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TECHNISCHE UNIVERSITÄT WIEN
Vienna University of Technology

DIPLOMA THESIS

Benzyloxycarbonyl protected thioglycosides for diastereoselective glycosylation

Institute of Applied Synthetic Chemistry

Vienna University of Technology

Under guidance of

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“The highest activity a human being can attain is learning for understanding, because to understand is to be free.”

Baruch de Spinoza

Zusammenfassung

In der Natur gibt es vielfältige Glycokonjugate, da diese unter anderem zur Zellerkennung und –kommunikation dienen. Weiters finden sie auch Anwendung als Stützstruktur und Energiespeicher, aber auch zur Verbesserung der Wasserlöslichkeit apolarer Substanzen. Enzyme bilden in der Regel überwiegend β-Anomere. Viele dieser Substanzen kommen nur in geringen Mengen vor und sind oft schwer zu isolieren. Daher ist es von Interesse, sie auf synthetischem Weg zugänglich zu machen. Bei der chemischen Glycosylierung wird eine glycosidische Bindung zwischen einem Glycosyldonor und einem Akzeptormolekül geknüpft, wobei, je nach Akzeptor, Oligosaccharide oder Glycoside synthetisiert werden können. Dabei kommt es am stereogenen anomeren Kohlenstoff zur Ausbildung einer neuen Bindung und infolgedessen meist zu einem Gemisch von α- und β- Produkt.

Da es sich bei Akzeptormolekülen oft um teure Verbindungen handelt und Anomerengemische schwer verlustfrei zu trennen sind, ist es von besonderem Interesse, Donorsysteme zu verwenden, mit denen eine diastereoselektive Glycosylierung möglich ist.

Bisher wurde das Selektivitätsproblem bei Zuckern mit äquatorialem 2-OH dadurch gelöst, dass man einfache Esterschutzgruppen einsetzte, die durch ihren Nachbargruppeneffekt die Bildung des β-Anomers bevorzugen. Bei Akzeptormolekülen, die Estergruppen enthalten, können diese Donoren nicht eingesetzt werden, da die Produkte unter den Entschützungsbedingungen nicht stabil sind.

Das Ziel dieser Arbeit ist folglich die Verwendung von *Benzoxycarbonyl-* (Cbz) sowie *2-(2-Benzyloxyphenyl)acetyl-* (BnPAc) als partizipierende Schutzgruppen, da die Entschützung orthogonal zu Estergruppen möglich und die Abtrennung der Spaltprodukte einfach ist.

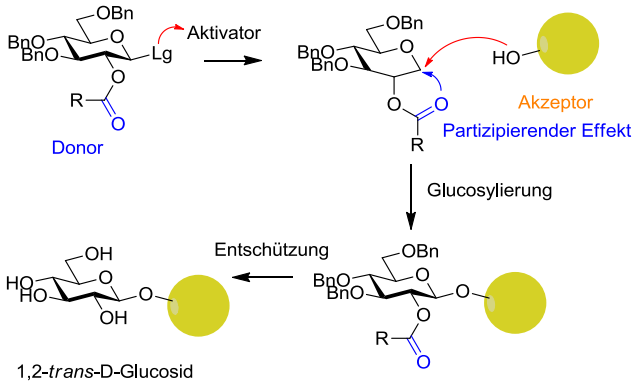

Abb.1 Glucosylierungsstrategie

Thioglycoside sind gut geeignet, da die Abgangsgruppen unter milden Bedingungen mit Lewissäure aktiviert werden können, sie aber gleichzeitig lagerstabil sind, da Monothioacetale als anomere Schutzgruppe fungieren.

Es wurden zwei unterschiedliche Syntheserouten angewandt, wobei eine Syntheseroute über Thioorthoester für ähnliche Substanzen literaturbekannt ist und eine neue Methode ausgehend von der Dihydroxylierung eines Glucals entwickelt wurde, die den Vorteil größerer Ausbeuten und weniger Reaktionsstufen bietet. Durch anomere Modifikationen wurden außerdem verschiedene Donoren ineinander überführt und auf diesem Weg Fluoro- und Imidoylglucoside zugänglich gemacht.

Mehrere Glycosylierungen erfolgten an einer Reihe von Akzeptormolekülen mit unterschiedlichen Aktivierungsmethoden, wobei eine Überprüfung mittels NMR den Umsatz zu reinem β-Produkt bestätigte.

Danach konnten orthogonale Entschützungen erfolgreich vorgenommen.

Abstract

In nature, various glycoconjugates occur for instance in cell communication processes, as scaffold molecules, or to increase the water-solubility of apolar compounds.

Mainly β-glycosides are found as natural products. Plenty of these substances only occur in very small amounts which often lead to difficulties in isolation. Therefore, the usage of synthetic methods is of great interest to make such compounds easier accessible.

In chemical glycosylation, formation of a glycosidic bond takes place between a glycosylic donor and an acceptor molecule. Depending on this acceptor, oligosaccharides or glycosides are synthesized.

During the reaction, bond formation at the stereogenic anomeric centre possibly causes a mixture of α- and β- product.

Acceptor molecules are often very expensive. Furthermore, separation of anomeric mixtures without much loss is a tough task. As a result of this, glycosyl donors for diastereoselective glycosylation are desirable.

Up to this point, the selectivity problem for glucose-like sugars at C2 was solved by using ester functionalities as protective groups, which favours formation of β-anomers due to a participating neighboring group effect.

Unfortunately, this method can not be applied for acceptors, which contain ester groups.

Cleavage of the protective groups may harm the product's ester functionalities as well.

This thesis aims at the implementation of *Benzoxycarbonyl*-(Cbz) and *2-(2-Benzyloxyphenyl)acetyl*- (BnPAc) as novel participating protective groups, that can be cleaved orthogonally. Furthermore by-products, that are formed during the deprotection step can be removed more easily.

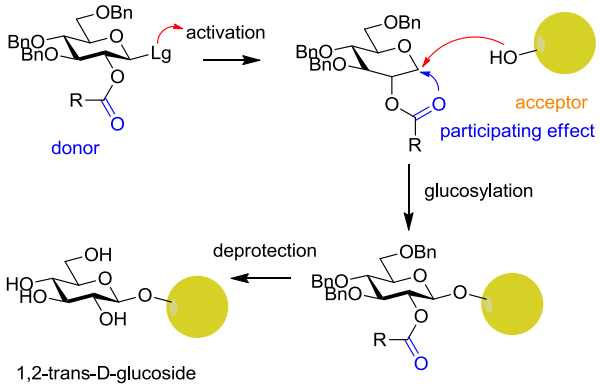

Abb.1 strategy for chemical glucosylation

Thioglycosides are particularly suitable for the planned application, because they can be activated under mild conditions using Lewis acids and monothioacetals act as anomeric protecting groups that show excellent storage capabilities.

For the donor synthesis, two different approaches were used. The thioorthoester-strategy is already known to literature for similar substances. By dihydroxylating glucals, a novel method was developed with the key advantage of higher yields over less reaction steps.

Anomeric modifications were done to interconvert different donor types and make fluoro- and imidoylglucosides accessible.

Finally, glycosylations were performed with several different acceptor molecules and activation strategies.

Examination of the products using NMR-spectroscopy confirmed the formation of β-product only.

In a last step, the protective groups were cleaved successfully.

Acknowledgment

I want to thank *Univ.Prof. Dipl.-Ing. Dr. Johannes Fröhlich* for the chance to work in his research group.

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Finally, I want to thank all of my friends, who always support what I am doing.

Index of Abbreviations

Besides abbreviations in common use of the English language and chemical symbols, the following short cuts are used in this thesis:

Ac	Acetyl
ACN	Acetonitrile
Bn	Benzyl
brine	saturated NaCl solution
CAN	Cer(IV)-ammoniumnitrate
Cbz	Benzyloxycarbonyl
Cbz-Cl	Benzylchloroformiate
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCM	Dichloromethane
DDQ	Dichlorodicyanobenzochinone
DMAP	4-(N,N-Dimethylamino)pyridine
DMF	N,N-Dimethylformamide
EE	Ethyl acetate
EtOH	Ethanol
HAc	Acetic acid
HSEt	Ethanethiol
HSPym	2-Mercaptopyrimidine
HSTaz	2-Mercaptothiazoline
HSTol	4-Methylbenzenethiol
LC/MS	Liquid chromatography – mass spectrometry coupling technique
Lg	Leaving group
MeOH	Methanol
MS	Mass spectrometry
NIS	N-iod-succinimide

Index of abbreviations

NMO	N-Methylmorpholin-N-oxide
NMR	Nuclear magnetic resonance
OTf	Triflate (Trifluormethane sulfonate)
PE	petroleum ether, boiling range 40-60 °C
Pg	„protective group“
Rf	Retention factor
rt	Room temperature
SP	Side product
SEt	Ethylthio moiety
SPym	2-Pyrimidyl thio moiety
STaz	1,3-Thiazolin-2-yl thio moiety
STol	p-Tolyl thio moiety
TBAB	Tetrabutylammoniumbromide
TBAF	Tetrabutylammoniumfluoride
TBDMS	tert-Butyldimethylsilyl
TCI	Trichloracetimidoyl
TEA	Triethylamine
TFI	N-Phenyltrifluoracetimidoyl
TfOH	Trifluormethanesulfonic acid
THF	Tetrahydrofurane
TLC	Thin-layer-chromatography
TLC-MS	Thin-layer-chromatography -MS-coupling technique
TMEDA	N,N,N‘,N‘-Tetramethylethylendiamine
TMS	Tetramethylsilane
TMSOTf	Trimethylsilyltrifluormethansulfonate

General remarks

Labeling of the described substances

Substances that are known to literature are labeled with Arabic numerals. If the synthesized substances are new to literature, the labeling is done with Roman figures.

References to Literature

Literature references are highlighted as superscripted Arabic numerals.

Nomenclature

Substances that are new to literature are named according to the Chemical Abstracts guidelines except literature-known compounds and reagents that in some cases are referred to with trivial or trade names.

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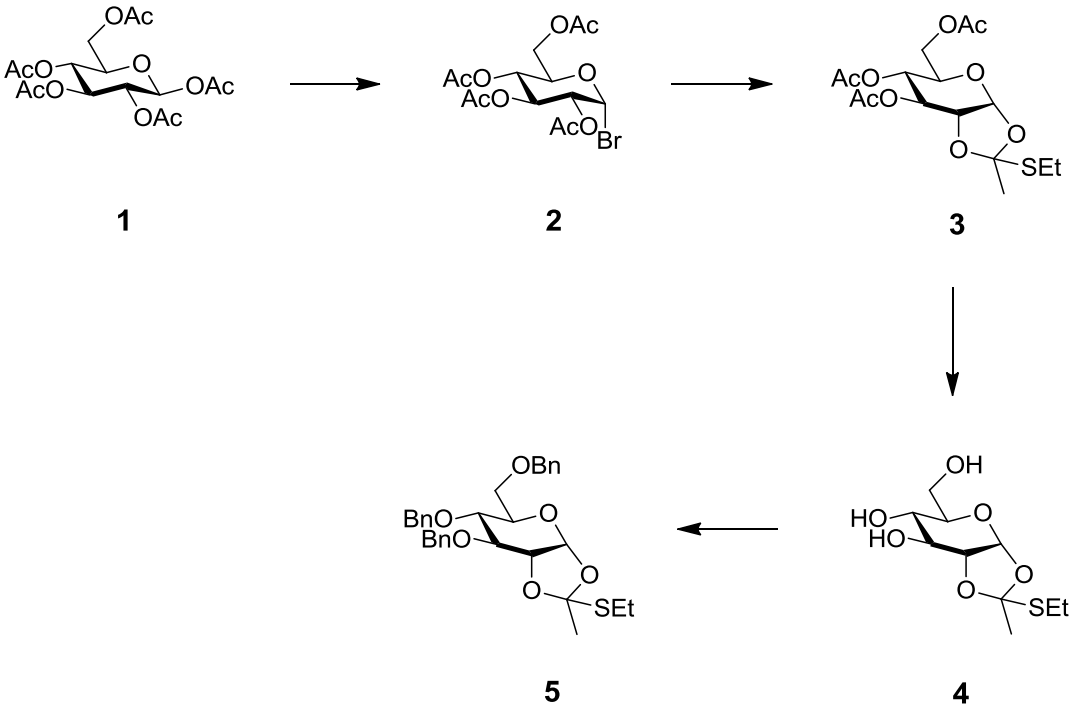

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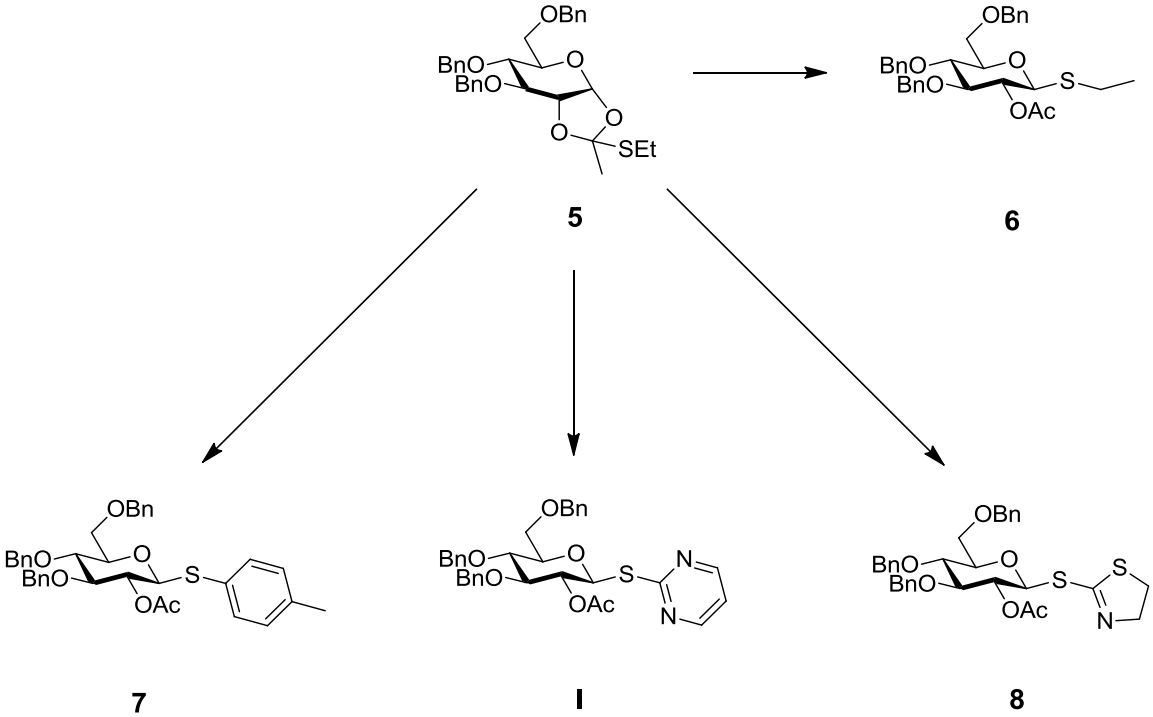

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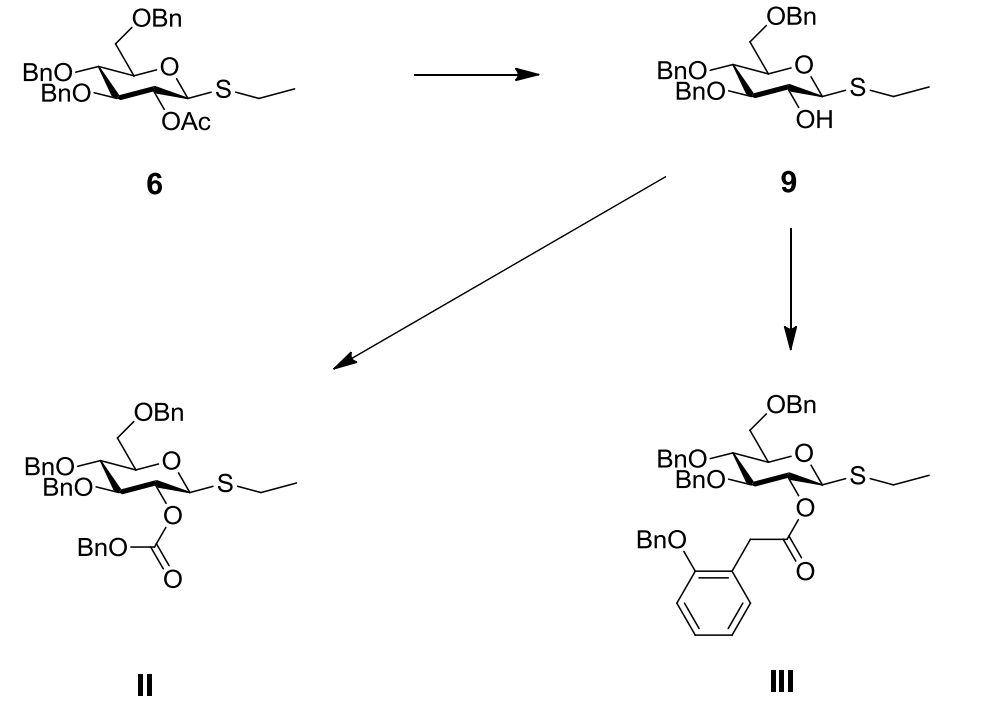

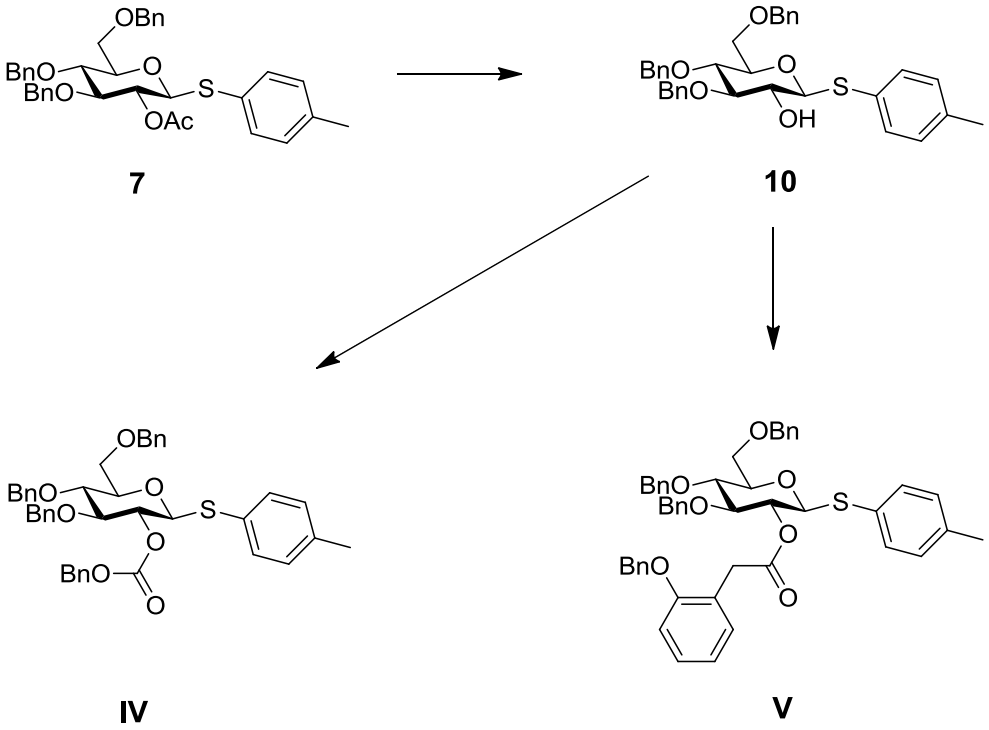

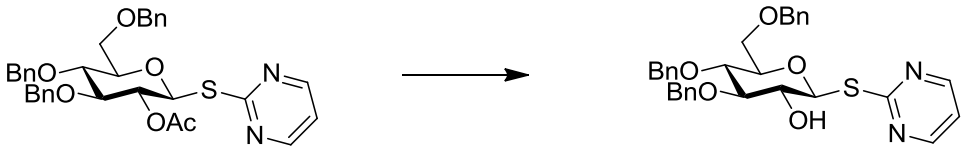

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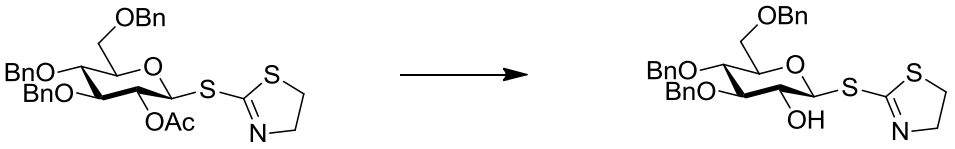

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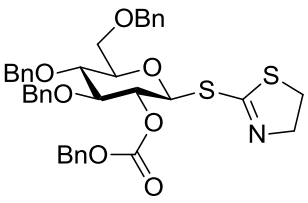

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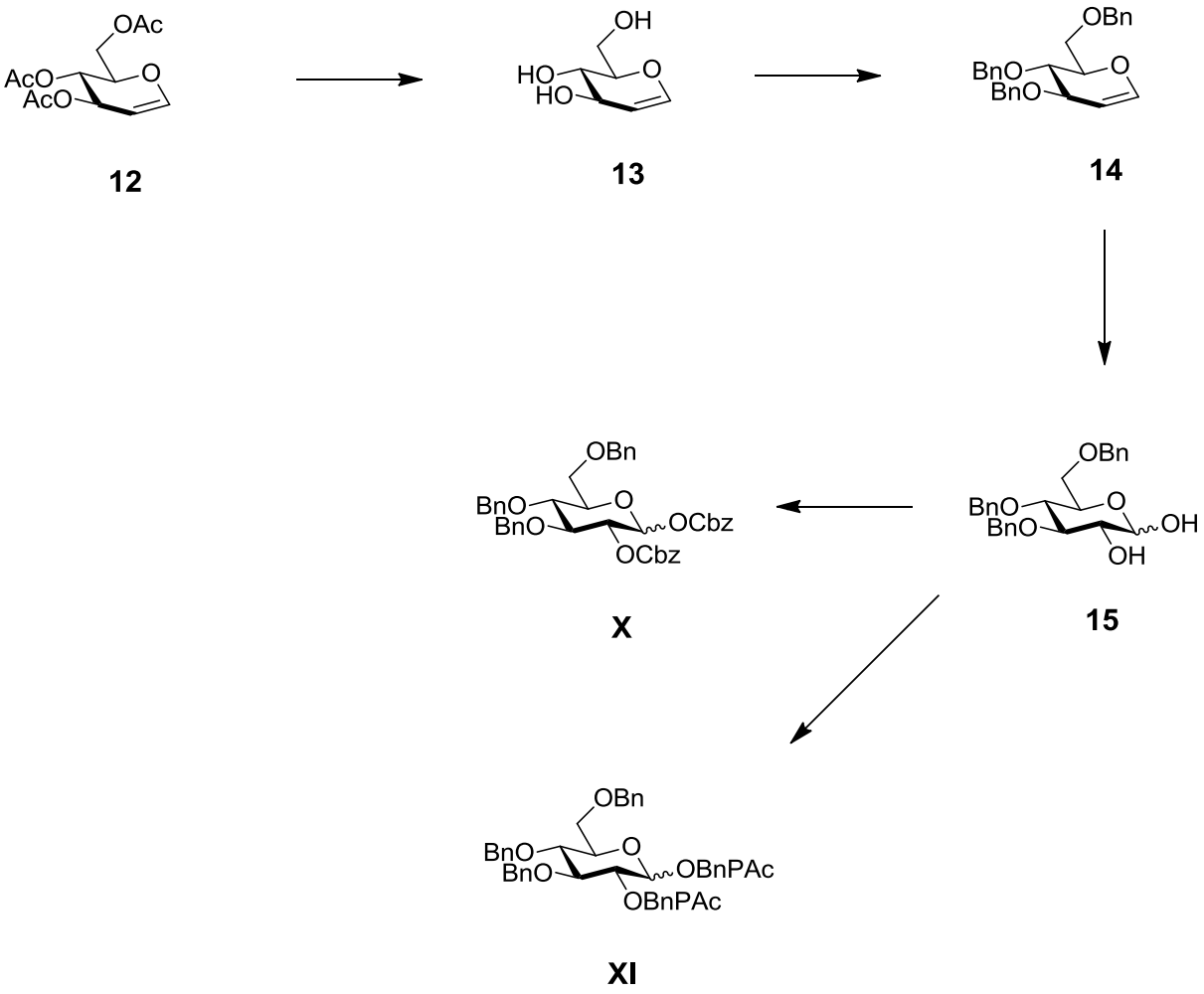

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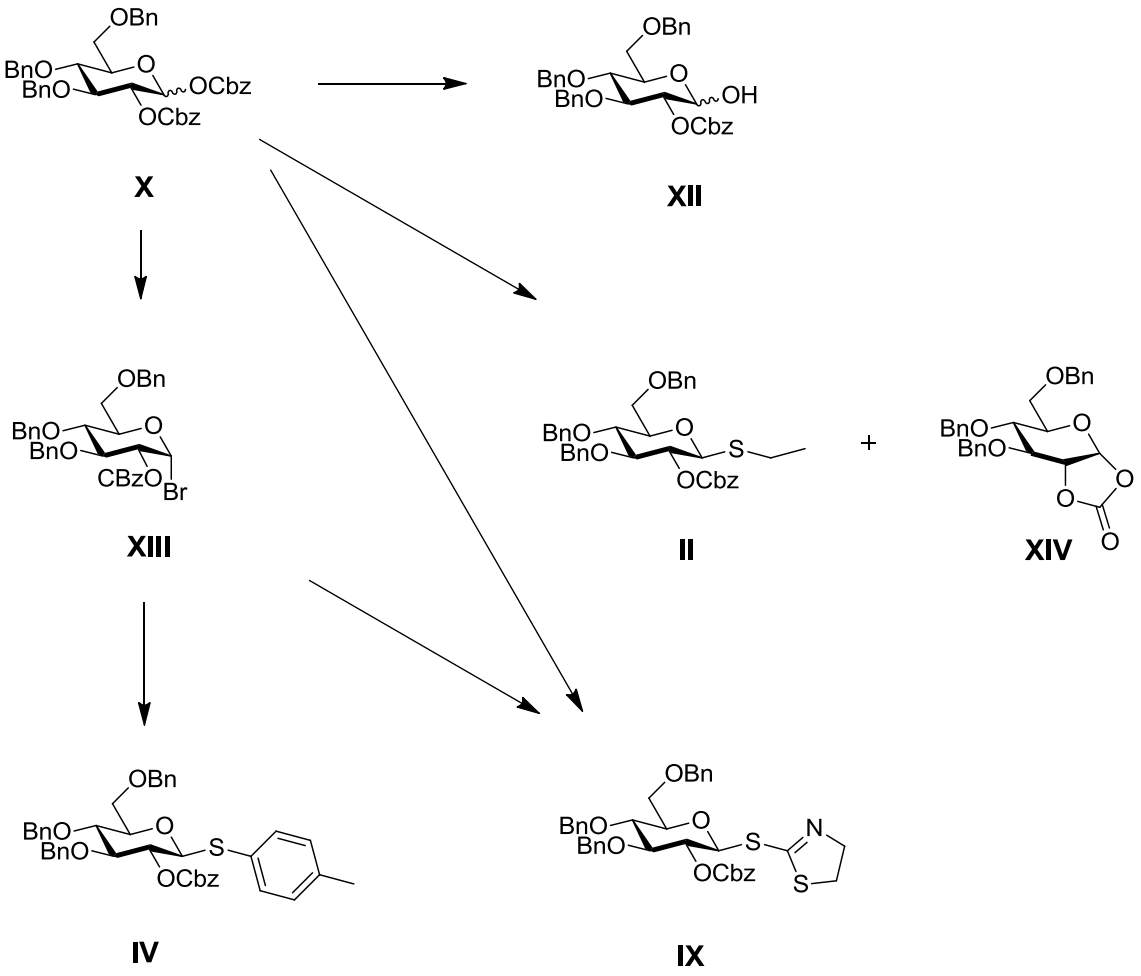

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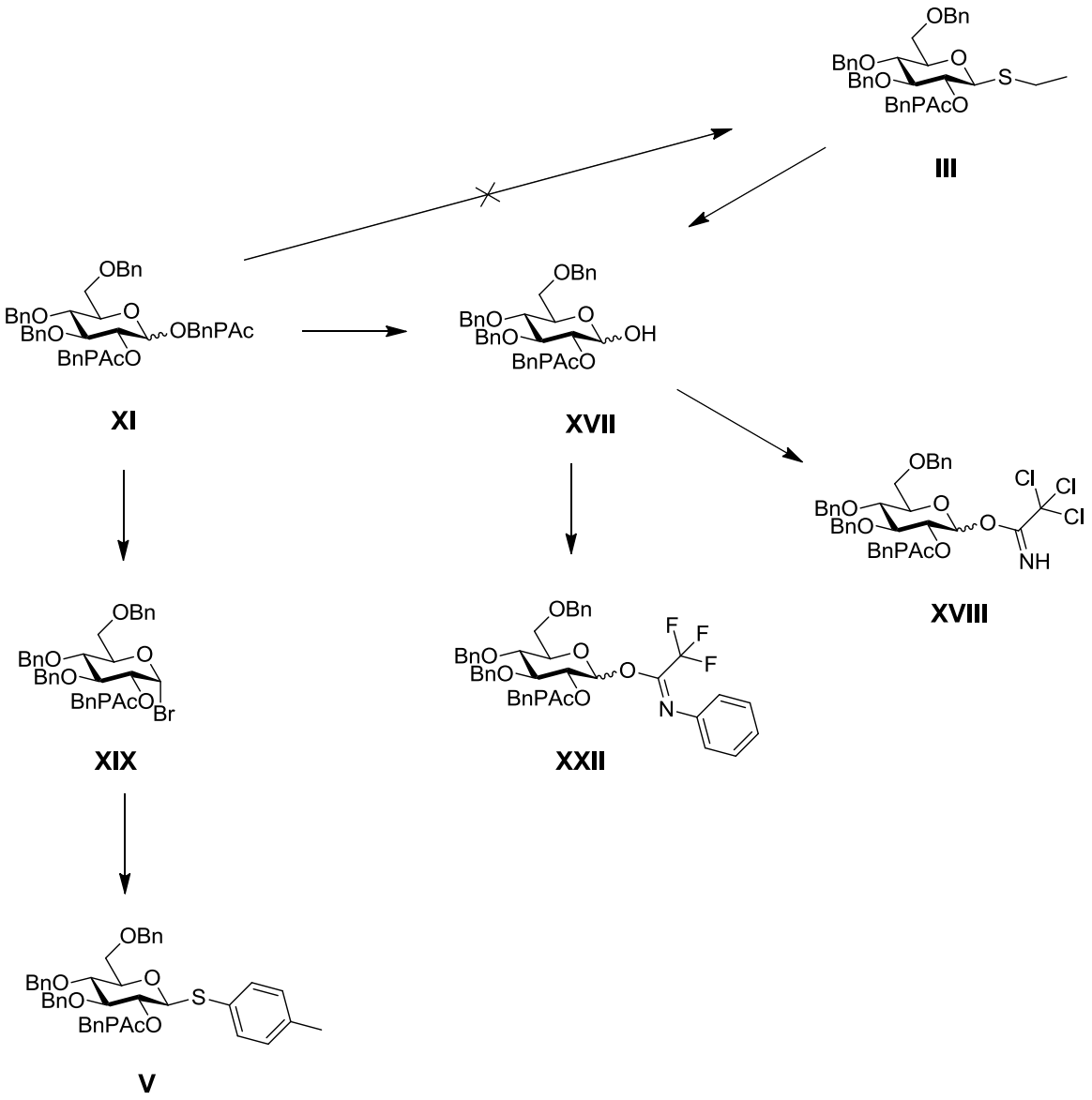

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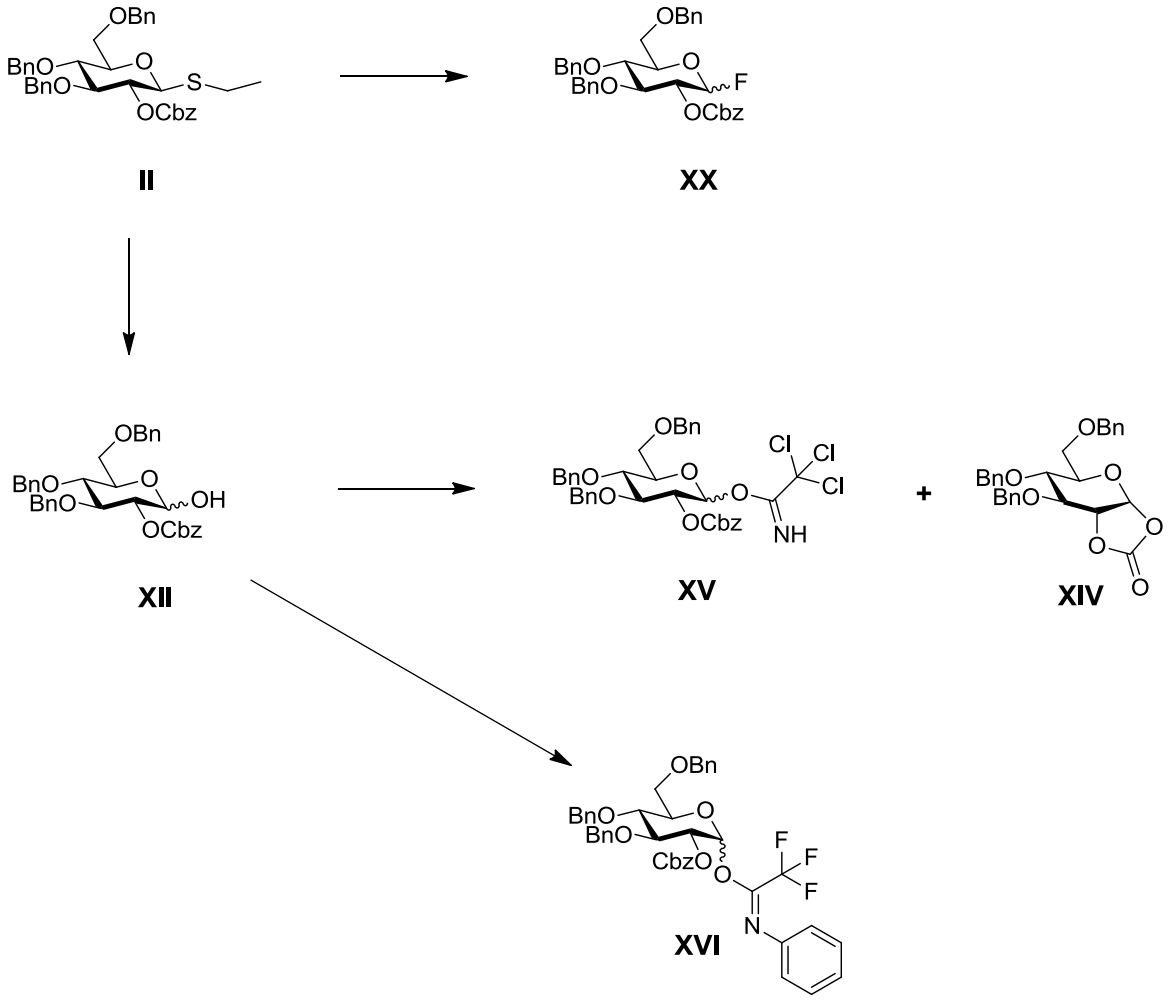

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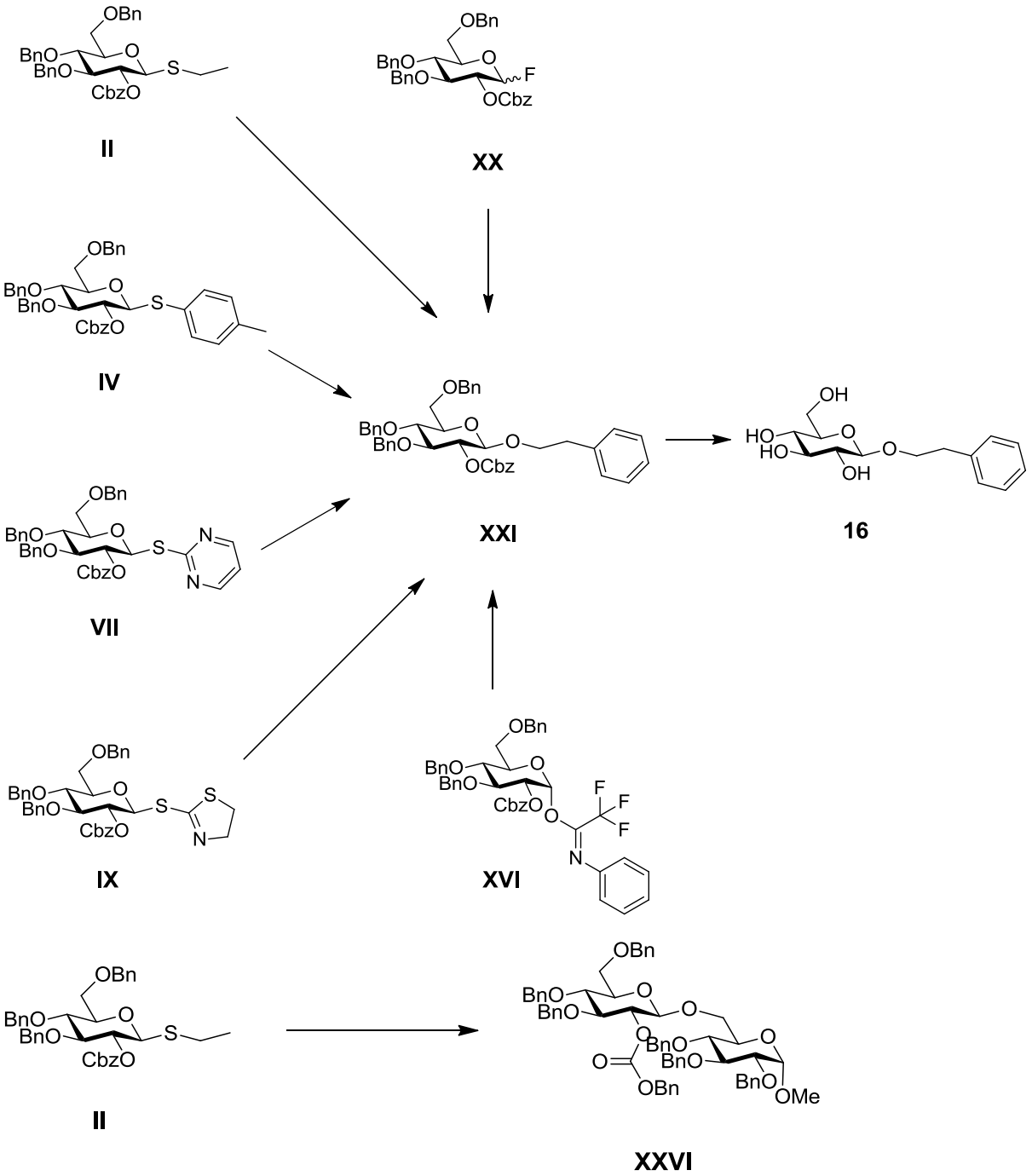

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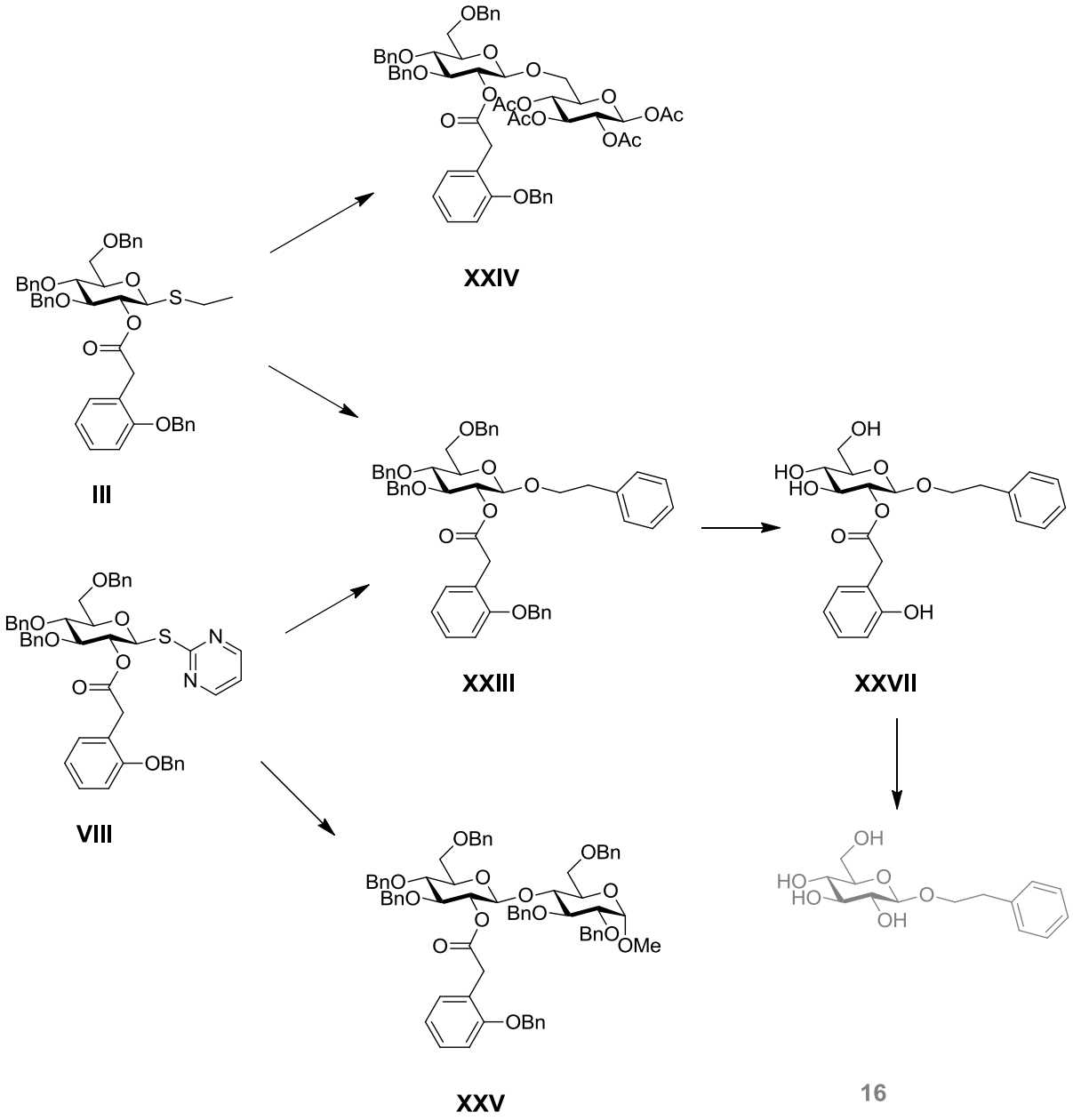

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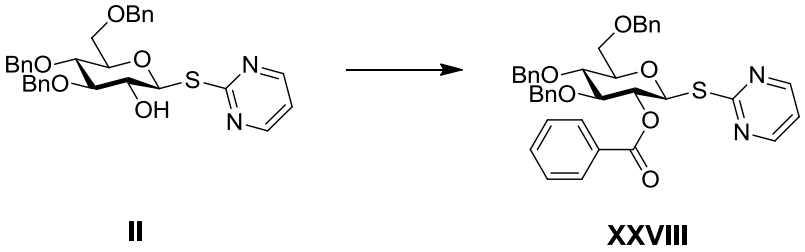

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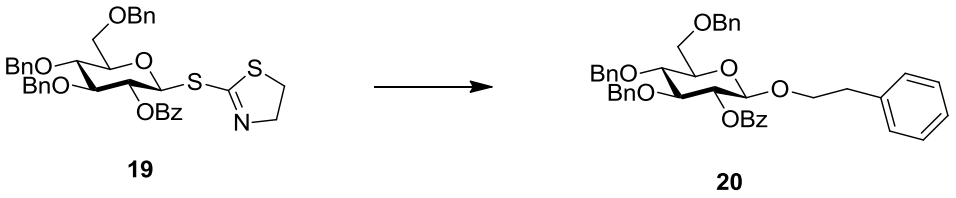

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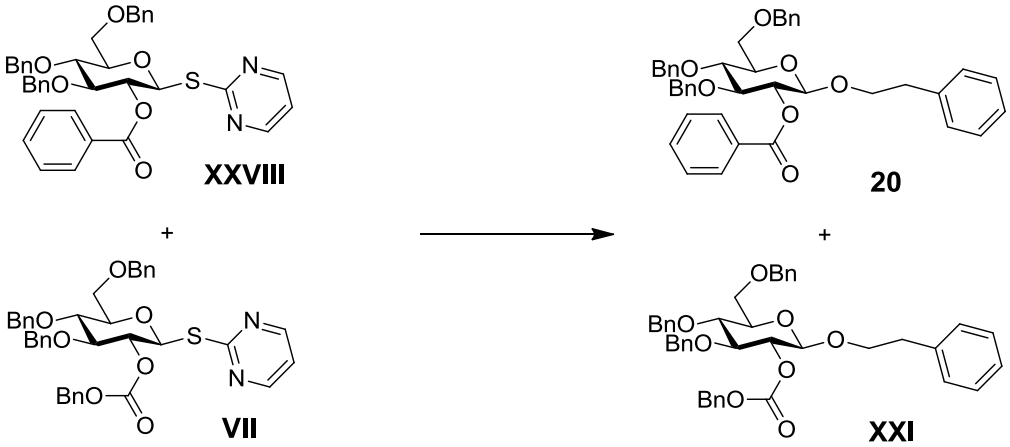

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B) Introduction

B.1) Introduction

Carbohydrates are not only one of the most abundant, but also one of the most important substance classes in nature. Besides their roles as scaffold molecules for tissues or as energy storage, other examples for natural applications are antigens in cell communication (e.g. blood types) or their use in metabolic detoxification. In phase-II-metabolism, xenobiotic substances are conjugated with sugar moieties to increase polarity and water-solubility. This is important for faster detoxification and the *trans*port of secondary plant products into their vacuoles. The solubility also significantly affects the biological activity. The increase of polarity by conjugate formation shifts the distribution coefficient towards the hydrophilic phase (water).

It is of high interest to obtain pure glycoconjugates as analytical reference material (e.g. "masked" mycotoxyins in agricultural research[1], antigens,…), because isolation from natural material often is too expensive or sometimes simply not possible in preparative amounts.

B.2) Biosynthesis of glucosides:

The formation of glucosidic bonds is done by glucosyl*trans*ferases which can be divided into inverting and retaining. Inverting glucosyl*trans*ferases act as catalytical bases, resulting in S_N2-like reactions of the glucosylacceptor at the anomeric carbon of activated sugar moieties (e.g. UDP-α-D-glycosides)[2] This leads to the formation of mainly β-glucosides (fig B-1). Acceptor molecules can be nucleophiles like other carbohydrates, proteins, nucleic acids, alcohols, thioles and amines.

Retaining glucosyl*trans*ferases act as nucleophiles at the anomeric carbon and form an intermediate that reacts with an acceptor molecule and releases the enzyme again. The original stereochemistry is retained (α-glucosides are formed).

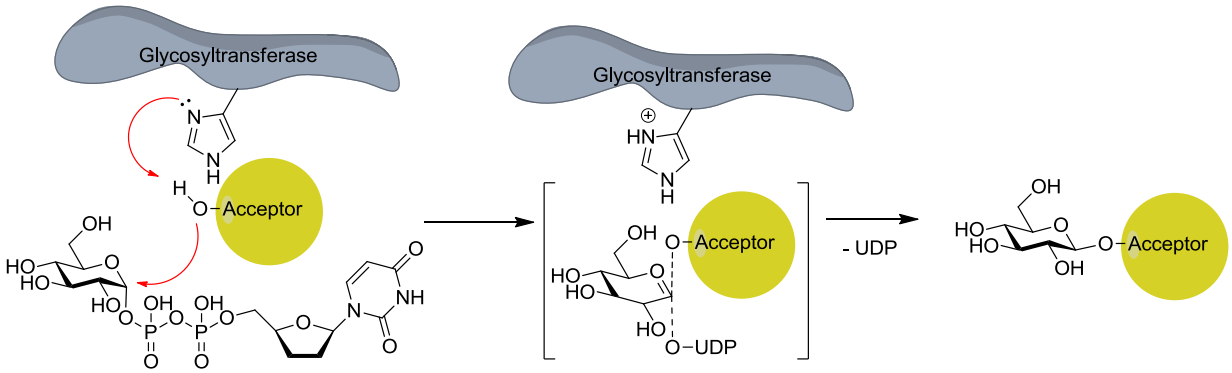


fig.B-1: biosynthesis of β-glucosides by inverting glucosyltransferase with UDP-glucose

B.3) Chemical glucosylation

A chemical glucosylation is the S_N1 reaction between a glucosyl donor and a glucosyl acceptor (which can be any nucleophile). In the first step the leaving group at the anomeric carbon is activated (by Lewis-acid for instance) and the oxocarbenium species is formed (fig. B-2). In a second step the nucleophilic attack of the glucosyl acceptor takes place and a glucosidic bond is formed. Because of the formation of a new stereocentre at the anomeric carbon, a mixture of α- and β-glycoside can occur.

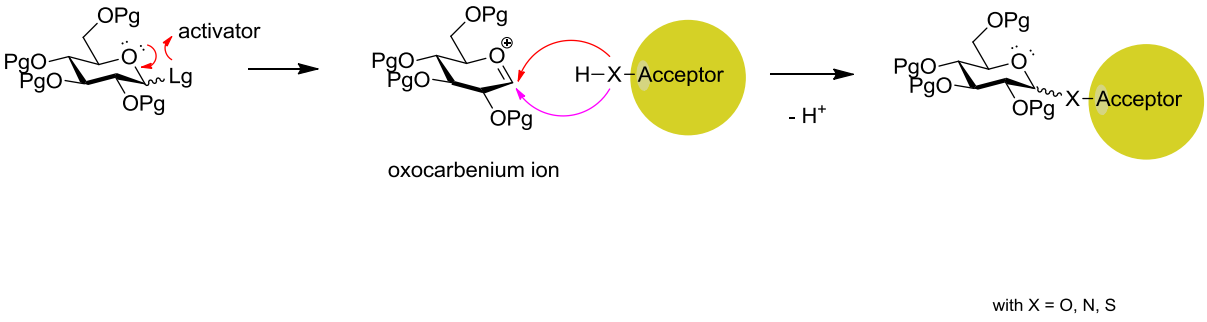


fig.B-2: S_N1-like mechanism of the chemical glucosylation

The anomeric mixture is a consequence of anomeric and steric effects. Although, the formation of β-glycoside is sterically preferred (equatorial position is less hindered), the α-product is thermodynamically more favored. This is caused by negative hyperconjugation of the ring-oxygen lone-pairs into the anti-bonding σ*(C-X)-orbital of the glucosidic bond. Only α-anomers allow this delocalization due to their orientation (fig. B-3). The α/β - ratio depends on the substituents (especially on C_2: ax. in mannose a lot stronger than eq. in glucose!), solvent effects and the conditions of the synthesis.

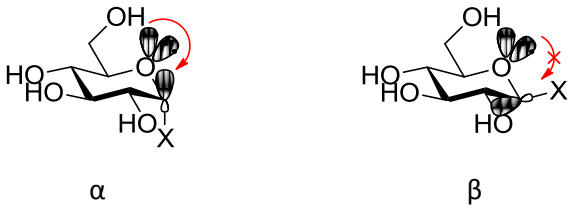


fig.B-3: anomeric effect

To achieve regioselectivity the use of protective groups is mandatory. Smart choice of the protective group pattern directly influences the reactivity and stereoselectivity of glycosyl donors.

B.4) Protective groups

Protective groups are used during organic synthesis to avoid unwanted sidereactions and to provide selectivity (see fig. B-4). Therefore competing groups are derivatized selectively in a step called protection. The substrate molecule is now ready to be reacted at a specific site without affecting other parts of the structure. In a last step the protective group has to be cleaved again to release the desired product. The use of this method leads to two additional steps in the overall synthesis of a molecule.

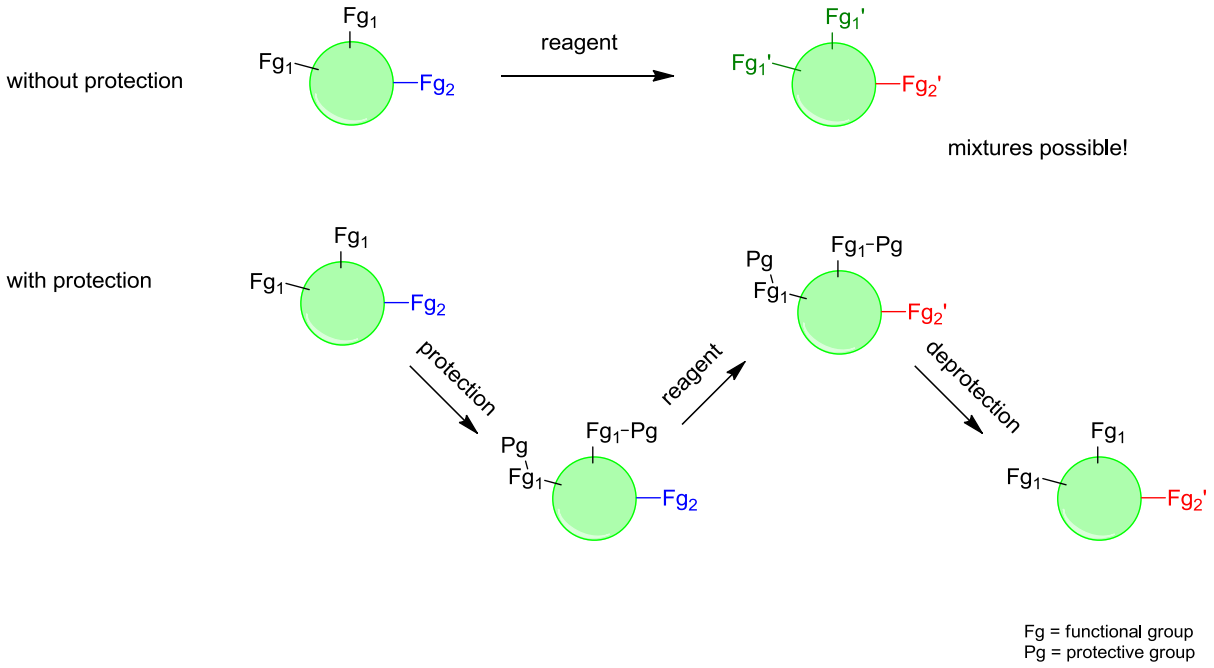


fig.B-4: schematic outline of the idea behind "protective groups"

B.5) Orthogonal protection patterns

The basic idea of orthogonal protection patterns is the use of different protective groups that can be cleaved each under specific conditions (as shown in fig.B-5) without affecting the others. Especially in carbohydrate chemistry, orthogonal protective group patterns are used to synthesize glycosids and oligosaccharids regio- and stereoselectively.

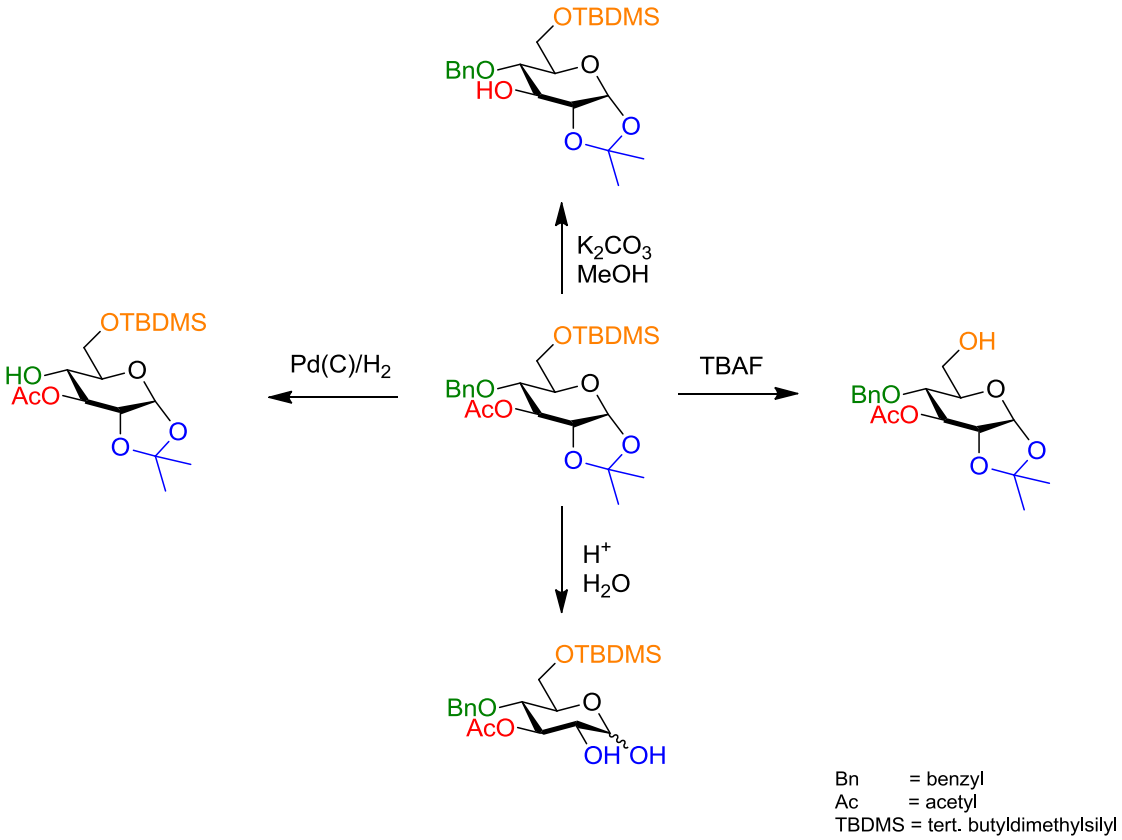


fig.B-5: example for an orthogonal protection pattern

There are loads of possible protective groups already known to literature to choose from (see [3]). No universal solution can be developed, because the reaction and cleaving conditions differentiate from case to case.

B.6) Stereoselectivity

Koenigs and Knorr were the first to develop a glucosylation method leading mainly to β-product.[4] They reacted 2,3,4,6-tetra-O-acetyl-1-bromo-1-deoxy-α-D-glucopyranose with methanol under Ag_2CO_3-activation. The 1,2-*trans*-selectivity is a result of neighboring group participation, the so-called anchimeric effect of the acetyl protective groups. Mechanistically (see fig.B-6), a stabilization of the oxocarbenium ion takes place, leading to an isomerization of the acetoxonium species. Now attack on the *si*-side is hindered and 1,2-*trans*-glycoside is formed selectively.

As a side-product an orthoester **(SP)** can be formed, which can be suppressed, if bulkier ester protective groups are used instead of acetyl (e.g. benzoxyl or pivaloyl).

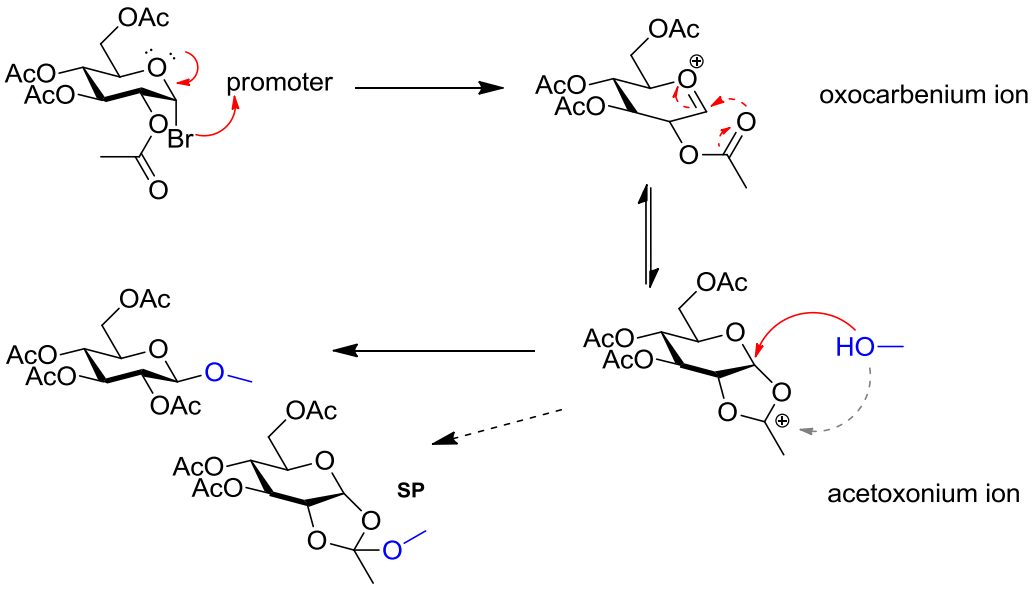


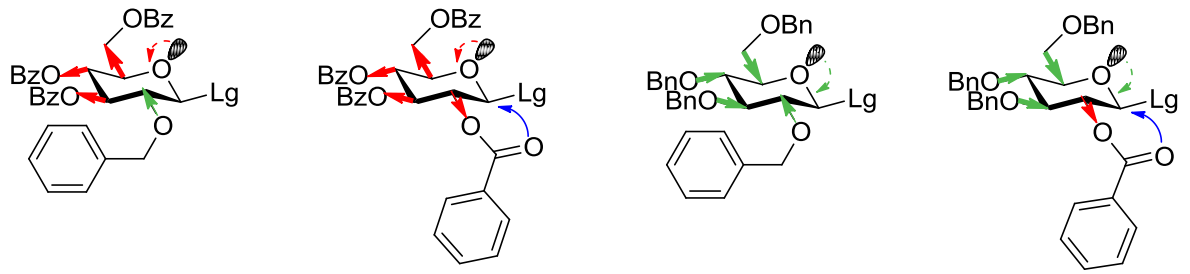
fig.B-6: Koenigs-Knorr-synthesis: mechanism

These simple ester protective groups are widely used and well established. However the basic cleaving conditions are a drawback because many glycosides contain ester functional groups which can also be cleaved during the deprotection step. Therefore, research in novel protective group patterns is of high interest.

B.7) Donor reactivity

The chosen protective group pattern, as well as the donor configuration affects the reactivity of glycosyl donors. This was first discovered by Fraser-Reid et al. in 1988, while studying n-pentenyl-glycosides[5]. They noticed that from a mixture of O-acetyl-protected and O-benzyl-protected n-pentenyl-glycosides, only the benzyl-protected reacted as a donor. They called their observation "armed and disarmed pair". This discovery allows the one-pot-synthesis of oligosaccharides, without formation of self-coupled product. Electron density in the ring is responsible for differences in reactivity. Electron-withdrawing groups like acetyl functionalities reduce the electronic density and thus destabilize the oxocarbenium species, formed during the reaction. Benzylethers, for example, act as electron-donators, whereby the intermediate is stabilized and the reactivity increases.

In 2005, Demchenko et al. researched mixed protective group patterns and reported unexpected reactivities.[6] While the perbenzoxylated species gave moderate yields, the 3,4,6-benzoxyl-2-benzyl-donor, which was thought to be more reactive, did not react at all. The further decrease in reactivity was explained by a "O-2-O-5 – cooperative effect". Although the electron density in the ring is reduced, the oxocarbenium intermediate of the perbenzoxylated donor at least is stabilized by neighboring group participation of the O-2-benzoxyl-group. In contrast, the oxocarbenium species of the 3,4,6-benzoxyl-2-benzyl-donor cannot be stabilized by these effects, which boosts the energy barrier. Later, they found the opposite effect[7] with the 2-benzoxyl-3,4,6-benzyl-donor, leading to an extension of the former "armed/dismarmed"-concept with the term "superarmed" for further increased and "superdisarmed" for even more decreased reactivity (see fig.B-7).[8] The term "superarmed" first was suggested by Bols et al. in 2007, when they were studying reactivity-enhancement caused by donor conformation.[9]



superdisarmed disarmed armed superarmed

fig.B-7: electronic influence on reactivity

Chrich and Li found out, that reactivity is also strongly influenced by the donor configuration.[10] Promotion of the donor activation by the O-2-participating group is stereoelectronically favoured for the β-donor.

Besides electronically superarmed donors, Bols et al. developed conformationally superarmed donors (see fig.B-8). They discovered, that axial hydroxyl groups are three times less electron withdrawing than equatorial groups and consequently, they used very bulky TBDMS-protective groups to force them from energetically favored $^4C_1$-configuration into axial position.

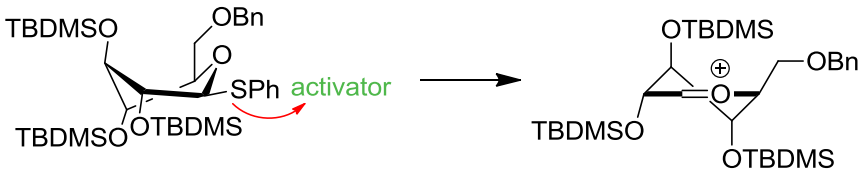


fig.B-8: conformationally superarmed donor

Demchenko et al. showed, that conformationally superarmed donors are more reactive than electronically superarmed ones, but their drawback is, that the glycosylation is not diastereoselective.[11] They combined both approaches to a new donor type by adding a O-2-participating group. This new donor showed a higher reactivity than conventional electronically superarmed donors, but less reactivity than Bols' system. By comparing it with the β-configuration (that has no participating effect) and a O-2-benzylated species (which was more reactive), they showed, that for conformationally superarmed donors, the participating effect is overruled by its electron-withdrawing properties.

B.8) Aim of this thesis

This thesis aims at the development of novel benzyloxycarbonyl-protected thioglycosides for diastereoselective 1,2-*trans*-glycosylation. Many natural glycosides occur only in β-configuration. As natural products they often are very expensive and anomeric mixtures are difficult to separate, so diastereoselective methods are very important. Lots of different donor types and methods have been developed by other research groups, usually based on O-2-anchimeric ester functionalities. However, these standard procedures cannot be applied for acceptor molecules that contain ester functionalities, because they are not stable under deprotection conditions. Benzyloxycarbonyl groups provide an anchimeric effect, necessary for the diastereoselectivity, but can also be cleaved under different conditions that do not affect ester functionalities (fig.B-9)

Furthermore, the new donors should be equipped with benzyl protective groups on O-3,O-4 and O-6 position to make them “superarmed”. Thioglycosides are chosen due to their good storage stability and mild activation conditions.

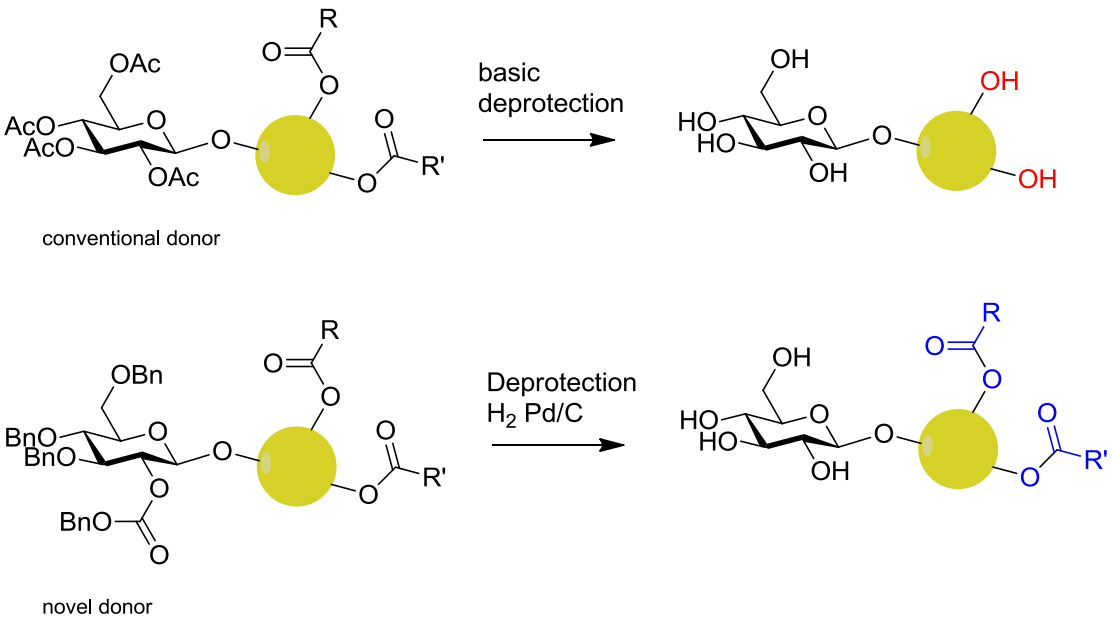
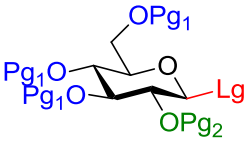


fig.B-9: deprotection step, compared between novel and conventional donors

C) Results & Discussion

C.1) Donor structure



protective groups:

Pg_1 = Bn
Pg_2 = CBz/BnPAc

leaving groups:

Lg = SEt, SPym, STaz, STol, F, OTCl, OTFl

fig.C-1 :lead structure for the donor design

In general the desired donor structure is 3,4,6-tri-O-Pg_1-2-O-Pg_2-1-Lg-1-deoxy-β-D-glucopyranose. (see fig. C-1). Pg_1 is chosen to be benzyl to allow a superarmed donor type. Pg_2 provided the anchimeric effect. A big variety of donors was successfully synthesized (figure C-2).

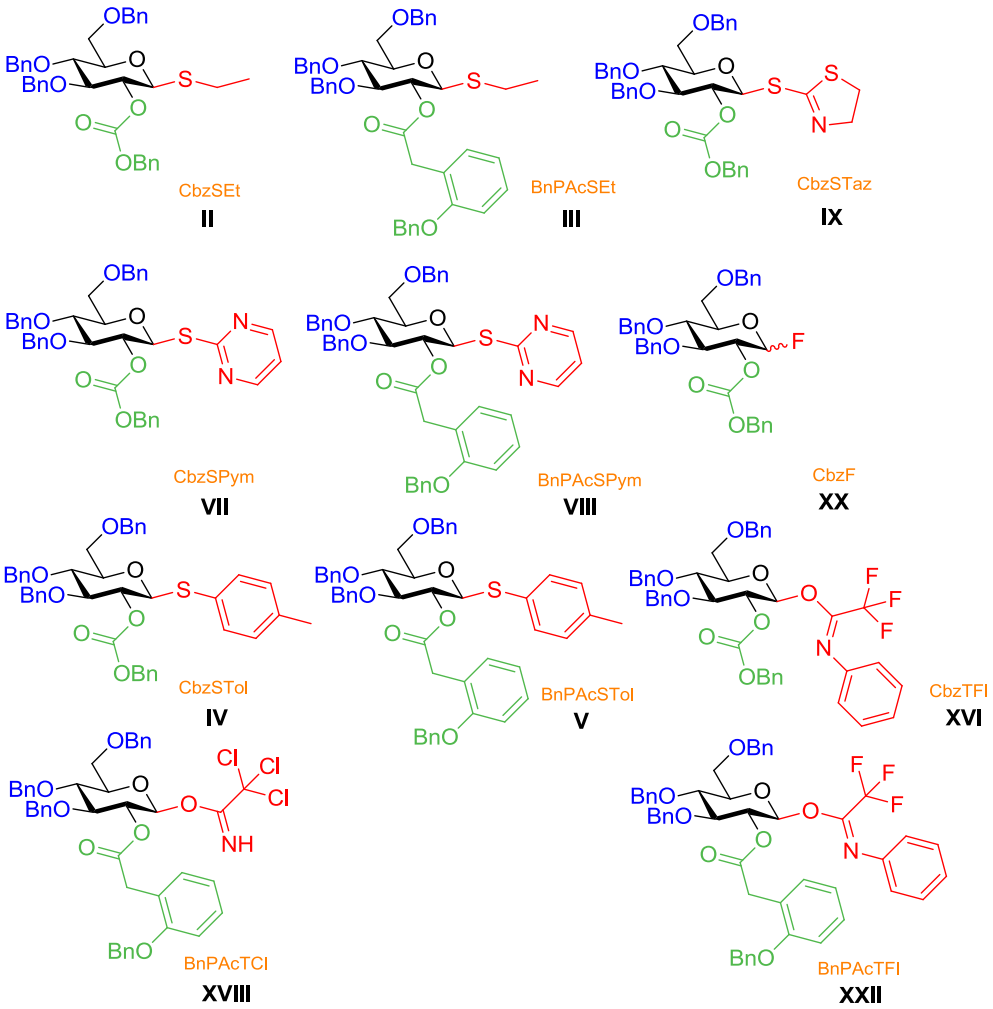


fig. C-2: synthesized donors

C.2) Protective group pattern

Protective groups (PGs) have to fulfill the following requirements:

- PGs have to be easy to introduce with high yields under mild conditions
- PGs must be stable under reaction conditions
- cleavage of PGs has to work under mild conditions providing high yields
- spectroscopic signals should not overlap with other structural elements of the molecule
- PGs should be cheap and easy accessible
- cleaving-products should be easy to separate from the main product

C.2.1) Benzyl protective groups

Besides cleaving benzylethers classically with acids, catalytic hydrogenation can also be used, which are very mild conditions. Pd on active charcoal is used as catalyst where dihydrogen is coordinated and dissociates. The activated hydrogen reacts with adsorbed starting material to cleave the benzylic C-O bond, releasing deprotected product and toluene. (see figure C-3)

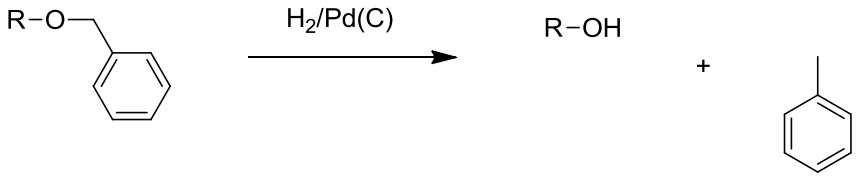


fig.C-3: deprotection of benzylethers by catalytic hydrogenation

C.2.2) Benzoxycarbonyl (Cbz) protective group

The Cbz protective group was developed by Zervas and Bergmann in 1932[12], initially thought for peptide-synthesis and is a standard method in that field today. For this thesis, Cbz was used as an alcohol protective group.

Cbz shows some very attractive properties that make it particularly suitable for superarmed glycosyl donors:

- deprotection is possible orthogonal to ester functionalities via catalytic hydrogenation
- reagent commercially available and cheap, due to widespread usage
- only one deprotection step for the whole molecule, when combined with 3,4,6-tri-O-benzyl protection
- cleavage products are easy to separate

During deprotection, the first step is the same as for the benzylether. The formed hydrogen carbonate is not stable and decomposes to CO_2 and the deprotected product (fig. C-4)

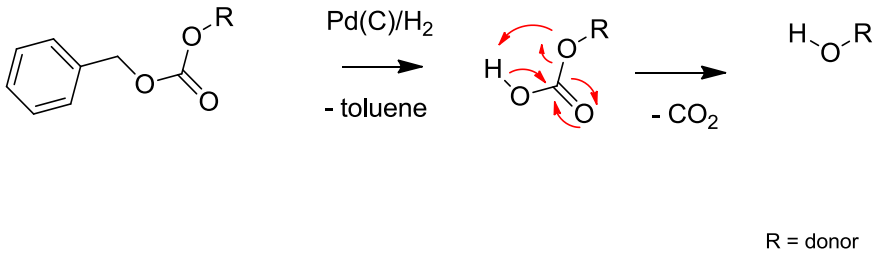


fig. C-4: cleavage of benzyloxycarbonyl protective group

C.2.3) 2-(2-(benzyloxy)phenyl)acetyl (BnPAc) protective group

The BnPAc group as protective group was developed by Theresa Weigl-Pollack within the research group during her bachelor thesis.[13] It shows some interesting properties that are of big advantage for the donor system:

- deprotection is possible orthogonally to ester functionalities via catalytic hydrogenation followed by an intramolecular ring formation reaction catalysed with proton sponge
- easy synthetically accessible
- cleavage products are easy to separate
- switching of protective groups is possible (for instance, switching from benzyl to sterically hindred silyl ethers would noticeable increase the reactivity of the donor)

Deprotection of BnPAc requires two steps. In the beginning catalytic hydrogenation leads to a stable isolable 2-(2-hydroxyphenyl)acetyl protected alcohol. Afterwards 1,8-Bis(N,N-dimethylamino)-naphthalin (proton sponge) is used as non-nucleophilic strong base, that deprotonates the phenolic hydroxygroup, followed by an entropically and energetically favoured intramolecular lactone formation of 2-Coumaranon, deprotecting the alcohol. (fig. C-5)

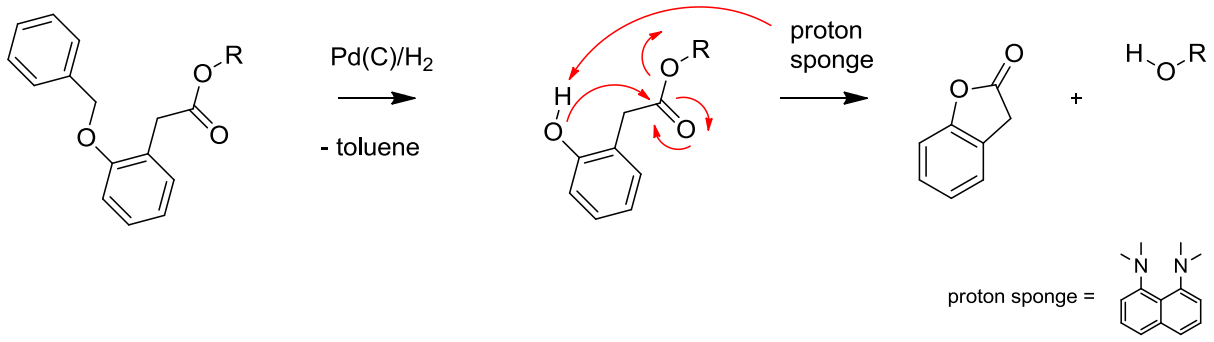


fig. C-5: cleavage of BnPAc protective group

C.3) Leaving groups

Leaving groups take significant influence on donor properties and are useful to regulate chemical glycosylations. Mild and orthogonal activation conditions are important in order to not affect acceptor molecules. There is a great number of different types but probably the most common three ones are glycosyl halides, glycosyl imidates and thioglycosides.[14]

Thioglycosides (on which this thesis is focused on) show excellent properties regarding to mild and selective activation (electrophilic). They also can serve as acceptors in abscence of thiophilic reagents (e.g. for glycosyl imidates), where the thioacetal function acts as an anomeric protective group.[15] Furthermore, thioglycosides are very stable under dry and non-electrophilic conditions and survive deacetylation, making protective group pattern changes possible.[16] In addition, they can be easily converted to other donor types like halides or imidates (as shown later).

Glycosyl acetimidates are a lot more delicate to handle because they hydrolyze very easily. Imidates need only catalytic amounts of promoter. N-phenyl-trifluoroacetimidates are less reactive than trichloroacetimidates but both are not stable to deacetylation conditions.[17] The anomeric α/β-ratio of the product depends on the strength of the used base. The stronger the base, the more thermodynamic product (α-anomer) is formed.

Glycosyl halides are less reactive than thioglycosides, which can lead to unwanted side reactions caused by more vigorous reaction conditions. Halides can be combined with thioglycosides in one-pot-reactions.

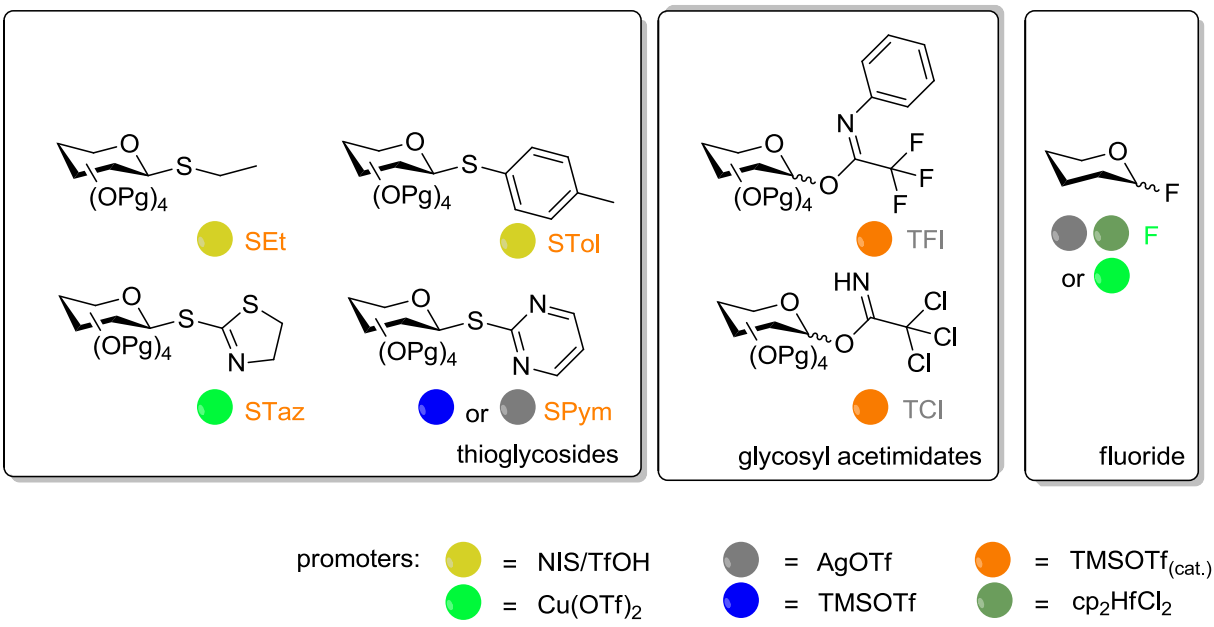


fig. C-6: used leaving groups and how they are activated

C.4) Retrosynthetic approach

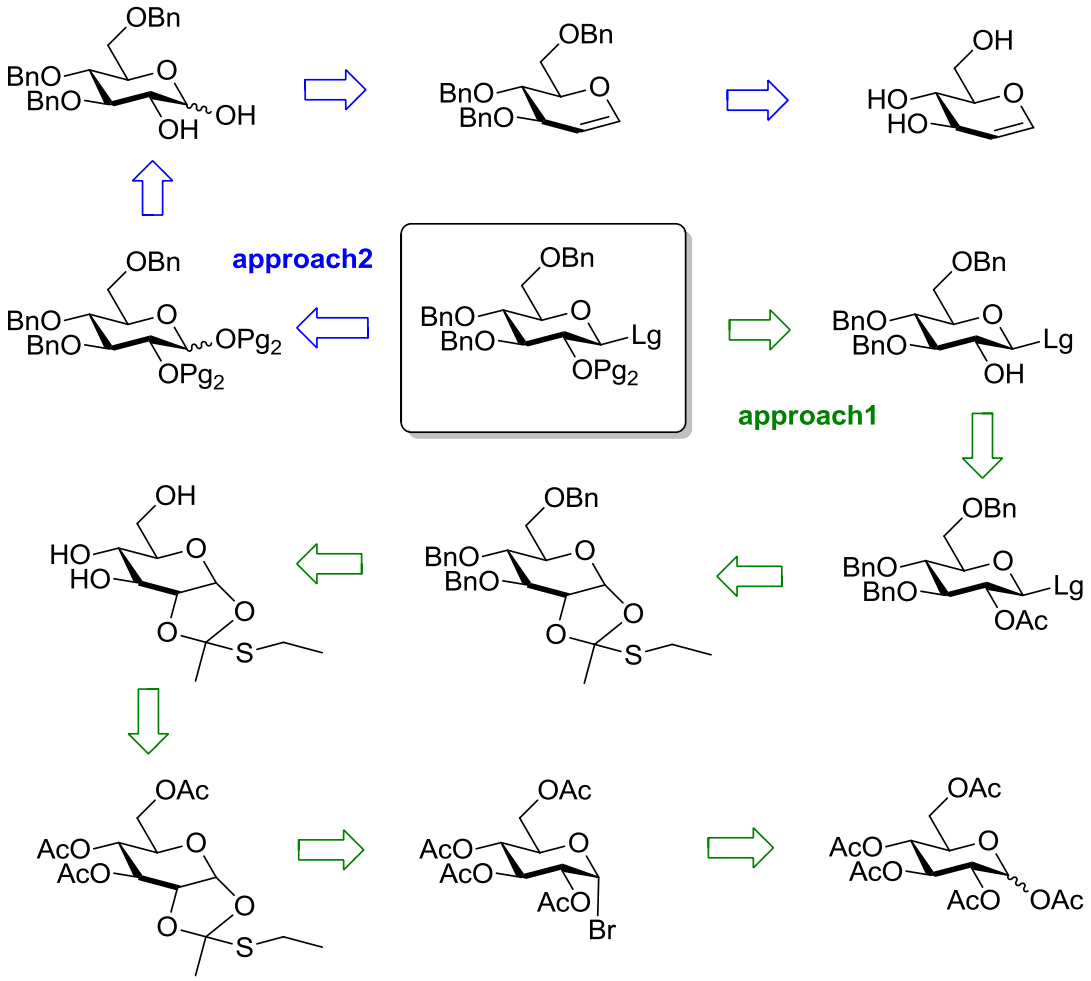


fig. C-7: retrosynthetic pathways

C.4.1) Approach 1: the orthoester method

Synthesizing thioglycosides out of thioorthoesters is already known to literature.[18] Protecting O-1 and O-2, selective benzylation of O-3, O-4 and O-6 is straightforward. Drawbacks are more reaction steps and a higher effort for purification.

C.4.2) Approach 2: the glucal method

The key step in the glucal method is the OsO_4-catalysed syn-(Upjohn)dihydroxylation, leading to anomeric mixtures of 3,4,6-protected D-glucose followed by introduction of the participating group at high yields. Final anomeric modification leads to desired donors.[19]

C.5) Donorsynthesis

C.5.1) The orthoester method

It is important to respect the order of events to avoid incompatibilities in further steps. Therefore, the strategy starts with the anomeric modification that takes place in strongly acidic environment. Introduction of ether protective groups first could lead to their cleavage during the anomeric modification. The next step is the formation of an 1,2-orthoester that acts as a protective group during the change of the protective group pattern and is not sensible to deacetylation conditions. Orthoesteropening, followed by deacetylation prepares the donor for the introduction of the new participating protective group on O-2. Afterwards, other glucosyl donors can be derived through anomeric modifications.

C.5.1.1) Preparation of the benzylated orthoester

Starting from 1,2,3,4,6-penta-o-acetyl-D-glucose **(1)**, 2,3,4,6-Tetra-O-acetyl-1-deoxy-1-bromo-glucopyranose **(2)** was synthesized with HBr in HAc (33%) (see fig. C-8) with 88% yield of pure α-anomer as yellowish oil.[20]

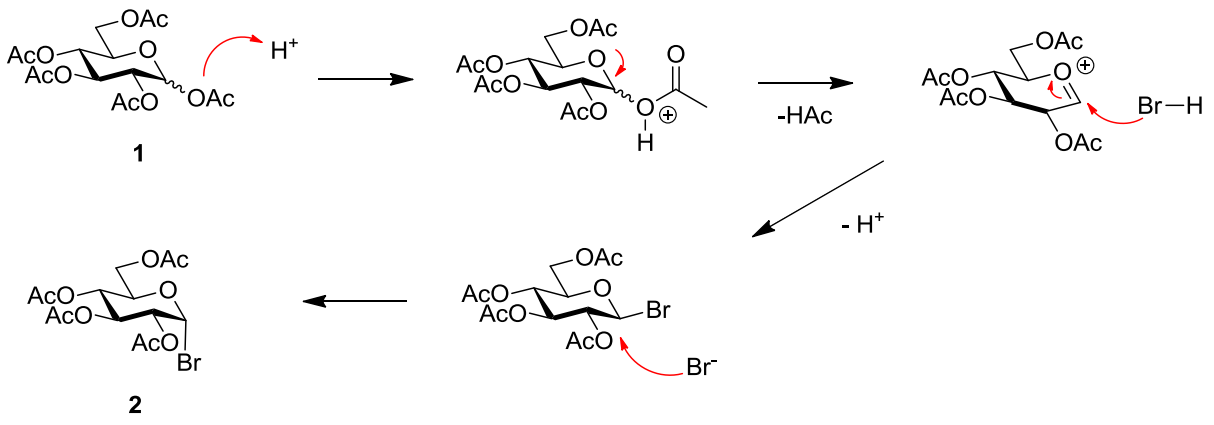


fig. C-8: synthesis of ***(2)***

Because of limited stability in acidic environments, **2** was used straight after workup without any further purification on silica to avoid product losses caused by donor hydrolysis.

In the next reaction step, 3,4,6-tri-O-acetyl-α-D-glucopyranose (R)-1,2-(ethylthioorthoacetate) **(3)** was the desired product. Hence, attack of the nucleophilic ethanethiol is possible on two different sites, control has to be taken on the reaction (described below) in order to obtain **3** only instead of the thioglycoside or a mixture of both. (see fig C-9)

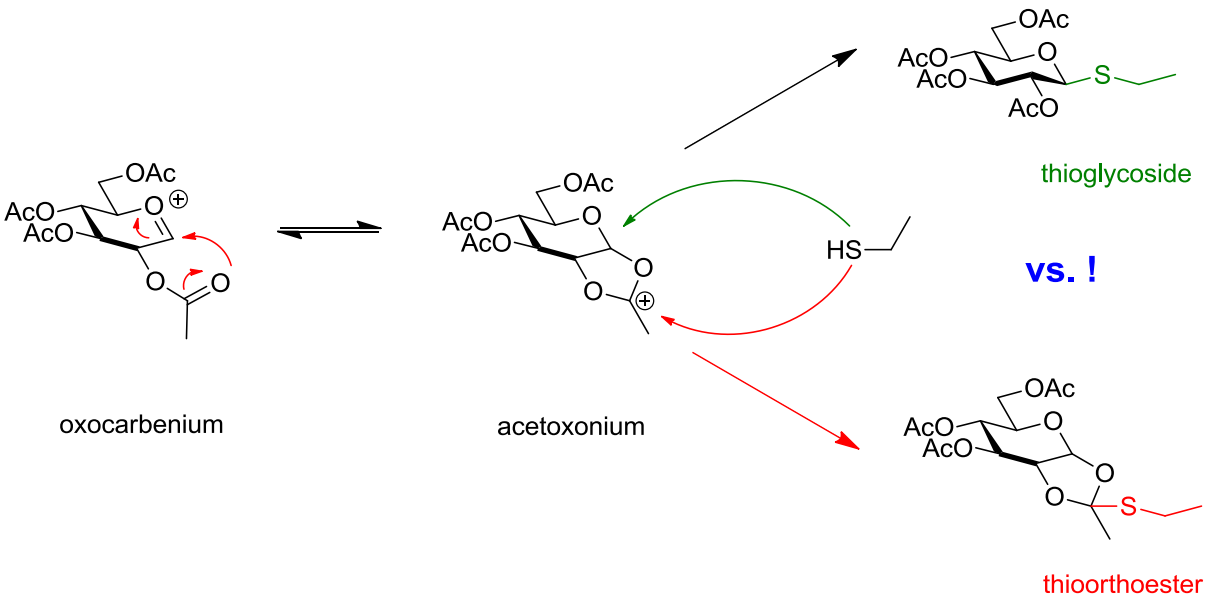


fig. C-9: thioorthoester vs. glycoside formation

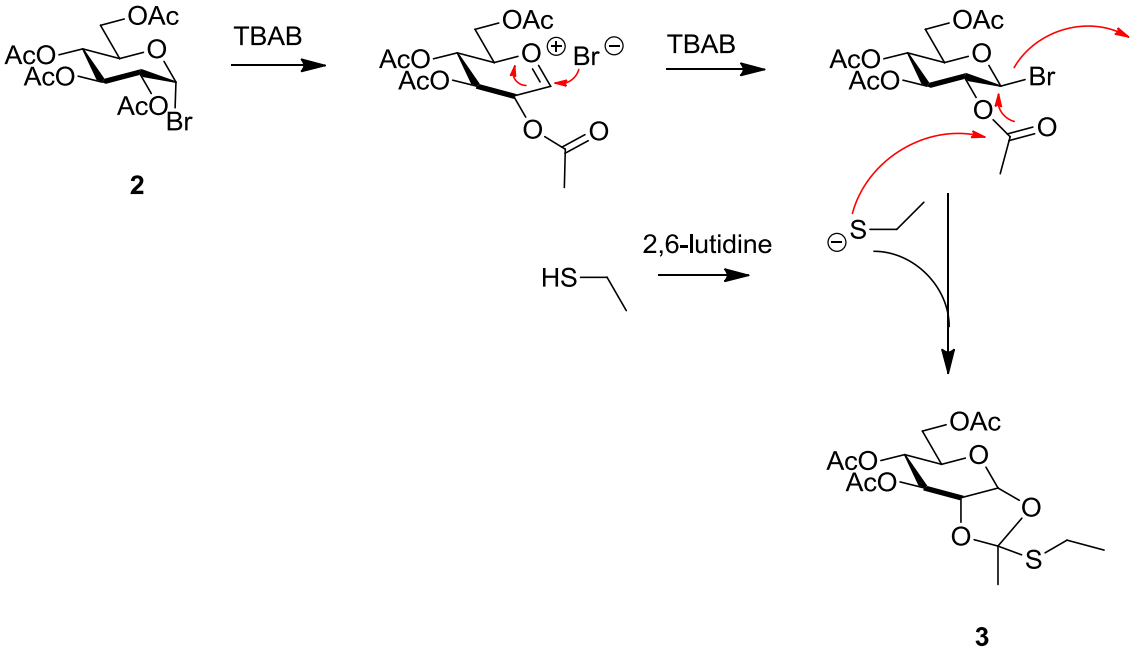
The formation of orthoesters over thioglycosides is favoured if:

- reaction conditions are neutral to basic
- 2-O-protective group is not bulky (e.g. acetylesters)
- β-attack is sterically hindred

To fulfill these requirements a method was developed by Lemieux and his coworkers. Mechanistically, Br^- forms a tight ion pair in presence of TBAB, leading to the much more reactive β-anomer ("in situ anomerization") that is reacted to α-product selectively (see fig C-10).[21]

The reaction was done according to [22] using 2,6-lutidine as a non-nuleophilic base that deprotonated ethanethiol.

95% of crude **3** were obtained. Because of the product's sensitivity to acidic environments, no further purification (using silica) was done and it was used directly in the next step.



2 **3**

*fig. C-10: synthesis of **(3)***

For the synthesis of α-D-glucopyranose (R)-1,2-(ethylthioorthoacetate) **(4)** deacetylation was done under basic conditions (K_2CO_3) as classical transesterification in methanol (see fig. C-11). In this case, a modification of the Zemplen method was used (K_2CO_3 in methanol instead of $CH_3O^-Na^+$) After full conversion the crude product was obtained with 95% yield.

As a consequence of the product's acidic lability and due to the complete conversion of **3**, it was not further purified via column chromatography but used directly for the next step.

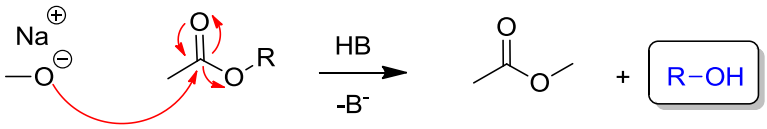


fig. C-11: Zemplen- transesterification

Next, 3,4,6-tri-O-benzyl-α-D-glucopyranose (R)-1,2-(ethylthioorthoacetate) **(5)** was synthesized using classic Williamson-ethersynthesis (see fig. C-12). First the three hydroxyl functionalities were deprotonated with NaH. Then, S_N2-attack on benzylbromide formed the benzylated product.

After workup, the product was purified via column chromatography with 1% TEA to avoid acidic hydrolysis. 30% were obtained as a colourless oil.

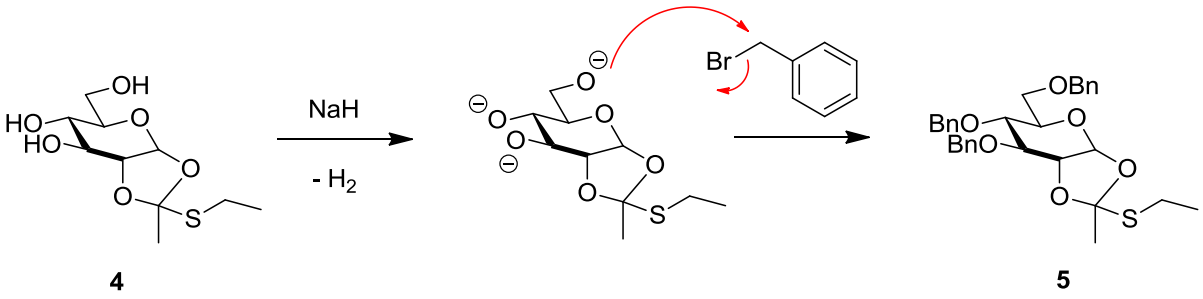


fig. C-12: benzylation

C.5.1.2) Orthoester opening and introduction of the leaving groups

By adding Lewis acid as promoter, orthoesters can be isomerized to 2-O-acetyl-protected glycosides under water-exclusion (molecular sieve addition). If no other nucleophilic reagent is added **5** forms ethyl 2-O-acetyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside **(6)**, a literature known donor. In contrast, if another nucleophilic reagent is added in high excess before activation, the introduction of different leaving groups is possible. (see fig. C-13) After workup, the products were purified using column chromatography. 1% TEA was added to the solvent because of the Lewis-acidic properties of silica to avoid product loss.

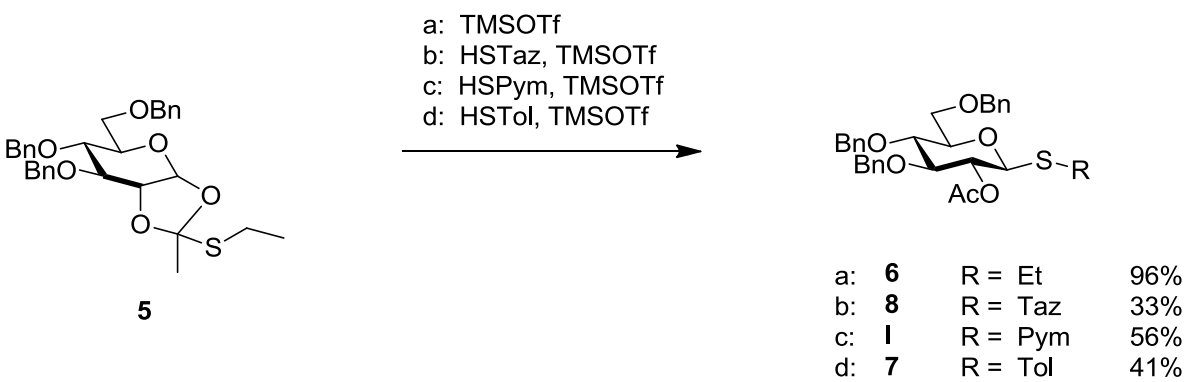
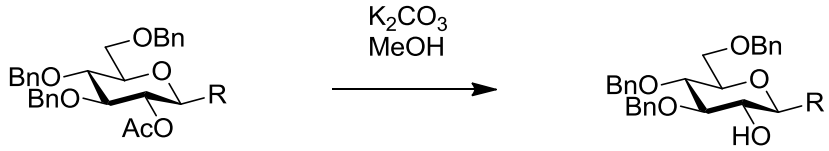


fig. C-13: leaving group introduction

Before Cbz and BnPAc could be introduced, the precursors had to be synthesized by deacetylating **6**, **7**, **8** and **I**, again using K_2CO_3-catalysed *trans*esterification in methanol giving ethyl- **(9)**; 1,3-thiazolin-2yl- **(11)**; 2-pyrimidyl- **(II)** and p-tolyl 3,4,6-tri-O-benzyl-1-thio-β,D-glucoside **(10)** in good yields. (see fig C-14).



6	R = SEt		**9**	R = SEt 94%
8	R = STaz		**11**	R = STaz 70%
I	R = SPym		**VI**	R = SPym 90%
7	R = STol		**10**	R = STol 70%

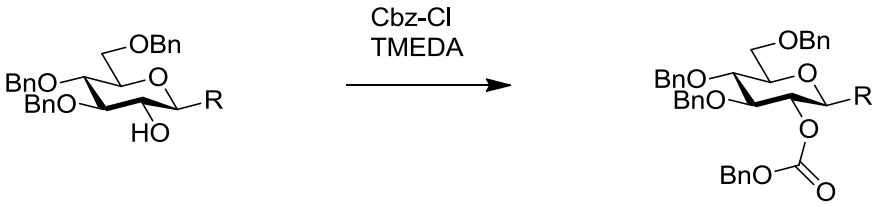
fig. C-14 : deacetylation

C.5.1.3) Introduction of the participating protective group

The introduction of the benzoxycarbonyl (Cbz) group was done based on a general method Adinolfi et al. developed for the installation of alkyloxycarbonyl groups on carbohydrates.[23] The free alcoholic functionality was reacted with benzylchloroformiate promoted by TMEDA in dichloromethane. (see fig. C-15). Interestingly, the reactions stopped between 40-58% conversion of the starting materials. Additional reagents or longer reaction times did not increase the amount of converted material. Residual reactants were recovered during the purification process.

obtained components: (% product based on conversion)

- Ethyl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside **(II)**: white solid (58%/57%)
- p-Tolyl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside **(IV)**: white solid (52%/40%)
- 2-Pyrimidyl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside **(VII)**: yellowish solid (60%/58%)
- 1,3-Thiazolin-2-yl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside **(IX)**: white solid (54%/50%)



9	R = SEt	**II**	R = SEt 58%
11	R = STaz	**IX**	R = STaz 54%
VI	R = SPym	**VII**	R = SPym 60%
10	R = STol	**IV**	R = STol 52%

fig. C-15: Cbz-introduction

Introduction of the novel participating protective group BnPAc was done under standard Steglich-esterification conditions (mechanism see fig. C-16).[24]

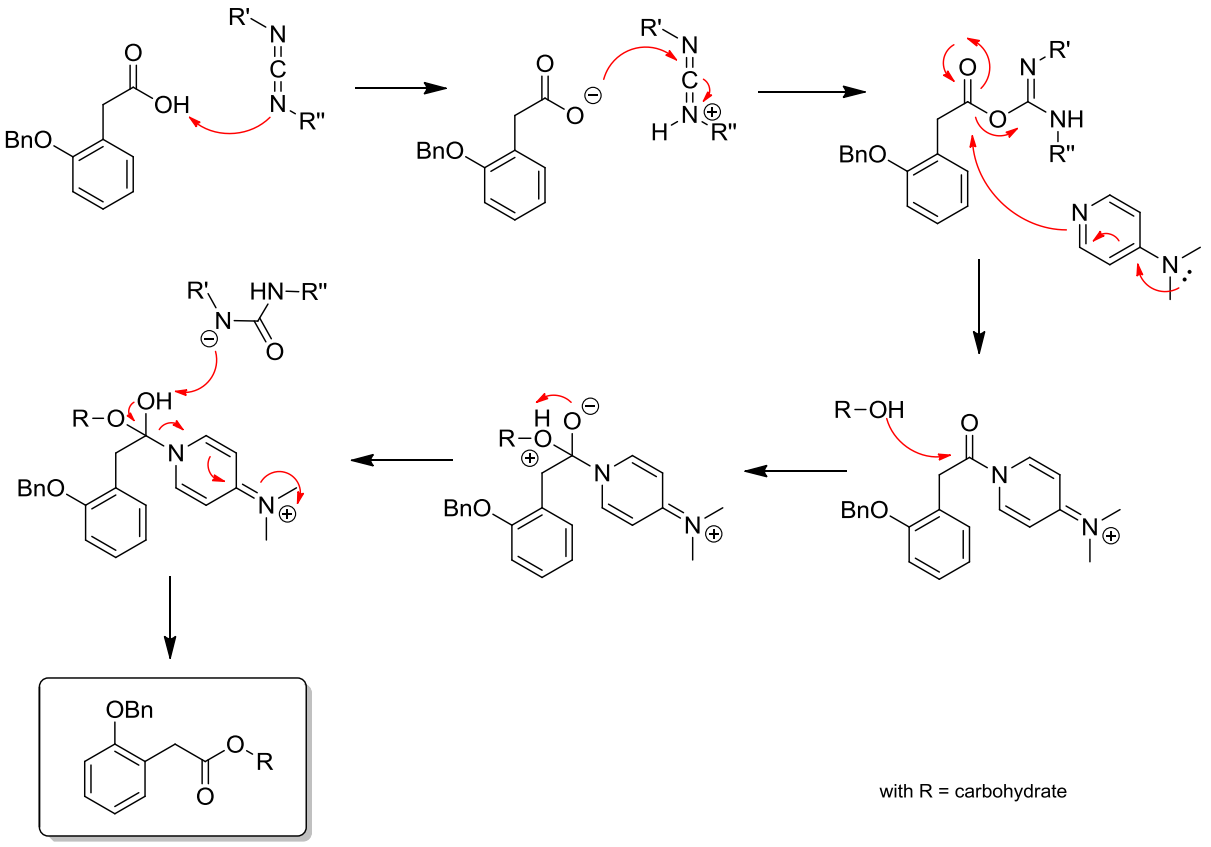


fig. C-16: mechanism of the Steglich-esterification

2-(2-(benzyloxy)phenyl)acetic acid is reacted with carbodiimid under very mild conditions (0°C). In this case EDCI (1-ethyl-3-(3-dimethylaminopropyl)carbodiimide) is used, because the carbamide side product it is easier to separate from the reaction mixture than dicyclohexylurea. In the next reaction step DMAP attacks the carbonylfunction as a nucleophile. Later the less nucleophilic alcohol adds to the activated carbonyl group. After another hydrogen-atom is abstracted, DMAP is released to proceed its catalytic activity.

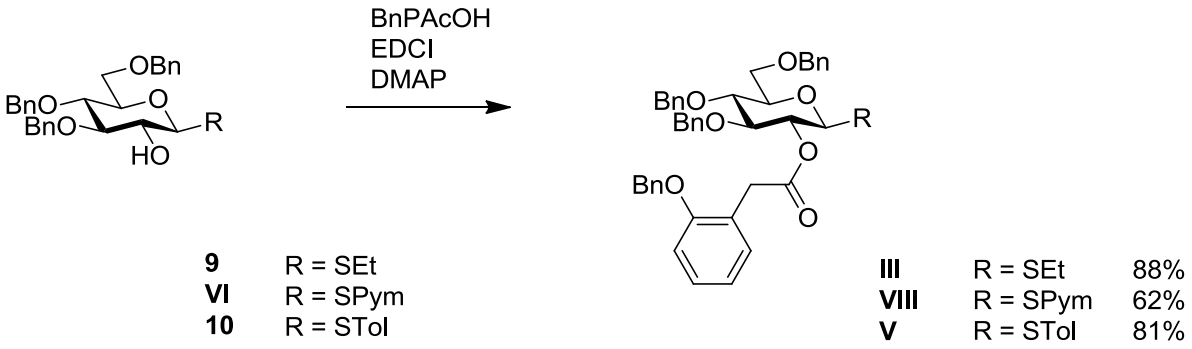


fig. C-17: BnPAc-introduction

Purification was done by column chromatography.

The following components were obtained with moderate to good yields:

- Ethyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-1-thio-β,D-glucoside **(III)**: white solid (88%)
- p-Tolyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-1-thio-β,D-glucoside **(V)**: white solid (81%)
- 2-Pyrimidyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-1-thio-β,D-glucoside **(VIII)**: colourless solid (62%)

C.5.2) The glucal method

Glucals as a starting material are quite common in carbohydrate chemistry. Usually, glucals are epoxidated diastereoselectively (due to sterical reasons) with epoxidising agents like DMDO (dimethyldioxirane), that are opened in a nucleophilic attack at the anomeric centre, which can be used to insert functionalities, that act as leaving groups later on. This is also a literature known and well established method (see fig. C-18).

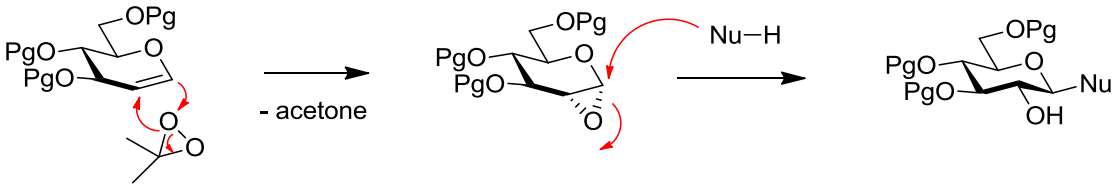


fig. C-18: glucal epoxidation

In this thesis instead of an epoxidation the key step is the catalytic dihydroxylation with OsO_4 which is regenerated *in situ*, using NMO (Upjohn process[19]). This method does work under mild conditions with excellent yields. Moreover, it is easy to handle and dihydroxylation gives glucose only. The mechanism will be discussed later on.

C.5.2.1) Preparation of the benzylated glucal

Starting material for the glucal approach was 3,4,6-Tri-O-acetyl-D-glucal **(12)**, which is commercially available. In the first step deacetylation was done the same way as in the orthoester-approach with full conversion (fig. C-19). After workup D-glucal **(13)** was used without further purification.

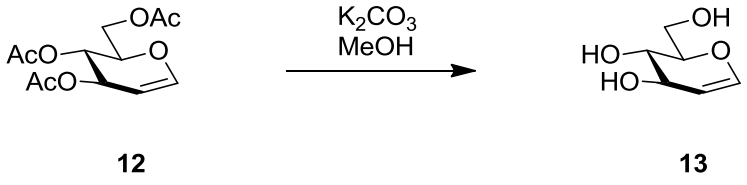


fig. C-19: glucal deacetylation

After the deacetylation step, **13** was benzylated. 3,4,6-tri-O-benzyl-D-glucal **(14)** was purified with column chromatography and a colorless oil was obtained (42%)

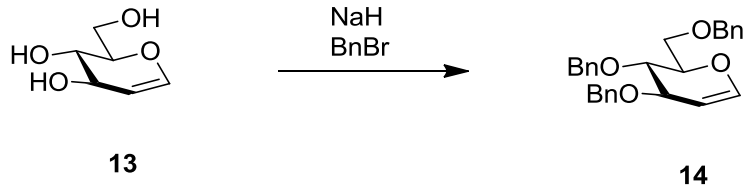


fig. C-20: glucal benzylation

C.5.2.2) Dihydroxylation

There were controversies concerning the exact mechanism of the first reaction step (the addition of OsO_4) whether a [3+2] or a [2+2] mechanism takes place. Quantum chemical calculations had shown, that [3+2]-cycloadditions are energetically more favourable.[25] After the syn-addition, NMO regenerates OsO_4 which makes it a catalyst. The osmate ester is hydrolysed by water.[26]

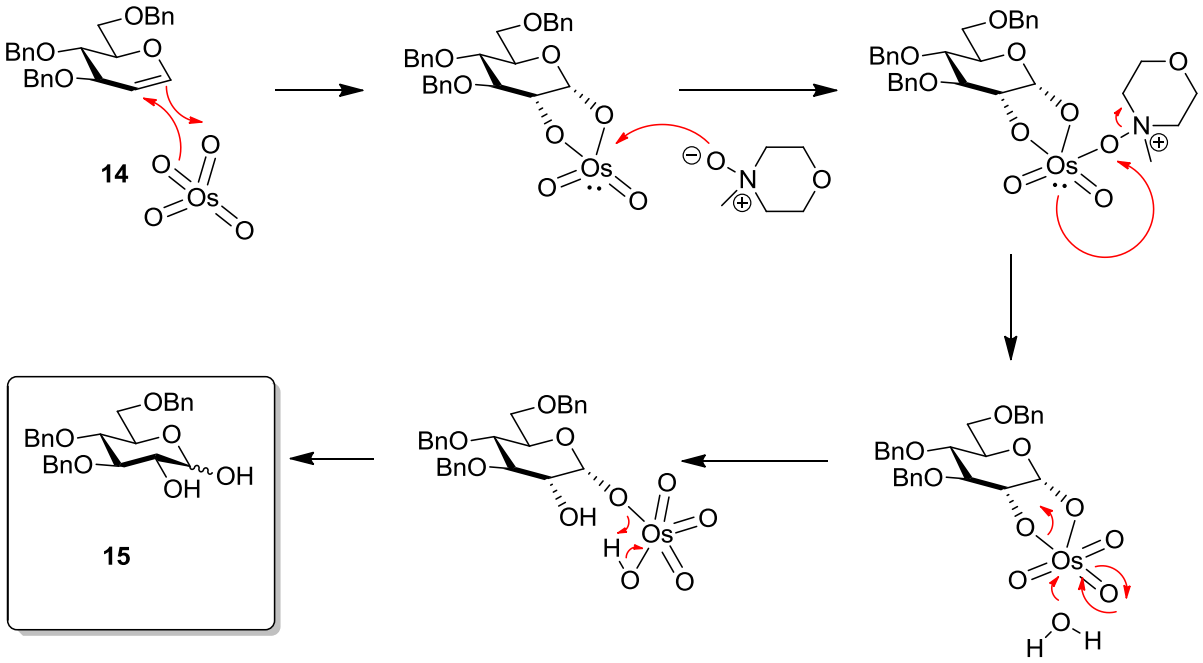


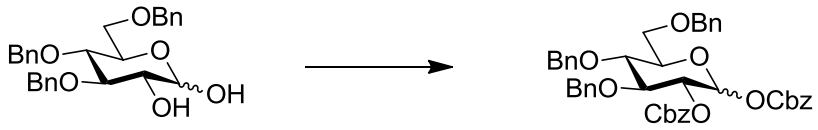
fig. C-21: mechanism of the dihydroxylation

14 was then reacted with OsO_4 and NMO in THF/t-BuOH/H_2O = 7/3/1 (according to [27]). After full conversion, the toxic Os(VIII)-species was reduced to less toxic OsO_2 (black solid) with $Na_2S_2O_3$ solution. 42% 3,4,6-tri-o-benzyl-D-glucoside **(15)** were obtained as white and waxy solid.

C.5.2.3) Introduction of the participating protective groups

C.5.2.3.1) Cbz-introduction

The same method as in the orthoester-strategy was used. The only difference was the usage of twice as much equivalents as for O-2-introduction only (fig. C-22). Surprisingly, the yields were a lot higher. After purification, 73% of 3,4,6-tri-O-benzyl-1,2-bis(benzyloxycarbonyl)-D-glucoside **(X)** were obtained as colorless oil (α/β ~ 1/1).

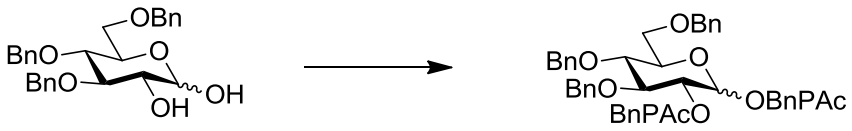


15 **X**

*fig. C-22: Cbz-introduction at **(15)***

C.5.2.3.2) BnPAc-introduction

Again, the same method as in the orthoester-strategy was used. 78% of 3,4,6-tri-O-benzyl-1,2-bis-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside **(XI)** were obtained as white, waxy solid (α/β ~ 3/2). This yield is good and comparable with the other method (62-88%).



15 **XI**

*fig. C-23: BnPac-introduction at **(15)***

C.6) Anomeric modifications

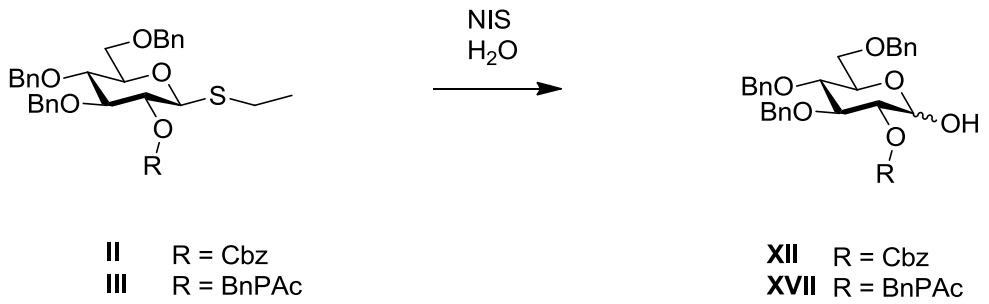
Anomeric modifications are interesting because other donor types become easily accessible within a divergent synthesis strategy. Besides thioglycosides, different and orthogonal activation methods can be used, allowing a broader range of reactivities fitting for each glycosylation problem. The most common are imidates and halides. In this thesis simple conversion to this other donor types while keeping the new protective group patterns should be shown.

C.6.1) Imidates

C.6.1.1) Preparing the OH-sugar

An important type of modification is the anomeric hydroxylation. These compounds are needed as precursors for the synthesis of imidates. Various methods were used to fulfill this task, starting either from thioglycosides or dialkyloxycarbonylated sugars.

The first method[28] can also be seen as a glycosylation with water as acceptor molecule. Sulfur is activated by an electrophile iodine species, formed by NIS. After workup and purification, 3,4,6-tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside **(XII)** (85%) and crude 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside **(XVII)** (99%) were obtained as white solids. (see fig. C-24)



II R = Cbz
III R = BnPAc

XII R = Cbz
XVII R = BnPAc

fig. C-24: anomeric hydroxylation of Set-donors

Another strategy was the Lewis-acidic catalysed, microwave assisted hydrolysis of the anomeric Cbz-group of 3,4,6-Tri-O-benzyl-1,2-bis(benzyloxycarbonyl)-D-glucoside **(X).** A few different conditions were tried, listed in table-1. Method A was too vigorous and nearly the whole reactand was destroyed. Method B produced desired product (confirmed by TLC-MS) and a remarkable more polar by-product. Method C led to formation of **XII** almost exclusively (according to TLC-control). (see Fig C-25)

method	temperature	time	solvent	result
A	120°C + 150°C	15 min + 30 min	THF/H_2O=9/1	overreaction
B	140°C	20 min	THF/H_2O=9/1	XII + by-product
C	130°C	20 min	THF/H_2O=9/1	mainly XII

table-1

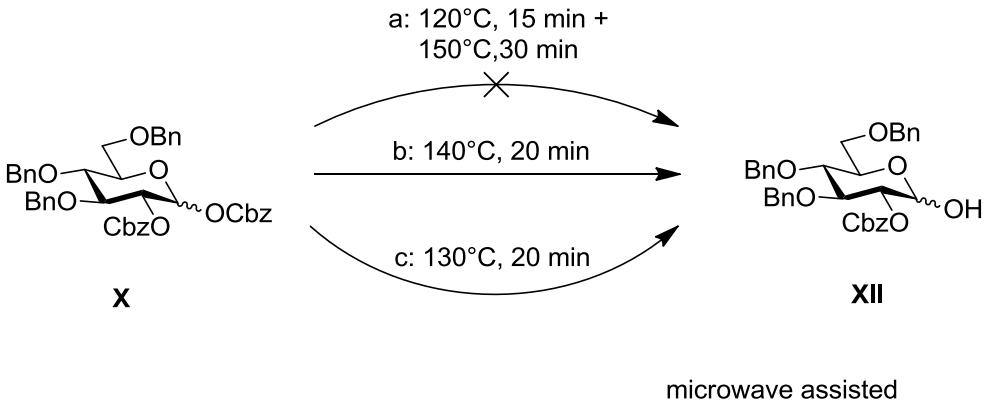


fig. C-25: anomeric hydroxylation of SEt-donors

Another approach for **XVII** is the use of benzylamine for nucleophilic substitution of the anomeric 2-(2-Benzyloxyphenyl)acetyl)-group (see fig C-26) in THF according to.[29] After purification, 86% white solid was obtained.

Small impurities of the byproduct N-benzyl-2-(2-(benzyloxy)phenyl)acetamide **(BP)** could not be separated from **XVII** because of a very similar retention time. Luckily, it did not affect the imidate synthesis.

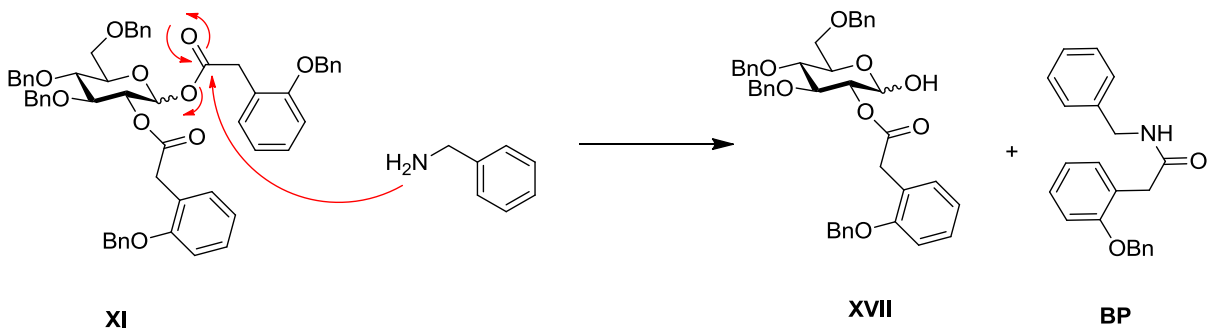


fig. C-25: anomeric hydroxylation of SEt-donors

C.6.1.2) Introduction of imidates

The standard procedure for synthesizing trichloroacetimidates is deprotonating the anomeric hydroxyl group with a strong non-nucleophilic base (DBU) that performs a nucleophilic attack on trichloroacetonitrile.[30] For **XVII** this approach leads to high yields (up to 97%) of the desired product trichloracetimidoyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside **(XVIII)** as a white solid, although the purification is quite challenging due to high reactivity and sensitivity to the acidic silica phase. However, when applying this strategy on **XII**, only 21% of the desired product (trichloracetimidoyl 3,4,6-tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside **(XV)**) were obtained whereas three quaters of the starting material were converted into a cyclic carbonate **(XIV)** (see fig.C-26). A connection between the α/β-ratio of **XII** and the amounts of **XIV** and **XV** could be possible, as NMR indicated a similar amount for the ratio. The problem did not occur for BnPAc-protected donors as no formation of **XIV** is possible in that case.

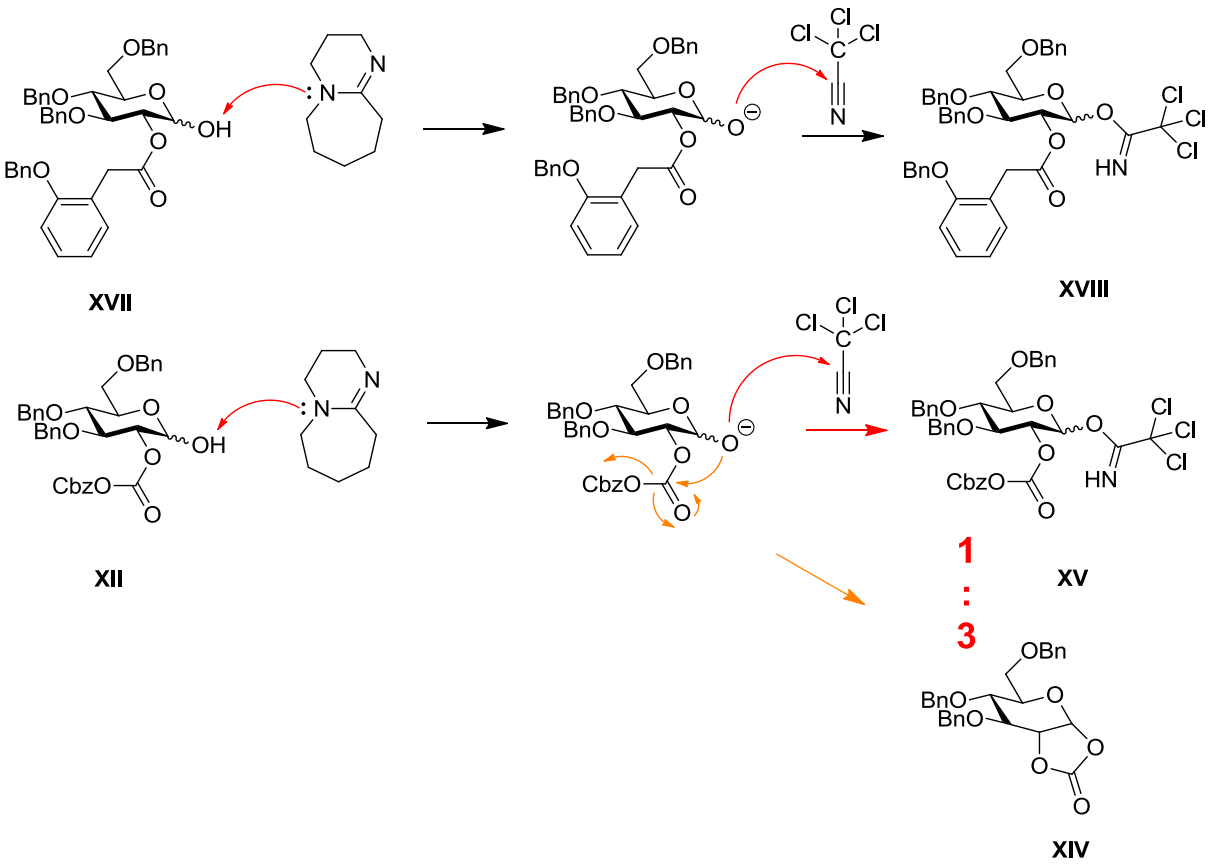


fig. C-26: synthesis of the trichloroacetimidates (XV) and (XVIII)

To handle the problem, N-phenyl-trifluoracetimidoyl chloride was chosen as a stronger electrophile combined with a weaker base (K_2CO_3) (see fig. C-27).[16] The electrophilic reagent **(19)** was prepared according to [31] with a yield of 65%.

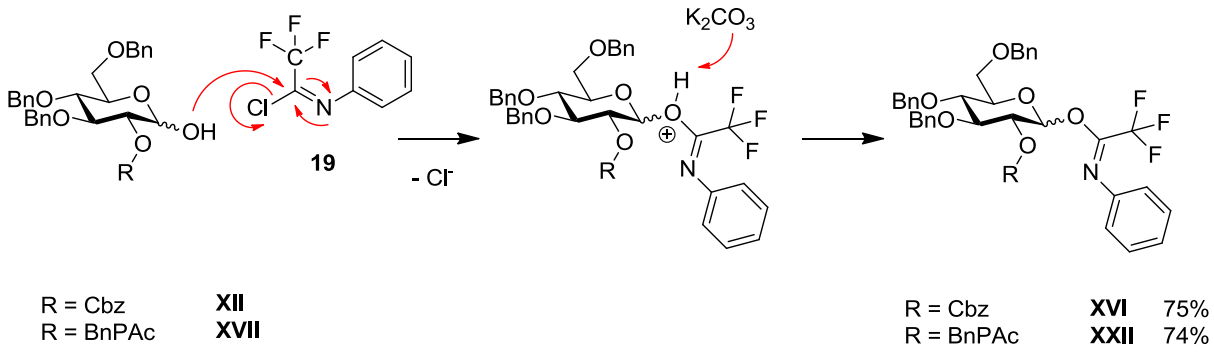


fig. C-27: synthesis of the N-phenyltrifluoroacetimidates (XVI) & (XXII)

This approach was successful, as both N-phenyltrifluoracetimidoyl 3,4,6-tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside **(XVI)** and N-phenyltrifluoracetimidoyl 3,4,6-Tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside **(XXII)** could be obtained at high yields (75% and 74% respectively). For purification, once again, a slight amount of TEA (1% of the solvent system) and short contact with silica is mandatory for high yields.

C.6.2) Glycosylfluorides from thioglycosides

Thioglycosides can be converted directly to fluorides at room temperature with DAST, a mild fluorinating agent, which is very interesting for oligosaccharide synthesis. First, the sulfuric leaving group is activated with NIS, forming the oxocarbenium intermediate.[32] Then, one equivalent of F^- is released by nucleophilic substitution on DAST. F^- attacks the anomeric centre to form an anomeric mixture of α and β- glycosyl fluoride (see fig. C-28). 49% of fluoro 3,4,6-tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside **(XX)** were obtained as a white solid after purification with column chromatography (α/β-ratio is 3/4 according to NMR).

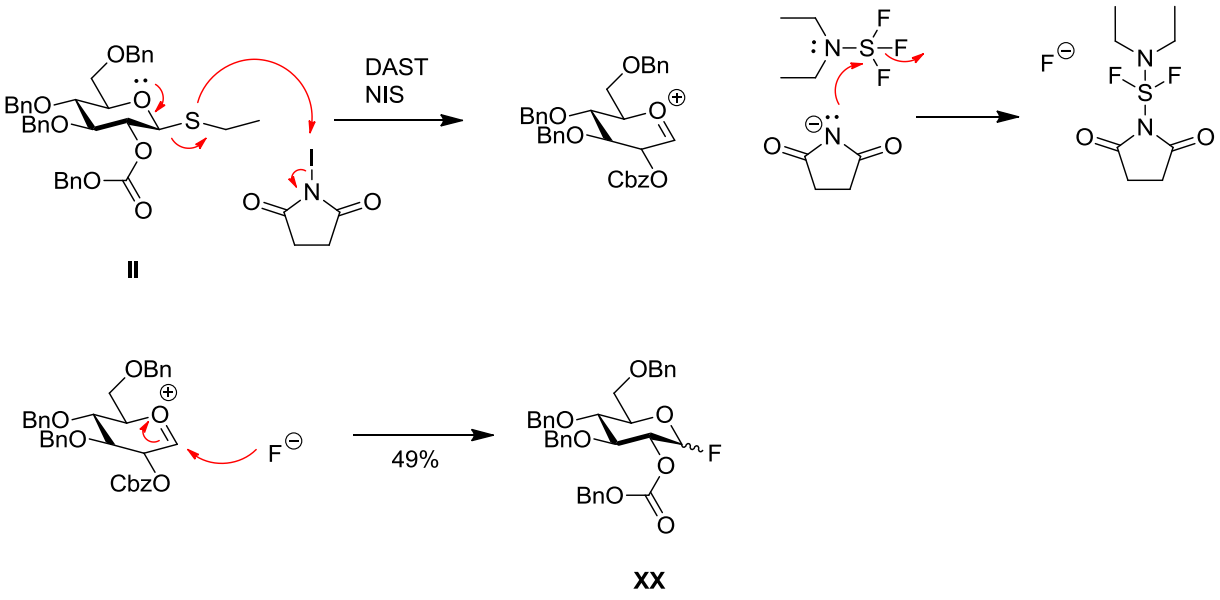


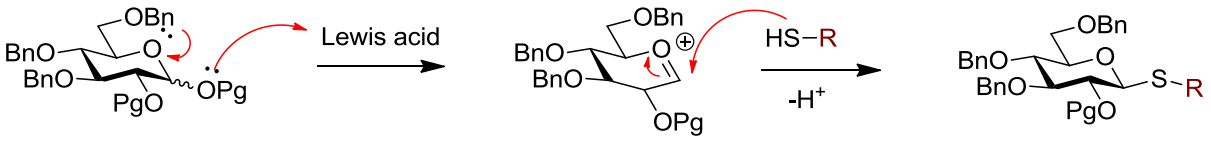
fig. C-28: synthesis of glycosylfluoride (XX)

C.6.3) Thioglycosides from 1-benzoxycarbonylglycosids

Starting from the donor precursors of the glucal strategy **X** and **XI**, two different approaches were used to make the desired thioglycosides accessible.

C.6.3.1) Lewis-*acidic promoted*

The general method was based on the leaving group introduction, discussed earlier. The starting material was dissolved in dry dichloromethane under water exclusion (stirring with molecular sieves) and Ar-atmosphere. An excess of the appropriate nucleophile and the Lewis acid promoter were added (see fig. C-29). After the reaction had finished (no more starting material on TLC), it was quenched with TEA, filtrated over Celite and concentrated *in vacuo*. A variation of different promoters and nucleophiles was used. All reactions were controlled by TLC and TLC/MS.



Pg = Cbz **X**
Pg = BnPAc **XI**

with Lewis acid = TMSOTf, $SnCl_4$, $BF_3 * Et_2O$
R = Et, Tol, Pym, Taz

fig. C-29: Lewis *acid promoted anomeric modification*

Table-2 shows that synthesizing the target molecules is possible under all applied reaction conditions. Nevertheless, only small amounts of the desired products were formed and further investigation and optimization is mandatory. It seems that the reaction conditions were too vigorous, which caused unwanted side reactions. A suggestion for the formation of the cyclic carbonate **(XIV)** is given in fig. C-30. Instead of the anomeric centre, the nucleophile may attack at the benzylic group of the benzyloxycarbonyl moiety (S_N2) and "traps" the carbonate in its anchimeric role.

starting material	promoter	nucleophile	product	product amount	by-product (XIV)
X	TMSOTf	EtSH	**II**	moderate	traces
X	$SnCl_4$	EtSH	**II**	moderate	moderate
X	TMSOTf	HSTol	**IV**	traces	high amount
X	TMSOTf	HSPym	**VII**	traces	high amount
X	$BF_3 \cdot Et_2O$	HSPym	**VII**	traces	high amount
X	TMSOTf	HSTaz	**IX**	traces	high amount
X	$BF_3 \cdot Et_2O$	HSTaz	**IX**	traces	high amount
XI	TMSOTf	EtSH	**III**	moderate	
XI	$SnCl_4$	EtSH	**III**	moderate	
XI	$BF_3 \cdot Et_2O$	HSTol	**V**	no product	

table-2

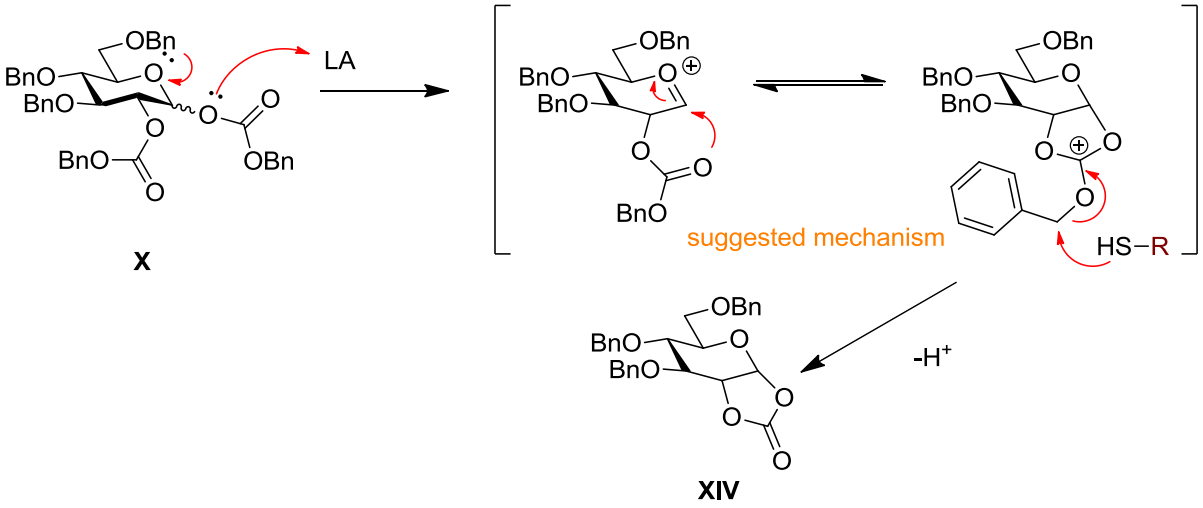


fig. C-30: suggested mechanism for the formation of the cyclic carbonate (XIV)

C.6.3.2) Through bromo-intermediate

To avoid the formation of cyclic carbonate, a new synthetic pathway was chosen that leads over a glycosylhalide intermediate followed by crown-ether catalysed nucleophilic substitution on the anomeric centre.

The first step was the formation of 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-deoxy-1-bromo-glucopyranose **(XIII)** respectively 2-O-(2-(2-benzyloxyphenyl)acetyl)-3,4,6-tri-O-benzyl-1-deoxy-1-bromo-glucopyranose **(XIX)**. Analogous to the formation of **2**, the starting material was reacted with HBr/HAc (33%), diluted with dichloromethane at -20°C. After full conversion, the reaction mixture was worked up and **XIII** respectively **XIX** were used directly for the second reaction step due to fast degradation.

Another approach that uses $TiBr_4$ for the bromination step led to the formation of the cyclic carbonate **(XIV)** predominantly (Only applied on **X**). Therefore, the other method was preferred.

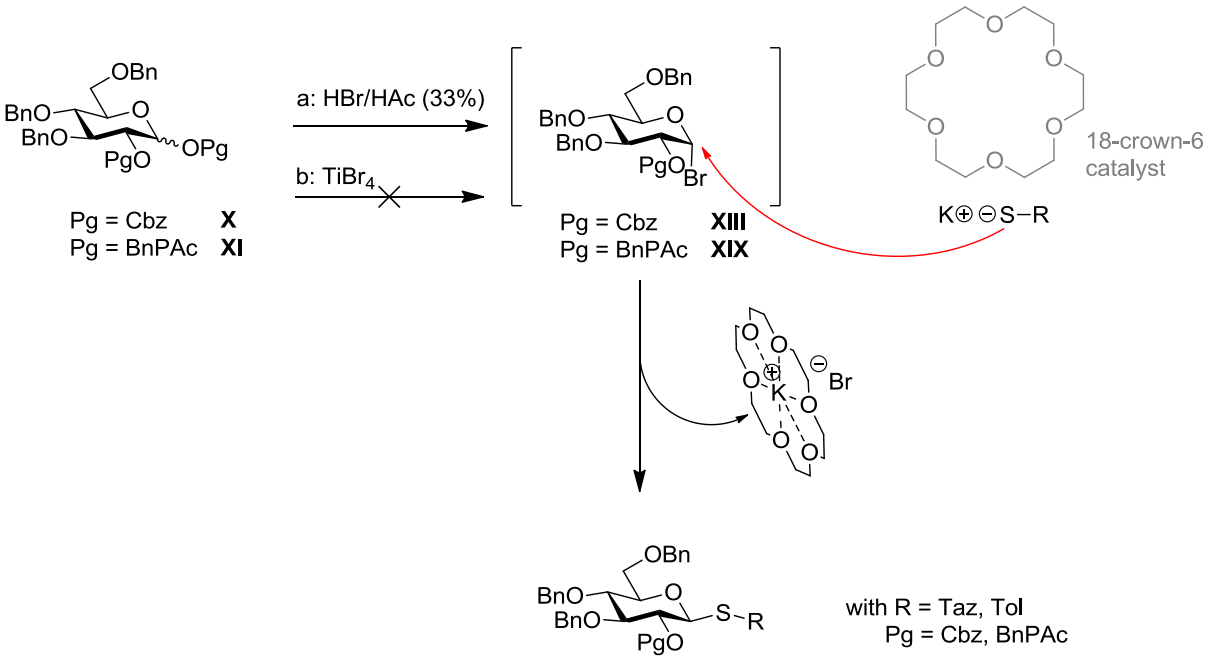


fig. C-31: anomeric modification to thioglycoside

For the second reaction step, potassium salts of the nucleophiles were used alongside 18-crown-6-ether catalyst. Potassium fits perfectly into the cavity of 18-crown-6. By complexing the K^+-species, the reactivity of the thiolate is enhanced (see fig. C-31). After consumption of the starting material, product formation was proved by TLC/MS as well as by comparison with TLC-references. **XIII** and **XIX** partially hydrolysed to **XII** and **XVII** (see (table-3)).

starting material	nucleophile	product	product amount	by-product
(XIII) (crude)	KSTaz	**(IX)**	91% (crude)	**(XIV), (XII)**
(XIII) (crude)	KSTol	**(IV)**	moderate yield*	**(XII)**
(XIX) (crude)	KSTol	**(V)**	moderate yield*	**(XVII)**

table-3

* as indicated by TLC

C.7) Glycosylations

C.7.1) Glycosylations with Cbz-donors

2-Phenylethanol was applied as simple acceptor molecule to prove the capability of the novel glycosyl donors to synthesize 1,2-*trans* glycosides stereoselectively. Different promoters were used all giving good yields and the selectivity was confirmed by NMR-spectroscopy. ($J_{anomeric}$ = 8.20 Hz, typical for β-glycosides) (see fig. C-32)

In general, the glycosyl donor was dissolved in dry dichloromethane together with 2-phenylethanol and molecular sieves (3Å) in vials under Ar-atmosphere. Then the suspension was stirred for 2-4 hours at the required temperature (regulated by a cryostat) followed by addition of the promoter, the mixture was stirred overnight at the adjusted temperature. TLC indicated full consumption of the glycosyl donor and the reaction was quenched with TEA. After dilution with dichloromethane, the molecular sieve was filtrated off with celite and the organic was washed with water and BRINE. Then, the phase was dried with Na_2SO_4 and concentrated *in vacuo*. The purification was done using column chromatography (silica, PE/EE gradient elution) to give **XXI** as colorless, high viscous oil in high yields. An overview is given in table-4.

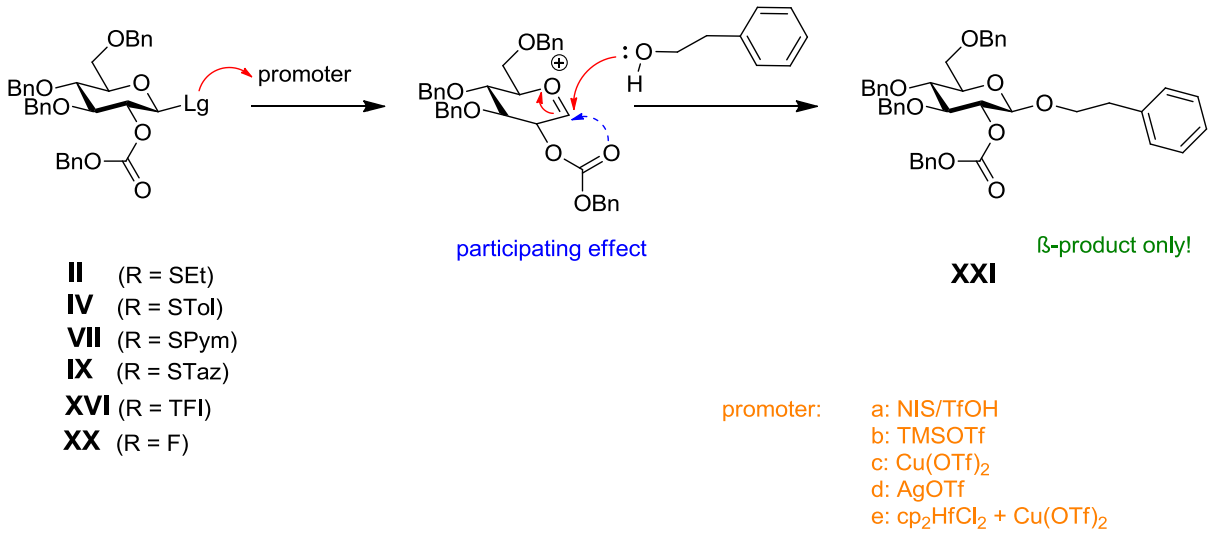


fig. C-32: mechanism of chemical glycosylation explained on 2-phenylethanol as acceptor

donor	leaving group	promoter system	temperature	yield
II	SEt	a: NIS/TfOH	-10°C	**83%**
IV	STol	a: NIS/TfOH	-10°C	**82%**
VII	SPym	b: TMSOTf	-10°C	**87%**
VII	SPym	d: AgOTf	0°C	**additional activation -> b**
IX	STaz	c: $Cu(OTf)_2$	-10°C	**77%**
XVI	TFI	b: TMSOTf (catalytic amount)	-20°C	**product***
XX	F	e: cp_2HfCl_2 + $Cu(OTf)_2$	-10°C	**product***

table-4: Glucosylation yields

*as indicated in TLC

Photographs C-1 and C-2 show the experimental assembly of the first glycosylation screening.

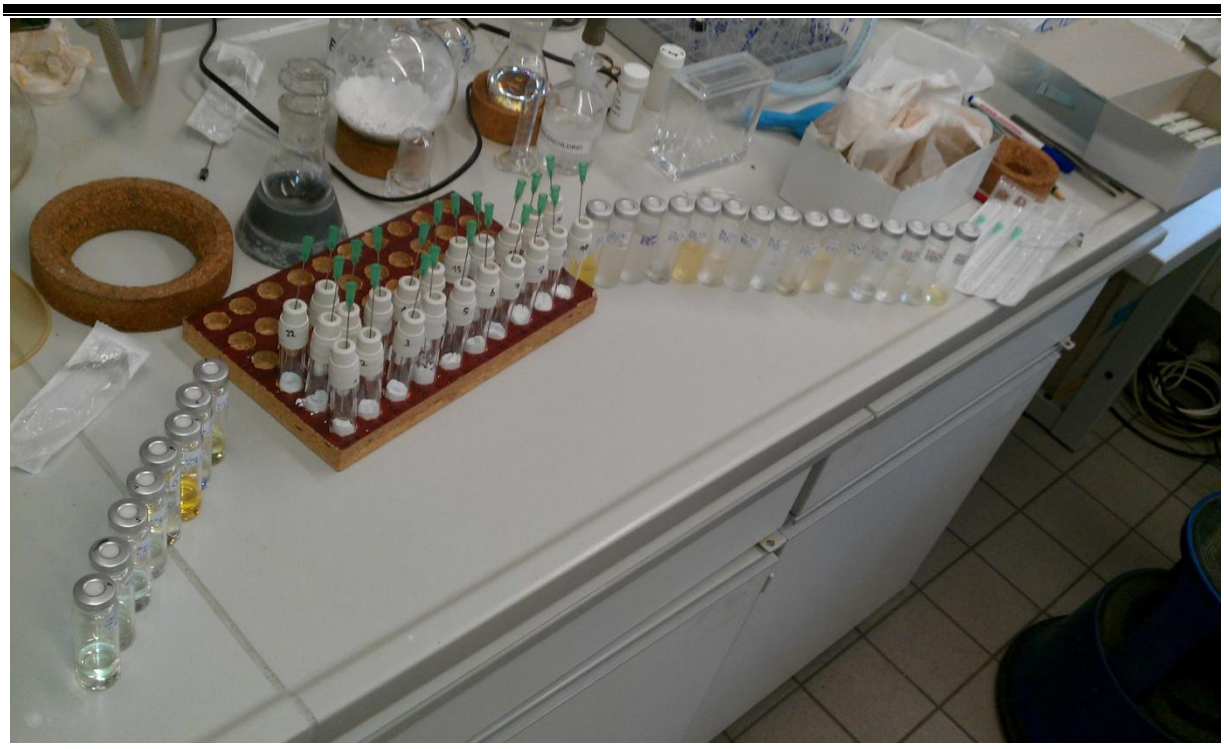
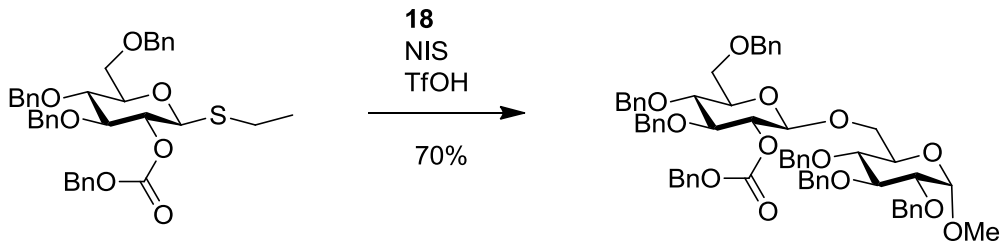


photo C-1:preparation of the glycosylations

photo C-2: glycosylations in progress

Furthermore, 2,3,6-tri-O-benzyl-1-O-methyl-α-D-glucopyranose **(18)** was used as acceptor to synthesize an orthogonal protected disaccharide (see fig. C-33). Following the general procedure at -15°C, the yield was 70% of 3,4,6-tri-O-benzyl-2-O-benzoxycarbonyl-β-D-glucopyranosyl-(1→6)-1,2,3,4-tetra-O-acetyl-β-D-glucopyranose **(XXVI)**.



II **XXVI**

*fig. C-33: glycosylation of **18***

C.7.2) Glycosylations with BnPAc-donors

Again, 2-phenylethanol was used as acceptor molecule to prove the stereoselectivity of the novel 2-O-(2-(2-benzyloxyphenyl)acetyl)-protected donors **III** and **VIII**. Excellent yields (82-95%) of 2-phenylethyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside **(XXIII)** were obtained with the general method discussed earlier. Again, exclusive formation of 1,2-*trans* products was confirmed using NMR-spectroscopy by analyzing the vicinal proton-proton coupling constants.
(fig. C-34). The relation between dihedral torsion angles and ^{3}J-coupling constants was first described by Martin Karplus in 1963.[33]

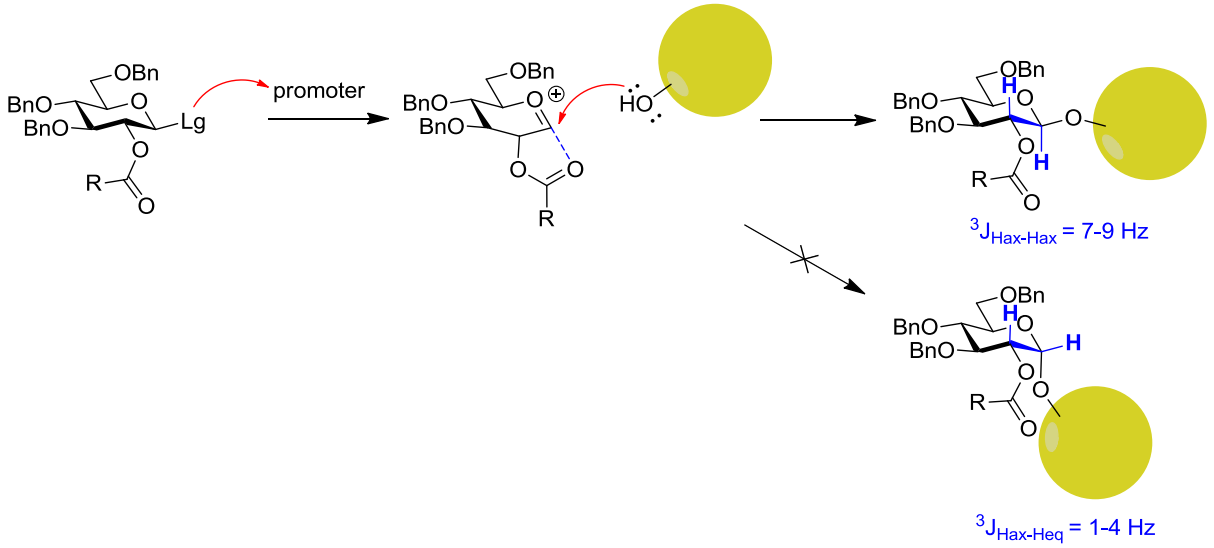


fig. C-34: formation of the β-anomer proved by NMR-spectroscopy

The connection between the anomeric hydrogen and the anomeric carbon atom can be deduced from HSQC-spectrum, giving the chemical shift value for the anomeric proton (fig. C-35). Couplings between different protons can be seen in the corresponding H,H-COSY spectra. For **XXIII**, J= 8.20 Hz, which is typical for β-glycosides (fig. C-36).

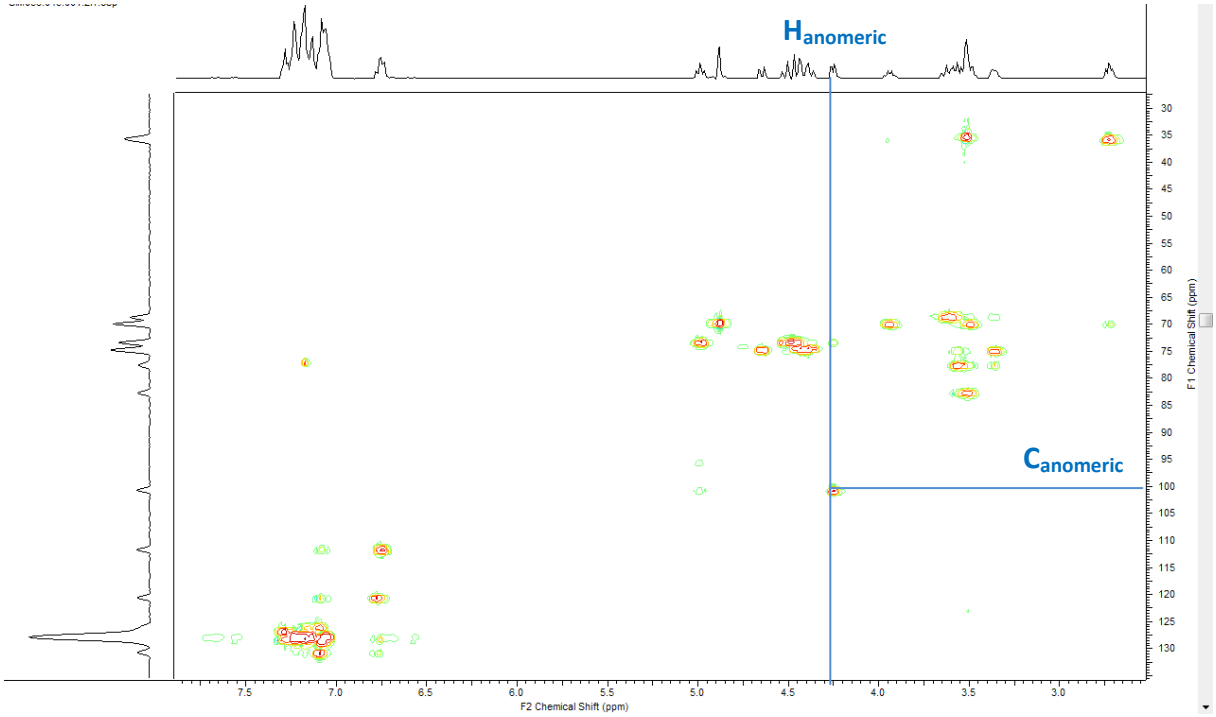


fig. C-35: Determination of the anomeric centre

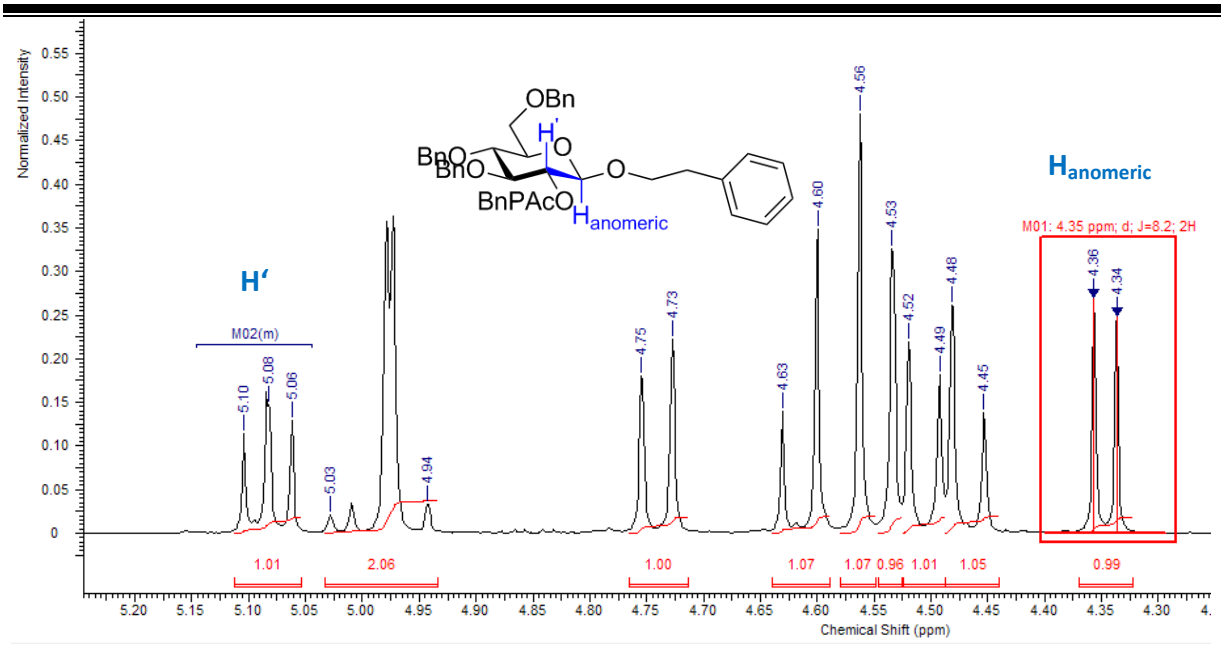


fig. C-36: Determination of the anomeric properties

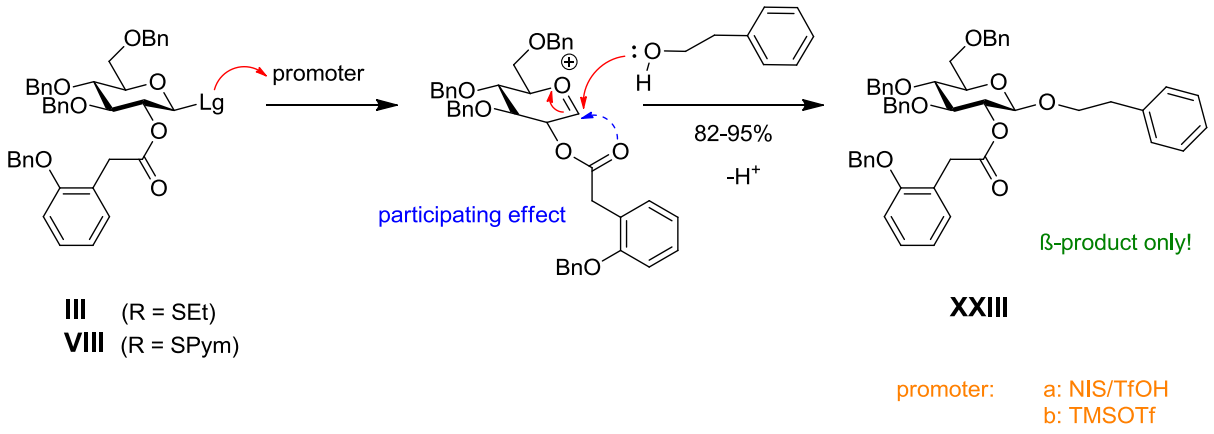


*fig. C-37: glycosylation of **2-phenylethanol***

After successfully applying the glycosylation method on 2-phenylethanol (see fig. C-37), more interest in the synthesis of disaccharids grew. Hence, two other acceptor molecules were envisaged (see fig. C-38):

- β-D-glucose-1,2,3,4-tetraacetat **(17)**
- 2,3,6-tri-O-benzyl-1-O-methyl-α-D-glucopyranose **(18)**

3,4,6-Tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-β-D-glucopyranosyl-(1→6)-1,2,3,4-tetra-O-acetyl-β-D-glucopyranose **(XXIV)** and 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)- β-D-glucopyranosyl-(1→4)- 2,3,6-tri-O-benzyl-1-O-methyl-α-D-glucopyranose **(XXV)** were both obtained in good yields (61% and 60%), both as highly viscous colorless oils.

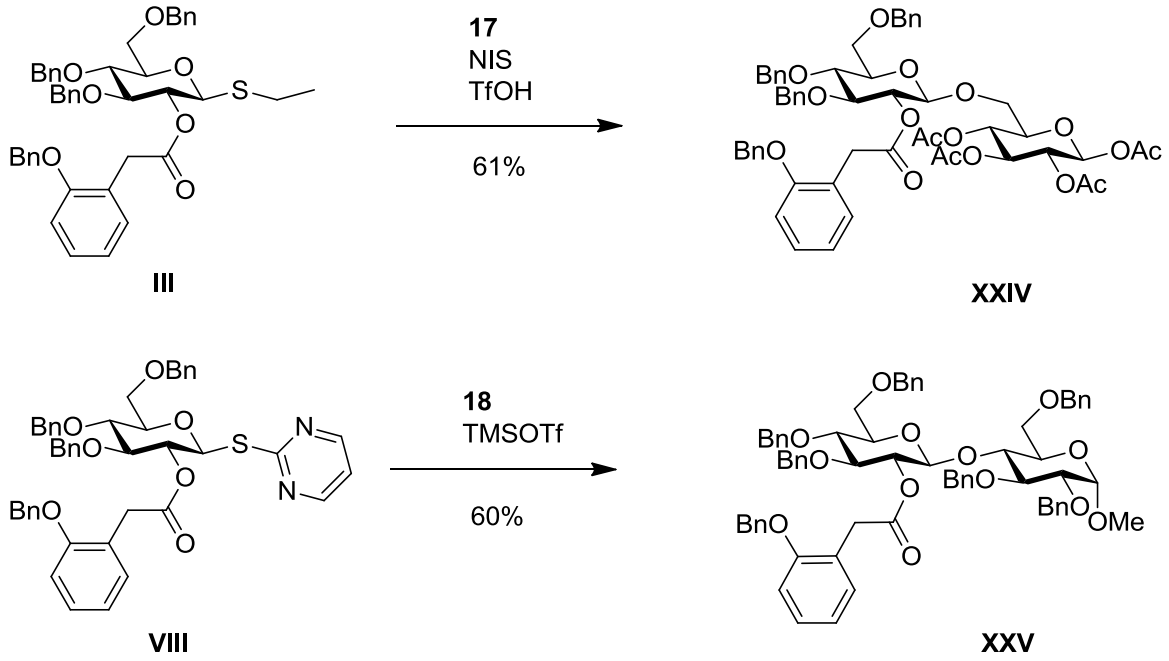


*fig. C-38: synthesis of **(XXIV)** and **(XXV)***

C.8) Competitive studies

To compare the reactivity of the novel glycosyl donors with literature-known 2-O-benzoxyl donors, 2-Pyrimidyl 3,4,6-tri-O-benzyl-2-O-benzoxyl-1-thio-β,D-glucoside **(XXVIII)** was synthesized. Afterwards, one equivalent of 2-phenylethanol was reacted with **VII** and **XXVIII** (one equivalent each) (see fig. C-39) and then, the ratio of 2-O-benzylated vs. 2-O-benzoxycarbonylated product was determined via LC/MS. For this purpose, **20** was synthesized as reference material. Preliminary studies have shown that more **20** than **XXI** was formed. The novel donor class seems to be less reactive than Demchenko's superarmed donor class, but still more reactive than the classical peracetylated donors.[5] For more pre*cis*e quantifications, further studies have to be done.

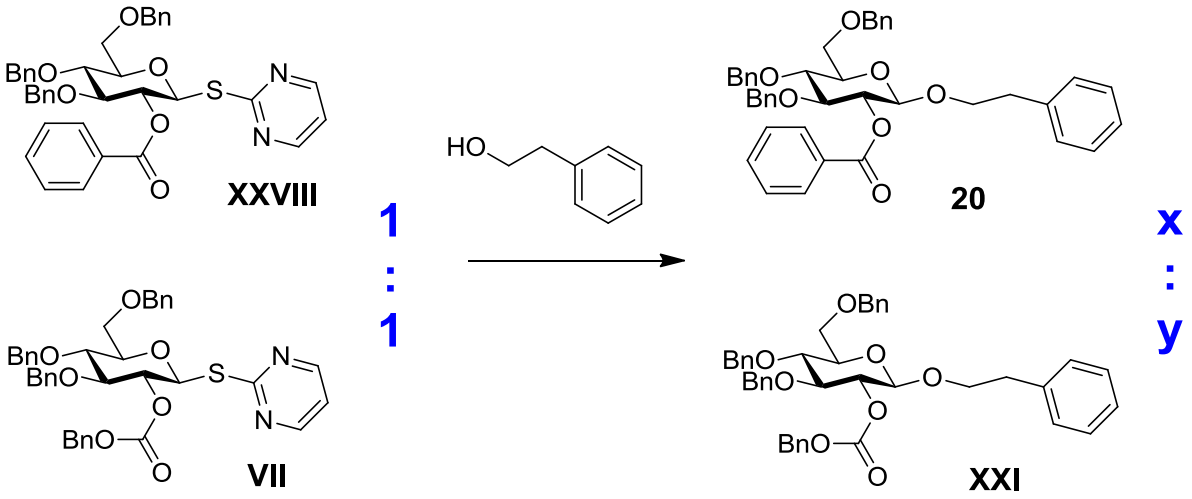


fig. C-39: competitive studies

C.9) Deprotection

For deprotecting the benzylic moieties the starting material (**XXI** and respectively **XXIII**) was dissolved in dry ethanol and bubbled with Ar. Then, the catalyst (Pd/C) was added and a balloon filled with hydrogen was attached. The deprotection went on very slowly (four benzyl moieties per molecule had to be deprotected) until it was finished after two weeks of stirring. Every time, the balloon grew empty due to diffusion, it was replaced by a new one. The reaction was monitored by TLC. After only traces of the partial hydrolysed glycosides were left, the activated catalyst was filtrated over celite and washed with solvent. During this process the catalyst was not left dry.

After washing the active catalyst species was destroyed. LC/MS-control showed the formation of the desired product almost exclusively (see fig. C-40). For **XXVII** a second deprotection step is necessary to obtain product **16**. For this purpose proton-sponge is used. Various preliminary tests were done within the research group that seem promising. Nevertheless, final cleavage of the 2-(2-hydroxyphenyl)acetyl-spacer was not done during this thesis for lack of time.

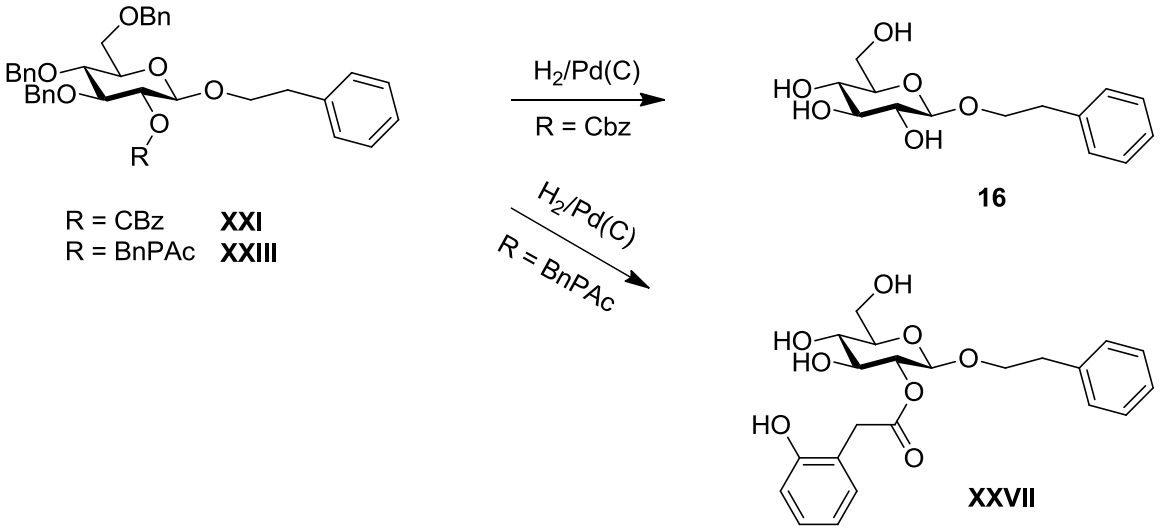


fig. C-40: cleavage of the benzylic moieties

D) Conclusion & Outlook

D.1) Summary

D.1.1) Donorsynthesis

All desired thioglycosides were synthesized using the literature-known orthoester-approach with moderate yields. Needing 7 reaction steps, this method leads to overall yields displayed in fig. D-1. The introduction step of the 2-O-benzoxycarbonyl protective group had a massive effect on the overall yield while the 2-O-(2-(2-benzyloxyphenyl)acetyl)-introduction worked very good.

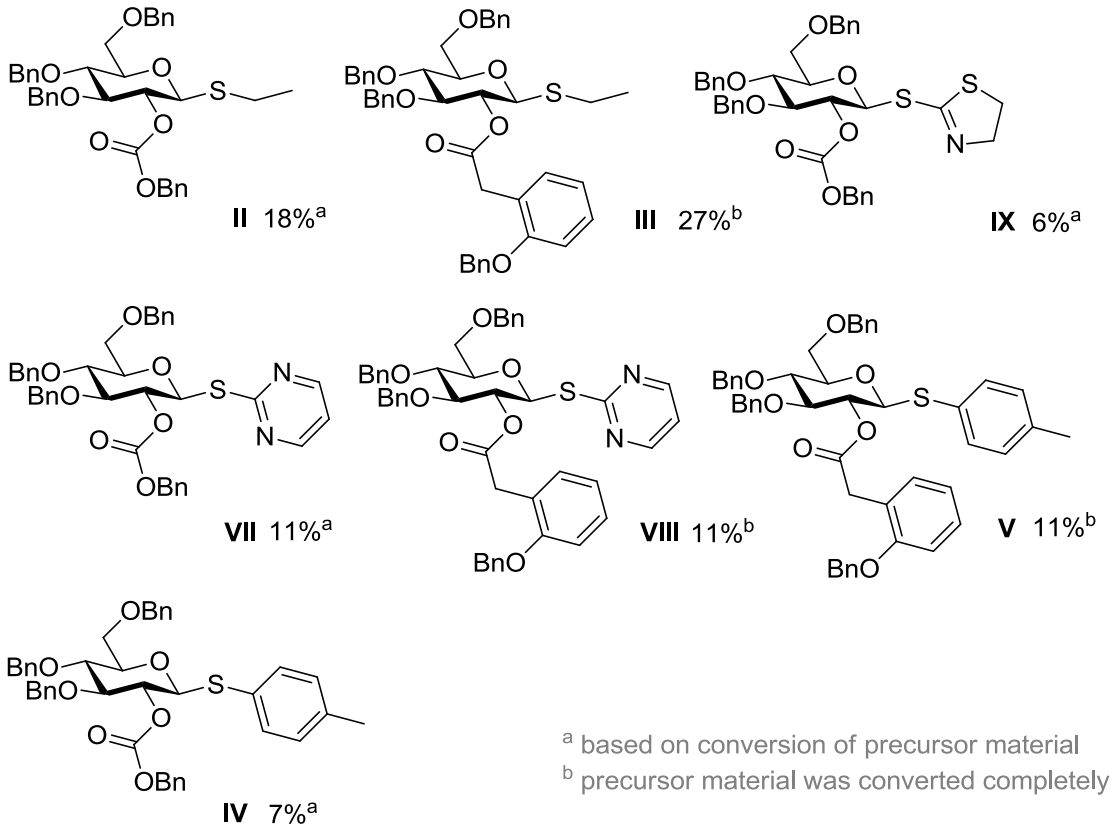


fig. D-1: overall yields

A promising new method has been implemented based on the dihydroxylation of a glucal. Although some more research has to be done in the last anomeric modification step to increase the yields, the viability of the new approach has been confirmed. Introduction of the benzyloxycarbonyl protective group gave good yields (73% at full conversion compared to about 55 at 60% conversion). The donor precursors were obtained at good overall yields (32% for **X** and 35% for **XI**) using less reaction steps (5). The final anomeric modification determines further yield calculations. More research has to be done in this field.

D.1.2) Anomeric modifications

The huge advantage of thioglycosides against other types of glycosyl donors besides the good storage stability is the capability of protecting the anomeric centre from nucleophilic attacks simultaneously. It was shown that *trans*forming thioglycosides into imidates and fluorides is easily possible. For the 2-O-benzoxycarbonyl-protected compounds, the synthesis of N-phenyl-trifluoracetimidoylglycosides was found to be better suiting than the classic trichloroacetimidates, because during the reaction the stronger electrophile **19** combined with a weaker base favor the formation of the desired imidate over the cyclic carbonate **XIV**. (3:1 compared to 1:4).
Also, the Fluoride could be synthesized directly from **(II)** with 49% yield.

D.1.3) Glycosylations

2-Phenylethanol, as well as carbohydrate acceptor molecules were successfully used as application examples for the novel glycosyl donors. These reaction gave good to excellent yields of pure 1,2-*trans* compounds, as proven by NMR-spectroscopy by analyzing the vicinal proton-proton coupling constants of the anomeric hydrogen atoms.

D.1.4) Deprotections

Deprotection of benzyl, as well as benzoxycarbonyl protective groups was done successfully, although the reaction time was long under mild conditions (up to 2 weeks). Therefore, different hydrogenation processes using the Thales Nano "H-Cube®" had already been performed within the research group but still have to be optimized for this project. The first deprotection step of 2-O-(2-(2-benzyloxyphenyl)acetyl)-protected products also was realized.

D.2) Outlook

D.2.1) Further competitive studies

To compare the reactivity of the novel glycosyl donors first experiments were done, but further investigations are necessary to integrate the new donor system into the reactivity scale for literature-known donors.

D.2.2) Variation of the protective group patterns

The novel method is limited to acceptor molecules that do not contain unsaturated moieties, which would also be hydrogenated during the cleavage of benzylic protective groups. Some possibilities are PmBoc/PMB (p-methoxybenzyloxycarbonyl/p-methoxybenzyl), alloc/allyl (allyloxycarbonyl/allyl), or NBoc/NB (o-nitrobenzyloxycarbonyl/o-nitrobenzyl) as similar patterns. (see fig. D-2)

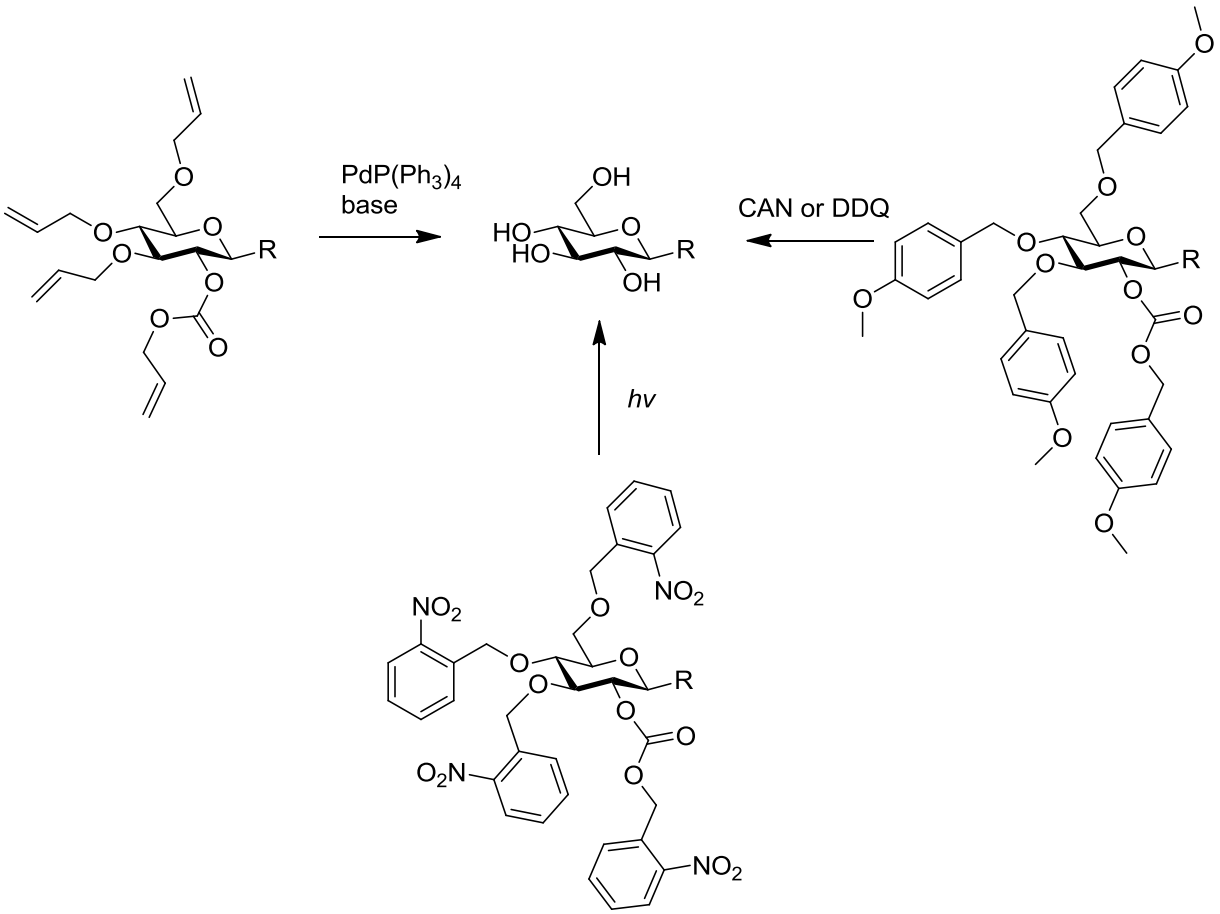


fig. D-2: other alkyloxycarbonyl protective group patterns

D.2.3) Further glycosylations & deprotections

A broader range of acceptor molecules with different protective group patterns or functionalities have to be tested with the novel glycosyl donors to determine the possible operating range. Furthermore, the final deprotection step of BnPAc has to be optimized to increase the yields. Deprotection of **(XXIV)** has to be done as a proof of concept to show, that the acetyl moieties are not affected.

D.2.4) Protective switch – change in reactivity?

Very interesting is the idea of switching the protective group pattern of the BnPAc-protected glycosyl donors after the catalytic hydrogenation step. Instead of cleaving the 2-(2-hydroxyphenyl)acetyl spacer by base induced intramolecular ring formation, another protective group could be attached to the spacer and the glycoside's hydroxyl functions to switch the protective group pattern. For example, TBDMS could be introduced, leading to conformationally superarmed donors, which may notable increase the reactivity (see fig. D-3). Moreover, switching the pattern could be of interest for synthesis of oligosaccharides.

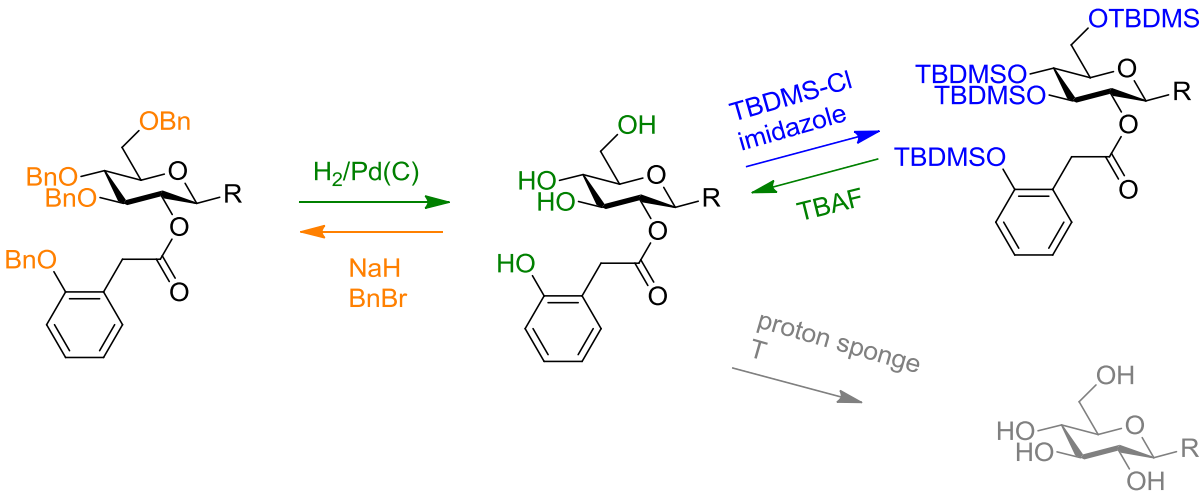


fig. D-3: "protective switch"

E) Experimental Part

E.1) General remarks

All reagents (if not noted otherwise) were purchased from commercial suppliers and used without any further purification. Dry DMF (Acros) and dry EtOH (Merck) were stored over molecular sieves (4Å). The solvents toluene, MeOH, DCM, diethylether and THF were dried using a *PURESOLVE*-system by *it - innovative technologie inc.* Microwave reactions were carried out in a *Biotage® Initiator Microwave Synthesizer.*

E.2) Chromatographic methods

E.2.1) TLC

TLC was realized on TLC-aluminum foil (*Merck*, Kieselgel 60 F254).

E.2.2) Column chromatography

Purification by column chromatography was done on a *Büchi Sepacore™ Flash System (see photo E-1)* consisting of the following modules:

- pump-system: 2 x *Büchi* pump module C-605
- *Büchi* pump manager C-615
- detector: *Büchi* UV photometer C-635
- fraction collector: *Büchi* fraction collector C-660

The polypropylene/glass- cartridges were packed with silica 60 (Si-OH, Merck, 40-63 µm).
Redistilled solvents were used as mobile phase. The exact composition of the eluents is noted at the particular synthesis in this chapter.

photo E-1: Büchi Sepacore Flash system

E.2.3) LC/MS

LC/MS measurements were realized on a HPLC system (photo E-2) from *Agilent Technologies* consisting of the following modules:

- *Agilent* 1200 Series G1367B HiP ALS Autosampler
- *Agilent* 1100 Series G1311A Quat Pump
- *Agilent* 1100 Series G1379A Degasser
- *Agilent* 1200 Series G1316B TCCSL
- Luna RP-C18 column (3.0 x 150 mm, 3 µm particle size, *Phenomenex*)

Detection was done with *Agilent* 1260 Infinity G1315D DAD and Esquire HCT Ion Trap MS by *Bruker*

photo E-2: Agilent HPLC system

E.2.4) TLC/MS

TLC/MS samples were measured with a TLC/ESI-MS-interface by „*Camag*“ that was attached to the HPLC-system (photo E-3)

photo E-3: TLC/MS-Interface

E.3) Physical methods

E.3.1) HR-MS

HR-MS samples were measured on a MALDI LTQ Orbitrap XL (*Thermo Scientific*) done by DI Dr. techn. Mikula.

E.3.2) NMR

NMR-samples were measured on Bruker DPX-200, Avance DRX-400 or Avance 600 Mhz spectrometers (*Bruker*). *TOPSPIN 1.3* (*Bruker Biospin*) was used for Data recording and evaluation (besides *ACD/Labs 12.01*). All chemical shifts are given in ppm referred to TMS. The NMR-spectra were calibrated by solvent signals.[34]
The multiplicities were indicated as:

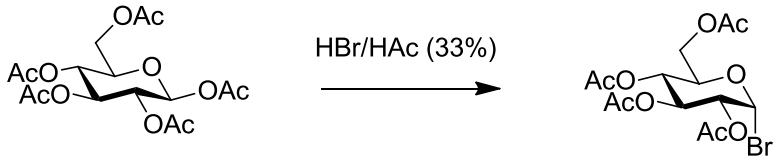
- s = singulett
- d = dublett
- t = triplett
- q = quartett
- m = multiplett
- bs = broad signal

photo E-4: Avance DRX-400 spectrometer

E.4) Synthesis and characterization of the compounds

E.4.1) Orthoester Strategy

Synthesis of 2,3,4,6-Tetra-O-acetyl-1-deoxy-1-bromo-glucopyranose (2)



1

$C_{16}H_{22}O_{11}$
390.34

2

$C_{14}H_{19}BrO_9$
411.20

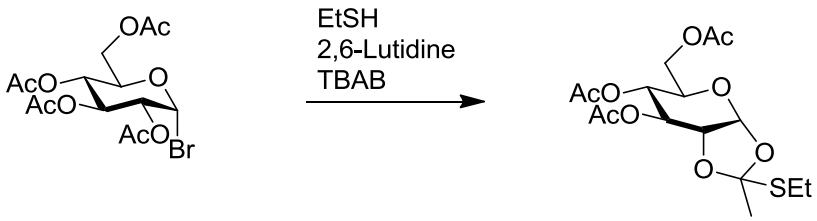
based on [20]

180 ml of HBr in acetic acid (33%) were cooled down to 0°C. Glucose pentaacetate **(1)** (100 g, 256 mmol, 1 eq) was added under stirring. After 2.5 hours TLC showed full conversion and the mixture was quenched with 300 ml iced water. The product precipitated as a white solid, which was dissolved in dichloromethane. The organic phase was washed with water (3x 200 ml), saturated $NaHCO_3$ solution (3x 200 ml) and water again. Afterwards, it was dried, using Na_2SO_4 and concentrated *in vacuo*. For stability reasons, the product was reacted crude without any further purification
93.3 g (88%) of **2** were obtained as yellowish oil.

Analytical data:

R_f : 0.56 (PE/EE = 1/1)

Synthesis of 3,4,6-Tri-O-acetyl-α-D-glucopyranose (R)-1,2-(ethylthioorthoacetate) (3)



2

$C_{14}H_{19}BrO_9$
411.20

3

$C_{16}H_{24}O_9S$
392.42

based on [22]

2 (93.3 g, 226.9 mmol, 1 eq) was dissolved in nitromethane (250 ml). Then ethanethiol (56.4 g, 67.15 ml, 907.6 mmol, 4 eq), TBAB (7.31 g, 22.7 mmol, 0.1 eq) and 2,6-lutidine (36.7 g, 39.7 ml, 340.3 mmol, 1.5 eq) were added to the solution. After 17 hours TLC indicated full consumption of the starting material. The reaction mixture was diluted with ethyl acetate (300 ml) and washed with saturated $NaHCO_3$-solution (200 ml). The aqueous phase was extracted with ethyl acetate two times and the combined organic phases were dried with Na_2SO_4 and concentrated *in vacuo*. The residue was dissolved in ethyl acetate (200 ml) and washed with 1N HCl (2x), water and saturated $NaHCO_3$-solution (2x).
The organic phase was dried with Na_2SO_4 and concentrated *in vacuo* and 84.1 g of **3** were obtained as yellowish oil (95 %)

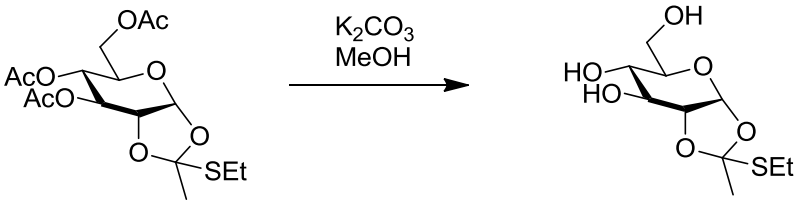
The product was reacted crude without any further purification.

Analytical data:

R_f : 0.51 (PE/EE = 3/2)

m/z $[M+Na]^+$ = 415 (TLC/MS)

Synthesis of α-D-Glucopyranose (R)-1,2-(ethylthioorthoacetate) (4)



3

$C_{16}H_{24}O_9S$
392.42

4

$C_{10}H_{18}O_6S$
266.31

3 (84.1 g, 214.3 mmol, 1 eq) was dissolved in dry methanol (450 ml) under Ar-atmosphere. K_2CO_3 (5.9 g, 42.9 mmol, 0.2 eq) was added and the reaction was stirred for 78 hours at room temperature. TLC showed full conversion of the starting material. The mixture was concentrated *in vacuo* and then treated with toluene (200 ml) to drag out traces of water. After a second concentration step, the residue was dried under high vacuum.

The product was reacted crude without any further purification.

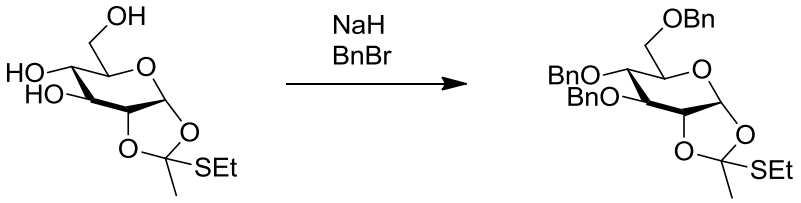
60.55 g of **4** were obtained as yellowish oil (>95 %).

Analytical data:

R_f : 0.03 (PE/EE = 3/2)

m/z $[M+Na]^+$ = 289

Synthesis of 3,4,6-Tri-O-benzyl-α-D-glucopyranose (R)-1,2-(ethylthioorthoacetate) (5)



4

$C_{10}H_{18}O_6S$
266.31

5

$C_{31}H_{36}O_6S$
536.68

4 (60.55 g, 266.31 mmol, 1 eq) was dissolved in dry DMF (800 ml) under Ar-atmosphere and cooled below 0°C. NaH (21.8 g ≙ 36.4 g of 60% in mineral oil, 909 mmol, 4 eq) was washed with dry THF and added to the mixture under Ar-stream. After stirring for 45 minutes, no more hydrogen was formed. Ice cooled benzyl bromide (155.4 g, 107.9 ml, 909 mmol, 4 eq) was added dropwise to the reaction mixture. After the addition was finished, the reaction was allowed to warm up to room temperature and 72 hours later the starting material was converted completely (TLC-control). The reaction mixture was cooled below 0°C again and quenched with methanol and iced water (some $NaHCO_3$ solution was added to adjust the pH value to basic). The aqueous phase was extracted with ethyl acetate three times. The combined organic phases were extracted with brine, dried with Na_2SO_4 and then concentrated *in vacuo*.

The residue was purified using column chromatography (900 g silica; PE/EE = 5/1, 1% TEA) to give a main fraction of 36.15 g **5** (30 %) as a colourless oil.

Analytical data:

R_f : 0.64 (PE/EE = 5/1)

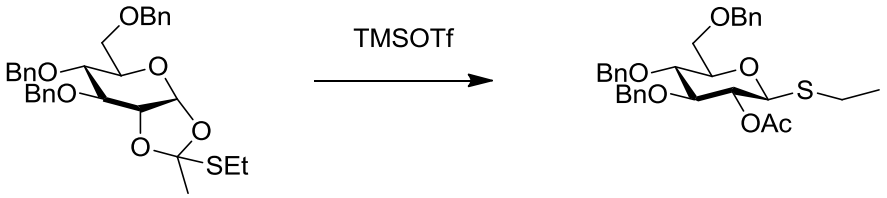
m/z: $[M+Na]^+$ = 559

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.30 – 7.07 (m, 15 H, Ar-H), 5.71 – 5.69 (d, J = 5.5 Hz, 1H), 4.63 – 4.18 (m, 7H), 3.85 – 3.82 (t, 1H), 3.78 – 3.55 (m, 4H), 2.60 – 2.49 (q, 3H), 1.84 (s, 3H), 1.22 – 1.15 (t, 3H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 138.0 (q, 1C), 137.7 (q, 1C), 137.5 (q, 1C), 128.5-127.4 (t, 15C), 115.6 (q, 1C), 98.1 (t, 1C) , 77.3 (t, 1C), 75.0 (t, 1C) , 74.5 (t, 1C), 73.3 (d, 1C), 72.3 (d, 1C), 71.7 (d, 1C) , 70.0 (t, 1C), 69.0 (d, 1C), 27.8 (s, 1C), 24.8 (d, 1C), 15.2 (s, 1C) ppm

E.4.1.2) Orthoester opening and introduction of the leaving groups

Synthesis of Ethyl 2-O-acetyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (6)



5

$C_{31}H_{36}O_6S$
536.68

6

$C_{31}H_{36}O_6S$
536.68

based on [35]

5 (18.075 g, 33.68 mmol, 1 eq) was dissolved in dry dichloromethane (90 ml) under Ar-atmosphere and molecular sieve (3 Å; 4.5 g) was added. After 45 minutes of stirring, the mixture was cooled down to 0°C. Then TMSOTf (374 mg, 304 µl, 1.68 mmol, 0.05 eq) was added and 24 hours later full conversion of **5** was detected via TLC. The reaction was quenched with TEA (5.4 ml), filtrated over celite (to seperate it from the molecular sieve) and washed with NaOH (1%) (3x) and water (3x). Then the organic phase was dried with Na_2SO_4 and concentrated *in vacuo*.
The product was purified by column chromatography (90 g silica; PE/EE = 5/1, 1% TEA) to give 17.3 g **6** (96%) as a reddish oil.

Analytical data:

R_f : 0.50 (PE/EE = 5/1)

m/z $[M+Na]^+$ = 559

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.38 – 7.11 (m, 15H), 5.06 – 4.91 (m, 1H), 4.79 – 4.45 (d, 6H), 4.33 – 4.28 (m, J= 10.0 Hz, 1H), 3.74 – 3.57 (m, 4H), 3.50 – 3.40 (m, 1H), 2.74 – 2.50 (m, 2H), 1.93 (s, 3H), 1.24 – 1.17 (t, J= 7.4 Hz, 3H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 169.3 (s, 1C), 138.0 (s, 1C), 138.0 (s, 1C), 137.8 (s, 1C), 128.2 (d, 1C), 128.15 (d, 1C)' 128.0 (d, 1C), 127.85 (d, 1C), 127.7 (d, 1C), 127.5 (d, 1C), 84.2 (d, 1C), 83.4 (d, 1C), 79.4 (d, 1C), 77.6 (d, 1C), 75.1 (t, 1C), 75.0 (t, 1C), 73.3 (t, 1C), 71.5 (d, 1C), 68.6 (t, 1C), 23.6 (t, 1C), 20.8 (q, 1C), 14.8 (q, 1C) ppm

Synthesis of p-Tolyl 2-O-acetyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (7)

5

$C_{31}H_{36}O_6S$
536.68

7

$C_{36}H_{38}O_6S$
598.75

based on [35]

5 (6.025 g, 11.23 mmol, 1 eq) and 4-methylthiophenol (11.16 g, 89.84 mmol, 8 eq) were dissolved in dry dichloromethane (80 ml) under Ar-atmosphere and molecular sieve (3 Å; 6 g) was added. After 45 minutes of stirring, the mixture was cooled down to 0°C and TMSOTf (624 mg, 507 µl, 2.81 mmol, 0.25 eq) was added. TLC showed full conversion of **5** after 24 h. The reaction was quenched with TEA (1.8 ml), filtrated over celite and washed with NaOH (1%) (3x) and water (3x). Then, the organic phase was dried with Na_2SO_4 and concentrated *in vacuo*.

The product was purified by column chromatography (90 g silica; PE/EE = 5/1, 1% TEA) and recrystallization from toluene (three times) to give 2.76 g **7** (41%) as white solid.

Analytical data:

R_f : 0.62 (PE/EE = 5/1)

m/z $[M+Na]^+$ = 621

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.37 – 7.33 (d, 2 H), 7.27 – 7.11 (m, 15H), 7.00 – 6.96 (d, 2H), 4.97 – 4.69 (m, 3H), 4.65 – 4.43 (m, 5H), 3.77 – 3.41 (m, 5H), 2.24 (s, 3H), 1.94 (s, 3H) ppm

13C-NMR (50 MHz, $CDCl_3$): δ = 169.5 (s, 1C), 138.3 (s, 1C), 138.1 (s, 2C), 137.9 (s, 1C), 133.2 (d, 2C), 129.6 (d, 2C), 128.5 (d, 4C), 128.4 (d, 2C), 128.0 (d, 2C), 127.9 (d, 3C), 127.8 (d, 1C), 127.7 (d, 2C), 127.6 (d, 1C), 86.1 (d, 1C), 84.4 (d, 1C), 84.2 (d, 1C), 79.4 (d, 1C), 77.8 (d, 1C), 75.3 (t, 1C), 75.1 (t, 1C), 73.5 (t, 1C), 71.8 (d, 1C), 68.9 (t, 1C), 21.1 (q, 1C), 21.0 (q, 1C) ppm

Synthesis of 1,3-Thiazolin-2-yl 2-O-acetyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (8)

5

$C_{31}H_{36}O_6S$
536.68

8

$C_{32}H_{35}NO_6S_2$
593.75

based on [35]

5 (6.025 g, 11.23 mmol, 1 eq) and 2-mercaptothiazoline (10.71 g, 89.84 mmol, 8 eq) were dissolved in dry dichloromethane (80 ml) under Ar-atmosphere and molecular sieve (3 Å; 6 g) was added. After 45 minutes of stirring, the mixture was cooled down to 0°C. Then, TMSOTf (624 mg, 507 µl, 2.81 mmol, 0.25 eq) was added and TLC showed full conversion of **5** after 24 h. The reaction was quenched with TEA (1.8 ml), filtrated over celite and washed with NaOH (1%) (3x) and water (3x). Then, the organic phase was dried with Na_2SO_4 and concentrated *in vacuo*.

The product was purified by column chromatography (90 g silica; PE/EE = 3/2, 1% TEA) to give 2.2 g **8** (33%) as white solid.

Analytical data:

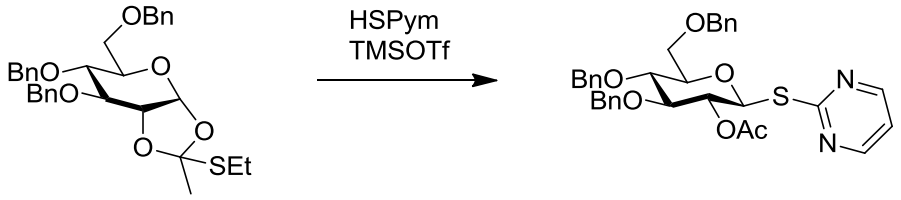
R_f : 0.39 (PE/EE = 3/2)

m/z $[M+Na]^+$ = 616

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.40 – 7.12 (m, 15 H), 5.32 – 5.27 (d, J = 10.5 Hz, 1H), 5.15 – 5.05 (t, 1H), 4.82 – 4.47 (m, 7H), 4.25 – 4.04 (m, 2H), 3.80 – 3.55 (m, 4H), 3.35 – 3.27 (t, 2H), 1.93 (s, 3H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 169.5 (s, 1C) , 163.5 (s, 1C), 138.0 (s, 2C), 137.8 (s, 1C), 128.4-127.5 (d, 15C), 84.2 (d, 1C) , 83.2 (d, 1C), 79.6 (d, 1C) , 77.5 (d, 1C), 75.2 (t, 1C) , 75.0 (t, 1C), 73.3 (t, 1C) , 71.3 (d, 1C), 68.3 (t, 1C) , 64.1 (t, 1C), 35.0 (t, 1C) , 20.8 (q, 1C) ppm

Synthesis of 2-Pyrimidyl 2-O-acetyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (I)



5

$C_{31}H_{36}O_6S$
536.68

I

$C_{33}H_{34}N_2O_6S$
586.70

based on [35]

(5) (6.025 g, 11.23 mmol, 1 eq) and 2-mercaptopyrimidine (10.07 g, 89.81 mmol, 8 eq) were dissolved in dry dichloromethane (80 ml) under Ar-atmosphere and molecular sieve (3 Å; 6 g) was added. After 45 minutes of stirring, the mixture was cooled down to 0°C and TMSOTf (624 mg, 507 µl, 2.81 mmol, 0.25 eq) was added. TLC showed full conversion of **5** after 24 h. The reaction was quenched with TEA (1.8 ml), filtrated over celite and washed with NaOH (1%) (3x) and water (3x). Then, the organic phase was dried with Na_2SO_4 and concentrated *in vacuo*.
The product was purified by column chromatography (90 g silica; PE/EE = 3/2, 1% TEA) to give 3.7 g **I** (56%) yellowish solid.

Analytical data:

R_f : 0.39 (PE/EE = 3/2)

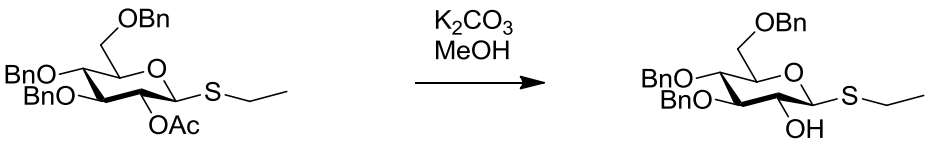
m/z $[M+Na]^+$ = 609 HRMS: 609.2042

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 8.52 – 8.49 (d, 2 H), 7.30 – 7.15 (m, 15 H), 7.01 – 6.96 (t, 1H), 5.69 – 5.64 (d, J = 10.6 Hz, 1H), 5.29 – 5.19 (m, 1H), 4.86 – 4.45 (m, 6H), 3.83 – 3.65 (m, 5H), 1.82 (s, 3H) ppm

^{13}C-NMR (50 MHz, d_6-Aceton): δ = 170.5 (s, 1C) , 170.1 (s, 1C), 158.8 (d, 2C), 139.7 (s, 1C), 139.6 (s, 1C), 139.5 (s, 1C), 129.3-128.2 (d, 15C), 118.8 (d, 1C), 85.3 (d, 1C) , 82.8 (d, 1C), 80.5 (d, 1C) , 80.0 (d, 1C), 75.6 (t, 1C) , 75.5 (t, 1C), 73.7 (t, 1C) , 72.00 (d, 1C), 69.8 (t, 1C), 21.0 (q, 1C) ppm

E.4.1.3) Cleavage of the ester protective group

Synthesis of Ethyl 3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (9)



6

$C_{31}H_{36}O_6S$
536.68

9

$C_{29}H_{34}O_5S$
494.64

To a solution of **6** (17.3 g, 32.24 mmol, 1 eq) in dry methanol (100 ml) K_2CO_3 (446 mg, 3.22 mmol, 0.1 eq) was added under Ar-atmosphere. After stirring for 72 hours at room temperature TLC indicated full conversion of the starting material. The organic phase was washed with water (3x) and brine (3x) and dried with Na_2SO_4. The solvent was removed *in vacuo* and the product was obtained without further purification as 14.88 g **9** (94%) of a yellowish, waxy solid.

Analytical data:

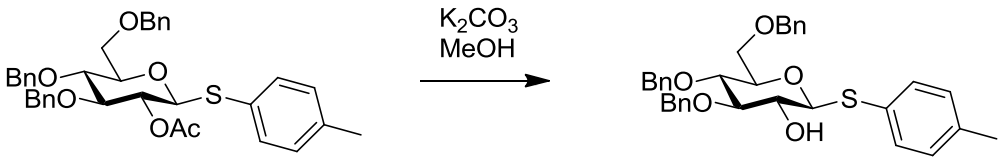
R_f : 0.41 (PE/EE = 4/1)

m/z $[M+Na]^+$ = 517

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.35 – 7.11 (m, 15H), 4.93 – 4.77 (m, 3H), 4.59 – 4.45 (m, 3H), 4.28 – 4.24 (d, J = 9.2 Hz, 1H), 3.75 – 3.42 (m, 6H), 2.75 – 2.63 (q, J = 7.4 Hz, 2H), 1.31 – 1.23 (t, J = 7.4 Hz, 3H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 138.7 (s, 1C), 138.3 (s, 1C), 138.1 (s, 1C), 128.6 (d, 2C), 128.5 (d, 2C), 128.4 (d, 2C), 128.1 (d, 2C), 128.0 (d, 2C), 127.9 (d, 1C), 127.8 (d, 3C), 127.7 (d, 1C), 86.2 (d, 1C), 86.1 (d, 1C), 79.5 (d, 1C), 77.5 (d, 1C), 75.3 (t, 1C), 75.2 (t, 1C), 73.5 (t, 1C), 73,4 (d, 1C), 69.1 (t, 1C), 24.4 (t, 1C), 15.5 (q, 1C) ppm

Synthesis of p-Tolyl 3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (10)



7

$C_{36}H_{38}O_6S$
598.75

10

$C_{34}H_{36}O_5S$
556.71

To a solution of **7** (2.7 g, 4.51 mmol, 1 eq) in dry methanol (25 ml), K_2CO_3 (62 mg, 0.45 mmol, 0.1 eq) was added under Ar-atmosphere. After stirring for 72 hours at room temperature no reaction had taken place, so the amount of K_2CO_3 was increased to 0.3 eq and 10 ml methanol were added. 48 hours later, low amounts of the starting material were converted. 10 ml dry THF were added to increase the solubility and after another 72 hours TLC indicated full conversion. The organic phase was washed with water (3x) and brine (3x) and dried with Na_2SO_4. The solvent was removed *in vacuo* and the product was purified using column chromatography (90 g silica, PE/EE = 5/1-3/1 + 1% TEA) to give 1.4 g **10** (70%) of a white solid.

Analytical data:

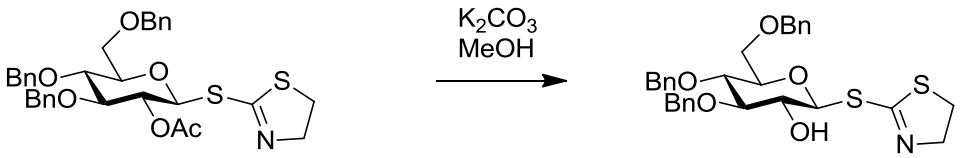
R_f : 0.48 (PE/EE = 5/1)

m/z $[M+Na]^+$ = 579

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.49 – 7.45 (d, J = 8.0 Hz, 2H), 7.37 – 7.18 (m, 15H), 7.08 – 7.04 (d, J = 8.0 Hz, 2H), 4.97 – 4.79 (m, 3H), 4.67 – 4.50 (m, 3H), 4.46 – 4.42 (d, J = 9.4 Hz, 1H), 3.78 – 3.44 (m, 6H), 1.32 (s, 3H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 138.6 (s, 1C), 138.6 (s, 1C), 138.5 (s, 1C), 138.2 (s, 1C), 133.8 (d, 2C), 129.9 (d, 2C), 128.60 (d, 2C), 128.56 (d, 2C), 128.5 (d, 2C), 128.1 (d, 2C), 128.08 (d, 2C), 127.9 (d, 2C), 127.8 (d, 2C), 127.7 (d, 1C), 127.6 (s, 1C), 88.2 (d, 1C), 86.0 (d, 1C), 79.6 (d, 1C), 77.5 (d, 1C), 75.5 (t, 1C), 75.2 (t, 1C), 73.6 (t, 1C), 72.6 (d, 1C), 69.1 (t, 1C), 21.3 (q, 1C) ppm

Synthesis of 1,3-Thiazolin-2-yl 3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (11)



8

$C_{32}H_{35}NO_6S_2$
593.75

11

$C_{30}H_{33}NO_5S_2$
551.72

To a solution of **8** (2.2 g, 3.71 mmol, 1 eq) in dry methanol (20 ml), K_2CO_3 (51 mg, 0.37 mmol, 0.1 eq) was added under Ar-atmosphere. After stirring for 72 hours at room temperature, TLC indicated full conversion of the starting material. The organic phase was washed with water (3x) and BRINE (3x) and dried with Na_2SO_4. The solvent was removed *in vacuo* and the product was purified via column chromatography (90 g silica, PE/EE = 5/1-2/1 + 1% TEA) to give 1.4 g **(11)** (70%) of a white solid.

Analytical data:

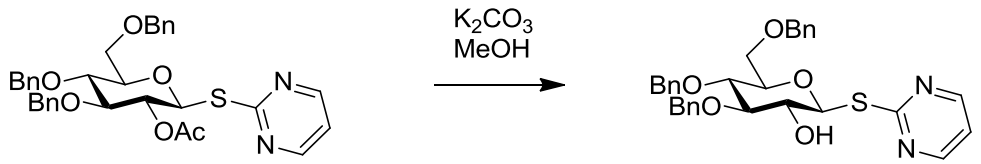
R_f : 0.22 (PE/EE = 3/2)

m/z $[M+Na]^+$ = 574

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.36 – 7.10 (m, 15 H), 5.15 – 5.11 (d, J = 9.2 Hz, 1H), 4.98 – 4.92(d, J = 11.2 Hz, 1H), 4.83 – 4.77 (d, J = 11.4 Hz, 1H), 4.82 – 4.76 (d, J = 11.0 Hz, 1H), 4.61 – 4.44 (m, 3H), 4.16 – 4.08 (t, 2H), 3.75 – 3.51 (m, 6H), 3.31 – 3.23 (t, 2H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 165.4 (s, 1C), 138.5 (s, 1C), 138.0 (s, 1C), 138.0 (s, 1C), 128.5-127.5 (d, 15C), 86.4 (d, 1C) , 85.5 (d, 1C), 79.6 (d, 1C), 75.3 (d, 1C), 74.9 (t, 1C) , 74.3 (t, 1C), 73.3 (d, 1C) , 68.5 (t, 1C), 63.7 (t, 1C) , 35.2 (t, 1C) ppm

Synthesis of 2-Pyrimidyl 3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (VI)



I $C_{33}H_{34}N_2O_6S$ 586.70

VI $C_{31}H_{32}N_2O_5S$ 544.66

To a solution of **I** (3.7 g, 6.31 mmol, 1 eq) in dry methanol (30 ml) K_2CO_3 (87 mg, 0.63 mmol, 0.1 eq) was added under Ar-atmosphere. After stirring for 72 hours at room temperature, TLC indicated full conversion of the starting material. The organic phase was washed with water (3x) and brine (3x) and dried with Na_2SO_4. The solvent was removed *in vacuo* and the product was purified via column chromatography (90 g silica, PE/EE = 4/1-2/1 + 1% TEA) to give 3.08 g **VI** (90%) of a yellowish solid.

Analytical data:

R_f : 0.24 (PE/EE = 3/2)

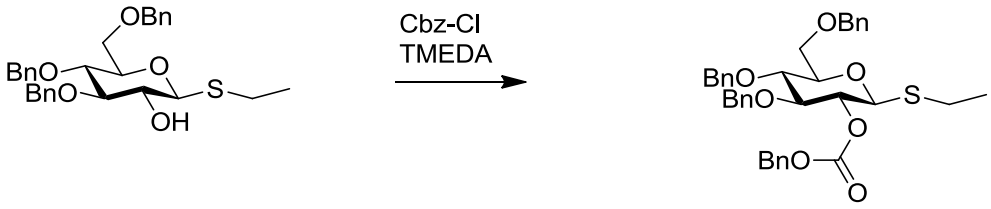
m/z $[M+Na]^+$ = 567 HRMS: 567.1909

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.51 (d, J = 4.9 Hz, 2H), 7.43-7.41 (m, 2H), 7.36-7.26 (m, 11H), 7.24-7.22 (m, 2H), 6.96 (t, J = 5.0 Hz, 1H), 5.65 (d, J = 9.8 Hz, 1H), 5.04 (d, J = 11.4 Hz, 1H), 4.93 (d, J = 11.4 Hz, 1H), 4.90 (d, J = 10.8 Hz, 1H), 4.63 (d, J = 12.2 Hz, 1H), 4.62 (d, J = 10.8 Hz, 1H), 4.53 (d, J = 12.2 Hz, 1H), 3.82-3.72 (m, 6H) ppm

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 170.3 (s, 1C), 157.6 (d, 2C), 138.7 (s, 1C), 138.3 (s, 1C), 138.2 (s, 1C), 128.5 (d, 2C), 128.4 (d, 2C), 128.3 (d, 2C), 128.02 (d, 2C), 127.96 (d, 2C), 127.9 (d, 2C), 127.7 (d, 2C), 127.6 (d, 1C), 117.5 (d, 1C), 86.6 (d, 1C), 84.6 (d, 1C), 79.6 (d, 1C), 77.4 (d, 1C), 75.4 (t, 1C), 75.0 (t, 1C), 73.4 (t, 1C), 73.3 (d, 1C), 68.8 (t, 1C) ppm

E.4.1.4) Introduction of Cbz protective group

Synthesis of Ethyl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (II)



9

$C_{29}H_{34}O_5S$
494.64

II

$C_{37}H_{40}O_7S$
628.77

based on [23]

9 (5 g, 10.11 mmol, 1 eq) was dissolved in dry dichloromethane (100 ml) under Ar-atmosphere. Next, the mixture was cooled down to 0°C. TMEDA (1.175 g, 1.526 ml, 10.11 mmol, 1 eq) and benzyl chloroformate (3.45 g, 2.899 ml, 20.22 mmol, 2 eq) were added. After one week TLC indicated an incomplete conversion, but additional reaction time did not led to any further product. The organic phase was washed with water, dried with Na_2SO_4 and concentrated *in vacuo*. Purification with column chromatography (silica 90 g, PE/EE = 8/1-5/1) gave 2.1 g **II** (58% at 57% conversion of the starting material) white solid.

Analytical data:

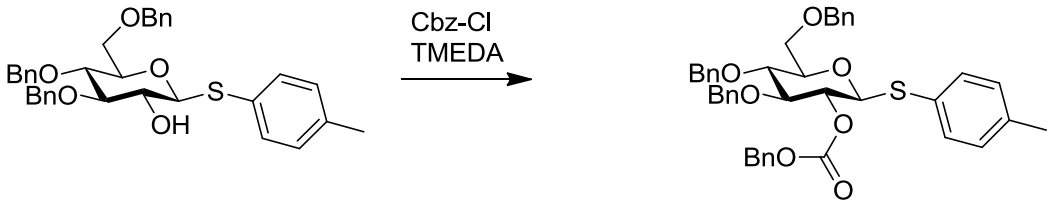
R_f : 0.49 (PE/EE = 4/1)

m/z $[M+Na]^+$ = 651 HRMS: 651.2402

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.30-7.27 (m, 2H), 7.26-7.23 (m, 6H), 7.22-7.17 (m, 8H), 7.15-7.12 (m, 2H), 7.11-7.08 (m, 2H), 4.79-4.75 (m, 1H), 4.72 (d, J = 10.9 Hz, 1H), 4.69 (d, J = 11.0 Hz, 1H), 4.62 (d, J = 11.0 Hz, 1H), 4.53 (d, J = 12.2 Hz, 1H), 4.50 (d, J = 10.9 Hz, 1H), 4.47 (d, J = 12.1 Hz, 1H), 4.34 (d, J = 10.0 Hz, 1H), 3.68 (dd, J = 11.0, 2.1 Hz, 1H), 3.66-3.59 (m, 3H), 3.42 (ddd, J = 9.2, 4.4, 1.8 Hz, 1H), 2.70-2.60 (m, 2H), 1.19 (t, J = 7.5 Hz, 3H) ppm

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 154.4 (s, 1C), 138.2 (s, 1C), 138.0 (s, 1C), 137.9 (s, 1C), 135.1 (s, 1C), 128.6 (d, 1C), 128.6 (d, 1C), 128.4 (d, 3C), 128.37 (d, 3C), 128.3 (d, 2C), 128.0 (d, 2C), 127.9 (d, 2C), 127.8 (d, 2C), 127.7 (d, 2C), 127.7 (d, 1C), 127.6 (d, 1C), 84.3 (d, 1C), 83.4 (d, 1C), 79.5 (d, 1C), 77.7 (d, 1C), 76.3 (d, 1C), 75.4 (t, 1C), 75.1 (t, 1C), 73.5 (t, 1C), 70.0 (t, 1C), 68.8 (t, 1C), 23.8 (t, 1C), 14.9 (q, 1C) ppm

Synthesis of p-Tolyl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (IV)



10

$C_{34}H_{36}O_5S$
556.71

IV

$C_{42}H_{42}O_7S$
690.84

based on [23]

10 (2 g, 3.5925 mmol, 1 eq) was dissolved in dry dichloromethane (50 ml) under Ar-atmosphere. Then, the mixture was cooled down to 0°C. TMEDA (0.545 ml, 3.5925 mmol, 1 eq) and benzyl chloroformate (1.03 ml, 7.185 mmol, 2 eq) were added. After one week, TLC indicated an incomplete conversion, but additional reaction time did not led to any further product. The organic phase was washed with water, dried with Na_2SO_4 and concentrated *in vacuo*. Purification with column chromatography (silica 90 g, PE/EE = 8/1-4/1 + 1% TEA) twice gave 0.51 g **IV** (52% at 40 % consumption of the starting material) white solid.

Analytical data:

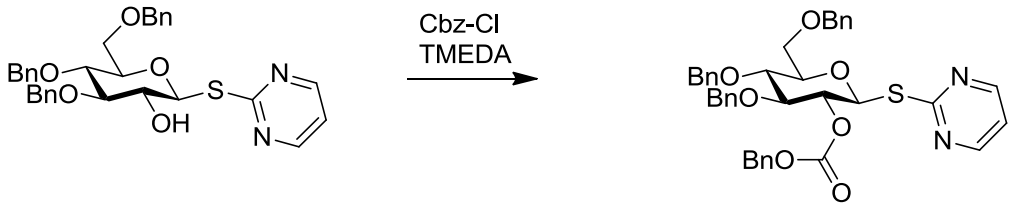
R_f : 0.59 (PE/EE = 5/1)

m/z $[M+Na]^+$ = 713 HRMS: 713.2570

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.37-7.05 (m, 22H), 6.93 (d, J = 6.9 Hz, 1H), 5.16 (d, J = 12.1 Hz, 1H), 5.08 (d, J = 12.1, 1H), 4.78-4.38 (m, 8H), 3.74-3.50 (m, 4H), 3.46-3.35 (m, 1H), 2.21 (s, 3H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 154.2 (s, 1C), 138.2 (s, 1C), 137.9 (s, 1C), 137.8 (s, 1C), 135.1 (s, 1C), 133.5 (d, 2C), 129.6 (d, 2C), 128.60 (d, 2C), 128.58 (d, 1C), 128.44 (d, 2 C), 128.36 (d, 6C), 128.0 (d, 2C), 127.9 (d, 1C), 127.8 (d, 2C), 127.7 (d, 1C), 127.7 (d, 2C), 127.6 (d, 1C), 86.0 (d, 1C), 84.4 (d, 1C), 79.4 (d, 1C), 77.6 (d, 1C), 76.3 (d, 1C), 75.5 (t, 1C), 75.1 (t, 1C), 73.5 (t, 1C), 70.1 (t, 1C), 68.8 (t, 1C), 21.2 (q, 1C) ppm

Synthesis of 2-Pyrimidyl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (VII)



II

$C_{31}H_{32}N_2O_5S$
544.66

VII

$C_{39}H_{38}N_2O_7S$
678.79

based on [23]

II (3 g, 5.507 mmol, 1 eq) was dissolved in dry dichloromethane (100 ml) under Ar-atmosphere. Then, the mixture was cooled down to 0°C. TMEDA (0.640 g, 0.831 ml, 5.507 mmol, 1 eq) and benzyl chloroformate (1.88 g, 1.58 ml, 11.015 mmol, 2 eq) were added. After one week, TLC indicated an incomplete conversion, but additional reaction time did not led to any further product. The organic phase was washed with water, dried with Na_2SO_4 and concentrated *in vacuo*. Purification with column chromatography (silica 90 g, PE/EE = 5/1-4/1) twice gave 1.31 g **VII** (60% at 58% consumption of the starting material) yellowish solid.

Analytical data:

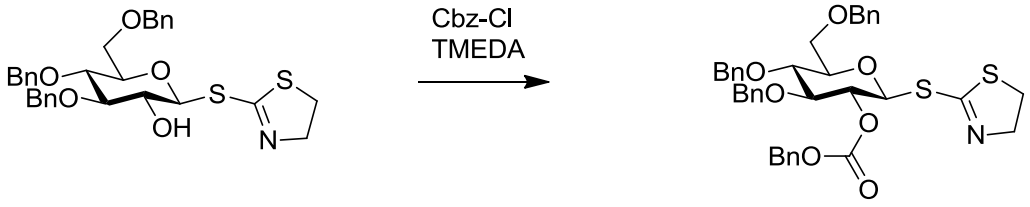
R_f : 0.46 (PE/EE = 3/2)

m/z $[M+Na]^+$ = 701 HRMS: 701.2306

^{1}H-NMR (600 MHz, d_6-Aceton): δ = 8.48 (d, J = 4.8 Hz, 2H), 7.24-7.10 (m, 20H), 7.08 (t, J = 5.4 Hz, 1H), 5.70 (d, J = 10.7 Hz, 1H), 5.08 (d, J = 12.2 Hz, 1H), 5.04 (d, J = 12.2 Hz, 1H), 4.81 (dd, J = 10.3, 9.3 Hz, 1H), 4.72 (d, J = 10.7 Hz, 1H), 4.70 (d, J = 11.0 Hz, 1H), 4.59 (d, J = 10.9 Hz, 1H), 4.54 (d, J = 11.1 Hz, 1H), 4.42 (d, J = 11.9 Hz, 1H), 4.36 (d, J = 12.1 Hz, 1H), 3.84 (t, J = 8.3 Hz, 1H), 3.66-3.56 (m, 4H) ppm

^{13}C-NMR (150 MHz, d_6-Aceton): δ = 169.4 (s, 1C), 157.9 (d, 2C), 154.5 (s, 1C), 138.6 (d, 1C), 138.5 (d, 1C), 138.4 (d, 1C), 135.6 (d, 1C), 128.5 (d, 2C), 128.3 (d, 1C), 128.2 (d, 4C), 128.15 (d, 2C), 128.1 (d, 2C), 127.9 (d, 2C), 127.7 (d, 2C), 127.6 (d, 2C), 127.54 (d, 1C), 127.49 (d, 1C), 127.3 (d, 1C), 118.0 (d, 1C), 84.2 (d, 1C), 81.6 (d, 1C), 79.5 (d, 1C), 77.8 (d, 1C), 75.6 (d, 1C), 75.0 (t, 1C), 74.6 (t, 1C), 72.7 (t, 1C), 69.6 (t, 1C), 68.8 (t, 1C) ppm

Synthesis of 1,3-Thiazolin-2-yl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (IX)



11

$C_{30}H_{33}NO_5S_2$
551.72

IX

$C_{38}H_{39}NO_7S_2$
685.85

based on [23]

11 (1.21 g, 2.193 mmol, 1 eq) was dissolved in dry dichloromethane (50 ml) under Ar-atmosphere. Next, the mixture was cooled down to 0°C. TMEDA (331 µl, 2.193 mmol, 1 eq) and benzyl chloroformate (748 mg, 629 µl, 4.316 mmol, 2 eq) were added. After one week, TLC indicated an incomplete conversion, but additional reaction time did not led to any further product. The organic phase was washed with water, dried with Na_2SO_4 and concentrated *in vacuo*. Purification with column chromatography (silica 90 g, PE/EE = 5/1-4/1) gave 400 m g **IX** (54% at 50% consumption of the starting material) white solid.

Analytical data:

R_f : 0.46 (PE/EE = 3/2)

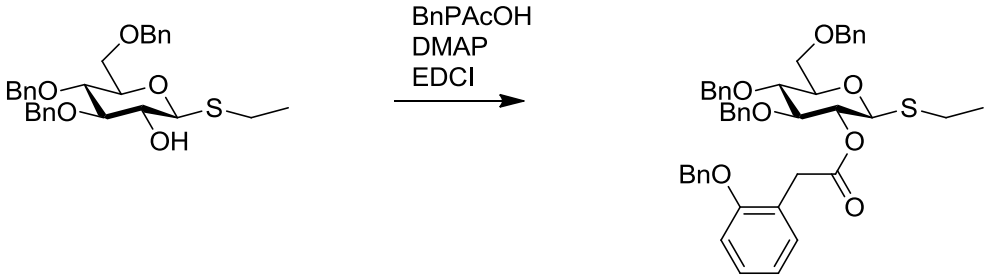
m/z $[M+Na]^+$ = 708

^{1}H-NMR (400 MHz, d_6-Aceton): δ = 7.43-7.23 (m, 20H), 5.56 (d, J = 10.6 Hz, 1H), 5.23 (s, 2H), 4.90-4.80 (m, 3H), 4.72 (d, J = 11.3 Hz, 1H), 4.68 (d, J = 10.6 Hz, 1H), 4.62 (d, J = 11.8 Hz, 1H), 4.56 (d, J = 11.8 Hz, 1H), 4.24-4.12 (m, 2H), 3.94 (t, J = 8.9 Hz, 1H), 3.84-3.68 (m, 4H), 3.44 (t, J = 8.2 Hz, 2H) ppm

^{13}C-NMR (100 MHz, d_6-Aceton): δ = 161.5 (s, 1C), 154.4 (s, 1C), 138.6 (s, 1C), 138.5 (s, 1C), 138.4 (s, 1C), 135.6 (s, 1C), 128.5 (d, 2C), 128.4 (d, 1C), 128.2 (d, 6C), 128.1 (d, 2C), 127.9 (d, 2C), 127.7 (d, 4C), 127.6 (d, 1C), 127.5 (d, 1C), 127.4 (d, 1C) ppm

E.4.1.5) Introduction of BnPAc protective group

Synthesis of Ethyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-1-thio-β,D-glucoside (III)



9

$C_{29}H_{34}O_5S$
494.64

III

$C_{44}H_{46}O_7S$
718.90

based on [24]

9 (4 g, 7.8 mmol, 1 eq) was dissolved in dry dichloromethane (100 ml) under Ar-atmosphere. Then the mixture was cooled down to 0°C. BnPAcOH (2.85 g, 11.75 mmol, 1.5 eq) and DMAP (0.192 g, 1.57 mmol, 0.2 eq) were added, followed by EDCI (3.76 g, 19.59 mmol, 2.5 eq) after a few minutes of stirring. Two days later TLC indicated full consumption of the starting material. The mixture was diluted with dichloromethane and washed with 0.05 M HCl, saturated $NaHCO_3$-solution and brine. The organic phase was dried with Na_2SO_4, concentrated *in vacuo* and purified, using column chromatography (silica 90 g, PE/EE = 6/1-4/1) to obtain 5.17 g **III** (88%) as a white solid.
Analytical data:

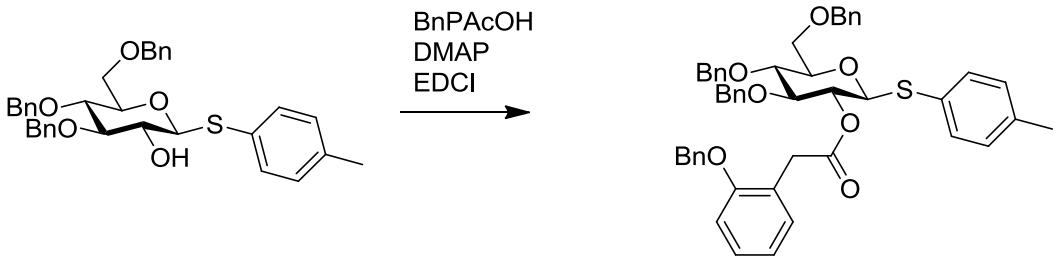
R_f : 0.53 (PE/EE = 4/1)

m/z $[M+Na]^+ = 741$

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.36 – 7.06 (m, 22H), 6.85 – 6.77 (m, 2H), 5.09 – 5.00 (dd, J = 9.8 Hz, 1H), 4.94 (s, 2H), 4.72 – 4.67 (d, J = 10.8 Hz, 1H), 4.59 – 4.42 (m, 5H), 4.29 – 4.24 (d, J = 10.0 Hz, 1H), 3.72 – 3.41 (m, 7H), 2.67 – 2.54 (m, 2H), 1.19 – 1.11 (t, 3H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 170.1 (s, 1C), 156.4 (s, 1C), 138.1 (s, 1C), 138.1 (s, 1C), 137.9 (s, 1C), 137.1 (s, 1C), 131.2 (d, 1C), 128.4-126.9 (d, 21C), 122.7 (s, 1C), 120.7 (d, 1C), 111.8 (d, 1C), 86.2 (d, 1C) , 83.4 (d, 1C), 79.4 (d, 1C), 77.6 (d, 1C), 75.0 (t, 1C) , 74.8 (t, 1C), 73.4 (t, 1C), 72.1 (d, 1C), 69.8 (t, 1C), 63.8 (t, 1C), 35.6 (t, 1C), 23.6 (t, 1C), 14.8 (q, 1C) ppm

Synthesis of p-Tolyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-1-thio-β,D-glucoside (V)



10

$C_{34}H_{36}O_5S$
556.71

V

$C_{49}H_{48}O_7S$
780.97

based on [24]

10 (500 mg, 0.898 mmol, 1 eq) was dissolved in dry dichloromethane (20 ml) under Ar-atmosphere. Then, the mixture was cooled down to 0°C. BnPAcOH (326 mg, 1.347 mmol, 1.5 eq) and DMAP (24 mg, 0.198 mmol, 0.2 eq) were added, followed by EDCI (430 mg, 2.245 mmol, 2.5 eq) after a few minutes of stirring. Two days later, TLC indicated full consumption of the starting material. The mixture was diluted with dichloromethane and washed with 0.05 M HCl, saturated $NaHCO_3$-solution and brine. The organic phase was dried with Na_2SO_4, concentrated *in vacuo* and purified, using column chromatography (silica 90 g, PE/EE = 6/1-4/1) to obtain 569 mg **V** (81%) as a white solid.

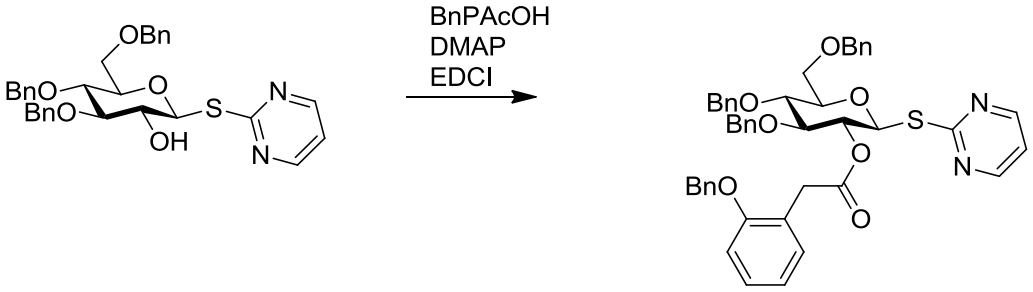
Analytical data:

R_f : 0.64 (PE/EE = 4/1)

m/z $[M+Na]^+$ = 803

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.42 – 7.13 (m, 24H), 7.01 – 6.84 (m, 4H), 5.09 – 4.98 (m, 3H), 4.75 – 4.70 (d, J = 11.0 Hz, 1H), 4.62 – 4.46 (m, 6H), 3.81 – 3.44 (m, 7H), 2.29 (s, 3H) ppm

Synthesis of 2-Pyrimidyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-1-thio-β,D-glucoside (VIII)



II

$C_{31}H_{32}N_2O_5S$
544.66

VIII

$C_{46}H_{44}N_2O_7S$
768.92

based on [24]

II (1 g, 1.89 mmol, 1 eq) was dissolved in dry dichloromethane (50 ml) under Ar-atmosphere. Then the mixture was cooled down to 0°C. BnPAcOH (688 mg, 2.84 mmol, 1.5 eq) and DMAP (46 mg, 0.38 mmol, 0.2 eq) were added, followed by EDCI (905 mg, 4.72 mmol, 2.5 eq) after a few minutes of stirring. Two days later, TLC indicated full consumption of the starting material. The mixture was diluted with dichloromethane and washed with 0.05 M HCl, saturated $NaHCO_3$-solution and brine. The organic phase was dried with Na_2SO_4, concentrated *in vacuo* and purified, using column chromatography (silica 90 g, PE/EE = 6/1-4/1) to obtain 900 mg **VIII** (62%) as a colourless solid.

Analytical data:

R_f : 0.49 (PE/EE = 4/1)

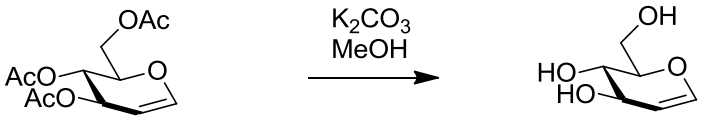
m/z $[M+Na]^+$ = 791

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 8.48 – 8.46 (d, 2H), 7.33 – 7.13 (m, 21H), 7.09 – 7.05 (d, 1H), 6.99 – 6.94 (t, 1H), 6.80 – 6.72 (t, 2H), 5.70 – 5.64 (d, J= 10.6 Hz, 1H), 5.36 – 5.26 (dd, J= 10.4 Hz, 1H), 4.95 (s, 2H), 4.79 – 4.44 (m, 6H), 3.79 – 3.64 (m, 7H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 170.2 (s, 1C), 170.1 (s, 1C), 157.3 (d, 2C), 156.4 (s, 1C), 138.2 (s, 1C), 138.1 (s, 1C), 138.0 (s, 1C), 137.1 (s, 1C), 131.1 (d, 1C), 128.4-126.8 (d, 21C), 122.6 (s, 1C), 120.6 (d, 1C), 117.1 (d, 1C), 111.7 (d, 1C), 84.5 (d, 1C) , 82.1 (d, 1C), 79.6 (d, 1C), 77.6 (d, 1C), 74.9 (t, 1C) , 74.9 (t, 1C), 73.3 (t, 1C), 71.5 (d, 1C), 69.8 (t, 1C), 68.6 (t, 1C), 35.7 (t, 1C) ppm

E.4.2) Glucal strategy

Synthesis of D-glucal (13)



12

$C_{12}H_{16}O_7$
272.25

13

$C_6H_{10}O_4$
146.14

12 (14.005 g, 51.74 mmol, 1 eq) was dissolved in dry methanol (100 ml) under Ar-atmosphere. K_2CO_3 (1.072 g, 7.76 mmol, 0.15 eq) was added and the reaction was stirred for 72 hours at room temperature. TLC showed full conversion of the starting material. The mixture was concentrated *in vacuo* and then treated with toluene (100 ml) to drag out water. After a second concentration step using a rotary evaporator, the residue was dried under high vacuum.
The crude product was reacted without any further purification.

Analytical data:

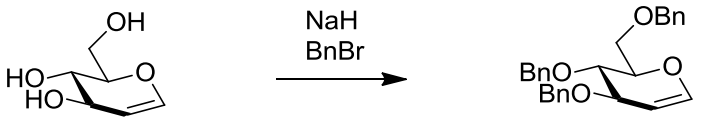
R_f : 0.06 (PE/EE = 1/1)

m/z $[M+Na]^+$ = not measured

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 6.26 (dd, J = 6.0, 1.6 Hz, 1H), 4.60 (dd, J = 6.0, 2.2 Hz, 1H), 4.04 (dt, J = 7.0, 1.9 Hz, 1H), 3.85-3.58 (m, 3H), 3.48 (dd, J = 9.5, 7.0 Hz, 1H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 146.5 (d, 1C), 106.1 (d, 1C), 81.9 (d, 1C), 72.5 (d, 1C), 72.1 (d, 1C), 63.8 (t, 1C) ppm

Synthesis of 3,4,6-Tri-O-benzyl-D-glucal (14)



13

$C_6H_{10}O_4$
146.14

14

$C_{27}H_{28}O_4$
416.51

A solution of **13** (9.48 g, 65 mmol, 1 eq) in dry DMF (150 ml) was cooled down to 0°C under Ar-atmosphere. NaH (6.24 g ≙ 10.4 g of 60% in mineral oil, 260 mmol, 4 eq) was washed with dry THF and added to the mixtur. After stirring for one hour, no more hydrogen was formed. Ice cooled benzyl bromide (44.45 g, 31 ml, 260 mmol, 4 eq) was added dropwise to the reaction mixture. After the addition had been finished, the reaction stirred for 20 hours. TLC-control showed full conversion of the starting material. The reaction mixture was cooled below 0°C again and quenched with methanol (50 ml). In the next step, it was poured on iced water (300 ml). The aqueous phase was extracted with ethyl acetate three times. The blended organic phases were washed with brine, dried with Na_2SO_4 and then concentrated *in vacuo*.
The residue was purified using column chromatography (900 g silica; PE/EE = 6/1) to give a main fraction of 11.27 g **14** (41.5 %) as a colourless oil.

Analytical data:

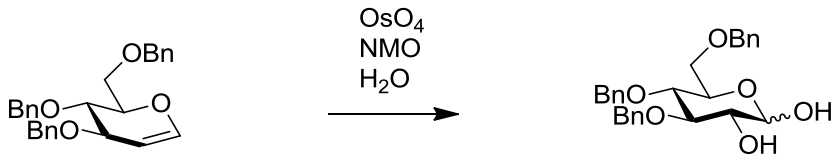
R_f : 0.52 (PE/EE = 5/1)

m/z $[M+Na]^+$ = 439

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.37 – 7.01 (m, 14H), 6.39 - 6.36 (d, J= 6.3 Hz, 1H), 4.85 – 4.76 (m, 2H), 4.62 – 4.47 (m, 5H), 4.21 – 4.14 (m, 1H), 4.06 – 3.98 (m, 1H), 3.85 – 3.68 (m, 3H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 144.8 (d, 1C), 138.4 (s, 1C), 138.2 (s, 1C), 138.1 (s, 1C), 128.5 (d, 6C), 128.0 (d, 2C), 127.8 (d, 2C), 127.7 (d, 3C), 127.7 (d, 2C), 100.0 (d, 1C), 76.8 (d, 1C), 75.8 (d, 1C), 74.5 (d, 1C), 73.8 (t, 1C), 73.6 (t, 1C), 70.5 (t, 1C), 68.6 (t, 1C) ppm

Synthesis of 3,4,6-Tri-O-benzyl-D-glucoside (15)



14

$C_{27}H_{28}O_4$
416.51

15

$C_{27}H_{30}O_6$
450.52

based on [27]

14 (11.27 g, 2.706 mmol, 1 eq) in (100 ml THF/t-BuOH/H_2O = 7/3/1) and NMO (9.51 g, 8.117 mmol, 3 eq) were stirred, until everything was dissolved. Then, OsO_4 (3 ml of 2.5% solution in THF/t-BuOH/H_2O = 7/3/1, 0.13528 mmol, 0.01 eq) was added and the reaction was stirred under Ar-atmosphere for 24 hours. After diluting the mixture with water, saturated $Na_2S_2O_3$-solution was added to destroy remaining OsO_4 and stirring continued for another 24 hours. The aqueous phase was extracted with ethyl acetate three times and the collected organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified using column chromatography (90 g silica; PE/EE = 2/1-0/1) to give 11.06 g **15** (41.5 %) as a white waxy solid (anomeric mixture).

Analytical data:

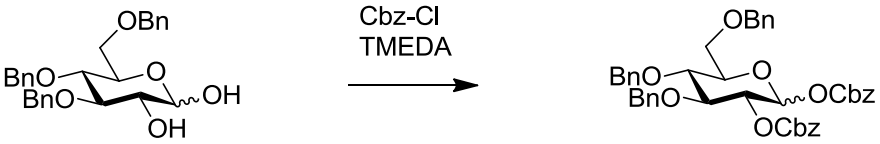
R_f : 0.03 (PE/EE = 3/1)

m/z $[M+Na]^+$ = 473

1H-NMR (200 MHz, $CDCl_3$): δ = 7.38 - 7.15 (m, 15H), 5.31 – 5.29 (d, J = 3.7 Hz, 0.6 $H_{1\alpha}$), 4.88 – 4.79 (m, 3H), 4.66 – 4.62 (d, J = 6.9 Hz, 0.4 $H_{1\beta}$), 4.59 – 4.48 (m, 3H), 4.08 – 4.00 (m, 1H), 3.82 – 3.48 (m, 6H) ppm

E.4.2.2) Introduction of participating protecting groups

Synthesis of 3,4,6-Tri-O-benzyl-1,2-bis(benzyloxycarbonyl)-D-glucoside (X)



15

$C_{27}H_{30}O_6$
450.52

X

$C_{43}H_{42}O_{10}$
718.79

based on [23]

15 (5.8 g, 12.87 mmol, 1 eq) was dissolved in dry dichloromethane (100 ml) under Ar-atmosphere. In the next step, the mixture was cooled down to 0°C. TMEDA (3 g, 3.9 ml, 25.75 mmol, 2 eq) and benzyl chloroformate (8.785 g, 7.383 ml, 51.5 mmol, 4 eq) were added. After 72 hours TLC indicated full conversion of the starting material. The organic phase was washed with water, extracted with dichloromethane, dried over Na_2SO_4 and concentrated *in vacuo*. Purification with column chromatography (silica 90 g, PE/EE = 4/1) gave 6.5 g **X** (73%) colorless oil. (α/β = 1/1)

Analytical data:

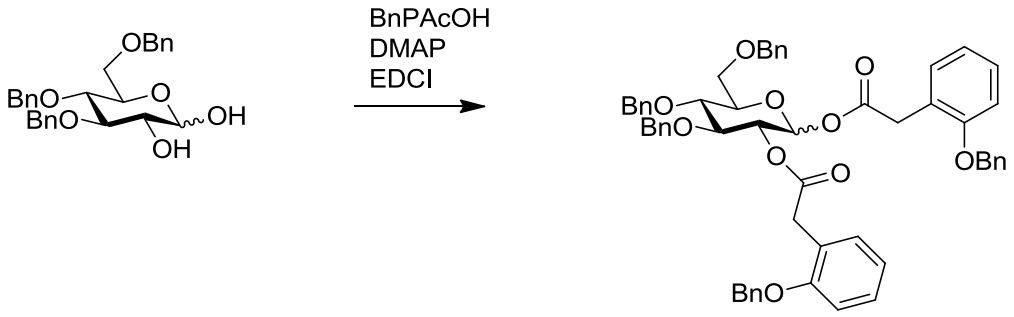
R_f : 0.61 (PE/EE = 3/1)

m/z $[M+Na]^+ = 741$

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.36 - 7.12 (m, 25H), 6.30 – 6.28 (d, J = 3.7 Hz, 0.5 $H_{1\alpha}$), 5.54 – 5.50 (d, J = 8.2 Hz, 0.5 $H_{1\beta}$), 5.17 – 4.45 (m, 11H), 4.10 – 3.59 (m, 5H) ppm

^{13}C-NMR (50 MHz, d_6-Acetone): δ = 155.3 (s, 1C), 155.2 (s, 1C), 154.4 (s, 1C), 139.5 (s, 1C), 139.4 (s, 1C), 139.3 (s, 1C), 136.5 (s, 1C), 136.5 (s, 1C), 136.3 (s, 1C), 136.2 (s, 1C), 129.5 - 128.4 (d, 25C), 96.3 (d, 1C), 94.3 (d, 1C), 83.2 (d, 1C), 80.6 (d, 1C), 78.4 (d, 1C), 78.0 (d, 1C), 77.3 (d, 1C), 76.7 (d, 1C), 76.5 (d, 1C), 76.1 (t, 1C), 75.8 (t, 1C), 75.7 (t, 1C), 75.5 (t, 1C), 74.4 (d, 1C), 73.9 (t, 1C), 73.8 (t, 1C), 70.8 (t, 1C), 70.7 (t, 1C), 70.7 (t, 1C), 70.6 (t, 1C), 69.3 (t, 1C), 69.2 (t, 1C).

Synthesis of 3,4,6-Tri-O-benzyl-1,2-bis-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside (XI)



15

$C_{27}H_{30}O_6$
450.52

XI

$C_{57}H_{54}O_{10}$
899,03

based on [24]

15 (3 g, 6.65 mmol, 1 eq) was dissolved in dry dichloromethane (100 ml) under Ar-atmosphere. Then, the mixture was cooled down to 0°C. BnPAcOH (4.85 g, 20 mmol, 3 eq) and DMAP (0.325 g, 2.66 mmol, 0.4 eq) were added, followed by EDCI (6.376 g, 33.26 mmol, 5 eq) after a few minutes of stirring. Two days later TLC indicated full consumption of the starting material. The mixture was diluted with dichloromethane and washed with 0.05M HCl, saturated $NaHCO_3$-solution and brine. The organic phase was dried with Na_2SO_4, concentrated *in vacuo* with toluene as a water-carrier and purified twice, using column chromatography (silica 90 g, PE/EE = 6/1-4/1) to obtain 4.85 g **XI** (78%) as a white, waxy solid. (α/β = 3/2)

Analytical data:

R_f : 0.38 (PE/EE = 4/1)

m/z $[M+Na]^+ = 922$

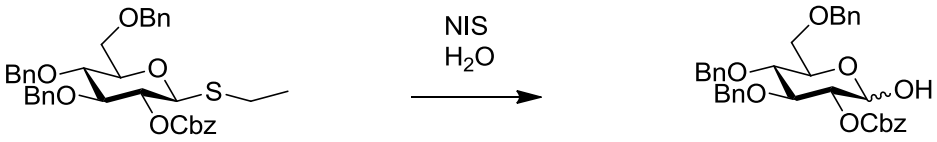
^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.36 - 7.26 (m, 14H), 7.23 - 7.20 (m, 5H), 7.16 – 6.99 (m, 9H), 6.99 – 6.77 (m, 5H), 6.30 – 6.28 (d, J = 3.3 Hz, 0.6 $H_{1α}$), 5.62 – 5.58 (d, J = 8.2 Hz, 0.4 $H_{1β}$), 5.20 – 4.91 (m, 5H), 4.75 – 4.67 (dd, J= 3.7, 11.0 Hz; 1H), 4.58 – 4.36 (m, 5H), 3.77 – 3.39 (m, 9H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 170.4 (s, 1C), 170.1 (s, 1C), 169.8 (s, 1C), 169.6 (s, 1C), 156.5 (s, 1C), 156.5 (s, 1C), 156.3 (s, 1C), 138.4 (s, 1C), 138.1 (s, 1C), 138.0 (s, 1C), 137.9 (s, 1C), 137.1 (s, 1C), 137.0 (s, 1C), 136.9 (s, 1C), 131.1 (d, 1C), 131.0 (d, 1C), 130.9 (d, 1C), 130.8 (d, 1C), 130.9 (d, 1C), 129.0 – 126.9 (d, 25C), 122.8 (s, 1C), 122.8 (s, 1C), 122.6 (s, 1C), 122.5 (s, 1C),

121.0 (d, 1C), 120.8 (d, 1C), 120.8 (d, 1C), 120.7 (d, 1C), 111.9 (d, 1C), 111.8 (d, 2C), 111.8 (d, 1C), 92.4 (d, 1C), 89.9 (d, 1C), 82.6 (d, 1C), 79.7 (d, 1C), 76.8 (d, 1C), 75.7 (d, 1C), 75.0 (t, 1C), 74.9 (t, 1C), 74.6 (t, 1C), 73.4 (t, 1C), 72.9 (d, 1C), 72.3 (d, 1C), 70.1 (t, 1C), 70.0 (t, 1C), 69.9 (t, 1C), 69.9 (t, 1C), 69.8 (t, 1C), 68.1 (t, 1C), 67.8 (t, 1C), 35.8 (t, 1C), 35.7 (t, 1C), 35.4 (t, 1C), 35.3 (t, 1C) ppm

E.4.3) Anomeric modifications: OH-sugar

Synthesis of 3,4,6-Tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside (XII)



II

$C_{37}H_{40}O_7S$
628.77

XII

$C_{35}H_{36}O_8$
584.66

based on [28]

To a solution of **II** (300 mg, 0.477 mmol, 1 eq) in ACN (3.6 ml), water (0.4 ml) and NIS (215 mg ≙ 239 mg 90%, 0,954 mmol, 2 eq) were added, changing the color to black. After stirring for five minutes, TLC indicated full conversion of the starting material. The reaction was quenched with saturated $Na_2S_2O_3$-solution and the mixture turned colorless. In the next step, it was diluted with dichloromethane and washed with $Na_2S_2O_3$-solution (2x) and brine (2x). The organic phase was dried over Na_2SO_4, concentrated *in vacuo* and purified via column chromatography (silica 90 g, PE/EE = 5/1) to obtain 235 mg **XII** (85%) as a white solid (anomeric mixture, NMR indicated more α than β-formation).

Analytical data:

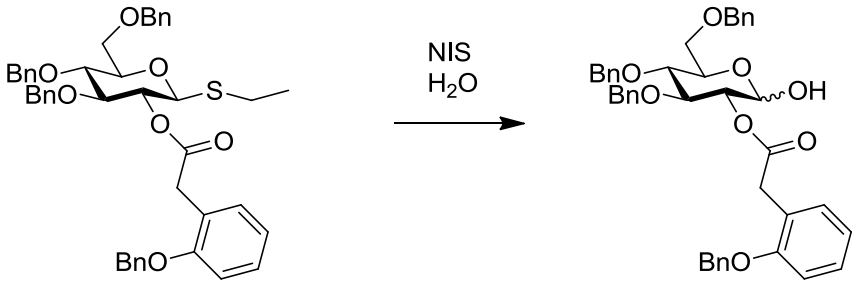
R_f : 0.03 (PE/EE = 4/1)

m/z $[M+Na]^+$ = 607

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.51 – 7.14 (m, 20H), 5.42 – 5.35 (m, 1H), 5.16 – 5.00 (m, 2H), 4.79 – 4.38 (m, 8H), 4.09 – 3.53 (m, 5H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 155.2 (s, 1C), 154.5 (s, 1C), 138.2 (s, 1C), 137.9 (s, 1C), 137.7 (s, 1C), 135.0 (s, 1C), 134.8 (s, 1C), 128.6 – 127.6 (d, 20C), 95.4 (d, 1C$_\beta$), 90.4 (d, 1C$_\alpha$), 82.4 (d, 1C), 79.7 (d, 1C), 79.5 (d, 1C), 77.8 (d, 1C), 77.1 (d, 1C), 75.6 (t, 1C), 75.4 (t, 1C), 75.0 (t, 1C), 75.0 (d, 1C), 73.5 (t, 1C), 73.4 (t, 1C), 70.2 (d, 1C), 70.2 (t, 1C), 69.9 (t, 1C), 68.6 (t, 1C) ppm

Synthesis of 3,4,6-Tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside (XVII)



III

$C_{44}H_{46}O_7S$
718.90

XVII

$C_{42}H_{42}O_8$
674.78

based on [28]

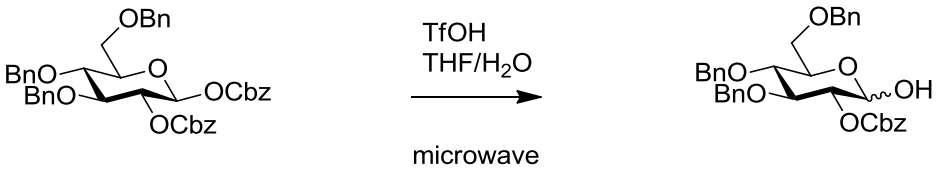
To a solution of **II** (300 mg, 0.417 mmol, 1 eq) in ACN (3.6 ml), water (0.35 ml) and NIS (188 mg, 0,835 mmol, 2 eq) were added, changing the color to black. After stirring for 30 minutes, TLC indicated full conversion of the starting material. The reaction was quenched with saturated $Na_2S_2O_3$-solution and the mixture turned colorless. In the next step, it was diluted with dichloromethane and washed with $Na_2S_2O_3$-solution (2x) and brine (2x). The organic phase was dried over Na_2SO_4, concentrated *in vacuo*. 299.6 mg crude **XVII** were obtained (including impurities of succinimide).

Analytical data:

R_f : 0.52 (PE/EE = 3/2)

m/z $[M+Na]^+ = 697$

Synthesis of 3,4,6-Tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside (XII)



X

$C_{43}H_{42}O_{10}$
718.79

a: 120°C, 15 min + 150°C, 30 min
b: 140°C, 20 min
c: 130°C, 20 min

XII

$C_{35}H_{36}O_8$
584.66

a:

X (500 mg, 0.696mmol, 1 eq) was dissolved in THF (1,8 ml) and H_2O (1 ml) and TfOH (52.2 mg, 30.52 µl, 0.348 mmol, 0.5 eq) was added. Then, the microwave vial was sealed and stirred at 120°C for 15 minutes using microwave radiation. TLC showed, that the desired product was formed, but conversion was incomplete, so the reaction was continued for 30 minutes at 150°C. These conditions turned out to be too vigorous, because not just the starting material, but also the product was consumed, leading to an unwanted side-product only (Due to the higher polarity, multiple protective groups are supposed to be cleaved).

b:

X (100 mg, 0. 139 mmol, 1 eq) was dissolved in THF (1.8 ml) and H_2O (0.2 ml) and TfOH (10 mg, 6.1 µl, 0.070 mmol, 0.5 eq) was added. Then, the microwave vial was sealed and stirred at 140°C for 20 minutes (7 bar), using microwave radiation. Besides the desired product, again, by-product was formed in small amounts (thought to be **15**)).

c:

X (100 mg, 0. 139 mmol, 1 eq) was dissolved in THF (1.8 ml) and H_2O (0.2 ml) and TfOH (10 mg, 6.1 µl, 0.070 mmol, 0.5 eq) was added. Then the microwave vial was sealed and stirred at 130°C for 20 minutes (5 bar), using microwave radiation. TLC showed full conversion of the starting material and comparison with reference material, as well as TLC/MS-measurement confirmed the formation of the desired product **XII**, almost exclusively.

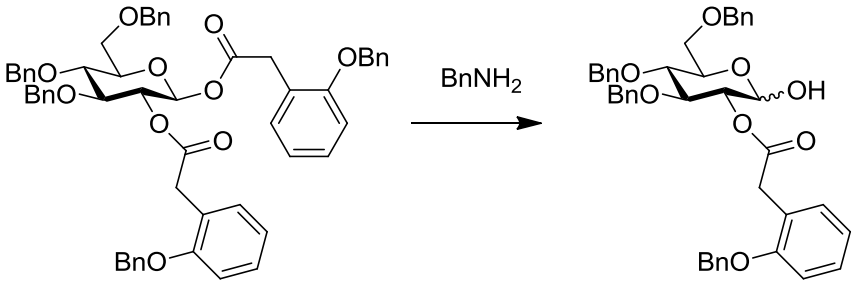
Analytical data:

R_f : 0.03 (PE/EE = 4/1)

^{1}H: see above

^{13}C: see above

Synthesis of 3,4,6-Tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside (XVII)



XI

$C_{57}H_{54}O_{10}$
899.03

XVII

$C_{42}H_{42}O_8$
674.78

based on [29]

To a solution of **XI** (1.5 g, 1.62 mmol, 1 eq) in THF (20 ml), $BnNH_2$ (191 mg, 194 µl, 1.78 mmol, 1.1 eq) was added and the mixture was stirred for two days at room temperature. Another 0.6 eq of $BnNH_2$ were added and 6 days later the reaction had been finished. After concentration *in vacuo*, the residue was diluted with dichloromethane and washed with HCl (1%) and water. The organic phase was dried over Na_2SO_4 and the solvent was removed *in vacuo*. The crude product was purified together with another batch via column chromatography (silica 90 g, PE/EE 9/1-3/1) twice to obtain 985 mg **XVII** (86 %).

Impurities of N-benzyl-2-(2-(benzyloxy)phenyl)acetamide could not be separated from the product due to very similar retentional behavior. Fortunately, it did not affect the following reaction step, where it was easy to divide from the desired product.

Analytical data:

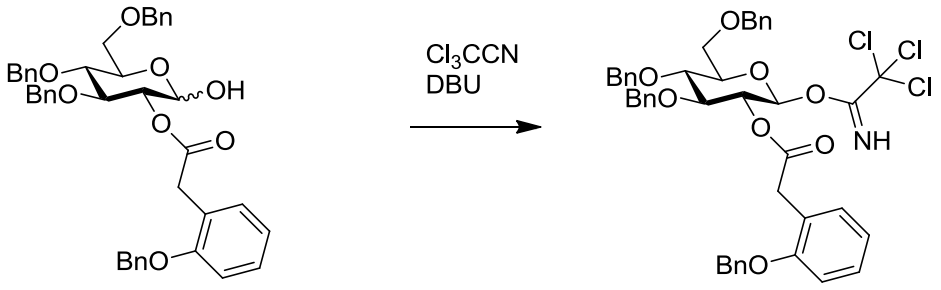
R_f : 0.30 (PE/EE = 4/1)

m/z Product: $[M+Na]^+ = 697$

Side-product: $[M+Na]^+ = 354$

E.4.4) Anomeric modifications: imidates

Synthesis of Trichloracetimidoyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside (XVIII)



XVII

$C_{42}H_{42}O_8$
674.78

XVIII

$C_{44}H_{42}Cl_3NO_8$
819.17

based on [30]

XVII (34 mg, 0.0472 mmol, 1 eq) was dissolved in dry dichloromethane (2.5 ml) under Ar-atmosphere. After bubbling the mixture with an Ar-balloon for 5 minutes, DBU (2.3 mg, 3 µl, 0.015 mmol, 0.3 eq) and trichloroacetonitrile (62.9 mg, 43.7 µl, 0.434 mmol, 9 eq) were added and the reaction stirred for 24 hours at room temperature. TLC indicated complete consumption of the starting material. The mixture was concentrated *in vacuo* and purification was done by column chromatography (silica 90 g, PE/EE = 9/1-3/1). 40 mg **XVIII** were obtained (97%, because the starting material was mixed with an unreactive byproduct of an earlier step)

Analytical data:

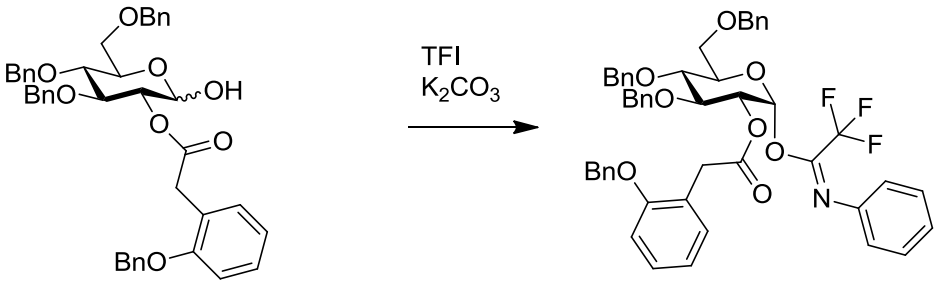
R_f : 0.44 (PE/EE = 4/1)

m/z $[M+Na]^+$ = 842

^{1}H-NMR (200 MHz, CD_2Cl_2): δ = 7.53 – 7.15 (m, 22H), 7.04 – 6.87 (m, 2H), 6.72 – 6.47 (bs, 1H), 6.13 – 5.98 (m, 1H), 5.26 – 4.28 (m, 9H), 4.07 – 3.12 (m, 7H) ppm

^{13}C-NMR (50 MHz, CD_2Cl_2): δ = 171.5 (s, 1C), 171.1 (s, 1C), 168.4 (s, 1C), 139.3 (s, 1C), 138.9 (s, 1C), 138.7 (s, 1C), 137.7 (s, 1C), 131.6 (d, 1C), 129.2 – 127.9 (m, 21C), 123.7 (s, 1C), 121.3 (d, 1C), 112.4 (d, 1C), 90.9 (d, 1C), 80.0 (d, 1C), 78.5 (d, 1C), 76.7 (d, 1C), 75.6 (t, 1C), 75.5 (t, 1C), 75.3 (1C), 74.7 (d, 1C), 73.9 (t, 1C), 70.8 (d, 1C), 70.5 (t, 1C), 69.7 (t, 1C), 36.6 (t, 1C) ppm

Synthesis of N-Phenyltrifluoracetimidoyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside (XXII)



XVII

$C_{42}H_{42}O_8$
674.78

XXII

$C_{50}H_{46}F_3NO_8$
845.90

based on [16], p174-179

XVII (150 mg, 0.218 mmol, 1 eq) and K_2CO_3 (60 mg, 0.436 mmol, 2 eq) were dissolved in dry dichloromethane (3 ml) under Ar-atmosphere. Then, the solution was bubbled with Ar and N-phenyl-trifluoracetimidoyl chloride (90 mg, 0.436 mmol, 2 eq) was added. After stirring at room temperature, TLC indicated full conversion. The mixture was filtrated over celite and reduced *in vacuo*. Purification was done by flash chromatography. 139 mg **XXII** were obtained (74%).

Analytical data:

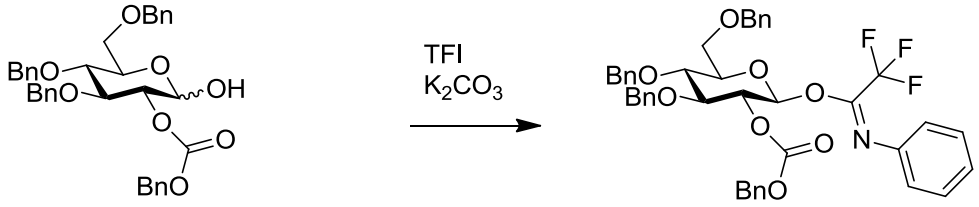
R_f : 0.56 (PE/EE = 4/1)

m/z $[M+Na]^+$ = 867

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.54 – 6.75 (m, 29H), 6.15 – 6.13 (d, J = 3.5 Hz, 0.5$H_{1\alpha}$), 5.24 – 4.81 (m, 3H), 4.75 – 4.33 (m, 6H), 4.19 – 3.88 (m, 1H), 3.71 – 3.39 (m, 6H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 170.9 (s, 1C), 170.1 (s, 1C), 156.5 (s, 1C), 138.5 (s, 1C), 138.1 (s, 1C), 137.8 (s, 1C), 136.8 (s, 1C), 131.0 (d, 1C), 130.9 (d, 1C), 129.4 – 126.3 (d, 23C), 123.0 (s, 1C), 121.1 (d, 1C), 120.4 (d, 2C), 112.0 (d, 1C), 111.8 (d, 1C), 92.3 (d, 1C), 90.3 (d, 1C), 82.6 (d, 1C), 79.6 (d, 1C), 76.8 (d, 1C), 75.3 (t, 1C), 75.1 (t, 1C), 74.9 (1C), 74.3 (d, 1C), 73.5 (t, 1C), 72.8 (d, 1C), 71.1 (d, 1C), 70.1 (t, 1C), 70.0 (t, 1C), 67.8 (t, 1C), 36.3 (t, 1C) ppm

Synthesis of N-Phenyltrifluoracetimidoyl 3,4,6-Tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside (XVI)



XII

$C_{35}H_{36}O_8$
584.66

XVI

$C_{43}H_{40}F_3NO_8$
755.77

based on [16]*, p174-179*

XII (300 mg, 0.513 mmol, 1 eq) and K_2CO_3 (142 mg, 1.026 mmol, 2 eq) were dissolved in dry dichloromethane (5 ml) under Ar-atmosphere. Then, the solution was bubbled with Ar and N-phenyl-trifluoracetimidoyl chloride (213 mg, 1.026 mmol, 2 eq) was added. After stirring overnight at room temperature, TLC indicated full conversion. The mixture was filtrated over celite and reduced *in vacuo*. Purification was done by flash chromatography. 290 mg **XVI** were obtained (**75%**).

Analytical data:

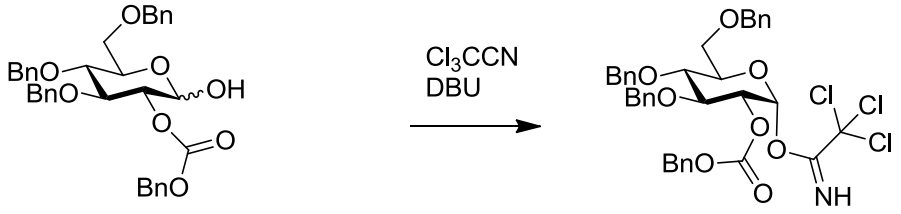
R_f : 0.56 (PE/EE = 4/1)

m/z $[M+Na]^+$ = 778

^{1}H-NMR (200 MHz, CD_2Cl_2): δ = 7.36-7.20 (m, 22H), 7.11-7.07 (t, J = 7.4 Hz, 1H), 6.82-6.79 (d, J = 7.4 Hz, 2H), 5.31-4.49 (m, 10H), 3.86-3.72 (m, 4H) ppm

^{13}C-NMR (50 MHz, CD_2Cl_2): δ = 154.7 (s, 1C), 143.8 (s, 1C), 138.6 (s, 1C), 138.6 (s, 2C), 135.7 (s, 1C), 129.3-128.2 (d, 25C), 125.0 (s, 1C), 119.8 (s, 1C), 95.5 (d, 1C), 82.8 (1C), 77.7 (1C), 77.0 (1C), 76.5 (1C), 75.8 (1C), 75.6 (1C), 73.9 (1C) 70.7 (1C), 68.7 (1C) ppm

Synthesis of Trichloracetimidoyl 3,4,6-Tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside (XV)



XII
$C_{35}H_{36}O_8$
584.66

XV
$C_{37}H_{36}Cl_3NO_8$
729.04

based on [30]

XII (994 mg, 1.7 mmol, 1 eq) was dissolved in an Ar-flushed flask and freshly distilled trichloroacetonitrile (736 mg, 510 µl, 3 eq) and DBU (39 mg, 40 µl, 0.255 mmol, 0.1 eq)) were added. After stirring for two hours TLC indicated full conversion of the starting material. The solvent was reduced *in vacuo* and purification was done by column chromatography (silica 90g, PE/EE = 4/1-3/2) to obtain **220** mg **XV** (21% besides 550 mg of the cyclic carbonate **XIV** as by-product).

Analytical data:

R_f : 0.57 (PE/EE = 3/1)

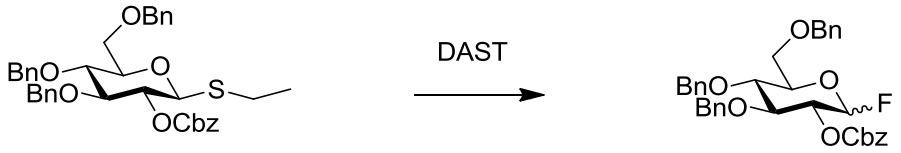
m/z $[M+Na]^+$ = 752

^{1}H-NMR (200 MHz, d_6-Aceton): δ = 9.31 (s, 1H), 7.41 – 7.23 (m, 20H), 6.66 – 6.58 (d, J = 2 Hz, 1H), 5.20 (s, 2H), 4.96 – 4.54 (m, 7H), 4.16 – 3.72 (m, 5H) ppm

^{13}C-NMR (50 MHz, d_6-Aceton): δ = 160.8 (s, 1C), 155.4 (s, 1C), 139.5 (s, 1C), 139.4 (s, 1C), 139.4 (s, 1C), 136.6 (s, 1C), 129.5-128.3 (d, 20C), 94.3 (d, 1C), 80.5 (d, 1C) , 78.0 (d, 1C), 77.1 (d, 1C) , 76.0 (t, 1C), 75.8 (t, 1C), 74.6 (d, 1C), 73.8 (t, 1C) , 70.6 (t, 1C), 69.2 (t, 1C) ppm

E.4.5) Anomeric modifications: F-sugar

Synthesis of Fluoro 3,4,6-tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside (XX)



II

$C_{37}H_{40}O_7S$
628.77

XX

$C_{35}H_{35}FO_7$
586.65

based on[36,37]

II (300 mg, 0.477 mmol, 1 eq) was dissolved in dry dichloromethane (25 ml) and bubbled with Ar for 5 minutes. After cooling down below 0°C, DAST (154 mg, 126 µl, 0.954 mmol, 2 eq) and 20 minutes later NIS (140 mg, 0.620 mmol, 1.3 eq) were added to the mixture and it was allowed to warm up to room temperature. 4 days later, TLC indicated only a partial conversion but the spot, which was thought to be starting material turned out to be one product of an anomeric mixture. The reaction mixture was blended with a second batch (starting from 0.636 mmol (II)) and washed with a mixture of saturated $NaHCO_3$-solution/saturated $Na_2S_2O_3$-solution/water = 1/1/1 two times. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified using column chromatography (silica 90 g, PE-PE/EE = 9/1) to obtain 318 mg **XX** (49%) as white solid. (α/β ~ 3/4)

Analytical data:

R_f : 0.39 (PE/EE = 5/1)

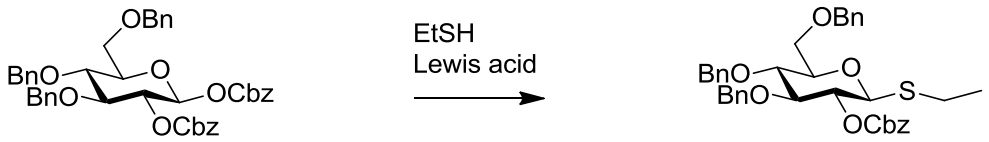
m/z $[M+Na]^+$ = 709

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.31 – 7.04 (m, 20H), 5.35-5.31 (d, J = 6.7 Hz, $0.5H_{1\alpha}$), 5.09 (s, 2H), 5.09 – 5.05 (d, J = 8.4 Hz, $0.5H_{1\beta}$), 4.92 – 4.79 (m, 1H), 4.72 – 4.42 (m, 6H), 3.80 – 3.52 (m, 5H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 154.1 (s, 1C), 137.8 (s, 1C), 137.6 (s, 1C), 134.8 (s, 1C), 128.7 – 127.8 (d, 20C), 108.8 (d, 1C), 81.7 (d, 1C), 81.5 (d, 1C), 76.6 (d, 1C), 75.1 (d, 1C), 75.0 (t, 1C), 74.9 (t, 1C), 73.6 (t, 1C), 70.3 (t, 1C), 68.2 (t, 1C) ppm

E.4.6) Anomeric modifications: thioglycosides from diCbz: Lewis acidic

Synthesis of Ethyl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (II)



X
$C_{43}H_{42}O_{10}$
718.79

a: TMSOTf
b: $SnCl_4$

II
$C_{37}H_{40}O_7S$
628.77

a: *based on* [38]

X (150 mg, 0.217 mmol, 1 eq) was dissolved in dry dichloromethane and molecular sieve (3 Å) (tip of a spatula) was added. The mixture was stirred, bubbled with Ar, cooled down below 0°C and EtSH (216 mg, 257 µl, 1.74 mmol, 8 eq) was added. After stirring for another 30 minutes, TMSOTf (12 mg, 10 µl, 0.0546 mmol, 0.25 eq) was added and 7 days later, the reaction had finished. The mixture was quenched with TEA and filtrated over Celite. Finally, the solvent was removed *in vacuo*. Because of relatively low yields (according to TLC), the product was not purified any further.

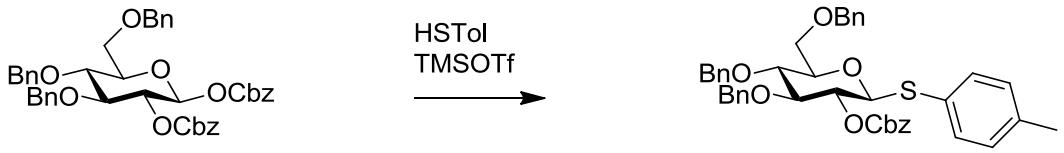
b: *based on* [39]

To a solution of **X** (300 mg, 0.434 mmol, 1 eq) in dry dichloromethane, EtSH (33 mg, 40 µl, 0.521 mmol, 1.2 eq) and $SnCl_4$ (17 mg, 8 µl, 0.065 mmol, 0.15 eq) were added under Ar-atmosphere. After stirring at room temperature for 3 days, TLC indicated full conversion of the starting material. The mixture was diluted with dichloromethane and washed with saturated $NaHCO_3$-solution (three times) and BRINE, changing the colour to white. The collected organic phases were dried over Na_2SO_4 and reduced *in vacuo*. Besides the desired product **II**, a big amount of **XIV** was formed.

Analytical data:

R_f :	(II):	0.49	(PE/EE = 4/1)
	(XIV):	0.53	(PE/EE = 7/3)
m/z	$[M+Na]^+$ = 651		

Synthesis of p-Tolyl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (IV)



X

$C_{43}H_{42}O_{10}$
718.79

IV

$C_{42}H_{42}O_7S$
690.84

based on [38]

X (346 mg, 0.500 mmol, 1 eq) was dissolved in dry dichloromethane (10 ml) and molecular sieve (3 Å) (500 mg) was added. The mixture was stirred, bubbled with Ar, cooled down below 0°C and HSTol (497 mg, 4 mmol, 8 eq) was added. After stirring for another 30 minutes, TMSOTf (12 mg, 10 µl, 0.0546 mmol, 0.25 eq) was added and 24 hours later, the starting material was consumed completely. No purification took place, because **only traces** of the desired product **IV** were formed.

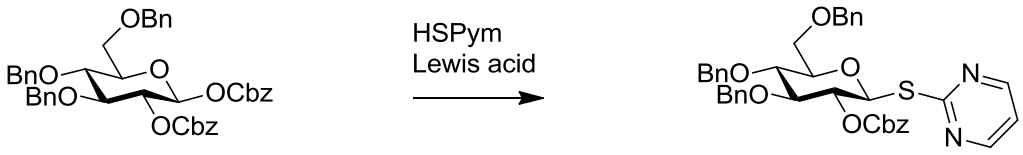
Analytical data:

R_f : (IV): 0.59 (PE/EE = 5/1)

(XIV): 0.53 (PE/EE = 7/3)

m/z $[M+Na]^+ = 713$

Synthesis of 2-Pyrimidyl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (VII)



X
$C_{43}H_{42}O_{10}$
718.79

a: TMSOTf
b: BF_3 * Et_2O

VII
$C_{39}H_{38}N_2O_7S$
678.79

a: *based on* [38]

X (90 mg, 0.125 mmol, 1 eq) was dissolved in dry dichloromethane (3 ml) and molecular sieve (3 Å) (100 mg) was added. The mixture was stirred, bubbled with Ar, cooled down below 0°C and HSPym (113 mg, 1 mmol, 8 eq) was added. After stirring for another 30 minutes TMSOTf (83 mg, 67 µl, 0.375 mmol, 3 eq) was added and 24 hours later, the starting material was consumed completely. No purification took place, because **only traces** of the desired **VII** were formed besides **XIV** as main product.

b: *based on* [40]

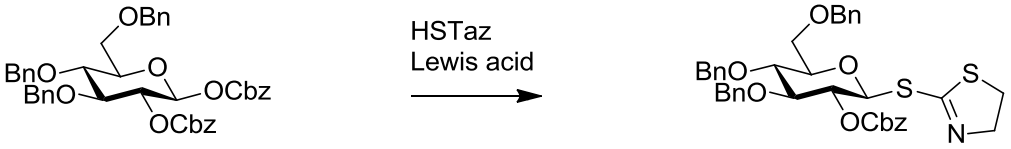
X (90 mg, 0.125 mmol, 1 eq) was dissolved in dry dichloroethane (2 ml) and molecular sieve (3 Å) (100 mg) was added. The mixture was stirred, bubbled with Ar, cooled down to 0°C with a cryostat and HSPym (28 mg, 0.250 mmol, 2 eq) was added. After stirring for 30 minutes, $BF_3 \cdot Et_2O$ (36 mg, 0.250 mmol, 2 eq) was added and the mixture was allowed to warm up to room temperature overnight. Because of the slightly conversion, the mixture was heated up to 50°C. TLC control indicated a predominantly formation of **XIV** besides **traces** of **VII.**

Analytical data:

R_f : (VII): 0.46 (PE/EE = 3/2)
(XIV): 0.53 (PE/EE = 7/3)

m/z $[M+Na]^+$ = 701

Synthesis of 1,3-Thiazolin-2-yl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (IX)



X

$C_{43}H_{42}O_{10}$

718.79

a: TMSOTf

b: BF_3 * Et_2O

IX

$C_{38}H_{39}NO_7S_2$

685.85

a: *based on* [38]

X (90 mg, 0.125 mmol, 1 eq) was dissolved in dry dichloromethane (3 ml) and molecular sieve (3 Å) (100 mg) was added. The mixture was stirred, bubbled with Ar, cooled down below 0°C and HSTaz (119 mg, 1 mmol, 8 eq) was added. After stirring for another 30 minutes, TMSOTf (83 mg, 67 µl, 0.375 mmol, 3 eq) was added and 24 hours later, the starting material was consumed completely. No purification took place, because **only traces** of the desired **IX** were formed (besides **XIV** as main product).

b: *based on* [40]

X (90 mg, 0.125 mmol, 1 eq) was dissolved in dry dichloroethane (2 ml) and molecular sieve (3 Å) (100 mg) was added. The mixture was stirred, bubbled with Ar, cooled down to 0°C with a cryostat and HSTaz (30 mg, 0.250 mmol, 2 eq) was added. After stirring for 30 minutes, $BF_3 \cdot Et_2O$ (36 mg, 0.250 mmol, 2 eq) was added and the mixture was allowed to warm up to room temperature overnight. Because of the slightly conversion, the mixture was heated up to 50°C. TLC control indicated a predominantly formation of **XIV** besides **traces** of **IX.**

Analytical data:

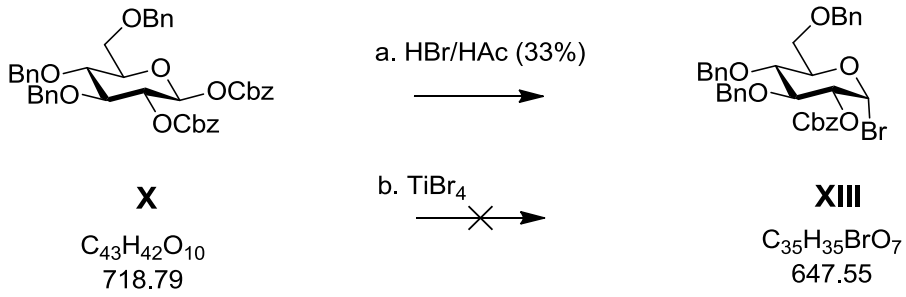
R_f : (IX): 0.46 (PE/EE = 3/2)

(XIV): 0.53 (PE/EE = 7/3)

m/z $[M+Na]^+ = 708$

E.4.7) Anomeric modifications: thioglycosides from diCbz: two steps through Br-sugar

Synthesis of 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-deoxy-1-bromo-glucopyranose (XIII)



X

$C_{43}H_{42}O_{10}$

718.79

XIII

$C_{35}H_{35}BrO_7$

647.55

a: *based on* [20]

X (500 mg, 0.696 mmol, 1 eq) was dissolved in dry dichloromethane (5 ml) under Ar-atmosphere and cooled down to -20°C with a freezing mixture (NaCl:ice = 1:3). Then, HBr/HAC (33%) (1.5 ml) was added dropwise. After 90 minutes, TLC indicated complete conversion of the starting material. The mixture was diluted with dichloromethane and washed with saturated $NaHCO_3$ – solution until it was neutral (three times). The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. For stability reasons, the product was reacted crude without any further purification. Therefore, no yield was determined and no NMR-spectrum measured.

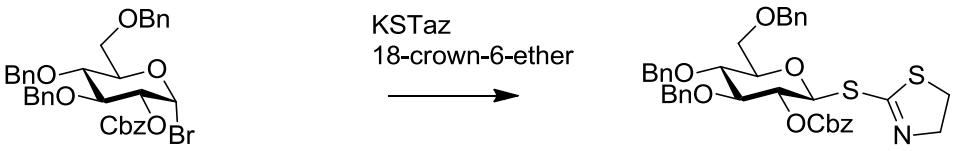
b:

A solution of **X** (108 mg, 150 mmol, 1 eq) in dry dichloromethane (3 ml) was cooled down to -20°C, using a freezing mixture (NaCl:ice = 1:3). Then, $TiBr_4$ (66 mg, 180 mmol, 1.2 eq) was added under Ar-atmosphere. After one hour of reaction time, TLC indicated a predominantly formation of **XIV**, which is why method a was preferred over method b.

Analytical data:

R_f : 0.67 (PE/EE = 4/1)

Synthesis of 1,3-Thiazolin-2-yl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (IX)



XIII
$C_{35}H_{35}BrO_7$
647.55

IX
$C_{38}H_{39}NO_7S_2$
685.85

XIII (2 g, 2.7 mmol, 1 eq) was dissolved in dry acetone (20 ml) under Ar-atmosphere and KSTaz (1 g, 5.4 mmol, 2 eq) and 18-crown-6-ether (143 mg, 0.54 mmol, 0.2 eq) were added. According to TLC-control, the reaction had finished after 20 hours. The solution was diluted with toluene and washed with saturated $NaHCO_3$-solution and water. Then, the organic phase was dried over Na_2SO_4 and reduced *in vacuo*, giving 1.94 of a mixture of **IX** and **XIV**.

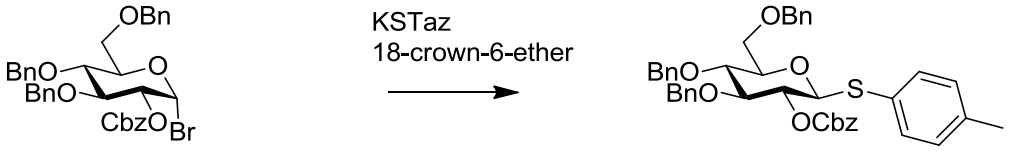
Analytical data:

R_f : (IX): 0.46 (PE/EE = 3/2)

(XIV): 0.53 (PE/EE = 7/3)

m/z $[M+Na]^+ = 708$

Synthesis of p-Tolyl 2-O-benzoxycarbonyl-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (IV)



XIII
$C_{35}H_{35}BrO_7$
647.55

IV
$C_{42}H_{42}O_7S$
690.84

XIII (97 mg, 0.150 mmol, 1 eq) was dissolved in dry acetone (2 ml) under Ar-atmosphere and KSTol (50 mg, 0.300 mmol, 2 eq) and 18-crown-6-ether (10 mg, 0.030 mmol, 0.2 eq) were added. According to TLC-control, the reaction had finished overnight. The solution was diluted with toluene and washed with NaOH-solution (1%) and water. Then, the organic phase was dried over Na_2SO_4 and reduced *in vacuo*.

No further purification took place, but TLC/MS and comparison with a reference proved formation of **IV.**

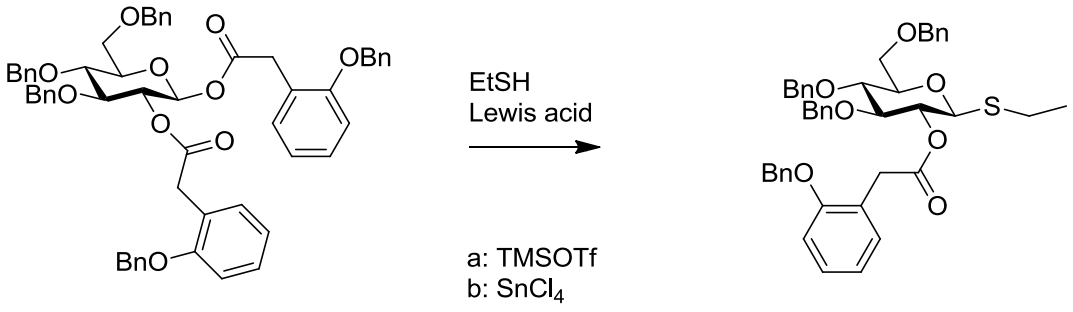
Analytical data:

R_f : 0.59 (PE/EE = 5/1)

m/z $[M+Na]^+ = 713$

E.4.8) anomeric modifications: thioglycosides from diBnPAc: Lewis acidic

Synthesis of Ethyl 2-O-(2-(2-benzyloxyphenyl)acetyl)-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (III)



XI

$C_{57}H_{54}O_{10}$
899.03

III

$C_{44}H_{46}O_7S$
718.90

a: *based on* [38]

XI (190 mg, 0.161 mmol, 1 eq) and EtSH (80 mg, 1.288 mmol, 8 eq) were dissolved in dry dichloromethane (3 ml) and Molecular sieve (3 Å) (tip of a spatula) was added. The mixture bubbled with Ar, stirred for 2 hours and cooled down below 0°C. Then, TMSOTf (10 µl, 0.051 mmol, 0.25 eq) was added and 7 days later, the reaction had finished. The mixture was quenched with TEA and filtrated over Celite. Finally, the solvent was removed *in vacuo*. Because of relatively low yields (according to TLC), the product was not purified any further.

b: *based on* [39]

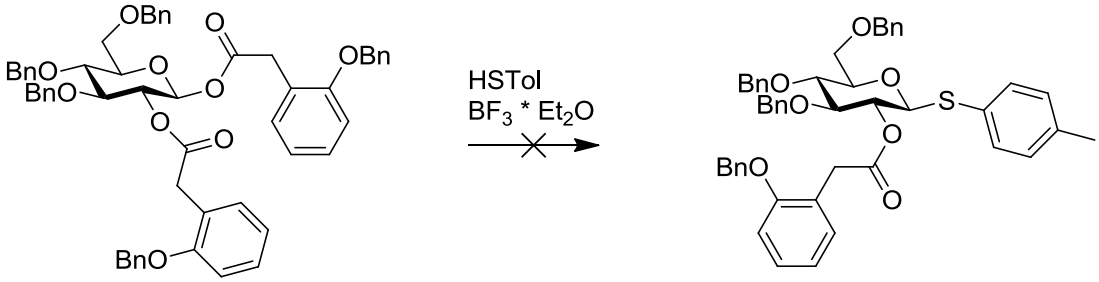
To a solution of **XI** (300 mg, 0.324 mmol, 1 eq) and EtSH (24 mg, 30 µl, 0.389 mmol, 1.2 eq) in dry dichloromethane (2 ml), $SnCl_4$ (13 mg, 6 µl, 0.05 mmol, 0.15 eq) was added. After stirring for 3 days, TLC indicated full consumption of the starting material. The mixture was diluted with dichloromethane, washed with sat. $NaHCO_3$-solution (three times) and brine and dried over Na_2SO_4. Then, the solvent was removed *in vacuo*. Unfortunately, **(III)** could not be isolated due to infrastructural issues, but nevertheless, TLC-MS confirmed the formation.

Analytical data:

R_f : 0.53 (PE/EE = 4/1)

m/z $[M+Na]^+$ = 741

Synthesis of p-Tolyl 2-O-(2-(2-benzyloxyphenyl)acetyl)-3,4,6-tri-O-benzyl-1-thio-β,D-glucoside (III)



XI

$C_{57}H_{54}O_{10}$
899.03

V

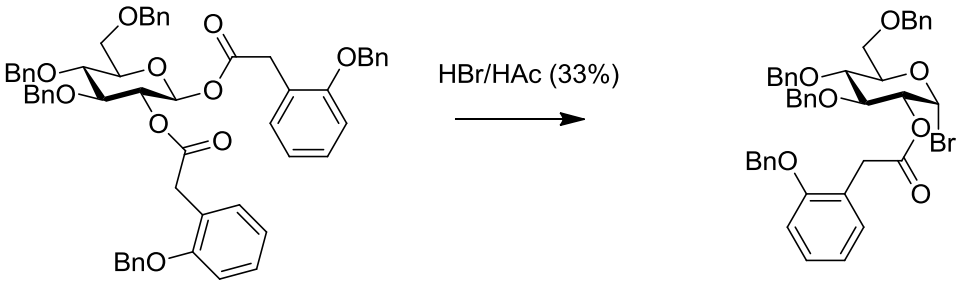
$C_{49}H_{48}O_7S$
780.97

based on [40]

XI (200 mg, 0.216 mmol, 1 eq) and HSTol (54 mg, 0.432 mmol, 2 eq) were dissolved in dry dichloromethane (3.5 ml) under Ar-atmosphere. $BF_3 \cdot Et_2O$ (3 mg, 0.022 mmol, 0.1 eq) was added over a syringe. After 48 h, TLC indicated full consumption of the starting material and the reaction was quenched with TEA. Then it was diluted with dichloromethane and washed with brine. The organic phase was dried over Na_2SO_4 and reduced *in vacuo*. Further purification was done with column chromatography (silica 90 g, PE-PE/EE = 3/1) to give two main fractions. Unfortunately, comparison with reference material and TLC-MS control did not show any product signals.

E.4.9) Anomeric modifications: thioglycosides from diBnPAc: two steps through Br-sugar

Synthesis of 2-O-(2-(2-benzyloxyphenyl)acetyl)-3,4,6-tri-O-benzyl-1-deoxy-1-bromo-glucopyranose (XIX)



XI

$C_{57}H_{54}O_{10}$
899.03

XIX

$C_{42}H_{41}BrO_7$
737.67

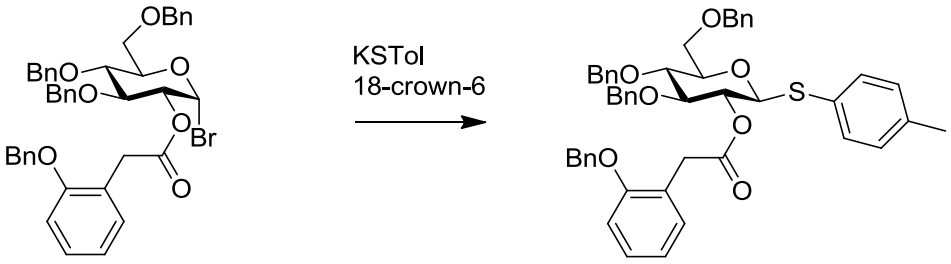
based on [20]

XI (50 mg, 0.054 mmol, 1 eq) was dissolved in dry dichloromethane (3 ml) under Ar-atmosphere and cooled down to -20°C with a freezing mixture (NaCl:ice = 1:3). Then, HBr/HAC (33%) (0.5 ml) was added dropwise. After 120 minutes TLC indicated complete conversion of the starting material. The mixture was diluted with dichloromethane and washed with saturated $NaHCO_3$ – solution (until it was neutral) and water. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. For stability reasons, the product was reacted crude without any further purification. Therefore, no yield was determined and no NMR-spectrum measured.

Analytical data:

R_f : 0.71 (PE/EE = 4/1)

Synthesis of p-Tolyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-1-thio-β,D-glucoside (V)



XIX

$C_{42}H_{41}BrO_7$

737.67

V

$C_{49}H_{48}O_7S$

780.97

XIX (245 mg, 0.150 mmol, 1 eq) was dissolved in dry acetone (5 ml) under Ar-atmosphere and KSTol (108 mg, 0.664 mmol, 2 eq) and 18-crown-6-ether (18 mg, 0.066 mmol, 0.2 eq) were added. According to TLC-control the reaction had finished overnight. The solution was diluted with toluene and washed with NaOH-solution (1%) and water. Then, the organic phase was dried over Na_2SO_4 and reduced *in vacuo*.

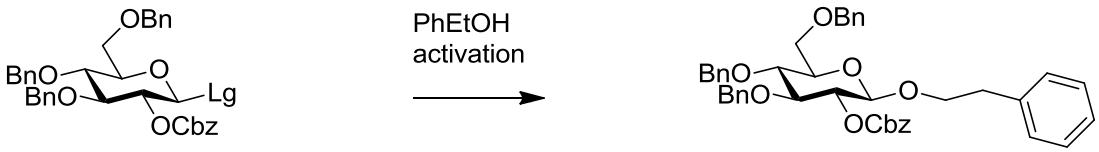
No further purification took place, but LC/MS and TLC-reference proved formation of **V.**

Analytical data:

m/z $[M+Na]^+ = 803$

E.4.10) Glycosylations: Cbz

Synthesis of 2-Phenylethyl 3,4,6-tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside (XXI)



II (R = SEt)
IV (R = STol)
VII (R = SPym)
IX (R = STaz)
XVI (R = TFI)
XX (R = F)

a: NIS/TfOH
b: TMSOTf
c: $Cu(OTf)_2$
d: AgOTf
e: cp_2HfCl_2 + $Cu(OTf)_2$

XXI

$C_{43}H_{44}O_8$
688.80

general procedures:

After preparative batches with **II** and **IX** (1 eq ≙ 0.2 mmol) for reference material, further glycosylations were done on analytical scale (1 eq ≙ 0.02 mmol, these were not purified). Yields were detected using LC/MS.

a: based on [41]

Donor (1 eq) was dissolved in dry dichloromethane (20 ml/ mmol donor) and acceptor (2.5 eq) and molecular sieves (3Å, 1g /mmol donor) were added under Ar-atmosphere. The mixture was stirred 4 hours at room temperature and then cooled down. NIS (2 eq) and TfOH (0.2 eq) were added and after reacting overnight, TLC indicated full conversion of the donor. The reaction was quenched with TEA, diluted with dichloromethane, filtrated over Celite and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. For purification in preparative scale, column chromatography (silica, PE/EE gradient elution) was used.

b: based on [41]

Donor (1 eq) was dissolved in dry dichloromethane (10 ml/ mmol donor) and acceptor (2.5 eq) and molecular sieves (3Å, 1g /mmol donor) were added under Ar-atmosphere. The mixture was stirred 4 hours at room temperature and then cooled down. TMSOTf (2 eq for **VII** and **IX**, 0.2 eq for others) added and after reacting overnight, TLC indicated full conversion of the donor. The reaction was quenched with TEA, diluted with dichloromethane, filtrated over Celite and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. For purification in preparative scale, column chromatography (silica, PE/EE gradient elution) was used.

c:

based on [35]

Donor (1 eq) was dissolved in dry dichloromethane (25 ml/ mmol donor) and acceptor (2.5 eq) and molecular sieves (3Å, 1g /mmol donor) were added under Ar-atmosphere. The mixture was stirred 2 hours at room temperature and then cooled down. $Cu(OTf)_2$(3 eq) added and after reacting overnight, TLC indicated full conversion of the donor. The reaction was quenched with TEA, diluted with dichloromethane, filtrated over Celite and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. For purification in preparative scale, column chromatography (silica, PE/EE gradient elution) was used.

d:

based on [42]

Donor (1 eq) was dissolved in dry dichloromethane (25 ml/ mmol donor) and **acceptor** (2.5 eq) and molecular sieves (3Å, 1g /mmol donor) were added under Ar-atmosphere. The mixture was stirred 20 minutes at room temperature and then cooled down. AgOTf (2 eq) added and after reacting overnight, TLC indicated full conversion of the donor. The reaction was quenched with TEA, diluted with dichloromethane, filtrated over Celite and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. For purification in preparative scale, column chromatography (silica, PE/EE gradient elution) was used.

e:

based on [43]

AgOTf (2 eq), cp_2HfCl_2 (1 eq) and molecular sieve (3 Å) were suspended under Ar-atmosphere in dry dichloromethane (18 ml/ mmol donor), stirred and cooled down. **Donor** (1 eq) and **acceptor** (2.5 eq) were dissolved in dry dichloromethane and added dropwise to the mixture. After reacting overnight, TLC indicated full conversion of the **donor** material and the mixture was filtered over Celite. The solution was washed with saturated $NaHCO_3$ – solution and water and then dried over Na_2SO_4. Finally, it was concentrated *in vacuo* and purified, using column chromatography (silica, PE/EE gradient elution).

donor	method	temperature	yield
II	a	-10	83
IV	a	-10	82
VII	b	-10	87
VII	d	0°C	additional activation -> b
IX	c	-10°C	77
XVI	b	-20°C	product*
XX	e	-10°C	product*

* according to TLC-control, product was formed

Analytical data:

R_f : 0.40 (PE/EE = 4/1)

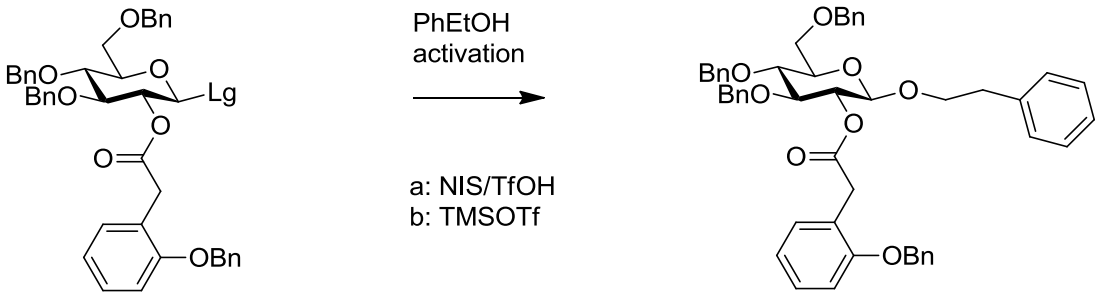
m/z: $[M+Na]^+$ = 711

^{1}H-NMR (400 MHz, d_6-acetone): δ = 7.41-7.16 (m, 25H), 5.22-5.14 (q, 2H), 4.84-4.80 (m, 2H), 4.76-4.63 (m, 3H), 4.61-4.60 (d, J= 6.1 Hz, $1H_{1\beta}$), 4.59-4.48 (m, 2H), 4.06-4.00 (m, 1H), 3.81-3.59 (m, 6H), 2.86-2.83 (t, 2H) ppm

^{13}C-NMR (100 MHz, d_6-acetone): δ = 155.4 (s, 1C), 139.9 (s, 1C), 139.7 (s, 1C), 139.5 (s, 2C), 136.9 (s, 1C), 129-9-127.0 (d, 25C), 101.4 (d, 1C), 83.7 (d, 1C), 79.0 (d, 1C), 78.6 (d, 1C), 75.9 (d, 1C), 75.7 (t, 1C), 75.4 (t, 1C), 73.8 (t, 1C), 71.0 (t, 1C), 70.2 (t, 1C), 69.8 (t, 1C), 36.8 (t, 1C) ppm

E.4.11) Glycosylations: BnPAc

Synthesis of 2-Phenylethyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside (XXIII)



III (R = SEt)
VIII (R = SPym)

XXIII

$C_{50}H_{50}O_8$
778.93

method a: based on [41]

III (231 mg, 0.321 mmol, 1 eq) was dissolved in dry dichloromethane (5 ml) and 2-phenylethanol (98 mg, 100 µl, 0.804 mmol, 2.5 eq) and molecular sieves (3Å) (300 mg) were added under Ar-atmosphere. The mixture was stirred 3 hours at room temperature and cooled down to -15°C. NIS (145 mg, 0.642 mmol, 2 eq) and TfOH (10 mg, 6 µl, 0.064 mmol, 0.2 eq) were added and after reacting overnight, TLC indicated full conversion of the donor. The reaction was quenched with TEA, diluted with dichloromethane, filtrated over Celite and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. After purification with column chromatography (silica 90 g, PE/EE = 8/1-4/1), 205 mg of **XXIII** were obtained (82%) as colorless oil.

method b: based on [41]

III (100 mg, 0.130 mmol, 1 eq) was dissolved in dry dichloromethane (2 ml) and 2-phenylethanol (40 mg, 40 µl, 0.325 mmol, 2.5 eq) and molecular sieves (3Å) (100 mg) were added under Ar-atmosphere. The mixture was stirred 3 hours at room temperature and cooled down to -15°C. TMSOTf (58 mg, 50 µl, 0.260 mmol, 0.2 eq) were added and after reacting overnight, TLC indicated full conversion of the donor. The reaction was quenched with TEA, diluted with dichloromethane, filtrated over Celite and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. After purification with column chromatography (silica 90 g, PE/EE = 8/1-4/1), 100 mg of **XXIII** were obtained (95%) as colorless oil.

Analytical data:

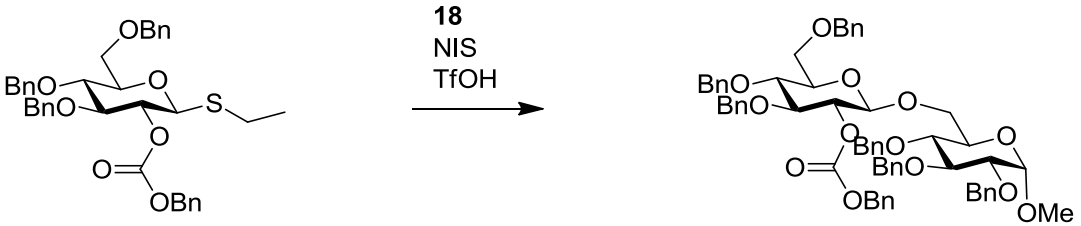
R_f : 0.50 (PE/EE = 4/1)

m/z: $[M+Na]^+$ = 801.4

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.40-7.12 (m, 27H), 6.88-6.83 (m, 2H), 5.10-5.06 (t, J= 8.2 Hz, 1H) 5.03-4.94 (m, 2H), 4.75-4.73 (d, J= 10.9 Hz, 1H), 4.63-4.60 (d, J= 12.5 Hz, 1H), 4.56 (s, 1H), 4.53 (s, 1H), 4.52-4.49 (d, J= 10.9 Hz, 1H), 4.48-4.45 (d, J= 11.3 Hz, 1H), 4.36-4.34 (d, J= 8.2 Hz, $1H_{1\beta}$), 4.07-4.01 (m, 1H), 3.75-3.72 (dd, J_1= 10.9 Hz, J_2= 2.0 Hz, 1H), 3.70-3.56 (m, 6H), 3.48-3.44 (m, 1H), 2.84-2.80 (t, 7.4 Hz, 2H) ppm

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 170.0 (s, 1C), 156.4 (s, 1C), 138.6 (s, 1C), 138.2 (s, 1C), 138.1 (s, 1C), 138.0 (s, 1C), 137.1 (s, 1C), 131.0 (d, 1C), 129.0-126.2 (d, 26C), 123.0 (s, 1C), 120.8 (d, 1C), 111.8 (s, 1C), 100.9 (d, 1C), 82.9 (d, 1C), 77.8 (d, 1C), 75.1 (d, 1C), 74.9 (t, 1C), 74.6 (t, 1C), 73.5 (d, 1C), 73.5 (t, 1C), 70.1 (t, 1C), 69.9 (t, 1C), 68.8 (t, 1C), 36.1 (t, 1C), 35. 6 (t, 1C), ppm

Synthesis of 3,4,6-Tri-O-benzyl-2-O-benzyloxycarbonyl-β-D-glucopyranosyl-(1→4)- 2,3,6-tri-O-benzyl-1-O-methyl-α-D-glucopyranose (XXVI)



II

$C_{37}H_{40}O_7S$
628.77

XXVI

$C_{63}H_{66}O_{13}$
1031.19

based on [41]

II (126 mg, 0.20 mmol, 1 eq) was dissolved in dry dichloromethane (2.5 ml) and β-D-glucose-1,2,3,4-tetraacetat (116 mg, 0.25 mmol, 2 eq) and molecular sieves (3Å) (300 mg) were added under Ar-atmosphere. The mixture was cooled down to -15°C and stirred for 2hours. NIS (90 mg, 0.400 mmol, 2 eq) and TfOH (6 mg, 3.5 µl, 0.040 mmol, 0.2 eq) were added and after reacting overnight, TLC indicated full conversion of the donor. The reaction was quenched with TEA, diluted with dichloromethane, filtrated over Celite and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. After purification with column chromatography (silica 8 g, PE/EE = 8/1-4/1), 95 mg of **XXVI** were obtained (46%) as colorless oil.

Analytical data:

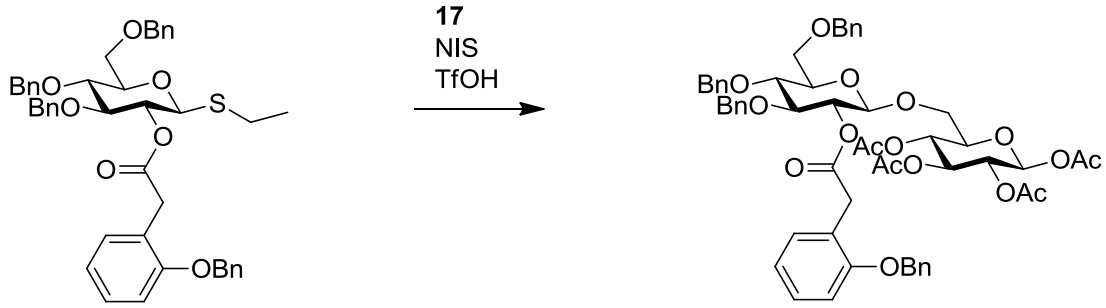
R_f : 0.45 (PE/EE = 4/1)

m/z: $[M+Na]^+$ = 1053

^{1}H-NMR (600 MHz, CD_2Cl_2): δ = 7.37-7.14 (m, 35H), 6.07-6.06 (d, J= 6.3 Hz, $1H_{1\beta}$), 5.17-5.05 (m, 2H), 4.77-4.71 (m, 2.5H), 4.69-4.68 (dd, J= 6.3 Hz, 2.5 Hz, $1H_2$), 4.67-4.42 (m, 10.5H), 4.37-4.31 (q, 1H), 3.94-3.93 (t, J= 4.6 Hz, $1H_{2'}$), 3.87-3.83 (m, 2H), 3.81-3.80 (d, J = 4.8 Hz, $1H_{1'\alpha}$), 3.80-3.22 (m, 9H) ppm

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 152.4 (s, 1C), 139.6 (s, 1C), 138.4 (s, 1C), 138.0 (s, 1C), 137.9 (s, 1C), 137.6 (s, 1C), 137.4 (s, 1C), 136.8 (s, 1C), 128.6-126.9 (d, 35C), 100.4 (d, 1C), 98.4 (d, 1C), 97.4 (d, 1C), 82.9 (d, 1C), 80.3 (d, 1C), 79.0 (d, 1C), 78.2 (d, 1C), 77.8 (d, 1C), 77.4 (d, 1C), 75.9 (d, 1C), 75.1 (t, 1C), 74.8 (t, 1C), 73.6 (t, 1C), 73.5 (t, 1C), 73.3 (t, 1C), 73.3 (d, 1C), 72.7 (t, 1C), 71.7 (d, 1C), 68.6 (t, 1C), 68.5 (t, 1C), 68.0 (t, 1C), 55.3 (q, 1C) ppm

Synthesis of 3,4,6-Tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)- β-D-glucopyranosyl-(1→6)-1,2,3,4-tetra-O-acetyl-β-D-glucopyranose (XXIV)



III

$C_{44}H_{46}O_7S$
718.90

XXIV

$C_{56}H_{60}O_{17}$
1005.07

based on [41]

III (200 mg, 0.278 mmol, 1 eq) was dissolved in dry dichloromethane (3.35 ml) and β-D-glucose-1,2,3,4-tetraacetat **(17)** (242 mg, 0.696 mmol, 2.5 eq) and molecular sieves (3Å) (223 mg) were added under Ar-atmosphere. The mixture was stirred 2.25 hours at room temperature and cooled down to 0°C. NIS (125 mg, 0.536 mmol, 2 eq) and TfOH (8 mg, 5 µl, 0.056 mmol, 0.2 eq) were added and after reacting overnight, TLC indicated full conversion of the donor. The reaction was quenched with TEA, diluted with dichloromethane, filtrated over Celite and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. After purification with column chromatography (silica 90 g, PE/EE = 8/1-4/1), 170 mg **XXIV** (61%) were obtained as colorless oil.

Analytical data:

R_f : 0.45 (PE/EE = 4/1)

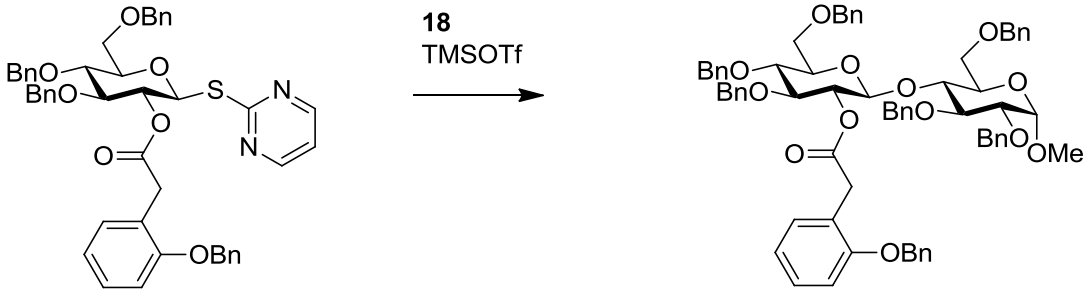
m/z: $[M+Na]^+$ = 1028

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.50-7.47 (dd, J_1= 9.0, J_2= 2.0, 1H), 7.40-7.10 (m, 22H), 6.64-6.61 (d, J= 9.0 Hz, 1H), 5.55-5.53 (m, J= 8.2 Hz, $1H_{\beta,OAc}$), 5.18-5.12 (t, 1H), 5.09-4.93 (m, 4H), 4.73-4.69 (m, 1H), 4.66-4.42 (m, 5H), 4.28-4.27 (d, J= 7.8 Hz, $1H_{\beta,glyc}$), 4.21-4.18 (m, 1H), 4.04-3.96 (m, 1H), 3.87-3.53 (m, 7H), 3.44-3.30 (m, 3H), 2.13-1.98 (m, 12H), ppm

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 170.2 (s, 1C), 169.9 (s, 1C), 169.6 (s, 1C), 169.0 (s, 1C), 168.8 (s, 1C), 156.5 (s, 1C), 139.3 (d, 1C), 138.0 (s, 1C), 137.8 (s, 1C), 137.6 (s, 1C), 137.4 (d, 1C), 136.5 (s, 1C), 128.7-126.8 (m, 20C), 125.2 (s, 1C), 120.8 (d, 1C), 114.2 (d, 1C), 100.7 (d, 1C), 91.6 (d, 1C), 83.2 (d, 1C), 82.9 (t, 1C), 75.0 (d, 1C), 74.9 (t, 1C), 73.4 (d, 1C), 73.4 (d, 1C), 73.3 (t, 1C),

72.8 (d, 1C), 72.3 (d, 1C), 70.5 (d, 1C), 70.2 (t, 1C), 68.6 (t, 1C), 67.7 (d, 1C), 61.5 (t, 1C), 35.0 (t, 1C), 20.8 (q, 1C), 20.8 (q, 1C), 20.6 (q, 1C), 20.5 (q, 1C) ppm

Synthesis of 3,4,6-Tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)- β-D-glucopyranosyl-(1→4)- 2,3,6-tri-O-benzyl-1-O-methyl-α-D-glucopyranose (XXV)



VIII

$C_{46}H_{44}N_2O_7S$
768.92

XXV

$C_{70}H_{72}O_{13}$
1121.31

based on [41]

VIII (66 mg, 0.0851 mmol, 1 eq) was dissolved in dry dichloromethane (1.3 ml) and 2,3,6-Tri-O-benzyl-1-O-methyl-α-D-glucopyranose **(18)** (100 mg, 0.215 mmol, 2.5 eq) and molecular sieves (3Å) (66 mg) were added under Ar-atmosphere. The mixture was stirred 2.5 hours at room temperature and cooled down to 0°C. TMSOTf (38 mg, 31 µl, 0.1722 mmol, 2 eq) was added and after reacting overnight, TLC indicated full conversion of the donor. The reaction was quenched with TEA, diluted with dichloromethane, filtrated over Celite and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. After purification with column chromatography (silica 90 g, PE/EE = 5/1-3/1), 58 mg of **XXV** (60%) were obtained as colorless oil.

Analytical data:

R_f : 0.45 (PE/EE = 4/1)

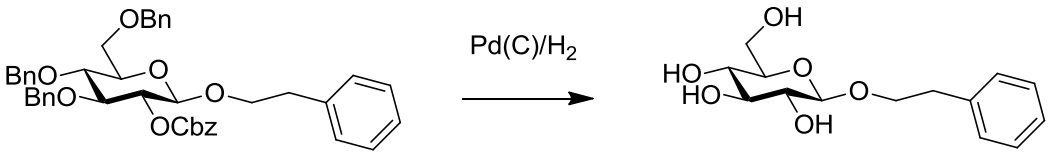
m/z: not detected

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.38-7.16 (m, 37 H), 6.92-6.85 (m, 2H), 5.07-4.91 (m, 4H), 4.79-4.16 (m, 13H), 3.91-3.39 (m, 11H), 3.35 (m, 3H), 3.28-3.21 (m, 2H) ppm

^{13}C-NMR (50 MHz, $CDCl_3$): δ = 169.8 (s, 1C), 156.4 (s, 1C), 139.6 (s, 1C), 138.5 (s, 1C), 138.4 (s, 1C), 138.2 (s, 1C), 138.1 (s, 1C), 137.7 (s, 1C), 136.8 (s, 1C), 130.9 (d, 1C), 128.6-127.0 (m, 36C), 122.8 (s, 1C), 120.8 (d, 1C), 111.7 (d, 1C), 99.8 (d, 1C), 98.6 (d, 1C), 83.0 (d, 1C), 80.2 (d, 1C), 78.7 (d, 1C), 78.1 (d, 1C), 76.1 (d, 1C), 75.4 (t, 1C), 75.4 (d, 1C), 74.8 (t, 1C), 74.7 (t, 1C), 73.9 (d, 1C), 73.6 (t, 1C), 73.4 (t, 1C), 73.4 (t, 1C), 70.0 (t, 1C), 69.8 (d, 1C), 68.8 (t, 1C), 67.6 (t, 1C), 55.3 (q, 1C), 35.9 (t, 1C) ppm

E.4.12) Deprotections: Cbz

Synthesis of 2-Phenylethyl β-D-glucoside (16)



XXI

$C_{43}H_{44}O_8$
688.80

16

$C_{14}H_{20}O_6$
284.31

XXI (3 mg, 0.0044 mmol, 1 eq) was dissolved in dry ethanol (1 ml), Pd/C (10%) (1 mg) was added and the solution was bubbled with Ar. Then a H_2-filled balloon was installed on the reaction vial and the mixture was stirred for two weeks at room temperature. The balloon was replaced every time it grew empty. After full conversion of the starting material (according to TLC), TLC-MS proved the formation of the desired product **16**. Due to the very low amount of product, no further purification was done.

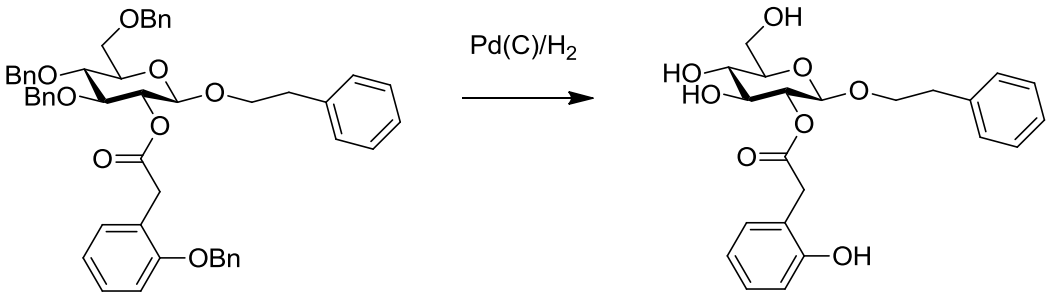
Analytical data:

R_f : 0.14 (PE/EE = 1/1)

m/z: $[M+Na]^+$ = 307

E.4.13) Deprotections: BnPAc

Synthesis of 2-Phenylethyl 2-O-(2-(2-benzyloxyphenyl)acetyl)-β-D-glucoside (XXVII)



XXIII

$C_{50}H_{50}O_8$

778.93

XXVII

$C_{22}H_{26}O_8$

418.44

XXIII (160 mg, 0.205 mmol, 1 eq) was dissolved in dry ethanol (14 ml), Pd/C (10%) (41 mg) was added and the solution was bubbled with Ar. Then a H_2-filled balloon was installed and the mixture was stirred for two weeks at room temperature. The balloon was replaced after 9 days, because the reaction had not finished and the hydrogen pressure was reduced drastically. Two weeks later, after full conversion of the starting material (according to TLC), LC-MS proved the formation of the desired product **XXVII**.

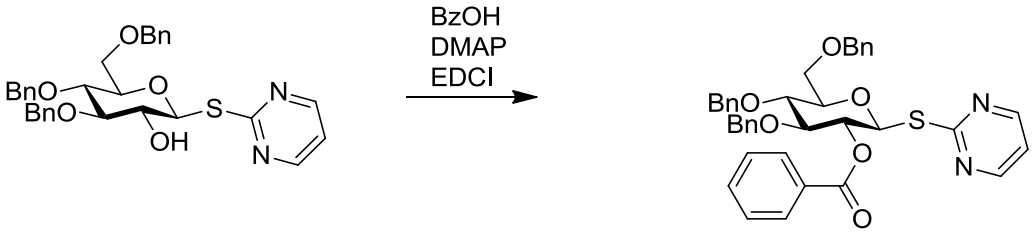
Analytical data:

R_f : 0.06 (PE/EE = 1/1)

m/z: $[M+Na]^+$ = 441

E.4.14) Competitive studies

Synthesis of 2-Pyrimidyl 3,4,6-tri-O-benzyl-2-O-benzoxyl-1-thio-β,D-glucoside (XXVIII)



II

$C_{31}H_{32}N_2O_5S$
544.66

XXVIII

$C_{38}H_{36}N_2O_6S$
648.77

based on [24]

II (500 mg, 0.92 mmol, 1 eq) was dissolved in dry dichloromethane (20 ml) under Ar-atmosphere. Then, the mixture was cooled down to 0°C. Benzoic acid (169 mg, 1.43 mmol, 1.5 eq) and DMAP (23 mg, 0.184 mmol, 0.2 eq) were added, followed by EDCI (441 mg, 2.30 mmol, 2.5 eq) after a few minutes of stirring. Three days later, TLC indicated half full conversion of the starting material and another 1.5 eq benzoic acid were added. After 14 more days, as conversion did not increase, the mixture was diluted with dichloromethane and washed with 0.05 M HCl, saturated $NaHCO_3$-solution and brine. The organic phase was dried with Na_2SO_4, concentrated *in vacuo* and purified, using column chromatography (silica 90 g, PE/EE = 6/1-4/1) to obtain 334 mg **VIII** (56%) as a colourless solid.

Analytical data:

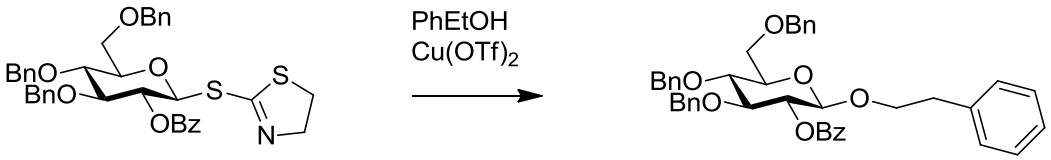
R_f : 0.33 (PE/EE = 1/1)

m/z $[M+Na]^+$ = 671.2203 (HRMS)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.62-8.61 (d, J= 4.8 Hz, 2H), 8.12-8.10 (dd, J= 8.3 Hz, J= 1.2 Hz, 2H), 7.67-7.64 (t, 1H), 7.53-7.50 (t, J= 7.9 Hz, 2H), 7.46-7.37 (m, 9H), 7.35-7.34 (m, 2H), 7.27 (m, 4H), 7.09-7.08 (t, J= 4.9 Hz, 1H), 5.99-5.98 (d, J= 10.5 Hz, 1H), 5.69-5.65 (dd, J= 10.4 Hz, J= 9.1 Hz, 1H), 4.99-4.97 (d, J= 10.9, 1H), 4.92-4.91 (d, J= 11.1 Hz, 1H), 4.86-4.84 (d, J= 11.1 Hz, 1H), 4.77-4.74 (dd, 2H), 4.67-4.65 (d, J= 12.1, 1H), 4.14-4.11 (t, J= 8.9 Hz, 1H), 4.03-3.99 (t, J= 9.2 Hz), 3.95-3.89 (m, 3H) ppm

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 170.2 (s, 1C), 165.2 (s, 1C), 157.3 (d, 2C), 138.1 (s, 1C), 138.1 (s,1C), 137.8 (s, 1C), 133.1 (d, 1C), 129.8 (d, 2C), 129.7 (s, 1C), 128.4 (d, 2C), 128.3 (d, 3C), 128.2 (d, 2C), 128.0 (d, 2C), 127.9 (d, 2C), 127.8 (d, 2C), 127.6, (d, 2C), 127.5 (d, 2C), 117.2 (d, 1C), 84.5 (d, 1C), 82.2 (d, 1C), 79.8 (d, 1C), 77.8 (d, 1C), 75.2 (t,1C), 75.0 (t, 1C), 73.4 (t, 1C), 71.8 (d, 1C), 68.7 (t, 1C) ppm

Synthesis of 2-Phenylethyl 3,4,6-tri-O-benzyl-2-O-benzoxyl-D-glucoside (19)



$C_{37}H_{37}NO_6S_2$
655.82
19

$C_{42}H_{42}O_7$
658.78
20

based on [41]

19 (131 mg, 0.2 mmol, 1 eq) was dissolved in dry dichloromethane (5 ml) and 2-phenylethanol (61 mg, 60 µl, 0.5 mmol, 2.5 eq) and molecular sieves (200 mg, 3Å) were added under Ar-atmosphere. The mixture was stirred 2 hours at room temperature and then cooled down. $Cu(OTf)_2$(217 mg, 0.6 mmol, 3 eq) added and after reacting overnight, TLC indicated full conversion of the donor. The reaction was quenched with TEA, diluted with dichloromethane, filtrated over Celite and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. For purification in preparative scale, column chromatography (silica, PE/EE gradient elution) was used to obtain 50 mg (38%) of **20**.

Analytical data:

R_f : 0.40 (PE/EE = 2/1)

m/z $[M+Na]^+$ = 681.2842 (HRMS)

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.13-8.11 (d, J= 7.3 Hz, 2H), 7.74-7.70 (t, J= 7.6 Hz, 1H), 7.60-7.56 (t, J= 7.6 Hz, 2H), 7.49-7.14 (m, 20H), 5.47-5.42 (t, J=8.3 Hz, 1H), 4.97-4.95 (d, J=10.8 Hz, 1H), 4.88-4.86 (d, J=11.1 Hz, 1H), 4.81-4.77 (m, 2H), 4.73-4.70 (d, J=12.9 Hz, 1H), 4.66-4.65 (d, J=7.9 Hz, $1H_{1\beta}$), 4.29-4.24 (m, 1H), 4.03-3.67 (m, 6H), 3.04-2.90 (m, 2H) ppm

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.2 (s, 1C), 138.6 (s, 1C), 138.1 (s, 1C), 137.4 (s, 1C), 137.8 (s, 1C), 133.0 (d, 1C), 130.0 (s, 1C), 129.8 (d, 2C), 128.8-127.7 (d, 21C), 126.0 (d, 1C), 101.0 (d, 1C), 82.8 (d, 1C), 78.0 (d, 1C), 75.3 (d, 1C), 75.1 (t, 2C), 73.7 (d, 1C), 73.6 (t, 1C), 70.4 (t, 1C), 68.8 (t, 1C), 36.0 (t, 1C) ppm

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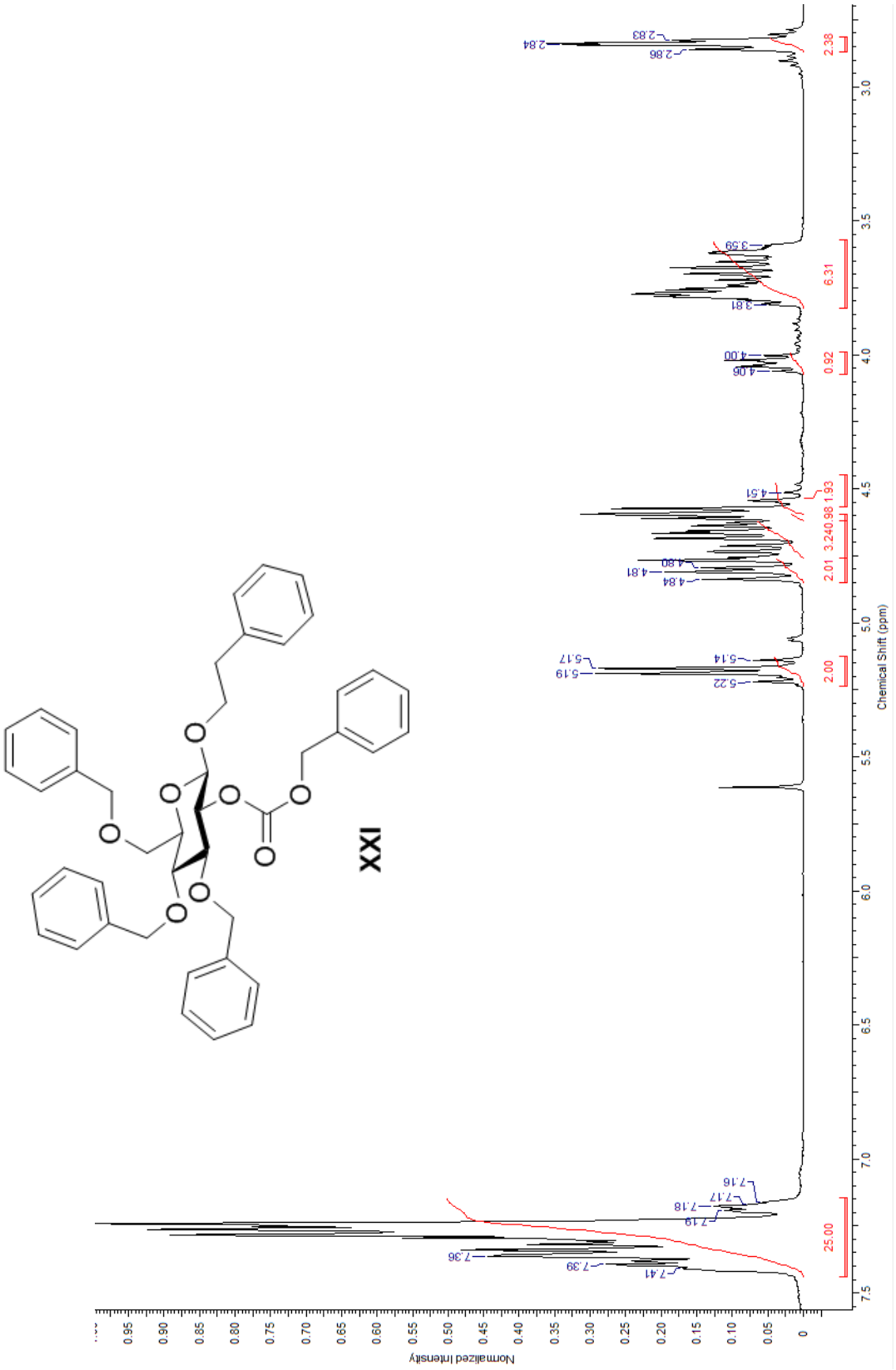
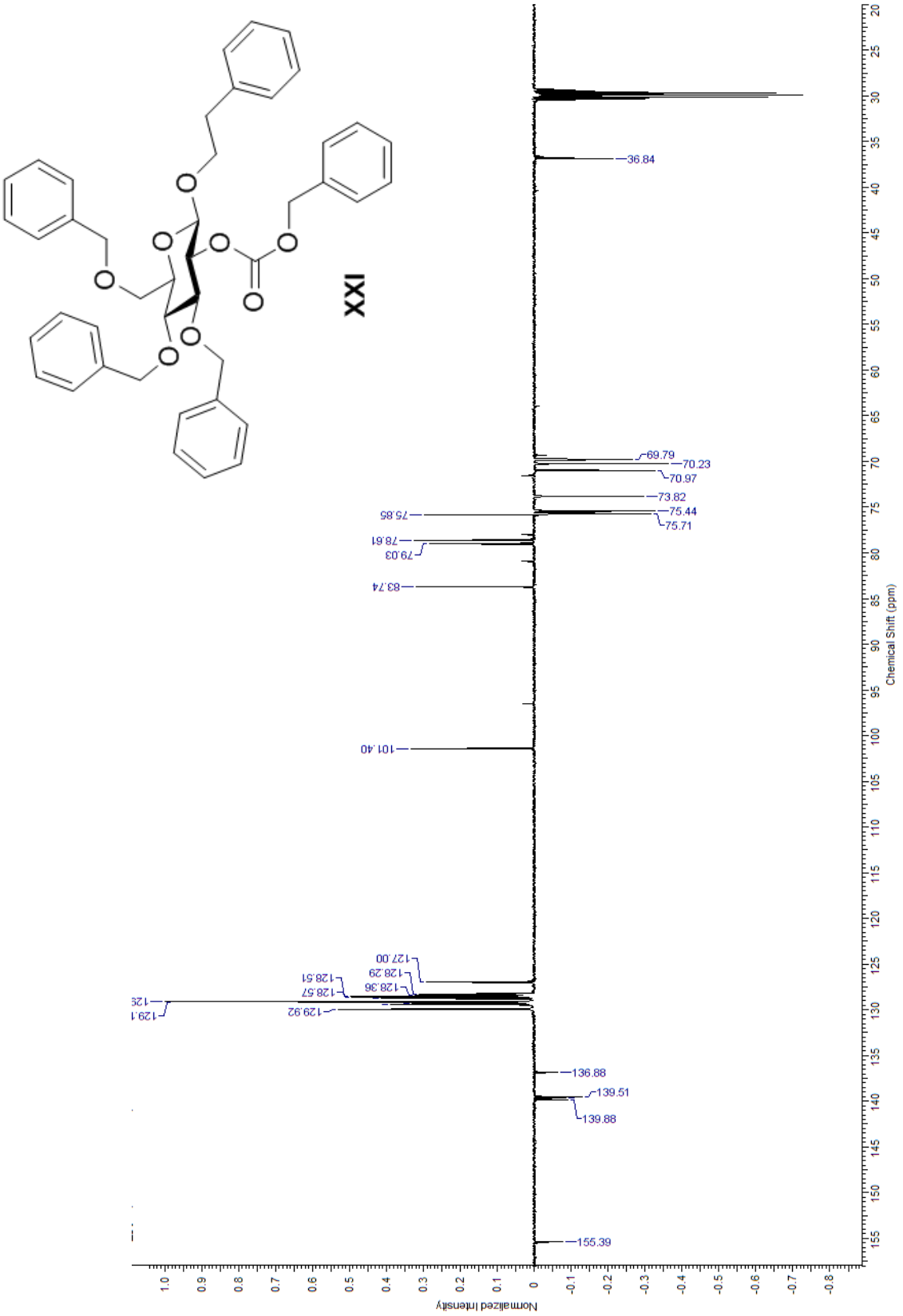
G) Appendix

G.1) NMR-spectra of 2-Phenylethyl 3,4,6-tri-O-benzyl-2-O-benzoxycarbonyl-D-glucoside (XXI)

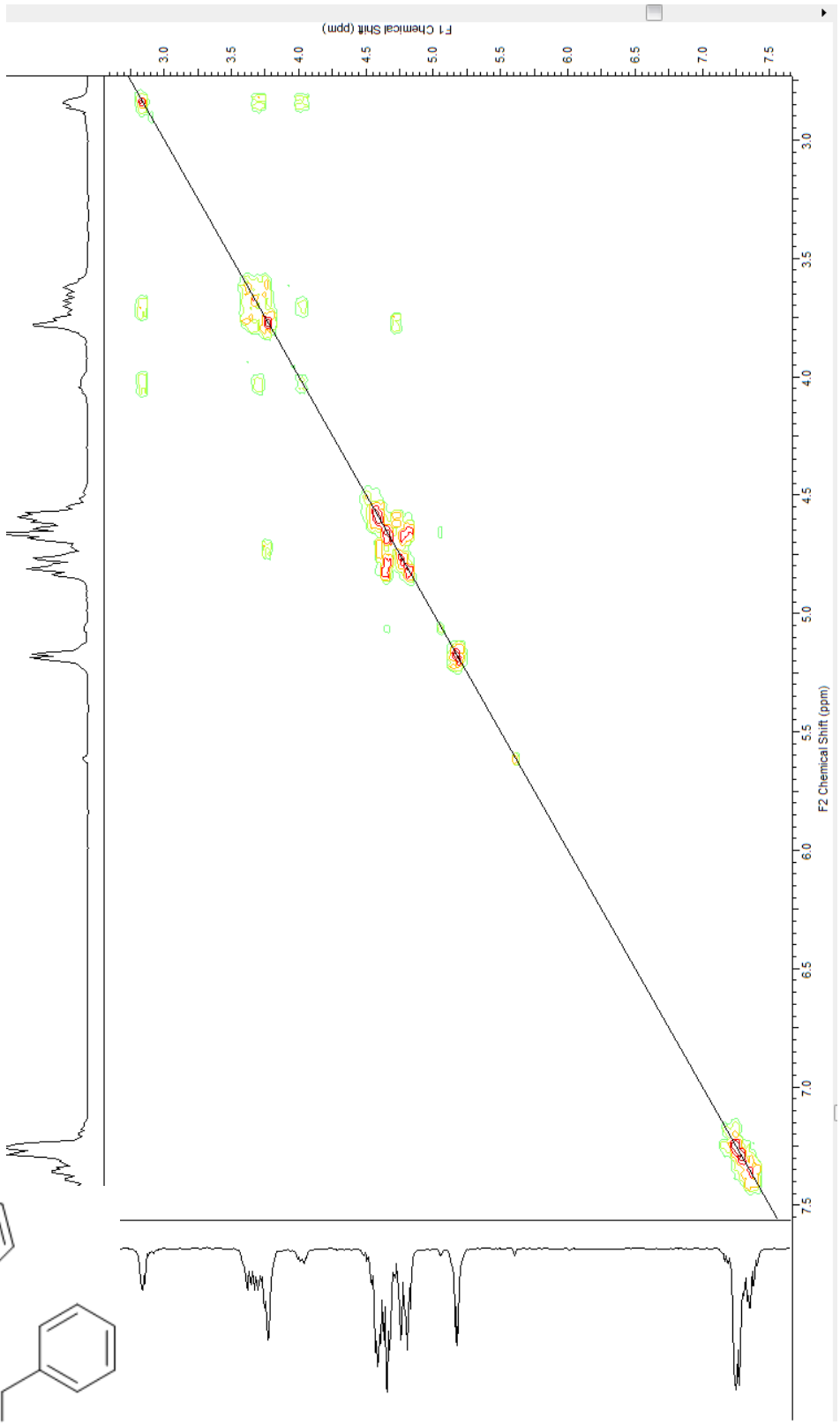
G.1.1) ^{1}H-NMR (400MHz, d_6-acetone)

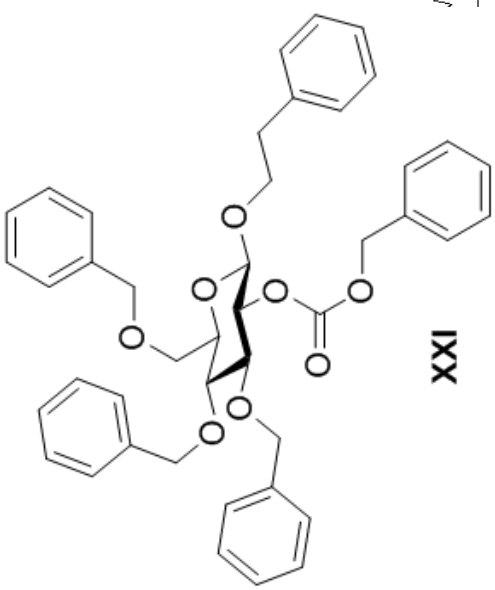


G.1.2) ^{13}C-NMR (100MHz, d_6-acetone)



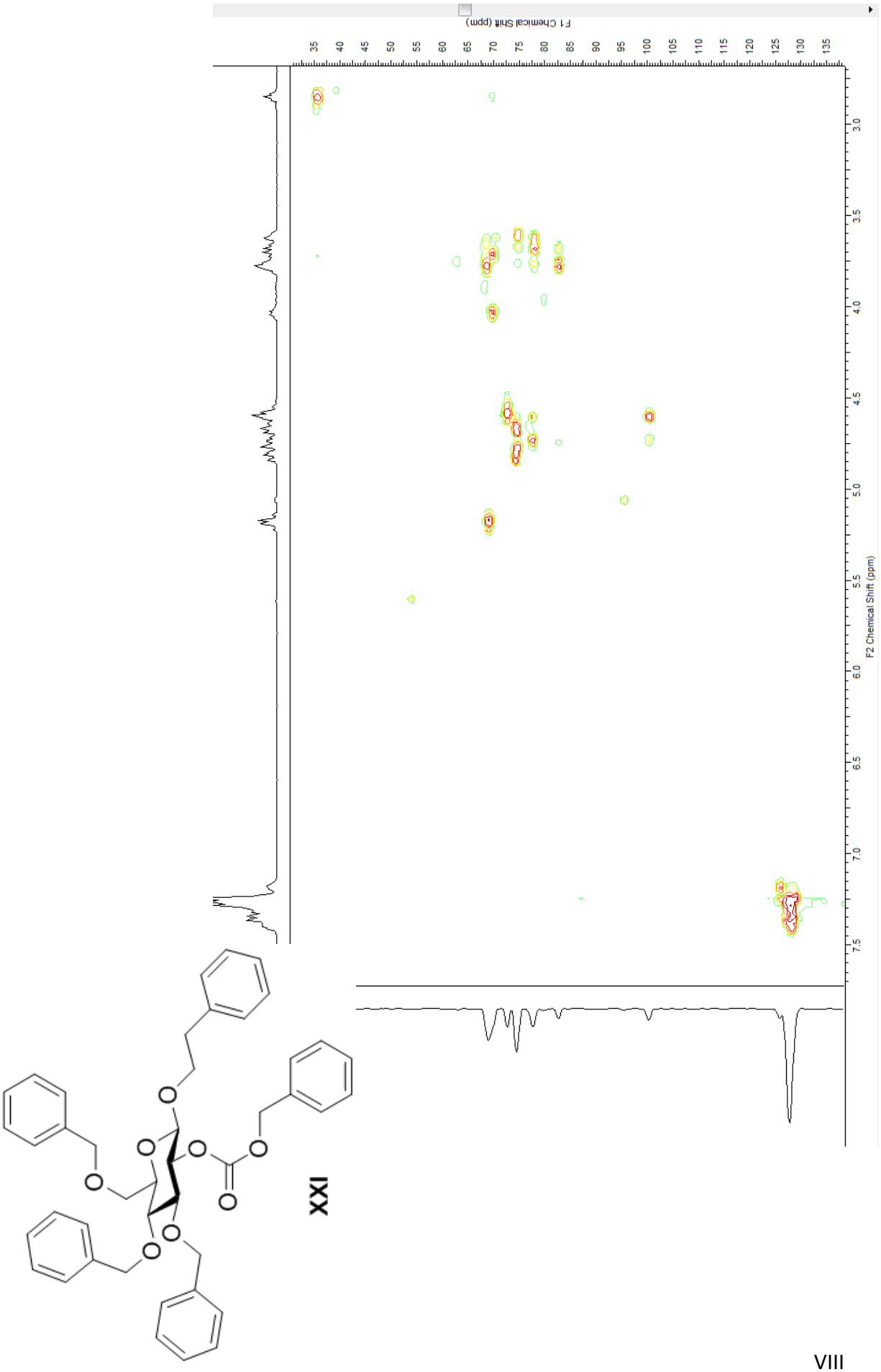
G.1.3) H,H-COSY (400MHz, d_6-acetone)





XXI

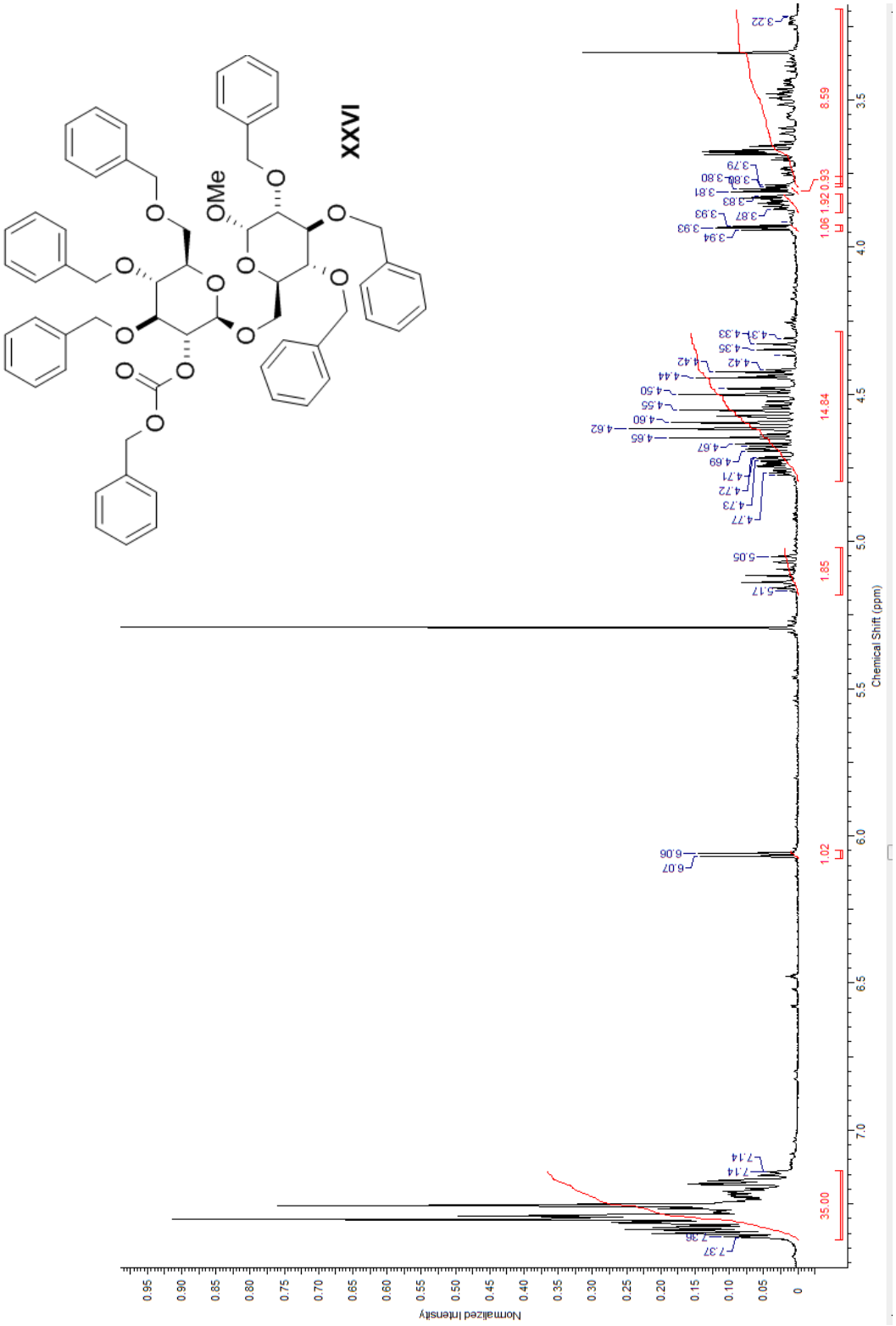
G.1.4) HSQC (400MHz, d_6-acetone)



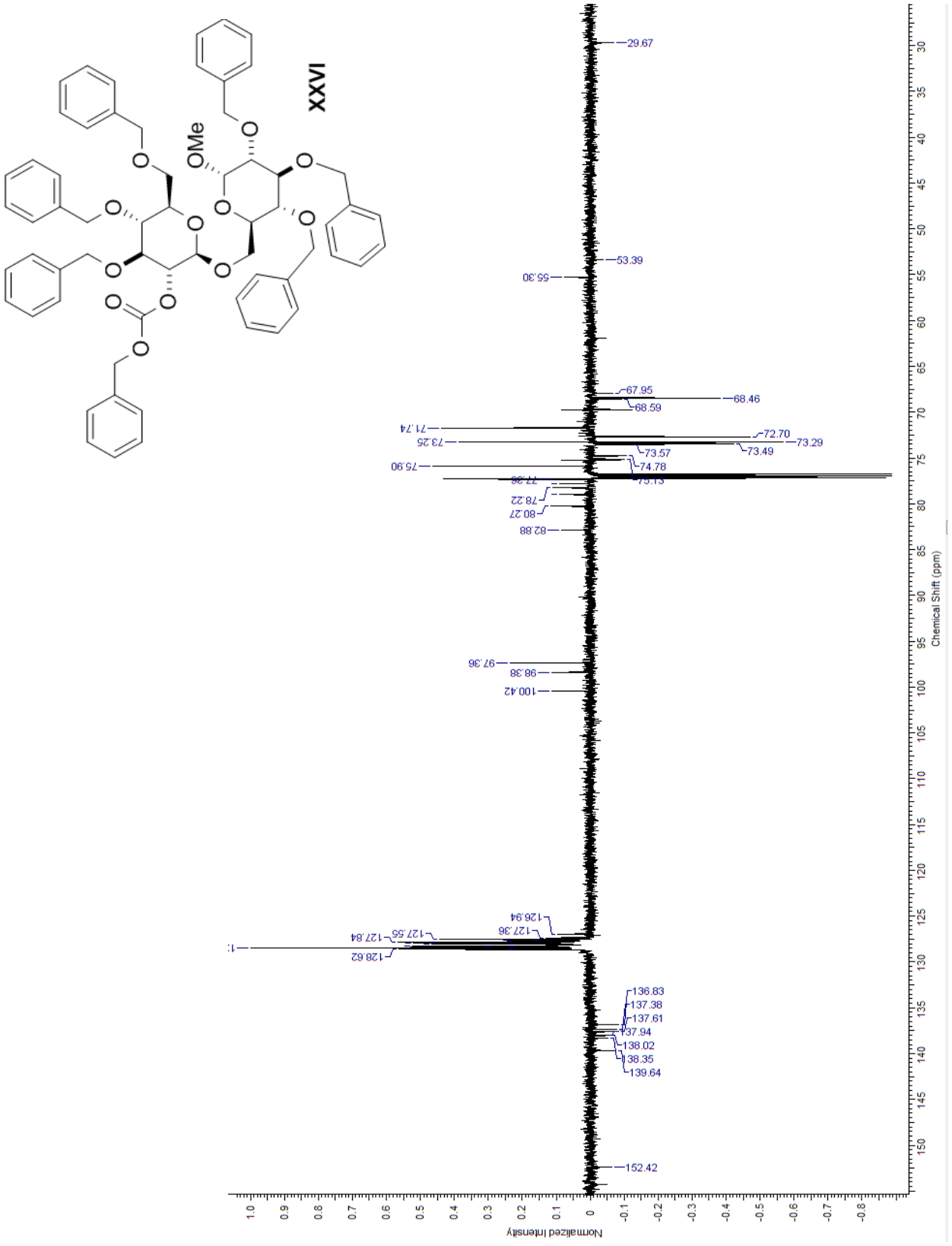
XXI

G.2) NMR-spectra of 3,4,6-Tri-O-benzyl-2-O-benzyloxycarbonyl-β-D-glucopyranosyl-(1→4)- 2,3,6-tri-O-benzyl-1-O-methyl-α-D-glucopyranose (XXVI)

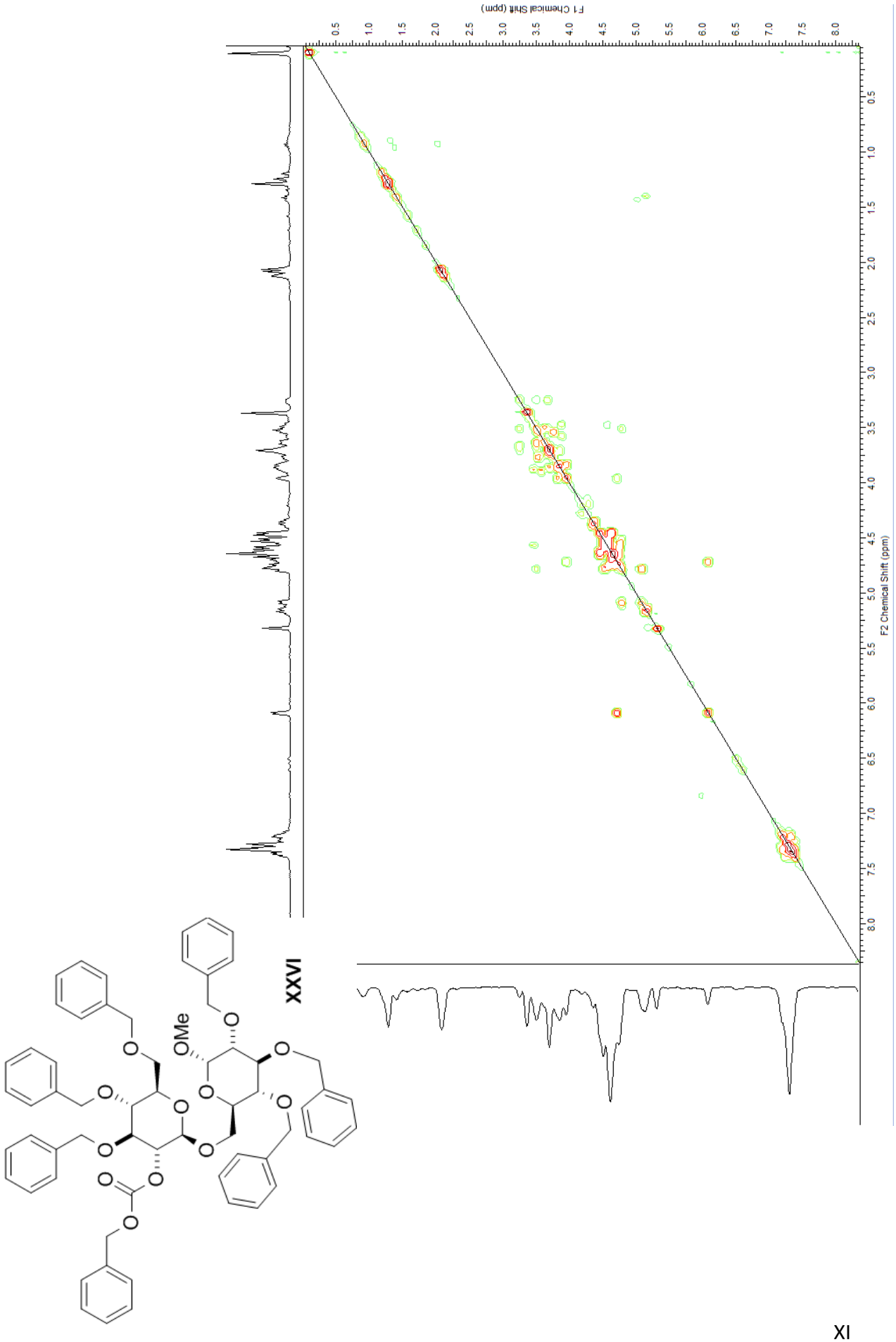
G.2.1) ^{1}H-NMR (600MHz, CD_2Cl_2)



G.2.2) ^{13}C-NMR (150MHz, CD_2Cl_2)

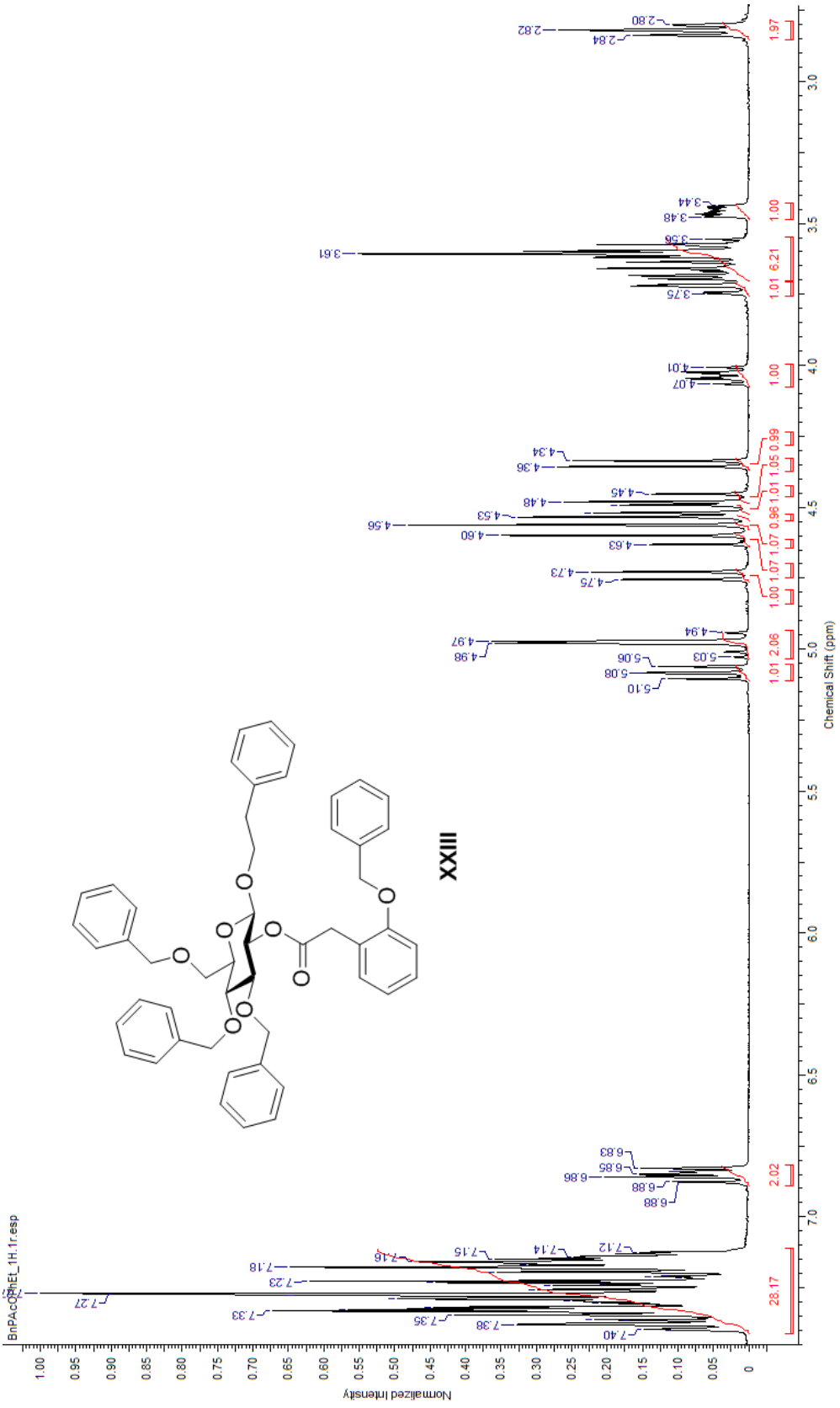


G.2.3) H,H-COSY (600MHz, CD_2Cl_2)

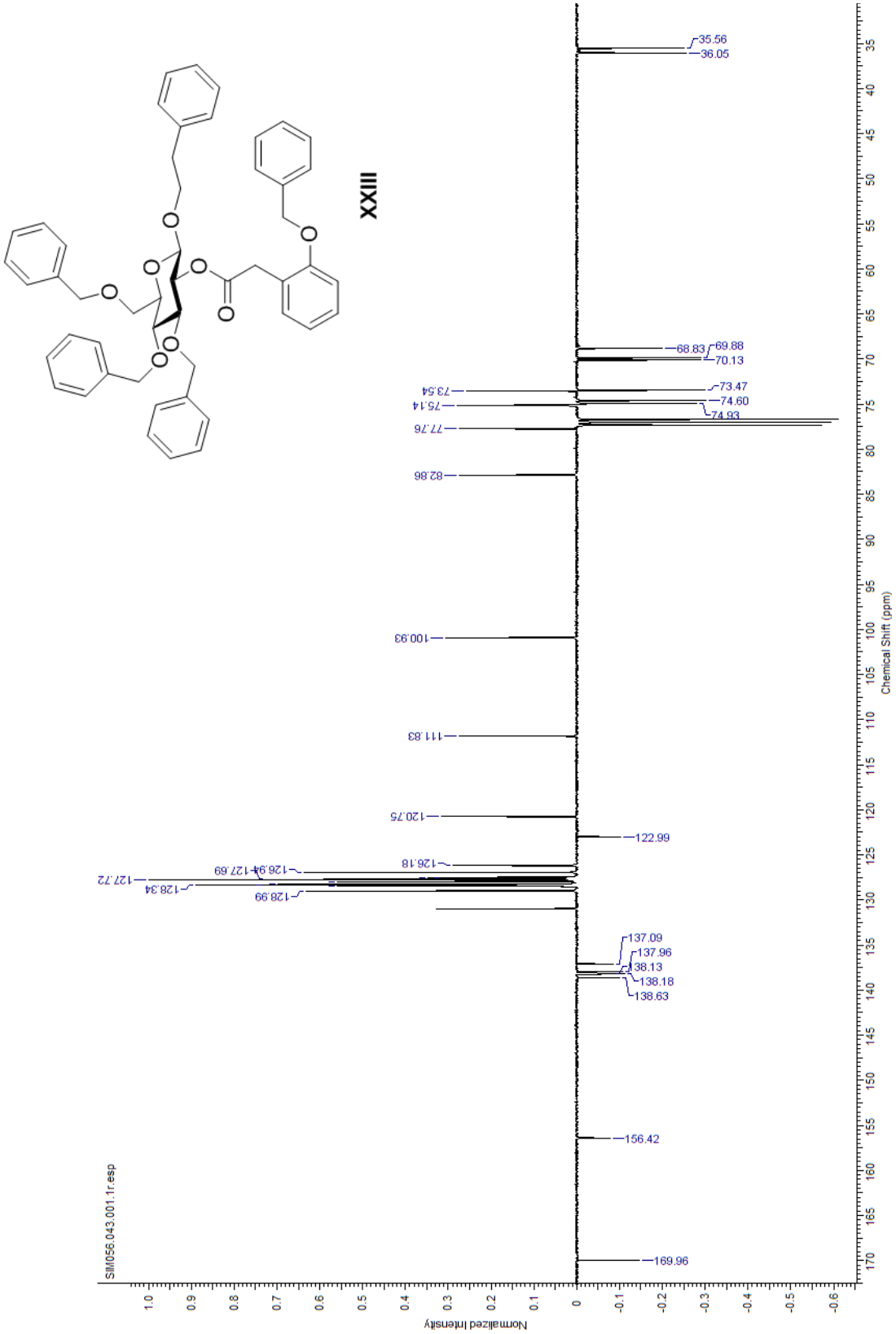


G.3) NMR-spectra of 2-Phenylethyl 3,4,6-tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-D-glucoside (XXIII)

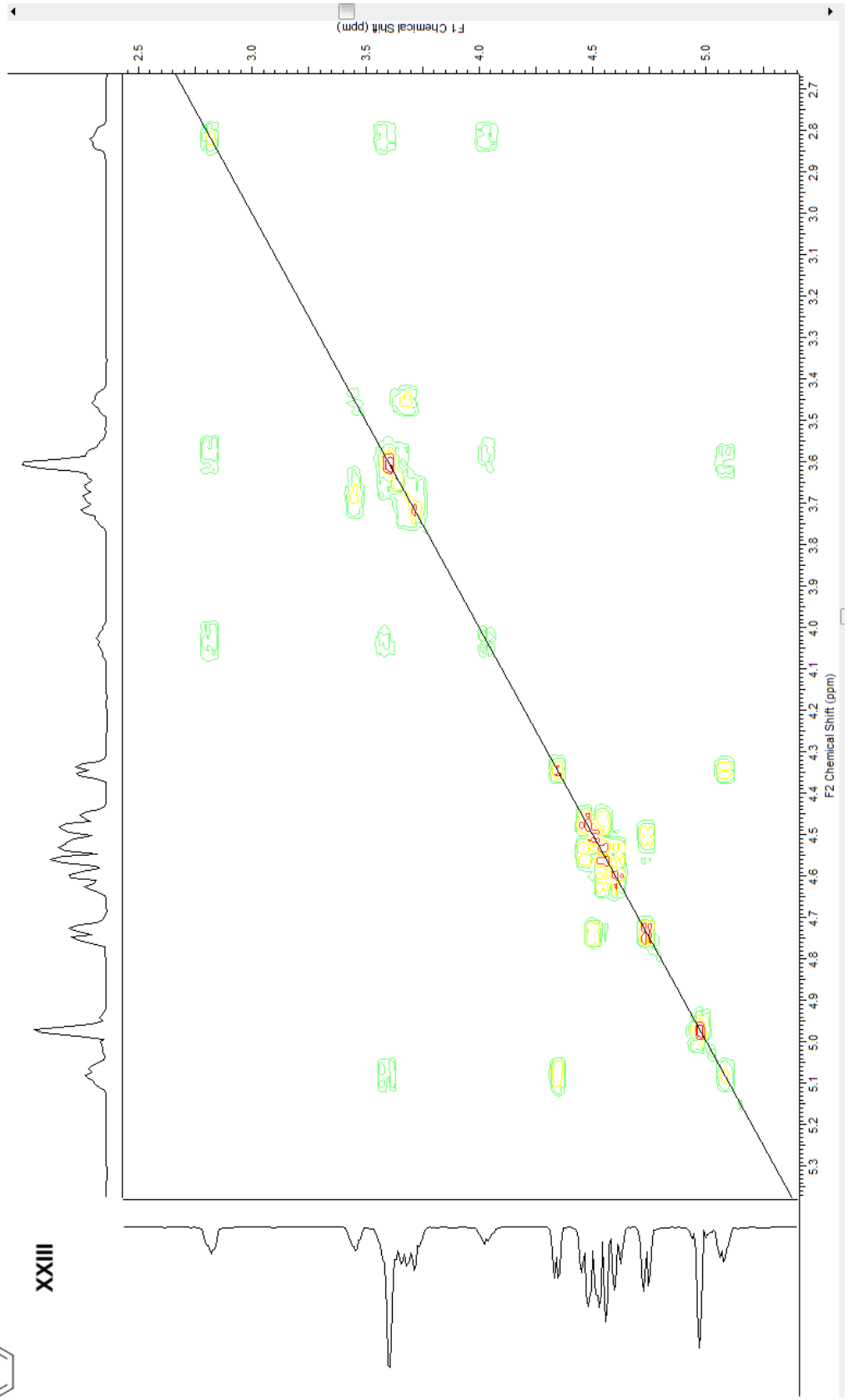
G.3.1) ^{1}H-NMR (400MHz, $CDCl_3$)

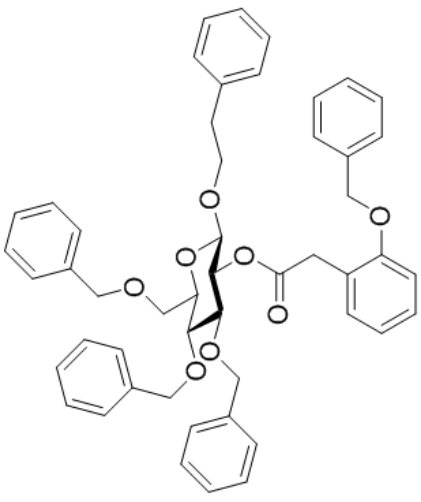


G.3.2) ^{13}C-NMR (100MHz, $CDCl_3$)



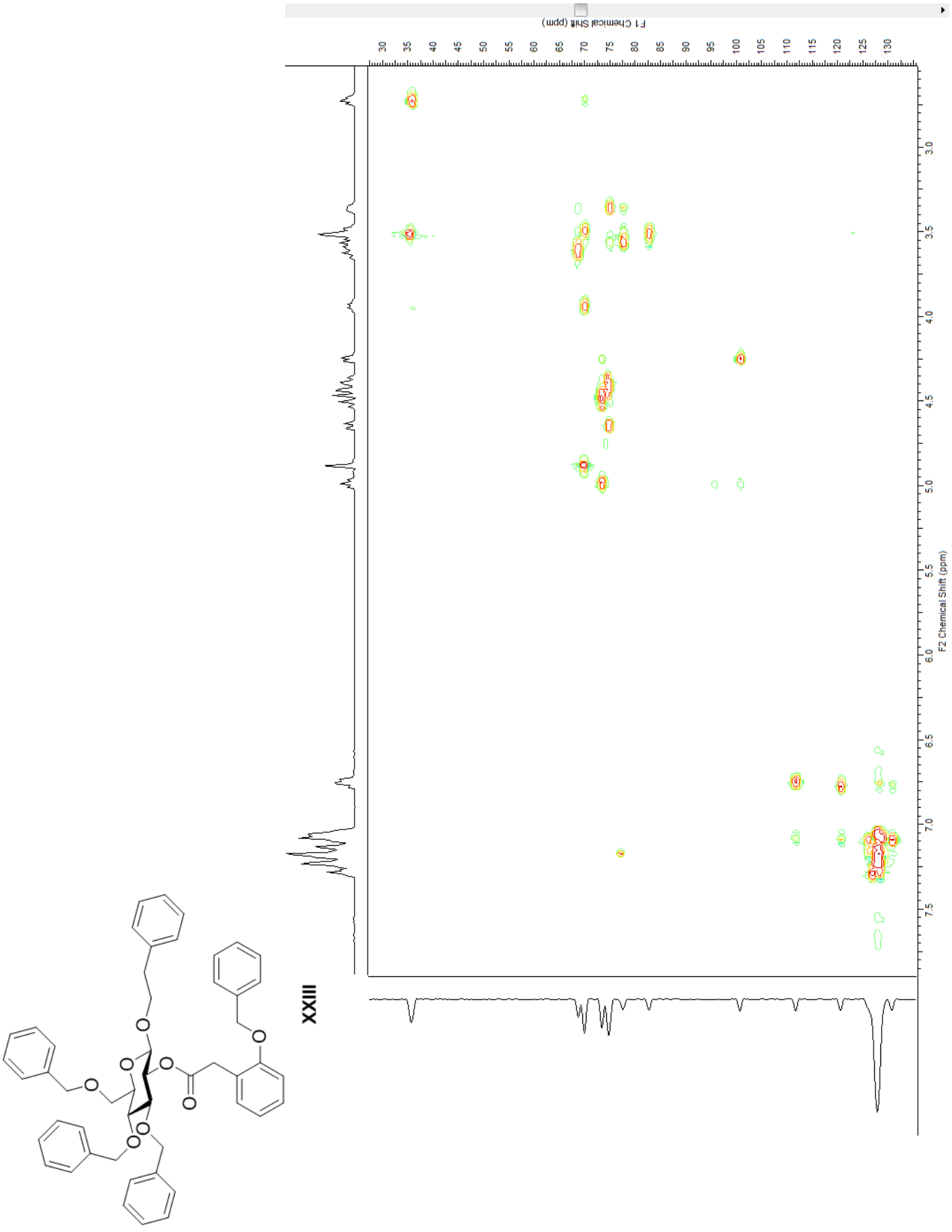
G.3.3) H,H-COSY (400MHz, $CDCl_3$)





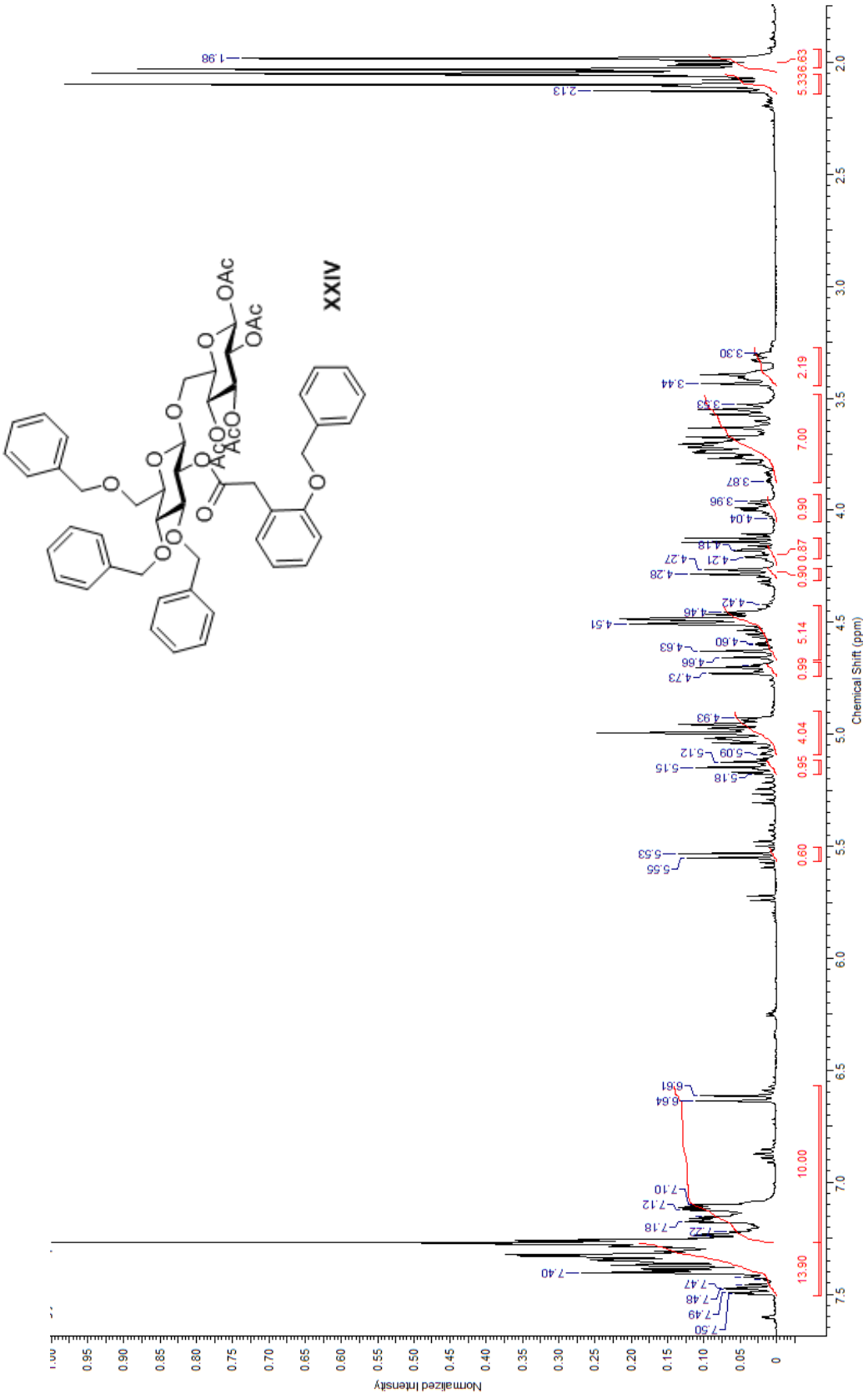
XXIII

G.3.4) HSQC (400MHz, $CDCl_3$)

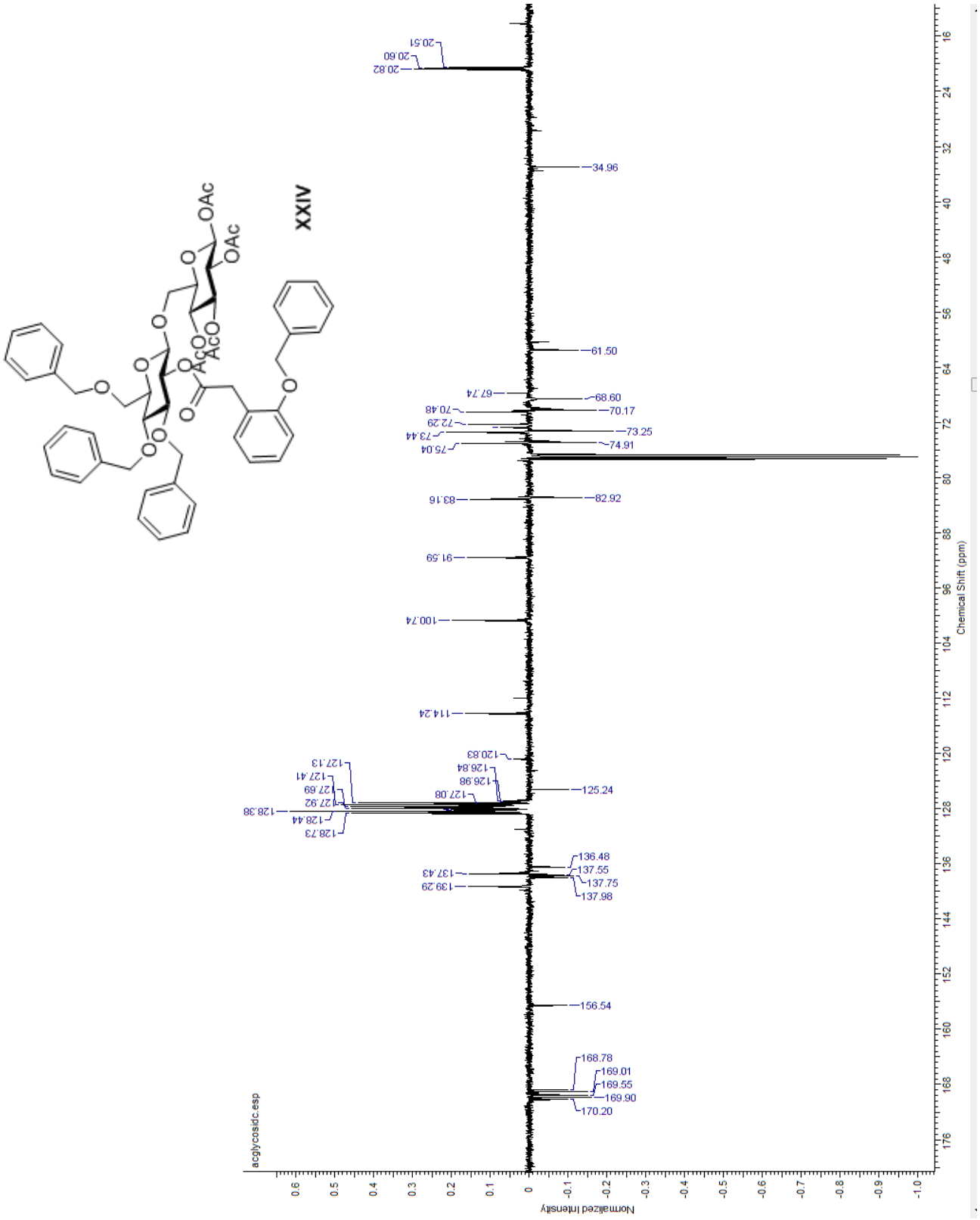


G.4) NMR-spectra of 3,4,6-Tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)- β-D-glucopyranosyl-(1→6)-1,2,3,4-tetra-O-acetyl-β-D-glucopyranose (XXIV)

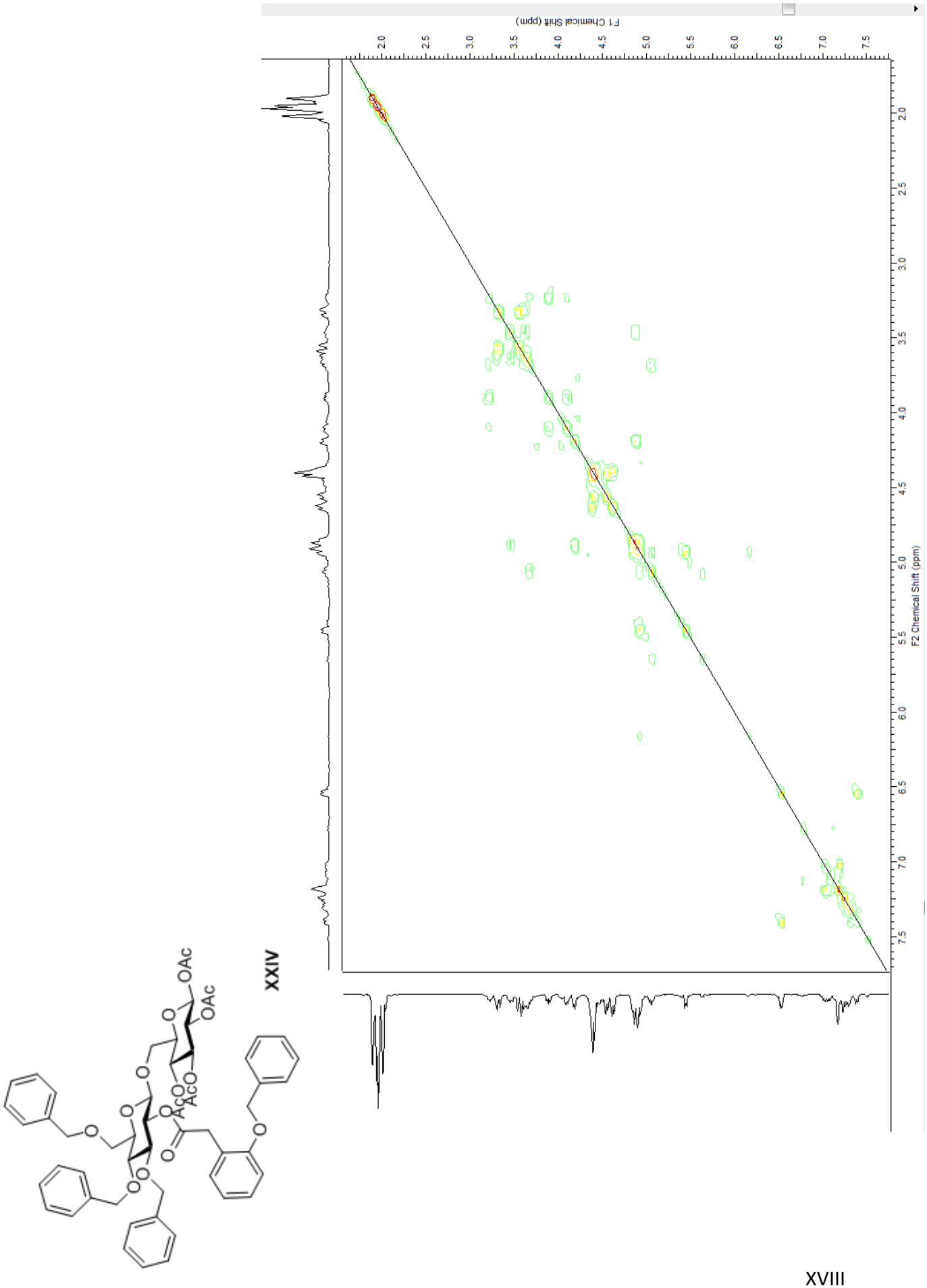
G.4.1) ^{1}H-NMR (400MHz, $CDCl_3$)



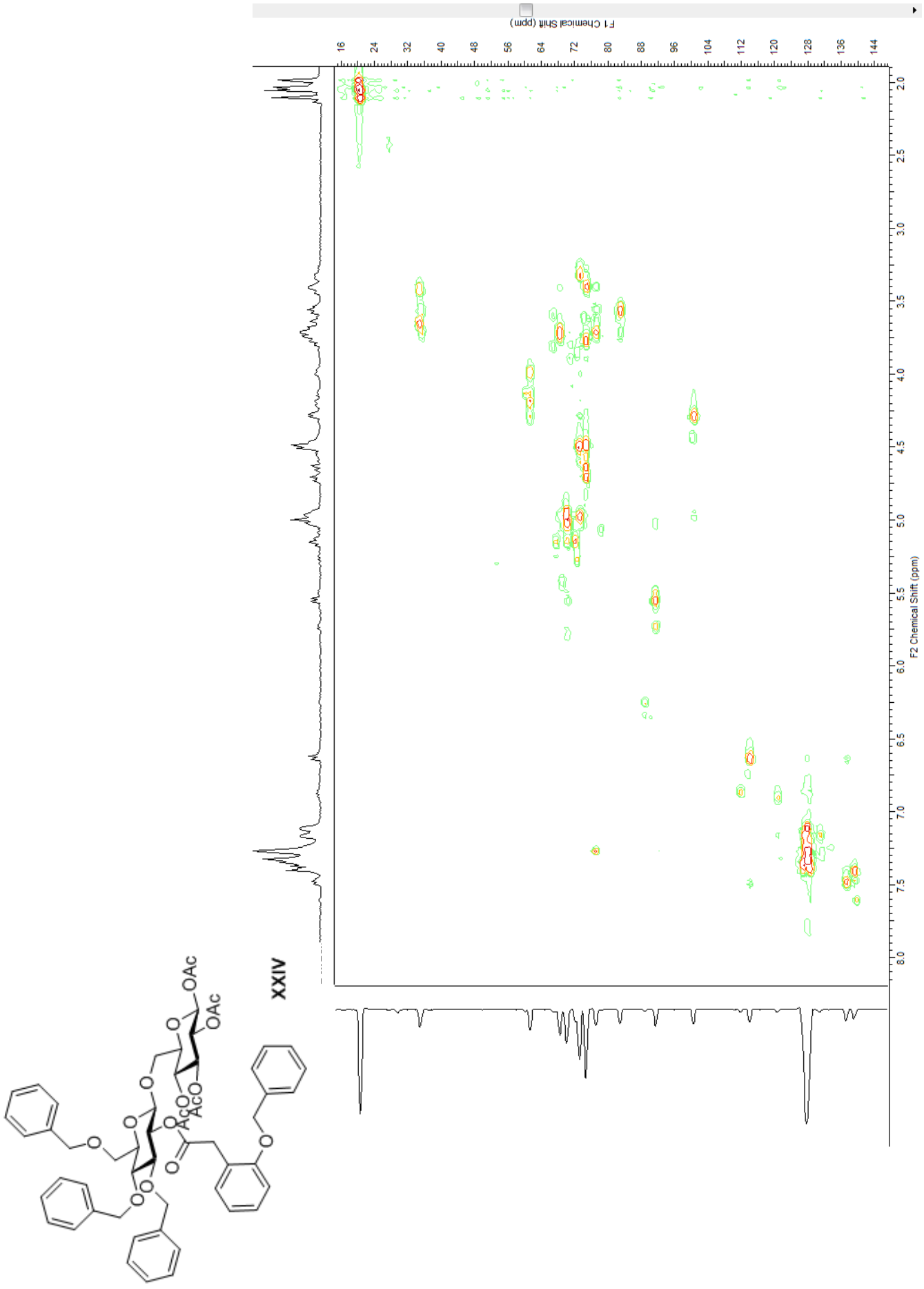
G.4.2) ^{13}C-NMR (100MHz, $CDCl_3$)



G.4.3) H,H-COSY (400MHz, $CDCl_3$)

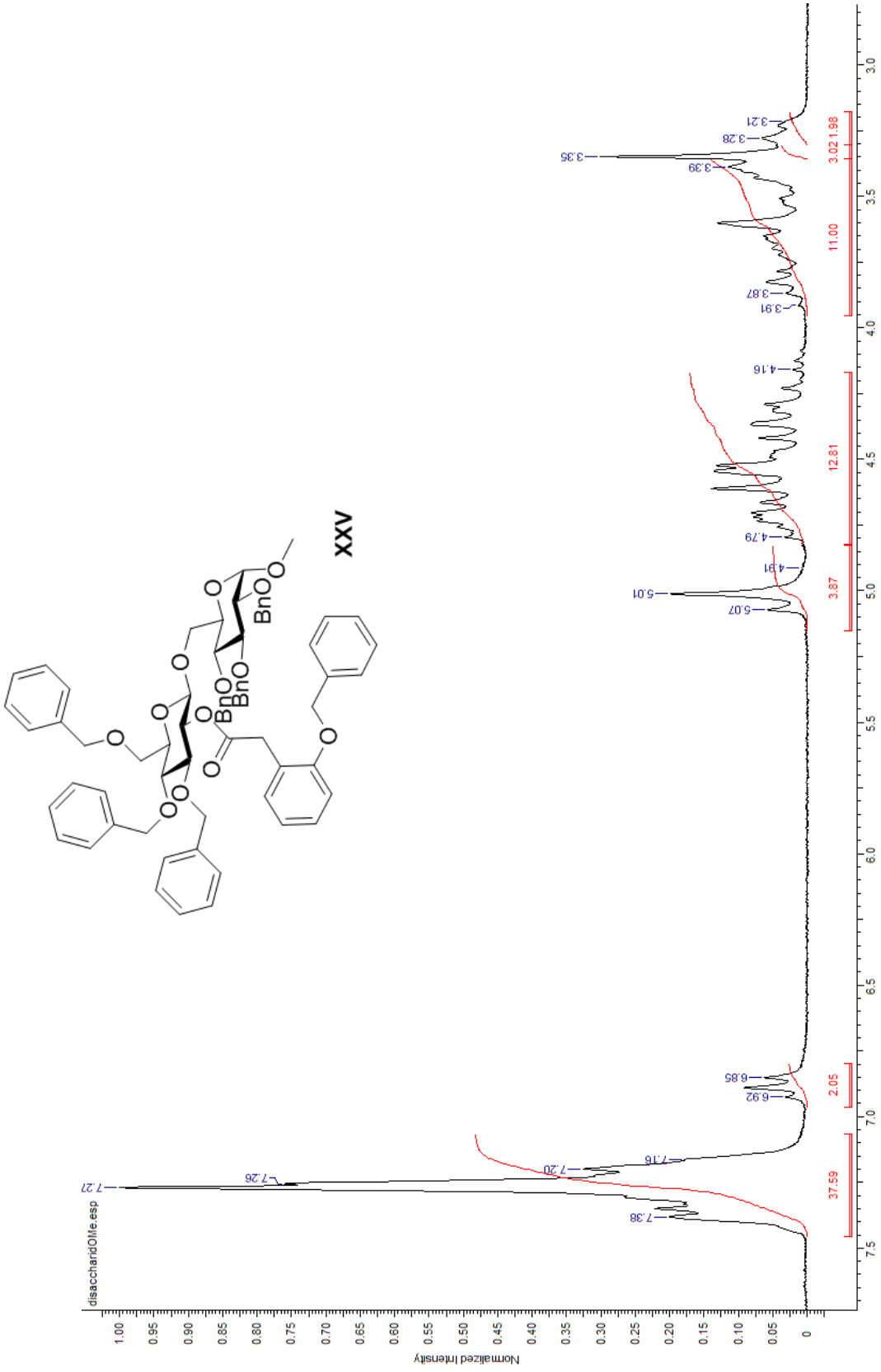


G.4.4) HSQC (400MHz, $CDCl_3$)



G.5) NMR-spectra of 3,4,6-Tri-O-benzyl-2-O-(2-(2-benzyloxyphenyl)acetyl)-β-D-glucopyranosyl-(1→4)- 2,3,6-tri-O-benzyl-1-O-methyl-α-D-glucopyranose (XXV)

G.5.1) ^{1}H-NMR (200MHz, $CDCl_3$)



G.5.2) ^{13}C-NMR (50MHz, $CDCl_3$)