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Synthesis of the globotetraose tetrasaccharide and terminal tri- and di-saccharide fragments

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ABSTRACT

The 2-(trimethylsilyl)ethyl (TMSEt) β-glycosides of globotetraose [β-D-GalNAc-(1 → 3)-α-D-Gal-(1 → 4)-β-D-Gal-(1 → 4)-D-Glc] and the terminal trisaccharide, as well as the methyl α-glycoside **1** of the terminal disaccharide, were synthesised by silver trifluoromethanesulfonate-promoted β-glycosylation of suitably protected galactoside, galabioside, and globotrioside alcohols with 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-galactopyranosyl chloride, followed by removal of protecting groups. Removal of the anomeric TMSEt group of the globotetraoside and of the terminal trisaccharide, using trifluoroacetic acid–dichloromethane, gave the corresponding hemiacetal sugars **8** and **3**. The TMSEt glycoside of the terminal trisaccharide was converted, via the 1-acetate, into the corresponding isobutyl (**4**) and 3-butylsulfonyl-2-[(butylsulfonyl)methyl]propyl (**5**) glycosides and into the TMSEt thioglycoside **6** via the glycosyl bromide.

INTRODUCTION

Antigens of the globoseries of glycolipids are recognized in vivo by antibodies of the P blood-group system and by various bacterial proteins, such as the pilus-associated PapG adhesin protein of uropathogenic *Escherichia coli*[1], verotoxin from *E. coli*[2], Shiga toxin from *Shigella dysenteriae*[3], and the adhesin from *Streptococcus suis*[4]. Furthermore, glycolipids of the globoseries have been suggested to be tumor-associated antigens on Burkitt lymphoma cells[5], human teratocarcinoma cells[6], and other tumor cells[7], and are also enriched in the body fluids of patients suffering from Fabry's disease[8].

Since different strains of uropathogenic *E. coli* recognize different epitopes on glycolipids of the globo series[9], we decided to synthesise the globoside tetrasaccharide and the corresponding terminal di- and tri-saccharides (**1–8**) for further use in various bio-assays and NMR investigations (Fig. 1). A preliminary account of this work has been published[10].

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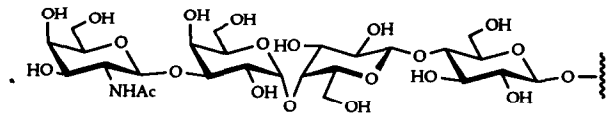


β-D-Gal*p*-NAc-(1→3)-α-D-Gal*p*-1-OMe (**1**)
β-D-Gal*p*-NAc-(1→3)-α-D-Gal*p*-(1→4)-β-D-Gal*p*-1-OTMSEt (**2**)
β-D-Gal*p*-NAc-(1→3)-α-D-Gal*p*-(1→4)-αβ-D-Gal*p*-1-OH (**3**)
β-D-Gal*p*-NAc-(1→3)-α-D-Gal*p*-(1→4)-β-D-Gal*p*-1-$OCH_2CH(CH_3)_2$ (**4**)
β-D-Gal*p*-NAc-(1→3)-α-D-Gal*p*-(1→4)-β-D-Gal*p*-1-$OCH_2CH(CH_2SO_2C_4H_9)_2$ (**5**)
β-D-Gal*p*-NAc-(1→3)-α-D-Gal*p*-(1→4)-β-D-Gal*p*-1-STMSEt (**6**)
β-D-Gal*p*-NAc-(1→3)-α-D-Gal*p*-(1→4)-β-D-Gal*p*-(1→4)-β-D-Glc*p*-1-OTMSEt (**7**)
β-D-Gal*p*-NAc-(1→3)-α-D-Gal*p*-(1→4)-β-D-Gal*p*-(1→4)-αβ-D-Glc*p*-1-OH (**8**)

TMSEt = 2-(Trimethylsilyl)ethyl

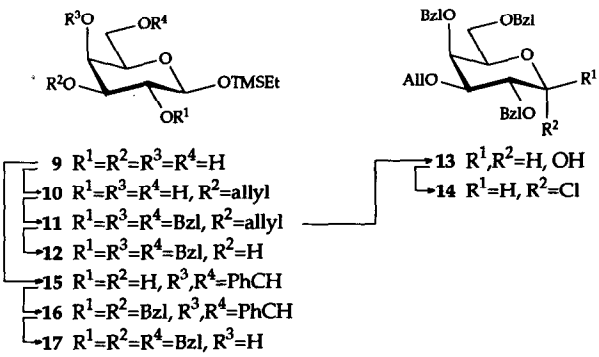
Fig. 1. Synthetic fragments of the globotetraose tetrasaccharide.

A detailed analysis of the molecular recognition of galabiose [α-D-Gal*p*-(1 → 4)-α,β-D-Gal*p*] by the PapG adhesin protein[11] of *E. coli* pili was performed by inhibition of hemagglutination by a collection of deoxy- and deoxyfluoro-galabioside analogues[12]. Galabiosides with hydrophobic aglycons (instead of a β-D-glucose residue as in the natural globoseries glycolipids) showed increased inhibitory power and it was also indicated that the β-D-GalNAc unit was important for binding to the PapG adhesin. This prompted us to convert the terminal trisaccharide into isobutyl (**4**), 3-butylsulfonyl-2-[(butylsulfonyl)methyl]propyl (**5**), and 2-(trimethylsilyl)ethylthio (**6**) glycosides.

The synthesis of the globotetraose tetrasaccharide in the form of the hemiacetal sugar[13] (**8**) and methyl and 1-octyl glycosides[14] has been reported by others. We decided to synthesise the globotetraose tetrasaccharide and the terminal trisaccharide as the 2-(trimethylsilyl)ethyl (TMSEt) glycosides which, via efficient deprotection–activation methods[15], permit high-yielding transformations of the complete oligosaccharides into glycoconjugates[16]. The synthetic strategy was based on β-glycosylation of suitably protected TMSEt glycosides of galactose, galabiose, and globotriose with a protected galactosamine donor, followed by deprotection. This strategy was successful, although a higher overall yield was obtained by block synthesis to furnish the TMSEt glycoside of globotetraose.

RESULTS AND DISCUSSION

The TMSEt galactoside, galabioside, and globotrioside acceptors were prepared as follows (Scheme 1). 2-(Trimethylsilyl)ethyl β-D-galactopyranoside[15] (**9**) was regioselectively allylated via a stannylidene acetal[17] to give **10** (70%) and then benzylated to given the protected glycoside **11** (92%). Deallylation of **11** with palladium(II) chloride in methanol[18] furnished the galactoside acceptor **12** (95%). The deallylation reaction had to be monitored carefully by TLC and worked up immediately, because prolonged reaction times and even leaving the crude product at −20°C overnight resulted in complete decomposition of **12**. The preparation of



Scheme 1.

12 by a similar route, using a 4-methoxybenzyl ether instead of an allyl ether in the 3-position, was recently described by Hasegawa et al.[19].

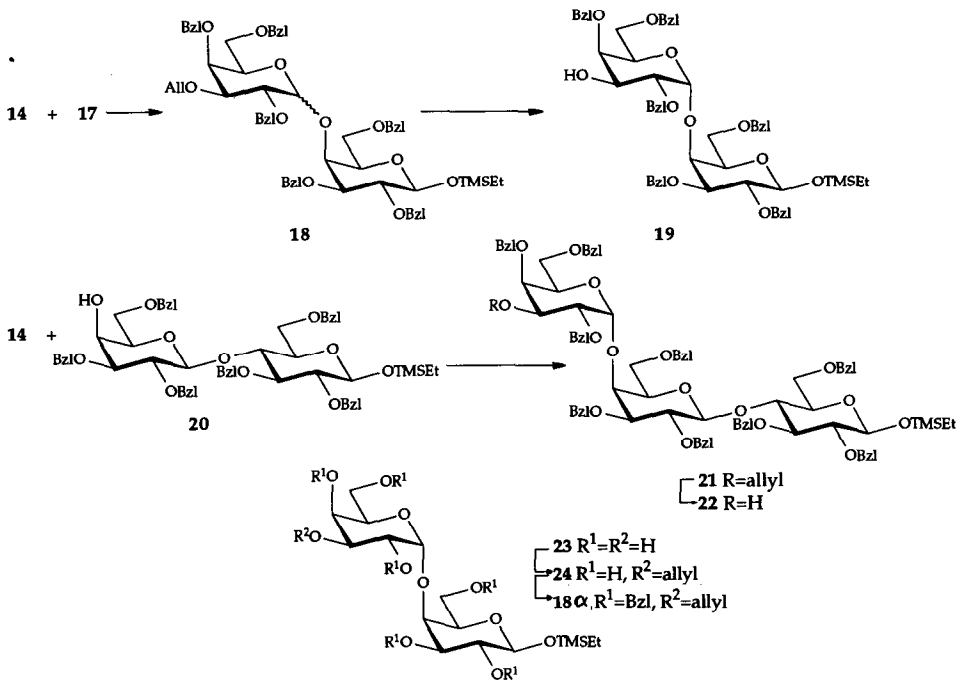
Removal of the TMSEt group[15] in **11** yielded the hemiacetal **13**[20] (89%), which was then treated with oxalyl chloride–*N*,*N*-dimethylformamide[21] to give the galactosyl chloride **14** in quantitative yield. Benzylation of 2-(trimethylsilyl)ethyl 4,6-*O*-benzylidene-β-D-galactopyranoside[15] (**15**) provided **16** (89%). Reductive ring opening of the benzylidene acetal[22] gave the galactoside acceptor **17** (80%).

Silver trifluoromethanesulfonate-promoted glycosylation of **17** and the corresponding lactoside alcohol[15] **20** with crude **14** afforded the disaccharide **18** (92%) as an inseparable mixture (α/β 5:1) and the globotrioside **21** (73% + 19% of the corresponding β-glycoside), respectively (Scheme 2). The α/β mixture of the trisaccharide **21** was separable on a silica gel column, in contrast to the disaccharide mixture **18**. Deallylation of **18** as described for **11** furnished a mixture of disaccharide alcohols, which was easily separated on a silica gel column to give the anomerically pure TMSEt galabioside alcohol **19** (75%). Deallylation of **21** afforded the TMSEt globotrioside alcohol **22** (75%).

Later, we found that anomerically pure **18α** could easily be prepared directly from the disaccharide 2-(trimethylsilyl)ethyl 4-*O*-α-D-galactopyranosyl-β-D-galactopyranoside[15] (**23**) via regioselective 3′-*O*-allylation to give **24** (48% + 28% recovered **23**), followed by benzylation (→ **18α**, 85%).

The β-GalNAc linkages were then established using 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-galactopyranosyl chloride[23] (**25**) as donor in a silver trifluoromethanesulfonate-promoted glycosylation of the galactoside alcohols[20] **26** and **12**, the galabioside alcohol **19**, and the globotrioside alcohol **22** to give the disaccharides **27** (83%) and **28** (70% + 9% α-glycoside), the trisaccharide **30** (78%, α/β 8:92), and the tetrasaccharide **32** (35%, α/β 15:85), respectively (Scheme 3). The anomeric mixtures of the tri- and tetra-saccharides **30** and **32** were not separable on a silica gel column.

Hydrogenolysis, hydrazinolysis, and *N*-acetylation of **27** gave the terminal disaccharide **1** (77%). Hydrogenolysis, hydrazinolysis, and acetylation of the trisaccha-



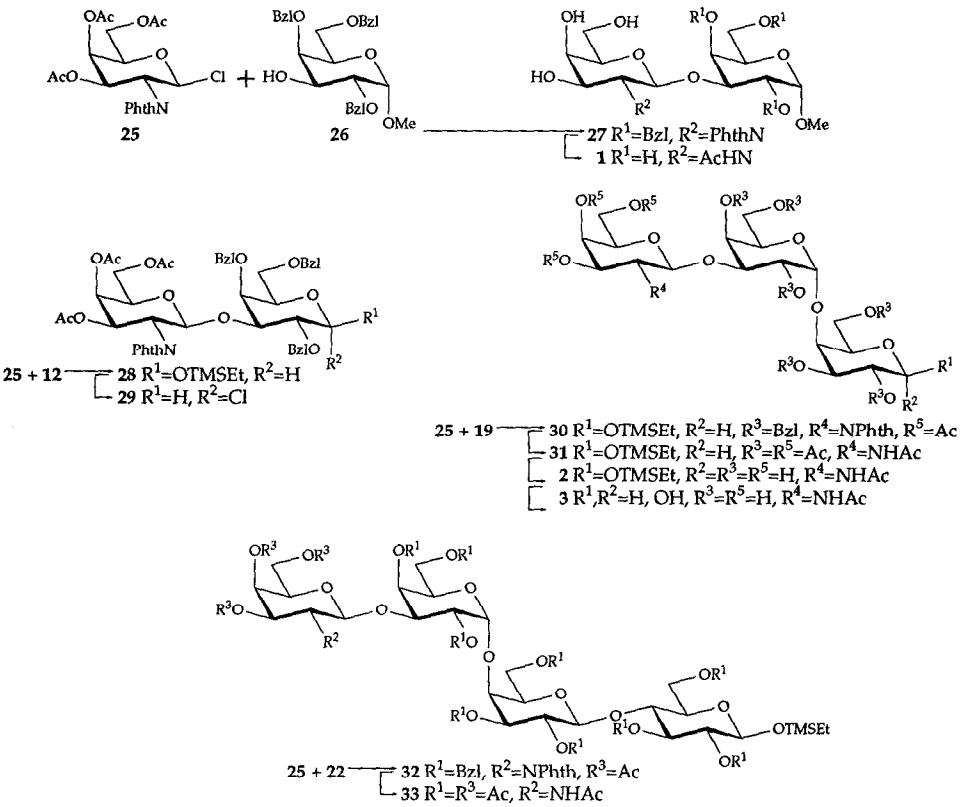
Scheme 2.

ride **30**, followed by separation of the anomeric mixture, gave fully acetylated **31** (90%), which was then *O*-deacetylated to give the deblocked trisaccharide **2** (95%). Deblocking, followed by acetylation and separation of the anomers of tetrasaccharide **32**, as described for **30**, afforded the fully acetylated globotetraoside **33** (55%).

With the trisaccharide acceptor **22**, the glycosylation yield (→ **32**) was disappointingly low (35%). This was mainly due to glycal formation by HCl elimination from **25** and consequently an alternative route based on a block strategy was investigated. Cleavage of the TMSEt group of **28** followed by treatment of the resulting hemiacetal with oxalyl chloride–*N*,*N*-dimethylformamide afforded a quantitative yield of the crude chloride **29**. Glycosylation of an excess of the lactoside alcohol[15] **20** with **29** (Scheme 4), using silver trifluoromethanesulfonate as promoter, furnished an anomeric mixture of products (60%, α/β 6:1), which was separated to give pure **32** (44% from **29**) (Scheme 4). The anomerically pure tetrasaccharide **32** was then deblocked in the usual manner to furnish the TMSEt globotetraoside **7**.

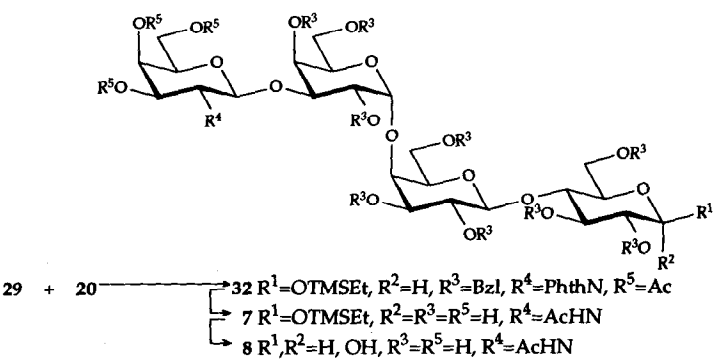
Anomeric deblocking of the trisaccharide **2** and the tetrasaccharide **7**, using trifluoroacetic acid–dichloromethane[15], gave the corresponding hemiacetal sugars **3** (83%) and **8** (98%).

In addition to the efficient anomeric deblocking of TMSEt glycosides, as exemplified by the synthesis of **13**, **29**, **3**, and **8** above, TMSEt glycosides undergo

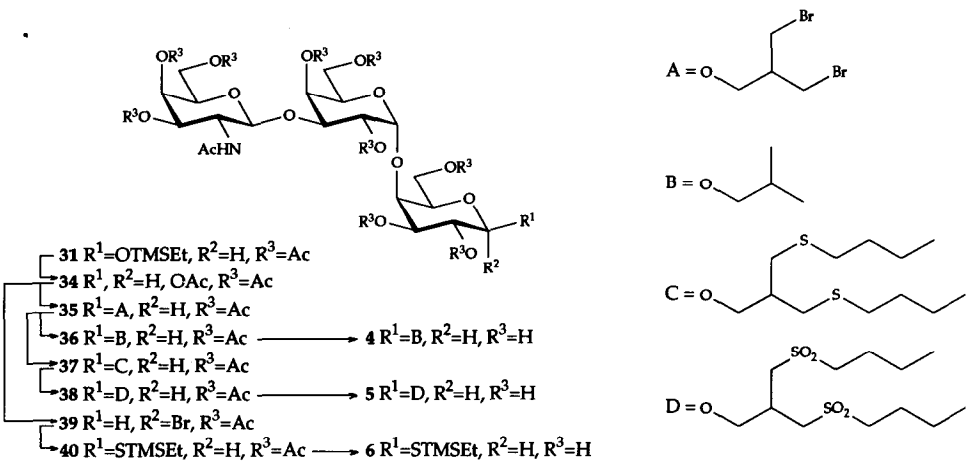


Scheme 3.

normally a highly stereoselective transformation to the corresponding β-1-*O*-acyl sugars[15]. Thus, treatment of the trisaccharide TMSEt glycoside **31** with acetic anhydride–boron trifluoride etherate afforded the acetate **34** (89%, β/α 3:1). In



Scheme 4.



Scheme 5.

this reaction, we had to use 2.0 equiv of boron trifluoride etherate (as compared with 0.8 equiv in the original conditions[14]), to compensate for the buffering capacity of the *N*-acetyl group. Still, the reaction was unusually slow and considerable anomerisation of the acetate **34** took place. Glycosylation of 3-bromo-(2-bromomethyl)propanol (DIBOL)[24] with **34**, using boron trifluoride etherate in acetonitrile as promoter[25], gave the DIB glycoside **35** (46%), together with the corresponding α-glycoside (0.3%) and the DIB α/β-glycoside having HO-2 unprotected (33%) (Scheme 5).

Reduction of the dibromide **35** with tributyltin hydride–azobisisobutyronitrile gave the isobutyl glycoside **36** (65%), which was deacetylated to give the trisaccharide **4** (93%). Similar reductions were earlier performed by hydrogenolysis[16], which gave a low yield and several byproducts with **35**.

Cesium carbonate-mediated nucleophilic substitution of the dibromide **35** with butanethiol[16] gave the bis-sulfide glycoside **37** (84%), which on oxidation[16] with 3-chloroperoxybenzoic acid furnished the corresponding bis-sulfone **38** (89%). Deacetylation of **38** afforded the bis-butylsulfone trisaccharide **5** (99%).

Finally, treatment of the acetate **34** with hydrogen bromide–acetic acid to give the crude bromide **39**, followed by bromide substitution with the sodium salt of 2-(trimethylsilyl)ethanethiol in *N*,*N*-dimethylformamide, gave the thioglycoside **40** (66% overall yield). *O*-Deacetylation furnished the terminal trisaccharide thioglycoside **6** (95%).

EXPERIMENTAL

General methods.—Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 polarimeter. ^1H and ^{13}C NMR spectra were recorded with a Varian XL-300 spectrometer. 1,4-Dioxane was used as internal reference (67.4 ppm) in ^{13}C NMR experiments in D_2O. Concentrations were made

using rotary evaporation with bath temperature at or below 40°C. Anhydrous Na_2SO_4 was used as drying agent for the organic extracts in the workup procedures. TLC was performed on Kieselgel 60 F_{254} plates (Merck). Column chromatography was performed using SiO_2 (Matrex LC-gel; 60 A, 35-70 MY, Grace).

Methyl 3-O-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-α-D-galactopyranoside (**1**).—Compound **27** (1.3 g, 1.72 mmol) and Pd–C (300 mg, 10%) in AcOH were stirred under H_2 (1 atm) for 2 days, and the solution was then filtered through Celite and concentrated. The residue was dissolved in EtOH (50 mL), hydrazine hydrate (4 mL) was added, and the mixture was heated at 85°C for 90 min, concentrated, and co-concentrated with EtOH (5 × 25 mL). *N*-Acetylation with Ac_2O (5 mL) in MeOH (50 mL) for 1 h, concentration, and column chromatography (10:4:1 CH_2Cl_2–MeOH–H_2O) followed by lyophilisation gave **1** (526 mg, 77%), $[\alpha]_D^{25}$ + 124° (*c* 0.5, H_2O). ^1H NMR data (D_2O): δ 4.75 (br s, 1 H, H-1), 4.57 (d, 1 H, *J* 8.4 Hz, H-1′), 4.14 (br s, 1 H, H-4), 3.35 (s, 3 H, OMe), 1.98 (s, 3 H, Ac). ^{13}C NMR data (D_2O): δ 176.0, 103.9, 100.4, 80.0, 75.8, 71.7, 71.1, 69.9, 68.6, 68.0, 62.0, 61.8, 55.8, 53.5, 23.1.

2-(Trimethylsilyl)ethyl 4-O-[3-O-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-α-D-galactopyranosyl]-β-D-galactopyranoside (**2**).—Compound **31** (260.9 mg, 0.254 mmol) was treated with methanolic NaOMe (3.3 mL, 0.02 M) for 20 min, then neutralised with Duolite (H^+) resin, filtered, and concentrated. Column chromatography (65:35:5 CH_2Cl_2–MeOH–H_2O) gave **2** (155.2 mg, 95%), $[\alpha]_D^{25}$ +42° (*c* 1, MeOH). An analytical sample was crystallised from MeOH; mp 157–160°C. ^1H NMR data (D_2O): δ 4.89 (d, 1 H, *J* 3.7 Hz, H-1′), 4.58 (d, 1 H, *J* 8.3 Hz, H-1″), 4.44 (d, 1 H, *J* 7.8 Hz, H-1), 4.36 (br t, 1 H, *J* 6.5 Hz, H-5′), 4.23 (br d, 1 H, *J* 2.0 Hz, H-4′), 3.49 (dd, 1 H, *J* 7.8, 10.2 Hz, H-2). 2.00 (s, 3 H, Ac), 1.09–0.87 (m, 2 H, CH_2CH_2Si), −0.01 (s, 9 H, $SiMe_3$). ^{13}C NMR data (CD_3OD): δ 173.7, 106.1 (2 C), 104.1, 82.4, 81.0, 78.3, 77.6, 76.4, 74.9, 74.5, 73.9, 72.3, 71.4, 71.1, 69.9, 64.2, 64.1, 62.7, 24.8, 22.1, 20.9, 0.2.

4-O-[3-O-(2-Acetamido-2-deoxy-β-D-galactopyranosyl)-α-D-galactopyranosyl]-α,β-D-galactopyranose (**3**).—Compound **2** (51.1 mg, 0.079 mmol) was stirred in dry CH_2Cl_2 (0.25 mL) and CF_3CO_2H (0.5 mL) under N_2. After 18 min, propyl acetate (1.5 mL) was added and the solution was concentrated. Column chromatography (65:35:5 CH_2Cl_2–MeOH–H_2O) of the residue gave **3** (35.9 mg, 83%), $[\alpha]_D^{25}$ + 90° (*c* 0.7, D_2O). Compound **3α** had: ^1H NMR data (D_2O): δ 5.28 (d, 1 H, *J* 3.7 Hz, H-1), 4.91 (d, 1 H, *J* 3.3 Hz, H-1′), 4.60 (d, 1 H, *J* 8.4 Hz, H-1″), 4.34 (br t, 1 H, *J* 6.8 Hz, H-5′), 4.23 (br d, 1 H, *J* 3.0 Hz, H-4′), 2.01 (s, 3 H, Ac). Compound **3β** had: ^1H NMR data (D_2O): δ 4.90 (d, 1 H, *J* 3.5 Hz, H-1′), 4.63 (d, 1 H, *J* 7.8 Hz, H-1), 4.60 (d, 1 H, *J* 8.3 Hz, H-1″), 4.36 (br t, 1 H, *J* 6.8 Hz, H-5′), 4.23 (br d, 1 H, *J* 3.0 Hz, H-4′), 3.51 (dd, 1 H, *J* 7.8, 10.2 Hz, H-2), 2.03 (s, 3 H, Ac). The α,β mixture had: ^{13}C NMR data (D_2O): δ 176.0, 104.14, 104.10, 101.4, 101.2, 97.5, 93.2, 79.8, 79.7, 79.6, 78.1, 75.9, 75.8, 73.3, 72.7, 71.6, 71.2, 71.1, 69.8, 68.6, 68.5, 66.2, 61.8, 61.3, 61.0, 23.1.

Isobutyl 4-O-[3-O-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-α-D-galacto-

pyranosyl]-β-D-galactopyranoside (**4**).—Compound **36** (102.0 mg, 0.104 mmol) was treated with methanolic NaOMe (4 mL, 50 mM) for 1.5 h, and the mixture was then neutralised with Duolite(H^+) resin, filtered, and concentrated. Column chromatography (65:35:5 CH_2Cl_2–MeOH–H_2O) of the residue gave **4** (58.0 mg, 93%), $[\alpha]_D^{25}$ + 99° (*c* 1, H_2O). ^1H NMR data (D_2O): δ 4.89 (d, 1 H, *J* 3.6 Hz, H-1′), 4.58 (d, 1 H, *J* 8.4 Hz, H-1″), 4.41 (d, 1 H, *J* 7.7 Hz, H-1), 4.39 (br t, 1 H, *J* 5.5 Hz, H-5′), 4.24 (br d, 1 H, *J* 1.6 Hz, H-4′), 3.52 (dd, 1 H, *J* 7.7, 10.2 Hz, H-2), 3.43 (dd, 1 H, *J* 6.5, 9.6 Hz, OCH_2CH), 2.00 (s, 3 H, Ac), 1.87 [m, 1 H, $CH_2CH(CH_3)_2$], 0.88 (d, 6 H, *J* 6.8 Hz, CH_3). ^{13}C NMR data (D_2O): δ 175.8, 104.2, 103.9, 101.1, 80.0, 78.0, 77.5, 75.81, 75.75, 73.2, 71.8, 71.7, 70.9, 69.7, 68.6, 68.5, 61.8, 61.2, 60.7, 53.4, 28.7, 23.1, 19.7, 19.3.

3-Butylsulfonyl-2-[(butylsulfonyl)methyl]propyl 4-O-[3-O-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-α-D-galactopyranosyl]-β-D-galactopyranoside (**5**).—Compound **38** (103.9 mg, 0.085 mmol) was treated with methanolic NaOMe (9 mL, 5 mM) for 2 h, and the mixture was then neutralised with Duolite(H^+) resin, filtered, and concentrated. Column chromatography (65:35:5 CH_2Cl_2–MeOH–H_2O) of the residue gave **5** (70.7 mg, 99%), $[\alpha]_D^{25}$ +70° (*c* 1, H_2O). ^1H NMR data (D_2O): δ 4.89 (d, 1 H, *J* 3.9 Hz, H-1′), 4.59 (d, 1 H, *J* 8.1 Hz, H-1″), 4.44 (d, 1 H, *J* 7.8 Hz, H-1), 4.37 (br t, 1 H, *J* 6.1 Hz, H-5′), 4.23 (br d, 1 H, *J* 2.1 Hz, H-4′), 3.52 [m, 4 H, $CH(CH_2SO_2Bu)_2$], 3.27 (m, 4 H, $SO_2CH_2CH_2$), 3.04 [m, 1 H, $CH(CH_2SO_2Bu)_2$], 2.00 (s, 3 H, Ac), 1.77 (m, 4 H, $CH_2CH_2CH_2$), 1.44 (m, 4 H, $CH_2CH_2CH_3$), 0.90 (t, 6 H, *J* 7.3 Hz, CH_3). ^{13}C NMR data (CD_3OD): δ 161.9, 106.5, 106.1, 78.3, 77.8, 74.2, 73.1, 71.3, 71.2, 64.18, 64.15, 62.9, 56.5, 55.9, 55.8, 54.8, 51.3, 50.2, 50.1, 50.0, 49.92, 49.87, 49.8, 26.5, 26.4, 24.7, 24.2, 15.5.

2-(Trimethylsilyl)ethyl 4-O-[3-O-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-α-D-galactopyranosyl]-1-thio-β-D-galactopyranoside (**6**).—Compound **40** (237.4 mg, 0.228 mmol) was treated with methanolic NaOMe (8.2 mL, 0.02 M) for 3.5 h, and the solution was then neutralised with Duolite (H^+) resin, filtered, and concentrated. Column chromatography (65:35:5 $CHCl_3$–MeOH–H_2O) gave **6** (144.0 mg, 95%), $[\alpha]_D^{25}$ +60° (*c* 1, H_2O). ^1H NMR data (D_2O): δ 4.89 (d, 1 H, *J* 3.4 Hz, H-1′), 4.59 (d, 1 H, *J* 8.8 Hz, H-1″), 4.55 (d, 1 H, *J* 10.7 Hz, H-1), 4.35 (br t, 1 H, *J* 6.4 Hz, H-5′), 4.23 (br s, 1 H, H-4′), 2.81 (m, 2 H, SCH_2CH_2), 2.01 (s, 3 H, Ac), 0.92 (m, 2 H, CH_2CH_2Si), −0.01 (s, 9 H, $SiMe_3$). ^{13}C NMR data (D_2O): δ 175.8, 104.1, 101.3, 86.6, 80.0, 79.6, 78.1, 75.7, 74.6, 71.7, 71.1, 70.8, 69.7, 68.6, 68.5, 61.8, 61.2, 60.7, 53.5, 27.2, 23.1, 18.1, −1.72.

2-(Trimethylsilyl)ethyl 4-O-{4-O-[3-O-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-α-D-galactopyranosyl]-β-D-galactopyranosyl}-β-D-glucopyranoside (**7**).—Compound **32** (624.4 mg, 0.340 mmol) was hydrogenated (1 atm) over Pd–C (180 mg, 10%) in AcOH (6 mL) for 17 h, and the solution was then filtered through Celite and concentrated. The residue was treated with hydrazine hydrate (340 mL) in EtOH (8.5 mL) at 85°C. After 50 min, the mixture was concentrated and co-concentrated 5 times with EtOH. The residue was acetylated in Ac_2O (10 mL) and pyridine (10 mL) for 17 h, and the solution was concentrated and then passed

through a silica gel column (20:1 toluene–EtOH) to remove most of the UV-active byproducts from the hydrazinolysis. The slightly impure, fully acetylated tetrasaccharide derivative was deacetylated in methanolic NaOMe (3.1 mL, 0.06 M) for 7 h, then the solution was neutralised with Duolite (H^+) resin, filtered, and concentrated. Column chromatography (65:35:5 CH_2Cl_2–MeOH–H_2O) of the residue gave **7** (250.1 mg, 91%), $[\alpha]_D^{25}$ +64° (*c* 1, H_2O). ^1H NMR data (D_2O): δ 4.87 (d, 1 H, *J* 3.4 Hz, H-1″), 4.59 (d, 1 H, *J* 8.3 Hz, H-1‴), 4.48 (d, 1 H, *J* 7.1 Hz, H-1′), 4.45 (d, 1 H, *J* 7.6 Hz, H-1), 4.33 (br t, 1 H, *J* 6.0 Hz, H-5″), 4.20 (br s, 1 H, H-4″), 2.00 (s, 3 H, Ac), 0.98 (m, 2 H, CH_2CH_2Si), −0.01 (s, 9 H, $SiMe_3$). ^{13}C NMR data (D_2O): δ 176.0, 104.12, 104.09, 102.2, 101.3, 79.5, 78.1, 76.3, 75.8, 75.6, 75.5, 73.8, 73.0, 71.7, 71.6, 71.1, 69.8, 69.2, 68.6, 68.5, 61.8, 61.24, 61.15, 60.9, 53.4, 23.1, 18.4, −1.6.

4-O-{4-O-[3-O-(2-Acetamido-2-deoxy-β-D-galactopyranosyl)-α-D-galactopyranosyl]-β-D-galactopyranosyl}-α,β-D-glucopyranose (**8**).—Compound **7** (17.3 mg, 21.4 mmol) was dissolved in dry CH_2Cl_2 (70 μL) and CF_3CO_2H (140 μL) under N_2. After 32 min, propyl acetate (0.75 mL) and toluene (5 mL) were added and the solution was concentrated. Column chromatography (10:10:1 CH_2Cl_2–MeOH–H_2O) of the residue gave **8** (14.9 mg, 98%), $[\alpha]_D^{25}$ +117° (*c* 1, D_2O); lit.[13] $[\alpha]_D^{25}$ +60° (*c* 0.25, H_2O). Compound **8α** had: ^1H NMR data (D_2O): δ 5.14 (d, 1 H, *J* 3.6 Hz, H-1), 4.82 (d, 1 H, *J* 3.6 Hz, H-1″), 4.54 (d, 1 H, *J* 8.3 Hz, H-1‴), 4.43 (d, 1 H, *J* 7.7 Hz, H-1′), 4.31 (br t, 1 H, *J* 6.0 Hz, H-5″), 4.17 (br s, 1-H, H-4″), 1.96 (s, 3 H, Ac). Compound **8β** had: ^1H NMR data (D_2O): δ 4.82 (d, 1 H, *J* 3.6 Hz, H-1″), 4.58 (d, 1 H, *J* 7.9 Hz, H-1), 4.54 (d, 1 H, *J* 8.3 Hz, H-1‴), 4.43 (d, 1 H, *J* 7.7 Hz, H-1′), 4.31 (br t, 1 H, *J* 6.0 Hz, H-5″), 4.17 (br s, 1 H, H-4″), 1.96 (s, 3 H, Ac). The α,β mixture had: ^{13}C NMR data (D_2O): δ 176.0, 104.1, 101.3, 96.6, 79.62, 79.56, 78.1, 76.3, 75.8, 75.7, 75.3, 74.8, 73.0, 72.4, 72.1, 71.8, 71.7, 71.15, 71.11, 71.0, 69.8, 68.6, 68.5, 67.6, 61.9, 61.3, 61.2, 60.9, 53.5, 23.1.

2-(Trimethylsilyl)ethyl 3-O-allyl-β-D-galactopyranoside (**10**).—A suspension of 2-(trimethylsilyl)ethyl β-D-galactopyranoside[15] (**9**; 649 mg, 2.32 mmol) and dibutyltin oxide (693 mg, 2.80 mmol) in benzene (40 mL) was refluxed with azeotropic removal of water for 24 h. Allyl bromide (3.82 mL, 44.2 mmol) and tetrabutylammonium bromide (373 mg, 1.16 mmol) were added, and the mixture was refluxed for another 3 h and then concentrated. Column chromatography (1:2 heptane–EtOAc) of the residue gave **10** (517 mg, 70%), $[\alpha]_D^{25}$ −8.5° (*c* 1, $CDCl_3$). ^1H NMR data ($CDCl_3$): δ 6.03–5.89 (m, 1 H, CH_2CHCH_2), 5.38–5.21 (m, 2 H, CH_2CH), 4.28 (d, 1 H, *J* 7.8 Hz, H-1), 4.24–4.19 (m, 2 H, $CHCH_2O$), 3.65–3.55 (m, 1 H, OCH_2CH_2), 3.53 (br t, 1 H, H-5), 3.40 (dd, 1 H, *J* 3.4, 9.5 Hz, H-3), 1.05–0.92 (m, 2 H, CH_2CH_2Si), 0.02 (s, 9 H, $SiMe_3$). Mass spectrum: calcd for $C_{14}H_{29}O_6Si$ (M + 1): *m/z* 321.1733; found: *m/z* 321.1728.

2-(Trimethylsilyl)ethyl 3-O-allyl-2,4,6-tri-O-benzyl-β-D-galactopyranoside (**11**).—To a solution of **10** (507 mg, 1.58 mmol) and NaH in mineral oil (0.31 g, 6.3 mmol) in N,N-dimethylformamide (DMF, 10.6 mL) was added benzyl bromide (1.31 mL, 11.0 mmol) under N_2. The mixture was left overnight and MeOH (10 mL) was

added. After 1 h, EtOAc was added, and the solution was washed with water twice, dried, and concentrated. Column chromatography (toluene) of the residue gave **11** (859 mg, 92%), $[\alpha]_D^{25}$ −13° (*c* 1, $CDCl_3$). ^1H NMR data ($CDCl_3$): δ 6.00–5.87 (m, 1 H, CH_2CHCH_2), 5.36–5.14 (m, 2 H, CH_2CH), 4.93 (d, 1 H, *J* 11.8 Hz, $PhCH_2$), 4.90 (d, 1 H, *J* 11.0 Hz, $PhCH_2$), 4.76 (d, 1 H, *J* 11.0 Hz, $PhCH_2$), 4.60 (d, 1 H, *J* 11.8 Hz, $PhCH_2$), 4.47 (d, 1 H, *J* 11.8 Hz, $PhCH_2$), 4.41 (d, 1 H, *J* 11.8 Hz, $PhCH_2$), 4.35 (d, 1 H, *J* 7.7 Hz, H-1), 4.21–4.17 (m, 2 H, $CHCH_2O$), 4.05–3.95 (m, 1 H, OCH_2CH_2), 3.85 (d, 1 H, *J* 2.9 Hz, H-4), 3.74 (dd, 1 H, *J* 7.7, 9.7 Hz, H-2), 3.42 (dd, 1 H, *J* 2.9, 9.7 Hz, H-3), 1.05–0.99 (m, 2 H, CH_2CH_2Si), 0.00 (s, 9 H, $SiMe_3$). Mass spectrum: calcd for $C_{35}H_{46}O_6Si$ (M + 1): *m/z* 590.3063; found: *m/z* 590.3059.

*2-(Trimethylsilyl)ethyl 2,4,6-tri-*O*-benzyl-β-*D*-galactopyranoside* (**12**). A mixture of **11** (3.96 g, 6.70 mmol) and palladium(II) chloride (400 mg) in MeOH (80 mL) was stirred for 3.5 h at room temperature, filtered through Celite, and concentrated. Column chromatography (3:1 heptane–EtOAc) of the residue gave **12** (3.51 g, 95%), $[\alpha]_D^{25}$ −1.54° (*c* 1, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ 4.36 (d, 1 H, *J* 7.4 Hz, H-1), 4.02 (m, 1 H, OCH_2CH_2), 3.87 (d, 1 H, *J* 3.2 Hz, H-4), 2.26 (d, 1 H, *J* 4.9 Hz, OH), 1.07–1.01 (m, 2 H, CH_2CH_2Si), 0.02 (s, 9 H, $SiMe_3$). Mass spectrum: calcd for $C_{32}H_{43}O_6Si$ (M + 1): *m/z* 551.2829; found *m/z*: 551.2828.

*3-*O*-Allyl-2,4,6-tri-*O*-benzyl-*D*-galactopyranose*[20] (**13**).—To a solution of **11** (842 mg, 1.43 mmol) in CH_2Cl_2 (7.2 mL) was added CF_3CO_2H (14.3 mL) at 0°C under N_2[15a]. After 25 min, propyl acetate (43 mL) and dry toluene (87 mL) were added, the mixture was concentrated, and traces of acid were removed by repeated evaporations with toluene. Column chromatography (3:1 heptane–EtOAc) of the residue gave **13** (625 mg, 89%), $[\alpha]_D^{25}$ +8° (*c* 0.8, $CHCl_3$); lit.[20] $[\alpha]_D^{20}$ +14° (*c* 2, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ 5.95–5.92 (m, 1 H, CH_2CHCH_2), 5.38–5.17 (m, 2 H, CH_2CH), 5.26 (d, 1 H, *J* 3.7 Hz, H-1α), 4.64 (d, 1 H, *J* 7.5 Hz, H-1β), 3.98 (dd, 1 H, *J* 3.6, 9.9 Hz, H-2α), 3.94 (br d, 1 H, H-4α), 3.87 (br d, 1 H, H-4β), 3.80 (dd, 1 H, *J* 2.7, 9.9 Hz, H-3α), 3.70 (dd, 1 H, *J* 7.5, 9.6 Hz, H-2β), 3.44 (dd, 1 H, *J* 2.9, 9.6 Hz, H-3β). Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.4; H, 7.0. Found: C, 73.3; H, 7.2.

*3-*O*-Allyl-2,4,6-tri-*O*-benzyl-*D*-galactopyranosyl chloride* (**14**).—To a solution of **13** (505 mg, 1.03 mmol) in CH_2Cl_2 (8 mL) was added DMF (0.55 mL) and oxalyl chloride (0.55 mL). After 45 min, the mixture was diluted with ice-cold toluene (40 mL), washed with ice-cold water and ice-cold satd aq $NaHCO_3$, dried, and concentrated to give crude **14** (520 mg, 99%). The crude product was used directly in glycosylation reactions with alcohols **17** and **20**.

*2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-*D*-galactopyranoside* (**16**).—To a solution of 2-(trimethylsilyl)ethyl 4,6-*O*-benzylidene-β-D-galactopyranoside[15] (**15**) (8.5 g, 23.1 mmol) and NaH (3.46 g, 72 mmol) in DMF (100 mL) was added benzyl bromide (7.5 mL, 65 mmol) at 0°C. After 5 h, MeOH was added and the mixture was poured into stirred ice–water (1.5 L). The solid product was filtered off and recrystallised from EtOH to give **16** (11.23 g, 89%),

mp 131–133°C, $[\alpha]_D^{25}$ +23° (*c* 1, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ 5.50 (s, 1 H, PhC*H*), 4.40 (d, 1 H, *J* 7.7 Hz, H-1), 4.31 (dd, 1 H, *J* 1.7, 12.4 Hz, H-6), 4.02 (dd, 1 H, *J* 1.7, 12.4 Hz, H-6), 3.84 (dd, 1 H, *J* 7.7, 9.7 Hz, H-2), 3.55 (dd, 1 H, *J* 3.6, 9.7 Hz, H-3), 1.09–1.01 (m, 2 H, CH_2CH_2Si), 0.03 (s, 9 H, $SiMe_3$). Mass spectrum: calcd for $C_{32}H_{44}NO_6Si$ ($M + NH_4$): *m/z* 566.2938; found: *m/z* 566.2963.

2-(Trimethylsilyl)ethyl 2,3,6-tri-O-benzyl-β-D-galactopyranoside (**17**).—Saturated ethereal HCl was added at 22°C to a mixture of **16** (24.1 g, 43.7 mmol), sodium cyanoborohydride (25.3 g, 402 mmol), and 3A powdered molecular sieves (32 g) in dry THF (320 mL). The addition was discontinued when the solution became acidic (pH-paper). The reaction was monitored by TLC (SiO_2, 2:1 toluene–EtOAc) and, when complete, solid $NaHCO_3$, CH_2Cl_2 (500 mL), and satd aq $NaHCO_3$ (500 mL) were added. The mixture was filtered, and the organic phase was dried and concentrated. Column chromatography (6:1 heptane–EtOAc) of the residue gave **17** (19.3 g, 80%), $[\alpha]_D^{25}$ −1.8° (*c* 1, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ 4.37 (d, 1 H, *J* 7.7 Hz, H-1) 4.09–3.98 (m, 1 H, OCH_2CH_2), 4.02 (br s, 1 H, H-4), 3.81 (dd, 1 H, *J* 6.0, 9.8 Hz, H-6), 3.74 (dd, 1 H, *J* 5.9, 9.8 Hz, H-6), 3.64 (dd, 1 H, *J* 7.7, 9.3 Hz, H-2), 3.62–3.53 (m, 1 H, OCH_2CH_2), 3.49 (dd, 1 H, *J* 3.4, 9.3 Hz, H-3), 1.08–1.01 (m, 2 H, CH_2CH_2Si), 0.02 (s, 9 H, $SiMe_3$). Mass spectrum: calcd for $C_{32}H_{43}O_6Si$ (M + 1): *m/z* 551.2828; found: *m/z* 551.2825.

2-(Trimethylsilyl)ethyl 4-O-(3-O-allyl-2,4,6-tri-O-benzyl-α-D-galactopyranosyl)-2,3,6-tri-O-benzyl-β-D-galactopyranoside (**18**).—(*a*) To a mixture of **17** (9.93 g, 18.0 mmol), silver trifluoromethanesulfonate (6.4 g, 25.0 mmol), tetramethylurea (3.6 mL, 30.0 mmol), and activated 4A molecular sieves (13 g) in dry toluene (225 mL) was added chloride **14** (11.8 g, 23.2 mmol) in dry toluene (65 mL) dropwise at −78°C under N_2. The temperature was allowed to rise to room temperature overnight, and the mixture was filtered through Celite and concentrated. Column chromatography (9:1 heptane–EtOAc) of the residue gave an inseparable α/β mixture (5:1) of **18** (16.99 g, 92%).

(*b*) To a mixture of **24** (172 mg, 0.36 mmol) and NaH (219 mg, 4.3 mmol, 50% in mineral oil) in DMF (10 mL) was added benzyl bromide (0.59 mL, 5.0 mmol) under N_2. After 2 h, MeOH (7 mL) was added and the mixture was diluted with CH_2Cl_2 (50 mL), washed with water, dried, and concentrated. Column chromatography (9:1 heptane–EtOAc) of the residue gave **18α** (312 mg, 85%), $[\alpha]_D^{25}$ +31° (*c* 1, $CDCl_3$). ^1H NMR data for the α anomer ($CDCl_3$): δ 6.01–5.84 (m, 1 H, CH_2CHCH_2), 5.00 (d, 1 H, *J* 3.4 Hz, H-1′), 4.32 (d, 1 H, *J* 7.6 Hz, H-1), 4.05 (dd, 1 H, *J* 3.4, 10.3 Hz, H-2′), 3.64 (dd, 1 H, *J* 7.6, 10.0 Hz, H-2), 3.37 (dd, 1 H, *J* 2.8, 10.0 Hz, H-3), 1.07–1.02 (m, 2 H, CH_2CH_2Si), 0.02 (s, 9 H, $SiMe_3$). Anal. Calcd for $C_{62}H_{74}O_{11}Si$: C, 72.8; H, 7.3. Found: C, 72.9; H, 7.4.

2-(Trimethylsilyl)ethyl 2,3,6-tri-O-benzyl-4-O-(2,4,6-tri-O-benzyl-α-D-galacto-pyranosyl)-β-D-galactopyranoside (**19**).—A mixture of **18** (16.99 g, 16.6 mmol, α/β 5:1) and palladium(II) chloride (1.0 g) in MeOH (200 mL) was stirred for 2 h at room temperature, filtered through Celite, and concentrated. A solution of the residue in toluene was washed with satd aq $NaHCO_3$ and water, dried, and

concentrated. Column chromatography (7:1 heptane–EtOAc) of the residue gave **19**.(12.26 g, 75%) and **19β** (2.06 g, 13%). An analytical sample of **19** was obtained by recrystallisation from heptane; mp 82–84°C, $[\alpha]_D^{25}$ +49° (*c* 1, $CDCl_3$). ^1H NMR data ($CDCl_3$): δ 5.05 (d, 1 H, *J* 3.2 Hz, H-1′), 4.33 (d, 1 H, *J* 7.6 Hz, H-1), 4.20 (dd, 1 H, *J* 3.2, 10.3 Hz, H-2′), 3.82 (dd, 1 H, *J* 3.4, 10.3 Hz, H-3′), 3.65 (dd, 1 H, *J* 7.6, 10.0 Hz, H-2), 3.39 (dd, 1 H, *J* 2.9, 10.0 Hz, H-3), 1.07–1.01 (m, 2 H, CH_2CH_2Si), 0.01 (s, 9 H, $SiMe_3$). Anal. Calcd for $C_{59}H_{70}O_{11}Si$: C, 72.1; H, 7.2. Found: C, 72.1; H, 7.1.

^1H NMR data for **19β** ($CDCl_3$): δ 4.85 (m, 1 H, virtual coupling, similar to compound 2 in ref 25, H-1′), 4.38 (d, 1 H, *J* 7.5 Hz, H-1), 1.02 (m, 2 H, CH_2CH_2Si), −0.01 (s, 9 H, $SiMe_3$).

2-(Trimethylsilyl)ethyl 4-O-[4-O-(3-O-allyl-2,4,6,tri-O-benzyl-α-D-galactopyranosyl)-2,3,6-tri-O-benzyl-β-D-galactopyranosyl]-2,3,6-tri-O-benzyl-β-D-glucopyranoside (**21**).—To a mixture of 2-(trimethylsilyl)ethyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside[15] (**20**; 2.27 g, 2.30 mmol), silver trifluoromethanesulfonate (0.83 g, 3.2 mmol), tetramethylurea (0.42 mL, 3.45 mmol), and activated 4A molecular sieves (1.6 g) in dry CH_2Cl_2 (30 mL) was added a solution of the chloride **14** (1.54 g, 3.03 mmol) in dry CH_2Cl_2 (8 mL) dropwise at −78°C under N_2. Cooling was continued for 1 h, the temperature was allowed to rise slowly to room temperature overnight, and the mixture was filtered through Celite and concentrated. Column chromatography (20:1 toluene–EtOAc) of the residue gave **21** (2.44 g, 73%), $[\alpha]_D^{25}$ +29° (*c* 1, $CHCl_3$) and 2-(trimethylsilyl)ethyl 4-*O*-[4-*O*-(3-*O*-allyl-2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl]-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**21β**; 643 mg, 19%). Compound **21** had: ^1H NMR data ($CDCl_3$): δ 5.84–5.71 (m, 1 H, CH_2CHCH_2), 5.02 (d, 1 H, *J* 3.2 Hz, H-1″), 4.54, 4.37 (2 d, 1 H each, *J* 7.2, 8.0 Hz, H-1,1′), 1.04 (m, 2 H, CH_2CH_2Si), 0.03 (s, 9 H, $SiMe_3$). ^{13}C NMR data ($CDCl_3$): δ 103.1, 102.9, 100.8. Anal. Calcd for $C_{89}H_{102}O_{16}Si$: C, 73.4; H, 7.1. Found: C, 73.4; H, 7.1.

Compound **21β** had: ^1H NMR data ($CDCl_3$): δ 5.96–5.83 (m, 1 H, CH_2CHCH_2), 4.93 (d, 1 H, *J* 7.4 Hz, H-1″), 4.44, 4.41 (2 d, 1 H each, *J* 8.0, 7.9 Hz, H-1,1′), 1.02 (m, 2 H, CH_2CH_2Si), 0.03 (s, 9 H, $SiMe_3$). ^{13}C NMR data ($CDCl_3$): δ 103.2, 102.9, 102.8.

2-(Trimethylsilyl)ethyl 2,3,6-tri-O-benzyl-4-O-[2,3,6-tri-O-benzyl-4-O-(2,4,6-tri-O-benzyl-α-D-galactopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (**22**).—Compound **21** (2.22 g, 1.53 mmol) was stirred with palladium(II) chloride (92 mg, 0.51 mmol) in MeOH (40 mL) for 2 h 40 min, then filtered through Celite and concentrated. Column chromatography (9:1 → 5:1 gradient heptane–EtOAc) of the residue gave **22** (1.63 g, 75%), $[\alpha]_D^{25}$ +36° (*c* 1, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ 5.13 (d, 1 H, *J* 3.4 Hz, H-1″), 4.50, 4.40 (2 d, 1 H each, *J* 7.0, 7.2 Hz, H-1,1′), 1.06 (m, 2 H, CH_2CH_2Si), 0.05 (s, 9 H, $SiMe_3$). Anal. Calcd for $C_{86}H_{98}O_{16}Si$: C, 73.0; H, 7.0. Found: C, 73.5; H, 7.1.

2-(Trimethylsilyl)ethyl 4-O-(3-O-allyl-α-D-galactopyranosyl)-β-D-galactopyrano-

side (**24**).—A suspension of 2-(trimethylsilyl)ethyl 4-*O*-α-D-galactopyranosyl-β-D-galactopyranoside[15] (**23**; 407 mg, 0.92 mmol) and dibutyltin oxide (270 mg, 1.08 mmol) in benzene (50 mL) was refluxed with azeotropic removal of water for 2 days. Allyl bromide (1.48 mL, 17.2 mmol) and tetrabutylammonium bromide (300 mg, 0.92 mmol) were added, and the mixture was refluxed for another 3 h and then concentrated. Column chromatography (9:1 CH_2Cl_2–MeOH) of the residue gave **24** (212 mg, 48%), $[\alpha]_D^{25}$ +77° (*c* 0.33, $CHCl_3$), together with unreacted **23** (114 mg, 28%). Compound **24** had: ^{1}H NMR data (D_2O): δ 5.97 (m, 1 H, CH_2CHCH_2), 5.35 (br d, 1 H, *J* 17.1 Hz, CH_2CH), 5.24 (br d, 1 H, *J* 10.4 Hz, CH_2CH), 4.95 (d, 1 H, *J* 3.9 Hz, H-1′), 4.45 (d, 1 H, *J* 7.7 Hz, H-1), 4.31 (br t, 1 H, *J* 6.4 Hz, H-5′), 3.50 (dd, 1 H, *J* 7.7, 9.1 Hz, H-2), 1.01 (m, 2 H, CH_2CH_2Si), 0.01 (s, 9 H, $SiMe_3$). ^{13}C NMR data (CD_3OD): δ 138.2, 118.9, 106.1, 104.1, 80.6, 80.4, 77.6, 76.3, 74.4, 74.1, 73.3, 71.5, 70.0, 69.6, 64.2, 62.5, 20.8, 0.2. Mass spectrum: calcd for $C_{20}H_{39}O_{11}Si$ (M + 1): *m/z* 483.2262; found: *m/z* 483.2261.

A fully acetylated sample of **24** had: ^{1}H NMR data ($CDCl_3$): δ 5.88–5.74 (m, 1 H, CH_2CHCH_2), 5.56 (br d, 1 H, *J* 3.2 Hz, H-4′), 5.26 (br dd, 1 H, *J* 17.2, 1.7 Hz, CH_2CH), 5.14 (br dd, 1 H, *J* 9.7 Hz, CH_2CH), 5.18 (dd, 1 H, *J* 7.7, 10.8 Hz, H-2), 5.08 (dd, 1 H, *J* 3.7, 10.7 Hz, H-2′), 4.96 (d, 1 H, *J* 3.7 Hz, H-1′), 4.82 (dd, 1 H, *J* 2.7, 10.7 Hz, H-3), 4.47 (d, 1 H, *J* 7.7 Hz, H-1), 4.43 (br t, 1 H, *J* 7.0 Hz, H-5′), 3.94 (dd, 1 H, *J* 3.4, 10.7 Hz, H-3′), 2.104, 2.095, 2.06, 2.044, 2.037 (5 s, 18 H, Ac), 1.01–0.84 (m, 2 H, CH_2CH_2Si), 0.01 (s, 9 H, $SiMe_3$).

*Methyl 2,4,6-tri-*O*-benzyl-3-*O*-(2-deoxy-2-phthalimido-β-D-galactopyranosyl)-α-D-galactopyranoside* (**27**).—A mixture of methyl 2,4,6-tri-*O*-benzyl-α-D-galactopyranoside[20] (**26**; 3.15 g, 6.78 mmol), silver trifluoromethanesulfonate (3.59 g, 14 mmol), tetramethylurea (2 mL, 16.7 mmol), and 4A molecular sieves (4 g) in dry CH_2Cl_2 (150 mL) was stirred at room temperature under N_2 for 30 min. The mixture was cooled to −30°C and 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-galactopyranosyl chloride[23] (**25**; 4.67 g, 10.3 mmol) was added. Stirring and cooling was continued for 5 h and the temperature was allowed to rise to room temperature overnight. The mixture was filtered through Celite, diluted with CH_2Cl_2 (200 mL), washed with satd aq $NaHCO_3$ and water, dried, and concentrated. The crude mixture was *O*-deacetylated in methanolic NaOMe (100 mL, 0.02 M), neutralised with Duolite(H^+) resin, filtered, and concentrated. Column chromatography (40:1 $CHCl_3$–MeOH) gave **27** (4.26 g, 83%), $[\alpha]_D^{25}$ −34° (*c* 0.7, $CHCl_3$). ^{1}H NMR data ($CDCl_3$): δ 5.47 (d, 1 H, *J* 8.1 Hz, H-1′), 4.23 (d, 1 H, *J* 3.7 Hz, H-1), 3.18 (s, 3 H, OMe). Anal. Calcd for $C_{42}H_{45}NO_{12}$: C, 66.7; H, 6.0; N, 1.9. Found: C, 66.0; H, 6.2; N, 1.9.

An acetylated sample of **27** had: ^{1}H NMR data ($CDCl_3$): δ 5.96 (dd, 1 H, *J* 3.5, 11.6 Hz, H-3′), 5.59 (d, 1 H, *J* 8.3 Hz, H-1′), 5.52 (br d, 1 H, *J* 3.2 Hz, H-4′), 4.63 (dd, 1 H, *J* 8.3, 11.6 Hz, H-2′), 4.22 (d, 1 H, *J* 3.6 Hz, H-1), 4.19 (dd, 1 H, *J* 3.0, 10.2 Hz, H-3), 3.96 (br d, 1 H, *J* 3.0 Hz, H-4), 3.67 (dd, 1 H, *J* 3.6, 10.2 Hz, H-2), 3.17 (s, 3 H, OMe), 2.16, 2.02, 1.86 (3 s, 3 H each, Ac). Anal. Calcd for $C_{48}H_{51}NO_{15}$: C, 65.4; H, 5.8; N, 1.6. Found: C, 65.2; H, 5.9; N, 1.5.

*2-(Trimethylsilyl)ethyl 2,4,6-tri-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-galactopyranosyl)-β-*D*-galactopyranoside* (**28**).—To a mixture of **12** (3.47 g, 6.30 mmol), silver trifluoromethanesulfonate (2.72 g, 10.7 mmol), tetramethylurea (1.29 mL, 10.7 mmol), and activated 4A molecular sieves (3 g) in dry CH_2Cl_2 (140 mL) was added chloride[23] **25** (4.30 g, 9.49 mmol) in dry CH_2Cl_2 (5 mL) dropwise at −30°C under N_2. After 20 h, silver trifluoromethanesulfonate (320 mg, 1.26 mmol) and tetramethylurea (150 mL, 1.26 mmol) were added. After 6 h, the mixture was filtered through Celite and concentrated. Column chromatography (5:1 heptane–EtOAc) of the residue gave **28** as an α/β mixture. Column chromatography in 30:1 CH_2Cl_2–diethyl ether separated the diastereomers and gave pure **28** (4.27 g, 70%), $[\alpha]_D^{25}$ −13.8° (*c* 1, $CHCl_3$), and **28α** (573 mg, 9%). Compound **28** had ^{1}H NMR data ($CDCl_3$): δ 5.87 (dd, 1 H, *J* 3.4, 11.5 Hz, H-3′), 5.65 (d, 1 H, *J* 8.4 Hz, H-1′), 5.49 (br d, 1 H, *J* 3.4 Hz, H-4′), 4.61 (dd, 1 H, *J* 8.4, 11.5 Hz, H-2′), 4.29 (d, 1 H, *J* 7.6 Hz, H-1), 3.91 (br d, 1 H, *J* 2.8 Hz, H-4), 3.79 (dd, 1 H, *J* 2.9, 9.6 Hz, H-3), 3.54 (dd, 1 H, *J* 7.6, 9.6 Hz, H-2), 2.18, 2.00, 1.84 (3 s, 3 H each, Ac), 0.80 (m, 2 H, CH_2CH_2Si), −0.10 (s, 9 H, $SiMe_3$). Mass spectrum: calcd for $C_{52}H_{61}NNaO_{15}Si$ (M + Na): *m/z* 990.3708; found: *m/z* 990.3704.

Compound **28α** had ^{1}H NMR data ($CDCl_3$): δ 6.68 (dd, 1 H, *J* 3.2, 12.2 Hz, H-3′), 5.42 (br d, 1 H, *J* 3.2 Hz, H-4′), 5.40 (d, 1 H, *J* 3.6 Hz, H-1′), 4.79 (dd, 1 H, *J* 3.6, 12.2 Hz, H-2′), 4.56 (br t, 1 H, *J* 6.1 Hz, H-5′), 2.14, 1.91, 1.88 (3 s, 3 H each, Ac), 1.04 (m, 2 H, CH_2CH_2Si), 0.01 (s, 9 H, $SiMe_3$).

*2,4,6-Tri-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-galactopyranosyl)-β-*D*-galactopyranosyl chloride* (**29**).—To a solution of **28** (1.60 g, 1.66 mmol) in CH_2Cl_2 (8.4 mL) was added CF_3CO_2H (16.6 mL) at 0°C under N_2. After 40 min, propyl acetate (50 mL) and toluene (100 mL) were added, and the solution was concentrated and co-concentrated with toluene 5 times. The residue was dissolved in dry CH_2Cl_2 (13 mL), and oxalyl chloride (0.9 mL) and DMF (0.9 mL) were added at 0°C under N_2. After 1 h 50 min, the mixture was diluted with cold toluene (50 mL), washed with cold water and cold satd aq $NaHCO_3$, dried, and concentrated to give a quantitative yield of crude **29**. The crude product was used without further purification in the synthesis of **32**.

*2-(Trimethylsilyl)ethyl 2,3,6-tri-*O*-benzyl-4-*O*-[2,4,6-tri-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-α,β-*D*-galactopyranosyl)-α-*D*-galactopyranosyl]-β-*D*-galactopyranoside* (**30**).—To a mixture of **19** (5.66 g, 5.75 mmol), silver trifluoromethanesulfonate (2.8 g, 11 mmol), tetramethylurea (1.6 mL, 13 mmol), and activated 4A molecular sieves (4.5 g) in dry CH_2Cl_2 (160 mL), was added chloride[23] **25** (3.92 g, 8.64 mmol) in dry CH_2Cl_2 (13 mL) dropwise at −78°C under N_2. The temperature was allowed to rise to room temperature and, after 17 h, **25** (1.18 g, 2.6 mmol) in dry CH_2Cl_2 (7 mL), silver trifluoromethanesulfonate (0.7 g, 2.7 mmol), and tetramethylurea (0.3 mL, 2.75 mmol) were added. After 12 h, the mixture was filtered through Celite and concentrated. Column chromatography (5:1 heptane–EtOAc) of the residue gave **30** (6.25 g, 78%; α/β 8:92) and unreacted **19** (1.08 g, 19%). Compound **30β** had: ^{1}H NMR data ($CDCl_3$): δ 5.92

(dd, 1 H, *J* 3.4, 11.5 Hz, H-3″), 5.71 (d, 1 H, *J* 8.3 Hz, H-1″), 5.53 (d, 1 H, *J* 3.4 Hz, H-4″), 4.79 (d, 1 H, *J* 3.7 Hz, H-1′), 4.67 (dd, 1 H, *J* 8.3, 11.5 Hz, H-2″), 4.29 (d, 1 H, *J* 7.6 Hz, H-1), 3.84 (d, 1 H, *J* 3.2 Hz, H-4′), 3.65 (dd, 1 H, *J* 7.6, 10.0 Hz, H-2), 3.32 (dd, 1H, *J* 2.7, 10.0 Hz, H-3), 2.11, 1.97, 1.83 (3 s, 3 H each, Ac), 1.11–1.04 (m, 2 H, CH_2CH_2Si), 0.04 (s, 9 H, $SiMe_3$). Anal. Calcd for $C_{79}H_{89}NO_{20}Si$: C, 67.7; H, 6.4. Found: C, 67.9; H, 6.4.

2-(Trimethylsilyl)ethyl 4-O-[3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl)-2,4,6-tri-O-acetyl-α-D-galactopyranosyl]-2,3,6-tri-O-acetyl-β-D-galactopyranoside (**31**).—Compound **30** (5.57 g, 3.98 mmol) was hydrogenated (1 atm) over Pd–C (5%, 2 g) in AcOH (70 mL) for 2 days, then the mixture was filtered through Celite and concentrated. The residue was dissolved in EtOH (100 mL) and hydrazine hydrate (4 mL) was added. The mixture was heated to 85°C for 55 min and then concentrated and co-concentrated with EtOH four times. The residue was stirred in pyridine (70 mL) and Ac_2O (70 mL) at room temperature overnight. The mixture was concentrated and column chromatography (100:1 → 20:1 gradient CH_2Cl_2–MeOH) gave **31** (3.66 g, 90%), $[\alpha]_D^{25}$ +58° (*c* 0.9, $CHCl_3$), and 2-(trimethylsilyl)ethyl 4-*O*-[3-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl)-2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl]-2,3,6-tri-*O*-acetyl-β-D-galactopyranoside (**31α**; 231.5 mg, 5%), $[\alpha]_D^{25}$ +99° (*c* 1, $CHCl_3$), mp 183–185°C (from heptane–EtOAc). Compound **31** had ^1H NMR data ($CDCl_3$): δ 5.68 (d, 1 H, *J* 8.8 Hz, NH), 5.54 (br d, 1 H, *J* 2.5 Hz, H-4′), 5.31 (br d, 1 H, *J* 3.2 Hz, H-4″), 5.17 (dd, 1 H, *J* 11.2, 3.4 Hz, H-3″), 5.16 (dd, 1 H, *J* 10.7, 3.7 Hz, H-2′), 5.14 (dd, 1 H, *J* 7.8, 10.8 Hz, H-2), 4.94 (d, 1 H, *J* 3.7 Hz, H-1′), 4.83 (dd, 1 H, *J* 2.8, 10.8 Hz, H-3), 4.74 (d, 1 H, *J* 8.3 Hz, H-1″), 4.45 (d, 1 H, *J* 7.8 Hz, H-1), 4.26 (dd, 1 H, *J* 3.4, 10.7 Hz, H-3′), 2.14, 2.12, 2.09, 2.043, 2.037, 2.029, 2.025, 2.015, 1.96, 1.91 (10 s, 3 H each, Ac), 1.01–0.81 (m, 2 H, CH_2CH_2Si), −0.01 (s, 9 H, $SiMe_3$). Anal. Calcd for $C_{43}H_{65}NO_{25}Si$: C, 50.4; H, 6.4; N, 1.4. Found: C, 50.2; H, 6.5; N, 1,4.

Compound **31α** had: ^1H NMR data ($CDCl_3$): δ 5.06 (d, 1 H, *J* 3.4 Hz, H-1″), 4.94 (d, 1 H, *J* 3.9 Hz, H-1′), 4.46 (d, 1 H, *J* 7.8 Hz, H-1).

2-(Trimethylsilyl)ethyl 2,3,6-tri-O-benzyl-4-O-{2,3,6-tri-O-benzyl-4-O-[2,4,6-tri-O-benzyl-3-O-(3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-α,β-D-galactopyranosyl)-α-D-galactopyranosyl]-β-D-galactopyranosyl}-β-D-glucopyranoside (**32αβ**).—To a mixture of **22** (1.55 g, 1.09 mmol), silver trifluoromethanesulfonate (0.61 g, 2.4 mmol), tetramethylurea (308 mL, 2.5 mmol), and activated 4A molecular sieves (0.9 g) in dry CH_2Cl_2 (30 mL) was added chloride[23] **25** (1.14 g, 2.5 mmol) in dry CH_2Cl_2 (3 mL) dropwise at −78°C under N_2. The temperature was allowed to rise to room temperature overnight, and the mixture was filtered through Celite and concentrated. Column chromatography (5:1 heptane–EtOAc) of the residue gave **32αβ** (710 mg, 35%; α/β, 15:85) and unreacted **22** (888 mg, 57%).

2-(Trimethylsilyl)ethyl 2,3,6-tri-O-benzyl-4-O-{2,3,6-tri-O-benzyl-4-O-[2,4,6-tri-O-benzyl-3-O-(3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-galactopyranosyl)-α-D-galactopyranosyl]-β-D-galactopyranosyl}-β-D-glucopyranoside (**32**).—To a mixture of **20** (ref 15) (1.80 g, 1.83 mmol), silver trifluoromethanesulfonate (0.51 g, 2.0 mmol),

tetramethylurea (257 mL, 2.15 mmol), and activated 4A molecular sieves (1.5 g) in dry toluene (30 mL) was added the crude chloride **29** (1.6 g, 1.66 mmol) in dry CH_2Cl_2 (6 mL) dropwise at −78°C under N_2. The temperature was maintained at −20°C for 4 h and then allowed to rise to room temperature overnight. Silver trifluoromethanesulfonate (260 mg, 1.0 mmol) was added at −25°C after 19 h, and after 26 h the mixture was filtered through Celite and concentrated. Column chromatography (5:1 heptane–EtOAc) of the residue gave **32** containing a small amount of the corresponding anomer **32β** (1.81 g, 60%). The mixture was partly separated by column chromatography in (30:1 CH_2Cl_2–diethyl ether) to give **32** (1.33 g, 44%), $[\alpha]_D^{25}$ +3.3° (*c* 1, $CHCl_3$), and **32β** (148 mg, 5%). Compound **32** had ^{1}H NMR data $CDCl_3$): δ 5.77 (dd, 1 H, *J* 3.4, 11.7 Hz, H-3‴), 5.40 (d, 1 H, *J* 8.3 Hz, H-1‴), 5.33 (d, 1 H, *J* 3.4 Hz, H-4‴), 4.81 (d, 1 H, *J* 3.5 Hz, H-1″), 4.61 (dd, 1 H, *J* 8.3, 11.7 Hz, H-2‴), 2.12, 1.97, 1.85 (3 s, 3 H each, Ac), 1.07 (m, 2 H, CH_2CH_2Si), 0.06 (s, 9 H, $SiMe_3$). ^{13}C NMR data ($CDCl_3$): δ 103.1, 103.0, 100.4, 99.8. Anal. Calcd for $C_{106}H_{117}NO_{25}Si$: C, 69.4; H, 6.4; N, 0.8. Found: C, 69.0; H, 6.5; N, 0.6.

*2-(Trimethylsilyl)ethyl 4-O-{4-O-[3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-*D*-galactopyranosyl)-2,4,6-tri-O-acetyl-α-*D*-galactopyranosyl]-2,3,6-tri-O-acetyl-β-*D*-galactopyranosyl}-2,3,6-tri-O-acetyl-β-*D*-glucopyranoside* (**33**).—Compound **32αβ** (678 mg, 0.370 mmol; α/β 35:65) and hydrazine hydrate (0.4 mL) in EtOH (10 mL) was heated to 85°C for 1 h 10 min, then more hydrazine hydrate (0.2 mL) was added and the temperature was raised to 90°C. After 1.5 h, the mixture was concentrated and co-concentrated several times with EtOH. The residue was acetylated with Ac_2O (10 mL) and pyridine (10 mL) overnight, concentrated, filtered through a silica gel column (1:1 heptane–EtOAc), and concentrated. The residue was hydrogenated (1 atm) over Pd–C (600 mg, 5%) in AcOH (15 mL) for 2 days, then the mixture was filtered through Celite, concentrated, filtered though a silica gel column (4:1 CH_2Cl_2–MeOH), and concentrated. Acetylation in Ac_2O (5 mL) and pyridine (5 mL) overnight, concentration, and column chromatography (20:1 toluene–EtOH) of the residue gave **33** (267 mg, 55%), $[\alpha]_D^{25}$ +41° (*c* 1, $CHCl_3$), and 2-(trimethylsilyl)ethyl 4-*O*-{4-*O*-[3-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl)-2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl]-2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl}-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (**33α**; 2.67 mg, 5.5%), $[\alpha]_D^{25}$ +70° (*c* 1, $CHCl_3$). Compound **33** had: ^{1}H NMR data ($CDCl_3$): δ 5.73 (d, 1 H, *J* 8.8 Hz, NH), 5.58 (br d, 1 H, *J* 2.9 Hz, H-4″), 5.31 (br d, 1 H, *J* 3.2 Hz, H-4‴), 5.22 (dd, 1 H, *J* 3.2, 11.2, Hz, H-3‴), 5.18 (t, 1 H, *J* 9.3 Hz, H-3), 5.17 (dd, 1 H, *J* 3.7, 11.2 Hz, H-2″), 5.10 (dd, 1 H, *J* 7.8, 10.9 Hz, H-2′), 4.93 (d, 1 H, *J* 3.7 Hz, H-1″), 4.84 (dd, 1 H, *J* 8.0, 9.3 Hz, H-2), 4.78 (d, 1 H, *J* 8.3 Hz, H-1‴), 4.73 (dd, 1 H, *J* 2.6, 10.9 Hz, H-3′), 4.54 (d, 1 H, *J* 7.8 Hz, H-1′), 4.46 (d, 1 H, *J* 8.0 Hz, H-1), 2.11, 2.092, 2.089, 2.08, 2.05, 2.04, 2.022, 2.016, 1.96, 1.89 (10 s, 3 H each, Ac), 0.88 (m, 2 H, CH_2CH_2Si), −0.03 (s, 9 H, $SiMe_3$). ^{13}C NMR data ($CDCl_3$): δ 101.0, 100.5, 99.9, 99.3, 76.7, 76.0, 73.3, 62.7, 72.6, 72.4, 72.0, 71.9, 70.6, 70.1, 69.85, 69.78,

69.0, 67.7, 67.5, 66.5, 62.5, 61.4, 61.2, 61.0, 51.6, 17.9, −1.4. Mass spectrum: calcd for $C_{55}H_{82}NO_{33}Si$ (M + 1): *m/z* 1312.4538 found: *m/z* 1312.4520.

Compound **33*α*** had: ^{1}H NMR data ($CDCl_3$): δ 4.98 (d, 1 H, *J* 3.9 Hz, H-1″), 4.94 (d, 1 H, *J* 3.4 Hz, H-1‴), 4.86 (dd, 1 H, *J* 8.1, 9.5 Hz, H-2), 4.69 (dd, 1 H, *J* 2.5, 10.9 Hz, H-3′), 4.50 (d, 1 H, *J* 7.8 Hz, H-1′), 4.47 (d, 1 H, *J* 8.1 Hz, H-1), 2.19, 2.12, 2.11, 2.08, 2.06, 2.04, 2.03, 2.024, 2.016, 1.97 (10 s, 3 H each, Ac), 0.91 (m, 2 H, CH_2CH_2Si), −0.02 (s, 9 H, $SiMe_3$). ^{13}C NMR data ($CDCl_3$): δ 101.0, 99.9, 99.7, 99.5, 77.0, 73.8, 73.51, 73.47, 72.8, 72.3, 71.7, 70.3, 69.0, 68.4, 67.6, 67.5, 67.33, 67.25, 66.8, 62.3, 61.3, 60.7, 60.1, 47.3, 17.9, −1.4.

4-O-[3-O-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl)-2,4,6-tri-O-acetyl-α-D-galactopyranosyl]-1,2,3,6-tetra-O-acetyl-α,β-D-galactopyranose (**34**).—To a solution of **31** (2.60 g, 2.54 mmol) in dry CH_2Cl_2 (12 mL) was added Ac_2O (2.36 mL, 25.4 mmol) and boron trifluoride etherate (0.693 mL, 5.59 mmol) under N_2. After 5 h 40 min, the mixture was diluted with CH_2Cl_2, washed with satd aq $NaHCO_3$, dried, and concentrated. Column chromatography (1 : 8 heptane–EtOAc) of the residue gave **34** (2.18 g, 89%; *α*/*β*, 25 : 75). Compound **34*β*** had: ^{1}H NMR data ($CDCl_3$): δ 5.68 (d, 1 H, *J* 8.1 Hz, H-1), 5.55 (br d, 1 H, *J* 3.5 Hz, H-4′), 5.54 (d, 1 H, *J* 8.5 Hz, NH), 5.32 (br d, 1 H, *J* 17.1 Hz, H-4″), 5.30 (dd, 1 H, *J* 8.1, 10.6 Hz, H-2), 5.26 (dd, 1 H, *J* 3.3, 11.2 Hz, H-3″), 5.18 (dd, 1 H, *J* 3.6, 10.6 Hz, H-2′), 4.94 (d, 1 H, *J* 3.6 Hz, H-1′), 4.89 (dd, 1 H, *J* 2.7, 10.6 Hz, H-3), 4.85 (d, 1 H, *J* 8.3 Hz, H-1″), 4.23 (dd, 1 H, *J* 3.4, 10.6 Hz, H-3′), 2.13, 2.10, 2.06, 2.052, 2.048, 2.03, 2.02, 1.97, 1.91 (9 s, 3 H each, Ac). Compound **34*β*** had: ^{13}C NMR ($CDCl_3$): δ 100.4, 99.0, 92.1, 75.9, 73.2, 72.42, 72.40, 70.8, 70.1, 69.6, 69.54, 67.9, 67.7, 66.6, 62.1, 61.5, 61.3, 51.9. Anal. Calcd for $C_{40}H_{55}NO_{26}$: C, 49.7; H, 5.7; N, 1.5. Found: C, 49.9; H, 5.8; N, 1.5.

3-Bromo-2-(bromomethyl)propyl 4-O-[3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl)-2,4,6-tri-O-acetyl-α-D-galactopyranosyl]-2,3,6-tri-O-acetyl-β-D-galactopyranoside (**35**).—To a solution of **34** (1.58 g, 1.63 mmol) and 3-bromo-2-(bromomethyl)propanol[24] (469 mg, 1.95 mmol) in dry MeCN (70 mL) was added boron trifluoride etherate (401 μL, 3.26 mmol) under N_2. After 3 h 50 min, the mixture was diluted with CH_2Cl_2, washed with satd aq $NaHCO_3$, dried, and concentrated. Column chromatography (25 : 1 → 10 : 1 gradient toluene–EtOH) of the residue gave **35** (857 mg, 46%), $[\alpha]_D^{25}$ +61° (*c* 1, $CHCl_3$), and 3-bromo-2-(bromomethyl)propyl 4-*O*-[3-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl]-2,3,6-tri-*O*-acetyl-α-D-galactopyranoside (**35*α***; 5.8 mg, 0.3%). Compound **35** had ^{1}H NMR data ($CDCl_3$): δ 5.55 (br d, 1 H, *J* 2.6 Hz, H-4′), 5.50 (d, 1 H, *J* 8.8 Hz, NH), 5.33 (br d, 1 H, *J* 2.9 Hz, H-4″), 5.24 (dd, 1 H, *J* 3.4, 11.2 Hz, H-3″), 5.18 (dd, 1 H, *J* 3.6, 10.5 Hz, H-2′), 5.17 (dd, 1 H, *J* 7.7, 10.7 Hz, H-2), 4.97 (d, 1 H, *J* 3.6 Hz, H-1′), 4.86 (dd, 1 H, *J* 2.9, 10.7 Hz, H-3), 4.84 (d, 1 H, *J* 8.1 Hz, H-1″), 4.45 (d, 1 H, *J* 7.7 Hz, H-1), 4.39 (br t, 1 H, H-5′), 4.23 (dd, 1 H, *J* 3.4, 10.5 Hz, H-3′), 3.63–3.49 [m, 4 H, $CH(CH_2Br)_2$], 3.45 (d, 2 H, *J* 6.3 Hz, OCH_2CH), 2.34 (m, 1 H, OCH_2CH), 2.14, 2.12, 2.08, 2.07, 2.06, 2.05, 1.99, 1.94 (8 s, 30 H, Ac). ^{13}C NMR data ($CDCl_3$): δ

101.7, 100.6, 98.8, 77.2, 75.7, 72.3, 72.2, 70.8, 70.1, 69.8, 69.42, 69.37, 68.7, 67.8, 66.5, 62.0, 61.6, 51.8, 42.6, 32.9, 31.7. Anal. Calcd for $C_{42}H_{59}Br_2NO_{25}$: C, 44.4; H, 5.2; N, 1.2. Found: C, 44.4; H, 5.3; N, 1.3.

Compound **35α** had ^{1}H NMR data ($CDCl_3$): δ 5.53 (br d, 1 H, *J* 3.0 Hz, H-4′), 5.43 (d, 1 H, *J* 8.6 Hz, NH), 5.34 (br d, 1 H, *J* 3.2 Hz, H-4″), 5.27 (dd, 1 H, *J* 3.2, 11.2 Hz, H-3″), 5.21 (dd, 1 H, *J* 3.6, 10.6 Hz, H-2′), 5.16, 5.10 (2 br s, 3 H, H-1,2,3), 4.92 (d, 1 H, *J* 3.6 Hz, H-1′), 4.86 (d, 1 H, *J* 8.3 Hz, H-1″), 4.20 (dd, 1 H, *J* 3.6, 10.6 Hz, H-3′), 3.57–3.47 [m, 6 H, $CH(CH_2Br)_2$ and OCH_2CH], 2.35 (m, 1 H, OCH_2CH), 2.16, 2.15, 2.13, 2.12, 2.091, 2.088, 2.08, 2.05, 1.99, 1.93 (10 s, 3 H each, Ac).

Isobutyl 4-O-[3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl)-2,4,6-tri-O-acetyl-α-D-galactopyranosyl]-2,3,6-tri-O-acetyl-β-D-galactopyranoside (**36**).—To a refluxing solution of **35** (205.7 mg, 0.181 mmol) and tributyltin hydride (300 mL, 1.13 mmol) in dry toluene (3 mL) under N_2 was added 2,2′-azobisisobutyronitrile (ca. 2 mg). The solution was refluxed for 3 h and then concentrated. Column chromatography (EtOAc) of the residue gave **36** (115.5 mg, 65%), $[\alpha]_D^{25}$ +66° (*c* 1, $CHCl_3$). ^{1}H NMR data ($CDCl_3$): δ 5.54 (br d, 1 H, *J* 2.7 Hz, H-4′), 5.48 (d, 1 H, *J* 8.8 Hz, NH), 5.33 (br d, 1 H, *J* 2.6 Hz, H-4″), 5.20 (dd, 1 H, *J* 3.1, 10.9 Hz, H-3″), 5.18 (dd, 1 H, *J* 7.8, 10.9 Hz, H-2), 5.16 (dd, 1 H, *J* 3.6, 10.7 Hz, H-2′), 4.96 (d, 1 H, *J* 3.6 Hz, H-1′), 4.84 (dd 1 H, *J* 2.8, 10.9 Hz, H-3), 4.78 (d, 1 H, *J* 8.2 Hz, H-1″), 4.41 (d, 1 H, *J* 7.8 Hz, H-1), 4.25 (dd, 1 H, *J* 3.4, 10.7 Hz, H-3′), 3.69 (dd, 1 H, *J* 5.9, 9.4 Hz, OCH_2CH), 3.17 (dd, 1 H, *J* 7.6, 9.4 Hz, OCH_2CH), 2.13, 2.12, 2.11, 2.064, 2.058, 2.05, 2.04, 2.03, 1.98, 1.93 (10 s, 3 H each, Ac), 1.85 [m, 1 H, $CH_2CH(CH_3)_2$], 0.88, 0.87 (2 d, 3 H each, *J* 6.6 and 6.6 Hz, CH_3). Mass spectrum: calcd for $C_{42}H_{62}NO_{25}$ (M + 1): *m/z* 980.3611; found: *m/z* 980.3614.

3-Bultylthio-2-[(butylthio)methyl]propyl 4-O-[3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl)-2,4,6-tri-O-acetyl-α-D-galactopyranosyl]-2,3,6-tri-O-acetyl-β-D-galactopyranoside (**37**).—To a solution of **35** (34.2 mg, 0.030 mmol) and butanethiol (9.6 mL, 0.090 mmol) in dry DMF (0.3 mL) was added cesium carbonate (23.4 mg, 0.072 mmol) under N_2. The mixture was left overnight, diluted with CH_2Cl_2, washed with water, dried, and concentrated. Column chromatography (1 : 1 heptane–EtOAc) gave **37** (29.0 mg, 84%), $[\alpha]_D^{25}$ +64° (*c* 0.84, $CHCl_3$). ^{1}H NMR data ($CDCl_3$): δ 5.54 (br d, 1 H, *J* 3.4 Hz, H-4′), 5.47 (d, 1 H, *J* 8.8 Hz, NH), 5.33 (br d, 1 H, *J* 3.2 Hz, H-4″), 5.21 (dd, 1 H, *J* 3.4, 11.2 Hz, H-3″), 5.18 (dd, 1 H, *J* 3.4, 10.5 Hz, H-2′), 5.17 (dd, 1 H, *J* 7.6, 10.8 Hz, H-2), 4.97 (d, 1 H, *J* 3.4 Hz, H-1′), 4.84 (dd, 1 H, *J* 2.9, 10.8 Hz, H-3), 4.80 (d, 1 H, *J* 8.3 Hz, H-1″), 4.43 (d, 1 H, *J* 7.6 Hz, H-1), 4.38 (br t, 1 H, *J* 6.2 Hz, H-5′), 4.23 (dd, 1 H, *J* 3.4, 10.5 Hz, H-3′), 3.59 (dd, 1 H, *J* 6.2 and 9.7 Hz, OCH_2CH), 2.65–2.53 [m, 4 H, $CH(CH_2SBu)_2$], 2.49 (br t, 4 H, *J* 5.5 Hz, SCH_2CH_2), 2.13, 2.11, 2.07, 2.06, 2.05, 2.04, 1.98, 1.93 (8 s, 30 H, Ac), 1.55 (m, 4 H, $CH_2CH_2CH_2$), 1.39 (m, 4 H, $CH_2CH_2CH_3$), 0.91 (t, 6 H, *J* 7.3 Hz, CH_3). Mass spectrum: calcd for $C_{50}H_{78}NO_{25}S_2$ (M + 1): *m/z* 1156.4304; found: *m/z* 1156.4280.

3-Butylsulfonyl-2-[(butylsulfonyl)methyl]propyl 4-O-[3-O-(2-acetamido-3,4,6-tri-

O-acetyl-2-deoxy-β-D-galactopyranosyl)-2,4,6-tri-O-acetyl-α-D-galactopyranosyl]-2,3,6-tri-O-acetyl-β-D-galactopyranoside (**38**).—To a solution of **37** (128.2 mg, 0.111 mmol) in EtOAc (4.0 mL) was added 3-chloroperoxybenzoic acid (128 mg, 0.554 mmol). After 1 h 40 min, the mixture was filtered through an alumina column and concentrated. Column chromatography (10:1 toluene–EtOH) gave **38** (121.0 mg, 89%), $[\alpha]_D^{25}$ +61° (*c* 1, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ 5.97 (d, 1 H, *J* 9.5 Hz, NH), 5.58 (br d, 1 H, *J* 2.7 Hz, H-4′), 5.30 (br d, 1 H, *J* 3.7 Hz, H-4″), 5.22 (dd, 1 H, *J* 7.8, 10.7 Hz, H-2), 5.20 (dd, 1 H, *J* 3.4, 10.7 Hz, H-2′), 5.10 (dd, 1 H, *J* 3.4, 11.2 Hz, H-3″), 4.96 (d, 1 H, *J* 3.4 Hz, H-1′), 4.81 (dd, 1 H, *J* 2.6, 10.7 Hz, H-3), 4.74 (d, 1 H, *J* 8.4 Hz, H-1″), 4.59 (d, 1 H, *J* 7.8 Hz, H-1), 4.36 (br t, 1 H, *J* 6.2 Hz, H-5′), 4.26 (dd, 1 H, *J* 3.2, 10.7 Hz, H-3′), 3.45–3.17 [m, 4 H, $CH(CH_2SO_2Bu)_2$], 3.12–2.93 [m, 5 H, $SO_2CH_2CH_2$ and $CH(CH_2SO_2Bu)_2$], 2.15, 2.12, 2.11, 2.074, 2.070, 2.041, 2.037, 1.97, 1.93 (9 s, 3 H each, Ac), 1.89–1.75 (m, 4 H, $CH_2CH_2CH_2$), 1.50 (m, 4 H, $CH_2CH_2CH_3$), 0.98 (t, 6 H, *J* 7.3 Hz, CH_3). ^{13}C NMR data ($CDCl_3$): δ 100.8, 100.1, 99.4, 76.4, 73.9, 72.5, 72.4, 70.7, 70.4, 70.0, 69.2, 68.2, 68.1, 67.9, 66.4, 62.1, 60.9, 54.0, 53.7, 52.1, 51.6, 51.0, 29.6, 23.9, 21.7, 13.5. Mass spectrum: calcd for $C_{50}H_{78}NO_{29}S_2$ (M + 1): *m/z* 1220.4100; found: *m/z* 1220.4100.

2-(Trimethylsilyl)ethyl 4-O-[3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl)-2,4,6-tri-O-acetyl-α-D-galactopyranosyl]-2,3,6-tri-O-acetyl-1-thio-β-D-galactopyranoside (**40**).—To a solution of **34** (406.1 mg, 0.420 mmol) in AcOH (205 μL) and Ac_2O (84 μL) was added 33% HBr in AcOH (591 μL) at 0°C. The mixture was allowed to reach room temperature and after 1.5 h it was diluted with CH_2Cl_2, washed with cold, satd aq $NaHCO_3$, dried, and concentrated. The crude bromide **39** was dissolved in DMF (3.6 mL) and a freshly prepared solution of 2-(trimethylsilyl)ethanethiol (89 μL, 0.547 mmol) and NaH (30 mg, 0.6 mmol, 50% in oil) in DMF (0.7 mL) was added under N_2. The mixture was diluted with CH_2Cl_2 after 30 min, washed with satd aq NaCl, dried, and concentrated. Column chromatography (15:1 toluene–EtOH) of the residue gave **40** (289.8 mg, 66%), $[\alpha]_D^{25}$ +58° (*c* 0.99, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ 5.55 (br d, 1 H, *J* 3.6 Hz, H-4′), 5.44 (d, 1 H, *J* 9.0 Hz, NH), 5.33 (br d, 1 H, *J* 3.3 Hz, H-4″), 4.97 (d, 1 H, *J* 3.7 Hz, H-1′), 4.89 (dd, 1 H, *J* 2.9, 10.3 Hz, H-3), 4.88 (d, 1 H, *J* 8.4 Hz, H-1″), 4.53 (d, 1 H, *J* 9.8 Hz, H-1), 4.23 (dd, 1 H, *J* 3.4, 10.4 Hz, H-3′), 2.73 (m, 2 H, SCH_2CH_2), 2.14, 2.12, 2.08, 2.062, 2.058, 2.05, 2.04, 1.99, 1.93 (9 s, 3 H each, Ac), 0.88 (m 2 H, CH_2CH_2Si), 0.04 (s, 9 H, $SiMe_3$). Mass spectrum: calcd for $C_{43}H_{66}NO_{24}SSi$ (M + 1): *m/z* 1040.3465; found: *m/z* 1040.3456.

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