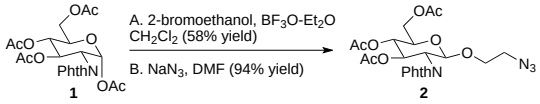
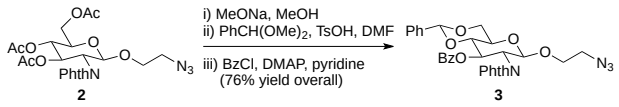
Supporting Information

^{1}H NMR and ^{13}C NMR spectra were recorded on Varian Unity 500 MHz instrument. Mass spectrometric data were obtained on Agilent 1100 series spectrometer. All solvents used in the experiments were dried by passage through a Glass Contour solvent drying system containing cylinders of activated alumina. Chemicals were obtained from Aldrich, Acros, TCI or Fluca and were used as received unless otherwise noted.



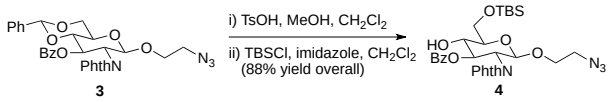
Synthesis of 2: Compound **1** (1.5 g, 3.14 mmol), 2-bromoethanol (0.472 g, 3.77 mmol), 4 Å molecular sieves (1 g), and dichloromethane (20 mL) were stirred for 30 min before BF_3-OEt_2 (0.668 g, 0.59 mL, 4.7 mmol) was added. After 20 h, the reaction was quenched with Et_3N (1 mL). The mixture was filtered through a pad of celite to remove the sieves. The filtrate was washed with saturated aqueous sodium bicarbonate (20 mL). The organic extract was dried over Na_2SO_4. Concentration under reduced pressure afforded the 2-bromoethylglycoside, which was purified by silica gel chromatography (EtOAc:hexane, 1:3 to 1:1) to yield the pure 2-bromoethylglycoside (Rf = 0.35, EtOAC/Hexane = 1/1) as a clear glass (990 mg, 58.3%). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.835 (dd, J = 3.00, 5.50 Hz, 2H), 7.20 (dd, J = 3.00, 5.50 Hz, 2H), 5.79 (dd, J = 9.00, 11.00 Hz, 1H), 5.41 (d, J = 8.50 Hz, 1H), 5.15 (t, J = 10.00 Hz, 1H), 4.31 (t, J = 10.5 Hz, 1H), 4.31 (dd, J = 4.50, 13.50 Hz, 1H), 4.16 (dd, J = 2.50, 12.50 Hz, 1H), 4.09 (tt, J = 5.5 Hz, 11.5 Hz, 1H), 3.87 (dddd, J = 2.00, 2.50, 4.50 Hz, 1H), 3.73 (dddd, J = 2.50, 6.00, 12.00 Hz, 1H), 3.35-3.27 (m, 2H), 2.09 (s, 3H), 2.01 (s, 3H), 1.85 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.65, 170.08, 169.44, 134.27, 131.88, 123.57, 98.28, 71.97, 70.65, 69.73, 68.85, 61.92, 54.39, 29.79. 20.77, 20.64, 20.46. HRESI-MS: $C_{22}H_{24}BrNO_{10}$ (541.0583). $[M+NH_4]^+$ cald: 559.0921; found: 559.0920. A mixture of 2-bromoethylglycoside (800 mg, 1.47 mmol),

sodium azide (2.0 g, 30.8 mmol), and DMF (30 mL) was stirred at 60 °C for 12 h. The DMF was removed under reduced pressure and water (50 mL) was added. The product was extracted with dichloromethane (100 mL). The organic solution was dried over anhydrous Na_2SO_4, concentrated, and the product was isolated by silica gel chromatography (EtOAc:hexane, 1:3 to 1:1), affording 700 mg of **2** (Rf = 0.3, EtOAc/Hexane = 1/1) as a white solid (94% yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.82-7.77 (m, 2H), 7.70-7.68 (m, 2H), 5.74 (dd, *J* = 9.50, 11.00 Hz, 1H), 5.42 (d, *J* = 8.50 Hz, 1H), 5.14 (t, *J* = 9.50 Hz, 1H), 4.30 (dd, *J* = 8.25, 10.50 Hz, 1H), 4.28 (dd, *J* = 4.50, 12.50 Hz, 1H), 4.15 (dd, *J* = 2.50, 12.50 Hz, 1H), 3.97 (dddd, *J* = 4.00, 5.00, 9.50 Hz, 1H), 3.854 (dddd, *J* = 2.50, 4.50, 10.00 Hz, 1H), 3.614 (dddd, *J* = 3.50, 8.50, 11.00 Hz, 1H), 3.348 (dddd, *J* = 3.50, 8.50, 13.50 Hz, 1H), 3.13 (dddd, *J* = 3.00, 4.00, 13.50 Hz, 1H), 2.07 (s, 3H), 1.98 (s, 3H), 1.81 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.60, 170.05, 169.39, 134.24, 131.41, 123.51, 98.15, 71.94, 70.63, 68.83, 68.79, 61.86, 54.41, 50.28, 20.96, 20.68, 20.55. HRESI-MS: $C_{22}H_{24}N_4O_{10}$ (504.1492). $[M+NH_4]^+$ cald: 522.1836; found: 522.1931.



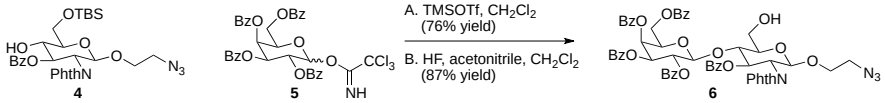
Synthesis of 3: To a solution of compound **2** (3.73 g, 7.4 mmol) in methanol (100 mL) was added NaOMe (1 mL, 1 *M* in methanol). The mixture was stirred for 2 h. Amberlite (10 g) was then added to quench the reaction, and the mixture was stirred for 30 min. The solid was removed by filtration. The filtrate was concentrated under vacuum. The crude material was dissolved in DMF (30 mL), followed by addition of dimethoxybenzaldehyde (2.22 mL, 14.8 mmol) and $TsOH{\cdot}H_2O$ (0.1 g, 0.5 mmol). The mixture was stirred at 65 °C for 2 h, and then Et_3N (1 mL) was added. The solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane (200 mL), and washed with water (100 mL). The organic phase was concentrated under vacuum. The resulting compound was dissolved in Et_3N (4 mL) and

dichloromethane (100 mL) and treated with BzCl (3.5 mL, 22.2 mmol), DMAP (0.1 g, 0.8 mmol) at 0 °C for 10 h. The reaction was quenched by addition of methanol (10 mL), diluted with dichloromethane (200 mL), washed with aqueous HCl (0.5 N, 300 mL), and saturated aqueous $NaHCO_3$ (400 mL). The organic phase was concentrated, and the product was isolated via silica gel chromatography (EtOAc:hexane, 1:2 – 1:1 eluent) giving **3** as 3.2 g of a clear glass (Rf = 0.63, EtOAc/Hexane = 1/1, 76% overall yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.88-7.26 (m, 9 H), 6.18 (t, *J* = 10.00 Hz, 1H), 5.60 (d, *J* = 8.50 Hz, 1H), 5.58 (s, 1H), 4.52 (dd, *J* = 9.50, 10.00 Hz, 1H), 4.46 (dd, *J* = 4.50, 10.50 Hz, 1H), 4.04 (dddd, *J* = 5.50, 10.00, 10.50 Hz, 1H), 3.95 (t, *J* = 9.50 Hz, 1H), 3.91 (t, *J* = 9.50 Hz, 1H), 3.86 (dd, *J* = 4.50, 9.50 Hz, 1H), 3.69 (dddd, *J* = 3.50, 8.00, 11.00 Hz, 1H), 3.36 (dddd, *J* = 3.50, 8.50, 12.50 Hz, 1H), 3.20 (dddd, *J* = 3.00, 5.00, 13.50 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 165.56, 136.77, 134.10, 133.13, 129.80, 129,16, 129.07, 128.55, 128.29, 128.20, 126.16, 126.03, 123.54, 101.59, 98.87, 79.65, 70.01, 68.86, 68.65, 66.46, 55.12, 50.42. HRESI-MS: $C_{30}H_{26}N_4O_8$ (570.1750). $[M+NH_4]^+$ cald: 588.2088; found: 588.2098.



Synthesis of 4: To a solution of **3** (1.2 g, 2.1 mmol) in dichloromethane (50 mL) and methanol (5 mL) was added $TsOH{\cdot}H_2O$ (0.2 g, 1.1 mmol). The mixture was stirred at room temperature for 3 h. The reaction was quenched with Et_3N (1 mL). The solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane (50 mL) and washed with water (40 mL). The organic phase was concentrated under reduced pressure. The residue was purified by silica gel chromatography (EtOAc:hexane, 1:1-3:1), giving the corresponding diol as 1.0 g of a clear oil (Rf = 0.12, EtOAc/Hexane = 1/1, 99 % yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.87-7.26 (m, 9H), 5.90 (dd, *J* = 9.00, 11.00 Hz, 1H), 5.55 (d, *J* = 8.50 Hz, 1H), 4.455 (dd, *J* = 8.50, 11.00

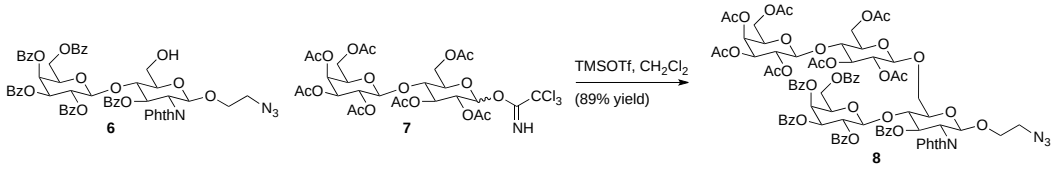
Hz, 1H), 4.09-4.01 (m, 2H), 3.97-3.93 (m, 2H), 3.756 (tt, *J* = 3.50, 10.50 Hz, 1H), 3.70 (dddd, *J* = 3.00, 8.00, 11.00 Hz, 1H), 3.374 (dddd, *J* = 3.50, 8.00, 13.50 Hz, 1H), 3.21 (dddd, *J* = 3.50, 5.50, 14.00 Hz, 1H), 2.56 (brs, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 167.07, 134.16, 133.39, 133.32, 131.39, 129.88, 128.43, 128.37, 98.21, 75.87, 74.53, 70.52, 68.68, 62.27, 60.48, 54.58, 50.38. HRESI-MS: $C_{23}H_{22}N_4O_8$ (482.1437). $[M+NH_4]^+$ cald: 500.1775; found: 500.1761. The crude diol was dissolved in dry dichloromethane (30 mL), followed by addition of TBSCl (0.375 g, 2.5 mmol) and imidazole (0.286 g, 4.2 mmol). The mixture was stirred at 0 °C for 5 h. MeOH (2 mL) was added to quench the reaction. The mixture was washed with water (60 mL), and the organic phase was concentrated under reduced pressure. The product, **4**, was isolated after silica gel chromatography (EtOAc:hexanes, 1:1, Rf = 0.82) as 1.1 g of a clear glass (89 % yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.88-7.30 (m, 9H), 5.915 (dd, *J* = 9.00, 11.50 Hz, 1H), 5.52 (d, *J* = 8.00 Hz, 1H), 4.422 (dd, *J* = 8.00, 10.50 Hz, 1H), 4.01 (dddd, *J* = 3.50, 4.50, 13.50 Hz, 1H), 3.999 (t, *J* = 6.50 Hz, 1H), 3.94 (dddd, *J* = 3.50, 9.00, 10.50 Hz, 1H), 3.72 (tt, *J* = 5.00, 9.50 Hz, 1H), 3.677 (dddd, *J* = 3.50, 8.00, 11.00 Hz, 1H), 3.56 (d, *J* = 3.50 Hz, 1H), 3.378 (dddd, *J* = 3.00, 8.00, 13.00 Hz, 1H), 3.19 (dddd, *J* = 3.50, 5.00, 13.00 Hz, 1H), 0.921 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.73, 134.06, 133.33, 131.49, 129.88, 128.98, 128.35, 123.45, 98.03, 75.12, 74.21, 72.20, 68.50, 64.19, 54.35, 50.41, 25.88, 18.32, -5.36, -5.388. HRESI-MS: $C_{29}H_{36}N_4O_8Si$ (596.2302). $[M+NH_4]^+$ cald: 614.2640; found: 614.2640.



Synthesis of 6: Donor **5** (0.45 g, 0.604 mmol) and acceptor **4** (0.3 g, 0.503 mmol) were mixed with molecular sieves (MS 4 Å, 600 mg) in dichloromethane (5 mL). The mixture was cooled to 0 °C, then TMSOTf (30 µL) was added. The mixture was allowed to warm to room temperature

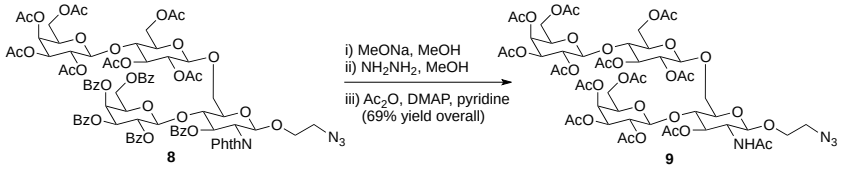
and stirred for 12 h. Et_3N (0.1 mL) was added, and the resulting mixture was filtered through a celite pad. The filtrate was concentrated, and the disaccharide was purified via silica gel chromatography (EtOAc:hexanes, 1:4-1:2). The disaccharide was recovered as 0.45 g of a white powder (Rf = 0.43, EtOAc/Hexane = 1/2, 76% yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.24-6.92 (m, 29H), 6.133 (dd, *J* = 9.00, 10.50 Hz, 1H), 5.77 (d, *J* = 2.5 Hz, 1H), 5.68 (dd, *J* = 7.50, 10.00 Hz, 1H), 5.45 (d, *J* = 9.00 Hz, 1H), 5.42 (dd, *J* = 3.50, 10.50 Hz, 1H), 5.13 (d, *J* = 8.00 Hz, 1H), 4.43 (dd, *J* = 8.00, 11.00 Hz, 1H), 4.27 (t, *J* = 9.00 Hz, 1H), 4.00 (t, *J* = 6.50 Hz, 1H), 3.98-3.78 (m, 4H), 3.64-3.62 (m, 3H), 3.35 (dddd, *J* = 3.00, 7.50, 13.50 Hz, 1H), 3.19 (dddd, *J* = 3.50, 6.00, 13.00 Hz, 1H), 0.93 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 165.73, 165.55, 165.48, 165.28, 164.60, 134.00, 133.60, 133.46, 133.35, 133.29, 132.87, 132.71, 129.96, 129.88, 129.75, 129.72, 129.68, 129.49, 129.60, 129.42, 129.17, 128.91, 128.69, 128.56, 128.46, 128.36, 128.26, 128.18, 128.11, 127.99, 123.48, 100.44, 97.92, 75.25, 72.15, 71.46, 70.92, 70.08, 69.69, 67.78, 61.56, 60.87,60.38, 54.87, 50.37, 25.86, 18.32, -5.04, -5.28. HRESI-MS: $C_{63}H_{62}N_4O_{17}Si$ (1174.3879). $[M+NH_4]^+$ cald: 1192.4223; found: 1192.4091. The disaccharide (0.10 g, 0.1 mmol) was dissolved in dichloromethane (5 mL) and acetonitrile (20 mL) in a 50 mL centrifuge tube . An aqueous solution of HF (48%, 2 mL) was added. After stirred at room temperature for 2 h. The mixture was poured onto the solid $NaHCO_3$ (10 g), and after agitation for 30 min, dichloromethane (100 mL) was added. The resulting organic solution was decanted from the salts and concentrated under reduced pressure. The product, **6** (Rf = 0.45, EtOAc/Hexane = 1/1), purified via silica gel chromatography (EtOAc:Hexanes, 1:1) giving 0.080 g of a clear oil (87 % yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.00-7.15 (m, 29H), 6.142 (dd, *J* = 8.50, 10.50 Hz, 1H), 5.773 (d, *J* = 2.50 Hz, 1H), 5.70 (dd, *J* = 8.00, 10.50 Hz, 1H), 5.52 (d, *J* = 8.50 Hz, 1H), 5.49 (dd, *J* = 3.50, 10.50 Hz, 1H), 5.03 (d, *J* = 8.00 Hz, 1H), 4.458 (dd, *J* =

8.50, 11.00 Hz, 1H), 4.28 (t, *J* = 9.5 Hz, 1H), 4.01 (t, *J* = 7.00 Hz, 1H), 3.95 (dddd, *J* = 3.50, 5.50, 11.00 Hz, 1H), 3.84-3.80 (m, 3H), 3.68-3.61 (m, 3H), 3.34 (dddd, *J* = 3.00, 7.50, 13.50 Hz, 1H), 3.19 (dddd, *J* = 3.50, 6.00, 13.50 Hz, 1H), 1.96 (brs, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 165.59, 165.47, 165.33, 165.23, 164.76, 134.08, 133.46, 133.38, 133.29, 133.22, 133.18, 131.48, 129.96, 129.75, 129.72, 129.66, 129.49, 129.42, 129.06, 128.91, 128.69, 128.56, 128.54, 128.51, 128.28, 128.24, 123.53, 100.94, 98.32, 75.54, 74.96, 71.82, 71.02, 71.00, 71.08, 68.83, 67.60, 60.85, 60.36, 54.74, 50.33. HRESI-MS: $C_{57}H_{48}N_4O_{17}$ (1060.3014). $[M+NH_4]^+$ cald: 1078.3352; found: 1078.3358.



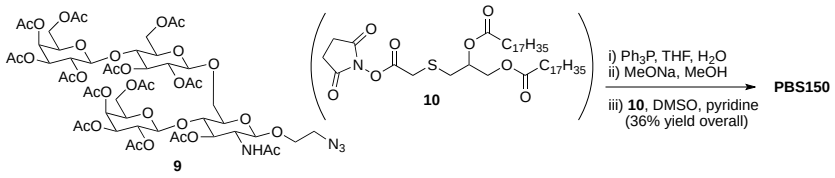
Synthesis of 8: Donor **7** (71 mg, 0.091 mmol), acceptor **6** (80 mg, 0.075 mmol), molecular sieves (4 Å, 300 mg) were mixed in dichloromethane (5 mL) followed by addition of TMSOTf (20 µL). The mixture was stirred at room temperature for 12 h. Et_3N (0.1 mL) was added, and solids were removed via filtration through a celite pad. The filtrate was concentrated under reduced pressure. The product was then purified by silica gel chromatography (EtOAc:hexanes, 1:1-1:3) giving **8** as 112 mg of a clear glass (Rf = 0.17, EtOAc/Hexane = 1/1, 89% yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.98-7.14 (m, 29H), 6.12 (dd, *J* = 8.50, 11.00 Hz, 1H), 5.75 (d, *J* = 3.50 Hz, 1H), 5.68 (dd, *J* = 8.00, 10.50 Hz, 1H), 5.50 (dd, *J* = 3.00, 10.00 Hz, 1H), 5.42 (d, *J* = 8.50Hz, 1H) , 5.365 (d, *J* = 3.50 Hz, 1H), 5.145 (dd, *J* = 8.50, 11.00 Hz, 1H), 4.98 (dd, *J* = 3.50, 10.00 Hz, 1H), 4.94 (d, *J* = 9.00 Hz, 1H), 4.88 (d, *J* = 9.00 Hz, 1H), 4.87 (d, *J* = 8.50 Hz, 1H), 4.52 (dd, *J* = 2.00, 10.50 Hz, 1H), 4.44 (d, *J* = 7.50 Hz, 1H), 4.46-4.42 (m, 1H), 4.14-4.07 (m, 3H), 4.11 (s, 1H), 4.03 (dd, *J* = 6.50, 11.50 Hz, 1H), 3.99-3.95 (m, 3H), 3.92-2.81 (m, 3H), 3.77 (dd, *J* = 6.00, 11.00 Hz, 1H), 3.70 (t, *J* = 9.50 Hz, 1H), 3.62 (dddd, *J* = 3.50, 5.50, 10.00 Hz, 1H),

4.47 (dd, J = 3.50, 10.50 Hz, 1H), 3.39 (dddd, J = 3.50, 6.00, 11.00 Hz, 1H), 3.20-3.12 (m, 2H), 2.26 (s, 3H), 2.16 (s, 3H), 2.13 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H), 1.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.61, 170.34, 170.14, 170.05, 169.76, 169.54, 169.26, 165.49, 165.40, 165.23, 165.19, 164.48, 134.15, 134.03, 133.54, 133.30, 133.22, 131.48, 129.96, 129.75, 129.71, 129.60, 129.45, 129.36, 128.93, 128.86, 128.62, 128.56, 128.54, 128.33, 128.27, 123.50, 101.45, 101.23, 100.97, 98.10, 77.67, 76.28, 74.39, 72.82, 72.73, 71.60, 71.48, 71.02, 70.98, 70.66, 70.16, 69.25, 68.99, 68.74, 67.52, 66.64, 61.96, 60.79, 60.50, 60.37, 54.60, 50.30, 20.91, 20.83, 20.79, 20.67, 20.64, 20.51. HRESI-MS: $C_{83}H_{82}N_4O_{34}$ (1678.4810). $[M+NH_4]^+$ cald: 1696.5148; found: 1696.5128.



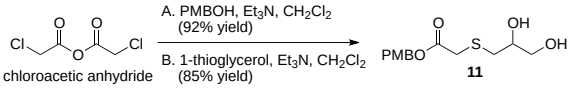
Synthesis of 9: To a solution of **8** (120 mg, 0.072 mmol) in methanol (2 mL) and THF (8 mL) was added NaOMe (1 mL, 1 *M* in methanol). The mixture was stirred at room temperature for 2 h. After quenching with acetic acid (0.10 mL), solvents were removed under reduced pressure. The resulting oil was dissolved in methanol (9 mL). To this solution was added anhydrous hydrazine (0.5 mL), and the solution was stirred at room temperature for 12 h. The solvents were then removed under reduced pressure. The resulting oil was dissolved in pyridine (12 mL), followed by addition of acetic anhydride (6 mL) and DMAP (10 mg, 0.082 mmol). The mixture was stirred for 12 h, quenched by methanol (7 mL), diluted with dichloromethane (150 mL), and washed with aqueous HCl (1 N, 200 mL), saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL). The organic phase was concentrated under reduced pressure, and the peracylated product was purified by silica gel chromatography (dichloromethane:methanol, 1: 0-9:1) affording **9** as a clear oil (Rf = 0.37, MeOH/DCM = 1/9, 63 mg, 69 % yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ

5.78 (d, *J* = 9.50 Hz, 1H), 5.36 (dd, *J* = 2.50, 8.50 Hz, 1H), 5.17 (t, *J* = 9.00 Hz, 1H), 5.11 (dd, *J* = 2.50, 8.00 Hz, 1H), 5.08 (t, *J* = 7.50 Hz, 1H), 5.06 (dd, *J* = 3.00, 10.00 Hz, 1H), 4.96 (dd, *J* = 3.50, 10.50 Hz, 1H), 4.89 (dd, *J* = 7.50, 9.00 Hz, 1H), 4.62 (d, *J* = 7.50 Hz, 1H), 4.54 (d, *J* = 7.00 Hz, 1H), 4.52-4.50 (m, 2H), 4.495 (d, *J* = 2.50 Hz, 1H), 4.15-3.95 (m, 10H), 3.89-3.74 (m, 4H), 3.64-3.57 (m, 3H), 3.45 (dddd, *J* = 3.00, 7.50 Hz, 13.50 Hz, 1H), 3.337 (dddd, *J* = 3.00, 5.50, 13.50 Hz, 1H), 2.15 (s, 3H), 2.14 (s, 3H), 2.12 (s, 3H), 2.057 (s, 6H), 2.053 (s, 3H), 2.050 (s, 6H), 2.04 (s, 3H), 2.03 (s, 3H), 1.97 (s, 3H), 1.967 (s, 3H), 1.96 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.43, 166.38, 166.36, 166.35, 166.27, 166.18, 166.14, 166.08, 166.01, 165.71, 165.61, 165.43, 165.11, 97.16, 96.82, 96.76, 96.56, 72.00, 71.12, 70.66, 68.98, 68.63, 67.90, 67.63, 67.01, 66.70, 66.67, 66.62, 65.27, 65.16, 64.21, 64.16, 62.86, 62.65, 58.03, 56.84, 56.76, 48.59, 46.76, 19.28, 16.87, 16.83, 16.78, 16.66, 16.56, 16.54. HRESI-MS: $C_{52}H_{72}N_4O_{33}$ (1280.4078). $[M+H]^+$ cald: 1281.4151; found: 1281.4156.



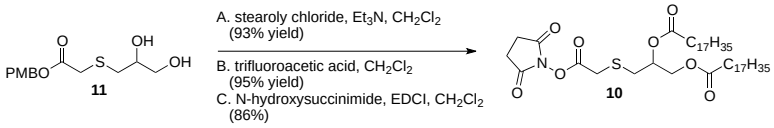
Synthesis of PBS150: A mixture of **9** (53 mg, 0.042 mmol) and Ph_3P (33 mg, 0.124 mmol) in THF (6 mL) and water (4 mL) was stirred at 55 °C under nitrogen for 48 h. The solvent was removed under reduced pressure, and the remaining oil was dissolved in methanol (7 mL) and water (0.5 mL), followed by addition of NaOMe (0.3 mL, 1 *M* in methanol). The mixture was stirred under nitrogen for 12 h. Solvents were removed under reduced pressure, and the crude amine was dissolved in DMSO (5 mL), followed by addition of **10** (58 mg, 0.073 mmol) in dichloromethane (2 mL) and pyridine (0.1 mL). The reaction was warmed to 50 °C for 30 min. The dichloromethane was removed under reduced pressure and the remaining DMSO and pyridine were removed via lyophilization. The product was purified by silica gel

chromatography (dichloromethane/methanol/water, 65/25/4, Rf = 0.42) yielding **PBS150** as a white solid (21.6 mg, 36%). ^{1}H-NMR (mixture of diastereoisomers, ratio: 1/5, 500 MHz, $CD_3OD/CDCl_3$): δ 7.78 (brs, 1H), 7.35 (brs, 1H), 5.34 (brs, minor isomer), 5.23 (brs, 1H), 4.49 (d, J = 7.00 Hz, 1H), 4.40 (d, J = 8.00 Hz, 1H), 4.36 (d, J = 8.00 Hz, 1H), 4.23 (d, J = 10.00 Hz, 1H), 4.19 (m, 1H), 3.95-3.49 (m, 42H), 3.43-3.37 (m, 2H), 3.27-3.20 (m, 2H), 2.90 (dd, J = 2.00, 6.00Hz, minor isomer), 2.87 (dd, J = 2.00, 6.00Hz, 1H), 2.84 (t, J = 7.00 Hz, 1H), 2.80 (t, J = 7.00Hz, minor isomer), 2.34 (q, J = 7.00Hz, 4H), 2.015 (s, 3H), 2.012 (s, minor isomer), 1.61 (m, 4H), 1.34-1.26 (m, 55H), 0.88 (t, J = 6.00 Hz, 6H). ^{13}C NMR (CD_3OD, 125 MHz): δ 177.86, 177.47, 176.29, 174.30, 107.57, 107.27, 106.80, 105.23, 83.66, 83.18, 79.39, 79.29, 78.85, 77.66, 77.36, 76.99, 76.47, 76.13, 75.29, 75.05, 73.86, 72.90, 71.77, 71.49, 67.73, 67.23, 65.37, 64.97, 59.20, 43.89, 43.42, 39.24, 338.14, 37.95, 36.58, 35.75, 33.51, 33.47, 33.35, 33.33, 33.17, 33.14, 33.13, 32.96, 28.95, 28.78, 28.72, 26.60, 26.48, 17.43, 75.53, 75.44, 74.98, 73.80, 73.51, 73.14, 72.61, 72.27, 71.43, 71.19, 70.00, 69.04, 67.91, 67.63, 63.87, 63.37, 61.51, 61.11, 55.34, 40.03, 39.56, 35.38, 34.28, 34.08, 32.72, 31.88, 29.65, 29.61, 29.49, 29.47, 29.31, 29.28, 29.27, 29.10, 25.09, 24.92, 24.86, 22.62, 13.87. HRESI-MS: $C_{69}H_{126}N_2O_{26}S$ (1430.8319). $[M+H]^+$ cald: 1431.8392; found: 1431.8367.



Synthesis of 11: Chloroacetic anhydride (10 g, 58.48 mmol) was dissolved in dichloromethane (150 mL) and triethylamine (8.97 mL). 4-Methoxybenzyl alcohol (PMBOH) (8.08 g, 58.48 mmol) was added at 0 °C. The reaction mixture was allowed to warm to room temperature and stir for 12 h. The resulting solution was washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL), and the organic solution was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting oil was subjected to silica gel chromatography

(EtOAc/Hexane, 1/4), yielding a clear oil (11.54 g, 92% yield, Rf = 0.89, EtOAc/Hexane = 1/1). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.37 (d, J = 14.57 Hz, 1H), 6.91 (d, J = 14.57 Hz, 1H), 5.84 (s, 2H), 4.08 (s, 2H), 3.82 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 167.55, 160.19, 130.71, 127.25, 114.29, 68.03, 55.54, 41.23. HRESI-MS: $C_{10}H_{11}ClO_3$ (214.0397). $[M+H]^+$ cald: 215.0475; found: 215.0491. The purified ester (1.98 g, 9.25 mmol) and 1-thioglycerol (1 g, 9.25 mmol) were dissolved in dichloromethane (30 mL) and triethylamine (5 mL). The resulting solution was stirred for 6 h, and then water (50 mL) was added. The organic material was removed, and the remaining water was extracted with dichloromethane (3 x 20 mL). Combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure, giving a light yellow oil. The desired product, **11**, was obtained after silica gel chromatography (EtOAc/Hexane, 1/1) as a clear oil (Rf = 0.08, EtOAc/Hexane = 1/1, 2.25 g, 85 % yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.34 (d, J = 15.00 Hz, 2H), 6.92 (d, J = 15.00 Hz, 2H), 5.14 (s, 2H), 3.83 (s, 3H), 3.80- 3.77 (m, 1H), 3.74-3.65 (m, 1H), 3.57-3.53 (m, 1H), 3.33 (d, J = 3.5 Hz, 2H), 3.75 (dddd, J = 7.50, 13.50, 23.25, 2H), 2.38 (brs, 1H), 1.68 (brs, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.03, 159.87, 130.43, 127.32, 114.04, 70.29, 67.41, 65.26, 55.35, 36.57, 34.23. HRESI-MS: $C_{13}H_{18}O_5S$ (286.0875). $[M+H]^+$ cald: 287.0947 ; found: 287.0959.



Synthesis of 10: To a solution of **11** (1.87 g, 6.58 mmol) in dichloromethane (150 mL) and triethylamine (10 mL) was added stearoyl chloride (8.0 g, 26.3 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. Saturated aqueous sodium bicarbonate (100 mL) was added. The organic layer was separated and concentrated under reduced pressure. The desired triester was isolated after silica gel chromatography

(EtOAc/Hexane, 1/3, Rf = 0.72) as a clear oil (5.0 g, 93% yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.31 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 5.22-5.18 (m, 1H), 5.11 (s, 2H), 4.22 (dddd, J = 3.00, 5.50, 11.50 Hz, 2H), 3.82 (s, 3H), 3.28 (dd, J = 14.5 Hz, 2H), 2.82 (dddd, J = 6.00 Hz, 7.00 Hz, 14.00 Hz, 2H), 2.307 (t, J = 7.00 Hz, 1H), 2.301 (t, J = 7.5 Hz, 1H), 1.66-1.58 (m, 4H), 1.30-1.25 (m, 56H), 0.88 (t, J = 6.50 Hz, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.33, 173.00, 169.95, 130.28, 127.53, 113.98, 69.56, 67.06, 63.57, 55.27, 34.26, 34.09, 33.76, 33.72, 32.66, 31.93, 29.71, 29.68, 29.65, 29.51, 29.37, 29.30, 29.25, 29.14, 29.11, 29.07, 24.91, 24.88, 24.70, 22.70, 14.13. HRESI-MS: $C_{49}H_{86}O_7S$ (818.6094). $[M+NH_4]^+$ cald: 836.6432 ; found: 836.6451. The triester (10 g, 12.2 mmol) was dissolved in dichloromethane (25 mL), and trifluoroacetic acid (4 mL) was added at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 30 min. Saturated aqueous sodium bicarbonate (50 mL) was added. The organic layer was isolated and concentrated under reduced pressure. Desired acid was isolated after silica gel chromatography (EtOAc/Hexane, 1/5-1/3) a light yellow solid (Rf = 0.1, EtOAc/Hexane = 1/1, 8.1 g, 95% yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 5.25-5.21 (m, 1H), 4.27 (dddd, J = 4.00 Hz, 5.50 Hz, 12.00 Hz, 2H), 3.32 (dd, J = 15.00 Hz, 2H), 2.88 (dddd, J = 5.50, 7.00, 14.00 Hz, 2H), 2.33 (t, J = 7.00 Hz, 2H), 2.32 (t, J = 7.00 Hz, 2H), 1.65-1.58 (m, 4H), 1.32-1.25 (m, 56H), 0.88 (t, J = 7.00 Hz, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.37, 173.11, 69.57, 63.55, 34.26, 34.09, 33.29, 32.85, 31.92, 29.70, 29.67, 29.66, 29.49, 29.36, 29.28, 29.13, 29.10, 24.89, 24.87, 22.68, 14.11. HRESI-MS: $C_{41}H_{78}O_6S$ (698.5519). $[M+NH_4]^+$ cald: 716.5863; found: 716.5840. A mixture of the acid (500 mg, 0.716 mmol), *N*-hydroxysuccinamide (82.5 mg, 0.76 mmol), EDCI (137.3 mg, 0.72 mmol) and dichloromethane (20 mL) was stirred at room temperature for 12 h. The solvent was removed under reduced pressure at room temperature. The remaining solid was subjected to silica gel chromatography (EtOAc/hexanes,1/2, Rf = 0.45) to yield **10** as a

viscous oil (487 mg, 86 %). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 5.31-5.25 (m, 1H), 4.27 (dddd, J = 3.50, 6.00, 11.50 Hz, 2H), 3.55 (dd, J = 15.00 Hz, 2H), 2.96 (dddd, J = 5.50, 7.50, 15.00 Hz, 2H), 2.84 (s, 4H), 2.33 (t, J = 9.00 Hz, 2H), 2.31 (t, J = 7.50 Hz, 2H), 1.64-1.57 (m, 4H), 1.25 (brs, 56H), 0.88 (t, J = 7.00 Hz, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.30, 173.02, 168.67, 165.48, 69.07, 63.59, 34.23, 34.06, 32.48, 31.92, 30.28, 29.71, 29.68, 29.66, 29.65, 29.50, 29.36, 29.29, 29.14, 29.10, 25.56, 24.91, 24.86, 22.69, 14.11. HRESI-MS: $C_{45}H_{81}NO_8S$ (795.5682). $[M+NH_4]^+$ cald: 813.6021; found: 813.6017.

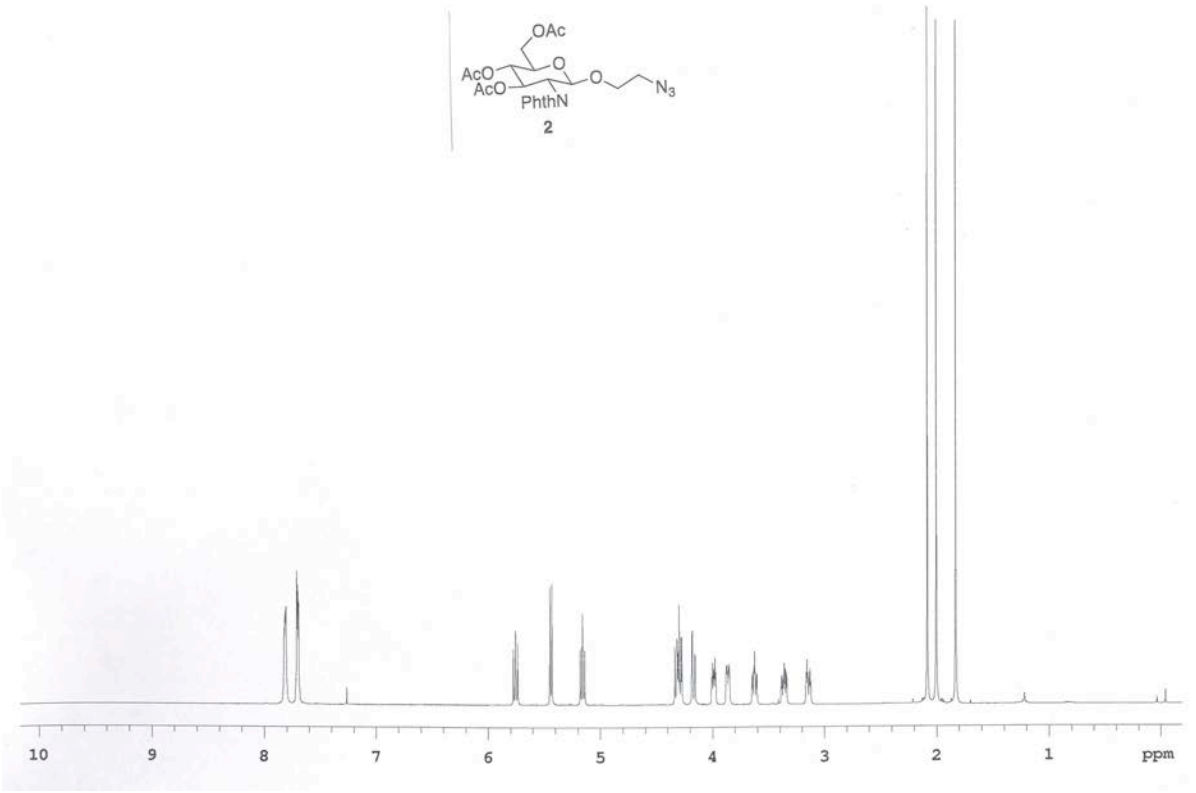
Vaccine Preparation: A chloroform mixture containing DOPC, cholesterol, PBS150 and PBS57 (or glc-DAG-s2) (35/40/20/5 molar ratio) was dried under a stream of nitrogen to remove chloroform, then hydrated and subjected to freeze/thaw cycles to produce multilamellar vesicles. Liposomes were sized by extrusion through a polycarbonate filter of 400 nm pore size (Whatman cat#80028) in the Avanti mini-extruder (AvantiPolar Lipids, cat# 610000). The quality and size of these 'pneumococcal' liposomes was monitored by cryoelectron microscopy. Liposomes were used immediately or within 1 week of storage at 4 ^{0}C.

Immunization: Mice (C57BL/6, Jackson Laboratory) were immunized intraperitoneally with Prevnar13[20] (Wyeth) concentrated over Amplicon Ultra Centrifugal Filters 0.5 mL-3K Membrane, Millipore, (Ref# UFC500324) to contain 2.2 μg of each polysaccharide in the injected 200 μL volume, or with 1 μg PBS57 + 4 μg PBS150 as a simple mixture or as liposomes in 200 μL phosphate buffered saline. The amount of each polysaccharide serotype in Prevnar is indicated by the manufacturer, and these values were used in calculating the dose of serotype 14 polysaccharide administered.

NKT-mediated cytokine release in vivo. Mice were injected intraperitoneally with PBS57/PBS150 or glc-DAG-s2/PBS150 liposomes and serum was collected at 2 h and 24 h to measure the release of IL-4 and IFN-γ, respectively, using BD mouse cytometric bead array kit.

Anti-polysaccharide antibody assay. DOPC/cholesterol liposomes containing 20% PBS150 were adsorbed onto 3-10 mM glass beads (Polysciences Inc., cat#07666) and incubated with serial dilutions of immune or naïve sera before adding FITC-conjugated isotype-specific goat antibodies from Southern Biotech (anti-IgM #1020-02, anti-IgG1 #1070-02) and measuring mean fluorescence intensity by flow cytometry. Arbitrary units/mL were determined by reference to a standard hyperimmune serum pool, with the following reciprocal end-point titer equivalences for 1 AU/mL: IgM, 16; IgG1, 32. s

Statistical analysis: For each vaccine group, it was of interest to identify the first time point at which IgG1 levels differed significantly from baseline. Comparisons between baseline and each subsequent time point were made through use of one-sided t-tests. Tests were performed on log transformed data; assumptions of normality were satisfied. All p-values were adjusted for multiple comparisons through use of the Bonferroni correction.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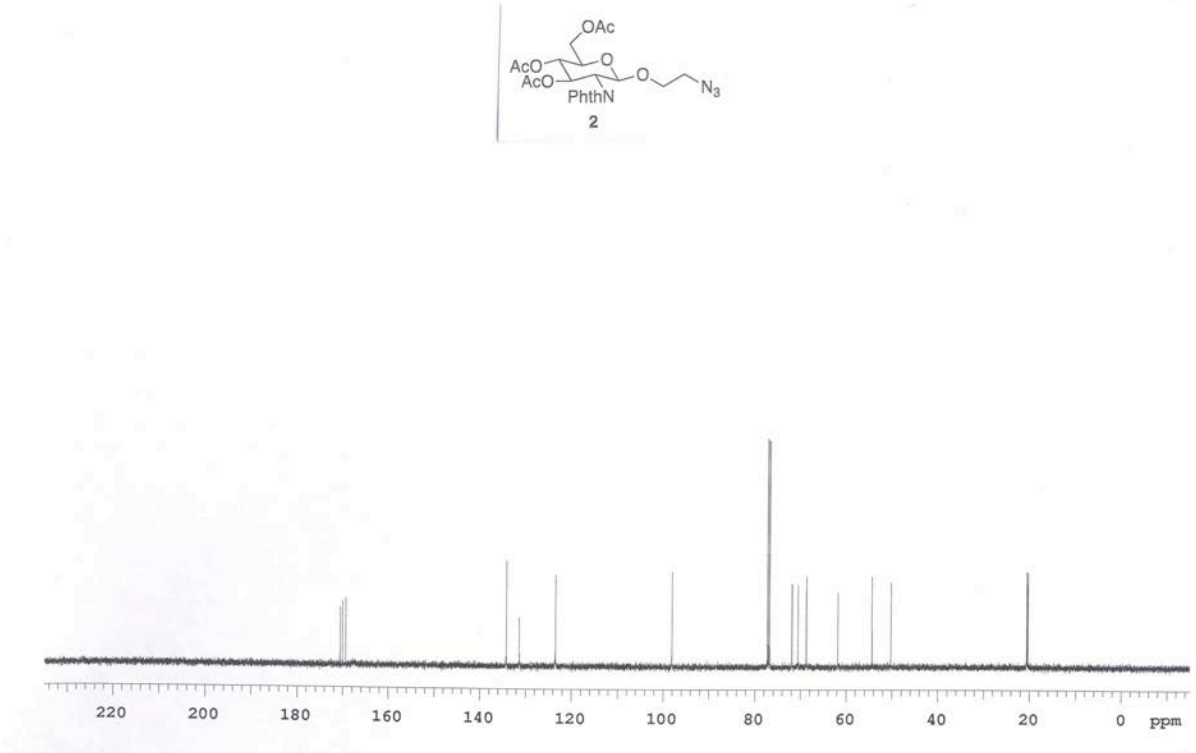
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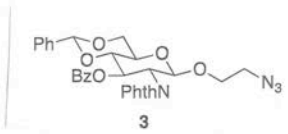
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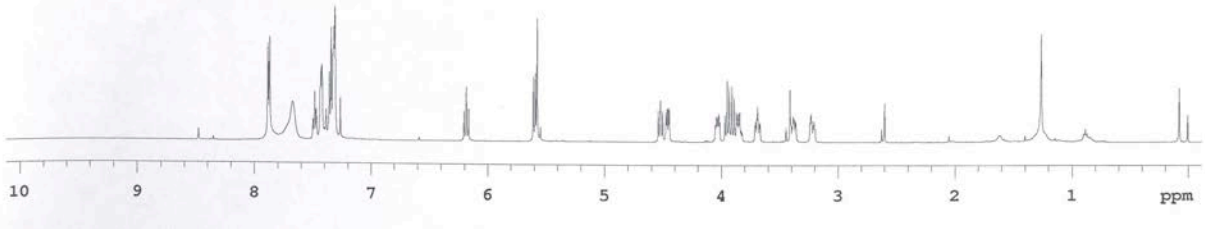
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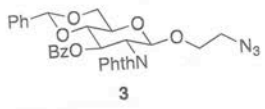
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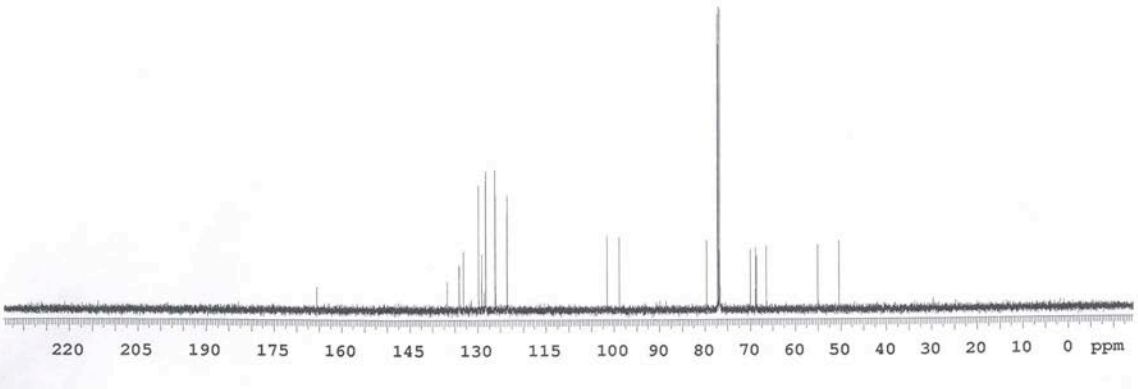
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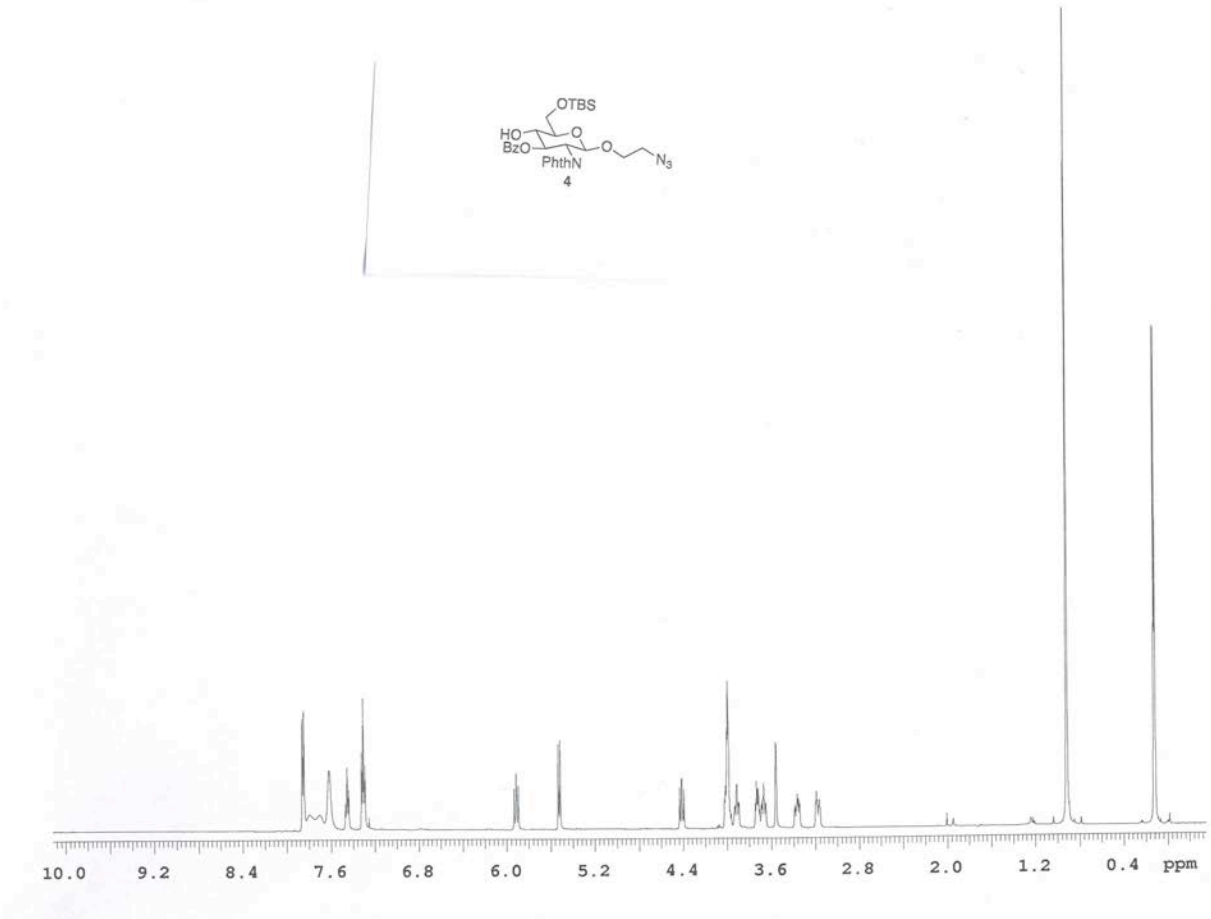
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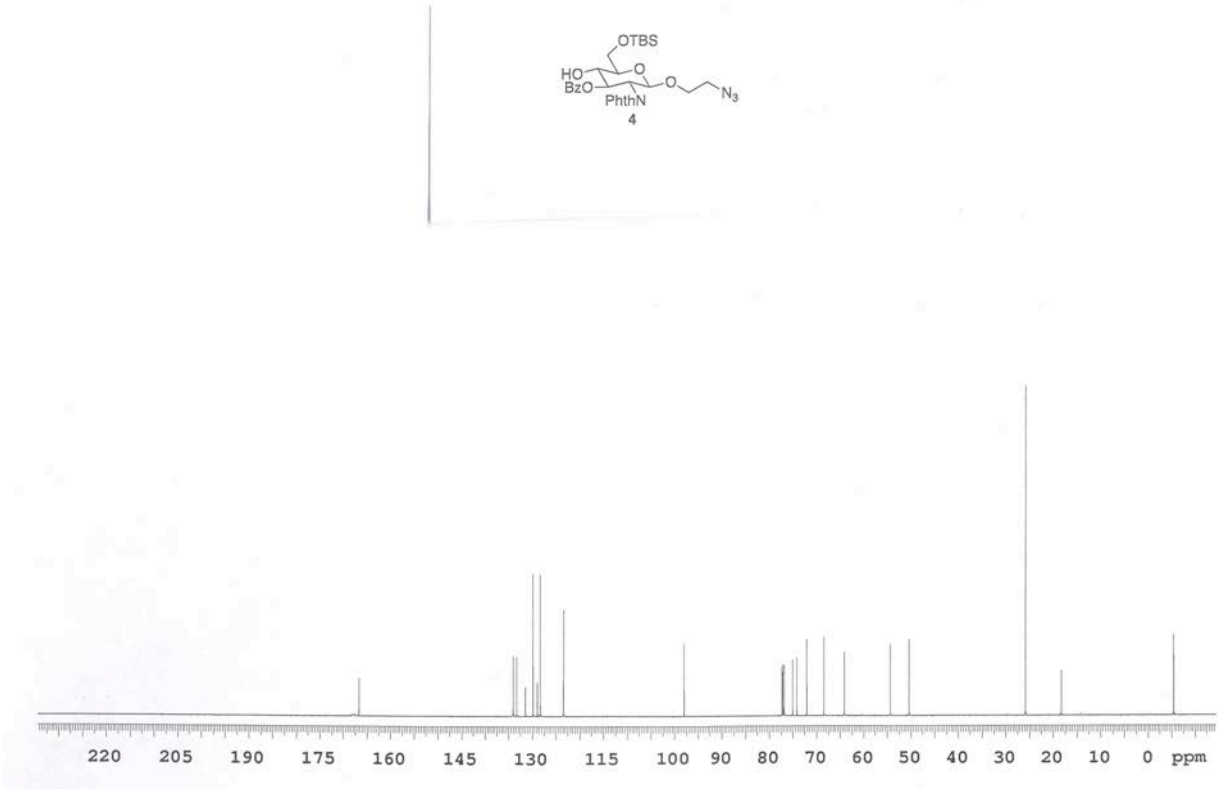
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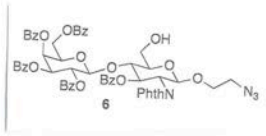
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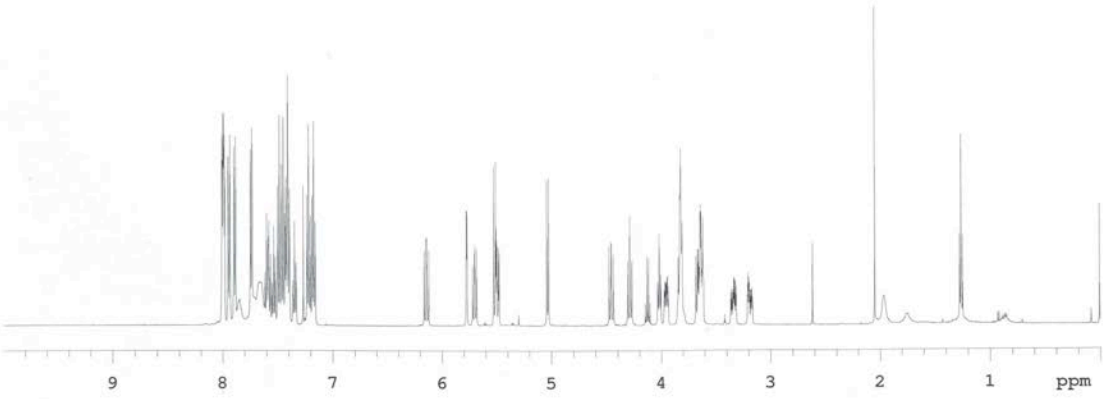
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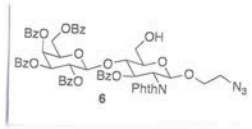
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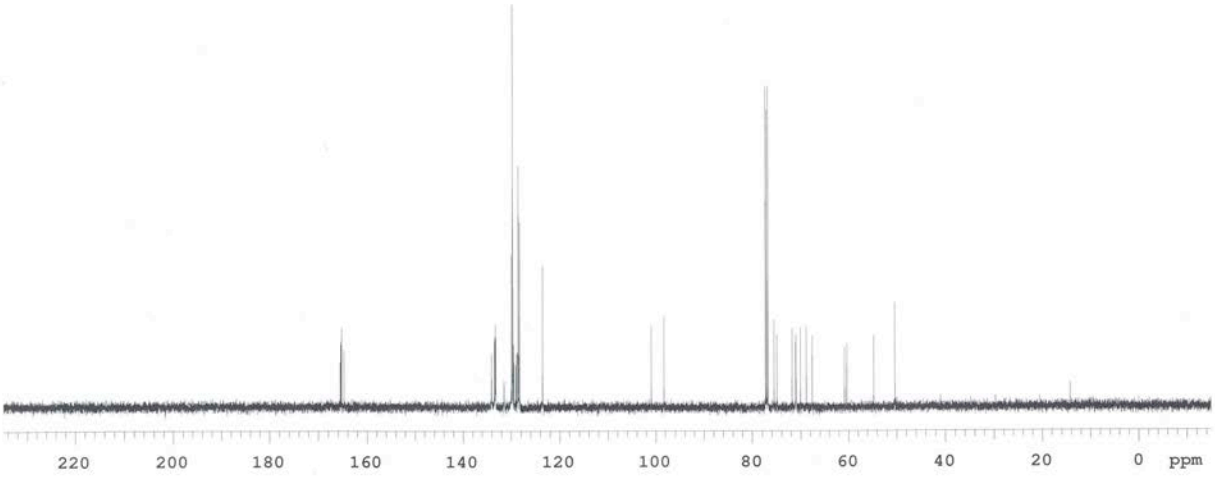
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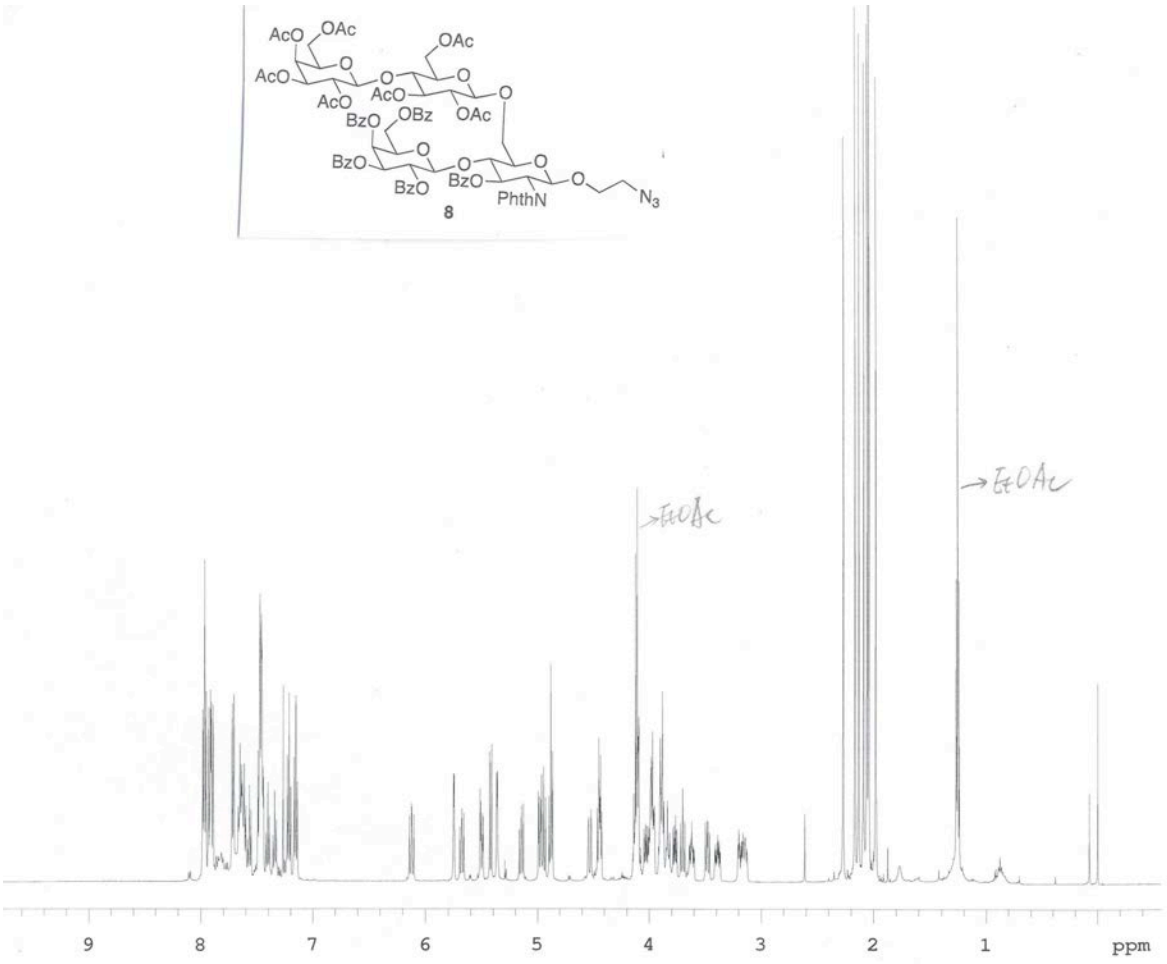
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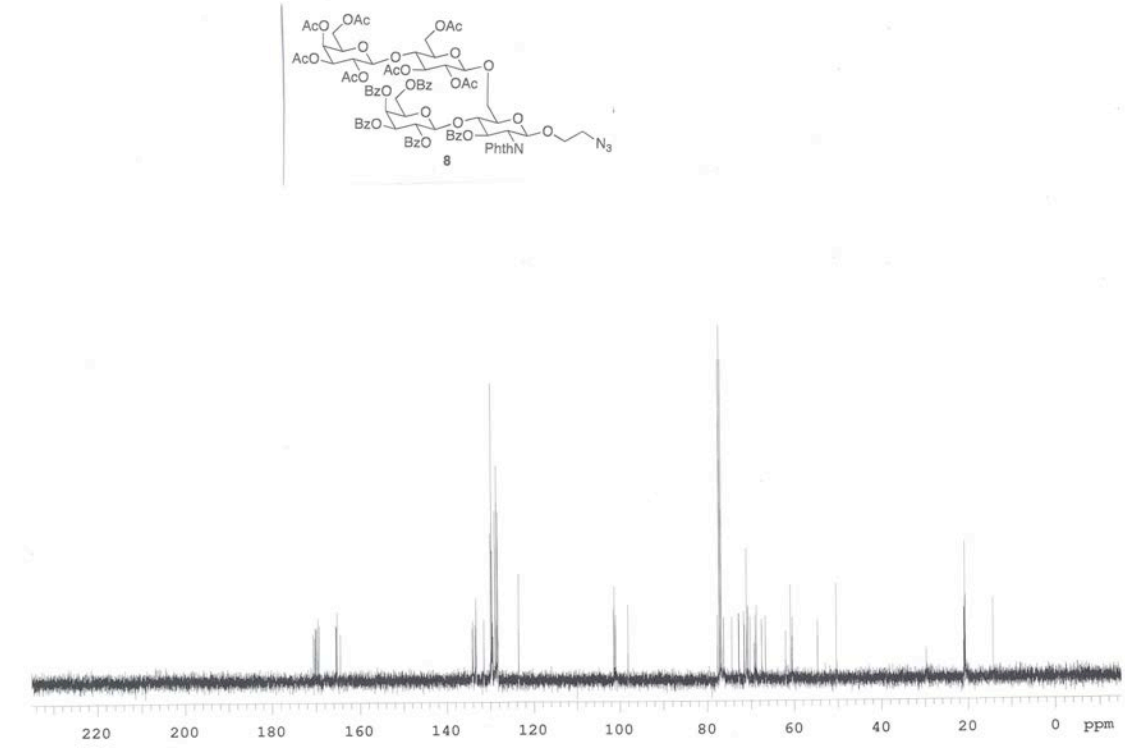
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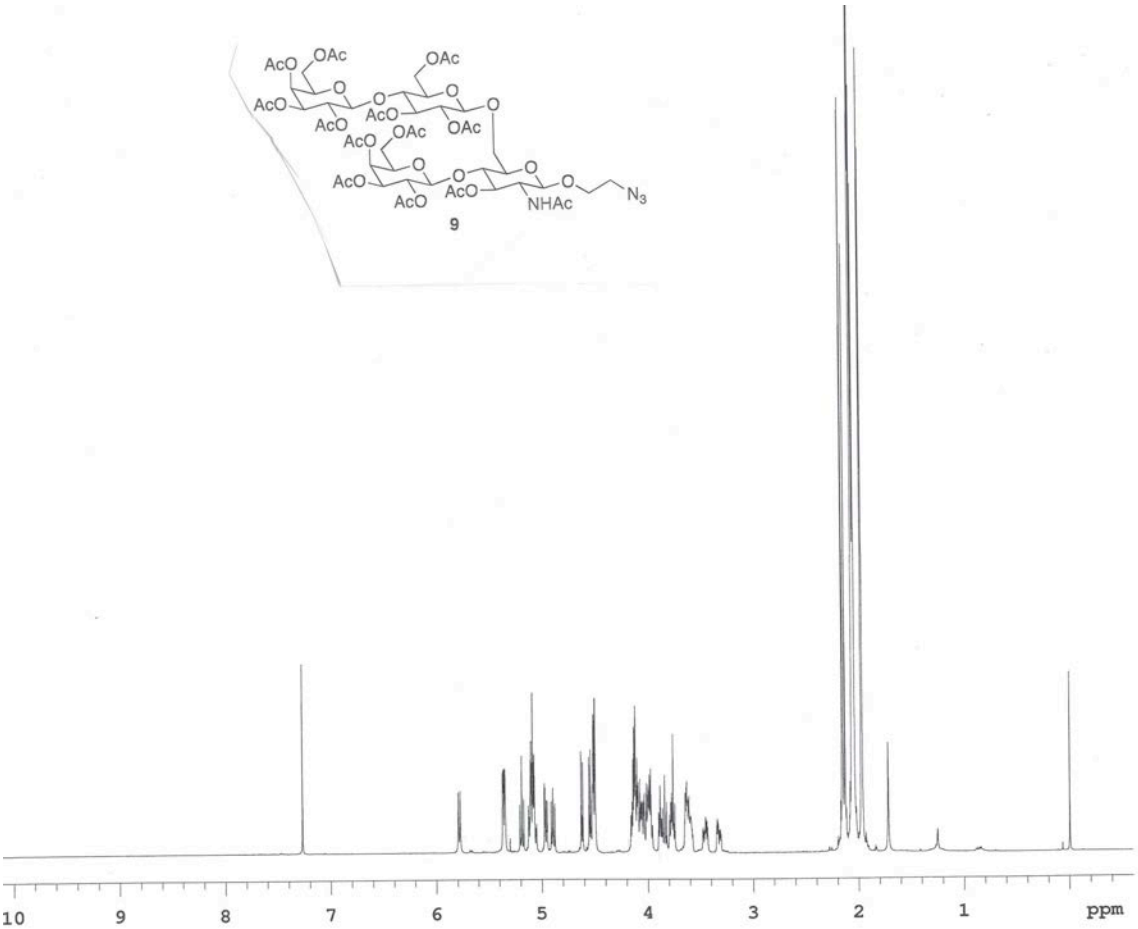
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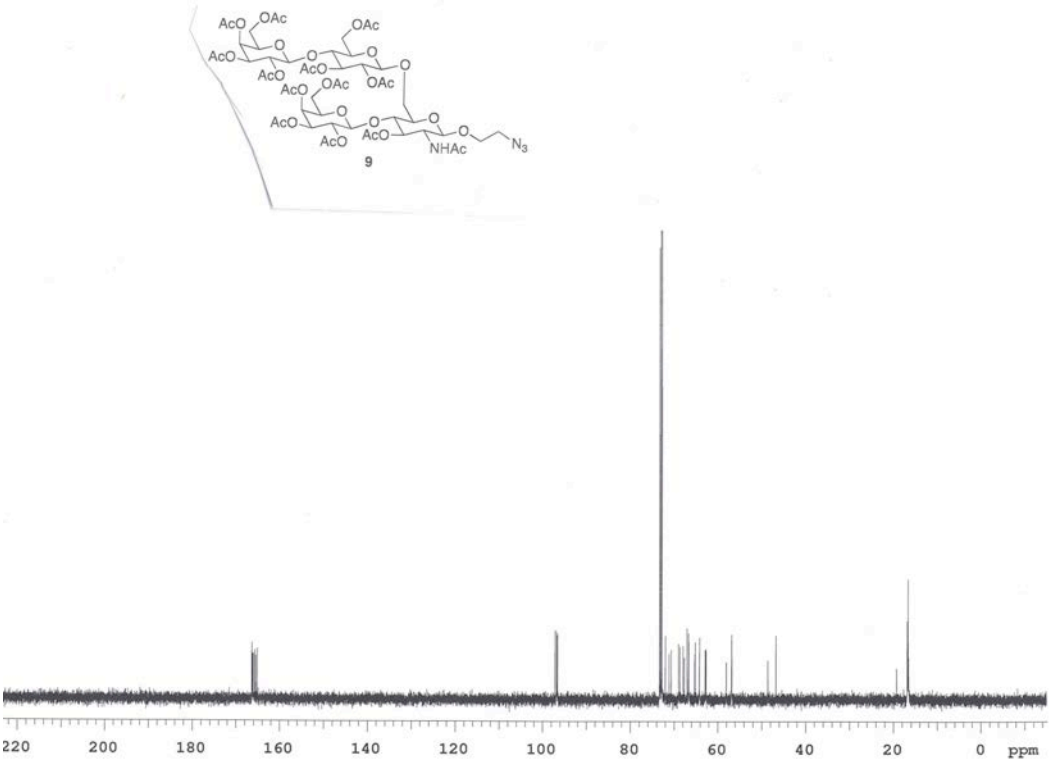
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STANDARD PROTON PARAMETERS

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Data collected on: Oct 26 2010

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Operator: sdeng

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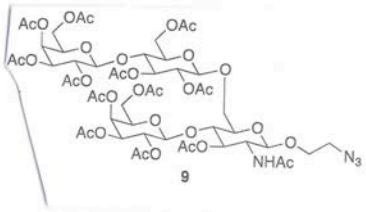

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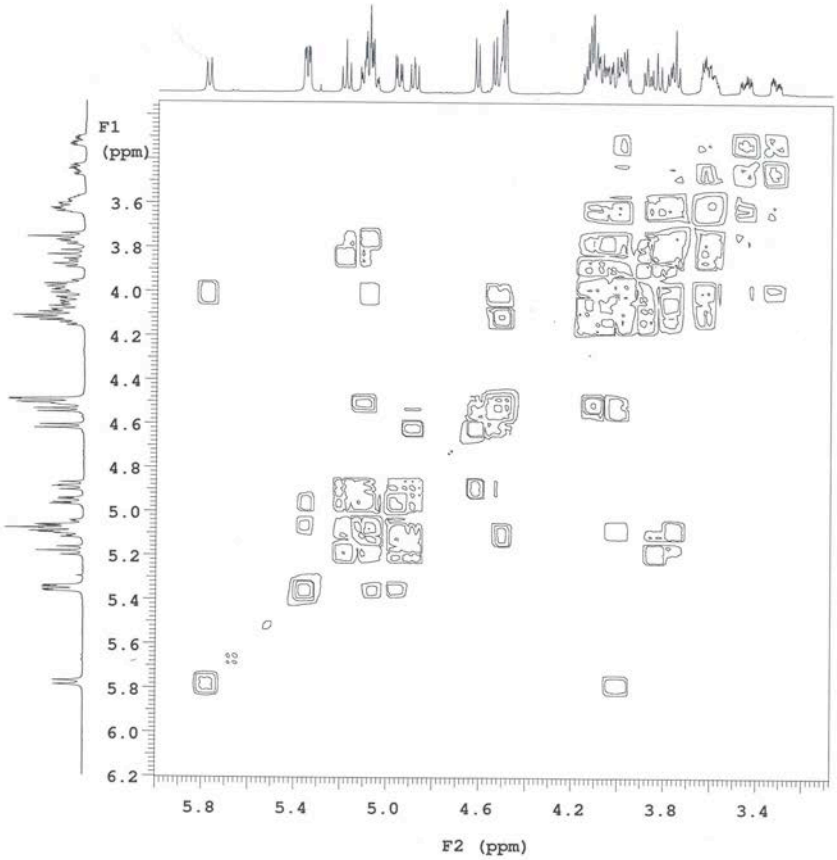

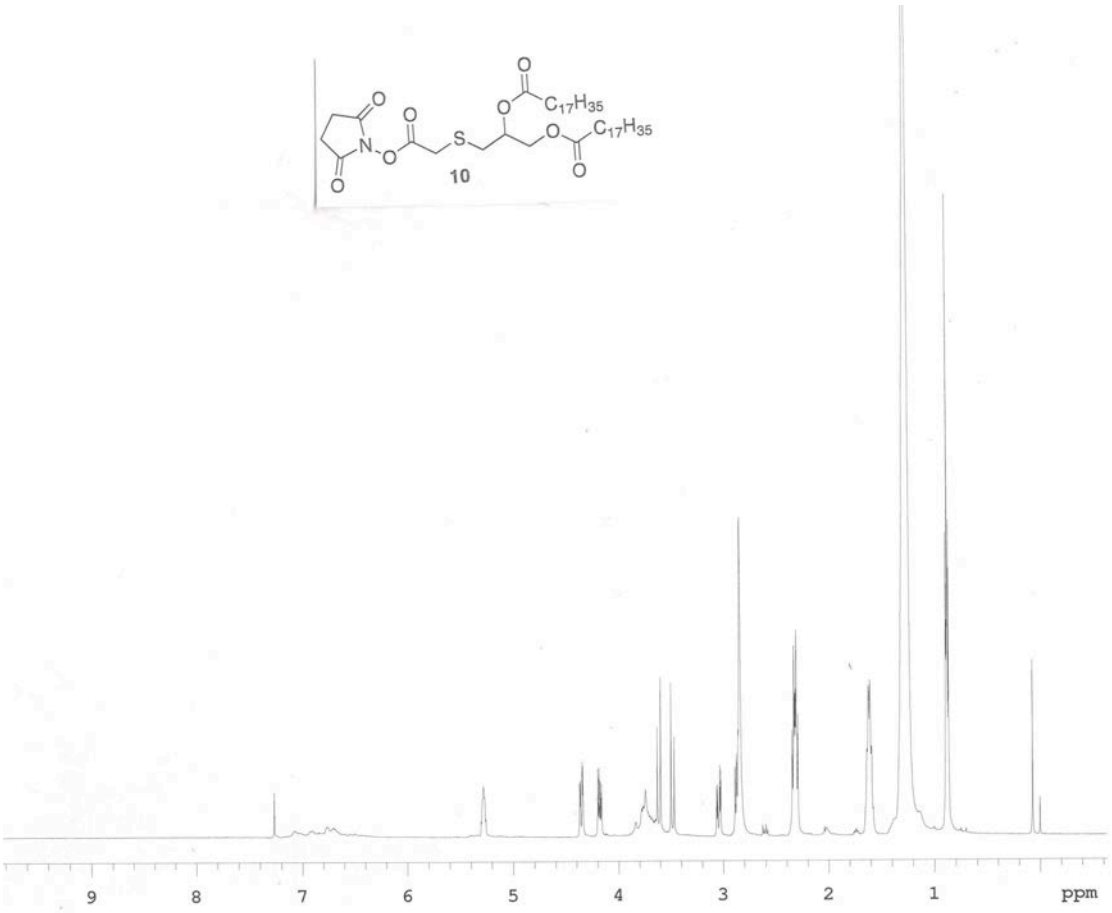
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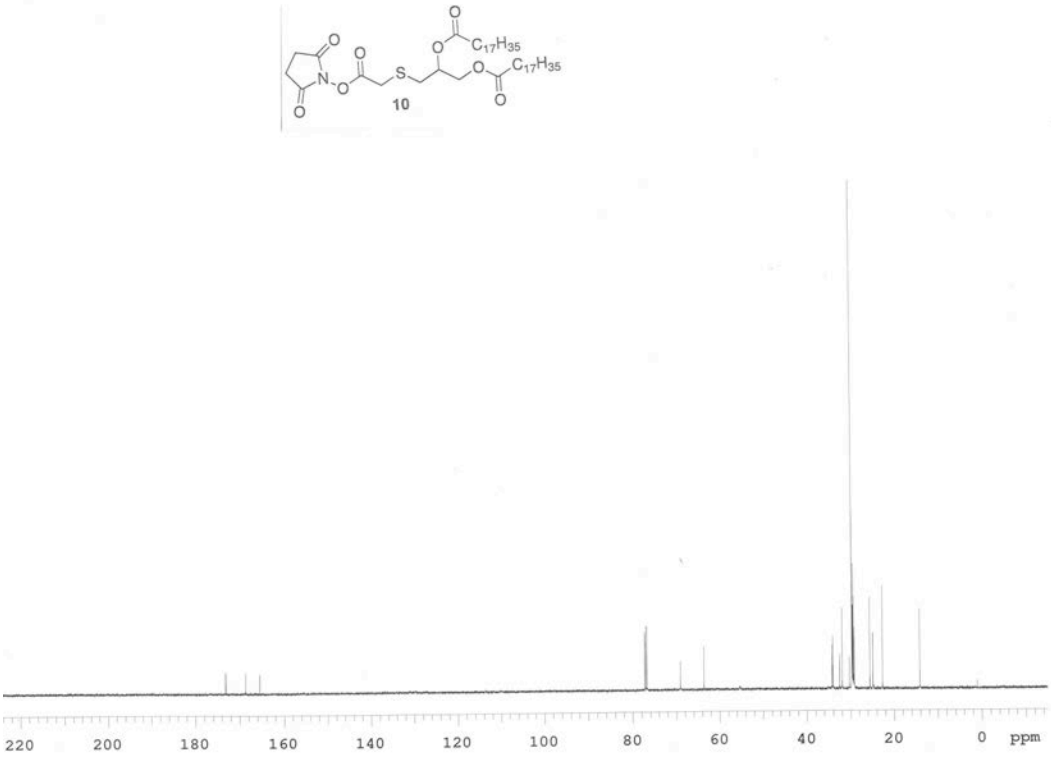
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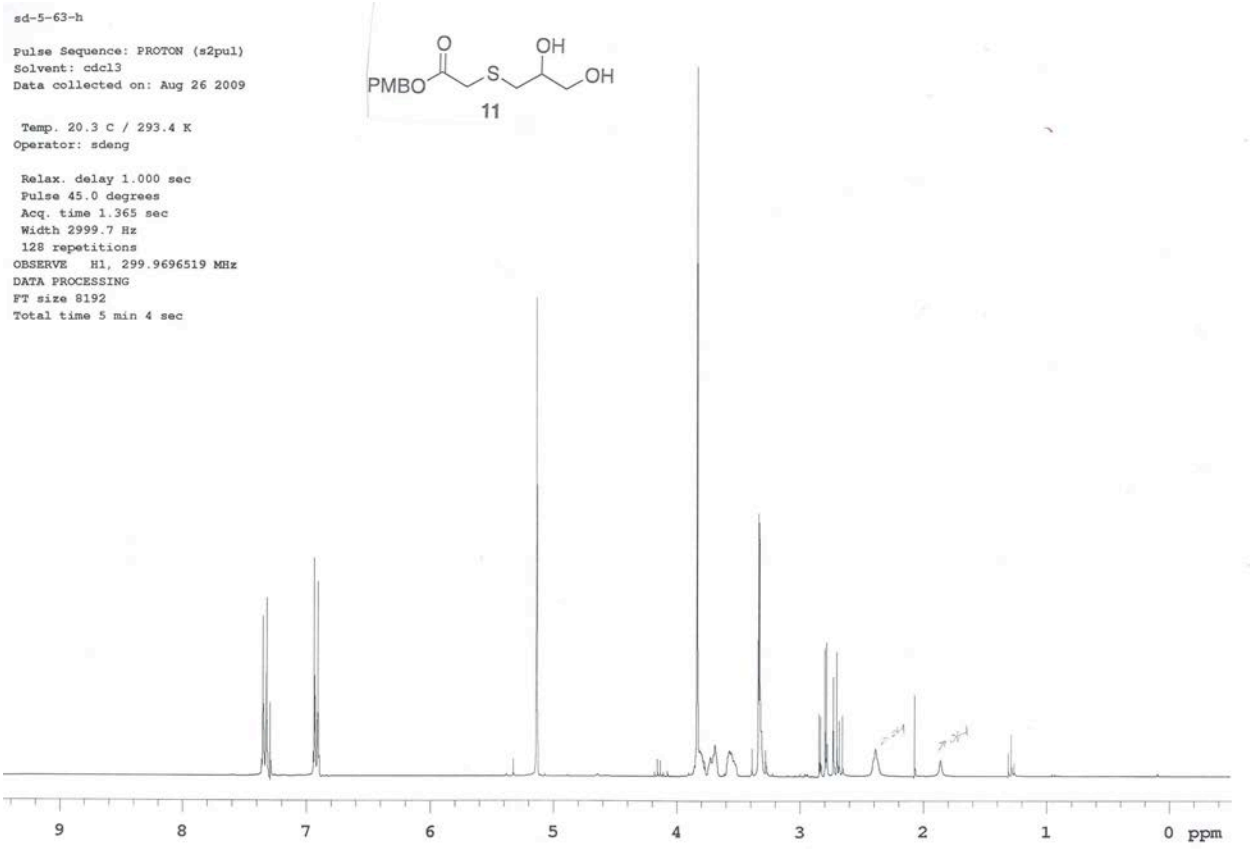
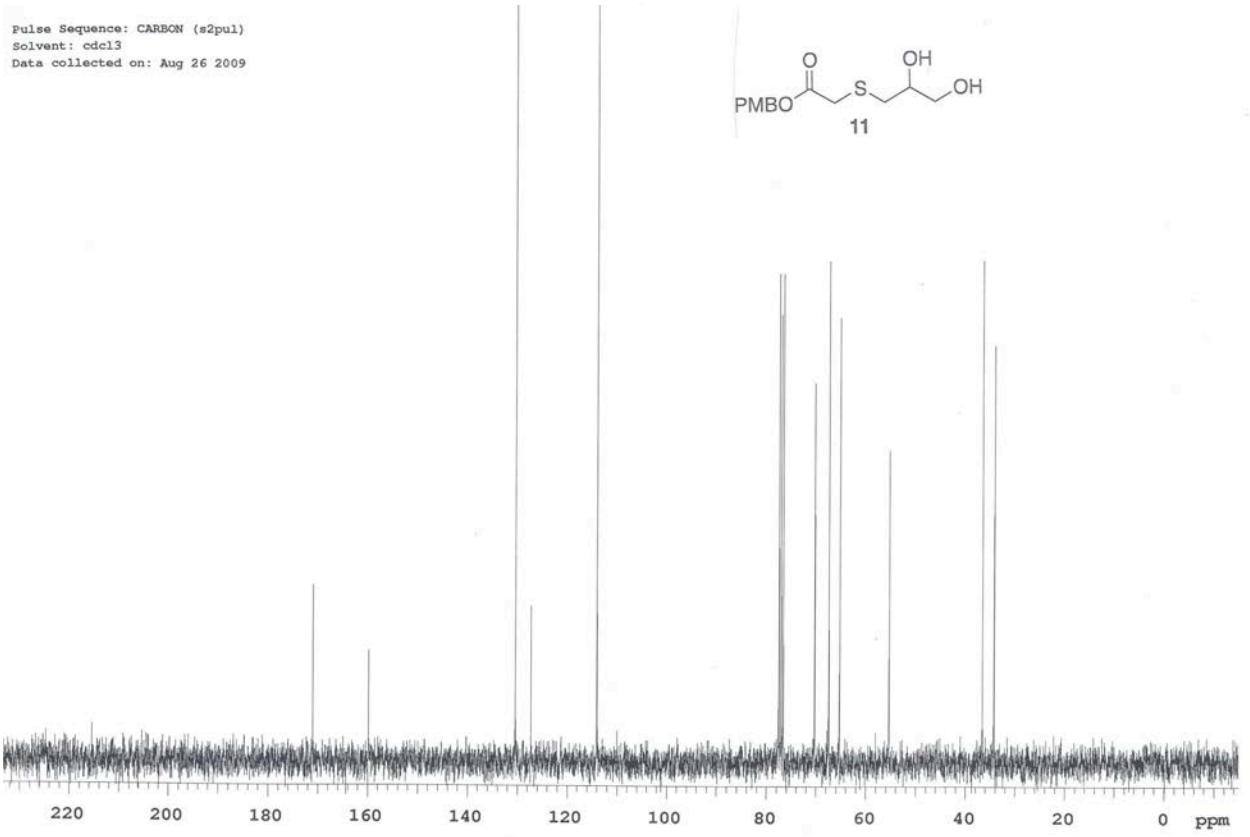
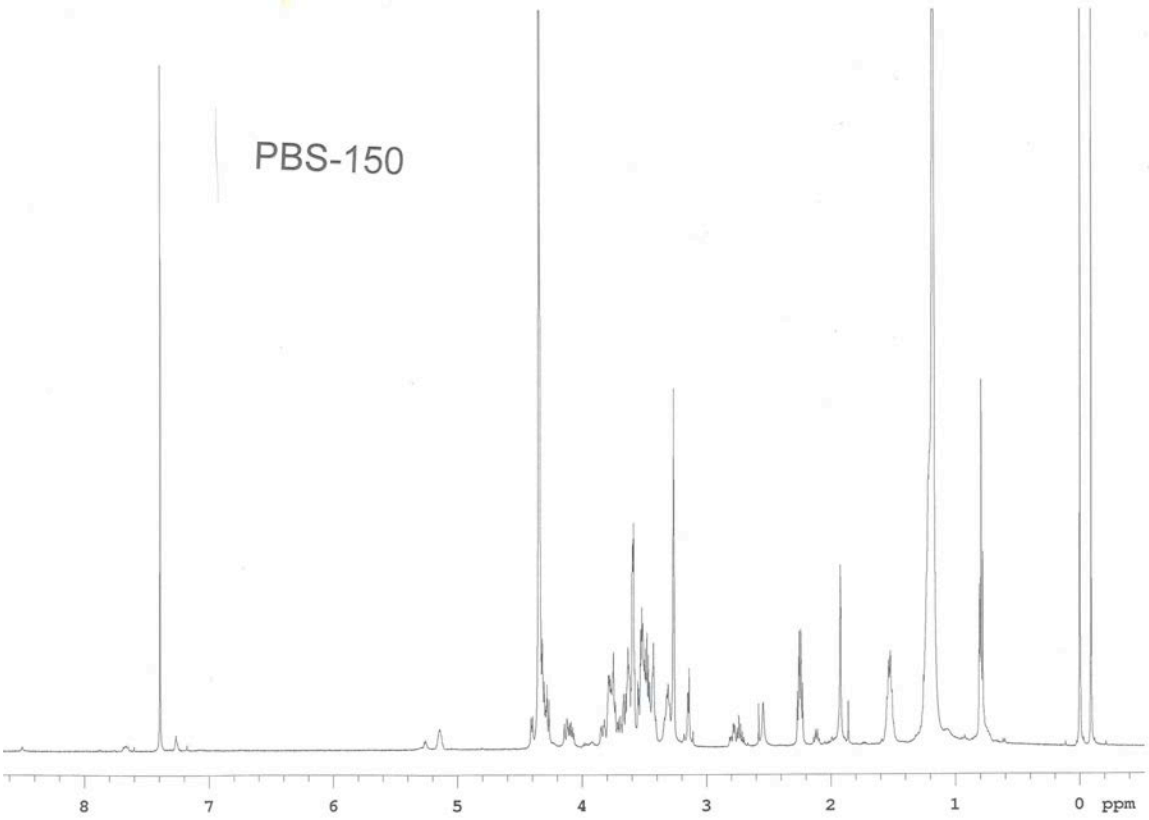
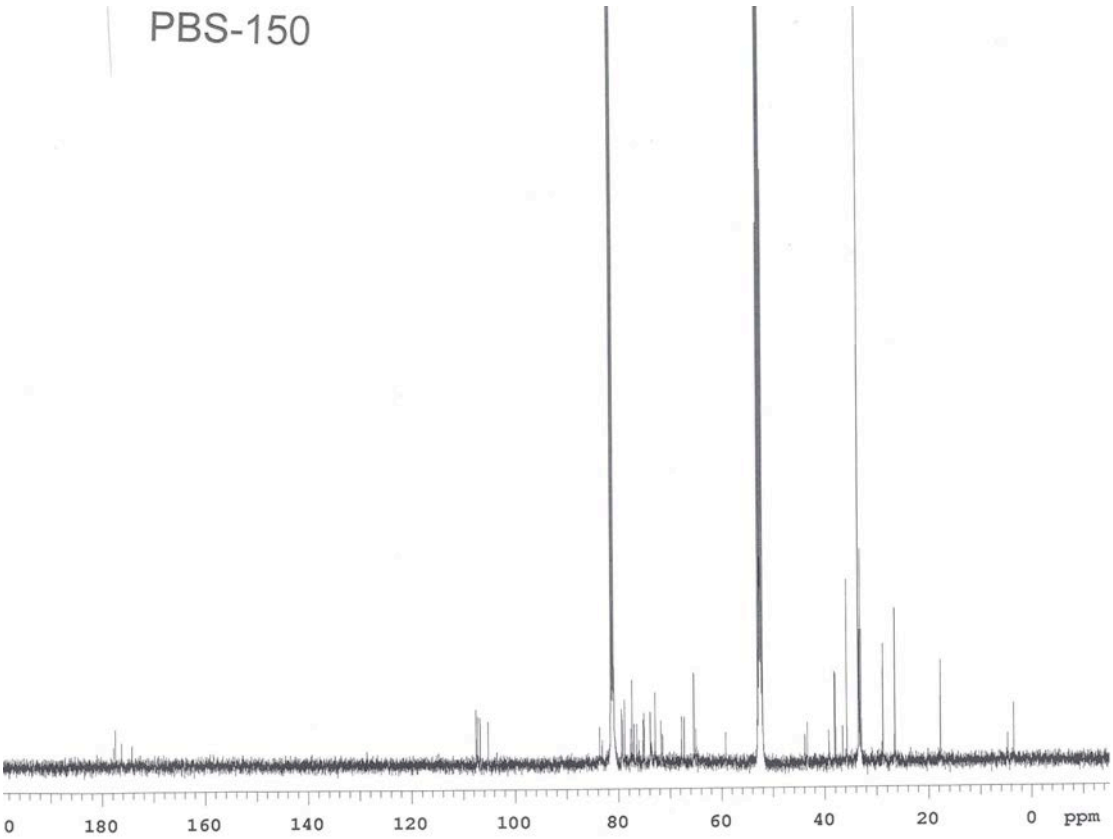
20
0
ppm


sd-5-63-h
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 26 2009
Temp. 20.3 C / 293.4 K
Operator: sdeng
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.365 sec
Width 2999.7 Hz
128 repetitions
OBSERVE H1, 299.9696519 MHz
DATA PROCESSING
FT size 8192
Total time 5 min 4 sec
PMBO
O
S
OH
OH
11
9
8
7
6
5
4
3
2
1
0 ppm

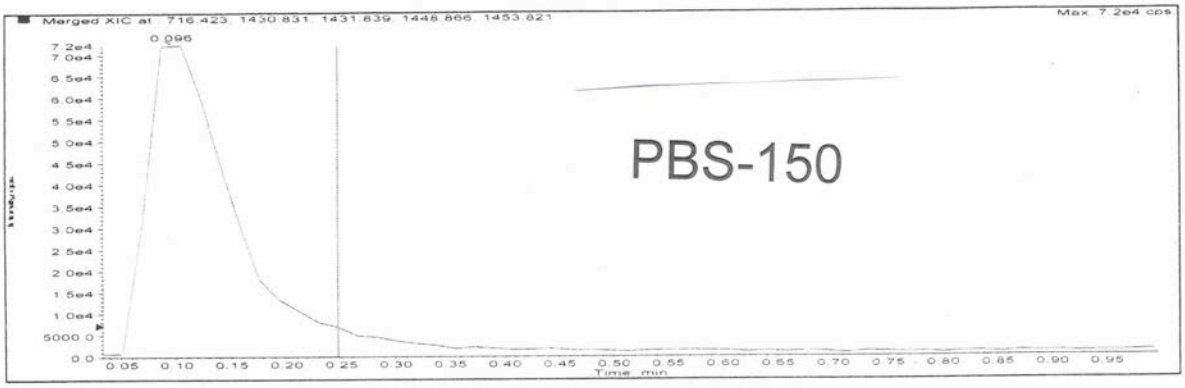

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 26 2009
PMBO
O
S
OH
OH
11
220
200
180
160
140
120
100
80
60
40
20
0 ppm


PBS-150
8
7
6
5
4
3
2
1
0
ppm

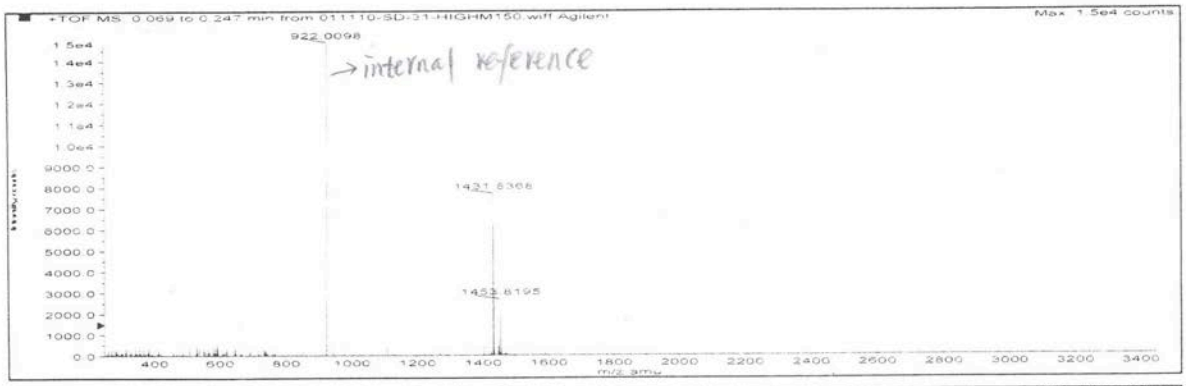

PBS-150
0
180
160
140
120
100
80
60
40
20
0
ppm

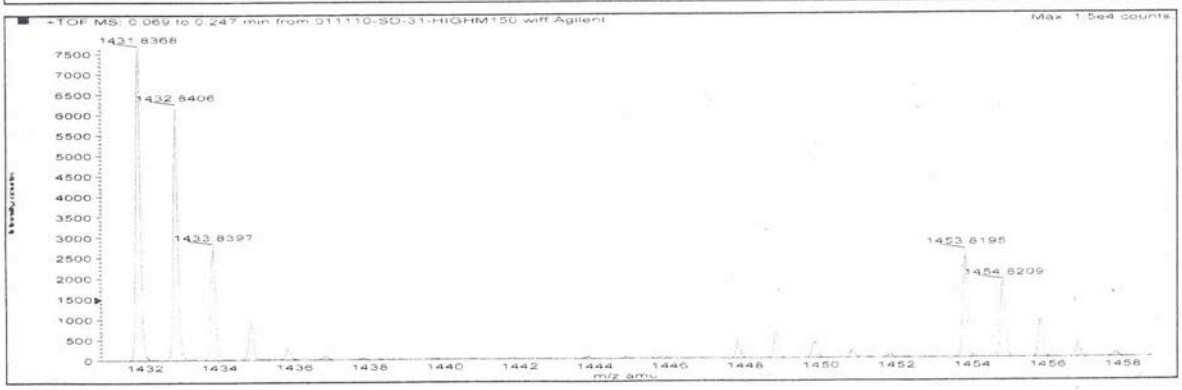
Sample Name: **SD-3** Sample Location: **72** Sample Id: **SD-3** Operator: **EasyAccess**
Data File Name: **d:\PE Sciex Data\Projects\chemist\11-10\Data\011110-SD-31-HIGHM150.wiff** Acq Time: **November 01 2010, 09:09:50 AM**
Method: **C:\Program Files\Agilent\TOF Software\damethods\BJJ.ANM\efc.xml**

One or more scans have failed IRM. Review the data file for details.



Merged XIC, Period# : 1 Experiment# : 1





Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C69H126N2O26S	--	1430.83195	0.10	3.97044 E5	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M+H]+	7986.34	1431.83923	1431.83676	-2.46877	-1.72	--
[M+Na]+	2688.18	1453.82117	1453.81951	-1.66040	-1.14	--