Building Biologics by Chemical Synthesis: Practical Preparation of Di- and Triantennary *N*-linked Glycoconjugates

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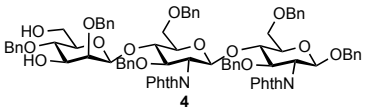
Experimental Section

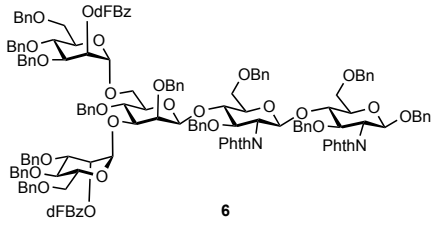
General Procedures: All reactions were carried out under dry Ar in an oven-dried glassware. CH_2Cl_2 was freshly distilled over CaH_2 and THF was filtered through a column of activated alumina prior to use. Anhydrous methanol was purchased from Aldrich. NIS was recrystallized from 1,4-dioxane/CCl_4 and was kept in dark. Ammonia was condensed (-78 ^oC) into a flask, dried with Na and then distilled into the reaction flask. All other reagents were used as received. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 500/600 MHz instruments are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. The residual solvent reference peaks were used from published literature.[1] 2D NMR experiments were performed using standard parameters (*200 and More NMR Experiments,* S. Berger, S. Braun, Wiley-VCH, **2004**). IR measurements were performed on Jasco ATR FT/IR-6100 instrument and optical rotations were measured on JASCO P-2000 and are reported as average of five data points. TLC analyses were performed on Merck TLC plates and visualizations were performed with UV light and/or Hanessian stain and/or sulfuric acid stain (5% H_2SO_4 in MeOH). Preparative purifications were performed using Silcacycle silica gel using HPLC grade solvents. Peptide synthesis was carried out using standard Fmoc-SPPS protocols.



4

Benzyl 2,4-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (4). Trisaccharide **3** (1.50 g, 10.8 mmol) was azeotropically dried with PhMe (3 x 5 mL) and then on high vacuum for 1 h. This compound was cooled to 0 ^oC, treated with a solution of BH_3 in THF (10.8 mL, 10.8 mmol, 1.0 M) and a solution of *n*-Bu_2BOTf in CH_2Cl_2 (3.20 mL, 3.20 mmol, 1.0 M). After 2 h at 0 ^oC, the reaction mixture was quenched with Et_3N and MeOH, and the volatiles were removed *in vacuo*. Purification by chrom. on SiO_2 (PhMe:EtOAc 3:1) afforded **4** (1.25 g, 83%) as a clear oil: $[\alpha]_D^{24}$ -7.8 (c 1.0, $CHCl_3$); IR (ATR) 3471, 2876, 1775, 1712, 1386 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.3 Hz, 1 H), 7.72 – 7.60 (m, 2 H), 7.58 (d, *J* = 4.2 Hz, 2 H), 7.53 (d, *J* = 7.0 Hz, 2 H), 7.44 – 7.29 (m, 1 H), 7.29 – 7.24 (m, 8 H),

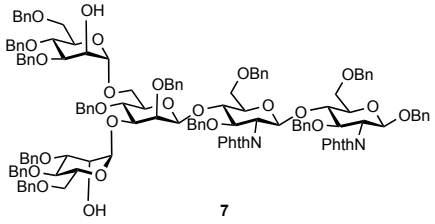
7.24 – 7.14 (m, 12 H), 6.98-6.91 (m, 1 H), 6.91 – 6.86 (m, 6 H), 6.83 (p, *J* = 3.8 Hz, 5 H), 6.67 (dd, *J* = 4.8, 1.9 Hz, 3 H), 5.21 (d, *J* = 8.0 Hz, 1 H), 4.93 (d, *J* = 11.6 Hz, 1 H), 4.90 – 4.84 (m, 2 H), 4.77 (d, *J* = 12.8 Hz, 1 H), 4.73 (d, *J* = 11.3 Hz, 1 H), 4.61 (d, *J* = 12.4 Hz, 1 H), 4.57 (d, *J* = 11.7 Hz, 1 H), 4.53 (s, 1 H), 4.50 – 4.42 (m, 5 H), 4.38 (d, *J* = 12.2 Hz, 1 H), 4.32 (d, *J* = 12.2 Hz, 1 H), 4.29 (d, *J* = 12.4 Hz, 1 H), 4.21 – 4.17 (m, 1 H), 4.16 – 4.12 (m, 2 H), 4.12 – 4.09 (m, 1 H), 4.06 (dd, *J* = 10.6, 8.3 Hz, 1 H), 3.96 (dd, *J* = 10.0, 8.2 Hz, 1 H), 3.64 – 3.59 (m, 1 H), 3.59-3.55 (m, 2 H), 3.49 (dd, *J* = 11.0, 1.6 Hz, 1 H), 3.42 (ddd, *J* = 15.2, 10.3, 3.4 Hz, 2 H), 3.39 – 3.30 (m, 3 H), 3.23 (ddd, *J* = 10.0, 3.8, 1.6 Hz, 1 H), 3.16 (dt, *J* = 10.0, 2.6 Hz, 1 H), 3.03 (ddd, *J* = 8.9, 5.6, 2.7 Hz, 1 H), 2.28 – 2.22 (m, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.6, 167.7, 167.6, 138.7, 138.6 (2), 138.3 (2), 137.7, 137.2, 134.1, 133.9, 133.5, 131.8, 131.7, 131.5, 129.1, 128.7, 128.6, 128.5, 128.4, 128.3 (3), 128.2 (2), 128.1 (3), 128.0 (2), 127.9 (2), 127.8 (2), 127.6 (2), 127.5, 127.4 (2), 127.2, 127.1, 126.9, 125.4, 123.8, 123.2 (2), 101.4, 97.2, 97.1, 79.0, 78.5, 76.6, 76.6, 75.9, 75.3, 75.3, 74.7, 74.7, 74.6, 74.5, 74.3, 73.5, 72.8, 70.6, 68.3, 67.7, 62.3, 56.5, 55.8. HRMS (ESI) calc for $C_{83}H_{80}N_2O_{18}Na$ ($M+Na^+$) 1415.5304, found 1415.5248.



6

Benzyl [3,4,6-tri-*O*-benzyl-2-*O*-(2,5-difluorobenzoyl)-α-D-mannopyranosyl-(1→ 6)]-[3,4,6-tri-*O*-benzyl-2-*O*-(2,5-difluorobenzoyl)-α-D-mannopyranosyl-(1→ 3)]-2,4-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (6). A mixture of donor **5** (0.806 g, 1.27 mmol) and acceptor **4** (0.475 g, 0.341 mmol) was azeotropically dried with PhMe (3 x 5 mL) and then on high vacuum for 1 h. This mixture was dissolved in anh. CH_2Cl_2 (6.82 mL), freshly activated 4Å MS (1.5 g) were added and, after 1 h, this mixture was cooled to -78 ^oC, AgOTf (0.175 g, 0.682 mmol) and NIS (0.286 g, 1.27 mmol) were added in one portion. The reaction mixture was allowed to warm up to -25 ^oC, stirred at this temp. for 2 h 30 min, quenched with Et_3N, filtered, washed with sat. $Na_2S_2O_3$, brine, dried ($MgSO_4$), and concentrated. Purification by chrom. on SiO_2 (CH_2Cl_2:EtOAc, 15:1 then PhMe:EtOAc 3:1) afforded **6** (0.770 g, 89%) as a clear oil: $[\alpha]_D^{23}$ -0.53 (c 1.0, $CHCl_3$), IR (ATR) 2930, 2867, 1780, 1713, 1492, 1391 cm^{-1}; ^{1}H NMR (600 MHz, CD_3CN) δ 7.86-7.70 (m, 6 H), 7.70-7.54 (m, 4 H), 7.49 (d, *J* = 7.5 Hz, 2 H), 7.43 (dp, *J* = 10.2, 3.3 Hz, 2 H), 7.40-7.14 (m, 50 H), 7.14-7.07 (m, 2 H), 7.01 (dd, *J* = 8.5,

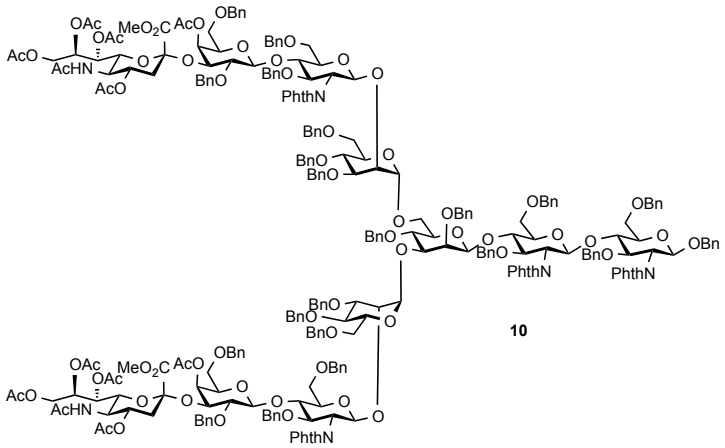
6.5 Hz, 2 H), 6.97 (d, *J* = 7.2 Hz, 2 H), 6.91-6.86 (m, 2 H), 6.84 (t, *J* = 7.3 Hz, 1 H), 6.77 (t, *J* = 7.1 Hz, 3 H), 6.69 (t, *J* = 7.4 Hz, 1 H), 6.59 (t, *J* = 7.5 Hz, 2 H), 5.72-5.66 (m, 1 H), 5.54 (t, *J* = 2.6 Hz, 1 H), 5.30-5.25 (m, 2 H), 5.13 (d, *J* = 12.2 Hz, 1 H), 5.05 (d, *J* = 2.0 Hz, 1 H), 4.92 (d, *J* = 8.5 Hz, 1 H), 4.89-4.81 (m, 3 H), 4.79 (d, *J* = 9.9 Hz, 1 H), 4.75 (d, *J* = 11.7 Hz, 1 H), 4.70 (br s, 1 H), 4.67-4.64 (m, 2 H), 4.62 (d, *J* = 12.3 Hz, 2 H), 4.59-4.54 (m, 4 H), 4.53 (d, *J* = 3.9 Hz, 3 H), 4.51-4.48 (m, 3 H), 4.48-4.45 (m, 2 H), 4.43 (d, *J* = 12.1 Hz, 2 H), 4.40-4.38 (m, 1 H), 4.37 (d, *J* = 4.8 Hz, 1 H), 4.33 (d, *J* = 11.3 Hz, 1 H), 4.21 (dq, *J* = 14.5, 6.6 Hz, 1 H), 4.13-3.99 (m, 7 H), 3.99-3.89 (m, 4 H), 3.89-3.81 (m, 2 H), 3.81-3.68 (m, 5 H), 3.65 (dd, *J* = 10.9, 4.5 Hz, 1 H), 3.58 (dt, *J* = 10.8, 3.1 Hz, 2 H), 3.52-3.47 (m, 1 H), 3.39 (dd, *J* = 10.9, 3.8 Hz, 1 H), 3.36-3.25 (m, 3 H); ^{13}C NMR (151 MHz, CD_3CN) δ 167.3, 138.9, 138.4, 138.3 (3), 138.2 (2), 138.1 (2), 137.7, 137.6, 137.0, 133.8, 131.0, 128.1(2), 128.0 (3), 127.9 (3), 127.8 (3), 127.7, 127.6 (2), 127.5 (2), 127.4 (2), 127.3 (4), 127.2 (2), 127.1 (2), 127.0 (3), 126.9, 126.7 (2), 122.9, 122.7, 117.4, 117.0, 101.3, 99.0, 97.1, 96.9, 96.6, 81.2, 79.1, 78.1, 77.6, 77.1, 76.5, 75.8, 75.3, 74.3 (2), 74.2, 74.1, 73.9, 73.8 (2), 73.7, 73.6, 72.6, 72.4 (2), 72.1, 72.0, 71.5, 71.1, 70.6, 70.2, 69.7, 69.1, 69.0, 68.7, 68.0, 67.8, 65.7, 56.1, 55.4; HRMS (ESI) calc for $C_{151}H_{140}N_2O_{30}F_4Na$ ($M+Na^+$) 2559.9325, found 2559.9351.



7

Benzyl [3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→ 6)]-[3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→ 3)]-2,4-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (7). A solution of **6** (0.333 g, 0.131 mmol) in anh. THF (0.76 mL) and MeOH (2.62 mL) was treated with a solution of NaOMe (0.26 mL, 0.52 mmol, 0.5 M in MeOH). After stirring at rt for 1 h, the mixture was quenched with DOWEX-50WX8, filtered, and concentrated. Purification by chrom. on SiO_2 (PhMe:EtOAc, 3:1) afforded **7** (0.296 g, 99%) as a clear oil: $[\alpha]_D^{21}$ +36.8 (c 1.0, $CHCl_3$); IR (ATR) 3426, 2933, 1716, 1389, 1075 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 – 7.64 (m, 1 H), 7.61 (t, *J* = 7.4 Hz, 1 H), 7.55 (t, *J* = 7.2 Hz, 2 H), 7.48 (d, *J* = 7.4 Hz, 1 H), 7.34 (d, *J* = 7.6 Hz, 2 H), 7.30 – 7.04 (m, 50 H), 7.04 – 6.99 (m, 2 H), 6.98 – 6.92 (m, 1 H), 6.92 – 6.79 (m, 6 H), 6.79 – 6.74 (m, 2 H), 6.71 – 6.56 (m, 5 H), 5.17 – 5.14 (m, 1 H), 5.08 (d, *J* = 1.9 Hz, 1 H), 4.94 (d, *J* = 11.8 Hz, 1 H), 4.91 – 4.82 (m, 3 H), 4.74 (dd, *J* = 12.0,

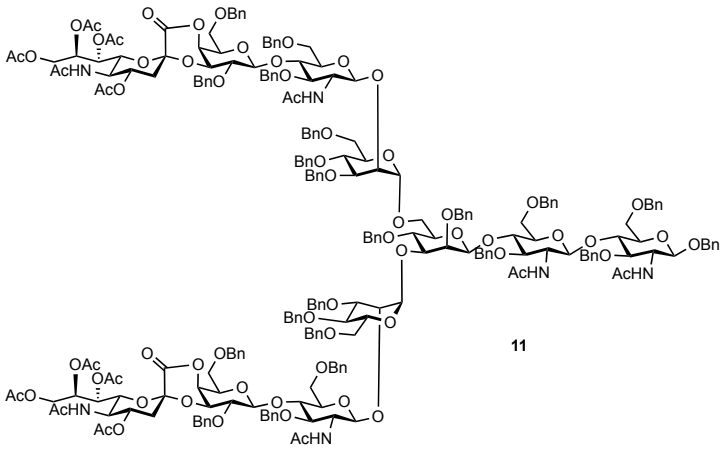
3.0 Hz, 2 H), 4.71 (d, *J* = 11.9 Hz, 1 H), 4.65 (d, *J* = 10.9 Hz, 1 H), 4.60 (d, *J* = 12.4 Hz, 1 H), 4.56 – 4.51 (m, 2 H), 4.51 – 4.48 (m, 2 H), 4.45 – 4.35 (m, 9 H), 4.35 – 4.30 (m, 1 H), 4.30 – 4.25 (m, 3 H), 4.23 (d, *J* = 11.5 Hz, 1 H), 4.12 – 4.06 (m, 4 H), 4.03 (td, *J* = 10.7, 7.6 Hz, 1 H), 3.97 (ddd, *J* = 11.6, 8.1, 3.8 Hz, 1 H), 3.90 – 3.84 (m, 2 H), 3.83 (d, *J* = 3.0 Hz, 1 H), 3.81 – 3.75 (m, 4 H), 3.75 – 3.69 (m, 2 H), 3.68 (d, *J* = 9.2 Hz, 1 H), 3.65 (d, *J* = 9.5 Hz, 1 H), 3.64 – 3.60 (m, 2 H), 3.60 – 3.51 (m, 4 H), 3.48 (dt, *J* = 8.5, 3.1 Hz, 2 H), 3.43 (d, *J* = 10.1 Hz, 1 H), 3.40 (dd, *J* = 10.8, 1.9 Hz, 1 H), 3.37 – 3.29 (m, 2 H), 3.20 (ddd, *J* = 9.8, 4.1, 1.7 Hz, 1 H), 3.09 (dt, *J* = 10.0, 2.8 Hz, 2 H), 2.25 (s, 2 H); ^{13}C NMR (150 MHz, CD_3CN) δ 167.3, 139.0, 138.6 (2), 138.4, 138.3 (3), 138.2 (4), 138.1, 137.0, 133.8, 131.0, 128.1 (2), 128.0 (3), 127.9 (4), 127.8 (3), 127.7 (2), 127.6 (2), 127.5 (4), 127.4 (3), 127.3 (2), 127.2 (3), 127.1 (5), 127.0 (2), 126.9 (2), 126.7, 122.9, 122.7, 117.2, 117.0, 116.9, 116.8, 101.9, 101.1, 99.6 (2), 96.7, 81.2, 79.4, 79.1, 78.8, 78.3, 76.5, 76.1, 75.4, 74.3 (3), 74.2, 74.1, 74.0 (2), 73.8 (3), 73.7, 73.6, 72.6, 72.4, 72.0, 71.8, 71.1, 70.6, 70.2, 70.1, 69.2, 68.9, 68.0, 67.8, 67.4, 66.9, 65.7, 56.1, 55.4; HRMS (ESI) calc for $C_{137}H_{136}N_2O_{28}Na$ ($M+Na^+$) 2279.9177, found 2279.9236.



10

Benzyl [2-[methyl[5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-2,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl]-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)]-[2-[methyl[5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-2,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl]-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (18). A mixture of donor **9** (0.245 g, 0.182 mmol) and acceptor **7** (0.0610 g,

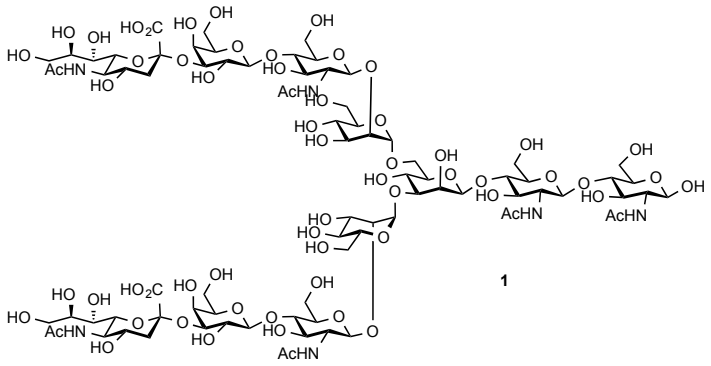
0.0270 mmol) was azeotropically dried with PhMe and then on high vacuum for 2 h. This mixture was dissolved in anh. CH_2Cl_2 (0.52 mL) and then added to a pre-cooled (0 ^oC) mixture of $Cp_2Zr(OTf)_2 \cdot THF$ (0.107 g, 0.181 mmol) and freshly activated 4Å MS (0.10 g). The reaction mixture was stirred at 0 ^oC for 1 h 30 min, quenched with Et_3N, filtered through a pad of Celite, and concentrated. Purification by chrom. on SiO_2 (PhMe:Acetone, 1:1 then Hexanes:Acetone, 1:1) afforded **10** (0.0984 g, 74%) as a clear oil: $[\alpha]_D^{23}$ +0.58 (c 1.0, $CHCl_3$); IR (ATR) 3398, 2926, 2870, 1745, 1714, 1388, 1368, 1224 cm^{-1}; ^1H NMR (600 MHz, CD_3CN) δ 7.84 – 7.72 (m, 6 H), 7.72 – 7.60 (m, 7 H), 7.60 – 7.50 (m, 4 H), 7.46 – 7.38 (m, 5 H), 7.38 – 7.26 (m, 33 H), 7.26 – 7.17 (m, 20 H), 7.17 – 7.06 (m, 21 H), 7.04 – 6.96 (m, 10 H), 6.96 – 6.89 (m, 9 H), 6.86 (tdd, *J* = 7.3, 4.5, 2.0 Hz, 1 H), 6.83 – 6.74 (m, 3 H), 6.64 – 6.58 (m, 1 H), 6.54 (dd, *J* = 8.8, 6.3 Hz, 1 H), 6.10 (dd, *J* = 10.0, 6.7 Hz, 2 H), 5.54 (ddd, *J* = 8.4, 5.5, 2.9 Hz, 1 H), 5.28 (ddt, *J* = 7.1, 5.0, 2.5 Hz, 2 H), 5.22 (dd, *J* = 8.6, 5.1 Hz, 1 H), 5.16 (dd, *J* = 10.1, 3.6 Hz, 2 H), 4.99 – 4.81 (m, 10 H), 4.81 – 4.74 (m, 2 H), 4.74 – 4.66 (m, 3 H), 4.64 (d, *J* = 12.4 Hz, 3 H), 4.57 – 4.46 (m, 10 H), 4.46 – 4.40 (m, 7 H), 4.40 – 4.35 (m, 5 H), 4.35 – 4.33 (m, 1 H), 4.33 – 4.23 (m, 5 H), 4.23 – 4.14 (m, 3 H), 4.12 – 3.97 (m, 16 H), 3.97 – 3.90 (m, 4 H), 3.90 – 3.87 (m, 1 H), 3.87 – 3.83 (m, 4 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.79 – 3.70 (m, 7 H), 3.70 – 3.64 (m, 3 H), 3.62 – 3.54 (m, 4 H), 3.54 – 3.49 (m, 3 H), 3.49 – 3.44 (m, 3 H), 3.44 – 3.41 (m, 2 H), 3.41 – 3.33 (m, 6 H), 3.32 – 3.22 (m, 5 H), 3.22 – 3.17 (m, 1 H), 3.15 (d, *J* = 10.7 Hz, 1 H), 2.94 – 2.88 (m, 2 H), 2.75 (dt, *J* = 11.0, 5.5 Hz, 2 H), 2.54 (dd, *J* = 12.6, 4.8 Hz, 1 H), 2.48 (dd, *J* = 12.7, 4.8 Hz, 1 H), 2.19 (s, 6 H), 2.06 – 2.03 (m, 3 H), 1.95 (s, 9 H), 1.93 (s, 6 H), 1.85 (s, 6 H), 1.80 – 1.79 (m, 2 H), 1.78 (s, 3 H), 1.77 (s, 3 H); ^{13}C NMR (150 MHz, CD_3CN) δ 170.0, 169.6 (2), 169.5 (2), 169.4, 169.3, 167.8 (2), 167.3, 139.1, 138.9, 138.8, 138.5, 138.4, 138.3 (2), 138.2 (3), 138.1 (2), 138.0, 137.8, 137.7, 137.0, 133.9, 133.8, 131.2 (2), 131.0, 129.2, 128.4, 128.3, 128.0 (4), 127.9 (7), 127.8 (6), 127.7 (2), 127.6 (4), 127.5 (4), 127.4 (2), 127.3 (4), 127.2, 127.1 (3), 127.0 (3), 126.9 (4), 126.8, 126.7, 126.1, 122.9, 122.7, 101.9, 101.6, 98.5, 97.4, 97.4, 96.9, 96.7, 96.3, 95.2, 78.6, 77.9, 77.2, 76.7, 76.5, 76.1, 75.5, 74.3, 74.2, 74.1, 74.0, 73.9, 73.8, 73.7, 73.6, 73.4, 72.5 (2), 72.4 (2), 72.3, 72.2, 72.0, 71.9, 71.7, 71.6 (2), 71.5, 70.2, 69.8, 69.2, 68.9, 68.7, 68.3, 68.2, 67.8, 67.7 (2), 67.0 (2), 66.5, 62.1, 61.7, 56.1, 55.4, 55.2, 53.9, 52.3, 48.1, 48.0, 45.9, 21.9, 21.8, 20.2, 19.8 (4), 19.7, 19.6 (2); MS (ESI) calc for $C_{277}H_{288}N_6O_{76}Na_2$ ($M+2Na^+$) 2481.62, $C_{277}H_{288}N_6O_{76}Na_3$ ($M+3Na^+$) 1662.08, found 2482.06, 1662.15.



11

Lactone 11. A solution of **10** (63.0 mg, 0.0128 mmol) in anh. CH_2Cl_2 (1.0 mL) and MeOH (3.0 mL) was treated with NaOMe (0.31 mL, 0.154 mmol, 0.5 M in MeOH) and stirred at rt for 12 h and water (0.20 mL) was added. After additional 12 h at rt, the mixture was quenched with DOWEX-MAC-3 resin to pH 6, filtered, and concentrated. The crude material was dissolved in EtOH (2.0 mL) and 1,2-ethylenediamine (0.10 mL), heated at 80 ^{o}C for 24 h, concentrated, and dissolved in anh. pyridine (3.0 mL) and acetic anhydride (1.5 mL). After 24 h at rt, the volatiles were removed *in vacuo* and the crude material was purified by chrom. on SiO_2 (Hexanes:Acetone, 1:1) to afford **11** (19.7 mg, 35%) as a clear oil: $[\alpha]_D^{22}$ -2.57 (c 1.0, $CHCl_3$), IR (ATR) 2925, 1475, 1661, 1369, 1220 cm^{-1}; ^{1}H NMR (600 MHz, CD_3CN) δ 7.41 – 7.08 (m, 105 H), 6.47 (d, *J* = 9.5 Hz, 1 H), 6.25 (t, *J* = 10.0 Hz, 3 H), 6.11 (t, *J* = 6.6 Hz, 1 H), 5.99 (d, *J* = 10.6 Hz, 1 H), 5.36 (dt, *J* = 11.3, 5.6 Hz, 3 H), 5.17 (d, *J* = 7.3 Hz, 2 H), 5.06 (s, 1 H), 5.00 – 4.91 (m, 4 H), 4.91 – 4.83 (m, 3 H), 4.83 – 4.73 (m, 8 H), 4.70 (td, *J* = 12.5, 12.1, 8.9 Hz, 3 H), 4.60 (ddt, *J* = 18.4, 11.1, 6.7 Hz, 6 H), 4.56 – 4.46 (m, 11 H), 4.46 – 4.37 (m, 8 H), 4.37 – 4.33 (m, 4 H), 4.28 (tq, *J* = 14.5, 7.0 Hz, 7 H), 4.24 – 4.19 (m, 4 H), 4.19 – 4.14 (m, 2 H), 4.10 (dt, *J* = 9.5, 2.8 Hz, 2 H), 3.99 (td, *J* = 12.2, 11.0, 5.6 Hz, 7 H), 3.95 – 3.77 (m, 7 H), 3.77 – 3.73 (m, 4 H), 3.73 – 3.65 (m, 8 H), 3.63 (dd, *J* = 11.2, 5.9 Hz, 2 H), 3.59 – 3.41 (m, 13 H), 3.43 – 3.32 (m, 4 H), 3.25 – 3.20 (m, 1 H), 3.18 (s, 1 H), 3.11 (d, *J* = 8.2 Hz, 2 H), 2.98 (d, *J* = 11.1 Hz, 1 H), 2.83 (d, *J* = 8.3 Hz, 1 H), 2.28 (s, 1 H), 2.16 (d, *J* = 14.8 Hz, 1 H), 2.12 – 2.01 (m, 9 H), 1.97 (t, *J* = 3.9 Hz, 15 H), 1.83 (s, 3 H), 1.80 – 1.76 (m, 6 H), 1.75 (s, 6 H), 1.73 – 1.63 (m, 5 H); ^{13}C NMR (150 MHz, CD_3CN) δ 170.1, 169.7 (2), 169.6, 169.4 (2), 169.1, 163.9, 139.2, 139.0, 138.9, 138.5 (2), 138.4, 138.3 (2), 138.2, 138.1 (3), 138.0 (2), 137.7, 133.8, 128.1 (5), 128.0 (6), 127.9 (2), 127.8 (3), 127.7 (4), 127.6, 127.5, 127.4 (2), 127.3 (2), 127.2 (2), 127.1 (3), 127.0 (3), 126.9 (2), 126.8, 126.1, 101.4, 101.3, 101.2, 100.2, 100.1, 99.8, 99.7, 99.5, 99.3, 94.8, 79.8, 79.1, 78.1, 76.1, 74.1 (2), 74.0, 73.5, 73.3, 73.1, 72.7 (2), 72.5, 72.4, 72.3, 72.2, 72.1, 71.9, 69.9 (2), 69.2, 68.7 (2), 68.6, 67.5, 67.2, 61.5, 54.7, 53.9, 48.1, 31.3, 30.9, 29.0, 28.7, 28.7, 28.6, 28.4, 26.5, 25.2, 22.3

(3), 22.1, 22.0, 21.8, 21.7, 19.8, 19.7 (2), 19.6, 13.1; MS (ESI) calc for $C_{247}H_{276}N_6Na_2O_{68}$ ($M+2Na^+$) 2231.41, found 2231.08.

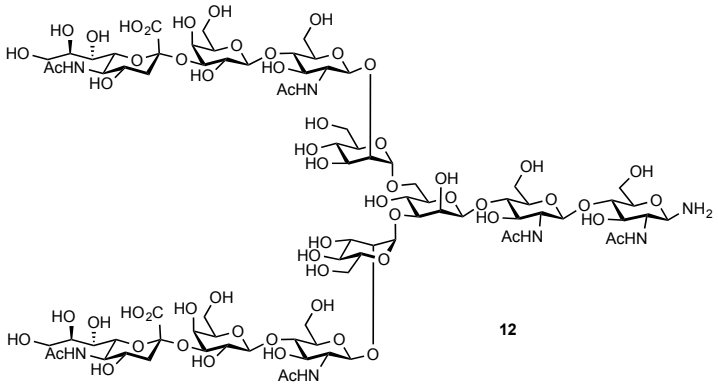


[2-[5-Acetamido-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-β-D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl]-α-D-mannopyranosyl-(1→3)]-[2-[5-acetamido-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-β-D-galactopyranosyl-(1→4)]-2-acetamido-2-deoxy-β-D-glucopyranosyl]-α-D-mannopyranosyl-(1→6)]- β-D-mannopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-D-glucopyranoside (1).

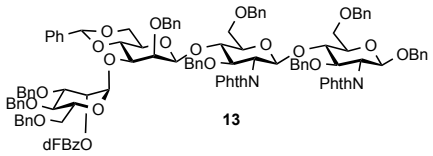
A solution of **11** (18.3 mg, 4.14 μmol) in anh. MeOH (1.0 mL) and anh. CH_2Cl_2 (1.0 mL) was treated with a solution of NaOMe in methanol (0.0830 mL, 0.092 mmol, 0.5 M) and stirred at rt for 18 h. Water (0.20 mL) was added and the reaction was continued for additional 20 h. The mixture quenched with DOWEX-MAC3 resin until pH was adjusted to 6, filtered, and concentrated: MS-ESI calc for $C_{231}H_{262}N_6O_{62}$ ($M-2H^+$) 2057.29, found 2057.56.

Ammonia (20 mL) was condensed at -78 ^oC into a RBF, dried with sodium (~100 mg) for 1 h and then transferred into an oven-dried RBF equipped with a Dewar condenser and a magnetic stir bar (total volume of ammonia: 15 mL). Sodium (0.080 g, 3.47 mmol) was added, followed by anh. THF (0.50 mL). After 1 h at -78 ^oC, a solution of diacid in anh. THF (0.50 mL plus 0.20 mL for washing) was added, the reaction was stirred at -78 ^oC for 4 h, and carefully quenched with NH_4Cl (0.185 g). The reaction was allowed to warm up to rt, and the solvent was removed under the stream of N_2 overnight. The crude white solid was dissolved in water (2.0 mL) and purified by gravity filtration on BioGel-P4 using water as eluent to afford **1** (7.1 mg, 77%) after lyophilization: ^1H NMR (600 MHz, D_2O) δ δ 5.15 – 5.08 (m, 2H), 5.07 – 4.83 (m, 4H), 4.55 – 4.37 (m, 16 H), 4.17 (s, 3 H), 4.11 (s, 1 H), 4.03 (d, *J* = 2.3 Hz, 3 H), 3.88 (s, 9 H), 3.80 (td, *J* = 16.6, 15.1, 9.3 Hz, 17 H), 3.73 – 3.59 (m, 23 H), 3.52 (d, *J* = 36.1 Hz, 29 H), 2.91 (s, 2 H), 2.83 (s, 2 H), 2.76 – 2.59

(m, 5 H), 2.00 (d, J = 4.8 Hz, 3 H), 1.98 – 1.79 (m, 15 H), 1.77 – 1.67 (m, 4 H); MS-ESI calc for $C_{84}H_{136}N_6O_{62}$ (M-2H$^+$) 1110.39, found 1110.45.

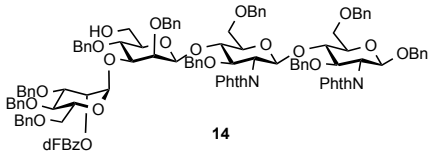


Amino [2-[5-acetamido-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-β-D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl]-α-D-mannopyranosyl-(1→3)]-[2-[5-acetamido-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-β-D-galactopyranosyl-(1→4)]-2-acetamido-2-deoxy-β-D-glucopyranosyl]-α-D-mannopyranosyl-(1→6)]- β-D-mannopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-D-glucopyranoside (12). A solution of **1** (5.0 mg) and NH_4HCO_3 (3.0 g) in water (2.5 mL) was heated at 40 ^{o}C for 3 days with slow stirring. The solution was then filtered through a plug of cotton and lyophilized to provide **12** (5.0 mg) as a white powder. This material was taken to the next step within 24 h. MS (ESI) calc for $C_{84}H_{138}N_7O_{61}$ (M-H$^+$), $C_{84}H_{137}N_7O_{61}$ (M-2H$^+$) 2222.01, 1110.50, found 2221.49, 1110.49; calc for $C_{84}H_{138}N_7O_{61}Na_2$ (M+2Na$^+$) 1134.50, found 1134.48.



Benzyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,5-difluorobenzoyl)-α-D-mannopyranosyl-(1→3)-2-*O*-benzyl-4,6-di-*O*-(*R*)-benzylidene-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (13). A mixture of thioether **5** (0.260 g, 0.409 mmol) and alcohol **3** (0.380 g, 0.273 mmol) was azeotropically dried with PhMe (3x) and then on high vacuum for 2 h. This mixture was dissolved in anh. CH_2Cl_2 (5.46 mL), freshly activated 4Å MS (0.50 g) were added and after 1 h at rt, this mixture as cooled to –50 ^{o}C, and NIS (0.0920 g, 0.409 mmol) and AgOTf

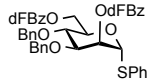
(0.0520 g, 0.205 mmol) were added. The reaction mixture was allowed to warm up to –20 °C, stirred at this temp. for 1 h 15 min, quenched with Et_3N, and filtered. The organic layer was washed with sat. $Na_2S_2O_3$, water, brine, dried ($MgSO_4$), and concentrated. Purification by chrom. on SiO_2 (Hexanes:EtOAc, 1:1) afforded **13** (0.490 g, 91%) as a clear oil: $[\alpha]_D^{22}$ +5.6 (c 1.0, $CHCl_3$); IR (ATR) 2870, 1714 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.3 Hz, 1 H), 7.72 – 7.54 (m, 3 H), 7.50 (dtd, *J* = 8.6, 6.0, 3.1 Hz, 3 H), 7.33 (dt, *J* = 7.9, 1.7 Hz, 4 H), 7.26 (d, *J* = 7.1 Hz, 2 H), 7.25 – 7.13 (m, 22 H), 7.13 – 7.06 (m, 9 H), 7.00 – 6.90 (m, 3 H), 6.90 – 6.85 (m, 6 H), 6.83 (dd, *J* = 7.2, 2.4 Hz, 2 H), 6.81 – 6.76 (m, 3 H), 6.70 – 6.62 (m, 3 H), 5.69 (t, *J* = 2.5 Hz, 1 H), 5.41 (s, 1 H), 5.34 (d, *J* = 1.9 Hz, 1 H), 5.20 (d, *J* = 8.2 Hz, 1 H), 4.87 (d, *J* = 8.4 Hz, 1 H), 4.80 (dd, *J* = 13.4, 11.5 Hz, 2 H), 4.76 – 4.71 (m, 3 H), 4.63 (d, *J* = 11.4 Hz, 1 H), 4.60 (d, *J* = 12.4 Hz, 1 H), 4.57 – 4.52 (m, 2 H), 4.47 (d, *J* = 11.9 Hz, 1 H), 4.44 (d, *J* = 9.0 Hz, 2 H), 4.42 – 4.40 (m, 3 H), 4.40 – 4.36 (m, 2 H), 4.32 (d, *J* = 8.5 Hz, 1 H), 4.31 – 4.26 (m, 2 H), 4.21 – 4.14 (m, 1 H), 4.14 – 4.08 (m, 3 H), 4.07 – 4.00 (m, 2 H), 4.00 – 3.95 (m, 3 H), 3.91 (t, *J* = 9.5 Hz, 1 H), 3.81 – 3.73 (m, 1 H), 3.72 (d, *J* = 3.5 Hz, 1 H), 3.68 (dd, *J* = 10.7, 4.4 Hz, 1 H), 3.61 – 3.56 (m, 1 H), 3.55 – 3.50 (m, 1 H), 3.50 – 3.45 (m, 1 H), 3.41 (d, *J* = 10.3 Hz, 1 H), 3.39 – 3.33 (m, 1 H), 3.29 (dd, *J* = 11.6, 3.0 Hz, 1 H), 3.22 (ddd, *J* = 10.0, 3.7, 1.7 Hz, 1 H), 3.11 (dt, *J* = 10.0, 2.4 Hz, 1 H), 2.99 (td, *J* = 9.6, 4.9 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.5, 168.6, 167.7, 167.6, 162.1 (3), 159.2, 159.1, 158.8 (2), 157.4 (2), 157.2 (2), 138.9, 138.7, 138.6, 138.5, 138.4 (4), 138.3, 138.2, 137.9, 137.8, 137.6, 137.3, 137.2, 134.1, 133.9, 133.5, 131.9, 131.7, 131.5, 128.8, 128.7, 128.5 (3), 128.4 (5), 128.3 (3), 128.2 (3), 128.1 (4), 128.0 (3), 127.9 (4), 127.8 (4), 127.7, 127.7 (3), 127.6 (3), 127.5 (2), 127.4 (2), 127.2, 127.0, 126.9, 126.1, 126.0, 123.7, 123.2, 121.6, 121.5, 121.4 (2), 119.6, 119.5 (2), 119.4, 118.6, 118.5 (2), 118.4 (3), 101.6, 101.2, 98.4, 97.2, 97.1, 79.0, 78.7, 78.5, 77.9, 77.1, 76.6, 75.8 (2), 75.5, 75.3, 74.8, 74.7, 74.6, 74.4, 74.3, 73.5, 73.3 (2), 72.8, 72.5, 71.6, 70.6, 69.5, 69.1, 68.5, 68.3, 67.8, 67.0, 56.7, 55.8; MS (ESI) calc for $C_{117}H_{108}F_2N_2NaO_{24}$ ($M+Na^+$)1987.13, found 1987.06.



14

Benzyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,5-difluorobenzoyl)-α-D-mannopyranosyl-(1→ 3)-2,4-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (14). Glycoside **13** (0.490 g, 0.249 mmol) was azeotropically dried with PhMe (3 x 5 mL) and then on

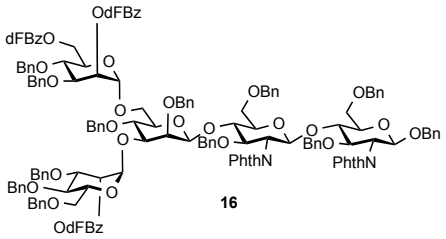
high vacuum for 1 h. The reaction flask was cooled to 0 °C, BH_3·THF (2.49 mL, 2.49 mmol, 1.0 M in THF) was added, followed by *n*-Bu_2BOTf (0.748 mL, 0.748 mmol, 1.0 M in CH_2Cl_2). After 4 h at 0 °C, the reaction was quenched with Et_3N (2.0 mL), methanol was added, and the volatiles were removed *in vacuo*. The crude mixture was dissolved in MeOH and concentrated, and this procedure was repeated one more time. Purification by chrom. on SiO_2 (PhMe:EtOAc, 6:1 to 3:1) afforded **14** (0.489 g, 99%) as a clear oil: $[\alpha]_D^{27}$ +34.3 (c 1.0, $CHCl_3$); IR (ATR) 3064, 2878, 1716, 1389 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.3 Hz, 1 H), 7.74 – 7.55 (m, 4 H), 7.53 (ddd, *J* = 12.1, 6.1, 3.5 Hz, 3 H), 7.31 (d, *J* = 7.5 Hz, 3 H), 7.26 (d, *J* = 7.5 Hz, 2 H), 7.25 – 7.14 (m, 23 H), 7.11 (hept, *J* = 5.2 Hz, 7 H), 7.07 – 7.03 (m, 2 H), 7.00 (td, *J* = 9.2, 4.1 Hz, 1 H), 6.94 (tq, *J* = 6.0, 3.7, 3.0 Hz, 1 H), 6.88 (q, *J* = 4.4, 4.0 Hz, 6 H), 6.81 (dq, *J* = 17.2, 3.4 Hz, 5 H), 6.64 (dt, *J* = 5.6, 2.9 Hz, 3 H), 5.58 (t, *J* = 2.5 Hz, 1 H), 5.26 – 5.17 (m, 2 H), 4.89 (d, *J* = 12.5 Hz, 1 H), 4.87 – 4.82 (m, 2 H), 4.76 (d, *J* = 11.9 Hz, 2 H), 4.71 (d, *J* = 11.8 Hz, 1 H), 4.65 (d, *J* = 11.2 Hz, 1 H), 4.63 – 4.54 (m, 3 H), 4.54 – 4.49 (m, 2 H), 4.47 – 4.42 (m, 4 H), 4.42 – 4.40 (m, 1 H), 4.40 – 4.36 (m, 2 H), 4.33 (d, *J* = 12.1 Hz, 1 H), 4.28 (dd, *J* = 12.3, 7.4 Hz, 2 H), 4.21 – 4.08 (m, 4 H), 4.05 (dd, *J* = 10.6, 8.3 Hz, 1 H), 3.99 – 3.93 (m, 2 H), 3.91 – 3.82 (m, 2 H), 3.78 (d, *J* = 3.0 Hz, 1 H), 3.74 (t, *J* = 9.5 Hz, 1 H), 3.59 (dd, *J* = 14.3, 10.6 Hz, 2 H), 3.54 (dd, *J* = 11.4, 5.4 Hz, 3 H), 3.48 (d, *J* = 10.9 Hz, 1 H), 3.39 – 3.26 (m, 3 H), 3.25 – 3.20 (m, 1 H), 3.14 (dt, *J* = 10.5, 2.3 Hz, 1 H), 2.99 (ddd, *J* = 8.3, 5.0, 2.5 Hz, 1 H), 1.78 (s, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.6, 167.7, 167.6, 162.2, 162.1, 159.2, 159.1, 158.8 (2), 157.5, 157.4, 157.2 (2), 138.7 (3), 138.5 (2), 138.2, 137.9, 137.8, 137.2, 134.1, 133.9, 133.5, 131.8, 131.7, 131.5, 128.7, 128.5 (2), 128.4 (3), 128.3 (3), 128.2 (2), 128.1 (3), 127.9 (2), 127.8 (5), 127.7 (3), 127.6 (2), 127.5 (3), 127.4, 127.1, 127.0, 126.9, 123.8, 123.1, 121.7, 121.6, 121.5, 121.4, 119.5, 119.4 (3), 118.6 (2), 118.5, 118.4 (3), 100.9, 99.4, 97.2 (2), 81.1, 78.5, 78.2, 77.9, 77.4, 76.0, 75.6, 75.1 (2), 74.9, 74.6 (2), 74.5, 74.4, 74.3, 73.5, 73.3, 72.8, 72.6, 71.8, 70.6, 69.9, 69.1, 68.2, 67.6, 62.0, 56.6, 55.8; MS (ESI) calc for $C_{117}H_{110}F_2N_2NaO_{24}$ ($M+Na^+$) 1987.73; found 1987.69.



15

Phenyl-3,4-di-*O*-benzyl-2,6-di-*O*-(2,5-difluorobenzoyl)-α-D-thiomannopyranose (15). A solution of phenyl-3,4-di-*O*-benzyl-α-D-thiomannopyranose (1.67 g, 3.69 mmol) in anh. pyridine (37.0 mL) was treated with 2,5-difluorobenzoyl chloride (1.83 mL, 14.8 mmol) and stirred at rt for 4 h. The reaction mixture was quenched with sat. $NaHCO_3$, extracted (3x) with EtOAc, and the combined organic layers were washed with water brine, dried ($MgSO_4$), and concentrated.

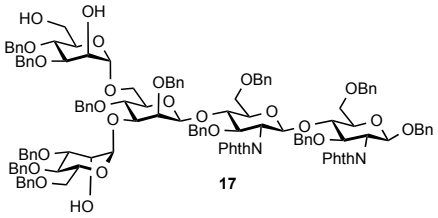
Purification by chrom. on SiO_2 (Hexanes:EtOAc, 4:1) afforded **15** (1.83 g, 67%) as a clear oil: $[\alpha]_D^{23}$ +86.6 (c 1.0, $CHCl_3$); IR (ATR) 2875, 1720, 1495, 1428, 1271, 1187 cm^{-1}; ^1H NMR (600 MHz, CD_3CN) δ 7.67 (ddd, *J* = 8.7, 5.5, 3.3 Hz, 1 H), 7.57 – 7.51 (m, 3 H), 7.45 – 7.36 (m, 4 H), 7.36 – 7.27 (m, 10 H), 7.27 – 7.19 (m, 3 H), 5.87 (dd, *J* = 2.8, 1.7 Hz, 1 H), 5.72 (d, *J* = 1.7 Hz, 1 H), 4.91 (d, *J* = 11.2 Hz, 1 H), 4.82 (d, *J* = 11.3 Hz, 1 H), 4.70 (d, *J* = 8.3 Hz, 1 H), 4.68 (d, *J* = 8.4 Hz, 1 H), 4.58 – 4.53 (m, 2 H), 4.51 – 4.47 (m, 1 H), 4.13 – 4.05 (m, 2 H); ^{13}C NMR (150 MHz, CD_3CN) δ 162.1 (4), 161.5 (2), 161.4 (2), 158.5 (5), 158.4, 156.9 (2), 156.8 (4), 137.9, 137.5, 132.4, 131.9, 128.9 (2), 128.1, 128.0, 127.9 (3), 127.8, 127.5, 127.4, 121.8 (2), 121.7, 121.6, 121.4, 121.3, 121.2 (2), 119.1 (2), 119.0 (2), 118.9, 118.8 (2), 118.7, 118.6 (2), 118.5, 118.4, 118.3 (2), 117.6, 117.4, 85.3, 78.1, 74.3, 73.4, 71.2, 70.7, 70.4, 63.5; HRMS (ESI) calc for $C_{40}H_{32}O_7F_4SNa$ ($M+Na^+$) 755.1703, found 755.1694.



16

Benzyl [3,4,6-tri-*O*-benzyl-2-*O*-(2,5-difluorobenzoyl)-α-D-mannopyranosyl-(1→ 3)]-[3,4-di-*O*-benzyl-2,6-di-*O*-(2,5-difluorobenzoyl)-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-β -D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (16). A mixture of donor **15** (0.0298 g, 0.0407 mmol) and acceptor **14** (0.040 g, 0.0204 mmol) was azeotropically dried with PhMe (3 x 5 mL) and then on high vacuum for 1 h. This mixture was dissolved in anh. CH_2Cl_2 (0.408 mL), freshly activated 4Å MS were added, and, after 1 h at rt, this mixture was cooled to -10 ^oC, treated with NIS (0.0183 g, 0.0814 mmol) and AgOTf (2.50 mg, 0.0102 mmol). After 2 h at -10 ^oC, the reaction mixture was quenched with Et_3N, filtered through a pad of Celite, washed with sat. $Na_2S_2O_3$, sat. $NaHCO_3$, water, brine, dried ($MgSO_4$), and concentrated. Purification by chrom. on SiO_2 (Hexanes:EtOAc, 2:1) afforded **16** (0.490 g, 87%) as a clear oil: $[\alpha]_D^{22}$ +13.9 (c 1.0, $CHCl_3$); IR (ATR) 2870, 1715, 1496, 1389 cm^{-1}; ^1H NMR (600 MHz, CD_3CN) δ 7.84 – 7.67 (m, 5 H), 7.61 (ddd, *J* = 8.6, 5.6, 3.4 Hz, 3 H), 7.56 (s, 1 H), 7.51 – 7.44 (m, 3 H), 7.39 (ddd, *J* = 7.5, 4.6, 2.7 Hz, 1 H), 7.38 – 7.08 (m, 47 H), 7.08 – 7.00 (m, 3 H), 7.00 – 6.92 (m, 5 H), 6.87 – 6.82 (m, 2 H), 6.82 – 6.78 (m, 1 H), 6.77 – 6.67 (m, 3 H), 6.62 (ddt, *J* = 8.7, 7.2, 1.4 Hz, 1 H), 6.56 – 6.44 (m, 2 H), 5.67 (dd, *J* = 3.2, 2.0 Hz, 1 H), 5.56 (dd, *J* = 3.2, 1.9 Hz, 1 H), 5.27 – 5.18

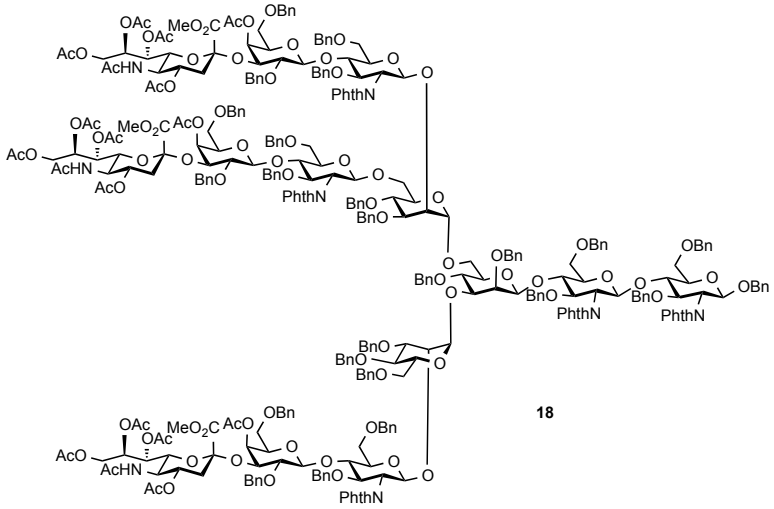
(m, 2 H), 5.09 (d, *J* = 12.2 Hz, 1 H), 5.05 (s, 1 H), 4.89 (d, *J* = 8.5 Hz, 1 H), 4.81 (dd, *J* = 11.6, 7.8 Hz, 2 H), 4.77 (dd, *J* = 11.6, 3.4 Hz, 3 H), 4.67 (s, 1 H), 4.65 (d, *J* = 11.5 Hz, 1 H), 4.60 (d, *J* = 12.0 Hz, 1 H), 4.56 (d, *J* = 9.3 Hz, 1 H), 4.54 (dd, *J* = 5.3, 2.7 Hz, 2 H), 4.53 – 4.51 (m, 2 H), 4.51 – 4.48 (m, 4 H), 4.47 – 4.44 (m, 1 H), 4.42 (d, *J* = 2.4 Hz, 1 H), 4.41 – 4.37 (m, 2 H), 4.36 – 4.29 (m, 4 H), 4.17 (dd, *J* = 10.6, 8.4 Hz, 1 H), 4.09 – 3.94 (m, 9 H), 3.93 (d, *J* = 9.7 Hz, 1 H), 3.91 – 3.85 (m, 4 H), 3.85 – 3.80 (m, 2 H), 3.75 – 3.66 (m, 4 H), 3.54 (dd, *J* = 11.1, 3.9 Hz, 1 H), 3.46 (dd, *J* = 10.9, 1.6 Hz, 1 H), 3.37 – 3.32 (m, 1 H), 3.30 – 3.20 (m, 3 H); ^{13}C NMR (150 MHz, CD_3CN) δ 168.6, 162.8, 158.3, 140.2, 139.6 (3), 139.5 (2), 139.4, 139.3, 139.1, 138.8, 138.3, 135.1, 132.3, 129.4 (2), 129.3 (4), 129.2 (4), 129.1 (3), 129.0, 128.9 (3), 128.8 (3), 128.7 (2), 128.6 (5), 128.5 (2), 128.4 (4), 128.3 (3), 128.0, 127.9, 124.2, 124.0, 122.9, 120.4, 119.8, 118.9, 118.7, 102.5, 100.3, 98.5, 98.2, 97.9, 82.4, 80.4, 79.4, 78.9, 78.7, 77.8, 77.1, 76.6, 75.7 (3), 75.6, 75.5, 75.4, 75.2, 75.1 (2), 74.8, 74.2, 73.9, 73.7, 73.4, 73.3, 72.5, 72.0, 71.5, 71.0, 70.7, 70.3, 69.3, 69.1, 67.0, 64.7, 63.0, 57.4, 56.7; HRMS (ESI) calc for $C_{151}H_{136}N_2O_{31}F_6Na$ ($M+Na^+$) 2609.8929, found 2609.9026.



17

Benzyl [3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→ 3)]-[3,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-β -D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (17). A solution of **16** (0.480 g, 1.86 mmol) in anh CH_2Cl_2 (5.0 mL) and MeOH (10.0 mL) was treated with NaOMe (1.11 mL, 0.556 mmol, 0.5 M in MeOH) and stirred at rt for 1 h 40 min. This mixture was quenched with DOWEX-50WX8, filtered, and concentrated. Purification by chrom. on SiO_2 (Hexanes:EtOAc, 1:2) afforded **17** (0.372 g, 93%) a clear oil: $[\alpha]_D^{22}$ +25.4 (c 1.0, $CHCl_3$); IR (ATR) 2877, 1716, 1389 cm^{-1}; ^{1}H NMR (600 MHz, CD_3CN) δ 7.84 – 7.68 (m, 5 H), 7.68 – 7.53 (m, 3 H), 7.44 – 7.38 (m, 2 H), 7.37 – 7.13 (m, 40 H), 7.13 – 7.09 (m, 2 H), 7.09 – 7.03 (m, 2 H), 6.98 (dd, *J* = 8.5, 6.7 Hz, 2 H), 6.96 – 6.93 (m, 2 H), 6.92 – 6.86 (m, 2 H), 6.86 – 6.78 (m, 4 H), 6.76 (tt, *J* = 6.2, 1.4 Hz, 2 H), 6.70 (dd, *J* = 8.7, 6.7 Hz, 2 H), 5.26 (d, *J* = 8.5 Hz, 1 H), 5.07 – 4.98 (m, 2 H), 4.90 (d, *J* = 8.5 Hz, 1 H), 4.86 (d, *J* = 12.8 Hz, 1 H), 4.84 (d, *J* = 1.8 Hz, 1 H), 4.82 – 4.77 (m, 2 H), 4.75 (d, *J* = 10.6 Hz, 1 H), 4.63

(dd, *J* = 9.3, 2.5 Hz, 3 H), 4.61 (d, *J* = 3.4 Hz, 1 H), 4.53 (d, *J* = 3.4 Hz, 1 H), 4.52 (d, *J* = 9.2 Hz, 1 H), 4.50 (t, *J* = 1.9 Hz, 3 H), 4.48 (dd, *J* = 9.4, 7.5 Hz, 2 H), 4.46 – 4.44 (m, 2 H), 4.41 (d, *J* = 11.9 Hz, 2 H), 4.38 (d, *J* = 12.4 Hz, 1 H), 4.35 (d, *J* = 12.3 Hz, 1 H), 4.28 (d, *J* = 11.6 Hz, 1 H), 4.19 (dd, *J* = 10.6, 8.5 Hz, 1 H), 4.11 – 4.01 (m, 3 H), 4.01 – 3.95 (m, 3 H), 3.92 – 3.86 (m, 4 H), 3.80 (d, *J* = 9.6 Hz, 1 H), 3.76 (dd, *J* = 6.2, 3.5 Hz, 1 H), 3.75 – 3.73 (m, 1 H), 3.71 (d, *J* = 9.2 Hz, 1 H), 3.70 – 3.67 (m, 1 H), 3.67 – 3.64 (m, 3 H), 3.64 – 3.59 (m, 3 H), 3.58 – 3.53 (m, 2 H), 3.53 – 3.49 (m, 2 H), 3.48 (t, *J* = 2.7 Hz, 1 H), 3.45 (ddd, *J* = 9.5, 4.8, 2.4 Hz, 1 H), 3.38 (dd, *J* = 11.0, 3.8 Hz, 1 H), 3.30 (ddd, *J* = 9.7, 3.8, 1.7 Hz, 1 H), 3.26 (ddd, *J* = 10.1, 3.9, 1.8 Hz, 1 H), 3.22 – 3.15 (m, 2 H), 2.90 (d, *J* = 3.9 Hz, 1 H), 2.54 (t, *J* = 6.1 Hz, 1 H); ^{13}C NMR (150 MHz, CD_3CN) δ 168.6, 140.3, 140.0, 139.9, 139.7, 139.6 (3), 139.5 (2), 139.4 (2), 138.3 (2), 135.1, 132.3, 129.4 (2), 129.3, 129.3, 129.2 (4), 129.1 (3), 129.0 (2), 128.9 (3), 128.8 (3), 128.7 (3), 128.6 (3), 128.5 (3), 128.4 (3), 128.3 (2), 128.2, 128.1 (2), 124.3, 124.0, 103.2, 102.5, 101.0, 98.2, 98.0, 82.5, 80.7, 80.4, 80.1, 79.6, 77.8, 77.4, 76.7, 75.6 (2), 75.5, 75.4 (2), 75.3, 75.1 (2), 75.0 (3), 74.0, 73.7, 73.5, 73.3, 73.1, 71.9, 71.5, 71.4, 70.5, 69.3, 69.2, 68.7, 68.2, 67.1, 62.3, 57.4, 56.7; HRMS (ESI) calc for $C_{130}H_{130}N_2O_{28}Na$ ($M+Na^+$) 2189.8708, found 2189.8782.

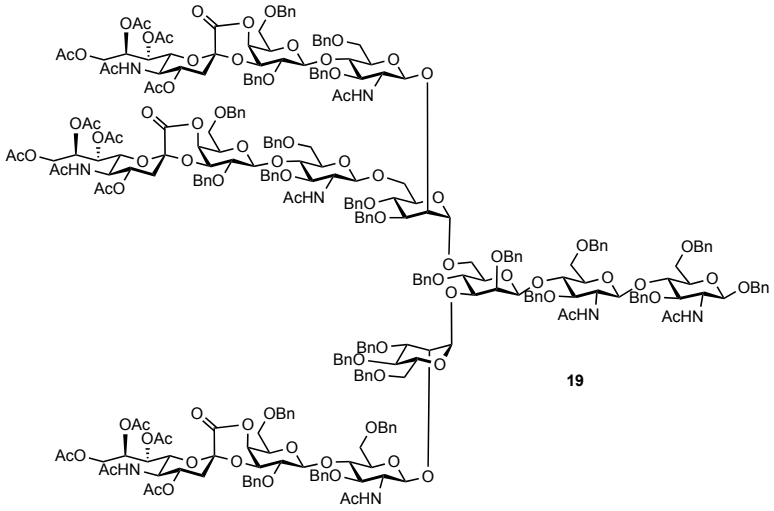


18

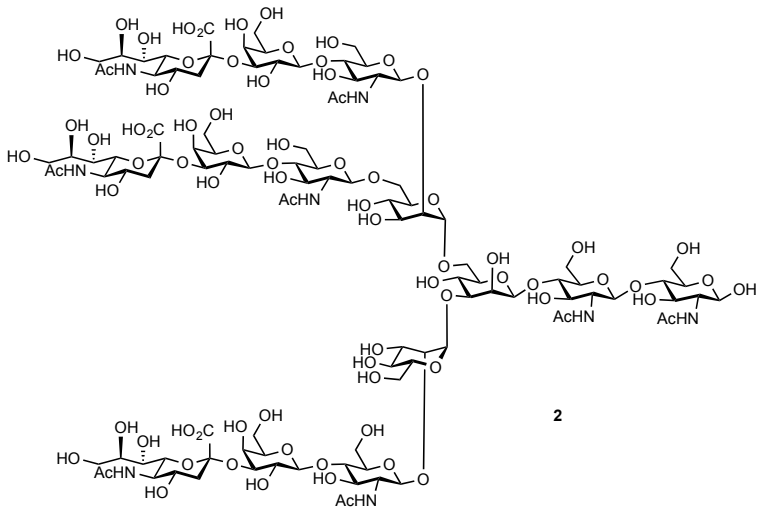
Benzyl [2-[methyl[5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-2,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl]-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)]-[2,4-bis[methyl[5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-2,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl]-3,4-di-*O*-benzyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzyl-β-D-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-

deoxy-2-phthalimido-β-D-glucopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (18). A mixture of donor **9** (0.360 g, 0.267 mmol) and acceptor **17** (0.0495 g, 0.0228 mmol) was azeotropically dried with PhMe (3 x 5 mL) and then on high vacuum for 1 h. This mixture was dissolved in anh. CH_2Cl_2 (0.46 mL + 0.10 mL for washing) and was added via cannula to a pre-cooled mixture of $Cp_2Zr(OTf)_2 \cdot THF$ (0.174 g, 0.294 mmol) and freshly activated 4Å MS (0.10 g). The reaction mixture was stirred at 0 ^oC for 1.5 h, quenched with Et_3N, filtered, and concentrated. Purification by chrom. on SiO_2 (Acetone:PhMe, 1:1) afforded **18** (0.100 g, 71%) as an off-white solid: $[\alpha]_D^{22}$ +52.5 (c 0.5, $CHCl_3$); IR (ATR) 2925, 2870, 1744, 1714 cm^{-1}; ^1H NMR (600 MHz, CD_3CN) δ 7.78 – 7.65 (m, 6 H), 7.65 – 7.49 (m, 10 H), 7.49 – 7.44 (m, 4 H), 7.44 – 7.37 (m, 4 H), 7.37 – 7.31 (m, 7 H), 7.31 – 7.06 (m, 54 H), 7.06 – 6.95 (m, 15 H), 6.95 – 6.77 (m, 25 H), 6.72 (tdd, *J* = 9.9, 4.5, 2.2 Hz, 6 H), 6.62 – 6.56 (m, 1 H), 6.53 (d, *J* = 7.6 Hz, 3 H), 6.50 – 6.43 (m, 2 H), 6.43 – 6.37 (m, 1 H), 6.34 (t, *J* = 7.4 Hz, 2 H), 6.05 – 5.93 (m, 3 H), 5.45 (dtd, *J* = 10.2, 5.3, 2.8 Hz, 1 H), 5.42 – 5.35 (m, 1 H), 5.27 (dd, *J* = 9.9, 5.3 Hz, 1 H), 5.25 – 5.08 (m, 4 H), 5.09 – 5.01 (m, 2 H), 4.98 (d, *J* = 3.4 Hz, 1 H), 4.96 – 4.85 (m, 3 H), 4.85 – 4.72 (m, 9 H), 4.72 – 4.59 (m, 5 H), 4.59 – 4.51 (m, 4 H), 4.51 – 4.22 (m, 27 H), 4.22 – 4.12 (m, 5 H), 4.07 – 3.89 (m, 13 H), 3.89 – 3.80 (m, 6 H), 3.80 – 3.75 (m, 2 H), 3.75 – 3.69 (m, 9 H), 3.69 – 3.55 (m, 10 H), 3.55 – 3.43 (m, 6 H), 3.43 – 3.34 (m, 5 H), 3.34 – 3.24 (m, 8 H), 3.24 – 3.13 (m, 4 H), 3.13 – 3.05 (m, 2 H), 3.05 – 2.93 (m, 3 H), 2.90 –2.75 (m, 2 H), 2.67 – 2.58 (m, 1 H), 2.53 – 2.34 (m, 6 H), 1.98 – 1.94 (m, 3 H), 1.94 (s, 3 H), 1.92 (s, 3 H), 1.91 (s, 3 H), 1.84 (s, 9 H), 1.82 (s, 3 H), 1.80 – 1.77 (m, 4 H), 1.76 (s, 3 H), 1.74 (s, 3 H), 1.72 (s, 3 H), 1.70 (s, 3 H), 1.69 – 1.68 (m, 3 H), 1.67 (s, 3 H), 1.66 (s, 9 H); ^{13}C NMR (151 MHz, CD_3CN) δ 170.02, 169.99, 169.89, 169.56, 169.55, 169.50, 169.48, 169.45, 169.42, 169.41, 169.39, 169.37, 169.34, 169.24, 167.79, 167.76, 167.75, 167.37, 167.30, 139.22, 139.11, 139.08, 139.01, 138.50, 138.46, 138.44, 138.35, 138.34, 138.31, 138.29, 138.25, 138.24, 138.21, 138.19, 138.17, 138.13, 138.11, 138.04, 138.02, 137.92, 137.89, 136.97, 134.00, 133.92, 133.81, 131.23, 130.97, 129.46, 129.41, 128.92, 128.37, 128.23, 128.16, 128.09, 128.07, 128.03, 128.02, 127.98, 127.94, 127.91, 127.90, 127.88, 127.86, 127.85, 127.84, 127.83, 127.81, 127.79, 127.77, 127.75, 127.71, 127.68, 127.66, 127.64, 127.62, 127.60, 127.57, 127.56, 127.54, 127.51, 127.49, 127.48, 127.46, 127.44, 127.43, 127.42, 127.36, 127.35, 127.31, 127.29, 127.26, 127.22, 127.20, 127.19, 127.17, 127.15, 127.11, 127.07, 127.05, 127.03, 127.01, 126.98, 126.96, 126.94, 126.91, 126.89, 126.87, 126.82, 126.80, 126.77, 126.74, 126.51, 126.48, 126.10, 122.89, 122.71, 122.50, 101.91, 101.64, 101.60, 98.86, 98.41, 98.31, 97.38, 97.36, 97.33, 96.86, 96.65, 96.11, 95.64, 95.38, 78.86, 78.83, 78.65, 78.48, 77.46, 76.61, 76.50, 76.43, 76.28, 76.08, 75.47, 75.25, 74.75, 74.54, 74.45, 74.30, 74.23, 74.17, 74.08, 74.00, 73.86, 73.75, 73.65, 73.58, 73.39, 73.13, 72.95, 72.89, 72.85, 72.68, 72.49, 72.47, 72.45, 72.43,

72.40, 72.39, 72.31, 72.19, 72.13, 71.95, 71.62, 71.60, 71.56, 71.52, 71.46, 71.36, 71.13, 70.58, 70.39, 70.15, 69.81, 69.72, 69.19, 69.15, 68.85, 68.80, 68.77, 68.73, 68.68, 68.64, 68.23, 68.21, 68.18, 68.06, 67.83, 67.81, 67.74, 67.68, 67.61, 67.43, 67.03, 66.98, 66.89, 62.04, 61.65, 61.62, 61.60, 56.28, 55.38, 55.18, 55.06, 53.84, 52.29, 52.28, 52.27, 52.22, 48.00, 47.96, 47.84, 36.65, 36.54, 34.78, 31.29, 29.12, 29.11, 28.84, 28.71, 28.63, 28.62, 28.60, 28.52, 28.37, 26.44, 24.98, 22.05, 21.92, 21.90, 21.82, 21.79, 21.77, 20.24, 20.20, 20.15, 19.89, 19.84, 19.82, 19.80, 19.78, 19.75, 19.74, 19.72, 19.69, 19.67, 19.65, 19.62, 19.59, 19.56, 19.55, 19.53, 19.50, 19.48; MS (ESI) calc for $C_{340}H_{358}N_8O_{100}Na_2$ ($M+2Na^+$) 3101.23, $C_{340}H_{358}N_8O_{100}Na_3$ ($M+3Na^+$) 2075.15, found 3101.19, 2075.15.



Lactone 19. A solution of **18** (100 mg, 0.0162 mmol) in anh. CH_2Cl_2 (1.5 mL) and MeOH (3.0 mL) was treated with NaOMe (1.12 mL, 0.56 mmol) and stirred at rt for 4 h. Water (0.20 mL) was added and the reaction was continued for 12 h. The mixture was quenched with DOWEX-MAC3 resin (pH 6), filtered, and concentrated. The crude material was dissolved in EtOH (4.0 mL), 1,2-ethylenediamine (1.0 mL) was added, and the mixture was stirred at 80 ^oC for 24 h, concentrated and then suspended in anh. pyridine (5.0 mL) and acetic anhydride (2.5 mL). After 24 h at rt, the volatiles were removed *in vacuo*, and purification by chrom. on SiO_2 (PhMe:Acetone 1:4) provided **19** (29.4 mg, 33%) as a light-yellow oil: MS (ESI) calc for $C_{301}H_{340}N_8O_{89}Na_2$ ($M+2Na^+$) 2769.95, $C_{301}H_{340}N_8O_{89}Na_3$ ($M+3Na^+$) 1854.30, found 2769.37, 1854.11.



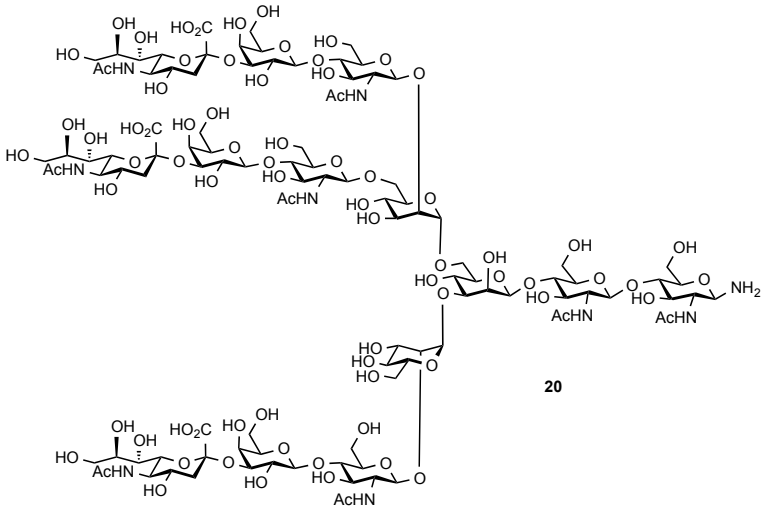
2

[2-[5-Acetamido-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-β-D-galactopyranosyl-(1→4)-2-deoxy-2-acetamido-β-D-glucopyranosyl]-α-D-mannopyranosyl-(1→3)]-[2,4-bis[5-acetamido-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-β-D-galactopyranosyl-(1→4)]-2-deoxy-2-acetamide-β-D-glucopyranosyl]-α-D-mannopyranosyl-(1→6)]-β-D-mannopyranosyl-(1→4)-2-deoxy-2-acetamido-β-D-glucopyranosyl-(1→4)-2-deoxy-2-acetamido-β-D-glucopyranoside (2).

Lactone **19** (8.0 mg, 1.46 μmol) was dissolved in anh. CH_2Cl_2 (0.50 mL) and MeOH (1.0 mL), treated with NaOMe (41 μL, 0.020 mmol, 0.5 M in MeOH), and stirred at rt for 7 h. Water (0.10 mL) was added and the reaction was continued at rt for 12 h, quenched with DOWEX-MAC3 resin (pH 6), filtered, and concentrated to provide crude triacid: MS (ESI) calc for $C_{277}H_{319}N_8O_{80}$ ($M-3H^+$) 1680.17, found 1680.13

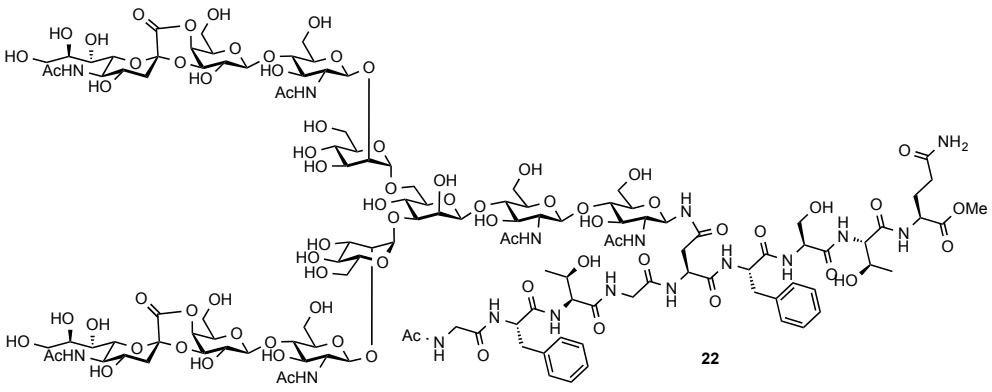
Ammonia was condensed at -78 ^oC into 100 mL RBF, dried with Na for 1 h, and then transferred into a pre-cooled (–78 ^oC) three-neck RBF equipped with a Dewar condenser and a magnetic stir bar (total volume 15 mL). Dry THF (0.20 mL) was added followed by freshly cut Na (42 mg), and the mixture was stirred at -78 ^oC for 1 h. A suspension of crude triacid in THF (0.50 mL + 0.50 mL for washing) was introduced via syringe, the mixture was stirred at -78 ^oC for 4 h, quenched with NH_4Cl (0.121 g), and the colorless solution was allowed to warp up to rt overnight under the stream of N_2. The residual white solid was dissolved in water (0.5 mL) and was purified on BioGel-P2 (water as an eluent). Fractions containing the desired product (21-27) were lyophilized to provide **2** (3.0 mg, 71%) as a white powder: ^1H NMR (600 MHz, D_2O) δ 5.14 – 5.03 (m, 5 H), 5.03 – 4.96 (m, 4 H), 4.78 – 4.73 (m, 7 H), 4.69 – 4.64 (m, 5 H), 4.52 – 4.37 (m, 8 H), 4.14 (s, 1 H), 4.08 (s, 4 H), 4.00 (d, J = 10.2 Hz, 6 H), 3.94 – 3.82 (m, 8 H), 3.82 – 3.70 (m, 14 H), 3.70 – 3.32 (m, 44 H), 3.32 – 3.22 (m, 6 H), 3.17 (s, 4 H), 3.02 (t, J = 5.9 Hz, 2 H), 2.95

(q, J = 7.4 Hz, 4 H), 2.73 – 2.60 (m, 8 H), 1.99 – 1.74 (m, 24 H), 1.68 (t, J = 12.3 Hz, 6 H), 1.54 – 1.42 (m, 6 H), 1.21 (dd, J = 12.0, 6.7 Hz, 5 H), 1.15 (q, J = 7.3, 6.6 Hz, 7 H); MS (ESI) calc for $C_{109}H_{176}N_8O_{80}$ ($M\text{-}2H^+$) 1438.50, $C_{109}H_{175}N_8O_{80}$ ($M\text{-}3H^+$) 958.67, found 1439.06, 958.80.

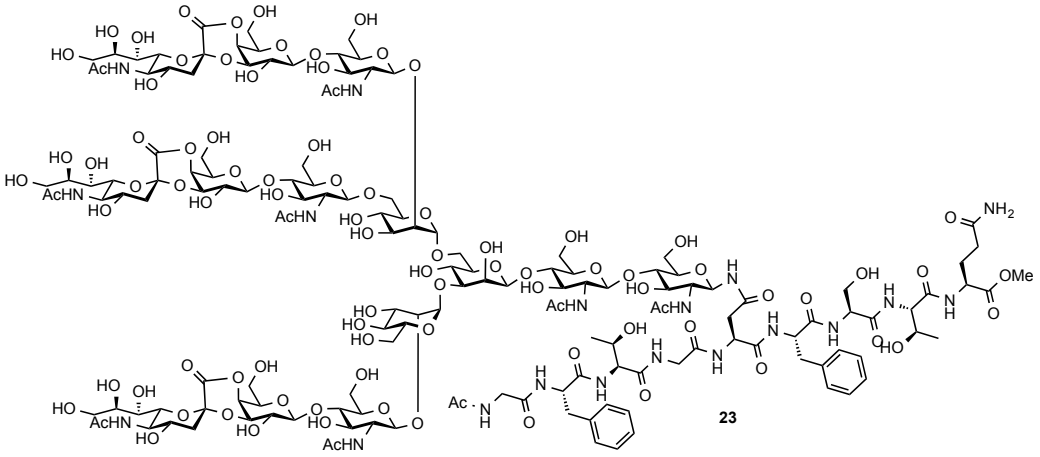


Amino [2-[5-acetamido-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-β-D-galactopyranosyl-(1→4)-2-deoxy-2-acetamido-β-D-glucopyranosyl]-α-D-mannopyranosyl-(1→3)]-[2,4-bis[5-acetamido-3,5-dideoxy-D-glycero-β-D-galacto-non-2-ulopyranosylate]-(2→3)-β-D-galactopyranosyl-(1→4)]-2-deoxy-2-acetamide-β-D-glucopyranosyl]-α-D-mannopyranosyl-(1→6)]-β-D-mannopyranosyl-(1→4)-2-deoxy-2-acetamido-β-D-glucopyranosyl-(1→4)-2-deoxy-2-acetamido-β-D-glucopyranoside (20).

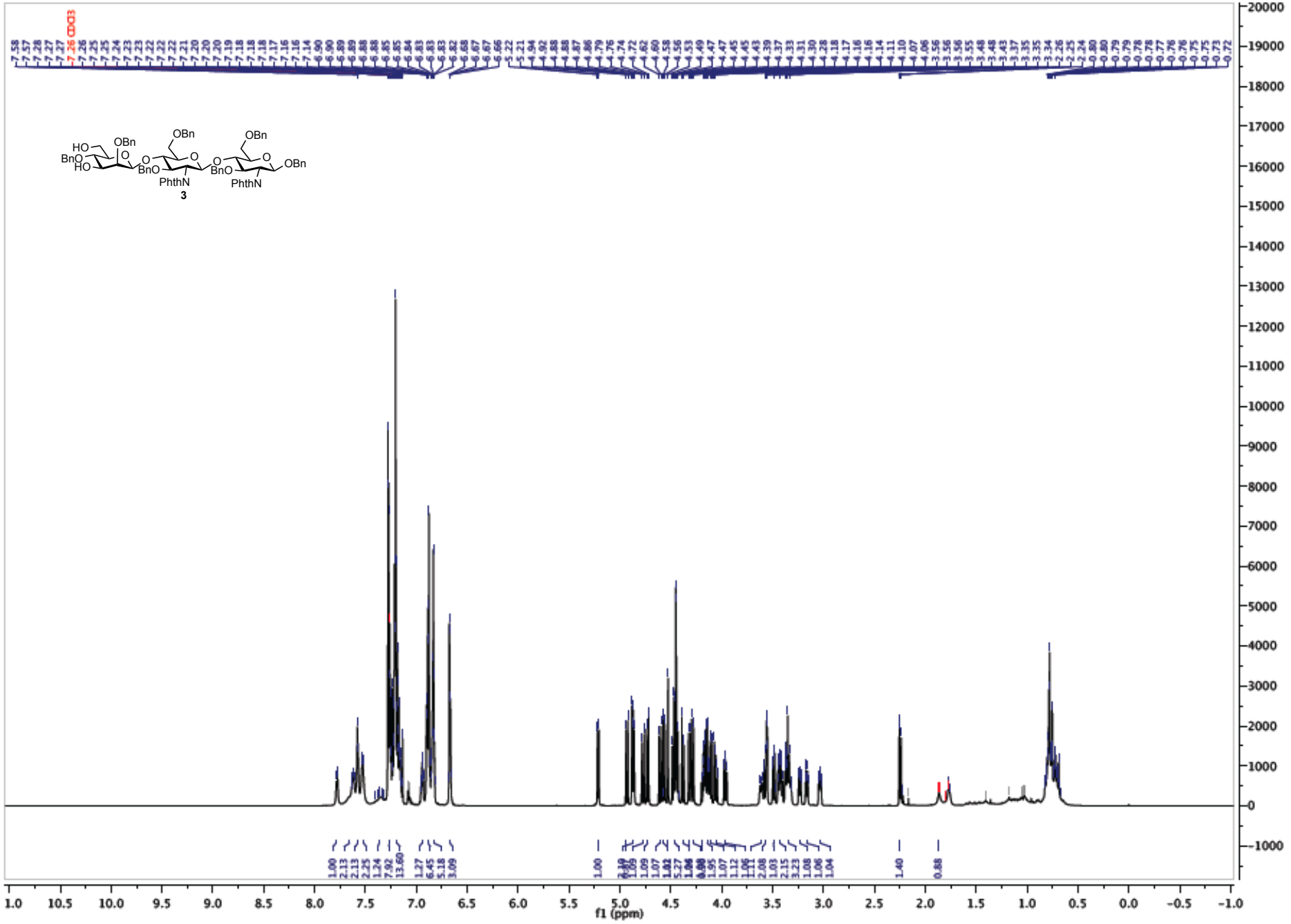
To a solution of **2** (2.2 mg) in water (2.5 mL), NH_4HCO_3 (3.0 g) was added, and the reaction mixture was stirred at 40 ^oC for 3 days. The mixture was then filtered through a pad of cotton, lyophilized until the mass remained constant to provide **20** (1.8 mg, 82%) a white powder. This material was used immediately crude in the next step.

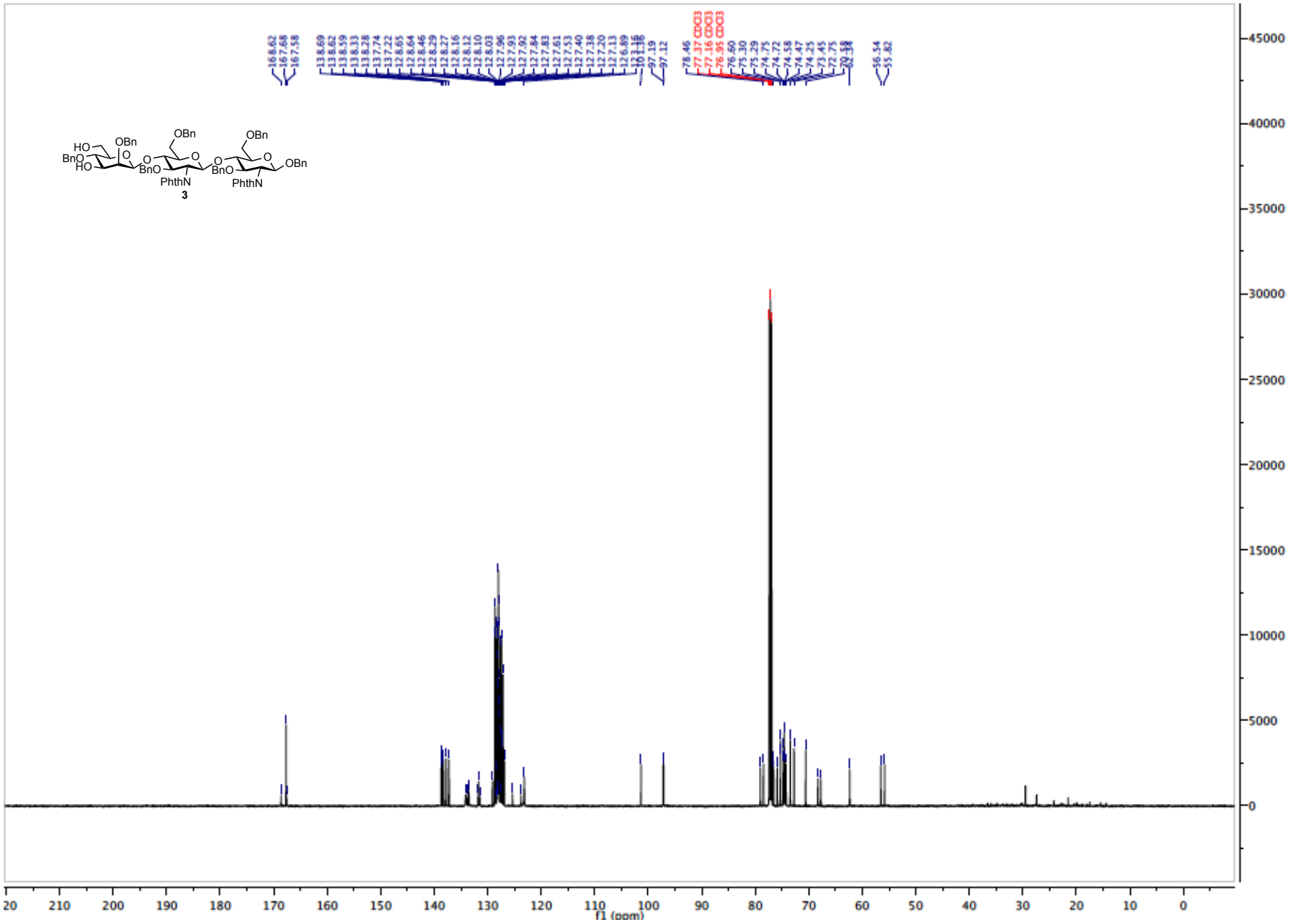


Glycoconjugate 22. A mixture of peptide **21** (2.3 mg, 2.25 μmol) and anomeric amine **12** (2.0 mg, 0.899 μmol) was dissolved in anh. DMSO (70 μL), treated with HATU (3.4 mg, 34 μL, 8.99 μmol, a solution of 100 mg of HATU in 1.0 mL of DMSO), and DIPEA (1.5 μL, 8.99 μmol). After 1.5 h at rt, this mixture was quenched with MeCN:H_2O 1:1 + 0.05% TFA and lyophilized. UPLC analysis (C18, 5-95%) showed 54% conversion (R_t = 2.39 min, calc for $C_{129}H_{197}N_{17}O_{75}$ ($M+2H^+$), $C_{129}H_{198}N_{17}O_{75}$ ($M+3H^+$) 1592.11, 1061.7, found: 1592.3, 1062.2).

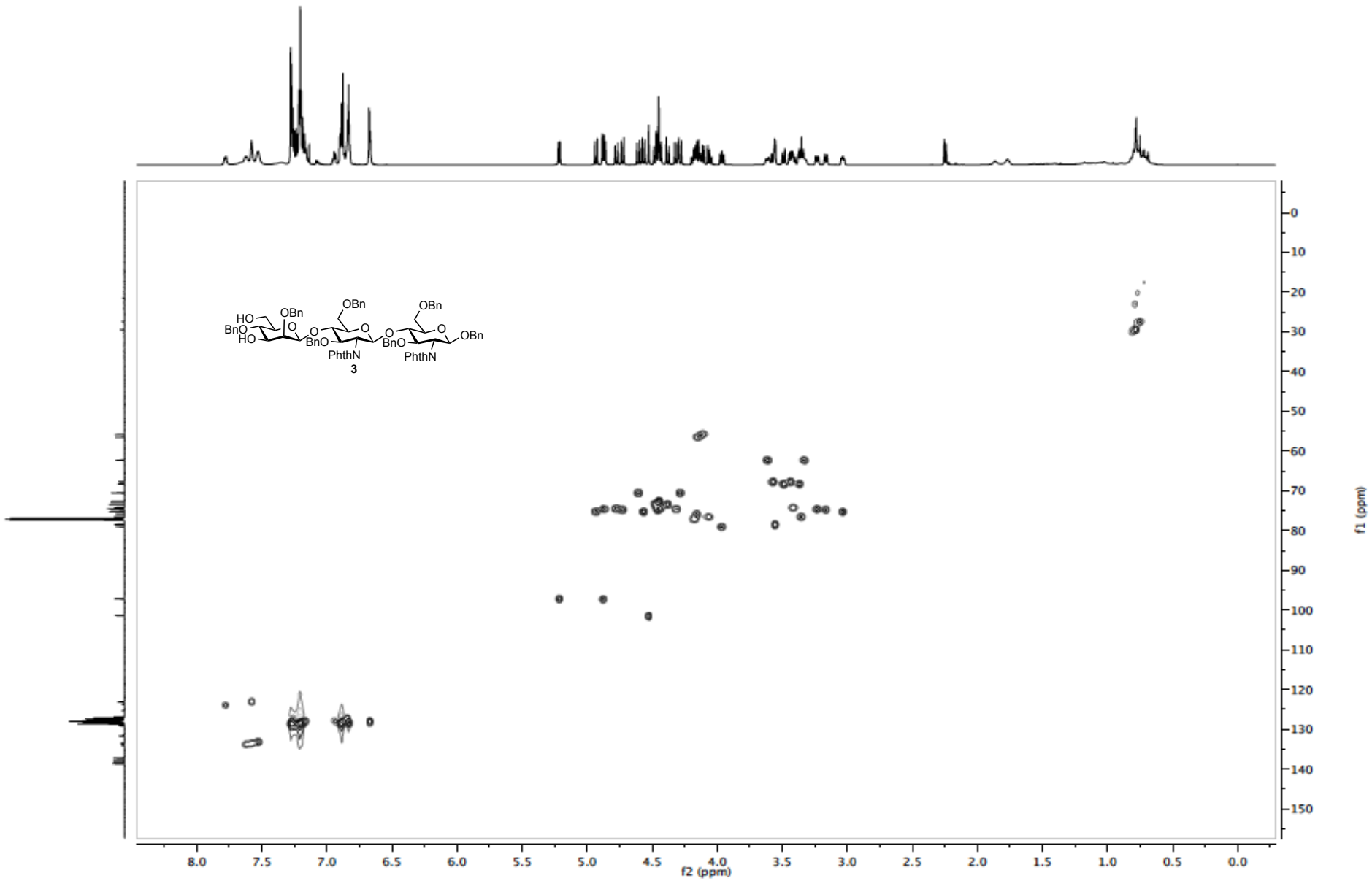


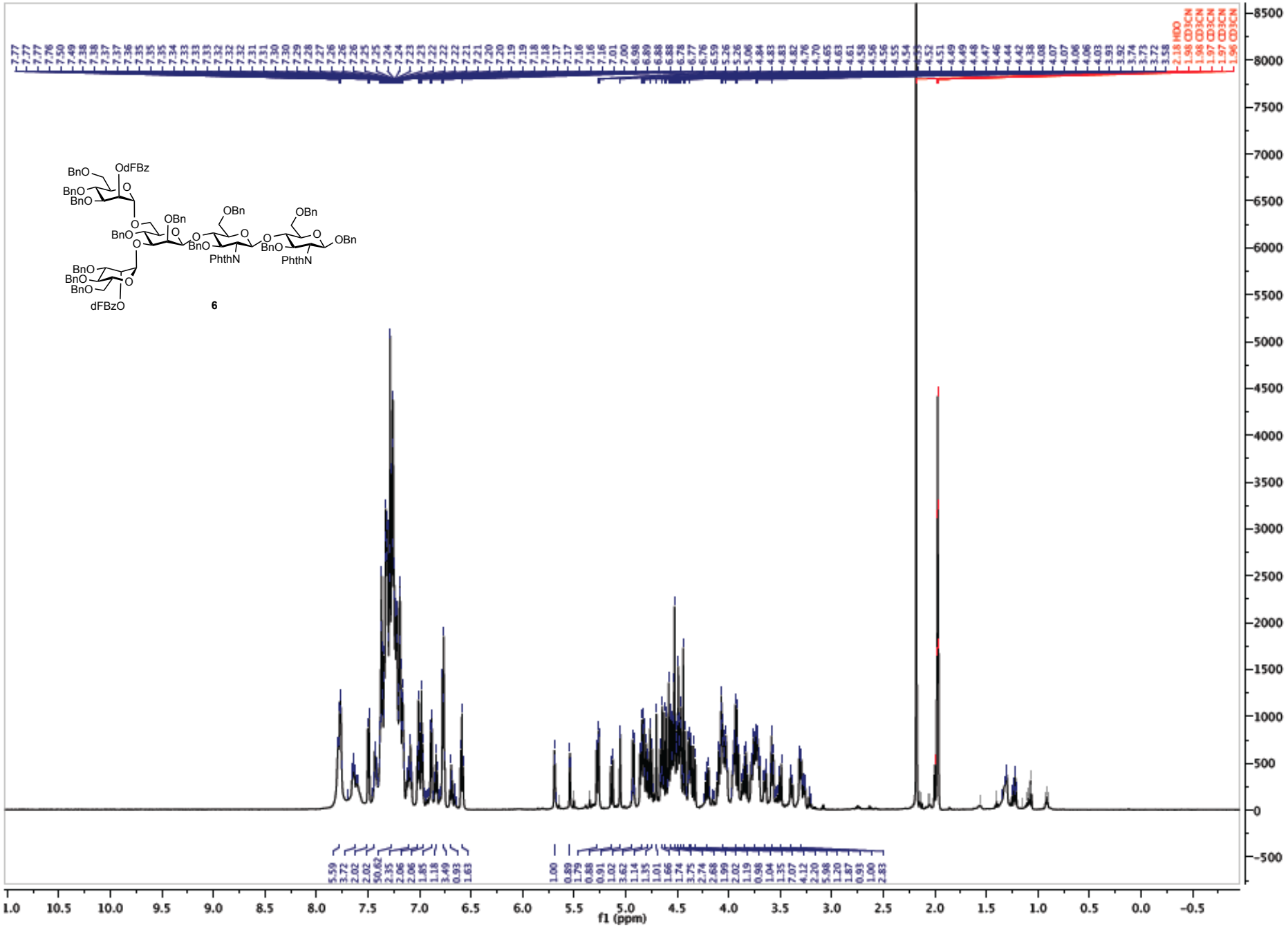
Glycoconjugate 23. A mixture of peptide **21** (3.1 mg, 3.06 μmol) and anomeric amine **12** (1.8 mg, 0.625 μmol) was dissolved in anh. DMSO (60 μL), treated with HATU (2.4 mg, 24 μL, 6.25 μmol, a solution of 100 mg of HATU in 1.0 mL of DMSO), and DIPEA (1.5 μL, 6.25 μmol). After 1.5 h at rt, this mixture was quenched with MeCN:H_2O 1:1 + 0.05% TFA and lyophilized. UPLC analysis (C18, 5-95%) showed 10% conversion (R_t = 2.37 min, calc for $C_{154}H_{236}N_{19}O_{92}$ ($M+3H^+$) 1274.5, found: 1275.2).

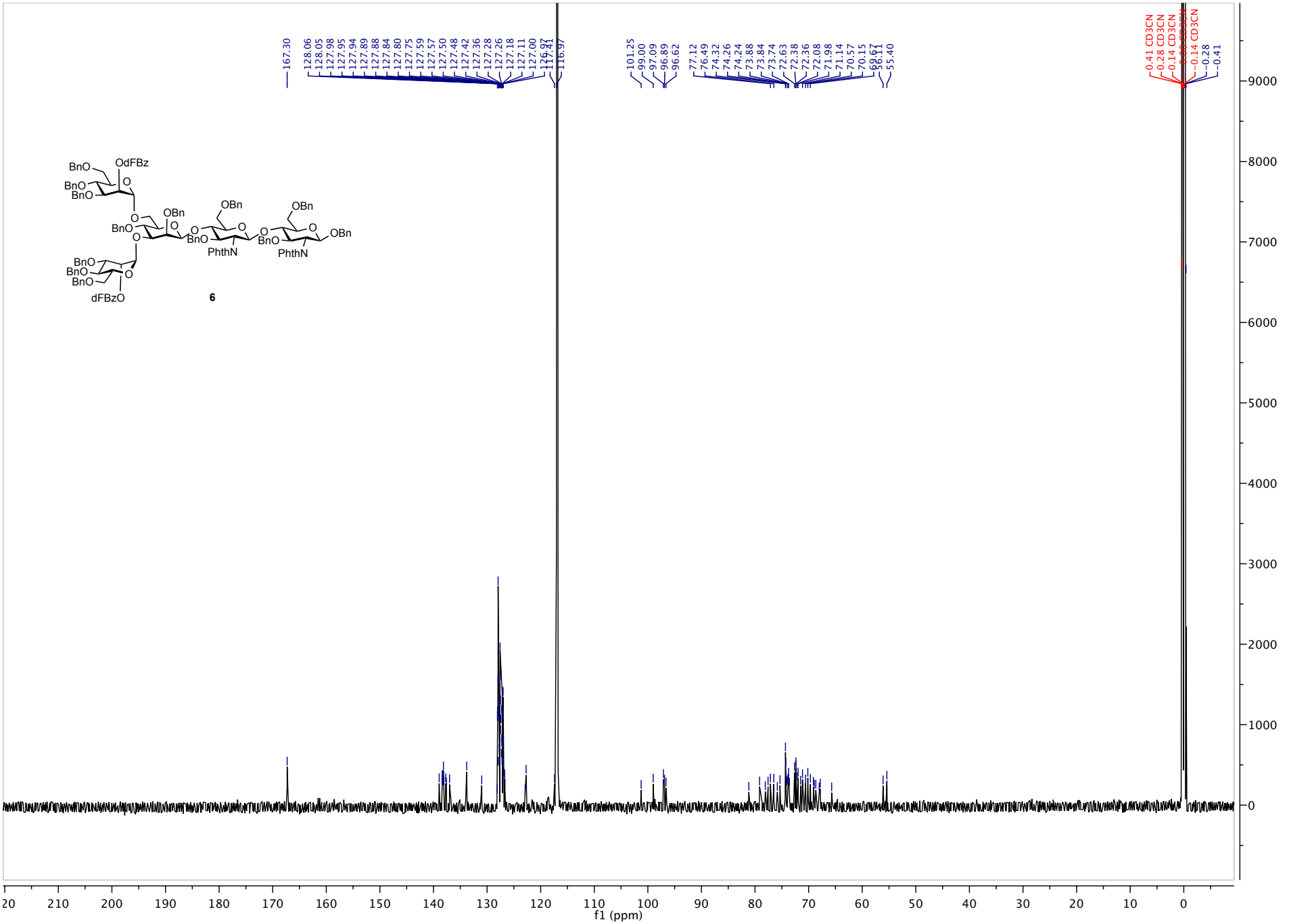

HO
OBn
BnO
HO
O
O
OBn
BnO
PhthN
3
O
OBn
BnO
PhthN
O
OBn
f1 (ppm)


HO
OBn
OBn
OBn
BnO
O
O
O
O
HO
BnO
BnO
BnO
OBn
PhthN
PhthN
3
168.62
167.68
167.58
138.69
138.62
138.59
138.33
138.28
137.74
137.22
128.65
128.64
128.46
128.29
128.27
128.16
128.12
128.10
128.03
127.96
127.93
127.92
127.84
127.83
127.61
127.53
127.40
127.38
127.20
127.13
126.89
97.19
97.12
78.46
77.37
77.16
76.95
CDCl3
76.60
75.30
75.29
74.75
74.72
74.58
74.47
74.25
73.45
72.75
70.58
70.54
56.54
55.82
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

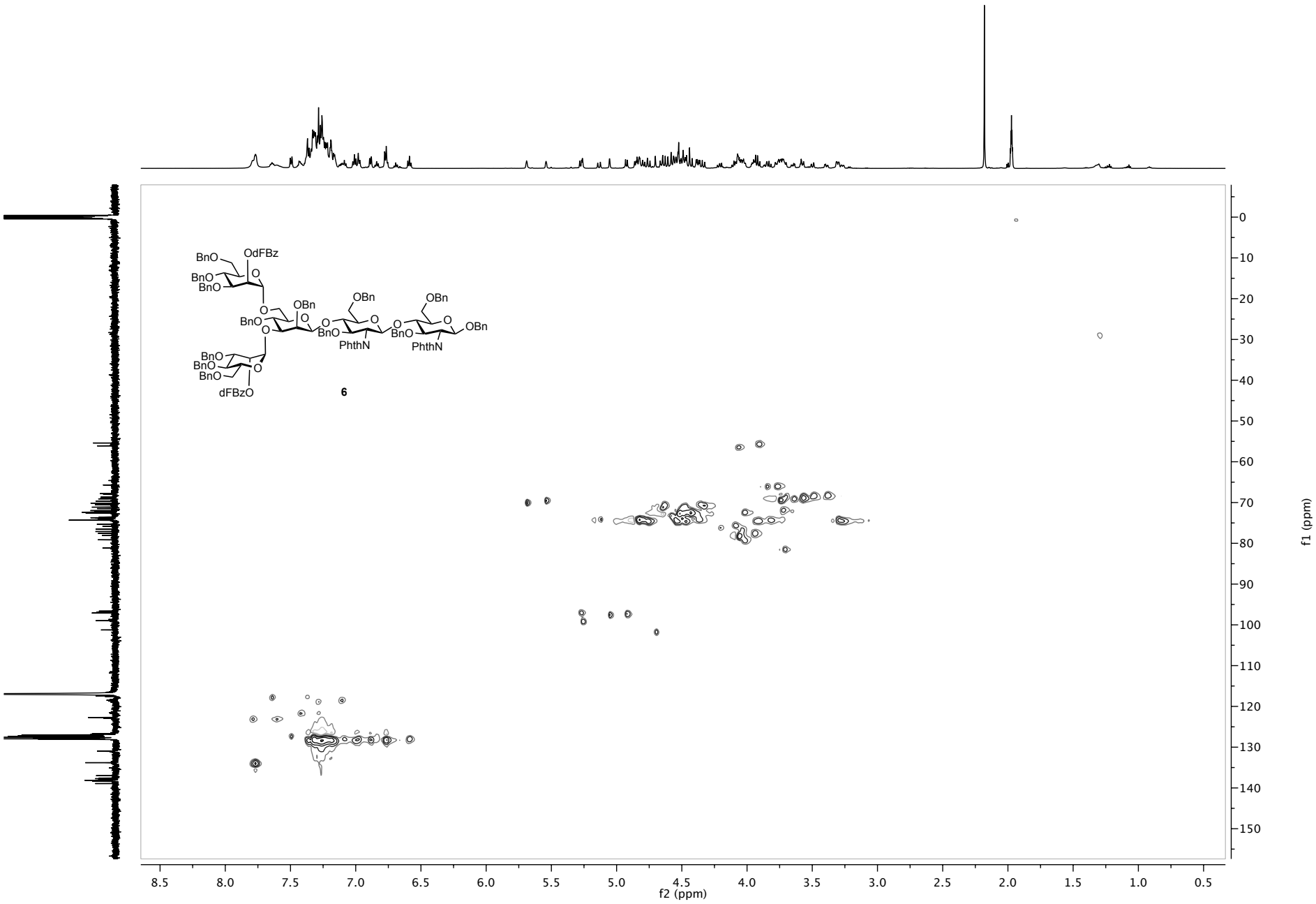
2D ^{1}H-^{13}C HSQC

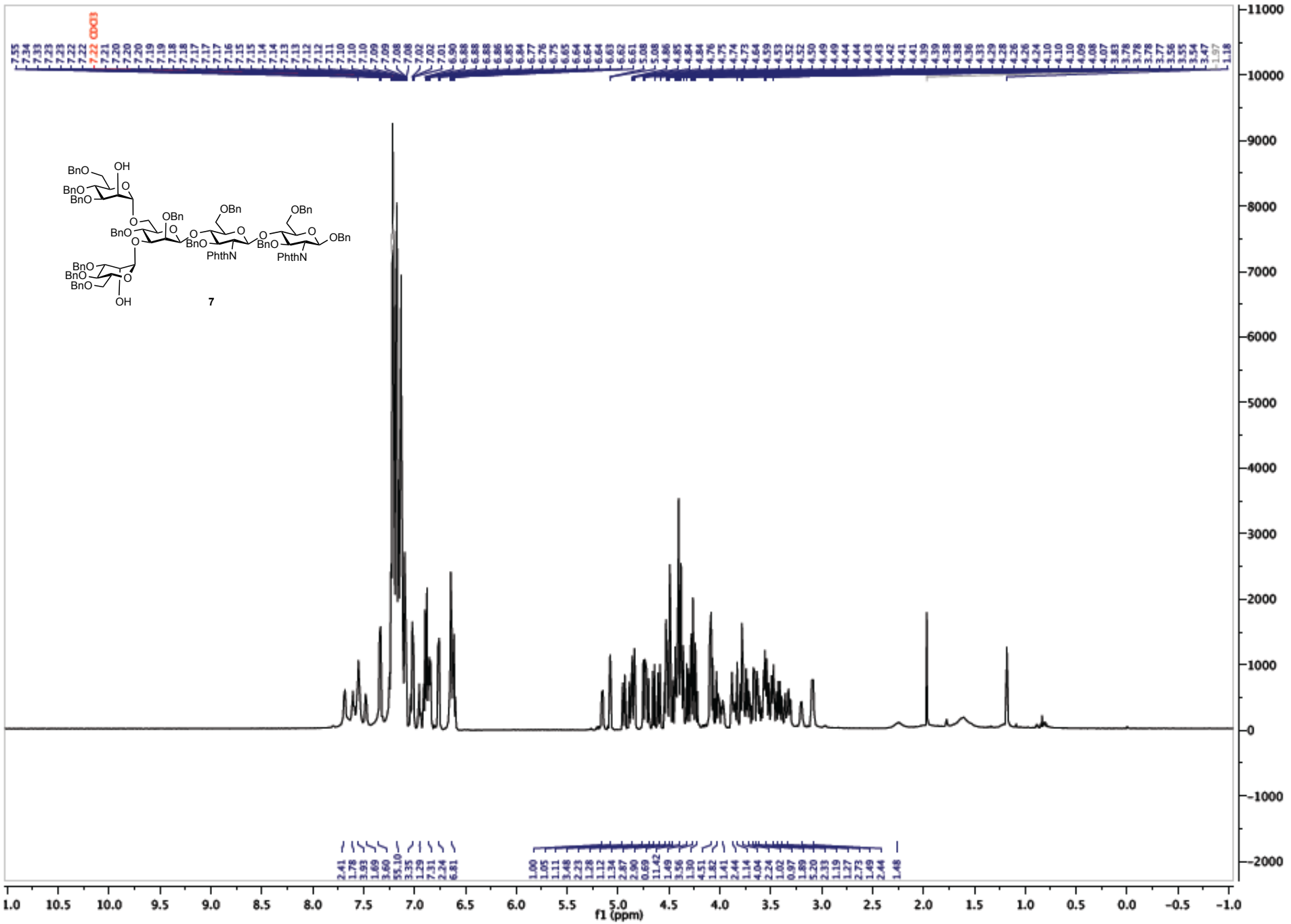


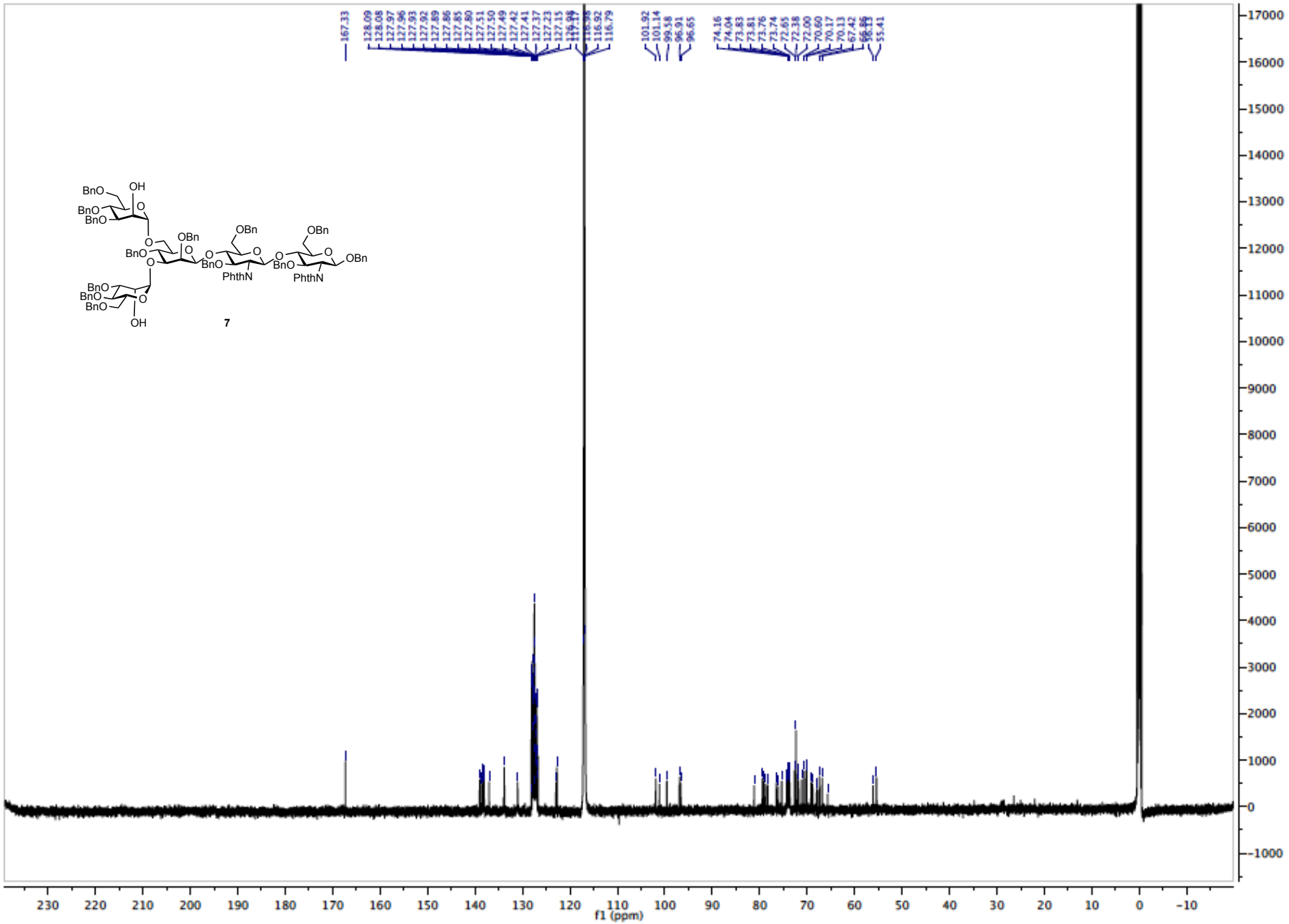

BnO
OdFBz
BnO
BnO
O
OBn
BnO
O
O
BnO
O
PhthN
OBn
O
BnO
O
PhthN
OBn
O
OBn
BnO
BnO
BnO
O
dFBzO
6
f1 (ppm)


167.30
128.06
128.05
127.98
127.95
127.94
127.89
127.88
127.84
127.80
127.75
127.59
127.57
127.50
127.48
127.42
127.36
127.28
127.26
127.18
127.11
127.00
116.97
101.25
99.00
97.09
96.89
96.62
77.12
76.49
74.32
74.24
73.88
73.84
73.74
72.63
72.38
72.36
72.08
71.98
71.14
70.57
70.15
55.40
0.41 CD3CN
0.28 CD3CN
0.14 CD3CN
-0.14 CD3CN
-0.28
-0.41
BnO
OdFBz
OBn
PhthN
dFBzO
6
f1 (ppm)

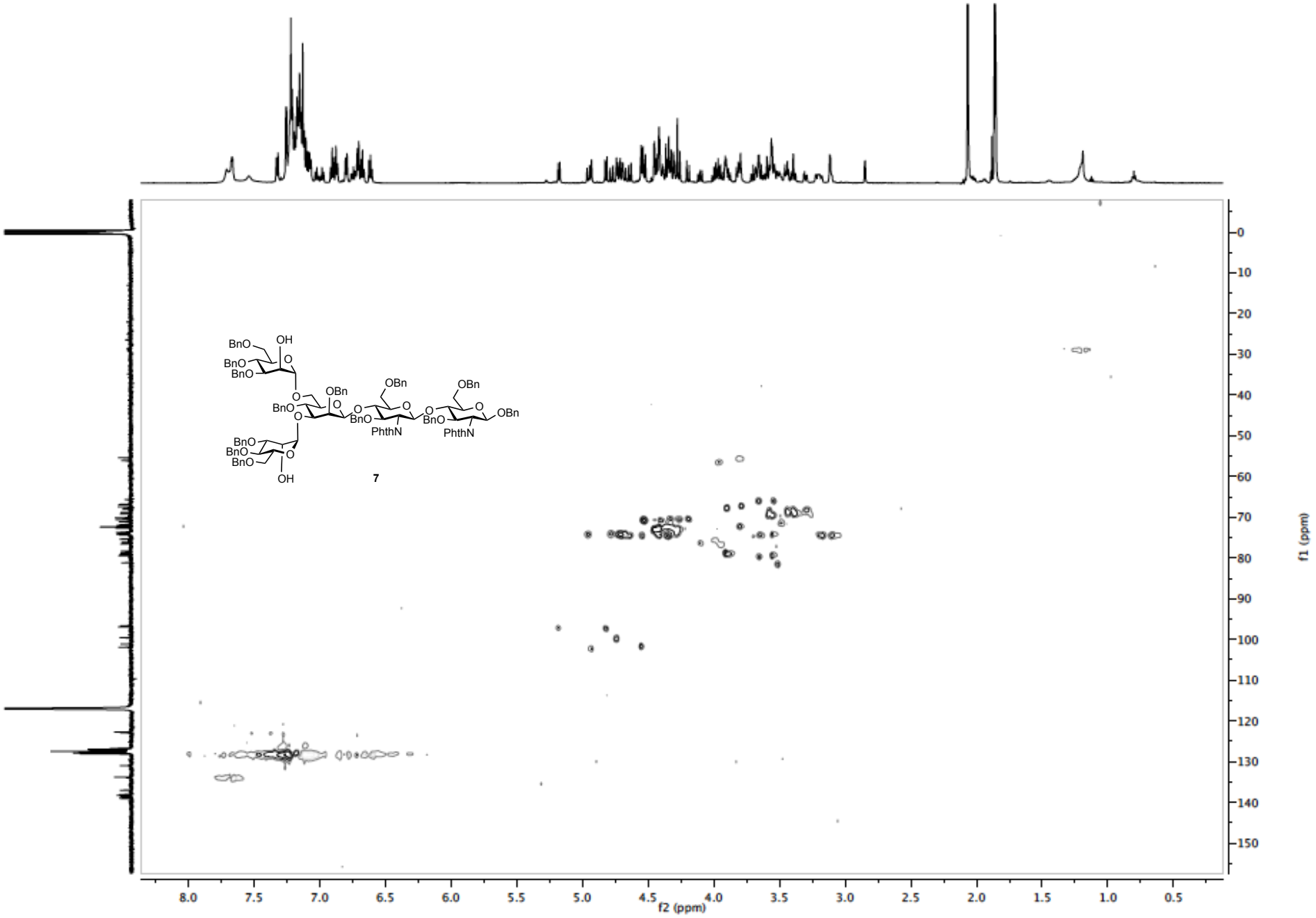
2D ^{1}H-^{13}C HSQC

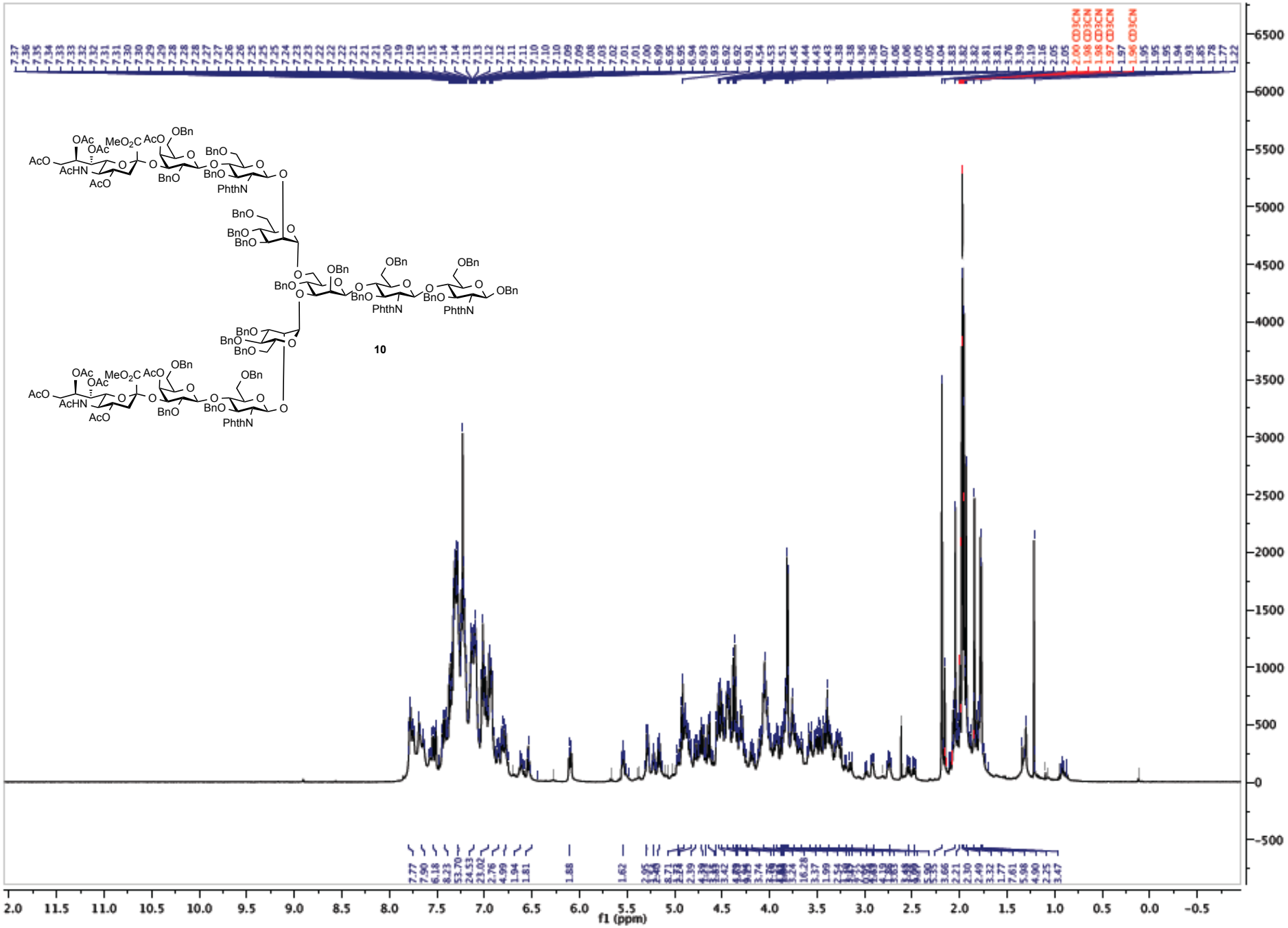


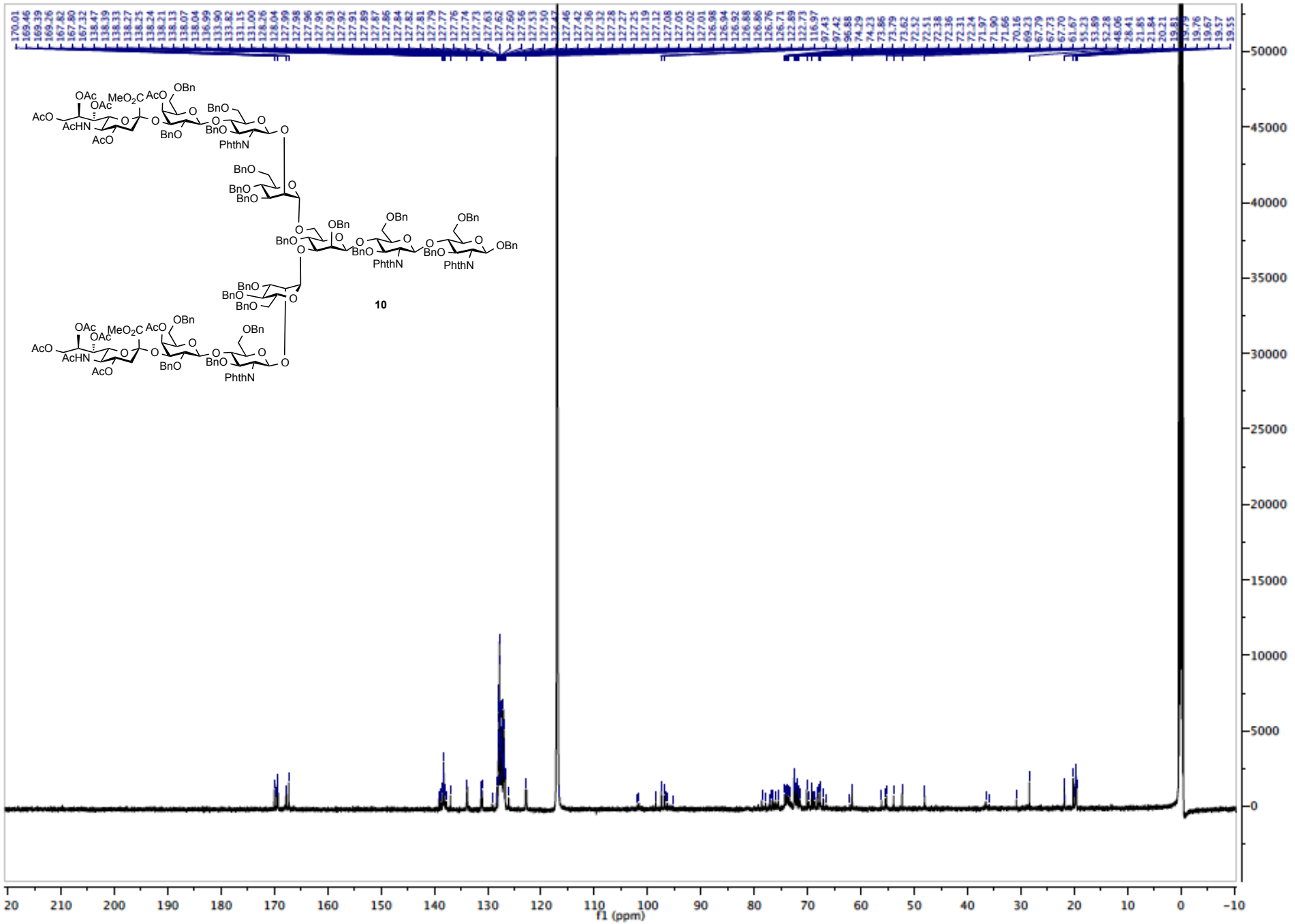

BnO
OH
BnO
BnO
O
OBn
BnO
O
O
BnO
PhthN
OBn
O
BnO
PhthN
OBn
O
OBn
BnO
BnO
BnO
O
OH
7
f1 (ppm)


167.33
128.09
128.08
127.97
127.96
127.93
127.92
127.89
127.86
127.85
127.80
127.51
127.50
127.49
127.42
127.41
127.37
127.23
127.15
116.92
116.79
101.92
101.14
99.58
96.91
96.65
74.16
74.04
73.83
73.81
73.76
73.74
72.65
72.38
72.00
70.60
70.17
70.13
67.42
55.41
BnO
OH
OBn
PhthN
7
f1 (ppm)

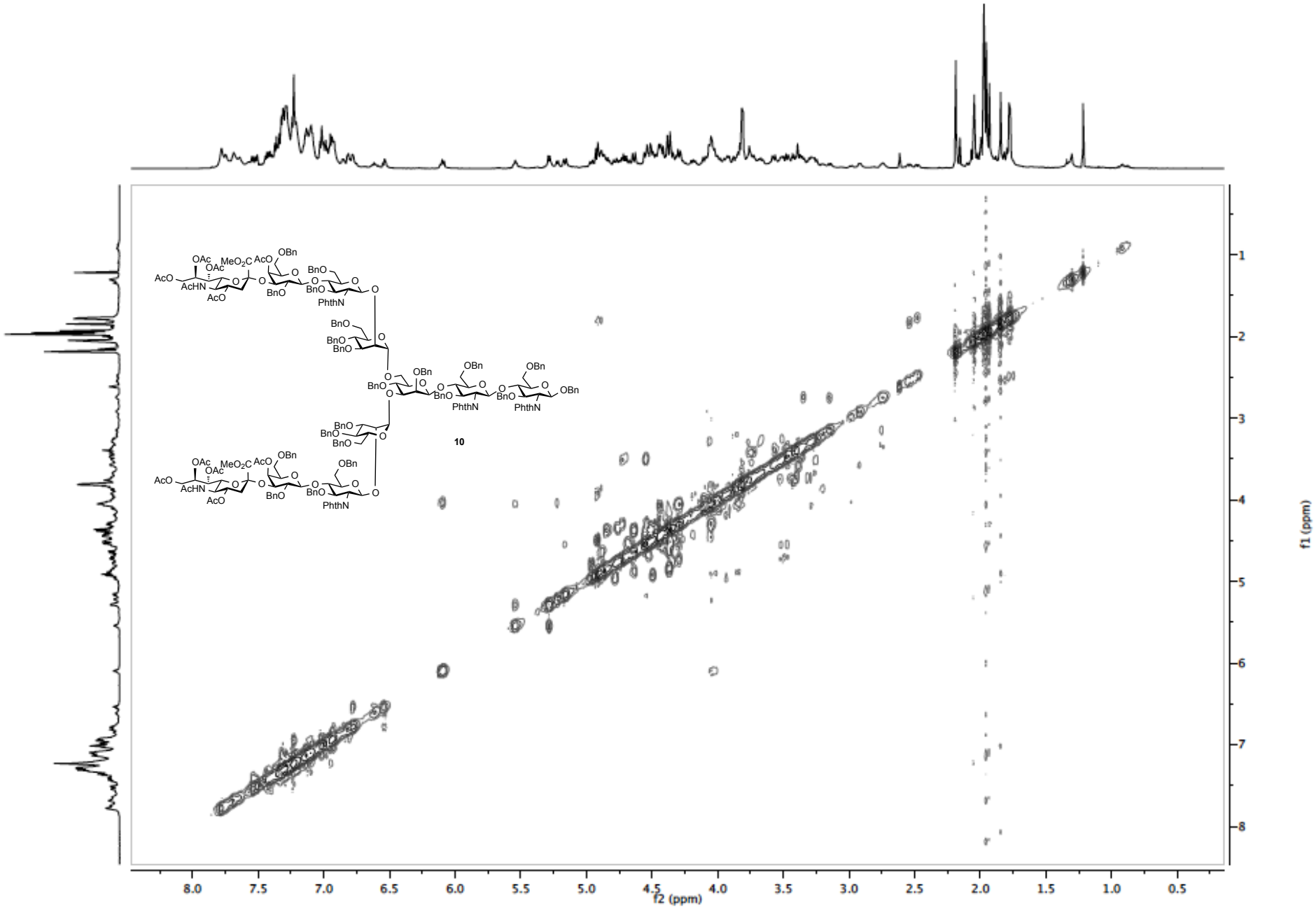
2D ^{1}H-^{13}C HSQC



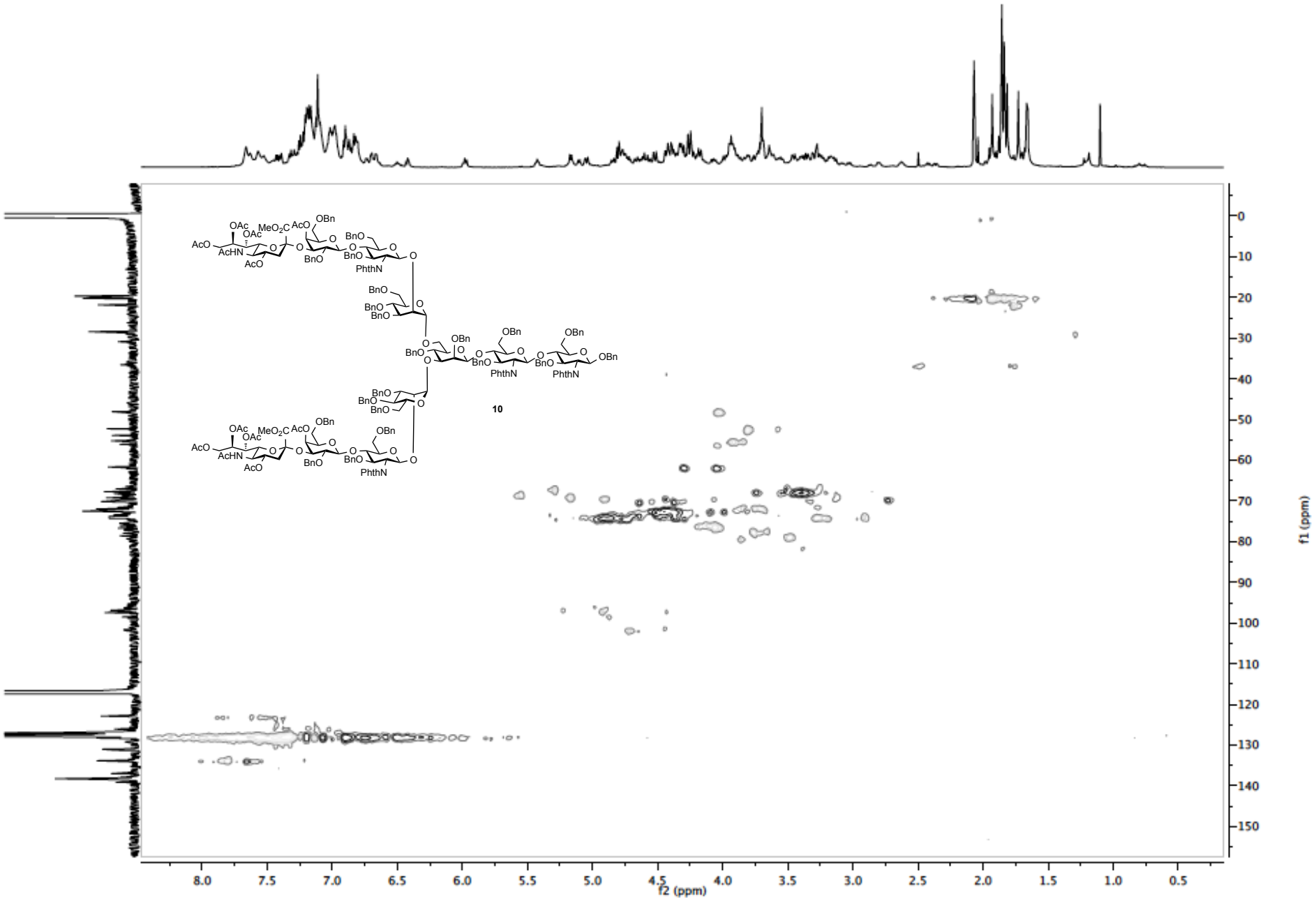

10
f1 (ppm)

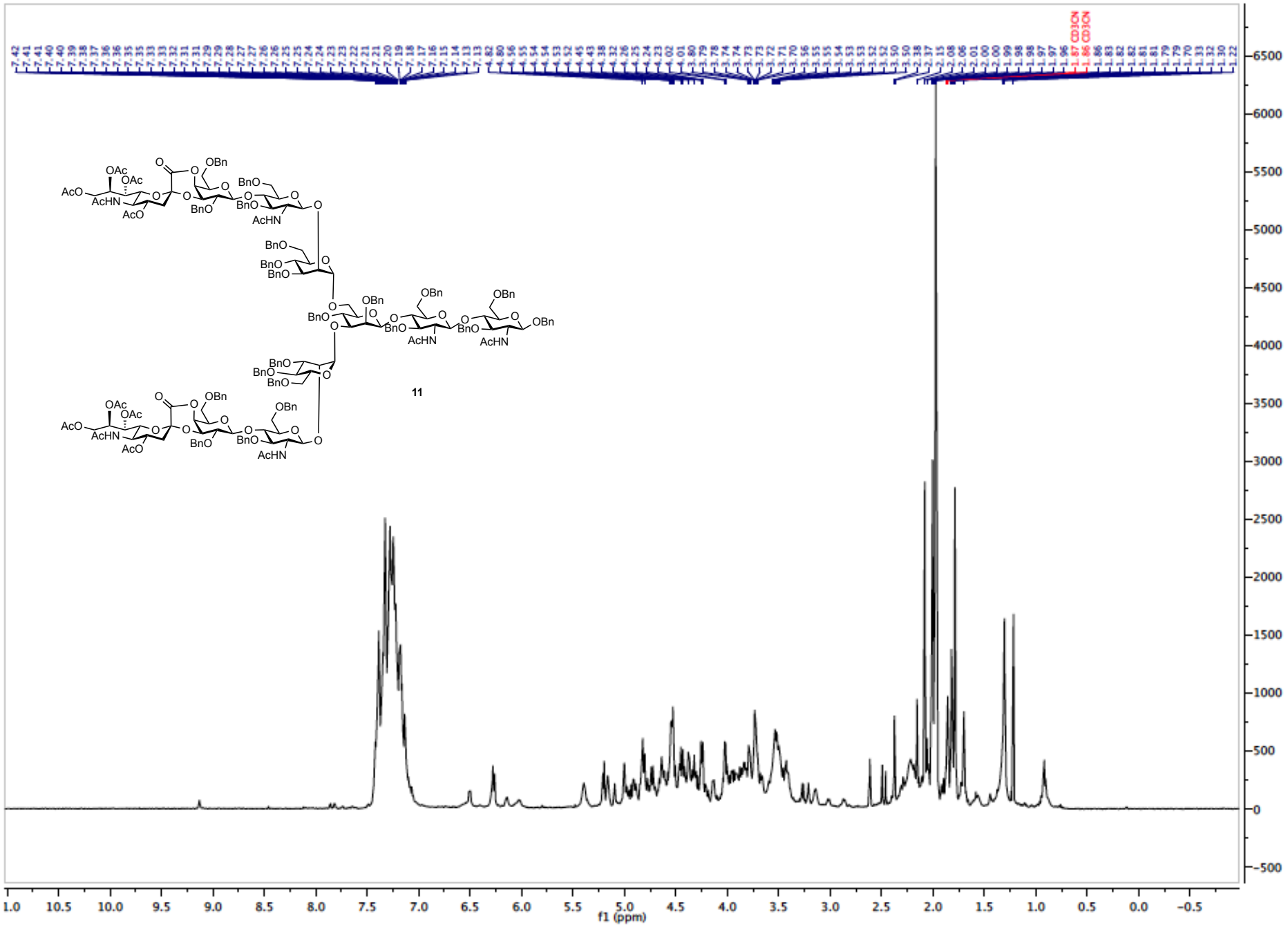

10
f1 (ppm)

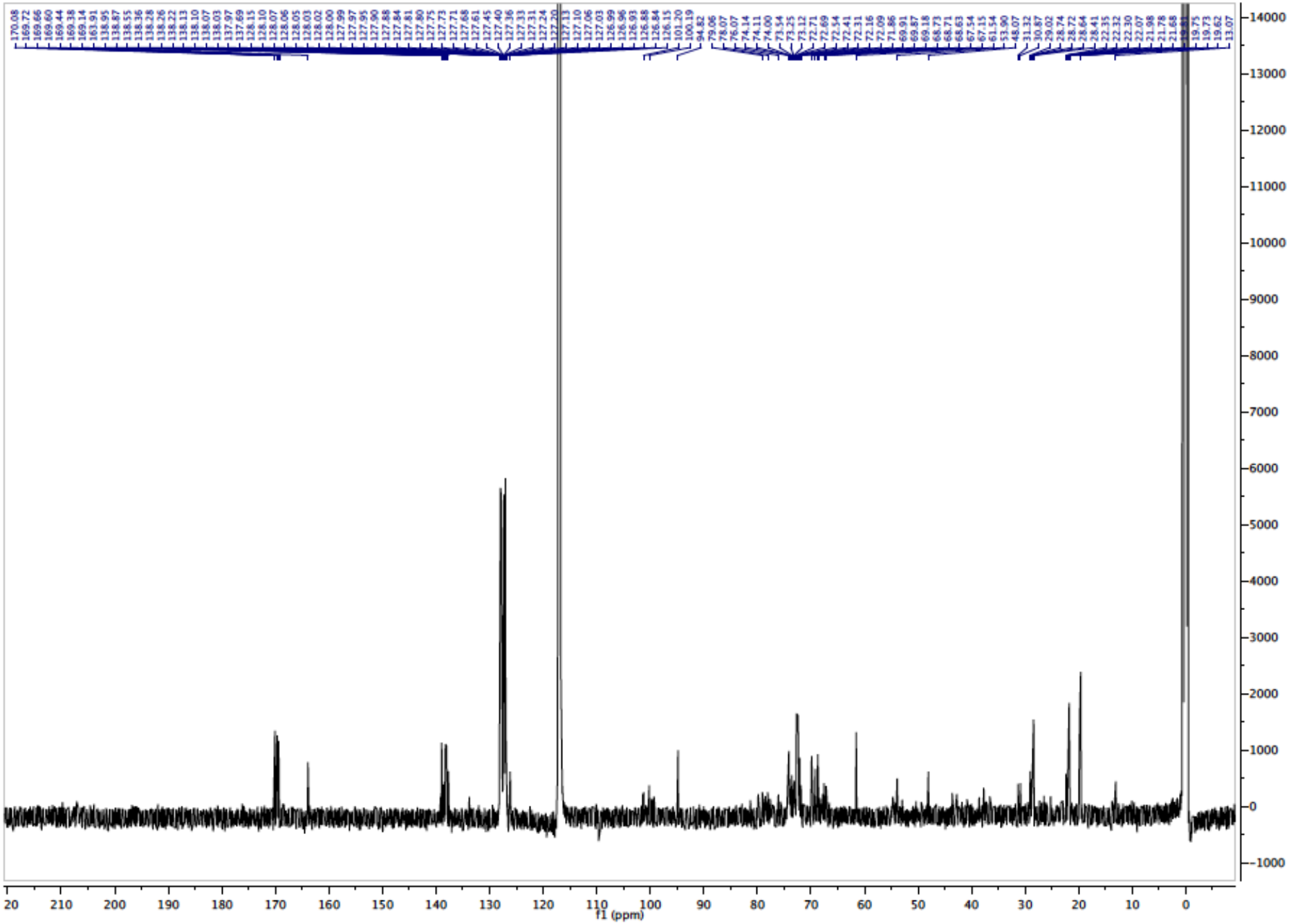
2D ^{1}H-^{1}H COSY



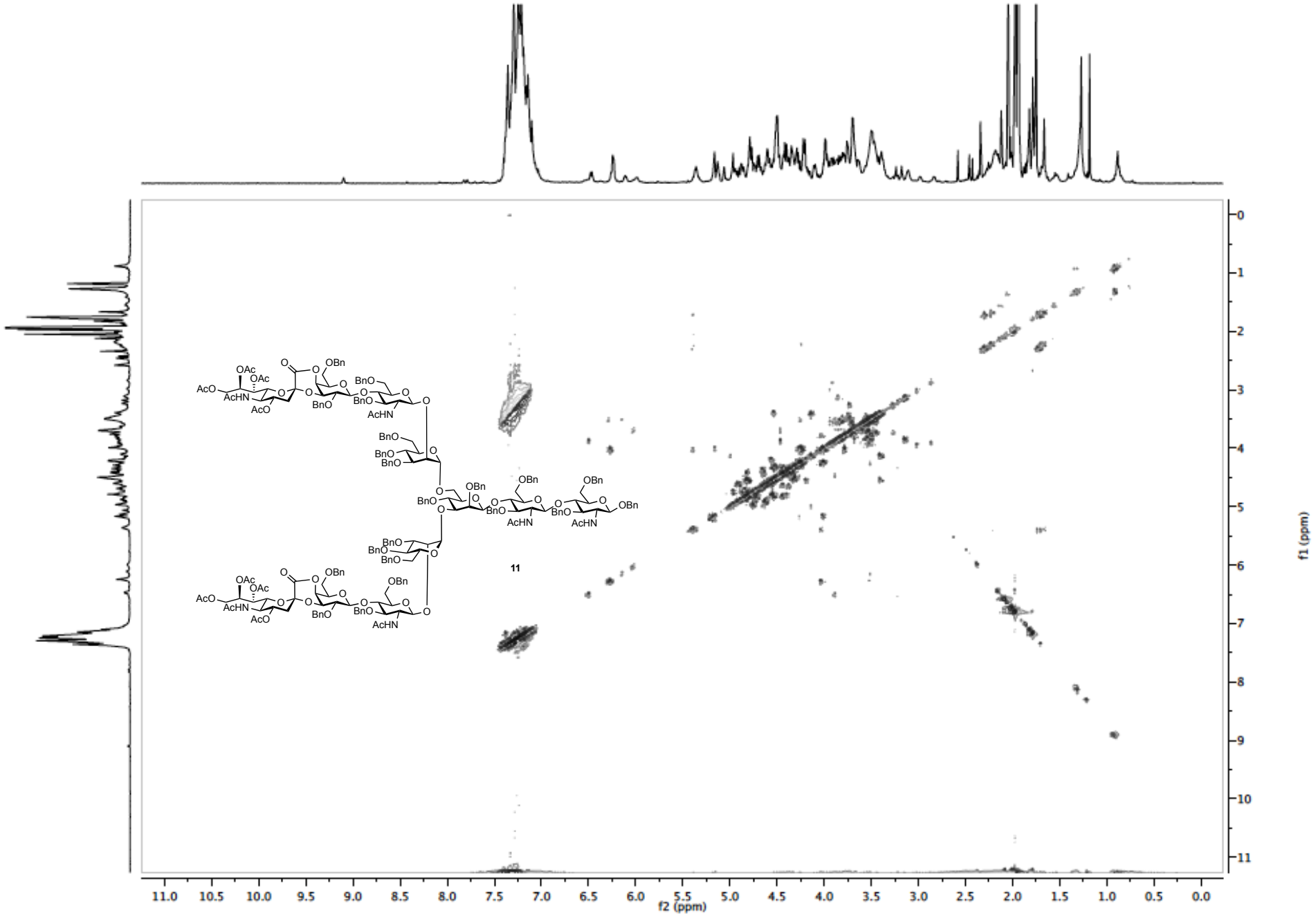
2D ^{1}H-^{13}C HSQC



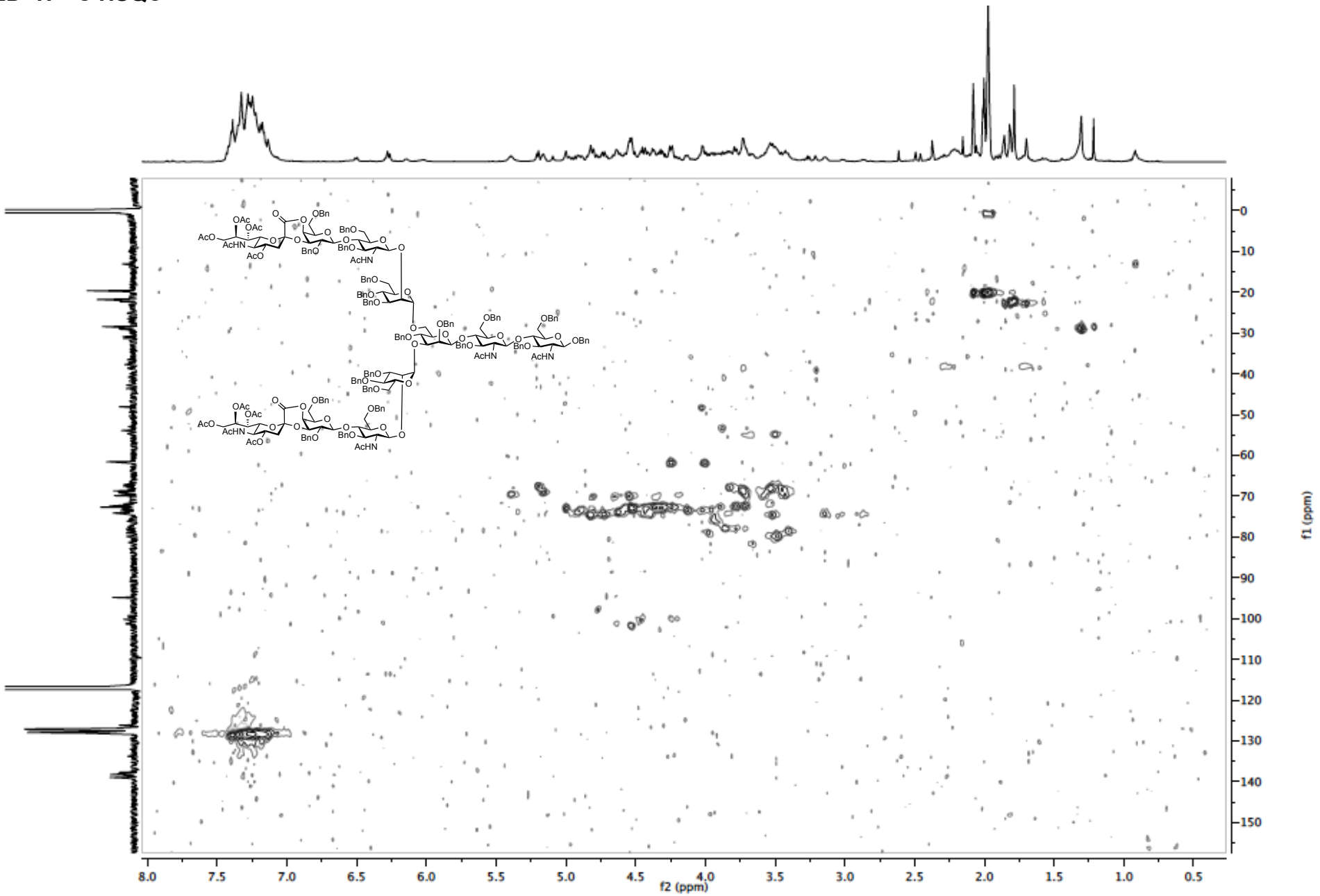

11
f1 (ppm)

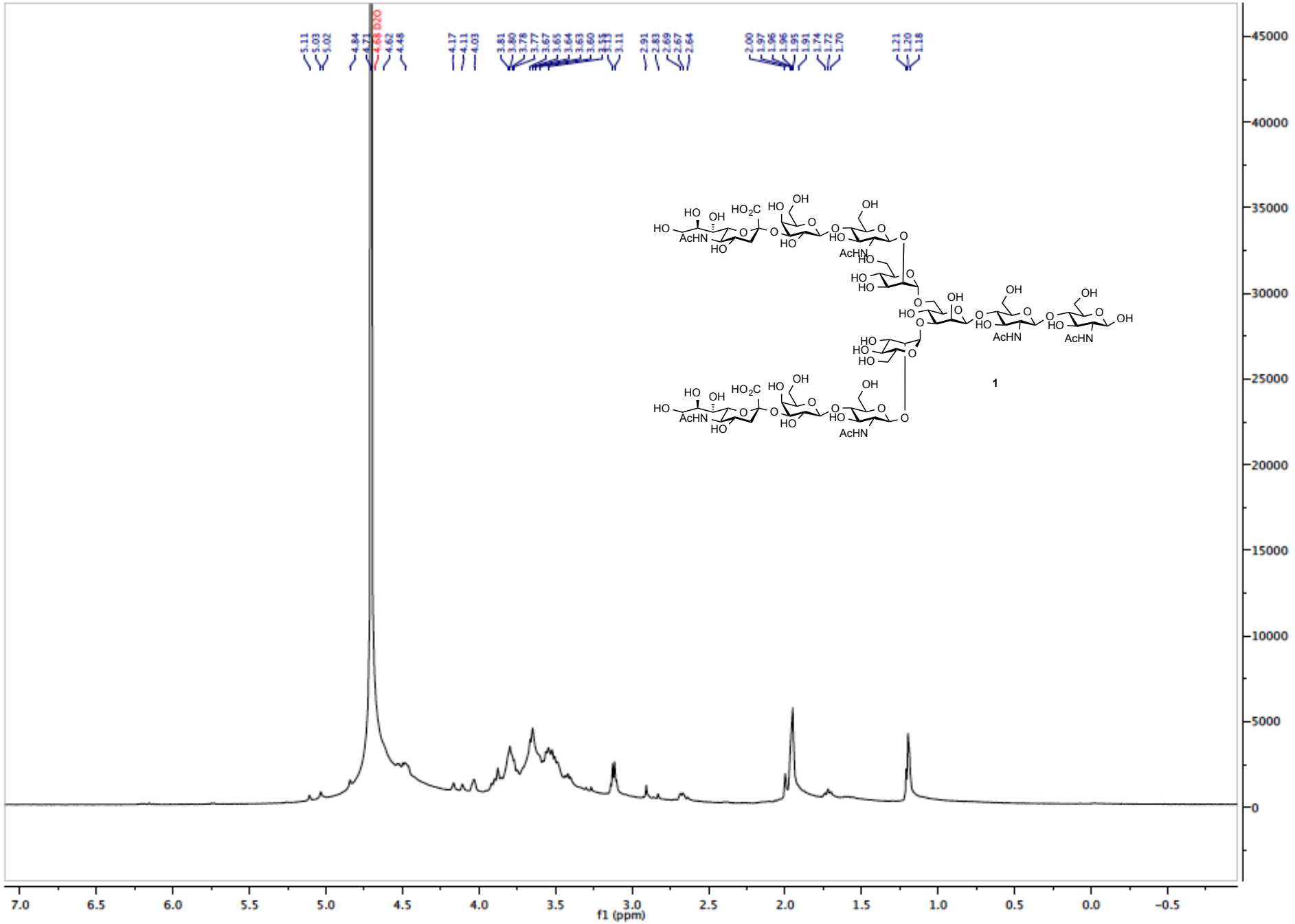

f1 (ppm)

2D ^{1}H-^{1H} COSY

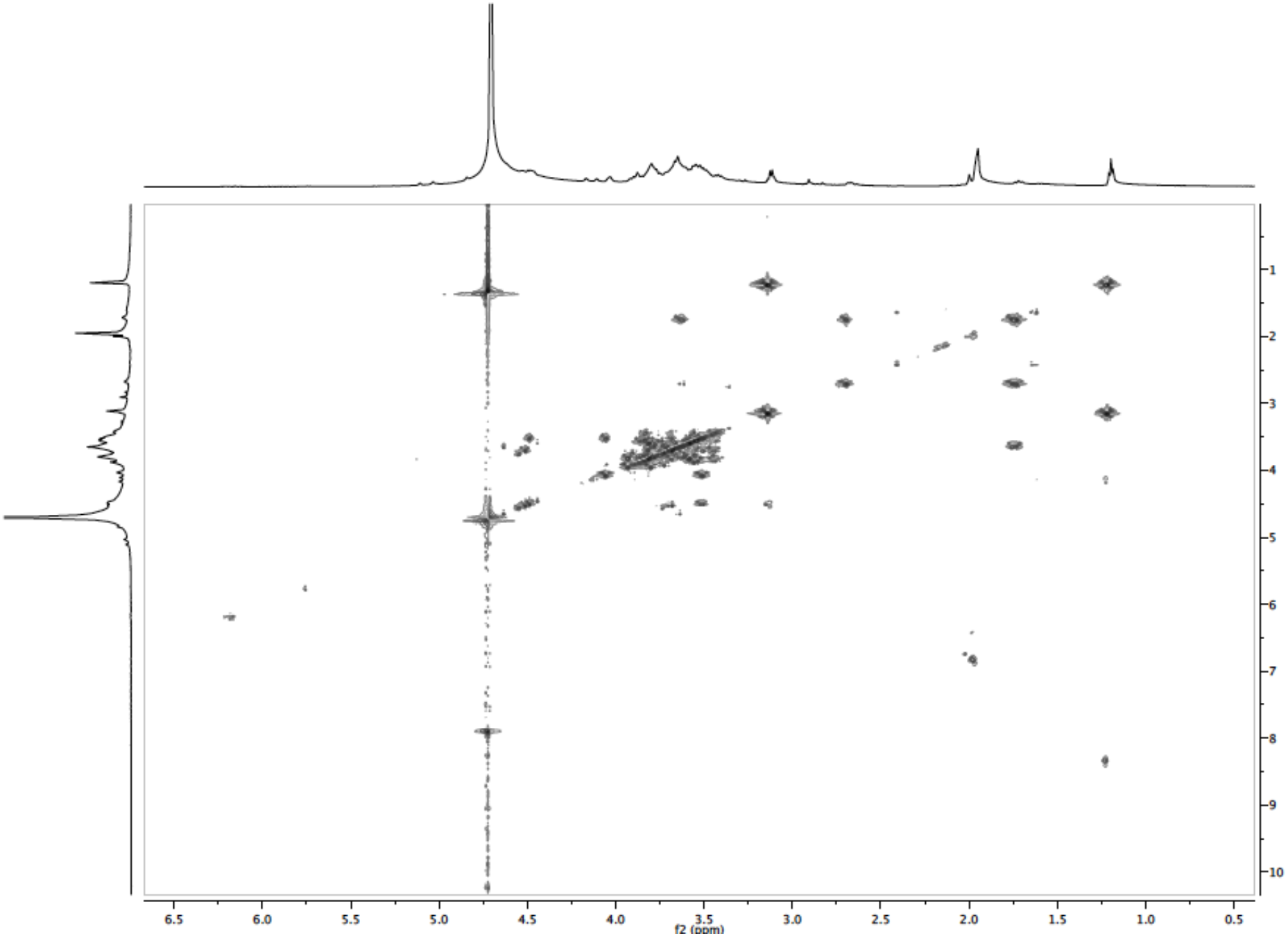

11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
f1 (ppm)
0
1
2
3
4
5
6
7
8
9
10
11

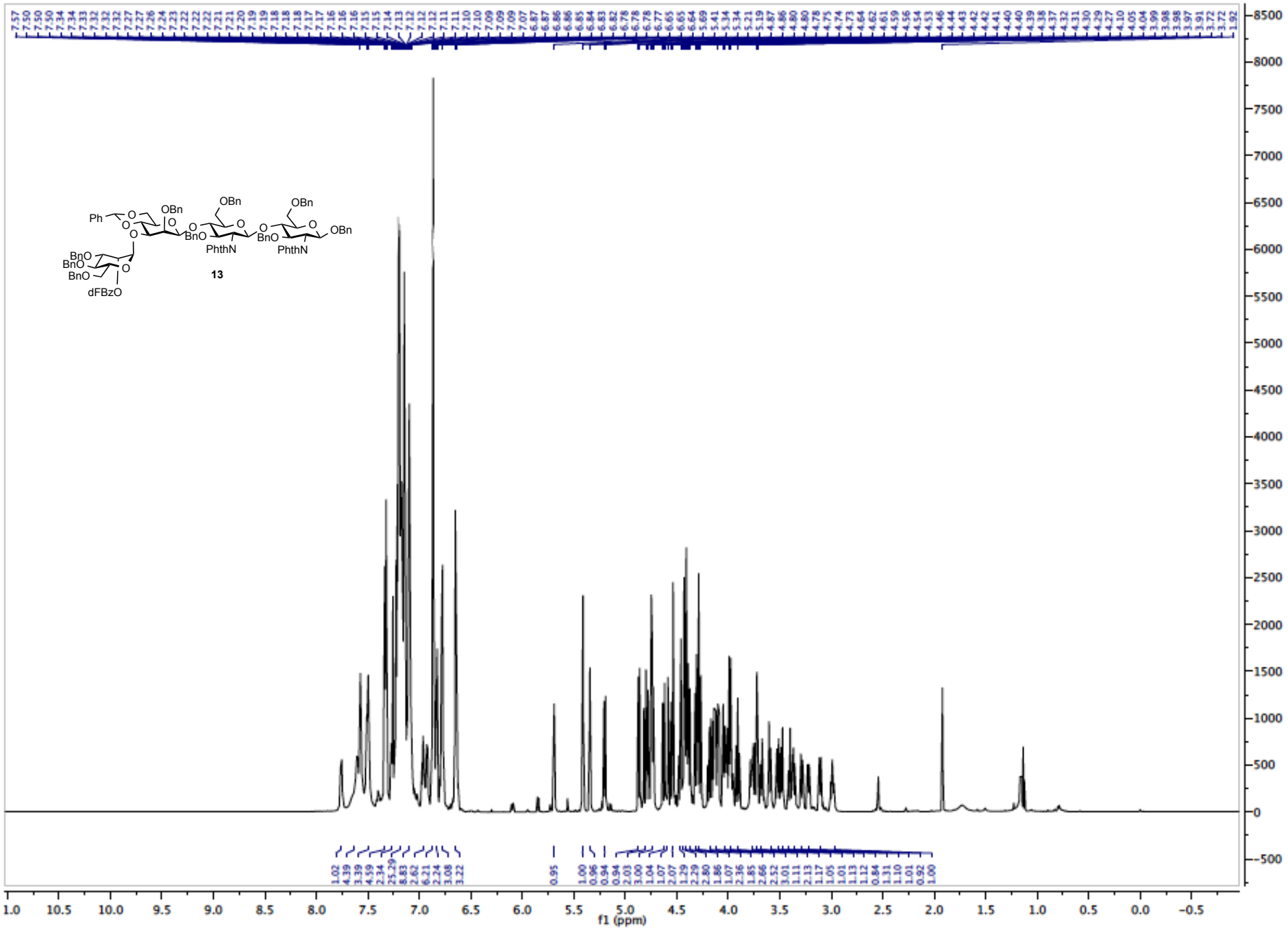
2D ^{1}H-^{13}C HSQC

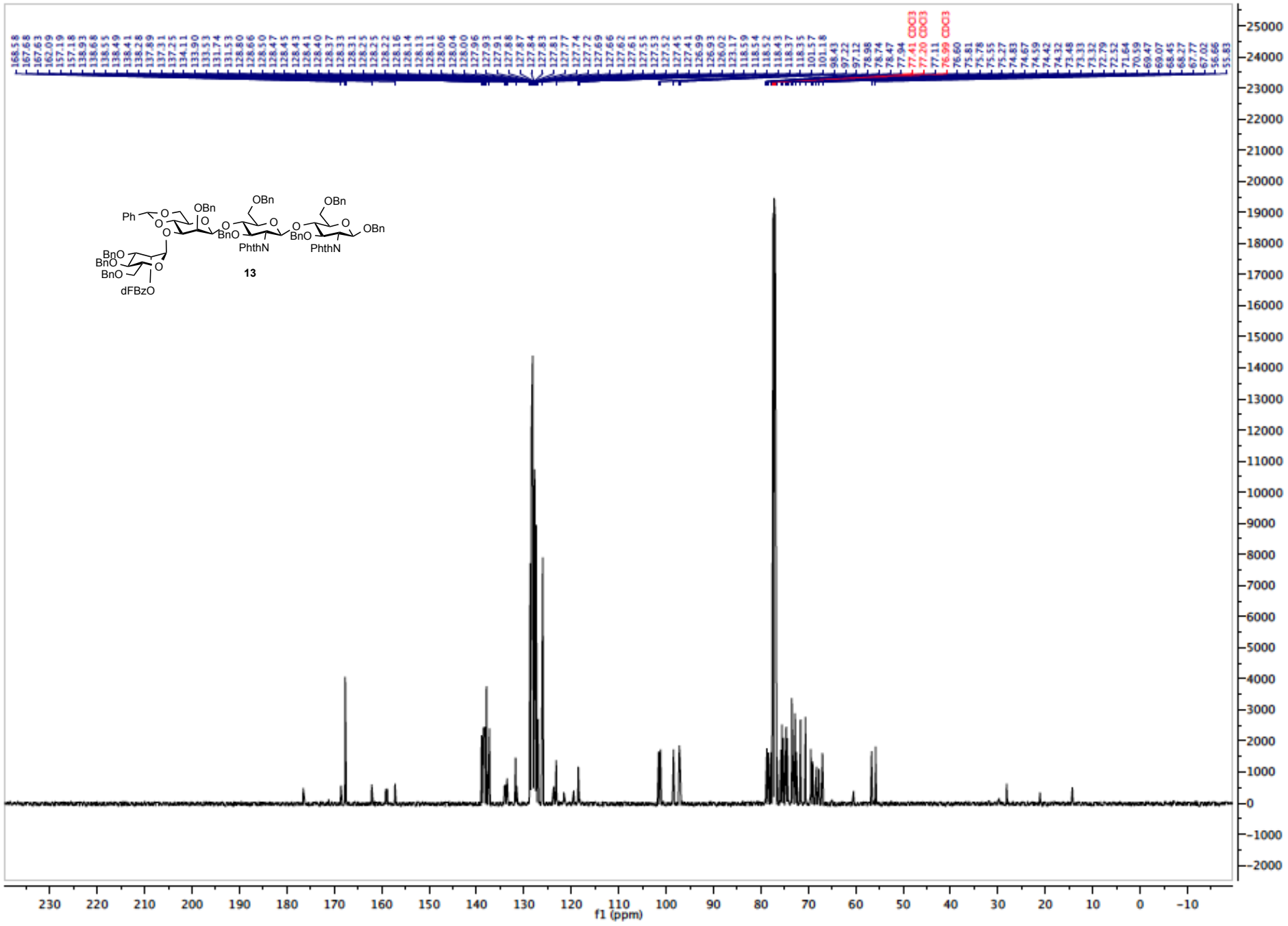



5.11
5.03
5.02
4.84
4.71
4.68 D2O
4.62
4.48
4.17
4.11
4.03
3.81
3.80
3.78
3.77
3.67
3.65
3.64
3.63
3.60
3.11
2.91
2.83
2.69
2.67
2.64
2.00
1.97
1.96
1.96
1.95
1.91
1.74
1.72
1.70
1.21
1.20
1.18
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
1

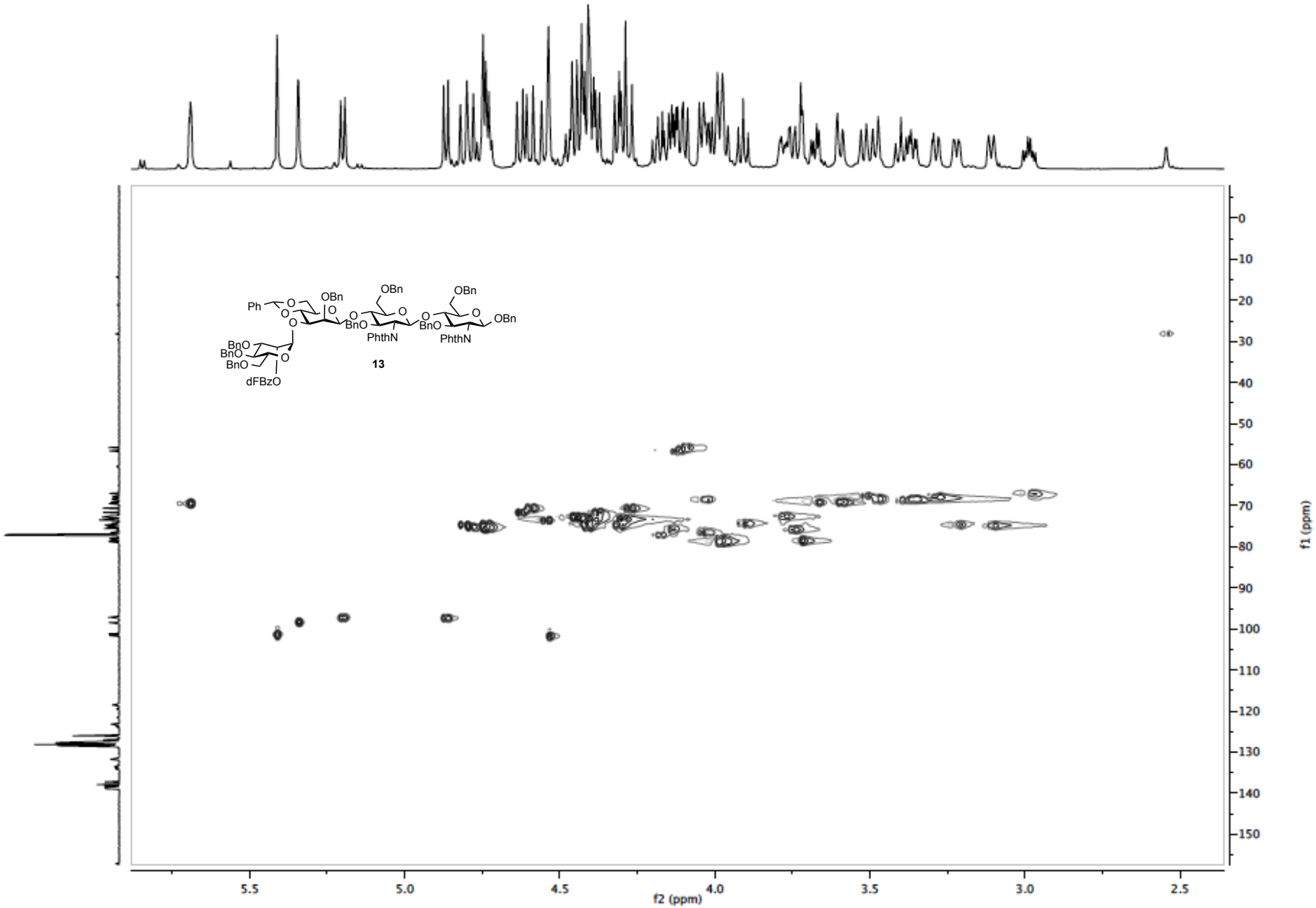
2D ^{1}H-^{1}H COSY

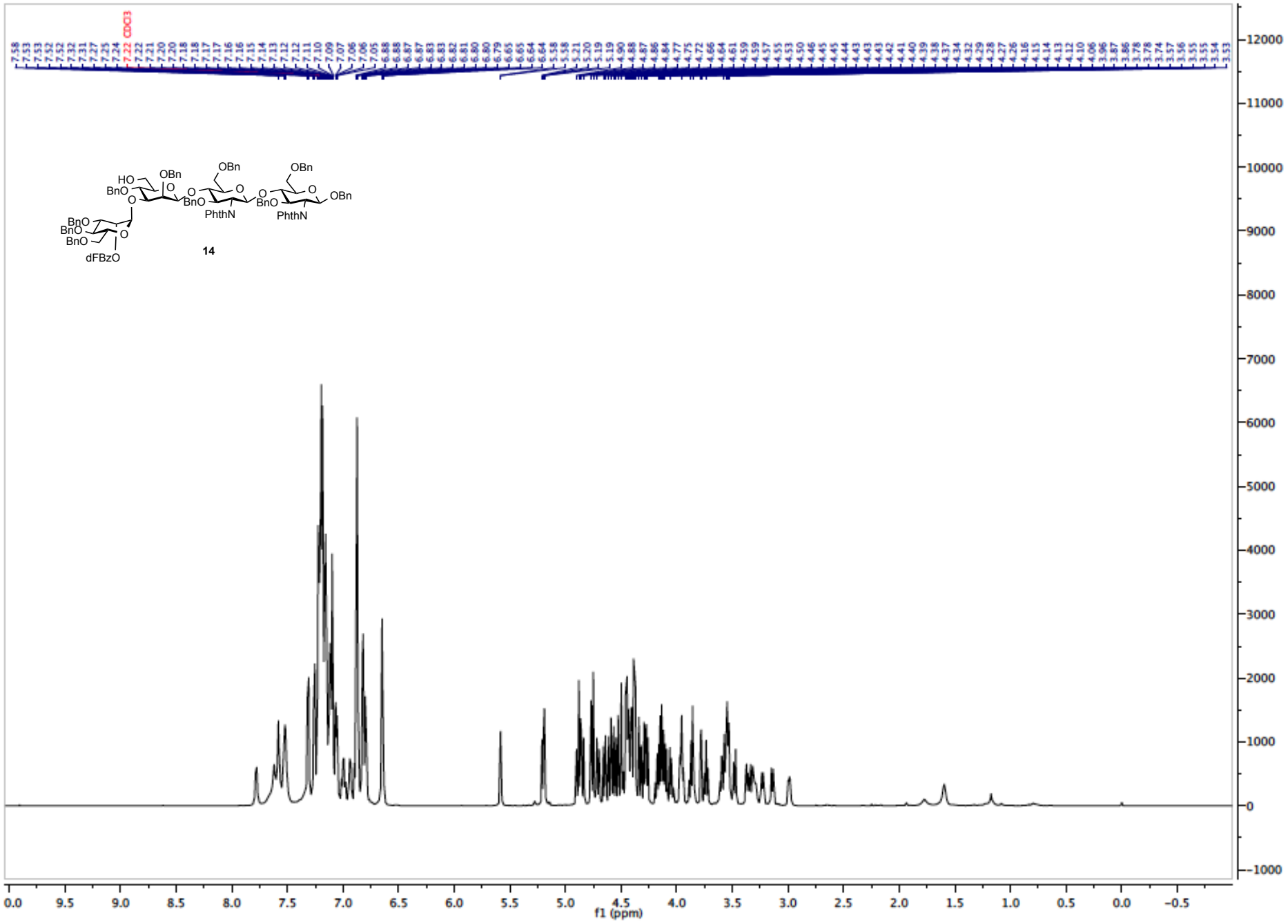


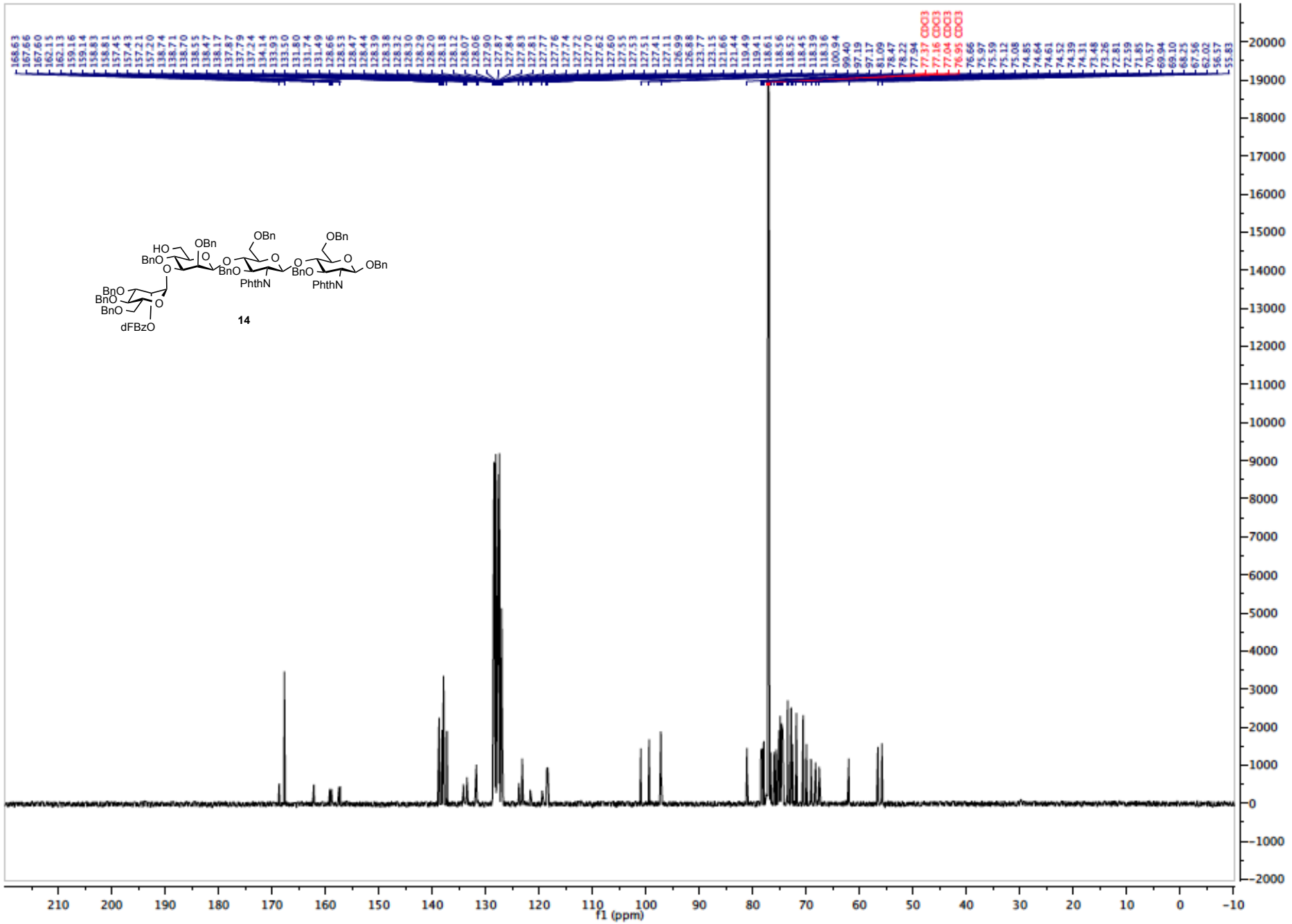

Ph
OBn
BnO
PhthN
dFBzO
13
f1 (ppm)


Ph
OBn
BnO
PhthN
dFBzO
13
f1 (ppm)

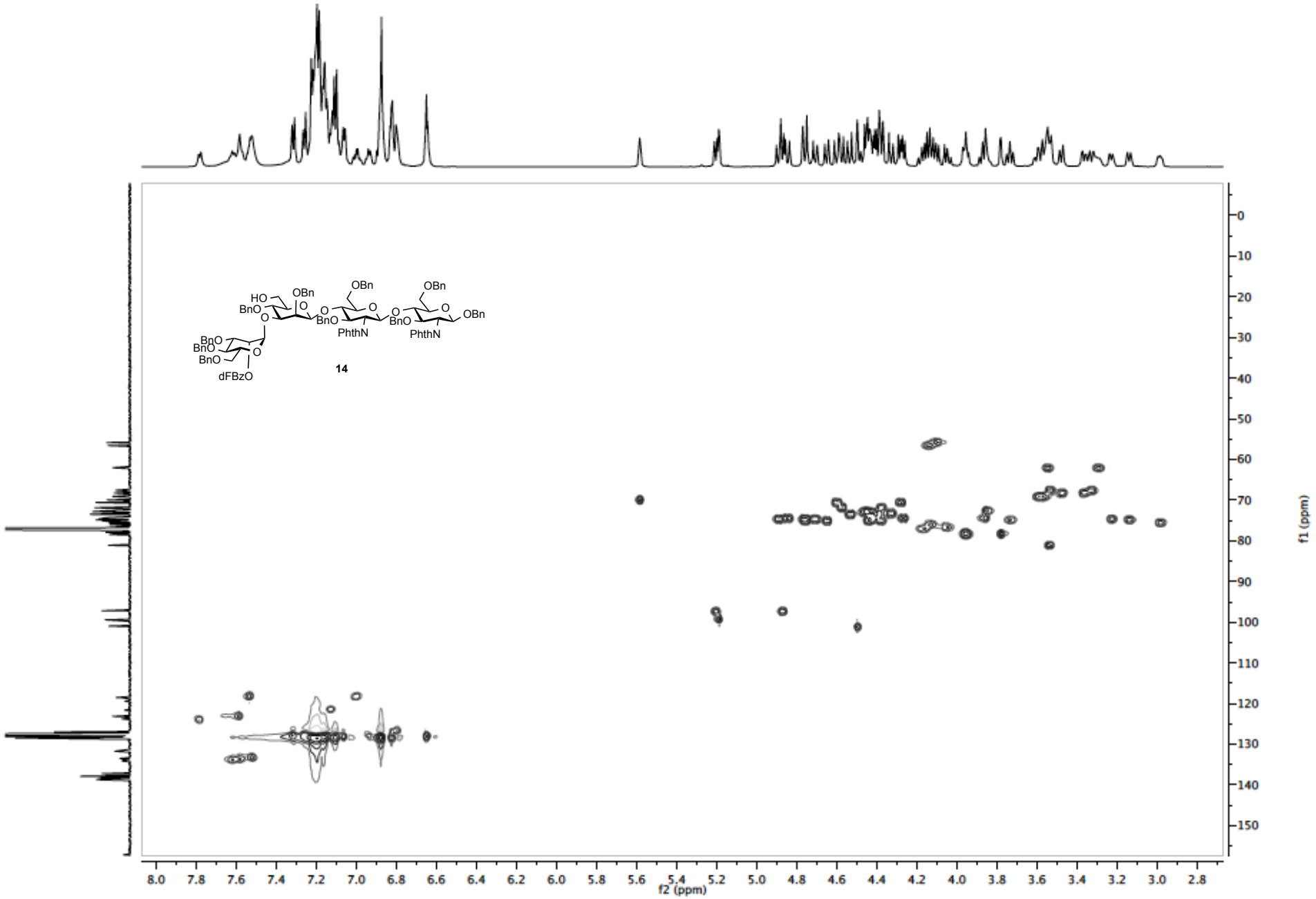
2D ^{1}H-^{13}C HSQC

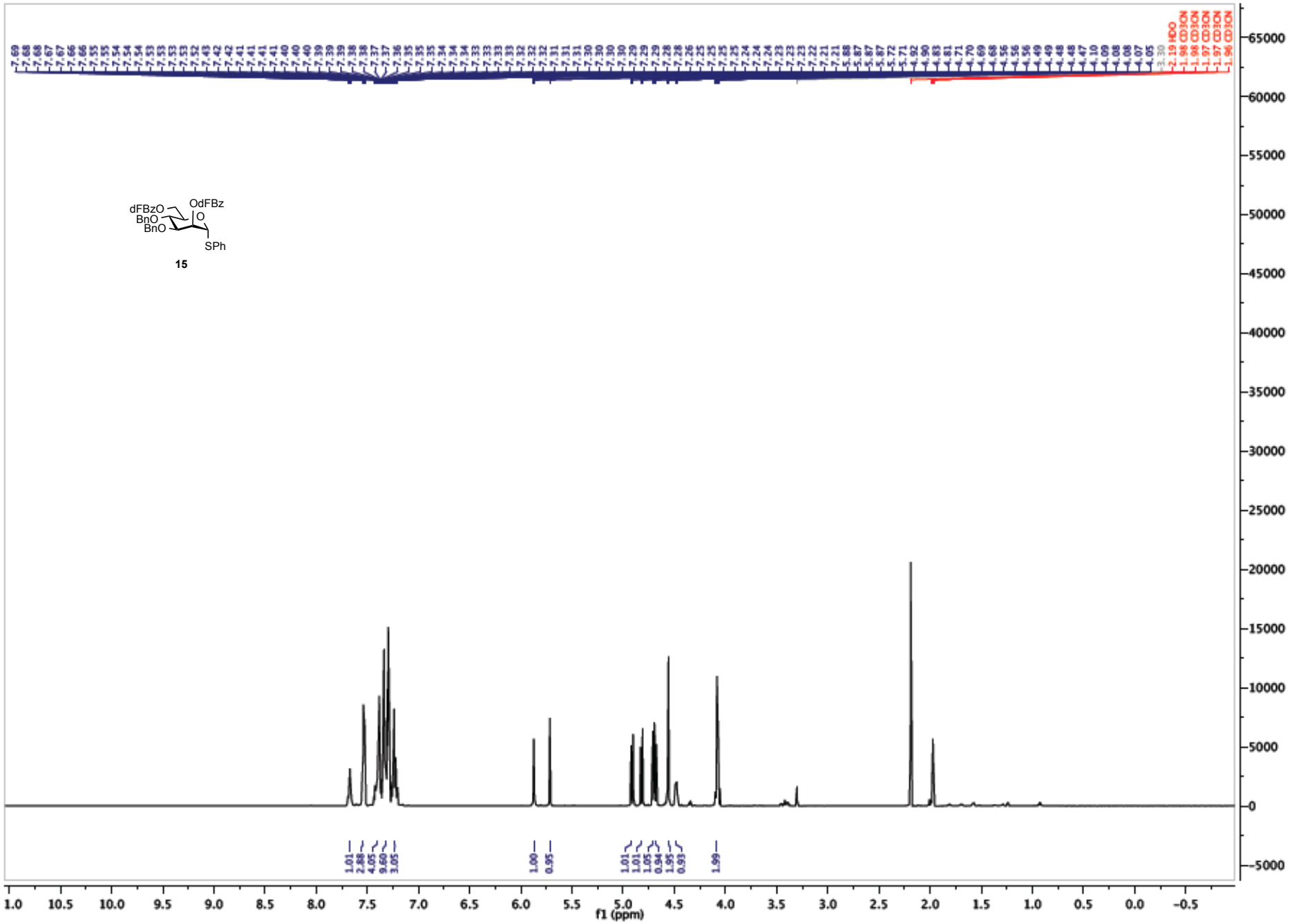


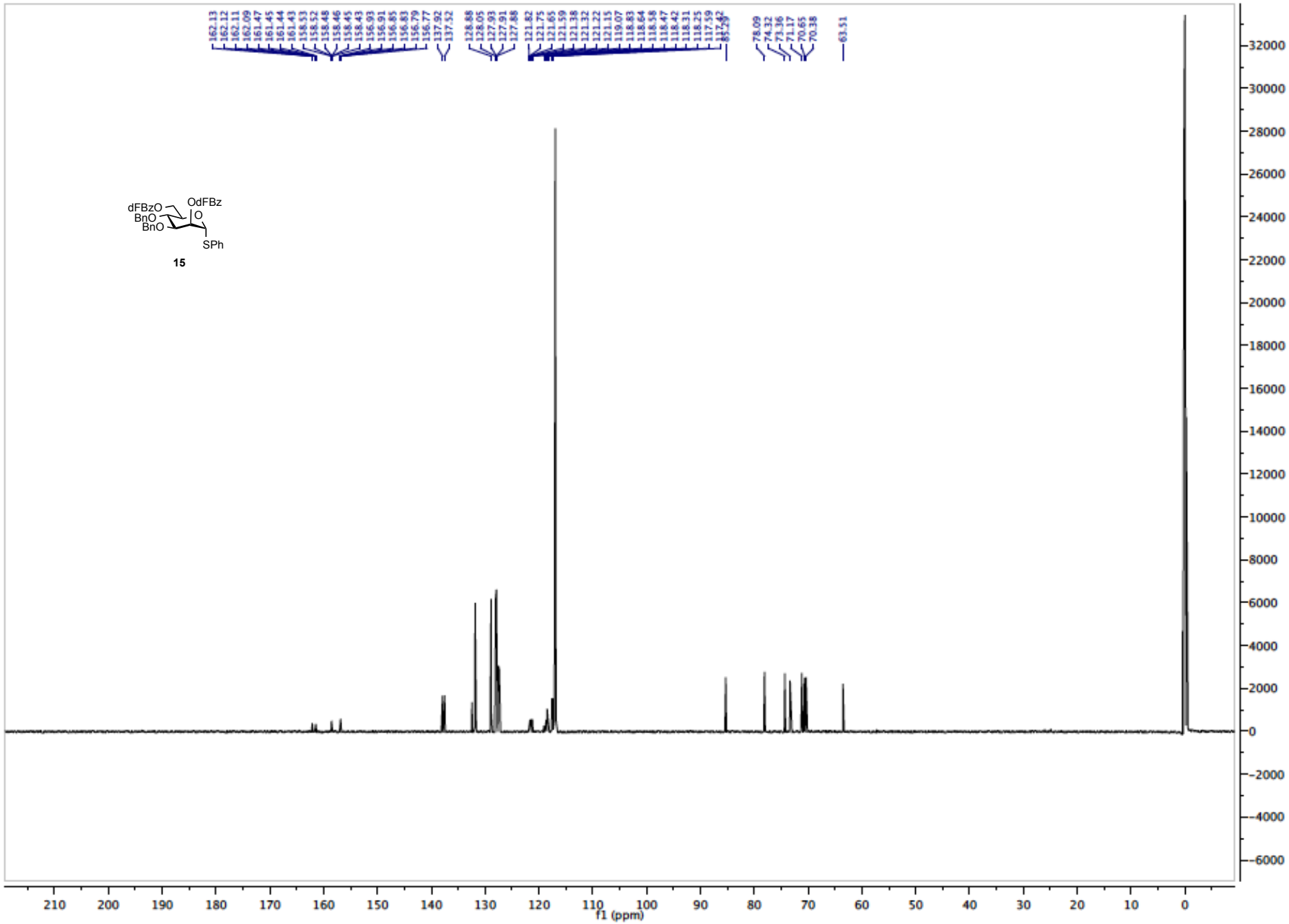

CDCl3
HO
OBn
BnO
PhthN
dFBzO
14
f1 (ppm)

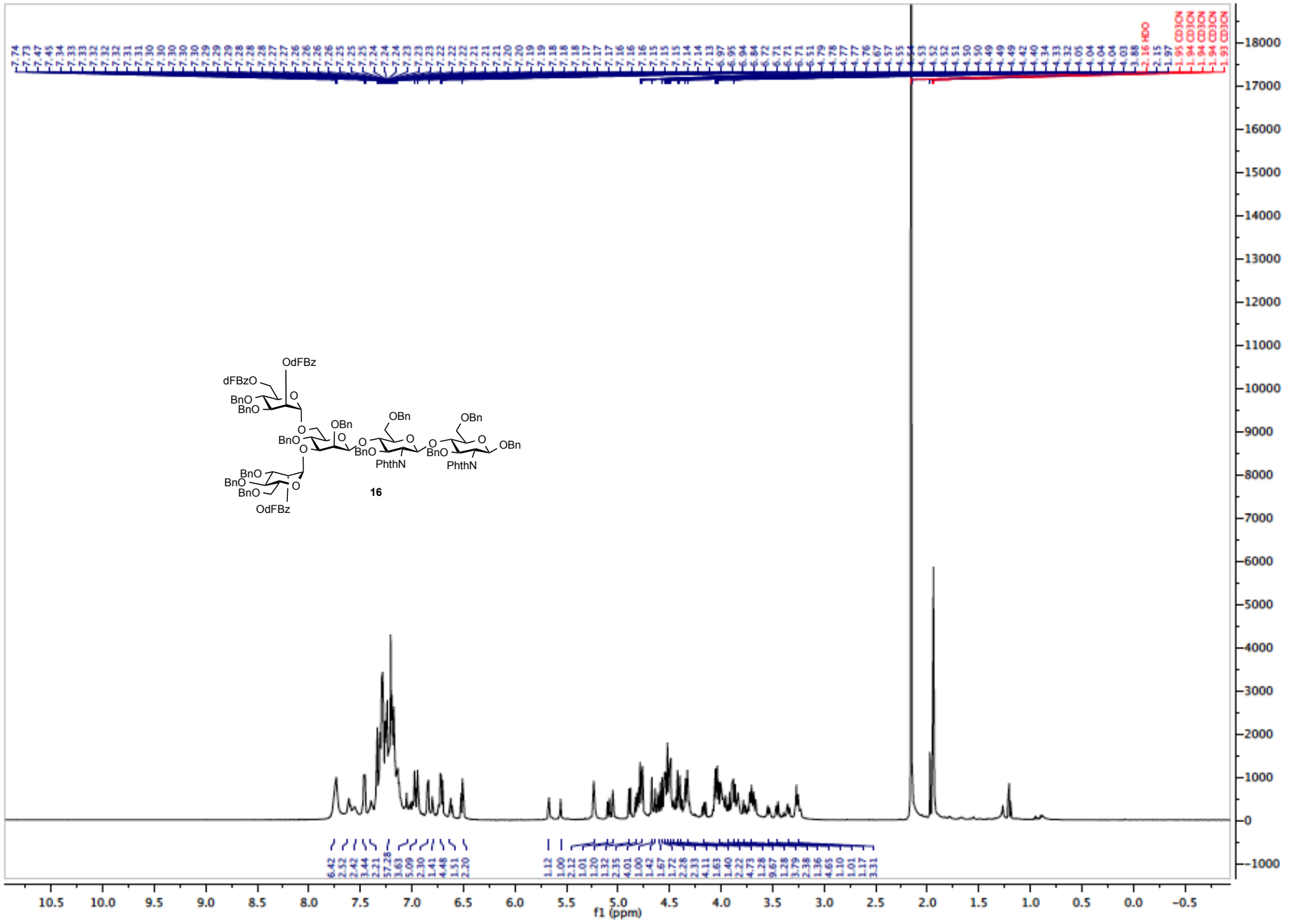

HO
OBn
BnO
O
BnO
PhthN
OBn
BnO
PhthN
OBn
OBn
BnO
BnO
BnO
dFBzO
14
f1 (ppm)

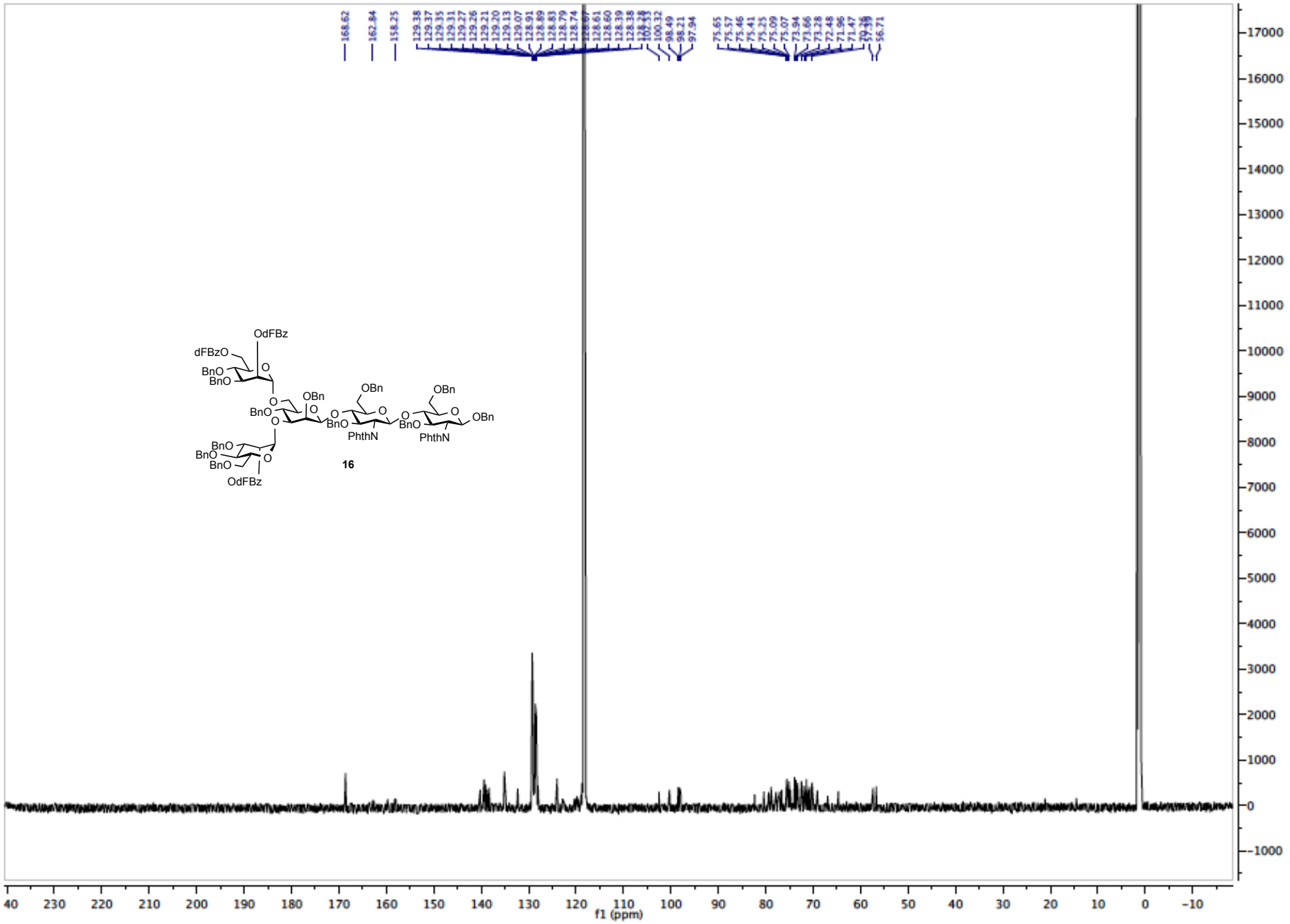
2D ^{1}H-^{13}C HSQC



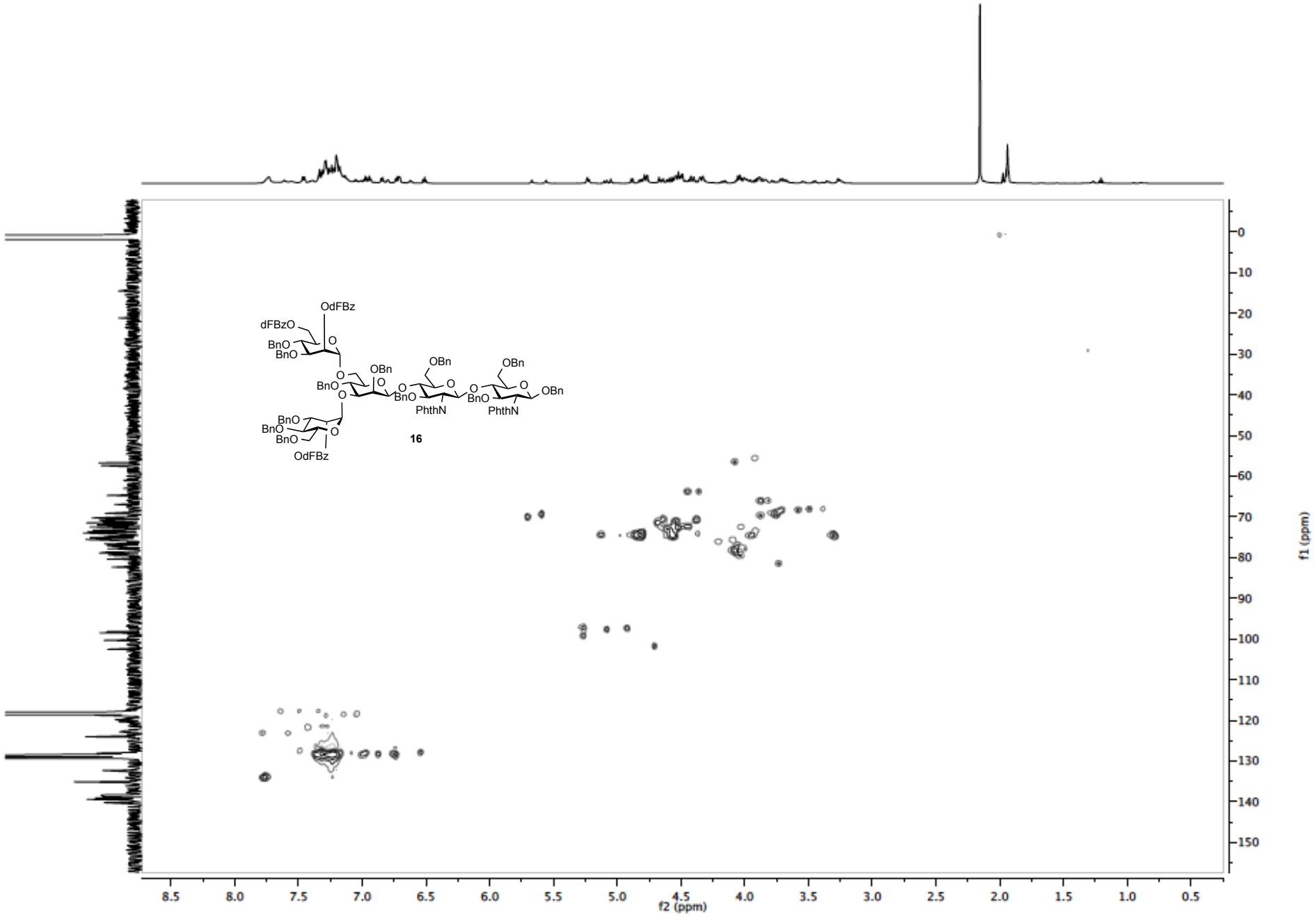

dFBzO
BnO
BnO
OdFBz
O
SPh
15
f1 (ppm)

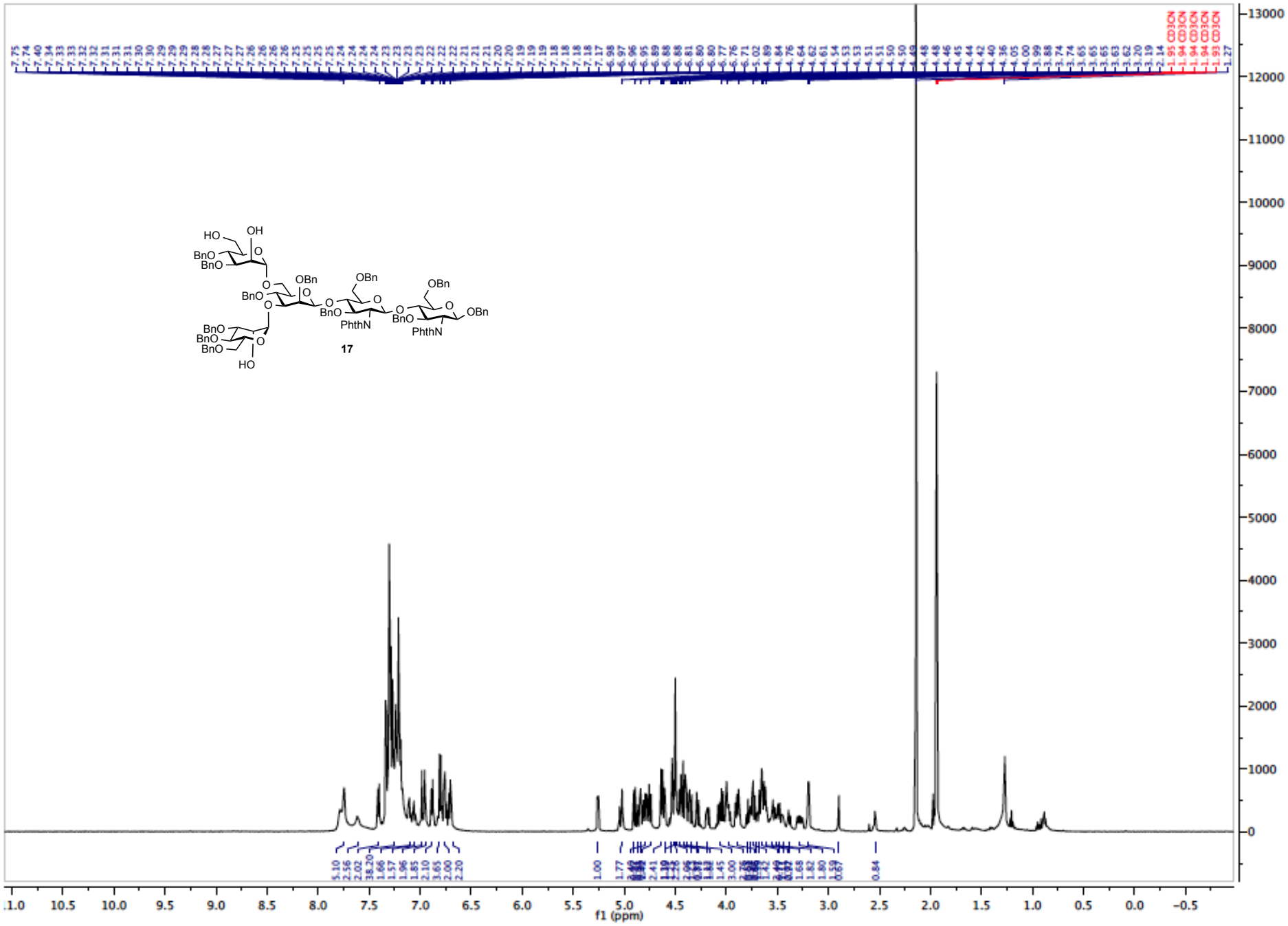

dFBzO
OdFBz
BnO
O
BnO
SPh
15
f1 (ppm)

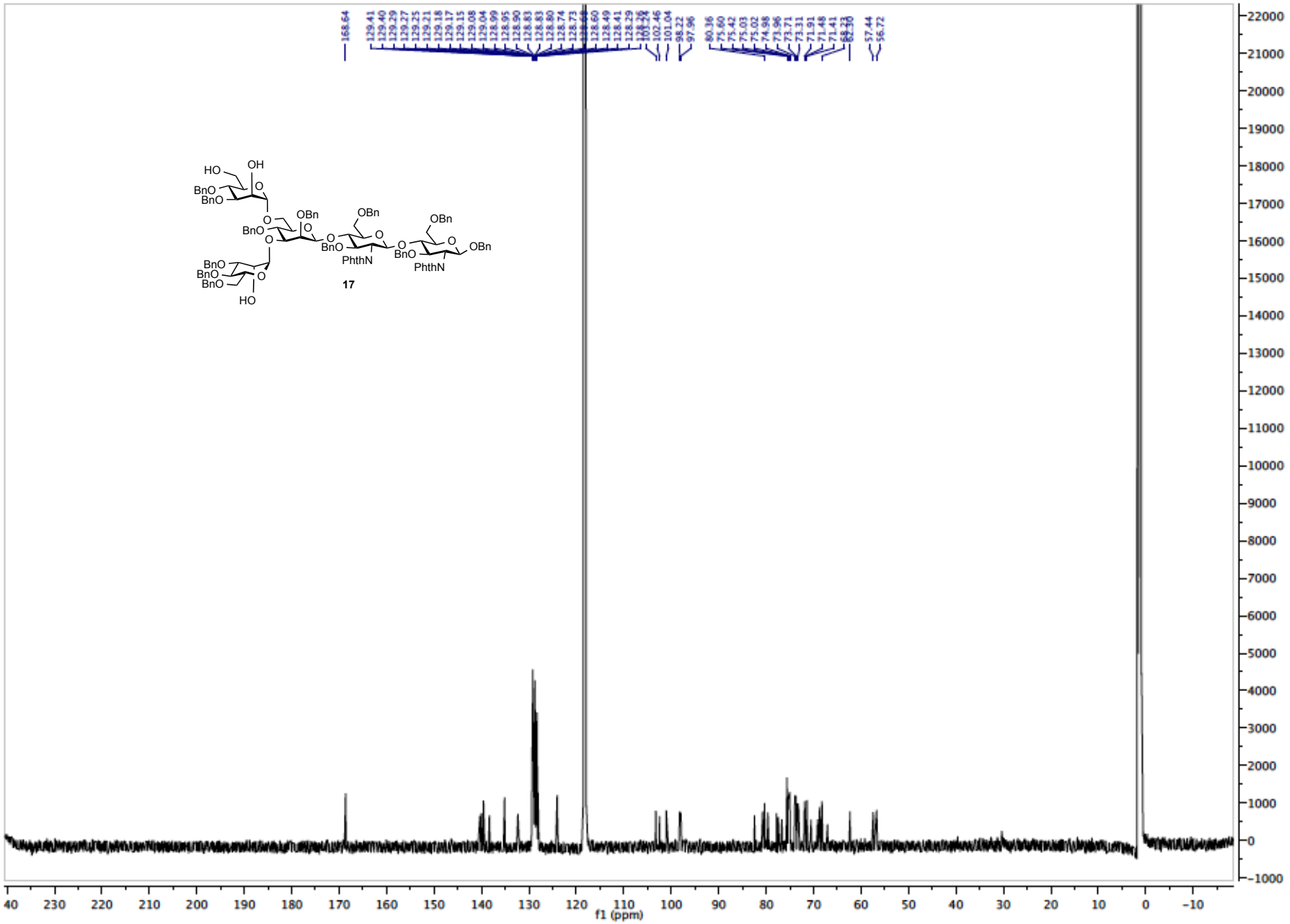

OdFBz
dFBzO
BnO
BnO
O
OBn
BnO
O
O
BnO
PhthN
OBn
BnO
O
O
BnO
PhthN
OBn
OBn
BnO
BnO
BnO
O
OdFBz
16
f1 (ppm)


168.62
162.84
158.25
129.38
129.37
129.35
129.31
129.27
129.26
129.21
129.20
129.13
129.07
128.91
128.89
128.83
128.79
128.74
128.67
128.61
128.60
128.39
128.38
100.32
98.49
98.21
97.94
75.65
75.57
75.46
75.41
75.25
75.09
75.07
73.94
73.66
73.28
72.48
71.96
71.47
56.71
OdFBz
dFBzO
BnO
BnO
O
OBn
BnO
O
O
O
BnO
PhthN
OBn
O
BnO
PhthN
OBn
O
OBn
BnO
BnO
BnO
O
OdFBz
16
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
40
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

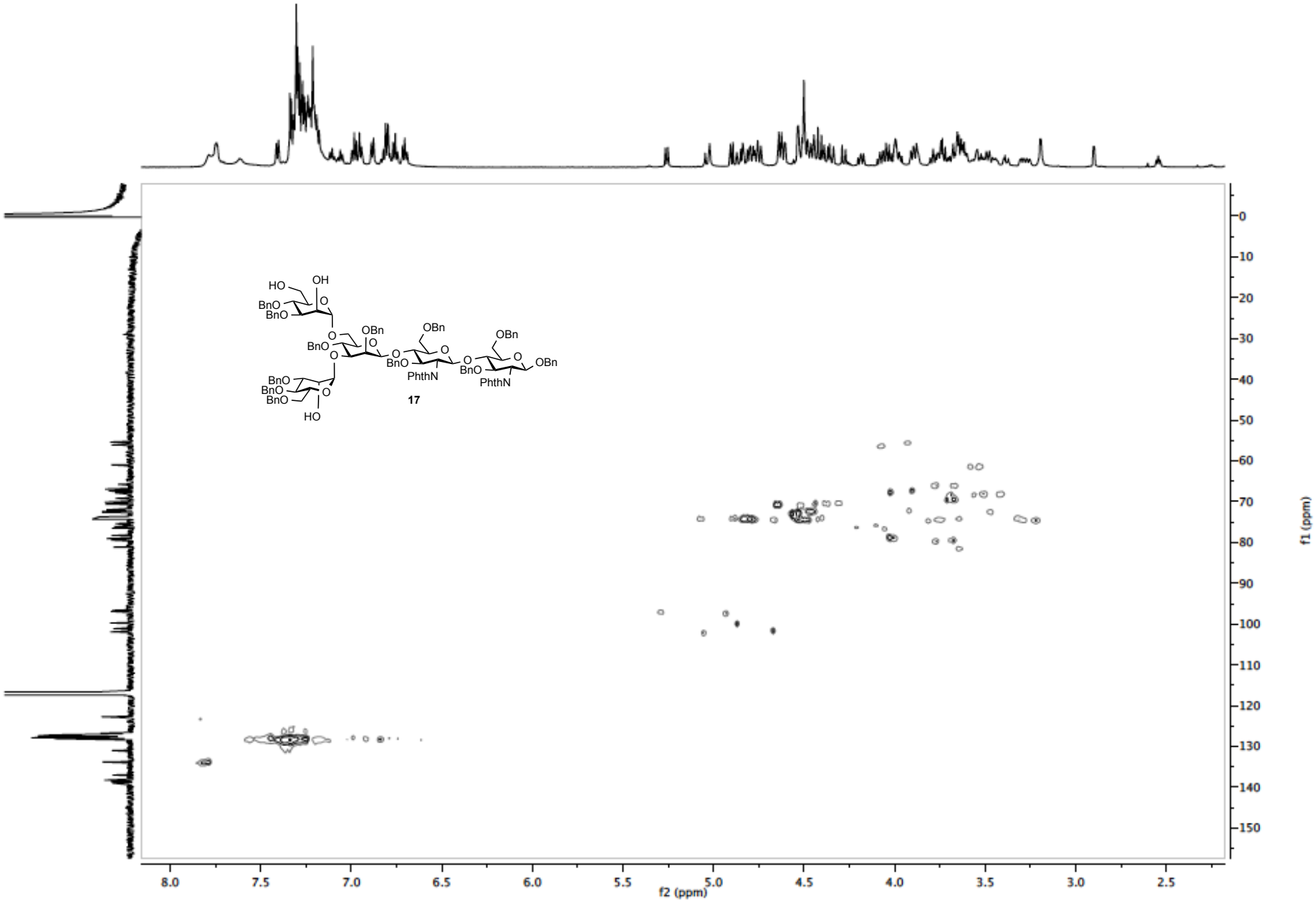
2D ^{1}H-^{13}C HSQC

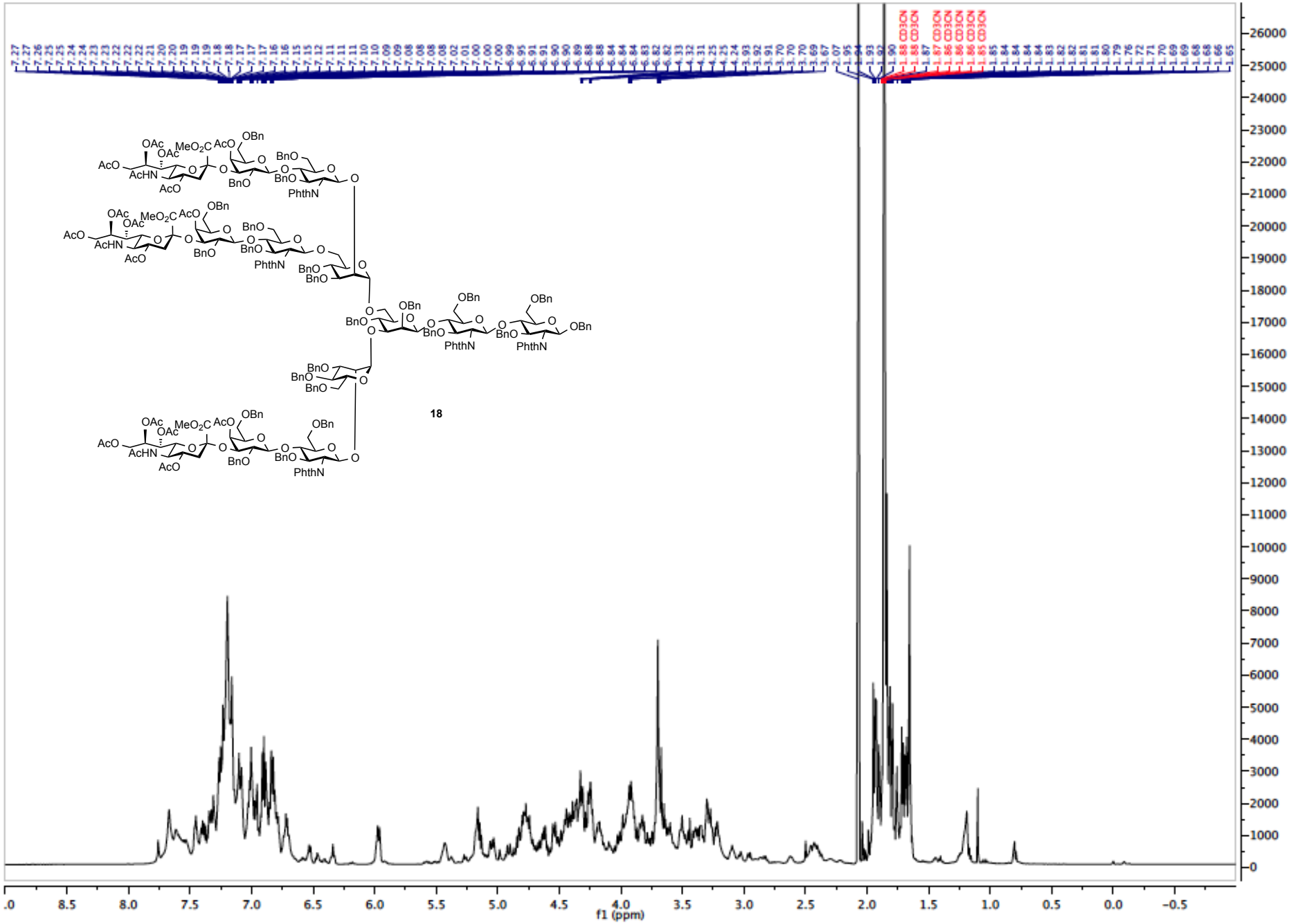


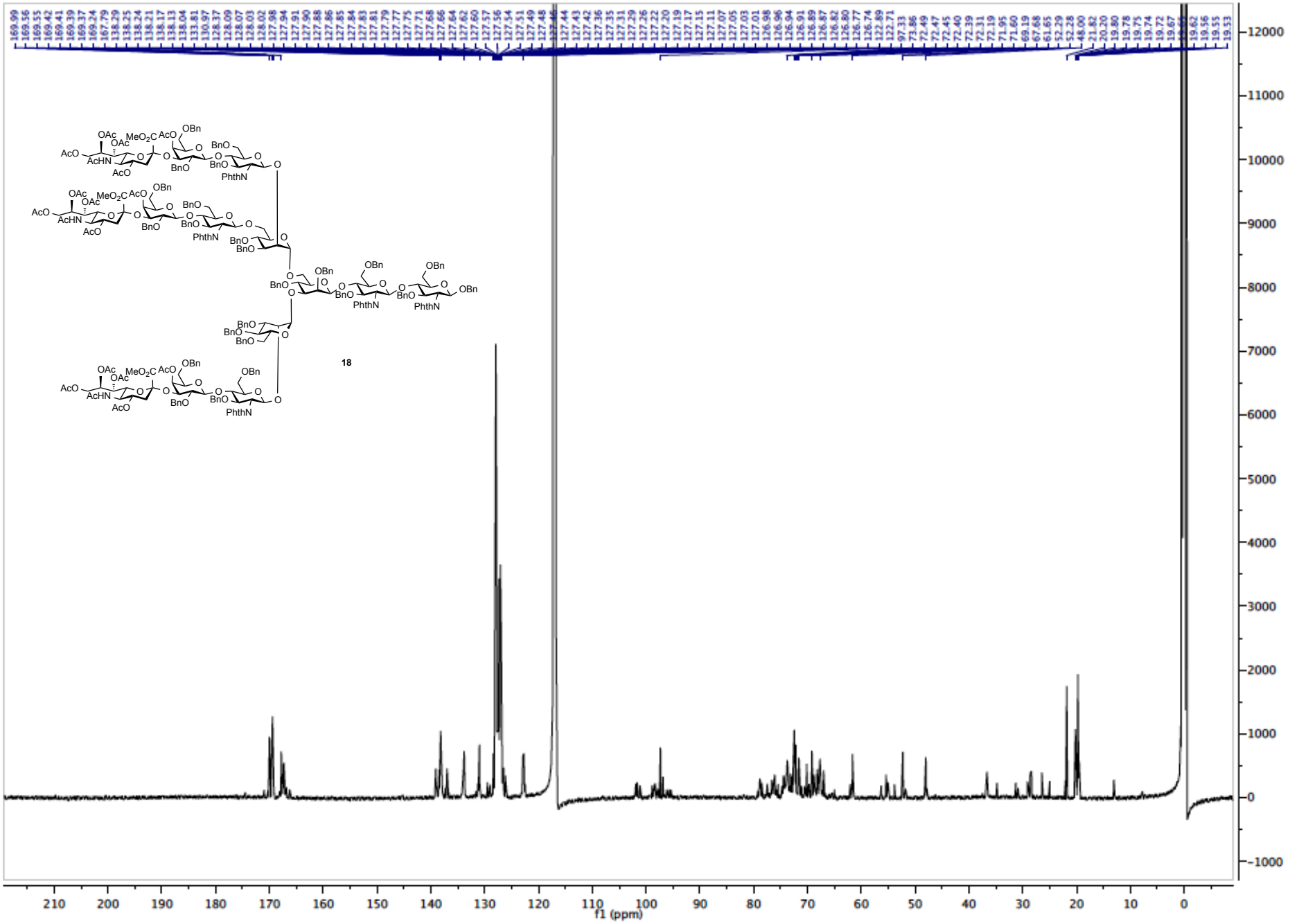

HO
OH
BnO
BnO
O
OBn
BnO
PhthN
BnO
PhthN
OBn
OBn
OBn
BnO
BnO
BnO
HO
17
f1 (ppm)


17
f1 (ppm)

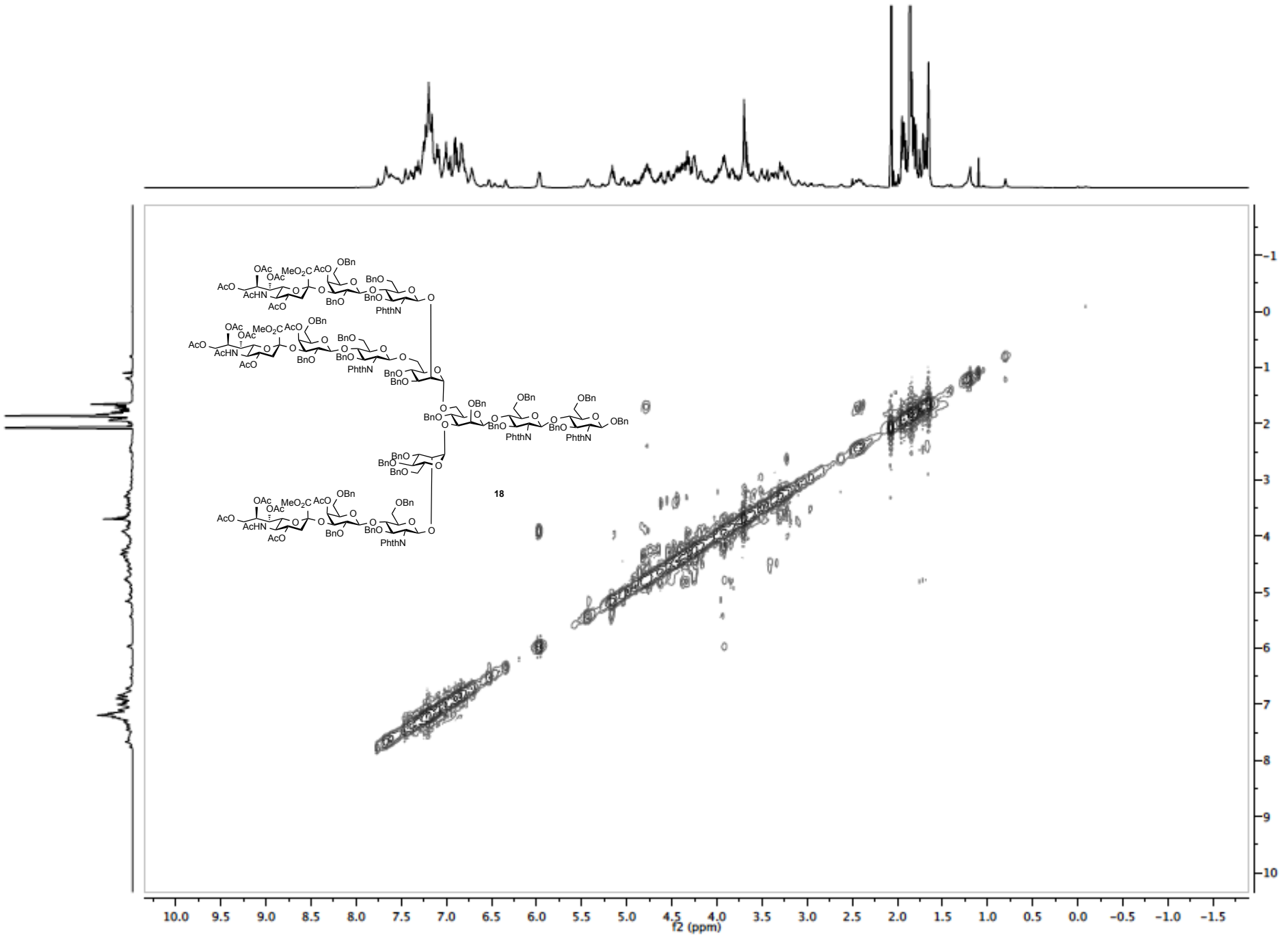
2D ^{1}H-^{13}C HSQC



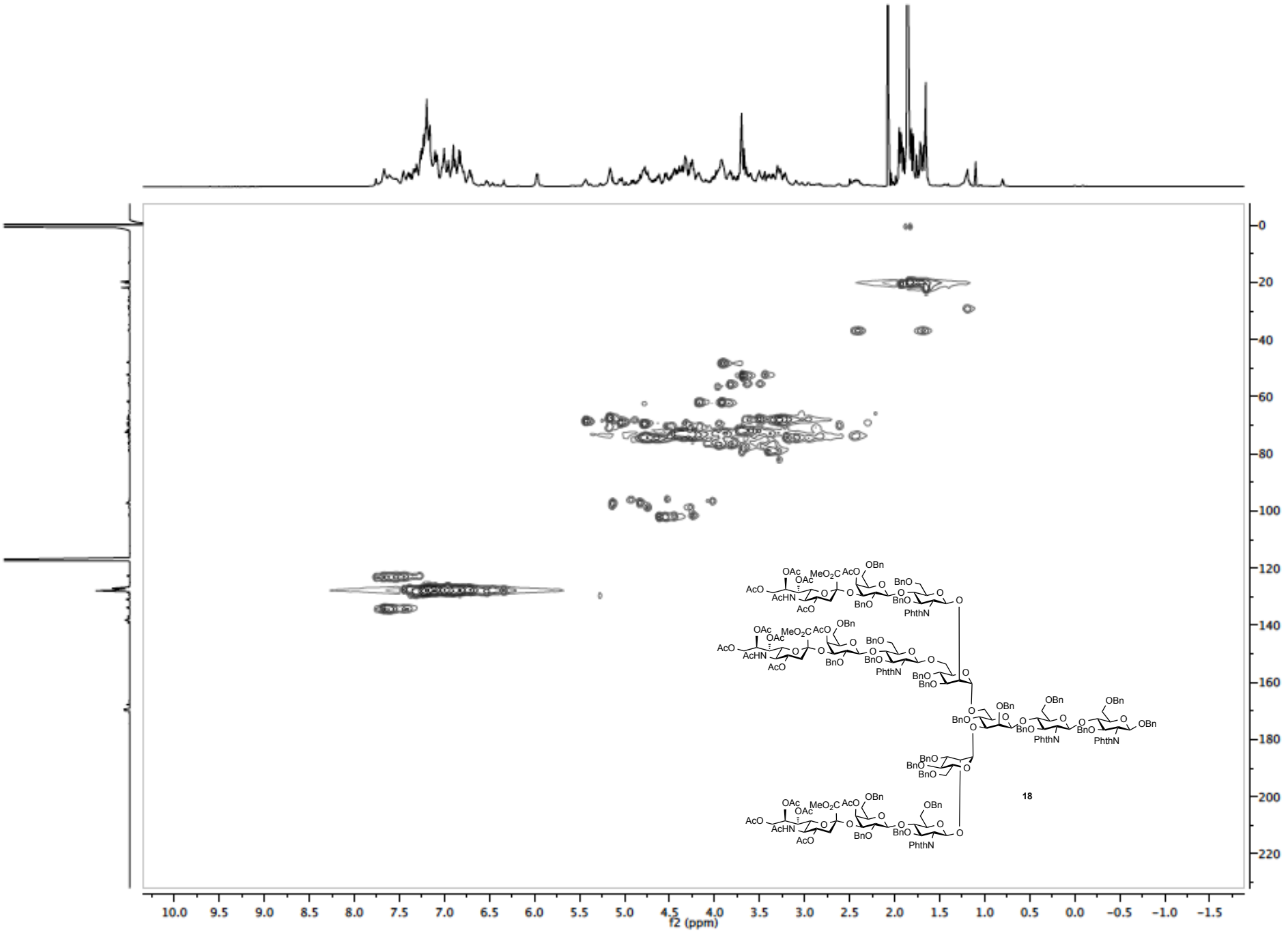

18
f1 (ppm)


18
f1 (ppm)

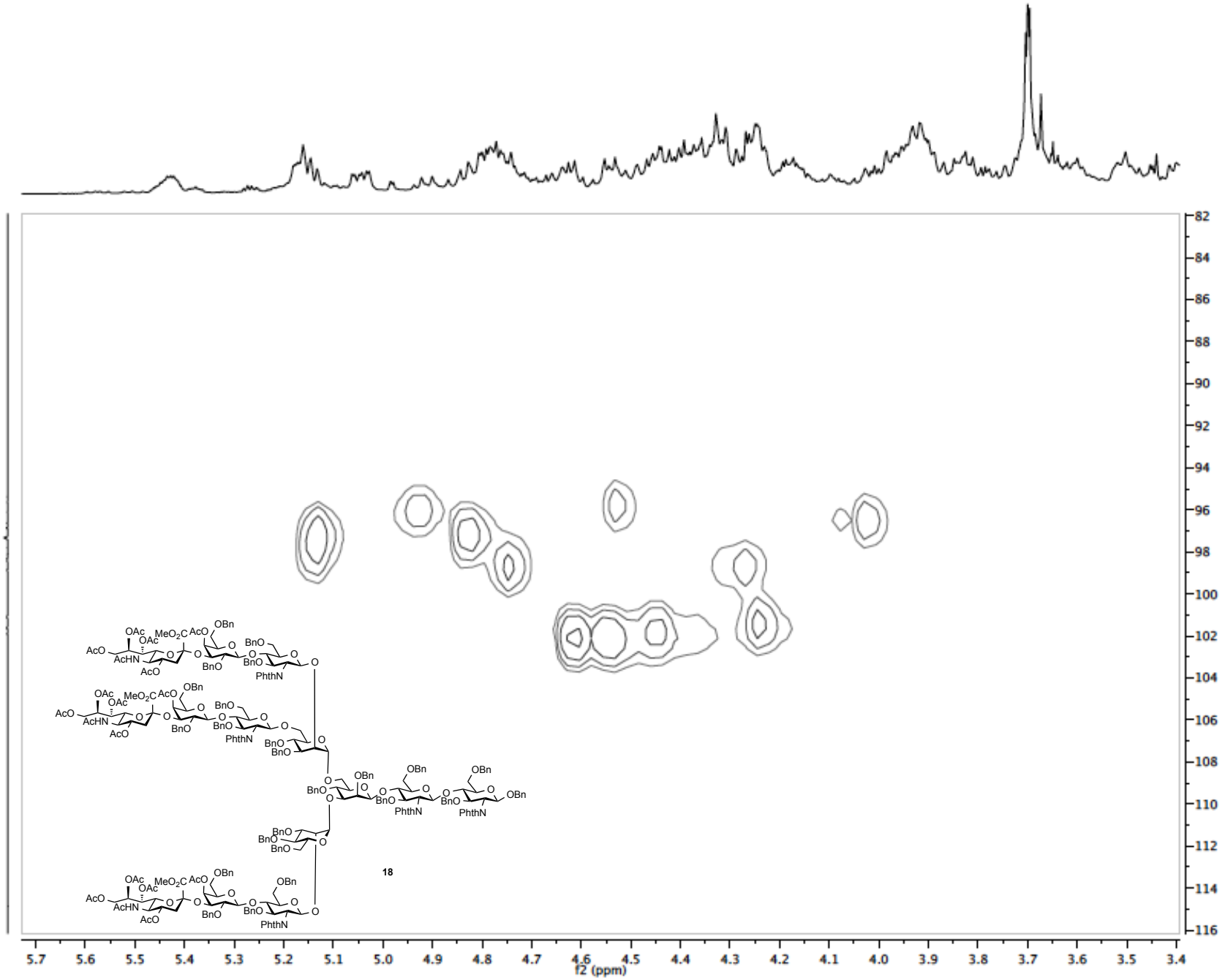
2D ^{1}H-^{1}H COSY

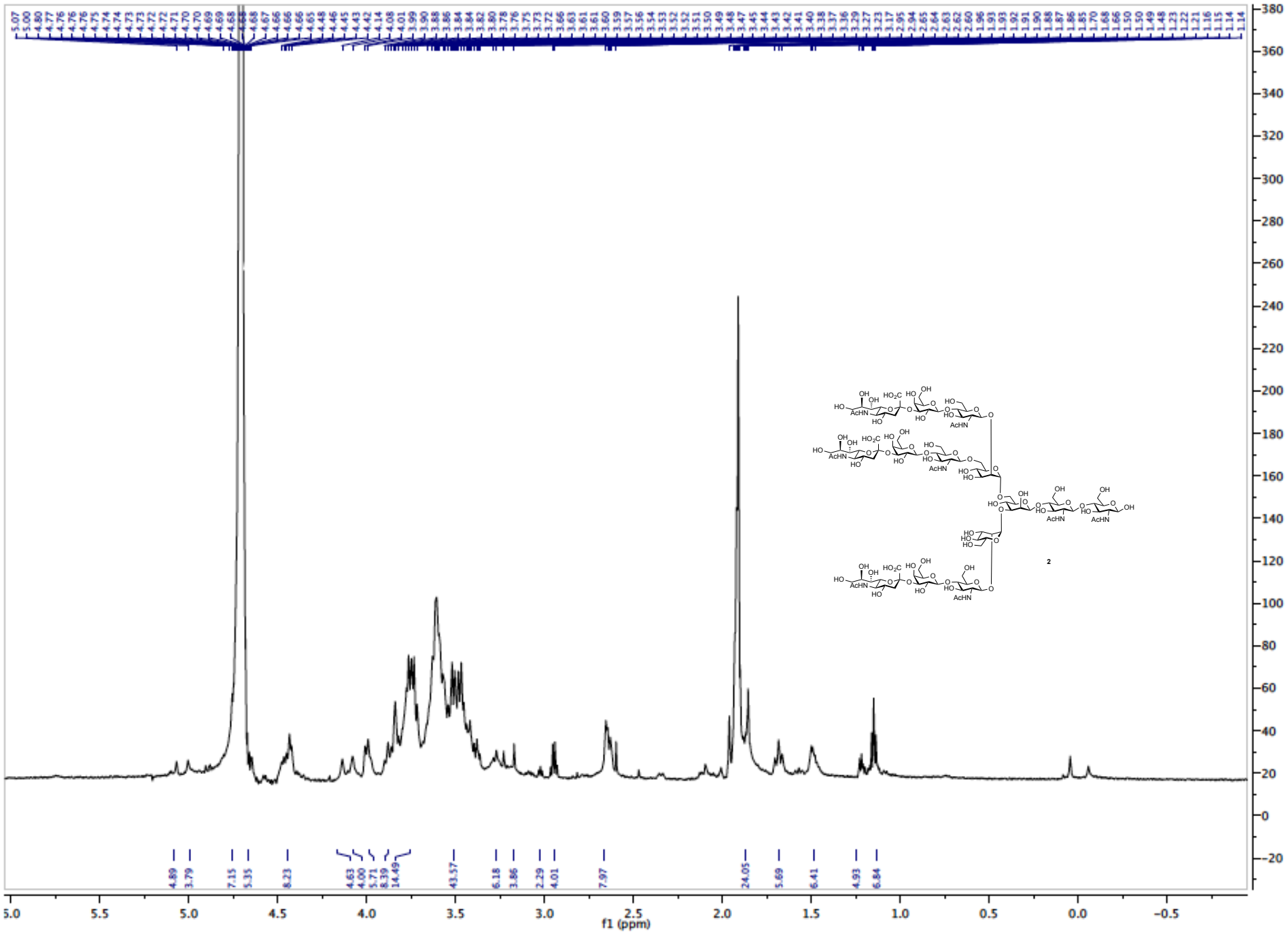


2D ^{1}H-^{13}C HSQC

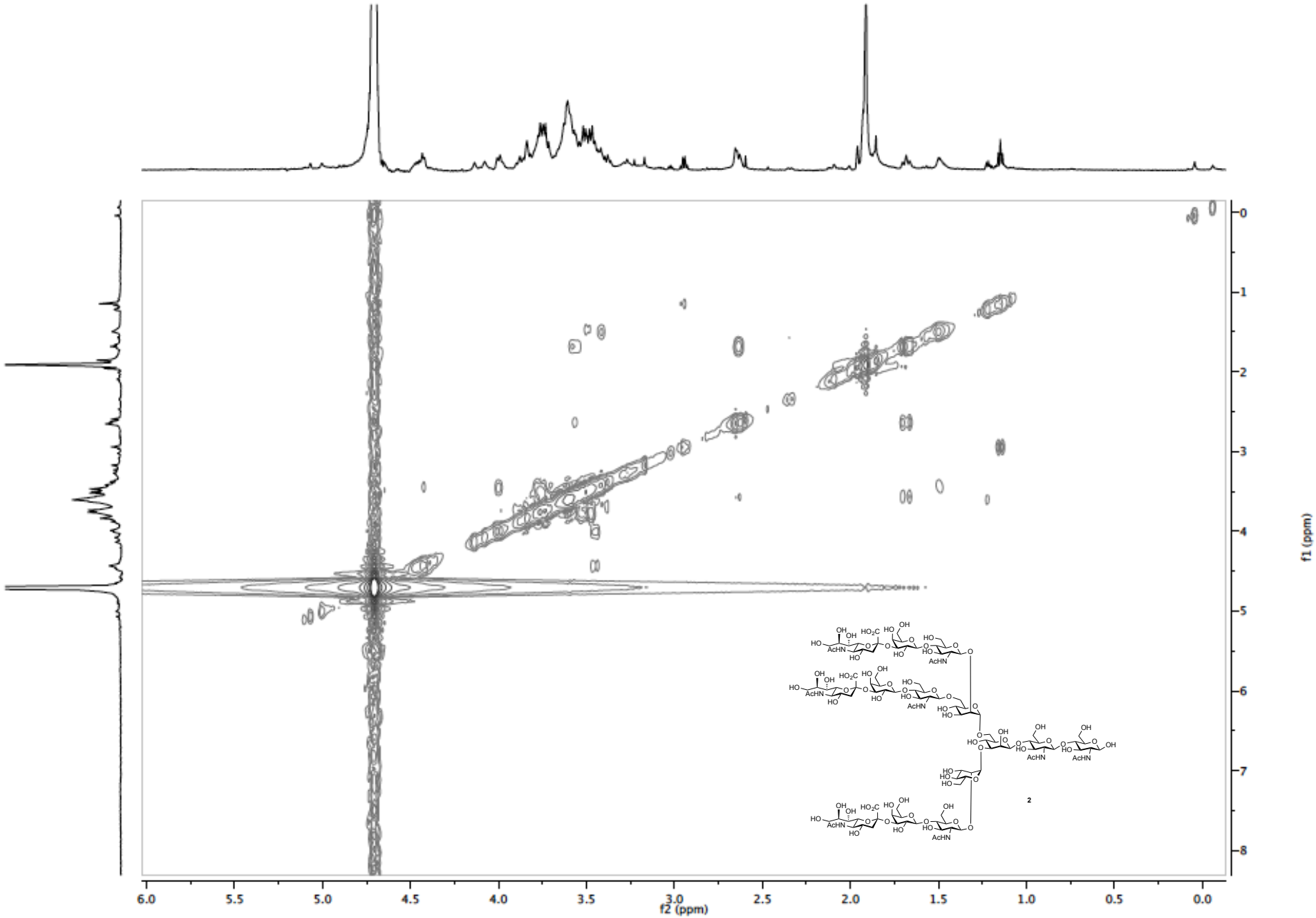


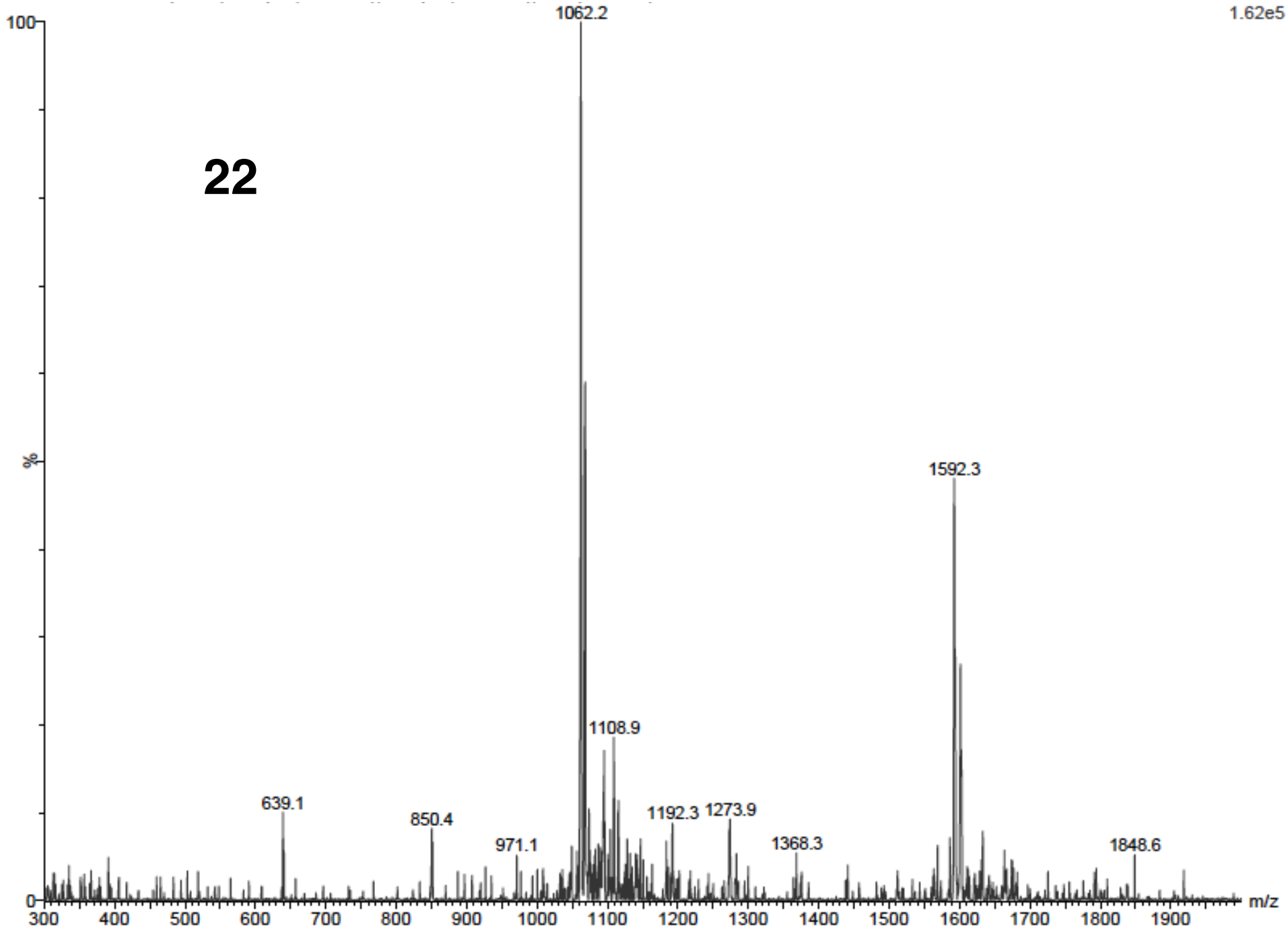
2D ^{1}H-^{13}C HSQC

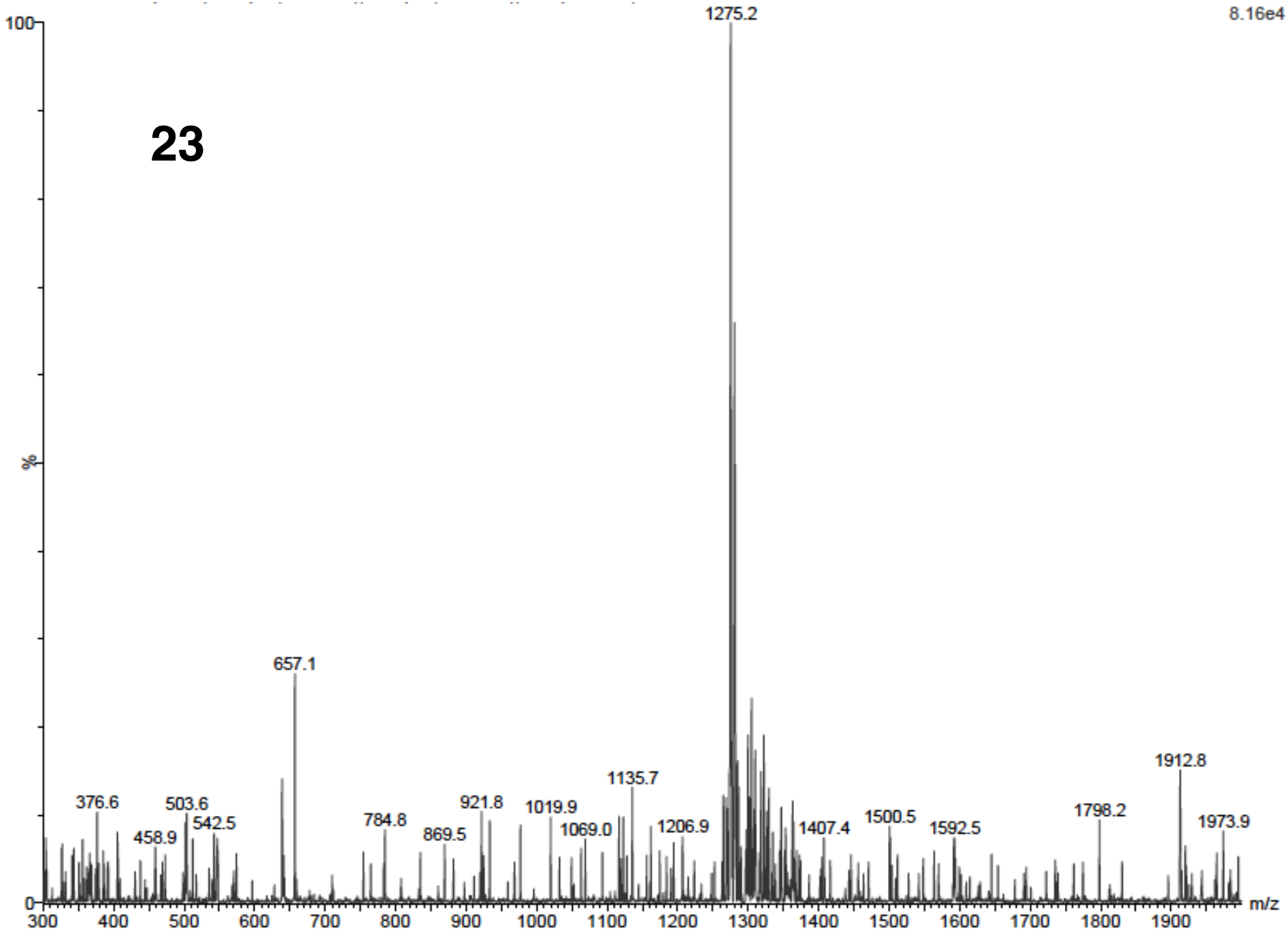



4.89
3.79
7.15
5.35
8.23
4.63
4.00
5.71
8.39
14.49
43.57
6.18
3.86
2.29
4.01
7.97
24.05
5.69
6.41
4.93
6.84
f1 (ppm)
2

2D ^{1}H-^{1}H COSY




22
1062.2
1.62e5
100
%
0
1592.3
1108.9
639.1
850.4
971.1
1192.3
1273.9
1368.3
1848.6
m/z
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900


23
100
%
0
8.16e4
1275.2
657.1
376.6
503.6
542.5
458.9
784.8
869.5
921.8
1019.9
1069.0
1135.7
1206.9
1407.4
1500.5
1592.5
1798.2
1912.8
1973.9
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
m/z