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Synthesis of selected aminodeoxy analogues of galabiose and globotriose

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Dedicated to Professor Sinäy on his 62nd birthday.

Abstract

Six aminodeoxy 2-(trimethylsilyl)ethyl (Me_3SiEt) glycoside analogues of galabiose (4′- and 6′-aminodeoxy) and globotriose (6″-, 4″-, 2″-, and 6′-aminodeoxy) were synthesized by glycosylation of protected Me_3SiEt galactoside and lactoside acceptors with azido-substituted monosaccharide donors, followed by reduction of the azido groups and removal of the protecting groups. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Galabiose analogues; Globotriose analogues; Aminodeoxy; Bacterial binding inhibitors

1. Introduction

Galabiose [Gal-α-(1→4)Gal-β-(1→] is an integral part of the globo series of glycolipids, where it constitutes the receptor epitope for several biologically important carbohydrate-binding proteins, as summarized in several review articles [1]. We have synthesized a large number of analogues (including the complete sets of monodeoxy analogues of both galabiose and globotriose) of galabiose-containing saccharides [2] and used these as probes in the mapping of receptor epitopes. In addition, the conformations of these compounds were determined by NMR and molecular mechanics investigations [2f,3]. Thus, the structural details of the recognition between galabiose and bacterial proteins were revealed for PapG adhesin [2l,4] (a pilus tip protein of uropathogenic, Gram negative, *Escherichia coli*), a surface protein from the Gram positive *Streptococcus suis* [2o,5], and verotoxin [6] (a protein toxin produced by *E. coli*). Results from these investigations indicated that some of the hydroxyl groups in the galabiose moiety were hydrogen bonded to carboxylic acid residues in the bacterial proteins. It is reasonable to expect that by changing some of these hydroxyl groups into amino groups, salt bridges might form, which would strengthen the galabiose–protein complex. Such compounds would constitute improved inhibitors of the complex formation and therefore be potentially useful as lead compounds for the development of antiadhesive drugs against bacterial infection or toxin action [7]. A prerequisite for successful use of receptor analogues is that the conformations are not changed compared to the parent compounds.

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We report here an MM3-minimization of the conformational energies of the trisaccharide analogues **3–6** (Fig. 1) for comparison with the low-energy conformations of the corresponding Me_3SiEt globotrioside.

The positions of the hydroxyl groups to be substituted by amino groups were chosen by analysis of the receptor epitopes of both the galabiose moiety and the proteins. As one example, it was postulated that the recognition between galabiose and PapG adhesin [2l] took place inter alia via cooperative hydrogen bonding of HO-6 and HO-2′ to a carboxylic acid residue in the adhesin. Another example comes from molecular modelling of the recognition between globotriose and the verotoxin b-subunit [6b], where two binding sites were suggested to employ HO-6, 6′, 4″, and 2″ of Gb3 for intermolecular hydrogen bonding.

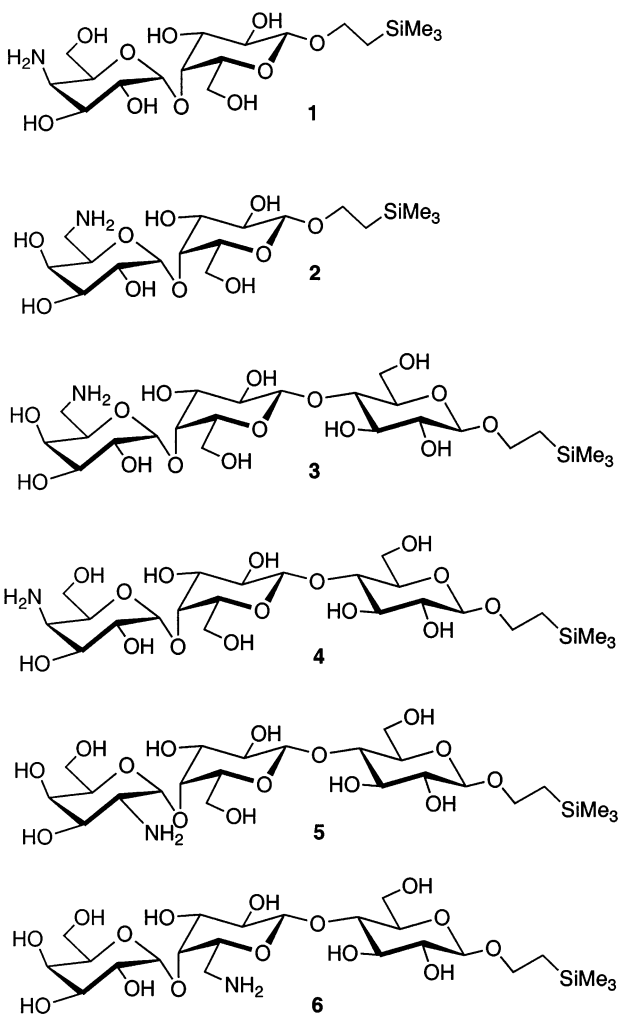


Fig. 1. Inhibitors of globotriose-binding proteins.

One of the binding sites suggested by this molecular modelling study was partly supported both by an X-ray crystal structure analysis [8] of a complex between verotoxin B-subunit pentamer and a Gb3 glycoside, and by an NMR study [9] of the same materials.

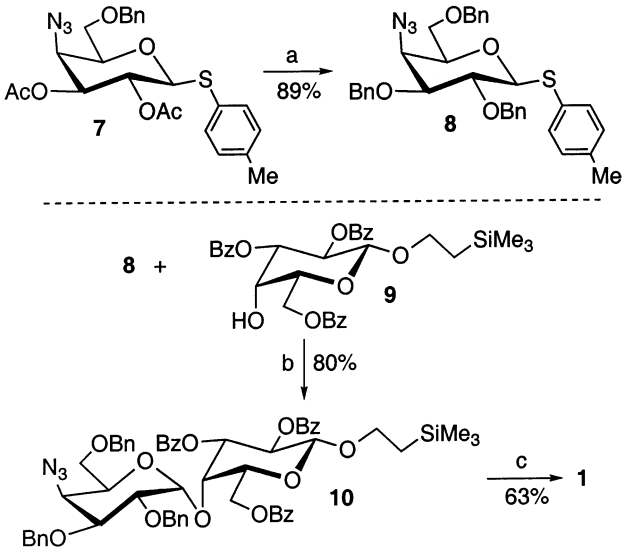
We now report the synthesis of six aminodeoxy-substituted 2-(trimethylsilyl)ethyl (Me_3SiEt) glycoside analogues of galabiose and globotriose (**1–6**, Fig. 1). It should be noted that the parent Me_3SiEt globotrioside was used in the NMR investigation [9] and that the corresponding methyl glycoside was used in a microcalorimetry investigation [10] of its binding to the b-subunit of verotoxin. Furthermore, Me_3SiEt glycosides [11] are easily transformed into anomerically activated saccharides for further glycosylation and transformation into various glycoconjugates useful for glycobiological investigations.

The exploitation of **1–6** as inhibitors of globotriose-binding proteins will be reported in due course.

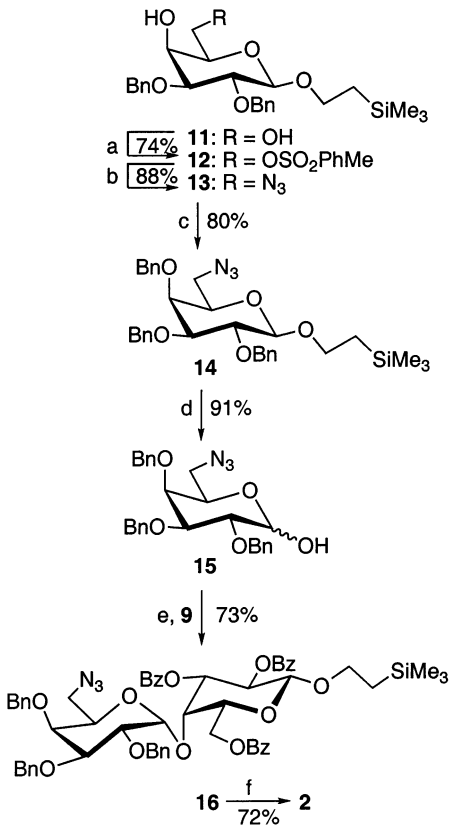
2. Results and discussion

Synthesis of compounds **1–6**.—An azido functionality was chosen as precursor of the amino groups in all the target compounds, since it is easily reduced by catalytic hydrogenation at the same time as the *O*-benzyl protecting groups are removed. For the α-galactosylation reactions, benzylated donors and benzoylated acceptors (having attenuated reactivity) were used in order to achieve good α-selectivity. The synthetic strategy employed here seems to be of general utility for the synthesis of aminodeoxy oligosaccharides.

Synthesis of the 4′-aminodeoxy galabioside **1**.—The 4-azidodeoxy galactosyl β-donor **7** was developed during our synthesis of sialyl Lewis x lactams [12] (Scheme 1). O-Deacetylation of **7**, followed by O-benzylation, gave the 4-azidodeoxy galactosyl α-donor **8** in 89% yield. The known [2n] Me_3SiEt galactoside acceptor **9** was α-galactosylated with the donor **8** under activation with *N*-iodosuccinimide (NIS)–triflic acid (TfOH) [13] to give the disaccharide derivative **10** (80%), devoid of the corresponding β-glycoside. Treatment of



Scheme 1. (a) NaOMe, MeOH, 14 h, then NaH, DMF, BnBr, 16 h. (b) NIS, TfOH, toluene, −45 °C, 5 h. (c) NaOMe, MeOH, 14 h, then H_2, Pd–C, EtOH, HCl.

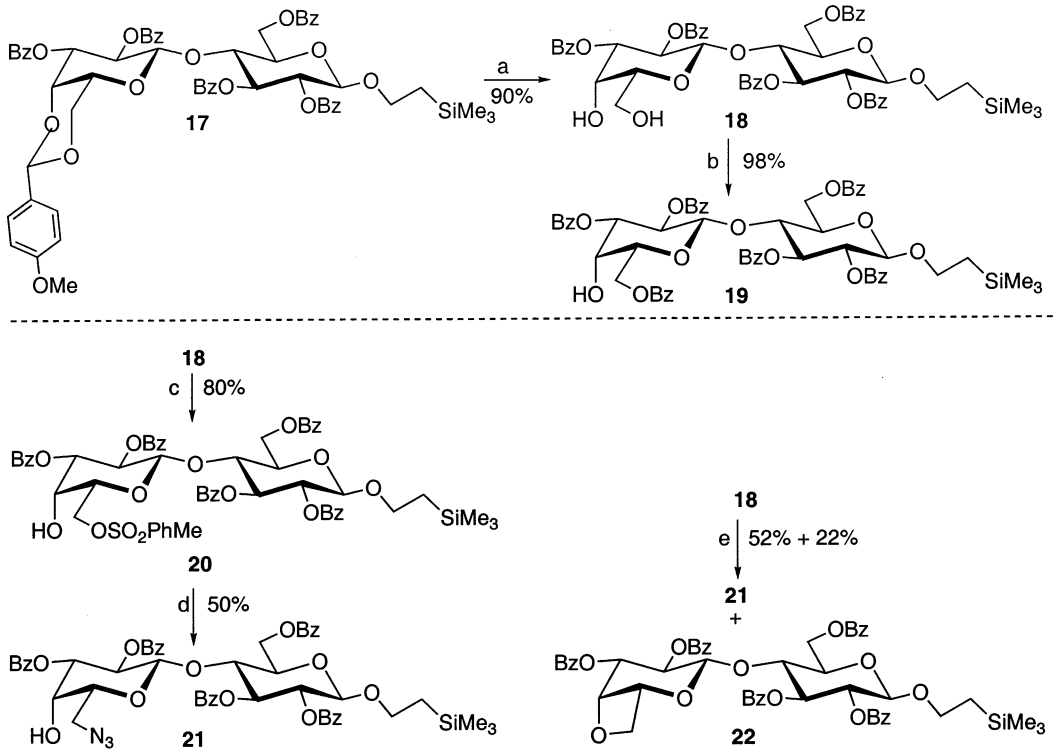


Scheme 2. (a) $MeC_6H_4SO_2Cl$, pyridine, −45→22 °C, 6 h. (b) NaN_3, 15-crown-5, DMF, 70 °C, 36 h. (c) NaH, BnBr, DMF, 0→22 °C, 12 h. (d) CF_3COOH, CH_2Cl_2, 0 °C, 30 min. (e) $(COCl)_2$, CH_2Cl_2, DMF, 30 min, then CF_3SO_2OAg, toluene, TMU, molecular sieves, −45 °C, 2.5 h and −10 °C, 14 h. (f) NaOMe, MeOH, 14 h, then H_2, Pd–C, EtOH, HCl.

10 with 0.5 mM methanolic sodium methoxide (NaOMe–MeOH), followed by catalytic hydrogenation of the product in acidic ethanol (1 equivalent HCl) gave the 4′-aminodeoxy analog **1** of Me_3SiEt galabioside in 63% overall yield. It should be noted that protonation of the amino group of **1** (and its precursor) by HCl in the hydrogenation mixture is crucial, since the catalyst is otherwise poisoned by the free amine.

Synthesis of the 6′-aminodeoxy galabioside **2**.—The known [2n] Me_3SiEt galactoside **11** was tosylated with *p*-toluenesulfonyl chloride in pyridine to give the tosylate **12** (74%, Scheme 2). Treatment of **12** with sodium azide in dimethyl formamide (DMF) in the presence of 15-crown-5 gave **13** in 88% yield. The unprotected hydroxyl group of **13** was then O-benzylated with benzyl bromide in DMF to furnish the 6-azidodeoxy galactoside **14** (80%). Cleavage of the Me_3SiEt group of **14** was performed by treatment with trifluoracetic acid in dichloromethane, followed by co-concentration with a mixture of toluene and propyl acetate [11], to yield the hemiacetal **15** (91%). Treatment of **15** with oxalyl chloride in DMF gave the corresponding α-chloro sugar in virtually quantitative yield. Further treatment with the galactoside acceptor **9** and silver triflate in a mixture of tetramethylurea and toluene provided the disaccharide **16** in 73% yield by α-stereoselective glycosylation. Compound **16** could also be prepared by glycosylation of **9** with the donor **25** (see Scheme 4) but the yield was lower (∼50%) and several unidentified byproducts were also formed. Treatment of **16** with NaOMe–MeOH, followed by catalytic hydrogenation of the product in acidic ethanol as above gave the 6′-aminodeoxy analog **2** of Me_3SiEt galabioside in 72% overall yield.

Synthesis of the Me_3SiEt lactoside acceptors **19** *and* **21**.—Deprotection of the known [2i] 4,6-*O*-*p*-methoxybenzylidene-protected lactoside **17** with aqueous acetic acid at 90 °C gave **18** (90%, Scheme 3). Compound **18** underwent regioselective benzoylation with benzoyl chloride in pyridine at −78 °C, thus furnishing the acceptor **19** in an excellent yield of 98%. Compound **19** was used in the preparation of **3–5** (Schemes 4–6). Compound **18** could also be regioselectively tosylated, and **20**

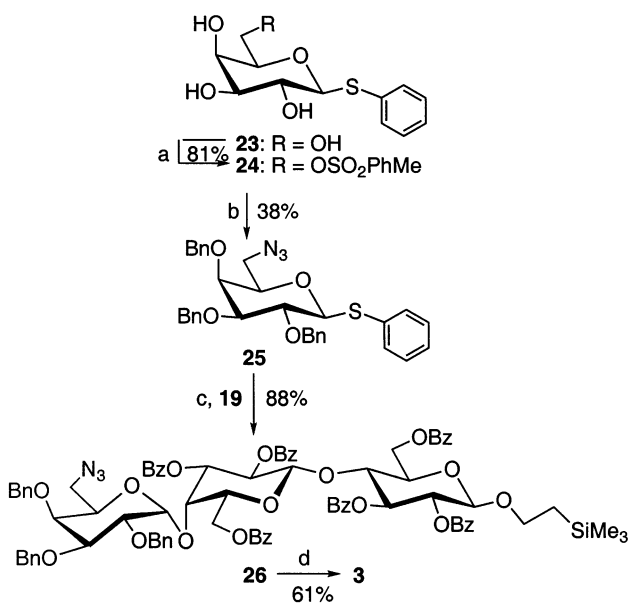


Scheme 3. (a) Aq AcOH, 90 °C, 30 min. (b) BzCl, pyridine, CH_2Cl_2, −78 °C, 6 h. (c) $MeC_6H_4SO_2Cl$, pyridine, −30→22 °C, 38 h. (d) NaN_3, 15-crown-5, DMF, 90 °C, 5 h. (e) CF_3SO_2Cl, 2,6-di-*t*-Bu-pyridine, CH_2Cl_2, −45 °C, 30 min, 0 °C, 30 min, then NaN_3, 15-crown-5, DMF, 22 °C, 2.5 h.

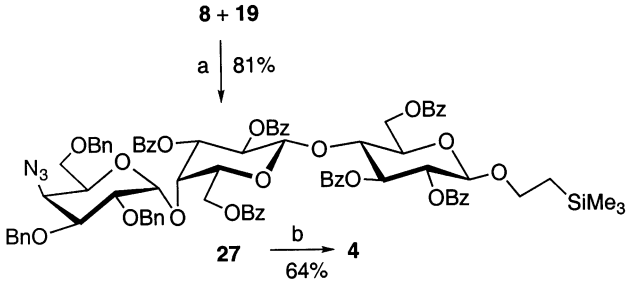
was obtained in 80% yield by treatment of **18** with tosyl chloride in pyridine at −30 °C. In a similar reaction, **18** was transformed into the corresponding triflate en route to **21** + **22**.

Nucleophilic substitution by azide ion at the 6′-position of both the tosylate and the triflate was complicated by benzoyl migration from position 3 to position 4, and formation of a 4,6-anhydro derivative (**22**), respectively, thus lowering the yields to approximately 50% in both reactions. We have observed such migrations earlier in attempted substitutions at the 6-position of different galactose derivatives [2k,2n].

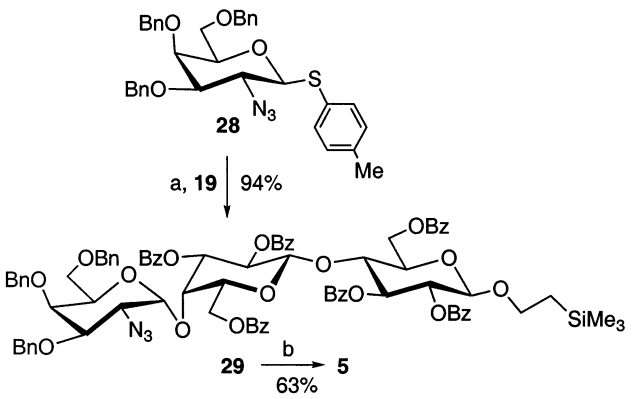
Treatment of **20** at 90 °C with sodium azide in DMF in the presence of 15-crown-5 gave **21** in 50% yield together with two byproducts formed by benzoyl migration. Acetylation of the byproducts permitted their identification as 2-(trimethylsilyl)ethyl (3-*O*-acetyl-2,4-di-*O*-benzoyl-6-*O*-*p*-toluenesulfonyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside and 2-(trimethylsilyl)ethyl (3-*O*-acetyl-6-azido-2,4-di-*O*-benzoyl-6-deoxy-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside. Treatment of **18** with triflic anhydride, followed by sodium azide in DMF in the presence of 15-crown-5 at 22 °C,



Scheme 4. (a) $MeC_6H_4SO_2Cl$, pyridine, −45→22 °C, 6 h. (b) NaN_3, DMF, 65 °C, 36 h, then NaH, DMF, BnBr, 15 h. (c) NIS, CF_3SO_2OH, toluene, −45 °C, 3.5 h. (d) NaOMe, MeOH, 14 h, then H_2, Pd–C, EtOH, HCl.



Scheme 5. (a) NIS, CF_3SO_2OH, toluene, −45 °C, 3.5 h. (b) NaOMe, MeOH, 16 h, then H_2, Pd–C, EtOH, HCl.



Scheme 6. (a) NIS, CF_3SO_2OH, toluene, −45 °C, 2 h. (b) NaOMe, MeOH, 13 h, then H_2, Pd–C, EtOH, HCl.

also gave **21** (52%). A byproduct (**22**) was isolated in 22% yield. The byproducts obtained from the reaction of **20** indicate that substitution by azide is only possible when position 4′ is unprotected (minimal steric hindrance [14]) and that benzoyl migration can occur in both compound **20** and **21**. When the substitution of triflate by azide was performed at 22 °C, no benzoyl migration occurred, but instead, partial intramolecular substitution by HO-4′ led to the 4,6-anhydro compound **22**.

Synthesis of the 6″-aminodeoxy globotrioside **3**.—The thiogalactoside **23** [15] was regioselectively tosylated in the 6-position by treatment with *p*-toluenesulfonyl chloride in pyridine at −45→22 °C, yielding the tosylate **24** in 81% yield (Scheme 4). Nucleophilic substitution at the 6-position of **24** by azide ion in DMF at 65 °C for 36 h, followed by O-benzylation of the hydroxyl groups, gave the donor **25** in an overall yield of 38%. The lactoside acceptor **19** was glycosylated with **25** under promotion by NIS–TfOH [13] in toluene at −45 °C, which furnished the protected trisaccharide **26** in 88% yield. Treatment of **26** with NaOMe–MeOH, followed by catalytic hydrogenation of the product in acidic ethanol, as in the preparation of **1** and **2**, gave the 6″-aminodeoxy analog **3** of Me_3SiEt globotrioside in 61% overall yield.

Synthesis of the 4″-aminodeoxy globotrioside **4**.—The lactoside acceptor **19** was glycosylated with the donor **8** under promotion by NIS–TfOH [13] in toluene at −45 °C, which furnished the protected trisaccharide **27** in 81% yield (Scheme 5). Treatment of **27** with NaOMe–MeOH, followed by catalytic hydrogenation of the product in acidic ethanol, as in the preparation of **1–3**, gave the 4″-aminodeoxy analog **4** of Me_3SiEt globotrioside in 64% overall yield.

Synthesis of the 2″-aminodeoxy globotrioside **5**.—The lactoside acceptor **19** was glycosylated with the donor **28** [2n] under promotion by NIS–TfOH [13] in toluene at −45 °C, which furnished the protected trisaccharide **29** in 94% yield (Scheme 6). Treatment of **29** with NaOMe–MeOH, followed by catalytic hydrogenation of the product in acidic ethanol, as in the preparation of **1–4**, gave the 2″-aminodeoxy analog **5** of Me_3SiEt globotrioside in 63% overall yield.

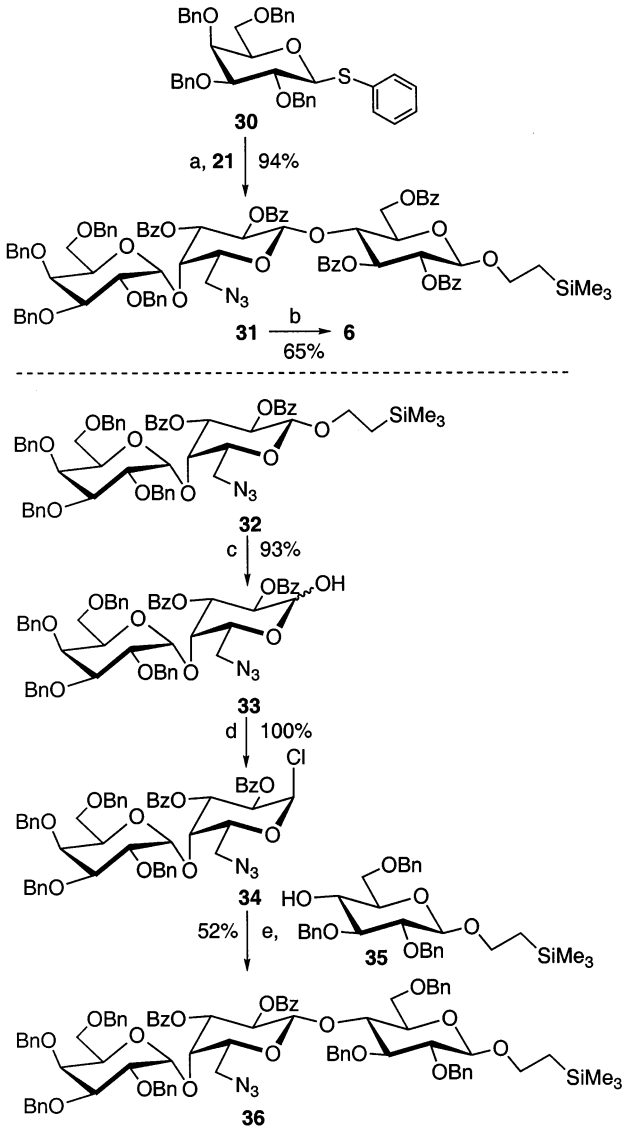
Synthesis of the 6′-aminodeoxy globotrioside **6**.—The lactoside acceptor **21** was glycosylated with the donor **30** [15,16] under promotion by NIS–TfOH [13] in diethyl ether or CH_2Cl_2 at −45 °C, which furnished the protected trisaccharide **31** in 94% yield (Scheme 7). Treatment of **31** with NaOMe–MeOH, followed by catalytic hydrogenation of the product in acidic ethanol, as in the preparation of **1–5**, gave the 6′-aminodeoxy analog **6** of Me_3SiEt globotrioside in 65% overall yield.

An alternative route to the 6′-aminodeoxy analog was also investigated. Thus, the known [2n] 6-azidodeoxy-galabioside **32** was treated with trifluoroacetic acid in dichloromethane to give the hemiacetal **33** (93%), which was then transformed into the chlorosugar **34** (100%) by treatment with oxalyl chloride in DMF. The known [11] acceptor **35** was then glycosylated with the donor **34** under promotion by silver trifluoromethanesulfonate, and the trisaccharide **36** was obtained in 52% yield. The chromatographed product contained a small amount of unidentified material.

Molecular mechanics (MM3) calculations of the conformations of **3–6**.—The parent Me_3SiEt globotrioside [4a] was constructed by the MacMimic program [17], and the structure was energy minimized with the MM3(92) molecular mechanics force field [18]. The corresponding methyl glycoside [2f,3] was used as a starting structure. Following the energy minimization, appropriate hydroxyl groups were substituted for amino groups and the resulting aminodeoxy trisaccharides (**3–6**) were each energy minimized. Finally, the low-energy conformations of the parent globotrioside and the four aminodeoxy analogues **3–6** were superimposed (by least-squares fitting of all ring atoms, using the MacMimic program), which gave the combination structure depicted in Fig. 2, clearly demonstrating that the low-energy conformations of all five compounds are very similar (rms < 0.047 Å). It is therefore reasonable to believe that introduction of the amino groups did not perturb the conformations to any substantial degree. This is important when structural analogues of natural compounds are to be used for mapping of receptor sites.

3. Experimental

NMR spectra were recorded with a 400 MHz instrument. ^1H NMR spectral assignments were made by double resonance techniques (COSY and HETCOR) and chemical shifts for ^1H-resonances are reported as if they were first order. Reactions were performed at room temperature (rt) unless stated otherwise. Concentrations were made using rotary evaporation with bath temperatures at or below 40 °C. Anhydrous Na_2SO_4 was used as drying agent for the organic extracts in the work-up procedures. Thin-layer chromatography (TLC) was performed on Kiselgel 60 F_{254} plates (E. Merck). Column chromatography was performed on SiO_2 (Matrex LC-gel: 60A, 35-70 MY, Grace) using the flash technique



Scheme 7. (a) NIS, CF_3SO_2OH, Et_2O, −45 °C, 2 h. (b) NaOMe, MeOH, 16 h, then H_2, Pd–C, EtOH, HCl. (c) CF_3COOH, CH_2Cl_2, 0 °C, 35 min. (d) $(COCl)_2$, CH_2Cl_2, DMF, 0 °C, 1 h. (e) CF_3SO_2OAg, CH_2Cl_2, TMU, molecular sieves, −30 °C, 1 h and 22 °C, 20 h.

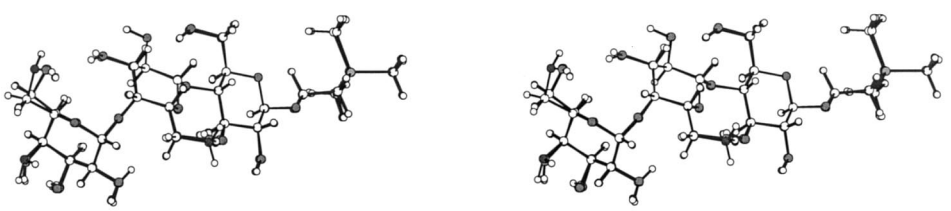


Fig. 2. Stereoview of the superimposed low-energy [(MM3(92)] conformers of Me_3SiEt globotrioside and the aminodeoxy analogues **3–6**.

[19]. The compounds **7** [12], **9** [2n], **11** [2n], **17** [2i], **18** [2i], **23** [15], **28** [2n], **30** [15,16], **32** [2n], and **35** [11], have been reported.

2-(Trimethylsilyl)ethyl (4-amino-4-deoxy-α-D-galactopyranosyl)-(1→4)-β-D-galactopyranoside (**1**).—Compound **10** (51 mg, 0.049 mm ol) was treated with NaOMe–MeOH (0.5 mM) for 14 h and the reaction mixture was neutralized with Duolite C436 (H^+) resin, filtered, and concentrated. The residue was chromatographed (SiO_2, 1:1 EtOAc–heptane → 1:1 EtOAc–MeOH). The product was dissolved in a mixture of EtOH (6 mL) and aqueous HCl (0.1 M, 0.5 mL) and hydrogenated (H_2, Pd-C, 1 atm). After 7.5 h, the mixture was filtered through Celite, treated with Duolite A147 resin, and concentrated. The residue was purified on a reverse-phase column (Varian Mega Bond Elut C18, water–MeOH 1:0 → 9:1 → 8:2 → 7:3 → 6:4 → 5:5 → 4:6, 6 mL of each), and then chromatographed (SiO_2, 4:4:1 CH_2Cl_2–MeOH–Et_3N) to give **1** (13.5 mg, 63%); $[\alpha]_D^{23}$ +63° (*c* 0.5, H_2O); ^1H NMR (D_2O): δ 4.87 (d, 1 H, *J* = 4.2 Hz, H-1′), 4.38 (d, 1 H, *J* = 7.8 Hz, H-1), 4.28 (br t, 1 H, *J* = 6.3 Hz, H-5′), 3.90–4.00 (m, 1 H, –O*CH*$_2$CH$_2$Si), 3.94 (d, 1 H, *J* = 2.7 Hz, H-4), 3.88 (dd, 1 H, *J* = 4.0, 10.6 Hz, H-3′), 3.58–3.83 (m, 8 H, H-2′,6′,3, and O*CH*$_2$CH$_2$Si), 3.44 (dd, 1 H, *J* = 7.7, 10.1 Hz, H-2), 3.14 (br dd, 1 H, *J* = 1.5, 4.0 Hz, H-4′), 0.85–1.03 (m, 2 H, CH_2Si), −0.06 (s, 9 H, $SiCH_3$); ^{13}C NMR (D_2O): δ 102.6, 100.7, 78.0, 75.3, 73.1, 71.5, 71.0, 69.6, 68.7, 68.65, 61.5, 60.5, 52.0, 18.1, −2.1; HRMS Anal. Calcd for $C_{17}H_{35}O_{10}NSiNa$ [M + Na]: 464.1928. Found: 464.1939.

2-(Trimethylsilyl)ethyl (6-amino-6-deoxy-α-D-galactopyranosyl)-(1→4)-β-D-galactopyranoside (**2**).—Compound **16** (110 mg, 0.105 mmol) was treated essentially as in the preparation of **1** to give **2** (33.4 mg, 72%); $[\alpha]_D^{24}$ +57° (*c* 0.7, H_2O); ^1H NMR (D_2O): δ 4.90 (d, 1 H, *J* = 3.8 Hz, H-1′), 4.42 (d, 1 H, *J* = 7.8 Hz, H-1), 4.22 (br t, 1 H, *J* = 6.5 Hz, H-5′), 3.63–4.03 (m, 10 H, H-2′, H-3′, –O*CH*$_2$-CH$_2$Si), 3.48 (dd, 1 H, *J* = 7.8, 10.1 Hz, H-2), 2.73 (d, 2 H, *J* = 6.6 Hz, H-6′), 0.88–1.08 (m, 2 H, CH_2Si), −0.03 (s, 9 H, $SiCH_3$); ^{13}C NMR (D_2O): δ 102.7, 100.5, 77.1, 75.5, 73.0, 72.1, 71.5, 69.9, 69.8, 69.3, 68.7, 60.4, 41.3, 18.2, −2.1; HRMS Anal. Calcd for $C_{17}H_{35}O_{10}NSiNa$ [M + Na]: 464.1928. Found: 464.1931.

2-(Trimethylsilyl)ethyl (6-amino-6-deoxy-α-D-galactopyranosyl)-(1→4)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (**3**).—Compound **26** (125.5 mg, 0.081 mmol) was treated essentially as in the preparation of **1** to give **3** (31.2 mg, 61%); $[\alpha]_D^{22}$ +46° (*c* 0.5, H_2O); ^1H NMR (D_2O): δ 4.78 (d, 1 H, *J* = 3.9 Hz, H-1″), 4.37 (d, 1 H, *J* = 7.8 Hz, H-1′ or H-1), 4.36 (d, 1 H, *J* = 8.1 Hz, H-1′ or H-1), 4.13 (br t, 1 H, *J* = 6.4 Hz, H-5″), 3.37–3.97 (m, 17 H), 3.14 (br t, 1 H, *J* = 8.1 Hz, H-2′ or H-2), 2.63 (br d, 1 H, *J* = 6.3 Hz, H-6″), 0.94 (dt, 1 H, *J* = 5.6, 13.2 Hz, CH_2Si), 0.83 (dt, 1 H, *J* = 5.3, 13.2 Hz, CH_2Si), −0.12 (s, 9 H, $SiCH_3$); ^{13}C NMR (D_2O): δ 103.5, 101.7, 100.4, 78.9, 76.9, 75.9, 75.1, 74.9, 73.3, 72.4, 71.3, 70.2, 69.2, 68.8, 68.6, 67.1, 60.40, 60.35, 40.8, 17.9, −2.2; HRMS Anal. Calcd for $C_{23}H_{45}O_{15}NSiNa$ [M + Na]: 626.2456. Found: 626.2460.

2-(Trimethylsilyl)ethyl (4-amino-4-deoxy-α-D-galactopyranosyl)-(1→4)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (**4**).—Compound **27** (66 mg, 0.043 mmol) was treated essentially as in the preparation of **1** to give **4** (16.8 mg, 64%); $[\alpha]_D^{22}$ +40° (*c* 0.5, H_2O); ^1H NMR (D_2O): δ 4.80 (d, 1 H, *J* = 4.0 Hz, H-1″), 4.37 (d, 1 H, *J* = 7.7 Hz, H-1′ or H-1), 4.35 (d, 1 H, *J* = 8.0 Hz, H-1′ or H-1), 4.23 (br t, 1 H, *J* = 6.3 Hz, H-5′), 3.75–3.93 (m, 5 H, H-3′ and O*CH*$_2$CH$_2$Si), 3.37–3.72 (m, 12 H), 3.14 (t, 1 H, *J* = 8.1 Hz, H-2′ or H-2), 3.08 (br d, 1 H, *J* = 3.8 Hz, H-4′), 0.93 (dt, 1 H, *J* = 5.5, 13.0 Hz, CH_2Si), 0.83 (dt, 1 H, *J* = 5.3, 13.0 Hz, OCH_2Si), −0.12 (s, 9 H, $SiCH_3$); ^{13}C NMR (D_2O): δ 103.6, 101.7, 100.8, 78.9, 78.1, 75.7, 75.1, 74.9, 73.3, 72.6, 71.3, 70.9, 69.5, 68.8, 68.5, 61.3, 60.8, 60.4, 51.9, 17.9, −2.2; HRMS Anal. Calcd for $C_{23}H_{46}O_{15}NSi$ [M + H]: 604.2637. Found: 604.2629.

2-(Trimethylsilyl)ethyl (2-amino-2-deoxy-α-D-galactopyranosyl)-(1→4)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (**5**).—Compound **29** (145 mg, 0.094 mmol) was treated essentially as in the preparation of **1** to give **5** (37 mg, 63%); $[\alpha]_D^{21}$ +46° (*c* 1.0, H_2O); ^1H NMR (D_2O): δ 4.81 (d, 1 H, *J* = 3.7 Hz, H-1′), 4.37 (d, 1 H, *J* = 7.9 Hz, H-1′ or H-1),

4.35 (d, 1 H, $J = 7.7$ Hz, H-1′ or H-1), 4.18 (t, 1 H, $J = 6.3$ Hz, H-5′), 3.38–3.94 (m, 17 H), 3.14 (t, 1 H, $J = 8.1$ Hz, H-2′ or H-2), 2.90 (dd, 1 H, $J = 3.6$, 10.8 Hz, H-2′), 0.93 (dt, 1 H, $J = 5.5$, 13.0 Hz, CH_2Si), 0.83 (dt, 1 H, $J =$ 5.3, 13.0 Hz, CH_2Si), −0.12 (s, 9 H, $SiCH_3$); ^{13}C NMR (D_2O): δ 103.7, 101.7, 100.7, 79.2, 77.5, 75.9, 75.1, 74.9, 73.2, 72.7, 71.8, 71.3, 70.3, 68.8, 68.7, 61.1, 60.9, 60.4, 51.4, 17.9, −2.2; HRMS Anal. Calcd for $C_{23}H_{45}O_{15}NSiNa$ [M + Na]: 626.2456. Found: 626.2449.

2-(Trimethylsilyl)ethyl (α-D-galactopyranosyl)-(1→4)-(6-amino-6-deoxy-β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (**6**).—Compound **31** (38 mg, 0.025 mmol) was treated essentially as in the preparation of **1** to give **6** (9.8 mg, 65%); $[\alpha]_D^{22}$ +41° (*c* 0.6, H_2O); ^1H NMR (D_2O): δ 4.87 (d, 1 H, $J = 3.1$ Hz, H-1′), 4.42 (d, 1 H, $J = 7.7$ Hz, H-1′ or H-1), 4.36 (d, 1 H, $J = 8.0$ Hz, H-1′ or H-1), 4.13 (br t, 1 H, $J = 6.4$ Hz, H-5′), 3.32–3.97 (m, 17 H), 3.24 (dd, 1 H, $J = 3.3$, 13.5 Hz, H-6 or H-6′), 3.14 (t, 1 H, $J = 8.6$ Hz, H-2′ or H-2), 0.94 (dt, 1 H, $J = 5.6$, 12.8 Hz, CH_2Si), 0.83 (dt, 1 H, $J = 5.3$, 12.8 Hz, CH_2Si), −0.11 (s, 9 H, –$SiCH_3$); ^{13}C NMR (D_2O): δ 103.1, 101.8, 101.5, 80.3, 77.2, 75.3, 74.7, 73.4, 72.2, 71.7, 71.0, 70.9, 69.5, 69.2, 68.8, 68.6, 60.9, 60.0, 40.4, 17.9, −2.2; HRMS Anal. Calcd for $C_{23}H_{46}O_{15}NSi$ [M + H]: 604.2638. Found: 604.2642.

4-Methylphenyl 4-azido-2,3,6-tri-O-benzyl-4-deoxy-1-thio-β-D-galactopyranoside (**8**).—4-Methylphenyl 2,3-di-*O*-acetyl-4-azido-6-*O*-benzyl-4-deoxy-1-thio-β-D-galactopyranoside [12] (**7**, 158 mg, 0.325 mmol) was treated with NaOMe–MeOH (0.5 mM) for 14 h, the mixture was neutralized with Duolite C436 (H^+) resin, filtered, and co-concentrated with EtOAc–toluene. The residue was dissolved in dry DMF (6 mL), and NaH (24.5 mg, 0.82 mmol, 80% in oil) was added. After 30 min, benzyl bromide (0.125 mL, 1.04 mmol) was added and the mixture was stirred under nitrogen for 16 h. NaH (25 mg, 0.84 mmol) and benzyl bromide (0.125 mL, 1.04 mmol) were added and the mixture was stirred for 24 h. MeOH (0.5 mL) and water (15 mL) were added and the mixture was extracted with Et_2O (2 × 20 mL). The ether phase was dried and concentrated and the residue was chromatographed (SiO_2, 1:5 EtOAc–heptane) to give **8** (168 mg, 89%); $[\alpha]_D^{23}$ −11° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.08–7.48 (2 m, 19 H, Ar–H), 4.83 (d, 1 H, $J = 10.2$ Hz, CH_2Ph), 4.78 (d, 1 H, $J = 11.4$ Hz, CH_2Ph), 4.76 (d, 1 H, $J = 10.2$ Hz, CH_2Ph), 4.72 (d, 1 H, $J = 11.5$ Hz, CH_2Ph), 4.51–4.58 (m, 3 H, H-1, and CH_2Ph), 4.06 (br s, 1 H, H-4), 3.66–3.76 (m, 4 H, H-2,3,6), 3.62 (ddd, 1 H, $J = 0.9$, 6.8, 13.1 Hz, H-5), 2.34 (s, 3 H, $ArCH_3$); ^{13}C NMR ($CDCl_3$): δ 128.3–138.6 (Ar), 88.7, 83.2, 77.6, 76.3, 75.9, 74.2, 73.2, 69.1, 60.4, 21.6; HRMS Anal. Calcd for $C_{34}H_{35}O_4N_3SNa$ [M + Na]: 604.2246. Found: 604.2263.

2-(Trimethylsilyl)ethyl (4-azido-2,3,6-tri-O-benzyl-4-deoxy-α-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-benzoyl-β-D-galactopyranoside (**10**).—To a cooled (−45 °C) solution of **8** (78.5 mg, 0.135 mmol) and 2-(trimethylsilyl)ethyl 2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside [2n] (**9**, 50 mg, 0.084 mmol) in dry toluene (5 mL) was added *N*-iodosuccinimide (55 mg, 0.24 mmol), followed by triflic acid (0.006 mL, 0.067 mmol). After 285 min at −45 °C, Et_3N (0.5 mL) and cyclohexene (2 mL) were added. The mixture was heated to ambient temperature and concentrated. The residue was chromatographed (SiO_2, EtOAc–heptane 1:5) to give **10** (70 mg, 80%); $[\alpha]_D^{23}$ +59° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.10–8.05 (m, 30 H, Ar–H), 5.72 (dd, 1 H, $J = 7.7$, 10.6 Hz, H-2), 5.23 (dd, 1 H, $J = 2.9$, 10.7 Hz, H-3), 4.80–4.88 (m, 5 H, incl. H-1′), 4.76 (dd, 1 H, $J = 2.1$, 6.7 Hz, H-6), 4.73 (d, 1 H, $J = 7.8$ Hz, H-1), 4.67 (d, 1 H, $J = 11.7$ Hz, CH_2Ph), 4.42 (ddd, 1 H, $J = 1.6$, 5.1, 9.5 Hz, H-5′), 4.38 (br d, 1 H, $J = 2.5$ Hz, H-4), 4.28 (dd, 1 H, $J = 3.4$, 10.0 Hz, H-3′), 4.17–4.23 (m, 2 H, H-4′, CH_2Ph), 4.14 (d, 1 H, $J = 11.8$ Hz, CH_2Ph), 4.01–4.10 (m, 2 H, incl. –OCH_2CH_2Si), 3.85 (dd, 1 H, $J = 3.5$, 10.0 Hz, H-2′), 3.63 (dt, 1 H, $J = 6.6$, 10.3 Hz, –OCH_2CH_2Si), 3.27 (t, 1 H, $J = 8.9$ Hz, H-6′), 3.00 (dd, 1 H, $J = 5.0$, 8.5 Hz, H-6′), 0.85–1.03 (m, 2 H, CH_2Si), −0.04 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 166.9, 166.5, 165.8, 128.0–138.5 (Ar), 101.32, 101.27, 78.2, 76.6, 76.3, 74.7, 73.5, 73.0, 70.2, 68.1, 68.0, 62.9, 61.4, 18.4, −1.0; HRMS Anal. Calcd for $C_{59}H_{63}O_{13}N_3SiNa$ [M + Na]: 1072.4028. Found: 1072.4023.

*2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzyl-6-*O*-p-toluenesulfonyl-β-*D*-galactopyranoside* (**12**). —To a solution of 2-(trimethylsilyl)ethyl 2,3-di-*O*-benzyl-β-D-galactopyranoside [2n] (**11**, 500 mg, 1.09 mmol) in dry pyridine (10 mL) under nitrogen at −45 °C, was added *p*-toluenesulfonyl chloride (249 mg, 1.2 mmol). The temperature was raised to ambient temperature. CH_2Cl_2 (30 mL) was added after 6 h and the mixture was washed with water and aq HCl (0.1 M). The organic phase was dried and concentrated and the residue was chromatographed (SiO_2, 1:1 EtOAc–heptane) to give **12** (496 mg, 74%); $[\alpha]_D^{21}$ −4° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.78–7.83 and 7.26–7.39 (14 H, Ar–H), 4.91 (d, 1 H, *J* = 11.2 Hz, CH_2Ph), 4.67–4.76 (m, 3 H, CH_2Ph), 4.34 (d, 1 H, *J* = 7.6 Hz, H-1), 4.27 (dd, 1 H, *J* = 5.8, 10.2 Hz, H-6), 4.19 (dd, 1 H, *J* = 6.7, 10.2 Hz, H-6), 3.98 (dt, 1 H, *J* = 8.0, 9.3 Hz, O*CH*$_2$CH$_2$Si), 3.92–3.96 (m, 1 H, H-4), 3.67 (br t, 1 H, *J* = 6.6 Hz, H-5), 3.53–3.62 (m, 2 H, H-2 and O*CH*$_2$CH$_2$Si), 3.49 (dd, 1 H, *J* = 3.5, 9.4 Hz, H-3), 2.46 (s, 3 H, $ArCH_3$), 2.34–2.37 (m, 1 H, 4-OH), 1.02 (dd, 2 H, *J* = 8.0, 9.3 Hz, CH_2Si), 0.04 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 145.5, 139.0, 138.1, 128.1–133.1, 103.5, 80.6, 79.2, 75.6, 73.1, 72.1, 69.0, 68.0, 66.7, 22.1, 18.9, −0.9; HRMS Anal. Calcd for $C_{32}H_{42}O_8SSiNa$ [M + Na]: 637.2267. Found: 637.2261.

*2-(Trimethylsilyl)ethyl 6-azido-2,3-di-*O*-benzyl-6-deoxy-β-*D*-galactopyranoside* (**13**).—To a solution of **12** (203 mg, 0.33 mmol) in dry DMF (4 mL), were added 15-crown-5 (0.065 mL, 0.33 mmol) and NaN_3 (107 mg, 1.65 mmol). The reaction mixture was stirred at 70 °C for 36 h, then cooled to rt, and water (15 mL) and CH_2Cl_2 (50 mL) were added. The organic layer was dried and concentrated and the residue was chromatographed (SiO_2, 1:1 EtOAc–heptane) to give **13** (141 mg, 88%); $[\alpha]_D^{21}$ −40° (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.28–7.44 (10 H, Ar–H), 4.98 (d, 1 H, *J* = 11.1 Hz, CH_2Ph), 4.70–4.80 (m, 3 H, CH_2Ph), 4.42 (d, 1 H, *J* = 7.7 Hz, H-1), 4.05–4.14 (m, 1 H, O*CH*$_2$CH$_2$Si), 3.87 (br s, 1 H, H-4), 3.78 (dd, 1 H, *J* = 8.4, 12.9 Hz, H-6), 3.60–3.69 (m, 2 H, H-2, and O*CH*$_2$CH$_2$Si), 3.57 (br dd, 1 H, *J* = 4.1, 8.3 Hz, H-5), 3.53 (dd, 1 H, *J* = 3.5, 9.4 Hz, H-3), 3.24 (dd, 1 H, *J* = 4.2, 12.9 Hz, H-6), 2.53 (br s, 1 H, 4-OH), 1.04–1.12 (m, 2 H, CH_2Si), 0.05 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 139.1, 138.1, 129.0, 128.8, 128.5, 128.48, 128.3, 128.1, 103.5, 80.6, 79.25, 75.6, 74.3, 73.2, 67.8, 51.6, 18.9, −1.0; HRMS Anal. Calcd for $C_{25}H_{35}O_5N_3SiNa$ [M + Na]: 508.2244. Found: 508.2236.

*2-(Trimethylsilyl)ethyl 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-β-*D*-galactopyranoside* (**14**).—A solution of **13** (130 mg, 0.268 mmol) in dry DMF (2 mL) was cooled to 0 °C and NaH (10.5 mg, 0.35 mmol, 80% in oil) was added, followed by benzyl bromide (0.039 mL, 0.32 mmol). The mixture was stirred under N_2 while the temperature was raised to ∼22 °C. After 12 h, methanol (0.2 mL) CH_2Cl_2 (20 mL) were added. The mixture was washed with water and satd aq $NaHCO_3$, dried, and concentrated. The residue was chromatographed (SiO_2, 1:3 EtOAc–heptane) to give **14** (123 mg, 80%); $[\alpha]_D^{21}$ −33° (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.2 7.5 (m, 15 H, Ar–H), 4.99 (d, 1 H, *J* = 11.7 Hz, CH_2Ph), 4.97 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.83 (d, 1 H, *J* = 11.8 Hz, CH_2Ph), 4.78 (d, 1 H, *J* = 10.9 Hz, CH_2Ph), 4.74 (d, 1 H, *J* = 11.9 Hz, CH_2Ph), 4.63 (d, 1 H, *J* = 11.7 Hz, CH_2Ph), 4.39 (d, 1 H, *J* = 7.7 Hz, H-1), 4.05 (dt, 1 H, *J* = 7.8, 9.6 Hz, O*CH*$_2$CH$_2$Si), 3.83 (dd, 1 H, *J* = 7.7, 9.8 Hz, H-2), 3.66–3.70 (m, 1 H, H-4), 3.62 (dd, 1 H, *J* = 4.5, 12.7, H-6), 3.57 (dt, 1 H, *J* = 7.7, 9.6 Hz, O*CH*$_2$CH$_2$Si), 3.52 (dd, 1 H, *J* = 2.9, 9.8 Hz, H-3), 3.46 (ddd, 1 H, *J* = 0.9, 4.3, 8.1 Hz, H-5), 2.81 (dd, 1 H, *J* = 4.2, 12.7 Hz, H-6), 1.02 (dd, 2 H, *J* = 8.0, 9.7 Hz, CH_2Si), 0.00 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 127.6–138.8 (Ar), 103.3, 82.1, 79.5, 75.2, 74.3, 74.2, 73.7, 73.5, 67.4, 51.4, 18.4, −1.5; HRMS Anal. Calcd for $C_{32}H_{41}O_5N_3SiNa$ [M + Na]: 598.2713. Found: 598.2712.

*6-Azido-2,3,4-tri-*O*-benzyl-6-deoxy-*D*-galactopyranose* (**15**).—A solution **14** (188 mg, 0.33 mmol) in CH_2Cl_2 (1.8 mL) was cooled to 0 °C under N_2 and trifluoroacetic acid (3.6 mL) was added [11]. After 30 min at 0 °C, *n*-propylacetate and toluene were added [11] and the mixture was concentrated. The residue was chromatographed (SiO_2, 1:2 EtOAc–heptane) to give **15** (141 mg, 91%); HRMS Anal. Calcd for $C_{27}H_{29}O_5N_3Na$ [M + Na]: 498.2005. Found: 498.2014.

*2-(Trimethylsilyl)ethyl (6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-α-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**16**).—To a solution of **15** (63.9 mg, 0.134 mmol) in a mixture of dry CH_2Cl_2 (4 mL) and DMF (0.2 mL) was added $(COCl)_2$ (0.085 mL, 0.99 mmol). The mixture was stirred for 30 min at ambient temperature under N_2. After 30 min, cold toluene (10 mL, 0 °C) and cold satd aq $NaHCO_3$ (5 mL, 0 °C) were added. The organic phase was isolated, dried, and concentrated to give the crude galactosyl chloride in quantitative yield. The chloride and compound **9** (50 mg, 0.084 mmol) were dissolved in dry toluene (4 mL), molecular sieves (AW-300) and *N*,*N*,*N*′,*N*′-tetramethylurea (0.050 mL, 0.42 mmol) were added, and the mixture was cooled to −45 °C under N_2. Silver trifluoromethanesulfonate (51 mg, 0.20 mmol) was added, and the reaction mixture was stirred at −45 °C for 2.5 h, the temperature was raised to −10 °C, and silver trifluoromethanesulfonate (50 mg, 0.19 mmol) was added. The reaction mixture was allowed to reach rt and after 14 h, the mixture was filtered through Celite and concentrated. The residue was chromatographed (SiO_2, 1:5 EtOAc–heptane) to give **16** (64.6 mg, 73%); $[\alpha]_D^{24}$ +49° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.90–8.07 and 7.10–7.63 (30 H, Ar–H), 5.74 (dd, 1 H, *J* = 7.7, 10.5 Hz, H-2), 5.26 (dd, 1 H, *J* = 2.9, 10.5 Hz, H-3), 5.00 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.94 (d, 1 H, *J* = 3.4 Hz, H-1′), 4.93 (d, 1 H, *J* = 11.8 Hz, CH_2Ph), 4.88 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.85 (d, 1 H, *J* = 11.8 Hz, CH_2Ph), 4.75–4.82 (m, 1 H, H-6), 4.75 (d, 1 H, *J* = 7.7 Hz, H-1), 4.73 (d, 1 H, *J* = 11.9 Hz, CH_2Ph), 4.57 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.42 (d, 1 H, *J* = 2.5 Hz, H-4), 4.21 (dd, 1 H, *J* = 2.6, 10.3 Hz, H-3′), 4.16 (br dd, 1 H, *J* = 6.3, 8.7 Hz, H-5′), 4.02–4.11 (m, 4 H, H-2′,5,6, and OCH_2CH_2Si), 3.95 (br s, 1 H, H-4′), 3.65 (dt, 1 H, *J* = 6.6, 10.0 Hz, OCH_2CH_2Si), 3.08 (dd, 1 H, *J* = 9.1, 11.5 Hz, H-6′), 2.83 (dd, 1 H, *J* = 5.6, 11.5 Hz, H-6′), 0.87–1.04 (m, 2 H, CH_2Si), −0.05 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 166.8, 166.5, 165.8, 128.0-139.0 (Ar), 101.3, 101.2, 79.3, 76.2, 76.0, 75.3, 74.9, 74.6, 74.4, 73.4, 73.0, 70.2, 70.1, 67.9, 62.9, 49.9, 18.4, −1.1; HRMS Anal. Calcd for $C_{59}H_{63}O_{13}N_3SiNa$ [M + Na]: 1072.4028. Found: 1072.4008.

*2-(Trimethylsilyl)ethyl (2,3-di-*O*-benzoyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-*D*-glucopyranoside* (**18**).—2-(Trimethylsilyl)ethyl (2,3-di-*O*-benzoyl-4,6-*O*-*p*-methoxybenzylidene-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-*D*-glucopyranoside [2i] (**17**, 1.8 g, 1.67 mmol) was dissolved in aq AcOH (80%) and the mixture was heated to 90 °C. After 30 min, the mixture was cooled to ambient temperature and CH_2Cl_2 (50 mL) was added. The mixture was washed with satd aq $NaHCO_3$ until neutral, then washed with water, dried, and concentrated. The residue was chromatographed (SiO_2, 2:1 toluene–EtOAc) to give **18** (1.44 g, 90%); $[\alpha]_D^{28}$ +75° (*c* 1.1, $CHCl_3$); Ref. [2i] $[\alpha]_D^{28}$ +77.2° (*c* 0.84, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.87–8.06 (m, 10 H, Ar–H), 7.19–7.61 (m, 15 H, Ar–H), 5.77 (dd, 1 H, *J* = 7.8, 10.3 Hz, H-2′), 5.75 (t, 1 H, *J* = 9.2 Hz, H-3), 5.42 (dd, 1 H, *J* = 7.9, 9.6 Hz, H-2), 5.10 (dd, 1 H, *J* = 3.1, 10.4 Hz, H-3′), 4.79 (d, 1 H, *J* = 7.9 Hz, H-1′), 4.73 (d, 1 H, *J* = 7.8 Hz, H-1), 4.60 (br dd, 1 H, *J* = 2.0, 12.0 Hz, H-6), 4.43 (dd, 1 H, *J* = 5.3, 12.0 Hz, H-6), 4.22 (d, 1 H, *J* = 3.0 Hz, H-4′), 4.17 (t, 1 H, *J* = 9.3 Hz, H-4), 3.84–3.95 (m, 2 H, H-5 and OCH_2CH_2Si), 3.54 (dt, 1 H, *J* = 6.6, 10.1 Hz, OCH_2CH_2Si), 3.41 (br t, 1 H, *J* = 4.9 Hz, H-5′), 3.35 (br dd, 1 H, *J* = 4.7, 12.0 Hz, H-6′), 3.25 (dd, 1 H, *J* = 5.4, 12.1 Hz, H-6′), 0.75–0.93 (m, 2 H, CH_2Si), −0.13 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 166.3, 166.2, 166.1, 165.7, 165.6, 128.8-133.9 (Ar), 101.8, 100.6, 77.2, 74.8, 74.7, 74.2, 73.3, 72.4, 70.2, 68.3, 67.9, 63.2, 62.6, 18.3, −1.1; HRMS Anal. Calcd for $C_{52}H_{54}O_{16}SiNa$ [M + Na]: 985.3079. Found: 985.3091.

*2-(Trimethylsilyl)ethyl (2,3,6-tri-*O*-benzoyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-*D*-glucopyranoside* (**19**).—Compound **18** (1025 mg, 1.06 mmol) was dissolved in a mixture of CH_2Cl_2 (20 mL) and pyridine (20 mL). The solution was cooled to −78 °C under N_2 and benzoyl chloride (0.133 mL, 1.17 mmol) was added. The mixture was stirred at −78 °C for 6 h, MeOH (5 mL) was added, and the resulting mixture was heated to rt and concentrated. The residue was chromatographed (SiO_2, 3:1 toluene–EtOAc) to give **19** (1.11 g, 98%); $[\alpha]_D^{22}$ +55° (*c* 1.0,

$CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.25–7.65 and 7.91–8.08 (30 H, Ar–H), 5.77 (t, 1 H, $J = 9.7$ Hz, H-3), 5.73 (dd, 1 H, $J = 8.0$, 10.4 Hz, H-2′), 5.44 (dd, 1 H, $J = 7.9$, 9.7 Hz, H-2), 5.14 (dd, 1 H, $J = 3.3$, 10.3 Hz, H-3′), 4.78 (d, 1 H, $J = 7.9$ Hz, H-1′), 4.71 (d, 1 H, $J = 7.9$ Hz, H-1), 4.59 (dd, 1 H, $J = 1.6$, 12.0 Hz, H-6), 4.46 (dd, 1 H, $J = 4.8$, 12.1 Hz, H-6), 4.21 (t, 1 H, $J = 9.7$ Hz, H-4), 4.04–4.15 (m, 2 H, incl. H-4′), 3.82–3.96 (m, 2 H, H-5 and OCH_2CH_2Si), 3.59–3.69 (m, 2 H), 3.54 (dt, 1 H, $J = 6.5$, 10.2 Hz, OCH_2CH_2Si), 0.77–0.94 (m, 2 H, CH_2Si), −0.12 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 166.5, 166.3, 166.2, 166.0, 165.7, 165.4, 128.7–133.9 (Ar), 101.5, 100.8, 76.7, 74.5, 73.6, 73.3, 72.9, 72.3, 70.1, 68.0, 67.2, 63.1,62.1, 18.3, −1.1; HRMS Anal. Calcd for $C_{59}H_{58}O_{17}SiNa$ [M + Na]: 1089.3341. Found: 1089.3330.

2-(Trimethylsilyl)ethyl (2,3-di-O-*benzoyl-6*-O-*p-toluenesulfonyl-β-*D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzoyl-β-*D-*glucopyranoside* (**20**).—Compound **18** (320 mg, 0.33 mmol) was dissolved in dry pyridine (5 mL) under N_2, *p*-toluenesulfonyl chloride (75 mg, 0.40 mmol) was added at −30 °C. The temperature was slowly raised to rt, and after 15 h, additional *p*-toluenesulfonyl chloride (20 mg, 0.10 mmol) was added. After 23 h, CH_2Cl_2 (30 mL) and water (10 mL) were added. The organic phase was isolated and washed with aqueous 1 M HCl and satd aq $NaHCO_3$, then dried and concentrated. The residue was chromatographed (SiO_2, 1:1 EtOAc–heptane) to give **20** (294 mg, 80%); $[\alpha]_D^{28}$ +59° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.23–8.03 (29 H, Ar–H), 5.69 (t, 1 H, $J = 9.5$ Hz, H-3), 5.64 (dd, 1 H, $J = 8.0$, 10.5 Hz, H-2′), 5.39 (dd, 1 H, $J = 7.9$, 9.7 Hz, H-2), 5.10 (dd, 1 H, $J = 3.2$, 10.3 Hz, H-3′), 4.74 (d, 1 H, $J = 7.9$ Hz, H-1′), 4.69 (d, 1 H, $J = 7.9$ Hz, H-1), 4.58 (br dd, 1 H, $J = 1.8$, 12.1 Hz, H-6), 4.40 (br dd, 1 H, $J = 4.8$, 12.0 Hz, H-6), 4.13 (t, 1 H, $J = 9.5$ Hz, H-4), 4.07 (br s, 1 H, H-4′), 3.85–3.95 (m, 1 H, OCH_2CH_2Si), 3.77–3.85 (m, 1 H, H-5), 3.44–3.63 (m, 4 H, H-5′,6′, and OCH_2CH_2Si), 2.47 (s, 3 H, $ArCH_3$), 0.75–0.92 (m, 2 H, CH_2Si), −0.13 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 166.3, 165.9, 165.6, 165.4, 145.6, 133.9-128.3 (Ar), 101.3, 100.7, 76.8, 74.1, 73.6, 73.3, 72.3, 69.9, 67.9, 66.4, 65.9, 63.0, 22.1, 18.2, −1.1; HRMS Anal. Calcd for $C_{59}H_{60}O_{18}SiNa$ [M + Na]: 1139.3167. Found: 1139.3176.

2-(Trimethylsilyl)ethyl (6-azido-2,3-di-O-*benzoyl-6-deoxy-α-*D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzoyl-β-*D-*galactopyranoside* (**21**).—(a) Compound **20** (266 mg, 0.238 mmol) was dissolved in dry DMF (7 mL), 15-crown-5 (0.052 mL, 0.26 mmol) and NaN_3 (78 mg, 1.2 mmol) were added, and the mixture was stirred at 90 °C for 5 h. The mixture was cooled to rt and water (20 mL) was added. The mixture was extracted with Et_2O (2 × 10 mL) and the organic phase was dried and concentrated. The residue was chromatographed (SiO_2, 1:5→1:3→1:2 EtOAc–heptane) to give **21** (118 mg, 50%); $[\alpha]_D^{28}$ +52° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.89–8.09 (10 H, Ar–H), 7.26–7.65 (15 H, Ar–H), 5.72 (t, 1 H, $J = 9.4$ Hz, H-3), 5.66 (dd, 1 H, $J = 7.9$, 10.5 Hz, H-2′), 5.43 (dd, 1 H, $J = 7.9$, 9.7 Hz, H-2), 5.09 (dd, 1 H, $J = 3.2$, 10.4 Hz, H-3′), 4.74 (d, 1 H, $J = 7.8$ Hz, H-1′), 4.70 (d, 1 H, $J = 7.9$ Hz, H-1), 4.58 (dd, 1 H, $J = 1.9$, 12.2 Hz, H-6), 4.42 (dd, 1 H, $J = 4.6$, 12.1 Hz, H-6), 4.21 (t, 1 H, $J = 9.4$ Hz, H-4), 4.03 (br d, 1 H, $J = 3.1$ Hz, H-4′), 3.86–3.96 (m, 1 H, OCH_2CH_2Si), 3.78–3.85 (m, 1 H, H-5), 3.54 (dt, 1 H, $J = 6.5$, 10.2 Hz, OCH_2CH_2Si), 3.39 (br t, 1 H, $J = 6.7$ Hz, H-5′), 2.80 (dd, 1 H, $J = 6.3$, 12.7 Hz, H-6′), 2.67 (dd, 1 H, $J = 6.7$, 12.8 Hz, H-6′), 0.76–0.93 (m, 2 H, CH_2Si), −0.13 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 166.3, 166.0, 165.6, 165.4, 128.7-134.0 (Ar), 101.2, 100.7, 76.5, 74.4, 74.0, 73.7, 73.2, 72.2, 70.0, 68.0, 67.5, 62.9, 49.5, 18.3, −1.1; HRMS Anal. Calcd for $C_{52}H_{53}O_{15}N_3SiNa$ [M + Na]: 1010.3145. Found: 1010.3164.

(b) To a solution of **18** (100 mg, 0.10 mmol) in a mixture of dry CH_2Cl_2 (4 mL) and 2,6-di-*tert*-butylpyridine (0.028 mL, 0.125 mmol) at −45 °C was added trifluoromethanesulfonic anhydride (0.019 mL, 0.114 mmol). The mixture was stirred at −45 °C for 30 min and at 0 °C for 30 min. Et_2O (10 mL) was added and the mixture was washed with saturated aqueous $NaHCO_3$, dried, and concentrated. Without further purification, the product was dissolved in dry DMF (5 mL), NaN_3 (33 mg, 0.52 mmol) and 15-crown-5 (0.021 mL, 0.1 mmol) were added, and the mixture was

stirred at rt under N_2 for 2.5 h. Water (10 mL) and Et_2O were added, and the organic phase was washed with water, dried, and concentrated. The residue was chromatographed (SiO_2, 3:1 heptane–EtOAc) to give **21** (53.3 mg, 52%) and 2-(trimethylsilyl)ethyl (4,6-anhydro-2,3-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside (**22**, 21.6 mg, 22%). Data for **22**: ^{1}H NMR ($CDCl_3$): δ 7.86–8.04, 7.25–7.61, 7.16–7.22 and 6.82–6.87 (25 H, Ar–H), 5.85 (t, 1 H, $J = 9.1$ Hz, H-3), 5.79 (dd, 1 H, $J = 8.0$, 10.5 Hz, H-2′), 5.31 (dd, 1 H, $J = 7.8$, 9.4 Hz, H-2), 5.15 (dd, 1 H, $J = 3.6$, 10.4 Hz, H-3′), 4.84 (d, 1 H, $J = 7.9$ Hz, H-1′), 4.71 (d, 1 H, $J = 7.8$ Hz, H-1), 4.63 (dd, 1 H, $J = 2.2$, 12.1 Hz, H-6), 4.38 (dd, 1 H, $J = 4.5$, 11.8 Hz, H-6), 4.29 (br d, 1 H, $J = 3.3$ Hz, H-4′), 4.22 (t, 1 H, $J = 9.3$ Hz, H-4), 3.84–3.93 (m, 2 H, H-5 and O$CH_2$$CH_2$Si), 3.75 (br d, 1 H, $J =$ 12.5 Hz, H-6′), 3.57 (br d, 1 H, $J = 12.7$ Hz, H-6′), 3.47–3.54 (m, 1 H, O$CH_2$$CH_2$Si), 2.97 (br s, 1 H, H-5′), 0.73–0.95 (m, 2 H, CH_2Si), −0.14 (s, 9 H, $SiCH_3$); HRMS Anal. Calcd for $C_{52}H_{52}O_{15}SiNa$ [M + Na]: 967.2973. Found: 967.2966.

*Phenyl 1-thio-6-*O*-p-toluenesulfonyl-β-*D*-galactopyranoside* (**24**).—To a solution of phenyl 1-thio-β-D-galactopyranoside [15] (**23**, 1.5 g, 5.51 mmol) in dry pyridine (15 mL) was added *p*-toluenesulfonyl chloride (1155 mg, 6.06 mmol) at −45 °C. The temperature was slowly raised to rt and after 6 h, MeOH (4 mL) was added. The mixture was stirred for 1 h and co-concentrated with toluene. The residue was chromatographed (SiO_2, 2:1:1 EtOAc–heptane–MeOH → 10:1 CH_2Cl_2–MeOH) to give **24** (1.9 g, 81%); $[\alpha]_D^{23}$ −61° (*c* 1.1, MeOH); ^{1}H NMR (CD_3OD): δ 7.20–7.80 (9 H, Ar–H), 4.53 (d, 1 H, $J = 9.6$ Hz, H-1), 4.15–4.22 (m, 2 H, H-6), 3.81 (dd, 1 H, $J =$ 1.0, 3.5 Hz, H-4), 3.76 (ddd, 1 H, $J = 1.0$, 5.3, 6.4 Hz, H-5), 3.54 (t, 1 H, $J = 9.4$ Hz, H-2), 3.46 (dd, 1 H, $J = 3.3$, 9.3 Hz, H-3), 2.40 (s, 3 H, $ArCH_3$); ^{13}C NMR (CD_3OD): δ 146.6, 136.0, 134.3, 132.1, 131.2, 130.0, 129.2, 128.2, 89.7, 77.5, 76.0, 71.3, 70.8, 70.4, 49.8, 49.6, 49.4, 49.2, 48.9, 48.7, 48.5, 21.7; HRMS Anal. Calcd for $C_{19}H_{22}O_7S_2Na$ [M + Na]: 449.0705. Found: 449.0708.

*Phenyl 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-1-thio-β-*D*-galactopyranoside* (**25**).—Compound **24** (1.46 g, 3.4 mmol) was dissolved in DMF (15 mL) and NaN_3 (1.1 g, 17 mmol) was added. The mixture was stirred at 65 °C for 36 h, then cooled to room temperature, filtered, and concentrated. The crude material was dissolved in dry DMF (12 mL) and treated with sodium hydride (340 mg, 11.2 mmol, 80% in oil) for 1 h. Benzyl bromide (1.3 mL, 10.9 mmol) was added and the mixture was stirred overnight at rt. Methanol (1.5 mL) and water were added and the aq phase was extracted with Et_2O. The organic phase was dried and concentrated, and the residue was chromatographed twice (SiO_2, 4:1 heptane–EtOAc, then 10:1 heptane–EtOAc) to give **25** (726 mg, 38%); $[\alpha]_D^{23}$ −29° (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.23–7.62 (m, 20 H, Ar–H), 5.05 (d, 1 H, $J = 11.5$ Hz, CH_2Ph), 4.86 (d 1 H, $J = 10.2$ Hz, CH_2Ph), 4.75–4.81 (m, 3 H, CH_2Ph), 4.65 (d, 1 H, $J = 9.7$ Hz, H-1), 4.64 (d, 1 H, $J = 11.5$ Hz, CH_2Ph), 3.94 (t, 1 H, $J = 9.5$ Hz, H-2), 3.83 (br d, 1 H, $J = 2.5$ Hz, H-4), 3.58–3.66 (m, 2 H, H-3,6), 3.49 (br t, 1 H, $J = 6.5$ Hz, H-5), 3.19 (dd, 1 H, $J = 5.8$, 12.4 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 127.8–138.7 (Ar), 88.6, 84.5, 77.5, 76.2, 74.8, 74.0, 73.6, 51.7; HRMS Anal. Calcd for $C_{33}H_{33}O_4N_3SNa$ [M + Na]: 590.2089. Found: 590.2101.

*2-(Trimethylsilyl)ethyl (6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-α-*D*-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzoyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-*D*-glucopyranoside* (**26**).—A mixture of **25** (123 mg, 0.216 mmol), **19** (144 mg, 0.13 mmol) and molecular sieves (AW-300) in dry toluene (7 mL) was cooled to −45 °C under N_2. *N*-Iodosuccinimide (80 mg, 0.36 mmol) was added, followed by trifluoromethanesulfonic acid (0.009 mL, 0.1 mmol). After 3.5 h at −45 °C, Et_3N (1 mL) was added, the mixture was heated to rt, filtered through Celite, and washed with satd aq $Na_2S_2O_3$ and water. The organic phase was dried (Na_2SO_4) and concentrated. The residue was chromatographed (SiO_2, 1:3 EtOAc–heptane) to give **26** (181 mg, 88%); $[\alpha]_D^{21}$ +49° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.94–8.07, 7.80–7.85, 7.07–7.64 (45 H, Ar–H), 5.82 (t, 1 H, $J = 9.3$ Hz, H-3), 5.73 (dd, 1 H, $J = 7.8$,

10.7 Hz, H-2′), 5.40 (dd, 1 H, $J = 7.9$, 9.5 Hz, H-2), 5.07 (dd, 1 H, $J = 2.6$, 10.7 Hz, H-3′), 4.94 (d, 1 H, $J = 11.1$ Hz, CH_2Ph), 4.91 (d, 1 H, $J = 7.8$ Hz, H-1′), 4.65–4.85 (m, 3 H), 4.71 (2 d, 1 H each, $J = 3.4$ Hz and $J = 7.8$ Hz, H-1′ and H-1), 4.49–4.60 (m, 5 H, incl. H-6′), 4.31 (d, 1 H, $J = 2.3$ Hz, H-4′), 4.27 (t, 1 H, $J = 9.5$ Hz, H-4), 4.20 (br dd, 1 H, $J = 6.2$, 11.2 Hz, H-6′), 4.05 (br dd, 1 H, $J = 6.2$, 8.9 Hz, H-5′), 3.86–3.98 (m, 5 H, incl. H-2′,5, and OCH_2CH_2Si), 3.73 (br t, 1 H, $J = 6.5$ Hz, H-5′), 3.53 (dt, 1 H, $J = 6.5$, 10.1 Hz, OCH_2CH_2Si), 3.08 (dd, 1 H, $J = 9.3$, 11.6 Hz, H-6′), 2.88 (dd, 1 H, $J = 5.5$, 11.5 Hz, H-6′), 0.78–0.95 (m, 2 H, CH_2Si), −0.11 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 166.8, 166.3, 166.1, 165.73, 165.66, 165.6, 127.8–139.2 (Ar), 101.5, 101.2, 100.7, 79.4, 76.9, 76.0, 75.8, 75.2, 74.84, 74.75, 73.8, 73.6, 73.5, 72.8, 70.2, 67.9, 63.1, 62.5, 49.9, 18.3, −1.1; HRMS Anal. Calcd for $C_{86}H_{85}O_{21}N_3SiNa$ [M + Na]: 1546.5343. Found: 1546.5347.

*2-(Trimethylsilyl)ethyl (4-azido-2,3,6-tri-*O*-benzyl-4-deoxy-α-*D*-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzoyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-*D*-glucopyranoside* (**27**).—To a solution of **8** (163 mg, 0.28 mmol) and **19** (150 mg, 0.14 mmol) in dry toluene (8 mL) was added molecular sieves (AW-300), and the mixture was cooled to −45 °C under N_2. *N*-Iodosuccinimide (95 mg, 0.42 mmol) and trifluoromethanesulfonic acid (0.01 mL, 0.11 mmol) were added and the reaction mixture was stirred for 3.5 h. Et_3N (2 mL) and CH_2Cl_2 (20 mL) were added, the mixture was filtered through Celite, and then washed with satd aq $Na_2S_2O_3$ and water. The organic phase was dried and concentrated and the residue was chromatographed (SiO_2, 3:1 heptane–EtOAc) to give **27** (174 mg, 81%); $[\alpha]_D^{22}$ +48° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.93–8.08, 7.80–7.84, 7.07–7.65 (45 H, Ar–H), 5.82 (t, 1 H, $J = 9.3$ Hz, H-3), 5.73 (dd, 1 H, $J = 7.9$, 10.6 Hz, H-2′), 5.40 (dd, 1 H, $J = 7.8$, 9.5 Hz, H-2), 5.08 (dd, 1 H, $J = 2.7$, 10.7 Hz, H-3′), 4.91 (d, 1 H, $J = 7.8$ Hz, H-1′), 4.72 (d, $J = 7.9$ Hz, H-1), 4.54 (d, $J = 3.5$ Hz, H-1′), 4.58–4.77 (m, 7 H) 4.41 (d, 1 H, $J =$ 11.9 Hz, CH_2Ph), 4.24–4.36 (m, 4 H, H-4,4′, 5′, and CH_2Ph), 4.19–4.22 (m, 1 H, H-4′), 4.17 (dd, 1 H, $J = 6.2$, 11.4 Hz, H-6′), 4.03 (dd, 1 H, $J = 3.4$, 10.1 Hz, H-3′), 3.86–3.96 (m, 2 H, H-5, OCH_2CH_2Si), 3.68–3.75 (m, 2 H, H-2′,5′), 3.49–3.61 (m, 1 H, OCH_2CH_2Si), 3.29 (t, 1 H, $J = 9.1$ Hz, H-6′), 3.18 (dd, 1 H, $J = 5.1$, 8.7 Hz, H-6′), 0.78–0.95 (m, 2 H, CH_2Si), −0.10 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 166.8, 166.3, 166.1, 165.8, 165.7, 165.5, 128.1–138.6 (Ar), 101.5, 101.3, 100.7, 78.4, 76.9, 76.6, 75.9, 74.7, 74.2, 73.6, 73.4, 73.1, 72.8, 70.2, 68.2, 68.0, 67.9, 63.1, 62.6, 61.4, 18.3, −1.1; HRMS Anal. Calcd for $C_{86}H_{85}O_{21}N_3SiNa$ [M + Na]: 1546.5343. Found: 1546.5348.

*2-(Trimethylsilyl)ethyl (2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-*D*-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzoyl-β-*D*-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-β-*D*-glucopyranoside* (**29**).—A mixture of 4-methylphenyl 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-1-thio-β-*D*-galactopyranoside [2n] (**28**, 100 mg, 0.17 mmol), **19** (115 mg, 0.107 mmol), molecular sieves (AW-300), and dry toluene (6 mL) was cooled to −45 °C under N_2. *N*-Iodosuccinimide (70 mg, 0.31 mmol) and trifluoromethanesulfonic acid (0.007 mL, 0.08 mmol) were added, and the reaction mixture was stirred for 2 h. Et_3N (1 mL) and CH_2Cl_2 (10 mL) were added, and the mixture was heated to rt, then filtered through Celite, and washed with satd aq $Na_2S_2O_3$ and water. The organic phase was dried and concentrated, and the residue was chromatographed (SiO_2, 1:3 EtOAc–heptane) to give **29** (154 mg, 94%); $[\alpha]_D^{21}$ +68° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.83–8.11 and 7.12–7.63 (45 H, Ar–H), 5.83 (t, 1 H, $J = 9.4$ Hz, H-3), 5.78 (dd, 1 H, $J = 7.9$, 10.6 Hz, H-2′), 5.41 (dd, 1 H, $J = 7.8$, 9.6 Hz, H-2), 5.09 (dd, 1 H, $J =$ 2.5, 10.8 Hz, H-3′), 4.93 (d, 1 H, $J = 7.8$ Hz, H-1′), 4.81 (d, 1 H, $J = 3.4$ Hz, H-1′), 4.73–4.80 (m, 3 H, CH_2Ph), 4.73 (d, 1 H, $J = 7.8$ Hz, H-1), 4.67 (br d, 1 H, $J = 11.8$ Hz, H-6), 4.56 (dd, 1 H, $J = 4.7$, 11.9 Hz, H-6), 4.41 (d, 1 H, $J = 11.0$ Hz, CH_2Ph), 4.35 (d, 1 H, $J = 2.6$ Hz, H-4′), 4.13–4.33 (m, 4 H, H-4,5′,6′), 3.85–4.08 (m, 7 H, incl. H-2′,5, OCH_2CH_2Si), 3.77 (br t, 1 H, $J = 7.0$ Hz, H-5′), 3.54 (dt, 1 H, $J = 6.8$, 10.2 Hz, OCH_2CH_2Si), 3.30 (t, 1 H, $J =$ 8.8 Hz, H-6′), 2.84 (dd, 1 H, $J = 5.1$, 8.1 Hz, H-6′), 0.78–0.95 (m, 2 H, CH_2Si), −0.11 (s, 9 H, $SiCH_3$);

^{13}C NMR ($CDCl_3$): δ 166.7, 166.4, 166.0, 165.8, 165.7, 165.5, 127.9–138.9 (Ar), 101.9, 100.7, 100.3, 77.7, 77.4, 75.4, 74.8, 74.6, 73.6, 73.5, 73.3, 73.1, 72.8, 72.7, 70.2, 70.1, 67.9, 67.6, 63.1, 61.6, 60.8, 18.3, −1.1; HRMS Anal. Calcd for $C_{86}H_{85}O_{21}N_3SiNa$ [M + Na]: 1546.5343. Found. 1546.5332.

2-(Trimethylsilyl)ethyl (2,3,4,6-tetra-O-*benzyl*-α-D-*galactopyranosyl)-(1→4)-(6-azido-2,3-di*-O-*benzoyl-6-deoxy*-β-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzoyl*-β-D-*glucopyranoside* (**31**).—A mixture of phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-galactopyranoside [15,16] (**30**, 62 mg, 0.098 mmol) and **21** (60.5 mg, 0.061 mmol) in Et_2O (4 mL) and CH_2Cl_2 (2 mL) was cooled to −45 °C under N_2 and *N*-iodosuccinimide (35 mg, 0.16 mmol) and trimethylsilyl trifluoromethanesulfonate (0.009 mL, 0.05 mmol) were added. After 2 h, Et_3N (0.5 mL) was added, and the mixture was co-concentrated with toluene (4 mL). The residue was chromatographed (SiO_2, 3:1 heptane–EtOAc) to give **31** (87 mg, 94%); $[\alpha]_D^{23}$ +56° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.12–8.07 (45 H, Ar–H), 5.79 (t, 1 H, $J = 9.2$ Hz, H-3), 5.70 (dd, 1 H, $J = 7.8$, 10.8 Hz, H-2′), 5.36 (dd, 1 H, $J = 7.9$, 9.4 Hz, H-2), 4.98 (dd, 1 H, $J = 2.7$, 10.8 Hz, H-3′), 4.86 (d, 1 H, $J = 7.8$ Hz, H-1′), 4.84 (d, 1 H, $J = 11.2$ Hz, CH_2Ph), 4.65–4.78 (m, 6 H, H-1,6,1′, and CH_2Ph), 4.61 (d, 1 H, $J = 11.9$ Hz, CH_2Ph), 4.51 (d, 1 H, $J = 11.1$ Hz, CH_2Ph), 4.41 (dd, 1 H, $J = 4.8$, 12.0 Hz, H-6), 4.21–4.31 (m, 4 H, incl. H-5′,4), 4.14 (br s, 1 H, H-4′), 3.84–3.99 (m, 4 H, H-5 and OCH_2CH_2Si), 3.45–3.59 (m, 2 H, H-6′ and OCH_2CH_2Si), 3.41 (br t, 1 H, $J = 8.8$ Hz, H-6′), 3.30 (br t, 1 H, $J = 6.5$ Hz, H-5′), 3.08 (dd, 1 H, $J = 4.9$, 8.4 Hz, H-6′), 2.88 (dd, 1 H, $J = 5.8$, 12.4 Hz, H-6′), 0.75–0.94 (m, 2 H, CH_2Si), −0.13 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 166.9, 166.2, 165.7, 165.52, 165.49, 127.7–139.2, 101.8, 101.6, 100.6, 79.4, 76.6, 76.1, 75.4, 74.9, 74.7, 74.3, 74.2, 73.5, 73.2, 72.78, 72.76, 70.3, 70.1, 67.84, 67.76, 62.9, 49.6, 18.3, −1.1; HRMS Anal. Calcd for $C_{86}H_{87}O_{20}N_3SiNa$ [M + Na]: 1532.5550. Found: 1532.5540.

(2,3,4,6-Tetra-O-*benzyl*-α-D-*galactopyranosyl)-(1→4)-6-azido-2,3-di*-O-*benzoyl-6-deoxy*D-*galactopyranose* (**33**).—2-(Trimethylsilyl)ethyl (2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-6-azido-2,3-di-*O*-benzoyl-6-deoxy-β-D-galactopyranoside [2n] (**32**, 143 mg, 0.138 mmol) was dissolved in CH_2Cl_2 (0.8 mL) and trifluoromethanesulfonic acid (1.6 mL) was added at 0 °C. The mixture was stirred at 0 °C under N_2 for 35 min, toluene (10 mL) and *n*-propylacetate (10 mL) were added [11], and the mixture was concentrated. The residue was chromatographed (SiO_2, 1:1 EtOAc–heptane) to give **33** (121 mg, 93%); HRMS Anal. Calcd for $C_{54}H_{53}O_{12}N_3Na$ [M + Na]: 958.3527. Found: 958.3525.

(2,3,4,6-Tetra-O-*benzyl*-α-D-*galactopyranosyl)-(1→4)-6-azido-2,3-di*-O-*benzoyl-6-deoxy*-α-D-*galactopyranosyl chloride* (**34**).—Compound **33** (115 mg, 0.125 mmol) was dissolved in a mixture of CH_2Cl_2 (4 mL) and DMF (0.1 mL) and $(COCl)_2$ (0.070 mL, 0.81 mmol) was added at 0 °C under N_2. The mixture was stirred at rt for 1 h, cold toluene and cold saturated aqueous $NaHCO_3$ were added, and the organic phase was dried and concentrated, to give **34** in quantitative yield. Crude **34** was used without further purification.

2-(Trimethylsilyl)ethyl (2,3,4,6-tetra-O-*benzyl*-α-D-*galactopyranosyl)-(1→4)-(6-azido-2,3-di*-O-*benzoyl-6-deoxy*-β-D-*galactopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl*-β-D-*glucopyranoside* (**36**).—To a solution of **34** (119 mg, 0.125 mmol) and 2-(trimethylsilyl)ethyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside [11] (**35**, 53 mg, 0.096 mmol) in CH_2Cl_2 (8 mL), were added *N*,*N*,*N*′,*N*′-tetramethylurea (0.026 mL, 0.21 mmol) and molecular sieves (AW-300). The mixture was cooled to −30 °C under N_2, silver trifluoromethanesulfonate (55 mg, 0.21 mmol) was added, and the reaction mixture was stirred at −30 °C for 1 h, slowly heated to rt, and stirred for 20 h. The mixture was filtered through Celite and concentrated, and the residue was chromatographed twice (SiO_2, 1:3 EtOAc–heptane, then 1:5:1 EtOAc–heptane–CH_2Cl_2) to give **36** (73 mg, 52%, contaminated with 5–10% of unidentified material); selected data for **36**: ^{1}H NMR ($CDCl_3$): δ 7.84–7.97 and 7.15–7.55 (45 H, Ar–H), 5.71 (dd, 1 H, $J = 8.0$, 10.8 Hz, H-2′), 5.04 (d, 1 H, $J = 11.3$ Hz, CH_2Ph), 4.96 (dd, 1 H, $J = 2.7$, 10.7 Hz, H-3′), 4.26 (br d, 1 H, $J = 2.5$ Hz, H-4′), 4.11 (br s, 1 H, H-4′), 3.03 (dd, 1 H, $J = 4.8$, 8.3 Hz, H-6′), 0.98–1.05 (m,

2 H, CH_2Si), 0.02 (s, 9 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): δ 167.0, 165.5, 127.6–139.3 (Ar), 103.4, 101.8, 101.1, 83.1, 82.3, 79.5, 76.8, 76.7, 75.4, 75.3, 75.0, 74.8, 74.71, 74.66, 74.4, 73.8, 73.4, 72.6, 70.8, 70.1, 67.8, 50.2, 18.9, –1.0.

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