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Synthesis of *E. faecium* wall teichoic acid fragments

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**Keywords**

E. faecium; wall teichoic acid; carbohydrate; glycosylation; phosphoramidite.

**Abstract**

The first synthesis of different *E. faecium* wall teichoic acids (WTA) fragments is presented. The structure of these major cell wall components was elucidated recently and it was shown that these glycerolphosphate (GroP) based polymers are built up from -6-(GalNAc-\(\alpha\)(1-3)-GalNAc-\(\beta\)(1-2)-GroP)- repeating units. We assembled WTA fragments up to three repeating units in length, in two series that differ in the stereochemistry of the glycerolphosphate moiety. The key GalNAc-GalNAc-GroP synthons, required for the synthesis, were generated from galactosazide building blocks that were employed in highly stereoselective glycosylation reactions to furnish both the \(\alpha\)- and \(\beta\)-configured linkages. By comparing the NMR spectra of the synthesized fragments with the isolated material it appears that the hereto undefined stereochemistry of the glycerolphosphate moiety is sn-glycerol-3-phosphate. The generated fragments will be valuable tools to study their immunological activity at the molecular level.
Introduction

The rise of multi-drug resistant bacteria is a great threat to public health and the development of novel therapeutic or prophylactic approaches represents a grand challenge to the medical and scientific community. Amongst the most resistant bacterial species are enterococci, of which the vancomycin resistant enterococci (VRE) are especially difficult to treat with currently available antibiotics. *Enterococcus faecium* and *Enterococcus faecalis* are the most prevalent enterococci cultured from humans, accounting for 90% of all clinical isolates and they are responsible for a large part of nosocomial infections (14% in the USA in 2009-2010). *E. faecium*, a commensal bacterium inhabiting the gastrointestinal tract, is responsible for most VRE infections. Novel ways to combat these bacteria are urgently needed and therefore different vaccination strategies are currently being developed. Teichoic acids (TAs), poly-alditol phosphate based glycopolymers, are major components of the cell wall of Gram-positive bacteria, accounting for up to 70% of the dry weight of the bacterial cell wall. Two types of TAs are commonly present in the Gram-positive cell wall. Lipoteichoic acids (LTAs) are generally built up from a poly-glycerol phosphate backbone with D-alanyl and carbohydrate residues randomly appended to the glycerol’s C-2-OH. They are functionalized with a glycolipid anchor, which inserts into the phospholipid cell membrane underneath the peptidoglycan (PG) layer. Wall teichoic acids (WTAs) are covalently attached to the PG layer and the structure of WTAs varies considerably between species and even different strains from the same bacterium. LTA is a target for opsonic (i.e. protective) antibodies and we have recently shown that synthetic fragments of *E. faecalis* LTA can be used as antigens in combination with a BSA-carrier protein to provide a semi-synthetic vaccine modality. Serum raised against this conjugate showed effective cross reactivity towards different *E. faecalis* and *E. faecium* strains indicating than an LTA based vaccine could provide broad protection against different enterococci and also several other gram-positive pathogens (such as group-B streptococci, *S. aureus* and *S. epidermidis*). Some strains of *E. faecium* however are not
opsonized by anti-LTA antibodies. One possible explanation for this lack of killing is that the *E. faecium* LTA is not or less available for antibodies, probably due to capsular polysaccharides that cover LTA epitopes and prevent binding of antibodies and activation of complement. WTAs are generally longer than LTAs and may also obscure the targets for the opsonic antibodies. Very recently, the first structure of an enterococcal WTA was elucidated. This structure was isolated from an *E. faecium* strain, resistant to anti-LTA opsonic antibodies and is shown in Figure 1. It is built up from pseudotrisaccharide repeats, composed of an α-N-acetyl galactosamine that is linked to a β-N-acetyl galactosamine which in turn is attached to a glycerol phosphate residue. The stereochemistry of the glycerol moiety has not been established.

![Figure 1](image.png)

**Figure 1.** Structure of *E. faecium* WTA (A) and the target structures of this study (B).

Synthetic teichoic acid fragments can be powerful tools to unravel the immunological mode of action of these molecules. Not only can they be used as components in (semi)-synthetic vaccines and employed for diagnostic purposes, they can also be used to probe the interaction with other players of the immune system, such as C-type lectin receptors (CLRs), carbohydrate receptors playing an important role in shaping the immune system, and Toll-like receptors (TLRs), receptors responsible for detecting pathogen associated molecular patterns (PAMPs). Therefore the structure depicted in Figure 1 is an attractive synthetic target. In addition synthetic fragments may be used to assign the stereochemistry of the as-yet unknown glycerol C-2. Here we report the assembly of a small library of *E. faecium* WTA structures, encompassing mono-, di- and trimeric repeats of both glycerol stereoisomers. Compounds 1-
3 represent members of the *sn*-glycerol-1-phosphate family, where compound 4-6 are *sn*-glycerol-3-phosphate based targets).

**Results and discussion**

We, and others, have described a number of approaches to generate synthetic TA fragments, including traditional solution phase studies, light fluorous approaches and fully automated solid phase assemblies. All of our syntheses hinged on the use of well-established synthetic “DNA-chemistry”, employing phosphoramidite building blocks bearing a dimethoxytrityl ether as a temporary protecting group for the nascent oligomer chain. To assemble the set of target compounds in Figure 1, we again resorted to this strategy here. All target structures were equipped with an aminohexanol spacer for conjugation purposes in the future. Thus, for the assembly of WTAs 1-6, spacer phosphoramidite 9 and diastereomeric building blocks 7 and 8 were required. To minimize protecting group manipulations on far-advanced building blocks, we reasoned that the use of galactosazide building blocks as precursors for the α- and β-GalNAc-moieties would be beneficial. We decided to explore two routes towards key pseudo trisaccharides 10 and 11. The first route builds up the target structure from the glycerol end, first introducing the β-galactosamine linkage and subsequently installing the α-GalN₃-GalN₃ linkage. The alternative route proceeds in opposite direction and it installs the Gal-α-(1-3)-Gal linkage first, after which the glycerol moieties are attached.

![Figure 2. Retrosynthetic analysis](image-url)
The synthesis of the building blocks required for the assembly of the central glycerol-disaccharide intermediate is depicted in Scheme 1. Both galactosazide synthons were accessed from azidoselenogalactoside 13, which was readily obtained through an azidoselenylation\(^{14}\) of commercially available 3,4,6-triacetylgalactal 12. To facilitate the installation of the \(\alpha\)-galactosamine bond, we investigated donors 14 and 15, featuring a bulky TBDPS-ether at C-6.\(^ {15-18}\) To synthesize these galactosides, triol 13 was selectively protected on C-6 with a TBDPS group and the remaining alcohols were benzylated yielding selenoglycoside 14. Hydrolysis of the anomeric selenoacetal and subsequent introduction of the trifluoroimidate\(^ {19}\) furnished donor 15 in 87% yield over 2 steps.

To install the \(\beta\)-galactosamine bond we aimed to exploit the nitrile assisted glycosylation system.\(^ {20}\) We thus equipped building block 18 with a “permanent” benzyl ether at C-4 and C-6 and a 2-naphthylmethyl (Nap) ether, which can be chemoselectively removed, at C-3. To introduce the Nap at C-3, the C-4 and C-6 alcohols in 13 were first masked with a silylidene-ketal yielding compound 16 in good yield. Subsequent naphthylation, desilylation and double benzylaion yielded 17 in 54% yield from 16. Donor 18 was obtained from 17 by executing the above described hydrolysis-imidate introduction sequence in 80% yield. Acceptor 19 was synthesized by selectively removing the naphthylmethyl group from 17 in 78% yield using DDQ in a biphasic solvent system.

\[
\begin{align*}
\text{Scheme 1. Building block synthesis.} \\
\text{Reagents and conditions:} & \quad \text{a) TBDPSCI, imidazole, DMF, 90%; b) BnBr, NaH, DMF, quant;} \\
& \quad \text{c) \text{NIS, THF/H}_2\text{O; d) CF}_3\text{C}(=\text{NPh})\text{Cl, K}_2\text{CO}_3, \text{acetone, 87% over 2 steps; e) (t-Bu)_2\text{Si(OTf)}_2, DMF, 97%; f) NapBr, NaH, DMF, 71%; g) NEt}_3\cdot3\text{HF, THF, 94%; h) BnBr, NaH, DMF, 83%; i) NIS, THF/H}_2\text{O; j) CF}_3\text{C}(=\text{NPh})\text{Cl, K}_2\text{CO}_3, \text{acetone, 80% over 2 steps; k) DDQ, DCM:H}_2\text{O, 78%; l) 2-aminoethyldiphenylborinate, KI, K}_2\text{CO}_3, \text{allylbromide, MeCN, 66%; m) 2-aminoethyldiphenylborinate, KI, K}_2\text{CO}_3, \text{allylbromide, MeCN, 62%.}}
\end{align*}
\]
Glycerol acceptors 21 and 23 were synthesized by the regioselective introduction of an allyl-ether on the primary alcohol of commercially available diols 20 and 22. Using a palladium-tin bimetallic catalysis system as reported by Onomura we obtained 21 from 20 with excellent regioselectivity in 84% yield. Scaling up this reaction proved troublesome and therefore we investigated alternative procedures. Using a tin-ketal mediated allylation, 21 was obtained in 66% as a single regioisomer. A similar yield was obtained by employing a 2-aminoethyl diphenylborinate-catalyzed allylation as described by Taylor and co-workers. Although this procedure also gave 20% of the undesired C-2-allyl ether, the regioisomers were readily separated and the reaction could be easily scaled up (62% yield on 6 mmol scale).

With all building blocks in hand we attended to the assembly of the glycerol-disaccharide building blocks 35 and 36 (Scheme 2). We first explored the combination of selenophenyl galactosides 14 and 16 in a pre-activation based glycosylation reaction. However, we found that activation of seleno donor 14 using the diphenyl sulfoxide (Ph$_2$SO)-triflic anhydride (Tf$_2$O) couple and the subsequent addition of selenogalactoside 16 led to a complex reaction mixture. We therefore switched to a chemoselective approach in which imidate donor 15 was paired with 16. This led to the desired disaccharide in good yield but with poor stereoselectivity. Even though we employed diethyl ether, a commonly employed solvent to promote the formation of cis-glycosidc linkages, the β-linked disaccharide was predominantly formed ($\alpha$/β = 1 : 3). Using dibenzyl acceptor 19 instead of 16, and changing the solvent to dichloromethane significantly improved the stereoselectivity of the reaction and disaccharide 24 was obtained as a single diastereomer in 58% yield. For the crucial condensation of the disaccharide donor and the glycerol acceptor we changed the anomeric seleno group into an imidate donor (24 to 26) to stay close to the condensation condition devised by Mong and co-workers. Gratifyingly, we found that condensation of the disaccharide imidate donor 26 with glycerol acceptor 21 under the agency of a catalytic amount of triflic acid (TfOH) in the presence of acetonitrile and propionitrile provided the target glycerol-disaccharide 10 as a single diastereoisomer in 90% yield.

In the alternative route towards the glycerol-disaccharide building block donor 18 was coupled to glycerol acceptor 21 using the aforementioned conditions to provide 27 with good stereoselectivity ($\alpha$/β = 1 : 19) and in good yield (Scheme 2). To unmask the C-3-napthyl ether we subjected 27 to a catalytic amount of HCl in hexafluoro-iso-propanol (HFIP), which produced galactosazide 28 in 63%. When DDQ was used in a biphasic DCM/H$_2$O
solvent system, the primary benzyl ether on the glycerol moiety was also partly cleaved. This side reaction could be circumvented by executing the oxidative cleavage in a phosphate buffer\textsuperscript{26} at pH=7.4 to yield glycerol-galactoside acceptor \textsuperscript{28} in 75% yield. To complete the assembly of the glycerol-disaccharide intermediate, donor \textsuperscript{15} was coupled to alcohol \textsuperscript{28} to provide the key building block \textsuperscript{10} as a single anomer in 88%.

Overall, both assembly routes feature highly stereoselective glycosylation reactions and both deliver the target glycerol-disaccharide in similar yields (Scheme 2). Because the first route allows the introduction of both glycerol epimers from a single far-advanced synthon we proceeded with this route to provide the diastereomeric glycerol-disaccharide \textsuperscript{11}. To this end donor \textsuperscript{26} and glycerol \textsuperscript{23} were united using the acetonitrile/propionitrile glycosylation conditions to provide glycerol-disaccharide \textsuperscript{11} in good yield and stereoselectivity.

Scheme 2. Glycerol-disaccharide building block synthesis.

Reagents and conditions: a) TfOH, DCM, 0°C, 58%; b) NIS, THF/H\textsubscript{2}O; c) CF\textsubscript{3}(=NPh)Cl, K\textsubscript{2}CO\textsubscript{3}, acetone, quant over 2 steps; d) \textsuperscript{21} or \textsuperscript{23}, TfOH, MeCN/EtCN/DCM, -40°C, \textsuperscript{10}90% \textsuperscript{11}:80%; e) TfOH, MeCN/EtCN/DCM, -40°C, 90%; f) DDQ, phosphate buffer, DCM, 75%; g) \textsuperscript{15}, TfOH, DCM, 0°C, 88%; h) PMe\textsubscript{3}, dioxane/H\textsubscript{2}O; i) Ac\textsubscript{2}O, NEt\textsubscript{3}, DCM, \textsuperscript{29}:59% over 2 steps, \textsuperscript{30}:76% over 2 steps; j) TBAF, THF, \textsuperscript{31}:77%, \textsuperscript{32}:89%; k) DMTrCl, NEt\textsubscript{3}, DCM, \textsuperscript{33}:89%, \textsuperscript{34}:86%; l) L.\textsubscript{Ir}(COD)(Ph\textsubscript{3}MeP)\textsubscript{2}, THF; \textsuperscript{2}NaHCO\textsubscript{3}, I\textsubscript{2}, H\textsubscript{2}O/THF, \textsuperscript{35}:70%, \textsuperscript{36}:80%; m) di-isopropylethylamine, N,N-di-isopropylamino-2-cyanoethyl-chlorophosphite, DCM, \textsuperscript{7}: 85% \textsuperscript{8}:62%.
To convert 10 and 11 into the necessary phosphoramidite building blocks 7 and 8 we transformed the azide functionalities using a Staudinger reduction and subsequent N-acetylation provided 29 and 30. Removal of the silyl ether in 29 and 30 was followed by installation of the dimethoxytrityl group to set the stage for the final de-allylation (Scheme 2). To this end we employed Ir(COD)(Ph2MeP)2, briefly activated with hydrogen gas, to isomerize the allyl ether into the enol ether and I2 in combination with aqueous NaHCO3 to unmask the alcohol. These mild conditions do not affect the acid labile dimethoxytrityl ether. Following this sequence of reactions glycerol-disaccharide 35 and epimeric glycerol-disaccharide 36 were obtained in 50% and 60% yield over 3 steps from 29 and 30, respectively. Finally, the alcohols were transformed into phosphoramidites 7 and 8.

With the building blocks in hand, we turned to the assembly of the oligomers. To this end we first coupled the phosphoramidite functionalized spacer 911 with alcohols 35 and 36 (Scheme 3) using dicyanoimidazole as an activator. Subsequently we oxidized the intermediate phosphite to the phosphotriester and unmasked the labile dimethoxytrityl ether with trichloroacetic acid (TCA). Because we found that the use of pyridine/H2O in combination with I2 for the oxidation of the phosphite intermediate led to partial removal of the cyanoethyl group, we employed the (10-camphorsulfonyl)oxaziridine (CSO) oxidation method27,28 to yield spacer-coupled products 37 and 40 in 72% and 80% yield.

Elongation of these molecules with phosphoramidites 7 and 8, gave the protected spacer functionalized dimers 38 and 41. Because we could not separate the target products from the
used excess of phosphoramidite by size exclusion chromatography or conventional flash column chromatography we used reversed phase automated flash column chromatography (20% – 100% MeOH in H2O) to purify dimers 38 and 41. These were obtained in 62% and 64%, respectively. The trimers 39 and 42 were obtained in a similar fashion and isolated in 69% and 67% yield.

The fully protected compounds were deprotected by a treatment with concentrated ammonia and dioxane to remove the cyanoethyl protecting groups from the phosphotriesters followed by a hydrogenation of the so-formed phosphodiesters (Scheme 4). To this end the oligomers were treated with H2 using palladium black as the catalyst in a mixture of water/dioxane under slightly acidic conditions. Progress of the reactions was monitored by NMR spectroscopy. If the crude reaction mixtures still contained aromatic functionalities the products were resubjected to the deprotection conditions. Final purification of the fully deprotected oligomers was affected by HW-40 gel filtration, after which the compounds were transformed into the sodium salts.

Scheme 4. Deprotection of the oligomers
Reagents and conditions: a) NH3(conc), dioxane; b) Pd(0), H2, AcOH, H2O, 1:73%, 2:57%, 3:44%, 4:45%, 5:49%, 6:56%.

The spectra of the diastereomeric mono- di- and trimer repeats are shown in Figure 3, alongside the spectrum for the E. faecium WTA obtained from natural sources as reported by Bychowska et al.9 When the spectra are compared it becomes clear that the spectrum of the sn-3-phosphate trimer 6 resembles the spectrum of the natural compound better than the spectrum of the corresponding sn-1-phosphate 3. Especially the set of signal belonging to the β-anomeric galactosamine residues (δ = 4.65 ppm) is indicative. Also the overall shape of the multiplet between 3.6-4.1 ppm is matched better to the spectrum of the natural WTA in the
spectrum of 6 than of its diastereomer 3. Based on the similarities between the spectrum of 6 and the spectrum of the isolated WTA we tentatively assign the stereocenter in *E. faecium* WTA as *R* and the stereochemistry of the glycerol as *sn*-glycerol-3-phosphate. Of note, the biosynthesis of WTA\textsuperscript{29–31} and LTA\textsuperscript{32} use different glycerolphosphate donors. Where LTA is assembled using phosphatidyl glycerol as building block, WTA is synthesized from cytidine diphosphate glycerol. In the latter process, the glycerol (or PG) alcohol of the nascent WTA chain attacks the pyrophosphate moiety and expels cytidine monophosphate as the leaving group.\textsuperscript{33} The stereochemistry is thus defined by the CDP-glycerol building block that is used. The natural configuration of this biological synthon is *sn*-glycerol-3-phosphate, which corroborates the assignment of the stereocenter using the NMR data presented above.

![Figure 3](image-url)

**Figure 3.** Part of the NMR spectra (solvent D\textsubscript{2}O) of WTA fragments 1-6 and WTA isolated from *E. faecalis*. (A) *sn*-glycerol-1-phosphate tri-, di- and monomer, (B) natural WTA, (C) *sn*-glycerol-3-phosphate tri-, di- and monomer. The triplet signal at $\delta = 2.95$ ppm is the resonance of the spacer’s CH\textsubscript{2}-NH\textsubscript{2} moiety.

**Conclusion**

In conclusion, we have assembled three *E. faecalis* WTA fragments alongside their three glycerol epimers. The fragments were built using a synthetic strategy that relied on the use of DMT-phosphoramidite based building blocks. The repeating unit building block, that featured both an $\alpha$- and a $\beta$-linked GalNAc moiety was assembled using galactosazide donors with excellent stereoselectivity. Based on the NMR spectra of the assembled structures and
biosynthesis arguments we assign the stereochemistry of the glycerol moiety in *E. faecium* WTA as *sn*-glycerol-3-phosphate. The synthesized structures will be evaluated in immunological assays in which they will be probed as synthetic antigens. Discovery of a potent antigen will pave the way to use the structures in (semi)-synthetic vaccine modalities.

**Experimental**

**General**

All chemicals (Acros, Fluka, Merck, Sigma-Aldrich, etc.) were used as received and reactions were carried out dry, under an argon atmosphere, at ambient temperature, unless stated otherwise. Column chromatography was performed on Screening Devices silica gel 60 (0.040-0.063 mm). TLC analysis was conducted on HPTLC aluminium sheets (Merck, silica gel 60, F245). Compounds were visualized by UV absorption (245 nm), by spraying with 20% H$_2$SO$_4$ in ethanol or with a solution of (NH$_4$)$_6$Mo$_7$O$_24·4$H$_2$O 25 g/l and (NH$_4$)$_4$Ce(SO$_4$)$_4·2$H$_2$O 10 g/l, in 10% aqueous H$_2$SO$_4$ followed by charring at +/- 140 ºC. Some unsaturated compounds were visualized by spraying with a solution of KMnO$_4$ (2%) and K$_2$CO$_3$ (1%) in water. Optical rotation measurements ([α]$_D^{20}$) were performed on a Propol automated polarimeter (Sodium D-line, λ = 589 nm) with a concentration of 10 mg/ml (c = 1), unless stated otherwise. Infrared spectra were recorded on a Shimadzu FT-IR 8300. $^1$H, $^{13}$C and $^{31}$P NMR spectra were recorded with a Bruker AV 400 (400, 101 and 162 MHz respectively), a Bruker AV 500 (500 and 202 MHz respectively) or a Bruker DMX 600 (600 and 151 MHz respectively). NMR spectra were recorded in CDCl$_3$ with chemical shift (δ) relative to tetramethylsilane, unless stated otherwise. High resolution mass spectra were recorded by direct injection (2 µl of a 2 µM solution in water/acetonitrile; 50/50; v/v and 0.1 % formic acid) on a mass spectrometer (Thermo Finnigan LTQ Orbitrap) equipped with an electrospray ion source in positive mode (source voltage 3.5 kV, sheath gas flow 10, capillary temperature 250 ºC) with resolution R = 60000 at m/z 400 (mass range m/z = 150-2000) and dioctylphthalate (m/z = 391.28428) as a lock mass. The high resolution mass spectrometer was calibrated prior to measurements with a calibration mixture (Thermo Finnigan).

**Experimental procedures**

**General procedure for phosphoramidite coupling**

The alcohol was coevaporated with acetonitrile four times, DCI (0.25M in MeCN) (1.5-3 eq), acetonitrile (0.06 M) and 3Å molsieves were added and the mixture was stirred for 15 minutes under an argon atmosphere. The phosphoramidite (1.5-3 eq) was added and the reaction was stirred for 1-4 h at RT. CSO (0.5M in MeCN) (1.5-3 eq) was added and the reaction was
stirred for 5 minutes. The mixture was diluted with EtOAc, washed with brine, dried over Na$_2$SO$_4$ and concentrated *in vacuo*. The residue was taken up in DCM (0.03 M). TCA (3% in DCM) (5 eq) was added and the mixture was stirred for 20 min. H$_2$O was added and the mixture was stirred for 15 minutes. The reaction mixture was diluted with DCM and was washed with a mixture of sat. aq. NaHCO$_3$ and brine (1/1 v/v). The aqueous layer was extracted with DCM and the combined organic layers were dried over Na$_2$SO$_4$ and concentrated *in vacuo.*

**General procedure for global deprotection**

The oligomer was dissolved in a mixture of ammonia (conc.) and dioxane (2 mM, 1/1 v/v). The mixture was stirred for 1h and was concentrated *in vacuo* yielding the phosphodiester intermediate. The residue was flushed over a Dowex Na$^+$ cation-exchange resin (type: 50WX4-200, stored on 0.5 M NaOH in H$_2$O, flushed with H$_2$O and MeOH before use) column to end up in a mixture of water and dioxane (2 mM, 2/1 v/v). ~0.1ml AcOH was added and the mixture was purged of oxygen. Pd-black (~20 mg) was added and subsequently, the reaction mixture was treated with Hydrogen gas for 3 days. Celite was added to the mixture and after short sonication (20-30 sec) the mixture was filtered over celite and Chelex 100 resin and concentrated *in vacuo* The residue was purified by size-exclusion chromatography (HW40, dimensions: 16/60 mm, eluent: 0.15 M NH$_4$OAc). After repeated lyophilization, the product was eluted through a small column containing Dowex Na$^+$ cation-exchange resin (type: 50WX4-200, stored on 0.5 M NaOH in H$_2$O, flushed with H$_2$O and MeOH before use).

**Phenyl 2-azido-3,4-di-O-benzyl-2-deoxy-1-seleno-6-O-(tert-butyl-di-phenylsilyl)-α-D-galactopyranoside (14)**

To a cooled (0°C) solution of 13 (4.7 g, 13.5 mmol) in DMF (50 ml) imidazole (1.4 g, 20.3 mmol) and TBDPSCl (3.7 ml, 14 mmol) were added. After stirring for 10 minutes, TLC analysis showed complete conversion of the starting material. H$_2$O was added and the mixture was diluted with Et$_2$O. The organic layer was washed with H$_2$O (5x), brine, dried over MgSO$_4$, filtered and concentrated *in vacuo*. Column chromatography yielded intermediate 2-azido-2-deoxy-1-seleno-6-O-(tert-butyl-di-phenylsilyl)-α-D-galacto-pyranoside (7.03 g, 12.1 mmol) in 90% yield. TLC: R$_f$ 0.8 (30% EtOAc/pentane); [α]$_D^{20}$ (CHCl$_3$, c 1): +172; IR (neat, cm$^{-1}$): 3432, 2929, 2889, 2110, 1113, 1055, 738, 702; $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.42 – 7.15 (m, 15H), 5.96 (d, $J$ = 5.2 Hz, 1H), 4.26 – 4.23 (m, 2H), 4.16 – 4.13 (m, 1H), 3.89 – 3.87 (m, 2H), 3.78 – 3.74 (m, 1H), 1.05 (s, 9H); $^{13}$C NMR (101 MHz, CDCl$_3$): δ = 135.7,
To a cooled (0°C) solution of the intermediate (6.1 g, 10.5 mmol) and BnBr (3.1 ml, 26.3 mmol) in DMF (70 ml) NaH (60% disp.) (1.1 g, 26.3 mmol) was added in portions over 20 minutes. The mixture was allowed to warm up to RT while stirring overnight. The mixture was cooled to 0°C and H₂O was added. The mixture was diluted with Et₂O, the organic layer was washed with H₂O (5x) and brine, dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded compound 14 (8.0 g, 10.5 mmol) in >98% yield. TLC: Rf 0.9 (20% EtOAc/pentane); [α]D²⁰ (CHCl₃, c 1): +131.6; IR (neat, cm⁻¹): 3066, 2929, 2856, 2110, 1103, 1062, 738, 700; ¹H NMR (400 MHz, CDCl₃): δ = 7.41 – 7.05 (m, 25H), 5.82 (d, J = 5.2 Hz, 1H), 4.92 (d, J = 11.2 Hz, 1H), 4.78 (q, J = 11.6 Hz, 2H), 4.59 (d, J = 11.2 Hz, 1H), 4.34 (dd, J = 5.2 Hz, 10.2 Hz, 1H), 4.23 (t, J = 7.6 Hz, 1H), 4.10 (s, 1H), 3.85 – 3.80 (m, 1H), 3.72 (dd, J = 2.4 Hz, 10.2 Hz, 1H), 3.58 – 3.54 (m, 1H), 1.05 (s, 9H); ¹³C NMR (101 MHz, CDCl₃): δ = 138.4, 137.6, 135.6, 135.1, 133.2, 133.1, 130.0, 129.9, 129.1, 128.7, 128.4, 128.2, 128.1, 127.9, 127.8, 85.7, 80.4, 75.2, 73.3, 73.2, 72.7, 61.7, 61.2, 27.0; HRMS: [C₄₂H₄₅N₃O₄SeSi + Na] requires 786.22411, found 786.22388.

2-azido-3,4-di-O-benzyl-2-deoxy-1-O-(N-phenyl-trifluoroacetimidoyl) -6-O-(tert-butyl-diphenylsilyl)-α/β-D-galactopyranoside (15)

To a cooled (0°C) solution of 14 (7.3 g, 9.5 mmol) in a mixture of H₂O/THF (1:1 v/v, 85 ml) NIS (2.4 g, 10.5 mmol) was added. The reaction was allowed to warm up towards RT and was stirred for 1h. The reaction mixture was diluted with EtOAc, the organic layer was washed with H₂O, brine, dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded intermediate 2-azido-3,4-di-O-benzyl-2-deoxy -6-O-(tert-butyl-diphenylsilyl)-α/β-D-galactopyranose (5.1 g, 8.3 mmol) in 87% yield. TLC: Rf 0.3 (10% EtOAc/pentane); IR (neat, cm⁻¹): 3389, 2956, 2929, 2856, 2110, 1112, 1060, 738, 700; ¹H NMR (400 MHz, CDCl₃): δ = 7.62 – 7.14 (m, 45H), 5.18 (d, J = 3.2 Hz, 1H), 4.93 – 4.90 (m, 2H), 4.74 – 4.54 (m, 6H), 4.34 (d, J = 8 Hz, 1H), 4.11 – 4.01 (m, 2H), 3.99 – 3.81 (m, 4H), 3.75 – 3.29 (m, 2H), 1.05 (s, 16H); ¹³C NMR (101 MHz, CDCl₃): δ = 138.5, 138.4, 137.7, 127.6, 135.6, 135.5, 133.2, 133.0, 129.9, 129.8, 129.1, 128.6, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 96.5, 92.4, 80.7, 77.2, 74.9, 74.8, 73.6, 72.6, 72.4, 70.8, 64.9, 61.1, 61.8, 60.4, 26.9; HRMS: [C₃₆H₄₈N₃O₅SeSi + Na] requires 646.27077, found 646.27081. To a stirred solution of the intermediate (0.31 g, 0.5 mmol) in acetone (5 ml) K₂CO₃ (82 mg, 0.6 mmol) and N-phenyl trifluoroacetimidoyl chloride (0.12 ml, 0.75 mmol) were added. After stirring for 2 days at RT
the reaction mixture was diluted with EtOAc and H₂O. The organic layer was washed with brine (2x), dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded compound 15 (0.4 g, 0.5 mmol) in >98% yield. TLC: Rf 0.8 (10% EtOAc/pentane); IR (neat, cm⁻¹): 2953, 2858, 2113, 1716, 1209, 1163, 1112, 738, 696; ¹H NMR (400 MHz, CDCl₃): δ = 7.63 – 6.74 (m, 43H), 6.25 (s, 1H), 5.49 (s, 0.7H), 4.92 – 4.87 (m, 2H), 4.80 – 4.69 (m, 4H), 4.59 – 4.55 (m, 2H), 4.07 – 4.04 (m, 1H), 4.01 – 3.99 (m, 1H), 3.96 – 3.93 (m, 1H), 3.89 – 3.87 (m, 3H), 3.82 – 3.72 (m, 4H), 3.38 – 3.35 (m, 2H), 1.04 (s, 15H); ¹³C NMR (101 MHz, CDCl₃): δ = 143.6, 143.5, 138.5, 137.6, 135.7, 133.5, 133.4, 130.0, 129.9, 129.4, 128.8, 128.7, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.4, 124.5, 120.8, 119.7, 119.6, 96.4, 95.1, 81.1, 77.8, 76.4, 75.1, 75.0, 74.1, 73.5, 73.1, 72.9, 72.7, 62.7, 62.5, 62.4, 59.6, 27.1; HRMS: [C₄₄H₄₅F₃N₄O₅Si + Na⁺] requires 817.30035, found 817.30042.

Phenyl 2-azido-4,6-O-silylidene-2-deoxy-1-seleno-α-D-galactopyranoside (16)

To a cooled (−40°C) solution of 13 (0.17 g, 0.5 mmol) in dry DMF (2 ml) di-tert-butylsilyl bis(trifluoromethanesulphonate) (0.17 ml, 0.5 mmol) was added. The mixture was stirred for 10 minutes, pyridine (0.12 ml, 1.5 mmol) was added and the mixture was stirred for 20 additional minutes at −40°C. Et₂O and H₂O were added and the organic layer was washed with H₂O (5x) and brine (2x). The aqueous layers were extracted with Et₂O, and the combined organic layers were dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded compound 16 (0.24 g, 0.49 mmol) in 97% yield. TLC: Rf 0.7 (10% EtOAc/pentane); [α]D²⁰ (CHCl₃): +196; ¹H NMR (400 MHz, CDCl₃): δ = 7.56 – 7.53 (m, 2H), 7.29 – 7.25 (m, 3H), 5.93 (m, J = 5.2 Hz, 1H), 4.48 – 4.47 (m, 1H), 4.30 – 4.26 (m, 1H), 4.18 (s, 1H), 4.04 – 4.00 (m, 2H), 3.81 – 3.77 (m, 1H), 2.81 (d, J = 10.4 Hz, 1H), 1.06 (s, 9H), 1.03 (s, 9H); ¹³C NMR (101 MHz, CDCl₃): δ = 134.4, 134.0, 129.2, 128.4, 127.9, 85.4, 72.3, 71.8, 69.8, 66.7, 62.1, 27.6, 27.3; HRMS: [C₂₀H₃₁N₃O₄SeSi + NH₄] requires 501.15983, found 501.15244.

Phenyl 2-azido-4,6-di-O-benzyl-2-deoxy-3-O-naphthylmethyl-1-seleno-α-D-galactopyranoside (17)

To a cooled (0°C) solution of 16 (0.24 g, 0.49 mmol) in DMF (2 ml) naphthyl bromide (0.12 g, 0.54 mmol) and NaH (60% disp.) (0.03 g, 0.68 mmol) were added. After stirring for 2h, H₂O and Et₂O were added, the organic layer was washed with H₂O (5x) and brine, dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded naphthylated intermediate 2-azido-4,6-silylidene-2-deoxy-3-O-naphthyl-1-seleno-α-D-galactopyranoside (0.35 g, 0.22 mmol) in 71% yield. TLC: Rf 0.82 (10% EtOAc/pentane); [α]D²⁰ (CHCl₃): +154; IR (neat, cm⁻¹): 3055, 2931, 2856, 2112, 1473, 1080, 823, 731, 690; ¹H NMR (400 MHz,
CDCl₃: δ = 7.89 – 7.78 (m, 4H), 7.56 – 7.32 (m, 3H), 7.48 – 7.46 (m, 2H), 7.27 – 7.22 (m, 4H), 5.95 (d, J = 5.2 Hz, 1H), 4.78 (q, J = 11.6 Hz, 2H), 4.59 – 4.57 (m, 1H), 4.35 (dd, J = 5.2 Hz, 10 Hz, 1H), 4.21 – 4.18 (m, 1H), 4.01, 3.96 (m, 2H), 3.68 (dd, J = 2.8 Hz, 10.2 Hz, 1H), 1.06 (s, 9H), 1.04 (s, 9H); ¹³C NMR (101 MHz, CDCl₃): δ = 135.2, 134.5, 133.4, 133.2, 129.4, 129.2, 128.6, 128.5, 128.3, 128.0, 127.9, 127.8, 126.7, 126.4, 126.3, 126.1, 125.9, 125.6, 85.9, 78.8, 71.0, 70.5, 70.3, 67.0, 59.8, 28.0, 27.4; HRMS: [C₃₁H₃₉N₃O₄SeSi + Na] requires 648.17697, found 648.17651. To a stirred solution of the intermediate (0.22 g, 0.35 mmol) in THF (7 ml) was added Et₃N●3HF (0.17 ml, 1.05 mmol). The mixture was stirred for 2h at RT, after which the reaction was diluted with EtOAc and washed with H₂O (1x). The aqueous layer was extracted with EtOAc (2x), and the combined organic layers were dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded intermediate diol 2-azido-2-deoxy-3-O-naphthyl-α-D-galactopyranoside (0.16 g, 0.33 mmol) in 94% yield. TLC: R₂f 0.4 (40% EtOAc/pentane); [α]D²⁰ (CHCl₃, c 1): +228; IR (neat, cm⁻¹): 3419, 2885, 2885, 2108, 1740, 1670, 1640, 1590, 1450, 1380, 1290, 1270, 1160; ¹H NMR (400 MHz, CDCl₃): δ = 7.78 – 6.99 (m, 13H), 5.90 (d, J = 5.2 Hz, 1H), 4.86 – 4.78 (m, 2H), 4.21 (dd, J = 5.2 Hz, 10 Hz, 1H), 4.16 – 4.13 (m, 1H), 4.12 – 4.02 (m, 1H), 3.82 – 3.76 (m, 1H), 3.71 – 3.65 (m, 1H), 2.98 (s, 1H), 2.18 (s, 1H); ¹³C NMR (101 MHz, CDCl₃): δ = 134.4, 133.3, 133.2, 133.1, 129.3, 128.7, 128.2, 128.1, 127.9, 127.1, 126.5, 126.5, 125.7, 84.7, 78.8, 72.3, 72.2, 67.2, 62.8, 60.3; HRMS: [C₂₃H₂₃N₃O₄Se + Na] requires 508.07474, found 508.07443. To a cooled (0°C) solution of the intermediate (1.4 g, 3.4 mmol) and BnBr (1.0 ml, 8.5 mmol) in DMF (23 ml) NaH (60% disp.) (0.34 g, 8.5 mmol) was added. After stirring overnight, H₂O was added at 0°C and the mixture was diluted with Et₂O. The organic layer was washed with H₂O (2x) and brine, dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded compound 17 (1.67 g, 2.8 mmol) in 83% yield. TLC: R₂f 0.8 (10% EtOAc/pentane); [α]D²⁰ (CHCl₃, c 1): +172; IR (neat, cm⁻¹): 3057, 3030, 2908, 2866, 2108, 1099, 1066, 817, 738, 696; ¹H NMR (400 MHz, CDCl₃): δ = 7.86 – 7.15 (m, 23H), 5.94 (d, J = 5.2 Hz, 1H), 4.97 – 4.55 (m, 4H), 4.43 – 4.36 (m, 4H), 4.08 – 4.07 (m, 1H), 4.77 (dd, J = 2.4 Hz, 10.6 Hz, 1H), 3.63 – 3.58 (m, 1H), 3.47 – 3.41 (m, 1H); ¹³C NMR (101 MHz, CDCl₃): 138.3, 137.9, 135.0, 134.8, 133.4, 133.2, 129.1, 128.5, 128.4, 128.1, 127.9, 127.7, 126.6, 126.3, 126.2, 125.7, 85.5, 80.3, 75.0, 73.5, 73.2, 72.5, 72.0, 68.4, 61.2; HRMS: [C₃₇H₃₅N₃O₄Se + Na] requires 688.16883, found 688.16858.

2-azido-4,6-di-O-benzyl-2-deoxy-3-O-naphthylmethyl-1-O-(N-phenyl-trifluoroacetimidoyl)-α/β-D-galactopyranoside (18)
To a cooled (0°C) solution of 17 (0.84 g, 1.4 mmol) in a mixture of THF/H₂O (14 ml, 1/1, v/v) NIS (0.35 g, 1.54 mmol) was added. The reaction was allowed to warm up to RT and stirred overnight. The mixture was diluted with EtOAc, washed with Na₂S₂O₃ (10% solution in H₂O), H₂O, brine, dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded intermediate 2-azido-4,6-di-O-benzyl-2-deoxy-3-O-napthyl-α/β-D-galactopyranose (0.64 g, 1.4 mmol) in >98% yield. TLC: Rf 0.4 (30% EtOAc/pentane); IR (neat, cm⁻¹): 3389, 3059, 2916, 2868, 2108, 1096, 1059, 818, 746, 696; ¹H NMR (400 MHz, CDCl₃): δ = 7.80 – 7.01 (m, 29H), 5.28 (d, J = 2.8 Hz, 1H), 4.87 – 4.30 (m, 10H), 4.15 – 4.12 (m, 1H), 3.99 – 3.82 (m, 4H), 3.77 – 3.76 (m, 1H), 3.56 – 3.52 (m, 1H), 3.28 – 3.25 (m, 1H); ¹³C NMR (101 MHz, CDCl₃): δ = 138.0, 137.9, 137.4, 137.1, 135.0, 134.9, 133.2, 133.1, 132.9, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.3, 126.8, 126.4, 126.3, 126.1, 126.0, 125.9, 125.6, 96.2, 92.1, 80.6, 77.2, 74.5, 73.5, 73.4, 73.3, 73.2, 72.3, 72.2, 72.1, 69.3, 69.2, 68.5, 64.3, 60.2; HRMS: [C₃₁H₃₁N₃O₅ + Na] requires 548.21559, found 548.21535. To a stirred solution of the intermediate (0.31 g, 0.5 mmol) in acetone (5 ml) K₂CO₃ (0.082 g, 0.6 mmol) and N-phenyl trifluoroacetimidoyl chloride (0.12 ml, 0.75 mmol) were added. After stirring for 4 days at RT, MgSO₄ was added, the mixture was filtered and concentrated in vacuo. Column chromatography yielded imidate 18 (0.32 g, 0.4 mmol) in 80% yield. TLC: Rf 0.75 (10% EtOAc/pentane); IR (neat, cm⁻¹): 3061, 3030, 2918, 2886, 2113, 1716, 1209, 1161, 1112, 736, 696; ¹H NMR (400 MHz, CDCl₃): δ = 7.84 – 7.90 (m, 10H), 7.51 – 7.46 (m, 8H), 7.31 -7.21 (m, 28H), 7.08 – 7.03 (m, 3H), 6.81 – 6.79 (m, 4H), 6.32 (s, 1H), 5.42 (d, J = 7.2 Hz, 1H), 4.93 – 4.84 (m, 6H), 4.62 – 4.40 (m, 6H), 4.17 – 4.00 (m, 5H), 3.94 – 3.93 (m, 1H), 3.68 – 3.36 (m, 6H); ¹³C NMR (101 MHz, CDCl₃): δ = 135.4, 133.6, 129.4, 129.1, 128.8, 128.4, 128.0, 127.8, 127.0, 126.5, 126.1, 124.7, 124.4 119.8, 119.5, 96.4, 96.1, 81.1, 77.9, 75.2, 75.1, 75.0, 73.9, 73.8, 73.6, 73.1, 72.9, 72.6, 62.7, 59.8 ; HRMS: [C₃₉H₃₅F₃N₄O₅ + Na] requires 719.24518, found 719.24518.

Phenyl 2-azido-4,6-di-O-benzyl-2-deoxy-1-seleno-α-D-galactopyranoside (19)

To a stirred solution of 17 (0.71 g, 1.2 mmol) in a mixture of DCM/H₂O (14 ml, 4/1, v/v), DDQ (0.63 g, 2.8 mmol) was added. The mixture was stirred for 2h, after which TLC analysis showed conversion of the starting material and formation of a lower running byproduct. Na₂S₂O₃ (10% solution in H₂O) was added, the mixture was diluted with DCM and the layers were separated. The organic layer was washed with sat. aq. NaHCO₃ (2x), dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded compound 19 (0.49 g, 0.94 mmol) in 78% yield. TLC: Rf 0.61 (20% EtOAc/pentane); [α]D²⁰ (CHCl₃, c 1): +174; IR (neat,
\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{)}: \delta = 7.30 - 6.79 (m, 15H), 5.90 (d, J = 5.2 Hz, 1H), 4.71 - 4.59 (m, 2H), 4.52 - 4.40 (m, 3H), 4.04 (dd, J = 5.2 Hz, 10.4 Hz, 1H), 3.89 - 3.88 (m, 1H), 3.76 - 3.70 (m, 1H), 3.67 - 3.62 (m, 1H), 3.51 - 3.45 (m, 1H), 2.52 (s, 1H); ^13\text{C NMR (101 MHz, CDCl}_3\text{)}: \delta = 137.9, 137.7, 134.7, 134.3, 129.3, 129.1, 128.6, 128.5, 128.5, 128.2, 128.1, 128.0, 127.9, 127.8, 125.3, 85.2, 76.1, 75.4, 73.4, 68.3, 68.1, 62.6 ; \text{HRMS: [C}_{26}\text{H}_{27}\text{N}_3\text{O}_4\text{Se + Na] requires 548.10607, found 548.10583.} \]

\[ ^1\text{-O-allyl-3-O-benzyl-sn-glycerol (21)} \]

**Bimetallic catalysis:** To a stirred solution of 20 (0.09 g, 0.5 mmol), DPPB (0.05 g, 0.13 mmol), Pd(OAc)\(_2\) (0.011 g, 0.05 mmol), Me\(_2\)SnCl\(_2\) (0.011 g, 0.05 mmol), and Cs\(_2\)CO\(_3\) (0.24 g, 0.75 mmol) in DCM (3 ml), allylacetate (0.16 ml, 1.5 mmol) was added. After stirring overnight at RT, H\(_2\)O was added and the mixture was extracted with EtOAc. The organic layer was washed with H\(_2\)O (2x), brine, dried over MgSO\(_4\) and concentrated \textit{in vacuo}. The residue was purified by column chromatography, yielding compound 21 (0.09 g, 0.42 mmol) in 84% yield.

**Tin ketal:** A mixture of 20 (0.09 g, 0.5 mmol) and dibutyltinoxide (0.12 g, 0.5 mmol) was refluxed in toluene (10 ml) for 3h. The mixture was concentrated \textit{in vacuo}, taken up in DMF (3 ml) and CsF (0.11 g, 0.725 mmol) and allylbromide (0.056 ml, 0.65 mmol) were added. The reaction was stirred for 1h, and refluxed for 1h, after which TLC analysis indicated complete conversion of the starting material. The mixture was concentrated \textit{in vacuo}, taken up in EtOAc, dried over MgSO\(_4\) and concentrated \textit{in vacuo}. The residue was purified by column chromatography, yielding compound 21 (0.073 g, 0.33 mmol) in 66% yield.

**Borinate catalysis:** To a stirred solution of 20 (0.09 g, 0.5 mmol), 2-aminooethyl diphenylborinate (0.011 g, 0.05 mmol), KI (0.08 g, 0.5 mmol), K\(_2\)CO\(_3\) (0.08 g, 0.55 mmol) in CH\(_3\)CN (2.5 ml) under an argon atmosphere, allyl bromide (0.065 ml, 0.75 mmol) was added, and the mixture was heated to 60°C. After stirring overnight, TLC analysis indicated complete conversion of the starting material. The mixture was diluted with EtOAc, washed with H\(_2\)O (2x), brine, dried over MgSO\(_4\) and concentrated \textit{in vacuo}. The residue was purified by column chromatography, yielding compound 21 (0.073 g, 0.33 mmol) in 66% yield. TLC: R\(_f\) 0.6 (50% EtOAc/pentane); ^1\text{H NMR (400 MHz, CDCl}_3\text{)}: \delta = 7.35 - 7.24 (m, 5H), 5.89 (ddd, J = 22.5 Hz, 10.8 Hz, 5.6 Hz, 1H), 5.27 - 5.15 (m, 2H), 4.53 (s, 2H), 3.94 (d, J = 5.6 Hz, 3H), 3.55 - 3.43 (m, 4H), 2.89 (s, 1H, OH); ^13\text{C NMR (101 MHz, CDCl}_3\text{)}: \delta = 138.0, 134.5, 128.4, 127.7, 117.2, 73.4, 72.3, 71.4, 71.3, 69.5.
3-O-allyl-1-O-benzyl-sn-glycerol (23)

To a stirred solution of 22 (1.8 g, 9.9 mmol), 2-aminoethyl diphenylborinate (0.22 g, 0.99 mmol), KI (1.64 g, 9.9 mmol), K₂CO₃ (1.5 g, 10.9 mmol) in CH₃CN (50 ml) under an argon atmosphere, allyl bromide (1.3 ml, 14.8 mmol) was added, and the mixture was heated to 60°C. After stirring overnight, TLC analysis indicated complete conversion of the starting material. The mixture was diluted with EtOAc, washed with H₂O (2x), brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography, yielding compound 23 (1.4 g, 6.1 mmol) in 62% yield. TLC: Rf 0.6 (50% EtOAc/pentane); ¹H NMR (400 MHz, CDCl₃): δ = 7.35 – 7.24 (m, 5H), 5.89 (ddd, J = 22.5 Hz, 10.8 Hz, 5.6 Hz, 1H), 5.27 – 5.15 (m, 2H), 4.53 (s, 2H), 3.94 (d, J = 5.6 Hz, 3H), 3.55 – 3.43 (m, 4H), 2.89 (s, 1H, OH); ¹³C NMR (101 MHz, CDCl₃): δ = 138.0, 134.5, 128.4, 127.7, 117.2, 73.4, 72.3, 71.4, 71.3, 69.5.

Phenyl 3-O-(2-azido-3,4-O-di-benzyl-2-deoxy-6-O-(tert-butyldi-phenylsilyl)-α-D-galactopyranosyl)-2-azido-4,6-O-di-benzyl-2-deoxy-1-seleno-α-D-galactopyranoside (24)

Donor 15 (6.86 g, 8.6 mmol) and acceptor 19 (5.43 g, 10.4 mmol) were coevaporated with toluene (2x) and dissolved in DCM (85 ml). Molecular sieves (3Å) were added and the mixture was stirred at 0°C for 10 minutes. TfOH (0.15 ml, 1.7 mmol) was added and the mixture was stirred for 30 minutes. After addition of NEt₃, DCM was added and the organic layer was washed with H₂O, brine, was dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded compound 24 (5.7 g, 5.0 mmol) in 58% yield as a single anomer. TLC: Rf 0.4 (10% EtOAc/pentane); [α]D²⁰ (CHCl₃, c 1): +102; IR (neat, cm⁻¹): 2927, 2856, 2110, 1726, 1112, 1051, 738, 700; ¹H NMR (400 MHz, CDCl₃): δ = 7.68 – 7.15 (m, 35H), 5.98 (d, J = 5.2 Hz, 1H), 5.20 (d, J = 3.6 Hz, 1H), 5.05 – 4.73 (m, 4H), 4.58 – 4.52 (m, 2H), 4.44 – 4.41 (m, 1H), 4.37 (s, 2H), 4.31 – 4.72 (m, 1H), 4.22 – 4.15 (m, 3H), 4.08 – 4.00 (m, 2H), 3.95 – 3.90 (m, 2H), 3.87 – 3.81 (m, 2H), 3.60 – 3.56 (m, 1H), 3.38 – 3.32 (m, 1H), 1.10 (s, 9H); ¹³C NMR (101 MHz, CDCl₃): δ = 138.5, 138.3, 137.8, 137.6, 135.6, 135.0, 134.9, 133.4, 133.0, 131.0, 129.9, 129.1, 128.9, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5, 94.4 (C-1’), 84.5 (C- 1), 77.5, 75.2, 75.0 (C-3’), 74.9, 73.7, 73.4, 72.7, 71.7, 71.6, 68.0, 61.9, 61.0, 59.6, 27.2; HRMS: [C₆₀H₆₆N₆O₈SeSi + 2H]²⁺ requires 566.20158, found 566.19305.

3-O-(2-azido-3,4-O-di-benzyl-2-deoxy-6-O-(tert-butyldi-phenylsilyl)-α-D-galactopyranosyl)-2-azido-4,6-O-di-benzyl-2-deoxy-α/β-D-galactopyranose (25)
To a cooled (0°C) solution of 24 (0.06 g, 0.05 mmol) in THF/H2O (0.5 ml, 1/1, v/v,) was added NIS (0.012 g, 0.05 mmol). The mixture was allowed to warm up to RT and stirred 2h, after which Na2S2O3 (10% solution in H2O) was added to the reaction and it was diluted with EtOAc. The organic layer was washed with H2O (2x), brine, dried over MgSO4 and concentrated in vacuo. Column chromatography yielded compound 25 (0.05 g, 0.05 mmol) in >98% yield. TLC: Rf 0.2 (20% EtOAc/pentane); IR (neat, cm⁻¹): 3390, 3030, 2927, 2856, 2108, 1496, 1103, 1047, 1026, 734, 696; ¹H NMR (400 MHz, CDCl3): δ = 7.65 – 7.15 (m, 80H), 5.34 (d, J = 3.2 Hz, 1H), 5.13 (d, J = 3.2 Hz, 2H), 5.03 – 5.01 (m, 2H), 4.91 – 4.87 (m, 2H), 4.76 – 4.73 (m, 4H), 4.56 – 4.52 (m, 5H), 4.47 – 4.33 (m, 3H), 4.18 – 4.02 (m, 8H), 3.91 – 3.72 (m, 6H), 3.59 – 3.40 (m, 4H) 1.05 (s, 20H); ¹³C NMR (101 MHz, CDCl3): δ = 138.5, 138.4, 138.3, 138.1, 137.7, 137.5, 135.6, 133.4, 133.3, 133.1, 129.9, 129.8, 128.9, 128.7, 129.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 96.6, 95.7, 94.3, 92.3, 77.7, 77.4, 75.5, 75.1 – 74.6, 74.0, 73.7, 73.6, 73.5, 73.4, 72.7, 72.6, 71.9, 70.5, 69.6, 69.0, 62.7, 62.0, 60.3, 60.0, 59.7, 27.0; HRMS: [C₅₆H₅₆O₉Si + Na] requires 952.95447, found 952.42582.

3-O-(2-azido-3,4-O-di-benzyl-2-deoxy-6-O-(tert-butyl-di-phenylsilyl)-α-D-galactopyranosyl)-2-azido-4,6-O-di-benzyl-2-deoxy-1-O-(N-phenyl-trifluoroacetimidoyl)-α/β-D-galactopyranoside (26)

To a stirred solution of 25 (0.05 g, 0.05 mmol) in acetone (0.5 ml) was added K₂CO₃ (8 mg, 0.06 mmol) and N-phenyl trifluoroacetimidoyl chloride (0.01 ml, 0.07 mmol) were added. The reaction mixture was stirred for 3 days under a dry atmosphere at RT. The reaction mixture was dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded compound 26 (0.056 g, 0.05 mmol) in >98% yield. TLC: Rf 0.76 (20% EtOAc/pentane); IR (neat, cm⁻¹): 3311, 2954, 2924, 2854, 2112, 1714, 1207, 1151, 1112, 731, 696; ¹H NMR (400 MHz, CDCl₃): δ = 7.65 – 6.78 (m, 35H), 5.17 – 5.16 (m, 1H), 5.06 – 5.03 (m, 1H), 4.94 – 4.89 (m, 1H), 4.80 – 4.75 (m, 3H), 4.59 – 4.55 (m, 3H), 4.46 – 4.37 (m, 1H), 4.15 – 3.91 (m, 6H), 3.78 – 3.58 (m, 5H), 1.07 (s, 9H); ¹³C NMR (101 MHz, CDCl₃): δ = 138.3, 138.2, 137.6, 137.5, 135.6, 133.3, 133.1, 129.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 124.5, 119.4, 94.5, 77.53, 75.6, 75.1, 74.9 74.5, 73.6, 73.6, 72.7, 72.0, 70.4, 67.8, 62.7, 61.7, 59.7, 27.0; HRMS: [C₆₈H₆₆F₃N₇O₉Si + Na] requires 1184.45356, found 1184.45410.

2-O-(2-azido-4,6-di-O-benzyl-2-deoxy-3-O-naphthylmethyl-β-D-galactopyranosyl)-1-O-allyl-3-O-benzyl-sn-glycerol (27)
Donor 18 (1.67 g, 2.4 mmol) and acceptor 21 (0.80 g, 3.6 mmol) were coevaporated with toluene (2x) and dissolved in a mixture of acetonitrile, propionitrile and DCM (24 ml, 2:1:1 v/v/v). Molecular sieves (3Å) were added and the mixture was stirred at -40°C for 10 minutes. TfOH (45 µl, 0.5 mmol) was added and the mixture was stirred for 20 minutes. After addition of NEt₃, DCM was added and the organic layer was washed with H₂O, brine, was dried over MgSO₄ and concentrated in vacuo. Size exclusion chromatography yielded compound 27 (1.6 g, 2.2 mmol) in 90% yield (α/β = 1 : 19). TLC: Rf 0.85 (20% EtOAc/pentane); [α]D²⁰ (CHCl₃, c 1): -8; IR (neat, cm⁻¹): 3061, 2922, 2860, 2110, 1454, 1064, 817, 732, 696; ¹H NMR (400 MHz, CDCl₃): δ = 7.85 – 7.80 (m, 4H), 7.51 – 7.46 (m, 3H), 7.32 – 7.22 (m, 16H), 5.90 (ddd, J = 22.7 Hz, 10.4 Hz, 5.6 Hz, 1H), 5.29 – 5.24 (m, 1H), 5.16 – 5.13 (m, 1H), 4.93 – 4.90 (m, 1H), 4.82 (s, 2H), 4.67 – 4.37 (m, 6H), 4.06 – 4.00 (m, 3H), 3.89 – 3.84 (m, 2H), 3.71 – 3.45 (m, 7H), 3.32 (dd, J = 2.8 Hz, 10.4 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ = 139.1, 138.9, 138.1, 127.8, 133.3, 131.9, 131.7, 128.6, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 126.6, 126.3, 126.1, 125.8, 116.9, 102.7, 80.6, 78.1, 74.4, 73.6, 73.5, 73.4, 72.7, 72.5, 72.4, 71.0, 70.3, 68.6, 63.5; HRMS: [C₄₄H₄₇N₃O₇ + Na] requires 752.33062, found 752.33026.

2-O-(2-azido-4,6-di-O-benzyl-2-deoxy-β-D-galactopyranosyl)-1-O-allyl-3-O-benzyl-sn-glycerol (28)

**HCl/HFIP method:** To a stirred solution of 27 (0.46 g, 0.6 mmol) in a mixture of HFIP/DCM (7 ml, 1/1 v/v) was added a solution of HCl (3.5 ml, 0.2M, 0.7 mmol) in HFIP. The mixture was stirred for 30 min, after which TLC analysis indicated complete conversion of the starting material. The mixture was poured into sat. aq. NaHCO₃, DCM was added and the layers were separated. The organic layer was washed with sat. aq. NaHCO₃, brine, dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded compound 28 (0.21 g, 0.35 mmol) in 63% yield.

**Buffered DDQ method:** To a cooled (0°C) solution of 27 (0.42 g, 0.57 mmol) in DCM (20 ml) a phosphate buffer (2 ml, pH=7.5, 10 mM) was added. DDQ (0.41 g, 1.8 mmol) was added over 1h in small portions, after which the mixture was allowed to warm up to RT and was stirred for 30 min. The mixture was diluted with NaHCO₃ and the aqueous layer was extracted with DCM (2x). The combined organic layers were dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded compound 28 (0.25 g, 0.42 mmol) in 75% yield. TLC: Rf 0.8 (20% EtOAc/pentane); [α]D²⁰ (CHCl₃, c 1): +42; IR (neat, cm⁻¹): 3447, 2916, 2863, 2110, 1454, 1064, 910, 732, 696; ¹H NMR (400 MHz, CDCl₃): δ = 7.34 –
7.21 (m, 15H), 5.90 (ddd, \( J = 22.6 \text{ Hz}, 10.6 \text{ Hz}, 5.6 \text{ Hz}, 1 \text{H} \)), 4.71 – 4.65 (m, 2H), 4.55 – 4.41 (m, 5H), 4.13 – 3.96 (m, 3H), 3.78 (d, \( J = 3.2 \text{ Hz}, 1 \text{H} \)), 3.72 – 3.35 (m, 7H), 3.43 -3.35 (m, 1H), 2.41 (d, \( J = 7.2 \text{ Hz}, 1 \text{H} \)); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \( \delta = 138.3, 138.2, 137.7, 134.4, 128.6, 128.5, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 116.9, 102.6, 78.0, 75.2, 75.2, 73.5, 73.4, 73.3, 72.6, 71.0, 70.2, 68.3, 64.8; HRMS: [C\(_{33}\)H\(_{39}\)N\(_3\)O\(_7\) + Na] requires 612.28602, found 612.28746.

2-O-(3-O-(2-azido-3,4-O-di-benzyl-2-deoxy-6-O-(tert-butyl-di-phenylsilyl)-\( \alpha \)-D-galactopyranosyl)-2-azido-4,6-O-di-benzyl-2-deoxy-\( \beta \)-D-galactopyranosyl)-1-O-allyl-3-O-benzyl-sn-glycerol (10)

From 28: Donor 15 (0.75 g, 1.3 mmol) and acceptor 28 (1.35 g, 1.7 mmol) were coevaporated with toluene (2x) and dissolved in DCM (15 ml). Molecular sieves (3Å) were added and the mixture was stirred at 0°C for 10 minutes. TfOH (23 µl, 0.26 mmol) was added and the mixture was stirred for 30 minutes. After addition of NEt\(_3\), DCM was added and the organic layer was washed with H\(_2\)O, brine, was dried over MgSO\(_4\) and concentrated in vacuo. Column chromatography yielded compound 10 (1.36 g, 1.14 mmol) in 88% yield as \( \alpha \)-anomer only.

From 26: Donor 26 (0.06 g, 0.05 mmol) and acceptor 21 (0.02 g, 0.1 mmol) were coevaporated with toluene (2x) and dissolved in a mixture of acetonitrile, propionitrile and DCM (0.5 ml, 2:1:1 v/v/v). Molecular sieves (3Å) were added and the mixture was stirred at -40°C for 10 minutes. TfOH (1 µl, 10 µmol) was added and the mixture was stirred for 20 minutes. After addition of NEt\(_3\), DCM was added and the organic layer was washed with H\(_2\)O, brine, was dried over MgSO\(_4\) and concentrated in vacuo. Size exclusion chromatography yielded compound 10 (0.37 g, 0.03 mmol) in 70% yield (\( \alpha / \beta = 1 : 19 \)). TLC: \( R_f \) 0.6 (10% EtOAc/toluene); \([\alpha]_D^{20}\) (CHCl\(_3\), c 1): +54; IR (neat, cm\(^{-1}\)): 2929, 2910, 2856, 2110, 1454, 1103, 1078, 1028, 736, 700; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.65 – 7.62 \) (m, 4H), 7.43 – 7.20 (m, 31H), 5.87 (ddd, \( J = 22.4 \text{ Hz}, 10.4 \text{ Hz}, 5.6 \text{ Hz}, 1 \text{H} \)), 5.25 – 5.21 (m, 1H), 5.14 -5.01 (m, 2H), 5.02 (d, \( J = 12 \text{ Hz}, 1 \text{H} \)), 4.88 (d, \( J = 11.2 \text{ Hz}, 1 \text{H} \)), 4.76 (s, 2H), 4.56 – 4.51 (m, 4H), 4.40 – 4.38 (m, 3H), 4.22 – 4.20 (m, 1H), 4.13 – 4.10 (m, 1H), 4.04 – 3.98 (m, 5H), 3.90 – 3.82 (m,2H), 3.76 – 3.47 (m, 9H), 3.44 – 3.41 (m, 1H), 1.06 (s, 9H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \( \delta = 138.5, 138.4, 137.9, 137.7, 135.7, 135.6, 134.9, 133.5, 133.2, 129.9, 129.8, 128.8, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.4, 116.9, 102.6, 94.5, 78.4, 77.7, 75.6, 75.0, 74.7, 73.7, 73.6, 73.4, 73.3, 72.6, 72.5, 71.8, 70.8, 70.4,
HRMS: [C_{69}H_{78}N_{6}O_{11}Si + Na] requires 1217.53900, found 1217.53846.

2-O-(3-O-[2-N-acetamido-3,4-di-O-benzyl-6-O-tert-butyl-di-phenylsilyl-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl)-1-O-allyl-3-O-benzyl-sn-glycerol (29)

Di-azido-pseudotrisaccharide 10 (0.93 g, 0.78 mmol) was dissolved in a mixture of dioxane (4.5 ml) and water (0.9 ml). PMe₃ (1M in THF, 3 ml, 3 mmol) was added to the mixture and it was stirred for 0.5h. The mixture was concentrated, coevaporated with toluene and dissolved in DCM (10 ml). Triethylamine (0.33 ml, 2.3 mmol) and Ac₂O (0.14 ml, 1.5 mmol) were added and the mixture was stirred for 1.25h. The organic layer was washed with sat.aq. NaHCO₃ and brine, dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded di-acetylated pseudotrisaccharide 29 (0.56 g, 0.46 mmol) in 59% yield. TLC: Rₚ=0.3 (50% EtOAc/pentane); [α]D²⁰ (CHCl₃, c 0.2): +113; IR (neat, cm⁻¹): 2859, 1661, 1454, 1112, 1056, 1027, 696, 667; ¹H NMR (400 MHz, CDCl₃) δ 7.69 – 7.54 (m, 6H), 7.48 – 7.37 (m, 8H), 7.37 – 7.21 (m, 44H), 7.18 (s, 5H), 5.82 (ddd, J = 22.7, 10.0, 4.7 Hz, 3H), 5.55 (d, J = 8.1 Hz, 1H), 5.26 – 5.17 (m, 2H), 5.15 – 5.09 (m, 3H), 4.94 (d, J = 11.7 Hz, 1H), 4.86 – 4.68 (m, 4H), 4.64 (d, J = 12.1 Hz, 1H), 4.55 (d, J = 12.2 Hz, 1H), 4.52 – 4.44 (m, 9H), 4.44 – 4.33 (m, 3H), 4.31 – 4.19 (m, 1H), 3.97 – 3.86 (m, 8H), 3.81 (s, 4H), 3.74 – 3.57 (m, 9H), 3.57 – 3.41 (m, 10H), 1.86 (s, 3H), 1.51 (s, 3H), 1.08 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 170.1, 170.0, 138.3, 138.0, 137.5, 135.6, 135.4, 135.3, 134.3, 132.9, 132.9, 129.8, 129.8, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.4, 127.2, 126.7, 126.6, 117.1, 102.1, 93.9, 78.5, 77.9, 77.3, 77.0, 76.7, 75.7, 74.1, 73.9, 73.2, 73.1, 73.1, 72.9, 72.3, 72.1, 71.8, 71.1, 69.9, 67.9, 63.5, 51.9, 48.7, 26.9, 23.5, 22.7, 19.1; HRMS: [C_{73}H_{86}N_{2}O_{13}Si +H] requires 1227.59719, found 1227.59871.

2-O-(3-O-[2-N-acetamido-3,4-di-O-benzyl-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl)-1-O-allyl-3-O-benzyl-sn-glycerol (31)

Silyl-protected pseudotrisaccharide 29 (0.6 g, 0.5 mmol) was coevaporated with toluene and was dissolved in THF (10 ml). TBAF (1M in THF, 0.54 ml, 0.54 mmol) was added and the reaction was stirred for 30 min. The mixture was concentrated and subsequent column chromatography yielded alcohol 31 (0.37 g, 0.37 mmol) in 77% yield. TLC: Rₚ=0.1 (50% EtOAc/pentane); [α]D²⁰ (CHCl₃, c 0.2): +61; IR (neat, cm⁻¹): 3331, 3063, 2912, 2870, 1699, 1645, 1538, 1118, 1014, 734, 695; ¹H NMR (400 MHz, Acetone-δ₆) δ 7.47 – 7.21 (m, 32H), 5.96 – 5.84 (m, 1H), 5.26 (dd, J = 17.8, 2.4 Hz, 2H), 5.12 (d,
J = 10.5 Hz, 1H), 4.95 (dd, J = 21.3, 11.5 Hz, 2H), 4.79 (d, J = 11.5 Hz, 1H), 4.74 – 4.66 (m, 2H), 4.66 – 4.58 (m, 2H), 4.56 – 4.42 (m, 4H), 4.39 – 4.28 (m, 1H), 4.15 (s, 1H), 4.10 (t, J = 6.3 Hz, 1H), 4.03 – 3.92 (m, 6H), 3.87 (dd, J = 11.2, 2.2 Hz, 1H), 3.81 (dd, J = 10.6, 7.0 Hz, 1H), 3.75 – 3.57 (m, 7H), 3.57 – 3.49 (m, 4H), 1.97 (s, 3H), 1.70 (s, 3H); 13C NMR (101 MHz, Acetone-d6) δ 170.7, 170.3, 140.1, 140.1, 139.7, 139.7, 139.4, 136.2, 129.0, 129.0, 128.9, 128.9, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 116.4, 103.0, 95.7, 78.6, 78.3, 77.0, 75.1, 75.0, 74.6, 74.0, 73.6, 73.5, 73.4, 72.6, 72.5, 71.1, 70.8, 69.7, 62.4, 52.2, 50.3, 30.4, 30.2, 30.0, 29.8, 29.6, 29.5, 23.7, 23.0; HRMS: [C57H68N2O13 +H] requires 989.47942, found 989.48077.

2-O-(3-O-[2-N-acetamido-3,4-di-O-benzyl-6-O-{4,4′-di-methoxy-tri-phenylmethyl]-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl)-1-O-allyl-3-O-benzyl-sn-glycerol (33)
Pseudotrisaccharide 31 (0.26 g, 0.26 mmol) was coevaporated with toluene three times and was dissolved in DCM (2.6 ml). Triethylamine (0.06 ml, 0.4 mmol) and 4,4′-dimethoxytritylchloride (0.098 g, 0.3 mmol) were added and the mixture was stirred for 23h. Water was added and the organic phase was washed with brine, dried over Na2SO4 and concentrated in vacuo. Column chromatography with neutralized silica yielded protected pseudotrisaccharide 33 (0.30 g, 0.24 mmol) in 89% yield. TLC: Rf=0.2 (50% EtOAc/pentane); [α]D20 (CHCl3, c 0.2): +43; IR (neat, cm⁻¹): 3032,2861, 1669, 1508, 1247, 1061, 1027, 736, 696; 1H NMR (400 MHz, Acetone-d6) δ 7.53 (d, J = 7.5 Hz, 2H), 7.46 (d, J = 7.3 Hz, 5H), 7.42 – 7.18 (m, 39H), 7.12 (dd, J = 6.5, 2.9 Hz, 3H), 6.91 (dd, J = 8.9, 5.4 Hz, 4H), 6.59 (d, J = 8.8 Hz, 1H), 5.92 – 5.79 (m, 1H), 5.35 (d, J = 3.5 Hz, 1H), 5.24 (dd, J = 17.3, 1.8 Hz, 1H), 5.09 (dd, J = 10.5, 1.7 Hz, 1H), 4.99 (d, J = 11.5 Hz, 1H), 4.93 – 4.86 (m, 1H), 4.83 (d, J = 10.3 Hz, 1H), 4.79 (s, 1H), 4.74 (ddd, J = 12.1, 9.0, 3.5 Hz, 2H), 4.68 (d, J = 11.7 Hz, 1H), 4.61 (d, J = 11.5 Hz, 1H), 4.53 (s, 2H), 4.52 – 4.41 (m, 3H), 4.36 (q, J = 8.7 Hz, 1H), 4.31 – 4.24 (m, 1H), 4.19 (s, 1H), 4.15 (dd, J = 10.9, 2.3 Hz, 1H), 4.10 – 4.03 (m, 3H), 3.98 – 3.90 (m, 3H), 3.77 (s, 9H), 3.73 – 3.65 (m, 4H), 3.65 – 3.53 (m, 7H), 3.26 (s, 2H), 3.14 (dd, J = 9.1, 4.7 Hz, 1H), 1.92 (s, 3H), 1.72 (s, 3H); 13C NMR (101 MHz, Acetone-d6) δ 170.4, 170.1, 159.4, 146.0, 139.9, 139.8, 139.6, 139.9, 139.2, 136.8, 136.4, 136.0, 131.0, 130.9, 129.0, 129.0, 128.9, 128.9, 128.9, 128.7, 128.6, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.5, 116.7, 113.9, 113.8, 102.9, 94.8, 86.9, 79.0, 78.4, 76.2, 75.1, 74.8, 74.7, 74.3, 73.6, 73.5, 72.8, 72.6, 72.6, 71.4, 71.1, 70.8, 69.5, 64.4, 55.5, 52.6, 50.0, 30.2, 30.0, 29.8, 29.6, 29.5, 23.8, 23.0; HRMS: [C78H86N2O15 +H] requires 1291.61010, found 1291.61161.
2-O-(3-O-[2-N-acetamido-3,4-di-O-benzyl-6-O-{4,4′-di-methoxy-tri-phenylmethyl}-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl)-3-O-benzyl-sn-glycerol (35)

Allyl-protected pseudotrisaccharide 33 (0.44, 0.34 mmol) was coevaporated with toluene three times and was dissolved in distilled THF (3.5 ml). The mixture was purged of oxygen by bubbling through argon for 10 minutes. (1,5-Cyclooctadiene)bis(methylidiphenylphosphine)iridium(I) hexafluorophosphate (0.035 g, 0.04 mmol) was added and H₂ gas was bubbled through for 5 seconds. Argon was applied and the reaction mixture was stirred for 2.5h, yielding the isomerised intermediate. The reaction mixture of was diluted with THF (5.5 ml) and sat. aq. NaHCO₃ (6 ml) was added. Iodine (0.13 g, 0.5 mmol) was added and the reaction was stirred for 1h. The mixture was diluted with EtOAc, washed with sat. aq. Na₂S₂O₃ and brine, dried over Na₂SO₄ and concentrated in vacuo. Column chromatography yielded deprotected pseudotrisaccharide 35 (0.30 g, 0.24 mmol) in 70 % yield. TLC: Rₖ=0.1 (75% EtOAc/pentane); [α]D₂₀ (CHCl₃, c 0.2): +25; IR (neat, cm⁻¹): 3100, 2929, 2910, 1699, 1509, 1247, 829, 732, 697; ¹H NMR (400 MHz, Acetone-d₆) δ 7.52 (d, J = 7.4 Hz, 2H), 7.49 – 7.42 (m, 6H), 7.42 – 7.19 (m, 42H), 7.11 (dd, J = 6.6, 2.9 Hz, 3H), 6.99 (d, J = 8.3 Hz, 1H), 6.91 (dd, J = 8.9, 6.8 Hz, 4H), 5.36 (d, J = 3.6 Hz, 1H), 5.00 (d, J = 3.4 Hz, 1H), 4.98 (s, 1H), 4.83 (dd, J = 17.9, 11.6 Hz, 2H), 4.78 – 4.69 (m, 2H), 4.67 (s, 0H), 4.60 (d, J = 11.5 Hz, 1H), 4.51 (s, 2H), 4.46 (d, J = 6.7 Hz, 2H), 4.44 – 4.40 (m, 1H), 4.39 – 4.30 (m, 1H), 4.27 (t, J = 6.0 Hz, 1H), 4.22 – 4.17 (m, 1H), 4.16 – 4.09 (m, 1H), 4.09 – 4.04 (m, 2H), 4.02 – 3.94 (m, 5H), 3.76 (s, 10H), 3.74 – 3.65 (m, 4H), 3.65 – 3.52 (m, 5H), 3.34 (s, 2H), 3.15 (dd, J = 9.0, 5.0 Hz, 1H), 1.96 (s, 3H), 1.71 (s, 3H); ¹³C NMR (101 MHz, Acetone-d₆) δ 171.2, 170.2, 159.4, 159.4, 145.9, 139.9, 139.7, 139.6, 139.5, 139.2, 136.8, 136.4, 132.6, 132.5, 130.9, 130.8, 129.4, 129.3, 129.0, 128.9, 128.9, 128.9, 128.7, 128.6, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.5, 113.9, 113.8, 103.0, 94.7, 86.9, 80.8, 78.3, 76.2, 75.0, 74.8, 74.7, 74.3, 73.6, 73.5, 72.8, 72.5, 71.4, 70.8, 69.5, 64.3, 63.5, 55.4, 52.9, 49.9, 30.2, 30.0, 29.8, 29.6, 29.5, 23.7, 23.0; HRMS: [C₇₅H₈₂N₂O₁₅ +H] requires 1251.57880, found 1251.57979.

2-O-(3-O-[2-N-acetamido-3,4-di-O-benzyl-6-O-{4,4′-di-methoxy-tri-phenylmethyl}-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl)-3-O-benzyl -1-O-([N, N'-di-isopropylaminol-2-cyanoethyl-phosphite]-sn-glycerol (7)
Pseudotrisaccharide 35 (0.37 g, 0.29 mmol) was dissolved in DCM (3 ml). Diisopropylethylamine (0.077 ml, 0.44 mmol) and 3Å molsieves were added and the resulting
solution was stirred for 45 minutes. \(N, N'\)-di-isopropylamino-2-cyanoethyl-chlorophosphite (0.078 ml, 0.35 mmol) was added and the reaction mixture was stirred for 2h. Water was added, the organic phase was washed with brine, dried over Na\(_2\)SO\(_4\) and concentrated *in vacuo*. Column chromatography with neutralized silica yielded phosphoramidite 7 (0.36 g, 0.25 mmol) in 85% yield. TLC: \(R_f=0.8\) (80% EtOAc/pentane); \(^1\)H NMR (400 MHz, CD\(_3\)CN) δ 7.50 (d, \(J = 7.7\) Hz, 2H), 7.45 – 7.22 (m, 42H), 7.13 – 7.03 (m, 3H), 6.93 – 6.76 (m, 4H), 6.39 – 6.29 (m, 1H), 5.44 (d, \(J = 2.4\) Hz, 1H), 5.21 (s, 1H), 4.85 (dd, \(J = 11.1, 2.1\) Hz, 1H), 4.81 – 4.71 (m, 3H), 4.59 (d, \(J = 11.6\) Hz, 1H), 4.55 – 4.40 (m, 7H), 4.35 (d, \(J = 11.3\) Hz, 1H), 4.19 – 4.14 (m, 1H), 4.14 – 4.03 (m, 3H), 4.03 – 3.92 (m, 3H), 3.83 – 3.53 (m, 17H), 3.47 (q, \(J = 8.0, 7.2\) Hz, 1H), 3.04 (td, \(J = 8.9, 4.4\) Hz, 1H), 2.64 – 2.47 (m, 5H), 1.93 (d, \(J = 5.7\) Hz, 3H), 1.70 (s, 3H), 1.26 – 1.09 (m, 12H); \(^{13}\)C NMR (101 MHz, CD\(_3\)CN) δ 171.2, 170.8, 159.6, 146.1, 139.7, 139.6, 139.3, 136.9, 136.6, 131.2, 131.1, 129.4, 129.3, 129.3, 129.2, 129.1, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 127.8, 119.6, 118.3, 114.1, 114.0, 102.4, 94.8, 87.1, 79.1, 78.3, 76.1, 76.0, 75.1, 75.0, 74.9, 74.3, 73.8, 73.7, 73.0, 72.7, 71.5, 70.6, 70.4, 69.6, 64.6, 61.0, 59.6, 59.4, 59.3, 59.1, 55.9, 52.4, 49.8, 43.9, 43.7, 25.1, 25.0, 23.9, 23.2, 21.0, 14.6; \(^{31}\)P NMR (162 MHz, CD\(_3\)CN) δ 147.8, 147.7.

2-\(O\)-(3-\(O\)-[2-azido-3,4-di-\(O\)-benzyl-2-deoxy-6-\(O\)-tert-butyl-di-phenylsilyl-\(\alpha\)-\(D\)-galactopyranosyl]-2-azido-4,6-di-\(O\)-benzyl-2-deoxy-\(\beta\)-\(D\)-galactopyranosyl)-3-\(O\)-allyl-1-\(O\)-benzyl-sn-glycerol (11)

Disaccharide donor 26 (2.33 g, 2.0 mmol) and glycerol acceptor 23 (0.67 g, 3.0 mmol) were coevaporated with toluene (2x) and dissolved in a mixture of acetonitrile, propionitrile and DCM (10 ml, 2:1:1 v/v/v). Molecular sieves (3Å) were added and the mixture was stirred at -40°C for 10 minutes. TfOH (35 µl, 0.4 mmol) was added and the mixture was stirred for 30 minutes. After addition of NEt\(_3\), DCM was added and the organic layer was washed with H\(_2\)O, brine, was dried over MgSO\(_4\) and concentrated in vacuo. Size exclusion chromatography yielded compound pseudotrisaccharide 11 (1.92 g, 1.61 mmol) in 80% yield as a single anomer. TLC: \(R_t\) 0.6 (15% EtOAc/pentane); [\(\alpha\)]\(_D\)\(^{20}\) (CHCl\(_3\), c 0.2): +48; IR (neat, cm\(^{-1}\)): 2915, 2856, 2109, 1454, 1207, 1097, 1028, 736; \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.69 – 7.56 (m, 4H), 7.47 – 7.13 (m, 28H), 5.21 (dd, \(J = 17.2, 1.6\) Hz, 1H), 5.17 – 5.07 (m, 2H), 5.03 (d, \(J = 11.2\) Hz, 1H), 4.89 (d, \(J = 11.2\) Hz, 1H), 4.76 (s, 1H), 4.61 – 4.49 (m, 4H), 4.40 (s, 2H), 4.24 (t, \(J = 6.6\) Hz, 1H), 4.16 (dd, \(J = 10.6, 2.4\) Hz, 1H), 4.09 – 3.99 (m, 3H), 3.96 (d, \(J = 5.3\) Hz, 3H), 3.93 – 3.84 (m, 2H), 3.84 – 3.76 (m, 1H), 3.76 – 3.67 (m, 2H), 3.67 – 3.62 (m, 2H), 3.62 – 3.49 (m, 3H), 3.46 – 3.41 (m, 1H), 1.06 (s, 9H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 138.2, 138.1,
137.5, 137.3, 135.4, 135.3, 134.6, 133.1, 132.8, 129.7, 129.6, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.3, 116.6, 102.2, 94.2, 78.0, 77.4, 77.3, 77.0, 76.7, 75.4, 74.7, 74.4, 73.4, 73.3, 73.2, 73.0, 72.3, 72.1, 71.5, 70.5, 70.2, 69.9, 68.0, 62.5, 59.6, 26.7, 26.7, 19.1; HRMS: \([C_{69}H_{78}N_6O_{11}Si + NH_4]\) requires 1213.58658, found 1213.58828.

2-O-(3-O-[2-N-acetamido-3,4-di-O-benzyl-6-O-tert-butyldi-phenylsilyl-\(\alpha\)-d-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-\(\beta\)-d-galactopyranosyl)-3-O-allyl-1-O-benzyl-sn-glycerol (30)

Di-azido-pseudotrisaccharide 11 (1.92 g, 1.6 mmol) was dissolved in a mixture of dioxane (9 ml) and water (1.8 ml). PMe₃ (1M in THF, 6.4 ml, 6.4 mmol) was added to the mixture and it was stirred for 1.7h. The mixture was concentrated, coevaporated with toluene and dissolved in DCM (20 ml). Triethylamine (0.7 ml, 4.8 mmol) and Ac₂O (0.45 ml, 4.8 mmol) were added and the mixture was stirred for 47h. The organic layer was washed with sat.aq. NaHCO₃, water and brine, dried over MgSO₄ and concentrated in vacuo. Column chromatography yielded di-acetylated pseudotrisaccharide 30 (1.49 g, 1.2 mmol) in 76% yield. TLC: \(R_f=0.3\) (50% EtOAc/pentane); \([\alpha]_D^{20}\) (CHCl₃, c 0.2): +44; IR (neat, cm\(^{-1}\)): 3067, 2930, 2857, 1663, 1305, 1112, 1027, 732, 696; \(^1\)H NMR (400 MHz, Acetone-\(d_6\)) δ 7.69 – 7.52 (m, 7H), 7.50 – 6.94 (m, 67H), 5.97 – 5.65 (m, 3H), 5.44 (d, \(J = 8.3\) Hz, 1H), 5.29 – 5.04 (m, 5H), 4.93 (d, \(J = 11.7\) Hz, 1H), 4.77 (td, \(J = 10.6, 3.4\) Hz, 3H), 4.70 (d, \(J = 11.7\) Hz, 1H), 4.63 (d, \(J = 12.1\) Hz, 1H), 4.56 – 4.44 (m, 11H), 4.41 (d, \(J = 6.7\) Hz, 3H), 4.30 – 4.19 (m, 2H), 4.08 (d, \(J = 7.1\) Hz, 0H), 3.98 – 3.86 (m, 8H), 3.86 – 3.78 (m, 4H), 3.71 (td, \(J = 9.9, 8.8, 3.6\) Hz, 5H), 3.68 – 3.39 (m, 19H), 1.74 (s, 3H), 1.51 (s, 3H), 1.07 (s, 9H); \(^{13}\)C NMR (101 MHz, Acetone-\(d_6\)) δ 169.9, 138.2, 138.2, 137.9, 137.8, 137.5, 135.4, 135.2, 134.4, 132.8, 129.8, 129.7, 128.2, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 127.4, 127.3, 127.2, 126.6, 126.5, 116.6, 101.7, 94.0, 78.2, 77.7, 77.3, 77.0, 76.7, 75.6, 74.0, 73.9, 73.1, 73.1, 73.0, 72.8, 72.2, 72.0, 71.7, 71.3, 70.7, 69.8, 67.9, 63.4, 51.8, 48.7, 26.8, 23.3, 22.6, 19.0; HRMS: \([C_{73}H_{87}N_2O_{13}Si + H]\) requires 1227.59719, found 1227.59868.

Silyl-protected pseudotrisaccharide 30 (1.53 g, 1.25 mmol) was coevaporated with toluene and was dissolved in THF (15 ml). TBAF (1M in THF, 1.4 ml, 1.4 mmol) was added and the reaction was stirred for 45 min. The mixture was concentrated and subsequent column
chromatography yielded alcohol 32 (1.1 g, 1.1 mmol) in 89% yield. TLC: Rf=0.1 (50% EtOAc/pentane); [α]D 20 (CHCl3, c 0.2): +39; IR (neat, cm⁻¹): 3282, 3029, 2869, 2865, 1652, 1539, 1553, 1370, 1061, 735, 696; ¹H NMR (400 MHz, Acetone-δ 6) δ 7.41 (d, J = 7.2 Hz, 6H), 7.38 – 7.21 (m, 43H), 7.14 (dd, J = 17.1, 9.0 Hz, 2H), 5.84 (ddt, J = 17.2, 10.6, 5.3 Hz, 1H), 5.22 (d, J = 3.1 Hz, 2H), 5.19 (q, J = 1.7 Hz, 1H), 5.06 (dq, J = 10.5, 1.4 Hz, 2H), 4.95 (dd, J = 19.9, 11.5 Hz, 3H), 4.83 – 4.71 (m, 2H), 4.67 (ddd, J = 11.9, 8.6, 3.7 Hz, 3H), 4.61 (dd, J = 11.4, 7.8 Hz, 3H), 4.54 (s, 3H), 4.51 (d, J = 3.3 Hz, 2H), 4.48 (d, J = 7.3 Hz, 2H), 4.20 – 4.12 (m, 3H), 4.07 (t, J = 6.2 Hz, 2H), 4.02 (d, J = 2.3 Hz, 2H), 3.99 – 3.91 (m, 7H), 3.86 (dd, J = 11.2, 2.6 Hz, 2H), 3.78 (dd, J = 10.6, 7.0 Hz, 2H), 3.72 – 3.65 (m, 4H), 3.65 – 3.61 (m, 3H), 3.58 (m, 7H), 3.49 (dd, J = 10.0, 6.5 Hz, 1H), 3.32 (s, 2H), 3.07 (s, 3H), 1.90 (s, 3H), 1.69 (s, 3H); ¹³C NMR (101 MHz, Acetone-δ 6) δ 206.2, 170.7, 170.2, 140.2, 140.2, 139.8, 139.7, 139.4, 136.2, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 128.5, 128.3, 128.3, 128.2, 128.1, 116.3, 103.0, 95.8, 78.6, 78.3, 77.1, 75.1, 75.1, 74.7, 74.1, 73.7, 73.7, 73.5, 72.7, 72.5, 72.5, 71.2, 70.7, 69.7, 62.5, 52.3, 50.3, 30.4, 30.2, 30.0, 29.8, 29.6, 29.5, 29.3, 23.7, 23.0; HRMS: [C₅₇H₆₈N₂O₁₃ +H] requires 989.47942, found 989.48061.

2-O-(3-O-[2-N-acetamido-3,4-di-O-benzyl-6-O-{4,4’-di-methoxy-tri-phenylmethyl]-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl)-3-O-allyl-1-O-benzyl-sn-glycerol (34)

Pseudotrisaccharide 32 (0.9 g, 0.9 mmol) was coevaporated with toluene three times and was dissolved in DCM (9 ml). Triethylamine (0.2 ml, 1.4 mmol) and 4,4’-dimethoxytrityl-chloride (0.34 g, 1.0 mmol) were added and the mixture was stirred for 2h. Water was added and the organic phase was washed with brine, dried over Na₂SO₄ and concentrated in vacuo. Column chromatography with neutralized silica yielded protected pseudotrisaccharide 34 (1.01 g, 0.78 mmol) in 86% yield. TLC: Rf=0.2 (50% EtOAc/pentane); [α]D 20 (CHCl₃, c 0.2): +40; IR (neat, cm⁻¹): 2930, 1699, 1508, 1247, 1060, 1027, 828, 736, 696; ¹H NMR (400 MHz, Acetone-δ 6) δ 7.56 (d, J = 7.7 Hz, 2H), 7.50 – 7.20 (m, 40H), 7.17 – 7.10 (m, 3H), 7.05 (d, J = 8.6 Hz, 1H), 6.92 (dd, J = 8.6, 5.9 Hz, 4H), 6.54 (d, J = 8.7 Hz, 1H), 5.95 – 5.82 (m, 1H), 5.38 (d, J = 3.4 Hz, 1H), 5.33 – 5.21 (m, 1H), 5.11 (d, J = 10.5 Hz, 1H), 4.98 (t, J = 9.5 Hz, 2H), 4.91 – 4.82 (m, 1H), 4.81 – 4.72 (m, 2H), 4.66 (dd, J = 16.4, 11.7 Hz, 2H), 4.55 – 4.44 (m, 6H), 4.43 – 4.27 (m, 2H), 4.20 (d, J = 8.3 Hz, 2H), 4.07 (d, J = 7.3 Hz, 2H), 4.01 – 3.91 (m, 4H), 3.81 (t, J = 6.3 Hz, 2H), 3.76 (s, 6H), 3.73 – 3.50 (m, 10H), 3.16 (dd, J = 9.0, 4.7 Hz, 1H), 1.85 (s, 3H), 1.75 (s, 3H); ¹³C NMR (101 MHz, Acetone-δ 6) δ 170.1, 170.0, 159.3, 154.9, 139.8, 139.7, 139.5, 139.4, 139.2, 136.8, 136.3, 136.0, 130.9, 130.8, 129.0, 128.9,
Allyl-protected pseudotrisaccharide 34 (1.01 g, 0.78 mmol) was coevaporated with toluene three times and was dissolved in distilled THF (5 ml). The mixture was purged of oxygen by bubbling through argon for 10 minutes. (1,5-Cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (0.02 g, 0.02 mmol) was added and H2 gas was bubbled through for 5 seconds. Argon was applied and the reaction mixture was stirred for 2h, yielding the isomerised intermediate. The reaction mixture of was diluted with THF (12.5 ml) and sat. aq. NaHCO3 (13.5 ml) was added. Iodine (0.30 g, 1.2 mmol) was added and the reaction was stirred for 1.5h. The mixture was diluted with EtOAc, washed with sat. aq. Na2S2O3 and brine, dried over Na2SO4 and concentrated in vacuo. Column chromatography yielded deprotected pseudotrisaccharide 36 (0.78 g, 0.63 mmol) in 80% yield. TLC: Rf=0.1 (75% EtOAc/pentane); [α]D20 (CHCl3, c 0.2): +28; IR (neat, cm⁻¹): 3061, 2862, 1674, 1508, 1248, 1053, 1026, 826, 735, 697; 1H NMR (400 MHz, Acetone-d6) δ 7.51 (d, J = 7.6 Hz, 2H), 7.44 (d, J = 7.4 Hz, 4H), 7.40 – 7.19 (m, 33H), 7.14 – 7.09 (m, 2H), 6.93 – 6.87 (m, 4H), 6.74 – 6.68 (m, 1H), 5.34 (d, J = 3.4 Hz, 1H), 4.97 (d, J = 11.4 Hz, 1H), 4.90 – 4.76 (m, 3H), 4.77 – 4.69 (m, 1H), 4.67 (d, J = 11.7 Hz, 1H), 4.58 (d, J = 11.4 Hz, 1H), 4.53 – 4.42 (m, 5H), 4.42 – 4.33 (m, 2H), 4.26 – 4.20 (m, 1H), 4.20 – 4.10 (m, 2H), 4.06 (s, 1H), 3.97 – 3.87 (m, 3H), 3.87 – 3.78 (m, 3H), 3.76 (s, 5H), 3.69 – 3.59 (m, 6H), 3.57 (d, J = 5.5 Hz, 2H), 3.53 – 3.42 (m, 2H), 3.35 (d, J = 4.9 Hz, 4H), 3.25 – 3.16 (m, 1H), 3.12 (dd, J = 9.1, 4.6 Hz, 1H), 1.85 (s, 3H), 1.72 (s, 3H); 13C NMR (101 MHz, Acetone-d6) δ 189.9, 189.4, 178.6, 165.1, 158.9, 158.8, 158.6, 158.3, 150.1, 150.0, 148.2, 148.1, 148.1, 147.9, 147.7, 147.7, 147.6, 147.6, 147.4, 147.4, 147.3, 147.3, 147.3, 146.7, 133.0, 133.0, 122.3, 114.0, 106.1, 101.8, 97.6, 95.4, 94.2, 94.0, 93.9, 93.6, 92.8, 92.7, 92.0, 91.7, 90.6, 90.1, 88.8, 83.7, 82.7, 74.6, 71.7, 69.1, 68.9, 49.5, 49.4, 49.2, 49.0, 48.8, 48.6, 48.4, 42.8, 42.2; HRMS: [C75H82N2O15 +H] requires 1251.57880, found 1251.58015.
2-O-(3-O-[2-N-acetamido-3,4-di-O-benzyl-6-O-[4,4'-di-methoxy-tri-phenylmethyl]-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl)- 1-O-benzyl -3-O-([N, N'-di-isopropylamino]-2-cyanoethyl-phosphite)-sn-glycerol (8)

Pseudotrisaccharide 36 (0.19 g, 0.15 mmol) was dissolved in DCM (1.5 ml). Diisopropylethylamine (0.045 ml, 0.26 mmol) and 3Å molsieves were added and the resulting solution was stirred for 45 minutes. N,N-di-isopropylamino-2-cyanoethyl-chlorophosphite (0.043 ml, 0.20 mmol) was added and the reaction mixture was stirred for 1.6h. Water was added, the organic phase was washed with brine, dried over Na₂SO₄ and concentrated in vacuo. Column chromatography with neutralized silica yielded phosphoramidite 8 (0.13 g, 0.09 mmol) in 62% yield. TLC: Rₚ=0.8 (80% EtOAc/pentane); ¹H NMR (400 MHz, CD₃CN) δ 7.48 (d, J = 7.5 Hz, 2H), 7.44 – 7.20 (m, 45H), 7.07 (dd, J = 6.3, 2.7 Hz, 3H), 6.93 – 6.82 (m, 4H), 6.64 (d, J = 9.1 Hz, 1H), 6.17 (dd, J = 9.1, 2.4 Hz, 1H), 5.19 (d, J = 3.6 Hz, 1H), 4.84 (d, J = 11.1 Hz, 1H), 4.78 – 4.68 (m, 3H), 4.62 – 4.41 (m, 9H), 4.34 (d, J = 11.3 Hz, 1H), 4.13 – 4.02 (m, 2H), 4.02 – 3.90 (m, 5H), 3.79 – 3.66 (m, 16H), 3.65 – 3.42 (m, 10H), 2.99 (dd, J = 9.2, 4.2 Hz, 1H), 2.63 – 2.38 (m, 5H), 1.78 (s, 3H), 1.66 (d, J = 1.6 Hz, 3H), 1.26 – 1.08 (m, 12H); ¹³C NMR (101 MHz, CD₃CN) δ 171.0, 170.7, 159.6, 146.0, 139.8, 139.6, 137.0, 136.6, 131.2, 131.0, 129.4, 129.3, 129.1, 128.9, 128.8, 128.6, 128.5, 128.4, 128.4, 127.8, 118.3, 114.1, 102.7, 95.0, 87.1, 78.3, 76.3, 75.1, 75.0, 74.9, 74.3, 73.9, 73.8, 72.9, 71.4, 70.6, 69.5, 64.6, 59.3, 55.9, 52.4, 49.8, 43.9, 43.8, 24.9, 23.8, 23.2, 21.0, 14.5, 1.9, 1.7, 1.5, 1.3, 1.1, 0.9; ³¹P NMR (162 MHz, CD₃CN) δ 148.0, 147.9.

1-O-(2-O-[3-O-[2-N-acetamido-3,4-di-O-benzyl-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl]-3-O-benzyl-sn-glycerol-1-[2-cyanoethylphosphate]-N-benzyloxycarbonyl-6-aminohexanol (37)

Phosphoramidite 9 (0.2M in MeCN, 1.1 ml, 227µmol) and alcohol 35 (189mg,151µmol) were coupled using the general procedure for phosphoramidite coupling. Size exclusion (Sephadex LH-20, DCM/MeOH, 1/1 v/v) column chromatography yielded spacer equipped monomer 37 (120mg, 91µmol) in 61% yield. IR (neat, cm⁻¹): 3420, 3275, 2914, 1699, 1653, 1539, 1454, 1248, 1026, 736, 696; ¹H NMR (400 MHz, Acetone-d₆) δ 7.56 – 7.19 (m, 30H), 6.38 (d, J = 6.3 Hz, 1H), 5.25 (d, J = 3.6 Hz, 1H), 5.06 (s, 2H), 4.96 (dd, J = 22.6, 11.4 Hz, 2H), 4.78 (t, J = 10.5 Hz, 2H), 4.74 – 4.60 (m, 3H), 4.54 – 4.49 (m, 3H), 4.49 – 4.43 (m, 2H), 4.25 (dt, J = 11.1, 5.4 Hz, 2H), 4.18 – 4.13 (m, 1H), 4.13 – 4.02 (m, 4H), 3.90 (ddd, J = 28.1, 11.0, 2.5 Hz, 2H), 3.80 (t, J = 9.1 Hz, 1H), 3.75 – 3.65 (m, 3H), 3.65 – 3.52 (m, 3H), 3.33 (s, 1H), 3.21 (s, 5H), 3.18 – 3.10 (m, 2H), 2.89 (t, J = 5.8 Hz, 2H), 2.02 (s, 3H), 1.72 – 1.62 (m, 5H), 1.56 –
1.46 (m, 2H), 1.45 – 1.29 (m, 5H); $^{13}$C NMR (101 MHz, Acetone-$d_6$) $\delta$ 171.3, 170.4, 159.5, 140.1, 140.0, 139.7, 139.4, 129.1, 129.0, 128.9, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.1, 118.3, 102.5, 102.2, 95.1, 78.3, 76.5, 75.1, 74.8, 74.3, 73.7, 73.6, 72.9, 69.6, 68.9, 66.3, 63.3, 62.4, 51.9, 50.1, 41.4, 30.5, 30.2, 30.0, 29.8, 29.6, 29.5, 29.3, 26.8, 25.7, 23.7, 23.0, 19.9; $^{31}$P NMR (162 MHz, Acetone-$d_6$) $\delta$ -1.5; HRMS: [C$_{71}$H$_{87}$N$_{4}$O$_{18}$P$^+$ +H$^+$] requires 1315.58257, found 1315.58397.

1-O-di(2-O-[3-O-{2-N-acetamido-3,4-di-O-benzyl-$\alpha$-D-galactopyranosyl}-2-N-acetamido-4,6-di-O-benzyl-$\beta$-D-galactopyranosyl}-3-O-benzyl-$sn$-glycerol-1-[2-cyanoethylphosphate])-N-benzylxoycarbonyl-6-aminohexanol (38)

Phosphoramidite 7 (0.05M in MeCN, 2.3 ml, 114µmol) and alcohol 37 (115mg, 87µmol) were coupled using the general procedure for phosphoramidite coupling. Automated reversed phase (C18, 10% $\rightarrow$ 100% MeOH/H$_2$O) column chromatography yielded spacer equipped dimer 38 (128mg, 54µmol) in 62% yield. IR (neat, cm$^{-1}$): 3520, 3275, 2915, 2870, 1641, 1549, 1454, 1250, 1026, 736, 697; $^1$H NMR (400 MHz, MeOD) $\delta$ 7.41 – 7.19 (m, 55H), 5.29 – 5.22 (m, 2H), 5.05 (s, 2H), 4.80 – 4.68 (m, 6H), 4.68 – 4.52 (m, 11H), 4.52 – 4.46 (m, 4H), 4.46 – 4.33 (m, 13H), 4.33 – 4.12 (m, 10H), 4.12 – 3.95 (m, 12H), 3.86 – 3.46 (m, 24H), 3.14 – 3.05 (m, 2H), 2.85 – 2.73 (m, 5H), 2.11 – 1.99 (m, 7H), 1.68 (d, J = 3.0 Hz, 8H), 1.53 – 1.42 (m, 2H), 1.42 – 1.23 (m, 4H); $^{31}$P NMR (162 MHz, MeOD) $\delta$ -0.7, -0.8, -0.8, -0.8, -1.2, -1.3; HRMS: [C$_{128}$H$_{153}$N$_7$O$_{33}$P$_2$ +2H$^+$] requires 1190.50815, found 1190.50915

1-O-tri(2-O-[3-O-{2-N-acetamido-3,4-di-O-benzyl-$\alpha$-D-galactopyranosyl}-2-N-acetamido-4,6-di-O-benzyl-$\beta$-D-galactopyranosyl}-3-O-benzyl-$sn$-glycerol-1-[2-cyanoethylphosphate])-N-benzylxoycarbonyl-6-aminohexanol (39)

Phosphoramidite 7 (0.05M in MeCN, 2.1 ml, 107µmol) and alcohol 38 (85mg, 36µmol) were coupled using the general procedure for phosphoramidite coupling. Automated reversed phase (C18, 10% $\rightarrow$ 100% MeOH/H$_2$O) column chromatography yielded spacer equipped trimer 39 (83mg, 24µmol) in 67% yield. IR (neat, cm$^{-1}$): 3522, 3285, 2920, 2868, 1653, 1557, 1454, 1254, 1024, 737, 696; $^1$H NMR (500 MHz, CD$_3$CN) $\delta$ 7.39 – 7.19 (m, 80H), 5.26 – 5.07 (m, 2H), 5.02 (s, 1H), 4.88 – 4.69 (m, 5H), 4.69 – 4.33 (m, 28H), 4.33 – 4.04 (m, 20H), 4.04 – 3.86 (m, 12H), 3.84 – 3.70 (m, 6H), 3.70 – 3.41 (m, 17H), 3.10 – 3.00 (m, 2H), 2.85 – 2.66 (m, 6H), 1.96 (s, 9H), 1.66 – 1.48 (m, 12H), 1.46 – 1.35 (m, 2H), 1.35 – 1.18 (m, 6H); $^{31}$P NMR (202 MHz, CD$_3$CN) $\delta$ -1.8, -1.9, -2.2, -2.3, -2.4, -2.5; HRMS: [C$_{185}$H$_{219}$N$_{10}$O$_{48}$P$_3$ +2H$^+$] requires 1722.72132, found 1722.72021.
1-O-(2-O-[3-O-[2-N-acetamido-3,4-di-O-benzyl-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl]-1-O-benzyl-sn-glycerol-3-[2-cyanoethylphosphate])]-N-benzyloxycarbonyl-6-aminohexanol (40)

Phosphoramidite 9 (0.2M in MeCN, 0.721 ml, 146µmol) and alcohol 36 (122mg, 97µmol) were coupled using the general procedure for phosphoramidite coupling. Size exclusion (Sephadex LH-20, DCM/MeOH, 1/1 v/v) column chromatography yielded spacer equipped monomer 40 (80mg, 61µmol) in 61% yield. IR (neat, cm⁻¹): 3499, 3283, 2934, 2866, 1659, 1549, 1454, 1254, 1026, 737, 698; ¹H NMR (400 MHz, CD₂CN) δ 7.41 – 7.24 (m, 30H), 6.58 (dd, J = 52.6, 9.1 Hz, 2H), 5.70 (s, 1H), 5.11 (d, J = 3.7 Hz, 1H), 5.03 (s, 2H), 4.82 (dd, J = 14.9, 11.1 Hz, 2H), 4.71 (d, J = 11.5 Hz, 1H), 4.61 – 4.37 (m, 11H), 4.18 – 4.01 (m, 10H), 4.01 – 3.87 (m, 9H), 3.79 (d, J = 11.0 Hz, 1H), 3.76 – 3.47 (m, 12H), 3.05 (s, 2H), 2.63 – 2.54 (m, 2H), 1.86 (s, 3H), 1.27 (s, 2H); ¹³C NMR (101 MHz, Acetone-d₆) δ 171.1, 171.0, 170.4, 157.2, 140.1, 139.7, 139.4, 138.5, 129.1, 128.9, 128.6, 128.5, 128.3, 128.3, 128.2, 128.1, 118.4, 118.3, 102.7, 95.7, 78.2, 77.6, 77.5, 77.3, 76.9, 75.3, 75.3, 75.1, 74.7, 74.1, 73.9, 73.8, 73.8, 73.3, 72.5, 69.6, 68.6, 68.5, 68.1, 68.0, 66.3, 63.0, 62.5, 55.5, 52.1, 50.3, 41.4, 30.8, 30.7, 30.5, 30.4, 30.2, 30.0, 29.8, 29.6, 29.5, 29.3, 26.8, 25.7, 23.6, 23.0, 19.9, 19.8, 31P NMR (162 MHz, CD₂CN) δ -1.8, -1.9; HRMS: [C₇₁H₈₇N₄O₁₈P +H] requires 1315.58257, found 1315.58421.

1-O-di(2-O-[3-O-[2-N-acetamido-3,4-di-O-benzyl-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl]-1-O-benzyl-sn-glycerol-3-[2-cyanoethylphosphate])]-N-benzyloxycarbonyl-6-aminohexanol (41)

Phosphoramidite 8 (73mg, 29µmol) and alcohol 40 (33mg, 25µmol) were coupled using the general procedure for phosphoramidite coupling. Automated reversed phase (C18, 10% → 100% MeOH/H₂O) column chromatography yielded spacer equipped dimer 41 (38mg, 16µmol) in 64% yield. IR (neat, cm⁻¹): 3275, 2926, 2866, 1637, 1558, 1456, 1252, 1026, 737, 698; ¹H NMR (500 MHz, CD₂CN) δ 7.40 – 7.20 (m, 55H), 6.66 (t, J = 9.3 Hz, 1H), 6.41 (t, J = 9.5 Hz, 1H), 6.31 (dd, J = 21.0, 8.7 Hz, 1H), 5.68 (s, 1H), 5.16 (dd, J = 5.8, 3.5 Hz, 1H), 5.10 (t, J = 3.3 Hz, 1H), 5.02 (s, 2H), 4.85 – 4.74 (m, 4H), 4.74 – 4.68 (m, 2H), 4.61 – 4.32 (m, 2H), 4.30 – 3.87 (m, 27H), 3.80 (d, J = 11.0 Hz, 1H), 3.76 – 3.40 (m, 21H), 3.05 (q, J = 6.7 Hz, 2H), 2.64 – 2.48 (m, 4H), 1.90 – 1.81 (m, 6H), 1.64 – 1.47 (m, 8H), 1.45 – 1.36 (m, 2H), 1.26 (d, J = 15.4 Hz, 4H); 31P NMR (202 MHz, CD₂CN) δ -0.4, -1.1, -1.3; HRMS: [C₁₂₈H₁₅₃N₇O₃₃P₂ +2H]²⁺ requires 1190.50815, found 1190.50890.
1-O-tri(2-O-[3-O-[2-N-acetamido-3,4-di-O-benzyl-α-D-galactopyranosyl]-2-N-acetamido-4,6-di-O-benzyl-β-D-galactopyranosyl]-1-O-benzyl(sn-glycerol-3-[2-cyanoethylphosphate])-N-benzylloxycarbonyl-6-aminohexanol (42)

Phosphoramidite 8 (42mg, 29µmol) and alcohol 41 (31mg, 13µmol) were coupled using the general procedure for phosphoramidite coupling. Automated reversed phase (C18, 10% → 100% MeOH/H2O) column chromatography yielded spacer equipped trimer 42 (30mg, 8.7µmol) in 67% yield. IR (neat, cm⁻¹): 3287, 3063, 2924, 2860, 1663, 1557, 1454, 1254, 1028, 739, 698; ¹H NMR (400 MHz, CD3CN) δ 7.41 – 7.14 (m, 80H), 6.74 (s, 3H), 6.46 – 6.26 (m, 3H), 5.68 (s, 1H), 5.20 – 5.06 (m, 3H), 5.02 (s, 2H), 4.87 – 4.65 (m, 12H), 4.62 – 4.29 (m, 40H), 4.29 – 3.85 (m, 40H), 3.85 – 3.42 (m, 35H), 3.05 (q, J = 6.4 Hz, 2H), 2.63 – 2.43 (m, 6H), 1.84 (dd, J = 8.3, 6.1 Hz, 9H), 1.63 – 1.44 (m, 11H), 1.40 (q, J = 9.1, 8.1 Hz, 2H), 1.25 (d, J = 18.9 Hz, 4H); ³¹P NMR (162 MHz, CD3CN) δ -0.6, -0.6, -1.3, -1.3, -1.4, -1.5, -1.5; HRMS: [C185H219N10O48P3 +2H]²⁺ requires 1722.72132, found 1722.72097.

1-O-(2-O-[3-O-[2-N-acetamido-α-D-galactopyranosyl]-2-N-acetamido-β-D-galactopyranosyl]-sn-glycerol-1-phosphate)-6-aminohexanol (1)

Spacer equipped pseudotrisaccharide monomer 37 was deprotected using the general procedure for global deprotection. Purification yielded deprotected 1 in 73% yield. Intermediate 43: ³¹P NMR (202 MHz, MeOD) δ 0.65; HRMS: [C₆₉H₈₂N₃O₁₈P +H] requires 1262.55603, found 1262.55694. Product 1: ¹H NMR (500 MHz , D₂O) δ 5.03 (d, J = 3.8 Hz, 1H), 4.68 (d, J = 8.5 Hz, 1H), 4.18 (dd, J = 11.0, 3.7 Hz, 1H), 4.08 (d, J = 3.1 Hz, 1H), 4.06 – 3.99 (m, 2H), 3.97 (d, J = 2.9 Hz, 1H), 3.94 – 3.87 (m, 1H), 3.86 – 3.66 (m, 11H), 3.66 – 3.59 (m, 2H), 2.95 (t, J = 7.1 Hz, 2H), 2.05 (s, 3H), 2.00 (s, 3H), 1.68 – 1.57 (m, 4H), 1.42 – 1.33 (m, 4H); ³¹P NMR (202 MHz, D₂O) δ 0.7; HRMS: [C₂₅H₄₈N₃O₁₆P +H] requires 678.28450, found 678.28411.

1-O-di(2-O-[3-O-[2-N-acetamido-α-D-galactopyranosyl]-2-N-acetamido-β-D-galactopyranosyl]-sn-glycerol-1-phosphate)-6-aminohexanol (2)

Spacer equipped pseudotrisaccharide dimer 38 was deprotected using the general procedure for global deprotection. Purification yielded deprotected 2 in 57% yield. Intermediate 44: ³¹P NMR (162 MHz, MeOD) δ 0.50, 0.33; HRMS: [C₁₂₂H₁₄₇N₅O₃₃P₂ +2H]²⁺ requires 1137.48161, found 1137.48890. Product 2: ¹H NMR (500 MHz, D₂O) δ 5.02 (t, J = 3.4 Hz, 2H), 4.68 (dd, J = 16.5, 8.5 Hz, 2H), 4.18 (dd, J = 11.0, 3.7 Hz, 2H), 4.11 – 3.58 (m, 37H), 2.96 (t, J = 7.4 Hz, 2H), 2.06 (s, 6H), 2.00 (s, 6H), 1.69 – 1.58 (m, 4H), 1.44 – 1.34 (m, 4H);
$^{31}$P NMR (202 MHz, D$_2$O) δ 0.7, 0.2; HRMS: [C$_{44}$H$_{81}$N$_5$O$_{31}$P$_2$ +H] requires 1238.44635, found 1238.44631.

1-O-tri(2-O-[3-O-{2-N-acetamido-α-D-galactopyranosyl}-2-N-acetamido-β-D-galactopyranosyl]-sn-glycerol-1-phosphate)-6-aminohexanol (3)

Spacer equipped pseudotrisaccharide trimer 39 was deprotected using the general procedure for global deprotection. Purification yielded deprotected 3 in 44% yield. Intermediate 45: $^{31}$P NMR (162 MHz, MeOD) δ 0.34, 0.25, 0.15; HRMS: [C$_{176}$H$_{210}$N$_7$O$_{48}$P$_3$ +2H]$^{2+}$ requires 1643.18151, found 1643.18103. Product 3: $^1$H NMR (500 MHz, D$_2$O) δ 5.08 – 4.97 (m, 3H), 4.73 – 4.63 (m, 3H), 4.18 (dd, J = 11.0, 3.7 Hz, 3H), 4.12 – 3.56 (m, 55H), 2.97 (t, J = 7.6 Hz, 2H), 2.07 (d, J = 6.1 Hz, 9H), 2.00 (s, 9H), 1.69 – 1.57 (m, 4H), 1.46 – 1.33 (m, 4H); $^{13}$C NMR (151 MHz, D$_2$O) δ 174.8, 174.7, 174.7, 174.5, 174.5, 174.5, 100.8, 93.6, 93.5, 93.2, 79.1, 79.1, 78.9, 78.9, 75.1, 74.9, 74.8, 74.5, 74.5, 71.2, 71.2, 70.0, 70.0, 68.2, 67.8, 67.8, 67.6, 67.5, 67.4, 66.0, 65.9, 64.7, 64.4, 64.3, 64.0, 63.7, 63.6, 63.4, 61.2, 61.0, 60.7, 50.8, 50.7, 49.2, 39.3, 29.4, 29.3, 26.5, 25.0, 24.3, 22.3, 22.3, 21.9, 21.9; $^{31}$P NMR (202 MHz, D$_2$O) δ 0.7, 0.2, 0.2; HRMS: [C$_{63}$H$_{114}$N$_7$O$_{46}$P$_3$ +2H]$^{2+}$ requires 899.80774, found 899.80953.

1-O-(2-O-[3-O-{2-N-acetamido-α-D-galactopyranosyl}-2-N-acetamido-β-D-galactopyranosyl]-sn-glycerol-3-phosphate)-6-aminohexanol (4)

Spacer equipped pseudotrisaccharide monomer 40 was deprotected using the general procedure for global deprotection. Purification yielded deprotected 4 in 45% yield. Intermediate 46: $^{31}$P NMR (202 MHz, MeOD) δ 0.46; HRMS: [C$_{68}$H$_{84}$N$_3$O$_{18}$P +H] requires 1262.55603, found 1262.55687. Product 4: $^1$H NMR (500 MHz, D$_2$O) δ 5.03 (d, J = 3.8 Hz, 2H), 4.65 (d, J = 8.5 Hz, 1H), 4.18 (dd, J = 11.0, 3.7 Hz, 1H), 4.07 (d, J = 3.0 Hz, 1H), 4.05 – 3.90 (m, 5H), 3.85 (q, J = 6.4 Hz, 2H), 3.83 – 3.57 (m, 11H), 2.95 (t, J = 7.6 Hz, 2H), 2.02 (s, 3H), 2.00 (s, 3H), 1.69 – 1.57 (m, 4H), 1.44 – 1.34 (m, 4H); $^{31}$P NMR (202 MHz, D$_2$O) δ 0.7; HRMS: [C$_{25}$H$_{48}$N$_3$O$_{18}$P +H] requires 678.28450, found 678.28431.

1-O-di(2-O-[3-O-{2-N-acetamido-α-D-galactopyranosyl}-2-N-acetamido-β-D-galactopyranosyl]-sn-glycerol-3-phosphate)-6-aminohexanol (5)

Spacer equipped pseudotrisaccharide dimer 41 was deprotected using the general procedure for global deprotection. Purification yielded deprotected 5 in 49% yield. Intermediate 47: $^{31}$P NMR (202 MHz, MeOD) δ 0.43, 0.21; HRMS: [C$_{122}$H$_{147}$N$_5$O$_{33}$P$_2$ +2H]$^{2+}$ requires 1137.48161, found 1137.48287. Product 5: $^1$H NMR (500 MHz, D$_2$O) δ 5.03 (d, J = 3.6 Hz, 2H), 4.70 – 4.62 (m, 2H), 4.17 (dd, J = 11.0, 3.6 Hz, 2H), 4.09 – 3.89 (m, 15H), 3.89 – 3.58
(m, 20H), 2.96 (t, J = 7.5 Hz, 2H), 2.04 (s, 3H), 2.02 (s, 3H), 2.00 (s, 6H), 1.70 – 1.58 (m, 4H), 1.45 – 1.35 (m, 4H); $^{31}$P NMR (202 MHz, D$_2$O) δ 0.7, 0.3; HRMS: $[C_{44}H_{81}N_5O_{31}P_2 + H]^{+}$ requires 1238.44635, found 1238.44620.

1-O-tri(2-O-[3-O-{2-N-acetamido-α-D-galactopyranosyl}-2-N-acetamido-β-D-galactopyranosyl]-sn-glycerol-3-phosphate)-6-aminohexanol (6)

Spacer equipped pseudotrisaccharide trimer 42 was deprotected using the general procedure for global deprotection. Purification yielded deprotected 6 in 56% yield. Intermediate 48: $^{31}$P NMR (162 MHz, MeOD) δ 0.41; HRMS: $[C_{176}H_{210}N_7O_{48}P_3 + 2H]^2^{+}$ requires 1643.18151, found 1643.18546. Product 6: $^1$H NMR (500 MHz, D$_2$O) δ 5.03 (d, J = 3.7 Hz, 3H), 4.69 – 4.63 (m, 3H), 4.17 (dd, J = 11.0, 3.6 Hz, 3H), 4.09 – 3.89 (m, 27H), 3.89 – 3.57 (m, 30H), 2.97 (t, J = 7.5 Hz, 2H), 2.04 (s, 6H), 2.02 (s, 3H), 2.00 (s, 9H), 1.69 – 1.57 (m, 4H), 1.43 – 1.37 (m, 4H); $^{13}$C NMR (151 MHz, D$_2$O) δ 174.7, 174.5, 174.5, 174.5, 101.3, 101.2, 93.4, 93.3, 79.6, 79.6, 79.4, 79.4, 75.1, 75.0, 74.9, 74.8, 74.7, 71.2, 70.1, 68.2, 67.9, 67.6, 67.5, 66.1, 66.0, 64.5, 64.3, 63.6, 63.5, 61.0, 60.8, 60.5, 60.4, 50.9, 50.8, 49.3, 49.2, 39.3, 29.3, 29.3, 26.5, 25.0, 24.3, 22.3, 22.1, 21.9; $^{31}$P NMR (202 MHz, D$_2$O) δ 0.7, 0.3; HRMS: $[C_{63}H_{114}N_7O_{46}P_3 + 2H]^2^{+}$ requires 899.80774, found 899.80953.

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Supplementary data

Supplementary data ($^1$H, $^{13}$C, $^{31}$P NMR spectra) associated with this article can be found, in the online version, at ...