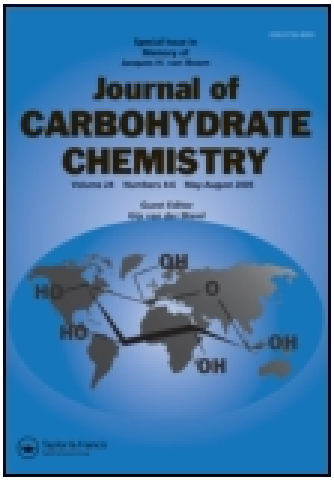

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Synthesis of Tetrasaccharide Repeating Unit of the O-Antigen from Enterohemorrhagic Escherichia coli O157 in the form of its 2-(trimethylsilyl)ethyl Glycoside

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Synthesis of Tetrasaccharide Repeating Unit of the O-Antigen from Enterohemorrhagic *Escherichia coli* O157 in the form of its 2-(trimethylsilyl)ethyl Glycoside

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Two α-linked disaccharide derivatives, ethyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl-(1 $\rightarrow$ 2)-4-azido-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopyranoside (**10**) and 2-(trimethylsilyl)ethyl 3-*O*-acetyl-4-*O*-benzoyl-2-*O*-benzyl-α-L-fucopyranosyl-(1 $\rightarrow$ 4)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-glucopyranoside (**16**), were prepared from appropriate monosaccharide synthons. The disaccharide **16** was deacetylated and debenzoylated to afford the acceptor **17**, which was allowed to react with the donor **10** to afford a tetrasaccharide derivative **18.** This tetrasaccharide was transformed in three steps into **21**, the desired repeating unit of the antigen from enterohemorrhagic *E. coli* type O157.

Keywords Synthesis, Tetrasaccharide, Enterohemorrhagic *Escherichia coli* type O157

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INTRODUCTION

The enterohemorrhagic *Escherichia coli* O157:H7 is probably the most important pathogen in the species *E. coli* that can cause hemorrhagic colitis and hemolytic uremic syndrome.[1] The structure of the O-antigen of enterohemorrhagic *E. coli* O157:H7 (**I**) has been reported by Perry and his coworkers.[2]

D C B A

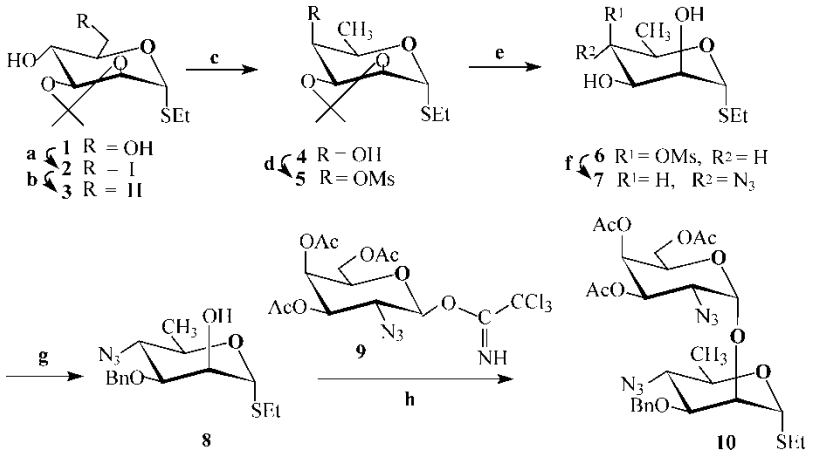
→3)-α-D-GalNAc*p*-(1→2)-α-D-PerNAc*p*-(1→3)-α-L-Fuc*p*-(1→4)-β-D-Glc*p*-(1→

I

As a continuation of our program to synthesize oligosaccharides[3,4] related to the O-antigens of enterohemorrhagic *E. coli* with the broader objective of developing glycoconjugate vaccines against these pathogens, we report here the synthesis of the tetrasaccharide repeating unit of the O-antigen from enterohemorrhagic *E. coli* type O157 in the form of its 2-(trimethylsilyl)ethyl glycoside. The strategy is to synthesize the blocks BA and DC and couple them together to prepare a blocked tetrasaccharide, which can then be transformed in three steps into the desired tetrasaccharide repeating unit.

RESULTS AND DISCUSSION

The known ethyl 2,3-*O*-isopropylidene-1-thio-α-D-mannopyranoside[5] (**1**) was converted to the corresponding 6-iodo compound (**2**) with triphenylphosphine, imidazole, and iodine.[6] Reduction of **2** with H_2[7] in the presence of 10% Pd-C gave the 6-deoxy compound (**3**). Oxidation of **3** with methyl sulfoxide[8] gave a ketohexose, which on reduction with sodium borohydride[8–10] gave ethyl 6-deoxy-2,3-*O*-isopropylidene-1-thio-α-D-talopyranoside (**4**). ^{1}H NMR signal of H-4 in compound **4** appeared at a downfield position compared to that for compound **3**. Treatment of **4** with methanesulfonyl chloride and triethylamine[10,11] gave the mesyl derivative **5.** Removal of isopropylidene group[12,13] from **5** followed by treatment of the resulting **6** with sodium azide[14] afforded the azido compound **7** (56% overall), which is a precurser for the D-perosamine moiety. Selective benzylation of **7** via stanylidene complex[15] gave ethyl 4-azido-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopyranoside (**8**). The acceptor **8** was allowed to react with the known 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl trichloroacetimidate[16,17] **9** in the presence of triethylsilyltrifluoromethanesulfonate (TESOTf)[17,18] at −25°C to give the disaccharide ethyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl-(1 → 2)-4-azido-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopy ranoside **(10)** (Sch. 1) in 57.3% yield. The structure of **10** was confirmed by its signals at δ 5.18 (H-1^{I}), 5.16 (H-1^{II}), 3.51 (H-2^{II}), and 1.55 (H-6^{I}) in its ^{1}H NMR



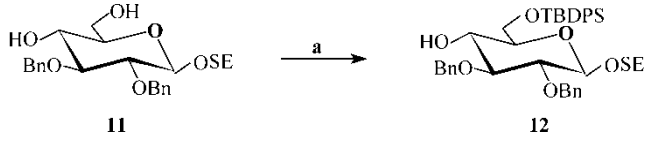
Scheme 1: (a) I_2, imidazole, PPh_3, toluene; (b) H_2, 10% Pd-C, EtOH-NEt_3 (19:1); (c) i. DMSO, $(COCl)_2$, CH_2Cl_2; ii. $NaBH_4$, EtOH; (d) MsCl, NEt_3, CH_2Cl_2; (e) 2*N* HCl in MeOH, MeOH, 0°C; (f) NaN_3, DMSO, 100°C; (g) i. Bu_2SnO, benzene; ii. BnBr, Bu_4NBr, 63°C, 62.9%; (h) TESOTf, CH_2Cl_2, 57.3%.

spectrum and at δ 99.86 (C-1^{I}), 83.70 (C-1^{II}), 64.84 (C-4^{I}), 57.76 (C-2^{II}), and 15.36 (C-6 ^{I}) in its ^{13}C NMR spectrum.

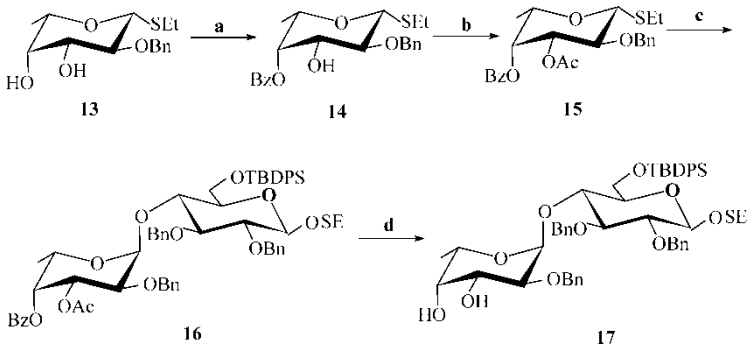
In another experiment, the known 2-(trimethylsilyl)ethyl 2,3-di-*O*-benzyl-β-D-glucopyranoside[19] **11**, prepared from D-glucose, on treatment with *tert*-butyldiphenylsilyl (TBDPS) chloride[20,21] and pyridine, afforded the acceptor **12** in 70% yield (Sch. 2).

In a separate experiment, ethyl 2-*O*-benzyl-1-thio-β-D-fucopyranoside[22,23] (**13**) was prepared by known technique starting from L-fucose. Treatment of **13** with trimethylorthobenzoate in the presence of *p*-TsOH[24] followed by mild hydrolysis of the product gave **14**, which on acetylation afforded the donor **15.** The acceptor **12** was then allowed to react with the thioglycoside donor **15** in the presence of *N*-iodosuccinimide (NIS) and trifluoromethanesulfonic acid[25,26] (TfOH) to give the disaccharide **16** in 72% yield. Removal of acetyl and benzoyl groups in **16** afforded the acceptor **17** having two hydroxyl groups (Sch. 3). The disaccharide **17** gave signals at δ 5.16 (H-1^{II}), 4.4 (H-1^{I}) and 0.8 (H-6^{II}) in its ^{1}H NMR spectrum and at δ 103.00 (C-1^{I}), and 95.86 (C-1^{II}) in its ^{13}C NMR spectrum.

The disaccharide acceptor **17**, having two hydroxyl groups, was allowed to react with the disaccharide donor **10** in the presence of NIS and

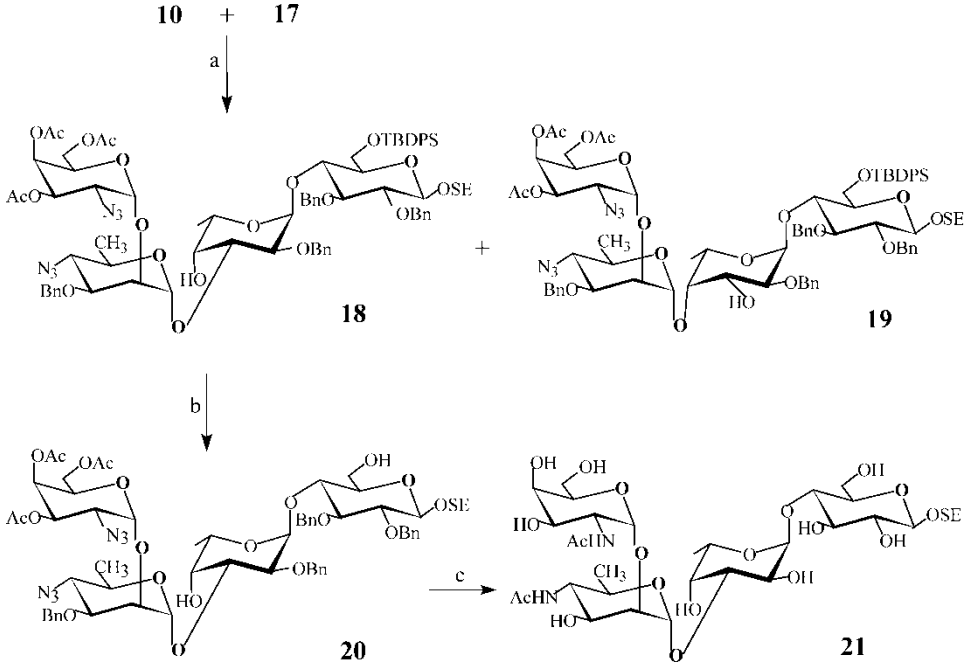


Scheme 2: (a) *t*-Butyldiphenylsilylchloride (TBDPSCl), Pyr, 12 h.



Scheme 3: (a) i. Triethylorthobenzoate, DMF, *p*-TsOH; ii. 80% AcOH, rt, 73.6%; (b) Ac_2O, Pyr, 85.8%; (c) **12**, NIS, TfOH, CH_2Cl_2, 1 h, 72%; (d) NaOMe, MeOH, rt.

TfOH[25,26] to afford the tetrasaccharide derivative 2-(trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl-(1 → 2)-4-azido-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranosyl-(1 → 3)-2-*O*-benzyl-α-L-fucopyranosyl-(1 → 4)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-glucopyranoside (**18**) in 57% yield together with the corresponding (1 → 4) linked tetrasaccharide derivative 2-(trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl-(1 → 2)-4-azido-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranosyl-(1 → 4)-2-*O*-benzyl-α-L-fucopyranosyl-(1 → 4)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-glucopyranoside (**19**) (Sch. 4) in 7.8% yield. The acceptor **17** had one equatorial and one axial hydroxyl groups, and it was expected that glycosidation would take place mostly at the equatorial 3-OH position. However, some reaction had also taken place at the axial 4-OH, probably because of the proximity of 6-deoxy status of the accepter **17**. The tetrasaccharide **18** was characterized by its ^{1}H NMR signals at δ 5.12 (H-1^{II}), 4.87 (H-1^{III}), 4.79 (H-1^{IV}), 4.23 (H-1^{I}), 4.50 (m, 1 H, H-3^{II}), and 3.87 (bs, 1 H, H-4^{II}); ^{13}C NMR signals at δ 102.90 (C-1^{I}), 97.90 (C-1^{IV}), 97.20 (C-1^{III}), and 96.20 (C-1^{II}); and DEPT 135 spectrum of the compound. The ^{13}C NMR and DEPT 135 spectra showed, apart from the characteristic peaks, all the carbon peaks clearly separated except those in the aromatic region. The tetrasaccharide **19** was also characterized by its ^{1}H NMR signals at δ 5.02 (H-1^{II}), 4.93 (H-1^{III}), 4.88 (H-1^{IV}), 4.83 (H-4^{II}), 4.20 (H-1^{I}), and 3.83 (H-3^{II}); ^{13}C NMR signals at δ 103.00 (C-1^{I}), 99.85 (C-1^{IV}), 99.00 (C-1^{III}), and 95.50 (C-1^{II}); and the DEPT 135 spectrum. That the linkage between the α-D-perosamine precurser and the α-L-fucose unit were 1 → 3 in compound **18** and 1 → 4 in compound **19** was confirmed by comparing the ^{1}H NMR signals of their acetyl derivatives. Acetylation of **18** gave 4^{II}-*O*-acetyl derivative **18A**, which manifested the shift of its ^{1}H NMR signal for H-4^{II} from δ 3.87 in **18** to δ 5.14 in the acetate **18A**, while the position of the signals for H-3^{II} remained practically unchanged. Similarly, the tetrasaccharide **19** manifested similar shift in **19A** where the



Scheme 4: (a) NIS, TfOH, CH_2Cl_2, 45 min; (b) Bu_4NF, THF, 51.5%; (c) i. H_2, 10% Pd-C, MeOH-Ac_2O (20:1), 3 d, rt; ii. MeOH, 0.05 *M* NaOMe, 3 h, rt, 56% overall.

^{1}H NMR signal for H-3^{II} had shifted from δ 3.83 in **19** to δ 4.86 in **19A** as expected, while the signals for H-4^{II} remained unchanged.

Compound **18** was treated with tetrabutylammoniumfluoride[27,28] in THF at 0°C to remove the t-butyldiphenylsilyl protecting group. The product **20** was hydrogenolyzed with hydrogen and 10% Pd-C[29] in the presence of acetic anhydride, a condition under which the azido groups were converted into acetamido groups, with simultaneous removal of the benzyl substituents. The product was then deacetylated with 0.05 M NaOMe to afford the desired tetrasaccharide repeating unit **21** of the antigen from *E. coli* O157. The final compound **21** was characterized from its ^{1}H NMR signals at δ 5.08 (H-1^{III}), 4.81 (H-1^{IV}), 4.69 (H-1^{II}), and 4.30 (H-1^{I}); and ^{13}C NMR signals at δ 102.5 (C-1^{I}), 100.5 (C-1^{IV}), 99.2 (C-1^{III}), and 97.2 (C-1^{II}); and DEPT spectrum.

EXPERIMENTAL

General

All the reactions were monitored by TLC on silica gel G (E. Merck). Column chromatography was performed on 100–200 mesh silica gel (SRL, India).

All solvents were distilled and/or dried before use and all evaporations were conducted below 50°C under reduced pressure unless stated otherwise. Petroleum ether used in this work has a boiling range of 60°C to 80°C. Optical rotations were measured with a Perkin Elmer model 241 MC polarimeter. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 300 Spectrometer using $CDCl_3$ as solvent. Tetramethylsilane was used as internal standard in ^{1}H NMR spectra unless otherwise mentioned. Melting points were determined on a paraffin oil bath and are uncorrected.

Ethyl 6-deoxy-6-iodo-2,3-*O*-isopropylidene-1-thio-α-D-mannopyranoside (2). To a solution of ethyl 2,3-*O*-isopropylidene-1-thio-α-D-mannopyranoside **1** (5.32 g, 20.1 mmol) in toluene (160 mL), triphenylphosphine (6.80 g, 25.9 mmol), imidazole (4.72 g, 69.3 mmol), and iodine (6.14 g, 24.2 mmol) were added and the mixture was boiled under reflux with vigorous stirring until the color disappeared (30 min). A solution of sodium hydrogen carbonate (6.7 g) and water (80 mL) were then introduced and after stirring for 5 min, iodine was added until the color of the mixture remained purple. Aqueous 10% sodium thiosulphate solution was added dropwise with stirring until the purple color of iodine disappeared. The mixture was then diluted with ethyl acetate, washed twice with water, and concentrated. A solution of the residue in ether (100 mL) was cooled to −10°C and after 1 h, the solution was filtered and concentrated to a syrup, which on column chromatography with 3:1 toluene-EtOAc gave compound **2** (6.80 g, 90.3%); $[\alpha]_D^{25}$ +106.2° (*c* 3.7, $CHCl_3$). ^{1}H NMR: δ 5.58 (s, 1 H, H-1), 4.19 (d, 1 H, $J_{2,3} = 5.5$ Hz, H-2), 4.10 (dd, 1 H, $J_{3,4} = 5.6$ Hz, $J_{4,5} = 7.2$ Hz, H-4), 3.79 (ddd, 1 H, $J_{4,5} = 9.0$ Hz, $J_{5,6a} = 2.5$ Hz, $J_{5,6b} = 6.9$ Hz, H-5), 3.58 (m, 1 H, H-3), 3.56 (dd, 1 H, $J_{5,6a} = 2.5$ Hz, $J_{6a,6b} = 10.5$ Hz, H-6a), 3.35 (dd, 1 H, $J_{5,6b} = 7.0$ Hz, $J_{6a,6b} = 10.8$, H-6b), 2.75 (m, 2 H, SCH_2CH_3), 1.54, 1.35 [2 s, 6 H, $C(CH_3)_2$], 1.31 (t, 3 H, J = 7.4 Hz, SCH_2CH_3).

Anal. Calcd for $C_{11}H_{19}O_4SI$: C, 35.3; H, 5.12. Found C, 35.05; H, 5.14.

Ethyl 6-deoxy-2,3-*O*-isopropylidene-1-thio-α-D-mannopyranoside (3). A solution of **2** (6.80 g, 18.2 mmol) in ethanol (75 mL) containing 5% triethylamine was stirred under hydrogen in the presence of 10% Pd-C (0.71 g) at rt. The reaction was completed in 4 d as ascertained by TLC with 5:1 toluene-EtOAc. The reaction mixture was filtered and the filtrate was concentrated to a syrup, which on column chromatography with 5:1 toluene-EtOAc gave **3** (2.5 g, 55.4%) as a syrup; $[\alpha]_D^{25}$ +145.1° (*c* 1.93, $CHCl_3$). ^{1}H NMR: δ 5.52 (s, 1 H, H-1), 4.18 (d, 1 H, $J_{2,3} = 5.5$ Hz, H-2), 4.04 (dd, 1 H, $J_{3,4} = 5.8$ Hz, $J_{4,5} = 7.5$ Hz, H-4), 3.97 (m, 1 H, H-5), 3.44 (dd, 1 H, $J_{2,3} = 5.6$ Hz, $J_{3,4} = 5.8$ Hz, H-3), 2.62 (m, 2 H, SCH_2CH_3), 1.54, 1.35 [2 s, 6 H, $C(CH_3)_2$], 1.30 (t, 3 H, J = 7.7 Hz, SCH_2CH_3), 1.29 (d, 3 H, J = 6.7 Hz, H-6).

Anal. Calcd for $C_{11}H_{20}O_4S$: C, 53.20; H, 8.12. Found: C, 52.98; H, 8.05.

Ethyl 6-deoxy-2,3-*O*-isopropylidene-1-thio-α-D-talopyranoside (4). A solution of oxalyl chloride (0.84 mL, 9.6 mmol) in dichloromethane (2.6 mL) under nitrogen was cooled to −78°C and a solution of methyl sulfoxide (1.3 mL, 18.0 mmol) in dichloromethane (2.4 mL) was added dropwise with stirring. After 30 min at −78°C, a solution of compound **3** (1.01 g, 4.1 mmol) in CH_2Cl_2 (28 mL) was slowly added to it. After another 40 min, *N,N*-diisopropylethylamine (4.80 mL, 27.6 mmol) was added and the mixture was kept at −70°C for 2.5 h and then allowed to attain rt. TLC with 5:1 toluene-EtOAc showed complete conversion of compound **3** into the corresponding ketohexose compound. The mixture was diluted with dichloromethane (50 mL), washed with water (50 mL × 3), dried (Na_2SO_4), and concentrated in vacuo. The syrupy residue was dissolved in ethanol (3 mL), sodium borohydride (450 mg, 11.8 mmol) was added to it and the mixture was stirred for 3 h at rt. The reaction was monitored by TLC with 5:1 toluene- EtOAc. Excess $NaBH_4$ was destroyed by adding a few drops of acetone and the solution was concentrated to dryness. The residue was diluted with dichloromethane (50 mL) and washed with water (2 × 50 mL), $NaHCO_3$ (2 × 50 mL), and water (2 × 50 mL), and the organic layer was concentrated. Column chromatography of the resulting syrupy residue with 7:1 toluene-EtOAc gave compound **4** (850 mg, 84.0%); $[\alpha]_D^{25}$ +152.8° (*c* 0.99, $CHCl_3$). ^{1}H NMR: δ 5.54 (d, 1 H, $J_{1,2} = 1.4$ Hz, H-1), 4.19 (dd, 1 H, $J_{3,4} = 5.5$ Hz, $J_{4,5} = 0.7$ Hz, H-4), 4.13 (dq, 1 H, $J_{4,5} = 0.7$ Hz, $J_{5,6} = 6.5$ Hz, H-5), 4.05 (dd, 1 H, $J_{1,2} = 1.5$ Hz, $J_{2,3} = 6.1$ Hz, H-2), 3.61 (t, 1 H, J = 5.6 Hz, H-3), 2.63 (m, 2 H, SCH_2CH_3), 1.60, 1.38 [2 s, 6 H, $C(CH_3)_2$], 1.33 (d, 3 H, J = 6.4 Hz, H-6), 1.32 (t, 3 H, J = 7.2 Hz, SCH_2CH_3).

Anal. Calcd for: $C_{11}H_{20}O_4S$: C, 53.20; H, 8.12. Found: C, 53.29; H, 8.15.

Ethyl 6-deoxy-2,3-*O*-isopropylidene-4-*O*-(methylsulfonyl)-1-thio-α-D-talopyranoside (5). A solution of **4** (1.33 g, 5.35 mmol) in CH_2Cl_2 (16 mL) was cooled to 0°C under nitrogen atmosphere and triethylamine (1.4 mL) and methanesulfonyl chloride (0.83 mL) were added to it. The reaction mixture was stirred for 10 min at 0°C and then allowed to attain rt. After 1.5 h the reaction was completed as revealed by TLC using 5:1 toluene-EtOAc. The reaction was quenched with saturated $NaHCO_3$ (2 mL) with stirring for 30 min. Dichloromethane (50 mL) was added and the organic phase was washed successively with saturated $NaHCO_3$, water, saturated $CuSO_4$ solution, and water; dried (Na_2SO_4); and concentrated to a syrup, which crystallized from ethanol to give **5** (1.6 g, 91.6%); m.p 105°C, $[\alpha]_D^{25}$ +67.7° (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 5.46 (d, 1 H, $J_{1,2} = 2.0$ Hz, H-1), 4.66 (dd, 1 H, $J_{4,5} = 1.9$ Hz, $J_{3,4} = 5.6$ Hz, H-4), 4.36 (t, 1 H, J = 6.0 Hz, H-3), 4.28 (dq, 1 H, $J_{4,5} = 1.8$ Hz, $J_{5,6} = 6.5$ Hz, H-5), 4.08 (dd, 1 H, $J_{1,2} = 2.1$ Hz, $J_{2,3} = 6.2$ Hz, H-2), 3.10 (s, 3 H, SO_2CH_3), 2.65 (m, 2 H, SCH_2CH_3), 1.60, 1.37 [2 s, 6 H, 2 $C(CH_3)_2$], 1.38 (d, 3 H, J = 6.1 Hz, H-6), 1.32 (t, 3 H, J = 7.5 Hz, CH_2CH_3).

Anal. Calcd for $C_{12}H_{22}O_6S_2$: C, 44.15; H, 6.79. Found: C, 44.17; H, 6.91.

Ethyl 4-azido-4,6-dideoxy-1-thio-α-D-mannopyranoside (7). To a solution of **5** (1.70 g, 5.3 mmol) in anhydrous methanol (59 mL), 2*N* HCl in MeOH (1.2 mL) was added and the mixture was stirred at 0°C for 2 h at rt. The solution was concentrated under diminished pressure to afford ethyl 6-deoxy-4-*O*-(methylsulfonyl)-α-D-talopyranoside **6**. The product **6** (1.52 g, 5.2 mmol) was quickly dissolved in DMSO (13.3 mL) and stirred with NaN_3 (1.80 g, 27.7 mmol) for 5 h at 100°C. Solvents were removed, and the syrupy residue was dissolved in ethanol (40 mL) and filtered through a Celite bed. The filtrate was concentrated and column chromatographed with 3:1 toluene-EtOAc to give **7** (700 mg, 56% overall), which crystallized from hexane; m.p. 88°C; $[\alpha]_D^{25}$ +210.6° (*c* 0.67, $CHCl_3$). ^{1}H NMR: δ 5.20 (s, 1 H, H-1), 3.96 (d, 1 H, $J_{2,3} = 3.5$ Hz, H-2), 3.91 (dd, 1 H, $J_{2,3} = 3.5$ Hz, $J_{3,4} = 10.0$ Hz, H-3), 3.74 (m, 1 H, H-5), 3.25 (t, 1 H, J = 9.8, H-4), 2.55 (m, 2 H, SCH_2CH_3), 1.28 (d, 3 H, J = 6.2 Hz, H-6), 1.22 (t, 3 H, J = 7.4 Hz, SCH_2CH_3); ^{13}C NMR: δ 84.31 (C-1), 72.12 (C-2), 71.36 (C-3), 67.60 (C-5), 66.49 (C-4), 25.57 (SCH_2CH_3), 18.63 (SCH_2CH_3), 15.24 (C-6). I.R: 2113.8 cm^{-1} (N_3).

Anal. Calcd for $C_8H_{15}O_3SN_3$: C, 41.19; H, 6.48; N, 18.01. Found: C, 40.88; H, 6.61; N, 18.39.

Ethyl 4-azido-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopyranoside (8). A mixture of **7** (579 mg, 2.48 mmol) and dibutyltinoxide (1.20 g, 4.82 mmol) was stirred under reflux in benzene (15 mL) with azeotropic removal of water for 20 h. The reaction mixture was then allowed to attain rt. Benzyl bromide (0.35 mL, 3.0 mmol) and Bu_4NBr (960 mg, 3.0 mmol) were then added and the mixture was stirred at 63°C for 6 h. The mixture was concentrated under reduced pressure and the residue dissolved in MeOH and kept at −10°C when the unwanted tin compounds were precipitated out from the mixture and filtered off. The filtrate was concentrated to dryness and the residue was chromatographed using 5:1 toluene-EtOAc and the product crystallized in ether-petroleum ether to afford **8** (505 mg, 62.9%); m.p. 82°C; $[\alpha]_D^{25}$ +120° (*c* 1.12, $CHCl_3$). ^{1}H NMR: δ 7.31–7.25 (m, 4 H, aromatic protons), 5.21 (s, 1 H, H-1), 4.61, 4.56 (2 d, 2 H, J = 11.4 Hz, $CH_2C_6H_4$), 3.95 (d, 1 H, $J_{2,3} = 3.2$ Hz, H-2), 3.81 (m, 1 H, H-5), 3.60 (dd, 1 H, $J_{2,3} = 3.2$ Hz, $J_{3,4} = 9.7$ Hz, H-3), 3.37 (t, 1 H, J = 9.9 Hz, H-4), 2.51 (m, 2 H, SCH_2CH_3), 1.24 (d, 3 H, $J_{5,6} = 6.2$ Hz, H-6), 1.19 (t, 3 H, J = 7.3 Hz, SCH_2CH_3); ^{13}C NMR: δ 137.40–128.60 (aromatic protons), 83.53 (C-1), 79.01, 72.48, 69.16, 67.49, 64.65 (C-4), 25.44 (SCH_2CH_3), 18.78 (SCH_2CH_3), 15.26 (C-6).

Anal. Calcd for $C_{15}H_{21}O_3N_3S$: C, 55.71; H, 6.54; N, 12.99. Found: C, 55.86; H, 6.75; N, 12.77.

Ethyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl-(1 → 2)-4-azido-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopyranoside (10). A solution of 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-β-D-galactopyranosyl

trichloroacetimidate[16,17] **9** (780 mg, 1.6 mmol) and acceptor **8** (390 mg, 1.2 mmol) in CH_2Cl_2 (15 mL) was stirred with MS 4 Å (2.50 g) under N_2 for 1 h. The mixture was then cooled to −25°C and TESOTf (45 mL, 200 mmol) was added dropwise. The reaction was allowed to proceed at −25°C for 1.5 h when TLC with12:1 toluene-EtOAc showed the disappearance of the acceptor **(8)**. The reaction was then quenched with the addition of Et_3N (0.5 mL) and the mixture was filtered through a Celite bed. The filtrate was concentrated and the syrupy product was purified by column chromatography with 10:1 toluene-EtOAc to afford **10** (600 mg, 57.3%), which crystallized as fine needles from hot ethanol; m.p. 96°C; $[\alpha]_D^{25}$ +115.6° (*c* 0.57, $CHCl_3$). ^{1}H NMR: δ 7.35–7.19 (m, 4 H, aromatic protons), 5.41 (d, 1 H, $J_{3,4} = 3.0$ Hz, H-4^{II}), 5.27 (dd, 1 H, $J_{3,4} = 3.2$ Hz, $J_{2,3} = 11.3$ Hz, H-3^{II}), 5.18 (d, 1 H, $J_{1,2} = 1.1$ Hz, H-1^{I}), 5.16 (d, 1 H, $J_{1,2} = 3.7$ Hz, H-1^{II}), 4.64, 4.59 (2 d, 2 H, J = 11.7 Hz, C*H*$_2$C$_6$H$_4$), 4.22 (m, 1 H, H-5^{II}), 4.01 (s, 1 H, H-2^{I}), 3.95 (m, 2 H, H-6^{I}), 3.78 (m, 1 H, H-5^{I}), 3.64 (dd, 1 H, $J_{2,3} = 2.7$ Hz, $J_{3,4} = 9.8$ Hz, H-3^{I}), 3.55 (t, 1 H, J = 9.7 Hz, H-4^{I}), 3.51 (dd, 1 H, $J_{1,2} = 3.7$ Hz, $J_{2,3} = 11.3$ Hz, H-2^{II}), 2.54 (m, 2 H, SC*H*$_2$CH$_3$), 2.09, 1.99, 1.98 (3 s, 9 H, 3 C*H*$_3$CO), 1.55 (d, 3 H, $J_{5,6} = 6.2$ Hz, H-6^{I}), 1.21 (t, 3 H, J = 7.5 Hz, SCH$_2$C*H*$_3$); ^{13}C NMR: δ 170.84, 170.42, 170.24 (3 CH$_3$*C*O), 137.69–128.34 (aromatic carbons), 99.86 (C-1^{I}), 83.7 (C-1^{II}), 78.65 (*C*H$_2$C$_6$H$_5$), 76.15, 72.66, 68.16, 68.05, 67.66,64.84 (C-4^{I}), 62.44 (C-6^{II}), 57.76 (C-2^{II}), 26.05 (S*C*H$_2$CH$_3$), 21.14, 21.08, 21.02 (3 *C*H$_3$CO), 18.76 (SCH$_2$*C*H$_3$), 15.36 (C-6^{I}).

Anal. Calcd for $C_{27}H_{36}O_{10}SN_6$: C, 50.94; H, 5.70. Found: C, 51.21; H, 5.92.

2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-glucopyranoside (12). To a solution of 2-(trimethylsilyl)ethyl 2,3-di-*O*-benzyl-*β*-D-glucopyranoside **11** (2 g, 4.3 mmol) in pyridine (15 mL), *tert*-butyldiphenylsilyl chloride (1.25 mL, 4.8 mmol) was added while stirring at rt. The reaction was monitored by TLC and after 12 h, the reaction was quenched with methanol and the mixture was concentrated to a thick glass. Column chromatography of the product with 5:1 toluene-EtOAc gave **12** (2.1 g, 70%); $[\alpha]_D^{25}$ −26° (*c* 2.8, $CHCl_3$). ^{1}H NMR: δ 7.55–7.10 (20 H, aromatic protons), 4.81, 4.56 (2 d, 2 H, J = 11.1 Hz, C*H*$_2$C$_6$H$_5$), 4.76, 4.59 (2 d, 2 H, J = 11.4 Hz, C*H*$_2$C$_6$H$_5$), 4.2 (d, 1 H, $J_{1,2} = 7.2$ Hz, 3.86 (t, 1 H, J = 9.3 Hz, H-3), 3.83 (dd, 1 H, $J_{1,2} = 7.2$ Hz, J $_{2,3} = 9.8$ Hz, H-2), 3.74 (m, 1 H, H-4), 3.45 (m, 2 H, OC*H*$_2$CH$_2$SiMe$_3$), 3.27 (m, 3 H, H-5, H-6), 0.89 [s, 9 H, C(C*H*$_3$)$_3$], 0.82 (m, 2 H, OCH$_2$C*H*$_2$SiMe$_3$), −0.15 [s, 9H, Si(C*H*$_3$)$_3$]; ^{13}C NMR: δ 135.6.–127.6 (aromatic carbons), 103.1 (C-1), 84.2, 81.9, 75.2, 74.8, 74.6, 71.6, 67.2, 64.4, 27.7 [SiC(*C*H$_3$)$_3$], 19.1 [Si*C*(CH$_3$)$_3$], 18.5 (CH$_2$*C*H$_2$SiMe$_3$), −1.5 [Si (*C*H$_3$)$_3$].

Anal. Calcd for $C_{41}H_{54}O_6Si_2$: C, 70.44; H, 7.78. Found: C, 70.79; H, 7.32.

Ethyl 4-*O*-benzoyl-2-*O*-benzyl-1-thio-β-L-fucopyranoside (14). To a stirred solution of ethyl 2-*O*-benzyl-1-thio-*β*-L-fucopyranoside **13** (2.5 g,

8.4 mmol) in anhydrous DMF (16 mL), trimethylorthobenzoate (2.2 mL, 12.8 mmol) and *p*-TsOH (30 mg) were added. Stirring was continued at rt for 3 h and after completion of the reaction as revealed by TLC with 5:1 toluene-EtOAc, NEt_3 was added to neutralize the solution. The solution was then concentrated and treated with 80% aqueous AcOH (10 mL) for 30 min. The reaction mixture was concentrated and immediately purified by column chromatography with 5:1 toluene-EtOAc. Crystallization of the column-purified material in ether gave **14** (2.48 g, 73.6%); m.p. 98°C; $[\alpha]_D^{25}$ −56.8° (*c* 2.6, $CHCl_3$). ^{1}H NMR: δ 8.09–7.12 (m, 9 H, aromatic protons), 5.43 (d, 1 H, $J_{3,4} = 3.1$ Hz, H-4), 4.98 (d, 1 H, $J_{1,2} = 10.7$ Hz, H-1), 4.67, 4.49 (2 d, 2 H, J = 9.5 Hz, $CH_2C_6H_4$), 3.90 (dd, 1 H, $J_{2,3} = 9.4$ Hz, $J_{3,4} = 3.2$ Hz, H-3), 3.81 (m, 1 H, H-5), 3.59 (t, 1 H, J = 9.4 Hz, H-2), 2.80 (m, 2 H, SCH_2CH_3), 1.35 (t, 3 H, J = 7.4 Hz, SCH_2CH_3), 1.24 (d, 3 H, J = 6.3 Hz, H-6); ^{13}C NMR: δ 167.22 (CO), 138.39–128.44 (aromatic carbons), 85.24 (C-1), 79.13, 75.89, 74.41, 73.99, 73.79, 25.40 (SCH_2CH_3), 17.16 (SCH_2CH_3), 15.40 (C-6).

Anal. Calcd for $C_{22}H_{26}O_5S$: C, 65.64; H, 6.51. Found: C, 65.68; H, 6.32.

Ethyl 3-*O*-acetyl-4-*O*-benzoyl-2-*O*-benzyl-1-thio-β-L-fucopyranoside (15). To compound **14** (600 mg, 1.5 mmol) dissolved in pyridine (5 mL), Ac_2O (2.5 mL) was added with cooling. After 3 h at rt, solvents were evaporated and then coevaporated with toluene to remove traces of pyridine. The residue was diluted with CH_2Cl_2 (25 mL); washed with 1*M* HCl (2 × 25 mL), $NaHCO_3$ (2 × 25 mL), and water (2 × 25 mL) in succession; dried (Na_2SO_4); and concentrated to a thick syrup. Column chromatography with 5:1 toluene-EtOAc gave **15** (580 mg, 85.8%), which crystallized from ether-petroleum ether to afford pure **15**; m.p. 105–107°C; $[\alpha]_D^{25}$ −65.3° (*c* 1.9, $CHCl_3$). ^{1}H NMR: δ 7.89–7.03 (10 H, aromatic protons), 5.28 (d, 1 H, $J_{3,4} = 3.1$ Hz, H-4), 4.65, 4.38 (2d, 2 H, J = 10.9 Hz, $CH_2C_6H_5$), 4.35 (d, 1 H, $J_{1,2} = 9.6$ Hz, H-1), 3.68 (m, 1 H, H-5), 3.51 (t, 1 H, J = 9.6 Hz, H-2), 2.60 (m, 2 H, SCH_2CH_3), 1.14 (t, 3 H, J = 7.4 Hz, SCH_2CH_3), 1.03 (d, 3 H, $J_{5,6} = 6.5$ Hz, H-6). ^{13}C NMR: 170.64 ($COCH_3$), 166.47 (COC_6H_5), 138.28–128.23 (aromatic carbons), 85.59 (C-1), 76.55, 75.15, 73.51, 71.90, 25.53 (SCH_2CH_3), 21.21 ($COCH_3$), 17.03 (SCH_2CH_3), 15.38 (C-6).

Anal. Calcd for $C_{24}H_{28}O_6S$: C, 64.84; H, 6.35. Found: C, 64.72; H, 6.28.

2-(Trimethylsilyl)ethyl 3-*O*-acetyl-4-*O*-benzoyl-2-*O*-benzyl-β-L-fucopyranosyl-(1 → 4)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-glucopyranoside (**16**). A solution of the donor **15** (420 mg, 940 μmol) and the acceptor **12** (550 mg, 770 μmol) in CH_2Cl_2 (10 mL) containing 4 Å MS (1 g) was stirred at rt for 1 h under N_2. The reaction mixture was cooled to −20°C and NIS (210 mg, 93 μmol) and TfOH (7 mL, 80 μmol) were added and stirring was continued at this temperature while the reaction was monitored by TLC in 10:1 tuluene-EtOAc. After 1 h, the concentration of the donor and the acceptor were

diminished to a negligible amount and a new spot appeared in between them. The reaction mixture was then diluted with CH_2Cl_2 (30 mL) and washed successively with water, 5% $Na_2S_2O_3$, saturated $NaHCO_3$, and water. The organic layer was dried (Na_2SO_4) and concentrated and the syrupy residue was column chromatographed with 15:1 toluene-EtOAc to give **16** (600 mg, 72%) as syrup; $[\alpha]_D^{25}$ −70.0° (*c* 1.8, $CHCl_3$). ^{1}H NMR: δ 7.79–6.81 (aromatic protons), 5.15 (dd, 1 H, $J_{2,3} = 10.7$ Hz, $J_{3,4} = 3.2$ Hz, H-3^{II}), 5.07 (d, 1 H, $J_{3,4} = 3.4$ Hz, H-4^{II}), 4.98 (d, 1 H, $J_{1,2} = 2.4$ Hz, H-1^{II}), 4.91, 4.47 (2 d, 2 H, J = 10.7 Hz, C*H*$_2$C$_6$H$_5$), 4.87, 4.56 (2 d, 2 H, J = 10.9 Hz, C*H*$_2$C$_6$H$_5$), 4.26 (d, 1 H, J = 7.7 Hz, H-1^{I}), 1.74 (s, 3 H, COC*H*$_3$), 0.94 [s, 9 H, C(C*H*$_3$)$_3$], 0.43 (d, 3 H, J = 6.6 Hz, H-6^{II}), −0.16 [s, 9 H, Si(C*H*$_3$)$_3$]. ^{13}C NMR: δ169.9 (*C*OCH$_3$), 165.9 (*C*OC$_6$H$_5$), 138.3–127.4 (aromatic carbons), 103.0 (C-1^{I}), 96.4 (C-1^{II}), 83.0, 82.9, 75.8, 74.5, 73.19, 73.2, 72.2, 67.0, 64.6, 62.5, 26.7 [SiC(*C*H$_3$)$_3$], 20.7 (CO*C*H$_3$), 19.2 [Si*C*(CH$_3$)$_3$], 18.5 (OCH$_2$*C*H$_2$SiMe$_3$), 15.3 (C-6^{II}),−1.5 [Si(*C*H$_3$)$_3$]; DEPT 135 spectrum: 135.8–127.4 (aromatic carbons), 103.0 (C-1^{I}), 96.43 (C-1^{II}), 82.9, 75.81, 75.80 (*C*H$_2$C$_6$H$_5$), 74.5 (*C*H$_2$C$_6$H$_5$), 73.5, 73.24 (*C*H$_2$C$_6$H$_5$), 73.18, 72.21, 70.15, 67.00 (C-6^{I}), 64.60, 62.50 (O*C*H$_2$CH$_2$SiMe$_3$), 26.74 [SiC(*C*H$_3$)$_3$], 20.70 (CO*C*H$_3$), 19.23 [Si*C*(CH$_3$)$_3$] 18.47 (OCH$_2$*C*H$_2$SiMe$_3$), 15.30 (C-6^{II}), -1.50 [Si (CH$_3$)$_3$].

Anal. Calcd for $C_{63}H_{76}O_{12}Si_2$: C, 69.97; H, 7.08. Found: C, 70.12; H, 7.34.

2-(Trimethylsilyl)ethyl 2-*O*-benzyl-α-L-fucopyranosyl-(1 → 4)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-glucopyranoside (17). Compound **16** (600 mg, 550 μmol) was treated with 0.05 *M* NaOMe in MeOH (15 mL) and stirred for 3 h. Column chromatography with 5:1 toluene-EtOAc of the product gave pure **17** (430 mg, 84%); $[\alpha]_D^{25}$ −90.2° (*c* 0.6, $CHCl_3$). ^{1}H NMR: δ 7.67–7.02 (aromatic protons), 5.16 (d, 1 H, J = 3.3 Hz,. H-1^{II}), 4.97 (d, 2 H, J = 10.9 Hz, C*H*$_2$C$_6$H$_5$), 4.68, 4.60 (2 d, 2 H, J = 10.9 Hz, C*H*$_2$C$_6$H$_5$), 4.40 (d, 1 H, J = 7.62 Hz, H-1^{I}), 4.28 (d, 1 H, J = 11.6 Hz, C*H*$_2$C$_6$H$_5$), 4.03 (m, 1 H, H-4^{II}), 1.00 [s, 9 H, SiC(C*H*$_3$)$_3$], 0.86 (d, 3 H, J = 6.6 Hz, H-6^{II}), -0.01 [s, 9 H, Si(C*H*$_3$)$_3$]. ^{13}C NMR: δ 138.40–125.20 (aromatic carbons), 103.00 (C-1^{I}), 95.86 (C-1^{II}), 83.20, 82.90, 76.60, 76.00, 75.40, 74.50, 73.80, 72.70, 71.40, 68.90, 67.03, 65.50, 62.90 (O*C*H$_2$CH$_2$SiMe$_3$), 26.70 [SiC(*C*H$_3$)$_3$], 19.10 [Si*C*(CH$_3$)$_3$], 18.50 (OCH$_2$*C*H$_2$SiMe$_3$), 15.60 (C-6^{II}), −1.50 [Si(*C*H$_3$)$_3$].

Anal. Calcd for $C_{54}H_{70}O_{10}Si_2$: C, 69.34; H, 7.54. Found: C, 69.57; H, 7.40.

2-(Trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl-(1 → 2)-4-azido-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranosyl-(1 → 3)-2-*O*-benzyl-α-L-fucopyranosyl-(1 → 4)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-glucopyranoside (**18**). NIS (58 mg, 260 μmol) and TfOH (3 mL, 30 μmol) were added to the stirred mixture of the acceptor **17** (200 mg, 210 μmol), the donor **10** (163 mg, 200 μmol), 4 Å molecular sieves (100 mg), and CH_2Cl_2 (3 mL) at (20°C under N_2 as described for compound **16**.

The reaction was monitored by TLC (10:1 toluene-ethyl acetate) and after 45 min, the spots for the donor and the accepter almost disappeared and a spot for the product appeared prominently. The reaction mixture was worked up as described for compound **16**. Column chromatography of the crude product with 15 : 1 toluene-EtOAc afforded **18** (180 mg, 57%) and another tetrasaccharide derivative **19** (25 mg, 7.8%).

For compound **18:** $[\alpha]_D^{25}$ +3.5° (*c* 0.01, $CHCl_3$). ^{1}H NMR: 7.53–6.99 (aromatic protons, 30 H), 5.23 (d, 1 H, J = 3.2 Hz, H-4^{IV}), 5.14 (m, 1 H, H-3^{IV}), 5.12 (s, 1 H, H-1^{II}), 4.87 (s, 1 H, H-1^{III}), 4.83 (s, 2 H, C*H*$_2$Ph), 4.79 (s, 1 H, H-1^{IV}), 4.52 (m, 2 H, C*H*$_2$Ph), 4.50 (m, 1 H, H-3^{II}), 4.46 (m, 2 H, C*H*$_2$Ph), 4.23 (d, 1 H, J = 7.6 Hz, H-1^{I}), 4.16 (m, 2 H, C*H*$_2$Ph), 3.95 (dd, 1 H, J = 0.5 Hz, J = 12.8 Hz, H-5^{IV}), 3.87 (bs, 1 H, H-4^{II}), 3.85 (m, 2 H, H-6^{IV}), 3.81 (s, 1 H, H-2^{III}), 3.75 (m, 1 H, H-2^{I}), 3.55 (dd, 1 H., J = 3.6 Hz, J = 9.9 Hz, H-3^{III}), 2.76 (m, 2 H, OC*H*$_2$CH$_2$SiMe$_3$), 1.94, 1.82, 1.73 (3 s, 9 H, 3 COC*H*$_3$), 1.07 (d, 3 H, J = 7.1 Hz, H-6^{III}), 0.87 [s, 9 H, SiC(C*H*$_3$)$_3$], 0.86 (m, 2 H, OCH$_2$C*H*$_2$SiMe$_3$), 0.73 (d, 3 H, J = 6.4 Hz, H-6^{II}), −0.15 [s, 9 H, Si(C*H*$_3$)$_3$; ^{13}C NMR: δ170.30, 169.80, 169.20 (3 *C*OCH$_3$), 135.80–127.30 (aromatic carbons), 102.90 (C-1^{I}), 97.90 (C-1^{IV}), 97.20 (C-1^{III}), 96.20 (C-1^{II}), 83.08, 82.85, 80.90, 78.70, 76.00, 75.00, 74.40, 74.10, 72.90, 72.80, 72.50, 72.10, 71.40, 70.60, 67.50, 67.40, 66.90, 66.30, 65.30, 63.80 (C-4^{III}), 62.70 (O*C*H$_2$CH$_2$SiMe$_3$), 61.40 (C-6^{IV}), 57.60 (C-2^{IV}), 26.90 [SiC(*C*H$_3$)$_3$], 20.40 (3 CO*C*H$_3$), 19.20 [Si*C*(CH$_3$)$_3$], 18.50 (OCH$_2$*C*H$_2$SiMe$_3$), 18.20 (C-6^{III}), 15.60 (C-6^{II}), −1.50 [Si(*C*H$_3$)$_3$]; DEPT 135 Spectrum: δ 136.10–127.60 (aromatic carbons), 103.20 (C-1^{I}), 98.2 0(C-1^{IV}), 97.50 (C-1^{III}), 96.50 (C-1^{II}), 83.30, 83.10, 81.10, 79.00, 77.30, 76.20, 75.20 (CH$_2$), 74.70 (CH$_2$), 74.30, 73.10, 73.00 (CH$_2$), 72.80, 72.30 (CH$_2$), 71.70, 70.80, 67.80, 67.60, 67.20 (C-6^{I}), 66.60, 65.50, 64.10 (C-4^{III}), 62.90 (O*C*H$_2$CH$_2$SiMe$_3$), 61.70 (C-6^{IV}), 57.90 (C-2^{IV}), 27.00 [SiC(*C*H$_3$)$_3$], 20.70 (3 CO*C*H$_3$), 18.70 (OCH$_2$*C*H$_2$SiMe$_3$), 18.50 (C-6^{III}), 15.90 (C-6^{II}), −1.20 [Si(*C*H$_3$)$_3$].

For compound **19:** $[\alpha]_D^{25}$ +6.2° (*c* 0.7, $CHCl_3$). ^{1}H NMR: δ 7.51–6.85 (aromatic protons, 30 H), 5.18 (d, 1 H, J = 1.9 Hz, H-4^{IV}), 5.09 (dd, 1 H, J = 2.8 Hz, J = 11.3 Hz, H-3^{IV}), 5.02 (d, 1 H, J = 2.9 Hz, H-1^{II}), 4.93 (s, 1 H, H-1^{III}), 4.88 (d, 1 H, J = 3.8 Hz, H-1^{IV}), 4.84, 4.82 (2d, 2 H, J = 10.8 Hz, C*H*$_2$Ph), 4.83 (s, 1 H, H-4^{II}), 4.55, 4.51 (2 s, 2 H, CH$_2$Ph), 4.40 (bs, 2 H, CH$_2$Ph), 4.20 (d, 1 H, J = 6.6 Hz, H-1^{I}), 4.01 (m, 2 H, CH$_2$Ph), 3.94 (t, 1 H, J = 6.5 Hz, H-5^{IV}), 3.85 (d, 1 H, J = 8.6 Hz, H-3^{I}), 3.83 (m, 1 H, H-3^{II}), 3.02 (m, 2 H, OC*H*$_2$CH$_2$SiMe$_3$) 1.94, 1.87, 1.73 (3 s, 9 H, 3 COC*H*$_3$), 1.23 (d, 3 H, J = 6.3 Hz, H-6^{III}), 0.88 [s, 9 H, SiC(C*H*$_3$)$_3$] 0.84 (m, 2 H, OCH$_2$C*H*$_2$SiMe$_3$), 0.56 (d, 3 H, J = 6.3 Hz, H-6^{II}) −0.15 [s, 9 H, Si (C*H*$_3$)$_3$]; ^{13}C NMR: δ 170.20, 169.80, 169.60 (3 *C*OCH$_3$), 135.90–127.30 (aromatic carbons), 103.00 (C-1^{I}), 99.85 (C-1^{IV}), 99.00 (C-1^{III}), 95.50 (C-1^{II}), 82.80, 82.50, 75.8000, 75.40, 75.30, 74.40, 74.20, 73.00, 72.20, 71.90, 68.00, 67.50, 67.40, 67.00, 66.90, 65.00, 63.80 (C-4^{III}), 62.10 (O*C*H$_2$CH$_2$Si), 61.7000 (C-6^{IV}), 57.30 (C-2^{IV}), 26.8000 [SiC(*C*H$_3$)$_3$], 20.80, 20.50, 20.40 (3 COCH$_3$), 19.20 [Si*C*(CH$_3$)$_3$], 18.50 (C-6^{III}), 18.40 (OCH$_2$*C*H$_2$Si), 15.30 (C-6^{II}),−1.50 [Si(CH$_3$)$_3$]; DEPT 135 Spectrum: δ 136.10–127.50 (aromatic

carbons), 103.10 (C-1^{I}), 100.00 (C-1^{IV}), 99.19 (C-1^{III}), 95.70 (C-1^{II}), 83.00, 82.70, 77.50, 77.20, 75.90, 75.50, 75.40 ($CH_2C_6H_5$), 74.60 ($CH_2C_6H_5$), 74.40, 73.20 ($CH_2C_6H_5$), 72.30, 72.10, 72.00, 68.10, 67.60, 67.10 (C-6^{I}), 67.00, 65.20, 63.90 (C-4^{III}), 62.30 ($OCH_2CH_2SiMe_3$), 61.90 (C-6^{IV}), 57.40 (C-2^{IV}), 26.90 [$SiC(CH_3)_3$], 20.90, 20.65, 20.63 (3 $COCH_3$), 18.70 (C-6^{III}), 18.60 (OCH_2CH_2Si), 15.50 (C-6^{II}), −1.30 [$Si(CH_3)_3$].

Anal. Calcd for $C_{79}H_{100}O_{20}N_6Si_2$: C, 62.84; H, 6.67; N, 5.57. Found for **18**: C, 62.58; H, 6.82; N, 5.48. Found for **19**: C, 62.61; H, 6.79; N, 5.42.

2-(Trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl-(1 → 2)-4-azido-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranosyl-(1 → 3)-2-*O*-benzyl-4-*O*-aetyl-α-L-fucopyranosyl-(1 → 4)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-glucopyranoside (18A). Compound **18** was acetylated as described for compound **15** to give **18A**.^{1}H NMR: δ 7.53–6.99 (aromatic protons, 30 H), 5.14 (d, 1 H, J = 2.6 Hz, H-4^{II}), 5.09 (d, 1 H, J = 3.5 Hz, H-4^{IV}), 5.03 (dd, 1 H, J = 3.2 Hz, J = 7.7 Hz, H-3^{IV}), 5.02 (s, 1 H, H-1^{II}), 4.88, 4.82 (2d, 2 H, J = 11.1 Hz, CH_2Ph), 4.80 (s, 1 H, H-1^{III}), 4.69 (d, 1 H, J = 3.1 Hz, H-1^{IV}), 4.58 (dd, 1 H, J = 3.2 Hz, J = 6.96 Hz, H-3^{II}), 4.51, 4.46 (2d, 2 H, J = 11.0 Hz, CH_2Ph), 4.41 (m, 2 H, CH_2Ph), 4.24 (d, 1 H, J = 6.5 Hz, H-1^{I}), 4.2 (bs, 2 H, CH_2Ph), 4.08 (d, 1 H, J = 6.4 Hz, H-5^{IV}), 3.99 (dd, 1 H, J = 8.6 Hz, J = 10.9 Hz, H-2^{I}), 3.92 (dd, 2 H, J = 3.5 Hz, J = 10.1 Hz, H-6^{IV}), 3.79 (s, 1 H, H-2^{III}), 2.92 (m, 2 H, OCH_2CH_2Si), 1.94, 1.91, 1.83, 1.66 (4 s, 12 H, 4 $COCH_3$), 1.14 (d, 3 H, J = 6 Hz, H-6^{III}), 0.87 (m, 2 H, OCH_2CH_2Si), 0.59 (d, 3 H, J = 6.6 Hz, H-6^{II}), −0.15 [s, 9 H, $Si(CH_3)_3$].

2-(Trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl-(1 → 2)-4-azido-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranosyl-(1 → 4)-2-*O*-benzyl-3-*O*-aetyl-α-L-fucopyranosyl-(1 → 4)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-glucopyranoside (19A). Compound **19** was acetylated as described for compound **15** to give **19A**. ^{1}H NMR: δ 7.50–6.88 (30 H, aromatic protons), 5.12 (s, 2 H, H-1^{III}, H-4^{IV}), 5.05 (dd, 1 H, J = 3.2 Hz, J = 11.4 Hz, H-3^{IV}), 5.02 (d, 1 H, J = 3.1 Hz, H-1^{II}), 4.92 (s, 1 H, H-1^{IV}), 4.86 (dd, 1 H, J = 8.1 Hz, J = 4.4 Hz, H-3^{II}), 4.81 (s, 2 H, CH_2Ph), 4.68 (d, 1 H, J = 3.0 Hz, H-4^{II}), 4.55, 4.51 (2 s, 2 H, CH_2Ph), 4.41, 4.39 (2d, 2 H, J = 5.3 Hz, CH_2Ph), 4.22 (d, 1 H, J = 7.3 Hz, H-1^{I}), 4.06 (bs, 2 H, CH_2Ph), 3.06 (d, 2 H, J = 8.9 Hz, OCH_2CH_2Si), 1.94, 1.86, 1.80, 1.75 (4 s, 12 H, 4 $COCH_3$), 1.18 (d, 3 H, J = 6 Hz, H-6^{III}), 0.89 (m, 2 H, OCH_2CH_2Si), 0.38 (d, 3 H, J = 6.3 Hz, H-6^{II}), −0.15 [s, 9 H, $Si(CH_3)_2$].

2-(Trimethylsilyl)ethyl 2-acetamido-2-deoxy-α-D-galactopyranosyl-(1 → 2)-4-acetamido-4,6-dideoxy-α-D-mannopyranosyl-(1 → 3)-α-L-fucopyranosyl-(1 → 4)-β-D-glucopyranoside (21). Tetrabutylammoniumfluoride (36 mg, 140 μmol) in 0.3 mL THF was added to a solution of **18** (103 mg,

68 μmol) in THF at 0°C with stirring. The mixture was then allowed to attain rt and after 12 h, the solution was concentrated. Column chromatography of the residue with 5:1 toluene-EtOAc gave pure compound **20** (45 mg, 51.5%). A solution of **20** (45 mg, 35 μmol) in aldehyde-free methanol (2 mL) containing acetic anhydride (0.1 mL) was stirred with 10% Pd on charcoal under hydrogen for 3 d when all the starting material was transformed into a clean, slower-moving compound as observed in the TLC. The mixture was filtered through a Celite bed, the filtrate was concentrated to a syrup, and the product was treated with 0.05 M NaOMe in methanol as described in the case of compound **17**. The deacetylated product was dissolved in water and filtered through Sep-Pak C-18 cartridge and concentrated to dryness to afford pure compound **21** (16 mg, 56%). $[\alpha]_D^{25}$ +52° (*c* 0.01, H_2O). ^{1}H NMR (D_2O): δ5.08 (s, 1 H, H-1^{III}), 4.81 (bs, 1 H, H-1^{IV}), 4.69 (d, 1 H, J = 4.2 Hz, H-1^{II}), 4.30 (d, 1 H, J = 7.9 Hz, H-1^{I}), 3.09 (m, 2H, $OCH_2CH_2SiMe_3$), 1.86, 1.83 (2 s, 6 H, 2 $NHCOCH_3$), 1.08, 1.02 (2d, 6 H, J = 6 Hz, H-6^{II}, H-6^{III}), 0.85 (m, 2H, $OCH_2CH_2SiMe_3$), -0.15 [$Si(CH_3)_3$]; ^{13}C NMR: δ175.90 (2 $NHCOCH_3$), 102.50 (C-1^{I}), 100.50 (C-1^{IV}), 99.20 (C-1^{III}), 97.20 (C-1^{II}), 78.30, 76.70, 76.20, 75.80, 74.60, 72.90, 72.50, 71.20, 70.40, 69.50, 69.40, 69.10, 68.10, 67.90 (C-6^{I}), 67.60, 67.50, 61.90 (OCH_2CH_2 $SiMe_3$), 61.10 (C-6^{IV}), 54.00 (C-4^{III}), 51.30 (C-2^{IV}), 23.20, 23.10 (2 $NHCOCH_3$), 18.60 ($OCH_2CH_2SiMe_3$), 17.70 (C-6^{III}), 16.30 (C-6^{II}), −1.50 [$Si(CH_3)_3$]; DEPT 135 Spectrum: δ 102.50 (C-1^{I}), 100.50 (C-1^{IV}), 99.10 (C-1^{III}), 97.10 (C-1^{II}), 78.30, 76.70, 76.20, 75.80, 74.60, 72.90, 72.50, 71.20, 70.40, 69.50, 69.40, 69.10, 68.10, 67.90 (C-6^{I}), 67.60, 67.50, 61.80 (OCH_2CH_2 $SiMe_3$), 61.10 (C-6^{IV}), 54.00 (C-4^{III}), 51.30 (C-2^{IV}), 23.20, 23.10 (2 $NHCOCH_3$), 18.60 ($OCH_2CH_2SiMe_3$), 17.70 (C-6^{III}), 16.30 (C-6^{II}), −1.50 [$Si(CH_3)_3$].

Anal. Calcd for $C_{33}H_{60}O_{19}N_2Si$: C, 48.52; H, 7.40; N, 3.43. Found: C, 48.38; H, 7.58; N, 3.25.

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