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Galacturonic Acid Lactones in the Synthesis of All Trisaccharide Repeating Units of the Zwitterionic Polysaccharide Sp1

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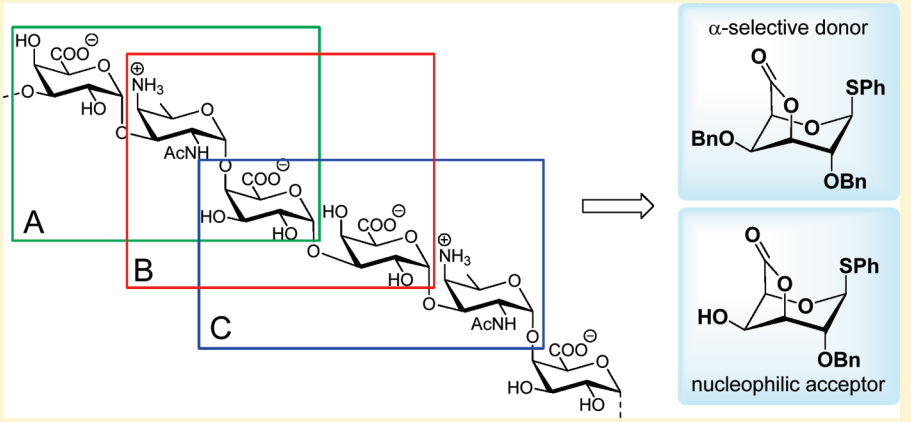
Supporting Information

ABSTRACT:



A modular approach toward the synthesis of all possible trimer repeating units of the type 1 capsular polysaccharide of *Streptococcus pneumonia*, Sp1, is described. This zwitterionic polysaccharide is built up from trisaccharide repeats, which in turn are composed of two galacturonic acid monomers and a 2,4,6-trideoxy-4-amino-2-acetamido-D-galactose moiety. All monomeric constituents are linked through *cis*-glycosidic bonds. To overcome the difficulty associated with the efficient stereoselective introduction of the α-galacturonic acid bonds, we have employed galacturonic acid-[3,6]-lactone building blocks. Not only did these building blocks perform well when used as donor galactosides, they were also shown to be reactive acceptor glycosides when equipped with a free hydroxyl function. All three frame-shifted trimer repeats were constructed via highly stereoselective glycosylation reactions, with one exception. The epimeric mixture of trisaccharides, formed in the nonselective glycosylation event, could be readily separated after global deprotection using high performance anion exchange chromatography (HPEAC).

INTRODUCTION

Zwitterionic polysaccharides (ZPs) present an unique class of polysaccharides from both a structural and a biological perspective.[1,2] These bacterial polysaccharides contain both basic amino functions and acidic carboxylate groups, accommodating them with a zwitterionic character at physiological pH. This not only distinguishes them from other naturally occurring polysaccharides but also bestows them with distinctive biological activity. ZPs are the only class of polysaccharides that is capable of eliciting a T-cell-dependent immune response, a mode of action that was long thought to be confined to peptides.[1,2] Indeed, the sole manner in which regular polysaccharides could be applied in effective vaccine formulations has been through conjugation to immunostimulatory carrier proteins.[3] Without these proteins, (capsular) polysaccharides are processed by antigen presenting cells but not presented by MHC class II proteins to T-cells, a key step in the realization of adaptive immune responses. In contrast, ZPs are capable of stimulating CD-4+ T-cell proliferation, after being presented via the MHC-II processing pathway.[2,4,5] In addition, ZPs have also been shown to stimulate the innate immune system through interaction with the Toll-like receptor 2 (TLR2).[6] To elucidate the mode of action of ZPs at the molecular level, well-defined ZPs fragments can serve as valuable tools.[7] We therefore set out to develop a strategy to synthesize fragments of the *S. pneumonia* zwitterionic polysaccharide. *S. pneumonia* is the causative agent of pneumonia, bacteremia, otitis media, meningitis, and peritonitis,[8] and one of its capsular polysaccharides, Sp1, is a prominent member of the ZPs family.[4,9] Sp1 is an overall anionic polysaccharide built up from nonbranching [→3)-α-2,4,6-trideoxy-4-amino-D-GalNAc-(1→4)-α-D-GalA*p*-(1→3)-α-D-GalA*p*-(1→]^{10} trisaccharide repeats, as depicted in Figure 1. The trimer repeat contains two α-D-galacturonic acids in addition to the rare α-2,4,

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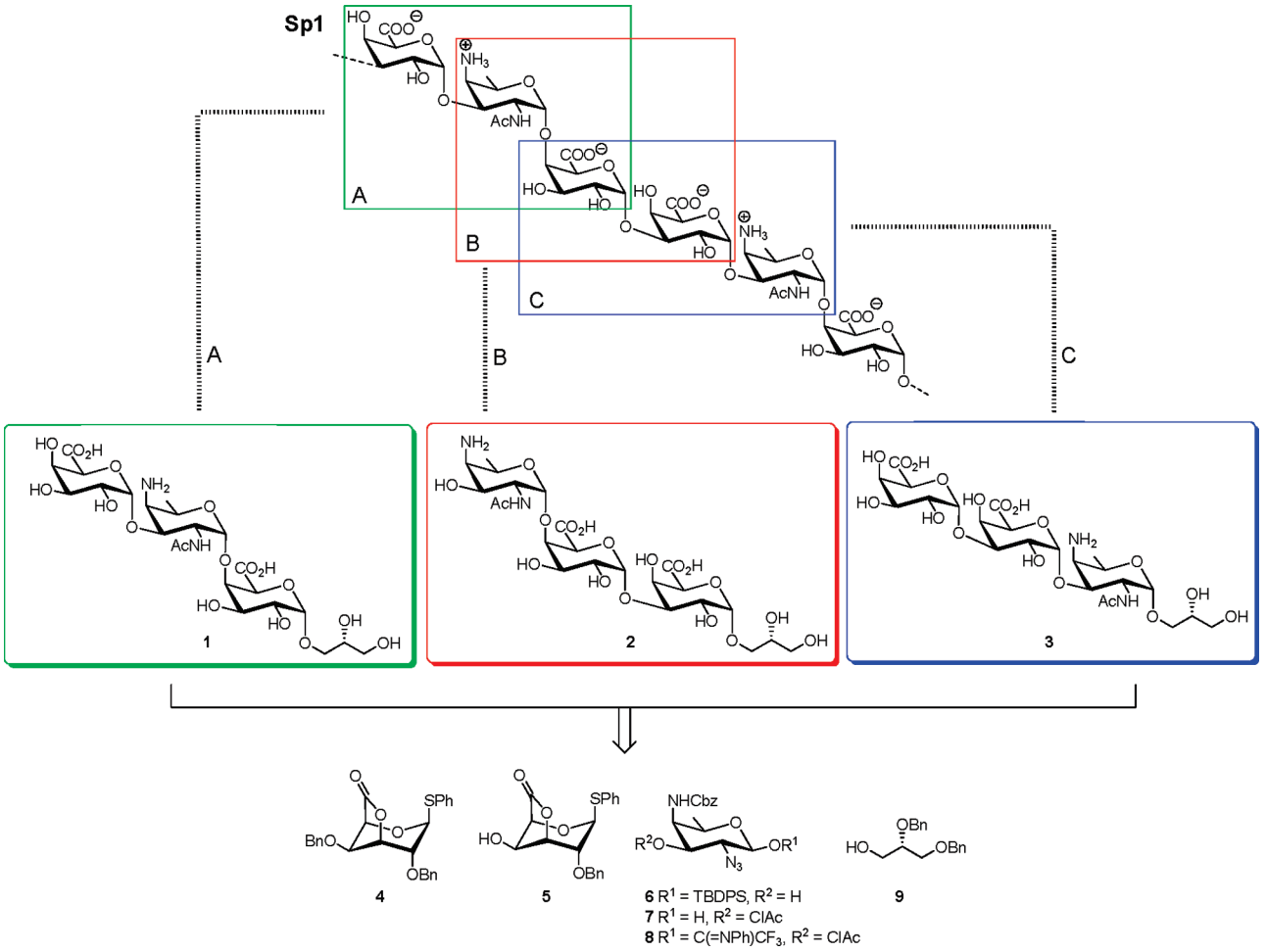

Figure 1. Sp1 polysaccharide and our retrosynthetic strategy toward the three frame-shifted trimer repeats **1**−**3**.

6-trideoxy-4-amino-2-acetamido-D-galactose moiety. We here report the assembly of all three possible spacers containing Sp1 repeating units **1**−**3** (Figure 1).

RESULTS AND DISCUSSION

The synthesis of (fragments of) the Sp1 oligosaccharide is complicated by the presence of the uronic acid moieties and the rare 2,4,6-trideoxy-4-amino-D-GalNAc monosaccharide,[7,11,12] which are interconnected through 1,2-*cis*-glycosidic bonds. Different approaches have been pursued for the introduction of uronic acids in oligosaccharide chains.[13] These can be introduced at the monosaccharide level in a pre-glycosylation oxidation strategy, which uses glycuronic acid building blocks as donor and acceptor in the construction of the target oligomer. Alternatively, a post-glycosylation−oxidation approach can be followed in which the oligosaccharide backbone is built up prior to the installment of the carboxylate functions. Galacturonic acids are generally considered to be relatively poor glycosyl donors[14,15] because of the electron-withdrawing effect of the C-5 carboxylic acid ester. Similarly, the C-5 carboxylate exerts a deactivating effect on the nucleophilicity of the proximal hydroxyl functions, which explains why the C-4 hydroxyl group in galacturonic acid acceptors has been regarded as a poor nucleophile.[16] In the first synthesis of two Sp1-oligomers, Bundle and co-workers therefore resorted to the use of nonoxidized galactose building blocks in a postglycosylation oxidation approach.[15] For the synthesis of all three frame-shifted repeating units of the Sp1 saccharide, we opted for a modular strategy in which monomeric building blocks can be combined in a flexible manner, as retrosynthetically depicted in Figure 1. To limit the amount of synthetic transformations at the oligosaccharide stage, and especially avoid the late-stage multiple oxidation step, we explored the use of C-6 oxidized galactosyl building blocks. We have previously described that conformationally locked 1-thiogalacturonic acid lactone donors show excellent reactivity[17,18] as well as anomeric selectivity in glycosidations to provide α-linked galacturonides in excellent yield.[19] This makes them attractive donor glycosides in the assembly of the target Sp1-oligomers. Additionally, the inverted $^{1}C_{4}$-chair conformation of the galacturonic acid-[3,6]-lactones positions the C4-OH equatorially, as opposed to the less accessible axial orientation in the normal $^{4}C_{1}$-chair.[20] In the synthesis of L-guluronate alginate oligomers, Hung and co-workers have shown that changing the orientation of the C4-OH of a gulosyl acceptor from an axial to an equatorial position, by locking the L-gulosyl ring in a $^{4}C_{1}$-conformation with an 1,6-anhydro bridge, increases the nucleophilicity of the C4-OH.[21] We reasoned that the inversion of the galacturonic acid chair conformation in the lactone synthons can have a similar beneficial effect on the galacturonic acid C4-hydroxyl. Thus, for our assembly of the Sp1-repeating units we envisaged two galacturonic

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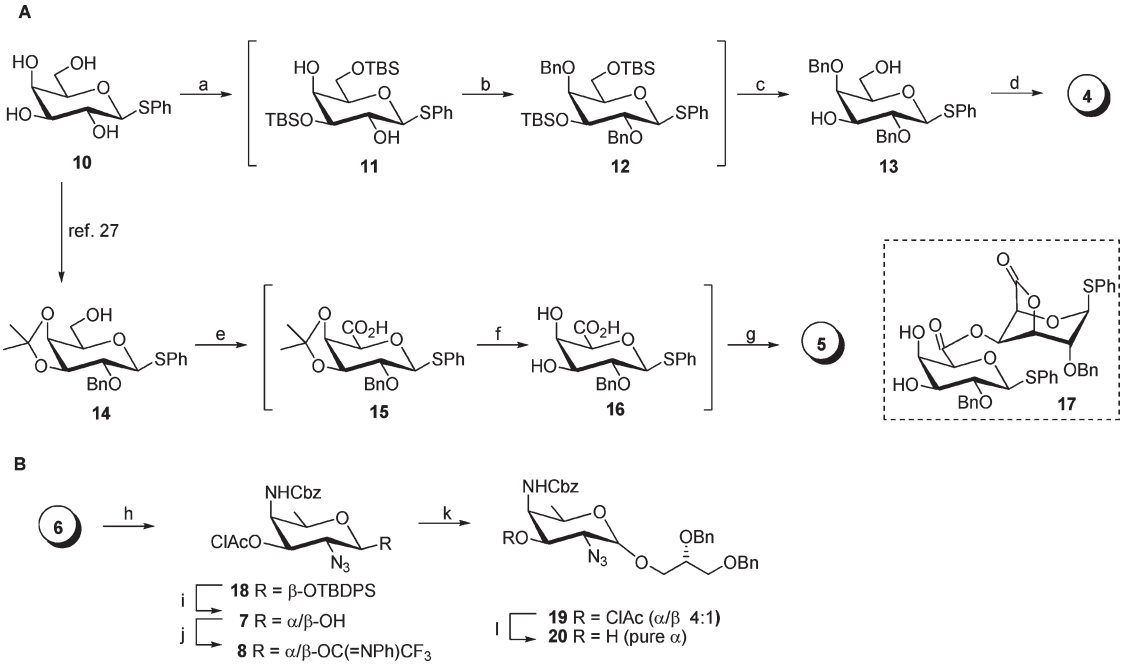
Scheme 1[a]



[a] Reagents and conditions: (a) TBDMSCl, imidazole, DMF; (b) BnBr, NaH, DMF, 0 °C; (c) TBAF, THF, 80% (over three steps); (d) TEMPO, BAIB, DCM, H_2O, 75%; (e) TEMPO, BAIB, DCM, H_2O; (f) AcOH/H_2O (4/1 v/v), 60 °C; (g) ethyl chloroformate, DiPEA, THF, 34% (over three steps); (h) $(ClAc)_2O$, pyridine, DCM, quant; (i) triethylamine·3HF, THF, 98%; (j) $ClC(=NPh)CF_3$, Cs_2CO_3, H_2O, acetone, 83% (α/β 1:3); (k) acceptor **9**, cat. TfOH, DCM/Et_2O (1/1 v/v), 0 °C, quant (α/β 4:1); (l) thiourea, EtOH, pyridine, 65°C, 78% for **20**, 16% for the β-anomer.

acid lactones: fully protected lactone thioglycoside **4** and acceptor lactone **5**. These will be combined with suitably protected 2,4,6-trideoxy-4-amino-D-galactosamine building blocks **6**−**8** bearing a nonparticipating azide functionality at C2 and a benzyloxycarbonyl (*Z*)-protected amine at C4 (Figure 1). In our synthetic plan, we capped the reducing ends of the trimer repeating units with a glycerol spacer.[22]

Synthesis of the Building Blocks. The synthesis of the required building blocks is depicted in Scheme 1. The assembly of the galacturonic acid lactone building blocks **4** and **5** started from known β-1-thiogalactoside **10** (Scheme 1A).[23] Selective silylation of the C-3 and C-6 hydroxyls in **10** led to diol **11**,[24] which was used without purification in the ensuing benzylation step to provide the fully protected galactoside **12**. Desilylation of crude **12** using tetrabutylammonium fluoride in THF led to the isolation of diol **13**, which was isolated in 80% yield over the three steps. 2,2,6,6-Tetramethyl-1-piperidinyloxy(TEMPO)/[bis(acetoxy)iodo]benzene (BAIB)-mediated oxidation[25,26] of the primary alcohol in **13** was followed by in situ lactone formation to provide the target galacturonic acid lactone **4** in one step, as we described previously.[19]

To construct galacturonic acid lactone acceptor **5**, β-1-thiogalactoside **10** was transformed into partially protected **14** following an one-pot procedure reported by Sinaÿ and coworkers.[27] TEMPO/BAIB-mediated oxidation of the primary hydroxyl and subsequent acidic hydrolysis of the acetonide gave crude acid **16**.[28] Lactonization of the acid was accomplished using ethyl chloroformate to generate the mixed anhydride, which cyclized to give **5** in 34% yield over the last three steps.[29] The concentration at which this lactonization step was performed turned out to be of vital importance to the outcome of the reaction. Insufficiently diluted conditions afforded **17** as a side

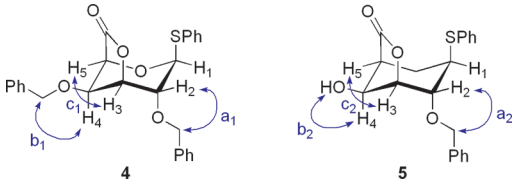


Figure 2. Schematic representation of observed crosspeaks from 2D NMR experiments with lactone building blocks **4** (a1, H2-CH_2 Bn (HMBC); b1, H4-CH_2 Bn (HMBC); c1, H3−H5 (COSY)) and **5** (a2, H2-CH_2 Bn (HMBC); b2, H4-OH (COSY); c2, H3−H5 (COSY)) whereupon the assignment of peaks was based.

product, providing an indication that the equatorially oriented hydroxyl function in lactone acceptor **5** is a reactive nucleophile. The structure of the lactone building blocks **4** and **5** was fully ascertained by NMR spectroscopy using ^1H, ^{13}C, $^1H-^1H$ COSY, and $^1H-^{13}C$ HSQC data (Figure 2). A vicinal coupling of H-4 with 4-OH in **5** led to spectral allocation of the H-4 proton signal in the spectrum of **5**. The resonance of H-3 was assigned on the basis of its relatively large chemical shift.[30] Because the ^1H NMR spectrum of **5** showed a coupling of H-3 with both H-2 and H-5,[31] the latter two protons were distinguished by a long-range $^1H-^{13}C$ HMBC NMR experiment, in which a clear cross peak between H-2 and the benzylic carbon was revealed. In this experiment, a crosspeak between C-6 and H-3 was also observed. Chemical shift similarities in the spectra of **4** and **5**, in combination with a $^1H-^{13}C$ HMBC NMR experiment, which revealed a crosspeak between H-4 of **4** and a benzylic carbon, led to the full assignment of the resonance sets belonging to lactone **4**.

The construction of the required 2,4,6-trideoxy-4-amino-D-galactosamine building blocks[7,11,18,32] is outlined in Scheme 1B.

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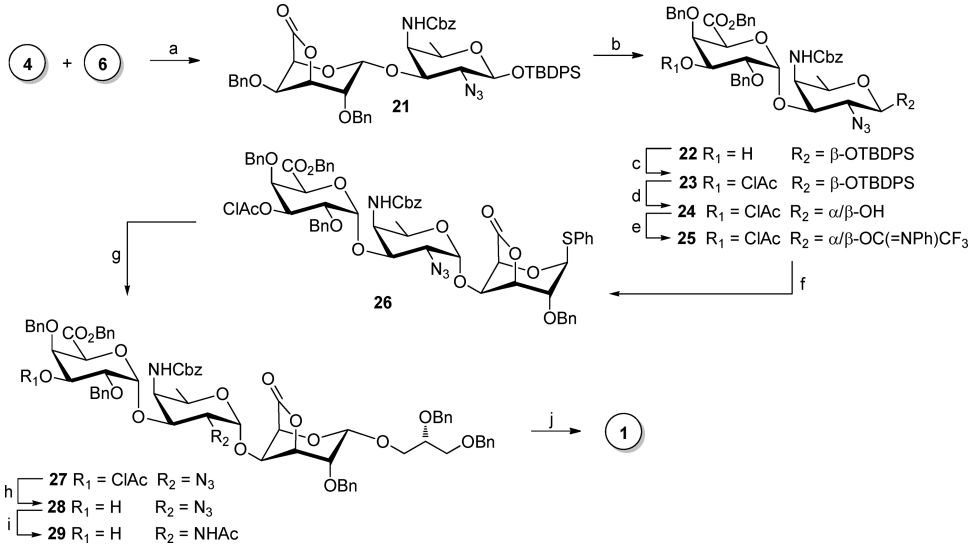
Scheme 2[a]



[a] Reagents and conditions: (a) **4**, Ph_2SO, Tf_2O, DCM, TTBP, −60 °C then acceptor **6**, 75%; (b) BnOH, AcCl, 50°C, overnight (quant); (c) $(ClAc)_2O$, pyridine, 93%; (d) triethylamine·3HF, THF, 84% (α/β 1:4); (e) ClC(=NPh)CF_3, Cs_2CO_3, H_2O, acetone, 85%; (f) acceptor **5**, cat. TfOH, DCM, 81% (α/β 8:1); (g) Ph_2SO, Tf_2O, DCM, TTBP, −60°C then acceptor **9** (81%); (h) thiourea, EtOH, pyridine, 65 °C, 76%; (i) AcSH/pyridine (1/1 v/v), 94%; (j) TMSONa, DCM, then H_2/Pd(C), *t*-BuOH, H_2O, HCl (52% over two steps).

We have recently reported the synthesis 2-azido-4-(benzyloxycarbonyl)amino-2,4,6-trideoxy-D-galactose building blocks in the context of the synthesis of the tetrasaccharide repeating unit of the *Bacteroides fragilis* ZPs,[7] and building block **6** was obtained from D-glucosamine using very similar procedures.[33] Lactol **7** was obtained from **6** by chloroacetylation of the C-3 OH, followed by anomeric desilylation. From **7**, donor **8** was readily obtained by installment of the *N*-phenyltrifluoroimidate function.[34] Imidate **8** was condensed with glycerol acceptor **9**, accessible from solketal following literature procedures,[35] under the agency of a catalytic amount of triflic acid (TfOH) in dichloromethane to provide **19** as a 1:1 mixture of inseparable anomers. Although the use of a DCM/Et_2O solvent system in this glycosylation event led to the preferential formation of the α-anomer,[36] the anomers remained inseparable at this stage. Fortunately, after dechloroacetylation of **19**, the epimers were separable by flash column chromatography, and 2,4,6-trideoxy-4-amino-D-galactosamine building block **20** was obtained in 78% from **19**, alongside 16% of its C1-epimer.

Assembly of the Trimer Repeats. With all monomeric building blocks in hand, we set out to assemble the three frame-shifted trimer repeats **1**−**3**. The synthesis of the first trisaccharide started with the coupling of lactone **4** and 2,4,6-trideoxy-4-amino-D-galactosamine **6** (Scheme 2). To this end, donor **4** was preactivated using in situ generated diphenylsulfonium bistriflate[37] and subsequently treated with acceptor **6** to give disaccharide **21** in good yield and excellent stereoselectivity. Opening of the lactone ring using benzyl alcohol under acidic conditions[19] afforded benzyl ester **22** quantitatively. Chloroacetylation of the liberated hydroxyl functionality, anomeric desilylation, and installment of the *N*-phenyltrifluoroimidate function then led to dimeric glycosyl donor **25**. Coupling of this donor with lactone acceptor **5** employing TfOH as a promoter gave *S*-phenyl trimer **26** in 81% yield and 8:1 α/β selectivity, showcasing the apt nucleophilicity of lactone acceptor **5**. The α-epimer of thioglycoside **26** could be isolated through column chromatoghraphy (64%) and was subsequently condensed with acceptor **9** in a Ph_2SO/Tf_2O-mediated preactivation glycosylation event furnishing the fully protected glycerol capped trisaccharide **27** as the sole anomer. Global deprotection started with removal of the chloroacetylgroup to give alcohol **28**. Reduction of the azide in **28** with either PMe_3 or dithiothreitol and ensuing acetylation of the amine and free C3″-OH gave only low yields of the desired product. The use of freshly distilled thiolacetic acid and pyridine on the other hand, gave acetamide **29** in 94% yield,[38] with the alcohol functionality still intact. Studies to open the lactone ring in compound **30** (vide infra) prompted us to use TMSONa as nucleophilic reagent to hydrolyze the lactone functionality in **29**.[39] Hydrogenolysis of the remaining benzyl ester, benzyloxy carbamate, and benzyl ethers then furnished the first target trisaccharide **1** in 52% yield over the last two steps.

For the construction of trisaccharide **2**, lactone donor **4** was converted into glycerol-capped galacturonic acid ester acceptor **31** (Scheme 3). To this end, lactone donor **4** was coupled with acceptor **9** in a Ph_2SO/Tf_2O-mediated glycosylation to yield **30** with excellent anomeric selectivity (α/β = 10:1). Unfortunately, the acid-catalyzed opening of lactone **30** in benzyl alcohol as described above did not lead to the anticipated product. Instead, we observed a product resulting from the endocyclic opening of the galactopyranosyl core (**32**). Use of Bu_2SnO[40] in BnOH did give the desired product, but only in low yields. Finally, we succeeded in opening the lactone ring using TMSONa to afford the free acid, which was subsequently treated with benzyl bromide and Cs_2CO_3 providing the reducing end galacturonic acid acceptor **31** in 75% yield. Next, hemiacetal **7** and key lactone acceptor **5** were coupled under the agency of Ph_2SO and Tf_2O to stereoselectively form the α-linked dimer **33** in 84% yield. The generated thioglycoside **33** was engaged next in a glycosylation event with spacer-capped galacturonic acid ester acceptor **31** to produce the fully protected trisaccharide **34**, again with complete α-selectivity. To deliver target compound **2**, the same global deprotection strategy was envisioned as used previously for the fully protected trisaccharide **27**. Thus, dechloroacetylation with

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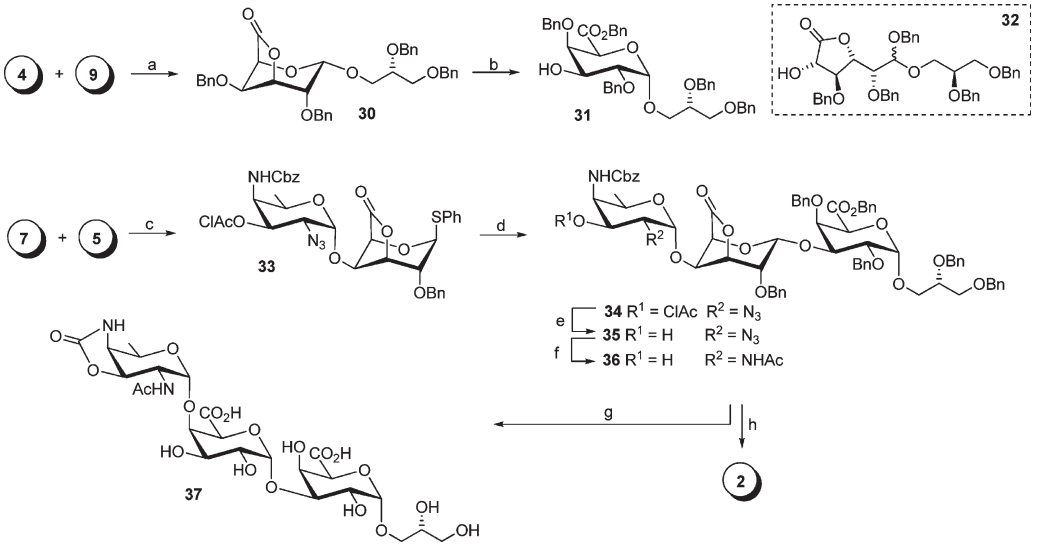
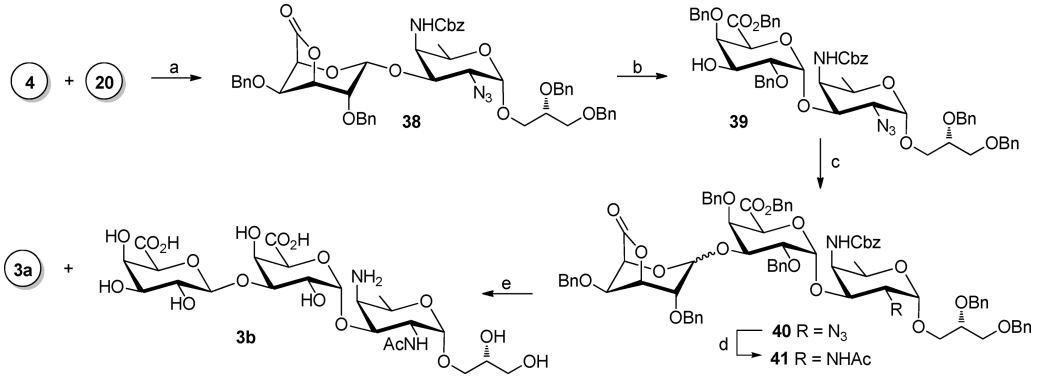
Scheme 3[a]



[a] Reagents and conditions: (a) **4**, Ph_2SO, Tf_2O, DCM, TTBP, −60 °C then acceptor **9**, 93% (α/β 10:1); (b) (1) TMSONa, DCM, (2) BnBr, Cs_2CO_3, DMF, 75% (two steps); (c) **7**, Ph_2SO, Tf_2O, DCM, TTBP, −60 °C then acceptor **5**, 84%; (d) **33**, Ph_2SO, Tf_2O, DCM, TTBP, −60°C then acceptor **31**, 60%; (e) thiourea, EtOH, pyridine, 65 °C, 62%; (f) thiolacetic acid/pyridine (1/1 v/v), 66%; (g) TMSONa, DCM, then H_2/Pd(C), *t*-BuOH, H_2O, HCl (38%); (h) H_2/Pd(C), *t*-BuOH, H_2O, HCl, then H_2O, HCl (38%).

Scheme 4[a]



[a] Reagents and conditions: (a) **4**, Ph_2SO, Tf_2O, DCM, TTBP, −60 °C then acceptor **20**, 70%; (b) (1) TMSONa, DCM, (2) BnBr, Cs_2CO_3, DMF, 88% (over two steps); (c) **4**, Ph_2SO, Tf_2O, DCM, TTBP, −60 °C then acceptor **39**, 78%; (d) AcSH, pyridine, 40%; (e) TMSONa, DCM, then H_2/Pd(C), *t*-BuOH, H_2O, HCl, **3a**: 28%, **3b**: 17%.

thiourea was followed by reduction of the azide group using AcSH and simultaneous N-acetylation to produce acetamide **36**. Unfortunately, treatment of **36** with TMSONa in dichloromethane and ensuing hydrogenolysis did not afford the anticipated trisaccharide **2**. Instead, oxazolidinone **37** was obtained as a result from intramolecular nucleophilic attack of the 3″-OH onto the nearby benzyl carbamate during the TMSONa treatment. The formation of the oxazolidinone could be circumvented by reversal of the lactone ring-opening and reduction steps. Hydrogenolysis of acetamide **36** under mildly acidic conditions provided the crude trimer lactone. The ^{1}H NMR spectrum of the crude lactone recorded directly after hydrogenolysis already showed partial hydrolysis of the lactone ring, and therefore, the crude lactone was further subjected to mild acidic hydrolysis conditions to provide the target trimer **2** in 38% over the last two steps.

The assembly of the third and last trisaccharide **3** commenced with the sulfonium bistriflate-mediated condensation of lactone donor **4** and acceptor **20**. As depicted in Scheme 4, disaccharide **38** was produced in a completely α-selective fashion in 70% yield. TMSONa opening of the lactone functionality in **38** and subsequent benzyl ester installment set the stage for the next glycosylation event, in which key lactone donor **4** was employed again. The coupling of **4** and **39**, proceeded without any selectivity, and trisaccharide **40** was isolated as an inseparable 1:1 mixture in 78% yield. Changing the solvent system to either toluene or acetonitrile in dichloromethane did not significantly alter the stereochemical outcome of the glycosylation. In light of the excellent α-selectivity of all previous condensations using the galacturonic acid-[3,6]-lactone donors, and especially the coupling of **33** with galacturonic acid acceptor **31**, the lack of selectivity in the condensation of **4** and **39** is surprising, and we have no adequate explanation for this result at this moment. Global deprotection of the epimeric mixture was accomplished by reduction of the azide in **40** and concomitant acetylation to

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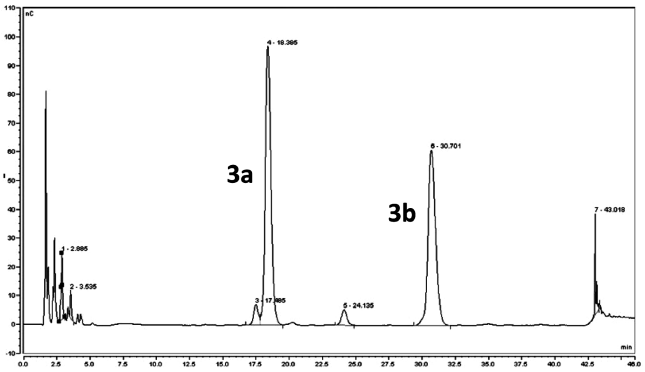

Figure 3. Dionex HPAEC (high performance an-ion exchange chromatography) trace of the epimeric mixture obtained after hydrogenation of **41** under acidic conditions, showing a retention time difference of 12.32 min between both epimers. Recovery: 28% for **3a** and 17% for **3b** (over two steps from **41**).

give acetamide **41** in moderate yield. Then, TMSONa-mediated lactone hydrolysis and ensuing removal of the remaining protective groups left us with a crude epimeric mixture of fully deprotected trisaccharides. The two anomers could be separated by high performance anion exchange chromatography (HPAEC).[41] The use of a gradient of 30−80 mM NaOAc in 100 mM NaOH led to the elution of the α- and β-epimers with a retention time difference of over 10 min, as depicted in Figure 3. Preparative ion-exchange chromatography gave us target C-1″-α-configured trisaccharide **3a** (28% over the last two steps) and its β-epimer **3b** (17% over the last two steps) in pure form. The structures of the trisaccharides were corroborated by NMR spectroscopy. The heteronuclear one-bond coupling constant of C-1″ and H-1″ in **3a** ($^1J_{C-H}$ = 170.3 Hz) and **3b** ($^1J_{C-H}$ = 161.5 Hz) unambiguously confirmed the α-anomeric configuration for the former and the β-anomeric configuration for the latter trisaccharide.

CONCLUSION

In summary, we have described the synthesis of all three frame-shifted trisaccharide repeats of the zwitterionic polysaccharide Sp1 of *S. pneumonia* exploiting the use of 1-thio galacturonic acid lactones as key donor and acceptor building blocks. The galacturonic acid-[3,6]-lactones proved to be efficient donor galactosides for the construction of the galacturonic acid-containing target compounds. The yields of the glycosylations using the lactone donors were good to excellent and in all but one of the galacturonylations very high α-selectivities were observed. For the unexpected lack of α-selectivity in the condensation of key lactone donor **4** and dimer acceptor **39** there currently is no satisfactory explanation. In addition to being adequate donor glycosides, the galacturonic acid lactones were also shown to be excellent nucleophiles when equipped with a free C4-hydroxyl function. The $^1C_4$-chair conformation of lactone **5** places the C4-hydroxyl in an equatorial position which makes it significantly more reactive toward incoming electrophiles. It is envisaged that this strategy can also be applied to other glycuronic acid acceptors. Finally, HPAEC proved to be a powerful purification technique for this class of compounds as the difference in one stereochemical center led to a significant difference in retention time, allowing the separation of the two epimers.

EXPERIMENTAL SECTION

General Procedure for Glycosylations Using Ph_2SO/Tf_2O. A solution of donor (1 equiv), diphenyl sulfoxide (1.1 equiv), and tri-*tert*-butylpyrimidine (1.5 equiv) in DCM (0.05M) was stirred over activated molecular sieves (3 Å) for 30 min. The mixture was cooled to −60 °C before triflic acid anhydride (1.1 equiv) was added. The mixture was allowed to warm to −45 °C and was subsequently recooled to −60 °C before a mixture (dried over 3 Å molecular sieves) of acceptor (1.5 equiv) and tri-*tert*-butylpyrimidine (1.0 equiv) in a small amount of DCM was added. Stirring was continued, and the reaction mixture was allowed to warm to −10 °C. The reaction mixture was quenched with triethylamine (5.0 equiv), diluted with DCM, and washed with satd aq $NaHCO_3$. The aqueous phase was extracted with DCM, and the combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Flash column chromatography and removal of the eluent afforded the coupled product.

Phenyl 2,4-Di-*O*-benzyl-1-thio-β-D-galactopyranoside (13). To a mixture of 10.0 g of phenyl-1-thiogalactopyranoside in 150 mL of DMF (36.8 mmol, 1 equiv) was added 8.77 g of imidazole (128.8 mmol, 3.5 equiv) and 16.64 g of TBSCl (110.4 mmol, 3 equiv). After 2 h of stirring, TLC analysis showed complete consumption of the starting material. The reaction was quenched by the addition of 3 mL of MeOH. The mixture was partitioned between H_2O and Et_2O, and the aqueous layer was extracted. The combined organic phases were washed with aq 1 M HCl, satd aq $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and evaporated. The crude product was dissolved in 150 mL of DMF, and to this solution were added 13.2 mL of BnBr (110.4 mmol, 3 equiv) and 4.42 g of NaH (60% in mineral oil, 110.4 mmol, 3 equiv) at 0 °C. After being stirred at ambient temperature overnight, the reaction was quenched with MeOH at 0 °C, taken up in Et_2O, and washed with 5% aq LiCl and brine. After drying over $MgSO_4$, filtration, and concentration under reduced pressure, the residue was dissolved in 40 mL of THF and treated with 146.8 mL of 1.0 M TBAF (in THF, 146.8 mmol, 4 equiv). The mixture was stirred for 3 h and subsequently taken up in EtOAc and H_2O. The water layer was further extracted with EtOAc, and the combined organic layers were dried ($MgSO_4$), filtered, and evaporated. Purification by flash column chromatography using EtOAc/PE (7/13 → 9/11) afforded the target compound **13** (13.4 g, 29.6 mmol, 80% over three steps): R_f 0.27 (EtOAc/PE, 1/1, v/v); $[\alpha]^{22}_D$ +1 (*c* 1.4, $CHCl_3$); IR (neat, cm^{-1}) 1311, 1049, 1018, 871, 732, 640, 694; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.53 (m, 2H, H_{arom}), 7.43−7.09 (m, 13H, H_{arom}), 4.90 (d, *J* = 10.8 Hz, 1H, CH_2 Bn), 4.76 (d, *J* = 11.6 Hz, 1H, CH_2 Bn), 4.68−4.54 (m, 3H, CH_2 Bn, H-1), 3.84 (dd, *J* = 11.0, 7.4 Hz, 1H, H-6), 3.75 (s, 1H, H-4), 3.74−3.65 (m, 2H, H-2, H-3), 3.56 (dd, *J* = 11.2, 4.5 Hz, 1H, H-6), 3.49−3.42 (m, 1H, H-5), 2.41 (bs, 1H, OH), 2.03 (bs, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 138.0, 137.9, 133.9 (C_q Ph), 131.2, 128.9, 128.5, 128.4, 128.3, 128.0, 127.9, 127.2 (CH_{arom}), 87.1 (C-1), 79.0 (C-5), 78.1 (C-2), 75.8, 75.7 (C-3, C-4), 75.2, 74.7 (CH_2 Bn), 62.1 (C-6); HRMS $[M + Na]^+$ calcd for $C_{26}H_{28}N_3O_5SNa$ 475.15497, found 475.15567.

Phenyl 2,4-Di-*O*-benzyl-1-thio-β-D-galactopyranosiduro-no-3,6-lactone (4). The thioglycoside lactone was synthesized as reported previously, and all physical and spectroscopic data were in accordance with the published data:[25] Previously, assignments of H-4 and H-5 as well as C-4 and C-5 were interchanged. See ref 25. ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.63−7.09 (m, 15H, H_{arom}), 5.41 (s, 1H, H-1), 4.80 (dd, *J* = 4.7, 1.3 Hz, 1H, H-3), 4.65 (d, *J* = 11.8 Hz, 1H, CH_2 Bn), 4.59 (2s, 2H, CH_2 Bn), 4.54 (d, *J* = 11.8 Hz, 1H, CH_2 Bn), 4.39 (br s, 1H, H-4), 4.27 (d, *J* = 4.7 Hz, 1H, H-2), 4.04 (br s, 1H, H-5); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC): δ 172.6 (C═O), 136.7, 136.5, 133.6 (C_q Ph), 132.7, 129.0, 128.7, 128.6, 128.5, 128.3, 128.1, 128.0, 127.8 (CH_{arom}), 85.8 (C-1), 78.9 (C-3), 78.6 (C-2), 76.0 (C-4), 73.0 (CH_2 Bn), 71.5 (CH_2 Bn), 70.8 (C-5).

Phenyl 2-*O*-Benzyl-1-thio-β-D-galactopyranosiduro-no-3,6-lactone (5). To a vigorously stirred solution of 3.59 g of

phenyl 2-*O*-benzyl-3,4-*O*-isopropylidene-1-thio-β-galactopyranoside (8.93 mmol, 1 equiv) in 30 mL of DCM and 15 mL of H_2O was added 279 mg of TEMPO (1.79 mmol, 0.2 equiv) and 7.19 g of BAIB (22.3 mmol, 2.5 equiv). After 2 h of stirring at room temperature, $Na_2S_2O_3$ solution (10% in H_2O) was added, and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and evaporated. The crude acid was stirred at 65 °C in 20 mL of AcOH/H_2O (4/1 v/v) until TLC analysis showed disappearance of the starting material. The mixture was concentrated in vacuo and coevaporated with toluene. The crude product was dissolved in 350 mL of anhydrous DCM followed by addition of 1.77 mL of Dipea (10.7 mmol, 1.2 equiv) and 939 μL of ethyl chloroformate (9.82 mmol, 1.1 equiv). After 3 h of stirring at ambient temperature, the mixture was evaporated, and lactone **5** was obtained in pure form after flash column chromatography using EtOAc/PE (1/4 → 1/3) (1.08 g, 3.0 mmol, 34% over three steps): R_f 0.26 (EtOAc/PE, 3/7, v/v); $[\alpha]^{22}_D$ −223 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 3440, 1794, 1095, 1055, 694; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.45−7.23 (m, 10H, H_{arom}), 5.39 (s, 1H, H-1), 4.77 (dd, *J* = 4.7, 1.3 Hz, 1H, H-3), 4.62−4.50 (m, 3H, H-4, CH_2 Bn), 4.22 (d, *J* = 4.7 Hz, 1H, H-2), 3.98 (t, *J* = 1.3 Hz, 1H, H-5), 3.29 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 174.1 (C═O), 136.4, 133.4 (C_q Ph), 132.5, 129.0, 128.6, 128.3, 128.1, 128.0 (CH_{arom}), 85.3 (C-1), 81.2 (C-3), 78.3 (C-2), 72.9 (CH_2 Bn), 72.5 (C-5), 69.5 (C-4); HRMS $[M + Na]^+$ calcd for $C_{19}H_{18}O_5SNa$ 381.07672, found 381.07675. When lactonization of the crude acid diol **16** was executed at a 0.21 M concentration, lactone **5** was isolated in 26% along with 19% of **2-*O*-benzyl-1-thio-β-D-galactopyranosiduronyl-3,6-lactone) 2-*O*-benzyl-1-thio-β-D-galactopyranosyluronate (17):** R_f 0.41 (EtOAc/PE, 2/3, v/v); $[\alpha]^{22}_D$ −158 (*c* 2.0, CH_2Cl_2); IR (neat, cm^{-1}) 3470, 1806, 1774, 1101, 741, 692; "a" designates signals belonging to the galacturonic acid ester, and "b" is used for signals stemming from the galacturonic acid lactone; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.0 Hz, 2H, H_{arom}), 7.48−7.20 (m, 18H, H_{arom}), 5.59 (s, 1H, H-4b), 5.44 (s, 1H, H-1b), 5.08 (d, *J* = 4.6 Hz, 1H, H-3b), 4.93 (d, *J* = 10.8 Hz, 1H, CH_2 Bn), 4.70−4.65 (m, 2H, CH_2 Bn), 4.62−4.54 (m, 2H, CH_2 Bn, H-1a), 4.35 (d, *J* = 4.8 Hz, 1H, H-2b), 4.20−4.16 (m, 2H, H-4a, H-5b), 4.09 (s, 1H, H-5a), 3.73−3.62 (m, 2H, H-3a, H-2a), 3.50 (d, *J* = 4.1 Hz, 1H, OH), 3.25 (d, *J* = 4.1 Hz, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 166.3 (C═O), 137.9, 136.3, 133.3 (C_q Ph), 133.0, 132.6, 132.4, 129.0, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9 (CH_{arom}), 87.6 (C-1a), 86.3 (C-1b), 78.4 (C-3b), 78.1 (C-2b), 77.2 (C-2a), 76.4 (C-5a), 75.4 (CH_2 Bn), 74.0 (C-3a), 72.9 (CH_2 Bn), 72.6 (C-4b), 70.0, 69.8 (C-4a, C-5b); HRMS $[M + Na]^+$ calcd for $C_{38}H_{36}O_{10}S_2Na$ 739.16421, found 739.16431.

***tert*-Butyldiphenylsilyl 4-(*N*-Benzyloxycarbonylamino)-2-azido-3-*O*-chloroacetyl-2,4,6-trideoxy-β-D-galactopyranoside (18).** To a mixture of alcohol **6** (860 mg, 1.54 mmol, 1 equiv), 5 mL of DCM, and 607 μL of pyridine (7.68 mmol, 5 equiv) was added 525 mg of chloroacetic anhydride (3.07 mmol, 2 equiv). After 1 h, 500 μL of H_2O was added, and the mixture was stirred for another 15 min. After evaporation, the residue was taken up in EtOAc and washed with aq 1 M HCl, satd aq $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, and evaporated to dryness yielding title compound **18** (984 mg, 1.54 mmol, quant): R_f 0.79 (EtOAc/PE, 1/3, v/v); $[\alpha]^{22}_D$ −9 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2114, 1713, 1504, 1165, 1057, 733; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.71−7.68 (m, 4H, H_{arom}), 7.46−7.25 (m, 11H, H_{arom}), 5.14 (d, *J* = 12.2 Hz, 1H, CH_2 Cbz), 5.02 (d, *J* = 12.2 Hz, 1H, CH_2 Cbz), 4.93 (d, *J* = 9.5 Hz, 1H, NH), 4.64 (dd, *J* = 10.7, 3.7 Hz, 1H, H-3), 4.44 (d, *J* = 7.7 Hz, 1H, H-1), 4.00 (dd, *J* = 9.5, 3.4 Hz, 1H, H-4), 3.95−3.81 (m, 2H, CH_2, ClAc), 3.48 (dd, *J* = 10.4, 8.0 Hz, 1H, H-2), 3.36 (q, *J* = 6.2 Hz, 1H, H-5), 1.11 (s, 9H, CH_3 *t*-Bu), 0.97 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 166.5, 156.45 (C═O), 136.2 (C_q Ph), 135.7 (CH_{arom}), 132.9, 132.4 (C_q Ph),, 129.9, 128.5, 128.3, 128.1, 127.5, 127.4 (CH_{arom}), 97.0 (C-1), 74.6 (C-3), 68.9 (C-5), 67.1 (CH_2 Cbz), 63.5 (C-2), 51.6 (C-4), 40.5 (CH_2 ClAc), 26.7 (CH_3 *t*-Bu), 19.0, (C_q *t*-Bu), 16.0 (C-6); HRMS $[M + Na]^+$ calcd for $C_{32}H_{37}ClN_4O_6$SiNa 659.20631, found 659.20672.

4-(*N*-Benzyloxycarbonylamino)-2-azido-3-*O*-chloroacetyl-2,4,6-trideoxy-D-galactopyranose (7). Galactosazide **18** (1.03 g, 1.62 mmol, 1 equiv) in 10 mL of THF was treated with 527 μL of $N_3Et \cdot 3HF$ (3.23 mmol, 2 equiv), and the mixture was stirred at 70 °C for 30 min. When the reaction mixture had cooled to ambient temperature, EtOAc was added, and the organic mixture was washed with satd aq $NaHCO_3$. The aqueous layer was extracted with DCM, and the combined organic layers were dried over $MgSO_4$, filtered, and evaporated. Purification by flash column chromatography using EtOAc/PE (1/3 → 3/7) yielded galactopyranose **7** (632 mg, 1.58 mmol, 98%, α/β 1:2) with a minor unidentified side product: R_f 0.42 (EtOAc/PE, 2/3, v/v); IR (neat, cm^{-1}) 3356 (br), 2361, 2114, 1701, 1526, 1061; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.42−7.29 (m, 5H, H_{arom}), 5.44 (d, *J* = 9.6 Hz, 0.7H, NH-α), 5.35−5.28 (m, 0.6H, H-1α, H-3α), 5.17−5.04 (m, 2H, CH_2 Cbz-α, CH_2 Cbz-β), 4.75 (dt, *J* = 13.2, 6.6 Hz, 0.7H, H-3β), 4.63 (d, *J* = 8.0 Hz, 0.7H, H-1β), 4.52−4.47 (m, 0.3H, H-5α), 4.33 (s, 0.7H, OH-β), 4.26−4.22 (m, 0.3H, H-4α), 4.18−4.12 (m, 0.7H, H-4β), 3.96−3.86 (m, 2H, CH_2 ClAc), 3.81−3.74 (m, 0.7H, H-5β), 3.56 (dd, *J* = 11.1, 3.7 Hz, 0.3H, H-2α), 3.50 (dd, *J* = 10.8, 8.0 Hz, 0.7H, H-2β), 3.42 (s, 0.3H, OH-α), 1.24 (d, *J* = 6.4 Hz, 0.7H, H-6β), 1.18 (d, *J* = 6.5 Hz, 0.3H, H-6α); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 166.9, 157.1, 157.0 (C═O), 136.1, 136.0 (C_q Ph), 128.6, 128.5, 128.3, 128.1, 127.9 (CH_{arom}), 96.2 (C-1β), 91.8 (C-1α), 74.6 (C-3β), 72.2 (C-3α), 69.2 (C-5β), 67.3, 67.2 (CH_2 Cbz), 64.1 (C-5α), 61.8 (C-2β), 58.0 (C-2α), 52.5 (C-4α), 51.8 (C-4β), 40.6, 40.5 (CH_2 ClAc), 16.4 (C-6β), 16.3 (C-6α); HRMS $[M + H]^+$ calcd for $C_{16}H_{20}ClN_4O_6$ 399.10659, found 399.10647.

4-(*N*-Benzyloxycarbonylamino)-2-azido-3-*O*-chloroacetyl-2,4,6-trideoxy-α/β-D-galactopyranosyl (*N*-Phenyl)trifluoroacetimidate (8). To a solution of 511 mg of hemiacetal **7** (1.28 mmol, 1 equiv) in 6.1 mL of acetone and 0.3 mL of H_2O were added 460 mg of $CsCO_3$ (1.41 mmol, 1.1 equiv) and 532 mg of ClC(C═NPh)CF_3 (2.56 mmol, 2 equiv). When TLC analysis showed complete consumption of the starting material, the mixture was coevaporated with toluene. Purification by flash column chromatography using EtOAc/PE (1/9 → 3/7) yielded 606 mg of imidate **8** (1.06 mmol, 83%, anomers α/β 1:3): R_f 0.54 (EtOAc/PE, 1/3, v/v); IR (neat, cm^{-1}) 2116, 1717, 1524, 1211, 1163, 1072, 696; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) (*T* = 333 K) δ 7.41−7.23 (m, 9.3H, H_{arom}), 7.09 (m, 1.4H, H_{arom}), 6.83 (m, 2.7H, H_{arom}), 6.35 (s, 0.3H, H-1α), 5.49 (d, *J* = 7.5 Hz, 1H, H-1β), 5.28 (dd, *J* = 11.1, 3.5 Hz, 0.3H, H-3α), 5.20−4.96 (m, 4H, CH_2 Cbz, NH), 4.81 (dd, *J* = 10.7, 3.9 Hz, 1H, H-3β), 4.38−4.26 (m, 0.7H, H-4α, H-5α), 4.16 (dd, *J* = 9.7, 3.1 Hz, 1H, H-4β), 3.89 (s, 2.7H, CH_2 ClAc), 3.81 (dd, *J* = 10.9, 3.9 Hz, 0.3H, H-2α), 3.75−3.59 (m, 2H, H-2β, H-5β), 1.20 (m, 4H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) (T=333K) δ 166.4, 156.7 (C═O), 143.1, 143.0, 136.3 (C_q Ph), 128.8, 128.6, 128.3, 128.0, 124.7, 124.6, 119.3, 119.2 (CH_{arom}), 95.9 (C-1β), 93.7 (C-1α), 74.6 (C-3β), 72.2 (C-3α), 70.6 (C-5β), 67.5 (C-5α), 67.4 (CH_2 Cbz), 60.2 (C-2β), 57.2 (C-2α), 52.4 (C-4α), 51.8 (C-4β), 40.3 (CH_2 ClAc), 16.2 (C-6); HRMS $[M - (C(N{=}Ph)CF_3) + H + Na]^+$ calcd for $C_{16}H_{19}ClN_4O_6$ 421.08853, found 421.08845.

4-(*N*-Benzyloxycarbonylamino)-2-azido-3-*O*-chloroacetyl-2,4,6-trideoxy-α/β-D-galactopyranosyl-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (19). A catalytic amount of triflic acid was added under anhydrous conditions to a mixture of 403 mg of imidate **8** (707 μmol, 1 equiv) and 578 mg of alcohol **9** (2.21 mmol, 3 equiv) in 7 mL of DCM/Et_2O (1/1 v/v) at 0 °C. After 20 min of stirring, TLC analysis

showed complete conversion of the starting material. The reaction was quenched by adding triethylamine, and the solvents were removed in vacuo. Purification by size-exclusion chromatography (DCM/MeOH 1/1 v/v) yielded the title compound as an anomeric mixture (460 mg, 704 μmol, α/β 4:1, quant): R_f 0.81 (EtOAc/PE, 3/7, v/v); IR (neat, cm^{-1}) 2936, 2111, 1768, 1718, 1520, 1041, 698; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.42−7.23 (m, 18.8H, H_{arom}), 5.25 (dd, J = 11.1, 3.7 Hz, 1H, H-3α), 5.13 (dd, J = 10.6, 7.5 Hz, 2.5H, CH_2 Cbz, NH), 5.01 (d, J = 12.3 Hz, 1,25H, CH_2 Cbz), 4.89 (d, J = 3.7 Hz, 1H, H-1α), 4.72−4.60 (m, 2.8H, CH_2 Bn, H-3β), 4.58−4.48 (m, 2.5H, CH_2 Bn), 4.28 (d, J = 8.0 Hz, 0.25H, H-1β), 4.18−4.04 (m, 2.25H, H-4α, H-5α, H-4β), 3.99−3.73 (m, 4.8H, CH_2 Gro, CH Gro, CH_2 ClAc), 3.63−3.57 (m, 4H, CH_2 Gro, H-5β), 3.45−3.35 (m, 1.3H, H-2β, H-2α), 1.19 (d, J = 6.3 Hz, 0.8H, H-6β), 1.04 (d, J = 6.4 Hz, 3H, H-6α); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 166.6, 156.6, 156.5 (C═O), 138.2, 137.9, 136.2 (C_q Ph), 128.5, 128.3, 128.2, 127.9, 127.6, 127.5 (CH_{arom}), 102.2 (C-1β), 97.9 (C-1α), 76.8 (CH Gro-β), 76.6 (CH Gro-α), 74.3 (C-3β), 73.3 (CH_2 Bn), 72.1, 72.0 (CH_2 Bn), 71.6 (C-3α), 69.5, 69.4, 69.2 (CH_2 Gro), 68.9 (C-5β), 67.9 (CH_2 Gro), 67.0 (CH_2 Cbz), 64.0 (C-5α), 60.8 (C-2β), 57.2 (C-2α), 52.3 (C-4α), 51.6 (C-4β), 40.5 (CH_2 ClAc), 16.3 (C-6β), 16.1 (C-6α); HRMS $[M + Na]^+$ calcd for $C_{33}H_{37}ClN_4O_8Na$ 675.21921, found 675.21973.

4-(*N*-Benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-α-D-galactopyranosyl-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (20α) and 4-(*N*-Benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-β-D-galactopyranosyl-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (20β). A mixture of 460 mg of azide **19** (704 μmol, 1 equiv), 454 μL of pyridine (5.63 mmol, 8 equiv), 161 mg of thiourea (2.11 mmol, 3 equiv), and 7 mL of ethanol was stirred for 3 h at 65 °C. The mixture was concentrated, and the crude residue was taken up in EtOAc. The organic phase was washed with aq 1 M HCl, satd aq $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and evaporated. Purification by flash column chromatography using EtOAc/PE (1/4 → 3/7) yielded 317 mg of **20α** (549 μmol, 78%) and 66 mg of **20β** (114 μmol, 16%). **20α**: R_f 0.3 (EtOAc/PE, 1/3, v/v); $[\alpha]^{22}_D$ +91 (c 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 3418, 2916, 2106, 1697, 1026, 725; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.40−7.23 (m, 15H, H_{arom}), 5.17−5.06 (m, 3H, NH, CH_2 Cbz), 4.81 (d, J = 3.7 Hz, 1H, H-1), 4.71−4.62 (m, 2H, CH_2 Bn), 4.54 (dd, J = 12.0, 12.0 Hz, 2H, CH_2 Bn), 4.14 (dd, J = 10.7, 3.5 Hz, 1H, H-3), 4.08 (q, J = 6.5 Hz, 1H, H-5), 3.96 (dd, J = 8.8, 2.5 Hz, 1H, H-4), 3.83−3.76 (m, 2H, CH Gro, CH_2 Gro), 3.63 (d, J = 4.7 Hz, 2H, CH_2 Gro), 3.57 (dd, J = 9.4, 4.3 Hz, 1H, CH_2 Gro), 3.24 (s, 1H, OH), 3.12 (dd, J = 10.7, 3.6 Hz, 1H, H-2), 1.07 (d, J = 6.5 Hz, 3H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 158.1 (C═O), 138.3, 138.0, 135.8 (C_q Ph), 128.6, 128.3, 128.1, 127.7, 127.6, 127.6 (CH_{arom}), 98.2 (C-1), 76.8 (CH Gro), 73.4 (CH_2 Bn), 72.1 (CH_2 Bn), 69.4 (CH_2 Gro), 68.5 (C-3), 67.6 (CH_2 Gro), 67.5 (CH_2 Cbz), 64.5 (C-5), 60.4 (C-2), 55.8 (C-4), 16.4 (C-6); HRMS $[M + Na]^+$ calcd for $C_{31}H_{36}N_4O_7Na$ 599.24762, found 599.24731. **20β**: R_f 0.16 (EtOAc/PE, 1/3, v/v); $[\alpha]^{22}_D$ −13 (c 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 3348, 2870, 2106, 1705, 1049, 741; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.47−7.17 (m, 15H, H_{arom}), 5.29−5.03 (m, 3H, NH, CH_2 Cbz), 4.67 (s, 2H, CH_2 Bn), 4.54 (s, 2H, CH_2 Bn), 4.22 (d, J = 8.0 Hz, 1H, H-1), 3.99−3.91 (m, 2H, CH_2 Gro, H-4), 3.83−3.78 (m, 1H, CH Gro), 3.72 (dd, J = 10.2, 5.2 Hz, 1H, CH_2 Gro), 3.63 (dd, J = 4.9, 1.5 Hz, 2H, CH_2 Gro), 3.60−3.53 (m, 2H, H-3, H-5), 3.22 (dd, J = 10.0, 8.2 Hz, 1H, H-2), 3.16 (d, J = 2.3 Hz, 1H, OH), 1.19 (d, J = 6.2 Hz, 3H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 158.0 (C═O), 138.6, 138.2, 136.0 (C_q Ph), 128.6, −128.4, 128.3, 128.1, 127.7, 127.6 (CH_{arom}), 102.5 (C-1), 77.0 (CH Gro), 73.5 (CH_2 Bn), 72.5 (C-3), 72.3 (CH_2 Bn), 69.8 (CH_2 Gro), 69.5 (C-5) (CH_2 Gro), 67.5 (CH_2 Cbz), 64.5 (C-2), 54.9 (C-4), 16.6 (C-6); HRMS $[M + H]^+$ calcd for $C_{31}H_{36}N_4O_7$ 577.26568, found 577.26583.

2,4-Di-*O*-benzyl-α-D-galactopyranosiduronyl-3,6-lactone-(1→3)-*tert*-butyldiphenylsilyl 4-(*N*-Benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-β-D-galactopyranoside (21). Lactone **4** (338 mg) was coupled to alcohol **6** (0.77 equiv instead of 1.5 equiv) according to the general procedure for glycosidations using Ph_2SO/Tf_2O. The reaction was quenched using triethylamine (5 equiv), and the title compound **21** was obtained in 75% yield (391 mg, 435 μmol): flash column chromatography eluent:EtOAc/toluene (0/1 → 1/49); R_f 0.78 (EtOAc/toluene, 1/4, v/v); $[\alpha]^{22}_D$ 27 (c 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2860, 2361, 2114, 1800, 1717, 1506, 1061; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.79−7.08 (m, 25H, H_{arom}), 5.13−5.00 (m, 3H, CH_2 Cbz, H-1′), 4.92 (d, J = 9.7 Hz, 1H, NH), 4.79 (d, J = 11.6 Hz, 1H, CH_2 Bn), 4.71 (d, J = 3.8 Hz, 1H, H-3′), 4.62−4.52 (m, 2H, CH_2 Bn), 4.50 (s, 1H, H-4′), 4.36 (d, J = 7.8 Hz, 1H, H-1), 4.27 (d, J = 11.6 Hz, 1H, CH_2 Bn), 4.18 (s, 1H, H-5′), 4.05 (dd, J = 4.9, 2.1 Hz, 1H, H-2′), 3.92 (dd, J = 10.0, 3.7 Hz, 1H, H-4), 3.68 (dd, J = 10.5, 4.0 Hz, 1H, H-3), 3.30−3.23 (m, 2H, H-2, H-5), 1.10 (s, 9H, CH_3 t-Bu), 1.00 (d, J = 6.3 Hz, 3H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 171.8 (C═O), 156.5 (C═O Cbz), 138.0, 136.8 (C_q Ph), 135.8 (CH_{arom}), 133.1, 132.5 (C_q Ph), 129.9, 129.8, 128.6, 128.5, 128.4, 128.3, 128.1, 127.8, 127.7, 127.5, 127.4 (CH_{arom}), 96.9 (C-1), 95.6 (C-1′), 80.4 (C-3′), 77.1 (C-3), 75.8 (C-4′), 75.0 (C-2′), 74.3 (CH_2 Bn), 72.2 (C-5′), 71.5 (CH_2 Bn), 69.0 (C-5), 67.2 (CH_2 Cbz), 64.8 (C-2), 50.9 (C-4), 26.8 (CH_3 t-Bu), 19.1 (C_q t-Bu), 16.3 (C-6); HRMS $[M + Na]^+$ calcd for $C_{50}H_{54}N_4O_{10}SiNa$ 921.35014, found 921.35091.

Benzyl 2,4-Di-*O*-benzyl-α-D-galactopyranosyluronate-(1→3)-*tert*-butyldiphenylsilyl 4-(*N*-benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-β-D-galactopyranoside (22). After addition of a catalytic amount of AcCl to a solution of 412 mg of lactone **21** (367 μmol) in 2 mL of BnOH, the mixture was allowed to stir overnight at 50 °C. Following neutralization using triethylamine, the mixture was diluted with EtOAc and washed with satd aq $NaHCO_3$ and brine. The organic phase was dried ($MgSO_4$), filtered, and concentrated in vacuo. Size-exclusion chromatography (DCM/MeOH 1/1 v/v) followed by flash column chromatography using EtOAc/toluene (1/19→1/9) gave 370 mg (367 μmol, quant) of the title compound **22**: R_f 0.51 (EtOAc/toluene, 1/4, v/v); $[\alpha]^{22}_D$ +34 (c 0.39, CH_2Cl_2); IR (neat, cm^{-1}) 3500, 2932, 2112, 1761, 1719, 1508, 1107, 1059; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.75−7.60 (m, 4H, H_{arom}), 7.49−7.16 (m, 24H, H_{arom}), 7.14−7.03 (m, 2H, H_{arom}), 5.54 (d, J = 3.3 Hz, 1H, H-1′), 5.14 (d, J = 12.2 Hz, 1H, CH_2 Bn), 5.06 (m, 2H, CH_2 Bn), 4.91 (d, J = 10.4 Hz, 1H, NH), 4.76 (d, J = 12.2 Hz, 1H, CH_2 Bn), 4.68−4.61 (m, 3H, H-5′, CH_2 Bn), 4.42−4.36 (m, 3H, H-1, CH_2 Bn), 4.30 (s, 1H, H-4′), 4.21 (dd, J = 10.0, 3.2 Hz, 1H, H-3′), 4.09 (dd, J = 10.1, 3.5 Hz, 1H, H-4), 3.90 (dd, J = 10.1, 3.3 Hz, 1H, H-2′), 3.57 (dd, J = 10.8, 4.2 Hz, 1H, H-3), 3.38 (dd, J = 10.9, 7.7 Hz, 1H, H-2), 3.23 (q, J = 6.1 Hz, 1H, H-5), 2.12 (s, 1H, OH), 1.09 (s, 9H, CH_3 t-Bu), 0.92 (d, J = 6.3 Hz, 3H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 168.3 (C═O), 156.7 (C═O Cbz), 138.2, 137.8, 136.0 (C_q Ph), 135.8, 135.7 (CH_{arom}), 135.1, 133.2, 132.8 (C_q Ph), 129.9, 129.8, 128.5, 128.4, 128.2, 128.0, 127.9, 127.6, 127.5, 127.4 (CH_{arom}), 97.2 (C-1), 92.1 (C-1′), 77.6 (C-4′), 74.9 (CH_2 Bn), 74.8 (C-2′), 72.3 (C-3), 72.0 (CH_2 Bn), 70.6 (C-5′), 69.8 (C-5), 69.3 (C-3′), 67.0 (CH_2 Cbz, CH_2 Bn), 65.3 (C-2), 49.9 (C-4), 26.8 (CH_3 t-Bu), 19.1 (C_q t-Bu), 16.0 (C-6); HRMS $[M + Na]^+$ calcd for $C_{57}H_{62}N_4O_{11}SiNa$ 1029.40766, found 1029.40828.

Benzyl 2,4-Di-*O*-benzyl-3-*O*-chloroacetyl-α-D-galactopyranosyluronate-(1→3)-*tert*-butyldiphenylsilyl 4-(*N*-Benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-β-D-galactopyranoside (23). Alcohol **22** (2.10 g, 2.09 mmol, 1 equiv) was coevaporated with toluene and dissolved in 10 mL of DCM. A 1.68 mL (20.9 mmol, 10 equiv) portion of pyridine and 1.07 g of $(ClAc)_2O$ (6.3 mmol, 3 equiv) were added at 0 °C, and the mixture was stirred at ambient temperature for 2.5 h. Next, H_2O and EtOAc were added, and the organic phase was washed with aq 1 M HCl, satd aq $NaHCO_3$ and brine.

The organic layer was dried ($MgSO_4$), filtered, and evaporated. Purification by flash column chromatography using EtOAc/Tol (0/1 → 1/19) yielded 2.11 g of chloroacetate **23** (1.94 mmol, 93%): R_f 0.81 (EtOAc/toluene, 1/4, v/v); $[\alpha]^{22}_D$ +78 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2936, 2112, 1760, 1718, 1508, 1063, 696; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.68 (dd, *J* = 7.0, 3.4 Hz, 4H, H_{arom}), 7.46−7.12 (m, 24H, H_{arom}), 7.08−6.97 (m, 2H, H_{arom}), 5.53 (d, *J* = 3.3 Hz, 1H, H-1′), 5.41 (dd, *J* = 10.5, 2.9 Hz, 1H, 3′), 5.15 (dd, *J* = 12.1, 12.1 Hz, 2H, CH_2 Bn), 5.03 (d, *J* = 12.2 Hz, 1H, CH_2 Bn), 4.89 (d, *J* = 10.4 Hz, 1H, NH), 4.78 (s, 1H, 5′), 4.67 (dd, *J* = 12.4, 12.4 Hz, 2H, CH_2 Bn), 4.44−4.37 (m, 3H, H-4′, H-1, CH_2 Bn), 4.31 (dd, *J* = 11.8, 11.8 Hz, 2H, CH_2 Bn), 4.14−4.02 (m, 2H, H-2′, H-4), 3.63 (d, *J* = 14.9 Hz, 1H, CH_2 ClAc), 3.58 (dd, *J* = 10.8, 4.1 Hz, 1H, H-3), 3.51 (d, *J* = 14.9 Hz, 1H, CH_2 ClAc), 3.42 (dd, *J* = 10.7, 7.7 Hz, 1H, H-2), 3.23 (q, *J* = 6.1 Hz, 1H, H-5), 1.10 (s, 9H, CH_3 *t*-Bu), 0.91 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 167.8, 166.4 (C═O), 156.6 (C═O Cbz), 138.0, 137.7, 136.0 (C_q Ph), 135.8, 135.7 (CH_{arom}), 134.9, 133.2, 132.8 (C_q Ph), 129.9, 129.8, 128.8, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 127.4 (CH_{arom}), 97.3 (C-1), 92.7 (C-1′), 76.8 (C-4′), 75.0 (CH_2 Bn), 72.9 (C-3′), 72.6 (C-3, CH_2 Bn), 72.2 (C-2′), 70.2 (C-5′), 69.7 (C-5), 67.2, 66.9 (CH_2 Bn), 65.1 (C-2), 49.9 (C-4), 40.3 (CH_2 ClAc), 26.8 (CH_3 *t*-Bu), 19.1 (C_q *t*-Bu), 16.0 (C-6); HRMS $[M + Na]^+$ calcd for $C_{59}H_{63}ClN_4O_{12}SiNa$ 1105.37925, found 1105.38018.

Benzyl 2,4-Di-*O*-benzyl-3-*O*-chloroacetyl-α-D-galactopyranosyluronate-(1→3)-4-(*N*-benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-D-galactopyranose (24). A mixture of 2.05 g of dimer **23** (1.89 mmol, 1 equiv), 20 mL of THF and 2.47 mL of triethylamine·3HF (15.13 mmol, 8 equiv) was stirred overnight at 70 °C. The solvent was removed using a rotary evaporator, and the crude anomers were purified by flash column chromatography using EtOAc/PE (7/13→9/11). The title compound **24** (1.35 g, 1.60 mmol, 84%, α/β 1:4) was obtained. Data of major anomer (β): R_f 0.24 (EtOAc/PE, 2/3, v/v); IR (neat, cm^{-1}) 3425, 2108, 1763, 1717, 1541, 1244, 1036; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.38−7.15 (m, 18H, H_{arom}), 7.08−7.00 (m, 2H, H_{arom}), 5.54 (d, *J* = 3.3 Hz, 1H, H-1′), 5.43−5.36 (m, 2H, H-3′, NH), 5.21−5.10 (m, 2H, CH_2 Bn), 5.06 (d, *J* = 12.3 Hz, 1H, CH_2 Cbz or CH_2 CO_2Bn), 4.85 (s, 1H, H-5′), 4.67 (m, 2H, CH_2 Bn), 4.55 (d, *J* = 7.0 Hz, 1H, H-1), 4.44−4.37 (m, 2H, CH_2 Bn, H-4′), 4.36−4.28 (m, 2H, CH_2 Bn), 4.20 (dd, *J* = 10.4, 4.3 Hz, 1H, H-4), 4.11 (dd, *J* = 10.5, 3.3 Hz, 1H, H-2′), 3.70 (dd, *J* = 10.8, 4.2 Hz, 1H, H-3), 3.66−3.44 (m, 4H, CH_2 ClAc, H-5, H-2), 1.19 (d, *J* = 6.3 Hz, 3H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 167.8, 166.3 (C═O), 156.9 (C═O Cbz), 137.7, 137.6, 136.0, 134.7 (C_q Ph), 128.9, 128.7, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4 (CH_{arom}), 96.5 (C-1), 92.5 (C-1′), 76.7 (C-4′), 74.9 (CH_2 Cbz or CH_2 CO_2Bn), 72.8, (C-3′), 72.5 (CH_2 Cbz or CH_2 CO_2Bn), 72.4 (C-3), 72.2 (C-2′), 70.1 (C-5′), 69.8 (C-5), 67.2, 66.7 (CH_2 Bn), 63.1 (C-2), 49.9 (C-4), 40.2 (CH_2 ClAc), 16.4 (C-6); HRMS $[M + Na]^+$ calcd for $C_{16}H_{19}ClN_4O_6Na$ 867.26147, found 867.26183.

Benzyl 2,4-Di-*O*-benzyl-3-*O*-chloroacetyl-α-D-galactopyranosyluronate-(1→3)-4-(*N*-benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-D-galactopyranosyl *N*-Phenyltrifluoroacetimidate (25). To a solution of 666 mg of hemiacetal **24** (0.787 mmol, 1 equiv) in 15 mLof acetone/H_2O (19/1) were added 282 mg of Cs_2CO_3 (0.866 mmol, 1.1 equiv) and 327 mg of ClC(C═NPh)CF_3 (1.57 mmol, 2.0 equiv). The mixture was stirred overnight at ambient temperature and evaporated to dryness after the addition of 328 μL of triethylamine (2.36 mmol, 3.0 equiv). Flash column chromatography of the crude product using EtOAc/PE (3/7) with 1% triethyamine as eluent afforded 680 mg (669 μmol, 85%) of the title imidate as one of the two possible epimers: R_f 0.64 (EtOAc/toluene, 1/4, v/v); IR (neat, cm^{-1}) 2112, 1759, 1717, 1516, 1209, 1078, 696; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.39−7.18 (m, 20H, H_{arom}), 7.13 (t, *J* = 7.5 Hz, 1H, H_{arom}), 7.08−7.00 (m, 2H, H_{arom}), 6.84 (d, *J* = 7.8 Hz, 2H, H_{arom}), 5.57 (d, *J* = 2.8 Hz, 1H, H-1′), 5.41 (dd, *J* = 10.6, 2.9 Hz, 1H, H-3′), 5.23−5.03 (m, 4H, NH, CH_2 Cbz or CH_2 CO_2Bn), 4.79 (s, 1H, H-5′), 4.74−4.64 (m, 2H, CH_2 Cbz or CH_2 CO_2Bn, CH_2 Bn), 4.46−4.38 (m, 2H, CH_2 Bn, H-4′), 4.37−4.22 (m, 3H, CH_2 Bn, H-4), 4.13 (dd, *J* = 10.5, 3.4 Hz, 1H, H-2′), 3.82−3.73 (m, 1H, H-5), 3.73−3.66 (m, 1H, H-2), 3.63 (d, *J* = 14.9 Hz, 1H, CH_2 ClAc), 3.52 (d, *J* = 14.9 Hz, 1H, CH_2 ClAc), 1.22 (d, *J* = 6.9 Hz, 3H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 167.6, 166.4 (C═O), 156.6 (C═O Cbz), 142.9, 137.8, 137.6, 135.8, 134.8 (C_q Ph), 128.8, 128.8, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 124.6, 119.2 (CH_{arom}), 92.9 (C-1′), 76.8 (C-4′), 75.1 (CH_2 Cbz or CH_2 CO_2Bn), 72.8 (C-3′), 72.7 (CH_2 Cbz or CH_2 CO_2Bn), 72.6 (C-3 or C-5), 72.1 (C-2′), 71.2 (C-3 or C-5), 70.3 (C-5′), 67.3, 67.0 (CH_2 Bn), 61.3 (C-2), 49.7 (C-4), 40.3 (CH_2 ClAc), 16.3 (C-6); HRMS $[M - (C(N{=}Ph)CF_3) + H + Na]^+$ calcd for $C_{43}H_{45}ClN_4O_{12}Na$ 867.26147, found 867.26164.

Benzyl 2,4-Di-*O*-benzyl-3-*O*-chloroacetyl-α-D-galactopyranosyluronate-(1→3)-4-(*N*-benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-D-galactopyranosyl-(1→4)-phenyl 2-*O*-benzyl-1-thio-β-D-galactopyranosidurono-3,6-lactone (26). Imidate donor (**25**) (600 mg, 590 μmol, 1 equiv) and 391 mg of lactone acceptor **5** (1.09 mmol, 1.85 equiv) were coevaporated with toluene and stirred over activated 3 Å molecular sieves in 6 mL of DCM for 30 min. The mixture was cooled to 0 °C before 5 μL of triflic acid (59 μmol, 0.1 equiv) was added. After 30 min of stirring, the reaction was quenched by the addition of 41 μL of triethylamine (295 μmol, 0.5 equiv). The mixture was diluted with DCM and washed with satd aq $NaHCO_3$. The aqueous phase was extracted with DCM, and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Size-exclusion chromatography (DCM/MeOH 1/1 v/v) gave 565 mg (476 μmol, 81%) of the two possible epimers. Partial separation of this mixture by flash column chromatography (eluent: EtOAc/PE 1/3 → 9/11) afforded the pure α-coupled product **26** (450 mg, 379 μmol, 64%): R_f 0.57 (EtOAc/toluene, 1/4, v/v); $[\alpha]^{22}_D$ +62 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2106, 1805, 1759, 1720, 1520, 1242, 1034; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.50−7.43 (m, 2H, H_{arom}), 7.41−7.14 (m, 26H, H_{arom}), 7.07−7.00 (m, 2H, H_{arom}), 5.54 (s, 1H, H-1″), 5.42 (s, 1H, H-1), 5.39 (dd, *J* = 10.7, 2.7 Hz, 1H, H-3″), 5.18 (s, 2H, CH_2), 5.09−4.96 (m, 3H, CH_2, H-1′, NH), 4.86 (d, *J* = 4.7 Hz, 1H, H-2), 4.69−4.63 (m, 4H, CH_2 Bn, H-5″), 4.58−4.55 (m, 2H, H-4, CH_2), 4.40−4.37 (m, 2H, H-4″, CH_2 Bn), 4.35−4.25 (m, 4H, H-4′, H-3, CH_2 Bn), 4.18 (dd, *J* = 10.6, 3.9 Hz, 1H, H-3′), 4.14−4.05 (m, 3H, H-2″, H-5′, H-5), 3.56 (d, *J* = 14.9 Hz, 1H, CH_2 ClAc), 3.46 (d, *J* = 14.9 Hz, 1H, CH_2 ClAc), 3.39 (dd, *J* = 11.0, 3.9 Hz, 1H, H-2′), 1.13 (d, *J* = 6.2 Hz, 3H, H-6′); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 171.7, 167.5, 166.4 (C═O), 156.7 (C═O Cbz), 138.0, 137.7, 136.3, 135.9, 134.9, 133.3 (C_q Ph), 132.8, 129.0, 128.8, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6 (CH_{arom}), 97.7 (C-1′), 93.1 (C-1″), 85.7 (C-1), 79.1 (C-2), 78.4 (C-3), 76.8 (C-4″), 76.3 (C-4), 75.1, 73.2 (CH_2 Bn), 72.8 (C-3″, CH_2 Bn), 72.3 (C-2″), 70.4 (C-5″), 70.2 (C-5′), 69.9 (C-3′), 67.4, 67.0 (CH_2), 66.5 (C-5), 58.8 (C-2′), 50.7 (C-4′), 40.3 (CH_2 ClAc), 16.3 (C-6′);

Benzyl 2,4-Di-*O*-benzyl-3-*O*-chloroacetyl-α-D-galactopyranosyluronate-(1→3)-4-(*N*-benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-D-galactopyranosyl-(1→4)-2-*O*-benzyl-α-D-galactopyranosiduronyl-3,6-lactone-(1→3)-*sn*-glycerol (27). Thioglycoside **26** (328 mg) was coupled to glycerol acceptor **9** (4.0 equiv instead of 1.5 equiv) according to the general procedure for glycosylations using Ph_2SO/Tf_2O. The reaction was quenched with triethylamine (5 equiv), and the title compound **27** was purified using size-exclusion chromatography: yield 81% (302 mg, 224 μmol); R_f 0.59 (EtOAc/PE, 2/3, v/v); $[\alpha]^{22}_D$ +99 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2874, 2108, 1803, 1761, 1719, 1028, 696; ^1H NMR

(400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.39−7.16 (m, 33H, H_{arom}), 7.06−6.99 (m, 2H, H_{arom}), 5.53 (d, J = 2.5 Hz, 1H, H-1″), 5.38 (dd, J = 10.6, 2.7 Hz, 1H, H-3″), 5.25−5.12 (m, 2H, CH_2 Bn), 5.05 (d, J = 12.2 Hz, 1H, CH_2 Bn), 4.99−4.97 (m, 2H, NH, H-1′), 4.90−4.86 (m, 2H, H-1, CH_2 Bn), 4.74−4.61 (m, 7H, H-4, H-3, H-5″, CH_2 Bn), 4.58−4.45 (m, 3H, CH_2 Bn), 4.40−4.37 (m, 2H, CH_2 Bn, H-4″), 4.34−4.26 (m, 3H, H-4′, CH_2 Bn), 4.21−4.14 (m, 2H, H-5, H-3′), 4.13−4.08 (m, 2H, CH_2 Gro, H-2″), 4.02 (q, J = 6.3 Hz, 1H, H-5′), 3.89 (dd, J = 5.0, 2.2 Hz, 1H, H-2), 3.87−3.82 (m, 1H, CH Gro), 3.70 (dd, J = 10.7, 6.9 Hz, 1H, CH_2 Gro), 3.59−3.52 (m, 3H, CH_2 Gro, CH_2 ClAc), 3.45 (d, J = 14.9 Hz, 1H, CH_2 ClAc), 3.38 (dd, J = 10.9, 3.9 Hz, 1H, H-2′), 1.11 (d, J = 6.3 Hz, 3H, H-6′); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 170.7, 167.5, 166.3 (C═O), 156.7 (C═O Cbz), 138.3, 137.9, 137.6, 137.4, 135.9, 134.9 (C_q Ph), 128.9, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6 (CH_{arom}), 99.3 (C-1), 97.5 (C-1′), 93.0 (C-1″), 80.6 (C-3), 77.2 (CH Gro), 76.8 (C-4″), 75.5 (C-4), 75.1 (CH_2 Bn), 74.5 (CH_2 Bn), 74.3 (C-2), 73.4 (CH_2 Bn), 72.8 (CH_2 Bn, C-3), 72.3 (CH_2 Bn, C-2″), 71.4 (C-5), 71.1 (CH_2 Gro), 70.4 (C-5″), 69.8 (C-3′), 69.5 (CH_2 Gro), 67.4, 67.0 (CH_2), 66.2 (C-5′), 58.7 (C-2′), 50.6 (C-4′), 40.3 (CH_2 ClAc), 16.2 (C-6′); HRMS $[M + Na]^+$ calcd for $C_{73}H_{75}ClN_4O_{19}Na$ 1369.46062, found 1369.46265.

Benzyl 2,4-Di-*O*-benzyl-α-D-galactopyranosyluronate-(1→3)-4-(*N*-benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-D-galactopyranosyl-(1→4)-2-*O*-benzyl-α-D-galactopyranosiduronyl-3,6-lactone-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (28). A solution of 302 mg of compound **27** (224 μmol, 1 equiv), 145 μL of pyridine (1.79 mmol, 8 equiv), and 51 mg of thiourea (672 μmol, 3 equiv) in 4 mL of EtOH was stirred at 65 °C for 3 h. The mixture was concentrated under reduced pressure, diluted with EtOAc, and washed with aq 1 M HCl, satd aq $NaHCO_3$, and brine. The organic phase was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Flash column chromatography using EtOAc/toluene (1/4→1/3) gave 218 mg (171 μmol, 76%) of the title compound **28**: R_f 0.62 (EtOAc/PE, 2/3, v/v); $[\alpha]^{22}_D$ +95 (c 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2924, 2106, 1805, 1759, 1713, 1535, 1034; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.39−7.12 (m, 33H, H_{arom}), 7.11−7.05 (m, 2H, H_{arom}), 5.55 (d, J = 2.2 Hz, 1H, H-1″), 5.15 (m, 2H, CH_2 Bn), 5.09−5.05 (m, 2H, NH, CH_2 Bn), 4.92 (d, J = 4.2 Hz, 1H, H-1′), 4.89−4.83 (m, 2H, H-1, CH_2 Bn), 4.74−4.58 (m, 7H, H-4, H-3, CH_2 Bn, CH_2), 4.55 (s, 1H, H-5″), 4.54−4.44 (m, 3H, CH_2 Bn), 4.43−4.28 (m, 3H, CH_2 Bn, H-4′), 4.24 (s, 1H, H-4″), 4.20−4.11 (m, 3H, H-5, H-3″, H-3′), 4.09 (dd, J = 10.7, 3.5 Hz, 1H, CH_2 Gro), 4.00 (q, J = 6.2 Hz, 1H, H-5′), 3.92−3.81 (m, 3H, H-2″, H-2, CH Gro), 3.68 (dd, J = 10.7, 6.9 Hz, 1H, CH_2 Gro), 3.54 (d, J = 5.3 Hz, 2H, CH_2 Gro), 3.36 (dd, J = 11.0, 3.9 Hz, 1H, H-2′), 2.04 (s, 1H, OH), 1.10 (d, J = 6.2 Hz, 3H, H-6′); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 170.6, 168.0 (C═O), 156.7 (C═O Cbz), 138.2, 138.0, 137.8, 137.7, 137.2, 135.8, 134.9 (C_q Ph), 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4 (CH_{arom}), 99.2 (C-1), 97.3 (C-1′), 92.3 (C-1″), 80.5 (C-3), 77.6 (C-4″), 77.1 (CH Gro), 75.1 (C-4), 74.8 (CH_2 Bn), 74.6 (C-2″), 74.3 (CH_2 Bn), 74.2 (C-2), 73.3 (CH_2 Bn), 72.2 (CH_2 Bn), 72.0 (CH_2 Bn), 71.2 (C-5), 71.0 (CH_2 Gro), 70.6 (C-5″), 69.3 (CH_2 Gro, C-3′), 69.0 (C-3″), 67.0, 66.9 (CH_2), 66.2 (C-5′), 58.6 (C-2′), 50.5 (C-4′), 16.1 (C-6′); HRMS $[M + Na]^+$ calcd for $C_{71}H_{74}N_4O_{18}Na$ 1293.48903, found 1293.49043.

Benzyl 2,4-Di-*O*-benzyl-α-D-galactopyranosyluronate-(1→3)-2-acetamido-4-(*N*-benzyloxycarbonylamino)-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-2-*O*-benzyl-α-D-galactopyranosiduronyl-3,6-lactone-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (29). To an ice-cooled solution of 94 mg of azide **28** (74 μmol) in 1 mL of pyridine was added 1 mL of freshly distilled thiolacetic acid. The mixture was stirred at room temperature for 4 h, concentrated under reduced pressure, and coevaporated with toluene. Flash column chromatography using EtOAc/PE (1/1→3/2) afforded the title acetamide (89 mg, 69 μmol, 94%): R_f 0.41 (EtOAc/PE, 3/2, v/v); $[\alpha]^{22}_D$ +97 (c 0.7, CH_2Cl_2); IR (neat, cm^{-1}) 3368, 2924, 1801, 1718, 1668, 1028, 697; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.40−7.19 (m, 33H, H_{arom}), 7.13 (d, J = 6.7 Hz, 2H, H_{arom}), 5.43 (d, J = 8.9 Hz, 1H, NH), 5.24 (d, J = 9.9 Hz, 1H, NH), 5.19−5.12 (m, 2H, CH_2, H-1″), 5.02 (d, J = 12.4 Hz, 1H, CH_2 Bn), 4.94 (d, J = 12.0 Hz, 1H, CH_2 Bn), 4.91−4.77 (m, 4H, CH_2 Bn, H-1′, H-1), 4.73−4.59 (m, 6H, CH_2 Bn, H-4, H-3), 4.53−4.37 (m, 6H, CH_2 Bn, H-5″), 4.20−4.05 (m, 5H, H-4′, H-4″, H-2′, H-5, CH_2 Gro), 3.98 (dd, J = 9.9, 2.7 Hz, 1H, H-3″), 3.93−3.80 (m, 4H, H-2, H-5′, CH Gro, H-2″), 3.75−3.65 (m, 2H, H-3′, CH_2 Gro), 3.55 (dd, J = 5.0, 1.7 Hz, 2H, CH_2 Gro), 1.71 (s, 3H, CH_3 NHAc), 1.12 (d, J = 6.4 Hz, 3H, H-6′); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 171.2, 170.4, 168.3 (C═O), 156.9 (C═O Cbz), 138.3, 138.1, 137.9, 137.3, 136.4, 134.8 (C_q Ph), 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5 (CH_{arom}), 99.2 (C-1), 96.4 (C-1′), 96.0 (C-1″), 80.9 (C-3), 77.2 (C-4″, CH Gro), 75.4 (C-2″), 74.7, 74.5 (CH_2 Bn), 74.2 (C-2), 73.9 (C-4), 73.4 (CH_2 Bn), 73.3 (C-3′), 72.7, 72.3 (CH_2 Bn), 71.2 (C-5 or C-5″), 71.1 (CH_2 Gro, C-5 or C-5″), 69.4 (CH_2 Gro), 69.2 (C-3″), 67.2, 66.6 (CH_2 Bn), 66.4 (C-5′), 52.1 (C-4′), 48.3 (C-2′), 22.8 (CH_3 NHAc), 16.4 (C-6′); HRMS $[M + Na]^+$ calcd for $C_{73}H_{78}N_2O_{19}Na$ 1309.50910, found 1309.50940.

α-D-Galactopyranosyluronate-(1→3)-2-acetamido-4-amino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-α-D-galactopyranosyluronate-(1→3)-*sn*-glycerol (1). To a solution of 21 mg (16 μmol, 1 equiv) of compound **29** in 1.5 mL of DCM was added 8.0 mg of TMSONa (71 μmol, 4.5 equiv). The mixture was stirred for 2.5 h, followed by the addition of 20 μL of AcOH (355 μmol, 22.5 equiv), evaporation, and elution over a plug of silica (eluent: EtOAc, then EtOAc/MeOH/H_2O/AcOH 88/10/1/1). After removal of the eluent, the crude product was dissolved in 7 mL of *t*-BuOH/H_2O (5/2 v/v) and stirred under argon atmosphere. A catalytic amount of palladium on activated charcoal and 125 μL of 1 M aq HCl were added, and the mixture was allowed to stir for 2 days under hydrogen atmosphere. Filtration over Celite, gel filtration (HW-40, 0.15 M Et_3NHOAc in H_2O), and subsequent lyophilization afforded 5.2 mg of the pure title compound **1** (8.3 μmol, 52% over two steps): ^{1}H NMR (600 MHz, D_2O, HH-COSY, HSQC, HMBC, TOCSY, T= 290 K) δ 5.07 (d, J = 2.4 Hz, 1H, H-1″), 5.04 (d, J = 3.7 Hz, 1H, H-1), 4.98 (d, J = 4.0 Hz, 1H, H-1′), 4.79 (q, J = 6.7 Hz, 1H, H-5′), 4.37 (d, J = 2.7 Hz, 1H, H-4), 4.34 (s, 1H, H-5), 4.27−4.25 (m, 2H, H-4″, H-3′), 4.14 (s, 1H, H-5″), 4.11 (dd, J = 11.4, 4.0 Hz, 1H, H-2′), 4.07 (dd, J = 10.6, 3.1 Hz, 1H, H-3), 3.96−3.91 (m, 1H, CH Gro), 3.89 (dd, J = 10.6, 3.8 Hz, 1H, H-2), 3.85 (m, 2H, H-2″, H-3″), 3.84−3.78 (m, 2H, H-4′, CH_2 Gro), 3.66 (dd, J = 11.8, 4.6 Hz, 1H, CH_2 Gro), 3.58 (dd, J = 11.8, 6.2 Hz, 1H, CH_2 Gro), 3.53 (dd, J = 10.6, 7.0 Hz, 1H, CH_2 Gro), 2.02 (s, 3H, CH_3 NHAc), 1.26 (d, J = 6.7 Hz, 3H, H-6′); ^{13}C NMR (151 MHz, D_2O, HH-COSY, HSQC, HMBC, TOCSY, T = 290 K) δ 175.6, 175.5, 174.7 (C═O), 99.6 (C-1), 99.1 (C-1′), 98.9 (C-1″), 80.0 (C-4), 73.3 (C-3′), 73.2 (C-5″), 71.5 (CH Gro), 71.3 (C-4″, C-5), 70.1 (C-3″, CH_2 Gro), 69.4 (C-3), 68.8 (C-2), 68.0 (C-2′), 63.7 (C-5′), 63.2 (CH_2 Gro), 53.5 (C-4′), 48.4 (C-2′), 23.0 (CH_3 NHAc), 16.3 (C-6′); ^{13}C-HMBC NMR (151 MHz, D_2O, T= 290 K) δ 99.6 (J_{C1-H1} = 171.1 Hz, C-1), 99.1 ($J_{C1'-H1'}$ = 174.4 Hz, C-1′), 98.9 ($J_{C1''-H1''}$ = 171.1 Hz, C-1″); HRMS $[M + H]^+$ calcd for $C_{23}H_{39}N_2O_{18}$ 631.21924, found 631.21934.

2,4-Di-*O*-benzyl-α-D-galactopyranosiduronyl-3,6-lactone-(1→3)-1,2-di-*O*-benzyl-sn-glycerol (30). 448 mg of lactone **4** was coupled to alcohol **9** according to the general procedure for glycosidations using Ph_2SO/Tf_2O, yielding 567 mg of the title compound **30** (928 μmol, α/β 10:1, 93%): flash column chromatography gradient EtOAc/PE (1/9 → 1/4); R_f 0.73 (EtOAc/toluene, 1/5, v/v); IR (neat, cm^{-1}) 3030, 2868, 1798, 1454, 1057, 696; NMR assignment of the major anomer (α), ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.37−7.25 (m, 18H, H_{arom}), 7.19 (dd, J = 6.7, 2.7 Hz, 2H,

H_{arom}), 4.86−4.83 (m, 2H, H-1, CH_2 Bn), 4.71−4.61 (m, 3H, H-3, CH_2 Bn), 4.56 (s, 2H, CH_2 Bn), 4.51 (d, J = 4.6 Hz, 2H, CH_2 Bn), 4.48−4.43 (m, 2H, H-4, CH_2 Bn), 4.14 (t, J = 1.6 Hz, 1H, H-5), 4.08 (dd, J = 10.7, 3.6 Hz, 1H, CH_2 Gro), 3.88 (dd, J = 5.0, 2.4 Hz, 1H, H-2), 3.86−3.81 (m, 1H, CH Gro), 3.67 (dd, J = 10.7, 6.9 Hz, 1H, CH_2 Gro), 3.54 (dd, J = 5.7, 4.7 Hz, 2H, CH_2 Gro); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 171.5 (C═O), 138.3, 137.8, 137.4, 136.6 (C_q Ph), 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.7, 127.6, 127.5 (CH_{arom}), 99.2 (C-1), 80.1 (C-3), 77.1 (CH Gro), 75.4 (C-5), 74.3 (C-2), 74.2 (CH_2 Bn), 73.2 (CH_2 Bn), 72.1 (CH_2 Bn), 71.8 (C-4), 71.3 (CH_2 Bn), 71.0 (CH_2 Gro), 69.4 (CH_2 Gro); HRMS $[M + Na]^+$ calcd for $C_{37}H_{38}O_8Na$ 633.24589, found 633.24698.

Benzyl 2,4-Di-*O*-benzyl-α-D-galactopyranosyluronate-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (31). To a solution of 831 mg of lactone **30** (1.36 mmol, 1 equiv) in 14 mL of DCM was added 160 mg of TMSONa (1.43 mmol, 1.05 equiv). After 30 min, TLC indicated complete consumption of the starting material, and the mixture was evaporated and filtered through a plug of silica gel using EtOAc/toluene/AcOH (20/79/1) as eluent. After removal of the eluent, the crude acid was dissolved in 14 mL of DMF. Next, 154 μL of BnBr (1.28 mmol, 1.1 equiv) and 418 mg of Cs_2CO_3 (1.28 mmol, 1.1 equiv) were added, and the reaction was stirred for 2 h. The mixture was diluted with EtOAc and washed with H_2O and brine. Drying over $MgSO_4$, filtration, and concentration under reduced pressure gave the crude product, which was purified by flash column chromatography using EtOAc/PE (1/4 → 1/3) to give ester **31** (729 mg, 1.01 mmol, 75% over two steps): R_f 0.52 (EtOAc/toluene, 1/3, v/v); $[\alpha]^{22}_D$ +44 (c 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 3030, 2870, 1759, 1454, 1107, 696; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.36−7.15 (m, 25H, H_{arom}), 5.09−4.95 (m, 3H, CH_2 Bn, H-1), 4.71 (d, J = 11.7 Hz, 1H, CH_2 Bn), 4.65−4.55 (m, 4H, CH_2 Bn), 4.49 (s, 3H, CH_2 Bn, H-5), 4.45 (d, J = 11.7 Hz, 1H, CH_2 Bn), 4.22 (dd, J = 3.1, 1.5 Hz, 1H, H-4), 4.11−4.05 (m, 1H, H-3), 3.88−3.80 (m, 2H, H-2, CH_2 Gro), 3.77−3.70 (m, 1H, CH Gro), 3.58 (d, J = 5.0 Hz, 2H, CH_2 Gro), 3.53 (dd, J = 10.4, 5.5 Hz, 1H, CH_2 Gro), 2.28 (d, J = 4.6 Hz, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 168.5 (C═O), 138.4, 138.3, 138.1, 138.0, 135.0 (C_q Ph), 128.6, 128.5, 128.4, 128.3, 128.3, 128.2, 127.9, 127.6, 127.5 (CH_{arom}), 97.4 (C-1), 78.0 (C-4), 76.7 (CH Gro), 76.6 (C-2), 74.9 (CH_2 Bn), 73.4 (CH_2 Bn), 72.6 (CH_2 Bn), 71.9 (CH_2 Bn), 70.4 (C-5), 69.7 (CH_2 Bn, C-3), 68.4 (CH_2 Gro), 66.9 (CH_2 COOBn); HRMS $[M + Na]^+$ calcd for $C_{44}H_{46}O_9Na$ 741.30340, found 741.30352.

1,2,4-Tri-*O*-benzyl-1-(1,2-di-*O*-benzyl-*sn*-glycerol)-D-galactopyranosiduronic Acid 3,6-Lactone (32). To a mixture of 57 mg of lactone **30** (93 μmol, 1 equiv), 96 μL of benzyl alcohol (933 μmol, 10 equiv), and 9.5 μL of thiophenol (93 μmol, 1 equiv) in 2 mL of dichloromethane was added 11 μL of $SnCl_4$ (93 μmol, 1 equiv). After being stirred for 2 days at ambient temperature, the mixture was neutralized with triethylamine, and 1 mL of satd aq $NaHCO_3$ was added. After rigorous stirring for 1 hr, the mixture was filtrated through a plug of Celite, and the solid material was rinsed with dichloromethane. The filtrate was washed with satd aq $NaHCO_3$ and brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by size-exclusion chromatography (DCM/MeOH 1/1 v/v) and flash column chromatography (eluent: EtOAc/PE 1/3) gave the title compound **32** (34 mg, 47 μmol, 51%) as an epimeric mixture: R_f 0.42 (EtOAc/toluene, 1/4, v/v); IR (neat, cm^{-1}) 3420, 2875, 1791, 1454, 1100, 1061, 698; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC, galacturonic acid based numbering, major epimer) δ 7.36−7.10 (m, 25H, H_{arom}), 4.81 (d, J = 7.2 Hz, 1H, H-1), 4.80−4.73 (m, 2H, CH_2 Bn), 4.65 (d, J = 2.2 Hz, 2H, CH_2 Bn), 4.62−4.57 (m, 2H, CH_2 Bn), 4.53 (dd, J = 6.8, 1.7 Hz, 1H, H-3), 4.49 (s, 2H, CH_2 Bn), 4.43 (dd, J = 6.8, 4.5 Hz, 1H, H-5), 4.33 (d, J = 11.7 Hz, 1H, CH_2 Bn), 4.28 (d, J = 11.5 Hz, 1H, CH_2 Bn), 4.11 (t, J = 6.8 Hz, 1H, H-4), 3.88−3.81 (m, 1H, CH_2 Gro), 3.81−3.74 (m, 2H, CH_2 Gro, CH Gro), 3.63−3.56 (m, 3H, H-2, CH_2 Gro), 2.85 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC, galacturonic acid based numbering, major epimer) δ 174.4 (C═O), 138.0, 137.3, 137.2, 137.0 (C_q Ph), 128.5, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5 (CH_{arom}), 103.4 (C-1), 79.5 (C-3, C-4), 77.1 (CH Gro), 76.3 (C-2), 74.4 (CH_2 Bn), 74.3 (C-5), 73.4 (CH_2 Bn), 72.2 (CH_2 Bn), 71.9 (CH_2 Bn), 70.5 (CH_2 Bn), 69.7 (CH_2 Gro), 69.3 (CH_2 Gro); HRMS $[M + Na]^+$ calcd for $C_{44}H_{46}O_9Na$ 741.30340, found 741.30347.

4-(*N*-Benzyloxycarbonylamino)-2-azido-3-*O*-chloroacetyl-2,4,6-trideoxy-D-galactopyranosyl-(1→4)-phenyl 2-*O*-Benzyl-1-thio-β-D-galactopyranosidurono-3,6-lactone (33). A mixture of 441 mg of hemiacetal **7** (1.11 mmol, 1 equiv), 559 mg of diphenyl sulfoxide (2.76 mmol, 2.5 equiv), and 330 mg of tri-*tert*-butylpyrimidine (1.33 mmol, 1.2 equiv) was coevaporated with toluene and stirred over activated molecular sieves (3 Å) for 30 min in 10 mL of DCM. The mixture was cooled to −60 °C before 202 μL of triflic acid anhydride (1.22 mmol, 1.1 equiv) was added. The mixture was allowed to warm to −40 °C before a mixture (dried over 3 Å molecular sieves) of 792 mg of acceptor **5** (2.21 mmol, 2 equiv) and 330 mg of tri-*tert*-butylpyrimidine (1.33 mmol, 1.2 equiv) in 2 mL of DCM was added. Stirring was continued, and the reaction mixture was allowed to warm to 4 °C overnight. The reaction mixture was quenched with 769 μL of triethylamine (5.53 mmol, 5.0 equiv), diluted with DCM, and washed with satd aq $NaHCO_3$. The aqueous phase was extracted with DCM, and the combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by size-exclusion chromatography (DCM/MeOH 1/1 v/v) and flash column chromatography (eluent: EtOAc/PE 1/4 → 3/7) gave the title compound **33** as a white foam (690 mg, 933 μmol, 84%): R_f 0.68 (EtOAc/PE, 2/3, v/v); $[\alpha]^{22}_D$ −38 (c 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2112, 1805, 1717, 1514, 1042; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.48−7.27 (m, 15H, H_{arom}), 5.42 (s, 1H, H-1), 5.24−5.12 (m, 2H, H-3′, CH_2 Cbz), 5.08−4.96 (m, 3H, CH_2 Cbz, NH, H-1′), 4.89 (dd, J = 4.9, 1.5 Hz, 1H, H-3), 4.69 (d, J = 11.8 Hz, 1H, CH_2 Bn), 4.63−4.54 (m, 2H, CH_2 Bn, H-4), 4.30 (d, J = 4.8 Hz, 1H, H-2), 4.27−4.20 (m, 2H, H-5′, H-4′), 4.11 (s, 1H, H-5), 3.98−3.83 (m, 2H, CH_2 ClAc), 3.48 (dd, J = 11.1, 3.8 Hz, 1H, H-2′), 1.17 (d, J = 6.4 Hz, 3H, H-6′); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 171.7, 166.5 (C═O), 156.6 (C═O Cbz), 136.3, 136.1, 133.2 (C_q Ph), 132.8, 129.0, 128.8, 128.6, 128.4, 128.3, 128.1, 128.0 (CH_{arom}), 97.9 (C-1′), 85.7 (C-1), 79.1 (C-3), 78.4 (C-2), 76.6 (C-4), 73.2 (CH_2 Bn), 71.6 (C-3′), 70.2 (C-5), 67.3 (CH_2 Cbz), 65.7 (C-5′), 57.1 (C-2′), 52.2 (C-4′), 40.5 (CH_2 ClAc), 16.3 (C-6′); HRMS $[M + Na]^+$ calcd for $C_{35}H_{35}ClN_4O_{10}SNa$ 761.16546, found 761.16560.

4-(*N*-Benzyloxycarbonylamino)-2-azido-3-*O*-chloroacetyl-2,4,6-trideoxy-D-galactopyranosyl-(1→4)-2-*O*-benzyl-α-D-galactopyranosiduronyl-3,6-lactone-(1→4)-benzyl 2,4-di-*O*-benzyl-α-D-galactopyranosyluronate-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (34). Lactone **33** (538 mg) was coupled to alcohol **31** (2 equiv instead of 1.5 equiv) according to the general procedure for glycosylations using Ph_2SO/Tf_2O. The reaction was quenched with triethylamine (5 equiv), and the title compound **34** was obtained in 60% yield (590 mg, 438 μmol) after size-exclusion chromatography (DCM/MeOH 1/1 v/v): R_f 0.58 (EtOAc/toluene, 1/3, v/v); $[\alpha]^{22}_D$ +101 (c 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2110, 1803, 1761, 1720, 1454, 1043; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.43−7.01 (m, 35H, H_{arom}), 5.17−5.14 (m, 2H, H-3″, CH_2 Bn), 5.08−4.94 (m, 6H, CH_2 Bn, H-1′, H-1, NH), 4.89−4.80 (m, 3H, H-1″, CH_2 Bn), 4.73−4.69 (m, 2H, H-4′, H-3′), 4.66−4.59 (m, 2H, CH_2 Bn), 4.57−4.48 (m, 4H, CH_2 Bn), 4.46 (s, 1H, H-5), 4.41−4.33 (m, 3H, H-3, CH_2 Bn), 4.25−4.21 (m, 3H, H-4, H-5′, H-4″), 4.18 (q, J = 6.6 Hz, 1H, H-5″), 3.99 (dd, J = 10.1, 3.5 Hz, 1H, H-2), 3.89 (d, J = 4.6 Hz, 2H, CH_2 ClAc), 3.88−3.80 (m, 2H, CH_2 Gro, H-2′), 3.80−3.74 (m, 1H, CH Gro), 3.65−3.57 (m, 3H, CH_2 Gro), 3.42 (dd, J = 11.2, 3.8 Hz,

1H, H-2″), 1.14 (d, J = 6.4 Hz, 3H, H-6″); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 170.7, 168.2, 166.5 (C═O), 156.5 (CH_2 Cbz), 138.6, 138.5, 138.2, 137.9, 137.1, 136.0, 134.8 (C_q Ph), 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5, 127.4, 127.2, 126.9 (CH_{arom}), 98.4 (C-1), 97.7 (C-1″), 94.9 (C-1′), 80.5 (C-3′), 76.5 (CH Gro), 75.7 (C-4), 75.5 (C-4′), 75.4 (C-3), 74.9 (C-2′), 74.7 (CH_2 Bn), 74.2 (CH_2 Bn), 73.9 (C-2), 73.3 (2 CH_2 Bn), 71.9 (CH_2 Bn), 71.5 (C-3″), 71.2 (C-5′), 70.1 (C-5), 69.7 (CH_2 Gro), 68.6 (CH_2 Gro), 67.3 (CH_2), 67.1 (CH_2), 65.4 (C-5″), 56.9 (C-2″), 52.1 (C-4″), 40.5 (CH_2 ClAc), 16.2 (C-6″); HRMS $[M + Na]^+$ calcd for $C_{73}H_{75}ClN_4O_{19}Na$ 1369.46062, found 1369.46158.

4-(*N*-Benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-D-galactopyranosyl-(1→4)-2-*O*-benzyl-α-D-galactopyranosiduronyl-3,6-lactone-(1→4)-benzyl 2,4-di-*O*-benzyl-α-D-galactopyranosyluronate-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (35). A solution of 76 mg of compound **34** (56 μmol, 1 equiv), 36 μL of pyridine (451 μmol, 8 equiv), and 13 mg (169 μmol, 3 equiv) of thiourea in 1 mL of EtOH was stirred at 65 °C for 6 h. The mixture was concentrated under reduced pressure, diluted with EtOAc, and washed with aq 1 M HCl, satd aq $NaHCO_3$, and brine. The organic phase was dried ($MgSO_4$), filtered, and concentrated in vacuo. Flash column chromatography using EtOAc/PE (7/13→9/11) gave 44 mg (34 μmol, 62%) of the title compound **35**: R_f 0.48 (EtOAc/PE, 3/7, v/v); $[\alpha]^{22}_D$ +97 (c 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 3400, 2874, 2110, 1081, 1717, 1705, 1028; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.45−6.99 (m, 35H, H_{arom}), 5.12 (s, 2H, CH_2 Bn), 5.08−4.98 (m, 4H, NH, CH_2 Bn, H-1′), 4.96 (d, J = 3.6 Hz, 1H, H-1), 4.87−4.78 (m, 3H, CH_2, H-1″), 4.71 (dd, J = 4.9, 1.8 Hz, 1H, H-3′), 4.69 (s, 1H, H-4′), 4.67−4.59 (m, 2H, CH_2 Bn), 4.58−4.48 (m, 4H, CH_2 Bn), 4.46 (s, 1H, H-5), 4.42−4.32 (m, 3H, CH_2 Bn, H-3), 4.23 (s, 2H, H-4, H-5′), 4.09 (m, 2H, H-3″, H-5″), 4.03−3.96 (m, 2H, H-4″, H-2), 3.85 (dd, J = 10.4, 4.5 Hz, 1H, CH_2 Gro), 3.81 (dd, J = 4.6, 2.5 Hz, 1H, H-2′), 3.79−3.73 (m, 1H, CH Gro), 3.65−3.55 (m, 3H, CH Gro), 3.14 (dd, J = 10.7, 3.8 Hz, 1H, H-2″), 1.13 (d, J = 6.4 Hz, 3H, H-6″); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 171.1, 168.3 (C═O), 158.0 (CH_2 Cbz), 138.6, 138.5, 138.2, 137.9, 137.2, 135.7, 134.9 (C_q Ph), 128.7, 128.6, 128.5, 128.5, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.40, 127.2, 126.9 (CH_{arom}), 98.5 (C-1), 98.4 (C-1″), 94.9 (C-1′), 80.6 (C-3′), 76.6 (CH Gro), 75.9 (C-4′), 75.8 (C-4), 75.5 (C-3), 74.9 (C-2′), 74.7, 74.2 (CH_2 Bn), 73.9 (C-2), 73.4, 73.3, 71.9 (CH_2 Bn), 71.4 (C-5′), 70.1 (C-5), 69.7, 68.6 (CH_2 Gro), 68.4 (C-3″), 67.6, 67.1 (CH_2), 65.8 (C-5″), 59.9 (C-2″), 55.5 (C-4″), 16.4 (C-6″); HRMS $[M + Na]^+$ calcd for $C_{71}H_{74}N_4O_{18}Na$ 1293.48903, found 1293.48964.

4-(*N*-Benzyloxycarbonylamino)-2-acetamido-2,4,6-trideoxy-D-galactopyranosyl-(1→4)-2-*O*-benzyl-α-D-galactopyranosiduronyl-3,6-lactone-(1→4)-benzyl 2,4-di-*O*-benzyl-α-D-galactopyranosyluronate-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (36). To an ice-cooled solution of 281 mg of azide **35** (221 μmol) in 5 mL of pyridine was added 5 mL of freshly distilled thiolacetic acid. The mixture was stirred at room temperature for 2.5 h, concentrated under reduced pressure, and coevaporated with toluene. Flash column chromatography using EtOAc/PE (7/3→1/0) afforded the title acetamide (188 mg, 146 μmol, 66%): R_f 0.30 (EtOAc/PE, 3/1, v/v); $[\alpha]^{22}_D$ +83 (c 0.8, CH_2Cl_2); IR (neat, cm^{-1}) 3300, 2924, 1801, 1759, 1717, 1661, 1540, 1028; ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.51−6.91 (m, 35H, H_{arom}), 5.67 (d, J = 8.4 Hz, 1H, NH), 5.40 (d, J = 9.7 Hz, 1H, NH), 5.18−4.99 (m, 5H, CH_2 Bn, H-1′), 4.95 (d, J = 3.5 Hz, 1H, H-1), 4.91 (d, J = 3.7 Hz, 1H, H-1″), 4.84−4.80 (m, 2H, CH_2 Bn), 4.69 (dd, J = 4.9, 1.5 Hz, 1H, H-3′), 4.66 (s, 1H, H-4′), 4.62 (m, 2H, CH_2 Bn), 4.59−4.48 (m, 4H, CH_2 Bn), 4.45 (s, 1H, H-5), 4.42−4.31 (m, 3H, CH_2 Bn, H-3), 4.22 (s, 1H, H-4), 4.12 (s, 1H, H-5′), 4.06−3.96 (m, 4H, H-2″, H-4″, H-5″, H-2), 3.86−3.73 (m, 4H, CH_2 Gro, H-3″, H-2′, CH Gro), 3.65−3.56 (m, 3H, CH_2 Gro), 1.92 (s, 3H, CH_3 NHAc), 1.12 (d, J = 6.2 Hz, 3H, H-6″); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 171.5, 168.2 (C═O), 157.7 (CH_2 Cbz), 138.4, 138.3, 138.2, 137.8, 137.1, 136.0, 134.8 (C_q Ph), 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.6, 127.4, 127.3, 127.0, 126.7 (CH_{arom}), 98.4 (C-1), 97.5 (C-1″), 94.9 (C-1′), 80.9 (C-3′), 76.4 (CH Gro), 75.7 (C-4), 75.6 (C-3), 74.7, 74.6 (C-2′, C-4′, CH_2 Bn), 74.0 (CH_2 Bn), 73.7 (C-2), 73.4, 73.1, 71.7 (CH_2 Bn), 71.3 (C-5′), 70.0 (C-5), 69.6, 68.4 (CH_2 Gro), 67.7 (C-3″), 67.0, 66.9 (CH_2), 66.1 (C-5″), 55.2 (C-4″), 50.2 (C-2″), 22.9 (CH_3 NHAc), 16.4 (C-6″); HRMS $[M + Na]^+$ calcd for $C_{73}H_{78}N_2O_{19}Na$ 1309.50910, found 1309.50986.

2-Acetamido-4-amino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-α-D-galactopyranosyluronate-(1→3)-α-D-galactopyranosyluronate-(1→3)-*sn*-glycerol (2). Compound **36** (54 mg, 42 μmol, 1 equiv) was dissolved in 7 mL of *t*-BuOH/H_2O (5/2 v/v) and stirred under argon atmosphere. A catalytic amount of palladium on activated charcoal and 105 μL of 1 M aq HCl were added, and the mixture was allowed to stir for 2 days under hydrogen atmosphere. Following filtration over Celite and removal of the eluent, the crude product was allowed to stir in 0.04 M aq HCl for an additional 2 days. Next, the mixture was concentrated in vacuo and purified by ion-exchange column chromatography (30 mM NaOAc (aq)/100 mM NaOH (aq) → 80 mM NaOAc (aq)/100 mM NaOH (aq)) and filtration (HW-40, 0.15 M Et_3NHOAc in H_2O) to afford 10 mg of the pure title compound **2** (16 μmol, 38%) after lyophilization: ^{1}H NMR (600 MHz, D_2O, HH-COSY, HSQC, HMBC, TOCSY, T = 293 K) δ 5.32 (d, J = 3.8 Hz, 1H, H-1′), 5.08 (d, J = 3.8 Hz, 1H, H-1), 5.03 (d, J = 3.8 Hz, 1H, H-1″), 4.85 (q, J = 6.5 Hz, 1H, H-5″), 4.68 (s, 1H, H-5′), 4.60 (d, J = 1.9 Hz, 1H, H-4), 4.44 (d, J = 2.4 Hz, 1H, H-4′), 4.39 (s, 1H, H-5), 4.27 (dd, J = 11.3, 4.3 Hz, 1H, H-3″), 4.21−4.18 (m, 2H, H-3′, H-3), 4.09 (dd, J = 11.3, 3.8 Hz, 1H, H-2″), 4.04−3.95 (m, 3H, H-2, CH Gro, H-2′), 3.88 (dd, J = 10.6, 3.6 Hz, 1H, CH_2 Gro), 3.74 (dd, J = 11.8, 4.5 Hz, 1H, CH_2 Gro), 3.70 (d, J = 3.7 Hz, 1H, H-4″), 3.66 (dd, J = 11.8, 6.2 Hz, 1H, CH_2 Gro), 3.57 (dd, J = 10.5, 7.1 Hz, 1H, CH_2 Gro), 2.17 (s, 3H, CH_3 NHAc), 1.33 (d, J = 6.7 Hz, 3H); ^{13}C NMR (151 MHz, D_2O, HH-COSY, HSQC, HMBC, TOCSY, T = 293 K) δ 176.1, 176.0, 175.3 (C═O), 99.7 (C-1″, C-1), 96.9 (C-1′), 81.0 (C-4′), 76.2 (C-3), 72.1, 72.0 (C-5, C-5′), 71.5 (CH Gro), 70.0 (CH_2 Gro), 69.4 (C-3′), 68.8 (C-2′), 68.5 (C-4), 67.5 (C-2), 65.5 (C-3″), 64.2 (C-5), 63.2 (CH_2 Gro), 56.2 (C-4″), 50.2 (C-2″), 23.2 (CH_3 NHAc), 16.3 (C-6″); ^{13}C-HMBC NMR (151 MHz, D_2O, T = 293 K) δ 99.7 ($J_{C1''-H1''}$ = 173.31 Hz, J_{C1-H1} = 170.6 Hz, C-1″, C-1), 96.9 ($J_{C1'-H1'}$ = 170.3 Hz, C-1′); HRMS $[M + H]^+$ calcd for $C_{23}H_{39}N_2O_{18}$ 631.21924, found 631.21928.

(1,3-Oxazolidino-2-one)[5,4-*c*]-2-acetamido-4-amino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-α-D-galactopyranosyluronate-(1→3)-α-D-galactopyranosyluronate-(1→3)-*sn*-glycerol (37). To a solution of 40.0 mg (31 μmol, 1 equiv) of compound **36** in 1.5 mL of DCM was added 14 mg of TMSONa (124 μmol, 4.0 equiv). The mixture was stirred for 1 h, followed by evaporation of the solvent and elution of the crude product over a plug of silica (eluent: EtOAc, then EtOAc/MeOH/H_2O/AcOH 93/5/1/1, then EtOAc/MeOH/H_2O/AcOH 88/10/1/1). After removal of the eluent, the crude product was dissolved in 5 mL of *t*-BuOH/H_2O (4/1 v/v) and stirred under argon atmosphere. A catalytic amount of palladium on activated charcoal and 190 μL of 1 M aq HCl were added, and the mixture was allowed to stir overnight under hydrogen atmosphere. Filtration over Celite, followed by gel filtration (HW-40, 0.15 M Et_3NHOAc in H_2O) and subsequent lyophilization, afforded 8.95 mg of the title compound **37** (11.8 μmol, 38% over two steps): ^{1}H NMR (600 MHz, D_2O, HH-COSY, HSQC, T = 306 K) δ 5.22 (d, J = 3.8 Hz, 1H, H-1′), 4.99 (d, J = 3.8 Hz, 1H, H-1), 4.95 (d, J = 3.8 Hz, 1H, H-1″), 4.79 (dd, J = 9.0, 7.2 Hz, 1H, H-3″), 4.70−4.61 (m, 2H, H-5′, H-5″), 4.52 (d, J = 2.0 Hz, 1H, H-4), 4.40−4.33 (m, 2H, H-5, H-4′), 4.16−4.06 (m, 4H, H-4″, H-3′, H-2″, H-3), 3.94−3.86 (m, 3H, H-2,

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CH Gro, H-2′), 3.78 (dd, J = 10.5, 3.7 Hz, 1H, CH_2 Gro), 3.64 (dd, J = 11.8, 4.6 Hz, 1H, CH_2 Gro), 3.56 (dd, J = 11.8, 6.2 Hz, 1H, CH_2 Gro), 3.49 (dd, J = 10.6, 7.0 Hz, 1H, CH_2 Gro), 3.19 (q, J = 7.3 Hz, 10H, CH_2 Et_3NHOAc), 2.07 (s, 3H, CH_3 NHAc), 1.28−1.24 (m, 18H, H-6″, CH_3 Et_3NHOAc); ^{13}C NMR (151 MHz, D_2O, HH-COSY, HSQC, T = 306 K) δ 175.5, 175.3, 174.8, 162.7 (C═O), 99.8 (C-1), 99.2 (C-1″), 96.9 (C-1′), 80.9 (C-4′), 76.7 (C-3″), 76.1 (C-3), 71.9, 71.8 (C-5, C-5′), 71.6 (CH Gro), 70.1 (CH_2 Gro), 69.5 (C-3′), 68.8 (C-2′), 68.4 (C-4), 67.5 (C-2), 63.3 (CH_2 Gro), 63.1 (C-5″), 56.9 (C-4″), 50.7 (C-2″), 47.6 (CH_2 Et_3NHOAc), 23.2 (CH_3 NHAc), 17.0 (C-6″), 9.2 (CH_3 Et_3NHOAc); ^{13}C-HMBC NMR (151 MHz, D_2O, T = 306 K) δ 99.9 (J_{C1-H1} = 170.9 Hz, C-1), 98.8 ($J_{C1''-H1''}$ = 172.5 Hz, C-1″), 97.1 ($J_{C1'-H1'}$ = 172.0 Hz, C-1′); HRMS $[M + H]^+$ calcd for $C_{24}H_{37}N_2O_{19}$ 657.19850, found 657.19866.

2,4-Di-*O*-benzyl-α-D-galactopyranosiduronyl-3,6-lactone-(1→3)-4-(*N*-benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-α-D-galactopyranosyl-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (38). Lactone **4** (257 mg) was coupled to 220 mg of alcohol **20** (382 μmol, 0.66 equiv) according to the general procedure for glycosidations using Ph_2SO/Tf_2O, yielding 244 mg of the title compound **38** (267 μmol, 70%) after size-exclusion chromatography (DCM/MeOH 1/1 v/v) and flash column chromatography (eluent: EtOAc/PE 1/3 → 3/7): R_f 0.68 (EtOAc/toluene, 1/4, v/v); $[\alpha]^{22}_D$ +106 (c 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2872, 2110, 1798, 1717, 1454, 1026, 696; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC); δ 7.55−7.11 (m, 25H, H_{arom}), 5.14 (d, J = 2.3 Hz, 1H, H-1′), 5.13−4.99 (m, 3H, NH, CH_2 Cbz), 4.82 (d, J = 3.8 Hz, 1H, H-1), 4.79 (d, J = 11.7 Hz, 1H, CH_2 Bn), 4.73−4.61 (m, 3H, CH_2 Bn, H-3′), 4.58−4.47 (m, 5H, CH_2 Bn, H-4′), 4.29−4.17 (m, 3H, CH_2 Bn, H-5′, H-3), 4.10 (dd, J = 5.0, 2.3 Hz, 1H, H-2′), 4.01 (dd, J = 9.6, 2.9 Hz, 1H, H-4), 3.94 (q, J = 6.1 Hz, 1H, H-5), 3.82−3.73 (m, 2H, CH Gro, CH_2 Gro), 3.62 (d, J = 4.5 Hz, 2H, CH_2 Gro), 3.60−3.53 (m, 1H, CH_2 Gro), 3.15 (dd, J = 10.8, 3.8 Hz, 1H, H-2), 1.05 (d, J = 6.4 Hz, 3H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 171.9 (C═O), 156.6 (C═O Cbz), 138.3, 138.0, 136.8, 135.8 (C_q Ph), 128.7, 128.5, 128.5, 128.3, 128.0, 127.7, 127.6, 127.4 (CH_{arom}), 98.2 (C-1), 95.6 (C-1′), 80.4 (C-3′), 76.7 (CH Gro), 75.8 (C-4′), 75.1 (C-2′), 74.3 (CH_2 Bn), 73.5 (C-3), 73.4 (CH_2 Bn), 72.0 (CH_2 Bn, C-5′), 71.4 (CH_2 Bn), 69.3 (CH_2 Bn), 67.9 (CH_2 Bn), 67.0 (CH_2 Cbz), 64.2 (C-5), 58.3 (C-2), 51.8 (C-4), 16.4 (C-6); HRMS $[M + Na]^+$ calcd for $C_{51}H_{54}N_4O_{12}Na$ 937.36304, found 937.36340.

Benzyl 2,4-Di-*O*-benzyl-α-D-galactopyranosyluronate-(1→3)-4-(*N*-benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-α-D-galactopyranosyl-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (39). To a solution of 88 mg of lactone **38** (96 μmmol, 1 equiv) in 2 mL of DCM was added 13 mg of TMSONa (115 μmol, 1.2 equiv). After 50 min, TLC indicated complete consumption of the starting material, and the reaction was quenched with 28 μL of AcOH (481 μmol, 5.0 equiv), after which the mixture was coevaporated with toluene and subsequently dissolved in 2 mL of DMF. Next, 17 μL of BnBr (144 μmol, 1.5 equiv) and 39 mg of Cs_2CO_3 (120 μmol, 1.25 equiv) were added, and the reaction was stirred until TLC analysis showed complete consumption of the starting material. The mixture was diluted with EtOAc and washed with H_2O and brine. Drying over $MgSO_4$, filtration, and concentration under reduced pressure gave the crude product. Purification by flash column chromatography using EtOAc/toluene (1/4) gave the title compound **39** in pure form (86 mg, 84 μmol, 88% over two steps): R_f 0.46 (EtOAc/toluene, 1/3, v/v); $[\alpha]^{22}_D$ +122 (c 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2880, 2104, 1761, 1719, 1094, 1026, 696; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.37−7.07 (m, 30H, H_{arom}), 5.59 (d, J = 3.0 Hz, 1H, H-1′), 5.11−4.96 (m, 4H, NH, CH_2 Bn), 4.88 (d, J = 3.8 Hz, 1H, H1), 4.75 (d, J = 12.2 Hz, 1H, CH_2 Bn), 4.70−4.58 (m, 5H, H-5′, CH_2 Bn), 4.55−4.45 (m, 2H, CH_2 Bn), 4.40 (m, 2H, CH_2 Bn), 4.28−4.20 (m, 4H, H-4′, H-4, H-3, H-3′), 3.97−3.90 (m, 2H, H-2′, H-5), 3.81−3.70 (m, 2H, CH_2 Gro, CH Gro), 3.61−3.53 (m, 3H, CH_2 Gro), 3.30 (dd, J = 10.5, 3.9 Hz, 1H, H-2), 2.18 (d, J = 4.0 Hz, 1H, OH), 1.03 (d, J = 6.4 Hz, 3H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 168.1 (C═O COOBn), 156.8 (C═O Cbz), 138.3, 138.1, 138.0, 137.8, 135.9, 134.9 (C_q Ph), 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 127.4 (CH_{arom}), 97.7 (C-1), 92.3 (C-1′), 77.6 (C-4′), 76.8 (CH Gro), 74.8 (CH_2 Bn), 74.8 (C-2′), 73.3 (CH_2 Bn), 72.1, 72.0 (CH_2 Bn), 70.6 (C-5′), 69.5 (C-3), 69.3 (CH_2 Gro), 69.1 (C-3′), 67.9 (CH_2 Gro), 66.9, 66.9 (CH_2 Cbz, CH_2 COOBn), 65.0 (C-5), 59.2 (C-2), 50.8 (C-4), 16.2 (C-6); HRMS $[M + Na]^+$ calcd for $C_{58}H_{62}N_4O_{13}Na$ 1045.42056, found 1045.42095.

2,4-Di-*O*-benzyl-α/*β*-D-galactopyranosiduronyl-3,6-lactone-(1→3)-benzyl 2,4-Di-*O*-benzyl-α-D-galactopyranosyluronate-(1→3)-4-(*N*-benzyloxycarbonylamino)-2-azido-2,4,6-trideoxy-α-D-galactopyranosyl-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (40). Lactone **4** (62 mg, 139 μmol) was coupled to 95 mg of alcohol **39** (93 μmol, 0.67 equiv) according to the general procedure for glycosidations using Ph_2SO/Tf_2O, yielding 99 mg of the title epimers (73 μmol, 78%, α/β 5:4) after size-exclusion chromatography (DCM/MeOH 1/1 v/v) and flash column chromatography (eluent: EtOAc/PE 1/4 → 3/7): R_f 0.42 (EtOAc/PE, 2/3, v/v); IR (neat, cm^{-1}) 2870, 2106, 1801, 1761, 1717, 1497, 1454, 1028, 696; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.42−6.81 (m, 72H, H_{arom}), 5.67 (d, J = 2.9 Hz, 0.8H, H-1′β), 5.49 (d, J = 2.5 Hz, 1H, H-1′α), 5.45 (s, 0.8H, H-1″β), 5.14−4.58 (m, 22H), 4.57−4.35 (m, 14.4H), 4.35−4.00 (m, 12.4H), 4.00−3.84 (m, 3.4H), 3.85−3.69 (m, 4.6H), 3.58−3.56 (m, 5.4H), 3.37 (dd, J = 10.6, 3.9 Hz, 0.8H, H-2β), 3.31 (dd, J = 10.6, 3.9 Hz, 1H, H-2α), 1.03−0.98 (m, 5.4H, H-6α, H-6β); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 173.5, 171.6, 168.0, 167.9, 156.7, 139.3, 138.5, 138.3, 138.1, 137.8, 137.3, 136.9, 136.8, 136.7, 136.2, 136.0, 135.1, 134.8, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 127.1, 126.9, 99.9 (C-1″β), 97.7 (C-1α, C-1β), 95.2 (C-1″α), 93.4 (C-1′α), 91.9 (C-1′β), 80.1, 79.0, 78.5, 77.2, 76.9, 76.4, 75.9, 75.8, 75.7, 75.4, 75.1, 74.7, 74.3, 74.0, 73.4, 73.0, 72.7, 72.4, 72.2, 72.1, 71.7, 71.4, 71.3, 71.2, 70.6, 70.3, 69.8 (C-3β), 69.6 (C-3α), 69.5, 68.1, 68.0, 67.1, 66.8, 66.7, 66.6, 65.1 (C-5β, C-5α), 59.5 (C-2β), 59.1 (C-2α), 50.8 (C-4α), 50.7 (C-4β), 16.3 (C-6α), 16.2 (C-6β); HRMS $[M + Na]^+$ calcd for $C_{78}H_{80}N_4O_{18}$-Na 1383.53598, found 1383.53760.

2,4-Di-*O*-benzyl-α/*β*-D-galactopyranosiduronyl-3,6-lactone-(1→3)-benzyl 2,4-Di-*O*-benzyl-α-D-galactopyranosyluronate-(1→3)-2-acetamido-4-(*N*-benzyloxycarbonylamino)-2,4,6-trideoxy-α-D-galactopyranosyl-(1→3)-1,2-di-*O*-benzyl-*sn*-glycerol (41). To an ice-cooled solution of 61 mg of epimeric azides **40** (45 μmol) in 1.5 mL of pyridine was added 1.5 mL of freshly distilled thiolacetic acid. The mixture was stirred at room temperature for 3 h, concentrated under reduced pressure, and coevaporated with toluene. Flash column chromatography using EtOAc/PE (2/3) afforded title epimers **41** (25 mg, 18 μmol, α/β 1:1, 40%): R_f 0.67 (EtOAc/PE, 3/2, v/v); IR (neat, cm^{-1}) 2930, 1802, 1718, 1668, 1497, 1454, 1027, 731, 695; ^1H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC) δ 7.48−6.84 (m, 80H, H_{arom}), 5.73 (dd, J = 15.8, 9.2 Hz, 2H, NH), 5.45 (s, 1H, H-1″β), 5.29 (d, J = 2.9 Hz, 1H, H-1′α or H-1′β), 5.22−4.99 (m, 8H), 4.95 (d, J = 12.4 Hz, 1H), 4.87 (m, 2H), 4.79 (d, J = 12.6 Hz, 1H), 4.75−4.26 (m, 34H), 4.26−4.07 (m, 7H), 4.05−3.65 (m, 13H), 3.62−3.39 (m, 6H), 1.72 (s, 3H, CH_3 NHAc), 1.71 (s, 3H, CH_3 NHAc), 1.06 (m, 6H, H-6α, H-6β); ^{13}C NMR (100 MHz, $CDCl_3$, HH-COSY, HSQC) δ 173.7, 171.7, 170.2, 170.1, 168.4, 168.2, 156.8, 139.3, 138.7, 138.2, 138.1, 138.0, 137.9, 137.8, 137.4, 136.9, 136.8, 136.4, 135.7, 135.0, 134.8, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.0, 126.9, 99.8 (C-1″β), 98.1 (C-1α or C1-β), 97.9 (C-1α or C1-β), 97.6 (C-1′α or C1′-β), 95.5 (C-1″α), 95.4 (C-1′α or C1′-β), 80.0, 79.2, 77.3, 77.1, 76.8, 76.6, 76.0, 75.7, 75.5, 75.4, 75.0, 74.5,

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74.2, 73.8, 73.7, 73.6, 73.5, 73.1, 72.4, 72.0, 71.9, 71.7, 71.6, 71.4, 71.2, 71.0, 70.6, 69.4, 69.3, 68.2, 67.1, 66.8, 66.5, 66.4, 65.7 (C-5α or C-5β), 65.5 (C-5α or C-5β), 52.5 (C-4α or C-4β), 52.1 (C-4α or C-4β), 48.8 (C-2α or C-2β), 48.5 (C-2α or C-2β), 22.9 (2 × CH_3 NHAc), 16.5 (C-6α, C-6β); HRMS $[M + Na]^+$ calcd for $C_{80}H_{84}N_2O_{19}Na$ 1399.55605 $C_{29}H_{35}N_3O_7S$, found 1399.55602.

α-D-Galactopyranosyluronate-(1→3)-α-D-galactopyranosyluronate-(1→3)-2-acetamido-4-amino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→3)-*sn*-glycerol (3a) and β-D-Galactopyranosyluronate-(1→3)-α-D-galactopyranosyluronate-(1→3)-2-acetamido-4-amino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→3)-*sn*-glycerol (3b). To a solution of 35 mg (25 μmol, 1 equiv) of epimeric mixture **41** in 1.5 mL of DCM was added 11.4 mg of TMSONa (102 μmol, 4 equiv). The mixture was stirred for 1 h, followed by evaporation and elution over a plug of silica (eluent: EtOAc, then EtOAc/MeOH/H_2O/AcOH 88/10/1/1). After removal of the eluent, the crude product was dissolved in *t*-BuOH/H_2O (4/1 v/v) and stirred under argon atmosphere. A catalytic amount of palladium on activated charcoal and 170 μL of 1 M aq HCl were added, and the mixture was allowed to stir for 2 days under hydrogen atmosphere. Filtration over Celite, gel filtration (HW-40, 0.15 M Et_3NHOAc in H_2O), and ion-exchange column chromatography (30 mM NaOAc (aq)/100 mM NaOH (aq) → 80 mM NaOAc (aq)/100 mM NaOH (aq)) yielded two fractions that were both subjected to another gel filtration step (HW-40, 0.15 M Et_3NHOAc in H_2O) to give the two title epimers in pure form after lyophilization (α-epimer **3a**: 4.4 mg, 7.0 μmol 28% over two steps, β-epimer **3b**: 2.7 mg, 4.3 μmol, 17% over two steps). α-Epimer **3a**: ^1H NMR (600 MHz, D_2O, HH-COSY, HSQC, HMBC, TOCSY, T= 298 K) δ 5.17 (d, *J* = 3.1 Hz, 1H, H-1″), 5.07 (d, *J* = 2.6 Hz, 1H, H-1′), 4.89 (d, *J* = 3.8 Hz, 1H, H-1), 4.66 (s, 1H, H-5′), 4.46 (s, 1H, H-4′), 4.35 (q, *J* = 6.4 Hz, 1H, H-5), 4.31−4.25 (m, 2H, H-4″, H-3), 4.19−4.13 (m, 2H, H-2, H-5″), 3.99−3.93 (m, 3H, H-3′, H-3″, H-2′), 3.93−3.89 (m, 1H, CH Gro), 3.87 (dd, *J* = 10.5, 3.2 Hz, 1H, H-2″), 3.82 (d, *J* = 4.0 Hz, 1H, H-4), 3.77 (dd, *J* = 10.6, 3.5 Hz, 1H, CH_2 Gro), 3.65 (dd, *J* = 11.7, 4.7 Hz, 1H, CH_2 Gro), 3.58 (dd, *J* = 11.7, 6.2 Hz, 1H, CH_2 Gro), 3.46 (dd, *J* = 10.5, 6.6 Hz, 1H, CH_2 Gro), 3.18 (q, *J* = 7.3 Hz, 1.2H, CH_2 Et_3NHOAc), 1.97 (s, 3H, CH_3 NHAc), 1.29 (d, *J* = 6.7 Hz, 3H, H-6), 1.26 (t, *J* = 7.3 Hz, 1.9H, CH_3 Et_3NHOAc); ^{13}C NMR (151 MHz, D_2O, HH-COSY, HSQC, HMBC, TOCSY, T= 298 K) δ 176.3, 175.5, 175.4 (C═O), 99.7 (C-1′), 98.3 (C-1), 97.4 (C-1″), 76.3 (C-3′), 73.8(C-3), 73.0 (C-5″), 72.6 (C-5), 71.6 (C-4″), 71.4 (CH Gro), 70.4 (C-3″), 70.0 (CH_2 Gro), 68.8 (C-2″), 68.5 (C-4′), 66.7 (C-2′), 63.4 (C-5), 63.2 (CH_2 Gro), 53.7 (C-4), 48.7 (C-2), 47.6 (CH_2 Et_3NHOAc), 22.7 (CH_3 NHAc), 16.5 (C-6), 9.2 (CH_3 Et_3NHOAc); ^{13}C-HMBC NMR (151 MHz, D_2O, *T* = 298 K) δ 99.7 ($J_{C1'-H1'}$ = 170.3 Hz, C-1′), 98.3 (J_{C1-H1} = 173.6 Hz, C-1), 97.4 ($J_{C1''-H1''}$ = 170.3 Hz,C-1″); HRMS $[M + H]^+$ calcd for $C_{23}H_{39}N_2O_{18}$ 631.21924, found 631.21927. β-Epimer **3b**: ^1H NMR (600 MHz, D_2O, HH-COSY, HSQC, HMBC, TOCSY, T= 298 K) δ 5.09 (d, *J* = 3.6 Hz, 1H, H-1′), 4.90 (d, *J* = 3.8 Hz, 1H, H-1), 4.61 (d, *J* = 7.8 Hz, 1H, H-1″), 4.58 (s, 1H, H-4′), 4.36 (q, *J* = 6.5 Hz, 1H, H-5), 4.29 (dd, *J* = 11.3, 4.4 Hz, 1H, H-3), 4.20−4.15 (m, 2H, H-4″, H-2), 4.14 (s, 1H, H-5′), 4.06 (s, 1H, H-5″), 4.05−3.98 (m, 2H, H-2′, H-3′), 3.91 (dd, *J* = 9.6, 5.3 Hz, 1H, CH Gro), 3.84 (d, *J* = 3.7 Hz, 1H, H-4), 3.77 (dd, *J* = 10.6, 3.6 Hz, 1H, CH_2 Gro), 3.70 (dd, *J* = 10.0, 3.5 Hz, 1H, H-3″), 3.65 (dd, *J* = 11.7, 4.7 Hz, 1H, CH_2 Gro), 3.63−3.56 (m, 2H, CH_2 Gro, H-2″), 3.46 (dd, *J* = 10.6, 6.6 Hz, 1H, CH_2 Gro), 1.97 (s, 3H, CH_3 NHAc), 1.89 (s, 1H, CH_3 AcOH), 1.31 (t, *J* = 6.7 Hz, 3H, H-6); ^{13}C NMR (151 MHz, D_2O, HH-COSY, HSQC, HMBC, TOCSY, T= 298 K) δ 176.1, 176.0, 175.5 (C═O), 104.7 (C-1″), 99.0 (C-1′), 98.3 (C-1), 80.3 (C-3′), 76.5 (C-5″), 73.6 (C-3″), 73.3 (C-3), 73.2 (C-5′), 71.5 (C-2″), 71.4 (CH Gro), 71.2 (C-4″), 70.7 (C-4′), 70.0 (CH Gro), 67.5 (C-2′), 63.2 (C-5), 53.7 (C-4), 48.7 (C-2), 22.7 (CH_3 NHAc), 16.5 (C-6); ^{13}C-HMBC NMR (151 MHz, D_2O, *T* = 298 K) δ 104.7 ($J_{C1''-H1''}$ = 161.5 Hz, C-1″), 99.0 ($J_{C1'-H1'}$ = 170.0 Hz, C-1′), 98.3 (J_{C1-H1} = 173.5 Hz, C-1); HRMS $[M + H]^+$ calcd for $C_{23}H_{39}N_2O_{18}$ 631.21924, found 631.21923.

■ ASSOCIATED CONTENT

Supporting Information. Spectroscopic data of the reported compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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