Supplementary Material

Synthesis and Characterization of a Template-Assembled Synthetic U-Quartet

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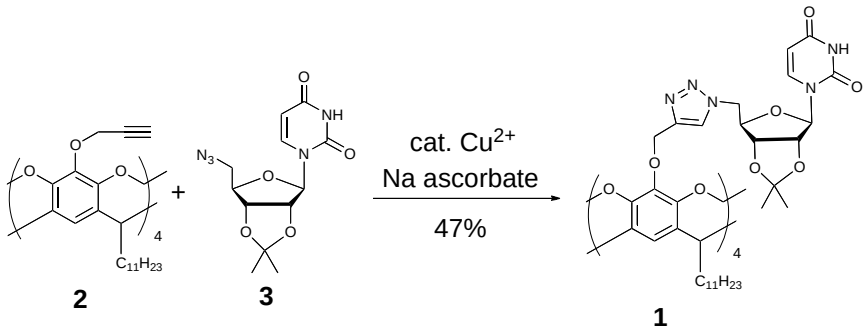
General information

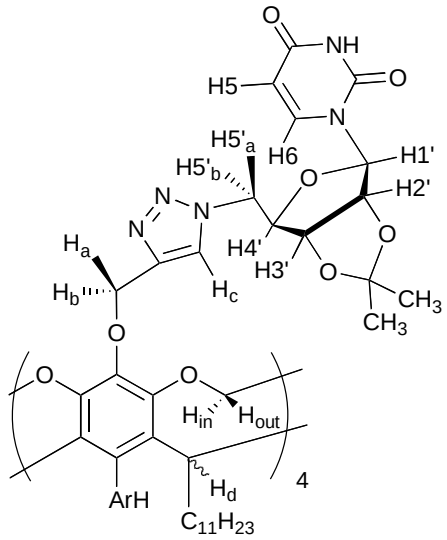
^{1}H NMR spectra were measured on a Bruker Avance 400 MHz spectrometer in $CDCl_3$ [using $CHCl_3$ (for 1H, δ = 7.26) as internal standard] or in DMSO-*d*6 [using DMSO (for 1H, δ = 2.50) as internal standard]. Chemical shifts are reported in ppm from tetramethylsilane. ^{13}C NMR spectra were measured on a Bruker Avance 400 MHz spectrometer in $CDCl_3$ [using $CDCl_3$ (for 13C, δ = 77.0) as internal standard. Chemical shifts are reported in ppm from tetramethylsilane. The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. 2D NOESY spectra were acquired with 800 ms mixing time and 1500 ms acquisition time. COSY45 spectra were obtained with 1500 ms acquisition time. DOSY experiments were carried out on a Bruker Avance 400inv spectrometer equipped with a 5mm BBI Z-gradient probe (inverse broadband probe with z-gradient coil). All measurements were performed using a BPLED gradient pulse sequence (ledbpgp2s). The length of the diffusion gradient was optimized for each sample to obtain at least 95% signal attenuation due to diffusion. Δ and δ values respectively were found to be 65 ms and 4000 ms (for **1** and **1**•Sr^{2+}), 65 ms and 5000 ms (for **4**). Eddy current (t_e) was set at 5 ms. All measurements were taken at 298K with sample concentrations of 3.2 mM. Diffusion coefficients were generated using the SimFit function on XWinNMR software. MALDI-TOF mass analyses were performed on a Bruker Biflex IV spectrometer in the reflectron mode using trans-3-indoleacrylic acid (3-IAA) as the matrix. Circular dichroism (CD) spectroscopy was performed on a Jasco J-810 spectrophotometer. Each spectrum is an average of three scans corrected for the baseline. All spectra were acquired with samples in a 1 mm path length quartz cuvette. Flash column chromatography was performed using Silicycle 60 silica gel and eluting solvents were used directly from their commercial bottles. Solvents and reagents for reactions were purchased commercially and used without further purification.

Synthesis of a uridine-cavitand conjugate (1)



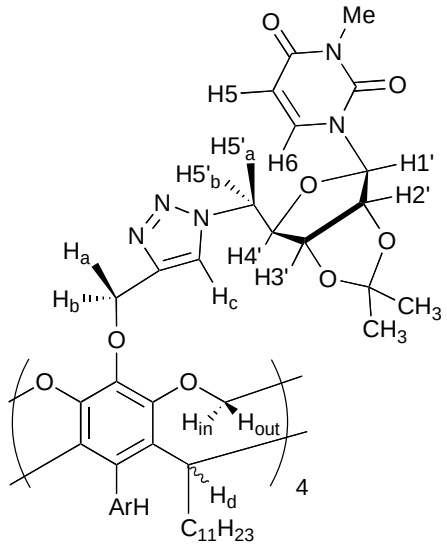
To a stirred solution of cavitand **2** (35.6 mg, 0.0345 mmol) and nucleoside **3** (46.9 mg, 0.152 mmol) in argon-purged DMSO (4 mL) was added a solution of copper(II) sulfate pentahydrate (87 μL, 0.04 M in argon-purged Milli-Q water, 0.00345 mmol) followed by a solution of sodium ascorbate (87 μL, 0.4 M in argon-purged Milli-Q water, 0.0345 mmol). The reaction was stirred at 60 °C for 20 h. The solvent was then removed in vacuo and the residue suspended in water. A few drops of ammonium hydroxide were added to remove the copper catalyst and the mixture was suction filtered. The residue, crude **1**, was washed with deionized water and allowed to air dry, whereupon it was purified via step gradient flash chromatography (100% ethyl acetate – ethyl acetate : methanol 98 : 2 – ethyl acetate : methanol 95 :5) to afford conjugate **1** in 47% yield (42.5 mg, 0.0163 mmol).

1:



Yield: 47%. White solid; ^{1}H (400 MHz, $CDCl_3$) δ(ppm) 0.92 (12H, t, *J* = 4 Hz, CH_3 feet), 1.29 – 1.38 (96H, m, long chain aliphatic feet and isopropylidene CH_3), 2.20 (8H, m, CH_2 feet), 4.37 (4H, d, *J* = 8 Hz, H_{in}), 4.56 – 4.60 (4H, m, H4′), 4.71 – 4.79 (12H, m, H5′$_a$ and H5′$_b$ and H_d), 5.02 – 5.05 (8H, m, H3′, H_a or H_b), 5.08 (4H, dd, *J* = 1.6, 8.0 Hz, H2′), 5.16 (4H, d, *J* = 12.0 Hz, H_a or H_b), 5.62 (4H, d, *J* = 1.6 Hz, H1′), 5.71 (4H, dd, *J* = 4.0, 8.0 Hz, H5), 5.79 (4H, d, *J* = 8.0 Hz, H_{out}), 6.85 (4H, s, ArH), 6.98 (4H, d, *J* = 8.0 Hz, H6), 7.74 (4H, s, H_c), 10.74 (4H, s, imino H); ^{1}H (400 MHz, DMSO-*d*6) δ(ppm) 0.85 (12H, t, *J* = 6.8 Hz, CH_3 feet), 1.24 – 1.30 (84H, m, long chain aliphatic feet and isopropylidene CH_3), 1.45 (12H, s, isopropylidene CH_3), 2.33 (8H, m, CH_2 feet), 4.28 (4H, d, *J* = 7.2 Hz, H_{in}), 4.40 (4H, m, H4′), 4.58 (4H, t, *J* = 8.0 Hz, H_d), 4.65 (4H, dd, *J* = 7.2, 14.0 Hz, H5′$_b$), 4.75 (4H, dd, *J* = 5.2, 14.0 Hz, H5′$_a$), 4.89 (4H, dd, *J* = 4.0, 6.4 Hz, H3′), 4.94 (8H, s, H_a and H_b), 5.12 (4H, dd, *J* = 1.6, 6.4 Hz, H2′), 5.61 (4H, d, *J* = 8.0 Hz, H5), 5.77 (4H, d, *J* = 2.0 Hz, H1′), 5.93 (4H, d, *J* = 7.2 Hz, H_{out}), 7.29 (4H, s, ArH), 7.64 (4H, d, *J* = 8.0 Hz, H6), 8.20 (4H, s, H_c), 11.46 (4H, s, imino H); ^{13}C (100 MHz, $CDCl_3$) δ(ppm) 163.8, 151.0, 148.4, 145.4, 144.4, 143.3, 139.1, 124.8, 115.0, 114.7, 103.4, 99.6, 96.3, 86.5, 84.5, 82.0, 67.6, 52.0, 37.1, 32.0, 30.1, 29.9, 29.7, 29.4, 28.2, 27.3, 25.6, 22.9, 14.1, 1.2; MS(MALDI-TOF): Found: *m/z* 2608.0. Calcd for $C_{136}H_{181}N_{20}O_{32}$: $(M+H)^+$ 2608.0.

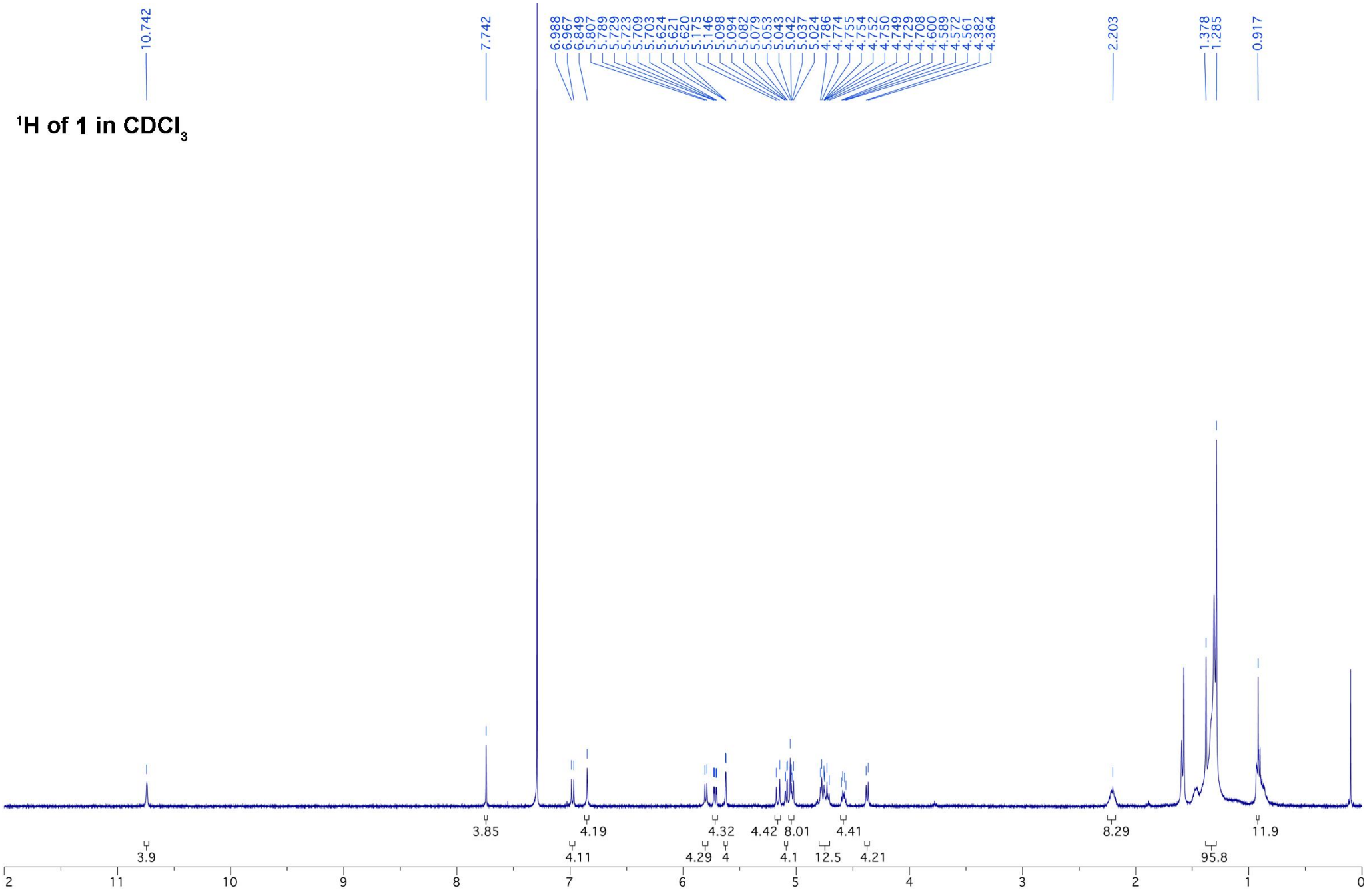
4: (preparation similar to that of compound 1)

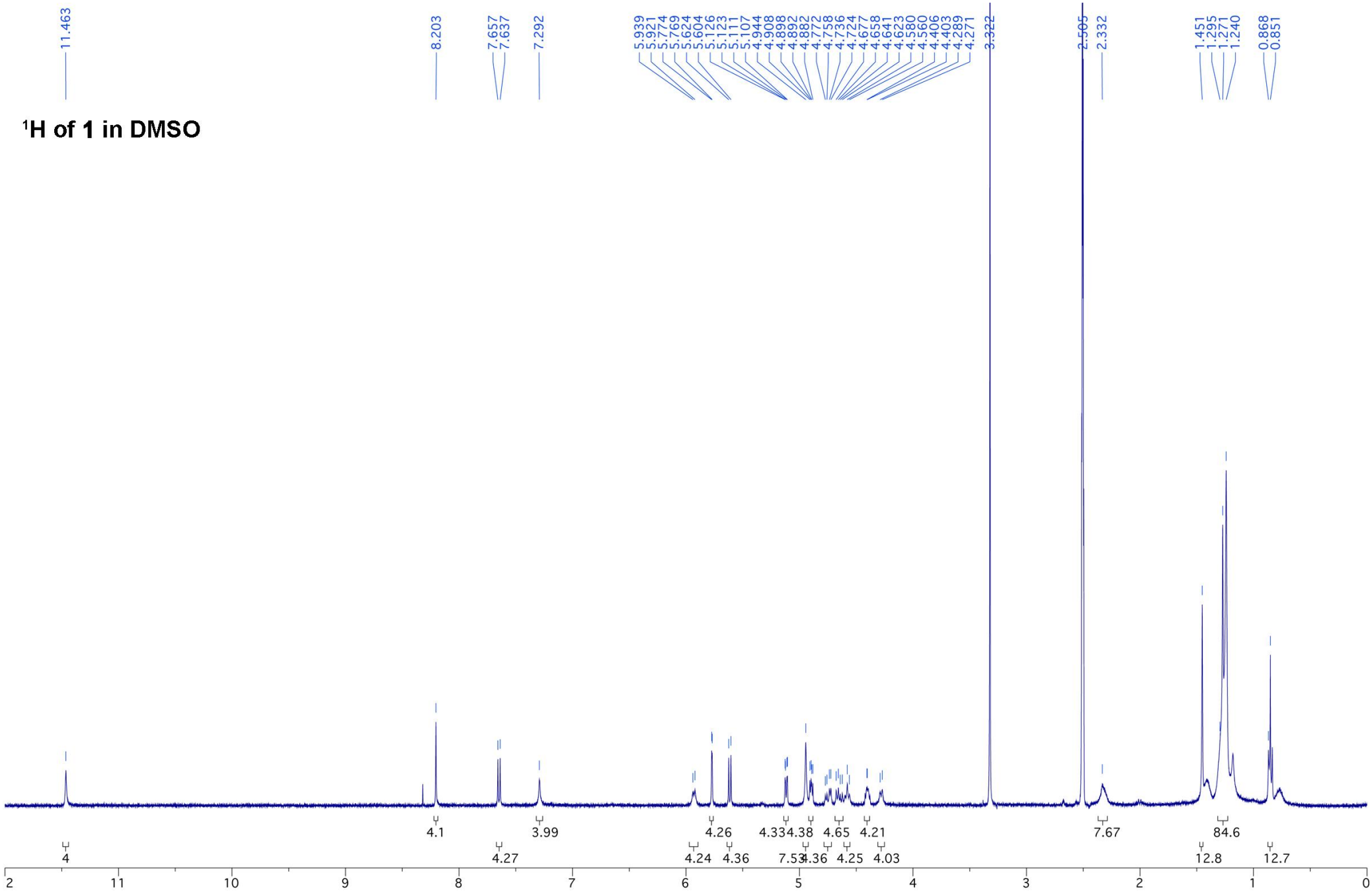


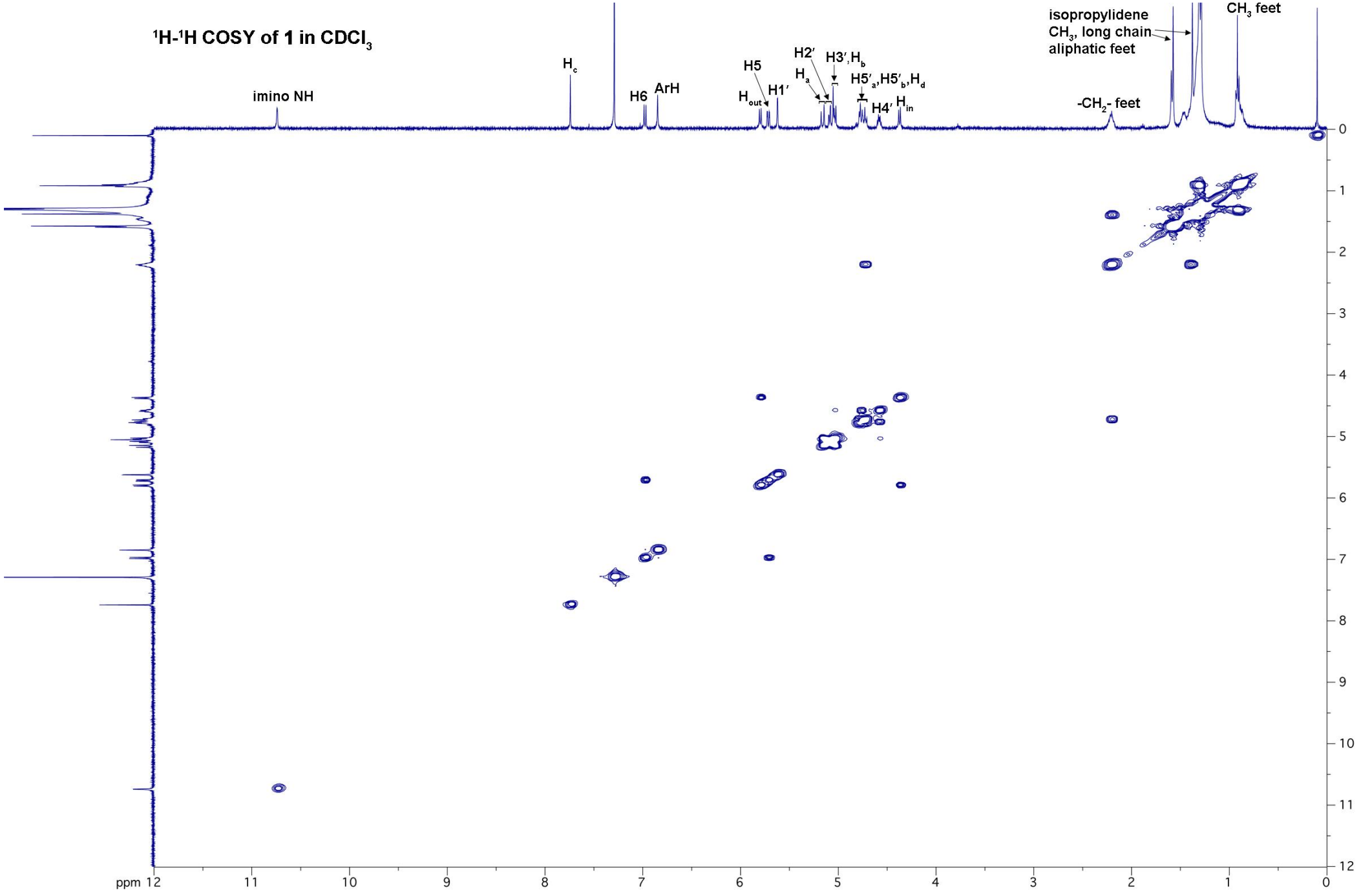
Yield: 47%. White solid; ^{1}H (400 MHz, $CDCl_3$) δ(ppm) 0.88 (12H, t, *J* = 7.2 Hz, CH_3 feet), 1.25 – 1.28 (84H, m, long chain aliphatic feet and isopropylidene CH_3), 1.54

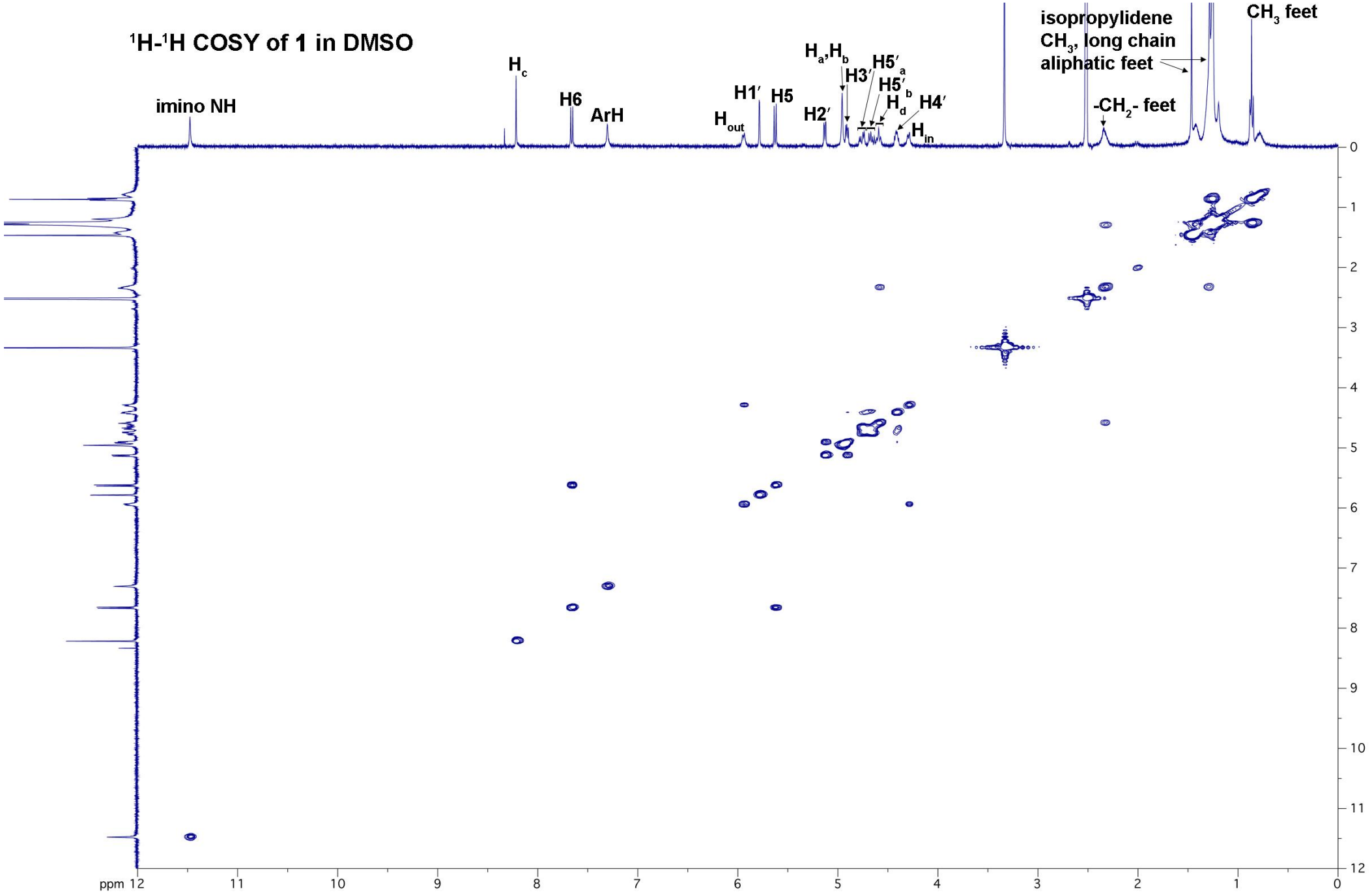
(12H, s, isopropylidene CH_3), 2.17 (8H, m, CH_2 feet), 3.30 (12H, s, NMe), 4.32 (4H, d, *J* = 7.2 Hz, H_{in}), 4.46 – 4.50 (4H, m, H4′), 4.65 – 4.70 (8H, m, H5′$_a$ and H_d), 4.77 (4H, dd, *J* = 3.6, 14.0 Hz, H5′$_b$), 4.98 – 5.09 (16H, m, H2′ and H3′ and H_a and H_b), 5.60 (4H, d, *J* = 1.2 Hz, H1′), 5.73 – 5.75 (8H, m, H5 and H_{out}), 6.80 (4H, s, ArH), 7.18 (4H, d, *J* = 8.0 Hz, H6), 7.67 (4H, s, H_c); ^{1}H (400 MHz, DMSO-*d*6) δ(ppm) 0.86 (12H, t, *J* = 6.4 Hz, CH_3 feet), 1.25 – 1.28 (84H, m, long chain aliphatic feet and isopropylidene CH_3), 1.47 (12H, s, isopropylidene CH_3), 2.33 (8H, m, CH_2 feet), 3.15 (12H, s, NMe), 4.28 (4H, d, *J* = 7.2 Hz, H_{in}), 4.40 – 4.44 (4H, m, H4′), 4.58 (4H, t, *J* = 8.0 Hz, H_d), 4.64 (4H, dd, *J* = 7.6, 14.0 Hz, H5′$_b$), 4.76 (4H, dd, *J* = 5.2, 14.0 Hz, H5′$_a$), 4.92 – 4.96 (12H, m, H_a and H_b and H3′), 5.13 (4H, dd, *J* = 1.6, 6.4 Hz, H2′), 5.75 (4H, d, *J* = 8.0 Hz, H5), 5.82 (4H, d, *J* = 1.6 Hz, H1′), 5.91 (4H, d, *J* = 7.2 Hz, H_{out}), 7.30 (4H, s, ArH), 7.70 (4H, d, *J* = 8.0 Hz, H6), 8.20 (4H, s, H_c); ^{13}C (100 MHz, $CDCl_3$) δ(ppm) 162.7, 151.1, 148.2, 145.2, 144.3, 141.4, 139.2, 124.4, 114.9, 114.8, 102.4, 99.7, 97.1, 86.7, 84.7, 82.3, 77.4 (overlapped), 67.4, 52.2, 37.2, 32.2, 30.2, 30.1, 29.95, 29.89, 29.6, 28.2, 27.8, 27.3, 25.4, 22.9, 14.3; MS(MALDI-TOF): Found: *m/z* 2686.0 Calcd for $C_{140}H_{188}N_{20}O_{32}Na$: $(M+Na)^+$ 2686.1

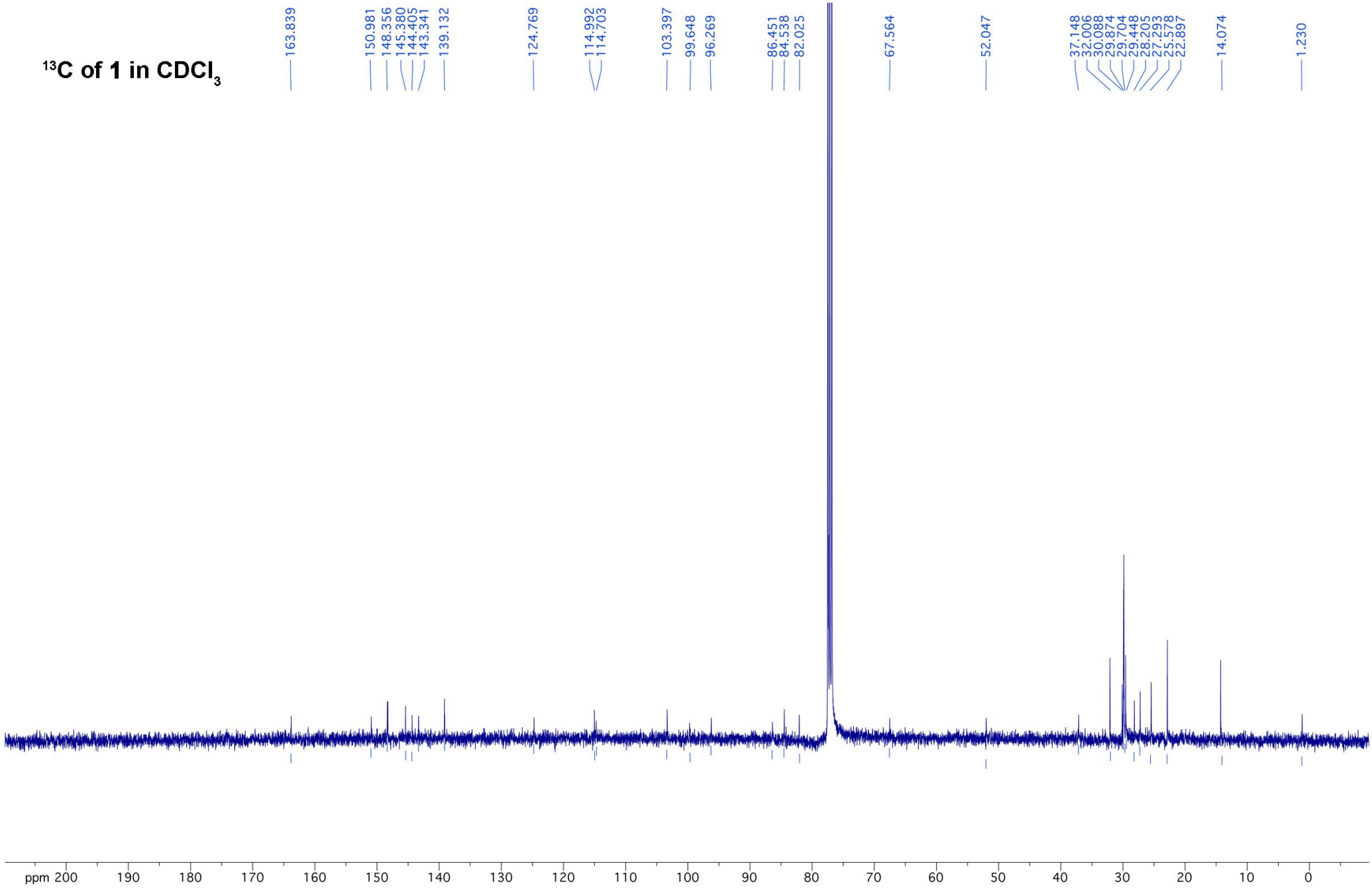
NMR spectra



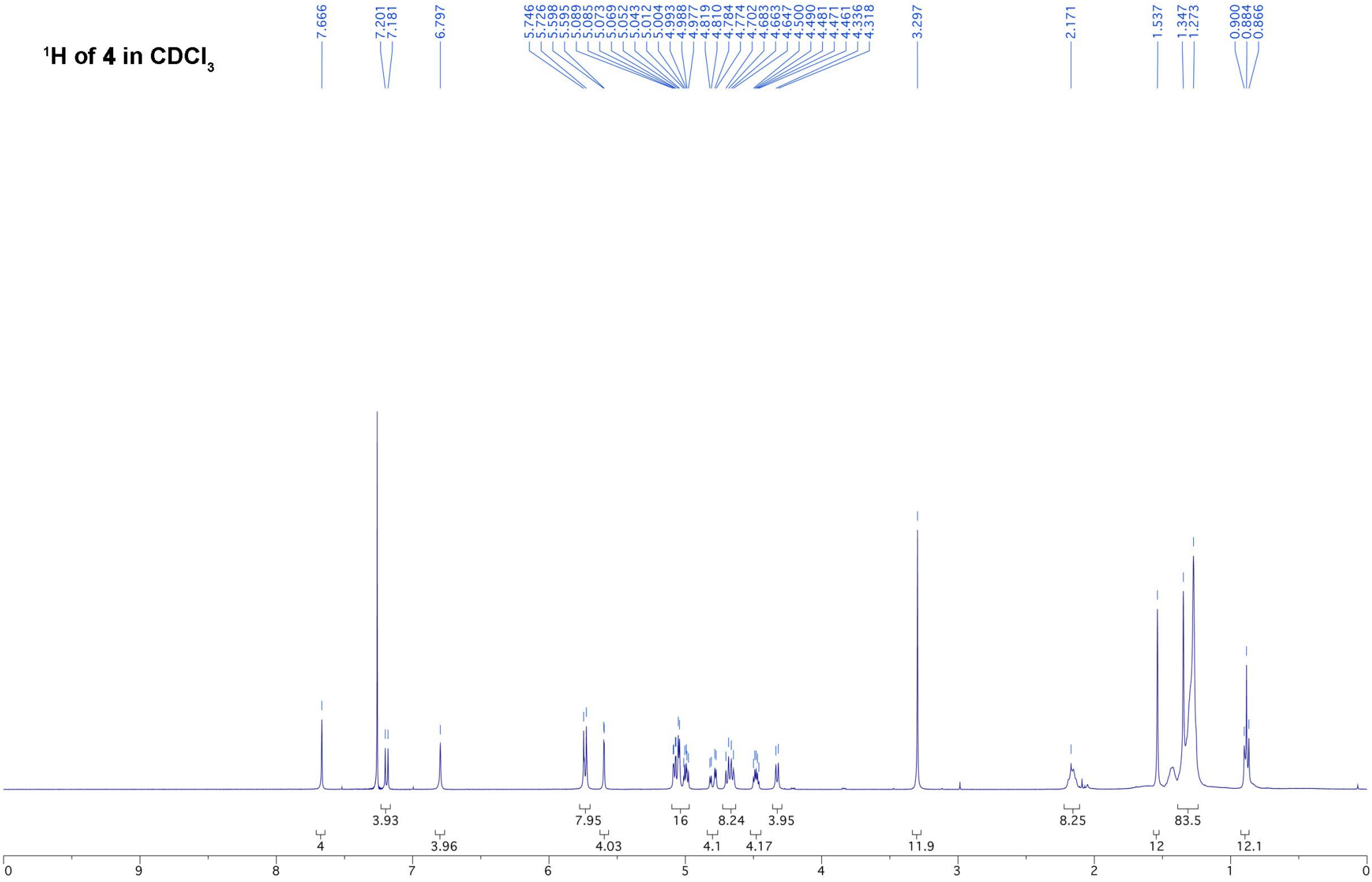


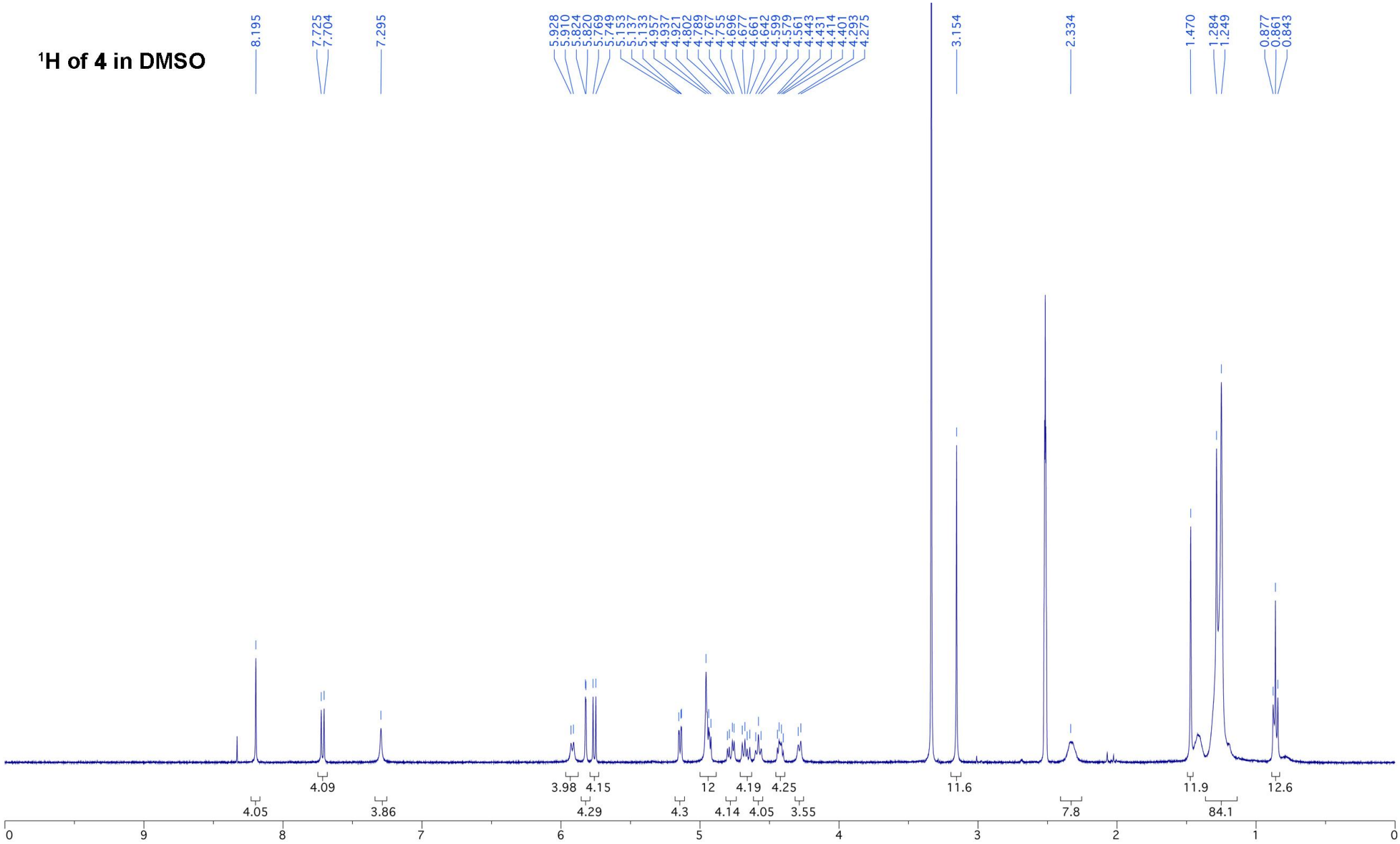


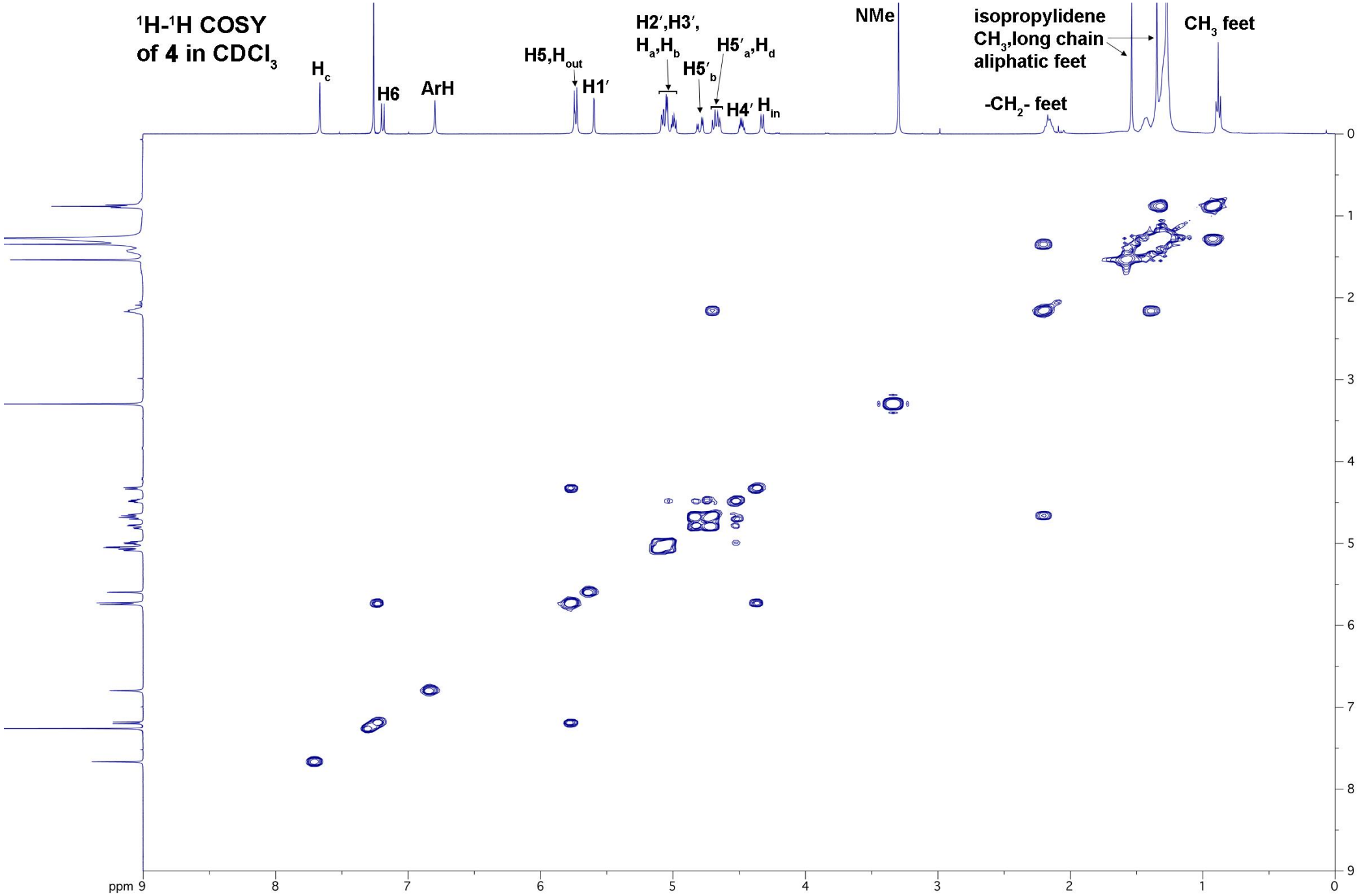


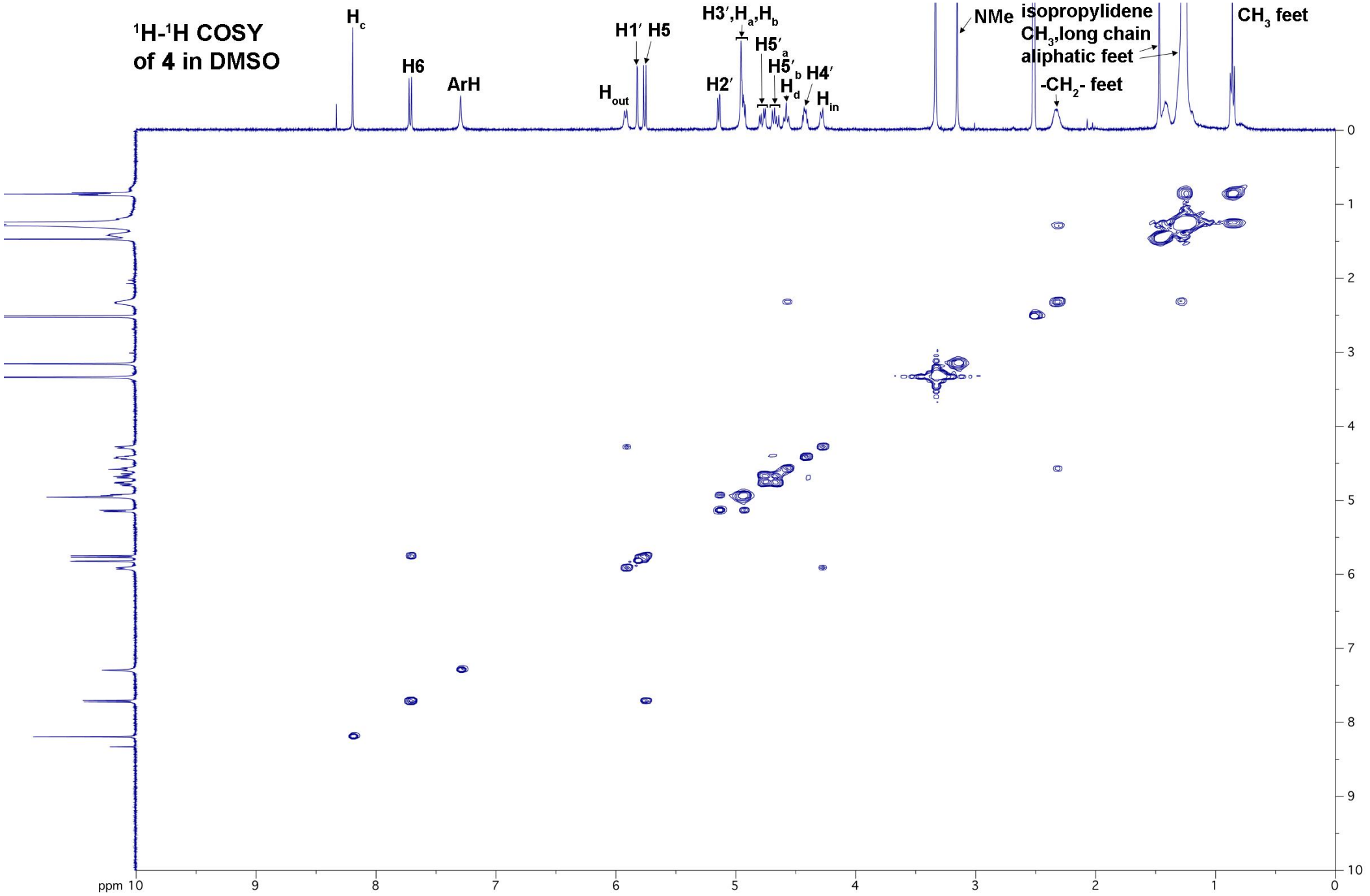


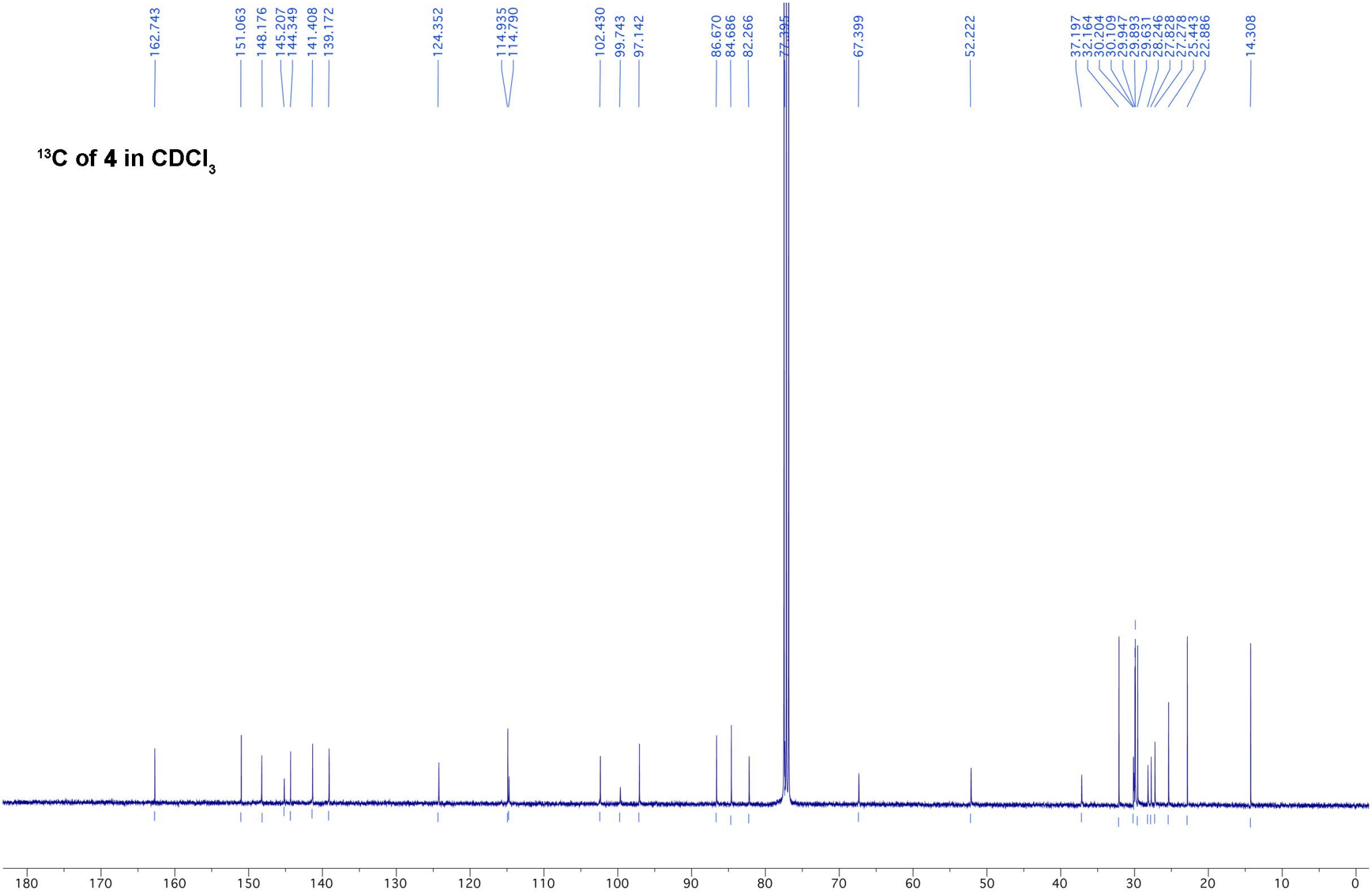
^{1}H of 4 in $CDCl_3$











^{13}C of 4 in $CDCl_3$