Solid-Phase Assisted Synthesis of Glycoconjugates, and Synthesis of ^{15}N-labelled Aminoglycosides

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Abstract

Janis Jaunzems

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Key words: glycoconjugates – glycosidation – polymer-assisted synthesis – olefin metathesis macrocyclisation – aminoglycosides

During the first part of this Ph. D. work, studies on the polymer-assisted synthesis of deoxyoligosaccharides and glycoconjugates were carried out. Here, their preparation on a polymer-support in direct comparison with solution-phase glycosidation using polymer-bound catalysts and reagents were carried out. In the second part of this work, synthetic approaches towards new artificial macrocyclic aminoglycosides with nucleic acid binding properties were developed. Particular focus was put on the synthesis of their ^{15}N-labelled analogues. Various 2-deoxyglycoconjugates were prepared on a new polystyrene resin which contains a silyl linker system. Glycals were employed as glycoside donors. This polymer showed excellent properties for non-destructive reaction monitoring using the gel-^{13}C-NMR technique. In a comparative study 2-deoxy glycoconjugates were prepared in excellent yields in solution using polymer-supported catalysts. The common Ferrier type side reactions were suppressed to a minimum which allowed to apply this approach for automated parallel glycoconjugate and oligosaccharide synthesis. Using 2-deoxythioglycosides as valuable glycosyl donors, two rapid and highly efficient glycosidation methods in solution were developed, utilizing new polymer-bound iodo(I)bistrifluoracetate and selectfluor™ as thiophilic promoters. Diphenyl disulphide liberated during the glycosidation process can quantitatively be removed by the first scavenging protocol for this purpose using polymer-supported borohydride in *iso*-propanol. Employing the elaborated orthogonal glycosidation strategy, a small library of various 2-deoxyoligosaccharides and glycoconjugates was synthesized with potential biological properties.

In the synthesis of new macrocyclic aminodeoxysaccharides allyl glycosides were employed in the olefin metathesis homodimerisation reaction. The amine function was introduced with high degree of stereo-selectivity by carrying out reductive amination on uloside using benzyl amine or ammonium acetate as nitrogen source. Olefin metathesis macrocyclisation proceeded in a highly diluted solution to avoid unfavored polymerizations. ^{15}N-labelled ammonium acetate was utilized in a elaborated reductive amination procedure to introduce ^{15}N into homodimeric uloside. The ^{14}N- and ^{15}N-labelled macrocyclic aminodeoxysaccharides obtained form tight complexes with TAR-RNA (HIV-1) and are therefore good tools for the evaluation of these complexes using NMR spectroscopy.

Zusammenfassung

Janis Jaunzems

Festphasen unterstützte Synthese von Glycoconjugaten und Synthese von ^{15}N-markierten Aminoglycosiden

Stichwörter: Glycokonjugate – Glycosidierung – Polymerunterstützte Synthese – Olefinmetathese – Makrocyclisierung – Aminoglycoside

Im ersten Teil der vorliegenden Dissertation wurden Untersuchungen zur polymerunterstützten Synthese von Desoxyoligosacchariden und Glycokonjugaten durchgeführt. Die Darstellung an der festen Phase wurde hierbei der Glycosidierung in Lösung unter Verwendung von polymergebundenen Katalysatoren und Reagenzien gegenübergestellt. Der zweite Teil dieser Arbeit richtete sich an die Synthese von neuen künstlichen makrocyclischen Aminoglycosiden, welche Nukleinsäure-Bindungsaffinitäten aufweisen. Besonderes Interesse wurde auf die Darstellung der ^{15}N-markierten Analoga gesetzt. Verschiedene 2-Desoxyglycokonjugate wurden auf einem neuen Polystyrolharz mit Silyl-Linkersystem hergestellt, wobei Glycale als Glycosiddonoren eingesetzt wurden. Dieses Polymer eignet sich hervorragend für die nichtzerstörende Reaktionskontrolle mittels Gel-^{13}C-NMR-Technik. In einer vergleichenden Studie wurden 2-Desoxyglycokonjugate in exzellenter Ausbeute unter Verwendung von polymerunterstützten Katalysatoren hergestellt. Die herkömmlichen Nebenreaktionen vom Ferriertyp wurden auf ein Minimum reduziert, so daß dieser Ansatz die automatisierte Parallelsynthese von Glycokonjugaten und Oligosacchariden erlaubte. Unter Verwendung von 2-Desoxythioglycosiden als nützliche Glycosyldonoren wurden zwei schnelle und hocheffiziente Glycosidierungsmethoden in Lösung entwickelt, welche das neue polymergebundene Iod-(I)-bistrifluoracetat und Selectfluor™ als thiophile Reagenzien benutzen. Das während der Glycosidierung freigesetzte Diphenyldisulfid kann quantitativ beseitigt werden durch das erste Abfangprotokoll für diesen Zweck, in welchem polymergebundenes Borhydrid in *iso*-Propanol eingesetzt wird. Durch Einsatz dieser ausgearbeiteten orthogonalen Glycosidierungsstrategie wurde eine kleine Bibliothek von verschiedenen 2-Desoxyoligosacchariden mit möglicher biologischer Aktivität synthetisiert.

Bei der Synthese von neuen makrocyclischen Aminodesoxysacchariden wurden Allylglycoside für die Homodimerisierung durch Olefinmetathese eingesetzt. Die Aminofunktion wurde mit hoher Stereoselektivität durch reduktive Aminierung an Ulosid mit Benzylamin oder Ammoniumacetat als Stickstoffquelle eingeführt. Die Olefinmetathesen zur Makrocyclisierung wurde in einer hochverdünnten Lösung durchgeführt, um unerwünschte Polymerisationsprodukte zu vermeiden. ^{15}N-markiertes Ammoniumacetat wurde in dem ausgearbeiteten reduktiven Aminierungsprotokoll verwendet, um ^{15}N in homodimeres Ulosid einzuführen. Die erhaltenen ^{14}N- und ^{15}N-markierten makrocyclischen Aminodesoxysaccharide bilden starke Komplexe mit TAR-RNA (HIV-1) und sind aus diesem Grunde nützliche Werkzeuge für die Untersuchung dieser Komplexe mittels NMR-Spektroskopie.

Contents

Abbreviations

abs.	absolute
Ac	acetyl
Bn	benzyl
Bu	butyl
Bz	benzoyl
Bn	benzyl
CSA	DL-camphersulfonic acid
CAN	ceric ammonium nitrate
CM	cross metathesis
CoA	coenzyme A
COSY	correlation spectroscopy
Cy	cyclohexyl
d	day(s)
DEPT	distortionless enhancement by polarization transfer
DIBAL	di*iso*butylaluminium hydride
DMAP	4-*N*,*N*-dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
DMTST	dimethyl(methylthio) sulfoniumtrifluoromethane sulfonate
eq.	equivalent
DNA	desoxyribonucleic acid
Et	ethyl
GC	gas chromatography
h	hour(s)
HIV	human immunodeficiency
HMQC	heteronuclear multiple quantum coherence
HPLC	high pressure liquid chromatography
IDCP	iodoniumdi-collidinperchlorat
IR	infrared spectroscopy
L	ligand
LiHMDS	lithium hexametyldisilazan
M	molecular ion
Me	methyl
Min	minute(s)
Ms	methanesulfonyl
MS	mass spectrometry or molecular sieves
NBS	*N*-bromsuccinimide
NIS	*N*-iodsuccinimide
NMR	nuclear magnetic resonance
NOE	nuclear overhauser enhancement
PE	petrol ether
Ph	phenyl
Piv	pivaloyl
Pr	propyl
Py	pyridine
RCM	ring closing metathesis
R_f	retention factor
RT	room temperature
TAR RNA	trans-activation response region
TASF	tris-(dimethylamino)-sulfur-(trimethylsilyl)-difluoride
TBAF	tetrabutylammonium floride
TBDPS	*tert*-butyldiphenylsilyl
TBS	*tert*-butyldimethylsilyl
t-Bu	*tert*-butyl
TES	triethylsilyl
Tf	trifluoromethylsulfonyl
Tfa	trifluoroacetyl
THF	tetrahydrofurane
THP	tetrahydropyrane
t.l.c.	thin layer chromatography
TMS	tetramethylsilyl
TMSOTf	trimethylsilyl trifluoromethanesulfonate
TOCSY	total correlation spectroscopy
Ts	toluol-4-sulfonyl

1. Introduction

1.1. Natural products and their role in human history and today

The first records on the use of natural products in form of plants to treat diseases can be dated back as early as 2700 B.C. in China, in the time of the Emperor Shennung. The Ebers papyrus describes a variety of plants used in the Egyptian medicine at about 1550 B.C. But plants were not only used as curatives. On Sumerian tablets that can be dated back to 3500 B.C. narcotic activity of *Papaver somniferum* was noted, making the Opium alkaloids to one of the oldest known drugs. Seminal from *Cannabis* were used during Skytten's steam-bath rituals as narcotic; the poisoning effect of deadly nightshade and henbane was well known. All kinds of biological effects were regarded as spiritual and attributed to divinity, and frequently some or other "magical recipes" were ascribed together with a certain folk. The first scientific classification of plants is dated back to 370-285 B.C. by Theophrastus, and three hundred years later Dioscorides in "de materia medica" (77 AD) described the use of more than 600 plants in medical and other use. Around this time and later chemistry or "Alchemy" was mostly based on chaotic experiments with common substances by means of distillations and sublimations. The alchemists efforts were directed to obtain the elixir of life or gold from lead. For more than 500 years much of the medicinal knowledge in Europe was centered in the Church, and only after the invention of the printing press (1500's AD) , herbal medicine became commonly available to the common people. Only in the 19th century prompted partly by Friedrich Wöhler's synthesis of urea (1828), organic chemistry gained its rapid growth. Urea synthesis overturned the belief that only living organisms could produce organic molecules. Robert Koch discovered microorganisms and disclosed (1876) some microorganism ability to cause infectious diseases. One year later Louis Pasteur reported that the bacterial disease anthrax, which can cause respiratory failure, could be overcome harmless in animals with the injection of soil bacteria. While at the end of the 19^{th} century some antibiotics were known, they were not being developed into an effective drug until the British scientist Alexander Flemings discovered in 1928 another antibacterial agent. Fleming observed bacterial cell lysis occurring in an area adjacent to a contaminant *Penicillium* mold growing on the plate. In fact he

rediscovered Penicillin, since more than thirty years earlier a French student Ernest Duchesne observed antibiotic properties of *Penicillium,* but was not able to resolve the connection between the fungus and the active substance. 1939 Howard Florey, Ernst Chain, and Norman Heatley obtained the *Penicillium* fungus from Fleming and were able to isolate *Penicillin* G in pure form. By 1946, *Penicillin* became widely distributed in clinics. *Penicillin* bioactivity is based on the beta-lactam ring opening followed by the irreversible covalent binding on the active site of the enzyme transpeptidase, which cross connects polysaccharide chains forming the bacterial cell walls. Thereby bacterial cell walls get structurally weak causing cell lysis. Fleming's invention was the first step in the beginning of the antibiotic era.

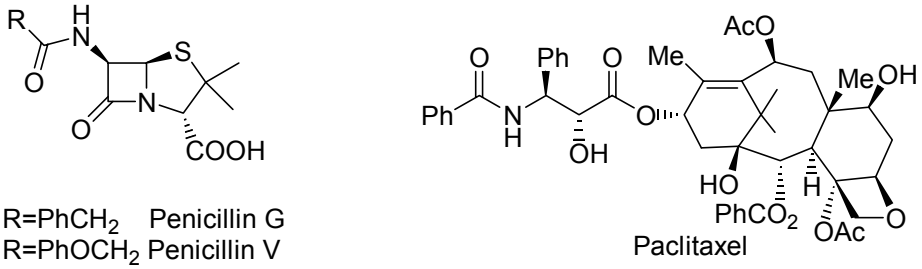


Figure 1

Many natural products that show medicinal properties or biological activity fall in the general class of terpenes. These compounds are made up from five-carbon (isoprene) units, put together in a regular pattern and often joined in a head-to-tail manner in terpenes up to 25 carbons. Head-to-head dimers are also common consisting from 30 and more carbons. Today one of the best known terpenoid with anticancer activity is Taxol®, first isolated from the bark of the Pacific yew *Taxus brevifolia* in the early 1960's. Taxol® stabilizes the mitotic apparatus in cells that suppresses rapid proliferation causing them to act as normal cells. Steroids, an another class of terpenes, are modified triterpenes that are one of the important natural products in human life. They are often familiar as androgens (testosterone) and estrogens (progesterone) due to their role as hormones. Steroid hormones are formed in the testicle, adrenal cortex and ovary; their main role in the organism is development of the sexual character, reproduction and metabolism. Another group of steroidal terpenes are cardiac glycosides that were firstly isolated from *Nerium Oleander* and different types of digitalis-foxglove plants. They exert a positive inotropic effect (increase myocardial contractility), negative chronotropic effect

(heart rate lowering), negative dromotropic effect (impede stimulus conduction), and positive bathmotropic effect (promote myocardial excitability). One of the best known cardiac glycoside is Digitoxin **2** which demonstrates also cytotoxic effect on some human tumor cells. It blocks cell proliferation and can introduce apoptosis in several malignant cell lines.

A great part of diseases is caused by insufficiency or excess of some specific metabolites in a living organism. These biologically active substances can originate from bacteria or viruses, or can be produced by organisms itself in some anomalous metabolism pathways. Enzymes are complex organic molecules that catalyses almost all synthetic and regulatory processes in living organisms. The enzyme activities can be suppressed or inhibited by specific metabolites or drugs. In case of malignant bacteria, viruses or cancer cells some essential enzyme inhibition can cause the termination of important metabolic processes leading to growth or replication slowdown or stop. Inhibition of bacterial Alanin-Racemase, which catalyzes the biosynthesis of specific peptidosaccharides, leads to the inhibition of bacterial cell wall synthesis. This is one example of many how humans fight with various diseases.[1e-s]

1.2. Antibiotic resistance

Already in the year 1945, Fleming reported about possible formation of resistant forms of bacteria in case of misuse of *Penicillin*. But not earlier than 1970s antibiotic resistance was considered to be a real threat, when cases of deaths from strains of bacteria that cause meningitis and gonorrhea were registered after 30 years of successful treatment of these infections. Bacteria can acquire resistance on specific or classes of antibiotics through random bacterial DNA mutations that can result in the formation of new resistance strains. These mutations are then inherited to all of the bacterial progeny resulting from the mutated cells. Among this vertical evolution, bacteria frequently undergo horizontal evolution where nearby bacteria cells can process gene exchange by transduction, transformation and conjugation mechanisms. Thus transferred genes can be incorporated into the bacterial genome forming new genotypes by a process known as genetic recombination. Resistance genes protect bacteria against the inhibitory effects of antibiotics by producing enzymes degrading antibiotics, by altering common

antibiotic binding sites on the bacteria cell or in other ways avoiding antibiotics to affect normal bacteria's metabolism. The fight between medicinal chemistry and bacteria still continues today: scientists develop new antibiotics or modify natural antibiotics that can be inert against bacteria defense; at the same time bacteria demonstrate constantly growing resistance against various antibiotics even against whole antibiotic classes. Many antibiotics that are widely used for a half of a century are now inactive against the designated bacterial infections leaving humanity with few still effective medicines. For how long more this will be the case is still unclear.[1e-s]

1.3. Carbohydrates and their role in biological processes

Already for more than a century carbohydrates and their chemistry have engaged the minds and hearts of many scientists and persist to be both dynamic and challenging. Carbohydrates can be found as monomers (glucose, fructose), oligomers, or polymers (starch, cellulose), or as components of biopolymers (RNA, DNA) and other naturally occurring substances. Prior to the recognition of the role of carbohydrate in biological processes, it seems that most oligomeric and polymeric carbohydrates rather play roles as structural and food storage elements, whereas the other main polymeric natural compounds, such as RNA, DNA and proteins, were left to control the complex functioning of organisms. Increased awareness of the vital biological roles exerted by oligosaccharides has led to an expanding interest and appreciation for those structures. These complex biomolecules, in the form of glycoprotein and glycolipid conjugates, carry detailed structural information and serve as mediators in a variety of biological events including imflammation,[1a-d] immunological response,[2] metastasis,[3] fertilization,[4] and many other biologically important processes.[5] Some cell surface carbohydrates are specific markers for certain types of tumors[6] while others function as binding sites for other substances, including bacterial and viral patogens.[7]

Deoxysugars are widely distributed in plant and animal species either as single structural elements or as components of oligosaccharides in antibiotic and anticancer agents such as erythromycin A **1** and altromycin B **3**, cardiac glycosides such as digitoxin **2** and others. (Figure 2) Kennedy and White[8a] listed more than a

hundred various naturally occurring deoxymonosaccharides. In glycoconjugate based natural products the deoxysugar moiety can be O- or C- glycosidically attached to the aglycone. Among the great diversity of glycoconjugates different macrolactones, peptides, steroids or oligoaromatic moieties can be found as aglycon parts. In many cases, the deoxysugar fragment in the glycoconjugate is vital for the bioactivity. Therefore, varying the sugar portion of the glycoconjugate or constructing fully new artificial fragments, may lead to new or improved bioactivity in various therapeutic areas[8b].

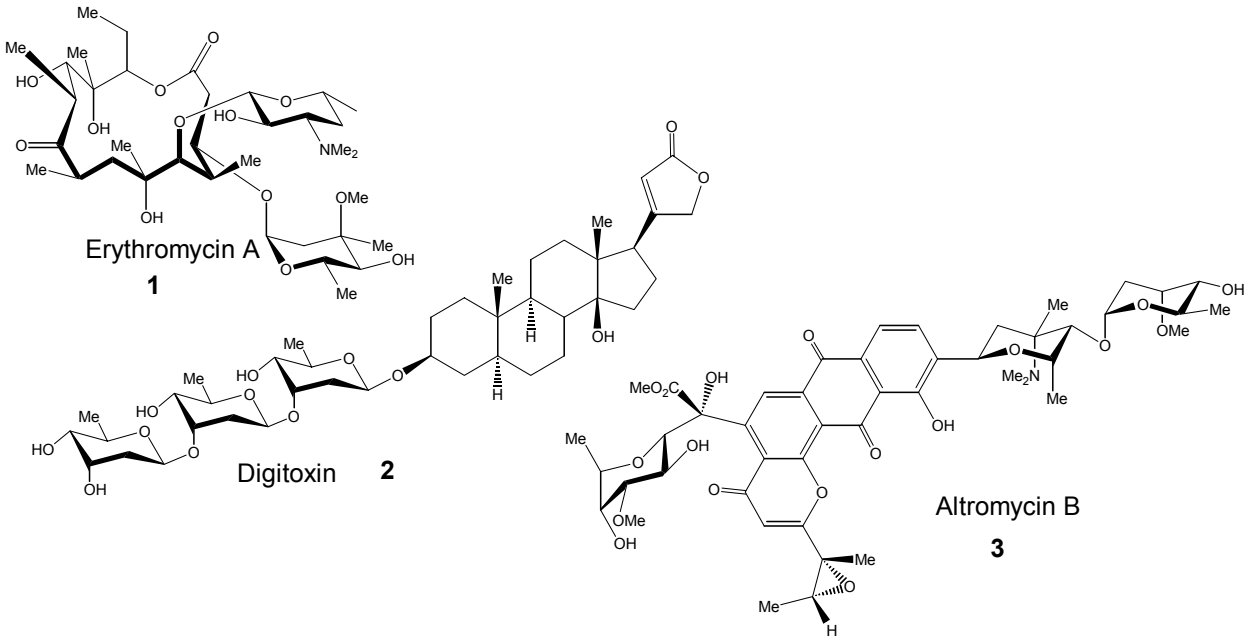
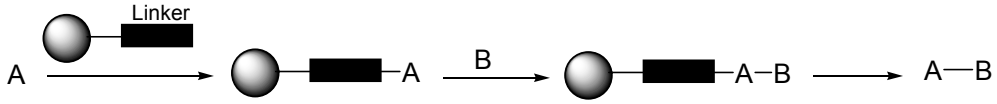


Figure 2 Structures of some glycoconjugate-based natural products

2. Polymer-supported synthesis of oligosaccharides

The preparation of biologically important oligosaccharides and glycoconjugates typically requires multistep transformations involving iterative protection-glycosidation-deprotection steps with chromatographic purification of intermediates at each stage of the synthesis. Such preparations could greatly benefit from developments in polymer-supported oligosaccharide synthesis. (Scheme 2)



Scheme 2 Polymer-bound synthesis

Seven years after the development of *Merrifield's* peptide synthesis[9] on solid support, *Frechet*, *Schuerch*,[10] and other scientists undertook pioneering efforts to investigate possibilities of polymer-supported oligosaccharide synthesis. Their attempts were impeded by lack of the suitable glycosylating activators that would be compatible with the special demands of solid-phase synthesis. Twenty years later, after substantial methodological progress in the solution-phase field was achieved which provided commodious choice of various protecting group strategies[11] and powerful glycosylation agents[12a], the interest in this field was reborn.[12b,c,d,e] In spite of many different polymer and linker systems developed so far a lot of challenges remained finding an ideal method of polymer-supported oligosaccharide synthesis. Such reactions require good swelling of the polymer by the solvent for achieving an efficient reaction. However, not all solvents that have good swelling properties are acceptable or compatible with the required glycosylation conditions. Furthermore, the problem to control the glycosidic bond geometry is still present due to limitations of solvent, glycosylating agent, and condition choice. Recently, controlled-pore glass (CPG)[13], commonly used for automated DNA synthesis, has been proposed as alternative to common polymers, because no pre-swelling is required. This removed the restrictions in the choice of solvents, however low loadings and incompatibility with silyl protecting groups widely used in sugar chemistry greatly reduces the applicability of such a method in the solid-phase synthesis area. Alternatively, various soluble polyethylene glycol (PEG)[14] resins were applied in the field of carbohydrates as polymeric carriers, but other difficulties, such as loss of material during the precipitation step after each stage of synthesis hampered further progress in this area. Nevertheless, progress in polymer-supported synthesis of oligosaccharides in the past decade is self-evident, and it is conceivable that the synthesis of simple oligosaccharide sequences may soon be automated in the similar fashion as oligonucleotides and oligopeptides.

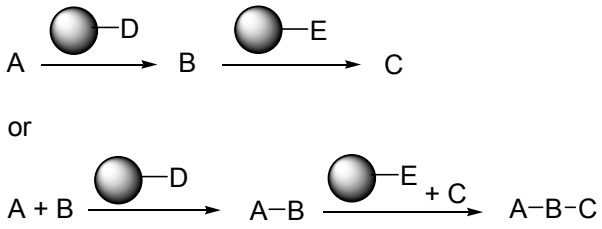
2.1. Analytical techniques

The modern organic chemist is commonly dependent on a dozen analytical techniques such as NMR spectroscopy that allow rapid analysis of the reaction process. Though, a major limitation in solid-supported oligosaccharide synthesis is associated with the difficulty in analyzing the reaction intermediates bound to the polymer. Normally, a small amount of polymer-bound intermediate or product is cleaved from the resin and analyzed using classical techniques that generally lead to product losses and require additional manipulations. Search for non-destructive and rapid analytical methods is essential for the success of solid-phase synthesis of oligosaccharides. While ^{13}C-NMR-gel spectroscopy is known in polymer-bound peptide chemistry for more than a decade[15], only recently this technique was adapted to solid-phase oligosaccharide synthesis.[16] In 1971 *Sternlicht* and co-workers[17] were the first to publish the application of ^{13}C-NMR for studying solvent swollen cross-linked polymers. In the field of solid phase peptide synthesis, *Manatt* and co-workers[15b] used ^{13}C-NMR spectroscopy to determine chlormetylation levels in cross-linked polystyrenes and investigated the application of ^{19}F-NMR to monitor peptide synthesis on a cross-linked polystyrene resin, employing fluorinated protecting groups.[15c] *Epton* and co-workers[15d] have employed gel-phase ^{13}C-NMR to characterize intermediates in peptide synthesis on a phenolic cross-linked poly(acryloylmorpholine) resin. Recently, the Magic Angle Spinning technique (HR-MAS) using high resolution probes proved to be extremely useful for the analysis of polymer-bound oligosaccharides.[18] Detailed ^{1}H-, ^{13}C and HMQC spectra could be obtained for polymer-bound intermediates. *Danishefsky* and co-workers used this technique to analyze a polymer-bound trisaccharide on Merrifield resin.[18b] However, HR-MAS technique requires special equipment which reduces broader application, therefore gel-^{13}C-NMR spectroscopy remains with its advantages and drawbacks to be the most widely used analytical tool for many chemists.

3. Polymer-assisted solution-phase synthesis

For more than thirty years polymer-supported synthesis pioneered by Merrifield dominated in polypeptide, polynucleotide and to a smaller extent also in oligosaccharide chemistry. In the shadow of solid-phase chemistry functionalized

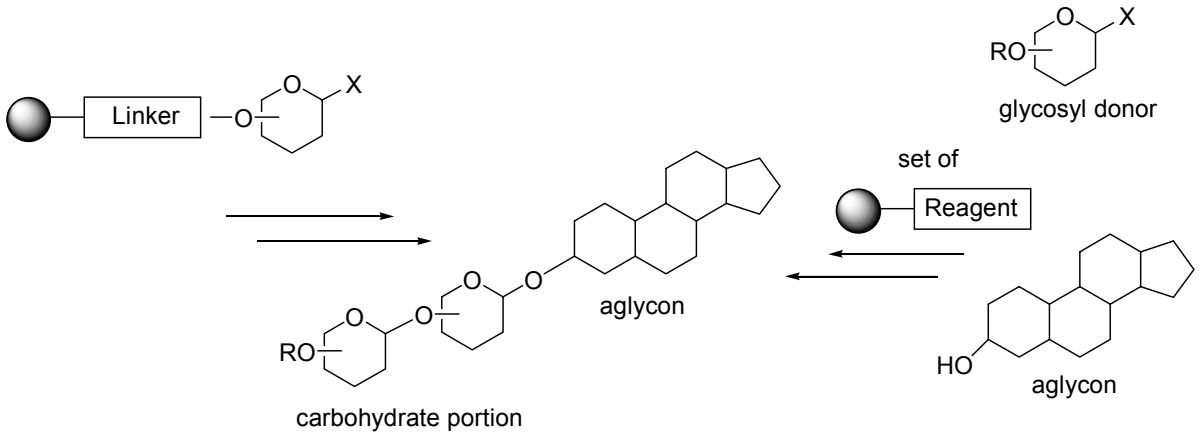
polymer techniques have developed quite slowly.[19] Recently, more and more scientific groups have recognized the value of this technique for classic solution-phase synthesis.[20] During this process the substrate remains in the solution during the whole reaction and various polymer-bound reagents or catalysts promote chemical transformations. After each step, polymer-supported reagents or catalysts were separated and only the product which could be directly used in the next step without additional purification remains in solution (Scheme 3). In fact, this approach is similar to the classical synthesis in solution and reactions can be monitored using common methods like the well known thin layer chromatography technique. The polymer-bound reagents and catalysts can be regenerated and reused again. In spite of growing interest for polymer-supported reagents, their application in sugar and oligosaccharide chemistry is scarce.[20b,21]



Scheme 3 Polymer-supported synthesis in solution

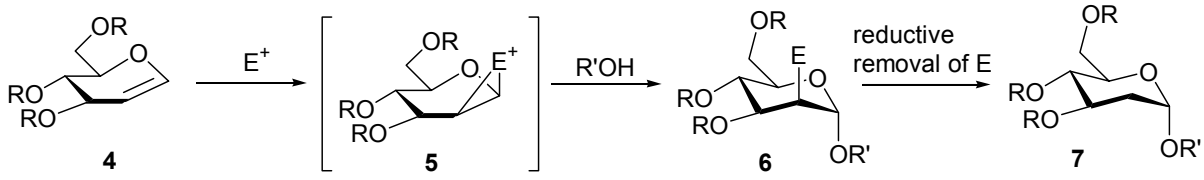
4. Objective

Polymer-supported deoxyoligosaccharide and deoxyglycoconjugate synthesis was studied in this work using a newly developed butyl diethylsilane polystyrene resin from Argonaut Technologies.[22] This resin evokes interest in several aspects: attaching of the first sugar moiety proceeds similar to classical silyl protection of alcohols; resin swelling capabilities in solvents such as dichloromethane or tetrahydrofuran is impressive (>8 ml/g); the resin contains a quite long linker which can greatly improves the option of carrying out gel-^{13}C-NMR spectroscopy. In a comparative study new polymer-supported reagents and catalysts were used to synthesize deoxyoligosaccharides and deoxyglycoconjugates in solution.



5. Polymer-supported 2-deoxyoligosaccharide and 2-deoxyglycoconjugate synthesis using PS-DES resin

Glycals can be used as classic glycosyl donors for the construction of complex glycosides and 2-deoxyglycosides. The possibility of utilizing them as glycosyl donors in 2-deoxyoligosaccharide synthesis has been demonstrated in the pioneering works of *Lemieux* and *Thiem*[23] through halonium-mediated glycosylation of the suitable acceptors. This strategy was successfully applied in 2-deoxyoligosaccharide and glycoconjugate synthesis by many other scientists.[24] Generally, I (IDCP, NIS, $PhIOAc_2$, $PhI(OCOCF_3)_2$), Br (NBS, $PhBrOAc_2$), SePh (PhSeCl) can serve as electrophiles (Scheme 4). The 2-deoxy-2-haloglycosides **6** formed can subsequently be reduced with various reducing agents (H_2/Pd, Bu_4SnH, AIBN).

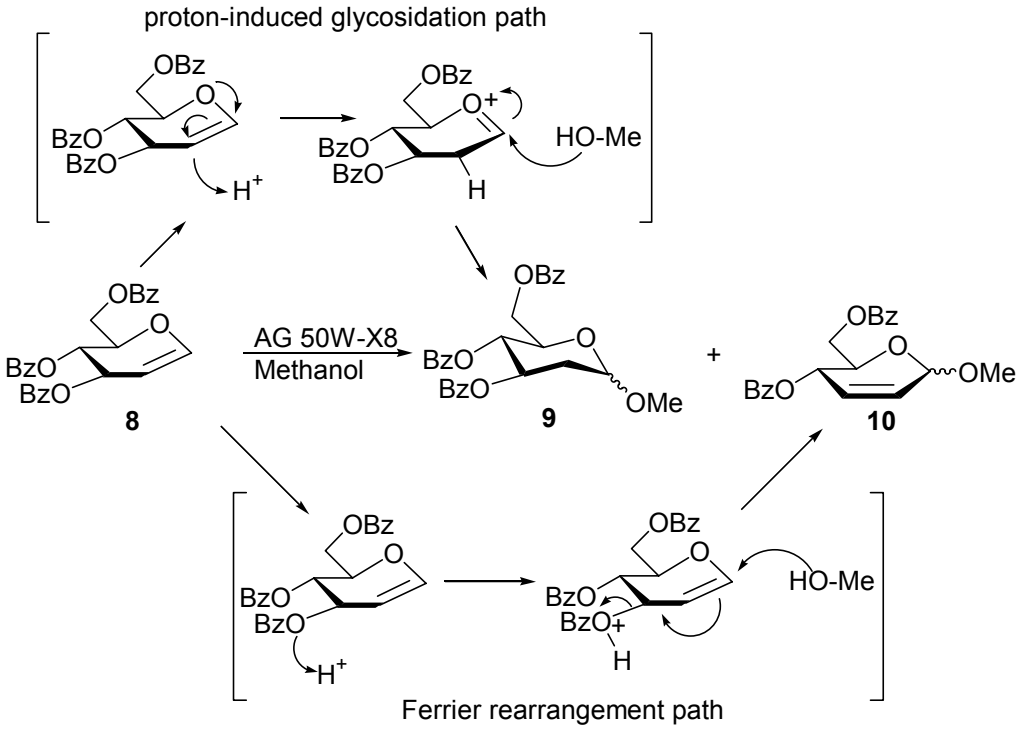


Scheme 4 Haloglycosidation

The stereochemistry of glycosidations is generally controlled by *trans*-diaxial addition usually yielding the α-linked glycoside.

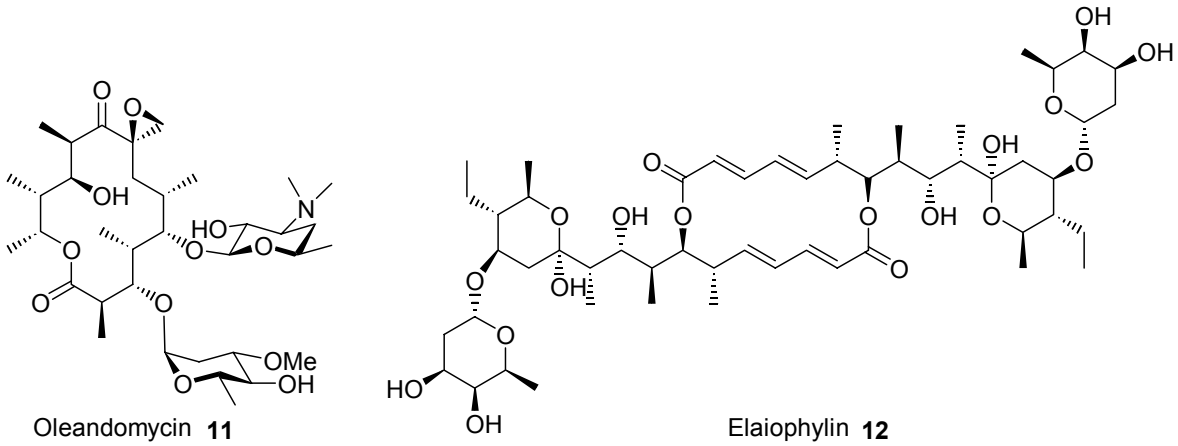
Earlier, *Hadfield* and *Sartorelli* reported on treatment of glucal tribenzoate **8** in refluxing methanol and the presence of cation exchange resin AG 50W-X8. They afforded an anomeric mixture of methyl 2-deoxy-3,4,6-tri-*O*-benzoyl-D-*arabino*-

hexopyranoside **9** in 38% yield (Scheme 5). Along with the product significant amounts of the *Ferrier* rearranged product **10** was isolated.[25b] As a result this direct method for preparing 2-deoxyglycosides remained synthetically unattractive.



Scheme 5 First glycosidation of methanol with glycal using acid catalysis.[25a] Mechanisms of proton-induced glycosidation and *Ferrier* rearrangement.

Later a similar strategy was used by *Wakamatsu*[26a] and *Tatsuta*[26b] groups in the synthesis of glycosylated macrocyclic antibiotics like elaiophylin **12** and oleandomycin **11** (Figure 3). They used campforsulfonic acid in dichloromethane to promote glycosidation. *Sabesan* and co-workers further developed *Satorelli's* idea in using polymer-bound sulfonic acid such as Dowex 50x8.[27a,c] To suppress the tendency of protonating the C-3 oxygen which usually leads to *Ferrier* rearrangement, aprotic solvents with low polarity ought to be used together with a "nonhydrated" proton source. Catalytic amounts of soluble bromide ions (LiBr, *n*-$Bu_4N^+Br^-$) have a great impact on the reaction speed, eventually due to traces of liberated HBr. *Falck* et al. reported a successful preparation of 2-deoxyglycopyranosides by using the triphenylphosphonium bromide catalyzed addition of alcohol to glycal triacetates.[27b] This work proves directly the necessity of a mild proton source as complexed HBr to avoid the unfavorable *Ferrier* rearrangement.



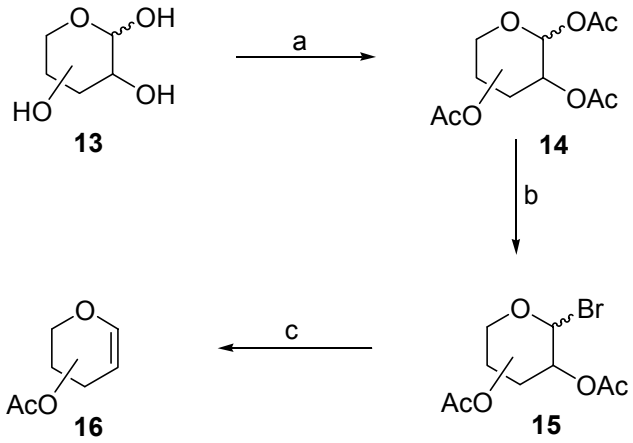
Oleandomycin **11** Elaiophylin **12**

Figure 3 macrocyclic antibiotics

5.1. Synthesis of carbohydrate monomers and test samples

5.1.1. Synthesis of glycals

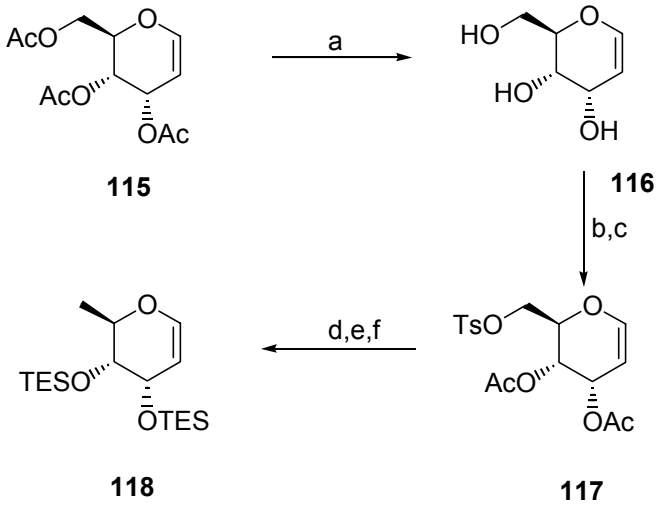
In 1944 *Reichstein* and co-workers published a three step transformation of unprotected sugars to glycals[28a]. In the first step carbohydrate **13** was peracetylated using acetic anhydride, and then anomeric acetate **14** was replaced by halogen. Halide **15** obtained was involved in a *Reformatsky*-type[28b,c] reaction with zinc and the intermediate organozinc glycoside was directly subjected to β-elimination affording glycal **16** with low to moderate yields. Later *Koreeda* and co-workers offered an improved one-pot procedure for the same sequence[29] (Scheme 7). After the pearcetylation process without use of any base, HBr in acetic acid was directly added to the reaction mixture to furnish haloglycoside **15**. Excess of HBr was neutralized with sodium acetate and the mixture was poured into a suspension of zinc in water/acetic acid buffered by sodium acetate. No intermediate had to be isolated and after workup crude peracetylated glycal **16** was obtained. In case of 3,4-di-*O*-acetyl-L-rhamnal and -L-fucal subsequent *kugelrohr*-destillation under reduced pressure is sufficient to afford pure compounds, otherwise purification by column chromatography is necessary.



Scheme 7 Reagents and conditions: (a) Ac_2O, HBr cat.; (b) HBr/AcOH, 12h; (c) Zn, $CuSO_4*5H_2O$, NaOAc, AcOH/H_2O, moderate cooling, 3h.

Using this methodology 3,4-bis-*O*-acetyl-L-rhamnal and -L-fucal were synthesized from the corresponding free sugars with 75% and 37% overall yields, respectively. Additional protecting group manipulations were performed if necessary.

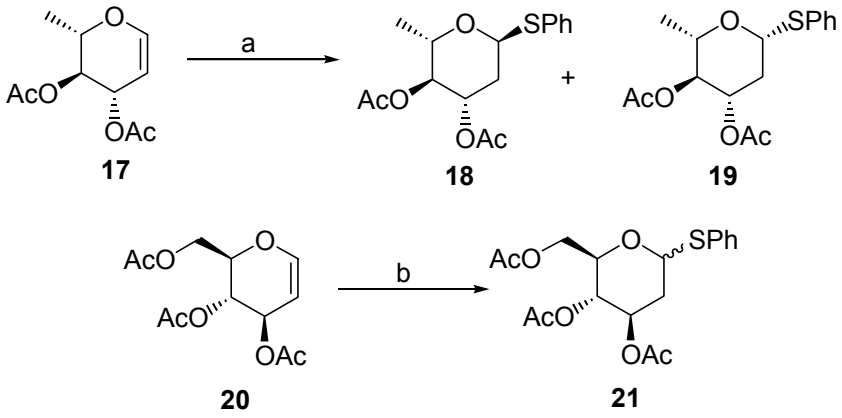
3,4,6-Tri-*O*-acetyl-D-allal **115** was taken as a staring material to synthesize 6-deoxy-D-allal **118**. After full deacetylation the hydroxyl group at C-6 was selectively tosylated in pyridine with subsequent addition of acetic anhydride. The tosylate **117** obtained was subjected to nucleophilic substitution with sodium iodide in acetone to yield 6-iodo-6-deoxy glycal. After reduction with lithium aluminiumhydride fully deprotected 6-deoxy-D-allal was silylated using TESCl to afford glycal **118** in excellent yields (Scheme 7a).



Scheme 7a Reagents and conditions: (a) Amberlyst A-26 $^-$OH form, MeOH, 99%; (b) TsCl, Py, RT; (c) Ac_2O, 90% for two steps; (d) NaI, Acetone, reflux, 12h, 97%; (e) $LiAlH_4$, THF, 2h, 90%; (f) TESCl, imidazole, DMAP, DMF, 92%.

5.1.2. Synthesis of 2-deoxyphenylthioglycosides

Thiophenol can be used as an acceptor in glycosylation reactions with glycals if induced by a mild proton source. Using the strategy of *Bolitt* as mentioned above 3,4-di-*O*-acetyl-L-rhamnal **17** was subjected in a glycosidation reaction to thiophenol and PPh_3*HBr. Anomeric product mixture was obtained with an α/β-ratio of 3.3:1 (59% yield). Both anomers can be separated using column chromatography to furnish α-glycoside **18** and β-glycoside **19** (Scheme 8). When camphorsulfonic acid was used as an alternative proton source, *Ferrier* rearrangement took place in considerable amounts. Using the same approach, glycal **20** was involved in glycosidation with thiophenol to yield an anomeric mixture **21** with an α/β ratio of 1:1.



Scheme 8 Reagents and conditions: (a) PhSH, PPh_3*HBr 1 eq, CH_2Cl_2, RT, 24h; (b) PhSH, PPH_3*HBr 0.6 eq, CH_2Cl_2, RT, 24h.

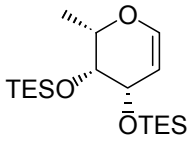
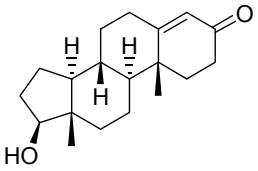
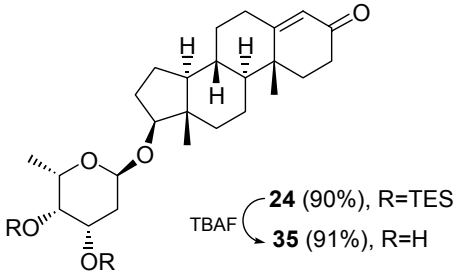
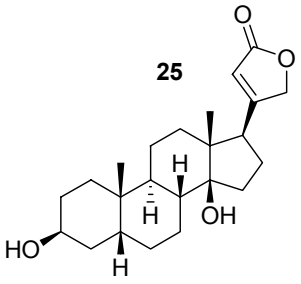
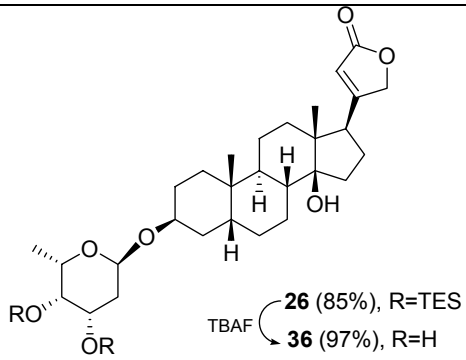
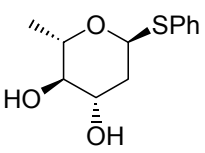
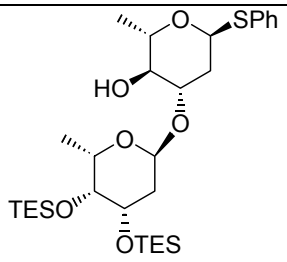
Thioglycosides obtained can directly be used as donors in glycosidation reactions or subjected to protecting group manipulations and used as glycosyl acceptors.

5.1.3. Synthesis of test samples

It is well known that solid-phase reactions can not be rapidly monitored by thin layer chromatography or gas chromatography. Therefore, all necessary optimizations and, if possible, also product analysis should be performed in solution prior to the solid-phase experiment.

Bis-*O*-TES-L-fucal **22** and testosterone **23** was chosen as a test system for optimizing the reaction conditions. Fucal **22** is best suited for reaction optimization

because it exclusively forms α-configured glycosides due to *ribo*-configured hydroxyl functions at C-3 and C-4, and actually it is one of the most reactive glycosyl donors in its class.[32c] These features ease reaction monitoring and subsequent analysis of products. After exhaustive optimization suitable reaction conditions were achieved using 5 to 10 mol% PPh_3*HBr as activator in dichloromethane. The glycosidation was completed within 30 minutes. The amount of the activator used depends on the donor activity and the nature of protection groups employed. For example, when silyl protection such as the triethylsilyl group is used, less catalyst is needed to initiate glycosidation which is in contradiction to benzoyl or pivaloyl groups.[34] It is worth to notice that PPh_3*HBr is able to cleave silyl ethers at higher concentrations. Generally 1 - 2 mg of activator per 5 ml dichloromethane is best for achieving initiation without side reactions. Glycosidation reactions of some steroids and sugars with L-fucal **22** are summarized in Table 1.

Donor	Acceptor	Product
 **22**	 **23**	 TBAF: **24** (90%), R=TES → **35** (91%), R=H
	 **25**	 TBAF: **26** (85%), R=TES → **36** (97%), R=H
	 **27**	 **28** (72%)

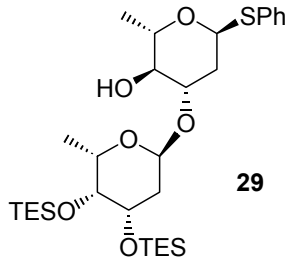
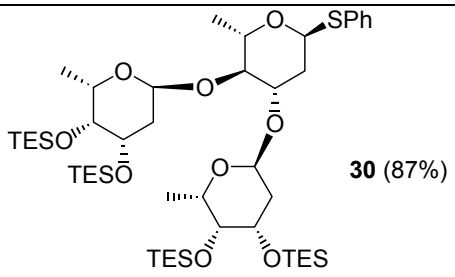
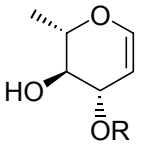
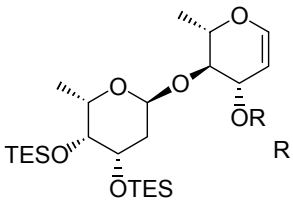
	 **29**	 **30** (87%)
	 R = Bz, Piv **31, 32**	 R = Bz, Piv **33, 34** (85%)

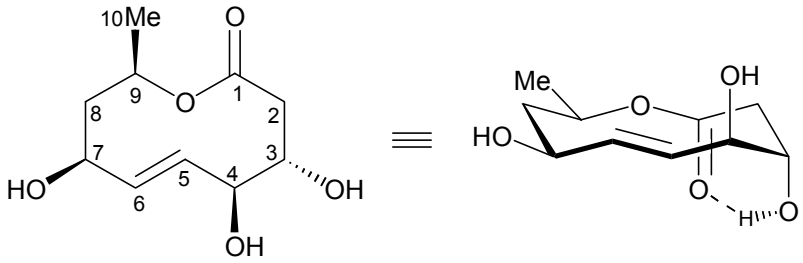
Table 1 Glycosidation of some alcohols

Among the commonly used leaving groups, thioglycoside **27** was chosen as a universal building block. It is well known that thioglycosides are stable under most reaction conditions frequently used in sugar chemistry, though they can be easily activated by various promoters such as NIS-TfOH, MeOTf, DMTST, IDCP, selectfluor™, and others.[30] These facts allow for the development of an orthogonal glycosidation strategy using thioglycoside **27** which can serve both as a donor or acceptor.

More than a decade ago, *Fraser-Reid* firstly reported on the concept of "armed" and "disarmed" glycosyl donors while investigating the chemistry of n-pentenyl glycosides.[31] Since then the laboratories of *Danishefsky*,[32a] *van Boom*,[30b,f] *Mereyala*, [32b] and others have extended this phenomenon to the various other glycosyl donors. A great contribution in field of thioglycosides was made by the *Wong* group who quantified reactivities of various glycosyl donors.[32c] Generally, glycosyl donors with ester protection groups undergo glycosylation reactions much more slowly than the corresponding donors with ether protection. The reason for this phenomenon is the electron withdrawing character of the ester group destabilizing the possible cationic transition state en route to glycoside formation.[33] The same strategy also works well with glycals as can be seen from experiments with glycals **31** and **32**. Bissilylated fucal **22** acts in this case as a donor while 3-*O*-benzylated rhamnal **31** is not activated under the given conditions and acts as a simple alcohol.

5.1.4. Selective decarestrictine D protecting methods

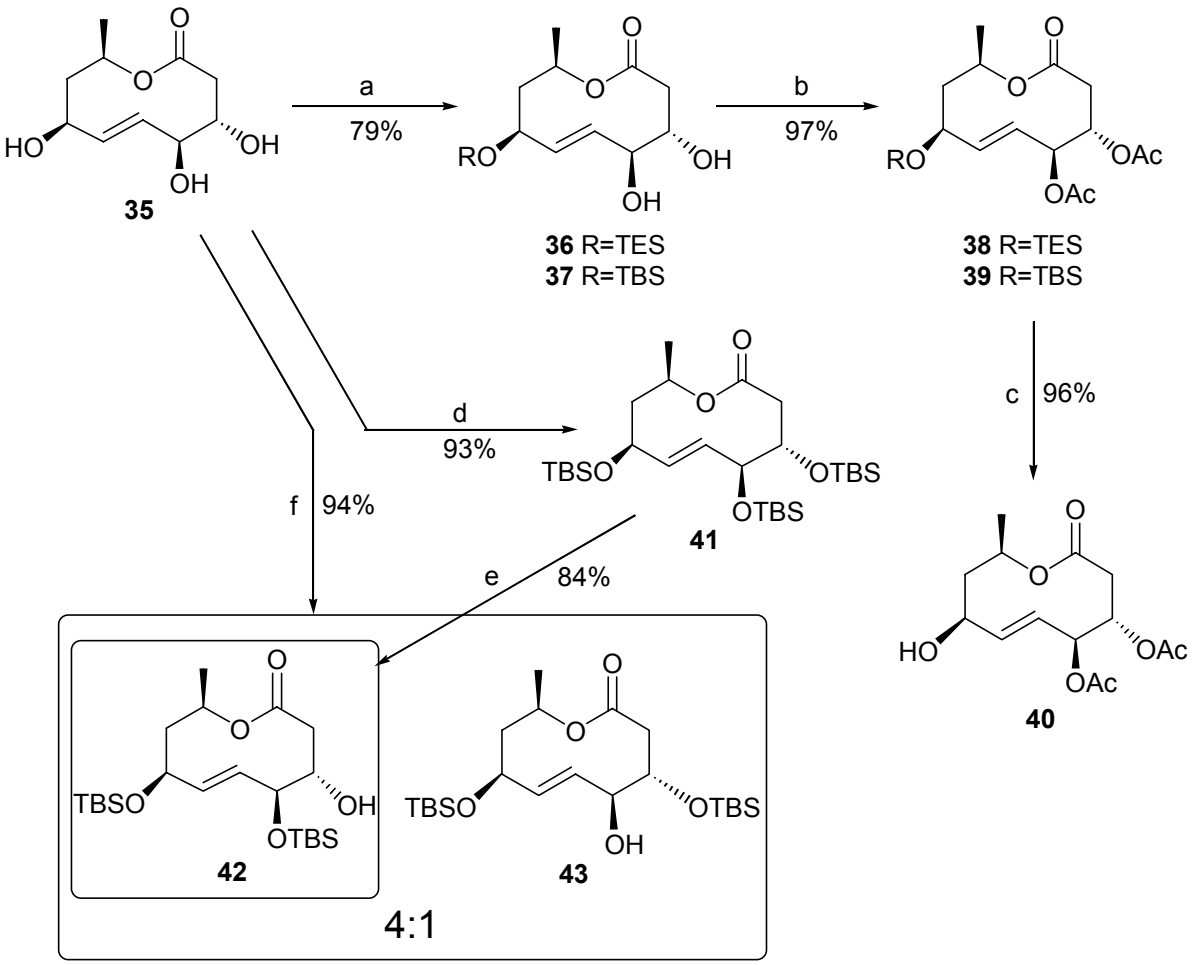
Decarestrictine D or Tuckolide **35** is a 10-membered lactone isolated from *Penicillum corylophilum, simplicissimum*[35a] and in an independent research from the Canadian Tuckahoe fungi *Polyporus tuberaster*.[35b] It potently inhibits liver cell HEP-G2 cholesterol biosynthesis (IC_{50} of 100 nm), but has no significant activity in antibacterial, antifungal, antiprotozoal, or antiviral area.



35

Scheme 9 Decarestrictine D

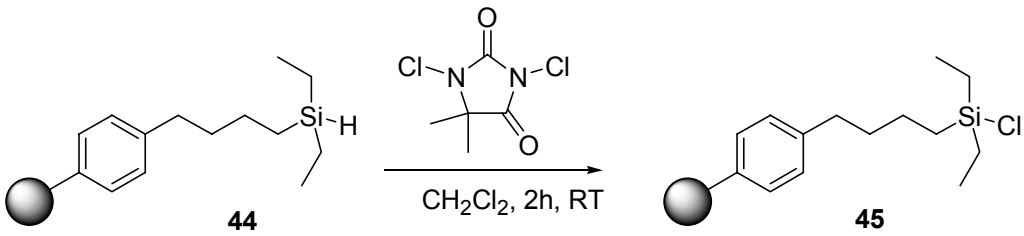
First glycosidation of decarestrictine D **35** was performed in the *Kirschning* group for investigating potential antibiotic activity.[24d] The different reactivities of the decarestrictine D hydroxyl groups have been investigated earlier.[36] The hydroxyl group at C-3 forms a hydrogen-bond with the ester carbonyl oxygen which reduces its reactivity. The most active hydroxyl group is the equatorially oriented one at C-7 while the axial oriented hydroxyl group at C-4 is somewhat less reactive. This observation allows to selectively protect the hydroxyl function at C-7. If decarestrictine **35** is fully silylated and then subjected to mild acidic silyl group cleavage with PPh_3*HBr in dichloromethane, clean deprotection of the hydroxyl function at C-3 takes place. The possible decarestrictine D protecting routes for affording various protecting group combinations are summarized in Scheme 10.



Scheme 10 Reagents and conditions: (a) TESCl or TBSCl 1.5 eq, DCM, imidazole, - 30° C, 1h; (b) Py, Ac_2O 4 eq, 50° C, 5 – 7h; (c) TBAF, AcOH ph 7, RT, 5d; (d) TBSCl 3.5 eq, imidazole, DMAP, DMF, 50° C, 2h; (e) PPh_3*HBr 5 mol%, DCM, RT, 6h; (f) TBSCl 2 eq, imidazole, DMAP, DMF, -30° C 1h, then → RT + 0.25 eq TBSCl, 1h.

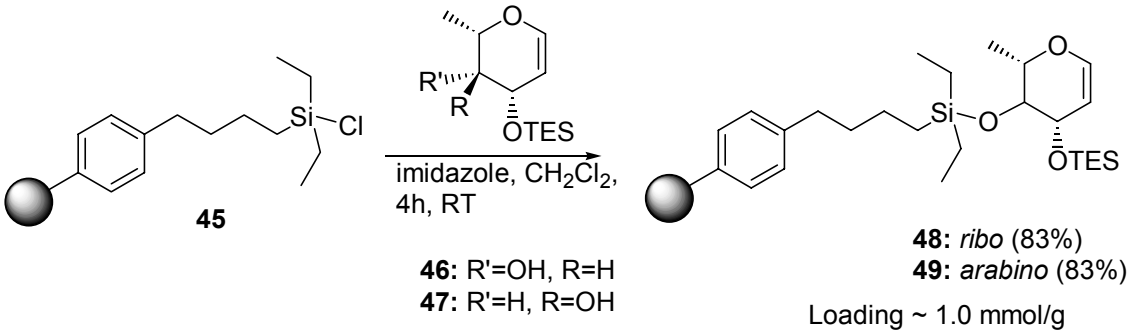
5.2. Activation of PS-DES resin and attaching the first carbohydrate

Commercially available silyl resin **44** has a silane (Si-H) moiety which offers a number of unique advantages: it is stable to moisture; alcohols, carbonyl, aromatic, or unsaturated derivatives can be attached directly using TBAF, rhodium-based or Wilkinson catalysts.[37] It also can be easily transformed into a reactive silyl chloride derivative, which can be used immediately in a classical sense (e.g TESCl). The silyl resin **44** was treated with 1,3-dichloro-5,5-dimethylhydantoin in dichloromethane according to the *Yonhang Hu*[22] protocol (Scheme 11). The resin **45** obtained was gently washed with abs. dichloromethane and THF several times.



Scheme 11 Chlorination of PS-DES resin

3-*O*-TES-L-fucal **46** and –rhamnal **47** were used as glycal moieties which contain a free hydroxyl group at C-4. Both sugars were attached to the resin with excellent results using the above mentioned protocol (Scheme 12).



Scheme 12 Attaching glycals to the PS-DES resin

The loading of the polymer can be monitored by weight difference or by gel-^{13}C-NMR spectroscopy according to the relative signal strength. Identically calculated loadings using gravimetry of both glycals indicate the actual resin loading capability. This was lower than certified by the manufacturer. In the IR spectra no Si-H bond absorption were detected at 2100 cm^{-1}, which clearly points to full possible resin loading. Nevertheless, this polymer showed excellent loading yields compared to the commercially available PSAMCOOH-resin which was involved in the same glycal attaching procedure before.[38]

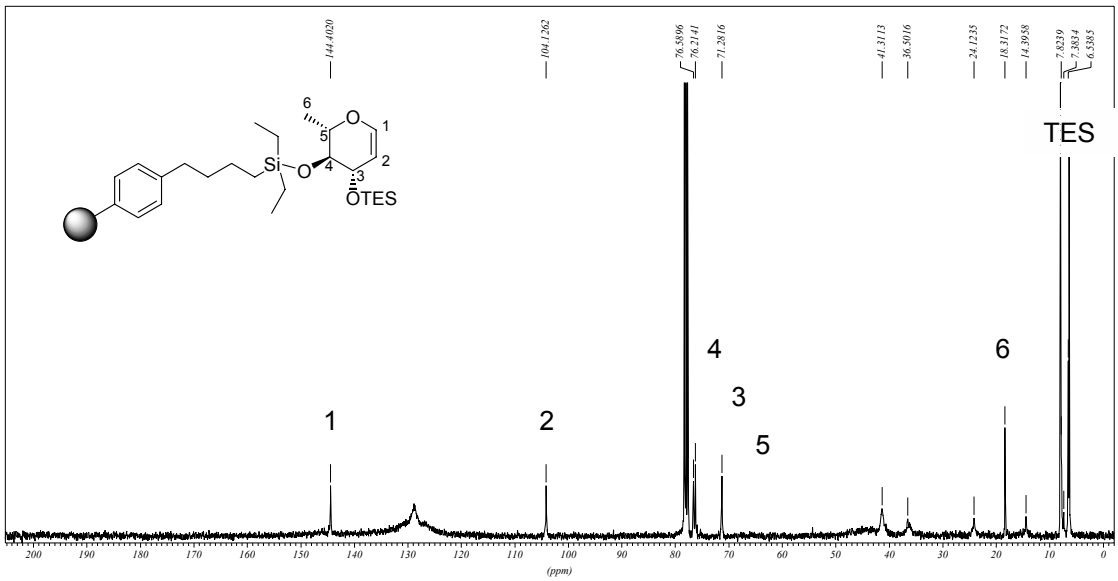
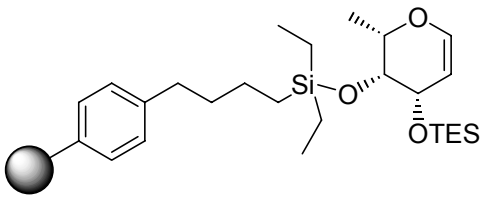
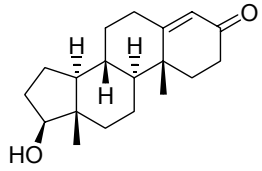
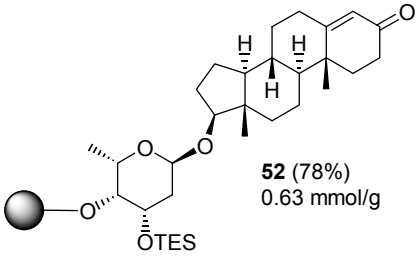
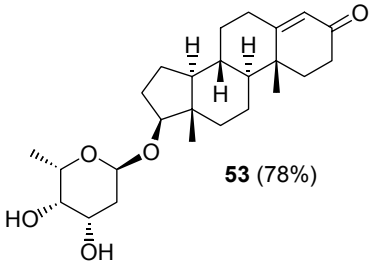
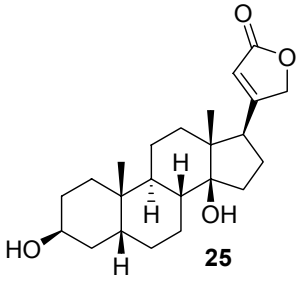
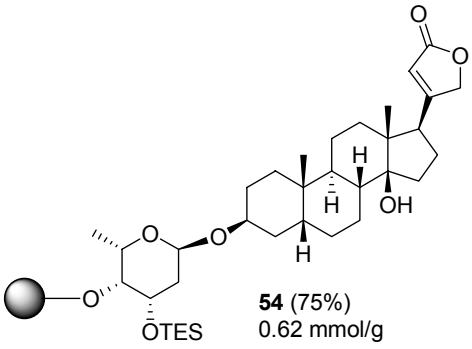
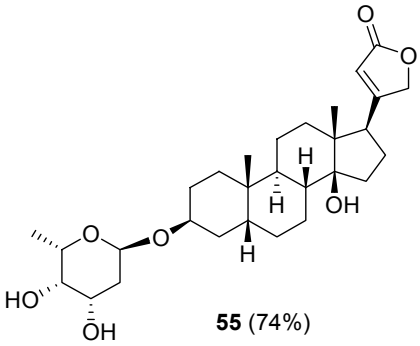
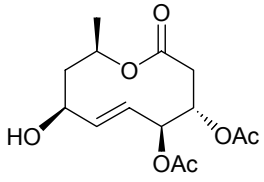
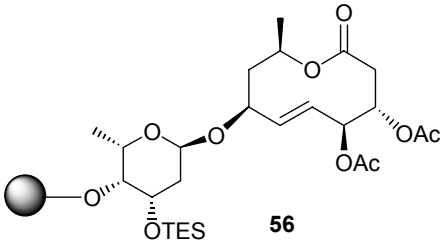
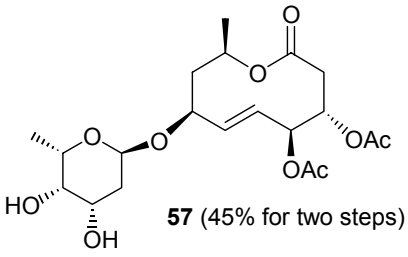
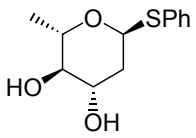
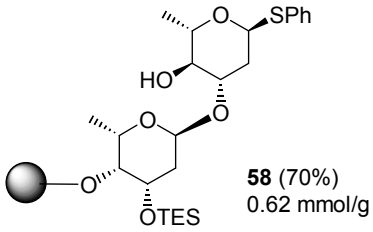


Figure 4 Representative Gel-^{13}C-NMR spectra from polymer-bound glycal **49**

5.3. Glycosidation of some aglycons and sugars using polymer-bound glycals 48 and 49

In the first solid-phase experiment polymer-bound fucal **48** was treated with testosterone as acceptor by adopting those reaction conditions which were optimized for solution chemistry. Only partial glycosidation was observed as judged by gel-^{13}C-NMR spectroscopy. The characteristic glycal signals (C-1' and C-2' at 143.1 and 102.7 ppm, respectively) did not fully disappear although signals from the product were clearly recognizable (C-3 at 199.2 from testosterone carbonyl, C-4 at 123.8 from testosterone olefinic double bond and C-1' at 98.8 for anomeric center). The data acquired indicate a reduced kinetics on the polymer compared to solution-phase synthesis. Further optimizations indicated that four hours are sufficient to drive the reaction to completion. Various natural products and some sugars were successfully glycosidated using polymer-bound fucal **48** and rhamnal **49** (Table 2 and Table 3).

Polymer-bound fucal **48**, loading 1.07 mmol/g		
		
Acceptor	Polymer-bound product	Cleaved product
 **23**	 **52** (78%) 0.63 mmol/g	 **53** (78%)
 **25**	 **54** (75%) 0.62 mmol/g	 **55** (74%)
 **40**	 **56**	 **57** (45% for two steps)
 **27**	 **58** (70%) 0.62 mmol/g	not subjected to cleavage

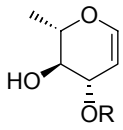
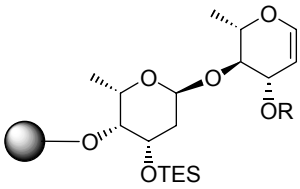
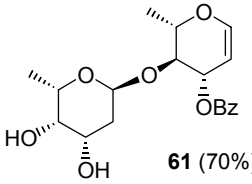
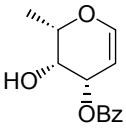
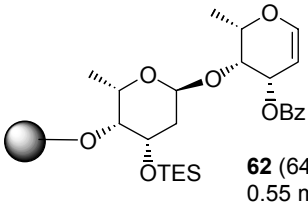
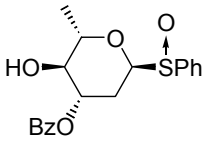
 R = Bz, Piv **31, 32**	 R = Bz **59** (70%, 0.60 mmol/g) Piv **60** (76%, 0.69 mmol/g)	 **61** (70%)
 **50**	 **62** (64%) 0.55 mmol/g	not subjected to cleavage
 **51**	decomposition	—

Table 2 Glycosidation conditions with polymer-bound fucal **48**: PPh_3*HBr 1 mg in 2.5 ml CH_2Cl_2, acceptor 3 eq, 4h, RT.

Yields on solid phase are generally slightly lower in comparison with previous tests in solution. The polymer-bound glycoconjugates and disaccharides can be easily analyzed using gel-^{13}C-NMR spectroscopy, but signals are significantly weaker in comparison to polymer-bound glycal spectra. It is already known[12b] that large molecules gave very poor gel-NMR spectra.

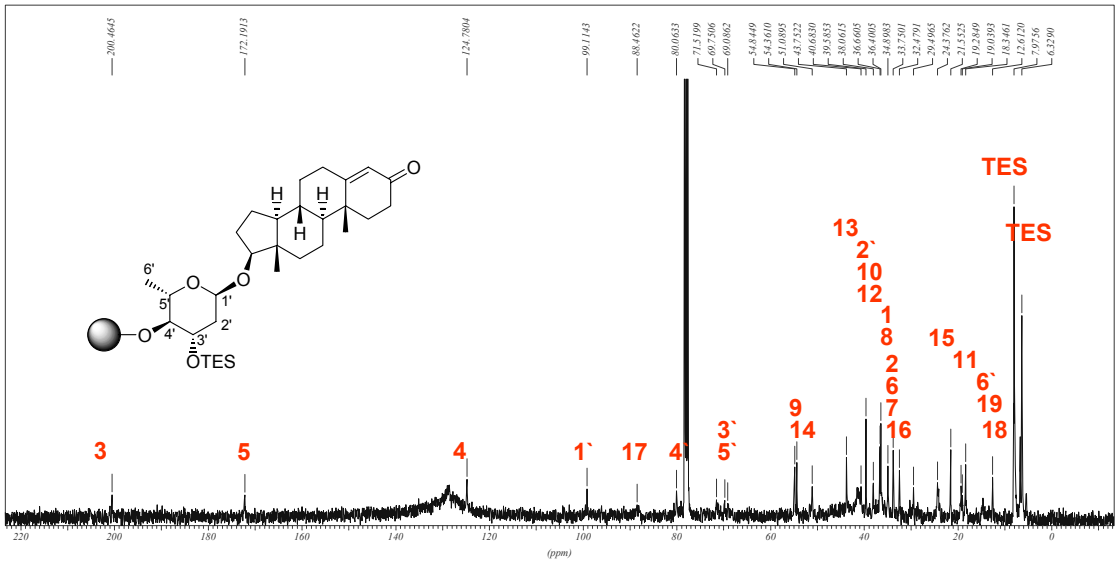


Figure 5 Representative Gel-^{13}C-NMR spectra from polymer-bound glycoconjugate **63**

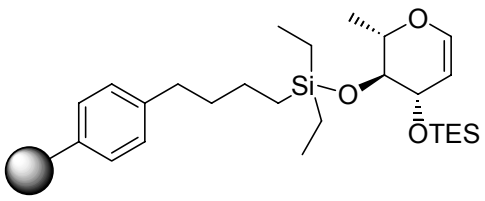
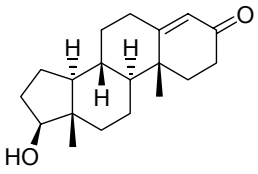
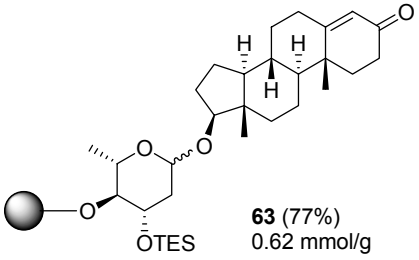
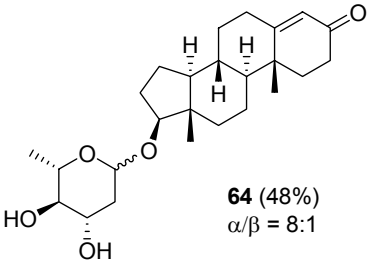
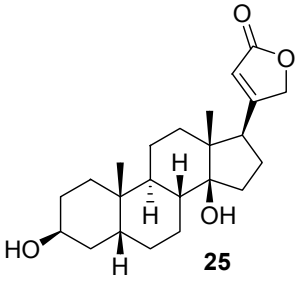
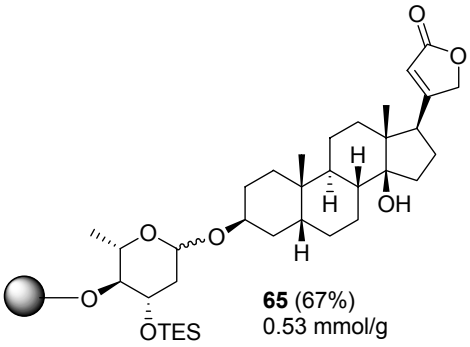
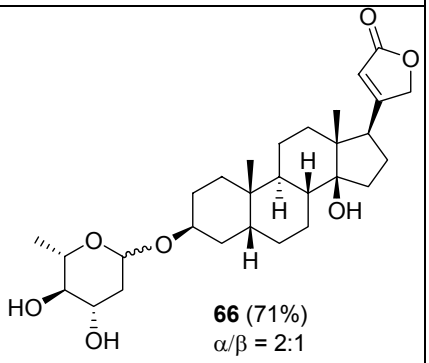
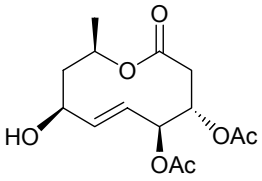
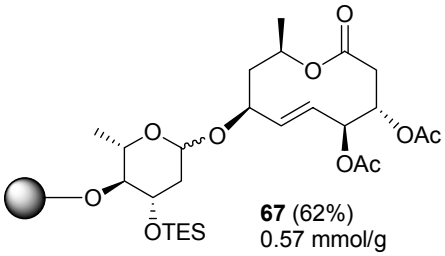
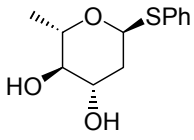
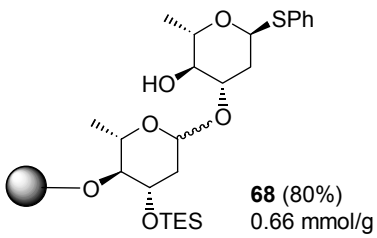
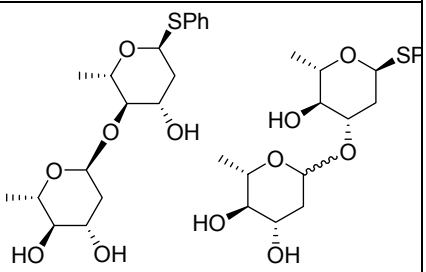
Polymer-bound rhamnal **49**, loading 0.99 mmol/g		
		
Acceptor	Polymer-bound product	Cleaved product
 **23**	 **63** (77%) 0.62 mmol/g	 **64** (48%) α/β = 8:1
 **25**	 **65** (67%) 0.53 mmol/g	 **66** (71%) α/β = 2:1
 **40**	 **67** (62%) 0.57 mmol/g	not subjected to cleavage
 **27**	 **68** (80%) 0.66 mmol/g	 **69** (19.1%) **70** (α - 47%) **71** (β - 33%)

Table 3 Glycosidation conditions with polymer-bound rhamnal **49**: PPh_3*HBr 1 mg in 2.5 ml CH_2Cl_2, acceptor 3 eq, 4h, RT.

The lower yield in experiment **62** compared with other trials (Table 2) could be explained with reduced reactivity of fucal **50** axial oriented hydroxyl function at C-4. Polymer-bound disaccharides with thiophenyl or glycal moiety such as **58** and **59** could be involved in further glycosidation reactions to build trisaccharides or glycoconjugates with two or more carbohydrate skeletons. Preliminary tests in solution to build similar substances gave good to excellent results which are summarized in Table 4.

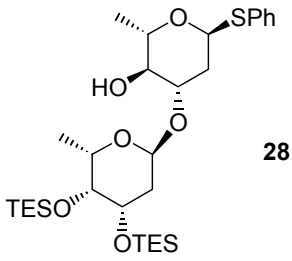
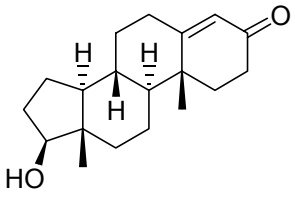
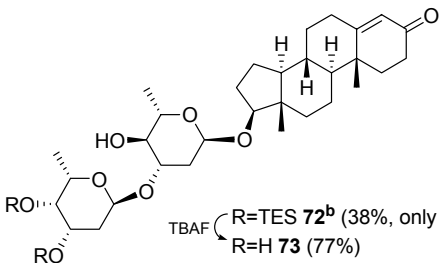
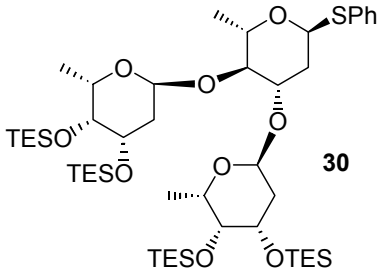
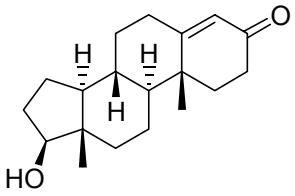
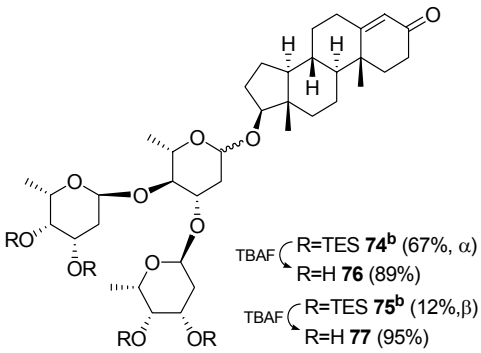
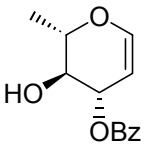
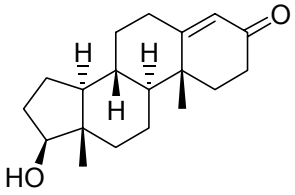
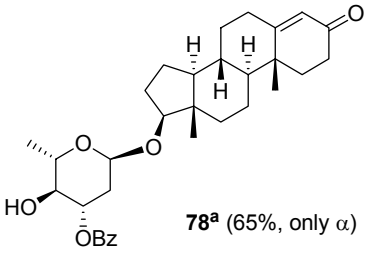
Donor	Acceptor	Product[(conditions)]
 **28**	 **23**	 TBAF → R=TES **72**[b] (38%, only α); R=H **73** (77%)
 **30**	 **23**	 TBAF → R=TES **74**[b] (67%, α); R=H **76** (89%); TBAF → R=TES **75**[b] (12%,β); R=H **77** (95%)
 **31**	 **23**	 **78**[a] (65%, only α)

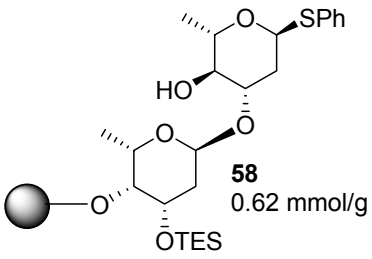
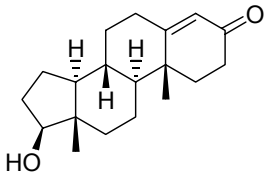
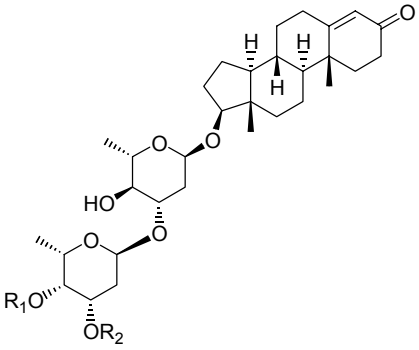
Table 4 Reagents and conditions: (a) **31** and **23** 0.1 mmol, PPh_3*HBr 8 mg in 5 ml CH_2Cl_2, RT, 5h; (b) Donor and acceptor 0.1 mmol, selectfluor™ 1 eq, acetonitrile 5 ml, 0^o C, 15 min.

Moderate yield in experiment **72** was caused by self-glycosidation at the free hydroxyl group in the disaccharide. This can not be considered in polymer-supported synthesis due to negligible self-interacting possibilities on solid support. Experiment **78** demonstrated the excellent selectivity of a reaction with two

possible acceptors: testosterone and glycal itself. Sterically hindered C-4 hydroxyl in benzoylated glycal **31** reacts significantly slower than the testosterone alcohol function. This approach could be employed to build glycoconjugate libraries using orthogonal synthesis strategy with possible automatization.

5.4. Attempts to attach a third component on solid-support and astounding results

Polymer-bound disaccharide **58** was subjected to the identical glycosidation reaction conditions as was described in experiment **72** but after the reaction no weight difference of polymer was observed and gel-NMR showed intact thioglycoside on polymer. No polymer swelling in the acetonitrile was observed which could be the main reason for this negative result. On the other hand, acetonitrile was essential for the thioglycoside activation with selectfluor™ therefore different solvent mixtures were tested. A 1:1-mixture of dichloromethane/acetonitrile was optimal in the means of polymer swelling and selectfluor™ solubility. This approach was tested with little success; only 17% of the product was isolated after cleavage from the resin. The remaining thioglycoside seemed to have been decomposed because no traces of it were detected in the cleaved mixture (Table 5).

Donor	Acceptor	Product
 **58** 0.62 mmol/g	 **23**	 TBAF: R_1=PS,R_2=TES: **79**[a]; R_1=R_2=H: **80** (17% for two steps)

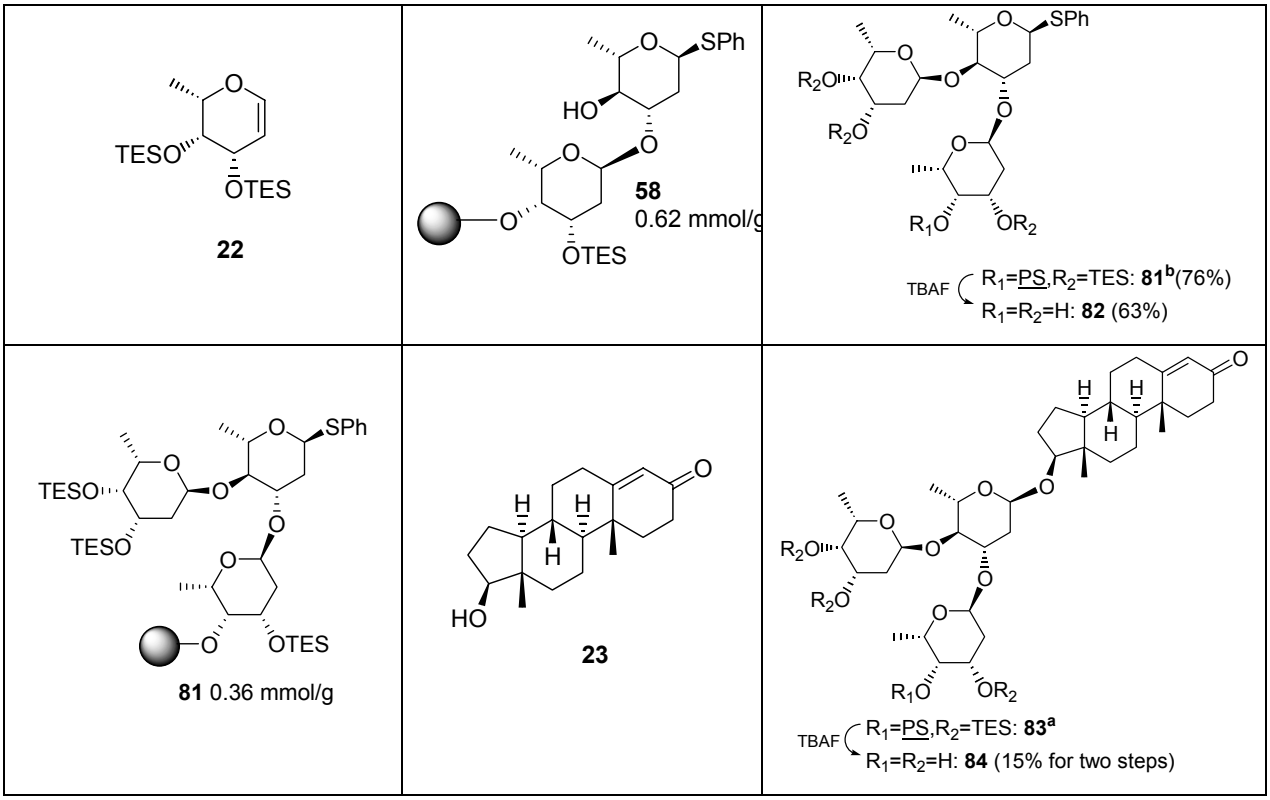
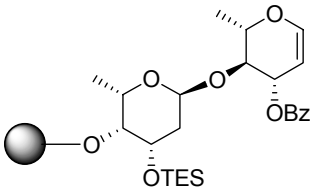
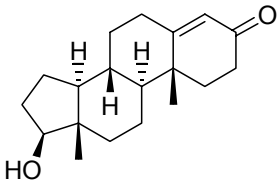
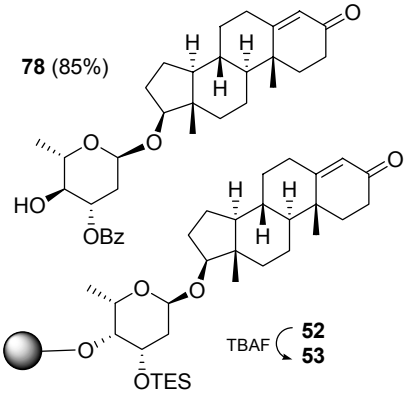
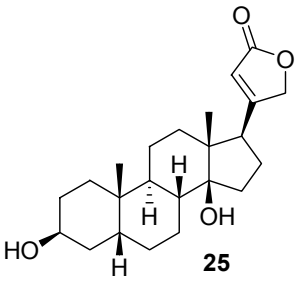
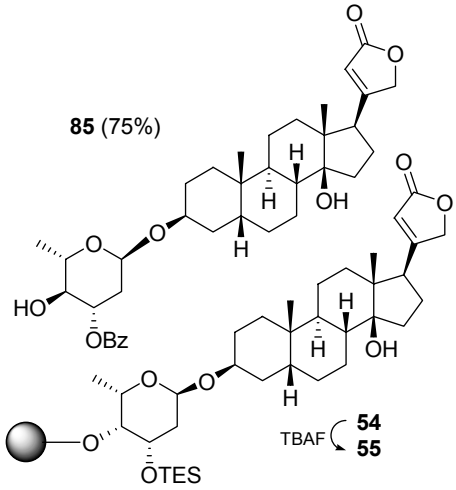
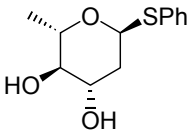
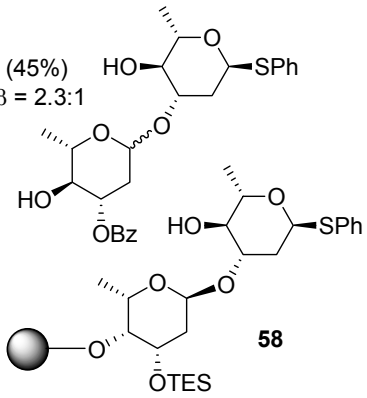


Table 5 Reagents and conditions: (a) Donor and acceptor 0.1 mmol, selectfluor™ 1 eq, acetonitrile 5 ml, RT, 4h; (b) PPh_3*HBr 1 mg in 2.5 ml CH_2Cl_2, acceptor 3 eq, 4h, RT.

Any attempt to modify glycosidation conditions or use other electrophilic promoters ($PhI(OAc)_2$ (5 eq), Et_4NI (5.5 eq) , CH_2Cl_2 , RT. overnight; NIS (1.6 eq), TMSOTf (cat.), CH_2Cl_2, -50°C → -20°C 3h) gave no better results. If more aggressive thiophilic promoters and conditions were used, immediate cleavage of the glycoside from the polymer support was observed. Any attempt to introduce other donors on solid support (2-deoxysulfoxides and -fluorides) failed due to high instability. For example, it was observed that PPh_3*HBr also activate sulfoxide **51** usually employed for glycal activation. This unusual activity compared to non 2-deoxysulfoxides can only be explained by the absence of the C-2 hydroxyl or other function with free electron pairs that could stabilize sulfoxides. There are also no literature evidences of applying 2-deoxysulfoxyglycosides in oligosaccharide synthesis.

Previously obtained polymer-bound disaccharides with glycal moiety can also serve as glycosyl donors in glycosidation reaction. Polymer-bound disaccharides **59**, **60**, and **62** were involved in glycosidation reactions with some steroids and sugars using a well optimized method for glycoconjugate synthesis on polymer-support (see Table 2). Surprisingly, no traces of the products were detected also after the resin was processed with TBAF solution to cleave the product. After

cleavage always two products were obtained which originated from glycosidation of each individual sugar unit (Table 6).

Polymer-bound donor	Acceptor	Products
 **59** 0.60 mmol/g	 **23**	**78** (85%) 
	 **25**	**85** (75%) 
	 **27**	**86** (45%) α/β = 2.3:1  **58**

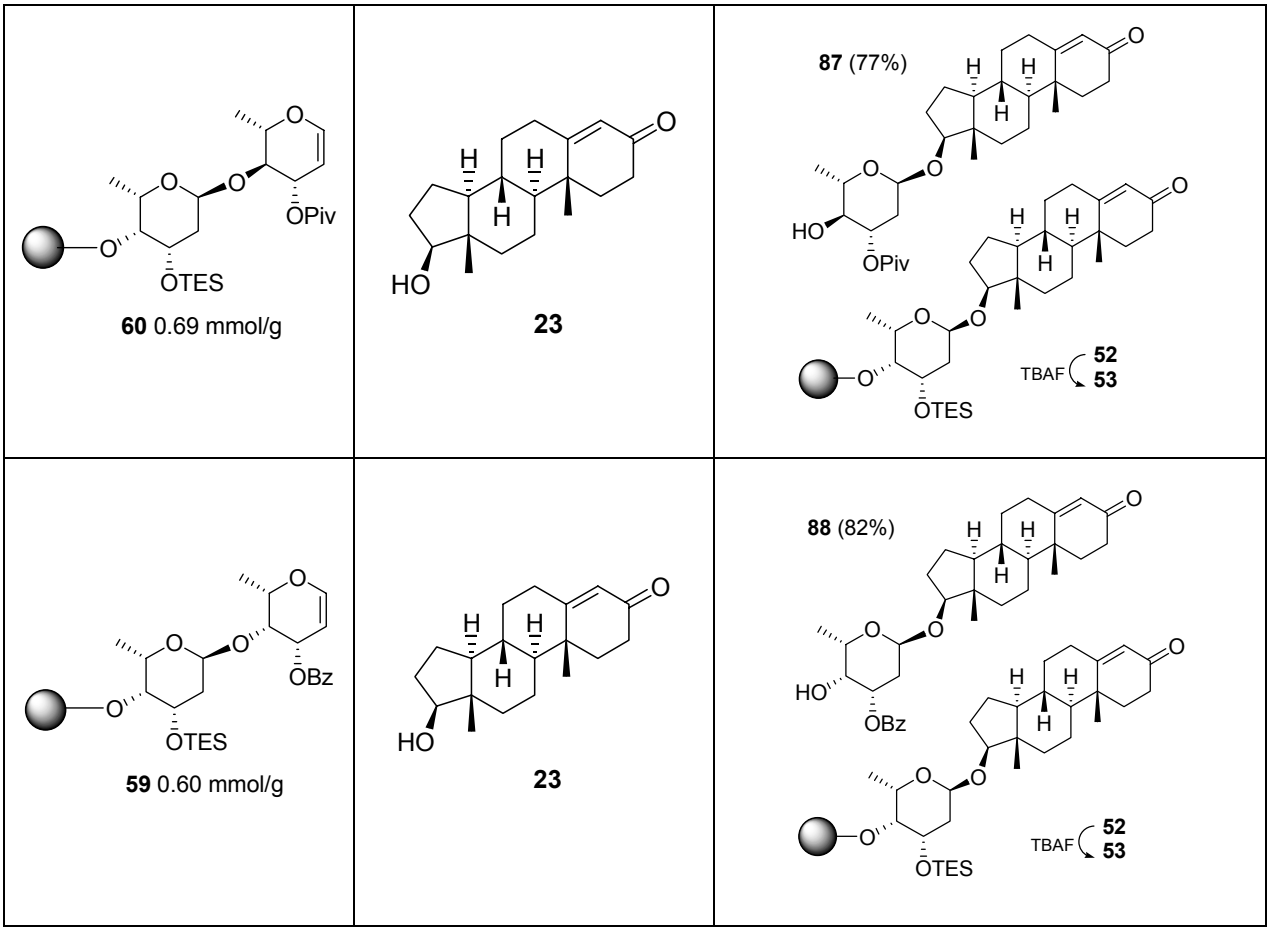
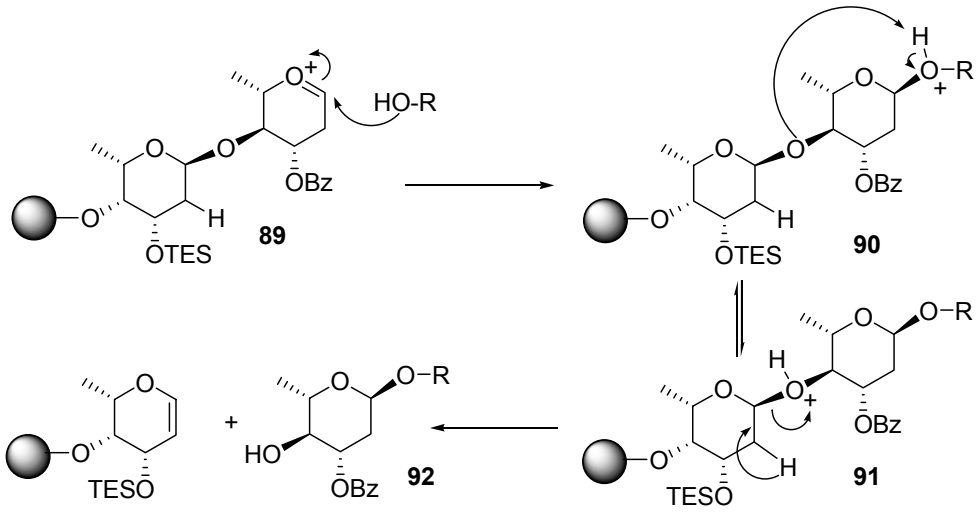


Table 6 Reagents and conditions: PPh_3*HBr 1 mg in 2.5 ml CH_2Cl_2, acceptor 3 eq, 6h, RT.

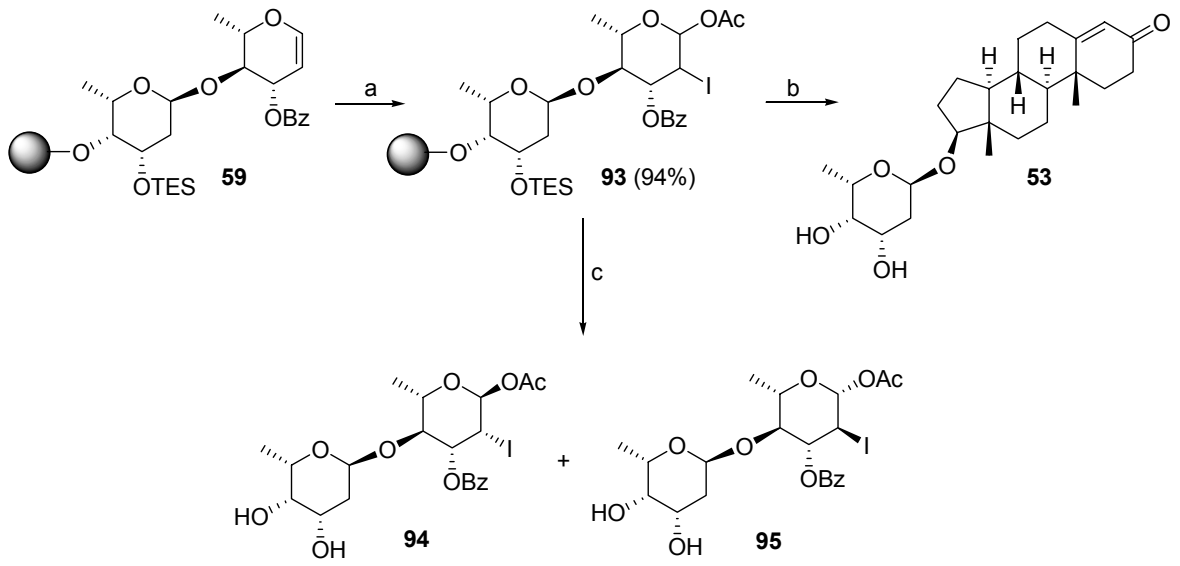
At first it seems that glycosidation conditions are too aggressive, therefore the glycosidic bond is cleaved. However, after careful analysis of the reaction pathway together with *in situ* monitoring, facts force to consider different reasons of failure. The glycosidated testosterones **78**, **87**, and **88** appears within minutes after the catalyst is added. If the catalyst concentration is lowered, no reaction takes place. Also, without an acceptor no cleavages were observed. These facts push to consider a “conjugate” glycosidation-cleavage mechanism (Scheme 13). Formation of the polymer-bound glycoconjugate **52** indicates that a fucal intermediate was present on the resin which subsequently is activated by the catalyst and reacts with the hydroxyl function of the aglycon.



Scheme 13 Proposed mechanism of "conjugated" glycosidation-cleavage on solid support

After protonation of the polymer-bound glycal**,** nucleophilic attack of an alcohol forms an oxonium ion **90**. Subsequently the released proton migrates to the neighboring glycosidic bond protonating the anomeric oxygen (**90 - 91**) which leads to the "retro glycosidation" reaction with glycosidic bond cleavage. If the glycosidic bond had been protonated and cleaved prior to the glycosidation, formation of free glycal **31** would have been observed in solution along with glycoconjugate **92**.

Recently, *Kirschning* and co-workers described the synthesis of 2-deoxyglycosides using the acetate glycosidation approach employing glycals in iodacetylation to yield desired donors.[39a] The corresponding 2-iodo-2-deoxyglycosyl acetates can be activated using silyl triflates that have proven to be powerful activating agents in solution.[39b,c,d] Iodoacetylation on polymer support was performed using hypervalent iodine - $PhI(OAc)_2$ in dichloromethane with excellent yields (Scheme 14). Further attempts to glycosidate testosterone with polymer-bound disaccharide **93** using TMSOTf as an activator[39a] failed. The glycoconjugate **53** was detected in the reaction solution that can originate from polymer-bound disaccharide "retro glycosidation"→glycosidation under acidic conditions.

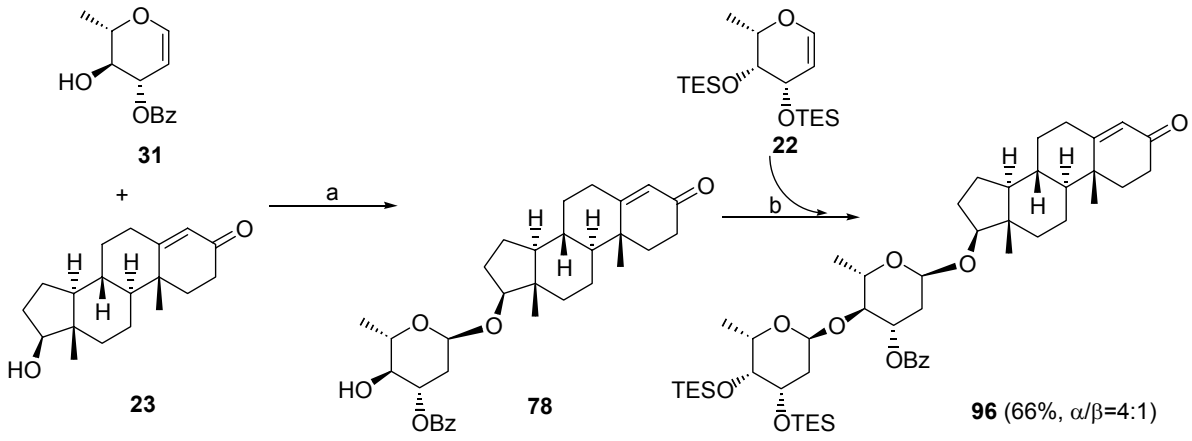


Scheme 14 Reagents and conditions: (a) $PhI(OAc)_2$ 10 eq, $Et_4N^+I^-$ 11eq, CH_2Cl_2, RT, 12; (b) **23**, TMSOTf 3 eq, CH_2Cl_2, -70° C → -30° C, 4h; (c) TBAF, THF, RT, 12h, 82%, *manno/gluco* = 2.3:1.

6. Polymer-assisted glycosidation of glycals and thioglycosides

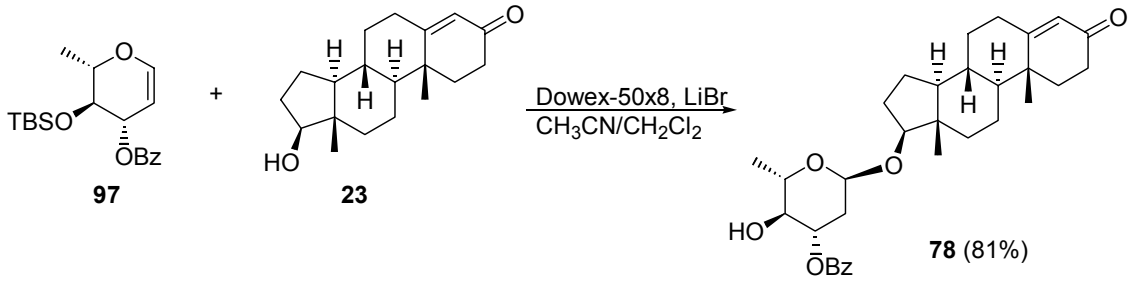
6.1.1. Polymer assisted glycosidation of glycals using new polymer-bound triphenylphosphonium bromide

The idea of automation of oligosaccharide and glycoconjugate synthesis is one of the greatest challenges in carbohydrate chemistry. One approach is the use of reagents or catalysts on solid-support which can be removed by simple filtration after the reaction yielding, in the best case, the pure product in solution. The preparation of glycoside **78** offers further synthetic options. It can directly be transformed into disaccharide **96** by adding a glycosyl donor, namely glycal **22** to the same reaction mixture which created glycoside **78**. By this “one pot” procedure very rapid access to complex glycoconjugates becomes frasable. This approach was first tested in solution using classic reagents (Scheme 15).



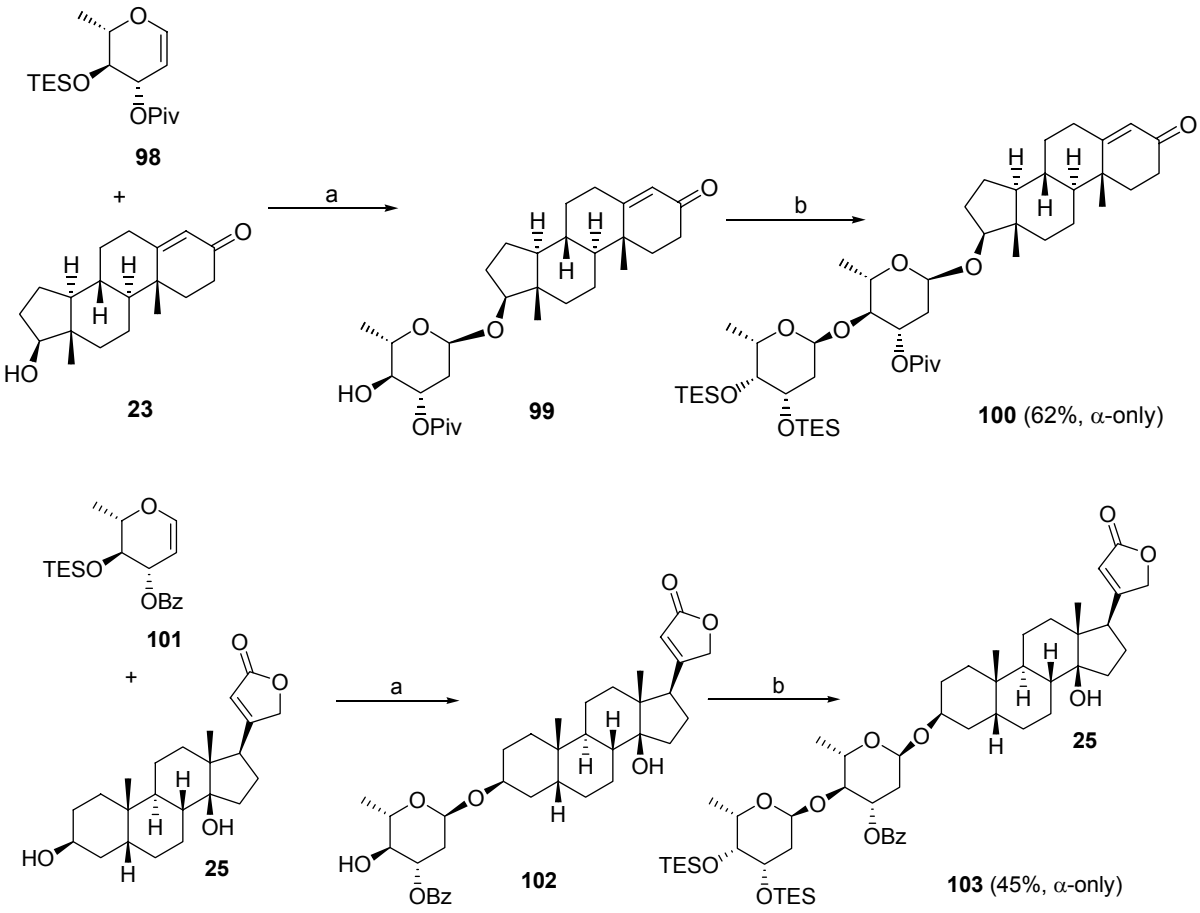
Scheme 15 Reagents and conditions: (a) **23** and **31** 1 eq, CSA cat., LiBr, CH_2Cl_2/CH_3CN – (1:1), RT, 4h; (b) **22** 1.1 eq, $+CH_2Cl_2$, RT, 6h.

The glycoconjugate **96** was obtained in good yield and only a final purification was necessary. In order to make the first glycosidation more efficient the remaining free hydroxyl group in glycal **31** C-4 should be protected with an easy removable protective group. Triethylsilyl or *t*-butyl-dimethylsilyl ethers can be used in this case, which can be later cleaved under mild acidic conditions or by using some fluoride source. Preliminary tests with the silylated glycal **97** gave better yields in comparison with the unprotected glycal **31**. The silyl group was removed using the same proton source, which was employed to initiate the glycosidation, at slightly elevated concentration with prolonged reaction time (Scheme 16).



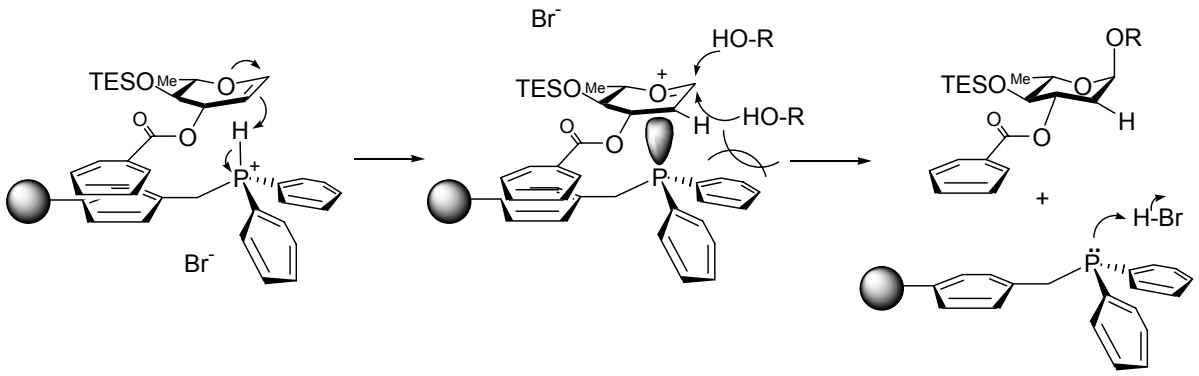
Scheme 16 Glycosidation using fully protected glycal

Both silyl ethers showed equal improvement as far as the yield of the glycosidation is concerned, though the TES ether was much easier cleaved under mild acidic conditions. However, further experiments employing polymer-bound catalysts gave no improvements in comparison to the model experiment (see Scheme 15) using non-polymer-bound catalysts (Scheme 17).



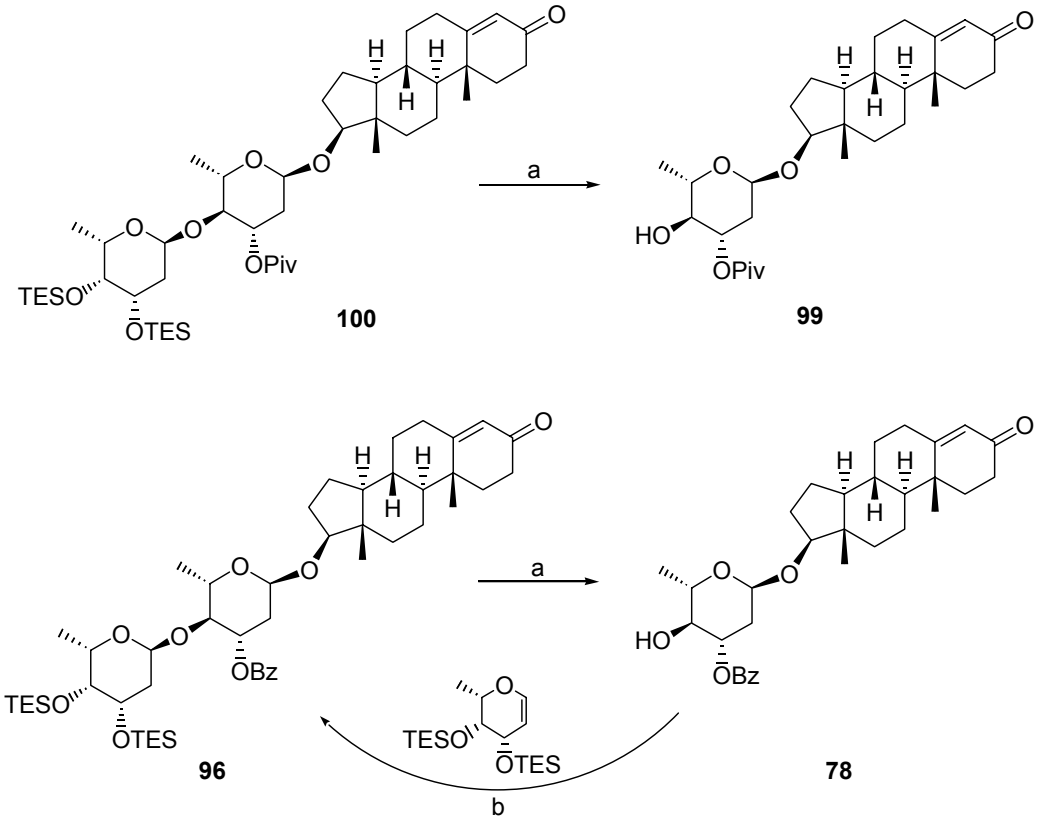
Scheme 17 Reagents and conditions: (a) PS-PPh_2*HBr cat., LiBr, CH_2Cl_2, RT, 4h, then Dowex 50x8 cat., +CH_3CN, 10h, RT; (b) **22** 1.1 eq, +CH_2Cl_2, RT, 5h.

Diluting the reaction mixture by adding dichloromethane or acetonitrile can allow to change catalyst concentration thus initiating or suppressing silyl group cleavage. The greatest benefit in all polymer-assisted experiments was an anomerically pure glycosidic bond formation generating exclusively α-glycosides. This phenomenon could be explained with the heterogeneous nature of the glycosidation reactions, as the glycal may form π-stack with polystyrene and is activated by proton on the surface of the polymer in a more favored manner. The oxonium ion intermediate then may be stabilized by free electron pair on phosphor forming tight sandwich-type complex. This complex hampers any nucleophilic attack from the bottom side; thereby an acceptor approaches oxonium species from the opposite side yielding exclusively α-configured glycoside (Scheme 18).



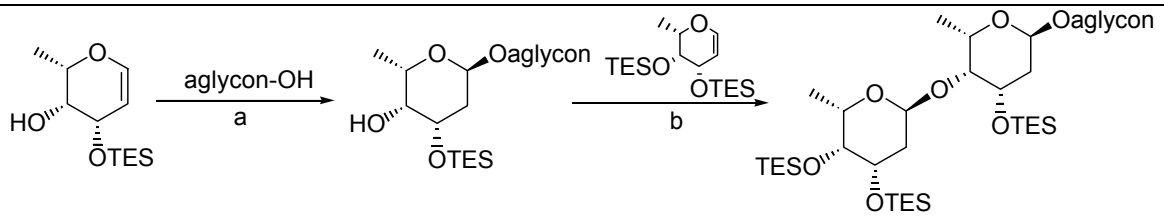
Scheme 18 Glycosidation with polymer-bound PPh_3*HBr catalysts

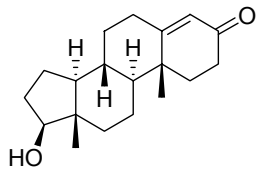
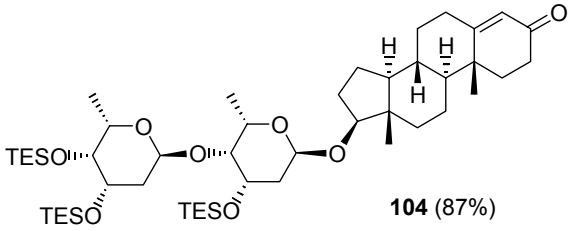
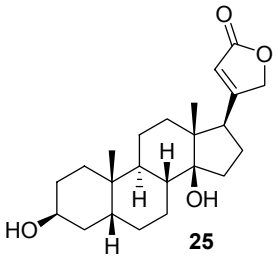
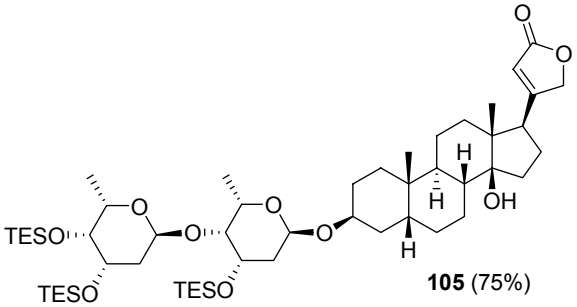
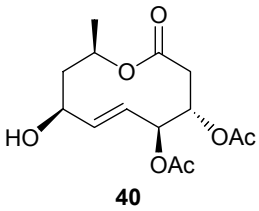
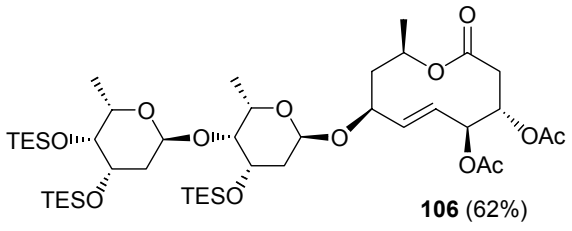
Utilizing the same mild acidic conditions that cleave silyl groups from the glycoconjugate **100** proved to be not successful since the glycosidic bond oxygen was protonated and the glycosidic bond was hydrolyzed faster than the silyl ethers. Any attempts to optimize proton-induced deprotection of the glycoconjugates **100** and **96** failed (Scheme 19). Reactions mainly yielded glycoconjugates **99** or **78** respectively. The glycoconjugate **78**, for example, could be glycosidated once more with fucal **22** to afford disaccharide **96** again.



Scheme 19 Reagents and conditions: (a) Dowex 50x8 1-5 mol%, CH_2Cl_2/acetonitrile; (b) PS-PPh_2*HBr cat., CH_2Cl_2, **22**, RT, 4h, 55% for two steps.

Additional experiments with the mono-substituted fucal **46** revealed excellent yields. At first, testosterone was glycosylated using glycal **46** as glycosyl donor. After the acceptor was completely consumed a second portion of glycal **22** was added. The axially oriented C-4 hydroxyl function in fucals is very unreactive compared to the aglycon alcohol. Therefore the oxonium ion species is attacked exclusively by the aglycon alcohol under kinetic control. The glycoconjugate formed can then slowly be glycosylated at the C-4 hydroxyl group. This “one-pot” system allows the easy production of various glycoconjugates in excellent yields without intermediate purification (Table 7).



Entry	Aglycon-OH	Product
1	 **23**	 **104** (87%)
2	 **25**	 **105** (75%)
3	 **40**	 **106** (62%)

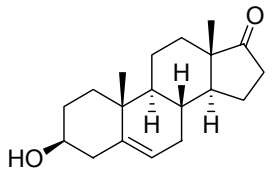
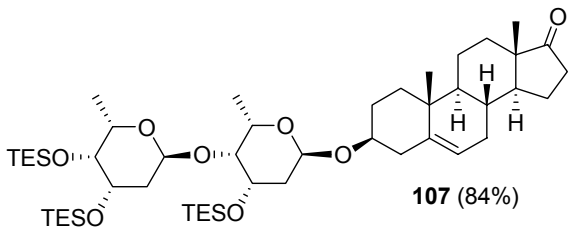
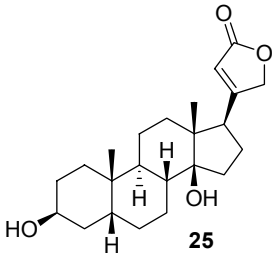
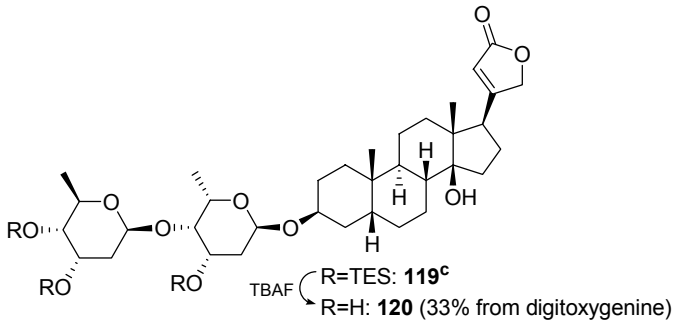
4		 **107** (84%)
5	 **25**	 R=TES: **119**[c] R=H: **120** (33% from digitoxygenine)

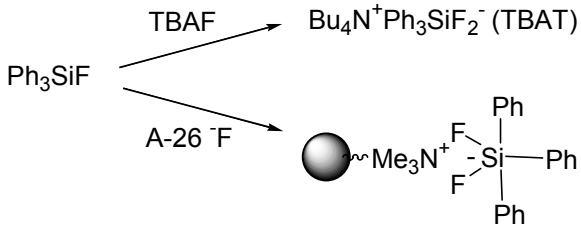
Table 7 Reagents and conditions: (a) PS-PPh_2*HBr cat., LiBr, CH_2Cl_2, RT, 2h; (b) +**22** 1.2 eq, + CH_2Cl_2, RT, 4h; (c) instead of glycal **22**, allal **118** was used in the step **b**, reaction time 24h. Allal **118** has demonstrated unusual low reactivity in the experiment **5**.

6.1.2. Towards the development of new polymer-bound fluorides for the deprotection of silylated alcohols

O-Silylation of alcohols was first introduced in the late fifties but silyl ethers were not widely appreciated as protecting groups in organic synthesis until the early seventies. Now silyl protecting groups play a major role in modern organic synthesis. They are readily formed and cleaved under mild conditions. Varying the substituents on silicon allows to finely tune their relative stability. The triethylsilyl group, for example, is more stable than trimethylsilyl but can be easier cleaved than the *t*-butyldimetylsilyl group. Not only the bulkiness of substituents affects silyl group stability but also their electronic nature. Thus, electron withdrawing groups, such as aryl substituents, enhance the stability under acidic conditions whereas the opposite effect can be noticed under basic conditions. Silicon has a high affinity for fluorine due to the greater strength of the silicon-fluorine bond (142 kcal/mol) compared to the silicon-oxygen bond (112 kcal/mol). Therefore, fluoride ions can be used to cleave silyl ethers under mild and highly specific conditions.

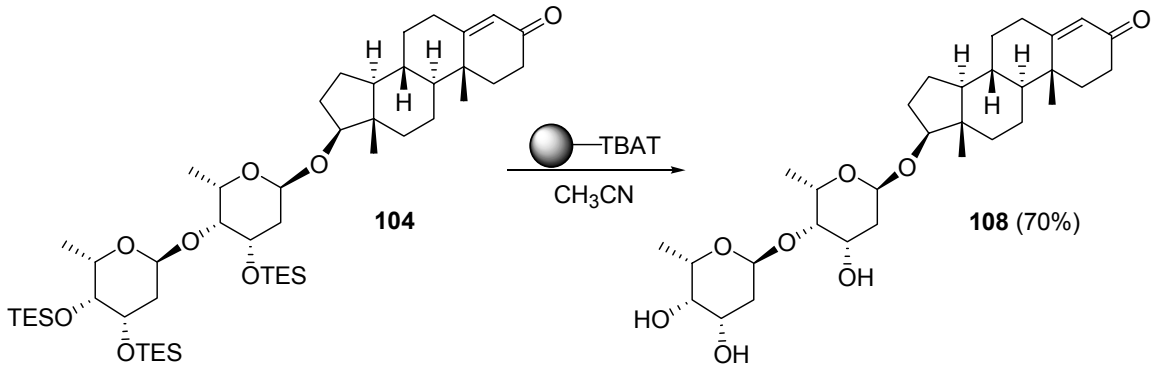
Nowadays, many methods have been developed to cleave silyl ethers in solution, but polymer-supported variants can rarely be found in the literature. The *Colonna* group in 1979 firstly reported the use of basic ion exchange resin to attach naked fluoride ions. They used it in various S_N2 fluorinations of steroids and sugars.[40a] Later *Huang* and co-workers used this resin to cleave various TMS-ethers.[40b]

Montmorillonite K-10 was used as acidic catalyst to cleave various silyl ethers.[40c,d] *Masaki* et al. offered polymer-bound π-acid dicyanoketene acetal catalyst for this purpose.[40e] Recently, *DeShong* and co-workers elaborated a new fluoride salt which is stable and compatible with most organic solvents.[41] They allowed triphenyl-silylfluoride to react with TBAF to form tetrabutylammonium (triphenyl-silyl)difluorosilicate (TBAT). It is not only a milder and non-basic fluorinating agent compared to TBAF but is also more stable and does not contain any molecular water. We used polymer-supported fluoride (Amberlyst A-26 F^- form) instead of TBAF, the silicate is formed directly on the polymer-bound amine.



Scheme 20 Synthesis of TBAT and its polymer-bound version

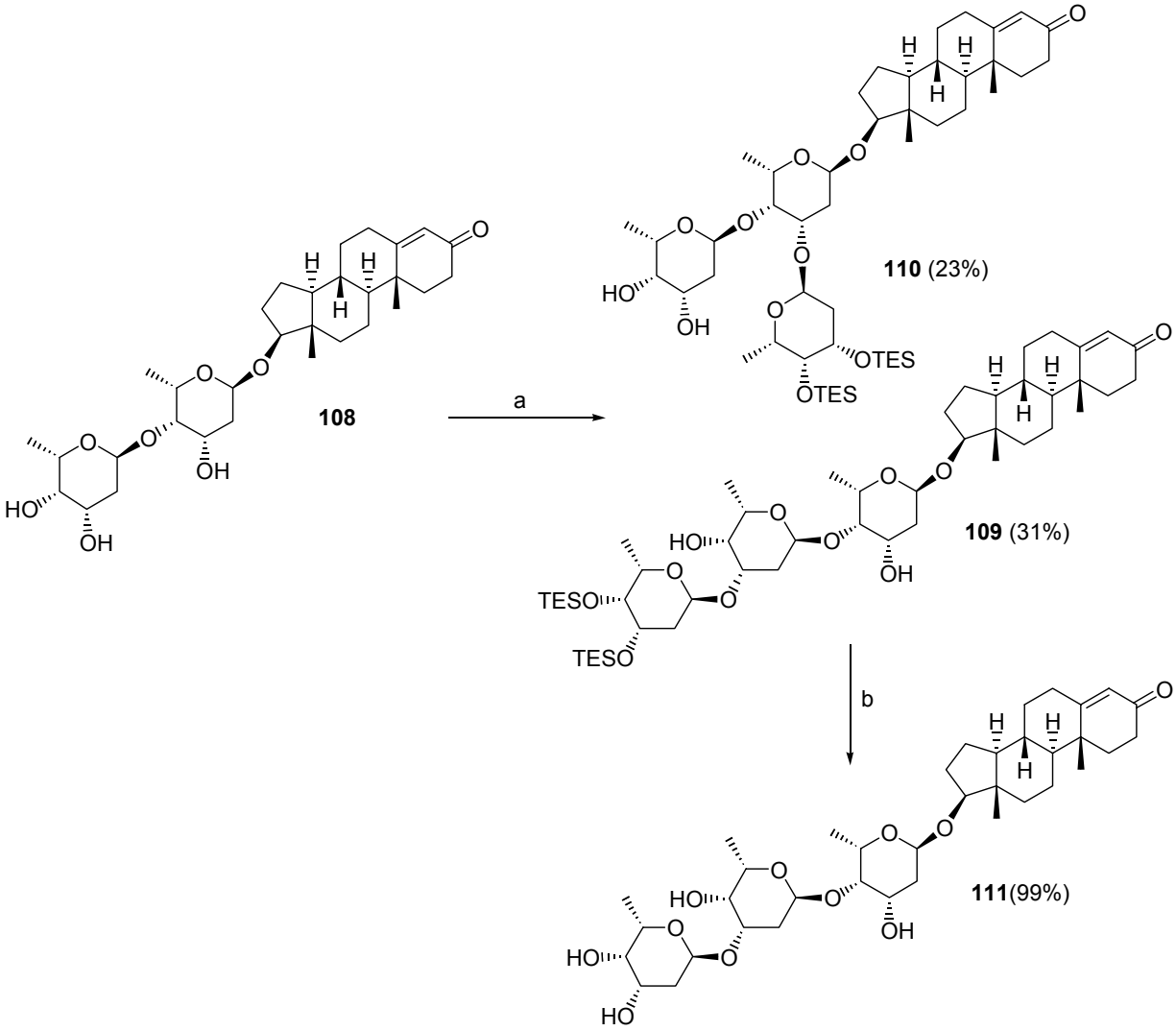
In such a way, a new polymer-bound TBAT was obtained and employed in some silyl ether deprotecting reactions to evaluate its capabilities in this area (Scheme 21). This new polymer is neutral to light acidic, and prior to reaction it should be gently washed with acetonitrile to remove any traces of free HF.



Scheme 21 Deprotection of silylated alcohols with polymer-bound TBAT

The resin developed only showed moderate results because significant extent (10-20%) of glycosidic bond cleavage was observed. However, in the same case, TBAF in tetrahydrofuran gave excellent yields without side reactions. The glycoconjugate **108** obtained was purified by short silica gel column filtration to eliminate unpolar triethylsilyl fluoride and employed in a glycosidation reaction with

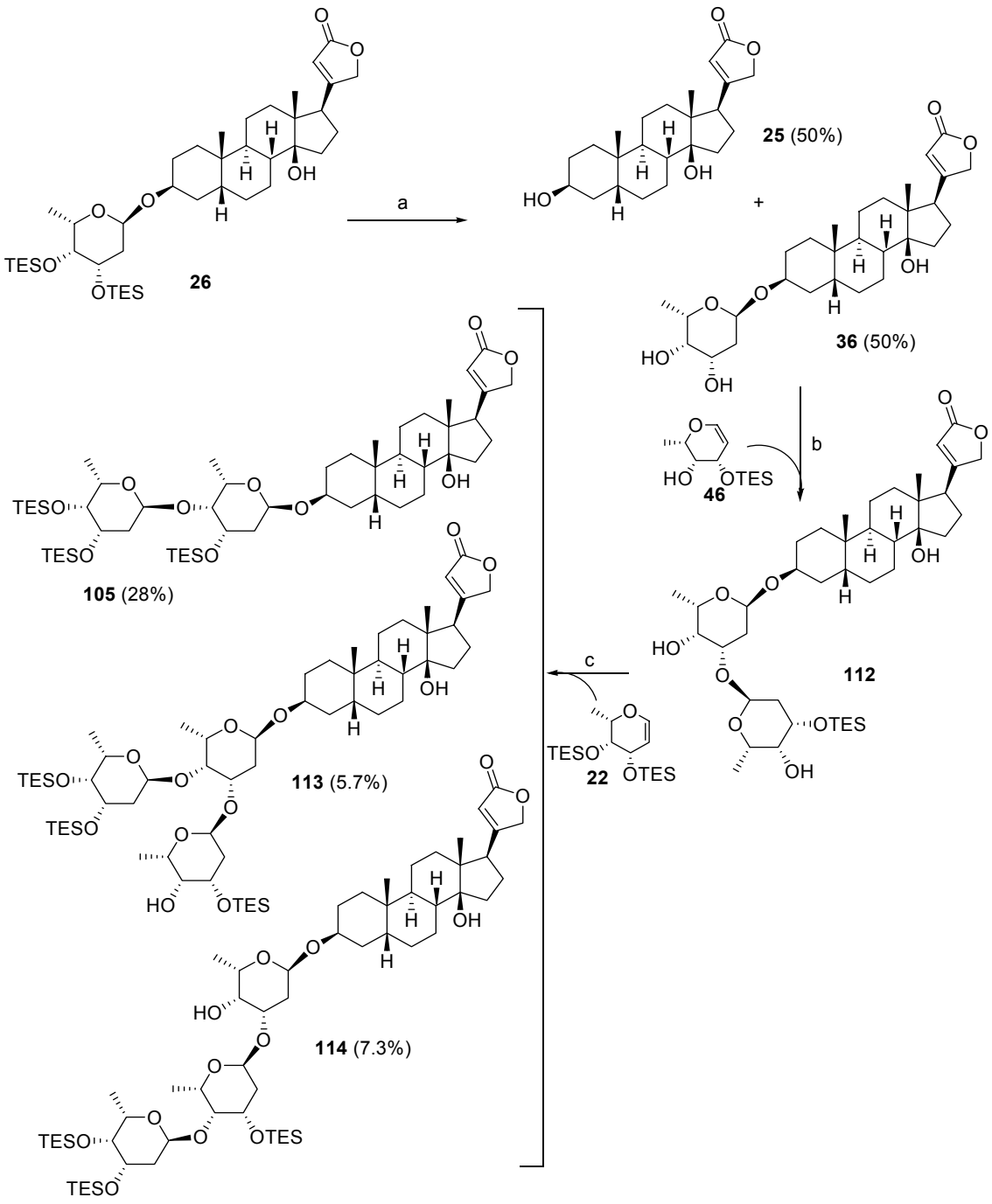
glycal **22** to afford two major products. Kinetically both C-3 hydroxyl groups in both fucals have similar activity but a hydroxyl function in the center of the glycoconjugate is slightly more hindered than on the terminal pyranose. This can also be observed in the current experiment (Scheme 22). The linear product **109** prevails over the branched trisaccharide **110**. The linear glycoconjugate was deprotected using TBAF solution in THF buffered with acetic acid to afford almost quantitative deprotection.



Scheme 22 Reagents and conditions: (a) **22**, PS-PPh_2*HBr cat. CH_2Cl_2, RT, 24h; (b) TBAF, THF, RT, 12h.

To evaluate the reactivity of Amberlyst A-26 (fluoride form) towards silyl ethers, the persilylated glycoconjugate **26** was chosen for a deprotection reaction using methanol as a solvent. No reaction was observed at room temperature for 10 hours. After elevating the temperature to 50^{o} C cleavage of the triethylsilyl groups

started. However, the glycosidic bond was also not stable under these conditions. Almost fifty percent of the starting material was deprotected within 20 hours. The second fraction isolated was free digitoxigenin (Scheme 23). The results observed allow to conclude that traces of acid in the polymer are capable to cleave the sensitive 2-deoxysugar glycosidic bond. The mixture of free digitoxigenin and glycoconjugate **36** was subjected to further glycosidation reaction without purification. Mono-protected fucal **46** was added together with polymer-bound PPh_3*HBr to the above afforded mixture in dichloromethane. When both starting materials **25** and **36** were fully consumed, glycal **22** was added to the reaction mixture. After 5 hours the reaction was quenched by addition of Amberlite A-21 and the resulting product mixture was purified by column chromatography. The disaccharide **105** originates from the free digitoxigenin which was formed in the first deprotection reaction. The other isolated trisaccharides **113** and **114** originate from glycoconjugate **36**.



Scheme 23 Reagents and conditions; (a) Amberlyst A-26 F^-, MeOH, 50^o C, 20h; (b) **46** 1.2 eq, PS-PPh_2*HBr, CH_2Cl_2, RT, 4h; (c) +**22** 1.2 eq, RT, 5h, yields are calculated from free digitoxigenin.

Summary

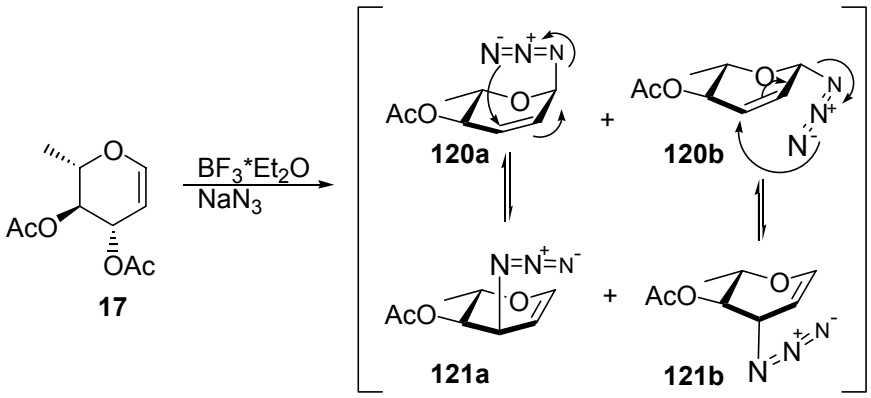
In order to secure excellent deprotection of 2-deoxyoligosaccharide and –glycoconjugate silyl ethers without undesirable side reactions, a polymer-bound reagent with the following qualities is necessary:

- it should be slightly basic
- it should contain fluoride ions with similar activity and substrate accessibility as in TBAF

- it should be compatible with various organic solvents (such as methanol, acetonitrile or CH_2Cl_2).

6.1.3. 3-Deoxy-3-azido-glycals as potential glycosyl donors

The reaction of L-rhamnal **17** with sodium azide in the presence of boron trifluoride which yields a mixture of α- and β-L-*erythro*-hex-2-enopyranosyl azides **120a** and **120b** is well documented.[41] The *Ferrier* products are in reversible equilibrium with the corresponding glycal-type azides **121a** and **121b** by means of a [3,3]-sigmatropic rearrangement (Scheme 24). It needs to be pointed out that these azidoglycals have not been regarded as proton-induced glycosyl donors in literature.

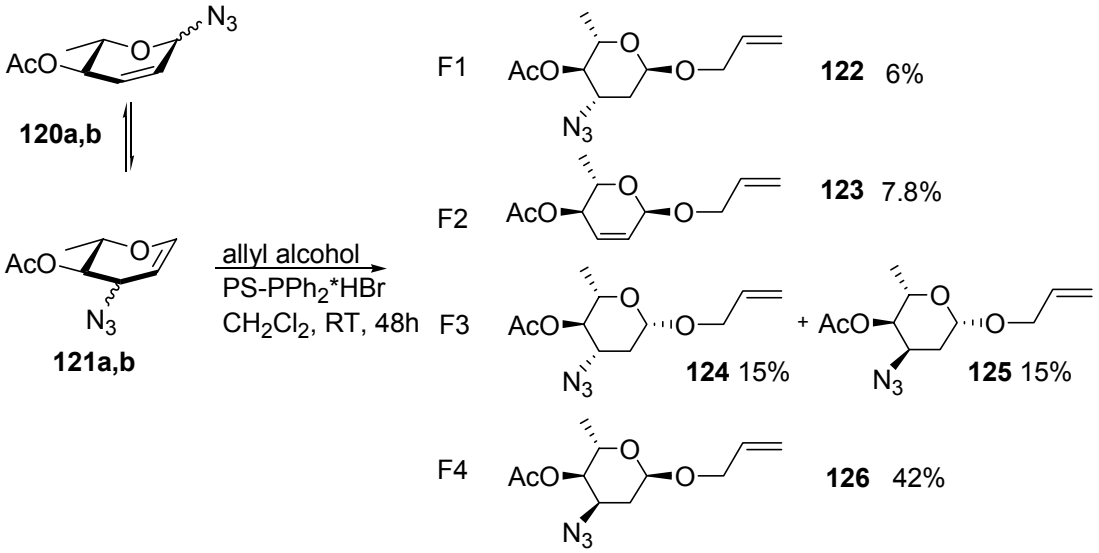


Scheme 24 Synthesis of 3-deoxy-3-azidoglycals

In the first minutes after the reaction is completed only Ferrier products **120a** and **b** were observed in the ^{1}H-NMR spectrum of the crude product in a about 1.2:1 ratio. Within 48 hours these *eno*-pyranosides rearrange to the corresponding azidoglycal **121a**, **b** which results in a mixture of regio- and stereoisomers in an approximate 60/40 ratio. Consequently, if these azidoglycals have similar donor capabilities as classic glycals, they could be activated with a proton source and can be utilized in glycosidation reactions in the presence of alcohols. This may lead to various azido-glycoconjugates. The [3,3]-sigmatropic rearrangement equilibrium could be then inclined in glycal direction, and in the best case the sugar could be fully consumed in the glycosidation reaction.

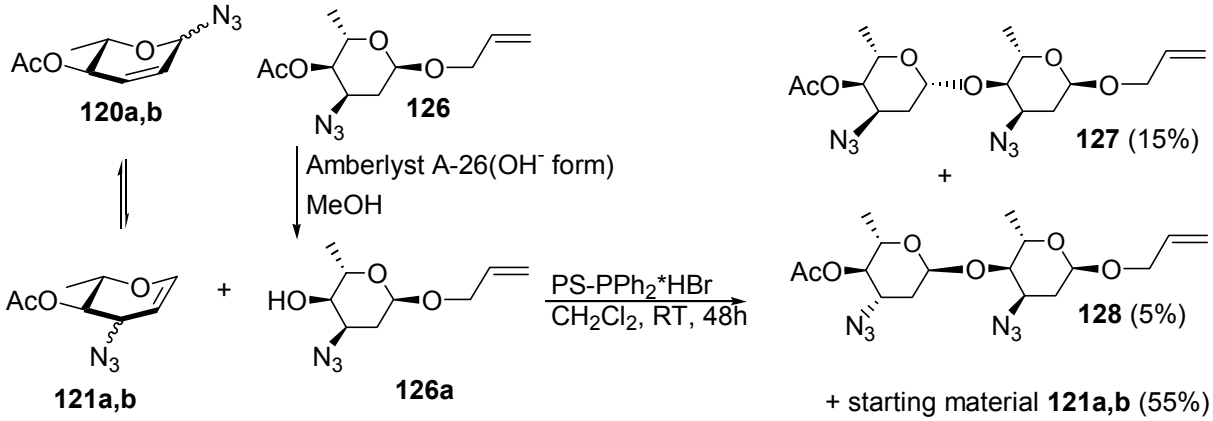
Thus, glycal mixture was employed in the glycosidation reaction with allyl alcohol catalyzed by the polymer-bound PPh_3*HBr (Scheme 25). Generally, this reaction

was significantly slower than the corresponding glycosidation with rhamnal **17**. Nevertheless, the overall yield was high enough to apply such a strategy in 2,3-deoxy-3-azido(amino)glycoconjugate synthesis.



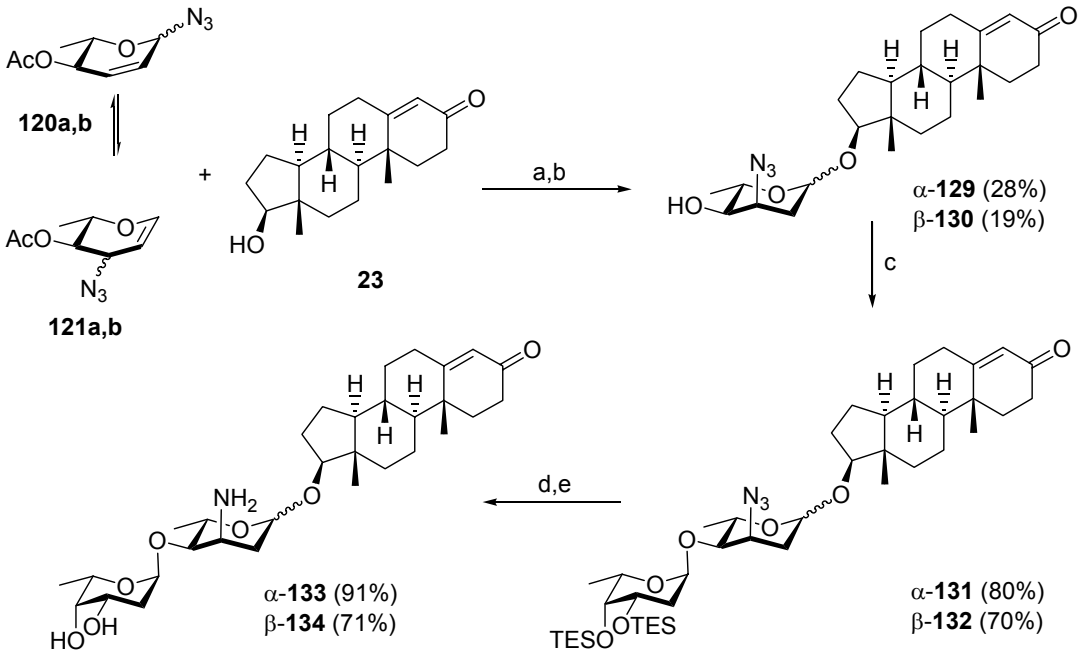
Scheme 25 Glycosidation of allyl alcohol with 3-deoxy-3-azidoglycals

The isolated allyl glycoside **126** was deacetylated under basic conditions and subjected once more in the proton-induced glycosidation with the azidoglycal mixture. After 48 hours the reaction was terminated and the product mixture was purified by column chromatography. *Ribo*-configured C-4 hydroxyl group in allylglycoside **126a** is sterically hindered, which hampers the accessibility of the substantially deactivated oxonium ion. Therefore, the two disaccharides **127** and **128** were isolated only in low yields together with the starting material (Scheme 26).



Scheme 26 Glycosidation of allylglycoside with 3-deoxy-3-azidoglycals

The scope and limitations of using this strategy in the synthesis of some amino-glycoconjugates is shown in Schemes 26 and 26a. Testosterone **23** was glycosidated with glycal mixture **121a**, **b** in moderate yields using the above mentioned reactions conditions. It is worth to notice a high kinetic selectivity of the given reaction, because only *ribo*-configured azidoglycal **121a** reacted within 24 hours yielding an anomeric mixture of glycoconjugates in excellent yields (about 80% when calculating only *ribo*-configured glycal). The *arabino*-configured azidoglycal **121b** remained unreacted and could be reisolated .



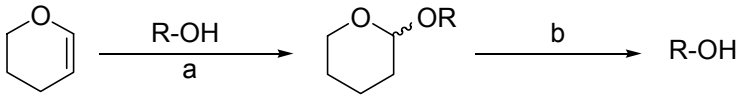
Scheme 26a Representative synthesis of glycoconjugates **133** and **134**; Reagents and conditions: (a) PS-PPh_2*HBr cat., CH_2Cl_2, RT, 24h; (b) Amberlyst A-26 (OH^- form), MeOH; (c) **22** 1 eq, PS-PPh_2*HBr cat., CH_2Cl_2, RT, 24h; (d) TBAF, THF, RT, 4h; (e) + PS-PPh_2, RT, 24h.

Both glycoconjugates were deacetylated and separated by column chromatography. Further glycosidation with fucal **22** afforded disaccharides **131** and **132.** After removing the TES groups with TBAF and subsequent *Staudinger* azide reduction with polymer-bound triphenylphosphine glycoconjugates **133** and **134** were obtained in excellent yields.

6.1.4. Polymer-bound triphenylphosphonium bromide as effective promoter for alcohol protection/deprotection with the tetrahydropyranyl (THP) group

Tetrahydropyranyl ethers, introduced as a protecting group for alcohols in 1948, are still widely used in modern chemistry.[42] They can both be formed under mild

acid-catalyzed conditions in CH_2Cl_2, and cleaved under similar conditions using other solvents such as methanol or a mixture of THF-water.[43] As substrate dihydropyran (DHP) is commonly used, which is protonated to build up an oxonium ion similar to glycals. This oxonium ion is attacked in the following by a nucleophilic alcohol. The similarities in the activation-addition mechanisms suggested to evaluate polymer-bound PPh_3*HBr as a potential reagent to introduce the THP group under very mild conditions. As test substances, some complex alcohols were employed and protected by proton-catalyzed addition to DHP. In a second set of experiments the THP-ethers were successfully deprotected using polymer-bound PPh_3*HBr as a mild proton source in methanol as a solvent (Table 8).



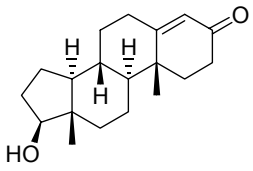
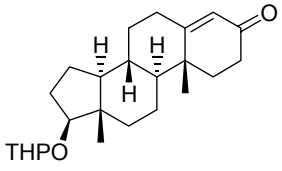
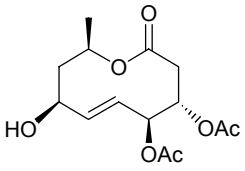
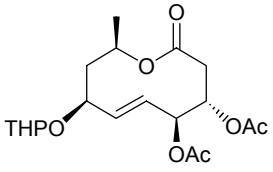
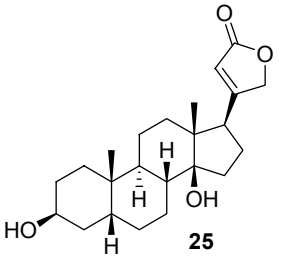
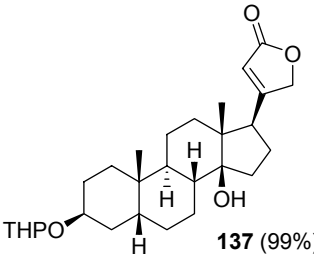
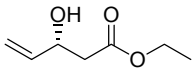
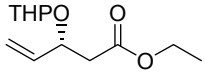
alcohol	THP-ether	cleaved alcohol (yield)
 **23**	 **135** (97%)	**23** (99%)
 **40**	 **136** (99%)	**40** (99%)
 **25**	 **137** (99%)	**25** (99%)
 **138** [90]	 **139** (99%)	**138** (99%)

Table 8 Reagents and conditions: (a) PS-PPh_2*HBr cat. DCM, RT, 3h; (b) PS-PPh_2*HBr cat., methanol, RT, 12h.

The mildness of the procedure is demonstrated for digitoxigenin **25** and the allyl alcohol **138** which easily can undergo retro-aldol reactions. In all cases, addition of alcohol to DHP proceeded almost quantitatively, and the following deprotection yielded chromatographically pure starting alcohol. Consequently, this reagent turned out to be a very powerful tool for the protection/deprotection of alcohols as the corresponding THP-ethers.

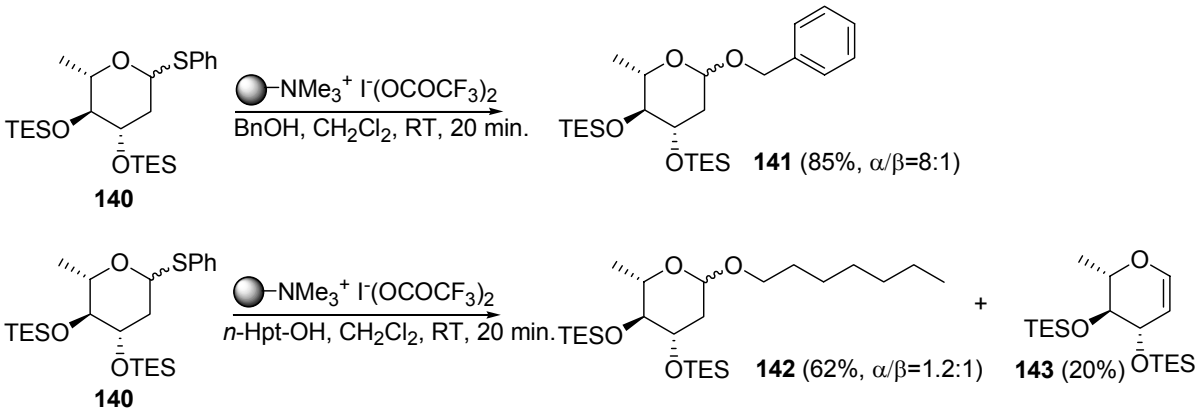
6.2. Polymer-assisted glycosidation of thioglycosides

6.2.1. Polymer-bound iodo(I)bis(trifluoroacetate), a versatile electrophilic promoter for the glycosidation of thioglycosides

Thioglycosides are widely utilized glycoside donors in carbohydrate chemistry. *Ferrier* et al. introduced the use of mercuric salts for the activation of thioglycosides due to high sulfur affinity to mercury.[44a] In the early eighties *Nicolaou* and co-workers offered the first thioglycoside-based glycosidation method using the halogen (I) based electrophilic reagent NBS.[44b] Later many other groups evaluated and further developed thioglycosides in electrophilic glycosidations by employing such electrophile catalysts as DMTST[44c], IDCP[44d], and NIS/TfOH[44e].

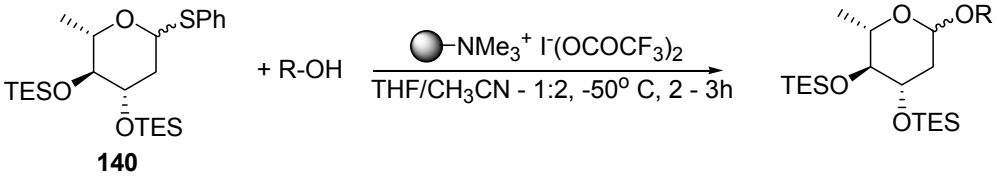
Recently, new halogenate (I)-complexes on solid support were developed in the *Kirschning* group.[45] One of these reagents, polymer-bound iodo(I)bis(trifluoroacetate), could be a very potent electrophilic activator of thioglycosides.

The first experiments were conducted by employing some simple alcohols as test systems in order to evaluate polymer capabilities for the activation of thioglycoside (Scheme 27).



Scheme 27 Glycosidation of some alcohols using polymer-bound iodo(I)bis(trifluoroacetate)

In both experiments glycosidation proceeded very rapidly, but formation of minor decomposition products were observed. In the second experiment, rhamnal **143** was also isolated as a by-product, which originated from the possible of a proton at C-2 when the oxonium cation is generated. A lower reaction temperature led to elongated reaction times without any improvements concerning the purity of the reaction products. In addition, liberated iodine and trifluoroacetic acid catalyzed silyl group cleavage which could be one of the reasons of the detected impurities.
To improve the yields, reaction conditions had to be thoroughly optimized. As an optimal reaction medium a bipolar aprotic solvent system (THF/CH_3CN 1:2) was chosen in which important reaction intermediates can be stabilized to avoid unfavorable side reactions. In the given conditions the reaction rate accelerated drastically, which meant lower reaction temperature (Table 9).



R-OH	Product

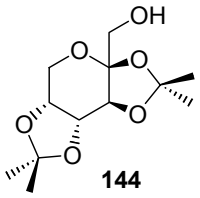
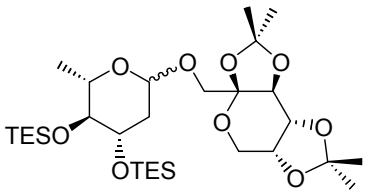
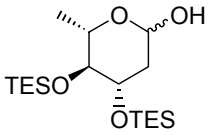
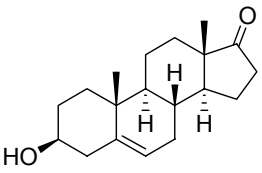
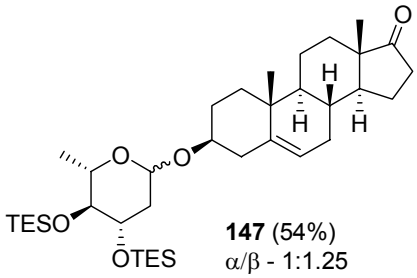
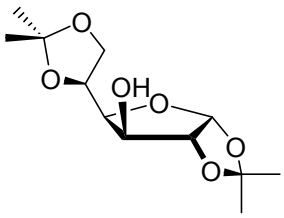
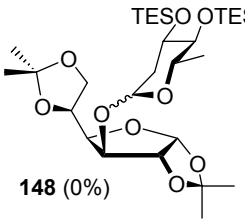
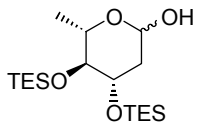
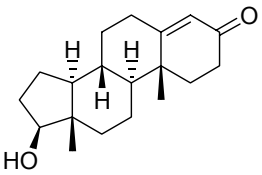
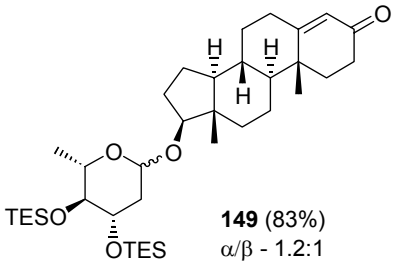
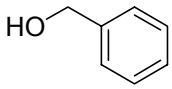
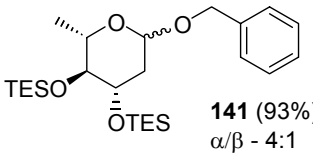
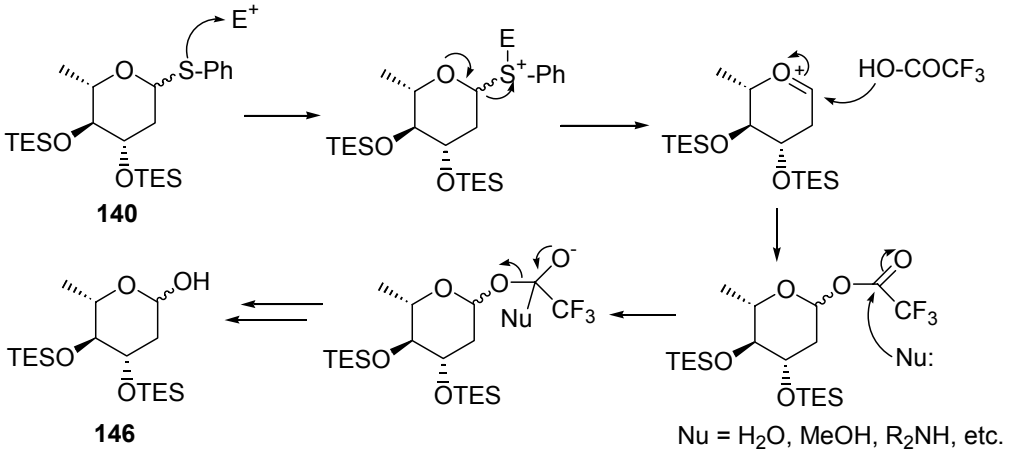
 **144**	 **145** (47%) α/β - 1.36:1 +  **146** (20-30%)
	 **147** (54%) α/β - 1:1.25
	 **148** (0%)  **146** (85%)
 **23**	 **149** (83%) α/β - 1.2:1
	 **141** (93%) α/β - 4:1

Table 9 Glycosidation using polymer-bound iodo(I)bis(trifluoroacetate)

All reactions were carried out at lower temperature in a 1:2 mixture of THF/CH_3CN using one equivalent of donor, acceptor, and polymer-bound activator. Isolated yields highly depend on the nature of glycosyl acceptors. Sterically inconveniently placed hydroxyl groups can be made responsible for reduced yields or may cause formation of other products. For example, the effort to glycosylate diacetonfructopyranose **144** led to the formation of pyranose **146** as a by-product. If diacetonglucofuranose is employed as an acceptor, this side reaction proceeds

exclusively leading to pyranose **146** in 85% isolated yield and none of the desired disaccharide **148** was formed. The extremely low reactivity of a hydroxyl group at C-3 is well documented, therefore this carbohydrate is well suited for determining the activity of different promoters. The trifluoroacetic acid liberated in the reaction medium after thioglycoside activation could be a reason for the formation of pyranose **146**. This acid can act as a weak nucleophilic acceptor, and if another nucleophile is not present in the reaction medium or is sterically inaccessible the intermediated anomeric, trifluoroacetate is formed (Scheme 28). In the following and upon work-up this ester easily hydrolyses to form free pyranose **146.**



Scheme 28 Mechanism of formation of monosaccharide **146**

These test reactions clearly demonstrate the applicability of the new polymer-attached activator in glycosidations of non-hindered alcohols. Indeed, polymer-bound iodo(I)bis(trifluoroacetate) showed excellent thiophylicity towards thioglycosides. The use of other more stable protecting groups could allow elevated reaction temperatures. Thereby, the trifluoroacetate intermediate, for which we collected evidence in some experiments (pyranose **146** were occasionally isolated), can itself be activated, thus driving the glycosidation to completion.

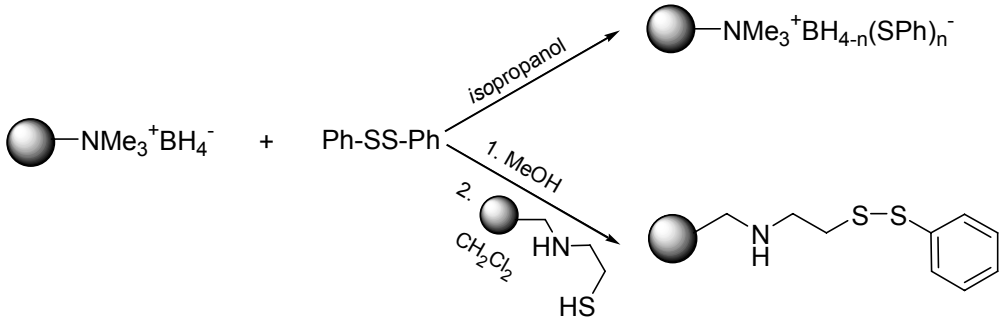
6.2.2. Polymeric scavenger reagent for diphenyl disulphide

Several reviews about polymer-supported scavenger reagents were recently published.[46] The clear advantage of this technology lies in the area of purification – simple addition of a polymeric scavengers to the reaction mixture with subsequent

filtration leads to the required target molecule in high purity. These functionalized polymers can be used to remove an excess of reactant or equally well liberated by-products. In addition to the known applications of solid-supported reagents this purification technique can also be applied in traditional solution-phase synthesis.

In all thioglycosidation reactions diphenyl disulphide is formed as a by-product. Commonly, it can be separated during the purification process by column chromatography. In the automated solution-phase synthesis such additional operations are not always feasible. Therefore, polymer-assisted purification techniques can help avoiding these additional procedures. Up to date no polymeric scavengers for disulphides are reported. Disulphides, if not removed, can slow down the oxidation and reduction processes and contaminate different transition-metal catalyzed reactions which are planned to be conducted in the next steps.

In this work a new method is disclosed which allows complete scavenging of diphenyl disulphide which is liberated during the thioglycosidation process (Scheme 29). Polymer-bound borohydride is used as a reagent of choice in *iso*propanol: borohydride resin reacts only sluggishly with *iso*propanol. Upon reaction thiophenol is formed and is attached to the polymer as thioboric acid ester. As an alternative polymer-bound 2-amino-1-thioethanol in CH_2Cl_2 could be used. In this case thiophenol, reduced by borohidride resin, forms disulphide with polymer-attached thiol in the presence of air. Both procedures allow quantitative removing of the diphenyl disulphide from the reaction medium, though, in second procedure employed polymer-bound thiol is fairly expensive that limits its application.



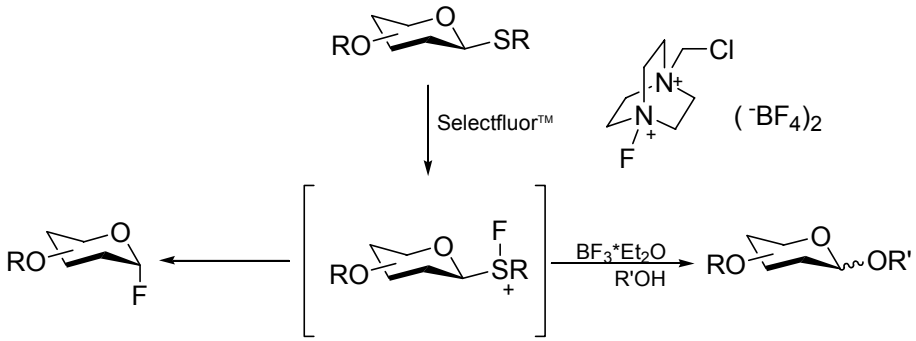
Scheme 29 Polymer-supported borhydride and 2-amino-1-thioethanol as a scavengers for disulphides.

In a typical procedure after workup of the thioglycosidation reaction, the crude product (0.1 mmol) containing diphenyl disulphide is dissolved in a 3 ml of

isopropyl alcohol. Subsequently 100 mg of polymer-supported borhydride is added. The resulting suspension is then allowed to shake for 12 hours whereupon disulphide is fully scavenged. This procedure can be repeated if the next step of synthesis is very sensible to sulfur traces such as catalytic debenzylation of benzyl ethers using hydrogen over Pd or Pt catalysts.

6.2.3. Selectfluor™ as powerful thiophilic activator for 2-deoxythioglycosides

In the last decade 1-chlormethyl-4-fluoro-1,4-diazonia-bicyclo[2.2.2]octane bis(tetrafluoroborate) (selectfluor™) was introduced as mild fluorinating agent.[47] Its application in sugar chemistry - especially in addition to glycals was extensively studied in the *Dax* and *Wong* laboratories.[48] *Wong* and co-workers were also the first to report on the ability of selectfluor™ to activate thioglycosides in the presence of boron trifluoride-etherate complex. No additional aspects more in the thioglycoside area were reported since then. *Wong* also proposed a mechanism for the activation of thioglycosides using selectfluor™ (Scheme 30).

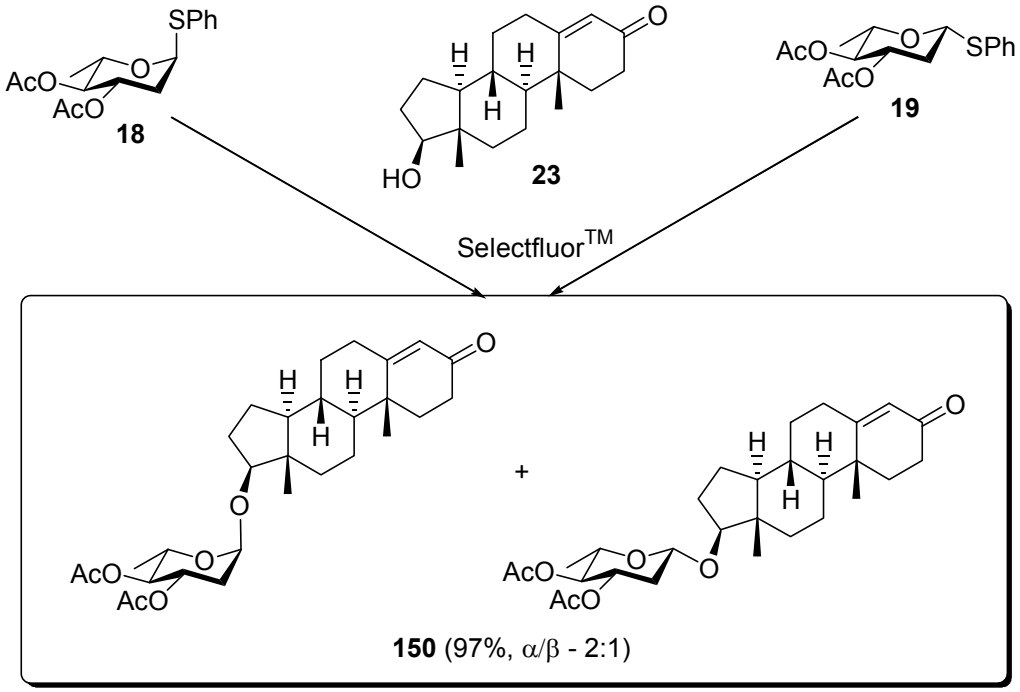


Scheme 30 Thioglycoside activation mechanism by *Wong*[48d]

Wong proposed a fluorosulfonium ion as an intermediate, which later decomposes to glycosyl fluoride or can be activated with boron trifluoride-etherate complex for further glycosidations with alcohols.

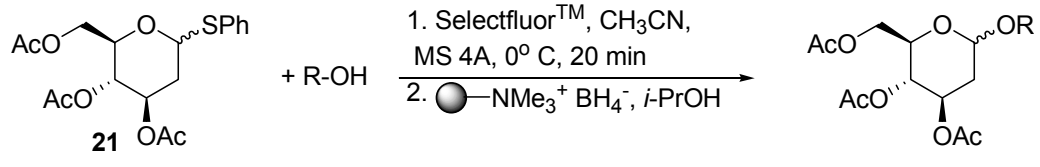
This activation method has briefly been evaluated on 2-deoxythioglycosides which allowed to prepare glycoconjugates **72** and **74** in excellent yields (See Table 4 in chapter 5.3). In the case of 2-deoxythioglycosides boron trifluoride is not necessary for glycosyl activation in conjunction with selectfluor™. As a test system for determining the stereospecificity of these glycosidations α- and β-configured

thioglycoside donors **18** and **19,** respectively, were chosen in the glycosidation with testosterone (Scheme 31).

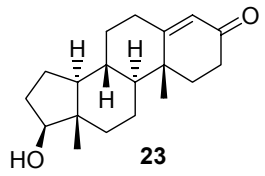
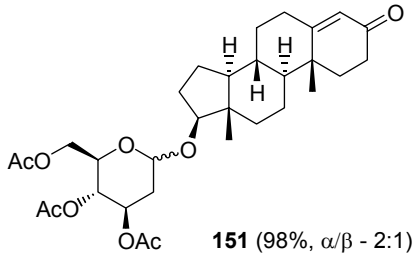
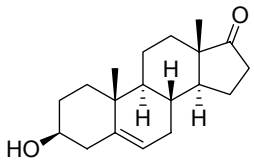
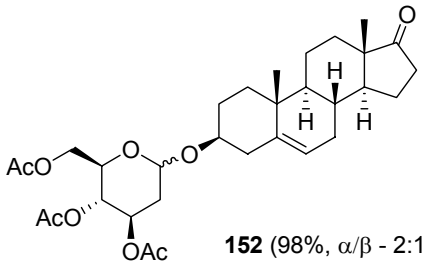
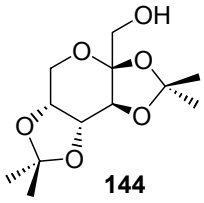
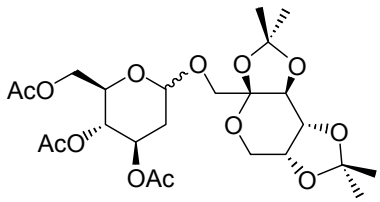
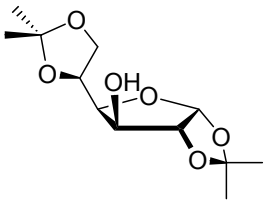
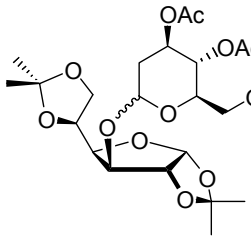
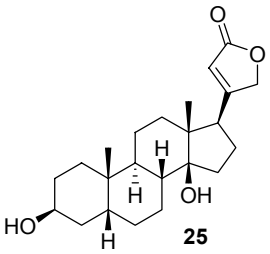
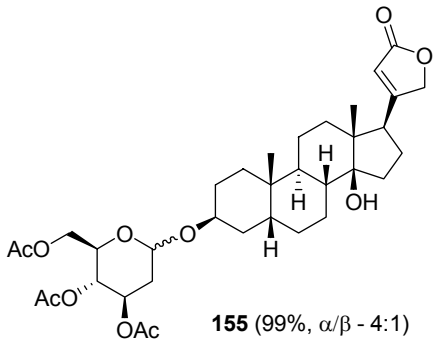
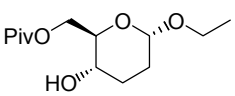
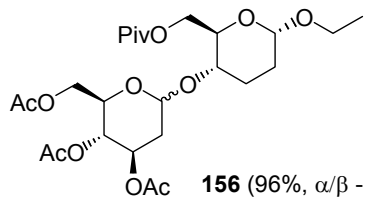


Scheme 31 Reagents and conditions: **18** or **19** 1 eq, **23** 1 eq, Selectfluor™ 1 eq, CH_3CN, MS 4Å, 0° C, 20 min.

Surprisingly, both anomers yielded the same α/β-ratio of glycosidation products. These observations point to an identical intermediate which in fact originates from different thioglycosides. Such an intermediate could be the oxonium ion that is a common species in glycosidation processes. Therefore, the fluorosulfonium ion (Scheme 30) decomposes before a nucleophile attacks the anomeric center with activated phenylthio group. The phenylfluorosulfide later forms diphenyldisulfide in a still obscure fashion. After diphenyldisulfid is removed by the scavenging protocol described above the products could be obtained in high yields and with excellent purity without necessity of additional purification. This strategy was tested on various aglyca and sugars (Table 10).



R-OH	Product

 **23**	 **151** (98%, α/β - 2:1)
	 **152** (98%, α/β - 2:1)
 **144**	 **153** (94%, α/β - 2:1)
	 **154** (79%, α/β - 4:1)
 **25**	 **155** (99%, α/β - 4:1)
	 **156** (96%, α/β - 2:1)

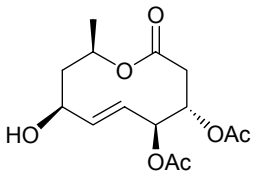
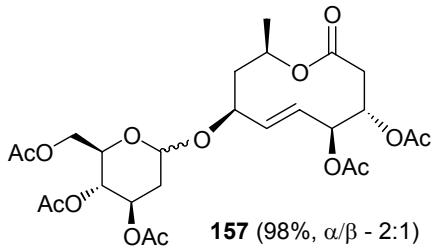
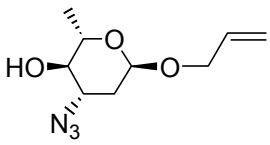
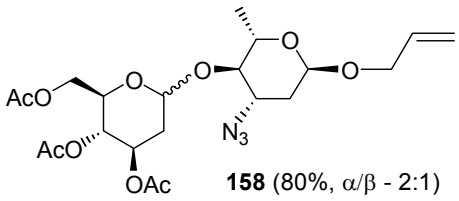
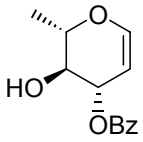
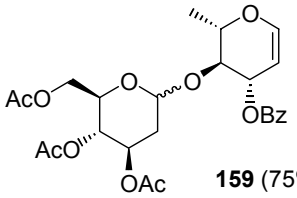
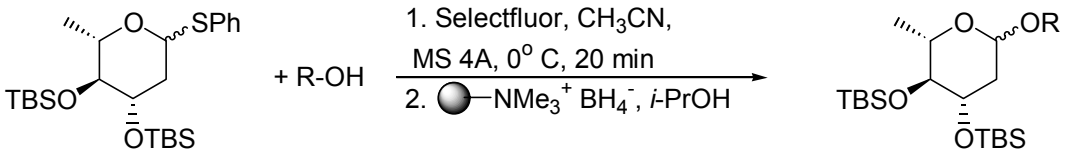
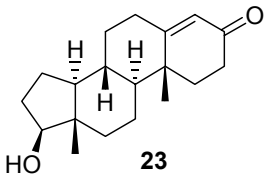
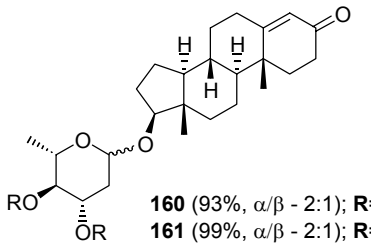
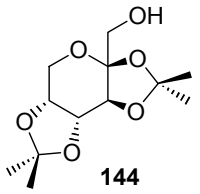
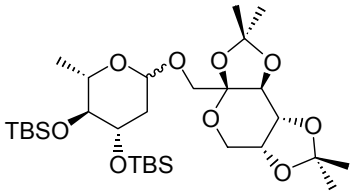
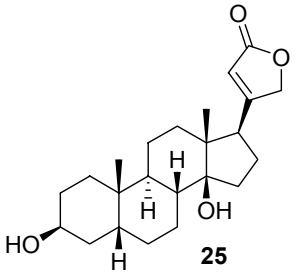
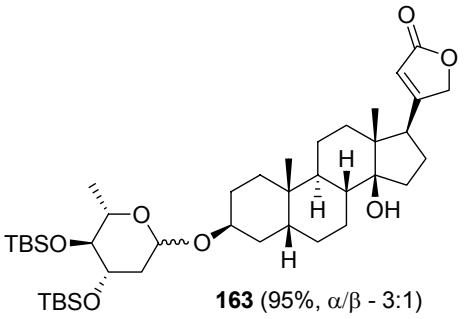
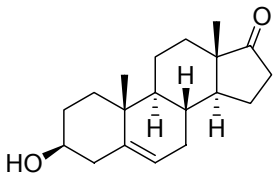
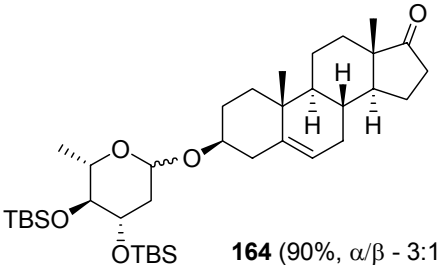
 **40**	 **157** (98%, α/β - 2:1)
	 **158** (80%, α/β - 2:1)
 **31**	 **159** (75%, α/β - 2:1)

Table 10 Glycosidation of thioglycosides with Selectfluor™ as an electrophilic activator (I)

Thioglycoside **21** was used as an anomeric mixture (α/β - 1:1) because the stereochemistry at the anomeric center was irrelevant for the stereochemical outcome of the glycosidation. It is obvious that the efficiency of the glycosidations conducted is hardly influenced by steric factors. Even diacetonglucofuranose can be glycosylated with excellent results which is in sharp contrast to the efforts using the polymer-attached iodate(I) complex mentioned above. This approach has clear advantages over the thioglycosidation procedures developed by *Nicolaou*[44b] and *van Boom*[44e], who employed NBS, NIS and combinations, where the liberated succinimide competes with the acceptor. Surprisingly, this method can also be employed using glycals despite the fact that selectfluor™ has been utilized as fluorinating agent for glycals[48]. These results testify a much greater affinity of selectfluor™ for sulfur than for the enolether double bond of glycals. One equivalent of boron trifluoride is liberated during the reaction, therefore basic molecular sieves are essential to buffer the reaction medium thus avoiding possible side reactions catalyzed by *Lewis* acids. After thioglycoside activation selectfluor™ is transformed into a salt with low solubility in most of organic solvents so that it can be separated by simple filtration through a pad of basic alumina. The remaining diphenyldisulphide is scavenged using the protocol mentioned above to

yield a pure product which can be used in the next step without additional purification. The anomeric mixture obtained can be separated chromatographically if pure anomers are needed. The given method was further evaluated for the 2-deoxy-L-rhamnoside thioglycoside with silyl protection in order to evaluate silyl group stability (Table 11).



R-OH	Product
 **23**	 **160** (93%, α/β - 2:1); **R**=TES **161** (99%, α/β - 2:1); **R**=TBS
 **144**	 **162** (60%, α/β - 1.8:1)
 **25**	 **163** (95%, α/β - 3:1)
	 **164** (90%, α/β - 3:1)

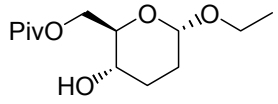
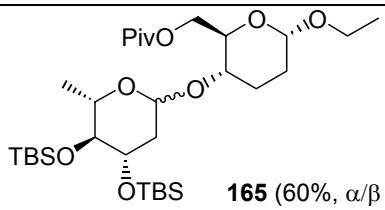
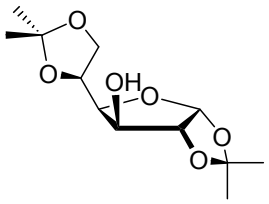
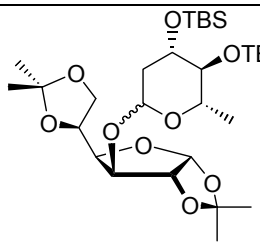
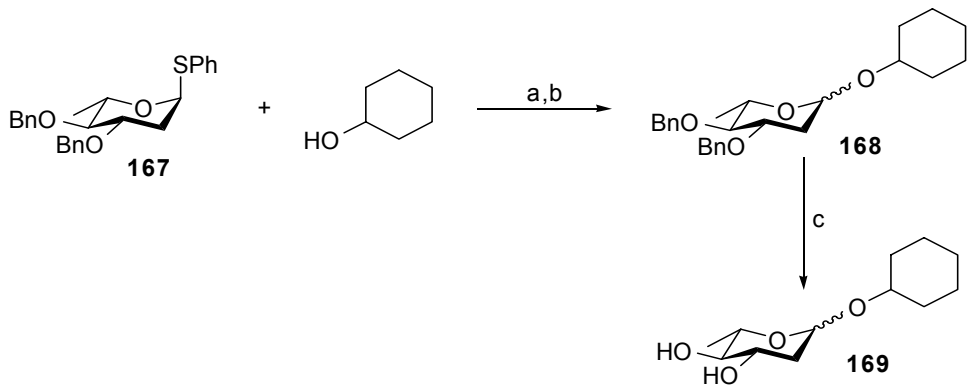
	 **165** (60%, α/β - 5:1)
	 **166** (55%, α/β - 2:1)

Table 11 Glycosidation of thioglycosides with Selectfluor™ as an electrophilic activator (II)

The overall yields are slightly lower compared to fully acetylated phenylthiodonor, but the general trend remains. Less hindered alcohols still gave almost quantitative yields and chromatographically pure products. With more hindered acceptors the yields slightly decrease.

An often employed protecting group in natural product synthesis is the benzyl ether which needs to be cleaved in the final step using H_2/Pd or H_2/Pt.[49] This hydrogenation may be hampered or completely suppressed if thioglycosidation is involved in the previous steps liberating thio impurities. To prove the quality and versatility of diphenyldisulphide scavenging an additional experiment was conducted with fully *O*-benzylated thioglycoside donor **167** (Scheme 32). The thioglycoside **167** was involved in a glycosidation reaction with cyclohexanol as acceptor with a subsequent scavenging procedure. The following palladium-catalyzed hydrogenation of the benzyl ethers was performed to determine whether the remaining sulfur traces (if such exist) were large enough to contaminate the catalyst.

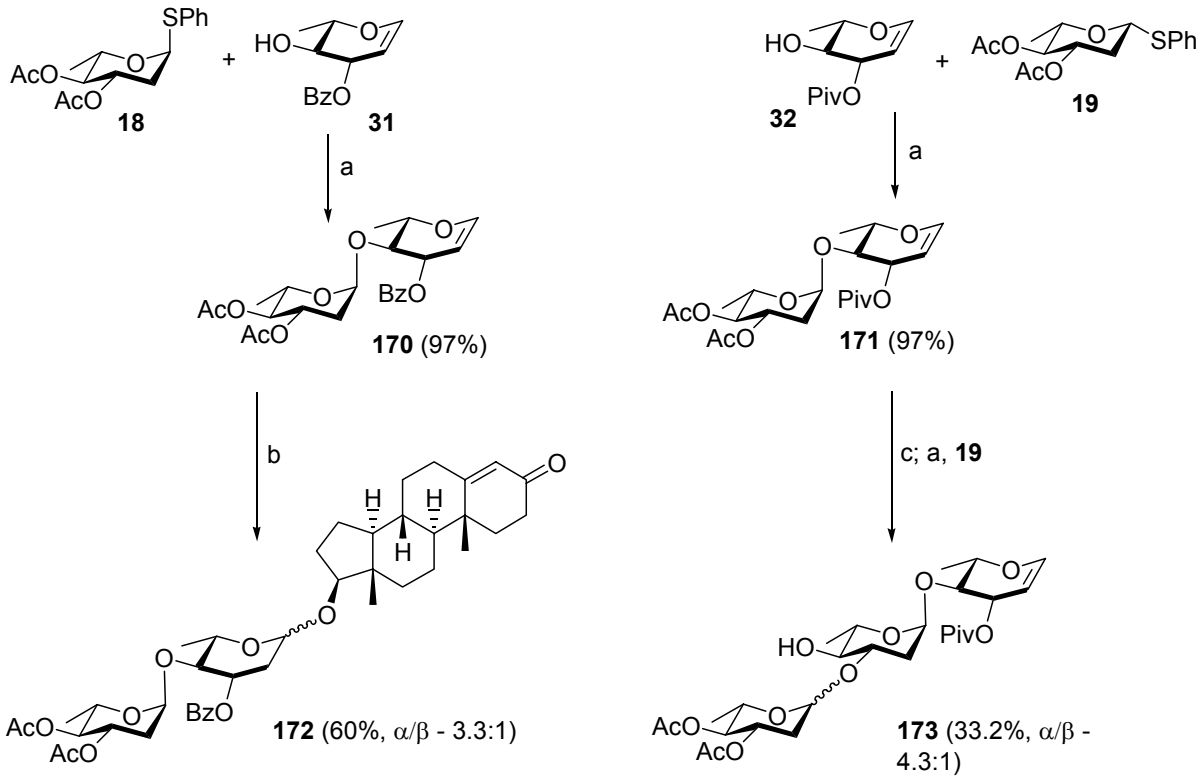


Scheme 32 Reagents and conditions: (a) Selectfluor™, CH_3CN, 0° C, 15 min; (b) polymer-bound-NMe_3 BH_4, *i*-PrOH, 12h, and repeat, 98%; (c) Pd/C-10%, H_2, 20 bar, 2h, 99%.

The standard scavenging procedure with a minimal amount of scavenger had to be be repeated because the traces of thiophenol, remaining after the first treatment with borhydride resin, deactivated the palladium catalyst. However, after the second scavenging step de-*O*-benzylation was achieved with large efficiency to yield glycoside **169**.

7. Orthogonal oligosaccharide and glycoconjugate synthesis employing polymer bound triphenylphosphonium bromide and selectfluor™ as activators for glycosidation

The thioglycosidation strategy which utilized glycals can be applied to an orthogonal oligosaccharide and glycoconjugate synthesis. The previously prepared disaccharide **159** which contains a glycal moiety may be directly activated for the next glycosidation step. In this work a new approach of obtaining oligosaccharides and glycoconjugates through polymer-assisted synthesis in solution is demonstrated. Disaccharides **170** and **171** are initally obtained using selectfluor™ thioglycoside activation (Scheme 33).



Scheme 33 Reagents and conditions: (a) Selectfluor™, CH_3CN, 0° C, 15 min; (b) PS-PPh_3*HBr cat, **23**, CH_3CN, RT, 24h; (c) Amberlyst A-26 OH^- , MeOH, RT, 12h.

In both disaccharides the glycosidic bond was established as pure α-epimers although in the first procedure α-thioglycoside **18** and in the second example the β-configured thioglycoside **19** was used. This proves once again that the proposed mechanism occurs through an identical intermediate in both cases. The disaccharides obtained were separately utilized in further glycosidation steps in which one of them acts as a donor and the other is applied as an acceptor after a deacetylation procedure. The products **172** and **173** were obtained in good yields without further optimizations which probably could improve the final outcome.

8. Conclusions and outlook

In this work polymer-bound 2-deoxyoligosaccharide and –glycoconjugate synthesis on PS-DES resin was compared with related polymer-assisted solution-phase synthesis using polymer-bound reagents and catalysts. The new polymer, developed by Argonaut technologies, demonstrated good to excellent results in disaccharide and small glycoconjugate synthesis on polymer-support. Attaching the first sugar onto the polymer proceeded with excellent yields and loading was much better (up to 1.1 mmol/g) compared with the other widely used polymers in solid-phase carbohydrate chemistry (0.1 – 0.65 mmol/g).[12d] Glycosidation of the second carbohydrate or the aglycon with the polymer-bound glycal gave good yields, though it was impossible to drive the glycosidation to completion in spite of 3-fold excess of the acceptor. In this way, glycoconjugates such as **52** and **54** were synthesized in 78 and 75% yields, respectively, and disaccharides, like **58**, **60** and **68,** were obtained in 70, 76, and 80% yield, respectively. Further attempts to attach a third acceptor onto the polymer-support were unsuccessful or gave low yields. The main problem was the elevated instability of the 2-deoxysugar glycosidic bond in the presence of a mild proton source in comparison to experiments in solution, where no decomposition was observed under identical conditions. The glycal activation on the polymer-supported disaccharide always led to the retroglycosidation. Further attempts to utilize the thioglycosidation strategy on polymer-support disclosed low reactivity of thioglycoside donors due to the restricted amount of thioglycoside activators, that may be compatible with the labile linker system used, and the limited choice of reaction conditions in which no decomposition of polymer-bound disaccharide was observed. Nevertheless, this polymer can be involved as a polymeric carrier in small disaccharide and glycoconjugate library synthesis with an acceptable outcome. This polymer has demonstrated excellent swelling capabilities in dichloromethane and chloroform that eases polymer-bound intermediate characterization using gel-^{13}C-NMR techniques. Both, polymer-bound disaccharides and glycoconjugates, could be easily monitored and characterized without cleavage from the polymeric carrier. Measuring the signal strength in gel-NMR spectra, it was possible to determine relative polymer loading and the glycosidation progress as the starting material

signals slowly disappeared a companied by the appearance of the successive product signals.

The first selective protecting strategy for decarestrictine-D was developed and the different reactivity of all the three hydroxyl functions was further[24d] evaluated. Partially protected decarestrictine **40** was successfully involved in glycosidation reactions on solid support and in solution using polymer-assisted techniques.

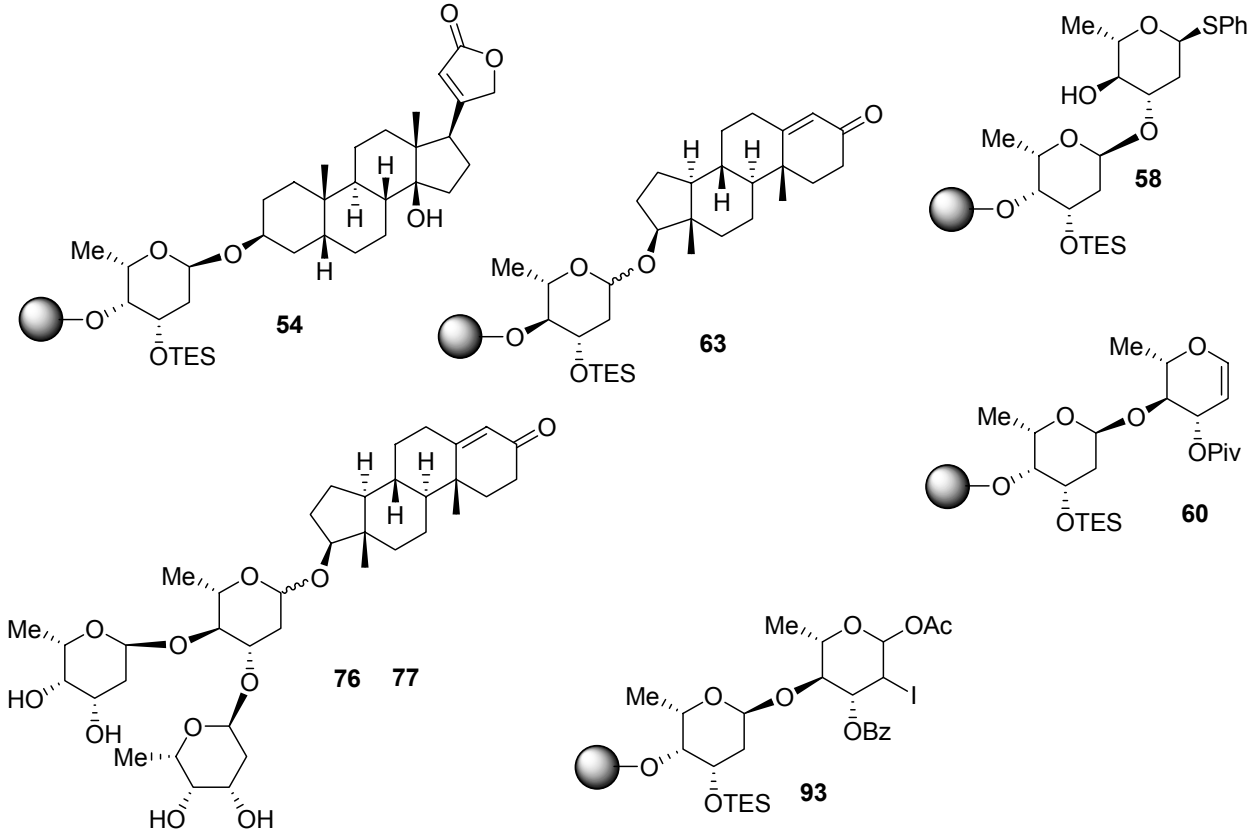


Figure 6 Selected substances from the polymer-bound synthesis chapter

The newly developed polymer-bound triphenylphosphonium bromide (P-TPHB) was involved in several glycosidation reactions as a mild proton source for glycal activation. Using an "armed-disarmed" donor technique a new one-pot glycoconjugate and oligosaccharide-synthesis method was developed based on different reactivities of the glycal and carbohydrate hydroxyl groups. Using this strategy, a small glycoconjugate library was synthesized with good to excellent yields (**96, 100, 103, 104, 105, 106, 107, 109, 110, 112, 113, 114** and **119**). This method can be automated if a proper and efficient polymer-bound reagent for the silyl ether cleavage is applied. The developed polymer-bound triphenyl difluorosilicate presented moderate affinity for silyl ethers. Traces of HF present in

polymer cavities frequently catalyzed side reactions which paralleled silyl ether cleavage.

Further P-TPHB was evaluated on 3-azidoglycals which could possibly undergo glycosidation reactions by protonation. Azidoglycals **121** showed acceptable activity as glycosidic donors in reactions with non-hindered alcohol acceptors. Applying this method several 2-deoxy-3-azidodisaccharides and 2-deoxy-3-aminoglycoconjugates were synthesized in good yields (**127, 128, 133** and **134**).

Dihydropyran is commonly used to introduce a tetrahydropyranyl protective group for alcohols under mild acidic conditions. This protecting group can be cleaved using slightly more acidic conditions in a protic solvent system. Polymer-bound triphenylphosphonium bromide was successfully tested for the introduction and cleavage of THP protecting groups. Several alcohols were quantitatively protected and deprotected with high purity of the final product.

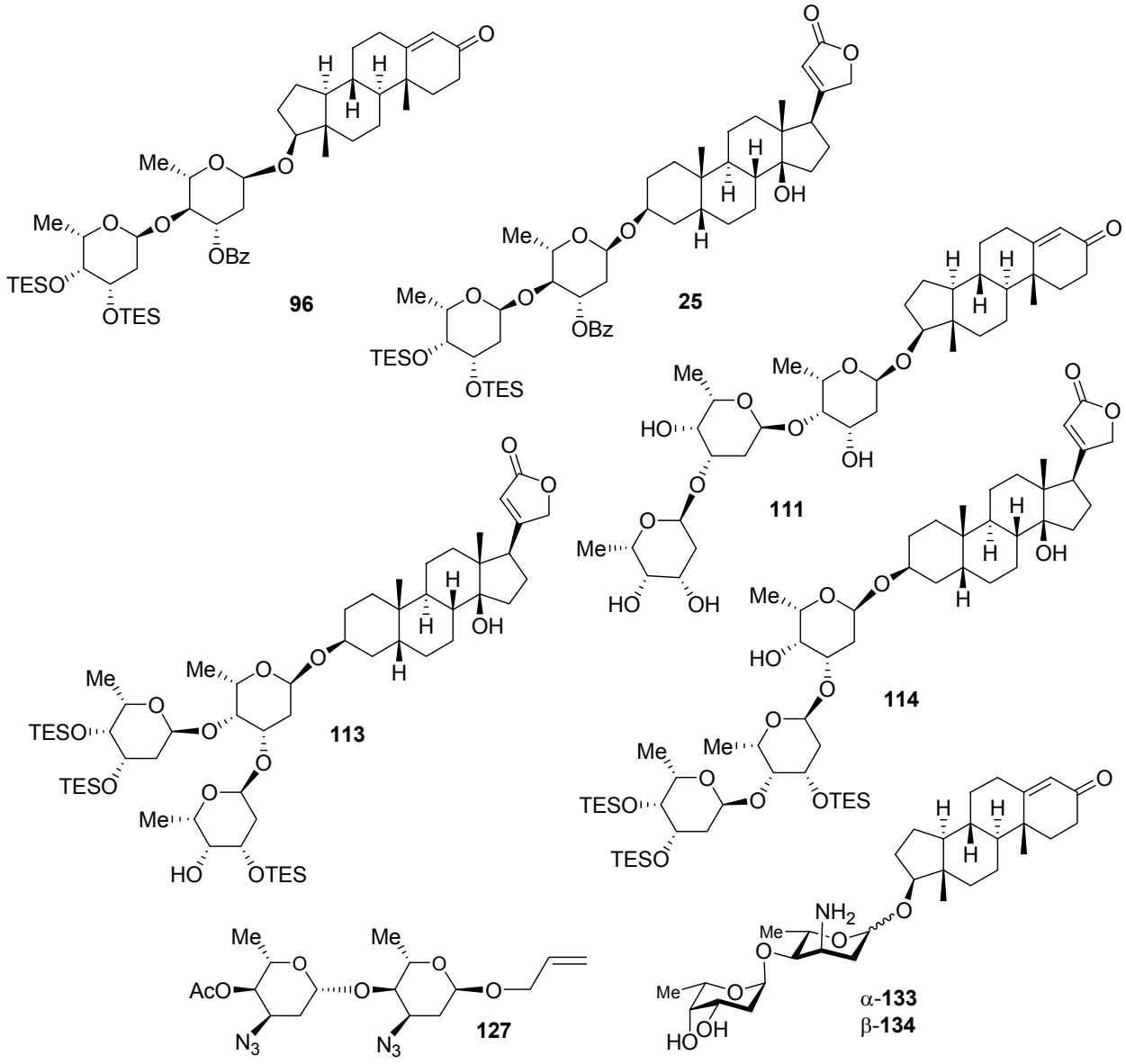


Figure 7 Selected substances from the polymer-assisted synthesis chapter (I)

Polymer-bound iodo(I)bis(trifluoroacetate)[45] was involved in electrophilic thioglycoside activations. Polymer-bound iodo(I) complex showed excellent affinity for sulfur. However, side-reactions, caused by the release of iodine and trifluoroacetic acid, hampered the use of the reagent with hindered alcohol acceptors, where liberated trifluoroacetic acid competes with the acceptor resulting in instable glycosyltrifluoroacetates.

A method using selectfluor™ as electrophilic thioglycoside activator, developed by the *Wong* group, was further developed in the 2-deoxythioglycoside area.[30g] This protocol showed excellent results: most of the reactions proceeded almost quantitatively and with superior product purity. Employing hindered acceptors such

as diacetonglycofuranose or 2,3,6-trideoxy-3-azido-α-L-allylglycoside in thioglycosidations was also successful. Thioglycosidations activated by selectfluor™ were compatible with silylated carbohydrates as well as disarmed glycals. Using the developed method, a small library of various disaccharides and glycoconjugates (**150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166** and **168**) was synthesized. Furthermore, employing the above elaborated glycal glycosidation protocol together with the selectfluor™ technique, some oligosaccharides and glycoconjugates were synthesized through an orthogonal synthesis strategy (**170, 171, 172** and **173**). The electrophilic thioglycoside activation with selectfluor™ always leads to the same intermediate regardless of the starting conformation of the anomeric center: α, β, or mixture of both. Stereocontrol during glycosidic bond formation depends exclusively on the solvent employed and the configuration of the acceptor. In all thioglycosidations diphenyldisulphide (or R-SS-R) is liberated as a by-product which can hamper or inhibit further transformations. Therefore a careful purification step is often a must. In this work a new and simple protocol using a polymer-bound scavenger technique to remove liberated diphenyldisulphide by simple filtration is presented. Polymer-bound borohydride is used to reduce disulphide to thiophenol, which is later attached to the polymer as phenylthioborate. Isopropanol is essential as a solvent for successful disulphide scavenging without undesired side reactions such as reduction of carbonyl functions or transesterifications. The quality of the given disulphide scavenging protocol is sufficient to allow sulfur sensitive reactions, such as palladium-catalyzed hydrogenations, without further purification.

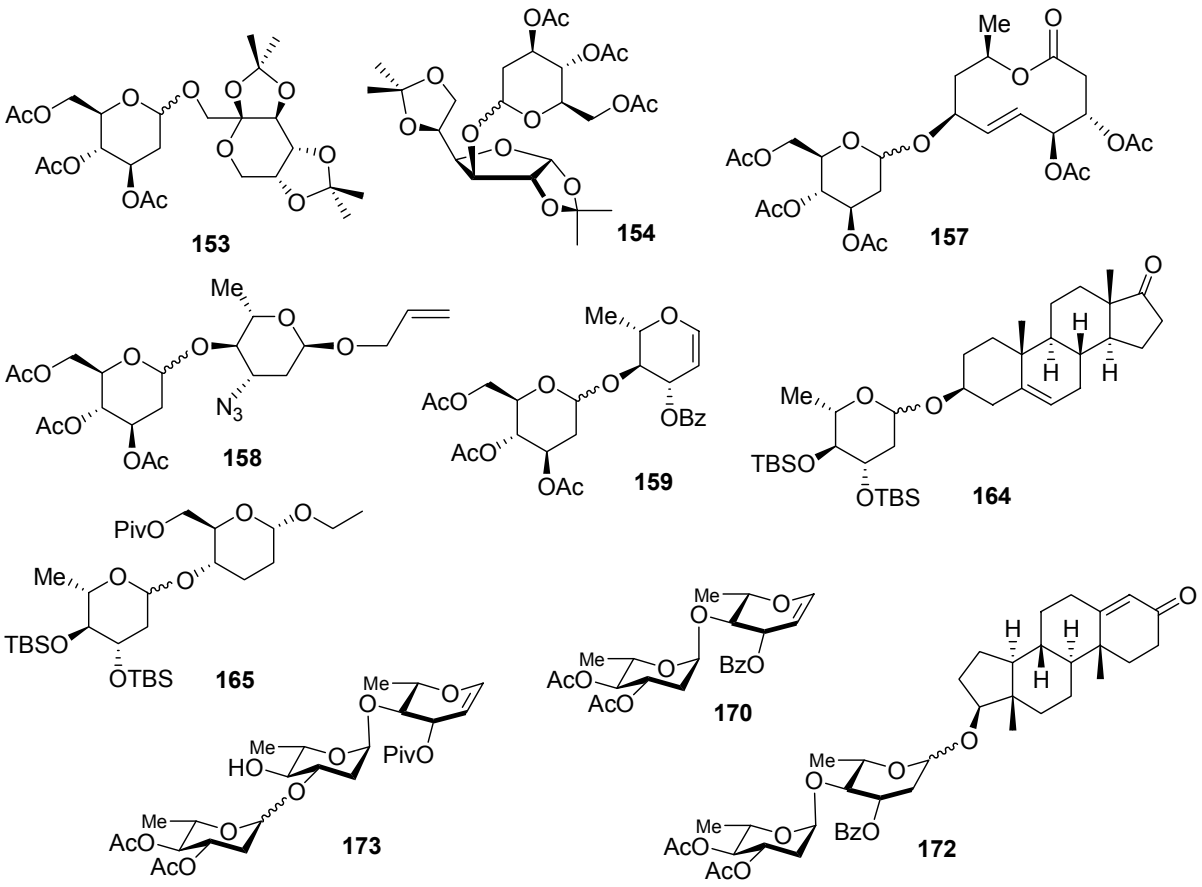


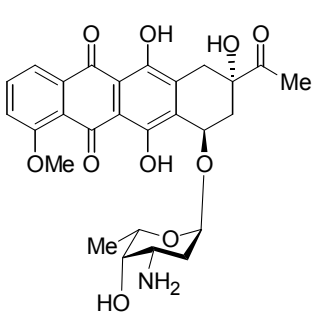
Figure 8 Selected substances from the polymer-assisted synthesis chapter (II)

Polymer-assisted solution-phase oligosaccharide synthesis showed several advantages over polymer-bound synthesis. The yields are generally higher with excellent product purity in most cases. There is no need of donor or acceptor excess – each of them is used equimolar which may save costs of complex saccharide building blocks. A standard sequence for a trisaccharide synthesis can be achieved in much shorter time as on a polymer-support. Elaborated polymer-assisted solution phase techniques for 2-deoxyoligosaccharide and glycoconjugate synthesis can be automated for parallel synthesis. In the nearest future this would allow to produce small glycoconjugate libraries in a short time using the recently developed PASSflow technique.[20a]

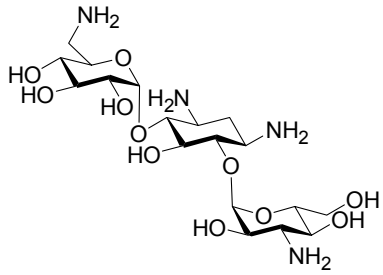
9. New ^{15}N-labelled neo-aminodeoxysaccharides

9.1. Introduction

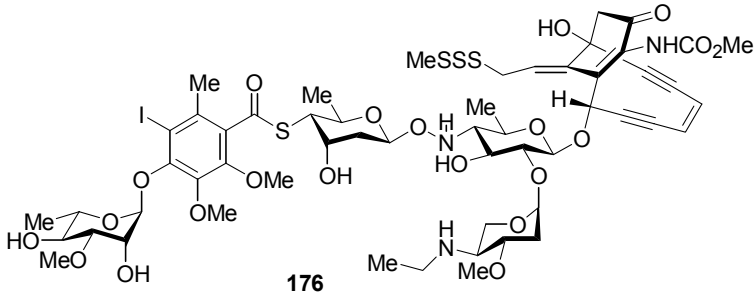
Carbohydrates, in particular protonable polyamines are fundamentally involved in many important biological processes. Their ability to specifically bind to polinucleotides could induce RNA conformation alterations and inhibit DNA or RNA synthesis.[38] Aminodeoxysugars are widely distributed in natural products as structural components of glycoconjugate and aminoglycoside antibiotics such as daunomycin **174** or kanamycin A **175**. (Figure 9).



174



175



176

Figure 9

These structures are well suited to form complexes with oligonucleotides, as the rigid feature of the sugar ring along with the flexibility of the glycosidic linkage gives them the ability of preorganization. *Tor et al*. showed that a spacer-linked dimer derived from **175** also recognizes RNA with enhanced binding properties in contradistinction to natural kanamycin. [87b] *Nicolaou* and co-workers presented a similar example where the head-to-head and head-to-tail 1,4-butanediol linked dimers of the oligosaccharide portion of calichamicin γ_1^I showed 1000 times higher affinity than the monomeric calichamicin γ_1^I **176** oligosaccharide by selectively binding to the TCCT-rich areas in DNA.[87f,g] In order to magnify the ability of

preorganization which could improve the binding capabilities *Kirschning* and co-workers recently initiated a project on the preparation of new 1,4-butanediol-linked oligomeric and macrocyclic aminodeoxysugars in order to search for specific oligonucleotide binders with therapeutic potentials.[83c,d,e]

9.2. Objective

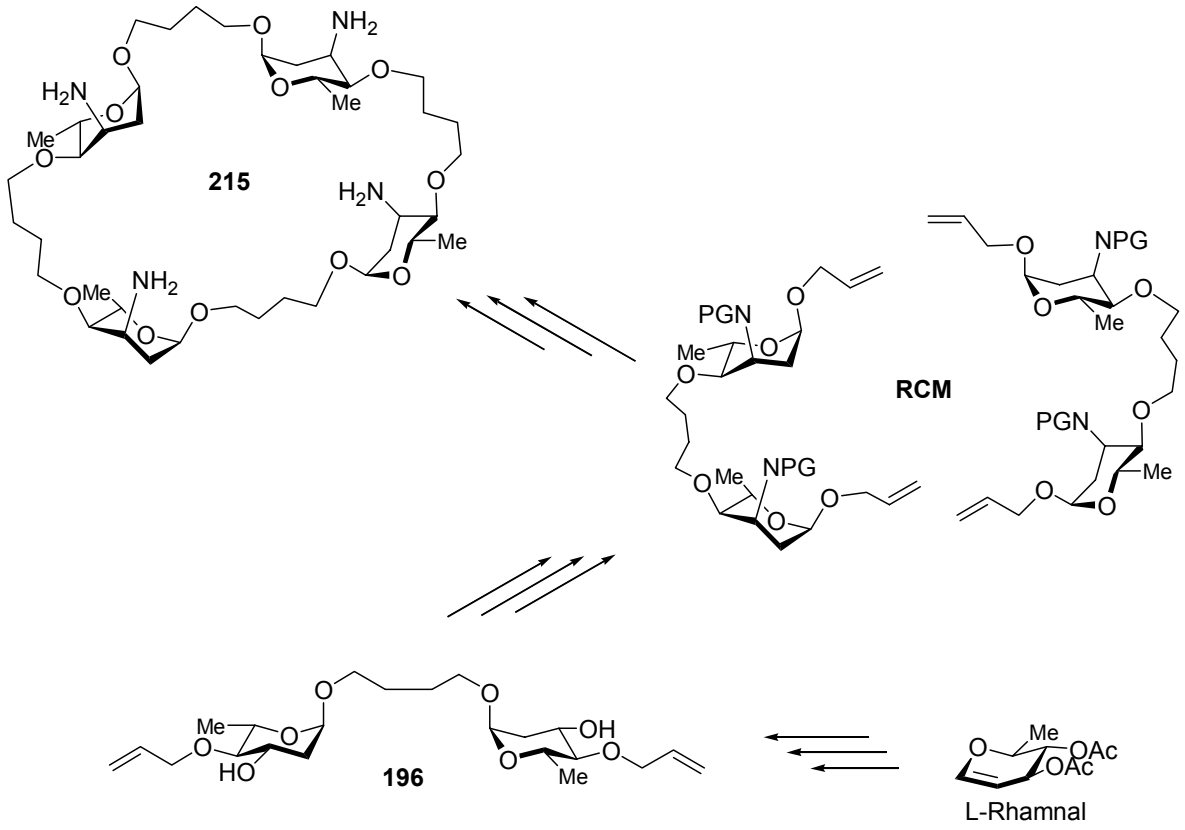
Based on the initial research by Dr. G.-W. Chen, who was involved in the development of the first spacer linked linear and cyclic aminoglycosides[58,79,85,] the preparation of correspondent ^{15}N-labelled analogues was envisaged. Some spacer-linked neooligosaccharides with TAR-RNA especially tetramer **215** (see Scheme 55) clearly indicated the strong formation of RNA/aminoglycoside complex in presence of Tat-protein. The HIV TAR-RNA was chosen as the target since the binding to the Tat-protein is well characterized and the known interactions between the RNA and the protein could therefore be used in competitive binding studies.[50]
In order to evaluate the RNA-binding properties and thoroughly explore the actual binding between the RNA and macrocyclic oligoaminodeoxysaccharides, NMR studies of labelled TAR-RNA, macrocyclic oligoaminodeoxyglycosides and the complexes of both should be carried out. For this purpose the novel non-labelled macrocycles **215**, **216** and fully ^{15}N-labelled macrocycles **220** and **221** should be synthesized on a “large scale”.

9.3. Strategy

In the earlier developed synthetic strategy for the preparation of macrocycles **215** and **216** the amino function has been introduced at an early stage of monosaccharide construction through the azide functionality. Such a way is not acceptable for the preparation of a ^{15}N-labelled macrocyclus assembly due to low overall yield of the macrocycle synthesis. High costs of $^{15}N_3$- and the fact that only one third of nitrogen isotope is used for introducing the amino function forced us to develop a truly new synthetic strategy towards ^{15}N-labelled macrocyclic oligoaminodeoxysaccharides. The key points of the new strategy should comprise following priorities:

- Introduction of nitrogen isotope into sugar molecule should occur as late as possible in order to reduce the nitrogen losses during the synthesis
- Cheap nitrogen source is desirable
- All nitrogen atoms should be involved for the introduction of the amino function (azide is not favorable).

After a careful study of possible synthetic routes the following strategy was proposed: (Scheme 34)



Scheme 34

As a key building block in the given strategy, spacer-linked bisallylated homodimer **196** with a free alcohol functionality at C-3 was chosen, which could be derived from well accessible L-rhamnal. This opens up various pathways to introduce the desirable ^{15}N-labelled amino functionality in the given molecule and at the same time furnishing *ribo*-configuration at the hexose moiety.

One approach could be activation of hydroxyl function by various means (such as triflate or *Mitsunobu* reaction) followed by nucleophilic attack of the eligible nitrogen nucleophile. (Figure 10)

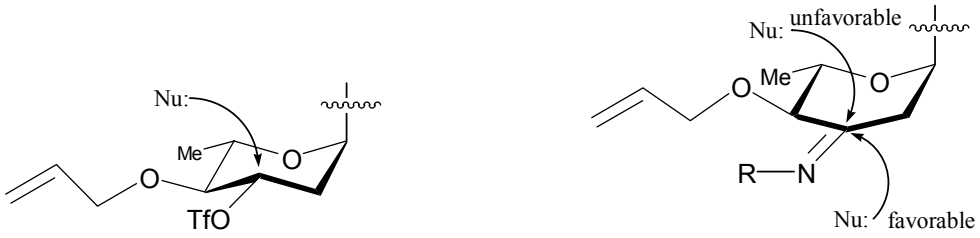
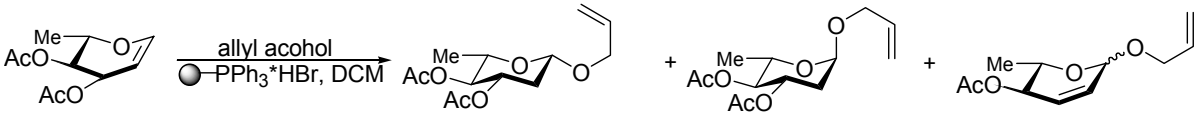


Figure 10

The other possibility could start with the corresponding ulose, which undergoes reductive amination using an appropriate amine. An impending sterical outcome should also lead predominantly to the *ribo*-configured 3-amino glycoside due to more favorable hydride attack from the bottom side of the imine.

9.4. Preparation of spacer-linked head to head dimer 196: the key building block in the synthesis of ^{15}N-labelled cyclic neooligoaminodeoxysaccharides.

Glycal **17** served as the starting carbohydrate-based building block for the synthesis of the spacer-linked diol **196**. Allyl rhamnosides **178** and **179** were prepared by treatment of L-rhamnal **17** with allyl alcohol using polymer-bound triphenylphosphonium bromide as a mild acidic promoter. The role of polymer-bound PPh_3*HBr as mild glycosidation promoter of glycals has been studied in the previous chapter. The isolated yield of both epimers was 72.6 % (α/β = 1.3:1). The required *α*-epimer **179** was easily separated after column chromatography. As byproducts the Ferrier rearranged glycosides **F** were formed.[51] (Scheme 37)



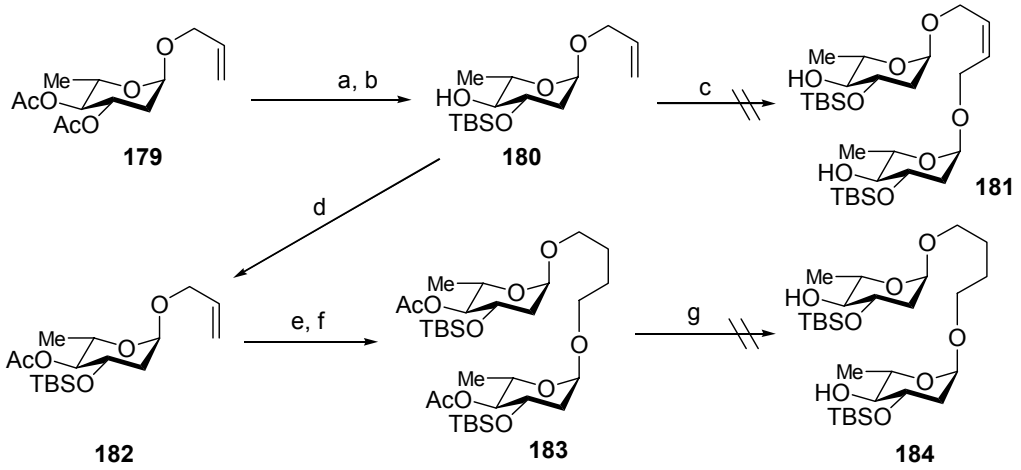
17 31.6% **178** 41% **179** 18.7% **F**

Scheme 37

Prior to metathesis dimerisation, the protecting groups in glycoside **179** should be manipulated in the advisable way for further allylation at C-4.

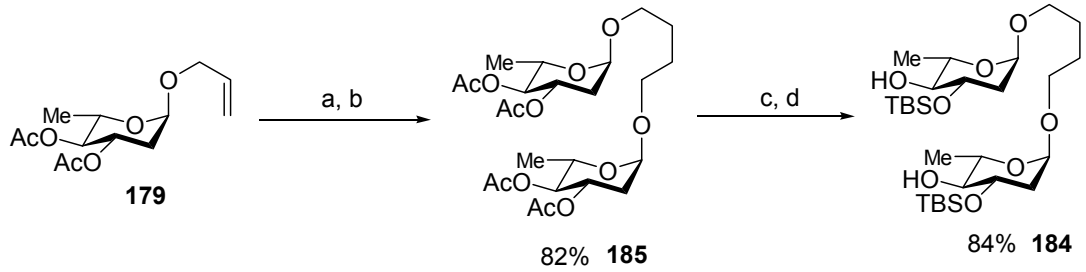
The obtained allyl rhamnoside **179** was deacetylated in methanol using Amberlyst A-26 in OH^- form as basic transesterification catalyst. Then the hydroxyl group at position C-3 of the protected diol **180** was protected as TBS ether in a well

established way.[52] Allyl glycoside **180** was subjected to the olefin metathesis reaction using Grubbs-1 catalyst, however the desired product **181** was not detected. A possible reason could be the free alcohol function at C-4. Therefore, an additional protection group was needed, which was introduced as an acetate using acetanhydride in pyridine to afford glycoside **182** in almost quantitative yield (Scheme 38).



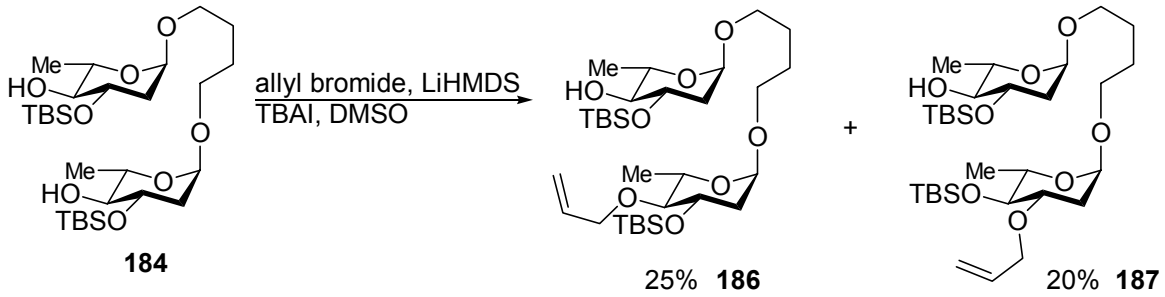
Scheme 38 Reagents and conditions: a) Amberlyst A-26 (OH^- form), methanol, RT, 12h, 98%; b) TBSCl, imidazole, DMF, 0^o C, 89%; c) Grubbs 1 (10 mol%), benzene, RT; d) Ac_2O, pyridine, RT, 99%, 12h; e) Grubbs 1 (10 mol%), benzene, RT, 48h, 72%; f) PtO_2/H_2, 99%; g) Amberlyst A-26 (OH^- form), methanol, RT, 12h.

Further dimerisation metathesis and successive hydrogenation of the double bond delivered **183** in good yields (72% for two steps). Nevertheless, glycoside **183** could not be deprotected in the usual manner without migration or cleavage of the silyl protecting groups. This failure led to the use of a slightly different approach towards target compound **184**. The new strategy avoids differentiation of the hydroxyl groups prior to dimerisation. The differentiation will be carried out on the level of homodimer, instead. Allyl rhamnoside **179** could also undergo olefin metathesis dimerisation to yield desired dimer **184** after hydrogenation, deprotection and 3-*O*-silylation (Scheme 39).



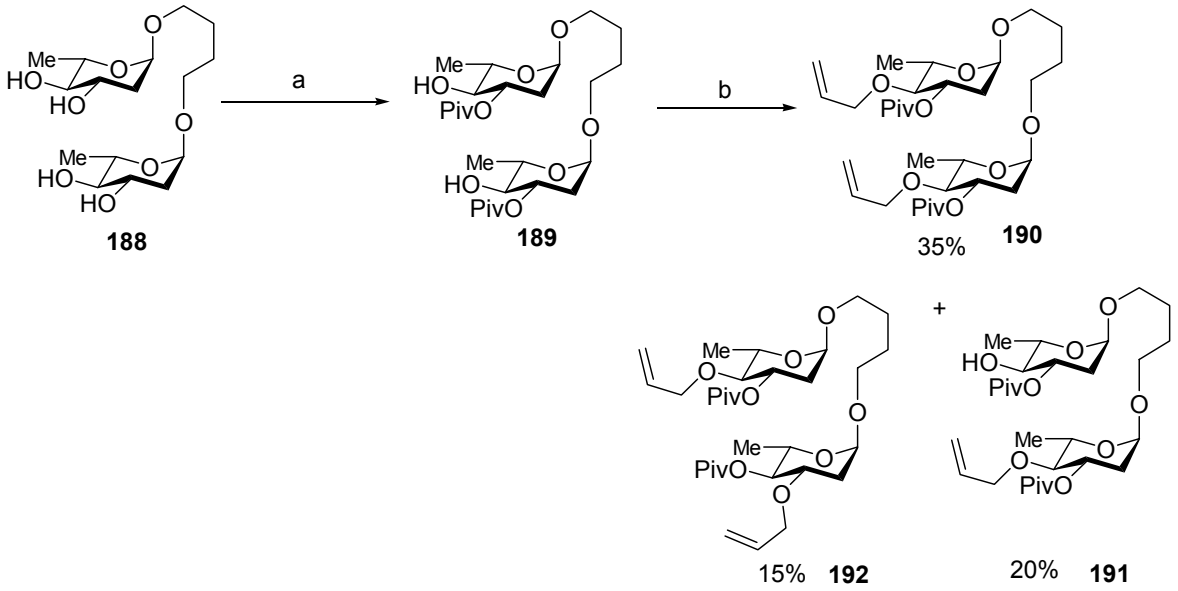
Scheme 39 Reagents and conditions: a) Grubbs 1 (10 mol%), RT, 48h; b) PtO_2/H_2; c) Amberlyst A-26 (OH^- form), methanol, RT, 12h; d) TBSCl, imidazole, DMF, 0^o C.

Allylation of the remaining hydroxyl groups in **184** was performed in various ways. The classical protocol using allyl bromide and sodium hydride showed an unspecific reaction due to pronounced silyl group (3→4) migration and deprotection at C-3.[53] Formation of the desired bisallylated glycoside was not observed. A milder method using freshly prepared, dried silver oxide and allyl iodide[54] gave no reaction. This result could be due to sterical hindrance by the bulky TBS group at C-3. *Wong et al*. described a modified procedure for the allylation of neamine at the sterically hindered C-5 alcohol of the cyclohexane ring system[55] where lithium hexamethyldisilazan was used as a deprotonating base together with tetrabutylammonium iodide as activator of allyl bromide. This approach gave no better results, either; the migration of silyl groups was still dominant (Scheme 40). In order to avoid this effect, a different protection group at the C-3 alcohol should be used with limited or no migration qualities under basic conditions. Such decent protecting group could be the pivaloyl- or TBDPS-group, which meet the desired requirements in compliance with early published data.[88]



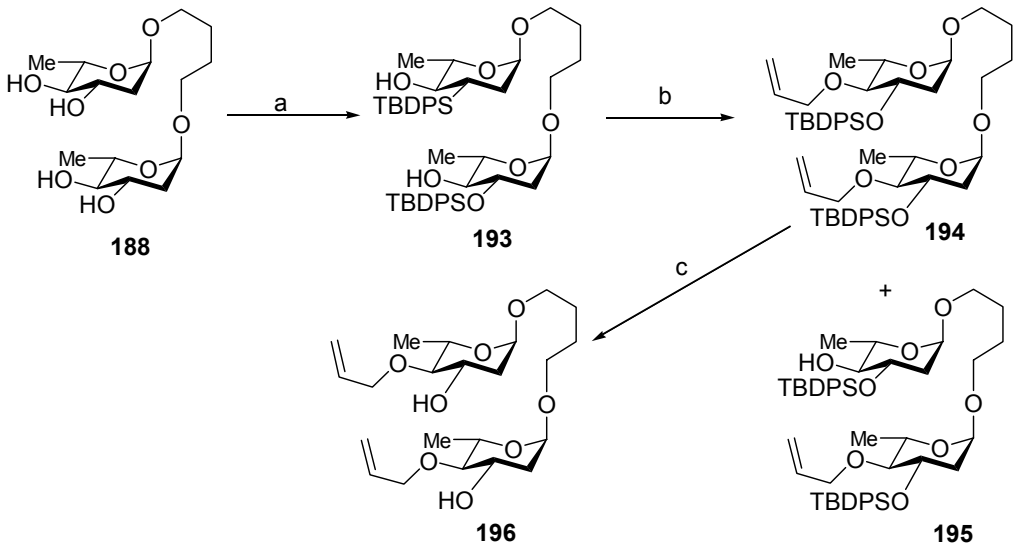
Scheme 40

For affording the 3-*O*-pivaloyl glycoside **189**, alcohol **188** was treated with pivaloyl chloride in pyridine. The reaction predominantly gave 3-*O*-pivaloylation which is in accordance with the different reactivity of both hydroxyl groups in the rhamnose ring system. Compound **189** was subjected to the allylation reaction using *Wong's* approach to afford bis-allyl glycoside in 35% yield (Scheme 8).



Scheme 41 Reagents and conditions: a) PivCl, pyridine, 0° C, 5h, 85%, b) allyl bromide, LiHMDS, TBAI, DMSO, RT.

However, again substantial migrations of the pivaloyl groups were observed which leads to highly reduced yields for the desired dimer **190**. Later, experiments with TBDPS protected dimer **193** gave decent results yielding almost 50% of expected bis-allylated glycoside **194** and 45% of mono-allylated glycoside **195**. No byproducts originating from silyl group migration were observed. It is worth to notice that the yield only 50% of bis-allylated glycoside **194**, although a high excess of reagents was used and the reaction conditions have thoroughly been optimized. Anyway, the monoallylated byproduct **195** can be recycled which increases the total yield to 85% (Scheme 42).



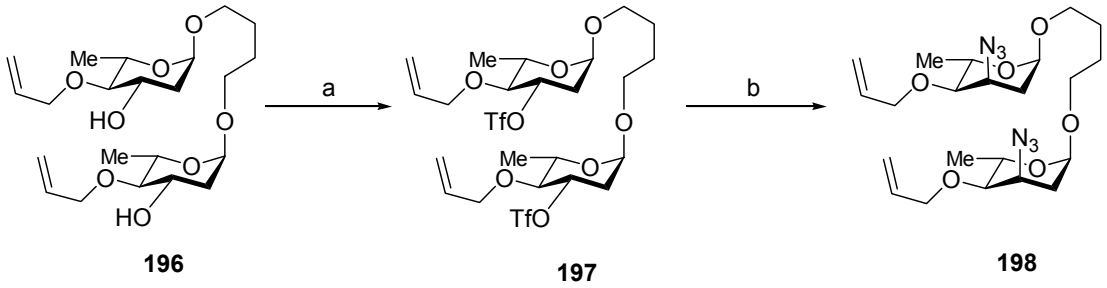
Scheme 42 Reagents and conditions: a) TBDPSCl, imidazole, DMF, 0° C, 12h, 85%; b) allyl bromide, LiHMDS, DMSO/THF = 1:1, 0° C, 5 min, 50% for **194**, 45% for **195**; c) TBAF, THF, RT, 20h, 85%.

Treatment of allylated dimer **194** with tetrabuthylammonium fluoride in tetrahydrofuran gave the title compound **196** in 85% yields.

9.5. ^{15}N-labelling of spacer linked head to head dimer 196

9.5.1. Activation of alcohol function

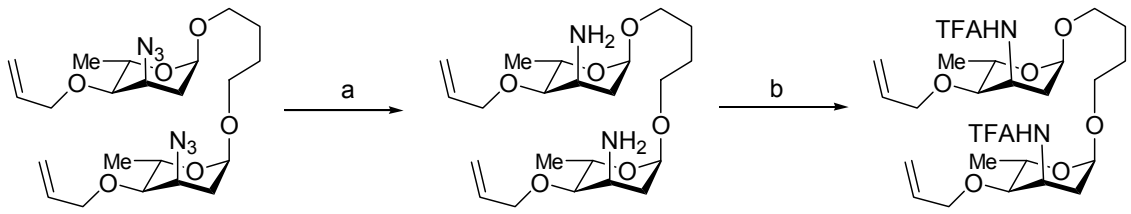
One of the oldest and simplest ways to convert an alcohol into an amino group is the activation of the hydroxyl group by sulphonating followed by displacement with azide in a S_N2 reaction. For this purpose *Guthrie* and *Richardson*[56] used the mesylate as a leaving group. On the other hand, the conversion of an alcohol to a mesylate followed by elimination under basic conditions is also a well known method to build up olefinic double bonds.[57] Under S_N2 conditions elimination frequently occurs when the nucleophilic attack lead to a strained transition state or an unfavorable geometry. Therefore, in this case the use of such an activating group can lead to undesired elimination products. An alternative could be the activation as the trifluormethylsulfonyl ester which shows a low elimination tendency. *Reckendorf* and later *Kirschning* and co-workers[58] used this approach to introduce azide in sugar molecules. *Nicolau et al.*[59] applied a similar strategy to introduce an amino functionality during the total synthesis of amphotericin B.
Alcohol **196** was successfully triflated with Tf_2O in dichloromethane and pyridine as a base in 96% yield. The colorless material **197** obtained is fairly unstable and must be used immediately in the next reaction step.[68] As an azide source, tetrabutylammonium azide in benzene was used, which can be prepared from sodium azide by a modified *Brändstrom* procedure.[86] The advantage of n-Bu_4NN_3 over sodium azide is based on its high solubility in organic solvents which allows more options to chose different solvents and conditions.[60] Unfortunately, this method gave only a moderate yield of product **198** (Scheme 43).



196 **197** **198**

Scheme 43 Reagents and conditions: a) Tf_2O, pyridine, CH_2Cl_2, - 15° C, 96%; b) n-Bu_4NN_3, benzene, 70° C, 10 min, 36%.

Such low yields in conjunction with the fact that azide was used as a nitrogen source were not acceptable for a ^{15}N-labelling strategy. The azide function can be reduced in various ways, such as: lithium aluminium hydride in THF, or following *Staudinger's* protocol with triphenyl phosphine[62] and its modifications.[63] In our case the reduction of azide **198** using $LiAlH_4$ or *Staudinger* protocol gave only moderate yields (Scheme 44).

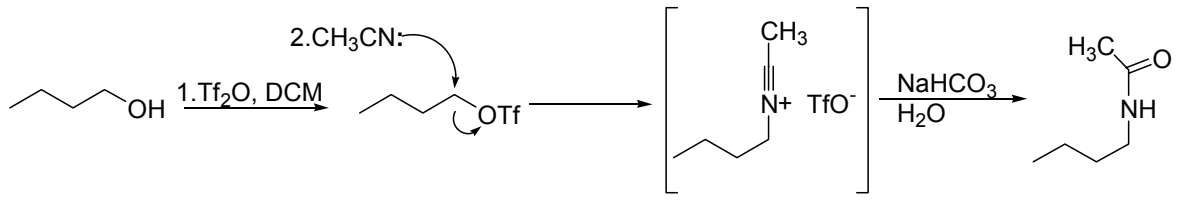


198 **199** **200**

Scheme 44 Reagents and conditions: a) $LiAlH_4$, THF, RT or PPh_3, THF/H_2O; b) TFAA, triethylamine, CH_2Cl_2, - 30° C, 1h, 60% from **198**.

The conversion of alcohols or alkenes to amides by the reaction with nitriles in the presence of sulfuric acid is named the *Ritter* reaction.[64] While the successful course of the reaction certainly depends on the reactivity of the nitrile, a major factor is the stability and reactivity of the carbocationic intermediates. Tertiary alcohols generally give good yields, secondary and primary alcohols give only mediocre results due to the instability of the primary and secondary carbenium ions in the common organic medium.[65] More than a decade ago *Jaouen* and co-workers[66] have published a modified approach of the *Ritter* reaction. They showed that this important limitation can sometimes be overcome using chromium tricarbonyl complex which directly influences the stability of the carbenium ions. However this method was limited to the conversion of benzyl alcohols. *Martinez* and *Hanack*[67] found an alternate strategy to stabilize the carbocationic

intermediate. They used alkyl triflates as masked carbocations which easily extends the scope of the reaction to secondary and primary aliphatic alcohols. For example n-butanol can be aminated with acetonitrile in the presence of 1 eq of Tf_2O in a 90% yield. (Scheme 45)

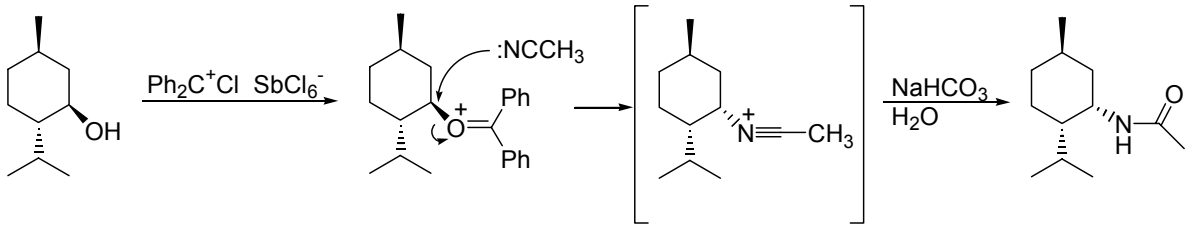


Scheme 45

Glycoside **197** was involved in this modified *Ritter* reaction, but only formation of decomposition products was observed. This could be explained in terms of the high instability of triflate **197** under acidic conditions where decomposition took place within minutes.

To our surprise, triflated alcohol **197** showed extraordinarily stability under basic conditions: heating in DMF in the presence of benzyl amine or refluxing in methanol with ammonia for several hours indicated no reaction or decomposition of the starting material.

Barton et al.[69] published different conditions for *Ritter*-type reactions. They used a stable chlorodiphenylmethyl hexachloroantimonate[70] as a free carbocation source to induce the activation of alcohols. This carbocation reacts with alcohols and yield an oxonium-type intermediate which is attacked by a free electron pair of the nitril. This intermediate is almost identical to the *Hanack* strategy (Scheme 45). Superficially the reaction seems to be a non-protic analogue of the *Ritter* reaction (Scheme 46).

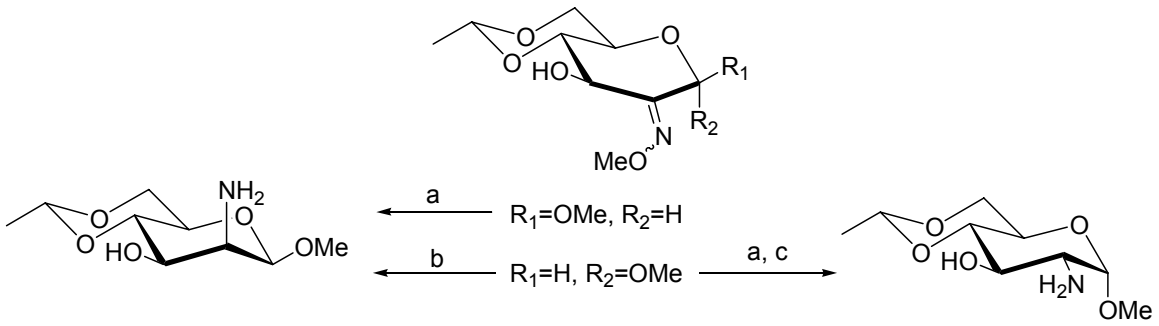


Scheme 46

Alcohol **196** was subjected to the same procedure as menthol in the Scheme 46, though again only decomposition of the starting material was observed.

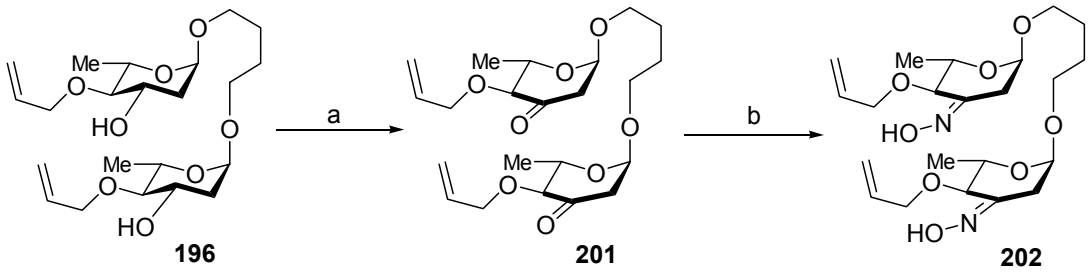
9.5.2. Reductive amination

A standard protocol for the preparation of amines is the reduction of oximes and their *O*-alkyl or –acyl derivatives by hydrogenation or the use of reagents such as lithium aluminium hydride, borane or a zinc-copper couple in acetic acid. Since the reductions can be highly stereoselective, this has become a very useful method for preparing amino sugar derivatives from oximes. The stereochemical outcome can depend upon the reducing conditions or disposition of substituents adjacent to the reaction center.[71] As shown in Scheme 47 catalytic hydrogenation of the β-methyl glycoside oxime gives exclusively the β-glycoside of mannosamine with an axial amino group at C-2. On the other hand, the α-anomer which has an axial methoxy group at C-1 gives predominantly the glucosamine derivative.[71b]



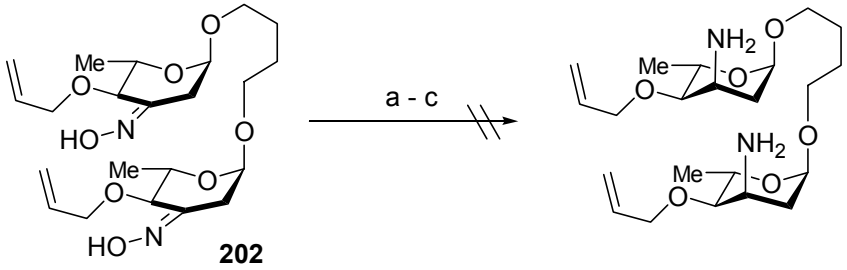
Scheme 47 Reagents and conditions: a) H_2, Pd/C; b) $LiAlH_4$, THF, RT; c) BH_3*THF, RT.

Alcohol **196** was easily oxidized with *Dess-Martin* periodinane to the corresponding ulose derivative **201** which was subsequently transformed to the oxime using well established techniques[89] (Scheme 48).



Scheme 48 Reagents and conditions: a) Dess-Martin periodinane, CH_2Cl_2, RT, 2h, 99%; b) hydroxylamine hydrochloride, sodium acetate, MeOH, RT, 3h, 96%.

Due to the allylic domain in **202** the correct reducing agent has to be well chosen. *Ipaktschi* has demonstrated an improved reduction method of oximes using sodium borohydride in the presence of transition metal compounds.[72] The combination of $NaBH_4$ with $NiCl_2$ * $6H_2O$ converted the unsaturated oximes through exhaustive reduction into saturated amines. If the reduction is carried out in the presence of MoO_3 olefinic double bonds were not attacked. Later on *Bandgar* and co-workers evaluated this strategy on polymer-support.[73] Lithium triethylborohydride and sodium cyanoborohydride do not react at all or the reduction is not complete.[74] Borane in THF or DIBALH are also not acceptable due to a possible attack of the allylic double bond or the induction of a Beckmann rearrangement.[75] Lithium aluminium hydride could be a suitable reductive agent for oximes.[76] However any attempts to reduce the oximine **202** failed in this case (Scheme 49).

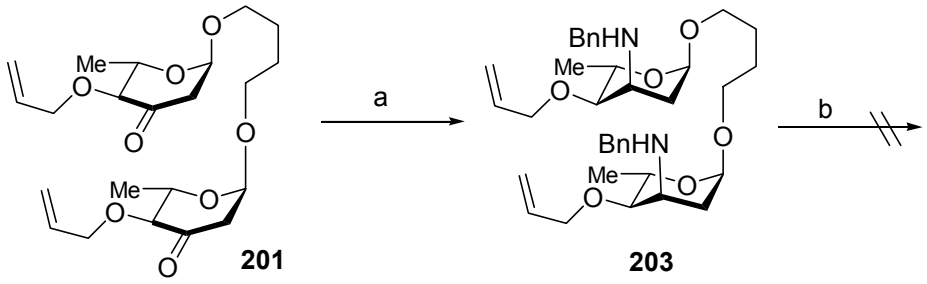


Scheme 49 Reagents and conditions: a) $NaBH_4$, MoO_3, MeOH, RT (decomposition); or b) $LiAlH_4$, THF, RT (decomposition); or c) Zn, AcOH, RT, 24h. (no reaction)

Another strategy for reductive amination of ketones could be the use of primary amines (such as benzyl amine) or ammonia salts. *Borch* and co-workers demonstrated a wide applicability of this method subjecting different primary and secondary amines (also ammonium salts) in the condensation with different aldehydes and ketones followed by *in situ* reduction using sodium cyanoborohydride.[74b] The reduction of aldehydes and ketones with sodium cyanoborohydride is *pH*- dependent. Under neutral conditions in water or methanol negligible reduction of aldehydes and ketones occur. As the *pH* is lowered the reduction becomes progressively more rapid. Therefore ideal conditions for the reductive amination should be at *pH* 6-7. To maintain the given *pH* level sodium acetate is used as a buffer.

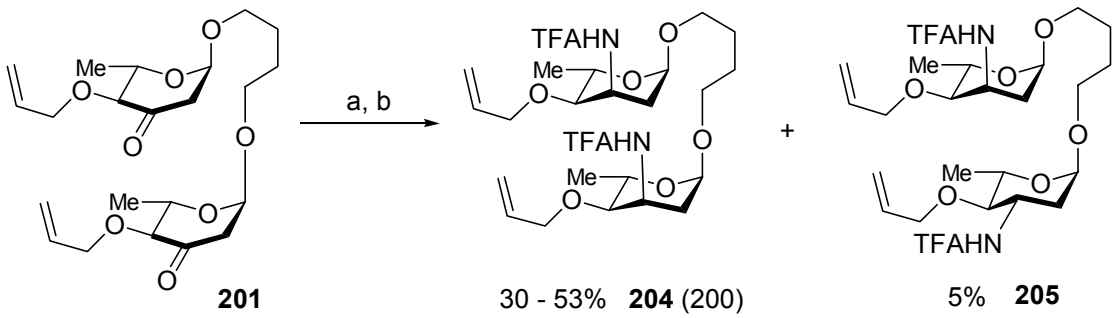
Diketone **201** reacted with benzyl amine acetate in methanol, and sodium cyanoborohydride was added. After four hours, the diketone was fully consumed

and t.l.c. indicated that only one product was established. NMR-spectroscopy and mass spectrometry surely yielded expected benzyl amine **203** with the desired *ribo*-configuration at C-3 and no *arabino*-configured amine would be detected. Such a high stereoselectivity has already been explained above (see scheme 35). Amine **203** was subjected to the ring closing olefin metathesis with Grubbs 1 catalyst without success. This is in compliance with prior investigations from the *Fürstner* group[77] (Scheme 50).



Scheme 50 Reagents and conditions: a) benzylamine, AcOH, NaOAc, $NaCNBH_3$, MeOH, 90%; b) Grubbs 1, benzene, 50° C; or Grubbs 2, benzene, RT.

In the total synthesis of Anatoxin *Danheiser* and co-workers employed a reductive amination step using ammonium acetate as a nitrogen source.[78] This procedure was adopted for the uloside system and finally the desired aminoglycoside **204** was synthesized in moderate yields. The diamine obtained was directly trifluoroacetylated using ethyl trifluoroacetate as mild acylating agent. As minor byproducts diastereomeric aminoglycosides **205** were isolated (Scheme 51).

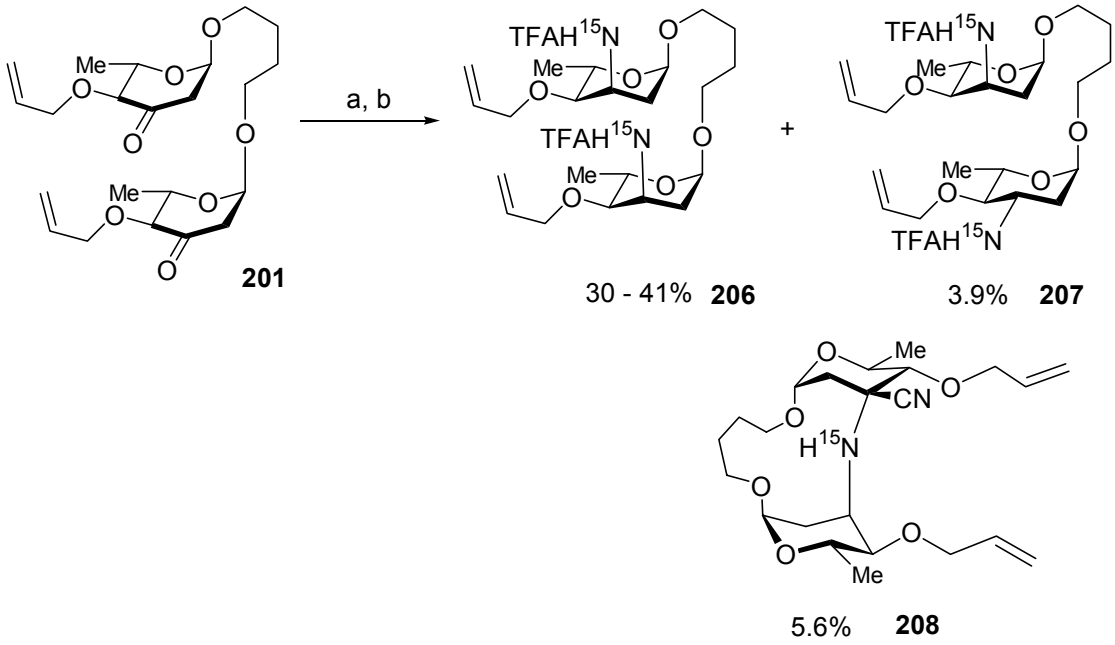


Scheme 51 Reagents and conditions: a) ammonium acetate, $NaCNBH_3$, MeOH, RT, 24h; b) CF_3COOEt, NEt_3, MeOH, RT, 12h.

In spite of moderate yields for the reductive amination step this strategy could be ideal for the ^{15}N-labelling of uloside **201**. The ^{15}N-labelled ammonium acetate is relatively cheap comparatively to other ^{15}N-nitrogen sources and yielded

aminoglycoside **204** is identical to the non-labelled macrocycle prepared before by an alternate route.[79] This can facilitate further steps such as ring closing olefin metathesis which leads to ^{15}N-labelled macrocyclic spacer linked oligoaminodeoxysaccharides.

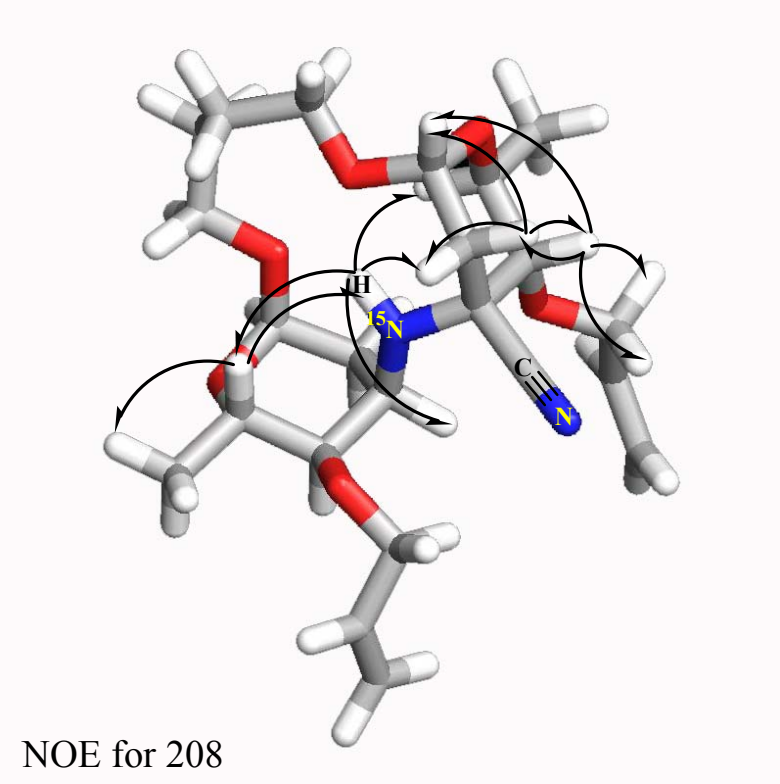
Uloside **201** was subjected to the reductive amination reaction employing ^{15}N-labelled ammonium acetate using the protocol described above. Along with the main product **206** two minor byproducts were isolated: one was the previously described diastereomeric aminoglycoside **207** (here ^{15}N-labelled) and the second one was the cyclic aminoglycoside **208** (Scheme 52).



Scheme 52 Reagents and conditions: a) ^{15}N-ammonium acetate, $NaCNBH_3$, MeOH, RT, 24h; b) CF_3COOEt, NEt_3, MeOH, RT, 12h.

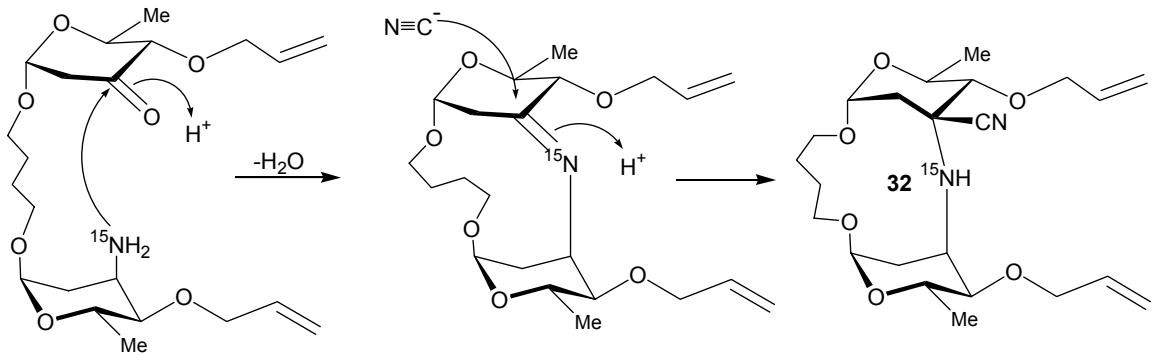
The structure and stereochemistry of cyclic aminoglycoside **208** was proven using NMR spectroscopy (^{1}H-NMR, ^{13}C-NMR, ^{1}H-^{1}H- and ^{1}H-^{13}C-COSY, NOE and TOCSY), mass spectrometry (ESI) and IR-absorption spectra to indicate CN moiety. ^{1}H-NMR-spectra clearly indicated two different allyl moieties, two different carbohydrate skeletons and one ^{15}NH with coupling constant 81.5 Hz at 4.7 ppm. In ^{13}C-NMR-spectra along with two different allylic fragments and pyranoses were detected two quaternary carbons: at 122 ppm, and 57.5 ppm with small coupling constant. Further ^{1}H-^{1}H- and ^{1}H-^{13}C-COSY-spectra allowed to characterize all signals indicating that C-3 from second carbohydrate skeleton now is quaternary and bound directly to ^{15}NH. C-3 from first sugar also is bound to ^{15}NH generating macrocyclic structure. Electro spray mass spectrometry data gave single molecular

ion [M^+] with mass 438.26. Acquired data pointed to one substituent at C-3'' with relative mass 26. Careful analysis of possible reaction routes and eventual product structures lead to consider the cyano group with the mass 26. Measured infrared spectra clearly detected a strong signal at 2279 cm^{-1} that could originate from the cyanide moiety. Prior observed quaternary carbon signal at 122 ppm in ^{13}C-NMR-spectra also is in accordance with the usually observed nitrile ^{13}C- shift. Molecular modeling calculations were made yielding a 3D-structure which meets the NOE-data.



NOE for 208

The formation of cyclic aminoglycoside **208** could be explained according to the following mechanism (Scheme 53).



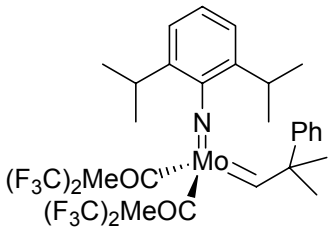
Scheme 53 Proposed mechanism for the formation of cyclic aminoglycoside **208**

Initially, only one keto function undergoes reductive amination. The amine attacks the second uloside yielding a Schiff-base. Subsequently cyanide anion originated from $NaCNBH_3$ attacks the intermediate cyclic imine carbon from the less hindered side to form the final cyclic cyanoamine **208**. Further reduction of this imine could be hampered by the actual cyclic disaccharide conformation which does not allow sodium cyanoborohydride to approach and form a complex with the imine double bond essential for hydride transfer.

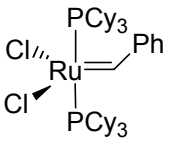
9.6. Synthesis of macrocyclic spacer-linked oligoaminodeoxysaccharides

9.6.1. Olefin metathesis reaction

Olefin metathesis which is catalyzed by transition metal complexes has been widely employed for the extension of carbon skeletons and various cyclisations in synthetic organic chemistry[80] since the introduction of highly active *Schrock's*[81] molybdenum catalyst **209** and particularly after the acquirement of the air and moisture stable ruthenium benzylidene catalyst **210** by the *Grubbs* group.[82] Recently more and more applications of olefin metathesis can be found in carbohydrate chemistry.[34]



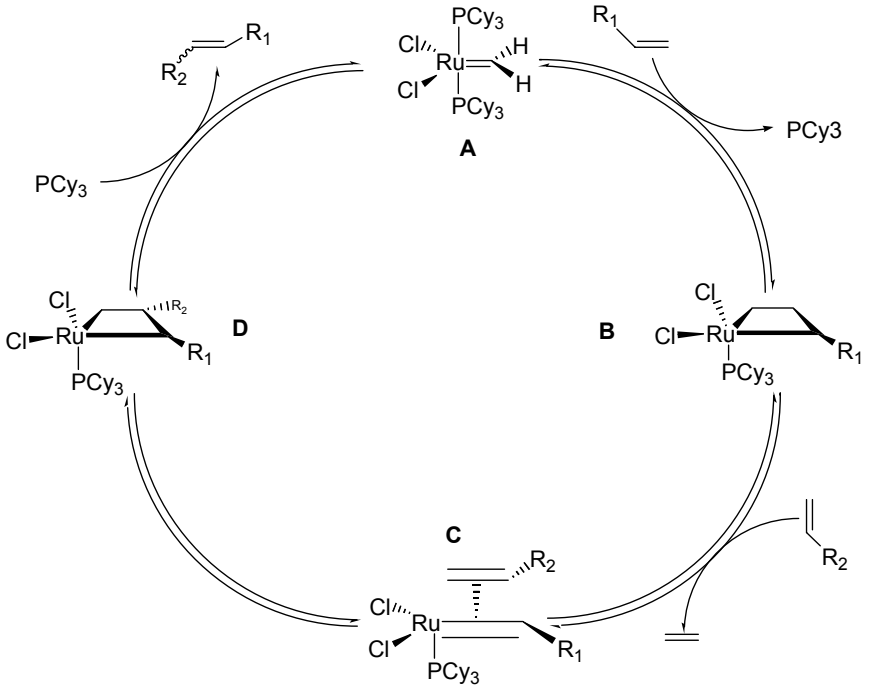
209



210

More than thirty years ago *Herrison* and *Chauvin* proposed a hypothetical mechanism of olefin metathesis reaction. A metallocyclobutane complex was proposed as the key intermediate in metathesis olefinations. Recently, *Grubbs* and co-workers provided substantial evidences for the existence of the key metallocyclobutane intermediate.[84] The catalytic cycle starts when the catalyst precursor transforms into the active methylidene form **A**. After the first alkene molecule is coordinated to the catalyst, one of the phosphine ligands dissociates during the formation of the metallocyclobutane **B**. With the release of ethylene, another alkene molecule coordinates to the catalytic center **C**. Subsequent

cycloaddition forms the second metallocyclobutane complex **D** which transfers again to catalyst **A** after cycloreversion, and liberates olefinic product (Scheme 54).



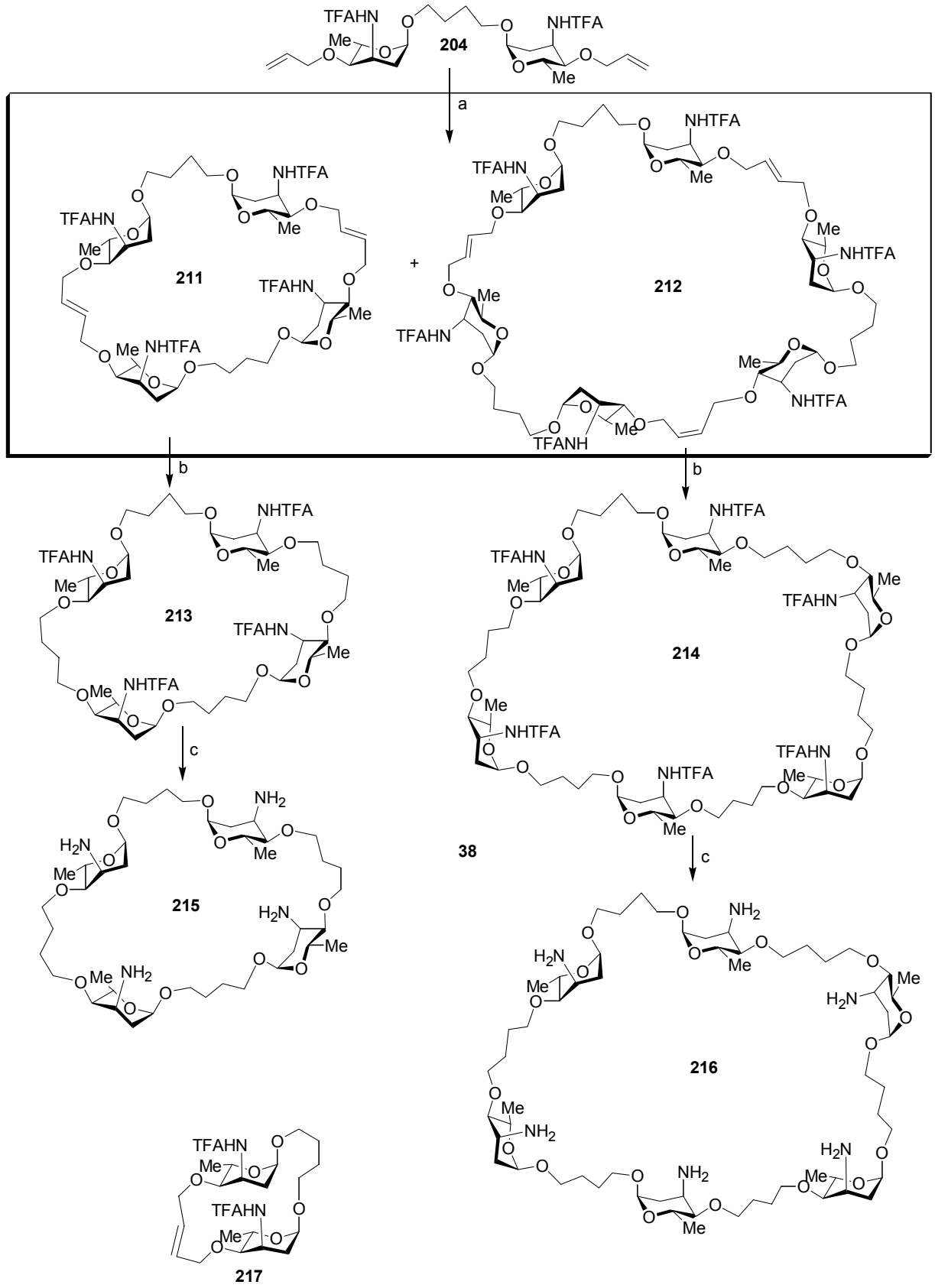
Scheme 54
$R_1 = R_2$ (ring-closing metathesis, self-metathesis)
$R_1 \neq R_2$ (ring-closing metathesis, cross-coupling metathesis)

9.6.2. Olefin metathesis macrocyclisation of dimer aminoglycosides 204 and 206

Previously obtained spacer linked dimer **204** was subjected to the olefin metathesis dimerisation with subsequent ring-closing metathesis macrocyclisation in the presence of *Grubbs* ruthenium benzylidene complex **210**. In order to avoid polymerization of the starting material, a diluted solution of glycoside **208** in DCM was used.[61] After 7 days of reaction at room temperature the desired tetracyclus **211** and small amount of hexacyclus **212** along with 30% of starting material was isolated. At elevated temperatures the yield of the desired macrocycle improves minimally, however, side reactions such as allylic double bond isomerisation prevail. No ring-closing metathesis product **217** was detected. This observation can be explained with the axial orientation of protected amino groups at C-3 that do not allow the molecule to take the right preorganization for smooth self-cyclisation. Instead, dimerisation and trimerization to linear tetra- and

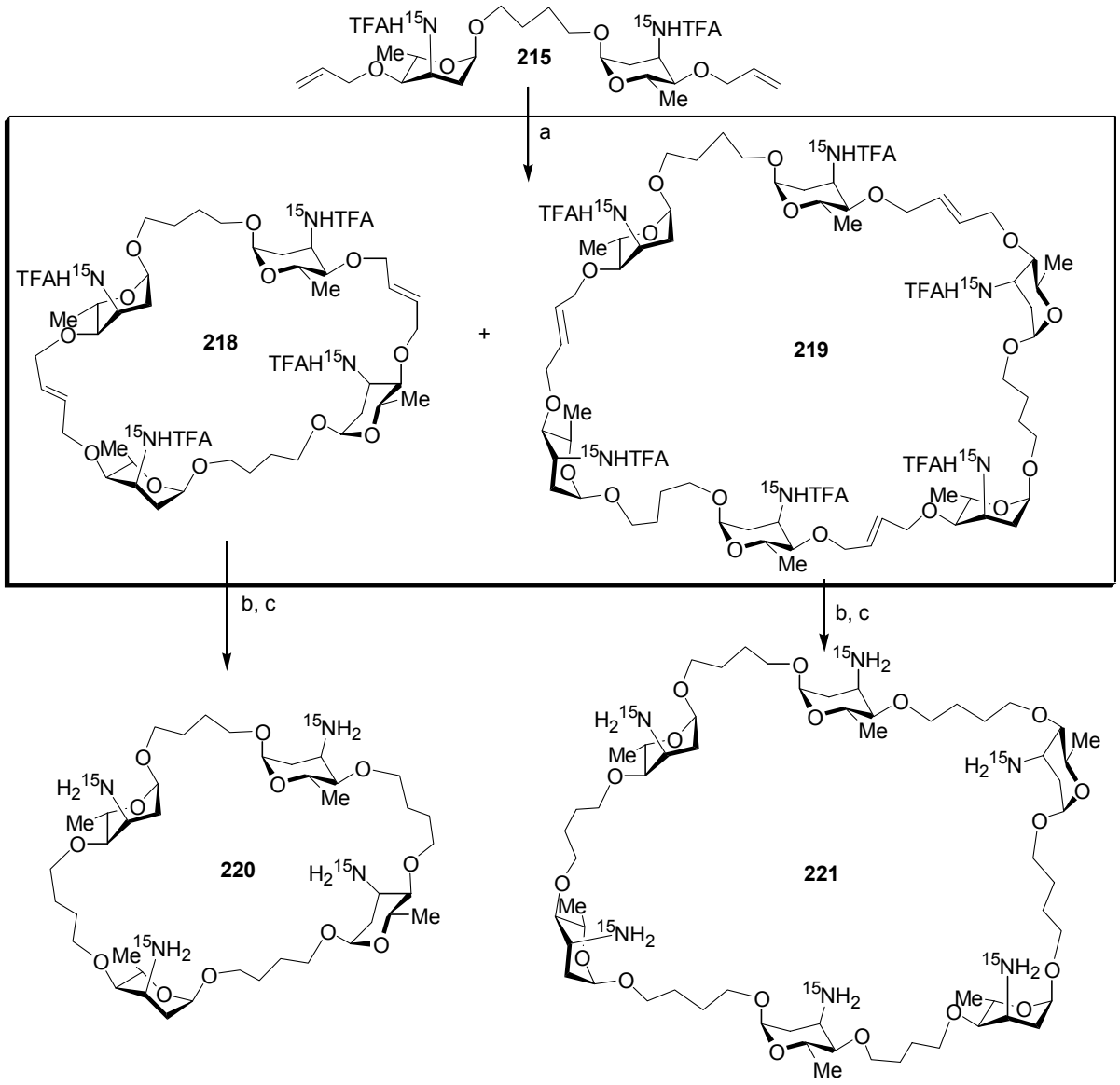
hexasaccharides occurs prior to macrocyclisation. On the other hand, if L-acosamine-based dimer with equatorial oriented protected amino groups at C-3 was allowed to macrocyclise under the same conditions, self-cyclisation was observed predominantly.[83e]

Spacer linked macrocycles **211** and **212** were hydrogenated over platinum oxide in ethyl acetate to afford **213** and **214**, and subsequent removal of the trifluoroacetyl groups in 1M NaOH-water/THF/methanol mixture led to the target cyclic tetramer **215** and hexamer **216** in almost quantitative yields (Scheme 55).



Scheme 55 Reagents and conditions: a) Grubbs **210**, CH_2Cl_2, RT, 7 days, 44% for **211**, 4.5% for **212**; b) PtO_2/H_2, ethyl acetate, RT, 12h, 99%; c) 1M NaOH/THF/MeOH = 3:1:2, RT, 24h, 95% for **215**, 99% for **216**.

After the successful preparation of the macrocyclic spacer-linked oligoaminosaccharides **215** and **216** the main efforts were directed towards the analogous synthesis of ^{15}N-labelled macrocyclic oligoaminosaccharides. Previously prepared ^{15}N-labelled dimer **206** was subjected to the olefin metathesis macrocyclisation conditions according to the previous protocol using non-labelled aminoglycoside **204**. The macrocycles **218** and **219** generated were hydrogenated and deprotected respectively to yield the target molecules **220** and **221** with similar yields as described above. (Scheme 56)



Scheme 56 Reagents and conditions: a) Grubbs **210**, CH_2Cl_2, RT, 7 days, 45% for **218**, 5% for **219**; b) PtO_2/H_2, ethyl acetate, RT, 12h, 99%; c) 1M NaOH/THF/MeOH = 3:1:2, RT, 24h, 99%.

10. Conclusions and outlook

The objective of the second part of this work was to develop a synthetic route for ^{15}N-labelled macrocyclic neooligoaminodeoxysaccharides, and synthesize the non-labelled and nitrogen ^{15}N-labeled macrocyclic spacer-linked oligoaminosaccharides on a “large scale” for NMR and biological evaluations with TAR-RNA. Uloside **201** was chosen as the key building block *en route* to the ^{15}N-labelled macrocycles. The intermediate satisfied the following parameters: it is easyly synthesized on a gram scale; it has proven to be an ideal structure for introducing a ^{15}N-label in a desirable axial configuration using readily available and cheap ^{15}N-labelled ammonium acetate; labeling leads to a well known structure which was previously prepared by Dr. G.-W. Chen [83e,85] for non-labelled linear and macrocyclic oligoamino-deoxysaccharide synthesis. By employing this well worked out strategy the following macrocyclic spacer-linked oligoaminodeoxysaccharides were prepared: (Figure 11)

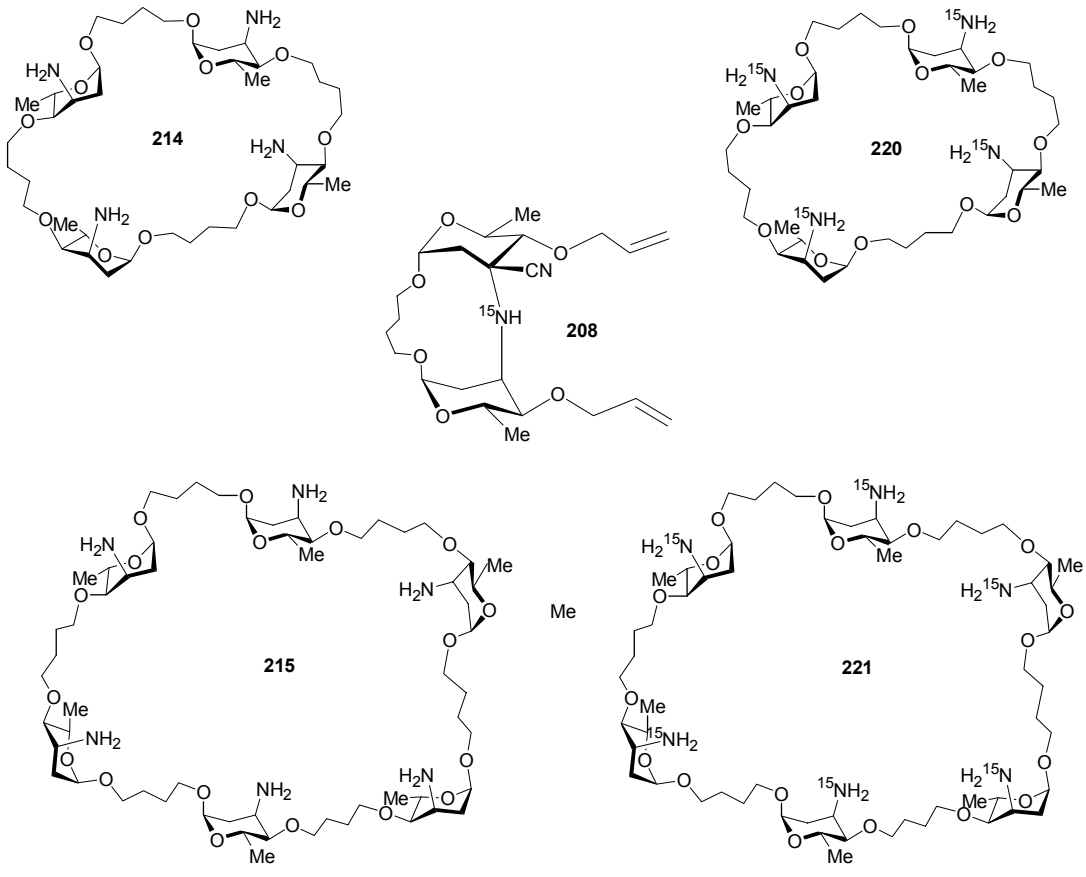


Figure 11

Along with the target aminoglycosides, also cyclic cyanamin **208** was isolated from this reductive amination process.

Further investigations in olefin metathesis process with homodimer **203** could open a new route in high-yielding macrocycle synthesis due to the perfect stereo control in the reduction process and excellent overall yields. The fluctuant yields in the reductive amination process with ammonium acetate points to still undiscovered influence of some reaction conditions, therefore the field of optimizations and hence improved yields is not yet exhausted. Preliminary affinity studies of spacer-linked neooligosaccharide **215** have been accomplished with TAR-RNA, the important m-RNA domain of HIV-1 virus.[85] An extraordinary binding property between TAR-RNA and **215** was observed, leading to formation of the aminoglycoside-RNA complex. Such complexation could force the TAR-RNA to adopt an alternative conformation. Further in-depth studies of TAR-RNA/aminoglycoside complex with contribution of ^{1}H-, ^{13}C-, and ^{15}N-NMR spectroscopy are in progress under guidance of Dr. T. Carlomagno in department of NMR-based structural biology (Prof. C. Griesinger) of Max-Planck-Institute for biophysical chemistry, Göttingen.

11. Experimental part

11.1. General methods:

Melting Points: All melting points were determined in glass capillaries on a Büchi or Gallenkamp apparatus and are uncorrected.

Polarimeter: Optical rotations were measured with a Perkin-Elmer model 243B polarimeter at the sodium line and given in deg per dm with the expression of concentration in g per 100 mL.

IR-Spectroscopy: IR spectra were recorded on a Bruker FT-IR aparatus Vector 22. The liquid substances spectra were recorded using NaCl plates or ATR unit, solid substances were pressed together with KBr.

^{1}H-NMR-Spectra: ^{1}H-NMR spectra were recorded on a Bruker DPX 200-NMR, Bruker ARX 400-NMR and Bruker AM 500-NMR spectrometer. Chemical shifts are reported in ppm (parts per million) relative to internal tetramethylsilane (δ = 0.00), chloroform (δ = 7.26), methanol (δ = 3.31), benzene (δ = 7.16), pyridine (δ = 8.71). Coupling constants *J* are given in Hertz (Hz). Multiplicities are described by using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad.

^{15}N-NMR-Spectra: ^{15}N-NMR spectra were recorded on a Bruker AM 500-NMR spectrometer. Chemical shifts are reported in ppm (parts per million) relative to internal nitromethane (δ = 0.00), Coupling constants *J* are given in Hertz (Hz). Multiplicities are described by using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad.

^{13}C-NMR-Spectra: ^{13}C-NMR spectra were recorded on a Bruker DPX 200-NMR (50 MHz), Bruker ARX 400-NMR (100 MHz) and Bruker AM 500-NMR (125 MHz) spectrometer. Chemical shifts are reported in ppm (parts per millions) relative to internal standards such as chloroform (δ = 77.0), methanol (δ = 49.0), benzene (δ = 128.06), pyridine (δ = 149.5). Multiplicities refer to the resonance in the off-

resonance spectra and were elucidated using the distortionless enhancement by polarization transfer (DEPT) spectral editing technique, with secondary pulses at 90° and 135°. $^{1}J_{CH}$ Coupling are described by using the following abbreviations: s = singlet (due to quaternary carbon), d (+) = doublet (methine), t (-) = triplet (methylene), q (+) = quartet (methyl).
Complete assignments of complex structures were performed employing a combination of homo- and heteronulear correlation experiments (^{1}H, ^{1}H-COSY and ^{13}C, ^{1}H-COSY), NOE, 1D-NOESY, ROSY, TOCSY and HMQC.

MS-Spectra: Mass spectra were obtained on Micromass LCT with Lock-Spray using electrospray ionization (ESI) mode. Ion mass (m/z) signals are reported as values in atomic mass units followed, in parentheses, by peak intensities relative to the base peak (100 %).

Chromatography: Elution of all reactions were monitored by analytical thin layer chromatography (t.l.c.) using silica gel 60 F^{254} precoated plates (E. Merck, Darmstadt) and spots were detected either by UV-absorption or by charring with H_2SO_4/4-methoxybenzaldehyde in methanol. R_f´s are given under these conditions too. Flash column chromatography were performed using E. Merck silica gel 60 of 230-400 meshes and normal column chromatography were done on E. Merck silica gel 60 of 35-70 meshes. The solvents for chromatography were freshly distilled before use.

Reagents and solvents: All commercial available chemicals were used without further purification unless otherwise stated, but some reagents were dried under vacuum before use.
All reactions involving air- or/and moisture-sensitive reagents were conducted under nitrogen or argon (high purity and dried over NaH, Firma Linde) atmosphere with dry, freshly distilled solvents using standard syringe-cannula/septa techniques. All solvents were dried by usual methods and stored under nitrogen atmosphere in the dark in well-stoppered bottles.

11.2. Typical protocols:

General procedure for the glycosidation with Selectfluor™. TP1

To a stirred solution of thioglycoside (0.1 mmol) and acceptor (0.1 mmol) in acetonitrile (5 ml), powdered molecular sieves 4A (50 mg) was added. The suspension was cooled to 0°C and selectfluor™ (0.105 mmol) was added. The reaction mixture was shaken for 20 min (t.l.c.: ethyl acetate / petroleum ether 1:1) and the reaction was terminated by addition of dry Amberlite A-21. The resulting suspension was filtered through a pad of Al_2O_3. The solvent was evaporated under reduced pressure and the residue was redissolved in isopropanol (5 ml). After addition of polymer-supported borohydride (100 mg) the mixture was shaken overnight in order to remove thio-derived impurities. The suspension was filtered and concentrated under reduced pressure. The purity of the crude products as well as the α/β-ratios were determined at this stage by NMR-spectroscopy. Separation of the anomers was achieved by column chromatography (silica gel; petroleum ether / ethyl acetate).

General procedure for the glycosidation with Selectfluor™. TP2

TP2 is identical to TP1 except for that the scale was downsized to 0.05 mmol.

General procedure for the metathesis olefinations. TP3

The sugar (1 mmol) was dissolved in 1 ml of benzene and Grubs 1 catalyst [17222-30-9] (1 mol%) was added under argon. The reaction mixture was stirred for 6 h, then a second portion of the catalyst (1 mol%) was added and the mixture was stirred for additional 12 h.

Then, the reaction temperature was elevated to 40°C and an additional portion of the catalyst was added (2 mol% in 24 h in 2 portions). The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (silica gel; petroleum ether / ethyl acetate) to yield main products and unreacted starting material. The isolated products were hydrogenated without further analysis.

General procedure for catalytic hydrogenation. TP4

The sugar (1 mmol) was dissolved in a mixture of solvents (ethyl acetate /CH_2Cl_2/MeOH 16:8:1) 10 ml and PtO_2 (7 mol%) was added. The suspension was

stirred for 5 h under positive H_2 pressure. The reaction mixture was filtered and concentrated under reduced pressure to give the product in almost quantitative yield.

General procedure for allylation. TP5

To a vigorously stirred solution of homodimeric diol (0.1 mmol) and allyl bromide (20 eq) in DMSO (0.5 ml) was added $LiN(SiMe_3)_2$ as solution in THF (200 µl) (7 eq) at 0°C. After 5 min the reaction was diluted with ethyl acetate and water. The organic layer was washed with water until neutral pH. The organic phase was dried ($MgSO_4$), filtered and concentrated in vacuum. The crude oil was purified by column chromatography (ethyl acetate / petroleum ether 1:10) to yield bisallylated homodimer, along with monoallylated product: yield 50-55% bisallylated homodimer, 40-45% monoallylated product. The latter can be used for another allylation step according to the procedure described above.

General procedure for introducing THP ethers. TP6

The chirale alcohol (0.033 mmol) was dissolved in CH_2Cl_2 abs. (3 ml). DHP 2.8 mg (3.3 µl, 1 eq) and polymer bound PPH_3HBr (cat.) were added, and the suspension was vigorously shaken for 3 h at room temperature. The reaction mixture was filtered through a pad of Celite and concentrated under reduced pressure.

General procedure for cleaving THP-ethers. TP7

To a stirred solution of THP protected alcohol (0.033 mmol) in methanol (5 ml) at room temperature was added polymer bound PPH_3HBr (2 mg). The mixture was stirred at room temperature for 12 h. The reaction mixture was filtered through a pad of Celite and concentrated under reduced pressure.

General procedure for deacetylation of alcohols. TP8

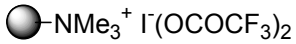
To a stirred solution of sugar (10.0 mmol) in methanol (50 ml) was added Amberlite A-26(OH^- form) (1 g). After 24h the reaction mixture was filtered and the solvent was removed under reduced pressure. The product was dried under reduced pressure for 4h and could directly be used for the next step.

11.3. Preparation of general reagents:

TBAF buffered solution (pH – 7) for mild silyl ether cleavage.

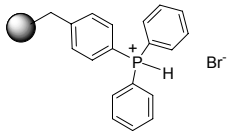
(TBAF /AcOH/THF – 266 mg/0.151 ml/8.4 ml).

Polymer-bound Iodo-bis-trifluoroacetate



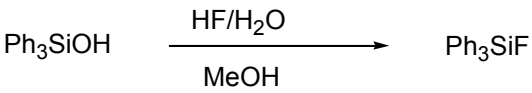
To a suspension of polymer-bound iodide A-26$^{+}I^{-}$ (5 g, 2.9mmol/g) in CH_2Cl_2 (30 ml) 11.22 g (26 mmol) $PhI(OCOCF_3)_2$ was added. The mixture was shaken for 2 h, polymer was filtered off, washed with CH_2Cl_2 (20 x 20 ml) and dried in high vacuum.

Polymer-bound triphenylphosphonium bromide



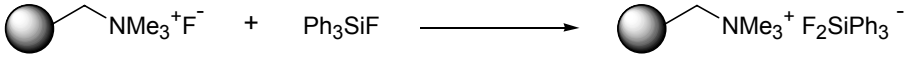
The suspension of polymer-bound triphenylphosphine (0.5g, 1.12 mmol/g) in HBr/AcOH (33%) 5ml was shaken for 24 h. The slurry washed with CH_2Cl_2 20x5ml and dried under reduced pressure to afford dark yellow polymer.

Polymer-bound tetramethylammonium triphenyldifluorosilicate TBAT



Triphenylsilanol was recrystallised from petroleum ether / ethyl acetate prior to use. A solution of triphenylsilanol (25 g, 90.4 mmol) in methanol (90 ml) in a polyethylene bottle was prepared and cooled to 5^{o}C. Aqueous HF (13 ml, 49%, 360 mmol) was slowly added and the resulting reaction mixture was allowed to warm to room temperature, followed by stirring for additional 30 min. Distilled water (50 ml) was added to induce further product precipitation. The resulting slurry was filtered in vacuum and washed with water. The crude product was recrystallised from solvent mixture (MeOH/water - 15:1) and dried under vacuum.

Yield: 23.9g (86 mmol, 95%).



Polymer-supported fluoride was washed with acetonitrile / ethyl acetate prior to use. A mixture of 2 g fluoride resin and triphenylsilylfluoride (3.3 g, 2 eq, 12 mmol) in CH_2Cl_2 (100 ml) was shaken for 30 min and the solvent was slowly evaporated under reduced pressure. The resulting polymer diluted with ethyl acetate (50 ml) and once more evaporated. This procedure was repeated more 3 times, and then resulted polymer-bound TBAT was filtered, washed with ethyl acetate and dried under high vacuum.

11.4.1. Experiments to the chapter 5.1.

3-*O*-TES-L-rhamnal (47)

To a solution of L-rhamnal (130 mg, 1 mmol), DMAP (24.9 mg, 0.2 mmol) and imidazole (102 mg, 1.5 mmol) in 10 ml of DMF was dropwise added TESCl (158 mg, 1.05 mmol) at - 50° C in 30 min. After all TESCl was added, the reaction mixture was stirred another 1 h at - 50° C. The resulting mixture was allowed to warm to RT and DMF was removed by filtration column (silica gel, petroleum ether / ethyl acetate 5:1). The crude product was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10:1, R_f- 0.26)

Yield: 170 mg (0.70 mmol, 70%), colorless oil.

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 6.15 (dd, *J* = 6.2, 1.7 Hz, 1H, 1-H), 4.55 (dd, *J* = 6.2, 2.0 Hz, 1H, 2-H), 4.19 (ddd, *J* = 6.7, 2.0, 1.7 Hz, 1H, 3-H), 3.90(dq, *J* = 9.2, 6.3 Hz, 1H, 5-H), 3.45 (ddd, *J* = 9.2, 6.7, 3.8 Hz, 1H, 4-H), 2.18 (d, *J* = 3.8 Hz, 1H, O<u>H</u>), 1.37 (d, *J* = 6.3 Hz, 3H, 6-H), 0.90 (t, *J* = 8.0 Hz, 9H, $SiCH_2C\underline{H_3}$), 0.57 (q, *J* = 8.0 Hz, 6H, $SiCH_2CH_3$).

^{13}**C-NMR** (50 MHz, $CDCl_3$, $CDCl_3$=77 ppm) δ:143.6 (+, C-1), 103.4 (+, C-2), 74.8 (+, C-4), 74.3 (+, C-5), 70.5 (+, C-3), 17.2 (+, C-6), 7.1 (+, $SiCH_2CH_3$), 5.3 (-, $SiCH_2CH_3$).

3-*O*-TES-L-Fucal (46)

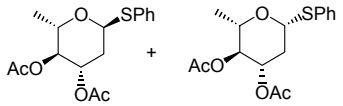
To a solution of L-fucal (2 g, 15.4 mmol), DMAP (0.35 g, 0.2 eq, cat.) and imidazole (1.5 g, 1.5 eq, 23.1 mmol) in DMF (20 ml) at - 60° C TESCl (2.3 g, 15.4 mmol) was added dropwise. The reaction mixture was stirred for 1 h at the same temperature and then allowed to warm up to RT. The DMF was removed by filtration column (silica gel, petroleum ether / ethyl acetate 5:1) and crude product was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10:1, R_f- 0.26)

Yield: 3 g (12.3, 80%), colorless oil.

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 6.30 (d, *J* = 5.8 Hz, 1H, 1-H), 4.45 (ddd, *J* = 5.8, 2.0, 1.4 Hz, 1H, 2-H), 4.41 (dd, *J* = 3.6, 2.0 Hz, 1H, 3-H), 3.92 (bq, *J* = 6.8, 1H, 5-H), 3.57 (ddd, *J* = 3.6, 2.0, 1.4 Hz, 1H, 4-H), 2.75 (dd, *J* = 1.4, 1.4 Hz, 1H, O<u>H</u>) 1.35 (d, *J* = 6.8 Hz, 3H, 6-H), 0.94 (t, *J* = 7.6 Hz, 9H, $Si(CH_2\underline{CH_3})_3$), 0.6 (q, *J* = 7.6 Hz, 6H, $Si(CH_2CH_3)_3$).

^{13}**C-NMR** (50 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 144.5 (+, C-1), 101.6 (+, C-2), 72.4, 68.0, 65.0 (3+, C-4, C-5, C-3), 16.7 (+, C-6), 6.5 (+, $Si(CH_2CH_3)_3$), 5.3 (-, $Si(CH_2CH_3)_3$).

Phenyl [3,4-di-*O*-acetyl-2,6-dideoxy]-1-thio-α(β)-L-glycopyranosides (18, 19)



18 **19**

3,4-Bis-*O*-acetyl-rhamnal (200 mg, 0.93 mmol) was added to a solution of thiophenol (0.10 g, 1.0 mmol) in dry CH_2Cl_2 (5 ml). Triphenylphosphine hydrobromid (343 mg, 1.0 mmol) was added and the solution was stirred for 24 h. The reaction mixture was evaporated in a nitrogen flow and the residue was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10/1, R_f- 0.32).

Yield: fraction-α: **18** 118 mg (0.364 mmol, 39%), colorless crystals.

fraction-β: **19** 36 mg (0.110 mmol, 12%), colorless crystals.

mix fraction (α/β) 24 mg (0.074 mmol, 8%), light yellow syrup.

fraction-α

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 7.46 (m, 2H, *Ph*), 7.3 (m, 3H, *Ph*), 5.62 (d, *J* = 5.6 Hz, 1H, *1-H*), 5.28 (ddd, *J* = 11.7, 9.5, 5.6 Hz, 1H, *3-H*), 4.80 (dd, *J* = 9.5, 9.5 Hz, 1H, *4-H*), 4.39 (dq, *J* = 9.5, 6.2 Hz, 1H, *5-H*), 2.46 (ddd, *J* = 13.3, 5.6, 1.1 Hz, 1H, *2-H*$_{ax}$), 2.22 (ddd, *J* = 13.3, 11.7, 5.6 Hz, 1H, *2-H*$_{eq}$), 2.01, 2.00 (2s, 6H, 2$COCH_3$), 1.21 (d, *J* = 6.2 Hz, 3H, *6-H*)

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 170.2, 170.1 (2s, 2 x *C*OCH_3), 134.5, 131.2, 129.0, 127.3 (s, 3d, *Ph*), 83.0 (d, C-1), 74.8, 69.3, 66.8 (3d, C-3, 4, 5), 35.9 (t, C-2), 21.0, 20.8 (2q, 2 x CO*C*H_3), 17.4 (q, C-6)

fraction-β

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 7.50 (m, 2H, *Ph*), 7.32 (m, 3H, *Ph*), 5.00 (ddd, *J* = 11.8, 9.5, 5.3 Hz, 1H, 3-H), 4.81 (dd, *J* = 11.8, 2.0 Hz, 1H, 1-H), 4.76 (dd, *J* = 9.5, 9.5 Hz, 1H, 4-H), 3.53 (dq, *J* = 9.5, 6.2 Hz, 1H, 5-H), 2.45 (ddd, *J* = 12.7, 5.3, 1.9 Hz, 1H, 2-H$_{ax}$), 2.06, 2.03 (2s, 6H, 2 x $COCH_3$), 1.84 (ddd, *J* = 12.7, 11.8, 11.8 Hz, 1H, 2-H$_{eq}$), 1.27 (d, *J* = 6.2 Hz, 3H, 6-H)

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 170.3, 170.0 (2s, 2 x *C*OCH_3), 132.9, 132.2, 128.9, 127.8 (s, 3d, *Ph*), 81.5 (d, C-1), 74.3, 73.7, 71.7 (3d, C-3, 4, 5), 36.5 (t, C-2), 20.9, 20.8 (2q, 2 x CO*C*H_3), 17.9 (q, C-6)

Phenyl [3,4,6-tri-*O*-acetyl-2-deoxy]-1-thio-α(β)-D-glycopyranoside (21)

3,4,6-Tri-*O*-acetyl-glucal (15 g, 0.055 mol) was added to a solution of thiophenol (6.1 g, 0.055 mol) in dry CH_2Cl_2 (150 ml). Triphenylphosphine hydrobromid (10 g, 60 mol%) was added and solution was stirred for 24 h. The reaction mixture was evaporated in a nitrogen flow and the residue was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10/1, R_f- 0.30).

Yield: 13 g (0.034 mol, 62%, α/β - 1:1), light yellow crystals.

α-anomer

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.38 (m, 2H, Ph-o), 7.21 (m, 3H, Ph-m, p), 5.68 (d, *J* = 5.5 Hz, H1, 1-H), 5.30 (ddd, *J* = 11.5, 9.5, 5.5 Hz, 1H, 3-H), 5.02 (dd, *J* = 9.5, 9.5 Hz, 1H, 4-H), 4.55 (ddd, *J* = 9.5, 5.5, 2.0 Hz, 1H, 5-H), 4.30 (dd, *J* = 12.0, 5.0 Hz, 1H, 6-H), 4.01 (dd, *J* = 12.5, 2.0 Hz, 1H, 6-H), 2.48 (ddd, *J* = 13.5, 5.5, 1.5 Hz, 1H, 2-H_{ax}), 2.22 (ddd, *J* = 13.5, 11,5 5.5 Hz, 1H, 2-H_{eq}), 2.03 (s, 3H, C*H*$_3$CO), 2.01 (2s, 6H, 2 x C*H*$_3$CO).

^{13}**C-NMR** (50 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 171.58, 170.41 (3 x *C*OCH_3), 134.21 (Ph-1), 131.73 (+, Ph-o), 129.75 (+, Ph-m), 128.01 (+, Ph-p), 83.62 (+, C-1), 69.88 (+, C-4), 69.71 (+, C-3), 69.11 (+, C-5), 62.73 (-, C-6), 35.51 (-, C-2), 21.35, 21.12 (3+, 3 x *C*H_3CO).

Phenyl (2,6-dideoxy)-1-thio-α-L-glycopyranoside (27)

To a solution of thioglycoside **18** (0.93 g, 2.87 mmol) in 50 ml of methanol 5 g of Amberlite A-26 (OH^- form) was added. The suspension was shaken overnight and then filtered from the polymer and evaporated under reduced pressure. The residue crystallizes as a colorless powder.

Yield: 630 mg (2.61 mmol, 91%).

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.38 (m, 2H, Ph-o), 7.21 (m, 3H, Ph-m, p), 5.58 (d, *J* = 5.5 Hz, 1H, 1-H), 4.17 (dq, *J* = 9.1, 6.2 Hz, 1H, 5-H), 3.95 (ddd, *J* = 11.8, 9.1, 5.0 Hz, 1H, 3-H), 3.16 (dd, *J* = 9.1, 9.1 Hz, 1H, 4-H), 2.72 (bs, 2H, 2 x O*H*), 2.37 (ddd, *J* = 13.0, 5.0, 1.0 Hz, 1H, 2-H^{eq}), 2.12 (ddd, *J* = 13.0, 11.8, 5.0 Hz, 1H, 2-H^{ax}), 1.31 (d, *J* = 6.2 Hz, 3H, 6-H).

^{13}**C-NMR** (50 MHz, $CDCl_3$, $CDCl_3$=77 ppm) 135.0 (P*1-H*), 131.1 (2x+, P*2-H*, 6), 128.9 (2x+, P*3-H*, 5), 127.1 (+, P*4-H*), 83.9 (+, C-1), 78.3 (+, C-3), 69.8 (+, C-4), 68.5 (+, C-5), 38.5 (-, C-2), 17.5 (+, C-6).

Phenyl (3-*O*-TES-2,6-dideoxy)-1-thio-α-L-glycopyranoside

To a solution of thioglycoside **27** (630 mg, 2.62 mmol), DMAP (64 mg, 0.2 eq, cat.) and imidazole (267 mg, 3.93 mmol) in DMF (10 ml) at - 60° C TESCl (0.396 g, 2.63

mmol) dropwise was added. The reaction mixture was stirred for 1 h at the same temperature then allowed to warm up to RT. DMF was removed by filtration through a short column (silica gel, petroleum ether / ethyl acetate 5:1). The crude product was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10:1, R_f- 0.24).

Yield: 0.8 g (2.26 mmol, 86%), colorless crystals.

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.38 (m, 2H, Ph-o), 7.21 (m, 3H, Ph-m, p), 5.56 (dd, *J* = 5.0, 1.0 Hz, 1H, 1-H), 4.18 (dq, *J* = 9.4, 6.2 Hz, 1H, 5-H), 3.9 (ddd, *J* = 11.3, 8.6, 5.4 Hz, 1H, 3-H), 3.14 (ddd, *J* = 9.4, 8.6,1.9 Hz, 1H, 4-H), 2.34 (d, *J* = 2.2 Hz, 1H, O*H*), 2.25 (ddd, *J* = 13.3, 5.4, 1.3 Hz, 1H, 2-H^{eq}), 2.10 (ddd, *J* = 13.3, 11.3, 5.4 Hz, 1H, 2-H^{ax}), 1.30 (d, *J* = 6.2 Hz, 3H, 6-H), 0.99 (t, *J* = 7.7 Hz, 9H, 3 x C*H*$_3$CH$_2$Si), 0.66 (q, *J* = 7.7 Hz, 6H, 3 x C*H*$_2$Si).

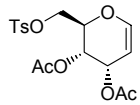
^{13}**C-NMR** (50 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) 135.0 (Ph-1), 131.1 (2+, Ph-o), 128.9 (2+, Ph-m), 127.1 (+, Ph-p), 83.9 (+, C-1), 78.1 (+, C-3), 70.9 (+, C-4), 68.5 (+, C-5), 39.5 (-, C-2), 17.7 (+, C-6), 6.8 (+, Si(CH$_2$*C*H$_3$)$_3$), 5.0 (-, Si(*C*H$_2$CH$_3$)$_3$).

D-Allal (116)

10 g (0.0367mol) of Tri-*O*-acetylallal **115** was dissolved in 100 ml of methanol and Amberlite A-26 (OH^- form, 5 g) was added. The mixture was shaken overnight. The reaction mixture was filtered and the solvent was evaporated to give a white crystalline substance.

Yield: 5.3g (0.0366 mmol, 99%).

3,4-Di-*O*-acetyl-6-tosyl-D-allal (117)



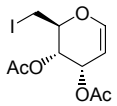
To a solution of allal **116** (4 g, 0.027 mol) in 30 ml of pyridine was added toluolsulfonyl chloride (5.22 g, 0.027 mmol). The mixture was stirred until no starting material was observed (t.l.c. ethyl acetate / petroleum ether – 1:2). Then acetanhydride (6 ml, 0.06 mmol) was added and the solution was allowed to stir for

12h more. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography over silica gel (ethyl acetate / petroleum ether - 2:2).

Yield: 9.4g (0.0245 mmol, 90%, R_f-0.5)

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.82 (bd, *J* = 8.1 Hz, 2H, Ph), 7.39 (bd, *J* = 8.1 Hz, 2H, Ph), 6.45 (d, *J* = 6.0 Hz, 1H, 1-H), 5.47 (dd, *J* = 6.0, 3.7 Hz, 1H, 3-H), 5.08 (ddd, *J* = 12.4, 6.0, 2.3 Hz, 1H, 5-H), 4.93 (bdd, *J* = 6.0, 6.0 Hz, 1H, 2-H), 4.1-4.4 (m, 3H, 4-H, 6-H), 2.50 (s, 3H, C$\underline{H}_3$-Ph), 2.10 (s, 3H, Ac), 2.00 (s, 3H, Ac).

3,4,-Di-*O*-acetyl-6-iodo-6-deoxy-D-allal



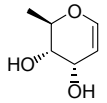
The sugar **117** (5 g, 0.013 mol) was dissolved in 100 ml of acetone and NaI (3.9 g, 0.026 mol) was added successively. The solution was refluxed for 12 h, whereupon t.l.c. (ethyl acetate / petroleum ether – 1:4) indicated the completion of the substitution. Solvent was evaporated under reduced pressure and the crude product was purified by column chromatography over silica gel (ethyl acetate / petroleum ether - 1:4).

Yield: 4.3g (0.0127 mmol, 97%, R_f-0.53)

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 6.56 (d, *J* = 5.8 Hz, 1H, 1-H), 5.47 (dd, *J* = 5.8, 3.8 Hz, 1H, 3-H), 4.99 (dd, *J* = 10.4, 3.8, 1H, 4-H), 4.95 (dd, *J* = 5.8, 5.8 Hz, 1H, 2-H), 3.92 (ddd, *J* = 10.4, 5.7, 2.8 Hz, 1H, 5-H), 3.48 (dd, *J* = 11.0, 2.8 Hz, 1H, 6-H), 3.35 (dd, *J* = 11.0, 5.7 Hz, 1H, 6-H') 2.10 (s, 3H, Ac), 2.07 (s, 3H, Ac).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 170.21 (s, CO), 169.13 (s, CO), 147.66 (d, C1), 97.80 (d, C2), 70.77, 70.74 (2d, C4, C3), 62.56 (d, C5), 20.98, 20.58 (2q, 2 x CO*C*H_3), 4.53 (t, -*C*H_2-I).

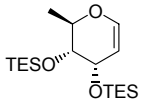
6-Deoxy-D-allal



A solution of 3,4-di-*O*-acetyl-6-iodo-6-deoxy-D-allal (3.1 g, 9.1 mmol) in 10 ml of THF was added to a suspension of $LiAlH_4$ in THF (1.897g, 50 mmol, 5.5 eq in 50 ml). After 2 h the reaction mixture was treated with NaF (23.76 g) and water 10 ml in 32.7 ml of THF at 0°C. The resulting suspension was stirred for 1 h and filtered through a pad of celite, solids were washed with THF and the solvent was evaporated to afford a white solid. The crude product was siliylated without further purification.

Yield: 1.05 g (8 mol, 88%).

6-Deoxy-3,4-diO-TES-D-allal (118)

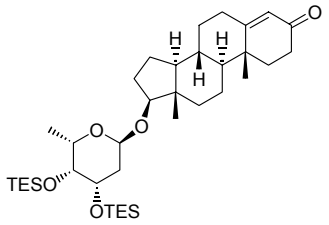


A solution of 6-deoxy-D-allal (1.1 g, 8 mmol), DMAP (50 mg, cat.) and imidazole (1.8 g, 24 mmol) in 20 ml of DMF was stirred, and dropwise TESCl (3.0 g, 20 mmol) was added. After all TESCl was added, the reaction mixture was stirred for another 5 h at RT. DMF was removed by filtration through a short silica gel column (petroleum ether / ethyl acetate - 5:1). The crude product was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10:1) to afford a colourless oil.

Yield: 2.6 g (7.2 mmol, 91%, R_f- 0.26)

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 6.33 (d, *J* = 5.8 Hz, 1H, 1-H), 4.82 (dd, *J* = 5.8, 5.7 Hz, 1H, 2-H), 4.16 (dq, *J* = 9.5, 6.3, 1H, 5-H), 4.05 (dd, *J* = 5.7, 3.3 Hz, 1H, 3-H), 3.55 (dd, *J* = 9.5, 3.3, 1H, 4-H), 1.33 (d, *J* = 6.3 Hz, 3H, 6-H), 1.00 (m, 18 H, TES), 0.65 (m, 12H, TES).

17-*O*-[3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl]-testosterone (24)



To a solution of testosterone (50 mg, 0.173 mmol), and 3,4-bis-*O*-TES-L-fucal **22** (0.312g, 4 eq, 0.692 mmol) in 3 ml of CH_2Cl_2 PPh_3HBr (3.7 mg, 5mol %) was added. The solution was stirred for 30 min then the reaction was terminated by addition of Amberlite A-21 and stirred for 10 min more. Polymer was filtered off, washed with ethyl acetate and the filtrate was evaporated under reduced pressure. Residue was purified by column chromatography (silica gel, petroleum ether / ethyl acetate -3:1, R_f-0.32).

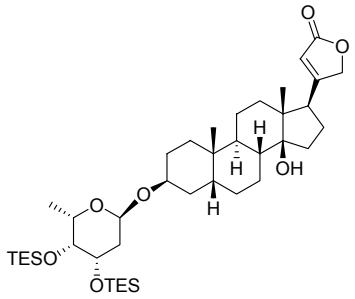
Yield: 101 mg (0.156 mmol, 90%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.68 (s, 1H, 4-H), 4.85 (d, *J* = 2.8 Hz, 1H, 1-H'), 3.99 (ddd, J = 11.5, 4.4, 2.4 Hz, 1H, 3-H'), 3.79 (bq, J = 6.7 Hz, 1H, 5-H'), 3.55 (bd, J = 2.4 Hz, 1H, 4-H'), 3.42 (t, J = 8.3 Hz, 1H, 17-H), 2.7 – 0.5 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.5 (C-3), 171.2 (C-5), 123.8 (+, C-4), 98.7 (+, C-1'),87.1 (+, C-17), 73.6 (+, C-4'), 67.6, 67.5 (2+, C-3', C-5'), 53.8 (+, C-9), 50.1 (+, C-14), 42.7 (C-13), 38.5 (C-10), 37.0 (-, C-12), 35.6 (-, C-1), 35.4 (+, C-8), 33.9 (-, C-2), 33.4 (-, C-2'), 32.7 (-, C-6), 31.4 (-, C-7), 28.5 (-, C-16), 23.3 (-, C-15), 20.5 (-, C-11), 17.3 (+, C-19), 17.2 (+, C-6'), 11.5 (+, C-18), 7.0, 6.8 (2+, 2 x $SiCH_2CH_3$), 5.1, 4.8 (2-, 2 x $SiCH_2CH_3$).

$[\alpha]_D^{23}$ = -14.76 ° (c=1.26, $CHCl_3$)

3-*O*-[3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl]-digitoxigenin (26)



To a solution of digitoxigenin (100 mg, 0.266 mmol) and 3,4-bis-*O*-TES-L-fucal **22** (0.3g, 3 eq, 0.8 mmol) in 5 ml of CH_2Cl_2 was added PPh_3HBr (10 mg, 10 mol %). The solution was stirred for 30 min then the reaction was terminated by addition of Amberlite A-21 and stirred for another 10 min. Polymer was filtered off, washed with ethyl acetate and the filtrate was evaporated under reduced pressure. Residue was purified by column chromatography (silica gel, petroleum ether / ethyl acetate -3:1, R_f-0.19). Treating with acetonitrile causes spontaneous crystallization.

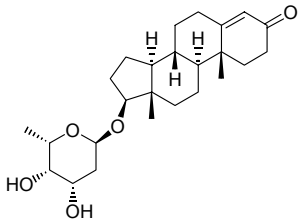
Yield: 165 mg (0.225 mmol, 85%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.84 (s, 1H, 22-H), 4.98 (dd, *J* = 18.1, 1.6 Hz, 1H, 21-H), 4.92 (d, *J* = 2.7 Hz, 1H, 1-H'), 4.78 (dd, *J* = 18.1, 1.6 Hz, 1H, 21-H), 4.05 (ddd, J = 11.9, 4.3, 2.7 Hz, 1H, 3-H'), 3.85 (bs, 1H, 14-H), 3.80 (bq, J = 6.7 Hz, 1H, 5-H'), 3.56 (bs, 1H, 4-H'), 2.75 (m, 1H, 3-H), 2.20 – 0.5 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 174.6 (s, C-20), 174.5 (s, C-23), 117.6 (d, C-22), 95.8 (d, C-1'), 85.6 (s, C-14), 73.8 (d, C-4'), 73.4 (t, C-21), 70.8 (d, C-3), 67.8 (d, C-3'), 67.6 (d, C-5'), 50.9 (d, C-17), 49.6 (s, C-13), 41.9 (d, C-8), 40.0 (t, C-12), 36.5 (d, C-5), 35.6 (d, C-9), 35.2 (s, C-10), 33.7 (t, C-2'), 33.2 (t, C-4), 30.4 (t, C-15), 29.9 (t, C-1), 26.8 (t, C-2), 26.7 (t, C-6), 26.6 (t, C-16), 23.8 (q, C-19), 21.4 (t, C-7), 21.2 (t, C-11), 17.3 (q, C-6'), 15.7 (q, C-18), 7.0, 6.9 (2q, 2 x $SiCH_2CH_3$), 5.2, 4.9 (2t, 2 x $SiCH_2CH_3$).

$[\alpha]_D^{23}$ = - 44.84 ° (c=1.22, $CHCl_3$)

17-*O*-[2,6-dideoxy-α-L-galactopyranosyl]-testosterone (35)



A solution of glycoside **24** (230 mg, 0.35 mmol) in "TBAF mixture" (10 ml) was stirred for 4 days. The resulted solution was evaporated and the crude product was purified by column chromatography over silica gel (ethyl acetate, Rf- 0.31)

Yield: 132.7 mg (0.318 mmol, 91%), crystalline powder.

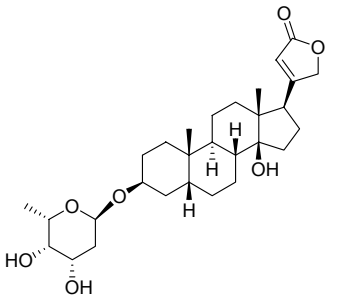
^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (s, 1H, 4-H), 4.92 (d, *J* = 3.5 Hz, 1-H'), 3.99 (m, 1H, 3-H'), 3.94 (bq, J = 6.7 Hz, 1H, 5-H'), 3.60 (bs, 1H, 4-H), 3.49 (t, J = 8.8 Hz, 1H, 17-H), 2.5 – 0.7 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.6 (C-3), 171.2 (C-5), 123.9 (+, C-4), 98.2 (+, C-1'), 87.1 (+, C-17), 71.4 (+, C-4'), 66.0 (+, C-3'), 65.6 (+, C-5'), 53.9 (+, C-9), 50.2 (+, C-14), 42,8 (C-13), 38.6 (C-10), 37.1 (-, C-12), 35.7 (-, C-1), 35.4 (+, C-8), 33.9 (-, C-2), 33.3 (-, C-2'), 32.8 (-, C-6), 31.5 (-, C-7), 28.4 (-, C-16), 23.3 (-, C-15), 20.6 (-, C-11), 17.4 (+, C-6'), 16.7 (+, C-19), 11.6 (+, C-18).

LC-MS (ESI) (-c): m/z (%): 417.24 (100) $[M - H]^-$; **HR-MS** $C_{25}H_{37}O_5$: calc. 417.2641, found 417.2646

$[\alpha]_D^{23}$ = -13 ° (c=1.0, $CHCl_3$)

3-*O*-[2',6'-dideoxy-α-L-galactopyranosyl]-digitoxigenin (36)



A solution of **26** (127 mg, 0.18 mmol) in "TBAF mixture" (20 ml) was stirred for 4 days. The resulted solution was evaporated and the crude product was purified by column chromatography over silica gel (ethyl acetate, R_f- 0.37).

Yield: 90 mg (0.179 mmol, 97%), crystalline powder.

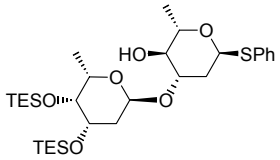
^{1}**H-NMR** (400 MHz, CD_3OD, CD_3OD = 3.31 ppm) δ: 5.84 (s, 1H, 22-H), 4.98 (dd, *J* = 18.1, 1.6 Hz, 1H, 21-H), 4.92 (d, *J* = 2.7 Hz, 1H, 1-H'), 4.78 (dd, *J* = 18.1, 1.6 Hz, 1H, 21-H), 4.0 -3.85 (m, 3H, 14-H, 3-H', 5-H'), 3.54 (bd, J = 2.7 Hz, 1H, 4-H'), 2.84 (bdd, J = 9., 5.4 Hz, 1H, 3-H), 2.25 – 0.85 (m).

^{13}**C-NMR** (100 MHz, CD_3OD, CD_3OD =50.2 ppm) δ: 179.6 (C-20), 178.4 (C-23), 119.0 (+, C-22), 98.3 (+, C-1'), 87.6 (C-14), 76.5 (+, C-4'), 74.2 (-, C-21), 73.6 (+, C-3), 68.9 (+, C-3'), 68.3 (+, C-5'), 53.3 (+, C-17), 52.3 (C-13), 43.9 (+, C-8), 42.1 (-, C-12), 39.3 (+, C-5), 38.0 (+, C-9), 37.6 (C-10), 35.1 (-, C-2'), 34.6 (-, C-4), 32.9 (-, C-15), 32.2 (-, C-1), 29.2 (-, C-2), 29.1 (-, C-6), 28.7 (-, C-16), 25.6 (+, C-19), 23.8 (-, C-7), 23.8 (-, C-11), 18.4 (+, C-6'), 17.6 (+, C-18).

LC-MS (ESI) (-c): m/z (%): 503.29 (100) $[M - H]^-$; **HR-MS** $C_{29}H_{43}O_7$: calc. 503.3009, found 503.3009

$[\alpha]_D^{23}$ = - 53.2 ° (c=0.5, MeOH)

Phenyl [3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl]-(1→3)-2,6-dideoxy-1-thio-α-L-glycopyranoside (28)



To a solution of 3,4-bis-*O*-TES-L-fucal **22** (50 mg, 0.139 mmol) and thioglycoside **27** (40 mg, 0.166 mmol) in CH_2Cl_2 (2 ml) was added PPh_3*HBr (1 mg, cat.). After 15 min reaction was terminated by addition of Amberlite A-21 and stirred for another 10 min. The polymer was filtered off, washed with ethyl acetate and the

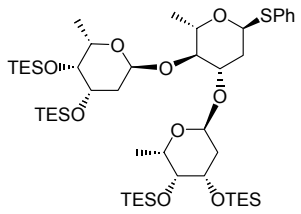
filtrate was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether / ethyl acetate 6:1, R_f- 0.25).

Yield: 60 mg (0.1 mmol, 72%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.38 (m, 2H, Ph-o), 7.21 (m, 3H, Ph-m, p), 5.54 (d, *J* = 5.3 Hz, 1H, 1-H), 5.11 (d, *J* = 3.2 Hz, 1H, 1-H'), 4.19 (dq, *J* = 9.1, 6.1 Hz, 1H, 5-H), 3.94 (ddd, *J* = 11.8, 4.9, 2.5 Hz, 1H, 3-H'), 3.81 (ddd, *J* = 11.4, 9.1, 4.8 Hz, 1H, 3-H), 3.79 (bq, *J* = 6.4 Hz, 1H, 5-H'), 3.57 (bdd, *J* = 2,5, 0.5 Hz, 1H, 4-H'), 3.21 (ddd, *J* = 9.1, 9.1, 2.1 Hz, 1H, 4-H), 2.48 (ddd, *J* = 13.2, 4.8, 0.9 Hz, 1H, 2-H), 2.31 (d, *J* = 2.5 Hz, 1H, O*H*), 2.08 (ddd, *J* = 12.0, 11.8, 3.2 Hz, 1H, 2-H'), 2.06 (ddd, *J* = 13.2, 5.3, 4.8 Hz, 1H, 2-H), 1.59 (ddd, *J* = 11.8, 4.9, 1.3 Hz, 1H, 2-H'), 1.28 (d, *J* = 6.1 Hz, 3H, 6-H), 1.15 (d, *J* = 6.4 Hz, 3H, 6-H'), 0.95 (t, 18H, 2 x (CH_3CH_2)$_3$Si), 0.62 (2q, 12H, 2 x (CH_3CH_2)$_3$Si).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) 135.2 (s, Ph-1), 131.2 (2d, Ph-o), 128.9 (2d, Ph-m), 127.0 (d, Ph-p), 100.02 (d, C-1'), 83.8 (d, C-1), 78.0 (d, C-3), 76.4 (d, C-4), 73.4 (d, C-4'), 68.5 (d, C-5), 68.0 (d, C-5'), 67.4 (d, C-3'), 37.4 (t, C-2), 33.5 (t, C-2'), 17.8 (q, C-6), 17.3 (q, C-6'), 7.0, 6.8 (2q, 2 x (CH_3CH_2)$_3$Si), 5.2, 4.8 (2t, 2 x (CH_3CH_2)$_3$Si).

Phenyl {di-[3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl]-(1→3),(1→4)}-2,6-dideoxy-1-thio-α-L-glycopyranoside (30)



To a solution of 3,4-di-*O*-TES-L-fucal **22** (300 mg, 0.84 mmol) and thioglycoside **27** (58 mg, 0.241 mmol) in CH_2Cl_2 (6 ml) was added PPh_3*HBr (1 mg, cat.). After 15 min, the disaccharides **29** (3-O, TLC: petroleum ether / ethyl acetate 3:1, R_f- 0.59) and regioisomer (4-O, R_f- 0.35) were fully formed (relationship ~6:1). The desired trisaccharide **30** has Rf- 0.76 (petroleum ether / ethyl acetate 3:1). The reaction mixture was stirred for another 5 h, and treated with saturated $NaHCO_3$ solution and 30 ml of ethyl acetate. The phases were separated and the aqueous phase

was extracted 3 times with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Residue was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10:1, Rf-0.25)

Yield: 200 mg (0.21 mmol, 87%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$=7.26 ppm) δ: 7.43 (m, 2H, Ph), 7.24 (m, 3H, Ph), 5.52 (d, *J* = 5.0 Hz, 1H, 1-H), 5.18, 5.03 (d, d, *J* = 3.6 Hz, *J* = 3.4 Hz, 2H, 1-H', 1-H''), 4.15 (dq, *J* = 9.3, 6.1 Hz, 1H, 5-H), 3.84 (m, 5H), 3.56 (dd, *J* = 9.4, 1.6 Hz, 2H, 4-H',4-H''), 3.20 (t, *J* = 9.3 Hz, 1H, 4-H), 2.43 (dd, *J* = 13.9, 4.5 Hz, 1H), 2.05 (m, 3H), 1.55 (m, 2H), 1.24 (d, *J* = 6.1 Hz, 3H, 6-H), 1.14 (d, *J* = 6.4 Hz, 3H, 6-H'), 1.13 (d, *J* = 6.4 Hz, 3H, 6-H''), 0.95(m, 36H, 4 x TES), 0.62(m, 24H, 4 x TES).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$=77 ppm): q-135.3, 131.1, 128.9, 126.9 (Ph), 100.8, 100.5 (2d, C-1', C-1''), 83.6 (d, C-1), 83.1 (d, C-4), 79.4 (d, C-3), 73.5, 73.4 (2d, C-4', C-4''), 68.0 (2d, C-5, C-5''), 67.7 (d, C-5'), 67.4, 67.3 (2d, C-3', C-3''), 38.1 (t, C-2), 33.6 (2t, C-2', C-2''), 18.1 (q, C-6), 17.3, 17.2 (2q, C-6', C-6''), 7.0, 6.99, 6.81, 6.77 (4q, 12x $\underline{C}H_3$-TES), 5.2, 4.8, 4.7 (3t, 12x $\underline{C}H_2$-TES).

3-*O*-Pivaloyl-L-rhamnal (32)

A solution of L-rhamnal (697 mg, 5.36 mmol) in dry pyridine (10 ml) was cooled to -50°C, and PivCl (646 mg, 1 eq, 5.36 mmol) was dropwise added. The reaction was stirred at the same temperature another 2h until full adduct consumption was observed (t.l.c., petroleum ether / ethyl acetate 5:1, R_f- 0.42). To the reaction mixture 1 ml of methanol was added, and solution was evaporated under reduced pressure. The crude product **32** was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 5:1, R_f- 0.42).

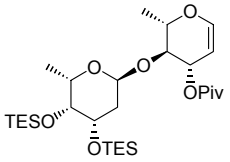
Yield: 610 mg (2.85 mmol, 53%).

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 6.43 (dd, *J* = 6.1, 1.3 Hz, 1H, 1-H), 5.17 (ddd, *J* = 6.1, 2.6, 1.5 Hz, 1H, 2-H), 4.67 (dd, *J* = 6.1, 2.6 Hz, 1H, 3-H),

3.93 (dq, *J* = 9.1, 6.3 Hz, 1H, 5-H), 3.59 (dd, *J* = 9.1, 6.1 Hz, 1H, 4-H), 3.37 (bs, 1H, OH), 1.40 (d, *J* = 6.3 Hz, 3H, 6-H), 1.22 (s, 9H, Piv).

^{13}**C-NMR** (50 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 180.6 (*C*O-Piv), 146.5 (+, C-1), 98.7 (+, C-2), 74.5, 73.5, 72.8 (3+, C-3, C-4, C-5), 38.9 (*C*$(CH_3)_3$-Piv), 27.1 (+, C(*C*$H_3)_3$-Piv), 17.0 (+, C-6).

(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-2,6-dideoxy-L-glycal (34)



To a solution of 3,4-bis-*O*-TES-L-fucal **22** (33.5 mg, 0.093 mmol) and glycal **32** (20 mg, 0.093 mmol) in CH_2Cl_2 (5 ml) was added PPh_3*HBr (1 mg, cat.). After 30 min, the reaction mixture was treated with saturated $NaHCO_3$ solution, phases were separated, and the aqueous phase was extracted 3 times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product **34** was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10:1, R_f- 0.45).

Yield: 45 mg (0.0785 mmol, 85%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 6.36 (dd, *J* = 6.0, 1.2 Hz, 1H, 1-H), 5.19 (dddd, *J* = 6.0, 3.2, 1.2, 0.6 Hz, 1H, 2-H), 5.12 (d, *J* = 3.2 Hz, 1H, 1-H'), 4.70 (dd, *J* = 5.8, 3.2 Hz, 1H, 3-H), 4.06 (dq, *J* = 7.7, 6.6 Hz, 1H, 5-H), 3.93 (ddd, *J* = 11.8, 4.4, 2.4 Hz, 1H, 3-H'), 3.86 (bq, *J* = 6.4 Hz, 1H, 5-H'), 3.70 (dd, *J* = 7.7, 5.8 Hz, 1H, 4-H), 3.58 (bd, *J* = 2.4 Hz, 1H, 4-H'), 2.04 (ddd, *J* = 12.3, 11.8, 3.2 Hz, 1H, 2-H'), 1.53 (ddd, *J* = 12.3, 4.4, 0.9 Hz, 1H, 2-H'), 1.36 (d, *J* = 6.6 Hz, 3H, 6-H), 1.19 (s, 9H, Piv), 1.16 (d, *J* = 6.4 Hz, 3H, 6-H'), 0.95, 0.94 (2t, *J* = 7.8 Hz, 18H, 2 x TES), 0.65, 0.64 (2q, *J* = 7.8 Hz, 12H, 2 x TES).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$=77 ppm) δ: 178.0 (*C*O-Piv), 145.6 (C-1), 99.0, 98.9 (2+, C-2, C-1'), 76.4, 73.6, 73.5, 70.9, 68.2, 67.3 (6+, C-3, C-4, C-5, C-3', C-4', C-5'), 38.7 (*C*$(CH_3)_3$-Piv), 33.4 (-, C-2'), 27.0 (+, C(*C*$H_3)_3$-Piv), 17.25, 17.20 (2+, C-6, C-6'), 7.0, 6.8 (2+, TES), 5.2, 4.8 (2-, TES).

3-*O*-Benzoyl-L-rhamnal (31)

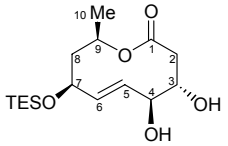
A solution of L-rhamnal (3 g, 0.023 mol) in dry pyridine (50 ml) was cooled to -30°C, and BzCl (3.24 g, 0.023 mol) dropwise was added. The reaction was stirred at the same temperature for another 2h until full adduct consumption was detected (t.l.c., petroleum ether / ethyl acetate 5:1, R_f- 0.45). To the reaction mixture 1 ml of methanol was added, and solution was evaporated under reduced pressure. The crude product **31** was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 5:1, R_f- 0.45).

Yield: 4.4 g (18.8 mmol, 83%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.65-7.40 (m, 5H, Ph), 6.49 (d, *J* = 6.1 Hz, 1H, 1-H), 5.47 (ddd, *J* = 6.4, 2.4, 1.5 Hz, 1H, 3-H), 4.83 (dd, *J* = 6.1, 2.4 Hz, 1H, 2-H), 4.01 (dq, *J* = 9.3, 6.4 Hz, 1H, 5-H), 3.78 (dd, *J* = 9.3, 6.4 Hz, 1H, 4-H), 1.45 (d, *J* = 6.4 Hz, 3H, 6-H).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 168.1 (*C*O-Ph), 146.8 (+, C-1), 133.4, 129.8, 128.4 (3+, Ph), 98.8 (+, C-2), 74.8, 74.3, 72.7 (3+, C-3, C-4, C-5), 17.1 (+, C-6).

7-*O*-TES-Decaristrictine D (36)



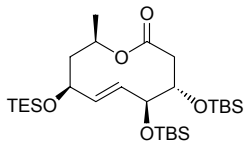
To a solution of decarestrictine D **35** (10 mg, 0.046 mmol) and imidazole (4.7 mg, 1.5 eq, 0.069 mmol) in CH_2Cl_2 (5 ml) at - 30° C dropwise was added TESCl (6.9 mg, 0.046 mmol). The reaction mixture was stirred another 1 h at the same temperature, then allowed to warm to RT and the solvent was evaporated under reduced pressure. The crude product **36** was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 2:1, R_f- 0.33)

Yield: 12 mg (0.0364, 79%), colorless crystals.

^{1}H-NMR (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.85 (ddd, *J* = 15.8, 9.5, 1.2 Hz, 1H, 6-H), 5.73 (dd, *J* = 15.8, 2.8 Hz, 1H, 5-H), 5.20 (ddq, *J* = 10.8, 6.2, 1.8 Hz, 1H, 9-H), 4.59 (bs, 1H, OH^3), 4.40 (bs, 1H, 4-H), 4.12 (ddd, *J* = 9.5, 9.5, 4.0 Hz, 1H, 7-H), 4.03 (dd, *J* = 6.3, 4.2 Hz, 1H, 3-H), 2.60, 2.37 (dd, *J* = 14.2, 1.8 Hz, 1H, 2-H, dd, *J* = 14.2, 6.3 Hz, 1H, 2-H), 1.88 - 1.79 (m, 2H, CH_2-8), 1.73 (bs, 1H, OH^4), 1.22 (d, *J* = 6.2 Hz, 3H, CH_3-10), 0.92 (t, *J* = 8.0 Hz, 9H, TES), 0.56 (q, *J* = 8.0 Hz, 6H, TES).

^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 174.9 (s, C-1), 134.7 (d, C-6), 127.8 (d, C-5), 73.8 (d, C-3), 72.9 (d, C-7), 72.2 (d, C-4), 68.3 (d, C-9), 44.4 (t, C-8), 33.3 (t, C-2), 21.3 (q, C-10), 6.8 (q, TES-CH_3), 4.9 (t, TES-CH_2).

3,4-Di-*O*-TBS-7-*O*-TES-decarestrictine D (41)



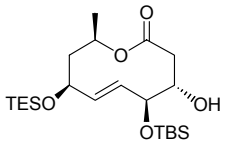
To a solution of decarestrictine D **35** (100 mg, 0.46 mmol) and imidazole (138 mg, 4.5 eq, 2.07 mmol) in CH_2Cl_2 (30 ml) at - 30° C dropwise was added TESCl (69 mg, 0.46 mmol). The reaction mixture was stirred for another 1 h at the same temperature and then evaporated under nitrogen flow allowing to warm up to RT. The resulted cake was dissolved in DMF (5 ml) and TBSCl (207 mg, 3 eq, 1.38 mmol) was added, and reaction temperature was raised to 50°C. After reaction completes (1-2 h), DMF was removed by filtration column (silica gel, petroleum ether / ethyl acetate 5:1) and crude product was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10:1, R_f- 0.26).

Yield: 240 mg (0.429 mmol, 93%), colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.85 (ddd, *J* = 15.8, 9.08, 1.2 Hz, 1H, 6-H), 5.65 (dd, *J* = 15.8, 2.5 Hz, 1H, 5-H), 5.20 (ddq, *J* = 11.4, 6.3, 1.7 Hz, 1H, 9-H), 4.15 (m, 2H, 4-H, 7-H), 3.89 (ddd, *J* = 8.6, 4.3, 2.0 Hz, 1H, 3-H), 2.55, (dd, *J* = 13.2, 2.0 Hz, 1H, 2-H), 2.15 (dd, *J* = 13.2, 6.8 Hz, 1H, 2-H), 1.88 - 1.60 (m, 2H, CH_2-8), 1.18 (d, *J* = 6.3 Hz, 3H, CH_3-10), 0.92 (t, *J* = 7.9 Hz, 9H, TES), 0.82 (s, 18H, 2 x TBS), 0.56 (q, *J* = 7.9 Hz, 6H, TES), 0.1 (2s, 12H, TBS).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 170.9 (s, C-1), 136.2 (d, C-6), 127.5 (d, C-5), 74.2 (d, C-3), 73.1 (d, C-7), 73.0 (d, C-4), 67.3 (d, C-9), 44.0 (t, C-8), 32.2 (t, C-2), 25.70 (TBS) 21.3 (q, C-10), 18.09 (TBS) 6.8 (q, TES-CH_3), 4.9 (t, TES-CH_2), -4.2, -4.9 (TBS).

4-*O*-Tbs-7-*O*-TES-Decarestrictine D (42)



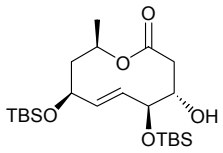
A solution of decarestrictine **41** (200 mg, 0.36 mmol) in CH_2Cl_2 (15 ml) was stirred with 3 mg of PPh_3*HBr at RT. After 6 h, TLC (petroleum ether / ethyl acetate 7:1, R_f- 0.39) showed completion of the reaction. The reaction mixture was treated with saturated $NaHCO_3$ solution, phases were separated and the aqueous phase was extracted 3 times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product **42** was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 7:1).

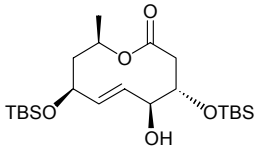
Yield: 134 mg (0.3 mmol, 84%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.85 (ddd, *J* = 15.5, 9.3, 1.4 Hz, 1H, 6-H), 5.64 (dd, *J* = 15.5, 2.7 Hz, 1H, 5-H), 5.20 (ddq, *J* = 10.9, 6.4, 1.9 Hz, 1H, 9-H), 4.65 (bs, 1H, OH[3]), 4.32 (bs, 1H, 4-H), 4.10 (ddd, *J* = 9.8, 9.3, 3.8 Hz, 1H, 7-H), 3.9 (bs, 1H, 3-H), 2.60, 2.31 (ddd, *J* = 14.0, 6.1, 1.7 Hz, 1H, 2-H, ddd, *J* = 14.1, 6.3, 3.13 Hz, 1H, 2-H), 1.84- 1.76 (m, 2H, CH_2-8), 1.22 (d, *J* = 6.4 Hz, 3H, CH_3-10), 0.95 (t, *J* = 7.9 Hz, 9H, TES), 0.85 (s, 9H), 0.56 (q, *J* = 7.9 Hz, 6H, TES), 0.0 (2s, 6H, 2 x CH_3 –*t*BuSi).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$=77 ppm) δ: 175.3 (C-1), 135.3 (+. C-6), 127.6 (+, C-5), 74.7 (+, C-3), 73.2 (+, C-7), 72.6 (+, C-4), 68.2 (+, C-9), 44.3 (-, C-8), 32.8 (-, C-2), 25.7 (3+, 3 x *C*H_3-t-Bu) 21.3 (+, C-10), 18.1 (*C*CH_3 t-Bu) 6.8 (+, TES-*C*H_3), 4.9 (-, TES-*C*H_2), -4.2, -4-9 (2+, 2 x *C*H_3 t-Bu).

4,7-Di-*O*-TBS-decarestrictine D (42); 3,7-di-*O*-TBS-decarestrictine D (43)





To a solution of decarestrictine D **35** (20 mg, 0.093 mmol), DMAP (1 mg, cat.) and imidazole (19.2 mg, 0.18 mmol) in DMF (2 ml) at - 30° C was added TBSCl (28 mg, 0.186 mmol). The reaction mixture was stirred for 1 h at the same temperature, then was allowed to warm to RT and more 5 mg (0.033 mmol) TBSCl was added. After the reaction was complete (TLC, petroleum ether / ethyl acetate 7:1, R_f- 0.39), it was quenched by a drop of methanol. DMF was removed by a filtration column (silica gel, petroleum ether / ethyl acetate 5:1) and the crude product mixture was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10:1, R_f- 0.26) to afford two fractions.

Yield: *1st fraction:* **42** (31 mg, 0.070 mmol, 75%)
2nd fraction: **43** *(*8 mg, 0.018 mmol, 19.4%).

1st fraction

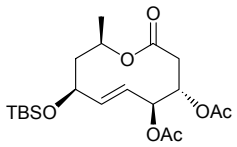
^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.83 (ddd, *J* = 15.5, 9.6, 1.6 Hz, 1H, 6-H), 5.64 (dd, *J* = 15.5, 2.7 Hz, 1H, 5-H), 5.19 (ddq, *J* = 10.9, 6.4, 1.8 Hz, 1H, 9-H), 4.69 (bs, 1H, OH[3]), 4.31 (m, 1H, 4-H), 4.10 (ddd, *J* = 9.9, 9.6, 3.9 Hz, 1H, 7-H), 3.87 (bs, 1H, 3-H), 2.58, 2.31 (dd, *J* = 14.0, 1.7 Hz, 1H, 2-H, dd, *J* = 14.0, 6.1 Hz, 1H, 2-H), 1.84-1.76 (m, 2H, CH_2-8), 1.22 (d, *J* = 6.4 Hz, 3H, CH_3-10), 0.91, 0.85 (2s, 18H, 6 x CH_3-tBuSi), 0.0 (3s, 12H, 4 x CH_3-tBuSi).

$[\alpha]_D^{23}$ = - 49.0° [C1, $CHCl_3$]

2nd fraction

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.79 (ddd, *J* = 16.3, 9.2, 0.8 Hz, 1H, 6-H), 5.67 (dd, *J* = 16.3, 4.3 Hz, 1H, 5-H), 5.11 (ddq, *J* = 10.0, 6.4, 2.8 Hz, 1H, 9-H), 4.12 (ddd, *J* = 9.3, 9.2, 4.6 Hz, 1H, 7-H), 3.99, 3.94 (m, 2H, *3-H*, 4-H), 2.56, 2.22 (dd, *J* = 13.9, 3.5 Hz, 1H, 2-H, dd, *J* = 13.9, 8.7 Hz, 1H, 2-H), 1.80- 1.70 (m, 2H, CH_2-8), 1.58 (bs, 1H, OH[4]), 1.20 (d, *J* = 6.4 Hz, 3H, CH_3-10), 0.92, 0.86 (2s, 18H, 6 x CH_3-tBuSi), 0.14, 0.03, 0.02 (3s, 12H, 4 x CH_3 -tBuSi).

3,4-Di-*O*-acetyl-7-*O*-TBS-decarestrictine D (39)

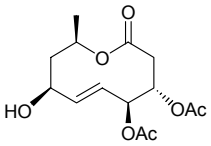


To a solution of decarestrictine D **35** (100 mg, 0.46 mmol) and imidazole (47 mg, 1.5 eq, 0.69 mmol) in CH_2Cl_2 (30 ml) at - 30° C was added TBSCl (69 mg, 0.46 mmol). The reaction mixture was stirred for 1 h at the same temperature, and then the solvent was evaporated under nitrogen flow, allowing mixture to warm up to RT. Dry pyridine (5 ml) and Ac_2O (187 µl, 4 eq) was added and the reaction temperature was raised to 50°C. After reaction completion (5-7 h), pyridine was evaporated under reduced pressure and the crude product was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 2:1, R_f- 0.53).

Yield: 185 mg (0.446, 97%), colorless oil.

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.70 (dd, *J* = 16.2, 9.2 Hz, 1H, 6-H), 5.59 (dd, *J* = 16.2, 3.3 Hz, 1H, 5-H), 5.20, 5.03 (2m, 3H, 9-H, 4-H, 3-H), 4.08 (ddd, *J* = 8.5, 8.4, 5.7 Hz, 1H, 7-H), 2.54 (m, 2H, 2-H), 2.06, 2.05 (2s, 6H, 2 x CH_3CO), 1.73 (m, 2H, 8-H), 1.16 (d, *J* = 6.4 Hz, 3H, 10-H), 0.79 (s, 9H, t-Bu), -0.04, -0.08 (2s, 6H, Si(*Me*)$_2$).

3,4-Di-*O*-acetyl-decarestrictine D (40)



A solution of decarestrictine **39** (160 mg, 0.38 mmol) in “TBAF mixture” (3 ml) was stirred for 5 days. The solution was evaporated and the crude product was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 2:1, R_f- 0.1).

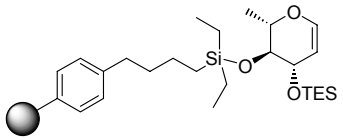
Yield: 109 mg (0.363 mmol, 96%), crystalline powder.

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (dd, *J* = 16.0, 7.9 Hz, 1H, 6-H), 5.66 (dd, *J* = 16.0, 2.6 Hz, 1H, 5-H), 5.22, 5.00 (2ddd, *J* = 5.2, 2.6, 2.6 Hz, *J* = 10.0, 5.2, 2.6 Hz, 2H, 4-H, 3-H), 5.08 (m, 1H, 9-H), 4.12 (ddd, *J* = 10.6, 7.9, 3.4 Hz, 1H, 7-H), 2.68 (bs, 1H, OH^7), 2.61, 2.52 (2ddd, *J* = 14.3, 10.0, 2.6 Hz, *J* = 14.3, 2.6, 2.6 Hz, 2H, 2-H), 2.08, 2.07(2s, 6H, 2 x CH_3CO), 1.83-1.73 (m, 2H, 8-H), 1.18 (d, *J* = 6.2 Hz, 3H, 10-H).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 169.8, 169.4, 169.2 (3s, C-1, 2 x CH_3CO), 136.9 (d, C-6), 123.4 (d, C-5), 72.1, 70.8 (3d, C-3, C-4, C-7), 68.0 (d, C-9), 42.3 (t, C-8), 33.7 (t, C-2), 21.2 (q, C-10), 20.9, 20.8 (2q, 2 x CH_3CO).

$[\alpha]_D^{23}$ = + 46.4° [C 0.5, $CHCl_3$]

11.4.2. Experiments to the chapter 5.2.
3-*O*-TES-4-*O*-(PS-DES)-L-rhamnal (49)

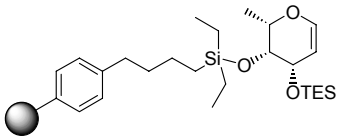


To a suspension of silane resin **44** (50 mg, 0.079 mmol) in 1 ml of CH_2Cl_2 was added 3 eq. (0.24 mmol, 47 mg) of 1,3-dichloro-5,5-dimethylhydantoine. The suspension was shaken for 2 h, and then polymer was filtered off and washed with CH_2Cl_2 (5x3 ml). This polymer bound silylchlorid **45** was used for further transformations immediately after washing. Obtained polymer-bound silylchlorid **45** was suspended in 1 ml of CH_2Cl_2 and solution of 3-*O*-TES-L-rhamnal **47** (3eq, 0.24 mmol, 58 mg) and imidazole (3.5 eq, 19 mg) in 1 ml of CH_2Cl_2 was added. The polymer was allowed to shake overnight, and then suspension was filtered and polymer-bound glycal washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. The loading of **49** was determined by resin weight difference.

Yield: (66 mg, 0.992 mmol/g, 83%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: GEL-NMR :143.4 (C-1), 103.1 (C-2), 75.6 (C-4), 75.3 (C-5), 70.3 (C-3), 17.4 (C-6), 6.9 ($SiCH_2\mathit{C}H_3$), 5.6 ($Si\mathit{C}H_2CH_3$).

3-*O*-TES-4-*O*-(PS-DES)-L-Fucal (48)



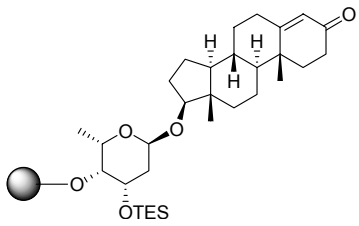
To a suspension of silane resin **44** (1.0 g, 1.58 mmol) in 10 ml of CH_2Cl_2 was added 3 equivalents (4.74 mmol, 934 mg) of 1,3-dichloro-5,5-dimethylhydantoine. The suspension was allowed to stir for 2h, and then polymer was filtered off and washed with CH_2Cl_2 (5x10 ml). Polymer-bound silylchlorid **45** was used for further transformations immediately after washing. Obtained silyl resin **45** was suspended in 5 ml of CH_2Cl_2 and solution of 3-*O*-TES-L-fucal **46** (3eq, 1.1 g, 4.74 mmol) and imidazole (3.5 eq, 0.38 g, 5 mmol) in 5 ml of CH_2Cl_2 was added. The polymer was allowed to shake overnight, and then suspension was filtered and polymer-bound glycal washed with CH_2Cl_2 (5x10 ml), acetonitrile (5x10 ml) and dried in high vacuum for 4 h. The loading of polymer **48** was determined by resin weight difference.

Yield: (1.355 g, 1.07 mmol/g, 83%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: GEL-NMR : 143.1 (C-1), 102.7 (C-2), 73.7 (C-5), 70.3 (C-4), 66.5 (C-3), 16.6 (C-6), 6.9 ($SiCH_2\mathit{C}H_3$), 5.3 ($Si\mathit{C}H_2CH_3$).

11.4.3. Experiments to the chapter 5.3.

17-*O*-[3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-α-L-galactopyranosyl]-testosterone (52)



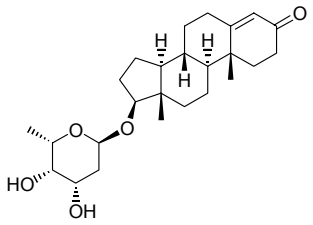
To a suspension of polymer-bound glycal **48** (200 mg, 0.214 mmol) in 5 ml of CH_2Cl_2 were added testosterone (0.172 g, 0.642 mmol) and 2 mg (cat.) of

PPh_3*HBr. The suspension was shaken for 4 h, then polymer filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. Resin **52** was weighted and loading was determined by weight difference.

Yield: 245 mg (0.625 mmol/g, 78%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: GEL-NMR : 199.2 (C-3), 171.2 (C-5), 123.8 (C-4), 98.8 (C-1'), 87.1 (C-17), 73.7 (C-4'), 67.7 (C-3'), 67.5 (C-5'), 53.8 (C-9), 50.0 (C-14), 42.7 (C-13), 38.6 (C-10), 37.0 (C-12), 35.7 (C-1), 35.4 (C-8), 33.9 (C-2), 33.4 (C-2'), 32.7 (C-6), 31.5 (C-7), 28.5 (C-16), 23.3 (C-15), 20.5 (C-11), 17.3 (C-6', C-19), 11.5 (C-18), 6.9 ($SiCH_2CH_3$), 5.2 ($SiCH_2CH_3$).

17-*O*-[2,6-dideoxy-α-L-galactopyranosyl]-testosterone (53)



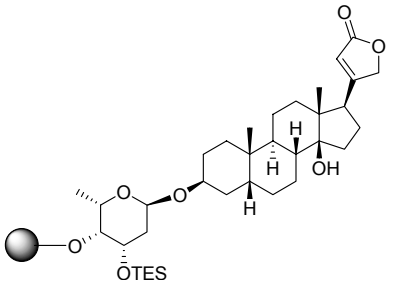
Polymer **52** (240 mg, 0.150 mmol) was suspended in "TBAF mixture" (10 ml). The suspension was shaken for 5 days, and then polymer was filtered off and filtrate evaporated under reduced pressure. The crude product was purified by column chromatography over silica gel (ethyl acetate, R_f- 0.31).

Yield: 49 mg (0.118 mmol, 78%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (s, 1H, 4-H), 4.92 (d, *J* = 3.5 Hz, 1-H'), 3.99 (m, 1H, 3-H'), 3.94 (bq, J = 6.7 Hz, 1H, 5-H'), 3.60 (bs, 1H, 4-H), 3.49 (t, J = 8.8 Hz, 1H, 17-H), 2.5 – 0.7 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.6 (C-3), 171.2 (C-5), 123.9 (+, C-4), 98.2 (+, C-1'), 87.1 (+, C-17), 71.4 (+, C-4'), 66.0 (+, C-3'), 65.6 (+, C-5'), 53.9 (+, C-9), 50.2 (+, C-14), 42,8 (C-13), 38.6 (C-10), 37.1 (-, C-12), 35.7 (-, C-1), 35.4 (+, C-8), 33.9 (-, C-2), 33.3 (-, C-2'), 32.8 (-, C-6), 31.5 (-, C-7), 28.4 (-, C-16), 23.3 (-, C-15), 20.6 (-, C-11), 17.4 (+, C-6'), 16.7 (+, C-19), 11.6 (+, C-18).

3-*O*-[3'-*O*-TES-4'-*O*-(PS-DES)-2',6'-dideoxy-α-L-galactopyranosyl]-digitoxigenin (54)

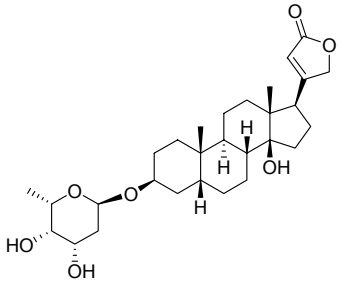


To a suspension of polymer-bound glycal **48** (140 mg, 0.150 mmol) in 5 ml of CH_2Cl_2 were added digitoxigenin (100 mg, 0.3 mmol) and 2 mg (cat.) of PPh_3*HBr. This suspension was shaken for 4 h, then polymer filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. Polymer **54** was weighted and loading was determined by weight difference.

Yield: 182 mg (0.62 mmol/g, 75%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) GEL-NMR δ: 174.5 (C-20), 174.5 (C-23), 117.5 (C-22), 95.8 (C-1'), 85.4 (C-14), 73.8 (C-4'), 73.6 (C-21), 70.8 (C-3), 67.7 (C-3'), 67.6 (C-5'), 50.9 (C-17), 49.5 (C-13), 41.8 (C-8), 40.0 (C-12), 36.5 (C-5), 35.6 (C-9), 35.1 (C-10), 33.7 (C-2'), 33.0 (C-4), 30.4 (C-15), 29.8 (C-1), 26.8 (C-2), 26.7 (C-6), 26.6 (C-16), 23.7 (C-19), 21.4 (C-7), 21.1 (C-11), 17.3 (C-6'), 15.7 (C-18), 7.0, 6.8 (2 x $SiCH_2CH_3$), 5.2, 4.9 (2 x $SiCH_2CH_3$).

3-*O*-[2,6-dideoxy-α-L-galactopyranosyl]-digitoxigenin (55)



A suspension of polymer-bound glycoside **54** (162 mg, 0.099 mmol) in "TBAF mixture" (10 ml) was stirred for 5 days. The polymer was filtered off and the resulted solution was evaporated. The residue was purified by column chromatography over silica gel (ethyl acetate, R_f- 0.37)

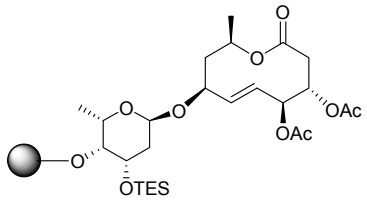
Yield: 37 mg (0.073 mmol, 74%), crystalline powder.

^{1}**H-NMR** (400 MHz, CD_3OD, CD_3OD = 3.31 ppm) δ: 5.84 (s, 1H, 22-H), 4.98 (dd, *J* = 18.1, 1.6 Hz, 1H, 21-H), 4.92 (d, *J* = 2.7 Hz, 1H, 1-H'), 4.78 (dd, *J* = 18.1, 1.6 Hz, 1H, 21-H), 4.0 -3.85 (m, 3H, 14-H, 3-H', 5-H'), 3.54 (bd, J = 2.7 Hz, 1H, 4-H'), 2.84 (bdd, J = 9.6, 5.4 Hz, 1H, 3-H), 2.25 – 0.85 (m).

^{13}**C-NMR** (100 MHz, CD_3OD, CD_3OD =50.2 ppm) δ: 179.6 (C-20), 178.4 (C-23), 119.0 (+, C-22), 98.3 (+, C-1'), 87.6 (C-14), 76.5 (+, C-4'), 74.2 (-, C-21), 73.6 (+, C-3), 68.9 (+, C-3'), 68.3 (+, C-5'), 53.3 (+, C-17), 52.3 (C-13), 43.9 (+, C-8), 42.1 (-, C-12), 39.3 (+, C-5), 38.0 (+, C-9), 37.6 (C-10), 35.1 (-, C-2'), 34.6 (-, C-4), 32.9 (-, C-15), 32.2 (-, C-1), 29.2 (-, C-2), 29.1 (-, C-6), 28.7 (-, C-16), 25.6 (+, C-19), 23.8 (-, C-7), 23.8 (-, C-11), 18.4 (+, C-6'), 17.6 (+, C-18).

$[\alpha]_D^{23}$ = - 53.2 ° (c=0.5, MeOH)

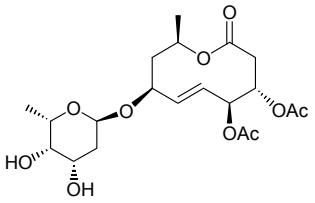
7-*O*-[3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-α-L-galactopyranosyl]-3,4-di-*O*-acetyl-decarestrictine D (56)



To a suspension of polymer-bound glycal **48** (100 mg, 0.107 mmol) in 5 ml of CH_2Cl_2 was added decarestrictine jj-67 (100 mg, 0.321 mmol) and 1.5 mg (cat.) of PPh_3*HBr. The suspension was shaken for 4 h, then polymer filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. Loading of polymer **56** was determined after cleaving of glycoconjugate from polymer support with "TBAF mixture"

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) GEL-NMR δ: 169.8, 169.4, 168.9 (2 x CH_3CO, C-1), 125.9 (C-5), 93.7 (C-1'), 74.3, 73.6, 71.9, 70.7, 68.3, 67.5 (C-3, C-4, C-7, C-9, C-3', C-4', C-5'), 40.9 (C-8), 33.4, 32.9 (C-2, C-2'), 21.4 (C-10), 20.9 (2 x CH_3CO), 17.4 (C-6'), 6.8, 6.4, 5.2 (TES).

7-*O*-[2,6-dideoxy-α-L-galactopyranosyl]-3,4-di-*O*-acetyl-decarestrictine D (57)

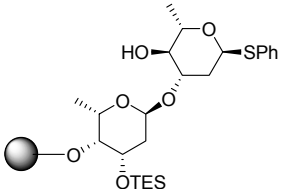


Yield: 21 mg (0.048 mmol, 45%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.82 (dd, *J* = 16.0, 3.3 Hz, 1H, 5-H), 5.60 (ddd, *J* = 16.0, 9.6, 1.3 Hz, 1H, 6-H), 5.34 (ddd, *J* = 5.1, 3.3, 1.2 Hz, 1H, 4-H), 5.16 (ddq, *J* = 10.1, 6.4, 2.8 Hz, 1H, 9-H), 5.02 (ddd, *J* = 7.2, 5.1, 2.3 Hz, 1H, 3-H), 4.85 (d, *J* = 3,1 Hz, 1H, 1-H'), 4.08 (ddd, *J* = 9.6, 9.6, 4.6 Hz, 1H, 7-H), 3.97 (ddd, *J* = 11.3, 5.4, 3.1 Hz, 1H, 3-H), 3.87 (bq, *J* = 6.4 Hz, 1H, 5-H'), 3.60 (bd, *J* = 2.9 Hz, 1H, 4-H'), 2.69 (dd, *J* = 13.9, 7.2 Hz, 1H, 2-H), 2.54 (dd, *J* = 13.9, 2.3 Hz, 1H, 2-H), 2.15, 2.13 (2s, 6H, 2 x C*H*$_3$CO), 1.9-1.7 (m, 4H, 8-H, 2-H'), 1.26, 1.23 (2d, *J* = 6.4, 6.4 Hz, 6H, 10-H, 6-H').

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 169.9, 169.5, 169.1 (2 x *C*OCH$_3$, C-1), 133.9 (+, C-6), 126.5 (+, C-5), 93.5 (+, C-1'), 74.8, 71.9, 71.2, 70.8, 68.1, 65.8, 65.79 (7+, C-3, C-4, C-7, C-9, C-3', C-4', C-5',), 40.9 (-, C-8), 33.3 (-, C-2), 32.8 (-, C-2'), 21.4 (+, C-10), 21.0, 20.9 (2+, 2 x CO*C*H$_3$), 16.8 (+, C-6').

Phenyl [3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-α-L-galactopyranosyl]-(1→3)-2,6-dideoxy-1-thio-α-L-glycopyranoside (58)

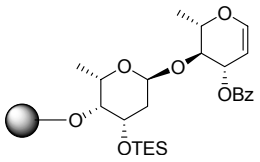


To a suspension of polymer-bound glycal **48** (200 mg, 0.214 mmol) in 5 ml of CH_2Cl_2 was added thioglycoside **27** (200 mg, 0.98 mmol) and 2 mg (cat.) of PPh_3*HBr. The suspension was shaken for 4 h, then polymer filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. Resin **58** was weighted and loading was determined by weight difference

Yield: 236 mg (0.62 mmol/g, 70%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): GEL-NMR: 135.2 (Ph-1), 131.1 (Ph-o), 128.9 (Ph-m), 127.7 (Ph-p), 99.9 (C-1'), 83.8 (C-1), 77.9 (C-3), 76.4 (C-4), 73.4 (C-4'), 68.6 (C-5), 67.9 (C-5'), 67.4 (C-3'), 37.4 (C-2), 33.5 (C-2'), 17.8 (C-6), 17.3 (C-6'), 6.8 (($CH_3CH_2)_3Si$), 5.3 (($CH_3CH_2)_3Si$).

[3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-α-L-galactopyranosyl]-(1→4)-3-*O*-benzoyl-2,6-dideoxy-L-glycal (59)



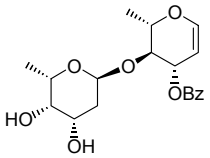
To a suspension of polymer-bound glycal **48** (500 mg, 0.5 mmol) in 10 ml of CH_2Cl_2 was added glycal **31** (351 mg, 1.5 mmol) and 5 mg of PPh_3*HBr. The suspension was shaken for 4 h, then polymer was filtered off and washed with CH_2Cl_2 (5x5 ml), acetonitrile (5x5 ml) and dried in high vacuum for 4 h. The resulted polymer was weighted and loading was determined by weight difference.

Yield: 181 mg (0.60 mmol/g, 70%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) GEL-NMR δ: 166.1 (Ph*C*O), 145.9 (C-1), 133.1, 129.6, 128.4 (Ph), 98.8, 98.6(C-2, C-1'), 76.0, 73.7, 73.5, 71.7, 68.2, 67.3 (C-3, C-4, C-5, C-3', C-4', C-5'), 33.4 (C-2'), 17.3 (C-6, C-6'), 6.9, 5.3 (TES).

IR (KBr) 1721.3 cm^{-1} (Ph*CO*).

[2,6-dideoxy-α-L-galactopyranosyl]-(1→4)-3-*O*-benzoyl-2,6-dideoxy-L-glycal (61)



A suspension of polymer-bound disaccharide **59** (190 mg, 0.6 mmol/g) in 10 ml of mixture (TBAF /AcOH/THF – 266 mg/0.151 ml/8.4 ml) was stirred for 2 days. The resulted mixture was filtered, solvent evaporated and flash chromatography over

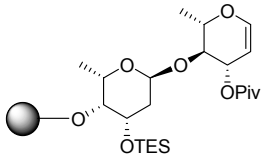
silica gel (ethyl acetate / petroleum ether = 1:1, R_f- 0.14) afforded **61** as a crystalline powder.

Yield: 29 mg (0.08 mmol, 70%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.0 (m, 2h, Ph), 7.5 (m, 3H, Ph) 6.45 (dd, *J* = 6.0, 1.2 Hz, 1H, 1-H), 5.50 (dd, *J* = 4.2, 5.4 Hz, 1H, 3-H), 5.26 (d, *J* = 3.2 Hz, 1H, 1-H'), 4.88 (dd, *J* = 6.0. 4.2 Hz, 1H, 2-H), 4.15 (dq, *J* = 7.1, 6.6 Hz, 1H, 5-H), 4.00 (bq, *J* = 6.3 Hz, 1H, 5-H'), 3.92 (dd, *J* = 7.1, 5.4 Hz, 1H, 4-H), 3.82 (m, 1H, 3-H'), 3.64 (d, *J* = 1.5 Hz, 1H, 4-H'), 1.85 (dd, *J* = 13.2, 5.5 Hz, 1H, 2-H'), 1.71 (dd, *J* = 13.2, 3.2 Hz, 1H, 2-H'), 1.43 (d, *J* = 6.3 Hz, 3H, 6-H'), 1.28 (d, *J* = 6.6 Hz, 3H, 6-H).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 166.0 (*C*O-Ph), 145.9 (C-1), 133.2, 129.6, 128.5 (Ph), 98.6, 97.5 (2+, C-2, C-1'), 75.4, 73.4, 71.1, 70.6, 66.4, 65.6 (6+, C-3, C-4, C-5, C-3', C-4', C-5'), 32.9 (-, C-2'), 17.2, 16.7 (2+, C-6, C-6').

[3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-α-L-galactopyranosyl]-(1$\rightarrow$4)-3-*O*-pivaloyl-2,6-dideoxy-L-glycal (60)



To a suspension of polymer bound glycal **48** (150 mg, 0.16 mmol) in 2.5 ml of CH_2Cl_2 was added glycal **32** (53 mg, 0.25 mmol) and 1 mg of PPh_3*HBr (cat.). The suspension was shaken for 6 h, then filtered, washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. Polymer bound glycoside **60** was weighted and loading was determined by weight difference.

Yield: 176 mg (0.69 mmol/g, 76%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) GEL-NMR δ: 178.1 (Piv*C*O), 145.7 (C-1), 98.9, 97.6(2x+, C-2, C-1'), 78.6, 76.1, 72.1, 70.9, 70.3, 69.4 (6x+, C-3, C-4, C-5, C-3', C-4', C-5'), 38.9 ($C(CH_3)_3$), 33.5 (-, C-2'), 26.9 (+, $C(CH_3)_3$), 17.3 (2x+, C-6, C-6'), 6.9, 5.3 (TES).

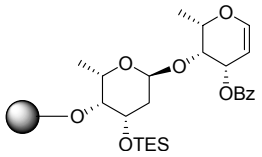
IR (KBr) 1730.9 cm^{-1} (Piv*CO*).

3-*O*-Benzoyl-L-fucal (50)

A solution of L-fucal (1 g, 7.7 mmol) in dry pyridine (20 ml) was cooled down to -30°C and benzoyl chloride (1.08 g, 7.7 mmol) was added dropwise. The reaction was stirred another 2h until t.l.c. (petroleum ether / ethyl acetate 5:1) showed full starting material consumption. The reaction was quenched by addition of methanol (1 ml), and the resulted solution was evaporated under reduced pressure. The crude product was purified by flash column chromatography over silica gel (petroleum ether / ethyl acetate 5:1, R_f- 0.45).

Yield: 1.56 g (6.67 mmol, 87%).

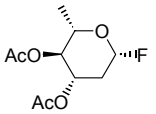
[3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-α-L-galactopyranosyl]-(1→4)-3-*O*-benzoyl-2,6-dideoxy-L-galactal (62)



To a suspension of polymer bound glycal **48** (157 mg, 0.55 mmol/g) in 2.5 ml of CH_2Cl_2 was added glycal **50** (150 mg, 2.75 mmol) and 1 mg of PPh_3*HBr. The suspension was shaken for 4 h, polymer filtered and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. The polymer **62** was weighted and loading was determined by weight difference

Yield: 14 mg (0.35 mmol/g, 64%).

1-Fluoro-3,4-di-*O*-acetyl 2,6-dideoxy-β-L-glucopyranoside



To an ice cooled mixture of thioglycoside **18** (0.62 g, 1.9 mmol) and MS 4A in dry acetonitrile was added selectfluor™ (2 g, 5.7 mmol) in 15 min under N_2. The mixture was stirred for 20 min, and then solid $NaHCO_3$ was added. The

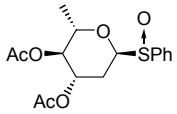
suspension was allowed to stir another 5 min., diluted with CH_2Cl_2 and filtered. The filtrate was evaporated and the crude product was purified by column chromatography over silica gel (ethyl acetate / petroleum ether=1:5, Rf-0.5). 2-Deoxy-fluoropyranose is highly unstable and can spontaneously decompose followed by intensive blue colour.

Yield: 0.4 g (1.71 mmol, 90%), white crystalline powder.

^{1}**H-NMR** (400 MHz, CD_2Cl_2, TMS = 0.00 ppm) δ: 5.69 (d, *J* = 51.3 Hz, H1, 1-H), 5.20 (ddd, *J* = 11.5, 9.6, 5.4 Hz, 1H, 3-H), 4.80 (dd, *J* = 9.9, 9.6 Hz, 1H, 4-H), 4.03 (dq, *J* = 9.9, 6.3 Hz, 1H, 5-H), 2.45 (dddd, *J* = 13.7, 5.1, 5.0, 1.2 Hz, 1H, 2-H_{ax}), 2.05 (s, 3H, C$\underline{H}_3$CO), 2.01 (s, 3H, C$\underline{H}_3$CO), 1.83 (dddd, *J* = 38.9, 13.7, 11,5, 2.7 Hz, 1H, 2-H_{eq}), 1.21 (d, *J* = 6.3 Hz, 3H, C$\underline{H}_3$CH).

^{13}**C-NMR** (100 MHz, CD_2Cl_2, TMS = 0.00 ppm) δ: 170.7 (2 x *C*OCH$_3$), 107.5, 105.4 (+, C-1), 73.8 (+, C-4), 68.8, 68.7 (+, C-3), 66.7 (+, C-5), 35.2, 35.0 (-, C-2), 21.0 (2+, 2 x *C*H$_3$CO), 17.6 (+, C-6).

3,4-Di-*O*-acetyl 2,6-dideoxy-α-L-glucopyranosyl-phenylsulfoxide



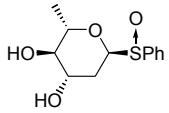
To a vigorously stirred mixture of thioglycoside **18** (325 mg, 1.0 mmol), Ac_2O (112 µl, 1.1 mmol) and SiO_2 (200 mg) in CH_2Cl_2 (5 ml) was added H_2O_2 (30%, 136 µl, 1.2 mmol). The reaction mixture was allowed to stir overnight, slurry extracted with ethyl acetate, organic layers combined and evaporated under reduced pressure. No product further purification is required.

Yield: 320mg (0.94 mmol, 94%).

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.67 (m, 2H, Ph-o), 7.56 (m, 3H, Ph-m, p), 5.55 (ddd, *J* = 10.5, 8.7, 5.4 Hz, 1H, 3-H), 4.82 (dd, *J* = 9.3, 8.7 Hz, 1H, 4-H), 4.51 (dd, *J* = 6.0, 2.2 Hz, 1H, 1-H), 4.26 (dq, *J* = 9.3, 6.1 Hz, 1H, 5-H), 2.86

(ddd, *J* = 14.4, 5.4, 2.2 Hz, 1H, 2-H_{ax}), 2.00 (ddd, *J* = 14,4, 10,5, 6.0 Hz, 1H, 2-H_{eq}), 2.13 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 1.24 (d, *J* = 6.1 Hz, 3H, 6-H).

2,6-Dideoxy-α-L-glucopyranosyl-phenylsulfoxide

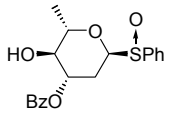


To a solution of 3,4-Di-*O*-acetyl 2,6-dideoxy-α-L-glucopyranosyl-phenylsulfoxide (320 mg, 0.94 mmol) in 10 ml of methanol 1 g of Amberlite A-26 (OH^- form) was added. The suspension was shaken for 12h and polymer was filtered off, washed with methanol and combined filtrates were evaporated under reduced pressure.

Yield: 235 mg (0.92 mmol, 98%), colourless crystalline powder.

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.60 (m, 5H, Ph), 4.53 (d, *J* = 5.7 Hz, 1H), 4.20 (m, 1H), 3.98 (dq, *J* = 9.3, 6.0 Hz, 1H, 5-H), 3.26 (dd, *J* = 9.3, 9.1 Hz, 1H, 4-H), 2.85 (dd, *J* = 14.5, 5.1 Hz, 1H, 2-H_{ax}), 1.98 (ddd, *J* = 14.5, 11.4, 5.7 Hz, 1H, 2-H_{eq}), 1.34 (d, *J* = 6.0 Hz, 3H, 6-H).

3-*O*-Benzoyl-2,6-dideoxy-α-L-glucopyranosyl-phenylsulfoxide (51)



A solution of 2,6-Dideoxy-α-L-glucopyranosyl-phenylsulfoxide (2.6 g, 0.01 mol) in dry pyridine (50 ml) was cooled down to -30°C, and benzoyl chloride (1.41 g, 0.01 mol) dropwise was added. The reaction mixture was allowed to stir another 1h at the same temperature, 1 ml of methanol was added to quench the acetylation and solution was evaporated under reduced pressure. The crude product was purified by column chromatography (petroleum ether / ethyl acetate 2:1, R_f- 0.48).

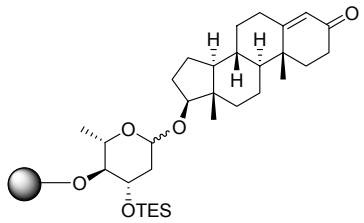
Yield: 3.2 g (8.9 mmol, 89%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.07 (m, 2H, Ph), 7.56 (m, 8H, Ph), 5.63 (ddd, *J* = 10.8, 9.0, 5.2 Hz, 1H, 3-H), 4.57 (dd, *J* = 5.8, 1.8 Hz, 1H, 1-H), 4.14 (dq, *J* = 9.2, 6.1 Hz, 1H, 5-H), 3.52 (dd, *J* = 9.2, 9.0 Hz, 1H, 4-H), 3.00 (ddd, *J*

= 14.4, 5.2, 1.8 Hz, 1H, 2-H_{ax}), 2.18 (ddd, *J* = 14.3, 10.8, 5.8 Hz, 1H, 2-H_{eq}), 1.39 (d, *J* = 6.1 Hz, 3H, 6-H).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 170.1 (*C*OPh), 135.4, 133.4 131.8, 131.7, 131.2, 130.4, 126.4, (Ph), 96.9 (+, C-1), 79.3, 76.9, 74.6 (+,C-3, C-4, C-5), 30.0 (-, C-2), 19.9 (+, C-6).

17-*O*-[3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-L-glycoopyranosyl]-testosterone (63)

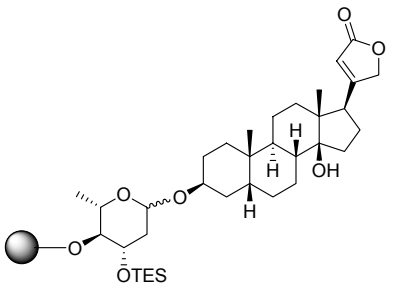


To a suspension of polymer-bound glycal **49** (200 mg, 0.198 mmol) in 5 ml of CH_2Cl_2 were added testosterone (0.172 g, 3 eq, 0.594 mmol) and 2 mg of PPh_3*HBr (cat.). The suspension was shaken for 4 h, and then the polymer was filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. Polymer bound glycoconjugate **63** was weighted and loading was determined by weight difference.

Yield: (244 mg, 0.623 mmol/g, 77%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: GEL-NMR : 199.4 (C-3), 171.2 (C-5), 123.8 (C-4), 98.1 (C-1'), 87.4 (C-17), 79.0 (C-4'), 70.5 (C-3'), 68.7 (C-5'), 53.8 (C-9), 50.1 (C-14), 42.7 (C-13), 39.7 (C-2'), 38.6 (C-10), 37.0 (C-12), 35.6 (C-1), 35.4 (C-8), 33.9 (C-2), 32.7 (C-6), 31.5 (C-7), 28.5 (C-16), 23.4 (C-15), 20.5 (C-11), 18.3 (C-6'), 17.3 (C-19), 11.6 (C-18), 7.0 ($SiCH_2CH_3$), 5.3 ($SiCH_2CH_3$).

3-*O*-[3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-L-glycoopyranosyl]-digitoxigenin (65)

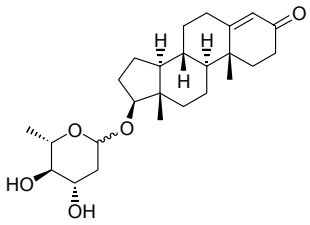


To a suspension of polymer-bound glycal **49** (100 mg, 0.099 mmol) in 2.5 ml of CH_2Cl_2 was added digitoxigenin (0.100 g, 3 eq, 0.3 mmol) and 1 mg (cat.) of PPh_3*HBr. The suspension was shaken for 4 h, then the polymer was filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. The obtained polymer-supported glycoconjugate **65** was weighted and loading was determined by weight difference

Yield: (125 mg, 0.53 mmol/g, 67%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: GEL-NMR : 174.5 (C-20), 174.4 (C-23), 117.5 (C-22), 94.6 (C-1'), 85.4 (C-14), 79.1 (C-4'), 73.5 (C-21), 73.4 (C-3'), 73.3 (C-5'), 70.3 (C-3), 50.9 (C-17), 49.6 (C-13), 41.7 (C-8), 40.2 (C-12), 39.9 (C-2'), 36.3 (C-5), 35.6 (C-9), 35.1 (C-10), 33.0 (C-4), 30.2 (C-15), 29.5 (C-1), 26.8 (C-2), 26.6 (C-6, C-16), 23.7 (C-19), 21.3 (C-7), 21.1 (C-11), 18.4 (C-6'), 15.7 (C-18), 6.9 ($SiCH_2CH_3$), 5.3 ($SiCH_2CH_3$).

17-*O*-[2,6-dideoxy-L-glycopyranosyl]-testosterone (64)



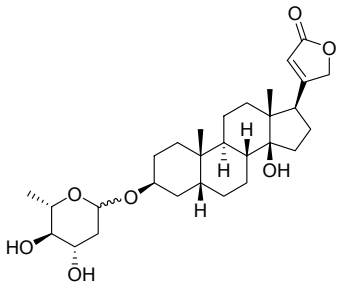
Polymer bound glycoside **63** (231 mg, 0.150 mmol) was suspended in CH_2Cl_2 (10 ml) and TASF (10 eq) was added. The suspension was shaken for 5 days, then filtered and the filtrate was evaporated under reduced pressure. The crude product was purified by column chromatography (ethyl acetate, R_f- 0.44). Partial cleavage was detected by later resin treating by TBAF in THF.

Yield: 30 mg (0.072 mmol, 48%), α/β = 8:1

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.71 (s, 1H, 4-H), 4.87 (d, *J* = 3.2 Hz, 1H, 1-H'α), 4.44 (dd, J = 9.8, 1.9 Hz, 0.1H, 1-H'β), 4.01 (ddd, J = 11.8, 5.4, 3.4 Hz, 1H, 3-H'), 3.66 (dq, J = 6.4, 9.3 Hz, 1H, 5-H'), 3.49 (t, J = 8.3 Hz, 1H, 17-H), 3.09 (t, J = 8.8 Hz, 1H, 3-H'), 2.5 – 0.7 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.7 (s, C-3), 171.4 (s, C-5), 123.8 (d, C-4), 98.0 (d, C-1'), 87.1 (d, C-17), 78.2 (d, C-4'), 69.3 (d, C-5'), 67.6 (d, C-3'), 53.8 (d, C-9), 50.2 (d, C-14), 42.8 (s, C-13), 38.6 (s, C-10), 38.0 (t, C-2'), 37.1 (t, C-12), 35.7 (t, C-1), 35.4 (d, C-8), 33.9 (t, C-2), 32.8 (t, C-6), 31.5 (t, C-7), 28.5 (t, C-16), 23.3 (t, C-15), 20.6 (t, C-11), 17.6 (q, C-6'), 17.4 (q, C-19), 11.6 (q, C-18).

3-*O*-[2',6'-dideoxy-L-glycopyranosyl]-digitoxigenin (66)



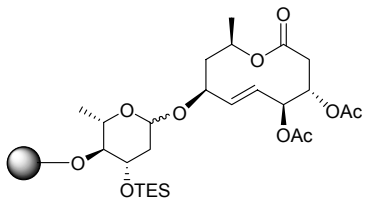
A suspension of polymer-bound glycoside **65** (100 mg, 0.081 mmol) in "TBAF mixture" (10 ml) was stirred for 5 days. The polymer was filtered off, resulted solution was evaporated and residue was purified by column chromatography over silica gel (ethyl acetate, R_f- 0.31).

Yield: 29 mg (0.0575 mmol, 71%), white powder, α/β = 2:1

^{1}**H-NMR** (400 MHz, CD_3OD, CD_3OD = 3.31 ppm) δ: 5.90 (s, 1H, 22-H), 5.07 (bd, J = 18.0 Hz, 1H, 21-H), 4.93 (bs, 0.7H, 1-H'α), 4.92 (bd, J = 18.0 Hz, 1H, 21-H), 4.59 (d, *J* = 9.3 Hz, 1.3H, 1-H'β), 4.03 (bs, 0.3H), 3.90 (bs, 0.7H), 3.82 (m, 0.7H, 3-H'), 3.67 (dq, J = 8.6, 6.7 Hz, 0.7H, 5-H'), 3.51 (m, 0.3H, 3-H'), 3.22 (dq, J = 8.3, 6.6 Hz, 0.3H, 5-H'), 2.95 – 2.80 (m, 2H, 4-H', 3-H), 2.25 – 0.8 (m).

^{13}**C-NMR** (100 MHz, CD_3OD, CD_3OD = 50.2 ppm) δ: 179.6 (C-20), 178.4 (C-23), 119.0 (C-22), 100.1 (C-1'β), 98.0 (C-1'α), 87.6 (C-14), 80.29, 79.73, 76.53, 75.83, 74.46, 74.33. 73.57, 71.00, 70.61, 62.72, 53.31, 52.25, 43.89, 42.37, 42.15, 40.99, 39.32, 39.14, 38.01, 37.56, 37.51, 34.58, 34.28, 32.85, 32.40. 32.11, 29.26, 29.10, 29.02, 28.79, 26.58, 25.57, 25.48, 23.77, 23.67, 23.57, 22.06, 19.46, 19.38, 17.60, 15.67

7-*O*-[3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-L-glycopyranosyl]-3,4-di-*O*-acetyl-decarestrictine D (67)

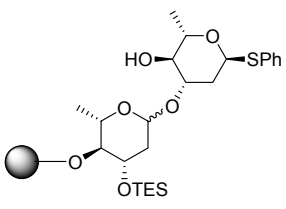


To a suspension of polymer-bound glycal **49** (100 mg, 0.107 mmol) in 5 ml of CH_2Cl_2 was added decarestrictine **40** (100 mg, 0.321 mmol) and 1.5 mg (cat.) of PPh_3*HBr. The suspension was shaken for 4 h, then polymer filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. Loading of polymer-bound glycoside **67** was determined by weight difference.

Yield: 121 mg (0.066 mmol, 62%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$=77 ppm) GEL-NMR δ: 169.8, 169.7, 168.9 (2x $CH_3\underline{C}O$, C-1), 134.4 (C-6), 125.7 (C-5), 93.0 (C-1'), 78.9, 74.2, 72.2, 71.9, 70.8, 68.0 (C-3, C-4, C-7, C-9, C-3', C-4', C-5'), 40.9 (C-8), 37.4 (C-2'), 33.3 (C-2), 21.4 (C-10), 20.9 (2x $\underline{C}H_3CO$), 18.2 (C-6'), 6.9, 5.3 (TES).

Phenyl [3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-α-L-glucoopyranosyl]-(1$\rightarrow$3)-2,6-dideoxy-1-thio-α-L-glycopyranoside (68)



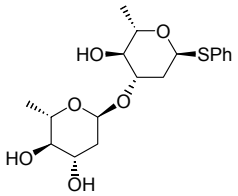
To a suspension of polymer bound glycal **49** (460 mg, 0.456 mmol) in 8 ml of CH_2Cl_2 were added thioglycoside **27** (327 mg, 3 eq, 1.368 mmol) and 4 mg of PPh_3*HBr. The suspension was shaken for 4 h, then polymer filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. Polymer-bound disaccharide **68** was weighted and loading was determined by weight difference

Yield: 547 mg (0.66 mmol/g, 80%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): GEL-NMR: 135.1 (Ph-1), 131.1 (Ph-o), 128.9 (Ph-m), 127.0 (Ph-p), 99.1 (C-1'), 83.7 (C-1), 78.7 (C-5'), 76.5 (C-4), 75.9 (C-4'), 72.7 (C-5), 70.4 (C-3), 68.5 (C-3'), 39.4 (C-2), 37.5 (C-2'), 18.2 (C-6), 17.7 (C-6'), 7.0, 6.9 (($CH_3CH_2)_3Si$), 5.7, 5.3 (($CH_3CH_2)_3Si$).

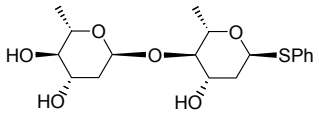
Polymer-bound glycoside **68** was treated with "TBAF mixture" for 3 days to determine the regioisomeric disaccharide ratio. The following disaccharides **70**, **69**, **71** (relative ratio was analyzed by ^{1}H-NMR spectroscopy: 47%, 19.1%, 33% respectively) were isolated.

Phenyl [2,6-dideoxy-α-L-glycopyranosyl]-(1→3)-2,6-dideoxy-1-thio-α-L-glycopyranoside (70)



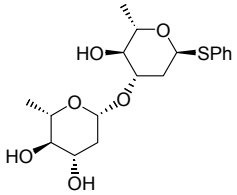
^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.38 (m, 2H, Ph-o), 7.21 (m, 3H, Ph-m, p), 5.54 (d, *J* = 5.4 Hz, 1H, 1-H), 5.12 (d, *J* = 3.5 Hz, 1H, 1-H'), 4.17 (dq, *J* = 9.1, 6.2 Hz, 1H, 5-H), 3.90 (ddd, *J* = 11.8, 9.1, 2.5 Hz, 1H, 3-H'), 3.82 (ddd, *J* = 11.4, 9.1, 4.8 Hz, 1H, 3-H), 3.68 (dq, *J* = 9.1, 6.2 Hz, 1H, 5-H'), 3.20 (t, *J* = 9.1 Hz, 1H, 4-H), 3.12 (t, *J* = 9.1, 1H, 4-H'), 2.5 – 1.5 (m, 4H, 2-H, 2-H'), 1.28 (d, *J* = 6.2 Hz, 3H, 6-H), 1.26 (d, *J* = 6.2 Hz, 3H, 6-H').

Phenyl [2,6-dideoxy-α-L-glycopyranosyl]-(1→4)-2,6-dideoxy-1-thio-α-L-glycopyranoside (69)



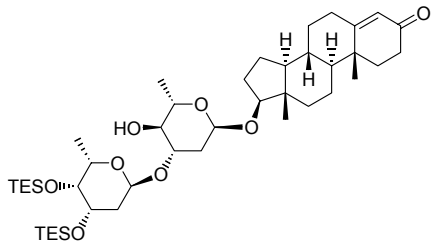
^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.38 (m, 2H, Ph-o), 7.21 (m, 3H, Ph-m, p), 5.54 (d, *J* = 5.4 Hz, 1H, 1-H), 5.36 (d, *J* = 3.5 Hz, 1H, 1-H'), 4.17 (dq, *J* = 9.1, 6.2 Hz, 1H, 5-H), 4.03 (ddd, *J* = 11.6, 8.6, 4.8 Hz, 1H, 3-H'), 3.81 (ddd, *J* = 11.4, 9.1, 4.8 Hz, 1H, 3-H), 3.72 (m, 1H, 5-H'), 3.20 (t, *J* = 9.1 Hz, 1H, 4-H), 3.11 (t, *J* = 9.1, 1H, 4-H'), 2.5 – 1.5 (m, 4H, 2-H, 2-H'), 1.28 (d, *J* = 6.2 Hz, 3H, 6-H), 1.26 (d, *J* = 6.5 Hz, 3H, 6-H').

Phenyl [2,6-dideoxy-β-L-glycopyranosyl]-(1→3)-2,6-dideoxy-1-thio-α-L-glycopyranoside (71)



^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.38 (m, 2H, Ph-o), 7.21 (m, 3H, Ph-m, p), 5.54 (d, *J* = 5.4 Hz, 1H, 1-H), 4.62 (dd, *J* = 9.7, 2.1 Hz, 1H, 1-H'), 4.15 (dq, *J* = 9.4, 6.2 Hz, 1H, 5-H), 3.75 (ddd, *J* = 11.9, 9.4, 5.4 Hz, 1H, 3-H), 3.63 (dd, *J* = 11.6, 5.6 Hz, 1H, 3-H'), 3.42 (q, J = 6.2 Hz, 1H, 5-H'), 3.17, 3.16 (t, *J* = 9.4 Hz, 2H, 4-H, 4-H'), 2.27 (m, 2H), 2.19 (dd, J = 11.6, 5.6 Hz, 1H), 1.70 (ddd, J = 12.1, 9.7, 9.7 Hz, 1H), 1.39 (d, *J* = 6.2 Hz, 3H, 6-H), 1.26 (d, *J* = 6.2 Hz, 3H, 6-H').

17-*O*-[(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1→3)-(2,6-dideoxy-α-L-glycopyranosyl)]-testosterone (72)



To an ice cooled solution of disaccharide **28** (60 mg, 0.1 mmol) and testosterone (29 mg, 0.1 mmol) in dry acetonitrile (5 ml) selectfluor™ (35 mg, 0.1 mmol) was added. After 15 min, the reaction mixture was treated with saturated $NaHCO_3$

solution and 5 ml of ethyl acetate. The phases were separated and the aqueous phase was extracted 3 times with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 3:1, R_f- 0.33)

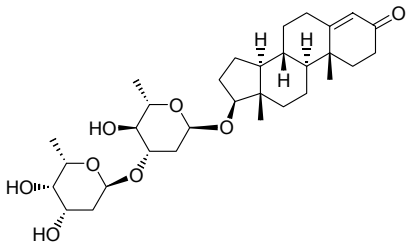
Yield: 30 mg (0.0386 mmol, 38%), crystalline powder.

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (s, 1H, 4-H), 5.08 (d, *J* = 3.1 Hz, 1H, 1-H'), 4.83 (d, *J* = 3.1 Hz, 1H, 1-H''), 3.95 (ddd, J = 11.9, 4.4, 2.2 Hz, 1H, 3-H''), 3.81 (m, 2H, 5-H'', 3-H'), 3.73 (dq, J = 9.5, 6.2 Hz, 1H, 5-H'), 3.57 (bd, J = 2.2 Hz, 1H, 4-H''), 3.47 (t, J = 8.6 Hz, 1H, 17-H), 3.16 (dt, J = 9.3, 1.7 Hz, 1H, 4-H'), 2.5 – 0.5 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.5 (C-3), 171.3 (C-5), 123.8 (+, C-4), 99.8 (+, C-1''), 98.1 (+, C-1'), 87.2 (+, C-17), 77.9 (+, C-3'), 76.1 (+, C-4'), 73.4 (+, C-4''), 67.7 (+, C-5''), 67.6 (+, C-5'), 67.4 (+, C-3''), 53.8 (+, C-9), 50.1 (+, C-14), 42.8 (C-13), 38.6 (C-10), 37.1 (-, C-2'), 37.0 (-, C-12), 35.7 (-, C-1), 35.4 (+, C-8), 33.9 (-, C-2), 33.5 (-, C-2''), 32.7 (-, C-6), 31.5 (-, C-7), 28.4 (-, C-16), 23.3 (-, C-15), 20.5 (-, C-11), 17.8 (+, C-19), 17.3 (+, C-6'), 17.2 (+, C-6''), 11.5 (+, C-18), 7.0, 6.8, 5.1, 4.8 (2 x TES).

$[\alpha]_D^{23}$ = - 36° [C1, $CHCl_3$]

17-*O*-[(2,6-dideoxy-α-L-galactopyranosyl)-(1$\rightarrow$3)-(2,6-dideoxy-α-L-glycopyranosyl)]-testosterone (73)



Glycoconjugate **72** (15 mg, 0.019 mmol) was stirred in "TBAF mixture" (5ml) for 3 days. The reaction mixture was concentrated under reduced pressure and crude product purified by column chromatography over silica gel (ethyl acetate, R_f- 0.22).

Yield: 8 mg (0.015 mmol, 77%).

^{1}**H-NMR** (400 MHz, CD_3OD, CD_3OD = 3.31 ppm) δ: 5.71 (s, 1H, 4-H), 5.15 (d, *J* = 2.7 Hz, 1H, 1-H''), 4.92 (1H, 1-H'), 3.92 (m, 2H, 3-H'', 5-H''), 3.83 (ddd, J = 11.7, 9.1, 5.3 Hz, 1H, 3-H'), 3.68 (dq, J = 9.6, 6.1 Hz, 1H, 5-H'), 3.52 (m, 2H, 17-H, 4-H''), 3.01 (t, J = 9.4 Hz, 1H, 4-H'), 2.5 – 0.5 (m).

^{13}**C-NMR** (100 MHz, CD_3OD, CD_3OD = 50.2 ppm) δ: 203.6 (C-3), 176.4 (C-5), 125.3 (+, C-4), 102.2 (+, C-1''), 100.7 (+, C-1'), 89.7 (+, C-17), 79.3 (+, C-3'), 78.1 (+, C-4'), 73.5 (+, C-4''), 68.9 (+, C-5''), 68.8 (+, C-5'), 68.1 (+, C-3''), 56.7 (+, C-9), 52.7 (+, C-14), 45.3 (C-13), 41.2 (C-10), 39.8 (-, C-2'), 39.6 (-, C-12), 38.0 (-, C-1), 37.9 (+, C-8), 35.9 (-, C-2), 35.1 (-, C-2''), 34.5 (-, C-6), 34.0 (-, C-7), 30.8 (-, C-16), 25.5 (-, C-15), 22.9 (-, C-11), 19.4 (+, C-19), 18.9 (+, C-6'), 18.4 (+, C-6''), 13.3 (+, C-18).

LC-MS (ESI) (-c): m/z (%): 547.31 (100) $[M - H]^-$; **HR-MS** $C_{31}H_{47}O_8$: calc. 547.3271, found 547.3269

$[\alpha]_D^{23}$ = - 56° [C 0.8, MeOH]

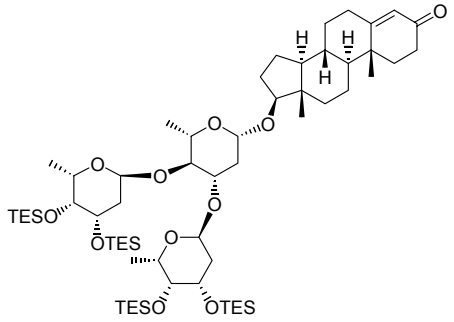
17-*O*-[{di-[3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl]-(1→3),(1→4)}-2,6-dideoxy-α-L-glycopyranosyl]-testosterone (fraction-2) (74); 17-*O*-[{di-[3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl]-(1→3),(1→4)}-2,6-dideoxy-β-L-glycopyranosyl]-testosterone (fraction-1) (75)

To an ice cooled solution of **30** (160 mg, 0.167 mmol) and testosterone (50 mg, 0.167 mmol) in dry acetonitrile (10 ml) was added selectfluor™ (60 mg, 0.167 mmol). After 15 min reaction mixture was treated with saturated $NaHCO_3$ water solution and 30 ml of ethyl acetate was added. The phases were separated and the aqueous phase was extracted 3 times with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 10:1) to yield three fractions.

Yield: *1st fraction*: **75** - 16 mg (0.0141 mmol, 8.4%),

2nd fraction: **74** - 116 mg (0.102 mmol, 61%),

3rd fraction: α/β mixture = 20 mg (0.0176 mmol, 10.5%).

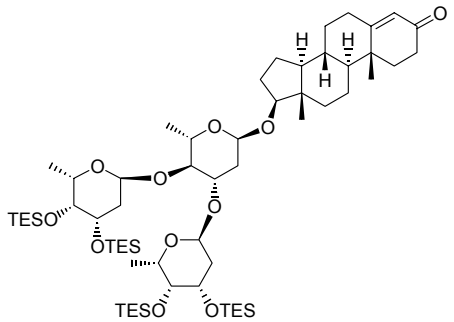


1st fraction

[1]**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (s, 1H, 4-H), 5.13 (d, *J* = 3.0 Hz, 1H, 1-H''), 4.96 (d, *J* = 3.0 Hz, 1H, 1-H'''), 4.38 (bd, *J* = 8.6 Hz, 1H, 1-H'), 3.90 (m, 2H, 3-H'', 3-H'''), 3.83, 3.82 (2q, J = 6.1 Hz, 2H, 5-H'', 5-H'''), 3.61 (t, J = 8.6 Hz, 1H, 17-H), 3.56 (bs, 2H, 4-H'', 4-H'''), 3.44 (ddd, J = 12.2, 9.1, 5.1 Hz, 1H, 3-H'), 3.22 (dq, J = 9.1, 6.1 Hz, 1H, 5-H'), 3.17 (t, J = 9.1 Hz, 1H, 4-H'), 2.5 – 0.5 (m).

[13]**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.6 (s, C-3), 171.4 (s, C-5), 123.8 (d, C-4), 98.7, 98.6 (2d, C-1'', C-1'''), 98.5 (d, C-1'), 87.2 (d, C-17), 82.9 (d, C-4'), 81.2 (d, C-3'), 73.5, 73.48 (2d, C-4'', C-4'''), 70.7 (d, C-5'), 67.9, 67.6 (2d, C-5'', C-5'''), 67.4, 67.3 (2d, C-3'', C-3'''), 54.0 (d, C-9), 50.6 (d, C-14), 42.4 (s, C-13), 39.2 (t, C-2'), 38.6 (s, C-10), 36.6 (t, C-12), 35.7 (t, C-1), 35.5 (d, C-8), 34.0 (t, C-2), 33.7, 33.6 (2t, C-2'', C-2'''), 32.8 (t, C-6), 31.6 (t, C-7), 27.6 (t, C-16), 23.3 (t, C-15), 20.6 (t, C-11), 18.3 (q, C-19), 17.4 (q, C-6'), 17.3, 17.2 (2q, C-6'', C-6'''), 11.6 (q, C-18), 7.0, 6.98, 6.8, 6.7, 5.2, 5.17, 4.8, 4.7 (4 x TES).

$[\alpha]_D^{23}$ = - 18.3° [C1, $CHCl_3$]



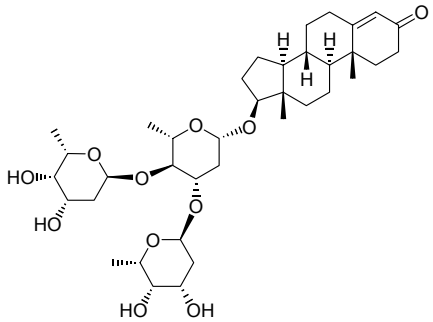
2nd fraction

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.71 (s, 1H, 4-H), 5.18 (d, *J* = 3.0 Hz, 1H, 1-H''), 4.99 (d, *J* = 3.0 Hz, 1H, 1-H'''), 4.08 (d, *J* = 3.1 Hz, 1H, 1-H'), 3.90 (m, 2H, 3-H'', 3-H'''), 3.84 (q, J = 6.2 Hz, 1H, 5-H''), 3.81 (m, 1H, 3-H'), 3.78 (q, J = 6.2 Hz, 1H, 5-H'''), 3.68 (dq, J = 9.1, 6.2 Hz, 1H, 5-H'), 3.57 (bdd, J = 5.0, 2.1 Hz, 2H, 4-H'', 4-H'''), 3.46 (t, J = 8.9 Hz, 1H, 17-H), 3.14 (t, J = 9.1 Hz, 1H, 4-H'), 2.5 – 0.5 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.5 (s, C-3), 171.3 (s, C-5), 123.8 (d, C-4), 100.5, 100.4 (2d, C-1'', C-1'''), 97.9 (d, C-1'), 87.2 (d, C-17), 82.9 (d, C-4'), 79.0 (d, C-3'), 73.5, 73.4 (2d, C-4'', C-4'''), 67.9, 67.4 (3d, C-5', C-5'', C-5'''), 67.38, 67.0 (2d, C-3'', C-3'''), 53.9 (d, C-9), 50.2 (d, C-14), 42.8 (s, C-13), 38.6 (s, C-10), 37.8 (t, C-2'), 37.1 (t, C-12), 35.7 (t, C-1), 35.4 (d, C-8), 34.0 (t, C-2), 33.7, 33.6 (2t, C-2'', C-2'''), 32.8 (t, C-6), 31.5 (t, C-7), 28.5 (t, C-16), 23.3 (t, C-15), 20.6 (t, C-11), 18.3 (q, C-19), 17.4 (q, C-6'), 17.3, 17.2 (2q, C-6'', C-6'''), 11.6 (q, C-18), 7.0, 6.98, 6.8, 6.7, 5.2, 5.17, 4.8, 4.7 (4 x TES).

$[\alpha]_D^{23}$ = - 38.7° [C1, $CHCl_3$]

17-*O*-[{di-[2,6-dideoxy-α-L-galactopyranosyl]-(1→3),(1→4)}-2,6-dideoxy-β-L-glycopyranosyl]-testosterone (77)



Glycoconjugate **75** (16 mg, 0.014 mmol) was stirred with "TBAF mixture" (2ml) for 3 days. The reaction mixture was concentrated under reduced pressure and purified by column chromatography over silica gel (ethyl acetate /MeOH 9:1, R_f-0.13).

Yield: 9 mg (0.013 mmol, 95%).

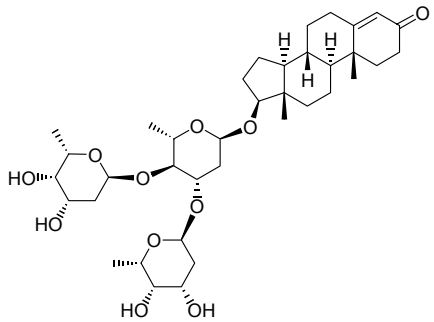
^{1}**H-NMR** (400 MHz, CD_3OD, CD_3OD = 3.31 ppm) δ: 5.71 (s, 1H, 4-H), 5.28 (d, *J* = 3.7 Hz, 1H, 1-H''), 5.04 (d, *J* = 3.3 Hz, 1H, 1-H'''), 4.49 (bd, *J* = 8.2 Hz, 1H, 1-H'), 4.0 – 3.85 (m, 4H, 5-H'', 5-H''', 3-H'', 3-H'''), 3.67 (t, J = 8.4 Hz, 1H, 17-H), 3.61 (m, 1H, 3-H'), 3.56 (bs, 2H, 4-H'', 4-H'''), 3.31 (dq, J = 8.6, 6.4 Hz, 1H, 5-H'), 3.15 (t, J = 8.6 Hz, 1H, 4-H'), 2.45 - 0.6 (m).

^{13}**C-NMR** (100 MHz, CD_3OD, CD_3OD = 50.2 ppm) δ: 202.3 (s, C-3), 175.2 (s, C-5), 124.1 (d, C-4), 101.6, 100.7 (2d, C-1'', C-1'''), 99.8 (d, C-1'), 88.7 (d, C-17), 83.1 (d, C-4'), 82.1 (d, C-3'), 72.2, 72.2 (2d, C-4'', C-4'''), 71.9.1 (d, C-5'), 68.3, 67.9 (2d, C-5'', C-5'''), 66.8, 66.7 (2d, C-3'', C-3'''), 55.5 (d, C-9), 51.9 (d, C-14), 43.6 (s, C-13), 40.5 (s, C-10), 40.0 (t, C-2'), 37.9 (t, C-12), 36.8 (t, C-1), 36.7 (d, C-8), 34.7 (t, C-2), 33.9, 33.8 (2t, C-2'', C-2'''), 33.6 (t, C-6), 32.8 (t, C-7), 28.6 (t, C-16), 24.1 (t, C-15), 21.7 (t, C-11), 19.0 (q, C-19), 17.7 (q, C-6'), 17.2, 17.1 (2q, C-6'', C-6'''), 12.1 (q, C-18).

LC-MS (ESI) (-c): m/z (%): 677.40 (100) $[M - H]^-$; **HR-MS** $C_{37}H_{57}O_{11}$: calc. 677.3901, found 677.3899

$[\alpha]_D^{23}$ = - 24.0° [C 0.5, MeOH]

17-*O*-[{di-[2,6-dideoxy-α-L-galactopyranosyl]-(1→3),(1→4)}-2,6-dideoxy-α-L-glycopyranosyl]-testosterone (76)



Glycoconjugate **74** (63 mg, 0.055 mmol) was stirred with "TBAF mixture" (5ml) for 3 days. The reaction mixture was concentrated under reduced pressure and crude product purified by column chromatography over silica gel (ethyl acetate /MeOH 9:1, R_f- 0.13).

Yield: 33 mg (0.049 mmol, 89%).

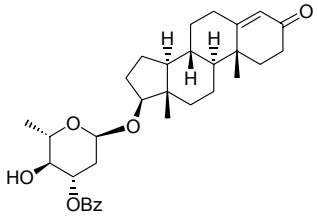
^{1}**H-NMR** (400 MHz, CD_3OD, CD_3OD = 3.31 ppm) δ: 5.71 (s, 1H, 4-H), 5.27 (d, *J* = 3.9 Hz, 1H, 1-H''), 5.03 (d, *J* = 3.5 Hz, 1H, 1-H'''), 4.85 (d, *J* = 3.1 Hz, 1H, 1-H'), 4.0 – 3.85 (m, 5H, 5-H'', 5-H''', 3-H'', 3-H''', 3-H'), 3.70 (dq, J = 9.4, 6.2 Hz, 1H, 5-H'), 3.58 – 3.50 (m, 3H, 17-H, 4-H'', 4-H'''), 3.17 (t, J = 9.4 Hz, 1H, 4-H'), 2.5 – 0.7 (m).

^{13}**C-NMR** (100 MHz, CD_3OD, CD_3OD = 50.2 ppm) δ: 203.4 (s, C-3), 176.2 (s, C-5), 125.4 (d, C-4), 102.5, 102.0 (2d, C-1'', C-1'''), 100.2 (d, C-1'), 89.6 (d, C-17), 84.8 (d, C-4'), 80.7 (d, C-3'), 73.4, 73.4 (2d, C-4'', C-4'''), 69.5, 67.4 (2d, C-5'', C-5'''), 69.1 (d, C-5'), 68.0, 67.9 (2d, C-3'', C-3'''), 56.6 (d, C-9), 50.7 (d, C-14), 45.2 (s, C-13), 41.2 (s, C-10), 40.0 (t, C-2'), 39.6 (t, C-12), 38.0 (t, C-1), 37.9 (d, C-8), 35.9 (t, C-2), 35.1, 35.0 (2t, C-2'', C-2'''), 34.8 (t, C-6), 34.0 (t, C-7), 30.8 (t, C-16), 25.5 (t, C-15), 22.9 (t, C-11), 20.0 (q, C-19), 18.9 (q, C-6'), 18.3, 18.3 (2q, C-6'', C-6'''), 13.3 (q, C-18).

LC-MS (ESI) (-c): m/z (%): 677.39 (100) $[M - H]^-$; **HR-MS** $C_{37}H_{57}O_{11}$: calc. 677.3901, found 677.3876

$[\alpha]_D^{23}$ = -97.8° [C 0.5, MeOH]

17-*O*-(3-*O*-benzoyl-2,6-dideoxy-α-L-glucopyranosyl)-testosterone (78)



To a solution of glycal **31** (35 mg, 0.1 mmol) and testosterone (28 mg, 0.1 mmol) in CH_2Cl_2 (5 ml) was added PPh_3*HBr (8 mg). After 5 h the reaction was quenched with addition of Amberlite A-21. The mixture was filtrated, solids were washed with ethyl acetate and filtrate was evaporated under reduced pressure. The crude product was purified by column chromatography over silica gel (ethyl acetate / petroleum ether=1:2, R_f-0.61).

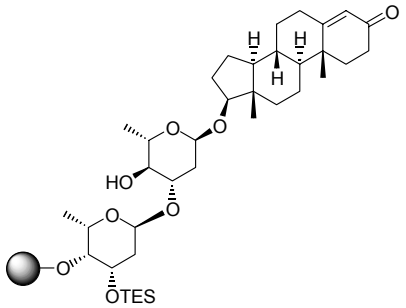
Yield: 41 mg (0.065 mmol, 65%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$=7.26 ppm) δ: 8.05 (m, 2h, Ph), 7.5 (m, 3H, Ph), 5.72 (s, 1H, 4-H), 5.35 (ddd, *J* = 11.4, 5.2, 9.3 Hz, 1H, 3-H'), 4.96 (d, *J* = 3.2 Hz, 1H, 1-H'), 3.83 (dq, *J* = 9.3, 6.2 Hz, 1H, 5-H'), 3.54 (dd, *J* = 8.5,, 8.51 Hz, 1H, 17-H), 3.40 (ddd, *J* = 9.3, 9.3, 4.1 Hz, 1H, 4-H'), 1.32 (d, *J* = 6.2 Hz, 3H, 6-H'), 2.5 – 0.7 (m)

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$=77 ppm) δ: 199.6 (C-3), 171.3 (C-5), 167.5 (COPh), 133.3, 129.7, 128.4, (Ph), 123.8 (+, C-4), 97.5 (+, C-1'), 87.2 (+, C-17), 75.9, 73.6, 68.1 (+, C-3', C-4', C-5'), 53.8 (+, C-9), 50.2 (+, C-14), 42.8 (C-13), 38.6 (C-10), 37.2 (-, C-12), 35.7 (-, C-1), 35.6 (-, C-2'), 35.4 (+, C-8), 33.9 (-, C-2), 32.8 (-, C-6), 31.5 (-, C-7), 28.4 (-, C-16), 23.3 (-, C-15), 20.6 (-, C-11), 17.7 (+, C-19), 17.4 (+, C-6'), 11.7 (+, C-18).

11.4.4. Experiments to the chapter 5.4.

17-*O*-[(3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-α-L-galactopyranosyl)-(1→3)-(2,6-dideoxy-α-L-glycopyranosyl)]-testosterone (79)

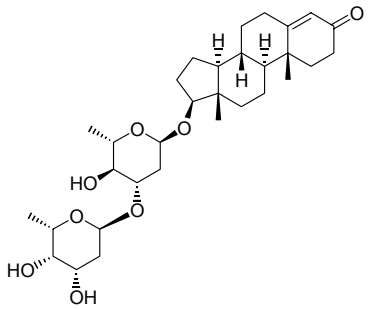


To a suspension of polymer-bound disaccharide **58** (200 mg, 0.116 mmol) in a mixture of solvents (CH_2Cl_2/acetonitrile 1:1, 8 ml) were added testosterone (0.1 g, 0.348 mmol) and selectfluor™ (61.6 mg, 1.5 eq). The suspension was shaken for 4 h, then polymer was filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. Loading of afforded polymer-bound glycoconjugate **79** was determined after cleavage with "TBAF mixture".

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) GEL-NMR δ: 199.6 (C-3), 171.3 (C-5), 123.7 (C-4), 98.9, 98.0 (C-1', C-1''), 86.9 (C-17), 79.0, 78.7 (C-4', C-4''), 72.7, 72.6 (C-3', C-3''), 70.3, 67.6 (C-5', C-5''), 53.8 (C-9), 50.2 (C-14), 42.7 (C-13), 38.6 (C-10), 38.4, 37.1 (C-2', C-2''), 36.9 (C-12), 35.6 (C-1), 35.4 (C-8), 33.8 (C-2), 32.7

(C-6), 32.4 (C-7), 28.4 (C-16), 23.2 (C-15), 20.5 (C-11), 18.1 (C-19), 17.8, 17.3 (C-6', C-6''), 11.6 (C-18), 6.9, 5.7, 5.3 (TES).

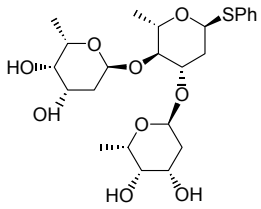
17-*O*-[(2,6-dideoxy-α-L-galactopyranosyl)-(1→3)-(2,6-dideoxy-α-L-glycopyranosyl)]-testosterone (80)



Yield: 11 mg (0.02 mmol, 17%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (s, 1H, 4-H), 5.13 (d, *J* = 3.7 Hz, 1H, 1-H'), 4.86 (d, *J* = 3.4 Hz, 1H, 1-H''), 4.02 – 3.93 (m, 2H, 3-H'', 5-H''), 3.84 (ddd, J = 11.4, 9.2, 4.5 Hz, 1H, 3-H'), 3.72 (dq, J = 9.2, 6.0 Hz, 1H, 5-H'), 3.63 (bs, 1H, 4-H''), 3.49 (t, J = 8.4 Hz, 1H, 17-H), 3.17 (t, J = 9.2 Hz, 1H, 4-H'), 2.5 – 0.7 (m).

Phenyl {di-[2,6-dideoxy-α-L-galactopyranosyl]-(1→3),(1→4)}-2,6-dideoxy-1-thio-α-L-glycopyranoside (82)



To a suspension of polymer bound thioglycoside **58** (174 mg, 0.83 mmol) in 2.5 ml of CH_2Cl_2 was added 3,4-bis-*O*-TES-L-fucal **22** (90 mg, 2.5 mmol) and 1 mg of PPh_3*HBr. The suspension was shaken for 6 h, polymer filtered off, washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. The polymer-bound trisaccharide **81** was weighted and loading was determined by weight difference

Yield: 196 mg (0.063 mmol, 22 mg, 76%).

Polymer bound trisaccharide **81** was successfully cleaved with TBAF in THF to afford 19.5 mg of trisaccharide **82** (0.039 mmol, 63%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.43 (m, 2H, Ph), 7.24 (m, 3H, Ph), 5.52 (d, *J* = 5.0 Hz, 1H, 1-H), 5.18, 5.03 (d, d, *J* = 3.7 Hz, *J* = 3.45 Hz, 2H, 1-H', 1''), 4.15 (dq, *J* = 9.3, 6.1 Hz, 1H, 5-H), 3.84 (m, 5H), 3.56 (dd, *J* = 9.4, 1.6 Hz, 2H, 4-H',4-H''), 3.20 (dd, *J* = 9.3, 8.8 Hz, 1H, 4-H), 2.43 (dd, *J* = 13.9, 4.5 Hz, 1H), 2.05 (m, 3H), 1.55 (m, 2H), 1.24 (d, *J* = 6.1 Hz, 3H, CH_3), 1.14 (d, *J* = 6.4 Hz, 3H, CH_3'), 1.13 (d, *J* = 6.4 Hz, 3H, CH_3'')

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$=77 ppm): 135.3, 131.1+, 128.9+, 126.9+ (Ph), 100.8, 100.5 (2d, C-1', C-1''), 83.6 (d, C-1), 83.1 (d, C-4), 79.4 (d, C-3), 73.5, 73.4 (2d, C-4', C-4''), 68.0 (2d, C-5, C-5''), 67.7 (d, C-5'), 67.4, 67.3 (2d, C-3', C-3''), 38.1 (t, C-2), 33.6 (2t, C-2', C-2''), 18.1 (q, C-6), 17.3, 17.2 (2q, C-6', C-6'').

The obtained polymer **81** was involved in the following glycosidation reactions with testosterone (3-5 eq) and different thioglycoside activators:

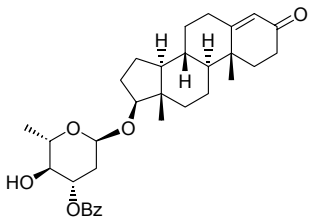
1. Selectfluor™ 2eq, CH_2Cl_2/CH_3CN, RT. overnight (after treating the polymer **83** with TBAF in THF glycoconjugate **84** was afforded in 15% yield).
2. $PhI(OAc)_2$ (5 eq), Et_4NI (5.5 eq) , CH_2Cl_2 , RT. overnight.
3. NIS (1.6 eq), TMSOTf (cat.), CH_2Cl_2, -50^{o}C – -20^{o}C 3h, (at higher temperatures cleavage of polymer-bound trisaccharide was observed).

In all reactions 17-Phenyl-S-testosterone was detected as a by-product.

17-Ph-S-Testosterone

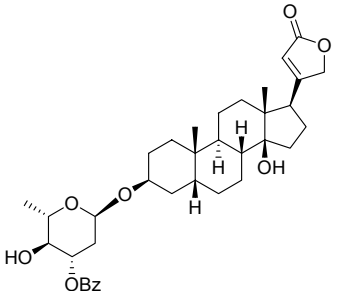
^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$=7.26 ppm) δ: 7.70 (m, 2H, Ph), 7.54 (m, 3H, Ph), 5.71(s, 1H, 4-H), 4.15 (dd, *J* = 8.3, 8.3 Hz, 0.5H, 17-H), 4.07 (dd, *J* = 9.0, 7.9 Hz, 0.5H, 17-H), 2.5-0.75 (m).

17-*O*-(3-*O*-benzoyl-2,6-dideoxy-α-L-glucopyranosyl)-testosterone (See table 6) (78)



To a suspension of polymer bound glycal **59** (147 mg, 0.07 mmol) in 2.5 ml of CH_2Cl_2 was added testosterone (60 mg, 3 eq, 0.21 mmol) and 1 mg of PPh_3*HBr (cat.). The suspension was shaken for 6 h, then filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. The filtrated solution was evaporated under reduced pressure and the residue was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 2:1, R_f- 0.63) to yield 31mg (0.059 mmol, 85%) of crystalline product **78**. After treating polymer with TBAF in THF the glycoside **53** was detected. NMR analysis see above.

3-*O*-(3-*O*-benzoyl-2,6-dideoxy-α-L-glucopyranosyl)-digitoxigenin (85)



To a suspension of polymer bound glycal **59** (73 mg, 0.033 mmol) in 1.5 ml of CH_2Cl_2 was added digitoxigenin (25 mg, 0.066 mmol) and 0.6 mg of PPh_3*HBr (cat.). The suspension was shaken for 6 h, then resin filtered and washed with CH_2Cl_2 (5x2 ml), acetonitrile (5x2 ml) and dried in high vacuum for 4 h. The filtrate was evaporated and residue was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 2:1, R_f- 0.45) to yield 15 mg (0.025 mmol, 75%) of crystalline product **85**. After treating resin with TBAF in THF the compound **55** was detected.

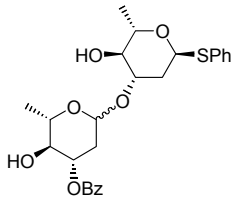
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.06 (m, 2H, Ph), 7.50 (m, 3H, Ph), 5.91 (dd, *J* = 1.5, 1.5 Hz, 1H, 22-H), 5.42 (ddd, *J* = 11.5, 9.3, 5.2 Hz, 1H, 3-

H'), 5.02 (dd, *J* = 18.1, 1.6 Hz, 1H, 21-H), 5.01 (d, *J* = 2.7 Hz, 1H, 1-H'), 4.80 (dd, *J* = 18.1, 1.6 Hz, 1H, 21-H), 3.85 (dq, *J* = 9.3, 6.3 Hz, 1H, 5-H'), 3.40 (dd, *J* = 9.3, 9.3 Hz, 1H, 4-H'), 2.71 (bs, 1H, OH), 2.28 (dd, *J* = 12.3, 5.2 Hz, 1H, 2-H'), 2.25 – 0.5 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 174.6 (s, C-20), 174.5 (s, C-23), 167.6 (s, *C*OPh), 133.4, 129.8, 129.7, 128.4 (Ph), 117.7 (t, C-22), 94.8 (t, C-1'), 85.6 (s, C-14), 76.7 (d, C-3'), 73.8 (d, C-4'), 73.4 (t, C-21), 71.5 (d, C-3), 68.1 (d, C-5'), 50.9 (d, C-17), 49.6 (s, C-13), 41.9 (d, C-8), 40.1 (s, C-12), 36.4 (d, C-5), 35.9 (t, C-2'), 35.7 (d, C-9), 35.2 (s, C-10), 33.2 (t, C-4), 30.4 (t, C-15), 29.7 (t, C-1), 29.6 (t), 26.9 (t, C-2), 26.61 (t, C-6), 26.60 (t, C-16), 23.7 (q, C-19), 21.4 (t, C-7), 21.2 (t, C-11), 17.7 (q, C-6'), 15.8 (q, C-18).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** - 1.35 ppm**:** 5.38 (ddd, 1H, 3-H'), 5.01 (d, 1H, 1-H'), 3.83 (dq, 1H, 5-H'), 3.40 (dd, 1H, 4-H'), 2.71 (bs, 1H, OH), 2.28 (dd, 1H, 2-H'), 1.93 (ddd, 1H, 2-H'), 1.35 (d, 3H, 6-H').

Phenyl [3-*O*-benzoyl-2,6-dideoxy-α/β-L-glycopyranosyl]-(1→3)-2,6-dideoxy-1-thio-α-L-glycopyranoside (86)

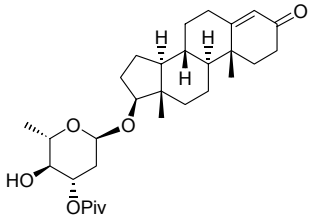


To a suspension of polymer bound glycal **59** (180 mg, 0.15 mmol) in mixture of solvents (3 ml, CH_2Cl_2/CH_3CN - 1:1) was added thioglycoside **27** (108 mg, 0.45 mmol), 1 mg of CSA (cat.) and 7 mg of LiBr. The suspension was shaken for 5 h, polymer filtered off and washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. The filtrate was evaporated and crude product **86** was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 3:1, R_f- 0.45). On the polymer no product was detected after treating with TBAF in THF for a 12h.

Yield: 32mg (0.067 mmol, 45%) as a diastereomeric mixture.

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.1 (m, 3H, Ph), 7.5 (m, 7H, Ph), 5.62 (d, *J* = 5.4 Hz, 1H, 1-H), 5.35 (ddd, *J* = 11.7, 9.1, 5.2 Hz, 1H, 3-H') 5.24 (d, *J* = 2.9 Hz, 0.7H, 1-H'$_\alpha$), 4.76 (dd, *J* = 9.8, 2.0 Hz, 0.3H, 1-H'$_\beta$), 4.23 (ddd, *J* = 11.2, 9.3, 6.1 Hz, 1H), 3.90 (m, 2H), 3.50 (m, 3H), 3.32 (ddd, *J* = 9.1, 9.1, 2.2 Hz, 0.7H), 3.20 (dd, *J* = 9.0, 9.0 Hz, 0.3H), 2.8- 2.7 (m, 1.7H), 2.6- 2.2 (m, 3.7H), 1.37 (d, *J* = 6.0 Hz, 3H, 6-H'), 1.35 (d, *J* = 6.1 Hz, 3H, 6-H)

17-*O*-(3-*O*-pivaloyl-2,6-dideoxy-α-L-glucopyranosyl)-testosterone (87)

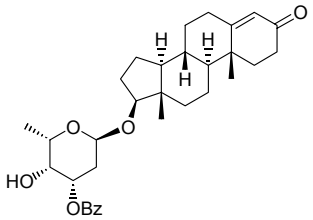


To the polymer bound glycoside **60** in CH_2Cl_2 (2.5 ml) testosterone (53mg, 0.186 mmol) and 1mg of PPh_3*HBr was added. The suspension was shaken for 8h, polymer was filtered off, washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. The filtrate was evaporated and residue was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 2:1, R_f-0.47) to yield 24 mg (0.048, 77%) of product **87**. After treating obtained polymer with TBAF in THF the compound **53** was detected.

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.76 (s, 1H, 4-H), 5.10 (ddd, *J* = 11.5, 5.2, 9.2 Hz, 1H, 3-H'), 4.95 (d, *J* = 3.0 Hz, 1H, 1-H'), 3.55 (dd, *J* = 8.6, 8.6 Hz, 1H, 17-H), 3.27 (ddd, *J* = 9.2, 8.9, 4.0 Hz, 1H, 4-H'), 1.24 (d, *J* = 6.2 Hz, 3H, 6-H'), 2.7 – 0.7 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.6 (C-3), 171.3 (C-5), 175.5 (*C*OPiv), 123.8 (+, C-4), 97.5 (+, C-1'), 87.2 (+, C-17), 81.3 (+, C-3'), 73.6, 68.1 (+, C-4', C-5'), 53.7 (+, C-9), 50.2 (+, C-14), 42.7 (C-13), 38.8 (s, *C*$(CH_3)_3$), 38.6 (C-10), 37.2 (-, C-12), 35.7 (-, C-1), 35.6 (-, C-2'), 35.4 (+, C-8), 33.9 (-, C-2), 32.8 (-, C-6), 31.5 (-, C-7), 28.4 (-, C-16), 27.2 (+, C(*C*$H_3)_3$), 23.3 (-, C-15), 20.6 (-, C-11), 17.7 (+, C-19), 17.4 (+, C-6'), 11.7 (+, C-18).

17-*O*-(3-*O*-benzoyl-2,6-dideoxy-α-L-galactopyranosyl)-testosterone (88)



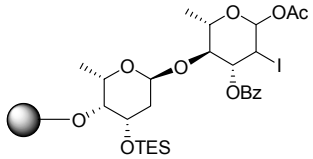
To a suspension of polymer bound glycal **59** (167 mg, 0.35 mmol/g) in 2.5 ml CH_2Cl_2 was added testosterone (48 mg, 0.175 mmol)) and 1 mg of PPh_3*HBr. The suspension was shaken for 6 h, polymer was filtered off, washed with CH_2Cl_2 (5x3 ml), acetonitrile (5x3 ml) and dried in high vacuum for 4 h. The filtrate was evaporated and crude glycoconjugate **88** was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 2:1). After treating resin with TBAF in THF the compound **53** was detected.

Yield: 25 mg (0.048 mmol, 82%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.05 (m, 2H, Ph), 7.5 (m, 3H, Ph), 5.68 (s, 1H, 4-H), 5.37 (1H, 3-H'), 4.85 (d, *J* = 2.8 Hz, 1H, 1-H'), 3.82 (bq, J = 6.5 Hz, 1H, 5-H'), 3.48 (t, J = 8.5 Hz, 1H, 17-H), 3.60 (bs, 1H, 4-H'), 2.7 – 0.5 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.5 (C-3), 171.2 (C-5), 167.5 (COPh), 133.3, 129.8, 128.5, (Ph), 123.8 (+, C-4), 99.3 (+, C-1'),87.1 (+, C-17), 75.9 (+, C-3'), 73.6 (+, C-4'), 67.5 (C-5'), 53.8 (+, C-9), 50.1 (+, C-14), 42.7 (C-13), 38.5 (C-10), 37.0 (-, C-12), 35.6 (-, C-1), 35.4 (+, C-8), 33.9 (-, C-2), 33.4 (-, C-2'), 32.7 (-, C-6), 31.4 (-, C-7), 28.5 (-, C-16), 23.3 (-, C-15), 20.5 (-, C-11), 17.3 (+, C-19), 18.0 (+, C-6'), 11.5 (+, C-18).

Acetyl [3-*O*-TES-4-*O*-(PS-DES)-2,6-dideoxy-α-L-glucoopyranosyl]-(1→3)-2-iodo-2,6-dideoxy-L-glyco/manno-pyranoside (93)



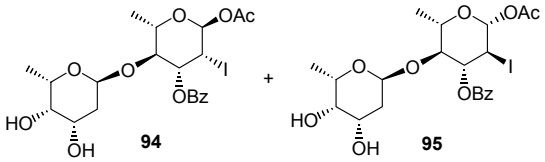
To a suspension of polymer bound glycal **59** (345 mg, 0.2 mmol) in 5 ml of CH_2Cl_2 was added $PhI(OAc)_2$ (644 mg, 2 mmol, 10 eq) and $Et_4N^+I^-$ (565mg, 2.2 mmol,

11eq). The suspension was shaken for 12 h, then filtered and washed with CH_2Cl_2 (5x5 ml), methanol (5x5 ml) and polymer was dried in high vacuum for 4 h. The polymer-bound carbohydrate **93** was weighted and loading was determined by weight difference.

Yield: 380 mg (0.188 mmol, 35 mg, 94%).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) GEL-NMR δ: 168.6 (Ph*C*O), 165.1 (CH_3*CO*), 133.6, 129.6, 128.6 (Ph), 100.3 (C-1') 95.0 (C-1, α) 93.9 (C-1, β), 78.9, 73.3, 71.7, 70.6, 68.3, 67.1 (C-3, C-4, C-5, C-3', C-4', C-5'), 33.1 (C-2'), 29.1 (C-2) 18.1, 17.3 (C-6, C-6'), 6.9, 5.3 (TES).

Acetyl [2,6-dideoxy-α-L-glucoopyranosyl]-(1→3)-2-iodo-2,6-dideoxy-α-L-mannopyranoside (**94), Acetyl [2,6-dideoxy-α-L-glucoopyranosyl]-(1→3)-2-iodo-2,6-dideoxy-β-L-glycopyranoside (95)**



150 mg Of the polymer **93** was treated with TBAF in THF for 12h. Polymer was filtered off and filtrate was evaporated under reduced pressure. Residue was purified by column chromatography over silica gel to afford compounds **94** and **95.**

Yield: 33 mg (0.06 mmol, 82%)

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.1 (m, 2H, Ph), 7.55 (m, 3H, Ph) 6.34 (d, *J* = 1.7 Hz, 0.7H, 1-H), 5.89 (d, *J* = 9.2, 0.3H, 1-H, β), 5.59 (dd, *J* = 11.3, 8.8 Hz 0.3H, 2-H), 5.21 (d, *J* = 2.2 Hz, 0.7H, 1-H'), 4.96 (d, *J* = 4.2 Hz, 0.3H, 1-H') 4.8 (dd, *J* = 8.4, 4.2 Hz, 0.7H), 4.60 (dd, *J* = 4.3, 1.8 Hz, 0.7H), 3.95 (m, 4H), 3.61 (d, *J* = 2.7 Hz, 0.7H), 3.57 (d, *J* = 2.9 Hz, 0.3H) 2.3- 1.5 (m), 1.39, 1.26 (2x d, *J* = 5.9, 6.6 Hz, 6H, 6-H', 6-H).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$=77 ppm) δ: 167.8 (*C*O-Ph), 164.3 (*C*O-CH_3), 133.0, 129.0, 127.9 (Ph), 98.6, 94.1 (2+, C-1, C-1'), 78.1, 71.1, 70.1, 69.9, 65.8,

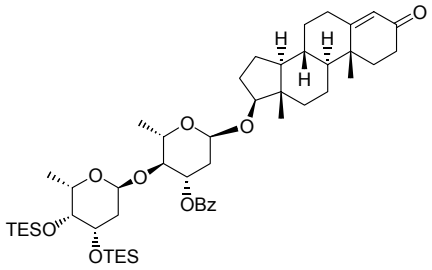
64.7 (6+, C-3, C-4, C-5, C-3', C-4', C-5'), 31.9 (-, C-2'), 27.8 (C-2), 17.3, 15.7 (2+, C-6, C-6').

Glycosidation of testosterone with polymer-bound disaccharide 93

To a suspension of polymer bound glycoside **93** (120 mg, 0.072 mmol) in 2.5 ml of CH_2Cl_2 was added testosterone (62 mg, 0.216 mmol). The reaction mixture was cooled down to –70°C and 50 μl (3 eq) of TMSOTf was added. The resulted suspension was shaken for 4 h, then allowed to warm up to -30°C, reaction was quenched with some drops of triethly amine. The polymer was filtered off, washed with CH_2Cl_2 (5x2 ml), acetonitrile (5x2 ml) and dried in high vacuum for 4 h. The filtrate was evaporated and residue was purified by column chromatography over silica gel (ethyl acetate, R_f- 0.25). The only compound **53** was isolated and analysed by NMR spectroscopy. After treating resin with TBAF in THF no desired product was detected.

11.5.1. Experiments to the chapter 6.1.1.

17-*O*-[(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-(3-*O*-benzoyl-2,6-dideoxy-α/β-L-glycopyranosyl)]-testosterone (96)



To a solution of rhamnal **31** (20 mg, 0.085 mmol) and testosterone (25mg, 0.085 mmol) in CH_2Cl_2 3 ml, was added solution of CSA (1mg, cat.) and LiBr (7 mg) in CH_3CN (3 ml). The reaction was stirred for 4 h, then 3,4-bis-*O*-TES-L-fucal (35 mg, 0.09 mmol) was added in a 2 ml of CH_2Cl_2. The resulted solution was allowed to stir another 6 h and the reaction was quenched with addition of Amberlite A-21. The polymer was filtered off and the filtrate was evaporated under reduced pressure. The crude product **96** was purified by column chromatography over silica gel (ethyl acetate / petroleum ether = 1:5) to afford three fractions: α-glycoside (40 mg, 0.045 mmol, 53%), β-glycoside (10 mg, 0.011 mmol, 13%), and 8 mg of by-product **24**.

α-glycoside:

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ =7.26 ppm) δ: 8.00 (m, 2H, Ph), 7.5 (m, 3H, Ph), 5.72 (s, 1H, 4-H), 5.40 (ddd, *J* = 10.8, 9.4, 5.2 Hz, 1H, 3-H'), 5.15 (d, *J* = 3.3 Hz, 1H, 1-H'), 4.89 (d, *J* = 3.1 Hz, 1H, 1-H''), 3.8 – 3.9 (m, 3H), 3.4 – 3.6 (m, 3H), 2.5 – 0.7 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.6 (C-3), 171.3 (C-5), 165.6 (*C*OPh), 133.1, 129.9, 129.5, 128.5 (Ph), 123.8 (+, C-4), 100.1 (+, C-1''), 97.5 (+, C-1'), 87.2 (+, C-17), 81.5 (+, C-3'), 73.4, 73.0, 68.0, 67.2, 66.8 (+, C-4', C-5', C-3'', C-4'', C-5''), 53.8 (+, C-9), 50.2 (+, C-14), 42.8 (C-13), 38.6 (C-10), 37.1 (-, C-12), 35.8 (-, C-1), 35.7 (-, C-2'), 35.4 (+, C-8), 33.9 (-, C-2), 33.2 (-, C-2''), 32.8 (-, C-6), 31.5 (-, C-7), 28.5 (-, C-16), 23.3 (-, C-15), 20.5 (-, C-11), 18.1 (+, C-19), 17.4 (+, C-6'), 17.2 (+, C-6''), 11.7 (+, C-18), 7.0, 6.7, 5.1, 4.6 (2 x TES).

β-glycoside:

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.00 (m, 2H, Ph), 7.5 (m, 3H, Ph), 5.72 (s, 1H, 4-H), 5.16 (d, J = 3.2 Hz, 1H, 1-H''), 5.10 (ddd, J = 11.5, 5.0, 3.7 Hz, 1H, 3-H'), 4.56 (dd, J = 9.8, 2.2 Hz, 1H, 1-H'), 3.4 – 3.9 (m, 5H), 2.5 – 0.4 (m).

3-*O*-Benzoyl-4-*O*-TES-6-deoxy-L-rhamnal (101)

To a solution of glycal **31** (1 g, 4.3 mmol), DMAP (300 mg, 0.2 eq, cat.) and imidazole (0.5 g, 1.3 eq) in 10 ml of DMF was added TESCl (0.79 ml, 4.7 mmol). The reaction mixture was stirred overnight. The crude product was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 15:1).

Yield: 1.4 g (4.0 mmol, 93%), colourless oil.

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.05 (m, 2H, Ph), 7.57 (m, 1H, Ph), 7.45 (m, 2H, Ph), 6.45 (dd, *J* = 6.0, 1.0 Hz, 1H, 1-H), 5.47 (ddd, *J* = 6.3, 2.5, 1.2 Hz, 1H, 3-H), 4.83 (dd, *J* = 6.0, 2.5 Hz, 1H, 2-H), 4.00 (dq, *J* = 8.8, 6.2 Hz, 1H, 5-H), 3.87 (dd, *J* = 8.8, 6.3 Hz, 1H, 4-H), 1.43 (d, *J* = 6.2 Hz, 3H, 6-H), 0.9 (t, *J* = 7.8 Hz, 9H, TES), 0.56 (q, *J* = 7.8 Hz, 6H, TES).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 166.2 (CO-Ph), 146.0 (+, C-1), 133.0, 129.6 128.4 (3+, Ph), 130.3 (q, Ph), 99.4 (+, C-2), 75.5, 73.7, 72.3 (3+, C-3, C-4, C-5), 17.4 (+, C-6), 6.4, 5.0 (+ -, TES).

3-*O*-Benzoyl-4-*O*-TBS-6-deoxy-L-rhamnal (97)

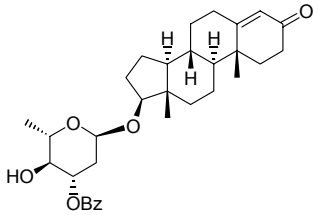
To a solution of glycal (jj-79) (1 g, 4.3 mmol), DMAP (300 mg, 0.2 eq, cat.) and imidazole (0.5 g, 1.3 eq) in 10 ml of DMF was added TESCl (0.79 ml, 4.7 mmol). The reaction mixture was stirred overnight. The crude product was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 15:1).

Yield: 1.44 g (4.1 mmol, 94%), colorless oil.

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.05 (m, 2H, Ph), 7.57 (m, 1H, Ph), 7.45 (m, 2H, Ph), 6.43 (dd, *J* = 6.0, 1.0 Hz, 1H, 1-H), 5.50 (ddd, *J* = 6.4, 2.5, 1.3 Hz, 1H, 3-H), 4.80 (dd, *J* = 6.0, 2.5 Hz, 1H, 2-H), 3.97 (dq, *J* = 9.0, 6.3 Hz, 1H, 5-H), 3.87 (dd, *J* = 9.0, 6.4 Hz, 1H, 4-H), 1.41 (d, *J* = 6.3 Hz, 3H, 6-H), 0.83 (s, 9H, TBS), 0.1, -0.2 (2s, 6H, TBS).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$=77 ppm) δ: 166.3 (*C*O-Ph), 146.1 (+, C-1), 133.0, 129.6 128.4 (3+, Ph), 130.3 (s, Ph), 99.6 (+, C-2), 75.5, 73.7, 72.4 (3+, C-3, C-4, C-5), 25.7 (+, t-Bu), 18.0 (s, t-Bu), 17.8 (+, C-6), -4.1, -4.6 (2+ , Si(*C*H_3)$_2$).

17-*O*-(3-*O*-benzoyl-2,6-dideoxy-α-L-glucopyranosyl)-testosterone (See scheme 16) (78)



To a solution of glycal **97** (30 mg, 0.086 mmol) and testosterone (23 mg, 0.080 mmol) in CH_2Cl_2/acetonitrile (1:1, 3 ml) were added MS 4A (55 mg), LiBr (30 mg) and Dowex 50x8 (15 mg, cat., the TBS group also be proposed to cleave). After 24 h reaction was quenched by addition of Amberlite A-21. The suspension was filtrated, solids were washed with ethyl acetate and the filtrate was evaporated under reduced pressure. The crude product **78** was purified by column

chromatography over silica gel (ethyl acetate / petroleum ether=1:2, R_f-0.61). Yield: 43 mg (0.070 mmol, 81%). NMR analyses see above.

3-*O*-Pivaloyl-4-*O*-TES-6-deoxy-L-rhamnal (98)

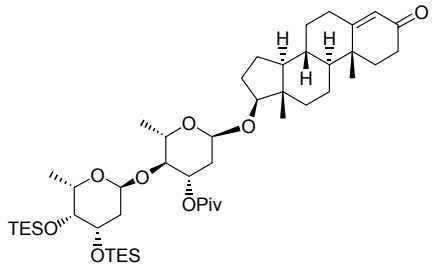
To a solution of glycal **32** (1 g, 4.7 mmol), DMAP (300 mg, 0.2 eq, cat.) and imidazole (0.5 g, 6.1 mmol) in 10 ml of DMF was added triethylsilyl chloride (0.77 g, 5.0 mmol). The reaction mixture was allowed to stir another 12h. The crude product solution in DMF directly was purified by column chromatography over silica gel (petroleum ether / ethyl acetate 15:1).

Yield: 1.5 g (4.46 mmol, 95%), colourless oil.

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 6.36 (dd, *J* = 6.2, 0.9 Hz, 1H, 1-H), 5.12 (dd, *J* = 5.4, 3.0 Hz, 1H, 3-H), 4.68 (dd, 6.2, 3.0 Hz, 1H, 2-H), 3.93 (dq, *J* = 7.4, 6.5 Hz, 1H, 5-H), 3.74 (dd, *J* = 7.4, 5.4 Hz, 1H, 4-H), 1.35 (d, *J* = 6.5 Hz, 3H, 6-H), 1.2 (s, 9H, Piv), 0.95 (t, 9H, TES), 0.6 (q, 6H, TES).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 178.2 (*C*O-Piv), 145.7 (+, C-1), 98.9 (+, C-2), 75.2, 72.3, 72.0 (3x+, C-3, C-4, C-5), 38.8 (q, *C*$(CH_3)_3$), 27.2 (+, C(*C*$H_3)_3$), 17.2 (+, C-6), 6.8 (+, TES), 5.0 (-, TES).

17-*O*-[(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1$\rightarrow$4)-(3-*O*-pivaloyl-2,6-dideoxy-α-L-glycopyranosyl)]-testosterone (100)



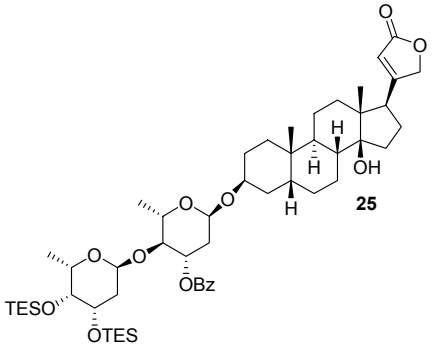
To a solution of rhamnal **98** (30 mg, 0.091 mmol) and testosterone (25mg, 0.091 mmol) in CH_3CN (3 ml) were added Dowex 50x8 (1 mg, cat.) and LiBr (5 mg). The reaction was shaken for 10 h, then 3,4-bis-*O*-TES-L-fucal (35 mg, 0.1 mmol) was added in a 2 ml of CH_2Cl_2. The resulted suspension was stirred another 5h, quenched with addition of Amberlite A-21, solids were filtered off and solvent was

evaporated under reduced pressure. The residue was purified by column chromatography (ethyl acetate / petroleum ether=1:5) to afford the glycoside **100**.

Yield: 48 mg (0.056 mmol, 62%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (s, 1H, 4-H), 5.16 (d, *J* = 3.3 Hz, 1H, 1-H') 5.12 (ddd, *J* = 11.7, 9.7, 4.9 Hz, 1H, 3-H'), 4.86 (d, *J* = 2.3 Hz, 1H, 1-H''), 4.0- 3.7 (m, 3H), 3.65- 3.35 (m, 3H), 2.5 – 0.7 (m).
^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ =77 ppm) δ: 199.6 (C-3), 171.3 (C-5), 175.1 (*C*OPiv), 123.8 (+, C-4), 100.1 (+, C-1''), 97.5 (+, C-1'), 87.2 (+, C-17), 81.5 (+, C-3'), 73.4, 73.0, 68.0, 67.2, 66.8 (+, C-4', C-5', C-3'', C-4'', C-5''), 53.8 (+, C-9), 50.2 (+, C-14), 42.8 (C-13), 38.7 (q, *C*$(CH_3)_3$), 38.6 (C-10), 37.1 (-, C-12), 35.8 (-, C-1), 35.7 (-, C-2'), 35.4 (+, C-8), 33.9 (-, C-2), 33.2 (-, C-2''), 32.8 (-, C-6), 31.5 (-, C-7), 28.5 (-, C-16), 27.0 (+, C(*C*$H_3)_3$), 23.3 (-, C-15), 20.5 (-, C-11), 18.1 (+, C-19), 17.4 (+, C-6'), 17.2 (+, C-6''), 11.7 (+, C-18), 7.0, 6.7, 5.1, 4.6 (2x TES).

3-*O*-[(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-(3-*O*-benzoyl-2,6-dideoxy-α-L-glycopyranosyl)]-digitoxigenin (103)



To a solution of rhamnal **101** (25 mg, 0.072 mmol) and digitoxigenin (26mg, 0.070 mmol) in 3 ml of CH_2Cl_2, were added polymer-bound PPh_3*HBr (1mg, cat.) and LiBr (5 mg). The reaction was shaken for 4 h, and then 1 ml of CH_3CN and 1 mg of Dowex 50x8 were added to initiate silyl ether cleavage. The resulted suspension was allowed to stir for 10h then 3,4-bis-*O*-TES-L-fucal (35 mg, 0.08 mmol) was added in 2 ml of CH_2Cl_2. Solution was stirred another 5h. The reaction was quenched by addition of Amberlite A-21, solids filtered off, washed with ethyl acetate and filtrate evaporated under reduced pressure. The crude product was

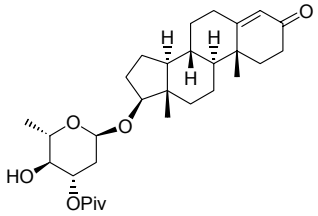
purified by column chromatography over silica gel (ethyl acetate / petroleum ether 1:1).

Yield: 30 mg (0.031 mmol, 45%).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.02 (m, 2H, Ph), 7.57 (m, 1H, Ph), 7.45 (m, 2H, Ph), 5.86 (s, 1H, 22-H), 5.45 (ddd, *J* = 11.3, 9.2, 5.1 Hz, 1H, 3-H'), 5.26 (d, *J* = 3.5 Hz, 1H, 1-H'), 4.98 (dd, *J* = 18.1, 1.6 Hz, 1H, 21-H), 4.95 (d, *J* = 3.1 Hz, 1H, 1-H''), 4.78 (dd, *J* = 18.1, 1.6 Hz, 1H, 21-H), 3.8 – 3.95 (m, 4H), 3.52 (bs, 1H, 4-H''), 3.45 (t, J = 9.2 Hz, 1H, 4-H'), 2.83 – 0.4 (m).

^{13}**C-NMR** (125 MHz, , $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 179.6 (C-20), 178.4 (C-23), 165.6 (s, *C*OPh), 133.1, 129.5 128.5 (3+, Ph), 130.0 (s, Ph), 117.7 (+, C-22), 100.1 (+, C-1''), 94.6 (+, C-1'), 85.6 (C-14), 81.6 (+, C-3'), 73.4 (-, C-21), 73.2, 71.3, 68.1, 67.2, 66.8 (5+, C-4', C-5', C-3'', C-4'', C-5''), 50.9 (+, C-17), 49.6 (C-13), 41.9 (+, C-8), 40.0 (-, C-12), 36.3 (+, C-5), 36.1 (-, C-2'), 35.7 (+, C-9), 35.2 (C-10), 33.3 (-, C-2'), 33.2 (+), 30.4 (-), 29.5 (-), 26.9 (+), 26.87 (+), 26.6 (-), 23.7 (-), 21.4(s), 21.2 (-), 18.4 (+, C-6'), 17.2 (+, C-6''), 15.7 (+, C-18), 7.0, 6.7 (+, TES), 5.2, 4.7 (-, TES).

17-*O*-(3-*O*-pivaloyl-2,6-dideoxy-α-L-glucopyranosyl)-testosterone (99)



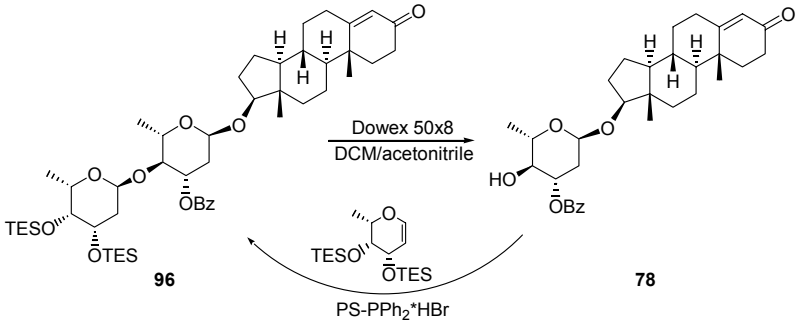
To a solution of glycoconjugate **100** (22 mg, 0.0255 mmol) in 2 ml mixture of solvents (CH_2Cl_2/Acetonitrile - 1:1) LiBr (5 mg) and Dowex 50x8 (2 mg, cat.) were added. The reaction mixture was allowed to stir for 4 h then the reaction was quenched by addition of Amberlite A-21. Solids were filtrated off and the filtrate was evaporated under reduced pressure. A crude product spectrum showed only glycoside **99** as a main product. No desired deprotection was observed.

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.76 (s, 1H, 4-H), 5.10 (ddd, *J* = 11.5, 5.2, 9.2 Hz, 1H, 3-H'), 4.95 (d, *J* = 3.0 Hz, 1H, 1-H'), 3.55 (dd, *J* = 8.6, 8.6 Hz,

1H, 17-H), 3.27 (ddd, *J* = 9.2, 8.9, 4.0 Hz, 1H, 4-H'), 1.24 (d, *J* = 6.1 Hz, 3H, 6-H'), 2.7 – 0.7 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.6 (C-3), 171.3 (C-5), 175.5 (*C*OPiv), 123.8 (+, C-4), 97.5 (+, C-1'), 87.2 (+, C-17), 81.3 (+, C-3'), 73.6, 68.1 (+, C-4', C-5'), 53.7 (+, C-9), 50.2 (+, C-14), 42.7 (C-13), 38.8 (s, *C*$(CH_3)_3$), 38.6 (C-10), 37.2 (-, C-12), 35.7 (-, C-1), 35.6 (-, C-2'), 35.4 (+, C-8), 33.9 (-, C-2), 32.8 (-, C-6), 31.5 (-, C-7), 28.4 (-, C-16), 27.2 (+, C(*C*$H_3)_3$), 23.3 (-, C-15), 20.6 (-, C-11), 17.7 (+, C-19), 17.4 (+, C-6'), 11.7 (+, C-18).

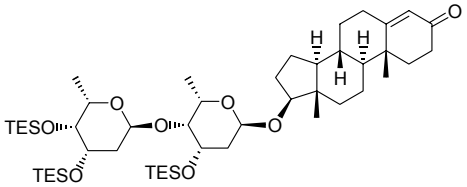
Attempts to deprotect glycoconjugate 96, with further glycosidation to afford trisaccharide.



To a solution of **96** (29 mg, 0.033 mmol) in a 4 ml mixture of solvents (CH_2Cl_2/Acetonitrile = 1:1) LiBr (5 mg) and Dowex 50x8 (5 mg) were added. After 2 h of stirring reaction was quenched by addition of Amberlite A-21. Solids were filtered off and the filtrate was evaporated under reduced pressure. The crude product was used in next step without further purification.

To a solution of crude product from the previous step in CH_2Cl_2 (3 ml), was added polymer-bound PPh_3HBr (1 mg, cat.), LiBr (5 mg) and 3,4-bis-*O*-TES-L-fucal (30 mg, 0.086 mmol). The reaction was shaken for 4 h and then quenched by addition of Amberlite A-21. The solids were filtered off and the filtrate was evaporated under reduced pressure. Residue was purified by column chromatography over silica gel (ethyl acetate / petroleum ether=1:2, Rf-0.33) to afford a product **96** (16 mg, 0.018 mmol, 55%). No desired trisaccharide was detected.

17-*O*-[(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-(3-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)]-testosterone (104)



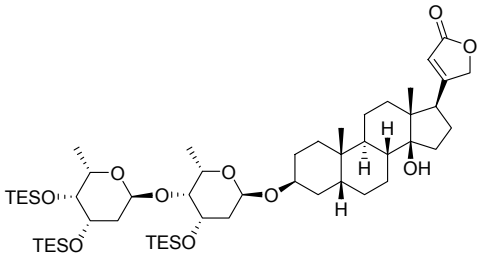
To a solution of fucal **46** (24 mg, 0.1 mmol) and testosterone (28mg, 0.1 mmol) in 3 ml of CH_2Cl_2 were added polymer-bound PPh_3*HBr (1mg, cat.) and LiBr (5 mg). The reaction mixture was shaken for 2 h, and then 3,4-bis-*O*-TES-L-fucal (40 mg, 0.12 mmol) was added in 1 ml of CH_2Cl_2. The resulted solution was stirred another 4 h, reaction quenched by addition of Amberlite A-21. The polymer was filtered off, washed with ethyl acetate and the filtrate was evaporated under reduced pressure. Residue was purified by column chromatography over silica gel (ethyl acetate / petroleum ether=1:4).

Yield: 77.5 mg (0.087 mmol 87%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (s, 1H, 4-H), 5.09 (d, *J* = 2.8 Hz, 1H, 1-H'), 4.89 (d, *J* = 2.9 Hz, 1H, 1-H''), 4.30 (bq, *J* = 6.3 Hz, 1H, 5-H''), 4.10 (m, 2H, 3-H', 3-H''), 3.80 (bq, *J* = 6.8 Hz, 1H, 5-H'), 3.65 (bd, *J* = 2.4 Hz, 1H, 4-H'), 3.55 (bs, 1H, 4-H''), 3.45 (t, *J* = 8.2 Hz, 1H, 17-H), 2.5 – 0.5 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.4 (C-3), 171.1 (C-5), 123.8 (+, C-4), 98.9 (+, C-1''), 97.7 (+, C-1'), 87.5 (+, C-17), 74.9, 73.9, 67.8, 67.6, 67.3, 66.9 (6+, C-3', C-4', C-5', C-3'', C-4'', C-5''), 53.9 (+, C-9), 50.1 (+, C-14), 42.8 (C-13), 38.6 (C-10), 37.1 (-, C-12), 35.7 (-, C-1), 35.5 (-, C-2'), 35.4 (+, C-8), 34.3 (-, C-2''), 33.9 (-, C-2), 32.9 (-, C-6), 31.5 (-, C-7), 28.6 (-, C-16), 26.9(-), 23.4 (-, C-15), 20.6 (-, C-11), 17.9 (+, C-19), 17.5 (+, C-6'), 17.4 (+, C-6''), 11.5 (+, C-18), 7.0, 6.8, 6.7, 5.2, 5.1, 4.9, 4.8 (3 x TES).

3-*O*-[(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-(3-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)]-digitoxigenin (105)



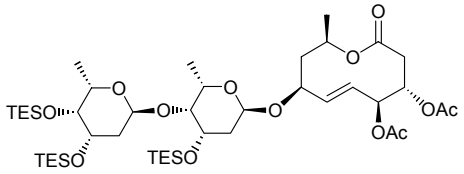
To a solution of fucal **46** (24 mg, 0.1 mmol) and digitoxigenin (37mg, 0.1 mmol) in 3 ml of CH_2Cl_2 were added polymer-bound PPh_3*HBr (1mg, cat.) and LiBr (5 mg). The reaction mixture was shaken for 2 h, and then 3,4-bis-*O*-TES-L-fucal (40 mg, 0.12 mmol) was added in 1 ml of CH_2Cl_2. The solution was stirred for another 4 h and then quenched by addition of Amberlite A-21. Solids were filtered off, washed with ethyl acetate and the filtrate was evaporated under reduced pressure. The residue was purified by column chromatography over silica gel (ethyl acetate / petroleum ether=1:2).

Yield: 73 mg (0.075 mmol, 75%).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.86 (s, 1H, 22-H), 5.26 (d, *J* = 2.7*,* Hz, 1H, 1-H'), 4.98 (dd, *J* = 18.1, 1.5 Hz, 1H, 21-H), 4.95 (d, *J* = 2.7 Hz, 1H, 1-H''), 4.78 (dd, *J* = 18.1, 1.5 Hz, 1H, 21-H),4.32 (bq, *J* = 6.5 Hz, 1H, 5-H''), 4.18 (dt, *J* = 11.8, 3.8 Hz, 1H, 3-H''), 4.12 (ddd, *J* = 11.5, 3.8, 2.4 Hz, 1H, 3-H'), 3.86 (bs, 1H, 14-H), 3.85 (bq, *J* = 6.5 Hz, 1H, 5-H'), 3.66 (bs, 1H, 4-H'), 3.55 (bs, 1H, 4-H''), 2.8 – 0.5 (m).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 174.5 (C-20), 174.4 (C-23), 117.7 (+, C-22), 97.8 (+, C-1''), 95.8 (+, C-1'), 85.6 (C-14), 75.1 (-, C-21), 73.9, 73.4, 70.9, 67.8, 67.6, 67.3 (6+, C-3', C-4', C-5', C-3'', C-4'', C-5''), 50.9 (+, C-17), 49.6 (C-13), 41.9 (+, C-8), 40.0 (-, C-12), 36.5 (+, C-5), 35.7 (+, C-9), 35.2 (C-10), 34.6 (-, C-2'), 33.3 (-, C-2'), 32.9 (+), 30.4 (-), 29.9 (-), 26.9 (+), 26.87 (+), 26.8 (-), 26.6 (-), 23.7 (-), 21.4(q), 21.2 (-), 17.9 (+, C-6'), 17.5 (+, C-6''), 15.7 (+, C-18), 7.0, 6.8 (2+, TES), 5.2, 4,7 (2-, TES).

7-*O*-[(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-(3-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)]-3,4-di-*O*-acetyl-decarestrictine D (106)



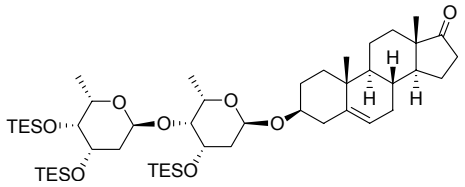
To a solution of fucal **46** (24 mg, 0.1 mmol) and decarestrictine **40** (30 mg, 0.1 mmol) in CH_2Cl_2 were added polymer-bound PPh_3*HBr (1 mg, cat.) and LiBr (5 mg). The reaction mixture was shaken for 2 h, and then 3,4-bis-*O*-TES-L-fucal (40 mg, 0.12 mmol) was added in 1 ml of CH_2Cl_2. The resulting solution was stirred for another 4 h and then quenched by addition of Amberlite A-21. Solids were filtered off, washed with ethyl acetate and the filtrate was evaporated under reduced pressure. The remaining residue was purified by column chromatography over silica gel (ethyl acetate / petroleum ether=1:2).

Yield: 56 mg (0.062 mmol, 62%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.77 (ddd, *J* = 16.0, 8.5, 3.5, Hz, 1H, 5-H), 5.60 (ddd, *J* = 16.0, 9.5, 1.5, Hz, 1H, 6-H), 5.33 (m, 1H, 4-H), 5.14 (ddd, J = 9.8, 6.6, 3.2 Hz, 1H, H-9), 5.06 (d, *J* = 3.0 Hz, 1H, 1-H'), 5.02 (ddd, *J* = 7.2, 5.0, 2.5 Hz, 1H, 3-H), 4.83 (d, *J* = 3,1 Hz, 1H, 1-H''), 4.30 (bq, *J* = 6.5 Hz, 1H, 5-H''), 4.15 – 4.0 (m, 3H), 3.75 (bq, *J* = 6.5 Hz, 1H, 5-H'), 3.63 (bd, *J* = 2.5 Hz, 1H, 4-H'), 3.53 (bs, 1H, 4-H''), 2.67 (dd, *J* = 14.0, 6.6 Hz, 1H, 8-H), 2.51 (dd, *J* = 14.0, 2.2 Hz, 1H, 8-H), 2.17, 2.14 (2s, 6H, 2 x AcO), 2.1 – 1.4 (m, 6H, 2-H, 2-H', 2-H''), 1.26, 1.23, 1.19 (3d, *J* = 6.6, 6.4, 6.4 Hz, 9H, 10-H, 6-H', 6-H''), 0.9 (m, 27H, 3 x TES), 0.6 (m, 18H, 3 x TES).

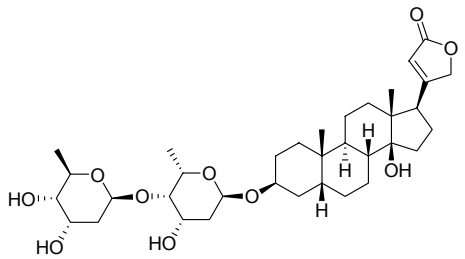
^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 169.9, 169.5, 169.0 (2 x *C*OCH_3, C-1), 134.0 (+, C-6), 125.9 (+, C-5), 97.7 (+, C-1''), 93.5 (+, C-1'), 74.5, 73.8, 71.9, 71.8, 70.8, 68.3, 67.7, 67.5, 67.3, 66.8, (10+, C-3, C-4, C-7, C-9, C-3'', C-4'', C-5'', C-3', C-4', C-5'), 40.9 (-, C-8), 33.8 (-, C-2''), 33.5 (-, C-2), 32.9 (-, C-2'), 21.4 (+, C-10), 21.0, 20.9 (2+, 2 x CO*C*H_3), 18.0 (+, C-6'), 17.3 (+, C-6''), 7.0, 6.8, 5.2, 4.9, 4.7 (3 x TES).

3-*O*-[(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-(3-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)]-dehydro-*epi*-androsterone (107)



To a solution of fucal **46** (24 mg, 0.1 mmol) and dehydroepiandrosteron (28mg, 0.1 mmol) in CH_2Cl_2 5 ml, was added PPh_3HBr-resin (1mg). The reaction was shaken for 2 h, and then 3,4-bis-*O*-TES-L-fucal (40 mg, 1,2 eq) was added in 1 ml of CH_2Cl_2. The solution was stirred for 5 h, quenched with A-21 and evaporated. After column chromatography (ethyl acetate / petroleum ether=1:3, Rf-0.62) the glycoconjugate **107** was obtained (71 mg, 84%).

3-*O*-[(2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-(2,6-dideoxy-α-L-galactopyranosyl)]-digitoxigenin (120)



To a solution of fucal **46** (24 mg, 0.1 mmol) and digitoxigenin (37mg, 0.1 mmol) in CH_2Cl_2 5 ml, polymer-bound PPh_3HBr (1mg, cat.) was added. The reaction was shaken for 2 h, and solution of allal **118** (35 mg, 0.1 mmol) in 1 ml of CH_2Cl_2 was added. The solution was stirred for another 24 h (reaction is very slow and not run to complete) and then quenched by addition of Amberlite A-21 (5 mg). The suspension was filtrated through a pad of celite and the solvent was evaporated under reduced pressure. The residue was dissolved in 10 ml of mixture (TBAF /AcOH/THF – 266 mg/0.151 ml/8.4 ml) and solution was allowed to stir overnight. The mixture was evaporated and crude product was purified by column chromatography over silica gel (ethyl acetate /MeOH = 10:1).

Yield: 21 mg (0.033 mmol, 33%)

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) δ: 5.92 (s, 1H, 22-H), 5.05 (dd, *J* = 18.4, 1.6 Hz, 1H, 21-H), 4.97 (d, *J* = 2.7 Hz, 1H, 1-H''), 4.93 (dd, *J* = 18.4, 1.6 Hz, 1H, 21-H), 4.06 (dd, *J* = 5.2, 2.4 Hz, 1H, 3-H'), 3.95 (m, 2H, 5-H'' 3-H''), 3.90 (bs, 1H), 3.86 (dq, *J* = 9.6, 6.2 Hz, 1H, 5-H'), 3.68 (bs, 1H, 4-H''), 3.22 (dd, *J* = 9.6, 2.8 Hz, 1H, 4-H'), 2.85 (bt, 1H, 3-H), 2.17 (m, 1H, 2-H'), 1.28 (d, *J* = 6.2 Hz, 3H, 6-H'), 1.19 (d, *J* = 6.4 Hz, 3H, 6-H''), 0.98 (s, 3H, 18-CH_3), 0.91 (s, 3H, 19-CH_3), 2.25 – 0.9 (m).

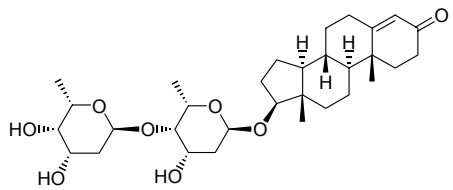
^{13}**C-NMR** (125 MHz, CD_3OD, = 49 ppm): 178.42 (s), 177.24(s), 117.78 (d, C-22), 101.08 (d, C-1'), 97.32 (d, C-1''), 86.43, 83.33 (d, C-4''), 79.52, 79.26, 79.00, 75.34 (t, C-21), 74.08 (d, C-4'), 73.25, 71.24 (d, C-5'), 69.05 (d, C-3'), 67.71 (d, C-3''), 66.24, 54.77, 52.15, 51.06, 42.72, 40.98, 38.97, 38.14, 36.84, 36.37, 35.76, 33.40, 31.67, 30.91, 28.06, 27.89, 27.54, 24.34, 22.57, 22.37, 18.37, 17.08, 16.40

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 1845 Hz = 3.67: 4.97 (d, 1H, 1-H''), 3.94, 3.95 (m, 2H, 3-H'', 5-H''), 3.68 (bs, 1H, 4-H''), 1.83 (ddd, 1H, 2-H''), 1.74 (dd, 1H, 2-H''), 1.19 (d, 3H, 6-H'').

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 1611 Hz = 3.22: 4.83 (bd, 1H, 1-H'), 4.05 (bd, 1H, 3-H'), 3.85 (bq, 1H, 5-H'), 3.22 (dd, 1H, 4-H'), 2.17 (dd, 1H, 2-H'), 1.80 (bdd, 1H, 2-H'), 1.26 (d, 3H, 6-H').

11.5.2. Experiments to the chapter 6.1.2.

17-*O*-[(2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-(2,6-dideoxy-α-L-galactopyranosyl)]-testosterone (108)



67 mg (0.075 mmol) of glycoconjugate **104** was mixed with polymer-bound TBAT (200 mg) in CH_3CN (10 ml). The reaction mixture was allowed to stir for 48 h, then the polymer was filtered off, washed with methanol and the filtrate was evaporated under reduced pressure. The crude product was purified by column chromatography over silica gel (ethyl acetate, Rf-0.14).

Yield: 29 mg (0.052 mmol, 70%).

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) δ: 5.73 (s, 1H, 4-H), 4.96 (d, J = 4.6 Hz, 1H, 1-H''), 4.95 (d, J = 3.7 Hz, 1H 1-H'), 4.28 (bq, J = 6.5 Hz, 1H, 5-H''), 4.04 (ddd, J = 11.8, 5.9, 3.0 Hz, 1H, 3-H''), 3.98 (ddd, *J* = 11.8, 4.9, 2.0 Hz, 1H, 3-H'), 3.95 (bq, *J* = 6.5 Hz, 1H, 5-H'), 3.62 (bd, *J* = 2.0 Hz, 1H, 4-H'), 3.59 (bd, *J* = 2.2 Hz, 1H, 4-H''), 3.54 (t, *J* = 8.5 Hz, 1H, 17-H), 1.26, 1.21 (2d, *J* = 6.5; 6.4 Hz, 2 x 3H, 6-H', 6-H''), 2.5 – 0.7 (m).

^{13}**C-NMR** (125 MHz, CD_3OD, = 49 ppm): 202.29 (s, C-3), 175.09 (s, C-5), 124.15 (d, C-4), 101.45 (d, C-1''), 99.87 (d, C-1'), 88.58 (d, C-17), 81.72 (d, C-4'), 72.32 (d, C-4''), 68.50 (d, C-5''), 68.14 (d, C-5'), 66.72, 66.70 (2d, C-3'', C-3'), 55.47 (d, C-9), 51.54 (d, C-14), 44.05 (s, C-13), 40.04 (s, C-10), 38.41 (t, C-12), 36.79 (t, C-1), 36.75 (d, C-8), 34.71 (2t, C-2', C-2), 33.88 (t, C-6), 33.30 (t, C-2''), 32.83 (t, C-7), 29.58 (t, C-16), 24.30 (t, C-15), 21.76 (t, C-11), 17.73 (q, C-19), 17.47, 17.10 (2q, C-6', C-6''), 12.09 (q, C-18).

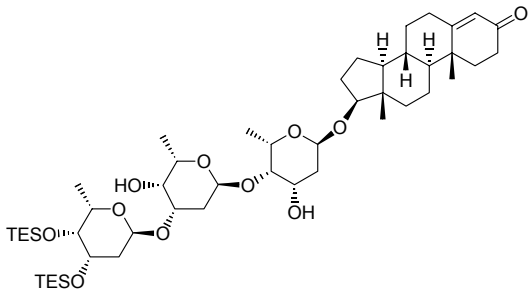
^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 2140 Hz = 4.28: 4.96 (d, 1H, 1-H''), 4.27 (q, 1H, 5-H''), 4.03 (dd, 1H, 3-H''), 3.59 (bd, 1H, 4-H''), 1.97 (ddd, 1H, 2-H_{ax}''), 1.91 (dd, 1H, 2-H_{eq}''), 1.21 (d, 3H, 6-H'').

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 1814 Hz = 3.63: 4.95 (bd, 1H, 1-H'), 3.99 (bd, 1H, 3-H'), 3.97 (bq, 1H, 5-H'), 3.63 (dd, 1H, 4-H'), 1.84 (dd, 1H, 2-H_{ax}'), 1.79 (bdd, 1H, 2-H_{eq}'), 1.20 (d, 3H, 6-H').

LC-MS (ESI) (-c): m/z (%): 547.33 (90) $[M - H]^-$, 548.33 (25) [M]; **HR-MS** $C_{31}H_{47}O_8$: calc. 547.3271, found 547.3278

17-*O*-[(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1→3)-(2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-(2,6-dideoxy-α-L-galactopyranosyl)]-testosterone (109), 17-*O*-[{(3,4-di-*O*-TES-2,6-dideoxy-α-L-galactopyranosyl)-(1→3);(2,6-dideoxy-α-L-galactopyranosyl)-(1→4)}-(2,6-dideoxy-α-L-galactopyranosyl)]-testosterone (110)

To a solution of fucal **22** (24 mg, 0.1 mmol) and glycoconjugate **108** (29 mg, 0.052 mmol) in CH_2Cl_2 (5 ml) was added polymer-bound PPh_3HBr (1mg). The reaction was allowed to stir for 24 h and quenched by addition of Amberlite A-21 (5 mg). The suspension filtrated through a pad of celite and solvent was evaporated under reduced pressure. After column chromatography over silica gel (ethyl acetate / petroleum ether = 1:4) the two products were isolated: trisaccharide **110** and trisaccharide **109**

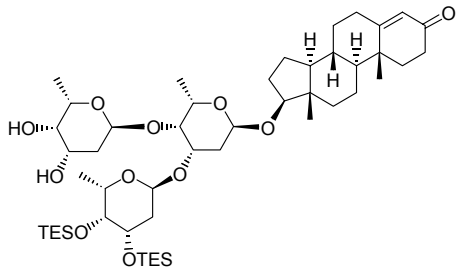


Yield: **109** 25 mg (0.028 mmol, 28% from testosterone).

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.75 (s, 1H, 4-H), 5.09 (d, *J* = 2.5 Hz, 1H'α), 4.96 (d, *J* = 2.2 Hz, 1H''α), 4.91 (bs, 1H'''α), 3.4-4.2 (m, 10H), 2.5 – 0.7 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.94, 171.65, 124.27, 101.08, 98.92, 96.37, 87.44, 83.92, 73.87, 70.31, 68.57, 67.79, 67.56, 66.71, 66.18, 54.32, 50.64, 43.24, 39.06, 36.13, 35.89, 34.36, 33.20, 28.80, 27.32, 23.74, 21.02, 17.82, 17.65, 17.46, 12.03, 7.43, 7.25, 5.63, 5.26.

LC-MS (ESI) (-c): m/z (%): 677.39 (100) $[M - H]^-$; **HR-MS** $C_{37}H_{57}O_{11}$: calc. 677.3901, found 677.3898

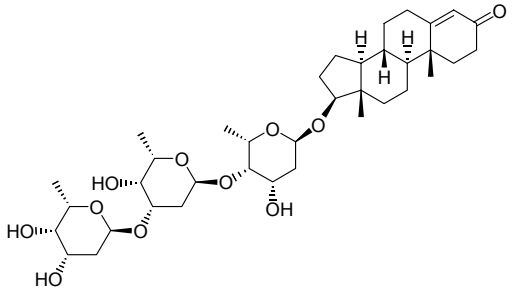


Yield: **110** 18mg (0.023 mmol, 23%, from testosterone)

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.76 (s, 1H, 4-H), 5.12 (d, *J* = 2.7 Hz, 1H, 1-H'), 4.97 (d, *J* = 2.3 Hz, 1H, 1-H''), 4.90 (bs, 1H'''α) 3.8-4.2 (m, 7H), 3.76 (bs, 1H, 4-H'), 3.63 (bs, 2H, 4-H'', 4-H'''), 3.51 (dd, *J* = 8.4, 8.4 Hz, 1H, 17-H), 2.5 – 0.7 (m).

^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.94, 171.65, 124.52+, 97.8+, 95.7+, 95.4+, 87.69+, 74.3+, 73.8+, 71.2+, 70.4+, 69.0+, 68.6+, 67.8+, 67.4+, 65.9+, 54.55+, 50.87+, 37.78-, 36.38-, 36.13+, 34.61-, 33.96-, 33.45-, 32.16-, 31.3-, 30.5-, 29.8-, 27.57-, 23.98-, 21.26-, 18.07+, 17.9+, 17.6+, 16.8+, 12.25+, 7.0+, 6.82+, 6.81+, 5.3-, 4.9-, 4.8-.

17-*O*-[(2,6-dideoxy-α-L-galactopyranosyl)-(1→3)-(2,6-dideoxy-α-L-galactopyranosyl)-(1→4)-(2,6-dideoxy-α-L-galactopyranosyl)]-testosterone (111)



Trisaccharide **109** (25mg, 0.028 mmol) was dissolved in 5 ml of mixture (TBAF /AcOH/THF – 266 mg/0.151 ml/8.4 ml). The solution was stirred overnight, solvent was evaporated under reduced pressure and crude product was purified by column chromatography over silica gel (ethyl acetate/MeOH – 10/1).

Yield: 19.3 mg (0.028 mmol, 99%, R_f- 0.45)

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) δ: 5.72 (s, 1H, 4-H), 5.13 (d, *J* = 2.5 Hz, 1H, 1-H'α), 4.98 (d, *J* = 2.2 Hz, 1H, 1-H''α), 4.95 (bs, 1H, 1-H'''α), 3.9-4.4 (m, 5H), 3.76 (bs, 1H, 4-H''), 3.63 (bs, 1H, 4-H'''), 3.56 (bs, 1H, 4-H'), 3.55 (m, 1H, 17-H), 2.4 – 0.7 (m).

^{13}**C-NMR** (125 MHz, CD_3OD, = 49 ppm): 210.09, 202.30, 175.10, 124.15+, 101.43+, 99.85+, 96.55+, 88.55+, 81.78+, 72.30+, 71.42+, 68.91+, 68.57+, 68.10+, 67.86+, 66.85+, 66.75+, 55.45+, 51.52+, 44.04, 40.03, 38.39-, 36.78-, 36.74+, 34.75-, 34.70-, 33.88-, 33.26-, 32.82-, 31.88-, 30.67-, 29.58-, 24.30-, 21.75-, 17.73+, 17.52+, 17.19+, 17.14+, 17.10+, 12.09+

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 2568 Hz = 5.13: 5.13 (d, 1-H'), 4.00 (m. 3-H', 5-H'), 3.56 (bs, 4-H'), 1.78-1.98 (2m, 2-H'), 1.25 (d, 6-H').

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 2492 Hz = 4.98: 4.98 (d, 1-H''), 4.10 (m. 3-H'', 5-H''), 3.76 (bs, 4-H''), 2.08 (ddd, 2-H''), 1.94 (m, 2-H''), 1.23 (d, 6-H').

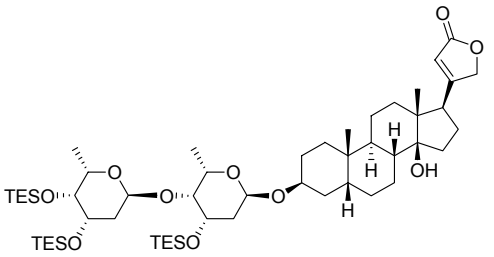
^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 2476 Hz = 4.95: 4.95 (d, 1-H'''), 3.96 (m. 3-H''', 5-H'''), 3.63 (bs, 4-H'''), 1.75-1.89 (m, 2-H'''), 1.20 (d, 6-H''').

Preparation of glycoconjugates 105, 113, 114

To a solution of 3,4-Bis-*O*-TES-fucal (35 mg, 1 mmol) and digitoxigenin (37 mg, 1 mmol) in CH_2Cl_2 (10 ml) polymer-bound PPH_3*HBr (1 mg) was added. The mixture was shaken until no starting material was observed (t.l.c. ethyl acetate / petroleum ether – 1:3). The polymer-bound catalyst was removed by filtration and the solvent was evaporated. The residue was dissolved in methanol (10 ml) and polymer supported fluoride (Amberlite A-26$^{+}F^{-}$, 100mg) was added. The resulting mixture was stirred at 50^{o}C for 20h. Polymer was removed by filtration and the solution was evaporated under reduced pressure. Yielded crude product mixture was involved in next step without purification (observed high ~50% glycoside-bond cleavage). The crude material was dissolved in 10 ml of CH_2Cl_2 and 3-*O*-TES-fucal **46** (30 mg, 1.2 mmol) and polymer-bound PPH_3*HBr (1 mg) were added. The mixture was shaken for 4 h, then 40 mg of 3,4-Bis-*O*-TES-fucal was added and the

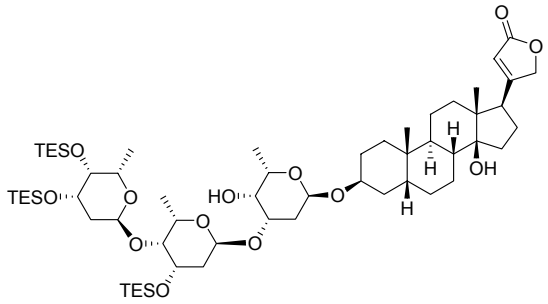
mixture was shaken for another 5 h. The reaction was quenched by addition of Amberlite A-21 (10 mg). The suspension was filtered and the filtrate was evaporated under reduced pressure.

Column chromatography over silica gel (ethyl acetate / petroleum ether - 1:3) yielded three main fractions: *1st fraction* **105** (R_f-48, 28 mg, 28%), *2nd fraction* **114** (R_f-0.21, 9 mg, 7.3%), *3rd fraction* **113** (R_f-0.09, 7 mg, 5.7%).



1st fraction **105**

[1]**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.86 (s, 1H, 22-H), 5.10 (d, *J* = 2.3 Hz, 1H, 1-H'), 4.98 (dd, *J* = 18.1, 1.4 Hz, 1H, 21-H), 4.97 (d, *J* = 2.3 Hz, 1H, 1-H''), 4.79 (dd, *J* = 18.1, 1.4 Hz, 1H, 21-H), 4.2-3.75 (m, 5H), 3.71 (bs, 1H, 4-H'), 3.60 (bs, 1H, 4-H''), 2.25 – 0.0 (m).



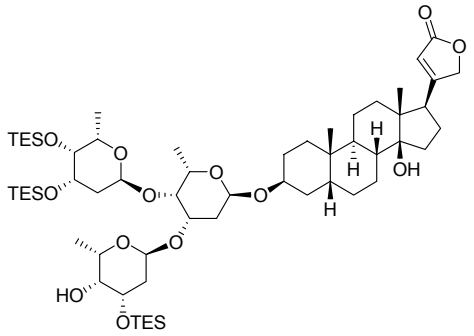
2nd fraction **114**

[1]**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.89 (s, 1H, 22-H), 5.14 (bd, *J* = 2.2 Hz, 1H, 1-H'), 5.05 (bd, *J* = 2.3 Hz, 1H, 1-H''), 4.98 (dd, *J* = 18.1, 1.4 Hz, 1H, 21-H), 4.89 (bd, *J* = 2.1 Hz, 1H, 1-H'''), 4.78 (dd, *J* = 18.1, 1.4 Hz, 1H, 21-H), 4.4-3.5 (m, 9H), 2.78 (m, 1H, 3-H), 2.25 – 0.0 (m).

[13]C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 174.4 (2s, C-20, C-23), 117.7 (d, C-22), 98.5 (d, C-1''), 95.8 (d, C-1'''), 94.2 (d, C-1'), 85.6 (s, C-14), 73.4 (t, C-21), 73.8, 72.3, 71.2, 71.1, 67.7, 67.6, 66.6 (9d, C-3', C-3'', C-3''', C-4', C-4'', C-4''', C-5', C-5'', C-5'''), 66.6 (d, C-3), 50.9 (d, C-17), 49.6 (s, C-13), 41.9 (d, C-8), 40.1 (t, C-12), 36.6, 35.7 (2d, C-5, C-9), 35.2 (s, C-10), 33.2, 32.9 (2t, C-4, C-15), 32.8, 30.5, 30.1 (3t, C-2', C-2'', C-2'''), 29.7 (t, C-1), 26.9, 26.8, 26.7 (3t, C-2, C-6, C-16), 23.8, (q, C-19), 21.4 (t, C-7), 21.2 (t, C-11), 17.9, 17.8, 16.6 (3q, C-6', C-6'', C-6'''),

15.8 (q, C-18), 7.0, 6.83, 6.81, 6.7 (4q, 3 x Si(CH$_2$CH$_3$)$_3$), 5.3, 5.2, 5.0, 4.9, 4.88 (5t, 3 x Si(CH$_2$CH$_3$)$_3$).

LC-MS (ESI) (+c): m/z (%): 1129.68 (30) $[M + Na]^+$; **HR-MS** $C_{59}H_{106}O_{13}Si_3$ +^{23}Na: calc. 1129.6839, found 1129.6831



3rd fraction **113**

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.89 (s, 1H, 22-H), 5.11 (bd, J = 2.2 Hz, 1H, 1-H'), 5.08 (bd, J = 2.2 Hz, 1H, 1-H''), 4.98 (dd, J = 18.1, 1.4 Hz, 1H, 21-H), 4.99 (bd, J = 2.1 Hz, 1H, 1-H'''), 4.78 (dd, J = 18.1, 1.4 Hz, 1H, 21-H), 4.4-3.5 (m, 9H), 2.80 (m, 1H, 3-H), 2.25 – 0.0 (m).

^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 174.4 (s, C-20), 174.3 (s, C-23), 117.7 (d, C-22), 97.9 (d, C-1''), 95.6 (d, C-1'), 95.5 (d, C-1'''), 85.6 (s, C-14), 73.4 (C-21), 74.7, 73.9, 71.3, 70.4, 68.3, 68.2, 67.6, 67.5, 65.6 (9d, C-3', C-3'', C-3''', C-4', C-4'', C-4''', C-5', C-5'', C-5'''), 66.7 (d, C-3), 51.0 (d, C-17), 49.6 (s, C-13), 41.9 (d, C-8), 40.1 (t, C-12), 36.5, 35.7 (2d, C-5, C-9), 35.2 (s, C-10), 33.2 (t, C-4, C-15), 31.3, 30.5, 29.8 (3t, C-2', C-2'', C-2'''), 29.7 (t, C-1), 26.9, 26.6 (3t, C-2, C-6, C-16), 23.8 (q, C-19), 21.4 (t, C-7), 21.2 (t, C-11), 17.9, 17.6, 16.8 (3q, C-6', C-6'', C-6'''), 15.8 (q, C-18), 7.0, 6.82, 6.81 (3q, 3 x Si(CH$_2$CH$_3$)$_3$), 5.3, 4.9, 4.8 (3t, 3 x Si(CH$_2$CH$_3$)$_3$).

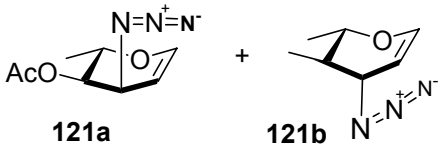
LC-MS (ESI) (+c): m/z (%): 1129.65 (30) $[M + Na]^+$; **HR-MS** $C_{59}H_{106}O_{13}Si_3$ +^{23}Na: calc. 1129.6839, found 1129.6799

11.5.3. Experiments to the chapter 6.1.3.

α-L-Erythro-hex-2-enopyranosylazide (120a), β-L-erythro-hex-2-enopyranosylazide (120b), 3-azido-4-*O*-acetyl-1,5-anhydro-2,3,6-trideoxy-L-ribo-hex-1-enit (121a), 3-azido-4-*O*-acetyl-1,5-anhydro-2,3,6-trideoxy-L-arabino-hex-1-enit (121b)

3,4-Di-*O*-acetyl-L-rhamnal **17** (1 g, 4.7 mmol) and solid NaN_3 (0.79 g, 0.012 mol) were suspended in 10 ml of abs. acetonitrile and 1 g of powdered molecular sieves 4A was added. After cooling down to –30° C BF_3*Et_2O (1.35 ml) was added dropwise within 30 min. The suspension was stirred at the same temperature for another 1h, then sodium bicarbonate (1 g) was added to the reaction mixture to neutralize the Lewis acid. The mixture was allowed to warm up with stirring within 30 min to RT. The resulted slurry was filtered, washed with ethyl acetate and the solvent was evaporated. The raw material was dissolved in ethyl acetate and washed with brine. The organic phase was separated and the solvent evaporated under reduced pressure. The crude product mixture was purified by column chromatography (ethyl acetate / petroleum ether 1:10) yielding colourless oil - mixture of Fierier product and glycal type product.

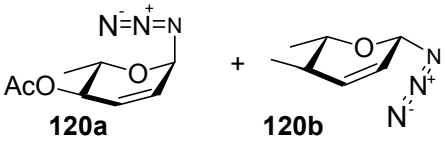
Yield: 0.9 g (4.6 mmol, 98%).



121a **121b**

121ab *(Glycal)*

[1]**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 6.53 (d, *J* = 6.0 Hz, 1H, 1-H), 4.87 (dd, *J* = 5.2, 5.2 Hz, 1H, 4-H), 4.3-3.9 (m, 2H, 3-H, 5-H), 2.19 (s, 3H, Ac), 1.34 (d, *J* = 6.4 Hz, 3H, 6-H).

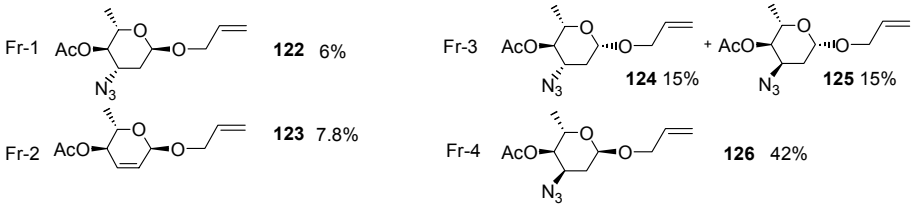


120a **120b**

120ab *(Ferier product)*

[1]**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.95 (bd, *J* = 10.1, 1H, 2-H), 5.77 (ddd, *J* = 10.1, 1.9, 3.0 Hz, 1H, 3-H), 5.50 (bs, 1H, 1-H), 5.09 (ddd, *J* = 9.0, 3.0, 1.9 Hz, 1H, 4-H), 3.98 (dq, *J* = 9.0, 6.3 Hz, 1H, 5-H), 1.29 (d, *J* = 6.3 Hz, 3H, 6-H).

Preparation of allylglycosides 122, 123, 126



Polymer-bound PPh_3*HBr (500 mg) was added to a solution of azidoglycal mixture **121ab** (1.0 g, 5 mmol) and allyl alcohol 1.7 ml (25 mmol, 5 eq) in 10 ml of dry CH_2Cl_2. The suspension was stirred at ambient temperature for 48 h. The reaction was quenched by addition of Amberlite A-21 (500 mg) and filtered through a pad of Celite. The solvent was removed under reduced pressure and the residue was purified by column chromatography (ethyl acetate / petroleum ether 1:10) to obtain four fractions.

Yield: *1st fraction:* **122** (77 mg, 0.302 mmol 6 %),
2nd fraction: **123** (100 mg, 0.47 mmol 7.8%),
3rd fraction: mixture containing **124** and **125** - 1:1
4th fraction: **126** (530 mg, 2.08 mmol 42 %),

1st fraction

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.88 (dddd, *J* = 17.2, 10.0, 6.0, 5.2 Hz, 1H, –C*H*=CH_2), 5.28 (dq, *J* = 17.2, 1.5 Hz, 1H, –CH=CH*H*'), 5.18 (dq, *J* = 10.0, 1.3 Hz, 1H, –CH=CH*H*'), 4.87 (d, *J* = 3.1 Hz, 1H, 1-H), 4.64 (dd, *J* = 9.7, 9.7 Hz, 1H, 4-H), 4.11 (ddt, *J* = 12.7, 5.2, 1.49 Hz, 1H, -*O*-CH*H*'-CH=), 3.93 (ddt, *J* = 12.7, 6.0, 1.3 Hz, 1H, -*O*-CH*H*'-CH=), 3.87 (ddd, *J* = 12.3, 9.7, 5.0 Hz, 1H, 3-H), 3.78 (dq, *J* = 9.7, 6.2 Hz, 1H, 5-H), 2.15 (ddd, *J* = 13.0, 5.0, 0.9 Hz, 1H, 2-H), 2.10 (s, 3H, AcO), 1.72 (ddd, *J* = 13.0, 12.3, 3.5 Hz, 1H, 2-H), 1.13 (d, *J* = 6.2 Hz, 3H, 6-H)

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 169.93 (s, C=O), 133.77 (d, -*C*H=CH_2), 117.28 (t, –CH=*C*H_2), 95.41 (d, C-1), 75.47 (d, C-4)), 67.84 (t, –*C*H_2-CH=), 65.97 (d, C-5), 57.63 (d, C-3), 35.11 (t, C-2), 20.76 (q, CO*C*H_3), 17.34 (q, C-6).

2nd fraction

^{1}H-NMR (400 MHz, $CDCl_3$, $CDCl_3$ =7.26 ppm) δ: 5.90 (dddd, *J* = 17.2, 10.4, 6.1, 5.1 Hz, 1H, –C*H*=CH_2), 5.82 (d, *J* = 10.2 Hz, 1H, 2-H), 5.77 (ddd, *J* = 10.2, 2.3, 1.5 Hz, 1H, 3-H), 5.27 (dq, *J* = 17.2, 1.4 Hz, 1H, –CH=CH*H*'), 5.16 (ddt, *J* = 10.4, 1.4, 1.3 Hz, 1H, –CH=CH*H*'), 5.02 (dq, *J* = 9.2, 1.5 Hz, 1H, 4-H), 4.97 (s, 1H, 1-H), 4.22 (ddt, *J* = 12.8, 5.1, 1.4 Hz, 1H, -*O*-CH*H*'-CH=), 4.03 (ddt, *J* = 12.8, 6.1, 1.2 Hz, 1H, -*O*-CH*H*'-CH=), 3.95 (dq, *J* = 9.2, 6.3 Hz, 1H, 5-H), 2.05 (s, 3H, AcO), 1.19 (d, *J* = 6.3 Hz, 3H, 6-H)

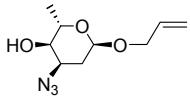
^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 170.36 (s, C=O), 134.36 (d, -*C*H=CH_2), 129.66, 127.69 (2d, C-2, C-3), 117.12 (t, –CH=*C*H_2), 93.50 (d, C-1), 70.82 (d, C-4), 68.97 (t, –*C*H_2-CH=), 64.76 (d, C-5), 20.94 (q, CO*C*H_3), 17.83 (q, C-6).

4th fraction

^{1}H-NMR (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.80 (dddd, *J* = 17.2, 10.5, 5.8, 4.7 Hz, 1H, –C*H*=CH_2), 5.22 (dddd, *J* = 17.2, 1.7, 1.6, 1.6 Hz, 1H, –CH=CH*H*'), 5.06 (dddd, *J* = 10.4, 1.5, 1.5, 1.4 Hz, 1H, –CH=CH*H*'), 4.71 (dd, *J* = 4.2, 1.2 Hz, 1H, 1-H), 4.53 (dd, *J* = 9.5, 3.7 Hz, 1H, 4-H), 4.13 (bq, *J* = 9.5, 6.4 Hz, 1H, 5-H), 4.08 (m, 1H, -*O*-C*H*$_2$-CH=), 4.01 (bddd, *J* = 3.7, 3.7, 3.7 Hz, 1H, 3-H), 3.86 (dddd, *J* = 13.3, 5.9, 1.3, 1.3 Hz, 1H -*O*-C*H*$_2$-CH=), 2.02 (ddd, *J* = 14.8, 3.2, 1.2 Hz, 1H, 2-H_{ax}), 2.00 (s, 3H, AcO), 1.94 (ddd, *J* = 14.8, 4.1, 3.7 Hz, 1H, 2-H_{eq}), 1.06 (d, *J* = 6.4 Hz, 3H, 6-H)

^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 169.64 (s, C=O), 133.80 (d, -*C*H=CH_2), 116.47 (t, –CH=*C*H_2), 94.18 (d, C-1), 73.56 (d, C-4), 67.77 (t, –*C*H_2-CH=), 61.61 (d, C-5), 55.31 (d, C-3), 32.40 (t, C-2), 20.31 (q, CO*C*H_3), 16.90 (q, C-6).

Allyl-3-azido-2,3,6-trideoxy-α-L-allopyranoside (126a)



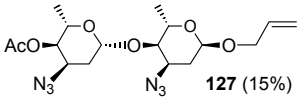
The reaction was carried out according to the protocol **TP8** except for the following details: starting material **126** (430 mg, 1.68 mmol).

Yield: 358 mg (1.67 mmol, >99%).

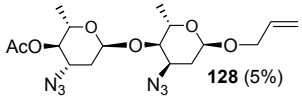
^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.89 (dddd, *J* = 17.2, 10.5, 5.7, 4.8 Hz, 1H, –C*H*=CH_2), 5.31 (dq, *J* = 17.2, 1.5 Hz, 1H, –CH=CH*H*'), 5.15 (dq, *J* = 10.5, 1.5 Hz, 1H, –CH=CH*H*'), 4.80 (d, *J* = 4.0 Hz, 1H, 1-H), 4.17 (ddt, *J* = 13.4, 4.8, 1.5 Hz, 1H, -*O*-CH*H*'-CH=), 4.03 (ddd, *J* = 3.7, 3.4, 3.7 Hz, 1H, 3-H), 3.93 (ddt, *J* = 13.4, 5.7, 1.4 Hz, 1H, -*O*-CH*H*'-CH=), 3.87 (dq, *J* = 9.3, 6.3 Hz, 1H, 5-H), 3.30 (ddd, *J* = 9.4, 9.3, 3.7 Hz, 1H, 4-H), 2.23 (d, J = 9.4 Hz, 1H, OH), 2.21 (ddd, *J* = 14.9, 3.4, 1.2 Hz, 1H. 2-H_{ax}), 2.02 (dt, *J* = 14.9, 4.0, Hz, 1H, 2-H_{eq}), 1.23 (d, *J* = 6.3, Hz, 3H, 6-H)

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 134.11 (d, -*C*H=CH_2), 116.34 (t, –CH=*C*H_2), 94.27 (d, C-1), 72.05 (d, C-4), 67.90 (t, –*C*H_2-CH=), 64.50 (d, C-5), 58.06 (d, C-3), 32.12 (t, C-2), 17.36 (q, C-6).

Preparation of disaccharides 127 and 128



127 (15%)



128 (5%)

Polymer-bound PPh_3*HBr (20 mg) was added to a solution of azidoglycal mixture **121ab** (335 mg, 1.7 mmol, 1.1 eq) and allylglycoside **126a** (350 mg, 1.65 mmol) in 10 ml of CH_2Cl_2. The suspension was stirred for 48 h at RT. The reaction mixture was quenched by addition of Amberlite A-21 (20 mg), filtered through a pad of Celite and concentrated under reduced pressure. The products were finally separated by flash column chromatography over silica gel (ethyl acetate / petroleum ether 1:10). The four fractions were isolated:

1st fraction: adduct mixture **121a,b** (183 mg, 0.92 mmol, 55%)

2nd fraction: **127** (100 mg, 0.24 mmol, 15%),

3rd fraction: mixture fraction (30 mg).

4th fraction: **128** (30 mg, 0.073 mmol, 5%).

2nd fraction

^{1}H-NMR (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.87 (dddd, *J* = 17.0, 10.2, 5.9, 5.0 Hz, 1H, –C*H*=CH_2), 5.28 (dq, *J* = 17.0, 1.5 Hz, 1H, –CH=CH*H*'), 5.13 (dq, *J* = 10.2, 1.4 Hz, 1H, –CH=CH*H*'), 4.76 (dd, *J* = 9.2, 1.5 Hz, 1H, 1-H'), 4.73 (d, *J* = 4.2 Hz, 1H, 1-H), 4.60 (dd, *J* = 9.7, 3.3 Hz, 1H, 4-H'), 4.13 (m, 3H), 4.05 (dq, *J* = 9.5, 6.2 Hz, 1H), 3.93 (m, 2H), 3.37 (dd, *J* = 9.4, 3.5 Hz, 1H, 4-H), 2.09 (s, 3H, AcO), 2.00 (m, 2H), 1.93 (ddd, *J* = 14.9, 4.3, 4.3 Hz, 1H), 1.82 (ddd, *J* = 13.9, 9.4, 3.3 Hz, 1H), 1.18 (d, *J* = 6.0 Hz, 3H), 1.17 (d, *J* = 6.2 Hz, 3H)

^{13}C-NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 169.82 (s, *C*OCH_3), 134.13 (d, -*C*H=CH_2), 116.88 (t, –CH=*C*H_2), 99.06 (d, C-1'), 94.29 (d, C-1), 81.38 (d, C-4), 74.18 (d, C-4'), 67.87 (t, –*C*H_2-CH=), 67.65 (d, C-5'), 62.26 (d, c-5), 2 x 58.01 (2d, C-3, C-3'), 35.71 (t, C-2'), 33.33 (t, C-2), 20.46 (q, CO*C*H_3), 17.72, 17.34 (2q, C-6, C-6').

^{1}H-NMR (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2949Hz = 5.90ppm: 5.89 (ddd, 1H, –C*H*=CH_2), 5.31 (dd, 1H, –CH=CH*H*'), 5.16 (d, 1H, –CH=CH*H*'), 4.15 (dd, 1H, -*O*-CH*H*'-CH=), 3.96 (dd, 1H, -*O*-CH*H*'-CH=).

^{1}H-NMR (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2316Hz = 4.63ppm: 4.79 (dd, 1H, 1-H'), 4.63 (dd, 1H, 4-H'), 4.18 (ddd, 1H, 3-H'), 3.93 (dq, 1H, 5-H'), 2.05 (dd, 1H, 2-H'$_{ax}$), 1.86 (dd, 1H, 2-H'$_{eq}$), 1.20 (dd, 3H, 6-H').

^{1}H-NMR (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2380Hz = 4.76ppm: 4.76 (d, 1H, 1-H), 4.15 (ddd, 1H, 3-H), 4.08 (dq, 1H, 5-H), 3.40 (dd, 1H, 4-H), 2.05 (dd, 1H, 2-H_{ax}), 1.95 (ddd, 1H, 2-H_{eq}), 1.19 (d, 3H, 6-H).

4th fraction

^{1}H-NMR (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.91 (dddd, *J* = 17.0, 10.5, 5.8, 5.1 Hz, 1H, –C*H*=CH_2), 5.32 (dq, *J* = 17.0, 1.5 Hz, 1H, –CH=CH*H*'), 5.17 (dq, *J* = 10.5, 1.4 Hz, 1H, –CH=CH*H*'), 5.07 (d, *J* = 3.4 Hz, 1H, 1-H'), 4.81 (d, *J* = 3.4 Hz, 1H, 1-H), 4.66 (dd, *J* = 9.7, 9.6 Hz, 1H, 4-H'), 4.19 (m, 2H), 4.10 (ddd, *J* = 4.0, 3.6, 3.6 Hz, 1H, 3-H), 3.97 (dd, *J* = 13.1, 6.0 Hz, -*O*-CH*H*'-CH=), 3.81 (dq, *J* = 9.7, 6.3 Hz, 1H, 5-H'), 3.47 (bdd, *J* = 9.0, 3.6 Hz, 1H, 4-H), 2.23 (dd, *J* = 13.3, 5.0 Hz, 1H,

2-H'$_{ax}$), 2.18 (ddd, *J* = 14.8, 1.3, 3.6 Hz, 1H, 2-H$_{ax}$), 2.12 (s, 3H, AcO), 1.97 (ddd, *J* = 14.8, 4.2, 4.0 Hz, 1H, 2-H$_{eq}$), 1.77 (ddd, *J* = 13.3, 12.8, 3.4 Hz, 1H, 2-H'$_{eq}$), 1.27 (d, *J* = 6.4 Hz, 3H, 6-H), 1.15 (d, *J* = 6.3 Hz, 3H, 6-H').

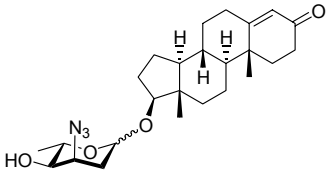
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 169.94 (s, *C*OCH$_3$), 134.06 (d, -*C*H=CH$_2$), 116.88 (t, –CH=*C*H$_2$), 94.48 (d, C-1), 92.35 (d, C-1'), 75.22 (d, C-4'), 68.11 (t, –*C*H$_2$-CH=), 66.75 (d, C-5'), 62.94 (d, C-5), 57.43 (d, C-3'), 53.45 (d, C-3), 34.72 (t, C-2'), 32.31 (t, C-2), 20.79 (q, CO*C*H$_3$), 18.14 (q, C-6), 17.30 (q, C-6').

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2969Hz = 5.93ppm: 5.93 (dd, 1H, –C*H*=CH$_2$), 5.35 (dq, 1H, –CH=CH*H*'), 5.20 (d, 1H, –CH=CH*H*'), 4.22 (dd, 1H, -*O*-CH*H*'-CH=), 4.00 (dd, 1H, -*O*-CH*H*'-CH=).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2348Hz = 4.69ppm: 5.10 (d, 1H, 1-H'), 4.69 (dd, 1H, 4-H'), 3.86 (ddd, 1H, 3-H'), 3.48 (dq, 1H, 5-H'), 2.25 (ddd, 1H, 2-H'$_{ax}$), 1.80 (ddd, 1H, 2-H'$_{eq}$), 1.18 (d, 3H, 6-H')

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 1753Hz = 3.51ppm: 4.84 (d, 1H, 1-H), 4.18 (dq, 1H, 5-H), 4.13 (ddd, 1H, 3-H), 3.51 (dd, 1H, 4-H), 2.21 (ddd, 1H, 2-H$_{ax}$), 2.00 (ddd, 1H, 2-H$_{eq}$), 1.29 (d, 3H, 6-H).

Testosteryl-3-azido-2,3,6-trideoxy-α-L-allopyranoside (129), testosteryl-3-azido-2,3,6-trideoxy-α-L-allopyranoside (130)



To a stirred mixture of testosterone 73 mg (0.25 mmol) and azidoglycal mixture **121ab** 50 mg (0.25 mmol) in dry CH_2Cl_2 (5 ml) polymer-bound PPh_3*HBr (2 mg) was added. The stirring was continued for 24 h, followed by quenching with Amberlite A-21 (10 mg). The mixture was filtered through a pad of Celite and the solvent was removed under reduced pressure. The products were finally separated by flash column chromatography over silica gel (ethyl acetate / petroleum ether 3:1) to afford the glycoconjugate 4-*O*-Ac-**129** (16 mg, 0.033 mmol, 13.2%),

glycoconjugate 4-*O*-Ac-**130** (15 mg, 0.031 mmol, 12.4%) and a mixture of both diastereomers (26 mg, 0.054 mmol, 21.6%).
The both products were separately deacetylated using the protocol **TP8**.

Yield: **129** (11.2 mg, 0.0253 mmol, 82%).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (s, 1H, 4-H), 4.83 (d, *J* = 3.8 Hz, 1H, 1-H'), 4.57 (dd, *J* = 9.6, 3.4 Hz, 1H, 4-H'), 4.22 (dq, *J* = 9.6, 6.2 Hz, 1H, 5-H'), 4.15 (ddd, *J* = 3.4, 3.4, 3.4 Hz, 1H, 3-H'), 3.45 (dd, *J* = 8.5, 8.5 Hz, 1H, 17-H), 2.5 – 0.7 (m).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.50 (s, C-3), 171.21 (s, C-5), 170.12 (s, C=O), 123.84 (d, C-4), 96.27 (d, C-1'), 88.36 (d, C-17), 73.55 (d, C-4'), 61.98 (d, C-5'), 55.01 (d, C-3), 53.92 (d, C-9), 50.08 (d, C-14), 42.98 (s, C-13), 38.64 (s, C-10), 37.05 (t, C-12), 35.72 (t, C-1), 35.42 (d, C-8), 33.93 (t, C-2), 32.77 (t, C-6), 32.29 (t, C-2'), 31.52 (t, C-7), 28.62 (t, C-16), 23.43 (t, C-15), 20.84 (q, CO*C*H_3), 20.58 (t, C-11), 17.39 (q, C-19), 17.15 (q, C-6'), 11.65 (q, C-18).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** = 2433Hz- 4.86ppm: 4.86 (d, 1H, 1-H'), 4.59 (dd, 1H, 4-H'), 4.25 (dq, 1H, 5-H'), 4.18 (ddd, 1H, 3-H'), 2.22 (dd, 1H, 2-H'$_{ax}$), 2.05 (dd, 1H, 2-H'$_{eq}$), 1.16 (d, 3H, 6-H')

Yield: **130** (11.6 mg, 0.0262 mmol, 80%),

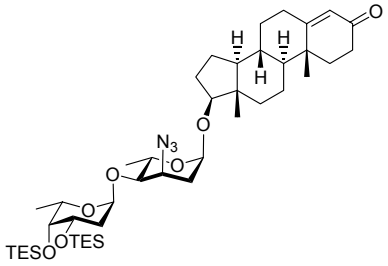
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.71 (s, 1H, 4-H), 4.66 (dd, *J* = 9.2, 2.3 Hz, 1H, 1-H'), 4.65 (dd, *J* = 9.3, 3.5 Hz, 1H, 4-H'), 4.16 (ddd, *J* = 3.5, 3.5, 3.5 Hz, 1H, 3-H'), 3.89 (dq, *J* = 9.3, 6.2 Hz, 1H, 5-H', 3.64 (dd, *J* = 8.4, 8.4 Hz, 1H, 17-H), 2.26 (ddd, *J* = 14.3, 4.0, 2.3 Hz, 1H), 1.68 (ddd, *J* = 14.3, 13.9, 4.8 Hz, 1H), 1.20 (d, *J* = 6.2 Hz, 3H, 6-H'), 2.5 – 0.7 (m).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.55 (s, C-3) , 171.21 (s, C-5), 170.13 (s, *C*=O), 123.82 (d, C-4), 96.42 (d, C-1'), 87.23 (d, C-17), 74.37 (d, C-4'), 67.96 (d, C-5'), 58.04 (d, C-3'), 53.95 (d, C-9), 50.62 (d, C-14), 42.40 (s, C-13), 38.64 (s, C-10), 37.00 (t, C-12), 36.56 (t, C-2'), 35.72 (t, C-1), 35.48 (d, C-8), 33.95

(t, C-2), 32.79 (t, C-6), 31.56 (t, C-7), 27.52 (t, C-16), 23.15 (t, C-15), 20.65 (q, CO*C*H$_3$), 20.57 (t, C-11), 17.90 (q, C-6'), 17.39 (q, C-19), 11.63 (q, C-18).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** = 2096 Hz - 4.19ppm: 4.68 (dd, 1H, 1-H'), 4.67 (dd, 1H, 4-H'), 4.19 (ddd, 1H, 3-H'), 3.92 (dq, 1H, 5-H'), 2.01 (ddd, 1H, 2-H'$_{ax}$), 1.83 (ddd, 1H, 2-H'$_{eq}$), 1.23 (d, 3H, 6-H')

Glycosidation of testosteryl-3-azido-2,3,6-trideoxy-α-L-allopyranoside (131)



To a stirred solution of **129** 11.2 mg (0.0253 mmol) and glycal **22** (10 mg, 1.05 eq) in dry CH_2Cl_2 (5 ml) polymer-bound PPh_3HBr (0.5 mg) was added. The stirring was continued for 24 h, followed by addition of Amberlite A-21 (5 mg). The mixture was filtered through a pad of Celite and concentrated under reduced pressure. The residue was purified by column chromatography.

Yield: 16.1 mg (0.02 mmol 80 %).

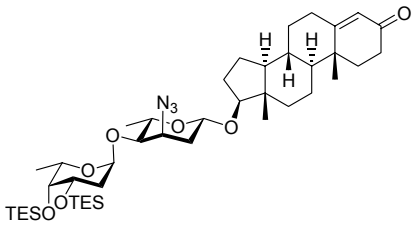
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (s, 1H, 4-H), 5.09 (d, *J* = 3.1 Hz,1H, 1-H''), 4.80 (d, *J* = 3.8 Hz, 1H, 1-H'), 4.12 (m, 2H, 3-H', 5-H'), 3.96 (ddd, *J* = 11.6, 2.4, 4.1 Hz, 1H, 3-H''), 3.74 (q, *J* = 6.3 Hz, 1H, 5-H''), 3.59 (s, 1H, 4-H''), 3.45 (dd, *J* = 8.5, 8.5 Hz, 1H, 17-H), 3.37 (dd, *J* = 9.0, 3.2 Hz, 1H, 4-H'), 2.5 – 0.7 (m).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.47 (s, C-3), 171.23 (s, C-5), 123.84 (d, C-4), 96.50 (d, C-1'), 93.41 (d, C-1''), 88.20 (d, C-17), 74.19 (d, C-4'), 73.40 (d, C-4''), 68.27 (d, C-5''), 67.50 (d, C-3''), 63.18 (d, C-3'), 53.98 (d, C-9), 52.94 (d, C-5'), 50.19 (d, C-14), 42.97 (s, C-13), 38.67 (s, C-10), 37.11 (t, C-12), 35.75 (t, C-1), 35.46 (d, C-8), 33.95 (t, C-2), 32.80 (t, C-6), 32.32 (t, C-2'), 32.27 (t, C-2''), 31.57 (t, C-7), 28.70 (t, C-16), 23.44 (t, C-15), 20.61 (t, C-11), 17.77 (q, C-19), 17.41 (q, C-6'), 17.26 (q, C-6''), 11.67 (q, C-18), 7.00, 6.80, 5.23, 4.81 (2t, 2q, 2 x TES).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2558Hz = 5.12ppm: 5.11 (d, 1H, 1-H''), 3.98 (ddd, 1H, 3-H''), 3.77 (q, 1H, 5-H''), 3.62 (s, 1H, 4-H''), 2.11 (ddd, 1H, 2-H''$_{ax}$), 1.67 (dd, 1H, 2-H''$_{eq}$), 1.19 (d, 3H, 6-H'')

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2415Hz = 4.83ppm: 4.83 (d, 1H, 1-H') 4.13 (m, 2H, 3-H', 5-H'), 3.39 (dd, 1H, 4-H'), 2.20 (dd, 1H, 2-H'$_{ax}$), 1.94 (ddd, 1H, 2-H'$_{eq}$), 1.21 (d, 3H, 6-H').

Glycosidation of testosteryl-3-azido-2,3,6-trideoxy-β-L-allopyranoside (132)



To a stirred solution of **130** 11.6 mg (0.026 mmol) and glycal **22** (10 mg, 1.05 eq) in dry CH_2Cl_2 (5 ml) polymer-bound PPh_3HBr (0.5 mg) was added. The stirring was continued for 24 h, followed by addition of Amberlite A-21 (5 mg). The mixture was filtered through a pad of Celite and concentrated under reduced pressure. The residue was purified by column chromatography.

Yield: 14.6 mg (0.0182 mmol, 70%).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (s, 1H, 4-H), 5.08 (d, *J* = 3.1 Hz, 1H, 1-H''), 4.65 (dd, *J* = 9.0, 1.5 Hz, 1H, 1-H'), 4.17 (ddd, *J* = 3.2, 3.2, 3.2 Hz, 1H, 3-H'), 3.95 (ddd, *J* = 11.7, 4.1, 2.4 Hz, 1H, 3-H''), 3.85 (dq, *J* = 8.9, 6.2 Hz, 1H, 5-H'), 3.79 (bq, *J* = 6.3 Hz, 1H, 5-H''), 3.64 (dd, *J* = 8.3, 8.3 Hz, 1H, 17-H), 3.60 (bs, 1H, 4-H''), 3.53 (dd, *J* = 8.9, 3.2 Hz, 1H, 4-H'), 1.25 (d, *J* = 6.2 Hz, 3H, 6-H'), 1.16 (d, *J* = 6.3 Hz, 3H, 6-H''), 2.5 – 0.7 (m).

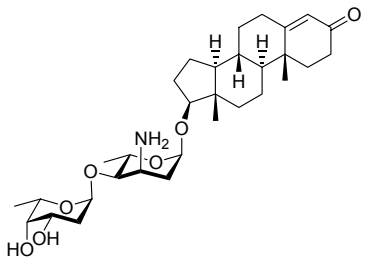
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.50 (s, C-3), 171.26 (s, C-5), 123.83 (d, C-4), 96.58 (d, C-1'), 94.33 (d, C-1''), 87.14 (d, C-17), 75.44 (d, C-4'), 73.36 (d, C-4''), 69.02 (d, C-5'), 68.41 (d, C-5''), 67.43 (d, C-3''), 55.80 (d, C-3'), 53.99 (d, C-9), 50.64 (d, C-14), 42.40 (s, C-13), 38.66 (s, C-10), 36.61 (t, C-12),

35.74 (t, C-1), 35.72 (t, C-2'), 35.51 (d, C-8), 33.96 (t, C-2), 32.81 (t, C-6), 31.95 (t, C-2''), 31.59 (t, C-7), 27.52 (t, C-16), 23.17 (t, C-15), 20.60 (t, C-11), 18.53 (q, C-6'), 17.41 (q, C-19), 17.22 (q, C-6''), 11.63 (q, C-18), 6.99, 6.77, 5.21, 4.79 (2t, 2q, 2 x TES).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2557Hz = 5.11ppm: 5.11 (d, 1H, 1-H''), 3.98 (ddd, 1H, 3-H''), 3.81 (q, 1H, 5-H''), 3.62 (bs, 1H, 4-H''), 2.12 (ddd, 1H, 2-H''$_{ax}$), 1.69 (dd, 1H, 2-H''$_{eq}$), 1.18 (d, 3H, 6-H'')

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2340Hz = 4.68ppm: 4.68 (d, 1H, 1-H'), 4.19 (ddd, 1H, 3-H'), 3.87 (q, 1H, 5-H'), 3.56 (dd, 1H, 4-H'), 1.98 (ddd, 1H, 2-H'$_{ax}$), 1.69 (ddd, 1H, 2-H'$_{eq}$), 1.27 (d, 3H, 6-H')

Preparation of aminoglycoconjugate 133



A solution of TBAF (1M, 0.06 ml, 3 eq) in THF was added to a solution of glycoconjugate **131** (16.1 mg, 0.02 mmol) in THF (1 ml). After the solution was stirred for 4 h, polymer bound PPH_3 (20 mg, 1.1 mmol/g) was added. The suspension was stirred at room temperature for 24 h and the polymer was filtered off. The resulting solution was evaporated under reduced pressure and the residue was purified by column chromatography (ethyl acetate / EtOH 6:1). The product was converted to an acetic acid salt to improve the stability.

Yield: 10 mg (0.0183 mmol, 91%).

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) δ: 5.75 (s, 1H, H-4), 5.10 (d, *J* = 3.3 Hz, 1H, 1-H''), 4.92 (d, *J* = 2.8 Hz, 1H, 1-H'), 3.98 (m, 3H), 3.61 (bd, *J* = 2.6 Hz, 1H, 4-H''), 3.59 (t, *J* = 8.5 Hz, 1H, 17-H), 3.52 (dd, *J* = 7.1, 3.8 Hz, 1H, 3-H'), 3.46 (dd, *J* = 9.4, 3.8 Hz, 1H, 4-H'), 2.6 – 0-7 (m).

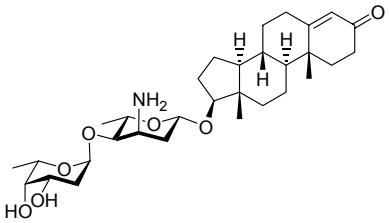
^{13}**C-NMR** (125 MHz, CD_3OD, = 49 ppm) δ: 202.27 (s, C-3), 174.98 (s, C-5), 124.18 (d, C-4), 99.07 (d, C-1'), 95.36 (d, C-1''), 89.70 (d, C-17), 76.33 (d, C-4'), 72.13 (d, C-4''), 68.51 , 66.83 (2d, C-3'', C-5''), 63.38 (d, C-5'), 55.42 (d, C-9), 51.35 (d, C-14), 45.62 (d, C-3''), 44.04 (s, C-13), 40.02 (s, C-10), 38.29 (t, C-12), 36.79 (t, C-1), 36.74 (d, C-8), 34.70 (t, C-2), 34.22 (t, C-2'), 33.86 (t, C-6), 32.97 (t, C-2''), 32.80 (t, C-7), 29.78 (t, C-16), 24.34 (t, C-15), 23.00 (q, CH_3COO^-), 21.73 (t, C-11), 18.62 (q, C-19), 17.72, 17.10 (2q, C-6', C-6''), 12.24 (q, C-18).

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 2542Hz = 5.08ppm: 5.08 (d, 1H, 1-H''), 3.95 (m, 2H, 3-H', 5-H''), 3.59 (d, 1H, 4-H''), 1.98 (ddd, 1H, 2-H''$_{ax}$), 1.84 (dd, 1H, 2-H''$_{eq}$), 1.24 (d, 3H, 6-H'').

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 2456Hz = 4.91ppm: 4.91 (d, 1H, 1-H'), 3.98 (dq, 1H, 5-H'), 3.50 (ddd, 1H, 3-H'), 3.44 (dd, 1H, 4-H'), 2.08 (dd, 1H, 2-H'$_{ax}$), 1.97 (ddd, 1H, 2-H'$_{eq}$), 1.25 (d, 3H, 6-H').

LC-MS (ESI) (-c): m/z (%): 546.34 (60) $[M - H]^-$; **HR-MS** $C_{31}H_{48}NO_7$: calc. 546.3431, found 546.3431

Preparation of aminoglycoconjugates 134



The reaction was carried out according to the experiment **133**: starting material **132** 14.6 mg (0.0182 mmol)

Yield: 7.1 mg (0.013 mmol, 71%)

^{1}**H-NMR** (500 MHz, CD_3OD, CD_3OD, = 3.35 ppm) δ: 5.75 (s, 1H, 4-H), 5.07 (d, *J* = 3.4 Hz, 1H, 1-H''), 4.93 (dd, *J* = 7.1, 2.6 Hz, 1H, 1-H'), 3.97 (m, 3H), 3.77 (t, *J* = 8.1, 8.1 Hz, 1H, H-17), 3.73 (bq, *J* = 6.2 Hz, 1H, 5-H''), 3.61 (bs, 1H, 4-H''), 3.53 (dd, *J* = 7.0, 3.6 Hz, 1H, 4-H'), 2.5-0.7 (m).

^{13}**C-NMR** (125 MHz, CD_3OD, = 49 ppm) δ: 202.32 (s, C-3), 175.11 (s, C-5), 124.14 (d, C-4), 97.66 (d, C-1''), 97.01 (d, C-1'), 87.31 (d, C-17), 77.14 (d, C-4'), 72.13 (d, C-4''), 70.66 (d, C-3'), 68.49 (d, C-3''), 66.83 (d, C-5''), 55.51 (d, C-9), 51.87 (d, C-14), 45.48 (d, C-5'), 43.65 (s, C-13), 40.04 (s, C-10), 38.12 (t, C-12), 36.80 (t, C-1), 36.75 (d, C-8), 35.00 (t, C-2') 34.70 (t, C-2), 33.88 (t, C-6), 33.05 (t, C-7), 32.86 (t, C-2''), 28.28 (t, C-16), 24.24 (t, C-15), 22.68 (t, C-11), 21.72 (q, CH_3COO^-), 19.82 (q, C-6'), 17.72 (q, C-19), 17.09 (q, C-6''), 12.15 (q, C-18).

^{1}**H-NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 2531Hz = 5.06ppm: 5.06 (d, 1-H'), 3.94 (m, 2H, 3-H', 5-H'), 3.59 (bd, 1H, 4-H'), 1.96 (ddd, 1H, 2-H'$_{ax}$), 1.86 (dd, 1H, 2-H'$_{eq}$), 1.23 (d, 3H, 6-H')

^{1}**H -NMR** (500 MHz, CD_3OD, = 3.35 ppm) **TOCSY** 2458Hz = 4.91ppm: 4.91 (dd, 1H, 1-H''), 3.99 (dd, 1H, 3-H''), 3.73 (q, 1H, 5-H''), 3.52 (dd, 1H, 4-H''), 2.04 (ddd, 1H, 2-H''$_{ax}$), 1.80 (ddd, 1H, 2-H''$_{eq}$), 1.32 (d, 3H, 6-H'')

11.5.4. Experiments to the chapter 6.1.4.

17-*O*-(1-THP)-testosterone (135)

The reaction was carried out according to the protocol **TP6** except the following details: testosterone (10 mg, 0.0347 mmol).

Yield: 12.5 mg (0.0337 mmol, 97%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.75 (s, 1H, 4-H), 4.65 (bd, J=3.7 Hz, 1H), 3.91 (ddd, J=10.9, 7.9, 2.9 Hz, 1H), 3.67 (ddd, J=8.1, 8.5, 4.7 Hz, 1H, 17-H), 3.5 (m, 1H), 2.5 – 0.7 (m).

7-*O*-(1-THP)-3,4-di-*O*-acetyl-decarestrictine D (136)

The reaction was carried out according to the protocol **TP6**:

Yield: 12.6 mg (0.0328 mmol, 99%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.87 (ddd, *J* = 16.0, 9.4, 1.1 Hz, 0.5H), 5.80 (dd, *J* = 16.0, 3.3 Hz, 0.5H), 5.71 (dd, *J* = 16.0, 3.5 Hz, 0.5H), 5.63 (ddd, *J* = 16.0, 9.4, 1.3 Hz, 0.5H), 5.32 (dddd, *J* = 16.2, 5.0, 3.3, 1.25 Hz, 1H), 5.13 (dddd, *J* = 21.7, 10.9, 6.3, 1.8 Hz, 1H), 5.03 (m, 1H), 4.61 (dd, *J* = 4.3, 2.9 Hz, 0.5H), 4.52 (dd, *J* = 4.5, 2.9 Hz, 0.5H), 4.24 (ddd, *J* = 10.4, 9.7, 3.5 Hz, 0.5H), 4.12 (ddd, *J* = 10.5, 9.6, 3.2 Hz, 0.5H), 3.80 (m, 1H), 3.43 (m, 1H), 2.66 (ddd, *J* = 14.2, 14.2, 7.2 Hz, 1H), 2.55 (ddd, *J* = 14.2, 11.6, 2.6 Hz, 1H), 2.14, 2.12, 2.11 (3s, 6H), 1.4-2.0 (m, 8H), 1.22, (d, *J* = 6.3 Hz, 3H)

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 169.88, 169.50, 169.41, 169.11, 169.10, 136.12+, 134.66+, 125.74+, 122.90+, 98.90, 97.20+, 95.21+, 94.64, 76.96+, 74.88+, 72.18+, 71.99+, 70.88+,68.38+, 68.27+, 62.86-, 62.71-, 41.11-, 40.08-, 33.87-, 33.43-, 30.77-, 30.71-, 30.68, 25.43-, 25.39-, 25.23-, 21.45+, 21.40+, 20.97+, 20.90+, 20.87+, 19.82-, 19.76-, 19.74-.

3-*O*-(1-THP)-digitoxigenin (137)

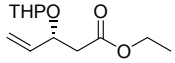
The reaction was carried out according to the protocol **TP6**: digitoxigenin (10 mg, 0.0267 mmol)

Yield: 12.2 mg (0.0265 mmol, 99%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.88 (s, 1H), 5.01 (ddd, *J* = 18.1, 1.6, 1.25 Hz, 1H), 4.82 (dd, *J* = 18.1, 1.6 Hz, 1H), 4.63 (m, 1H), 3.98 (bs, 1H), 3.90 (m, 1H), 3.50 (m, 1H), 2.80 (m, 1H), 2.4-0.7 (m).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 174.54 (s, C-20), 174.47 (s, C-23), 117.64 (d, C-22), 96.94+, 96.75+, 94.63+, 85.59, 73.41-, 71.09+, 70.79+, 62.90-, 62.87-, 62.81-, 50.94+, 50.92+, 49.58, 49.57, 41.88+, 40.05-, 36.49+, 36.36+, 35.70+, 35.66+, 35.19, 33.18-, 33.15-, 32.23-, 31.40-, 30.67-, 30.39-, 30.05-, 29.88-, 26.87-, 26.85-, 26.78-, 26.67-, 26.56-, 25.57-, 25.55-, 25.43-, 24.14-, 23.68+, 21.42-, 21.32-, 21.16-, 20.07-, 20.01-, 19.72-, 15.74+

(3R)-3-OTHP-pent-4-enic acid ethyl ester (139)



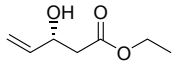
The reaction was carried out according to the protocol **TP6**: alcohol **138** (20 mg, 0.139 mg)

Yield: 31.2 mg (0.137 mmol, 99%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.91 (ddd, *J* = 17.2, 10.5, 6.5 Hz, 0.34H, 4-H), 5.66 (ddd, *J* = 17.2, 10.2, 7.7 Hz, 0.66H, 4-H), 5.29 (dd, *J* = 17.1, 1.5 Hz, 0.66H, 5-H), 5.25 (d, *J* = 17.2, 1.2 Hz, 0.34H, 5-H), 5.21, (dd, *J* = 10.2, 1.5 Hz, 0.66H, 5-H'), 5.11 (ddd, *J* = 10.5, 1.5, 1.2 Hz, 0.34H, 5-H'), 4.73 (dd, *J* = 4.1, 3.0 Hz, 0.34H, H-a), 4.69 (dd, *J* = 3.1, 3.1 Hz, 0.66H, H-a), 4.55 (ddd, *J* = 7.9, 7.7, 5.7 Hz, 0.66H, 3-H), 4.50 (ddd, *J* = 8.0, 6.5, 5.6 Hz, 0.34H, 3-H), 4.14, 4.12 (2q, *J* = 7.3 Hz, 2H, C*H*$_2$-CH_3), 3.84, 3.48 (2m, 2H, H-e), 2.64 (dd, *J* = 14.9, 8.1 Hz, 0.66H, 2-H), 2.61 (dd, *J* = 14.9, 8.0 Hz, 0.34H, 2-H), 2.48 (dd, *J* = 14.7, 5.7 Hz, 0.66H, 2-H), 2.47 (dd, *J* = 15.1, 5.5 Hz, 0.34H, 2-H), 1.4-1.8 (m, 6H, H-b, H-c, H-d), 1.25, 1.23 (2d, *J* = 7.3 Hz, 3H, CH_2-C*H*$_3$).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 170.92 (s, C=O), 170.79 (s, C=O), 138.34 (d, -*C*H=CH_2), 136.75 (d, -*C*H=CH_2), 118.37 (t, –CH=*C*H$_2$), 115.53 (t, –CH=*C*H$_2$), 98.68 (d, C-a), 94.56 (d, C-a), 74.94 (d, C-3), 72.80 (d, C-3), 61.59 (t, *C*H$_2$-CH_3), 60.40 (t, *C*H$_2$-CH_3), 41.23 (t, C-2), 40.58 (t, C-2), 30.70-, 30.40-, 25.46-, 25.33-, 19.52-, 18.93-, 14.19 (q, *C*H$_3$)

(3R)-3-Hydroxy-pent-4-enic acid ethyl ester (138)



The reaction was carried out according to the protocol **TP7**: protected alcohol **139** (31.2 mg, 0.137 mmol)

Yield: 19.59 mg (0.136 mmol, 99%)

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.87 (ddd, *J* = 17.1, 10.5, 545 Hz, 1H, 4-H), 5.31 (ddd, *J* = 17.1, 1.4, 1.4 Hz, 1H, 5-H), 5.14 (ddd, *J* = 10.5, 1.4, 1.4

Hz, 1H, 5-H), 4.53 (ddd, *J* = 8.7, 4.6, 2.8 Hz, 1H, 3-H), 4.16 (q, *J* = 7.1 Hz, 2H, CH_2), 3.02 (bs, 1H, OH), 2.57 (dd, *J* = 16.1, 4.6 Hz, 1H, 2-H), 2.50 (dd, *J* = 16.1, 8.7 Hz, 1H, 2-H), 1.26 (t, *J* = 7.1 Hz, 3H, CH_3)

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 172.22 (s, C=O), 138.78 (d, C-4), 115.35 (t, C-5), 68.90 (d, C-3), 60.75 (t, *C*H_2-CH_3), 41.13 (t, C-2), 14.13 (q, CH_3).

Deprotection of 3-*O*-THP-digitoxigenine (25)

The reaction was carried out according to the protocol **TP7**: protected alcohol **137** (12.2 mg, 0.0265 mmol)

Yield: 9.8 mg (0.0262 mmol, 99%)

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.86 (ddd, *J* = 1.7, 1.7, 0.6 Hz, 1H), 4.98 (ddd, *J* = 18.1, 1.7, 0.5 Hz, 1H), 4.80 (dd, *J* = 18.1, 1.7 Hz, 1H), 4.12 (bdd, *J* = 2.6, 2.6 Hz, 1H), 2.77 (dd, *J* = 9.1, 5.5 Hz, 1H), 2.4 - 0.7 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 174.46 (s, C-20), 174.45 (s, C-23), 117.68 (d, C-22), 85.57 (s, C-14), 73.41 (t, C-21), 66.79 (d, C-3), 50.91 (d, C-17), 49.58 (s, C-13), 41.82 (d, C-8), 40.02 (t, C-12), 35.95, 35.47 (2d, C-5, C-9), 35.38 (s, C-10), 33.31, 33.14 (2t , C-4, C-15), 29.61 (t, C-1), 27.89, 26.86, 26.44 (3t, C-2, C-6, C-16), 23.69 (q, C-19), 21.33 (t, C-7), 21.14 (t, C-11), 15.75 (q, C-18).

Deprotection of 7-*O*-THP-3,4-di-*O*-acetyl-decarestrictine D (40)

The reaction was carried out according to the protocol **TP7**: protected alcohol **136** (12.6 mg, 0.0328 mmol).

Yield: 9.75 mg (0.0325 mmol, 99%)

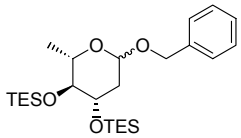
^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.72 (dd, *J* = 16.0, 7.9 Hz, 1H, 6-H), 5.66 (dd, *J* = 16.0, 2.6 Hz, 1H, 5-H), 5.22, 5.00 (2ddd, *J* = 5.2, 2.6, 2.6 Hz, *J* = 10.0, 5.2, 2.6 Hz, 2H, 4-H, 3-H), 5.08 (m, 1H, 9-H), 4.12 (ddd, *J* = 10.6, 7.9, 3.4 Hz, 1H, 7-H), 2.68 (bs, 1H, OH^7), 2.61, 2.52 (2ddd, *J* = 14.3, 10.0, 2.6 Hz, *J* = 14.3,

2.6, 2.6 Hz, 2H, 2-H), 2.08, 2.07(2s, 6H, 2 x CH_3CO), 1.83-1.73 (m, 2H, 8-H), 1.18 (d, *J* = 6.2 Hz, 3H, 10-H).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 169.86, 169.44, 169.21, 136.88+, 123.86+, 72.45+, 72.28+, 70.92+, 68.06+, 42.46-, 33.81-, 21.36+, 20.96+, 20.87+

11.6.1. Experiments to the chapter 6.2.1.

Benzyl 2´,6´-dideoxy-3´,4´-di-*O*-triethylsilyl-α/β-L-*arabino*-hexopyranoside (141)

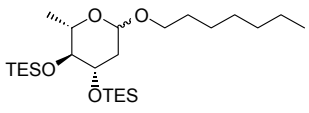


To a shaken suspension of thioglycoside **140** (40 mg, 0.085 mmol), molecular sieves 4A (100 mg) and benzyl alcohol (20 mg, 0.17 mmol) in CH_2Cl_2 (5 ml) polymer-bound Iodo-*bis*-trifluoroacetat (1 eq, 2.5 mmol/g) was added. The reaction was gently shaken for 1h at rt. Amberlite A-21 (40 mg) was added and the suspension was filtered and concentrated under reduced pressure. Removal of thio impurities was achieved as described in protocol **TP1** (see above). The crude product was purified by column chromatography over silica gel (ethyl acetate / petroleum ether=1:10, Rf-0.30) to yield an inseparable mixture of α,β-isomers.

Yield: 32 mg (0.068 mmol, 85%, α/β - 8:1).

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$=7.26 ppm) δ: 7.37 (m, 5H, Ph), 4.90 (d, *J* = 3.2 Hz, 1H, 1-H), 4.59 (2d, *J* = 47.2, 12.1 Hz, 2H, CH_2Ph), 4.01 (ddd, *J* = 11.3, 8.4, 5.0 Hz, 1H, 3-H), 3.71 (dq, *J* = 8.9, 6.3 Hz, 1H, 5-H), 3.22 (dd, *J* = 8.9, 8.4 Hz, 1H, 4-H), 2.16 (ddd, *J* = 13.0, 5.0, 1.2 Hz, 1H, 2-H_{ax}), 1.70 (ddd, *J* = 13.0, 11.3, 3.2 Hz, 1H, 2-H_{eq}), 1.28 (d, *J* = 6.3 Hz, 3H, 6-H').

n-Heptyl 2',6'-dideoxy-3',4'-di-*O*-triethylsilyl-α/β-L-*arabino*-hexopyranoside (142)



To a solution of thioglycoside **140** (47 mg, 0.1 mmol), *n*-heptanol (15 mg, 0.14 mmol) in CH_2Cl_2 were added molecular sieves 4Å (100 mg) and polymer-bound Iodo-*bis*-trifluoroacetate (40 mg, with 2.5 mmol x g^{-1}). The crude product was purified by flash column chromatography (ethyl acetate / petroleum ether 1:15; R_f= 0.36) to yield an inseparable mixture of α,β-isomers.

Yield: 29 mg (0.061 mmol, 62%, α/β 1.2:1, R_f-0.36)

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$=7.26 ppm) δ: 4.78 (d, *J* = 2.6 Hz, 0.55H, 1-Hα), 4.45 (dd, *J* = 9.6, 1.8 Hz, 0.45H, 1-Hβ), 3.91 (m, 1H, 3-H), 3.63 (m, 2H), 3.22 (m, 2H), 2.11 (ddd, *J* = 13.0, 5.0, 1.2 Hz, 1H, 2-H), 1.65 (m, 3H), 1.30 (m, 13H), 1.00 (m, 18H, TES-C<u>H</u>$_3$), 0.70 (m, 12H, TES-C<u>H</u>$_2$).

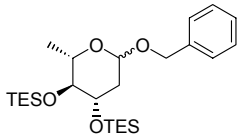
3,4-Di-*O*-TES-rhamnal (143)

Yield: 7.1 mg (0.02 mmol, 20%, R_f-0.4)

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$=7.26 ppm) δ: 6.27 (d, *J* = 6.1, 1.0 Hz, 1H, 1-H), 4.66 (dd, *J* = 6.1, 2.9 Hz, 1H, 2-H), 4.13 (ddd, *J* = 5.5, 1.0, 2.9 Hz, 1H, 3-H), 3.86 (dq, *J* = 6.7, 7.5 Hz, 1H, 5-H), 3.53 (dd, *J* = 7.5, 5.5 Hz, 1H, 4-H), 1.32 (d, *J* = 6.7 Hz, 3H, 6-H), 0.95 (m, 18H, TES), 0.65 (m, 12H, TES).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$=77 ppm) δ: 143.0 (+, C-1), 102.8 (+, C-2), 75.1, 74.7, 69.3 (3+, C-4, C-5, C-3), 17.2 (+, C-6), 6.4, 5.0 (+ -, TES).

Benzyl 2',6'-dideoxy-3',4'-di-*O*-triethylsilyl-α/β-L-*arabino*-hexopyranoside (141)



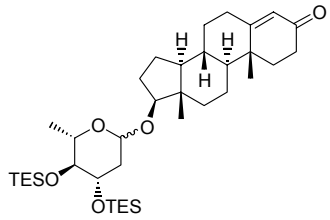
A solution of thioglycoside **140** (23 mg, 49 μmol) and benzyl alcohol (10 mg, 0.1 mmol) was shaken in THF/CH_3CN (1:2; 5 ml) at –50°C. Polymer-bound Iodo-*bis*-trifluoroacetate (20 mg, 2.5 mmol/g) was added and shaking was continued for 1 h at –50°C. Amberlite A-21 (20 mg) was added and the suspension was filtered through a pad of Al_2O_3. The filtrate was concentrated under reduced pressure.

Removal of thio impurities was achieved as described in protocol **TP1** (see above). The crude product was purified by flash column chromatography (ethyl acetate / petroleum ether= 1:10; R_f-0.30) to yield an inseparable mixture of α,β-isomers.

Yield: 21 mg (93%, 45.6 μmol, α/β - 4:1).

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.37 (m, 5H, Ph), 4.90 (d, *J* = 3.2 Hz, 0.8H, 1-Hα), 4.59 (2d, *J* = 47.2, 12.1 Hz, 2H, *CH*$_2$Ph), 4.26 (dd, *J* = 5.8, 1.8 Hz, 0.2H, 1-Hβ), 4.01 (ddd, *J* = 11.3, 8.5, 5.0 Hz, 0.8H, 3-Hα), 3.71 (dq +m, *J* = 8.9, 6.3 Hz, 1H+0.2H, 5-H+3-Hβ), 3.22 (dd, *J* = 8.9, 8.5 Hz, 1H, 4-H), 2.16 (ddd, *J* = 13.1, 5.0, 1.2 Hz, 1H, 2-H), 1.70 (ddd, *J* = 13.1, 11.3, 3.2 Hz, 1H, 2-H), 1.28 (d, *J* = 6.3 Hz, 3H, 6-H'), 0.95 (m, 18H, TES), 0.65 (m, 12H, TES).

Testosteryl 2´,6´-dideoxy-3´,4´-di-*O*-triethylsilyl-α/β-L-*arabino*-hexopyranoside (149)



To a shaken solution of thioglycoside **140** (40 mg, 85 μmol) and testosterone (25 mg, 87 μmol) in THF/CH_3CN (1:2; 5 ml) polymer-bound Iodo-*bis*-trifluoroacetate (37 mg, 2.5 mmol x g^{-1}) was added at –50°C and shaking was continued for 3 h at that temperature. Amberlite A-21 (40 mg) was added and after 30 min the suspension was filtered and concentrated under reduced pressure. Removal of thio impurities was achieved as described in protocol **TP1** (see above). The crude product was purified by column chromatography (ethyl acetate / petroleum ether= 1:3) to yield two fractions.

Yield: *1st fraction:* **149**α 25 mg (0.039 mmol, 46%, R_f - 0.6).

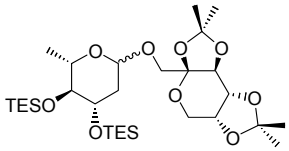
^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$=7.26 ppm) δ: 5.76 (s, 1H, 4-H), 4.84 (d, *J* = 2.7 Hz, 1H, 1-H'α), 3.95 (ddd, *J* = 11.0, 8.7, 4.7 Hz, 1H, 3-H'), 3.67 (dq, *J* = 8.7, 6.4

Hz, 1H, 5-H'), 3.47 (dd, *J* = 8.4, 8.4 Hz, 1H, 17-H), 3.16 (dd, *J* = 8.7, 8.7 Hz, 1H, 4-H'), 2.5 – 0.7 (m).

Yield: *2nd fraction:* **149**β 21 mg (0.032 mmol, 37%, R_f - 0.53).

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.76 (s, 1H, 4-H), 4.40 (dd, *J* = 9.3, 1.8 Hz, 1H, 1-H'β), 4.00 (ddd, *J* = 11.2, 8.5, 4.7 Hz, 1H, 3-H'), 3.87 (dq, *J* = 8.6, 6.3 Hz, 1H, 5-H'), 3.62 (dd, *J* = 8.4, 8.4 Hz, 1H, 17-H), 3.20 (dd, *J* = 8.6, 8.5 Hz, 1H, 4-H'), 2.5 – 0.7 (m).

1-*O*-(2´,6´-deoxy-3´,4´di-*O*-triethylsilyl-α/β-D-*arabino*-hexopyranosyl) (2:3, 4:5-di-*O*-isopropyliden)-α-D-*fructo*-hexopyranoside (145)



To a solution of thioglycoside **140** (40 mg, 85 μmol) and diacetonfructopyranose (22.3 mg, 85 μmol) in THF/CH_3CN (2:3, 5 ml) polymer-bound Iodo-*bis*-trifluoroacetate (37 mg, 2.5 mmol x g^{-1}) was added at –50°C and shaken was continued for 3 h at that temperature. Amberlite A-21 (40 mg) was added and after 30 min the suspension was filtered and concentrated under reduced pressure. Removal of thio impurities was achieved as described in protocol **TP1** (see above). The crude product was purified by column chromatography (ethyl acetate / petroleum ether 1:6; R_f= 0.52) to yield an inseparable mixture of α,β-isomers. As a byproduct 2,6-dideoxy-3,4-di-*O*-triethylsilyl-α/β-L-*arabino*-hexopyranose **146** was formed (R_f= 0.3).

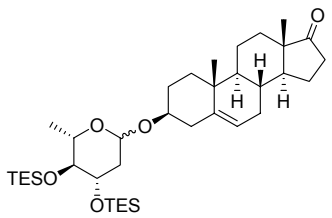
Yield: 25 mg (0.040 mmol, 47%, α/β – 1.36:1).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 4.88 (d, *J* = 3.0 Hz, 0.56H, 1-Hα), 4.63 (ddd, *J* = 7.7, 7.7, 2.5 Hz, 1H), 4.51 (dd, *J* = 9.6, 1.8 Hz, 0.42H, 1-Hβ), 4.33, 4.43 (2d, *J* = 2.5 Hz, 1H), 4.25 (bd, *J* = 7.9 Hz, 1H), 4.05 (d, 0.44H), 3.85-4.00 (m, 2H), 3.73 (m, 1.6H), 3.60 (m, 1H), 3.50 (d, 1H), 3.18 (m, 1.6H), 2.17 (ddd, 1H), 1.3-

1.6 (8s, 12H, 4xCH_3), 1.27, 1.23 (2d, *J* = 5.7, 6.2 Hz, 3H, 6-H),), 0.95 (m, 18H, TES), 0.65 (m, 12H, TES).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 108.98, 108.92, 108.50, 108.37, 102.53, 102.42, 99.26+, 97.40+, 78.88+, 78.55+, 72.98+, 72.51+ 71.06+, 71.03+, 70.75+, 70.37+, 70.29+, 70.08+, 69.81+, 68.78+, 67.32-, 61.01-, 60.99-, 40.29-, 39.00-, 26.91-, 26.55+, 26.53+, 25.94+, 25.87+, 25.42+, 25.17+, 24.13+, 23.99+, 18.30+, 18.19+, 7.04+, 6.92+, 6.93+, 5.38-, 5.37-, 5.30-

Dehydro-*epi*-androsteronyl 2´,6´-dideoxy-3´,4´-di-*O*-triethylsilyl-α/β-L-*arabino*-hexopyranoside (147)



To a shaken solution of thioglycoside **140** (55 mg, 0.117 mmol) and dehydro-*epi*-androsteron (33 mg, 0.117 mmol) in THF/CH_3CN (1:2; 5 ml) polymer-bound Iodo-*bis*-trifluoroacetate (47 mg, 2.5 mmol x g^{-1}) was added at –50°C and shaking was continued for 3 h at that temperature. Amberlite A-21 (50 mg) was added and after 30 min the suspension was filtered through a pad of celite and concentrated under reduced pressure. Removal of thio impurities was achieved as described in protocol **TP1** (see above). The crude product was purified by column chromatography (ethyl acetate / petroleum ether 1:8; R_f= 0.53) to yield an inseparable mixture of α,β-isomers.

Yield: 46 mg (0.071 mmol, 54%, R_f-0.53, α/β – 1:1.25).

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.38 (dd, *J* = 14.3, 5.3 Hz, 1H, steroid), 4.94 (d, *J* = 2.8 Hz, 0.43H, 1-Hα), 4.57 (dd, *J* = 9.7, 1.8 Hz, 0.55H, 1-Hβ), 3.92 (ddd, *J* = 11.2, 8.1, 4.9 Hz, 0.43H, 3-H), 3.55-3.75 (m, 1.6H), 3.4 (m, 0.43H), 3.15-3.25 (m, 1.55H), 2.5 – 0.7 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 221.15, 221.13, 141.20, 120.91, 120.69, 97.29, 95.26, 79.11, 78.50, 77.64, 76.09, 73.16, 72.38, 70.58, 68.48,

51.78, 51.76, 50.28, 47.53, 41.16, 40.20, 39.77, 38.62, 37.32, 37.09, 36.90, 36.84, 35.83, 35.82, 31.50, 31.49, 31.44, 30.80, 29.45, 28.08, 26.89, 21.86, 20.34, 20.33, 19.43, 19.36, 18.44, 18.35, 13.53, 7.05, 7.01, 6.96, 5.35, 5.34, 5.33

3,4-Di-*O*-triethylsilyl-2,6-dideoxy-L-*arabino*-hexopyranoside (146)

To a shaken solution of sugar **140** (40 mg, 0.085 mmol) and diacetonglucose (21 mg, 0.085mmol) in a mixture of solvents (THF/CH_3CN -1:2, 5 ml) at –50^oC polymer bound Iodo-*bis*-trifluoroacetat (37 mg, 2.5 mmol/g) was added. The reaction was shaken for 2-3 h at the same temperature, then quenched with addition of Amberlite A-21(40 mg), shaken another 30 min, filtrated through a pad of celite and solvent was evaporated under reduced pressure. The crude product was purified by column chromatography over silica gel (ethyl acetate / petroleum ether=1:6). No expected product was detected. As a main product 2,6-dideoxy-3,4-di-*O*-triethylsilyl-α/β-L-*arabino*-hexopyranose **146** was formed (R_f= 0.3).

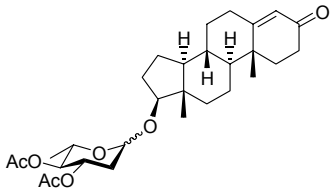
Yield: 27 mg (0.072 mmol, 85%, R_f-0.3).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.27 (ddd, *J* = 3.2, 3.0, 1.8 Hz, 0.57H, 1-Hα), 4.82 (ddd, *J* = 9.2, 6.5, 2.2 Hz, 0.42H, 1-Hβ), 3.98 (ddd, *J* = 10.9, 8.1, 4.8 Hz, 0.57H, 3-H), 3.87 (dq, *J* = 8.6, 6.3 Hz, 0.57H, 5-H), 3.64 (ddd, *J* = 11.1, 8.1, 4.9 Hz, 0.44H, 3-H'), 3.31 (dq, *J* = 8.5, 6.3 Hz, 0.41H, 5-H'), 3.18 (dd, *J* = 8.5, 8.1 Hz, 1H, 4-H, 4-H'), 3.17 (bd, *J* = 8.0 Hz, 0.45H, OHβ), 2.54 (dd, *J* = 3.2, 2.5 Hz, 0.54H, OHα), 2.25 (ddd, *J* = 12.5, 4.9, 1.8 Hz, 0.42H, 2-H), 2.10 (ddd, *J* = 13.0, 4.9, 1.7 Hz, 0.58H, 2-H'), 1.67 (dddd, *J* = 13.0, 11.1, 2.2, 3.5 Hz, 0.5H, 2-H'), 1.56 (ddd, *J* = 12.5, 11.3, 9.5 Hz, 0.5H, 2-H), 1.31 (d, *J* = 6.3 Hz, 1.3H, 6-H), 1.25 (d, *J* = 6.3 Hz, 1.8H, 6-H'), 0.95 (m, 18H, TES), 0.65 (m, 12H, TES).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 93.60, 91.79 (C1), 78.75, 78.09 (C4), 72.72, 72.71 (C3, C5), 70.06 (C3), 69.04 (C5), 41.76, 39.12 (C2), 18.52, 18. 43 (C6), 7.02, 6.93 (+), 5.30 (-).

11.6.2. Experiments to the chapter 6.2.3.

Testosteryl 2´,6´-dideoxy-3´,4´-di-*O*-acetyl-α/β-L-*arabino*-hexopyranoside (150)



The two reactions were carried out according to the protocol **TP1** except the following details:

First reaction: thioglycoside **18** (32 mg, 0.1 mmol), testosterone (28 mg, 0.1 mmol), selectfluor™ (35.4 mg, 0.1 mmol).

Second reaction: thioglycoside **19** (32 mg, 0.1 mmol), testosterone (28 mg, 0.1 mmol), selectfluor™ (35.4 mg, 0.1 mmol).

Both reactions gave the same yield and α/β ratio of diastereomers.

Yield: 49 mg (0.097 mmol, 97%, α/β - 2:1).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.71 (s, 1H, 4-H), 5.27 (ddd, *J* = 11.5, 9.6, 5.3 Hz, 0.66H, 3-H'α), 4.94 (ddd, *J* = 11.7, 9.4, 5.2 Hz, 0.33H, 3-H'β), 4.92 (d, *J* = 3.0 Hz, 0.66H, 1-H'α), 4.75 (dd, *J* = 9.4, 9.4 Hz, 0.33H, 4-H'β), 4.71 (dd, *J* = 9.6, 9.6 Hz, 0.66H, 4-H'α), 4.51 (dd, *J* = 9.6, 1.8 Hz, 0.33H, 1-H'β), 3.89 (dq, *J* = 9.6, 6.2 Hz, 0.66H, 5-H'α), 3.66 (t, *J* = 8.4 Hz, 0.33H, 17-Hβ), 3.51 (t, *J* = 8.5 Hz, 0.66H, 17-Hα), 3.42 (dq, *J* = 9.4, 6.1 Hz, 0.33H, 5-H'β), 2.5-0.7 (m)

^{13}**C-NMR α-anomer** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 199.3 (s, C-3), 170.9, 170.2 (2s, $\underline{C}OCH_3$), 123.8 (d, C-4), 97.3 (d, C-1'), 87.2 (d, C-17), 74.9, 69.1, 65.6 (3d, C-3', 4', 5'), 53.8 (d, C-9), 50.2 (d, C-14), 42.8 (s, C-13), 38.6 (s, C-10), 37.1(t, C-12), 35.6 (t, C-1), 35.5 (t, C-2'), 35.4 (d, C-8), 33.8 (t, C-2), 32.7 (t, C-6), 31.4 (t, C-7), 28.3 (t, C-16), 23.2 (t, C-15), 20.7, 20.5 (2q, $2CO\underline{C}H_3$), 17.4 (q, C-19), 17.3 (q, C-6'), 11.6 (q, C-18)

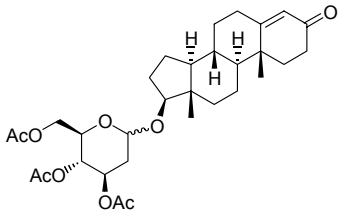
^{13}**C-NMR β-anomer** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 199.3 (s, C-3), 171.1, 170.3 (2s, $\underline{C}OCH_3$), 123.8 (d, C-4), 98.1 (d, C-1'), 87.3 (d, C-17), 74.1, 70.9, 69.8 (3d, C-3', 4', 5'), 53.9 (d, C-9), 50.6 (d, C-14), 42.4 (s, C-13), 38.6 (s, C-10), 36.8(t,

C-12), 36.5 (t, C-2'), 35.6 (t, C-1), 35.4 (d, C-8), 33.9 (t, C-2), 32.7 (t, C-6), 31.5 (t, C-7), 27.4 (t, C-16), 23.1 (t, C-15), 20.9, 20.8 (2q, 2CO<u>C</u>H_3), 17.6 (q, C-19), 17.3 (q, C-6'), 11.5 (q, C-18)

^{1}**H-NMR α-anomer** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 2641 Hz = 5.28 ppm: δ = 5.28 (ddd, 3-H'), 4.92 (d, 1-H'), 4.71 (dd, 4-H'), 3.89 (dq, 5-H'), 2.22 (dd, 2-H'$_{ax}$), 1.76 (ddd, 2-H'$_{eq}$), 1.15 (d, 6-H')

^{1}**H-NMR β-anomer** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 2254 Hz = 4.51 ppm: δ = 4.94 (ddd, 3-H'), 4.75 (dd, 4-H'), 4.50 (dd, 1-H'), 3.42 (dq, 5-H'), 2.27 (ddd, 2-H'$_{ax}$), 1.70 (ddd, 2-H'$_{eq}$), 1.21 (d, 6-H')

Testosteryl 2´-deoxy-3´,4´,6´-tri-*O*-acetyl-α/β-D-*arabino*-hexopyranoside (151)



The reaction was carried out according to the protocol **TP1**:

Yield: 55 mg (0.098 mmol, 98%, α/β - 2:1)

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.69 (s, 1H, 4-H), 5.27 (ddd, *J* = 11.5, 9.5, 5.3 Hz, 0.68H, 3-H'α), 5.26 (m, 1H), 4.94 (m, 2H, 0.32H, 0.68H, 1H, 3-H'β, 1-H'α, 4-H'βα), 4.57 (dd, *J* = 9.6, 1.6 Hz, 0.32H, 1-H'β), 4.28 (m, 1.6H), 4.2-3.95 (m, 2.6H), 3.60 (m, 1.3H), 2.5 – 0.7 (m).

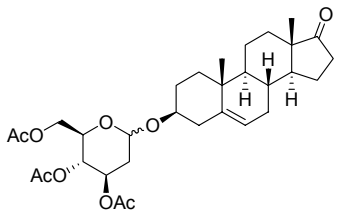
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 199.25, 199.23, 170.87, 170.82, 170.59, 170.56, 170.25, 170.12, 169.78, 169.64, 123.84+, 99.93+, 95.01+, 89.07+, 84.37+, 71.86+, 70.76+, 69.50, 69.22, 69.08, 67.72, 62.62, 62.39, 53.92, 53.82, 50.47, 50.20, 42.79, 42.30, 38.56, 38.55, 37.26, 36.95, 36.34, 35.66, 35.34, 35.29, 33.85, 32.66, 31.43, 28.82, 26.82, 26.71, 23.28, 23.25, 20.89, 20.81, 20.71, 20.67, 20.64, 20.63, 20.52, 20.50, 17.35, 17.32, 11.61

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 1096 Hz = 2.19 **α**: 5.30 (ddd, 1H, 3-H), 4.97 (dd, 1H, 4-H), 4.95 (d, 1H, 1-H), 4.27 (dd, 1H, 6-H), 4.04 (dd, 1H, 6-H'), 3.99 (ddd, 1H, 5-H), 2.19 (dd, 1H, 2-H), 1.82 (ddd, 1H, 2-H')

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2302 Hz = 4.60 **β**: 4.98 (ddd, 1H, 3-H), 4.95 (dd, 1H, 4-H), 4.60 (dd, 1H, 1-H), 4.26 (dd, 1H, 6-H), 4.09 (dd, 1H, 6-H'), 3.56 (ddd, 1H, 5-H), 2.32 (ddd, 1H, 2-H), 1.73 (ddd, 1H, 2-H').

LC-MS (ESI) (+c): m/z (%): 583.29 (100) $[M + Na]^+$; **HR-MS** $C_{31}H_{44}O_9$ +^{23}Na: calc. 583.2883, found 583.2888.

Dehydro-*epi*-androsteryl 2´-deoxy-3´,4´,6´-tri-*O*-acetyl-α/β-D-*arabino*-hexopyranoside (152)



The reaction was carried out according to the protocol **TP1**:

Yield: 55 mg (0.098 mmol, 98%, α/β - 2:1)

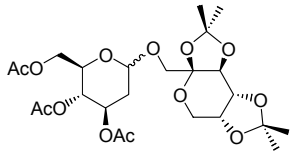
^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.38 (dd+m, *J* = 14.3, 5.3 Hz, 1H+0.32H, 6-H + 3-H'α), 5.12 (d, *J* = 3.1 Hz, 0.6H, 1-H'α), 5.00 (m, 1.32H, 4-H', 3-H'β), 4.70 (dd, *J* = 9.8, 1.6 Hz, 0.32H, 1-H'β), 4.4-4.0 (m, 2.7H, 6-H', 5-H'α), 3.5 (m, 0.33H, 5-H'β), 2.5 – 0.7 (m)

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 220.98, 220.95, 170.71, 170.20, 169.91, 140.91, 140.71, 97.84+, 95.04+, 81.81+, 78.71+, 70.77+, 69.65+, 69.15+, 67.87+, 64.35+, 62.53-, 51.73+, 50.23+, 47.49, 42.69, 39.93-, 38.79-, 37.14-, 36.97-, 36.82-, 36.65-, 36.54-, 35.79-, 35.50-, 31.90+, 31.45+, 31.40-, 30.77-, 30.47-, 29.64-, 29.43-, 27.68-, 25.31+, 23.39+, 21.83-, 20.94+, 20.73+, 20.70+, 20.30-, 19.33+, 13.50+, 10.91+

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$=7.26 ppm) **TOCSY**: 2567 Hz = 5.13 **α**: 5.37 (ddd, 1H, 3-H), 5.13 (d, 1H, 1-H) 4.97 (dd, 1H, 4-H), 4.28 (dd, 1H, 6-H), 4.07 (dd, 1H, 6-H'), 4.06 (ddd, 1H, 5-H), 2.20 (dd, 1H, 2-H), 1.82 (ddd, 1H, 2-H')

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$=7.26 ppm) **TOCSY**: 2302 Hz = 4.60 **β**: 5.05 (ddd, 1H, 3-H), 4.97 (dd, 1H, 4-H), 4.70 (dd, 1H, 1-H), 4.30 (dd, 1H, 6-H), 4.09 (dd, 1H, 6-H'), 3.60 (ddd, 1H, 5-H), 2.30 (ddd, 1H, 2-H), 1.77 (ddd, 1H, 2-H').

1-*O*-(2´-deoxy-3´,4´,6´-tri-*O*-acetyl-α/β-D-*arabino*-hexopyranosyl) (2:3, 4:5-di-*O*-isopropyliden)-α-D-*fructo*-hexopyranoside (153)



The reaction was carried out according to the protocol **TP1**:

Yield: 50 mg (0.094 mmol, 94%, α/β - 2:1)

α-anomer

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.30 (ddd, *J* = 11.5, 9.6, 5.1 Hz, 1H 3-H'), 5.01 (dd, *J* = 9.6, 9.6 Hz, 1H, 4-H'), 4.99 (d, *J* = 3.1 Hz, 1H, 1-H'), 4.62 (dd, *J* = 7.9, 2.6 Hz, 1H, 3-H), 4.40 (d, *J* = 2.6 Hz, 1H, 2-H), 4.29 (dd, *J* = 12.2, 4.6 Hz, 1H, 6-H'), 4.24 (dd, *J* = 7.9, 1.5 Hz, 1H, 4-H), 4.05 (m, 2H, 6-H', 5-H'), 3.93 (dd, *J* = 12.9, 1.5 Hz, 1H, 5-H), 3.82 (d, *J* = 10.3 Hz, 1H, 6-H), 3.73 (d, *J* = 12.9 Hz, 1H, 5-H), 3.45 (d, *J* = 10.3 Hz, 1H, 6-H), 2.30 (dd, *J* = 12.8, 5.1 Hz, 1H, 2-H'), 2.08, 2.03, 1.99 (3s, 9H, 3xAc), 1.83 (ddd, *J* = 12.8, 11.5, 3.1 Hz, 1H, 2-H'), 1.55, 1.50, 1.46, 1.34 (4s, 12H, 4xCH_3)

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 170.73, 170.11, 169.87, 109.04, 108.82, 101.96, 96.88, 71.02, 70.19, 69.87, 69.06, 69.00, 68.20, 68.15, 62.17, 61.12, 34.82, 26.55, 25.91, 25.49, 24.05, 20.91, 20.76, 20.71

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 1880 Hz= 3.76 *fructose*: 4.64 (dd, 1H, 3-H), 4.43 (d, 1H, 2-H), 4.26 (dd, 1H, 4-H), 3.95 (dd, 1H, 5-H), 3.75 (d, 1H, 5-H).
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 1738 Hz= 3.48 *fructose*: 3.85 (d, 1H, 6-H), 3.47 (d, 1H, 6-H).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 1164 Hz= 2.33 *glucose*: 5.32 (ddd, 1H, 3-H), 5.04 (dd, 1H, 4-H), 5.02 (d, 1H, 1-H), 4.31 (dd, 1H, 6-H), 4.08 (m, 2H, 6-H, 5-H), 2.32 (dd, 1H, 2-H), 1.85 (ddd, 1H, 2-H).

LC-MS (ESI) (+c): m/z (%): 555.16 (100) $[M + Na]^+$; **HR-MS** $C_{24}H_{36}O_{13}$ +^{23}Na: calc. 555.2054, found 555.2066.

$[\alpha]^{25}_{D}$ = + 44.5^{o} (c = 1 in $CHCl_3$).

β-anomer
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.00 (m, 1H, 3-H'), 4.96 (dd, *J* = 9.3, 9.3 Hz, 1H, 4-H'), 4.70 (dd, *J* = 9.5, 1.6 Hz, 1H, 1-H'), 4.59 (dd, *J* = 8.0, 2.6 Hz, 1H, 3-H), 4.38 (d, *J* = 2.6 Hz, 1H, 2-H), 4.26 (dd, *J* = 12.4, 5.1 Hz, 1H, 6-H'), 4.23 (dd, *J* = 8.3, 8.0 Hz, 1H, 4-H), 4.27 (m, 1H, 6-H'), 4.12-3.90 (m, 2H, 5-H, 6-H'), 3.72 (m, 2H, 5-H, 6-H), 3.59 (ddd, *J* = 9.3, 5.0, 2.3 Hz, 1H, 5-H'), 2.36 (ddd, *J* = 12.2, 4.7, 1.6 Hz, 1H, 2-H'), 2.07, 2.03, 2.02 (3s, 9H, 3xAc), 1.74 (ddd, *J* = 11.6, 12.2, 9.5 Hz, 1H, 2-H'), 1.54, 1.45, 1.38, 1.33 (4s, 12H, 4xCH_3)

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 170.72, 170.23, 169.78, 109.01, 108.62, 102.27, 99.97, 72.01, 70.92, 70.59, 70.10, 69.99, 69.57, 69.18, 62.55, 61.14, 35.87, 26.58, 25.85, 25.50, 23.97, 20.89, 20.74, 20.70

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2365 Hz= 4.73 *glucose*: 5.04 (ddd, 1H, 3-H), 4.99 (dd, 1H, 4-H), 4.73 (dd, 1H, 1-H), 4.28 (dd, 1H, 6-H), 4.12 (dd, 1H, 6-H), 3.62 (ddd, 1H, 5-H), 2.38 (ddd, 1H, 2-H), 1.77 (ddd, 1H, 2-H)

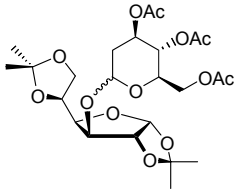
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2310 Hz= 4.62 *fructose*: 4.61 (dd, 1H, 3-H), 4.41 (d, 1H, 2-H), 4.24 (dd, 1H, 4-H), 3.93 (dd, 1H, 5-H), 3.76 (d, 1H, 5-H)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 1738 Hz= 3.48 *fructose*: 3.85 (d, 1H, 6-H), 3.47 (d, 1H, 6-H).

LC-MS (ESI) (+c): m/z (%): 555.17 (100) $[M + Na]^+$; **HR-MS** $C_{24}H_{36}O_{13}$ +^{23}Na: calc. 555.2054, found 555.2054.

$[\alpha]^{25}_D$ = - 5.2^o (c = 0.5 in $CHCl_3$).

3-*O*-(2´-deoxy-3´,4´,6´-tri-*O*-acetyl-α/β-D-*arabino*-hexopyranosyl) (1:2, 5:6-di-*O*-isopropyliden)-α-D-*gluco*-hexofuranoside (154)



The reaction was carried out according to the protocol **TP1**.

Yield: 42 mg (0.079 mmol, 79%, α/β - 4:1)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.97 (d, *J* = 3.7 Hz, 0.2H, 1-H), 5.88 (d, *J* = 3.5 Hz, 0.8H, 1-H), 5.26 (ddd, *J* = 11.7, 9.6, 5.4 Hz, 1H, 3-H'), 5.23 (d, *J* = 2.4 Hz, 0.8H, 1-H'α), 4.99 (dd, *J* = 9.6, 1.5 Hz, 0.2H, 1-H'β), 4.95 (dd, *J* = 9.6, 9.6 Hz, 1H, 4-H'), 4.56 (d, *J* = 3.7 Hz, 0.2H, 2-H), 4.55 (d, *J* = 3.5 Hz, 0.8H, 2-H), 4.32 (dd, *J* = 6.8, 3.8 Hz, 0.2H), 4.27 (dd, *J* = 12.0, 5.6 Hz, 1H), 4.23 (d, *J* = 2.7 Hz, 0.8H), 4.21 (d, *J* = 4.1 Hz, 0.2H), 4.11 (m, 2.6H), 4.05 (m, 2.2H), 3.96 (dd, *J* = 8.1, 4.8 Hz, 0.8H), 3.7 (m, 0.6H), 2.25 (dd, *J* = 13.0, 5.4 Hz, 1H, 2-H'), 2.08, 2.07, 2.03, 2.01, 2.00, 1.99 (6s, 9H, 3xAc), 1.82 (ddd, *J* = 13.0, 11.7, 3.7 Hz, 1H, 2-H') 1.48, 1.41, 1.38, 1.34, 1.31, 1.30, 1.29 (5s, 12H, 4xCH_3)

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) **α'α**-diastereomer δ: 170.66, 170.10, 169.81, 111.97, 109.22, 105.29, 98.07, 84.00, 81.33, 80.71, 72.40, 69.57, 68.63, 67.78, 62.60, 34.64, 26.86, 26.82, 26.31, 25.31, 20.88, 20.66

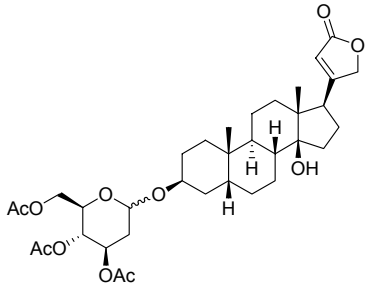
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) **β'α** -diastereomer δ: 170.69, 170.10, 169.86, 112.21, 106.35, 100.94, 96.68, 84.04, 81.33, 79.15, 75.02, 71.11, 69.27, 69.07, 67.84, 67.28, 62.16, 34.81, 29.65, 27.16, 27.16, 26.88, 26.54, 23.97, 23.95, 20.93, 20.72

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 926 Hz= 1.85 *pyranose* **α'**α + **β**α: 5.29 (ddd, 1H, 3-H), 5.26 (s, 0.8H, 1-Hα), 5.00 (dd, 0.2H, 1-Hβ), 4.98 (dd, 1H, 4-H), 4.29 (dd, 1H, 6-H), 4.14 (dd, 1H, 6-H), 4.04 (ddd, 1H, 5-H), 2.27 (dd, 1H, 2-H), 1.85 (ddd, 1H, 2-H)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2957 Hz= 5.91 *furanose* α'**α**: 5.91 (d, *J* = 3.47 Hz, 1-H), 4.57 (d, *J* = 5.99 Hz, 2-H), 4.25 (d,), 4.15 (dd,), 4.06 (dd, 6-H), 3.99 (dd, 6-H)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 3000 Hz= 6.00 *furanose* β'α : 6.00 (d, 1-H), 4.59 (d, 2-H), 4.34 (dd,), 4.23 (d,), 3.72 (bdd, 6-H)

Digitoxigenyl 2-deoxy-3,4,6-tri-*O*-acetyl-α/β-D-*arabino*-pyranoside (155)



The reaction was carried out according to the protocol **TP1**.

Yield: 64 mg (0.099 mmol, 99%, α/β - 4:1)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.86 (s, 1H, 22-H), 5.35 (ddd, *J* = 11.5, 9.5, 5.3 Hz, 0.8H, 3-H'), 5.03 (d, *J* = 3.0 Hz, 0.8H, 1-H'), 4.97 (bdd, *J* = 8.0,

8.44 Hz, 1.0H+0.2H, 4-H', 3-H'), 4.97 (d, *J* = 18.0 Hz, 1H, 21-H), 4.79 (d, *J* = 18.0 Hz, 1H, 21-H), 4.61 (dd, *J* = 9.6, 1.5 Hz, 0.2H, 1-H'), 4.28 (dd, *J* = 12.4, 4.6 Hz, 1H, 6-H'), 4.11 (bdd, *J* = 14.2, 7.0 Hz, 1.2H, 6-H'), 4.00 (m, 1.8H), 3.91 (bs, 0.8H), 2.75 (m, 1H, 3-H), 2.27 (ddd, *J* = 12.7, 3.0, 1.5 Hz, 0.2H, 2-H'), 2.4 – 0.7 (m).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) **α**-anomer δ: 174.40, 170.68, 170.32, 169.88, 117.68, 94.61, 85.51, 73.38, 71.65, 69.75, 69.21, 67.93, 62.46, 60.34, 50.90, 49.57, 41.83, 39.99, 36.53, 35.68, 35.53, 35.21, 33.13, 31.88, 29.97, 26.85, 26.51, 23.77, 23.65, 21.27, 21.14, 20.97, 20.73, 20.71, 15.73, 14.16

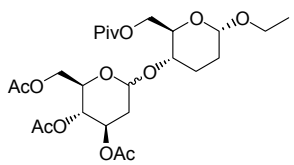
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) **β**-anomer δ: 174.43, 171.08, 170.37, 169.72, 117.68, 97.45, 85.52, 73.60, 71.90, 70.95, 69.29, 67.93, 62.67, 60.34, 50.90, 49.57, 41.83, 40.02, 36.69, 36.29. 35.75, 35.15, 33.10, 30.04, 29.91, 26.88, 26.55, 26.47, 23.60, 21.35, 21.14, 20.99, 20.76, 15.73, 14.16

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2535 Hz= 5.07, **α**-anomer: 5.38 (ddd, 1H, 3-H), 5.07 (d, 1H, 1-H), 5.00 (dd, 1H, 4-H), 4.31 (dd, 1H, 6-H), 4.04 (dd, 1H, 6-H), 4.01 (ddd, 1H, 5-H), 2.20 (ddd, 1H, 2-H), 1.87 (ddd, 1H, 2-H)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2321 Hz= 4.61, **β**-anomer: 5.03 (ddd, 1H, 3-H), 4.99 (dd, 1H, 4-H), 4.64 (dd, 1H, 1-H), 4.28 (dd, 1H, 6-H), 4.11 (dd, 1H, 6-H), 3.59 (ddd, 1H, 5-H), 2.30 (dd, 1H, 2-H), 1.79 (ddd, 1H, 2-H).

LC-MS (ESI) (+c): m/z (%): 669.32 (100) $[M + Na]^+$; **HR-MS** $C_{35}H_{50}O_{11}$ +^{23}Na: calc. 669.3251, found 669.3248.

Ethyl 4-*O*-(2´-deoxy-3´,4´,6´-tri-*O*-acetyl-α/β-D-*arabino*-hexopyranosyl) 2,3-dideoxy-6-pivaloyl-α-*threo*-D-hexopyranoside (156)



The reaction was carried out according to the protocol **TP1**.

Yield: 51 mg (0.096 mmol, 96%, α/β - 2: 1)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.22 (ddd, *J* = 11.5, 9.4, 5.2 Hz, 0.7H, 3-H'α), 5.17 (d, *J* = 3.0 Hz, 0.7H, 1-H'α), 5.00 (dd, *J* = 9.6, 9.8 Hz, 0.7H, 4-H'α), 4.99 (ddd, *J* = 11.2, 9.3, 5.1 Hz, 0.3H, 3-H'β), 4.94 (dd, *J* = 9.3, 9.3 Hz, 0.3H, 4-H'β), 4.77 (d, *J* = 2.2 Hz, 0.7H, 1-Hα), 4.76 (d, *J* = 2.8 Hz, 0.3H, 1-Hβ), 4.59 (dd, *J* = 9.6, 2.5 Hz, 0.3H, 1-H'β), 4.39 (dd, *J* = 11.5, 2.2 Hz, 0.7H, 6-Hα), 4.30 (dd, *J* = 12.2, 4.6 Hz, 0.7H, 6-Hα), 4.26 (m, 0.6H, 6-Hβ), 4.17 (dd, *J* = 11.5, 6.7 Hz, 0.7H, 6-H'α), 4.14 (dd, *J* = 11.6, 5.9 Hz, 0.3H, 6-H'β), 4.10 (dd, *J* = 12.0, 2.6 Hz, 0.3H, 6-H'β), 4.03 (dd, *J* = 12.2, 2.2 Hz, 0.7H, 6-H'α), 3.92 (ddd, *J* = 10.0, 4.5, 2.2 Hz, 0.7 H, 5-Hα), 3.89 (ddd, *J* = 9.4, 6.8, 2.2 Hz, 0.7H, 5-H'α), 3.83 (ddd. *J* = 9.7, 6.0, 1.9 Hz, 0.3H, 5-Hβ), 3.74 (dq, *J* = 9.7, 7.1 Hz, 0.7H, H-Et-$CH_2\alpha$), 3.70 (dq, *J* = 9.7, 7.1 Hz, 0.3H, H-Et-$CH_2\beta$), 3.6-3.48 (m, 1.3H, 5-H'α, 4-Hα, 4-Hβ), 3.45 (dq, *J* = 9.7, 7.1 Hz, 0.7H, H-Et-$CH_2\alpha$), 3.43 (dq, *J* = 9.7, 7.1 Hz, 0.3H, H-Et-$CH_2\beta$), 2.28 (ddd, *J* = 12.8, 4.8, 2.0 Hz, 0.3H, 2-H'β), 2.20 (ddd, *J* = 12.9, 5.2, 1.3 Hz, 0.7H, 2-H'α), 2.09, 2.04, 2.00 (3s, 6H, 3 x Ac α), 2.06, 2.02, 2.01 (3s, 3H, 3 x Ac β), 1.22 (s, 6H, Piv α), 1.22 (m, 3H, Et), 1.21 (s, 3H, Piv β).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 178.19, 170.63, 170.17, 170.08, 169.86, 169.73, 100.27+, 95.71+, 95.54+, 92.40+, 75.67+, 71.94+, 70.40+, 69.74+, 69.69+, 69.39+, 69.19+, 69.08+, 69.04+, 68.70+, 63.72-, 62.54-, 38.81-, 35.14-, 29.66-, 28.64-, 27.24+, 22.59-, 20.93+, 20.83+, 20.70+, 20.68+, 15.00+

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2209 Hz= 4.42, α**'α**-diastereomer: 4.80 (d, 1H, 1-H), 4.41 (d, 1H, 6-H), 4.20 (dd, 1H, 6-H), 3.92 (ddd, 1H, 5-H), 3.57 (ddd, 1H, 4-H), 2.1-1.6 (m, 4H, 3-H, 2-H).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 1928 Hz= 3.86, β**'α**-diastereomer: 4.78 (d, 1-H), 4.30 (dd, 1H, 6-H), 4.17 (dd, 1H, 6-H), 3.86 (ddd, 1H, 5-H), 3.52 (ddd, 1H, 4-H), 2.1-1.6 (m, 4H, 3-H, 2-H).

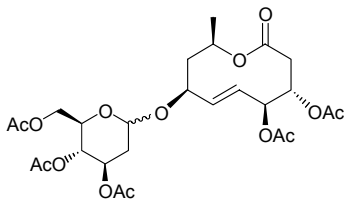
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2310 Hz= 4.62, **β'**α-diastereomer: 5.01 (ddd, 1H, 3-H'), 4.96 (dd, 1H, 4-H'), 4.62 (dd, 1H, 1-H'), 4.28

(dd, 1H, 6-H'); 4.12 (dd, 1H, 6-H'), 3.60 (ddd, 1H, 5-H'), 2.31 (ddd, 1H, 2-H'), 1.76 (ddd, 1H, 2-H').

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2601 Hz= 5.20, **α'**α-diastereomer: 5.25 (ddd, 1H, 3-H'), 5.20 (d, 1H, 1-H'), 5.03 (dd, 1H, 4-H'), 4.33 (dd, 1H, 6-H'); 4.06 (dd, 1H, 6-H'), 3.94 (ddd, 1H, 5-H'), 2.23 (ddd, 1H, 2-H'), 1.87 (ddd, 1H, 2-H').

LC-MS (ESI) (+c): m/z (%): 555.19 (100) $[M + Na]^+$; **HR-MS** $C_{25}H_{40}O_{12}$ +^{23}Na: calc. 555.2417, found 555.2402.

7-*O*-(2´-Deoxy-3´,4´,6´-tri-*O*-acetyl-α/β-D-*arabino*-pyranosyl)-3,4-di-*O*-acetyl-decarestrictine (157)



The reaction was carried out according to the protocol **TP1**.

Yield: 56 mg (0.098 mmol, 98%, α/β - 2:1)

1st fraction: **157**β

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.81 (dd, J = 16.0, 3.6 Hz, 1H, 5-H), 5.63 (ddd, J = 16.0, 9.6, 1.1 Hz, 1H, 6-H), 5.34 (ddd, J = 4.8, 3.6, 0.91 Hz, 1H, 4-H), 5.16 (ddq, J = 17.6, 6.3, 1.6 Hz, 1H, 9-H), 5.04 (ddd, J = 7.3, 4.8, 2.5 Hz,1H, 3-H), 4.95 (m, 2H, 3-H', 4-H'), 4.50 (dd, J = 9.6, 1.8 Hz, 1H, 1-H'β), 4.33 (ddd, J = 10.8, 9.6, 4.0 Hz, 1H, 7-H), 4.28 (dd, J = 12.2, 4.9 Hz, 1H, 6-H'), 4.07 (dd, J = 12.1, 2.2 Hz, 1H, 6-H'), 3.51 (ddd, J = 9.4, 5.0, 2.3 Hz, 1H, 5-H'), 2.69 (dd, J = 14.1, 7.3 Hz, 1H, 2-H), 2.54 (dd, J = 14.1, 2.5 Hz, 1H, 2-H), 2.23 (ddd, J = 12.3, 4.0, 1.6 Hz, 1H, 8-H), 2.19, 2.13, 2.10 (3s, 9H, 3 x CH_3CO'), 2.02, 2.01 (2s, 6H, 2 x CH_3CO), 1.95 (bd, J = 12.3 Hz, 1H, 8-H), 1.65 – 1.90 (m, 2H, 2 x 2-H'), 1.21 (d, J = 6.3 Hz, 3H, 10-H).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 170.6, 170.3, 169.8, 169.4, 169.1, 133.8, 127.0, 95.3, 72.0, 72.0, 70.9, 70.8, 69.1, 68.1, 62.5, 40.8, 36.1, 33.5, 21.3, 21.0, 20.9, 20.8, 20.7.

LC-MS (ESI) (+c): m/z (%): 595.17 (100) $[M + Na]^+$; **HR-MS** $C_{27}H_{38}O_{13}$ +^{23}Na: calc. 595.2003, found 595.2003.

[α]$^{25}_{D}$ = - 3.7^{o} (c = 0.5 in $CHCl_3$).

2nd fraction **157**α

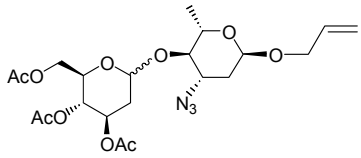
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.79 (dd, J = 16.6, 9.0 Hz, 1H, 6-H), 5.72 (dd, J = 16.6, 3.1, 1H, 5-H), 5.32 (dd, J = 5.2, 3.1, 0.9 Hz, 1H, 4-H), 5.27 (ddd, J = 11.3, 10.0, 5.3 Hz, 1H, 3-H'), 5.01 (ddq, J = 11.1, 6.4, 1.7 Hz, 1H, 9-H), 5.04 (ddd, J = 7.2, 5.2, 2.8 Hz,1H, 3-H), 5.00 (d, J = 2.7 Hz, 1H, 1-H'α), 4.98 (t, J = 10.0 Hz, 1H, 4-H'), 4.27 (dd, J = 12.3, 3.7 Hz, 1H, 6-H'), 4.07 (ddd, J = 10.6, 9.0, 3.5 Hz, 1H, 7-H), 3.92 (dd, J = 12.3, 2.2 Hz, 1H, 6-H'), 3.87 (ddd, J = 10.0, 3.7, 2.3 Hz, 1H, 5-H'), 2.67 (dd, J = 14.1, 7.2 Hz, 1H, 2-H), 2.56 (dd, J = 14.1, 2.8 Hz, 1H, 2-H), 2.16 (m, 1H, 8-H), 2.17, 2.11, 2.09 (3s, 9H, 3 x CH_3CO'), 2.02, 2.00 (2s, 6H, 2 x CH_3CO), 1.89 (ddd, J = 14.0, 3.3, 1.7 Hz, 1H, 8-H), 1.80 (bt, J = 11.3 Hz, 2H, 2 x 2-H'), 1.22 (d, J = 6.4 Hz, 3H, 10-H).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 170.6, 170.3, 169.8, 169.79, 169.4, 169.0, 135.1, 124.0, 95.6, 72.1, 70.7, 69.2, 69.0, 68.1, 67.9, 62.0, 40.1, 35.1, 33.7, 21.4, 21.0, 20.9, 20.87, 20.71, 20.70.

LC-MS (ESI) (+c): m/z (%): 595.17 (100) $[M + Na]^+$; **HR-MS** $C_{27}H_{38}O_{13}$ +^{23}Na: calc. 595.2003, found 595.2007.

[α]$^{25}_{D}$ = + 105.5^{o} (c = 1 in $CHCl_3$).

Allyl 4-*O*-(2´-deoxy-3´,4´,6´-tri-*O*-acetyl-α/β-D-*arabino*-pyranosyl)-3-azido-2,3,6-trideoxy-α-L-*arabino*-pyranoside (158)



The reaction was carried out according to the protocol **TP1**.

Yield: 39 mg (0.08 mmol, 80%, α/β - 2:1)

anomeric mixture

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.92 (ddd, *J* = 22.4, 10.5, 6.0 Hz, 1H, C*H*=CH_2), 5.35-5.20 (m, 3H, 3-H, CH=CH_2), 5.1 (bs, 1H), 5.07 (dd, *J* = 9.4, 9.4 Hz, 1H, 4-H), 4.91 (d, *J* = 2.8 Hz, 0.9H, 1-Hα), 4.4 (m, 1.8H), 4.1 (m, 2.6H), 3.95 (dd, *J* = 12.8, 6.1 Hz, 1H), 3.75 (m, 2H), 3.14 (dd, *J* = 9.4, 9.4 Hz, 1H, 4-H'), 2.28 (dd, *J* = 12.9, 5.0 Hz, 2H), 2.11, 2.07, 2.04 (3s, 9H, 3Ac), 2.06 (m, 2H), 1.84 (dddd, *J* = 20.8, 11.9, 11.9, 3.4 Hz, 2H), 1.25 (d, *J* = 6.3 Hz, 3H, 6-H').

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 170.82, 170.26, 169.92, 133.74+, 117.50-, 98.36+, 95.22+, 81.83+, 68.95+, 68.69+, 67.86-, 67.25+, 62.22-, 58.17+, 35.19-, 35.01-, 29.67-, 20.97+, 20.75+, 18.04+

α'α-diastereomer

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.91 (ddd, J = 16.8, 11.1, 5.5, 5.4 Hz, 1H, -C*H*=CH_2), 5.30 (dq, J = 17.0, 1.5 Hz, 1H, -CH=CH*H*'), 5.29 (ddd, J = 11.6, 9.6, 5.1 Hz, 1H, 3-H'), 5.21 (dq, J = 10.4, 1.1 Hz, 1H, -CH=C*H*H'), 5.08 (d, J = 3.0 Hz, 1H, 1-H'), 5.04 (t, J = 9.6 Hz, 1H, 4-H'), 4.89 (d, J = 2.8 Hz, 1H, 1-H), 4.39 (m, 2H, 5-H', 6-H'), 4.12 (dd, J = 13.0, 5.3 Hz, 1H, O-C*H*H'-CH=), 4.10 (m, 1H, 6-H'), 3.94 (dd, J = 12.8, 6.1 Hz, 1H, O-C*H*H'-CH=), 3.74 (dq, J = 9.4, 6.2 Hz, 1H, 5-H), 3.73 (m, 1H, 3-H), 3.13 (t, J = 9.4 Hz, 1H, 4-H), 2.26 (bd, J = 12.9 Hz, 2H, 2-H_{ax}, 2-H_{ax}'), 2.09, 2.05, 2.02 (3s, 9H, 3 x CH_3CO), 1.85 (dt, J = 12.6, 3.4 Hz, 1H, 2-H_{eq}'), 1.80 (dt, J = 12.6, 3.45 Hz, 1H, 2-H_{eq}), 1.23 (d, J = 6.2 Hz, 3H, 6-H).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 170.8, 170.2, 169.9 (3s, 3 x CH_3CO), 133.8 (d, -*C*H=CH_2), 117.5 (t, -CH=*C*H_2), 98.4 (d, C-1'), 95.3 (d, C-1), 81.9 (d, C-4), 69.1 (d, C-4'), 69.0 (d, C-3'), 68.7 (d, C-5'), 67.9 (t, O-*C*H_2-CH=), 67.3 (d, C-5), 62.3 (t, C-6'), 58.2 (d, C-3), 35.2, 35.1 (2t, C-2, C-2'), 20.9 (q, *C*H_3CO), 20.7 (q, 2 x *C*H_3CO), 18.1 (q, C-6).

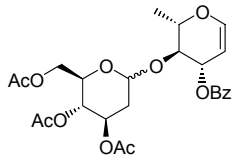
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2461 Hz = 4.92: 4.92 (d, 1H, 1-H), 3.75 (m, 2H, 3-H, 5-H), 3.15 (dd, 1H, 4-H), 2.29 (ddd, 1H, 2-H_{ax}), 1.82 (ddd, 1H, 2-H_{eq}), 1.26 (d, 3H, 6-H).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2205 Hz = 4.41: 5.31 (ddd, 1H, 3-H'), 5.10 (d, 1H, 1-H'), 5.07 (t, 1H, 4-H'), 4.42 (dd, 1H, 5-H'), 4.40 (dd, 1H, 6-H'), 4.12 (dd, 1H, 6-H'), 2.29 (dd, 1H, 2-H_{ax}'), 1.88 (dd, 1H, 2-H_{eq}').

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2622 Hz = 5.24: 5.94 (ddd, 1H, -C*H*=CH_2), 5.33 (dq, 1H, -CH=C*H*H'), 5.24 (dq, 1H, -CH=CH*H*'), 4.15 (ddd, 1H, O-C*H*H'-CH=), 3.97 (dd, 1H, O-CH*H*'-CH=).

LC-MS (ESI) (+c): m/z (%): 595.17 (100) $[M + Na]^+$; **HR-MS** $C_{27}H_{38}O_{13}$ +^{23}Na: calc. 595.2003, found 595.2003.

4-*O*-(3',4',6´-Tri-*O*-acetyl-2'-deoxy-α/β-D-*arabino*-hexopyranosyl)-1,5-anhydro-3-*O*-benzoyl-2,6-dideoxy-L-*arabino*-hex-1-enit (159)



The reaction was carried out according to the protocol **TP1**.

Yield: 38 mg (0.075 mmol, 75%, α/β - 2:1).

anomeric mixture

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 8.05 (d, 2H, Ph), 7.5 (m, 3H, Ph), 6.51 (dd, *J* = 6.0, 1.0 Hz, 1H, 1-H'), 5.59 (dd, *J* = 4.6, 3.7 Hz, 1H, 3-H'), 5.32 (ddd, *J* = 11.5, 9.6, 5.1 Hz, 1H, 3-H), 5.23 (d, *J* = 2.6 Hz, 0.7H, 1-Hα), 5.02 (dd, *J* =

9.6, 9.6 Hz, 1H, 4-H), 4.91 (dd, *J* = 5.9, 3.5 Hz, 1H, 2-H'), 4.3-3.8 (m, 5H), 2.32 (ddd, *J* = 12.8, 5.1, 0.9 Hz, 1H, 2-H), 2.04, 2.02, 2.01 (3s, 9H, 3Ac), 1.88, (ddd, *J* = 12.8, 11.5, 3.54 Hz, 1H, 2-H), 1.46 (d, *J* = 6.6 Hz, 3H, 6-H).

α-anomer

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 8.01 (d, J = 7.3 Hz, 2H, Ph-o), 7.57 (t, J = 7.3 Hz, 1H, Ph-p), 7.44 (t, J = 7.3 Hz, 2H, Ph-m), 6.47 (d, J = 6.0 Hz, 1H, 1-H), 5.55 (dd, J = 4.8, 3.7 Hz, 1H, 3-H), 5.28 (ddd, J = 11.8, 9.6, 5.0 Hz, 1H, 3-H'), 5.19 (d, J = 2.8 Hz, 1H, 1-H'), 4.98 (t, J = 9.6, 1H, 4-H'), 4.87 (dd, J = 6.0, 3.7 Hz, 1H, 2-H), 4.20 (dq, J = 6.5, 6.5 Hz, 1H, 5-H), 4.06 (m, 2H, 5-H', 6-H'), 3.90 (dd, J = 6.5, 4.8 Hz, 1H, 4-H), 3.82 (dd, J = 12.0, 1.3 Hz, 1H, 6-H'), 2.27 (dd, J = 12.5, 5.0 Hz, 1H, 2-H_{ax}'), 1.99, 1.98, 1.97 (3s, 9H, 3 x C*H*$_3$CO), 1.84 (ddd, J = 12.5, 11.8, 2.8 Hz, 1H, 2-H_{eq}'), 1.42 (d, J = 6.5 Hz, 3H, 6-H).

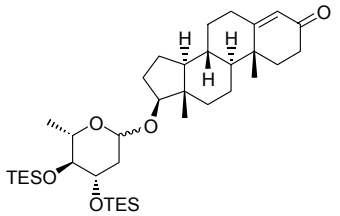
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 170.6, 170.1, 169.8 (3s, 3 x CH_3*C*O), 166.0 (s, Ph*C*O), 146.1 (d, C-1), 133.2 (d, Ph–p), 130.0 (s, P1-H), 129.6 (d, Ph-o), 128.5 (d, Ph-m), 98.3 (d, C-2), 97.1 (d, C-1'), 77.0 (d, C-4), 72.3 (d, C-5), 69.3 (d, C-3), 68.9, 68.8, 68.6 (3d, C-3', C-4', C-5'), 61.8 (t, C-6'), 35.1 (t, C-2'), 20.9, 20.64, 20.60 (3q, 3 x *C*H_3CO), 16.8 (q, C-6).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 3250 Hz= 6.50: 6.50 (d, 1H, 1-H), 5.58 (m, 1H, 3-H), 4.89 (dd, 1H, 2-H), 4.22 (dq, 1H, 5-H), 3.92 (dd, 1H, 4-H), 1.46 (d, 3H, 6-H).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2608 Hz= 5.21: 5.30 (ddd, 1H, 3-H'), 5.21 (d, 1H, 1-H'), 5.01 (t, 1H, 4-H'), 4.10 (d, 1H, 6-H'), 4.07 (dd, 1H, 5-H'), 3.85 (d, 1H, 6-H'), 2.30 (ddd, 1H, 2-H_{ax}'), 1.86 (dt, 1H, 2-H_{eq}').

LC-MS (ESI) (+c): m/z (%): 529.17 (100) $[M + Na]^+$; **HR-MS** $C_{25}H_{30}O_{11}$ +^{23}Na: calc. 529.1686, found 529.1669.

Testosteryl [2´,6´-dideoxy-3´,4´-di-*O*-triethylsilyl]-α/β-L-*arabino*-hexopyranoside (160)

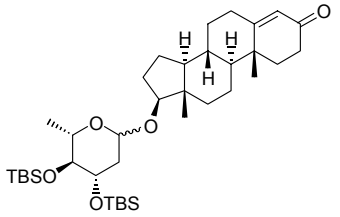


The reaction was carried out according to the protocol **TP2**.

Yield: 30 mg (0.046 mmol, 93%, α/β - 2:1)

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.76 (s, 1H, 4-H), 4.83 (d, *J* = 2.6 Hz, 0.7H, 1-H', α), 4.44 (dd, *J* = 9.7, 1.8 Hz, 0.3H, 1-H', β), 3.96 (ddd, *J* = 11.3, 8.6, 4.8 Hz, 0.7H, 3-H'), 3.73 (ddq, *J* = 9.0, 6.1 , 5.9 Hz, 1H, 5-H'), 3.51 (dd, *J* = 9.0, 8.6 Hz, 1H, 4-H'), 3.12 (dd, *J* = 8.5, 8.5 Hz, 1H, 17-H), 1.32 (d, *J* = 6.1 Hz, 3H, 6-H'), 2.5 – 0.7 (m).

Testosteryl [2´,6´-dideoxy-3´,4´-di-*O*-(*tert*-butyldimethylsilyl)]-α/β-L-*arabino*-hexopyranoside (161)



The reaction was carried out according to the protocol **TP2**.

Yield: 32 mg (0.049 mmol, 99%, α/β - 2:1)

1st fraction: **161**β

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.72 (s, 1H, 4-H), 4.38 (dd, J = 9.7, 1.6 Hz, 1H 1-H'), 3.63 (t, J = 8.5 Hz, 1H, 17-H), 3.60 (m, 1H, 5-H'), 3.15 (m, 2H, 3-H', 4-H'), 2.5 – 0.7 (m).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 199.5, 171.3, 123.8, 98.4, 87.2, 77.9, 73.3, 72.6, 54.0, 50.7, 42.4, 41.3, 38.7, 36.6, 35.7, 35.5, 34.0, 32.8, 31.6, 27.7, 26.9, 26.3, 26.1, 23.2, 20.6, 18.8, 18.3, 18.1, 17.4, 11.7, -2.7, -3.0, -3.8, -4.0

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2204 Hz= 4.41: 4.41 (d, 1H, 1-H'), 3.62 (ddd, 1H, 5-H'), 3.18 (m, 2H, 3-H', 4-H'), 2.07 (ddd, 1H, 2-H_{ax}'), 1.61 (dd, 1H, 2-H_{eq}'), 1.27 (d, 3H, 6-H').

LC-MS (ESI) (+c): m/z (%): 669.43 (100) $[M + Na]^+$; **HR-MS** $C_{37}H_{66}O_5Si_2$ +^{23}Na: calc. 669.4347, found 669.4354.

[α]$^{25}_{D}$ = + 64.6^{o} (c = 1 in $CHCl_3$).

2nd fraction: **161**α

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.72 (s, 1H, 4-H), 4.79 (d, J = 2.0 Hz, 1H 1-H'), 3.93 (ddd, J = 11.0, 8.7, 4.3 Hz, 1H, 3-H'), 3.63 (dq, J = 8.7, 6.4 Hz, 1H, 5-H'), 3.44 (t, J = 8.5 Hz, 1H, 17-H), 3.12 (t, J = 8.7 Hz, 1H, 4-H'), 2.5 – 0.7 (m).

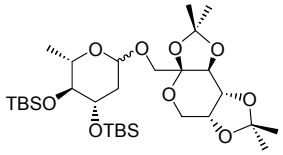
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 199.4, 171.2, 123.9, 98.2, 87.6, 78.5, 70.8, 69.3, 53.9, 50.2, 42.8, 39.9, 38.7, 37.1, 35.7, 35.5, 33.9, 32.8, 31.5, 28.6, 26.9, 26.3, 26.1, 23.4, 20.6, 18.6, 18.4, 18.1, 17.4, 11.6, -2.8, -3.0, -4.1, -4.4

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2412 Hz= 4.82: 4.82 (d, 1H, 1-H'), 3.95 (ddd, 1H 3-H'), 3.65 (dq, 1H, 5-H'), 3.15 (t, 1H, 4-H'), 2.07 (ddd, 1H, 2-H_{ax}'), 1.61 (dd, 1H, 2-H_{eq}'), 1.27 (d, 3H, 6-H').

LC-MS (ESI) (+c): m/z (%): 647.45 (100) $[M + Na]^+$; **HR-MS** $C_{37}H_{67}O_5Si_2$: calc. 647.4527, found 647.4545.

[α]$^{25}_{D}$ = + 3.7^{o} (c = 1 in $CHCl_3$).

1-*O*-(2´,6´-deoxy-3´,4´di-*O*-(*tert*-butyldimethylsilyl)-α/β-D-*arabino*-hexopyranosyl) (2:3, 4:5-di-*O*-isopropyliden)-α-D-*fructo*-hexopyranoside (162)

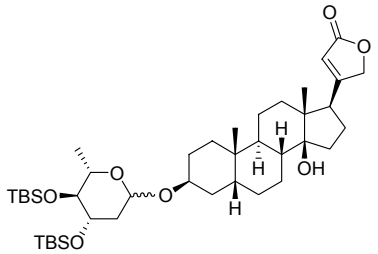


The reaction was carried out according to the protocol **TP2**.

Yield: 19 mg (0.03 mmol, 60%, α/β - 1.8:1).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 4.89 (d, *J* = 2.7 Hz, 0.6H, 1-H'α), 4.67 (dd, *J* = 7.9, 2.6 Hz, 1H), 4.47 (d, *J* = 2.5 Hz, 1H), 4.33 (dd, *J* = 9.0, 2.3 Hz, 0.4H, 1-H'β), 4.28 (bd, *J* = 8.0 Hz, 1H), 4.1-3.5 (m, 5H), 3.20 (dd, *J* = 8.5, 8.5 Hz, 1H, 4-H'), 2.16 (ddd, *J* = 13.0, 4.9, 1.1 Hz, 1H), 1.64, 1.58, 1.51, 1.47 (4s, 12H, 4 x CH_3), 1.24 (d, *J* = 6.1 Hz, 1H, 6-H'), 0.95 (m, 18H), 0.1 (m, 12H).

Digitoxigenyl [2,6-dideoxy-3,4-di-*O*-(*tert*-butyldimethylsilyl)]-α/β-L-*arabino*-pyranoside (163)



The reaction was carried out according to the protocol **TP2**.

Yield: 35 mg (0.048 mmol, 95%, α/β - 3:1).

1st fraction: **163**β

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.86 (s, 1H, 22-H), 4.98 (dd, *J* = 18.0, 1.5 Hz, 1H, 21-H), 4.80 (dd, *J* = 18.0, 1.5 Hz, 1H, 21-H), 4.46 (dd, *J* = 9.6, 1.8 Hz, 1H, 1-H'), 3.99 (bs, 1H), 3.62 (ddd, J = 11.5, 4.7, 7.1 Hz, 1H, 3-H'), 3.17 (m, 1H, 4-H'), 3.16 (dq, J = 8.2, 6.8 Hz, 1H, 5-H'), 2.75 (m, 1H, 3-H), 2.2 – 0.0 (m).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 174.41, 174.40, 117.7, 97.3, 85.6, 77.9, 73.4, 73.4, 72.9, 72.6, 51.0, 49.6, 41.9, 41.5, 40.1, 36.2, 35.7, 35.2, 33.2, 32.0, 30.0, 26.9, 26.88, 26.4, 26.3, 26.1, 24.6, 23.6, 21.3, 21.2, 18.8, 18.3, 18.1, 15.8, 14.2, -2.7, -3.0, -3.9, -4.0

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2246 Hz= 4.49: 4.49 (d, 1H, 1-H'), 3.64 (ddd, 1H, 3-H'), 3.20 (t, 1H, 4-H'), 3.19 (dq, 1H, 5-H'), 2.06 (ddd, 1H, 2-H_{ax}'), 1.65 (dd, 1H, 2-H_{eq}'), 1.27 (d, 3H, 6-H').

LC-MS (ESI) (+c): m/z (%): 755.46 (30) $[M + Na]^+$, 796.48 (100) $[M + CH_3CN + Na]^+$; **HR-MS** $C_{41}H_{72}O_7Si_2$ + Na: calc. 755.4714, found 755.4700.

[α]$^{25}_{D}$ = + 25.2^{o} (c = 1 in $CHCl_3$).

2nd fraction: **163**α

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.87 (s, 1H, 22-H), 4.98 (d, *J* = 18.0 Hz, 1H, 21-H), 4.86 (d, J = 1.9 Hz, 1H, 1-H'), 4.80 (dd, *J* = 18.0, 1.5 Hz, 1H, 21-H), 3.99 (ddd, J = 11.2, 8.5, 4.1 Hz, 1H, 3-H'), 3.88 (bs, 1H), 3.63 (dq, J = 8.5, 6.3 Hz, 1H, 5-H'), 3.14 (t, J = 8.5 Hz, 1H, 4-H'), 2.75 (m, 1H, 3-H), 2.2 – 0.0 (m).

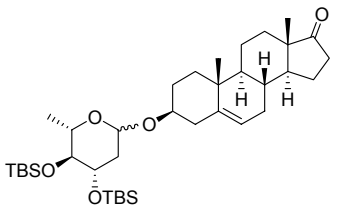
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 174.5, 174.4, 117.7, 94.5, 85.6, 78.6, 73.4, 70.8, 70.4, 69.3, 50.9, 49.6, 41.9, 40.14, 40.1, 36.4, 35.7, 35.2, 33.2, 30.4, 29.5, 26.9, 26.88, 26.74, 26.7, 26.3, 26.2, 23.8, 21.5, 21.2, 18.7, 18.5, 18.1, 15.8, -2.8, -2.9, -4.1, -4.4

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2446 Hz= 4.89: 4.89 (d, 1H, 1-H'), 4.01 (ddd, 1H, 3-H'), 3.66 (dq, 1H, 5-H'), 3.16 (t, 1H, 4-H'), 2.04 (ddd, 1H, 2-H_{ax}'), 1.67 (dd, 1H, 2-H_{eq}'), 1.22 (d, 3H, 6-H').

LC-MS (ESI) (+c): m/z (%): 796.48 (100) $[M + CH_3CN + Na]^+$; **HR-MS** $C_{43}H_{75}O_7NSi_2$ + Na: calc. 796.4980, found 796.4982.

[α]$^{25}_{D}$ = - 29.6^{o} (c = 1 in $CHCl_3$).

Dehydro-*epi*-androsteryl [2´,6´-dideoxy-3´,4´-di-*O*-(*tert*-butyldimethyl silyl)]-α/β-L-*arabino*-hexopyranoside (164)



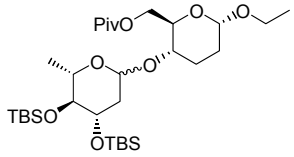
The reaction was carried out according to the protocol **TP2**.

Yield: 29 mg (0.045 mmol, 90%, α/β - 3:1).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.36 (ddd, *J* = 13.1, 13.1, 5.0 Hz, 1H, 6-H), 4.94 (d, *J* = 2.7 Hz, 0.75H, 1-H'α), 4.58 (dd, *J* = 9.6, 1.6 Hz, 0.25H, 1-H'β), 3.94 (ddd, *J* = 10.9, 7.9, 4.5 Hz, 0.75H, 3-H'α), 3.7-3.5 (m, 2H), 3.4 (m, 0.7H), 3.2-3.1 (m, dd *J* = 8.2, 8.2 Hz, 1.8H), 2.7 – 0.0 (m).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 221.12, 221.10, 141.18, 141.17, 130.71+, 128.97+, 127.11+, 120.88+, 120.67+, 97.15+, 95.43+, 78.47+, 76.44+, 73.21+, 72.60+, 70.78+, 68.94+, 64.38+, 51.75+, 50.27+, 47.52, 39.91-, 38.76-, 37.30-, 36.89-, 36.84, 35.82-, 31.49+, 31.48-, 30.80-, 29.53-, 26.29+, 26.25+, 26.11+, 25.33+, 21.86-, 20.32-, 19.42+, 18.62+, 18.28+, 18.27+, 18.08, 18.03, 13.51+, -2.82+, -3.09+, -4.01+, -4.29+

Ethyl 4-*O*-[2´,6´-dideoxy-3´,4´-di-*O*-(*tert*-butyldimethylsilyl)-α/β-L-*arabino*-hexopyranosyl]-2,3-dideoxy-6-pivaloyl-α-D-*threo*-hexopyranoside (165)



The reaction was carried out according to the protocol **TP2**.

Yield: 19 mg (0.031 mmol, 60%, α/β - 5:1)

1st fraction: **165**β

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 4.77 (d, *J* = 2.7 Hz, 1H, 1-H), 4.51 (dd, *J* = 9.6, 1.8 Hz, 1H, 1-H'), 4.47 (dd, *J* = 11.9, 1.6 Hz, 1H, 6-H), 4.10 (dd, *J* = 11.9, 7.5 Hz, 1H, 6-H), 3.82 (ddd, *J* = 9.4, 7.5, 1.6 Hz, 1H, 5-H), 3.73 (dq, *J* = 9.6, 7.0 Hz, 1H, O-CH*H*'-CH_3), 3.62 (m, 2H, 3-H', 4-H), 3.44 (dq, *J* = 9.6, 7.0 Hz, 1H, O-CH*H*'-CH_3), 3.13 (m, 2H, 4-H', 5-H'), 2.03 (ddd, *J* = 12.5, 4.9, 2.0 Hz, 1H, 2-H'$_{ax}$), 1.92 (m, 1H, 3-H), 1.80 (m, 2H, 3-H, 2-H), 1.69 (m, 1H, 2-H), 1.55 (m, 1H, 2-H'$_{eq}$), 1.21 (m, 15H, 6-H', $COC(CH_3)_3$, O-CH_2-CH_3), 0.90, 0.89 (2s, 18H, 2 x Si-*t-Bu*), 0.10, 0.09, 0.08 (3s, 12H, 2 x $Si(CH_3)_2$).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 178.3 (s, CO), 95.6, 95.4 (2d, C-1', C-1), 77.9 (d, C-4'), 73.2 (d, C-3'), 72.7 (d, C-5'), 70.6 (d, C-4), 70.0 (d, C-5), 64.5 (t, C-6), 62.1 (t, O*C*H_2CH_3), 41.3 (t, C-2'), 38.8 (s, CO*C*$(CH_3)_3$), 28.9 (t, C-2), 27.3 (q, $COC(CH_3)_3$), 26.3, 26.1 (2q, 2 x $SiC(CH_3)_3$), 23.7 (t, C-3), 18.7, 18.1 (2q, 2 x $SiC(CH_3)_3$), 18.3 (q, C-6'), 15.0 (q, O-CH_2-CH_3), -2.8, -3.0, -3.9, -4.1 (4q, 2 x $Si(CH_3)_2C(CH_3)_3$).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2400Hz= 4.80: 4.80 (d, 1H, 1-H), 4.50 (dd, 1H, 6-H), 4.13 (dd, 1H, 6-H), 3.85 (ddd, 1H, 5-H), 3.66 (ddd, 1H, 4-H), 1.94 (m, 1H, 3-H), 1.83 (m, 2H, 3-H, 2-H), 1.72 (m, 1H, 2-H).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2273 Hz= 4.55: 4.55 (d, 1H, 1-H'), 3.63 (ddd, 1H, 3-H'), 3.16 (m, 2H, 5-H', 4-H'), 2.06 (dd, 1H, 2-H'$_{ax}$), 1.58 (ddd, 1H, 2-H'$_{eq}$), 1.26 (q, 3H, 6-H').

LC-MS (ESI) (+c): m/z (%): 641.41 (100) $[M + Na]^+$; **HR-MS** $C_{31}H_{62}O_8Si_2$ + Na: calc. 641.3881, found 641.3894.

$\mathbf{[\alpha]^{25}_D}$ = + 22.7° (c = 1 in $CHCl_3$).

2nd fraction: **165**α

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 4.81 (d, *J* = 2.8 Hz, 1H, 1-H'), 4.76 (d, *J* = 2.8 Hz, 1H, 1-H), 4.21 (dd, *J* = 11.7, 1.7 Hz, 1H, 6-H), 4.17 (dd, *J* = 11.7, 5.2 Hz, 1H 6-H), 3.90 (ddd, *J* = 11.0, 9.0, 4.5 Hz, 1H, 3-H'), 3.79 (ddd, *J* = 10.0, 5.2, 2.0 Hz, 1H, 5-H), 3.73 (dq, *J* = 9.0, 6.6 Hz, 1H, 5-H'), 3.70 (dq, *J* = 9.0,

6.8 Hz, 1H, O-CH*H*'-CH_3), 3.45 (dq, *J* = 9.0, 6.8 Hz, 1H, O-CH*H*'-CH_3), 3.42 (dd, *J* = 10.0, 4.4 Hz, 1H, 4-H), 3.13 (t, *J* = 9.0 Hz, 1H, 4-H'), 2.01 (m, 2H, 2-H'$_{ax}$, 3-H), 1.92 (ddt, *J* = 12.9, 4.4 Hz, 1H, 3-H), 1.79 (bd, *J* = 14.0 Hz, 1H, 2-H), 1.70 (ddt, *J* = 14.0, 12.9, 4.0 Hz, 1H, 2-H), 1.60 (ddd, *J* = 13.4, 11.0, 3.6 Hz, 1H, 2-H'$_{eq}$), 1.23 (t, *J* = 6.8 Hz, 3H, O-CH_2-CH_3), 1.21 (s, 9H, COC(CH_3)$_3$), 1.18 (d, *J* = 6.6 Hz, 3H, 6-H'), 0.90, 0.89 (2s, 18H, 2 x Si-*t*-Bu), 0.10, 0.09, 0.07 (3s, 12H, 2 x Si(CH_3)$_2$).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 178.2 (s, CO), 99.4 (d, C-1'), 96.0 (d, C-1), 78.4 (d, C-4'), 74.9 (d, C-4), 70.6 (d, C-3'), 70.0 (d, C-5), 69.3 (d, C-5'), 63.8 (t, C-6), 62.4 (t, O*C*$H_2$$CH_3$), 39.8 (t, C-2'), 38.8 (s, CO*C*(CH_3)$_3$), 29.2 (t, C-2), 27.2 (q, COC(*C*H_3)$_3$), 26.9 (t, C-3), 26.2, 26.1 (2q, 2 x SiC(*C*H_3)$_3$), 18.5, 18.1 (2q, 2 x Si*C*(CH_3)$_3$), 18.3 (q, C-6'), 15.1 (q, O-CH_2-*C*H_3), -2.8, -3.1, -4.0, -4.4 (4q, 2 x Si(*C*H_3)$_2$C(CH_3)$_3$).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 631 Hz= 1.26: 3.75 (dq, 1H, O-CH*H*'-CH_3), 3.48 (dq, 1H, O-CH*H*'-CH_3), 1.26 (t, 3H, OCH_2C*H*$_3$).

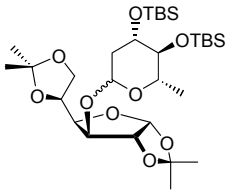
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 2397 Hz= 4.79: 4.79 (d, 1H, 1-H), 4.24 (dd, 1H, 6-H), 4.20 (dd, 1H, 6-H), 3.82 (ddd, 1H, 5-H), 3.45 (ddd, 1H, 4-H), 2.04 (ddd, 1H, 3-H), 1.94 (dq, 1H, 3-H), 1.81 (d, 1H, 2-H), 1.74 (ddd, 1H, 2-H).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY**: 1580 Hz= 3.16: 4.83 (dd, 1H, 1-H'), 3.92 (ddd, 1H, 3-H'), 3.72 (dq, 1H, 5-H'), 3.16 (t, 1H, 4-H'), 2.03 (dd, 1H, 2-H'$_{ax}$), 1.63 (ddd, 1H, 2-H'$_{eq}$), 1.20 (q, 3H, 6-H').

LC-MS (ESI) (+c): m/z (%): 641.36 (100) $[M + Na]^+$; **HR-MS** $C_{31}H_{62}O_8Si_2$ + Na: calc. 641.3881, found 641.3904.

[α]$^{25}_D$ = + 19.6^o (c = 1 in $CHCl_3$).

3-*O*-[2´,6´-dideoxy-3´,4´-di-*O*-(*tert*-butyldimethylsilyl)-α/β-L-*arabino*-hexopyranosyl]-(1:2,5:6-di-*O*-isopropylidene)-α-D-*gluco*-hexofuranosid (166)



The reaction was carried out according to the protocol **TP2**.

Yield: 17 mg (0.0275 mmol, 55%, α/β - 2:1)

diastereomeric mixture

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.91 (d, *J* = 3.5 Hz, 1H, 1-H), 4.99 (d, *J* = 3.3 Hz, 0.7H, 1-H'α), 4.82 (dd, *J* = 9.8, 1.7 Hz, 0.33H, 1-H'β), 4.53 (d, *J* = 3.7 Hz, 0.7H), 4.4-3.8 (m, 4H), 3.6 (m, 0.6H), 3.18 (dd, *J* = 8.6, 8.6 Hz, 1H, 4-H'), 2.1 (m, 1H), 1.54, 1.44, 1.39, 1.34 (4s, 12H, 4 x CH_3), 1.22 (d, *J* = 6.2 Hz, 3H, 6-H'), 0.93 (m, 18H, 2 x t-*Bu*$SiMe_2$), 0.11 (m, 12H, 2 x t-BuSi*Me*$_2$).

Cyclohexyl α/β-L-rhamnoside (169)

A suspension of phenylthio 3,4-di-*O*-benzyl-2,6-dideoxy-α-L-*arabino*-hexopyranoside **167** (42 mg, 0.1 mmol) and powdered molecular sieves 4A (50 mg) in acetonitrile (5 ml) was cooled to 0°C and treated with selectfluor™ (0.105 mmol). The reaction mixture was shaken for 20 minutes (t.l.c: ethyl acetate / petroleum ether 1:15) after which time the reaction was terminated by addition of dry Amberlite A-21 (10 mg). The resulting suspension was filtered through a pad of Al_2O_3 and washed with ethyl acetate (2x 1 ml). The solvent was evaporated in vacuo and the residue was dissolved in isopropanol (5 ml). To this solution polymer-supported borohydride (200 mg) was added. The suspension was shaken overnight and the polymer was removed by filtration which was followed by washing with isopropanol (1 ml). A second portion of polymer-supported borohydride (200 mg) was added to the filtrate in order to remove final traces of diphenyl disulfide. The suspension was shaken for additional 12 h, filtered and the solvent was removed under reduced pressure. The resulting material **168** was

subjected to hydrogenation conditions by dissolving it in methanol (20 ml) in the presence of Pd/C (10 mol%) over hydrogen atmosphere (20 bar) to yield fully debenzylated disaccharide **169** within 2h as an inseparable mixture of isomers.

Yield: 21.4 mg, 93 μmol; 93% (α/β= 2:1, inseparable mixture of isomers);

1-*O*-Cyclohexyl-3,4-bis-*O*-benzyl-α/β-L-rhamnoside (168)

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 7.31 (m, 10H, 2 x Ph), 5.02 (d, *J* = 3.0 Hz, 0.6H, 1-Hα), 4.96 (d, *J* = 10.9 Hz, 1H, Ph-C*H*H), 4.67 (s, 2H, Ph-CH_2), 4.66 (d, *J* = 10.9 Hz, 1H, Ph-CH*H*), 4.56 (dd, *J* = 9.8, 1.9 Hz, 0.4H, 1-Hβ), 4.00 (ddd, *J* = 11.3, 9.3, 5.0 Hz, 0.6H, 3-Hα), 3.83 (dq, *J* = 9.3, 6.2 Hz, 0.6H, 5-Hα), 3.64 (m, 0.4H, 3-Hβ), 3.52 (m, 1H, Cy^{1}), 3.33 (dq, *J* = 9.0, 6.1 Hz, 0.4H, 5-Hβ), 3.16 (t, *J* = 9.0 Hz, 0.4H, 4-Hβ), 3.14 (t, *J* = 9.3 Hz, 0.6H, 4-Hα), 2.31 (ddd, *J* = 12.3, 5.0, 1.8 Hz, 0.4H, 2-H_{ax}β), 2.26 (ddd, *J* = 12.7, 5.0, 1.2 Hz, 0.6H, 2-H_{ax}α), 2.0 - 1.28 (m 14H), 1.33 (d, *J* = 6.1 Hz, 6-Hβ), 1.29 (d, *J* = 6.2 Hz, 6-Hα).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 128.37, 128.33, 128.32, 128.08, 128.02, 127.65, 127.60, 127.57, 127.44 (2 x Ph), 97.28 (C-1β), 94.73 (C-1α), 84.55 (C-4α), 83.67 (C-4β), 79.45, 77.60, 75.22, 74.17, 71.71, 71.23, 67.15 (C-3α, C-3β, C-5α, C-5β, 2 x Bn-*C*H_2, C-cy^{1}), 37.53, (C-2β), 36.31 (C-2α), 33.63, 33.41, 31.90, 31.45, 29.66, 25.69, 25.61, 24.25, 24.10, 23.97 (Cy^{2,3,4,5,6}), 18.22 (C-6β), 18.11 (C-6α).

1-*O*-Cyclohexyl-α/β-L-rhamnoside (169)

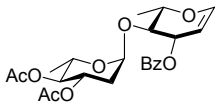
^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 4.99 (d, *J* = 3.2 Hz, 0.6H, 1-Hα), 4.61 (dd, *J* = 9.6, 1.8 Hz, 0.4H, 1-Hβ), 3.92 (ddd, *J* = 11.6, 9.0, 5.0 Hz, 0.6H, 3-Hα), 3.70 (dq, *J* = 9.1, 6.2 Hz, 0.6H, 5-Hα), 3.65 – 3.43 (m, 1.4H), 3.25 (dq, *J* = 9.1, 6.1 Hz, 0.4H, 5-Hβ), 3.13 (bs, 2H, 2 x OH), 3.07 (bt, *J* = 9.0 Hz, 1H, 4-H), 2.14 (ddd, *J* = 12.4, 5.0, 1.8 Hz, 0.4H, 2-H_{ax}β), 2.7 (ddd, *J* = 12.7, 5.0, 1.1 Hz, 0.6H, 2-H_{ax}α), 2.0 - 1.15 (m 14H), 1.32 (d, *J* = 6.1 Hz, 6-Hβ), 1.26 (d, *J* = 6.2 Hz, 6-Hα).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 97.31 (C-1β), 94.95 (C-1α), 78.20 (C-4α), 77.56 (C-4β), 74.50, 71.90, 71.55, 69.30, 67.52 (C-3α, C-3β, C-5α,

C-5β, C-cy[1]), 39.64, (C-2β), 38.32 (C-2α), 33.57, 33.48, 31.87, 31.51, 25.66, 25.59, 24.26, 24.28, 23.98 (Cy[2,3,4,5,6]), 17.75 (C-6β), 17.68 (C-6α).

11.7. Experiments to the chapter 7.

4-*O*-(3',4'-Di-*O*-acetyl-2',6'-dideoxy-α-L-*arabino*-hexopyranosyl)-3-*O*-benzoyl-2,6-dideoxy-L-*arabino*-hex-1-enit (170)



The reaction was carried out according to the protocol **TP1** except for the following details: thioglycoside **18** was used.

Yield: 43.4 mg (0.097 mmol, 97%).

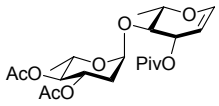
[1]**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 8.01 (d, *J* = 7.1 Hz, 2H, *Ph*-o), 7.57 (dd, *J* = 7.1, 7.1 Hz, 1H, *Ph*-p), 7.45 (dd, *J* = 7.1, 7.1 Hz, 2H, *Ph*-m), 6.45 (d, *J* = 6.1 Hz, 1H, 1-H), 5.51 (bdd, *J* = 4.1, 3.5 Hz, 1H, 3-H), 5.25 (d, *J* = 3.7 Hz, 1H, 1-H'), 5.23 (ddd, *J* = 11.5, 9.6, 5.2 Hz, 1H, 3-H'), 4.87 (dd, *J* = 6.1, 3.5 Hz, 1H, 2-H), 4.71 (dd, *J* = 9.6, 9.6 Hz, 1H, 4-H'), 4.18 (dq, *J* = 6.7, 6.5 Hz, 1H, 5-H), 3.94 (dq, *J* = 9.6, 6.3 Hz, 1H, 5-H'), 3.93 (m, 1H, 4-H), 2.15 (dd, *J* = 13.0, 5.2 Hz, 1H, 2-H'$_{ax}$), 2.04, 1.96 (2s, 6H, 2C$\underline{H}_3$CO), 1.75 (ddd, *J* = 13.0, 11.5, 3.7 Hz, 1H, 2-H'$_{eq}$), 1.46 (d, *J* = 6.5 Hz, 3H, 6-H), 1.18 (d, *J* = 6.3 Hz, 3H, 6-H');

[13]**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 170.1 (s, CH_3*C*O), 170.11 (s, CH_3*C*O), 165.9 (s, Ph*C*O), 146.0 (d, C-1), 133.2 (d, *Ph*-o), 129.9 (s, *Ph*-1), 129.6 (d, *Ph*-o), 128.5 (d, *Ph*-m), 98.5 (d, C-2), 96.4 (d, C-1'), 75.4 (d, C-4), 74.7 (d, C-4'), 73.3 (d, C-5), 70.8 (d, C-3), 68.6 (d, C-3'), 66.5 (d, C-5'), 35.4 (t, C-2'), 20.9, 20.8 (2q, 2 x *C*H_3CO), 17.4 (q, C-6'), 17.3 (q, C-6).

[1]**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 3442 Hz = 6.48 ppm: δ = 6.48 (d, 1-H), 5.54 (ddd, 3-H), 4.90 (dd, 2-H), 4.20 (dq, 5-H), 3.96 (dd, 4-H), 1.49 (d, 6-H);

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 1094 Hz = 2.19 ppm: δ = 5.28 (d, 1-H'), 5.25 (ddd, 3-H'), 4.73 (dd, 4-H'), 3.97 (dq, 5-H'), 2.19 (dd, 2-H'$_{ax}$), 1.78 (ddd, 2-H'$_{eq}$), 1.21 (d, 6-H')

4-*O*-(3',4'-Di-*O*-acetyl-2',6'-dideoxy-α-L-*arabino*-hexopyranosyl)-3-*O*-pivaloyl-2,6-dideoxy-L-*arabino*-hex-1-enit (171)



The reaction was carried out according to the protocol **TP1** except for the following details: thioglycoside **19** (65 mg, 0.2 mmol), glycal **32** (43 mg, 0.2 mmol), selectfluor™ (71 mg, 0.2 mmol).

Yield: 83 mg (0.194 mmol, 97%).

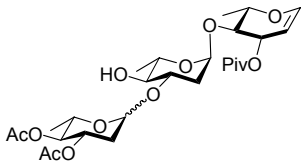
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm)*:* δ = 6.43 (dd, *J* = 6.1, 1.2 Hz, 1H, 1-H), 5.21 (bdd, *J* = 3.1, 5.8 Hz, 1H, 3-H), 5.23 (d, *J* = 3.7 Hz, 1H, 1-H'), 5.23 (ddd, *J* = 11.6, 9.7, 5.2 Hz, 1H, 3-H'), 4.71 (dd, *J* = 6.1, 3.1 Hz, 1H, 2-H), 4.70 (dd, *J* = 9.7, 9.7 Hz, 1H, 4-H'), 4.15 (bdq, *J* = 6.6, 6.6 Hz, 1H, 5-H), 3.95 (dq, *J* = 9.7, 6.5 Hz, 1H, 5-H'), 3.74 (dd, *J* = 7.0, 5.8 Hz, 1H, 4-H), 2.19 (dd, *J* = 13.0, 5.2 Hz, 1H, 2-H'$_{ax}$), 2.04, 1.96 (2s, 6H, 2C$\underline{H}_3$CO), 1.75 (ddd, *J* = 13.0, 11.6, 3.7 Hz, 1H, 2-H'$_{eq}$), 1.40 (d, *J* = 6.6 Hz, 3H, 6-H), 1.20 (s, 9H, (C$\underline{H}_3$)$_3$C), 1.19 (d, *J* = 6.4 Hz, 3H, 6-H');

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ =178.0 s, 170.1 s, 170.1 s, 146.0 d, 98.5 d, 96.5 d, 75.7 d, 74.7 d, 73.2 d, 70.2 d, 68.7 d, 66.4 d, 38.7 s, 35.4 t, 27.0 q 20.9 q, 20.8 q, 17.3 q, 17.2 q;

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 3210 Hz = 6.42 ppm: δ = 6.42 (d, 1-H), 5.22 (ddd, 3-H), 4.72 (dd, 2-H), 4.11 (dq, 5-H), 3.75 (dd, 4-H), 1.40 (d, 6-H);

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 1094 Hz = 2.19 ppm: δ = 5.22 (d, 1-H'), 5.25 (ddd, 3-H'), 4.73 (dd, 4-H'), 3.95 (dq, 5-H'), 2.19 (dd, 2-H'$_{ax}$), 1.75 (ddd, 2-H'$_{eq}$), 1.21 (d, 6-H')

4-*O*-(3'-*O*-(3'',4''-Di-*O*-acetyl-2'',6''-dideoxy-β-L-*arabino*-hexopyranosyl)-2',6'-dideoxy-α-L-arabino-hexopyranosyl)-3-*O*-pivaloyl-2,6-dideoxy-L-*arabino*-hex-1-enit (173β); 4-*O*-(3'-*O*-(3'',4''-Di-*O*-acetyl-2'',6''-dideoxy-α-L-*arabino*-hexopyranosyl)-2',6'-dideoxy-α-L-arabino-hexopyranosyl)-3-*O*-pivaloyl-2,6-dideoxy-L-*arabino*-hex-1-enit (173α)



The reaction was carried out according to the protocol **TP1** except for the following details: thioglycoside **18** (52 mg, 0.16 mmol), deprotected disaccharide **171** (55 mg, 0.16 mmol), selectfluor™ (55 mg, 0.16 mmol). Column chromatography (CH_2Cl_2/Acetone 12:1). The two fractions were isolated.

1st fraction: **173**β 5.5 mg (0.0099 mmol, 6.2%).

*2nd fraction:***173**α 24 mg (0.043 mmol, 27%)

1st fraction

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 6.40 (d, *J* = 5.8 Hz, 1H, 1-H), 5.19 (dd, *J* = 4.0, 3.9 Hz, 1H, 3-H), 5.13 (d, *J* = 3.3 Hz, 1H, 1-H'), 4.95 (ddd, *J* = 11.8, 9.4, 5.2 Hz, 1H, 3-H''), 4.75 (dd, *J* = 9.4, 9.4 Hz, 1H, 4-H''), 4.72 (dd, *J* = 5.8, 3.2 Hz, 1H, 2-H), 4.63 (dd, *J* = 9.6, 1.6 Hz, 1H, 1-H''), 4.10 (dq, *J* = 6.6, 6.4 Hz, 1H, 5-H), 3.8-3.9 (m, 2H, 3-H', 4-H), 3.69 (dq, *J* = 9.2, 6.2 Hz, 1H, 5-H'), 3.57 (dq, *J* = 9.4, 6.1 Hz, 1H, 5-H''), 3.11 (dd, *J* = 9.2, 9.2 Hz, 1H, 4-H'), 2.33 (ddd, *J* = 12.6, 5.2, 1.6 Hz, 1H, 2-H''$_{ax}$), 2.04, 2.02 (2s, 6H, 2CH_3CO), 2.00 (m, 1H, 2-H'$_{ax}$), 1.7-1.8 (m, 2H, 2-H'$_{eq}$, 2-H''$_{eq}$), 1.39 (d, *J* = 6.6 Hz, 3H, 6-H), 1.30 (d, *J* = 6.2 Hz, 3H, 6-H'), 1.25 (d, *J* = 6.1 Hz, 3H, 6-H''), 1.19 (s, 9H, Piv)

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 177.9 (s, *C*OPiv), 170.2, 169.9 (2s, *C*OAc), 145.7 (d, C-1), 99.4 (d, C-1''), 98.4 (d, C-2), 97.2 (d, C-1'), 80.3 (d, C-4), 75.6 (d, C-3'), 75.4 (d, C-4'), 73.6 (d, C-4''), 73.4 (d, C-5), 70.4 (d, C-3''), 70.3 (d, C-5''), 69.6 (d, C-3), 68.6 (d, C-5'), 38.8 (s, *C*$(CH_3)_3$), 36.6, 36.5 (2t, C-2', 2''), 27.0 (q, C(*C*$H_3)_3$), 20.9, 20.8 (2q, 2CO*C*H_3), 17.7 (q, C-6), 17.5 (q, C-6'), 17.2 (C-6'')

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 2613 Hz = 5.22 ppm: δ = 6.43 (d, 1-H), 5.22 (dd, 3-H), 4.75 (dd, 2-H), 4.13 (dq, 5-H), 3.77 (dd, 4-H), 1.42 (d, 6-H)

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 2581 Hz = 5.16 ppm: δ =: 5.16 (d, 1-H'), 3.76 (ddd, 3-H'), 3.72 (dq, 5-H'), 3.14 (dd, 4-H'), 2.04 (dd, 2-H'$_{ax}$), 1.76 (ddd, 2-H'$_{eq}$), 1.32 (d, 6-H')

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 2330 Hz = 4.66 ppm: δ = 4.98 (ddd, 3-H''), 4.78 (dd, 4-H''), 4.66 (dd, 1-H''), 3.60 (dq, 5-H''), 2.36 (ddd, 2-H''$_{ax}$), 1.76 (ddd, 2-H''$_{eq}$), 1.28 (d, 6-H'')

2nd fraction

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 6.38 (d, *J* = 5.7 Hz, 1H, H-1), 5.22 (m, 2H, 3-H, 3-H''), 5.11 (bs, 2H, 1-H', 1-H''), 4.73 (dd, *J* = 9.7, 9.7 Hz, 1H, 4-H''), 4.69 (dd, *J* = 5.7, 3.2 Hz, 1H, 2-H), 4.07 (dq, *J* = 6.8, 6.6 Hz, 1H, 5-H), 3.86 (dq, *J* = 9.7, 6.1 Hz, 1H, 5-H''), 3.8-3.7 (m, 3H, 3-H', 4-H, 5-H'), 3.20 (ddd, *J* = 9.1, 9.1, 2.7 Hz, 1H, 4-H'), 2.43 (d, *J* = 3.0 Hz, 1H, OH), 2.25 (dd, *J* = 12.5, 5.2 Hz, 1H, 2-H''$_{ax}$), 2.18 (dd, *J* = 12.7, 4.7 Hz, 1H, 2-H'$_{ax}$), 2.05, 2.00 (2s, 6H, 2CH_3CO), 1.78 (ddd, *J* = 12.7, 12.0, 3.6 Hz, 1H, 2-H''$_{eq}$), 1.70 (ddd, *J* = 12.7, 11.7, 3.7 Hz, 1H, 2-H'$_{eq}$), 1.37 (d, *J* = 6.6 Hz, 3H, 6-H), 1.28 (d, *J* = 6.1 Hz, 3H, 6-H'), 1.18 (s, 9H, Piv),1.14 (d, *J* = 6.1 Hz, 3H, 6-H'')

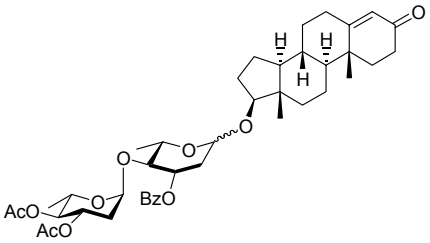
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 177.9 (s, <u>C</u>OPiv), 170.4, 170.1 (2s, <u>C</u>OAc), 145.7 (d, C-1), 98.6, 98.57 (2d, C-1', 2), 97.1 (d, C-1''), 77.8 (d, C-3'), 75.9 (d, C-4'), 75.5 (d, C-5'), 74.6 (d, C-4''), 73.4 (d, C-5), 70.3 (d, C-3), 69.0 (d, C-3''), 68.3 (d, C-4), 66.1 (d, C-5''), 38.7 (s, <u>C</u>$(CH_3)_3$), 37.1 (t, C-2'), 35.6 (t, C-2''), 27.0 (q, C(<u>C</u>$H_3)_3$), 20.9, 20.8 (2q, 2CO<u>C</u>H_3), 17.7 (q, C-6'), 17.4, 17.3 (2q, C-6, 6'')

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 3250 Hz = 6.41 ppm: δ = 6.41 (d, 1-H), 5.23 (dd, 3-H), 4.72 (dd, 2-H), 4.10 (dq, 5-H), 3.76 (dd, 4-H), 1.40 (d, 6-H)

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 1612 Hz = 3.22 ppm: δ = 5.13 (d, 1-H'), 3.81 (ddd, 3-H'), 3.77 (dq, 5-H'), 3.22 (dd, 4-H'), 2.46 (s, OH), 2.21 (dd, 2-H'$_{ax}$), 1.73 (ddd, 2-H'$_{eq}$), 1.30 (d, 6-H')

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 1140 Hz = 2.28 ppm: δ = 5.24 (ddd, 3-H''), 5.13 (d, 1-H''), 4.75 (dd, 4-H''), 3.88 (dq, 5-H''), 2.28 (ddd, 2-H''$_{ax}$), 1.80 (ddd, 2-H''$_{eq}$), 1.17 (d, 6-H'')

17-*O* [4-*O*-(3',4'-Di-*O*-acetyl-2',6'-dideoxy-α-L-*arabino*-hexopyranosyl)-3-*O*-benzoyl-2,6-dideoxy-β-L-*arabino*-hexopyranosyl]-testosterone (172β); 17-*O* (4-*O*-(3',4'-Di-*O*-acetyl-2',6'-dideoxy-α-L-*arabino*-hexopyranosyl)-3-*O*-benzoyl-2,6-dideoxy-α-L-*arabino*-hexopyranosyl)-testosteron (172α)



To a mixture of testosterone (28 mg, 0.1 mmol) and disaccharide **170** (44 mg, 0.1 mmol) in dry acetonitrile (5 ml) Dowex 50w2 (2 mg) was added. Stirring was continued for 24 h followed by quenching with amberlite A-21 (10 mg). The mixture was filtered through a pad of Celite and the solvent was removed under reduced pressure. The isomers were finally separated by flash column chromatography (ethyl acetate/petroleum ether 1:5).

1st fraction: **173**β 10.3 mg (0.014 mmol, 14%),

2nd fraction: **173**α 33.9 mg (0.046 mmol, 46%).

1st fraction

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 7.99 (d, *J* = 7.5 Hz, 2H, *Ph*-o), 7.58 (dd, *J* = 7.5, 7.5 Hz, 1H, *Ph*-p), 7.45 (dd, *J* = 7.5, 7.5 Hz, 2H, *Ph*-m), 5.72 (s, 1H, 4-H), 5.23 (d, *J* = 3.3 Hz, 1H, 1-H''), 5.15 (m, 2H, 3-H', 3''), 4.65 (dd, *J* = 9.6, 9.5 Hz, 1H, 4-H''), 4.56 (dd, *J* = 9.5, 1.7 Hz, 1H, 1-H'), 3.93 (dq, *J* = 9.6, 6.2 Hz, 1H, 5-H''), 3.69 (t, *J* = 8.3 Hz, 1H, 17-H), 3.59 (dd, *J* = 9.0, 9.0 Hz, 1H, 4-H'), 3.44 (dq, *J* = 9.0, 6.08 Hz, 1H, 5-H'), 2.5-0.7 (m)

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 199.5 (s, C-3), 171.3 (s, C-5), 170.1, 170.0 (2s, $\underline{C}OCH_3$), 165.4 (s, $\underline{C}O$*Ph*), 133.3 (s, *Ph*), 129.7 (d, *Ph*-p), 129.5 (d, *Ph*-o), 128.6 (d, *Ph*-m), 123.8 (d, C-4), 98.1 (d, C-1'), 97.7 (d, C-1''), 87.21 (d,

C-17), 79.6 (d, C-4'), 75.0 (d, C-3'), 74.7 (d, C-4''), 70.5 (d, C-5'), 68.5(d, C-3''), 66.4 (d, C-5''), 54.0 (d, C-9), 50.6 (d, C-14), 42.4 (s, C-13), 38.7 (s, C-10), 37.1 (t, C-12), 36.6 (t, C-2'), 35.7 (t, C-1), 35.5 (t, C-2''), 35.3 (d, C-8), 34.0 (t, C-2), 32.8 (t, C-6), 31.6 (t, C-7), 27.5 (t, C-16), 23.2 (t, C-15), 20.9, 20.8 (2q, 2CO<u>C</u>H_3), 20.6 (t, C-11), 18.6 (q, C-6'), 17.4 (q, C-19), 17.3 (q, C-6''), 11.6 (q, C-18)

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 2298 Hz = 4.59 ppm: δ = 5.18 (ddd, 3-H'), 4.59 (dd, 1-H'), 3.62 (dd, 4-H'), 3.47 (dq, 5-H'), 2.44 (ddd, 2-H'$_{ax}$), 1.73 (ddd, 2-H'$_{eq}$), 1.41 (d, 6-H')

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 2344 Hz = 4.69 ppm: δ = 5.26 (d, 1-H''), 5.18 (ddd, 3-H''), 4.68 (dd, 4-H''), 3.96 (dq, 5-H''), 1.99 (ddd, 2-H''$_{ax}$), 1.64 (ddd, 2-H''$_{eq}$), 1.19 (d, 6-H'')

2nd fraction

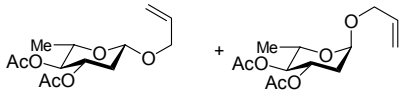
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 8.00 (d, *J* = 7.5 Hz, 2H, *Ph*-o), 7.58 (dd, *J* = 7.5, 7.5 Hz, 1H, *Ph*-p), 7.45 (dd, *J* = 7.5, 7.5 Hz, 2H, *Ph*-m), 5.73 (s, 1H, 4-H), 5.47 (ddd, *J* = 11.2, 9.1, 5.1 Hz, 1H, 3-H'), 5.24 (d, *J* = 3.1 Hz, 1H, 1-H''), 5.19 (ddd, *J* = 11.4, 9.2, 5.1 Hz, 1H, 3-H''), 4.91 (d, *J* = 2.7 Hz, 1H, 1-H'), 4.66 (dd, *J* = 9.5, 9.2 Hz, 1H, 4-H''), 3.96 (dq, *J* = 9.5, 6.2 Hz, 1H, 5-H''), 3.91 (dq, *J* = 9.3, 6.2 Hz, 1H, 5-H'), 3.55 (dd, *J* = 9.3, 9.1 Hz, 1H, 4-H'), 3.52 (t, *J* = 8.5, 8.5 Hz, 1H, 17-H), 2.5 – 0.7 (m)

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 199.5 (s, C-3), 171.3 (s, C-5), 170.1, 170.0 (2s, 2<u>C</u>OCH_3), 165.4(s, <u>C</u>O*Ph*), 133.2 (s, *Ph*), 129.9 (d, *Ph*-p), 129.5 (d, *Ph*-o), 128.6 (d, *Ph*-m), 123.8 (d, C-4), 97.8 (d, C-1''), 97.4 (d, C-1'), 87.5 (d, C-17), 80.6 (d, C-4'), 74.8 (d, C-4''), 73.4 (d, C-3'), 68.5 (d, C-3''), 66.4 (d, C-5''), 66.4 (d, C-5'), 53.9 (d, C-9), 50.3 (d, C-14), 42.9 (s, C-13), 38.7 (s, C-10), 37.2 (t, C-12), 35.7 (t, C-1), 35.7 (t, C-2''), 35.5 (t, C-2'), 35.4 (d, C-8), 33.9 (t, C-2), 32.8 (t, C-6), 31.6 (t, C-7), 28.5 (t, C-16), 23.4 (t, C-15), 20.9, 20.8 (2q, CO<u>C</u>H_3), 20.6 (t, C-11), 18.4 (q, C-6'), 17.4 (q, C-19), 17.3 (q, C-6''), 11.7 (q, C-18)

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 2472 Hz = 4.94 ppm: δ = 5.50 (ddd, 3-H'), 4.94 (d, 1-H'), 3.94 (dq, 5-H'), 3.57 (dd, 4-H'), 2.42 (ddd, 2-H'$_{ax}$), 1.78 (ddd, 2-H'$_{eq}$), 1.35 (d, 6-H')

^{1}**H-NMR** (500 MHz, $CDCl_3$ = 7.26 ppm) **TOCSY** - 2343 Hz = 4.68 ppm: δ = 5.27 (d, 1-H''), 5.21 (ddd, 3-H''), 4.68 (dd, 4-H''), 3.98 (dq, 5-H''), 2.01 (dd, 2-H''$_{ax}$), 1.65 (ddd, 2-H''$_{eq}$), 1.19 (d, 6-H'')

11.8.1. Experiments to the chapter 9.4.
Allyl-3,4-di-*O*-acetyl-2,6-dideohy-α-L-glucopyranoside (179)



31.6% **178** 41% **179**

To a stirred solution of 3,4-di-*O*-acetyl-L-rhamnal (5 g, 23 mmol) and allyl alcohol (2 g, 34.5 mmol, 1.5 eq) in dry CH_2Cl_2 (50 ml) polymer-bound PPh_3*HBr (20 mg) was added. The reaction mixture was stirred at room temperature for 24 h, filtered through a pad of Celite and concentrated under reduced pressure. The products were finally separated by flash column chromatography over silica gel (ethyl acetate / petroleum ether 1:6).

Yield: α-anomer (2.6g, 9.56 mmol, 41%),
β-anomer (2.0 g, 7.35 mmol 31.6%),
Ferrier product mixture (1.0 g, 4.72 mmol, 18.7%).

α-anomer

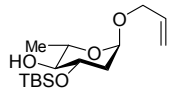
^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.89 (dddd, *J* = 17.0, 10.7, 5.8, 5.3 Hz, 1H, –C*H*=CH_2), 5.30 (ddd, *J* = 11.7, 9.7, 5.3 Hz, 1H, 3-H), 5.29 (dq, *J* = 17.0, 1.5 Hz, 1H, –CH=CH*H*'), 5.18 (dq, *J* = 10.7, 1.3 Hz, 1H, –CH=CH*H*'), 4.90 (d, *J* = 3.1 Hz, 1H, 1-H), 4.73 (t, *J* = 9.7 Hz, 1H, 4-H), 4.13 (ddt, *J* = 12.9, 5.3, 1.5 Hz, 1H, -*O*-CH*H*'-CH=), 3.94 (ddt, *J* = 12.9, 5.8, 1.3, Hz, 1H, -*O*-CH*H*'-CH=), 3.86 (dq, *J* = 9.7, 6.2 Hz, 1H, 5-H), 2.24 (ddd, *J* = 12.8, 5.3, 1.19 Hz, 1H, 2-H_{ax}), 2.04, 1.99 (2s, 6H, 2 x AcO), 1.79 (ddd, *J* = 12.8, 11.7, 3.1 Hz, 1H, 2-H_{eq}), 1.17 (d, *J* = 6.2 Hz, 3H, 6-H).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 170.51 (2s, 2 x *C*OCH_3), 134.27 (d, -*C*H=CH_2), 117.46 (t, –CH=*C*H_2), 96.21 (d, C-1), 75.20, 69.40, 66.00 (3d, C-4, C-3, C-5), 68.21 (t, –*C*H_2-CH=), 35.58 (t, C-2), 21.30, 21.12 (2q, 2 x CO*C*H_3), 17.82 (q, C-6).

LC-MS (ESI) (+c): m/z (%): 336.15 (100) $[M + CH_3CN + Na]^+$; **HRMS** (ESI) for $C_{15}H_{23}NO_6 + ^{23}Na$: calc: 336.1423, found: 336.1431.

$[\alpha]^{26}_D$ = - 156.3° (c = 1, $CHCl_3$).

Allyl-3-*O*-(*tret*-butyldimethylsilyl)-2,6-dideohy-α-L-glucopyranoside (180)



The reaction was carried out according to the protocol **TP8**: starting material **179**. Yield: 1.90 g (10.0 mmol, >98%). The crude product was used for the next step without further purification.

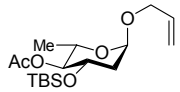
To a stirred solution of 2-deoxy-α-allyl-L-rhamnoside (1.90 g, 0.01 mol), imidazole (1.0 g, 0.015 mol, 1.5 eq) and DMAP (cat.) in DMF (15 ml) was slowly added TBSCl (1.55g, 0.01 mol, 1 eq) at 0°C. The solution was stirred at 0°C for 4 h and then at room temperature for additional 12 h. The pure product **180** was isolated after purification by flash column chromatography as colorless oil.

Yield: 2.68 g (8.86 mmol, 89 %).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.90 (dddd, *J* = 17.1, 10.5, 4.9, 5.8 Hz, 1H, –C*H*=CH_2), 5.27 (dq, *J* = 17.1, 1.6 Hz, 1H, –CH=CH*H*'), 5.16 (dq, *J* = 10.5, 1.5 Hz, 1H, –CH=CH*H*'), 4.85 (d, *J* = 3.4 Hz, 1H, 1-H), 4.12 (ddt, *J* = 13.2, 4.9, 1.5 Hz, 1H, -*O*-CH*H*'-CH=), 3.93 (m, 2H, -*O*-CH*H*'-CH=, 3-H), 3.68 (dq, *J* = 9.1, 6.2 Hz, 1H, 5-H), 3.10 (dt, *J* = 9.1, 2.0 Hz, 1H, 4-H), 2.23 (d, *J* = 2.0 Hz, 1H, OH), 2.02 (ddd, *J* = 12.9, 5.1, 1.1 Hz, 1H, 2-H_{ax}), 1.68 (ddd, *J* = 12.9, 11.3, 3.4 Hz, 1H, 2-H_{eq}), 1.28 (d, *J* = 6.2 Hz, 3H, 6-H), 0.89 (s, 9H, t-Bu-Si), 0.11, 0.09 (2s, 6H, Si(C*H*$_3$)$_2$).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 134.40 (d, -*C*H=CH_2), 116.58 (t, –CH=*C*H_2), 96.61 (d, C-1), 78.02, 70.56, 67.46, (3d, C-3, C-4, C-5), 67.55 (t, –*C*H_2-CH=), 38.63 (t, C-2), 25.76 (q, Si-C(*C*H_3)$_3$), 17.98 (s, Si-*C*(CH_3)$_3$), 17.84 (q, C-6), -4.20, -4.64 (2q, Si(*C*H_3)$_2$).

Allyl-3-*O*-(*tret*-butyldimethylsilyl)-4-*O*-acetyl-2,6-dideohy-α-L-glucopyranoside (182)



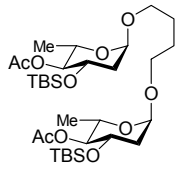
The sugar **180** (2.58 g, 8.5 mmol) was dissolved in pyridine (10 ml) and Ac_2O (1.02 ml, 11.05 mmol, 1.3 eq) was added. The reaction mixture was stirred overnight. The solvent was evaporated under reduced pressure and the residue was extracted with ethyl acetate, washed with water, dried over $MgSO_4$ and again concentrated under reduced pressure.

Yield: 2.9 g (8.4 mmol, 99%)

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.90 (dddd, *J* = 17.2, 10.5, 5.8, 5.0 Hz, 1H, –C*H*=CH_2), 5.27 (dq, *J* = 17.2, 1.6 Hz, 1H, –CH=CH*H*'), 5.18 (dq, *J* = 10.5, 1.4 Hz, 1H, –CH=CH*H*'), 4.86 (d, *J* = 3.3 Hz, 1H, 1-H), 4.63 (t, *J* = 9.5 Hz, 1H, 4-H), 4.11(ddt, *J* = 13.1, 5.0, 1.5 Hz, 1H, -*O*-CH*H*'-CH=), 4.05 (ddd, *J* = 11.3, 9.5, 5.3 Hz, 1H, 3-H), 3.92 (ddt, *J* = 13.1, 5.8, 1.3, Hz, 1H, -*O*-CH*H*'-CH=), 3.73 (dq, *J* = 9.5, 6.2 Hz, 1H, 5-H), 2.06 (s, 3H, AcO), 2.06 (ddd, *J* = 13.1, 5.3, 1.1 Hz, 1H, 2-H_{ax}), 1.75 (ddd, *J* = 13.1, 11.3, 3.3 Hz, 1H, 2-H_{eq}), 1.13 (d, *J* = 6.2 Hz, 3H, 6-H), 0.84 (s, 9H, t-BuSi), 0.04, 0.03 (2s, 6H, Me_2Si).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 170.33 (s, *C*OCH_3), 134.61 (d, -*C*H=CH_2), 117.06 (t, –CH=*C*H_2), 96.74 (d, C-1), 68.03 (t, –*C*H_2-CH=), 78.12, 67.80, 66.29 (3d, C-3, C-4, C-5), 39.42 (t, C-2), 25.88 (q, Si-C(*C*H_3)$_3$), 21.46 (q, CO*C*H_3), 18.12 (s, Si-*C*(CH_3)$_3$, 17.91 (q, C-6), -4.18, -4.58 (2q, Si(*C*H_3)$_2$).

Dimerization of allyl glycoside 182 and catalytic hydrogenation (183)



The reaction was carried out according to the protocol **TP3** except for the following details: starting material **182** (100 mg, 0.29 mmol) in dry benzene (3 ml), Column chromatography (ethyl acetate / petroleum ether 1:10)
Yield: 69 mg (0.104 mmol, 72%); recovery of starting material 20 mg (0.058 mmol, 20%). Obtained olefin was directly involved in catalytic hydrogenation.

The reaction was carried out according to the protocol **TP4** except for the following details: olefin (69 mg, 0.104 mmol) in the solvent mixture (5 ml).

Yield: 70 mg (0.103 mmol, 99%).

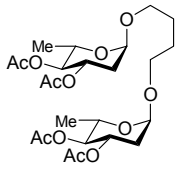
^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 4.79 (d, *J* = 2.7 Hz, 1H, 1-H), 4.61 (dd, *J* = 9.1, 9.5 Hz, 1H, 4-H), 4.00 (ddd, *J* = 10.8, 9.1, 5.2 Hz, 1H, 3-H), 3.69 (dq, *J* = 9.5, 6.3 Hz, 1H, 5-H), 3.60 (m, 1H, –O-CH*H*'-CH_2-), 3.36 (m, 1H, –O-CH*H*'-CH_2-), 2.05 (s, 3H, AcO), 2.01 (dd, *J* = 13.3, 5.2 Hz, 1H, 2-H_{ax}), 1.72 (ddd, *J* = 13.3, 10.8, 3.5 Hz, 1H, 2-H_{eq}), 1.62 (m, 2H, –O-CH_2-CH_2-), 1.12 (d, *J* = 6.3 Hz, 3H, 6-H), 0.83 (s, 9H, t-Bu), 0.03, 0.02 (2s, 6H, 2xMe)

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 169.92 (s, *C*OCH_3), 97.12 (d, 1-H), 77.79 (d, 4-H), 67.53, 65.87 (2d, C-3, C-5), 67.05 (t, –O-*C*H_2-CH_2-), 39.23 (t, C-2), 26.36 (t, –O-CH_2-*C*H_2-), 25.54 (q, SiC(*C*H_3)$_3$), 21.12 (q, CO*C*H_3), 17.79 (s, Si*C*$(CH_3)_3$), 17.63 (q, C-6), -4.50, -4.90 (2q, Si(*C*H_3)$_2$).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2410Hz = 4.82ppm: 4.81 (d, 1H, 1-H), 4.63 (dd, 1H, 4-H), 4.03 (ddd, 1H, 3-H), 3.72 (dq, 1H, 5-H), 2.04 (dd, 1H, 2-H), 1.74 (ddd, 1H, 2-H), 1.14 (d, 3H, 6-H)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 1697Hz = 3.39ppm: 3.63 (bd, –O-CH*H*'-CH_2-), 3.39 (ddd, 1H, –O-CH*H*'-CH_2-), 1.65 (ddd, 2H, –O-CH_2-CH_2-).

Dimerization of allyl glycoside 179 and catalytic hydrogenation (185)

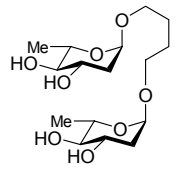


The reaction was carried out according to the protocol **TP3**: starting material **179** (4 g, 15 mmol) in dry benzene (30 ml), Column chromatography (ethyl acetate / petroleum ether 1:7). Yield: 3.1 g (6.0 mmol, 80%).
The product was involved in catalytic hydrogenation according to the protocol **TP4**: starting material 3.1 g (6.0 mmol) in the mixture of solvents (50 ml).

Yield: 3.1 g (5.97 mmol, >99%).

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.25 (ddd, *J* = 11.6, 9.5, 5.4 Hz, 1H, 3-H), 4.84 (d, *J* = 2.8 Hz, 1H, 1-H), 4.72 (dd, *J* = 9.7, 9.5 Hz, 1H, 4-H), 3.83 (dq, *J* = 9.7, 6.4 Hz, 1H, 5-H), 3.63 (m, 1H, –O-CH*H*'-CH_2-), 3.35 (m, 1H, –O-CH*H*'-CH_2-), 2.20 (ddd, *J* = 12.7, 5.4, 0.9 Hz, 1H, 2-H_{ax}), 2.04, 1.99 (2s, 6H, 2 x AcO), 1.77 (ddd, *J* = 12.7, 11.6, 3.7 Hz, 1H, 2-H_{eq}), 1.64 (m, 2H, –O-CH_2-C*H*$_2$-), 1.16 (d, *J* = 6.4 Hz, 3H, 6-H)

Deacetylation of homodimer 185 and preparation of tetrol (188)



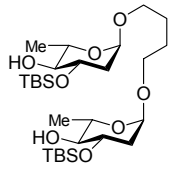
The reaction was carried out according to the protocol **TP8**: acylated alcohol **185** 3.1 g (5.97 mmol). The crude product was used for the next step without further purification.

Yield: 2.08 g (5.95 mmol, >99%)

^{1}**H-NMR** (200 MHz, CD_3OD, = 3.35 ppm) δ: 4.80 (d, *J* = 3.0 Hz, 1H, 1-H), 3.77 (ddd, *J* = 11.7, 9.1, 5.1 Hz, 1H, 3-H), 3.66 (m, 1H, –O-CH*H*'-CH_2-), 3.58 (dq, *J* = 9.3, 6.2 Hz, 1H, 5-H), 3.44 (m, 1H, –O-CH*H*'-CH_2-), 2.93 (dd, *J* = 9.3, 9.1 Hz, 1H,

4-H), 2.05 (ddd, *J* = 12.9, 5.1, 0.9 Hz, 1H, 2-H_{ax}), 1.70 (m, 2H, –O-CH*H*'-CH_2-), 1.6 (ddd, *J* = 12.9, 11.7, 3.0 Hz, 1H, 2-H_{eq}), 1.24 (d, *J* = 6.2 Hz, 3H, 6-H)

Silylation of homodimeric tetrol (184)



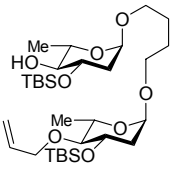
To an ice cooled stirred solution of tetrol **188** (383 mg, 1.1 mmol), imidazole (223 mg, 3.3 mmol, 3.0 eq) and DMAP (cat.) in DMF (10 ml) TBSCl (330 mg, 2.2 mmol, 2 eq) was slowly added. The solution was stirred at 0°C for 4 h and then allowed to warm up to RT. After additional 12h the reaction was terminated by addition of *n*-hexane (10 ml). The DMF phase was extracted with *n*-hexane (2x 5 ml) and the combined hexane phases were concentrated under reduced pressure. The crude material was subjected to gel filtration (petroleum ether / ethyl acetate 10:1) after which it could be directly employed for the next step.

Yield: 507 mg (0.875 mmol, 84%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 4.79 (d, *J* = 3.3 Hz, 1H, 1-H), 3.90 (ddd, *J* = 11.3, 9.0, 4.9 Hz, 1H, 3-H), 3.65 (dq, *J* = 9.3, 6.3 Hz, 1H, 5-H), 3.60 (m, 1H, –O-CH*H*'-CH_2-), 3.35 (m, 1H, –O-CH*H*'-CH_2-), 3.09 (ddd, *J* = 9.0, 9.0, 2.0 Hz, 1H, 4-H), 2.24 (d, *J* = 2.0 Hz, 1H, OH), 1.99 (dd, *J* = 12.7, 4.9 Hz, 1H, 2-H_{ax}), 1.66 (ddd, *J* = 12.7, 11.3, 3.3 Hz, 1H, 2-H_{eq}), 1.28 (d, *J* = 6.3 Hz, 3H, 6-H), 0.89 (s, 9H, t-Bu), 0.11, 0.09 (2s, 6H, Me_2Si).

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 97.34 (d, C-1), 78.04, 70.64, 67.37 (3d, C-3, C-4, C-5), 66.90 (t, –O-*C*H_2-CH_2-), 38.76 (t, C-2), 26.40 (t, –O-CH_2-*C*H_2-), 25.77 (q, Si-C(*C*H_3)$_3$), 17.99 (s, Si-*C*$(CH_3)_3$), 17.89 (q, C-6), -4.18, -4.61 (2q, Si(*C*H_3)$_2$).

O-Allylation of diol 184 (186)



The reaction was carried out according to the protocol **TP5**: starting material **184** (50 mg, 0.086 mmol) in DMSO (0.5 ml), allylbromid 208 mg (1.72 mmol, 20 eq), $LiN(SiMe_3)_2$ 100 mg (0.6 mmol) in THF (0.5 ml). Column chromatography (ethyl acetate / petroleum ether 1:10).

Yield: 13.3 mg (0.021 mmol, 25%),
isolated starting material 16 mg (0.027 mmol, 32%)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.94 (dddd, *J* = 17.0, 10.5, 5.8, 5.8 Hz, 1H, –C*H*=CH_2), 5.24 (dd, *J* = 17.0, 1.5 Hz, 1H, –CH=CH*H*'), 5.14 (d, *J* = 10.5 Hz, 1H, –CH=CH*H*'), 4.78, 4.75 (2d, *J* = 3.0 Hz, 2H, 1-H, 1-H'), 4.34 (dd, *J* = 12.0, 5.4 Hz, 1H, -*O*-CH*H*'-CH=), 4.08 (dd, *J* = 12.0, 6.0 Hz, 1H, -*O*-CH*H*'-CH=), 3.99 (ddd, *J* = 10.9, 9.0, 5.0 Hz, 1H, 3-H'), 3.90 (ddd, *J* = 11.1, 8.8, 4.9 Hz, 1H, 3-H), 3.62 (m, 4H, 5-H, 5-H', –O-CH_2-CH_2-), 3.34 (m, 2H, –O-CH_2-CH_2-), 3.09 (ddd, *J* = 9.2, 8.8, 2.0 Hz, 1H, 4-H), 2.83 (dd, *J* = 9.0, 9.0 Hz, 1H, 4-H'), 2.22 (d, *J* = 2.0 Hz, 1H, OH), 1.99 (ddd, *J* = 13.0, 4.0, 3.7 Hz, 2H, 2-H_{ax}, 2-H_{ax}'), 1.61 (m, 6H, 2 x –O-CH_2-CH_2-, 2-H_{eq}, 2-H'$_{eq}$), 1.28 (d, *J* = 6.1 Hz, 3H, 6-H), 1.26 (d, *J* = 6.1 Hz, 3H, 6-H'), 0.89 (s, 18H, 2 x t-BuSi), 0.11, 0.10, 0.09, 0.08 (4s, 12H, 2 x Me_2Si).

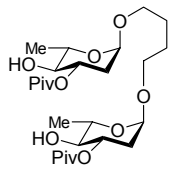
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 135.14 (d, -*C*H=CH_2), 116.81 (t, –CH=*C*H_2), 97.31 (d, C-1), 97.14 (d, C-1'), 85.36 (d, C-4'), 78.05 (d, C-4), 74.31 (t, –*C*H_2-CH=), 70.65 (d, C-3), 70.18 (d, C-3'), 67.35, 67.20 (2d, C-5, C-5'), 66.90, 66.82 (2t, 2 x –O-*C*H_2-CH_2-), 39.56, 38.76 (2t, C-2, C-2'), 26.40, 26.39 (2t, 2 x –O-CH_2-*C*H_2-), 25.84, 25.78 (2q, 2 x SiC(*C*H_3)$_3$), 18.13, 17.99 (2s, Si*C*$(CH_3)_3$), 17.95, 17.89 (2q, C-6, C-6'), -4.17, -4.55, -4.57, -4.61 (4q, 2 x $SiMe_2$).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2186Hz = 4.37ppm: 5.95 (ddd, 1H, –C*H*=CH_2), 5.27 (dd, 1H, –CH=CH*H*'), 5.17 (d, 1H, –CH=CH*H*'), 4.37 (ddd, 1H, -*O*-CH*H*'-CH=), 4.11 (ddd, 1H, -*O*-CH*H*'-CH=)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 1561Hz = 3.12ppm: 4.81 (d, 1H, 1-H), 3.92 (ddd, 1H, 3-H), 3.67 (dq, 1H, 5-H), 3.12 (ddd, 1H, 4-H), 2.25 (d, 1H, OH), 2.02 (dd, 1H, 2-H_{ax}), 1.68 (ddd, 1H, 2-H_{eq}), 1.31 (d, 3H, 6-H).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 1428Hz = 2.68ppm: 4.78 (d, 1H, 1-H'), 4.03 (ddd, 1H, 3-H'), 3.66 (dq, 1H, 5-H'), 2.85 (dd, 1H, 4-H'), 2.01 (dd, , 1H, 2-H'$_{ax}$), 1.67 (ddd, 1H, 2-H'$_{eq}$), 1.28 (d, 3H, 6-H')

Pivaloylation of homodimeric tetrol (189)



The sugar **188** (0.3 g, 0.856 mmol) was dissolved in pyridine (10 ml) and PivCl (0.21 ml, 1.72 mmol, 2.2 eq) was added. The reaction mixture was stirred overnight. The solvent was evaporated under reduced pressure and the residue was extracted with ethyl acetate, washed with water, dried over $MgSO_4$ and again concentrated under reduced pressure.

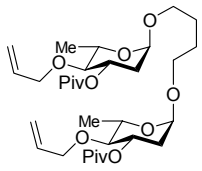
Yield: 377 mg (0.727 mmol, 85%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.13 (ddd, *J* = 11.6, 9.2, 5.2 Hz, 1H, 3-H), 4.89 (d, *J* = 3.0 Hz, 1H, 1-H), 3.71 (dq, *J* = 9.2, 6.2 Hz, 1H, 5-H), 3.70 (m, 1H, –O-CH*H*'-CH_2-), 3.35 (m, 1H, –O-CH*H*'-CH_2-), 3.22 (dd, *J* = 9.2, 9.2 Hz, 1H, 4-H), 2.87 (bs, 1H, OH), 2.12 (ddd, *J* = 12.6, 5.2, 1.0 Hz, 1H, 2-H_{ax}), 1.74 (ddd, *J* = 12.6, 11.6, 3.0 Hz, 1H, 2-H_{eq}), 1.65 (m, 2H, –O-CH_2-CH_2-), 1.31 (d, *J* = 6.2 Hz, 3H, 6-H), 1.19 (s, 9H, PivO)

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 179.90 (s, *C*O$C(CH_3)_3$), 96.62 (d, C-1), 76.00, 72.47, 68.26 (3d, C-3, C-4, C-5), 66.60 (t, –O-*C*H_2-CH_2-), 38.84 (s, CO*C*$(CH_3)_3$), 35.29 (t, C-2), 27.06 (q, COC(C*H*$_3)_3$), 26.28 (t, –O-CH_2-*C*H_2-), 17.74 (q, C-6).

***O*-Allylation of diol 189 (190, 192)**

The reaction was carried out according to the protocol **TP5**: starting material **189** (50 mg, 0.096 mmol), allylbromide 232 mg (1.92 mmol), $LiN(SiMe_3)_2$ 112 mg (0.67 mmol). Column chromatography (ethyl acetate / petroleum ether 1:10). Three fractions were isolated.



Yield: **190** 20 mg (0.034 mmol, 35%)

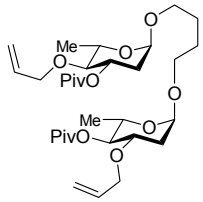
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.86 (dddd, *J* = 17.1, 11.0, 5.9, 5.2 Hz, 1H, –C*H*=CH_2), 5.23 (dd, *J* = 17.1, 1.5 Hz, 1H, –CH=CH*H*'), 5.17 (ddd, *J* = 11.1, 9.1, 5.1 Hz, 1H, 3-H), 5.13 (dd, *J* = 11.0, 1.2 Hz, 1H, –CH=CH*H*'), 4.78 (d, *J* = 2.7 Hz, 1H, 1-H), 4.18 (dd, *J* = 12.1, 5.2 Hz, 1H, -*O*-CH*H*'-CH=), 4.08 (dd, *J* = 12.3, 5.9 Hz, 1H, -*O*-CH*H*'-CH=), 3.74 (dq, *J* = 9.2, 6.2 Hz, 1H, 5-H), 3.60 (ddd, *J* = 9.2, 6.2, 5.9 Hz, 1H, –O-CH*H*'-CH_2-), 3.32 (ddd, *J* = 9.2, 5.9, 5.2 Hz, 1H, –O-CH*H*'-CH_2-), 3.06 (dd, *J* = 9.2, 9.1 Hz, 1H, 4-H), 2.21 (ddd, *J* = 12.6, 5.2, 0.9 Hz, 1H, 2-H), 1.61 (m, 3H, 2-H, –O-CH_2-CH_2-), 1.29 (d, *J* = 6.2 Hz, 3H, 6-H), 1.19 (s, 9H, COC(CH_3)$_3$)

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 177.39 (s, *C*=O), 134.72 (d, -*C*H=CH_2), 116.76 (t, –CH=*C*H_2), 96.70 (d, C-1), 82.27 (d, C-4), 73.44 (t, –*C*H_2-CH=), 71.62 (d, C-3), 66.92 (t, –O-*C*H_2-CH_2-), 66.90 (d, C-5), 38.61 (s, CO*C*$(CH_3)_3$), 35.37 (t, C-2), 27.11 (q, COC(*C*H_3)$_3$), 26.30 (t, –O-CH_2-*C*H_2-), 18.19 (q, C-6).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2057Hz = 4.11ppm: 5.88 (dddd, 1H, –C*H*=CH_2), 5.27 (dd, 1H, –CH=CH*H*'), 5.15 (d, 1H, –CH=CH*H*'), 4.20 (dd, 1H, -*O*-CH*H*'-CH=), 4.11 (dd, 1H, -*O*-CH*H*'-CH=)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2404Hz = 4.81ppm: 5.19 (ddd, 1H, 3-H), 4.81 (d, 1H, 1-H), 3.77 (dq, 1H, 5-H), 3.09 (dd, 1H, 4-H), 2.23 (ddd, 1H, 2-H), 1.62 (ddd, 1H, 2-H), 1.31 (d, 3H, 6-H)

[1]**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 1675Hz = 3.35ppm: 3.63 (d, 1H, –O-CH*H*'-CH_2-), 3.35 (ddd, 1H, –O-CH*H*'-CH_2-), 1.64 (ddd, 2H, –O-CH_2-C*H*$_2$-)



Yield: **192** 8.6 mg (0.014 mmol, 15%).

[1]**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.84 (bdddd, *J* = 17.4, 10.3, 5.4, 5.2 Hz, 2H, 2 x –C*H*=CH_2), 5.23 (ddd, *J* = 17.4, 9.4, 1.5 Hz, 2H, 2 x –CH=CH*H*'), 5.21 (m, 1H, 3-H'), 5.14 (d, *J* = 10,3 Hz, 1H, –CH=CH*H*'), 5.11 (dd, *J* = 10.3, 1.3 Hz, 1H, –CH=CH*H*'), 4.85 (d, *J* = 3.0 Hz, 1H, 1-H'), 4.79 (d, *J* = 3.1 Hz, 1H, 1-H), 4.70 (dd, *J* = 9.4, 9.4 Hz, 1H, 4-H), 4.20 (dd, *J* = 12.2, 5.3 Hz, 1H, -*O*-CH*H*'-CH=), 4.10 (dd, *J* = 12.2, 5.9 Hz, 1H, -*O*-CH*H*'-CH=), 4.07 (dd, *J* = 12.8, 5.4 Hz, 1H, -*O*-CH*H*'-CH=), 3.93 (dd, *J* = 12.8, 5.3 Hz, 1H, -*O*-CH*H*'-CH=), 3.76 (m, 3H), 3.62 (m, 2H), 3.35 (m, 2H), 3.08 (dd, *J* = 9.2, 9.2 Hz, 1H, 4-H'), 2.24 (ddd, *J* = 12.6, 6.6, 5.6 Hz, 2H, 2-H, 2-H'), 1.62 (m, 6H), 1.30 (d, *J* = 6.3 Hz, 3H, 6-H'), 1.22, 1.20 (2s, 18H, 2 x PivO), 1.13 (d, *J* = 6.2 Hz, 3H, 6-H)

[13]**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 177.52, 177.48 (2s, 2 x *C*OC$(CH_3)_3$), 134.90, 134.64 (2d, 2 x -*C*H=CH_2), 116.94, 116.34 (2t, 2 x –CH=*C*H_2), 97.27 (d, C-1), 96.78 (d, C-1'), 82.26 (d, C-4'), 75.83 (d, C-4), 74.36 (d, C-5'), 73.64, 70.45 (2t, 2 x –*C*H_2-CH=), 71.71 (d, C-3'), 67.25 (d, C-3), 67.00 (t, 2 x –O-*C*H_2-CH_2-), 66.01 (d, C-5), 38.79, 38.65 (2s, 2 x CO*C*$(CH_3)_3$), 35.68, 35.38 (2t, C-2, C-2'), 27.16, 27.13 (2q, COC(*C*$H_3)_3$), 26.41, 26.37 (2t, 2 x –O-CH_2-*C*H_2-), 18.22 (q, C-6'), 17.54 (q, C-6).

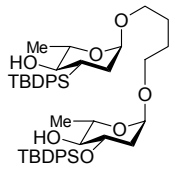
[1]**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2115Hz = 4.23ppm: 5.90 (dddd, 1H, –C*H*=CH_2'), 5.26 (dd, 1H, –CH=CH*H*'), 5.18 (d, 1H, –CH=CH*H*'), 4.22 (dd, 1H, -*O*-CH*H*'-CH='), 4.13 (dd, 1H, -*O*-CH*H*'-CH=')

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 1981Hz = 3.96ppm: 5.86 (dddd, 1H, –C*H*=CH_2), 5.25 (dd, 1H, –CH=CH*H*'), 5.14 (d, 1H, –CH=CH*H*'), 4.10 (dd, 1H, -*O*-CH*H*'-CH=), 3.96 (dd, 1H, -*O*-CH*H*'-CH=)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 1554Hz = 3.11ppm: 5.21 (ddd, 1H, 3-H'), 4.82 (d, 1-H'), 3.79 (dq, 1H, 5-H'), 3.11 (dd, 1H, 4-H'), 2.26 (dd, 1H, 2-H'), 1.63 (ddd, 1H, 2-H'), 1.32 (d, 3H, 6-H')

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2365Hz = 4.73ppm: 4.88 (d, 1H, 1-H), 4.73 (dd, 1H, 4-H), 3.79 (ddd, 1H, 3-H), 3.77 (dq, 1H, 5-H), 2.27 (dd, 1H, 2-H), 1.71 (ddd, 1H, 2-H), 1.16 (d, 3H, 6-H)

Silylation of homodimeric tetrol (193)

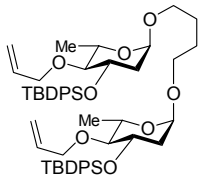


To a solution of tetrol **188** (393 mg, 1.13 mmol), imidazole (223 mg, 3.3 mmol), DMAP (cat.) in DMF (10 ml) was slowly added TBDPSCl (565 mg, 2.26 mmol) at 0°C. The solution was stirred at 0°C for 4h and then temperature was raised to rt. After additional 12h the reaction was terminated by addition of *n*-hexane (10 ml). The DMF phase was extracted with *n*-hexane (2x 5 ml) and the combined hexane phases were concentrated under reduced pressure. The crude material was subjected to gel filtration (petroleum ether / ethyl acetate 10:1) after which it could directly be employed for the next step.

Yield: 857 mg (1.034 mmol, 94%).

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.68 (m, 4H, Ph), 7.38 (m, 6H, Ph), 4.63 (d, *J* = 3.0 Hz, 1H, 1-H), 4.01 (ddd, *J* = 11.2, 9.0, 5.1 Hz, 1H, 3-H), 3.50 (dq, *J* = 9.1, 6.2 Hz, 1H, 5-H), 3.44 (m, 1H, –O-CH*H*'-CH_2-), 3.23 (ddd, *J* = 9.1, 9.0, 2.5 Hz, 1H, 4-H), 3.15 (m, 1H, –O-CH*H*'-CH_2-), 2.14 (d, *J* = 2.5 Hz, 1H, OH), 1.84 (ddd, *J* = 12.6, 5.1, 0.9 Hz, 1H, 2-H_{ax}), 1.67 (ddd, *J* = 12.6, 11.2, 3.0 Hz, 1H, 2-H_{eq}), 1.33 (m, 2H, –O-CH_2-CH_2-), 1.25 (d, *J* = 6.2 Hz, 3H, 6-H), 1.08 (s, 9H, t-Bu)

_O_-Allylation of diol 193 (194)



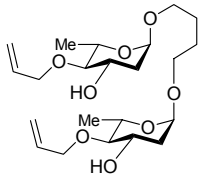
The reaction was carried out according to the protocol **TP5**: starting material **193** 4.6 g (5.5 mmol), allylbromide 9.4 ml (0.11 mmol), $LiN(SiMe_3)_2$ 6.45 g (0.0385 mol), moderate cooling required (ice bath). Column chromatography (ethyl acetate / petroleum ether 1:10).

Yield: 2.4 g (2.64 mmol, 48%),
mixfraction 100 mg (~2%),
isolated monoallylated product **195** 2.39 g (2.75 mmol, 50%).

^{1}**H-NMR** (400 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 7.76 (dd, *J* = 7.9, 1.5 Hz, 2H, Ar), 7.71 (dd, *J* = 7.9, 1.5 Hz, 2H, Ar), 7.36 (m, 6H, Ar), 5.97 (dddd, *J* = 17.2, 10.3, 5.7, 5.7 Hz, 1H, –C*H*=CH_2), 5.28 (dd, *J* = 17.2, 1.6 Hz, 1H, –CH=CH*H*'), 5.20 (dd, *J* = 10.3, 1.7 Hz, 1H, –CH=CH*H*'), 4.52 (bs, 1H, 1-H), 4.50 (dd, *J* = 11.9, 5.7 Hz, 1H, -*O*-CH*H*'-CH=), 4.25 (ddd, *J* = 10.1, 8.9, 5.9 Hz, 1H, 3-H), 4.18 (dd, *J* = 11.9, 5.7 Hz, 1H, -*O*-CH*H*'-CH=), 3.60 (dq, *J* = 9.1, 6.2 Hz, 1H, 5-H), 3.39 (m, 1H, –O-CH*H*'-CH_2-), 3.05 (m, 1H, –O-CH*H*'-CH_2-), 3.02 (dd, *J* = 9.1, 8.9 Hz, 1H, 4-H), 1.54 (m, 2H, 2-H), 1.28 (d, *J* = 6.2 Hz, 3H, 6-H), 1.27 (m, 2H, –O-CH_2-C*H*$_2$-), 1.10 (s, 9H, t-Bu)

^{13}**C-NMR** (100 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm) δ: 135.92 (d, Ar), 135.85 (d, Ar), 135.10 (d, -*C*H=CH_2), 134.94 (s, Ar), 133.80 (s, Ar), 129.55, 129.47, 127.49 (3d, 3 x Ar), 116.78 (t, –CH=*C*H_2), 96.95 (d, C-1), 85.68 (d, C-4), 74.27 (t, –*C*H_2-CH=), 71.15 (d, C-3), 67.21 (d, C-5), 66.49 (t, –O-*C*H_2-CH_2-), 38.95 (t, C-2), 27.05 (q, SiC(*C*H_3)$_3$), 26.01 (t, –O-CH_2-*C*H_2-), 19.17 (s, Si*C*$(CH_3)_3$), 18.19 (q, C-6).

Desilylation of homodimer 194 (196)



A solution of tetra-*n*-butyl ammonium fluoride (1M, 1.65 mmol, 1.65 ml, 3 eq) in THF was added to a solution of homodimer (0.5 g, 0.55 mmol) in THF (10 ml). The solution was stirred overnight, the solvent was removed under reduced pressure and the crude material was purified by column chromatography (petroleum ether / ethyl acetate 1:3) to give the corresponding diol.

Yield: 200 mg (0.465 mmol, 85 %) colorless, amorphous powder.

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) δ: 5.97 (dddd, *J* = 17.2, 10.3, 5.7, 5.7 Hz, 1H, –C*H*=CH_2), 5.32 (dq, *J* = 17.2, 1.6 Hz, 1H, –CH=CH*H*'), 5.22 (dq, *J* = 10.3, 1.4 Hz, 1H, –CH=CH*H*'), 4.83 (d, *J* = 3.3 Hz, 1H, 1-H), 4.25 (dq, *J* = 5.7, 1.3 Hz, 2H, -*O*-CH_2-CH=), 4.00 (dddd, *J* = 11.7, 9.0, 5.1, 3.1 Hz, 1H, 3-H), 3.66 (dq, *J* = 9.2, 6.2 Hz, 1H, 5-H), 3.63 (dt, *J* = 9.4, 6.4, Hz, 1H, –O-CH*H*'-CH_2-), 3.36 (dt, *J* = 9.4, 6.4 Hz, 1H, –O-CH*H*'-CH_2-), 2.87 (dd, *J* = 9.2, 9.0 Hz, 1H, 4-H), 2.34 (d, *J* = 3.1 Hz, 1H, OH), 2.13 (ddd, *J* = 12.9, 5.1, 1.1 Hz, 1H, 2-H_{ax}), 1.69 (ddd, *J* = 12.9, 11.7, 3.3 Hz, 1H, 2-H_{eq}), 1,63 (ddd *J* = 6.4, 6.4, 6.4 Hz, 2H, –O-CH_2-CH_2-), 1.30 (d, *J* = 6.2 Hz, 3H, 6-H).

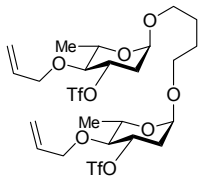
^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm)δ: 134.87 (d, -*C*H=CH_2), 117.24 (t, –CH=*C*H_2), 97.11 (d, C-1), 86.37 (d, C-4), 73.97 (t, –*C*H_2-CH=), 68.73 (d, C-3), 66.96 (d, C-5), 66.86 (t, –O-*C*H_2-CH_2-), 37.69 (t, C-2)), 26.41 (t, –O-CH_2-*C*H_2-), 18.16 (q, C-6).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2134Hz = 4.25ppm: 5.97 (dddd, 1H, –C*H*=CH_2), 5.32 (dq, 1H, –CH=CH*H*'), 5.22 (dq, 1H, –CH=CH*H*'), 4.24 (dd, 2H, -*O*-C*H*$_2$-CH=).

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 2414Hz = 4.83ppm: 4.83 (d, 1H, 1-H), 4.01 (dddd, 1H, 3-H), 3.67 (dq, 1H, 5-H), 2.88 (dd, 1H, 4-H), 2.34 (d, 1H, OH), 2.13 (ddd, 1H, 2-H_{ax}), 1.69 (ddd, 1H, 2-H_{eq}), 1.30 (d, 3H, 6-H)

^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm) **TOCSY** 1680Hz = 3.36ppm: 3.63 (dt, 1H, –O-CH*H*'-CH_2-), 3.36 (ddd, 1H, –O-CH*H*'-CH_2-), 1.63 (dq, 2H, –O-CH_2-C*H*$_2$-).

11.8.2. Experiments to the chapter 9.5.1.
Trifluorosulfonation of allylated homodimeric diol 196 (197)

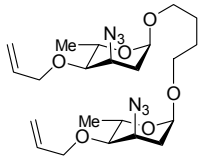


To a solution of sugar **196** (100 mg, 0.232 mmol) in dry CH_2Cl_2 (20 ml) with pyridine as a base (100μl) at – 15°C Tf_2O (138 mg, 0.49 mmol) in dry CH_2Cl_2 (5 ml) was added. The reaction mixture was stirred for 2h, diluted with water and extracted with petrol ether (2 x 40 ml). The organic extracts were combined, washed with water, dried over an $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude product was dissolved in a small amount of CH_2Cl_2 and filtered through a small column of silica gel.

Yield: 125 mg (0.22 mmol, 96%). very unstable colourless film.

^{1}**H-NMR** (200 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 5.93 (ddt, *J* = 17.2, 10.3, 5.5 Hz, 2H, 2 x -CH=), 5.41 (ddd, *J* = 12.3, 9.2, 5.3 Hz, 2H, 2 x 3-H), 5.27 (dq, *J* = 17.2, 1.5 Hz, 2 x H, -CH=CH*H*'), 5.11 (dq, *J* = 10.3, 1.5 Hz, 2H, 2 x -CH=CH*H*'), 4.51 (d, *J* = 3.1 Hz, 2H, 2 x 1-H), 4.18 (ddt, *J* = 12.1, 5.5, 1.2 Hz, 2H, 2 x =CH-CH*H*'-*O*-), 3.91 (ddt, *J* = 12.1, 5.5, 1.0 Hz, 2H, 2 x =CH-CH*H*'-*O*-), 3.77 (dq, *J* = 9.2, 6.2 Hz, 2H, 2 x 5-H), 3.38 (m, 2H, 2 x –O-CH*H*'-CH_2-), 3.05 (m, 2H, 2 x –O-CH*H*'-CH_2-), 2.90 (t, *J* = 9.2 Hz, 2H, 2 x 4-H), 2.29 (ddd, *J* = 12.3, 5.3, 0.9 Hz, 2H, 2 x 2-H_{ax}), 1.63 (dt, *J* = 12.3, 3.1 Hz, 2H, 2 x 2-H_{eq}), 1.38 (m, 4H, 2 x –O-CH_2-CH_2-), 1.29 (d, *J* = 6.2 Hz, 6H, 2 x 6-H).

Nucleophilic substitution of trifluorsulfonate ester with azide in the homodimer 197 (198)



The solution of sugar **197** (200 mg, 0.465 mmol) in benzene (1 ml) was treated with *n*-BuN^+ N_3^- (300 mg, 1.06 mmol, 2.3 eq). The reaction mixture was heated at 70°C for 15 min, diluted with water and extracted with ethyl acetate (3 x 30 ml).

The organic extracts were combined, dried over an $MgSO_4$ and solvent was evaporated under reduced pressure. The crude product was purified by column chromatography over silica gel (ethyl acetate / petroleum ether 1:12).

Yield: 80 mg (0.167 mmol, 36%).

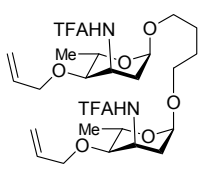
^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 5.78 (ddt, *J* = 17.2, 10.4, 5.4 Hz, 2H, 2 x –C*H*=CH_2), 5.18 (dq, *J* = 17.2, 1.6 Hz, 2H, 2 x –CH=CH*H*'), 5.01 (bdd, *J* = 10.4, 1.3 Hz, 2H, 2 x –CH=CH*H*'), 4.53 (d, *J* = 4.1 Hz, 2H, 2 x 1-H), 4.25 (dq, *J* = 9.1, 6.2 Hz, 2H, 2 x 5-H), 3.85 (dd, *J* = 12.7, 5.4 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 3.70 (m, 2H, 2 x –O-CH*H*'-CH_2-), 3.60 (dd, *J* = 12.7, 5.4 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 3.41 (dt, *J* = 3.8, 3.4 Hz, 2H, 2 x 3-H), 3.26 (m, 2H, 2 x –O-CH*H*'-CH_2-), 2.82 (dd, *J* = 9.1, 3.8 Hz, 2H, 2 x 4-H), 1.85 (ddd, *J* = 14.5, 3.4, 0.9 Hz, 2H, 2 x 2-H_{ax}), 1.76 (m, 4H, 2 x –O-CH_2-C*H*$_2$-), 1.33 (dt, *J* = 14.5, 4.1 Hz, 2H, 2 x 2-H_{eq}), 1.31 (d, *J* = 6.2 Hz, 6H, 2 x 6-H).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 135.1 (d, 2 x -*C*H=CH_2), 116.7 (t, 2 x –CH=*C*H_2), 95.6 (d, 2 x C-1), 80.1 (d, 2 x C-4), 69.9 (t, 2 x –*C*H_2-CH=), 67.4 (t, 2 x –O-*C*H_2-CH_2-), 63.4 (d, 2 x C-5), 54.8 (d, 2 x C-3), 33.0 (t, 2 x C-2), 26.9 (t, 2 x –O-CH_2-*C*H_2-), 18.2 (q, 2 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2324 Hz = 4.65 ppm: δ = 4.65 (d, 2H, 2 x 1-H), 4.37 (dq, 2H, 2 x 5-H), 3.53 (dt, 2H, 2 x 3-H), 2.94 (dd, 2H, 2 x 4-H), 1.96 (ddd, 2H, 2 x 2-H_{ax}), 1.44 (dt, 2H, 2 x 2-H_{eq}), 1.41 (d, 6H, 2 x 6-H).

LC-MS (ESI) (+c): m/z (%): 453.26 (100) $[M - N_2]^+$, 487.26 (92) $[M + Li]^+$, 503.24 (88) $[M + Na]^+$; **HR-MS** $C_{22}H_{36}N_6O_6$ +^{23}Na: calc. 503.2594, found 503.2593

Reduction of homodimeric azide 198 and trifluoroacetation the obtained amine (200)



A solution of azide **198** (80 mg, 0.167 mmol) in THF (5 ml) is added to a solution of $LiAlH_4$ (25 mg, 0.658 mmol) in THF (10 ml). The reaction mixture was stirred 45 min. at RT, then NaF (500 mg) was added followed by addition of a water/THF mixture (1 ml water, 4 ml THF). The resulted suspension was stirred for additional 1 h, filtered and the solvent was evaporated under reduced pressure. The crude amine **199** was directly acetylated without further purifications.
To a solution of crude amine **199** in CH_2Cl_2 (25 ml) was added dry triethly amine (50 mg, 0.5 mmol, 3 eq) at 0°C followed by addition of trifluoroacetic anhydride (105 mg, 0.5 mmol). The mixture was allowed to stir at RT for 30 min, whereupon t.l.c (ethyl acetate / petroleum ether 1:5) showed that acetylation was complete. The mixture was concentrated under reduced pressure to afford a crude product which was purified by column chromatography over silica gel (ethyl acetate / petroleum ether 1:7).

Yield: 62 mg (0.1 mmol, 60% in two steps).

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 8.00 (d, *J* = 8.5 Hz, 2H, 2 x NH), 5.97 (dddd, *J* = 17.2, 10.4, 6.0, 5.3 Hz, 2H, 2 x –C*H*=CH_2), 5.34 (dq, *J* = 17.2, 1.5 Hz, 2H, 2 x –CH=CH*H*'), 5.15 (bdd, *J* = 10.4, 1.1 Hz, 2H, 2 x –CH=CH*H*'), 4.50 (m, 2H, 2 x 3-H), 4.48 (d, *J* = 3.0 Hz, 2H, 2 x 1-H), 4.38 (dd, *J* = 12.5, 5.3 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 3.85 (dd, *J* = 12.5, 6.0 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 3.84 (dq, *J* = 9.5, 6.2 Hz, 2H, 2 x 5-H), 3.56 (m, 2H, 2 x –O-CH*H*'-CH_2-), 3.06 (m, 2H, 2 x –O-CH*H*'-CH_2-), 2.89 (dd, *J* = 9.5, 3.9 Hz, 2H, 2 x 4-H), 1.3 – 1.6 (m, 8H, 2 x 2-H_{ax}, 2 x 2-H_{eq}, 2 x –O-CH_2-C*H*$_2$-), 1.41 (d, *J* = 6.2 Hz, 6H, 2 x 6-H).

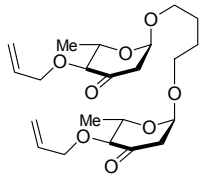
^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 135.1 (d, 2 x -*C*H=CH_2), 117.1 (t, 2 x –CH=*C*H_2), 96.8 (d, 2 x C-1), 78.1 (d, 2 x C-4), 70.5 (t, 2 x –*C*H_2-CH=), 67.4 (t, 2 x –O-*C*H_2-CH_2-), 63.5 (d, 2 x C-5), 43.7 (d, 2 x C-3), 32.7 (t, 2 x C-2), 26.6 (t, 2 x –O-CH_2-*C*H_2-), 18.3 (q, 2 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2551 Hz = 4.50 ppm: δ = 8.00 (d, 2H, 2 x NH), 4.50 (ddd, 2H, 2 x 3-H), 4.48 (d, 2H, 2 x 1-H), 3.84 (dq, 2H, 2 x 5-H), 2.89 (dd, 2H, 2 x 4-H), 1.53 (ddd, 2H, 2 x 2-H_{ax}), 1.41 (d, 6H, 2 x 6-H), 1.38 (dt, 2H, 2 x 2-H_{eq}).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2192 Hz = 4.38 ppm: δ = 5.98 (dddd, 2H, 2 x –C*H*=CH_2), 5.34 dq, 2H, 2 x –CH=CH*H*'), 5.15 (bdd, 2H, 2 x –CH=CH*H*'), 4.38 (dd, 2H, 2 x -*O*-CH*H*'-CH=), 3.85 (dd, 2H, 2 x -*O*-CH*H*'-CH=).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1783 Hz = 3.57 ppm: δ = 3.57 (m, 2H, 2 x –O-CH*H*'-CH_2-), 3.06 (m, 2H, 2 x –O-CH*H*'-CH_2-), 1.48 (m, 4H, 2 x –O-CH_2-C*H*$_2$-).

11.8.3. Experiments to the chapter 9.5.2.
Preparation of diketone 201



To a solution of the diol **196** (51 mg, 0.118 mmol) in dry CH_2Cl_2 (10 ml) was added the Dess-Martin periodinane (111 mg, 0.261 mmol). The mixture was stirred at RT for 3h, after which t.l.c. (ethyl acetate / petroleum ether 1:3) revealed that oxidation was completed. Remaining oxidant was removed by washing with aqueous $Na_2S_2O_3$-solution. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel; ethyl acetate / petroleum ether 1:5).

Yield: 50 mg (0.117 mmol, 99%).

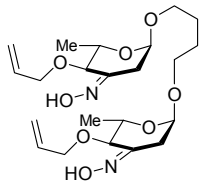
^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 5.98 (dddd, *J* = 17.12 10.6, 6.0, 5.0 Hz, 2H, 2 x –C*H*=CH_2), 5.31 (dq, *J* = 17.2, 1.6 Hz, 2H, 2 x –CH=CH*H*'), 5.13 (dq, *J* = 10.6, 1.3 Hz, 2H, 2 x –CH=CH*H*'), 4.79 (d, *J* = 4.3 Hz, 2H, 2 x 1-H), 4.56 (bddt, *J* = 12.7, 5.0, 1.3 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 4.17 (dq, *J* = 9.6, 6.2 Hz, 2H, 2 x 5-H), 3.99 (bdd, *J* = 12.7, 6.0 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 3.46 (dt, *J* = 9.6, 6.3 Hz, 2H, 2 x –O-CH*H*'-CH_2-), 3.43 (bd, *J* = 9.6 Hz, 2H, 2 x 4-H), 3.10 (dt, *J* = 9.6, 5.7 Hz, 2H, 2 x –O-CH*H*'-CH_2-), 2.50 (bd, *J* = 14.1 Hz, 2H, 2 x 2-H_{ax}), 2.27 (dd, *J* = 14.1, 4.3 Hz, 2H, 2 x 2-H_{eq}), 1.52 (d, *J* = 6.2 Hz, 6H, 2 x 6-H), 1.43 (bq, *J* = 5.7 Hz, 4H, 2 x –O-CH_2-C*H*$_2$-).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 202.2 (s, 2 x C-3), 135.2 (d, 2 x -*C*H=CH_2), 116.8 (t, 2 x –CH=*C*H_2), 98.6 (d, 2 x C-1), 85.0 (d, 2 x C-4), 72.4 (t, 2 x –*C*H_2-CH=), 69.4 (d, 2 x C-5), 67.2 (t, 2 x –O-*C*H_2-CH_2-), 46.9 (t, 2 x C-2), 26.4 (t, 2 x –O-CH_2-*C*H_2-), 19.1 (q, 2 x C-6).).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 759 Hz = 1.52 ppm: δ = 4.79 (d, 2H, 2 x 1-H), 4.18 (dq, 2H, 2 x 5-H), 3.43 (d, 2H, 2 x 4-H), 2.50 (d, 2H, 2 x 2-H_{ax}), 2.26 (dd, 2H, 2 x 2-H_{eq}), 1.52 (d, 6H, 2 x 6-H).).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1549 Hz = 3.10 ppm: δ = 3.46 (dt, 2H, 2 x –O-CH*H*'-CH_2-), 3.09 (dt, 2H, 2 x –O-CH*H*'-CH_2-), 1.43 (bq, 4H, 2 x –O-CH_2-C*H*$_2$-).

Preparation of homodimeric oxime 202



To a solution of hydroxylamine hydrochloride (7 mg, 0.1 mmol), NaOAc (25 mg, 0.3 mmol) and molecular sieves 4-Å (50 mg) in methanol (1.5 ml) the ketone **201** (10 mg, 0.0233 mmol) was added. The suspension was stirred for 1h, then the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography over silica gel (ethyl acetate / petroleum ether 1:4).

Yield: 10.2 mg (0.0224 mmol, 96%).

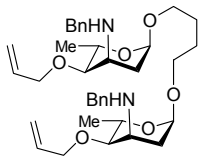
^{1}**H-NMR** (500 MHz, $CDCl_3$, $CDCl_3$ = 7.26 ppm): δ = 8.57 (bs, 2H, 2 x =N-OH), 5.92 (dddd, *J* = 17.2, 10.4, 6.4, 5.2 Hz, 2H, 2 x –C*H*=CH_2), 5.28 (dq, *J* = 17.2, 1.5 Hz, 2H, 2 x –CH=CH*H*'), 5.19 (dq, *J* = 10.4, 1.3 Hz, 2H, 2 x –CH=CH*H*'), 4.88 (dd, *J* = 4.1, 2.3 Hz, 2H, 2 x 1-H), 4.33 (bdd, *J* = 12.5, 5.2 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 3.99 (dd, *J* = 12.5, 6.4 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 3.91 (dq, *J* = 8.3, 6.3 Hz, 2H, 2 x 5-H), 3.63 (m, 2H, 2 x –O-CH*H*'-CH_2-), 3.59 (d, *J* = 8.3 Hz, 2H, 2 x 4-H), 3.34 (m, 2H, 2 x –O-CH*H*'-CH_2-), 3.30 (dd, *J* = 14.3, 2.3 Hz, 2H, 2 x 2-H_{ax}), 2.31 (dd, *J* = 14.3,

4.1 Hz, 2H, 2 x 2-H_{eq}), 1.61 (m, 4H, 2 x –O-CH_2-CH_2-), 1.31 (d, *J* = 6.3 Hz, 6H, 2 x 6-H).

^{13}**C-NMR** (125 MHz, $CDCl_3$, $CDCl_3$ = 77 ppm): δ = 153.5 (s, 2 x C-3), 134.5 (d, 2 x -*C*H=CH_2), 117.6 (t, 2 x –CH=*C*H_2), 96.4 (d, 2 x C-1), 79.3 (d, 2 x C-4), 71.8 (t, 2 x –*C*H_2-CH=), 69.2 (d, 2 x C-5), 66.5 (t, 2 x –O-*C*H_2-CH_2-), 29.9 (t, 2 x C-2), 26.4 (t, 2 x –O-CH_2-*C*H_2-), 18.2 (q, 2 x C-6).).

LC-MS (ESI) (+c): m/z (%): 457.25 (40) $[M + H]^+$, 479.23 (100) $[M + Na]^+$; **HR-MS** $C_{22}H_{37}N_2O_8$: calc. 457.2550, found 457.2550

Reductive amination of homodimeric ketone 201 (203)



Ketone **201** (10 mg, 0.0233 mmol), benzylamine (25 mg, 0.233 mmol) and $NaBH_3CN$ (4 mg, 0.064 mmol) were stirred in methanol (2 ml) for 4h until t.l.c. (ethyl acetate /MeOH 10:1) showed that the reaction was complete. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography over RP-18 silica gel (MeOH, R_f = 0.5).

Yield: 12.7 mg (0.021 mmol, 90%).

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 7.57 (m, 4H, 2 x Ph), 7.2-7.4 (m, 6H, 2 x Ph), 5.94 (ddt, *J* = 17.2, 10.5, 5.1 Hz, 2H, 2 x –C*H*=CH_2), 5.33 (dq, *J* = 17.2, 1.7 Hz, 2H, 2 x –CH=CH*H*'), 5.13 (dq, *J* = 10.5, 1.6 Hz, 2H, 2 x –CH=CH*H*'), 4.77 (dd, *J* = 4.1, 1.9 Hz, 2H, 2 x 1-H), 4.37 (dq, *J* = 8.6, 6.3 Hz, 2H, 2 x 5-H), 4.06 (d, *J* = 13.3 Hz, 2H, 2 x Ph-CH*H*'-), 4.01 (ddt, *J* = 12.8, 5.1, 1.6 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 3.88 (d, *J* = 13.3 Hz, 2H, 2 x Ph-C*H*H'-), 3.79 (ddt, *J* = 12.8, 5.1, 1.5 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 3.75 (m, 2H, 2 x –O-CH*H*'-CH_2-), 3.30 (m, 2H, 2 x –O-C*H*H'-CH_2-), 3.13 (dd, *J* = 8.6, 3.7 Hz, 2H, 2 x 4-H), 3.07 (dt, *J* = 4.1, 3.7 Hz, 2H, 2 x 3-H), 2.13 (ddd, *J* = 14.0, 4.3, 1.9 Hz, 2H, 2 x 2-H_{ax}), 1.61 (dt, *J* = 14.0, 4.1 Hz, 2H, 2 x 2-H_{eq}), 1.5 – 1.8 (m, 4H, 2 x –O-CH_2-CH_2-), 1.52 (d, *J* = 6.3 Hz, 6H, 2 x 6-H).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 142.1 (s, 2 x Ph), 135.8 (d, 2 x -*C*H=CH_2), 128.5, 127.1, 126.9 (3d, 6 x Ph), 116.0 (t, 2 x –CH=*C*H_2), 97.4 (d, 2 x C-1), 81.2 (d, 2 x C-4), 69.5 (t, 2 x –*C*H_2-CH=), 67.3 (t, 2 x –O-*C*H_2-CH_2-), 64.1 (d, 2 x C-5), 52.0 (t, 2 x Ph-*C*H_2-), 50.7 (d, 2 x C-3), 32.7 (t, 2 x C-2), 27.0 (t, 2 x –O-CH_2-*C*H_2-), 18.7 (q, 2 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2387 Hz = 4.77 ppm: δ = 4.77 (dd, 2H, 2 x 1-H), 4.38 (dq, 2H, 2 x 5-H), 3.13 (dd, 2H, 2 x 4-H), 3.07 (dt, 2H, 2 x 3-H), 2.13 (ddd, 2H, 2 x 2-H_{ax}), 1.61 (dt, 2H, 2 x 2-H_{eq}), 1.52 (d, 6H, 2 x 6-H).

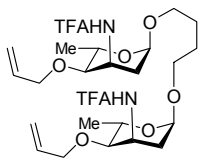
LC-MS (ESI) (+c): m/z (%): 609.39 (100) $[M]^+$, 610.39 (30) $[M + H]^+$, 611.40 (30) $[M + 2H]^+$; **HR-MS** $C_{36}H_{53}N_2O_6$: calc. 609.3925, found 609.3917

Reductive amination of homodimeric ketone 201 using ammonium acetate(204)

Ketone **201** (10 mg, 0.0233 mmol), ammonium acetate (18 mg, 0.233 mmol) and $NaBH_3CN$ (2 mg, 0.032 mmol) were stirred in methanol (5 ml) for 24h followed by the addition of a second portion of $NaBH_3CN$ (2 mg, 0.032 mmol). The reaction mixture was allowed to stir another 24h. To the yielded reaction mixture triethylamine (23 mg, 0.233 mmol) and CF_3COOEt (100 mg, 0.7 mmol) were added and the mixture was allowed to stir overnight. The solvent was evaporated under reduced pressure. Prior to column chromatography the crude product was separated from trifluoracatamide by sublimation in high vacuum (0.01 mbar, 60°C) then the residue was purified by column chromatography over silica gel (ethyl acetate / petroleum ether 1:5) to yield two fractions:

1st fraction: **204** (6 mg, 0.0097 mmol, 41%),

2nd fraction: **205** (1.3 mg, 0.0021 mmol, 9%).



1st fraction

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 8.00 (d, *J* = 8.5 Hz, 2H, 2 x NH), 5.97 (dddd, *J* = 17.2, 10.4, 6.0, 5.3 Hz, 2H, 2 x –C*H*=CH_2), 5.34 (dq, *J* = 17.2, 1.5

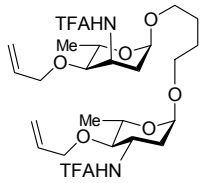
Hz, 2H, 2 x –CH=CH*H'*), 5.15 (bdd, *J* = 10.4, 1.1 Hz, 2H, 2 x –CH=CH*H'*), 4.50 (m, 2H, 2 x 3-H), 4.48 (d, *J* = 3.0 Hz, 2H, 2 x 1-H), 4.38 (dd, *J* = 12.5, 5.3 Hz, 2H, 2 x -*O*-CH*H'*-CH=), 3.85 (dd, *J* = 12.5, 6.0 Hz, 2H, 2 x -*O*-CH*H'*-CH=), 3.84 (dq, *J* = 9.5, 6.2 Hz, 2H, 2 x 5-H), 3.56 (m, 2H, 2 x –O-CH*H'*-CH_2-), 3.06 (m, 2H, 2 x –O-CH*H'*-CH_2-), 2.89 (dd, *J* = 9.5, 3.9 Hz, 2H, 2 x 4-H), 1.3 – 1.6 (m, 8H, 2 x 2-H_{ax}, 2 x 2-H_{eq}, 2 x –O-CH_2-CH_2-), 1.41 (d, *J* = 6.2 Hz, 6H, 2 x 6-H).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 135.1 (d, 2 x -*C*H=CH_2), 117.1 (t, 2 x –CH=*C*H_2), 96.8 (d, 2 x C-1), 78.1 (d, 2 x C-4), 70.5 (t, 2 x –*C*H_2-CH=), 67.4 (t, 2 x –O-*C*H_2-CH_2-), 63.5 (d, 2 x C-5), 43.7 (d, 2 x C-3), 32.7 (t, 2 x C-2), 26.6 (t, 2 x –O-CH_2-*C*H_2-), 18.3 (q, 2 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2551 Hz = 4.50 ppm: δ = 8.00 (d, 2H, 2 x NH), 4.50 (ddd, 2H, 2 x 3-H), 4.48 (d, 2H, 2 x 1-H), 3.84 (dq, 2H, 2 x 5-H), 2.89 (dd, 2H, 2 x 4-H), 1.53 (ddd, 2H, 2 x 2-H_{ax}), 1.41 (d, 6H, 2 x 6-H), 1.38 (dt, 2H, 2 x 2-H_{eq}).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2192 Hz = 4.38 ppm: δ = 5.98 (dddd, 2H, 2 x –C*H*=CH_2), 5.34 dq, 2H, 2 x –CH=CH*H'*), 5.15 (bdd, 2H, 2 x –CH=CH*H'*), 4.38 (dd, 2H, 2 x -*O*-CH*H'*-CH=), 3.85 (dd, 2H, 2 x -*O*-CH*H'*-CH=).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1783 Hz = 3.57 ppm: δ = 3.57 (m, 2H, 2 x –O-CH*H'*-CH_2-), 3.06 (m, 2H, 2 x –O-CH*H'*-CH_2-), 1.48 (m, 4H, 2 x –O-CH_2-CH_2-).



2nd fraction

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 8.08 (d, *J* = 8.1 Hz, 1H, NH^1), 6.05 (dd, *J* = 8.1 Hz, 1H, NH^2), 5.99 (dddd, *J* = 17.2, 10.4, 6.4, 5.2 Hz, 1H, –C*H*=CH_2^2), 5.82 (dddd, *J* = 17.1, 10.5, 5.3, 5.2 Hz, 1H, –C*H*=CH_2^1), 5.35 (dq, *J* = 17.2, 1.5 Hz, 1H, –CH=CH*H'*^{2}), 5.26 (dq, *J* = 17.1, 1.6 Hz, 1H, –CH=CH*H'*^{1}), 5.12 (dq, *J* = 10.4, 1.5 Hz, 1H, –CH=CH*H'*^{2}), 5.11 (dq, *J* = 10.5, 1.5 Hz, 1H, –CH=CH*H'*^{1}), 4.65 (d, *J* = 3.1 Hz, 1H, 1-H^2), 4.51 (d, *J* = 3.3 Hz, 1H, 1-H^1), 4.44 (m, 1H, 3-H^1), 4.37 (dd, *J* = 12.3, 5.2 Hz, 1H, -*O*-CH*H'*-CH=^{1}), 4.32 (m, 1H, 3-H^2), 4.01

(dd, *J* = 12.6, 5.2 Hz, 1H, -*O*-CH*H*'-CH=^{2}), 3.91 (dq, *J* = 9.2, 6.3 Hz, 1H, 5-H^2), 3.8 – 3.9 (m, 3H, -*O*-CH*H*'-CH=^{1}, -*O*-CH*H*'-CH=^{2}, 5-H^1), 3.60, 3.22, 3.08 (3m, 4H, 2 x –O-C*H*$_2$-CH$_2$-), 2.91 (t, *J* = 9.2 Hz, 1H, 4-H^2), 2.89 (dd, *J* = 9.5, 3.6 Hz, 1H, 4-H^1), 1.96 (dd, *J* = 12.5, 4.6 Hz, 1H, 2-H$_{ax}^2$), 1.68 (dd, *J* = 12.5, 3.1 Hz, 1H, 2-H$_{eq}^2$), 1.55 (m, 5H, 2-H$_{ax}^1$, 2 x –O-CH$_2$-C*H*$_2$-), 1.41 (d, *J* = 6.2 Hz, 3H, 6-H^1), 1.39 (d, *J* = 6.3 Hz, 3H, 6-H^2), 1.38 (m, 1H, 2-H$_{eq}^1$).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ =156.7, 156.5 (2s, 2 x *C*OCF$_3$), 135.3, 135.0 (2d, -*C*H=CH$_2^1$, -*C*H=CH$_2^2$), 117.3, 117.2 (2t, –CH=*C*H$_2^1$, –CH=*C*H$_2^2$), 96.99 (d, C-1^1), 96.51 (d, C-1^2), 82.15 (d, C-4^2), 78.29 (d, C-4^1), 73.43 (t, –*C*H$_2$-CH=^{2}), 70.61 (t, –*C*H$_2$-CH=^{1}), 68.23 (d, C-5^2), 67.82, 67.09 (2t, 2 x –O-*C*H$_2$-CH$_2$-), 63.64 (d, C-5^1), 49.79 (d, C-3^2), 43.90 (d, C-3^1), 35.37 (t, C-2^2), 32.88 (t, C-2^1), 27.11, 26.58 (2t, 2 x –O-CH$_2$-*C*H$_2$-), 18.64, 18.51 (2q, C-6^1, C-6^2).

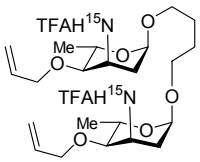
Reductive amination and introduction of ^{15}N label (206)

Bisketone **201** (350 mg, 0.821 mmol), ^{15}N-ammonium acetate (700 mg, 9.0 mmol) and $NaBH_3CN$ (105 mg, 1.64 mmol) were stirred in methanol (100 ml) for 24h followed by the addition of a second portion $NaBH_3CN$ (105 mg, 1.64 mmol). The reaction mixture was allowed to stir for another 24h after which triethylamine (1.5 ml, 10 mmol) and CF_3COOEt (3.6 ml, 30 mmol) were added and stirring was continued overnight. The solvent was evaporated under reduced pressure. Prior to column chromatography the crude product was separated from trifluoroacetamide by sublimation in high vacuum (0.01 mbar, 60 ^{o}C). The remaining residue was purified by column chromatography over silica gel (ethyl acetate / petroleum ether 1:5) to yield three fractions:

1st fraction: **206** (177 mg, 0.284 mmol, 35%).

2nd fraction: **207** (20 mg, 0.032 mmol, 3.9%)

3rd fraction: **208** (20 mg, 0.046 mmol, 5.6%).



1st fraction

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 7.89 (dd, *J* = 92.1, 9.1 Hz, 2H, 2 x NH), 5.86 (dddd, *J* = 17.2, 10.4, 6.4, 5.1 Hz, 2H, 2 x –C*H*=CH$_2$), 5.22 (dq, *J* = 17.2,

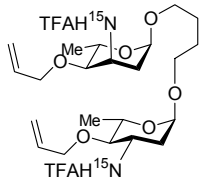
1.5 Hz, 2H, 2 x –CH=CH*H*'), 5.03 (bdd, *J* = 10.4, 1.3 Hz, 2H, 2 x –CH=CH*H*'), 4.38 (m, 2H, 2 x 3-H), 4.37 (d, *J* = 3.1 Hz, 2H, 2 x 1-H), 4.27 (dd, *J* = 12.4, 5.1 Hz, 2H, 2 x -*O*-CH*H*'-CH=), 3.85 (m, 4H, 2 x -*O*-CH*H*'-CH=, 2 x 5-H), 3.44 (m, 2H, 2 x –O-CH*H*'-CH_2-), 2.95 (m, 2H, 2 x –O-CH*H*'-CH_2-), 2.77 (ddd, *J* = 9.6, 3.8, 3.8 Hz, 2H, 2 x 4-H), 1.2 – 1.5 (m, 8H, 2 x 2-H_{ax}, 2 x 2-H_{eq}, 2 x –O-CH_2-C*H*$_2$-), 1.30 (d, *J* = 6.2 Hz, 6H, 2 x 6-H).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 157.10, 156.95, 156.81, 156.67, 156.53, 156.38, 156.24 (s, 2 x *CO*CF_3), 135.13 (d, 2 x -*C*H=CH_2), 117.1 (t, 2 x –CH=*C*H_2), 96.82 (d, 2 x C-1), 78.1 (d, 2 x C-4), 70.5 (t, 2 x –*C*H_2-CH=), 67.4 (t, 2 x –O-*C*H_2-CH_2-), 63.5 (d, 2 x C-5), 43.75, 43.68 (d, 2 x C-3), 32.7 (t, 2 x C-2), 26.6 (t, 2 x –O-CH_2-*C*H_2-), 18.3 (q, 2 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2241 Hz = 4.48 ppm: δ = 8.00 (dd, 2H, 2 x NH), 4.50 (ddd, 2H, 2 x 3-H), 4.48 (d, 2H, 2 x 1-H), 3.84 (dq, 2H, 2 x 5-H), 2.89 (ddd, 2H, 2 x 4-H), 1.53 (ddd, 2H, 2 x 2-H_{ax}), 1.42 (d, 6H, 2 x 6-H), 1.38 (dt, 2H, 2 x 2-H_{eq}).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2193 Hz = 4.39 ppm: δ = 5.98 (dddd, 2H, 2 x –C*H*=CH_2), 5.34 dq, 2H, 2 x –CH=CH*H*'), 5.15 (bdd, 2H, 2 x –CH=CH*H*'), 4.39 (dd, 2H, 2 x -*O*-CH*H*'-CH=), 3.85 (dd, 2H, 2 x -*O*-CH*H*'-CH=).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1782 Hz = 3.56 ppm: δ = 3.56 (m, 2H, 2 x –O-CH*H*'-CH_2-), 3.06 (m, 2H, 2 x –O-CH*H*'-CH_2-), 1.48 (m, 4H, 2 x –O-CH_2-C*H*$_2$-).



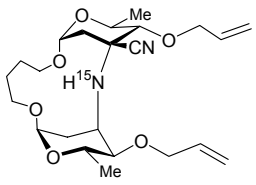
2nd fraction

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 8.08 (dd, *J* = 92.2, 9.1 Hz, 1H, ^{15}NH^1), 6.00 (dd, *J* = 90.9, 8.1 Hz, 1H, ^{15}NH^2), 5.97 (dddd, *J* = 17.2, 10.5, 6.4, 5.1 Hz, 1H, –C*H*=CH_2^2), 5.83 (dddd, *J* = 17.2, 10.6, 5.4, 5.3 Hz, 1H, –C*H*=CH_2^1), 5.33 (dq, *J* = 17.2, 1.5 Hz, 1H, –CH=CH*H*'^{2}), 5.26 (dq, *J* = 17.2, 1.6 Hz, 1H, –CH=CH*H*'^{1}), 5.15 (dq, *J* = 10.5, 1.6 Hz, 1H, –CH=CH*H*'^{2}), 5.11 (dq, *J* = 10.6, 1.4

Hz, 1H, –CH=CH*H*'^{1}), 4.65 (d, *J* = 2.7 Hz, 1H, 1-H^2), 4.51 (d, *J* = 3.0 Hz, 1H, 1-H^1), 4.50 (m, 1H, 3-H^1), 4.38 (dd, *J* = 12.3, 5.3 Hz, 1H, -*O*-CH*H*'-CH=^{1}), 4.32 (m, 1H, 3-H^2), 4.01 (dd, *J* = 12.6, 5.1 Hz, 1H, -*O*-CH*H*'-CH=^{2}), 3.91 (dq, *J* = 9.0, 6.2 Hz, 1H, 5-H^2), 3.8 – 3.9 (m, 3H, -*O*-CH*H*'-CH=^{1}, -*O*-CH*H*'-CH=^{2}, 5-H^1), 3.60, 3.22, 3.08 (3m, 4H, 2 x –O-C*H*$_2$-CH$_2$-), 2.95 (t, *J* = 9.9 Hz, 1H, 4-H^2), 2.88 (ddd, *J* = 9.5, 3.6, 3.6 Hz, 1H, 4-H^1), 1.97 (dd, *J* = 12.8, 4.5 Hz, 1H, 2-H$_{ax}$^{2}), 1.68 (dt, *J* = 12.8, 3.6 Hz, 1H, 2-H$_{eq}$^{2}), 1.55 (m, 5H, 2-H$_{ax}$^{1}, 2 x –O-CH$_2$-C*H*$_2$-), 1.39 (d, *J* = 6.2 Hz, 3H, 6-H^1), 1.38 (d, *J* = 6.2 Hz, 3H, 6-H^2), 1.38 (m, 1H, 2-H$_{eq}$^{1}).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ =156.7, 156.5 (2s, 2 x *C*OCF$_3$), 135.3, 135.0 (2d, -*C*H=CH$_2$^{1}, -*C*H=CH$_2$^{2}), 117.3, 117.2 (2t, –CH=*C*H$_2$^{1}, –CH=*C*H$_2$^{2}), 97.00, 96.98 (2d, C-1^1), 96.53, 96.51 (2d, C-1^2), 82.17, 82.14 (2d, C-4^2), 78.29 (d, C-4^1), 73.43 (t, –*C*H$_2$-CH=^{2}), 70.61 (t, –*C*H$_2$-CH=^{1}), 68.24, 68.22 (2d, C-5^2), 67.82, 67.09 (2t, 2 x –O-*C*H$_2$-CH$_2$-), 63.64 (d, C-5^1), 49.84, 49.74 (2d, C-3^2), 43.95, 43.85 (2d, C-3^1), 35.37 (t, C-2^2), 32.88 (t, C-2^1), 27.11, 26.58 (2t, 2 x –O-CH$_2$-*C*H$_2$-), 18.64, 18.51 (2q, C-6^1, C-6^2).

LC-MS (ESI) (+c): m/z (%): 645.15 (100) [M + Na]$^+$.



3rd fraction

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 6.29 (dddd, *J* = 17.2, 10.4, 6.2, 5.3 Hz, 1H, –C*H*=CH$_2$^{2}), 5.94 (ddt, *J* = 17.2, 10.5, 5.2 Hz, 1H, –C*H*=CH$_2$^{1}), 5.47 (dq, *J* = 17.2, 1.7 Hz, 1H, –CH=CH*H*'^{2}), 5.35 (dq, *J* = 17.2, 1.7 Hz, 1H, –CH=CH*H*'^{1}), 5.22 (dq, *J* = 10.4, 2.0 Hz, 1H, –CH=CH*H*'^{2}), 5.16 (dq, *J* = 10.5, 1.6 Hz, 1H, –CH=CH*H*'^{1}), 4.76 (d, *J* = 3.5 Hz, 1H, 1-H^1), 4.70 (dd, *J* = 81.5, 9.2 Hz, 1H, ^{15}NH), 4.70 (ddt, *J* = 12.3, 5.3, 1.3 Hz, 1H, -*O*-CH*H*'-CH=^{2}), 4.49 (ddt, *J* = 12.7, 5.2, 1.4 Hz, 1H, -*O*-CH*H*'-CH=^{1}), 4.42 (bd, *J* = 3.6 Hz, 1H, 1-H^2), 4.33 (dq, *J* = 9.6, 6.3 Hz, 1H, 5-H^2), 4.30 (dq, *J* = 9.5, 6.3 Hz, 1H, 5-H^1), 4.05 (m, 2H, -*O*-CH*H*'-CH=^{1}, -*O*-CH*H*'-CH=^{2}), 3.91 (m, 1H, 3-H^1), 3.72 (ddd, *J* = 9.5, 8.4, 1.7 Hz, 1H, –O-CH*H*'-CH$_2$-^{2}), 3.53 (ddd, *J* = 9.6, 7.6, 3.2 Hz, 1H, –O-CH*H*'-CH$_2$-^{1}), 3.22 (dd, *J* = 9.6, 1.3 Hz, 1H, 4-H^2), 3.17 (m, –O-CH*H*'-CH$_2$-^{1}), 3.09 (ddd, *J* = 9.5, 7.0, 2.13 Hz, 1H, –O-

CH*H'*-CH_2-^{2}), 3.01 (ddd, *J* = 9.5, 4.0, 4.0 Hz, 1H 4-H^1), 2.48 (bd, *J* = 13.6 Hz, 1H, 2-H_{ax}^2), 2.46 (dd, *J* = 14.0, 2.8 Hz, 1H, 2-H_{ax}^1), 1.94 (ddd, *J* = 13.6, 5.7, 4.0 Hz, 1H, 2-H_{eq}^2), 1.78 (ddt, *J* = 14.0, 3.5, 3.7 Hz, 1H, 2-H_{eq}^1), 1.65 (m, 1H, –O-CH_2-CH*H'*-^{2}), 1.54 (d, *J* = 6.3 Hz, 3H, 6-H^1), 1 52 (m, 2H, –O-CH_2-CH_2-^{1}), 1.45 (m, 1H, –O-CH_2-CH*H'*-^{2}), 1.34 (d, *J* = 6.3 Hz, 3H, 6-H^2).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 136.6 (d, -*C*H=CH_2^2), 135.1 (d, -*C*H=CH_2^1), 122.3 (s, C≡N),116.6 (t, –CH=*C*H_2^2), 116.5 (t, –CH=*C*H_2^1), 98.4 (d, C-1^1), 96.2 (d, C-1^2), 87.1 (d, C-4^2), 82.0, 81.9 (2d, C-4^1), 74.7 (t, –*C*H_2-CH=^{1}), 71.5 (t, –*C*H_2-CH=^{2}), 68.7 (t, –O-*C*H_2-CH_2-^{2}), 68.5 (t, –O-*C*H_2-CH_2-^{1}), 64.0, 63.9 (2d, C-5^1, C-5^2), 57.6, 57.5 (s, C-3^2), 49.4, 49.3 (2d, C-3^1), 41.5, 41.4 (2t, C-2^2), 36.4 (t, C-2^1), 29.1 (t, –O-CH_2-*C*H_2-^{2}), 28.7 (t, –O-CH_2-*C*H_2-^{1}), 18.7 (q, C-6^1), 17.9 (q, C-6^2).

LC-MS (ESI) (+c): m/z (%): 438.26 (100) $[M + H]^+$.

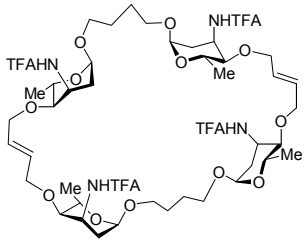
11.8.4. Experiments to the chapter 9.6.2.
Macrocyclization of bisallylated homodimer 204 (211, 212)

The reaction was carried out according to the protocol **TP3** except for the following details: olefin **204** (55 mg, 0.089 mmol), benzol (50 ml), Grubbs 1 catalyst (20 mol%), reaction time 7 days, RT. After column chromatography over silica gel, three fractions were isolated:

1st fraction: tetracyclus **211** (23 mg, 0.0194 mmol, 44%),

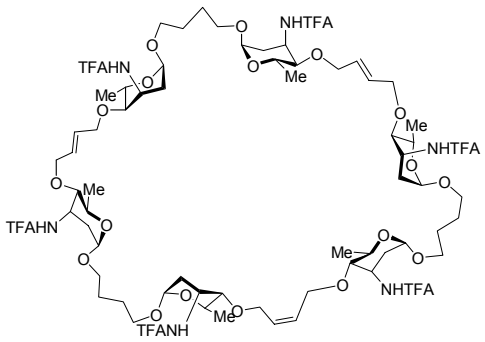
2nd fraction: hexacyclus **212** (3.6 mg, 0.002 mmol, 4.5 %),

and starting material **204** 16.5 mg (0.0267 mmol, 30%).



1st fraction

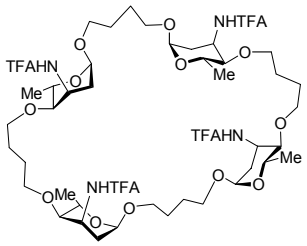
LC-MS (ESI) (+c): m/z (%): 1202.86 (60) $[M + H_2O]^+$, 1207.81 (100) $[M + Na]^+$



2nd fraction

LC-MS (ESI) (+c): m/z (%): 1794.53 (70) $[M + H_2O]^+$, 1799.51 (100) $[M + Na]^+$.

Catalytic hydrogenation of macrocyclus 211 (213)



The reaction was carried out according to the protocol **TP4** except for the following details: tetracyclus **211** (23 mg, 0.0194 mmol), solvent ethyl acetate, reaction time 12h.

Yield: 23 mg (0.0193 mmol, > 99%).

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 7.94 (d, *J* = 9.1 Hz, 4H, 4 x NH), 4.52 (bdd, *J* = 9.1, 3.8 Hz, 4H, 4 x 3-H), 4.48 (d, *J* = 2.6 Hz, 4H, 4 x 1-H), 3.93 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 3.74 (dq, *J* = 9.7, 6.0 Hz, 4H, 4 x 5-H), 3.63 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 3.20 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 3.07 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 2.78 (dd, *J* = 9.7, 3.8 Hz, 4H, 4 x 4-H), 1.78 (m, 8H, 4 x –O-CH_2-C*H*$_2$-^{tail}), 1.4 - 1.6 (m, 16H, 4 x 2-H, 4 x –O-CH_2-C*H*$_2$-^{head}), 1.40 (d, *J* = 6.0 Hz, 12H, 4 x 6-H).

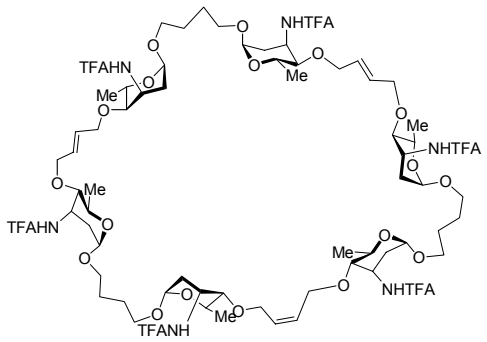
^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 156.6 (q, *J* = 35.9 Hz, 4 x *C*OCF_3), 117.1 (q, *J* = 288.7 Hz, 4 x CO*C*F_3), 96.9 (d, 4 x C-1), 79.3 (d, 4 x C-4), 70.2 (t, 4 x –O-*C*H_2-CH_2-^{tail}), 67.5 (t, 4 x –O-*C*H_2-CH_2-^{head}), 63.8 (d, 4 x C-5), 44.2 (d, 4 x C-3), 32.9 (t, 4 x C-2), 27.7 (t, 4 x –O-CH_2-*C*H_2-^{tail}), 27.2 (t, 4 x –O-CH_2-*C*H_2-^{head}), 18.4 (q, 4 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 3971 Hz = 7.94 ppm: δ = 7.94 (d, 4H, 4 x NH), 4.52 (dd, 4H, 4 x 3-H), 4.48 (d, 4H, 4 x 1-H), 3.74 (dq, 4H, 4 x 5-H), 2.78 (dd, 4H, 4 x 4-H), 1.53 (dd, 4H, 4 x 2-H_{ax}), 1.43 (dd, 4H, 4 x 2-H_{eq}), 1.40 (d, 12H, 4 x 6-H).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1969 Hz = 3.94 ppm: δ = 3.93 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 3.20 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 1.78 (m, 8H, 4 x –O-CH_2-CH_2-^{tail}).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1817 Hz = 3.63 ppm: δ = 3.63 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 3.06 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 1.55 (m, 8H, 4 x –O-CH_2-CH_2-^{head}).

Catalytic hydrogenation of macrocyclus 212 (214)



The reaction was carried out according to the protocol **TP4** except for the following details: hexacyclus **212** (27 mg, 0.0152 mmol), solvent ethyl acetate, reaction time 12h.

Yield: 27 mg (0.01519 mmol, > 99%).

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 7.99 (d, *J* = 9.0 Hz, 6H, 6 x NH), 4.57 (bdd, *J* = 9.0, 3.7 Hz, 6H, 6 x 3-H), 4.51 (d, *J* = 2.3 Hz, 6H, 6 x 1-H), 4.00 (m, 6H, 6 x –O-CH*H*'-CH_2-^{tail}), 3.82 (dq, *J* = 9.5, 6.2 Hz, 6H, 6 x 5-H), 3.60 (m, 6H, 6 x –O-CH*H*'-CH_2-^{head}), 3.29 (m, 6H, 6 x –O-CH*H*'-CH_2-^{tail}), 3.08 (m, 6H, 6 x –O-CH*H*'-CH_2-^{head}), 2.87 (dd, *J* = 9.5, 3.7 Hz, 6H, 6 x 4-H), 1.80 (m, 12H, 6 x –O-CH_2-CH_2-^{tail}), 1.4 - 1.6 (m, 24H, 6 x 2-H, 6 x –O-CH_2-CH_2-^{head}), 1.45 (d, *J* = 6.2 Hz, 18H, 6 x 6-H).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 156.6 (q, *J* = 35.9 Hz, 6 x *C*OCF$_3$), 117.1 (q, *J* = 288.8 Hz, 6 x CO*C*F$_3$), 96.9 (d, 6 x C-1), 79.3 (d, 6 x C-4), 69.7 (t, 6 x –O-*C*H$_2$-CH$_2$-^{tail}), 67.4 (t, 6 x –O-*C*H$_2$-CH$_2$-^{head}), 63.7 (d, 6 x C-5), 44.0 (d, 6 x C-3), 32.8 (t, 6 x C-2), 26.9 (t, 6 x –O-CH$_2$-*C*H$_2$-^{tail}), 26.8 (t, 6 x –O-CH$_2$-*C*H$_2$-^{head}), 18.3 (q, 6 x C-6).

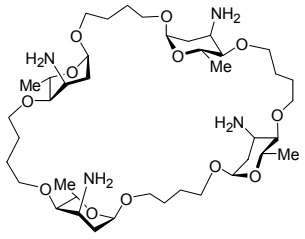
^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1438 Hz = 2.87 ppm: δ = 7.99 (d, 6H, 6 x NH), 4.57 (dd, 6H, 6 x 3-H), 4.51 (d, 6H, 6 x 1-H), 3.82 (dq, 6H, 6 x 5-H), 2.87 (dd, 6H, 6 x 4-H), 1.58 (dd, 6H, 6 x 2-H$_{ax}$), 1.50 (dd, 6H, 6 x 2-H$_{eq}$), 1.45 (d, 18H, 6 x 6-H).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1999 Hz = 4.00 ppm: δ = 4.00 (m, 6H, 6 x –O-CH*H*'-CH$_2$-^{tail}), 3.30 (m, 6H, 6 x –O-CH*H*'-CH$_2$-^{tail}), 1.80 (m, 12H, 6 x –O-CH$_2$-C*H*$_2$-^{tail}).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1543 Hz = 3.09 ppm: δ = 3.60 (m, 6H, 6 x –O-CH*H*'-CH$_2$-^{head}), 3.09 (m, 6H, 6 x –O-CH*H*'-CH$_2$-^{head}), 1.52 (m, 12H, 6 x –O-CH$_2$-C*H*$_2$-^{head}).

LC-MS (ESI) (+c): m/z (%): 1807.50 (100) $[M + Na]^+$.

Preparation of macrocycle 215 by N-deprotection



The hydrogenated product **213** (21 mg, 0.0177 mmol) was dissolved in 12 ml THF/1.0M aqueous NaOH (1:3) and methanol (5 ml) was added to homogenise the solution. This mixture was allowed to stir at RT for 20 h, at which time t.l.c. (CH_3CN/25% aqueous NH_3 10:1, R_f – 0.5, t.l.c. should be exposed to aq. ammonia vapor prior to use) indicated that the detrifluoroacetylation was complete. The mixture was extracted with CH_2Cl_2 (3 x 50 ml). The organic

phase was dried over a Na_2SO_4 and evaporated under reduced pressure. Amin **215** was lyophilised from benzol to yield a very hygroscopic gray-green powder.

Yield: 13.5 mg (0.0168 mmol, 95%).

^{1}**H-NMR** (500 MHz, Py, Py = 8.71 ppm): δ = 4.83 (d, *J* = 3.5 Hz, 4H, 4 x 1-H), 4.06 (dq, *J* = 9.3, 6.2 Hz, 4H, 4 x 5-H), 3.77 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 3.69 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 3.50 (bs, 4H, 4 x 3-H), 3.39 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 3.34 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 3.02 (dd, *J* = 9.3, 3.5 Hz, 4H, 4 x 4-H), 2.23 (bd, *J* = 14.13 Hz, 4H, 4 x 2-H_{ax}), 1.89 (dt, *J* = 14.00, 4.35 Hz, 4H, 4 x 2-H_{eq}), 1.6 – 1.8 (m, 16H, 4 x –O-CH_2-C*H*$_2$-^{tail}, 4 x –O-CH_2-C*H*$_2$-^{head}), 1.40 (d, *J* = 6.2 Hz, 12H, 4 x 6-H).

^{13}**C-NMR** (125 MHz, Py, Py = 149.5 ppm): δ = 97.5 (d, 4 x C-1), 81.9 (d, 4 x C-4), 69.2 (t, 4 x –O-*C*H_2-CH_2-^{head}), 67.7 (t, 4 x –O-*C*H_2-CH_2-^{tail}), 62.1 (d, 4 x C-5), 45.8 (d, 4 x C-3), 34.6 (t, 4 x C-2), 27.6 (t, 4 x –O-CH_2-*C*H_2-^{head}), 27.3 (t, 4 x –O-CH_2-*C*H_2-^{tail}), 18.6 (q, 4 x C-6).

^{1}**H-NMR** (500 MHz, Py) **TOCSY** - 2417 Hz = 4.83 ppm: δ = 4.83 (d, 4H, 4 x 1-H), 4.06 (dq, 4H, 4 x 5-H), 3.50 (bs, 4H, 4 x 3-H), 3.02 (dd, 4H, 4 x 4-H), 2.24 (bd, 4H, 4 x 2-H_{ax}), 1.89 (dt, 4H, 4 x 2-H_{eq}), 1.40 (d, 12H, 4 x 6-H).

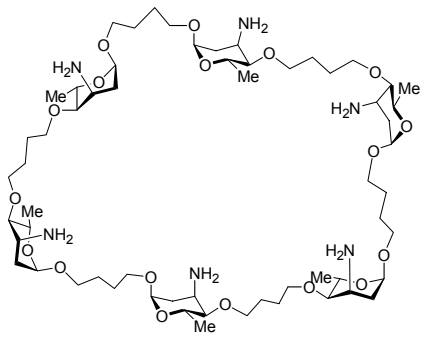
^{1}**H-NMR** (500 MHz, Py) **TOCSY** - 1886 Hz = 3.77 ppm: δ = 3.77 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 3.33 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 1.70 (m, 8H, 4 x –O-CH_2-C*H*$_2$-^{tail}).

^{1}**H-NMR** (500 MHz, Py) **TOCSY** - 1846 Hz = 3.69 ppm: δ = 3.69 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 3.39 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 1.74 (m, 8H, 4 x –O-CH_2-C*H*$_2$-^{head}).

LC-MS (ESI) (+c): m/z (%): 403.29 (100) $[M + 2H]^{2+}$, 805.56 (80) $[M + H]^+$, 827.56 (30) $[M + Na]^+$; **HR-MS** $C_{40}H_{77}N_4O_{12}$: calc. 805.5538, found 805.5519.

$[\alpha]^{25}_D$ = - 127.7^o (c = 1 in $CHCl_3$).

Preparation of macrocycle 216 by N-deprotection



The hydrogenated product **214** (27 mg, 0.0152 mmol) was dissolved in 12 ml THF/1.0M aqueous NaOH (1:3) and methanol (5 ml) was added to homogenise a solution. This mixture was allowed to stir at RT for 20 h, at which time t.l.c. (CH_3CN/25% aqueous NH_3 10:1, R_f – 0.5, t.l.c. should be exposed to aq. ammonia vapor prior to use) indicated that the detrifluoroacetylation was complete. The mixture was extracted with CH_2Cl_2 (3 x 50 ml). The organic phase was dried over a Na_2SO_4 and evaporated under reduced pressure. Amin **216** was lyophilised from benzol to yield a very hygroscopic gray-green powder.

Yield: 18 mg (0.0151 mmol, 99%).

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 4.65 (d, *J* = 3.1 Hz, 6H, 6 x 1-H), 4.01 (dq, *J* = 9.5, 6.1 Hz, 6H, 6 x 5-H), 3.62 (m, 6H, 6 x –O-CH*H*'-CH_2-^{tail}), 3.45 (m, 6H, 6 x –O-CH*H*'-CH_2-^{head}), 3.33 (bs, 6H, 6 x 3-H), 3.13 (m, 12H, 6 x –O-CH*H*'-CH_2-^{head}, 6 x –O-CH*H*'-CH_2-^{tail}), 2.81 (dd, *J* = 9.5, 3.2 Hz, 6H, 6 x 4-H), 2.16 (bd, *J* = 14.4 Hz, 6H, 6 x 2-H_{ax}), 1.35 – 1.7 (m, 30H, 6 x –O-CH_2-C*H*$_2$-^{tail}, 6 x –O-CH_2-C*H*$_2$-^{head}, 6 x 2-H_{eq}), 1.42 (d, *J* = 6.1 Hz, 18H, 6 x 6-H).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 97.76 (d, 6 x C-1), 82.3 (d, 6 x C-4), 69.0 (t, 6 x –O-*C*H_2-CH_2-^{head}), 67.7 (t, 4 x –O-*C*H_2-CH_2-^{tail}), 62.3 (d, 4 x C-5), 45.9 (d, 4 x C-3), 34.7 (t, 4 x C-2), 27.6 (t, 4 x –O-CH_2-*C*H_2-^{head}), 27.3 (t, 4 x –O-CH_2-*C*H_2-^{tail}), 18.7 (q, 4 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2384 Hz = 4.77 ppm: δ = 4.77 (d, 6H, 6 x 1-H), 4.12 (dq, 6H, 6 x 5-H), 3.45 (bs, 6H, 6 x 3-H), 2.92 (dd, 6H, 6 x 4-H), 2.27 (bd, 6H, 6 x 2-H_{ax}), 1.78 (dt, 6H, 6 x 2-H_{eq}), 1.54 (d, 18H, 6 x 6-H).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1871 Hz = 3.74 ppm: δ = 3.74 (m, 6H, 6 x –O-CH*H*'-CH_2-^{tail}), 3.26 (m, 6H, 6 x –O-CH*H*'-CH_2-^{tail}), 1.66 (m, 12H, 6 x –O-CH_2-CH_2-^{tail}).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1787 Hz = 3.57 ppm: δ = 3.57 (m, 6H, 6 x –O-CH*H*'-CH_2-^{head}), 3.25 (m, 6H, 6 x –O-CH*H*'-CH_2-^{head}), 1.71 (m, 12H, 6 x –O-CH_2-CH_2-^{head}).

LC-MS (ESI) (+c): m/z (%): 604.41 (10) $[M + 2H]^{2+}$, 1207.80 (30) $[M + H]^+$; **HR-MS** $C_{60}H_{115}N_6O_{18}$: calc. 1207.8268, found 1207.8284.

$[\alpha]^{25}_D$ = - 112.3^o (c = 1 in $CHCl_3$).

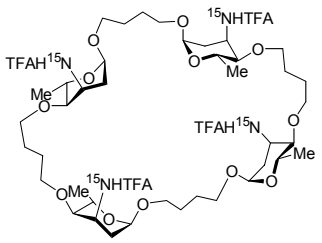
Macrocyclization of ^{15}N-labelled bisallylated homodimer 215 and catalytic hydrogenation of macrocycle 218 and 219

The reaction was carried out according to the protocol **TP3** except for the following details: olefin **215** (150 mg, 0.24 mmol), CH_2Cl_2 (150 ml), Grubbs 1 catalyst (20 mol %), reaction time 7 days, RT. The products were hydrogenated without further purification.

Yield: tetracyclus **218** (65 mg, 0.0543 mmol, 45%).

Yield: hexacyclus **219** (7 mg, 0.004 mmol, 5%).

The reaction was carried out according to the protocol **TP4** except for the following details: tetracyclus **218** (130 mg, 0.1086 mmol), solvent ethyl acetate, reaction time 12h.



Yield: 130 mg (0.1086 mmol, >99%).

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 7.84 (dd, *J* = 91.6, 9.2 Hz, 4H, 4 x NH), 4.40 (bdd, *J* = 8.6, 3.8 Hz, 4H, 4 x 3-H), 4.35 (bs, 4H, 4 x 1-H), 3.82 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 3.63 (dq, *J* = 9.3, 6.0 Hz, 4H, 4 x 5-H), 3.51 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 3.08 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 2.94 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 2.66 (ddd, *J* = 9.3, 3.8, 3.8 Hz, 4H, 4 x 4-H), 1.66 (m, 8H, 4 x –O-CH_2-C*H*$_2$-^{tail}), 1.2 - 1.6 (m, 16H, 4 x 2-H, 4 x –O-CH_2-C*H*$_2$-^{head}), 1.28 (d, *J* = 6.0 Hz, 12H, 4 x 6-H).

^{15}N**-NMR** (50 MHz, C_6D_6, CH_3NO_2 = 0 ppm): δ = -266.56 (d, J = 91.6 Hz, 4 x NH).

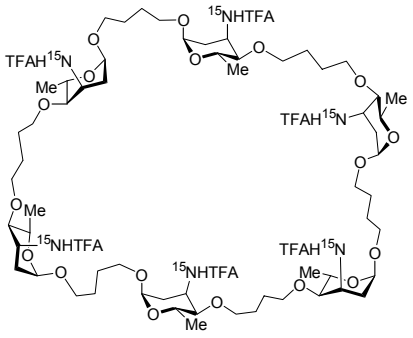
^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 156.67 (q, *J* = 35.9 Hz, 4 x *C*OCF_3), 117.2 (q, *J* = 288.7 Hz, 4 x CO*C*F_3), 96.9 (d, 4 x C-1), 79.25 (d, 4 x C-4), 70.2 (t, 4 x –O-*C*H_2-CH_2-^{tail}), 67.5 (t, 4 x –O-*C*H_2-CH_2-^{head}), 63.8 (d, 4 x C-5), 44.2, 44.1 (2d, 4 x C-3), 32.9 (t, 4 x C-2), 27.7 (t, 4 x –O-CH_2-*C*H_2-^{tail}), 27.2 (t, 4 x –O-CH_2-*C*H_2-^{head}), 18.4 (q, 4 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2257 Hz = 4.51 ppm: δ = 7.95 (dd, 4H, 4 x NH), 4.52 (dd, 4H, 4 x 3-H), 4.47 (d, 4H, 4 x 1-H), 3.74 (dq, 4H, 4 x 5-H), 2.78 (dd, 4H, 4 x 4-H), 1.53 (dd, 4H, 4 x 2-H_{ax}), 1.42 (dd, 4H, 4 x 2-H_{eq}), 1.40 (d, 12H, 4 x 6-H).

LC-MS (ESI) (+c): m/z (%): 1215.45 (100) $[M + Na]^+$; **HR-MS** $C_{48}H_{72}{}^{15}N_4O_{16}$ +Na: calc. 1215.4531, found 1215.4532.

$[\alpha]^{25}_D$ = - 115.6^o (c = 1 in $CHCl_3$).

The reaction was carried out according to the protocol **TP4** except for the following details: hexacyclus **219** (11 mg, 0.0062 mmol), solvent ethyl acetate, reaction time 12h.



Yield: 11mg (0.0062 mmol, >99%)

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 7.90 (dd, *J* = 92.4, 9.2 Hz, 6H, 6 x NH), 4.57 (bdd, *J* = 8.3, 3.5 Hz, 6H, 6 x 3-H), 4.38 (d, *J* = 2.4 Hz, 6H, 6 x 1-H), 3.90 (m, 6H, 6 x –O-CH*H*'-CH_2-^{tail}), 3.71 (dq, *J* = 9.5, 6.2 Hz, 6H, 6 x 5-H), 3.48 (m, 6H, 6 x –O-CH*H*'-CH_2-^{head}), 3.17 (m, 6H, 6 x –O-CH*H*'-CH_2-^{tail}), 2.95 (m, 6H, 6 x –O-CH*H*'-CH_2-^{head}), 2.75 (ddd, *J* = 9.5, 3.8, 3.5 Hz, 6H, 6 x 4-H), 1.74, 1.65 (2m, 12H, 6 x –O-CH_2-C*H*$_2$-^{tail}), 1.2 - 1.5 (m, 24H, 6 x 2-H, 6 x –O-CH_2-C*H*$_2$-^{head}), 1.34 (d, *J* = 6.2 Hz, 18H, 6 x 6-H).

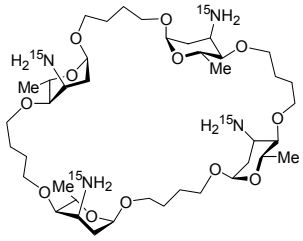
^{15}N-**NMR** (50 MHz, C_6D_6, CH_3NO_2 = 0 ppm): δ = -266.36 (d, J = 92.4 Hz, 6 x NH).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 156.5 (q, *J* = 35.9 Hz, 6 x *C*OCF_3), 117.2 (q, *J* = 288.8 Hz, 6 x CO*C*F_3), 96.8 (d, 6 x C-1), 79.2 (d, 6 x C-4), 69.7 (t, 6 x –O-*C*H_2-CH_2-^{tail}), 67.3 (t, 6 x –O-*C*H_2-CH_2-^{head}), 63.6 (d, 6 x C-5), 43.9, 43.8 (2d, 6 x C-3), 32.7 (t, 6 x C-2), 26.9 (t, 6 x –O-CH_2-*C*H_2-^{tail}), 26.8 (t, 6 x –O-CH_2-*C*H_2-^{head}), 18.3 (q, 6 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2286 Hz = 4.57 ppm: δ = 8.02 (dd, 6H, 6 x NH), 4.57 (dd, 6H, 6 x 3-H), 4.50 (d, 6H, 6 x 1-H), 3.82 (dq, 6H, 6 x 5-H), 2.86 (ddd, 6H, 6 x 4-H), 1.56 (dd, 6H, 6 x 2-H_{ax}), 1.50 (m, 6H, 6 x 2-H_{eq}), 1.46 (d, 18H, 6 x 6-H).

LC-MS (ESI) (+c): m/z (%): 1811.18 (100) $[M + Na]^+$.

Preparation of macrocycle 220 by N-deprotection



The hydrogenated tetracyclus (130 mg, 0.109 mmol) was dissolved in THF/1.0M aqueous NaOH (1:3, 72 ml) and methanol (20 ml) was added in order to obtain a clear solution. This mixture was allowed to stir at RT for 20 h, at which time t.l.c. (CH_3CN/25% aqueous NH_3 10:1, R_f – 0.5, t.l.c. should be exposed to aq. ammonia vapor prior to use) indicated that the deprotection step was completed. The mixture was extracted with CH_2Cl_2 (3 x 50 ml), the organic phase was dried over a Na_2SO_4 and evaporated under reduced pressure. Amine **220** was lyophilized from benzene to yield macrocycle as a hygroscopic gray crystalline powder.

Yield: 88 mg (0.109 mmol, >99%).

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 4.63 (d, *J* = 3.4 Hz, 4H, 4 x 1-H), 3.98 (dq, *J* = 9.3, 6.1 Hz, 4H, 4 x 5-H), 3.62 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 3.39 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 3.25 (bs, 4H, 4 x 3-H), 3.08 (m, 8H, 4 x –O-CH*H*'-CH_2-^{head}, 4 x –O-CH*H*'-CH_2-^{tail}), 2.77 (dd, *J* = 9.3, 3.0 Hz, 4H, 4 x 4-H), 2.10 (bd, *J* = 14.1 Hz, 4H, 4 x 2-H_{ax}), 1.64 (dt, *J* = 14.1, 4.7 Hz, 4H, 4 x 2-H_{eq}), 1.54 (m, 16H, 4 x –O-CH_2-C*H*$_2$-^{tail}, 4 x –O-CH_2-C*H*$_2$-^{head}), 1.41 (d, *J* = 6.1 Hz, 12H, 4 x 6-H).

^{15}N-**NMR** (50 MHz, C_6D_6, CH_3NO_2 = 0 ppm): δ = - 360.81 (s, 4 x NH).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 97.8 (d, 4 x C-1), 82.7 (d, 4 x C-4), 68.9 (t, 4 x –O-*C*H_2-CH_2-^{head}), 67.7 (t, 4 x –O-*C*H_2-CH_2-^{tail}), 62.1 (d, 4 x C-5), 45.9 (d, 4 x C-3), 34.9 (t, 4 x C-2), 27.8 (t, 4 x –O-CH_2-*C*H_2-^{head}), 27.5 (t, 4 x –O-CH_2-*C*H_2-^{tail}), 18.7 (q, 4 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2374 Hz = 4.75 ppm: δ = 4.75 (d, 4H, 4 x 1-H), 4.09 (dq, 4H, 4 x 5-H), 3.36 (bs, 4H, 4 x 3-H), 2.88 (dd, 4H, 4 x 4-H), 2.22 (bd, 4H, 4 x 2-H_{ax}), 1.75 (dt, 4H, 4 x 2-H_{eq}), 1.51 (d, 12H, 4 x 6-H).

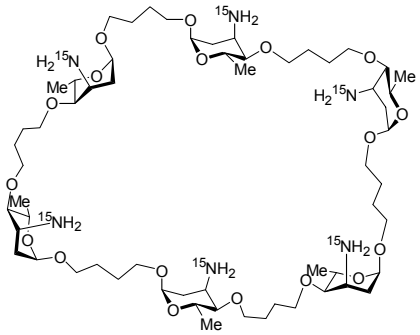
^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1864 Hz = 3.73 ppm: δ = 3.73 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 3.21 (m, 4H, 4 x –O-CH*H*'-CH_2-^{tail}), 1.65 (m, 8H, 4 x –O-CH_2-C*H*$_2$-^{tail}).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1752 Hz = 3.50 ppm: δ = 3.50 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 3.19 (m, 4H, 4 x –O-CH*H*'-CH_2-^{head}), 1.67 (m, 8H, 4 x –O-CH_2-C*H*$_2$-^{head}).

LC-MS (ESI) (+c): m/z (%): 809.54 (90) $[M + H]^+$, 831.49 (100) $[M + Na]^+$; **HR-MS** $C_{40}H_{77}{}^{15}N_4O_{12}$: calc. 809.5419, found 809.5403.

$[\alpha]^{25}_D$ = - 139.9^o (c = 1 in $CHCl_3$).

Preparation of macrocycle 221 by N-deprotection



The hydrogenated hexacyclus (11 mg, 6.2 μmol) was dissolved in 10 ml THF/1.0M aqueous NaOH (1:3) and methanol (5 ml) was added in order to obtain a clear solution. This mixture was allowed to stir at RT for 20 h, at which time t.l.c. (CH_3CN/25% aqueous NH_3 10:1, R_f – 0.5, t.l.c. should be exposed to aq. ammonia vapor prior to use) indicated that the deprotection was completed. The mixture was extracted with CH_2Cl_2 (3 x 10 ml), organic phase was dried over Na_2SO_4 and evaporated under reduced pressure. Amine **221** was lyophilized from benzene to yield macrocycle as a hygroscopic gray crystalline powder.

Yield: 7.4 mg (0.0061 mmol, 99%).

^{1}**H-NMR** (500 MHz, C_6D_6, C_6D_6 = 7.16 ppm): δ = 4.65 (d, *J* = 3.7 Hz, 6H, 6 x 1-H), 4.01 (dq, *J* = 9.4, 6.2 Hz, 6H, 6 x 5-H), 3.61 (m, 6H, 6 x –O-CH*H*'-CH_2-^{tail}), 3.40 (m, 6H, 6 x –O-CH*H*'-CH_2-^{head}), 3.27 (bs, 6H, 6 x 3-H), 3.12 (m, 12H, 6 x –O-CH*H*'-CH_2-^{head}, 6 x –O-CH*H*'-CH_2-^{tail}), 2.79 (dd, *J* = 9.4, 3.1 Hz, 6H, 6 x 4-H), 2.12 (bd, *J* = 14.0 Hz, 6H, 6 x 2-H_{ax}), 1.2 – 1.8 (m, 30H, 6 x –O-CH_2-C*H*$_2$-^{tail}, 6 x –O-CH_2-C*H*$_2$-^{head}, 6 x 2-H_{eq}), 1.43 (d, *J* = 6.2 Hz, 18H, 6 x 6-H).

^{15}N-**NMR** (50 MHz, C_6D_6, CH_3NO_2 = 0 ppm): δ = - 360.77 (s, 6 x NH).

^{13}**C-NMR** (125 MHz, C_6D_6, C_6D_6 = 128.06 ppm): δ = 97.86 (d, 6 x C-1), 82.67 (d, 6 x C-4), 68.80 (t, 6 x –O-*C*H_2-CH_2-^{head}), 67.67 (t, 4 x –O-*C*H_2-CH_2-^{tail}), 62.15 (d, 4 x C-5), 45.93, 45.91 (d, 4 x C-3), 34.97 (t, 4 x C-2), 27.60 (t, 4 x –O-CH_2-*C*H_2-^{head}), 27.31 (t, 4 x –O-CH_2-*C*H_2-^{tail}), 18.74 (q, 4 x C-6).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 2384 Hz = 4.77 ppm: δ = 4.77 (d, 6H, 6 x 1-H), 4.12 (dq, 6H, 6 x 5-H), 3.38 (bs, 6H, 6 x 3-H), 2.91 (dd, 6H, 6 x 4-H), 2.24 (bd, 6H, 6 x 2-H_{ax}), 1.77 (dt, 6H, 6 x 2-H_{eq}), 1.55 (d, 18H, 6 x 6-H).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1864 Hz = 3.73 ppm: δ = 3.73 (m, 6H, 6 x –O-CH*H*'-CH_2-^{tail}), 3.25 (m, 6H, 6 x –O-CH*H*'-CH_2-^{tail}), 1.65 (m, 12H, 6 x –O-CH_2-C*H*$_2$-^{tail}).

^{1}**H-NMR** (500 MHz, C_6D_6) **TOCSY** - 1758 Hz = 3.51 ppm: δ = 3.51 (m, 6H, 6 x –O-CH*H*'-CH_2-^{head}), 3.22 (m, 6H, 6 x –O-CH*H*'-CH_2-^{head}), 1.68 (m, 12H, 6 x –O-CH_2-C*H*$_2$-^{head}).

LC-MS (ESI) (+c): m/z (%): 607.90 (10) $[M + 2H]^{2+}$, 1213.80(30) $[M + H]^{+}$; **HR-MS** $C_{60}H_{115}{}^{15}N_6O_{18}$: calc. 1213.8090, found 1213.8068.

12. References

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