Supporting Information

Lipid structure-dependent CD1d functional stabilization and immunomodulation of endogenous glucosyl ceramides

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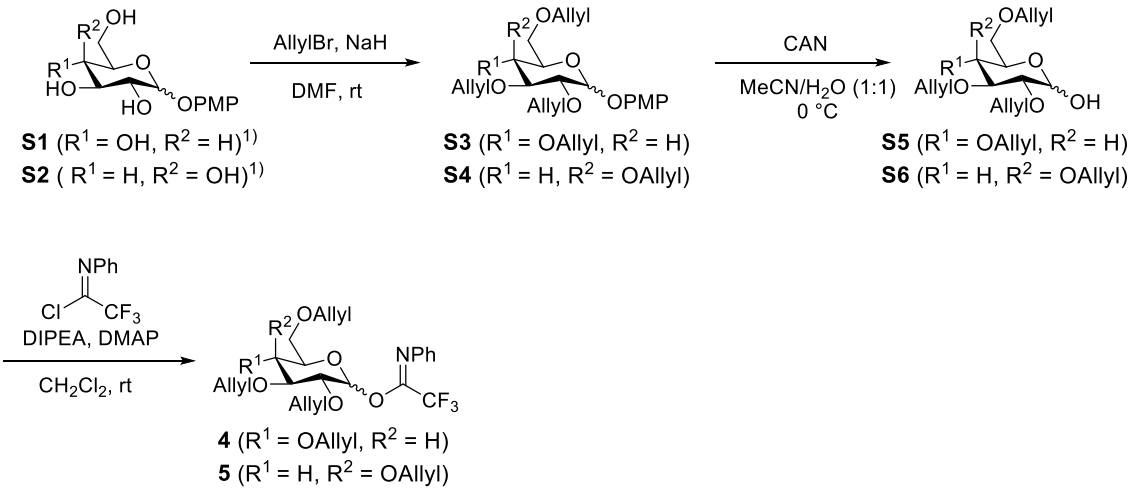
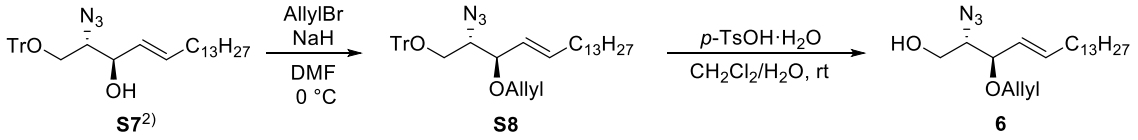
Ethics approval

Ethics approval for the genetic recombination experiments and the animal experiments was obtained from the Institutional Review Board of Keio University, in accordance with national and institutional guidelines for the safe and ethical conduct of genetic research.

Supplemental Figures and Data



Scheme S1. Synthesis of compounds **4** and **5**



Scheme S2. Synthesis of compounds **6**

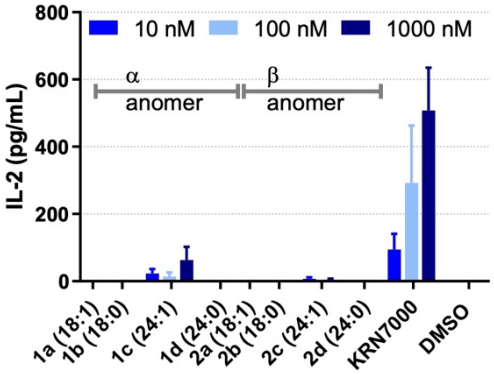


Figure S1. Antigen presenting cell (APC)-free assay for lipid binding to mCD1d-Fc fusion protein using the indicated a) GlcCer **1a**–**d**, **2a**–**d**. α-GalCer (KRN7000) was used as a reference. The graphs show the mean ± SD of triplicate measurements, and the results shown are representative of at least three independent experiments. b) Overview of antigen presenting cell (APC)-free assay for lipid binding to mCD1d-Fc fusion protein.

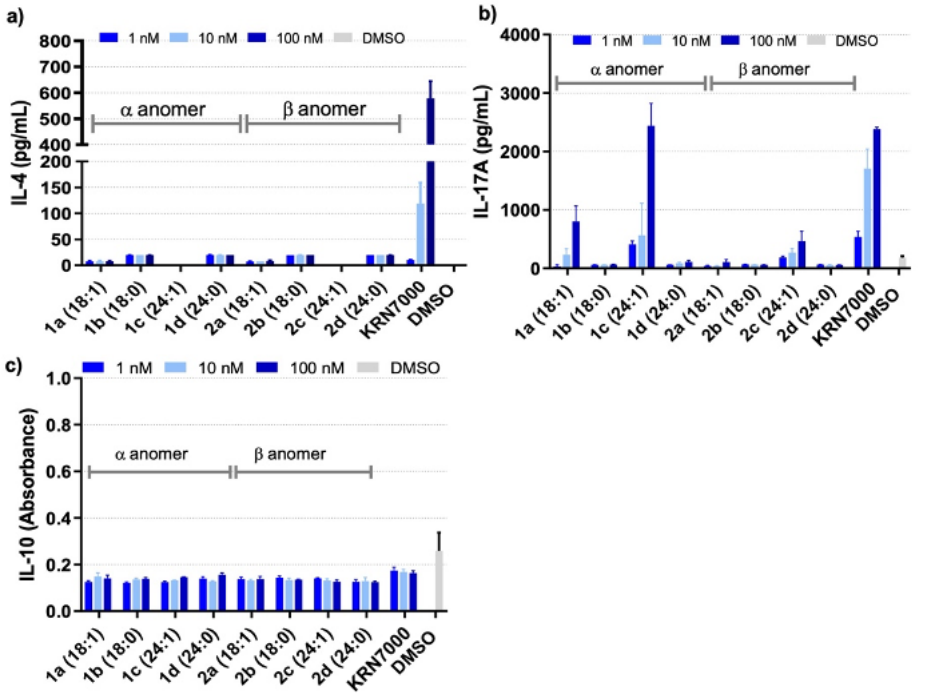


Figure S2. Cytokines, IL-4, IL-17A and IL-10, secretion by mouse splenocytes following stimulation by ligands **1a–d** and **2a–d**. The graphs show the mean ± SD of triplicate measurements, and the results shown are representative of at least three independent experiments. a) IL-4, b) IL-17A and c) IL-10 secretion stimulated with GlcCer **1a**–**d** and **2a**–**d**.

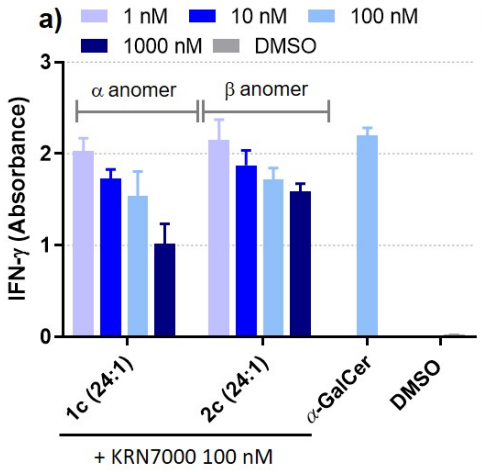
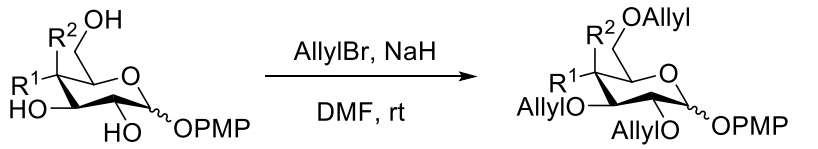


Figure S3. Inhibitory activities of GlcCer (**1c**, **2c**) along with KRN7000 100 nM against IFN-γ induction in mouse splenocytes.

Experimental Section

Synthesis: General procedures

Nuclear magnetic resonance (^{1}H NMR, ^{13}C NMR) spectra were measured in an indicated solvent with either JEOL AL400, ECX 400 or ECS 400. The proton chemical shifts in $CDCl_3$ are reported in parts per million (δ) using tetramethylsilane as an internal standard and coupling constants are in Heltz (Hz). The chemical shifts in other solvents are reported in ppm from the residual proton signal of the solvent. The chemical shifts for ^{13}C NMR are reported in ppm from the internal solvent signal ($CDCl_3$, δ 77.16). High-resolution mass spectra (HRMS) of synthetic compounds were obtained on an electron spray ionization quadrupole time of flight (ESI-QTOF) mass spectrometer (micrOTOF-QII-HC; BRUKER). Analytical thin layer chromatography (TLC) was performed on Silica gel 60 F_{254} Plates (Merck, 0.25 mm thickness). Silica gel column chromatography was performed using Silica gel 60 N [spherical neutral (Kanto Chemical Co., Inc., 40–50 mm)] at medium pressure (2–4 $kgcm^{-2}$ using indicated solvent systems. Reagents were purchased from commercial suppliers (TCI, nacalai tesque, FUJIFILM Wako Pure Chemical Corporation, Merck, Kanto Chemical Co., Inc., Watanabe Chemical Industries, ltd.) and were used without further purification. Unless otherwise noted, non-aqueous reactions were carried out under an argon atmosphere. Anhydrous dichloromethane, tetrahydrofuran, N, N-dimethylformamide, methanol, and toluene were purchased from Kanto Chemical Co., Inc.

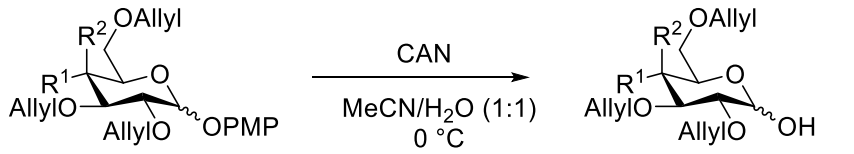


S1 (R^1 = OH, R^2 = H)[1)] **S3** (R^1 = OAllyl, R^2 = H)

S2 (R^1 = H, R^2 = OH)[1)] **S4** (R^1 = H, R^2 = OAllyl)

Compound S3: To a stirred solution of **S1**[1] (1.00 g, 3.49 mmol) in anhydrous DMF (15.2 mL) were added NaH 60% suspension in mineral oil (616 mg, 15.4 mmol) and AllylBr (1.28 mL, 14.7 mmol) at 0 °C, and the mixture was stirred at room temperature for 18 h. The reaction was quenched with ice water, and the whole was extracted with Et_2O and washed with H_2O and brine, dried over anhydrous Na_2SO_4, filtered, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 7/1) to afford **S3** (1.23 g, 79%) as clear oil; ^{1}H NMR ($CDCl_3$) δ 7.06–6.97 (m, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 6.06–5.84 (m, 4H), 5.34–5.23 (m, 4H), 5.18–5.15 (m, 4H), 4.47–4.39 (m, 1H), 4.30 (ttt, *J* = 21.3, 7.4, 2.3 Hz, 3H), 4.21–4.11 (m, 2H), 4.08–3.80 (m, 3H), 3.76 (t, *J* = 3.1 Hz, 3H), 3.63 (dt, *J* = 11.9, 4.1 Hz, 1H), 3.58–3.51 (m, 2H), 3.45 (t, *J* = 4.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 155.2, 154.9, 150.7, 135.3, 134.9, 134.7, 134.4, 118.4, 118.1, 117.6, 117.3, 117.1, 116.9, 116.8, 116.5, 102.7, 96.5, 84.1, 81.4, 79.3, 75.0, 74.5, 73.9, 72.4, 70.6, 68.2, 55.6; HRMS (ESI-QTOF) calcd for $C_{25}H_{34}O_7$ $[M+Na]^+$ 469.2197, found 469.2203.

Compound S4: To a stirred solution of **S2**[1] (4.00 g, 14.0 mmol) in anhydrous DMF (60.7 mL) were added NaH 60% suspension in mineral oil (2.46 g, 61.5 mmol) and AllylBr (5.32 mL, 61.5 mmol) at 0 °C, and the mixture was stirred at room temperature for 24 h. The reaction was quenched with ice water, and the whole was extracted with Et_2O and washed with H_2O and brine, dried over anhydrous Na_2SO_4, filtered, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 6/1) to afford **S4** (5.16 g, 83%) as clear oil; ^{1}H NMR ($CDCl_3$) δ 7.05–6.92 (m, 2H), 6.84–6.68 (m, 2H), 6.03–5.73 (m, 4H), 5.46–5.43 (m, 1H), 5.36-5.09 (m, 8H), 4.77–4.72 (m, 1H), 4.44–3.87 (m, 13H), 3.84–3.79 (m, 1H), 3.70–3.54 (m, 1H), 3.49–3.30 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 155.2, 151.8, 135.5, 135.4, 135.3, 135.2, 135.1, 135.0, 134.5, 118.7, 118.7, 117.4, 117.2, 117.1, 116.8, 116.7, 116.5, 114.5, 114.4, 103.2, 97.6, 81.5, 79.0, 78.3, 76.1, 74.5, 74.2, 74.0, 73.6, 72.5, 72.3, 72.0, 71.8, 69.7, 68.5, 55.7; HRMS (ESI-QTOF) calcd for $C_{25}H_{34}O_7$ $[M+Na]^+$ 469.2197, found 469.2203.



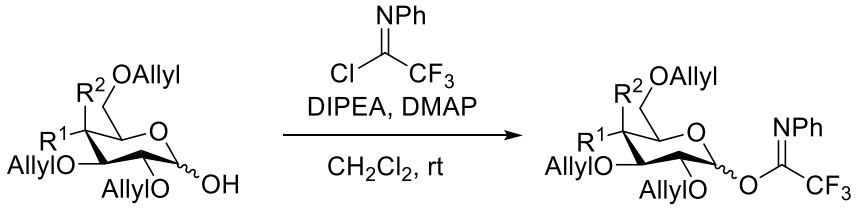
S3 (R^1 = OAllyl, R^2 = H)
S4 (R^1 = H, R^2 = OAllyl)

S5 (R^1 = OAllyl, R^2 = H)
S6 (R^1 = H, R^2 = OAllyl)

Compound S5: To a stirred solution of **S3** (30.4 mg, 0.068 mmol) in MeCN (419 μL) and H_2O (419 μL) was added CAN (73.5 mg, 0.134 mmol), and the mixture was stirred at 0 °C for 15 min. The mixture was diluted with brine, and the whole was extracted with EtOAc, dried over anhydrous Na_2SO_4, filtered, and then concentrated under reduced pressure to affrd the residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2/1) to afford **S5** (19.9 mg, 86%) as a brown solid; ^{1}H NMR ($CDCl_3$) δ: 6.02–5.86 (m, 4H), 5.27 (dt, *J* = 17.2, 5.1 Hz, 4H), 5.14 (m, 4H), 4.39–3.93 (m, 9H), 3.74–3.58 (m, 3H), 3.38 (m, 2H), 3.24–3.14 (1H, m); ^{13}C NMR ($CDCl_3$) δ 135.7, 135.4, 115.8, 115.6, 115.4, 115.2, 89.6, 80.4, 79.6, 77.5, 73.5, 72.9, 72.8, 72.5, 72.4, 71.1, 70.3, 69.1; HRMS (ESI-QTOF) calcd for $C_{18}H_{28}O_6$ $[M+Na]^+$ 363.1778, found 363.1787.

Compound S6: To a stirred solution of **S4** (2.42 g, 5.42 mmol) in MeCN (33.9 mL) and H_2O (33.9 mL) was added CAN (5.94 g, 10.8 mmol), and the mixture was stirred at 0 °C for 40 min. The mixture was diluted with brine, and the whole was extracted with EtOAc, dried over anhydrous Na_2SO_4, filtered, and then concentrated under reduced pressure to afford the residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2/1 to 1/1) to afford **S6** (1.55 g, 84%) as a brown solid; ^{1}H NMR ($CDCl_3$) δ: 6.00–5.86 (m, 4H), 5.42–5.10 (m, 9H), 4.97–4.76 (m, 1H), 4.60 (dd,

J = 7.5, 1.5 Hz, 1H), 4.42–3.94 (m, 9H), 3.84–3.81 (m, 1H), 3.78–3.67 (m, 2H), 3.67–3.54 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 135.3, 134.9, 134.7, 134.3, 117.8, 117.5, 117.4, 116.9, 116.7, 97.6, 92.0, 74.5, 74.0, 72.7, 72.5, 71.6, 69.4, 68.9; HRMS (ESI-QTOF) calcd for $C_{18}H_{28}O_6$ $[M+Na]^+$ 363.1778, found 363.1787.

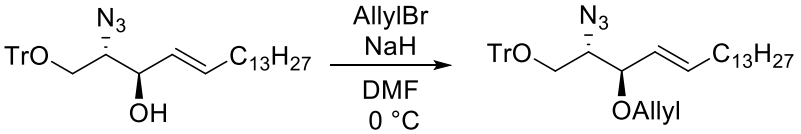


S5 (R^1 = OAllyl, R^2 = H)
S6 (R^1 = H, R^2 = OAllyl)

5 (R^1 = OAllyl, R^2 = H)
6 (R^1 = H, R^2 = OAllyl)

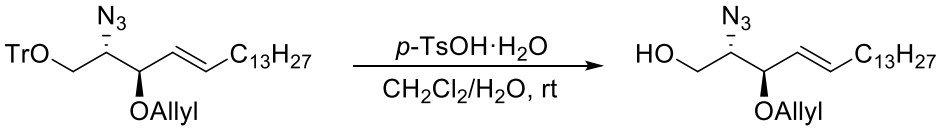
Compound 5: To a stirred solution of **S5** (261 mg, 0.767 mmol) in CH_2Cl_2 (15.3 mL) were added 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (145 μL, 0.922 mmol), DIPEA (261 μL, 1.53 mmol), and DMAP (81.5 mg, 0.667 mmol). The mixture was stirred at room temperature for 4 h, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 9/1) to afford **5** (373 mg, 95%) as yellow oil; ^{1}H NMR ($CDCl_3$) δ: 7.28 (dd, *J* = 13.2, 4.9 Hz, 2H), 7.09 (t, *J* = 7.3 Hz, 1H), 6.83 (d, *J* = 7.3 Hz, 2H), 6.03–5.84 (m, 4H), 5.32–5.26 (m, 4H), 5.19 (tt, *J* = 9.0, 3.6 Hz, 4H), 4.41–3.98 (m, 9H), 3.85 (s, 1H), 3.74 (q, *J* = 7.8 Hz, 1H), 3.66 (dd, *J* = 12.7, 8.3 Hz, 2H), 3.52 (dd, *J* = 21.5, 11.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 135.0, 134.7, 134.5, 134.4, 129.1, 128.7 (3C), 127.4, 120.6, 117.6 (2C), 117.5, 117.2, 117.1 (2C), 116.8 (2C), 116.7, 80.3, 74.4, 74.1, 73.9, 73.0, 72.5, 72.4; HRMS (ESI-QTOF) calcd for $C_{26}H_{32}F_3O_6$ $[M+Na]^+$ 534.2174, found 534.2074.

Compound 6: To a stirred solution of **S6** (1.10 g, 3.23 mmol) in CH_2Cl_2 (64.6 mL) were added 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (558 μL, 3.55 mmol), DIPEA (1.10 mL, 6.46 mmol), and DMAP (276 mg, 2.26 mmol). The mixture was stirred at room temperature for 14 h, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 9/1) to afford **6** (1.40 g, 85%) as yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.34–7.03 (m, 4H), 7.10–6.98 (m, 1H), 6.80 (d, *J* = 7.2 Hz, 2H), 5.98–5.82 (m, 4H), 5.42–5.14 (m, 8H), 4.41–4.34 (m, 1H), 4.27–3.91 (m, 8H), 3.80–3.74 (m, 2H), 3.67–3.53 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 135.3, 135.2, 134.9, 134.8, 134.7 (2C), 134.4 (3C), 129.5, 128.8, 128.7, 126.5, 124.2, 120.5, 119.6, 119.4, 117.6 (2C), 117.3, 117.2, 117.0, 116.7 (2C), 81.4, 75.5, 74.3, 74.3, 74.2, 74.1, 72.9, 72.5, 72.0, 71.9, 68.3, 67.9; HRMS (ESI-QTOF) calcd for $C_{26}H_{32}F_3O_6$ $[M+Na]^+$ 534.2174, found 534.2074.



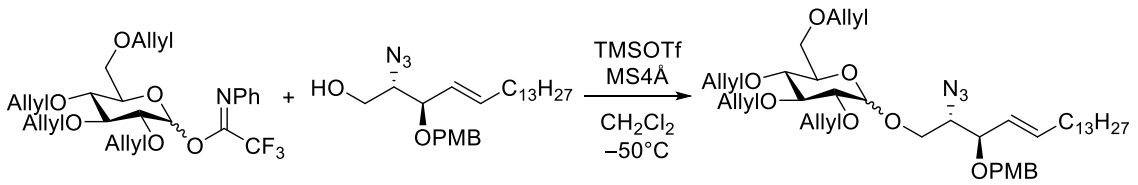
S7[2)] **S8**

Compound S8: To a stirred solution of **S7**[2] (877 mg, 1.55 mmol) in DMF (15.5 mL) were added NaH 60% suspension in mineral oil (99.2 mg, 2.48 mmol) and AllylBr (201 μL, 2.32 mmol) at 0 °C, and the mixture was stirred at room temperature for 23 h. The mixture was diluted with ice water. The whole was extracted with Et_2O and washed with H_2O and brine, dried over anhydrous Na_2SO_4, filtrated, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 15/1) to afford **S8** (891 mg, 95%) as a white solid; ^{1}H NMR ($CDCl_3$) δ 7.51–7.41 (m, 5H), 7.35–7.22 (m, 10H), 5.80 (dq, *J* = 11.1, 5.4 Hz, 1H), 5.68–5.61 (m, 1H), 5.30–5.11 (m, 2H), 4.01 (dd, *J* = 13.1, 5.0 Hz, 1H), 3.90 (dd, *J* = 8.4, 5.7 Hz, 1H), 3.76 (dd, *J* = 12.9, 5.7 Hz, 1H), 3.63–3.56 (m, 1H), 3.30 (dd, *J* = 9.7, 6.6 Hz, 1H), 3.21 (q, *J* = 4.7 Hz, 1H), 2.05–1.98 (m, 2H), 1.44–1.16 (m, 20H), 0.93–0.84 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 143.8 (3C), 137.7, 134.7 (2C), 128.8, 127.9, 127.2, 127.1, 126.0, 116.7, 87.1, 79.6, 77.5, 77.1, 76.8, 69.0, 65.0, 63.1, 53.5, 32.4, 32.0, 29.8 (2C), 29.7, 29.6 (2C), 29.5, 29.3, 29.1, 22.8, 14.3; HRMS (ESI-QTOF) calcd for $C_{40}H_{53}O_2$ $[M+Na]^+$ 630.4030, found 630.4022.



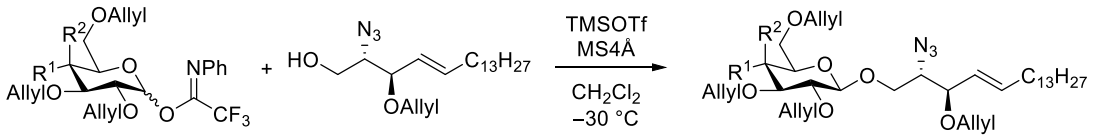
S8 **7**

Compound 7: To a stirred solution of compound **S8** (810 mg, 1.33 mmol) in CH_2Cl_2 (6.8 mL) and MeOH (3.4 mL) was added *p*-TsOH·H_2O (278 mg, 1.46 mmol), and the mixture was stirred at room temperature for 2.5 h. The mixture was quenched with saturated aqueous $NaHCO_3$, and the whole was extracted with EtOAc and washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtrated, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 5/1) to afford **7** (443 mg, 91%) as colorless oil; ^{1}H NMR ($CDCl_3$) δ 5.94–5.84 (m, 1H), 5.77 (dt, *J* = 15.1, 6.8 Hz, 1H), 5.39 (q, *J* = 8.0 Hz, 1H), 5.29–5.18 (m, 2H), 4.16–4.07 (m, 1H), 3.92–3.80 (m, 2H), 3.80–3.70 (m, 2H), 3.50 (q, *J* = 5.4 Hz, 1H), 2.17 (t, *J* = 6.3 Hz, 1H), 2.10 (q, *J* = 6.8 Hz, 2H), 1.41 (t, *J* = 6.8 Hz, 2H), 1.27–1.20 (m, 20H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 138.2, 134.3, 126.1, 117.3, 80.9, 77.4, 77.1, 76.8, 69.1, 66.0, 62.7, 32.4, 32.0, 29.7 (3C), 29.5 (2C), 29.5 (2C), 29.2, 29.0, 22.8, 14.2; HRMS (ESI-QTOF) calcd for $C_{21}H_{39}O_2$ $[M+Na]^+$ 388.2934, found 388.2930.



5 **S9**[3)] **S10a** (α), **S10** (β)

Compound <u>S10α</u> and <u>S10β</u>: To a solution of compound **5** (1284 mg, 2.52 mmol), and compound **S9**[3] (860 mg, 1.93 mmol) in CH_2Cl_2 (29.7 mL) was stirred for 30 min in the presence of MS 4Å. The mixture was cooled to –50 °C then TMSOTf (90.8 μL, 0.50 mmol). After stirring for 19 h, the reaction was quenched with Et_3N, the mixture was filtered, and the solvent was concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 6/1) to afford **<u>S10α</u>** (597 mg, 33%) as yellow solid, and **<u>S10β</u>** (732 mg, 40%) as yellow oil; **<u>S10α</u>**: ^{1}H NMR ($CDCl_3$) δ: 7.22 (t, *J* = 7.3 Hz, 2H), 6.83 (t, *J* = 13.5 Hz, 2H), 6.01–5.82 (m, 4H), 5.79–5.71 (m, 1H), 5.41 (dd, *J* = 15.5, 8.5 Hz, 1H), 5.27 (d, *J* = 17.1 Hz, 4H), 5.16 (dd, *J* = 16.3, 10.0 Hz, 4H), 4.87 (d, *J* = 3.1 Hz, 1H), 4.52 (d, *J* = 11.4 Hz, 1H), 4.29 (m, 4H), 4.14–4.07 (m, 4H), 4.00 (m, 2H), 3.89 (t, *J* = 6.8 Hz, 1H), 3.78 (s, 3H), 3.71 (dd, *J* = 17.7, 8.8 Hz, 2H), 3.62 (t, *J* = 5.3 Hz, 3H), 3.53 (t, *J* = 8.9 Hz, 1H), 3.43 (t, *J* = 9.4 Hz, 1H), 3.35 (dd, *J* = 9.5, 3.3 Hz, 1H), 2.08 (dd, *J* = 15.9, 9.0 Hz, 2H), 1.41 (s, 2H), 1.26 (s, 20H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 159.0, 138.0, 135.3, 135.1, 134.9, 134.8, 134.4, 130.1, 129.2, 129.1, 126.3, 125.9, 120.6, 120.1, 117.3, 117.1, 117.0, 116.7, 116.3, 114.2, 113.7, 97.9, 81.2, 79.3, 79.1, 74.1, 73.8, 72.4, 71.9, 70.4, 69.6, 68.3, 67.5, 64.3, 55.2, 32.3, 31.9, 29.6 (2C), 29.4, 29.3, 29.2, 29.0, 22.6; HRMS (ESI-QTOF) calcd for $C_{44}H_{69}N_3O_8$ $[M+Na]^+$ 790.4977, found 790.4991; **<u>S10β</u>**: ^{1}H NMR ($CDCl_3$) δ: 7.25 (dd, *J* = 16.6, 7.3 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.00–5.83 (m, 4H), 5.77–5.69 (m, 1H), 5.41 (dd, *J* = 15.6, 8.8 Hz, 1H), 5.26–5.22 (m, 3H), 5.15 (d, *J* = 10.2 Hz, 4H), 4.54 (d, *J* = 11.7 Hz, 1H), 4.29 (tt, *J* = 21.0, 6.6 Hz, 6H), 4.11 (dd, *J* = 12.7, 5.9 Hz, 3H), 4.02 (td, *J* = 12.6, 7.2 Hz, 2H), 3.94 (dd, *J* = 10.2, 6.8 Hz, 1H), 3.87 (dd, *J* = 8.3, 5.4 Hz, 1H), 3.78 (s, 3H), 3.68 (t, *J* = 5.6 Hz, 2H), 3.59 (dt, *J* = 17.4, 5.9 Hz, 2H), 3.37–3.32 (m, 3H), 3.18 (t, *J* = 8.3 Hz, 1H), 2.10 (q, *J* = 6.8 Hz, 2H), 1.40 (d, *J* = 6.8 Hz, 2H), 1.25 (d, *J* = 10.7 Hz, 20H), 0.88 (t, *J* = 6.6 Hz, 3H) ; ^{13}C NMR ($CDCl_3$) δ 159.0, 138.0, 135.1, 135.0, 134.9, 134.7, 134.6, 134.5, 134.3, 130.0, 129.1, 125.7, 117.0, 116.9, 116.8 (2C), 116.5, 113.6, 103.2, 84.0, 81.3, 78.9, 76.7, 74.8, 74.3, 73.7, 73.5, 72.4, 69.4, 68.6, 68.4, 64.3, 55.1, 32.3, 31.8, 29.6 (2C), 29.4, 29.3, 29.1, 29.0, 22.6, 14.1, 14.0; HRMS (ESI-QTOF) calcd for $C_{44}H_{69}N_3O_8$ $[M+Na]^+$ 790.4977, found 790.4991.



5 (R^1 = OAllyl, R^2 = H)
6 (R^1 = H, R^2 = OAllyl)

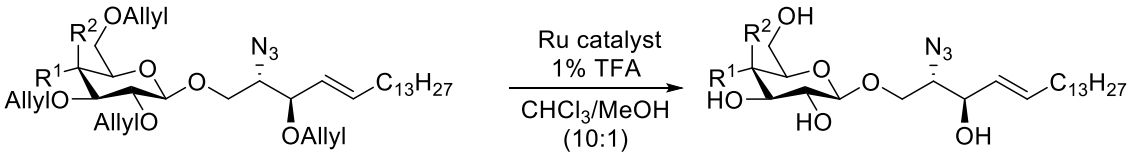
7

8: (: = 43:57) (R^1 = OAllyl, R^2 = H)
9: (: = 54:46) (R^1 = H, R^2 = OAllyl)

Compound 8α and 8β: To a solution of compound **5** (294 mg, 0.57 mmol), and compound **7** (268 mg, 0.44 mmol) in CH_2Cl_2 (8.8 mL) was stirred for 30 min in the presence of MS 4Å. The mixture was cooled to –30 °C then TMSOTf (27 μL, 0.15mmol). After stirring for 7 h, the reaction was quenched with Et_3N, the mixture was filtered, and the solvent was concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 6/1) to afford **8α** (160 mg, 53%) as yellow solid, and **8β** (121 mg, 40%) as yellow oil; **8α**: ^{1}H NMR ($CDCl_3$) δ 5.96–5.78 (m, 5H), 5.73–5.65 (m, 1H), 5.37–5.17 (m, 5H), 5.16–5.05 (m, 5H), 4.34–4.13 (m, 6H), 4.12–3.96 (m, 5H), 3.91–3.73 (m, 3H), 3.70–3.50 (m, 4H), 3.39–3.31 (m, 3H), 3.20–3.09 (m, 1H), 2.08–1.95 (m, 2H), 1.34 (d, *J* = 5.0 Hz, 2H), 1.31–1.23 (m, 20H), 0.85 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 135.3, 135.1 (2C), 134.9 (2C), 134.8 (2C), 129.3, 126.2, 120.7, 117.1, 117.0, 116.9, 116.8, 116.7, 103.4, 84.2, 81.5, 77.5, 77.3, 77.1, 76.8, 75.0, 74.9, 74.5, 73.9, 72.5, 69.0, 68.9, 32.4, 32.0, 29.7 (3C), 29.5 (2C), 29.4 (2Cs), 29.3, 29.2, 29.1, 22.8, 14.2; HRMS (ESI-QTOF) calcd for $C_{39}H_{65}N_3O_{87}$ $[M+Na]^+$ 710.4715, found 710.4711; **8β**: ^{1}H NMR ($CDCl_3$) δ 5.99–5.82 (m, 5H), 5.75–5.66 (m, 1H), 5.38–5.30 (m, 1H), 5.28–5.22 (m, 5H), 5.18–5.13 (m, 5H), 4.39–4.21 (m, 5H), 4.19–3.97 (m, 5H), 3.93–3.77 (m, 3H), 3.69–3.51 (m, 4H), 3.36–3.31 (m, 3H), 3.22–3.17 (m, 1H), 2.09–2.03 (m, 2H), 1.37 (t, *J* = 7.0 Hz, 2H), 1.26–1.21 (m, 20H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 138.0, 137.8, 135.3, 135.2, 134.9, 134.8, 134.4, 117.1, 117.0, 116.9, 116.8, 116.7, 84.2, 84.1, 81.5, 79.7, 79.5, 77.5, 77.2, 76.8, 75.0, 74.9, 74.4, 73.9, 73.7, 72.5, 69.0, 67.5, 64.4, 58.5, 53.5, 49.6, 32.4, 32.0, 29.7, 29.5, 29.4, 29.3, 29.2, 29.1, 22.7, 14.2; HRMS (ESI-QTOF) calcd for $C_{39}H_{65}N_3O_{8¥7}$ $[M+Na]^+$ 710.4715, found 710.4720.

Compound 9α and 9β: To a solution of compound **6** (1.63 g, 3.19 mmol), and compound **7** (1.06 g, 2.90 mmol) in CH_2Cl_2 (44.6 mL) was stirred for 30 min in the presence of MS 4Å. The mixture was cooled to –30 °C then TMSOTf (136 μL, 0.75 mmol). After stirring for 15 h, the reaction was quenched with Et_3N, the mixture was filtered, and the solvent was concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography (*n*-hexane/EtOAc = 6/1) to afford **9α** (734 mg, 37%) as yellow solid, and **9β** (861 mg, 43%) as yellow oil; **14β**: ^{1}H NMR ($CDCl_3$) δ 5.98–5.81 (m, 5H), 5.75–5.68 (m, 1H), 5.38–4.97 (m, 14H), 4.37–4.29 (m, 2H), 4.24–4.10 (m, 4H), 4.06–3.95 (m, 2H), 3.95–3.68 (m, 4H), 3.66–3.47 (m, 5H), 3.37–3.29 (m, 1H), 2.20–2.04 (m, 2H), 1.55–1.11 (m, 22H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 138.1, 135.5, 135.4, 135.1, 135.0, 134.8, 134.4, 129.5, 128.0, 126.5, 125.6, 120.6, 117.6, 117.1, 116.8, 116.7, 116.6, 103.8, 81.6,

79.6, 79.0, 74.1, 74.0, 73.4, 73.2, 72.5, 71.9, 69.0, 68.6, 64.4, 32.5, 32.0, 29.8, 29.6, 29.5, 29.3, 29.1, 22.8, 14.2; HRMS (ESI-QTOF) calcd for $C_{44}H_{69}N_3O_8$ $[M+Na]^+$ 710.4715, found 710.4519.



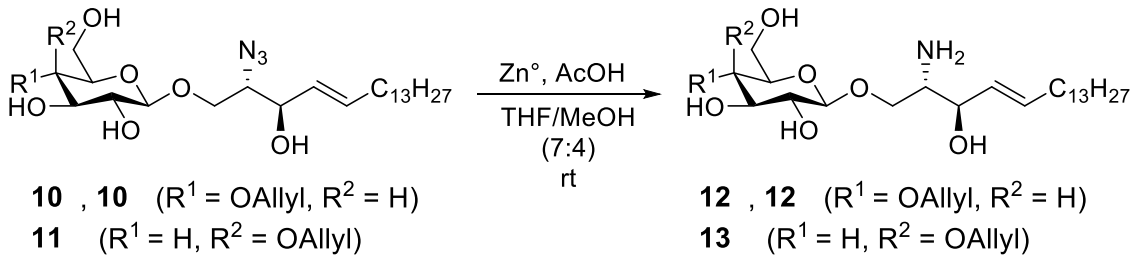
8 , **8** (R^1 = OAllyl, R^2 = H)
9 (R^1 = H, R^2 = OAllyl)

10 , **10** (R^1 = OAllyl, R^2 = H)
11 (R^1 = H, R^2 = OAllyl)

Compound 10α: To a stirred solution of **8α** (148 mg, 0.22 mmol) in $CHCl_3$ (6.5 mL), MeOH (0.65 mL) and TFA (72 μL) was added $[CpRu(C_3H_5)(C_9H_6NCOO)]PF_6$ (9.0 mg, 17.2 μmol), and the mixture was stirred at room temperature for 15 h, and the reaction was quenched with SilicaMet® DMT, and the mixture was stirred at room temperature for 30 min, and filtered, and the solvent was concentrated to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1) to afford **10α** (97.4 mg, 93%) as a brown solid; ^{1}H NMR (CD_3OD) δ: 5.72–5.64 (m, 1H), 5.43 (dd, *J* = 15.4, 7.5 Hz, 1H), 4.72 (dd, *J* = 9.5, 5.7 Hz, 1H), 4.09 (t, *J* = 6.1 Hz, 1H), 3.80–3.75 (m, 1H), 3.70 (dd, *J* = 11.8, 2.4 Hz, 1H), 3.58 (dt, *J* = 15.1, 4.5 Hz, 1H), 3.54–3.42 (m, 2H), 3.32–3.28 (m, 1H), 3.20 (dq, *J* = 9.7, 2.7 Hz, 3H), 1.98 (q, *J* = 6.7 Hz, 2H), 1.31 (d, *J* = 6.3 Hz, 2H), 1.19 (s, 20H), 0.82–0.77 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 135.8, 129.8, 101.0, 74.9, 74.0 (2C), 73.5, 73.4 (2C), 71.6 (2C), 68.8, 67.2, 62.5 (2C), 33.4, 33.1, 30.8 (2C), 30.6, 30.5, 30.3, 30.2, 23.7; HRMS (ESI-QTOF) calcd for $C_{24}H_{45}N_3O_7$ $[M+Na]^+$ 510.3150, found: 510.3164.

Compound 10β: To a stirred solution of **8β** (244.3 mg, 0.36 mmol) in $CHCl_3$ (10.8 mL), MeOH (1.1 mL) and TFA (118 μL) was added $[CpRu(C_3H_5)(C_9H_6NCOO)]PF_6$ (14.9 mg, 28.4 μmol), and the mixture was stirred at room temperature for 16 h, and the reaction was quenched with SilicaMet® DMT, and the mixture was stirred at room temperature for 30 min, and filtered, and the solvent was concentrated to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH = 7/1) to afford**10β** (150 mg, 87%) as a brown solid; ^{1}H NMR (CD_3OD) δ: 5.70–5.63 (m, 1H), 5.41 (dd, *J* = 15.4, 7.5 Hz, 1H), 4.19 (t, *J* = 9.6 Hz, 1H), 4.08 (dd, *J* = 7.3, 5.5 Hz, 1H), 3.83–3.75 (m, 2H), 3.61–3.51 (m, 3H), 3.28–3.14 (m, 3H), 3.10 (dd, *J* = 8.8, 7.9 Hz, 1H), 1.97 (q, *J* = 7.0 Hz, 2H), 1.30 (d, *J* = 6.7 Hz, 2H), 1.14 (d, *J* = 36.8 Hz, 20H), 0.80 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 135.9, 129.6, 104.5, 78.0 (2C), 75.0, 73.5 (2C), 71.5 (2C), 70.1, 67.3, 62.7 (2C), 33.4, 33.1, 30.8 (2C), 30.6, 30.5, 30.3, 30.2, 23.7, 14.5; HRMS (ESI-QTOF) calcd for $C_{24}H_{45}N_3O_7$ $[M+Na]^+$ 510.3150, found 510.3163.

Compound 11α: To a stirred solution of **9α** (448 mg, 0.65 mmol) in $CHCl_3$ (19.8 mL), MeOH (1.98 mL) and TFA (217 μL) was added $[CpRu(C_3H_5)(C_9H_6NCOO)]PF_6$ (27.3 mg, 52.0 μmol), and the mixture was stirred at room temperature for 18 h, and the reaction was quenched with SilicaMet® DMT, and the mixture was stirred at room temperature for 30 min, and filtered, and the solvent was concentrated to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1) to afford **11α** (259 mg, 82%) as a brown solid; ^{1}H NMR (CD_3OD) δ 5.78–5.70 (m, 1H), 5.51–5.46 (m, 1H), 4.22 (d, *J* = 7.7 Hz, 1H), 4.17 (dd, *J* = 7.0, 5.7 Hz, 1H), 3.90–3.83 (m, 2H), 3.78–3.71 (m, 2H), 3.70–3.59 (m, 2H), 3.55–3.44 (m, 2H), 3.29–3.28 (m, 1H), 2.07–1.99 (m, 2H), 1.38 (q, *J* = 6.8 Hz, 2H), 1.32–1.21 (m, 20H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 134.5, 128.3, 103.8, 75.2 (3C), 73.6, 72.2, 71.1(2C), 69.1, 68.7, 66.0, 61.2 (2C), 48.3, 48.1, 47.9, 47.7, 47.5, 47.3, 47.0, 32.1, 31.8, 29.5, 29.3, 29.2, 28.9, 28.9, 22.4, 13.2; HRMS (ESI-QTOF) calcd for $C_{24}H_{45}N_3O_7$ $[M+Na]^+$ 510.3150, found: 510.3164.



10 , **10** (R^1 = OAllyl, R^2 = H)
11 (R^1 = H, R^2 = OAllyl)

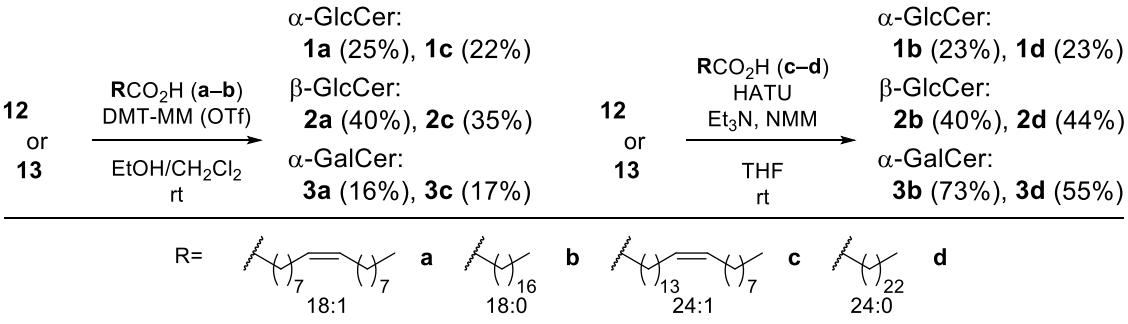
12 , **12** (R^1 = OAllyl, R^2 = H)
13 (R^1 = H, R^2 = OAllyl)

Compound 12α: To a compound **10α** (68.1 mg, 0.14 mmol) in THF (7.4 mL), MeOH (12.9 mL) and AcOH (5.5 mL), zinc dust (1.84 g, 28.3 mmol) was added. The mixture was subjected to sonication (bath sonication) for 20 min then filtered, and the filtrate was concentrated under the reduced pressure. The residue was dissolved in MeOH and treated with aqueous NH_4OH at room temperature for 1 h. The solvent was removed under reduced pressure to afford a residue, which was purified by silica gel column chromatography (CH_2Cl_2/MeOH/H_2O = 60/25/4) to afford **10α** (59.5 mg, 92%) as purple oil; ^{1}H NMR (CD_3OD) δ: 5.81–5.74 (m, 1H), 5.39 (dd, *J* = 15.2, 6.6 Hz, 1H), 4.73 (d, *J* = 3.6 Hz, 1H), 4.23 (dd, *J* = 12.2, 6.8 Hz, 1H), 3.94–3.84 (m, 1H), 3.71 (dd, *J* = 11.8, 1.8 Hz, 1H), 3.55 (dt, *J* = 16.9, 6.0 Hz, 2H), 3.42 (m, 3H), 3.29 (t, *J* = 5.0 Hz, 1H), 3.19 (dt, *J* = 14.3, 6.7 Hz, 1H), 2.00 (q, *J* = 6.9 Hz, 2H), 1.30 (s, 2H), 1.19 (s, 20H), 0.80 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (CD_3OD) δ 136.7, 126.1, 100.6, 74.9, 74.2, 73.3, 71.4 (2C), 62.5, 57.0, 33.4, 33.1, 30.9, 30.8 (3C), 30.7 (2C), 30.5, 30.4 (2C), 30.2, 23.7, 14.5; HRMS (ESI-QTOF) calcd for $C_{24}H_{47}NO_7$ $[M+Na]^+$ 484.3245, found: 484.3241.

Compound 12β: To a compound **10β** (10.7 mg, 22.0 μmol) in THF (1.2 mL), MeOH (2.0 mL) and AcOH (870 μL), zinc dust (290 mg, 4.43 mmol) was added. The mixture was subjected to sonication (bath sonication) for 30 min then filtered, and the filtrate was concentrated under the reduced pressure. The residue was dissolved in MeOH and treated with aqueous NH_4OH at room temperature for 1 h.

The solvent was removed under reduced pressure to afford a residue, which was purified by silica gel column chromatography (CH_2Cl_2/MeOH/H_2O = 60/25/4) to afford **12β** (6.3 mg, 62%) as purple oil; ^{1}H NMR (CD_3OD) δ: 5.80–5.72 (m, 1H), 5.39 (dd, *J* = 15.4, 6.8 Hz, 1H), 4.21 (t, *J* = 6.3 Hz, 1H), 3.83 (ddd, *J* = 19.1, 13.5, 4.9 Hz, 3H), 3.56 (dd, *J* = 11.6, 5.7 Hz, 1H), 3.30–3.11 (m, 6H), 2.00 (q, *J* = 6.9 Hz, 2H), 1.32 (t, *J* = 7.5 Hz, 2H), 1.19 (s, 20H), 0.80 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (CD_3OD) δ 136.5, 128.5, 104.1, 78.1, 77.8, 74.8, 71.5, 71.1, 62.5, 56.7, 35.4, 33.4, 33.1, 30.9, 30.8 (3C), 30.7, 30.5 (2C), 30.4, 30.2, 23.7, 14.5; HRMS (ESI-QTOF) calcd for $C_{24}H_{47}NO_7$ $[M+Na]^+$ 484.3245, found 484.3243.

Compound 13α: To a compound **11α** (148 mg, 0.30 mmol) in THF (11.1 mL), MeOH (19.4 mL) and AcOH (1.0 mL), zinc dust (4.0 g, 60.8 mmol) was added. The mixture was subjected to sonication (bath sonication) for 30 min then filtered, and the filtrate was concentrated under the reduced pressure. The residue was dissolved in MeOH and treated with aqueous NH_4OH at room temperature for 1 h. The solvent was removed under reduced pressure to afford a residue, which was purified by silica gel column chromatography (CH_2Cl_2/MeOH/H_2O = 60/25/4) to afford **13α** (67.9 mg, 48%) as purple oil; ^{1}H NMR (CD_3OD) δ 5.83 (dd, *J* = 15.0, 7.0 Hz, 1H), 5.47 (dd, *J* = 15.4, 6.6 Hz, 1H), 4.84 (d, *J* = 3.6 Hz, 1H), 4.30 (t, *J* = 5.5 Hz, 1H), 4.02–3.97 (m, 1H), 3.88 (t, *J* = 3.1 Hz, 1H), 3.82 (dd, *J* = 10.1, 3.6 Hz, 1H), 3.76–3.64 (m, 3H), 3.50–3.43 (m, 1H), 3.38 (dd, *J* = 7.5, 4.4 Hz, 1H), 3.30–3.27 (m, 1H), 2.07 (q, *J* = 6.7 Hz, 2H), 1.91 (d, *J* = 7.2 Hz, 2H), 1.39 (d, *J* = 6.1 Hz, 2H), 1.27 (s, 22H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (CD_3OD) δ 135.3, 127.0, 99.6, 71.6 (2C), 69.9, 69.6, 68.8, 64.5, 61.4, 55.5, 48.4, 48.1, 47.9, 47.7, 47.5, 47.3, 47.1, 32.1, 31.8, 29.5 (3C), 29.4 (2C), 29.2, 29.1, 28.9, 22.4, 21.8, 13.2; HRMS (ESI-QTOF) calcd for $C_{24}H_{47}NO_7$ $[M+Na]^+$ 484.3245, found: 484.3241.



Compound 1a: To a stirring solution of compound **12α** (12.1 mg, 26.2 μmol) and oleic acid (8.14 mg, 28.8 μmol) in EtOH (250 μL) and CH_2Cl_2 (80 μL) at room temperature was added DMT-MM(OTf) (12.3 mg, 31.4 μmol). The mixture was stirred for 13 h at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$, the whole was extracted with EtOAc and washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtrated, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography

($CHCl_3$/MeOH= 9/1 to 6/1) to afford **1a** (4.0 mg, 21%) as a white solid. ^{1}H NMR ($CDCl_3$/CD_3OD = 3/1) δ 5.67–5.61 (m, 1H), 5.36 (m, J = 15.5, 7.2 Hz, 1H), 5.26 (dq, J = 15.6, 5.1 Hz, 2H), 4.74 (d, J = 3.7 Hz, 1H), 4.01 (t, J = 7.0 Hz, 1H), 3.89–3.86 (m, 1H), 3.67 (m, 4H), 3.58 (t, J = 9.3 Hz, 1H), 3.48–3.45 (m, 1H), 3.37 (dd, J = 9.7, 3.7 Hz, 1H), 3.30 (t, J = 4.9 Hz, 1H), 3.27–3.26 (m, 2H), 2.16–2.03 (m, 2H), 1.93 (d, J = 3.7 Hz, 6H), 1.51 (s, 2H), 1.20 (s, 44H), 0.80 (t, J = 6.9 Hz, 6H); ^{13}C–NMR ($CDCl_3$/CD_3OD = 3/1) δ 174.3, 133.8, 129.5, 129.3, 128.8, 99.0, 73.4, 71.7, 71.6, 69.8, 66.8, 61.0, 55.4, 53.2, 36.0, 32.0, 31.5 (2C), 29.4, 29.3 (5C), 29.2 (2C), 29.1 (2C), 29.0 (4C), 28.9 (4C), 28.8 (2C), 25.5, 22.3, 13.5 (2C); HRMS (ESI-QTOF) calcd for $C_{42}H_{79}NO_8$: $[M+Na]^+$, 748.5698; found: 748.5698.

Compound 2a: To a stirring solution of compound **12β** (14.9 mg, 32.3 μmol) and oleic acid (10.0 mg, 35.5 μmol) in EtOH (300 μL) and CH_2Cl_2 (100 μL) at room temperature was added DMT-MM(OTf) (11.0 mg, 38.8 μmol). The mixture was stirred for 21 h at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$, the whole was extracted with EtOAc and washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtrated, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 9/1 to 6/1) to afford **2a** (4.8 mg, 20%) as a white solid. ^{1}H NMR ($CDCl_3$/CD_3OD = 3/1) δ 5.61 (m, 1H), 5.38 (m, 1H), 5.26 (m, 2H), 4.19 (m, 1H), 4.09 (m, 1H), 4.01 (m, 1H), 3.95 (t, J = 5.3 Hz, 2H), 3.79 (m, 1H), 3.64 (m, 1H), 3.49 (m, 1H), 3.26 (m, 2H), 3.20 (m, 1H), 2.09 (m, 2H), 1.93 (m, 4H), 1.50 (m, 2H), 1.18 (m, 44H), 0.80 (m, 6H); ^{13}C–NMR ($CDCl_3$/CD_3OD = 3/1) δ 173.6, 133.3, 128.8, 128.6, 128.2,102.0, 75.3, 72.5, 71.0, 69.0, 67.5, 60.3, 54.6, 52.2, 35.3, 31.3, 30.8, 28.6 (6C), 28.4 (4C), 28.3 (4C), 28.2 (3C), 28.1, 26.1, 24.9, 21.6, 12.8 (2C); HRMS (ESI-QTOF) calcd for $C_{42}H_{79}NO_8$: $[M+Na]^+$, 748.5698; found: 748.5698

Compound 3a: To a stirring solution of compound **13α** (16.9 mg, 34.7 μmol) and oleic acid (14.7 mg, 52.0 μmol) in EtOH (325 μL) and CH_2Cl_2 (110 μL) at room temperature was added DMT-MM(OTf) (30.4 mg, 78.0 μmol). The mixture was stirred for 13 h at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$, the whole was extracted with EtOAc and washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtrated, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1 to 5/1) to afford **3a** (11.9 mg, 47%) as a white solid. ^{1}H NMR ($CDCl_3$/CD_3OD = 10/1) δ 5.54–5.47 (m, 1H), 5.23 (dd, J = 15.4, 6.8 Hz, 1H), 5.15–5.11 (m, 2H), 4.66 (d, J = 3.6 Hz, 1H), 4.29–4.19 (m, 3H), 3.89–3.73 (3, 11H), 3.62–3.40 (m, 6H), 2.05–1.96 (m, 2H), 1.79 (d, J = 5.4 Hz, 6H), 1.38 (s, 2H), 1.09–0.97 (m, 44H), 0.68–0.64 (m, 6H); ^{13}C–NMR ($CDCl_3$/CD_3OD = 10/1) δ 174.6, 133.9, 129.8, 129.5, 129.0, 99.8, 77.6, 77.2, 76.9, 72.1, 70.1, 69.6, 68.9, 67.4, 61.6, 55.6, 53.6, 49.2, 48.9, 48.7, 48.5, 48.3, 48.1, 47.9, 36.3, 32.2, 31.7, 29.5, 29.5, 29.4 (5C), 29.3 (2C), 29.2 (4C), 29.1 (4C), 27.0 (4C), 25.8, 22.5, 13.7 (2C); HRMS (ESI-QTOF) calcd for $C_{42}H_{79}NO_8$: $[M+Na]^+$, 748.5698; found: 748.5698.

Compound 1b: To a stirring solution of compound **12β** (11.4 mg, 24.7 μmol) and stearic acid (7.0 mg, 24.7 μmol) in THF (310 μL) at room temperature was added HATU (9.4 mg, 24.7 μmol), Et_3N (10.9 μL, 49.4 μmol) and NMM (5.4 μL, 49.4 μmol). The mixture was stirred at room temperature for 21 h, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1 to 5/1) to afford **1b** (4.2 mg, 23%) as a white solid. ^{1}H NMR ($CDCl_3/CD_3OD$ = 3/1) δ 5.68–5.61 (m, 1H), 5.36 (dd, J = 15.4, 7.2 Hz, 1H), 4.74 (d, J = 3.6 Hz, 1H), 4.01 (t, J = 7.0 Hz, 1H), 3.88 (dd, J = 6.8, 3.6 Hz, 1H), 3.72–3.63 (m, 4H), 3.58 (dd, J = 12.7, 5.9 Hz, 1H), 3.46 (t, J = 4.3 Hz, 1H), 3.38–3.35 (m, 1H), 3.29 (t, J = 9.3 Hz, 1H), 2.12–2.07 (m, 2H), 1.94 (tt, J = 29.2, 8.9 Hz, 2H), 1.51 (m, 2H), 1.18 (m, 50H), 0.81–0.78 (m, 6H); ^{13}C–NMR ($CDCl_3/CD_3OD$ = 3/1) δ 174.2, 133.6, 128.7, 98.8, 73.2, 71.6, 71.5, 71.2, 69.6, 66.5, 60.8, 53.1, 35.8 (2C), 31.8 (2C), 31.3 (2C), 29.1 (5C), 29.0 (3C), 28.9 (3C), 28.8 (3C), 28.7 (4C), 25.4 (2C), 22.0 (2C), 13.2 (2C); HRMS (ESI-QTOF) calcd for $C_{42}H_{81}NO_8$: $[M+Na]^+$, 750.5854; found: 750.5862.

Compound 2b: To a stirring solution of compound **12β** (10.4 mg, 22.5 μmol) and stearic acid (6.4 mg, 22.5 μmol) in THF (280 μL) at room temperature was added HATU (8.56 mg, 22.5 μmol), Et_3N (10.0 μL, 45.1 μmol) and NMM (5.0 μL, 45.1 μmol). The mixture was stirred at room temperature for 21 h, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1 to 5/1) to afford **2b** (6.5 mg, 40%) as a white solid. ^{1}H NMR ($CDCl_3/CD_3OD$ = 3/1) δ 5.61 (t, J = 7.8 Hz, 1H), 5.37 (dd, J = 15.1, 7.3 Hz, 1H), 4.18 (d, J = 7.8 Hz, 1H), 4.08 (t, J = 5.0 Hz, 1H), 4.01 (t, J = 7.5 Hz, 1H), 3.92 (m, 1H), 3.78 (d, J = 9.6 Hz, 1H), 3.63 (dd, J = 11.9, 5.0 Hz, 1H), 3.49 (d, J = 7.3 Hz, 1H), 3.35–3.26 (m, 2H), 3.18 (t, J = 8.5 Hz, 2H), 2.09 (t, J = 7.5 Hz, 2H), 1.92 (t, J = 11.0 Hz, 2H), 1.50 (m, 2H), 1.18 (m, 50H), 0.80 (t, J = 6.6 Hz, 6H); ^{13}C–NMR ($CDCl_3/CD_3OD$ = 3/1) δ 174.3, 134.0, 128.8, 102.7, 76.0, 75.8, 73.2, 71.6, 69.7, 68.2, 61.0, 52.9, 36.0 (2C), 31.9 (2C), 31.5 (2C), 29.3 (2C), 29.2 (3C), 29.1 (6C), 29.0 (3C), 28.9 (2C), 28.8 (2C), 25.5 (2C), 22.2 (2C), 13.4 (2C); HRMS (ESI-QTOF) calcd for $C_{42}H_{81}NO_8$: $[M+Na]^+$, 750.5854; found: 750.5861.

Compound 3b: To a stirring solution of compound **13α** (15.6 mg, 32.0 μmol) and stearic acid (13.7 mg, 48.0 μmol) in THF (400 μL) at room temperature was added HATU (18.2 mg, 48.0 μmol), Et_3N (14.1 μL, 64.0 μmol) and NMM (7.0 μL, 64.0 μmol). The mixture was stirred at room temperature for 20 h, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1 to 5/1) to afford **3b** (10.1 mg, 43%) as a white solid. ^{1}H NMR ($CDCl_3/CD_3OD$ = 10/1) δ 5.71–5.62 (m, 1H), 5.38 (dd, J = 15.4, 6.8 Hz, 1H), 4.86–4.80 (m, 1H), 4.09–4.00 (m, 2H), 3.95–3.80 (m, 3H), 3.77–3.57 (m, 5H), 2.14–2.07 (m, 2H), 2.02–1.90 (m, 2H), 1.53 (s, 2H), 1.29–1.08 (m, 50H), 0.87–0.80 (m, 6H); ^{13}C NMR ($CDCl_3/CD_3OD$ = 10/1) δ 174.7, 134.0, 128.9, 99.8, 77.5, 77.2, 76.9, 72.2, 70.5, 70.1, 69.6, 68.9, 67.5, 61.6, 53.6, 49.3, 49.1, 48.8, 48.6, 48.4, 48.2, 48.0, 36.4, 32.3 (3C), 31.8 (3C), 29.6 (3C), 29.4 (3C), 29.3 (2C), 29.2 (2C), 29.1 (2C), 25.8

(3C), 22.5 (4C), 13.8 (2C); HRMS (ESI-QTOF) calcd for $C_{42}H_{81}NO_8$: $[M+Na]^+$, 750.5854; found: 750.5862.

Compound 1c: To a stirring solution of compound **12β** (10.8 mg, 23.5 μmol) and nervonic acid (12.9 mg, 35.2 μmol) in EtOH (220 μL) and CH_2Cl_2 (70 μL) at room temperature was added DMT-MM (OTf) (14.4 mg, 37.6 μmol). The mixture was stirred for 16 h at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$, the whole was extracted with EtOAc and washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtrated, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1 to 5/1) to afford **1c** (4.2 mg, 22%) as a white solid. ^{1}H NMR ($CDCl_3$/CD_3OD = 3/1) δ 5.74–5.67 (m, 1H), 5.43 (dd, J = 15.4, 7.5 Hz, 1H), 5.33 (t, J = 4.5 Hz, 2H), 4.82 (d, J = 3.6 Hz, 1H), 4.08 (t, J = 8.1 Hz, 1H), 3.95–3.92 (m, 1H), 3.77 (t, J = 5.4 Hz, 1H), 3.67–3.62 (m, 2H), 3.53 (t, J = 2.6 Hz, 1H), 3.40 (dd, J = 9.6, 3.8 Hz, 1H), 3.29 (dt, J = 8.3, 4.3 Hz, 3H), 2.19–2.15 (m, 2H), 2.02 (d, J = 5.2 Hz, 6H), 1.57 (m, 2H), 1.28 (m, 54H), 0.89 (dd, J = 8.5, 4.7 Hz, 6H); ^{13}C NMR ($CDCl_3$/CD_3OD = 3/1) δ 174.3, 133.8 (2C), 129.4, 128.8, 99.0, 73.4, 71.7, 71.6, 71.5, 69.8, 66.8, 61.0, 53.2, 36.0, 32.0, 31.5 (4C), 29.3 (6C), 29.2 (3C), 29.1 (6C), 29.0 (2C), 28.9 (6C), 26.7, 25.5, 22.2, 13.5 (2C); HRMS (ESI-QTOF) calcd for $C_{48}H_{91}NO_8$: $[M+Na]^+$, 832.6637; found: 832.6642.

Compound 2c: To a stirring solution of compound **12β** (10.6 mg, 23.0 μmol) and nervonic acid (12.7 mg, 34.6 μmol) in EtOH (220 μL) and CH_2Cl_2 (70 μL) at room temperature was added DMT-MM (OTf) (14.4 mg, 36.9 μmol). The mixture was stirred for 16 h at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$, the whole was extracted with EtOAc and washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtrated, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1 to 5/1) to afford **2c** (6.6 mg, 35%) as a white solid. ^{1}H NMR ($CDCl_3$/CD_3OD = 3/1) δ 5.65–5.57 (m, 1H), 5.36 (dd, J = 15.3, 7.6 Hz, 1H), 5.30–5.22 (m, 2H), 4.18 (d, J = 7.9 Hz, 1H), 4.09 (dd, J = 10.1, 4.5 Hz, 1H), 4.01 (t, J = 7.6 Hz, 1H), 3.91 (dd, J = 8.9, 4.6 Hz, 1H), 3.78 (d, J = 12.1 Hz, 1H), 3.63 (dd, J = 12.0, 5.3 Hz, 1H), 3.49 (t, J = 5.0 Hz, 1H), 3.31 (dq, J = 22.0, 4.5 Hz, 2H), 3.17 (t, J = 8.4 Hz, 2H), 2.08 (t, J = 7.6 Hz, 2H), 1.93 (t, J = 6.2 Hz, 6H), 1.50 (m, 2H), 0.81 (dd, J = 15.6, 9.1 Hz, 6H); ^{13}C NMR ($CDCl_3$/CD_3OD = 3/1) δ 174.3, 133.9, 129.4 (2C), 128.8, 102.6, 76.0, 75.8, 73.2, 71.6, 69.7, 68.1, 61.0, 52.9, 36.0, 31.9, 31.5, 31.4, 29.3 (6C), 29.2 (3C), 29.1 (4C), 29.0 (4C), 28.9 (2C), 28.8 (4C), 26.7, 25.5, 25.5, 22.2, 13.4 (2C); HRMS (ESI-QTOF) calcd for $C_{48}H_{91}NO_8$: $[M+Na]^+$, 832.6637; found: 832.6645.

Compound 3c: To a stirring solution of compound **13α** (15.0, 30.8 μmol) and nervonic acid (16.9 mg, 46.1 μmol) in EtOH (290 μL) and CH_2Cl_2 (100 μL) at room temperature was added DMT-MM (OTf) (27.0 mg, 69.2 μmol). The mixture was stirred for 24 h at room temperature. The reaction was

quenched with saturated aqueous $NaHCO_3$, the whole was extracted with EtOAc and washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtrated, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1 to 5/1) to afford **3c** (11.2 mg, 45%) as a white solid. ^{1}H NMR ($CDCl_3$/CD_3OD = 10/1) δ 5.68–5.61 (m, 1H), 5.37 (dd, *J* = 15.3, 7.0 Hz, 1H), 5.28–5.23 (m, 2H), 4.80 (d, *J* = 3.6 Hz, 1H), 4.43–4.32 (m, 3H), 3.89–3.86 (m, 1H), 3.76–3.63 (m, 7H), 2.11 (t, *J* = 7.6 Hz, 2H), 1.96–1.92 (m, 6H), 1.51 (d, *J* = 6.7 Hz, 2H), 1.35–1.19 (m, 50H), 0.80 (t, *J* = 6.7 Hz, 6H); ^{13}C NMR ($CDCl_3$/CD_3OD = 10/1) δ 174.6, 134.0 (2C), 129.7, 129.0, 99.7, 77.6, 77.2, 76.9, 72.0, 70.5, 70.1, 69.6, 68.9, 67.4, 61.6, 53.6, 49.1, 48.9, 48.7, 48.5, 48.3, 48.1, 47.8, 36.3 (3C), 32.2 (3C), 31.7 (3C), 29.5 (3C), 29.4 (3C), 29.3 (3C), 29.2 (3C), 29.1 (3C), 27.0 (3C), 25.8 (3C), 22.5 (3C), 13.7 (2C); HRMS (ESI-QTOF) calcd for $C_{48}H_{91}NO_8$: $[M+Na]^+$, 832.6637; found: 832.6642.

Compound 1d: To a stirring solution of compound **12α** (15.5 mg, 33.6 μmol) and lignoceric acid (12.4 mg, 33.6 μmol) in THF (420 μL) at room temperature was added HATU (12.8 mg, 33.6 μmol), Et_3N (14.8 μL, 67.2 μmol) and NMM (7.4 μL, 67.2 μmol). The mixture was stirred at room temperature for 21 h, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1 to 5/1) to afford **1d** (6.3 mg, 23%) as a white solid. ^{1}H NMR ($CDCl_3$/CD_3OD = 3/1) *δ* 5.64 (dd, *J* = 14.1, 7.3 Hz, 1H), 5.36 (dd, *J* = 15.4, 7.1 Hz, 1H), 4.74 (d, *J* = 3.9 Hz, 1H), 4.03 (dd, *J* = 13.9, 7.1 Hz, 1H), 3.89 (m, 1H), 3.70 (t, *J* = 5.1 Hz, 2H), 3.64 (d, *J* = 8.8 Hz, 2H), 3.58 (t, *J* = 9.3 Hz, 1H), 3.46 (m, 1H), 3.37 (dd, *J* = 9.5, 3.7 Hz, 1H), 3.30 (t, *J* = 9.3 Hz, 1H), 2.09 (dt, *J* = 18.7, 7.0 Hz, 2H), 1.95 (d, *J* = 7.3 Hz, 2H), 1.51 (m, 2H), 1.30–1.04 (m, 62H), 0.80 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$/CD_3OD = 3/1) *δ* 174.3, 133.6, 128.8, 98.9, 73.3, 71.7, 71.6, 71.3, 69.7, 66.7, 60.9, 53.2, 35.9 (2C), 31.9 (2C), 31.4 (2C), 29.2 (6C), 29.1 (3C), 29.0 (6C), 28.9 (3C), 28.8 (6C), 25.5 (2C), 22.2 (2C), 13.4 (2C); HRMS (ESI-QTOF) calcd for $C_{42}H_{81}NO_8$: $[M+Na]^+$, 834.6793; found: 834.6802.

Compound 2d: To a stirring solution of compound **12β** (10.2 mg, 22.1 μmol) and lignoceric acid (8.10 mg, 22.1 μmol) in THF (280 μL) at room temperature was added HATU (8.4 mg, 22.1 μmol), Et_3N (9.7 μL, 44.2 μmol) and NMM (4.8 μL, 44.2 μmol). The mixture was stirred at room temperature for 20 h, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1 to 5/1) to afford **2d** (7.9 mg, 44%) as a white solid. ^{1}H NMR ($CDCl_3$/CD_3OD = 3/1) *δ* 5.60 (d, *J* = 15.4 Hz, 1H), 5.36 (dd, *J* = 15.4, 7.7 Hz, 1H), 4.18 (d, *J* = 7.7 Hz, 1H), 4.10 (dd, *J* = 10.0, 4.5 Hz, 1H), 4.00 (t, *J* = 7.7 Hz, 1H), 3.91 (m, 1H), 3.78 (t, *J* = 5.9 Hz, 1H), 3.64–3.57 (m, 1H), 3.55–3.47 (m, 1H), 3.29 (t, *J* = 3.2 Hz, 1H), 3.25–3.24 (m, 2H), 3.17 (dd, *J* = 10.2, 6.6 Hz, 1H), 2.21 (dd, *J* = 16.5, 9.3 Hz, 2H), 2.08 (t, *J* = 7.7 Hz, 2H), 1.93 (d, *J* = 6.8 Hz, 2H), 1.51 (d, *J* = 7.2 Hz, 2H), 1.33–1.09 (m, 58H), 0.79 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$/CD_3OD = 3/1) *δ* 174.3, 134.0, 128.8, 102.6, 76.0, 75.8, 73.2, 71.7, 69.7, 68.2, 61.0, 52.0, 36.1, 34.2 (2C), 32.0

(2C), 31.5 (2C), 29.3 (4C), 29.2 (6C), 29.1 (2C), 29.0 (2C), 28.9 (4C), 28.8 (4C), 25.6 (2C), 24.7 (2C), 22.2, 13.5 (2C); HRMS (ESI-QTOF) calcd for $C_{42}H_{81}NO_8$: $[M+Na]^+$, 834.6793; found: 834.6787.

Compound 3d: To a stirring solution of compound **13α** (15.1 mg, 31.0 μmol) and lignoceric acid (17 .1mg, 46.4 μmol) in THF (390 μL) at room temperature was added HATU (17.7 mg, 46.4 μmol), Et_3N (13.7 μL, 61.9 μmol) and NMM (6.8 μL, 61.9 μmol). The mixture was stirred at room temperature for 24 h, and then concentrated under reduced pressure to afford a residue, which was purified by silica gel column chromatography ($CHCl_3$/MeOH= 7/1 to 5/1) to afford **3d** (4.8 mg, 19%) as a white solid. ^{1}H NMR ($CDCl_3/CD_3OD$ = 10/1) δ 5.67–5.60 (m, 1H), 5.35 (dd, *J* = 15.3, 7.0 Hz, 1H), 4.78 (d, *J* = 3.8 Hz, 1H), 4.04–3.97 (m, 1H), 3.92–3.79 (m, 3H), 3.73–3.61 (m, 6H), 2.12–2.04 (m, 2H), 1.99–1.87 (m, 2H), 1.50 (s, 2H), 1.25 (m, 65H), 0.79 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3/CD_3OD$ = 10/1) *δ* 174.3, 133.6, 128.8, 98.9, 73.3, 71.7, 71.6, 71.3, 69.7, 66.7, 60.9, 53.2, 35.9 (2C), 31.9 (2C), 31.4 (2C), 29.2 (6C), 29.1 (3C), 29.0 (6C), 28.9 (3C), 28.8 (6C), 25.5 (2C), 22.2 (2C), 13.4 (2C); HRMS (ESI-QTOF) calcd for $C_{42}H_{81}NO_8$: $[M+Na]^+$, 834.6793; found: 834.6802.

AlphaScreen® assay for CD1d-Ligand Binding

The Mouse IgG Detection Kit (Perkin-Elmer Life Sciences) was used to determine CD1d-ligand interactions. Mouse CD1d:Ig fusion protein (BD Biosciences) in PBS containing 0.005% Tween 20 (final concentration: 5 nM, 10 μL/well) was mixed with anti-mouse IgG acceptor beads in PBS containing 0.005% Tween 20 (final concentration: 10 μg/mL, 10 μL/well). After 60 min, Biotinyl-PE (Avanti) in PBS containing 0.005% Tween 20, 1% DMSO and 1% EtOH (final concentration; 2 mM, 10 μL/well), and ligands in PBS containing 0.005% Tween 20 and 3% DMSO (final concentration range: 3-10000 nM, 10 mL/well) were added to the plate. After incubation at 37 °C for 23 h, Streptavidin Donor beads in PBS containing 0.005% Tween 20 (final concentration: 10 μg/mL, 10 μL/well) was added, and incubated for another 60 min. Samples were measured at 520-620 nm in a Spark® 10M microplate reader (TECAN).

APC (Antigen Presenting Cell)-free Assay for CD1d-Ligand Binding

Initially, 96-well microplates (multiwell plate 96F, Sumitomo Bakelite Co., Ltd.) were coated with mouse CD1d:Ig fusion protein (0.25 μg/well, BD Biosciences) in PBS (100 μL) at 37 °C for 24 h. After washing with PBS, various concentrations of ligand solution were added and incubated at 37 °C for 24 h. The above ligand solution was prepared by diluting the ligand stock solution in DMSO with PBS containing DMSO and Triton®X-100 (the final concentration: 1% DMSO and 0.005% Triton®X-100). After washing with PBS, 2E10 NKT hybridoma cells (5.0×10^4 cells/well, Ref.: Nyambayar, D.; Iwabuchi, K.; Hedlund, E.; Murakawa, S.; Shirai, K.; Iwabuchi, C.; Kon, Y.; Miyazaki, Y.; Yanagawa, Y.; Onoe, K. *J. Clin. Exp. Hematop.* **2007**, *47*, 1-8.) were added and cultured

at 37 °C for 48 h. IL-2 in the supernatant was measured by ELISA kit (Biolegend).

Cytokine Secretion Assay Using Mouse Splenocyte

Spleen cell suspension (from C57BL/6*J* mice) was prepared in complete medium (RPMI 1640 media supplemented with 5% fetal bovine serum (FBS), and 1% penicillin-streptomycin) and seeded into 96 well plates (6.0×10^5 cells/well). Ligands were added and incubated at 37 °C for 50 h. IFN-γ, IL-4, IL-10 and IL-17A in the supernatant were measured by ELISA kit (Biolegend).

Cytokine Secretion Assay Using Mouse Splenocyte (inhibition of α-GalCer)

Spleen cell suspension (from C57BL/6*J* mice) was prepared in complete medium (RPMI 1640 media supplemented with 5% fetal bovine serum (FBS), and 1% penicillin-streptomycin) and seeded into 96 well plates (6.0×10^5 cells/well). The mixtures of a-GalCer (100 nM) and ligand were added and incubated at 37 °C for 50 h. IFN-γ in the supernatant were measured by ELISA kit (Biolegend).

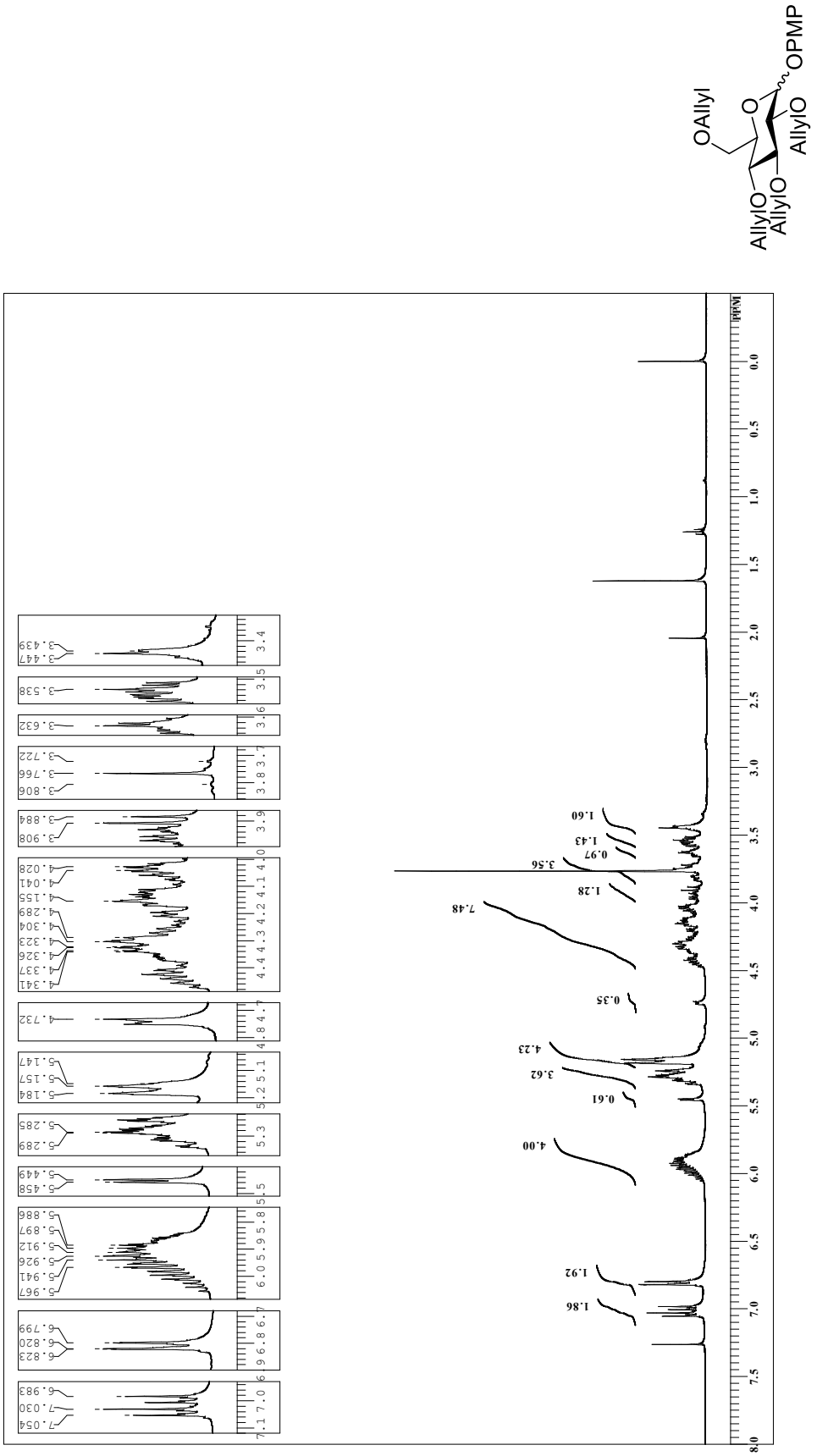
Mincle Reporter Assay[4]

The ligands were dissolved in CH_2Cl_2/MeOH (2/1) at 1 mM, were diluted in isopropanol and added to 96-well plates with the indicated concentrations, followed by evaporation of the solvent. The 2B4 NFAT-GFP reporter cells expressing human Mincle/FcRγ were seeded before incubation at 37 °C for 18 h. The activation of NFAT-GFP reporter cells was monitored by flow cytometry.

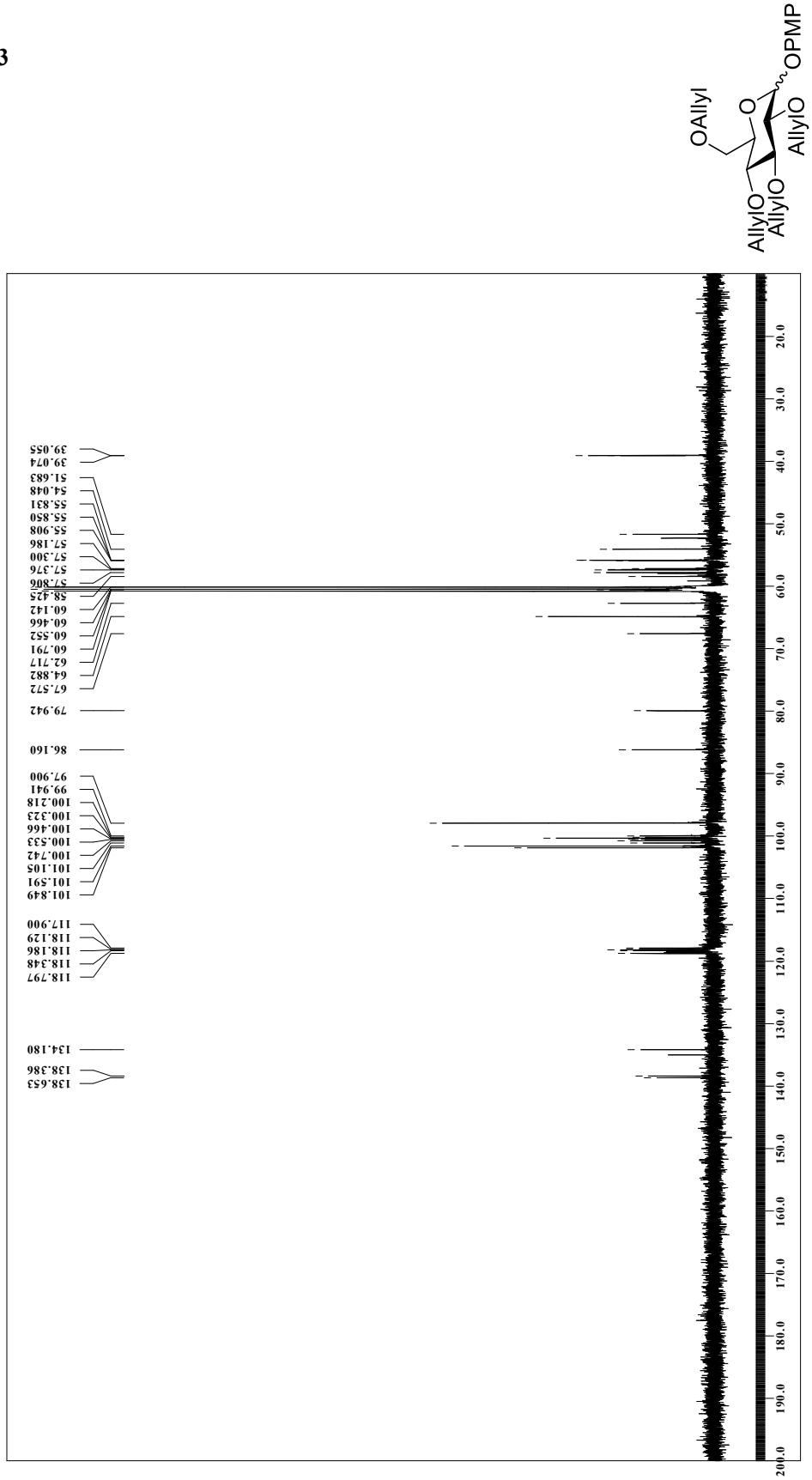
References

1) (a) Meng, X. B.; Yang, L. D.; Li, H.; Li, Q.; Cheng, T. M.; Cai, M. S.; Li, Z. J. *Carbohydr. Res.* **2002,** *337*, 977-981. (b) Dasgupta, S.; Rajput, V. K.; Roy, B.; Mukhopadhyay, B. *J. Carbohydr. Chem.* **2007,** *26*, 91-106.
2) Strelkov, I. S. et al. *J. Org. Chem*. **2009**, *74*, 8669.
3) Cairo, C. W.; Sandbhor, M. S.; Key, J. A.; Strelkov, I. S. *J. Org. Chem*. **2009**, *74*, 8669.
4) Yamasaki, S.; Ishikawa, E.; Sakuma, M.; Hara, H.; Ogata, K.; Saito, T. *Nat. Immunol.* **2008**, *9*, 1179-1188.

Compound **S3**


OAllyl
O
OPMP
AllylO
AllylO
AllylO
1.86
1.92
4.00
0.61
3.62
4.23
0.35
7.48
1.28
3.56
0.97
1.43
1.60
PPM

Compound **S3**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O
OPMP
AllylO
AllylO
AllylO
39.055
39.074
51.683
54.048
55.831
55.850
55.908
57.186
57.300
57.376
57.806
58.425
60.142
60.466
60.552
60.791
62.717
64.882
67.572
79.942
86.160
97.900
99.941
100.218
100.323
100.466
100.533
100.742
101.105
101.591
101.849
117.900
118.129
118.186
118.348
118.797
134.180
138.386
138.653
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
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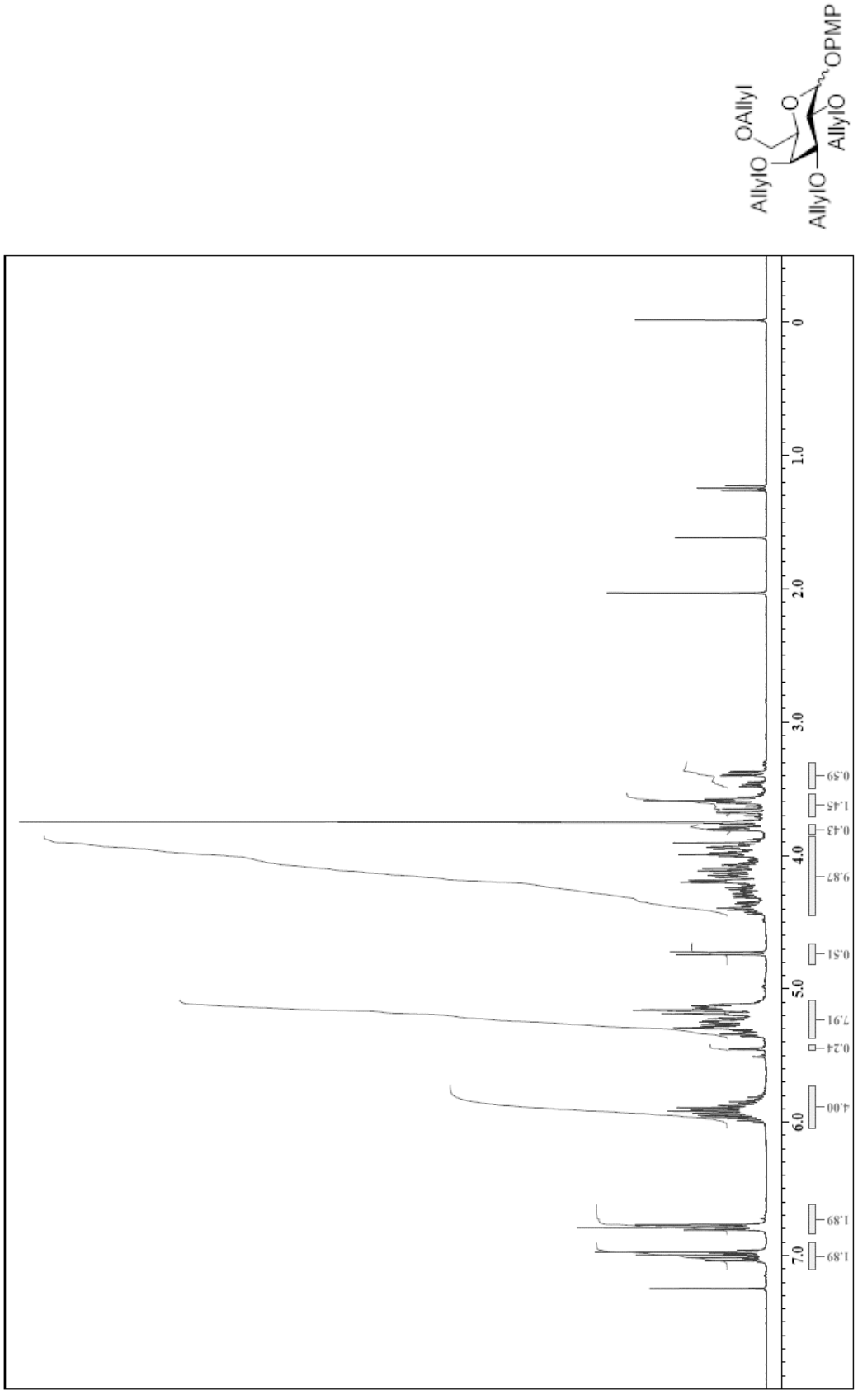
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0

Compound **S4**


AllylO
OAllyl
O
AllylO
AllylO
OPMP
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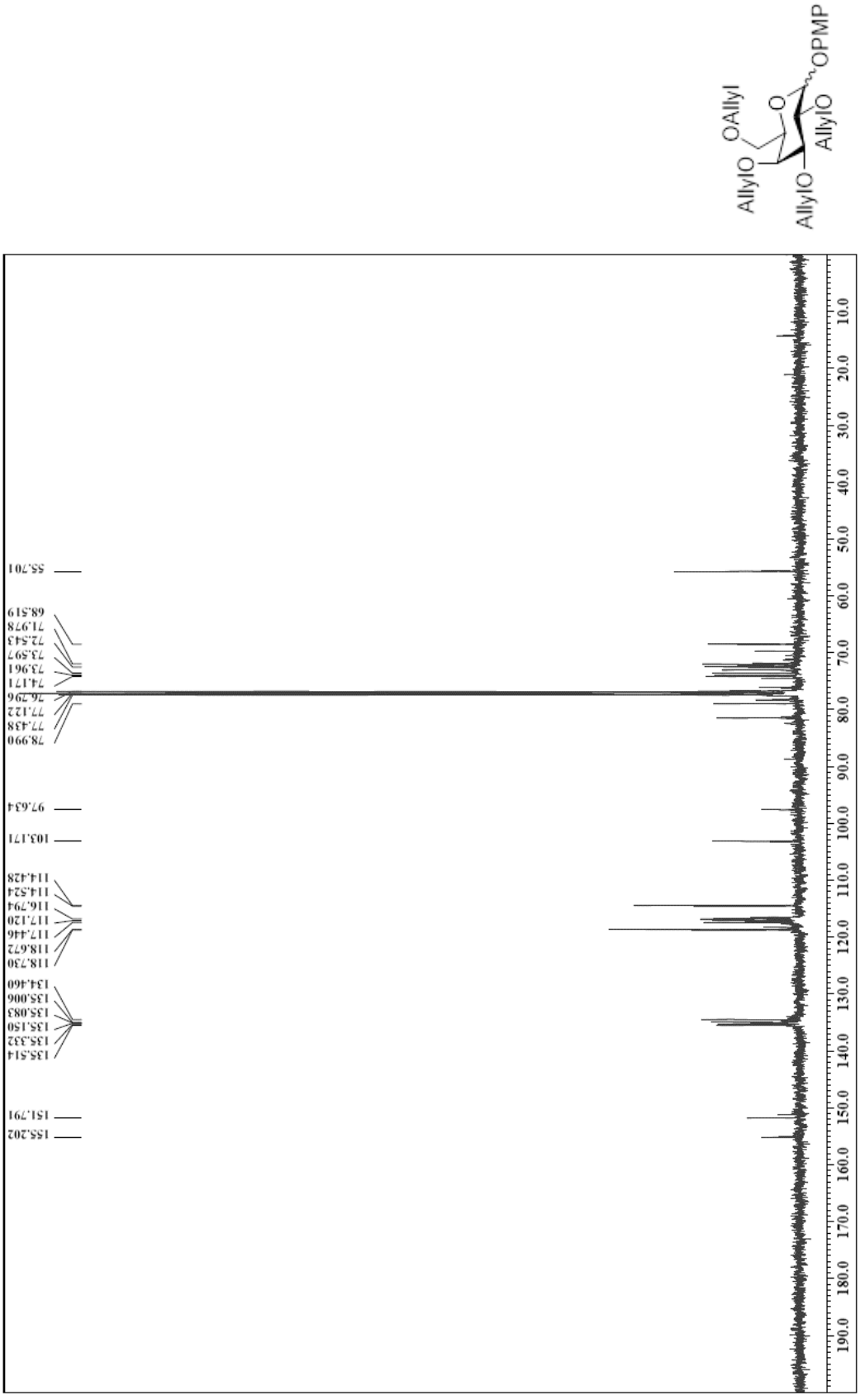
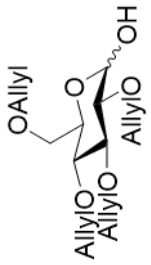
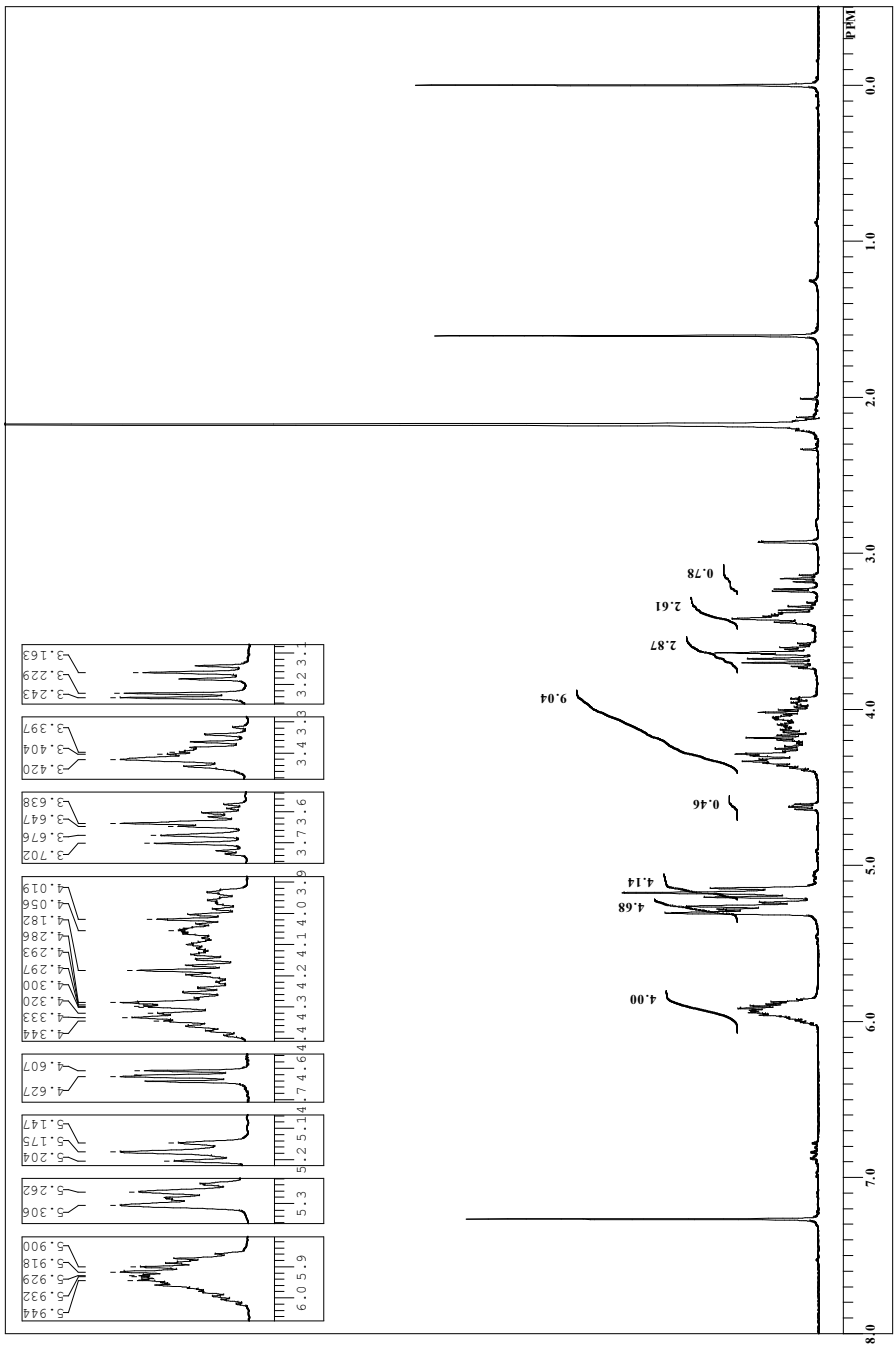
6.0
5.0
4.0
3.0
2.0
1.0
0
1.89
1.89
4.00
0.24
7.91
0.51
9.87
0.43
1.45
0.59

Compound **S4**

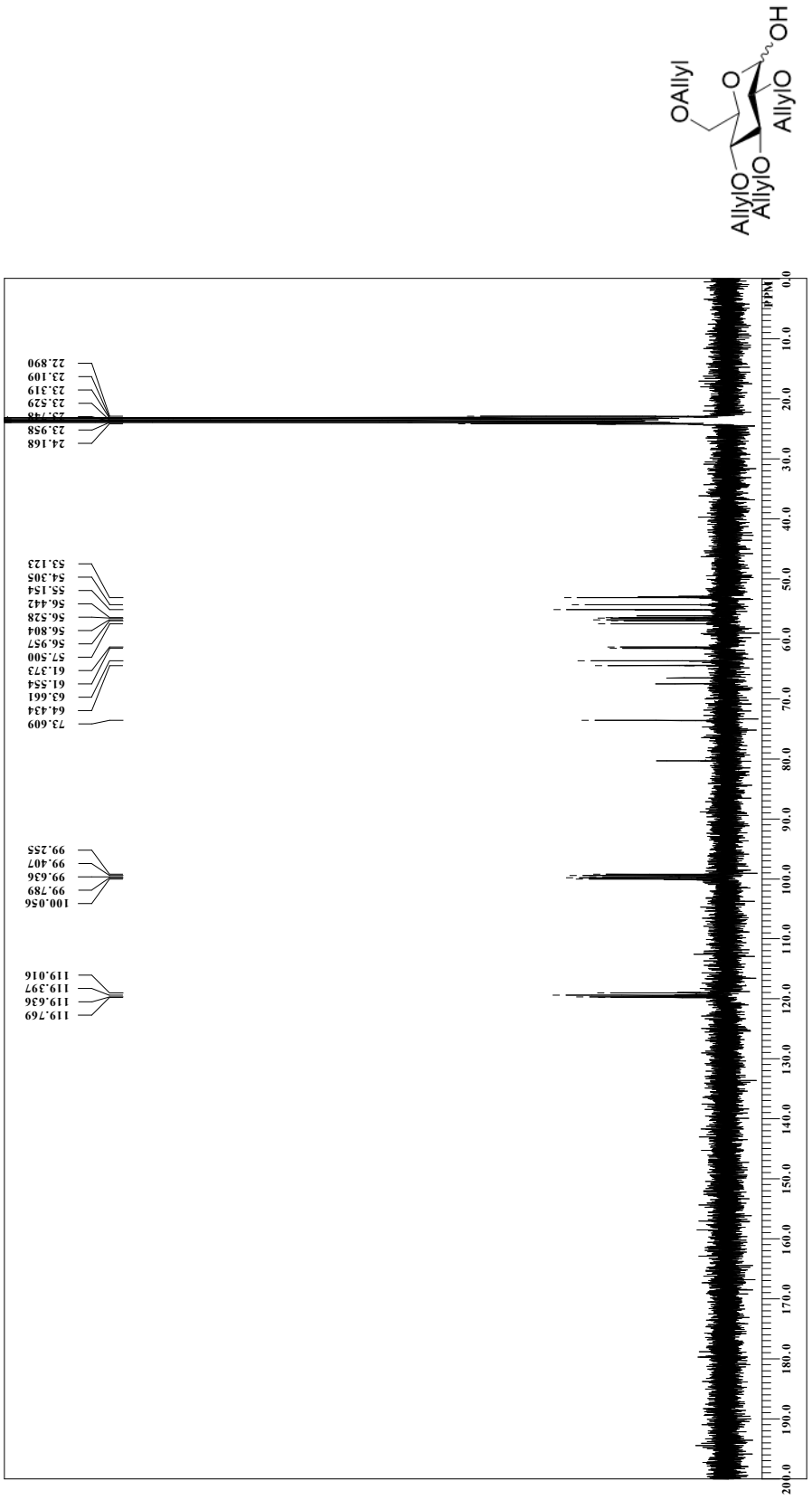

AllylO
OAllyl
O
AllylO
AllylO
OPMP
55.701
68.519
71.978
72.543
73.597
73.961
74.171
76.796
77.122
77.438
78.990
97.634
103.171
114.428
114.524
116.794
117.120
117.446
118.672
118.730
134.460
135.006
135.083
135.150
135.332
135.514
151.791
155.202
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0

Compound **S5**

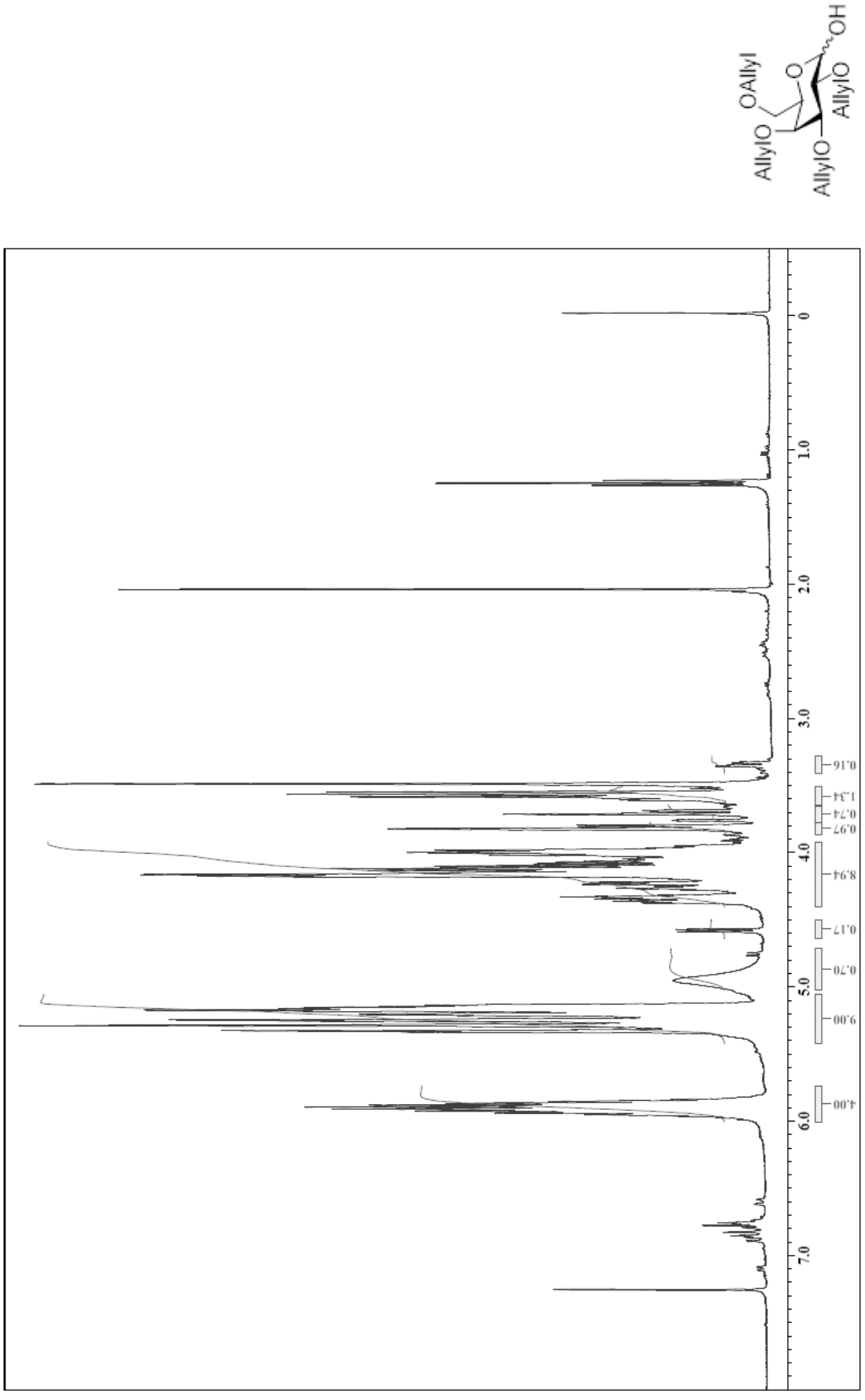

OAllyl
O
OH
AllylO
AllylO
AllylO


PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
0.78
2.61
2.87
9.04
0.46
4.14
4.68
4.00
3.163
3.229
3.243
3.397
3.404
3.420
3.638
3.647
3.676
3.702
4.019
4.056
4.182
4.286
4.293
4.297
4.300
4.320
4.333
4.344
4.607
4.627
5.147
5.175
5.204
5.262
5.306
5.900
5.918
5.929
5.932
5.944

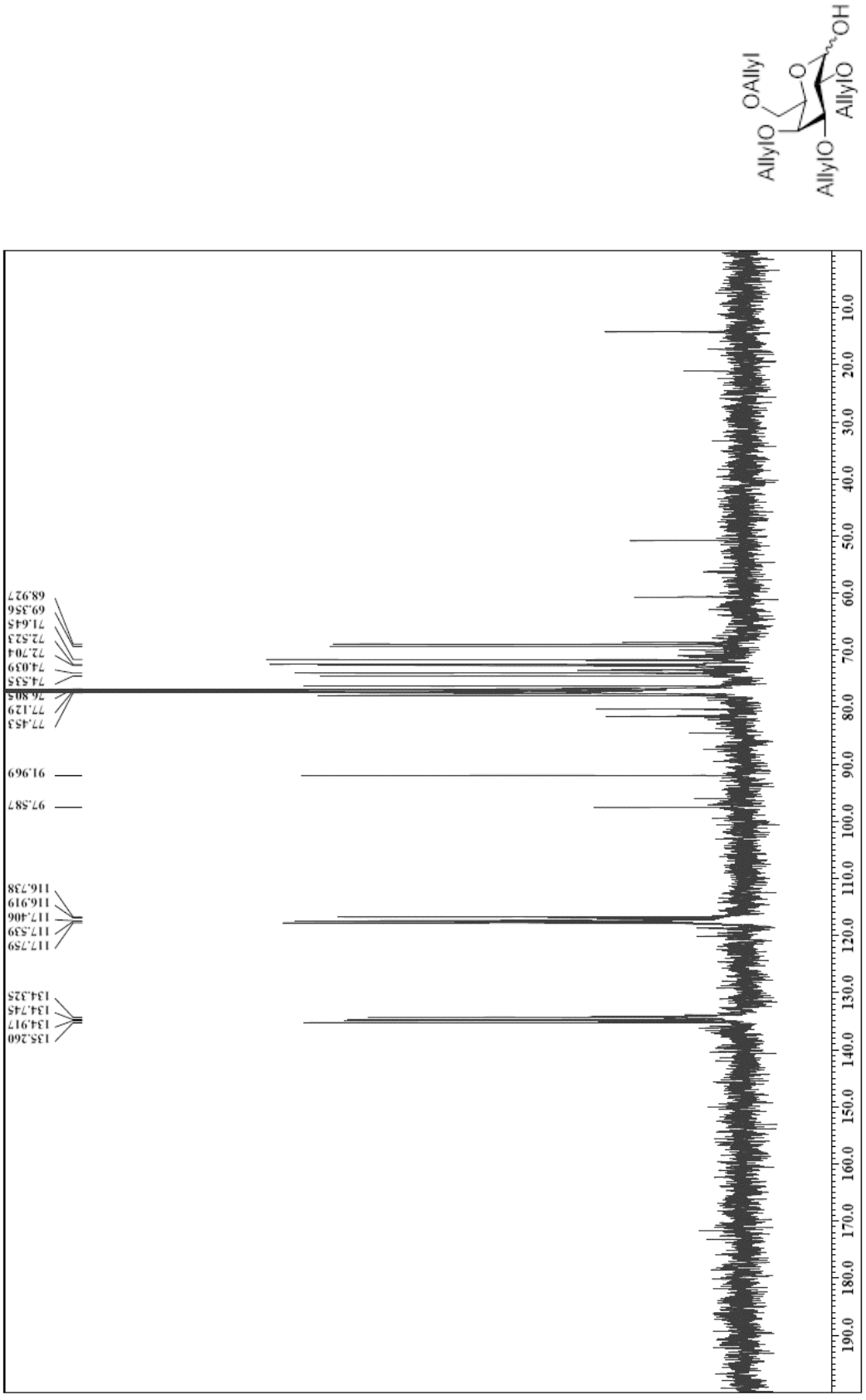
Compound **S5**


OAllyl
O
OH
AllylO
AllylO
AllylO
PPM
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
22.890
23.109
23.319
23.529
23.748
23.958
24.168
53.123
54.305
55.154
56.442
56.528
56.804
56.957
57.500
61.373
61.554
63.661
64.434
73.609
99.255
99.407
99.636
99.789
100.056
119.016
119.397
119.636
119.769

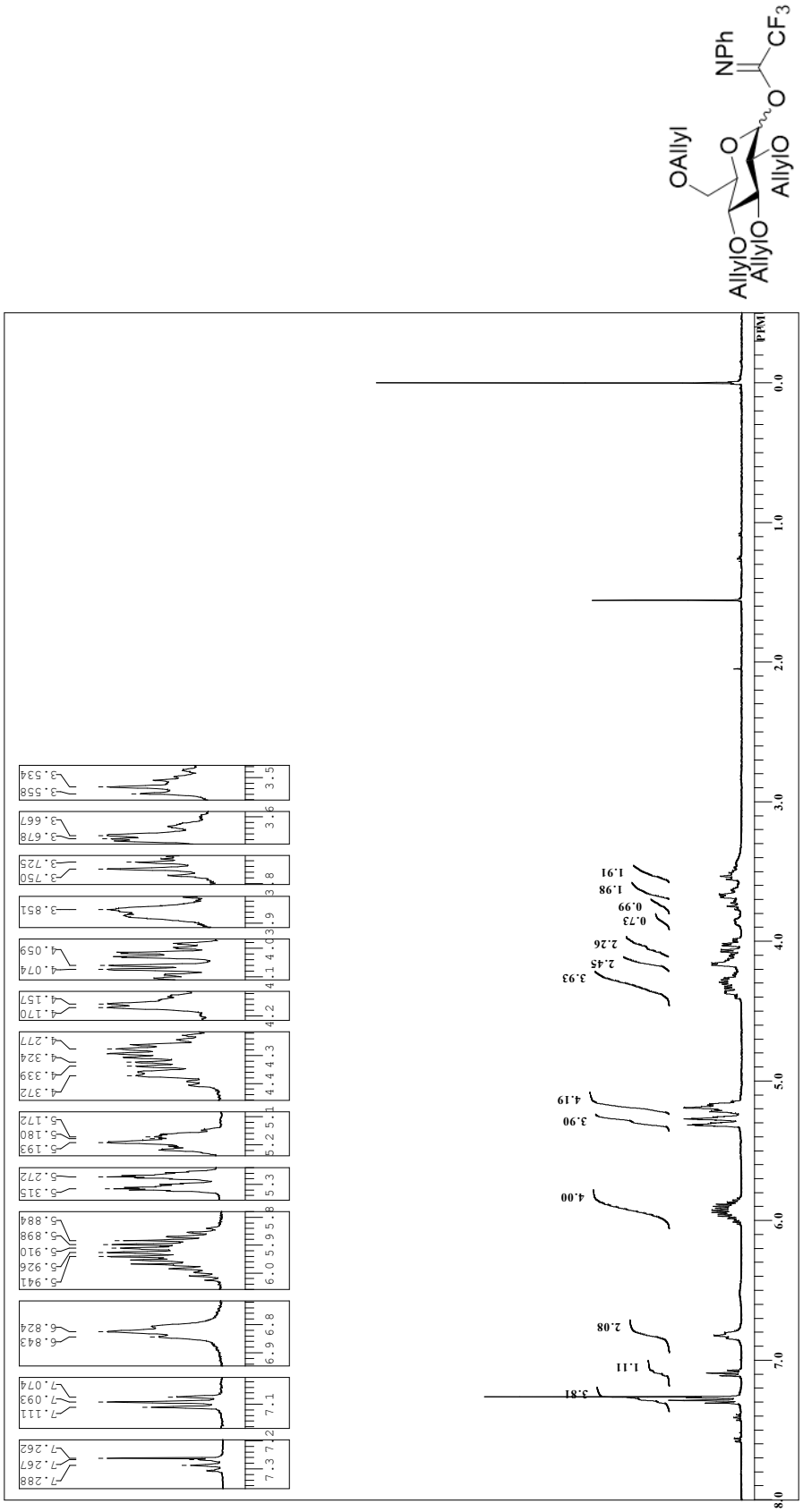
Compound **S6**


AllylO
OAllyl
O
AllylO
AllylO
OH
0.16
1.34
0.74
0.97
8.94
0.17
0.70
9.00
4.00
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0

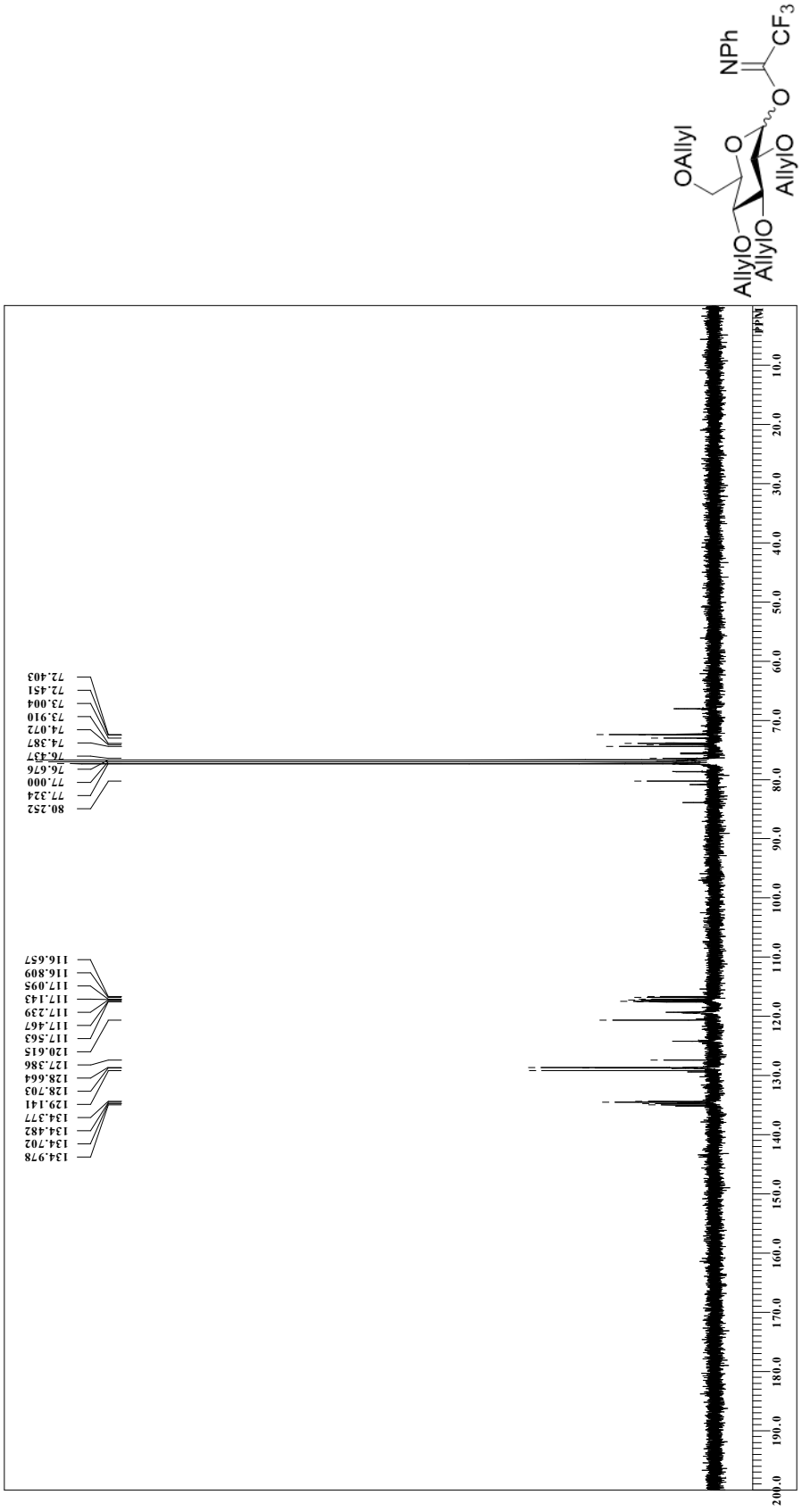
Compound **S6**


AllylO
OAllyl
O
OH
AllylO
AllylO
135.260
134.917
134.745
134.325
117.759
117.539
117.406
116.919
116.738
97.587
91.969
77.453
77.129
76.805
74.535
74.039
72.704
72.523
71.645
69.356
68.927

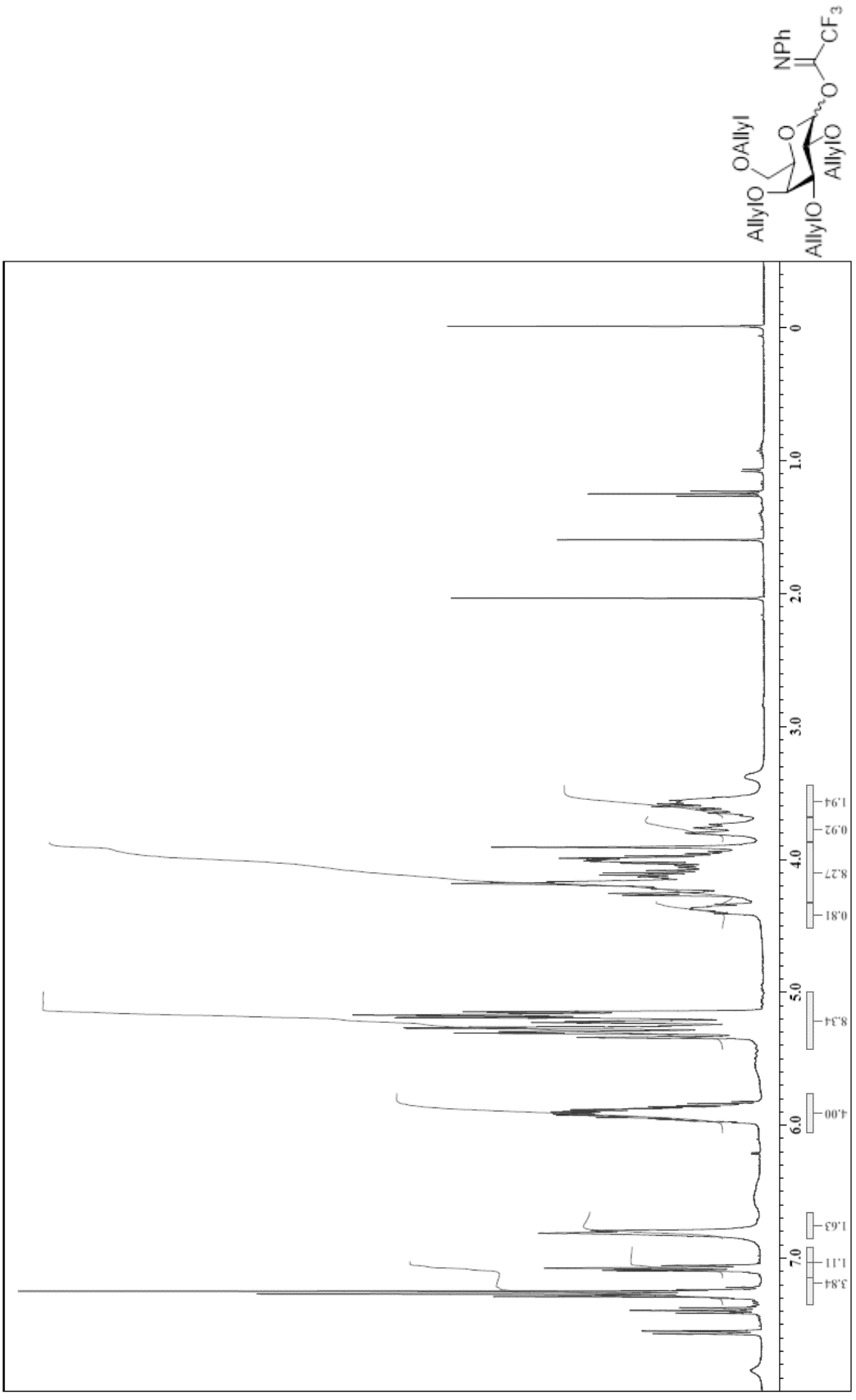
Compound **4**


OAllyl
AllylO
AllylO
AllylO
O
O
NPh
CF3
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
3.81
1.11
2.08
4.00
3.90
4.19
3.93
2.45
2.26
0.73
0.99
1.98
1.91

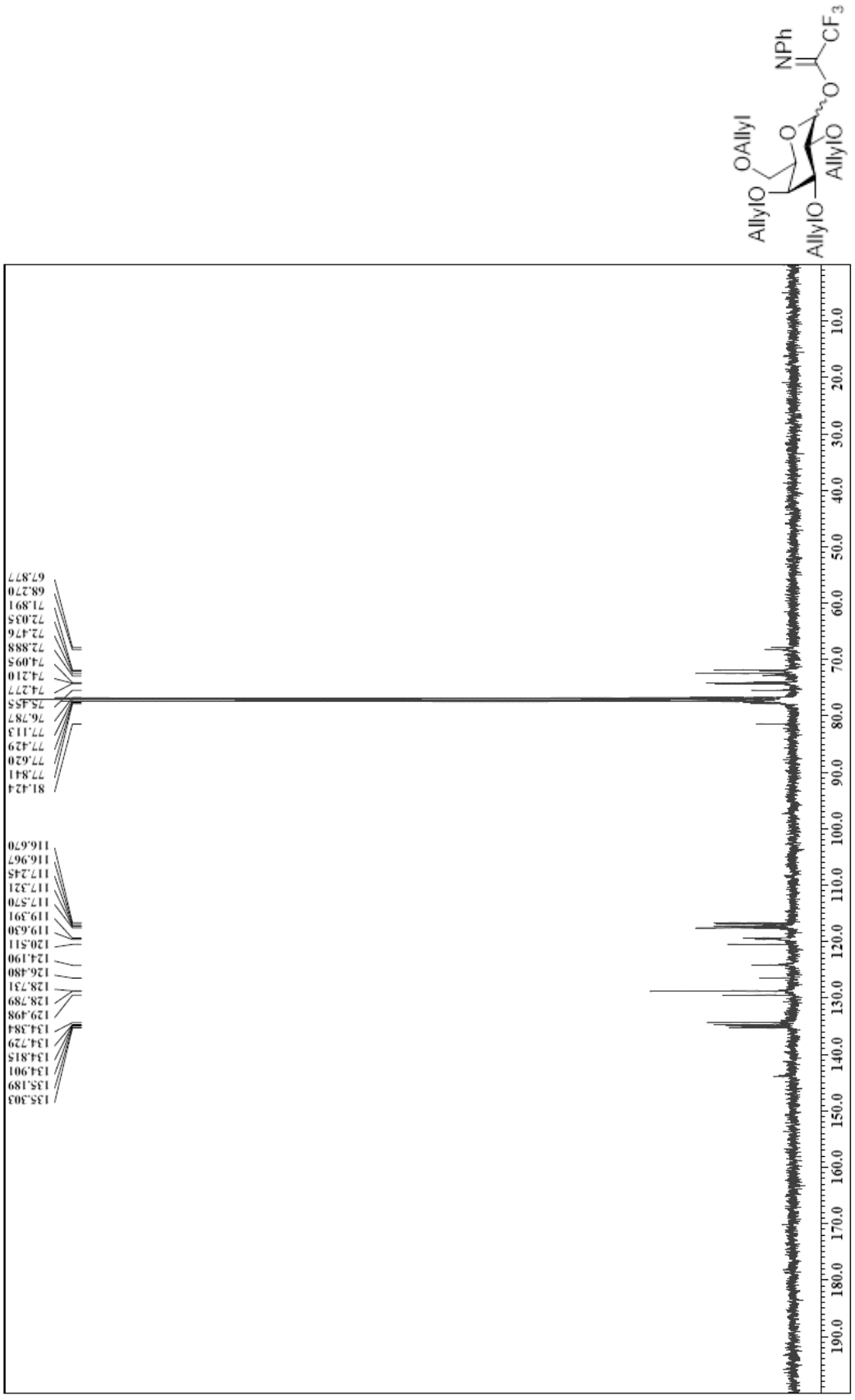
Compound **4**


NPh
CF3
O
OAllyl
O
AllylO
AllylO
AllylO
80.252
77.324
77.000
76.676
76.437
74.387
74.072
73.910
73.004
72.451
72.403
134.978
134.702
134.482
134.377
129.141
128.703
128.664
127.386
120.615
117.563
117.467
117.239
117.143
117.095
116.809
116.657
PPM
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0

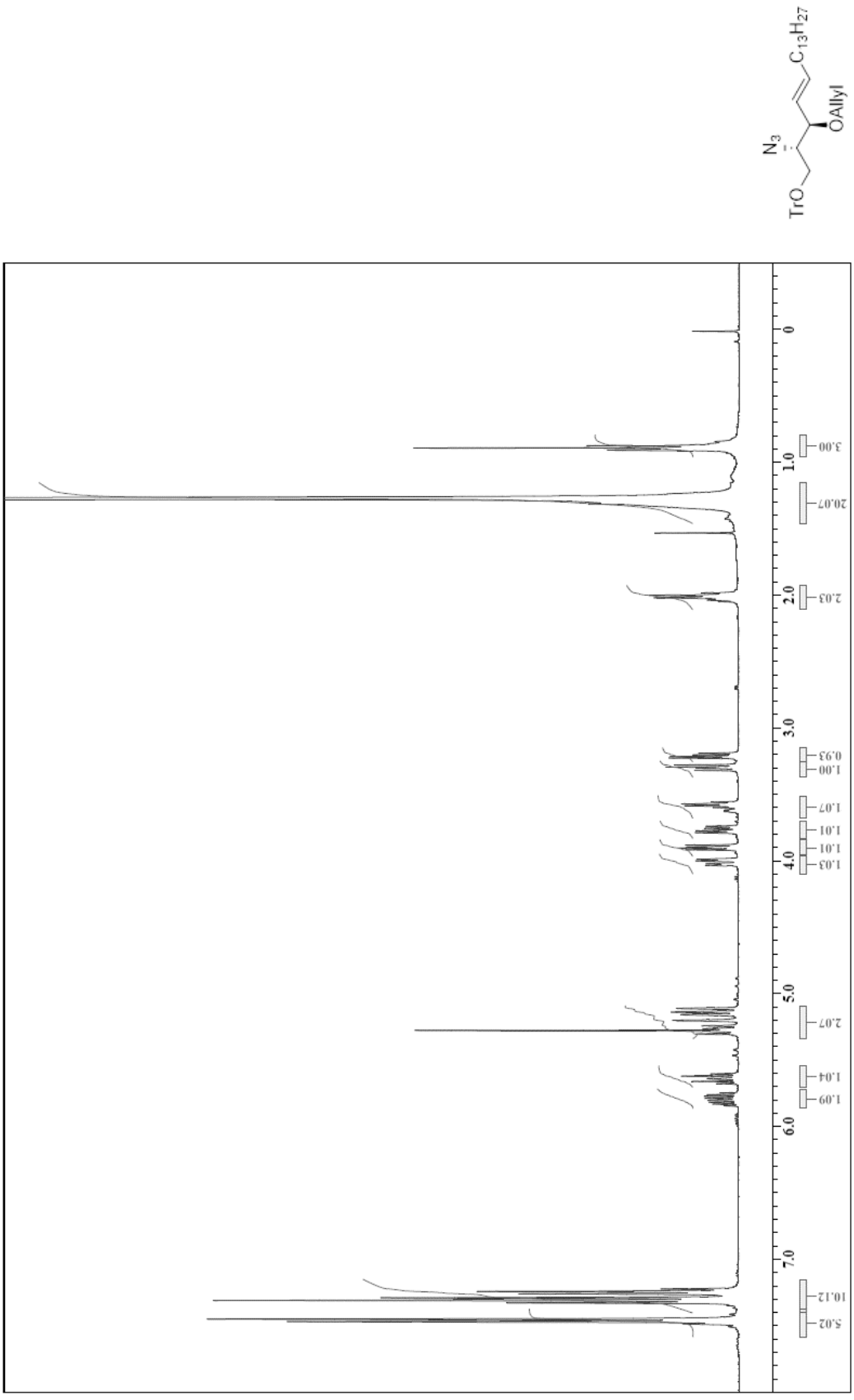
Compound **5**


AllylO
OAllyl
O
AllylO
AllylO
O
NPh
CF3
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
0.81
8.27
0.92
1.94
8.34
4.00
1.63
1.11
3.84

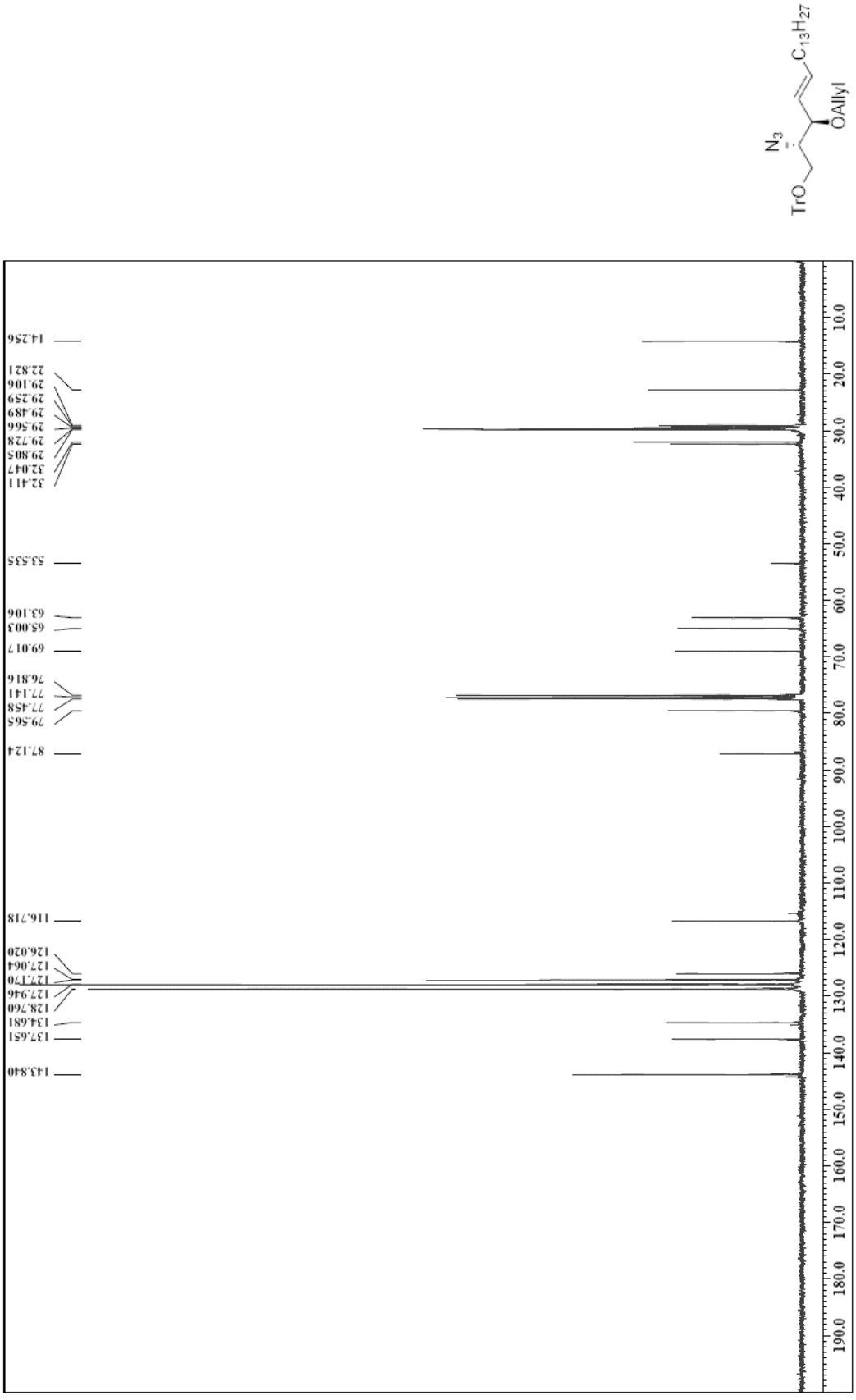
Compound **5**


AllylO
OAllyl
O
AllylO
AllylO
O
NPh
CF3
67.877
68.270
71.891
72.035
72.476
72.888
74.095
74.210
74.277
75.455
76.787
77.113
77.429
77.620
77.841
81.424
116.670
116.967
117.245
117.321
117.570
119.391
119.630
120.511
124.190
126.480
128.731
128.789
129.498
134.384
134.729
134.815
134.901
135.189
135.303
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0

Compound **S8**


TrO
N3
OAllyl
C13H27
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
3.00
20.07
2.03
0.93
1.00
1.07
1.01
1.01
1.03
2.07
1.04
1.09
10.12
5.02

Compound **S8**


TrO
N3
OAllyl
C13H27
14.256
22.821
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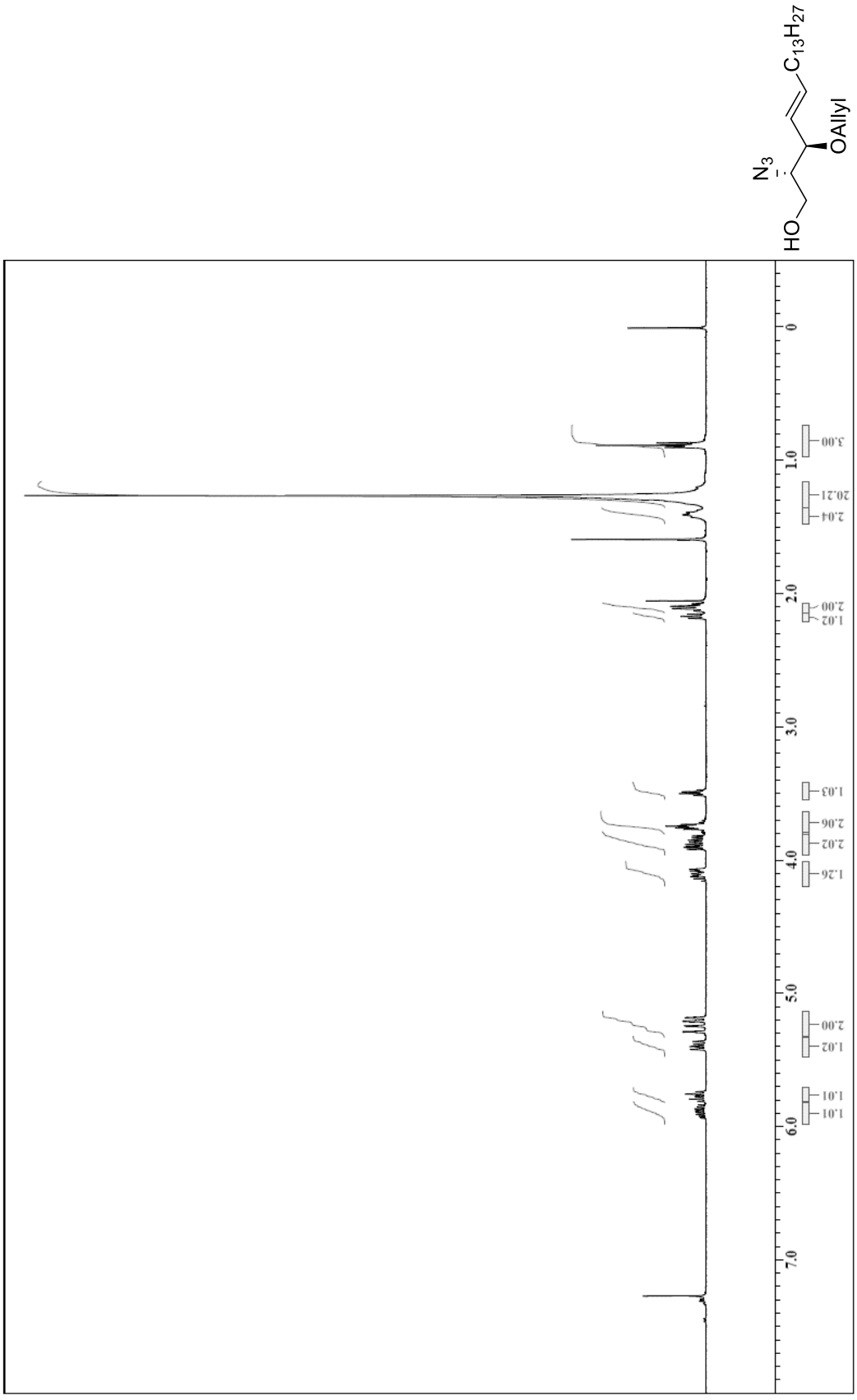
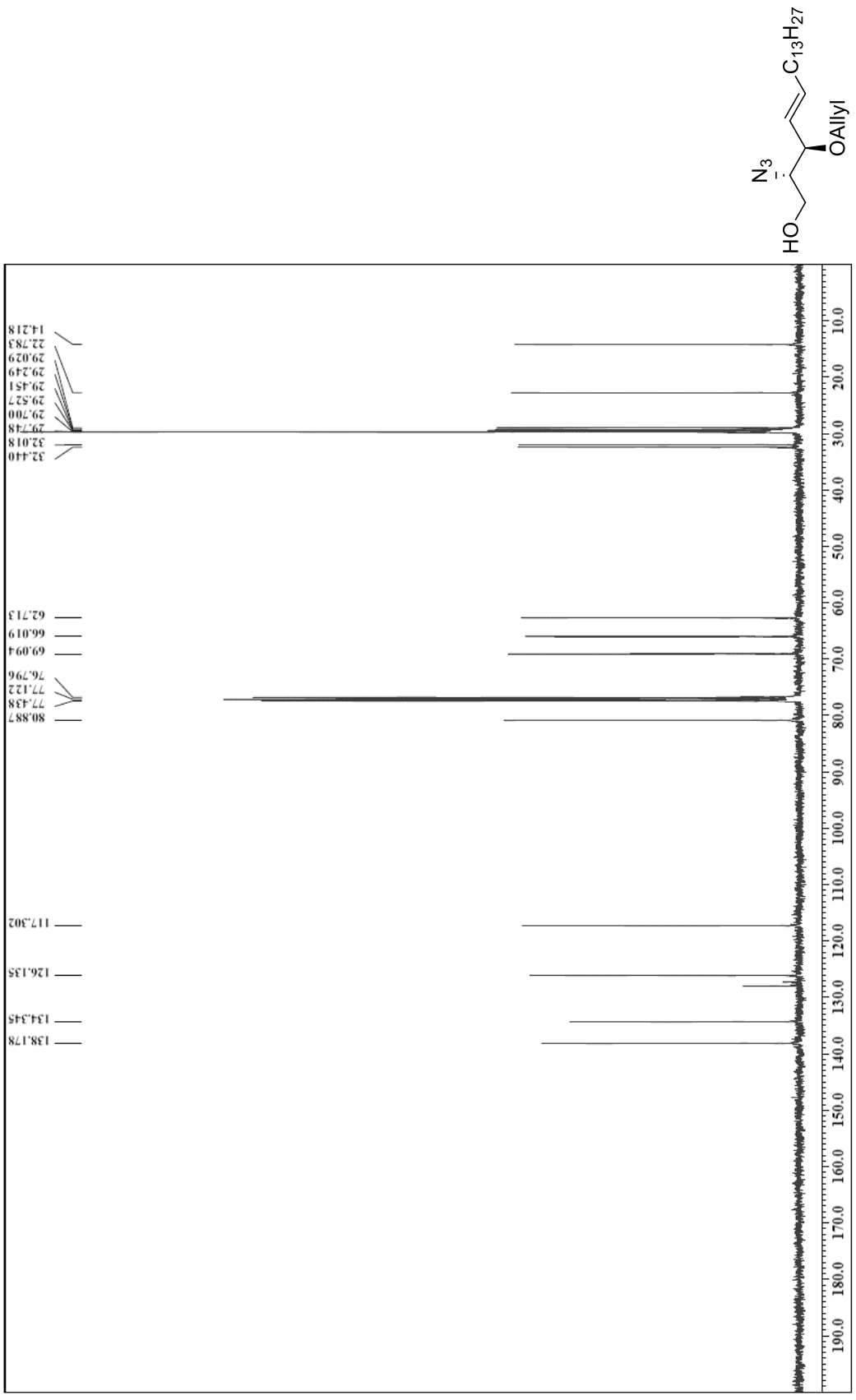
29.259
29.489
29.566
29.728
29.805
32.047
32.411
53.535
63.106
65.003
69.017
76.816
77.141
77.458
79.565
87.124
116.718
126.020
127.064
127.170
127.946
128.760
134.681
137.651
143.840

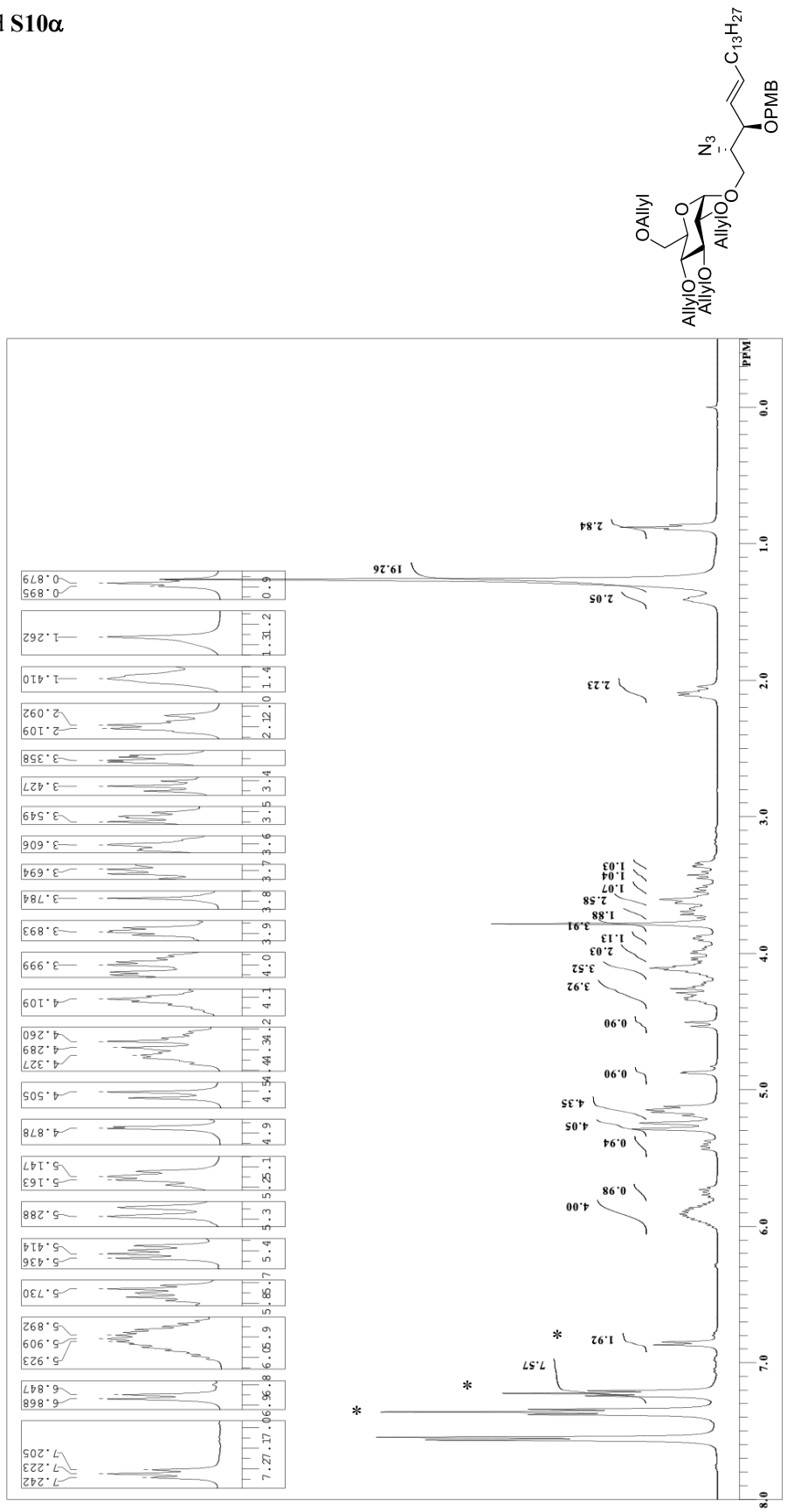
Compound **6**


HO
N3
OAllyl
C13H27
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
3.00
20.21
2.04
1.02
2.00
1.03
2.06
2.02
1.26
1.02
2.00
1.01
1.01

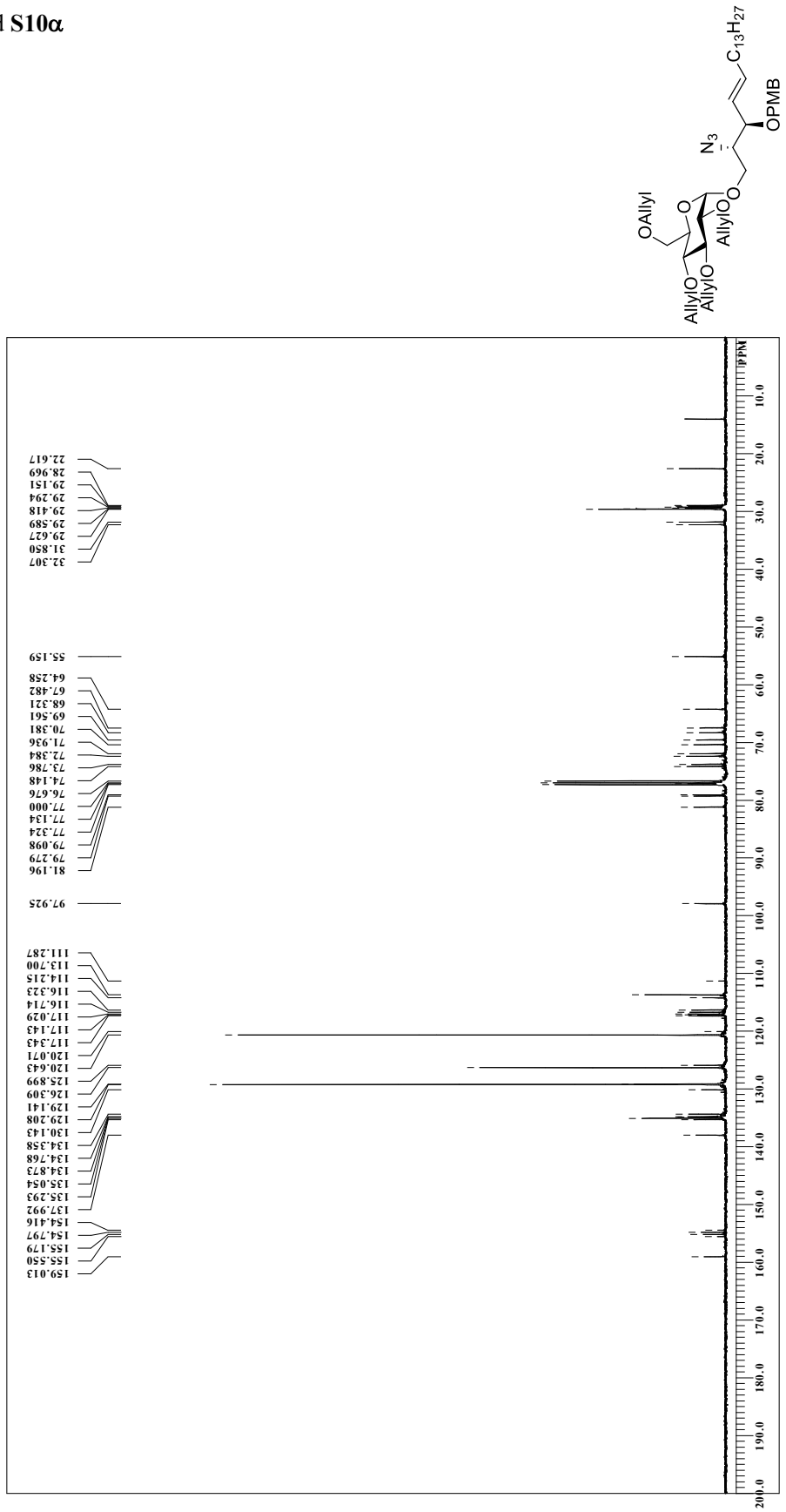
Compound **6**


C13H27
OAllyl
N3
HO
14.218
22.783
29.029
29.249
29.451
29.527
29.700
29.748
32.018
32.440
62.713
66.019
69.094
76.796
77.122
77.438
80.887
117.302
126.135
134.345
138.178

Compound **S10α**



Compound **S10α**



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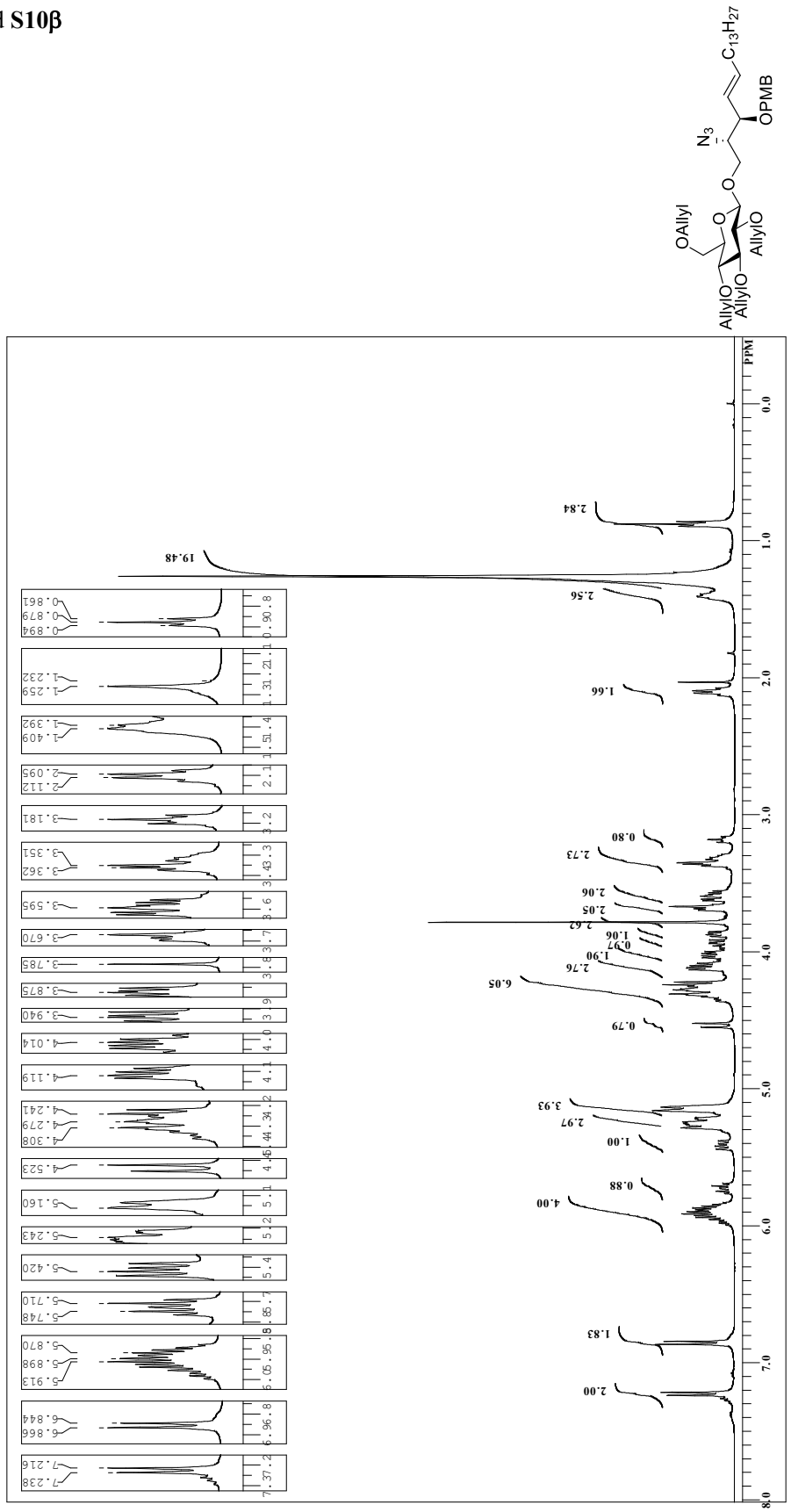
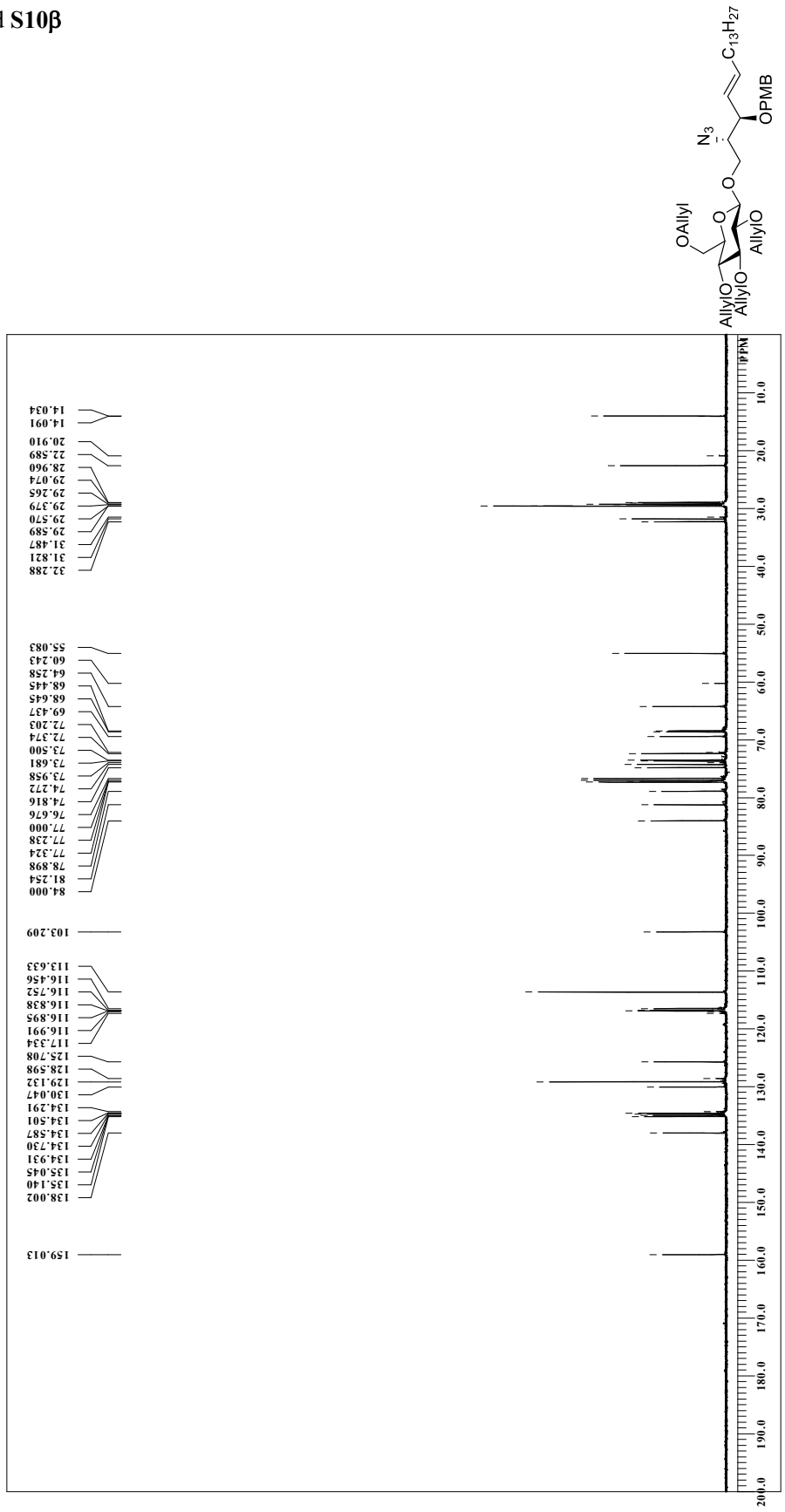
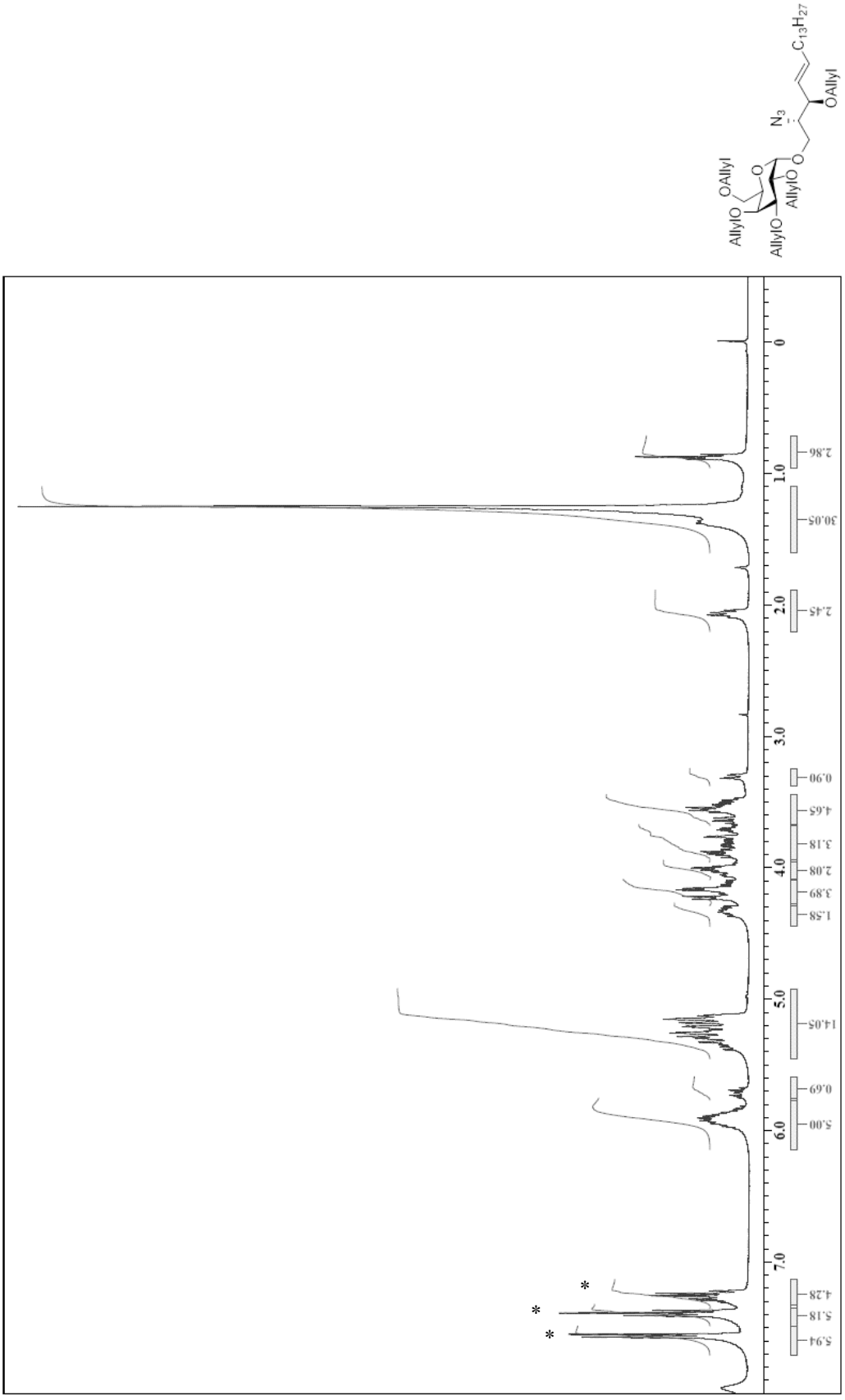


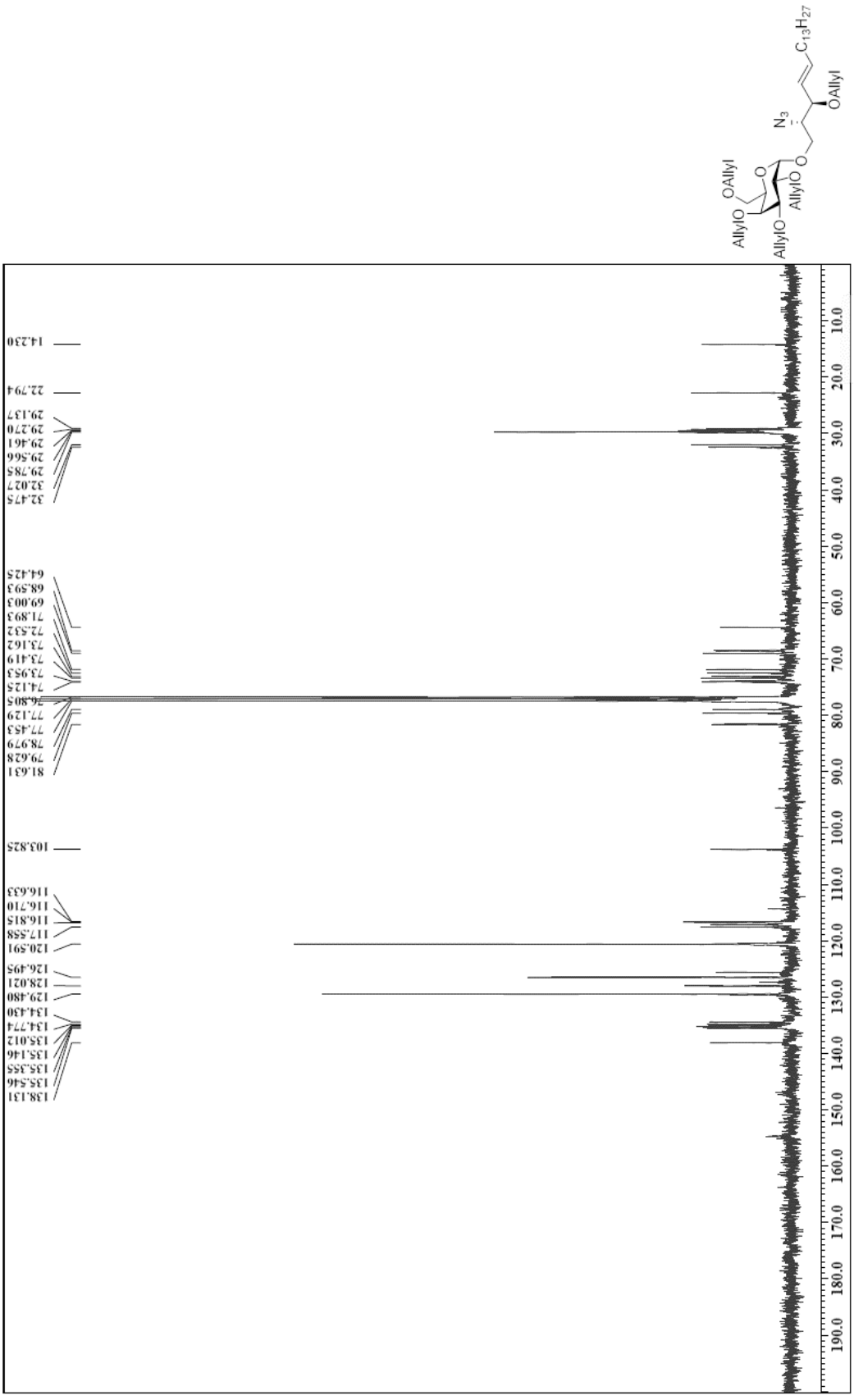
Compound **S10β**



Compound **7α**


AllylO
OAllyl
AllylO
AllylO
O
O
N3
C13H27
OAllyl
*
*
*
5.94
5.18
4.28
7.0
0.69
5.00
6.0
14.05
5.0
1.58
3.89
2.08
3.18
4.65
0.90
4.0
3.0
2.45
2.0
30.05
1.0
2.86
0

Compound **7α**


AllylO
OAllyl
AllylO
AllylO
O
O
N3
C13H27
OAllyl
14.230
22.794
29.137
29.270
29.461
29.566
29.785
32.027
32.475
64.425
68.593
69.003
71.893
72.532
73.162
73.419
73.953
74.125
76.805
77.129
77.453
78.979
79.628
81.631
103.825
116.633
116.710
116.815
117.558
120.591
126.495
128.021
129.480
134.430
134.774
135.012
135.146
135.355
135.546
138.131
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
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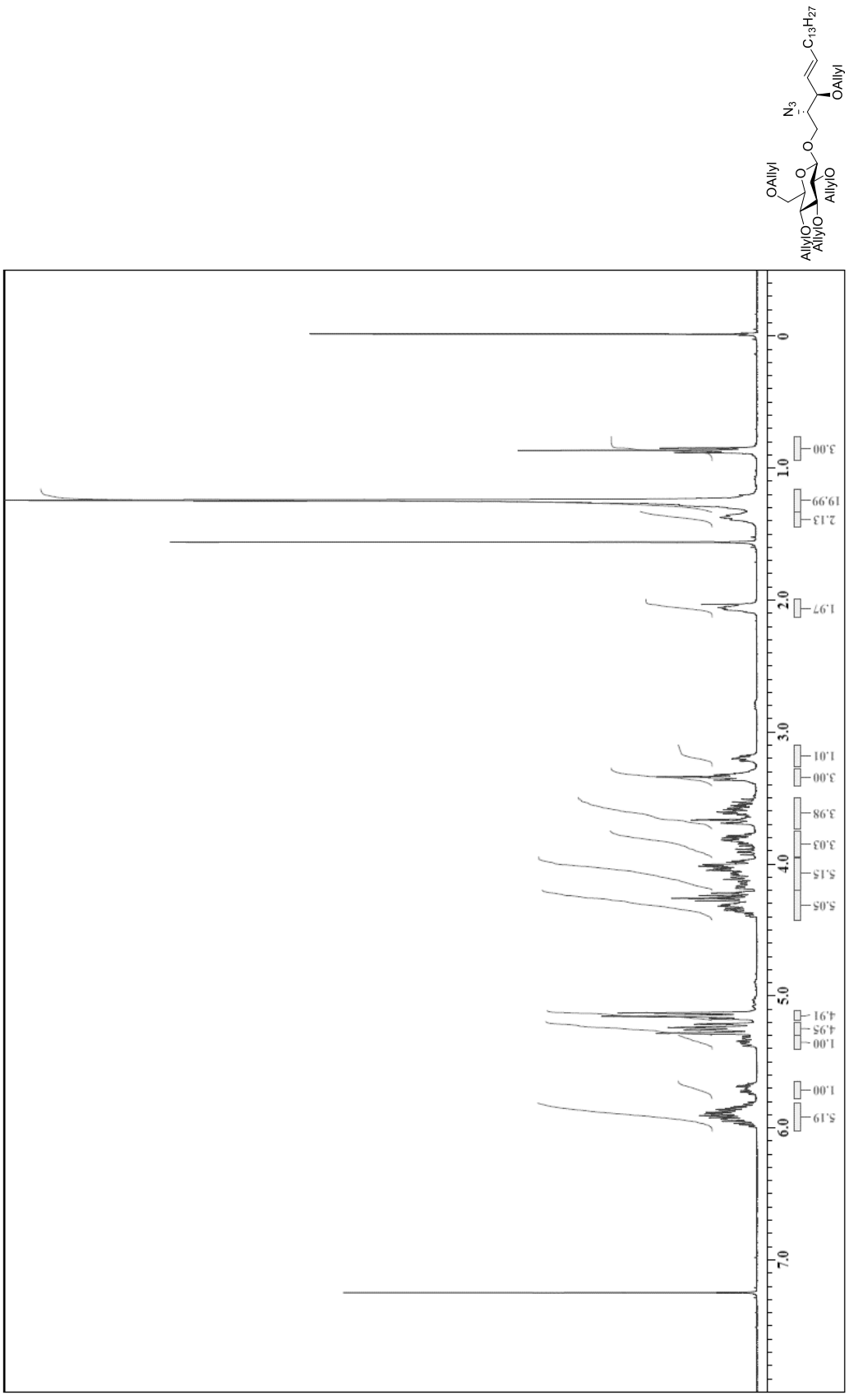
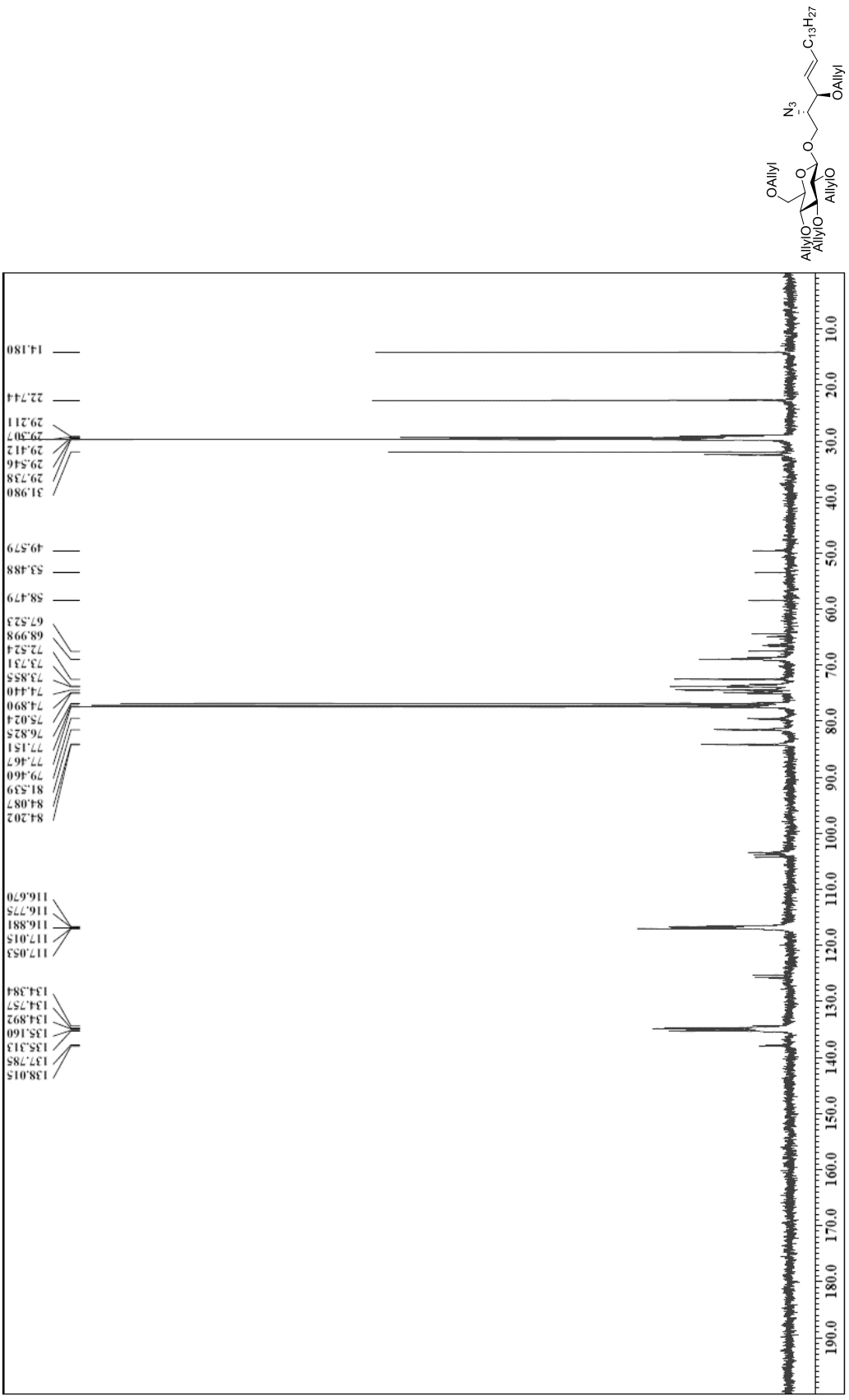
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0

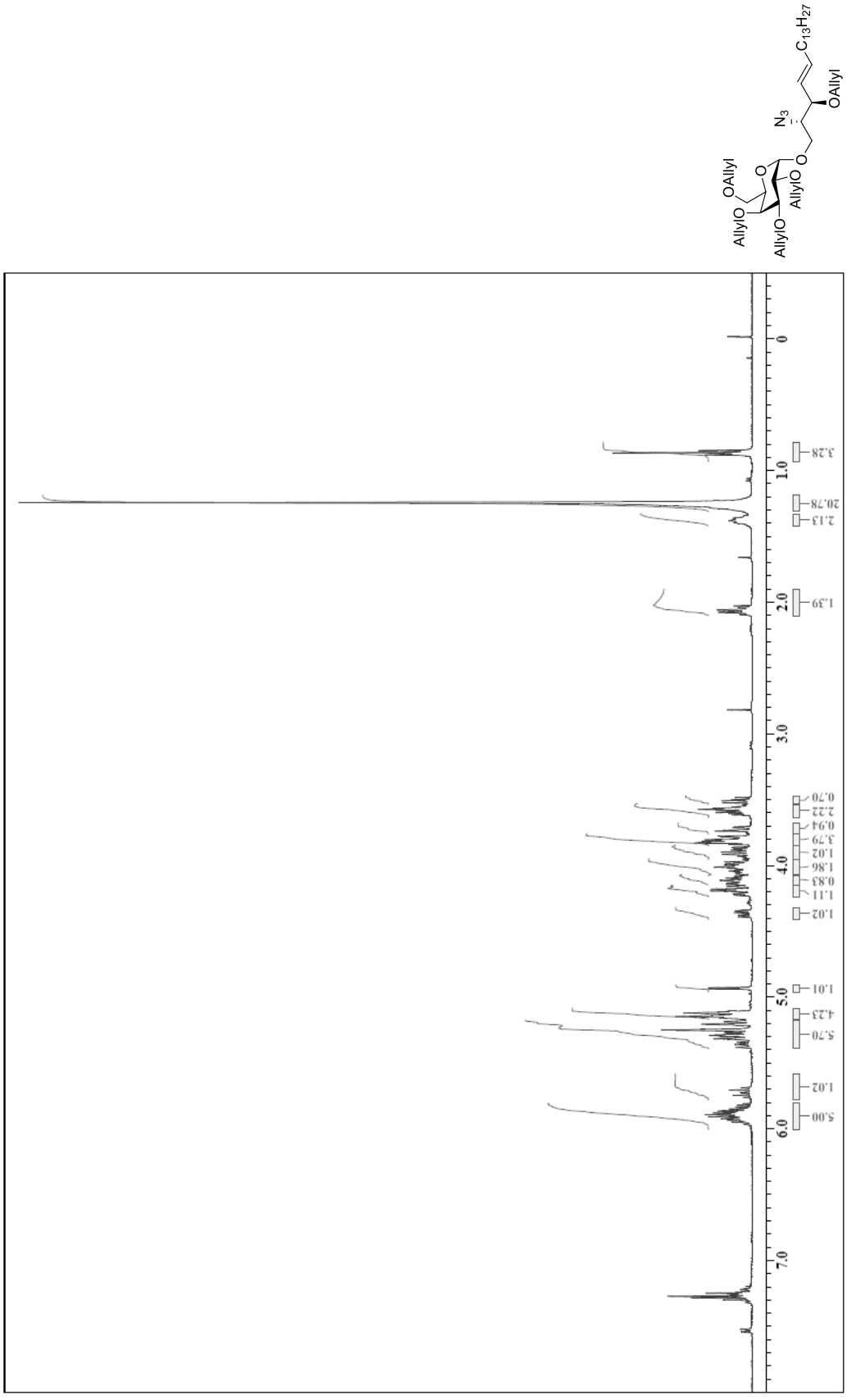
Compound **7β**


OAllyl
AllylO
AllylO
AllylO
N3
C13H27
OAllyl
3.00
19.99
2.13
1.97
1.01
3.00
3.98
3.03
5.15
5.05
1.00
4.95
4.91
1.00
5.19
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0

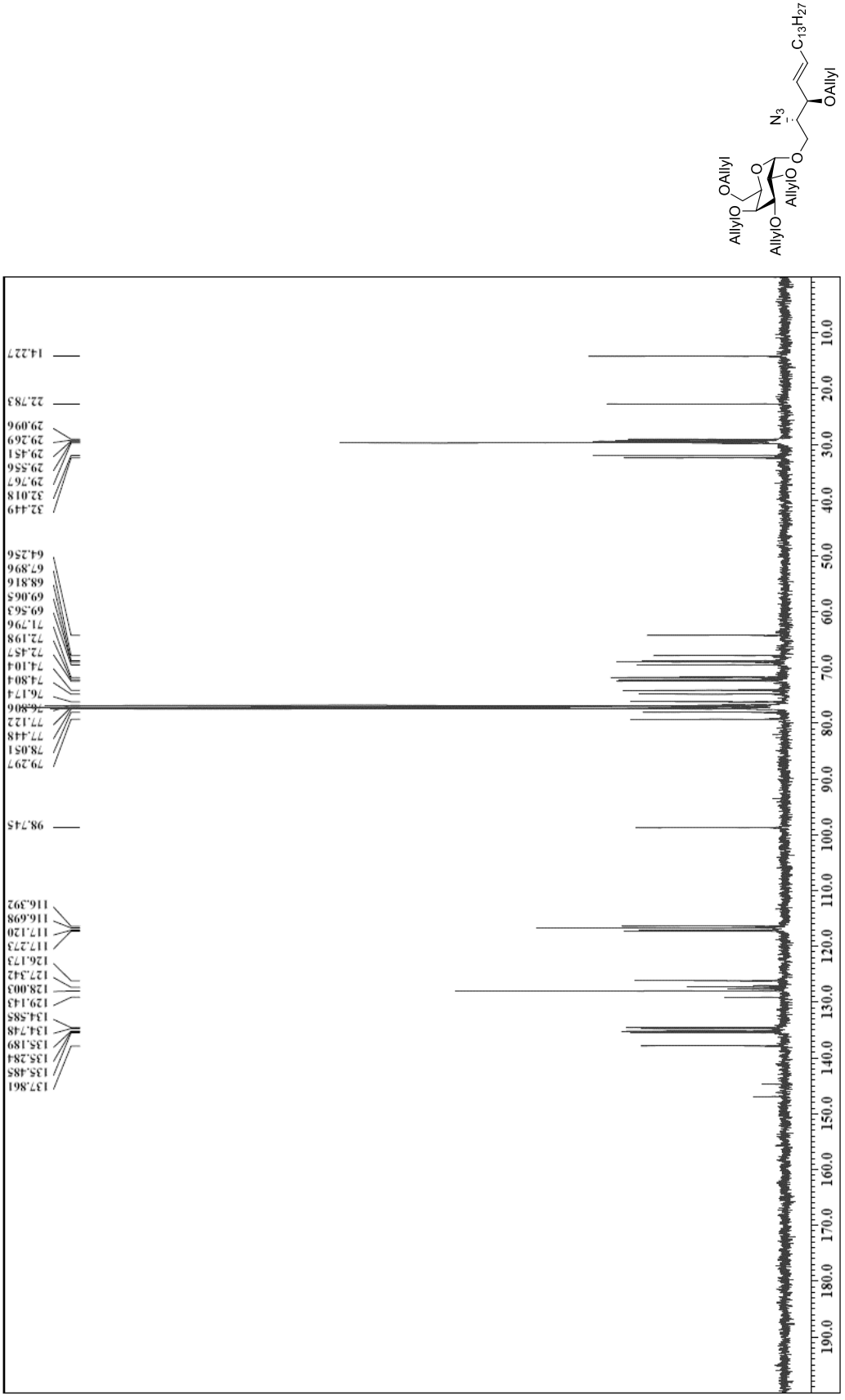
Compound **7β**


OAllyl
AllylO
AllylO
AllylO
N3
C13H27
OAllyl
14.180
22.744
29.211
29.307
29.412
29.546
29.738
31.980
49.579
53.488
58.479
67.523
68.998
72.524
73.731
73.855
74.440
74.890
75.024
76.825
77.151
77.467
79.460
81.539
84.087
84.202
116.670
116.775
116.881
117.015
117.053
134.384
134.757
134.892
135.160
135.313
137.785
138.015

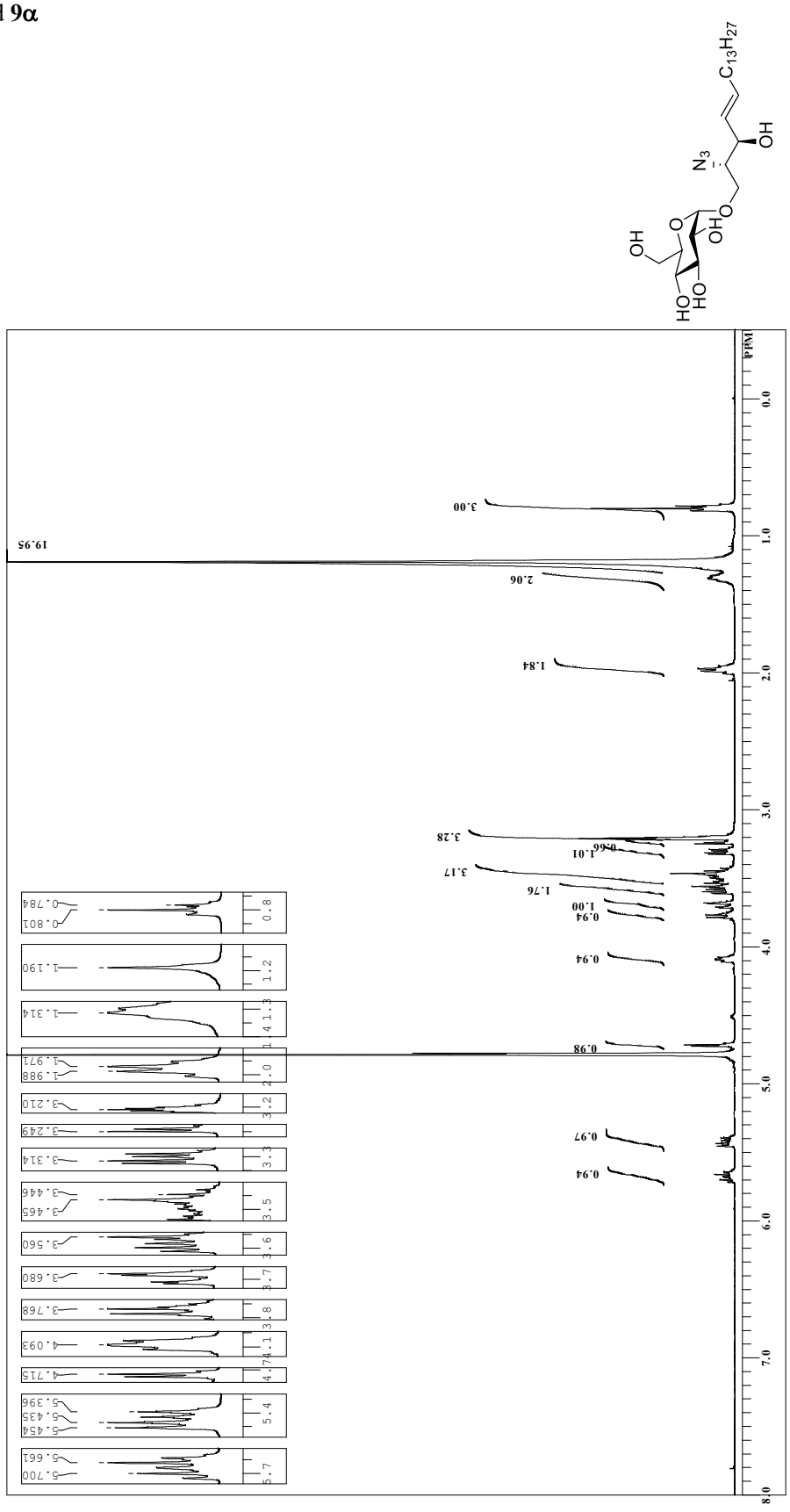
Compound **8α**


AllylO
OAllyl
AllylO
AllylO
O
O
N3
C13H27
OAllyl
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
5.00
1.02
4.23
5.70
1.01
1.02
1.11
0.83
1.86
1.02
3.79
0.94
2.22
0.70
1.39
2.13
20.78
3.28

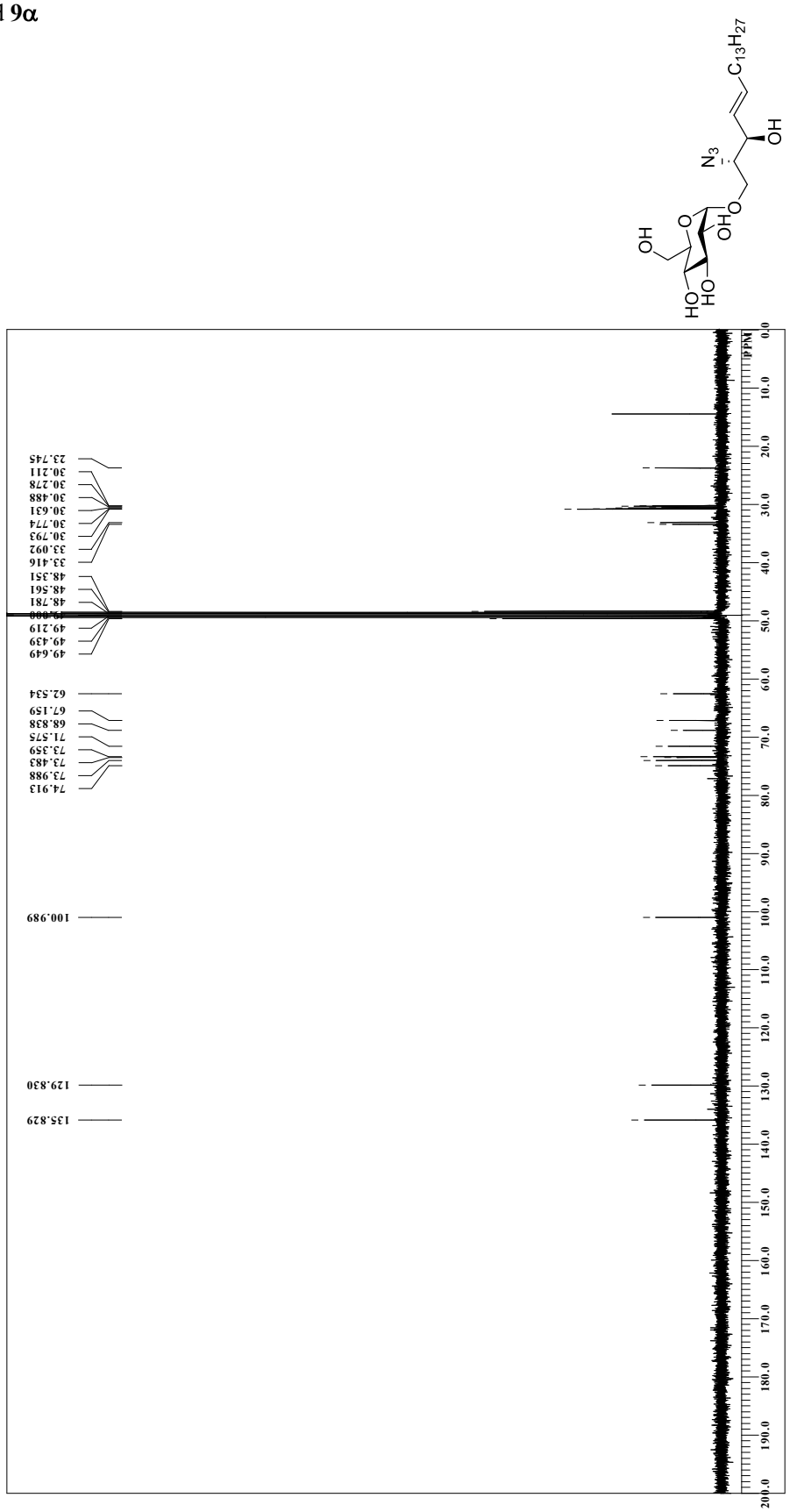
Compound **8α**


AllylO
OAllyl
AllylO
AllylO
O
O
N3
C13H27
OAllyl
14.227
22.783
29.096
29.269
29.451
29.556
29.767
32.018
32.449
64.256
67.896
68.816
69.065
69.563
71.796
72.198
72.457
74.104
74.804
76.174
76.806
77.122
77.448
78.051
79.297
98.745
116.392
116.698
117.120
117.273
126.173
127.342
128.003
129.143
134.585
134.748
135.189
135.284
135.485
137.861
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0

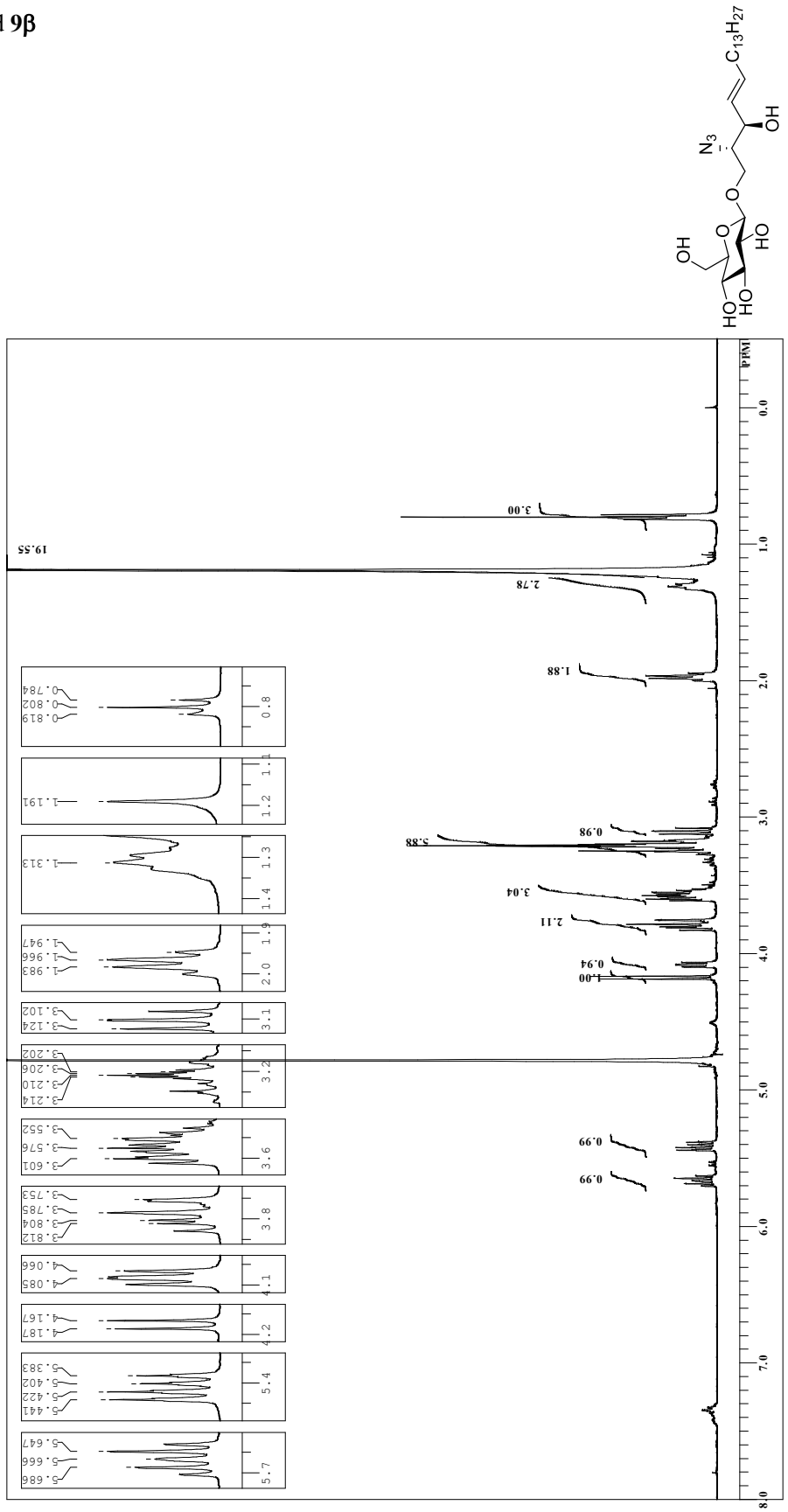
Compound **9α**


C13H27
N3
OH
HO
HO
OH
O
O
OH
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
19.95
3.00
2.06
1.84
3.28
1.01
0.66
3.17
1.76
1.00
0.94
0.94
0.98
0.97
0.94
5.700
5.661
5.454
5.435
5.396
4.715
4.093
3.768
3.680
3.560
3.465
3.446
3.314
3.249
3.210
1.988
1.971
1.314
1.190
0.801
0.784

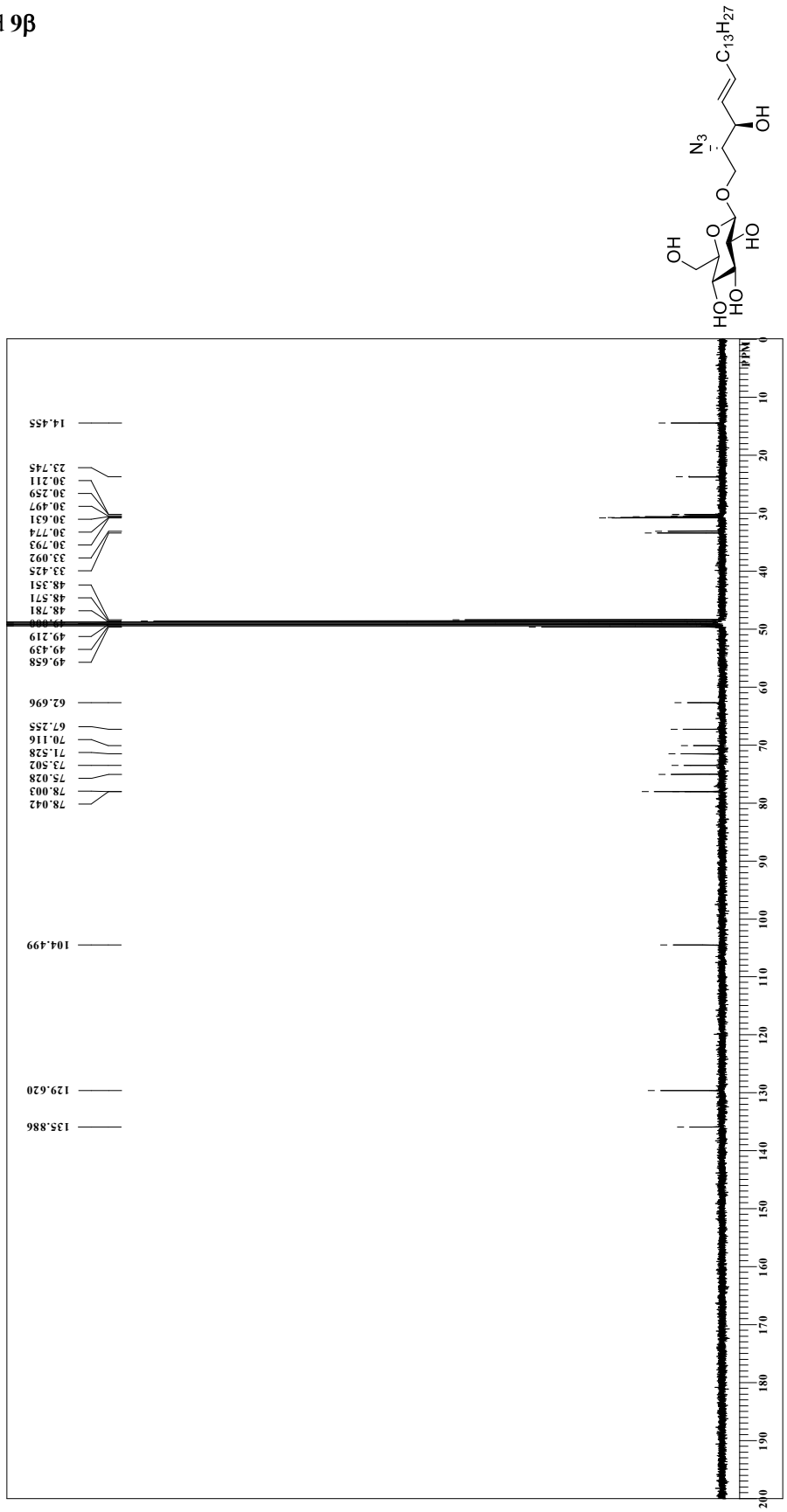
Compound **9α**


C13H27
N3
OH
OH
OH
HO
HO
O
O
PPM
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
23.745
30.211
30.278
30.488
30.631
30.774
30.793
33.092
33.416
48.351
48.561
48.781
49.008
49.219
49.439
49.649
62.534
67.159
68.838
71.575
73.359
73.483
73.988
74.913
100.989
129.830
135.829

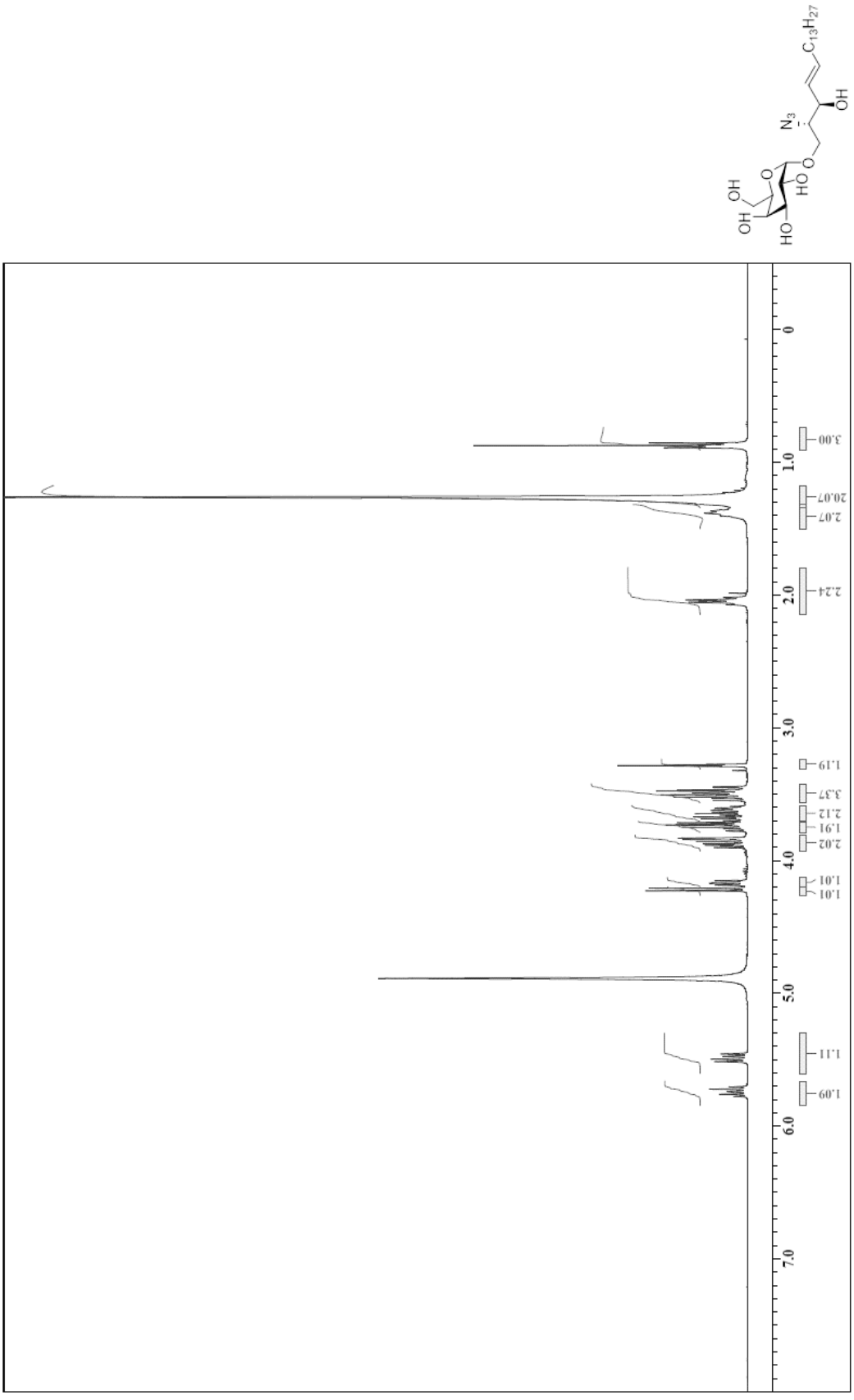
Compound **9β**



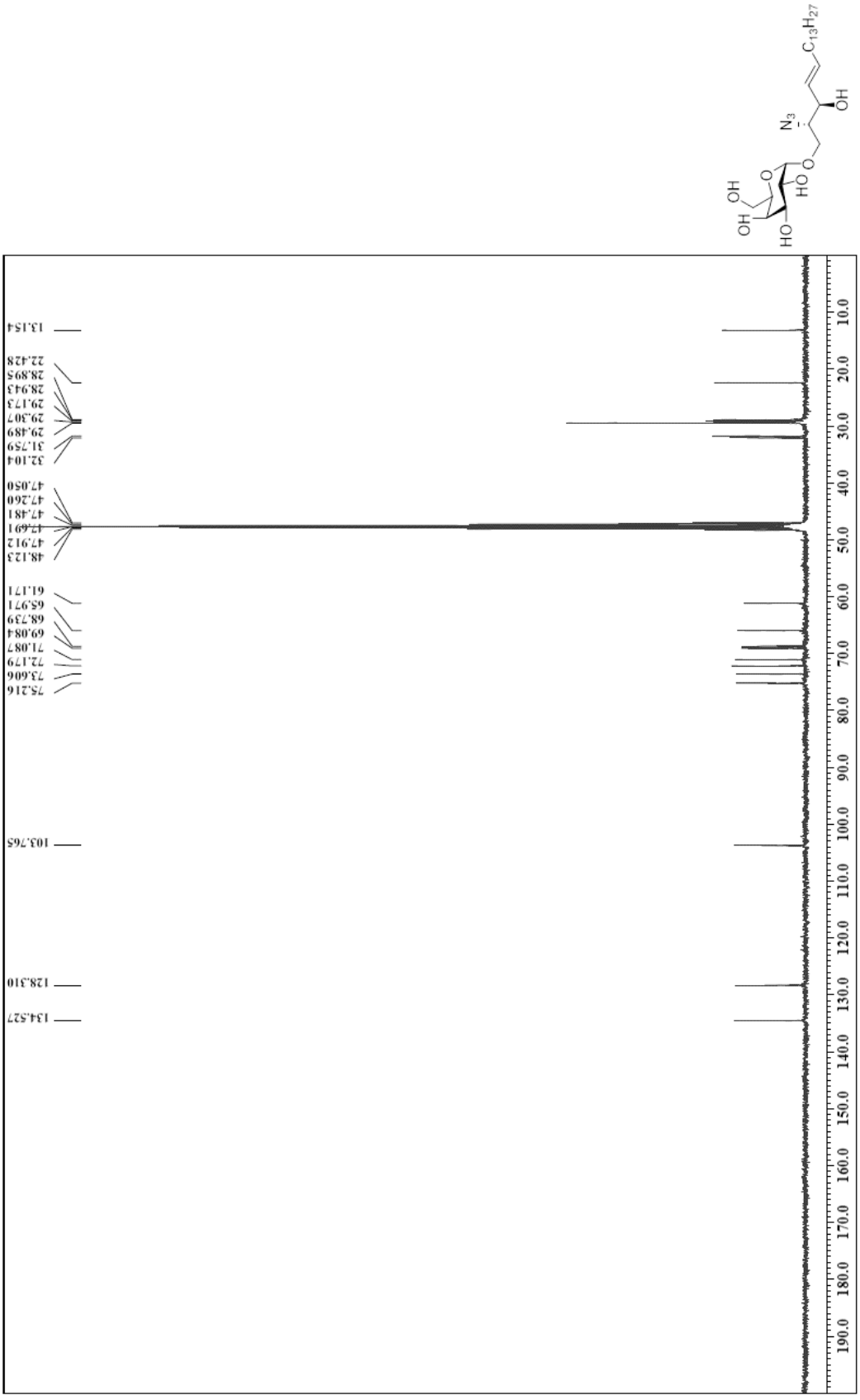
Compound **9β**


C13H27
OH
N3
O
O
HO
OH
HO
HO
PPM
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
14.455
23.745
30.211
30.259
30.497
30.631
30.774
30.793
33.092
33.425
48.351
48.571
48.781
49.219
49.439
49.658
62.696
67.255
70.116
71.528
73.502
75.028
78.003
78.042
104.499
129.620
135.886

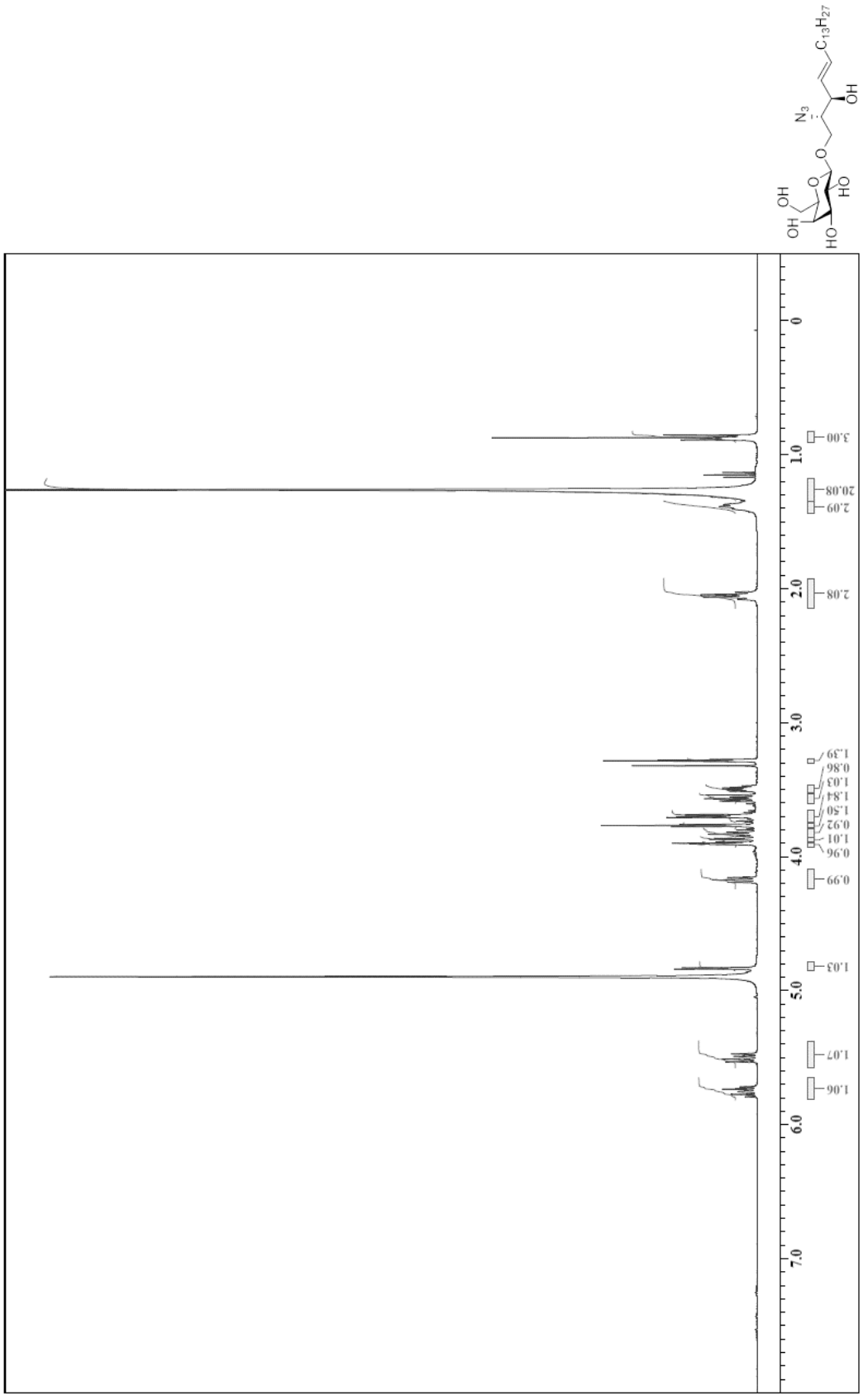
Compound **10α**



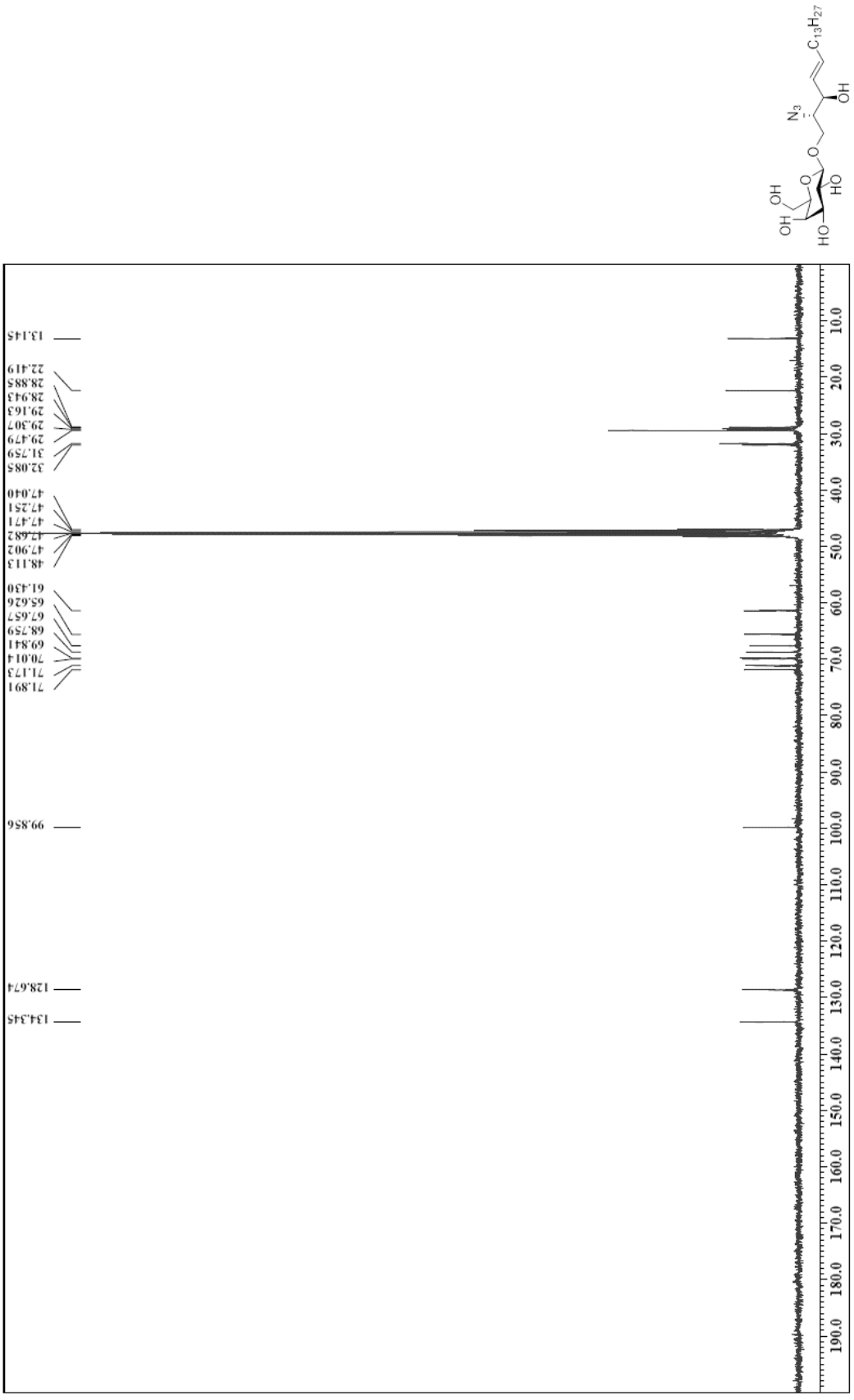
Compound **10α**



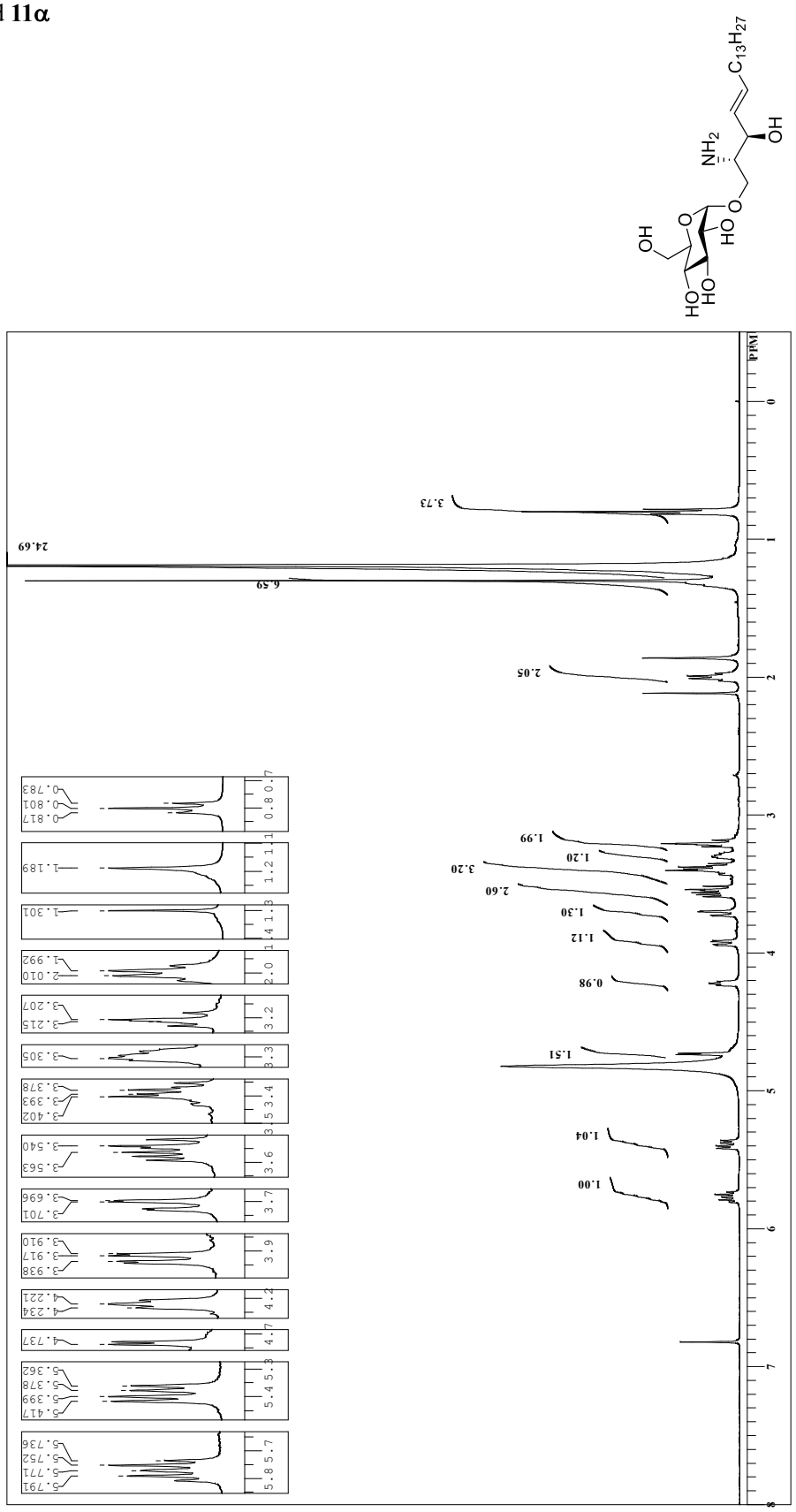
Compound **10β**



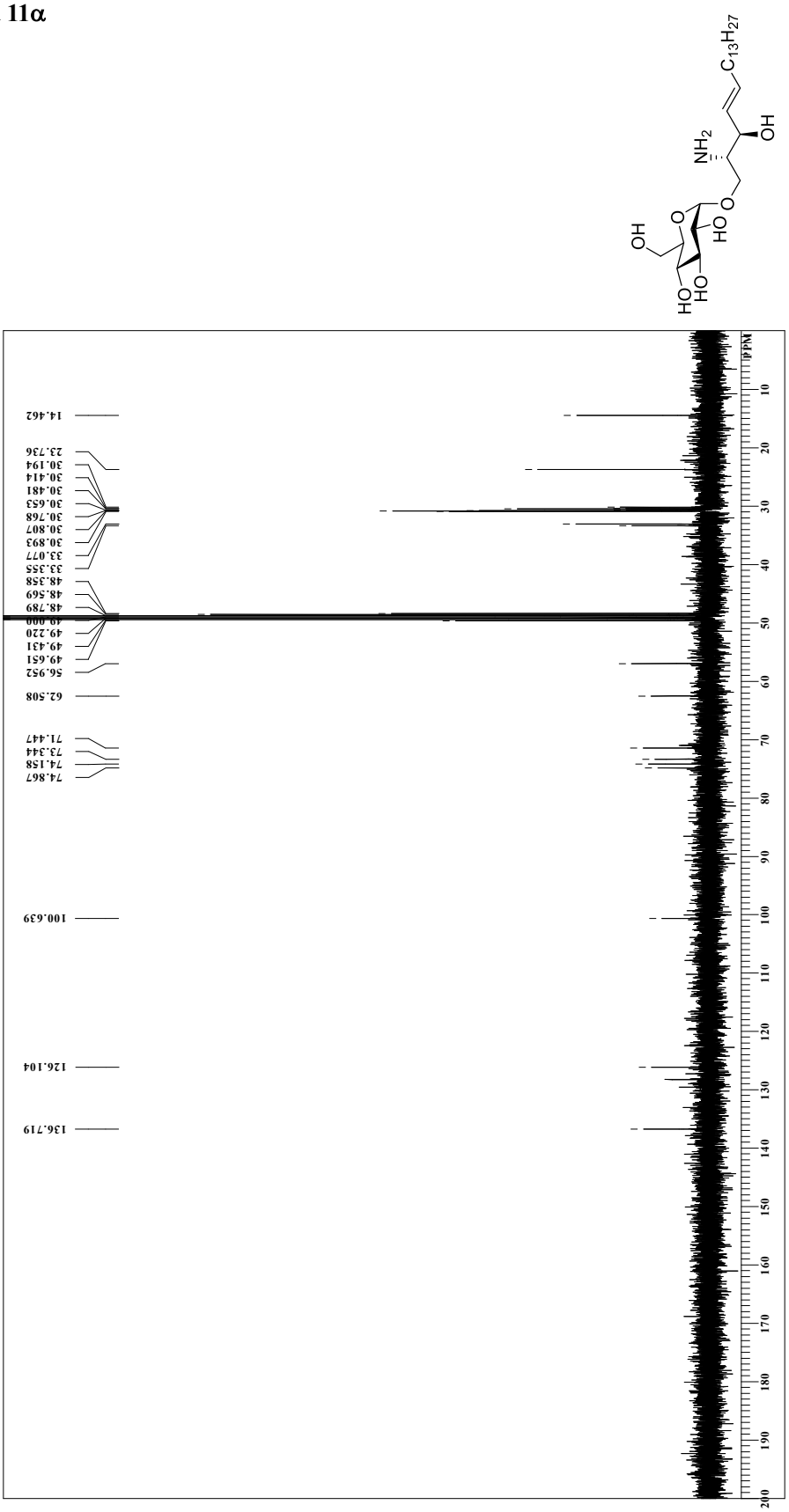
Compound **10β**



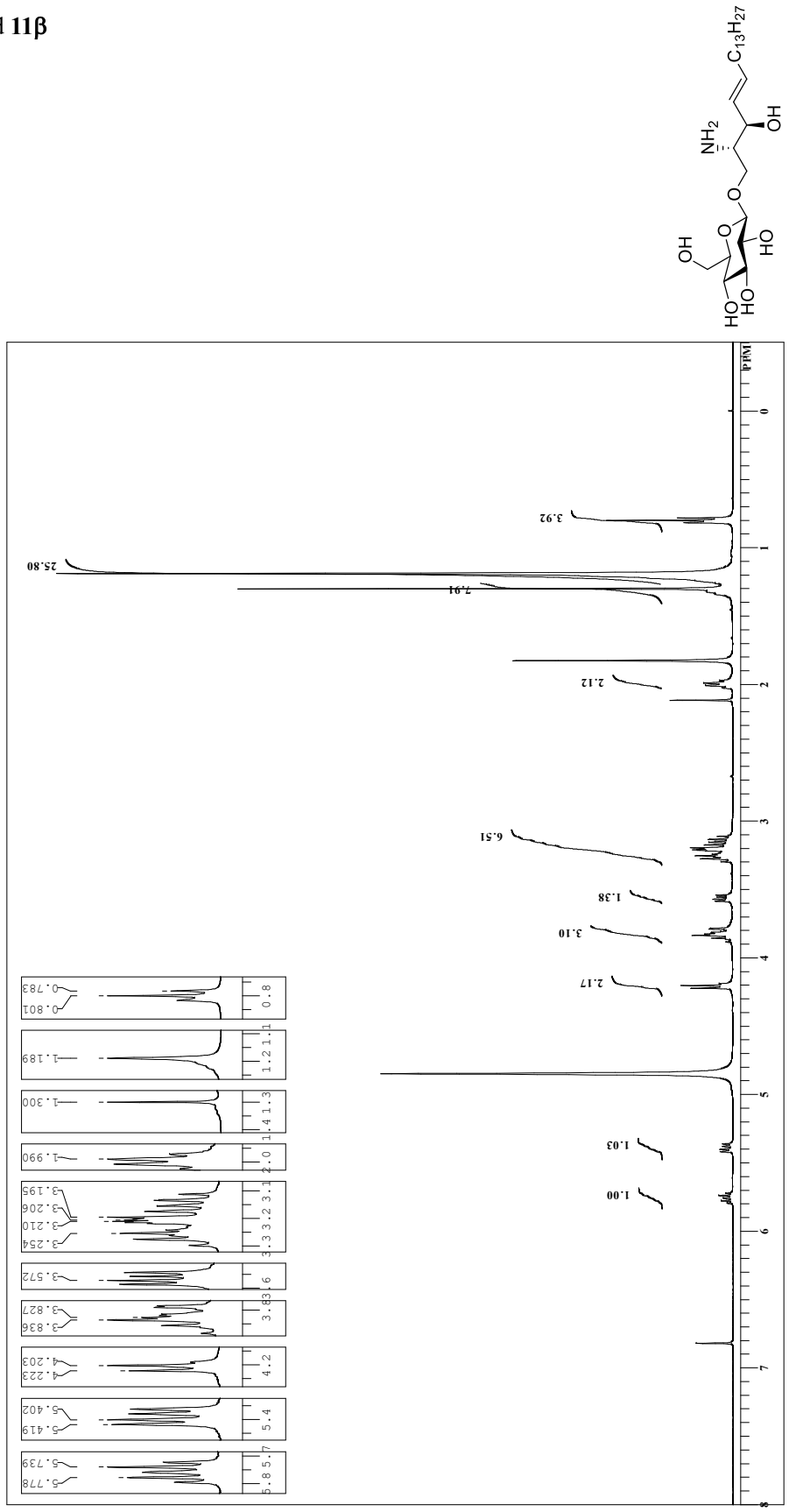
Compound **11α**



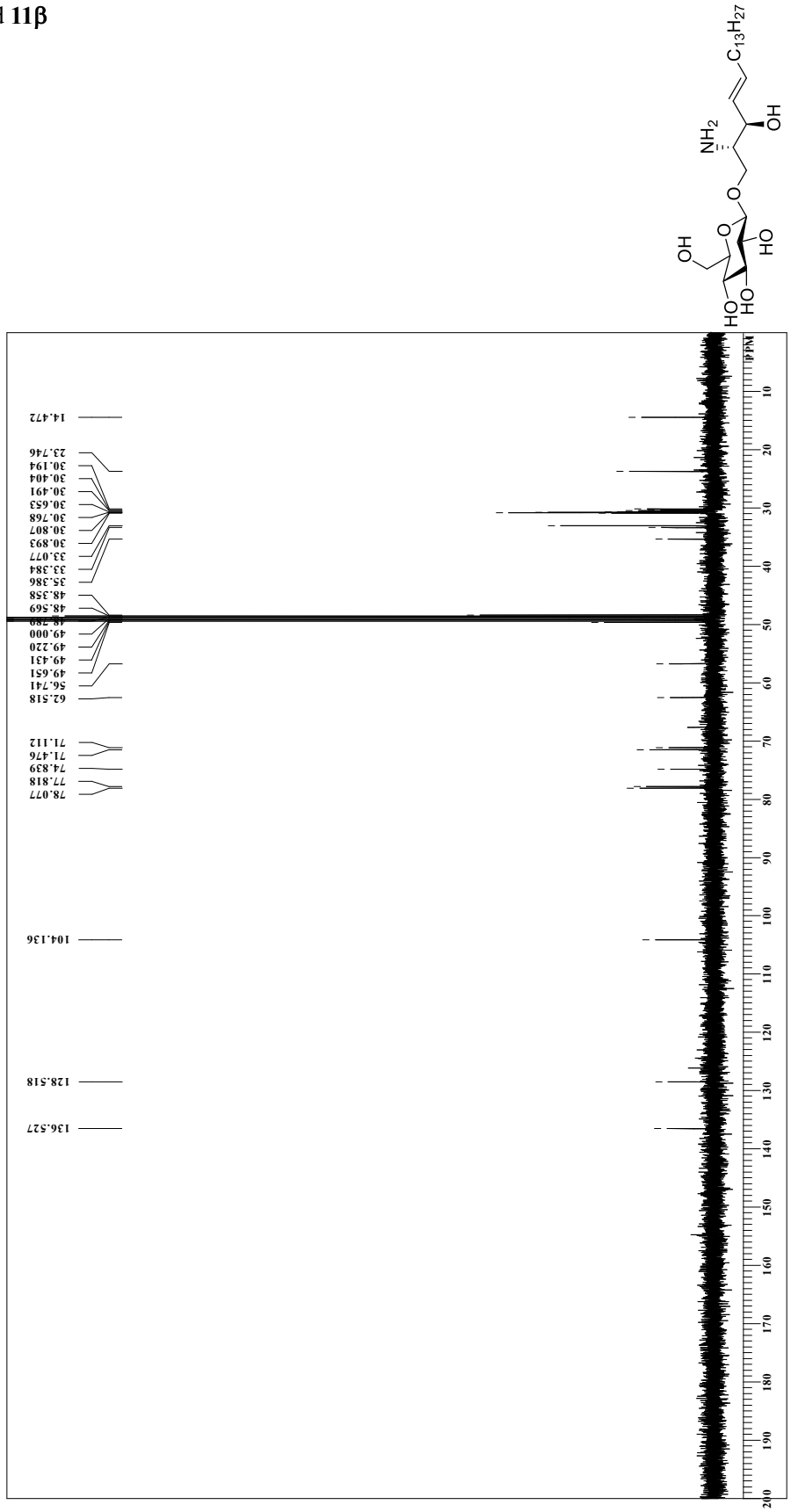
Compound **11α**



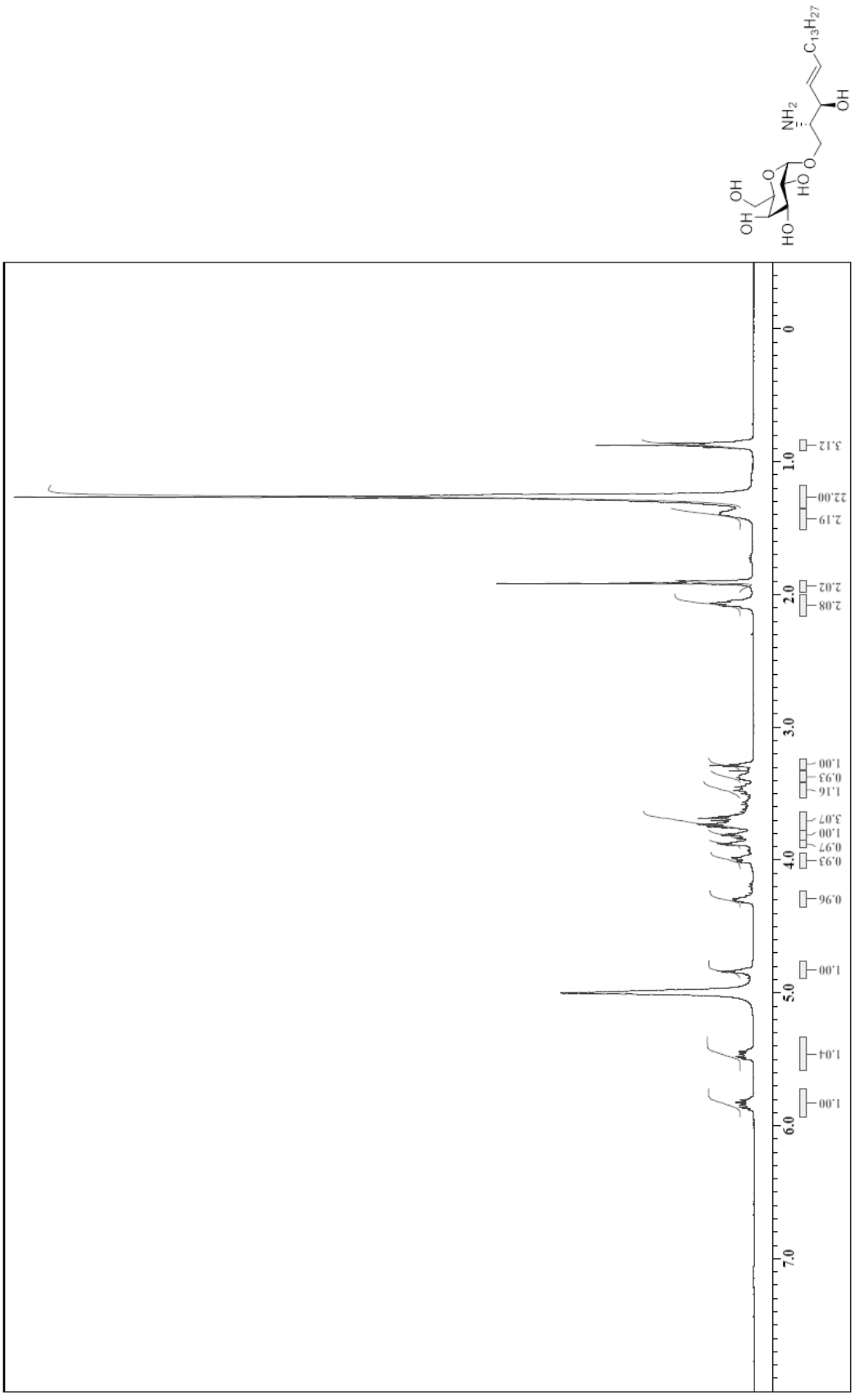
Compound **11β**



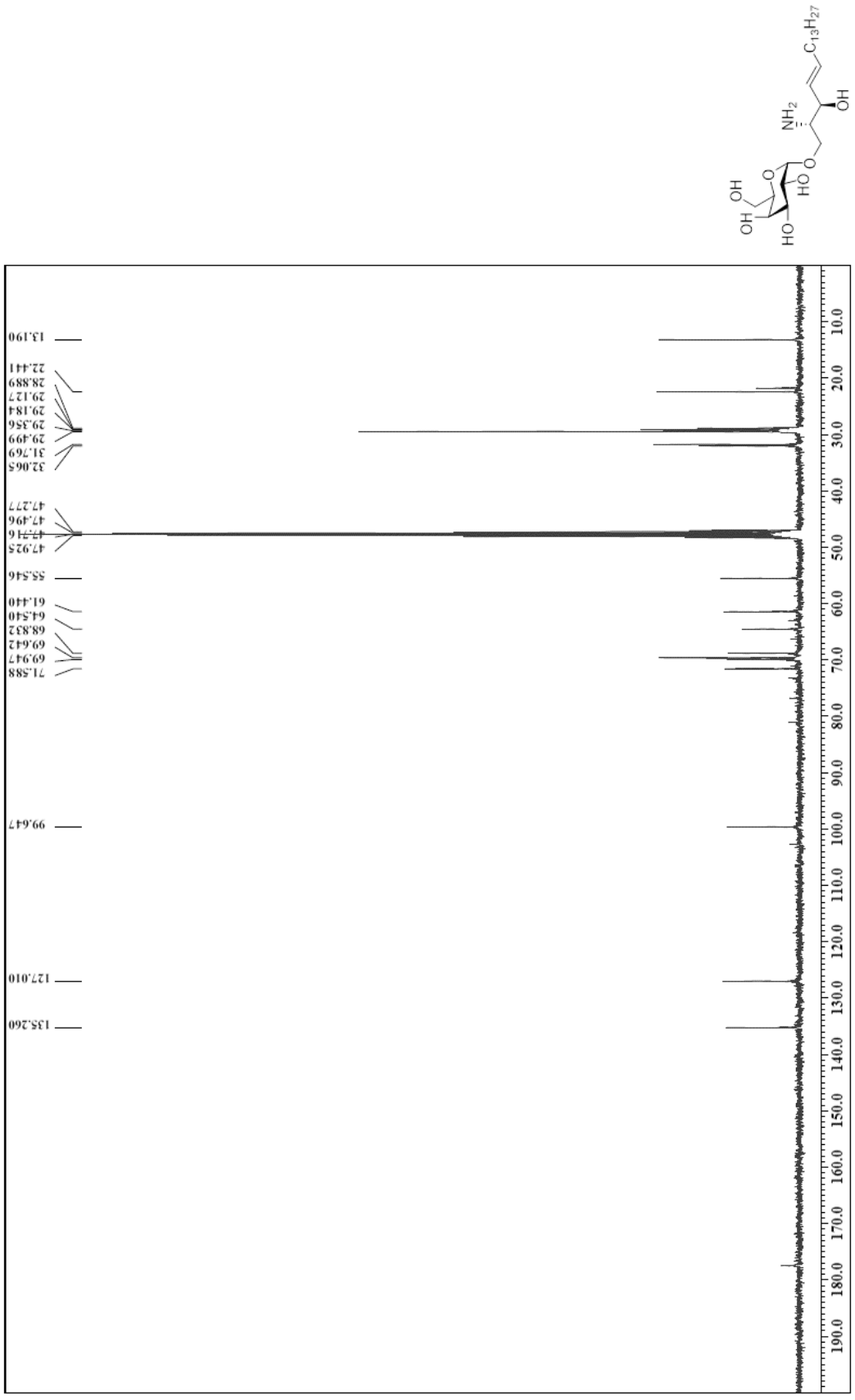
Compound **11β**



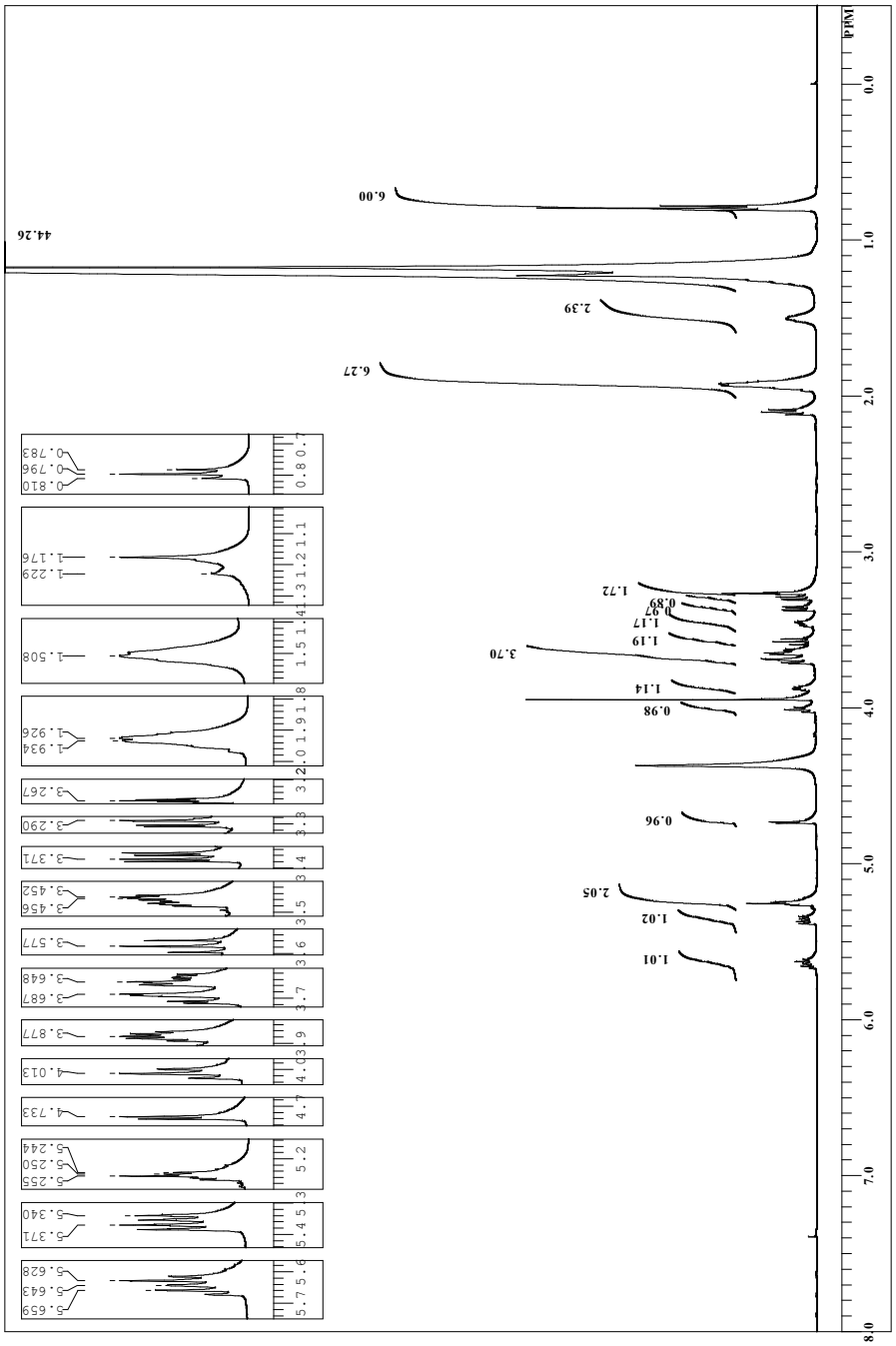
Compound **12α**



Compound **12α**



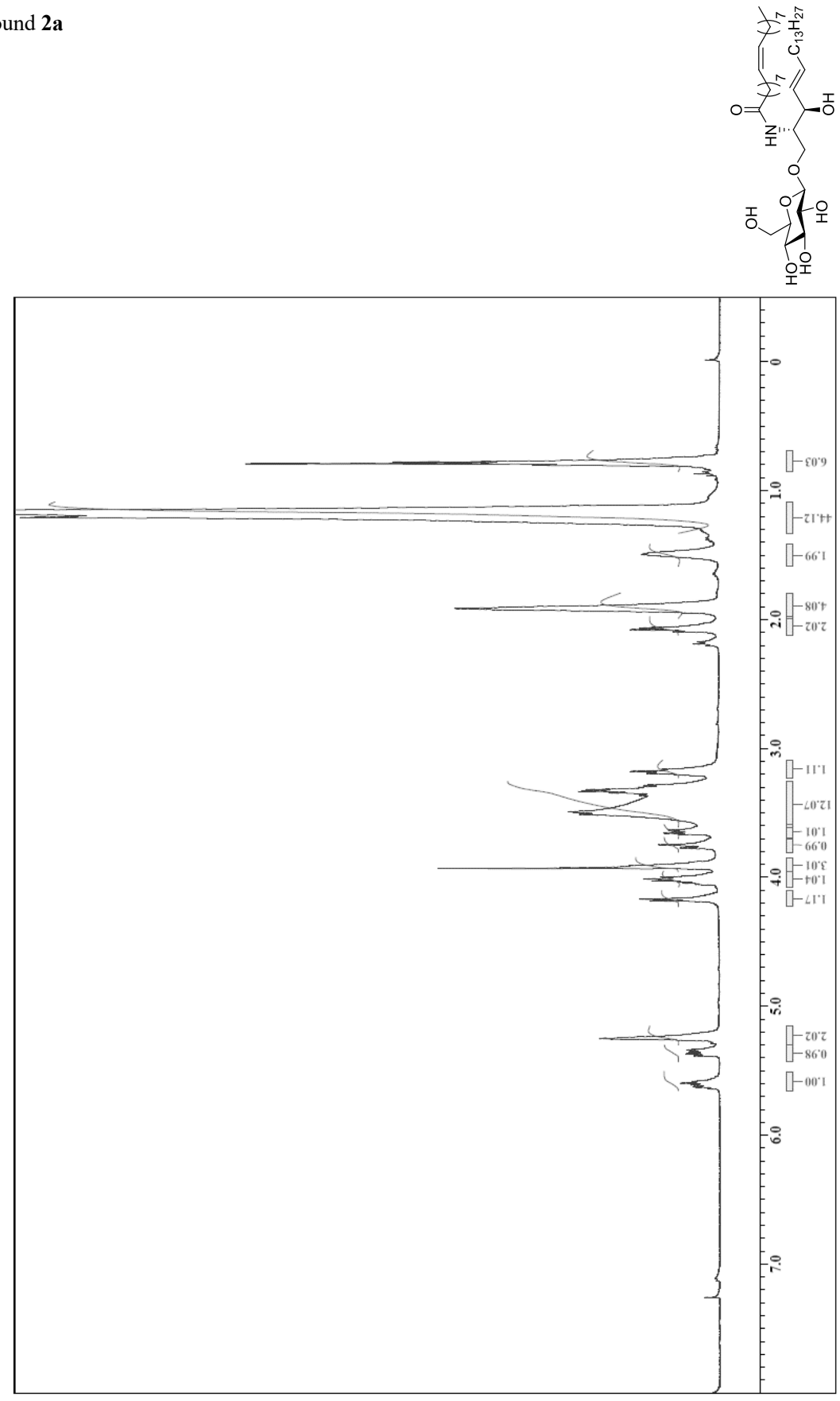
Compound **1a**



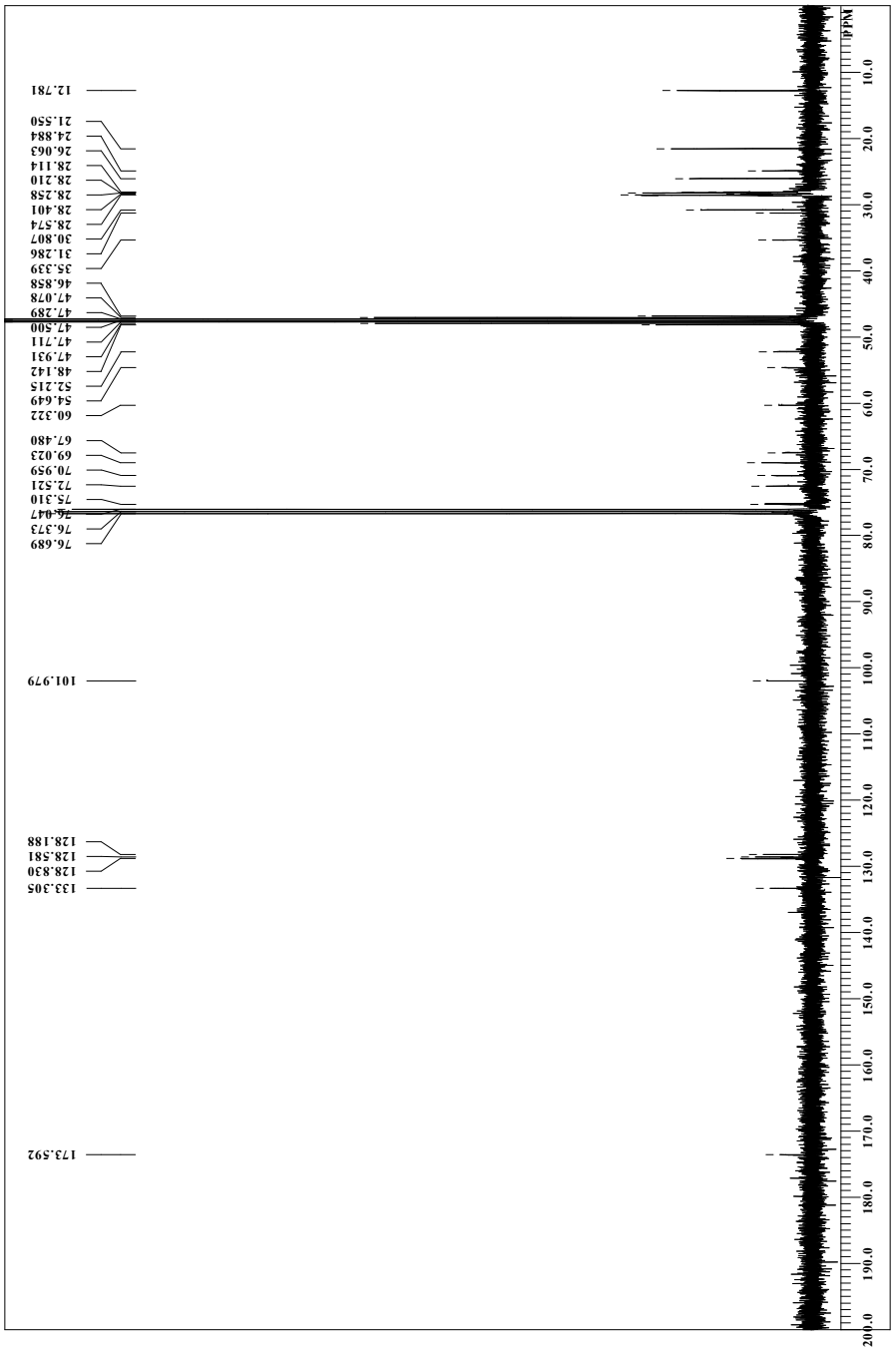
Compound **1a**

13.518
22.250
25.541
26.771
28.822
28.894
28.908
28.937
28.956
28.984
29.108
29.175
29.256
29.299
29.313
29.342
29.385
31.498
31.521
31.994
36.004
47.765
47.937
48.109
48.280
48.447
48.619
48.791
53.207
55.448
61.014
66.837
69.765
71.639
71.687
73.385
76.747
77.000
77.258
99.029
128.779
129.289
129.546
133.839
174.314
PPM
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
HO
HO
HO
O
HO
O
HN
O
OH
$C_{13}H_{27}$
7
7

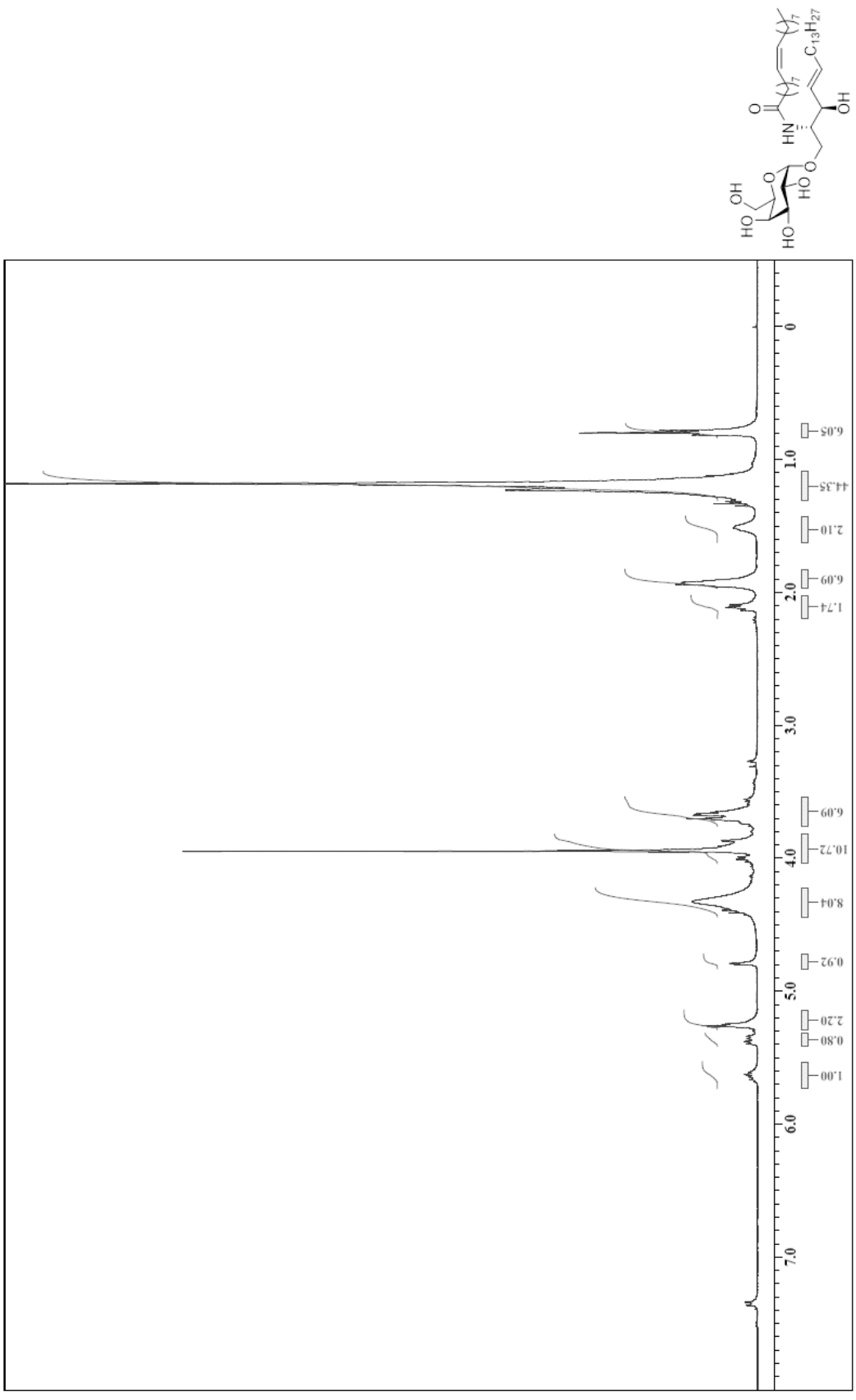
Compound **2a**



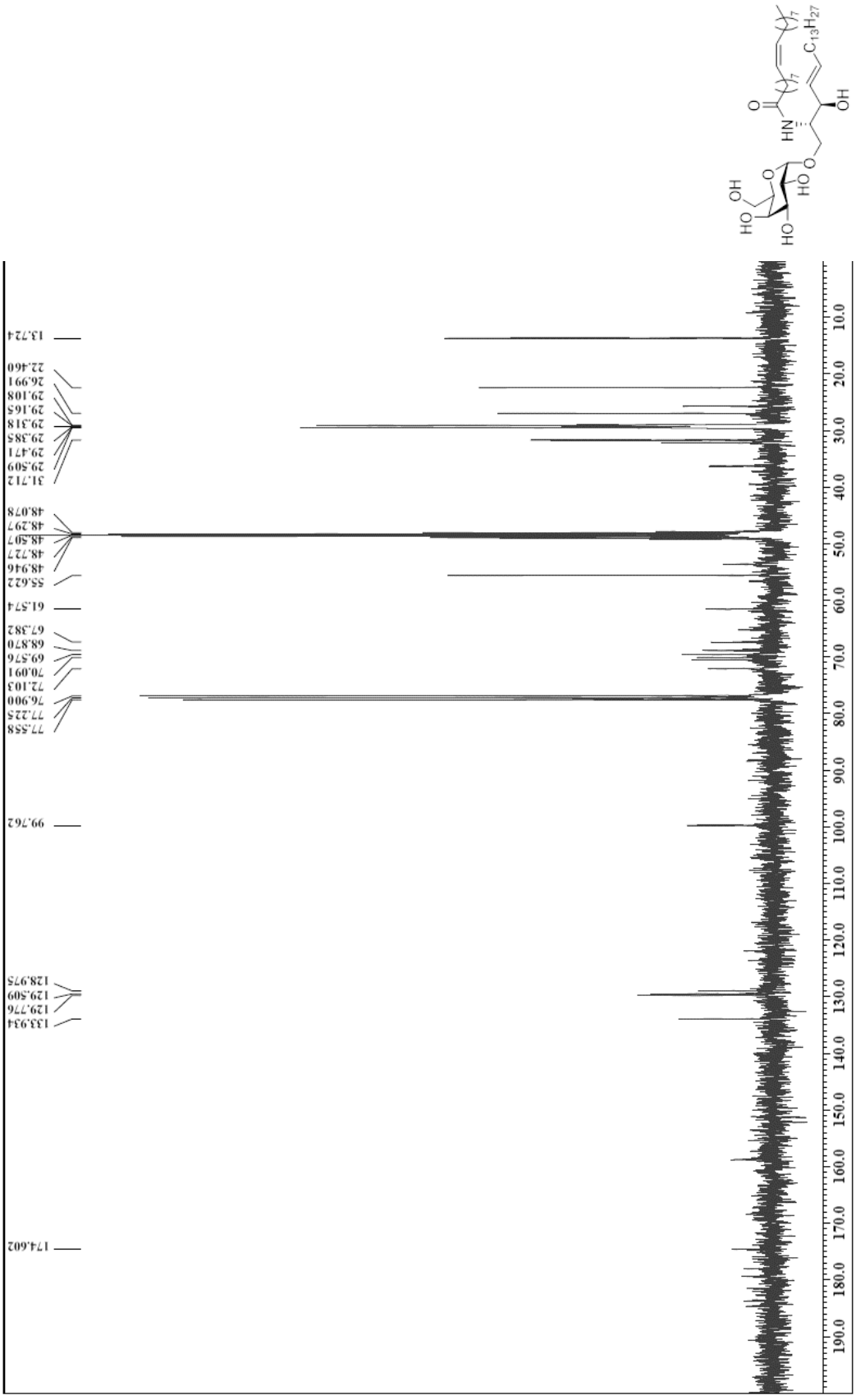
Compound **2a**


12.781
21.550
24.884
26.063
28.114
28.210
28.258
28.401
28.574
30.807
31.286
35.339
46.858
47.078
47.289
47.500
47.711
47.931
48.142
52.215
54.649
60.322
67.480
69.023
70.959
72.521
75.310
76.047
76.373
76.689
101.979
128.188
128.581
128.830
133.305
173.592
PPM

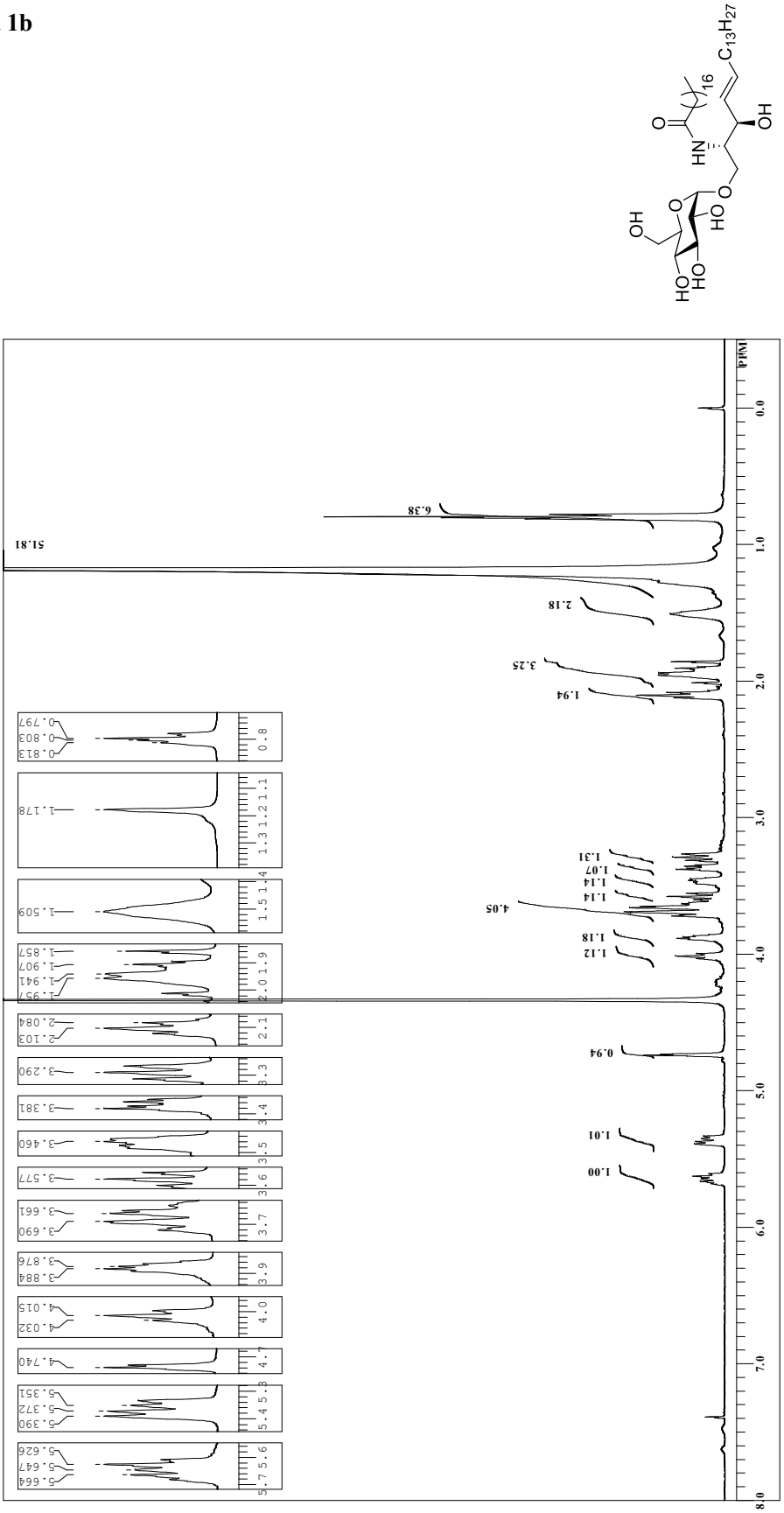
Compound **3a**



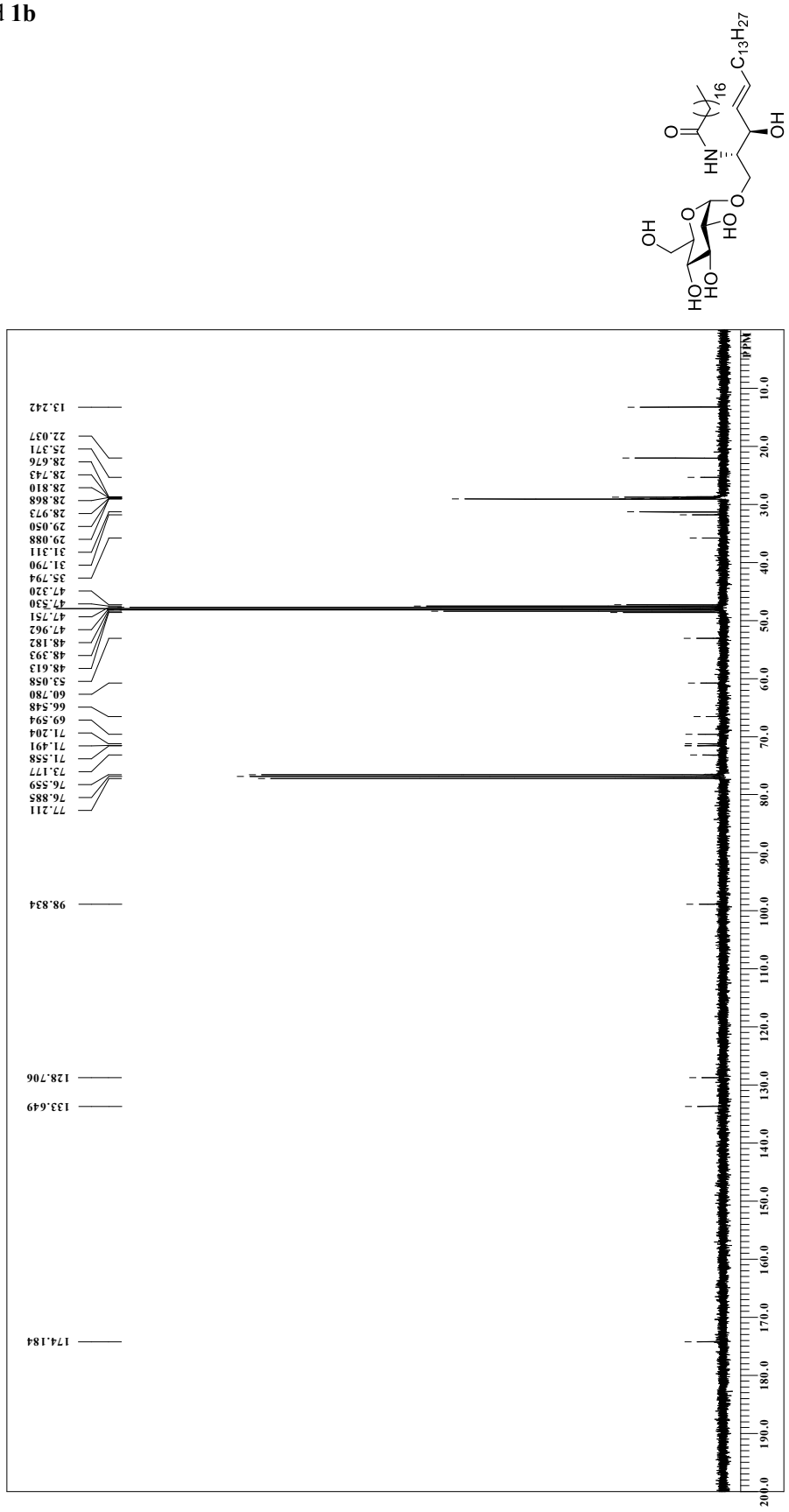
Compound **3a**


13.724
22.460
26.991
29.108
29.165
29.318
29.385
29.471
29.509
31.712
48.078
48.297
48.507
48.727
48.946
55.622
61.574
67.382
68.870
69.576
70.091
72.103
76.900
77.225
77.558
99.762
128.975
129.509
129.776
133.934
174.602
HO
OH
HO
O
HO
O
HN
O
OH
$C_{13}H_{27}$
$_7$
$_7$
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0

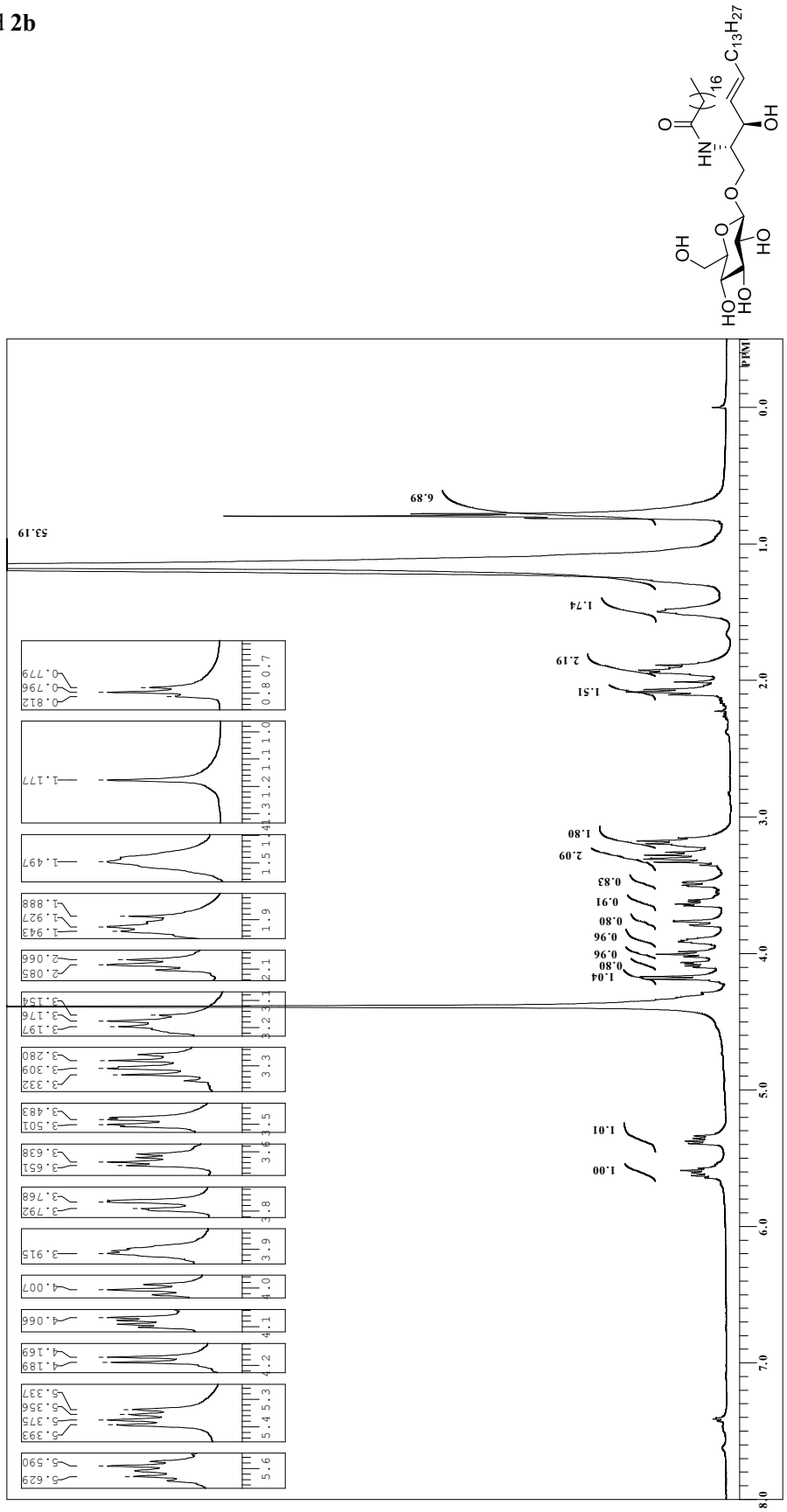
Compound **1b**


C13H27
16
HN
O
OH
HO
HO
HO
OH
51.81
6.38
2.18
3.25
1.94
4.05
1.14
1.14
1.07
1.31
1.12
1.18
0.94
1.01
1.00
PPM

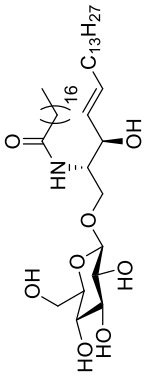
Compound **1b**

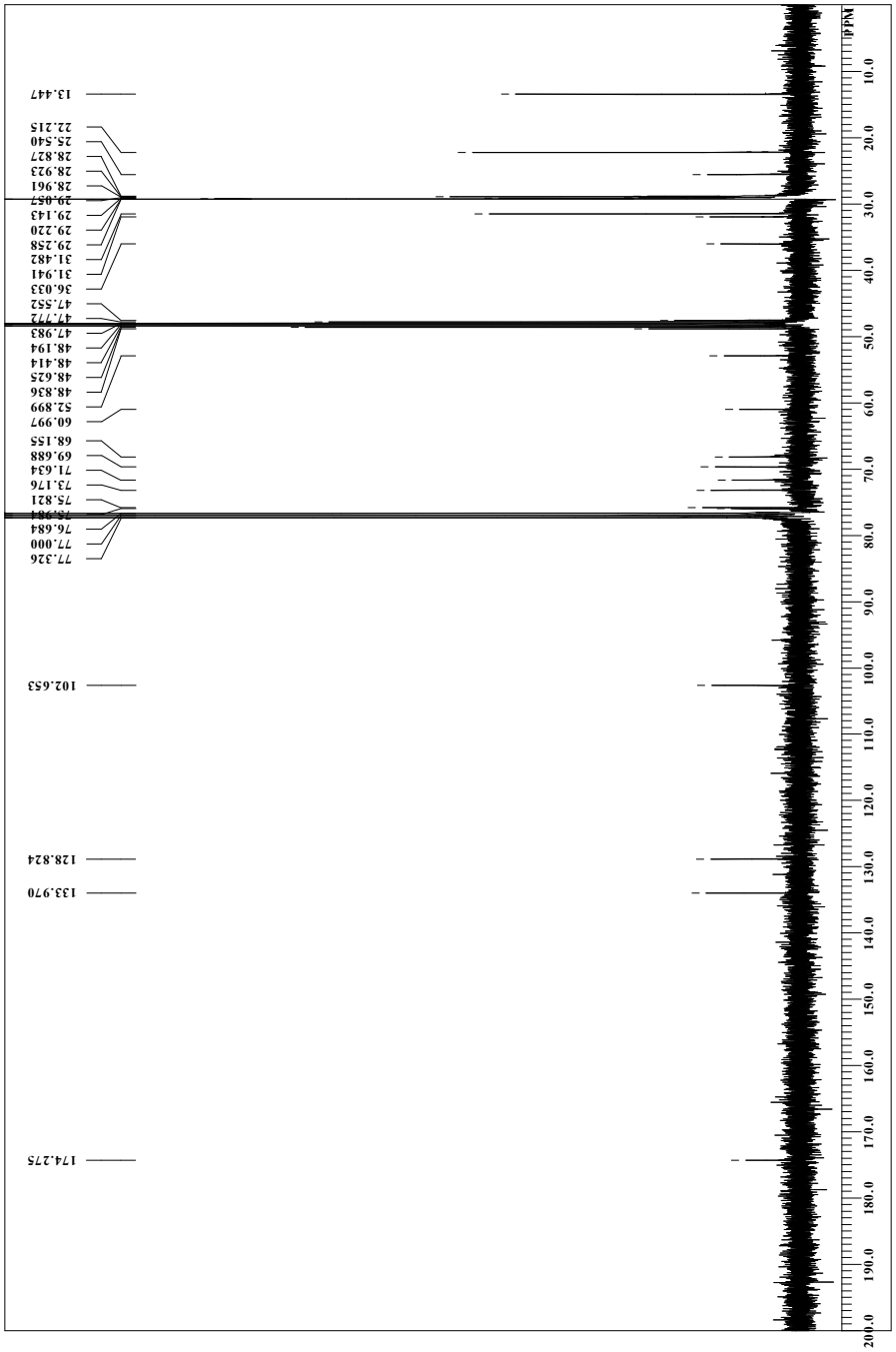

C13H27
16
HN
O
OH
HO
HO
HO
OH
13.242
22.037
25.371
28.676
28.743
28.810
28.868
28.973
29.050
29.088
31.311
31.790
35.794
47.320
47.530
47.751
47.962
48.182
48.393
48.613
53.058
60.780
66.548
69.594
71.204
71.491
71.558
73.177
76.559
76.885
77.211
98.834
128.706
133.649
174.184
PPM

Compound **2b**

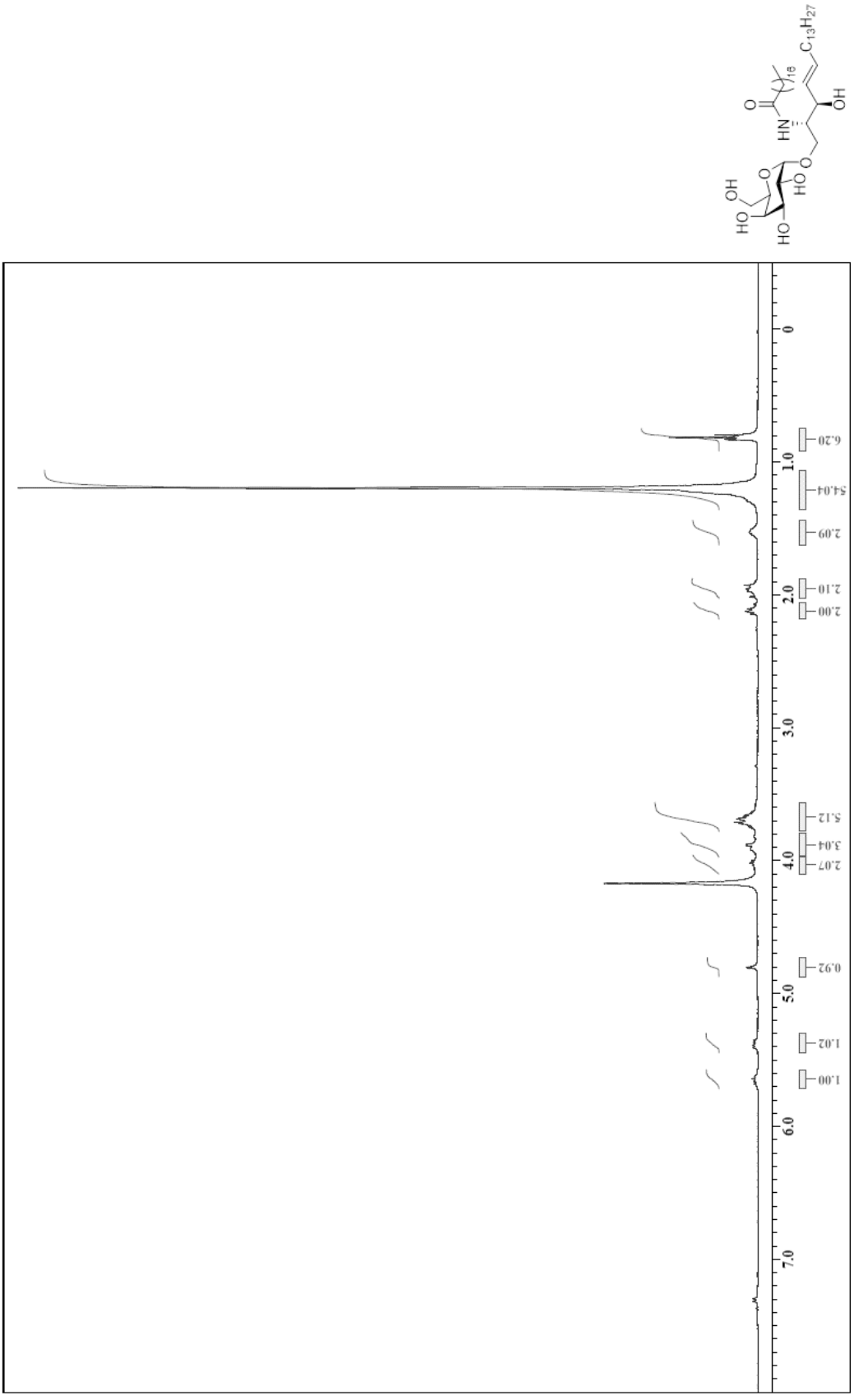

C13H27
16
NH
O
OH
OH
OH
OH
O
O
53.19
6.89
1.74
2.19
1.51
1.80
2.09
0.83
0.91
0.80
0.96
1.04
0.80
0.96
1.00
1.01
PPM

Compound **2b**

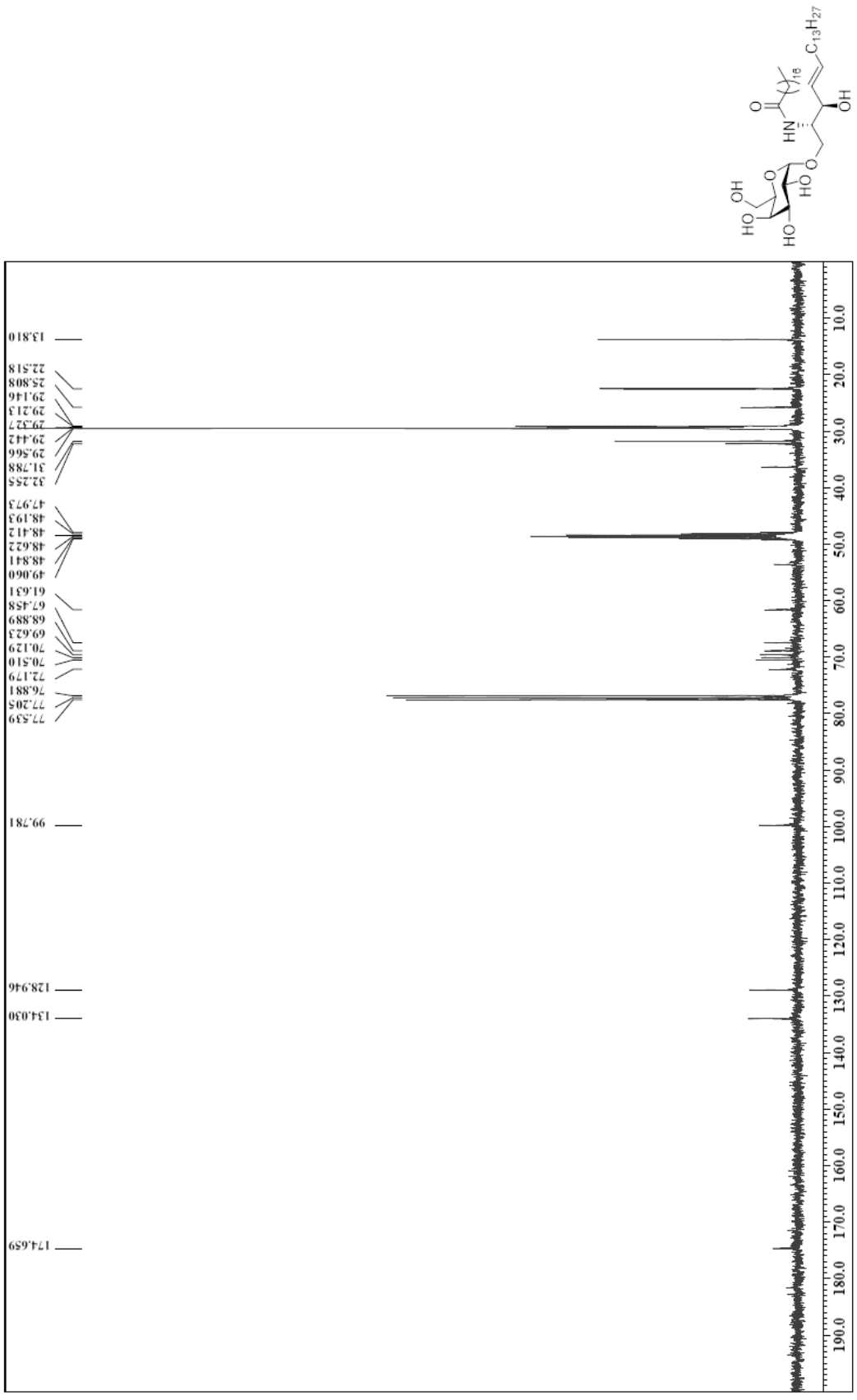

$C_{13}H_{27}$
16
O
HN
OH
O
O
OH
HO
HO
HO


13.447
22.215
25.540
28.827
28.923
28.961
29.057
29.143
29.220
29.258
31.482
31.941
36.033
47.552
47.772
47.983
48.194
48.414
48.625
48.836
52.899
60.997
68.155
69.688
71.634
73.176
75.821
76.684
77.000
77.326
102.653
128.824
133.970
174.275
PPM
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0

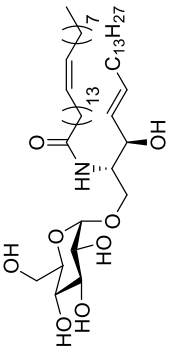
Compound **3b**

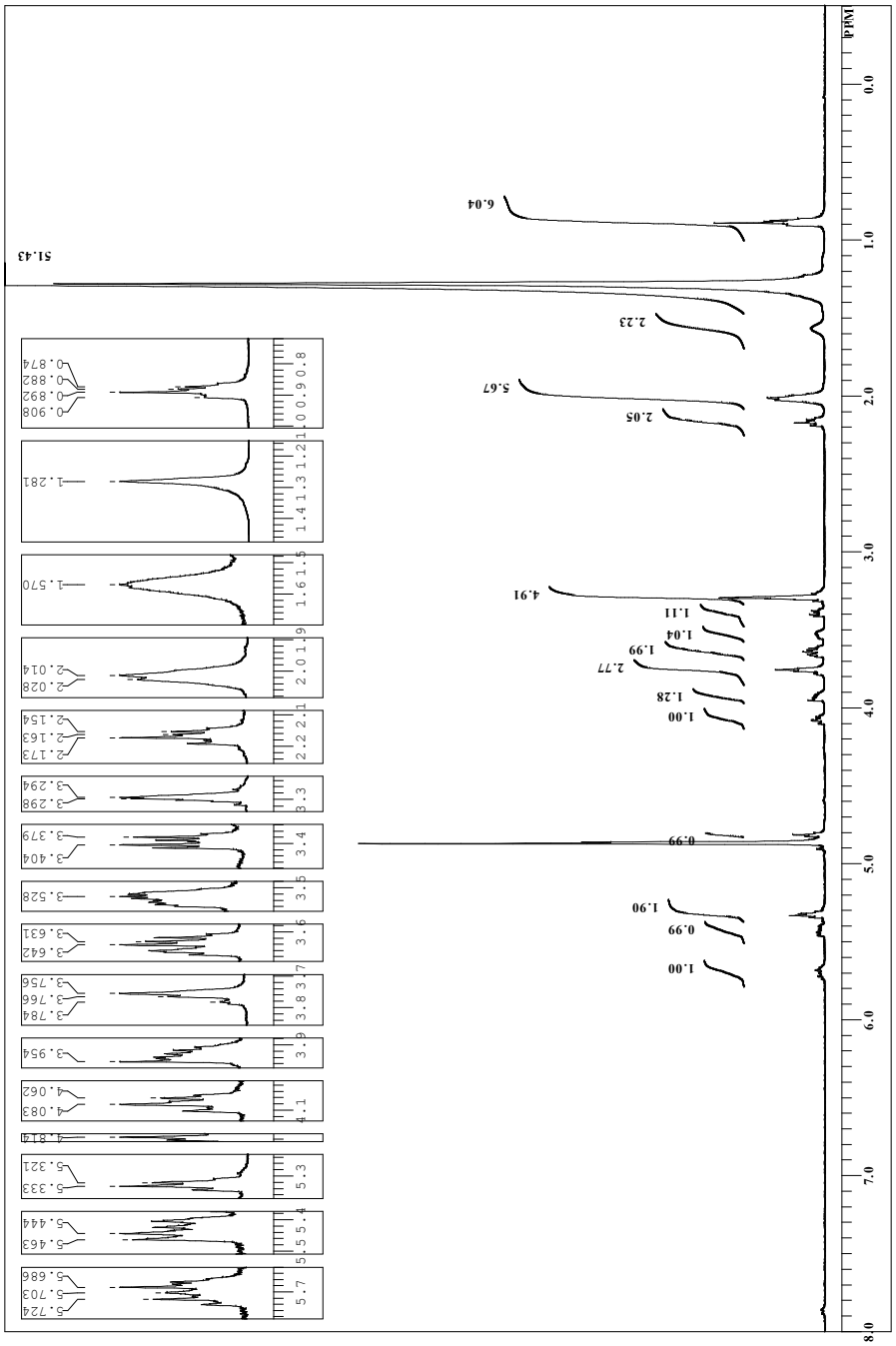


Compound **3b**

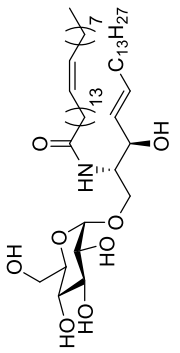

13.810
22.518
25.808
29.146
29.213
29.527
29.442
29.566
31.788
32.254
47.973
48.193
48.412
48.622
48.841
49.060
61.631
67.458
68.889
69.623
70.129
70.510
72.179
76.881
77.205
77.539
99.781
128.946
134.030
174.659
HO
OH
O
HO
HO
O
HN
O
OH
C13H27
16

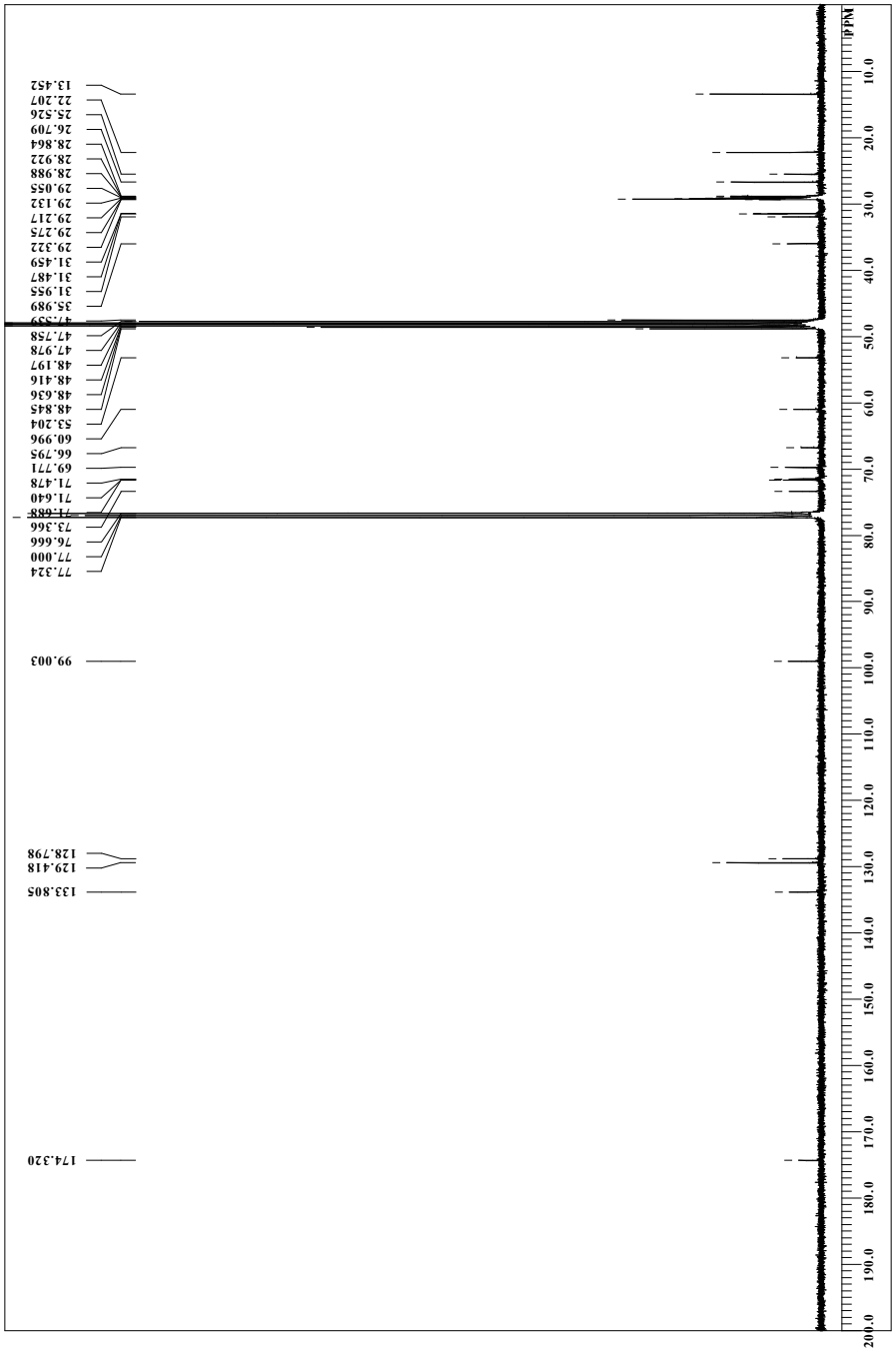
Compound **1c**


OH
HO
HO
O
O
HO
O
HN
OH
13
7
$C_{13}H_{27}$

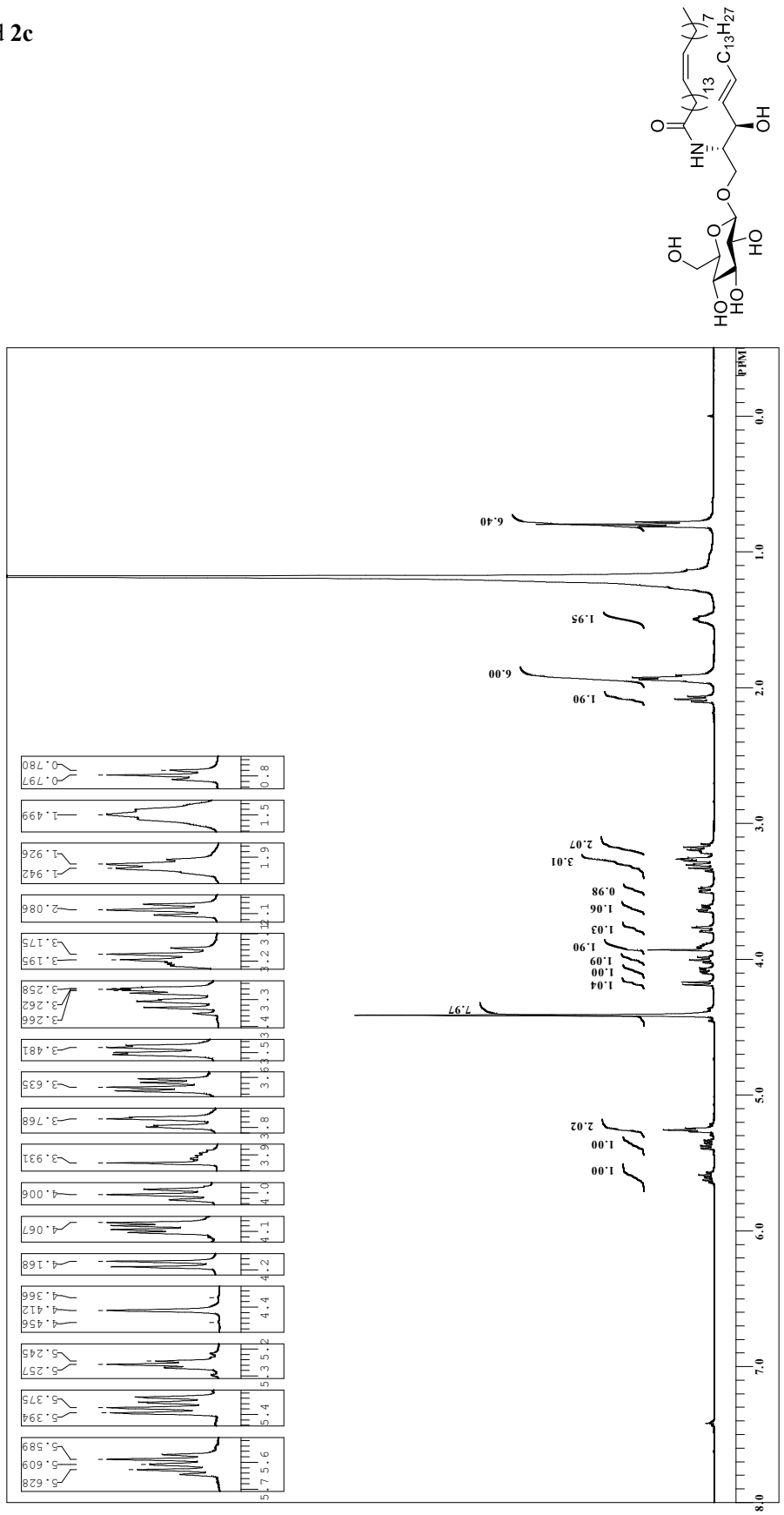

PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
51.43
6.04
2.23
5.67
2.05
4.91
1.11
1.04
1.99
2.77
1.28
1.00
0.99
1.90
1.00
0.99
5.724
5.703
5.686
5.463
5.444
5.333
5.321
4.814
4.083
4.062
3.954
3.784
3.766
3.756
3.642
3.631
3.528
3.404
3.379
3.298
3.294
2.173
2.163
2.154
2.028
2.014
1.570
1.281
0.908
0.892
0.882
0.874

Compound **1c**

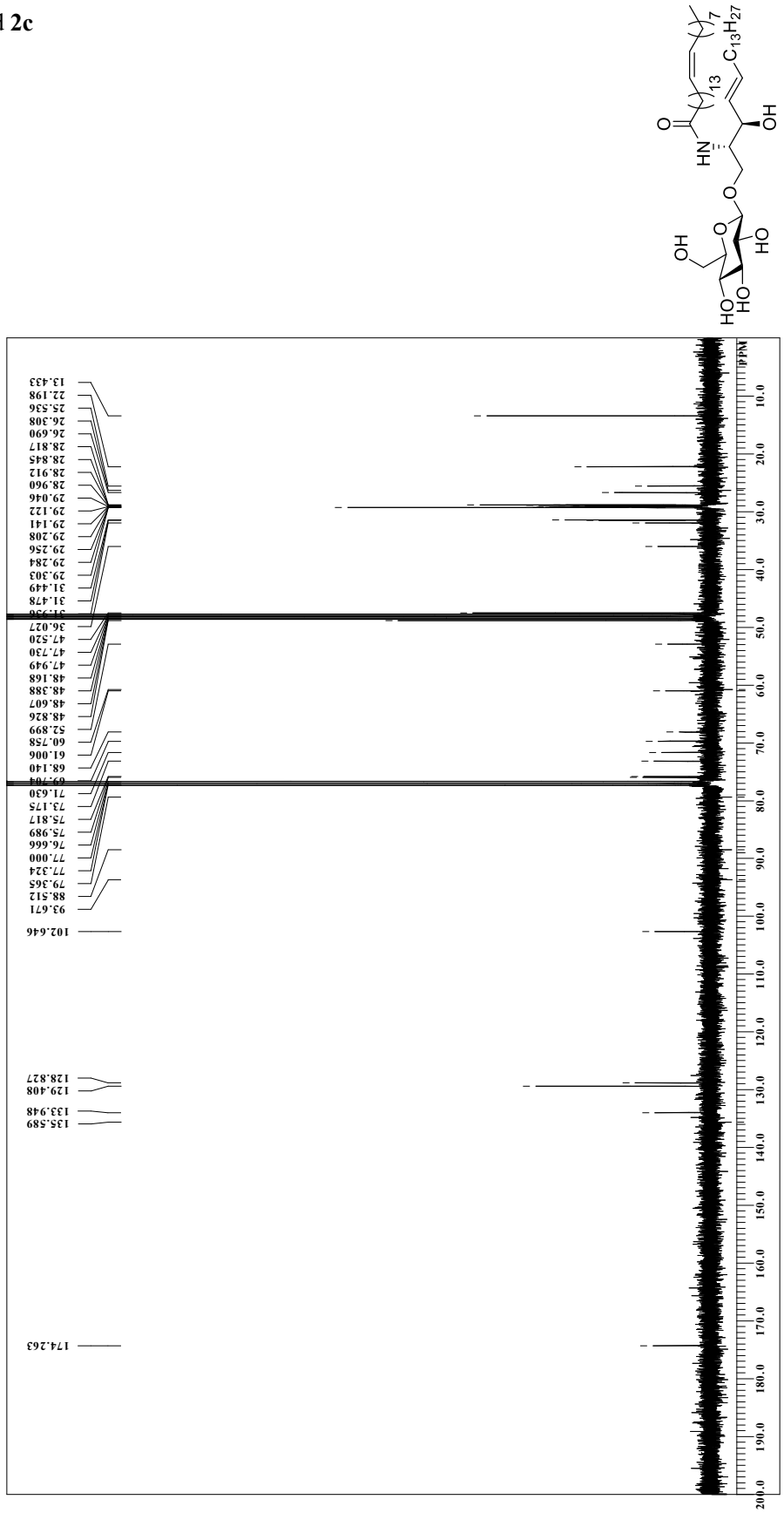

C13H27
13
7
O
HN
OH
O
HO
OH
HO
HO


174.320
133.805
129.418
128.798
99.003
77.324
77.000
76.666
73.366
71.640
71.478
69.771
66.795
60.996
53.204
48.845
48.636
48.416
48.197
47.978
47.758
47.539
35.989
31.955
31.487
31.459
29.322
29.275
29.217
29.132
29.055
28.988
28.922
28.864
26.709
25.526
22.207
13.452
PPM

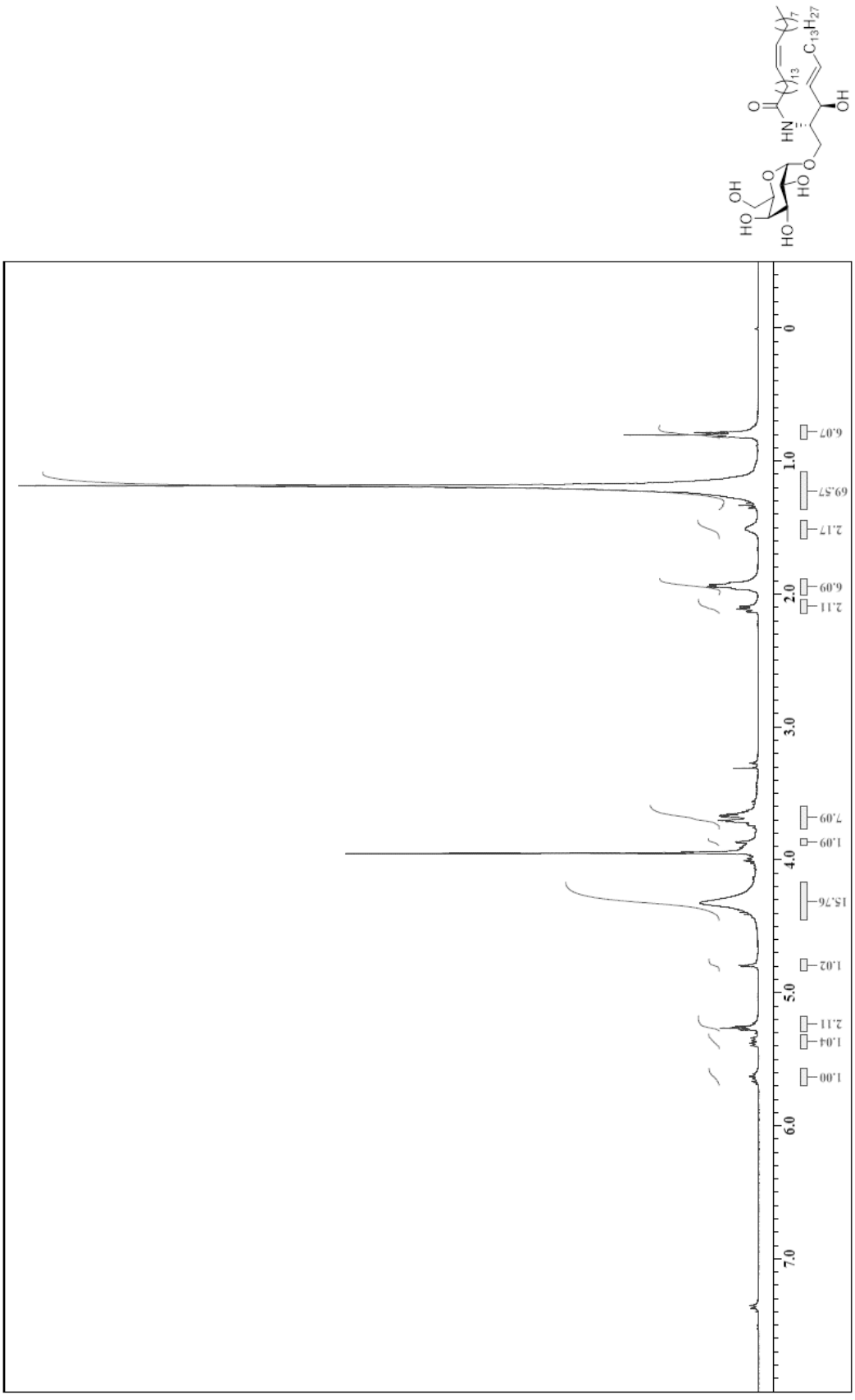
Compound **2c**


OH
HO
HO
HO
O
HN
O
OH
13
7
C13H27
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
6.40
1.95
6.00
1.90
2.07
3.01
0.98
1.06
1.03
1.90
1.09
1.00
1.04
7.97
2.02
1.00
1.00
5.628
5.609
5.589
5.394
5.375
5.257
5.245
4.456
4.412
4.366
4.168
4.067
4.006
3.931
3.768
3.635
3.481
3.266
3.262
3.258
3.195
3.175
2.086
1.942
1.926
1.499
0.797
0.780

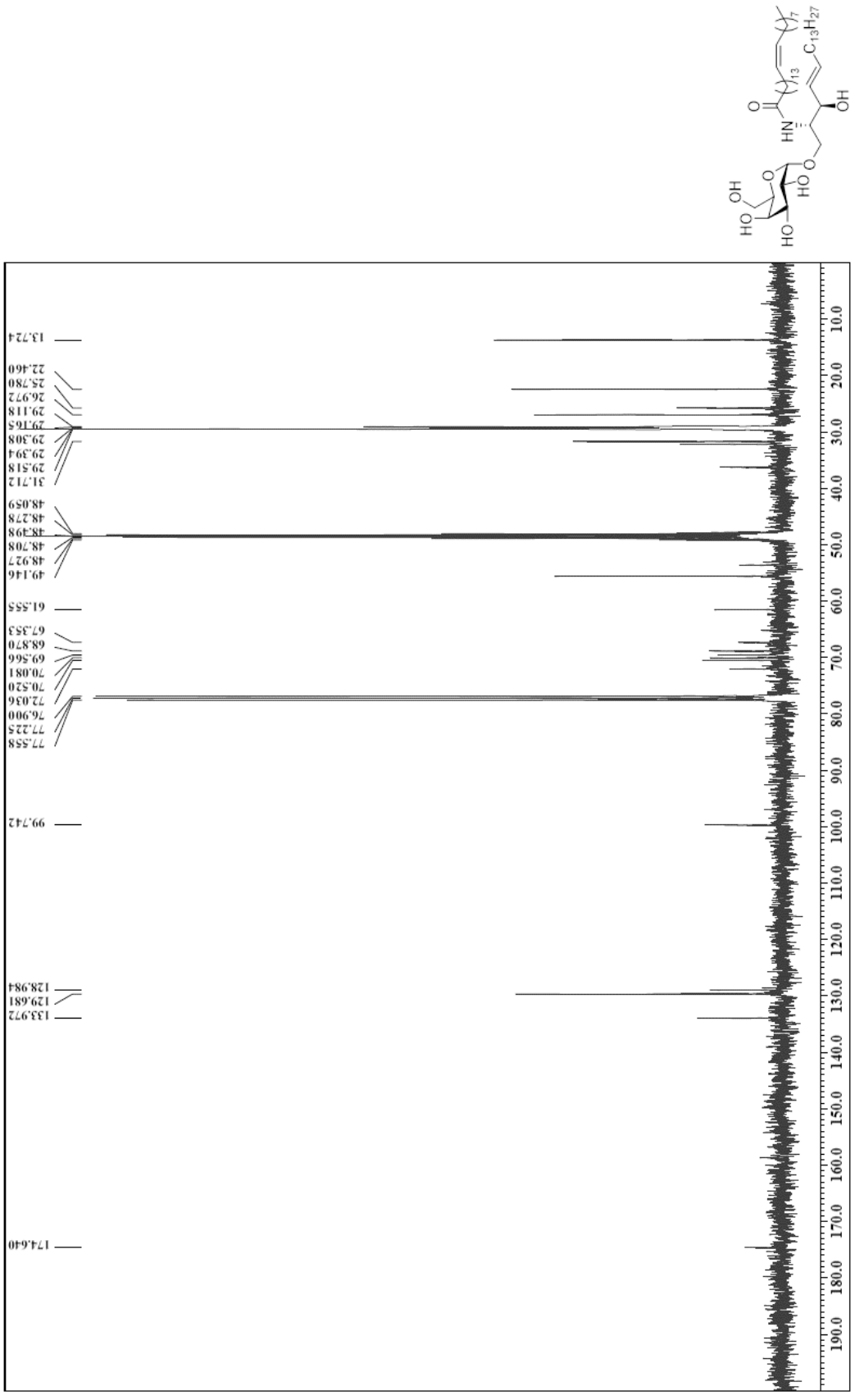
Compound **2c**


13.433
22.198
25.536
26.308
26.690
28.817
28.845
28.912
28.960
29.046
29.122
29.141
29.208
29.256
29.284
29.303
31.449
31.478
36.027
47.520
47.730
47.949
48.168
48.388
48.607
48.826
52.899
60.758
61.006
68.140
71.630
73.175
75.817
75.989
76.666
77.000
77.324
79.365
88.512
93.671
102.646
128.827
129.408
133.948
135.589
174.263
PPM
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0

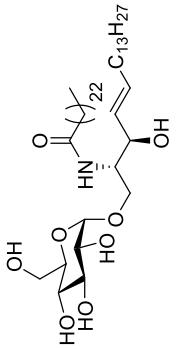
Compound **3c**

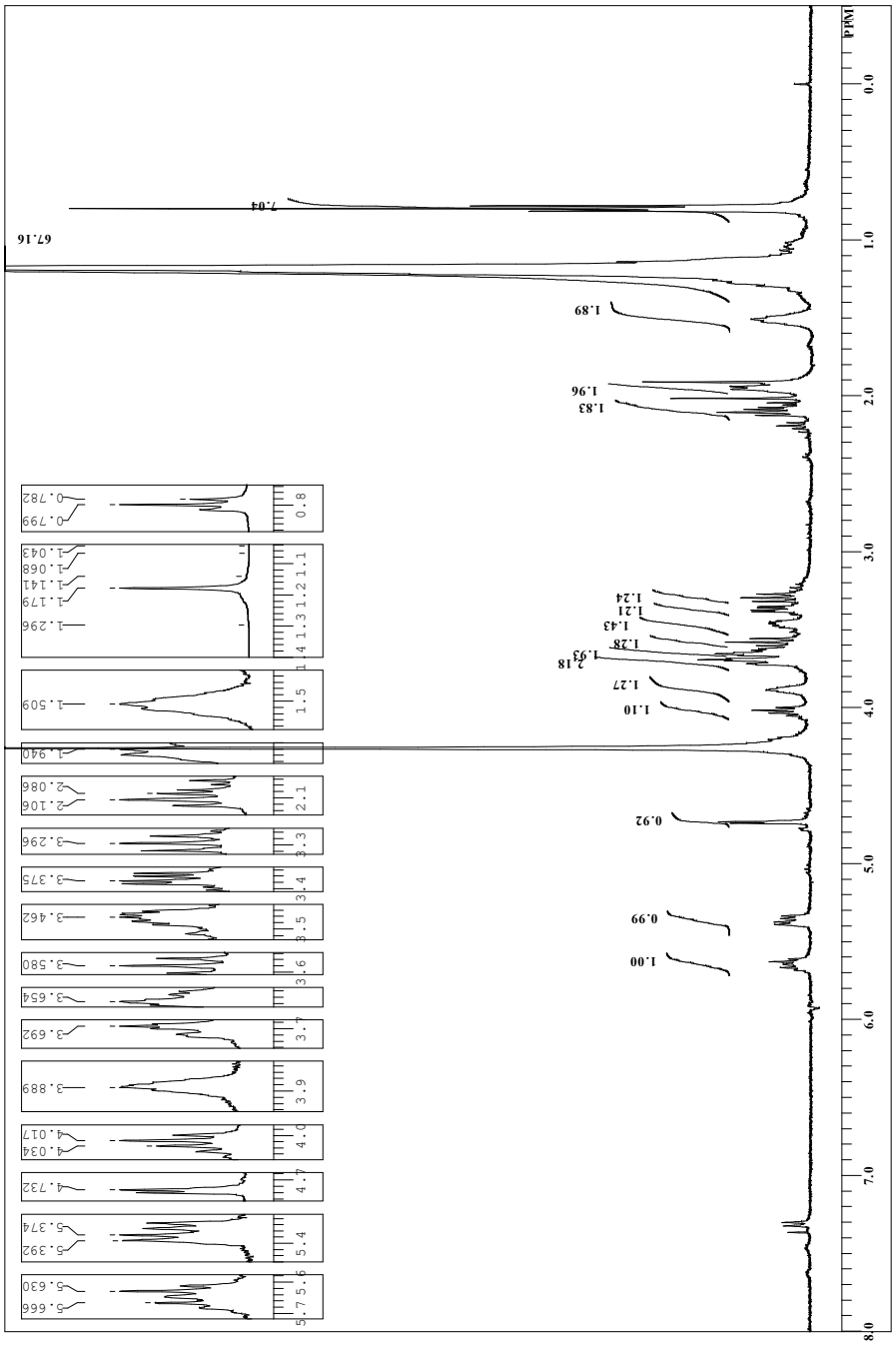


Compound **3c**

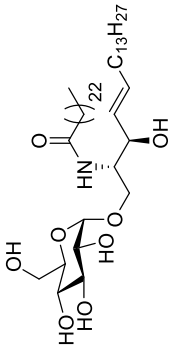

13.724
22.460
25.780
26.972
29.118
29.765
29.308
29.394
29.518
31.712
48.059
48.278
48.398
48.708
48.927
49.146
61.555
67.353
68.870
69.566
70.081
70.520
72.036
76.900
77.225
77.558
99.742
128.984
129.681
133.972
174.640

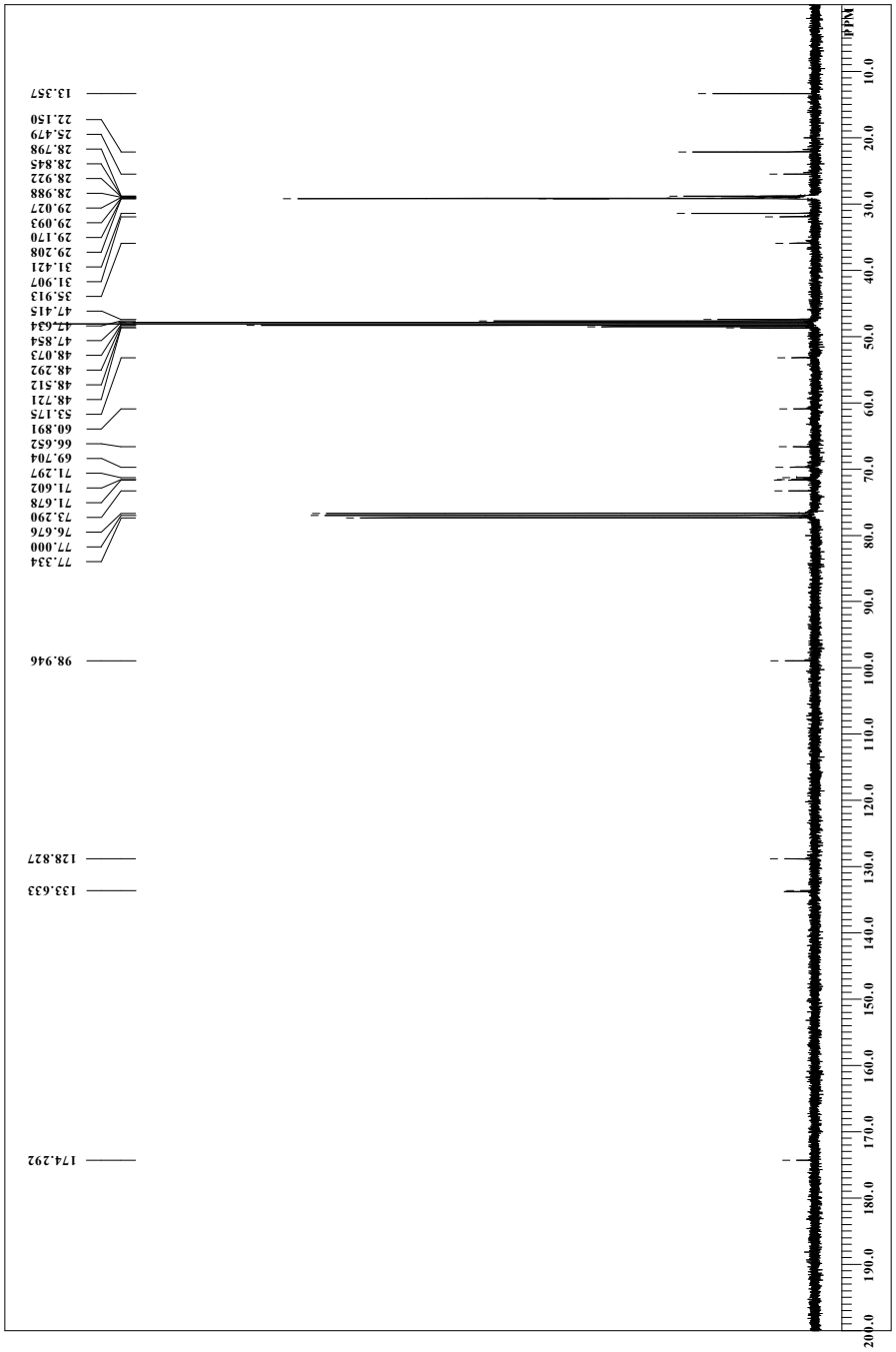
Compound **1d**


$C_{13}H_{27}$
22
O
HN
OH
O
HO
HO
OH
HO

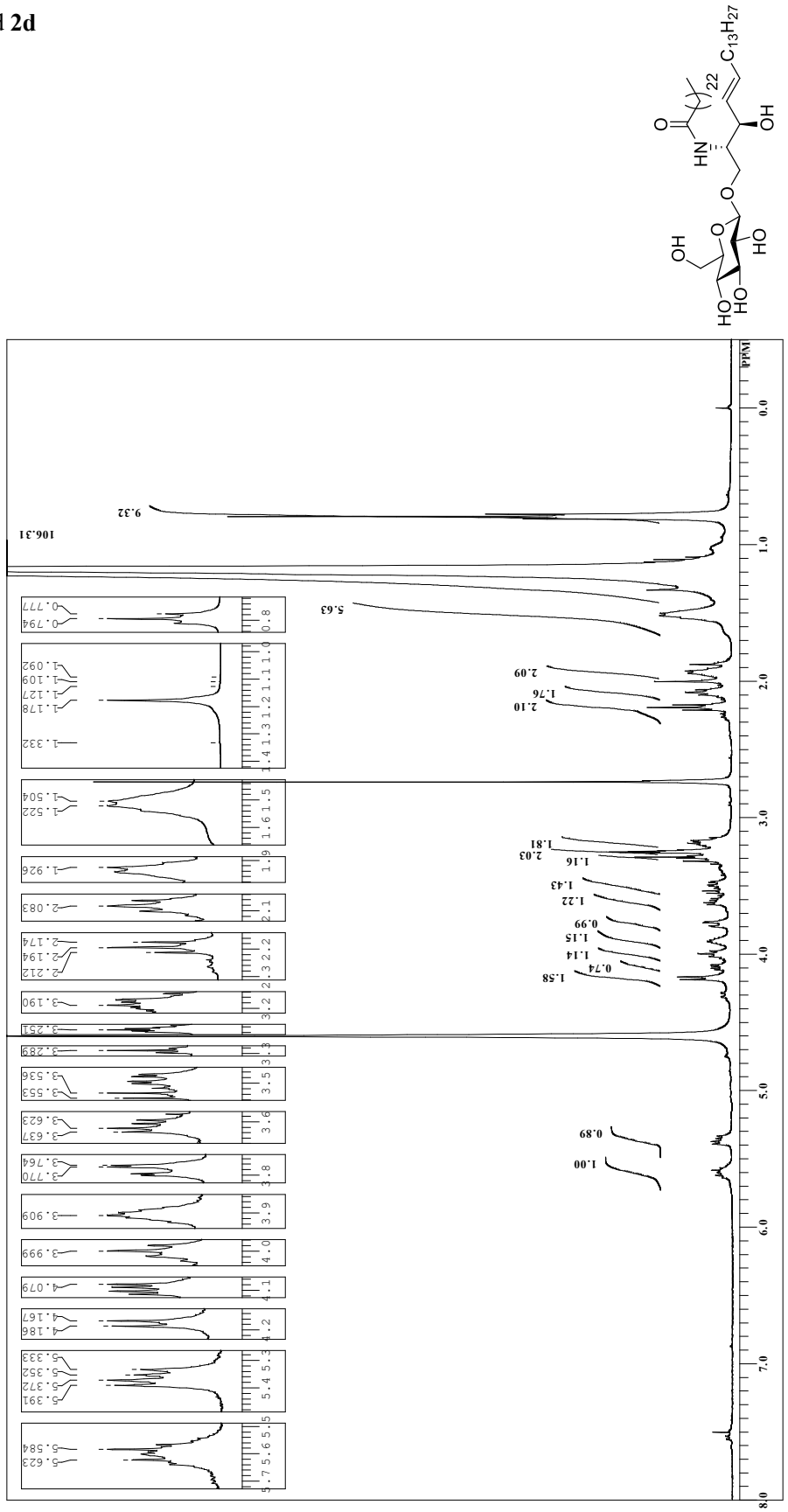

PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
67.16
7.04
1.89
1.83
1.96
0.92
0.99
1.00
1.10
1.27
2.18
1.93
1.28
1.43
1.21
1.24
1.179
1.141
1.068
1.043
1.296
1.509
1.940
2.106
2.086
3.296
3.375
3.462
3.580
3.654
3.692
3.889
4.034
4.017
4.732
5.392
5.374
5.666
5.630
0.799
0.782

Compound **1d**

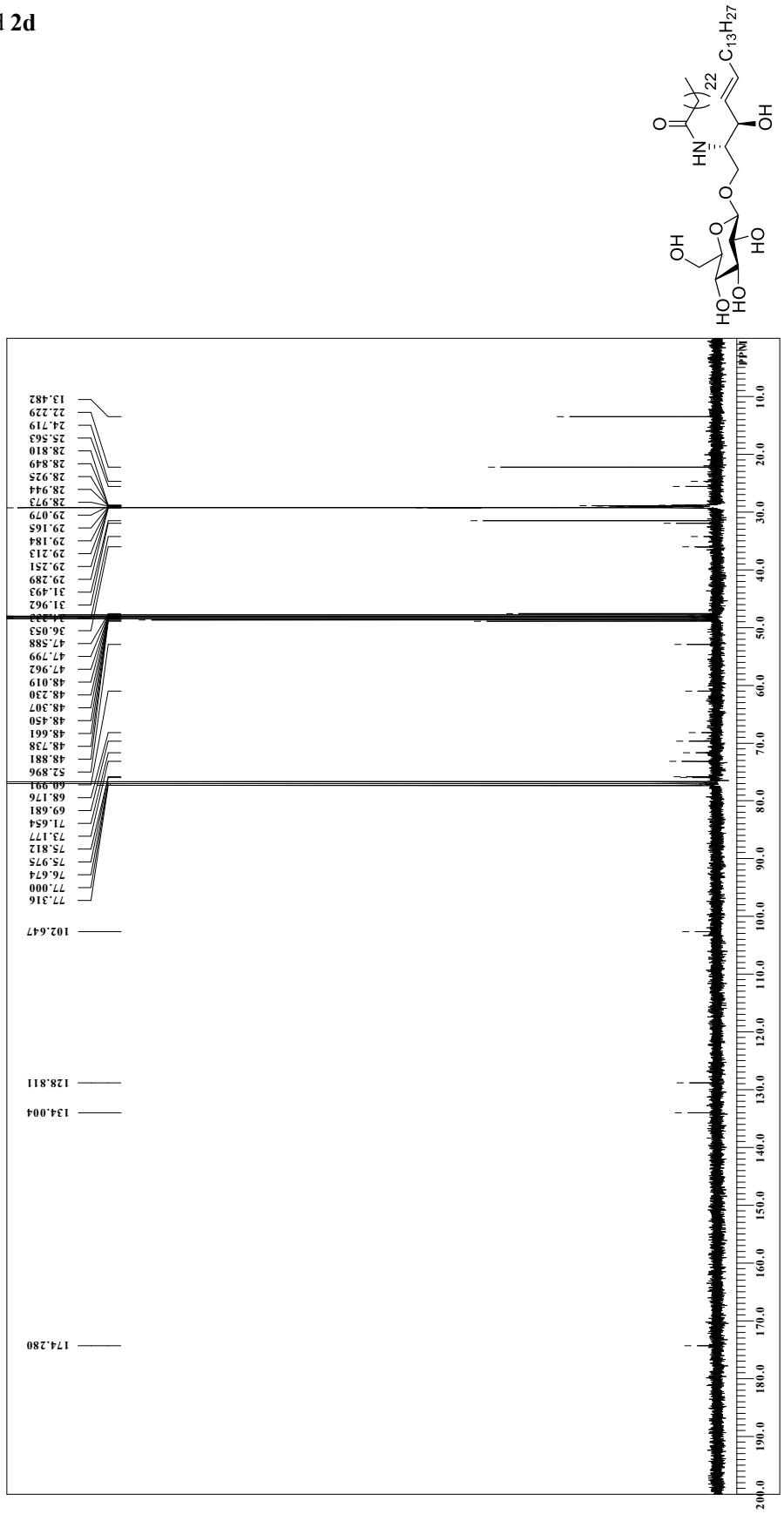

C13H27
22
O
HN
OH
O
HO
OH
HO
HO


13.357
22.150
25.479
28.798
28.845
28.922
28.988
29.027
29.093
29.170
29.208
31.421
31.907
35.913
47.415
47.634
47.854
48.073
48.292
48.512
48.721
53.175
60.891
66.652
69.704
71.297
71.602
71.678
73.290
76.676
77.000
77.334
98.946
128.827
133.633
174.292
PPM
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0

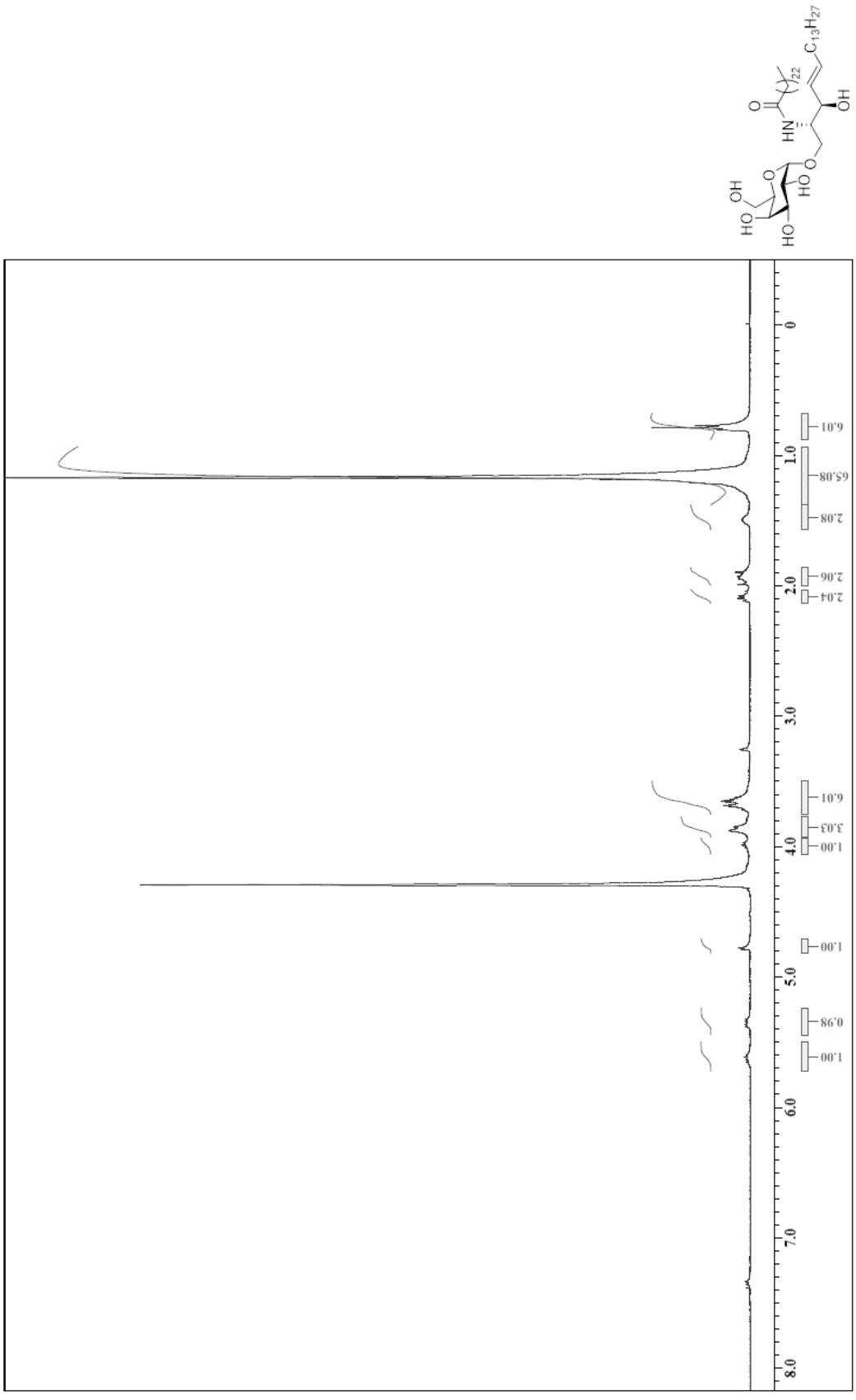
Compound **2d**


HO
HO
HO
OH
O
O
HN
O
22
C13H27
OH
PPM
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
106.31
9.32
5.63
2.09
2.10
1.76
1.81
2.03
1.16
1.58
0.74
1.14
1.15
0.99
1.22
1.43
1.00
0.89

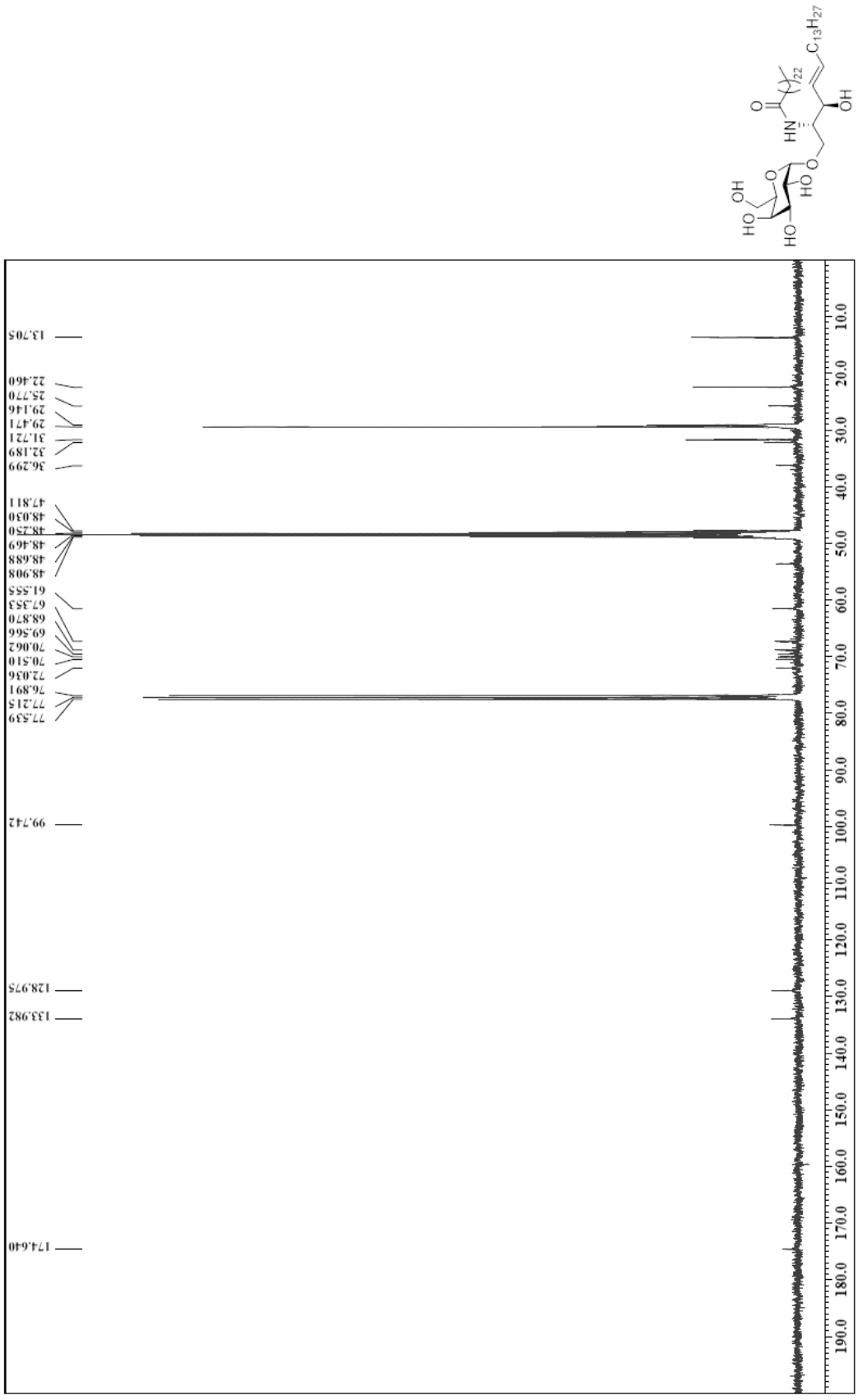
Compound **2d**



Compound **3d**



Compound **3d**


13.705
22.460
25.770
29.146
29.471
31.721
32.189
36.299
47.811
48.030
48.250
48.469
48.688
48.908
61.555
67.353
68.870
69.566
70.062
70.510
72.036
76.891
77.215
77.539
99.742
128.975
133.982
174.640
HO
OH
HO
HO
O
HN
O
OH
$C_{13}H_{27}$
$_{22}$