Chemical synthesis of fragments of streptococcal cell wall polysaccharides

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Chapter 4

The First Total Synthesis of Acetylated Zwitterionic Polysaccharide Sp1 Fragments

Introduction

Bacterial cell-surface carbohydrates play a significant role in binding events with components from the host immune system.[1] Bacterial capsular polysaccharides (CPS) are excellent targets for designing carbohydrate-based antibacterial vaccines. Typically, bacterial capsular polysaccharides can only be recognized by B-cell receptors, thereby eliciting IgM responses, without inducing immunoglobulin class switching to form IgG isotypes.[2] They are considered to be "T-cell-independent antigens" which cannot be used as stand-alone vaccine entities, because they do not induce immunological memory.

Zwitterionic polysaccharides (ZPSs) are a rare class of immunomodulatory agents that can provoke a T-cell mediated immune responses. It has been shown that they can be processed by antigen-presenting cells and presented by major histocompatibility complex (MHC) class II-molecules to T helper cells.[3] Several ZPSs showed in Fig. 1 have been verified, such as Sp1 isolated from *Streptococcus pneumoniae*[4], CP5 and CP8 isolated from *Staphylococcus aureus*[5], PS A1, PS A2 and PS B isolated from *Bacteroides fragilis*[6]. Structurally, each of these molecules has both positively charged amino and negatively charged carboxylate or phosphate groups, which shape the unusual immunologic properties.[7] To explore structure–activity relationships and immunomodulatory mechanisms of ZPSs, pure and structurally well-defined oligosaccharides are required and therefore various chemical syntheses of these ZPSs have reported.[8]

The Sp1-polysaccharide is built up from trisaccharide repeating units, that in turn are composed of the rare α-2,4-di-amino-2,4,6-tri-deoxygalactose (D-AAT) and two α-D-galacturonic acid residues. The polysaccharide can carry *O*-acetyl groups at two thirds of the C-2 or C-3 positions of the 4-linked galacturonic acid residues. Recently, the assembly of zwitterionic, non-acetylated Sp1-oligosaccharides, up to the dodecasaccharide, has been achieved by combining pre-glycosylation oxidation and post-glycosylation oxidation chemistry.[8g] The 3D-structure of these Sp1 oligomers was analyzed via molecular dynamics simulations and NMR spectroscopy studies, and they were shown to adopt a right-handed helical structure with the nonasaccharide completing a full turn. It was found in ELISA and STD NMR[9] experiments that the longer oligosaccharides showed better binding to anti-Sp1 antibodies, but only a slight difference was shown between the nona- and dodecasaccharide, indicating that a single complete turn of the oligomers is sufficient for binding. This indicates that the Sp1-nonasaccharide can be a promising candidate for the development of a synthetic carbohydrate-based vaccine against *Streptococcus pneumoniae*. The role of the acetyl groups in the poly- and oligosaccharides however remain to be established.[4a, 10]

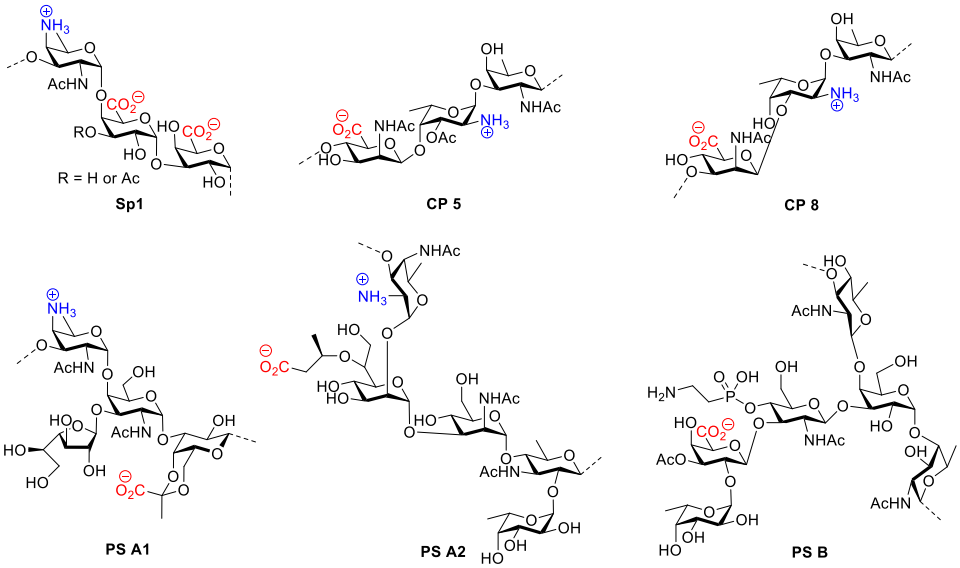


Figure 1. The chemical structures of naturally occurring ZPSs.

Streptococcus pneumoniae (or *pneumococcus*) is a dreaded alpha-hemolytic Gram-positive pathogen that can cause many types of fatal illnesses, including pneumonia, septicemia, meningitis, leading to high morbidity and mortality rates worldwide.[11] Pneumococcal infections can transmit via person-to-person contact, and mainly occur in individuals with weaker immune systems, such as infants, young children and the elderly, especially in developing countries, common during the winter and early spring months. Although antibiotic treatment for most pneumococcal infections is effective, it does induce the evolution of drug-resistant pneumococcal bacteria.

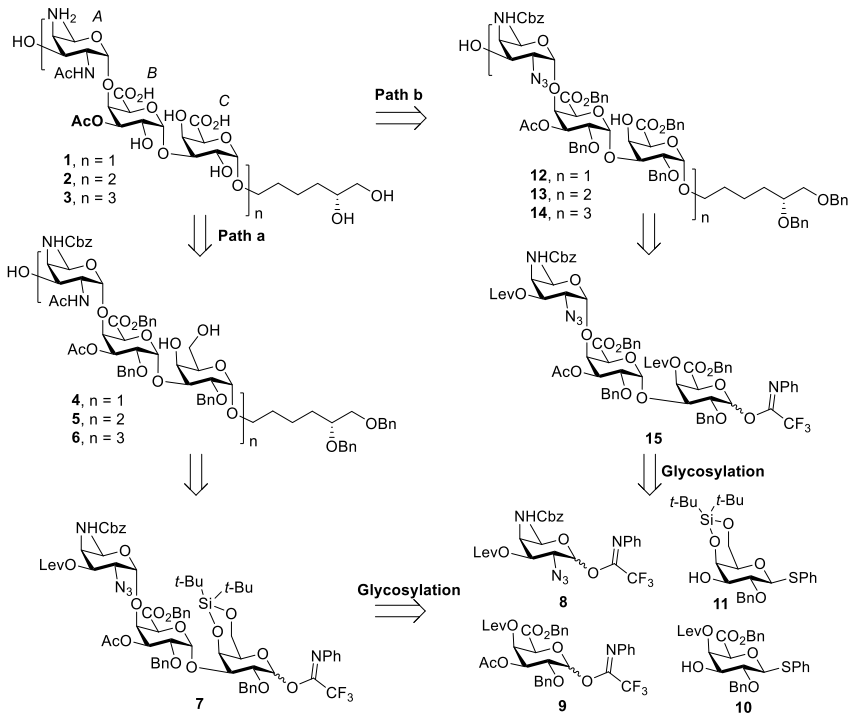
As early as 1946, the first pneumococcal polysaccharide vaccine was licensed.[12] Currently, two vaccines are available against the pneumococcal infections, including a 23-valent pneumococcal polysaccharide vaccine (PPSV23, Pneumovax, Merck) approved in 1983 and a 13-valent pneumococcal conjugate vaccine (PCV13, Prevnar, Pfizer) approved in 2010. Of the more than 90 serotypes of *pneumococcus*, only 25 serotypes were covered in these two vaccines.[13] Even though these vaccines have been very successful, the immunologic mechanism is not well understood and the large death tolls to date stimulate the development of novel well-defined vaccines.

To complement the series of de-acetylated Sp1 fragments described above, this chapter describes the development of a synthesis route to generate acetylated Sp1 fragments, which have been generated in multi-milligram amounts. The generated C-3-

O-acetyl Sp1 oligomers will be powerful tools to probe the effect of the acetyl groups on the structure of the oligosaccharides and binding to antibodies.

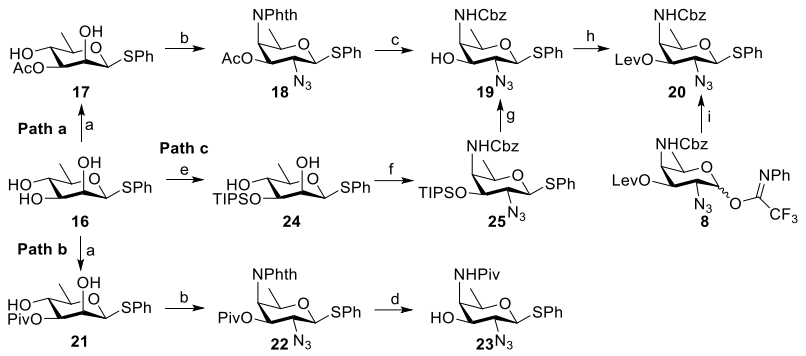
Result and discussion

The acetylated Sp1-fragments targeted in this chapter are shown in Scheme 1. The previously reported route towards the Sp1 oligosaccharides, combined a pre-glycosylation oxidation strategy with a post-glycosylation oxidation approach (path a in Scheme 1) to minimize the difficult oxidation events required on large oligosaccharides while enabling a robust and highly stereoselective glycosyl protocol. The de-OAc-Sp1 oligosaccharides were generated with a butenol spacer to enable thiol-ene conjugation chemistry. A Birch reduction was employed at the end of the syntheses to unmask all benzyl-type protecting groups. Taking the acetyl groups in the target compounds into consideration, a Birch reduction cannot be used for the deprotection and therefore a hydrogenation step will be required at the end of the synthesis. This thus precludes the use of an alkene-based linker and therefore a vicinal diol terminated spacer was chosen for the new targets. A selective oxidation by a Malaprade reaction can give the aldehyde for further modification. The oxidation and benzyl-ester formation steps in the syntheses of the long oligosaccharides proved to be extremely difficult. Therefore, another retrosynthetic plan built on a novel dual pre-glycosylation oxidation strategy (path b of Scheme 1), employing trisaccharide **15** as the pivotal building block. The required α-selectivity was expected to be controlled by the remote levulinoyl ester for the [3 + 3] and [3 + 6] glycosylations. It was planned to assemble the key trisaccharide **15** using glycosylation of the monosaccharide building blocks **8** – **10**.



Scheme 1. The designed fragments of *O*-Ac-Sp1 **1** – **3** and their retrosynthetic analysis.

The previously developed synthetic route (path a in Scheme 2) of the rare building block 2-acetamido-4-amino-2,4,6-trideoxy-D-galactose (D-AAT) **8**, which followed a modification of Kulkarni's protocol,[14] delivered **19** from triol **16** in only 19% yield.[8g] The most important side-products that were detected in this transformation were C-4-azido or C-4-hydroxyl substituted derivatives of the D-AAT building block. Therefore, different bulky protecting groups, such as Piv, TBS and TIPS groups, on the C-3 position of 6-deoxy-D-mannose **16** were probed to inhibit the formation of these side-products (routes b and c in Scheme 2). The three-step reaction sequence, involving triflation, azido substitution and phthalimide inversion delivered **22** from **21** in 37% yield. Unmasking the phthaloyl group however led to migration of the Piv group, generating the C-4-NHPiv compound **23**. In contrast, when the TIPS group was employed as the C-3-*O*-protecting group and ammonia as the nucleophile instead of potassium phthalimide, **16** was transformed into **19** in 50% yield over six steps (path c, Scheme 2). Following this route, the D-AAT sugar **8** can be rapidly obtained on multi-gram scale.

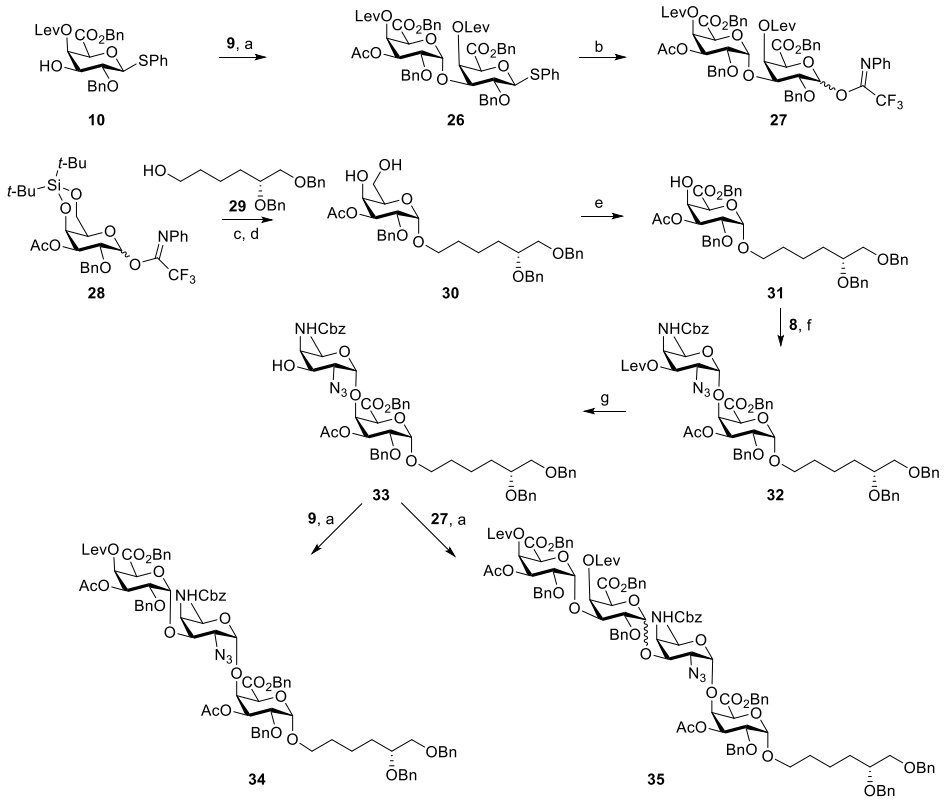


Scheme 2. The synthesis of building block D-AAT **8**.

Reagents and conditions: a) AcCl or pivaloyl chloride (PivCl), Me_2SnCl_2, DIPEA, THF, **17**, 90%; **21**, 89%. b) i, Tf_2O, pyridine, DCM; (ii) $TBAN_3$, CH_3CN, -30 °C; (iii) PhthNK, DMF, **18**, 30%; **22**, 37% (over three steps). c) i, Ethylenediamine, *n*-BuOH, reflux; (ii) CbzCl, $NaHCO_3$, THF/H_2O, 69%. d) i, Ethylenediamine, *n*-BuOH, reflux, 44%. e) TIPSCl, imidazole, DMF, 88%. f) i, Tf_2O, pyridine, DCM; (ii) $TBAN_3$, CH_3CN, -30 °C; (iii) NH_3 in MeOH; (iv) CbzCl, $NaHCO_3$, THF/H_2O, 62% (over four steps). g) TBAF, AcOH, THF, 91%. h) LevOH, EDCI, DIPEA, DMAP, DCM, 98%. i) i, NIS, TFA, DCM; ii, *N*-phenyltrifluoroacetimidoyl chloride, K_2CO_3, acetone; 91%.

The synthesis of the target oligosaccharides started with a feasibility study to see whether the designed strategy (path b in Scheme 1) could be used for the stereoselective fusion of the trisaccharides (*ABC*). It has been reported that the glycosylation of a C-4-*O*-Lev decorated D-galactopyranosyl uronate donor and silylidene galactose acceptor **11** can be achieved with effective stereoselectivity (α/β = 13 : 1).[8g] To further investigate the feasibility of the [*ABC* + *ABC* or *ABCABC*] glycosylation, two more model reactions were performed using [*C* + *AB*] and [*BC* + *AB*] glycosylations (Scheme 3). The detailed procedures for the synthesis of all required building blocks can be found in Experimental Section. Glycosylation between galactoside imidate donor **9** (*B*) and acceptor **10** (*C*) using TfOH as promotor provided a disaccharide **26** (*BC*) along with a side product resulting from an aglycon transfer of thioglycoside. Thereafter, disaccharide imidate donor **27** (*BC*) was generated by hydrolysis of thioglycoside **26** and installation of the imidate moiety in excellent yield. To accomplish the synthesis of disaccharide acceptor **33** (*AB*), spacer **29** (*vide infra*) was glycosylated with silylidene galactoside imidate donor **28** under the promotion of TBSOTf and ensuing desilylation delivered diol intermediate **30** in good yield. Then, selective oxidation of the diol **30** was performed under TEMPO-BAIB conditions, after benzylation of the carboxylate, to provide the C-4-OH galacturonic acid **31** in 94% yield. The desired disaccharide acceptor **33** (*AB*) was synthesized via glycosylation of **31** and D-AAT donor **8** (*A*) using TBSOTf as promotor,

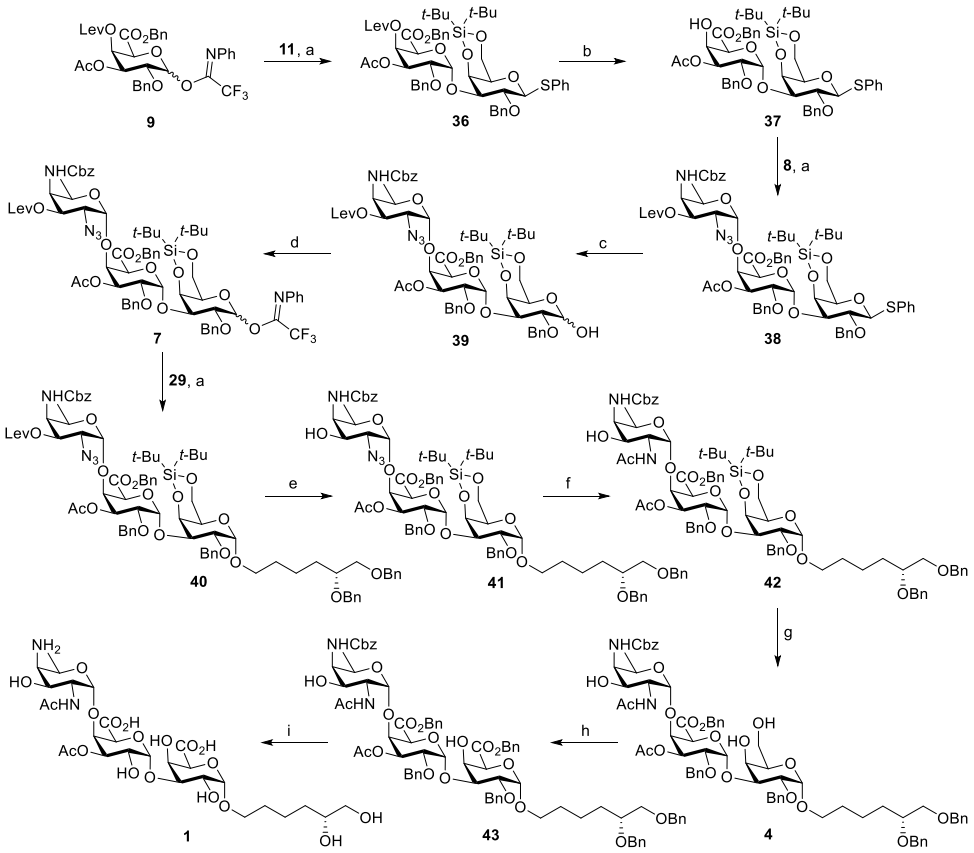
followed by delevulination by treatment with N_2H_4•H_2O in excellent yield. Next, the disaccharide acceptor **33** (*AB*) was investigated in the model glycosylations with the monosaccharide galactoside donor **9** (*B*) and a disaccharide donor **27** (*BC*). The stereoselectivity of [*B* + *AB*] glycosylation was excellent, and only α trisaccharide product **34** (*BAB*) was obtained. However, the model [*BC* + *AB*] glycosylation provided the tetrasaccharide **35** (*BCAB*) with very poor stereoselectivity (α/β = 2/1). Apparently, the functional group at the C-3-OH of the galacturonic acid donor plays a crucial role in determining the glycosylation stereoselectivity. The last model reaction clearly indicates a great risk to obtain the wanted stereoselectivity for the glycosylations to be used following route (b) for the synthesis of hexa- and nonasaccharides.



Scheme 3. The model glycosylation reactions.

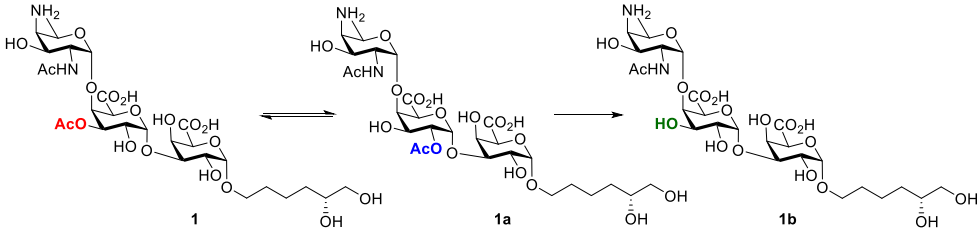
Reagents and conditions: a) TfOH, DCM, 5Å MS, 0 °C, **26**, 34%; **34**, 55% (α only); **35**, 52% (α/β = 2:1). b) i, NIS, TFA, DCM, 0 °C, 90%. ii, *N*-phenyltrifluoroacetimidoyl chloride, Cs_2CO_3, acetone, 91%. c) **29**, TBSOTf, DCM, 4Å MS, 0 °C, 94%. d) HF•Py, THF, pyridine, 0 °C, 85%. e) i, TEMPO, BAIB, *t*-BuOH, H_2O, DCM, 4 °C; ii, BnBr, Cs_2CO_3, DMF, 96% (over two steps). f) TBSOTf, DCM, 4Å MS, 0 °C, 83% (α/β = 9:1). g) N_2H_4•H_2O, pyridine, AcOH, 92%.

Because of the model experiments indicated route (b) to be challenging, attention was next focused on route (a), realizing that a difficult oxidation step was to be overcome. The synthesis commenced with the assembly of the trisaccharide target **1** (Scheme 4). First, the glycosylation between the imidate donor **9** and the acceptor **11** was performed in the presence of TBSOTf to provide the disaccharide **36** in 75% yield with excellent stereoselectivity. Subsequently, selective deprotection of the levulinoyl protecting group was affected by treatment with hydrazine acetate under acidic conditions to inhibit possible migration of the C-3-OAc, delivered the C4'-OH disaccharide **37** in 95% yield. Next, the glycosylation between acceptor **37** and the 6-deoxy-D-galactose analogue **8** was carried out under the promotion of TBSOTf to provide **38**/**38a** in 82% yield and a 5/1 α/β-ratio. The anomers could be separated at this stage and the synthesis was continued with the hydrolysis of the thioglycoside using the NIS-TFA system[15], to provide the corresponding hemiacetal **39**, which was followed by installation the imidate moiety in Cs_2CO_3 condition to provide the pivotal trisaccharide imidate donor **7**. As a spacer entity, (*R*)-5,6-bis(benzyloxy)hexan-1-ol **29** was selected, which was stereoselectively prepared according to literature procedures.[16] Taking advantage of the stereoselectivity controlled by the bulky silylidene, the glycosylation between the key trisaccharide donor **7** and this linker proceeded smoothly to furnish **40** in 85% yield, with complete stereoselectivity. Subsequently, hydrolysis of the levulinoyl group was performed using hydrazine monohydrate to provide the trisaccharide **41** in excellent yield. Reduction of the azido group using a Staudinger reaction, followed by selective *N*-acetylation provided the acetamide **42** in quantitative yield. Triol intermediate **4** could be prepared in 95% yield from **42** by treatment with hydrogen fluoride in pyridine. Regioselective oxidation to provide the carboxylic moiety was achieved using the TEMPO-BAIB oxidation system in a *tert*-butanol-DCM-water solution at 4 °C, which was followed by benzylation using BnBr in DMF to provide trisaccharide **43** in 81% yield. To complete the synthesis of the trisaccharide target **1**, all benzyl ethers, the benzyl esters and the benzyl carbamate were removed via a hydrogenation using $Pd(OH)_2$ as catalyst. After purification by gel filtration column, however, it was observed that the product was impure and NMR indicated the presence of side-products, in which the acetyl group had migrated (**1a**) and was hydrolyzed (**1b**) (see Scheme 5).[4c] Presumably, the acetyl group in the trisaccharide is very labile and cannot withstand the slightly basic conditions used for the gel filtration.[17] Therefore, the purity of the trisaccharide was checked, immediately after the hydrogenation reaction. After filtration of the catalyst and concentration, the trisaccharide proved to be pure and no sign of acetyl migration was detected by NMR spectroscopy.



Scheme 4. Assembly of the trisaccharide **1**.

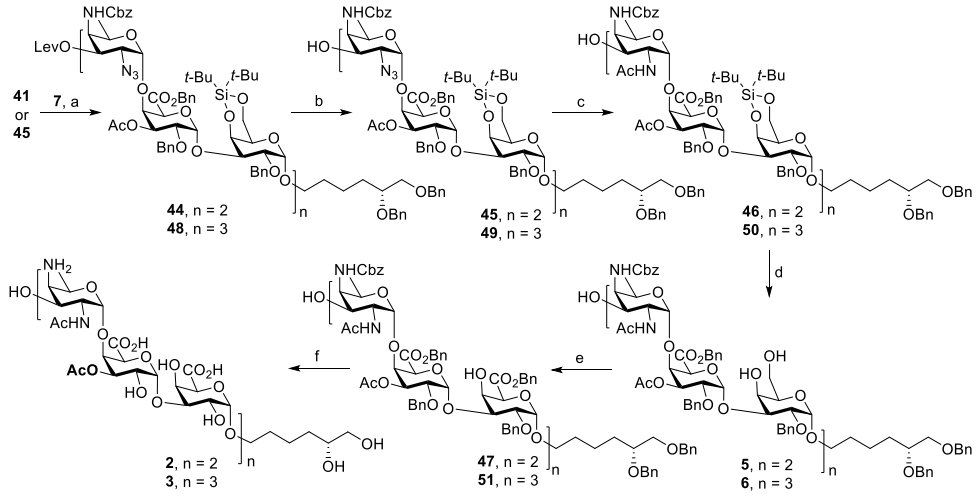
Reagents and conditions: a) TBSOTf, DCM, 5Å MS, 0 °C, **36**, 75%; **38**, 68% (β anomer **38a**, 14%); **40**, 85%. b) N_2H_4•AcOH, AcOH, THF, MeOH, 0 °C, 95%. c) NIS, TFA, DCM, 0 °C, 95%. d) *N*-phenyltrifluoroacetimidoyl chloride, Cs_2CO_3, acetone, 93%. e) N_2H_4•H_2O, pyridine, AcOH, 0 °C - RT, 95%. f) i, PPh_3, pyridine, H_2O, THF, 70 °C, 7 h; ii, Ac_2O, $NaHCO_3$, THF, H_2O, quantitative. g) HF•Py, THF, pyridine, 0 °C, 94%. h) i, TEMPO, BAIB, *t*-BuOH, H_2O, DCM, 4 °C; ii, BnBr, Cs_2CO_3, DMF, 81% (over two steps). i) $Pd(OH)_2$/C, H_2, *t*-BuOH, H_2O, 3 days, quantitative.



Scheme 5. Acetyl migration and hydrolysis in trisaccharide **1**.

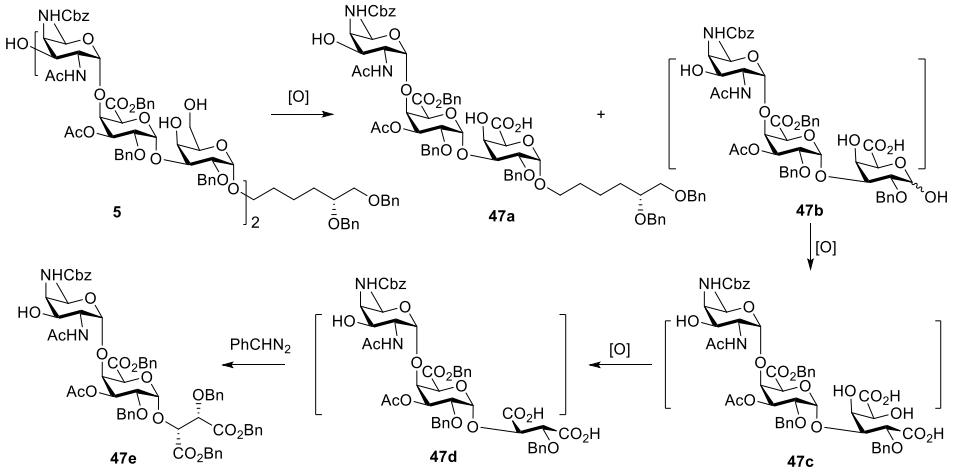
With the trisaccharide imidate donor **7** and acceptor **41** in hand, hexasaccharide **44** was synthesized via a [3 + 3] glycosylation mediated by TBSOTf in 83% yield as a single diastereoisomer (Scheme 6). Removal of the levulinoyl group using hydrazine monohydrate, as described for the synthesis of **41**, furnished hexasaccharide **45**. Subsequently, a [3 + 6] glycosylation and delevulination cycle was carried to provide the nonasaccharide **49**. Following the synthetic approach for trisaccharide target **1**, a similar functionalization and deprotection sequence were performed with hexasaccharide **45** and nonasaccharide **49** to provide the partially protected hexasaccharide **5** and nonasaccharide **6**, respectively. Previously it was shown that the regioselective oxidation of multiple primary alcohols in the longer oligosaccharide became increasingly difficult with increasing substrate length. The oxidation conditions, as previously optimized,[8g] were initially applied on hexasaccharide **5**, containing five free hydroxyls. Unfortunately, these conditions proved to be incompatible for the oxidation of **5**, and a major side-product was isolated. The structure of this compound was established using NMR and HRMS analysis and proved to be truncated disaccharide **47e**. A possible mechanism for the formation of **47e** is shown in Scheme 7. [18] Apparently, the oxidative conditions led to cleavage of the glycosydic bond at the junction of the trisaccharide repeating units. This would lead to two trisaccharide fragments **47a**, and **47b**. Subsequently, the hemiacetal **47b** can undergo a further oxidation to the di-acid intermediate **47c**, the diol of which can be oxidatively cleaved to provide, after another oxidation, di-acid **47d**, which upon benzylation provided **47e**. The formation of this side product indicated that the long time (3 days) used for the oxidation and the large excess of oxidants were too harsh for the substrate. Therefore, shorter reaction times were explored. The reaction was therefore monitored from 10 hours to 3 days, by thin-layer chromatography, indicating 24h to be optimal for the conversion of **5** into **47**. Thus, hexasaccharide **47** could be obtained in 58% yield after a reaction with the TEMPO/BAIB reagent combination for 24 hours at 4 ℃ in *t*-BuOH-water-EtOAc solution, followed by a benzylation using phenyldiazomethane. Similarly, the three primary alcohols of the nonasaccharide **6** were oxidized and benzylated to provide the corresponding nonasaccharide **51** in 66% yield over two steps. The cleavage of the nonasaccharide could not be completely prevented as LC-MS analysis of the reaction, which indicated the formation of trisaccharides and hexasaccharides, including **43** and **47**. The formation of these side products confirms the regioselectivity of the cleavage reactions, taking place at the anomeric center of the galactose residues that have to be oxidized. Unexpectedly, the deprotection procedure used for trisaccharide **1** was not suitable for the hexasaccharide, as products of acetyl migration and hydrolysis were detected by NMR and LC-MS. After various

optimizations of the solvent and reaction pH, the global deprotection was accomplished by performing the hydrogenation under mild acidic conditions to provide the target hexasaccharide **2** in 91% and nonasaccharide **3** in 90% yield (Figure 2).



Scheme 6. Assembly of the larger targets **2** and **3**.

Reagents and conditions: a) TBSOTf, DCM, 5Å MS, 0 °C, **44**, 83%; **48**, 85%. b) N_2H_4•H_2O, pyridine, AcOH, 0 °C - RT, **45**, 94%; **49**, 89%. c) i, PPh_3, pyridine, H_2O, THF, 70 °C, 7 h; ii, Ac_2O, $NaHCO_3$, THF, H_2O, **46**, 88%; **50**, 99%. d) HF•Py, THF, pyridine, 0 °C, **5**, 92%; **6**, 96%. e) i, TEMPO, BAIB, *t*-BuOH, H_2O, EtOAc or MeCN, 4 °C, 1d; ii, $PhCHN_2$, DCM, **47**, 58%; **51**, 66% (over two steps). f) $Pd(OH)_2$/C, H_2, *t*-BuOH, 0.1% AcOH in H_2O, 3 days, **2**, 91%; **3**, 90%.



Scheme 7. The possible mechanism for the formation of **47e**.

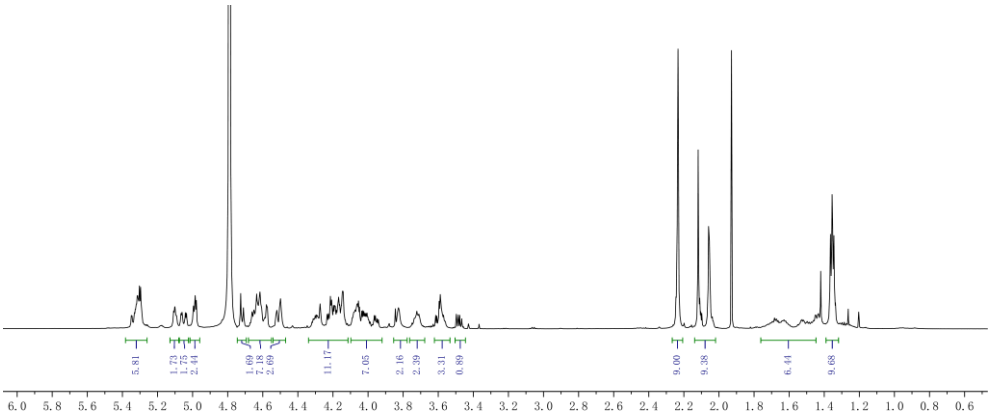


Figure 2. ^{1}H NMR spectrum of synthesized target nonasaccharide **3** in D_2O.

The syntheses of the acetylated oligomers clearly indicated the C-3-*O*-acetyl to be labile. To evaluate the stability of the acetyl group more accurately, a set of NMR experiments was set up. NMR analyses were performed on samples of **1** in D_2O phosphate buffer at different pD values (pD = pH + 0.4), ranging from pD 5.0 to pD 8.0. As shown in Figure 3 and 4, the acetyl group can migrate and hydrolyze from **1** to **1a** and **1b** under slightly basic conditions (pD = 8.0), and unexpectedly, migration also occurred, albeit sluggishly, at pD 7.0, which indicates that the acetyl may be labile also under very mild acidic conditions (pH = 6.6). At pD = 8.0 the 3-OAc ↔ 2-OAc migration was fast (Figure 4), with more than 50% of the 3-OAc migrating in the first 15 days. Recently a detailed acetyl migration study was performed on a β-mannosyl trisaccharide, carrying a C-3-*O*-acetyl. In this mannose system migration occurred much faster, because of the *cis*-relationship of the substituents at the C-2 and C-3 position of the mannose ring.[17] After 380 days the ratio of **1**, **1a** and **1b** was approximately 5:5:90. At lower pD (pD = 5.0 and 6.0) no migration or hydrolysis was observed over a period as long as 380 days. The stability studies underpinned the requirement for slightly acidic condition during the deprotection of the oligosaccharides. They also indicate that care should be taken when interaction studies are performed with these synthetic fragments or isolated Sp1-polysaccharides.

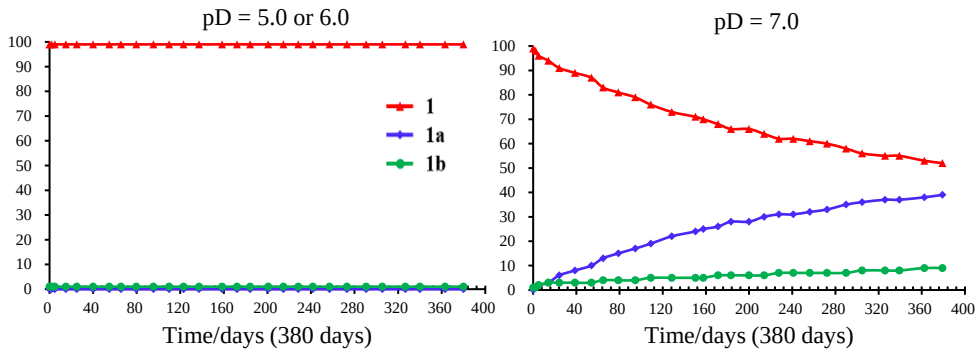


Figure 3. The *O*-Ac migration and hydrolysis of trisaccharide **1** in pD = 5, 6 and 7.

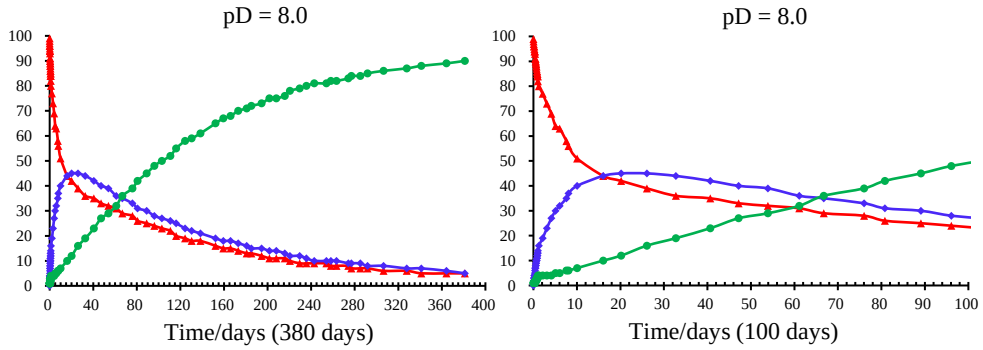


Figure 4. The *O*-Ac migration and hydrolysis of trisaccharide **1** in pD = 8.

Conclusion

In conclusion, three acetylated Sp1 fragments, a trisaccharide, hexasaccharide and nonasaccharide, were successfully assembled building on the previously developed synthesis approach, which strategically combined pre- and post-glycosylation oxidation events. The target molecules each contain a novel spacer, carrying a vicinal diol at its terminus, for future conjugation purposes. An alternative strategy that was devised to assemble the target oligosaccharides, hinging on the use of building blocks with the galacturonic acid moieties pre-installed (*i.e.* the use of a pre-glycosylation oxidation approach) was abandoned in an early stage as model experiments indicated that the glycosylation reactions proceeded with poor stereoselectivity. The regioselective oxidation of multiple primary alcohols in the complex oligosaccharide was accomplished using a modified TEMPO-BAIB oxidation. The formation of over-oxidized side products indicated the need to closely monitor the progress of the reactions. The pure trisaccharide was used to probe the stability of the C-3-*O*-acetyl group, which was shown to be labile under neutral and slightly basic conditions. At slightly acidic pH, the acetyl

group is stable, without migration and cleavage taking place. The structure of the acetylated Sp1 fragments will be investigated employing molecular dynamics simulations and NMR spectroscopy to evaluate the role of the acetyl on the 3-D structure of these oligomers. Binding studies using the ELISA and STD NMR experiments will reveal the role of the acetyl groups in the interaction with anti-Sp1 antibodies.

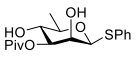
Experimental Section

General experimental procedures

All reagents were of commercial grade and used as received. All moisture sensitive reactions were performed under an argon atmosphere. DCM used in the glycosylation reactions was dried with flamed 4Å molecular sieves before being used. Reactions were monitored by TLC analysis with detection by UV (254 nm) and where applicable by spraying with 20% sulfuric acid in EtOH or with a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (25 g/L) and $(NH_4)_4Ce(SO_4)_4\cdot 2H_2O$ (10 g/L) in 10% sulfuric acid (aq.) followed by charring at ~150 °C. Flash column chromatography was performed on silica gel (40-63µm). ^1H and ^{13}C spectra were recorded on a Bruker AV 400 or Bruker AV 500 or Bruker AV 600 and Bruker AV 850 in $CDCl_3$ or D_2O. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard (^1H NMR in $CDCl_3$) or the residual signal of the deuterated solvent. Coupling constants (*J*) are given in Hz. All ^{13}C spectra are proton decoupled. NMR peak assignments were made using COSY and HSQC experiments, where applicable Clean TOCSY, HMBC and GATED experiments were used to further elucidate the structure. The anomeric product ratios were analyzed through integration of proton NMR signals.

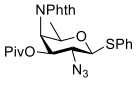
Experimental Procedures and Characterization Data of Products

Phenyl 3-*O*-pivaloyl-6-deoxy-1-thio-β-D-mannopyranoside (21)



Phenyl 6-deoxy-1-thio-β-D-mannopyranoside **16**[14b] (100 mg, 0.39 mmol, 1.0 eq) was dissolved in dry THF (2 mL). DIPEA (134 µL, 0.78 mmol, 2.0 eq), Me_2SnCl_2 (4.3 mg, 0.02 mmol, 0.05 eq) were added and stirred for 15 min. Then pivaloyl chloride (PivCl) (55 mg, 0.46 mmol, 1.1 eq) was added and the reaction was stirred at rt for 1 hour. After TLC showed complete consumption of the starting material, the reaction was quenched with 3% HCl solution and washed with H_2O (2x), brine. The organic phase was dried with $MgSO_4$, filtered and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/Acetone 20:1 - 10:1) to yield compound **21** (118 mg, 0.35 mmol, 89%). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.49 – 7.42 (m, 2H), 7.31 – 7.21 (m, 3H), 4.91 (d, *J* = 1.1 Hz, 1H, H-1), 4.78 (dd, *J* = 9.8, 3.2 Hz, 1H, H-3), 4.30 – 4.24 (m, 1H, H-2), 3.71 (t, *J* = 9.5 Hz, 1H, H-4), 3.49 – 3.38 (m, 1H, H-5), 2.81 (s, 1H), 1.39 (d, *J* = 6.1 Hz, 3H, H-6), 1.23 (s, 9H, Piv). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.96 (Piv), 134.26, 131.17, 129.06, 127.53, 87.01 (C-1), 76.89 (C-5), 76.62 (C-3), 71.11 (C-2), 70.70 (C-4), 39.10, 27.14, 17.94 (C-6). HR-MS: Calculated for $C_{17}H_{24}O_5S$ $[M+Na]^+$: 363.12367, found: 363.12347. $[\alpha]^{20}_D$ = - 48.1° (c = 1, $CHCl_3$). TLC: Rf = 0.6 (DCM/Acetone = 10/1, v/v).

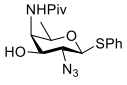
Phenyl 2-azido-3-*O*-pivaloyl-4-*N*-phthaloyl-6-deoxy-1-thio-β-D-galactopyranoside (22)



The compound **21** (115 mg, 0.338 mmol, 1.0 eq) was dissolved in DCM (6 ml) with pyridine (0.36 mL, 4.4 mmol, 13.0 eq), then Tf_2O (0.35 mL, 2.0 mmol, 6.0 eq) was added to the reaction mixture at -10 °C, and slowly warm up to 10 °C in 2 h. After TLC showed complete consumption of the starting material, the reaction mixture was diluted with DCM and washed with 1M HCl solution and saturated aqueous sodium bicarbonate. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was

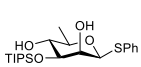
dissolved in dry CH_3CN (5 mL), $TBAN_3$ (96 mg, 0.338 mmol, 1.0 eq) solution in CH_3CN (1 mL) was slowly added to the reaction mixture at -30 ℃. The reaction was allowed to stir for 2 d at same temperature and then concentrated *in vacuo* under nitrogen. The residue was dissolved in DMF (2 mL), and then phthalimide potassium (135 mg, 0.73 mmol, 2.1 eq) was added to the reaction mixture and stirred for overnight at room temperature. The reaction mixture was diluted with EtOAc and washed with water and brine and then dried over Na_2SO_4 and concentrated *in vacuo*. The product was purified by column chromatography (PE/EA, 20:1 – 10:1) to yield compound **22** (61.4 mg, 0.124 mmol, 37%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 – 7.83 (m, 2H), 7.82 – 7.72 (m, 3H), 7.67 – 7.58 (m, 2H), 7.40 – 7.29 (m, 2H), 5.14 (dd, *J* = 9.2, 7.0 Hz, 1H, H-3), 4.88 (dd, *J* = 7.0, 2.9 Hz, 1H, H-4), 4.75 – 4.60 (m, 2H, H-2, H-1), 4.01 – 3.88 (m, 1H, H-5), 1.17 (d, *J* = 6.4 Hz, 3H, H-6), 0.98 (s, 9H, Piv). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.90 (Piv), 134.45, 133.63, 132.33, 129.09, 128.01, 123.73, 88.71 (C-1), 73.29 (C-5), 72.40 (C-3), 62.10 (C-2), 51.27 (C-4), 38.74, 26.82, 16.99 (C-6). HR-MS: Calculated for $C_{25}H_{26}N_4O_5S$ $[M+Na]^+$: 517.15161, found: 517.15180. $[\alpha]^{20}_D$ = + 62.9° (c = 1, $CHCl_3$). TLC: Rf = 0.4 (PE/EA = 4/1, v/v).

Phenyl 2-azido-4-*N*-pivaloyl-6-deoxy-1-thio-β-D-galactopyranoside (23)



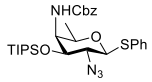
The compound **22** (31 mg, 0.06 mmol, 1.0 eq) was dissolved in butanol (3 mL) with ethylenediamine (0.3 mL), the reaction mixture was refluxed for 24 h. The reaction mixture concentrated *in vacuo*. The product was purified by column chromatography (DCM/MeOH 100:1 - 20:1) to yield product **23** (10 mg, 0.0274 mmol, 44%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 – 7.57 (m, 2H), 7.41 – 7.31 (m, 3H), 5.66 (d, *J* = 8.0 Hz, 1H, N*H*Piv), 4.37 (d, *J* = 10.2 Hz, 1H, H-1), 4.21 – 4.13 (m, 1H, H-4), 3.86 – 3.75 (m, 2H, H-5, H-3), 3.08 (t, *J* = 9.8 Hz, 1H, H-2), 2.36 (s, 1H), 1.24 (d, *J* = 6.7 Hz, 3H, H-6), 1.12 (s, 9H, Piv). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.94 (Piv), 135.07, 129.29, 129.17, 129.15, 85.47 (C-1), 75.68 (C-3), 73.74 (C-5), 62.68 (C-2), 53.56 (C-4), 39.10, 27.59, 17.31 (C-6). $[\alpha]^{20}_D$ = - 34.0° (c = 0.1, $CHCl_3$). TLC: Rf = 0.4 (PE/EA = 4/1, v/v).

Phenyl 6-deoxy-3-*O*-triisopropylsilyl-1-thio-β-D-mannopyranoside (24)

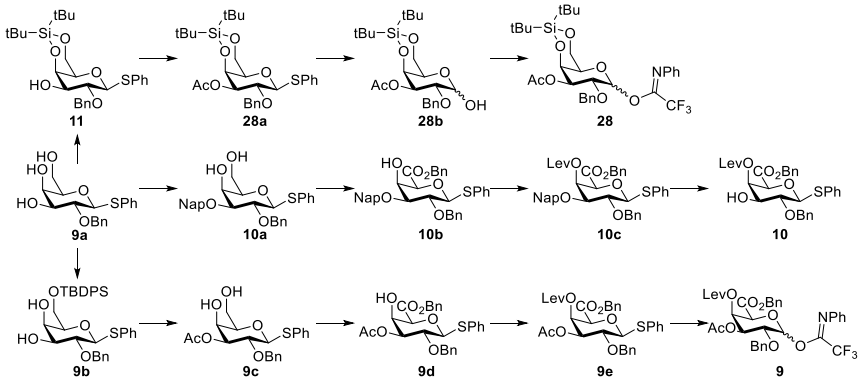


Compound phenyl 2-*O*-benzyl-1-thio-β-D-galactopyranoside **16**[14b] (19.7 g, 76.9 mmol, 1.0 eq) was dissolved in DMF (154 mL) and cooled to 0 ℃. Triisopropylsilyl chloride (TIPSCl) (33 mL, 153.8 mmol, 2.0 eq) and imidazole (31 g, 455 mmol, 6.0 eq) were added at 0 ℃. It was stirred at RT for 24 hours and checked by TLC. After completed consumption of the starting material, diluted with EtOAc, and washed with water and brine. The organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 20:1 - 8:1) to yield compound **24** (28 g, 67.9 mmol, 88%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.55 – 7.49 (m, 2H), 7.34 – 7.23 (m, 3H), 4.89 – 4.81 (m, 1H, H-1), 4.16 – 4.08 (m, 1H, H-2), 3.74 (dd, *J* = 8.8, 3.5 Hz, 1H, H-3), 3.63 – 3.54 (m, 1H, H-4), 3.41 – 3.29 (m, 1H, H-5), 2.66 (t, *J* = 1.8 Hz, 1H, 2-OH), 2.08 (d, *J* = 3.4 Hz, 1H, 4-OH), 1.41 (d, *J* = 6.1 Hz, 3H, H-6), 1.17 – 1.07 (m, 21H, TIPS). ^{13}C NMR (126 MHz, $CDCl_3$) δ 130.86, 129.01, 127.31, 86.39 (C-1), 76.62 (C-3), 75.94 (C-5), 73.34, 73.33 (C-2, C-4), 18.15, 18.14, 18.05 (C-6), 12.56. HR-MS: Calculated for $C_{21}H_{36}O_4SSi$ $[M+Na]^+$: 435.19958, found: 435.19957. $[\alpha]^{20}_D$ = - 40.0° (c = 1, $CHCl_3$). TLC: Rf = 0.5 (PE/EA = 4/1, v/v).

Phenyl 2-azido-4-*N*-benzyloxycarbonyl-6-deoxy-3-*O*-triisopropylsilyl-1-thio-β-D-galactopyranoside (25)

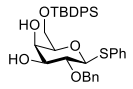


The compound **24** (1.57 g, 3.81 mmol, 1.0 eq) was dissolved in DCM (54 ml) with pyridine (4 mL, 50 mmol, 13.0 eq), then Tf_2O (3.8 mL, 22.9 mmol, 6.0 eq) was added to the reaction mixture at -10 ℃, and slowly warm up to 10 ℃ in 2 h. After TLC showed complete consumption of the starting material, the reaction mixture was diluted with DCM and washed with 1M HCl solution and saturated aqueous sodium bicarbonate. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was dissolved in dry CH_3CN (50 mL), $TBAN_3$ (1.11 g, 3.90 mmol, 1.02 eq) solution in CH_3CN (5 mL) was slowly added to the reaction mixture at -30 ℃ and stirred for one day. The reaction was warmed slowly to -20℃ and stir for additional 2 days. After TLC showed complete consumption of the starting material, 7N NH_3 in methanol (10 mL) was added in -20℃. The reaction was slowly warmed to 5 ℃ and stirred for 3 days. After TLC showed complete consumption of the starting material, the mixture was concentrated *in vacuo*. The residue was dissolved in THF (28 mL) and water (19 mL), and then sodium bicarbonate (1.28 g, 15.2 mmol, 4.0 eq) was added and cooled to 0 ℃. After benzyl chloroformate (CbzCl) (1.1 mL, 7.6 mmol, 2.0 eq). the mixture was stirred for overnight at room temperature. After TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate and diluted with EtOAc. The solution was washed with water (2x) and brine. The aqueous layer was extracted with EA (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 5:1 - 3:1) to yield compound **25** (3.0 mg, 3.0 mmol, 75%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 – 7.53 (m, 2H), 7.40 – 7.26 (m, 8H), 5.08 (q, *J* = 12.2 Hz, 2H, Cbz), 4.79 (d, *J* = 10.0 Hz, 1H, N*H*Cbz), 4.42 (d, *J* = 10.2 Hz, 1H, H-1), 4.01 – 3.93 (m, 1H, H-4), 3.77 (dd, *J* = 9.5, 4.4 Hz, 1H, H-3), 3.63 – 3.53 (m, 1H, H-5), 3.09 (t, *J* = 9.8 Hz, 1H, H-2), 1.24 (d, *J* = 6.3 Hz, 3H, H-6), 1.15 – 1.00 (m, 21H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.76 (Cbz), 133.08, 129.19, 128.57, 128.47, 128.21, 128.16, 87.37 (C-1), 74.64 (C-5), 73.86 (C-3), 67.01 (Cbz), 64.73 (C-2), 55.62 (C-4), 18.05, 18.02, 17.22 (C-6), 12.78. HR-MS: Calculated for $C_{29}H_{42}N_4O_4SSi$ [M+H$^+$]: 571.27688, found: 571.27703. $[\alpha]^{20}_D$ = + 0.6° (c = 1, $CHCl_3$). TLC: Rf = 0.3 (PE/EA = 20/1, v/v).



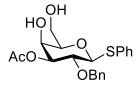
Scheme I. The synthesis of building blocks of galactose.

Phenyl 2-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-1-thio-β-D-galactopyranoside (9b)



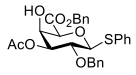
Compound phenyl 2-*O*-benzyl-1-thio-β-D-galactopyranoside **9a**[8g] (16.4 g, 45.3 mmol, 1.0 eq) was dissolved in DMF (91 mL) and cooled to 0 °C. *tert*-Butyl(chloro)diphenylsilane (TBDPSCl) (14.2 mL, 54.5 mmol, 1.2 eq) and imidazole (4.7 g, 69.0 mmol, 1.5 eq) were added at 0 °C. It was stirred at RT for 4 hours and checked by TLC. After completed consumption of the starting material, diluted with EtOAc, and washed with water and brine. The organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 6:1 - 3:1) to yield compound **9b** (26 g, 43.3 mmol, 96%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 – 7.64 (m, 4H), 7.59 – 7.51 (m, 2H), 7.46 – 7.16 (m, 14H), 4.89 (d, *J* = 10.9 Hz, 1H, C*H*$_2$), 4.69 (d, *J* = 10.9 Hz, 1H, C*H*$_2$), 4.64 – 4.55 (m, 1H, H-1), 4.06 – 4.01 (m, 1H, H-4), 3.98 – 3.87 (m, 2H, H-6), 3.66 – 3.57 (m, 2H, H-3, H-2), 3.49 – 3.42 (m, 1H, H-5), 2.74 (s, 1H), 1.06 (s, 9H, TBDPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.16, 135.65, 135.57, 134.21, 132.84, 132.66, 131.33, 129.90, 128.92, 128.52, 128.25, 127.98, 127.83, 127.82, 127.22, 87.59 (C-1), 78.10 (C-3), 77.84 (C-5), 75.35, 75.23 (C-2), 69.60 (C-4), 63.88 (C-6), 26.80, 19.14. HR-MS: Calculated for $C_{35}H_{40}O_5SSi$ [M+Na$^+$]: 623.2258, found: 623.2256. $[\alpha]^{20}_D$ = + 6.8° (c = 1, $CHCl_3$). TLC: Rf = 0.4 (PE/EA = 3/1, v/v).

Phenyl 2-*O*-benzyl-3-*O*-acetyl-1-thio-β-D-galactopyranoside (9c)



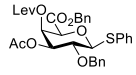
Compound **9b** (2.5 g, 4.24 mmol, 1.0 eq) was dissolved in dry THF (22 mL). DIPEA (1.5 mL, 8.5 mmol, 2.0 eq), Me_2SnCl_2 (50 mg, 0.23 mmol, 0.05 eq) were added and stirred for 15 min. Then acetyl chloride (362 µL, 5.07 mmol, 1.2 eq) was added and the reaction was stirred at rt for overnight. After TLC showed complete consumption of the starting material, the reaction was quenched with 3% HCl solution and washed with H_2O (2x), brine. The organic phase was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was dissolved in THF (30 mL) and pyridine (30 mL), then cooled to 0 °C and hydrogen fluoride (HF)/pyridine (70%) (3 mL) was added dropwise. The solution was stirred for overnight. After TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate slowly and diluted with EtOAc. The solution was washed with water (2x) and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/Acetone 20:1 - 5:1) to yield compound **9c** (1.5 g, 3.6 mmol, 85%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 – 7.52 (m, 2H), 7.37 – 7.23 (m, 8H), 4.92 (dd, *J* = 9.5, 3.1 Hz, 1H, H-3), 4.86 (d, *J* = 10.9 Hz, 1H, C*H*$_2$), 4.73 (d, *J* = 9.7 Hz, 1H, H-1), 4.58 (d, *J* = 11.0 Hz, 1H, C*H*$_2$), 4.19 (dd, *J* = 3.1, 1.0 Hz, 1H, H-4), 3.92 – 3.80 (m, 3H, H-2, H-6), 3.59 – 3.52 (m, 1H, H-5), 2.85 (s, 2H), 2.02 (s, 3H, OAc). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.41 (OAc), 137.99, 133.49, 131.76, 129.19, 128.50, 128.03, 127.96, 127.77, 88.02 (C-1), 77.42 (C-5), 76.78 (C-3), 75.64 (*C*H$_2$), 75.42 (C-2), 68.77 (C-4), 62.98 (C-6), 21.10 (OAc). HR-MS: Calculated for $C_{21}H_{24}O_6S$ [M+Na$^+$]: 427.1186, found: 427.1185. $[\alpha]^{20}_D$ = +21.1° (c = 1, $CHCl_3$). TLC: Rf = 0.5 (DCM/Acetone = 4/1, v/v).

Benzyl phenyl 3-*O*-acetyl-2-*O*-benzyl-1-thio-β-D-galactopyranosyl uronate (9d)



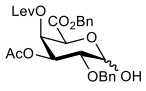
Compound **9c** (7.8 g, 19.3 mmol, 1.0 eq) was dissolved in DCM/*tert*-BuOH/H_2O (146 mL, 4/4/1, v/v/v). The mixture was cooled to 0 ℃ and treated with TEMPO (608 mg, 3.9 mmol, 0.2 eq) and BAIB (16 g, 48.2 mmol, 2.5 eq). After stirring for overnight at 4 ℃ and TLC showed complete consumption of the starting material, saturated aqueous sodium thiosulphate was added and diluted with EtOAc, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was dissolved in DMF (77 mL), followed by addition of Cs_2CO_3 (6.4 g, 19.6 mmol, 1.0 eq) and BnBr (4.6 mL, 38.5 mmol, 2.0 eq) at 0ºC. The mixture was allowed to stir overnight at rt, and then diluted with EtOAc, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/DCM/EA, 7/2/1) yielded **9d** (7.6 g, 14.9 mmol, 77%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 – 7.60 (m, 2H), 7.41 – 7.21 (m, 13H), 5.28 – 5.19 (m, 2H, CH_2), 4.97 (dd, *J* = 9.6, 3.1 Hz, 1H, H-3), 4.88 (d, *J* = 11.0 Hz, 1H, CH_2), 4.67 (d, *J* = 9.7 Hz, 1H, H-1), 4.59 (d, *J* = 11.0 Hz, 1H, CH_2), 4.44 (dd, *J* = 3.1, 1.2 Hz, 1H, H-4), 4.19 (d, *J* = 1.2 Hz, 1H, H-5), 3.81 (t, *J* = 9.6 Hz, 1H, H-2), 2.23 (s, 1H), 2.01 (s, 3H, OAc). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.10 (OAc), 167.21, 137.87, 135.06, 133.24, 132.63, 129.06, 128.72, 128.66, 128.64, 128.51, 128.44, 128.24, 128.04, 128.00, 87.99 (C-1), 76.84 (C-5), 75.82 (C-3), 75.67 (*C*H_2), 74.96 (C-2), 68.54 (C-4), 67.50 (*C*H_2), 21.00 (OAc). HR-MS: Calculated for $C_{28}H_{28}O_7S$ [M+Na^+]: 531.1448, found: 531.1448. $[\alpha]^{20}_D$ = + 4.5º (c = 1, $CHCl_3$). TLC: Rf = 0.1 (PE/DCM/EA = 7/2/1, v/v/v).

Benzyl phenyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-levulinoyl-1-thio-β-D-galactopyranosyl uronate (9e)



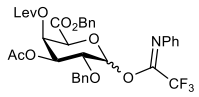
Compound **9d** (1.05 g, 2.1 mmol, 1.0 eq) was co-evaporated with anhydrous toluene three times under nitrogen and dissolved in DCM (20 mL). Reduced to 0 ℃, levulinic acid (668 mg, 5.8 mmol, 2.8 eq), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDCI) (640 mg, 4.1 mmol, 2.0 eq) and 4-dimethylaminopyridine (DMAP) (50 mg, 0.41 mmol, 0.2 eq) were added. The reaction was stirred for 2 days. The reaction was diluted with DCM and washed with saturated aqueous sodium bicarbonate and brine. The organic phase was dried with $MgSO_4$, filtered and concentrated *in vacuo*. The compound was purified by flash chromatography (Tol/EA 20:1 - 10:1) to yield compound **9e** (1.21 g, 2.0 mmol, 99%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 – 7.62 (m, 2H), 7.41 – 7.23 (m, 13H), 5.76 – 5.71 (m, 1H, H-4), 5.23 (d, *J* = 11.9 Hz, 1H, CH_2), 5.12 (d, *J* = 11.9 Hz, 1H, CH_2), 5.02 (dd, *J* = 9.6, 3.4 Hz, 1H, H-3), 4.85 (d, *J* = 10.9 Hz, 1H, CH_2), 4.69 (d, *J* = 9.7 Hz, 1H, CH_2), 4.59 (d, *J* = 10.9 Hz, 1H, CH_2), 4.28 (d, *J* = 1.4 Hz, 1H, H-5), 3.70 (t, *J* = 9.7 Hz, 1H, H-2), 2.64 – 2.44 (m, 3H, Lev), 2.34 – 2.23 (m, 1H, Lev), 2.16 (s, 3H, Lev), 1.92 (s, 3H, OAc). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.12 (Lev), 171.49 (Lev), 170.15 (OAc), 165.87 (CO_2Bn), 137.88, 135.14, 133.33, 132.78, 129.11, 129.04, 128.76, 128.74, 128.70, 128.52, 128.27, 128.22, 128.04, 128.03, 87.93 (C-1), 75.72, 75.37 (C-5), 74.84 (C-2), 73.85 (C-3), 68.95 (C-4), 67.60 (CO_2Bn), 37.72, 29.98 (Lev), 27.68, 20.69 (OAc). HR-MS: Calculated for $C_{33}H_{34}O_9S$ [M+Na^+]: 629.18157, found: 629.18103. $[\alpha]^{20}_D$ = + 4.6º (c = 1, $CHCl_3$). TLC: Rf = 0.2 (Tol/EA = 9/1, v/v).

Benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-levulinoyl-α/β-D-galactopyranosyl uronate (9f)



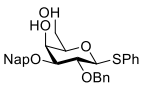
Compound **9e** (490 mg, 0.79 mmol, 1.0 eq) was dissolved in DCM (8 mL) and reduced to 0 °C. NIS (195 mg, 0.87 mmol, 1.1 eq) and TFA (67 µL, 0.87 mmol, 1.1 eq) were added and the solution stirred for 2 hours. After analysis by TLC showed complete consumption of the starting material, the reaction was quenched with triethyl amine and saturated aqueous sodium thiosulphate. The solution was diluted with DCM and washed with brine (3x). The organic phase was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 2:1 - 1:1) to yield the titled compound (390 mg, 0.76 mmol, 96%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.16 (m, 10H), 5.82 – 5.63 (m, 1H, H-4), 5.45 – 5.32 (m, 2H, H-1, H-3), 5.29 – 5.19 (m, 1H, CH_2), 5.13 – 5.00 (m, 1H, CH_2), 4.88 – 4.80 (m, 1H, H-5), 4.74 – 4.56 (m, 2H, CH_2), 3.93 – 3.65 (m, 2H, H-2), 2.66 – 2.35 (m, 3H, Lev), 2.31 – 2.09 (m, 4H, Lev), 2.01 – 1.89 (m, 3H, OAc). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.27, 206.19 (Lev), 171.52 (Lev), 170.35z, 170.33 (OAc), 167.42, 166.62 (CO_2Bn), 138.25, 137.69, 135.04, 134.92, 129.22, 128.73, 128.68, 128.65, 128.60, 128.40, 128.16, 128.01, 127.92, 127.82, 97.52, 91.95 (C-1), 77.01, 74.87, 73.51, 73.21 (C-2), 72.09, 71.92, 69.55 (C-4), 69.15 (C-3), 68.72, 68.53 (C-5), 67.78, 67.55 (C-6), 37.70, 37.68, 29.89, 27.58, 20.78 (OAc). HR-MS: Calculated for $C_{27}H_{30}O_{10}$ $[M+NH_4]^+$: 537.17312, found: 537.17302. TLC: Rf = 0.3 (PE/EA = 10/1, v/v).

Benzyl *N*-phenyl-trifluoroacetimidate 3-*O*-acetyl-2-*O*-benzyl-4-*O*-levulinoyl-α/β-D-galactopyranosyl uronate (9)



The corresponding hemiacetal (5.5 g, 10.7 mmol, 1.0 eq) was dissolved in acetone (110 mL) and cooled to 0 °C. Cesium carbonate (3.3 g, 12.9 mmol, 1.2 eq) was added. After 15 min, N-phenyl trifluoroacetimidoyl chloride (3.3 g, 15.9 mmol, 1.5 eq) was added, and then the reaction was allowed to stir for overnight at RT. After analysis by TLC showed complete consumption of the starting material, quenched by triethyl amine, filtered and concentrated *in vacuo*, and the product purified by column chromatography (PE/EA 5:1 – 2/1) to yield compound **9** (6.62 g, 9.66 mmol, 91%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.01 (m, 13H), 6.85 – 6.68 (m, 2H), 5.95 – 5.30 (m, 2H, H-4, H-3), 5.29 – 5.19 (m, 1H, CH_2), 5.15 – 4.88 (m, 2H, H-5, CH_2), 4.86 – 4.76 (m, 1H, CH_2), 4.73 – 4.64 (m, 1H, CH_2), 3.96 – 3.73 (m, 1H, H-2), 2.68 – 2.43 (m, 3H, Lev), 2.33 – 2.24 (m, 1H, Lev), 2.20 – 2.13 (m, 3H, Lev), 2.01 – 1.82 (m, 3H, OAc). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.07 (Lev), 171.39 (Lev), 170.11 (OAc), 165.26 (CO_2Bn), 137.44, 134.89, 129.31, 129.29, 128.86, 128.78, 128.74, 128.72, 128.70, 128.58, 128.56, 128.20, 128.12, 124.49, 119.36, 96.57 (C-1), 75.39, 74.91, 72.81, 71.89, 68.43, 67.79, 37.64, 29.91, 27.60, 20.61. HR-MS: Calculated for $C_{35}H_{34}F_3NO_{10}$ $[M+Na^+]$: 708.20270, found: 708.20297. TLC: Rf = 0.2 (PE/EA = 7/3, v/v).

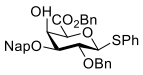
Phenyl 2-*O*-benzyl-3-*O*-(2-naphthylmethyl)-1-thio-β-D-galactopyranoside (10a)



The compound phenyl 2-*O*-benzyl-1-thio-β-D-galactopyranoside **9a**[8g] (4.47 g, 12.3 mmol, 1.0 eq) was dissolved in acetonitrile DCM (60 ml). Benzaldehyde dimethyl acetal (2.8 mL, 18.5 mmol, 1.5 eq) and *p*-Toluenesulfonic acid monohydrate (TsOH) (235 mg, 1.23 mmol, 0.1 eq) were added successively to the reaction mixture at RT. After stirred for overnight and TLC showed complete

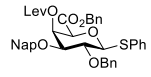
consumption of the starting material, the reaction mixture was quenched with triethyl amine and concentrated *in vacuo*. The intermediate was crystalized in ethanol and dissolved in dry DMF (35 mL). The reaction was cooled to 0 ℃, sodium hydride (1.0 g, 24.7 mmol, 2 eq) was added and stirred for 15 min. 2-(bromomethyl)naphthalene (4.1 g, 18.5 mmol, 1.5 eq) was added at 0 ℃. It was slowly wormed to RT and stirred for overnight. After analysis by TLC showed complete consumption of the starting material, quenched with MeOH and water. Diluted with EtOAc and washed with water and brine. The organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude was dissolved in MeOH (150 mL) and DCM (150 mL). TsOH was added until the solution pH about 2. After analysis by TLC showed complete consumption of the starting material, the reaction was quenched by triethylamine and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/Acetone 40:1 - 10:1) to yield compound **10a** (4.1, 8.2 mmol, 66%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.84 – 7.69 (m, 4H), 7.57 – 7.52 (m, 2H), 7.49 – 7.37 (m, 5H), 7.36 – 7.20 (m, 6H), 4.90 – 4.79 (m, 3H, CH_2), 4.76 (d, *J* = 10.3 Hz, 1H, CH_2), 4.64 (d, *J* = 9.8 Hz, 1H, H-1), 4.07 (d, *J* = 3.2 Hz, 1H, H-4), 3.94 (dd, *J* = 11.8, 6.6 Hz, 1H, H-6), 3.84 – 3.73 (m, 2H, H-6, H-2), 3.61 (dd, *J* = 8.9, 3.2 Hz, 1H, H-3), 3.49 – 3.41 (m, 1H, H-5), 2.80 (s, 1H, 4-OH), 2.37 (s, 1H, 6-OH). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.21, 135.03, 133.79, 133.28, 133.18, 131.82, 129.09, 128.56, 128.52, 128.36, 128.02, 127.98, 127.83, 127.58, 126.91, 126.40, 126.27, 125.85, 87.72 (C-1), 82.31 (C-3), 78.07 (C-5), 77.10 (C-2), 75.89, 72.40, 67.50 (C-4), 62.80 (C-6). HR-MS: Calculated for $C_{30}H_{30}O_5S$ $[M+Na]^+$: 525.17062, found: 525.17051. $[\alpha]^{20}_D$ = + 5.3° (c = 1, $CHCl_3$). TLC: Rf = 0.4 (DCM/Acetone = 10/1, v/v).

Benzyl phenyl 2-*O*-benzyl-3-*O*-(2-naphthylmethyl)-1-thio-β-D-galactopyranosyl uronate (10b)



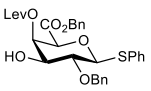
Compound **10a** (4.1 g, 8.2 mmol, 1.0 eq) was dissolved in DCM/*tert*-BuOH/H_2O (80 mL, 4/4/1, v/v/v). The mixture was cooled to 0 ℃ and treated with TEMPO (255 mg, 1.6 mmol, 0.2 eq) and BAIB (6.8 g, 20.4 mmol, 2.5 eq). After stirring for overnight at 4 ℃ and TLC showed complete consumption of the starting material, saturated aqueous sodium thiosulphate was added and diluted with EtOAc, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was dissolved in DMF (32 mL), followed by addition of Cs_2CO_3 (4.0 g, 12.3 mmol, 1.5 eq) and BnBr (2.0 mL, 16.3 mmol, 2.0 eq) at 0 ℃. The mixture was allowed to stir overnight at rt, and then diluted with EtOAc, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (silica gel, PE/EA, 5/1 – 3/1) yielded **10b** (2.9 g, 4.78 mmol, 59%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 – 7.76 (m, 2H), 7.76 – 7.69 (m, 2H), 7.68 – 7.61 (m, 2H), 7.51 – 7.30 (m, 13H), 7.28 – 7.19 (m, 3H), 5.27 (s, 2H, CO_2Bn), 4.93 – 4.74 (m, 4H, CH_2), 4.58 (d, *J* = 9.6 Hz, 1H, CH_2), 4.47 – 4.41 (m, 1H, H-4), 4.07 (d, *J* = 1.5 Hz, 1H, H-5), 3.77 (t, *J* = 9.3 Hz, 1H, H-2), 3.66 (dd, *J* = 8.9, 3.2 Hz, 1H, H-3), 2.50 (s, 1H, 4-OH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.62 (CO_2Bn), 138.13, 135.38, 134.82, 133.36, 133.29, 133.23, 132.95, 129.00, 128.73, 128.60, 128.57, 128.44, 128.42, 128.10, 128.06, 128.04, 127.85, 127.00, 126.42, 126.30, 125.86, 87.73 (C-1), 81.70 (C-2), 76.96 (C-5), 76.54 (C-2), 75.96 (*C*H_2), 72.46 (Nap), 67.93 (C-4), 67.38 (CO_2Bn). HR-MS: Calculated for $C_{37}H_{34}O_6S$ $[M+Na]^+$: 629.19683, found: 629.19680. $[\alpha]^{20}_D$ = - 5.0° (c = 1, $CHCl_3$). TLC: Rf = 0.1 (PE/EA = 4/1, v/v).

Benzyl phenyl 2-*O*-benzyl-4-*O*-levulinoyl-3-*O*-(2-naphthylmethyl)-1-thio-β-D-galactopyranosyl uronate (10c)



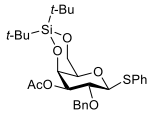
Compound **10b** (2.0 g, 3.3 mmol, 1.0 eq) was co-evaporated with anhydrous toluene three times under nitrogen and dissolved in DCM (33 mL). Reduced to 0 °C, levulinic acid (1.1 g, 9.5 mmol, 2.9 eq), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDCI) (1.0 g, 6.4 mmol, 2.0 eq) and 4-dimethylaminopyridine (DMAP) (81 mg, 0.66 mmol, 0.2 eq) were added. The reaction was stirred for overnight. The reaction was diluted with DCM and washed with H_2O (2x), brine. The organic phase was dried with $MgSO_4$, filtered and concentrated *in vacuo*. The compound was purified by flash chromatography (Tol/EA 50:1 - 30:1) to yield compound **10c** (2.1 g, 2.98 mmol, 90%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 – 7.61 (m, 6H), 7.45 – 7.19 (m, 16H), 5.85 (dd, *J* = 3.1, 1.3 Hz, 1H, H-4), 5.19 (s, 2H, CH_2), 4.85 (d, *J* = 11.4 Hz, 1H, CH_2), 4.81 – 4.70 (m, 2H, CH_2), 4.63 – 4.55 (m, 2H, CH_2, H-1), 4.11 (d, *J* = 1.3 Hz, 1H, H-5), 3.73 – 3.57 (m, 2H, H-3, H-2), 2.65 – 2.43 (m, 4H, Lev), 2.08 (s, 3H, Lev). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.89 (Lev), 171.40 (Lev), 166.22 (CO_2Bn), 138.00, 135.01, 134.79, 133.14, 133.07, 132.88, 132.60, 128.85, 128.70, 128.49, 128.46, 128.26, 128.09, 128.04, 127.87, 127.81, 127.73, 127.53, 126.85, 125.99, 125.94, 125.85, 87.21 (C-1), 80.24 (C-3), 75.92 (C-2), 75.64, 75.40 (C-5), 71.78, 67.68 (C-4), 67.45 (C-6), 37.76, 29.65, 27.79 (Lev). HR-MS: Calculated for $C_{42}H_{40}O_8S$ [M+Na$^+$]: 727.23361, found: 727.23321. $[\alpha]^{20}_D$ = + 38.6° (c = 1, $CHCl_3$). TLC: Rf = 0.4 (Tol/EA = 9/1, v/v).

Benzyl phenyl 2-*O*-benzyl-4-*O*-levulinoyl-3-*O*-acetyl-1-thio-β-D-galactopyranosyl uronate (10)



The compound **10c** (2.0 g, 2.98 mmol, 1.0 eq) was dissolved in DCM (60 mL) and water (6 mL). After cooled to 0 °C, 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) (745 mg, 3.3 mmol, 1.1 eq) was added. The reaction was stirred at RT for 7 hours. After analysis by TLC showed complete consumption of the starting material, the reaction was quenched by saturated aqueous sodium thiosulphate, extracted with DCM, and washed with water and brine. The organic layer was dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo*, and the product purified by column chromatography (PE/EA 5:1 – 2:1) to yield compound **10** (1.45 g, 2.6 mmol, 86%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.67 – 7.59 (m, 2H), 7.43 – 7.17 (m, 13H), 5.51 (dd, *J* = 3.4, 1.3 Hz, 1H, H-4), 5.12 (s, 2H, CO_2Bn), 4.80 (d, *J* = 10.6 Hz, 1H, CH_2), 4.71 (d, *J* = 10.6 Hz, 1H, CH_2), 4.53 (d, *J* = 9.6 Hz, 1H, H-1), 3.98 (d, *J* = 1.4 Hz, 1H, H-5), 3.75 (dd, *J* = 9.2, 3.4 Hz, 1H, H-3), 3.47 (t, *J* = 9.4 Hz, 1H, H-2), 3.27 (s, 1H), 2.61 – 2.52 (m, 2H, Lev), 2.49 – 2.34 (m, 2H, Lev), 2.08 (s, 3H, Lev). ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.14 (Lev), 172.06 (Lev), 166.42 (*C*H_2), 138.11, 135.15, 133.00, 132.93, 128.88, 128.85, 128.57, 128.55, 128.44, 128.24, 127.93, 127.91, 87.13 (C-1), 77.35 (C-2), 75.48 (CO_2Bn), 75.41 (C-5), 73.29 (C-3), 71.35 (C-4), 67.42 (CO_2Bn), 38.02 (Lev), 29.76 (Lev), 27.96 (Lev). HR-MS: Calculated for $C_{31}H_{32}O_8S$ [M+Na$^+$]: 587.17101, found: 587.17111. $[\alpha]^{20}_D$ = -19.2 ° (c = 1, $CHCl_3$). TLC: Rf = 0.2 (PE/EA = 3/2, v/v).

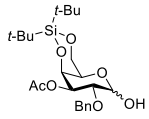
Phenyl 3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylidene-β-D-galactopyranoside (28a)



Compound **11** (1.76 g, 3.5 mmol, 1.0 eq) was dissolved in pyridine (35 mL). After reduced to 0 °C and 4- added dimethylaminopyridine (DMAP) (214 mg, 1.75 mmol, 0.5 eq), the acetyl chloride (AcCl) (275 µL, 3.9 mmol, 1.1 eq) was added dropwise. After stirred for overnight at RT and checked by TLC complete consumption of the starting material, the reaction was quenched by MeOH. The

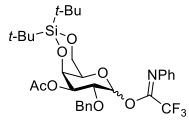
mixture was diluted with EtOAc and washed with H_2O (2x), brine. The organic phase was dried with $MgSO_4$, filtered and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 30:1 - 15:1) to yield compound **28a** (1.42 g, 2.61 mmol, 75%). ^{1}H NMR (500 MHz, Chloroform-*d*)f δ 7.57 – 7.50 (m, 2H), 7.40 – 7.30 (m, 4H), 7.30 – 7.19 (m, 4H), 4.94 (d, *J* = 10.8 Hz, 1H, CH_2), 4.79 – 4.69 (m, 3H, H-3, H-1, CH_2), 4.68 – 4.63 (m, 1H, H-4), 4.23 – 4.12 (m, 2H, H-6), 3.90 (t, *J* = 9.6 Hz, 1H, H-2), 3.37 (d, *J* = 2.0 Hz, 1H, H-5), 2.06 (s, 3H, OAc), 1.12 (s, 9H), 1.01 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.57 (OAc), 138.13, 134.39, 132.20, 128.90, 128.41, 128.12, 127.86, 127.56, 88.59 (C-1, J_{CH} = 157.0 Hz), 77.33 (C-3), 75.79 (C-2), 75.74, 74.48 (C-5), 70.28 (C-4), 67.18 (C-6), 27.65, 27.60, 23.29, 21.00 (OAc), 20.76. HR-MS: Calculated for $C_{29}H_{40}O_6SSi$ [M+Na^+]: 567.22071, found: 567.22100. $[\alpha]^{20}_D$ = + 49.8º (c = 1, $CHCl_3$). TLC: Rf = 0.5 (PE/EtOAc = 9/1, v/v).

3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylidene-α/β-D-galactopyranoside (28b)



Compound **28a** (1.18 g, 2.17 mmol, 1.0 eq) was dissolved in DCM (22 mL) and reduced to 0 °C. NIS (537 mg, 2.39 mmol, 1.1 eq) and TFA (184 µL, 2.39 mmol, 1.1 eq) were added and the solution stirred for 2 hours. After analysis by TLC showed complete consumption of the starting material, the reaction was quenched with triethyl amine and saturated aqueous sodium thiosulphate. The solution was diluted with DCM and washed with brine (3x). The organic phase was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 5:1 - 3:1) to yield compound **28b** (823 mg, 1.82 mmol, 84%). α anomer: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.27 (m, 5H), 5.22 (d, *J* = 3.6 Hz, 1H, H-1), 5.06 (dd, *J* = 10.2, 3.0 Hz, 1H, H-3), 4.79 – 4.64 (m, 3H, Bn, H-4), 4.27 – 4.17 (m, 1H, H-6), 4.12 (dd, *J* = 12.6, 1.7 Hz, 1H, H-6), 4.01 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2), 3.97 (dd, *J* = 2.2, 1.2 Hz, 1H, H-5), 3.05 (s, 1H, 1-OH), 2.11 (s, 3H, OAc), 1.01 – 0.96 (m, 18H). α anomer: ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.88 (OAc), 137.77, 128.65, 128.49, 128.24, 128.22, 128.06, 127.86, 92.03 (C-1), 73.64 (Bn), 73.19 (C-2), 72.74 (C-3), 71.02 (C-4), 67.17 (C-6), 67.10 (C-5), 27.66, 27.35, 23.37, 21.17 (OAc), 20.76. HR-MS: Calculated for $C_{23}H_{36}O_7Si$ [M+Na^+]: 475.21225, found: 475.21208. TLC: Rf = 0.2 (PE/EA = 4/1, v/v).

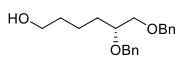
***N*-phenyl-trifluoroacetimidate 3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylidene-α/β-D-galactopyranoside (28)**



The hemiacetal **28b** (788 mg, 1.74 mmol, 1.0 eq) was dissolved in acetone (20 mL) and cooled to 0 °C. Cesium carbonate (688 mg, 2.11 mmol, 1.2 eq) was added. After 15 min, *N*-phenyl trifluoroacetimidoyl chloride (600 mg, 2.89 mmol, 1.7 eq) was added, and then the reaction was allowed to stir for overnight at RT. After analysis by TLC showed complete consumption of the starting material, quenched by triethyl amine, filtered and concentrated *in vacuo*, and the product purified by column chromatography (PE/EA 50:1 – 20:1) to yield compound **28** (1.05 g, 1.68 mmol, 97%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.78 – 7.67 (m, 1H), 7.47 – 7.27 (m, 5H), 7.27 – 7.19 (m, 1H), 7.13 (qt, *J* = 7.3, 1.2 Hz, 1H), 6.94 – 6.75 (m, 2H), 5.12 (dd, *J* = 10.4, 2.9 Hz, 1H, H-3), 4.89 – 4.60 (m, 3H, Bn, H-4), 4.47 – 3.99 (m, 4H, H-6, H-2, H-5), 2.10 (s, 3H, OAc), 1.10 – 0.95 (m, 18H). ^{13}C NMR (101 MHz, Acetone) δ 170.83, 170.67, 144.84, 139.31, 139.20, 130.00, 129.79, 129.32, 129.20, 128.87, 128.82, 128.74, 128.62, 126.69, 121.78, 120.23, 95.71 (C-

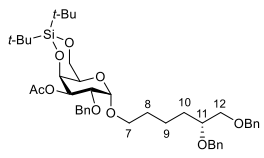
1), 76.08, 75.57, 73.97 (Bn), 72.95, 72.76, 72.66, 71.67, 70.63, 67.40 (C-6), 28.05, 28.02, 27.89, 27.76, 23.83, 21.34, 21.05, 20.98. HR-MS: Calculated for $C_{31}H_{40}F_3NO_7Si$ [M+Na$^+$]: 646.24183, found: 646.24202. TLC: Rf = 0.2/0.4 (α/β) (PE/EA = 20/1, v/v).

(*R*)-5,6-bis(benzyloxy)hexan-1-ol (29)



AD-mix-β (28.5 g) was dissolved in *tert*-BuOH/H_2O (192 mL, 1/1, v/v). The mixture was cooled to 0 °C and 2-((hex-5-en-1-yloxy)methyl)naphthalene[16b] (4.88 g, 20.3 mmol, 1.0 eq) was added and stirred for overnight. After TLC showed complete consumption of the starting material, solid sodium sulfite (25 g) was added slowly at 0 °C. The resultant suspension was allowed to warm to room temperature, stirred for an additional 1 h, and diluted with DCM. diluted with EtOAc, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The aqueous phase was extracted with DCM, and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated.[16a] The crude residue was dissolved in DMF (32 mL), sodium hydride (3.3 g, 81.2 mmol, 4.0 eq) was added and stirred for 15 min. Benzyl bromide (7.3 mL, 60.9 mmol, 3.0 eq) was added at 0 °C. It was slowly wormed to RT and stirred for overnight. After analysis by TLC showed complete consumption of the starting material, quenched with MeOH and water. Diluted with EtOAc and washed with water and brine. The organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude was dissolved in DCM (400 mL) and water (40 mL). After cooled to 0 °C, 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) (5.5 g, 24.2 mmol, 1.2 eq) was added. The reaction was stirred at RT for 7 hours. After analysis by TLC showed complete consumption of the starting material, the reaction was quenched by saturated aqueous sodium thiosulphate, extracted with DCM and washed with water and brine. The organic layer was dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo*, and the product purified by column chromatography (PE/EA 10:1 – 4:1) to yield compound **29** (3.1 g, 9.9 mmol, 49%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 – 7.10 (m, 10H), 4.69 (d, *J* = 11.6 Hz, 1H, Bn), 4.59 – 4.52 (m, 3H, Bn), 3.65 – 3.47 (m, 5H), 1.64 – 1.31 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.94, 138.44, 128.47, 128.41, 127.93, 127.73, 127.69, 127.60, 78.10 (CH), 73.45, 72.85, 72.12, 62.81, 32.79, 31.80, 21.69. HR-MS: Calculated for $C_{20}H_{26}O_3$ [M+Na$^+$]: 337.1774, found: 337.1781. $[\alpha]^{20}_D$ = +13.7° (c = 1, $CHCl_3$). TLC: Rf = 0.1 (PE/EA = 4/1, v/v).

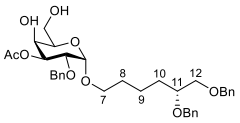
(*R*)-5,6-bis(benzyloxy)hexyl 3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylidene-α-D-galactopyranoside (30a)



Known compound donor **28** (1.06 g, 1.7 mmol, 1.0 eq) and the linker acceptor **29** (1.07 g, 3.4 mmol, 2.0 eq) were co-evaporated with anhydrous toluene three times under nitrogen. Dry DCM (17 mL) and 4Å molecular sieves were added and then the solution stirred for 20 minutes at RT. The reaction was cooled to 0 °C and *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (80 µL, 0.34 mmol, 0.2 eq) was added. After stirred for 2 hours and TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The solution was washed with water (2x) and brine. The aqueous layer was extracted with DCM (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 15:1 - 8:1) to yield compound **30a** (1.13 g, 1.59 mmol, 94%). ^{1}H

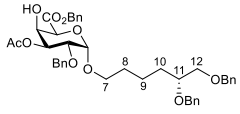
NMR (500 MHz, Chloroform-*d*) δ 7.37 – 7.22 (m, 15H), 5.05 (dd, *J* = 10.4, 3.1 Hz, 1H, H-3), 4.78 – 4.63 (m, 4H, H-1, H-4, CH_2), 4.59 (d, *J* = 12.1 Hz, 1H, CH_2), 4.56 – 4.50 (m, 3H, CH_2), 4.15 (dd, *J* = 12.5, 2.2 Hz, 1H, H-6), 4.05 (dd, *J* = 12.6, 1.8 Hz, 1H, H-6), 4.00 (dd, *J* = 10.4, 3.6 Hz, 1H, H-2), 3.73 – 3.65 (m, 1H, H-5), 3.63 – 3.46 (m, 4H, H-7, H-11, H-12), 3.43 – 3.31 (m, 1H, H-7), 2.09 (s, 3H, OAc), 1.64 – 1.29 (m, H-8, H-9, H-10), 0.98 (d, *J* = 4.4 Hz, 18H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.77 (OAc), 139.01, 138.53, 138.38, 128.50, 128.48, 128.42, 128.22, 127.94, 127.92, 127.88, 127.72, 127.67, 127.60, 127.58, 97.84 (C-1), 78.17 (C-11), 73.45, 73.23, 72.94 (C-12), 72.91 (C-3), 72.72 (C-2), 72.18, 71.05 (C-4), 68.24 (C-7), 67.14 (C-6), 66.82 (C-5), 31.87, 29.57, 27.68, 27.35, 23.36, 22.15, 21.16 (OAc), 20.74. HR-MS: Calculated for $C_{43}H_{60}O_9Si$ [M+Na^+]: 771.3899, found: 771.3927. $[\alpha]^{20}_D$ = + 92.4º (c = 1, $CHCl_3$). TLC: Rf = 0.4 (PE/EA = 9/1, v/v).

(*R*)-5,6-bis(benzyloxy)hexyl 3-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranoside (30)



Compound **30a** (166 mg, 0.235 mmol, 1.0 eq) was dissolved in THF (2 mL) and pyridine (2 mL), then cooled to 0 ℃ and hydrogen fluoride (HF)/pyridine (70%) (0.2 mL) was added dropwise. The solution was stirred for overnight. After TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate slowly and diluted with EtOAc. The solution was washed with water (2x) and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 2:1 - 1:2) to yield compound **30** (120 mg, 0.2 mmol, 84%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.19 (m, 15H), 5.17 (dd, *J* = 10.4, 3.2 Hz, 1H, H-3), 4.79 (d, *J* = 3.7 Hz, 1H, H-1), 4.71 – 4.61 (m, 2H, CH_2), 4.60 – 4.45 (m, 4H, CH_2), 4.02 (d, *J* = 3.2 Hz, 1H, H-4), 3.92 (dd, *J* = 10.5, 3.7 Hz, 1H, H-2), 3.83 – 3.73 (m, 1H, H-5), 3.71 – 3.61 (m, 2H, H-6, H-7), 3.61 – 3.46 (m, 4H, H-11, H-6, H-12), 3.42 – 3.31 (m, 1H, H-7), 3.15 (s, 1H, 4-OH), 3.02 (s, 1H, 6-OH), 2.12 – 2.03 (m, 3H, OAc), 1.78 – 1.33 (m, 6H, H-8, H-9, H-10). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.34 (OAc), 138.54, 138.34, 138.27, 128.42, 128.39, 128.09, 127.79, 127.71, 127.69, 127.66, 127.63, 97.38 (C-1, J_{CH} = 167.0 Hz), 78.43 (C-11), 73.72 (C-2), 73.35, 72.91, 72.73 (C-12), 72.38, 72.29 (C-3), 69.23 (C-4), 69.05 (C-5), 67.65 (C-7), 62.75 (C-6), 31.46 (C-10), 29.21 (C-8), 21.94 (C-9), 21.12 (OAc). HR-MS: Calculated for $C_{35}H_{44}O_9$ [M+Na^+]: 631.2878, found: 631.2892. $[\alpha]^{20}_D$ = + 208.1º (c = 1, $CHCl_3$). TLC: Rf = 0.15 (PE/EA = 1/1, v/v).

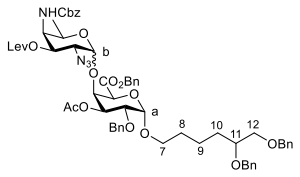
Benzyl (*R*)-5,6-bis(benzyloxy)hexyl 3-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranosyl uronate (31)



Compound **30** (116 mg, 0.19 mmol, 1.0 eq) was dissolved in DCM/*tert*-BuOH/H_2O (4.5 mL, 4/4/1, v/v/v). The mixture was cooled to 0 ℃ and treated with TEMPO (6.0 mg, 0.04 mmol, 0.2 eq) and BAIB (158 mg, 0.48 mmol, 2.5 eq). After stirring for overnight at 4 ℃ and TLC showed complete consumption of the starting material, saturated aqueous sodium thiosulphate was added and diluted with EtOAc, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was dissolved in DMF (4 mL), followed by addition of Cs_2CO_3 (62 g, 0.19 mmol, 1.0 eq) and BnBr (65 µL, 0.38 mmol, 2.0 eq) at 0℃. The mixture was allowed to stir overnight at rt, and then diluted with EtOAc, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*.

Purification by column chromatography (PE/EA 7/3) yielded **31** (130 mg, 0.18 mmol, 96%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.20 (m, 20H), 5.31 – 5.14 (m, 3H, H-3, CO_2Bn), 4.89 (d, *J* = 3.6 Hz, 1H, H-1), 4.66 (dd, *J* = 12.0, 2.1 Hz, 2H, CH_2), 4.58 – 4.48 (m, 5H, CH_2, H-5), 4.48 – 4.41 (m, 1H, H-4), 3.92 (dd, *J* = 10.5, 3.5 Hz, 1H, H-2), 3.71 – 3.32 (m, 5H, H-7, H-11, H-12), 2.49 – 2.35 (m, 1H, 4-OH), 2.07 (s, 3H, OAc), 1.65 – 1.30 (m, 6H, H-8, H-9, H-10). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.13 (OAc), 168.39 (CO_2Bn), 138.87, 138.40, 138.10, 135.13, 128.63, 128.49, 128.47, 128.38, 128.32, 127.95, 127.85, 127.82, 127.63, 127.58, 127.49, 97.62 (C-1, J_{CH} = 170.0 Hz), 77.88 (C-11), 73.33, 73.09, 73.06 (C-2), 72.75 (C-12), 72.01, 71.38 (C-3), 69.80 (C-5), 69.04 (C-4), 68.96 (C-7), 67.22 (C-6), 31.72 (C-10), 29.37 (C-8), 21.92 (C-9), 21.05 (OAc). HR-MS: Calculated for $C_{42}H_{48}O_{10}$ [M+Na$^+$]: 735.3140, found: 735.3161. $[\alpha]^{20}_{D}$ = + 35.8° (c = 1, $CHCl_3$). TLC: Rf = 0.2 (PE/EA = 7/3, v/v).

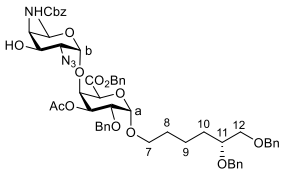
Benzyl ((*R*)-5,6-bis(benzyloxy)hexyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-azido-3-*O*-levulinoyl-4-*N*-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl uronate) (32)



Known compound donor *N*-phenyl-trifluoroacetimidate 2-azido-3-*O*-levulinoyl-4-*N*-benzyloxycarbonyl-6-deoxy-α/β-D-galactopyranoside **8**[8g] (430 mg, 0.73 mmol, 2.5 eq) and the acceptor **31** (210 mg, 0.30 mmol, 1.0 eq) were co-evaporated with anhydrous toluene three times under nitrogen. Dry DCM (5 mL) and 4Å molecular sieves were added and then the solution stirred for 20 minutes at RT. The reaction was cooled to 0 °C and *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (7 µL, 0.03 mmol, 0.1 eq) was added. After stirred for 5 hours and TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The solution was washed with water (2x) and brine. The aqueous layer was extracted with DCM (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 4:1 - 3:2) to yield 9:1 ratio of α/β mixed compound **32** (275.5 mg, 0.25 mmol, 83%). **α anomer 32**: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.18 (m, 25H), 5.32 – 4.95 (m, 8H, H-1a, H-3a, H-3b, NHCbz, CH_2), 4.70 – 4.43 (m, 9H, H-1b, H-5b, H-4a, H-5a, CH_2), 4.23 – 4.07 (m, 2H, H-4b, H-5b), 3.91 (dd, *J* = 10.8, 3.5 Hz, 1H, H-2a), 3.69 – 3.36 (m, 5H, H-7, H-11, H-12), 3.20 (dd, *J* = 11.3, 3.9 Hz, 1H, H-2b), 2.84 – 2.36 (m, 4H, Lev), 2.14 (s, 3H, Lev), 2.00 (s, 3H, OAc), 1.62 – 1.28 (m, 6H), 1.05 (d, *J* = 6.3 Hz, 3H, H-6b). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.16 (Lev), 171.80 (Lev), 170.01 (OAc), 167.70 (CO_2Bn), 156.49 (Cbz), 138.75, 138.27, 137.60, 136.24, 134.67, 128.65, 128.55, 128.49, 128.44, 128.37, 128.29, 128.24, 128.19, 128.17, 127.92, 127.83, 127.71, 127.67, 127.48, 127.43, 127.34, 98.18 (C-1b, J_{CH} = 172.5 Hz), 97.03 (C-1a, J_{CH} = 170.0 Hz), 77.69 (C-11), 76.49 (C-4a), 73.15, 72.83, 72.60 (*C*H$_2$), 72.53 (C-2a), 71.84 (*C*H$_2$), 70.22 (C-3a), 70.07 (C-3b), 69.28 (C-5a), 68.76 (C-7), 67.27 (CO_2Bn), 66.92 (Cbz), 64.64 (C-5b), 57.45 (C-2b), 52.35 (C-4b), 37.79, 31.51, 29.64, 29.20, 27.84, 21.74, 21.16, 16.53 (C-6b). HR-MS: Calculated for $C_{61}H_{70}N_4O_{16}$ [M+Na$^+$]: 1137.4679, found: 1137.4712. $[\alpha]^{20}_{D}$ = + 116.0° (c = 1, $CHCl_3$). TLC: Rf = 0.4 (PE/EA = 3/2, v/v). **β anomer:** ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.19 (m, 25H), 5.32 (d, *J* = 12.6 Hz, 1H, CH_2), 5.22 (dd, *J* = 10.5, 3.1 Hz, 1H, H-3a), 5.15 (d, *J* = 12.3 Hz, 1H, CH_2), 5.09 – 4.93 (m, 3H, CH_2), 4.79 (d, *J* = 3.7 Hz, 1H, H-1a), 4.75 – 4.63 (m, 2H, CH_2), 4.60 – 4.47 (m, 7H, H-4a, H-3b, H-5a, CH_2), 4.19 (d, *J* = 8.0 Hz, 1H, H-1b), 4.11 (dd, *J* = 10.4, 3.7 Hz, 1H, H-2a), 4.02 (dd, *J* = 10.2, 4.0 Hz, 1H, H-4b), 3.63 – 3.45 (m, 6H, H-5b,

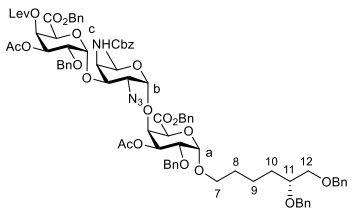
H-7, H-11, H-12, H-2b), 3.38 – 3.28 (m, 1H, H-7), 2.81 – 2.70 (m, 1H, Lev), 2.65 – 2.53 (m, 2H, Lev), 2.41 – 2.31 (m, 1H, Lev), 2.15 (d, *J* = 16.3 Hz, 6H, Lev), 1.62 – 1.25 (m, 6H, Lev, OAc), 1.10 (d, *J* = 6.3 Hz, 3H, H-6b). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.60 (Lev), 172.17 (Lev), 170.82 (OAc), 167.53 (CO_2Bn), 156.67 (Cbz), 138.96, 138.49, 138.37, 136.47, 135.07, 128.77, 128.67, 128.56, 128.54, 128.47, 128.40, 128.32, 128.04, 128.03, 127.97, 127.94, 127.91, 127.84, 127.73, 127.67, 127.58, 103.44 (C-1b, J_{CH} = 163.7 Hz), 97.93 (C-1a), 77.96 (C-11), 77.29 (C-4a), 73.67 (C-2a), 73.61, 73.43, 72.93 (C-3b), 72.85 (C-12), 72.12, 71.61 (C-3a), 69.58 (C-5b), 69.35 (C-5a), 69.25 (C-7), 67.15 (Bn), 67.12 (Bn), 61.40 (C-2b), 51.73 (C-4b), 37.90 (Lev), 31.84, 29.93 (Lev), 29.44, 27.92 (Lev), 21.97, 21.00 (OAc), 16.82 (C-6b). $[\alpha]^{20}_D$ = + 38.2º (c = 1, $CHCl_3$).

Benzyl ((*R*)-5,6-bis(benzyloxy)hexyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-azido-4-*N*-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl uronate) (33)



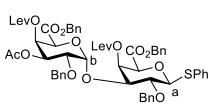
Compound **32** (234 mg, 0.21 mmol, 1.0 eq) was dissolved in pyridine (4 mL) and acetic acid (1 mL). After cooled to 0 °C, hydrazine hydrate (N_2H_4 • H_2O 50-60 %) (31 µL, 0.64 mmol, 3.0 eq) was added slowly. After stirred 20 min at RT, checked by TLC complete consumption of the starting material, quenched by acetone. The solution was washed with water (2x) and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 5:1 - 2:1) to yield compound **33** (196 mg, 0.19 mmol, 92%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.19 (m, 25H), 5.28 – 5.19 (m, 2H, H-3a, CH_2), 5.19 – 5.03 (m, 4H, CH_2), 5.00 (d, *J* = 3.7 Hz, 1H, H-1a), 4.70 – 4.44 (m, 9H, CH_2, H-1b, H-4a, H-5a), 4.16 – 4.03 (m, 2H, H-3b, H-5b), 4.01 – 3.92 (m, 1H, H-4b), 3.88 (dd, *J* = 10.7, 3.7 Hz, 1H, H-2a), 3.70 – 3.59 (m, 1H, H-7), 3.59 – 3.30 (m, 5H, H-7, H-11, H-12, 3b-OH), 3.02 (dd, *J* = 10.7, 3.9 Hz, 1H, H-2b), 2.03 (s, 3H, OAc), 1.63 – 1.28 (m, 6H, H-8, H-9, H-10), 1.08 (d, *J* = 6.4 Hz, 3H, H-6b). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.19 (OAc), 167.76 (CO_2Bn), 158.05 (Cbz), 138.86, 138.38, 137.80, 135.92, 134.81, 128.70, 128.63, 128.61, 128.52, 128.38, 128.36, 128.34, 128.30, 128.27, 128.15, 128.13, 127.99, 127.81, 127.77, 127.59, 127.53, 127.44, 98.75 (C-1b), 97.14 (C-1a), 77.84 (C-11), 76.89 (C-4a), 73.28, 72.73, 72.62 (C-2a), 71.96, 71.91, 70.61 (C-3a), 69.46 (C-5a), 68.90 (C-7), 68.36 (C-5b), 67.50 (Cbz), 67.42 (CO_2Bn), 65.19 (C-3b), 60.60 (C-2b), 55.78 (C-4b), 31.65, 29.33, 21.85, 21.27, 16.78 (C-6b). HR-MS: Calculated for $C_{56}H_{64}N_4O_{14}$ $[M+Na]^+$: 1039.4311, found: 1039.4344. $[\alpha]^{20}_D$ = + 98.8º (c = 1, $CHCl_3$). TLC: Rf = 0.2 (Tol/EA = 8/2, v/v).

Benzyl ((*R*)-5,6-bis(benzyloxy)hexyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-azido-3-O-(Benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-levulinoyl-α-D-galactopyranosyl urinate)-4-*N*-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl uronate) (34)



Donor **9** (111.3 mg, 0.162 mmol, 3.0 eq) and acceptor **33** (55.8 mg, 55 µmol, 1.0 eq) were co-evaporated with anhydrous toluene three times under nitrogen. Dry DCM (1 mL) and 5Å molecular sieves were added and then the solution stirred for 20 minutes at RT. The reaction was cooled to 0 °C and Trifluoromethanesulfonic acid (TfOH) (2.0 µL, 0.02 mmol, 0.4 eq) was added. After stirred for 5 hours and TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The solution was washed with water (2x) and brine. The aqueous layer was extracted with DCM (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 3:1 – 1:1) to yield desired α anomer compound **34** (46 mg, 30.4 µmol, 55%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.17 (m, 35H), 5.83 – 5.77 (m, 1H, H-4c), 5.48 (d, *J* = 3.5 Hz, 1H, H-1c), 5.41 (dd, *J* = 10.7, 3.4 Hz, 1H, H-3c), 5.34 (d, *J* = 11.9 Hz, 1H, CO_2Bn), 5.28 – 5.19 (m, 2H, CH_2, H-3a), 5.12 – 5.03 (m, 2H, CH_2), 5.02 – 4.95 (m, 2H, CH_2), 4.92 (d, *J* = 3.6 Hz, 1H, H-1a), 4.79 (d, *J* = 1.8 Hz, 1H, H-5c), 4.75 – 4.44 (m, 12H, CH_2, H-1b, H-4a, H-5a), 4.31 – 4.20 (m, 1H, H-4b), 4.14 (dd, *J* = 10.5, 4.2 Hz, 1H, H-3b), 4.09 – 4.01 (m, 1H, H-5b), 3.90 – 3.81 (m, 2H, H-2a, H-2c), 3.77 – 3.43 (m, 4H, H-7, H-11, H-12), 3.43 – 3.32 (m, 1H, H-7), 3.12 (dd, *J* = 10.5, 3.9 Hz, 1H, H-2b), 2.60 – 2.29 (m, 4H, Lev), 2.12 (s, 3H, Lev), 2.04 (s, 3H, OAc), 1.85 (s, 3H, OAc), 1.62 – 1.28 (m, 6H, H-8, H-9, H-10), 1.05 (d, *J* = 6.5 Hz, 3H, H-6b). ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.99 (Lev), 171.26 (Lev), 170.32 (OAc), 169.97 (OAc), 167.76 (CO_2Bn), 166.88 (CO_2Bn), 156.87 (Cbz), 138.96, 138.49, 138.09, 137.98, 136.15, 135.08, 134.78, 129.30, 128.90, 128.83, 128.73, 128.67, 128.61, 128.58, 128.53, 128.46, 128.42, 128.40, 128.29, 128.26, 128.02, 127.93, 127.90, 127.81, 127.71, 127.66, 127.57, 97.61 (C-1b, J_{CH} = 172.0 Hz), 97.33 (C-1a, J_{CH} = 171.0 Hz), 93.98 (C-1c, J_{CH} = 171.0 Hz), 77.98 (C-11), 76.19 (C-4a), 73.42, 73.27 (C-2a), 73.21, 73.09, 72.87 (C-12), 72.11, 71.82 (C-2c), 70.47 (C-3a), 69.66 (C-4c), 69.37 (C-5a), 69.11 (C-5c), 69.01 (C-7), 68.83 (C-3c), 67.57 (6c-CO_2Bn), 67.48 (6a-CO_2Bn), 67.07 (Cbz), 65.82 (C-5b), 59.63 (C-2b), 50.56 (C-4b), 37.65 (Lev), 31.80, 29.89 (Lev), 29.46, 27.56 (Lev), 22.00, 21.36 (OAc), 20.68 (OAc), 16.57 (C-6b). HR-MS: Calculated for $C_{83}H_{92}N_4O_{23}$ [M+Na$^+$]: 1535.6045, found: 1535.6095. $[\alpha]^{20}_D$ = + 97.1° (c = 1, $CHCl_3$). TLC: Rf = 0.4 (PE/EA = 3/2, v/v).

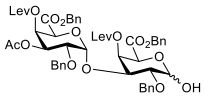
Benzyl (Phenyl 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-levulinoyl-α-D-galactopyranosyl urinate)-4-*O*-levulinoyl-1-thio-β-D-galactopyranosyl uronate) (26)



Donor **9** (572.3 mg, 0.84 mmol, 2.2 eq) and acceptor **10** (211 mg, 0.37 mmol, 1.0 eq) were co-evaporated with anhydrous toluene three times under nitrogen. Dry DCM (5 mL) and 5Å molecular sieves were added and then the solution stirred for 20 minutes at RT. The reaction was cooled to 0 °C and Trifluoromethanesulfonic acid (TfOH) (13 µL, 0.15 mmol, 0.4 eq) was added. After stirred 2 hours and TLC showed complete consumption of the starting material, the reaction was

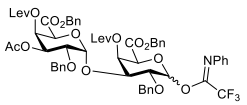
quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The solution was washed with water (2x) and brine. The aqueous layer was extracted with DCM (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 4:1 - 3:2) to yield compound **26** (136 mg, 0.13 mmol, 34%) and SPh transferred byproduct **9e**[19] (140 mg, 0.23 mmol, 62%). **26**: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.72 – 7.67 (m, 2H), 7.51 – 7.47 (m, 2H), 7.42 – 7.20 (m, 18H), 7.18 – 7.13 (m, 2H), 7.13 – 7.08 (m, 1H), 5.89 – 5.83 (m, 1H, H-4a), 5.49 – 5.44 (m, 1H, H-4b), 5.41 – 5.34 (m, 2H, H-3b, H-1b), 5.27 (d, *J* = 12.0 Hz, 1H, CH_2), 5.18 – 5.04 (m, 3H, CH_2), 4.75 – 4.66 (m, 2H, H-5b, CH_2), 4.65 – 4.59 (m, 2H, CH_2, H-1a), 4.57 – 4.48 (m, 2H, CH_2), 4.21 (d, *J* = 1.3 Hz, 1H, H-5a), 3.97 (dd, *J* = 9.5, 3.2 Hz, 1H, H-3a), 3.79 (dd, *J* = 10.5, 3.3 Hz, 1H, H-2b), 3.70 (t, *J* = 9.5 Hz, 1H, H-2a), 2.51 – 2.20 (m, 8H, Lev), 2.10 (s, 3H, Lev), 2.02 (s, 3H, Lev), 1.93 (s, 3H, OAc). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.04 (Lev), 205.95 (Lev), 171.42 (Lev), 171.28 (Lev), 170.20 (OAc), 166.76 (6b-CO_2Bn), 166.08 (6a-CO_2Bn), 138.02, 137.15, 135.19, 135.05, 133.18, 132.53, 129.02, 128.98, 128.81, 128.69, 128.64, 128.61, 128.58, 128.46, 128.40, 128.37, 128.23, 128.21, 127.81, 127.69, 93.14 (C-1b, J_{CH} = 174.0 Hz), 87.43 (C-1a, J_{CH} = 157.0 Hz), 76.32, 75.64 (C-5a), 75.26 (C-2a), 74.54 (C-3a), 73.65, 72.60 (C-2b), 69.41 (C-4b), 68.89 (C-3b), 68.39 (C-5b), 67.70, 67.09, 66.04 (C-4a), 37.76, 37.56, 29.83, 29.68, 27.90, 27.48, 20.73. HR-MS: Calculated for $C_{58}H_{60}O_{17}S$ [M+Na$^+$]: 1083.3443, found: 1083.3462. $[\alpha]^{20}_D$ = + 77.1° (c = 1, $CHCl_3$). TLC: Rf = 0.4 (PE/EA = 3/2, v/v).

Benzyl (2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-levulinoyl-α-D-galactopyranosyl urinate)-4-*O*-levulinoyl-α/β-D-galactopyranosyl uronate) (27a)



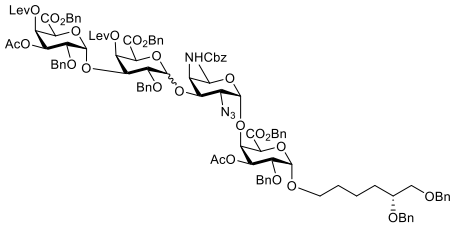
Compound **26** (112 mg, 0.11 mmol, 1.0 eq) was dissolved in DCM (4 mL) and reduced to 0 °C. NIS (26 mg, 0.12 mmol, 1.1 eq) and TFA (9.0 µL, 0.13 mmol, 1.1 eq) were added and the solution stirred for 2 hours. After analysis by TLC showed complete consumption of the starting material, the reaction was quenched with triethyl amine and saturated aqueous sodium thiosulphate. The solution was diluted with DCM and washed with brine (3x). The organic phase was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 3:1 - 3:2) to yield α/β mixed compound **27a** (92 mg, 0.095 mmol, 90%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.45 – 7.07 (m, 20H), 5.89 – 5.75 (m, 1H), 5.58 – 5.48 (m, 1H), 5.46 – 5.37 (m, 1H), 5.37 – 5.30 (m, 1H), 5.25 – 5.00 (m, 4H), 4.92 (dd, *J* = 44.2, 1.8 Hz, 1H), 4.78 – 4.45 (m, 6H), 4.30 (dd, *J* = 10.1, 3.5 Hz, 1H), 4.18 – 4.06 (m, 1H), 3.95 – 3.74 (m, 2H), 2.56 – 2.03 (m, 11H), 1.95 (dd, *J* = 24.8, 6.2 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.53, 206.26, 206.08, 206.05, 171.40, 171.38, 171.33, 171.29, 170.23, 170.15, 167.57, 166.98, 166.78, 138.19, 138.13, 137.53, 137.02, 128.95, 128.92, 128.89, 128.72, 128.65, 128.59, 128.56, 128.50, 128.45, 128.42, 128.40, 128.34, 128.31, 128.28, 127.69, 127.58, 127.56, 97.87, 93.59, 93.26, 91.06, 78.49, 75.90, 74.77, 73.58, 73.56, 73.13, 72.93, 72.86, 72.58, 72.29, 69.58, 69.50, 68.93, 68.82, 68.66, 68.51, 68.29, 67.81, 67.63, 67.07, 65.92, 37.74, 37.73, 37.55, 29.78, 29.77, 29.58, 29.52, 27.88, 27.49, 27.47, 20.69. HR-MS: Calculated for $C_{52}H_{56}O_{18}$ [M+Na$^+$]: 991.33589, found: 991.33578. TLC: Rf = 0.15 (PE/EA = 3/2, v/v).

Benzyl (*N*-phenyl-trifluoroacetimidate 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-levulinoyl-α-D-galactopyranosyl urinate)-4-*O*-levulinoyl-α/β-D-galactopyranosyl uronate) (27)



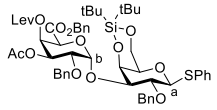
Hemiacetal **27a** (92 mg, 0.095 mmol, 1.0 eq) was dissolved in acetone (3 mL) and cooled to 0 ℃. Cesium carbonate (34 mg, 0.104 mmol, 1.1 eq) was added. After 15 min, *N*-phenyl trifluoroacetimidoyl chloride (30 mg, 0.14 mmol, 1.5 eq) was added, and then the reaction was allowed to stir for overnight at RT. After analysis by TLC showed complete consumption of the starting material, quenched by triethyl amine, filtered and concentrated *in vacuo*, and the product purified by column chromatography (PE/EA 5:1 – 2:1) to yield compound **27** (99 mg, 0.09 mmol, 91%). The crude compound was used for the further reaction without any purification. TLC: Rf = 0.5 (PE/EA = 3/2, v/v).

Benzyl ((*R*)-5,6-bis(benzyloxy)hexyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-azido-3-O-(Benzyl 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-levulinoyl-α-D-galactopyranosyl urinate)-4-*O*-levulinoyl-α/β-D-galactopyranosyl urinate)-4-*N*-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl uronate) (35)



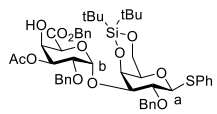
Donor **27** (60.0 mg, 52.6 µmol, 1.9 eq) and acceptor **33** (27.8 mg, 27.3 µmol, 1.0 eq) were co-evaporated with anhydrous toluene three times under nitrogen. Dry DCM (1 mL) and 5Å molecular sieves were added and then the solution stirred for 20 minutes at RT. The reaction was cooled to 0 ℃ and Trifluoromethanesulfonic acid (TfOH) (1.0 µL, 0.01 mmol, 0.4 eq) was added. After stirred 5 hours and TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The solution was washed with water (2x) and brine. The aqueous layer was extracted with DCM (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 3:1 - 3:2) to yield 2:1 ratio of α/β mixed compound **35** (28 mg, 14.2 µmol, 52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.15 (m, 45H), 5.95 – 5.78 (m, 1H), 5.68 – 5.50 (m, 1H), 5.45 – 4.41 (m, 23H), 4.39 – 3.96 (m, 5H), 3.94 – 3.44 (m, 12H), 3.44 – 3.32 (m, 1H), 3.17 – 2.98 (m, 1H), 2.54 – 2.16 (m, 8H), 2.10 (d, *J* = 6.2 Hz, 3H), 2.04 (d, *J* = 5.3 Hz, 3H), 1.98 – 1.86 (m, 6H), 1.63 – 1.31 (m, 6H), 1.09 – 1.00 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.20, 206.03, 205.99, 171.34, 171.32, 171.18, 170.39, 170.12, 170.03, 167.87, 167.75, 167.05, 167.02, 166.88, 165.92, 156.92, 156.43, 138.98, 138.51, 138.32, 138.06, 138.01, 137.39, 135.99, 135.50, 135.34, 135.25, 135.12, 134.91, 129.11, 129.04, 129.03, 128.93, 128.81, 128.76, 128.72, 128.71, 128.64, 128.59, 128.55, 128.49, 128.47, 128.45, 128.40, 128.38, 128.36, 128.25, 128.20, 128.16, 128.09, 128.03, 128.02, 127.97, 127.94, 127.72, 127.67, 127.59, 127.58, 102.08, 98.46, 97.90, 97.45, 97.31, 93.45, 93.32, 78.00, 76.66, 73.71, 73.52, 73.44, 73.38, 73.33, 73.19, 73.00, 72.90, 72.74, 72.61, 72.54, 72.12, 72.08, 71.39, 70.62, 70.59, 70.30, 69.70, 69.59, 69.50, 69.42, 69.37, 69.05, 68.82, 68.62, 67.83, 67.61, 67.52, 67.41, 67.24, 67.01, 66.96, 66.89, 61.99, 60.66, 59.94, 50.60, 37.81, 37.67, 37.64, 31.82, 31.77, 29.86, 29.61, 29.48, 27.98, 27.59, 27.55, 22.01, 21.39, 21.37, 20.79, 20.77, 19.37, 16.58, 14.02. HR-MS: Calculated for $C_{108}H_{118}N_4O_{31}$ [M+Na^+]: 1989.7672, found: 1989.7719. TLC: Rf = 0.2 (PE/EA = 3/2, v/v).

Phenyl 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-levulinoyl-α-D-galactopyranosyl urinate)-4,6-*O*-di-*tert*-butylsilylidene-1-thio-β-D-galactopyranoside (36)



The donor **9** (3.1 g, 4.52 mmol, 1.1 eq) and the acceptor **11** (2.0 g, 3.98 mmol, 1.0 eq) were co-evaporated with anhydrous toluene three times under nitrogen. Dry DCM (35 mL) and 5Å molecular sieves were added and then the solution stirred for 20 minutes at RT. The reaction was cooled to -70 °C and *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (182 µL, 0.79 mmol, 0.2 eq) was added. After stirred overnight and TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The solution was washed with water (2x) and brine. The aqueous layer was extracted with DCM (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 5:1 - 3:1) to yield compound **36** (3.0 mg, 3.0 mmol, 75%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.59 – 7.48 (m, 4H), 7.35 – 7.23 (m, 13H), 7.22 – 7.17 (m, 2H), 7.17 – 7.10 (m, 1H), 5.63 – 5.58 (m, 1H, H-4b), 5.56 (dd, *J* = 10.5, 3.4 Hz, 1H, H-3b), 5.47 (d, *J* = 3.4 Hz, 1H, H-1b), 5.14 (d, *J* = 12.0 Hz, 1H, C*H*$_2$), 5.06 (d, *J* = 9.7 Hz, 1H, C*H*$_2$), 4.83 – 4.71 (m, 4H, H-5b, C*H*$_2$), 4.70 – 4.65 (m, 2H, H-1a, H-4a), 4.62 (d, *J* = 12.0 Hz, 1H, C*H*$_2$), 4.26 – 4.14 (m, 2H, H-6a), 3.96 (dd, *J* = 10.5, 3.3 Hz, 1H, H-2b), 3.89 (t, *J* = 9.5 Hz, 1H, H-2a), 3.71 (dd, *J* = 9.4, 2.9 Hz, 1H, H-3a), 3.32 (d, *J* = 2.3 Hz, 1H, H-5a), 2.55 – 2.32 (m, 3H, Lev), 2.16 – 2.07 (m, 4H, Lev), 1.94 (s, 3H, OAc), 1.09 (s, 9H), 1.02 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.87 (Lev), 171.29 (Lev), 170.06 (OAc), 166.91 (CO_2Bn), 137.83, 137.52, 134.99, 131.97, 128.97, 128.88, 128.73, 128.56, 128.45, 128.39, 128.32, 128.01, 127.73, 127.67, 127.45, 92.87 (C-1b, J_{CH} = 171.0 Hz), 88.89 (C-1a, J_{CH} = 157.2 Hz), 77.82 (C-3a), 76.39, 76.08 (C-2a), 74.54 (C-5a), 72.08, 71.90 (C-2b), 69.47 (C-4b), 69.03 (C-3b), 68.55 (C-5b), 68.18 (C-4a), 67.33, 67.18, 37.56, 29.78, 27.73, 27.69, 27.65, 27.49, 23.34, 20.69 (OAc). HR-MS: Calculated for $C_{54}H_{66}O_{14}SSi$ [M+Na$^+$]: 1021.3835, found: 1021.3843. $[\alpha]^{20}_D$ = + 94.3° (c = 1, $CHCl_3$). TLC: Rf = 0.3 (PE/EA = 7/3, v/v).

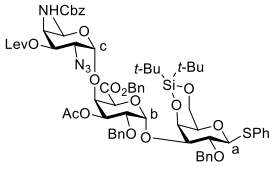
Phenyl 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranosyl urinate)-4,6-*O*-di-*tert*-butylsilylidene-1-thio-β-D-galactopyranoside (37)



The compound **36** (3.0 g, 3.0 mmol, 1.0 eq) was dissolved in THF (30 mL), MeOH (3 mL) and acetic acid (3 mL). After cooled to 0 °C, hydrazine acetate (N_2H_4 • AcOH) (830 mg, 9.01 mmol, 3.0 eq) was added. After stirred 2 hours at RT, checked by TLC complete consumption of the starting material, the reaction was quenched by acetone. The solution was diluted by EtOAc and then washed with water (2x) and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA/DCM 10:1:1 – 5:1:1) to yield compound **37** (2.6 g, 2.89 mmol, 95%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 – 7.52 (m, 2H), 7.52 – 7.46 (m, 2H), 7.36 – 7.15 (m, 16H), 5.54 (d, *J* = 3.5 Hz, 1H, H-1b), 5.49 (dd, *J* = 10.4, 3.2 Hz, 1H, H-3b), 5.18 (d, *J* = 12.4 Hz, 1H, C*H*$_2$), 5.03 (d, *J* = 9.9 Hz, 1H, C*H*$_2$), 4.95 (d, *J* = 12.3 Hz, 1H, C*H*$_2$), 4.87 – 4.79 (m, 2H, C*H*$_2$), 4.75 – 4.65 (m, 3H, H-1a, H-4a, H-5b), 4.56 (d, *J* = 12.1 Hz, 1H, C*H*$_2$), 4.32 – 4.26 (m, 1H, H-4b), 4.26 – 4.14 (m, 2H, H-6a), 4.06 (dd, *J* = 10.4, 3.4 Hz, 1H, H-2b), 3.89 (t, *J* = 9.5 Hz, 1H, H-2a), 3.73 (dd, *J* = 9.3, 2.9 Hz, 1H, H-3a), 3.32 (d, *J* = 2.2 Hz, 1H, H-5a), 2.06 (s, 3H, OAc), 1.08 (s, 9H), 1.02 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.98

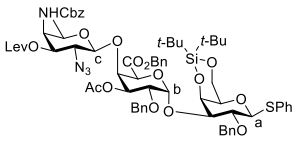
(OAc), 168.09 (CO_2Bn), 137.96, 137.79, 132.00, 129.08, 128.89, 128.62, 128.53, 128.46, 128.36, 128.27, 128.14, 127.87, 127.72, 127.49, 127.44, 125.35, 92.41 (C-1b, J_{CH} = 171.0 Hz), 88.83 (C-1a, J_{CH} = 157.0 Hz), 77.68 (C-3a), 76.28, 76.12 (C-2a), 74.50 (C-5a), 72.05 (C-2b), 71.72, 71.15 (C-3b), 69.90 (C-5b), 68.86 (C-4b), 68.21 (C-4a), 67.30 (C-6a), 67.00, 27.74, 27.65, 23.34, 21.03 (OAc), 20.71. HR-MS: Calculated for $C_{49}H_{60}O_{12}SSi$ [M+Na^+]: 923.3467, found: 923.3487. $[\alpha]^{20}_D$ = + 104.6º (c = 1, $CHCl_3$). TLC: Rf = 0.3 (PE/DCM/EA = 3/1/1, v/v/v).

Phenyl 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-azido-3-*O*-levulinoyl-4-*N*-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-4,6-*O*-di-*tert*-butylsilylidene-1-thio-β-D-galactopyranoside (38)



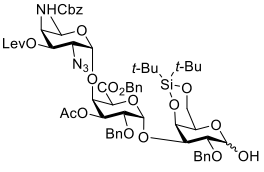
The donor **8**[8g] (1.6 g, 2.7 mmol, 1.5 eq) and the acceptor **37** (1.64 g, 1.82 mmol, 1.0 eq) were co-evaporated with anhydrous toluene three times under nitrogen. Dry DCM (18 mL) and 5Å molecular sieves were added and then the solution stirred for 20 minutes at RT. The reaction was cooled to 0 ºC and *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (84 µL, 0.37 mmol, 0.2 eq) was added. After stirred 2 hours and TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The solution was washed with water (2x) and brine. The aqueous layer was extracted with DCM (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA/DCM 5:1:1 - 3:1:1) to yield desired α anomer compound **38** (1.6 g, 1.23 mmol, 68%) and byproduct β anomer **38a** (332 mg, 0.25 mmol, 14%). α anomer **38**: ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.57 – 7.53 (m, 2H), 7.51 – 7.46 (m, 2H), 7.41 – 7.20 (m, 21H), 5.57 (d, *J* = 3.6 Hz, 1H, H-1b), 5.45 (dd, *J* = 10.7, 2.9 Hz, 1H, H-3b), 5.24 – 5.12 (m, 2H, CH_2), 5.09 – 4.97 (m, 3H, H-3c, CH_2), 4.89 – 4.79 (m, 4H, CH_2), 4.73 (d, *J* = 3.0 Hz, 1H, H-4a), 4.66 (d, *J* = 9.8 Hz, 1H, H-1a), 4.61 (s, 1H, H-5b), 4.54 (d, *J* = 3.9 Hz, 1H, H-1c), 4.49 (d, *J* = 11.9 Hz, 1H, CH_2), 4.38 (d, *J* = 2.9 Hz, 1H, H-4b), 4.26 – 4.16 (m, 2H, H-6a), 4.16 – 4.10 (m, 1H, H-4c), 4.08 – 4.00 (m, 2H, H-2b, H-5c), 3.89 (t, *J* = 9.6 Hz, 1H, H-2a), 3.73 (dd, *J* = 9.4, 2.9 Hz, 1H, H-3a), 3.29 (d, *J* = 2.2 Hz, 1H, H-5a), 3.11 (dd, *J* = 11.3, 3.9 Hz, 1H, H-2c), 2.84 – 2.37 (m, 4H, Lev), 2.17 (s, 3H, Lev), 1.99 (s, 3H, OAc), 1.06 (d, *J* = 21.5 Hz, 21H, H-6c). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.37 (Lev), 171.97 (Lev), 170.24 (OAc), 167.20 (CO_2Bn), 156.61 (Cbz), 137.86, 132.03, 128.91, 128.70, 128.67, 128.55, 128.50, 128.45, 128.44, 128.27, 128.10, 127.93, 127.47, 98.50 (C-1c, J_{CH} = 170.8 Hz), 91.85 (C-1b, J_{CH} = 171.5 Hz), 88.89 (C-1a, J_{CH} = 158.0 Hz), 77.61 (C-3a), 76.76 (C-4b), 76.25, 76.04 (C-2a), 74.56 (C-5a), 71.93, 71.72 (C-2b), 70.31 (C-3b), 70.19 (C-3c), 69.55 (C-5b), 68.08 (C-4a), 67.38, 67.29, 67.21, 64.80 (C-5c), 57.64 (C-2c), 52.53 (C-4c), 38.00, 29.87, 28.01, 27.78, 27.66, 23.35, 21.39 (OAc), 20.74, 16.74 (C-6c). HR-MS: Calculated for $C_{68}H_{82}N_4O_{18}SSi$ [M+Na^+]: 1325.50063, found: 1325.50063. $[\alpha]^{20}_D$ = + 122.2º (c = 1, $CHCl_3$). TLC: Rf = 0.3 (PE/EA/DCM = 3:1:1, v/v).

Phenyl 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-azido-3-*O*-levulinoyl-4-*N*-benzyloxycarbonyl-6-deoxy-β-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-4,6-*O*-di-*tert*-butylsilylidene-1-thio-β-D-galactopyranoside (38a)



β anomer **38a**: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 – 7.46 (m, 4H), 7.41 – 7.19 (m, 20H), 7.16 – 7.10 (m, 1H), 5.59 (d, *J* = 3.6 Hz, 1H, H-1b), 5.46 (dd, *J* = 10.3, 3.1 Hz, 1H, H-3b), 5.21 – 5.11 (m, 2H, C*H*$_2$), 5.11 – 4.99 (m, 2H, C*H*$_2$), 4.99 – 4.78 (m, 4H, C*H*$_2$), 4.78 – 4.48 (m, 6H, H-5b, H-4a, H-1a, H-3c, H-4b, C*H*$_2$), 4.28 (dd, *J* = 10.4, 3.5 Hz, 1H, H-2b), 4.25 – 4.13 (m, 3H, H-1c, H-6a), 4.09 – 3.98 (m, 1H, H-4c), 3.88 (t, *J* = 9.5 Hz, 1H, H-2a), 3.66 (dd, *J* = 9.3, 2.9 Hz, 1H, H-3a), 3.56 – 3.41 (m, 2H, H-5c, H-2c), 3.33 – 3.24 (m, 1H, H-5a), 2.84 – 2.28 (m, 4H), 2.15 (d, *J* = 2.0 Hz, 3H, Lev), 2.10 (s, 3H, OAc), 1.15 – 0.98 (m, 21H, H-6c). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.57 (Lev), 172.18 (Lev), 170.64 (OAc), 167.31 (CO_2Bn), 156.68 (Cbz), 138.14, 137.90, 135.04, 134.86, 132.14, 129.10, 128.94, 128.80, 128.75, 128.70, 128.66, 128.56, 128.54, 128.48, 128.43, 128.37, 128.06, 127.95, 127.78, 127.52, 127.47, 124.91, 103.15 (C-1c, J_{CH} = 163.8 Hz), 92.90 (C-1b, J_{CH} = 172.0 Hz), 88.84 (C-1a, J_{CH} = 157.0 Hz), 78.40 (C-3a), 76.86 (C-4b), 76.35, 76.16 (C-2a), 74.57 (C-5a), 73.10 (C-3c), 73.04 (C-2b), 72.27, 71.53 (C-3b), 69.90 (C-5b), 69.39 (C-5c), 68.54 (C-4a), 67.36, 67.16, 67.03, 61.43 (C-2c), 51.78 (C-4c), 37.92, 30.45, 29.83, 29.80, 27.84, 27.70, 23.45, 22.83, 21.00 (OAc), 20.78, 16.72 (C-6c). HR-MS: Calculated for $C_{68}H_{82}N_4O_{18}SSi$ [M+Na$^+$]: 1325.5006, found: 1325.5015. $[\alpha]^{20}_D$ = + 118.6º (c = 1, $CHCl_3$). TLC: Rf = 0.25 (PE/EA/DCM = 3:1:1, v/v).

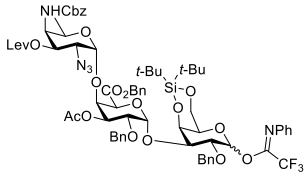
2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-azido-3-*O*-levulinoyl-4-*N*-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-4,6-*O*-di-*tert*-butylsilylidene-α/β-D-galactopyranoside (39)



The compound **38** (1.56 g, 1.2 mmol, 1.0 eq) was dissolved in DCM (15 mL) and reduced to 0 °C. NIS (405 mg, 1.8 mmol, 1.5 eq) and TFA (111 µL, 1.44 mmol, 1.2 eq) were added and the solution stirred for 2 hours. After analysis by TLC showed complete consumption of the starting material, the reaction was quenched with triethyl amine and saturated aqueous sodium thiosulphate. The solution was diluted with DCM and washed with brine (3x). The organic phase was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA 2:1 - 1:1) to yield compound **39** (1.38 g, 1.14 mmol, 95%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.45 – 7.15 (m, 20H), 5.57 – 5.50 (m, 1H), 5.50 – 5.39 (m, 1H), 5.31 – 5.21 (m, 1H), 5.21 – 5.13 (m, 2H), 5.10 – 4.96 (m, 3H), 4.94 – 4.84 (m, 1H), 4.84 – 4.75 (m, 2H), 4.74 – 4.61 (m, 4H), 4.56 – 4.43 (m, 2H), 4.24 – 4.08 (m, 4H), 4.07 – 3.94 (m, 3H), 3.88 – 3.65 (m, 1H), 3.20 – 3.08 (m, 1H), 3.04 (s, 1H), 2.86 – 2.37 (m, 4H), 2.21 – 2.14 (m, 3H), 2.02 – 1.95 (m, 3H), 1.08 – 0.88 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.50, 172.04, 170.25, 167.55, 167.39, 156.64, 138.14, 137.80, 137.71, 137.55, 136.32, 134.86, 134.83, 128.83, 128.75, 128.74, 128.72, 128.65, 128.58, 128.44, 128.43, 128.20, 128.16, 128.12, 128.10, 128.03, 127.96, 127.90, 127.84, 98.49, 98.46, 97.91, 92.16, 91.77, 77.97, 76.79, 76.76, 75.77, 75.52, 73.69, 73.61, 72.71, 72.09, 71.90, 71.82, 71.36, 70.31, 70.28, 70.21, 70.18, 69.74, 69.48, 69.24, 68.21, 67.42, 67.28, 67.22, 67.18,

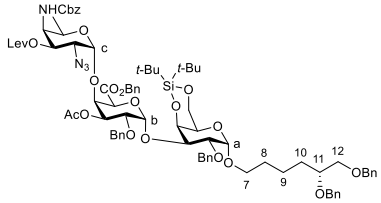
64.80, 57.66, 57.61, 52.54, 52.52, 38.01, 28.02, 27.75, 27.46, 27.29, 23.32, 21.38, 20.67, 16.74. HR-MS: Calculated for $C_{62}H_{78}N_4O_{19}Si$ [M+Na^+]: 1233.4922, found: 1233.4943. TLC: Rf = 0.2 (PE/EA/DCM = 1/1/1, v/v/v).

_N_-phenyl-trifluoroacetimidate 2-_O_-benzyl-3-_O_-(benzyl 3-_O_-acetyl-2-_O_-benzyl-4-_O_-(2-azido-3-_O_-levulinoyl-4-_N_-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-4,6-_O_-di-_tert_-butylsilylidene-α/β-D-galactopyranoside (7)



The hemiacetal **39** (1.53 g, 1.26 mmol, 1.0 eq) was dissolved in acetone (13 mL) and cooled to 0 ℃. Cesium carbonate (617 mg, 1.89 mmol, 1.5 eq) was added. After 15 min, N-phenyl trifluoroacetimidoyl chloride (524 mg, 2.5 mmol, 2.0 eq) was added, and then the reaction was allowed to stir for overnight at RT. After analysis by TLC showed complete consumption of the starting material, quenched by triethyl amine, filtered, and concentrated *in vacuo*, and the product purified by column chromatography (PE/EA 4:1 – 3/1) to yield compound **7** (1.64 mg, 1.19 mmol, 94%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.49 – 7.21 (m, 22H), 7.19 – 7.10 (m, 1H), 6.95 – 6.76 (m, 2H), 6.48 – 6.36 (m, 1H), 5.60 – 5.46 (m, 2H), 5.30 – 4.75 (m, 12H), 4.70 – 4.52 (m, 2H), 4.41 – 4.09 (m, 7H), 3.71 (dd, J = 11.5, 3.8 Hz, 1H), 2.87 – 2.33 (m, 4H), 2.16 – 2.12 (m, 3H), 2.09 (s, 3H), 1.20 – 1.13 (m, 3H), 1.12 – 0.92 (m, 18H). ^{13}C NMR (101 MHz, Acetone) δ 206.15, 206.04, 172.25, 170.63, 170.54, 168.33, 168.05, 157.75, 144.51, 144.30, 139.06, 139.01, 138.59, 138.57, 138.07, 136.18, 136.15, 129.53, 129.50, 129.35, 129.25, 129.18, 129.15, 129.11, 129.08, 129.03, 129.01, 128.94, 128.90, 128.86, 128.79, 128.74, 128.73, 128.67, 128.58, 128.46, 128.43, 128.31, 128.29, 125.06, 120.07, 119.93, 99.57, 99.49, 93.78, 93.68, 77.12, 76.84, 76.54, 75.86, 73.78, 73.33, 73.19, 73.03, 72.90, 72.63, 72.42, 72.40, 71.01, 70.97, 70.34, 70.23, 70.01, 69.97, 69.26, 67.57, 67.36, 67.22, 66.75, 65.78, 58.03, 57.99, 55.25, 53.49, 38.04, 29.78, 29.60, 28.58, 27.99, 27.79, 27.66, 23.64, 23.60, 21.36, 21.34, 21.14, 21.09, 17.01. HR-MS: Calculated for $C_{70}H_{82}F_3N_5O_{19}Si$ [M+Na^+]: 1404.5218, found: 1404.5259. TLC: Rf = 0.2 (PE/EA = 3/1, v/v).

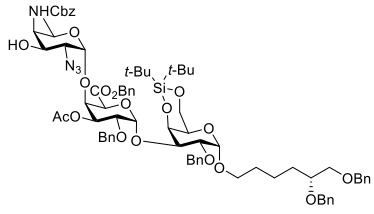
(_R_)-5,6-bis(benzyloxy)hexyl 2-_O_-benzyl-3-_O_-(benzyl 3-_O_-acetyl-2-_O_-benzyl-4-_O_-(2-azido-3-_O_-levulinoyl-4-_N_-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-4,6-_O_-di-_tert_-butylsilylidene-α-D-galactopyranoside (40)



Donor **7** (540 mg, 0.39 mmol, 1.0 eq) and the linker acceptor **29** (368 mg, 1.17 mmol, 3.0 eq) were co-evaporated with anhydrous toluene three times under nitrogen. Dry DCM (5 mL) and 4Å molecular sieves were added and then the solution stirred for 20 minutes at RT. The reaction was cooled to 0 ℃ and *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (18 μL, 0.08 mmol, 0.2 eq) was added. After stirred 2 hours and TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The solution was washed with water (2x) and brine. The aqueous layer was extracted with DCM (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA/DCM 8:1:1 - 4:1:1) to yield desired α anomer

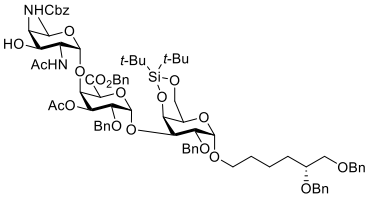
compound **40** (501 mg, 0.33 mmol, 85%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.45 – 7.17 (m, 30H), 5.59 (d, *J* = 3.5 Hz, 1H, H-1b), 5.51 (dd, *J* = 10.7, 2.9 Hz, 1H, H-3b), 5.31 – 5.23 (m, 1H, CH_2), 5.16 (d, *J* = 12.3 Hz, 1H, CH_2), 5.11 – 4.98 (m, 3H, H-3c, CH_2), 4.87 – 4.74 (m, 4H, CH_2, H-5b), 4.72 – 4.60 (m, 5H, CH_2, H-4a, H-1a, H-1c), 4.59 – 4.44 (m, 5H, CH_2, H-4b), 4.19 – 4.09 (m, 3H, CH_2, H-4c, H-5c), 4.09 – 3.99 (m, 3H, CH_2, H-3a, H-2b), 3.95 (dd, *J* = 10.2, 3.7 Hz, 1H, H-2a), 3.61 – 3.47 (m, 5H, H-5a, H-7, H-12, H-11), 3.43 – 3.35 (m, 1H, H-7), 3.16 – 3.10 (m, 1H, H-2c), 2.86 – 2.39 (m, 4H, Lev), 2.18 (s, 3H, Lev), 1.97 (s, 3H, OAc), 1.63 – 1.28 (m, 6H, H-8, H-9, H-10), 1.07 – 0.97 (m, 12H, H-6c), 0.87 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.48 (Lev), 172.09 (Lev), 170.21 (OAc), 167.62 (CO_2Bn), 156.67 (Cbz), 138.98, 138.50, 138.36, 138.06, 136.39, 134.94, 128.90, 128.75, 128.64, 128.59, 128.50, 128.48, 128.46, 128.42, 128.14, 127.92, 127.91, 127.88, 127.86, 127.84, 127.75, 127.72, 127.70, 127.64, 98.56 (C-1c, J_{CH} = 171.5 Hz), 97.65 (C-1a, J_{CH} = 167.6 Hz), 92.05 (C-1b, J_{CH} = 171.0 Hz), 78.23 (C-11), 77.04 (C-4b), 73.65, 73.45, 73.16 (C-2a), 73.00 (C-3a), 72.95 (C-12), 72.41 (C-2b), 72.24, 71.65, 70.26 (C-3c), 70.22 (C-3b), 69.97 (C-5b), 69.52 (C-4a), 68.11 (C-7), 67.45 (CO_2Bn), 67.25 (Cbz), 66.92 (C-5a), 64.80 (C-5c), 57.69 (C-2c), 52.61 (C-4c), 38.07 (Lev), 31.86, 29.94 (Lev), 29.46, 28.08 (Lev), 27.87, 27.31, 23.35, 22.02, 21.43 (OAc), 20.69, 16.79 (C-6c). HR-MS: Calculated for $C_{82}H_{102}N_4O_{21}Si$ [M+NH_4^+]: 1524.71440, found: 1524.71125. $[\alpha]^{20}_D$ = + 140.4° (c = 1, $CHCl_3$). TLC: Rf = 0.1 (PE/EA/DCM = 4:1:1, v/v).

(*R*)-5,6-bis(benzyloxy)hexyl 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-azido-4-*N*-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-4,6-*O*-di-*tert*-butylsilylidene-α-D-galactopyranoside (41)



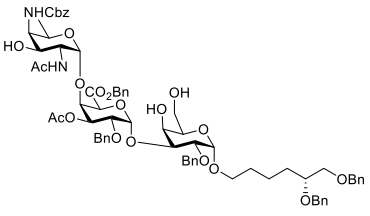
The compound **40** (356.6 mg, 0.237 mmol, 1.0 eq) was dissolved in pyridine (4 mL) and acetic acid (1 mL). After cooled to 0 °C, hydrazine hydrate (N_2H_4 • H_2O 50-60 %) (57 µL, 1.18 mmol, 5.0 eq) was added slowly. After stirred 20 min at RT, checked by TLC complete consumption of the starting material, quenched by acetone. The solution was washed with water (2x) and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (PE/EA/DCM 10:1:1 – 6:1:1) to yield compound **41** (317 mg, 0.225 mmol, 95%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.14 (m, 30H), 5.60 (d, *J* = 3.6 Hz, 1H, H-1b), 5.54 (dd, *J* = 10.7, 2.8 Hz, 1H), 5.30 – 5.19 (m, 1H), 5.18 – 4.98 (m, 4H), 4.87 – 4.74 (m, 3H), 4.73 – 4.57 (m, 5H, H-1a, H-1c), 4.57 – 4.41 (m, 5H), 4.19 – 3.85 (m, 8H), 3.64 – 3.33 (m, 7H), 2.95 (dd, *J* = 10.7, 3.8 Hz, 1H), 2.00 (s, 3H), 1.65 – 1.28 (m, 6H), 1.06 (d, *J* = 6.5 Hz, 3H), 1.01 (d, *J* = 5.7 Hz, 9H), 0.89 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.04, 167.54, 158.06, 138.83, 138.34, 138.19, 138.00, 135.88, 134.83, 128.64, 128.60, 128.54, 128.47, 128.37, 128.34, 128.33, 128.30, 128.27, 128.17, 128.15, 127.74, 127.69, 127.68, 127.63, 127.58, 127.55, 127.53, 127.47, 98.79 (C-1), 97.45 (C-1), 91.94 (C-1), 78.04, 76.93, 73.39, 73.26, 73.02, 72.85, 72.75, 72.13, 72.06, 71.21, 70.19, 69.91, 69.44, 68.18, 67.91, 67.49, 67.30, 67.11, 66.76, 65.02, 60.40, 55.79, 31.66, 29.29, 27.72, 27.18, 23.18, 21.86, 21.28, 20.55, 16.79. HR-MS: Calculated for $C_{77}H_{96}N_4O_{19}Si$ [M+NH_4^+]: 1426.67763, found: 1426.67712. $[\alpha]^{20}_D$ = + 120.5° (c = 1, $CHCl_3$). TLC: Rf = 0.25 (PE/DCM/EA = 6/1/1, v/v/v).

(*R*)-5,6-bis(benzyloxy)hexyl 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-acetylamino-4-*N*-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-4,6-*O*-di-*tert*-butylsilylidene-α-D-galactopyranoside (42)



The compound **41** (97 mg, 0.07 mmol, 1.0 eq) was dissolved in THF (2 mL) and water (20 µL). Pyridine (88 µL, 1.1 mmol, 15 eq) and Ph_3P (72 mg, 0.27 mmol, 4.0 eq) were added and the reaction was allowed to stir for 7 h at 70 °C. After TLC showed complete consumption of the starting material, the reaction mixture was concentrated *in vacuo* and co-evaporated by toluene. The residue was dissolved in THF (2 ml) and water (0.5 mL), then sodium bicarbonate (24 mg, 0.29 mmol, 4.0 eq) and acetic anhydride (14 µL, 0.15 mmol, 2.0 eq) were added and stirred for overnight. After TLC showed complete consumption of the starting material, the reaction mixture was diluted with EtOAc and then washed with saturated aqueous sodium bicarbonate and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/Acetone 10:1 – 5:1) to yield compound **42** (98 mg, 0.07 mmol, quantitative). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.19 (m, 30H), 5.98 (d, *J* = 8.6 Hz, 1H), 5.61 – 5.50 (m, 2H), 5.41 – 5.17 (m, 2H), 5.15 – 4.89 (m, 3H), 4.88 – 4.72 (m, 3H), 4.72 – 4.59 (m, 4H), 4.58 – 4.43 (m, 4H), 4.38 – 4.20 (m, 2H), 4.18 – 4.10 (m, 1H), 4.09 – 3.78 (m, 8H), 3.76 – 3.68 (m, 1H), 3.65 – 3.47 (m, 5H), 3.45 – 3.36 (m, 1H), 2.14 – 1.97 (m, 6H), 1.65 – 1.28 (m, 6H), 1.12 – 0.83 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.63, 170.07, 168.27, 157.62, 138.92, 138.39, 138.25, 137.84, 136.33, 134.04, 129.11, 129.00, 128.94, 128.60, 128.55, 128.47, 128.45, 128.41, 128.39, 128.33, 128.21, 128.16, 127.87, 127.83, 127.79, 127.76, 127.66, 127.60, 98.51, 97.57, 92.29, 78.13, 76.42, 73.64, 73.40, 73.28, 73.14, 72.86, 72.19, 72.12, 71.51, 70.11, 69.87, 69.49, 69.13, 68.13, 67.71, 67.20, 67.16, 66.77, 66.04, 55.37, 50.80, 31.81, 29.41, 27.85, 27.25, 23.43, 23.38, 21.98, 21.41, 20.65, 16.95. HR-MS: Calculated for $C_{79}H_{100}N_2O_{20}Si$ [M+H$^+$]: 1425.67115, found: 1425.67113. $[\alpha]^{20}_D$ = + 104° (c = 1, $CHCl_3$). TLC: Rf = 0.4 (DCM/Acetone = 4/1, v/v).

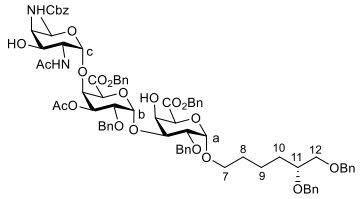
(*R*)-5,6-bis(benzyloxy)hexyl 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-acetylamino-4-*N*-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-α-D-galactopyranoside (4)



The compound **42** (94 mg, 0.066 mmol, 1.0 eq) was dissolved in THF (1 mL) and pyridine (1 mL), then cooled to 0 °C and hydrogen fluoride (HF)/pyridine (70%) (0.1 mL) was added dropwise. The solution was stirred for overnight. After TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate slowly and diluted with EtOAc. The solution was washed with water (2x) and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/Acetone 3:1 - 2:1) to yield compound **4** (80 mg, 0.062 mmol, 94%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.09 (m, 30H), 5.97 (dd, *J* = 8.2, 4.1 Hz, 1H), 5.37 – 5.26 (m, 2H), 5.21 (d, *J* = 12.2 Hz, 1H), 5.10 – 4.97 (m, 3H), 4.90 – 4.78 (m, 2H), 4.76 –

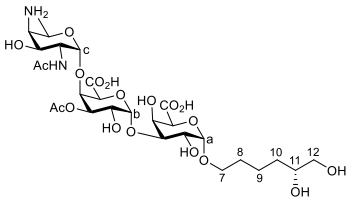
4.45 (m, 9H), 4.29 – 4.23 (m, 1H), 4.16 – 4.00 (m, 4H), 3.99 – 3.46 (m, 13H), 3.41 – 3.29 (m, 2H), 2.82 – 2.68 (m, 1H), 2.22 – 1.94 (m, 6H), 1.76 – 1.28 (m, 6H), 1.12 – 0.95 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.01, 170.37, 167.95, 157.77, 138.81, 138.37, 138.21, 136.70, 136.29, 134.03, 129.00, 128.90, 128.81, 128.73, 128.62, 128.50, 128.45, 128.42, 128.26, 128.15, 128.05, 127.84, 127.82, 127.77, 127.71, 127.68, 127.65, 98.31, 96.71, 94.18, 78.43, 76.11, 75.06, 74.56, 74.32, 73.41, 72.83, 72.75, 72.41, 72.34, 72.01, 70.46, 70.19, 69.15, 68.75, 67.64, 67.28, 67.12, 66.07, 62.85, 55.29, 50.72, 31.60, 29.31, 23.36, 21.99, 21.41, 16.99. HR-MS: Calculated for $C_{71}H_{84}N_2O_{20}$ [M+H$^+$]: 1285.56902, found: 1285.56928. $[\alpha]^{20}_D$ = + 105 ° (c = 1, $CHCl_3$). TLC: Rf = 0.2 (DCM/Acetone = 2/1, v/v).

Benzyl ((*R*)-5,6-bis(benzyloxy)hexyl 2-*O*-benzyl-3-*O*-(benzyl 3-*O*-acetyl-2-*O*-benzyl-4-*O*-(2-acetylamino-4-*N*-benzyloxycarbonyl-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-α-D-galactopyranosyl uronate) (43)



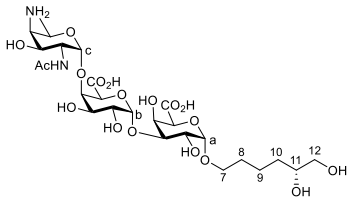
The compound **4** (62 mg, 0.05 mmol, 1.0 eq) was dissolved in DCM/*tert*-BuOH/H_2O (2.25 mL, 4/4/1, v/v/v). The mixture was cooled to 0 ℃ and treated with TEMPO (2.0 mg, 12.8 μmol, 0.25 eq) and BAIB (40.4 mg, 0.12 mmol, 2.5 eq). After stirring for overnight at 4 ℃ and TLC showed complete consumption of the starting material, saturated aqueous sodium thiosulphate was added and diluted with EtOAc, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was dissolved in DMF (2 mL), followed by addition of Cs_2CO_3 (19 mg, 0.06 mmol, 1.2 eq) and BnBr (12 μL, 0.1 mmol, 2.0 eq) at 0℃. After the mixture was allowed to stir overnight at rt and TLC showed complete consumption of the starting material, the reaction was diluted with EtOAc and washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (DCM/Acetone 10:1 – 5:1) yielded **43** (54.6 mg, 0.039 mmol, 81%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.08 (m, 35H), 5.90 (d, *J* = 7.7 Hz, 1H, N*H*Ac), 5.33 (d, *J* = 12.3 Hz, 1H, CH_2), 5.27 (dd, *J* = 10.7, 2.7 Hz, 1H, H-3b), 5.25 – 5.16 (m, 2H, CH_2), 5.12 (d, *J* = 9.8 Hz, 1H, CH_2), 5.07 (d, *J* = 12.2 Hz, 1H, CH_2), 5.01 (d, *J* = 11.8 Hz, 1H, CH_2), 4.93 (d, *J* = 3.6 Hz, 2H, H-1b, H-1a), 4.82 (d, *J* = 11.9 Hz, 1H, CH_2), 4.70 – 4.61 (m, 2H, CH_2, H-5b), 4.61 – 4.48 (m, 7H, CH_2), 4.40 (s, 1H, H-5a), 4.31 – 4.22 (m, 2H, H-4a, H-4b), 4.17 – 4.06 (m, 2H, H-3a, H-1c), 4.06 – 3.98 (m, 2H, H-4c, H-5c), 3.87 (dd, *J* = 9.8, 3.5 Hz, 1H, H-2a), 3.81 (dd, *J* = 10.6, 3.6 Hz, 1H, H-2b), 3.77 – 3.64 (m, 3H, H-3c, H-2c), 3.64 – 3.57 (m, 1H, H-7), 3.57 – 3.45 (m, 3H, H-11, H-12), 3.40 – 3.29 (m, 2H, H-7), 2.11 – 1.98 (m, 6H, NHAc, OAc), 1.61 – 1.49 (m, 4H), 1.49 – 1.38 (m, 1H), 1.38 – 1.28 (m, 1H), 1.06 (d, *J* = 6.3 Hz, 3H, H-6c). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.84 (NHAc), 170.04 (OAc), 168.44, 167.98 (CO_2Bn), 157.62 (Cbz), 138.98, 138.47, 138.02, 136.72, 136.32, 135.50, 134.07, 129.02, 128.99, 128.95, 128.86, 128.70, 128.67, 128.61, 128.59, 128.55, 128.50, 128.46, 128.43, 128.40, 128.31, 128.22, 127.99, 127.94, 127.88, 127.85, 127.81, 127.69, 127.67, 127.57, 98.36 (C-1c), 97.08 (C-1a), 94.54 (C-1b), 77.98 (C-11), 76.22 (C-4b), 74.79 (C-3a), 74.13, 74.07 (C-2a), 73.43, 72.85, 72.81, 72.73, 72.15 (C-2b), 72.09, 70.68 (C-3b), 70.13 (C-5b), 69.48, 69.43 (C-5a, H-5c), 68.82 (C-7), 67.68, 67.34 (Cbz), 67.20, 67.09 (C-4a), 66.12 (C-5c), 55.37 (C-4c), 50.89 (C-2c), 31.87 (C-10), 29.49 (C-8), 23.34 (NHAc), 21.97 (C-9), 21.42 (OAc), 17.05 (C-6c). HR-MS: Calculated for $C_{78}H_{88}N_2O_{21}$ [M+H$^+$]: 1389.59523, found: 1389.59579. $[\alpha]^{20}_D$ = + 90.2° (c = 1, $CHCl_3$). TLC: Rf = 0.4 (DCM/Acetone = 4/1, v/v).

(*R*)-5,6-diol-hexyl 3-*O*-(2-*O*-acetyl-4-*O*-(2-acetylamino-4-amino-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-α-D-galactopyranosyl uronate (1)



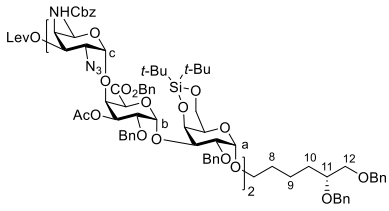
The protected trimer **43** (15 mg, 10.8 µmol, 1.0 eq) was dissolved in *tert*-butanol (7 mL) and water (3 mL). After $Pd(OH)_2/C$ (60 mg) was added, the reaction was stirred for 3 days under a H_2 atmosphere, filtered and concentrated *in vacuo* to yield compound **1** (7.5 mg, 10.5 µmol, quantitative). ^{1}H NMR (500 MHz, Deuterium Oxide) δ 5.33 (dd, *J* = 10.9, 2.9 Hz, 1H, H-3b), 5.30 (d, *J* = 3.9 Hz, 1H, H-1b), 5.02 – 4.96 (m, 2H, H-1c, H-1a), 4.84 (s, 1H, H-5b), 4.68 – 4.59 (m, 2H, H-5c, H-4b), 4.58 – 4.55 (m, 1H, H-4a), 4.53 (d, *J* = 1.4 Hz, 1H, H-5a), 4.23 (dd, *J* = 11.4, 4.4 Hz, 1H, H-3c), 4.18 – 4.12 (m, 1H, H-2b), 4.07 (dd, *J* = 10.3, 3.1 Hz, 1H, H-3a), 3.98 – 3.91 (m, 2H, H-2c, H-2a), 3.73 – 3.62 (m, 3H, H-7, H-11, H-4c), 3.58 – 3.50 (m, 2H, H-7, H-12), 3.46 – 3.40 (m, 1H, H-12), 2.19 (s, 3H, OAc), 2.03 (s, 3H, NHAc), 1.71 – 1.34 (m, 6H, H-8, H-9, H-10), 1.31 (d, *J* = 6.7 Hz, 3H, H-6c). ^{13}C NMR (101 MHz, D_2O) δ 174.90, 173.35, 172.69, 171.96, 98.46, 97.91 (C-1a, C-1c), 95.82 (C-1b), 76.30 (C-4b), 74.90 (C-3a), 71.63 (C-11), 71.24 (C-3b), 70.21 (C-5a), 70.07 (C-5b), 68.59 (C-7), 67.03 (C-4a), 66.13 (C-2b), 66.03 (C-2a), 65.38 (C-12), 63.73 (C-3c), 63.32 (C-5c), 55.16 (C-4c), 49.21 (C-2c), 31.90, 28.48, 22.23 (NHAc), 21.40, 20.80 (OAc), 16.03 (C-6c). HR-MS: Calculated for $C_{28}H_{46}N_2O_{19}$ [M+H$^+$]: 715.27675, found: 715.27682.

(*R*)-5,6-diol-hexyl 3-*O*-(4-*O*-(2-acetylamino-4-amino-6-deoxy-α-D-galactopyranosyl)-α-D-galactopyranosyl urinate)-α-D-galactopyranosyl uronate (1b)



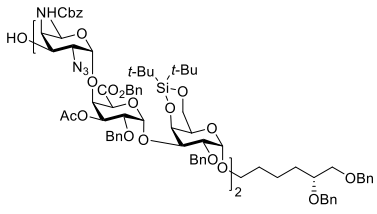
^{1}H NMR (500 MHz, Deuterium Oxide) δ 5.22 (d, *J* = 3.9 Hz, 1H, H-1b), 4.98 – 4.93 (m, 2H, H-1a, H-1c), 4.78 – 4.71 (m, 1H, H-5c), 4.56 (d, *J* = 1.3 Hz, 1H, H-5b), 4.48 (dd, *J* = 3.3, 1.4 Hz, 1H, H-4a), 4.35 (dd, *J* = 3.2, 1.2 Hz, 1H, H-4b), 4.24 (d, *J* = 1.5 Hz, 1H, H-5a), 4.18 (dd, *J* = 11.3, 4.4 Hz, 1H, H-3c), 4.10 (dd, *J* = 10.6, 3.1 Hz, 1H, H-3b), 4.05 – 3.97 (m, 2H, H-3a, H-2c), 3.93 – 3.85 (m, 2H, H-2a, H-2b), 3.74 – 3.65 (m, 2H, H-7, H-11), 3.63 – 3.51 (m, 3H, H-4c, H-12, H-7), 3.49 – 3.41 (m, 1H, H-12), 2.09 (s, 3H, NHAc), 1.73 – 1.34 (m, 6H, H-8, H-9, H-10), 1.25 (d, *J* = 6.7 Hz, 3H, H-6c). ^{13}C NMR (214 MHz, D_2O) δ 175.96, 175.79, 175.14, 99.68 (C-1c, J_{CH} = 174.0 Hz), 99.27 (C-1a, J_{CH} = 172.0 Hz), 97.15 (C-1b, J_{CH} = 170.0 Hz), 80.89 (C-4b), 76.63 (C-3a), 72.56 (C-11), 72.01 (C-5b), 71.84 (C-5a), 69.41 (C-3b), 69.29 (C-7), 68.89 (C-2b), 68.57 (C-4a), 67.39 (C-2a), 66.31 (C-12), 65.51 (C-3c), 64.20 (C-5c), 56.21 (C-4c), 50.26 (C-2c), 32.83, 29.43, 23.24, 22.34, 16.35 (C-6c). HR-MS: Calculated for $C_{26}H_{44}N_2O_{18}$ [M+H$^+$]: 673.26619, found: 673.26633.

Hexamer of two repeating units 44



The donor **7** (194 mg, 0.14 mmol, 2.0 eq) and the acceptor **41** (99 mg, 0.07 mmol, 1.0 eq) were co-evaporated with anhydrous toluene three times under nitrogen. Dry DCM (3 mL) and 4Å molecular sieves were added and then the solution stirred for 20 minutes at RT. The reaction was cooled to 0 °C and TBSOTf (3.2 µL, 13.9 µmol, 0.2 eq) was added. After stirred 2 hours and TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The solution was washed with water (2x) and brine. The aqueous layer was extracted with DCM (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (Tol/EA 8:1 - 8:3) to yield desired α anomer compound **44** (151 mg, 58 µmol, 83%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.43 – 7.15 (m, 50H), 5.61 (d, *J* = 3.5 Hz, 1H, H-1), 5.56 (d, *J* = 3.5 Hz, 1H, H-1), 5.53 – 5.43 (m, 2H), 5.25 – 5.13 (m, 5H, H-1a$_1$), 5.12 – 4.90 (m, 6H), 4.88 – 4.62 (m, 15H, H-1a), 4.59 (dd, *J* = 11.5, 3.8 Hz, 2H, H-1c, H-1c$_1$), 4.56 – 4.40 (m, 8H), 4.29 – 4.09 (m, 7H), 4.09 – 3.97 (m, 6H), 3.97 – 3.86 (m, 2H), 3.71 (s, 1H), 3.62 – 3.44 (m, 5H), 3.43 – 3.35 (m, 1H, H-7), 3.14 (dd, *J* = 11.3, 4.0 Hz, 1H, H-2c$_1$), 3.07 (dd, *J* = 10.8, 3.8 Hz, 1H, H-2c), 2.86 – 2.36 (m, 4H), 2.17 (s, 3H), 2.01 (d, *J* = 8.7 Hz, 6H), 1.62 – 1.27 (m, 6H), 1.08 – 0.97 (m, 21H), 0.88 (s, 9H), 0.80 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.38, 172.00, 170.30, 170.03, 167.39, 167.33, 156.93, 156.57, 138.90, 138.41, 138.26, 138.01, 137.95, 137.92, 136.33, 136.13, 135.00, 134.88, 128.86, 128.68, 128.66, 128.57, 128.53, 128.50, 128.48, 128.42, 128.38, 128.33, 128.31, 128.12, 128.05, 127.83, 127.76, 127.70, 127.65, 127.63, 127.60, 127.56, 127.55, 98.24 (C-1c, C-1c$_1$), 97.58 (C-1a), 93.52 (C-1a$_1$), 92.00 (C-1b), 91.65 (C-1b$_1$), 78.09 (C-11), 77.07, 76.68, 73.50, 73.37, 73.01, 72.94, 72.91, 72.82, 72.58, 72.30, 72.13, 71.37, 71.31, 70.50, 70.33, 70.30, 70.15, 69.87, 69.47, 69.30, 68.08, 67.41, 67.25, 67.19, 67.15, 66.85, 65.92, 64.76, 59.80 (C-2c), 57.66 (C-2c$_1$), 52.51 (C-4c$_1$), 50.41 (C-4c), 37.98, 31.78, 29.85, 29.39, 28.00, 27.91, 27.82, 27.30, 27.24, 27.14, 23.30, 21.93, 21.37, 21.32 (OAc), 20.62, 20.54, 16.69, 16.57 (C-6c, C-6c$_1$). HR-MS: Calculated for $C_{139}H_{172}N_8O_{37}Si_2$ [M+ NH_4^++NH_4^+]/2: 1318.60192, found: 1318.60143. $[\alpha]^{20}_D$ = + 136.5 ° (c = 1, $CHCl_3$). TLC: Rf = 0.4 (Tol/EA = 8:3, v/v).

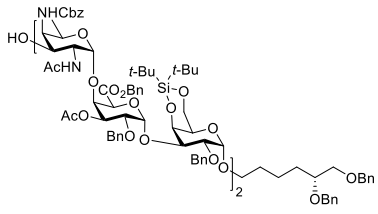
Hexamer of two repeating units 45



The compound **44** (585.1 mg, 0.225 mmol, 1.0 eq) was dissolved in pyridine (4 mL) and acetic acid (1 mL). After cooled to 0 °C, hydrazine hydrate (N_2H_4 • H_2O 50-60 %) (83 µL, 1.7 mmol, 7.5 eq) was added slowly. After stirred 20 min at RT, checked by TLC complete consumption of the starting material, quenched by acetone. The solution was washed with water (2x) and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/Acetone 30:1 – 20:1) to yield compound **45** (530 mg, 0.212 mmol, 94%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.14 (m, 50H), 5.61 (d, *J* = 3.5 Hz, 1H), 5.55 (d, *J* = 3.5 Hz, 1H), 5.51 – 5.43 (m, 2H), 5.25 – 5.10 (m, 6H), 5.05 (d, *J* = 12.2 Hz, 1H), 5.03 – 4.87 (m, 3H), 4.87 – 4.39 (m, 23H), 4.30 –

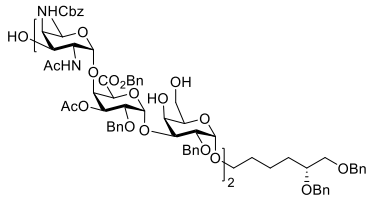
4.10 (m, 6H), 4.10 – 3.86 (m, 11H), 3.72 (s, 1H), 3.62 – 3.45 (m, 5H), 3.44 – 3.34 (m, 1H), 3.08 (dd, *J* = 10.8, 3.7 Hz, 1H), 2.97 (dd, *J* = 10.6, 3.8 Hz, 1H), 2.90 (s, 1H), 2.07 – 1.97 (m, 6H), 1.62 – 1.27 (m, 6H), 1.10 – 0.98 (m, 21H), 0.92 – 0.77 (m, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.36, 170.07, 167.43, 158.26, 156.99, 138.97, 138.47, 138.32, 138.10, 138.02, 136.19, 135.92, 135.07, 134.91, 128.89, 128.78, 128.75, 128.68, 128.62, 128.58, 128.57, 128.54, 128.48, 128.43, 128.38, 128.34, 128.32, 128.17, 127.89, 127.82, 127.71, 127.68, 127.62, 127.54, 98.64, 98.31, 97.64, 93.54, 92.07, 91.72, 78.16, 76.90, 73.56, 73.44, 73.05, 72.89, 72.40, 72.19, 71.43, 71.12, 70.63, 70.36, 70.01, 69.94, 69.53, 69.44, 68.95, 68.16, 67.74, 67.47, 67.38, 67.25, 66.91, 65.97, 65.11, 60.92, 59.89, 55.80, 50.48, 31.84, 29.45, 27.98, 27.88, 27.29, 27.19, 23.36, 21.98, 21.42, 21.38, 20.68, 20.60, 16.91, 16.64. HR-MS: Calculated for $C_{134}H_{166}N_8O_{35}Si_2$ [M+H$^+$]: 2504.10669, found: 2504.10992. $[\alpha]^{20}_D$ = + 140.9° (c = 1, $CHCl_3$). TLC: Rf = 0.1 (DCM/Acetone = 20/1, v/v).

Hexamer of two repeating units 46



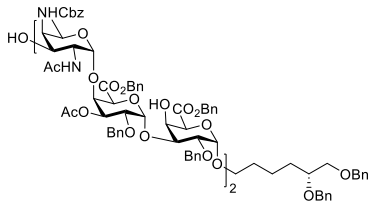
The compound **45** (85 mg, 34 μmol, 1.0 eq) was dissolved in THF (2 mL) and water (20 μL). Pyridine (42 μL, 0.5 mmol, 15 eq) and Ph_3P (37 mg, 0.14 mmol, 4.0 eq) were added and the reaction was allowed to stir for 7 h at 70 °C. After TLC showed complete consumption of the starting material, the reaction mixture was concentrated *in vacuo* and co-evaporated by toluene. The residue was dissolved in THF (1 ml) and water (0.5 mL), then sodium bicarbonate (12 mg, 0.14 mmol, 4.0 eq) and acetic anhydride (14 μL, 0.15 mmol, 4.0 eq) were added and stirred for overnight. After TLC showed complete consumption of the starting material, the reaction mixture was diluted with EtOAc and then washed with saturated aqueous sodium bicarbonate and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/Acetone 5:1 – 4:1) to yield compound **46** (75.6 mg, 29.8 μmol, 88%). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.51 – 6.96 (m, 50H), 6.17 – 6.05 (m, 1H), 5.63 – 5.46 (m, 5H), 5.34 – 4.88 (m, 10H), 4.88 – 4.59 (m, 13H), 4.59 – 4.41 (m, 5H), 4.40 – 4.29 (m, 2H), 4.29 – 3.81 (m, 16H), 3.78 – 3.31 (m, 11H), 2.61 (s, 1H), 2.16 – 1.92 (m, 12H), 1.65 – 1.29 (m, 6H), 1.13 – 0.74 (m, 42H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.88, 170.27, 170.16, 169.86, 168.35, 157.59, 156.96, 139.02, 138.46, 138.37, 138.28, 137.96, 137.91, 136.76, 136.42, 134.59, 134.08, 129.17, 128.94, 128.88, 128.82, 128.63, 128.50, 128.46, 128.40, 128.35, 128.25, 128.21, 128.04, 127.93, 127.86, 127.81, 127.68, 127.58, 99.10, 98.48, 97.54, 96.40, 92.84, 91.70, 78.15, 76.62, 73.46, 73.30, 73.19, 72.98, 72.91, 72.86, 72.43, 72.16, 72.05, 71.76, 71.59, 71.21, 70.21, 70.06, 69.96, 69.69, 69.64, 69.29, 68.31, 68.21, 67.80, 67.71, 67.64, 67.26, 67.23, 67.13, 66.93, 66.67, 66.61, 66.03, 55.47, 51.66, 51.09, 48.78, 31.87, 29.49, 27.91, 27.81, 27.30, 27.21, 23.46, 23.39, 23.31, 22.00, 21.42, 21.37, 20.68, 17.03, 16.94. HR-MS: Calculated for $C_{138}H_{174}N_4O_{37}Si_2$ [M+H$^+$+NH$_4^+$]/2: 1277.09032, found: 1277.09029. $[\alpha]^{20}_D$ = + 128.3° (c = 1, $CHCl_3$). TLC: Rf = 0.3 (DCM/Acetone = 4/1, v/v).

Hexamer of two repeating units 5



The compound **46** (73 mg, 28.8 µmol, 1.0 eq) was dissolved in THF (1 mL) and pyridine (1 mL), then cooled to 0 °C and hydrogen fluoride (HF)/pyridine (70%) (0.1 mL) was added dropwise. The solution was stirred for overnight. After TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate slowly and diluted with EtOAc. The solution was washed with water (2x) and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/Acetone 4:1 - 1:1) to yield compound **5** (60 mg, 26.6 µmol, 92%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.09 (m, 50H), 6.09 – 5.92 (m, 2H), 5.40 – 4.86 (m, 13H), 4.86 – 4.41 (m, 17H), 4.38 (d, *J* = 3.7 Hz, 1H), 4.33 (d, *J* = 2.9 Hz, 1H), 4.25 (d, *J* = 10.8 Hz, 1H), 4.19 – 3.46 (m, 27H), 3.41 – 3.27 (m, 3H), 2.93 – 2.55 (m, 3H), 2.14 – 1.96 (m, 12H), 1.72 – 1.32 (m, 6H), 1.11 – 0.97 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.98, 170.85, 170.03, 169.87, 167.71, 157.55, 156.91, 138.79, 138.34, 138.25, 138.12, 137.03, 136.70, 136.45, 136.30, 134.20, 134.00, 129.06, 128.85, 128.83, 128.79, 128.78, 128.72, 128.66, 128.62, 128.59, 128.50, 128.43, 128.41, 128.15, 128.06, 127.87, 127.74, 127.72, 127.69, 127.66, 127.27, 98.61, 98.26, 96.72, 94.40, 94.25, 78.45, 78.02, 76.15, 75.54, 75.21, 74.55, 74.32, 74.22, 74.14, 73.99, 73.40, 72.87, 72.81, 72.54, 72.34, 72.09, 72.00, 70.71, 70.36, 70.23, 70.13, 69.28, 68.83, 67.62, 67.59, 67.22, 66.94, 66.81, 66.60, 66.03, 63.27, 62.87, 55.28, 50.95, 50.85, 48.50, 31.56, 29.73, 29.26, 23.56, 23.29, 21.96, 21.38, 21.35, 17.00, 16.98. HR-MS: Calculated for $C_{122}H_{142}N_4O_{37}$ $[M+2H^+]/2$: 1128.47492, found: 1128.47435. $[\alpha]^{20}_D$ = + 137.6 ° (c = 1, $CHCl_3$). TLC: Rf = 0.1 (DCM/Acetone = 3/2, v/v).

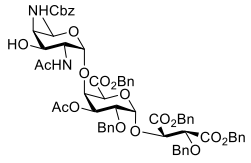
Hexamer of two repeating units 47



The compound **5** (11.6 mg, 5.14 µmol, 1.0 eq) was dissolved in EtOAc/*tert*-BuOH/H_2O (375 µL, 2/2/1, v/v/v). The mixture was cooled to 0 °C and treated with TEMPO (1.4 mg, 8.96 µmol, 1.7 eq), BAIB (14 mg, 42 mmol, 8 eq) and $NaHCO_3$ (4.5 mg, 53.6 µmol, 10 eq). After stirring for 24 hours at 4 °C and TLC showed complete consumption of the starting material, saturated aqueous sodium thiosulphate was added and diluted with EtOAc, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was dissolved in DCM (2 mL), followed by addition of 0.2M phenyldiazomethane ($PhCHN_2$) in Et_2O (1 mL) at RT. After the mixture was allowed to stir overnight at rt and TLC showed complete consumption of the starting material, the reaction was diluted with EtOAc and washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by preparative TLC plates (Macherey-Nagel, pre-coated TLC plates SIL G-100 UV254) (DCM/Acetone/MeOH 16:4:0.4) yielded **47** (7.4 mg, 3.0 µmol, 64%). ^{1}H NMR (850 MHz, Chloroform-*d*) δ 7.41 – 7.14 (m, 60H), 5.94 (s, 1H), 5.74 (d, *J* = 9.3 Hz, 1H), 5.32 – 5.28 (m, 2H), 5.27 – 5.22 (m, 3H), 5.20 – 5.14 (m, 2H), 5.13 – 5.10 (m, 1H), 5.02 (d, *J* = 11.8 Hz, 1H), 5.00 – 4.95 (m, 2H), 4.95 – 4.90 (m, 3H), 4.88 – 4.81 (m, 2H), 4.76 (d, *J* = 11.5 Hz, 1H), 4.72 (d, *J* = 12.2 Hz, 1H), 4.67

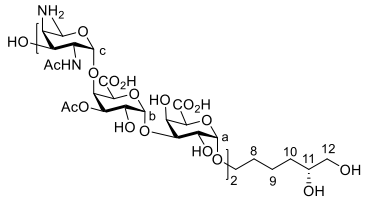
(d, *J* = 11.7 Hz, 2H), 4.63 (s, 1H), 4.60 – 4.45 (m, 14H), 4.40 – 4.36 (m, 2H), 4.30 – 4.20 (m, 4H), 4.13 – 4.07 (m, 2H), 4.06 – 4.01 (m, 1H), 3.98 – 3.90 (m, 4H), 3.89 – 3.82 (m, 2H), 3.82 – 3.75 (m, 2H), 3.68 – 3.46 (m, 9H), 3.40 – 3.30 (m, 3H), 2.09 (s, 3H), 2.03 – 1.96 (m, 9H), 1.59 – 1.28 (m, 6H), 1.06 – 0.99 (m, 6H). ^{13}C NMR (214 MHz, $CDCl_3$) δ 173.09, 170.88, 170.19, 169.90, 168.56, 168.51, 167.84, 167.73, 157.59, 156.83, 138.97, 138.48, 138.31, 138.03, 137.00, 136.65, 136.49, 136.23, 135.51, 135.38, 134.13, 134.06, 129.22, 128.99, 128.97, 128.95, 128.87, 128.82, 128.78, 128.76, 128.73, 128.64, 128.59, 128.57, 128.56, 128.54, 128.52, 128.48, 128.45, 128.39, 128.37, 128.06, 127.94, 127.86, 127.83, 127.74, 127.73, 127.64, 127.45, 98.62, 98.09, 97.09, 95.48, 94.53, 77.99, 76.23, 76.14, 74.82, 74.32, 74.10, 74.02, 73.86, 73.46, 73.12, 72.84, 72.76, 72.14, 72.12, 72.06, 70.55, 70.34, 70.28, 70.16, 69.94, 69.45, 68.84, 67.74, 67.63, 67.49, 67.26, 67.19, 67.11, 66.61, 65.91, 55.32, 50.99, 31.89, 29.85, 29.49, 23.52, 23.33, 22.85, 21.98, 21.45, 17.18, 17.12. HR-MS: Calculated for $C_{136}H_{150}N_4O_{39}$ [M+Na$^+$]: 2485.97694, found: 2485.97705. $[\alpha]^{20}_D$ = + 117° (c = 1, $CHCl_3$). TLC: Rf = 0.3 (DCM/Acetone/MeOH = 16/4/0.4, v/v/v).

Side-product from the oxidation 47e



^{1}H NMR (850 MHz, Chloroform-*d*) δ 7.42 – 7.16 (m, 30H), 5.90 (d, *J* = 8.4 Hz, 1H, N*H*Ac), 5.42 (d, *J* = 3.5 Hz, 1H, H-1b), 5.24 (dd, *J* = 10.8, 2.7 Hz, 1H, H-3b), 5.17 (d, *J* = 11.8 Hz, 1H, C*H*$_2$), 5.14 – 4.99 (m, 6H, C*H*$_2$), 4.92 (d, *J* = 11.8 Hz, 1H, C*H*$_2$), 4.86 (d, *J* = 9.8 Hz, 1H, N*H*Cbz), 4.81 (d, *J* = 5.9 Hz, 1H, H-3a), 4.71 – 4.66 (m, 2H, C*H*$_2$), 4.60 (s, 1H, H-5b), 4.54 – 4.48 (m, 1H, H-2a), 4.43 (d, *J* = 11.1 Hz, 1H, C*H*$_2$), 4.35 (d, *J* = 12.3 Hz, 1H, C*H*$_2$), 4.21 – 4.17 (m, 1H, H-4b), 4.08 (d, *J* = 3.8 Hz, 1H, , H-1c), 3.92 – 3.88 (m, 2H, H-5c, H-4c), 3.82 – 3.77 (m, 1H, H-2b), 3.70 – 3.52 (m, 2H, H-3c, H-3c), 3.19 (d, *J* = 6.5 Hz, 1H, 3c-OH), 2.11 – 2.07 (m, 3H, NHAc), 2.03 (s, 3H, OAc), 1.02 (d, *J* = 6.3 Hz, 3H, H-6c). ^{13}C NMR (214 MHz, $CDCl_3$) δ 172.79 (NHAc), 170.08 (OAc), 169.21, 168.24, 168.02, 157.67 (Cbz), 137.58, 136.74, 136.27, 135.20, 134.86, 134.27, 129.01, 128.98, 128.93, 128.85, 128.83, 128.82, 128.76, 128.73, 128.65, 128.58, 128.57, 128.53, 128.52, 128.47, 128.45, 128.43, 128.36, 128.23, 128.15, 127.94, 127.75, 98.36 (C-1c), 95.70 (C-1b), 78.58 (C-2a), 76.15 (C-4b), 75.09 (C-3a), 73.67, 71.73, 71.06 (C-2b), 70.26 (C-5b), 69.79 (C-3b, C-3c), 67.66, 67.61, 67.49, 67.40, 65.92 (C-5c), 55.44 (C-4c), 50.95 (C-2c), 23.38 (NHAc), 21.46 (OAc), 17.08 (C-6c). HR-MS: Calculated for $C_{63}H_{66}N_2O_{18}$ [M+H$^+$]: 1139.43834, found: 1139.43641. $[\alpha]^{20}_D$ = + 63° (c = 0.1, $CHCl_3$). TLC: Rf = 0.5 (DCM/Acetone/MeOH = 16/4/0.4, v/v/v).

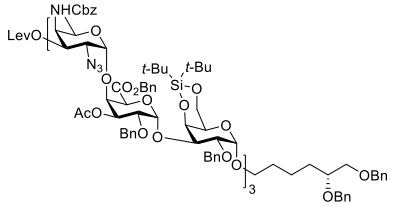
The deprotection of Hexamer 2



The protected hexamer **47** (9.8 mg, 4.3 µmol, 1.0 eq) was dissolved in *tert*-butanol (7 mL) and 0.1% AcOH in water (2 mL). After $Pd(OH)_2$/C (60 mg) was added, the reaction was stirred for 3 days under a H_2 atmosphere, filtered and concentrated *in vacuo* to yield compound **2** (5.1 mg, 3.94 µmol, 91%). ^{1}H NMR (850 MHz, Deuterium Oxide) δ 5.30 – 5.21 (m, 4H, H-3b, H-1b, H-1b$_1$, H-3b$_1$), 5.04 (d, *J* = 4.2 Hz, 1H, H-1a$_1$), 5.00 (d, *J* = 4.0 Hz, 1H, H-1c), 4.92 (dd, *J* = 12.0, 3.9 Hz, 2H, H-1a, H-1c$_1$), 4.66 (s, 1H, H-5b$_1$), 4.62 – 4.49 (m, 5H, H-5c, H-5b, H-4b, H-5c$_1$, H-4b$_1$),

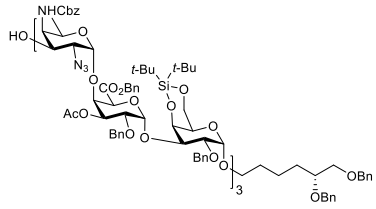
4.47 – 4.41 (m, 2H, H-4a, H-4a$_1$), 4.25 – 4.19 (m, 2H, H-3c, H-5a), 4.16 – 4.06 (m, 5H, H-2b, H-2b$_1$, H-3c$_1$, H-2c, H-5a$_1$), 4.04 – 3.97 (m, 3H, H-3a, H-3a$_1$, H-2c$_1$), 3.94 (dd, *J* = 10.3, 4.1 Hz, 1H, H-2a$_1$), 3.89 (dd, *J* = 10.3, 3.9 Hz, 1H, H-2a), 3.74 (s, 1H, H-4c), 3.69 – 3.63 (m, 2H, H-7, H-11), 3.55 – 3.49 (m, 2H, H-12, H-7), 3.49 – 3.43 (m, 1H, H-4c$_1$), 3.44 – 3.39 (m, 1H, H-12), 2.19 – 2.14 (m, 6H, OAc), 2.05 (s, 3H, 2c$_1$-NHAc), 1.99 (s, 3H, 2c-NHAc), 1.68 – 1.34 (m, 6H, H-8, H-9, H-10), 1.32 – 1.23 (m, 6H, H-6c, H-6c$_1$). ^{13}C NMR (214 MHz, D_2O) δ 176.51 (CO_2H), 176.01 (NHAc), 175.87 (CO_2H), 175.57 (NHAc), 175.16 (CO_2H), 175.01 (CO_2H), 174.51 (OAc), 174.40 (OAc), 99.42 (C-1a$_1$, C-1c$_1$), 99.26 (C-1a), 98.62 (C-1c), 97.11 (C-1b$_1$), 96.93 (C-1b), 78.25 (C-4b$_1$), 77.51 (C-4b), 76.83 (C-3a), 76.54 (C-3a$_1$), 74.05 (C-3c), 73.12 (C-5a$_1$), 72.90 (C-3b), 72.81 (C-3b$_1$), 72.59 (C-11), 72.13 (C-5a), 71.92 (C-5b$_1$), 71.74 (C-5b), 69.22 (C-7), 68.69 (C-4a, C-4a$_1$), 67.43 (C-2a), 67.19 (C-2b$_1$), 67.16 (C-2b), 66.62 (C-2a$_1$), 66.31 (C-12), 66.01 (C-3c$_1$), 65.29 (C-5c$_1$), 64.18 (C-5c), 55.82 (C-4c$_1$), 53.59 (C-4c), 50.20 (C-2c$_1$), 48.48 (C-2c), 32.85, 29.46, 23.32, 23.22, 22.40, 21.75, 21.74, 16.99, 16.95 (C-6c, C-6c$_1$). HR-MS: Calculated for $C_{50}H_{78}N_4O_{35}$ [M+2H$^+$]/2: 648.22961, found: 648.22942.

Nomamer of three repeating units 48



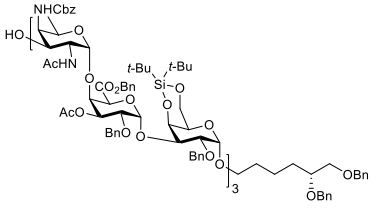
The donor **7** (248 mg, 0.18 mmol, 2.0 eq) and the acceptor **45** (224 mg, 0.09 mmol, 1.0 eq) were co-evaporated with anhydrous toluene three times under nitrogen. Dry DCM (3 mL) and 4Å molecular sieves were added and then the solution stirred for 20 minutes at RT. The reaction was cooled to 0 °C and TBSOTf (5 µL, 19.5 µmol, 0.2 eq) was added. After stirred 2 hours and TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate and diluted with DCM. The solution was washed with water (2x) and brine. The aqueous layer was extracted with DCM (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (Tol/EA 8:1 - 8:3) to yield desired α anomer compound **48** (283 mg, 76.5 µmol, 85%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 – 7.12 (m, 72H), 5.66 – 5.54 (m, 3H), 5.53 – 5.42 (m, 3H), 5.26 – 4.90 (m, 14H), 4.90 – 4.62 (m, 19H), 4.62 – 4.37 (m, 12H), 4.32 – 3.86 (m, 23H), 3.71 (s, 2H), 3.63 – 3.46 (m, 5H), 3.45 – 3.35 (m, 1H), 3.20 – 3.02 (m, 3H), 2.86 – 2.36 (m, 4H), 2.16 (s, 3H), 2.08 – 1.95 (m, 9H), 1.62 – 1.26 (m, 6H), 1.12 – 0.71 (m, 63H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.35, 171.99, 170.27, 170.17, 170.01, 167.36, 167.33, 167.08, 156.92, 156.57, 138.90, 138.40, 138.26, 137.99, 137.97, 137.94, 137.91, 136.32, 136.14, 135.00, 134.93, 134.82, 128.84, 128.69, 128.66, 128.64, 128.56, 128.52, 128.46, 128.42, 128.37, 128.32, 128.30, 128.24, 128.11, 128.04, 127.83, 127.79, 127.76, 127.69, 127.64, 127.62, 127.55, 127.38, 98.20, 97.95, 97.57, 93.48, 91.99, 91.67, 91.62, 78.08, 77.36, 77.04, 76.63, 73.50, 73.36, 73.04, 72.99, 72.94, 72.91, 72.87, 72.81, 72.60, 72.30, 72.12, 71.99, 71.36, 71.31, 71.15, 70.50, 70.32, 70.27, 70.15, 69.89, 69.47, 69.34, 68.18, 68.08, 67.42, 67.22, 67.14, 66.84, 65.90, 64.75, 59.90, 59.81, 57.65, 52.51, 50.43, 37.97, 31.76, 29.83, 29.37, 27.94, 27.90, 27.82, 27.23, 27.14, 27.12, 23.30, 23.28, 21.91, 21.35, 21.31, 20.62, 20.53, 16.68, 16.60, 16.56. HR-MS: Calculated for $C_{196}H_{242}N_{12}O_{53}Si_3$ [M+H$^+$+NH$_4^+$]/2: 1857.31645, found: 1857.32031. $[\alpha]^{20}_D$ = + 161.8 ° (c = 1, $CHCl_3$). TLC: Rf = 0.3 (Tol/EA = 8:3, v/v).

Nonamer of three repeating units 49



The compound **48** (128 mg, 34.6 µmol, 1.0 eq) was dissolved in pyridine (2 mL) and acetic acid (0.5 mL). After cooled to 0 °C, hydrazine hydrate (N_2H_4 • H_2O 50-60 %) (8.4 µL, 0.17 mmol, 5 eq) was added slowly. After stirred 20 min at RT, checked by TLC complete consumption of the starting material, quenched by acetone. The solution was washed with water (2x) and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/Acetone 25:1 – 15:1) to yield compound **49** (111.4 mg, 30.9 µmol, 89%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.11 (m, 70H), 5.65 – 5.54 (m, 3H), 5.49 (d, *J* = 10.6, 2.2 Hz, 3H), 5.25 – 4.92 (m, 15H), 4.89 – 4.36 (m, 31H), 4.30 – 3.87 (m, 24H), 3.71 (s, 2H), 3.67 – 3.45 (m, 6H), 3.44 – 3.34 (m, 1H), 3.23 – 3.08 (m, 2H), 2.99 (dd, *J* = 10.6, 3.8 Hz, 1H), 2.10 – 1.94 (m, 9H), 1.64 – 1.28 (m, 6H), 1.12 – 0.97 (m, 36H), 0.92 – 0.73 (m, 27H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.29, 170.17, 170.02, 167.36, 167.07, 158.16, 156.98, 152.90, 138.89, 138.39, 138.25, 138.03, 137.96, 137.92, 137.88, 136.16, 135.90, 135.01, 134.91, 134.81, 128.79, 128.69, 128.63, 128.60, 128.54, 128.52, 128.46, 128.44, 128.42, 128.37, 128.32, 128.29, 128.25, 128.21, 128.09, 127.83, 127.79, 127.76, 127.71, 127.64, 127.62, 127.56, 127.45, 127.37, 98.57, 98.30, 97.99, 97.56, 93.41, 91.99, 91.65, 91.58, 78.08, 77.36, 77.06, 76.77, 73.49, 73.36, 73.04, 72.99, 72.90, 72.88, 72.79, 72.74, 72.62, 72.40, 72.28, 72.11, 71.98, 71.37, 71.13, 71.04, 70.50, 70.28, 69.95, 69.91, 69.47, 69.41, 69.32, 68.70, 68.08, 67.61, 67.42, 67.30, 67.21, 67.13, 66.84, 65.91, 65.09, 60.78, 59.93, 59.81, 55.77, 50.44, 31.75, 29.37, 27.95, 27.91, 27.82, 27.23, 27.12, 23.30, 23.28, 21.90, 21.35, 21.31, 20.62, 20.53, 16.83, 16.60. HR-MS: Calculated for $C_{191}H_{236}N_{12}O_{51}Si_3$ $[M+H^+ + H^+]/2$: 1799.78479, found: 1799.78658. $[\alpha]^{20}_D$ = + 139.5 ° (c = 1, $CHCl_3$). TLC: Rf = 0.5 (DCM/MeOH = 60/1, v/v).

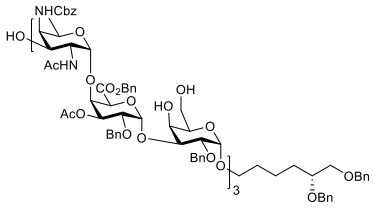
Nonamer of three repeating units 50



The compound **49** (105 mg, 29.2 µmol, 1.0 eq) was dissolved in THF (2 mL) and water (24 µL). Pyridine (106 µL, 1.31 mmol, 45 eq) and Ph_3P (92 mg, 0.35 mmol, 12.0 eq) were added and the reaction was allowed to stir for 7 h at 70 °C. After TLC showed complete consumption of the starting material, the reaction mixture was concentrated *in vacuo* and co-evaporated by toluene. The residue was dissolved in THF (3 ml) and water (1 mL), then sodium bicarbonate (30 mg, 0.36 mmol, 12.0 eq) and acetic anhydride (17 µL, 0.18 mmol, 6.0 eq) were added and stirred for overnight. After TLC showed complete consumption of the starting material, the reaction mixture was diluted with EtOAc and then washed with saturated aqueous sodium bicarbonate and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/MeOH 60:1 – 30:1) to yield compound **50** (106 mg, 29.0 µmol, 99%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.09 (m, 70H), 6.21 – 6.06 (m, 1H), 5.72 (d, *J* = 9.4 Hz, 1H), 5.67 – 5.37 (m, 9H), 5.23 – 5.13 (m, 4H), 5.13 – 4.89 (m, 9H), 4.89 – 4.72 (m, 13H), 4.72 – 4.60 (m, 6H), 4.57 – 4.42 (m, 6H), 4.36 – 4.23 (m, 5H), 4.23 – 3.86 (m, 23H), 3.78 – 3.63 (m, 4H),

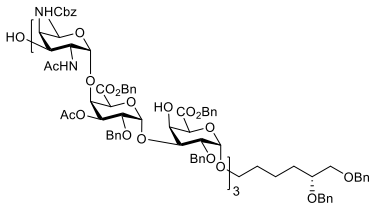
3.62 – 3.46 (m, 7H), 3.45 – 3.35 (m, 1H), 2.90 (s, 2H), 2.12 (s, 3H), 2.09 – 1.93 (m, 15H), 1.64 – 1.28 (m, 6H), 1.12 – 0.73 (m, 63H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.89, 170.66, 170.43, 170.17, 169.95, 169.84, 168.44, 168.39, 157.56, 157.10, 138.94, 138.39, 138.19, 138.11, 138.05, 137.84, 137.78, 137.77, 136.79, 136.65, 136.33, 134.53, 134.29, 133.88, 129.14, 129.04, 129.01, 128.95, 128.93, 128.87, 128.83, 128.78, 128.62, 128.57, 128.49, 128.45, 128.43, 128.39, 128.35, 128.32, 128.25, 128.22, 128.01, 127.95, 127.85, 127.80, 127.79, 127.76, 127.69, 127.66, 127.57, 127.54, 127.49, 127.43, 99.54, 99.13, 98.47, 97.43, 95.86, 92.81, 91.56, 91.34, 78.07, 77.36, 77.01, 76.68, 73.49, 73.43, 73.41, 73.25, 73.15, 72.85, 72.82, 72.79, 72.40, 72.35, 72.13, 72.10, 72.02, 71.56, 71.28, 71.14, 71.01, 70.39, 70.24, 70.07, 69.86, 69.78, 69.65, 69.15, 68.25, 68.14, 67.78, 67.72, 67.69, 67.26, 67.19, 66.86, 66.68, 66.59, 66.46, 65.95, 55.42, 51.55, 51.26, 51.03, 48.54, 31.82, 29.42, 27.90, 27.86, 27.78, 27.26, 27.13, 27.11, 23.43, 23.36, 23.32, 23.31, 21.96, 21.46, 21.38, 20.65, 20.62, 20.61, 17.04, 17.01, 16.95. HR-MS: Calculated for $C_{197}H_{248}N_6O_{54}Si_3$ $[M+H^+ + H^+]/2$: 1823.81489, found: 1823.81474. $[\alpha]^{20}_D$ = + 130.8° (c = 1, $CHCl_3$). TLC: Rf = 0.1 (DCM/MeOH = 50/1, v/v).

Nonamer of three repeating units 6



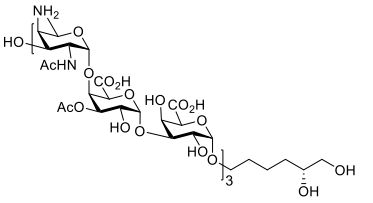
The compound **50** (102 mg, 28.0 µmol, 1.0 eq) was dissolved in THF (2 mL) and pyridine (2 mL), then cooled to 0 °C and hydrogen fluoride (HF)/pyridine (70%) (0.15 mL) was added dropwise. The solution was stirred for overnight. After TLC showed complete consumption of the starting material, the reaction was quenched with saturated aqueous sodium bicarbonate slowly and diluted with EtOAc. The solution was washed with water (2x) and brine. The aqueous layer was extracted with EtOAc (3x), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The compound was purified by flash chromatography (DCM/Acetone/MeOH 10:3:0.2 – 10:3:0.3) to yield compound **6** (86.2 mg, 26.7 µmol, 96%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.07 (m, 70H), 6.14 – 5.93 (m, 2H), 5.38 – 4.97 (m, 15H), 4.97 – 4.89 (m, 3H), 4.88 – 4.28 (m, 27H), 4.28 – 3.48 (m, 42H), 3.46 – 3.16 (m, 7H), 2.78 (d, *J* = 7.0 Hz, 1H), 2.51 (s, 1H), 2.14 – 1.94 (m, 18H, OAc, NHAc), 1.73 – 1.31 (m, 6H), 1.11 – 0.90 (m, 9H, H-6c). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.03, 171.13, 170.87, 170.01, 169.92, 169.86, 167.77, 167.72, 167.59, 157.53, 156.94, 138.80, 138.43, 138.36, 138.33, 138.14, 136.97, 136.90, 136.73, 136.43, 136.30, 134.21, 134.00, 133.95, 129.09, 128.96, 128.91, 128.89, 128.85, 128.80, 128.72, 128.68, 128.61, 128.59, 128.51, 128.46, 128.44, 128.42, 128.40, 128.36, 128.17, 128.09, 127.87, 127.74, 127.72, 127.70, 127.67, 127.23, 127.02, 98.69, 98.40, 98.18, 96.71, 95.23, 94.42, 94.23, 78.50, 78.00, 76.52, 76.15, 75.72, 75.23, 74.55, 74.26, 74.16, 74.05, 73.93, 73.40, 72.85, 72.81, 72.74, 72.61, 72.53, 72.47, 72.37, 72.00, 71.96, 71.82, 71.64, 70.77, 70.64, 70.40, 70.29, 70.12, 69.43, 68.83, 67.70, 67.61, 67.55, 67.33, 67.24, 66.97, 66.88, 66.56, 66.41, 65.98, 63.25, 63.01, 62.91, 55.28, 50.85, 48.41, 31.54, 29.73, 29.26, 23.60, 23.52, 23.28, 21.95, 21.39, 21.35, 17.01, 16.97, 16.91. HR-MS: Calculated for $C_{173}H_{200}N_6O_{54}$ $[M+2H^+]/2$: 1613.66170, found: 1613.66372. $[\alpha]^{20}_D$ = + 147.6 ° (c = 1, $CHCl_3$). TLC: Rf = 0.2 (DCM/Acetone/MeOH 10:3:0.3, v/v/v).

Nonamer of three repeating units 51



The compound **6** (16.1 mg, 4.99 µmol, 1.0 eq) was dissolved in MeCN/*tert*-BuOH/H_2O (700 µL, 4/1/2, v/v/v). The mixture was cooled to 0 °C and treated with TEMPO (1.9 mg, 12.2 µmol, 2.4 eq), BAIB (20 mg, 0.06 mmol, 12 eq) and $NaHCO_3$ (6.3 mg, 75 µmol, 15 eq). After stirring for 24 hours at 4 °C and TLC showed complete consumption of the starting material, saturated aqueous sodium thiosulphate was added and diluted with EtOAc, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was dissolved in DCM (2 mL), followed by addition of 0.2M phenyldiazomethane ($PhCHN_2$) in Et_2O (1 mL) at RT. After the mixture was allowed to stir overnight at rt and TLC showed complete consumption of the starting material, the reaction was diluted with EtOAc and washed with brine. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by preparative TLC plates (Macherey-Nagel, pre-coated TLC plates SIL G-100 UV254) (DCM/Acetone/MeOH 10:2:0.5) yielded **51** (11.6 mg, 3.28 µmol, 66%). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.49 – 6.99 (m, 85H), 6.03 – 5.79 (m, 3H), 5.40 – 5.20 (m, 10H), 5.20 – 5.09 (m, 4H), 5.07 – 4.80 (m, 10H), 4.77 (d, *J* = 11.8 Hz, 1H), 4.74 – 4.41 (m, 19H), 4.41 – 4.33 (m, 3H), 4.31 – 4.15 (m, 7H), 4.15 – 3.72 (m, 20H), 3.71 – 3.44 (m, 14H), 3.43 – 3.27 (m, 3H), 2.09 (s, 3H), 2.05 – 1.92 (m, 15H), 1.65 – 1.36 (m, 6H), 1.07 – 0.90 (m, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.10, 171.16, 170.96, 170.18, 169.98, 169.89, 168.56, 168.49, 167.83, 167.71, 167.49, 157.60, 156.94, 138.96, 138.46, 138.21, 138.01, 136.95, 136.71, 136.62, 136.52, 136.25, 135.49, 135.43, 135.38, 134.17, 134.06, 134.02, 129.22, 129.06, 129.00, 128.96, 128.87, 128.86, 128.81, 128.77, 128.74, 128.72, 128.64, 128.61, 128.58, 128.55, 128.53, 128.51, 128.45, 128.36, 128.34, 128.09, 128.06, 127.93, 127.91, 127.86, 127.79, 127.77, 127.73, 127.67, 127.63, 127.46, 127.44, 98.65, 98.59, 98.10, 97.08, 95.48, 95.25, 94.52, 77.98, 76.31, 76.24, 76.11, 74.85, 74.28, 74.11, 73.96, 73.83, 73.71, 73.46, 73.12, 73.01, 72.83, 72.72, 72.62, 72.12, 72.06, 70.67, 70.46, 70.26, 70.17, 69.98, 69.81, 69.46, 68.84, 67.75, 67.65, 67.46, 67.27, 67.18, 67.13, 66.59, 65.92, 64.75, 55.33, 51.96, 51.28, 50.94, 48.50, 32.06, 31.87, 29.50, 29.48, 23.48, 23.33, 22.84, 21.97, 21.44, 19.25, 17.15, 17.10. HR-MS: Calculated for $C_{194}H_{212}N_6O_{57}$ $[M+NH_4^+ + NH_4^+]/2$: 1778.21429, found: 1778.21433. $[\alpha]^{20}_D$ = + 127.1° (c = 1, $CHCl_3$). TLC: Rf = 0.35 (DCM/Acetone/MeOH 10:2:0.5, v/v/v).

The deprotection of Nonamer 3



The protected nonamer **51** (13 mg, 3.68 µmol, 1.0 eq) was dissolved in *tert*-butanol (7 mL) and 0.1% AcOH in water (2 mL). After $Pd(OH)_2$/C (60 mg) was added, the reaction was stirred for 3 days under a H_2 atmosphere, filtered and concentrated *in vacuo* to yield compound **3** (6.2 mg, 3.3 µmol, 90%). ^{1}H NMR (600 MHz, Deuterium Oxide) δ 5.38 – 5.26 (m, 6H), 5.13 – 5.08 (m, 2H), 5.08 – 5.02 (m, 2H), 5.02 – 4.96 (m, 2H), 4.75 – 4.69 (m, 2H), 4.68 – 4.55 (m, 7H), 4.54 – 4.47 (m, 3H), 4.34 – 4.11 (m, 11H), 4.10 – 3.92 (m, 7H), 3.85 – 3.78 (m, 2H), 3.76 – 3.68 (m, 2H), 3.62 – 3.53 (m, 3H), 3.50 – 3.44 (m, 1H), 2.27 – 2.21 (m, 9H), 2.14 – 2.09 (m, 4H), 2.08 – 2.02 (m, 5H), 1.76 – 1.45

(m, 6H), 1.39 – 1.32 (m, 9H). ^{13}C NMR (151 MHz, D_2O) δ 176.02, 175.55, 175.13, 175.03, 174.51, 174.43, 100.17, 99.79, 99.38, 99.26, 98.71, 98.62, 97.37, 97.04, 96.92, 78.32, 77.67, 77.60, 76.82, 76.45, 74.18, 73.89, 73.17, 72.91, 72.84, 72.67, 72.59, 72.14, 71.89, 71.78, 71.65, 69.24, 68.83, 68.68, 67.45, 67.18, 67.15, 66.67, 66.58, 66.32, 65.63, 64.80, 63.94, 55.99, 53.86, 53.71, 50.25, 48.53, 35.38, 32.85, 29.46, 23.31, 23.22, 22.38, 21.74, 21.73, 16.92. HR-MS: Calculated for $C_{72}H_{110}N_6O_{51}$ $[M+2H^+]/2$: 938.31720, found: 938.31596.

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