Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Concise Access to C2-ethylidene Pyrrolo[1,4]benzodiazepine Natural Products

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Supporting Information

General Experimental Details

Commercially available reagents and starting materials were used as received. All reactions in anhydrous solvents were performed under an atmosphere of argon. DME and THF were dried over Na and benzophenone and distilled before use, others were purchased from commercial sources labeled as anhydrous over molecular sieves. For analytical thin-layer chromatography used Merk TLC Silica gel 60 F_{254} plates. Flash chromatography was carried out using Zeochem silica gel ZEOprep 60 (40-63μm) for the direct phase and Biotage KP-C18-HS for the reverse phase. NMR spectra were recorded on Varian Mercury (400 MHz) and Bruker (300 MHz) spectrometers. Chemical shift values were referenced against residual protons in the deuterated solvents. Cross peaks multiplicity marked as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad). Infrared spectra were recorded in the range 4000-500 cm^{-1} as a film. HRMS spectra were obtained on Micromass AutoSpec Ultima Magnetic sector mass spectrometer (TOF). Optical rotations were measured on a Rudolph Research Analytical Autopol VI polarimeter. Melting points were determined on the Stanford Research System MPA100 apparatus and are uncorrected. Chromatographic analyses for determination of *E*/*Z* isomers were performed on Apollo $C_{18\text{-}12}$ 5μm (4.6×150 mm, isocratic 25-60% ACN/ (0.1% H_3PO_4), flow rate 1 mL/min at 40 °C) column at 210 nm.

PBDs **27a, b, d, e** and Julia-Kocienski reagents **SI-1a, b, d, e, g** and **26a** were prepared according to the literature procedures.[1]

Table S1. ^{1}H Data comparison of oxo-prothracarcin (**6**)

Literature, 400MHz, CD_3OD[2]	**Synthetic**, *major isomer*, 400MHz, CD_3OD
7.86 (1H, d, J = 7.82 Hz)	7.87 (1H, ddd, J = 7.9, 1.6 Hz)
7.54 (1H, t, J = 7.82 Hz)	7.55 (1H, (1H, td, J = 7.3, 1.6 Hz)
7.28 (1H, t, J = 7.82 Hz)	7.29 (1H, td, J = 7.3, 1.1 Hz)
7.13 (1H, d, J = 7.82 Hz)	7.14 (1H, m)
5.56 (1H, m)	5.57 (1H, m)
4.35 (1H, dd, J=9.39, 2.35 Hz)	4.36 (1H, dd, J = 9.2, 2.5 Hz)
4.31 (1H, m)	4.31 (1H, m)
4.12 (1H, d, J = 16.04 Hz)	4.13 (1H, dq, J = 15.7, 1.8 Hz)
3.44 (1H, d, J = 16.04 Hz)	3.45 (1H, br d, J = 16.3 Hz)
2.69 (1H, m)	2.69 (1H, m)
1.74 (3H, d, J = 6.65)	1.74 (3H, m)

Table S2. ^{13}C Data comparison of oxo-prothracarcin (**6**)

Literature, 100MHz, CD_3OD[2]	**Synthetic**, *major isomer*, 100MHz, CD_3OD
170.76	170.7
166.27	166.2
136.35	136.3
133.04	133.0
132.44	132.4
129.92	129.9
126.27	126.2
124.35	124.3
121.09	121.1
117.61	117.6
56.94	56.9
51.07	51.0
26.80	26.7
13.09	13.0

Table S3. ^{1}H Data comparison boseongazepine B (**8**)

Literature, 900MHz, DMSO-d_6[3]	**Synthetic**, *major isomer*, 400MHz, DMSO-d_6
9.54 (1H, s)	9.54 (1H, br.s)
7.33 (1H, dd, J = 6.2, 2.9 Hz)	7.32 (1H, dd, J = 5.4, 4.1 Hz)
7.24 (1H, t, J = 5.8 Hz)	7.26–7.20 (2H, m)
7.22 (1H, d, J = 5.0 Hz)	
5.49 (1H, dd, J = 4.5, 2.1 Hz)	5.49 (1H, m)
4.30 (1H, dd, J = 9.3, 2.1 Hz)	4.30 (1H, dd, J = 9.4, 2.6 Hz)
4.21 (1H, d, J = 15.7 Hz)	4.20 (1H, m)
4.01 (1H, d, J = 15.8 Hz)	4.00 (1H, m)
3.86 (3H, s)	3.86 (3H, s)
3.24 (1H, d, J = 16.2 Hz)	3.24 (1H, d, J = 16.4 Hz)
2.60 (1H, dd, J = 15.1, 9.9 Hz)	2.59 (1H, m)
1.66 (3H, d, J = 6.5 Hz)	1.66 (3H, d, J = 6.7 Hz)

Table S4. ^{13}C Data comparison of boseongazepine B (**8**)

Literature, 225MHz, DMSO-d_6[3]	**Synthetic**, *major isomer*, 100MHz, DMSO-d_6
169.7	169.7
164.3	164.3
149.8	149.8
133.9	133.9
127.9	128.0
125.5	125.5
124.8	124.8
121.1	121.1
116.9	116.9
113.7	113.7
56.4	56.4
56.2	56.2
51.0	51.0
27.2	27.2
14.3	14.3

Table S5. ^{1}H Data comparison of oxo-tomaymycin (**7**)

Literature, 200MHz, DMSO-d_6[4]	**Synthetic**, *major isomer*, 400MHz, DMSO-d_6
10.24 (1H, s)	10.24 (1H, br.s)
9.91 (1H, s)	9.94 (1H, br.s)
7.20 (1H, s)	7.20 (1H, s)
6.56 (1H, s)	6.56 (1H, s)
5.46 (1H, d, J = 6.5 Hz)	5.47 (1H, m)
4.21 (2H, m)	4.25 (1H, dd, J = 9.4, 2.7 Hz)
	4.21 (1H, m)
3.94 (1H, d, J = 16 Hz)	3.91 (1H, m)
3.77 (3H, s)	3.78 (3H, s)
3.24(1H, d, J = 16 Hz)	3.25 (1H, br.d, J = 16.2 Hz)
2.56 (1H, m)	2.59 (1H, m)
1.65 (3H, d, J = 6.5 Hz)	1.66 (3H, m)

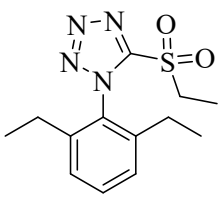
Table S6. ^{13}C Data comparison of oxo-tomaymycin (**7**)

Literature, 50MHz, DMSO-d_6[4]	**Synthetic**, *major isomer*, 100MHz, DMSO-d_6
170.0	170.0
164.55	164.6
150.2	150.3
144.6	144.6
134.1	134.1
130.9	131.0
117.1	117.1
116.6	116.7
112.2	112.3
107.7	107.8
56.4	56.4
55.65	55.7
51.1	51.1
27.1	27.2
14.2	14.3

EXPERIMENTAL SECTION

Synthesis of aryltetrazolyl sulfones

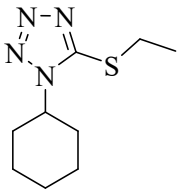
1-(2,6-Diethylphenyl)-5-(ethylsulfonyl)-1*H*-tetrazole (SI-1c)



Sulfone synthesis was performed by analogy literature described method.[1] Following the procedure 1.400 g of the title compound was obtained as a white solid starting from commercially available 2,6-diethylphenyl isothiocyanate in 3 steps with an overall yield of 91%. Intermediates were not purified and characterized, and used in the next step as they were.

R_f = 0.67 (PE 1 : EA 1). **^{1}H NMR** (400 MHz; $CDCl_3$): δ 7.52 (1H, m), 7.29 (1H, d, *J* = 7.7 Hz), 3.71 (2H, q, *J* = 7.5 Hz), 2.33 (2H, dq, *J* = 15.1, 7.6 Hz), 2.06 (2H, dq, *J* = 15.1, 7.6 Hz), 1.52 (3H, t, *J* = 7.5 Hz), 1.13 (6H, t, *J* = 7.6 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.2, 141.5, 132.1, 130.3, 126.8, 50.7, 24.0, 14.2, 7.0. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{13}H_{19}N_4O_2S$, 295.1229; found 295.1237. **IR** (ν_{max}, film): 2974, 2925, 2877, 1458, 1342, 1151, 781, 735, 548, 502 cm^{-1}. **MP** = 79-80 °C.

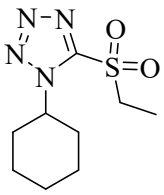
1-Cyclohexyl-5-(ethylthio)-1*H*-tetrazole (SI-2f)



Sulfide synthesis was performed by analogy with literature described method[1] starting from commercially available cyclohexyl isothiocyanate in 2 steps with an overall yield of 87%. After purification on silica gel (PE 3 : EA 1) 16.400 g of the title compound was obtained as a colourless oil. **The product is unstable, keep it in the freezer**!

R_f = 0.36 (PE 3 : EA 1). **^{1}H NMR** (400 MHz; $CDCl_3$): δ 4.12 (1H, m), 3.35 (1H, q, *J* = 7.3 Hz), 2.06–1.86 (6H, m), 1.77–1.69 (1H, m), 1.45 (3H, t, *J* = 7.3 Hz), 1.46–1.23 (3H, m). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 152.7, 58.2, 32.1, 27.7, 25.3, 24.9, 14.9. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_9H_{17}N_4S$, 213.1174; found 213.1182.

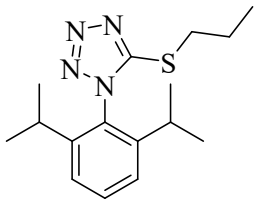
1-Cyclohexyl-5-(ethylsulfonyl)-1*H*-tetrazole (SI-1f)



Oxidation was performed in analogy with the literature.[1] After purification on silica gel (PE 3 : EA 1) 6.200 g (yield 84%) the title compound was isolated as a white solid.

R_f = 0.44 (PE 3 : EA 1). **^{1}H NMR** (400 MHz; $CDCl_3$): δ 4.96–4.86 (1H, m), 3.72 (2H, q, *J* = 7.5 Hz), 2.19 (2H, m), 2.08–1.92 (4H, m), 1.78 (1H, m), 1.53 (3H, t, *J* = 7.5 Hz), 1.48 (2H, m), 1.34 (1H, tt, *J* = 12.5, 3.3 Hz). **HRMS-ESI** (*m/z*): [M+H] calculated for $C_9H_{17}N_4O_2S$, 245.1072; found 245.1064. **MP** = 57-58 °C

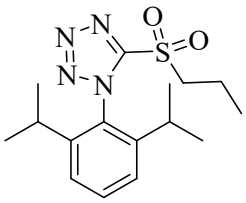
1-(2,6-Diisopropylphenyl)-5-(propylthio)-1*H*-tetrazole (SI-3)



Sulfide synthesis was performed by analogy with literature described method[1] starting from commercially available 2,6-diisopropylphenyl isothiocyanate in 2 steps with an overall yield of 88%. The product was obtained in 2.07 g scale and was not purified.

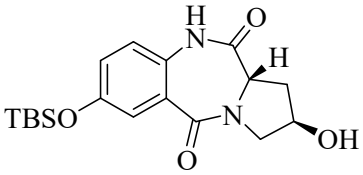
R_f = 0.54 (PE 6 : EA 1). **^{1}H NMR** (400 MHz; $CDCl_3$): δ 7.57–7.49 (1H, m), 7.31 (2H, d, *J* = 7.7 Hz), 3.38–3.30 (2H, m), 2.13 (2H, hept, *J* = 6.8 Hz), 1.83 (2H, h, *J* = 7.3 Hz), 1.18 (6H, d, *J* = 6.8 Hz), 1.10 (6H, d, *J* = 6.8 Hz), 1.03 (3H, t, *J* = 7.3 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.2, 146.8, 131.9, 128.5, 124.5, 34.8, 28.7, 24.5, 23.2, 22.8, 13.2. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{16}H_{25}N_4S$, 305.1800; found 305.1806. **IR** (ν_{max}, film): 2966, 2872, 1457, 1387, 1275, 1255, 1219, 1085, 1059, 1015, 805, 759.

1-(2,6-Diisopropylphenyl)-5-(propyl sulfonyl)-1*H*-tetrazole (26b)



Oxidation was performed in analogy with the literature[1] and the product was obtained in 1.91 g (yield 89%) scale as a white solid.
R_f = 0.47 (PE 1 : DCM 2). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.57 (1H, t, *J* = 7.9 Hz), 7.33 (2H, d, *J* = 7.9 Hz), 3.71–3.63 (2H, m), 2.10–1.91 (4H, m), 1.24 (6H, d, *J* = 6.8 Hz), 1.14 (3H, t, *J* = 7.5 Hz), 1.08 (6H, d, *J* = 6.8 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 154.7, 146.2, 132.4, 128.6, 124.3, 57.5, 29.2, 25.3, 22.2, 16.0, 13.0. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{16}H_{25}N_4O_2S$, 337.1698; found 337.1720. **IR** (ν_{max}, film): 2973, 2876, 1463, 1337, 1147, 1060, 859, 810, 762, 624, 536. **MP** = 95-96 °C

(2*R*,11a*S*)-7-((*tert*-Butyldimethylsilyl)oxy)-2-hydroxy-1,2,3,11a-tetrahydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11(10*H*)-dione (27c)

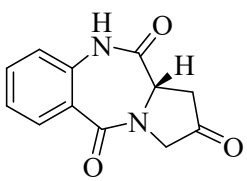


To a stirred solution of anthranilic acid **23c**[5] (2.254 g, 8.429 mmol, 1.0 equiv) and HBTU (6.400 g, 16.858 mmol, 2.0 equivs) in DCM (70 mL) TEA (11.7 mL, 84.3 mmol, 10.0 equivs) was added at room temperature and the mixture stirred for 15 min. Then **22** (1.611 g, 8.429 mmol, 1.0 equiv) was added and stirring was continued for 5 days. Next solution was washed twice with water, then volatiles were removed under reduced pressure and the residue was subjected to reverse phase chromatography (water/MeCN, full gradient) to obtain 2.503 g (82%) of the title compound as white solid. **R_f** = 0.60 (DCM 5 : MeOH 1). **^{1}H NMR** (400 MHz; $CDCl_3$): δ 7.84 (1H, br. s), 7.43 (1H, d, *J* = 2.9 Hz), 6.96 (1H, dd, *J* = 8.6, 2.9 Hz), 6.87 (1H, d, *J* = 8.6 Hz), 4.64 (1H, m), 4.29 (1H, dd, *J* = 8.2, 6.2 Hz), 3.95 (1H, m), 3.69 (1H, dd, *J* = 12.6, 4.7 Hz), 2.93 (1H, dt, *J* = 13.5, 5.6 Hz), 2.16 (1H, m), 2.03 (1H, d, *J* = 3.5 Hz), 1.59 (1H, s), 0.98 (9H, s), 0.22 (6H, s). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.3, 165.7, 153.3, 128.7, 127.9, 124.9, 122.6, 121.7, 69.1, 55.6, 54.5, 34.9, 25.7, 18.3, -4.3. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{18}H_{27}N_2O_4Si$, 363.1740; found 363.1754. **IR** (ν_{max}, film): 3393, 3267, 2951, 2930, 2858, 1691, 1623, 1611, 1495, 1440, 1278, 1229, 993, 914, 845, 779 cm^{-1}. **$[\alpha]_D^{20}$** = 278° (*c* = 0.1, MeOH). **MP** = 220-222 °C.

General procedure for oxidation of 27

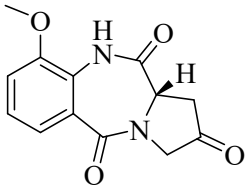
To a mixture containing **27** (5.241 mmol, 1.0 equiv), PIDA (2.026 g, 6.290 mmol, 1.2 equivs) and KBr (62.4 mg, 0.524 mmol, 0.1 equiv) in a mixture of DCM (37 mL) and water (3.7 mL) under vigorous stirring was added TEMPO (16.4 mg, 0.104 mmol, 0.02 equivs) at 0 °C and mixture was stirred at the same temperature for 3 h. Then, to the reaction mixture were added more PIDA (0.844 g, 2.620 mmol, 0.5 equivs) and TEMPO (8.2 mg, 0.052 mmol, 0.01 equiv), and the mixture was stirred vigorously for 16 h at 0 °C. Then to suspension was added petroleum ether (40 mL) and the formed precipitate was collected by filtration. The filter cake was washed with petroleum ether (20 mL) and water (5 mL) and dried under vacuum (at 45 °C over P_2O_5) to give the title compound.

(*S*)-1,11a-Dihydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-2,5,11(3*H*,10*H*)-trione (24a)



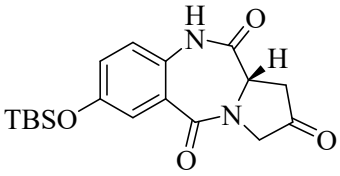
Following the general oxidation procedure 0.724 g (73%) of the title compound was prepared as off white solid starting from 27a (1.00 g, 4.306 mmol, 1 eq).
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (1H, br. s), 8.01 (1H, dd, J = 8.0, 1.7 Hz), 7.56 (1H, ddd, J = 8.0, 7.3, 1.7 Hz), 7.40–7.29 (1H, m), 7.08 (1H, dd, J = 8.0, 1.2 Hz), 4.61 (1H, dd, J = 10.2, 3.5 Hz), 4.38 – 4.24 (1H, m), 4.00–3.92 (1H, m), 3.70–3.55 (1H, m), 2.92–2.76 (1H, m). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.7, 169.7, 166.2, 135.1, 133.4, 131.5, 126.0, 121.5, 54.1, 52.9, 36.8.

(*S*)-9-Methoxy-1,11a-dihydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-2,5,11(3*H*,10*H*)-trione (24b)



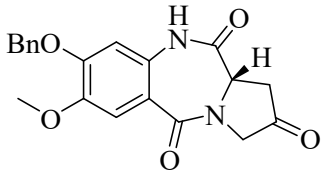
Following the general oxidation procedure 5.51 g (64%) of the title compound was prepared as a dark brown solid starting from **27b** (8.70 g, 33.173 mmol, 1.0 equiv). $\mathbf{R_f}$ = 0.50 (DCM 20 : MeOH 1). **^{1}H NMR** (400 MHz; $CDCl_3$): δ 8.01 (1H, br. s), 7.57 (1H, dd, *J* = 8.1, 1.3 Hz), 7.27 (1H, t, *J* = 8.1 Hz), 7.08 (1H, dd, *J* = 8.1, 1.3 Hz), 4.58 (1H, dd, *J* = 10.3, 3.7 Hz), 4.32 (1H, m), 3.95 (1H, m), 3.94 (3H, s), 3.64 (1H, ddt, *J* = 19.6, 3.6, 1.2 Hz), 2.83 (1H, ddd, *J* = 19.6, 10.2, 1.6 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 206.8, 168.9, 166.1, 148.9, 126.1, 125.6, 125.1, 122.6, 113.6, 56.4, 54.4, 53.0, 36.8. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{13}H_{13}N_2O_4$, 261.0875; found 261.0881. **IR** (ν_{max}, film): 3266, 2930, 1760, 1694, 1639, 1492, 1412, 1257, 1070, 752 cm^{-1}. **$[\alpha]_D^{20}$** = 538° (*c* = 0.1, $CHCl_3$). **MP** = 206-207 °C.

(*S*)-7-((*tert*-Butyldimethylsilyl)oxy)-1,11a-dihydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-2,5,11(3*H*,10*H*)-trione (24c)



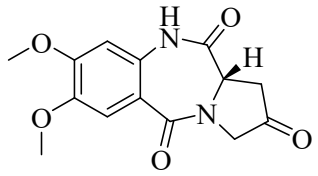
Following the general oxidation procedure 0.504 g (97%) of the title compound was prepared as a beige solid starting from **27c** (0.522 g, 1.440 mmol, 1.0 equiv). $\mathbf{R_f}$ = 0.25 (PE 1: EA 1). **^{1}H NMR** (400 MHz; $CDCl_3$): δ 8.34 (1H, br. s), 7.43 (1H, d, *J* = 2.8 Hz), 7.02 (1H, dd, *J* = 8.6, 2.8 Hz), 6.95 (1H, d, *J* = 8.6 Hz), 4.61 (1H, dd, *J* = 10.2, 3.5 Hz), 4.30 (1H, m), 3.95 (1H, m), 3.61 (1H, m), 2.83 (1H, m), 0.99 (9H, s), 0.23 (6H, s). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 206.8, 169.4, 165.8, 153.7, 128.7, 127.3, 125.4, 123.0, 121.6, 54.1, 52.9, 36.8, 25.7, 18.3, -4.3. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{18}H_{25}N_2O_4Si$, 361.1584; found 361.1598. **IR** (ν_{max}, film): 3220, 2955, 2930, 2859, 1767, 1698, 1644, 1495, 1437, 1279, 1231, 997, 922, 859 cm^{-1}. **$[\alpha]_D^{20}$** = 289° (*c* = 0.1, $CHCl_3$).

(*S*)-8-(Benzyloxy)-7-methoxy-1,11a-dihydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-2,5,11(3*H*,10*H*)-trione (24d)



Following the general oxidation procedure 1.680 g (87%) of the title compound was prepared as off white solid starting from **27d** (1.931 g, 5.241 mmol, 1.0 equiv). $\mathbf{R_f}$ = 0.60 (DCM 10 : MeOH 1). **^{1}H NMR** (400 MHz; DMSO-d_6): δ 10.51 (1H, br. s), 7.50−7.33 (5H, m), 7.29 (1H, s), 6.85 (1H, s), 5.11 (2H, m), 4.59 (1H, dd, *J* = 10.1, 3.6 Hz), 4,13 (1H, m), 3.84 (1H, m), 3.80 (3H, s), 3.18 (1H, m), 2,87 (1H, m). **^{13}C NMR** (100 MHz, DMSO-d_6): δ 208.7, 169.4, 165.3, 151.0, 145.8, 136.1, 130.7, 128.5, 128.2, 128.1, 117.6, 112.0, 105.8, 70.1, 55.8, 54.2, 52.8, 36.8. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{20}H_{19}N_2O_5$, 367.1294; found 367.1299. **IR** (ν_{max}, film): 3213, 3137, 3062, 2931, 1764, 1699, 1627, 1436, 1226, 1115, 1002, 735 cm^{-1}. **$[\alpha]_D^{20}$** = 341° (*c* = 0.1, DMSO). **MP** = 220 °C (dec).

(*S*)-7,8-Dimethoxy-1,11a-dihydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-2,5,11(3*H*,10*H*)-trione (24e)

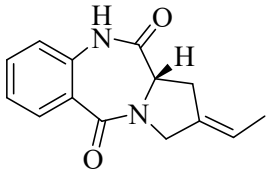


Following the general oxidation procedure 0.880 g (65%) of the title compound was prepared as off white solid starting from **27e** (1.359 g, 4.650 mmol, 1.0 equiv). $\mathbf{R_f}$ = 0.26 (EA). **^{1}H NMR** (400 MHz; $CDCl_3$): δ 8.53 (1H, br. s), 7.42 (1H, s), 6.51 (1H, s), 4.60 (1H, dd, *J* = 10.2, 3.6 Hz), 4.31 (1H, m), 3.93 (1H, m and 6H, s (partially overlapping)), 3.60 (1H, m), 2.83 (1H, ddd, *J* = 19.4, 10.1, 1.2 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 206.9, 169.4, 166.1, 153.1, 147.2, 129.5, 118.1, 112.3, 104.1, 56.4, 54.3, 53.0, 36.8. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{14}H_{15}N_2O_5$, 291.0981; found 291.0981. **IR** (ν_{max}, film): 3240, 2937, 1763, 1698, 1608, 1516, 1428, 1259, 1228, 1006, 754 cm^{-1}. **$[\alpha]_D^{20}$** = 500° (*c* = 0.1, $CHCl_3$). **MP** = 240 °C (dec).

General procedure for olefination of PBD triones

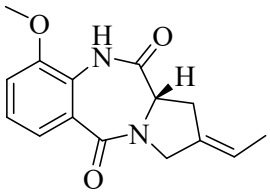
To a solution of sulfone **26** (12.000 mmol, 3.0 equivs) in DME (30 mL; freshly distilled from Na/Ph_2CO) at −40 °C was added 1 M KHMDS (made before use: 2.394 g, 12.000 mmol, 3.0 equivs dissolved in 12 mL of DME), and the mixture was stirred at the same temperature for 15 min. Next, a solution of **24** (4.000 mmol, 1.0 equiv) in DME (70 mL) was added, and the resulting mixture was stirred for 4h at −40 °C before being quenched with sat. NH_4Cl (20 mL). Then, brine (20 mL) was added, the organic layer was separated, and the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4), and volatiles were evaporated *in vacuo*. At this point, the qNMR spectrum was measured. The product was further purified by flash column chromatography.

(*S*,*E*)-2-Ethylidene-1,2,3,11a-tetrahydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11(10*H*)-dione (*Oxo-prothracarcin*) (6)



Following the general olefination procedure 0.217 g (65%) of the title compound was prepared as off white solid starting from **24a** (0.340 g, 1.373 mmol, 1 eq). $\mathbf{R_f}$ = 0.35 (DCM 20: MeOH 1). **^{1}H NMR** (400 MHz; MeOH-d_4): δ 7.87 (1H, ddd, *J* = 7.9, 1.6, 0.3 Hz), 7.55 (1H, ddd, *J* = 8.2, 7.4, 1.7 Hz), 7.29 (1H, m) 7.14 (1H, m) 5.57 (1H, m) 4.37 (1H, dd, *J* = 9.2, 2.4 Hz) 4.31 (1H, m) 4.13 (1H, dq, *J* = 16.0, 1.8 Hz) 3.45 (1H, br d, *J* = 16.2 Hz) 2.69 (1H, m) 1.75 (3H, m). **^{13}C NMR** (100 MHz, MeOH-d_4): δ 170.8, 166.3, 136.4, 133.0, 132.5, 130.0, 126.3, 124.4, 121.1, 117.7, 57.0, 51.1, 26.8, 13.1. **HRMS-ESI** (*m*/*z*): [M+H] calculated for $C_{14}H_{15}N_2O_2$, 243.1134; found 243.1140. **IR** (ν_{max}, film): 3218, 2920, 2854, 1694, 1622, 1446, 1257, 760 cm^{-1}. **$[\alpha]_D^{20}$** = +481.0° (*c* = 0.1, MeOH).

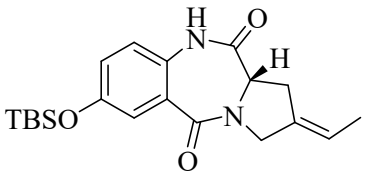
(*S*,*E*)-2-Ethylidene-9-methoxy-1,2,3,11a-tetrahydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11(10*H*)-dione (*Boseogazepine B*) (8)



Following the general olefination procedure 243 mg (43%) of the title compound was prepared as colorless foam starting from **24b** (0.553 g, 2.125 mmol, 1.0 equiv).

$\mathbf{R_f}$ = 0.45 (DCM 40:MeOH 1). ^{1}H NMR (400 MHz; MeOH-d_4): δ 7.47−7.39 (1H, m), 7.31−7.19 (2H, m), 5.57 (1H, m), 4.39−4.22 (2H, m), 4.12 (1H, m), 3.94 (3H, s), 3.44 (1H, br.d, *J* = 16.2 Hz), 2.69 (1H, m), 1.74 (3H, m). **^{13}C NMR** (100 MHz, MeOH-d_4): δ 171.9, 167.5, 151.3, 134.5 and 134.4 (isomers), 128.6, 127.1, 126.3, 122.4, 119.4 and 119.1 (isomers), 114.8, 58.5 and 58.0 (isomers), 56.8, 52.5, 32.3 and 28.2 (isomers), 14.8 and 14.5 (isomers). **HRMS-ESI** (*m*/*z*): [M+H] calculated for $C_{15}H_{17}N_2O_3$, 273.1239; found 273.1252. **IR** (ν_{max}, film): 3257, 2982, 2920, 2860, 1693, 1413, 1261, 1068, 750 cm^{-1}. **$[\alpha]_D^{20}$** = 571° (*c* = 0.1, MeOH). **MP** = 108-109 °C.

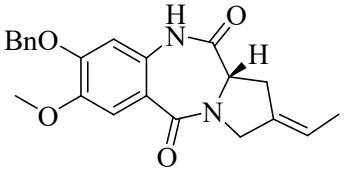
(*S*,*E*)-7-((*tert*-Butyldimethylsilyl)oxy)-2-ethylidene-1,2,3,11a-tetrahydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11(10*H*)-dione (25c)



Following the general olefination procedure 20 mg (38%) of the title compound was prepared as colorless foam starting from **24c** (50.0 mg, 0.138 mmol, 1.0 equiv).

$\mathbf{R_f}$ = 0.32 (petrol ether 1: ethyl acetate 1). **^{1}H NMR** (400 MHz; $CDCl_3$): δ 8.33 (1H, br. s), 7.42 (1H, d, *J* = 2.8 Hz), 6.95 (1H, dd, *J* = 8.6, 2.8 Hz), 6.90 (1H, d, *J* = 8.6 Hz), 5.53 (1H, m), 4.39 (1H, m), 4.25 (1H, dd, *J* = 9.4, 2.8 Hz), 4.15 (1H, m), 3.49 (1H, m), 2.66 (1H, m), 1.72 (3H, m), 0.98 (9H, s), 0.21 (6H, s). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.8, 165.1, 153.1, 132.8, 129.1, 128.3, 124.8, 122.6, 121.3, 118.5, 56.9, 51.7, 27.7, 25.7, 18.3, 14.6, -4.3. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{20}H_{29}N_2O_3Si$, 373.1947; found 373.1953. **IR** (ν_{max}, film): 3227, 2928, 2858, 1702, 1641, 1494, 1438, 1278, 1229, 995, 914, 859, cm^{-1}. **$[\alpha]_D^{20}$** = 673° (*c* = 0.1, $CHCl_3$).

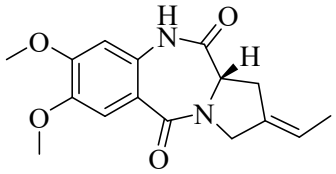
(*S*,*E*)-8-(Benzyloxy)-2-ethylidene-7-methoxy-1,2,3,11a-tetrahydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11(10*H*)-dione (25d)



Following the general olefination procedure 1.00 g (66%) of the title compound was prepared as beige foam starting from **24d** (1.465 g, 4.000 mmol, 1.0 equiv).

$\mathbf{R_f}$ = 0.22 (DCM 10: MeOH 0.2). **^{1}H NMR** (400 MHz; $CDCl_3$): δ 8.00 (1H, br. s), 7.44 (1H, s), 7.43−7.29 (5H, m), 6.46 (1H, s), 5.52 (1H, m), 5.21−5.13 (2H, m), 4.39 (1H, m), 4.22 (1H, dd, *J* = 9.4, 2.9 Hz), 4.13 (1H, m), 3.92 (3H, s), 3.48 (1H, m), 2.64 (1H, m), 1.72 (3H, m). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.5, 165.3, 151.5, 147.2, 136.0, 132.9, 129.3, 128.9, 128.5, 127.4, 119.5, 118.5, 112.6, 106.0, 71.2, 57.0, 56.4, 51.8, 27.6, 14.6. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{22}H_{23}N_2O_4$, 379.1658; found 379.1650. **IR** (ν_{max}, film): 3229, 2930, 1695, 1607, 1516, 1433, 1375, 1255, 1228, 1118, 753 cm^{-1}. $\mathbf{[\alpha]_D^{20}}$ = 325° (*c* = 0.1, $CHCl_3$). **MP** = 89-90 °C.

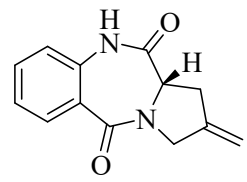
(*S*,*E*)-2-Ethylidene-7,8-dimethoxy-1,2,3,11a-tetrahydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11(10*H*)-dione (25e)



Following the general olefination procedure 21.8 mg (46%) of the title compound was prepared as a white solid starting from **24e** (46 mg, 0.158 mmol, 1.0 equiv).

$\mathbf{R_f}$ = 0.46 (ethyl acetate). **^{1}H NMR** (400 MHz; DMSO-d_6): δ 10.30 (1H, br. s), 7.23 (1H, s), 6.70 (1H, s), 5.48 (1H, m), 4.27 (1H, dd, *J* = 9.5, 2.7 Hz), 4.21 (1H, m), 3.97 (1H, m), 3.78 (3H, s), 3.77 (3H, s), 3.25 (1H, m), 2.60 (1H, m), 1.66 (3H, m). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 170.0, 164.4, 151.7, 145.3, 134.0, 130.8, 118.1, 116.8, 111.6, 104.4, 56.4, 55.6 (2×C), 51.2, 27.1, 14.2. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{16}H_{19}N_2O_4$, 303.1345; found 303.1347. $\mathbf{[\alpha]_D^{20}}$ = 217° (*c* = 0.1, MeOH). **MP** = 282-283 °C.

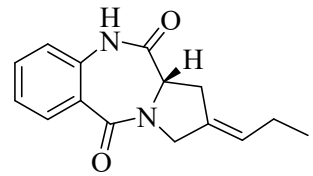
(*S*)-2-Methylene-1,2,3,11a-tetrahydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11(10*H*)-dione (25f)



Following the general olefination procedure 46 mg (50%) of the title compound was prepared as white solid starting from **24a** (92 mg, 0.400 mmol, 1.0 equiv).

Title compound was isolated in reverse phase using H_2O/MeCN gradient. $\mathbf{R_f}$ = 0.33 (DCM 20: MeOH 1). **^{1}H NMR** (400 MHz; CD_3OD): δ 7.88 (1H, dd, *J* = 7.9, 1.5 Hz), 7.55 (1H, ddd, *J* = 8.2, 7.4, 1.7 Hz), 7.29 (1H, ddd, *J* = 7.9, 7.3, 1.1 Hz), 7.17–7.11 (1H, m), 5.19–5.11 (2H, m), 5.19–5.11 (2H, m), 4.22–4.14 (1H, m), 3.41–3.34 (1H, m), 2.93–2.83 (1H, m). **^{13}C NMR** (100 MHz, CD_3OD) δ 172.1, 167.8, 143.5, 137.8, 134.0, 131.4, 127.6, 125.8, 122.6, 109.0, 58.2, 52.3, 32.6. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{13}H_{13}N_2O_2$, 229.0977; found 229.0977. **IR** (ν_{max}, film): 3225, 3006, 2914, 1694, 1622, 1480, 1448, 1412, 1260, 1163, 1053, 881, 758 cm^{-1}. $\mathbf{[\alpha]_D^{20}}$ = +532° (*c* = 0.1, MeOH). **MP** = 189-190 °C.

(*S*,*E*)-2-Propylidene-1,2,3,11a-tetrahydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11(10*H*)-dione (25g)

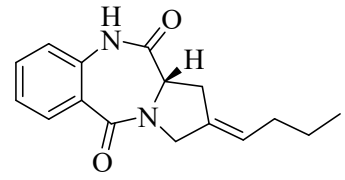


Following the general olefination procedure 28 mg (32%) of the title compound was prepared as a white solid starting from **24a** (90.0 mg, 0.336 mmol, 1.0 equiv). $\mathbf{R_f}$ = 0.30 (DCM 20: MeOH 1).

^{1}H NMR (400 MHz; $CDCl_3$): δ 8.00 (1H, dd, *J* = 7.9, 1.7 Hz), 7.70 (1H, s), 7.49 (1H, td, *J* = 7.9, 1.7 Hz), 7.29 (1H, m), 6.97 (1H, dd, *J* = 7.9, 1.3 Hz), 5.53–5.44 (1H, m), 4.45–4.36 (1H, m), 4.25 (1H, dd, *J* = 9.3, 2.9 Hz), 4.19 (1H, dt, *J* = 15.9, 1.7 Hz), 3.54–3.46 (1H, m), 2.74–2.62 (1H, m), 2.26–2.01 (2H, m), 1.03 (3H, t, *J* = 7.6 Hz). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.5, 165.3, 135.0, 132.6, 131.2, 131.1, 127.0, 125.9, 125.4, 120.8, 56.8, 51.7, 27.6,

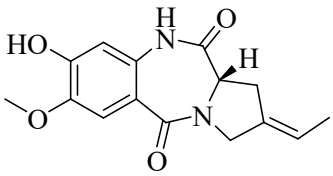
22.6, 13.9. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{15}H_{17}N_2O_2$, 257.1290; found 257.1294. **IR** (ν_{max}, film): 3235, 2973, 2935, 1690, 1629, 1481, 1445, 1412, 1257, 1216, 1162, 756 cm^{-1}. **$[\alpha]_D^{20}$** = 303° (*c* = 0.1, MeOH). **MP** = 173-174 °C.

(*S*,*E*)-2-Butylidene-1,2,3,11a-tetrahydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11(10*H*)-dione (25h)



Following the general olefination procedure 20 mg (22%) of the title compound was prepared as colorless wax starting from **24a** (90 mg, 0.336 mmol, 1.0 equiv). Title compound was isolated in reverse phase using H_2O/MeCN gradient. **^{1}H NMR** (400 MHz; $CDCl_3$): δ 8.37 (1H, br.s), 7.99 (1H, dd, *J* = 7.9, 1.7 Hz), 7.54 – 7.42 (1H, m), 7.27 (1H, m), 7.01 (1H, d, *J* = 7.9 Hz), 5.49 (1H, m), 4.46 – 4.30 (1H, m), 4.28 – 4.12 (2H, m), 3.50 (1H, br. d, *J* = 15.5 Hz), 2.67 (1H, m), 2.10 (2H, m), 1.51 – 1.35 (2H, m), 0.93 (3H, t, *J* = 7.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 165.5, 135.3, 132.6, 132.0, 131.3, 127.0, 125.4, 124.3, 121.1, 56.9, 51.8, 31.4, 27.9, 22.6, 14.0. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{16}H_{19}N_2O_2$, 271.1447; found 271.1451. **IR** (ν_{max}, film): 3229, 2955, 2925, 2858, 1694, 1615, 1485, 1460, 1418, 1258, 1223, 1201, 1180, 757 cm^{-1}. **$[\alpha]_D^{20}$** = +510° (*c* = 0.1, MeOH).

(*S*,*E*)-2-Ethylidene-8-hydroxy-7-methoxy-1,2,3,11a-tetrahydro-5*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11(10*H*)-dione (*Oxo-tomaymycin*) (7)



To a solution of **25d** (0.200 g, 0.528 mmol) in DCM/H_2O (3 mL, 1:1) at 0 °C anisole (1.00 mL, 8.985 mmol, 17.0 equivs) and MsOH (0.538 mL, 8.985 mmol, 17.0 equivs) were added and the mixture was stirred at RT for 40 min. Then, the DCM was removed *in vacuo* and the residue was purified by flash column chromatography in reverse phase using full gradient water/MeCN to obtain 120 mg (79%) of the title compound as a yellowish wax. **^{1}H NMR** (400 MHz; DMSO-d_6): δ 10.24 (1H, br.s) 9.94 (1H, br.s) 7.20 (1H, s) 6.56 (1H, s) 5.47 (1H, m) 4.25 (1H, dd, J = 9.4, 2.7 Hz) 4.21 (1H, m) 3.91 (1H, m) 3.78 (3H, s) 3.25 (1H, br.d, J = 16.2 Hz) 2.59 (1H, m) 1.66 (3H, m). **^{13}C NMR** 170.0, 164.6, 150.3, 144.6, 134.1, 131.0, 117.1, 116.7, 112.3, 107.8, 56.4, 55.7, 51.1, 27.2, 14.3. **HRMS-ESI** (*m/z*): [M+H] calculated for $C_{15}H_{17}N_2O_4$, 289.1188; found 289.1202. **IR** (ν_{max}, film): 3403, 3069, 2919, 2859, 2610, 2417, 1677, 1611, 1482, 1268, 1207, 1008, 960, 878, 787, 759 cm^{-1}. **$[\alpha]_D^{20}$** = +391° (*c* = 0.3, MeOH).

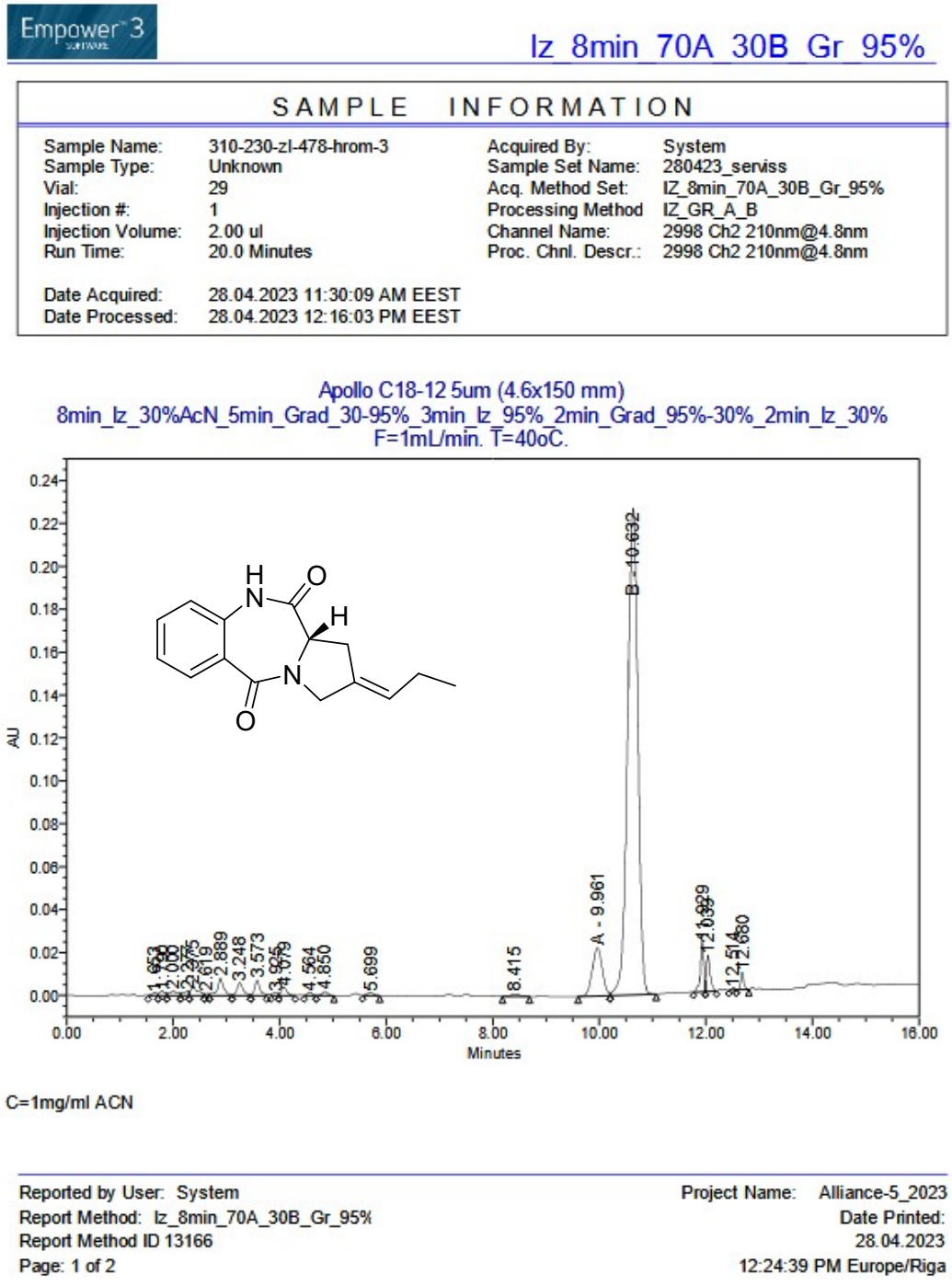
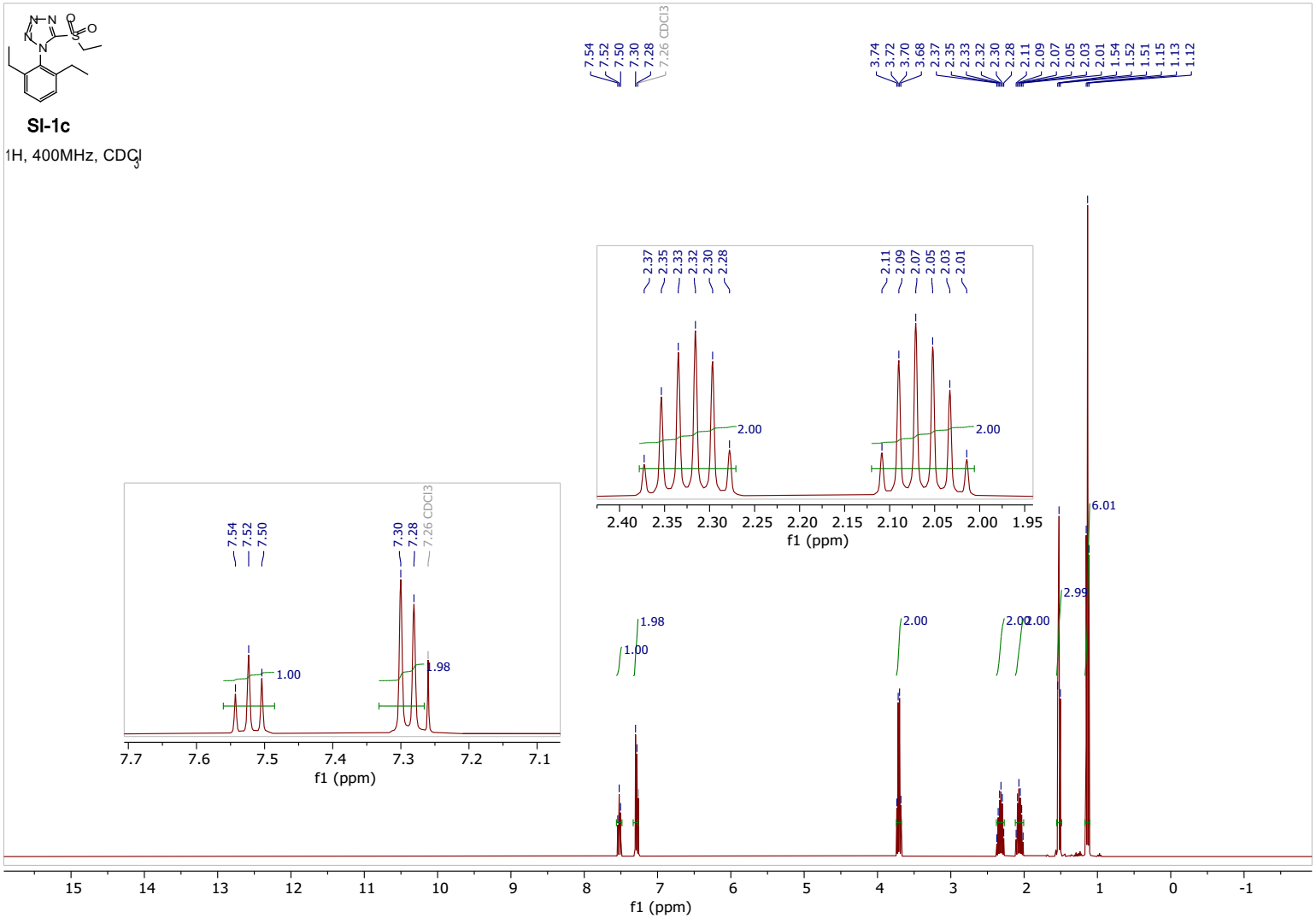


Figure SI-1. Typical plot for *E*/*Z*- determination of olifinated PBDs **6, 7** and **25**.
Method: Apollo C_{18} (4.6×150mm), 8 min, isocratic 30% ACN/ 70% H_2O (0.1% H_3PO_4), 5 min gradient to 95% ACN, flow =1.0 mL/min, 40 °C, 210 nm

NMR spectra


SI-1c
1H, 400MHz, CDCl3
7.54
7.52
7.50
7.30
7.28
7.26 CDCl3
3.74
3.72
3.70
3.68
2.37
2.35
2.33
2.32
2.30
2.28
2.11
2.09
2.07
2.05
2.03
2.01
1.54
1.52
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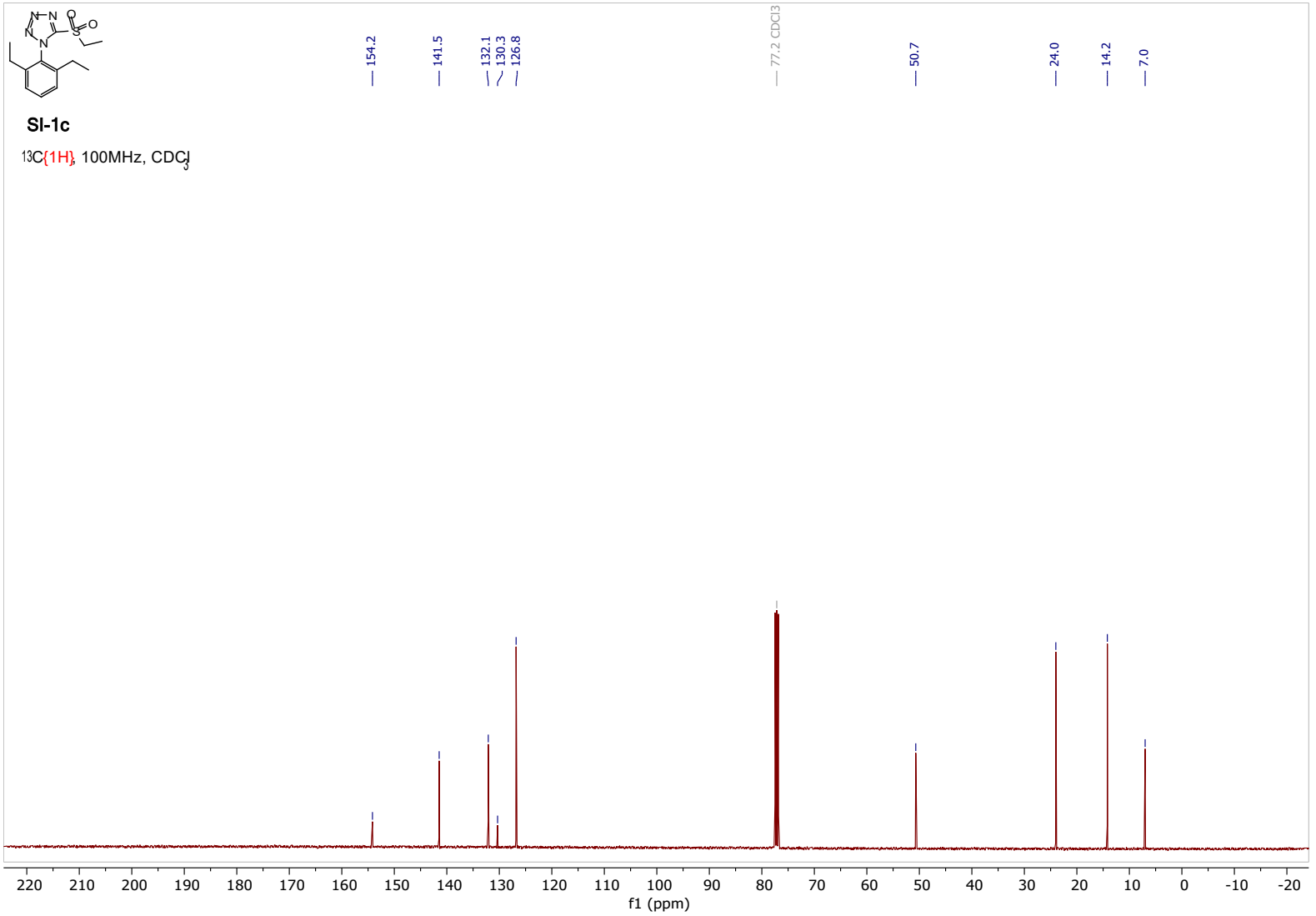
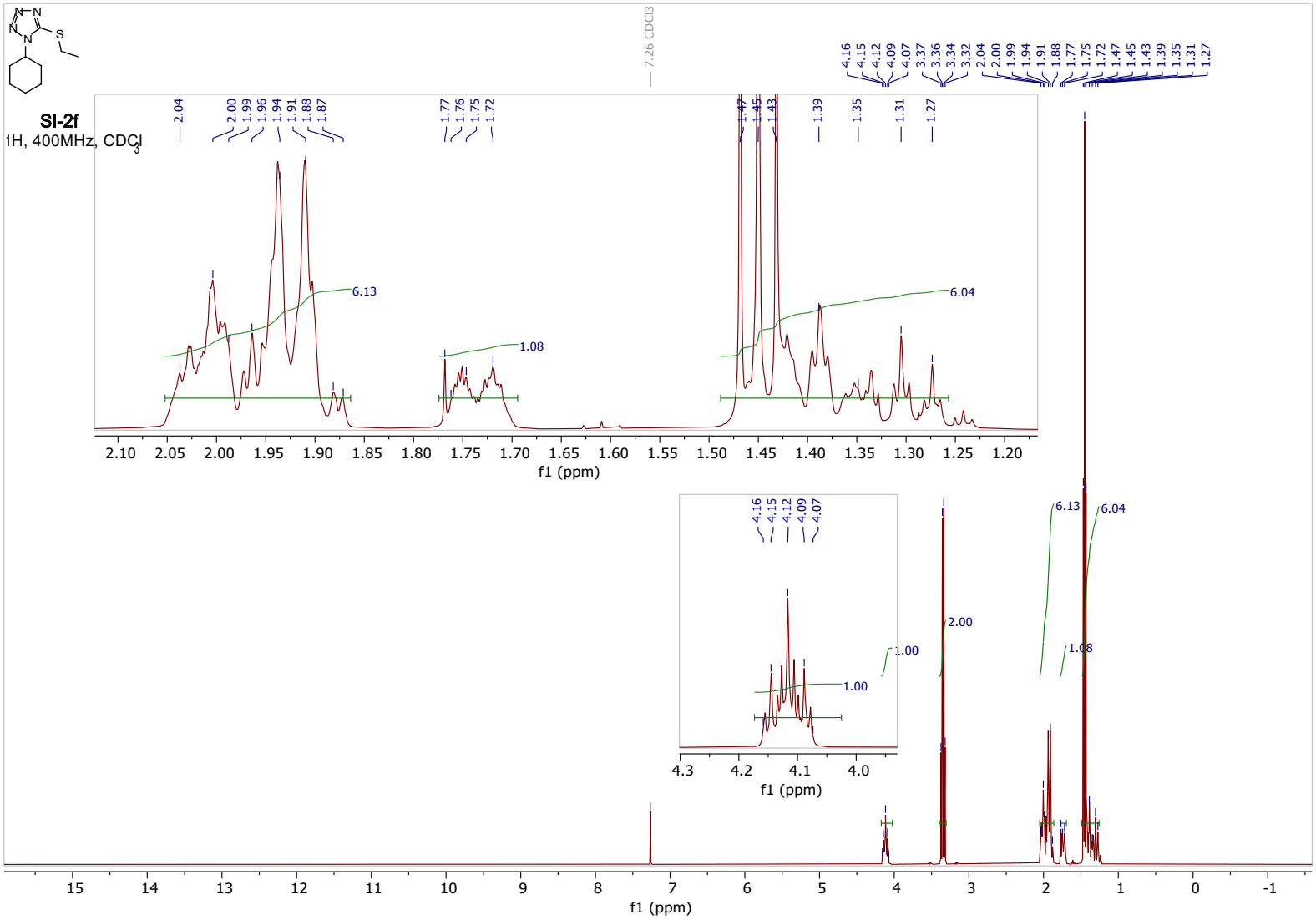
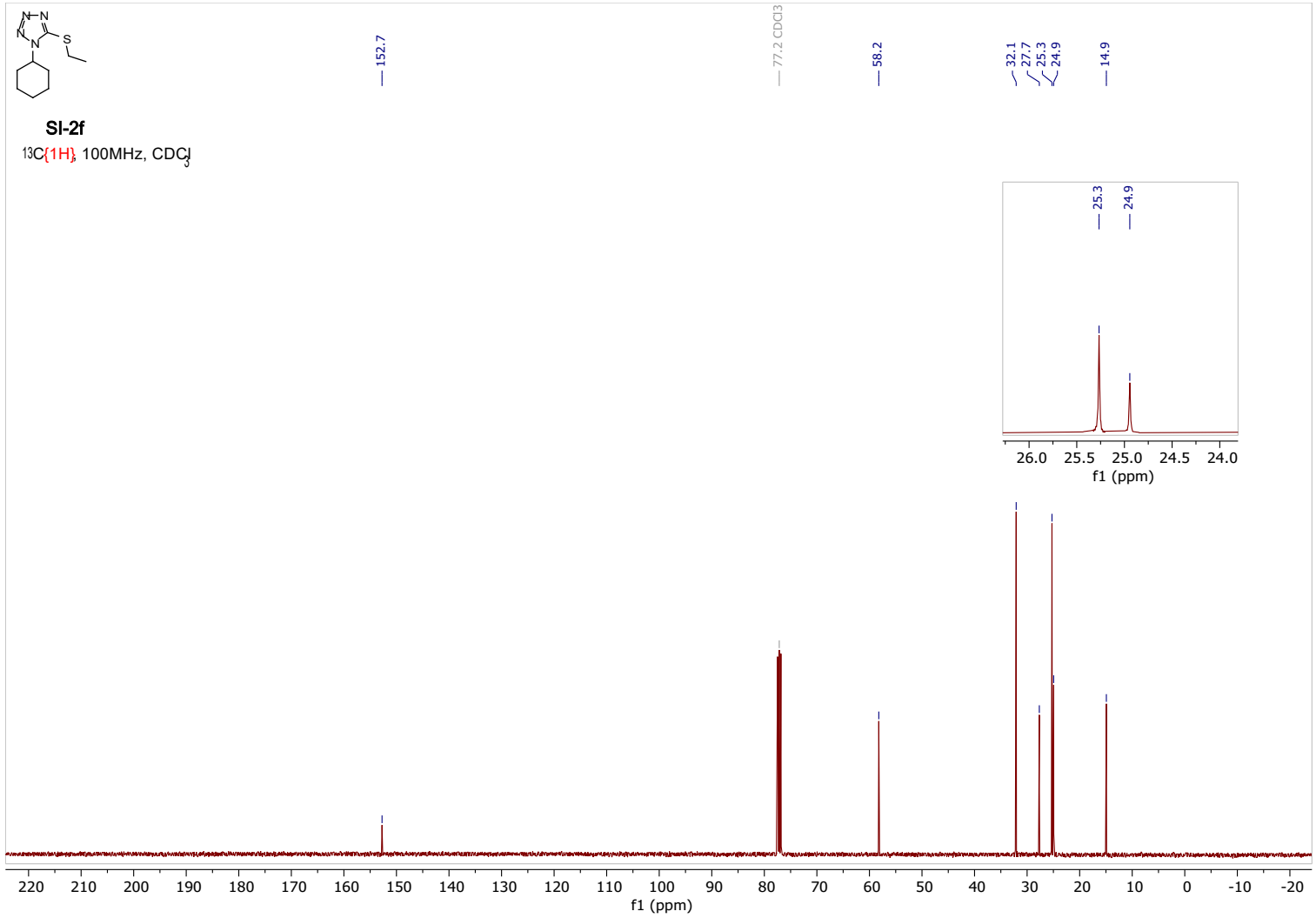
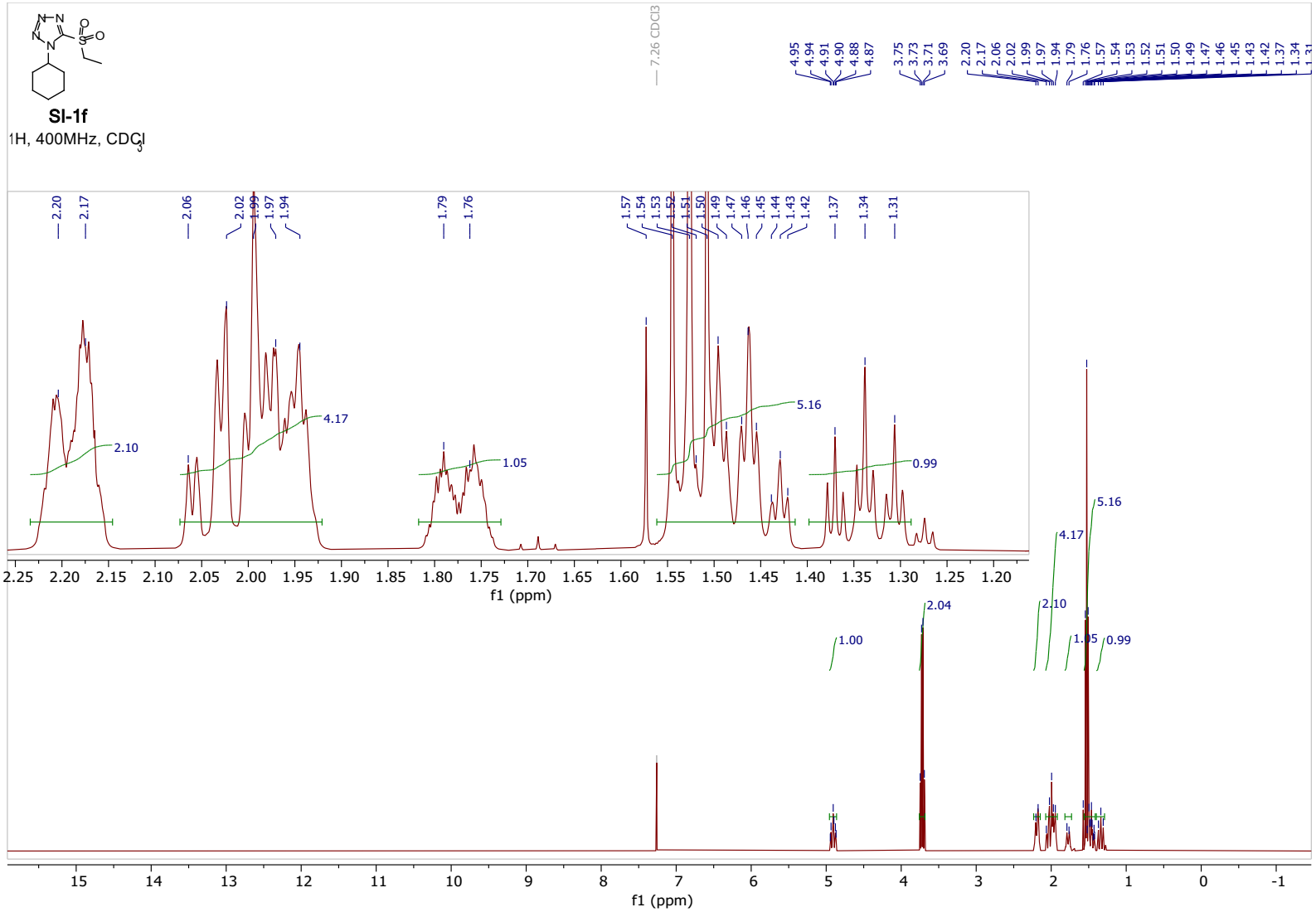
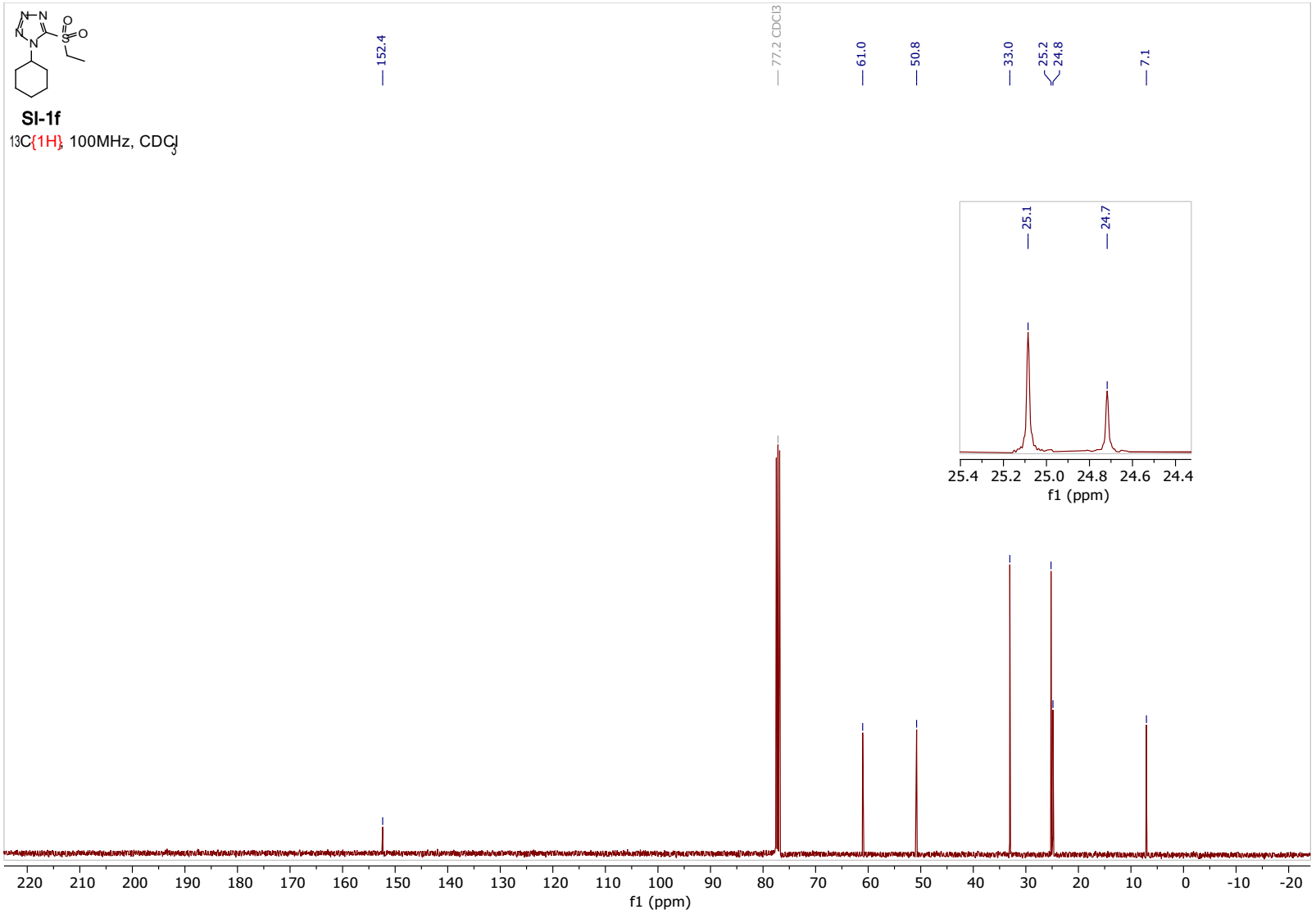
2.00
2.00
2.00
2.99
6.01
f1 (ppm)

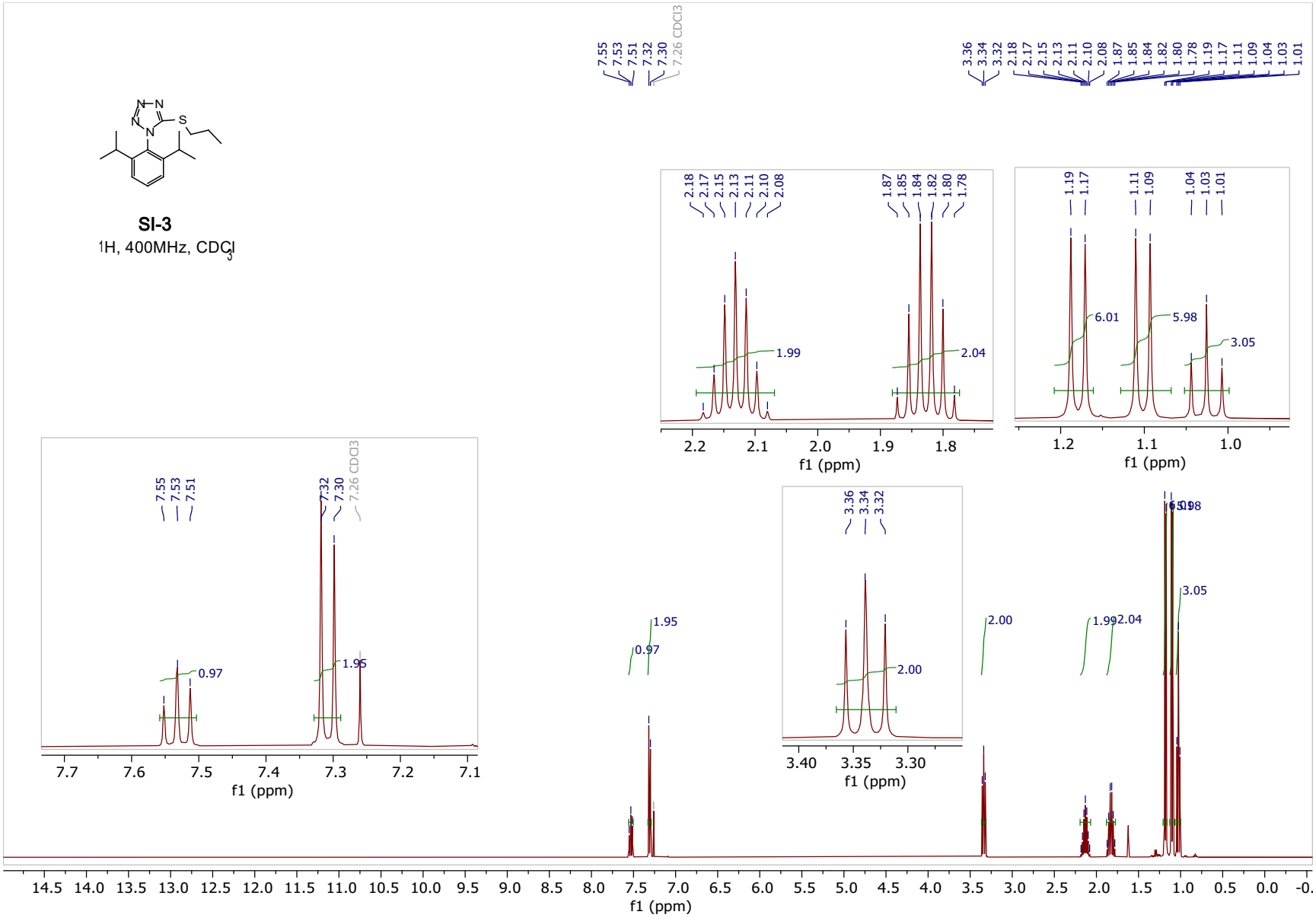

154.2
141.5
132.1
130.3
126.8
77.2 CDCl3
50.7
24.0
14.2
7.0
SI-1c
13C{1H}, 100MHz, CDCl3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

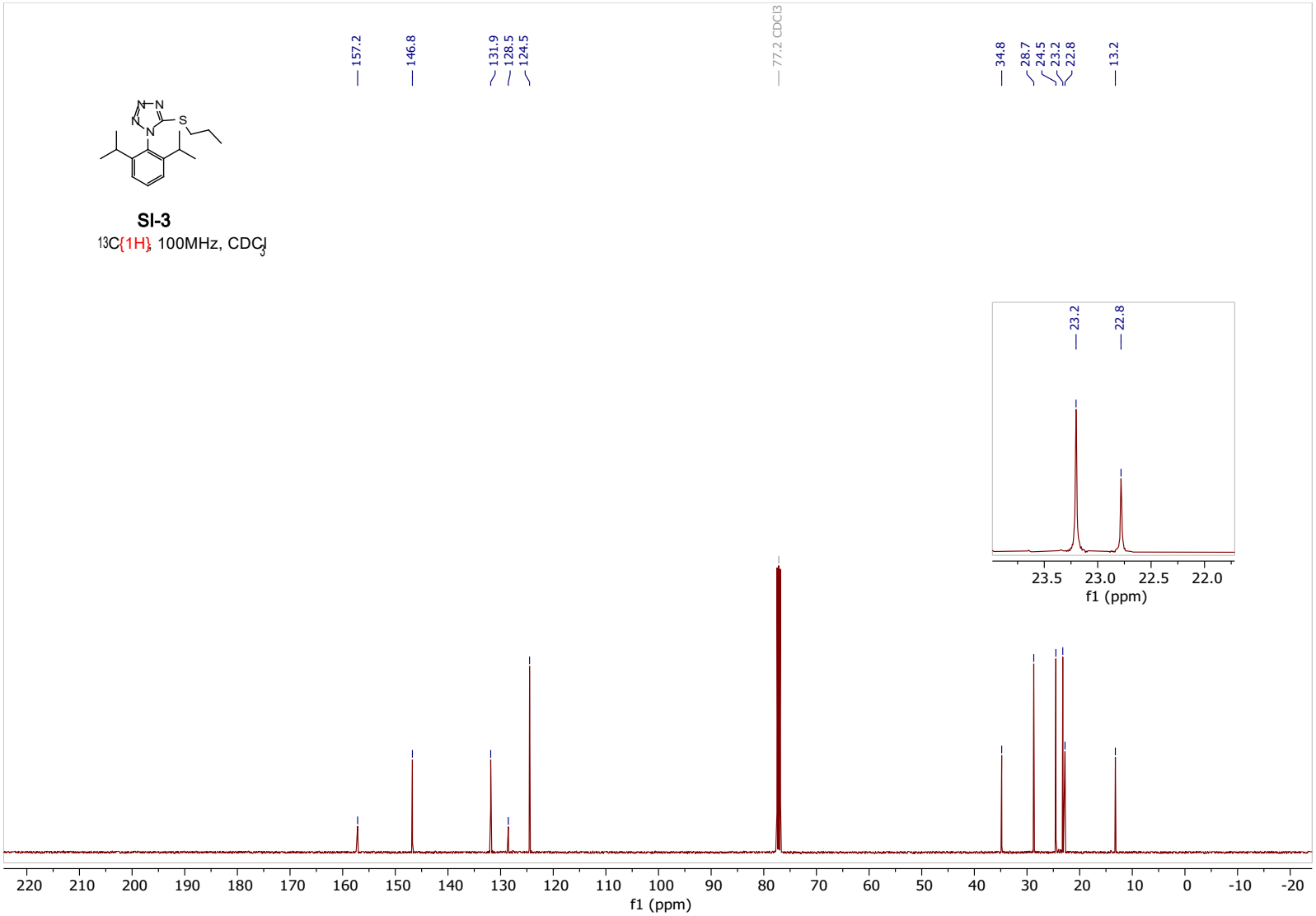

SI-2f
1H, 400MHz, CDCl3
7.26 CDCl3
f1 (ppm)
6.13
1.08
6.04
1.00
1.00
2.00
1.08

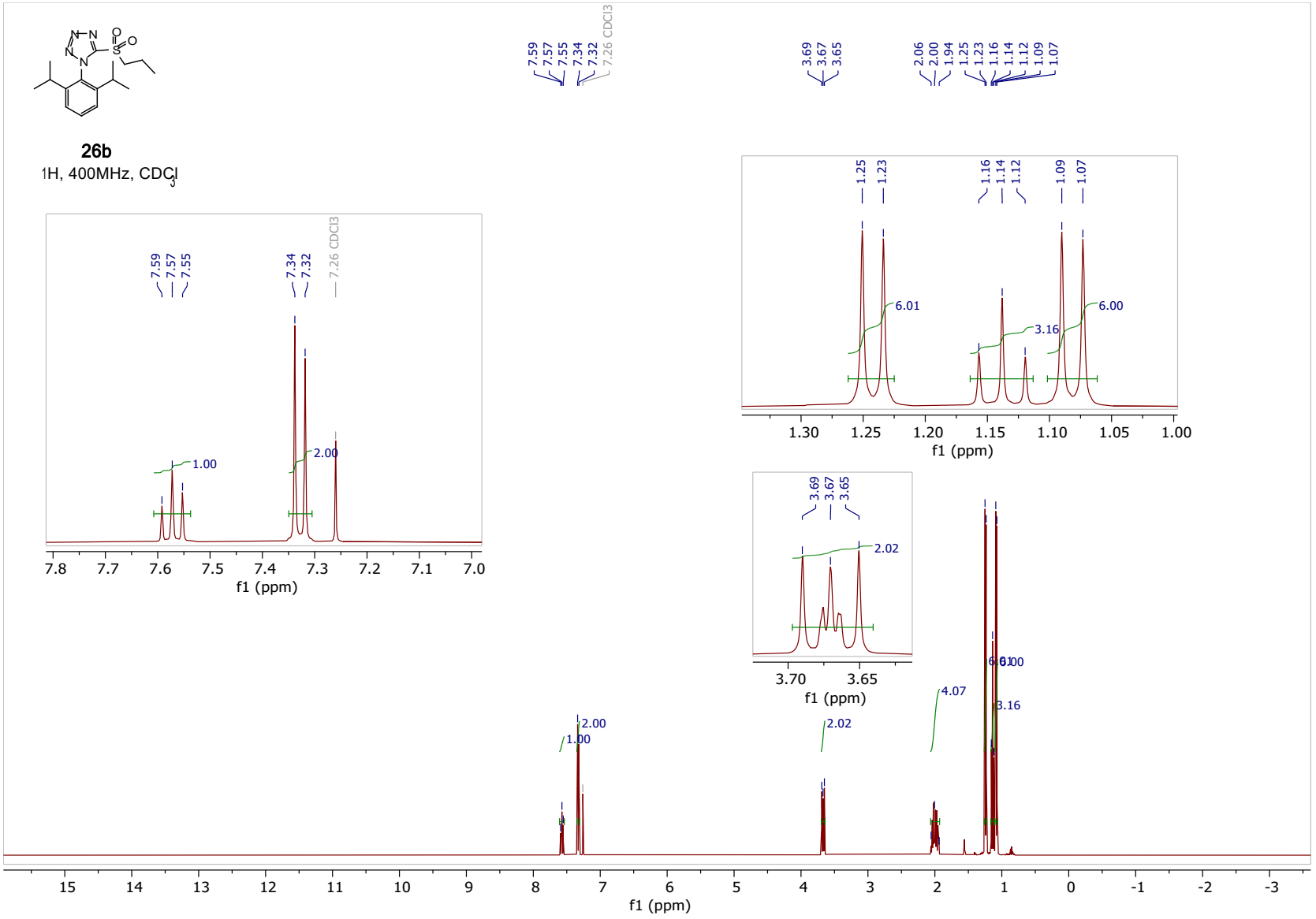

152.7
77.2 CDCl3
58.2
32.1
27.7
25.3
24.9
14.9
SI-2f
13C{1H}, 100MHz, CDCl3
25.3
24.9
26.0 25.5 25.0 24.5 24.0
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

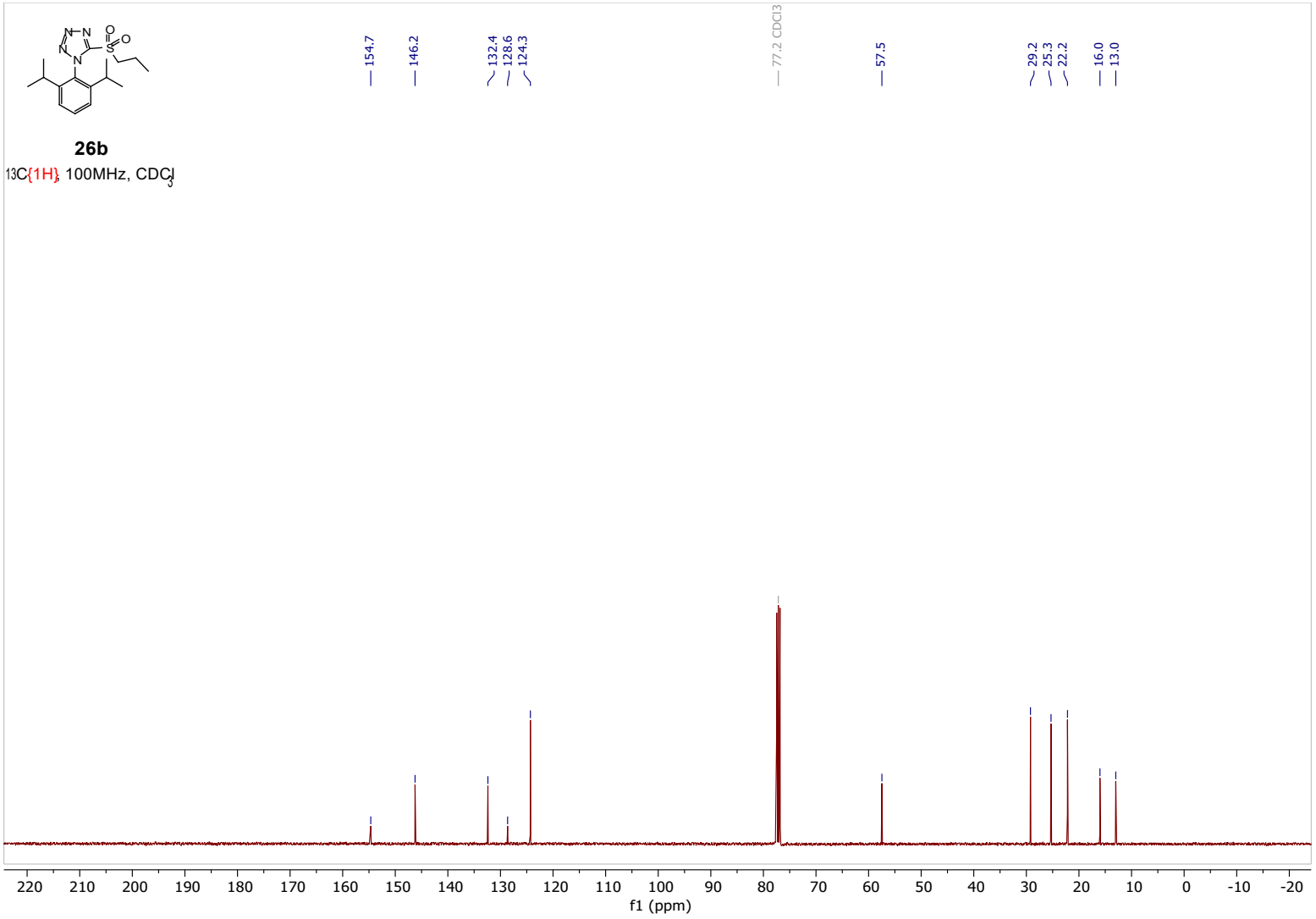

SI-1f
1H, 400MHz, CDCl3
7.26 CDCl3
4.95 4.94 4.91 4.90 4.88 4.87
3.75 3.73 3.71 3.69
2.20 2.17 2.06 2.02 1.99 1.97 1.94 1.79 1.76 1.57 1.54 1.53 1.52 1.51 1.50 1.49 1.47 1.46 1.45 1.43 1.42 1.37 1.34 1.31
2.10
4.17
1.05
5.16
0.99
1.00
2.04
f1 (ppm)

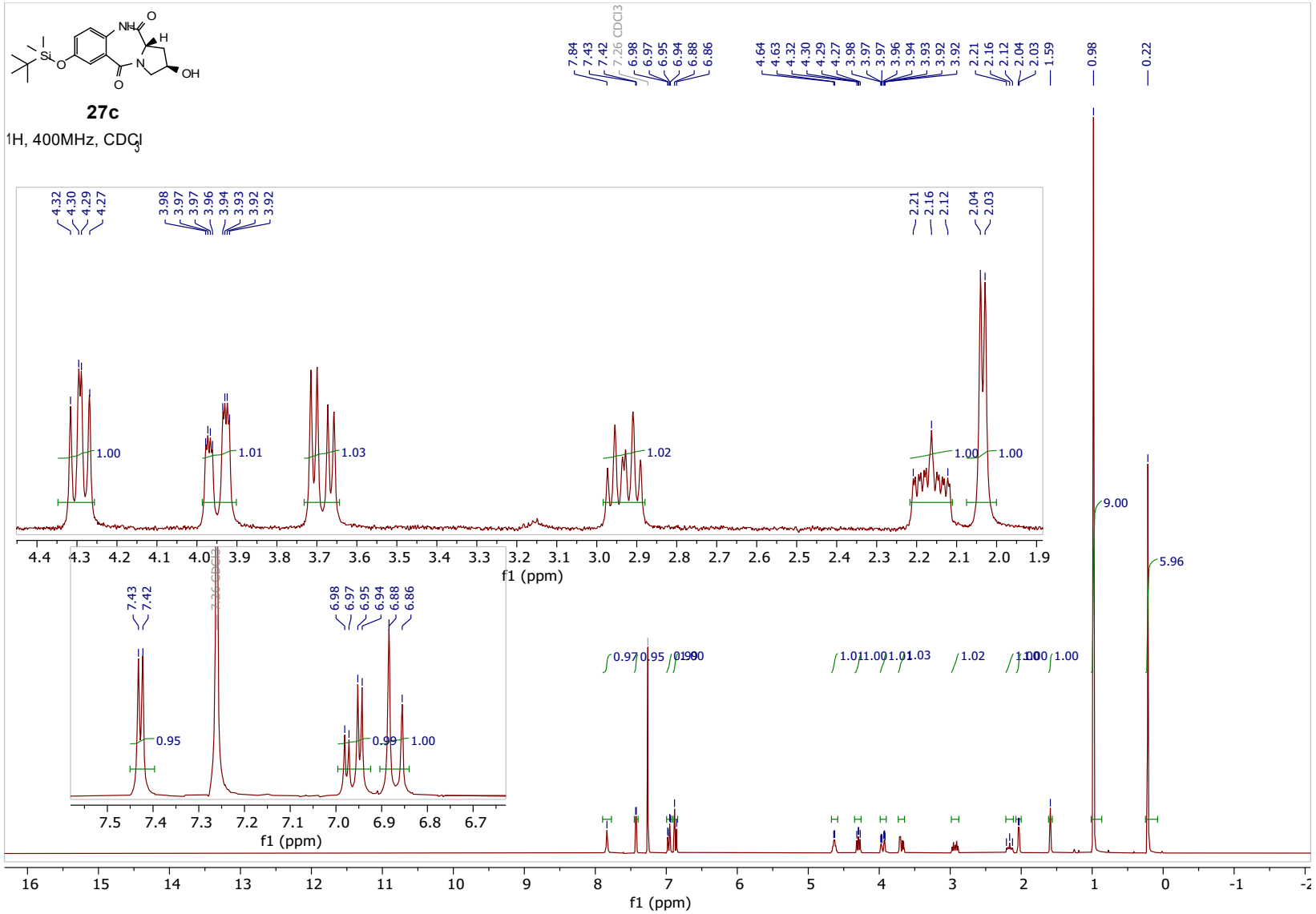

SI-1f
13C{1H}, 100MHz, CDCl3
152.4
77.2 CDCl3
61.0
50.8
33.0
25.2
24.8
7.1
25.1
24.7
25.4 25.2 25.0 24.8 24.6 24.4
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

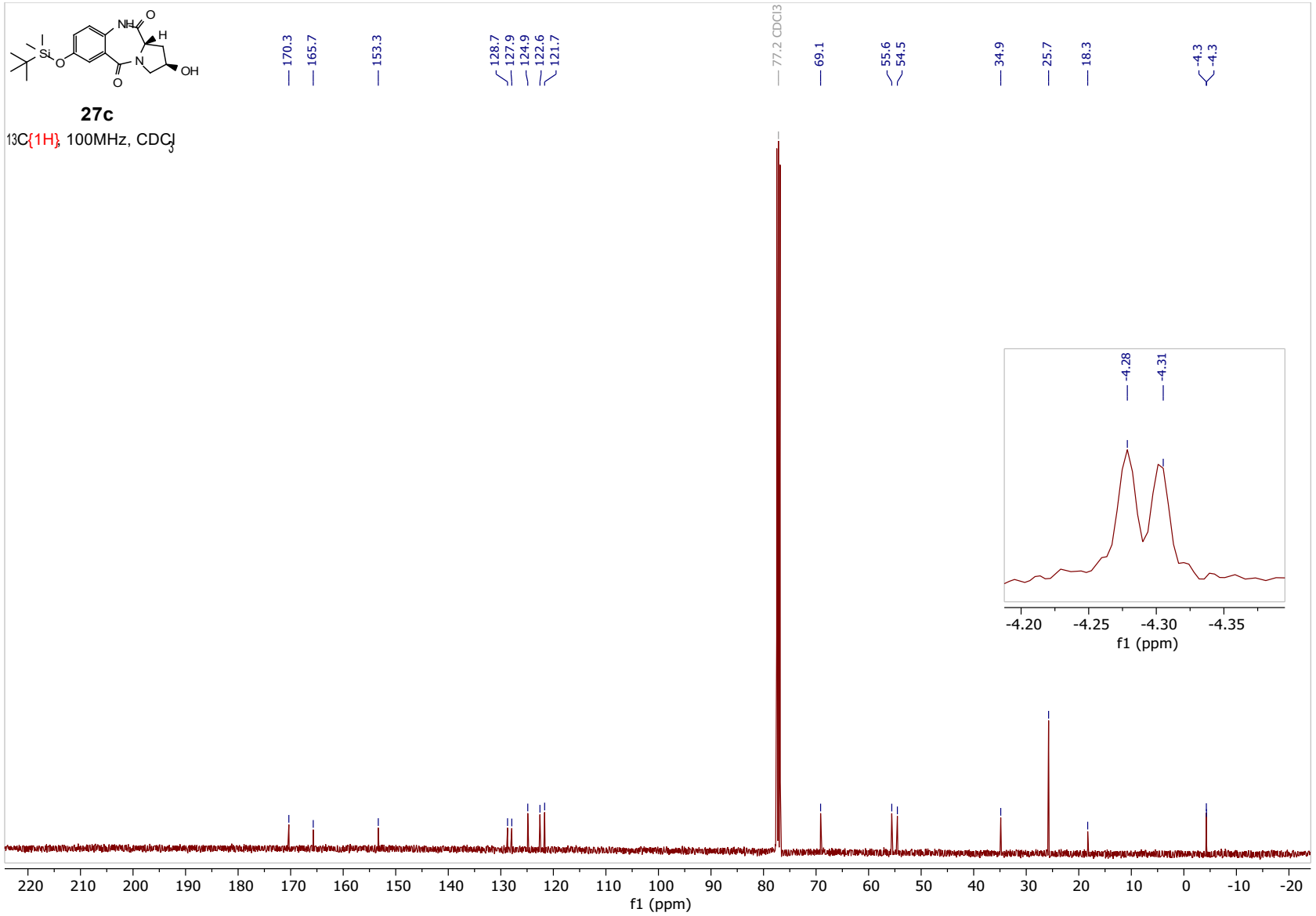

SI-3
1H, 400MHz, CDCl3
7.55
7.53
7.51
7.32
7.30
7.26 CDCl3
3.36
3.34
3.32
2.18
2.17
2.15
2.13
2.11
2.10
2.08
1.87
1.85
1.84
1.82
1.80
1.78
1.19
1.17
1.11
1.09
1.04
1.03
1.01
1.99
2.04
6.01
5.98
3.05
0.97
1.95
2.00
f1 (ppm)

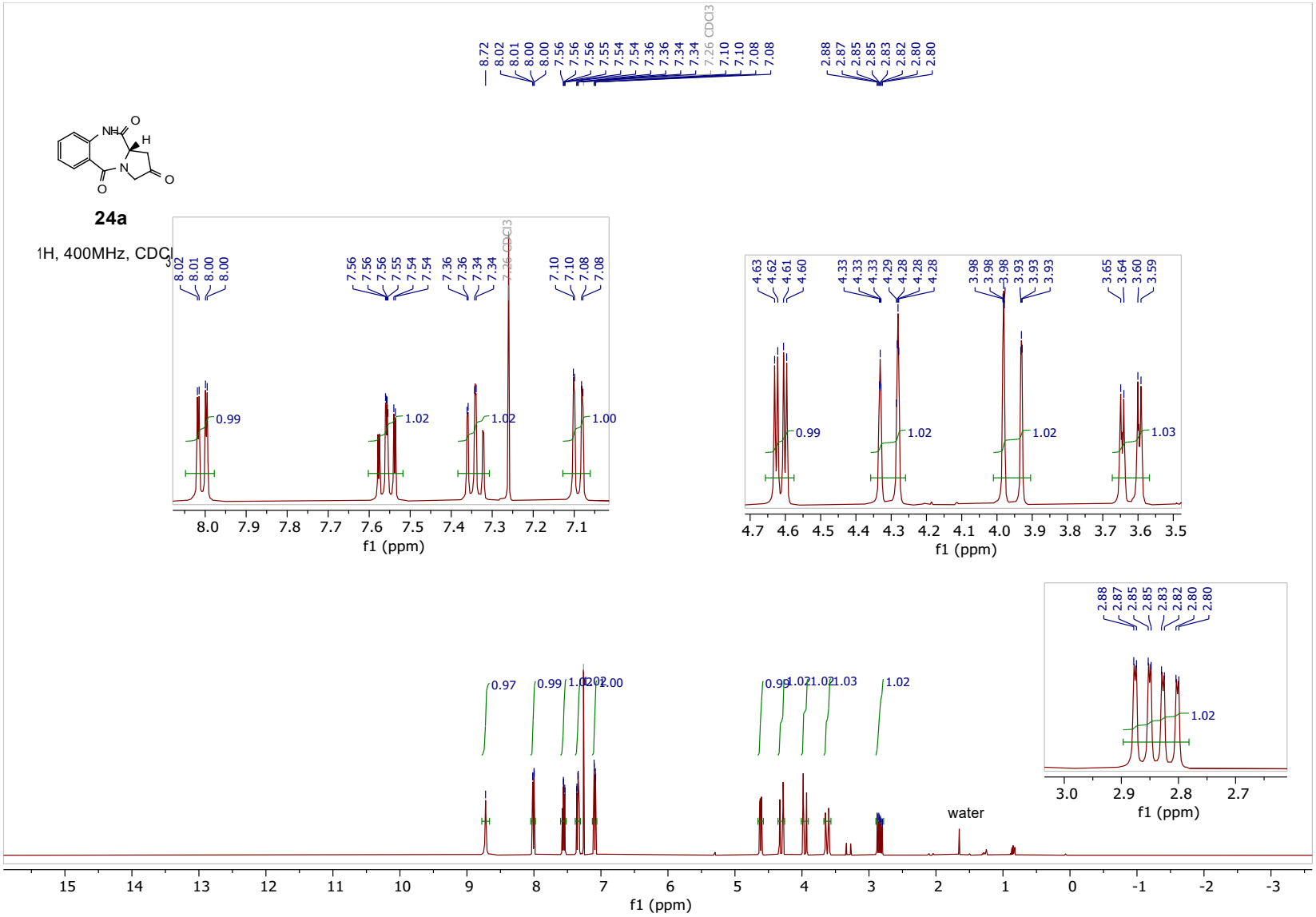

157.2
146.8
131.9
128.5
124.5
77.2 CDCl3
34.8
28.7
24.5
23.2
22.8
13.2
SI-3
13C{1H}, 100MHz, CDCl3
23.2
22.8
23.5
23.0
22.5
22.0
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

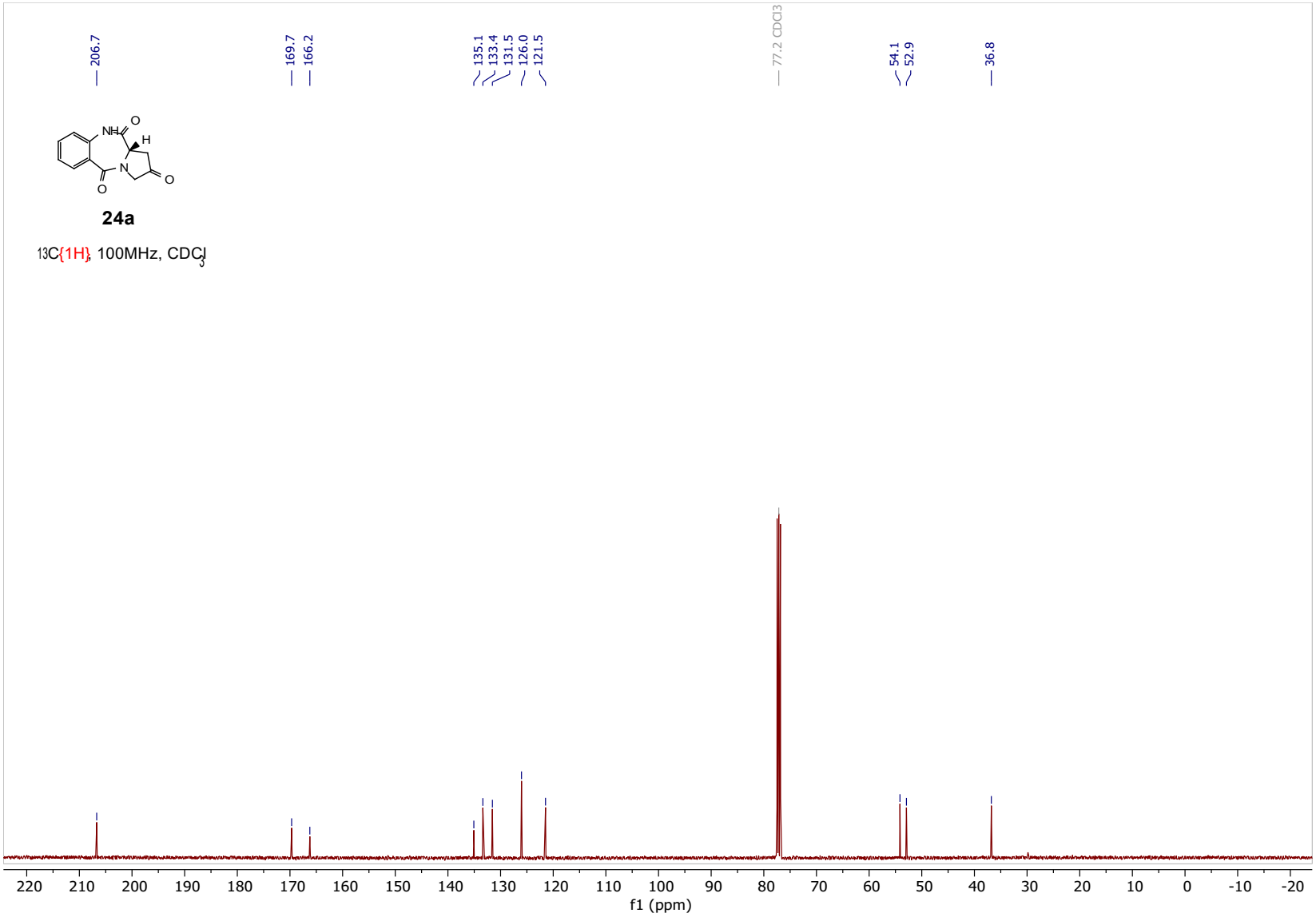

26b
1H, 400MHz, CDCl3
7.59
7.57
7.55
7.34
7.32
7.26 CDCl3
3.69
3.67
3.65
2.06
2.00
1.94
1.25
1.23
1.16
1.14
1.12
1.09
1.07
1.00
2.00
6.01
3.16
6.00
2.02
4.07
f1 (ppm)

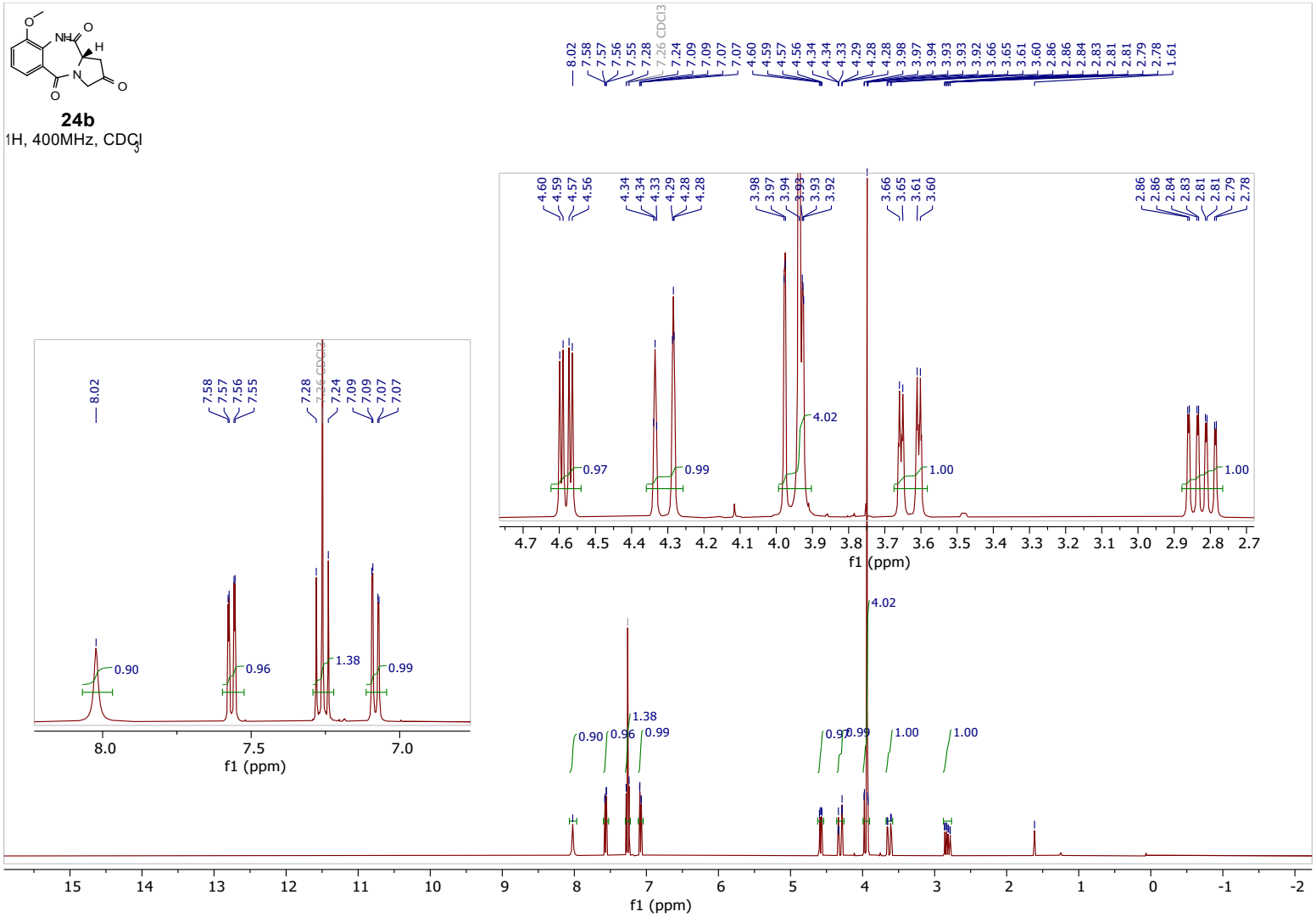

26b
13C{1H}, 100MHz, CDCl3
154.7
146.2
132.4
128.6
124.3
77.2 CDCl3
57.5
29.2
25.3
22.2
16.0
13.0
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

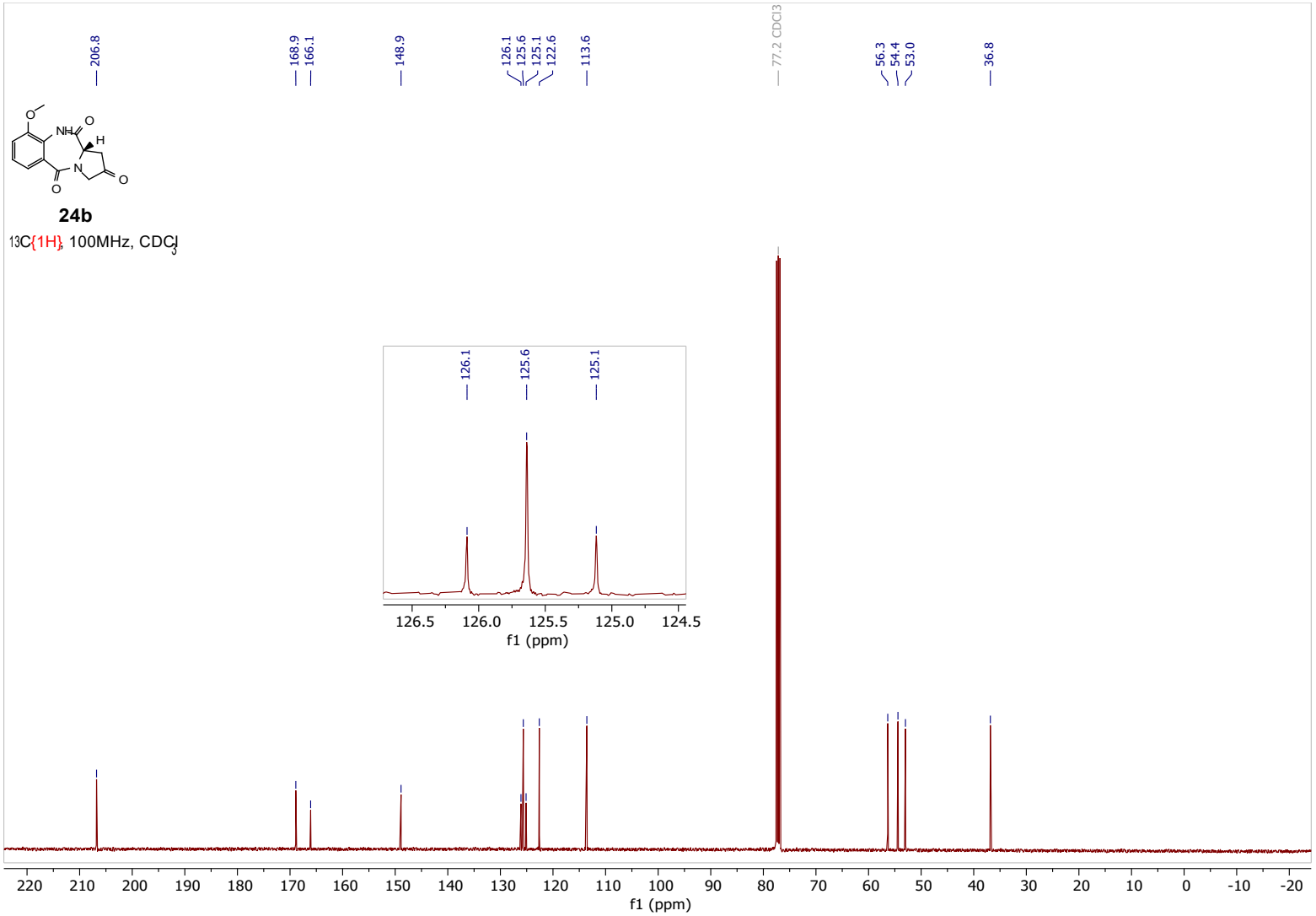

27c
1H, 400MHz, CDCl3
f1 (ppm)

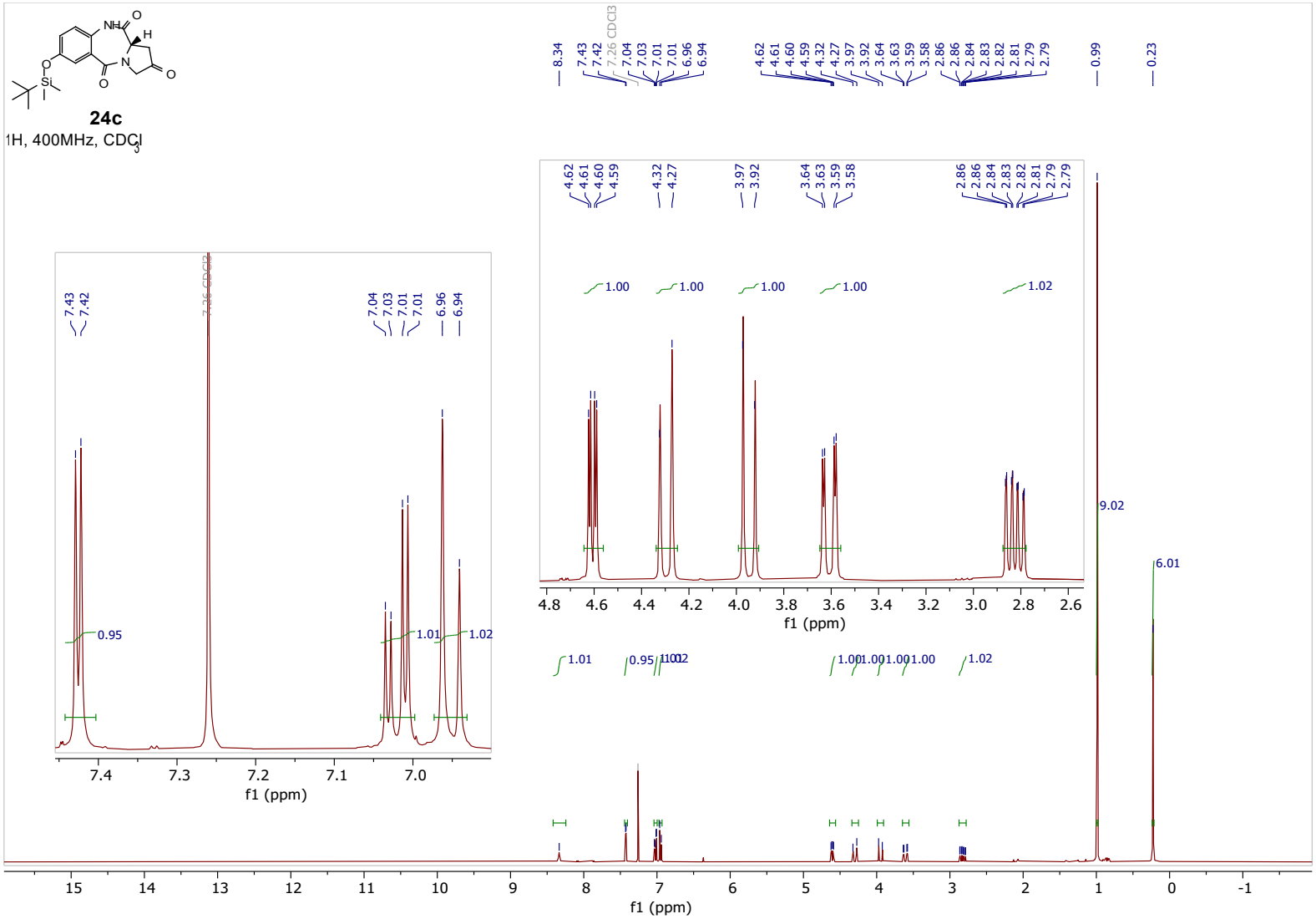

27c
13C{1H}, 100MHz, CDCl3
170.3
165.7
153.3
128.7
127.9
124.9
122.6
121.7
77.2 CDCl3
69.1
55.6
54.5
34.9
25.7
18.3
-4.3
-4.3
-4.28
-4.31
-4.20
-4.25
-4.30
-4.35
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

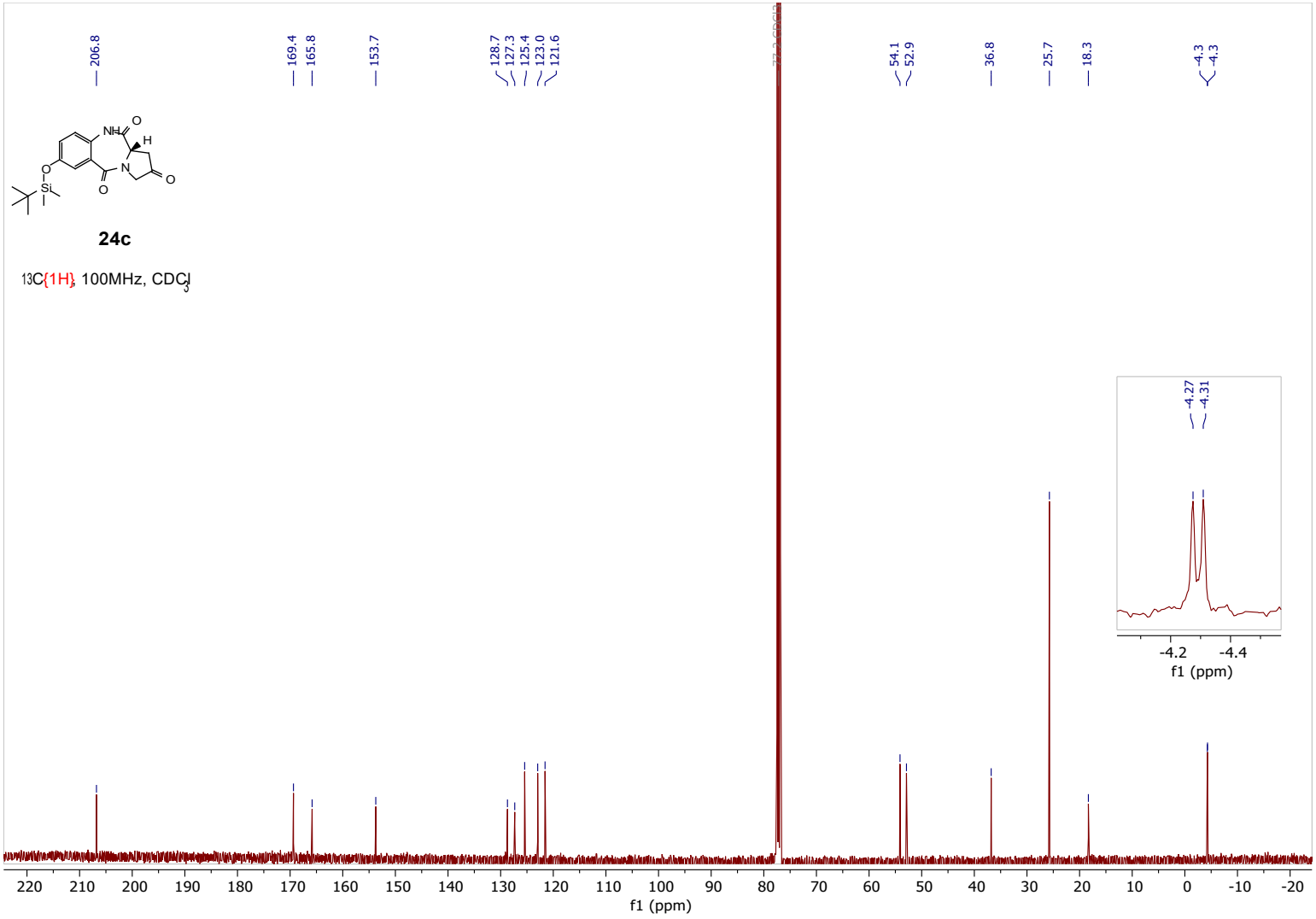

24a
1H, 400MHz, CDCl3
f1 (ppm)
water

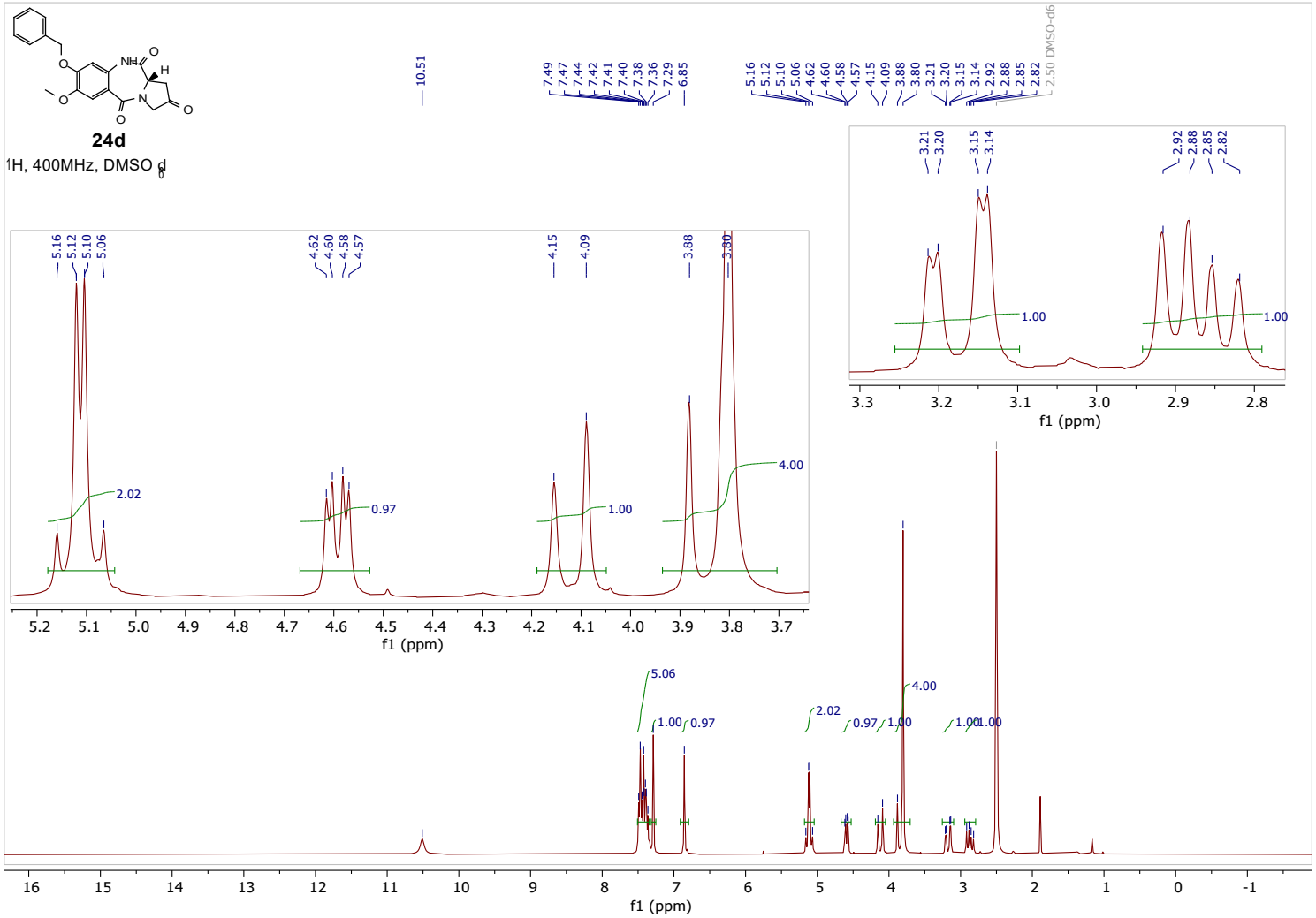

206.7
169.7
166.2
135.1
133.4
131.5
126.0
121.5
77.2 CDCl3
54.1
52.9
36.8
NH
O
H
N
O
O
24a
13C{1H}, 100MHz, CDCl3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

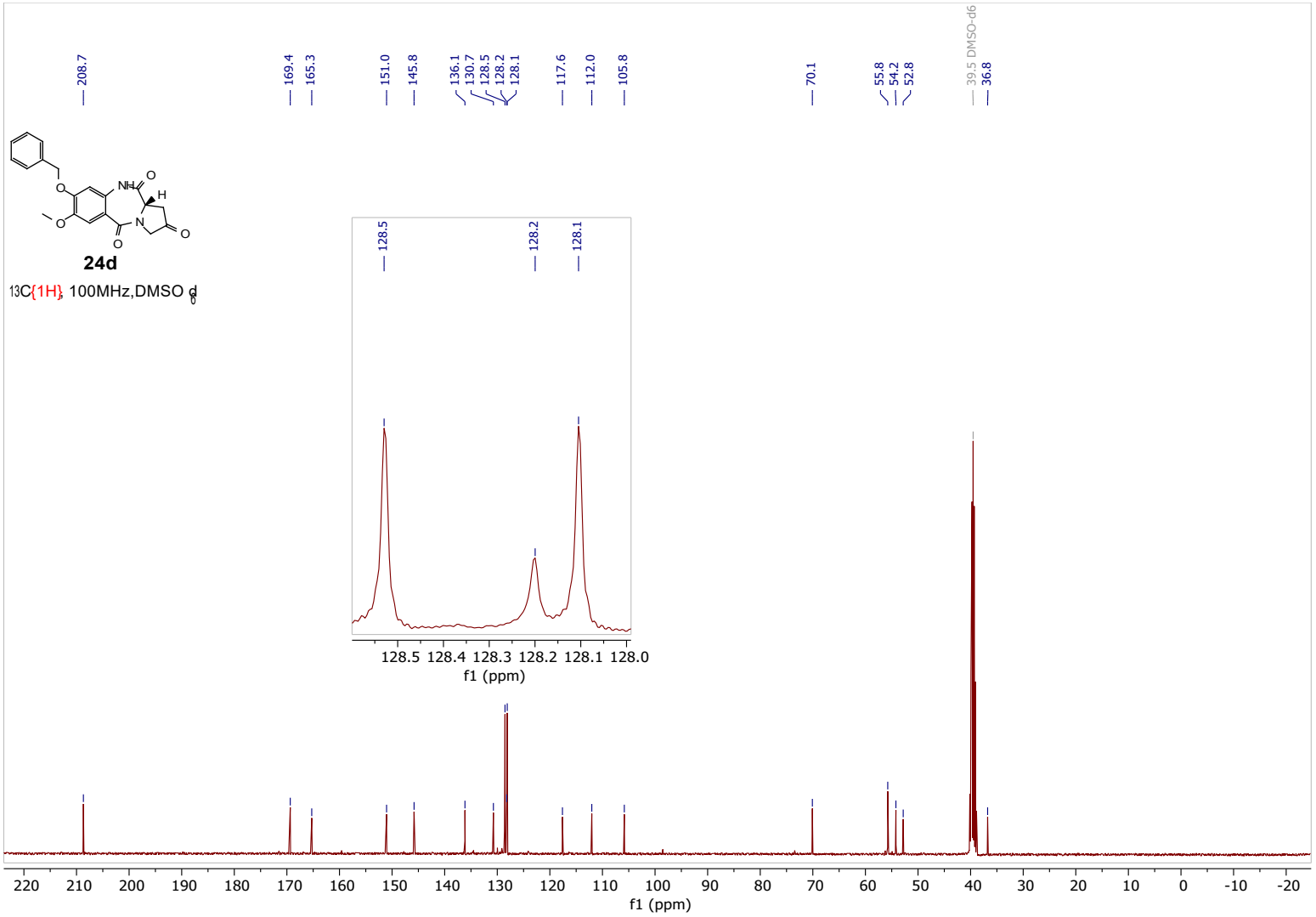

24b
1H, 400MHz, CDCl3
f1 (ppm)

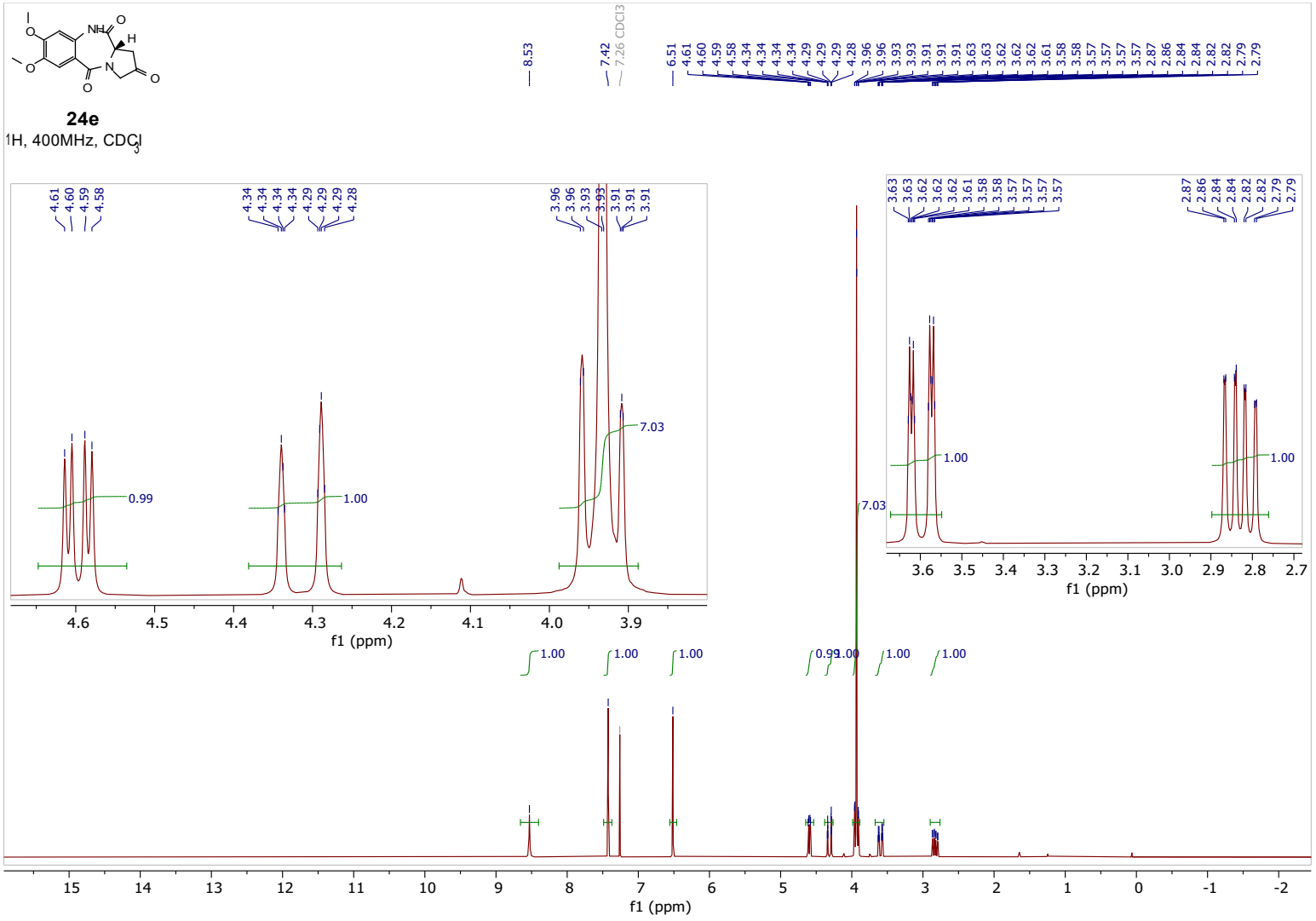

206.8
168.9
166.1
148.9
126.1
125.6
125.1
122.6
113.6
77.2 CDCl3
56.3
54.4
53.0
36.8
24b
13C{1H}, 100MHz, CDCl3
126.1
125.6
125.1
126.5
126.0
125.5
125.0
124.5
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

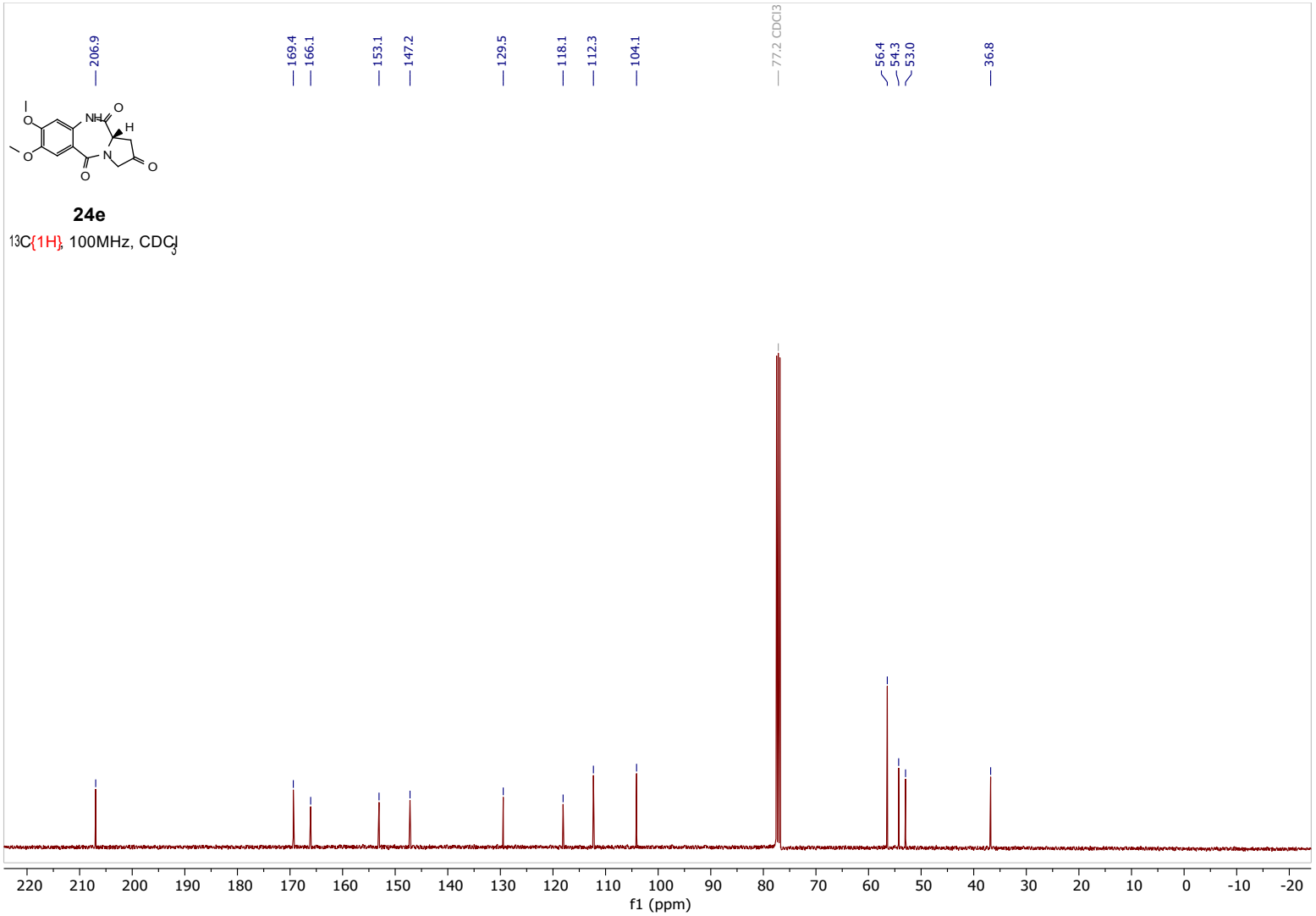

24c
1H, 400MHz, CDCl3
f1 (ppm)

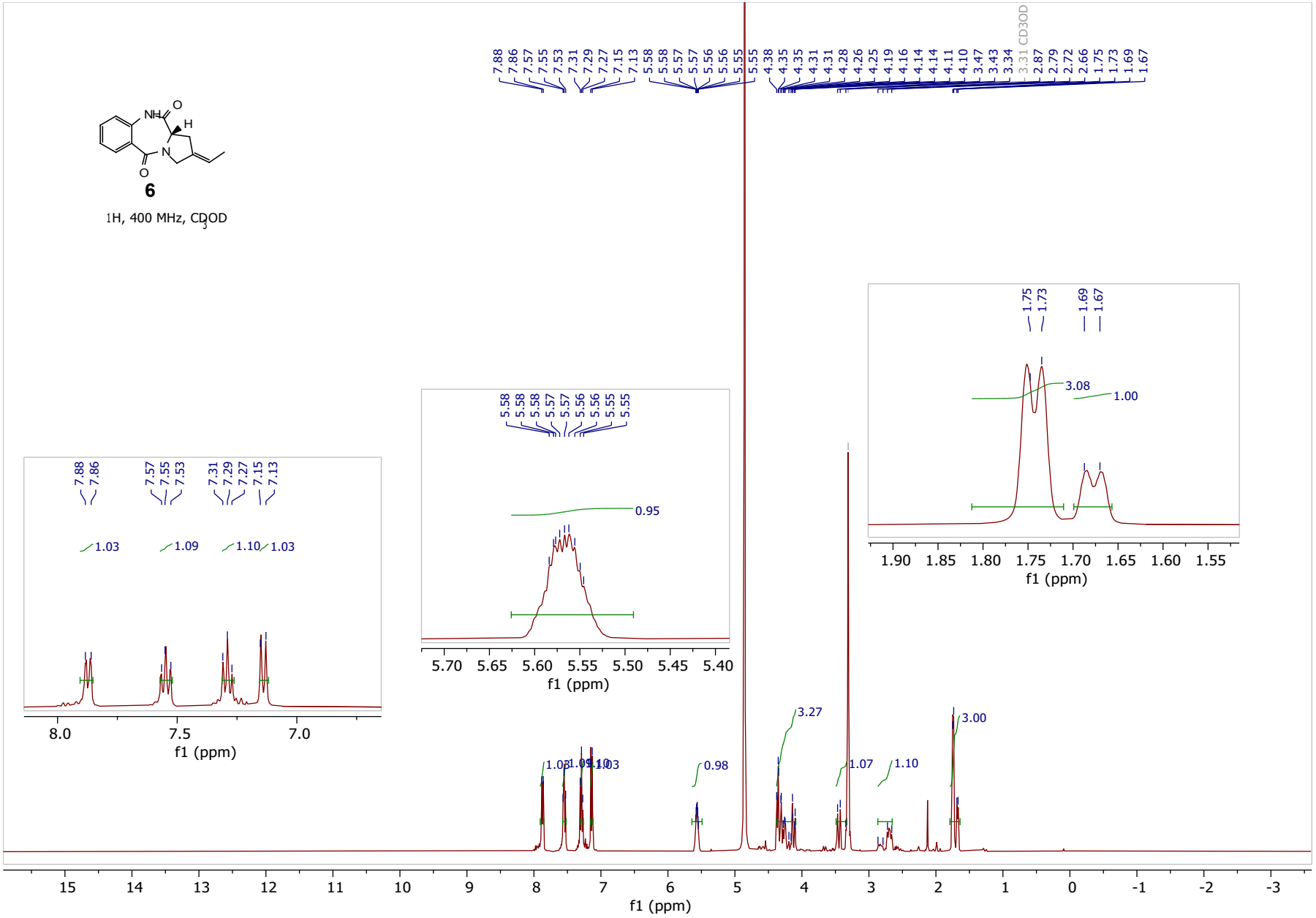

206.8
169.4
165.8
153.7
128.7
127.3
125.4
123.0
121.6
77.2 CDCl3
54.1
52.9
36.8
25.7
18.3
-4.3
-4.3
NH
O
H
N
O
O
O
Si
24c
13C{1H}, 100MHz, CDCl3
-4.27
-4.31
-4.2
-4.4
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

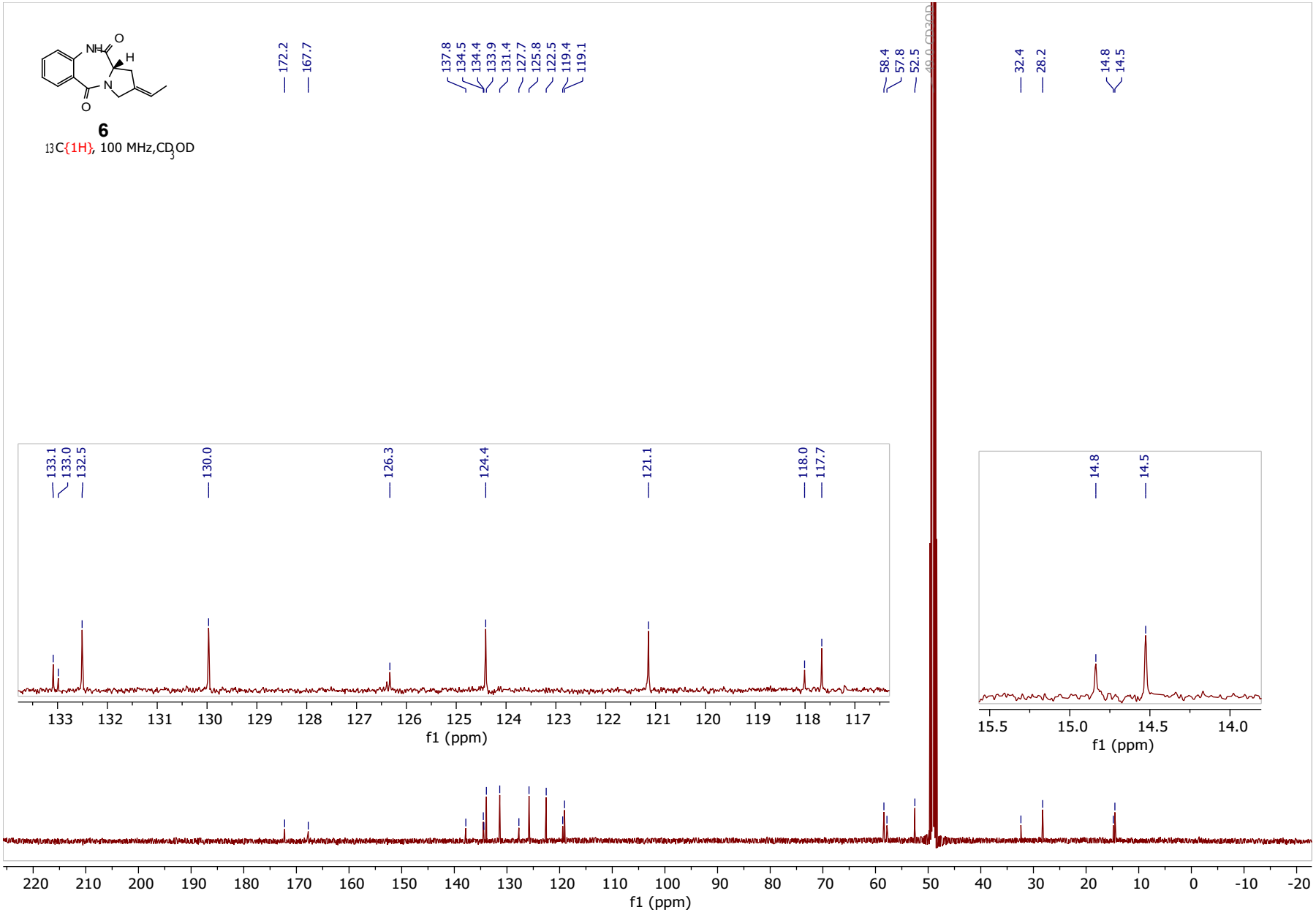

24d
1H, 400MHz, DMSO d6
10.51
7.49
7.47
7.44
7.42
7.41
7.40
7.38
7.36
7.29
6.85
5.16
5.12
5.10
5.06
4.62
4.60
4.58
4.57
4.15
4.09
3.88
3.80
3.21
3.20
3.15
3.14
2.92
2.88
2.85
2.82
2.50 DMSO-d6
2.02
0.97
1.00
4.00
f1 (ppm)

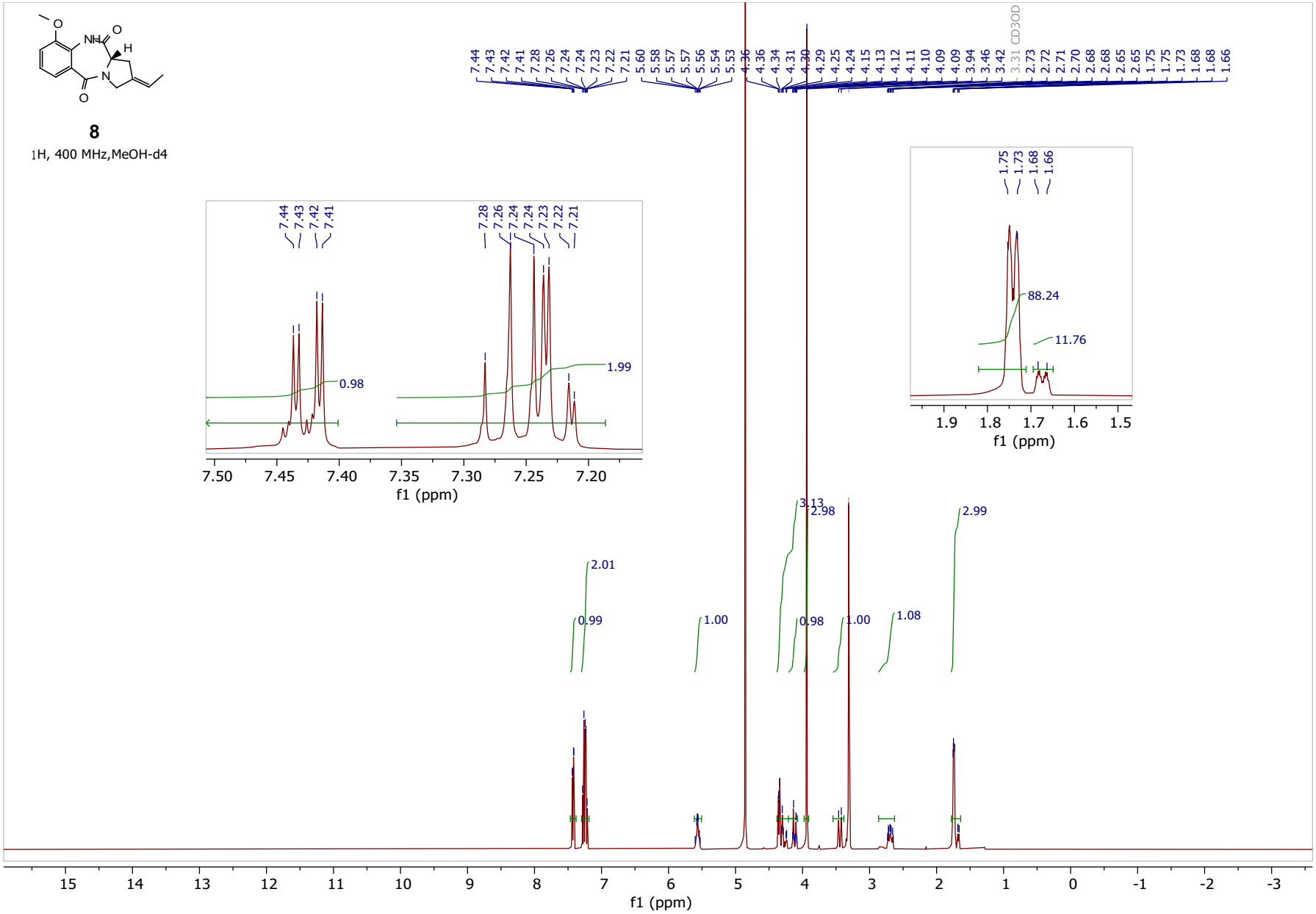

208.7
169.4
165.3
151.0
145.8
136.1
130.7
128.5
128.2
128.1
117.6
112.0
105.8
70.1
55.8
54.2
52.8
39.5 DMSO-d6
36.8
24d
13C{1H}, 100MHz,DMSO d6
128.5 128.4 128.3 128.2 128.1 128.0
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

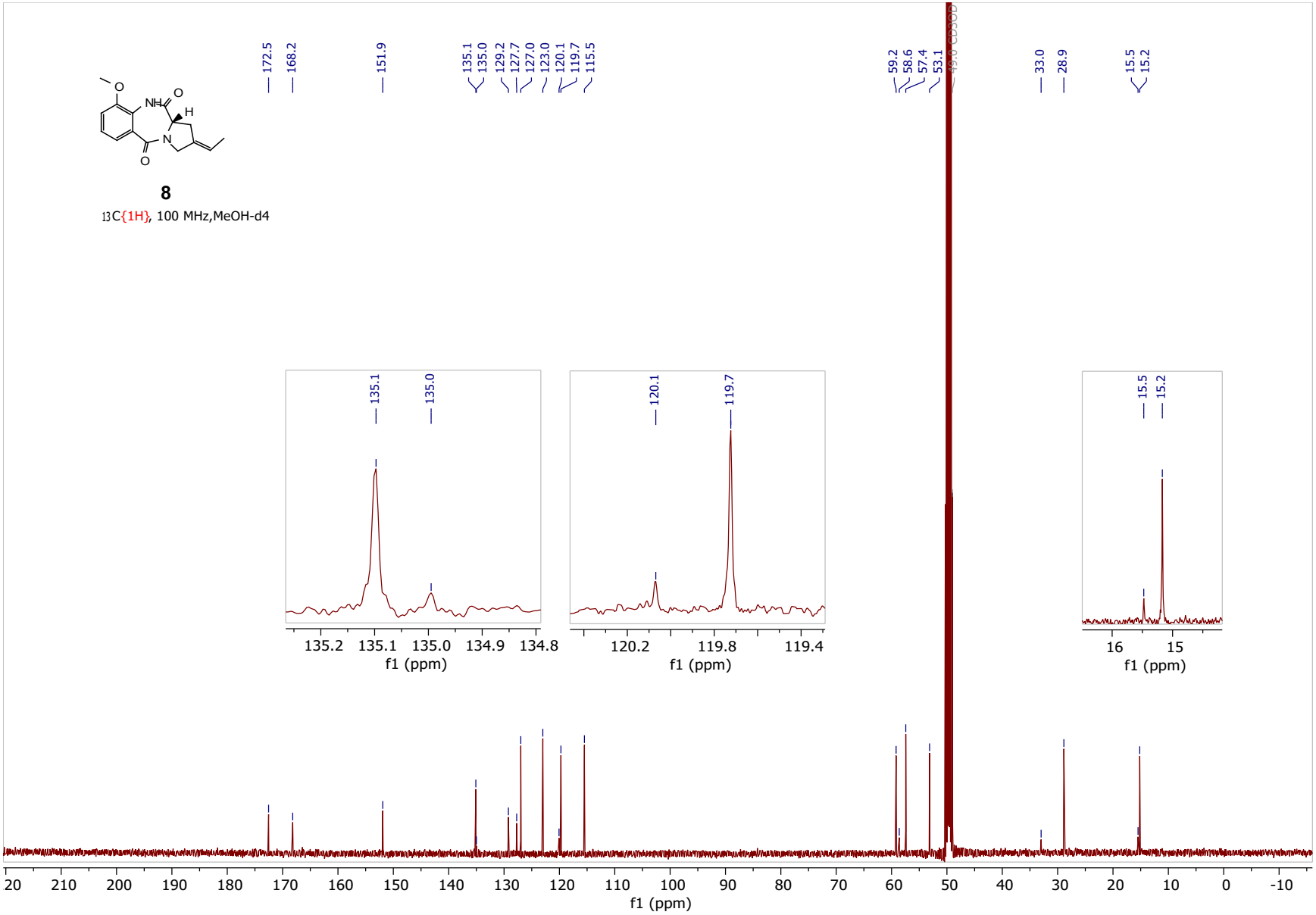

24e
1H, 400MHz, CDCl3
8.53
7.42
7.26 CDCl3
6.51
4.61
4.60
4.59
4.58
4.34
4.34
4.34
4.34
4.29
4.29
4.29
4.28
3.96
3.96
3.93
3.93
3.91
3.91
3.91
3.63
3.63
3.62
3.62
3.62
3.61
3.58
3.58
3.57
3.57
3.57
3.57
2.87
2.86
2.84
2.84
2.82
2.82
2.79
2.79
0.99
1.00
7.03
1.00
1.00
f1 (ppm)
7.03
1.00
1.00
f1 (ppm)
1.00
1.00
1.00
0.99
1.00
1.00
1.00
f1 (ppm)

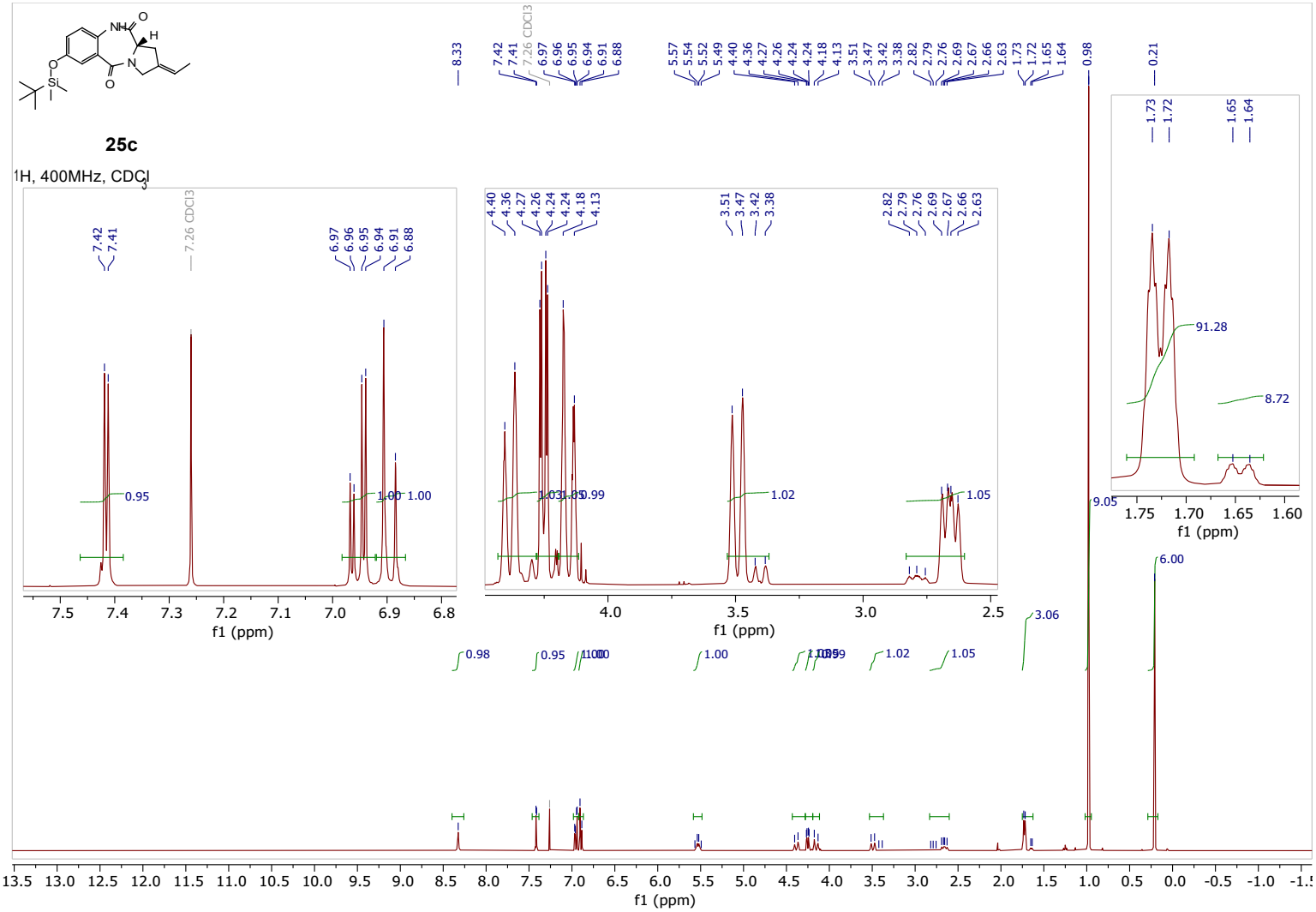

206.9
169.4
166.1
153.1
147.2
129.5
118.1
112.3
104.1
77.2 CDCl3
56.4
54.3
53.0
36.8
24e
13C{1H}, 100MHz, CDCl3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

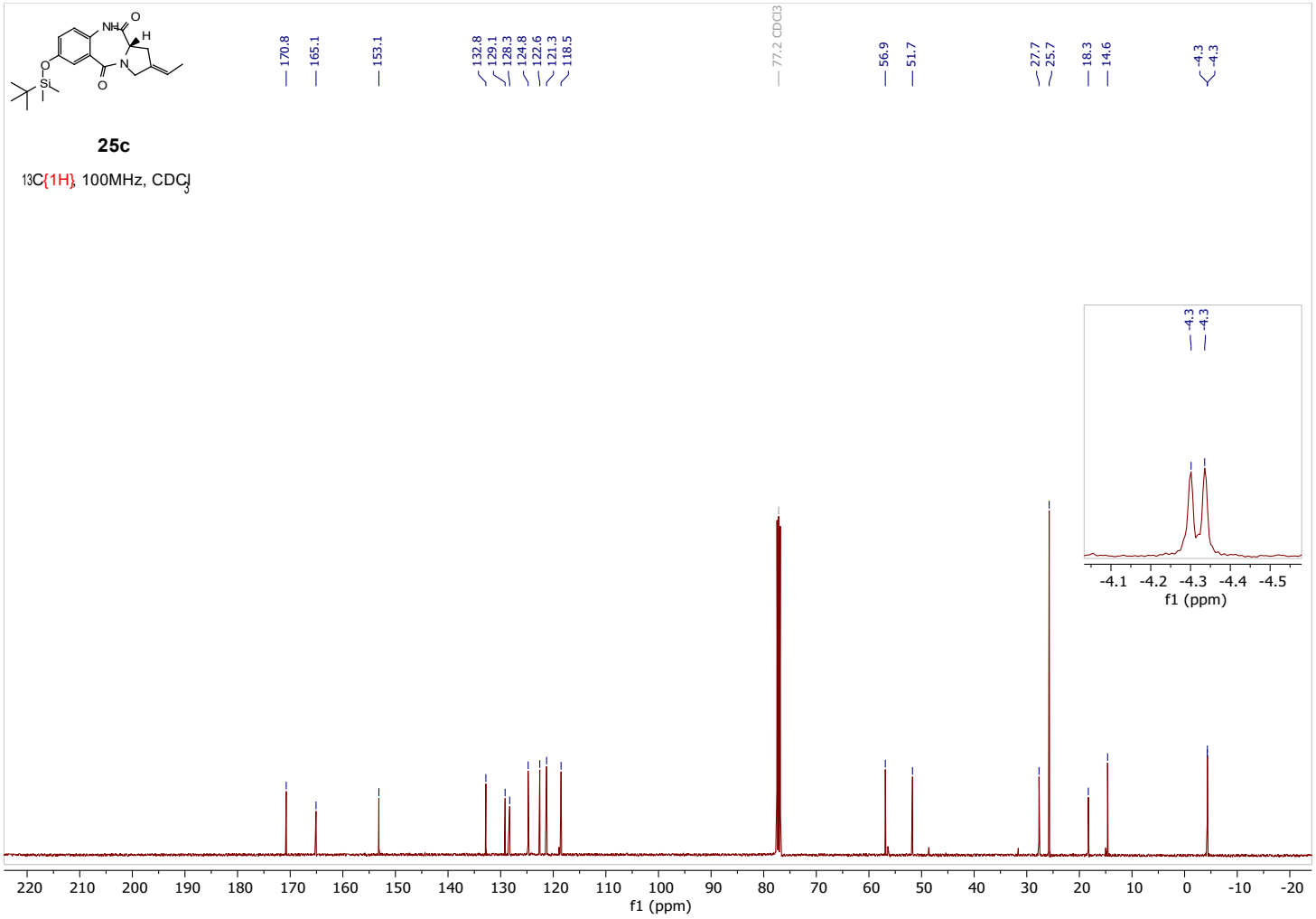

6
1H, 400 MHz, CD3OD
7.88 7.86 7.57 7.55 7.53 7.31 7.29 7.27 7.15 7.13 5.58 5.58 5.57 5.57 5.56 5.56 5.55 5.55 5.55 4.38 4.35 4.35 4.31 4.31 4.28 4.26 4.25 4.19 4.16 4.14 4.14 4.11 4.10 3.47 3.43 3.34 3.31 CD3OD 2.87 2.79 2.72 2.66 1.75 1.73 1.69 1.67
1.03 1.09 1.10 1.03
f1 (ppm)
0.95
f1 (ppm)
1.75 1.73 1.69 1.67
3.08 1.00
f1 (ppm)
1.03 1.09 1.10 1.03 0.98 3.27 1.07 1.10 3.00
f1 (ppm)

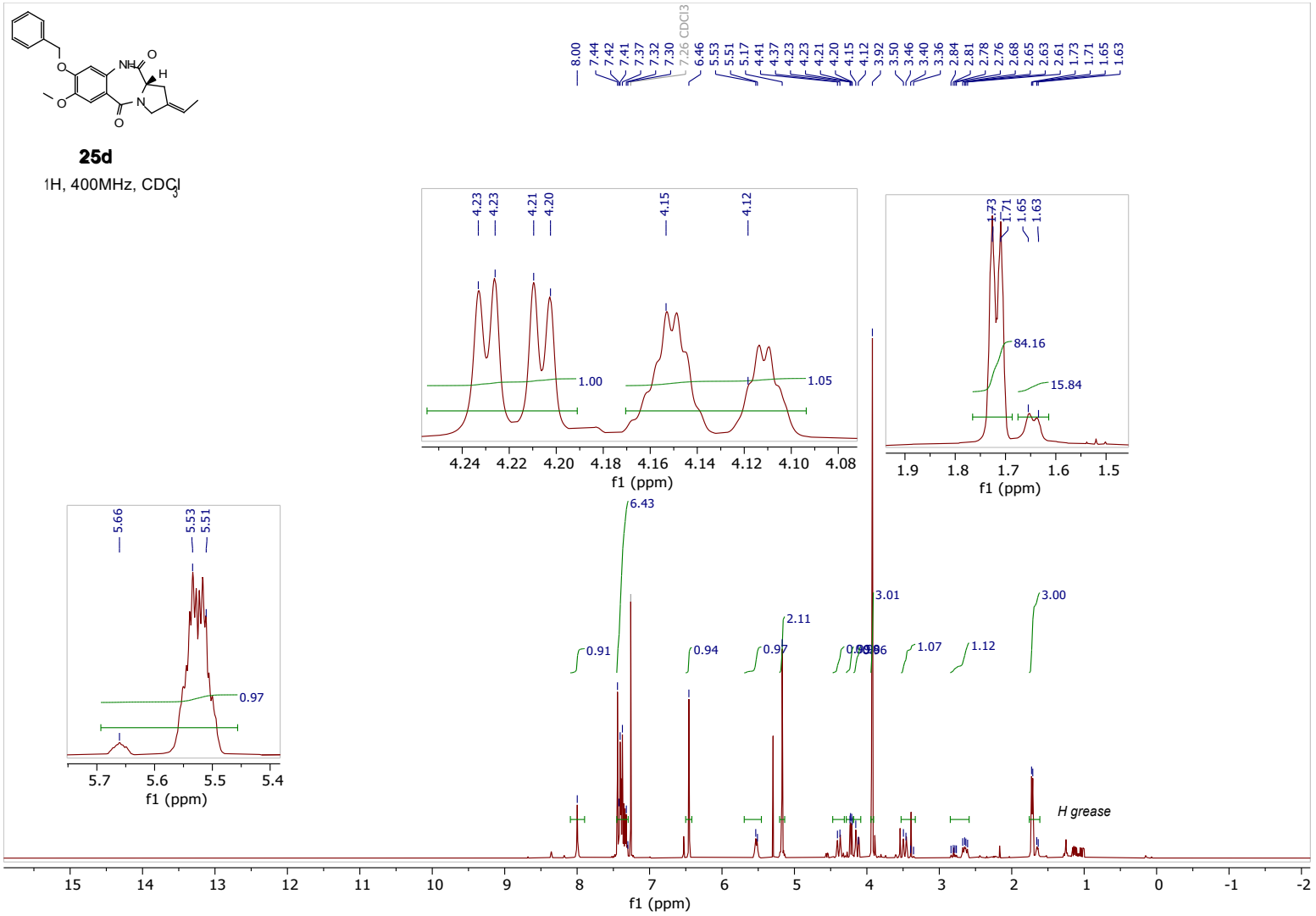

6
13C{1H}, 100 MHz, CD3OD
172.2
167.7
137.8
134.5
134.4
133.9
131.4
127.7
125.8
122.5
119.4
119.1
58.4
57.8
52.5
49.0 CD3OD
32.4
28.2
14.8
14.5
133.1
133.0
132.5
130.0
126.3
124.4
121.1
118.0
117.7
f1 (ppm)
f1 (ppm)
f1 (ppm)

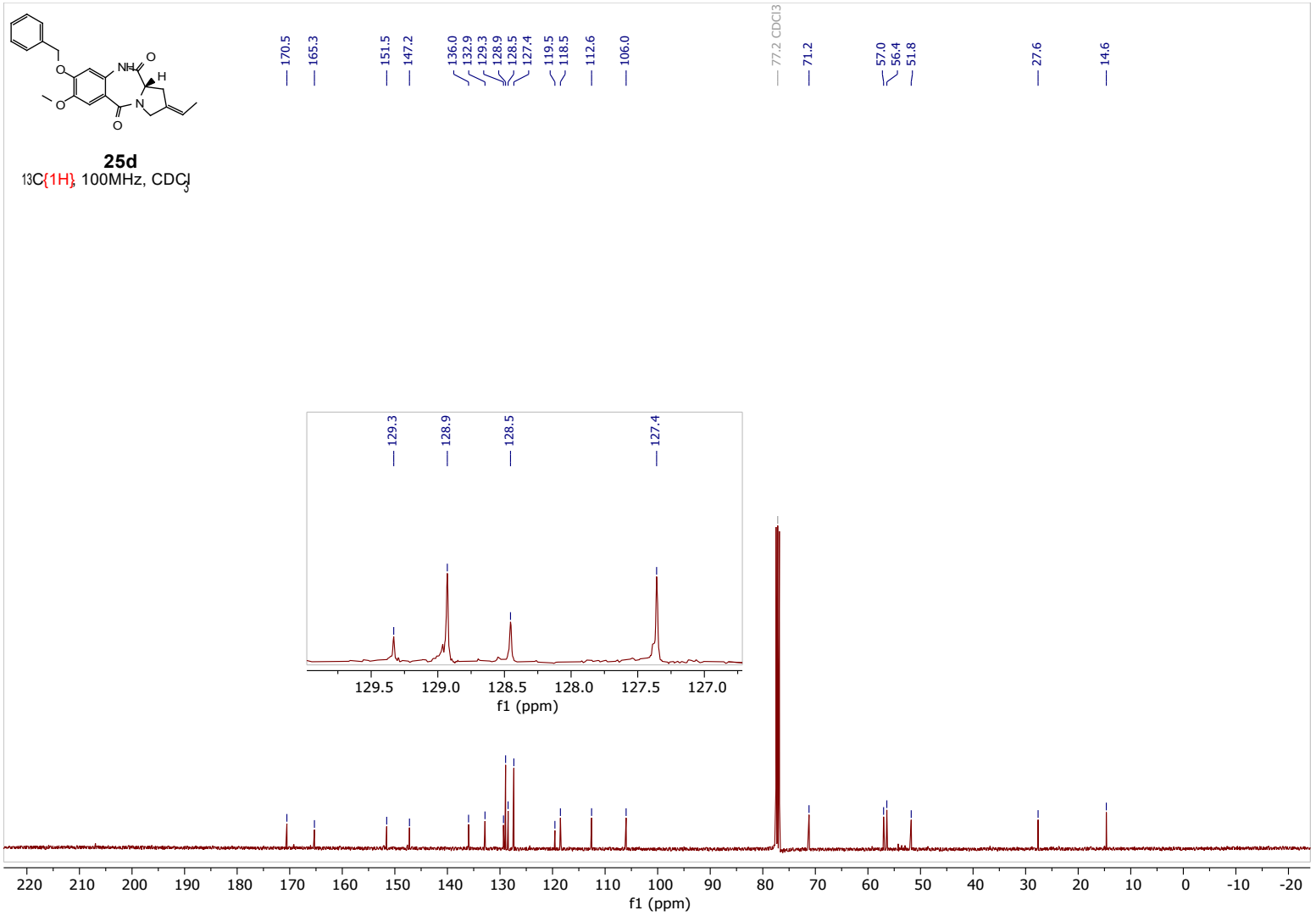

8
1H, 400 MHz,MeOH-d4
7.44 7.43 7.42 7.41 7.28 7.26 7.24 7.24 7.23 7.22 7.21 5.60 5.58 5.57 5.57 5.56 5.54 5.53 4.36 4.36 4.34 4.31 4.30 4.29 4.25 4.24 4.15 4.13 4.12 4.11 4.10 4.09 4.09 3.94 3.46 3.42 3.31 CD3OD 2.73 2.72 2.71 2.70 2.68 2.68 2.65 2.65 1.75 1.75 1.73 1.68 1.68 1.66
0.98
1.99
f1 (ppm)
1.75 1.73 1.68 1.66
88.24
11.76
f1 (ppm)
2.01
0.99
1.00
3.13
2.98
0.98
1.00
1.08
2.99
f1 (ppm)

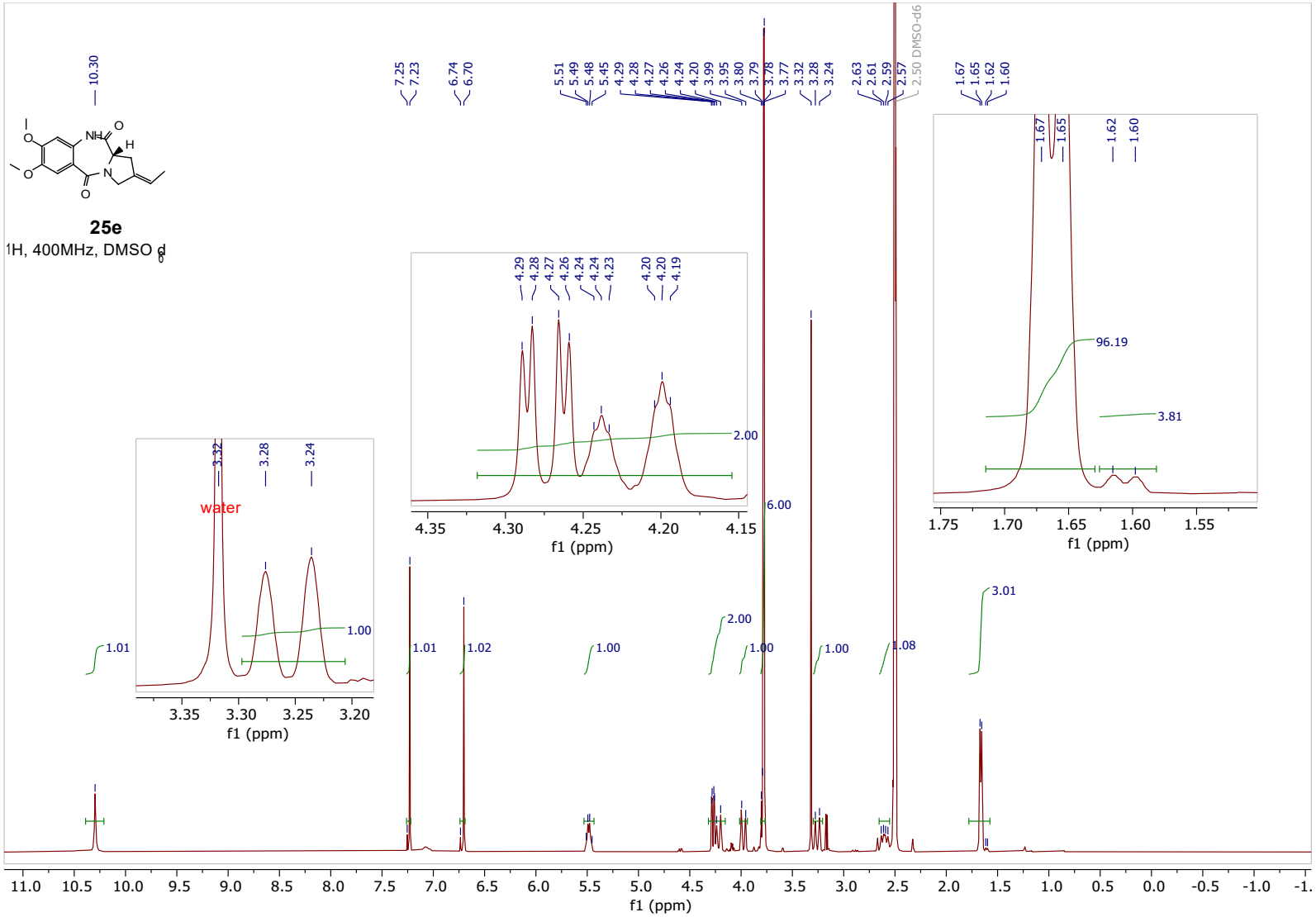

172.5
168.2
151.9
135.1
135.0
129.2
127.7
127.0
123.0
120.1
119.7
115.5
59.2
58.6
57.4
53.1
49.0 CD3OD
33.0
28.9
15.5
15.2
8
13C{1H}, 100 MHz,MeOH-d4
135.1
135.0
135.2 135.1 135.0 134.9 134.8
f1 (ppm)
120.1
119.7
120.2 119.8 119.4
f1 (ppm)
15.5
15.2
16 15
f1 (ppm)
f1 (ppm)

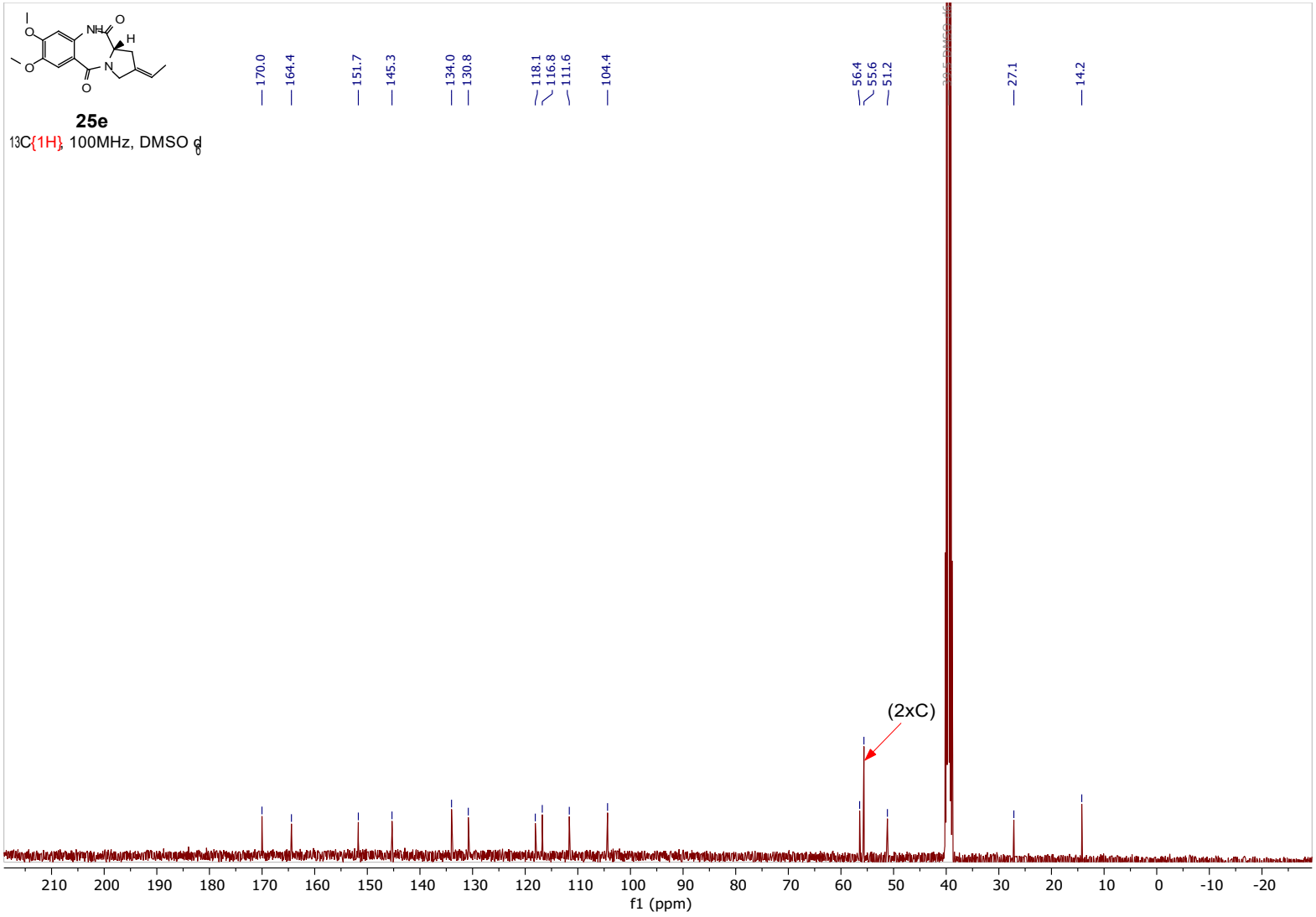

25c
1H, 400MHz, CDCl3
f1 (ppm)

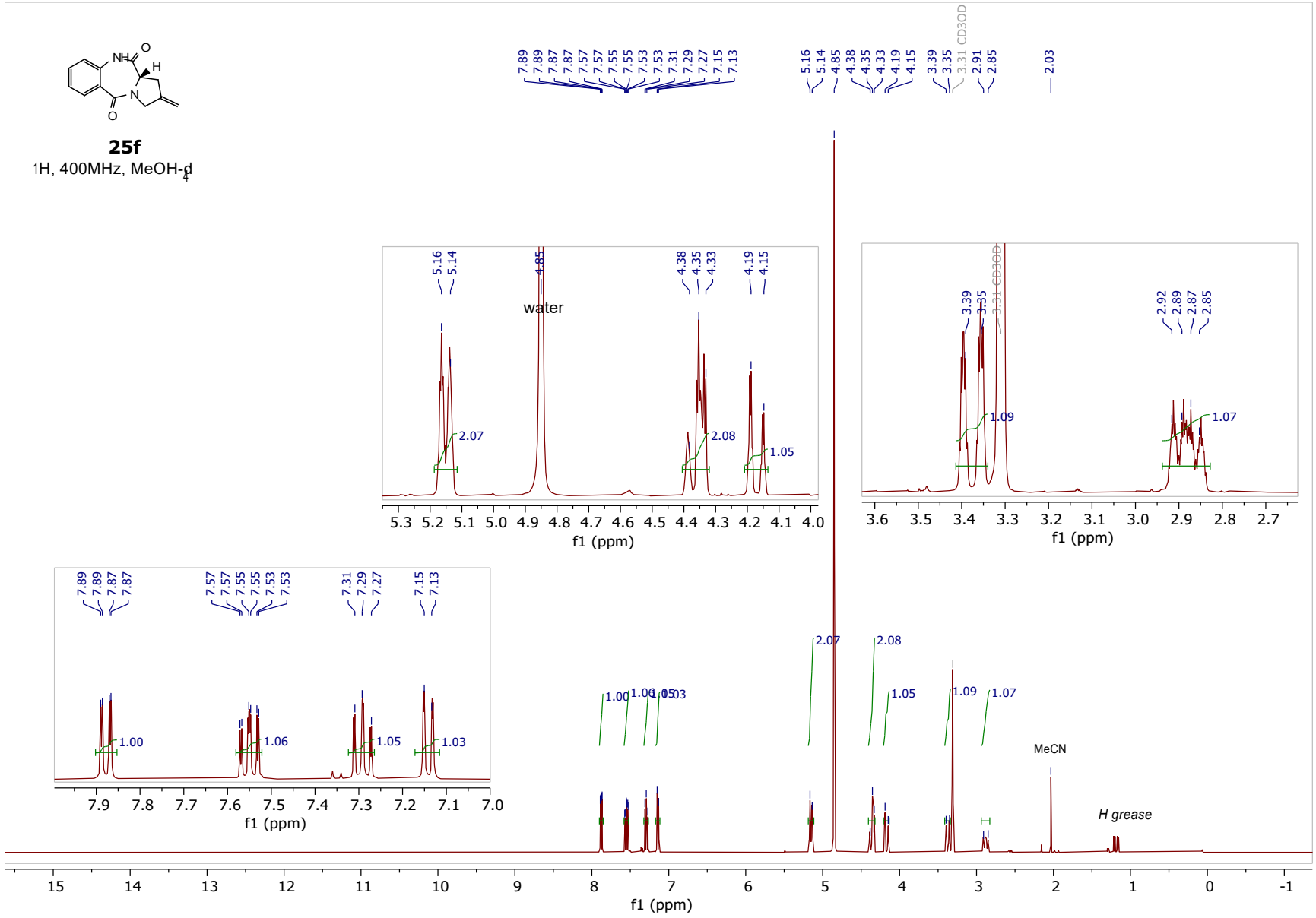

25c
13C{1H}, 100MHz, CDCl3
170.8
165.1
153.1
132.8
129.1
128.3
124.8
122.6
121.3
118.5
77.2 CDCl3
56.9
51.7
27.7
25.7
18.3
14.6
-4.3
-4.3
f1 (ppm)

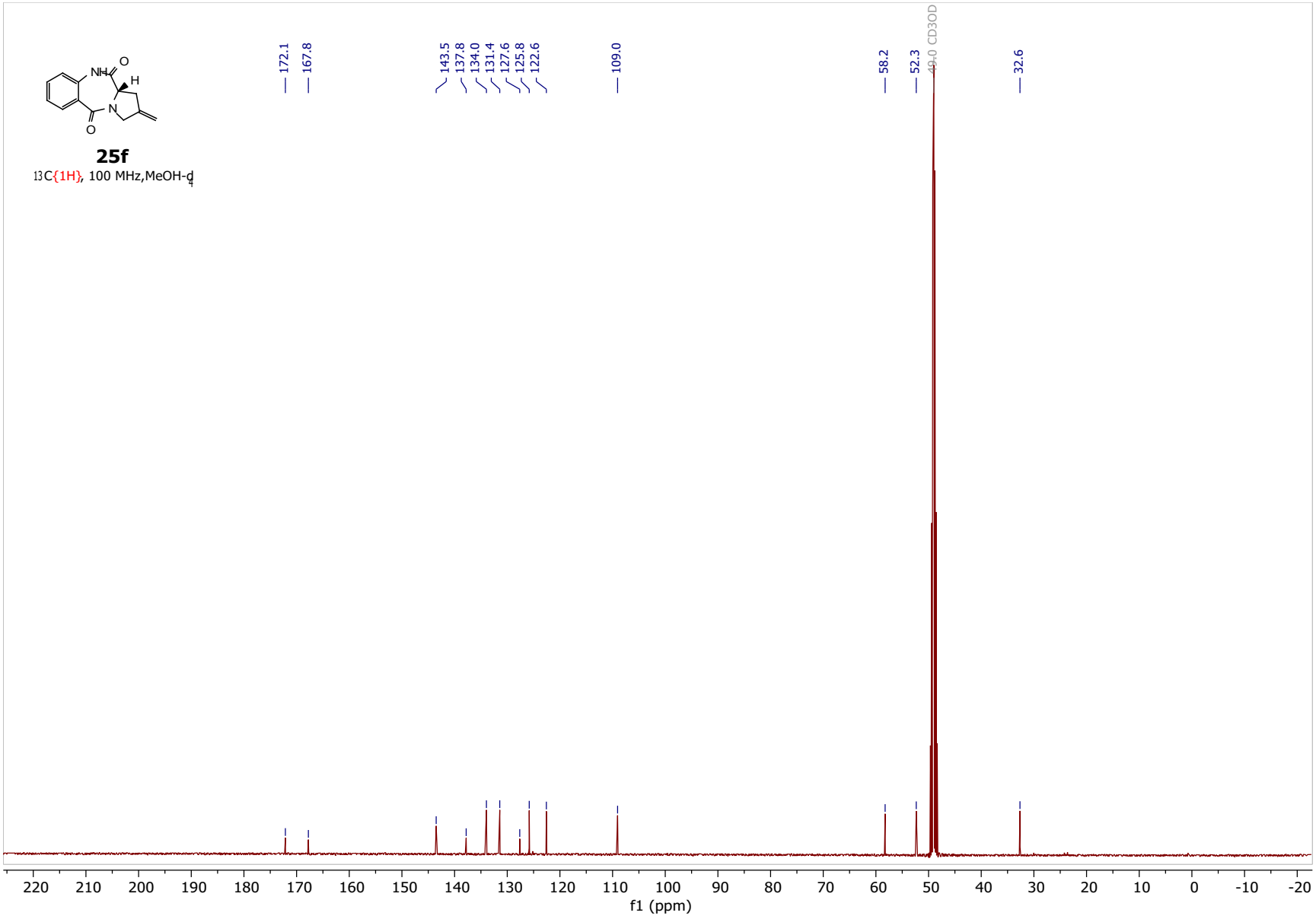

25d
1H, 400MHz, CDCl3
8.00
7.44
7.42
7.41
7.37
7.32
7.30
7.26 CDCl3
6.46
5.53
5.51
5.17
4.41
4.37
4.23
4.23
4.21
4.20
4.15
4.12
3.92
3.50
3.46
3.40
3.36
2.84
2.81
2.78
2.76
2.68
2.65
2.63
2.61
1.73
1.71
1.65
1.63
1.00
1.05
84.16
15.84
0.91
6.43
0.94
0.97
2.11
3.01
1.07
1.12
3.00
0.97
H grease
f1 (ppm)

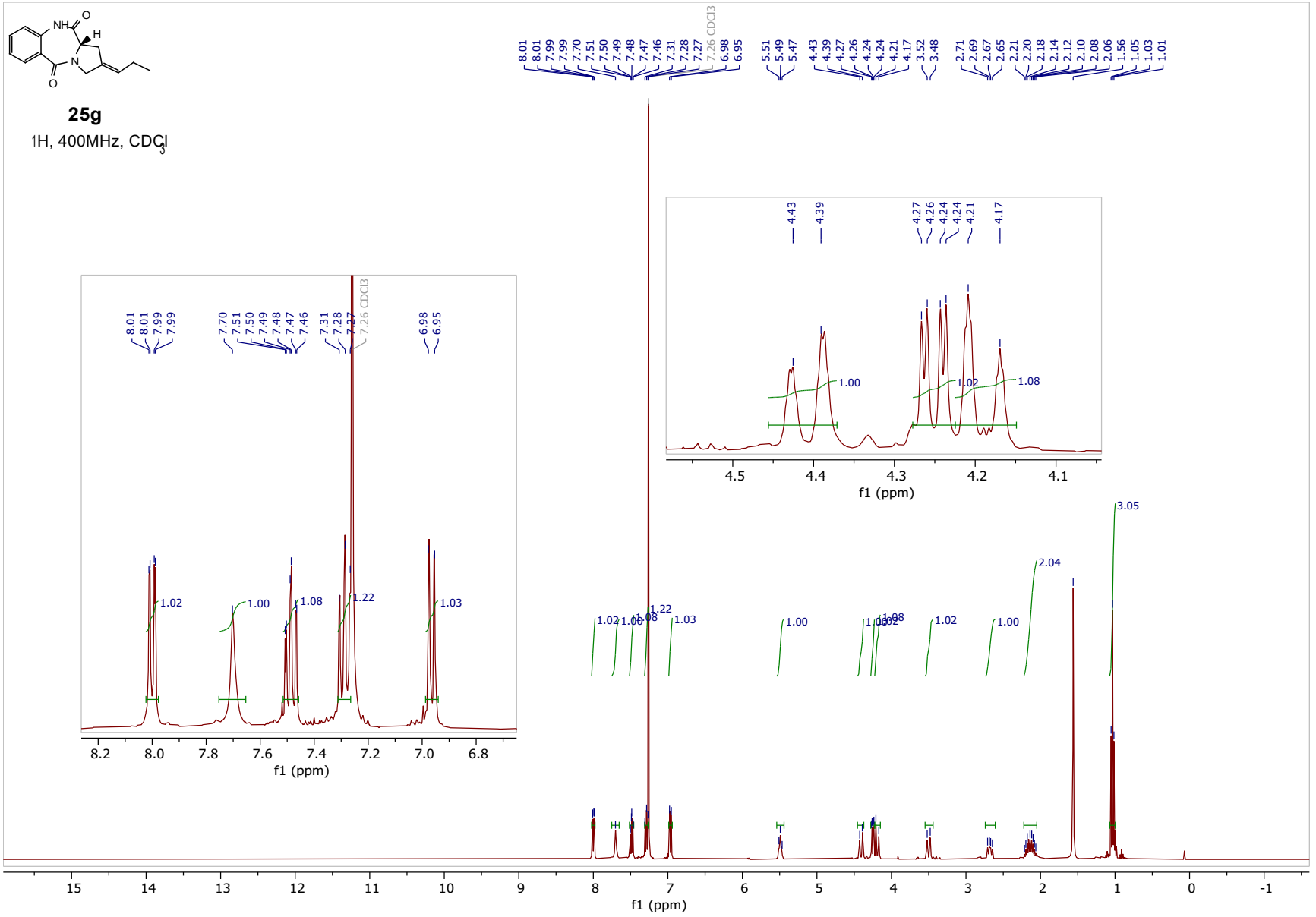

25d
13C{1H}, 100MHz, CDCl3
170.5
165.3
151.5
147.2
136.0
132.9
129.3
128.9
128.5
127.4
119.5
118.5
112.6
106.0
77.2 CDCl3
71.2
57.0
56.4
51.8
27.6
14.6
129.3
128.9
128.5
127.4
129.5
129.0
128.5
128.0
127.5
127.0
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

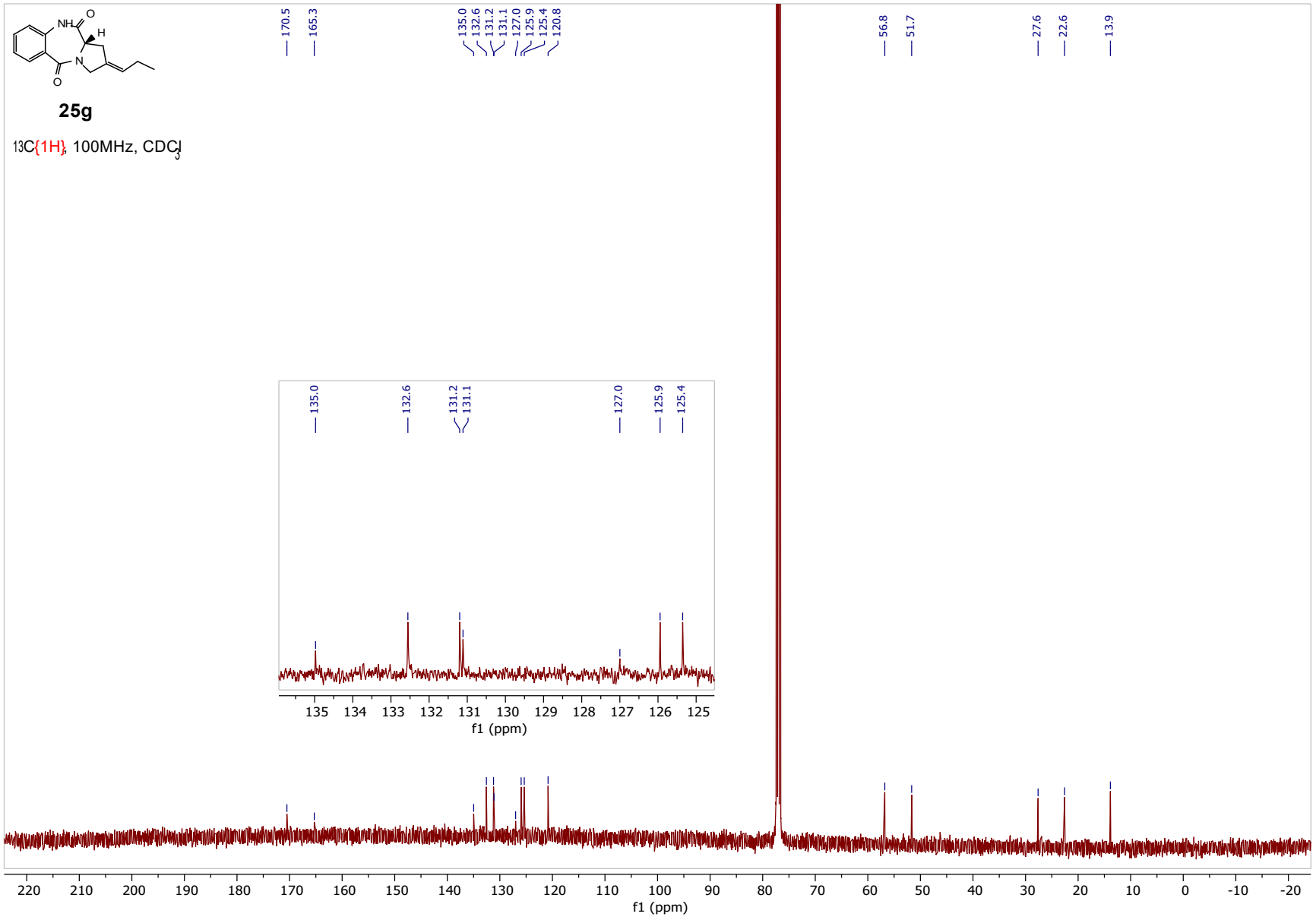

25e
1H, 400MHz, DMSO d6
water
DMSO-d6
f1 (ppm)

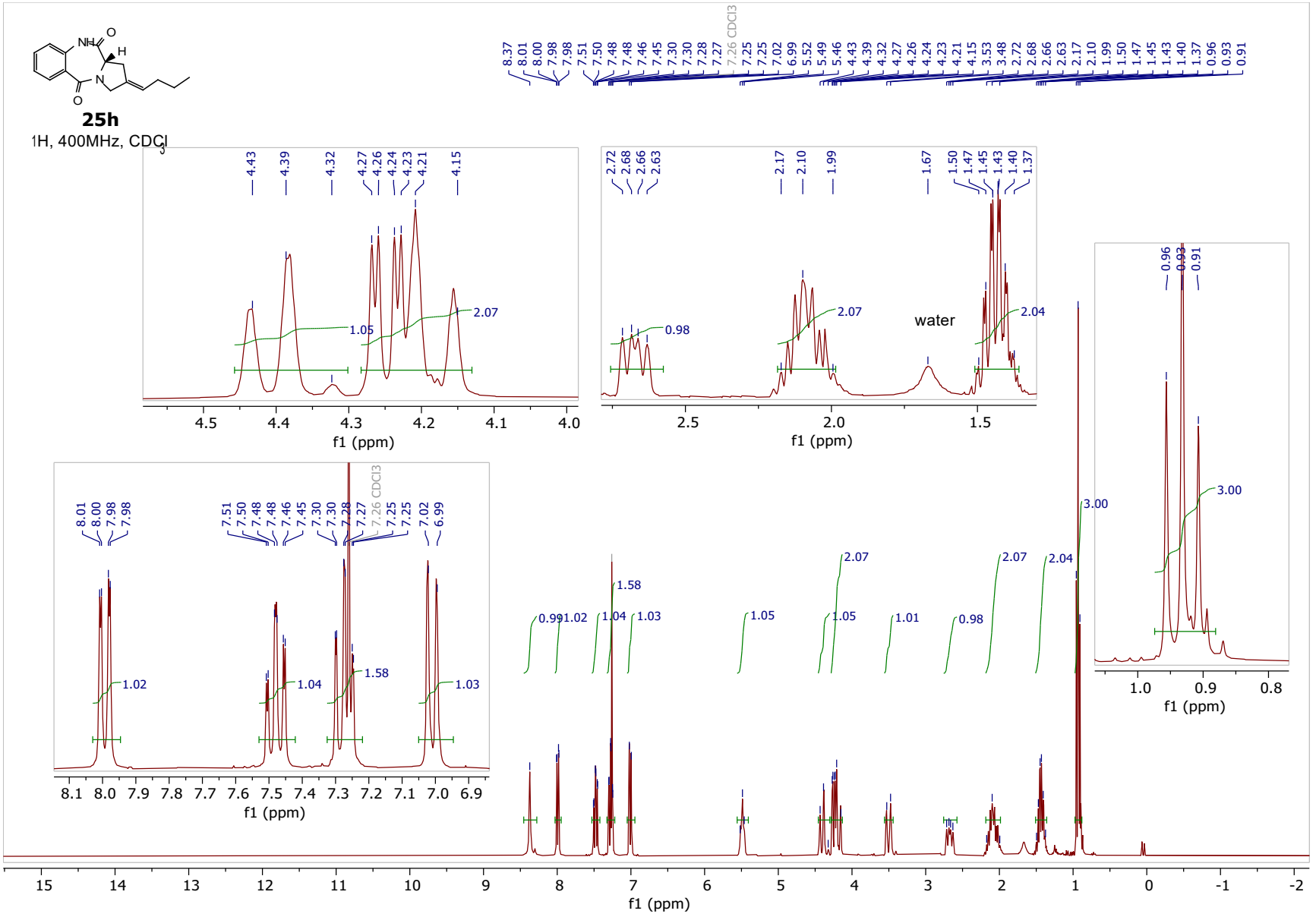

25e
13C{1H}, 100MHz, DMSO d6
170.0
164.4
151.7
145.3
134.0
130.8
118.1
116.8
111.6
104.4
56.4
55.6
51.2
27.1
14.2
(2xC)
f1 (ppm)

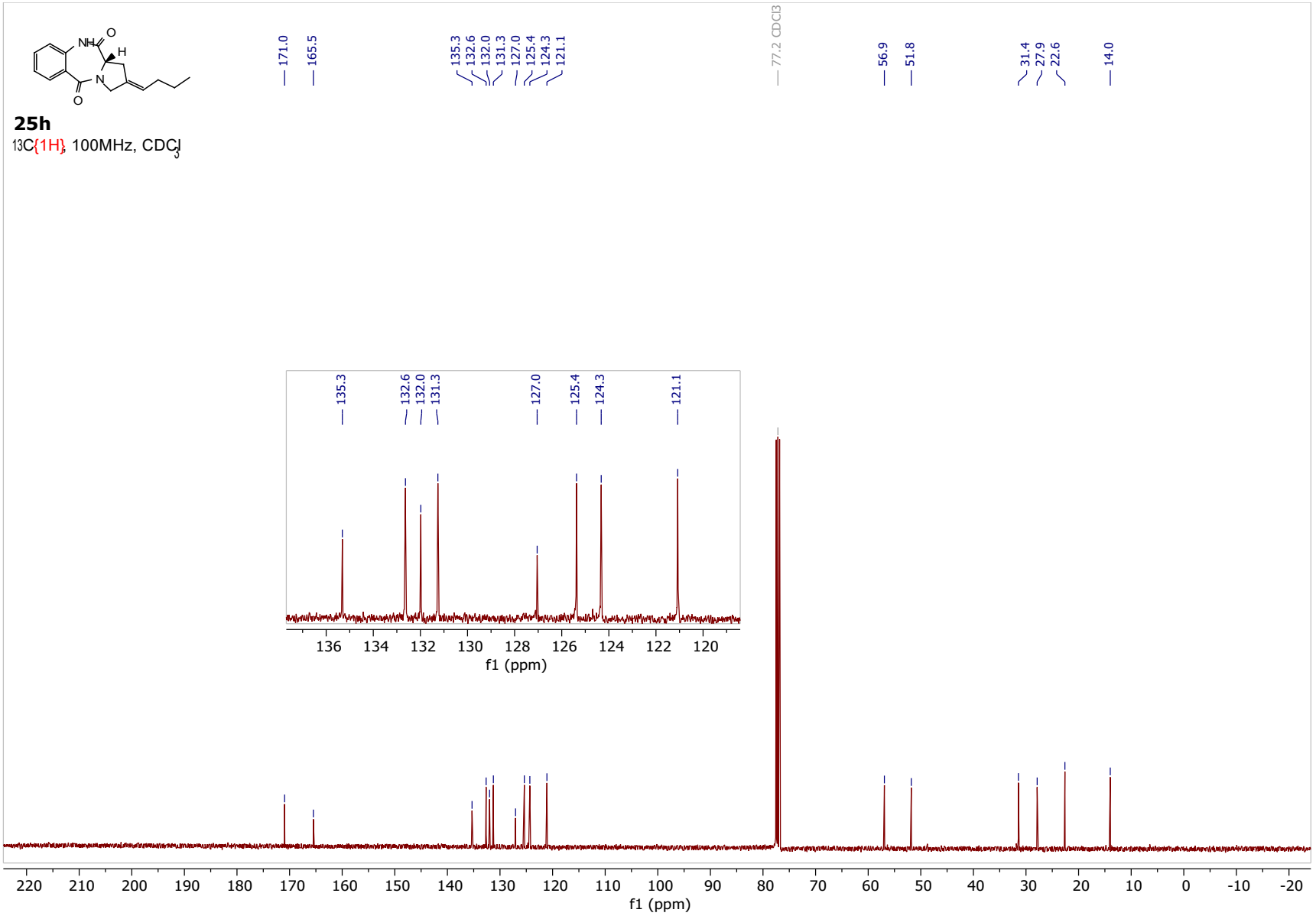

25f
1H, 400MHz, MeOH-d4
water
MeCN
H grease
f1 (ppm)

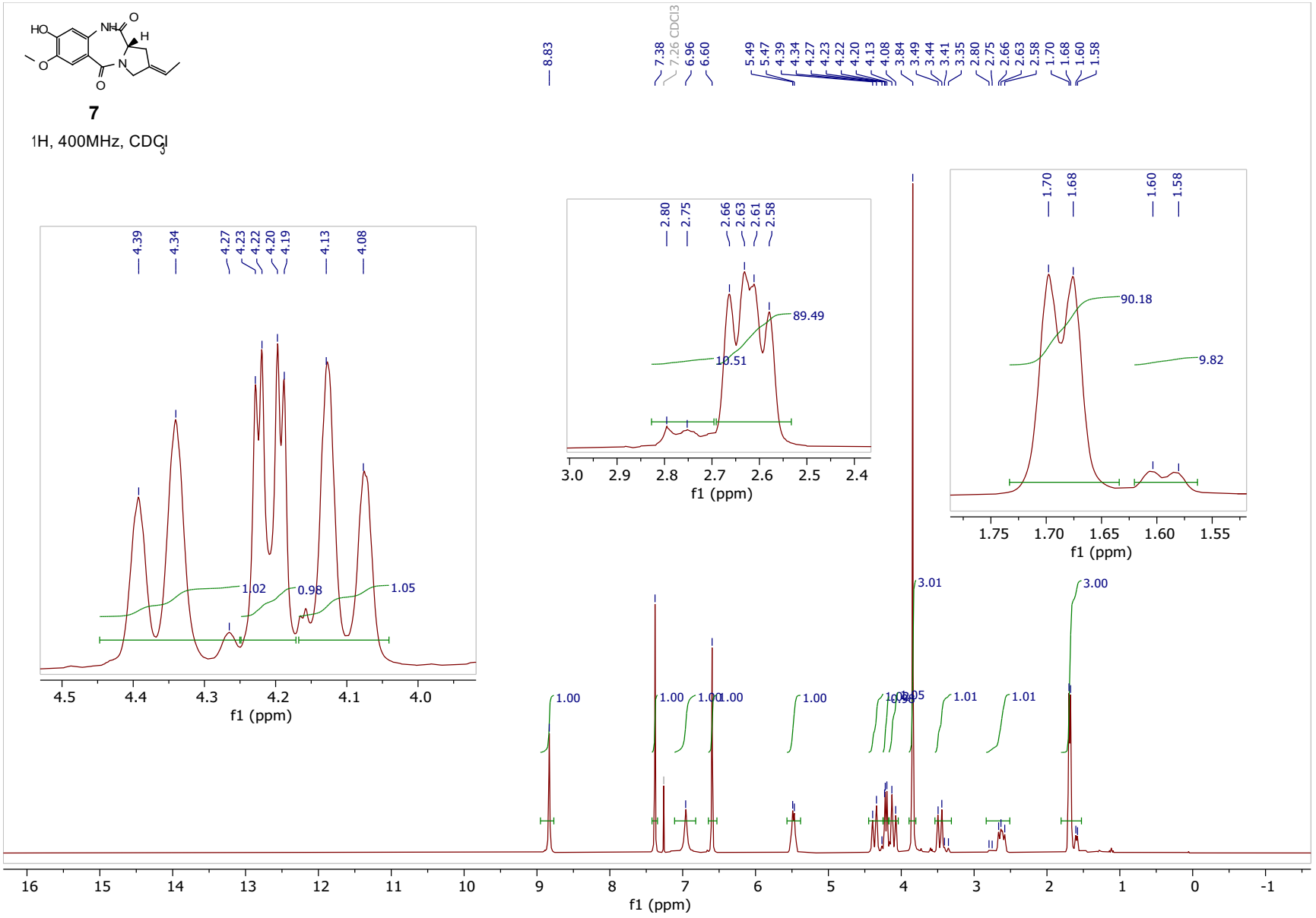

25f
13C{1H}, 100 MHz,MeOH-d4
172.1
167.8
143.5
137.8
134.0
131.4
127.6
125.8
122.6
109.0
58.2
52.3
49.0 CD3OD
32.6
f1 (ppm)

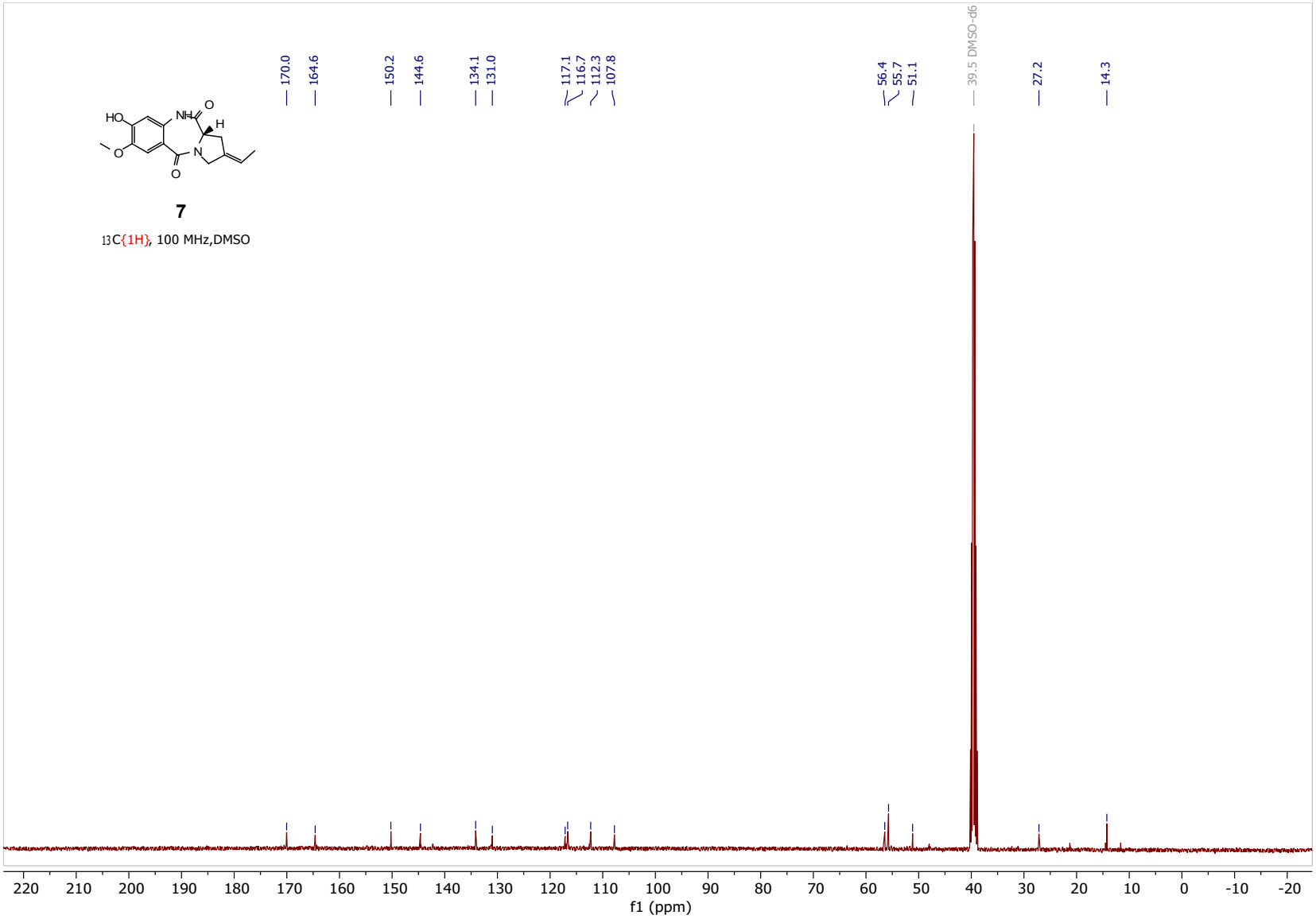

25g
1H, 400MHz, CDCl3
f1 (ppm)


25g
13C{1H}, 100MHz, CDCl3
170.5
165.3
135.0
132.6
131.2
131.1
127.0
125.9
125.4
120.8
56.8
51.7
27.6
22.6
13.9
f1 (ppm)
f1 (ppm)


25h
1H, 400MHz, CDCl3
water
CDCl3
f1 (ppm)


171.0
165.5
135.3
132.6
132.0
131.3
127.0
125.4
124.3
121.1
77.2 CDCl3
56.9
51.8
31.4
27.9
22.6
14.0
25h
13C{1H}, 100MHz, CDCl3
f1 (ppm)


7
1H, 400MHz, CDCl3
8.83
7.38
7.26 CDCl3
6.96
6.60
5.49
5.47
4.39
4.34
4.27
4.23
4.22
4.20
4.13
4.08
3.84
3.49
3.44
3.41
3.35
2.80
2.75
2.66
2.63
2.58
1.70
1.68
1.60
1.58
1.00
1.00
1.00
1.00
1.00
3.01
1.01
1.01
3.00
f1 (ppm)
4.39
4.34
4.27
4.23
4.22
4.20
4.19
4.13
4.08
1.02
0.98
1.05
f1 (ppm)
2.80
2.75
2.66
2.63
2.61
2.58
89.49
10.51
f1 (ppm)
1.70
1.68
1.60
1.58
90.18
9.82
f1 (ppm)


HO
O
NH
O
H
N
O
7
13C{1H}, 100 MHz,DMSO
170.0
164.6
150.2
144.6
134.1
131.0
117.1
116.7
112.3
107.8
56.4
55.7
51.1
39.5 DMSO-d6
27.2
14.3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

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