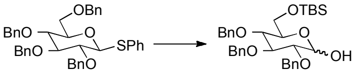
Supporting Information

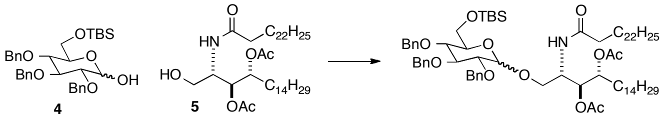
General Methods: ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian Unity 500 MHz or 300 MHz instruments. Mass spectrometric data were obtained on an Agilent 1100 series spectrometer. Methylene chloride, THF, DMF, pyridine, and DMSO were dried by passage through a Glass Contour solvent drying system containing cylinders of activated alumina. Chemicals were obtained from Fluka, Aldrich, Acros, and Sigma and were used as received unless otherwise noted. LC-MS was performed on Agilent LCMS TOF spectrometer with C3 reverse phase column (Agilent) 100×3 mm. Gradient eluent was used (for compounds 1 and 2, CH_3CN/H_2O(50/50) to CH_3CN/H_2O(30/70); for compound GSL-1C, CH_3CN/H_2O(30/70) to CH_3CN/H_2O(30/70)). KRN7000 was prepared as described.[25]

Synthesis of 1 (Scheme 1).

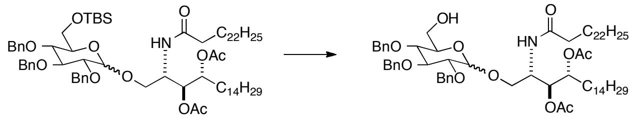


3 **4**

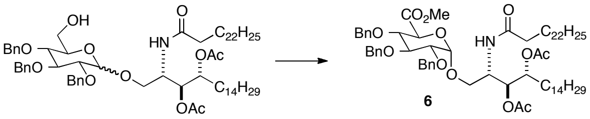
To a solution of 2,3,4,6-tetrabenzyl-1-β-D-phenylthioglucoside (**3**) (600 mg, 0.950 mmol) in CH_2Cl_2 (30 mL) was added Ac_2O (0.228 mL, 2.468 mmol) at -78° C, then TMSOTf (0.228 mL, 2.468 mmol) was added slowly. The mixture was allowed to slowly warm to room temperature. After 4 h, water (5 mL) and ether (50 mL) were added. The organic phase was washed with 1 N HCl and saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated. The resulting oil was subjected to silica gel chromatography (R_f = 0.25, EtOAc/hexanes = 1/4), affording the 1,6-diacetate (210 mg, 41% yield) as a mixture of α and β anomers. ^{1}H NMR ($CDCl_3$, 500 MHz) of α anomer: δ 7.42-7.33 (m, 15 H), 6.415 (d, J = 3.5 Hz, 1H), 5.06 (d, J = 10.5 Hz, 1H), 4.96 (d, J = 11.0 Hz, 1H), 4.90 (d, J = 11.0 Hz, 1H), 4.77 (d, J = 11.0 Hz, 1H), 4.69 (d, J = 11.0 Hz, 1H), 4.65 (d, J = 10.5 Hz, 1H), 4.36 (dd, J = 4.0, 12.0 Hz, 1H), 4.31 (dd, J = 2.00, 12.00 Hz, 1H), 4.05 (t, J = 9.00 Hz, 1H), 4.03-4.01 (m, 1H), 3.74 (dd, J = 3.50, 10.00 Hz, 1H), 3.64 (t, J = 9.50 Hz, 1H), 2.19 (s, 3H), 2.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) of α isomer: (CD_3CO_2D/DMSO-D_6, 125 MHz, ppm): δ 165.93, 164.60, 133.77, 132.95, 132.82, 123.84, 123.79, 123.60, 123.45, 123.29, 123.17, 84.94, 76.93, 74.16, 71.85, 71.03, 70.55, 68.48, 66.39, 57.95, 16.46, 16.27; HRESI-MS: $C_{31}H_{34}O_8$ (534.22537). $[M+NH_4]^+$: Calcd: 552.25919; found: 552.25819. To a solution of the 1,6-diacetate (250 mg, 0.286 mmol) in a mixture of THF (7 mL) and MeOH (3 mL) was added NaOMe (1 *M* in methanol, 0.5 mL). The mixture was stirred for 1 h, then AcOH (1 mL) was added. The solvent was removed, and the residue was dissolved in THF (10 mL) and CH_3CN (30 mL). Imidazole (50 mg, 0.74 mmol) was added, and the mixture was cooled to -15° C with an ice-acetone bath. TBSCl (64.65 mg, 0.429 mmol) was added. The reaction mixture was stirred for 2 h at -15 °C. MeOH (1 mL) was added, and the solvent was removed. The residue was subjected to silica gel chromatography (R_f = 0.45, EtOAc/hexanes = 1/4), affording **4** as a thick oil (160 mg, mixture of α and β isomers, 82% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.40-7.26 (m), 5.25 (d, J = 3.00 Hz), 5.00-4.65 (m), 4.02-3.81 (m), 3.71-3.63 (m), 3.56 (dd, J = 4.00, 9.00 Hz), 3.40-3.34 (m), 3.18 (brs), 1.77 (brs), 0.93 (s), 0.11 (s), 0.10 (s), 0.09 (s), 0.08 (s); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 138.69, 138.55, 138.50, 138.34, 137.96, 128.52, 128.47, 128.44, 128.43, 128.41, 128.36, 128.29, 128.09, 128.04, 128.00, 127.98, 127.96, 127.87, 127.80, 127.73, 127.70, 97.42, 91.21, 84.59, 83.52, 81.74, 80.49, 77.48, 76.10, 75.85, 75.78, 75.03, 75.01, 74.79, 73.30, 71.68, 62.39, 62.13, 26.04, 26.00, -5.01, -5.05, -5.27, -5.31; HRESI-MS: $C_{33}H_{44}O_6Si$ (564.2907). $[M+NH_4]^+$ Calcd: 582.3245; Found: 582.3379.



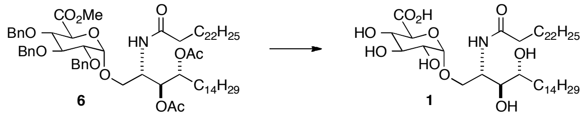
Donor **4** (200 mg, 2.362 mmol) was mixed with Ph_2SO (153 mg, 0.754 mmol), TTBP (0.262 g, 1.055 mmol) and 3 Å ms (700 mg) in CH_2Cl_2 (6 mL) and stirred for 30 min. The mixture was cooled to -60° C, and Tf_2O (0.119 g, 0.427 mmol) was added. The reaction mixture was allowed to warm to -40° C, and the acceptor **5** (0.22 g, 0.30 mmol) in CH_2Cl_2 (1.5 mL) was added. The reaction mixture was allowed to slowly warm to room temperature over the span of 4 h. Et_3N (0.1 mL) was added, and the solvent was removed. The resulting mixture was subjected to silica gel chromatography (R_f = 0.7, EtOAc/hexanes = 1/4), affording 198 mg of the glycosylated product as a mixture of anomers (51 % yield). ^1H NMR ($CDCl_3$, 500 MHz) of mixture: δ 7.39-7.26 (m, 15H), 6.58 (d, J = 9.0 Hz), 5.88 (d, J = 9.5 Hz) 5.29 (dd, J = 2.5, 9.0 Hz), 5.19 (dd, J = 2.0, 9.5 Hz), 4.96 (dt, J = 3.00, 10.5 Hz), 4.92-4.59 (m), 4.36-4.35 (m), 3.96-3.89 (m), 3.86-3.76 (m), 3.65-3.47 (m), 3.38 (dd, J = 3.0, 11.0 Hz), 2.18-2.15 (m), 2.08 (s), 2.03 (s), 2.02 (s), 2.00 (s), 1.71-1.58 (m), 1.31-1.24 (m), 0.88 (t, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.08, 172.85, 171.38, 171.07, ,171.05, 170.36, 170.05, 139.02, 139.0, 138.72, 138.25, 128.62, 128.58, 128.47, 128.38, 128.31, 128.18, 128.01, 127.94, 127.85, 99.14, 97.99, 81.92, 80.58, 79.61, 75.99, 75.22, 74.58, 73.88, 73.48, 73.18, 72.75, 72.39, 71.89, 66.90, 66.86,62.50, 62.16, 48.23, 47.94, 37.01, 32.17, 29.96, 29.61, 27.97, 26.16, 25.96, 25.86, 22.94, 21.28, 18.54, 14.43, 14.37; HRESI-MS: $C_{79}H_{131}NO_{11}Si$ (1297.9491). $[M+H]^+$ Calcd: 1298.9564; Found; 1298.9834.



To a solution of the glycoside from above (198 mg, 0.155 mmol) in a mixture of CH_3CN (15 mL) and CH_2Cl_2 (4 mL) was added HF_{aq} (48%, 4 mL). The mixture was stirred for 5 h, then diluted with CH_2Cl_2 (20 mL) and washed with saturated aqueous $NaHCO_3$. The organic phase was dried over Na_2SO_4 and concentrated to an oil. The product was isolated by silica gel chromatography (R_f =0.3-0.5, EtOAc/hexanes = 1/2) to give 151 mg of a clear oil (84% yield). ^1H NMR ($CDCl_3$, 500 MHz, α isomer, ppm): δ 7.40-7.29 (m, 15H), 6.05 (d, J = 9.50 Hz, 1H), 5.36 (dd, J = 2.50, 10.00 Hz, 1H), 4.93 (d, J = 10.5 Hz, 1H), 4.85 (d, J = 11.50 Hz, 1H), 4.82 (m, 1H), 4.81 (d, J = 10.5 Hz, 1H), 4.75 (d, J = 12. 0 Hz, 1H), 4.64 (d, J = 11.50 Hz, 1H), 4.60 (d, J = 11.5 Hz, 1H), 4.565 (d, J = 3.5 Hz, 1H), 4. 27 (m, 1H), 4.01 (m, 2 H), 3.89 (t, J = 9.5 Hz, 1H), 3.83 (m, 1H), 3.50 (dd, J = 4.0, 10.0 Hz, 1H), 3.45 (m, 2H), 3.29 (t, J = 10.0 Hz, 1H), 3.16 (brs, 1H), 2.19 (t, J = 9.0 Hz, 2H), 2.11 (s, 3H), 2.02 (s, 3H), 1.66-1.58 (m, 4 H), 1.40-1.11 (m, 64 H), 0.88 (t, J = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz, α isomer, ppm): δ 173.51, 172.23, 170.14, 138.88, 138.14, 128.66, 128.38, 128.33, 128.19, 128.09, 127.89, 100.47, 81.77, 80.50, 78.38, 75.98, 74.78, 74.03, 73.75, 72.88, 72.11, 70.48, 48.58, 36.77, 32.18, 29.96, 29.89, 28.63, 29.52, 27.12, 25.93, 25.82, 22.95, 21.38, 21.24, 14.38; HRESI-MS: $C_{73}H_{117}NO_{11}$ (1183.86266). $[M+NH_4]^+$ Calcd: 1201.89649; found: 1201.89081.

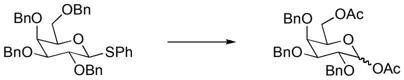


The alcohol from above (120 mg, 0.101 mmol), TBAI (81.66 mg, 0.254 mmol), TEMPO (3.17 mg, 0.0203 mmol) in CH_2Cl_2 (10 mL) was stirred for 12 h, then diluted with CH_2Cl_2, washed with water. The organic phase was dried and concentrated to 5 mL. To this solution was added a solution of excess CH_2N_2 in Et_2O. AcOH (2 mL) was added, and the solution was washed with aqueous $NaHCO_3$ and water. The organic layer was concentrated and subjected to silica gel chromatography (R_f = 0.25, EtOAc/hexanes = 1/3), affording 45.4 mg of the α isomer in (37% yield) and 31 mg of the β anomer (25% yield). ^{1}H NMR ($CDCl_3$, 500 MHz, α anomer, ppm): δ 7.36-7.22 (m, 15 H), 6.46 (d, J = 9.0 Hz, 1H), 5.27 (dd, J = 3.0, 9.0 Hz, 1H), 4.98 (dt, J = 3.0, 10.50 Hz, 1H), 4.93 (d, J = 11.0 Hz, 1H), 4.81 (d, J = 10.5 Hz, 1H), 4.802 (d, J = 2.5 Hz, 1H), 4.78 (d, J = 11.00 Hz, 1H), 4.75 (d, J = 11.50 Hz, 1H), 4.66 (d, J = 11.50 Hz, 1H), 4.57 (d, J = 11.00 Hz, 1H), 4.38 (m, 1H), 4.15 (d, J = 9.50 Hz, 1H), 3.93 (t, J = 9 .5 Hz, 1H), 3.73-3.67 (m, 1H), 3.70 (s, 3H), 3.57 (dd, J = 3.0, 9.5 Hz, 1H), 3.53 (dd, J = 2.5, 10.5 Hz, 1H), 2.18 (m, 3H), 2.08 (s, 3H), 2.01 (s, 3H), 1.67 (m, 4H), 1.36-1.40 (m, 64 H), 0.89 (t, J = 6.5 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz, α anomer, ppm): δ 173.09, 171.15, 171.01, 169.90, 138.71, 138.24, 137.98, 128.71, 128.63, 128.47, 128.17, 128.07, 127.91, 98.42, 81.14, 79.49, 75.97, 75.38, 73.38, 72.112, 70.89, 67.51, 52.76, 48.14, 36.96, 32.17, 29.96, 29.61, 28.14, 25.90, 22.94, 21.26, 21.17, 14.38; HRESI-MS: $C_{74}H_{117}NO_{12}$ (1211.85758). $[M+NH_4]^+$ Calcd: 1229.8914; found: 1229.89155. ^{1}H NMR ($CDCl_3$, 500 MHz, β anomer, ppm): δ: 7.36-7.22 (m, 15 H), 6.11 (d, J = 8.50 Hz, 1H), 5.23 (dd, J = 2.0, 9.0 Hz, 1H), 4.95-4.92 (m, 2H), 4.72 (d, J = 12.50 Hz, 1H), 4.69 (d, J = 12.5 Hz, 1H), 4.63 (d, J = 11.50 Hz, 1H), 4.60 (d, J = 11.5 Hz, 1H), 4.58 (d, J = 12.50 Hz, 1H), 4.53 (d, J = 11.50 Hz, 1H), 4.35-4.31 (m, 1H), 4.23 (d, J = 5.5 Hz, 1H), 4.16 (t, J = 7.50 Hz, 1H), 3.795 (dd, J = 3.0, 7.5 Hz, 1H), 3.76-3.69 (m, 2H), 3.65 (s, 3H), 2.16 (t, J = 7.5 Hz, 2H), 2.03 (s, 6H), 1.62-1.59 (m, 4H), 1.30-1.24 (m, 64H), 0.88 (s, J = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 500 MHz, β anomer, ppm): δ: 173.08, 171.17, 170.08, 169.82, 138.61, 138.21, 138.06, 128.66, 128.55, 128.17, 128.14, 128.08, 127.91, 127.82, 99.69, 75.91, 74.45, 74.13, 73.49, 73.38, 73.22, 72.87, 72.45, 71.91, 68.76, 52.49, 48.03, 37.04, 32.18, 29.97, 29.81, 29.67, 29.62, 27.98, 25.91, 22.95, 21.32, 21.08, 14.39; HRESI-MS: $C_{74}H_{117}NO_{12}$ (1211.85758). $[M+H]^+$ Calcd: 1212.86485; found: 1212.85890.

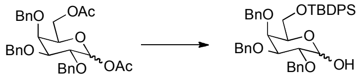


Compound **6** (42 mg, 0.037 mmol) was dissolved in THF (3.5 mL) and MeOH (3.5 mL). Pd/C (5%, 100 mg) was added. The suspension was subjected to hydrogenation at 500 psi for 3 days. The Pd/C was then removed via filtration through a celite pad. The filtrate was concentrated, and the residue was dissolved in pyridine (10 mL). To this solution was added DMAP (0.05 g) and Ac_2O (2 mL). The mixture was stirred overnight and then concentrated. The residue was diluted with CH_2Cl_2 (50 mL), washed with HCl (1 N, 100 mL) and saturated aqueous $NaHCO_3$. The organic phase was dried and concentrated. The resulting oil was subjected to silica gel chromatography (R_f = 0.5, EtOA/hexanes = 1/2), yielding 27.2 mg of the peracetate (68% yield). Formation of the peracetate was confirmed by HRESI-MS: $[M+H]^+$ 1068.7557; Found: 1068.7571. The peracetate was dissolved in THF (4 mL) and MeOH (4 mL). NaOMe (1 *M* in MeOH, 1 mL) was added. The mixture was stirred for 5 h, and then one drop of water was added. The mixture was stirred for 12 h, and then 2 drops of AcOH were added. The mixture was concentrated and subjected to silica gel chromatography (R_f = 0.3, $MeOH/CH_2Cl_2/H_2O$ = 25/65/4) affording 12.3 mg of **1** as a white solid (57% yield). ^{1}H NMR (CD_3CO_2D/DMSO-D_6, 500 MHz, ppm): *δ* 4.74 (d, *J* = 3.5 Hz, 1H, H-1’), 4.03 (dd, *J* = 4.5, 9.0 Hz, 1H), 3.86 (d, *J* = 9.5 Hz, 1H), 3.74 (dd, *J* = 4.5, 10.5 Hz, 1H), 3.50 (dd, *J* = 4.5, 10.5 Hz, 1H), 3.47-3.88 (m, 3H), 3.35 (t, *J* = 9.5 Hz, 1H), 3.26 (dd, *J* = 3.5, 9.5 Hz, 1H), 2.07 (t, *J* = 7.5 Hz, 2H), 1.49-1.44 (m, 4H), 1.25-1.14 (m, 64H), 0.79 (t, *J* = 7.5 Hz, 6H); ^{13}C NMR (CD_3CO_2D/DMSO-D_6, 125 MHz, ppm): *δ* 172.9, 171.55, 100.02 (C-1’), 74.37, 73.56, 72.26, 72.08, 71.37, 67.63, 50.42, 36.13, 32.30, 31.87, 29.66, 29.57, 29.29, 25.28, 25.92, 22.64, 14.25; HRESI-MS: $C_{84}H_{93}NO_{10}$ (843.67995). [M+H]$^+$ Calcd: 844.68722; found: 844.70387.

Synthesis of 2 (Scheme 1).



To a solution of 2,3,4,6-tetrabenzyl-1-*α*-D-phenylthiogalactoside (300 mg, 0.475 mmol) in CH_2Cl_2 (15 ml) was added Ac_2O (0.114 ml, 1.234 mmol) at -78 °C, then TMSOTf (0.114 ml, 1.234 mmol) was added slowly. After completion of addition, the mixture as allowed to warm to room temperature. The reaction was quenched with water (2 mL) and diluted with diethyl ether (50 ml). The organic layer was washed with aqueous HCl (1 N) and saturated aqueous $NaHCO_3$ and dried over Na_2SO_4. After removal of solvent, the residue was purified by silica gel column chromatography (R_f = 0.2, EtOAc/hexanes = 1/4), affording 54.0 mg of *α* isomer and 40.3 mg of *β* isomer with overall yield of 37%. *β*-isomer: ^{1}H-NMR (500 MHz; $CDCl_3$, ppm): *δ* 7.42-7.23 (m, 15H), 6.40 (d, *J* = 3.5 Hz, 1H), 5.23 (dd, *J* = 3.0, 11.0 Hz, 1H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.6 (dd, *J* = 9.0, 5.5 Hz, 1H), 4.58 (dd, *J* = 11.0, 11.0 Hz, 2H), 4.51 (dd, *J* = 5.5, 5.5 Hz, 2H), 4.43 (d, *J* = 12.0 Hz), 4.12-4.11 (m, 3H), 4.6 (dd, *J* = 9.0, 5.5 Hz, 1H), 2.13 (s, 3H), 1.97 (s, 3H); ^{13}C NMR of *β*-isomer (125 Hz, $CDCl_3$, ppm) *δ* 170.8, 169.6, 138.7, 137.97, 137.9, 128.7, 128.5, 128.2, 128.1, 90.6, 75.5, 75.3, 73.8, 73.4, 72.9, 72.4, 71.4, 68.7, 21.3, 21.1. HRESI-MS: $C_{31}H_{34}O_8$ (534.225). [M+Na]$^+$, calcd: 557.2145; found: 557.2245.
α-isomer: ^{1}H-NMR (500MHz; $CDCl_3$, ppm) *δ* 7.42-7.27 (m, 15H), 6.42 (d, *J* = 3.0 Hz, 1H), 5.01 (d, *J* = 11.50 Hz, 1H), 4.89 (d, *J* = 11.50Hz, 1H), 4.78 (d, *J* = 11.50 Hz, 1H), 4.73 (d, *J* = 11.0 Hz, 1H), 4.70 (d, *J* = 11.00 Hz, 1H), 4.64 (d, *J* = 11.50 Hz, 1H), 4.20 (dd, *J* = 3.50 Hz, 10.0 Hz, 1H), 4.16 (dd, *J* = 7.00 Hz, 11.50 Hz, 1H), 4.09 (dd, *J* = 5.05, 11.50 Hz, 1H), 4.04 (dd, *J* = 5.5, 7.00 Hz, 1H), 3.95 (dd, *J* = 2.0, 3.0 Hz, 1H), 3.91 (dd, *J* = 3.00, 10.00 Hz, 1H), 2.13 (s, 3H), 2.02 (s, 3H); ^{13}C NMR of *α*-isomer (125 Hz, $CDCl_3$, ppm): *δ* 170.8, 169.6, 138.7, 138.3, 138.2, 128.7, 128.6, 128.3, 128.1, 128.0, 127.9, 127.7, 90.92, 78.8, 75.6, 74.9, 74.5, 73.7, 73.65, 71.1, 63.3, 21.8, 21.0. HRESI-MS: $C_{31}H_{34}O_8$ (534.225). [M+Na]$^+$ calcd: 557.2145; found: 557.2245.



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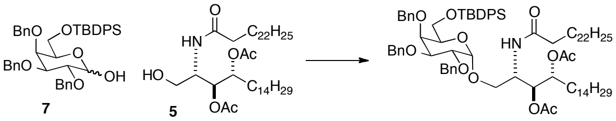
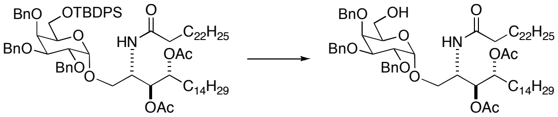
2,3,4-Tribenzyl-1,6-diacetylgalactose (250 mg, 0.286 mmol, mixture of anomers) was dissolved in a mixture of THF (5 mL) and MeOH (7 mL), and NaOMe (1 *M* in methanol, 0.5 mL) was added dropwise. The mixture was stirred for 1 h, then 3 drops of AcOH were added. The mixture was stirred for another 10 min, and the solvent was removed. The crude product was then directly dissolved in dry CH_2Cl_2 (10 mL) and CH_3CN (30 mL). Imidazole (50 mg, 0.74 mmol) was added, and the mixture was cooled to -15° C on ice-acetone bath. Then TBDPSCl (94 mg, 0.344 mmol) was added, and the reaction was stirred for 2 h at -15° C. MeOH (1 mL) was added, and the mixture was stirred for 15 min at room temperature. The solvent was removed, and the residue was subjected to silica gel chromatography (R_f = 0.45, EtOAc/hexanes = 1/4), affording

149.6 mg of **15** as a thick oil (mixture of α and β anomers,76% yield). ^{1}H-NMR (500 MHz; $CDCl_3$): *δ* 7.74-7.26 (m), 5.22 (d, *J* = 4.0 Hz), 5.02 (d, *J* = 11.50 Hz), 5.01 (d, *J* = 11.50Hz), 4.91 (d, *J* = 11.00 Hz), 4.87 (d, *J* = 11.0 Hz), 4.85-4.80 (m), 4.77 (d, *J* = 3.5 Hz), 4.72 (d, *J* = 12.0 Hz), 4.66 (d, *J* = 11.00 Hz), 4.62 (d, *J* = 11.0 Hz,), 4.11-4.08 (m), 4.07-4.00 (m), 3.92 (dd, *J* = 2.5, 9.5 Hz), 3.88 (dd, *J* = 1.5, 10.0 Hz), 3.85 (brs), 3.83 (brs), 3.80-3.70 (m), 3.56 (brs), 3.54 (dd, *J* = 3.0, 10.0 Hz), 3.45 (dd, *J* = 7.50, 9.0 Hz), 3.00 (brs), 2.83 (brs), 1.09 (brs), 1.07 (brs). ^{13}C NMR ($CDCl_3$, 125 Hz): *δ* 139.5, 138.94, 138.79, 138.76, 138.43, 135.82, 135.05, 133.55, 130.05, 129.97, 128.66, 128.58, 128.41, 128.27, 128.13, 128.03, 127.97, 127.87, 127.79, 127.64, 97.97, 92.19, 82.42, 81.16, 79.01, 76.94, 75.24, 75.12, 75.03, 74.01, 73.82, 73.23, 73.16, 71.17, 65.24, 63.97, 62.26, 29.95, 27.19, 27.11, 19.44. HRESI-MS: $C_{43}H_{48}O_6Si$ (688.3220). $[M+H]^+$ cald: 689.3298; found: 689.3274.

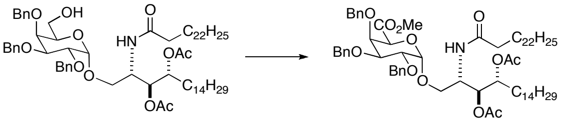


Donor **7** (145 mg, 0.209 mmol), diphenyl sulfoxide (87.99 mg, 0.435 mmol), TTBP (151.3 mg, 0.609 mmol), and 3 Å ms (500 mg) were mixed in CH_2Cl_2 (5 mL) for 1 h. After the mixture was cooled to -60° C, Tf_2O (68.73 mg, 40.98 µl, 0.244 mmol) was added. The reaction was then allowed to warm to -40 °C, and acceptor **5** (131 mg, 0.174 mmol) in CH_2Cl_2 (1.5 mL) was added. The reaction was allowed to warm to ambient temperature and quenched with Et_3N (0.1 mL). The solvent was removed, and the resulting material was subjected to silica gel chromatography (R_f = 0.4, EtOAc/hexanes =1/4) giving 200 mg of a clear oil (81 % yield). ^{1}H NMR (500 MHz; $CDCl_3$): *δ* 7.64-7.27 (m, 25H), 6.22 (d, *J* = 9.5 Hz, 1H), 5.26 (dd, *J* = 2.5, 9.0 Hz, 1H), 4.99 (dt, *J* = 2.50, 10.5 Hz, 1H), 4.97 (d, *J* = 11.50 Hz, 1H), 4.88 (d, *J* = 12.0 Hz, 1H), 4.81 (d, *J*= 3.5 Hz, 1H), 4.78 (d, *J* = 11.00 Hz, 1H), 4.76 (d, *J* = 11.5 Hz, 1H), 4.72 (d, *J* = 11.50 Hz, 1H), 4.58 (d, *J* = 11. 0 Hz, 1H), 4.38-4.33 (m, 1H) 4.03 (dd, *J* = 3.5, 11.0 Hz, 1H), 4.02 (brs), 3.9 (dd, *J* = 3.0, 10.0 Hz, 1H), 3.80-3.74 (m, 2H), 3.71-3.67 (m, 1H), 3.57 (dd, *J* = 3.5, 11.0 Hz, 1H), 3.51 (dd, *J* = 3.5, 11.0 Hz, 1H), 2.10-2.07 (m, 2H), 2.03 (s, 3H), 2.00 (s, 3H), 1.63-1.58 (m, 4H), 1.44-1.20 (m, 64H), 1.06 (s, 9H), 0.903 (t, *J* = 7.0, 6H); ^{13}C NMR ($CDCl_3$, 125 Hz) *δ* 173.05, 170.99, 170.28, 139.07, 138.91, 138.65, 135.79, 135.78, 133.42, 130.06, 130.01, 128.61, 128.50, 128.41, 128.25, 128.01, 127.91, 127.78, 127.68, 98.73, 78.98, 76.90, 75.12, 75.09, 73.44, 73.33, 72.29, 71.68, 66.93,, 62.56, 48.25, 36.95, 32.19, 29.88, 29.98, 29.85, 29.71, 29.63, 29.52, 28.21, 27.13, 25.95, 25.91, 22.96, 21.26, 21.14, 19.42, 14.39; HRESI-MS; $C_{89}H_{135}NO_{11}Si$. $[M]^+$ Calcd: 1421.9804; Found: 1421.9845.

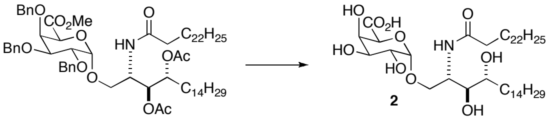


To the solution of galactoside from above (200 mg) in THF (25 mL) was added HF-pyridine-THF solution (10%, 20 mL). The mixture was stirred for 6 h, then diluted with CH_2Cl_2 (100 mL), and washed with saturated aqueous $NaHCO_3$, dilute aqueous HCl and water sequentially. The organic layer was concentrated, and the residue was subjected to silica get chromatography (R_f = 0.5, EtOAc/hexanes = 1/2) yielding 150 mg of desired alcohol (89% yield). ^{1}H-NMR ($CDCl_3$, 500 MHz): *δ* 7.67-7.28 (m, 15H), 5.37 (dd, *J* = 2.0, 11.0, 1H), 4.93 (d, *J* = 12.0 Hz, 1H), 4.84 (d, *J* = 4.0 Hz, 1H), 4.82 (d, *J* = 5.0 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.70 (dt, *J* = 2.0, 9.5 Hz, 1H), 4.66 (d, *J* = 3.0 Hz, 1H), 4.65 (d, *J* = 7.5 Hz, 1H), 4.63 (d, *J* = 7.5 Hz, 1H), 4.25 (d, *J* =

11.5 Hz, 1H), 4.26-4.22 (m, 1H), 4.06 (dd, *J* = 3.5, 10.0 Hz, 1H), 3.95-3.91 (m, 2H), 3.85 (dd, *J* = 3.0, 10.0 Hz, 1H), 3.81-3.75 (m, 2H), 3.60-3.56 (m, 1H), 3.38 (d, *J* = 12.0 Hz, 1H), 2.18 (t, *J* = 7.5 Hz, 2H), 2.1 0 (s, 3H), 1.99 (s, 3H), 1.66-1.55 (m, 4H), 1.32-1.14 (m, 64H), 0.88 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125Hz): δ 173.59, 172.76, 170.36, 138.86, 138.48, 138.48, 138.29, 128.89, 128.76, 128.64, 128.31, 128.21, 128.18, 127.83, 127.73, 102.40, 79.34, 76.92, 74.69, 74.61, 74.35, 74.05, 73.71, 73.57, 69.56, 63.05, 48.49, 36.72, 32.18, 29.96, 29.86, 29.67, 29.63, 29.52, 29.48, 26.64, 25.92, 25.83, 22.95, 21.48, 21.33, 14.39; HRESI-MS: $C_{73}H_{117}NO_{11}$. [M+H]$^+$ Calcd: 1189.86994; Found: 1184.86083.



A mixture of the alcohol from above (60 mg, 0.5 mmol), BAIB (41 mg, 0.12 mmol), TEMPO (1.6 mg, 0.01 mmol), CH_2Cl_2 (8 mL) and water (3 mL) was stirred for 12 h. The mixture was diluted with CH_2Cl_2 (50 mL) and washed with water. The organic phase was dried over Na_2SO_4 and concentrated. The residue was dissolved in CH_2Cl_2 (5 mL). To this solution was added a solution of excess CH_2N_2 in Et_2O. AcOH (3 mL) was added to quench excess CH_2N_2. The reaction solution was then washed with aqueous $NaHCO_3$, and the organic phase was dried and concentrated. The resulting clear oil was subjected to silica gel chromatography (R_f = 0.2, EtOAc/hexanes = 1/2), affording 33 mg of the methyl ester (54% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.41-7.24 (m, 15H), 6.77 (d, *J* = 10.0 Hz, 1H), 5.13 (dd, *J* = 2.5, 10.0 Hz, 1H), 4.91 (d, *J* = 11.0 Hz, 1H), 4.82-4.75 (m, 5H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.63 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 1.5 Hz, 1H), 4.38 (m, 1H), 4.29 (ddd, *J* = 2.5, 10.0, 10.0 Hz, 1H), 4.09 (dd, *J* = 3.5 Hz, 1H), 3.93 (dd, *J* = 3.5, 10.0 Hz, 1H), 3.91 (dd, *J* = 2.0, 7.5 Hz, 1H), 3.68 (s, 3H), 3.52 (dd, *J* = 3.0, 11.5 Hz 1H), 2.17 (t, *J* = 7.5 Hz, 2H), 2.05 (s, 3H), 1.96 (s, 3H), 1.64-1.57 (m, 4H), 1.37-1.24 (m, 64H), 0.88 (t, *J* =7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.37, 171.02, 170.34, 168.90, 138.62, 138.41, 138.35, 128.72, 128.67, 128.48, 128.45, 128.41, 128.19, 127.89, 127.75, 100.61, 78.31, 76.12, 76.04, 75.00, 74.03, 73.49, 73.46, 71.59, 71.44, 52.55, 48.22, 36.92, 32.18, 29.97, 29.85, 29.69, 29.61, 29.57, 27.61, 25.94, 25.89, 22.95, 21.20, 14.38; HRESI-MS: $C_{74}H_{117}NO_{12}$ (1211.8575). [M+H]$^+$ Calcd: 1212.86485; found: 1212.86626.

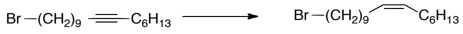


The methyl ester from above (25 mg, 0.021 mmol) was dissolved in a mixture of THF (3 mL) and MeOH (3 mL). Pd/C (10%, 50 mg) was added, and the mixture was subjected to hydrogen at 500 psi for 72 h. The catalyst was removed via filtration through a cellite pad. The solvent was removed. The structure of deprotected compound was confirmed via HRESI-MS: $C_{53}H_{99}NO_{12}$ (941.7167). [M+H]$^+$ Calcd: 942.72400. Found: 942.72426. The resulting oil was dissolved in pyridine (6 mL), and acetic anhydride (1.5 mL) and DMAP (5 mg) were added at 0 °C. The reaction was allowed to warm to room temperature and stir overnight. The solvent was removed, and the residue was dissolved in CH_2Cl_2 (30 mL) and washed with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4 and concentrated. The resulting mixture was purified by silica gel chromatography (R_f = 0.5, EtOA/hexanes = 1/2), affording 13 mg of the peracetate. The peracetate (13 mg, 0.012 mmol) was dissolved in a mixture of THF (3.5 mL) and MeOH (3.5 mL). To this solution was added NaOMe (1 *M* in methanol, 0.5 mL). The solution was stirred for 5 h, and then one drop of water was added. The reaction was allowed to continue for an additional 12 h. One more drop of acetic acid was added, and solvent was removed. The residue was subjected to silica gel chromatography (R_f = 0.4, MeOH/CH_2Cl_2/H_2O = 25/64/4) giving **2** as 7.7 mg of a white solid (65% yield). ^{1}H NMR (CD_3CO_2D/DMSO-D_6, 500 MHz, ppm): δ 4.77 (d, J = 3.0 Hz, 1H, H-1'), 4.25 (brs, 1H), 4.01 (brs, 2H), 3.71-3.67 (m, 1H), 3.64 (dd, J = 2.0, 10.5 Hz, 1H), 3.58 (dd, J = 3.0, 10.0 Hz, 1H), 3.51-3.48 (m, 1H), 3.43 (dd, J = 5.5, 6.0 Hz, 1H), 3.40-3.36 (m, 1H), 2.05 (t, J = 7.5 Hz, 2H), 1.46 (m, 4H), 1.28-1.14 (m, 64H), 0.79 (t, J = 6.5 Hz, 6H); ^{13}C NMR (CD_3CO_2D/DMSO-D_6, 125 MHz, ppm): δ 173.05, 170.69, 99.68 (C-1'), 74.45, 71.43, 71.28, 70.91, 70.16, 68.57, 67.79, 50.19, 36.08, 32.21, 31.84, 29.63, 29.53, 29.43, 29.23, 25.93, 22.59, 14.16; HRESI-MS: $C_{48}H_{93}NO_{10}$ (843.6799). $[M+H]^+$ Calcd: 844.6872; found: 844.6867.

Synthesis of GSL-1B (Scheme 2)

$H{-}{\equiv}{-}C_6H_{13} \longrightarrow Br{-}(CH_2)_9{-}{\equiv}{-}C_6H_{13}$

To a stirred solution of 1-octyne (1.28 g, 1.72 mL, 0.0117 mol) in dry THF (30 mL) was added BuLi (2.5 M in hexane, 4.68 mL, 0.117 mol. After stirring at -25° C for 1 h, the solution was transferred to a solution of 1,9-dibromononane (10 g, 0.035 mol, 3 eq) in HMPA (5 mL) dropwise *via* canula at -25° C. The mixture was stirred for another 2.5 h, and allowed stir for 12 h at room temperature. Aqueous NH_4Cl (50 mL) was added. The mixture was extracted with diethyl ether. The organic layer was dried over Na_2SO_4, concentrated to dryness, and the crude product was purified by silica gel chromatography (R_f= 0.7, hexanes), giving 3.3 g of a clear oil (90% yield). HRESI-MS: $C_{17}H_{31}Br$ (314.1609). $[M+H]^+$ calcd: 315.1682; found: 315.1489.



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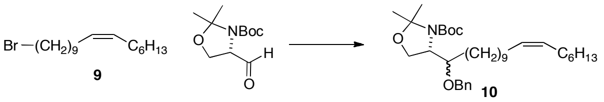
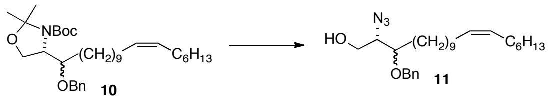
The alkyne from above was dissolved in CH_2Cl_2 (50 mL). To this solution was added quinonine (0.5 mL) and Lindlar catalyst (1.5 g). The mixture was subjected to hydrogenation (50 psi) at room temperature overnight. After TLC showed that the starting material was completely consumed, the solids were removed by filtration. The filtrate was concentrated. The crude mixture was purified by silica gel chromatography (R_f = 0.85, hexanes), giving 2.3 g of **9** (70 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 5.36-5.34 (m, 2H), 3.41 (t, J = 7.50 Hz, 2H), 2.04-2.00 (m, 4H), 1.88-1.82 (m, 2H), 1.44-1.26 (m, 18H), 0.89 (t, J = 7.00 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 130.20, 130.05, 34.28, 33.07, 32.03, 29.97, 29.66, 29.48, 29.23, 29.00, 28.42, 27.46, 27.42, 22.91, 14.36; HRESI-MS: $C_{17}H_{33}Br$. $[M]^+$: Calcd: 316.17656; found: 316.16979.

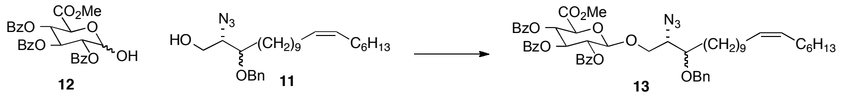


To a three-necked round bottom flask (250 mL) was added Mg° (0.15 g, 6.31 mmol, 2 eq), THF (25 mL), dibromoethane (5 drops), and **9** (2 g, 6.31 mmol). The mixture was heated to reflux for 3 h. The resulting solution was cooled to -78° C. A solution of Garner's aldehyde (0.72 g, 0.00315 mol, 1 eq) in Et_2O (5 mL) was added dropwise. The reaction mixture was warmed to room temperature and stirred for 3 h, quenched with aqueous NH_4Cl, and extracted with EtOAc. The organic phase was dried over Na_2SO_4. After removal of solvent, the crude mixture was subjected to silica gel chromatography (R_f = 0.5, EtOAc/hexanes = 1/4), giving 0.8 g as a clear oil (54% yield). HRESI-MS: $C_{28}H_{53}NO_4$. $[M]^+$ Calcd: 467.3974; Found: 467.3938. The alcohol

(2.0 g, 4.3 mmol) was treated with NaH (60%, 0.343 g, 2 eq) in DMF (40 mL). To this stirred suspension was added BnBr (0.805 g, 4.7 mmol, 1.1 eq). The mixture was stirred for 4 h. MeOH (10 mL) was added. The mixture was stirred for 10 min and concentrated under reduced pressure. The resulting mixture was purified by silica gel chromatography (R_f = 0.65, EtOAc/hexanes = 1/4), affording 2.1 g of **10** as a clear oil (mixture of diastereomers, 88% yield). ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 7.39-7.01 (m), 5.43-5.36 (m), 4.76-4.39 (m), 4.31 (m), 4.17-4.07 (m), 3.98-3.92 (m), 3.79-3.76 (m), 2.05-2.01 (m), 1.66-1.50 (m), 1.38-1.29 (m), 0.916 (t, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, ppm): δ 152.86, 152.19, 138.72, 137.24, 131.19, 131.10, 130.85, 130.38, 129.93, 128.43, 128.37, 128.31, 128.02, 127.87, 127.73, 127.58, 127.48, 126.84, 126.65, 104.87, 104.76, 94.54, 93.93, 80.32, 79.93, 79.08, 78.33, 72.52, 63.68, 63.41, 58.02, 57.47, 29.65, 29.37, 28.54, 27.26, 26.84, 26.49, 26.00, 24.02, 22.69, 14.16; HRESI-MS: $C_{35}H_{59}NO_4$. $[M+H]^+$ Calcd: 558.45169; Found: 558.45202.

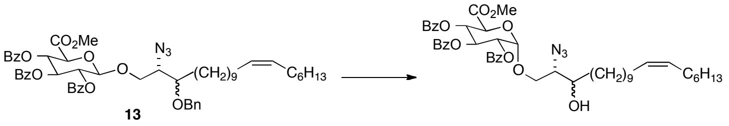


Mixture **10** (2.1 g) was dissolved in TFA (10 mL) and CH_2Cl_2 (10 mL) and stirred at 0° C for 30 min. The solution was warmed to room temperature and stirred for another 30 min. The solvent was removed. The residue was purified by silica gel chromatography (R_f = 0.15, MeOH/CH_2Cl_2= 1/19), affording 1.6 g of the corresponding amine. The amine was dissolved in CH_2Cl_2 (15 mL), followed by addition of K_2CO_3 (700 mg), water (6 mL), Cu_2SO_4 (30 mg), MeOH (500 mL). The reaction mixture was stirred vigorously while TfN_3 in CH_2Cl_2 was added dropwise. The mixture was stirred for 12 h, concentrated and the product was isolated by silica gel chromatography (R_f = 0.5, EtOAc/hexanes = 1/4), affording 1.2 g of **11** as a clear oil (mixture of isomers 74% overall yield). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.37-7.26 (m), 5.40-5.33 (m), 4.63 (t, J = 11.50 Hz), 4.58 (t, J = 9.00 Hz), 3.81-3.68 (m), 3.60-3.53 (m), 2.04-1.96 (m), 1.71-1.54 (m), 1.41-1.25 (m), 0.89 (t, J = 7.00 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 138.14, 130.17, 130.09, 128.72, 128.21, 128.17, 79.85, 79.53, 72.84, 72.67, 65.59, 65.42, 62.81, 62.70, 32.83, 32.02, 31.38, 30.83, 30.03, 29.98, 29.75, 29.53, 29.22, 27.46, 25.44, 25.32, 22.89, 14.33. HRESI-MS: $C_{27}H_{45}N_3O_2$ (443.35118). $[M+NH_4]^+$. Calcd: 461.38500; found: 461.37269.

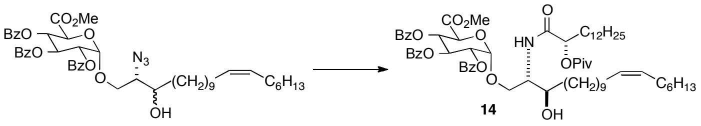


Donor **12** (285 mg, 0.55 mmol) was dissolved in a mixture of CH_2Cl_2 (5 mL) and CCl_3CN (8 mL). K_2CO_3 (500 mg) was added. The mixture was stirred at room temperature for 3 h. The solid was then removed via filtration through a celite pad. The filtrate was concentrated and was mixed with acceptor **11** (243 mg, 0.55 mmol), 3 Å MS (600 mg) and CH_2Cl_2 (7 mL). The mixture was stirred at room temperature for 1 h and cooled to 0°C. TMSOTf (35 μl) was added. The reaction was allowed to warm to room temperature and stir for 12 h. Et_3N (1 mL) was added, and the solids were removed by filtration. The filtrate was concentrated, and the product was purified via silica gel chromatography (R_f = 0.6, EtOAc/hexanes = 1/3), affording 356 mg **13** as a clear oil (69% yield). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 8.01-7.22 (m), 5.96-5.89 (m), 5.77-5.66 (m), 5.62-5.55 (m), 5.42-5.38 (m), 4.95 (d, J = 7.5 Hz), 4.79 (d, J = 8.0 Hz), 4.60-4.35 (m), 4.29 (d, J = 9.5 Hz), 4.24 (d, J = 11.5 Hz), 4.17 (dd, J = 6.0, 11.0 Hz), 4.13 (d, J = 7.0 Hz), 4.09 (dd, J = 5.0, 10.5 Hz), 3.82 (dd, J = 6.0, 10.5 Hz), 3.76 (dd, J = 5.0, 10.0 Hz), 3.71 (s), 3.69 (s), 3.66-3.60 (m), 3.49-3.44 (m), 2.05-1.69 (m), 1.60-1.12 (m), 0.89 (t, J = 7.5 Hz); ^{13}C NMR

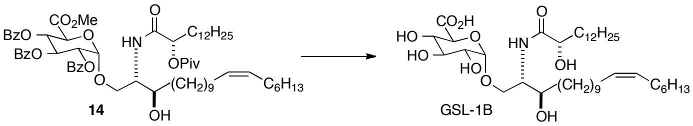
($CDCl_3$, 125 MHz, ppm): δ 167.40; 165.86, 165.386, 165.14, 165.08, 138.48, 138.40, 133.71, 133.58, 130.16, 130.06, 129.40, 128.97, 128.70, 128.61, 128.22, 128.05, 127.95, 127.90, 101.49, 101.40, 78.70, 78.54, 77.54, 77.29, 77.04, 73.29, 73.17, 72.76, 72.33, 72.18, 71.75, 71.66, 70.41, 70.36, 69.35, 68.71, 63.33, 63.12, 53.12, 32.85, 32.01, 31.06, 30.96, 30.03, 29.98, 29.91, 29.78, 29.56, 29.22, 27.47, 25.66, 25.48, 25.26, 22.89, 14.33; HRESI-MS: $C_{55}H_{67}N_3O_{11}$ (945.47756) $[M+NH_4]^+$ Calcd: 963.51139: Found: 963.51141.



Compound **13** (200 mg, 0.212 mmol) was dissolved in dry CH_2Cl_2 (9 mL). To this stirred solution was added $TiCl_4$ (1 *M* in CH_2Cl_2, 0.423 mmol, 0.423 mL) dropwise over 30 min. The reaction was stopped by the addition of aqueous $NaHCO_3$ as soon as TLC showed that the starting material was consumed. The product was then extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The product was purified by silica gel chromatography (R_f = 0.2, EtOAc/hexanes = 1/3), affording 167 mg of a clear oil (92% yield). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm, mixture of isomers): δ 8.01-7.26 (m), 6.22 (t, *J* = 10.5 Hz), 6.21 (t, *J* = 10.5 Hz), 5.87 (t, *J* = 9.5 Hz), 5.66-5.66 (m), 5.48-5.51 (m), 5.37-5.34 (m), 5.52 (d, *J* = 8.5 Hz), 4.70-4.64 (m), 4.38 (d, *J* = 9.5 Hz), 4.18-4.08 (m), 3.88-3.27 (m), 3.70 (s), 3.69 (s), 3.59-3.56 (m), 3.53-3.49 (m), 2.04-1.95 (m), 1.72 (m), 1.70-1.67 (m), 1.5-1.25 (m), 0.89 (t, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 500 MHz, ppm): δ 168.22, 165.94, 165.73, 165.54, 133.94, 133.69, 133.45, 130.30, 130.19, 130.09, 129.96, 129.22, 129.03, 128.92, 128.69, 128.57, 97.33, 97.06, 71.58, 71.48, 70.26, 69.87, 69.66, 69.43, 69.23, 65.75, 65.53, 65.44, 60.61, 38.76, 34.55, 33.88, 32.83, 32.01, 30.0, 29.96, 29.76, 29.54, 29.41, 29.21, 27.45, 26.73, 25.77, 22.87, 21.25, 14.42, 14.33; HRESI-MS: $C_{48}H_{61}N_3O_{11}$ (855.43061). :$[M+NH_4]^+$ Calcd: 873.46444; Found: 873.46468.

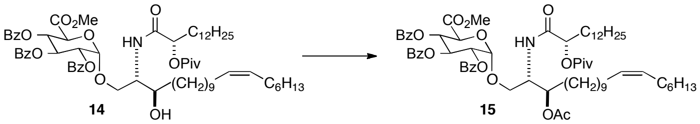


The azide (from above) (160 mg, 0.187 mmol) was dissolved in CH_2Cl_2 (7 mL), followed by addition of tributylphosphine (75 µl, 0.374 mmol, 2 eq). The mixture was stirred at room temperature for 1 h. MeOH (0.5 mL) and water (1 mL) were added. The mixture was stirred for an additional 2 h, diluted with CH_2Cl_2 (50 mL) and washed with water. The organic layer was dried over Na_2SO_4 and concentrated. The resulting clear oil was used in the next step without further purification. The pivaloyl ester of (*S*)-2-hydroxytetradecanoic acid (67.5 mg, 0.206 mmol), EDCI (39.49 mg, 0.206 mmol) and HOBT (27.83 mg, 0.206 mmol) in THF (10 mL) were stirred together for 1 h. To this solution was added the amine described above in THF (4 mL). The mixture was stirred for 12 h, diluted with CH_2Cl_2 (150 mL), washed with aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated. The residue was subjected to silica gel chromatography (R_{f1} = 0.5, upper spot; R_{f2} = 0.4, lower spot; EtOAc/hexanes = 1/3), affording 55.4 mg of C3-epi-**14** (upper spot) (26% yield) and with 102 mg of **14** (48% yield). ^{1}H NMR of **14** ($CDCl_3$, 500 MHz, ppm): δ 7.97-7.31 (m, 15 H), 7.01 (d, *J* = 9.00 Hz, 1H), 6.10 (t, *J* = 9.50 Hz, 1H), 5.67 (t, *J* = 10.00 Hz, 1H), 5.49 (d, *J* = 3.50 Hz, 1H), 5.39-5.32 (m, 3H), 5.19 (dd, *J* = 3.50, 8.00 Hz, 1H), 4.56 (d, *J* = 9. 50 Hz, 1H), 4.09 (dd, *J* = 2.50, 10.50 Hz, 1H), 4.00-3.98 (m, 1H), 3.78 (dd, *J* = 3.00, 10.50 Hz, 1H), 3.67 (s, 3H), 3.52 (m, 1H), 2.09 (d, *J* = 9.00 Hz, 1H), 2.05-1.61 (m, 8H), 1.34 (s, 9H), 1.32-1.11 (m, 42H), 0.88 (t, *J* = 7.00 Hz, 6H); ^{13}C NMR of **13** ($CDCl_3$, 125 MHz, ppm): δ 177.43, 170.32, 167.87, 165.62, 165.40, 134.04, 133.74, 133.59, 130.11, 130.00, 129.95, 129.12, 128.87, 128.63, 128.47, 96.75, 73.94, 73.05, 71.67, 70.08, 69.55, 69.12, 53.13, 51.41, 39.15, 38.77, 35.16, 32.19, 32.13, 32.00, 30.00, 29.87, 29.79, 29.56, 29.37, 29.21, 27.45, 27.39, 26.74, 26.14, 25.37, 22.90, 14.32; HRESI-MS: $C_{67}H_{97}NO_{14}$ (1139.69091). $[M]^+$. Calcd: 1139.69036; Found: 1139.76100.

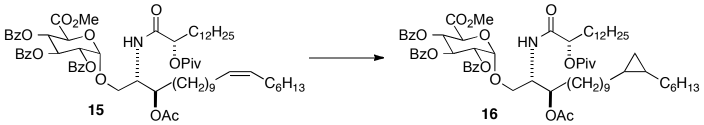


A solution of **14** (40 mg, 0.0338 mmol) in a mixture of THF (5 mL) and MeOH (5 mL) was treated with sodium methoxide (1 *M* in methanol, 0.5 mL). The reaction mixture was stirred for 4 h. Water (0.1 mL) was added. The reaction was stirred for another 12 h. Acetic acid (0.01 mL) was added. The solvent was removed. The product was isolated by silica gel chromatography (R_f = 0.65, $MeOH/CH_2Cl_2/H_2O$=25/65/4) as 18.7 mg of a white solid (76% yield). ^{1}H NMR (CD_3CO_2D/DMSO-D_6, 500 MHz, ppm): δ 7.54 (d, *J* = 9.00 Hz, 1H), 5.31-5.26 (m, 2H), 4.72 (d, *J* = 4.00 Hz, 1H, H-1$'$), 3.83 (dd, *J* = 4.50, 8.00 Hz, 1H), 3.78 (d, *J* = 10.00 Hz, 1H), 3.75-3.71 (m, 1H), 3.64 (dd, *J* = 3.50, 10.00 Hz, 1H), 3.56 (dd, *J* = 4.50, 10.00 Hz, 1H), 3.52 (dt, *J* = 2.50, 7.50 Hz, 1H), 3.41 (t, *J* = 9.00 Hz, 1H), 3.30 (t, *J* = 9.50 Hz, 1H), 3.22 (dd, *J* = 4.50, 9.50 Hz, 1H), 1.95-1.89 (m, 4H), 1.61-1.57 (m, 2H), 1.46-1.39 (m, 4H), 1.29-1.12 (m, 40 H), 0.80 (t, *J* = 6.50 Hz, 6H); ^{13}C NMR (CD_3CO_2D/DMSO-D_6, 125 MHz, ppm): δ 174.55, 171.72, 130.17, 100.23 (C-1$'$), 73.39, 72.27, 72.18, 72.05, 71.44, 70.15, 53.29, 34.90, 34.10, 31.91, 31.73, 29.81, 29.69, 29.55, 29.50, 29.33, 29.27, 29.15, 28.87, 27.16, 25.84, 25.18, 22.67, 14.27; HRESI-MS: $C_{40}H_{75}NO_{10}$ (729.53910). $[M+H]^+$. Calcd: 730.54637; found: 730.54503.

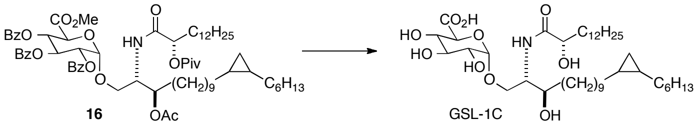
Synthesis of GSL-1C (Scheme 2)



Compound **14** (92 mg, 0.081 mmol) was dissolved in CH_2Cl_2 (8 mL). To this stirred solution was added triethylamine (1 mL) and acetic anhydride (0.3 mL). The mixture was stirred for 6 h and then washed with aqueous $NaHCO_3$. The organic phase was concentrated. The remaining clear oil was subjected to silica gel chromatography (R_f = 0.5, EtOAc/hexanes = 1/3), affording **15** as 91 mg of a clear oil (95% yield). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.96-7.32 (m, 15H), 6.55 (d, *J* = 9.00 Hz, 1H), 6.12 (t, *J* = 10.00 Hz, 1H), 5.65 (t, *J* = 10.00 Hz, 1H), 5.44 (d, *J* = 3.50 Hz, 1H), 5.37 (dd, *J* = 3.50, 10.00 Hz, 1H), 5.36-5.34 (m, 2H), 5.15 (dd, *J* = 4.00, 8.00 Hz, 1H), 4.87 (dt, *J* = 4.50, 8.50 Hz, 1H), 4.64 (d, *J* = 9.50 Hz, 1H), 4.40-4.35 (m, 1H), 3.86 (dd, *J* = 5.50, 10.50 Hz, 1H), 3.68 (s, 3H), 3.63 (dd, *J* = 4.00, 10.50 Hz, 1H), 2.02 (s, 3H), 2.04-1.59 (m, 8H), 1.39-1.11 (m, 51H), 0.88 (t, *J* = 6.50 Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 170.93, 170.41, 168.15, 165.82, 165.60, 165.41, 133.67, 133.49, 130.14, 130.04, 129.94, 129.15, 128.62, 97.08, 74.19, 74.05, 71.29, 70.36, 69.69, 69.29, 67.93, 53.09, 50.46, 32.24, 32.13, 32.00, 31.59, 30.03, 29.89, 29.85, 29.79, 29.63, 29.56, 29.36, 29.21, 27.45, 27.33, 25.57, 25.22, 22.89, 21.08, 14.32; HRESI-MS: $C_{69}H_{99}NO_{15}$ (1181.70147). $[M+NH_4]^+$. Calcd: 1199.73530; found: 1199.73372.



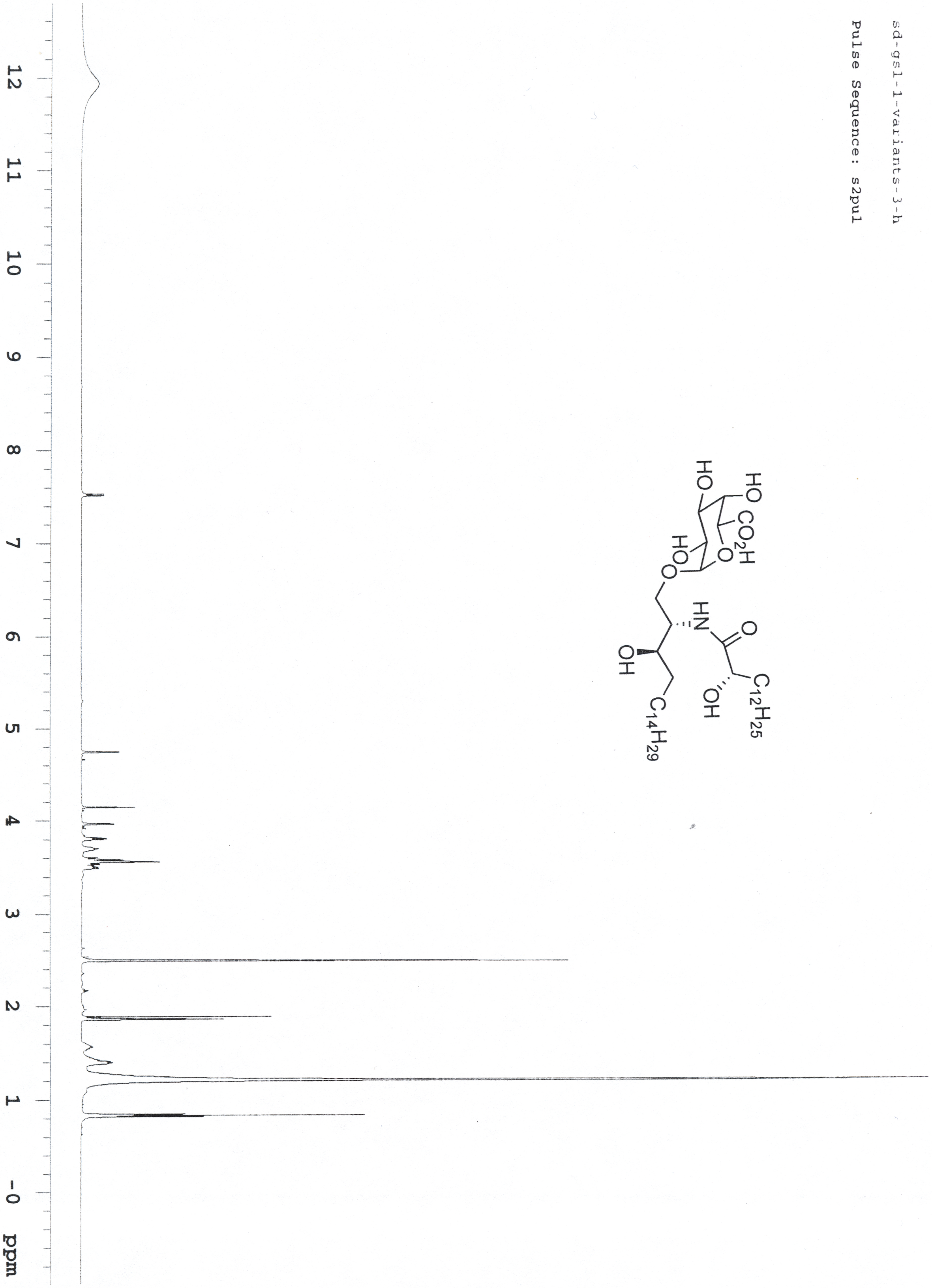
Compound **15** (20 mg, 0.027 mmol) was dissolved in CH_2Cl_2 (4 mL) at 0° C. To this stirred solution was added CH_2I_2 (110 mg, 0.408 mmol, 34 μl). The mixture was stirred for 10 min at 0° C, followed by addition of diethylzinc (52 mg, 0.41 mmol, 0.21 mL). The reaction was allowed to warm to room temperature and stir overnight. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed with water. The organic phase was dried over Na_2SO_4 and concentrated. The crude mixture was subjected to silica gel chromatography (R_f = 0.4, EtOAc/hexanes = 1/3), affording **16** as 18.2 mg of white solid (91% yield). ^{1}H NMR (CD_3Cl, 500 MHz, ppm): δ 7.97-7.28 (m, 15H), 6.54 (d, J = 9.0 Hz, 1H), 6.12 (t, J = 9.5 Hz, 1H), 5.65 (t, J = 9.0 Hz, 1H), 5.44 (d, J = 3.5 Hz, 1H), 5.37 (dd, J = 3.5, 10.0 Hz, 1H), 5.15 (dd, J = 4.0, 8.0 Hz, 1H), 4.87 (dt, J = 5.0, 8.0 Hz, 1H), 4.64 (d, J = 9.5 Hz, 1H), 4.40-4.35 (m, 1H), 3.86 (dd, J = 5.0, 10.5 Hz, 1H), 3.68 (s, 3H), 3.63 (dd, J = 4.0, 10.5 Hz, 1H), 2.35 (t, J = 7.5 Hz, 1H), 2.02 (s, 3H), 1.93-1.57 (m, 7H), 1.52-1.20 (m, 52H), 0.90 (t, J = 7.0 Hz, 3H), 0.89 (t, J = 7.0 Hz, 3H), 0.64 (m, 1H), 0.57-0.54 (m, 1H), -0.32--0.344 (m, 1H); ^{13}C NMR (CD_3Cl, 125 MHz, ppm): δ 177.34, 170.93, 170.38, 168.14, 165.82, 165.60, 165.52, 133.67, 133.49, 130.14, 130.03, 129.94, 129.14, 128.62, 97.08, 74.20, 74.04, 71.30, 70.37, 69.69, 69.29, 67.94, 53.10, 50.47, 32.24, 32.15, 31.61, 30.48, 30.41, 29.92, 29.83, 29.64, 29.57, 29.47, 29.37, 29.30, 28.96, 27.34, 25.58, 25.22, 22.91, 16.00, 14.33; HRESI-MS: $C_{70}H_{101}NO_{15}$ (1195.71712) $[M+H]^+$ Calcd:1196.72440; Found:1196.72457



Compound **16** (12 mg, 0.01 mmol) was dissolved in a mixture of THF (3 mL) and MeOH (3 mL). NaOMe (1 *M* in MeOH, 0.2 mL) was added, and the mixture was stirred for 4 h. Water (0.2 mL) was added. The mixture was stirred overnight. AcOH (1 mL) was added, and the mixture was concentrated. The remaining oil was subjected to silica gel chromatography (R_f = 0.55, MeOH/CH_2Cl_2 = 1/3), affording GSL-1C as 5.8 mg of white solid (73% yield). ^{1}H NMR (CD_3CO_2D/DMSO-D_6, 500 MHz, ppm): δ 7.55 (d, J = 9.0 Hz,1H), 4.71 (d, J = 4.00 Hz, 1H, H-1$'$), 3.84 (dd, J = 4.5, 8.0 Hz, 1H), 3.79 (d, J = 10.0 Hz, 1H), 3.74 (dt, J = 4.0, 7.5 Hz, 1H), 3.64 (dd, J = 3.5, 10.0 Hz, 1H), 3.56 (dd, J = 4.5, 10.0 Hz, 1H), 3.51 (dt, J = 3.0, 7.0 Hz, 1H), 3.41 (t, J = 9.5 Hz, 1H), 3.31 (t, J = 9.50, 1H), 3.23 (dd, J = 3.5, 9.0 Hz, 1H), 1.62-1.33 (m, 4H), 1.32-1.10 (m, 47H), 0.80 (t, J = 6.5, 3H), 0.79 (t, J = 7.0 Hz, 3H), 0.58 (m, 1H), 0.49-0.45 (m, 1H), -0.38--0.41 (m, 1H); ^{13}C NMR (CD_3CO_2D/DMSO-D_6, 500 MHz, ppm): δ 174.53, 171.55, 100.25 (C-1$'$), 73.39, 72.32, 72.15, 72.06, 71.44, 70.14, 67.87, 53.29, 34.90, 34.08, 31.90, 30.31, 30.25, 29.82, 29.69, 29.51, 29.34, 29.28, 28.71, 25.83, 25.17, 22.66, 15.88, 14.27, 11.13; HRESI-MS: $C_{41}H_{77}NO_{10}$ (743.55475); $[M+H]^+$ Calcd:744.56202; Found: 744.56147.

Stimulation experiments with B6 mouse splenocytes:[20] Spleen cell suspensions (5 x 10^5 cells/well) were exposed to the indicated concentrations of glycolipids in 96-well round-bottom plates in RPMI 1640 (Biofluids) supplemented with glutamine, antibiotics, mercaptoethanol (5 x10^{-5} *M*) and 10% FCS. After 48 h, IL-4 and IFN-γ concentrations were determined by ELISA (R&D Systems; lower detection limit of 15 pg/mL).

NMR Spectra of 1, 2, GSL-1B and GSL-1C and LC-MS data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OH
C$_{14}$H$_{29}$
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11
10
9
8
7
6
5
4
3
2
1
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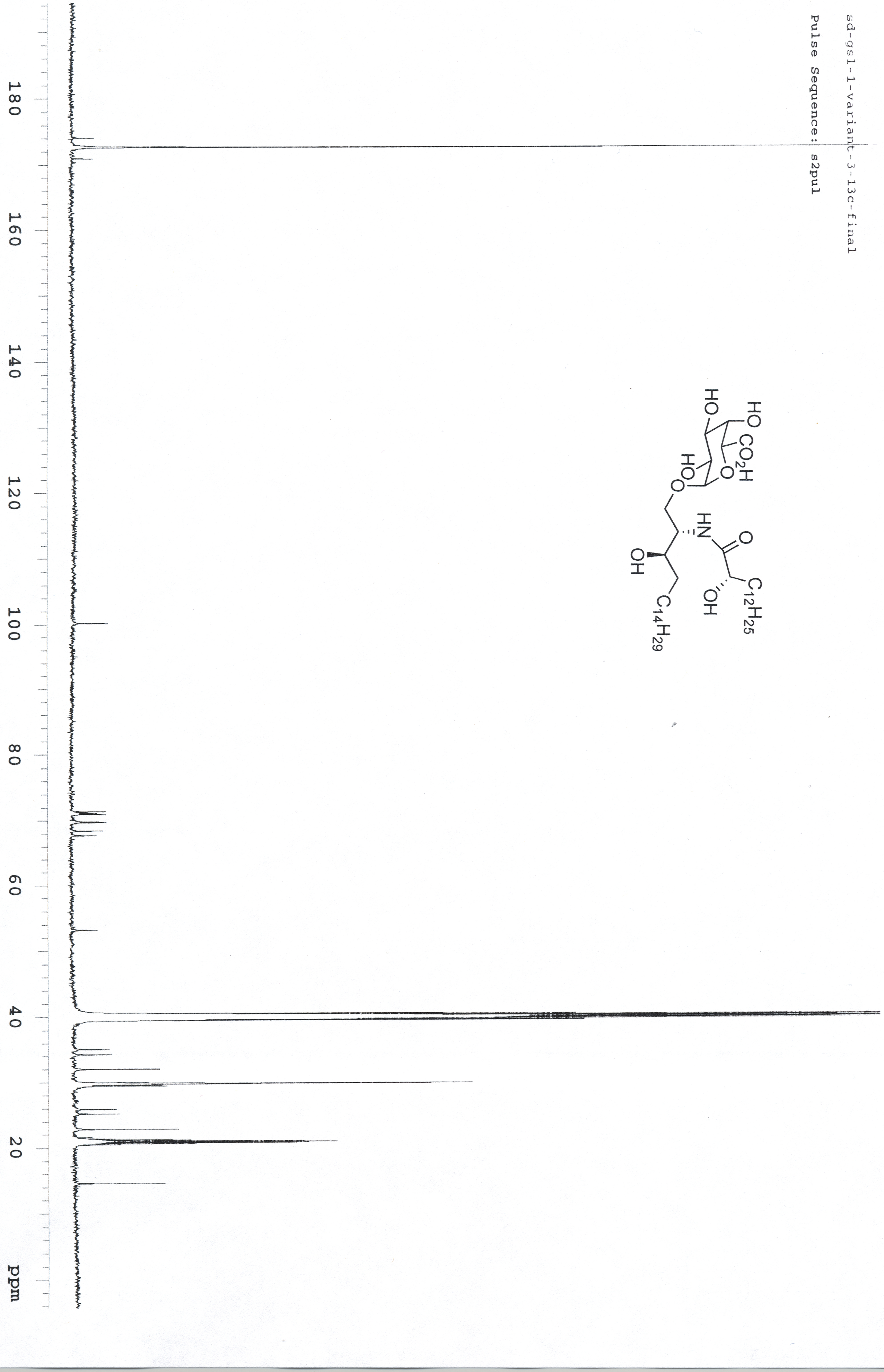
ppm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HO
HO
O
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C$_{14}$H$_{29}$
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160
140
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80
60
40
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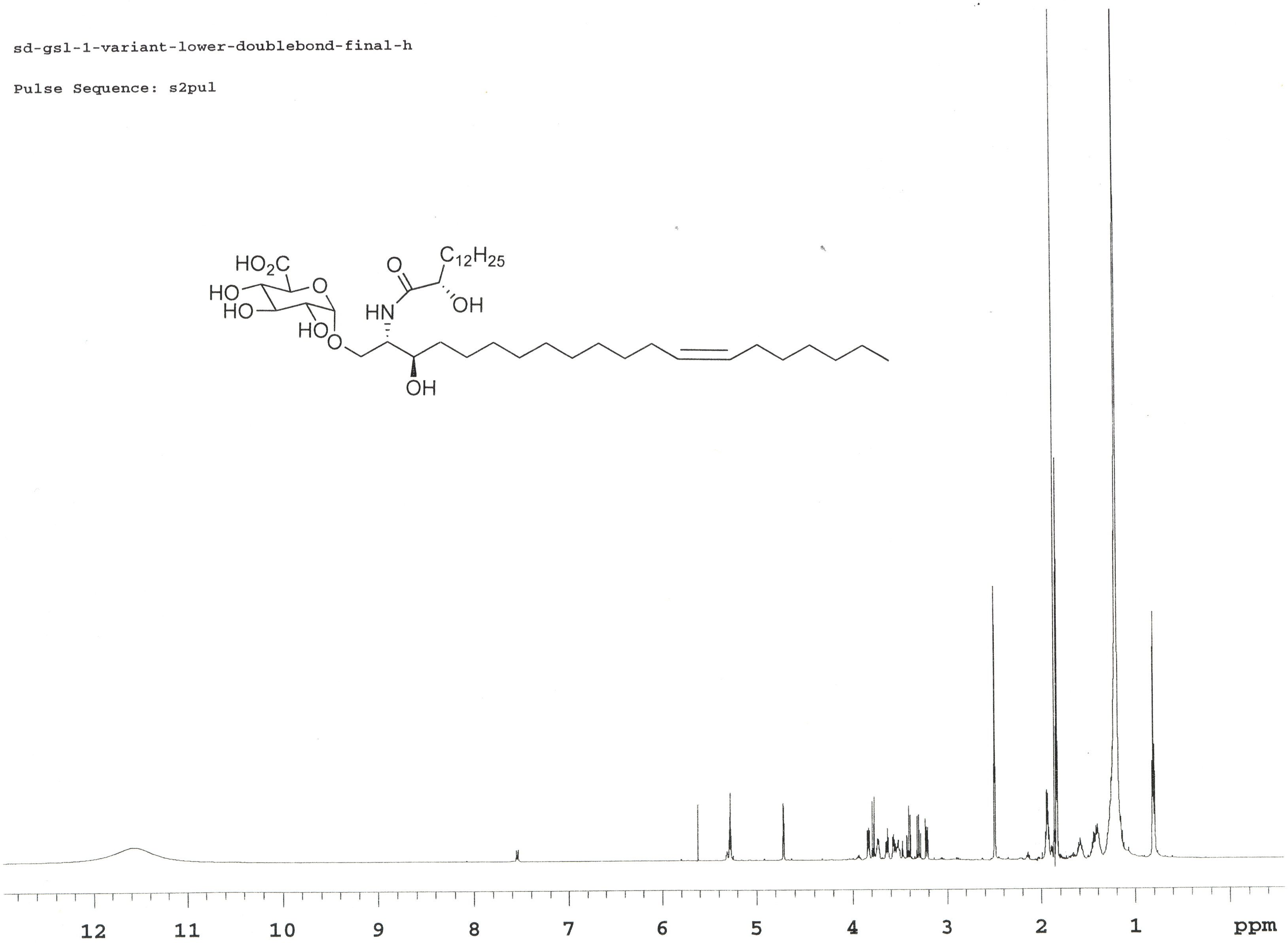
ppm



sd-gs1-1-variant-lower-doublebond-final-h

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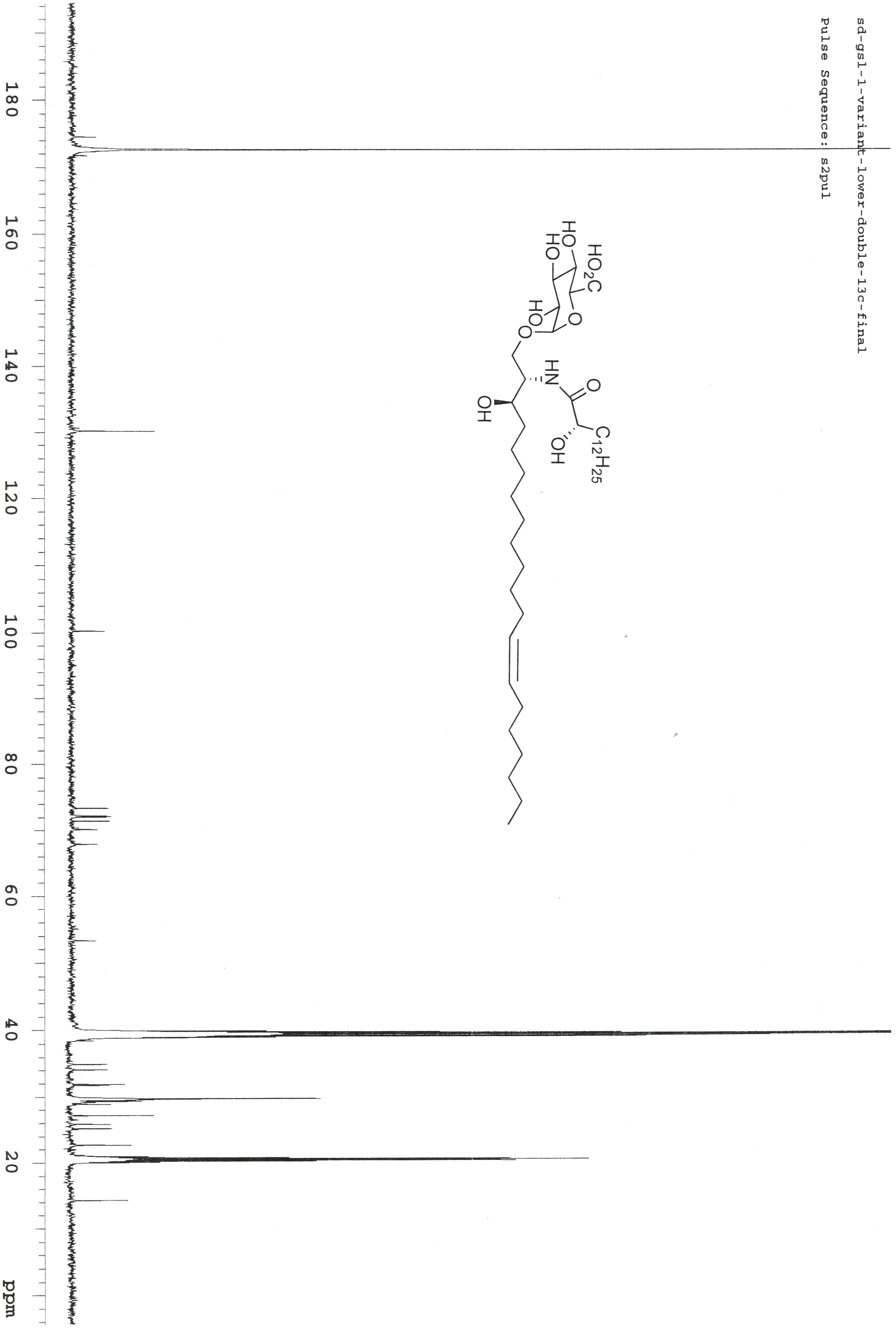
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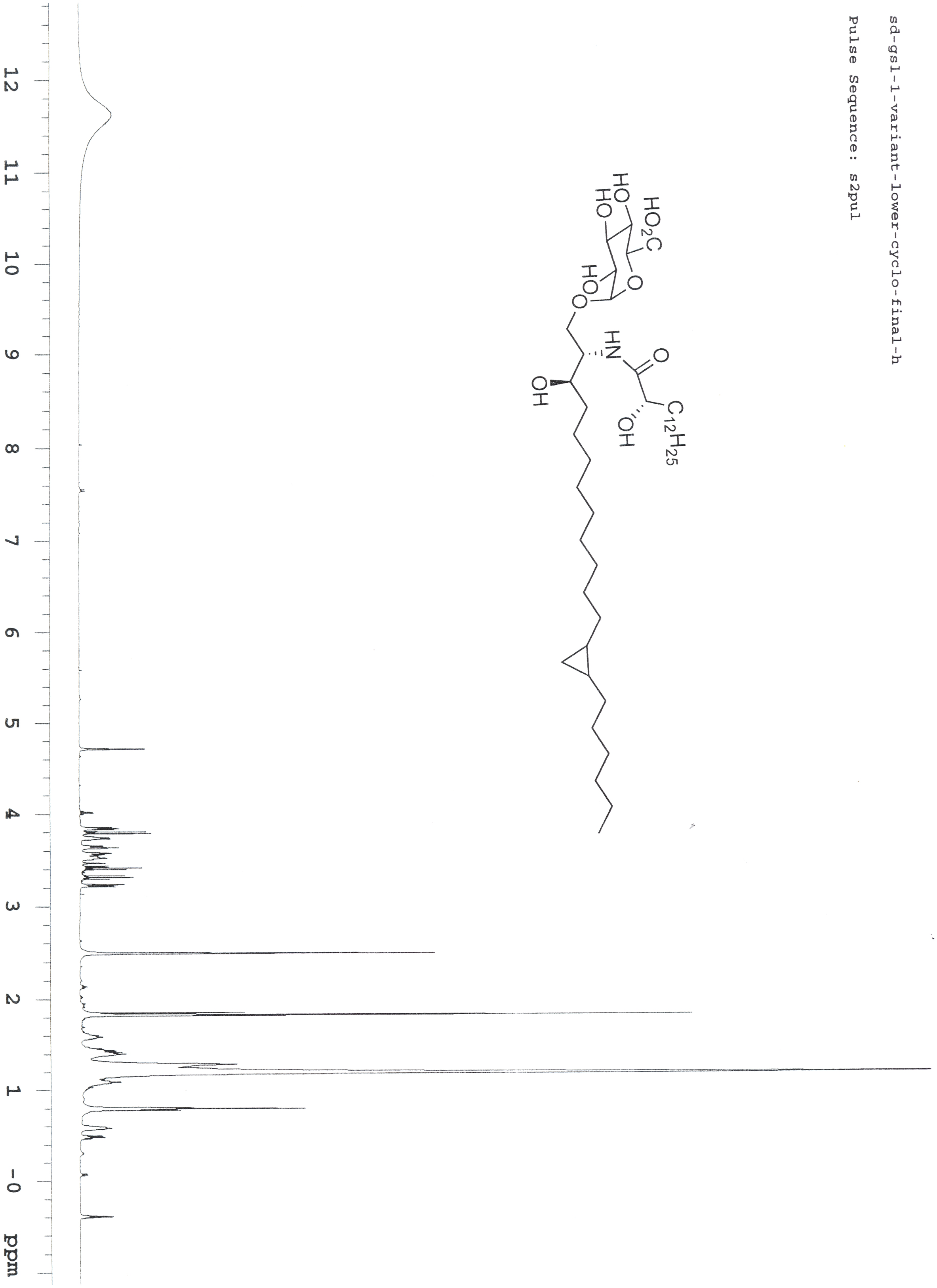
20
ppm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HO
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1
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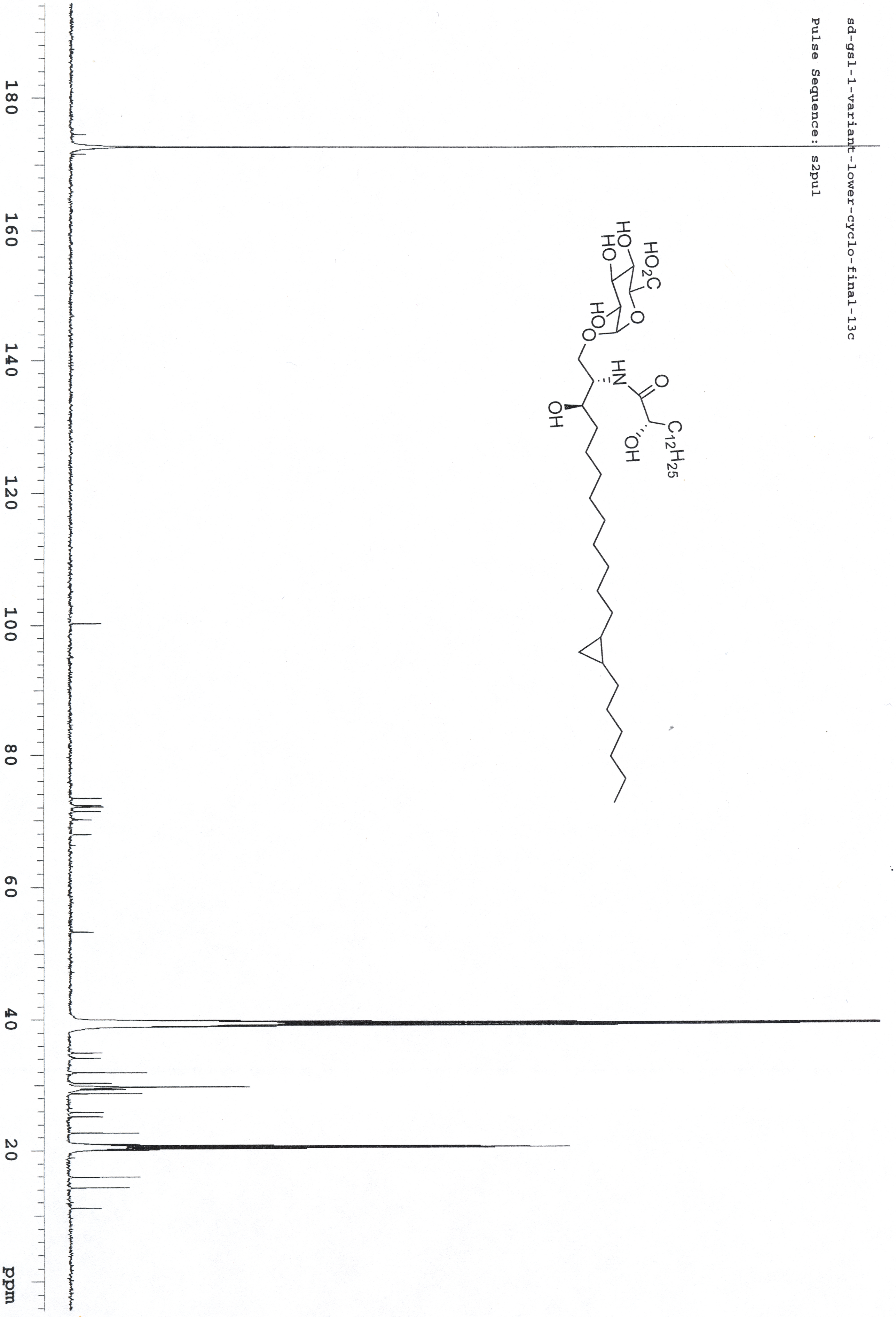
ppm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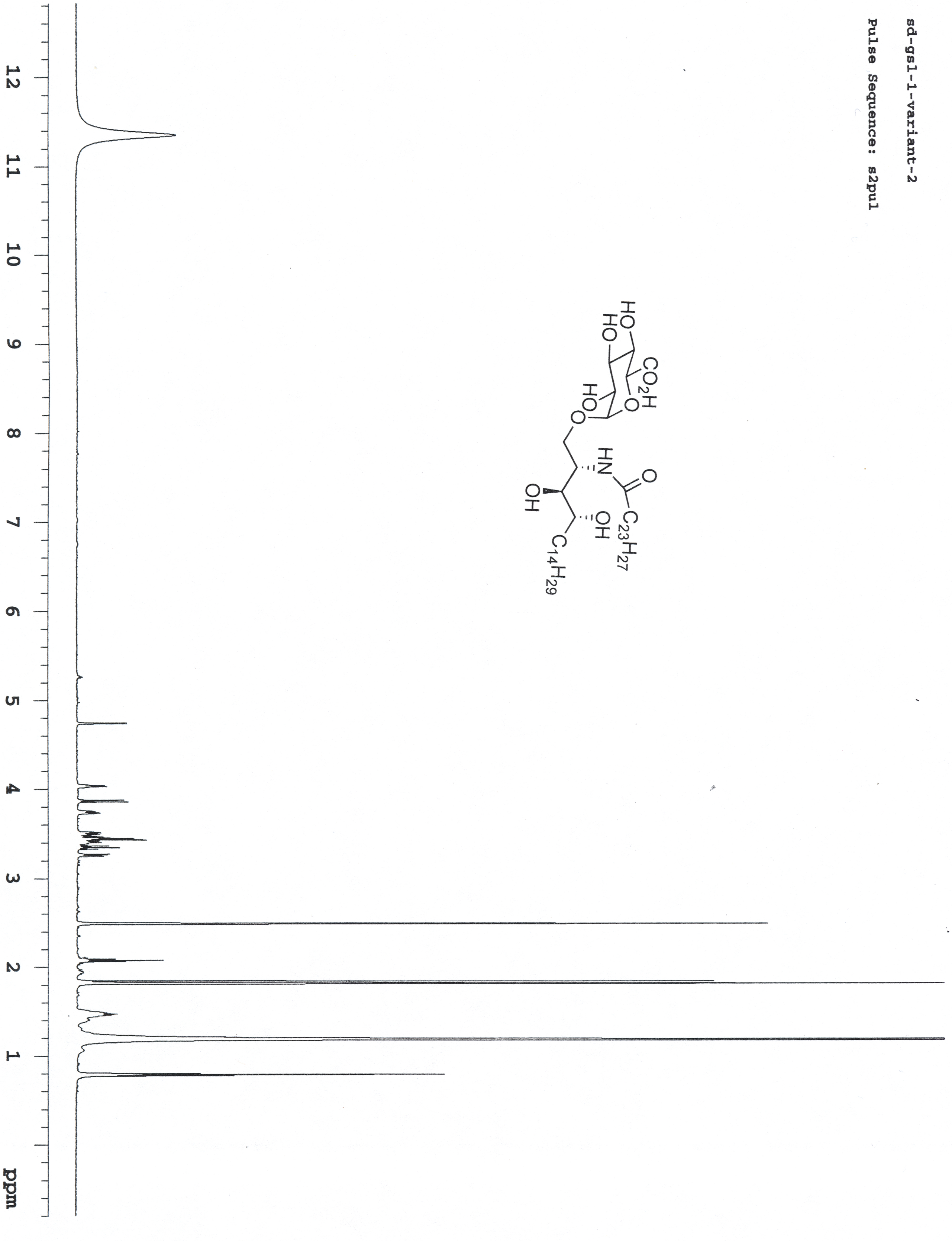
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4
3
2
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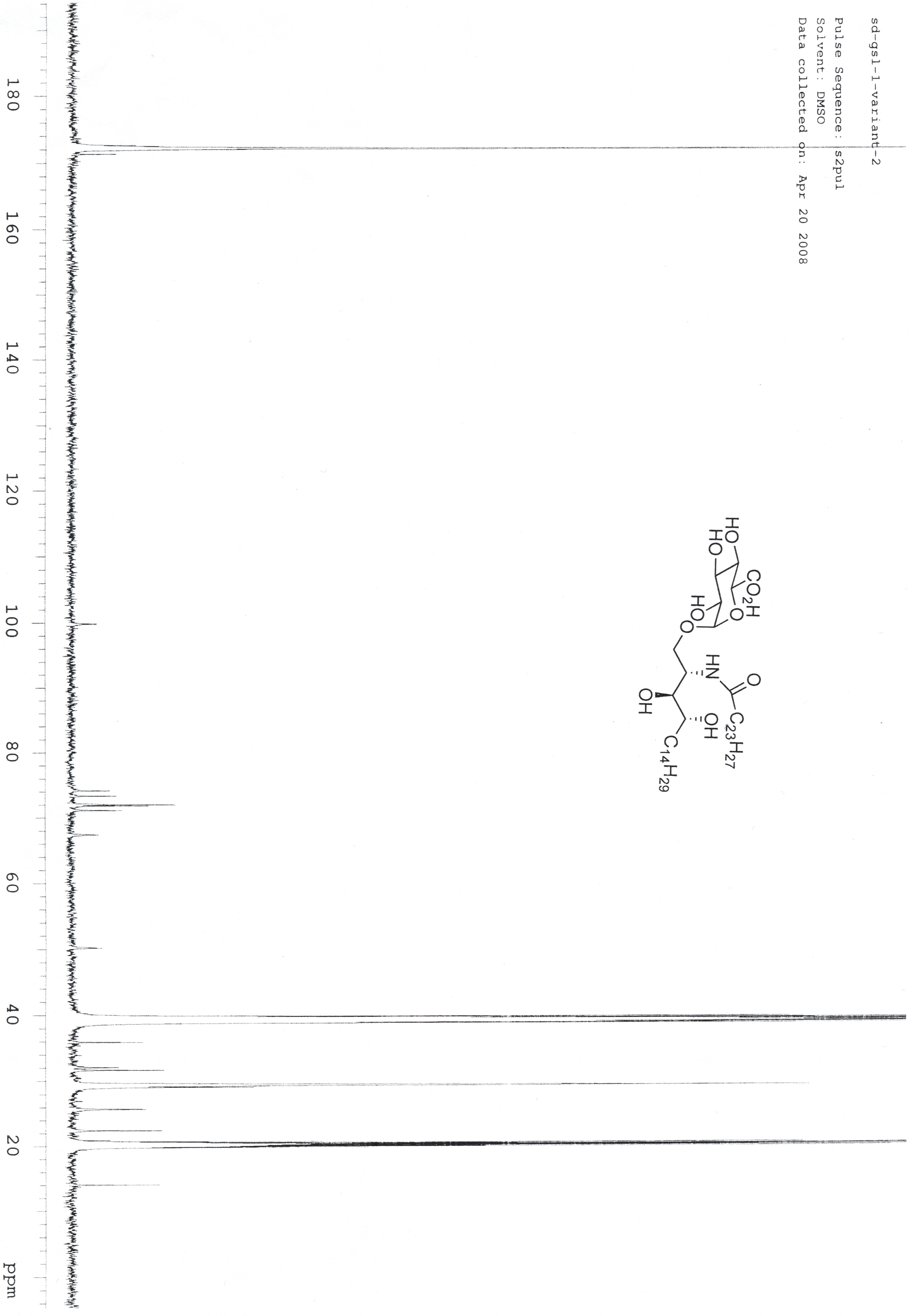
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OH
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140
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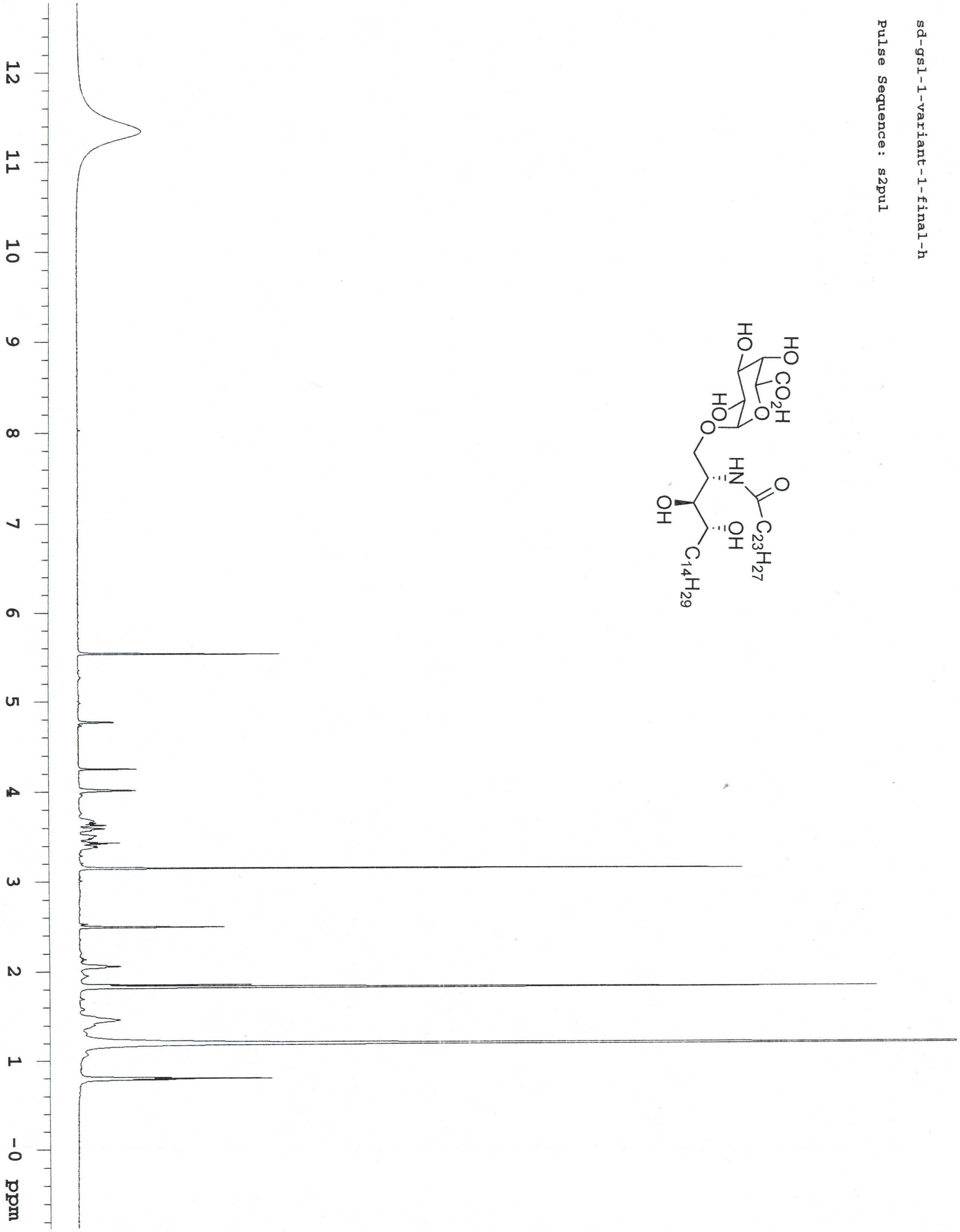
80
60
40
20
ppm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CO2H
O
HO
HO
O
HN
O
C23H27
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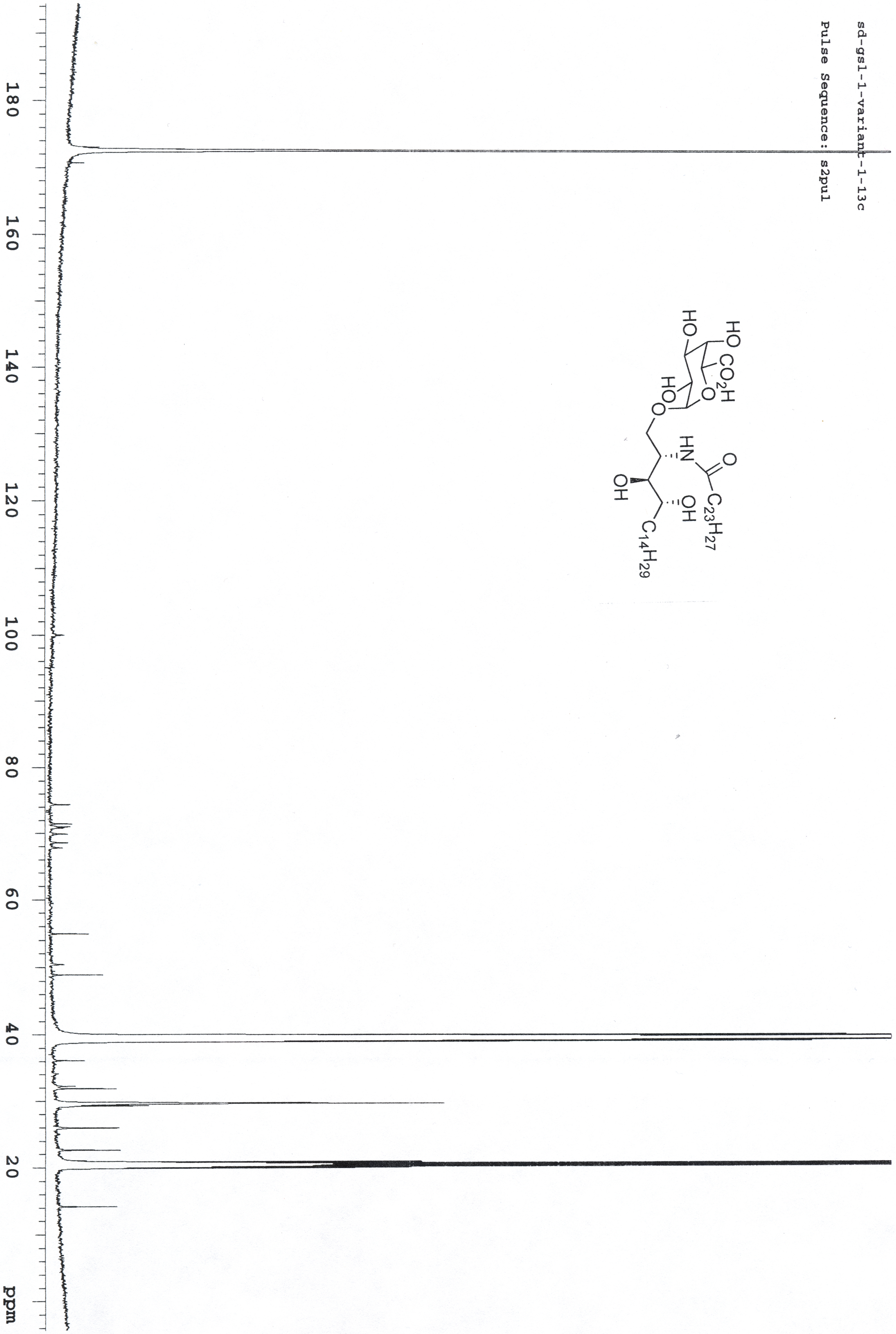
11
10
9
8
7
6
5
4
3
2
1
-0
ppm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OH
C14H29
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80
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ppm

Qualitative Analysis Report

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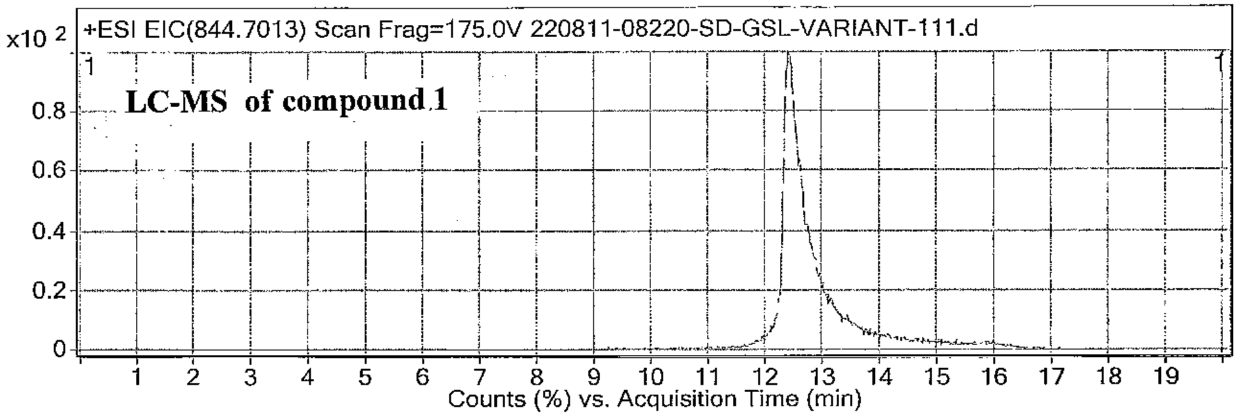
Sample Type	Unknown	**Position**	16
Instrument Name	Instrument 1	**User Name**	J. Chemist
Acq Method	VINOD ASP.M	**IRM Calibration Status**	Success
DA Method	unknown.m	**Comment**	Easy-Access Method: 'Vinod Asp'|C59H105NO15

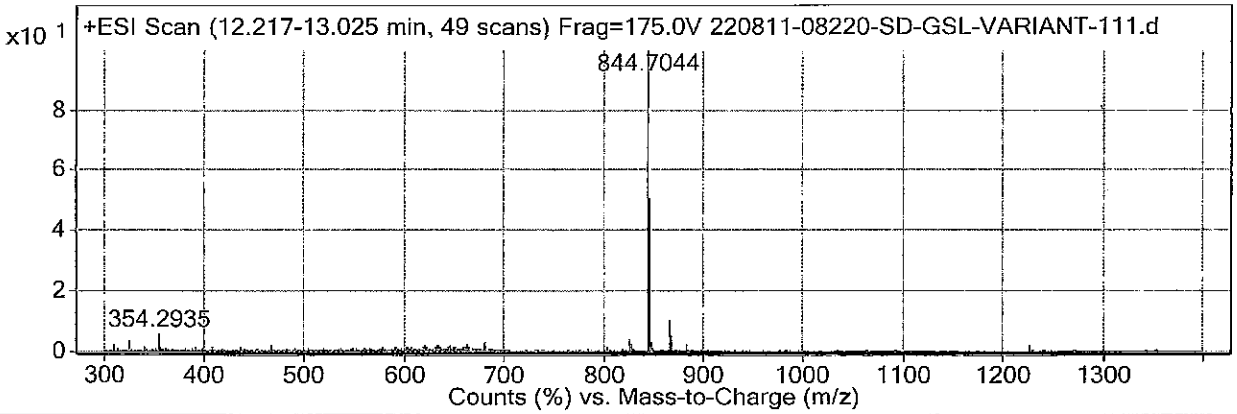
User Chromatograms

Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** Esl



User Spectra

Fragmentor Voltage	**Collision Energy**	**Ionization Mode**
175	0	Esl



Fragmentor Voltage	**Collision Energy**	**Ionization Mode**
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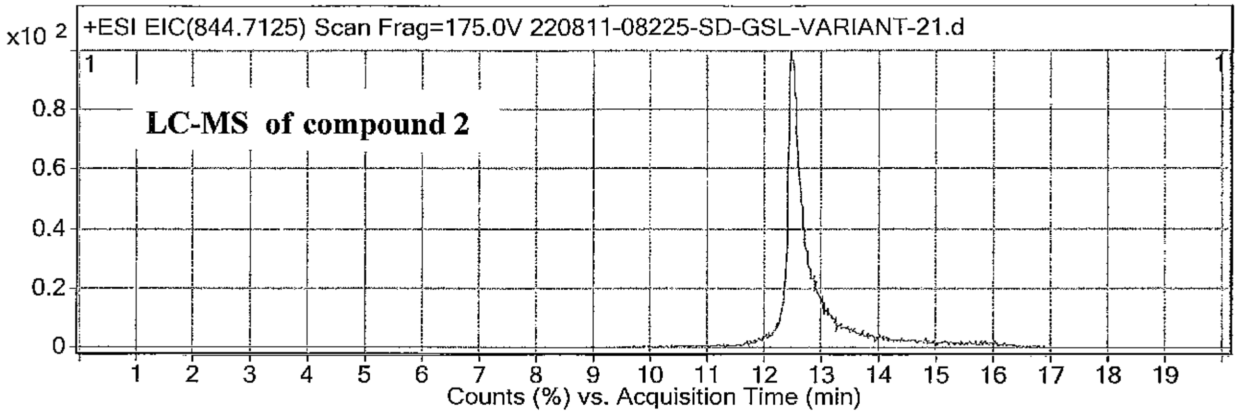
Qualitative Analysis Report

Data Filename	220811-08225-SD-GSL-VARIANT-21.d	**Sample Name**	sd-gsl-variant-2
Sample Type	Unknown	**Position**	21
Instrument Name	Instrument 1	**User Name**	J. Chemist
Acq Method	VINOD ASP.M	**IRM Calibration Status**	Success
DA Method	unknown.m	**Comment**	Easy-Access Method: 'Vinod Asp'|C84H93NO10

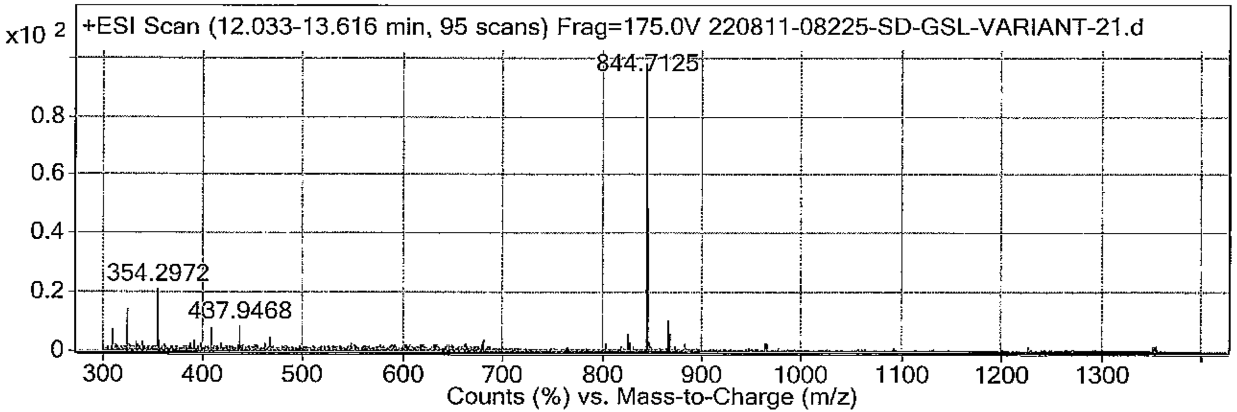
User Chromatograms

Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** Esi



User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	Esi



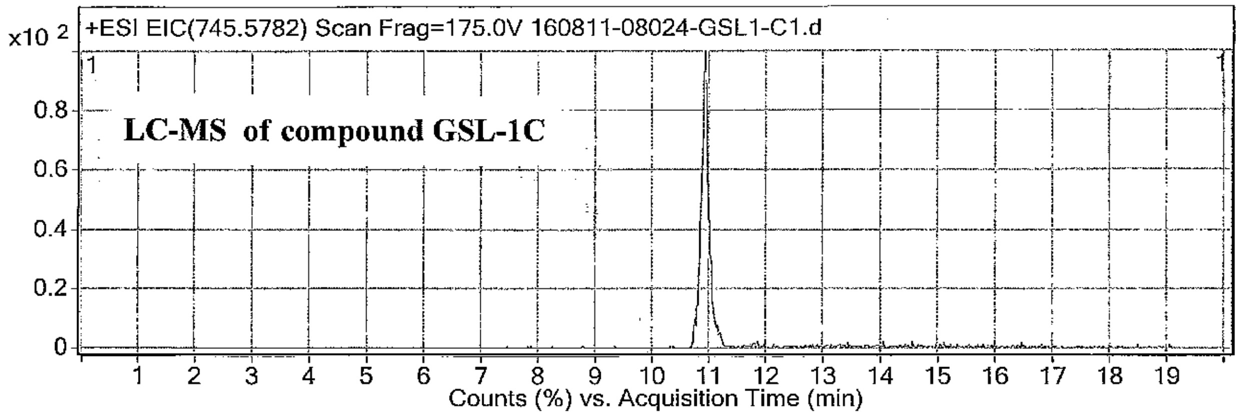
Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	Esi

Qualitative Analysis Report

Data Filename	160811-08024-GSL1-C1.d	**Sample Name**	GSL1-C
Sample Type	Unknown	**Position**	82
Instrument Name	Instrument 1	**User Name**	J. Chemist
Acq Method	VINOD ASP.M	**IRM Calibration Status**	Success
DA Method	unknown.m	**Comment**	Easy-Access Method: 'Vinod Asp'|C41H77NO10

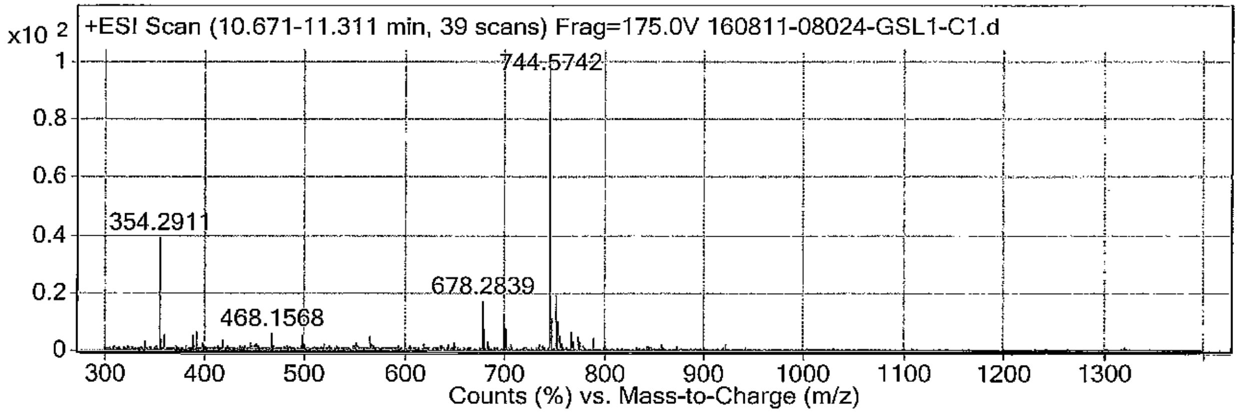
User Chromatograms

Fragmentor Voltage 175 **Collision Energy** 0 **Ionization Mode** Esi



User Spectra

Fragmentor Voltage	**Collision Energy**	**Ionization Mode**
175	0	Esi



Fragmentor Voltage	**Collision Energy**	**Ionization Mode**
175	0	Esi