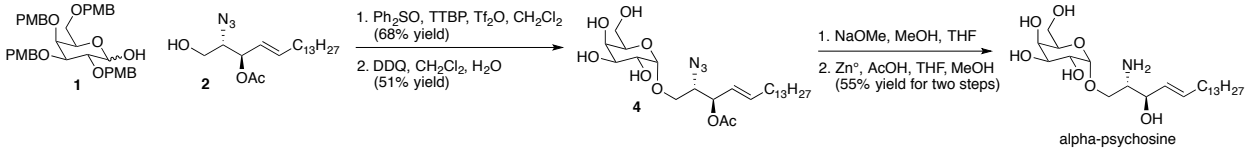
Supporting Information

^{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 Sigma-Aldrich, Acros, TCI or Fluka and were used as received unless otherwise noted.

Scheme 1. Synthesis of alpha-psychosine.

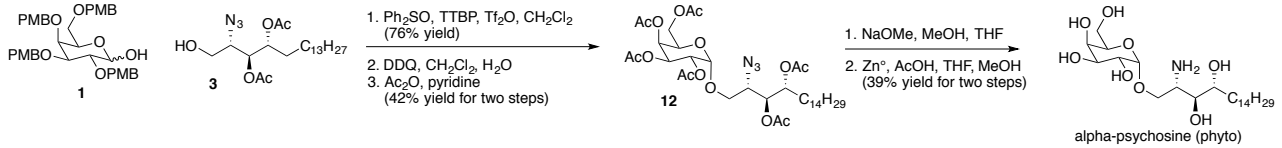


Preparation of 4: To a solution of **1** (330 mg, 0.5 mmol, 1.3 eq) in dry dichloromethan (6 mL) was added diphenylsulfoxide (194.7 mg, 0.963 mmol, 2.5 eq), 2,4,6-tri-*tert*-butylpyrimidine (TTBP) (334.72 mg, 1.35 mmol, 3.5 eq) and 3 Å molecular sieves (600 mg). The mixture was stirred at room temperature for 1 h and then cooled to -60 °C. Triflic anhydride (90.7 µl, 152.67 mg, 0.539 mmol, 1.4 eq) was added. The mixture was warmed to -40 °C, and a solution of **2** (141.2 mg, 0.385 mmol, 1 eq) in dichloromethane (1.5 mL) was added drop wise. The mixture was allowed to warm to room temperature over 30 min. After removal of molecular sieves by filtration, the filtrate was concentrated and subjected to silica gel column chromatography (EtOAc:hexanees - 1:5 to 1:2 (v:v)) to give the alpha-glycoside as a colorless oil (264 mg, 68% yield) (R_f =0.3, EtOAc:hexanes 1:3). ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 7.45-6.78 (m, 16 H), 5.758 (dt, J = 15.0, 8.0 Hz, 1 H), 5.41 (dd, J = 15.0, 8.0 Hz, 1 H), 5.32 (dd, J = 8.0, 8.0 Hz, 1 H), 4.829 (d, J = 11.0 Hz, 1 H), 4.792 (d, J = 3.5 Hz, 1 H, anomeric), 4.73 (d, J = 11.50 Hz, 1 H), 4.70 (d, J = 11.50 Hz, 1 H), 4.627 (d, J = 10.50 Hz, 1 H), 4.604 (d, J = 11.50 Hz, 1H), 4.478 (d, J = 11.0 Hz, 1 H), 4.401 (d, J = 11.5 Hz, 1 H), 4.301 (d, J = 11.50 Hz, 1 H), 3.98 (dd, J = 9.50, 3.50 Hz, 1 H), 3.91-3.85 (m, 3 H), 3.83 (m, 1 H), 3.758 (s, 3 H), 3.749 (s, 3 H), 3.740 (s, 3 H), 3.735 (s, 3 H), 3.66 (dd, J = 10.50, 4.0 Hz, 1 H), 3.50-3.40 (m, 3 H), 2.019 (s, 3 H), 1.98 (m, 2 H), 1.32-1.23 (m, 21 H), 0.85 (t, J = 6.50 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ = 169.56, 159.23, 159.16, 159.06, 138.31, 131.28, 131.05, 130.78, 130.04, 129.89, 129.75, 129.49, 129.32, 129.17, 129.09, 124.95, 124.83, 124.72, 124.47, 123.07, 113.82, 113.76, 113.67, 113.59, 98.84, 78.32, 77.45, 77.20, 76.94, 76.07, 74.65, 74.29, 73.08, 72.88, 72.74, 69.93, 68.80, 67.71, 63.67, 55.20, 32.30, 31.91, 29.68, 29.60, 29.44, 29.34, 29.17, 28.68, 22.68, 21.08, 14.15. HRMS (ESI) calcd for $C_{58}H_{80}N_3O_{12}$ $[M+H]^+$: 1010.5664; found: 1010.5781.

The clear oil was dissolved in dichloromethane (20 mL), to which DDQ (0.78 g, 3.44 mmol, 10 eq) and water (3 mL) were added at 0 °C. The mixture was stirred at room temperature overnight, then diluted with chloroform (100 mL). The mixture was washed with water (100 mL x 2) and the organics were concentrated under vacuum. The crude mixture was subjected to column chromatography (MeOH (2 to 10%) in dichloromethane) to give **4** as a colorless oil (70 mg, 51% yield). ^{1}H NMR (500 MHz, CD_3OD, ppm): δ = 5.758 (dt, J = 15.0, 8.0 Hz, 1 H), 5.41 (dd, J = 15.0, 8.0 Hz, 1H), 5.32 (dd, J = 8.0, 8.0 Hz, 1H), 4.847 (d, J = 3.50 Hz, 1H, anomeric), 3.91 (brs, 1 H), 3.83-3.67 (m, 7 H), 3.485 (dd, J = 10.50,7.50 Hz, 1 H), 2.10 (s, 3 H), 2.09 (m, 2 H), 1.40-1.29 (m, 22 H), 0.905 (t, J = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, CD_3OD, ppm): δ = 173.94, 141.73, 127.46, 103.81, 78.06, 75.42, 73.88, 73.57, 72.64, 70.94, 67.51, 65.27, 35.84, 35.61, 33.33, 33.32, 33.30, 33.29, 33.27, 33.07, 33.02, 32.69, 32.42, 26.27, 23.53, 16.98. HRMS (ESI) calcd for $C_{26}H_{51}N_4O_8$ $[M+NH_4]^+$: 547.3707; found: 547.3509.

Preparation of alpha-psychosine: To a solution of **4** (20 mg, 0.038 mmol) in a mixture of MeOH (2 mL) and THF (3.5 mL) was added NaOMe (1 *M* in MeOH, 0.1 mL). The mixture was stirred for 2 h. Zinc dust (500 mg, 7.69 mmol) and AcOH (1.5 mL) were added. The mixture was subjected to sonication (bath sonicator) for 10 min. Residual zinc dust was removed by filtration, and the filtrate was concentrated under reduced pressure. The resulting material was dissolved in methanol (6 mL) and treated with 3 mL of ammonium hydroxide. After 1 h, the solvent was removed under vacuum, and the product was purified by silica gel column (MeOH:dichloromethane:H_2O- 25:60:4), affording alpha psychosine (9.6 mg, 55% yield) as a white powder. ^{1}H NMR (500 MHz, CD_3OD, ppm): 5.82 (dt, *J* = 15.0, 7.0 Hz, 1 H), 5.49 (dd, *J* = 15.5, 7.0 Hz, 1 H), 4.84 (d, *J* = 4.0 Hz, 1 H, anomeric), 4.19 (t, *J* = 6.0 Hz, 1 H), 3.99 (dd, *J* = 10.5, 2.5 Hz, 1 H), 3.89 (d, *J* = 3.0 Hz, 1 H), 3.82 (dd, *J* = 10.0, 3.50 Hz, 1 H), 3.77 (t, *J* = 6.0 Hz, 1H), 3.75 (dd, J = 7.0, 3.5 Hz, 1 H), 3.73-3.67 (m, 3 H), 3.41 (t, J = 9.5 Hz, 1H), 3.21 (m, 1 H), 2.10 (q, *J* = 7.0 Hz, 2 H), 1.42 (m, 2 H), 1.29 (m, 20 H), 0.90 (t, *J* = 6.5 Hz, 3 H). ^{13}C NMR (125 MHz, CD_3OD, ppm); δ = 134.84, 127.70, 99.61, 71.40, 70.98, 69.97, 69.60, 68.83, 66.14, 61.37, 55.41, 31.98, 31.66, 29.39, 29.35, 29.23, 29.07, 28.99, 28.84, 22.27, 13.02. HRMS (ESI) calcd for $C_{24}H_{48}NO_7$ $[M+H]^+$: 462.3431; found: 462.3290.

Scheme S1. Synthesis of alpha-psychosine (phyto).



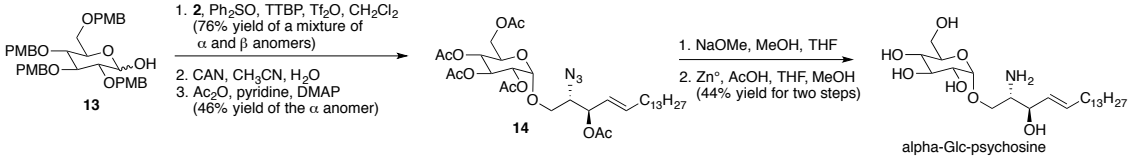
Preparation of 12: To a solution of **1** (660 mg, 1 mmol, 1.3 eq) in dichloromethane (7 mL) was added diphenylsulfoxide (390 mg, 1.92 mmol, 2.5 eq), TTBP (669 mg, 2.7 mmol, 3.5 eq), and 3 Å molecular sieves (800 mg). The mixture was stirred at room temperature for 1 h, then cooled to -60 °C. Triflic anhydride (181 µl, 305 mg, 1.078 mmol, 1.4 eq) was added. The mixture was warmed to -40 °C, and a solution of acceptor **3** (328.8 mg, 0.77 mmol, 1 eq) in dichloromethane (2 mL) was added drop wise. The mixture was allowed to warm to room temperature over 50 min. After removal of molecular sieves by filtration, the filtrate was concentrated and subjected to silica gel column chromatography, affording the alpha glycoside (626 mg, 76% yield) as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 7.32-6.81 (m, 16 H), 5.09 (m, 2H), 4.84 (d, *J* = 11.00 Hz, 1 H), 4.81 (d, *J* = 3.50 Hz, 1H, anomeric), 4.76 (d, J = 11.00 Hz, 1 H), 4.72 (d, *J* = 11.50 Hz, 1H), 4.64 (d, *J* = 11.0 Hz, 1H), 4.63 (d, *J* = 11.50 Hz, 1H), 4.49 (d, *J* = 11.50 Hz, 1 H), 4.41 (d, *J* = 11.50 Hz, 1 H), 4.32 (d, *J* = 11.50 Hz, 1 H), 3.98 (dd, *J* = 10.0, 3.5 Hz, 1 H), 3.92 (t, *J* = 6.5 Hz, 1H), 3.904 (d, *J* = 3.0 Hz, 1 H), 3.86 (m, 3 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.80 (s, 3H), 3.79 (s, 3H), 3.605 (dd, *J* = 10.5, 8.5 Hz, 1 H), 3.458 (dd, *J* = 9.5, 6.0 Hz, 1 H), 3.398 (dd, *J* = 9.50, 6.5 Hz, 1H), 2.03 (s, 3 H), 2.02 (s, 3H), 1.59 (m, 2 H), 1.26 (m, 24 H), 0.89 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ = 170.29, 169.68, 159.24, 159.18, 159.11, 159.05, 131.07, 130.87, 130.78, 130.03, 129.96, 129.47, 129.39, 129.17, 113.76, 113.72, 113.66, 113.59, 99.22, 78.41, 76.04, 74.65, 74.20, 73.06, 72.94, 72.81, 72.29, 72.18, 69.99, 68.95, 68.44, 60.85, 55.27, 55.24, 31.93, 29.71, 29.70, 29.69, 29.67, 29.65, 29.58, 29.51, 29.38, 29.37, 25.33, 22.70, 20.93, 20.73, 14.14. HRMS (ESI) calcd for $C_{60}H_{87}N_4O_{14}$ $[M+NH_4]^+$: 1087.6219; found: 1087.6343.

The clear oil from above (300 mg, 0.28 mmol) was dissolved in dichloromethane (30 mL), to which DDQ (0.637 g, 2.8 mmol, 10 eq) and water (6 mL) were added at 0 °C. The mixture was stirred at room temperature overnight. The mixture was diluted with chloroform (100 mL). The separated organic phase was further washed with water (100 mL x 2) and concentrated. The crude mixture was subjected to acetylation immediately by treatment with acetic anhydride (8 mL) in the presence of pyridine (10 mL) at room temperature. After stirred overnight, the reaction was quenched with

methanol (10 mL) at 0 °C. The mixture was further diluted with dichloromethane (150 mL), washed with aqueous HCl (10%, 500 mL) and aqueous $NaHCO_3$ (sat. 200 mL) sequentially. The organic material was concentrated, and the product was purified by silica gel column chromatography (EtOAc:Hexane- 1:3), affording **12** as a clear oil (89 mg, 42% yield for two steps). ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 5.49 (d, J = 3.0 Hz, 1 H), 5.35 (dd, J = 10.50, 3.0 Hz, 1 H), 5.16 (dd, J = 11.0, 3.5 Hz, 1 H), 5.124-5.07(m, 3 H), 4.22 (t, J = 7.0 Hz, 1 H), 4.12 (d, J = 6.5 Hz, 1 H), 4.004 (dd, J = 10.5, 2.5 Hz, 1 H), 3.73 (m, 1 H), 3.507 (dd, J = 11.0, 8.5 Hz, 1 H), 2.15 (s, 3 H), 2.09 (s, 3 H), 2.08 (s, 3 H), 2.06 (s, 3 H), 2.05 (s, 3 H), 1.99 (s, 3 H). 1.61 (m, 2 H), 1.29 (m, 25 H), 0.88 (t, J = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ = 170.72, 170.38, 170.27, 170.18, 169.99, 169.57, 97.02, 72.13, 71.75, 68.21, 67.87, 67.62, 67.43, 66.62, 61.67, 60.41, 31.91, 29.94, 29.68, 29.66, 29.65, 29.63, 29.55, 29.47, 29.39, 29.36, 29.32, 25.34, 22.68, 20.93, 20.74, 20.71, 20.68, 20.66, 20.64, 14.12. HRMS (ESI) calcd for $C_{36}H_{60}N_3O_{14}$ $[M+H]^+$: 758.4075; found: 758.4103.

Preparation of alpha-psychosine (phyto): To a solution of **12** (38 mg, 0.05 mmol) in a mixture of methanol (3 mL) and THF (3 mL) was added NaOMe (1 *M* in methanol, 0. 4 mL). The mixture was stirred for 3 h. Acetic acid (1.5 mL) was added to the reaction mixture, followed by addition of zinc dust (162 mg, 50 eq). The mixture was sonicated for 15 min. After removal of zinc dust by filtration, the filtrate was concentrated under reduced pressure. The resulting crude mixture was dissolved in MeOH (6 mL) and combined with ammonium hydroxide (6 mL). After stirred for 30 min, the solvent was removed on under vacuum, and the residue was purified by silica gel column chromatography (MeOH:dichloromethane:H_2O- 25:60:4), affording alpha psychosine (phyto) as a white powder (9.34 mg, 39% for two steps). ^{1}H NMR (500 MHz, CD_3OD, ppm): δ = 4.85 (d, J = 3.5 Hz, 1 H, anomeric), 4.13 (dd, J = 10.5, 3.0 Hz, 1 H), 3.895 (d, J = 3.0 Hz, 1 H), 3.86 (dd, J = 10.0, 4.0 Hz, 1 H), 3.80-4.74 (m, 3 H), 3.70 (dd, J = 10.5, 4.0 Hz, 1 H), 3.65 (m, 1 H), 3.54 (m, 2 H), 3.45 (m, 1 H), 1.80 (m, 1 H), 1.57 (m, 1 H), 1.29 (m, 24 H), 0.91 (t, J = 6.5 Hz, 3 H). ^{13}C NMR (125 MHz, CD_3OD, ppm): δ = 99.47, 72.55, 71.60, 71.53, 69.88, 69.62, 68.71, 64.02, 61.52, 53.45, 34.04, 31.66, 29.38, 29.34, 29.06, 24.93, 22.32. 13.02. HRMS (ESI) calcd for $C_{24}H_{50}NO_8$ $[M+H]^+$: 480.3536; found: 480.3572.

Scheme S2. Synthesis of alpha-Glc-psychosine.

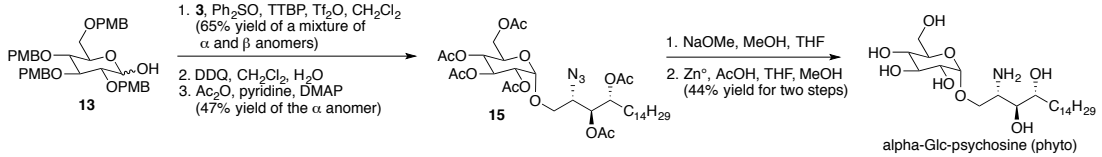


Preparation of 14: To a solution of **13** (165 mg, 0.25 mmol, 1.3 eq) in dry dichloromethane (5 mL) was added diphenylsulfoxide (98 mg, 0.48 mmol, 2.5 eq), TTBP (168 mg, 0.68 mmol, 3.5 eq), and 3 Å molecular sieves (600 mg). The mixture was stirred at room temperature for 1 h then cooled to -60 °C. Triflic anhydride (46 µl, 77 mg, 0.27 mmol, 1.4 eq) was subsequently added at that temperature. After the mixture was warmed to -40 °C, a solution of acceptor **2** (71 mg, 0.193 mmol, 1 eq) in dichloromethane (1 mL) was added drop wise. The mixture was allowed to warm up to room temperature over 30 min. After removal of the molecular sieves by filtration, the filtrate was concentrated and subject to silica gel column chromatography (EtOAc:hexanes- 1:4 to 1:2) to give a colorless oil (147 mg as a mixture of α and β anomers, 76% yield) HRMS (ESI) calcd for $C_{58}H_{80}N_3O_{12}$ $[M+H]^+$: 1010.5742; found: 1010.5765. The crude mixture (147 mg, 0.146 mmol) was dissolved in acetonitrile (6 mL) and water (1 mL) and cooled to 0 °C. CAN (800 mg, 1.46 mmol, 10 eq) was added to the mixture, which was stirred for 30 min. A solution of NaS_2O_3 (2 g) in water (10 mL) was added,

and the mixture was stirred for 30 min before chloroform (100 mL) was added. The organic phase was collected and concentrated. The resulting crude product was used immediately without further purification. The crude product, acetic anhydride (5 mL), pyridine (10 mL), and DMAP (0.02 g) were stirred together for 8 h. Methanol (7 mL) was added, and the reaction mixture was diluted with dichloromethane (100 mL), washed with aqueous HCl (10% 50 mL). The organic phase was concentrated and purified by column chromatography (EtOAc: hexanes- 1:3), affording **14** (alpha anomer) as a clear oil (49 mg, 46% overall yield). ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 5.85 (dt, J = 15.00, 6.50 Hz, 1 H), 5.49 (t, J = 9.50 Hz, 1 H), 5.44 (dd, J = 15.0, 6.5 Hz, 1 H), 5.32 (m, 1 H), 5.11 (d, J = 3.5 Hz, 1 H, anomeric), 5.08 (t, J = 10.0 Hz, 1 H), 4.90 (dd, J = 10.0, 3.0 Hz, 1 H), 4.27 (dd, J = 12.50, 4.50 Hz, 1 H), 4.12 (d, J = 12.0 Hz, 1 H), 4.01 (d, J = 8.0 Hz, 1H), 3.79 (m, 2 H), 3.42 (t, J = 7.5 Hz, 1H), 2.21 (m, 2H), 2.10 (s, 3 H), 2.09 (s, 3 H), 2.07 (s, 3H), 2.04 (s, 3 H), 2.02 (s, 3 H), 1.26 (m, 24 H), 0.88 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ = 170.52, 170.37, 169.98, 169.54, 138.76, 122.88, 96.49, 73.72, 70.42, 69.90, 68.39, 67.88, 63.35, 61.75, 32.29, 31.89, 29.66, 29.63, 29.56, 29.39, 29.32, 29.15, 28.65, 22.65, 21.04, 20.67, 20.64, 20.58, 14.09. HRMS (ESI) calcd for $C_{34}H_{59}N_4O_{12}$ $[M+NH4]^+$: 715.4129; found: 715.3879.

Preparation of alpha-Glc-psychosine: To a solution of **14** (35 mg, 0.05 mmol) in a mixture of methanol (4 mL) and THF (2 mL) was added NaOMe (1 *M* in methanol, 0.5 mL). The mixture was stirred for 5 h. Acetic acid (1.0 mL) was added to the reaction mixture, followed by addition of zinc dust (162 mg, 50 eq). The mixture was sonicated for 13 min. After removal of zinc dust by filtration, the filtrate was concentrated under vacuum. The resulting crude mixture was dissolved in MeOH (6 mL) and treated with ammonium hydroxide (6 mL). After stirring for 30 min, the solvents were removed undervacuum, and the product was purified by silica gel column chromatography (MeOH:dichloromethane:H_2O- 25:60:4), affording alpha-Glc-psychosine as a white powder (10 mg, 44% for 2 steps). ^{1}H NMR (500 MHz, CD_3OD, ppm): δ = 5.82 (dt, J = 15.0, 7.0 Hz, 1 H), 4.48 (dd, J = 15.0, 7.0 Hz, 1 H), 4.80 (d, J = 3.5 Hz, 1 H, anomeric), 4.20 (t, J = 6.0 Hz, 1 H), 3.98 (dd, J = 10.5, 3.0 Hz, 1 H), 3.79 (dd, J = 10.5, 2.5 Hz, 1 H), 3.66 (dd, J = 12.0, 4.5 Hz, 1 H), 3.62 (t, J = 4.5 Hz, 1 H), 3.507 (ddd, J = 9.50, 5.5, 2.0 Hz, 1 H), 3.44 (dd, J = 9.5, 3.5 Hz, 1 H), 3.40 (t, J = 10.5 Hz, 1 H), 3.26 (m, 1 H), 3.22 (m, 1 H), 2.08 (q, J = 7.0 Hz, 2 H), 1.41 (m, 2 H), 1.27 (m, 20 H), 0.89 (t, J = 7.0 Hz, 3H). ^{13}NMR (125 MHz, CD_3OD, ppm): δ = 138.84, 131.51, 103.25, 77.51, 76.59, 76.00, 74.69, 74.09, 69.73, 65.08, 59.40, 35.90, 35.59, 33.32, 33.28, 33.16, 32.99, 32.92, 32.78, 26.25, 16.95. HRMS (ESI) calcd for $C_{24}H_{47}NO_7$ $[M+H]^+$: 462.3431; found: 462.3492.

Scheme S3. Synthesis of alpha-Glc-psychosine (phyto).

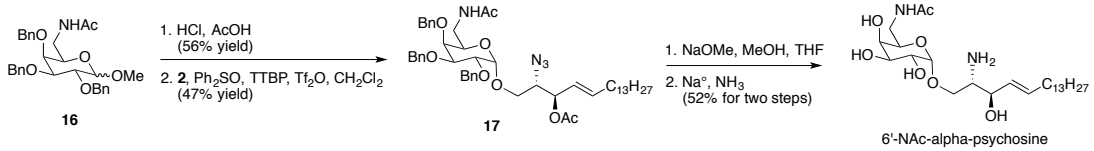


Preparation of 15: To a solution of **13** (250 mg, 0.38 mmol, 1.2 eq) in dichloromethane (6 mL) was added diphenylsulfoxide (160 mg, 0.79 mmol, 2.5 eq), TTBP (275 mg, 1.11 mmol, 3.5 eq), and 3 Å molecular sieves (600 mg). The mixture was stirred at room temperature for 1 h, and then cooled to -60 °C. Triflic anhydride (74 µl, 125 mg, 0.44 mmol, 1.4 eq) was added at that temperature. After the mixture was warmed to -40 °C, and a solution of acceptor **3** (135 mg, 0.316 mmol, 1 eq) in

dichloromethane (1 mL) was added drop wise. The reaction was allowed to warm to room temperature with stirring over 30 min. After removal of molecular sieves by filtration, the filtrate was concentrated and subjected to silica gel column chromatography (EtOAc:hexanes- 1:4 to 1:1) to give of a colorless oil (210 mg as a mixture of α and β anomers, 65% yield). HRMS (ESI) calcd for $C_{60}H_{87}N_4O_{14}$ $[M+NH4]^+$: 1087.6219; found: 1087.6276. The clear oil (200 mg, 0.187 mmol) was dissolved in dichloromethane (35 mL) to which DDQ (0.24 g, 2.1 mmol, 11 eq) and water (7 mL) were added at 0 °C. The mixture was stirred at room temperature overnight. The mixture was diluted with chloroform (150 mL), and the organic phase was further washed with water (100 mL x 3) and concentrated. The crude mixture was subject to acetylation immediately by treatment with acetic anhydride (10 mL) in the presence of pyridine (15 mL) and DMAP (0.05 g) at room temperature. After stirring overnight, the mixture was quenched with methanol (10 mL) at 0 °C. The mixture was further diluted with dichloromethane (150 mL) and washed with aqueous HCl (10%, 500 mL), $NaHCO_3$ (sat. 200 mL) sequentially. The organic phase was concentrated, and the product was purified by silica gel column chromatography (EtOAc:Hexane- 1:3), affording **15** as a clear oil (52 mg, 47% for two steps). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 5.44 (t, J = 10.0 Hz, 1 H), 5.04 (d, J = 7.5 Hz, 1 H, anomeric), 5.02 (m, 2 H), 4.88(m, 1 H), 3.69 (m, 1 H), 3.64 (brs, 1 H), 3.46 (t, J = 9.5 Hz, 1 H), 2.43 (m, 2 H), 2.04 (s, 3 H), 2.02 (s, 6 H), 1.99 (s, 3 H), 1.96 (s, 3 H), 1.55 (m, 2 H), 1.20 (m, 22 H), 0.82 (t, J = 6.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm); δ = 170.532, 170.352, 170.188, 169.97, 169.51, 169.49, 96.53, 71.98, 71.80, 70.29, 69.87, 68.38, 68.18, 67.58, 61.75, 60.37, 31.86, 29.89, 29.62, 29.60, 29.59, 29.57, 29.49, 29.47, 29.39, 29.30, 29.25, 25.24, 22.63, 21.31, 21.08, 20.90, 20.68, 20.65, 20.62, 20.56, 20.54, 14.08. HRMS (ESI) calcd for $C_{36}H_{60}N_3O_{14}$ $[M+NH4]^+$: 775.4341; found: 775.4336.

Preparation of alpha-Glc-psychosine (phyto): To a solution of **15** (80 mg, 0.11 mmol) in a mixture of methanol (5 mL) and THF (4 mL) was added NaOMe (1 *M* in methanol, 0.3 mL). The mixture was stirred for 5 h. Acetic acid (1.5 mL) was added to the reaction mixture, followed by addition of zinc dust (200 mg, 28 eq). The mixture was subsequently sonicated for 13 min. After removal of the excess zinc dust by filtration, the filtrate was concentrated under vacuum. The mixture was dissolved in MeOH (8 mL) and treated with ammonium hydroxide (8 mL). After stirring for 30 min, the solvent was removed under vacuum, and the product was purified by silica gel column chromatography (MeOH:dichloromethane:H_2O- 25:60:4), affording alpha-Glc-psychosine (phyto) as white powder (23 mg, 44% for two steps). ^{1}H NMR (500 MHz, pyridine-D5, ppm): δ = 5.45 (d, J = 3.7 Hz, 1 H), 4.94 (dd, J = 10.7, 3.5, 1 H), 4.78 (t, J = 9.5 Hz, 1 H), 4.65 (m, 2 H), 4.45 (t, J = 10.5 Hz, 1 H), 3.36 (m, 2 H), 4.29 (dd, J = 11.5, 5.0 Hz, 1 H), 4.19 (t, J = 9.0 Hz, 1 H), 4.12 (m, 2 H), 3.61 (brs, 1 H), 2.22 (m, 1 H), 1.81 (m, 1 H), 1.71 (m, 1 H), 1.60 (m, 1 H), 1.28 (m, 20 H), 0.89 (t, J = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, pyridine-d5, ppm): δ = 100.05, 73.72, 73.19, 72.56, 72.52, 70.96, 70.39, 64.65, 61.12, 53.46, 33.98, 30.70, 28.78, 28.63, 28.57, 28.50, 28.19, 24.66, 21.52, 12.87. HRMS (ESI) calcd for $C_{24}H_{50}NO_8$ $[M+H]^+$: 480.3536; found: 480.3437.

Scheme S4. Synthesis of 6'-NAc-alpha-psychosine.

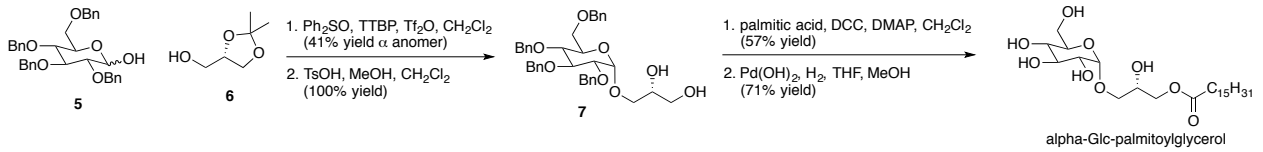


Compound 17: To a solution of **16** (150 mg, 0.297 mmol) in AcOH (9 mL) was added concentrated aqueous HCl (35%, 2 mL). The reaction mixture was warmed to 80 °C and stirred for 1 h. To the

mixture was added dichloromethane (100 mL), followed by saturated aqueous $NaHCO_3$ (50 mL). The organic phase was collected and concentrated. The crude mixture was subject to column chromatography (MeOH (5%) in dichloromethane) affording a clear oil (81.7 mg, 56% yield). HRMS (ESI) calcd for $C_{29}H_{34}NO_6$ $[M+H]^+$: 492.2386; found: 492.2336. To a solution of clear oil (77 mg, 0.157 mmol, 1.0 eq) in dichloromethane (6 mL) was added diphenylsulfoxide (79.4 mg, 0.393 mmol, 2.5 eq), TTBP (136.5 mg, 0.55 mmol, 3.5 eq), and 3 Å molecular sieves (600 mg). The mixture was stirred at room temperature for 1 h and then cooled to -60 °C. Triflic anhydride (37 µl, 62 mg, 0.219 mmol, 1.4 eq) was added at that temperature, and the mixture was warmed to -40 °C. A solution of acceptor **2** (57 mg, 0.157 mmol, 1 eq) in dichloromethane (1 mL) was then added drop wise. The mixture was allowed to warm to room temperature over 30 min. After removal of molecular sieves by filtration, the filtrate was concentrated and subjected to silica gel column chromatography (EtOAc:hexanes- 1:4 to 1:1) to give **17** as a clear oil (62 mg 47% yield). ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 7.42-7.27 (m, 15 H), 5.80 (dt, *J* = 15.0, 6.5 Hz, 1 H), 5.44 (dd, *J* = 15.5, 7.5 Hz, 1 H), 5.32 (dd, *J* = 7.0, 5.0 Hz, 1 H), 5.26 (t, *J* = 5.0 Hz, 1 H), 4.99 (d, *J* = 11.5 Hz, 1 H), 4.90 (d, *J* = 11.5 Hz, 1 H), 4.86 (d, *J* = 3.0 Hz, 1 H, anmeric), 4.82 (d, *J* = 12.0 Hz, 1H), 4.76 (d, *J* = 12.0 Hz, 1 H), 4.72 (d, *J* = 12.0 Hz, 1 H), 4.64 (d, *J* = 11.5 Hz, 1 H), 4.05 (dd, *J* = 10.0 Hz, 1 H), 3.93 (dd, *J* = 10.0, 1.5 Hz, 1 H), 3.80 (m, 2 H), 3.76 (m, 1 H), 3.65 (dd, *J* = 11.0, 3.5 Hz, 1 H), 3.46 (dd, *J* = 10.5, 8.5 Hz, 1 H), 3.34 (m, 1 H), 3.23 (m, 1 H), 2.07 (s, 3 H), 2.04 (q, *J* = 6.5 Hz, 1H), 1.76 (s, 3 H), 1.36 (m, 2 H), 1.26 (m, 20H), 0.89 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm); δ = 170.03, 169.65, 138.66, 138.60, 138.52, 138.25, 128.92, 128.61, 128.45, 128.40, 128.34, 128.11, 127.83, 127.65, 127.64, 127.61, 123.08, 98.63, 78.70, 75.11, 74.43, 74.12, 73.71, 73.21, 68.72, 67.67, 63.67, 40.15, 32.33, 31.93, 29.70, 29.69, 29.68, 29.66, 29.61, 29.45, 29.36, 29.19, 28.71, 23.01, 22.70, 21.13, 14.13. HRMS (ESI) calcd for $C_{49}H_{69}N_4O_8$ $[M+H]^+$: 841.5115; found: 841.5099.

Preparation of 6'-NAc-alpha psychosine: To a solution of **17** (62 mg, 0.074 mmol) in a mixture of MeOH (4 mL) and THF (4 mL) was added NaOMe (1 *M* in methanol, 0.1 mL) and the mixture was stirred for 30 min. The mixture was concentrated under vacuum, and the resulting alcohol was purified by a flash column chromatography (EtOAc:Heaxne- 1:1) giving the desired product in quantitative yield. This alcohol was then dissolved in THF (1 mL) and added to a mixture of sodium and ammonia at -78 °C. The mixture was stirred for 8 h at that temperature, then methanol (10 mL) was added, and the mixture was allowed to warm to room temperature. After removal of solvent, the product was purified by silica gel column chromatography (MeOH:dichloromethane:H_2O- 65:25:4) giving the product as a in of white powder (19.3 mg, 52% yield for two steps. ^{1}H NMR (500 MHz, CD_3OD, ppm): δ = 5.87 (td, *J* = 15.5 Hz, 6.5 Hz, 1 H), 5.49 (dd, *J* = 15.5, 7.0 Hz, 1 H), 4.84 (d, *J* = 3.5 Hz, 1 H, anomeric), 4.24 (t, *J* = 6.0 Hz, 1 H), 3.95 (dd, *J* = 10.5, 2.5, 1 H), 3.83 (dd, *J* = 10.5, 3.5 Hz, 1 H), 3.82 (d, *J* = 3.5 Hz, 1 H), 3.74 (dd, *J* = 10.0, 3.0 Hz, 1 H), 3.49 (dd, *J* = 14.0, 5.0 Hz, 1 H), 3.45 (t, *J* = 10.5 Hz, 1 H), 3.27 (dd, *J* = 13.5, 8.0 Hz, 1 H), 2.21 (m, 2 H), 1.97 (s, 3H), 1.94 (s, 3 H), 1.49 (m, 2 H), 1.29 (m, 20 H), 0.93 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, CD_3OD, ppm): δ = 172.39, 135.41, 127.17, 99.57, 70.15, 69.68, 69.58, 69.02, 68.62, 64.99, 55.41, 39.76, 32.01, 31.66, 29.38, 29.35, 29.24, 29.06, 29.00, 28.82, 28.79, 23.20, 22.32, 22.27, 21.24, 13.02. HRMS (ESI) calcd for $C_{26}H_{51}N_2O_7$ $[M+H]^+$: 503.3696; found: 503.3684.

Scheme 2. Synthesis of alpha-Glc-palmitoyl glycerol.

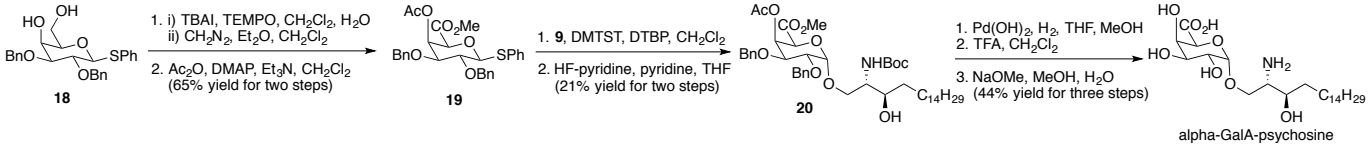


Preparation of 7: To a solution of **5** (500 mg, 0.928 mmol, 1.0 eq) in dichloromethane (8 mL) was added diphenylsulfoxide (469.24 mg, 2.32 mmol, 2.5 eq), TTBP (806.8 mg, 3.25 mmol, 3.5 eq), and 3 Å molecular sieves (700 mg). The mixture was stirred at room temperature for 1 h, and then cooled to -60 °C. Triflic anhydride (219 µl, 367 mg, 1.29 mmol, 1.4 eq) was added. The mixture was then warmed to -40 °C, and a solution of acceptor **6** (134.6 mg, 1.02 mmol, 1.1 eq) in dichloromethane (2 mL) was added drop wise. The mixture was allowed to warm to room temperature over 45 min. After removal of the molecular sieves by filtration, the filtrate was concentrated and subject to silica gel column chromatography (EtOAc:hexanes- 1:5 to 1:3) to give the alpha anomer of the glycoside as a clear oil (248.8 mg, 41% yield). ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 7.38-7.14 (m, 20 H), 4.99 (d, J = 11.0 Hz, 1 H), 4.88 (d, J = 3.5 Hz, 1 H), 4.84 (d, J = 12.0 Hz, 1 H), 4.82 (d, J = 11.5 Hz, 1 H), 4.80 (d, J = 13.0 Hz, 1 H), 4.67 (d, J = 12.0 Hz, 1H), 4.62 (d, J = 12.0 Hz, 1 H, anmeric), 4.49 (d, J = 10.0 Hz, 1 H), 4.48 (d, J = 12.0 Hz, 1 H), 4.37 (quintet, J = 6.0 Hz, 1 H), 4.086 (dd, J = 8.0, 6.5 Hz, 1 H), 3.97 (t, J = 9.0 Hz, 1H), 3.80-3.72 (m, 3 H), 3.67-3.55 (m, 5 H), 1.42 (s, 3 H), 1.38 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ = 138.83, 138.26, 138.24, 137.89, 131.06, 129.34, 128.46, 128.40, 128.38, 128.35, 128.04, 128.00, 127.96, 127.93, 127.90, 127.71, 127.60, 124.80, 109.45, 97.51, 81.93, 79.97, 77.58, 75.71, 75.10, 74.59, 73.49, 73.12, 70.35, 69.06, 68.42, 67.07, 26.85, 25.46. HRMS (ESI) calcd for $C_{40}H_{50}NO_8$ $[M+H]^+$: 672.3536; found: 672.3514. The glycoside from above (130 mg, 0.199 mmol) was dissolved in a mixture of dichloromethane (15 mL) and methanol (10 mL), and TsOH-H_2O (100 mg, 0.57 mmol) was added. The mixture was stirred at room temperature. After 3 h, triethylamine (1 mL) was added, and the mixture was stirred for 5 min. After removal of solvent under vacuum, the residue was purified by silica gel column chromatography (EtOAc:hexane- 1:1), affording the desired diol as a colorless oil (122 mg, quantitative yield). HRMS (ESI) calcd for $C_{37}H_{46}NO_8$ $[M+NH4]^+$: 632.3223; found: 632.3200.

Preparation of alpha-Glc-palmitoylglycerol: A mixture of diol **7** (120 mg, 0.195 mmol), DCC (24.7 mg, 0.120 mmol), DMAP (10 mg, 0.082 mmol) and palmitic acid (30.7 mg, 0.12 mmol) in dichloromethane (30 mL) was stirred at 0 °C for 1 h, then the mixture was allowed to warm to room temperature overnight. After solvent was removed, the mixture was subjected to column chromatography (EtOAc:hexane- 1:2), affording the ester as a colorless oil (94.7 mg, 57% yield). ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 7.38-7.14 (m, 20 H), 4.96 (d, J = 11.0 Hz, 1 H), 4.83 (d, J = 11.0 Hz, 2 H), 4.79 (d, J = 12.0 Hz, 1 H), 4.77 (d, J = 4.0 Hz, 1 H), 4.65 (d, J = 11.5 Hz, 1 H), 4.60 (d, J = 12.5 Hz, 1 H), 4.48 (d, J = 12.0 Hz, 1 H), 4.15 (dd, J = 12.0, 4.5 Hz, 1 H), 4.115 (dd, J = 11.5, 6.0 Hz, 1 H), 3.96 (t, J = 9.0 Hz,1 H), 3.83 (m, 1 H), 3.75 (dd, J = 11.0, 3.5 Hz, 1 H), 3.68 (dd, J = 10.5, 4.0 Hz, 1 H), 3.64-3.55 (m, 4 H), 3.46 (dd, J = 11.0, 8.0 Hz, 1 H), 3.12 (brs, 1 H, OH), 2.33 (t, J = 7.5 Hz, 2 H), 1.61 (m, 4 H), 1.29 (m, 22 H), 0.89 (t, J = 6.5 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm); δ = 173.885, 138.67, 138.10, 137.94, 137.74, 128.54, 128.42, 128.40, 128.38, 128.11, 128.02, 127.94, 127.91, 127.86, 127.77, 127.73, 127.64, 98.84, 82.00, 79.90, 77.61, 77.26, 77.22, 77.01, 76.76, 75.71, 75.08, 73.54, 73.51, 70.92, 70.64, 68.94, 68.41, 64.88, 34.14, 31.93, 29.70, 29.66, 29.62, 29.48, 29.37, 29.29, 29.16, 24.91, 22.70, 14.13. HRMS (ESI) calcd for $C_{53}H_{76}NO_9$ $[M+NH4]^+$: 870.5520; found: 870.5584. To a solution of the ester from above (50 mg, 0.059 mmol) in a mixture of THF (5 mL) and methanol (5 mL) in hydrogenation chamber was added $Pd(OH)_2$ (10% on carbon, 50 mg). The reaction mixture was subject to hydrogenation at 200 psi at room temperature overnight. After removal of the

catalyst by filtration through a celite pad, the filtrate was concentrated and the product was purified by silica gel column chromatography (10% MeOH in dichloromethane), affording targeted compound as a waxy solid (20.5 mg, 71% Yield). ^{1}H NMR (500 MHz, CD_3OD, ppm): δ = 4.80 (d, J = 3.5 Hz, 1 H), 4.12 (dd, J = 11.5, 4.5 Hz, 1 H), 4.05 (dd, J = 11.5, 60 Hz, 1 H), 4.00 (m, 1 H), 3.81-3.76 (m, 2 H), 3.71(dd, J = 12.0, 5.0 Hz, 1 H), 3.63 (t, J = 9.0 Hz, 1 H), 3.54 (m, 1 H), 3.42 (dd, J = 9.5, 3.5 Hz, 1 H), 3.36-3.2 (m 2H), 2.31 (t, J = 7.5 Hz, 2 H), 1.58 (m, 4 H), 1.26 (m, 22 H), 0.84 (t, J = 6.5 Hz, 3 H). ^{13}C NMR (125 MHz, CD_3OD, ppm): δ = 174.379, 99.231, 77.02, 73.75, 72.11, 71.95, 70.20, 69.55, 68.40, 64.88, 61.45, 55.58, 31.82, 29.57, 29.53, 29.50, 29.36, 29.24, 29.17, 29.03, 24.76, 22.56, 13.82. HRMS (ESI) calcd for $C_{25}H_{52}NO_9$ $[M+NH4]^+$: 510.3642; found: 510.3453.

Scheme S5. Synthesis of alpha-GalA-psychosine.



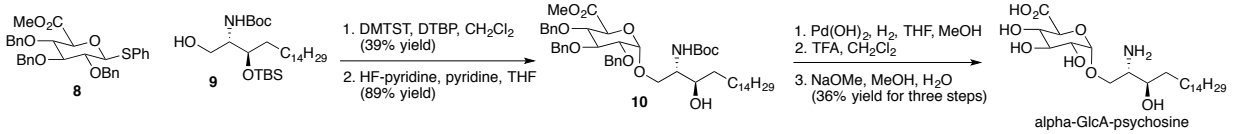
Preparation of 19: A mixture of **18** (430 mg, 0.951 mmol), TEMPO (29.72 mg, 0.19 mmol) and BAIB (766 mg, 2.38 mmol) was dissolved in a mixture of dichloromethane (10 mL) and water (3 mL). The mixture was stirred at room temperature overnight. After dilution with dichloromethane (50 mL), the reaction mixture was washed with H_2O (2 x 30 mL) and dried over Na_2SO_4. Solvent was removed under vacuum, and the crude acid was then dissolved in dichloromethane (10 mL). A solution of diazomethane in diethyl ether was added in small portions until complete conversion of the methyl ester was verified by TLC and HRMS. HRMS (ESI) calcd for $C_{27}H_{32}NO_6S$ $[M+NH_4]^+$: 498.1950, found: 498.1912. Acetic acid (2 mL) was added, and the reaction mixture was concentrated under vacuum. The methyl ester was then mixed with Et_3N (10 mL), Ac_2O (4 mL), DMAP (0.05 g) in dichloromethane (15 mL) at 0 °C. The mixture was stirred for 2 h. Then the mixture was diluted with dichloromethane (100 mL), washed with aqueous HCl (10%, 100 mL), and saturated aqueous $NaHCO_3$ (100 mL) sequentially. The organic layer was dried over Na_2SO_4 and concentrated. The product was purified by silica gel column chromatography (EtOAc:hexane- 1:3) giving **19** as a clear oil (323 mg, 65% yield for two steps). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.71 (d, J = 6.5 Hz, 2 H), 7.45-7.29 (m, 13 H), 5.87 (s, 1 H), 4.80 (dd, J = 17.0, 10.5 Hz, 2 H), 4.68 (d, J = 8.50 Hz, 1 H), 4.55 (d, J = 6.00 Hz, 1 H), 3.80 (s, 3 H), 3.74 (m, 3 H), 2.14 (s, 3 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 169.96, 167.19, 138.15, 137.36, 133.04, 132.99, 128.91, 128.56, 128.52, 128.42, 128.26, 128.01, 127.96, 127.91, 87.77, 80.63, 76.17, 75.83, 75.67, 72.09, 67.71, 52.70, 20.84. HRMS (ESI) calcd for $C_{29}H_{31}O_7S$ $[M+H]^+$: 523.1790, found: 523.1782.

Preparation of 20: A mixture of donor **19** (0.15 g, 0.29 mmol), acceptor **9** (0.15 g, 0.29 mmol), and DTBMP (0.27 g, 1.32 mmol) was dissolved in dichloromethane (7 mL). The solution was stirred with MS 4 Å (650 mg) at room temperature. After 30 min, freshly prepared promoter DMTST (0.27 g, 1.05 mmol) was added. The mixture was stirred overnight. Triethylamine (1 mL) was added to quench the reaction. The mixture was filtered through a silica gel pad. The filtrate was concentrated, and the product was purified by silica gel column chromatography, affording a light yellow oil as a mixture of inseparable anomers (150.5 mg). The product (150 mg) was dissolved in THF (7 mL) and pyridine (5 mL), followed by addition of HF-pyridine (50% in pyridine, 3 mL) at 0 °C. The mixture was stirred overnight. After dilution with dichloromethane (50 mL), the reaction mixture was washed with 10% HCl in water (30 mL), and saturated aqueous $NaHCO_3$ (100 mL). The organic phase was concentrated, and the product was purified by silica gel column chromatography (EtOAc:hexane- 1:2), affording the

alpha anomer **20**) as a clear oil (27.8 mg, 21% yield for 2 steps). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.38-7.27 (m, 10 H), 5.84 (d, J = 1.0 Hz, 1 H), 5.38 (d, J = 8.5, 1 H), 4.90 (d, J = 3.6 Hz, 1 H), 4.85 (d, J = 12.00 Hz, 1 H), 4.78 (d, J = 11.0 Hz, 1 H), 4.62 (d, J = 11.5 Hz, 1 H), 4.57 (d, J = 11.0 Hz, 1 H), 4.49 (s, 1 H). 3.98 (dd, J = 9.5, 2.0 Hz, 1 H), 3.82 (dd, J = 10.0, 3.0 Hz, 1 H), 3.75 (s, 3 H), 2.90 (d, J = 9.0 Hz, 1 H), 2.08 (s, 3 H), 1.57 (m, 2 H), 1.46 (s, 9 H), 1.26 (m, 24 H), 0.88 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 169.86, 167.89,137.64, 137.51, 128.46, 128.44, 128.09, 128.05, 128.02, 127.86, 99.20, 75.92, 74.2, 74.33, 74.13, 73.40, 72.08, 70.06, 69.16, 68.40, 52.98, 52.64, 35.10, 34.50, 31.93, 29.71, 29.67, 29.66, 29.62, 29.59, 29.55, 29.37, 28.39, 28.38, 26.10, 22.70, 20.74, 14.14. HRMS (ESI) calcd for $C_{46}H_{72}NO_{11}$ $[M+H]^+$: 814.5105, found: 814.5014.

Preparation of alpha-GalA-psychosine: To a solution of **20** (27 mg, 0.033 mmol) in a mixture of THF (6 mL) and methanol (6 mL) in a hydrogenation chamber was added $Pd(OH)_2$ (10% on carbon, 50 mg). The reaction mixture was subject to hydrogenation at 200 psi at room temperature overnight. After removal of the catalyst by filtration through a celite pad, the filtrate was concentrated and dried under vacuum. The crude product was dissolved in dry dichloromethane (2 mL). The solution was cooled to 0 °C, and TFA (4 mL) was added. The mixture was stirred for 2 h. The solvent and TFA were then evaporated under vacuum. The residue was subsequently dissolved in MeOH (6 mL), followed by addition of NaOMe (1 *M* in methanol, 0.5 mL). The mixture was stirred for 3 h before water (0.1 mL) was introduced. The mixture was stirred overnight. After removal of solvent under vacuum, the residue was subject to silica gel column chromatography (dichloromethane:MeOH:H_2O-65:25:4), affording the product as a white solid (7 mg, 44% yield for three steps). ^{1}H NMR (CD_3CO_2D/DMSO-D_6, 500 MHz): δ = 4.768 (d, J = 3.5 Hz, 1 H), 4.25 (s, 1 H), 4.007 (t, J = 1.5 Hz, 1 H), 3.82 (dd, J = 10.5, 3.5 Hz, 1 H), 3.66 (dd, J = 10.0, 3.0 Hz, 1 H), 3.64 (m, 1H), 3.55 (dd, J = 10.0, 4.0 Hz, 1 H), 3.45 (dd, J = 10.5, 8.5 Hz, 1 H), 3.23 (m, 1 H), 1.37 (m, 2 H), 1.19 (m, 24H), 0.80 (t, J = 7. Hz, 3 H). ^{13}C NMR (CD_3CO_2D/DMSO-D6, 125 MHz): δ = 170.65, 99.96, 70.97, 70.65, 69.47, 68.50, 68.34, 64.68, 63.20, 54.88, 32.83, 31.67, 29.45, 29.44, 29.39, 29.26, 29.09, 25.77, 22.45, 20.86, 20.79, 20.71, 20.63, 20.55, 20.48, 20.39, 20.32, 20.24, 20.16, 20.01, 19.85, 14.10. HRMS (ESI) calcd for $C_{24}H_{48}NO_8$ $[M+H]^+$: 478.3380, found: 478.3337.

Scheme 3. Synthesis of alpha-GlcA-psychosine.

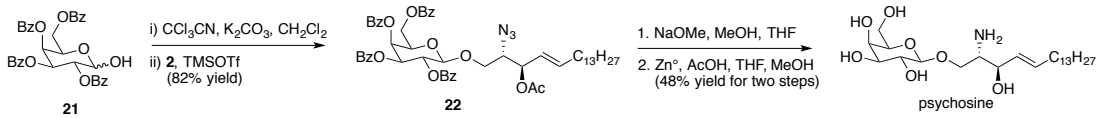


Preparation of 10: A mixture of donor **8** (0.15 g, 0.263 mmol), acceptor **9** (0.135 g, 0.263 mmol) and DTBMP (0.27 g, 1.05 mmol) was dissolved in dichloromethane (6 mL). The solution was stirred with MS 3 Å (600 mg) at room temperature. After 30 min, freshly prepared promoter DMTST (0.272 g, 1.05 mmol) was added. The mixture was stirred overnight. Triethylamine (1 mL) was added to quench the reaction. The mixture was filtered through a silica gel pad. The filtrate was concentrated, and the product was purified by silica gel chromatography (EtOAc:hexanes- 1:4) affording the alpha anomer as a light yellow oil (100 mg, 39% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.38-7.25 (m, 15 H), 4.94 (d, J = 10.5 Hz, 1 H), 4.81 (d, J = 4.0, 1 H), 4.794 (d, J = 4.0 Hz, 1 H, anomeric), 4.76 (d, J = 12.00 Hz, 1 H), 4.65 (d, J = 12.0 Hz, 1 H), 4.59 (d, J = 10.5 Hz, 1 H), 4.22 (d, J = 10.0 Hz, 1 H), 3.97 (t, J = 9.0 Hz, 1 H). 3.92 (m, 1 H), 3.82 (m, 1 H), 3.72 (m, 2 H), 3.70 (s, 3 H), 3.57 (dd, J = 9.5, 3.5 Hz, 1 H), 3.48 (m, 1 H), 1.63 (s, 3H), 1.51 (s, 6 H), 1.50 (m, 2 H), 1.26 (m, 24 H), 0.89 (s, 9 H), 0.87 (t, J = 0.65 Hz, 3 H), 0.093 (s, 3 H), 0.074 (s, 3 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 138.57, 138.17, 128.45,

128.42, 128.38, 128.31, 127.96, 127.86, 127.83, 127.79, 127.68, 127.65, 98.50, 81.25, 79.53, 79.48, 75.78, 75.00, 73.19, 70.46, 52.42, 31.94, 29.97, 29.71, 29.68, 29.67, 29.59, 29.37, 28.43, 25.91, 22.70, 18.10, 14.14, -4.30, -4.58. HRMS (ESI) calcd for $C_{57}H_{93}N_2O_{10}Si$ $[M+NH4]^+$: 993.6599, found: 993.6855. The resulting oil (70 mg, 0.072 mmol) was dissolved in THF (5 mL) and pyridine (5 mL), followed by addition of HF-pyridine complex (50% in pyridine, 2 mL) at 0 °C. The mixture was stirred overnight. After dilution with dichloromethane (30 mL), the reaction mixture was washed with 10% aqueous HCl (30 mL), and saturated aqueous $NaHCO_3$ (100 mL) sequentially. The organic phase was concentrated under vacuum, and the product was purified by silica gel column chromatography (EtOAc:hexane- 1:3), affording **10** as a clear oil (55 mg, 89% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.35-7.24 (m, 15 H), 5.43 (d, J = 8.0 Hz, 1 H), 4.92 (dd, J = 11.0, 1 H), 4.90 (d, J = 11.0 Hz, 1 H), 4.80 (d, J = 10.50 Hz, 1 H), 4.78 (d, J = 11.0 Hz, 1 H), 4.745 (d, J = 3.5 Hz, 1 H), 4.66 (d, J = 11.5 Hz, 1 H), 4.58 (d, J = 10.5 Hz, 1 H), 4.20 (d, J = 10.0 Hz, 1 H), 3.99 (d, J = 3.5, 1 H), 3.94 (t, J = 9.0 Hz, 1 H), 3.735 (dd, J = 9.0, 7.5 Hz, 1 H), 3.72 (s, 3H), 3.65 (d, J = 8.5 Hz, 2 H), 3.59 (dd, J = 9.5 Hz, 1 H), 2.94 (d, J = 9.5 Hz, 1 H), 1.48 (s, 9 H), 1.46 (m, 2 H), 1.26 (m, 24 H), 1.26 (m, 24 H), 0.88 (t, J = 7.0 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 169.83, 155.64, 138.25, 137.62, 137.39, 128.62, 128.57, 128.50, 128.47, 128.44, 128.18, 128.17, 128.13, 128.04, 128.02, 127.98, 127.94, 127.88, 127.84, 127.78, 98.65, 81.50, 79.62, 79.52, 78.59, 75.87, 75.38, 73.91, 70.47, 52.58, 52.53, 35.24, 31.93, 29.71, 29.67, 29.65, 29.63, 29.38, 28.42, 28.40, 28.38, 26.11, 26.03, 22.71, 14.14. HRMS (ESI) calcd for $C_{51}H_{79}N_2O_{10}$ $[M+NH4]^+$: 879.5735 found: 879.5658.

Preparation of alpha-GlcA-psychosine: To a solution of **10** (30 mg, 0.035 mmol) in a mixture of THF (4 mL) and methanol (4 mL) in hydrogenation chamber was added $Pd(OH)_2$ (10% on carbon, 50 mg). The reaction mixture was subject to hydrogenation at 200 psi at room temperature overnight. After removal of the catalyst by filtration through a celite pad, the filtrate was concentrated and dried under vacuum. The crude product was dissolved in dry dichloromethane (2 mL), and the solution was cooled down to 0 °C. TFA (4 mL) was added, and the mixture was stirred for 2 h. The solvent and TFA were then removed under vacuum. The residue was subsequently dissolved in MeOH (6 mL), followed by addition of NaOMe (1 *M* in methanol, 0.5 mL). The mixture was stirred for 3 h before water (0.1 mL) was introduced. After removal of solvent under vacuum, the residue was subject to silica gel column chromatography (DCM:MeOH:H_2O- 65:25:4) affording the desired product as a white solid (6 mg, 36% yield for three steps). ^{1}H NMR (CD_3CO_2D/DMSO-D6, 500 MHz): δ = 4.73 (d, J = 4.0 Hz, 1 H), 3.86 (dd, J = 10.5, 3.5 Hz, 1H), 3.81 (d, J = 10.0 Hz, 1 H), 3.66 (m, 1 H), 3.47-3.42 (m, 2 H), 3.32 (t, J = 9.0 Hz, 1 H), 1.83 (m, 2 H), 1.37 (m, 2 H), 1.18 (m 22 H), 0.80 (t, J = 7.0 Hz, 3 H). ^{13}C NMR (CD_3CO_2D/DMSO-D6, 125 MHz): δ = 172.75, 172.53, 172.30, 171.51, 100.03, 73.22, 72.07, 71.96, 71.93, 68.47, 64.62, 55.09, 39.69, 39.60, 39.52, 39.43, 39.35, 39.26, 39.18, 39.10, 39.01, 38.93, 38.76, 38.59, 32.79, 31.65, 29.44, 29.42, 29.38, 29.24, 29.08, 25.74, 22.44, 20.81, 20.74, 20.65, 20.58, 20.42, 20.34, 20.27, 20.18, 20.11. HRMS (ESI) calcd for $C_{24}H_{48}NO_8$ $[M+H]^+$: 478.3380, found: 478.3404

Scheme S6. Synthesis of psychosine.

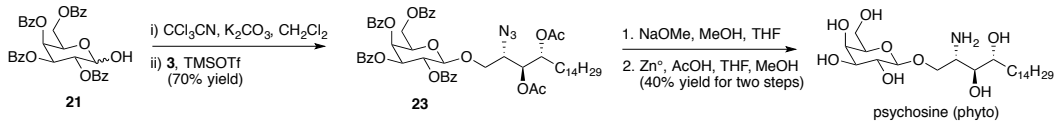


Preparation of 22: Compound **21** (174 mg, 0.291 mmol) was dissolved in dichloromethane (20 mL), and solid potassium carbonate (750 mg) was added followed by excess trichloroacetonitrile (291 µl, 2.91 mmol). The reaction was stirred for 16 h at room temperature. The solid was removed by

filtration, and the filtrate was concentrated under vacuum. The resulting trichloroacetimidate (75 mg, 0.1 mmol), acceptor **2** (56 mg, 0.152 mmol) and 4 Å MS (300 mg) were stirred together for 1 h in dichloromethane (5 mL). To this mixture was added TMSOTf (9 ul, 0.051 mmol). The reaction was stirred for another 10 h, then quenched with triethyl amine (0.1 mL). After removal of molecular sieves by filtration, the filtrate was concentrated and the crude subjected to silica gel column chromatography (EtOAc:hexane- 1:4), affording **22** as a clear oil (78.8 mg, 82% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.10 (dt, J = 7.2, 1.4 Hz, 2 H), 8.03 (dd, *J* = 8.1, 1.5 Hz, 2 H), 7.98-7.91 (m, 2 H), 7.78 (dd, *J* = 8.2, 1.4 Hz, 2 H), 7.66-7.61 (m, 2 H), 7.57 (td, *J* = 7.2, 1.4 Hz, 2 H), 7.53-7.34 (m, 6 H), 7.28-7.21 (m, 2 H), 5.97 (d, *J* = 3.4 Hz, 1 H), 5.80 (m, 1 H), 5.71 (dd, *J* = 15.5, 6.8 Hz, 1 H), 5.57 (dd, *J* = 10.4, 3.5 Hz, 1 H), 5.29-5.21 (m, 1 H), 4.87 (d, *J* = 8.0 Hz, 1 H), 4.65 (dd, *J* = 11.4, 6.9 Hz, 1H), 4.42 (dd, *J* = 11.4, 6.2 Hz, 1 H), 4.34 (dd, *J* = 8.7, 5.2 Hz, 1 H), 4.30-4.23 (m, 1 H), 4.19-4.03 (m, 2 H), 3.76 (m, 1 H), 3.70-3.64 (m, 1H), 2.05 (m, 5 H), 1.41-1.34 (m, 2 H), 1.26 (q, *J* = 7.3 Hz, 22 H), 0.87 (dt, *J* = 6.9, 2.2 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 171.11, 170.75, 170.4, 165.96, 165.57, 165.53, 165.01, 139.96, 136.39, 133.59, 133.35, 133.25, 133.15, 130.05, 129.77, 129.74, 129.71, 129.69, 129.67, 129.46, 129.38, 128.95, 128.73, 128.67, 128.64, 128.49, 128.47, 128.41, 128.33, 128.31, 128.26, 127.22, 123.55, 97.55, 78.36, 77.25, 77.20, 77.00, 76.74, 2.63, 71.74, 71.40, 69.59, 68.06, 64.53, 63.69, 63.28, 62.98, 62.08, 60.37, 32.32, 32.28, 31.91, 29.70, 29.67, 29.65, 29.64, 29.62, 29.57, 29.44, 29.41, 29.34, 29.25, 29.15, 28.86, 28.77, 22.67, 21.03, 20.73, 20.70, 14.18, 14.10. HRMS (ESI) calcd for $C_{54}H_{67}N_4O_{12}$ $[M+NH4]^+$: 963.4755, found: 963.4771.

Preparation of psychosine: Compound **22** (60 mg, 0.064 mmol) was dissolved in a mixture of THF (3 mL) and MeOH (3 mL), followed by addition of NaOMe (1 *M* in methanol, 0.2 mL). The mixture was stirred for 10 h, then zinc powder (200 mg) and acetic acid (1 mL) was added. The mixture was subject to sonication for 13 min. The excess zinc was removed by filtration, and the filtrate was concentrated and dried under vacuum. The crude product was then dissolved in methanol (5 mL), followed by addition of ammonium hydroxide (5 mL). The mixture was stirred for 2 h then the solvent was removed by evaporation under reduced pressure. The product was purified by silica gel column chromatography (MeOH:dichloromethane:H_2O- 65:25:4), affording psychosine as a white solid (14 mg, 48% yield for two steps). ^{1}H NMR (CD_3OD, 500 MHz): δ = 5.85 (dt, *J* = 15.5, 6.5 Hz, 1 H), 5.49 (dd, *J* = 15.5, 7.0 Hz, 1 H), 4.28 (t, *J* = 6.5 Hz, 1H), 4.27 (d, *J* = 7.5 Hz, 1 H), 3.93 (d, *J* = 6.0 Hz, 1 H), 3.825 (d, *J* = 3.0 Hz, 1 H), 3.78 (dd, *J* = 11.5, 7.5 Hz, 1 H), 3.72 (dd, *J* = 11.5, 4.5 Hz, 1 H), 3.57-3.52 (m, 2 H), 3.49 (dd, *J* = 10.0, 3.5 Hz, 1 H), 3.31 (m, 2 H), 2.10 (q, *J* = 7.0 Hz, 2 H), 1.42 (m, 2 H), 1.29 (m, 20 H), 0.90 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (CD3OD, 125 MHz): δ = 134.96, 127.37, 103.27, 75.54, 73.34, 71.02, 70.00, 68.88, 66.47, 61.20, 55.46, 31.98, 31.67, 29.40, 229.34, 29.24, 29.07, 28.99, 28.81, 22.33, 13.04. HRMS (ESI) calcd for $C_{24}H_{47}NO_7$ $[M+H]^+$: 462.3353, found: 462.3387.

Scheme S7. Synthesis of psychosine (phyto).

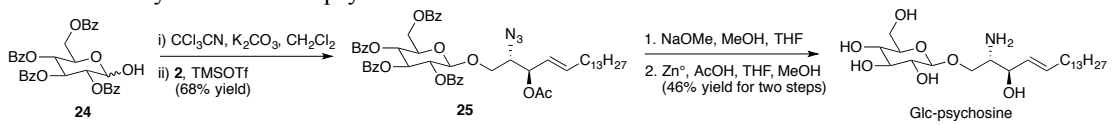


Preparation of 23: Compound **21** (348 mg, 0.582 mmol) was dissolved in dichloromethane (30 mL), and solid potassium carbonate (1,200 mg) was added followed by addition of excess trichloroacetonitrile (592 µl, 5.82 mmol). The mixture was stirred for 28 h at room temperature. The solid was removed by filtration, and the filtrate was concentrated on under vacuum. A portion of the crude donor (125 mg, 0.169 mmol), acceptor **3** (108 mg, 0.254 mmol) and 4 Å molecular sieves (600

mg) was stirred together for 1 h in dichloromethane (6 mL). To this mixture was added TMSOTf (16 µl, 0.0845 mmol). The mixture was stirred for 12 h then quenched with triethyl amine (0.5 mL). After removal of molecular sieves by filtration, the filtrate was concentrated, and the crude mixture was subjected to silica gel column chromatography (EtOAc:hexane- 1:4), affording **23** as a clear oil (114 mg, 70% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.10-8.06 (m, 2 H), 8.03-7.98 (m, 2 H), 7.98-7.93 (m, 1 H), 7.81-7.74 (m, 2 H), 7.66-7.59 (m, 1 H), 7.57 (td, J = 7.2, 1.4 Hz, 2 H), 7.53-7.34 (m, 6 H), 7.2-7.20 (m, 2 H), 5.99 (d, J = 1.2 Hz, 1 H), 5.81 (dd, J = 10.3, 7.9 Hz, 1 H), 5.61 (dd, J = 10.4, 3.4 Hz, 1 H), 5.11-5.02 (dd, 2 H), 4.91 (d, J = 8.0 Hz, 1 H), 4.69 (dd, J = 11.5, 6.5 Hz, 1H), 4.47-4.31 (m, 2 H), 4.15-4.04 (m, 1 H), 3.93 (dd, J = 10.0, 3.0 Hz, 1 H), 3.70 (m, 1 H), 2.03 (m, 6 H), 1.98 (s, 3 H), 1.55 (d, J = 6.5 Hz, 2 H), 1.26 (m, 24 H), 0.87 (t, J = 6.5 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 171.14, 170.23, 169.45, 166.02, 165.56, 165.49, 165.01, 133.61, 133.32, 133.29, 133.20, 130.05, 129.79, 129.76, 129.34, 128.93, 128.70, 128.67, 128.65, 128.52, 128.49, 128.48, 128.32, 128.30, 128.27, 100.77, 77.25, 77.00, 76.80, 76.74, 72.34, 71.93, 71.67, 71.41, 69.58, 68.48, 67.93, 61.90, 60.39, 60.23, 31.91, 29.68, 29.66, 29.64, 29.62, 29.55, 29.51, 29.46, 29.35, 29.32, 25.35, 22.68, 1.04, 20.85, 20.72, 14.18, 14.11. HRMS (ESI) calcd for $C_{56}H_{71}N_4O_{14}$ $[M+NH4]^+$: 1023.4967, found: 1023.4751.

Preparation of psychosine (phyto): Compound **23** (60 mg, 0.06 mmol) was dissolved in THF (6 mL) and methanol (4 mL), followed by addition of NaOMe (1 *M* in methanol, 0.2 mL). The mixture was stirred for 6 h, then zinc (200 mg) and acetic acid (1 mL) were added. The mixture was subjected to sonication for 12 min. The excess zinc was removed by filtration, and the filtrate was concentrated under vacuum. The crude product was then dissolved in methanol (5 mL) followed by addition of ammonium hydroxide (5 mL). The mixture was stirred for 2 h then the solvent was removed under reduced pressure. The product was purified by silica gel column chromatography (MeOH:dichloromethane:H_2O- 65:25:4) giving the desired product as a white solid (12 mg, 40% yield for two steps). ^{1}H NMR (CD_3OD, 500 MHz): δ = 4.28 (d, J = 7.5 Hz, 1 H), 4.02-3.97 (m, 2 H), 3.832 (d, J = 3.0 Hz, 1 H), 3.78 (dd, J = 11.5, 7.5 Hz, 1 H), 3.73 (dd, J = 11.5, 5.0 Hz, 1 H), 3.554 (dd, J = 14.5, 7.5 Hz, 2 H), 3.52-3.47 (m, 3 H), 3.32 (m, 1 H), 1.79 (m, 2 H), 1.57 (m, 2 H), 1.29 (m, 20 H), 0.90 (t, J = 7.0 Hz, 3 H). ^{13}C NMR (CD3OD, 125 MHz): δ = 103.26, 75.53, 73.36, 72.60, 72.18, 71.01, 68.91, 61.23, 53.43, 33.86, 31.66, 29.46, 29.39, 29.35, 29.07 24.93, 22.69, 22.32, 13.03. HRMS (ESI) calcd for $C_{24}H_{49}NO_8$ $[M+H]^+$: 480.3458, found: 480.3529.

Scheme S8. Synthesis of Glc-psychosine.

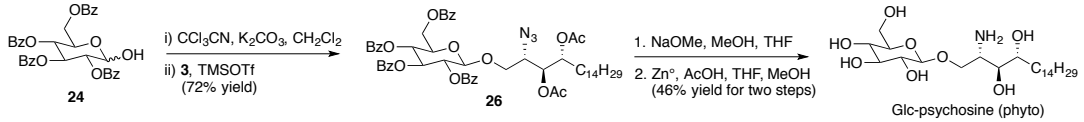


Preparation of 25: Compound **24** (298 mg, 0.5 mmol) was dissolved in dichloromethane (18 mL), and solid potassium carbonate (600 mg) was added, followed by addition of trichloroacetonitrile (3 mL). The reaction was stirred for 18 h at room temperature. The solid was removed by filtration, and the filtrate was concentrated under vacuum. A portion of the resulting trichloroacetimidate (159 mg, 0.169 mmol), **2** (93 mg, 0.254 mmol) and 4 Å molecular sieves (600 mg) were stirred together for 1 h in dichloromethane (6 mL). To this mixture was added TMSOTf (16 µl, 0.0845 mmol). The mixture was stirred 12 h then quenched with triethyl amine (0.5 mL). After removal of molecular sieves by filtration, the filtrate was concentrated and the crude mixture was subjected to silica gel column chromatography (EtOAc:hexane- 1:4), affording **25** as a clear oil (108.6 mg, 68% yield). ^{1}H NMR (CDCl3, 500 MHz): δ = 8.08-7.26 (m, 20 H), 5.92 (t, J = 7.0 Hz, 1 H), 5.70 (t, J = 10.5 Hz, 1 H), 5.62

(dt, J = 14.0, 6.5 Hz, 1 H), 5.58 (t, J = 9.5 H, 1 H), 5.35 (dd, J = 15.0, 8.25 Hz, 1H), 4.88 (d, J = 8.0 Hz, 1 H), 4.66 (dd, J = 12.5, 3.0 Hz, 1 H), 4.52 (dd, J = 12.0, 5.0 Hz, 1 H), 4.18 (m, 1H), 3.90 (dd, J = 10.5, 7.0 Hz, 1 H), 3.80 (m, 1 H), 3.60 (dd, J = 10.0, 5.5 Hz, 1 H), 2.01 (s, 3 H), 1.92 (m, 2 H), 1.26 (m, 22 H), 0.89 (t, J = 7.0 Hz, 3 H). HRMS (ESI) calcd for $C_{54}H_{63}N_3O_{12}$ $[M]^+$: 945.4412, found $[M+NH4]^+$: 963.4771.

Preparation of Glc-psychosine: Compound **25** (70 mg, 0.075 mmol) was dissolved in THF (4 mL) and methanol (6 mL), followed by addition of NaOMe (1 *M* in methanol, 0.3 mL). The mixture was stirred for 5 h then zinc (200 mg) and acetic acid (1 mL) were added. The mixture was subjected to sonication for 12 min. The excess zinc was removed by filtration, and the filtrate was concentrated under vacuum. The crude product was then dissolved in methanol (5 mL), followed by addition of ammonium hydroxide (5 mL). The mixture was stirred for 2 h then the solvent was removed under reduced pressure. The residue was subjected to silica gel column chromatography (MeOH:dichloromethane:H_2O- 65:25:4), affording Glc-psychosine as a white solid (16 mg, 46% for two steps). ^{1}H NMR (CD_3OD, 500 MHz): δ = 5.77 (dt, J = 15.0, 7.0 Hz, 1 H), 5.49 (dd, J = 15.5, 7.5 Hz, 1 H), 4.26 (d, J = 7.5 Hz, 1 H), 3.99 (t, J = 7.0 Hz, 1 H), 3.86 (dd, J = 12.0, 1.5 Hz,1 H), 3.845 (d, J = 10.5, 7.0 Hz, 1 H), 3.77 (dd, J = 10.5, 3.5 Hz, 1 H), 3.67-3.64 (m, 1 H), 3.37-3.34 (m, 1H), 3.28-3.26 (m, 2 H), 3.20 (dd, J = 9.0, 8.0 Hz,1 H), 2.93 (m, 1 H), 2.09 (q, J = 7.0 Hz, 2 H), 1.42 (m, 2 H), 1.29 (m, 20 H), 0.90 (t, J = 7.0 Hz, 3 H). ^{13}C NMR (CD_3OD, 125 MHz): δ = 134.35, 129.20, 102.97, 76.58, 76.50, 73.62, 72.96, 70.19, 69.89, 61.28, 54.87, 32.02, 31.66, 29.38, 29.35, 29.23, 29.07, 28.96, 28.94, 22.32, 13.02. HRMS (ESI) calcd for $C_{24}H_{47}NO_7$ $[M+H]^+$: 462.3353, found $[M+H]^+$: 462.3349.

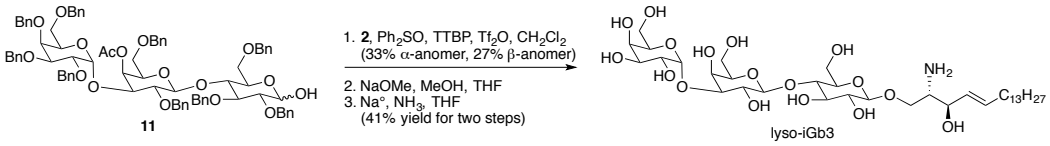
Scheme S9. Synthesis of Glc-psychosine (phyto).



Preparation of 26: Compound **24** (298 mg, 0.5 mmol) was dissolved in dichloromethane (18 mL), and solid potassium carbonate (600 mg) was added, followed by addition of trichloroacetonitrile (3 mL). The mixture was stirred for 18 h at room temperature. The solid was removed by filtration, and the filtrate was concentrated under vacuum. A portion of the trichloroacetimidate donor (159 mg, 0.169 mmol), acceptor **3** (110 mg, 0.254 mmol) and 4 Å molecular sieves (600 mg) were stirred together for 1 h in dichloromethane (6 mL). To this mixture was added TMSOTf (16 µl, 0.0845 mmol). The mixture was stirred for 12 h then quenched with triethyl amine (0.5 mL). After removal of the molecular sieve by filtration, the filtrate was concentrated, and the crude mixture was subjected to silica gel column chromatography (EtOAc:hexane- 1:4) affording **26** as a clear oil (115 mg, 72% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.06-8.00 (m, 2 H), 7.93 (m, 4 H), 7.85-7.79 (m, 2 H), 7.59-7.46 (m, 3 H), 7.46-7.24 (m, 7 H), 5.91 (t, J = 9.6 Hz, 1 H), 5.70 (t, J = 9.7 Hz, 1 H), 5.54 (dd, J = 9.7, 7.8 Hz, 1H), 5.08-4.98 (m, 2 H), 4.93 (d, J = 7.8 Hz, 1 H), 4.65 (dd, J = 12.2, 3.2 Hz, 1 H), 4.51 (dd, J = 12.2, 5.1 Hz, 1 H), 4.18 (m, 1H), 4.03 (dd, J = 10.5, 7.7 Hz, 1H), 3.88 (dd, J = 10.5, 3.1 Hz, 1 H), 3.66 (m, 1 H), 1.98 (m, J = 14.2 Hz, 6 H), 1.52 (q, J = 6.6, 6.0 Hz, 2 H), 1.24 (d, J = 8.9 Hz, 24 H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 170.21, 169.45, 166.10, 165.78, 165.11, 164.87, 133.44, 133.24, 133.19, 133.15, 129.82, 129.75, 129.73, 129.51, 129.27, 128.72, 128.39, 128.30, 128.27, 100.59, 77.25, 77.20, 76.99, 76.74, 72.82, 72.40, 72.29, 71.96, 71.67, 69.52, 68.61, 62.99, 60.22, 31.92, 29.69, 29.66, 29.65, 29.62, 29.55, 29.46, 29.35, 29.31, 25.33, 22.69, 20.84, 20.66, 14.12. HRMS (ESI) calcd for $C_{56}H_{67}N_3O_{14}$ $[M]^+$: 1005.4623, found $[M+NH4]^+$: 1023.4756.

Preparation of Glc-psychosine (phyto): Compound **26** (75 mg, 0.075 mmol) was dissolved in THF (4 mL) and methanol (6 mL), followed by addition of NaOMe (1 *M* in methanol, 0.3 mL). The mixture was stirred for 5 h, then zinc (200 mg) and acetic acid (1 mL) were added. The mixture was subjected to sonication for 12 min. The excess zinc removed by filtration, and the filtrate was concentrated under vacuum. The resulting crude product was dissolved in methanol (5 mL), followed by addition of ammonium hydroxide (5 mL). The mixture was stirred for 2 h then the solvent was removed under reduced pressure. The residue was subjected to silica gel column chromatography (MeOH:dichloromethane:H_2O- 65:25:4), affording desired compound as a white solid (16.5 mg, 46% for two steps). ^{1}H NMR (CD_3OD, 500 MHz): δ = 4.33 (d, *J* = 8.0 Hz, 1 H), 4.04-3.98 (m, 2 H), 3.90 (dd, *J* = 12.0 Hz, 1 H), 3.66 (dt, *J* = 11.5, 6.0 Hz, 1 H), 3.54 (m, 2 H), 3.46 (m, 1 H), 3.39-3.22 (m, 4 H), 1.78 (m, 2 H), 1.57 (m, 2 H), 1.29 (m, 22 H), 0.90 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (CD_3OD, 125 MHz): δ = 102.76, 76.67, 76.46, 73.49, 72.22, 70.11, 61.13, 53.29, 48.20, 33.85, 31.66, 29.45, 29.39, 29.35, 29.06, 24.96, 22.32, 13.02. HRMS (ESI) calcd for $C_{24}H_{50}NO_8$ $[M+H]^+$: 480.3536, found: 480.3591.

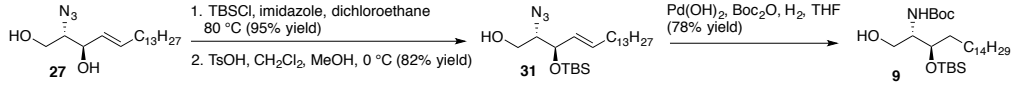
Scheme 4. Synthesis of lyso-iGb3.



Preparation of lyso-iGb3: To a solution of **11** (190 mg, 0.14 mmol) in dry dichloromethane (6 mL) was added diphenylsulfoxide (70.8 mg, 0.35 mmol), TTBP (121.7 mg, 0.49 mmol), and 4 Å molecular sieves (500 mg). The mixture was stirred at room temperature for 1 h, and then cooled to -60 °C. Triflic anhydride (33 µl, 55.4 mg, 0.196 mmol) was added. The mixture was warmed to -40 °C, and a solution of **2** (61.66 mg, 0.168 mmol) in dichloromethane (1 mL) was added drop wise. The reaction was allowed to warm to room temperature with stirring over 45 min. After removal of molecular sieves by filtration, the filtrate was concentrated and subjected to silica gel column chromatography (EtOAc:Hexane- 1:3 to 1:1) to give the alpha anomer as a clear oil (78 mg, 33% yield) and the beta anomer as a clear oil (65 mg, 27% yield). ^{1}H NMR (500 MHz, $CDCl_3$, beta-anomer): δ = 7.44-7.15 (m, 45 H), 5.77 (dt, *J* = 15.0, 8.0 Hz, 1 H), 5.73 (m, 1 H), 5.71 (dd, *J* = 12.0, 4.0 Hz, 1 H), 5.66 (m, 2 H), 5.57-5.55 (m, 3 H), 5.44 (t, *J* = 7.5 H, 1 H), 5.40 (t, *J* = 3.5 Hz, 1H), 5.38 (m, 1 H), 5.35-5.28 (m, 3 H), 5.03 (d, *J* = 10.5, 1 H), 4.84 (t, *J* = 11.0 Hz, 2H), 4.74 (t, *J* = 11.0 Hz, 2 H), 4.70 (dd, *J* = 11.0, 4.5 Hz, 2 H), 4.58 (d, *J* = 12.0 Hz, 1 H), 4.53 (d, *J* = 8.0 Hz, 1 H), 4.42 (q, *J* = 12.5 Hz, 2H), 4.34-4.24 (m, 4 H), 4.15 (t, *J* = 6.5 Hz, 1 H), 4.05 (t, *J* = 6.0 Hz, 1 H), 4.03-3.83 (m, 7 H), 3.73 (m, 1 H), 3.63 (m, 2 H), 3.56-3.46 (m, 2 H), 3.29 (m, 2 H), 2.04 (s, 3 H), 2.01 (m, 2H), 1.78 (s, 3 H), 1.89-1.70 (m, 2 H), 1.25 (m, 20 H), 0.87 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 170.19, 169.63, 145.55, 139.11, 138.64, 138.51, 138.26, 138.04, 137.75, 134.73, 128.67, 128.52, 128.39, 128.20, 128.00, 127.78, 127.63, 127.39, 127.27, 103.45, 102.72, 95.24, 80.12, 79.36, 78.68, 78.45, 78.01, 76.23, 75.73, 75.37, 75.01, 74.86, 74.65, 74.45, 73.81, 73.57, 73.27, 73.01, 72.65, 70.79, 69.61, 68.77, 68.62, 67.72, 64.64, 63.96, 32.38, 31.93, 29.71, 29.51, 29.37, 29.04, 22.70, 21.10, 20.61, 14.14. HRMS (ESI) calcd for $C_{103}H_{127}N_4O_{19}$ $[M+NH4]^+$: 1723.9095, found: 1723.9013. The beta anomer (65 mg, 0.038 mmol) was dissolved in a mixture of THF (3 mL) and MeOH (3 mL), and NaOMe (1 *M* in methanol, 0.1 mL) was added. The reaction mixture was stirred for 1 h, and the solvent was removed under vacuum. The product was purified by silica gel column chromatography (EtOAc:hexane- 1:2) affording desired diol (61.6 mg, 98%). ^{1}H NMR (500 MHz, $CDCl_3$): 7.51-7.21 (m, 45 H), 5.02 (d, *J* = 10.0 Hz, 1 H), 4.90 (d,

J = 11.0 Hz, 1 H) 4.85 (d, *J* = 12.0 Hz, 1 H), 4.82 (d, *J* = 3.5 Hz, 1 H), 4.75 (t, *J* = 8.5 Hz, 1 H), 4.74 (s, 2 H), 4.71 (q, *J* = 11.5 Hz, 2 H), 4.53 (d, *J* = 11.0 HZ, 1 H), 4.48 (t, *J* = 12.0 H,z 1H), 4.41 (t, *J* = 12.0 Hz, 1 H), 4.37 (d, *J* = 7.5 Hz, 4.33-4.24 (m, 3 H), 4.07 (t, *J* = 7.0 Hz, 1 H), 4.04 (dd, *J* = 9.5, 3.5 Hz, 1 H), 3.90 (s, 5 H), 3.886 (d, *J* = 1.5 Hz,1 H), 3.83 (dd, *J* = 11.0, 3.5 Hz, 1 H) 3.74 (dd, *J* = 9.5, 7.0 Hz, 1 H), 3.70 (dd, *J* = 10.5, 4.5 Hz,1 H), 3.64 (s, 1 H), 3.62 (s, 1 H), 3.59 (d, *J* = 7.5 Hz, 1 H), 3.56-3.50 (m, 2 H), 3.48 (t, *J* = 8.0 Hz, 1 H), 3.44-3.39 (m, 2 H), 3.35 (m, 1 H), 2.87 (s, 1 H), 2.37 (m, 1 H), 2.06 (m, 2 H), 1.60 (m, 2 H), 1.38 (m, 2 H), 1.26 (m, 20 H), 0.89 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 138.95, 138.55, 138.01, 137.86, 137.69, 135.22, 128.53, 128.36, 128.21, 128.07, 127.89, 127.77, 127.63, 127.54, 127.38, 127.29, 103.45, 102.64, 95.31, 82.69, 81.68, 79.36, 78.90, 78.19, 76.62, 75.52, 75.35, 75.09, 74.86, 74.58, 74.48, 73.54, 73.25, 72.90, 72.61, 71.18, 69.66, 68.80, 68.54, 68.41, 65.13, 64.62, 32.41, 31.93, 29.69, 29.51, 29.37, 29.23, 29.01, 22.70, 14.14. HRMS (ESI) calcd for $C_{99}H_{123}N_4O_{17}$ $[M+NH4]^+$: 1639.8883, found: 1639.8959. The diol (61.6 mg) was dissolved in THF (1 mL) and added a solution of sodium (1 g) and ammonia (50 mL) at -78 °C. The mixture was stirred for 8 h at -78 °C, then methanol (10 mL) was added, and the mixture was allowed to warm to room temperature. After removal of solvent under vacuum, the crude mixture was subjected to silica gel column chromatography (MeOH:EtOAc:H_2O- 25:60:20) giving the desired compound as a white solid (12.3 mg, 41% yield). ^{1}H NMR (500 MHz, D_2O): 5.71 (m, 1 H), 5.33 (m, 1 H), 4.97 (m, 1 H), 4.78 (d, *J* = 3.5 Hz,1 H), 4.35 (m, 1 H), 4.25 (m, 1 H), 4.03 (m, 2 H), 3.80-3.30 (m, 32 H), 2.20 (m, 2 H), 1.23 (m, 22 H), 0.67 (t, *J* = 6.5 Hz, 3 H). ^{13}C NMR (125 MHz, D_2O): 131.57, 128.95, 125.27, 102.79, 102.31, 95.38, 88.21, 81.67, 78.49, 77.12, 75.00, 74.66, 74.23, 72.68, 72.28, 71.99, 71.66, 70.76, 69.51, 69.21, 69.08, 68.42, 68.12, 66.12, 64.76, 62.42, 61.12, 60.94, 60.86, 59.98, 59.43, 55.30, 48.83, 46.08, 39.37, 28.03, 23.33, 23.12, 21.83, 21.24, 20.01, 19.30, 19.23, 13.16. HRMS (ESI) calcd for $C_{36}H_{67}NNaO_{17}$ $[M+Na]^+$: 808.4307, found: 808.4296.

Scheme S10. Synthesis of **9**.



Preparation of 9: A mixture of **27** (1.479 g, 0.0046 mol), TBSCl (2.74 g, 0.0182 mol), imidazole (1.877 g, 0.0276 mol) in dichloroethane (50 mL) was warmed to 80 °C and stirred for 7 h. To this reaction mixture was added MeOH (10 mL), and the mixture was stirred for 20 min then washed with water (40 mL). The organic phase was concentrated, and the crude mixture was purified by silica gel column chromatography (EtOAc:hexane- 1:1) affording bis-TBS ether (2.43 g, 95%) as a clear oil. This material (2.4 g, 0.004 mol) was dissolved in a mixture of methanol (5 mL) and dichloromethane (5 mL), followed by addition of TsOH (0.1 g) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min before Et_3N (3 mL) was added. The mixture was further concentrated under vacuum, and the primary alcohol was purified by silica gel column chromatography (EtOAc:hexane- 1:9) giving **31** as a clear oil (1.45 g 82 % yield). This alcohol (1.0 g, 0.0023 mmol) was dissolved in THF (25 mL) in a hydrogenation chamber, followed by addition of di-*tert*-butyl bicarbonate (0.596 g, 0.00273 mol, 1.2 eq) and Pd/C (10%, 0.5 g). Hydrogen was introduced and the pressure was kept at 500 psi overnight. The mixture was filtered through celite pad to remove the catalyst, and the solvent was removed under vacuum. The crude product was purified by silica gel column chromatography (EtOAc:hexane- 1:4) resulting in isolation of **9** as a clear oil (0.925 g, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$): 5.31(d, *J* = 7.5 Hz, 1 H), 4.02 (d, *J* = 11.5 Hz, 1 H), 3.95 (m, 1 H), 3.57 (t, *J* = 10.0 Hz, 1 H), 3.52 (d, *J* = 4.0 Hz, 1 H), 3.13 (d, *J* = 9.5 Hz, 1 H), 1.52 (m, 2 H), 1.42 (s, 9 H), 1.35 (m, 1 H), 1.23 (m, 24 H), 0.87 (s, 9 H), 0.85 (t, *J* = 7.0 Hz, 1 H), 0.079 (s, 3 H), 0.055 (s, 3 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 155.70,

79.26, 75.78, 62.10, 53.18, 34.72, 31.90, 29.75, 29.67, 29.66, 29.65, 29.63, 29.59, 29.54, 29.42, 29.34, 28.37, 25.78, 25.50, 22.66, 17.89, 14.08, -4.65, -4.84. HRMS (ESI) calcd for $C_{29}H_{62}NO_4Si$ $[M+H]^+$: 516.4448, found: 516.4422.

Measurement of stimulation of murine NKT cells.
For observation of NKT cell stimulation with cell lines, 50,000 cells of the NKT cell hybridoma DN32.D3 were incubated with the indicated glycolipid (dissolved in DMSO, final concentration less than 0.01 vol%) in the presence of 100,000 RBL cells. Cell culture supernatants were assayed after 24 h for IL-2 release with an IL-2-dependent NK cell line reporter system.[4]

Measurement of stimulation of human NKT cells
CD1d-transfeted C1R cells (initially provided by De Libero and Mori, Basel University, Switzerland) were cultured for 4 h with several concentrations of alpha-psychosine and alpha-Glc-psychosine, followed by addition of human NKT cell lines.[21] After 40 h, supernatant from the cultures was collected and GM-CSF concentration determined by ELISA.

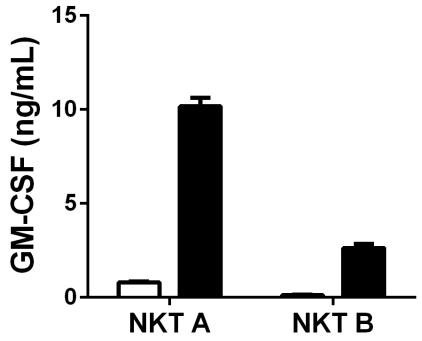


Figure S1. Response of two human NKT cell lines (A and B) to alpha-galactosylceramide (50 ng/mL) (filled bars). Empty bars represent cytokine production in the absence of antigen. CD1d-transfected C1R cells were used for antigen presentation.

Measurement of NKT cell expansion
Experiments were performed in compliance with relevant laws and institutional guidelines and approved by the Institutional Animal Care and Use Committee at Scripps Research Institute. Mice (C57BL/6J) were injected (IV) with glycolipids (seven mice per glycolipid). After three days, the mice were sacrificed, and NKT cell percentages in the spleen were quantified by flow cytometry using CD1d tetramers empty or loaded with PBS-57. Samples were acquired on a MACSQuant analyzer with MACSQuantify software (both Miltenyi Biotec) and analyzed with FlowJo software (Tree Star).

Cytokines were measured in blood plasma as described previously,[6] and results are shown in Figure S2.

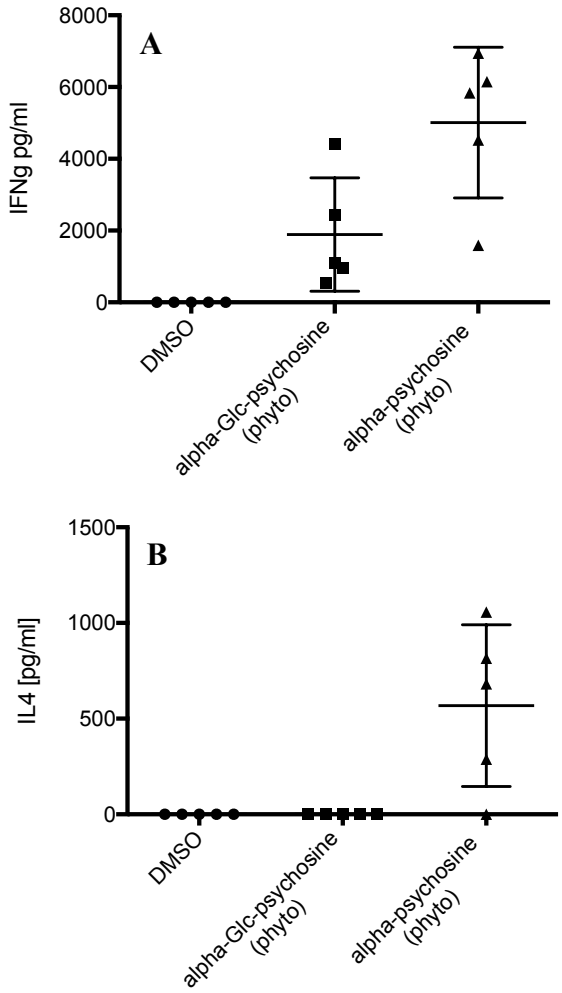
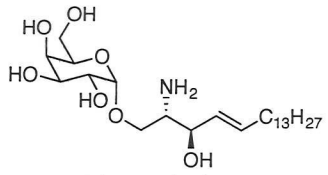


Figure S2. Cytokine release from wild-type C57BL/6J mice after injection (IV) with the indicated glycolipid (2.5 μg/mouse). **A:** IFN-γ measured 16 h after injection. **B:** IL-4 measured 24 h after injection.

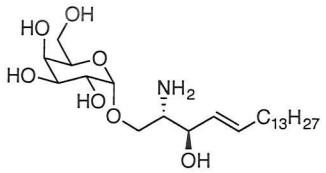
^{1}H and ^{13}C NMR Spectra

Alpha-psychosine
Alpha-psychosine (phyto)
Alpha-Glc-psychosine
Alpha-Glc-psychosine (phyto)
6'-NAc-alpha-psychosine
Alpha-Glc-palmitoylglycerol
Alpha-GalA-psychosine
Alpha-GlcA-psychosine
Psychosine
Psychosine (phyto)
Glc-psychosine
Glc-psychosine (phyto)
Lyso-iGb3
Compound **9**



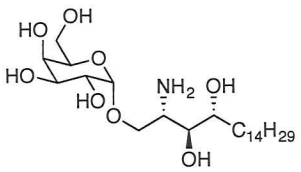
alpha-psychosine

^{1}H NMR, CD_3OD, 500 MHz



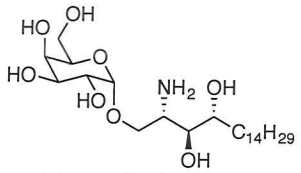
alpha-psychosine

^{13}C NMR, CD_3OD, 125 MHz



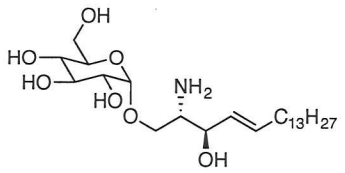
alpha-psychosine (phyto)

^{1}H NMR, CD_3OD, 500 MHz

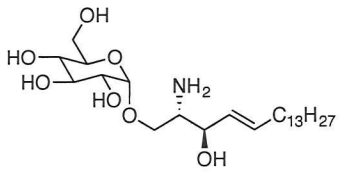


alpha-psychosine (phyto)

^{13}C NMR, CD_3OD, 125 MHz

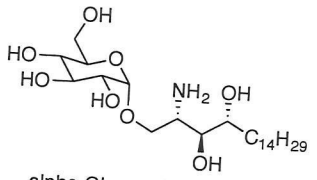


alpha-Glc-psychosine
^{1}H NMR, CD_3OD, 500 MHz



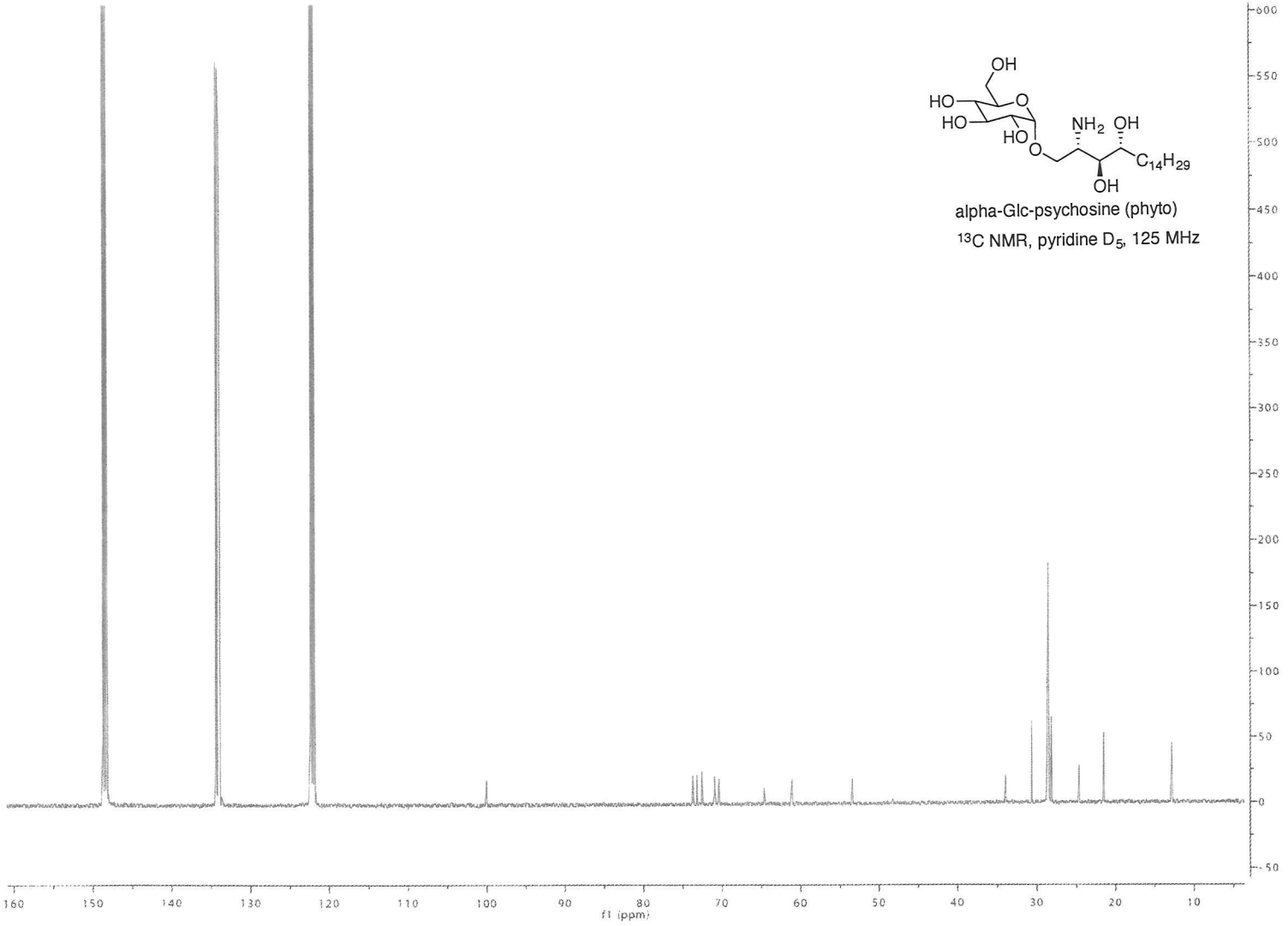
alpha-Glc-psychosine

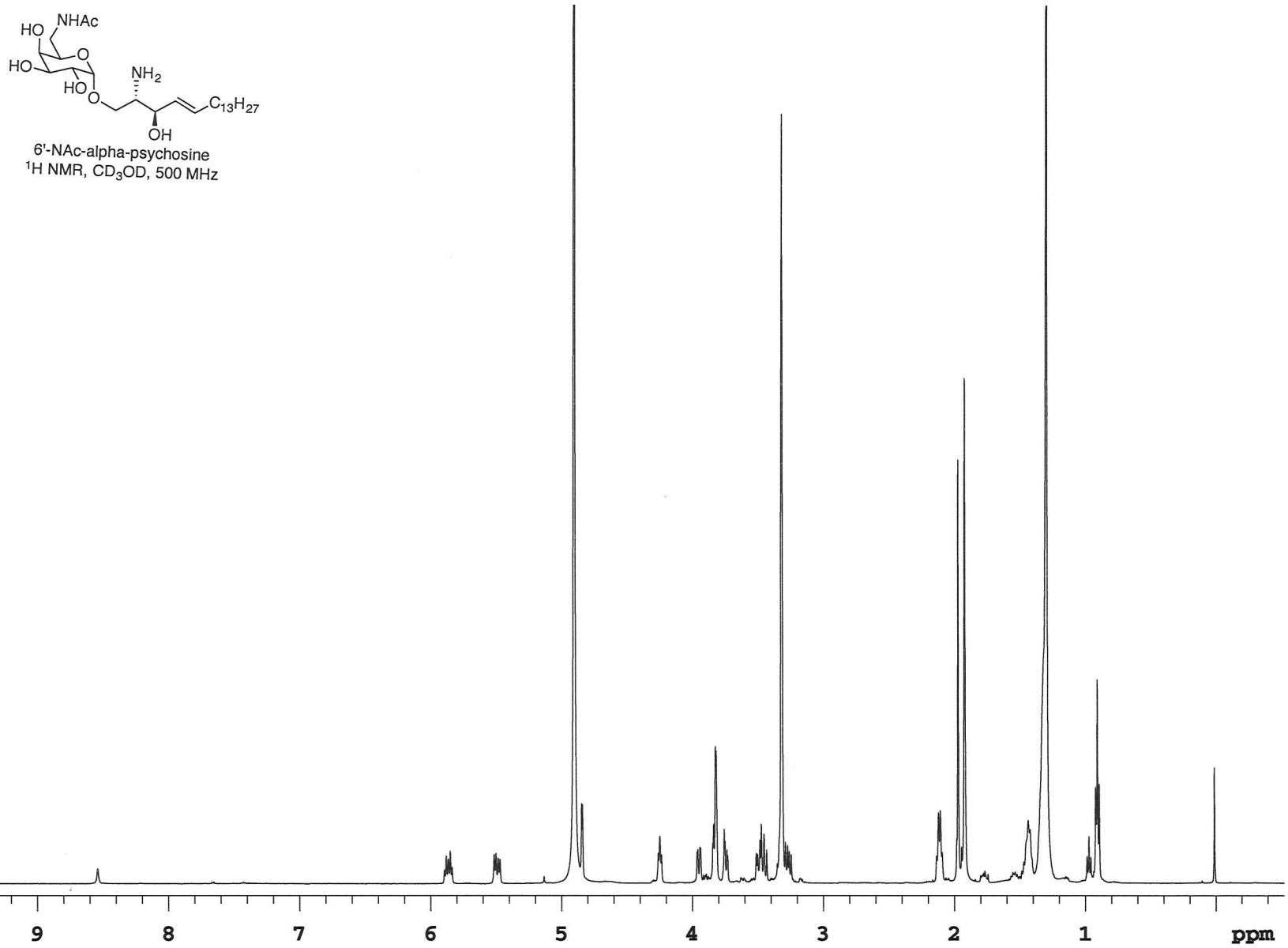
^{13}C NMR, CD_3OD, 125 MHz



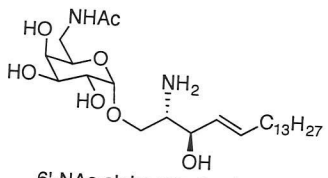
alpha-Glc-psychosine (phyto)

^{1}H NMR, pyridine D_5, 500 MHz


OH
HO
HO
HO
O
O
NH2 OH
C14H29
OH
alpha-Glc-psychosine (phyto)
13C NMR, pyridine D5, 125 MHz
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

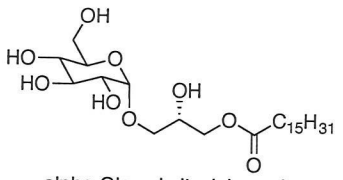


6'-NAc-alpha-psychosine
^{1}H NMR, CD_3OD, 500 MHz



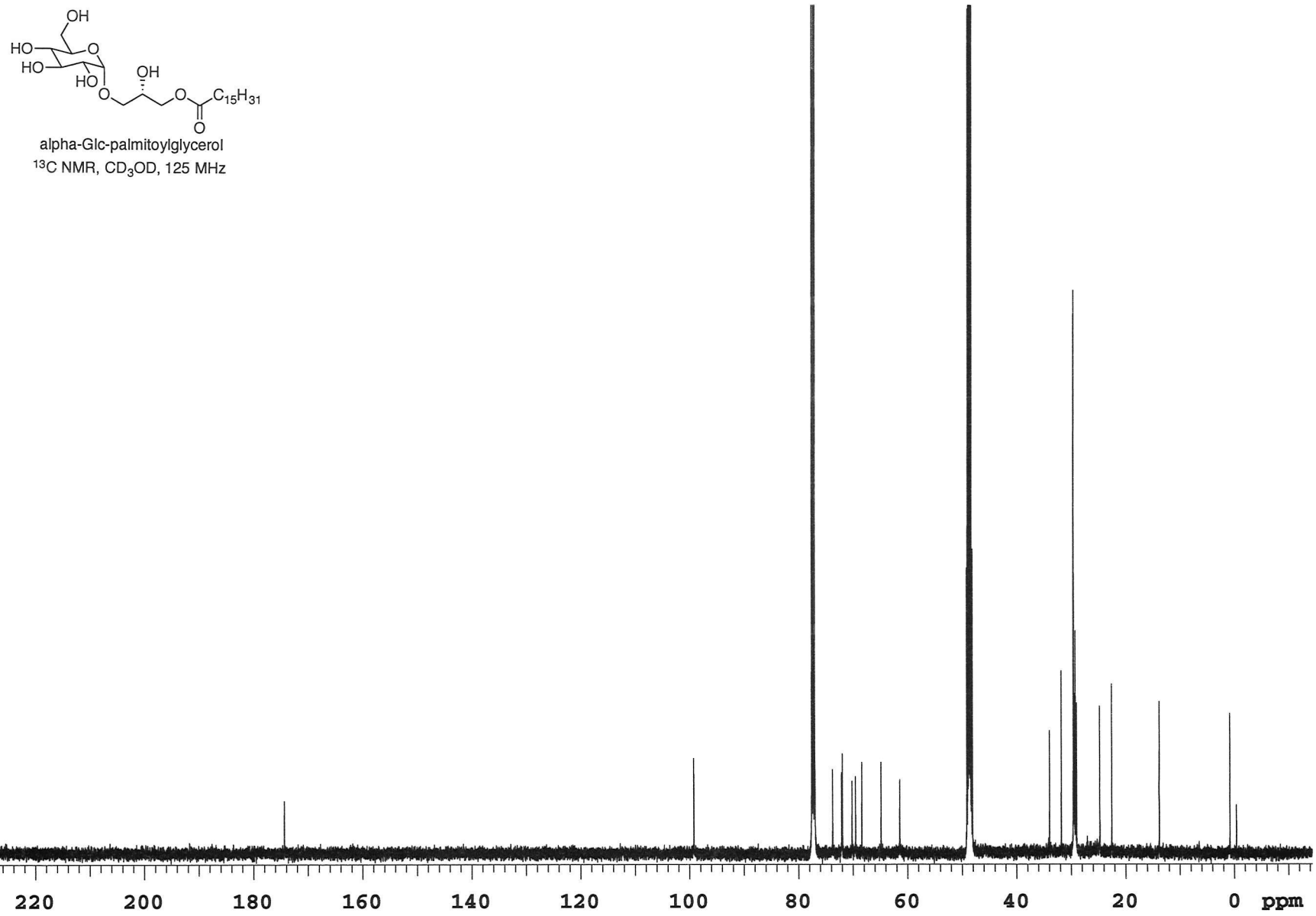
6'-NAc-alpha-psychosine

^{13}C NMR, CD_3OD, 125 MHz



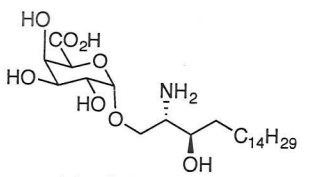
alpha-Glc-palmitoylglycerol

^{1}H NMR, CD_3OD, 500 MHz



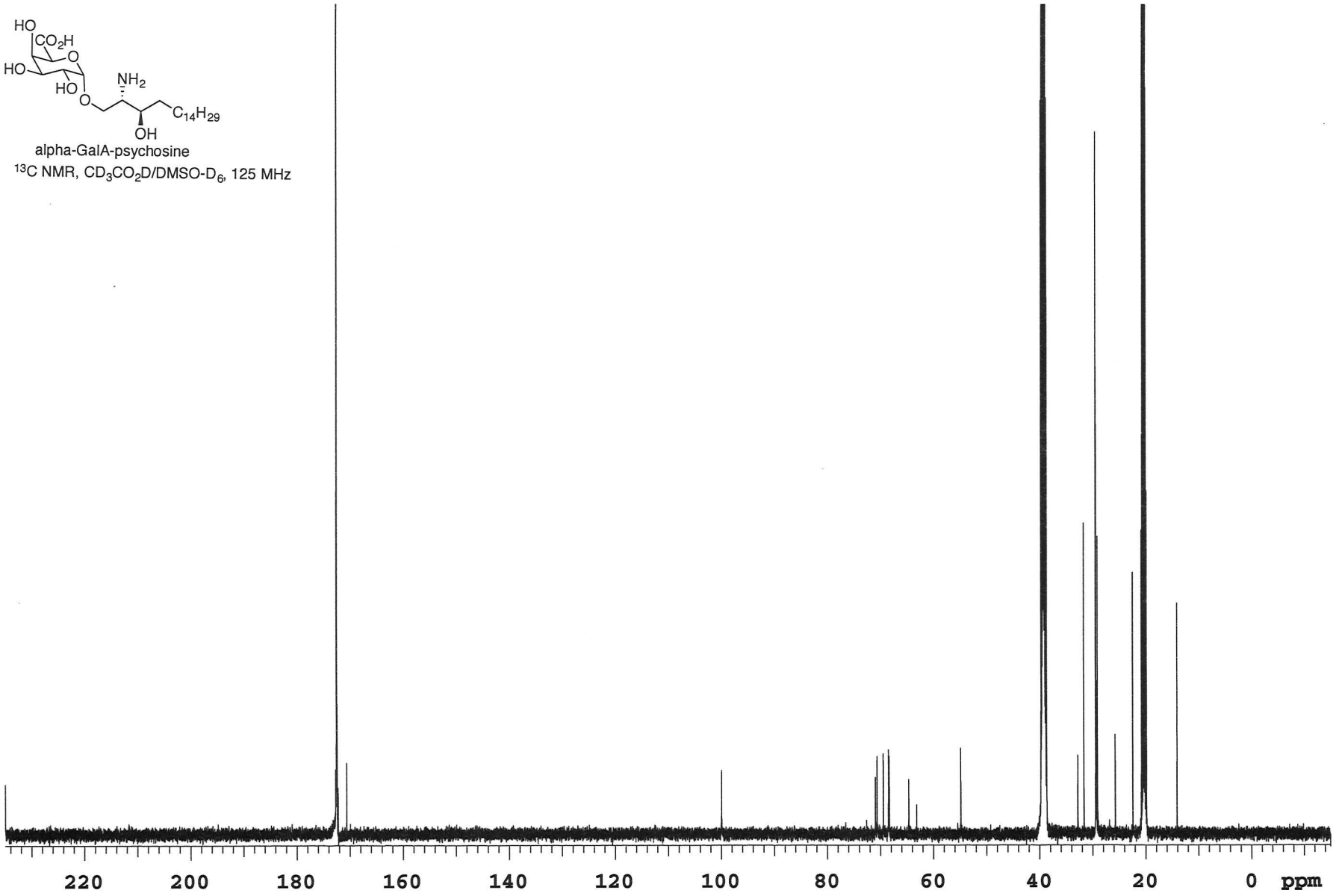
alpha-Glc-palmitoylglycerol

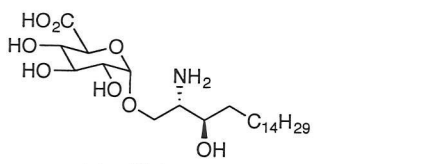
^{13}C NMR, CD_3OD, 125 MHz



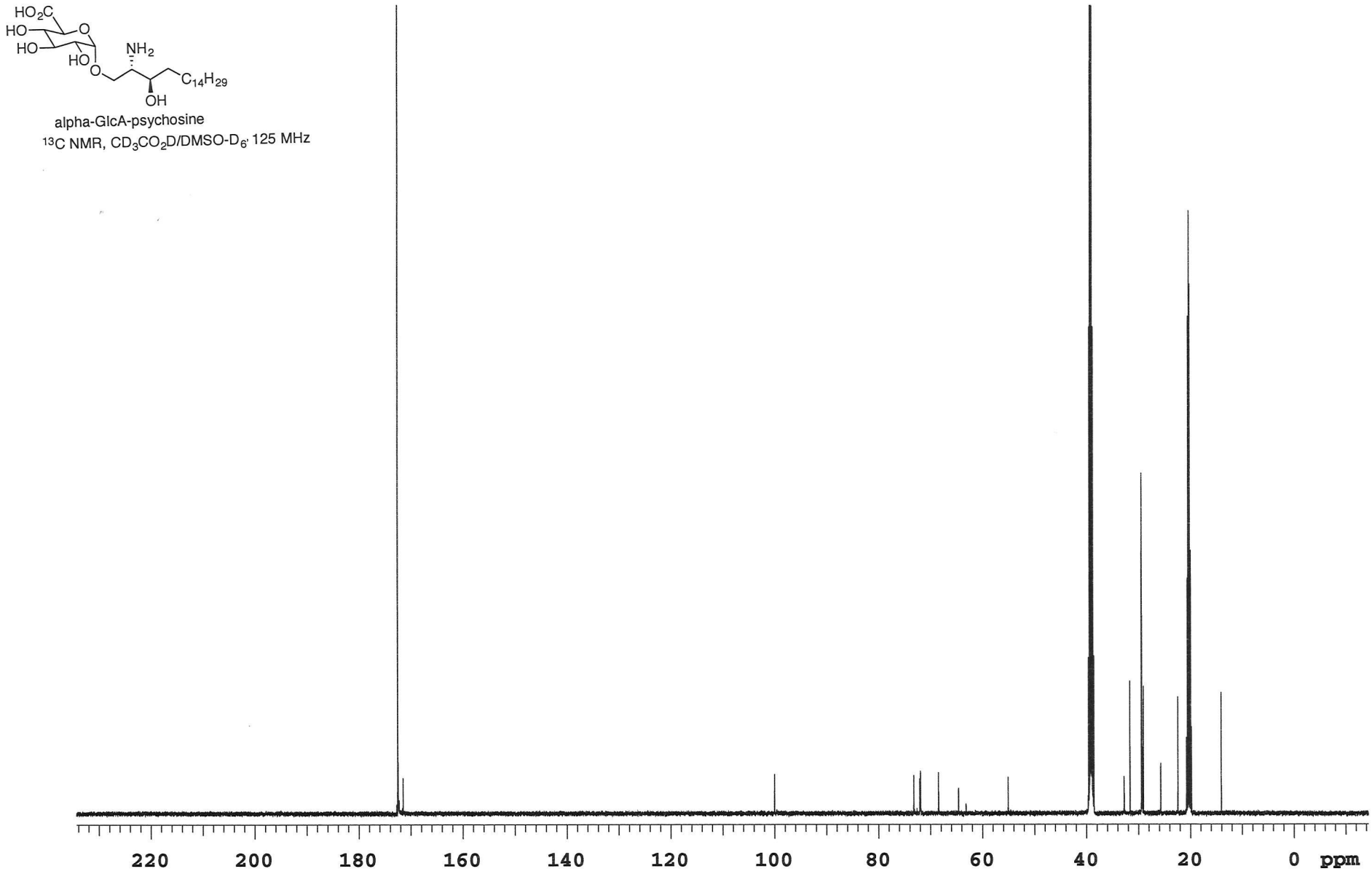
alpha-GalA-psychosine

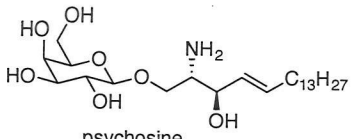
^{1}H NMR, CD_3CO_2D/DMSO-D_6, 500 MHz


HO
CO2H
O
HO
HO
NH2
O
C14H29
OH
alpha-GalA-psychosine
13C NMR, CD3CO2D/DMSO-D6, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0
ppm

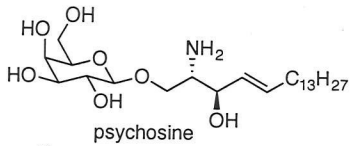


alpha-GlcA-psychosine
^{1}H NMR, CD_3CO_2D/DMSO-D_6, 500 MHz


HO2C
HO
HO
HO
O
NH2
C14H29
OH
alpha-GlcA-psychosine
13C NMR, CD3CO2D/DMSO-D6, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0
ppm

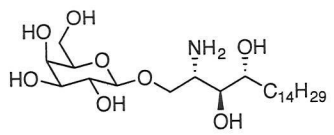


psychosine
^{1}H NMR, CD_3OD, 500 MHz



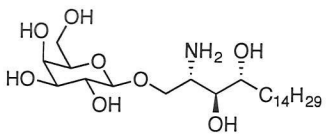
psychosine

^{13}C NMR, CD_3OD, 125 MHz

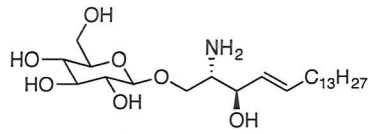


psychosine (phyto)

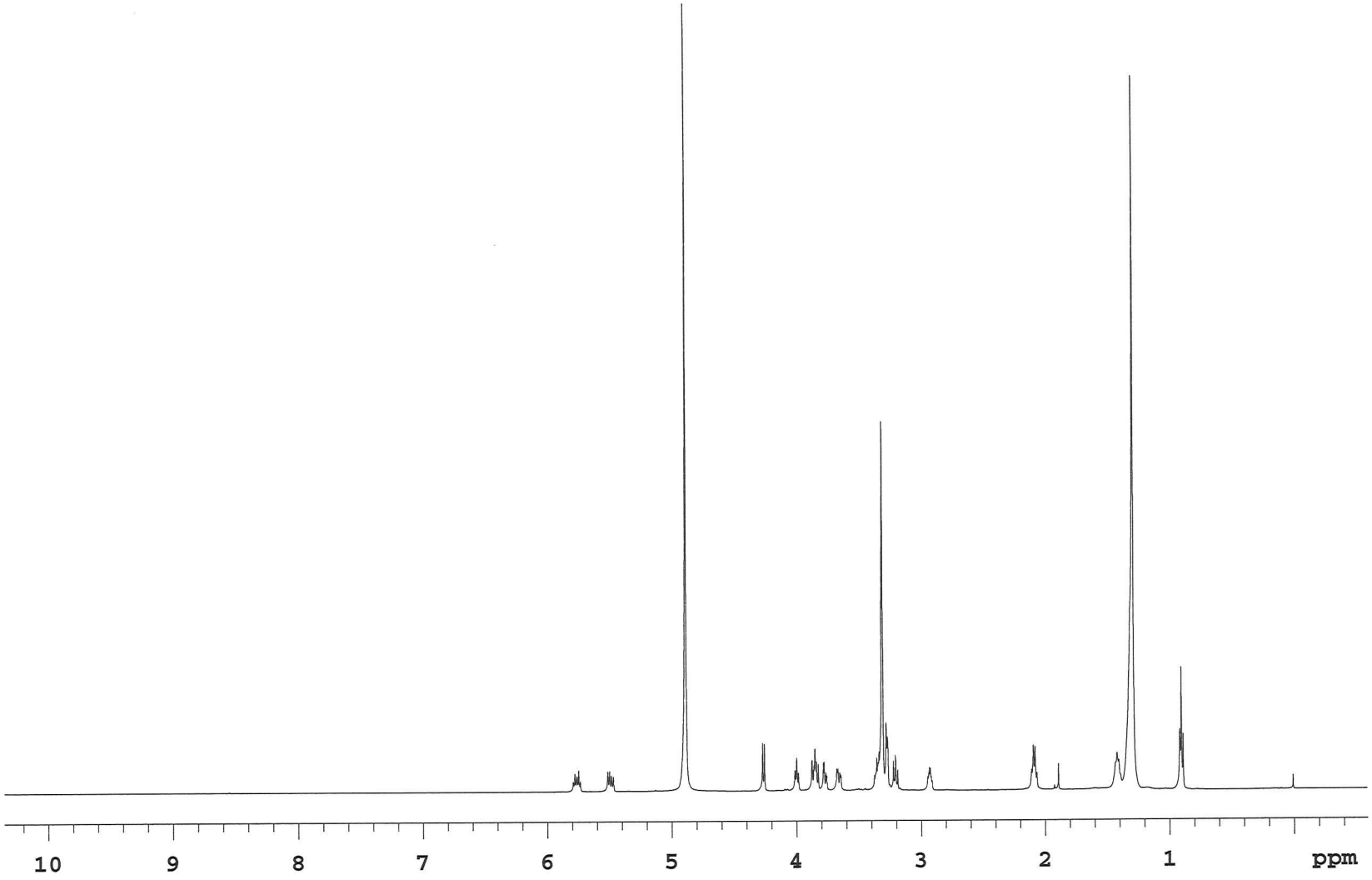
^{1}H NMR, CD_3OD, 500 MHz

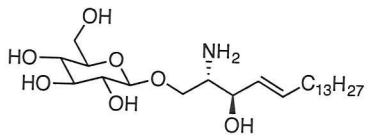


psychosine (phyto)
^{13}C NMR, CD_3OD, 125 MHz



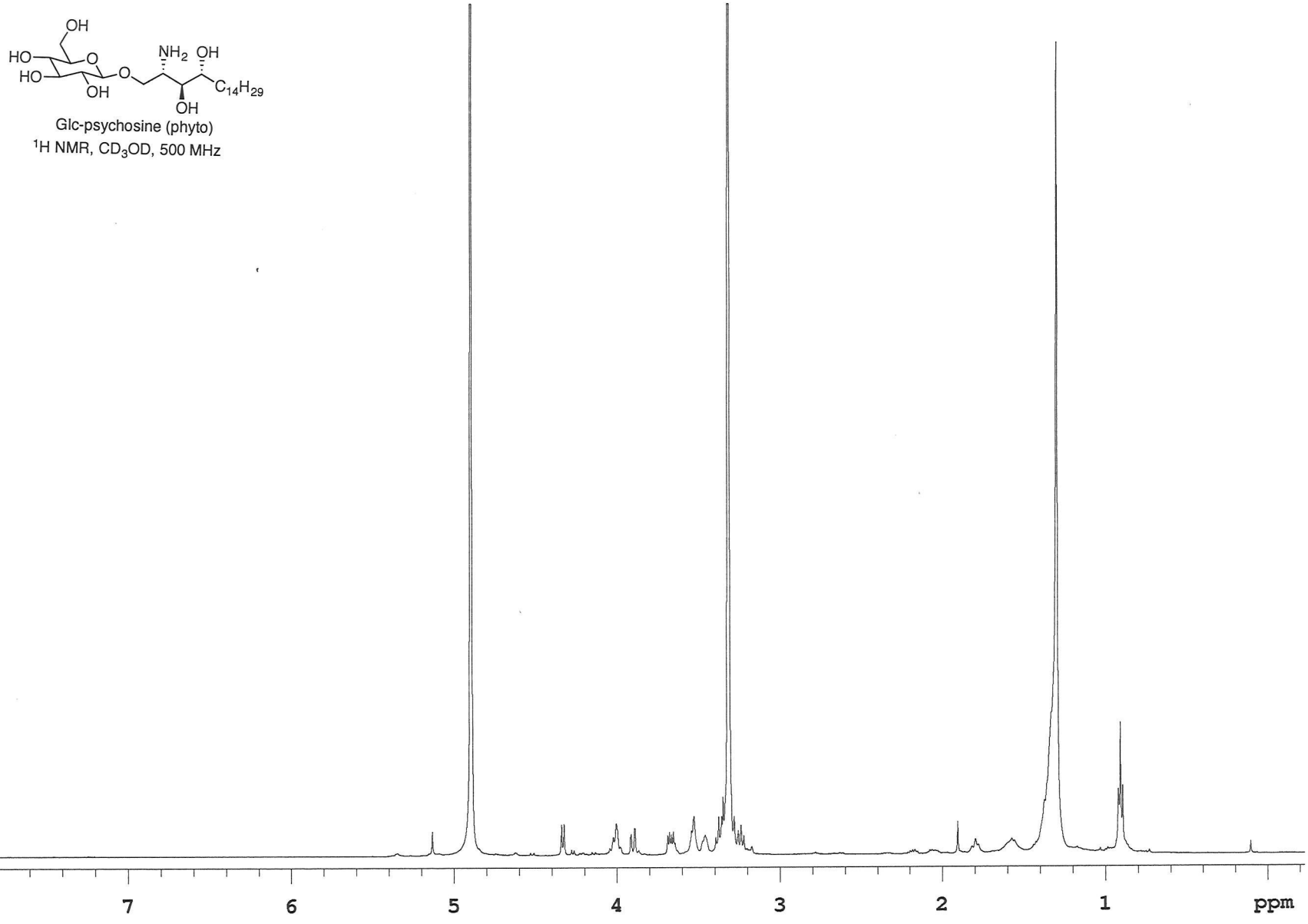
Glc-psychosine
^{1}H NMR, CD_3OD, 500 MHz





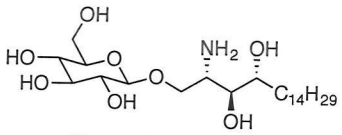
Glc-psychosine

^{13}C NMR, CD_3OD, 125 MHz

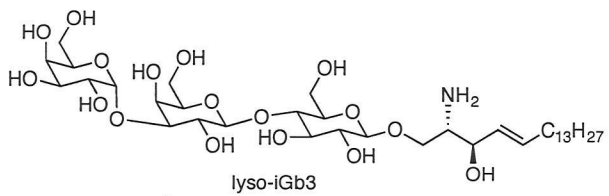


Glc-psychosine (phyto)

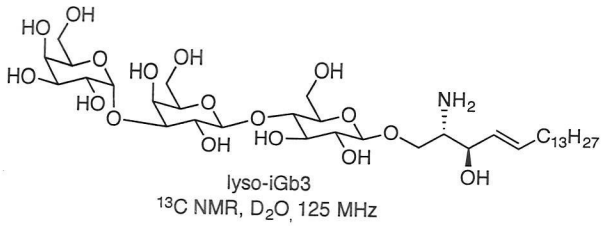
^{1}H NMR, CD_3OD, 500 MHz



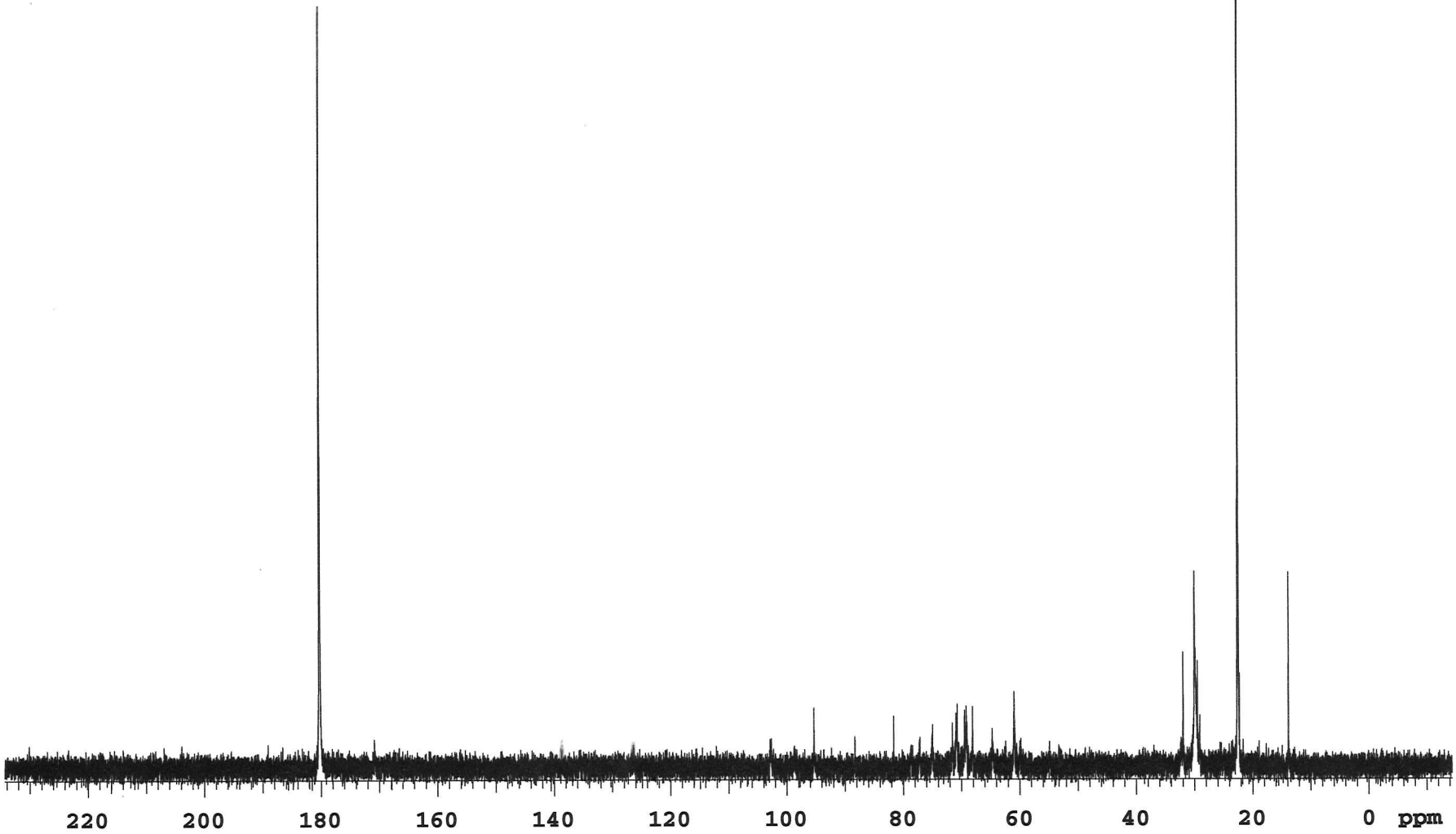
Glc-psychosine (phyto)
^{13}C NMR, CD_3OD, 125 MHz

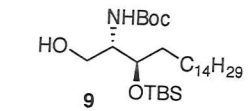


lyso-iGb3
^{1}H NMR, D_2O, 500 MHz



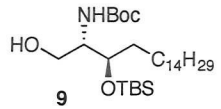
lyso-iGb3
^{13}C NMR, D_2O, 125 MHz





9

^{1}H NMR, $CDCl_3$, 500 MHz



9

^{13}C NMR, $CDCl_3$, 125 MHz