Synthesis of ribitol phosphate based wall teichoic acids

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Synthesis of glycosylated ribitol phosphates and their binding to human langerin

INTRODUCTION

The skin provides the first line of defense against microbes and the skin immune system relies on a rich network of professional antigen-presenting dendritic cells (DCs) on the epidermis and dermis.[1-2] Langerhans cells (LCs) are a subset of DCs, present in the epidermis and they express high levels of langerin, a CD207 C-type lectin receptor[3], which aids in the detection of invading pathogens by binding to pathogen-associated molecular patterns (PAMPs). Langerin is involved in the detection and uptake of a wide set of pathogens, including viruses like HIV[4] and measles[5], fungi[6], and (myco)bacteria.[7] Langerin is a type II C-type lectin receptor that has been shown to bind mannose, fucose, glucose, galactose-6-phosphate as well as *N*-acetyl glucosamine and sulfated heparin disaccharides, in a calcium dependent manner through its carbohydrate-recognition domain.[8]

Ali, S., Hendriks, A., van Dalen, R., Bruyning, T., Meeuwenoord, N., Overkleeft, H., Filippov, D., van der Marel, G., van Sorge, N., Codée, J.D.C., (Automated) Synthesis of Well-defined Staphylococcus Aureus Wall Teichoic Acid Fragments. *Chem. Eur. J.* **2021**, 27 (40): 10461-10469.

Staphylococcus aureus (*S. aureus*) is a commensal bacterium residing on our skin and LCs play a crucial role in the host defence against the bacterium. The cell wall of *S. aureus* is densely functionalized with wall teichoic acids (WTAs), ribitol phosphate (RboP) polymers decorated with *N*-acetyl glucosamine (GlcNAc) and D-alanine residues. As described in Chapter 1 and 2, WTAs are involved in host interaction, biofilm formation, cation homeostasis and autolysin activity. It has previously been shown that langerin can recognize β-GlcNAc modifications on *S. aureus* contributing to LC activation and production of Th1- and Th17-polarizing cytokines, while α-GlcNAcylation was found to impair langerin interaction, weakening the functional response of LCs.[9] This latter finding implies that *S. aureus* can modulate immune detection and subsequent inflammation in the epidermis. van Dalen *et al.*[9] reported langerin as the first human innate receptor to discriminate between the α-GlcNAc and β-GlcNAc modifications. Unraveling the interactions of *S. aureus* WTAs and langerin at the molecular level is of importance for the development of a vaccine specifically targeting skin and soft tissue infections and may also open up possibilities for the targeted delivery of vaccines.[10-11]

Since the isolation of WTA from bacterial sources results in heterogenous fragments with possible bacterial contaminations, the synthesis of well-defined fragments is of great interest. This Chapter describes the synthesis of a set of glycosylated ribitol phosphate oligomers, varying in length of the ribitol phosphate chain as well as the substitution pattern. Both C-4-α- and C-4-β-GlcNAc are incorporated (Fig 1). The GlcNAc-WTAs fragments will be equipped with an aminohexanol linker that serves as a ligation handle to attach the molecules to surfaces, biotin affinity handles or carrier proteins for example. The short trimer fragments are intended for future crystallization studies. These latter fragments lack the flexible spacer entity as its presence may hamper crystallization.

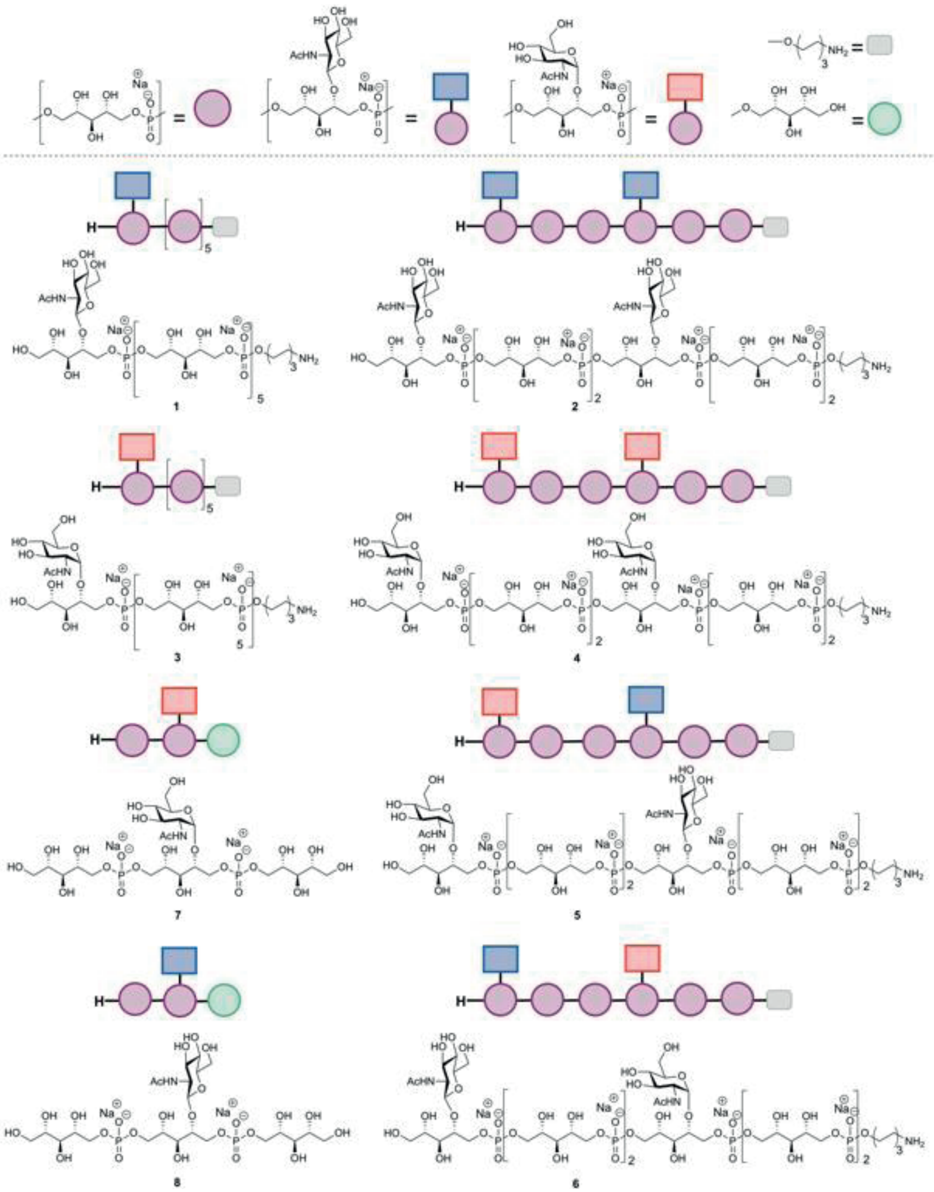


Figure 1. Library of glycosylated ribitol phosphates targeted in this Chapter.

RESULTS AND DISCUSSION

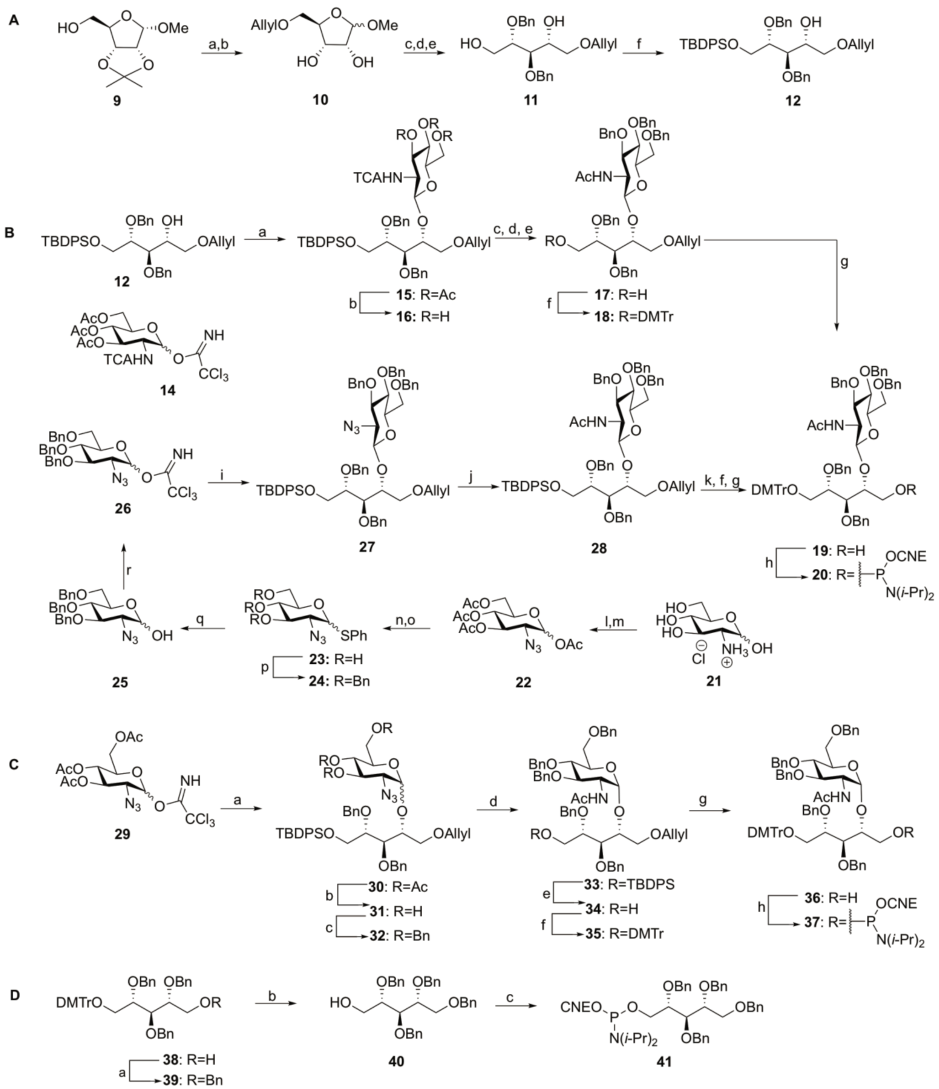
As discussed in Chapter 1, a team at Sanofi Pasteur synthesized two octamers with either an α- or a β-GlcNAc on the C-4 of each ribitol phosphate moiety and a nonamer bearing a C-3 β-GlcNAc on each ribitol phosphate repeating unit using a block coupling approach.[12] The spacer was installed in the last coupling event to the ribitol phosphate chain, on the opposite position on the WTA chain with respect to the peptidoglycan binding site. Jung *et al.*[13] also used a block approach to generate ribitol phosphate tetramers bearing an α- or β-GlcNAc moiety at C-4 of the RboP motifs, and D-alanine amides at C-2. This Chapter outlines a strategy for the assembly of well-defined WTA fragments based on repetitive coupling cycles using monomeric RboP building blocks to allow for maximum flexibility in terms of substitution patterns that can be targeted. The spacer will be attached at the site of the WTA chain where the peptidoglycan is attached in the bacterial structures.

Scheme 1 depicts the synthesis of the required phosphoramidite building blocks **20**, **37**, and **41**, which will be used alongside building block **42** (Scheme 2), the synthesis and use of which has been described in Chapter 2. Scheme 1A shows the synthesis of C4-OH ribitol **12**, and starts from compound **9** by allylation of the primary alcohol, followed by isopropylidene hydrolysis to yield **10**. Benzylation and ensuing acidic hydrolysis of the methyl riboside yielded the corresponding hemi-acetal intermediate and subsequent ring opening using sodium borohydride provided primary alcohol **11**. Protection with a TBDPS group then gave acceptor **12.** Two approaches were explored to introduce the β-GlcNAc as shown in scheme 1B. In the first approach, acceptor **12** was coupled with trichloroacetimidate donor **14**. The TCA protecting group on the glucosamine donor can participate in the stabilization of the oxocarbenium ion formed upon activation of the donor, forcing the nucleophilic attack to the other side of the pyranose ring leading to the desired β-product and coupling of acceptor **12** and donor **14** afforded the desired β-product **15** in 92% yield. Subsequent deacetylation under Zemplén conditions yielded triol **16**, after which the alcohols were benzylated. To avoid benzylation of the trichloroacetamide the reaction was kept at 0ºC although this also led to slower and incomplete conversion of the starting material. The TCA was removed using $CsCO_3$ in DMF at 70ºC,[14] followed by acetylation of the free amine and TBAF mediated TBDPS removal to yield β-product **17** in 42% over 4 steps. The primary alcohol was protected with a DMTr group in 53% yield, after which an iridium catalyzed allyl isomerization and iodine mediated enol ether hydrolysis delivered alcohol **19** in 79%. Equipment of the alcohol with a cyanoethyl protected phosphoramidite yielded key building block **20** for the upcoming oligomerization. Although the TCA protecting group served well to provide a β-selective glycosylation reaction, its undesired reactivity in the benzylation reaction and relatively difficult removal made the assembly of **20** using donor **14** suboptimal. To circumvent the use of a TCA group, a second route was developed in which glucose azide **26** was coupled to acceptor **12**. This donor[15] was synthesized starting from commercially available glucosamine **21**, of which the amine was masked with an azide using Stick's reagent[16] after which acetylation gave **22**. Subsequent introduction of a thiophenol and deacetylation under Zemplén conditions led to compound **23** in 56% over 2 steps. Benzylation of the free alcohols gave **24** in 98% yield and hydrolysis of the anomeric thiophenyl gave hemiacetal **25** in 62% yield. The hemiacetal was equipped with an imidate moiety, completing the synthesis of donor **26**. The use of acetonitrile as a β-directing solvent in combination with a low reaction temperature ensured the stereoselective formation of the desired β-glucosamine linkage and **27** was obtained in 85%.[17-24] Propanedithiol mediated azide reduction, followed by acetylation delivered acetamide **28** in 59% over 2 steps and removal of the TBDPS afforded alcohol **19** in 68% yield. Overall this latter route proved significantly more efficient than the route using TCA-donor **14**.

The synthesis of amidite **37**, bearing the α-GlcNAc appendage is shown in Scheme 1C. Azide donor **29** was coupled with acceptor **12** to yield **30** as a 7:1 α/β mixture. The two anomers could be separated after Zemplén deacetylation, leading to the pure α-product **31** in 70% yield.[25] Benzylation of the liberated alcohols, followed by Staudinger reduction and subsequent acetylation of the amine yielded **33** in 89% yield over 3 steps. Removal of the TBDPS group gave **34** in 86% yield and protection of the primary alcohol with a DMTr group afforded **35**. Allyl removal as described above yielded the primary alcohol **36** which was functionalized with a cyanoethyl phosphoramidite to give the second key building block **37** in 81% yield.

Where the spacer is required for conjugation and biological purposes, it may impede crystallization studies. Therefore, a terminal building block was generated with a benzyl group at the terminating alcohol. To this end phosphoramidite **41** was assembled by benzylation of alcohol **38** which was followed by detritylation to yield intermediate **40** in 66% over 2 steps. Conversion into the amidite yielded **41**.

With all the required phosphoramidites in hand, the stage was set to assemble the target library (Fig 1). Scheme 2A schematically depicts the assembly of the fragments. For the elongation of the oligomers, the condensation procedure described in Chapter 2 was employed: in the first step the phosphoramidite is activated by DCI, after which the activated group is replaced by the incoming alcohol of the growing chain to yield the phosphite triester. Subsequent oxidation using CSO affords the phosphate triester, after which a detritylation step using 3% DCA in DCM liberates the alcohol for the next coupling event. Purification was achieved by size exclusion or silica gel column chromatography.

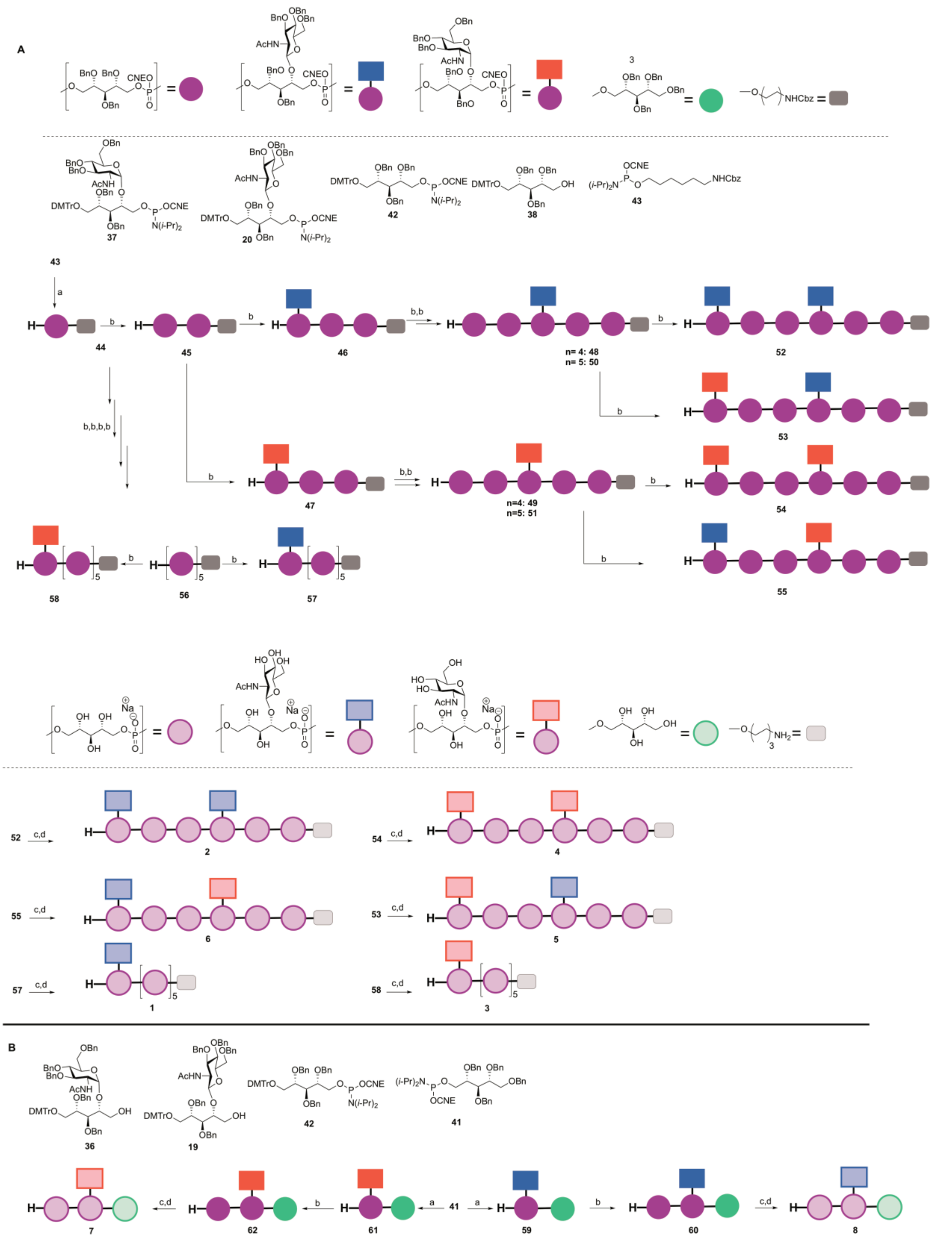


Scheme 1. A Building block synthesis; *Reagents and conditions:* a) AllylBr, NaH, THF/DMF (v/v= 7/1), 0ºC to rt; b) AcOH/H_2O (v/v= 1/1), 50ºC, 300 mbar, 62% 2 steps; c) BnBr, NaH, THF/DMF (v/v= 7/1), 0ºC to rt; d) 4M HCl dioxane, 80ºC; e) $NaBH_4$, MeOH, 0ºC, 50% over 3 steps; f) TBDPSCl, TEA, DCM 0ºC to rt, 95%.
B Building block synthesis; *Reagents and conditions:* a) **14**, TMSOTf, DCM, 0ºC, 92%; b) NaOMe, MeOH, 85%; c) BnBr, NaH, DMF, 0ºC; d) i. $CsCO_3$, DMF, 70ºC; ii. Ac_2O, pyridine; e) TBAF, THF, rt, 42% 4 steps; f) DMTrCl, TEA, DCM, 53%; g) i. Ir(COD)$(Ph_2MeP)_2PF_6$, H_2, THF, ii. I_2, sat. aq. $NaHCO_3$, THF, 79%; h) 2-cyanoethyl-*N,N*-diisopropylchlorophosphoramidite, DIPEA, DCM, 78%; i) **12**, TMSOTf, ACN, -40°C to 0°C, 85%; j) propane dithiol, pyridine, H_2O, TEA, rt; ii. Ac_2O, pyridine, 59% 2 steps; k) TBAF, THF, rt, 68%; l) Stick reagent, K_2CO_3, $CuSO_4{\cdot}5\ H_2O$, MeOH; m) Ac_2O, pyridine, 99% over 2 steps; n), PhSH, $BF_3{\cdot}OEt_2$, DCM; o) NaOMe, MeOH, 56% over 2 steps; p) BnBr, NaH, THF/DMF (v/v= 1/1), 98%; q) NBS, acetone, 62%; r) TCAN, K_2CO_3, DCM, 89%. **C Building block synthesis;** *Reagents and conditions:* a) **12**, TMSOTf, DCM, rt, 92%, α/β (7:1); b) NaOMe, MeOH, rt, 70% α-anomer; c) BnBr, NaH, THF/DMF (v/v= 7/1), 0ºC to rt, 73%; d) i. PMe_3, KOH, THF; ii. Ac_2O, pyridine, 89% 2 steps; e) TBAF, THF, rt, 86%; f) DMTrCl, TEA, DCM, 78%; g) i. Ir(COD)$(Ph_2MeP)_2PF_6$, H_2, THF, ii. I_2, sat. aq. $NaHCO_3$, THF, 88%; h) 2-cyanoethyl-*N,N*-diisopropylchlorophosphoramidite, DIPEA, DCM, 81%.
D Building block synthesis; *Reagents and conditions:* a) BnBr, NaH, THF/DMF (v/v= 7/1) 0°C to rt, 84%; b) 3% DCA in DCM, 87%; c) 2-cyanoethyl-*N,N*-diisopropylchlorophosphoramidite, DIPEA, DCM, 82%.

As described in Chapter 2, alcohol **38** was coupled with spacer phosphoramidite **43** to give monomer **44**. Detritylation then set the stage for a second coupling cycle with amidite **42** to deliver dimer **45**, which was coupled to β-GlcNAc amidite **20** or α-GlcNAc amidite **37** to give trimers **46** and **47**. Both trimers were extended by two coupling cycles using **42** to yield pentamers **50** and **51**. Both pentamers were coupled to **20** or **37** yielding four double glycosylated hexamers **52**, **53**, **54**, **55** with a different substitution pattern. In addition, unsubstituted pentamer **56** (Chapter 2) was coupled to amidite **20** and **37** to yield hexamers **57** and **58** bearing a single terminal GlcNAc moiety. Global deprotection using aqueous ammonia and subsequent hydrogenolysis of the semi protected fragments yielded hexamers **1**, **2**, **3**, **4**, **5**, and **6**.

Scheme 2B depicts the generation of the α- and β-GlcNAc trimers, designed for crystallization studies. Phosphoramidite **41** was coupled to α- and β-GlcNAc ribitol alcohol **36** and **19** giving dimers **59** and **61,** which were coupled with amidite **42** to afford trimers **60** and **62**. Global deprotection as described above yielded trimers **7** and **8**.

To study the interactions of glycosylated and non-glycosylated WTAs with human langerin, a micro array interaction study was undertaken. As previously reported by van der Es *et al.*,[26] teichoic acid (TA) micro arrays can be employed to rapidly report on the sequence binding specificity of biomolecules interaction with TAs. Thus, amino spacer functionalized WTA fragments **1**-**5** as well as non-glycosylated trimer **63**, tetramer **64**, octamer **65**, and dodecamer **66** (Chapter 2) were coupled to epoxide functionalized micro array slides and the generated arrays were interrogated using langerin-FITC.[8, 27] As can be seen in Figure 2, the WTAs that bear a β-GlcNAc show selective binding to langerin, with fragment **2** having 2 β-GlcNAcs showing highest binding. The α-GlcNAc WTAs (**3**, **4**) did not bind to langerin, nor did the unsubstituted WTAs (**63** - **66**). WTA **5** that bears an α- and a β-GlcNAc shows binding comparable to the mono-β-GlcNAc WTA **1**. The array clearly reveals that langerin does not bind to the RboP-backbone and that a β-GlcNAc is required for binding. These results support the data of van Dalen *et al.*[9], who studied binding of langerin-FITC to a panel of *S. aureus* strains, expressing either the glycosyltransferase TarM or TarS, responsible for the introduction of WTA-α- and WTA-β-GlcNAc residues, respectively. It was shown that the knock-out of both enzymes (ΔTarS/TarM) decreased langerin binding compared to the wild-type indicating that a GlcNAc is required for binding. The ΔTarM species showed increased binding to langerin compared to the *S. aureus* wild-type, while the ΔTarS bacterium showed 7-8 fold lower binding compared to the wild type. These results showed that at the bacterial level the WTA β-GlcNAc is required for langerin binding and that the α-GlcNAc-moieties could hinder langerin binding. The micro array results confirm langerin WTA β-GlcNAc binding at the molecular level, and show that a single α-GlcNAc-residue (as in **5**) does



Scheme 2. WTA hexamer assembly **A**; *Reagents and conditions:* a) i. DCI, ACN, **38**; ii. CSO; iii. 3% DCA in DCM, **44**: 85%; b) i. DCI, ACN, phosphoramidite **20** or **37** or **42**; ii. CSO; iii. 3% DCA in DCM, **45**: 74%, **47**: 53%, **46**: 88%, **49**: 82%, **48**: 90%, **51**: 89%, **50**: 68%, **54**: 88%, **52**: 79%, **53**: 76%, **55**: 61%, **58**: 73%, **57**: 85%; c) i. NH_3 (30-33% aqueous solution), dioxane; d) Pd black, H_2, AcOH, H_2O/dioxane, **4**: 55%, **2**: 78%, **5**: 88%, **6**: 16%, **3**: 96%, **1**: 68%;
WTA trisaccharide assembly **B**: a) i. DCI, ACN, alcohol **36** or **19**, **61**: 80%, **59**: 46%; b) i. DCI, ACN, amidite **42**, **60**: 91%, **62**: 91%; c) i. NH_3 (30-33% aqueous solution), dioxane; d) Pd black, H_2, AcOH, H_2O/dioxane, **7**: 90%, **8**: 85%.

not adversely affect interaction of the C-type lectin with the WTA β-GlcNAc-moieties. The differences between the *S. aureus* study of van Dalen *et al*. and the here presented results may be explained by the different number of GlcNAc residues per RboP unit and/or the difference in density of the WTAs on the array *vs* the bacterial cell wall. In addition, D-alanine residues may also play a role in WTA-langerin interaction.

A

B

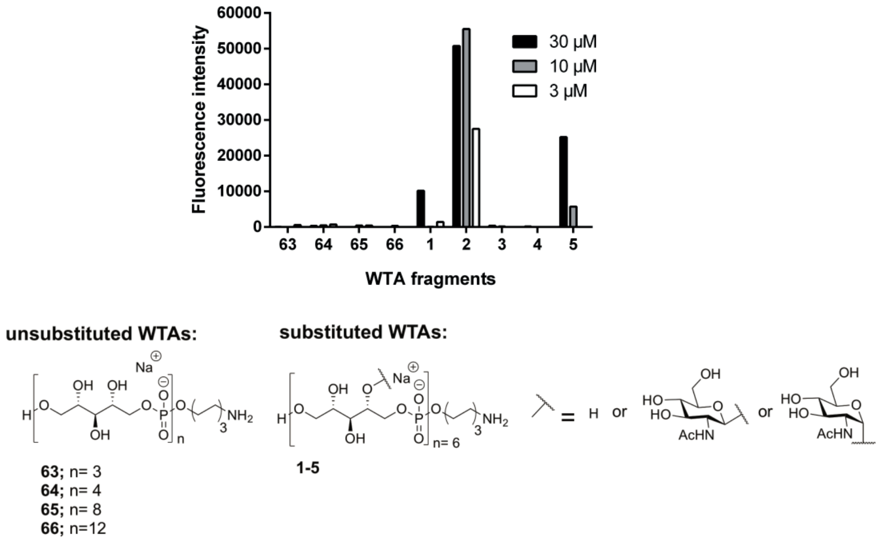


Figure 2. A) Human langerin binding on a RboP micro array. X-as represents the WTA fragments printed with 3 different concentrations on the slide; B) WTA fragments included on micro array for their langerin binding.

To further probe langerin WTA binding with fragments having a higher density of GlcNAc residues, an assay using WTA functionalized magnetic beads was employed. Thus, as described in Chapter 2, the biotinylated non-glycosylated RboP-hexamer and RboP-dodecamer were enzymatically glycosylated using the enzymes TarS, TarM and TarP generating β-(1,4)-GlcNAc-WTA, α-(1,4)-GlcNAc-WTA and β-(1,3)-GlcNAc-WTA respectively, which were then captured on streptavidin functionalized beads. Figure 3 shows langerin-FITC binding to these beads and reveals that both the β-(1,4)- and β-(1,3)-GlcNAc-WTAs are recognized by langerin, with equal binding efficiency. The dodecamer shows significantly higher binding than the hexamers. Thus, although the microarray has indicated that a single β-GlcNAc can already provide langerin binding, the presence of more copies of the sugar ligand on the RboP chains leads to stronger binding with the lectin.

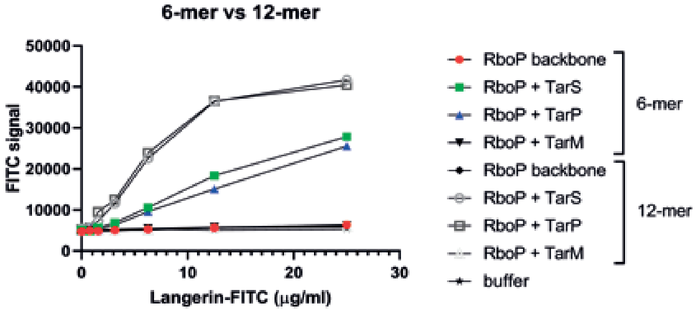


Figure 3. Magnetic beads functionalized with enzymatically glycosylated 6-mer and 12-mer can bind langerin in an anomeric configuration dependent manner.

CONCLUSION AND OUTLOOK

This Chapter described the successful synthesis of a set of C-4 glycosylated WTAs on milligram scale. Here, the phosphoramidite chemistry developed in Chapter 2 was further extended by synthesizing α- and β-linked C4-GlcNAc ribitol phosphoramidite building blocks. The synthetic route towards β-glycosylated amidites was realized following two approaches with different donors. The trichloroacetamide protecting group, chosen for the excellent beta selectivity during the glycosylation reaction, showed to be less optimal for the overall efficiency in the rest of the route. It presented an obstacle during the benzylation and its removal proved challenging. Meanwhile, the glucose azide donor, bearing a non-participating group on the C-2 gave excellent beta-selectivity in a nitrile-assisted glycosylation reaction and no further laborious steps in the synthesis route were encountered, making the approach using this latter donor the preferred one to generate the required building block on multigram scale. The activity of the synthesized WTAs towards langerin has been established on a micro array platform and it was found that langerin binds in selective manner to the β-epitope. A similar outcome was found using WTA-functionalized beads, carrying TarS, TarM or TarP modified synthetic ribitol phosphate hexa- or dodecamers. The α-GlcNAc WTA beads did not capture langerin, while the β-GlcNAc functionalized beads effectively bound the C-type lectin. The position of the GlcNAc on the ribitol phosphates seems to be of less importance for binding. These results clearly demonstrate β-GlcNAc-WTA to be an epitope for human langerin. Establishing the molecular interaction of langerin and *S. aureus* using well-defined WTA fragments is of great importance for the development of treatments against *S. aureus* soft skin and tissue infections. The activity of the glycosylated WTA-fragments against monoclonal antibodies will be presented in Chapter 4 to reveal the role of these antigens in adaptive immunity.

EXPERIMENTAL SECTION

General information

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_2SO_4 in ethanol or with a solution of $(NH_4)_6Mo_7O_{24}\cdot4H_2O$ 25 g/L and $(NH_4)_4Ce(SO_4)_4\cdot2H_2O$ 10 g/L, in 10% aqueous H_2SO_4 followed by charring at +/- 140°C. Some unsaturated compounds were visualized by spraying with a solution of $KMnO_4$ (2%) and K_2CO_3 (1%) in water. Optical rotation measurements ($[\alpha]_D^{20}$) were performed on an Anton Paar Modular Circular Polarimeter MCP 100/150 with a concentration of 10 mg/mL (*c* 1), unless stated otherwise. Infrared spectra were recorded on a Shimadzu FT-IR 8300. ^1H, ^{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°C) 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).

Phosphoramidite coupling, oxidation, and detritylation

The starting alcohol was co-evaporated 2 times with toluene before being dissolved in acetonitrile (ACN, 0.15 M). 4,5-dicyanoimidazole (DCI) (1.6-2.4 eq; 0.25 M in ACN) was added and the mixture was stirred over freshly activated molecular sieves under an argon atmosphere for 20 min. Then phosphoramidite (1.3-2.0 eq; 0.20 M) was added and the mixture was stirred at rt until total conversion of the starting material (15 - 45 min). Subsequently, (10-camphorsulfonyl)oxaziridine (CSO) (2.0 eq; 0.5 M in ACN) was added and the stirring was continued for 15 min. The mixture was diluted with DCM and washed with a 1:1 solution of saturated $NaCl/NaHCO_3$. The water layer was extracted 3 times with DCM and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was dissolved in DCM, DCA was added (5 eq; 0.18 M in DCM), and the mixture was stirred at rt. After 40–60 min an aqueous solution of methanol (1:1) was added, stirred for an additional 30-40 min, and diluted with DCM.

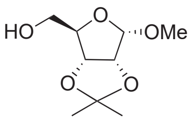
The organic layer was washed with saturated NaCl/$NaHCO_3$ solution (1:1), the water layer was extracted 3 times with DCM, and the combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by either flash chromatography (DCM/acetone) or size exclusion chromatography (sephadex LH-20, MeOH/DCM, 1/1).

3

General procedure for global deprotection

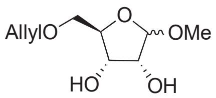
The oligomer was dissolved in a 1:1 solution of NH_3 (30-33% aqueous solution) and dioxane (1.2-2.4 mM) and stirred overnight. The mixture was concentrated *in vacuo* and loaded on a Dowex Na^+ cation-exchange resin (50WX4-200, stored on 0.5 M NaOH, flushed with H_2O and MeOH before use) column and flushed with water/dioxane (1:1). The fractions were then concentrated *in vacuo*, dissolved in water/dioxane (2 ml per 10 µmol) and 4 drops of glacial AcOH were added. After purging the mixture with argon, Pd black was added (32-59 mg), and the mixture was repurged with N_2. The mixture was stirred under hydrogen gas for 3 - 7 days, filtered over celite, and concentrated *in vacuo*. The crude product was purified by size-exclusion chromatography (Toyopearl HW-40, NH_4OAc buffer) and the fractions were concentrated. The product was co-evaporated repeatedly with MilliQ water to remove NH_4OAc/ NH_4HCO_3 traces and eluted through a Dowex Na^+ cation-exchange resin column, and lyophilized.

Methyl 2,3-*O*-isopropylidene-α-D-ribofuranoside (9)



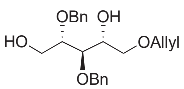
D-Ribose (40.0 g; 266 mmol; 1.0 eq.) was dissolved in MeOH (950 ml; 0.28 M) and AcCl (5.7 ml; 0.3 eq.) was added and the mixture was stirred for 2h at rt. Then the mixture was quenched with Na_2CO_3, filtrated and concentrated. The crude was dissolved in acetone (750 ml, 0.35 M), HCl (16 ml) was added and the mixture was stirred overnight at rt. The mixture was quenched with Na_2CO_3, filtrated and concentrated under reduced pressure. Column purification pentane/EtOAc 9:1 to 6:4 pentane/EtOAc afforded the title compound **9** in 72% over 2 steps (39.0 g; 190.9 mmol). IR (neat, cm^{-1}): 3431, 2988, 2940, 1456, 1373, 1089, 1040, 866; ^1H NMR (400 MHz, $CDCl_3$) δ= 1.32 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 3.33 (dd, 1H, *J*= 10.0 Hz, 3.2 Hz, O*H*), 3.43 (d, 3H, *J*= 2.8 Hz, CH_3O), 3.59 - 3.70 (m, 2H, H-5), 4.41 (d, 1H, *J*= 2.8 Hz, H-4), 4.58 - 4.60 (m, 1H, H-3), 4.82 - 4.84 (m, 1H, H-2), 4.97 (d, 1H, *J*= 2.4 Hz, H-1); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 24.7, 26.4 (CH_3), 55.5 (CH_3O), 64.0 (C-5), 81.5 (C-2), 85.8 (C-3), 88.3 (C-4), 109.9 (C-1), 112.1 (Cq); HRMS: $[M+Na]^+$ calculated for $C_9H_{16}O_5Na$ 227.0895, found 227.0896.

Methyl 5-*O*-allyl-α/β-D-ribofuranoside (10)



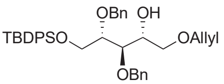
Compound **9** (38.7 g; 189 mmol; 1.0 eq.) was dissolved in a mixture of THF/DMF (540 ml; 0.35 M; v/v= 7/1). The mixture was cooled to 0°C and NaH (11.3 g; 284 mmol; 1.5 eq.) was added in portions followed by dropwise addition of AllylBr (24.5 ml; 284 mmol; 1.5 eq.) and the mixture was allowed to warm up to rt and was stirred overnight. Then the mixture was quenched with MeOH at 0°C and diluted with Et_2O. The organic layer was washed 5x with H_2O, 1x with brine, dried over $MgSO_4$, filtrated and concentrated under reduced pressure. The crude was dissolved in a mixture of AcOH/H_2O (v/v= 1:1, 528 ml; 0.35M) and the mixture was stirred under a pressure of 300 mbar at 50°C. Then the mixture was concentrated under reduced pressure and the crude was purified by column chromatography 8:2 pentane/EtOAc to 2:8 pentane/EtOAc affording the title compound **10** in 62% yield over 2 steps as an α/β mixture with a ratio of 11:1 (24.1 g; 118 mmol). IR (neat, cm-[1]): 3441, 2914, 1558, 1449, 1103, 1051, 1026, 1005, 974; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 3.35 (s, 3H, OCH_3 α anomer), 3.47 (s, 0.3 H, OCH_3 β anomer), 3.51 - 3.61 (m, 2.2H, H-5 α/β anomer), 3.97- 4.16 (m, 6.7H, H-2/H-3, H-4, C*H*$_2$-CH α/β anomer), 4.24 (d, 1H, *J*= 4.4 Hz, H-2/H-3), 4.83 (s, 1H, H-1 α anomer), 4.92 (d, 0.09H, *J*= 4.8 Hz, β anomer), 5.18 - 5.32 (m, 2H, CH=C*H*$_2$), 5.86 - 5.96 (m, C*H*=CH_2); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 55.1 (CH_3O α anomer), 55.5 (CH_3 β anomer), 70.0 (C-5/*C*H$_2$-CH β anomer), 70.8, 71.7 (C2/C3 β anomer), 72.0, 72.4 (C-5/*C*H$_2$-CH α anomer), 72.4, 74.7 (C-2/C-3 α anomer), 81.8 (C-4 α anomer), 83.6 (C-4 β anomer), 102.9 (C-1 β anomer), 108.2 (C-1 α anomer), 117.5 (CH=*C*H$_2$), 134.4 (*C*H=CH_2); HRMS: $[M+Na]^+$ calculated for $C_9H_{16}O_5Na$ 227.0895, found 227.0895.

5-*O*-allyl-2,3-*O*-benzyl-D-ribitol (11)



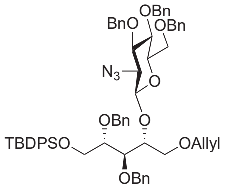
Compound **10** (24.1 g; 118 mmol; 1.0 eq.) was co-evaporated twice with toluene before use and was dissolved in a mixture of THF/DMF (590 ml; 0.30 M; v/v= 7:1). The solution was cooled to 0°C and NaH (7.1 g; 177 mmol; 1.5 eq.) was added, followed by dropwise addition of BnBr (21.0 ml; 177 mmol; 1.5 eq.). The remaining NaH (7.1 g; 177 mmol; 1.5 eq.) was added followed by the dropwise addition of BnBr (21.0 ml; 177 mmol; 1.5 eq.) and the mixture was allowed to warm up to rt and was stirred overnight. Then the mixture was quenched with MeOH at 0°C, diluted with Et_2O and the organic layer was washed 5x with H_2O. The organic layer dried over $MgSO_4$, filtrated and concentrated *in vacuo*. Purification by column chromatography pentane/EtOAc 9:1 to 1:1 pentane/EtOAc yielded the crude (63.2 g) with benzyl alcohol traces. The crude was dissolved in a mixture of 4M HCl (aq) /dioxane (800 ml, 0.15M v/v= 1:1) and the mixture was heated at 80°C for 2.5h and was then left stirring overnight at rt. The mixture was reheated at 80°C for 1.5 h and was then poured into 200 ml sat aq. $NaHCO_3$ after cooling down. Na_2CO_3 was added to neutralize the mixture and the mixture was diluted with EtOAc. The organic layer was washed with water and brine, dried over $MgSO_4$, filtrated and concentrated in vacuo. Purification by column chromatography pentane/EtOAc 8:2 to 4:6 pentane/EtOAc yielded a mixture of product and starting material. The mixture was dissolved in MeOH (375 ml; 0.20 M) and $NaBH_4$ (3.7 g; 98.0; 1.3 eq.) was added at 0°C in 2 portions and the mixture was stirred 4 days at rt. Then the reaction was quenched with EtOAc, concentrated under reduced pressure and co-evaporated with toluene. Purification by column chromatography pentane/EtOAc 1:0 to 2:8 pentane/EtOAc yielded the product **11** in 50% over 3 steps (21.7 g; 58.3 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 1): + 19.4; IR (neat, cm^{-1}): 3383, 2924, 2872, 1717, 1506, 1456, 1096, 1070, 1028, 737, 698; ^1H NMR (400 MHz, $CDCl_3$) δ= 2.86 (bs, 1H, O*H*), 3.22 (bs, 1H, O*H*), 3.49 - 3.56 (m, 2H, *H*-C-OH, C*H*H), 3.74 - 3.87 (m, 4H, C*H*$_2$-OH, 2x C*H*-Rbo), 3.91 - 4.00 (m, 3H, C*H*H, CH-C*H*$_2$), 4.58 - 4.66 (m, 3H, C*H*$_2$-Bn), 4.73 (d, 1H, *J*= 11.2 Hz, C*H*H-Bn), 5.14 - 5.27 (m, 2H, CH=C*H*$_2$), 5.82 - 5.92 (m, 1H, C*H*=CH_2), 7.24 - 7.35 (m, 10H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 60.9 (CH_2-OH), 70.5 (CH-OH), 71.1 71.9, 72.2, 73.9 (CH_2-Rbo/*C*H$_2$-CH, 2x CH_2-Bn), 79.4 (2x CH-Rbo), 117.4 (CH=*C*H$_2$), 127.8, 127.9, 128.0, 128.4, 128.4 (C-arom), 134.5 (*C*H=CH_2), 138.1, 138.1 (Cq-arom); HRMS: $[M+Na]^+$ calculated for $C_{22}H_{28}O_5Na$ 395.1834, found 395.1831.

5-*O*-allyl-2,3-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-D-ribitol (12)



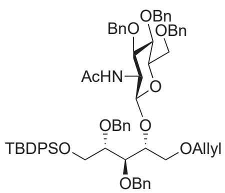
Compound **11** (17.8 g; 47.8 mmol; 1.0 eq.) was dissolved in DCM (480 ml; 0.1M) and the solution was cooled to 0°C. TEA (40 ml; 6.0 eq.) was added followed by dropwise addition of TBDPSCl (13.7 ml; 52.6 mmol: 1.1 eq.). The mixture was allowed to warm up to rt and was stirred overnight. The reaction was quenched by the addition of MeOH at 0°C and was concentrated under reduced pressure. Purification by column chromatography pentane/EtOAc 1:0 to 6:4 pentane/EtOAc yielded the product in 95% yield (27.7 g; 45.3 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 1): + 26.7; IR (neat, cm^{-1}): 3545, 2930, 2884, 1717, 1506, 1456, 1111, 1028, 824, 739, 700; ^1H NMR (400 MHz, $CDCl_3$) δ= 1.07 (s, 9H, *t*Bu), 2.86 (d, 1H, *J*= 4.0 Hz, O*H*), 3.52 - 3.55 (m, 1H, H-4), 3.81 - 3.82 (m, 2H, H-2, H-3), 3.89 - 4.03 (m, 6H, C*H*$_2$-CH, 2x CH_2-Rbo), 4.53 (d, 1H, *J*= 11.6 Hz, C*H*H Bn), 4.60 - 4.67 (m, 2H, CH_2-Bn), 4.70 (d, 1H, *J*= 11.6 Hz, C*H*H Bn), 5.13 - 5.26 (m, 2H, CH=C*H*$_2$), 5.84 - 5.91 (m, 1H, C*H*=CH_2), 7.19 - 7.42 (m, 15H, H-arom), 7.68 - 7.72 (m, 5H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 19.3 (Cq *t*Bu), 26.7, 26.9, 27.0 (CH_3 *t*Bu), 63.3 (CH_2-Rbo), 71.2 (C4-OH), 71.3, 72.3, 72.6, 73.8 (CH_2-Bn, CH_2-Rbo, *C*H$_2$-CH), 78.9, 80.7 (C-2, C-3), 117.2 (CH=*C*H$_2$), 127.6, 127.7, 127.8, 127.8, 128.0, 128.4, 129.7, 129.8 (CH-arom), 133.3, 133.4 (Cq-arom), 134.8, 134.9, 135.6, 135.8, 135.8, 138.4 (*C*H=CH_2, C-arom), 138.5 (Cq-arom); HRMS: $[M+Na]^+$ calculated for $C_{38}H_{46}O_5SiNa$ 633.3012, found 633.3015.

O-(3,4,6-tri-*O*-benzyl-2-azido-2-deoxy-β-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-D-ribitol (27)



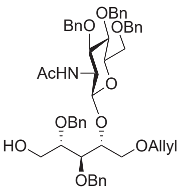
Alcohol **12** (1.83 g; 3.00 mmol; 1.0 eq.) was co-evaporated with toluene under a N_2 atmosphere and dissolved in dry ACN (30.0 ml; 0.10 M). Activated molecular sieves (3Å) were added and the solution was stirred for 30 minutes under N_2 atmosphere. The mixture was cooled to -40°C and TMSTOTf (55 µl; 0.30 mmol; 0.1 eq.) was added. Imidate **26** (2.79 g; 4.5 mmol; 1.5 eq.) was co-evaporated with toluene under a N_2 atmosphere and dissolved in dry ACN (30 ml; 0.15M). The donor was added to the reaction mixture and the mixture was stirred from -40°C to 0°C in a timeframe of 3 hours. Subsequently, 3 drops TEA were added and the mixture was diluted in DCM. The organic phase was washed with sat. aq. $NaHCO_3$; NaCl (v/v= 1:1) and the water layer was extracted with DCM. The organic layer was dried over $MgSO_4$, filtrated and concentrated *in vacuo*. Purification by column chromatography Et_2O/pentane 2:98 to 14:86 Et_2O/pentane yielded compound **27** in 85% yield (2.71 g; 2.54 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 1): + 6.6; IR (neat, cm-[1]): 2931, 2858, 2109, 1454, 1361, 1089, 1075, 1029, 737, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 1.05 (s, 9H, 3x CH_3-*t*Bu), 3.34 - 4.01 (m, 14H, H-2, 2x CH_2-Rbo, CH_2-CH, 3x CH-Rbo, H-3, H-4, H-6', H-6"), 4.38 (d, 1H, *J*= 12.1 Hz, *C*HH-Bn), 4.43 (m, 1H, H-5), 4.48 - 4.60 (m, 4H, CH_2-Bn), 4.67 (d, 1H, *J*= 8.0 Hz, H-1), 4.72 - 4.91 (m, 5H, CH_2-Bn), 5.10 - 5.28 (m, 2H, CH_2=CH), 5.90 (m, 1H, CH_2=C*H*), 7.13 - 7.42 (m, 30H, H-arom), 7.68 (m, 5H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 19.3 (Cq-*t*Bu), 27.0 (CH_3-*t*Bu), 63.8 (CH_2-Rbo), 66.8 (C-2), 68.8 (C-6), 71.0 (CH_2-Rbo), 72.4, 72.7, 73.9, 74.1, 75.1 (CH_2-CH, CH_2-Bn), 75.2 (CH-Rbo, C-3, C-4), 75.5 (CH_2-CH, CH_2-Bn), 79.5 (C-5), 79.8, 83.2 (CH-Rbo, C-3, C-4), 102.5 (C-1), 116.8 (CH_2=CH), 127.5, 127.5, 127.5, 127.6, 127.6, 127.8, 127.8, 127.9, 127.9, 127.9, 128.0, 128.1, 128.1, 128.3, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 129.7, 129.7 (CH-arom), 133.4, 133.6 (Cq-arom), 135.0 (CH_2=CH), 135.8, 135.9 (CH-arom), 138.2, 138.2, 138.3, 138.3, 138.7, 138.8 (Cq-arom); HRMS: $[M+Na]^+$ calculated for $C_{65}H_{73}N_3NaO_9Si$ 1090.5014, found 1090.5023.

O-(2-acetylamino-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-D-ribitol (28)



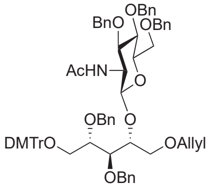
Compound **27** (1.65 g; 1.55 mmol; 1.0 eq.) was dissolved in pyridine/H_2O (27 ml; 0.058M; v/v= 5:1). TEA (0.1 ml) and propanedithiol (0.78 ml; 7.75 mmol; 5.0 eq.) were added and the mixture was stirred overnight at rt. Then the mixture was concentrated under reduced pressure and was 3x co-evaporated with toluene. The mixture was dissolved in pyridine/Ac_2O (27 ml; v/v= 2:1) and the mixture was stirred overnight at rt. The mixture was then quenched with MeOH, concentrated under reduced pressure and purified by column chromatography 1:0 pentane/EtOAc to 1:1 pentane/EtOAc affording the title compound **28** in 59% yield over 2 steps (1.00 g; 0.92 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 1): + 11.8; IR (neat, cm-[1]): 2929, 2858, 1653, 1454, 1362, 1112, 1070, 1029, 738, 698; ^{1}H NMR (500 MHz, $CDCl_3$) δ= 1.06 (s, 9H, 3x CH_3-*t*Bu), 1.77 (s, 3H, CH_3-NAc), 3.49 (m, 1H, CH-Rbo/H-3), 3.54 - 3.64 (m, 2H, CH_2-Rbo), 3.64 - 3.81 (m, 7H, H-2, H-4, CH_2-Rbo, 2x CH-Rbo), 3.83 (m, 2H, C*H*$_2$-CH), 3.88 (dd, 1H, *J*= 11.3 Hz, 5.4 Hz, H-6'), 3.93 - 4.00 (m, 2H, H-6", CH-Rbo/H-3), 4.30 (m, 1H, H-5), 4.42 (d, *J*= 12.1 Hz, 1H, C*H*H-Bn), 4.46 - 4.83 (m, 10H, CH_2-Bn, H-1), 5.08 - 5.22 (m, 2H, C*H*$_2$=CH), 5.59 (d, 1H, *J*= 7.0 Hz, N*H*), 5.82 (m, 1H, CH_2=C*H*), 7.08 - 7.38 (m, 30H, H-arom), 7.69 (m, 5H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 19.3 (Cq-*t*Bu), 23.6 (CH_3-NAc), 27.0 (CH_3-*t*Bu), 56.4 (C-2), 63.8 (C-6), 69.1 (CH_2-Rbo), 71.3 (CH_2-Rbo), 72.1, 72.3, 73.6, 74.0, 74.5, 74.8, 75.0 (*C*H$_2$-CH, CH_2-Bn), 75.3 (CH-Rbo/C-3), 78.3, 79.5, 79.5, 82.1 (C-5, CH-Rbo/C-3, C-4, 2x CH-Rbo), 101.6 (C-1), 116.9 (CH_2=*C*H), 127.5, 127.5, 127.6, 127.7, 127.8, 127.8, 127.8, 127.9, 128.0, 128.1, 128.1, 128.3, 128.3, 128.3, 128.4, 128.5, 128.5, 129.7 (CH-arom), 133.4, 133.6 (Cq-arom), 134.7 (*C*H=CH_2), 135.8, 135.8 (CH-arom), 138.3, 138.4, 138.6, 138.7, 138.7 (Cq-arom), 170.3 (C=O); HRMS: $[M+Na]^+$ calculated for $C_{67}H_{77}NNaO_{10}Si$ 1106.5214, found 1106.5231.

***O*-(2-acetylamino-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-D-ribitol (17)**



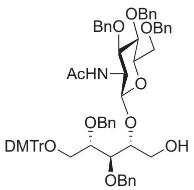
Compound **28** (0.93 g; 0.85 mmol; 1.0 eq.) was dissolved in THF (5.0 ml; 0.17M). TBAF (1M in THF: 1.7 ml; 1.70 mmol; 2.0 eq.) was added and the mixture was stirred at rt. After 1h TBAF (1M in THF: 2.6 ml; 2.60 mmol; 3.0 eq.) was added and stirring was continued until the starting material was completely converted. The mixture was concentrated under reduced pressure and purified by column chromatography pentane/EtOAc 1:0 to 4:6 pentane/EtOAc yielding the title compound **17** in 68% yield (0.49 g; 0.58 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 1): +14.4; IR (neat, cm-[1]): 3288, 3064, 2923, 2868, 1653, 1454, 1371, 1069, 1029, 736, 697; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 1.83 (s, 3H, CH_3-NAc), 2.86 (m, 1H, O*H*), 3.42 - 3.57 (m, 4H, H-3, H-4, CH_2-Rbo), 3.61 - 3.80 (m, 5H, H-2, H-6', CH_2-Rbo, CH-Rbo), 3.81 – 3.97 (m, 5H, H-6", C*H*$_2$-CH, 2x CH-Rbo), 4.07 (td, 1H, *J*= 7.2 Hz, 2.4 Hz, H-5), 4.43 - 4.55 (m, 3H, CH_2-Bn), 4.55 - 4.82 (m, 8H, CH_2-Bn, H-1), 5.11 - 5.25 (m, 2H, C*H*$_2$=CH), 5.75 (d, 1H, *J*= 7.9 Hz, N*H*), 5.84 (m, 1H, CH_2=C*H*), 7.16 (m, 2H, H-arom), 7.28 (m, 23H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 23.5 (CH_3-NAc), 56.3 (C-2), 61.4 (C-6), 68.9 (CH_2-Rbo), 71.4, 71.8, 72.1, 73.4, 73.9 (CH_2-Rbo, C*H*$_2$-CH, CH_2-Bn), 74.5 (C-3/C-4), 74.6, 74.7 (CH_2-Bn), 78.3 (C-3/C-4), 78.4, 78.7, 79.3, 82.0 (C-5, 3x CH-Rbo), 101.2 (C-1), 117.0 (*C*H$_2$=CH), 127.5, 127.6, 127.7, 127.8, 127.8, 128.0, 128.2, 128.3, 128.4, 128.4 (CH-arom), 134.5 (CH_2=*C*H), 137.6, 137.8, 138.3, 138.3, 138.6 (Cq-arom), 170.4 (C=O); HRMS: $[M+H]^+$ calcd for $C_{51}H_{60}NO_{10}$846.42117, found 846.42055.

O-(2-acetylamino-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-1-*O*-(4,4'-dimethoxytrityl)-D-ribitol (18)



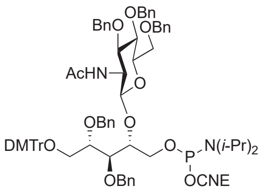
Compound **17** (0.47 g; 0.55 mmol; 1.0 eq.) was dissolved in DCM (5.5 ml; 0.10M) followed by the addition of TEA (0.12 ml; 0.83 mmol; 1.5 eq.) and the mixture was cooled to 0°C. DMTrCl (0.23 g; 0.67 mmol; 1.2 eq.) was added and the mixture was allowed to warm up to rt and stirring was continued for 2 days. The reaction was then quenched with MeOH at 0°C, diluted with DCM and washed with sat. aq. $NaHCO_3$/NaCl. The organic layer was dried over Na_2SO_4, filtrated and concentrated under reduced pressure. Purification by TEA neutralized column chromatography pentane/EtOAc 1:0 to 1:1 pentane/EtOAc yielded the title **18** compound in 53% yield (0.34 g; 0.30 mmol). $[\alpha]_D^{20}$ (DCM *c* 1): + 2.7; IR (neat, cm-^{1}): 2928, 2869, 1653, 1454, 1364, 1251, 1069, 1029, 751, 737, 698; ^{1}H NMR (400 MHz, CD_3CN) δ= 1.85 (s, 3H, CH_3-NAc), 3.24 (d, 1H, *J*= 10.4 Hz, H-6'), 3.42 - 3.55 (m, 2H, H-6", CH-Rbo), 3.55 - 3.75 (m, 12H, H-3, 2x CH_2-Rbo, CH-Rbo, 2x CH_3O), 3.75 - 3.91 (m, 2H, H-5, H-2), 3.91 - 4.02 (m, 3H, H-4, C*H*$_2$-CH), 4.30 - 4.33 (m, 1H, CH-Rbo), 4.41 (m, 2H, CH_2-Bn), 4.49 (d, 1H, *J*= 12.1 Hz, C*H*H-Bn), 4.60 (d, 2H, *J*= 11.2 Hz, CH_2-Bn), 4.70 - 4.86 (m, 6H, CH_2-Bn, H-1), 5.12 - 5.33 (m, 2H, C*H*$_2$=CH), 5.90 - 6.00 (m, 1H, CH_2=C*H*), 6.54 (d, 1H, *J*= 9.1 Hz, NH), 6.73 - 6.83 (m, 4H, H-arom), 7.11 (m, 2H, H-arom), 7.16 - 7.54 (m, 32H, H-arom); ^{13}C-APT NMR (126 MHz, CD_3CN) δ= 23.6 (CH_3-NAc), 55.8 (CH_3O), 56.5 (C-2), 64.2 (C-6), 70.1 (CH_2-Rbo), 71.2, 72.7, 73.2, 74.0, 74.3, 75.3, 75.5, (CH_2-Rbo, *C*H$_2$-CH, CH_2-Bn), 75.8 (CH-Rbo), 79.4, 79.5, 79.5, 80.5 (C-3, C-4, C-5, CH-Rbo), 83.6 (CH-Rbo), 86.8 (Cq-DMTr), 102.1 (C-1), 114.0 (CH-arom), 116.9 (*C*H$_2$=CH), 127.7, 128.3, 128.4, 128.4, 128.5, 128.6, 128.7, 128.7, 128.8, 128.9, 128.9, 129.0, 129.0, 129.2, 129.3, 129.3, 131.1, 131.1 (CH-arom), 136.3 (*C*H=CH_2), 137.0, 137.1, 139.5, 139.6, 139.8, 139.8, 139.9, 146.5, 159.5 (Cq-arom), 170.6 (C=O).

O-(2-acetylamino-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1-4)-2,3-di-*O*-benzyl-1-*O*-(4,4'-dimethoxytrityl)-D-ribitol (19)



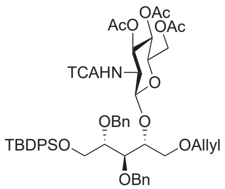
A solution of compound **18** (0.27 g; 0.21 mmol) in destilled THF (2.1 ml; 0.10M) was degassed with N_2. Ir(COD)(Ph_2MeP)$_2PF_6$ (6 mg; 0.03 eq.) was added and the solution was degassed with N_2. Then the red solution was purged with H_2 until the color became yellow (~5 seconds) and hereafter the solution was degassed with argon to remove traces of H_2 from the solution and stirring was continued under N_2 atmosphere until complete conversion of the substrate occured according to TLC analysis. The mixture was diluted with THF (2.0 ml) and aq. sat. $NaHCO_3$ (2.0 ml) followed by the addition of I_2 (0.08 g; 0.31 mmol; 1.5 eq.) and stirred for +/- 30 mins. The reaction was quenched by the addition of sat. aq. Na_2SO_3, diluted with EtOAc and the organic layer was washed with sat. aq. $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtrated and concentrated under reduced pressure. Purification by TEA neutralized column chromatography DCM/aceton 96:4 to 9:1 DCM/aceton yielded the title compound **19** in 79% yield. $[\alpha]_D^{20}$ (DCM *c* 1): + 3.6; IR (neat, cm-^{1}): 3288, 3064, 2929, 2870, 1653, 1508, 1453, 1362, 1251, 1070, 1029, 736, 698; ^{1}H NMR (400 MHz, CD_3CN) δ= 1.87 (s, 3H, CH_3-NAc), 3.25 (dd, 1H, *J*= 10.3 Hz, 5.3 Hz, H-6'), 3.47 - 3.50 (m, 2H, H-6'', CH-Rbo), 3.58 - 3.67 (m, 2H, C*H*H-Rbo, CH-Rbo), 3.67 - 3.77 (m, 10H, 2x CH_3O, C*H*H-Rbo, H-3, CH_2-Rbo), 3.77 - 3.90 (m, 2H, H-5, H-2), 4.03 (dd, 1H, *J*= 7.4 Hz, 3.0 Hz, H-4), 4.09 - 4.13 (m, 1H, CH-Rbo), 4.39 (dd, *J*= 11.6, 3.6 Hz, 2H, CH_2-Bn), 4.48 (d, *J*= 12.0 Hz, 1H, C*H*H-Bn), 4.59 (dd, 2H, *J*= 11.2, 5.7 Hz, CH_2-Bn), 4.70 - 4.85 (m, 6H, CH_2-Bn, H-1), 6.72 - 6.82 (m, 4H, H-arom), 6.85 (d, 1H, *J*= 9.0 Hz, N*H*), 7.09 - 7.12 (m, 2H, *J*= 6.6 Hz, 2.2 Hz, H-arom), 7.17 - 7.44 (m, 30H, H-arom), 7.47 - 7.53 (m, 2H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 23.6 (CH_3-NAc), 55.8 (CH_3O), 56.9 (C-2), 62.2 (CH_2-Rbo), 64.1 (C-6), 70.0 (CH_2-Rbo), 73.3, 74.0, 74.5, 75.3, 75.5 (CH_2-Bn), 75.7(CH-Rbo), 79.3, 79.5 (CH-Rbo, C-5), 80.4 (C-4), 82.0 (C-3), 83.4 (CH-Rbo), 86.9 (Cq-DMTr), 102.4 (C-1), 114.0, 127.7, 128.3, 128.4, 128.5, 128.5, 128.6, 128.6, 128.8, 128.9, 128.9, 128.9, 129.0, 129.1, 129.2, 129.2, 129.3, 131.1, 131.1 (CH-arom), 137.0, 137.1, 139.4, 139.5, 139.7, 139.8, 146.4, 159.5 (Cq-arom), 171.6 (C=O); HRMS: $[M+Na]^+$ calculated for $C_{69}H_{73}NNaO_{12}$ 1130.5030 found, 1130.5049.

O-(2-acetylamino-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1-4)-2,3-di-*O*-benzyl-5-*O*-(2-cyanoethyl-*N,N*-diisopropylphosphoramidite)-1-*O*-(4,4'-dimethoxytrityl)-D-ribitol (20)



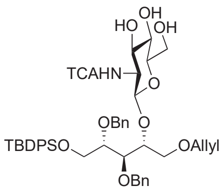
To a solution of compound **19** (0.19 g; 0.15 mmol; 1.0 eq.) in DCM (1.5 ml; 0.10 M) was added DIPEA (43 µl; 0.25 mmol; 1.6 eq.). The mixture was stirred over activated MS 4Å for +/- 15 min. *N,N'*-di-isopropylamino-2-cyanoethyl-chlorophosphite (45 µl; 0.20 mmol; 1.3 eq.) was added and the mixture was stirred for 1h. Water was added, the mixture was diluted with DCM and the organic layer was washed with sat. aq. $NaHCO_3$:NaCl (v/v= 1:1), dried over Na_2SO_4, filtrated and concentrated *in vacuo*. Purification by TEA neutralized column chromatography pentane/EtOAc 1:0 to 6:4 pentane/EtOAc yielded phosphoramidite **20** in 61% yield (0.13 g; 0.09 mmol). ^{1}H NMR (400 MHz, CD_3CN) δ= 1.08 - 1.23 (m, 12H, 4x CH_3-isopropylamine), 1.83 (bs, 3H, CH_3-NAc), 2.54 - 2.64 (m, 2H, CH_2-cyanoethyl), 3.19 (ddd, 1H, *J*= 10.0 Hz, 8.1 Hz, 5.1 Hz, H-6'), 3.45 (m, 2H, H-6'', CH-Rbo), 3.51 - 3.75 (m, 15H, 2x CH-isopropylamine, 2x CH_2-cyanoethyl, 2x CH_3O, CH_2-Rbo, CH-Rbo, CH-Rbo/H-3/H-4), 3.75 - 4.02 (m, 5H, H-2, H-5, CH_2-Rbo, CH-Rbo/H-3/H-4), 4.23 - 4.34 (m, 1H, CH-Rbo/H-3/H-4), 4.34 - 4.81 (m, 11H, 5x CH_2-Bn, H-1), 6.40 (d, 1H, *J*= 9.2 Hz, N*H*), 6.74 - 6.78 (m, 4H, H-arom), 7.07 - 7.11 (m, 2H, H-arom), 7.12 - 7.49 (m, 32H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 21.1, 21.1 (CH_2-cyanoethyl), 23.7 (CH_3-NAc), 24.9, 25.0, 25.1, 25.2 (CH_3-isopropylamine), 43.7, 43.7, 43.8, 43.8 (CH-isopropylamine), 55.8 (CH_3O), 56.4 (C-2), 59.2, 59.4, 59.6 (CH_2-cyanoethyl), 63.5, 63.6, 64.0, 64.2, 64.3, 64.4 (CH_2-Rbo, C-6), 70.0, 70.0 (CH_2-Rbo), 73.3, 73.9, 74.0, 74.2, 75.3, 75.4 (CH_2-Bn), 75.8 (CH-Rbo), 79.3, 79.3, 79.4, 79.5, 79.6, 79.7, 80.1, 80.1, 83.6, 83.6 (C-3, C-4, C-5, 2x CH-Rbo), 86.8 (Cq-DMTr), 101.8, 101.8 (C-1), 113.9 (CH-arom), 126.2, 127.6, 128.3, 128.3, 128.3, 128.5, 128.6, 128.6, 128.7, 128.7, 128.7, 128.9, 128.9, 129.0, 129.2, 129.2, 129.9, 131.1 (CH-arom), 137.1, 137.2, 139.5, 139.6, 139.7, 139.7, 139.9, 140.0, 140.0, 146.5, 159.5 (Cq-arom), 170.6 (C=O); ^{31}P NMR (162 MHz, CD_3CN) δ= 148.3, 147.9.

O-(3,4,6-tri-*O*-acetyl-2-trichloroacetylamino-2-deoxy-β-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-D-ribitol (15)



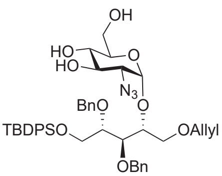
Donor **14** (3.86 g; 6.48 mmol; 1.2 eq.) and acceptor **12** (3.29 g; 5.39 mmol; 1.0 eq.) were co-evaporated with toluene twice under a N_2 atmosphere in 1 pot. The mixture was dissolved in dry DCM (65.0 ml; 0.10 M) and stirred on activated MS 4Å and cooled to 0°C. TMSOTf (125.0 µl; 0.69 mmol; 0.1 eq.) was added and the reaction was quenched with TEA after complete conversion of the acceptor according to TLC analysis. The mixture was diluted with DCM and was washed with water and brine. The organic layer was dried over $MgSO_4$, filtrated and concentrated *in vacuo*. Purification by column chromatography pentane/EtOAc 9:1 to 7:3 pentane/EtOAc. The combined eluate was concentrated *in vacuo* and purified by size exclusion chromatography affording the title compound **15** in 92% yield (5.44 g; 5.93 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 1): - 0.5; IR (neat, cm^{-1}): 2931, 2858, 1749, 1723, 1457, 1368, 1232, 1112, 1039, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 1.06 (s, 9H, CH_3-*t*Bu), 1.97 (s, 3H, CH_3-Ac), 2.02 (d, 6H, *J*= 2.2 Hz, CH_3-Ac), 3.52 - 3.71 (m, 4H, H-5, CH-Rbo, C*H*$_2$-CH), 3.77 - 3.97 (m, 5H, 2x CH_2-Rbo, CH-Rbo), 4.04 (dd, 1H, *J*= 12.2 Hz, 2.4 Hz, H-6'), 4.14 (q, 1H, *J*= 10.4 Hz, H-2), 4.26 (dd, *J*= 12.2 Hz, 4.9 Hz, 1H, H-6"), 4.36 - 4.39 (m, 1H, H-4), 4.48 (dd, 2H, *J*= 14.3 Hz, 11.4 Hz, CH_2-Bn), 4.73 (dd, 2H, *J*= 15.2 Hz, 11.4 Hz, CH_2-Bn), 4.93 (d, 1H, *J*= 8.5 Hz, H-1), 5.10 - 5.26 (m, 4H, C*H*$_2$=CH, H-3, CH-Rbo), 5.79 - 5.89 (m, 1H, CH_2=C*H*), 7.07 (d, 1H, *J*= 8.8 Hz, N*H*), 7.16 - 7.44 (m, 16H, H-arom), 7.66 - 7.68 (m, 4H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 19.3 (Cq-*t*Bu), 20.7, 20.7 (CH_3-Ac) 26.9 (CH_3-*t*Bu), 56.0 (C-2), 62.2 (C-6), 63.3 (CH_2-Rbo), 68.5 (C-3/CH-Rbo), 71.4 (CH_2-Rbo/*C*H$_2$-CH/CH_2-Bn), 72.1 (C-3/CH-Rbo), 72.2, 72.3 (CH_2-Rbo/*C*H$_2$-CH/CH_2-Bn), 72.7 (C-3/CH-Rbo), 74.2 (CH_2-Rbo/*C*H$_2$-CH/CH_2-Bn), 79.2, 79.4, 79.5 (C-4, C-5, CH-Rbo), 92.5 (CCl_3), 101.3 (C-1), 117.4 (*C*H$_2$=CH), 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.7, 127.8, 128.2, 128.2, 128.3, 128.3, 128.3, 129.8 (CH-arom), 133.2, 133.5 (Cq-arom), 134.5 (CH_2=CH), 135.7, 135.8 (CH-arom), 138.3, 138.5 (Cq-arom), 162.1, 169.4, 170.8, 171.0 (C=O); HRMS: $[M+Na]^+$ calcd for $C_{52}H_{62}Cl_3NNaO_{13}Si$ 1064.2954, found 1064.2965.

O-(2-trichloroacetylamino-2-deoxy-β-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-D-ribitol (16)



To a solution of Compound **15** (4.23 g; 3.90 mmol; 1.0 eq.) in MeOH (39.0 ml; 0.10 M) was added NaOMe (21.0 mg; 0.39 mmol; 0.1 eq.) and the mixture was stirred overnight. A small piece of Na was added and the mixture was stirred for 3h. Then the mixture was quenched with amberlite H^+ resin, filtrated and concentrated *in vacuo*. Purification by column chromatography pentane/EtOAc 9:1 to 0:1 pentane/ EtOAc afforded fractions of the starting compound and the product. The fractions of the starting compound were combined, concentrated *in vacuo* and treated for deacetylation according to the described procedure above. The crude was purified using column chromatography pentane/EtOAc 7:3 to 3:7 pentane/ EtOAc affording the title compound **16** in a total yield of 73% (2.63 g; 2.86 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 1): + 5.0; IR (neat, cm^{-1}): 3348, 2931, 2858, 1701, 1457, 1112, 1076, 1028, 701; ^1H NMR (400 MHz, $CDCl_3$) δ= 3.35 (ddd, 1H, *J*= 9.1 Hz, 5.2 Hz, 3.2 Hz, CH-Rbo), 3.47 (dd, 1H, *J*= 10.7, 2.5 Hz, H-6'), 3.52 - 3.97 (m, 12H, 2x CH_2-Rbo, CH_2-CH, H-6", H-2, H-3, H-4, 2x CH-Rbo), 4.22 (dt, *J*= 9.2 Hz, 2.9 Hz, 1H, H-5), 4.48 (dd, 2H, *J*= 29.1, 11.6 Hz, CH_2-Bn), 4.65 (dd, 2H, *J*= 14.5, 11.6 Hz, CH_2-Bn), 4.78 (d, 1H, *J*= 7.7 Hz, H-1), 5.12 - 5.22 (m, 2H, CH_2=CH), 5.77 - 5.86 (m, 1H, CH_2=C*H*), 7.13 - 7.17 (m, 2H, H-arom), 7.22 - 7.35 (m, 11H, H-arom), 7.37 - 7.44 (m, 2H, H-arom), 7.49 (d, 1H, *J*= 5.1 Hz, H-arom), 7.65 - 7.48 (m, 4H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 19.3 (Cq-*t*Bu), 27.0 (CH_3-*t*Bu), 59.1 (C-2), 62.4, 63.0 (CH_2-Rbo), 71.2 (C-6), 71.8 (C-3/C-4/CH-Rbo), 72.1, 72.4, 74.1 (CH_2-CH, CH_2-Bn), 75.7, 76.1 (C-3/C-4/CH-Rbo), 78.7, 79.3, 79.5 (C-3/C-4/C-5/CH-Rbo), 101.3 (C-1), 117.6 (CH_2=CH), 127.8, 127.8, 127.8, 128.0, 128.1, 128.4, 128.5, 129.8, 129.9 (CH-arom), 133.3, 133.4 (Cq-arom), 134.4 (CH_2=*C*H), 135.8, 135.9 (CH-arom), 138.2 (Cq-arom), 164.3 (C=O); HMRS: $[M+Na]^+$ calcd for $C_{46}H_{56}Cl_3NNaO_{10}Si$ 938.2637, found 938.2653.

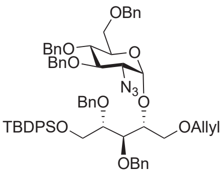
O-(2-azido-2-deoxy-α-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-D-ribitol (31)



Donor **29** (11.5 g; 24.1 mmol; 1.0 eq.) and acceptor **12** (17.7 g; 29.0 mmol; 1.2 eq.) were co-evaporated together twice with toluene under an N_2 atmosphere. The mixture was dissolved in DCM (240 ml; 0.10 M) and stirred on activated MS 4Å for +/- 30 min. TMSOTf (0.44 ml; 2.41 mmol; 0.1 eq.) was added at rt and the reaction was stirred until full conversion of the donor was achieved according to TLC analysis. The reaction was quenched with TEA, concentrated under reduced pressure and purified by column chromatography pentane/EtOAc 1:0 to 8:2 pentane/EtOAc yielding the product as an α/β mixture (7:1). The mixture was dissolved in MeOH (165 ml; 0.13 M) followed by addition of 4.3M NaOMe (0.82 ml; 0.15

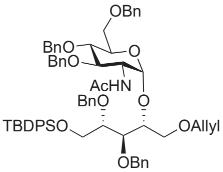
eq.) and the mixture was stirred for 2h. The reaction was neutralized with amberlite H^+, filtrated and concentrated under reduced pressure. Purification by column chromatography pentane/EtOAc 85:15 to 30:70 pentane/EtOAc yielded the product in 64% over 2 steps as the α anomer (12.3 g; 15.4 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 4.2): + 57.1; IR (neat, cm-^{1}): 3352, 2930, 2857, 2108, 1454, 1362, 1103, 1024, 741, 700; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 1.05 (s, 9H, CH_3-*t*Bu), 2.87 (bs, 1H, O*H*), 3.32 (dd, 1H, *J*= 10.4 Hz, 3.6 Hz, H-2), 3.52 (dd, 1H, *J*= 10.8 Hz, 2.4 Hz, H-6′), 3.60 - 4.00 (m, 12H, H-3, H-4, H-6″, 3x CH-Rbo, 2x CH_2-Rbo, C*H*$_2$-CH), 4.17 (bs, 1H, O*H*), 4.23 - 4.25 (m, 1H, H-5), 4.31 (bs, 1H, O*H*), 4.47 (d, 1H, *J*= 11.6 Hz, C*H*H-Bn), 4.58 (d, 1H, *J*= 11.2 Hz, C*H*H-Bn), 4.67 (d, 1H, *J*= 11.6 Hz, C*H*H-Bn), 4.82 (d, 1H, *J*= 11.2 Hz, C*H*H-Bn), 5.09 - 5.19 (m, 3H, H-1, CH=C*H*$_2$), 5.77 - 5.84 (m, 1H, C*H*=CH_2), 7.19 - 7.40 (m, 15H, H-arom), 7.65 - 7.69 (m, 5H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 19.3 (Cq-*t*Bu), 27.0 (CH_3-*t*Bu), 61.8, 62.9 (CH_2-Rbo, *C*H$_2$-CH), 63.6 (C-2), 70.4 (C-6), 70.7 (C-4), 71.2 (C-3/CH-Rbo), 72.1 (CH_2 Bn/CH_2-Rbo), 72.3, (C-3/CH-Rbo), 72.3 (CH_2 Bn/CH_2-Rbo), 74.0 (CH_2 Bn/CH_2-Rbo), 77.6 (C-5), 78.8, 78.9 (CH-Rbo), 96.8 (C-1), 117.3 (CH=*C*H$_2$), 127.6, 127.8, 127.8, 127.8, 127.9, 128.1, 128.4, 129.8 (CH-arom), 133.3, 133.6 (Cq-arom), 134.7 (*C*H=CH_2), 135.7, 135.9 (CH-arom), 138.4, 138.5 (Cq-arom); HRMS: $[M+Na]^+$ calcd for $C_{44}H_{55}N_3NaO_9Si$ 820.3605, found 820.3616.

O-(2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-D-ribitol (32)



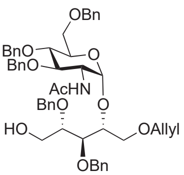
To a solution of compound **31** (12.7 g; 15.9 mmol; 1.0 eq.) in THF/DMF (160 ml; 0.1M; v/v= 7:1) at 0°C was added NaH (2.50 g; 63.6 mmol; 4.0 eq.) in portions followed by BnBr (9.5 ml; 79.5 mmol; 5.0 eq.) and the mixture was allowed to warm up to rt and stirred for 2 days. The mixture was then quenched with MeOH at 0°C, diluted with EtOAc (260 ml), washed with water (5x 150 ml) and brine. Column chromatography afforded the product and partly benzylated intermediate (3.00 mmol) that was recovered and dissolved in THF/DMF (30.0 ml; 0/1 M; v/v= 7:1) followed by addition of NaH (0.16 g; 4.1 mmol; 1.4 eq.) and BnBr (0.46 ml; 3.8 mmol; 1.3 eq.) at 0°C and the reaction was allowed to warm up to rt and was stirred overnight. The mixture was quenched with MeOH at 0°C and worked up as described above leading to a total yield of the title compound in 73% (12.36 g; 11.57 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 4.2): + 48.3; IR (neat, cm-^{1}): 2928, 2857, 2106, 1454, 1362, 1105, 1074, 1028, 737, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 1.06 (s, 9H, CH_3-*t*Bu), 3.55 (dd, 1H, *J*= 9.2 Hz, 3.6 Hz, H-2), 3.59 - 3.65 (m, 3H, H-6′, CH_2-Rbo), 3.77 - 3.84 (m, C*H*$_2$-CH, H-6″, 2x CH-Rbo), 3.91 (dd, 1H, *J*= 11.2 Hz, 4.4 Hz, C*H*H-Rbo), 3.98 - 4.03 (m, 3H, C*H*H-Rbo, H-3, H-4), 4.17 - 4.20 (m, 1H, CH-Rbo), 4.25 - 4.27 (m, 1H, H-5), 4.44 - 4.88 (m, 10H, CH_2-Bn), 7.18 - 7.39 (m, 30H, H-arom), 7.67 - 7.71 (m, 5H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 19.3 (Cq-*t*Bu), 26.9 (CH_3-*t*Bu), 62.9 (CH_2-Rbo), 64.3 (C-2), 68.4 (C-6), 70.3 (CH_2-Rbo), 70.7 (CH-Rbo), 72.0, 72.2 (*C*H$_2$-CH, CH_2-Bn), 73.6, 73.9, 74.9, 75.4 (CH_2-Bn), 77.8, 78.5, 78.8, 79.1, 80.6 (C-5, C-3, C-4, 2x CH-Rbo), 97.2 (C-1), 116.8 (CH_2=CH), 127.4, 127.5, 127.7, 127.8, 127.9, 127.9, 128.0, 128.2, 128.3, 128.4, 128.4, 128.5, 128.8, 129.1, 129.7 (CH-arom), 133.3, 133.6 (Cq-arom), 134.9 (*C*H=CH_2), 135.7, 135.7, 135.9 (Cq-arom), 138.1, 138.3, 138.6, 138.6 (Cq-arom); HRMS: $[M+Na]^+$ calculated for $C_{65}H_{73}N_3NaO_9Si$ 1090.5014, found 1090.5040.

O-(2-acetylamino-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-D-ribitol (33)



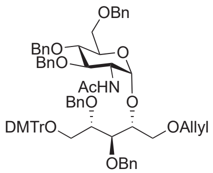
Compound **32** (12.4 g; 11.6 mmol; 1.0 eq.) was dissolved in pyridine/H_2O (200 ml; 0.058M; v/v= 5:1) followed by the addition of TEA (0.93 ml) and 1,3-propaandithiol (5.80 ml; 57.8 mmol; 5.0 eq.) and the mixture was stirred overnight at rt. Then the mixture was concentrated under reduced pressure, co-evaporated with toluene (3x), dissolved in pyr/Ac_2O (200 ml; v/v= 2:1) and stirred overnight. The mixture was then quenched with MeOH, concentrated under reduced pressure and purified by column chromatography pentane/EtOAc 1:0 to 1:1 pentane/EtOAc affording the title compound **27** in 92% yield (11.66 g; 10.8 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 2.6): + 53.3; IR (neat, cm-^{1}): 2930, 2857, 1684, 1454, 1271, 1111, 1070, 1028, 741, 700; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 1.05 (s, 9H, CH_3-*t*Bu), 1.43 (s, 3H, CH_3-NAc), 3.54 - 5.06 (m, 14H, 3x CH-Rbo, 2x CH_2-Rbo, H-3, H-4, H-5, H-6', H-6", *CH_2*-CH), 4.19 - 4.25 (m, 1H, H-2), 4.41 (d, 1H, *J*= 11.6 Hz, C*H*H-Bn), 4.64 - 4.67 (m, 8H, CH_2-Bn), 4.81 (d, 1H, *J*= 10.8 Hz, C*H*H-Bn), 4.92 (d, 1H, *J*= 3.2 Hz, H-1), 5.08 - 5.20 (m, 2H, CH=C*H*$_2$), 5.59 (d, 1H, *J*= 9.2 Hz, N*H*), 5.77 - 5.84 (m, 1H, C*H*=CH_2), 7.17 - 7.38 (m, 30H, H-arom), 7.62 - 7.68 (m, 5H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 19.2 (Cq-*t*Bu), 22.9 (*C*H_3-NAc), 26.8 (CH_3-*t*Bu), 52.8 (C-2), 63.2 (*C*H_2-CH), 68.6, 69.5 (CH_2-Rbo, C-6), 71.4 (CH-Rbo), 71.9, 72.4, 73.4, 74.7, 74.9 (CH_2-Rbo, 5x CH_2-Bn), 78.1, 78.2, 79.3, 79.4, 80.6 (2x CH-Rbo, C-3, C-4, C-5), 99.3 (C-1), 116.7 (*C*H_2=CH), 127.6, 127.7, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 128.5, 128.9 129.8, 129.8 (C-arom), 133.0, 133.2 (Cq-arom), 134.7 (*C*H=CH_2), 135.5, 135.6 (C-arom), 138.0, 138.0, 138.1, 138.4 (Cq-arom), 169.7 (C=O); HRMS: $[M+H]^+$ calculated for $C_{67}H_{78}NO_{10}Si$ 1084.5395, found 1084.5394.

O-(2-acetylamino-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-D-ribitol (34)



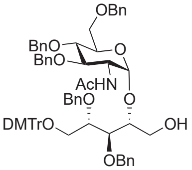
Compound **33** (11.2 g; 10.4 mmol; 1.0 eq.) was dissolved in THF (61 ml; 0.17 M) and to this solution was added TBAF (15.5 ml; 15.5 mmol; 1.5 eq.) and the mixture was stirred at rt. When TLC analysis showed a small amount of starting material, TBAF (5.2 ml; 5.2 mmol; 0.5 eq.) was added and the reaction was stirred for 40 min, after which the mixture was concentrated under reduced pressure. Purification by column chromatography pentane/EtOAc 1:0 to 3:7 pentane/EtOAc yielded the title compound **34** in 86% yield (7.93 g; 8.9 mmol). $[\alpha]_D^{20}$ ($CHCl_3$ *c* 1.6): + 42.4; IR (neat, cm-^{1}): 3447, 3420, 2920, 2862, 1684, 1558, 1456, 1097, 1070, 1047, 1028, 737, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 1.51 (s, 3H, CH_3-NAc), 2.59 (bs, 1H, O*H*), 3.48 (dd, 1H, *J*= 10.4 Hz, 5.6 Hz, H-6'), 3.57 (dd, 1H, *J*= 10.4 Hz, 5.6 Hz, H-6''), 3.62 - 3.83 (m, 9H, 2x CH_2-Rbo, CH_2-CH, H-3, 2x CH-Rbo), 3.92 - 3.95 (m, 2H, H-4, CH-Rbo), 4.01 (q, 1H, *J*= 3.6 Hz, H-5), 4.22 (ddd, *J* = 10.5 Hz, 9.0 Hz, 3.6 Hz, H-2), 4.48 - 4.68 (m, 8H, CH_2-Bn), 4.82 (dd, *J*= 11.2 Hz, 3.3 Hz, 2H, CH_2-Bn), 4.94 (d, *J*= 3.6 Hz, 1H, H-1), 5.09 - 5.20 (m, 2H, CH=CH_2), 5.77 (m, 1H, C*H*=CH_2), 5.86 (d, *J*= 9.1 Hz, 1H, N*H*), 7.17 - 7.38 (m, 25H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 22.9 (CH_3-NAc), 52.9 (C-2), 61.9 (CH_2-CH), 68.7 (CH_2-Rbo), 69.3 (C-6), 71.6 (CH-Rbo), 71.7, 72.2, 73.6, 74.2, 74.8, 75.2 (CH_2-Rbo, 5x CH_2-Bn), 78.0, 78.4, 78.9, 79.2, 80.1, (2x CH-Rbo, C-3, C-4, C-5), 100.1 (C-1), 117.3 (CH=CH_2), 127.8, 127.8, 127.9, 127.9, 128.0, 128.0, 128.0, 128.0, 128.1, 128.1, 128.2, 128.2, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7 (C-arom), 134.5 (*C*H=CH_2), 137.7, 137.9, 138.1, 138.2, 138.4 (Cq-arom), 170.3 (C=O); HRMS: $[M+H]^+$ calcd for $C_{51}H_{60}NO_{10}$846.4217, found 846.4230.

***O*-(2-acetylamino-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1-4)-5-*O*-allyl-2,3-di-*O*-benzyl-1-*O*-(4,4'-dimethoxytrityl)-D-ribitol (35)**



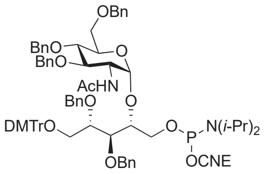
To a solution of compound **34** (7.61 g; 9.0 mmol; 1.0 eq.) in DCM (60.0 ml; 0.15 M) was added DMTrCl (3.66 g; 10.8 mmol; 1.2 eq.) and TEA (2.0 ml; 13.5 mmol; 1.5 eq.) and the reaction was stirred for 2h at rt. The reaction was then quenched with MeOH at 0°C, diluted with DCM and washed with sat. aq. $NaHCO_3$/NaCl. The organic layer was dried over Na_2SO_4, filtrated and concentrated under reduced pressure. Purification by TEA neutralized column chromatography pentane/EtOAc 1:0 to 1:1 pentane/EtOAc yielded the title compound **35** in 78% yield (8.05 g; 7.00 mmol). $[\alpha]_D^{20}$ (DCM *c* 1): + 44.1; IR (neat, cm-^{1}): 2909, 2868, 1684, 1508, 1454, 1250, 1088, 1072, 1029, 829, 737, 698; ^{1}H NMR (400 MHz, CD_3CN) δ= 1.69 (s, 3H, CH_3-NAc), 3.21 (dd, 1H, *J*= 10.2 Hz, 4.9 Hz, C*H*H-Rbo), 3.47 (dd, 1H, *J*= 10.2 Hz, 2.9 Hz, CH*H*-Rbo), 3.59 - 3.77 (m, 13H, H-6', H-6'', H-3, 2x CH_3O, CH_2-Rbo, 2x CH-Rbo), 3.87 (ddt, 2H, *J*= 8.1 Hz, 5.3 Hz, 1.6 Hz, CH_2-CH), 3.95 (dd, 1H, *J*= 7.2, 2.6 Hz, H-4), 4.01 - 4.10 (m, 2H, H-2, CH-Rbo), 4.14 - 4.17 (m, 1H, H-5), 4.42 (d, 1H, *J*= 11.1 Hz, C*H*H-Bn), 4.49 (d, 1H, *J*= 12.0 Hz, C*H*H-Bn), 4.53 - 4.85 (m, 8H, CH_2-Bn), 4.93 (d, 1H, *J*= 3.6 Hz, H-1), 5.05 - 5.26 (m, 2H, CH_2=CH), 5.85 (m, 1H, CH_2=C*H*), 6.30 (d, 1H, *J*= 9.0 Hz, N*H*), 6.74 - 6.83 (m, 4H, H-arom), 7.08 - 7.50 (m, 34H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 23.3 (CH_3-NAc), 54.1 (C-2), 55.8 (CH_3O), 63.6 (CH_2-Rbo), 70.0, 70.7 (C-6, CH_2-Rbo), 71.8 (CH-Rbo), 72.5, 73.3, 73.9, 74.4, 75.4, 75.5 (*C*H_2-CH, 5x CH_2-Bn), 77.8 (C-5), 79.2, 79.2, 79.6, 81.2 (2x CH-Rbo, C-3, C-4), 86.8 (Cq-DMTr), 97.7 (C-1), 114.0 (CH-arom), 116.8 (*C*H_2=CH), 127.7, 128.5, 128.5, 128.5, 128.6, 128.8, 128.8, 128.8, 128.9, 129.2, 129.3, 129.3, 131.0, 131.0 (CH-arom), 136.2 (*C*H=CH_2), 137.0, 137.1 (Cq-arom), 139.5, 139.5, 139.6, 139.7, 139.9, 146.4, 159.5 (Cq-arom), 170.3 (C=O); HRMS: [M+Na]$^+$ calculated for $C_{72}H_{77}NNaO_{12}$ 1170.5343, found 1170.5337.

O-(2-acetylamino-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1-4)-2,3-di-*O*-benzyl-1-*O*-(4,4'-dimethoxytrityl)-D-ribitol (36)



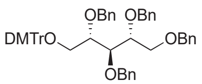
A solution of compound **35** (0.85 g; 0.74 mmol; 1.0 eq.) in destilled THF (7.4 ml; 0.10 M) was degassed with N_2. Ir(COD)$(Ph_2MeP)_2PF_6$ (14 mg; 0.02 eq.) was added and the solution was degassed with N_2. Then the red solution was purged with H_2 until the color became yellow (~25 seconds) and hereafter the solution was degassed with argon to remove traces of H_2 from the solution and the reaction was warmed up to 30°C for 5 mins under argon atmosphere. The mixture was diluted with THF (7.4 ml) and aq. sat. $NaHCO_3$ (7.4 ml) followed by the addition of I_2 (0.28 g; 1.12 mmol; 1.5 eq.) and stirred for +/- 30 min. The reaction was quenched by the addition of sat. aq. Na_2SO_3, diluted with EtOAc and the organic layer was washed with sat. aq. $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtrated and concentrated under reduced pressure. Purification by TEA neutralized column chromatography pentane/EtOAc 1:0 to 1:1 pentane/EtOAc yielded the title compound **36** in 77% yield (0.70 g; 0.63 mmol). $[\alpha]_D^{20}$ (DCM *c* 1): + 31.7; IR (neat, cm^{-1}): 3567, 3064, 3031, 2931, 1668, 1508, 1454, 1368, 1251, 1069, 1029, 737, 698; ^{1}H NMR (400 MHz, CD_3CN) δ= 1.66 (s, 3H, CH_3-NAc), 3.25 (t, 1H, *J*= 6.3 Hz, O*H*), 3.30 (dd, 1H, *J*= 10.2 Hz, 5.0 Hz, H-6'), 3.50 (dd, 1H, *J*= 10.1 Hz, 2.8 Hz, H-6''), 3.58 (dd, 1H, *J*= 10.1, 8.9 Hz, CH-Rbo), 3.64 - 3.81 (m, 11H, 2x CH_2-Rbo, 2x CH_3O, H-3), 3.87 (m, 1H, H-5), 3.93 - 4.02 (m, 2H, H-4, CH-Rbo), 4.09 (ddd, 1H, *J*= 10.2 Hz, 5.5 Hz, 2.0 Hz, CH-Rbo), 4.16 (ddd, 1H, *J*= 10.7 Hz, 9.1 Hz, 3.7 Hz, H-2), 4.45 - 4.86 (m, 10H, CH_2-Bn), 4.94 (d, 1H, *J*= 3.7 Hz, H-1), 6.33 (d, 1H, *J*= 9.1 Hz, N*H*), 6.77 - 6.84 (m, 4H, H-arom), 7.14 - 7.23 (m, 3H, H-arom), 7.24 (s, 27H, H-arom), 7.46 (dt, 2H, *J*= 6.5 Hz, 1.5 Hz, H-arom), 7.49 - 7.54 (m, 2H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 23.3 (CH_3-NAc), 54.0 (C-2), 55.8, 55.8 (CH_3O), 62.7 (CH_2-Rbo), 64.2 (C-6), 70.0 (CH_2-Rbo), 72.1 (CH-Rbo), 73.4, 73.9, 74.2, 75.5, 75.6 (CH_2-Bn), 79.3, 79.5, 79.7 (C-4, C-5, CH-Rbo), 81.4 (C-3), 82.3 (C-4, C-5, CH-Rbo), 86.9 (Cq-DMTr), 98.8 (C-1), 114.0 (CH-arom), 127.7, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.8, 128.8, 128.9, 129.0, 129.2, 129.2, 129.3, 129.4, 131.0, 131.1 (CH-arom), 137.0, 137.1, 139.2, 139.4, 139.4, 139.5, 139.8, 146.4, 159.5 (Cq-arom), 170.4 (C=O); HRMS: [M+Na]$^+$ calculated for $C_{69}H_{73}NNaO_{12}$ 1130.50250, found 1130.50183.

***O*-(2-acetylamino-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1-4)-2,3-di-*O*-benzyl-5-*O*-(2-cyanoethyl-*N,N*-diisopropylphosphoramidite)-1-*O*-(4,4'-dimethoxytrityl)-D-ribitol (37)**



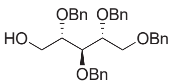
To a solution of alcohol **36** (0.70 g; 0.63 mmol; 1.0 eq.) in DCM (6.3 ml; 0.10 M) was added DIPEA (0.16 ml; 0.94 mmol; 1.5 eq.). The mixture was stirred over activated MS 4Å for +/- 30 min. *N,N'*-di-isopropylamino-2-cyanoethyl-chlorophosphite (0.17 ml; 0.75 mmol; 1.2 eq.) was added and the mixture was stirred for 1h. Water was added, the mixture was diluted with DCM and the organic layer was washed with sat. aq. $NaHCO_3$:NaCl (v/v= 1:1), dried over Na_2SO_4, filtrated and concentrated *in vacuo*. Purification by TEA neutralized column chromatography pentane/EtOAc 1:0 to 1:1 pentane/EtOAc yielded phosphoramidite **37** in 81% yield (0.67 g; 0.51 mmol). ^{1}H NMR (400 MHz, CD_3CN) δ= 1.07 - 1.18 (m, 12H, 4x CH_3-isopropylamine), 1.72 (d, 3H, *J*= 14.7 Hz, CH_3-NAc), 2.37 - 2.51 (m, 2H, CH_2-cyanoethyl), 3.22 (dt, 1H, *J*= 9.8 Hz, 4.7 Hz, H-6'), 3.45 (dd, 1H, *J*= 10.3 Hz, 2.9 Hz, H-6"), 3.52 - 3.96 (m, 15H, 2x CH_3O, 2x CH_2-Rbo, 2x CH-isopropylamine, H-5, H-3, CH-Rbo), 3.98 - 4.22 (m, 4H, H-2, H-4, 2x CH-Rbo), 4.45 (dd, 1H, *J*= 11.0 Hz, 4.3 Hz, C*H*H-Bn), 4.52 (dd, 1H, *J*= 12.0 Hz, 5.3 Hz, C*H*H-Bn), 4.56 - 4.67 (m, 4H, CH_2-Bn), 4.70 - 4.84 (m, 4H, CH_2-Bn), 4.98 (dd, 1H, *J*= 9.8 Hz, 3.6 Hz, H-1), 6.36 (dd, 1H, *J*= 16.4 Hz, 9.0 Hz, N*H*), 6.74 - 6.83 (m, 4H, H-arom), 7.11 - 7.22 (m, 3H, H-arom), 7.22 - 7.51 (m, 31H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 20.8, 20.9, 21.0, 21.0 (CH_2-cyanoethyl), 23.3, 23.3 (CH_3-NAc), 24.9, 25.0, 25.1, 25.2, 25.2, 25.3 (CH_3-isopropylamine), 43.7, 43.7, 43.8, 43.8, 43.9 (CH-isopropylamine), 54.1 (C-2), 55.8 (CH_3O), 59.3, 59.4, 59.5, 59.6 (CH_2-cyanoethyl), 63.6, 63.7, 63.7, 63.8, 63.9, 64.0 (CH_2-Rbo, C-6), 69.8, 69.9 (CH_2-Rbo), 71.8 (CH-Rbo), 73.3, 73.3, 73.9, 74.0, 74.3, 74.5, 75.4, 75.5, 75.5, 75.6 (CH_2-Bn), 78.1, 78.1, 78.4, 78.5, 78.6, 79.0, 79.3, 79.4, 79.6, 79.7, 81.0 (2x CH-Rbo, C-3, C-4, C-5), 86.9 (Cq-DMTr), 97.6, 97.7 (C-1), 114.0 (CH-arom), 127.7, 128.5, 128.5, 128.6, 128.6, 128.6, 128.7, 128.7, 128.7, 128.8, 128.9, 128.9, 129.0, 129.0, 129.2, 129.2, 129.3, 129.3, 131.0, 131.0, 131.0 (CH-arom), 137.0, 137.1, 137.1, 139.5, 139.5, 139.6, 139.6, 139.8, 139.9, 140.0, 146.4, 159.5, 159.5 (Cq-arom), 170.3, 170.4 (C=O); ^{31}P NMR (162 MHz, CD_3CN) δ= 148.9.

2,3,4,5-tetra-*O*-benzyl-1-*O*-(4,4'-dimethoxytrityl)-D-ribitol (39)



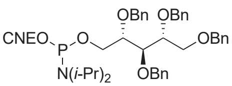
To a solution of compound **38** (887 mg; 1.16 mmol; 1.0 eq.) in a mixture of THF/DMF (10.0 ml; 0.12 M: v/v= 7:1) at 0°C was added NaH (100 mg; 2.32 mmol, 2.0 eq.) followed by the addition of BnBr (0.20 ml; 1.74 mmol; 1.5 eq.) and the mixture was allowed to warm up to rt and was stirred overnight. The mixture was quenched with MeOH at 0°C, was diluted with Et_2O and the organic layer was washed with 4x water and brine. The organic layer was dried over Na_2SO_4, filtrated and concentrated *in vacuo*. Purification by column chromatography pentane/EtOAc 1:0 to 8:2 pentane/EtOAc yielded compound **39** in 84% yield (836 mg; 0.98 mmol). $[\alpha]_D^{25}$ (DCM *c* 1): +11.9; IR (neat, cm^{-1}): 3567, 2931, 2355, 1608, 1508, 1454, 1251, 1176, 1093, 829, 736, 697; ^1H NMR (400 MHz, CD_3CN) δ= 3.25 - 3.38 (m, 2H, CH_2-Rbo), 3.66 (dd, 1H, *J*= 10.5 Hz, 5.6 Hz, C*H*H-Rbo), 3.71 (d, 6H, *J*= 1.4 Hz, CH_3O), 3.76 (dd, 1H, *J*= 10.6 Hz, 3.1 Hz, CH*H*-Rbo), 3.84 - 3.95 (m, 3H, CH-Rbo), 4.46 (s, 2H, CH_2-Bn), 4.48 - 4.61 (m, 3H, CH_2-Bn), 4.61 - 4.67 (m, 2H, CH_2-Bn), 4.72 (d, 1H, *J*= 11.6 Hz, C*H*H-Bn), 6.77 (dd, 4H, *J*= 9.0 Hz, 2.7 Hz, H-arom), 7.09 - 7.48 (m, 29H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 55.8 (CH_3O), 64.7 (CH_2-Rbo), 71.0 (CH_2-Rbo), 72.9, 73.3, 73.7, 74.2 (CH_2-Bn), 79.6, 79.8 (CH-Rbo), 86.8 (Cq-DMTr), 113.9 (CH-arom), 127.6, 128.3, 128.4, 128.6, 128.6, 128.7, 128.8, 129.0, 129.1, 129.2, 129.3, 129.3, 131.0, 131.0 (CH-arom), 137.1, 137.2, 139.6, 139.7, 139.9, 146.4, 159.5 (Cq-arom); HRMS: $[M+Na]^+$ calcd for $C_{54}H_{54}O_7Na$ 837.3767, found 837.3784.

2,3,4,5-tetra-*O*-benzyl-D-ribitol (40)



Compound **39** (1.04 g, 1.27 mmol; 1.0 eq.) was dissolved in a solution of 3% DCA in DCM (23 ml, 0.18 M, 3.3 eq.) and the reaction mixture was stirred for 1h at rt. A mixture of $MeOH/H_2O$ (23 ml; v/v= 1:1) was added, and the reaction mixture was stirred for 45 minutes. The mixture was diluted in DCM, and the organic phase was washed with sat. aq. $NaHCO_3$:brine (1:1) (v/v). The water layer was extracted with DCM (3x), and the combined organic layers were dried over $MgSO_4$, filtrated and concentrated *in vacuo*. Column chromatography pentane/EtOAc 1:0 to 8:2 pentane/EtOAc yielded title compound **40** (0.56 g, 1.08 mmol) in 87% yield. $[\alpha]_D^{25}$ ($CHCl_3$ *c* 1.0): -9.8; IR (neat, cm^{-1}): 3031, 2866, 2354, 1507, 1454, 1098, 1029, 736, 697; ^1H NMR (400 MHz, $CDCl_3$) δ= 2.32 (s, 1H, O*H*), 3.61 - 3.79 (m, 5H, H-1, H-3, H-5), 3.88 (td, 1H, *J*= 5.1, 3.7 Hz, H-4), 3.94 (t, 1H, *J*= 4.7 Hz, H-2), 4.37 - 4.85 (m, 8H, 4x CH_2-Bn), 7.23 - 7.47 (m, 20H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 61.5 (C-1), 69.8 (C-5), 72.0 - 74.1 (4x CH_2-Bn), 78.3 (C-4), 78.9 (C-3), 79.2 (C-2), 127.8 - 128.5 (C-arom), 138.2 - 138.4 (Cq-arom); HRMS: $[M+Na]^+$ calcd for $C_{33}H_{36}O_5Na$ 535.2460, found 535.2435.

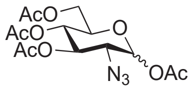
2,3,4,5-tetra-*O*-benzyl-1-*O*-(2-cyanoethyl-*N,N*-diisopropylphosphoramidite)-D-ribitol (41)



To a solution of alcohol **40** (388 mg; 0.76 mmol; 1.0 eq.) in DCM (7.6 ml; 0.10 M) was added DIPEA (0.20 ml; 1.14 mmol; 1.5 eq.). The mixture was stirred over activated MS 4Å for +/- 30 min. *N,N'*-di-isopropylamino-2-cyanoethyl-chlorophosphite (0.20 ml; 0.91 mmol; 1.2 eq.) was added and the mixture was stirred for 1h. Water was added, the mixture was diluted with DCM and the organic layer was washed with sat. aq. $NaHCO_3$:NaCl (v/v= 1:1), dried over Na_2SO_4, filtrated and concentrated *in vacuo*. Purification by TEA neutralized column chromatography pentane/EtOAc 1:0 to 8:2 pentane/EtOAc yielded phosphoramidite **41** in 82% yield (442 mg; 0.62 mmol). ^1H NMR (400 MHz, CD_3CN) δ= 1.15 - 1.19 (m, 12H, 4x

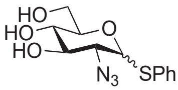
CH_3 isopropylamino), 2.53 - 2.60 (m, 2H, CH_2-cyanoethyl), 3.59 - 4.04 (m, 11H, 2x CH-isopropylamino, 2x CH_2-Rbo, 3x CH-Rbo, CH_2-cyanoethyl), 4.49 - 4.74 (m, 8H, 4x CH_2 -Bn), 7.28 - 7.38 (m, 20H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 21.0, 21.0 (CH_2-cyanoethyl), 24.9, 25.0, 25.0, 25.1 (CH_3-isopropylamino), 59.2, 59.3, 59.4, 59.5 (CH_2-cyanoethyl), 63.7, 63.8 (CH_2-Rbo), 71.0 (CH_2-Rbo), 72.8, 72.8, 72.9, 73.7, 74.5 (CH_2-Bn), 79.4, 79.6, 80.0, 80.1 (CH-Rbo), 119.5 (Cq-cyanoethyl), 128.3 - 129.2 (CH-arom), 139.7-139.9 (Cq-arom 4x); ^{31}P NMR (162 MHz, CD_3CN) δ= 149.1, 149.0.

1,3,4,6-tetra-*O*-acetyl-2-azido-2-deoxy-D-glucopyranose (22)



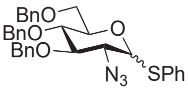
Glucosamine · HCl (17.8 g, 82.8 mmol; 1.0 eq.) was dissolved in MeOH (410 mL, 0.2 M). K_2CO_3 (30.8 g, 223 mmol, 2.7 eq.), $CuSO_4 \cdot 5\ H_2O$ (0.21 g, 1.32 mmol, 0.02 eq.), and the stick reagent (31.3 g, 99.3 mmol, 1.2 eq.) were added at rt. The reaction mixture was stirred for 3 hours, and the mixture was filtrated over celite. The mixture was concentrated *in vacuo*, co-evaporated with toluene (2x), and continued without purification to give the crude glucoseazide. The crude compound (17.0 g) was dissolved in pyridine (410 mL, 0.2 M). Ac_2O (62.6 mL, 662 mmol, 8.0 eq.) was added at 0°C and the reaction mixture was stirred from 0°C to rt overnight, followed by the addition of MeOH at 0°C. The mixture was diluted in EtOAc, and washed with 3M HCl (3x), sat. aq. $NaHCO_3$ (2x), and brine (1x). The organic layer was dried over $MgSO_4$, filtrated, and concentrated *in vacuo* to give title compound **22** (30.6 g, 81.9 mmol) as an α:β mixture with a ratio of 1 : 2.3 in 99% yield over 2 steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ= 1.97 – 2.25 (m, 12H, 4x C*H*$_3$-Acetyl), 3.63 – 3.76 (m, 1H, H-2), 3.88 (ddd, *J*= 9.8, 4.4, 2.1 Hz, 1H, H-5β), 4.01 – 4.35 (m, 2H, H-6), 4.97 – 5.20 (m, 2H, H-3β, H-4), 5.45 (dd, *J*= 10.6, 9.4 Hz, 0.44H, H-3 α), 5.62 (d, *J*= 8.6 Hz, 1H, H-1β), 6.31 (d, *J*= 3.6 Hz, 0.44H, H-1 α); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 20.2 – 20.6 (4x *C*H$_3$- Acetyl α, 4x *C*H$_3$-Acetyl β), 59.9 (C- 2α), 61.2 (C-6), 62.3 (C-2β), 67.6 (C-4β, C-4 α), 69.5 (C-5 α), 70.5 (C-3 α), 72.3 (C-3β, C-5β), 89.7 (C-1α), 92.2 (C-1β), 168.3 – 170.2 (4x C=O- α, 4x C=O- β); HRMS: $[M+Na]^+$ calcd for $C_{14}H_{19}N_3O_9Na$ 396.1019, found 396.1021.

Phenyl 2-azido-2-deoxy-thio-D-glucopyranose (23)



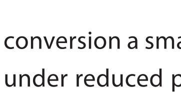
Compound **22** (30.6 g, 81.9 mmol; 1.0 eq.) was dissolved in dry DCM (275 mL, 0.3 M). Thiophenol (8.35 mL, 81.9 mmol, 1.0 eq.) and $BF_3 \cdot OEt_2$ (31.1 mL, 246 mmol, 3.0 eq.) were added and the reaction mixture was refluxed for 7 days. TEA was added, and the organic layer was washed with sat. aq. $NaHCO_3$ (3x), 1M NaOH (3x), and brine (1x). The organic layer was dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Column chromatography (100% toluene to 32% Et_2O in toluene) yielded the crude product. The crude compound (25.0 g) was dissolved in MeOH (300 mL, 0.2 M), followed by the dropwise addition of NaOMe (5.4 M) in MeOH (4.4 mL, 23.6 mmol, 0.4 eq.). The reaction mixture was stirred at rt overnight, followed by the addition of H^+ amberlite. The H^+ amberlite was filtered off, and the mixture was concentrated *in vacuo*. Column chromatography (100% DCM to 9% MeOH in DCM) yielded triol **23** (13.7 g, 46.0 mmol) as an α:β mixture with a ratio of 2.9 : 1 in 56% yield over 2 steps. ^{1}H NMR (400 MHz, MeOD) δ= 3.30 – 3.40 (m, 1H, H-4α), 3.53 – 3.60 (m, 1H, H-5α), 3.62 – 3.70 (m, 3H, H-2α, H-6), 3.99 (dt, *J* = 10.0, 3.6 Hz, 1H, H-3α), 4.43 (d, *J* = 10.1 Hz, 0.34H, H-1β), 5.46 (d, *J* = 5.2 Hz, 1H, H-1α), 6.95 – 7.90 (m, 5H, H-arom); ^{13}C-APT NMR (101 MHz, MeOD) δ= 62.2 (C-6α), 65.5 (C-2α), 71.9 (C-4α), 74.8 – 75.0 (C-3α, C-5α), 87.3 (C-1β), 89.2 (C-1α), 128.8 – 133.9 (C-arom), 135.5 (Cq-arom); HRMS: $[M+Na]^+$ calcd for $C_{12}H_{15}N_3O_4SNa$ 320.0681, found 320.0685.

Phenyl 3,4,6-tri-*O*-benzyl-2-azido-2-deoxy-thio-D-glucopyranose (24)



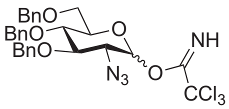
Triol **23** (13.7 g, 46.0 mmol; 1.0 eq.) was co-evaporated with toluene, and dissolved in a (v/v= 1:1) mixture of DMF/THF (130 mL, 0.35 M). The mixture was cooled to 0°C and NaH (8.3 g, 207 mmol, 4.5 eq., 60% in mineral oil) was added portion wise. BnBr (21.3 mL, 180 mmol, 3.9 eq.) was added dropwise, and the reaction was stirred from 0°C to rt overnight, followed by the slow addition of a small amount of MeOH at 0°C. The mixture was diluted in Et_2O, and the organic phase was washed with H_2O (4x), and brine (1x). The organic layer was dried over $MgSO_4$, filtrated and concentrated *in vacuo*. Column chromatography (100% pentane to 12% EtOAc in pentane) yielded title compound **24** (25.7 g, 45.2 mmol) as an α/β mixture with a ratio of 2:3 in 98% yield. IR (neat, cm^{-1}): 3595, 3064, 2550, 2108, 1457, 1054, 1027, 738, 697; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 3.29 – 3.39 (m, 1H, H- 2β), 3.41 – 3.55 (m, 2H, H-3β, H-5β), 3.55 – 3.67 (m, 2.3H, H-4β, H-6α), 3.68 – 3.87 (m, 4H, H-6β, H-3α, H-4α, H-5α), 3.94 (dd, *J*= 10.1, 5.3 Hz, 1H, H-2α), 4.40 (d, *J*= 10.2 Hz, 1H, H-1β), 4.33 – 4.95 (m, 10H, 3x CH_2-Cq α, 3x CH_2-Cq β), 5.60 (d, *J*= 5.3 Hz, 1H, H-1α), 6.81 – 7.88 (m, 33H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 64.1 (C-2α), 65.1 (C-2β), 68.4 (C-6α), 68.8 (C-6β), 71.9 (C-3α/C-3β/C-5α/C-5β), 77.6 (C-4β), 78.3 (C-4α), 79.4 (C-3α/C-3β/C-5α/C-5β), 81.9 (C-3α/C-3β/C-5α/C-5β), 85.1 (C-3α/C-3β/C-5α/C-5β), 86.0 (C-1β), 87.3 (C-1α), 127.6 – 133.7 (C-arom), 131.2 – 138.3 (Cq-arom); HRMS: $[M+Na]^+$ calcd for $C_{33}H_{33}N_3O_4SNa$ 590.2089, found 590.2094.

3,4,6-tri-*O*-benzyl-2-azido-2-deoxy-D-glucopyranose (25)



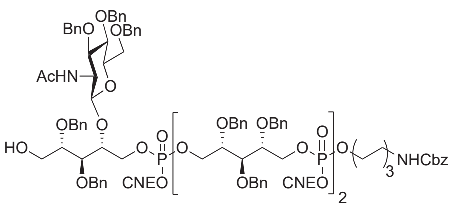
Compound **24** (17.9 g, 31.5 mmol; 1.0 eq.) was dissolved in acetone (650 mL, 0.05 M), followed by the addition of NBS (22.5 g, 126 mmol, 4.0 eq.). The reaction mixture was stirred for 3 hours, and after full conversion a small amount of sat. aq. $Na_2S_2O_3$ was added. The mixture was concentrated under reduced pressure and diluted in EtOAc. The organic phase was washed with sat. aq. $Na_2S_2O_3$ (2x), sat. aq. $NaHCO_3$ (1x), and brine (1x). The organic layer was dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Column chromatography (100% pentane to 30% EtOAc in pentane) yielded hemiacetal **25** (9.31 g, 19.6 mmol) as an α/β mixture with a ratio of 1.3:1 in 62% yield. IR (neat, cm^{-1}): 3410, 2345, 2106, 1457, 1120, 1052, 1027, 736, 697; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 2.96 (dd, *J*= 3.4, 1.3 Hz, 1H, OH), 3.33 – 3.53 (m, 4H, H-2α, H-2β, H-3β, H-5β), 3.54 – 3.74 (m, 6H, H-4α, H- 4β, H-6α, H-6β), 4.02 (dd, *J*= 10.2, 8.9 Hz, 1H, H-3α), 4.08 (ddd, *J*= 10.0, 4.4, 2.2 Hz, 1H, H-5α), 4.41 – 4.95 (m, 12, H-1β, 3x CH_2-Bn α, 3x CH_2-Bn β), 5.33 (t, *J*= 3.4 Hz, 1H, H-1α), 6.94 – 8.16 (m, 25H, H-arom); ^{13}C-APT NMR (101 MHz, $CDCl_3$) δ= 64.1 (C-2α), 68.6 (C-6α), 70.8 (C-5α), 73.6 – 75.7 (3x CH_2-Bn), 78.6 (C-4α), 80.2 (C-3α), 92.2 (C-1α), 96.3 (C-1β), 127.9 – 128.6 (C-arom), 137.8 – 137.9 (Cq-arom); HRMS: $[M+Na]^+$ calcd for $C_{27}H_{29}N_3O_5Na$ 498.2005, found 498.1999.

O-(3,4,6-tri-*O*-benzyl-2-azido-2-deoxy-α/β-D-glucopyranosyl) trichloroacetimidate (26)



Hemiacetal **25** (4.3 g, 9.0 mmol; 1.0 eq.) was co-evaporated with toluene (2x) under a N_2 atmosphere and dissolved in dry DCM (45 mL, 0.2 M). The mixture was cooled to 0°C and K_2CO_3 (3.7 g, 27 mmol, 3.0 eq.) and TCAN (5.4 mL, 54 mmol, 6.0 eq.) were added. The reaction mixture was stirred from 0°C to rt overnight. K_2CO_3 was filtered off after full conversion and the mixture was concentrated *in vacuo* at 30°C. Column chromatography with neutralized silica (100% pentane to 15% EtOAc in pentane) yielded title compound **26** (4.9 g, 8.0 mmol) as an α/β mixture with a ratio of 1:8.3 in 89% yield. IR (neat, cm^{-1}): 3336, 2866, 2360, 2110, 1457, 1057, 1029, 737, 697; ^{1}H NMR (400 MHz, CD_3CN) δ= 3.51 – 3.80 (m, 7H, H-2, H-3, H-4, H-5β, H-6), 3.88 – 4.00 (0.13 H, H-5α), 4.35 – 5.17 (m, 7H, 3x CH_2-Bn), 5.69 (d, *J*= 7.6 Hz, 1H, H-1β), 6.37 (d, *J*= 3.4 Hz, 0.13H, H-1α), 7.06 – 7.57 (m, 19H, H-arom), 9.07 (s, 0.13H, NH-α), 9.17 (s, 1H, NH-β); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 66.6 (C-2β), 69.2 (C-6β), 73.8 – 76.1 (3x CH_2-Bn), 76.6 (C-5β), 78.4 (C-4β), 83.6 (C-3β), 95.6 (C-1α), 97.3 (C-1β), 128.7 – 129.4 (C-arom), 139.2 (Cq-arom), 161.1 (NH=*Cq*); HRMS: $[M+Na]^+$ calcd for $C_{27}H_{29}N_3O_5Na$ (hydrolysed form of compound **26**) 498.2005, found 498.2000.

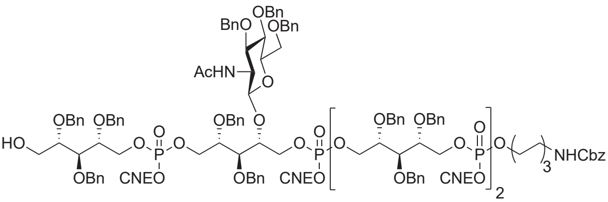
Trimer (46)



According to the general procedure above, alcohol **45** (276 mg; 0.208 mmol; 1.0 eq.) was coupled with phosphoramidite **20** (431 mg; 0.305 mmol; 1.5 eq.) and the title compound was synthesized in 88% yield (432 mg; 0.184 mmol). IR (neat, cm^{-1}): 3546, 2931, 2868, 1717, 1560, 1453, 1262, 1025, 1005, 736, 697; ^{1}H NMR (400 MHz, CD_3CN) δ= 1.22 - 1.29 (m, 4H, CH_2-hexylspacer), 1.37 - 1.44 (m, 2H, CH_2-hexylspacer), 1.53 - 1.59 (m, 2H, CH_2-hexylspacer), 1.86 (d, 3H, *J*= 4.6 Hz, CH_3-NAc), 2.50 – 2.70 (m, 6H, CH_2-

cyanoethyl), 2.89 - 2.93 (m, 1H, OH), 3.04 (q, 2H, *J*= 4.5 Hz, CH_2-N hexylspacer), 3.40 - 4.12 (m, 24H, CH_2-Rbo, CH_2-O, 3x CH_2 cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, CH-Rbo), 4.12 - 4.32 (m, 11H, 5x CH_2-Rbo, CH-Rbo/H-3/H-4/H-5), 4.40 - 4.79 (m, 23H, CH_2-Bn, H-1), 5.03 (s, 2H, CH_2-Cbz), 5.67 (bs, 1H, N*H*), 6.72 (dd, 1H, *J*= 9.1 Hz, 2.3 Hz, N*H*Ac), 7.21 - 7.36 (m, 60H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 20.1, 20.2, 20.2, 20.2, (CH_2 cyanoethyl), 23.7 (CH_3-NAc), 25.7, 26.8, 30.4, 30.7, 30.8 (CH_2-hexylspacer), 41.4 (CH_2-N hexylspacer), 56.4 (C-2), 61.5 (CH_2-Rbo), 63.1, 63.1, 63.3, 63.4 (CH_2 cyanoethyl), 66.6 (CH_2-Cbz), 67.5, 67.8, 68.6, 68.9, 69.0, 70.0 (CH_2-Rbo, C-6), 72.6, 73.1, 74.0, 74.5, 75.3, 75.5, (CH_2-Bn), 75.6, 78.3, 78.6, 79.3, 79.4, 79.7, 80.3, 83.6, 83.8 (CH-Rbo, C-3, C-4, C-5), 101.7, 101.8 (C-1), 118.5, 118.5, 118.6, 118.7 (Cq-cyanoethyl), 128.4, 128.5, 128.5, 128.6, 128.7, 128.7, 128.8, 128.9, 128.9, 129.2, 129.2, 129.2, 129.3, 129.3, 129.3, 129.4 (CH-arom), 139.1, 139.3, 139.4, 139.6, 139.8 (Cq-arom), 171.0 (C=O); ^{31}P NMR (162 MHz, CD_3CN) δ= 0.2, 0.2, -0.1, -0.1, -0.2, -0.2; HRMS: $[M+2H]^{2+}$ calculated for $C_{123}H_{144}N_5O_{29}P_3$ 1124.4591, found 1124.4622.

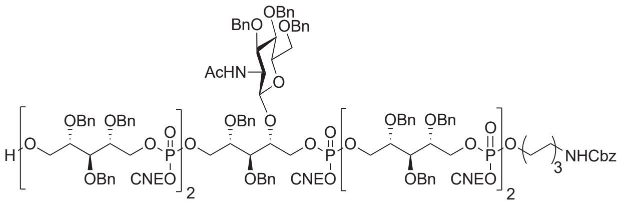
Tetramer (48)



According to the general procedure above, alcohol **46** (225 mg; 0.100 mmol; 1.0 eq.) was coupled with phosphoramidite **42** (109 mg g; 0.15 mmol; 1.5 eq.) and the title compound was synthesized in 90% yield (250 mg; 89.7 μmol). IR (neat, cm-[1]): 3567, 2935, 2868, 1717, 1560, 1454, 1265, 1092, 1025, 1003, 734, 697; ^{1}H NMR (400 MHz, CD_3CN) δ= 1.22 - 1.31 (m, 4H, CH_2-hexylspacer), 1.37 - 1.42 (m, 2H, CH_2-hexylspacer), 1.55 - 1.60 (m, 2H, CH_2-hexylspacer), 2.47 - 2.71 (m, 8H, 4x CH_2-cyanoethyl), 3.05 (q, 2H, *J*= 6.7 Hz, CH_2-N hexylspacer), 3.43 - 4.13 (m, 29H, CH_2-Rbo, CH_2-O, 4x CH_2-cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, 11x CH-Rbo), 4.13 - 4.45 (m, 15H, 7x CH_2-Rbo, H-1), 4.45 - 4.78 (m, 29H, 14x CH_2-Bn, H-1), 5.03 (s, 2H, CH_2-Cbz), 5.72 (t, 1H, *J*= 6.2 Hz, N*H*), 6.80 - 6.86 (m, 1H, N*H*Ac), 7.18 – 7.42 (m, 75H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 20.0, 20.1, 20.1, 20.1, 20.2, 20.2, 20.2 (CH_2-cyanoethyl), 23.7 (CH_3-NAc), 25.7, 26.8, 30.4, 30.7, 30.8 (CH_2-hexylspacer), 41.4 (CH_2-N hexylspacer), 56.3, 56.5 (C-2), 61.5 (CH_2-Rbo), 63.1, 63.1, 63.2, 63.2, 63.3, 63.4, 63.5, 63.5 (CH_2-cyanoethyl), 66.6 (CH_2-Cbz), 67.5, 67.5, 67.8, 67.9, 68.2, 68.2, 68.9, 68.9, 69.0, 69.0, 70.0 (CH_2-Rbo, C-6), 72.7, 72.9, 73.0, 73.0, 73.1, 73.1, 73.2, 73.9, 74.4, 74.5, 74.5, 74.6, 75.3, 75.5, 75.5 (CH_2-Bn), 75.7, 75.7, 78.3, 78.3, 78.3, 78.4, 78.6, 78.7, 78.8, 78.9, 78.9, 79.0, 79.1, 79.2 (CH-Rbo, C-3, C-4, C-5), 80.6 (CH-Rbo), 83.5, 83.7 (CH-Rbo, C-3, C-4, C-5), 101.3, 101.4 (C-1), 118.5, 118.5, 118.6, 118.7, 118.7 (Cq-cyanoethyl), 128.4, 128.4, 128.4, 128.5, 128.5, 128.6, 128.7, 128.7, 128.7, 128.8, 128.8, 128.8, 128.9, 129.0, 129.1, 129.2, 129.2, 129.2, 129.3, 129.3, 129.4, 129.4 (CH-arom), 138.5, 139.1, 139.2, 139.3, 139.3, 139.5, 139.7, 139.8, 139.8 (Cq-arom), 157.3, 171.1 (C=O); ^{31}P NMR (162 MHz, CD_3CN)

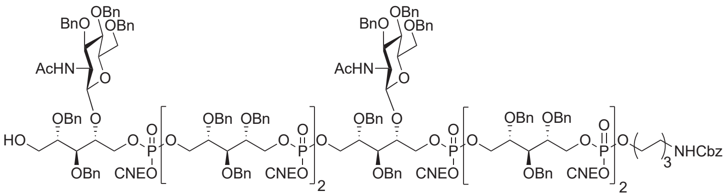
δ= 0.5, 0.3, 0.3, 0.0, 0.0, 0.0; HRMS: $[M+2H]^{2+}$ calculated for $C_{152}H_{176}N_6O_{36}P_4$ 1393.0549, found 1393.0590.

Pentamer (50)



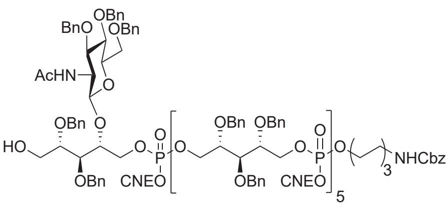
According to the general procedure above, alcohol **48** (210 mg; 75.4 µmol; 1.0 eq.) was coupled with phosphoramidite **42** (71.0 mg; 98.0 µmol; 1.3 eq.) and the title compound was synthesized in 68% yield (171 mg; 51.5 µmol). IR (neat, cm^{-1}): 3567, 2935, 2868, 1717, 1560, 1457, 1262, 1093, 1027, 1009, 747, 698; ^{1}H NMR (500 MHz, CD_3CN) δ= 1.20 - 1.31 (m, 4H, CH_2-hexylspacer), 1.38 - 1.42 (m, 2H, CH_2-hexylspacer), 1.55 - 1.60 (m, 2H, CH_2-hexylspacer), 1.84 - 1.85 (m, 3H, CH_3-NAc), 2.46 - 2.70 (m, 10H, 5x CH_2-cyanoethyl), 3.05 (q, 2H, *J*= 6.9 Hz, CH_2-N hexylspacer), 3.42 (td, 1H, *J*= 13.9 Hz, 13.3 Hz, 6.7 Hz, CH-Rbo/H-3/H-4/H-5), 3.55 (t, 1H, *J*= 9.2 Hz, CH-Rbo/H-3/H-4/H-5), 3.60 - 4.12 (m, 35H, 1x CH_2-Rbo, CH_2-O, 5x CH_2-cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, CH-Rbo), 4.17 - 4.45 (m, 19H, 9x CH_2-Rbo, C*H*H-Bn, CH-Rbo/H-3/H-4/H-5), 4.45 - 4.77 (m, 34H, 16.5x CH_2-Bn, H-1), 5.03 (s, 2H, CH_2-Cbz), 5.66 (s, 1H, N*H*), 6.74 (d, 1H, *J*= 9.3 Hz, N*H*Ac), 7.19 - 7.35 (m, 90H, H-arom); ^{13}C-APT NMR (126 MHz, CD_3CN) δ= 20.1, 20.1, 20.2, 20.2, 20.2, 20.2, 20.3 (CH_2-cyanoethyl), 23.7 (CH_3-NAc), 25.7, 26.8, 30.4, 30.8, 30.8 (CH_2-hexylspacer), 41.4 (CH_2-N hexylspacer), 56.4, 56.4 (C-2), 61.6 (CH_2-Rbo), 63.1, 63.1, 63.2, 63.2, 63.2, 63.3, 63.4, 63.5 (CH_2-cyanoethyl), 66.6 (CH_2-Cbz), 67.5, 67.9, 68.2, 68.3, 68.9, 69.0, 70.1 (CH_2-Rbo, C-6), 72.8, 73.0, 73.0, 73.1, 73.1, 73.2, 73.2, 74.0, 74.5, 74.5, 74.6, 74.6, 75.3, 75.5, 75.5 (CH_2-Bn), 75.8, 75.8, 78.3, 78.3, 78.4, 78.4, 78.5, 78.6, 78.7, 78.8, 78.9, 78.9, 79.0, 79.1, 79.1, 79.1, 79.2, 79.2, 79.3, 79.3, 79.3 (CH-Rbo, C-3, C-4, C-5), 80.6, 80.6 (CH-Rbo), 83.6, 83.7 (CH-Rbo, C-3, C-4, C-5), 101.3, 101.5 (C-1), 118.4, 118.5, 118.5, 118.5, 118.6, 118.6, 118.7, 118.7 (Cq-cyanoethyl), 128.4, 128.4, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 128.7, 128.7, 128.8, 128.8, 128.8, 128.9, 128.9, 129.0, 129.0, 129.1, 129.2, 129.2, 129.3, 129.3, 129.4 (CH-arom), 139.1, 139.2, 139.2, 139.2, 139.3, 139.4, 139.6, 139.7, 139.8, 139.8, 139.8 (Cq-arom), 157.3, 171.0 (C=O); ^{31}P NMR (202 MHz, CD_3CN) δ= 0.5, 0.4, 0.3, 0.2, 0.1, 0.1, 0.0, 0.0; HRMS: $[M+2H]^{2+}$ calculated for $C_{181}H_{208}N_7O_{43}P_5$ 1661.6508, found 1661.6587.

Hexamer (52)



According to the general procedure above, alcohol **50** (150 mg; 45.0 μmol; 1.0 eq.) was coupled with phosphoramidite **20** (75.9. mg; 58.0 μmol; 1.3 eq.) and the title compound was synthesized in 79% yield (151 mg; 35.6 μmol). IR (neat, cm-[1]): 3567, 2933, 2866, 1717, 1558, 1454, 1262, 1070, 1025, 1004, 737, 697; ^{1}H NMR (400 MHz, CD_3CN) δ= 1.23 - 1.31 (m, 4H, CH_2-hexylspacer), 1.36 - 1.45 (m, 2H, CH_2-hexylspacer), 1.55 - 1.61 (m, 2H, CH_2-hexylspacer), 1.86 - 1.89 (m, 6H, CH_3-NAc), 2.47 - 2.70 (m, 12H, CH_2-cyanoethyl), 3.06 (q, 2H, *J*= 6.8 Hz, CH_2-N hexylspacer), 3.38 – 4.14 (m, 41H, 1x CH_2-Rbo, CH_2-O, 5x CH_2 cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, 17x CH-Rbo), 4.14 – 4.41 (m, 23H, 11x CH_2-Rbo, CH-Rbo/H-3/H-4/H-5), 4.43 - 4.78 (m, 46H, 22x CH_2-Bn, 2x H-1), 5.04 (s, 2H, CH_2-Cbz), 5.72 (s, 1H, NH), 6.75 - 6.79 (m, 2H, N*H*Ac), 7.21 - 7.35 (m, 115H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 20.0, 20.1, 20.1, 20.1, 20.2, 20.2, 20.2 (CH_2-cyanoethyl), 23.7 (CH_3-NAc), 25.7, 26.8, 30.4, 30.7, 30.8 (CH_2 hexylspacer), 41.4 (CH_2-N hexylspacer), 55.8, 56.3, 56.4 (C-2), 61.5 (CH_2-Rbo), 63.0, 63.1, 63.2, 63.4, 63.4 (CH_2-cyanoethyl), 66.6 (CH_2-Cbz), 67.4, 67.7, 67.8, 68.5, 68.9, 69.0, 70.0 (CH_2-Rbo, C-6), 72.6, 73.0, 73.1, 73.0, 74.5, 74.5, 75.3, 75.5 (CH_2-Bn), 75.7, 77.6, 78.2, 78.3, 78.6, 79.2, 79.4, 79.7, (CH-Rbo, C-3, C-4, C-5), 80.3 (CH-Rbo), 83.5, 83.6, 83.7 (CH-Rbo, C-3, C-4, C-5), 101.3, 101.6, 101.8 (C-1), 118.4, 118.5, 118.5, 118.5, 118.6, 118.6 (Cq-cyanoethyl), 127.6, 128.4, 128.5, 128.5, 128.6, 128.7, 128.7, 128.8, 128.9, 129.2, 129.3, 129.4 (CH-arom), 138.5, 139.1, 139.1, 139.2, 139.4, 139.5, 139.6, 139.7, 139.8 (Cq-arom), 157.3, 159.4, 170.9, 171.0 (C=O); ^{31}P NMR (162 MHz, CD_3CN) δ= 0.4, 0.2, 0.2, 0.1, -0.1, -0.1, -0.2, -0.2; HRMS: $[M+2H]^{2+}$ calculated for $C_{232}H_{265}N_9O_{55}P_6$ 2122.3349, found 2122.3276.

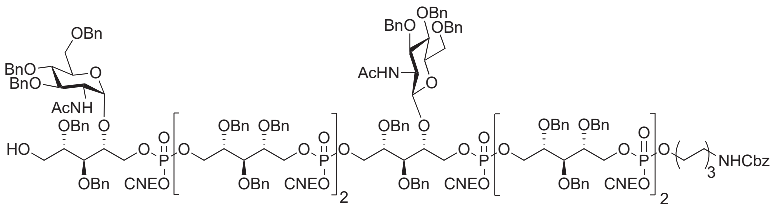
Hexamer (57)



According to the general procedure above, alcohol **56** (29.0 mg; 9.89 μmol; 1.0 eq.) was coupled with phosphoramidite **20** (16.7 mg; 12.8 μmol; 1.3 eq.) and the title compound was synthesized in 85% yield (32.3 mg; 8.36 μmol). IR (neat, cm-[1]): 3567, 2935, 2865, 1717, 1560, 1457, 1275, 1262, 1095, 1027, 750, 698; ^{1}H NMR (400 MHz, CD_3CN) δ= 1.23 - 1.30 (m, 4H, CH_2-hexylspacer), 1.36 - 1.41 (m, 2H, CH_2-hexylspacer), 1.53 - 1.59 (m, 2H, CH_2-hexylspacer), 1.83 - 1.85 (m, 3H, CH_3-NAc), 2.49 - 2.69 (m, 12H, CH_2-cyanoethyl), 3.03 (m, 2H, *J*= 6.5 Hz, CH_2-N hexylspacer), 3.39 - 4.10 (CH_2-Rbo, CH_2-O, 6x

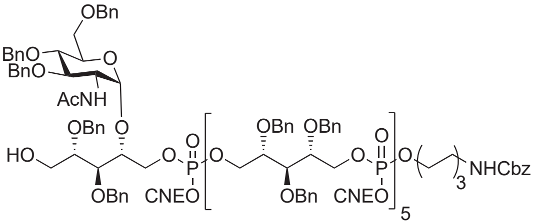
CH_2 cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, 18x CH-Rbo), 4.12 - 4.34 (m, 22H, 11x CH_2-Rbo), 4.40 - 4.77 (m, 42H, CH_2-Bn, H-1, CH-Rbo/H-3/H-4/H-5), 5.02 (s, 2H, CH_2-Cbz), 5.65 (bs, 1H, N*H*), 6.73 (d, *J*= 9.1 Hz, 1H, N*H*Ac), 7.18 – 7.35 (m, 105H); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 20.1, 20.1, 20.2, 20.2, 20.2, 20.3 (CH_2-cyanoethyl), 23.7 (CH_3-NAc), 25.7, 26.8, 30.4, 30.8, 30.8 (CH_2-hexylspacer), 41.4 (CH_2-N hexylspacer), 56.3 (C-2), 61.5 (CH_2-Rbo), 63.1, 63.1, 63.3, 63.4 (CH_2-cyanoethyl), 66.6 (CH_2-Cbz), 67.7, 67.7, 67.7, 67.7, 67.8, 67.8, 67.8, 67.8, 67.9, 68.9, 69.0, 70.0 (CH_2-Rbo, C-6), 72.6, 73.0, 73.1, 74.0, 74.5, 74.6, 75.3 (CH_2-Bn), 75.6, 78.3, 78.6, 79.3, 79.4 (CH-Rbo, C-3, C-4, C-5), 80.3 (CH-Rbo), 83.6, 83.8 (CH-Rbo, C-3, C-4, C-5), 101.7 (C-1), 118.5, 118.5 (Cq-cyanoethyl), 128.4, 128.5, 128.6, 128.7, 128.7, 128.8, 128.8, 128.9, 129.0, 129.3, 129.3, 129.3, 129.3, 129.4 (CH-arom), 139.2, 139.2, 139.5, 139.7 (Cq-arom), 171.1 (C=O); ^{31}P NMR (162 MHz, CD_3CN) δ= 0.2, 0.2, 0.2, 0.1, -0.1, -0.2, -0.2, -0.2, -0.2, -0.2; HRMS: $[M+2H]^{2+}$ calculated for $C_{210}H_{240}N_8O_{50}P_6$ 1930.7483, found 1930.7478.

Hexamer (53)



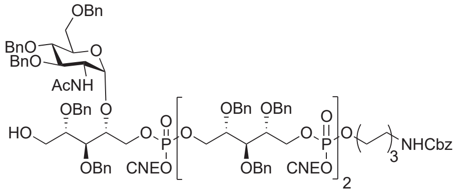
According to the general procedure above, alcohol **50** (129 g; 39.0 μmol; 1.0 eq.) was coupled with phosphoramidite **37** (76.6 mg; 58.5 μmol; 1.5 eq.) and the title compound was synthesized in 76% yield (126 mg; 29.5 μmol). IR (neat, cm-^{1}): 2932, 2869, 1717, 1560, 1455, 1274, 1262, 1093, 1027, 1007, 748, 698; ^{1}H NMR (500 MHz, CD_3CN) δ= 1.22 - 1.29 (m, 4H, CH_2-hexylspacer), 1.36 - 1.41 (m, 2H, CH_2-hexylspacer), 1.54 - 1.59 (m, 2H, CH_2-hexylspacer), 1.72 (s, 3H, CH_3-NAc), 1.85 (m, 3H, CH_3-NAc), 2.45 - 2.58 (m, 12H, CH_2-cyanoethyl), 3.03 - 3.06 (m, 2H, CH_2-N hexylspacer), 3.41 - 4.41 (m, 68H, 12x CH_2-Rbo, CH_2-O, 6x CH_2-cyanoethyl, 2x H-2, 2x H-3, 2x H-4, 2x H-5, 4x H-6, 18x CH-Rbo), 4.42 - 4.79 (m, 45H, 22x CH_2-Bn, H-1 β), 4.99 - 5.03 (m, 3H, CH_2-Cbz, H-1 α), 5.68 (bs, 1H, N*H*), 6.40 (d, 0.6H, *J*= 9.0 Hz, N*H*Ac), 6.47 (d, 0.3 H, *J*= 9.0 Hz, N*H*Ac), 6.76 (bs, 1H, N*H*Ac), 7.21 - 7.37 (m, 115H, H-arom); ^{13}C-APT NMR (126 MHz, CD_3CN) δ= 20.1, 20.2, 20.2, 20.2, 20.3 (CH_2-cyanoethyl), 23.2, 23.7 (CH_3-NAc), 25.7, 26.8, 30.4, 30.8, 30.8 (CH_2-hexylspacer), 41.4 (CH_2-N hexylspacer), 54.0, 56.4 (C-2), 60.9 (CH_2-Rbo), 63.1, 63.1, 63.2, 63.2, 63.4, 63.5 (CH_2-cyanoethyl), 66.6 (CH_2-Cbz), 67.5, 67.7, 67.8, 68.2, 68.6, 69.0, 69.0, 69.7, 70.0 (CH_2-Rbo, C-6), 72.0, 72.1 (CH-Rbo/C-3/C-4/C-5), 72.7, 72.7, 73.0, 73.1,73.1, 73.9, 74.0, 74.4, 74.5, 74.6, 74.6, 75.3, 75.5, 75.6, 75.6 (CH_2-Bn), 75.8, 76.9, 77.6, 77.6, 78.3, 78.4, 78.6, 79.2, 79.4, 79.9, 80.0, (CH-Rbo, C-3, C-4, C-5), 80.6, 81.0, 81.0 (CH-Rbo), 83.6, 83.7, (CH-Rbo, C-3, C-4, C-5), 97.3, 97.9 (C-1 α), 101.3, 101.4 (C-1 β), 118.5, 118.5, 118.6, 118.6, 118.7 (Cq-cyanoethyl), 128.4, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 128.8, 128.8, 128.9, 128.9, 129.0, 129.0, 129.2, 129.2, 129.3, 129.3, 129.4 (CH-arom), 139.1, 139.2, 139.2, 139.3, 139.5, 139.5, 139.8, 139.9 (Cq-arom), 157.3, 170.6, 171.0 (C=O); ^{31}P NMR (202 MHz, CD_3CN) δ= 0.5, 0.5, 0.4, 0.3, 0.3, 0.2, 0.1, 0.0, 0.0, 0.0; HRMS: $[M+2H]^{2+}$ calculated for $C_{232}H_{265}N_9O_{55}P_6$ 2122.3349, found 2122.3345.

Hexamer (58)



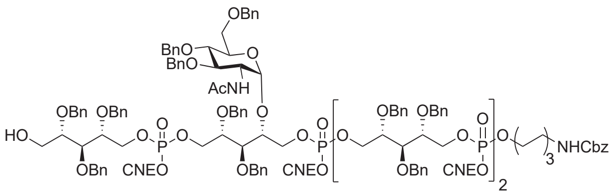
According to the general procedure above, alcohol **56** (361 mg; 0.272 mmol; 1.0 eq.) was coupled with phosphoramidite **37** (569 mg; 0.435 mmol; 1.6 eq.) and the title compound was synthesized in 53% yield (325 mg; 0.144 mmol). IR (neat, cm^{-1}): 3580, 2933, 2865, 1717, 1560, 1454, 1262, 1093, 1025, 1002, 736, 697; ^1H NMR (400 MHz, CD_3CN) δ= 1.20 - 1.32 (m, 4H, CH_2-hexylspacer), 1.36 - 1.41 (m, 2H, CH_2-hexylspacer), 1.52 - 1.59 (m, 2H, CH_2-hexylspacer), 1.72 (s, 3H, CH_3-NAc), 2.38 (td, 1H, *J*= 6.0 Hz, 2.6 Hz, CH_2-cyanoethyl), 2.45 (t, 1H, *J*= 5.9 Hz, CH_2-cyanoethyl), 2.51 - 2.59 (m, 2H, CH_2-cyanoethyl), 2.60 - 2.70 (m, 2H, CH_2-cyanoethyl), 3.03 (q, 1H, *J*= 8.3 Hz, CH_2-N hexylspacer), 3.54 - 4.39 (m, 35H, 6x CH_2-Rbo, CH_2-O, 3x CH_2-cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, 9x CH-Rbo), 4.39 - 4.82 (m, 22H, CH_2-Bn), 4.99 (d, 1H, *J*= 3.6 Hz, H-1), 5.02 (s, 2H, CH_2-Cbz), 5.66 (s, 1H, N*H*), 6.43 (d, 0.5H, *J*= 8.9 Hz, N*H*Ac), 6.52 (d, 0.3H, *J*= 9.5 Hz, N*H*Ac), 7.20 - 7.37 (m, 60H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 19.9, 20.0, 20.0, 20.1, 20.1, 20.2, 20.2, 20.2 (CH_2-cyanoethyl), 23.1 (CH_3-NAc), 25.7, 26.8, 30.4, 30.7, 30.8 (CH_2-hexylspacer), 41.4 (CH_2-N hexylspacer), 54.0 (C-2), 60.8, 60.9 (CH_2-Rbo), 63.1, 63.1, 63.2, 63.2, 63.2, 63.3 (CH_2-cyanoethyl), 66.6 (CH_2-Cbz), 67.5, 67.8, 68.6, 68.9, 69.0, 69.6, 69.7 (CH_2-Rbo, C-6), 72.0, 72.0 (CH-Rbo/C-3/C-4/C-5), 72.6, 72.7, 73.0, 73.0, 73.1, 73.1, 73.8, 74.5, 74.6, 74.6, 75.5, 75.6, 75.6 (CH_2-Bn), 76.7, 76.7, 77.4, 77.5, 78.2, 78.2, 78.3, 78.5, 78.6, 78.6, 79.2, 79.3, 79.8, 79.9, 80.9, 81.0 (CH-Rbo, C-3, C-4, C-5), 97.1, 97.8 (C-1), 118.5, 118.5, 118.5, 118.6 (Cq-cyanoethyl), 128.4, 128.5, 128.5, 128.6, 128.7, 128.7, 128.7, 128.8, 128.9, 128.9, 128.9, 129.0, 129.0, 129.1, 129.3, 129.4 (CH-arom), 139.0, 139.0, 139.0, 139.1, 139.1, 139.2, 139.4, 139.4, 139.5, 139.9 (Cq-arom), 157.3, 170.6, 170.6 (C=O); ^{31}P NMR (162 MHz, CD_3CN) δ= 0.5, 0.3, 0.0; HRMS: $[M+2H]^{2+}$ calculated for $C_{210}H_{240}N_8O_{50}P_6$ 1930.7483, found 1930.7495.

Trimer (47)



According to the general procedure above, alcohol **45** (24.0 mg; 8.17 μmol; 1 eq.) was coupled with phosphoramidite **37** (21.4 mg; 16.3 μmol; 2.0 eq.) and the title compound was synthesized in 73% yield (23.0 mg; 5.96 μmol). IR (neat, cm-[1]): 3567, 2928, 2865, 1717, 1560, 1457, 1262, 1093, 1026, 1007, 738, 698; ^{1}H NMR (500 MHz, CD_3CN) δ= 1.25 - 1.27 (m, 4H, CH_2-hexylspacer), 1.39 (m, 2H, CH_2-hexylspacer), 1.52 - 1.58 (m, 2H, CH_2-hexylspacer), 1.71 (s, 3H, CH_3-NAc), 2.45 - 2.64 (m, 12H, CH_2-cyanoethyl), 3.02 - 3.04 (m, 2H, CH_2-N hexylspacer), 3.55 - 4.35 (m, 62H, 12x CH_2-Rbo, CH_2-O, 6x CH_2-cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, 18x CH-Rbo), 4.44 - 4.80 (m, 40H, CH_2-Bn), 4.96 - 5.02 (m, 3H, CH_2-Cbz, H-1), 5.63 (bs, 1H, N*H*), 6.35 (d, 0.4H, *J*= 8.5 Hz, N*H*Ac), 6.42 (d, 0.3H, *J*= 9.0 Hz, N*H*Ac), 7.19 - 7.36 (m, 105H, H-arom); ^{13}C-APT NMR (126 MHz, CD_3CN) δ= 20.0, 20.1, 20.2, 20.3, 20.3, (CH_2-cyanoethyl), 23.2 (CH_3-NAc), 25.8, 26.9, 30.5, 30.8, 30.8 (CH_2-hexylspacer), 41.4 (CH_2-N hexylspacer), 54.0 (C-2), 60.9, (CH_2-Rbo), 63.1, 63.2, 63.2, 63.3, 63.3 (CH_2-cyanoethyl), 66.6 (CH_2-Cbz), 67.5, 67.7, 67.8, 68.6, 69.0, 69.0, 69.7 (CH_2-Rbo, C-6), 72.1 (CH-Rbo/C-3/C-4/C-5), 72.7, 73.1, 73.1, 73.2, 73.9, 74.6, 74.6, 75.5, 75.6, 75.7 (CH_2-Bn), 77.6, 77.7, 78.3, 78.4, 78.7, 78.7, 78.8, 79.4, 79.9, 80.0, 81.0, 81.0 (CH-Rbo, C-3, C-4, C-5), 97.4, 98.0 (C-1), 118.5, 118.6 (Cq-cyanoethyl), 128.5, 128.5, 128.6, 128.7, 128.8, 128.8, 128.8, 128.9, 129.0, 129.1, 129.2, 129.4, 129.4 (CH-arom), 139.2, 139.2, 139.5, 139.6, 139.9 (Cq-arom), 170.5 (C=O); ^{31}P NMR (202 MHz, CD_3CN) δ= 0.5, 0.3, 0.3, 0.0, 0.0, -0.1; HRMS: $[M+2H]^{2+}$ calculated for $C_{123}H_{144}N_5O_{29}P_3$ 1124.4591 found 1124.4624.

Tetramer (49)

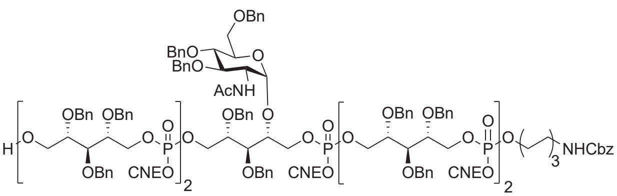


According to the general procedure above, alcohol **47** (298 mg; 0.133 mmol; 1.0 eq.) was coupled with phosphoramidite **42** (215 mg; 0.231 mmol; 1.7 eq.) and the title compound was synthesized in 82% yield (302 mg; 0.108 mmol). IR (neat, cm-[1]): 3587, 2935, 2866, 1717, 1560, 1457, 1262, 1095, 1026, 1009, 748, 698; ^{1}H NMR (400 MHz, CD_3CN) δ= 1.21 - 1.30 (m, 4H, CH_2-hexylspacer), 1.38 - 1.43 (m, 2H, CH_2-hexylspacer), 1.54 - 1.61 (m, 2H, CH_2-hexylspacer), 1.74 - 1.75 (m, 3H, CH_3-NAc), 2.36 - 2.71 (m, 8H, CH_2-cyanoethyl), 3.06 (q, 2H, *J*= 6.7 Hz, CH_2-N hexylspacer), 3.64 - 4.40 (m, 44H, 8x CH_2-Rbo, CH_2-O, 4x CH_2-cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, 12x CH-Rbo), 4.40 - 4.86 (m, 28H, CH_2-Bn), 5.04 - 5.09 (m, 3H, CH_2-Cbz, H-1), 5.74 (t, 1H, *J*= 6.1 Hz, NH), 6.64 (d, 0.4H, *J*= 8.8 Hz, N*H*Ac), 6.72 (d, 0.3H, *J*= 8.8 Hz, N*H*Ac), 7.22 - 7.38 (m, 75H, H-arom); ^{13}C-APT NMR (101

MHz, CD_3CN) δ= 20.0, 20.0, 20.1, 20.1, 20.1, 20.2, 20.2, 20.2 (CH_2-cyanoethyl), 23.2 (CH_3-NAc), 25.7, 26.8, 30.4, 30.7, 30.8 (CH_2-hexylspacer), 41.4 (CH_2-N hexylspacer), 54.1 (C-2), 61.5, 61.5 (CH_2-Rbo), 63.1, 63.1, 63.2, 63.2, 63.3, 63.3 (CH_2-cyanoethyl), 66.6 (CH_2-Cbz), 67.0, 67.1, 67.1, 67.5, 67.5, 67.7, 67.7, 67.8, 67.9, 67.9, 68.2, 68.3, 68.3, 68.4, 68.4, 68.5, 68.9, 69.0, 69.6, 69.7 (CH_2-Rbo, C-6), 72.1, 72.1 (CH-Rbo/C-3/C-4/C-5), 72.7, 72.9, 73.0, 73.1, 73.1, 73.8, 74.4, 74.5, 74.5, 74.6, 75.5, 75.6 (CH_2-Bn), 77.3, 77.9, 77.9, 78.0, 78.1, 78.1, 78.3, 78.6, 78.6, 78.8, 78.9, 79.0, 79.1, 79.4, 80.5, 80.8, 80.8 (CH-Rbo, C-3, C-4, C-5), 97.5, 97.6, 98.2, 98.2 (C-1), 118.5, 118.5, 118.6 (Cq-cyanoethyl), 128.4, 128.5, 128.5, 128.6, 128.7, 128.7, 128.8, 128.9, 129.0, 129.1, 129.3, 129.3, 129.4, 129.4 (CH-arom), 138.5, 138.8, 138.9, 139.0, 139.0, 139.1, 139.1, 139.2, 139.3, 139.4, 139.5, 139.5, 139.5, 139.7, 139.9, 139.9 (Cq-arom), 157.3, 170.7, 170.7, 170.7 (C=O); ^{31}P NMR (162 MHz, CD_3CN) δ= 0.5, 0.3, 0.3, 0.2, 0.0, 0.0, 0.0; HRMS: $[M+2H]^{2+}$ calculated for $C_{152}H_{176}N_6O_{36}P_4$ 1393.0549, found 1393.0587.

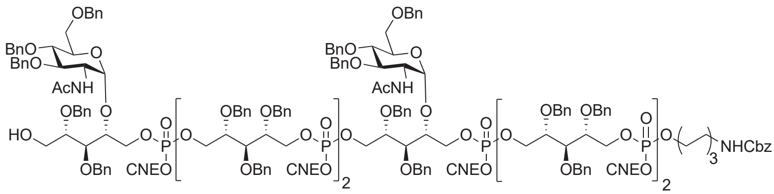
3

Pentamer (51)



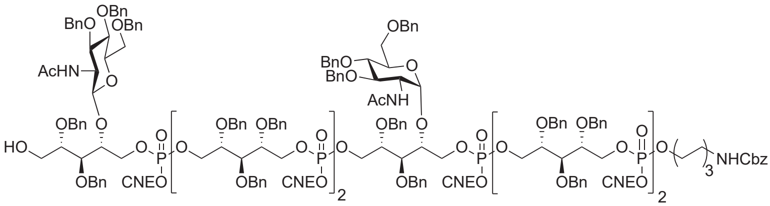
According to the general procedure above, alcohol **49** (270 mg; 97.0 μmol; 1.0 eq.) was coupled with phosphoramidite **42** (153 mg; 0.165 mmol; 1.7 eq.) and the title compound was synthesized in 89% yield (287 mg; 86.4 μmol). IR (neat, cm^{-1}): 3562, 2931, 2865, 1717, 1560, 1457, 1274, 1262, 1096, 1027, 748, 698; ^{1}H NMR (400 MHz, CD_3CN) δ= 1.20 - 1.33 (m, 4H, CH_2-hexylspacer), 1.38 - 1.44 (m, 2H, CH_2-hexylspacer), 1.54 - 1.61 (m, 2H, CH_2-hexylspacer), 1.74 - 1.75 (m, 3H, CH_3-NAc), 2.33 - 2.71 (m, 10H, CH_2-cyanoethyl), 3.06 (q, 2H, *J*= 6.7 Hz, CH_2-N hexylspacer), 3.62 - 4.40 (m, 53H, 10x CH_2-Rbo, CH_2-O, 5x CH_2-cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, 15x CH-Rbo), 4.40 - 4.86 (m, 34H, CH_2-Bn), 5.03 - 5.11 (m, 3H, CH_2-Cbz, H-1), 5.74 (t, 1H, *J*= 6.0 Hz, N*H*), 6.58 - 6.67 (m, 1H, N*H*Ac), 7.21 - 7.37 (m, 90H, H-arom); ^{13}C-APT NMR (101 MHz, CD_3CN) δ= 20.0, 20.0, 20.1, 20.1, 20.2, 20.2, 20.3 (CH_2-cyanoethyl), 23.2 (CH_3-NAc), 25.7, 26.8, 30.4, 30.7, 30.8 (CH_2-hexylspacer), 41.4 (CH_2-N hexylspacer), 54.1 (C-2), 61.5 (CH_2-Rbo), 63.1, 63.1, 63.1, 63.2, 63.2, 63.2, 63.3, 63.3, 63.4 (CH_2-cyanoethyl), 66.6 (CH_2-Cbz), 67.2, 67.5, 67.7, 67.7, 67.8, 68.2, 68.2, 68.9, 69.0, 69.6 (CH_2-Rbo, C-6), 72.1, 72.1 (CH-Rbo/C-3/C-4/C-5), 72.7, 72.9, 73.0, 73.0, 73.1, 73.1, 73.9, 74.5, 74.5, 74.5, 74.6, 75.5, 75.5, 75.5, 75.6 (CH_2-Bn), 78.1, 78.2, 78.3, 78.6, 78.6, 78.6, 78.8, 78.9, 79.0, 79.1, 79.1, 79.1, 79.4, 80.5, 80.6, 80.8, 80.8 (CH-Rbo, C-3, C-4, C-5), 97.6, 97.7, 98.2, 98.3 (C-1), 118.5, 118.5, 118.6 (Cq-cyanoethyl), 128.4, 128.5, 128.5, 128.6, 128.6, 128.6, 128.7, 128.7, 128.7, 128.8, 128.9, 128.9, 129.0, 129.0, 129.2, 129.2, 129.3, 129.3, 129.3, 129.3, 129.4, 129.4, 129.4 (CH-arom), 138.5, 138.8, 138.9, 139.0, 139.1, 139.1, 139.1, 139.2, 139.2, 139.3, 139.4, 139.5, 139.5, 139.5, 139.7, 139.7, 139.9, 139.9 (Cq-arom), 157.3, 170.6, 170.6, 170.7 (C=O); ^{31}P NMR (162 MHz, CD_3CN) δ= 0.7, 0.6, 0.6, 0.4, 0.3, 0.3, 0.3, 0.1, 0.1, 0.0, 0.0; HRMS: $[M+2H]^{2+}$ calculated for $C_{181}H_{208}N_7O_{43}P_5$ 1661.6508, found 1661.6509.

Hexamer (54)



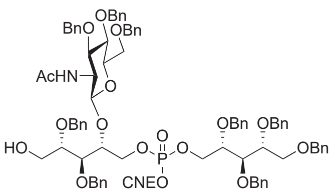
According to the general procedure above, alcohol **51** (257 mg; 77.0 μmol; 1.0 eq.) was coupled with phosphoramidite **37** (182 mg; 0.139 mmol; 1.8 eq.) and the title compound was synthesized in 88% yield (290 mg; 68.0 μmol). IR (neat, cm-[1]): 3553, 2931, 2866, 1717, 1560, 1454, 1264, 1093, 1070, 1024, 1005, 737, 697; ^{1}H NMR (500 MHz, CD_3CN) δ= 1.27 (m, 4H, CH_2-hexylspacer), 1.41 - 1.42 (m, 2H, CH_2-hexylspacer), 1.58 - 1.59 (m, 2H, CH_2-hexylspacer), 1.74 (s, 3H, CH_3-NAc), 1.75 (3H, CH_3-NAc), 2.41 - 2.68 (m, 12H, CH_2-cyanoethyl), 3.06 - 3.07 (m, 2H, CH_2-N hexylspacer), 3.60 - 4.37 (m, 68H, 12x CH_2-Rbo, CH_2-O, 6x CH_2-cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, 18x CH-Rbo), 4.42 - 4.84 (m, 44H, CH_2-Bn), 5.05 - 5.09 (m, 4H, CH_2-Cbz, 2x H-1), 5.75 (bs, 1H, N*H*), 6.47 (d, 0.6H, *J*= 9.0 Hz, N*H*Ac), 6.55 - 6.57 (m, 0.4H, N*H*Ac), 6.63 - 6.70 (m, 1H, N*H*Ac), 7.25 - 7.40 (m, 115H, H-arom); ^{13}C-APT NMR (126 MHz, CD_3CN) δ= 20.0, 20.1, 20.1, 20.1, 20.2, 20.2, 20.3 (CH_2-cyanoethyl), 23.2, 23.2 (CH_3-NAc), 25.7, 26.8, 30.4, 30.8, 30.8, (CH_2-hexylspacer), 41.4 (CH_2-N hexylspacer), 54.0, 54.1 (C-2), 60.9, 60.9 (CH_2-Rbo), 63.1, 63.1, 63.2, 63.3, 63.3, 63.4, (CH_2-cyanoethyl), 66.6 (CH_2-Cbz), 67.2, 67.5, 67.8, 68.2, 68.6, 69.0, 69.0, 69.7 (CH_2-Rbo, C-6), 72.0, 72.1, 72.1, 72.1 (CH-Rbo/C-3/C-4/C-5), 72.7, 72.7, 73.0,73.1, 73.1, 73.1, 73.9, 73.9, 75.5, 75.6, 75.6, 75.5, 75.6, 75.6 (CH_2-Bn), 76.8, 76.8, 77.3, 77.5, 77.6, 78.0, 78.2, 78.2, 78.3, 78.4, 78.6, 78.6, 78.8, 79.4, 79.8, 80.0, 80.1, 80.9, 81.0, 81.0 (CH-Rbo, C-3, C-4, C-5), 97.2, 97.7, 97.9, 98.3 (C-1), 118.5, 118.5, 118.6 (Cq-cyanoethyl), 128.5, 128.5, 128.5, 128.6, 128.7, 128.8, 128.8, 128.8, 128.9, 128.9, 128.9, 129.0, 129.0, 129.1, 129.3, 129.4, 129.4, 138.5, 138.8, 138.9, 139.0, 139.1, 139.2, 139.2, 139.4, 139.4, 139.5, 139.5, 139.9 (Cq-arom), 157.3, 170.6, 170.6, 170.6, 170.7 (C=O); ^{31}P NMR (202 MHz, CD_3CN) δ= 0.7, 0.6, 0.6, 0.6, 0.4, 0.4, 0.3, 0.3, 0.1, 0.0, 0.0; HRMS: $[M+3H]^{3+}$ calculated for $C_{232}H_{266}N_9O_{55}P_6$ 1415.22569, found 1415.22566.

Hexamer (55)



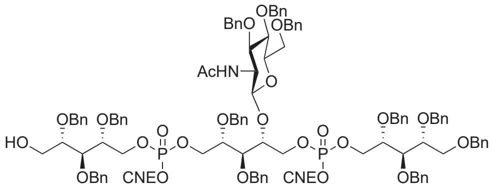
According to the general procedure above, alcohol **51** (25.0 mg; 7.5 μmol; 1.0 eq.) was coupled with phosphoramidite **20** (21.2 mg; 15.0 μmol; 2.0 eq.) and the title compound was synthesized in 61% yield (19.6 mg; 4.6 μmol). IR (neat, cm-^{1}): 3567, 2926, 2858, 1717, 1560, 1457, 1266, 1095, 1027, 1009, 747, 698; ^{1}H NMR (500 MHz, $CDCl_3$) δ= 1.26 - 1.28 (m, 4H, CH_2-hexylspacer), 1.44 (m, 2H, CH_2-hexylspacer), 1.57 - 1.60 (m, 8H, CH_2-hexylspacer, CH_3-NAc), 2.26 - 2.57 (m, 12H, CH_2-cyanoethyl), 3.13 - 3.14 (m, 2H, CH_2-N hexylspacer), 3.43 – 4.35 (m, 68H, 12x CH_2-Rbo, CH_2-O, 6x CH_2-cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6, 18x CH-Rbo), 4.35 – 4.85 (m, 45H, CH_2-Bn, H-1), 5.05 – 5.15 (m, 3H, CH_2-Cbz, H-1), 5.69 (m, 1H, N*H*), 5.82 - 5.83 (m, 0.3H, N*H*Ac), 5.95 - 6.00 (m, 0.1H, N*H*Ac), 6.06 - 6.09 (m, 0.2H, N*H*Ac), 6.50 - 6.53 (m, 0.2H, N*H*Ac), 7.12 - 7.35 (m, 115H, H-arom); ^{13}C-APT NMR (126 MHz, $CDCl_3$) δ= 19.2, 19.3, 19.3, 19.3, 19.5, 19.5, 19.6, 19.6 (CH_2-cyanoethyl), 23.0, 23.0 (CH_3-NAc), 25.1, 26.2, 29.8, 29.9, 30.1, 30.2 (CH_2-hexylspacer), 41.0 (CH_2-N hexylspacer), 53.1, 53.1, 53.2, 53.6 (C-2), 61.2, 61.2 (CH_2-Rbo), 61.8, 61.8, 61.8, 61.9, 62.0, 62.0, 62.0, 62.1 (CH_2-cyanoethyl), 66.7 (CH_2-Cbz), 66.8, 66.9, 67.0, 67.1, 67.1, 67.2, 67.3, 67.4, 67.4, 67.5, 67.6, 68.3, 68.4, 68.4 (CH_2-Rbo, C-6), 71.5, 71.6 (CH-Rbo/C-3/C-4/C-5), 72.2, 72.4, 72.5, 72.5, 72.6, 72.6, 72.7, 73.5, 73.6, 73.9, 73.9, 73.9, 74.0, 74.1, 74.1, 74.6, 74.7, 74.9, 75.1, 75.3 (CH_2-Bn), 77.3, 77.5, 77.6, 77.7, 77.7, 77.8, 77.9, 78.0, 78.1, 78.2, 78.2, 78.9, 78.9, 79.6, 79.7 (CH-Rbo, C-3, C-4, C-5), 98.2, 98.2 (C-1 α), 100.8, 101.1 (C-1 β), 116.5, 116.6, 116.7, 116.7, 116.9, 116.9, 116.9 (Cq-cyanoethyl), 127.8, 127.9, 128.0, 128.0, 128.0, 128.1, 128.2, 128.2, 128.3, 128.6, 128.6, 128.6, 128.7 (CH-arom), 136.8, 137.4, 137.5, 137.6, 137.7, 137.8, 137.9, 137.9, 137.9, 138.0, 138.1, 138.2, 138.3, 138.6 (Cq-arom), 156.5, 170.2, 170.2, 170.3 (C=O); ^{31}P NMR (202 MHz, $CDCl_3$) δ= 0.1, -0.1, -0.3, -0.3, -0.3, -0.4, -0.7, -0.7, -0.8, -0.8, -0.9, -0.9, -1.0, -1.4.

Dimer (59)



According to the general procedure above, alcohol **19** (179 mg; 0.162 mmol; 1.0 eq.) was coupled with phosphoramidite **41** (162 mg; 0.227 mmol; 1.4 eq.) and the title compound was synthesized in 46% yield (107 mg; 74.6 μmol). IR (neat, cm-^{1}): 3567, 2919, 2866, 1717, 1560, 1454, 1266, 1069, 1027, 737, 697; ^{1}H NMR (500 MHz, $CDCl_3$) δ= 1.90 (d, 3H, *J*= 2.5 Hz, CH_3-NAc), 2.26 - 2.30 (m, 2H, CH_2-cyanoethyl), 3.40 – 3.53 (m, 3H, C*H*H-Rbo, H-3/H-4/H-5/CH-Rbo), 3.56 - 3.76 (m, 6H, C*H*H-Rbo, CH_2-Rbo, 2x H-6, H-3/H-4/H-5/CH-Rbo), 3.76 - 3.97 (m, 10H, CH_2-cyanoethyl, H-2, CH-Rbo, H-3/H-4/H-5), 4.04 - 4.38 (m, 6H, CH_2-Rbo, H-3/H-4/H-5/CH-Rbo), 4.41 - 4.78 (m, 19H, CH_2-Bn, H-1), 6.61 (d, 0.7H, *J*= 8.6 Hz, N*H*Ac), 6.65 6.61 (d, 0.5H, *J*= 8.6 Hz, N*H*Ac), 7.10 - 7.35 (m, 45H, H-arom); ^{13}C-APT NMR (126 MHz, $CDCl_3$) δ= 19.2, 19.3, 19.3 (CH_2-cyanoethyl), 23.5, 23.5 (CH_3-NAc), 55.9, 56.1 (C-2), 61.3, 61.9, 61.9, 61.9, 62.0 (C-6, CH_2-cyanoethyl), 67.8, 67.8, 68.2, 68.2, 68.4, 68.4, 69.1, 69.1, 69.4, 69.5 (CH_2-Rbo), 72.1, 72.4, 72.5, 72.5, 72.6, 73.4, 73.5, 73.5, 73.8, 73.8, 73.9 (CH_2-Bn), 74.5, 74.6 (CH-Rbo/C-3/C-4/C-5), 74.8, 74.8, 75.0 (CH_2-Bn), 77.0, 77.0, 77.2 (CH-Rbo/C-3/C-4/C-5), 77.9, 78.0, 78.0, 78.1, 78.1, 78.1, 78.2, 78.2, 78.3, 78.9, 79.1, 79.2, 82.8, 82.9 (CH-Rbo/C-3/C-4/C-5), 100.8, 101.0 (C-1), 116.6, 116.7 (Cq-cyanoethyl), 127.6, 127.6, 127.7, 127.7, 127.7, 127.8, 127.8, 127.8, 127.8, 127.9, 127.9, 127.9, 128.0, 128.0, 128.0, 128.1, 128.1, 128.2, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5 (CH-arom), 137.6, 137.6, 137.9, 137.9, 138.0, 138.0, 138.1, 138.1, 138.2, 138.2, 138.3, 138.3, 138.4, 138.4, 138.5, 138.6 (Cq-arom), 171.0, 171.0 (C=O); ^{31}P NMR (202 MHz, $CDCl_3$) δ= -0.8, -1.4; HRMS: $[M+H]^+$ calculated for $C_{84}H_{94}N_2O_{17}P$ 1433.62846, found 1433.62819.

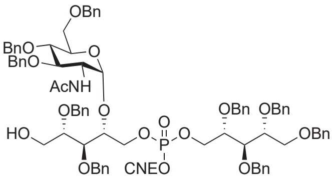
Trimer (60)



According to the general procedure above, alcohol **59** (88.4 mg; 61.7 μmol; 1.0 eq.) was coupled with phosphoramidite **42** (85.7 mg; 92.6 μmol; 1.5 eq.) and the title compound was synthesized in 91% yield (111 mg; 56.3 μmol). IR (neat, cm-^{1}): 3567, 2919, 2865, 1684, 1560, 1507, 1457, 1261, 1093, 1029, 750, 698; ^{1}H NMR (500 MHz, $CDCl_3$) δ= 1.87 (d, 3H, *J*= 2.2 Hz, CH_3-NAc), 2.18 - 2.31 (m, 4H, CH_2-cyanoethyl), 3.47 - 4.37 (m, 32H, 6x CH_2-Rbo, 9x CH-Rbo, 2x CH_2-cyanoethyl, H-2, H-3, H-4, H-5, H-6', H6''), 4.39 - 4.77 (m, 25H, CH_2-Bn, H-2), 6.67 (dd, 1H, *J*= 17.3, 8.8 Hz, N*H*Ac), 7.12 – 7.34 (m, 60H, H-arom); ^{13}C-APT NMR (126 MHz, $CDCl_3$) δ= 19.1, 19.1, 19.1, 19.2, 19.2, 19.3, 19.3 (CH_2-cyanoethyl), 23.4 (CH_3-NAc), 55.8, 55.9, 56.0 (C-2), 61.1, 61.2, 61.7, 61.8, 61.8, 61.9, 61.9, 62.0 (C-6, CH_2-cyanoethyl), 66.8, 67.3, 67.3, 67.5, 67.5, 67.8, 67.8, 68.2, 69.2, 69.2, 69.3, 69.5 (CH_2-Rbo), 72.1, 72.4, 72.4, 72.4, 72.5, 72.5, 72.5, 72.5, 73.3, 73.4, 73.4, 73.5, 73.7, 73.8, 73.8, 73.9, 74.0, 74.8, 74.8, 74.9, 74.9, 74.9 (CH_2-Bn), 75.2, 75.2, 76.3, 76.3, 77.8, 77.9, 78.0, 78.0, 78.0, 78.0, 78.1, 78.1, 78.2, 78.2, 78.3, 78.8, 78.9, 82.7, 82.7, 83.0, (CH-Rbo/C-3/C-4/C-5), 100.0, 100.1, 100.1 (C-1), 116.6, 116.6, 116.7, 116.7, 116.8, 116.8 (Cq-cyanoethyl), 127.6, 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.8, 127.8, 127.8, 127.9, 127.9, 128.0, 128.0, 128.0, 128.0, 128.1, 128.1, 128.4, 128.5, 128.5, 128.7 (CH-arom), 137.8, 137.8, 137.8, 137.9, 137.9, 138.0, 138.1, 138.1, 138.1, 138.2, 138.2, 138.2, 138.3, 138.3, 138.3, 138.3, 138.3, 138.4, 138.5, 138.5 (Cq-arom),170.7, 170.8 (C=O); ^{31}P NMR (202 MHz,

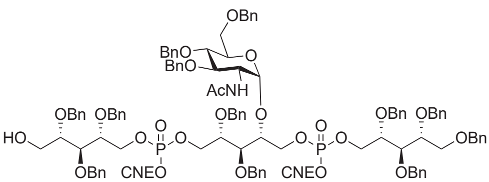
$CDCl_3$) δ= -0.2, -0.3, -0.6, -0.6, -0.7, -0.7, -1.1; HRMS: $[M+H]^+$ calculated for $C_{113}H_{126}N_3O_{24}P_2$ 1971.82346, found 1971.82551.

Dimer (61)



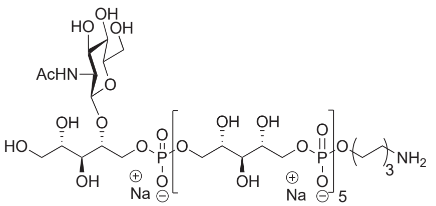
According to the general procedure above, alcohol **36** (528 mg; 0.476 mmol; 1.0 eq.) was coupled with phosphoramidite **41** (435 mg; 0.611 mmol; 1.3 eq.) and the title compound was synthesized in 80% yield (538 mg; 0.375 mmol). IR (neat, cm-[1]): 3567, 2915, 2868, 1684, 1560, 1457, 1275, 1261, 1096, 1043, 1027, 747, 697; ^{1}H NMR (500 MHz, CD_3CN) δ= 1.73 (s, 3H, CH_3-NAc), 2.40 (t, 1H, *J*= 5.1 Hz, CH_2-cyanoethyl), 2.46 (t, 1H, *J*= 5.6 Hz, CH_2-cyanoethyl), 2.92 - 2.99 (m, 1H, OH), 3.56 – 3.91 (m, 12H, H-6, 2x CH_2-Rbo, H-3/H-4/H-5, CH-Rbo), 4.03 (m, 4H, CH_2-cyanoethyl, H-2, H-3/H-4/H-5/CH-Rbo), 4.18 – 4.39 (m, 5H, 2x CH_2-Rbo, H-3/H-4/H-5/CH-Rbo), 4.39 – 4.83 (m, 18H, CH_2-Bn), 5.03 (dd, *J* = 11.6, 3.6 Hz, 1H, H-1), 6.45 (dd, *J*= 33.2, 9.0 Hz, 1H, N*H*Ac), 7.21 – 7.40 (m, 45H, H-arom); ^{13}C-APT NMR (126 MHz, CD_3CN) δ= 20.0, 20.1, 20.1, 20.1 (CH_2-cyanoethyl), 23.2, 23.2 (CH_3-NAc), 54.0 (C-2), 60.9, 60.9, 63.2, 63.2, 63.2, 63.3 (C-6, CH_2-cyanoethyl), 68.0, 68.0, 68.2, 68.2, 68.5, 68.5, 68.6, 69.7, 69.7 (CH_2-Rbo), 70.6, 70.7 (CH_2-Bn), 72.0, 72.1 (C-3/C-4/C-5/CH-Rbo), 72.7, 72.7, 72.9, 72.9, 73.0, 73.8, 73.9, 74.5, 74.6, 74.6, 75.5, 75.5, 75.6, 75.6 (CH_2-Bn), 76.9, 76.9, 77.5, 77.6, 78.6, 78.7, 78.8, 78.9, 78.9, 78.9, 79.1, 79.2, 79.2, 79.4, 79.4, 79.9, 80.0, 81.0, 81.0 (CH-Rbo/C-3/C-4/C-5), 97.3, 97.9 (C-1), 118.5, 118.5 (Cq-cyanoethyl), 128.4, 128.5, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.7, 128.7, 128.8, 128.8, 128.8, 128.9, 128.9, 129.0, 129.0, 129.1, 129.2, 129.3, 129.3, 129.3 (CH-arom), 139.2, 139.3, 139.5, 139.5, 139.5, 139.5, 139.5, 139.5, 139.6, 139.6, 139.6, 139.7, 139.8, 139.9 (Cq-arom), 170.6 (C=O); ^{31}P NMR (202 MHz, CD_3CN) δ= 0.5, 0.3; HRMS: $[M+H]^+$ calculated for $C_{84}H_{94}N_2O_{17}P$ 1433.62846, found 1433.62744.

Trimer (62)



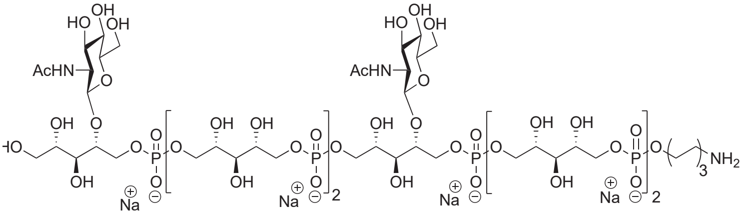
According to the general procedure above, alcohol **61** (508 mg; 0.354 mmol; 1.0 eq.) was coupled with phosphoramidite **42** (426 mg; 0.461 mmol; 1.3 eq.) and the title compound was synthesized in 91% yield (636 mg; 0.323 mmol). IR (neat, cm-[1]): 3567, 2928, 2866, 1684, 1560, 1457, 1265, 1093, 1070, 1027, 731, 697; ^{1}H NMR (500 MHz, CD_3CN) δ= 1.71 - 1.73 (m, 3H, CH_3-NAc), 2.40 (q, 1H, *J*= 6.0 Hz, CH_2-cyanoethyl), 2.45 (q, 1H, *J*= 5.6 Hz, CH_2-cyanoethyl), 2.54 (td, 1H, *J*= 6.0 Hz, 2.4 Hz, CH_2-cyanoethyl), 2.59 (td, 1H, *J*= 6.0 Hz, 2.5 Hz, CH_2-cyanoethyl), 2.89 (bs, 1H, OH), 3.60 - 4.35 (m, 33H, 6x CH_2-Rbo, 9x CH-Rbo, 2x CH_2-cyanoethyl, H-2, H-3, H-4, H-5, 2x H-6), 4.40 - 4.83 (m, 24H, CH_2-Bn), 5.01 – 5.07 (m, 1H, H-1), 6.56 (d, 0.5H, *J*= 8.9 Hz, N*H*Ac), 6.61 (dd, 0.5H, *J*= 8.9 Hz, 2.6 Hz, N*H*Ac), 7.19 - 7.36 (m, 60H, H-arom); ^{13}C-APT NMR (126 MHz, CD_3CN) δ= 20.0, 20.1, 20.1, 20.2 (CH_2-cyanoethyl), 23.2 (CH_3-NAc), 54.1, 54.1 (C-2), 61.6, 61.6, 63.2, 63.3, 63.3, 63.3, 63.4 (C-6, CH_2-cyanoethyl), 67.1, 67.1, 67.1, 67.1, 67.2, 67.2, 67.2, 68.1, 68.2, 68.2, 68.2, 68.4, 68.4, 68.5, 68.5, 69.7, 69.7, 70.7, 70.8, (CH_2-Rbo), 72.1, 72.2 (CH-Rbo/C-3/C-4/C-5), 72.8, 72.9, 73.0, 73.0, 73.0, 73.1, 73.1, 73.8, 73.9, 74.5, 74.5, 74.5, 74.6, 74.6, 74.6, 75.5, 75.5, 75.6, 75.6, 75.6 (CH_2-Bn), 76.7, 76.7, 76.8, 76.8, 77.4, 77.4, 77.4, 77.5, 77.9, 77.9, 78.0, 78.0, 78.1, 78.1, 78.2, 78.9, 78.9, 78.9, 79.0, 79.0, 79.1, 79.1, 79.1, 79.2, 79.2, 79.2, 79.4, 80.6, 80.8, 80.8, 80.9, 80.9 (CH-Rbo, C-3, C-4, C-5), 97.7, 97.8, 98.3, 98.3 (C-1), 118.5, 118.5 (Cq-cyanoethyl), 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 128.8, 128.8, 128.9, 128.9, 128.9, 129.0, 129.0, 129.1, 129.3, 129.3, 129.3, 129.4, 129.4, 129.4 (CH-arom), 138.9, 138.9, 139.1, 139.1, 139.2, 139.3, 139.4, 139.4, 139.5, 139.5, 139.5, 139.5, 139.6, 139.6, 139.6, 139.7, 139.8, 139.8, 139.9, 140.0 (Cq-arom), 170.6, 170.7, 170.7 (C=O); ^{31}P NMR (202 MHz, CD_3CN) δ= 0.6, 0.5, 0.3, 0.3; HRMS: $[M+2H]^{2+}$ calculated for $C_{113}H_{127}N_3O_{24}P_2$ 986.41537, found 986.41536.

Hexamer (1)



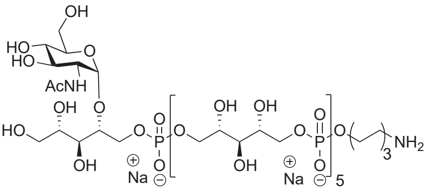
According to the general procedure described above, compound **57** (26.0 mg; 6.74 μmol) was deprotected affording the target compound in 67% yield (8.0 mg; 4.5 μmol). ^{1}H NMR (500 MHz, D_2O) δ= 1.41 - 1.42 (m, 4H, 2x CH_2-hexylspacer), 1.64 - 1.67 (m, 4H, 2x CH_2-hexylspacer), 2.08 (s, 3H, CH_3-NAc), 2.99 (t, 3H, *J*= 7.5 Hz, CH_2-N hexylspacer), 3.43 - 3.45 (m, 2H, CH-Rbo/CH-GlcNAc), 3.54 - 3.57 (m, 1H, CH-Rbo/CH-GlcNAc), 3.59-3.63 (m, 1H, C*H*H), 3.71- 3.76 (m, 2H, H-2, C*H*H), 3.78-4.14 (m, 47H, 2x C*H*H, 12x CH_2, 2x H-6, 17x CH-Rbo/CH-GlcNAc, CH_2O), 4.72 (d, 1H, *J*= 8.5 Hz, H-1); ^{13}C-APT NMR (126 MHz, D_2O) δ= 22.4 (CH_3-NAc), 24.5, 25.2, 26.7, 29.4, 29.5 (CH_2-hexylspacer), 39.5 (CH_2-N hexylspacer), 55.7 (C-2), 60.7, 62.7, 65.0, 66.2, 66.2, 66.4, 66.5, 66.5 (CH_2-Rbo, C-6, CH_2O), 70.0, 70.9, 70.9, 71.2, 71.3, 71.6, 71.7, 73.8, 75.8 (CH-Rbo/C-GlcNAc), 79.4, 79.5 (*C*-O-C-1), 101.4 (C-1), 175.1 (C=O); ^{31}P NMR (202 MHz, D_2O) δ= 2.0, 2.0, 1.8, 1.7; HRMS: $[M+H]^+$ calculated for $C_{44}H_{95}N_2O_{48}P_6$ 1605.3475, found 1605.3480.

Hexamer (2)



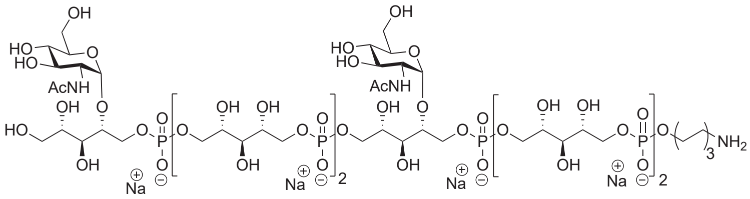
According to the general procedure described above, compound **52** (120 mg; 28.2 µmol) was deprotected affording the target compound in 78% yield (43.0 mg; 22.3 µmol). ^{1}H NMR (500 MHz, D_2O) δ= 1.39 - 1.40 (m, 4H, 2x CH_2-hexylspacer), 1.61 - 1.65 (m, 4H, 2x CH_2-hexylspacer), 2.06 (s, 6H, 2x CH_3-NAc), 2.97 (t, 2H, *J*= 7.5 Hz, CH_2-N hexylspacer), 3.41 - 3.44 (m, 4H, CH-Rbo/CH-GlcNAc), 3.51 - 3.53 (m, 2H, CH-Rbo/CH-GlcNAc), 3.56 - 3.61 (m, 1H, C*H*H), 3.69 - 4.12 (m, 53H, 12x CH-Rbo, 12x CH_2, 10x CH-GlcNAc, 4x H-6, 1x CH*H*, CH_2O), 4.70 (dd, 2H, *J*= 8.0 Hz, *J*= 4.0 Hz, H-1); ^{13}C-APT NMR (126 MHz, D_2O) δ= 22.4 (CH_3-NAc), 24.5, 25.2, 26.6, 29.4, 29.5 (CH_2-hexylspacer), 39.5 (CH_2-N hexylspacer), 55.7, 55.7 (C-2), 60.6, 60.7, 62.6, 65.0, 66.2, 66.2, 66.4, 66.4, 66.5, 66.7 (CH_2-Rbo, CH_2-O, C-6), 69.9, 70.2, 70.2, 70.9, 70.9, 71.0, 71.2, 71.6, 71.7, 73.8, 73.9, 75.8, 75.8 (CH-Rbo, C-3, C-4, C-5), 79.4, 79.5, 79.7, 79.7 (*C*-O-C-1), 101.4, 101.6 (C-1), 175.1, 175.1 (C=O); ^{31}P NMR (202 MHz, D_2O) δ= 2.0, 2.0, 1.8, 1.7; HRMS: $[M+H]^+$ calculated for $C_{52}H_{108}N_3O_{53}P_6$ 1808.42682, found 1808.42555.

Hexamer (3)



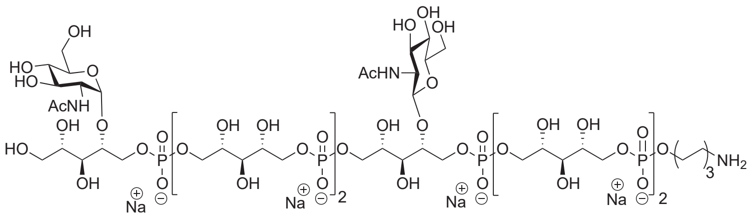
According to the general procedure described above, compound **58** (18.0 mg; 4.66 µmol) was deprotected affording the target compound in 96% yield (7.74 mg; 4.45 µmol). ^{1}H NMR (500 MHz, D_2O) δ= 1.41 - 1.43 (m, 4H, 2x CH_2-hexylspacer), 1.64 - 1.69 (m 4H, 2x CH_2-hexylspacer), 2.05 (s, 3H, CH_3-NAc), 2.99 (t, 2H, *J*= 7.5 Hz, CH_2-N hexylspacer), 3.48 (t, 1H, *J*= 9.5 Hz, CH-Rbo/CH-GlcNAc), 3.61 - 3.63 (m, 1H, C*H*H), 3.77 - 4.12 (m, 48H, 11x CH_2-Rbo, 1x CH*H*, 21x CH-Rbo/CH-GlcNAc, 2x H-6, CH_2O), 5.03 (d, 1H, *J*= 3.5 Hz, H-1); ^{13}C-APT NMR (126 MHz, D_2O) δ= 22.0 (CH_3-NAc), 24.5, 25.2, 26.7, 29.4, 29.5 (CH_2-hexylspacer), 39.5 (CH_2-N hexylspacer), 53.9 (C-2), 60.6, 62.7, 64.4, 66.2, 66.2, 66.4, 66.4, 66.5, 66.5, 66.6 (CH_2-Rbo, C-6, CH_2-O), 70.1, 70.9, 70.9, 71.1, 71.2, 71.3, 72.0 (CH-Rbo/CH-GlcNAc), 77.6, 77.6 (*C*-O-C-1), 96.4 (C-1), 174.5 (C=O); ^{31}P NMR (202 MHz, D_2O) δ= 2.0, 2.0, 1.8, 1.6; HRMS: $[M+H]^+$ calculated for $C_{44}H_{95}N_2O_{48}P_6$ 1605.34745, found 1605.34696.

Hexamer (4)



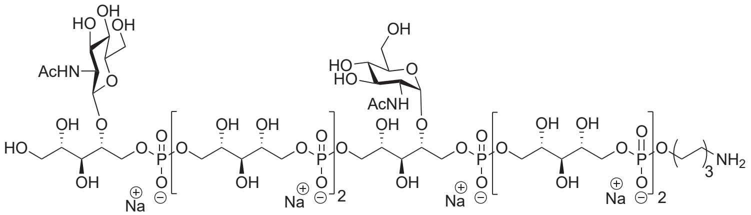
According to the general procedure described above, compound **54** (145 mg; 34.0 µmol was deprotected affording the target compound in 49% yield (34.4 mg; 16.7 µmol). ^{1}H NMR (500 MHz, D_2O) δ= 1.41 - 1.43 (m, 4H, 2x CH_2-hexylspacer), 1.64 - 1.67 (m, 4H, 2x CH_2-hexylspacer), 2.05 (s, 3H, CH_3-NAc), 2.07 (s, 3H, CH_3-NAc), 2.99 (t, 2H, *J*= 7.5 Hz, CH_2-N hexylspacer), 3.49 (t, 2H, *J*= 9.0 Hz, CH-Rbo/CH), 3.63 (q, 1H, *J*= 5.5 Hz, C*H*H-Rbo), 3.77 - 4.12 (m, 53H, CH-GlcNAc, CH-Rbo, CH_2-Rbo, CH_2O), 5.03 (d, 1H, *J*= 3.5 Hz, H-1), 5.06 (d, 1H, *J*= 3.5 Hz, H-1); ^{13}C-APT NMR (126 MHz, D_2O) δ= 22.0, 22.1 (CH_3-NAc), 24.5, 25.2, 26.6, 29.4, 29.5 (CH_2-hexylspacer), 39.5 (CH_2-N hexylspacer), 53.9 (C-2), 60.6, 62.7, 64.4, 64.5, 66.2, 66.2, 66.4, 66.4, 66.5, 66.5, 66.6 (CH_2-Rbo, CH_2-O, C-6), 69.9, 69.9, 70.1, 70.1, 70.9, 70.9, 71.1, 71.2, 71.2, 71.3, 72.0 (CH-Rbo, C-3/C-4/C-5), 77.6, 77.7, 77.8 (*C*-O-C-1 GlcNAc), 96.4, 96.5 (C-1), 174.5 (C=O); ^{31}P NMR (202 MHz, D_2O) δ= 2.0, 2.0, 1.9, 1.8, 1.6, 1.6; HRMS: $[M+2Na]^{2+}$ calculated for $C_{52}H_{107}N_3O_{53}P_6 Na_2$ 926.6990, found 926.7034.

Hexamer (5)



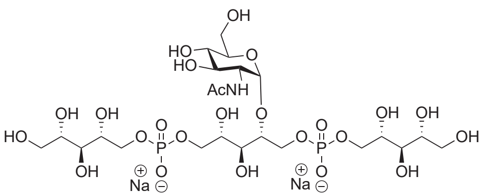
According to the general procedure described above, compound **53** (106 mg; 25.0 µmol) was deprotected affording the target compound in 88% yield (42.5 mg; 21.9 µmol). ^{1}H NMR (500 MHz, D_2O) δ= 1.41 - 1.42 (m, 4H, 2x CH_2-hexylspacer), 1.63 - 1.68 (m, 4H, 2x CH_2-hexylspacer), 2.04 (s, 3H, CH_3-NAc), 2.08 (s, 3H, CH_3-NAc), 2.99 (t, 3H, *J*= 7.5 Hz, CH_2-N hexylspacer), 3.45 - 3.50 (m, 3H, CH-Rbo/CH-GlcNAc), 3.53 - 3.57 (m, 1H, CH-Rbo/CH-GlcNAc), 3.59 - 3.66 (m, 2H, CH_2), 3.72 - 4.15 (m, 52H, 14x CH_2, 22x CH-Rbo/CH-GlcNAc, CH_2-O), 4.73 (d, 1H, *J*= 8.0 Hz, H-1 β), 5.03 (d, 1H, *J*= 3.5 Hz, H-1 α); ^{13}C-APT NMR (126 MHz, D_2O) δ= 22.0, 22.4 (CH_3-NAc), 24.5, 25.2, 26.6, 29.4, 29.5 (CH_2-hexylspacer), 39.5 (CH_2-N hexylspacer), 53.9, 55.7 (C-2), 60.6, 60.6, 62.4, 62.7, 64.4, 64.5, 64.9, 66.2, 66.2, 66.4, 66.4, 66.5, 66.6 (CH_2-Rbo, C-6, CH_2-O), 69.9, 70.1, 70.3, 70.9, 70.9, 71.0, 71.1, 71.2, 71.3, 71.7, 72.0, 72.1, 73.9, 75.8 (CH-Rbo/CH-GlcNAc), 77.6, 77.7 (*C*-O-C-1 α), 79.7, 79.7 (*C*-O-C-1 β), 96.4 (C-1 α), 101.6 (C-1 β), 174.5, 175.1 (C=O); ^{31}P NMR (202 MHz, D_2O) δ= 2.0, 2.0, 1.8, 1.7, 1.6; HRMS: $[M+2H]^{2+}$ calculated for $C_{52}H_{109}N_3O_{53}P_6$ 904.7172, found 904.7208.

Hexamer (6)



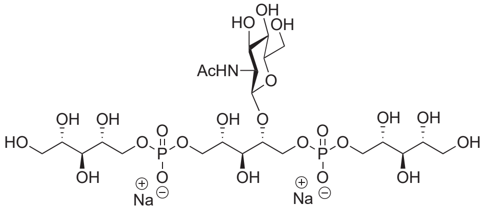
According to the general procedure described above, compound **55** (19.6 mg; 4.6 µmol) was deprotected affording the target compound in 16% yield (1.4 mg; 0.73 µmol). ^{1}H NMR Presat D_2O (500 MHz, D_2O) δ= 1.39 - 1.42 (m, 4H, CH_2-hexylspacer), 1.61 - 1.69 (m, 4H, CH_2-hexylspacer), 2.06 (d, 6H, *J*= 7.3 Hz, CH_3-NHAc), 2.96 - 3.01 (m, 2H, CH_2-N hexylspacer), 3.40 - 4.15 (m, 56H, CH_2-Rbo, CH-Rbo, 2x H-2, 2x H-3, 2x H-4, 2x H-5, 2x H-6', 2x H-6'', CH_2-O), 4.72 (d, 0.25H, *J*= 8.6 Hz, H-1 β), 5.05 (d, 1H, *J*= 3.7 Hz, H-1 α); ^{31}P NMR (202 MHz, D_2O) δ= 2.0, 2.0, 1.9, 1.8, 1.7, 1.6; HRMS: $[M+2H]^{2+}$ calculated for $C_{52}H_{109}N_3O_{53}P_6$ 904.7171, found 904.7202.

Trimer (7)



According to the general procedure described above, compound **62** (318 mg; 0.161 mmol) was deprotected affording the target compound in 90% yield (120.3 mg; 0.145 mmol). ^{1}H NMR (500 MHz, D_2O) δ= 2.05 (s, 3H, CH_3-NAc), 3.48 (dd, 1H, *J*= 10.1 Hz, 9.0 Hz, CH-Rbo), 3.63 (dd, 2H, *J*= 11.9 Hz, 7.2 Hz, CH_2-Rbo), 3.73 (t, *J*= 6.2 Hz, 2H, CH-Rbo), 3.75 – 4.12 (m, 22H, 5x CH_2-Rbo, 6x CH-Rbo, H-2, H-3, H-4, H-5, 2x H-6), 5.04 (d, 1H, *J*= 3.7 Hz, H-1); ^{13}C-APT NMR (126 MHz, D_2O) δ= 22.0 (CH_3-NAc), 53.8 (C-2), 60.5, 62.3, 64.4, 64.4, 66.5, 66.6, 66.6 (CH_2-Rbo, C-6), 69.8, 69.9, 70.1, 70.9, 70.9, 71.0, 71.0, 71.7, 71.7, 72.0, 72.1, 72.1 (CH-Rbo, C-3, C-4, C-5), 77.7, 77.7 (*C*O-C1), 96.5 (C-1), 174.5 (C=O); ^{31}P NMR (202 MHz, D_2O) δ= 1.9, 1.6; HRMS: $[M+H]^{+}$ calculated for $C_{23}H_{48}NO_{24}P_2$ 784.20360, found 784.20354.

Trimer (8)



According to the general procedure described above, compound **60** (105 mg; 53.2 µmol) was deprotected affording the target compound in 85% yield (37.5 mg; 45.3 µmol). ^{1}H NMR presat D_2O (400 MHz, D_2O) δ= 2.06 (s, 3H, CH_3-NAc), 3.43 - 3.47 (m, 2H, CH-ribitol/CH-GlcNAc), 3.49 - 3.56 (m, 1H, CH-Rbo/CH-GlcNAc), 3.62 (dd, 2H, *J*= 11.6 Hz, 7.2 Hz, CH_2-Rbo), 3.70 - 4.14 (m, 24H, 5x CH_2-Rbo, 11x CH-Rbo/CH-GlcNAc), 4.71 (d, 1H, *J*= 8.4 Hz, H-1); ^{13}C-APT NMR (101 MHz, D_2O) δ= 22.4 (CH_3-NAc), 55.7 (C-2), 60.6, 62.3, 64.9, 64.9, 66.5, 66.5, 66.6, 66.7 (CH_2-ribitol/C-6), 69.8, 70.1, 70.2, 70.9, 70.9, 71.0, 71.0, 71.0, 71.7, 71.7, 72.0, 72.1, 73.9, 75.7 (CH-Rbo, C-3, C-4, C-5), 79.7, 79.7 (*C*-O-C-1), 101.6 (C-1), 175.0 (C=O); ^{31}P NMR (162 MHz, D_2O) δ= 2.0, 1.7; HRMS: $[M+H]^+$ calculated for $C_{23}H_{48}NO_{24}P_2$ 784.2036, found 784.2062.

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