Supporting Information

S-Linked Ganglioside Analogues for Use in Conjugate Vaccines

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General

All chemical reagents were of analytical grade, used as supplied without further purification unless indicated. Solvents used in reactions were distilled under an inert atmosphere, except *N,N*-dimethylformamide, which was stored over 3Å molecular sieves and subjected to reduced pressure for several minutes (<0.5mm Hg) prior to use. Pyridine was dried over solid KOH and used without further purification. Molecular sieves were stored in an oven (>170 °C) and cooled in vacuo. The acidic ion-exchange resin used was Rexyn-101 (H⁺ form). Analytical thin layer chromatography (TLC) was conducted on silica gel 60-F₂₅₄ (Merck). Plates were visualized under UV light, and/or by treatment with either acidic cerium ammonium molybdate or 5% ethanolic sulfuric acid, followed by heating. Medium pressure chromatography was conducted using silica gel (230-400 mesh) from SiliCycle at flow rates of 5-10 mL min⁻¹. HPLC purification was conducted on a Waters Delta 600 system using a UV absorbance detector. Separations were performed on Phenomenex C₈/C₁₈-silica semi-preparative columns with combinations of water and methanol (flow rate 2 mL min⁻¹) as eluants.

¹H and ¹³C NMR spectra were recorded on Varian INOVA 400, 500 and 600 MHz spectrometers. Chemical shifts are reported in δ (ppm) units using ¹³C and residual ¹H signals from deuterated solvents as references. ¹H and ¹³C NMR spectra were assigned with the assistance of COSY, HMQC, HMBC, TOCSY and TROESY spectra where necessary. NMR data for compounds containing sphingosine/ceramide and derivatives as the aglycone were labeled as follows. Carbon and hydrogen atoms of sphingosine and the truncated 2-azido/amino-4-pentene-1,3-diol sphingosine homologue are denoted C-X_{sphing}/H-X_{sphing}, where numbering begins with C1/H1 at the glycosyl linkage.

Electrospray ionization mass spectra were recorded on a Micromass Zabspec TOF mass spectrometer. For high resolution mass determination, spectra were obtained by voltage scan over a narrow range at a resolution of approximately 10000. Optical rotations were determined with a Perkin-Elmer model 241 polarimeter at 22 °C.

2-(Trimethylsilyl)ethyl (2,3-di-O-acetyl-4,6-O-benzylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (5)

2-(Trimethylsilyl)ethyl lactose (5.012g; 11.3 mmol) was suspended in freshly distilled acetonitrile (175 mL) and benzaldehyde dimethyl acetal (3.45 mL; 23.1 mmol; 2 eq.). *p*-Toluenesulfonic acid (100 mg) was added, and the mixture stirred for 80 minutes. After this time the solution was made basic with triethylamine, then concentrated. The residue was taken up in pyridine (100 mL) and acetic anhydride (25 mL) and stirred overnight. After concentration, the residue was dissolved in dichloromethane (500 mL), washed successively with 1M HCl, saturated NaHCO₃ solution, and water, then dried over sodium sulfate, filtered and concentrated. Crystallization from ethyl acetate/hexanes yielded **5** (3.784g; 5.1 mmol; 45%). Chromatography of the mother liquor afforded a further (3.236 g; 4.36 mmol) 39% of the desired compound. All spectral data matched those reported earlier for synthesis of this compound under different conditions.⁸

2-(Trimethylsilyl)ethyl (2,3-di-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside

Acetal **5** (3.260g; 4.4 mmol) was combined with 80% acetic acid (80 mL) and heated at 50 °C for nine hours, then concentrated. Recrystallization of the residue from hexanes/ethyl acetate gave the diol (2.470g; 3.8 mmol; 86%). All spectral data matched those reported earlier for synthesis of this compound under different conditions.⁸

2-(Trimethylsilyl)ethyl (2,3-di-O-acetyl-6-O-trifluoromethanesulfonyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (6)

The diol (0.310 g; 0.47 mmol) was dissolved in dichloromethane (8.0 mL) and pyridine (0.150 mL; 1.85 mmol; 3.9 eq.) with stirring under argon, and was then cooled to – 30 °C. Trifluoromethanesulfonic anhydride (0.088 mL; 0.52 mmol; 1.1 eq.) was added dropwise over a one minute period, and the mixture was stirred for one hour, then diluted with dichloromethane (25 mL), washed successively with 1M hydrochloric acid, saturated sodium bicarbonate solution, and water, then dried over sodium sulfate, filtered and concentrated. The residue was chromatographed on silica gel using hexanes/ethyl acetate (3:2) as eluant affording the title compound (0.264g; 0.34 mmol; 71%): [α]_D -16° (c 0.55, CHCl₃); ¹H NMR (500 MHz, CDCl₃, δ) 5.19 (dd, 1H, H-3, *J*_{3,2} = *J*_{3,4} = 9.3 Hz), 5.14 (dd, 1H, H-2', *J*_{2',1'} = 7.8 Hz, *J*_{2',3'} = 10.1 Hz), 4.93 (dd, 1H, H-3', *J*_{3',4'} = 3.3 Hz), 4.86 (dd, 1H, H-2, *J*_{2,1} = 7.9 Hz), 4.67 (dd, 1H, H-6a', *J*_{6a',6b'} = 10.6 Hz, *J*_{6a',5'} = 5.5 Hz), 4.61 (dd, 1H, H-6b', *J*_{6b',5'} = 6.9 Hz), 4.51 (d, 1H, H-1'), 4.48 (dd, H-6a, *J*_{6a,5} = 12.0 Hz, *J*_{6a,6b} = 2.1 Hz), 4.45 (d, 1H, H-1), 4.10 (dd, 1H, H-6b, *J*_{6b,5} = 5.1 Hz), 4.06 (d, 1H, H-4', *J*_{4',3'} = 2.7 Hz), 3.91 (m, 1H, OCH₂CH₂), 3.85 (m, 1H, H-5'), 3.81 (dd, 1H, H-4, *J*_{4,3} = *J*_{4,5} = 9.3 Hz), 3.60 (m, 1H, H-5), 3.53 (m, 1H, OCH₂CH₂), 2.58 (bs, 1H, OH-4'), 2.09, 2.06, 2.03, 2.01, 2.00 (5 x s, 15H,

C(O)CH₃), 0.90 (m, 2H, CH₂TMS), -0.05 (s, 9H, Si(CH₃)₃); ¹³C NMR (100 MHz, CDCl₃, δ) 170.4, 170.0, 69.8, 169.4, 169.2, 118.6 (q, CF₃, ¹J_{C,F} = 320 Hz), 100.1 (C-1'), 99.9 (C-1), 75.7, 72.8, 72.7, 72.6, 72.5, 71.9, 71.8, 69.2, 67.4, 66.3, 62.1, 20.75, 20.68, 20.56 (3 x C), 17.8, -1.5; ESI HRMS calc'd for C₂₈H₄₃O₁₈SSiNa: 807.17837. Found: 807.17827. (Note: Although this compound was found to exhibit reasonable stability (<5% decomposition observed by ¹H NMR after 1 month at -20 °C), satisfactory elemental analyses could not be obtained even after repeated purification.)

2-(Trimethylsilyl)ethyl S-(Methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-2-thio-β-D-glycero-α-D-galacto-non-2-ulopyranosylate)-(2→6)-(2,3-di-O-acetyl-6-thio-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (8)

2-(Trimethylsilyl)ethyl (2,3-di-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (0.240 g; 0.37 mmol) was dissolved in freshly distilled dichloromethane (5.0 mL) and pyridine (0.119 mL; 1.47 mmol; 4 eq.) with stirring under argon. After cooling the solution to -25°C, trifluoromethanesulfonic anhydride (0.074 mL; 0.44 mmol; 1.2 eq.) was added dropwise over approximately one minute. After stirring at constant temperature for 45 minutes, the reaction mixture was diluted with dichloromethane (30 mL), washed successively with 1M HCl, saturated NaHCO₃ solution, and water. The organic layer was dried over Na₂SO₄, filtered, and concentrated. The crude residue was combined with Methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2-S-acetyl-3,5-dideoxy-2-thio-β-D-glycero-α-D-galacto-non-2-ulopyranosylate (0.202g; 0.37 mmol; 1 eq.), and the mixture was dissolved in dimethylformamide (3.0 mL) under argon. After cooling to -25°C, diethylamine (0.380 mL, 3.7 mmol, 10eq.) was added and the solution was stirred for 2 hours, after which time it was concentrated under reduced pressure. Column chromatography of the residue in methanol/dichloromethane (3:97) afforded **8** (0.301 g; 0.27 mmol; 73 %) and a small amount of **9**¹⁰ (0.031 g; 0.26 mmol; 7%): [α]_D +2° (c 0.94, CHCl₃). ¹H NMR (500 MHz, CDCl₃, δ) 5.29 (dd, 1H, J_{7'',8''} = 9.6 Hz J_{7'',6''} = 2.0 Hz, H-7''), 5.21 (m, 1H, H-8''), 5.15-5.08 (m, 3H, NHAc, H-2'', H-3), 4.93-4.87 (m, 3H, H-4'', H-3', H-2), 4.58 (d, 1H, J_{1'',2''} = 7.91 Hz, H-1''), 4.46-4.43 (m, 2H, H-1', H-6a), 4.26 (dd, 1H, J_{9a'',8''} = 2.88 Hz, J_{9a'',9b''} = 12.5Hz, H-9a'') 4.19 (d, 1H, J_{4',3'} = 3.2 Hz, H-4'), 4.15-4.08 (m, 2H, H-9''b, H-6b), 3.95-3.88 (m, 2H, H-5'', CH₂CH₂Si), 3.83-3.77 (m, 5H, CO₂CH₃, H-6'', H-4), 3.62-3.58 (m, 2H, H-5', H-5), 3.53 (ddd, 1H, CH₂CH₂Si), 2.85 (dd, 1H, J_{6'a,6'b} = 14.3 Hz, J_{6'a,5} = 7.2 Hz, H-6'a), 2.78 (dd, J_{6'b,6'a} = 14.3 Hz, J_{6'b,5} = 6.9 Hz, H-6'b), 2.73 (dd, J_{3''eq,3''ax} = 12.8 Hz, J_{3''eq,4''} = 4.6 Hz, H-3''eq), 2.18-2.00 (27H, 9 x OC(O)CH₃), 1.96 (dd, 1H, J_{3''ax,4''} = 12.5 Hz), 1.87 (s, 3H, NHC(O)CH₃), 0.89 (m, 2H, CH₂CH₂Si), -0.03 (s, 9H, SiCH₃); 170.7, 170.6, 170.28, 170.23, 170.0 (2 x C), 169.9, 169.7, 169.5, 169.2, 168.1, 100.2 (C-1'), 100.0 (C-1), 83.8, 73.95, 73.87, 73.4, 73.0, 72.7, 71.8, 69.6, 69.3, 68.1, 67.3, 66.7, 62.6, 62.0, 53.3, 49.6, 38.1, 29.8, 23.3, 21.3, 21.1, 20.90, 20.87 (multiple C), 20.81, 20.76, 17.98, -1.3; ESI MS calc'd for C₄₇H₇₁NO₂₇SSiNa: 1164. Found: 1164. Anal. calc'd for C₄₇H₇₁NO₂₇SSi: C 49.42, H 6.27, N 1.24. Found: C 49.60, H 6.25, N 1.40.

Alternatively, direct acetylation of the crude reaction mixture afforded **9** in 83% yield after chromatography. All spectral data were found to be in accord with those reported previously. Removal of the 2-(Trimethylsilyl)ethyl protecting group and generation of the hemiacetal proceed smoothly under previously reported conditions.¹⁰

S-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero- α -*D*-galacto-2-nonulopyranosylate)-(2 $\rightarrow$ 6)-*O*-(2,3-di-*O*-acetyl-6-thio- β -*D*-galactopyranosyl)-(1 $\rightarrow$ 4)-*O*-(2,3,6-tri-*O*-acetyl- β -*D*-glucopyranosyl)-(1 $\rightarrow$ 1)-(2*S*, 3*R*)-2-azido-3-*O*-benzoyl-pent-4-ene-1,3-diol. (**10**)

(2*S*, 3*R*)-2-azido-3-*O*-benzoyl-4-pentene-1,3-diol (0.020 g; 0.08 mmol; 0.8 eq), the glycosyl trichloroacetimidate (0.120 g; 0.10 mmol; 1.0 eq), and Drierite (0.170 g) were combined under an argon atmosphere in freshly distilled dichloromethane (1.5 mL). The mixture was stirred for 45 minutes and then cooled to $-10\text{ }^{\circ}\text{C}$ prior to addition of boron trifluoride-diethyl etherate (30 μ L; 0.23 mmol; 2.4 eq). After 1 hour, the temperature was increased to $0\text{ }^{\circ}\text{C}$ for 50 minutes, and then to room temperature for a further 30 minutes. The reaction mixture was diluted with dichloromethane (20 mL), washed with saturated NaHCO_3 solution (20 mL) followed by water (20 mL). The organic layer was dried over Na_2SO_4 , filtered, and concentrated. Column chromatography of the residue in methanol/dichloromethane (3:97) afforded the glycosyl-sphingosine analogue **10** (0.075 g; 0.06 mmol; 71 %): $[\alpha]_D - 19^{\circ}$ (*c* 0.50, CHCl_3); ^1H NMR (600 MHz, CDCl_3 , δ) 8.04 (m, 2H, Ar), 7.56 (m, 1H, Ar), 7.44 (m, 2H, Ar), 5.92 (m, 1H, H-4_{sphing}), 5.64 (dd, 1H, H-3_{sphing}, $J = 4.0, 7.0\text{ Hz}$), 5.60 (d, 1H, H-4', $J_{4',3'} = 3.0\text{ Hz}$), 5.44 (bd, 1H, H-5a_{sphing}, $J_{5a,4} = 17.3\text{ Hz}$), 5.39 (bd, 1H, H-5b_{sphing}, $J_{5b,4} = 10.5\text{ Hz}$), 5.29 (d, 1H, H-7'', $J = 11.4\text{ Hz}$), 5.19 (m, 1H, H-8''), 5.17 (dd, 1H, H-3, $J_{3,2} = J_{3,4} = 9.4\text{ Hz}$), 5.11 (d, 1H, NHAc , $J_{\text{NH},5''} = 9.2\text{ Hz}$), 5.02 (m, 2H, H-2', H-3'), 4.96 (dd, 1H, H-2, $J_{2,1} = 8.0\text{ Hz}$), 4.93 (m, 1H, H-4''), 4.69 (d, 1H, H-1', $J_{1',2'} = 7.3\text{ Hz}$), 4.50 (d, 1H, H-1), 4.47 (dd, 1H, H-6a, $J_{6a,5} = 3.9\text{ Hz}$, $J_{6a,6b} = 12.6\text{ Hz}$), 4.26 (dd, 1H, H-9a'', $J_{9a,8} = \text{Hz}$, $J_{9a,9b} = \text{Hz}$), 4.15 (dd, 1H, H-9b'', $J_{9b'',8''} = 4.4\text{ Hz}$), 4.10 (dd, 1H, H-6b, $J_{6b,5} = 6.6\text{ Hz}$), 3.97 (m, 1H, H-2_{sphing}), 3.92-3.84 (m, 5H, H-1a_{sphing}, H-4, H-5', H-5'', H-6''), 3.83 (s, 3H, OCH_3), 3.63 (ddd, 1H, H-5, $J_{5,4} = 2.0\text{ Hz}$), 3.59 (dd, 1H, H-1b_{sphing}, $J_{1b,1a} = 10.5\text{ Hz}$, $J_{1b,2} = 6.4$), 2.78 (dd, 1H, H-6a', $J_{6a',5'} = 6.9\text{ Hz}$, $J_{6a',6b'} = 14.4\text{ Hz}$), 2.70 (dd, 1H, H-3eq'', $J_{3e'',3a''} = 12.8\text{ Hz}$, $J_{3e'',4''} = 4.7\text{ Hz}$), 2.52 (dd, 1H, H-6b', $J_{6b',5'} = 7.7\text{ Hz}$), 2.18, 2.16, 2.11, 2.10, 2.03, 2.02, 2.014, 2.009, 2.001 (9 x s, 27H, $\text{C}(\text{O})\text{CH}_3$), 1.96 (dd, 1H, H-3ax, $J_{3a'',4''} = 12.8\text{ Hz}$), 1.91, 1.87 (2 x s, 6H, $\text{C}(\text{O})\text{CH}_3$); ^{13}C NMR (125 MHz, CDCl_3 , δ) 170.7, 170.5, 170.3, 170.2, 169.94, 169.88 (2C), 169.74, 169.6, 169.5, 169.1, 167.8, 164.9, 133.2, 131.2, 129.7, 129.6, 128.4, 120.7, 100.4 (C-1), 100.1 (C-1'), 84.2, 75.7, 74.6, 73.8, 73.3, 72.49, 72.45, 71.5, 71.3, 69.3, 69.1, 67.8, 67.7, 66.7, 63.2, 62.3, 62.2, 53.3, 49.7, 44.1, 29.9, 23.3, 21.2, 21.1, 20.92, 20.85 (multiple C), 20.81, 20.78 (multiple C). ESI MS calc'd for $\text{C}_{56}\text{H}_{72}\text{N}_4\text{O}_{30}\text{SNa}$: 1335. Found: 1335.

S-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero- α -*D*-galacto-2-nonulopyranosylonate)-(2 $\rightarrow$ 6)-*O*-(2,3-di-*O*-acetyl-6-thio- β -*D*-galactopyranosyl)-(1 $\rightarrow$ 4)-*O*-(2,3,6-tri-*O*-acetyl- β -*D*-glucopyranosyl)-(1 $\rightarrow$ 1)-(2*S*, 3*R*)-3-*O*-benzoyl-2-octadecylamido-pent-4-ene-1,3-diol

Compound **10** (0.0806 g; 0.06 mmol) and triphenylphosphine (0.032 g; 0.12 mmol; 2 eq.) were combined in pyridine/water (10:1) (3.0 mL) and heated at 50 °C. After four hours, *N*-(octadecanoyloxy)-succinimide (0.117 g; 0.31 mmol; 5 eq) was added, and heating was continued for 4-5 hours. The solution was then cooled and concentrated. The residue was chromatographed on silica gel using a gradient of 0 to 4% methanol in dichloromethane to afford the title compound (0.084 g; 0.05 mmol; 88%): $[\alpha]_D -16^\circ$ (*c* 1.0 , CHCl₃); ¹H NMR (600 MHz, CDCl₃, δ) 8.00 (m, 2H, Ar), 7.54 (m, 1H, Ar), 7.42 (m, 2H, Ar), 5.88 (ddd, 1H, H-4_{sphing}, $J_{4,3} = 6.3$ Hz, $J_{4,5a} = 17.0$ Hz, $J_{4,5b} = 10.6$ Hz), 5.78 (d, 1H, NH_{sphing}, $J_{NH,H2} = 9.0$ Hz), 5.60 (ddd, 1H, H-3_{sphing}, $J_{3,5a} = J_{3,2} = 1.2$ Hz), 5.40 (dd, 1H, H-4', $J_{4',3'} = 3.2$ Hz, $J_{4',5'} = 1.0$ Hz), 5.37 (ddd, 1H, H-5a_{sphing}, $J_{5a,5b} = 1.2$ Hz), 5.30-5.26 (m, 2H, H-5b_{sphing}, H-7"), 5.20-5.14 (m, 2H, H-3, H-8"), 5.12 (d, 1H, NHAc, $J_{NH,5''} = 8.8$ Hz), 5.02 (dd, 1H, H-2', $J_{2',1'} = 7.8$ Hz, $J_{2',3'} = 10.6$ Hz), 4.97 (dd, 1H, H-3'), 4.93 (m, 1H, H-4"), 4.90 (dd, 1H, H-2, $J_{2,1} = 7.9$ Hz, $J_{2,3} = 9.7$ Hz), 4.64 (d, 1H, H-1'), 4.50 (m, 1H, H-3_{sphing}), 4.43 (d, 1H, H-1), 4.38 (dd, 1H, H-6a, $J_{6a,5} = 2.2$ Hz, $J_{6a,6b} = 11.9$ Hz), 4.26 (dd, 1H, H-9a", $J_{9a'',8''} = 3.0$ Hz, $J_{9a'',9b''} = 12.6$ Hz), 4.13 (dd, 1H, H-9b", $J_{9b'',8''} = 4.4$ Hz), 4.02 (dd, 1H, H-6b, $J_{6b,5} = 6.4$ Hz), 3.92-3.81 (m, 7H, H-1a_{sphing}, H-4, H-5', H-5", OCH₃), 3.63 (dd, 1H, H-1b_{sphing}, $J_{1b,2} = 4.9$ Hz, $J_{1b,1a} = 10.2$ Hz), 3.59 (ddd, 1H, H-5, $J_{5,4} = 8.7$ Hz, $J_{5,6b} = 8.8$ Hz), 2.78 (dd, 1H, H-6a', $J_{6a',5'} = 7.1$ Hz, $J_{6a',6b'} = 14.5$ Hz), 2.70 (dd, 1H, H-3"eq., $J_{3''eq,3''ax} = 12.8$ Hz, $J_{3''eq,4''} = 4.7$ Hz), 2.52 (dd, 1H, H-6b', $J_{6'b,5'} = 7.5$ Hz), 2.16, 2.15 (2 x s, 6H, 2 x C(O)CH₃), 2.13 (m, 2H, CH_{2cer}), 2.10, 2.03, 2.012, 2.008, 2.006, 1.998 (6 x s, 18H, 6 x C(O)CH₃), 1.96 (dd, 1H, H-3"ax, $J_{3''ax,4''} = 11.8$ Hz), 1.91 (s, 6H, 2 x C(O)CH₃), 1.87 (s, 3H, C(O)CH₃), 1.66-1.54 (m, 4H, 2 x CH_{2cer}), 1.30-1.20 (m, 26H, 13 x CH_{2cer}), 0.85 (t, 3H, CH_{3cer}); ¹³C NMR (125 MHz, CDCl₃, δ) 171.1, 170.8, 170.6, 170.4, 170.2, 170.1, 170.0, 169.9, 169.8, 169.70, 169.69, 169.2, 167.9, 165.1, 133.10, 133.05, 129.9, 129.6, 128.4, 119.0, 100.4 (C-1), 100.1 (C-1'), 84.1, 75.6, 74.1, 73.8, 73.1, 72.8, 72.5, 72.1, 71.8, 71.3, 71.2, 69.2, 69.0, 68.0, 67.6, 67.2, 66.6, 62.2, 62.1, 53.2, 50.4, 49.6, 38.0, 36.7, 31.9, 29.9-29.2 (multiple C), 25.7, 23.2, 22.6, 21.11, 20.97, 20.78, 20.73, 20.72 (multiple C), 20.64, 20.63, 20.53, 20.48, 14.1; ES MS calc'd for C₇₄H₁₀₈N₂O₃₁SNa: 1575.6. Found: 1575.6; Anal. calc'd for C₇₄H₁₀₈N₂O₃₁S: C 57.20, H 7.01, N 1.80 Found: C 56.86, H 6.99, N 1.69.

S-(5-acetamido-3,5-dideoxy-*D*-glycero- α -*D*-galacto-non-2-ulopyranosylonic acid)-(2-6)-(6-thio- β -*D*-galactopyranosyl)-(1-4)- β -*D*-glucopyranosyl)-(1 $\rightarrow$ 1)-(2*S*, 3*R*)-2-octadecylamido-pent-4-ene-1,3-diol (**4**)

S-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero- α -*D*-galacto-2-nonulopyranosylonate)-(2 $\rightarrow$ 6)-*O*-(2,3-di-*O*-acetyl-6-thio- β -*D*-galactopyranosyl)-(1 $\rightarrow$ 4)-*O*-(2,3,6-tri-*O*-acetyl- β -*D*-glucopyranosyl)-(1 $\rightarrow$ 1)-(2*S*, 3*R*)-3-*O*-benzoyl-2-

octadecylamido-pent-4-ene-1,3-diol (0.027 g; 27 μ mol) was combined with dry methanol (3.0 mL) and a small piece of sodium (~5mg) was added. The solution was stirred for 24 hours and then water (300 μ L) was added. Stirring was continued for a further 24 hours, then the mixture was neutralized with H⁺ resin, filtered, and concentrated. The residue was loaded onto a preconditioned tC₁₈ SepPak cartridge in 10% methanol, washed extensively with water and eluted with methanol. Concentration of the eluates gave a residue which was further purified by reverse-phase C₁₈ HPLC (methanol/water gradient) to afford compound **4** (0.015g; 84%): $[\alpha]_D + 17^\circ$ (c 0.71, MeOH); ¹H NMR (600 MHz, MeOD, δ) 5.86 (ddd, 1H, H-4_{sphing}, $J_{4,3} = 6.8$ Hz, $J_{4,5a} = 17.2$ Hz, $J_{4,5b} = 10.4$ Hz), 5.27 (ddd, 1H, H-5a_{sphing}, $J = 17.2$ Hz, 1.3 Hz, 1.7 Hz), 5.13 (ddd, 1H, H-5b_{sphing}, $J = 10.4$ Hz, 1.2 Hz, 1.8 Hz), 4.39 (d, 1H, H-1', $J_{1',2'} = 7.5$ Hz), 4.30 (d, 1H, H-1, $J_{1,2} = 7.9$ Hz), 4.19-4.13 (m, 2H, H-1a_{sphing}, H-3_{sphing}), 4.02-3.98 (m, 2H, H-4', H-3_{sphing}), 3.90 (dd, 1H, H-6a, $J_{6a,6b} = 12.0$ Hz $J_{6a,5} = 2.7$ Hz), 3.86-3.77 (m, 4H, H-6b, H-9a'', H-9b'', H-5'), 3.74-3.64 (m, 2H, H-4'', H-5''), 3.61-3.56 (m, 3H, H-1_{sphing}, H-4, H-8''), 3.55-3.40 (m, 6H, H-3, H-3', H-7'', H-6'', H-2', H-5), 3.32 (dd, 1H, H-2, $J_{2,3} = 9.0$ Hz), 2.99 (d, 2H, H-6a', H-6b', $J_{6a,6b} = 7.1$ Hz, 2.89 (dd, 1H, H-3_{eq}'', $J_{3e,4} = 4.8$ Hz, $J_{3e,3a} = 12.5$ Hz), 2.18 (t, 2H, C(O)CH₂, $J = 7.5$ Hz), 1.99 (s, 3H, NHAc), 1.64 (dd, 1H, H-3_{ax}'', $J_{3a,4} = 10.8$ Hz), 1.62-1.54 (m, 2H, C(O)CH₂CH₂), 1.35-1.25 (m, 28H, alkyl), 0.89 (t, 3H, CH₃, $J = 7$ Hz); ¹³C NMR (125 MHz, MeOD, δ) 176.2, 175.5, 174.8, 139.7, 117.0, 104.7, 104.4, 87.6, 80.5, 76.8, 76.6, 76.4, 76.0, 74.9, 74.7, 73.3, 73.2, 72.4, 70.4, 70.1, 64.8, 64.5, 62.0, 54.7, 54.0, 43.2, 37.2, 33.1, 30.78 (multiple C), 30.75, 30.66, 30.49, 30.47, 30.37, 27.1, 23.7, 22.6, 14.4; ESI HRMS calc'd for C₄₆H₈₂O₂₀SNa: 1037.507936. Found: 1037.508042

2-(Trimethylsilyl)ethyl 2-O-benzoyl-4,6-O-benzylidene-3-O-(4-methoxybenzyl)- β -D-galactopyranoside

Triol **11** (2.246 g; 5.6 mmol) was dissolved in acetonitrile (40.0 mL) and benzaldehyde dimethyl acetal (842 μ L; 3.0 eq.). A catalytic amount of *p*-toluenesulfonic acid was added, and the mixture was stirred for 25 minutes and neutralized with triethylamine. Following concentration, the residue was dissolved in pyridine (25.0 mL) and benzoyl chloride (781 μ L; 1.2 eq.). After stirring overnight, the mixture was concentrated, then redissolved in dichloromethane (100 mL) and washed with an equal volume of water. The organic extract was dried (Na₂SO₄) and concentrated. Recrystallization from ethyl acetate-hexanes yielded the title compound (2.526 g; 4.3 mmol; 76%): $[\alpha]_D + 33^\circ$ (c 0.76, CHCl₃); ¹H NMR (500 MHz, CDCl₃, δ) 8.03-7.99 (m, 2H, Ar), 7.58-7.52 (m, 3H, Ar), 7.45-7.41 (m, 2H, Ar), 7.38-7.31 (m, 3H, Ar), 7.14-7.10 (m, 2H, Ar), 6.70-6.66 (m, 2H, Ar), 5.57 (dd, 1H, H-2, $J_{2,1} = 8.0$ Hz, $J_{2,3} = 9.9$ Hz), 5.51 (s, 1H, CHPh), 4.62-4.48 (m, 3H, H-1, CH₂Ar), 4.33 (dd, 1H, H-6a, $J_{6a,5} = 1.3$ Hz, $J_{6a,6b} = 12.2$ Hz), 4.19 (d, 1H, H-4, $J_{4,3} = 3.5$ Hz), 4.05 (dd, 1H, H-6b, $J_{6b,5} = 1.7$ Hz), 3.98 (m, 1H, OCH₂CH₂TMS), 3.73 (s, 3H, OCH₃), 3.69 (dd, 1H, H-3), 3.51 (m, 1H, OCH₂CH₂TMS), 3.39 (s, 1H, H-5), 0.84 (m, 2H, CH₂TMS), -0.10 (s, 9H, Si(CH₃)₃); ¹³C NMR (125 MHz, CDCl₃, δ) 165.1, 159.2, 137.7, 132.7, 130.5, 129.9, 129.8, 129.3, 128.9, 128.2, 128.1, 126.5, 113.6, 101.2, 100.7, 76.6, 73.3,

70.9, 70.5, 69.2, 66.7, 66.5, 55.2, 17.9, -1.5; ES HRMS calc'd for C₃₃H₄₀O₈SiNa: 615.239017. Found: 615.239105. Anal. calc'd for C₃₃H₄₀O₈Si: C 66.87, H 6.80. Found: C 66.55 H 6.83.

2-(Trimethylsilyl)ethyl 2-O-benzoyl-4,6-O-benzylidene-3-O-β-D-galactopyranoside (12)

2-(Trimethylsilyl)ethyl 2-O-benzoyl-4,6-O-benzylidene-3-O-(4-methoxybenzyl)-β-D-galactopyranoside (2.123 g; 3.6 mmol) was dissolved in a mixture of acetonitrile and water (16:1; 68 mL) and ceric ammonium nitrate (6.033 g; 11.0 mmol; 3.0 eq.) was added. After stirring for 30 minutes, the yellow solution was poured into dichloromethane (200 mL) and washed with water (2 x 150 mL). The organics were dried over sodium sulfate, filtered through cotton and concentrated. Chromatography on silica gel with hexanes/ethyl acetate (2:1) as eluant gave **12** (1.431 g; 85%). All spectral data were in accord with those reported for the synthesis of **12** by a different method.¹⁸

2-(Trimethylsilyl)ethyl 2-O-benzyl-4,6-O-benzylidene-3-O-(4-methoxybenzyl)-β-D-galactopyranoside

Triol **11** (0.854g; 2.13 mmol) was dissolved in acetonitrile (20.0 mL) and benzaldehyde dimethyl acetal (960 μL; 3.0 eq.). A catalytic amount of *p*-toluenesulfonic acid was added, and the mixture was stirred for 25 minutes then neutralized with triethylamine. After concentration and further evaporation from toluene, the residue was dissolved in *N,N*-dimethylformamide (10 mL) and sodium hydride (0.170 g of a 60% dispersion in oil; 4.25 mmol; 2 eq.) was added. After stirring for several minutes, benzyl bromide (0.303 mL; 2.56 mmol; 1.2 eq.) was added dropwise, and stirring was continued for a further 3 hours, then diluted with 1 mL of methanol. The reaction mixture was concentrated to roughly 1/3 of its initial volume, ethyl acetate (20 mL) was added, and the solids were removed by filtration. After concentration, the residue was recrystallized from ethanol to give the title compound (0.877 g; 1.51 mmol; 71%): [α]_D + 20.6° (c 1.23, CHCl₃); ¹H NMR (500 MHz, CDCl₃, δ) 7.56-7.52 (m, 2H, Ar), 7.39-7.23 (m, 10H, Ar), 6.84-6.79 (m, 2H, Ar), 5.47 (s, 1H, CHPh), 4.92 (d, 1H, Ar, *J* = 10.9 Hz), 4.76 (d, 1H, Ar, *J* = 10.9 Hz), 4.68 (ABq, 2H, Ar), 4.37 (d, 1H, H-1, *J*_{1,2} = 7.8 Hz), 4.29 (dd, 1H, H-6a, *J*_{6a,5} = 2.4 Hz, *J*_{6a,6b} = 12.2 Hz), 4.07-3.96 (m, 3H, H-4, H-6b, OCH₂CH₂TMS), 3.80 (dd, 1H, H-2, *J*_{2,3} = 9.7 Hz), 3.78 (s, 3H, OCH₃), 3.56 (m, 1H, OCH₂CH₂TMS), 3.52 (dd, 1H, H-3, *J*_{3,4} = 3.7 Hz), 3.28 (bs, 1H, H-5), 1.04 (m, 2H, OCH₂CH₂TMS), 0.01 (s, 9H, Si(CH₃)₃); ¹³C NMR (125 MHz, CDCl₃, δ) 159.2, 139.1, 137.2, 130.5, 129.3, 128.9, 128.2, 128.1, 128.0, 127.4, 126.6, 113.7, 103.2, 101.4, 78.8, 78.6, 75.2, 74.1, 71.6, 69.3, 67.3, 66.4, 55.2, 18.5, -1.4; ES HRMS calc'd for C₃₃H₄₂O₇SiNa: 601.259752. Found: 601.259680. Anal. calc'd for C₃₃H₄₂O₇Si: C 68.48, H 7.31. Found: C 68.27. H 7.40.

2-(Trimethylsilyl)ethyl 2-O-benzyl-4,6-O-benzylidene-β-D-galactopyranoside (13)

2-(Trimethylsilyl)ethyl 2-O-benzyl-4,6-O-benzylidene-3-O-(4-methoxybenzyl)- β -D-galactopyranoside (0.137 g; 0.24 mmol) was dissolved in a mixture of acetonitrile and water (5 mL; 16:1), and then ceric ammonium nitrate (0.390 g; 0.71 mmol; 3 eq) was added. After stirring for one hour, the mixture was diluted with dichloromethane (30 mL) and washed with water (2 x 20 mL), then dried over sodium sulfate, filtered, and concentrated. Chromatography on silica gel with hexanes:ethyl acetate (2:1) as eluant afforded compound **13** (0.083 g; 0.18 mmol; 77%): $[\alpha]_D^{+5}$ (c 0.80, CHCl₃); ¹H NMR (500 MHz, CDCl₃, δ) 7.53-7.47 (m, 2H, Ar), 7.39-7.24 (m, 8H, Ar), 5.54 (s, 1H, CHPh), 4.98 (d, 1H, Ar, $J = 11.3$ Hz), 4.76 (d, 1H, Ar, $J = 11.2$ Hz), 4.40 (d, 1H, H-1, $J_{1,2} = 7.7$ Hz), 4.32 (d, 1H, H-6a, $J_{6a,6b} = 12.4$ Hz), 4.20 (d, 1H, H-4, $J_{4,3} = 3.8$ Hz), 4.08-4.02 (m, 2H, H-6b, OCH₂CH₂TMS), 3.72 (m, 1H, H-3), 3.62-3.55 (m, 2H, H-2, OCH₂CH₂TMS), 3.52 (bs, 1H, H-5), 1.04 (m, 2H, OCH₂CH₂TMS), 0.02 (s, 9H, Si(CH₃)₃); ¹³C NMR (125 MHz, CDCl₃, δ) 138.6, 137.7, 129.0, 128.3, 128.1, 127.9, 127.5, 126.4, 103.1, 101.4, 79.4, 75.6, 74.8, 72.5, 69.2, 67.4, 66.5, 18.6, -1.3; ES HRMS calc'd for C₂₅H₃₄O₆SiNa: 481.20169. Found: 481.20187. Anal. calc'd for C₂₅H₃₄O₆Si: C 65.47, H 7.47. Found: C 65.62. H 7.67.

2-(Trimethylsilyl)ethyl 2-O-benzoyl-4,6-O-benzylidene- β -D-gulopyranoside (14)

Alcohol **13** (0.780 g; 1.6 mmol) was dissolved in freshly distilled dichloromethane (15 mL) and pyridine (0.33 mL; 4.1 mmol; 2 eq.), then cooled to -20 °C with stirring under an argon atmosphere. Trifluoromethanesulfonic anhydride (0.450 mL; 2.6 mmol; 1.6 eq.) was added dropwise over a period of approximately one minute, and stirring was continued for 30 minutes. The reaction mixture was then diluted with dichloromethane (50 mL), washed with water (2 x 50 mL), dried over Na₂SO₄, filtered and concentrated. The residue was dissolved in freshly distilled acetonitrile (12 mL) and solid tetrabutylammonium nitrite (1.430g; 4.95 mmol; 3 eq.) was added. After stirring overnight at room temperature, the solution was concentrated and the residue chromatographed using 3:1 hexanes/ethyl acetate as eluant to afford **14** (0.560g; 1.2 mmol; 72%): $[\alpha]_D^{-39.4}$ (c 0.18, CHCl₃); ¹H NMR (500 MHz, CDCl₃, δ) 8.04 (m, 2H, Ar), 7.60-7.52 (m, 3H, Ar), 7.46-7.42 (m, 2H, Ar), 7.38-7.32 (m, 3H, Ar), 5.56 (s, 1H, CHPh), 5.34 (dd, 1H, H-2, $J_{2,1} = 8.4$ Hz, $J_{2,3} = 3.2$ Hz), 5.05 (d, 1H, H-1), 4.39-4.34 (m, 2H, H-3, H-6a), 4.12-4.00 (m, 3H, H-6b, H-4, OCH₂CH₂TMS), 3.87 (d, 1H, H-5, $J = 1.3$ Hz), 3.57 (ddd, 1H, OCH₂CH₂TMS), 2.24 (d, 1H, OH-3, $J_{OH3,3} = 2.4$ Hz), 0.90 (m, 2H, CH₂TMS), -0.09 ((s, 9H, Si(CH₃)₃); ¹³C NMR (125 MHz, CDCl₃, δ) 165.0, 137.6, 133.2, 129.9, 129.8, 129.0, 128.4, 128.1, 126.4, 101.3, 97.4, 76.2, 71.4, 69.4, 69.3, 66.8, 65.6, 18.0, -1.5; ES HRMS calc'd for C₂₅H₃₂O₇SiNa: 495.18095. Found: 495.18107.

2-(Trimethylsilyl)ethyl 2-O-benzyl-4,6-O-benzylidene- β -D-gulopyranoside (15)

Alcohol **13** (0.150g; 0.33 mmol) was dissolved in freshly distilled dichloromethane (8 mL) and pyridine (0.053 mL; 0.65 mmol; 2 eq.), then cooled to -20 °C with stirring under an argon atmosphere. Trifluoromethanesulfonic anhydride (0.078

mL; 0.46 mmol; 1.4 eq.) was added dropwise, and stirring was continued for 1 hour. The reaction mixture was then diluted with dichloromethane (30 mL), washed with water (2 x 15 mL), dried over Na₂SO₄, filtered and concentrated. The residue was dissolved in freshly distilled acetonitrile (5 mL) and solid tetrabutylammonium nitrite (0.283 g; 0.98 mmol; 3 eq.) was added. No reaction was observed after stirring for one hour at room temperature, so the solution was heated to 50 °C. After stirring for a further two hours the solution was concentrated and the residue chromatographed using 7:2 hexanes/ethyl acetate as eluant to afford **15** (0.060g; 0.13 mmol; 40%); ¹H NMR (500 MHz, CDCl₃, δ) 7.53-7.49 (m, 2H, Ar), 7.40-7.29 (m, 8H, Ar), 5.55 (s, 1H, CHPh), 4.94 (d, 1H, CH₂Ar, *J*_{Ha,Hb} = 11.5 Hz), 4.81 (d, 1H, H-1, *J*_{1,2} = 8.1 Hz), 4.67 (d, 1H, CH₂Ar), 4.35 (d, 1H, H-6a, *J*_{6a,6b} = 12.6 Hz), 4.18 (dd, 1H, H-3, *J*_{3,2} = *J*_{3,4} = 3.1 Hz), 4.12-4.04 (m, 3H, H-4, H-6b, OCH₂CH₂), 3.78 (bs, 1H, H-5), 3.66 (dd, 1H, H-2), 3.59 (m, 1H, OCH₂CH₂), 2.62 (bs, 1H, OH-3), 1.05 (m, 2H, CH₂SiMe₃), 0.18 (s, 9H, SiMe₃); ¹³C NMR (125 MHz, CDCl₃ δ) 138.4, 137.9, 129.1, 128.4, 128.2, 127.82, 127.79, 126.4, 101.3, 99.9, 75.99, 75.96, 73.5, 69.8, 69.4, 67.1, 65.4, 18.5, -1.4; ES HRMS calc'd for C₂₅H₃₄O₆SiNa: 481.20169. Found: 481.20165. Anal. calc'd for C₂₅H₃₄O₆Si: C 65.47, H 7.47. Found: C 65.33. H 7.89.

2-(Trimethylsilyl)ethyl 3-S-acetyl-2-O-benzoyl-4,6-O-benzylidene-β-D-galactopyranoside (16)

Alcohol **14** (0.450 g; 0.95 mmol) was dissolved in dry dichloromethane and pyridine (0.385 mL; 4.76 mmol; 5.0 eq.), then cooled to -20 °C. Trifluoromethanesulfonic anhydride (0.640 mL; 3.80 mmol; 4.0 eq.) was added over approximately five minutes and the mixture was allowed to warm to room temperature. After 50 minutes dichloromethane (50 mL) was added, and the solution was washed with water (2 x 25 mL), dried over sodium sulfate, filtered, and concentrated. The residue was combined with potassium thioacetate (0.650 g; 5.80 mmol; 6.1 eq), and *N,N*-dimethylformamide (10 mL) was added. The mixture was stirred overnight at 60 °C then diluted with ethyl acetate (75 mL), washed with water (2 x 50 mL), dried over sodium sulfate and concentrated. Chromatography on silica gel using hexanes:ethyl acetate (4.5:1-3.5:1) as eluant yielded **15** (0.398 g; 0.75 mmol; 79%): [α]_D + 73.8° (*c* 0.32, CHCl₃); ¹H NMR (600 MHz, CDCl₃, δ) 7.98 (m, 2H, Ar), 7.55-7.50 (m, 3H, Ar), 7.43-7.32 (m, 5H, Ar), 5.54 (s, 1H, CHPh), 5.42 (dd, 1H, H-2, *J*_{2,1} = 7.8 Hz, *J*_{2,3} = 11.5 Hz), 4.71 (d, 1H, H-1), 4.36 (dd, 1H, H-6a, *J*_{6a,5} = 1.4 Hz, *J*_{6a,6b} = 12.3 Hz), 4.22 (dd, 1H, H-3, *J*_{3,4} = 3.3 Hz), 4.11 (dd, 1H, H-4, *J*_{4,5} = 1.0 Hz), 4.08 (dd, 1H, H-6b, *J*_{6b,5} = 1.7 Hz), 4.00 (1H, ddd, OCH₂CH₂TMS), 3.78 (m, 1H, H-5), 3.53 (m, 1H, OCH₂CH₂TMS), 2.18 (s, 3H, SC(O)CH₃), 0.85 (m, 2H, CH₂TMS), -0.12 (s, 9H, Si(CH₃)₃); ¹³C NMR (125 MHz, CDCl₃ δ) 195.0, 165.2, 137.4, 132.9, 129.87, 129.82, 129.0, 128.3, 128.1, 126.3, 101.9, 101.3, 75.9, 69.2, 69.0, 68.4, 66.8, 47.1, 30.5, 17.9, -1.5; ES HRMS calc'd for C₂₇H₃₄O₇SSi Na: 553.169224. Found: 553.169271. Anal. calc'd for C₂₇H₃₄O₇SSi: C 61.11, H 6.46. Found: C 61.55. H 6.33.

2-(Trimethylsilyl)ethyl S-(Methyl 5-acetamido-4,5,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosylonate)-(2-3)-2-O-benzoyl-4,6-O-benzylidene-3-thio- β -D-galactopyranoside

Thioacetate **16** (0.253 g; 0.48 mmol) was dissolved in degassed N,N-dimethylformamide and hydrazinium acetate (0.066g; 0.72 mmol; 1.5 eq.) was added. After stirring under an argon atmosphere for 90 minutes, the reaction mixture was diluted with ethyl acetate (80 mL) and washed with water (2 x 40 mL). After drying over sodium sulfate, the organics were filtered and concentrated. The residue was dissolved in a small volume of dichloromethane and passed through a short pad of silica gel. Concentration of the eluant yielded a white solid (0.224 g) which was dissolved in degassed N,N-dimethylformamide (6.0 mL). Solid sodium hydride (0.021g of a 60% dispersion in mineral oil; 1.1 eq.), and the mixture was stirred for ~one minute before **17** (0.485g; 0.95 mmol; 2 eq.) was added as a solid. The reaction mixture was stirred overnight, then diluted with ethyl acetate (50 mL) and washed successively with 1M HCl, saturated sodium bicarbonate solution, and water then dried over sodium sulfate, filtered and concentrated. Chromatography on a column of silica gel using hexanes/ethyl acetate/acetone (8:7:2) as eluant afforded **18** (0.309g; 0.32 mmol; 67%): $[\alpha]_D + 75.2^\circ$ (c 0.71, CHCl₃); ¹H NMR (600 MHz, CDCl₃, δ) 8.14-8.11 (m, 2H, Ar), 7.56-7.50 (m, 3H, Ar), 7.47-7.43 (m, 2H, Ar), 7.36-7.30 (m, 3H, Ar), 5.62 (ddd, 1H, H-8'), 5.45 (s, 1H, CHPh), 5.22 (dd, 1H, H-2, $J_{2,1} = 7.8$ Hz, $J_{2,3} = 11.8$ Hz), 5.20 (dd, 1H, H-7', $J = 2.2$ Hz, 10.0 Hz), 5.05 (d, 1H, NH, $J_{NH,H-5'} = 10.1$ Hz), 4.95 (d, 1H, H-1, $J_{1,2}$), 4.80 (ddd, 1H, H-4'), 4.37-4.30 (m, 2H, H-9a', H-6a'), 4.09-4.03 (m, 2H, H-9b', H-6b'), 3.98 (ddd, 1H, OCH₂CH₂), 3.90-3.82 (m, 2H, H-5', H-3), 3.76 (bs, 4H, OMe, H-5), 3.73-3.70 (m, 2H, H-4, H-6'), 3.59 (ddd, 1H OCH₂CH₂), 2.56 (dd, 1H, H-3''_{eq}, $J_{3eq,3ax} = 12.7$ Hz, $J_{3eq,4} = 4.6$ Hz), 1.89 (dd, 1H, H-3''_{ax}, $J_{3ax,4} = 12.0$ Hz), 2.20, 2.05, 1.96, 1.82, 1.67, (5 x C(O)CH₃), 0.82 (m, 2H, CH₂SiMe₃), -0.13 (s, 9H, SiMe₃); ¹³C NMR (125 MHz, CDCl₃ δ) 170.9, 170.6, 170.21, 170.49, 170.10, 169.8, 165.8, 137.7, 132.7, 130.7, 130.1, 128.8, 128.2, 128.0, 126.3, 101.38, 101.33, 81.0, 76.2, 73.6, 69.4, 69.3, 69.2, 67.8, 67.5, 66.90, 66.86, 62.5, 52.9, 49.2, 45.7, 37.4, 23.1, 21.5, 20.8 (2C), 20.5, 18.1, -1.5; ES HRMS calc'd for C₄₅H₅₉NO₁₈SSiNa: 984.311688. Found: 984.311756. Anal. calc'd for C₄₅H₅₉NO₁₈SSi: C 56.18, H 6.18 N 1.46. Found: C 55.75. H 6.39. N 1.38.

Note: Attempts to characterize the intermediate thiol were unsuccessful, owing to the rapid formation of a mixture of thiol and disulfide. Exposure of a solution of the thiol in chloroform to the atmosphere for several days resulted in clean conversion to the disulfide, which has been characterized:

2-(Trimethylsilyl)ethyl -2-O-benzoyl-4,6-O-benzylidene-3-thio- β -D-galactopyranoside disulfide

$[\alpha]_D + 106.7^\circ$ (c 1.36, CHCl_3); ^1H NMR (500 MHz, CDCl_3 , δ) 8.14-8.10 (m, 2H, Ar), 7.63-7.59 (m, 1H, Ar), 7.52-7.45 (m, 4H, Ar), 7.33-7.28 (m, 3H, Ar), 5.45 (s, 1H, CHPh), 5.26 (dd, 1H, H-2, $J_{2,1} = 7.7$ Hz, $J_{2,3} = 11.6$ Hz), 4.28 (d, 1H, H-1), 4.18 (dd, 1H, H-6a, $J_{6a,6b} = 12.3$ Hz, $J_{2,3} = 1.3$ Hz), 4.14 (d, 1H, H-4, $J_{4,3} = 3.2$ Hz), 3.95-3.83 (m, 2H, OCH_2CH_2 , H-6b), 3.44 (m, 1H, OCH_2CH_2), 3.08 (dd, 1H, H-3), 2.89 (bs, 1H, H-5), 0.81 (m, 2H, CH_2TMS), -0.11 (s, 9H, SiMe_3); ^{13}C NMR (125 MHz, CDCl_3 , δ) 164.9, 137.4, 133.2, 130.3, 129.9, 128.8, 128.5, 128.0, 126.2, 101.5, 101.1, 74.6, 70.2, 68.9, 68.5, 66.6, 58.5, 17.9, -1.5; ES HRMS calc'd for $\text{C}_{50}\text{H}_{62}\text{O}_{12}\text{S}_2\text{Si}_2\text{Na}$: 997.311898. Found: 997.311601. Anal. calc'd for $\text{C}_{50}\text{H}_{62}\text{O}_{12}\text{S}_2\text{Si}_2$: C 61.57, H 6.41. Found: C 61.37, H 6.73.

2-(Trimethylsilyl)ethyl (2-O-benzoyl-4,6-O-benzylidene-3-O-(4-methoxybenzyl)- β -D-galactopyranosyl)-(1-4)-2,3,6-tri-O-benzoyl- β -D-glucopyranoside (22)

To a solution of **21** (0.186 g; 0.33 mmol) in dry N,N-dimethylformamide (6.0 mL) was added benzaldehyde dimethyl acetal (95 μL ; 0.63 mmol; 1.9 eq.). *p*-Toluenesulfonic acid monohydrate (10 mg) was added, and the mixture was stirred for 13 hours at room temperature, then neutralized with triethylamine and concentrated. The crude residue was taken up in pyridine (5 mL) and benzoyl chloride (305 μL ; 2.64 mmol; 8 eq.), and stirred overnight. The mixture was concentrated, and the residue dissolved in dichloromethane (45 mL), washed with 1M HCl, followed by saturated NaHCO_3 solution and water, then dried over Na_2SO_4 . Following evaporation to dryness, the residue was chromatographed in toluene/ethyl acetate (10:1) to afford as a white solid **22** (0.215 g, 70%): $[\alpha]_D + 75^\circ$ (c 0.83, CHCl_3). ^1H NMR (600 MHz, CDCl_3 , δ) 7.96-7.83 (8H, Ar), 7.56-7.21 (17H, Ar), 7.01 (2H, Ar), 6.63 (2H, Ar), 5.75 (t, 1H, $J_{2,1} = J_{2,3} = 9.1$ Hz, H-3), 5.49 (dd, 1H, $J_{2',1'} = 8.1$ Hz, $J_{2',3'} = 10.1$ Hz, H-2'), 5.27 (dd, 1H, $J_{2,1} = 7.8$ Hz, $J_{2,3} = 9.3$ Hz, H-2), 5.25 (s, 1H, CHPh), 4.65 (d, 1H, $J_{1,2} = 7.8$ Hz, H-1), 4.63 (d, 1H, $J_{1',2'} = 8.0$ Hz, H-1'), 4.57 (dd, 1H, $J_{6a,6b} = 11.8$ Hz, $J_{6a,5} = 2.0$ Hz, H-6a), 4.44 (d, 1H, $J_{\text{gem}} = 12.55$ Hz, $\text{CH}_2\text{PhOCH}_3$), 4.40-4.33 (m, 2H, H-6b, CH_2PhOMe), 4.09 (t, 1H, $J_{4,3} = J_{4,5} = 9.1$ Hz, H-4), 3.92 (d, 1H, $J_{4',3'} = 3.1$ Hz, H-4'), 3.86-3.77 (m, 2H, $\text{CH}_2\text{CH}_2\text{Si}$, H-5), 3.71 (s, 3H, $\text{CH}_2\text{PhOCH}_3$), 3.67 (d, 1H, $J_{6'a-6'b} = 11.58$ Hz, H-6'a), 3.65-3.44 (m, 3H, H-6'b, H-3', $\text{CH}_2\text{CH}_2\text{Si}$), 2.75 (s, 1H, H-5'), 0.76 (m, 2H, $\text{CH}_2\text{CH}_2\text{Si}$), -0.19 (s, (9H, $\text{Si}(\text{CH}_3)_3$). ^{13}C NMR (125 MHz, CDCl_3 , δ) 165.5, 165.2, 164.81, 164.76, 159.0, 137.5, 132.84, 132.78, 132.74, 132.73, 129.78, 129.74, 129.67, 129.66, 129.65, 129.56, 129.52, 129.0, 129.4, 129.0, 128.7, 128.17, 128.14, 128.12, 128.11, 127.9, 126.5, 113.6, 101.63, 100.90 ($\text{C}1'$), 100.02 ($\text{C}1$), 76.5, 74.2, 72.8, 72.6, 72.4, 71.2, 70.4, 68.2, 67.4, 66.7, 62.8, 55.2, 17.90, -1.48; ES HRMS calc'd for $\text{C}_{60}\text{H}_{63}\text{O}_{16}\text{SiNa}$: 1089.3705. Found: 1089.3697. Anal. calc'd for $\text{C}_{60}\text{H}_{63}\text{O}_{16}\text{Si}$: C 67.46, H 5.94. Found: C 67.32 H 5.84.

2-(Trimethylsilyl)ethyl-(2-O-benzoyl-4,6-O-benzylidene- β -D-galactopyranosyl)-(1-4)-2,3,6-tri-O-benzoyl- β -D-glucopyranoside (23)

Compound **22** (3.980 g; 3.7 mmol) was dissolved in 95% aqueous acetonitrile (125 mL), and ceric ammonium nitrate (12.267 g; 22.4 mmol; 6 eq.) was added. The solution was stirred at room temperature for 40 minutes and was then diluted with dichloromethane (500 mL), washed with water (2x250 mL), dried over anhydrous sodium sulfate, and concentrated. Crystallization of the solid residue from acetonitrile/water afforded compound **23** (3.032 g; 3.20 mmol; 86%). Column chromatography of the mother liquor in ethyl acetate/chloroform (1:49) yielded additional product (0.254 g; 0.26 mmol; 7%): $[\alpha]_D^{+29}$ (c 0.73, CHCl_3). ^1H NMR (500 MHz, CDCl_3 , δ) 8.02-7.88 (8H, Ar), 7.60-7.24 (17H, Ar), 5.75 (t, 1H, $J_{3,2} = J_{3,4} = 9.1$ Hz, H-3), 5.32 (dd, 1H, $J_{2,1} = 7.8$ Hz, $J_{2,3} = 9.6$ Hz, H-2), 5.30 (s, 1H, CHPh), 5.27 (dd, 1H, $J_{2',1'} = 8.0$ Hz, $J_{2',3'} = 10.0$ Hz, H-2'), 4.67 (d, 1H, $J_{1,2} = 7.8$ Hz, H-1), 4.63 (d, 1H, $J_{1',2'} = 7.9$ Hz, H-1'), 4.57 (dd, 1H, $J_{6a,6b} = 11.8$ Hz, $J_{6a,5} = 2.1$ Hz, H-6a), 4.44 (dd, 1H, $J_{6b,6a} = 11.8$ Hz, $J_{6b,5} = 4.9$ Hz, H-6b), 4.12 (t, 1H, $J_{4,3} = J_{4,5} = 9.5$ Hz, H-4), 3.97 (d, 1H, $J_{4',3'} = 3.2$ Hz, H-4'), 3.83 (m, 2H, H-5, $\text{CH}_2\text{CH}_2\text{Si}$), 3.70 (dd, 1H, $J_{3',2'} = 10.6$ Hz, $J_{3',4'} = 3.2$ Hz, H-3'), 3.65 (dd, 1H, $J_{6'a,6'b} = 12.4$ Hz, $J_{6'a,5'} = 1.0$ Hz, H-6'a), 3.57 (dd, 1H, $J_{6'b,6'a} = 12.4$, $J_{6'b,5'} = 1.8$ Hz, H-6'b), 3.50 (ddd, 1H, CHCH_2Si), 2.93 (d, 1H, $J_{5',6'a} = 1.0$ Hz, H-5'), 2.38 (d, 1H, $J_{3'\text{OH},3'} = 11.6$ Hz, $\text{OH}3'$), 0.81 (ddd, 2H, $\text{CH}_2\text{CH}_2\text{Si}$), -0.17 (s, 9H, $\text{Si}(\text{CH}_3)_3$). ^{13}C NMR (125 MHz, CDCl_3 , δ) 165.7, 165.6, 165.2, 164.9, 137.2, 133.1, 133.0, 132.9, 132.82, 129.76, 129.73, 129.70, 129.69, 129.65, 129.60, 129.5, 129.2, 129.1, 128.28, 128.25, 128.157, 128.151, 128.0, 126.5, 101.23, 101.19 ($\text{C}1'$), 100.2 ($\text{C}1$), 76.95, 75.7, 73.8, 73.1, 72.3, 71.5, 69.2, 68.2, 67.4, 65.8, 62.8, 17.9, -1.5. ES HRMS calc'd for $\text{C}_{52}\text{H}_{55}\text{O}_{15}\text{SiNa}$: 969.31297, found: 969.31314. Anal. calc'd for $\text{C}_{52}\text{H}_{55}\text{O}_{15}\text{Si}$: C 65.95, H 5.75. Found: C 65.95, H 5.75.

2-(Trimethylsilyl)ethyl-(2-O-benzoyl-4,6-O-benzylidene- β -D-gulopyranosyl)-(1-4)-2,3,6-tri-O-benzoyl- β -D-glucopyranoside.

Crystalline **23** (0.918 g; 0.97 mmol) was dissolved in freshly distilled dichloromethane (20 mL) and pyridine (0.470 mL; 5.81 mmol; 6.0 eq) with stirring under an argon atmosphere. The solution was cooled to -40 $^{\circ}\text{C}$, and trifluoromethanesulfonic anhydride (0.650 mL; 3.88 mmol; 4.0 eq) was added dropwise over approximately one minute. After 70 minutes at constant temperature, the reaction mixture was diluted with dichloromethane (40 mL) and washed successively with 1M HCl, saturated NaHCO_3 solution, water. The organic layer was then dried over Na_2SO_4 , filtered, and concentrated. The crude residue was taken up in N,N -dimethylformamide (15 mL), and tetrabutylammonium nitrite (2.21 g; 7.76 mmol; 8.0 eq.) was added. The mixture was stirred overnight at room temperature and then evaporated to dryness. The residue was taken up in dichloromethane (20 mL), washed with water, dried (Na_2SO_4), and then concentrated. Chromatography in methanol/dichloromethane (1:99) gave the title compound (0.837 g; 0.88 mmol; 91%): $[\alpha]_D^{+5}$ (c 0.84, CHCl_3). ^1H NMR (500 MHz, CDCl_3 , δ) 8.14-7.89 (8H, Ar), 7.60-7.22 (17H, Ar), 5.74 (t, 1H, $J_{3,2} = J_{3,4} = 9.5$ Hz, H-3), 5.33 (dd, 1H, $J_{2,1} = 7.8$ Hz, $J_{2,3} = 9.6$ Hz, H-2), 5.30-5.27 (m, 2H, H-2', CHPh), 5.05 (d, 1H, $J_{1',2'} = 8.4$ Hz, H-1'), 4.67 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1), 4.59 (dd, 1H, $J_{6a,6b} = 11.9$ Hz, $J_{6a,5} =$

4.6 Hz, H-6a), 4.54 (dd, 1H, $J_{6b,6a} = 11.9$ Hz, $J_{6b,5} = 2.3$ Hz, H-6b), 4.21 (t, 1H, $J_{3',2'} = J_{3',4'} = 3.1$ Hz, H-3'), 4.13 (t, 1H, $J_{4,3} = J_{4,5} = 9.5$ Hz, H-4), 3.88 (ddd, 1H, $\text{CH}_2\text{CH}_2\text{Si}$), 3.83-3.78 (m, 2H, H-4', H-5), 3.62 (dd, 1H, $J_{6'a,6'b} = 11.8$ Hz, $J_{6'a,5'} = 1.1$ Hz), 3.57-3.47 (m, 2H, H-6b, $\text{CH}_2\text{CH}_2\text{Si}$), 3.29 (d, 1H, $J_{5',6'a} = 1.1$ Hz, H-5'), 0.80 (ddd, 2H, $\text{CH}_2\text{CH}_2\text{Si}$), -0.15 (s, 9H, $\text{Si}(\text{CH}_3)_3$). ^{13}C NMR (125 MHz, CDCl_3 , δ) 165.9, 165.20, 165.18, 165.12, 137.6, 133.3, 133.0, 132.9, 132.7, 129.75, 129.74, 129.71, 129.65 (2C), 129.55, 129.1, 128.8, 128.5, 128.3, 128.13, 128.08, 127.92, 127.90, 126.4, 101.0, 100.26 (C1), 98.50 (C1'), 76.8, 75.7, 73.8, 73.1, 72.3, 71.5 (C3'), 69.2, 68.2, 67.4, 65.8, 62.8, 18.0, -1.4; ES HRMS calc'd for $\text{C}_{52}\text{H}_{55}\text{O}_{15}\text{SiNa}$: 969.31297. Found: 969.31315. Anal. calc'd for $\text{C}_{52}\text{H}_{55}\text{O}_{15}\text{Si}$: C 65.95, H 5.75. Found: C 66.05, H 5.74.

2-Trimethylsilyl(ethyl) (3-S-acetyl-2-O-benzoyl-4,6-O-benzylidene- β -D-galactopyranosyl)-(1-4)-2,3,6-tri-O-benzoyl- β -D-glucopyranoside (24)

2-(Trimethylsilyl)ethyl-(2-O-benzoyl-4,6-O-benzylidene- β -D-gulopyranosyl)-(1-4)-2,3,6-tri-O-benzoyl- β -D-glucopyranoside (0.615 g; 0.65 mmol) was dissolved in dichloromethane (10.0 mL) containing pyridine (1.05 mL; 13 mmol; 20 eq.). The solution was cooled to -65 °C and trifluoromethanesulfonic anhydride (0.41 mL, 3.81 mmol, 12.0 eq.) was added dropwise over a period of roughly one minute. The reaction mixture was allowed to warm to room temperature over 30 minutes. After stirring for a total of 1 hour, dichloromethane (50 mL) was added, and solution was washed with water (75 mL), dried over sodium sulfate, filtered, and concentrated (<25 °C bath temperature). The residue was taken up in *N,N*-dimethylformamide (10.0 mL), and potassium thioacetate (0.445 g; 3.90 mmol; 6.0 eq) was added. The suspension was stirred for one hour at 70 °C, then concentrated. The residue was dissolved in ethyl acetate (50 mL), washed with water (3x50 mL), dried over sodium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel using a mixture of hexanes/ethyl acetate (7:2 – 11:4) as eluant, affording **24** (0.516 g; 0.51 mmol; 79%): $[\alpha]_D^{+118}$ (c 0.8, CHCl_3); ^1H NMR (600 MHz, CDCl_3 , δ) 8.0-7.8 (8H, Ar), 7.7-7.2 (17H, Ar), 5.79 (dd, 1H, H-3, $J_{3,2} = J_{3,4} = 9.0$ Hz), 5.36 (dd, 1H, H-2', $J_{2',1'} = 7.9$ Hz, $J_{2',3'} = 11.5$ Hz), 5.29 (s, 1H, CHPh), 5.26 (dd, 1H, H-2, $J_{2,1} = 7.6$ Hz, $J_{2,3} = 9.3$ Hz), 4.81 (d, 1H, H-1), 4.65 (d, 1H, H-1'), 4.59 (dd, 1H, H-6a, $J_{6a,5} = 2.2$ Hz, $J_{6a,6b} = 11.7$ Hz), 4.26 (dd, 1H, H-6b, $J_{6b,5} = 4.6$ Hz), 4.16 (dd, 1H, H-4, $J_{4,3} = J_{4,5} = 9.0$ Hz), 4.04 (dd, 1H, H-3') 3.81 (m, 3H, H-4', H-5, OCH_2CH_2), 3.77 (dd, 1H, H-6a', $J_{6'a,5'} = 1.3$ Hz, $J_{6'a,6'b} = 12.5$ Hz), 3.48 (m, 2H, H-6'b, OCH_2CH_2), 2.96 (m, 1H, H-5'), 2.08 (s, 3H, $\text{C}(\text{O})\text{CH}_3$), 0.76 (m, 2H, CH_2TMS), -0.19 (s, 9H, $\text{Si}(\text{CH}_3)_3$); ^{13}C NMR (100 MHz, CDCl_3 , δ) 194.8, 165.5, 165.3, 165.1, 164.8, 137.3, 133.1, 133.0, 132.9, 132.8, 129.81, 129.76, 129.70, 129.66, 129.62, 129.61, 129.58, 128.84, 128.83, 128.4, 128.3, 128.2, 128.1, 128.0, 126.3, 102.6 (C1'), 100.9, 100.0 (C1), 75.3, 74.4, 72.7, 72.5, 69.5, 68.4, 68.0, 67.3, 62.4, 46.8 (C3'), 30.4, 17.8, -1.6; ESI HRMS calc'd for $\text{C}_{54}\text{H}_{56}\text{O}_{15}\text{SSi}$: 1027.300692. Found: 1027.300228. Anal. calc'd for $\text{C}_{54}\text{H}_{56}\text{O}_{15}\text{SSi}$: C 64.52, H 5.62. Found: C 64.34, H 5.71.

2-(Trimethylsilyl)ethyl S-(Methyl 5-acetamido-4,5,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosylonate)-(2-3)-(2-O-benzoyl-4,6-O-benzylidene-3-thio- β -D-galactopyranosyl)-(1-4)-2,3,6-tri-O-benzoyl- β -D-glucopyranoside (25)

Thioacetate **24** (0.313 g; 0.31 mmol) was dissolved in dry, degassed *N,N*-dimethylformamide (5.0 mL) and argon was bubbled through the solution. Hydrazinium acetate (0.057 g; 0.62 mmol; 2.0 eq.) was added and the mixture was stirred for 1.5 hours, then diluted with ethyl acetate (100 mL), washed with water, dried over sodium sulfate, and concentrated. The residue was dissolved in degassed dichloromethane and passed through a short plug of silica gel (4cm), using 2:1 hexanes/ethyl acetate (degassed) as the mobile phase. After concentration the residue was combined with 1,4,10-Trioxa-7,13-diazacyclopentadecane (0.010 g; 0.05 mmol; 0.15 eq) and dissolved in dry, degassed *N,N*-dimethylformamide (5.0 mL). Sodium hydride (12.5 mg; 60% dispersion in oil; 1.5 eq.) was added, followed after 10 minutes by solid Methyl (5-acetamido-4,7,8,9-O-acetyl-3,5-dideoxy-D-glycero- β -D-galacto-2-nonulopyranosyl chloride)onate (0.210 g; 0.41 mmol; 1.5 eq.). After stirring overnight, the reaction mixture was diluted with ethyl acetate (50 mL), washed with saturated sodium bicarbonate solution, then water, and the organic layers dried over sodium sulfate and concentrated. The residue was chromatographed on silica gel using a gradient of 1% to 2% methanol in dichloromethane as eluant, affording **25** (0.292g; 0.20 mmol; 65%): $[\alpha]_D^{+71}$ (*c* 0.83, CHCl₃). ¹H NMR (600 MHz, CDCl₃, δ) 8.14-8.10 (m, 2H, Ar), 7.96-7.92 (m, 4H, Ar), 7.89-7.86 (m, 2H, Ar), 7.43-7.17 (m, 15H, Ar), 5.72 (dd, 1H, H-3, $J_{3,2} = J_{3,4} = 9.3$ Hz), 5.65 (ddd, 1H, H-8'', $J_{8'',7''} = 10.1$ Hz, $J_{8'',9a''} = 2.5$ Hz, $J_{8'',9b''} = 4.8$ Hz), 5.27 (dd, 1H, H-2, $J_{2,1} = 7.8$ Hz, $J_{2,3} = 9.6$ Hz), 5.23 (dd, 1H, H-7, $J_{7,6} = 2.4$ Hz), 5.21-5.14 (m, 3H, CHPh, H-1', H-2'), 4.98 (d, 1H, NH, $J_{NH,5''} = 9.9$ Hz), 4.77 (ddd, 1H, H-4'', $J_{4'',5''} = 10.4$ Hz, $J_{4'',3'e} = 4.6$, $J_{4'',3'a} = 11.7$ Hz), 4.62 (d, 1H, H-1), 4.68 (dd, 1H, H-6a, $J_{6a,5} = 2.3$ Hz, $J_{6a,6b} = 11.8$ Hz), 4.40 (dd, 1H, H-9a'', $J_{9a'',9b''} = 12.8$ Hz), 4.31-4.25 (m, 2H, H-4, H-6b), 4.19 (dd, 1H, H-9b''), 3.86-3.73 (m, 5H, OCH₂CH₂, H-5, H-3', H-4', H-5'), 3.69-3.65 (m, 4H, OCH₃, H-6''), 3.57 (dd, 1H, H-6a', $J_{6a',6b'} = 12.2$ Hz, $J_{6a',5'} = 1.85$ Hz), 3.47-3.41 (m, 2H, OCH₂CH₂, H-6b'), 3.30 (m, 1H, H-5'), 2.49 (dd, 1H, H-3e'', $J_{3e'',3a''} = 12.7$ Hz), 2.13, 1.98, 1.92, 1.80 (4 x s, 12H, C(O)CH₃), 1.78 (dd, 1H, H-3a''), 1.70, 1.58 (2 x s, 6H, C(O)CH₃), 0.75 (m, 2H, CH₂TMS), -0.2 (s, 9H, Si(CH₃)₃); ¹³C NMR (100 MHz, CDCl₃, δ) 170.8, 170.7, 170.15, 170.10, 169.8, 169.6, 165.5, 165.4, 165.3, 165.2, 137.6, 132.9, 132.8, 132.7, 132.5, 130.2, 130.0, 129.83, 129.77, 129.71, 129.64, 129.62, 129.59, 128.6, 128.3, 128.13, 128.12, 128.0, 127.9, 126.3, 101.6 (C1'), 101.1, 100.0 (C1), 81.1, 76.2, 75.6, 74.1, 73.5, 73.0, 72.4, 69.3, 69.1, 68.2, 67.8, 67.2, 67.2, 66.6, 63.0, 62.3, 59.5, 52.8, 49.2, 45.5, 38.1, 37.2, 31.9, 31.2, 29.6, 23.1, 21.3, 20.9, 20.7, 20.6, 17.8, -1.6; ES MS calc'd for C₇₂H₈₁O₂₆SSiNa: 1458.4. Found: 1458.4. Anal. calc'd for C₇₂H₈₁O₂₆SSi: C 60.20, H 5.68. Found: C 60.01, H 5.87.

2-(Trimethylsilyl)ethyl S-(Methyl 5-acetamido-4,5,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosylonate)-(2-3)-(2-O-benzoyl-3-thio- β -D-galactopyranosyl)-(1-4)-2,3,6-tri-O-benzoyl- β -D-glucopyranoside

The trisaccharide **25** (0.201 g; 0.14 mmol) was dissolved in 80% acetic acid solution (10.0 mL) and stirred at 45 °C for a period of 48 hours. After this time, the reaction mixture was concentrated on a rotary evaporator while the bath temperature was maintained below room temperature. The residue was evaporated several times from toluene, then chromatographed on silica gel using 2-2.5% methanol in dichloromethane as eluant to give the diol (0.153 g; 0.11 mmol; 81%): $[\alpha]_D +46^\circ$ (c 1.2, CHCl₃); ¹H NMR (600 MHz, CDCl₃, δ) 8.11 (m, 2H, Ar), 8.00 (m, 2H, Ar), 7.96 (m, 2H, Ar), 7.90 (m, 2H, Ar), 7.56-7.32 (m, 12H, Ar), 5.60 (dd, 1H, H-3, $J_{3,2} = J_{3,4} = 9.2$ Hz), 5.56 (ddd, 1H, H-8'', $J_{8'',7''} = 10.1$ Hz, $J_{8'',9a''} = 2.5$ Hz, $J_{8'',9b''} = 4.0$ Hz), 5.39 (dd, 1H, H-2, $J_{2,1} = 7.8$ Hz, $J_{2,3} = 9.6$ Hz), 5.21 (dd, 1H, H-7'', $J_{7'',6''} = 2.3$ Hz), 5.12 (dd, 1H, H-2', $J_{2',1'} = 7.6$ Hz, $J_{2',3'} = 11.6$ Hz), 5.07 (d, 1H, H-1'), 4.96 (d, 1H, NH, $J_{NH,5''} = 10.0$ Hz), 4.76 (ddd, 1H, H-4'', $J_{4'',3e''} = 4.7$ Hz, $J_{4'',3a''} = 11.7$ Hz, $J_{4'',5''} = 10.3$ Hz), 4.63 (m, 2H, H-1, H-6b), 4.37 (m, 2H, H-6b, H-9a''), 4.25 (dd, 1H, H-4, $J_{4,5} = 9.2$ Hz), 4.21 (dd, 1H, H-9b'', $J_{9b'',9a''} = 12.9$ Hz), 3.84 (m, 1H, OCH₂CH₂), 3.77-3.70 (m, 2H, H-5, H-5''), 3.68-3.64 (m, 4H, OCH₃, H-6''), 3.56-3.45 (m, 3H, H-3', H-5', OCH₂CH₂), 3.30 (m, 1H, H-4'), 3.26 (m, 1H, H-6a'), 3.14 (m, 1H, H-6b'), 2.57 (d, 1H, OH-4', $J_{OH-4',H4'} = 4.9$ Hz), 2.52 (dd, 1H, H-3e'', $J_{3e'',3a''} = 12.8$ Hz), 2.08, 1.93, 1.86 (3 x s, 9H, C(O)CH₃), 1.82 (dd, 1H, H-3a''), 1.79, 1.64 (2 x s, 6H, C(O)CH₃), 1.55 (m, 1H, OH-6'), 0.79 (m, 2H, OCH₂CH₂Si), -0.18 (s, 9H, Si(CH₃)₃); ¹³C NMR (125 MHz, CDCl₃, δ) 170.7(2C), 170.1, 169.91, 169.87, 169.2, 133.1, 133.0 (2C), 132.8, 130.19, 130.17, 130.1, 130.0, 129.75, 129.66, 129.65, 129.5, 128.5, 128.4, 128.3, 128.2, 101.5 (C1'), 100.1(C1), 81.4, 75.5, 75.3, 74.1, 73.4, 73.0, 71.9, 70.3, 69.2, 69.1, 67.3, 67.2, 66.4, 62.9, 62.7, 62.0, 53.0, 49.2, 47.8, 37.2, 23.14, 21.1, 20.9, 20.7, 20.5, 17.8, -1.6; ES MS calc'd for C₆₅H₇₇NO₂₆SSiNa: 1370.4. Found: 1370.4. Anal. calc'd for C₆₅H₇₇NO₂₆SSi: C 57.90, H 5.76. Found: C 57.81, H 5.97.

2-(Trimethylsilyl)ethyl S-(Methyl 5-acetamido-4,5,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero- α -D-galacto-2-nonulopyranosylonate)-(2-3)-(4,6-di-O-acetyl-2-O-benzoyl-3-thio- β -D-galactopyranosyl)-(1-4)-2,3,6-tri-O-benzoyl- β -D-glucopyranoside

The diol (0.101 g; 75 μ mol) was dissolved in pyridine/acetic anhydride (1:1) and stirred overnight at ambient temperature. After concentration of the solution, chromatography on silica gel with 1.5% methanol in dichloromethane as eluant afforded the title compound (0.102 g; 71 μ mol ; 95%): $[\alpha]_D +55^\circ$ (c 1.2, CHCl₃); ¹H NMR (600 MHz, CDCl₃, δ) 8.11 (m, 2H, Ar), 8.01-7.96 (m, 4H, Ar), 7.90 (m, 2H, Ar), 7.55 (m, 1H, Ar), 7.48-7.31 (m, 11H, Ar), 5.61 (dd, 1H, H-3, $J_{3,2} = J_{3,4} = 9.5$ Hz), 5.56 (ddd, 1H, H-8'', $J_{8'',7''} = 10.3$ Hz, $J_{8'',9a''} = J_{8'',9b''} = 3.0$ Hz), 5.37 (dd, 1H, H-2, $J_{2,1} = 7.9$ Hz), 5.23 (dd, 1H, H-7'', $J_{7'',6''} = 2.4$ Hz), 5.10 (d, 1H, H-1', $J_{1',2'} = 7.6$ Hz), 4.99-4.93 (m, 2H, H-2', NH), 4.75 (ddd, 1H, H-4'', $J_{4'',3e''} = 4.5$ Hz, $J_{4'',3a''} = 11.7$ Hz, $J_{4'',5''} = 10.6$ Hz), 4.68 (dd, 1H, H-4', $J_{4',3'} = 3.0$ Hz, $J_{4',5'} = 0.7$ Hz), 4.65

(dd, 1H, H-6a, $J_{6a,5} = 1.9$ Hz, $J_{6a,6b} = 12.0$ Hz), 4.61 (d, 1H, H-1), 4.38 (m, 2H, H-6b, H-9a"), 4.27 (dd, 1H, H-9b", $J_{9b",9a"} = 13.1$ Hz), 4.22 (dd, 1H, H-4, $J_{4,5} = 9.5$ Hz), 3.91-3.82 (m, 2H, OCH₂CH₂, H-5), 3.75 (s, 3H, OCH₃), 3.74-3.66 (m, 3H, H-5, H-3', H-5"), 3.58 (dd, 1H, H-6", $J_{6",5"} = 10.8$ Hz), 3.47 (ddd, 1H, OCH₂CH₂), 3.41 (dd, 1H, H-6a', $J_{6a',5} = 6.8$ Hz, $J_{6a',6b'} = 11.4$ Hz), (dd, 1H, H-6a', $J_{6b',5} = 6.6$ Hz), 2.48 (dd, 1H, H-3e, $J_{3e',3a'} = 12.8$ Hz), 2.08, 2.01, 1.91, 1.84, 1.82, 1.78 (6 x s, 18H, C(O)CH₃), 1.72 (dd, 1H, H-3a"), 1.61 (s, 3H, C(O)CH₃), 0.79 (m, 2H, OCH₂CH₂Si), -0.18 (s, 9H, Si(CH₃)₃); ¹³C NMR (125 MHz, CDCl₃, δ) 170.71, 170.66, 170.2, 170.1, 170.0, 169.9, 169.8, 168.8, 165.8, 165.23, 165.18, 165.12, 133.0, 132.9, 132.79, 132.78, 130.3, 130.1, 130.0, 129.8, 129.66, 129.59, 129.56, 129.0, 128.4, 128.23, 128.20, 128.0, 100.8 (C1'), 100.4 (C1), 81.2, 74.8, 73.3, 73.2, 73.0, 72.1, 71.9, 69.3, 69.2, 68.5, 67.4, 67.1, 66.1, 62.8, 61.8, 61.7, 53.0, 49.1, 45.0, 36.7, 23.1, 20.9 (2C), 20.68, 20.66, 20.5, 20.3, 17.8, -1.6; ES MS calc'd for C₆₉H₈₁NO₂₈SSiNa: 1454.4. Found: 1454.4. Anal. calc'd for C₆₉H₈₁NO₂₈SSi: C 57.85, H 5.70, N 0.98 Found: C 57.71, H 6.04, N 0.91.

S-(Methyl 5-acetamido-4,5,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero- α -*D*-galacto-2-nonulopyranosylonate)-(2-3)-(4,6-di-*O*-acetyl-2-*O*-benzoyl-3-thio- β -*D*-galactopyranosyl)-(1-4)-2,3,6-tri-*O*-benzoyl- α / β -*D*-glucopyranose

The trisaccharide (0.092 g; 64 μ mol) was dissolved in a mixture of anhydrous toluene (2.0 mL) and trifluoroacetic acid (3.0 mL) with stirring under argon. After two hours, the reaction was judged to be complete by TLC, and the solution was diluted with toluene (5.0 mL) and concentrated at room temperature to a volume of approximately 1 mL. The process was repeated three times, and then evaporated to dryness. Chromatography of the residue on silica gel with 2.5% methanol in dichloromethane as eluant afforded the hemiacetal as a mixture of anomers (82 mg; 62 μ mol; 96%): ES MS calc'd for C₆₄H₆₉NO₂₈SNa: 1354.4. Found: 1354.4. Anal. calc'd for C₆₄H₆₉NO₂₈S: C 57.70, H 5.22. Found: C 57.58, H 5.52.

S-(Methyl 5-acetamido-4,5,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero- α -*D*-galacto-2-nonulopyranosylonate)-(2-3)-(4,6-di-*O*-acetyl-2-*O*-benzoyl-3-thio- β -*D*-galactopyranosyl)-(1-4)-2,3,6-tri-*O*-benzoyl- β -*D*-glucopyranosyl)-(1 $\rightarrow$ 1)-(2*S*, 3*R*)-2-azido-3-*O*-benzoyl-4-pentene-1,3-diol (**26**)

The hemiacetal (0.088 g; 66 μ mol) was concentrated from dry toluene (10 mL) and dissolved in dichloromethane (4.0 mL) containing trichloroacetonitrile (0.132 mL; 1.32 mmol; 20 eq.). 1,8-diazabicyclo-[5.4.1]-undec-7-ene (5.0 μ L; 0.5 eq) was added, and the reaction mixture was stirred under argon for 90 minutes, then concentrated to approximately one quarter of the initial volume (bath temperature < room temp). The remaining solution was passed through a short plug (2cm) of silica gel using toluene/acetone (5:2) as eluant. The residue obtained after concentration was combined with (2*S*, 3*R*)-2-azido-3-*O*-benzoyl-4-pentene-1,3-diol (0.020g; 86 μ mol; 1.3 eq.), and the mixture was dried in vacuo for one hour. Drierite (~ 0.1 g) was added, followed by dichloromethane, and the

mixture was stirred under an argon atmosphere for 30 minutes, then cooled to –15 °C. After this time boron trifluoride-diethyl etherate (25 µL; 0.2 mmol; 3 eq) was added, and stirring was continued for 24 hours. The mixture was made basic with pyridine (0.1 mL) diluted with dichloromethane (25 mL), filtered, washed with water, and the organic layers dried over sodium sulfate then filtered and concentrated. The residue was chromatographed on silica gel employing toluene acetone (5:2) as eluant to afford **26** (0.082g; 53 µmol; 80%): $[\alpha]_D^{+31^\circ}$ (c 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃, δ) 8.12-8.08 (m, 2H, Ar), 7.99-7.89 (m, 8H, Ar), 7.55-7.30 (m, 15H, Ar), 5.74 (ddd, 1H, H-4_{Sphing}, $J_{4,5b} = 10.5$ Hz, $J_{4,5a} = 17.3$ Hz, $J_{4,3} = 7.0$ Hz, 5.63 (dd, 1H, H-3, $J_{3,2} = J_{3,4} = 9.4$ Hz), 5.57 (ddd, 1H, H-8'', $J_{8'',7''} = 2.7$ Hz, $J_{8'',9a''} = J_{8'',9b''} = 9.8$ Hz, 3.2 Hz), 5.50 (dd, 1H, H-3_{N-acyl}, $J_{3,4} = 3.7$ Hz), 5.41 (dd, 1H, H-2, $J_{2,1} = 7.7$ Hz, $J_{2,3} = 9.7$ Hz), 5.23 (dd, 1H, H-7'', $J_{7'',6''} = 10.4$ Hz), 5.19 (ddd, 1H, H-5a_{Sphing}), 5.13 (ddd, 1H, H-5b_{Sphing}), 5.11 (d, 1H, H-1', $J_{1',2'} = 7.6$ Hz), 5.0-4.94 (m, 2H, H-2', NH), 4.75 (ddd, 1H, H-4'', $J_{4'',3e''} = 4.6$ Hz, $J_{4'',3a''} = 11.7$ Hz, $J_{4'',5''} = 10.4$ Hz), 4.70-4.62 (m, 3H, H-1, H-6a, H-4'), 4.40-4.35 (m, 2H, H-6b, H-9a''), 4.28-4.22 (m, 2H, H-4, H-9b''), 3.93-3.80 (m, 3H, H-5', H-2_{Sphing}, H-1a_{Sphing}), 3.76 (s, 3H, OCH₃), 3.74-3.66 (m, 3H, H-5, H-3', H-5''), 3.57 (m, 2H, H-1b_{Sphing}), H-6''), 3.44 (dd, 1H, H-6a', $J_{6a',5} = 6.7$ Hz, $J_{6a',6b'} = 11.3$ Hz), 3.33 (dd, 1H, H-6a'', $J_{6a'',5} = 6.6$ Hz), 2.48 (dd, 1H, H-3e'', $J_{3e'',3a''} = 12.7$ Hz), 2.07, 2.02, 1.91, 1.84, 1.83, 1.77 (6 x s, 18H, C(O)CH₃), 1.72 (dd, 1H, H-3a''), 1.62 (s, 3H, C(O)CH₃); ¹³C NMR (125 MHz, CDCl₃, δ) 170.69, 170.66, 170.13, 170.08, 170.02, 169.91, 161.8, 168.8, 165.66, 165.18, 165.13, 165.06, 164.8, 133.12, 133.11, 133.09, 132.88, 132.82, 131.1, 130.1, 130.0, 129.80, 129.78, 129.68, 129.63, 129.60, 129.52, 129.3, 128.42, 128.34, 128.28, 128.26, 128.1, 120.4, 100.82 (C-1'), 100.78 (C-1), 81.2, 74.6, 74.5, 73.4, 73.3, 72.8, 72.1, 71.5, 69.4, 69.1, 68.5, 67.9, 67.1, 66.1, 63.1, 62.5, 61.9, 61.7, 53.0, 49.0, 44.9, 36.7, 23.1, 20.92, 20.85, 20.7 (2C), 20.5, 20.3; ES MS calc'd for C₇₆H₈₀N₄O₃₀SNa: 1583.4. Found: 1583.4.

S-(Methyl 5-acetamido-4,5,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero- α -*D*-galacto-2-nonulopyranosylonate)-(2-3)-(4,6-di-*O*-acetyl-2-*O*-benzoyl-3-thio- β -*D*-galactopyranosyl)-(1-4)-2,3,6-tri-*O*-benzoyl- β -*D*-glucopyranosyl)-(1 $\rightarrow$ 1)-(2*S*, 3*R*)-3-*O*-benzoyl-2-octadecylamido-pent-4-ene-1,3-diol

Azide **26** (0.028 g; 18 µmol) was dissolved in pyridine/water (9:1) with stirring. Triphenylphosphine (0.007 g; 27 µmol; 1.5 eq.) was added, and the mixture was stirred at 40 °C for 7 hours. *N*-(octadecanoyloxy)-succinimide (0.020g; 54 µmol; 3 eq.) was added, and stirring was continued overnight. Concentration of the solution, followed by chromatography on silica gel using a gradient of 0 to 2.25% methanol in dichloromethane as eluant afforded a white solid (0.023g; 13 µmol; 71%): $[\alpha]_D^{+47^\circ}$ (c 0.2, CHCl₃); ¹H NMR (500 MHz, CDCl₃, δ) 8.10-7.86 (m, 10H, Ar), 7.56-7.22 (m, 15H, Ar), 5.79 (ddd, 1H, H-4_{Sphing}, $J_{4,5b} = 10.8$ Hz, $J_{4,5a} = 17.2$ Hz, $J_{4,3} = 6.3$ Hz, 5.66-5.59 (m, 2H, HNC(O)C₁₇H₃₅, H-3), 5.56 (m, 1H, H-8''), 5.48 (dd, 1H, H-3_{Sphing}, $J_{3,4} = J_{3,2} = 6.3$ Hz), 5.36 (dd, 1H, H-2, $J_{2,1} = 7.9$ Hz, $J_{2,3} = 10.0$ Hz), 5.26-5.20 (m, 2H, H-5a_{Sphing}, H-7''), 5.13 (ddd, 1H, H-5b_{Sphing}), 5.08 (d, 1H, H-1', $J_{1',2'} = 7.5$ Hz), 5.0-4.9 (m, 2H, H-2', NH), 4.75 (ddd, 1H, H-4'',

$J_{4'',3e''} = 4.7$ Hz), 4.69 (dd, 1H, H-4', $J_{4',3'} = 3.2$ Hz, $J_{4',5'} = < 1$ Hz), 4.56 (d, 1H, H-1, $J_{1,2} = 7.7$ Hz), 4.52 (dd, 1H, H-6a, $J_{6a,5} = 1.9$ Hz, $J_{6a,6b} = 12.2$ Hz), 4.44-4.34 (m, 2H, H-2_{Sphing}, H-9a''), 4.28-4.22 (m, 2H, H-6b, H-9b''), 4.20 (dd, 1H, H-4, $J_{4,3} = J_{4,5} = 9.6$ Hz), 4.04 (dd, 1H, H-1a_{Sphing}, $J_{1a,1b} = 10.0$ Hz, $J_{1a,2} = 3.3$ Hz), 3.90 (ddd, 1H, H-5', $J_{5',6a'} = J_{5',6b'} = 6.5$ Hz), 3.75 (s, 3H, OCH₃), 3.74-3.67 (m, 2H, H-3', H-5''), 3.64 (m, 1H, H-5), 3.59 (dd, 1H, H-6'', $J = 10.7$ Hz, 2.4 Hz), 3.44 (dd, 1H, H-6a', $J_{6a',6b'} = 11.4$ Hz), 3.33 (dd, 1H, H-6a'), 2.48 (dd, 1H, H-3e'', $J_{3e'',3a''} = 12.8$ Hz), 2.08, 2.03, 1.91, 1.85, 1.81, 1.78 (6 x s, 18H, C(O)CH₃), 1.76-1.70 (m, 2H, H-3a'', H-1a_{N-acyl}, H-1b_{N-acyl}), 1.62 (s, 3H, C(O)CH₃), 1.36-1.10 (m, 30H), 0.86 (t, 3H, CH_{3-N-acyl}); ¹³C NMR (125 MHz, CDCl₃, δ) 172.67, 170.71, 170.66, 170.11, 170.09, 170.03, 169.9, 169.8, 168.8, 165.6, 165.3, 165.11, 165.09, 164.08, 133.4, 133.13, 133.07, 132.9, 132.8, 130.1, 130.0, 129.98, 129.96, 129.85, , 129.78, 129.74, 129.6, 129.50, 129.49, 129.1, 128.47, 128.40, 128.24, 128.23, 128.1, 118.7, 114.7, 100.80 (C-1'), 100.73 (C-1), 81.2, 74.3, 74.2, 73.4, 73.2, 72.6, 72.10, 72.08, 69.3, 69.1, 68.5, 67.3, 67.1, 66.1, 62.5, 61.9, 61.7, 53.0, 50.2, 49.0, 44.9, 38.1, 36.7, 36.4, 31.9, 31.2, 29.67 (multiple C), 29.64, 29.62, 29.61, 29.5, 29.32, 29.28, 29.1, 25.4, 23.1, 22.7, 20.93, 20.87, 20.69, 20.68, 20.47, 20.32, 14.8; ESI MS calc'd for C₉₄H₁₁₆N₂O₃₁SNa: 1824.7. Found: 1824.7.

S-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-non-2-ulopyranosylonic acid)-(2-3)-(3-thio-β-D-galactopyranosyl)-(1-4)- β-D-glucopyranosyl)-(1→1)-(2S, 3R)-2-octadecylamido-4-pentene-1,3-diol (**27**)

S-(Methyl 5-acetamido-4,5,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylate)-(2-3)-(4,6-di-O-acetyl-2-O-benzoyl-3-thio-β-D-galactopyranosyl)-(1-4)-2,3,6-tri-O-benzoyl-β-D-glucopyranosyl)-(1→1)-(2S, 3R)-3-O-benzoyl-2-octadecylamido-pent-4-ene-1,3-diol (0.015 g; 8.3 μmol) was combined with dry methanol (4.0 mL) and a small piece of sodium (~5mg) was added. The solution was stirred for 24 hours and then water (400 μL) was added. Stirring was continued for a further 24 hours, then the mixture was neutralized with H⁺ resin, filtered, and concentrated. The residue was loaded onto a preconditioned tC₁₈ SepPak cartridge in 10% methanol, washed extensively with water and eluted with methanol. Concentration of the eluate gave a residue which was further purified by reverse-phase C₁₈ HPLC (elute ~90% methanol) to afford compound **27** (6.4 mg; 76%): [α]_D + 21° (c 0.2, MeOH); ¹H NMR (500 MHz, MeOD, δ) 5.86 (ddd, 1H, H-4_{Sphing}, $J_{4,5a} = 17.2$ $J_{4,5b} = 10.4$ Hz $J_{4,3} = 6.7$ Hz), 5.26 (ddd, 1H, H-5a_{Sphing}, $J = 17.1$ Hz, 1.3 Hz, 1.7 Hz), 5.13 (ddd, 1H, H-5b_{Sphing}, $J = 10.4$ Hz, 1.2 Hz, 1.9 Hz), 4.46 (d, 1H, H-1', $J_{1',2'} = 7.6$ Hz), 4.29 (d, 1H, H-1, $J_{1,2} = 7.8$ Hz), 4.19-4.12 (m, 2H, H-1a_{Sphing}, H-3_{Sphing}), 4.02-3.95 (m, 2H, H-2_{Sphing}, H-8''), 3.93 (d, 2H, H-6a, H-6b, $J = 3.4$ Hz), 3.87-3.84 (m, H-4', H-9a''), 3.73-3.66 (m, H, H-4'', H-5'', H-6a'), 3.67-3.49 (m, 8H, H-5', H-6b', H-4, H-1b_{Sphing}, H-9b'', H-3, H-6'', H-3'), 3.44-3.38 (m, 3H, H-5, H-7'', H-2'), 3.28 (dd, 1H, H-2, $J_{2,3} = 9.3$ Hz), 2.91 (dd, 1H, H-3_{eq}'', $J_{3e,4} = 4.4$ Hz, $J_{3e,3a} = 12.3$ Hz), 2.18 (t, 2H, C(O)CH₂, $J = 7.6$ Hz), 1.99 (s, 3H, NHAc), 1.70 (dd, 1H, H-3_{ax}'', $J_{3a,4} = 10.8$ Hz), 1.62-1.56 (m, 2H, C(O)CH₂CH₂), 1.36-1.24 (m, 28H, alkyl), 0.50 (t, 3H, CH₃); ¹³C NMR (125 MHz, MeOD, δ) 176.2, 175.4, 175.2, 139.7, 116.9,

106.4, 104.5, 85.3, 80.7, 79.8, 77.2, 76.5, 76.2, 74.9, 73.2, 72.9, 70.8, 70.41, 70.39, 64.9, 62.9, 61.70, 49.6, 37.2, 33.1, 30.78 (multiple C), 30.75, 30.74, 30.6, 30.49, 30.46, 30.35, 27.1, 23.7, 22.5, 14.4; ESI HRMS calc'd for $C_{46}H_{82}N_2O_{20}SNa$: 1037.507936. Found: 1037.507814.

S-(Methyl 5-acetamido-4,5,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero- α -*D*-galacto-2-nonulopyranosylate)-(2-3)-(4,6-di-*O*-acetyl-2-*O*-benzoyl-3-thio- β -*D*-galactopyranosyl)-(1-4)-2,3,6-tri-*O*-benzoyl- β -*D*-glucopyranosyl)-(1 $\rightarrow$ 1)-(2*S*, 3*R*)-3-*O*-benzoyl-2-(*S*-Acetyl-16-mercaptohexadecan-amido)-pent-4-ene-1,3-diol

Azide **26** (0.038 g; 24 μ mol) and triphenylphosphine (0.013 g; 49 μ mol; 2.0 eq) were dissolved in a mixture of pyridine and water (9:1) (4.0 mL). The solution was heated at 45 °C for three hours until all starting material had been consumed, as judged by TLC. *N*-(*S*-Acetyl-16-mercaptohexadecanoyloxy)-succinimide (0.052 g; 96 μ mol; 4.0 eq.) was added, and stirring was continued at elevated temperature for five hours. The solution was then concentrated and the residue chromatographed on silica gel using 2.2% methanol in dichloromethane as eluant, yielding the thioacetate (0.034g; 18 μ mol; 74%): $[\alpha]_D + 49^\circ$ (c 1.0, $CHCl_3$); 1H NMR (600 MHz, $CDCl_3$, δ) 8.08 (m, 2H, Ar), 7.97 (m, 2H, Ar), 7.94-7.86 (m, 6H, Ar), 7.56-7.28 (m, 15H, Ar), 5.79 (ddd, 1H, H-4_{Sphing}, $J_{4,5b} = 10.6$ Hz, $J_{4,5a} = 16.9$ Hz, $J_{4,3} = 6.2$ Hz), 5.66-5.61 (m, 2H, $HNC(O)C_{15}H_{30}SAc$, H-3), 5.56 (ddd, 1H, H-8", $J = 2.7$ Hz, 3.0 Hz, 10.0 Hz), 5.49 (dd, 1H, H-3_{Sphing}, $J_{3,4} = J_{3,2} = 6.3$ Hz), 5.36 (dd, 1H, H-2, $J_{2,1} = 7.8$ Hz, $J_{2,3} = 9.9$ Hz), 5.26-5.21 (m, 2H, H-5-a_{Sphing}, H-7"), 5.13 (ddd, 1H, H-5b_{Sphing}, $J = 1.2$ Hz, 1.2 Hz, 10.6 Hz), 5.07 (d, 1H, H-1', $J_{1',2'} = 7.6$ Hz), 4.94-4.91 (m, 2H, H-2', NH), 4.75 (ddd, 1H, H-4", $J_{4'',3e''} = 4.7$ Hz, $J = 10.3$ Hz, $J = 11.6$ Hz), 4.69 (dd, 1H, H-4', $J_{4',3'} = 3.0$ Hz, $J_{4',5'} < 1$ Hz), 4.56 (d, 1H, H-1, $J_{1,2} = 7.8$ Hz), 4.53 (dd, 1H, H-6a, $J_{6a,5} = 1.6$ Hz, $J_{6a,6b} = 11.9$ Hz), 4.41-4.36 (m, 2H, H-2_{Sphing}, H-9a"), 4.31-4.24 (m, 2H, H-6b, H-9b"), 4.19 (dd, 1H, H-4, $J_{4,3} = J_{4,5} = 9.5$ Hz), 4.04 (dd, 1H, H-1a_{Sphing}, $J_{1a,1b} = 10.0$ Hz, $J_{1a,2} = 3.3$ Hz), 3.90 (ddd, 1H, H-5', $J_{5',6a'} = J_{5',6b'} = 6.5$ Hz), 3.75 (s, 3H, OCH_3), 3.77-3.64 (m, 2H, H-3', H-5"), 3.65 (m, 1H, H-5), 3.58 (dd, 1H, H-6", $J = 10.8$ Hz, 2.5 Hz), 3.43 (dd, 1H, H-6a', $J_{6a',6b'} = 11.3$ Hz), 3.36 (dd, 1H, H-6a'), 2.83 (dd, 2H, CH_2SAc , $J = 7.4$ Hz), 2.48 (dd, 1H, H-3e", $J_{3e'',3a''} = 12.6$ Hz), 2.29, 2.08, 2.03, 1.91, 1.86, 1.81, 1.78 (7 x s, 21H, $C(O)CH_3$), 1.76-1.69 (m, 3H, H-3a", $CH_{2N-acyl}$), 1.62 (s, 3H, $C(O)CH_3$), 1.53 (m, 2H, $CH_{2N-acyl}$), 1.36-1.02 (m, 24H); ^{13}C NMR (100 MHz, $CDCl_3$, δ) 196.0, 172.6, 170.72, 170.65, 170.10, 170.08, 170.03, 169.9, 169.8, 165.5, 165.3, 165.10, 165.08, 165.06, 133.4, 133.11, 133.07, 132.91, 132.90, 132.8, 130.1, 129.96, 129.93, 129.8, 129.7, 129.6, 129.49, 129.46, 129.1, 128.5, 128.44, 128.39, 128.38, 128.23, 128.22, 128.06, 118.7, 100.78, 100.70, 81.1, 74.3, 74.1, 73.3, 73.2, 72.5, 72.07, 72.04, 69.3, 69.1, 68.5, 67.30, 67.29, 67.1, 66.1, 62.5, 61.8, 61.6, 53.0, 50.1, 49.0, 44.9, 36.6, 36.3, 30.6, 29.61, 29.60, 29.5, 29.4 (multiple C), 29.3, 29.12, 29.08, 28.8, 25.4, 23.1, 20.92, 20.86, 20.69, 20.68, 20.46, 20.30; ESI MS calc'd for $C_{94}H_{114}N_2O_{32}SNa$: 1870.7 Found: 1870.7.

S-(5-acetamido-3,5-dideoxy-*D*-glycero- α -*D*-galacto-non-2-ulopyranosylonic acid)-(2-3)-(3-thio- β -*D*-galactopyranosyl)-(1-4)- β -*D*-glucopyranosyl)-(1 $\rightarrow$ 1)-(2*S*, 3*R*)-2-(16-mercaptohexadecan-amido)-pent-4-ene-1,3-diol (**28**)

S-(Methyl 5-acetamido-4,5,8,9-tetra-*O*-acetyl-3,5-dideoxy-*D*-glycero- α -*D*-galacto-2-nonulopyranosylate)-(2-3)-(4,6-di-*O*-acetyl-2-*O*-benzoyl-3-thio- β -*D*-galactopyranosyl)-(1-4)-2,3,6-tri-*O*-benzoyl- β -*D*-glucopyranosyl)-(1 $\rightarrow$ 1)-(2*S*, 3*R*)-3-*O*-benzoyl-2-(*S*-Acetyl-16-mercaptohexadecan-amido)-pent-4-ene-1,3-diol (0.010 g; 5.4 μ mol) was dissolved in dry degassed methanol (2.0 mL) and a small piece of sodium was added. A gentle stream of argon was bubbled through the solution, and stirring was continued for approximately 24 hours. Water (350 μ L) was added, and the solution was heated at 40 °C for 48 hrs. The solution was then cooled and dithiothreitol (0.010g) was added. After stirring overnight, the mixture was neutralized with acidic resin, filtered, and concentrated. The residue was redissolved in 10% methanol and applied to a tC18 Sep Pak cartridge (0.39 g). Gradient elution (MeOH-H₂O) afforded **28** which was further purified by HPLC (0.0045g; 4.4 μ mol; 82 %): [α]_D + 18° (*c* 0.26, MeOH); ¹H NMR (600 MHz, MeOH, δ) 5.86 (ddd, 1H, H-4_{Sphing}, $J_{4,5a}$ = 17.1 $J_{4,5b}$ = 10.4 Hz $J_{4,3}$ = 6.7 Hz), 5.26 (ddd, 1H, H-5a_{sphing}, J = 17.1 Hz, 1.4 Hz, 1.8 Hz), 5.13 (ddd, 1H, H-5b_{sphing}, J = 10.4 Hz, 1.1 Hz, 1.8 Hz), 4.46 (d, 1H, H-1', $J_{1',2'}$ = 7.5 Hz), 4.29 (d, 1H, H-1, $J_{1,2}$ = 7.8 Hz), 4.18-4.12 (m, 2H, H-1a_{sphing}, H-3_{sphing}), 4.02-3.96 (m, 2H, H-2_{sphing}, H-8''), 3.92 (d, 2H, H-6a, H-6b, J = 3.3 Hz), 3.87-3.83 (m, H-4', H-9a''), 3.75-3.67 (m, H, H-4'', H-5'', H-6a'), 3.67-3.50 (m, 8H, H-5', H-6b', H-4, H-1b_{sphing}, H-9b'', H-3, H-6'', H-3'), 3.44-3.37 (m, 3H, H-5, H-7'', H-2'), 3.28 (dd, 1H, H-2, $J_{2,3}$ = 9.1 Hz), 2.90 (dd, 1H, H-3_{eq}'', $J_{3e,4}$ = 4.2 Hz, $J_{3e,3a}$ = 12.4 Hz), 2.44 (t, 2H, CH₂SH, J = 7.5 Hz),), 2.18 (t, 2H, C(O)CH₂, J = 7.1 Hz), 1.99 (s, 3H, NHAc), 1.69 (dd, 1H, H-3_{ax}'', $J_{3a,4}$ = 10.7 Hz), 1.61-1.54 (m, 4H, alkyl), 1.42-1.25 (m, 22H, alkyl); ESI HRMS calc'd for C₄₄H₇₇ N₂O₂₀S₂Na₂: 1063.43028 Found: 1063.43010.

1-O-Benzoyl-3,5-O-benzylidene-2-deoxy-4-O-formyl-D-threo-pent-1-enitol (**32**)

[α]_D + 12.2 ° (*c* 0.82, CHCl₃); ¹H NMR (600 MHz, CDCl₃, δ) 8.22 (bs, 1H, OCHO), 8.09-8.05 (m, 2H, Ar), 7.72 (dd, 1H, H-1, $J_{1,2}$ = 12.5 Hz, $J_{1,3}$ = 1.0 Hz), 7.62-7.57 (m, 1H, Ar), 7.55-7.52 (m, 2H, Ar), 7.48-7.44 (m, 2H, Ar), 7.39-7.32 (m, 3H, Ar), 5.72 (dd, 1H, H-2, $J_{2,3}$ = 7.3 Hz), 5.70 (s, 1H, CHPh), 4.94 (m, 1H, H-5), 4.71 (m, 1H, H-4), 4.37 (dd, 1H, H-6a, $J_{6a,6b}$ = 13.0 Hz, $J_{6a,5}$ = 1.6 Hz), 4.20 (dd, 1H, H-6b), ¹³C NMR (125 MHz, CDCl₃, δ) 163.6 (COPh), 160.7 (OCHO), 140.0 (C-1), 137.5, 134.0, 130.3, 129.4, 128.78, 128.75, 128.5, 126.3 (8*Ar), 110.4 (C-2), 101.5 (CHPh), 75.5 (C-3), 69.3 (C-5), 67.5 (C-4); ESI HRMS calc'd for C₂₀H₁₈O₆Na: 377.09956. Found: 377.09943; Anal. calc'd for C₂₀H₁₈O₆: C 67.79, H 5.12. Found: C 67.51, H 5.13.