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Ammonium persulfate activated DMSO as the one-carbon synthon for the synthesis of methylenebisamides and other applications

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General information

All reagents and solvents were used as received from commercial sources unless otherwise noted. All amides were procured from commercial sources and used as it is. All experiments were carried out under air atmosphere. Pre-coated plates (silica gel 60 PF254, 0.25 mm or 0.5 mm) were utilized for thin layer chromatography (TLC). Column chromatographic purifications were carried out on flash silica-gel (240–400 mesh) using petroleum ether and ethyl acetate as eluents. The ^{1}H, ^{13}C NMR spectra were recorded on 200/400/500 MHz, and 50/100/125 MHz NMR spectrometers, respectively in $CDCl_3$/DMSO-d_6. Chemical shifts were reported as δ values from standard peaks. Melting points are uncorrected. Mass spectra were taken on LC-MS (ESI) mass or GC-MS mass spectrometer. HRMS were scanned on Quadrupole-Orbitrap Mass Spectrometer available at our institutional facility.

General procedure for the synthesis of methylenebisamides

A solution of amide (50 mg, 1 equiv), ammonium persulfate [$(NH_4)_2S_2O_8$] (2 equiv) and DMSO (6 equiv) in 1,4-dioxane (2 mL) was heated at 100 ^{o}C in a round bottom flask, equipped with a stirring bar and water condenser, until the reaction was complete as indicated by thin layer chromatography. After completion, the reaction mixture was filtered through a cotton plug and 1,4-dioxane was removed under vacuum. The residue was then dissolved in ethyl acetate (10 mL) and washed with warm water (4 mL) and brine (3 mL x 2). The organic layer was dried over anhydrous sodium sulfate and the crude product was purified by flash column chromatography to furnish corresponding methylenebisamides in good to excellent yields.

N,N'-methylenedibenzamide ***(2)****.*[1] Reaction time: 6 h; R*f*: 0.5 (1:1, EtOAc:Pet. Ether); White solid; mp 210-212 ^{o}C; 51 mg, 98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.70 (m, 6H),

7.43 (t, *J* = 5.9 Hz, 2H), 7.40-7.30 (m, 4H), 5.00 (t, *J* = 5.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 133.4, 132.0, 128.6, 127.3, 45.7; HRMS-ESI (*m/z*) calcd $[(C_{15}H_{14}O_2N_2)+Na]^+$: 277.0947, found: 277.0946.

N,N'-methylenebis(2-(trifluoromethyl)benzamide) ***(3)***. Reaction time: 18 h; R_f = 0.6 (EtOAc:Pet. Ether, 1:1). White solid; 36 mg, 70%, mp 213-215 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.26 (t, *J* = 5.6, 2H), 7.78 (d, *J* = 7.8, 2H), 7.74 (t, *J* = 7.6, 2H), 7.65 (t, *J* = 7.6, 2H), 7.51(d, *J* = 7.3, 2H), 4.69 (t, *J* = 5.6, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.6, 132.5, 130.0, 128.8, 125.3-126.4 (m, CF_3), 126.0, 122.6, 44.4; HRMS-ESI (m/z) calcd $[C_{17}H_{12}O_2N_2F_6+Na]^+$: 413.0695, found 413.0687.

N,N'-methylenebis(2-bromobenzamide) ***(4)***. Reaction time: 30 h; R*f*: 0.5 (1:1, EtOAc:Pet. Ether); White solid; mp 213-215 ^{o}C; 37 mg, 72%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.13 (t, *J* = 5.6 Hz, 2H), 7.65 (d, *J* = 7.3 Hz, 2H), 7.46-7.34 (m, 6H), 4.71 (t, *J* = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.7, 138.7, 132.9, 131.2, 129.2, 127.7, 119.1, 44.5; HRMS-ESI (*m/z*) calcd $[(C_{15}H_{12}O_2N_2{}^{79}Br_2)+H]^+$: 410.9338, found: 410.9345.

N,N'-methylenebis(2-iodobenzamide) ***(5)***. Reaction time: 16 h; R*f*: 0.5 (3:2, EtOAc:Pet. Ether); White solid; mp 231-233 ^{o}C; 35 mg, 68%; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.07 (t, *J* = 5.5 Hz, 2H), 7.88 (d, *J* = 8.0 Hz, 2H), 7.47-7.43 (m, 2H), 7.40-7.35 (m, 2H), 7.20-7.14 (m, 2H), 4.70 (t, *J* = 5.5 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 142.4, 139.3, 131.1, 128.5, 128.1, 93.6, 44.7; HRMS-ESI (*m/z*) calcd $[(C_{15}H_{12}O_2N_2I_2)+H]^+$: 506.9061, found: 506.9056.

N,N'-methylenebis(2-methyl-3-nitrobenzamide) ***(6)***. Reaction time: 30 h; R*f*: 0.5 (9:1, EtOAc:Pet. Ether); White solid; mp 277-279 ^{o}C; 34 mg, 65%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.28 (t, 5.5 Hz, 2H), 7.94 (d, *J* = 7.8 Hz, 2H), 7.61 (d, *J* = 7.8 Hz, 2H), 7.51 (t, *J* = 7.8 Hz, 2H),

4.77 (t, J = 5.5 Hz, 2H), 2.40 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.1, 150.7, 140.0, 131.5, 129.1, 127.4, 124.9, 44.6, 15.6; HRMS-ESI (*m/z*) calcd $[(C_{17}H_{16}O_6N_4)+Na]^+$: 395.0962, found: 395.0960.

N,N'-methylenebis(4-methylbenzamide) (7). [1] Reaction time: 5 h; R_f = 0.5 (EtOAc:Pet. Ether, 2:3). White solid; 39 mg, 74%, mp 205-207 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.93 (t, J = 5.5 Hz, 2H), 7.81(d, J = 7.9 Hz, 4H), 7.26 (d, J = 7.9 Hz, 4H), 4.84 (t, J = 5.5 Hz, 2H), 2.34 (s, 6H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.5, 141.4, 131.4, 128.9, 127.6, 45.3, 21.1; ESI-MS (*m/z*): 305 (M+Na).

*N,N'-methylenebis(4-isopropylbenzamide) (**8**).* [2] Reaction time: 7 h; R_f = 0.3 (EtOAc:Pet. Ether, 1:1). White solid; 49 mg, 94%, mp 181-183 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.96 (t, J = 5.6 Hz, 2H), 7.83 (d, J = 8.3 Hz, 4H), 7.32 (d, J = 8.3 Hz, 4H), 4.84 (t, J = 5.6 Hz, 2H), 2.98-2.87 (m, 2H), 1.20 (d, J = 6.8 Hz, 12H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.6, 152.2, 131.8, 127.8, 126.4, 45.2, 33.5, 23.8; HRMS-ESI (*m/z*) calcd $[C_{21}H_{26}O_2N_2+Na]^+$: 361.1886, found 361.1881.

*N,N'-methylenebis(4-methoxybenzamide) (**9**).* [1] Reaction time: 4 h; R*f*: 0.5 (13:7, EtOAc:Pet. Ether); White solid; mp 199-201 ^{o}C; 48 mg, 93%; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.88 (t, J = 5.6 Hz, 2H), 7.89 (d, J = 8.8 Hz, 4H), 6.98 (d, J = 8.8 Hz, 4H), 4.82 (t, J = 5.6 Hz, 2H), 3.80 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.1, 161.9, 129.5, 126.4, 113.6, 55.5, 45.3; HRMS-ESI (*m/z*) calcd $[(C_{17}H_{18}N_2O_4)+Na]^+$: 337.1159, found: 337.1156.

*N,N'-methylenebis(4-nitrobenzamide) (**10**).* [1] Reaction time: 18 h; R*f*: 0.5 (7:3, EtOAc:Pet. Ether); White solid; mp 247-249 ^{o}C; 37 mg, 71%; ^{1}H NMR (500 MHz, DMSO-d_6) : δ 9.5 (bs, 2H), 8.33-8.31 (m, 4H), 8.14-8.12 (m, 4H), 4.9 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) : δ

165.2, 149.3, 139.7, 129.2, 123.7, 45.5; HRMS-ESI (*m/z*) calcd $[(C_{15}H_{12}O_6N_4)+Na]^+$: 367.0649, found: 367.0647.

N,N'-methylenebis(4-chlorobenzamide) ***(11)***.[1] Reaction time: 9 h; R*f*: 0.5 (9:11, EtOAc:Pet. Ether); White solid; mp 248-250 ^oC; 44 mg, 84%; ^1H NMR (400 MHz, DMSO-d_6): δ 9.18 (t, 5.5 Hz, 2H), 7.92 (d, J = 8.6 Hz, 4H), 7.54 (d, J = 8.6 Hz, 4H), 4.84 (t, 5.5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.7, 136.5, 132.9, 129.6, 128.6, 45.4; HRMS-ESI (*m/z*) calcd $[(C_{15}H_{12}O_2N_2{}^{35}Cl_2)+Na]^+$: 345.0168, found: 345.0166.

N,N'-methylenebis(2-naphthamide) ***(12)***.[2] Reaction time: 24 h; R*f*: 0.5 (1:1, EtOAc:Pet. Ether); White solid; mp 235-237 ^oC; 38 mg, 73%; ^1H NMR (400 MHz, DMSO-d_6): δ 9.27 (t, J = 5.4 Hz, 2H), 8.55 (s, 2H), 8.04-7.95 (m, 8H), 7.65-7.57 (m, 4H), 4.99 (t, J = 5.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.8, 134.4, 132.3, 131.5, 129.1, 128.1, 128.0, 127.9, 127.8, 126.9, 124.5, 45.5; HRMS-ESI (*m/z*) calcd $[(C_{23}H_{18}N_2O_2)+Na]^+$: 377.1260, found: 377.1266.

N,N'-methylenebis(thiophene-2-carboxamide) ***(19)***.[3] Reaction time: 6 h; R*f*: 0.6 (EtOAc:Pet. Ether, 1:1). White solid; 48 mg, 91%, mp 224-226 ^oC; ^1H NMR (400 MHz, DMSO-d_6): δ 9.16 (t, J = 5.6 Hz, 2H), 7.88 (d, J = 3.7 Hz, 2H), 7.77 (d, J = 4.9 Hz, 2H), 7.14 (t, J = 4.9 Hz, 2H), 4.78 (t, J = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.7, 139.7, 131.5, 128.9, 128.3, 44.7; HRMS-ESI (m/z) calcd $[C_{11}H_{10}O_2N_2S_2+Na]^+$: 289.0076, found 289.0072.

(2E,2'E)-N,N'-methylenebis(3-phenylacrylamide) ***(21)***. [1] Reaction time: 5 h; R*f*: 0.5 (3:2, EtOAc:Pet. Ether); White solid; mp 256-258 ^oC; 38 mg, 74%; ^1H NMR (400 MHz, DMSO-d_6): δ 8.81 (t, J = 6.1 Hz, 2H), 7.58-7.53 (m, 4H), 7.48 (d, J = 15.6 Hz, 2H), 7.45-7.36 (m, 6H), 6.69 (d, J = 15.6 Hz, 2H), 4.64 (t, J = 6.1 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.6, 139.7,

135.0, 129.9, 129.2, 127.8, 122.0, 43.8; HRMS-ESI (*m/z*) calcd $[(C_{19}H_{18}N_2O_2)+Na]^+$: 329.1260, found: 329.1259.

N,N'-methylenebis(2-phenylacetamide) ***(22)***.[1] Reaction time: 11 h; R*f*: 0.5 (1:1, EtOAc:Pet. Ether); White solid; mp 213-215 ^oC; 40 mg, 77%; ^1H NMR (400 MHz, DMSO-d_6): δ 8.73 (t, J = 5.9 Hz, 2H), 7.30-7.19 (m, 10H), 4.38 (t, J = 5.9 Hz, 2H), 3.41 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.9, 136.4, 129.2, 128.4, 126.6, 43.6, 42.2; HRMS-ESI (*m/z*) calcd $[(C_{17}H_{18}O_2N_2)+Na]^+$; 305.1260, found: 305.1259.

N,N'-methylenebis(2-(2,6-difluorophenyl)acetamide) ***(23)***. Reaction time: 24 h; R*f*: 0.5 (2:3, EtOAc:Pet. Ether); White solid; mp 281-283 ^oC; 31 mg, 60%; ^1H NMR (400 MHz, DMSO-d_6): δ 8.80 (t, J = 5.9 Hz, 2H), 7.43-7.28 (m, 2H), 7.15-6.98 (m, 4H), 4.42 (t, J = 5.9 Hz, 2H), 3.52 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.8, 161.4 (dd, J_{CF} = 245.8, 8.5 Hz), 129.2 (t, J_{CF} = 10.0 Hz), 112.0 (t, J_{CF} = 20.0 Hz), 111.4 (dd, J_{CF} = 19.3, 6.9 Hz), 43.8, 28.8; HRMS-ESI (*m/z*) calcd $[(C_{17}H_{14}N_2O_2F_4)+H]^+$: 355.1064, found: 355.1061.

N,N'-methylenebis(2-(XXXaphthalene-1-yl)acetamide) ***(24)***. Reaction time: 30 h; R*f*: 0.5 (7:3, EtOAc:Pet. Ether); White solid; mp 279-281^oC; 22 mg, 40%; ^1H NMR (400 MHz, DMSO-d_6): δ 8.87 (t, J = 6.1 Hz, 2H), 8.06 (d, J = 8.8 Hz, 2H), 7.92 (d, J = 9.0 Hz, 2H), 7.82 (d, J = 9.0 Hz, 2H), 7.59 – 7.39 (m, 8H), 4.44 (t, J = 6.1 Hz, 2H), 3.90 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.9, 133.6, 132.8, 132.2, 128.6, 127.9, 127.3, 126.2, 125.9, 125.8, 124.6, 43.7, 39.65; HRMS-ESI (*m/z*) calcd $[(C_{25}H_{22}O_2N_2)+H]^+$: 383.1754, found: 383.1750.

N,N'-(methylene-d_2)dibenzamide ***(2a)***. DMSO-d_6 was used instead of DMSO. Reaction time: 6 h; R*f*: 0.5 (1:1, EtOAc:Pet. Ether); White solid; mp 224-226 ^oC; 50 mg, 94%; ^1H NMR

(400 MHz, $CDCl_3$): δ 7.74 (d, J = 7.3 Hz, 4H), 7.61 (bs, 2H), 7.44 (t, J = 7.2 Hz, 2H), 7.34 (t, 7.5 Hz, 4H); HRMS-ESI (*m/z*) calcd $[(C_{15}H_{12}{}^2H_2O_2N_2)+Na]^+$: 279.1073, found: 279.1078.

Procedure for the synthesis of pthalimide (16). The solution of amide **15** (50 mg, 1 equiv, 0.30 mmol), ammonium persulfate $[(NH_4)_2S_2O_8]$ (138 mg, 2 equiv, 0.60 mmol) and DMSO (130 µL, 6 equiv, 1.82 mmol) in 1,4-dioxane (2 mL) was heated at 100 ^oC in a round bottom flask, equipped with a stirring bar and water condenser, until the reaction was complete (3 h) as indicated by thin layer chromatography. After completion, the reaction mixture was filtered through a cotton plug and 1,4-dioxane was removed under vacuum. The residue was then dissolved in ethyl acetate (10 mL) and washed with warm water (4 mL) and brine (3 mL x 2). The organic layer was dried over anhydrous sodium sulfate and the crude product was purified by flash column chromatography to furnish pthalimide (**16**) in 98% yield (44 mg).

*Isoindoline-1,3-dione (**16**).*[4] Reaction time: 3 h; R*f*: 0.5 (1:4, EtOAc:Pet. Ether); White solid; mp 237-239 ^oC; 44 mg, 98%; ^1H NMR (400 MHz, DMSO-d_6): δ 11.33 (s, 1H), 7.82 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.5, 134.5, 132.8, 123.2; GC-MS (M^+) : 147.0

Procedure for the synthesis of diphenylthiadiazole (18). The solution of thiamide **17** (50 mg, 1 equiv, 0.36 mmol), ammonium persulfate $[(NH_4)_2S_2O_8]$ (166 mg, 2 equiv, 0.72 mmol) and DMSO (154 µL, 6 equiv, 2.16 mmol) in 1,4-dioxane (2 mL) was heated at 100 ^oC for 5 minutes in a round bottom flask, equipped with a stirring bar and water condenser. The reaction mixture was filtered through a cotton plug and 1,4-dioxane was removed under vacuum. The residue was then dissolved in ethyl acetate (10 mL) and washed with warm water (4 mL) and brine (3 mL x 2). The organic layer was dried over anhydrous sodium sulfate and the crude

product was purified by flash column chromatography to furnish 3,5-diphenyl-1,2,4-thiadiazole (**18**) in 92% yield (40 mg).

*3,5-diphenyl-1,2,4-thiadiazole (**18**).*[5] Reaction time: 5 min; R*f*: 0.5 (1:19, EtOAc:Pet. Ether); White solid; mp 95-97 ^{o}C; 40 mg, 92%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (dd, J = 7.6, 1.9 Hz, 2H), 7.98 (dd, J = 7.4, 2.1 Hz, 2H), 7.50-7.42 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.1, 173.8, 132.8, 131.9, 130.7, 130.4, 129.3, 128.7, 128.3, 127.5; HRMS-ESI (*m/z*) calcd $[(C_{14}H_{10}N_2S)+H]^+$: 239.0637, found: 239.0636.

Procedure for the synthesis of 2-(3-oxo-3-phenylpropyl)benzo[d]isothiazol-3(2*H*)-one 1,1-dioxide (30). The solution of acetophenone (**29**, 50 mg, 1 equiv, 0.42 mmol), saccharine (**28**, 152 mg, 2 equiv, 0.83 mmol), ammonium persulfate $[(NH_4)_2S_2O_8]$ (190 mg, 2 equiv, 0.83 mmol) and DMSO (177 µL, 6 equiv, 2.46 mmol) in 1,4-dioxane (2 mL) was heated for 20 h at 120 ^{o}C in a Schlenk tube equipped with a stirring bar. The reaction mixture was filtered through a cotton plug and 1,4-dioxane was removed under vacuum. The residue was then dissolved in ethyl acetate (10 mL) and washed with warm water (4 mL) and brine (3 mL x 2). The organic layer was dried over anhydrous sodium sulfate and the crude product was purified by flash column chromatography to furnish 2-(3-oxo-3-phenylpropyl)benzo[d]isothiazol-3(2*H*)-one 1,1-dioxide (**30**) in 52% yield (68 mg).

*2-(3-oxo-3-phenylpropyl)benzo[d]isothiazol-3(2H)-one 1,1-dioxide (**30**).*[6] Reaction time: 20 h; R*f*: 0.5 (3:7, EtOAc:Pet. Ether); White solid; mp 137-139 ^{o}C; 68 mg, 52%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.98 (m, 1H), 7.92 – 7.74 (m, 5H), 7.51 (t, J = 7.7 Hz, 1H), 7.39 (t, 7.7 Hz, 2H), 4.19 (t, 7.8 Hz, 2H), 3.50 (t, 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.8, 158.8,

137.7, 136.2, 134.8, 134.4, 133.5, 128.7, 128.0, 127.3, 125.2, 120.9, 36.8, 34.4; HRMS-ESI (*m/z*) calcd $[(C_{16}H_{13}O_4NS)+Na]^+$: 338.0457, found: 338.0452.

Mechanistic aspect study:

Procedure for Radical trapping experiment. The solution of amide **1** (50 mg, 1 equiv, 0.41 mmol), ammonium persulfate $[(NH_4)_2S_2O_8]$ (188 mg, 2 equiv, 0.82 mmol), TEMPO (128 mg, 2 equiv, 0.82 mmol) and DMSO (175 µL, 6 equiv, 2.46 mmol) in 1,4-dioxane (2 mL) was heated for 24 h at 100 ^oC in a round bottom flask, equipped with a stirring bar and water condenser. Only a trace amount of product was seen on TLC. Repetition of the same reaction using BHT (145 mg, 4 equiv, 0.66 mmol) as a radical scavenger showed the same result.

Procedure using DMS instead of DMSO. The solution of amide **1** (50 mg, 1 equiv, 0.41 mmol), ammonium persulfate $[(NH_4)_2S_2O_8]$ (188 mg, 2 equiv, 0.82 mmol), and DMS (232 mg, 6 equiv, 2.47 mmol) in 1,4-dioxane (2 mL) was heated for 6 h at 100 ^oC in a round bottom flask, equipped with a stirring bar and water condenser. Usual work-up followed by column chromatographic (2:3, ethyl acetate: petroleum ether) purification furnished 23 mg, 44% of **2**.

Procedure using NH_4I instead of $(NH_4)_2S_2O_8$. The solution of amide **1** (50 mg, 1 equiv, 0.41 mmol), ammonium iodide $[NH_4I]$ (119 mg, 2 equiv, 0.82 mmol) and DMSO (175 µL, 6 equiv, 2.46 mmol) in 1,4-dioxane (2 mL) was heated at 100 ^oC in a round bottom flask, equipped with a stirring bar and water condenser. Even after heating for 24 h there was no reaction and the starting material was recovered unchanged.

Procedure for trapping the formaldehyde equivalent intermediate to furnish compound 32. To the solution of compound **31** (250 mg, 1.48 mmol, 1 eq) in 2 mL 1,4-dioxane added sequentially APS (628 mg, 2.97 mmol, 2 eq) and DMSO (0.64 mL, 8.91 mmol, 6 eq) and heated at 100 ^{o}C for 5 h then solvents were evaporated under vacuum and added 10 mL ethyl acetate and washing of brine was given (5 mL X 2). Organic layer was separated dried over sodium sulfate and column chromatography was done with 3:7 (ethyl acetate: petroleum ether) to give 104 mg, 40% of **32**.

Bis(2,4,6-trimethoxyphenyl)methane (32).[7] R*f*: 0.5 (1:5, EtOAc:Pet. Ether); White solid; mp 110-112 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.10 (s, 4H), 3.85 (s, 2H), 3.78 (s, 6H), 3.71 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 158.6, 111.9, 91.1, 56.0, 55.2, 16.6; HRMS-ESI (*m/z*) calcd[$(C_{19}H_{25}O_6)$+H]$^{+}$; 349.1646, found: 349.1646.

Compound 34 as a plausible intermediate. The compound **33** was prepared as per the literature procedure.[8] To the solution of compound **33** (80 mg, 0.44 mmol, 1 eq) in 2 mL 1,4-dioxane added sequencially 4-methoxy benzamide (66 mg, 0.44 mmol, 1 eq), APS (50 mg, 0.22 mmol, 0.5 eq) and heated at 50 ^{o}C for 5 h then reaction mixture was directly loaded on column and purification done with 1:1 (ethylacetate: petroleum ether) to give 63 mg, 50% of **35** and 10 mg, 18% of benzamide **1** (based on ^{1}H NMR) and 10 mg, 15% of compound **9** (corresponding to 4-methoxy benzamide).

N-((methylthio)methyl)benzamide(33).[8] R*f*: 0.3 (1:5, EtOAc:Pet. Ether); White Solid; mp 105-107 ^{o}C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.84-7.78 (m, 2H), 7.58-7.41 (m, 3H), 6.49 (bs, 1H), 4.60 (d, J = 6.3 Hz, 2H), 2.22 (S, 3H).

N-(benzamidomethyl)-4-methoxybenzamide (35). R*f*: 0.3 (1:1, EtOAc:Pet. Ether); White Solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 7.3 Hz, 2H), 7.79 (d, J = 8.9 Hz, 2H), 7.74 (t, J = 6.1 Hz, 1H), 7.64 (t, J = 6.1 Hz, 1H), 7.46 (t, J = 7.3 Hz, 1H), 7.42 (t, J =7.3 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 5.04 (t, J = 6.1 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 168.0, 162.6, 133.5, 132.0, 129.1, 128.6, 127.2, 125.7, 113.8, 55.4, 45.6; HRMS-ESI (*m/z*) calcd[$(C_{16}H_{16}N_2O_3)$+Na]$^{+}$; 307.1053, found: 307.1046.

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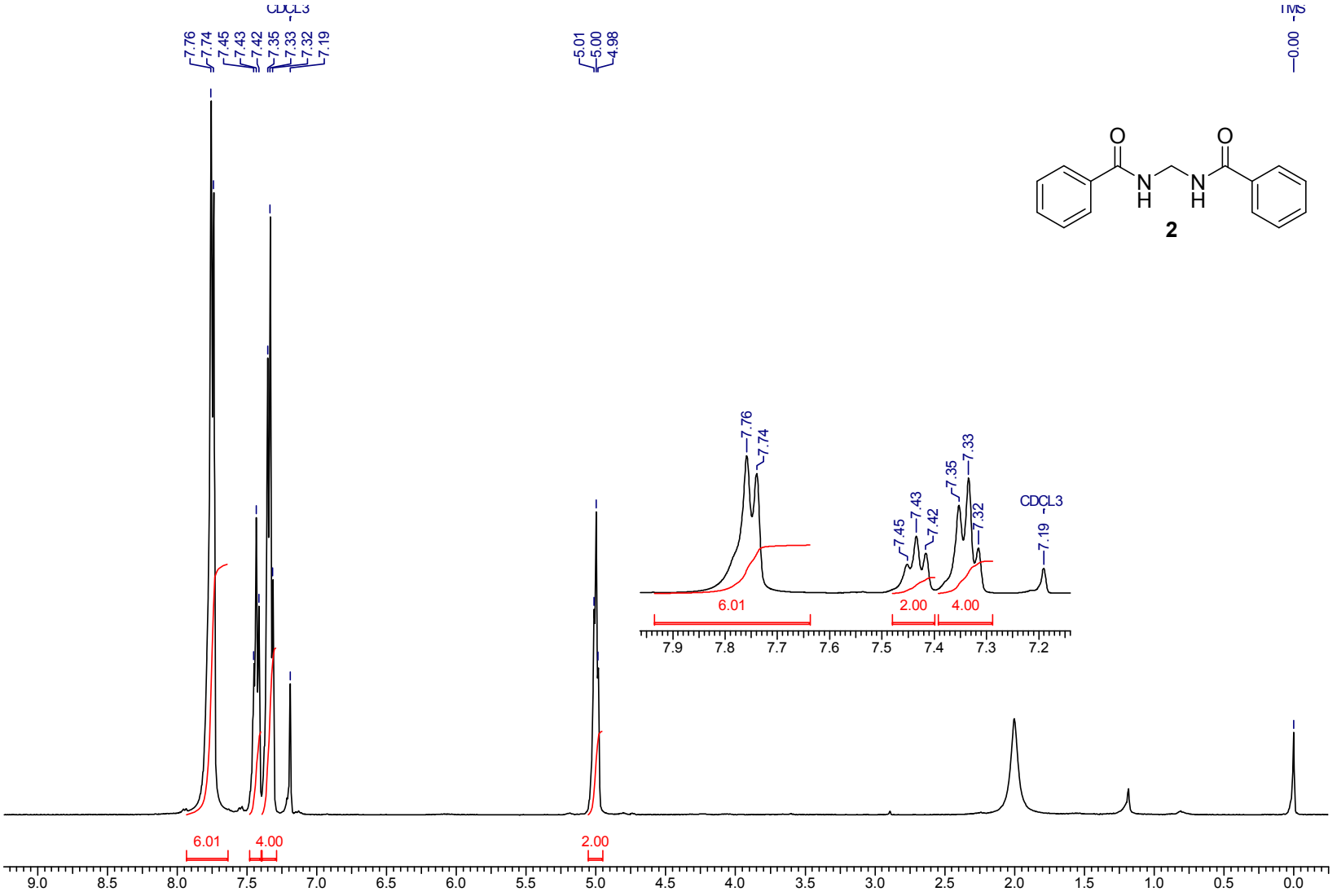
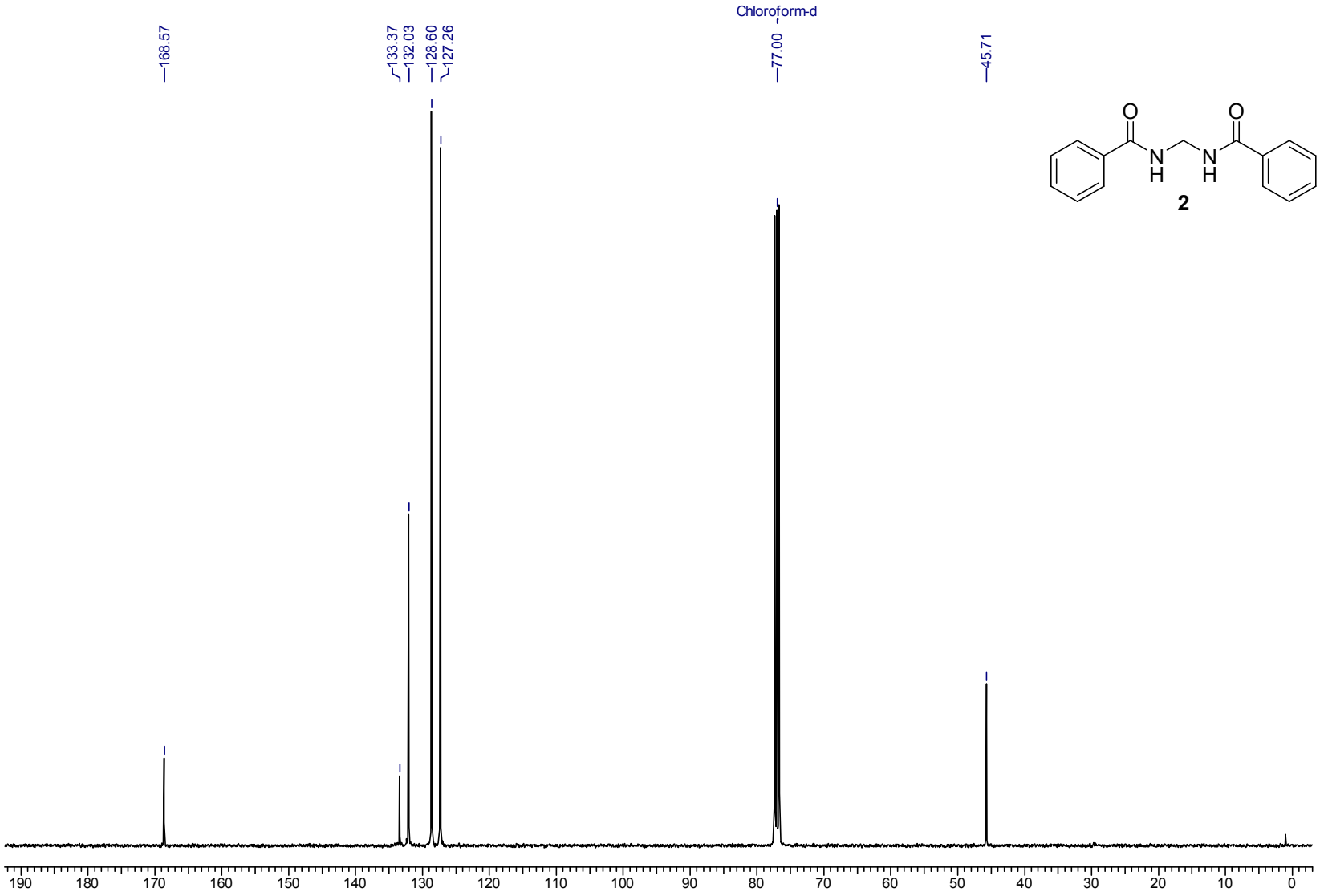
^{1}H NMR, 400 MHz

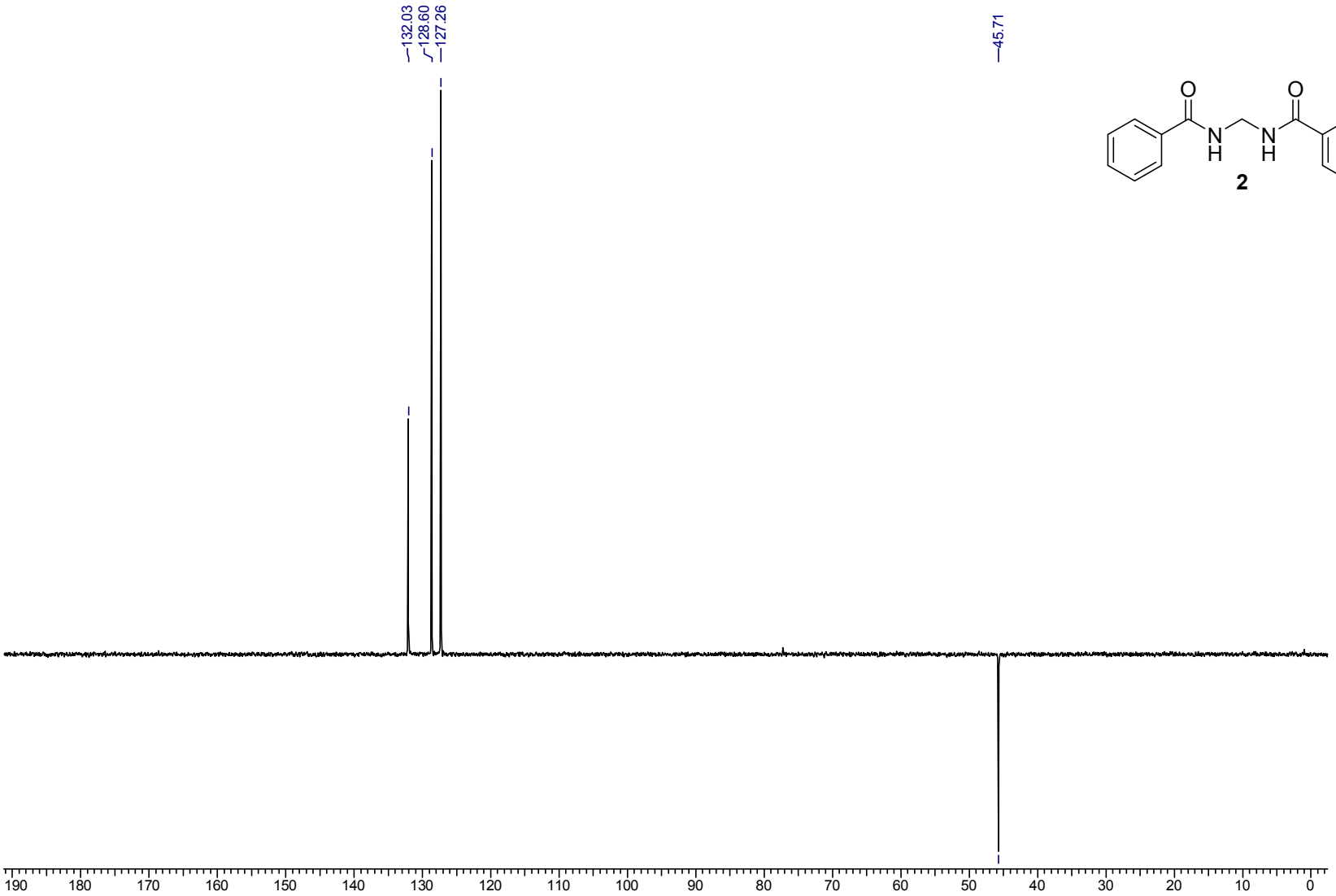


2

^{13}C NMR, 100 MHz

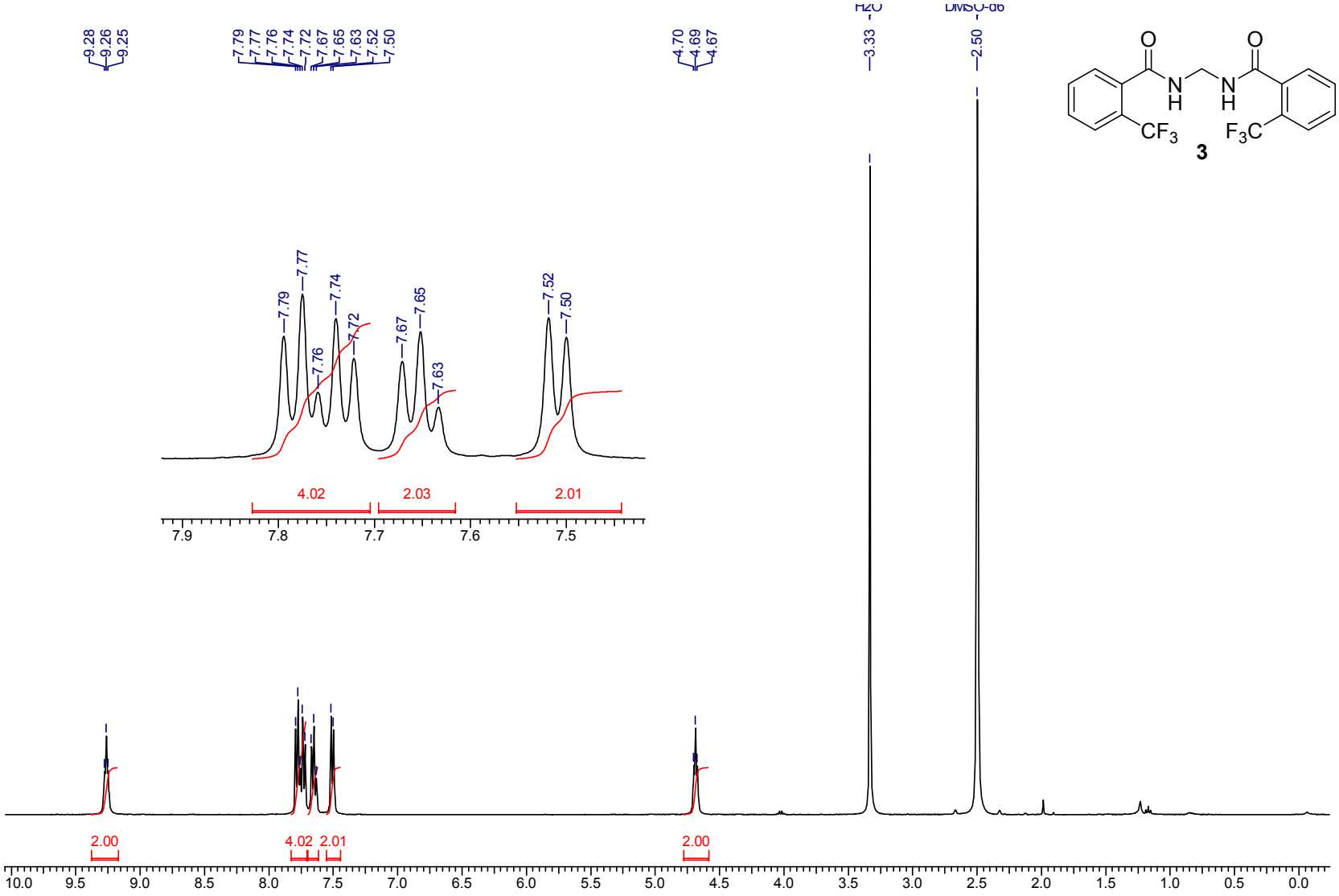


DEPT NMR, 100 MHz

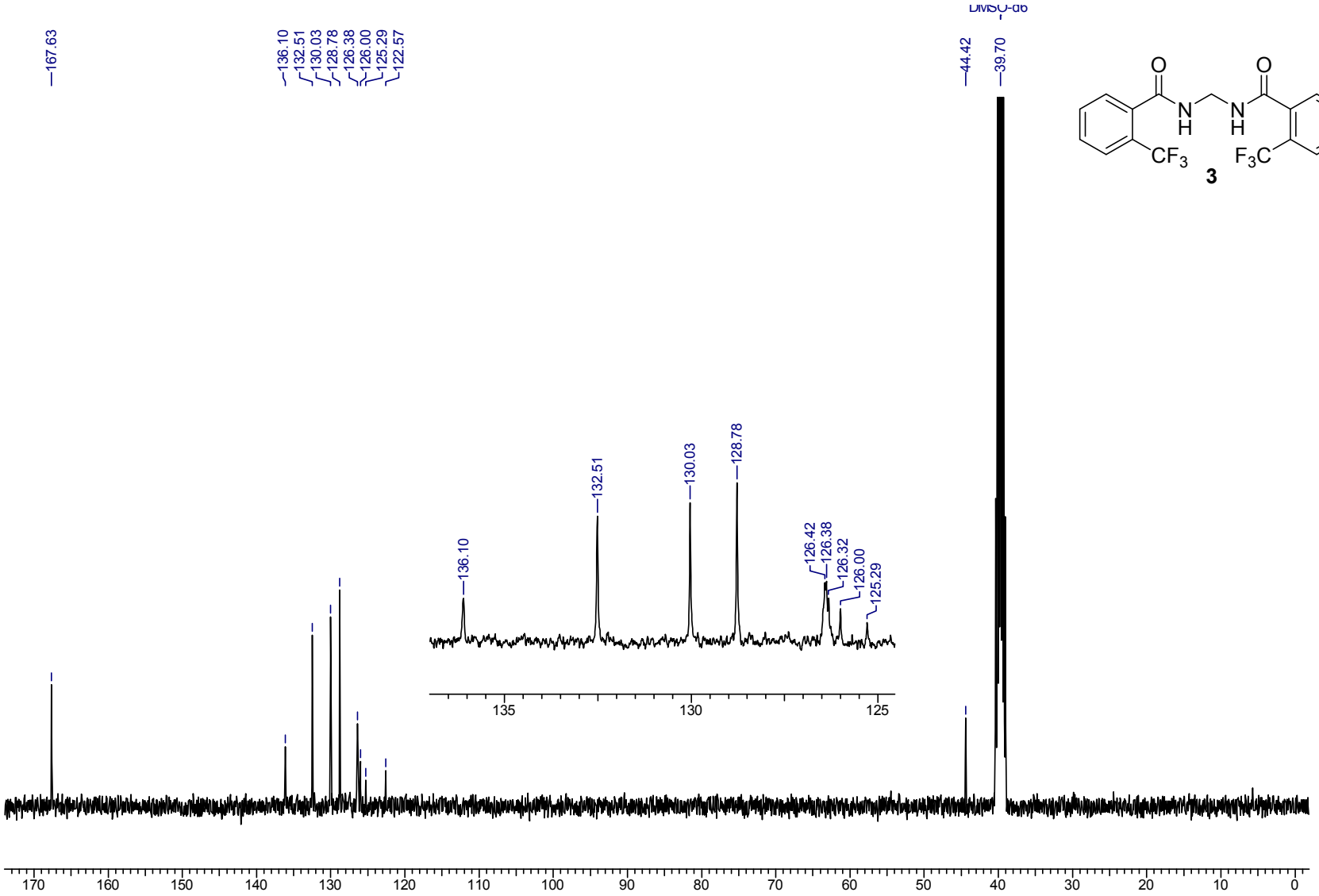


2

^{1}H NMR, 400 MHz

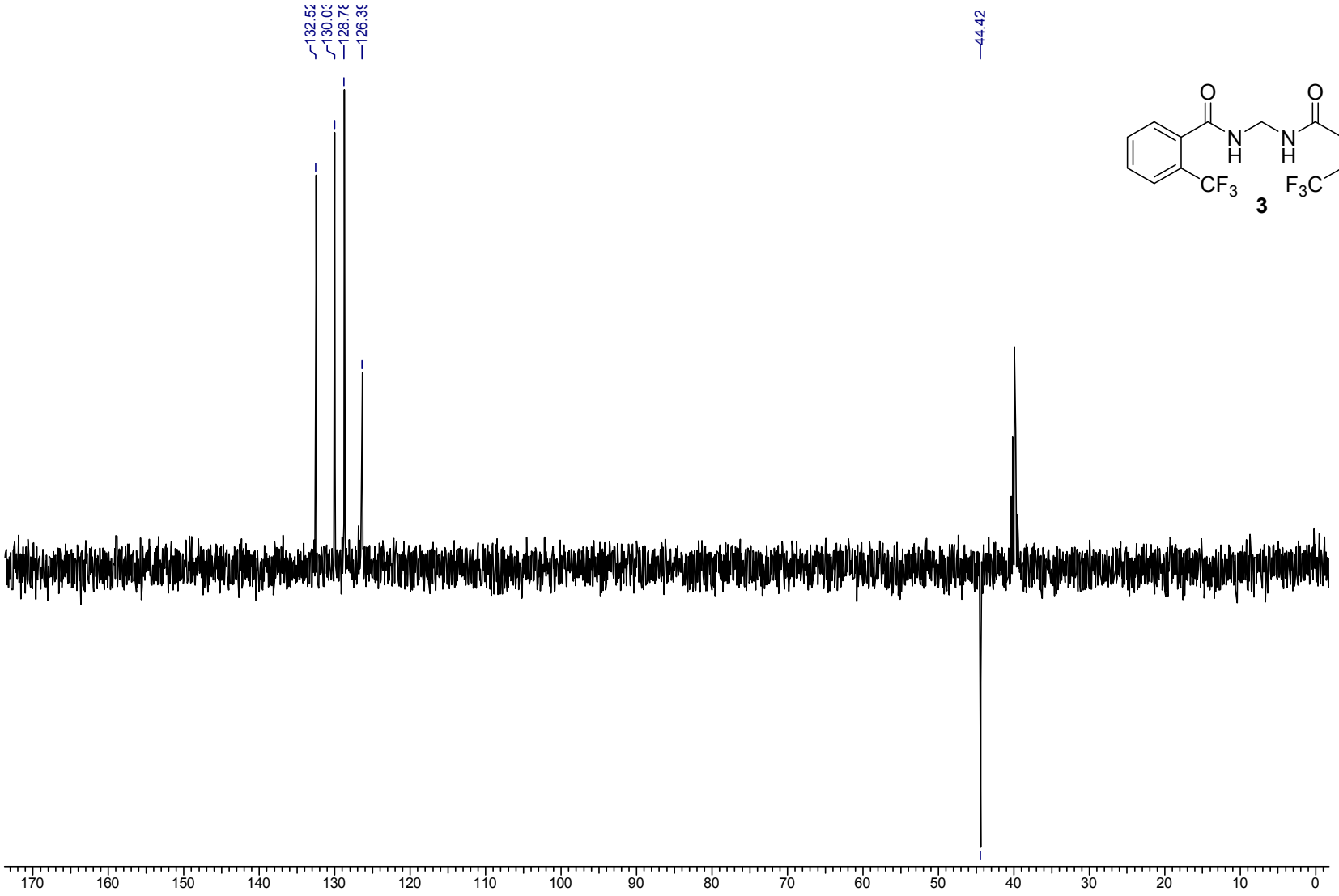


^{13}C NMR, 100 MHz



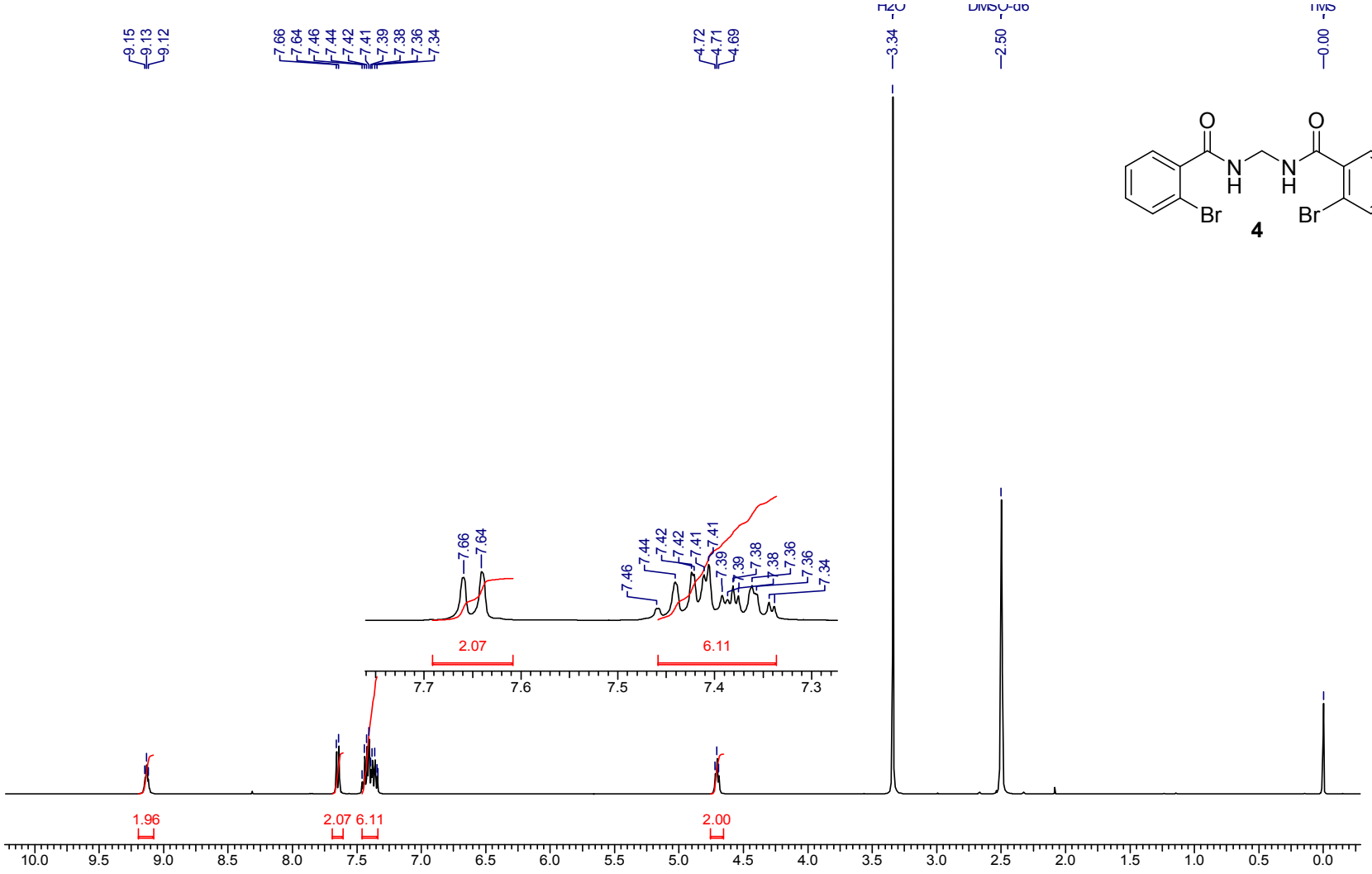
3

DEPT NMR, 100 MHz

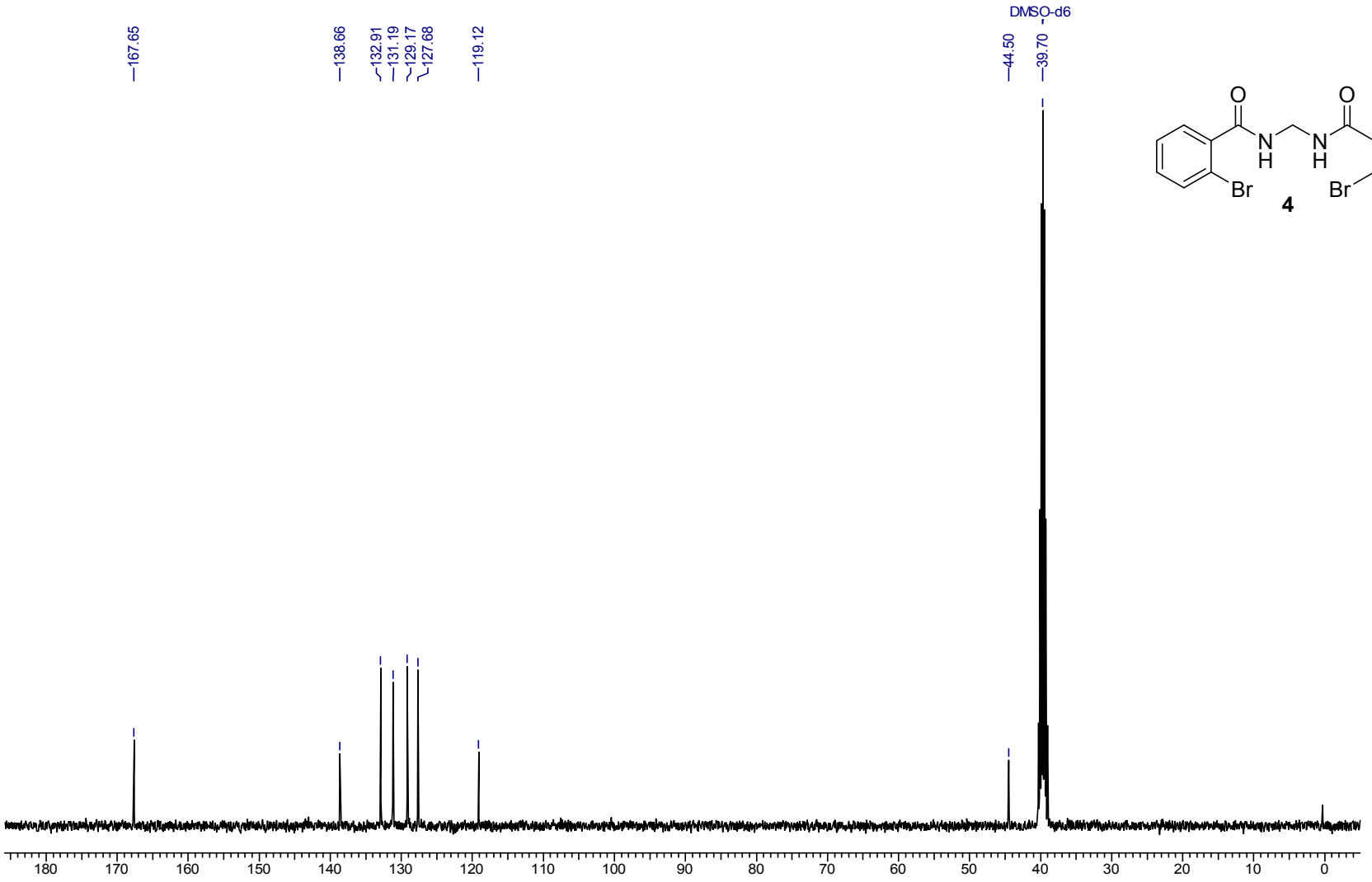


3

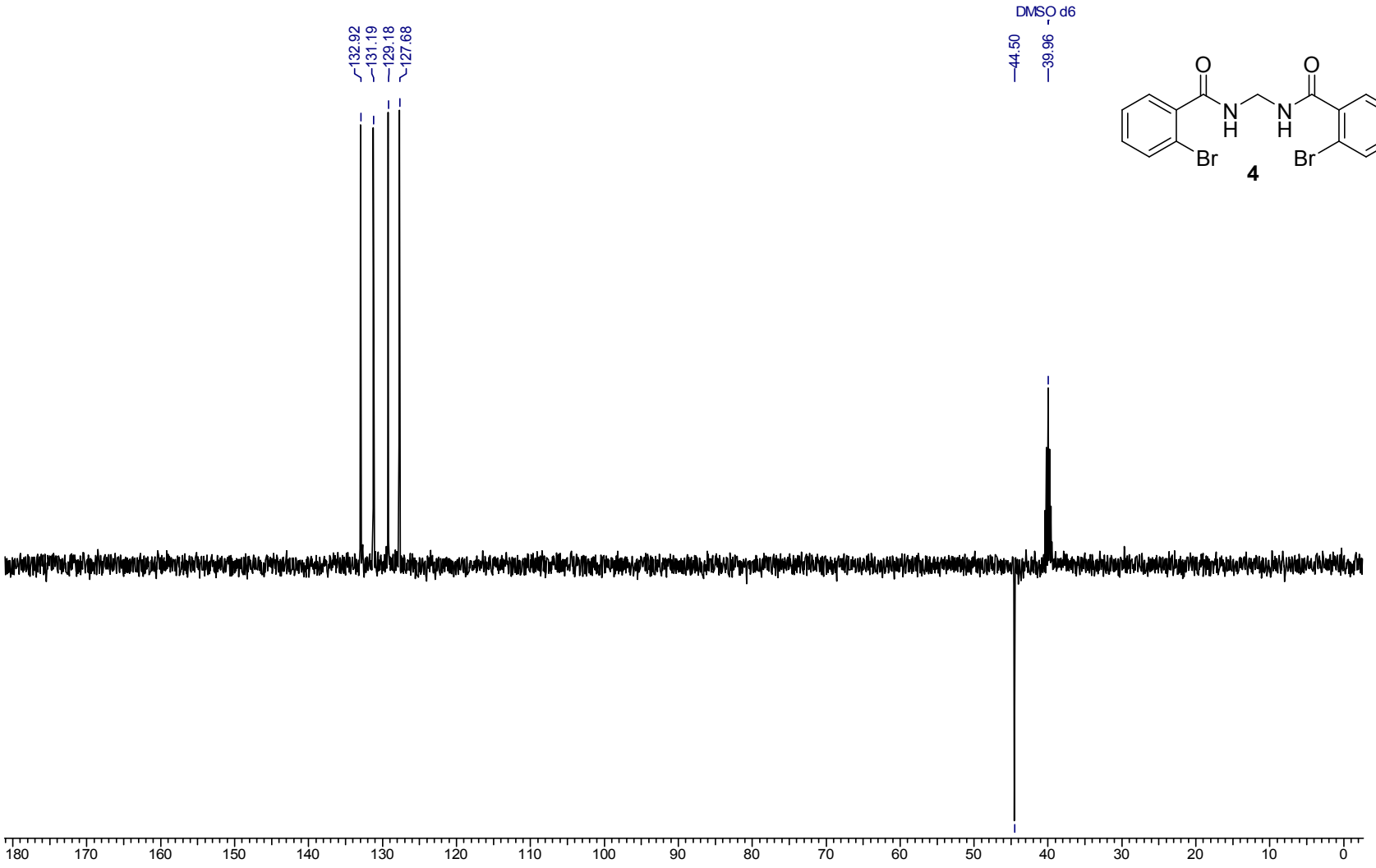
^{1}H NMR, 400 MHz



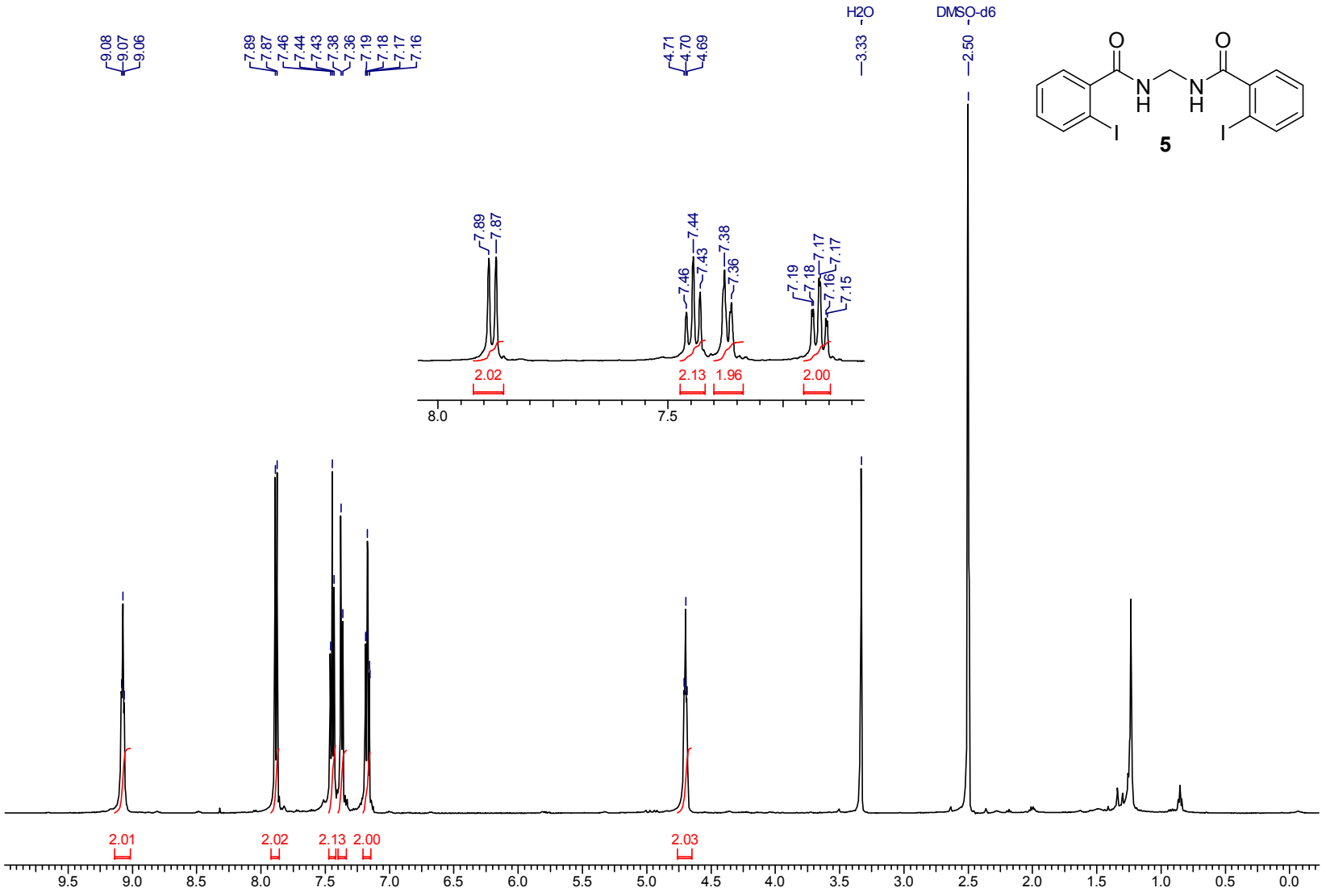
^{13}C NMR, 100 MHz



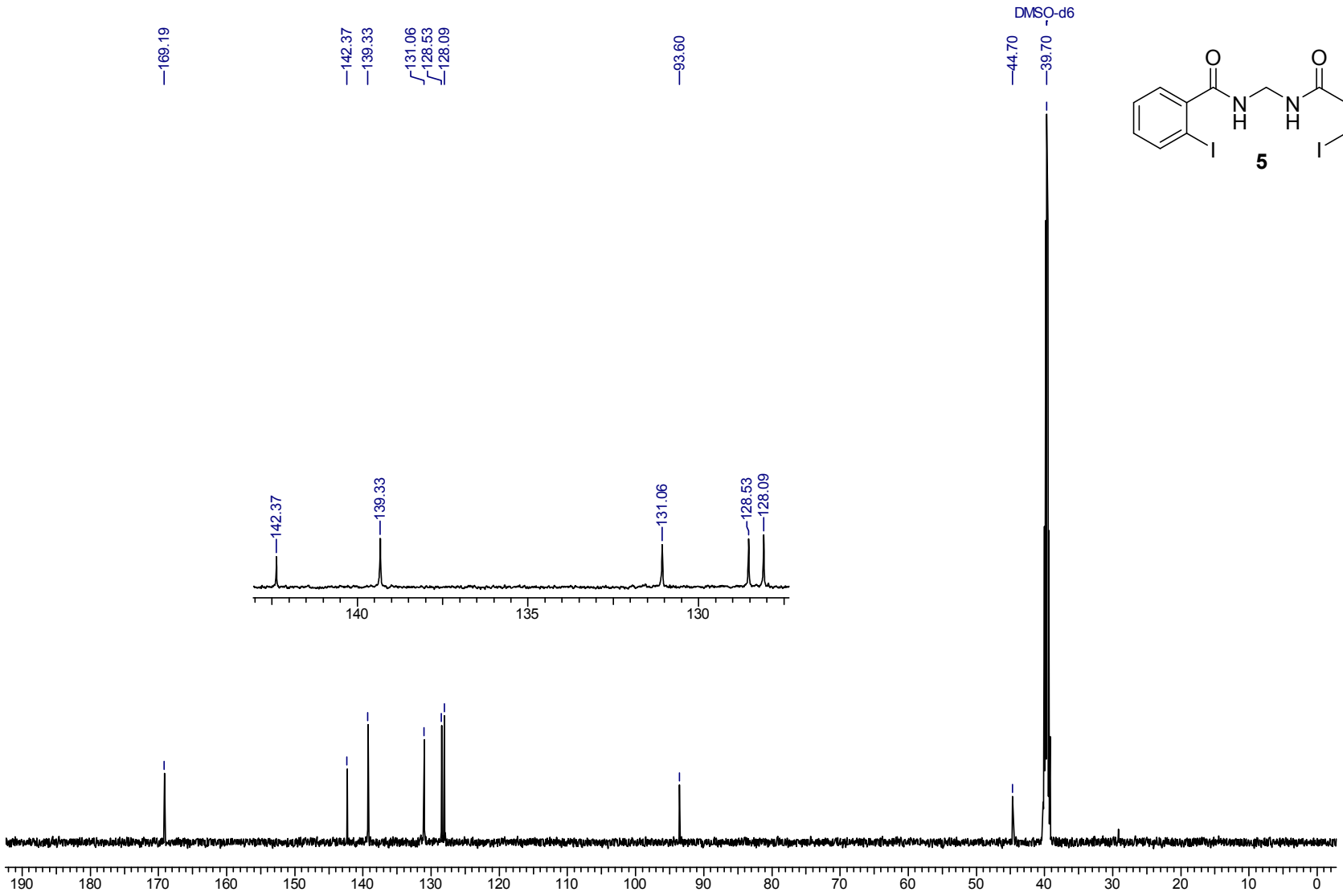
DEPT NMR, 100 MHz



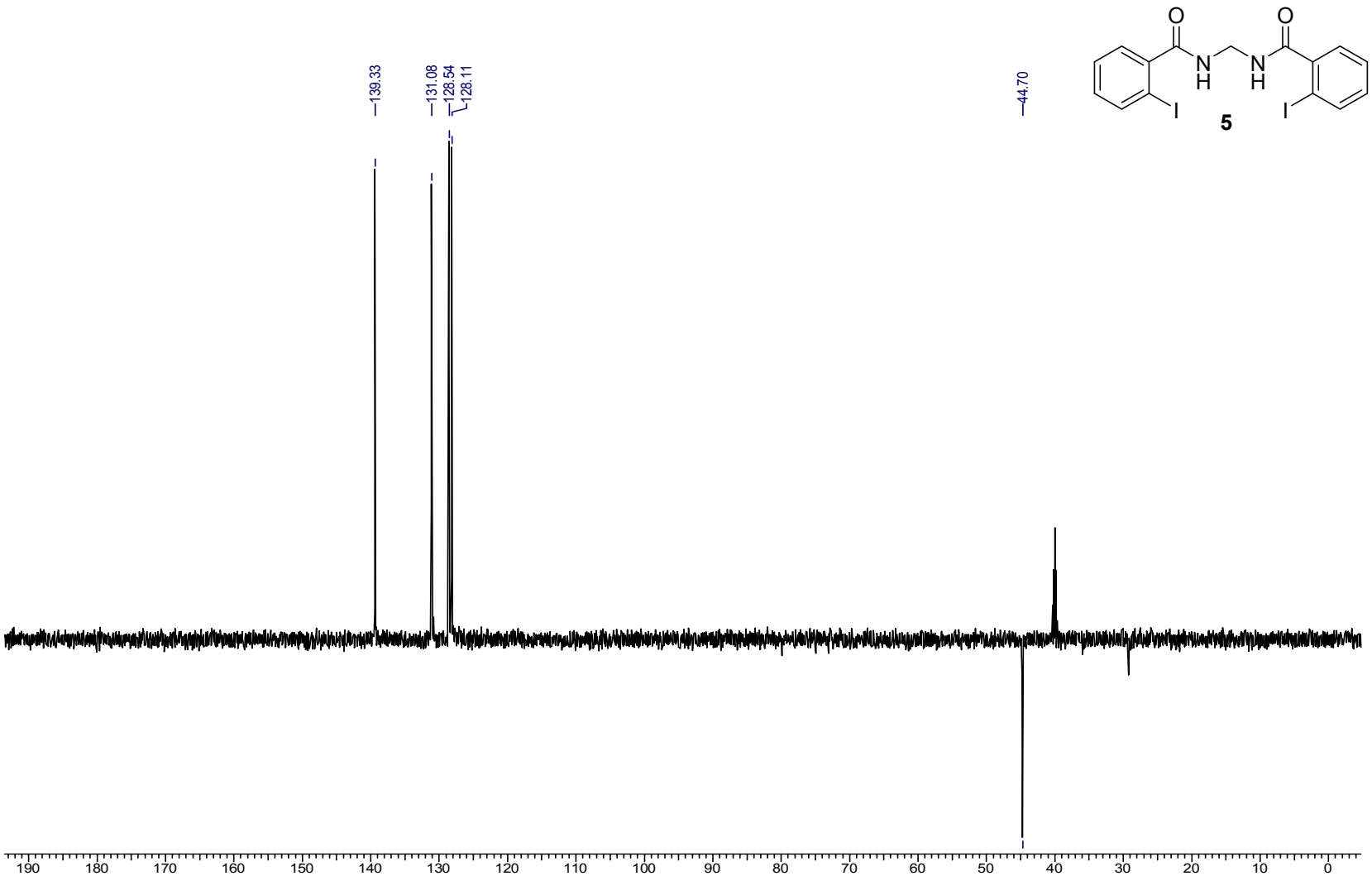
^{1}H NMR, 500 MHz



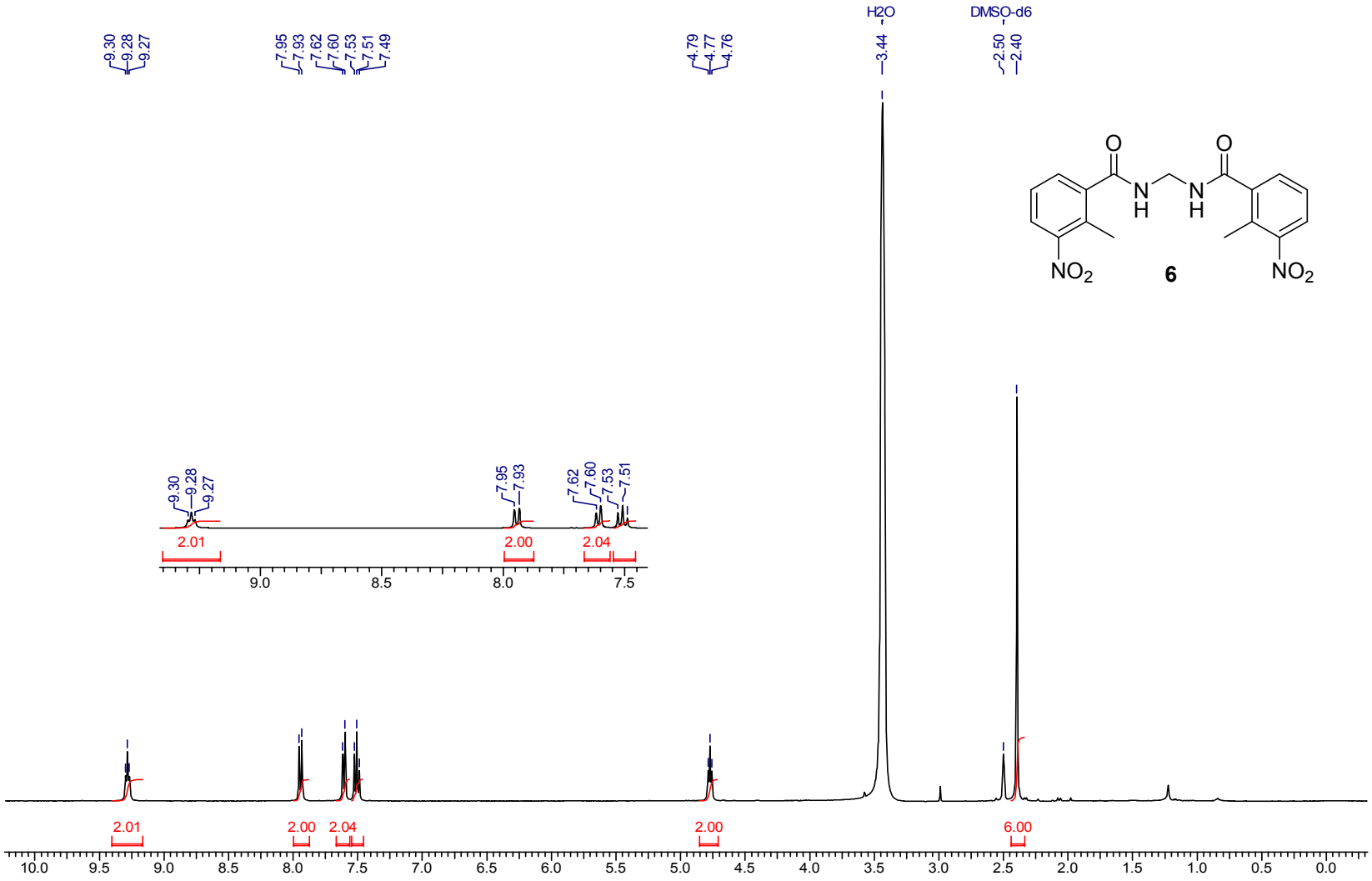
^{13}C NMR, 125 MHz



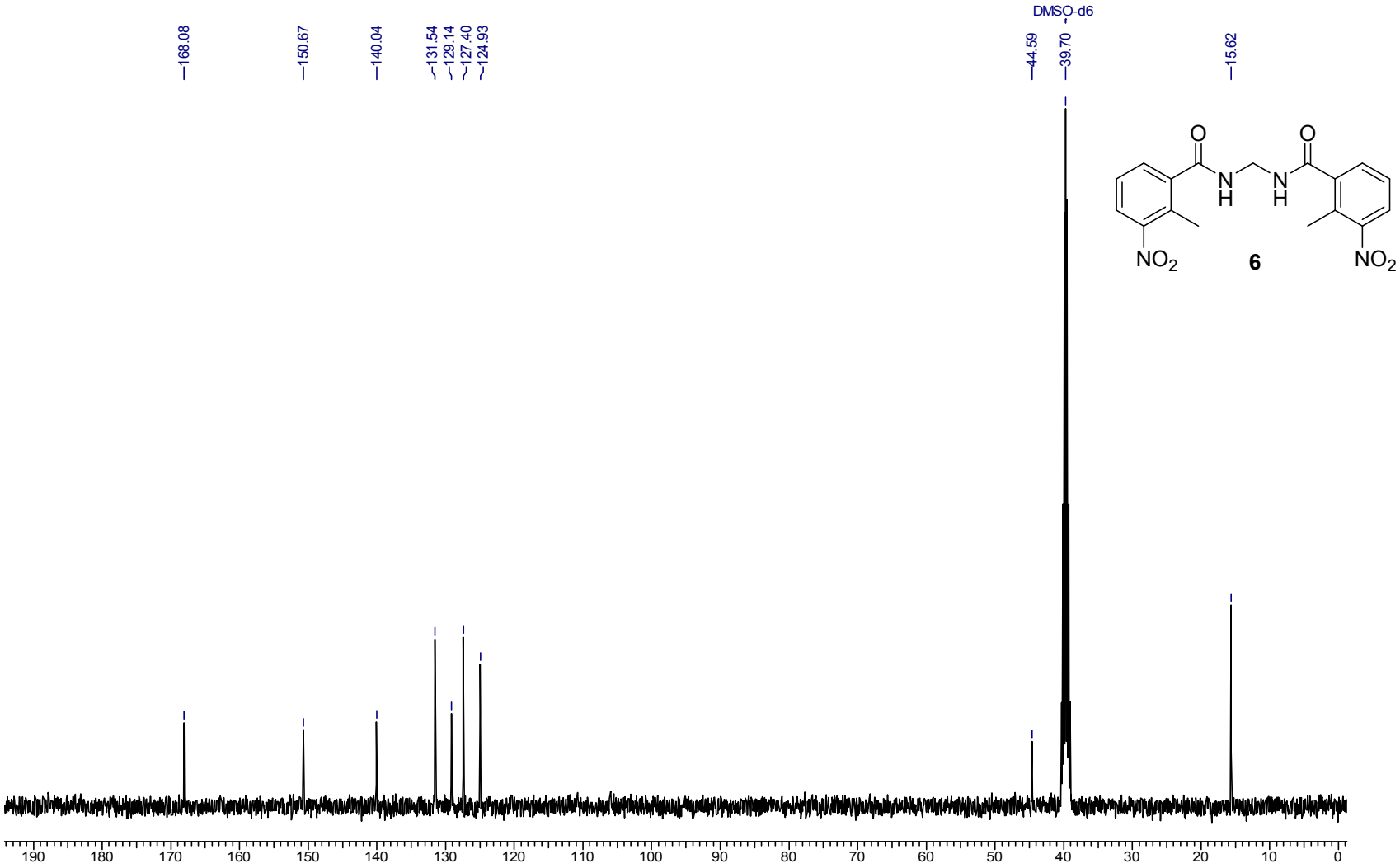
DEPT NMR, 125 MHz



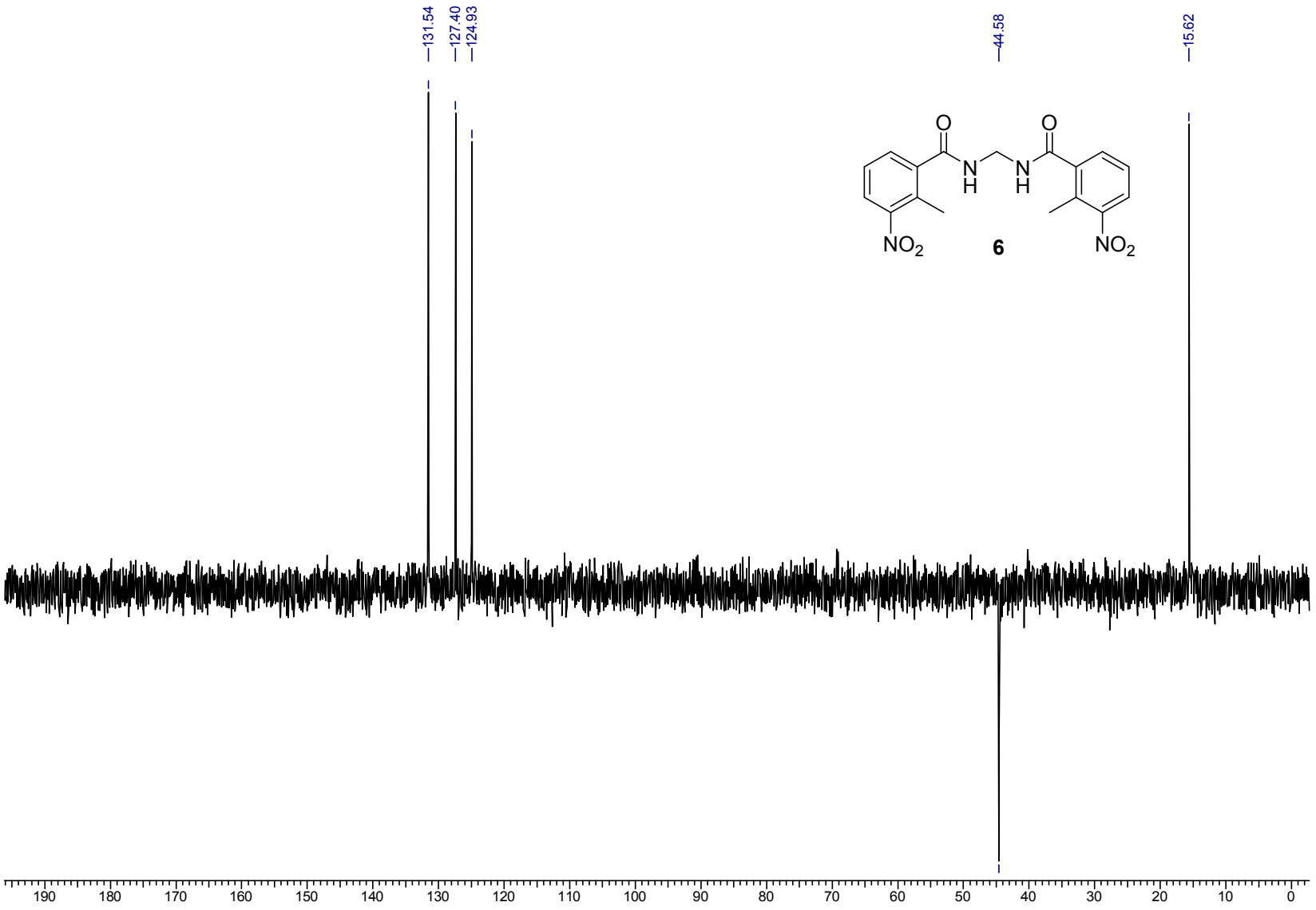
^{1}H NMR, 400 MHz



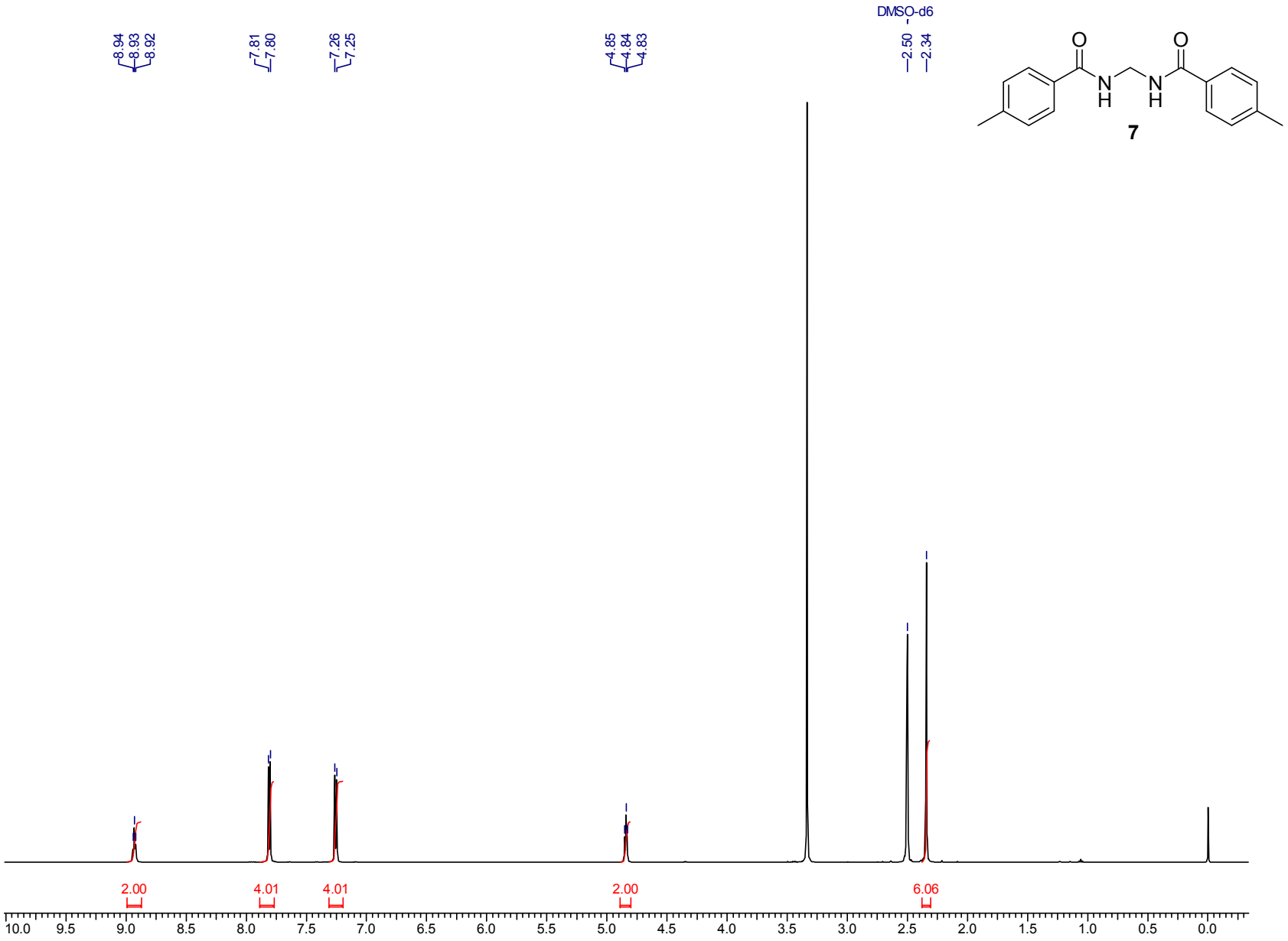
^{13}C NMR, 100 MHz



DEPT NMR, 100 MHz

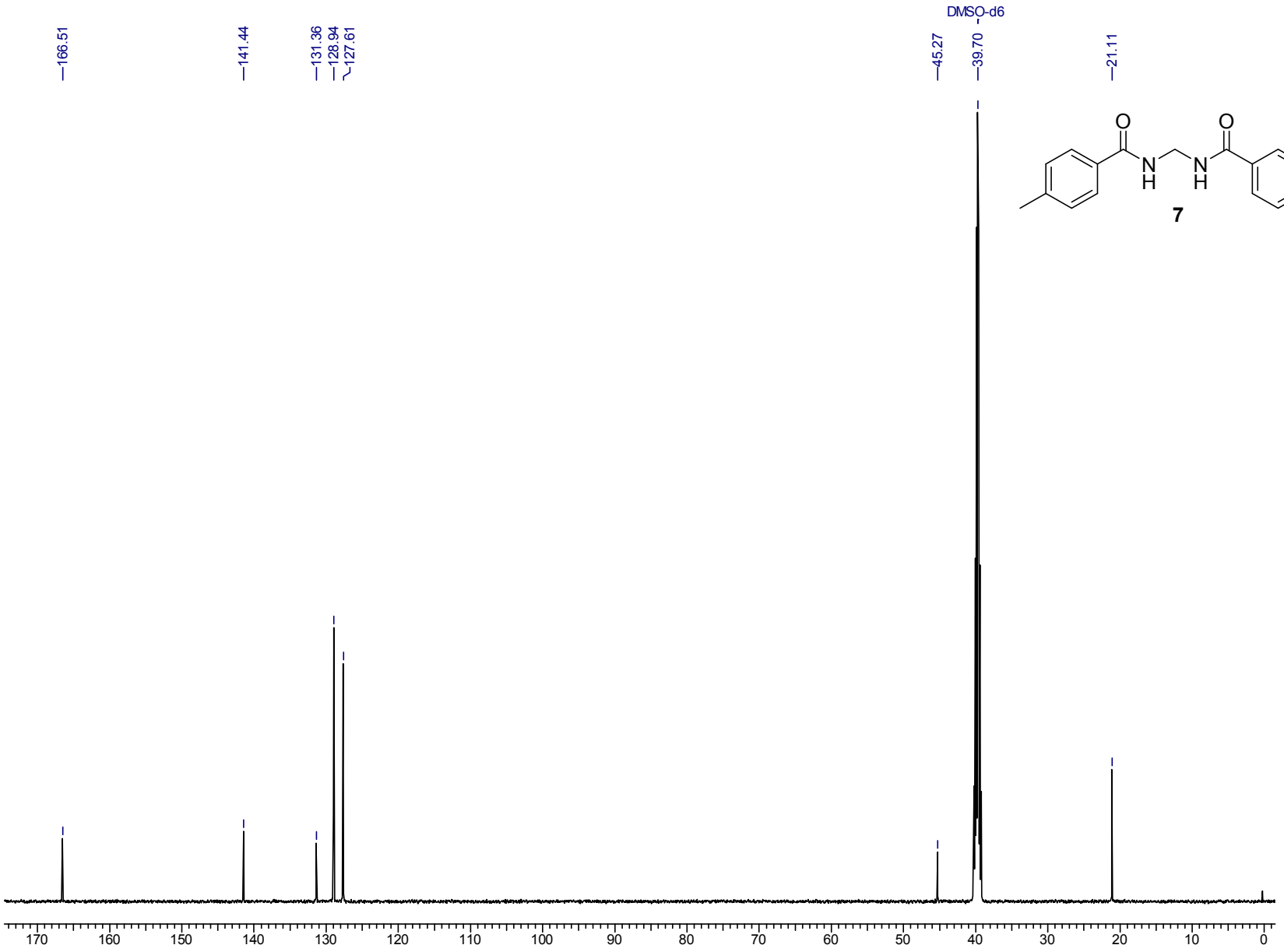


^{1}H NMR, 500 MHz

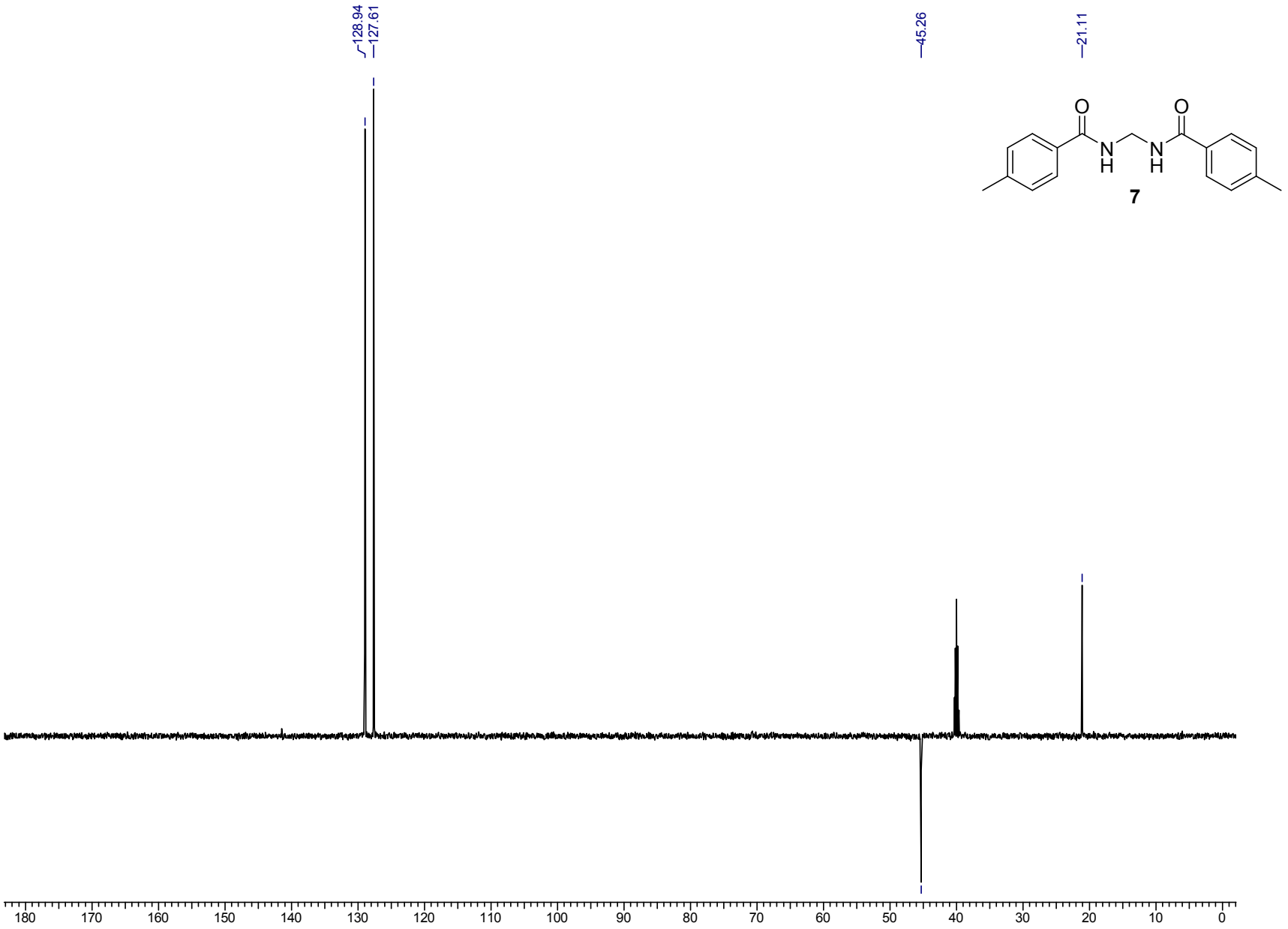


7

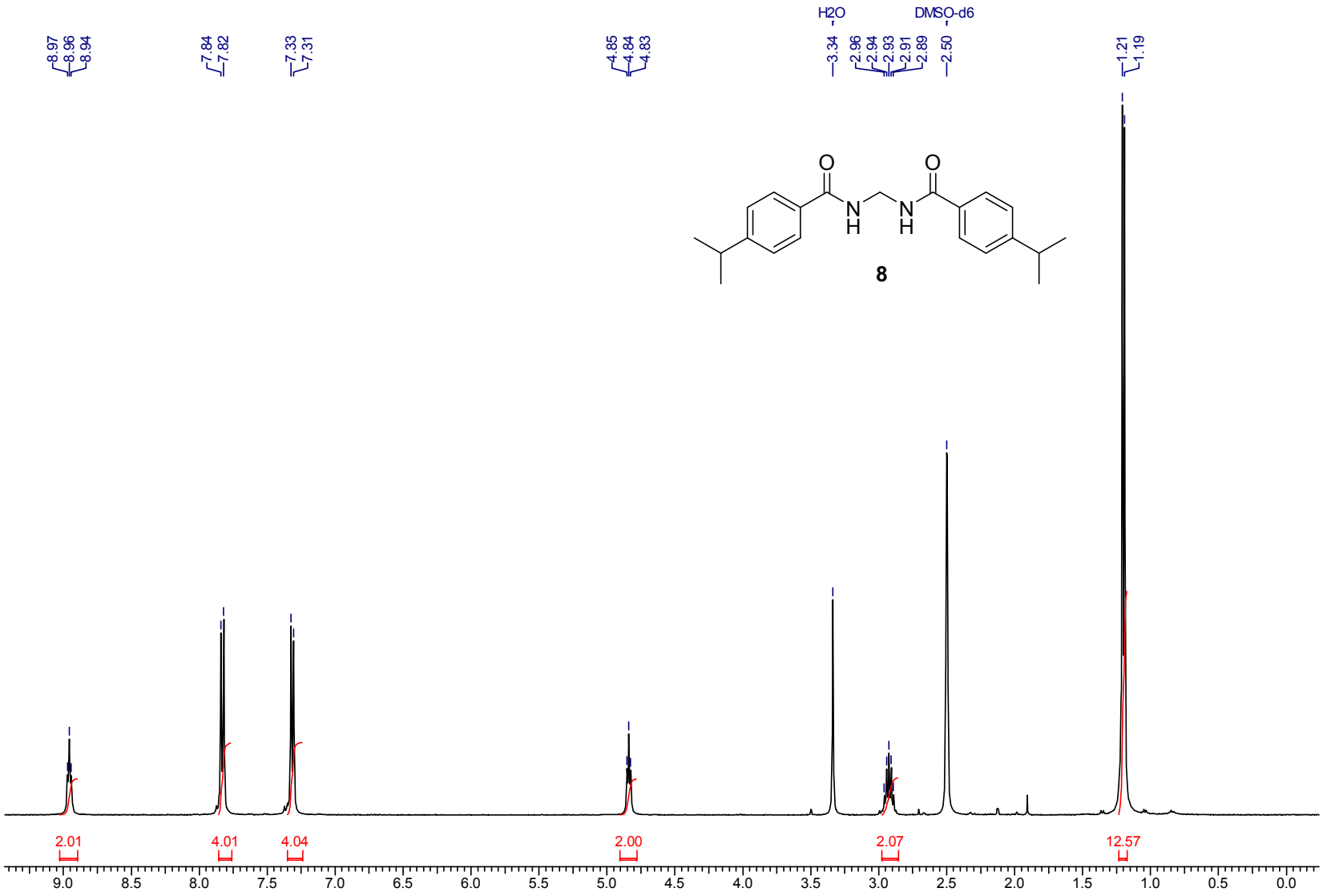
^{13}C NMR, 125 MHz



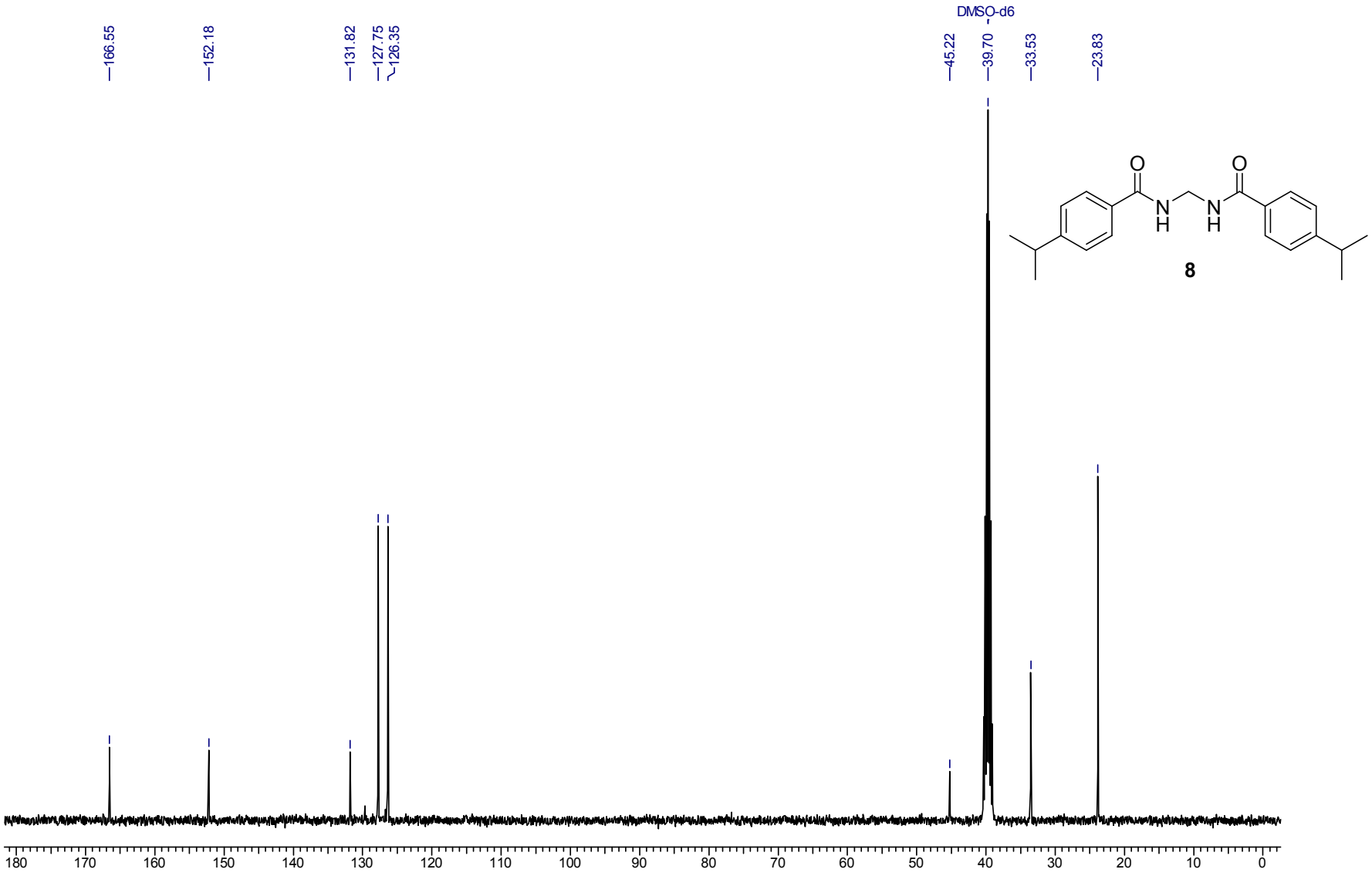
DEPT NMR, 125 MHz



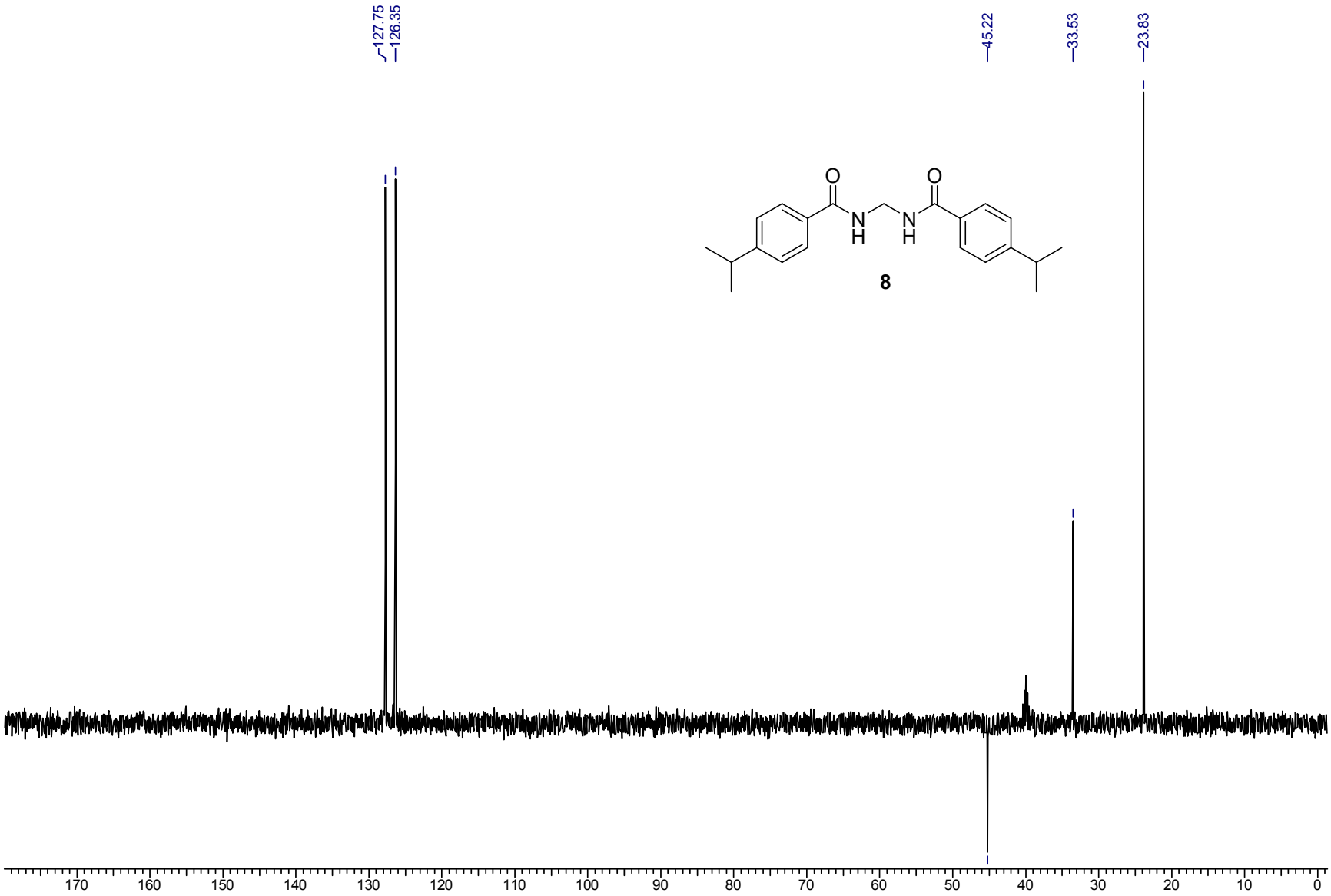
^{1}H NMR, 400 MHz



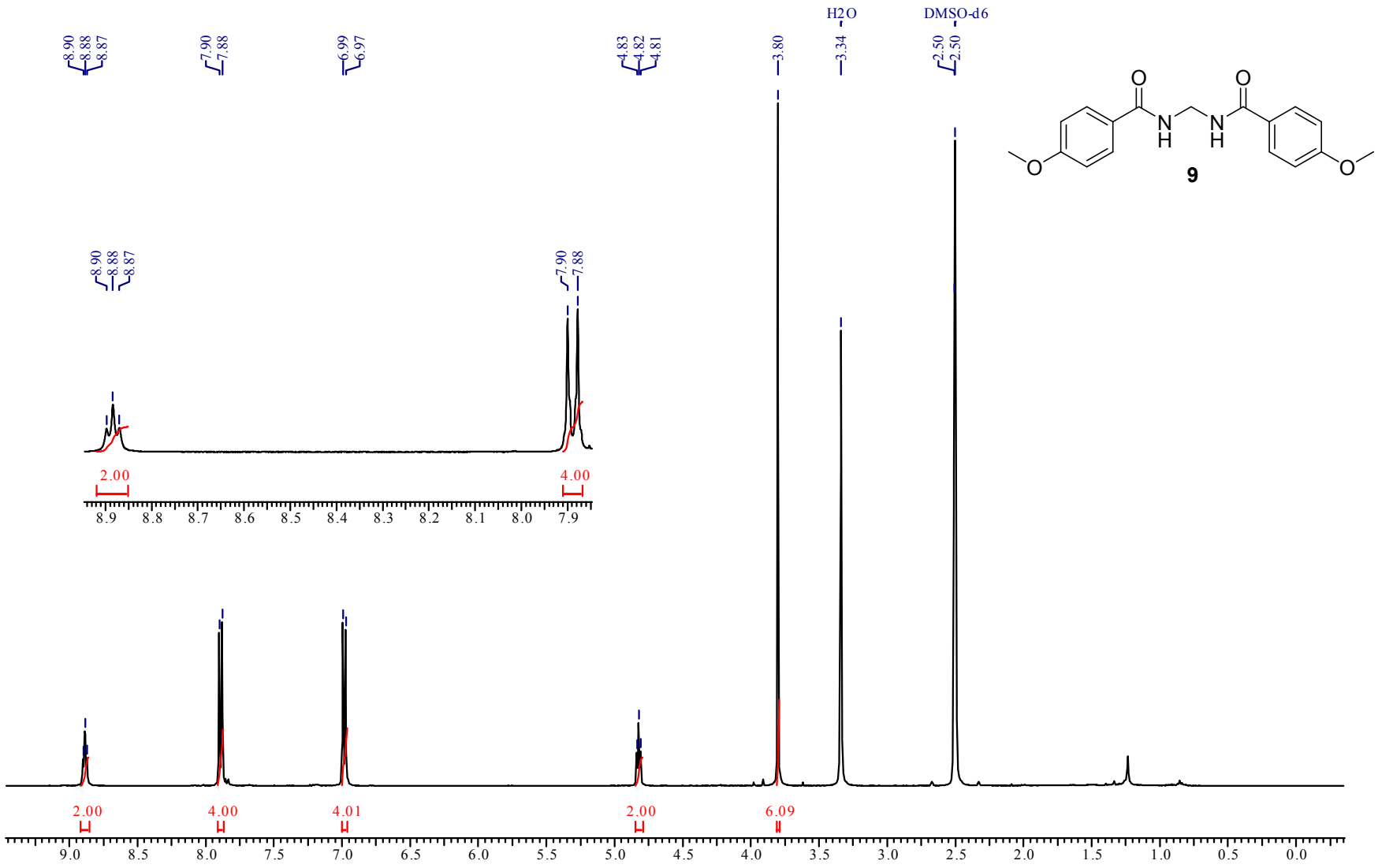
^{13}C NMR, 100 MHz



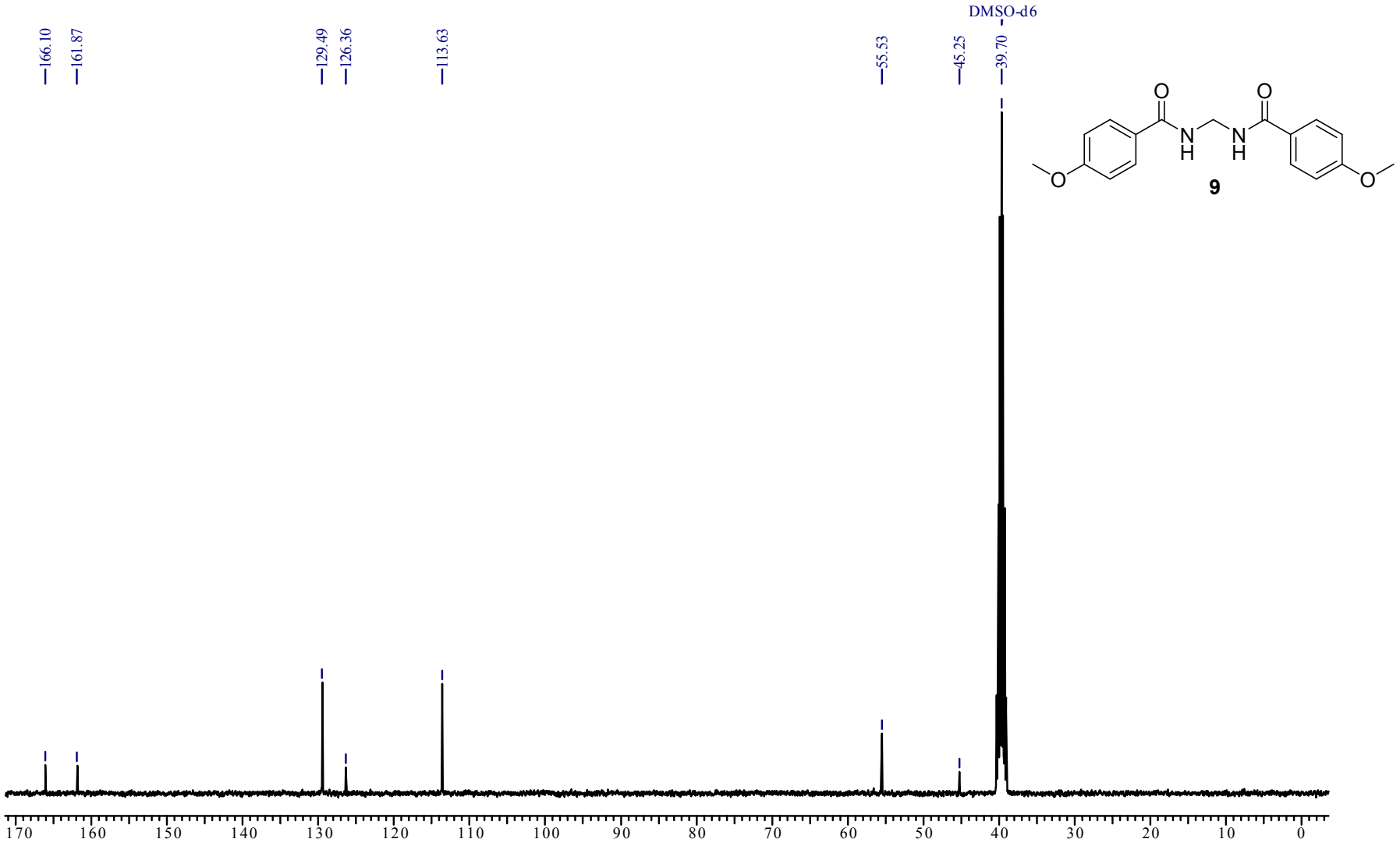
DEPT NMR, 100 MHz



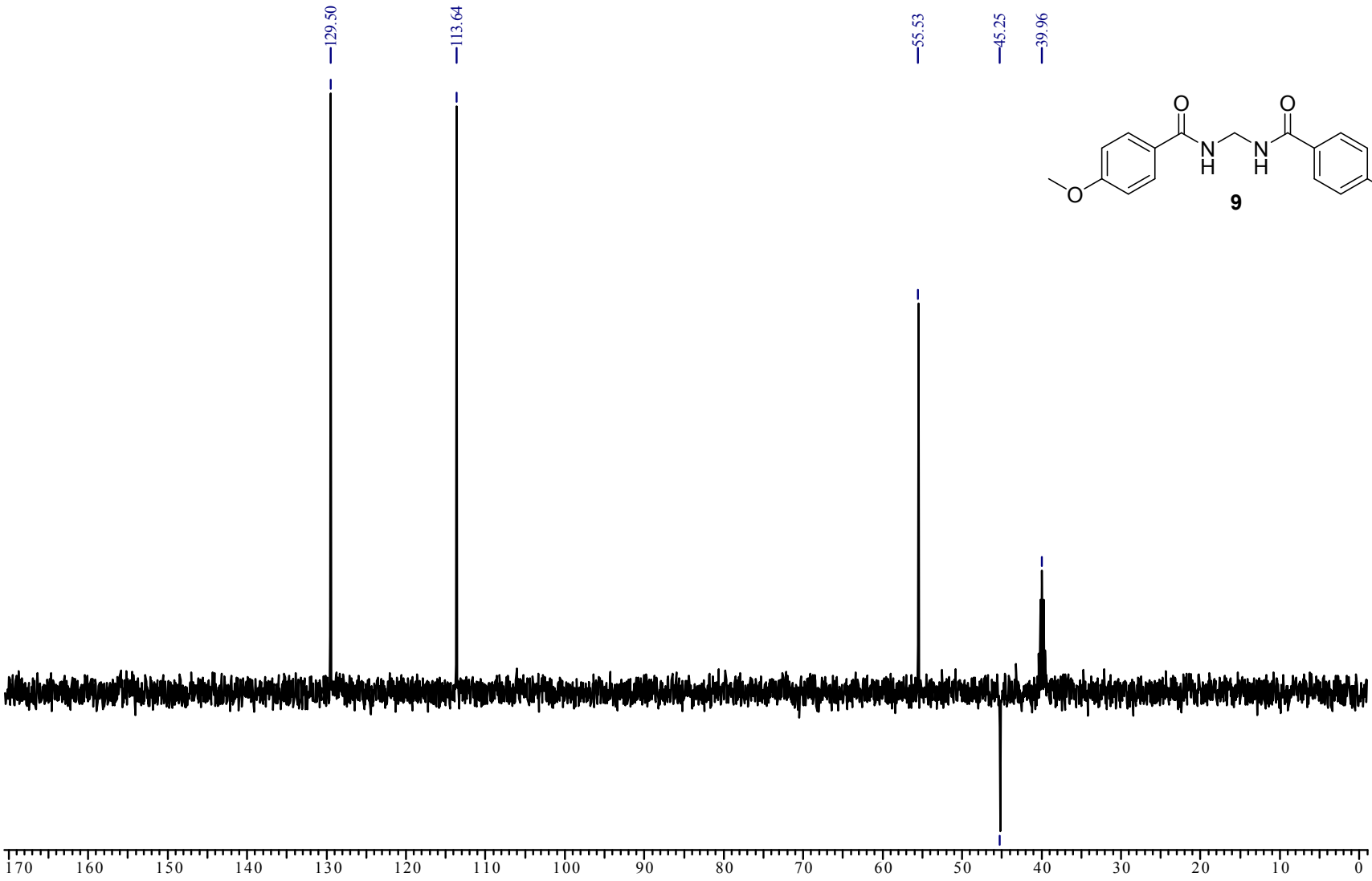
^{1}H NMR, 400 MHz



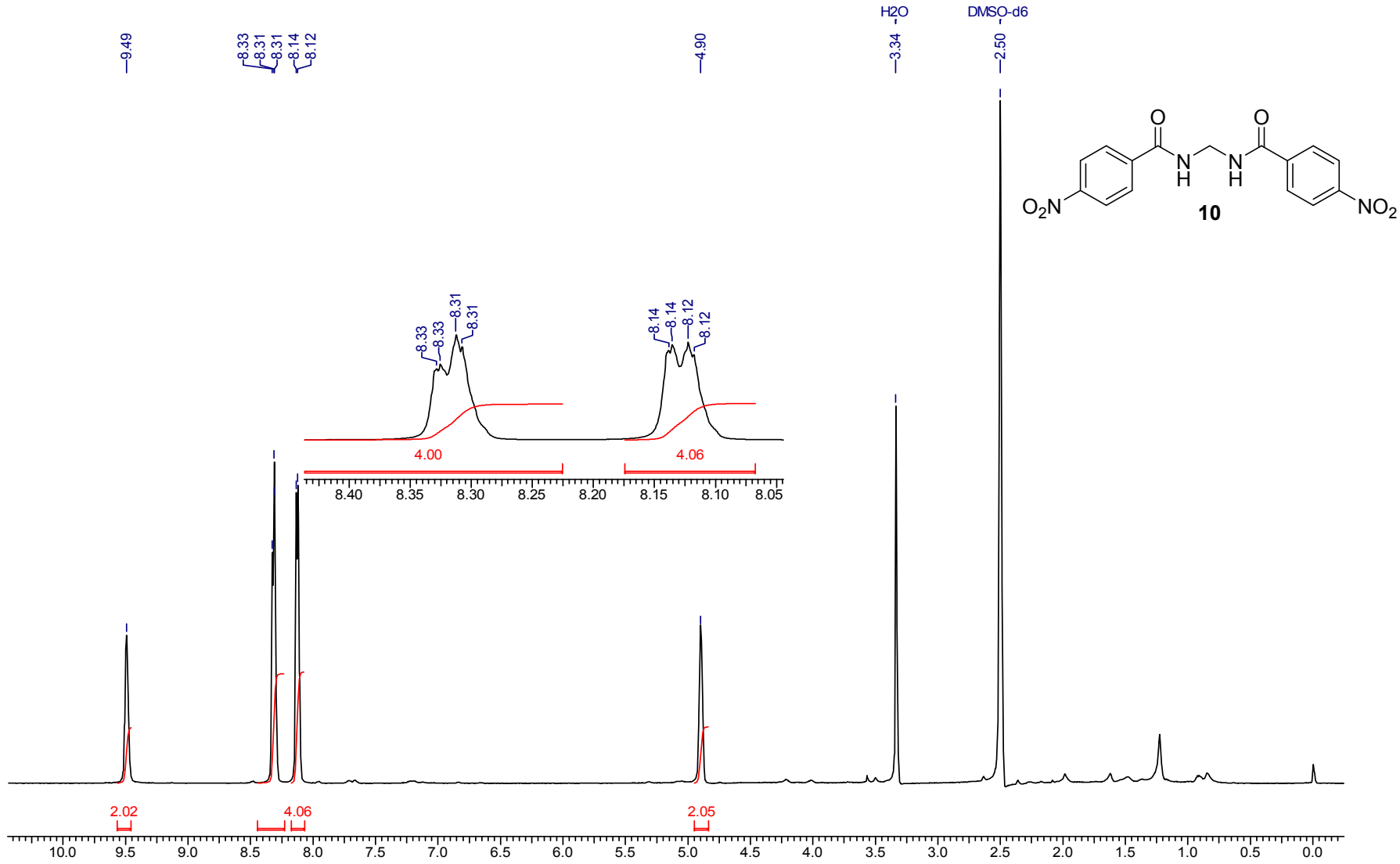
^{13}C NMR, 100 MHz



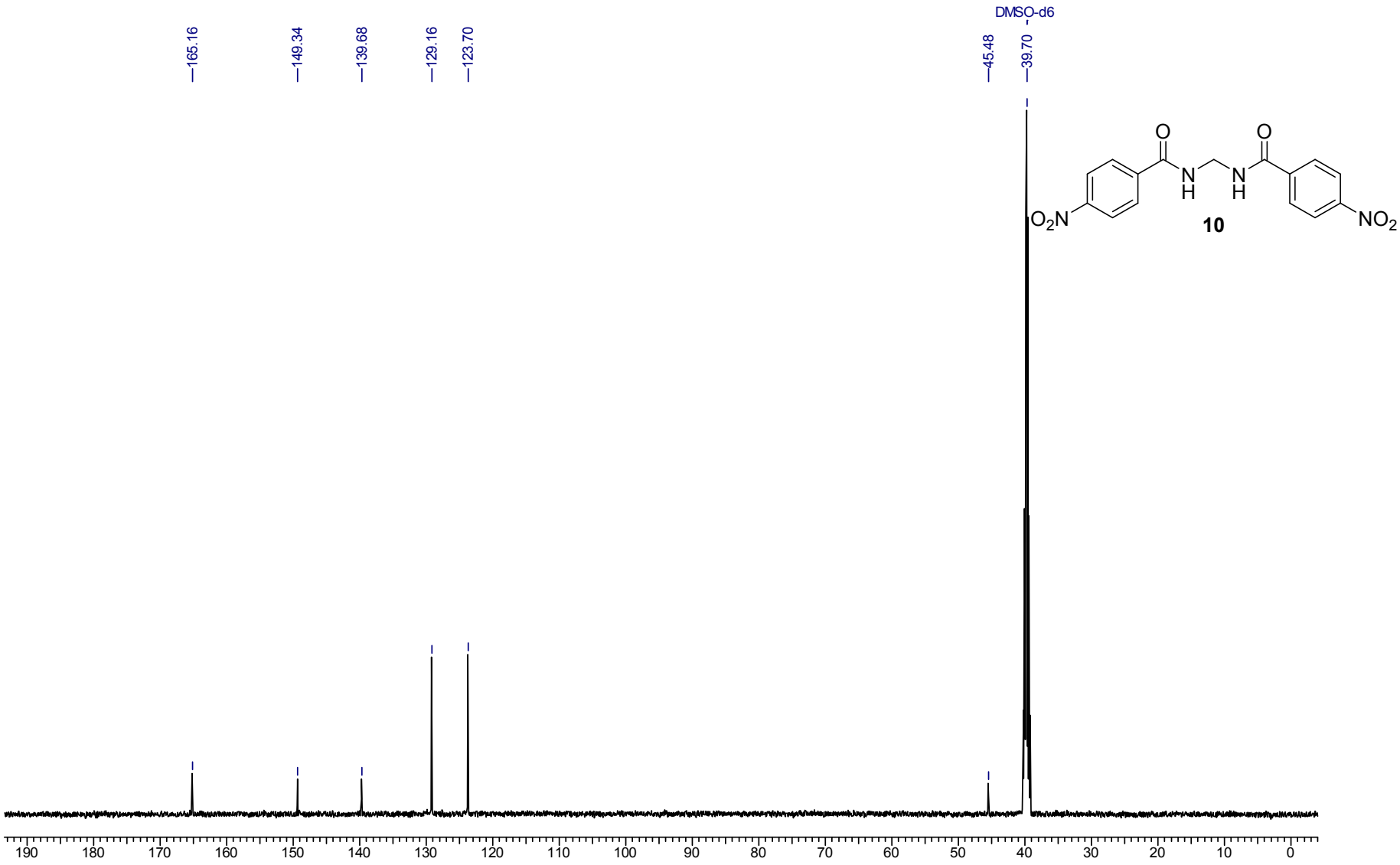
DEPT NMR, 100 MHz



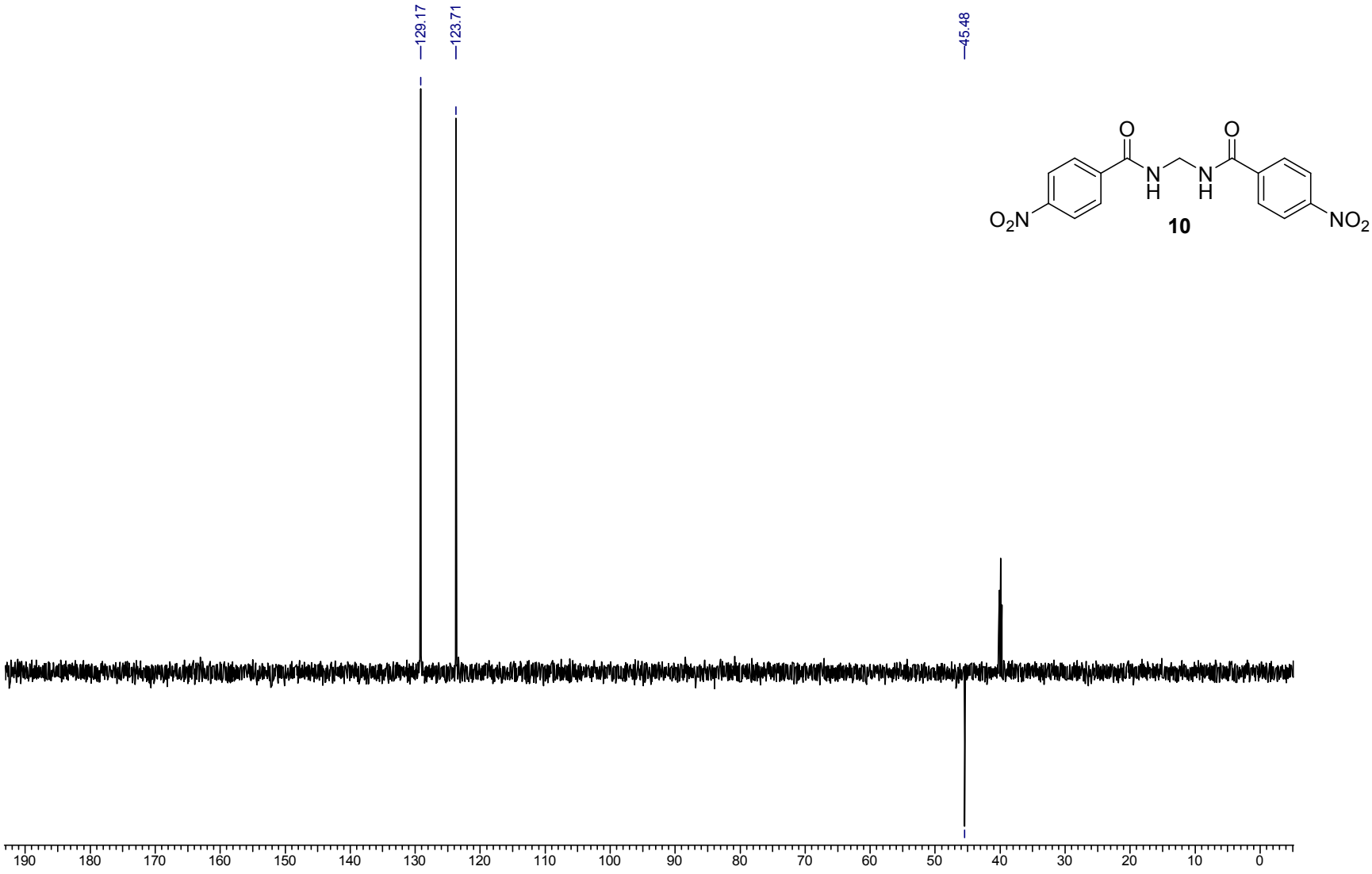
^{1}H NMR, 500 MHz



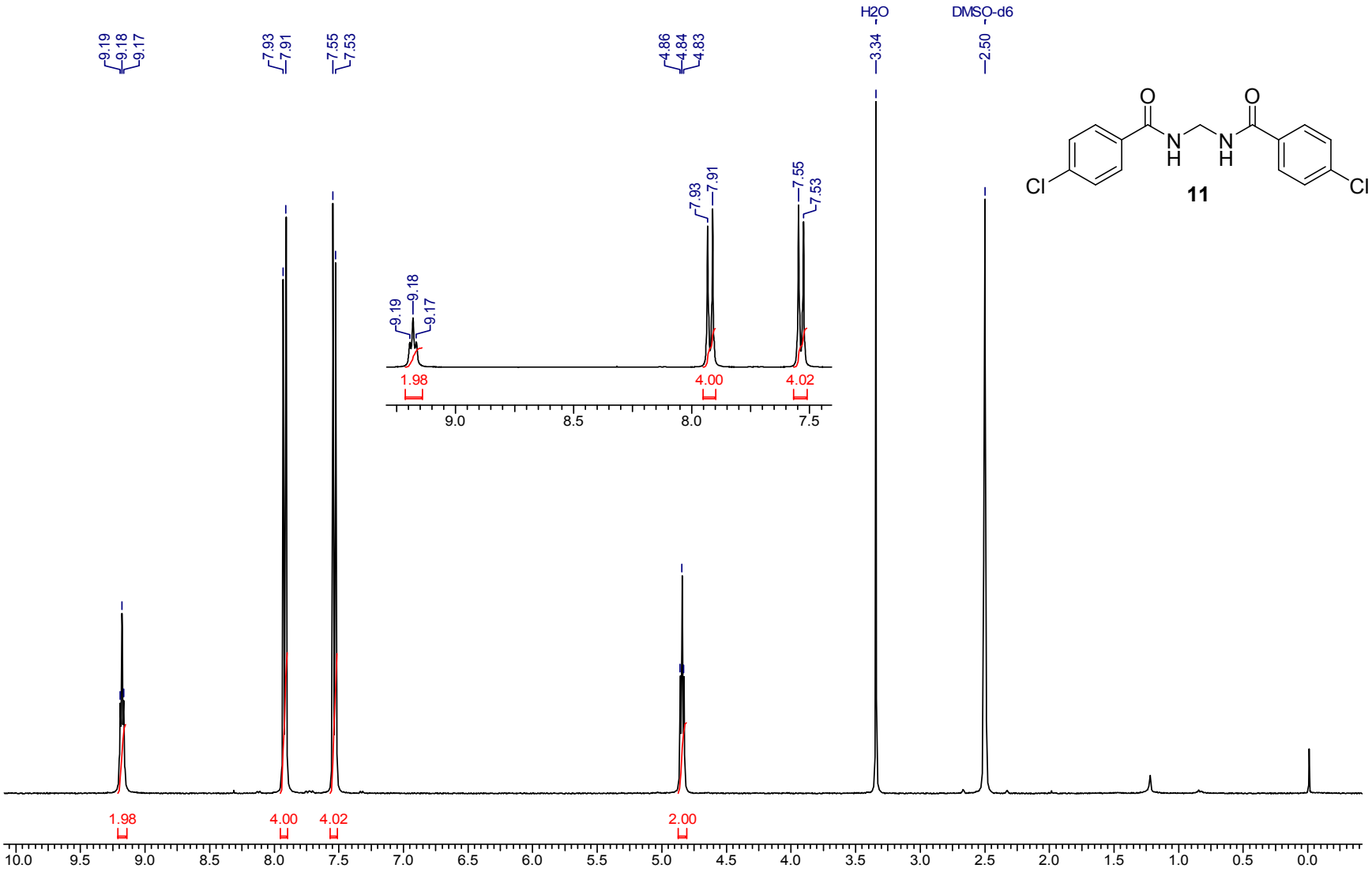
^{13}C NMR, 125 MHz



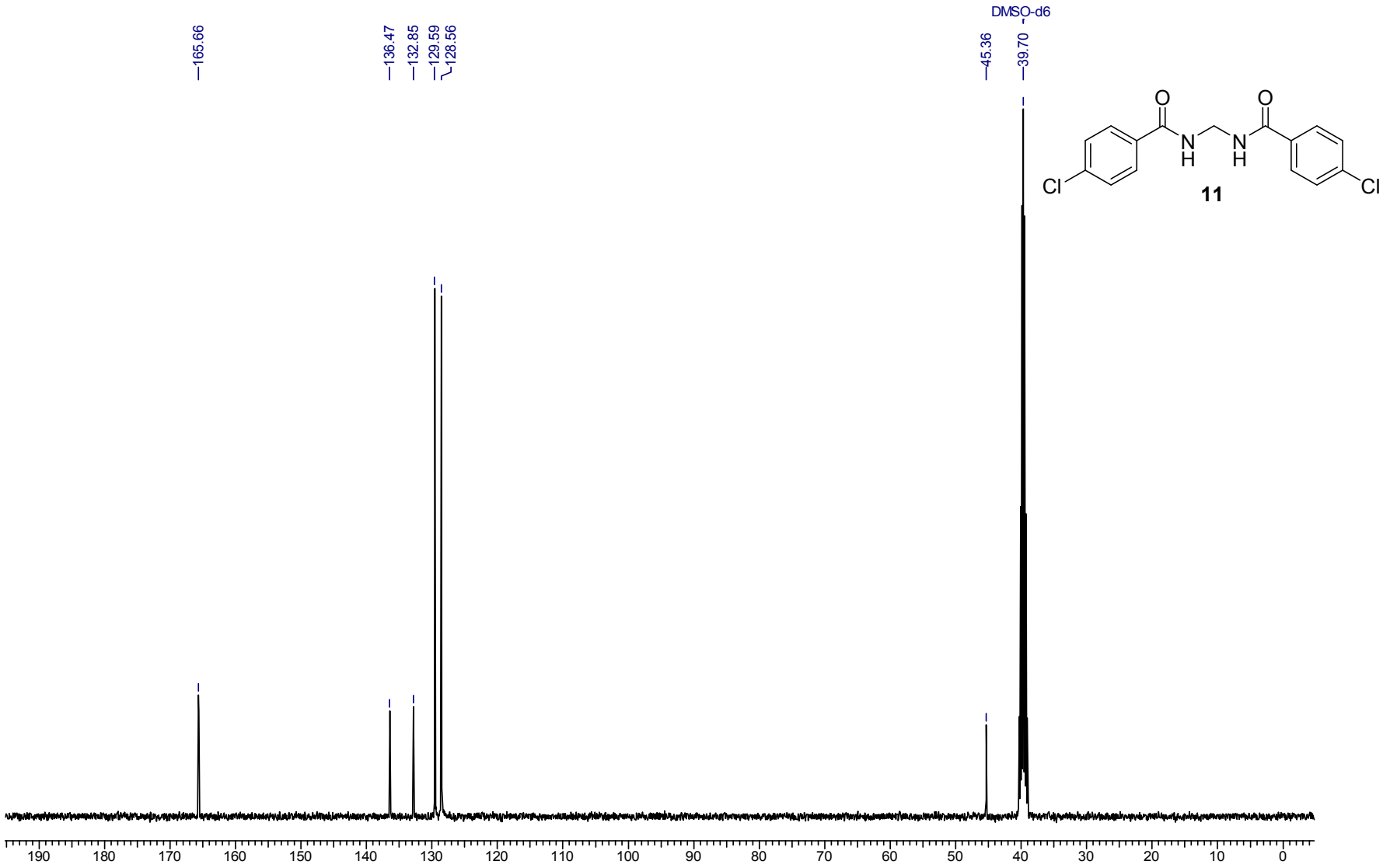
DEPT NMR, 125 MHz



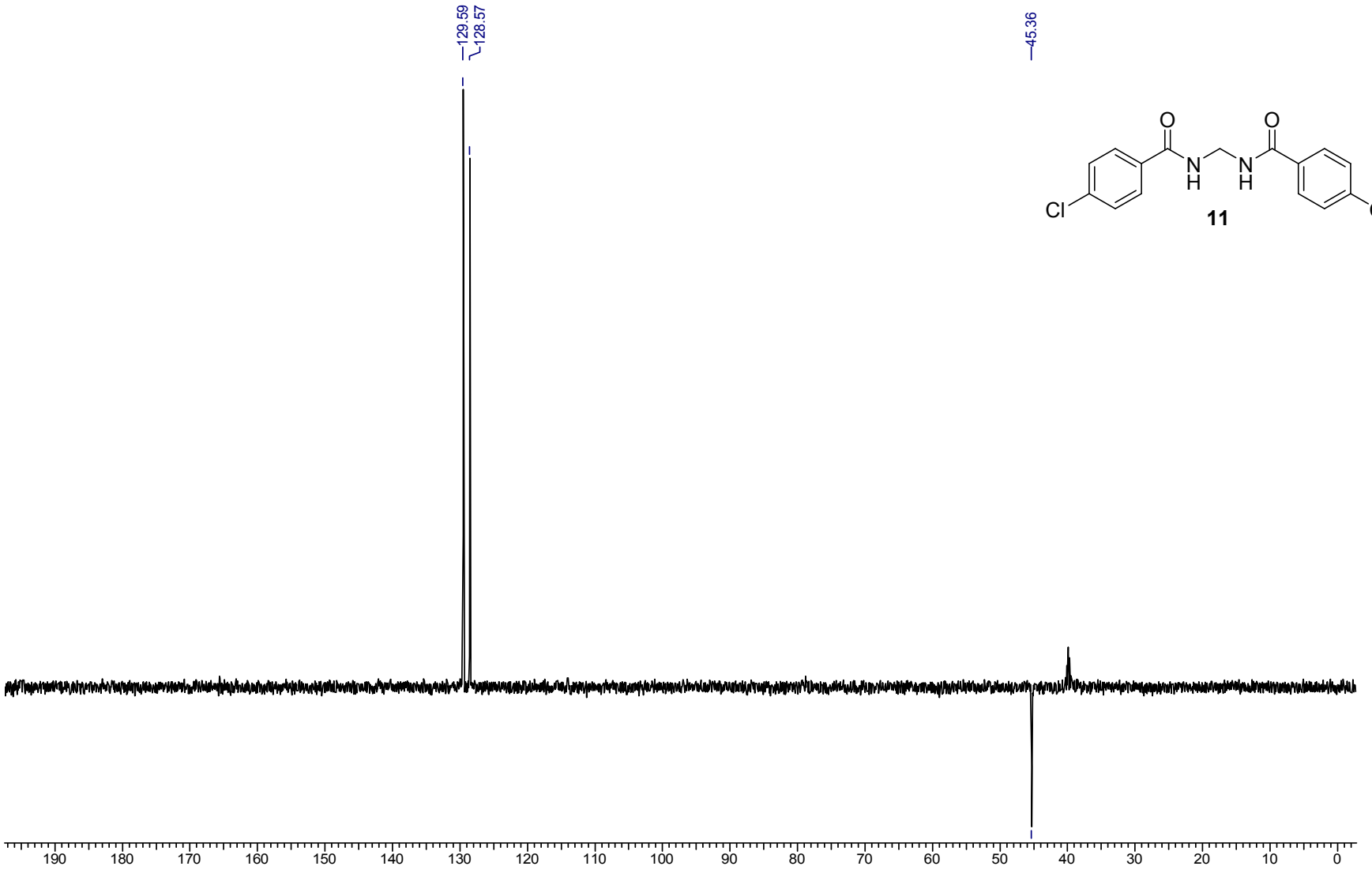
^{1}H NMR, 400 MHz



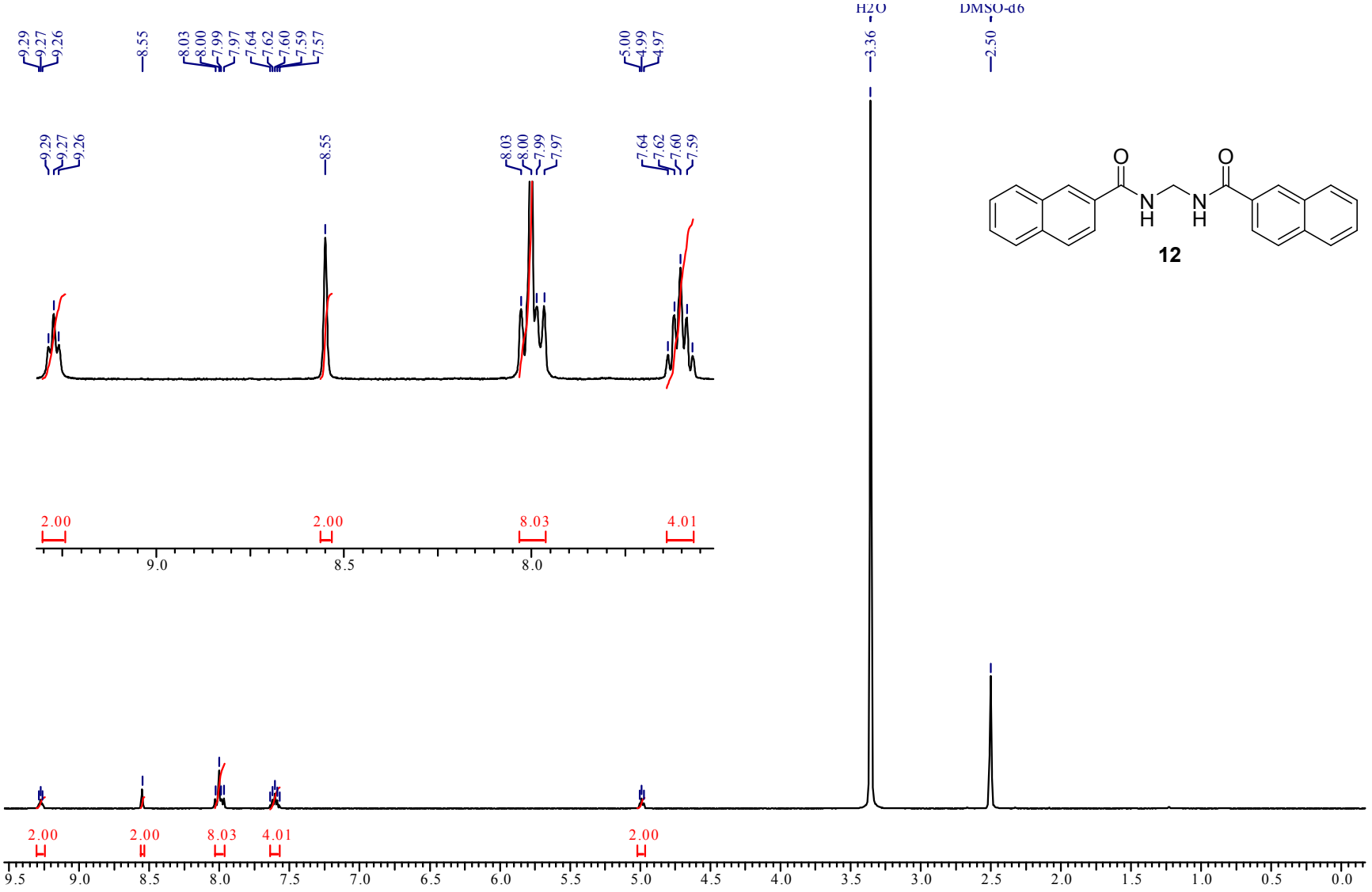
^{13}C NMR, 100 MHz



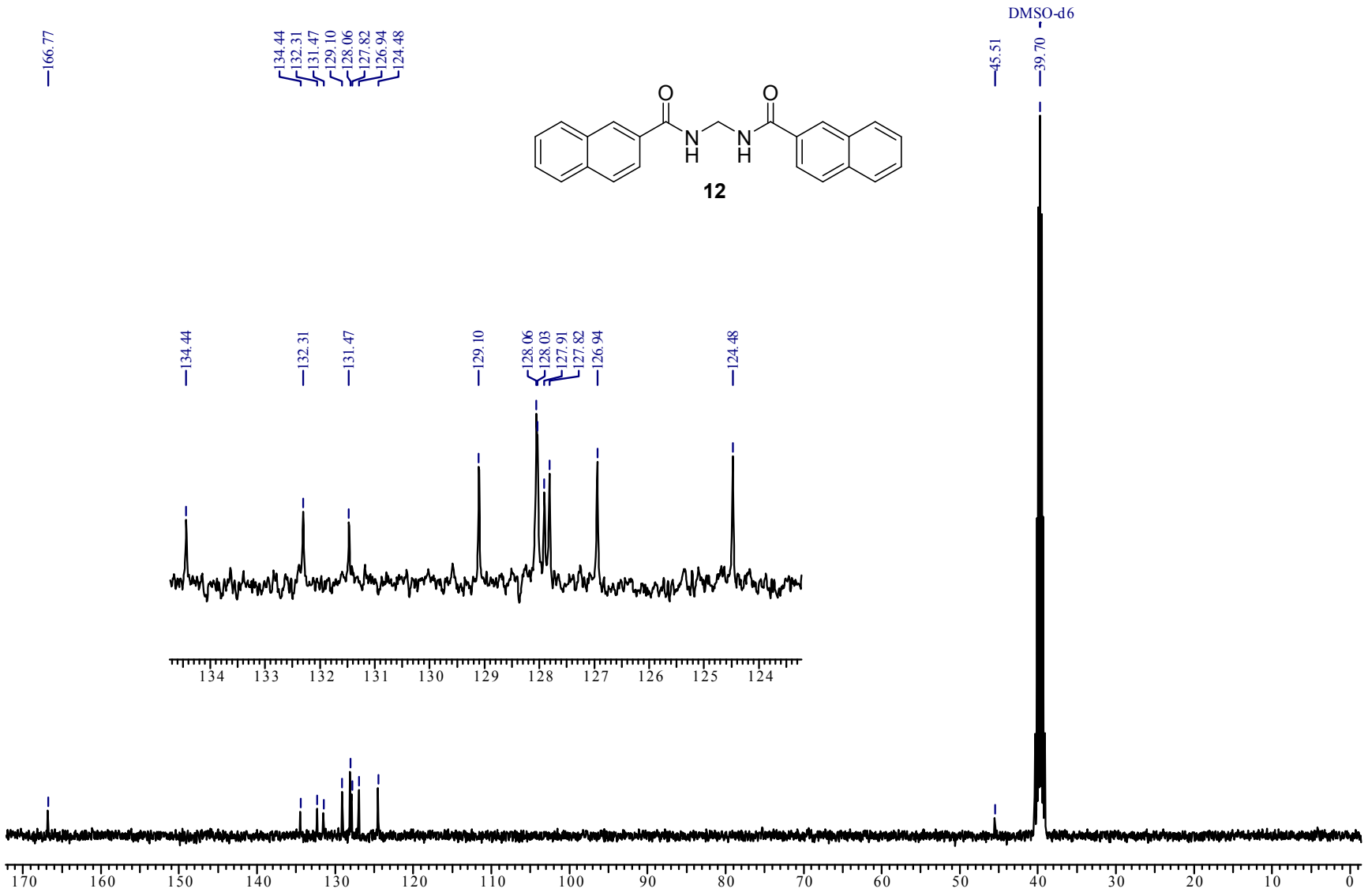
^{13}DEPT NMR, 100 MHz



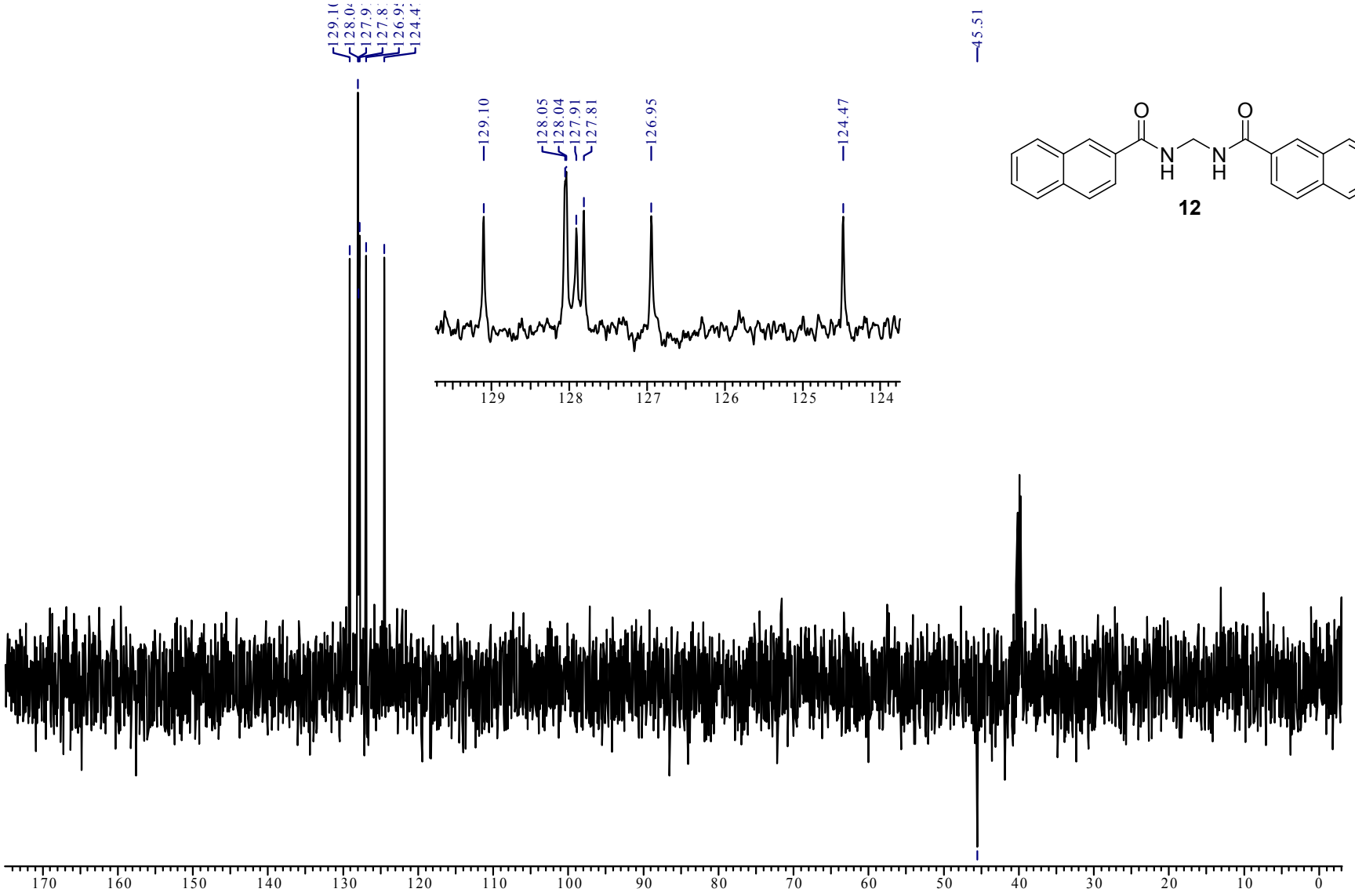
^{1}H NMR, 400 MHz



^{13}C NMR, 100 MHz

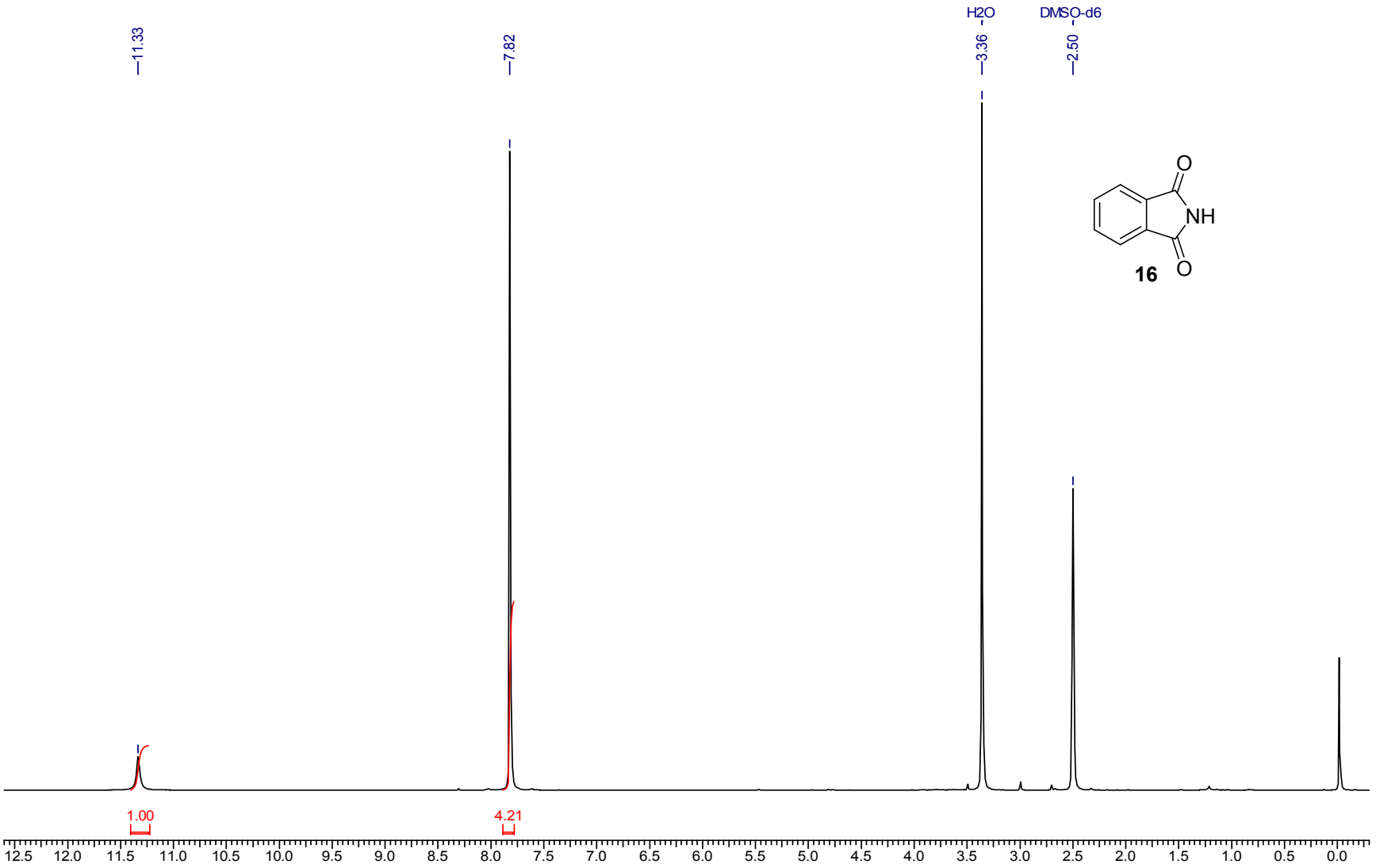


DEPT NMR, 100 MHz

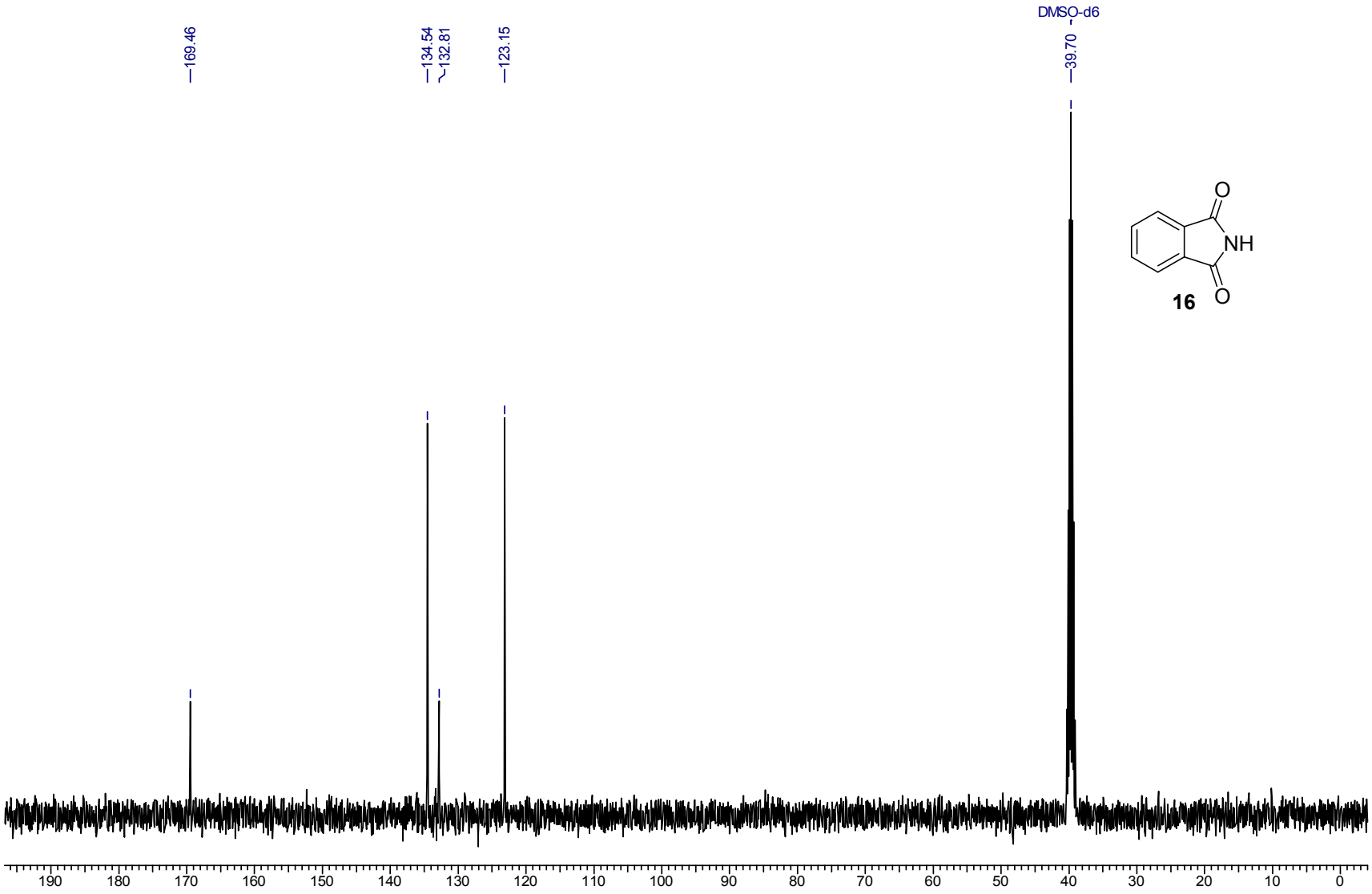


12

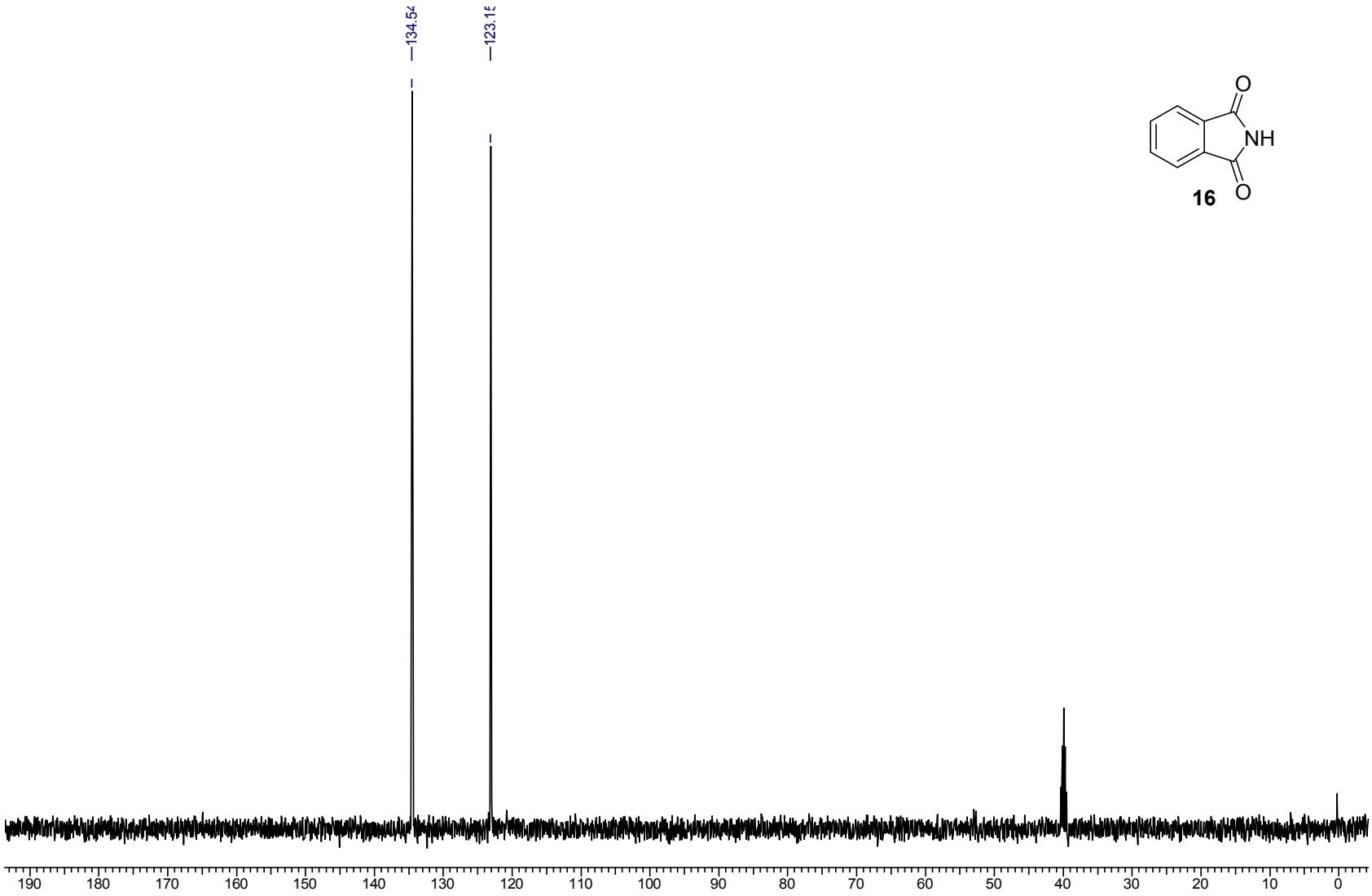
^{1}H NMR, 400 MHz



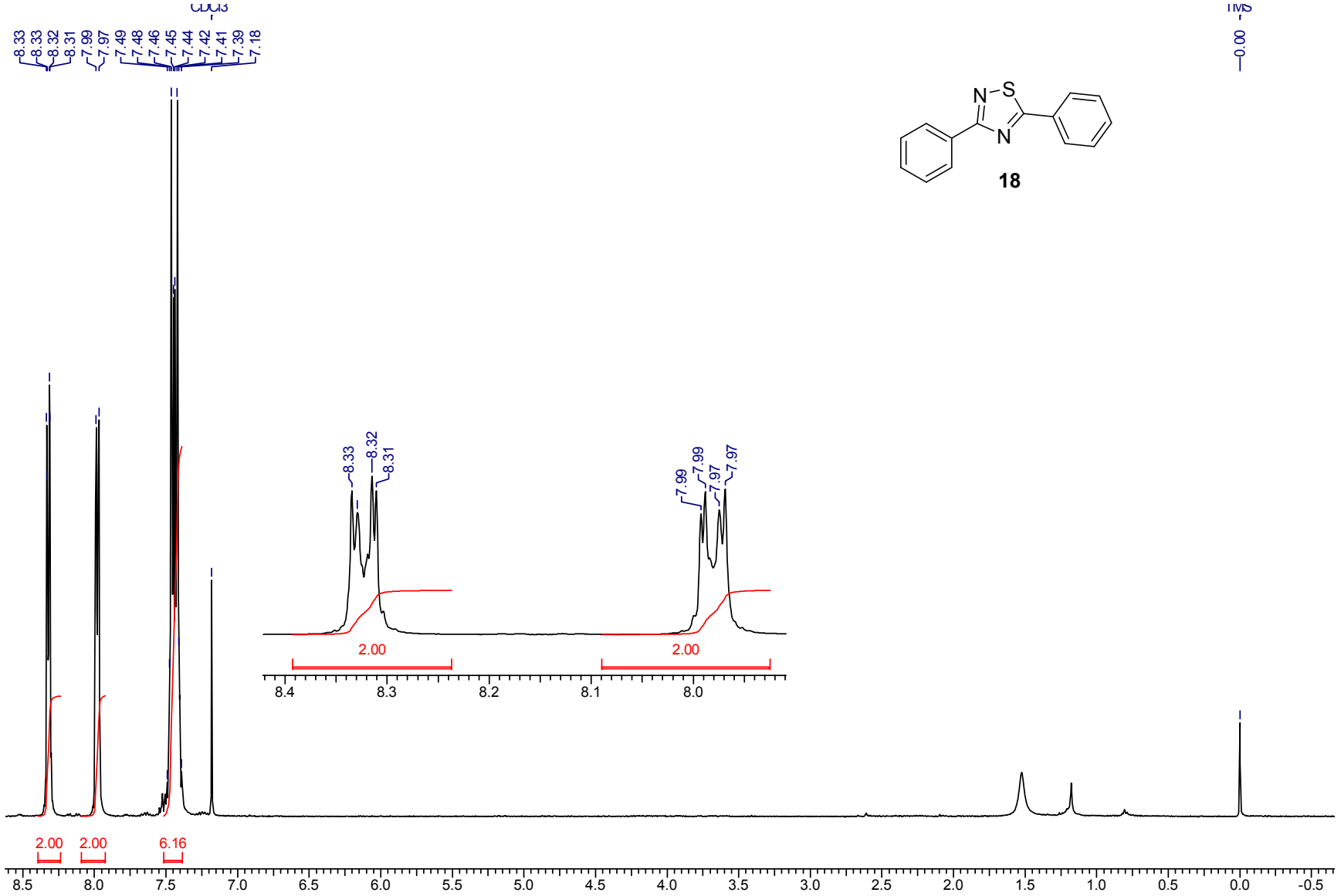
^{13}C NMR, 100 MHz



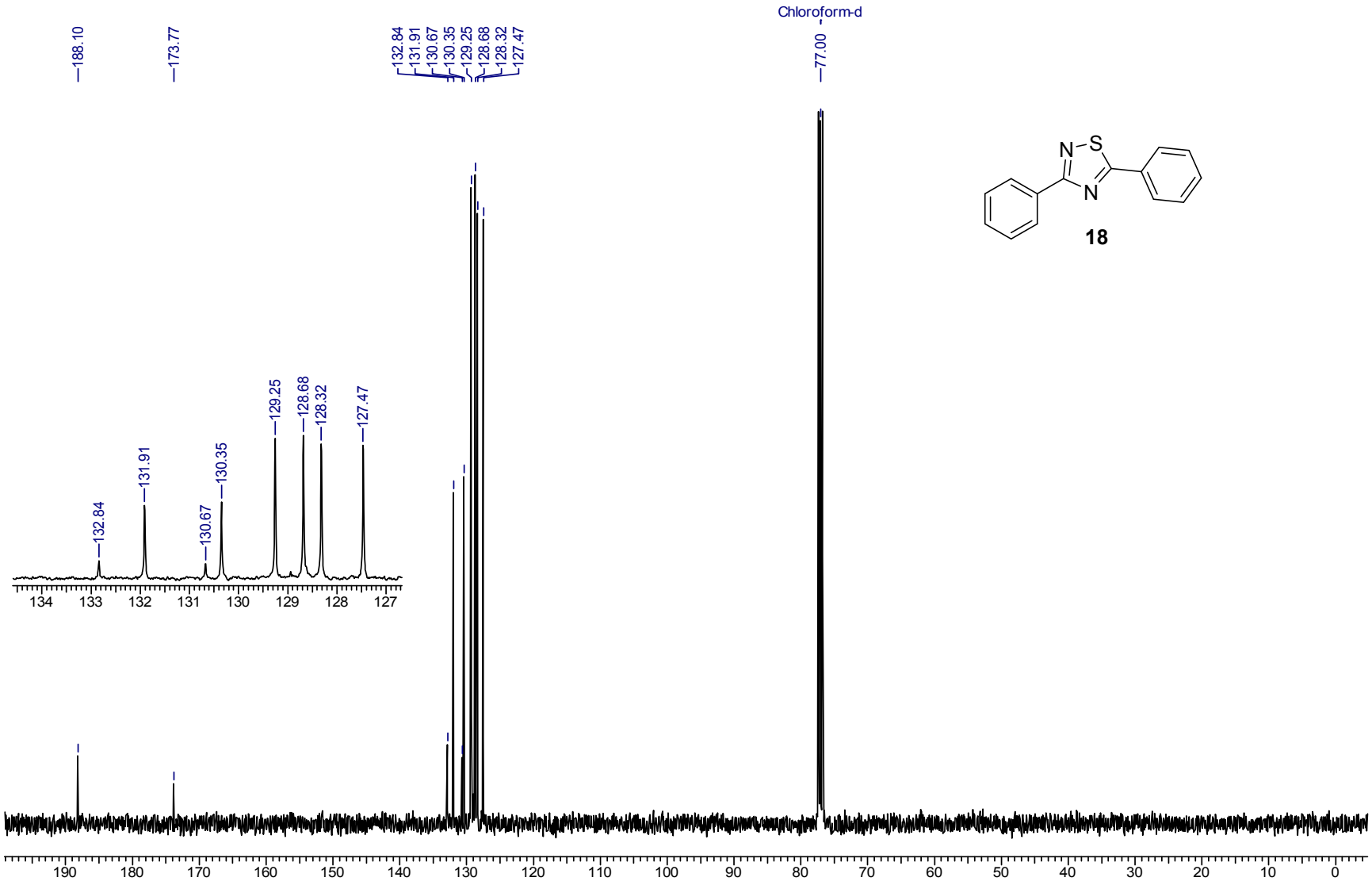
DEPT NMR, 100 MHz



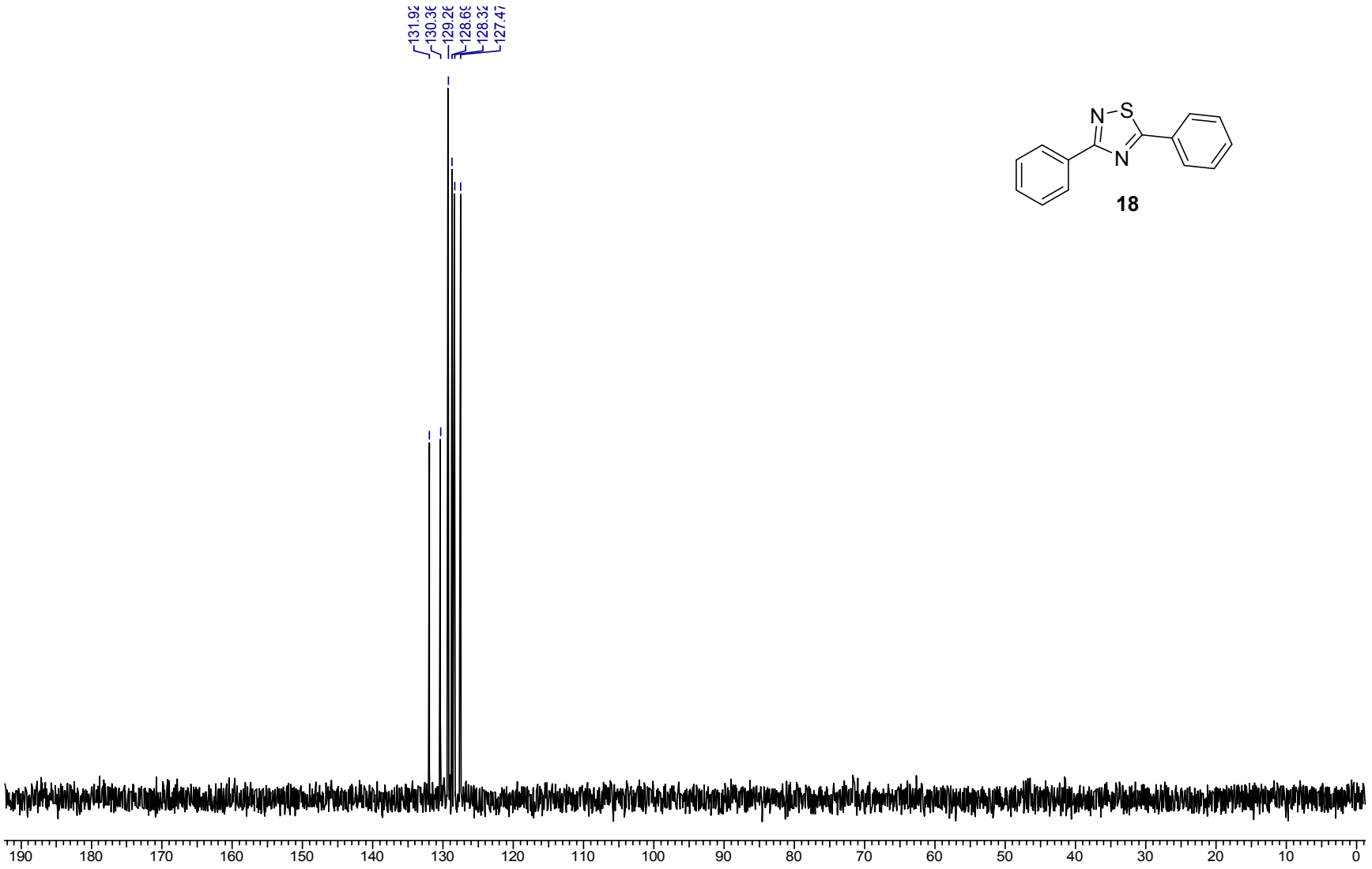
^{1}H NMR, 400 MHz



^{13}C NMR, 100 MHz

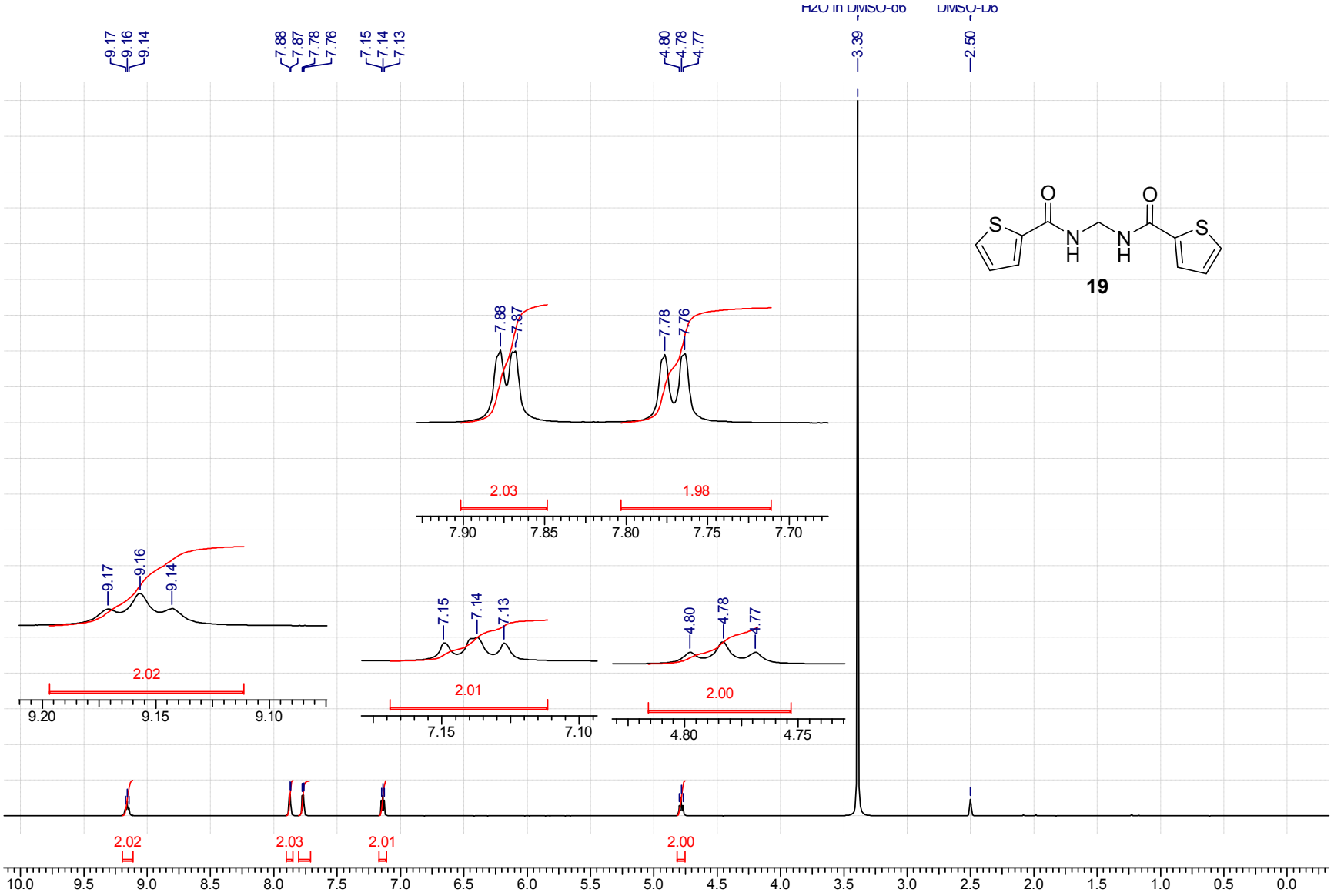


DEPT NMR, 100 MHz

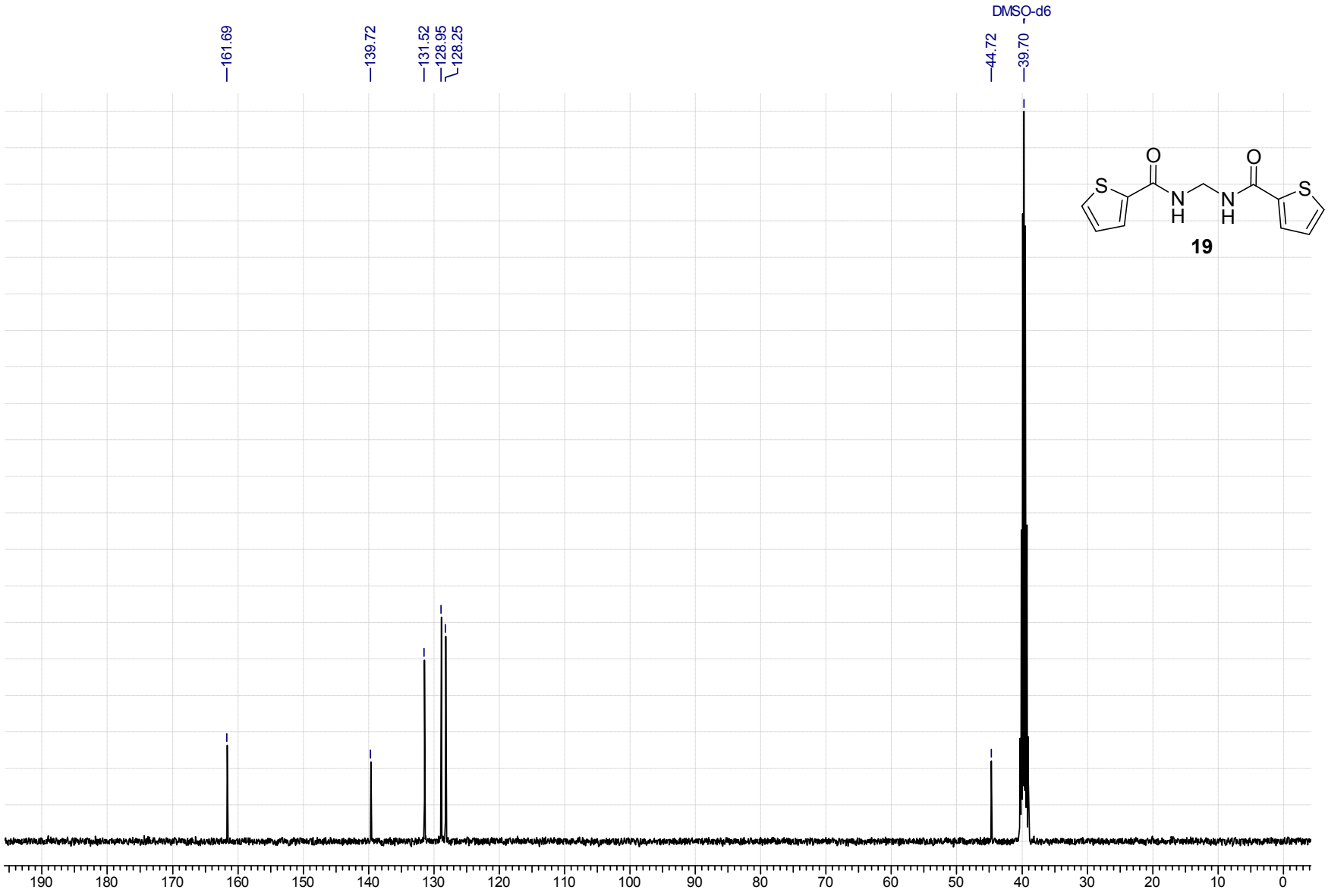


18

^{1}H NMR, 400 MHz

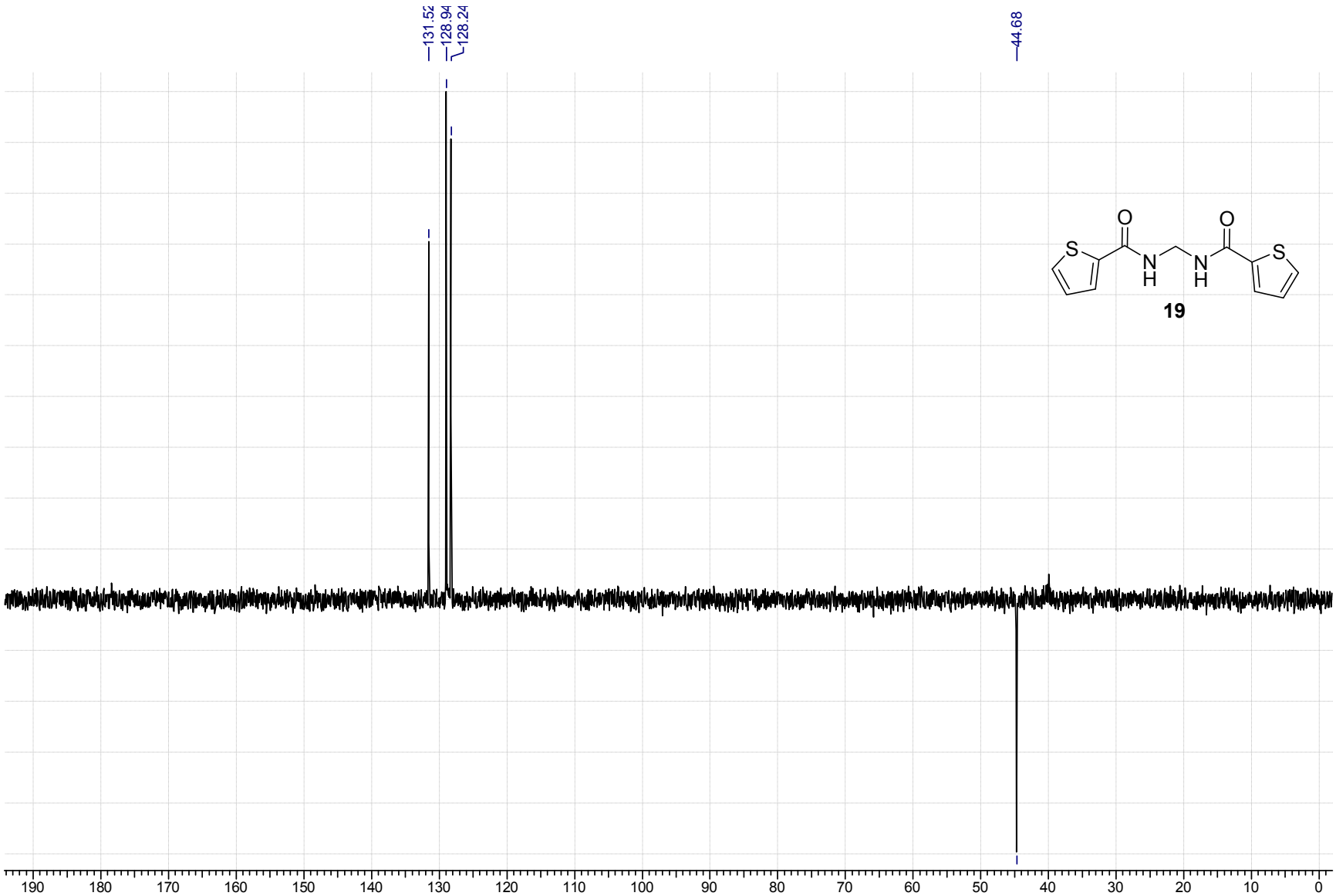


^{13}C NMR, 100 MHz

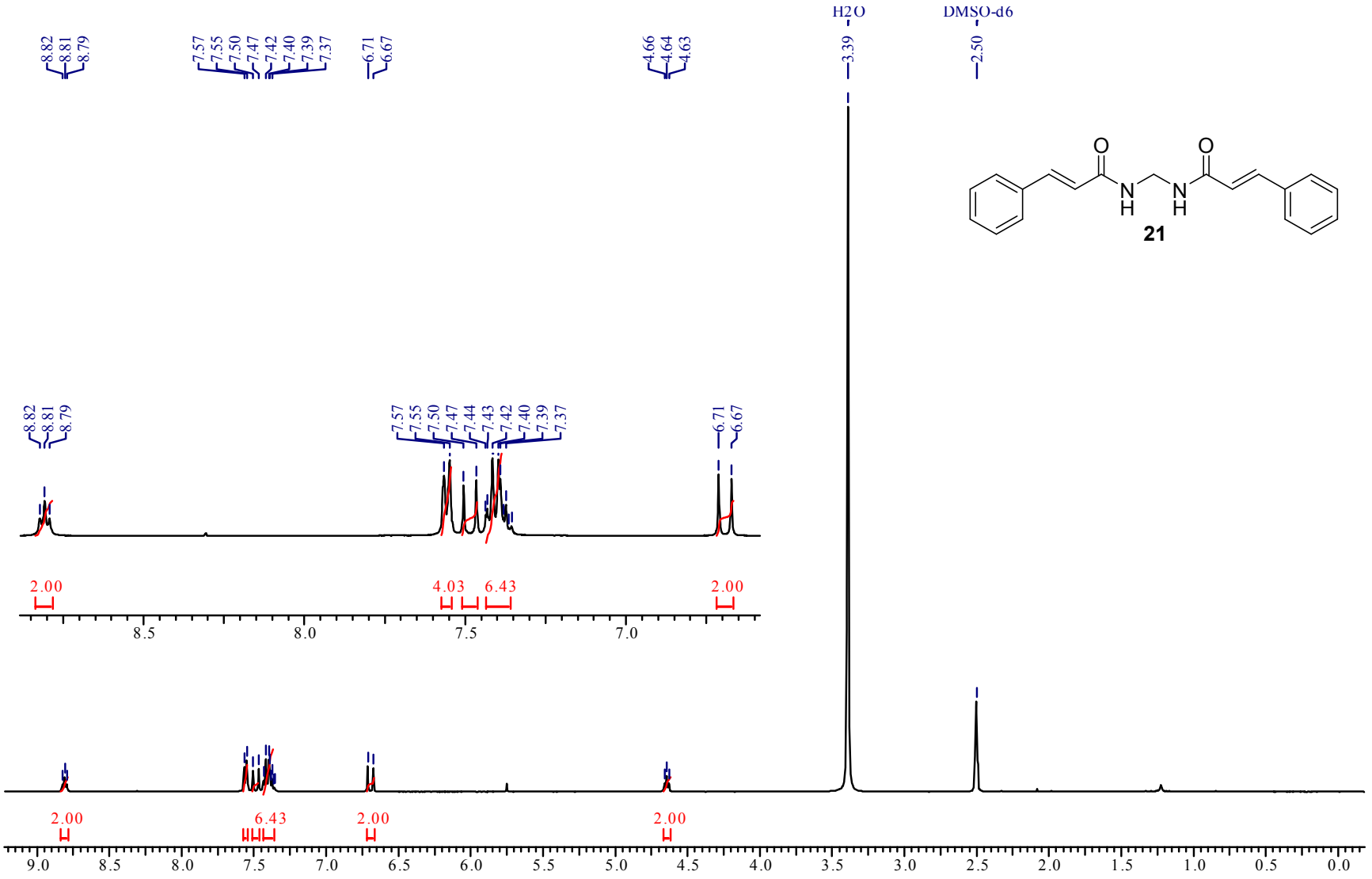


19

DEPT NMR, 100 MHz

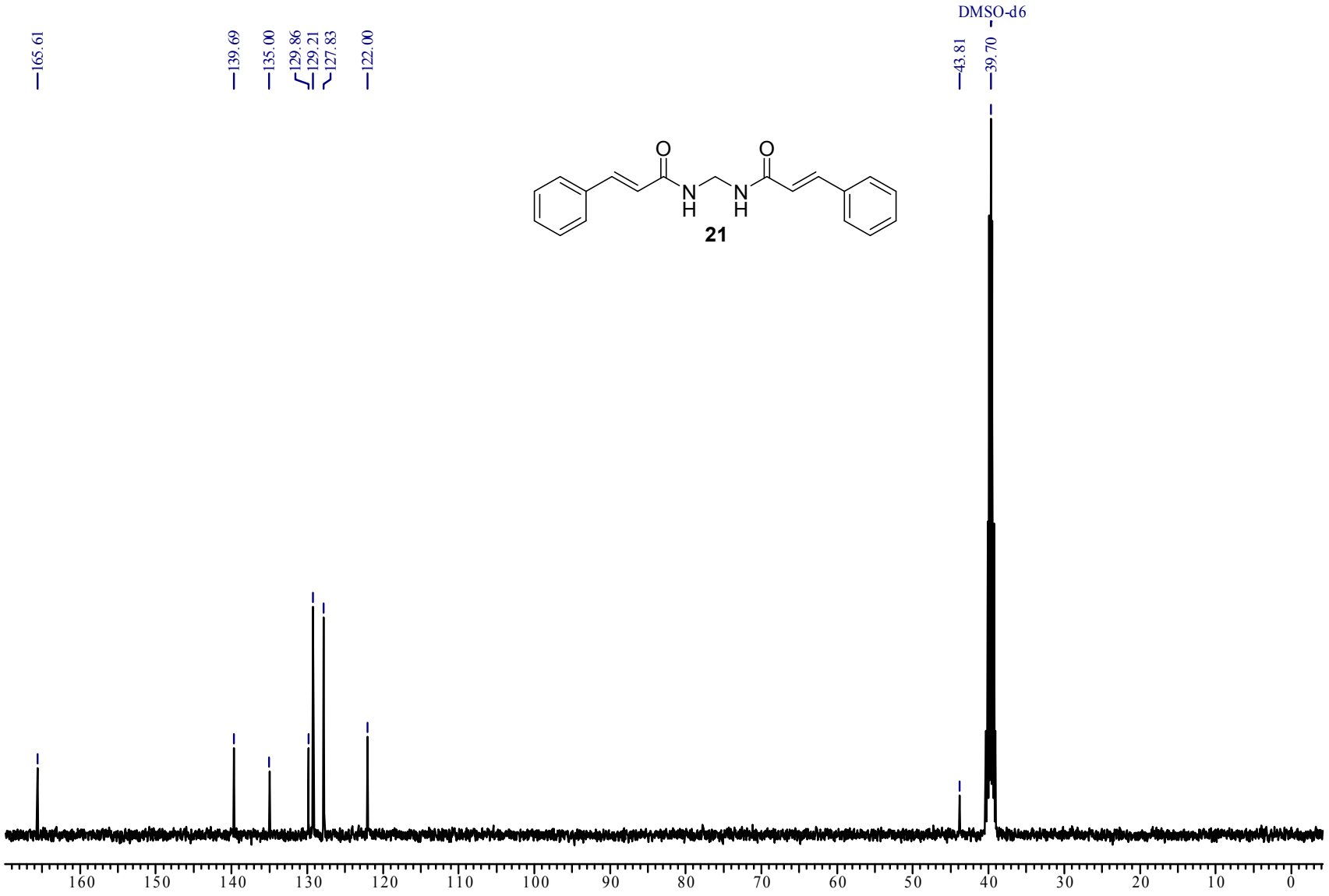


^{1}H NMR, 400 MHz

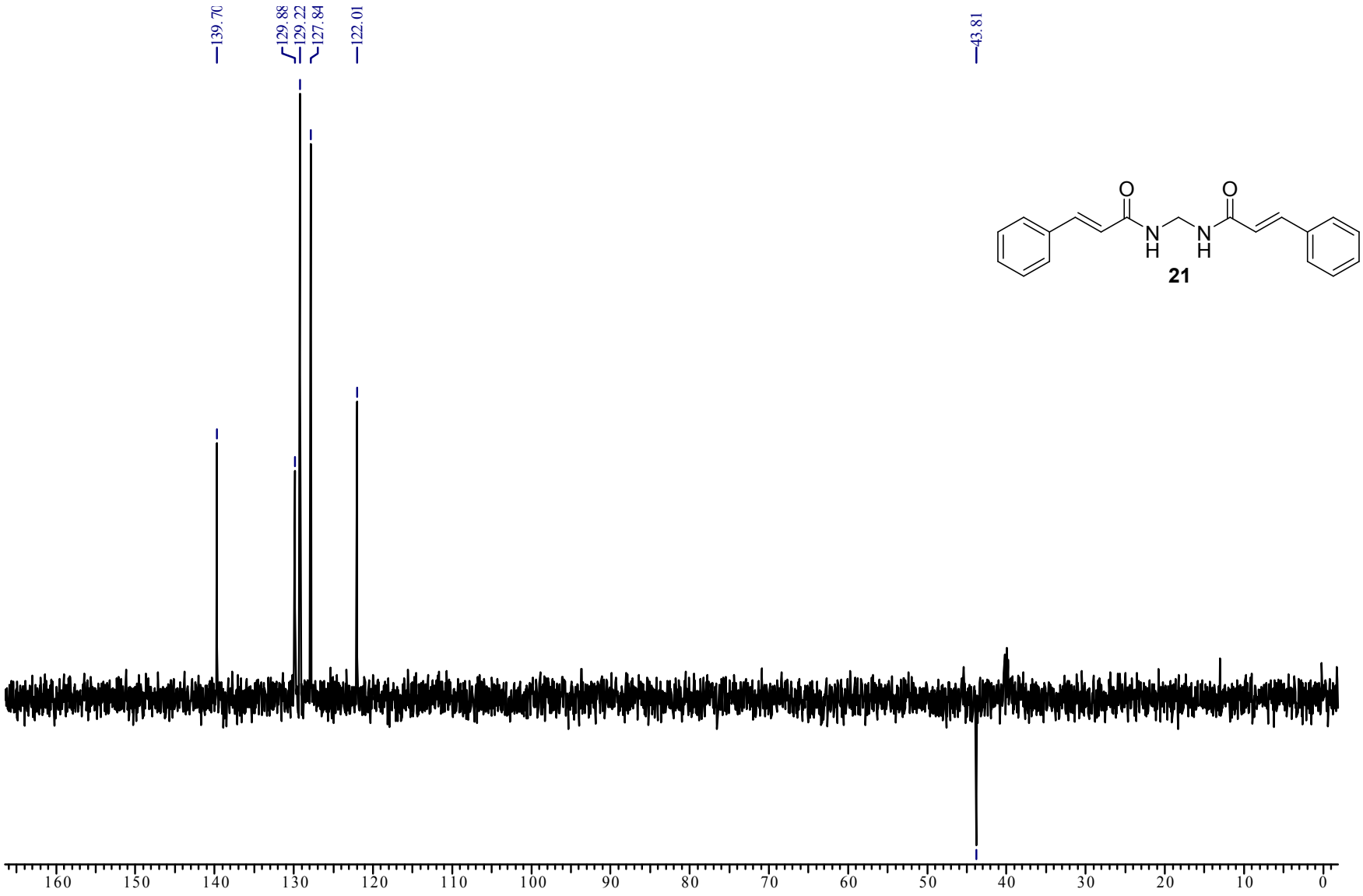


21

^{13}C NMR, 100 MHz

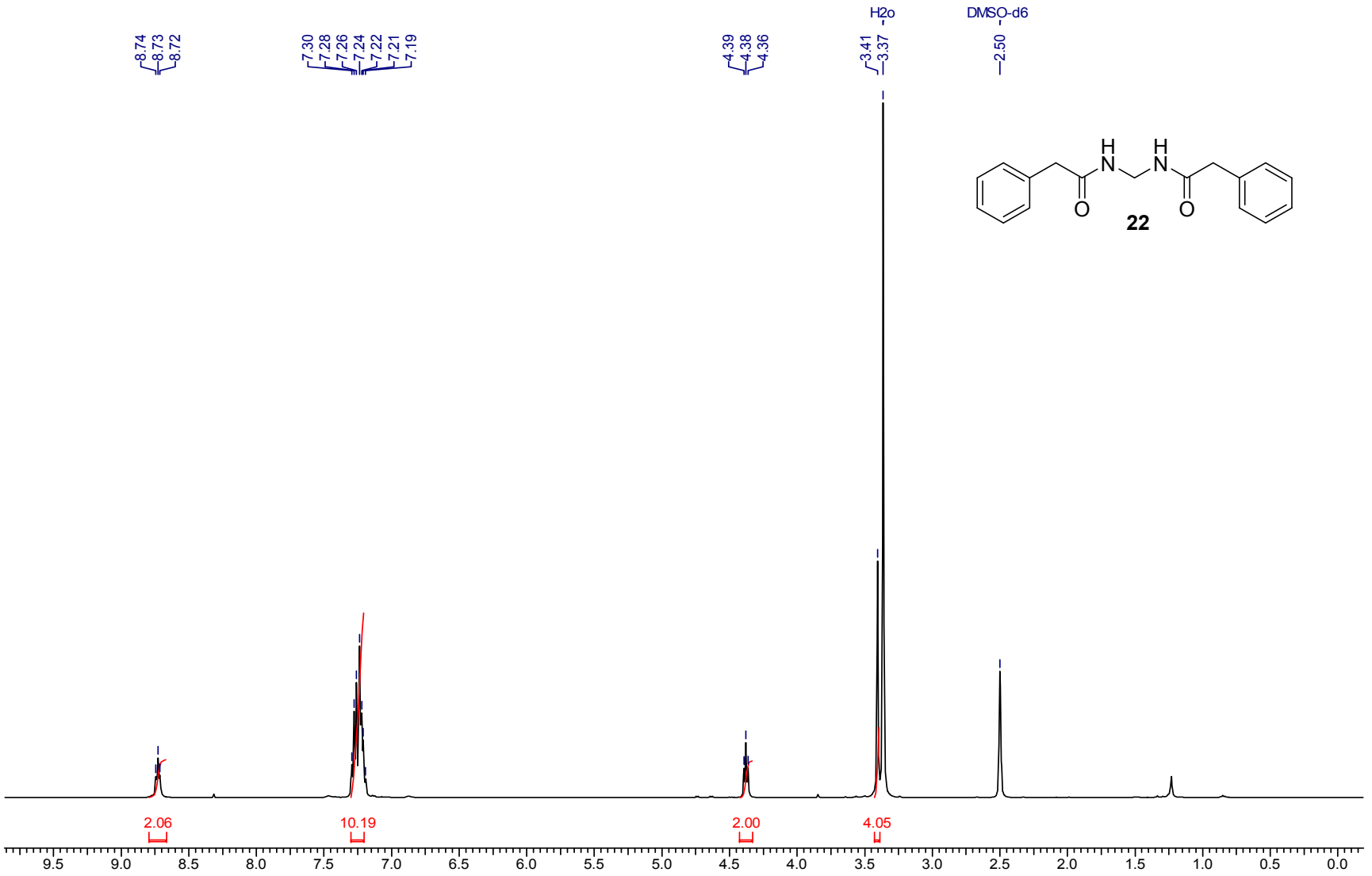


DEPT NMR, 100 MHz



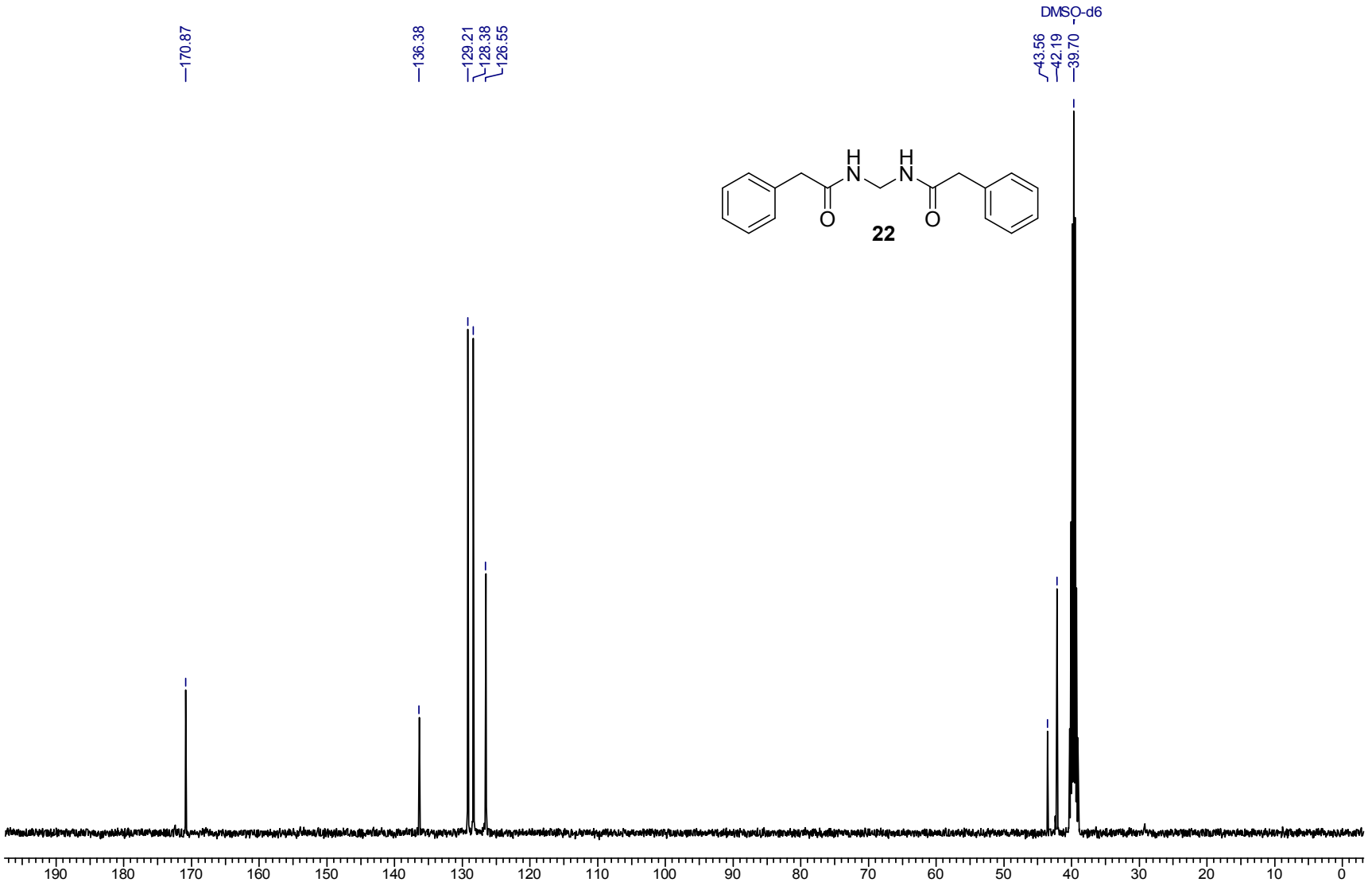
21

^{1}H NMR, 400 MHz

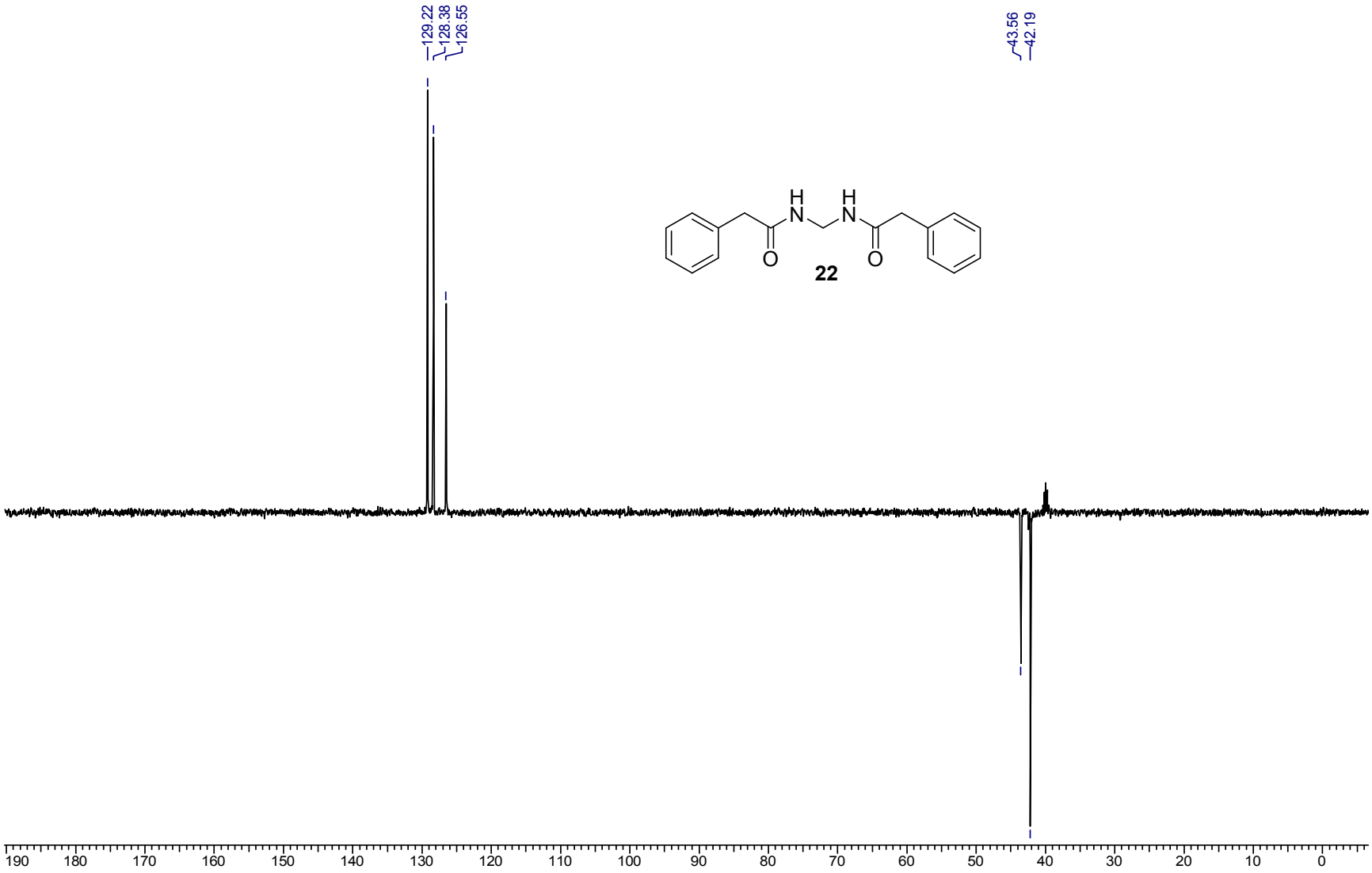


22

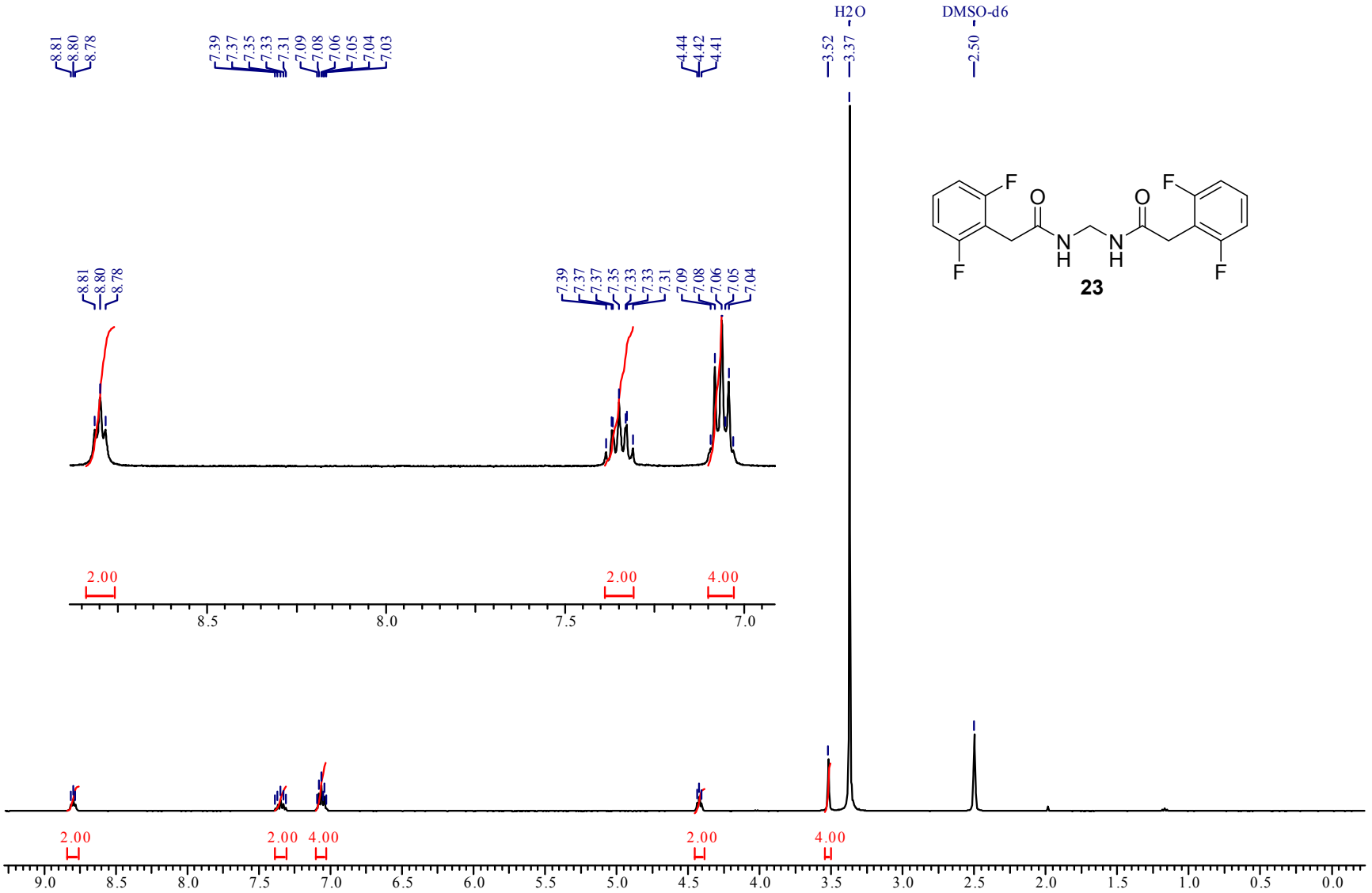
^{13}C NMR, 100 MHz



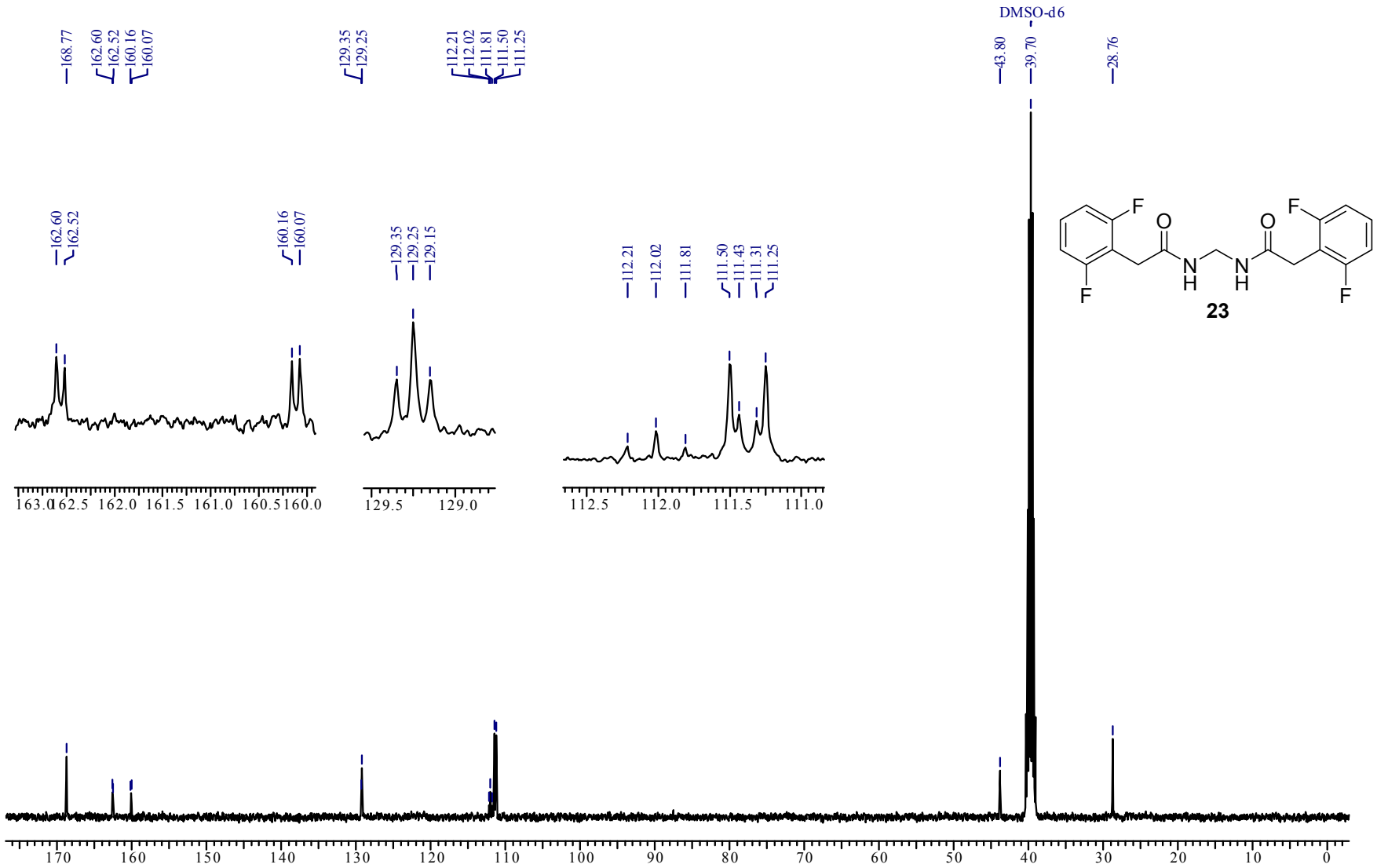
DEPT NMR, 100 MHz



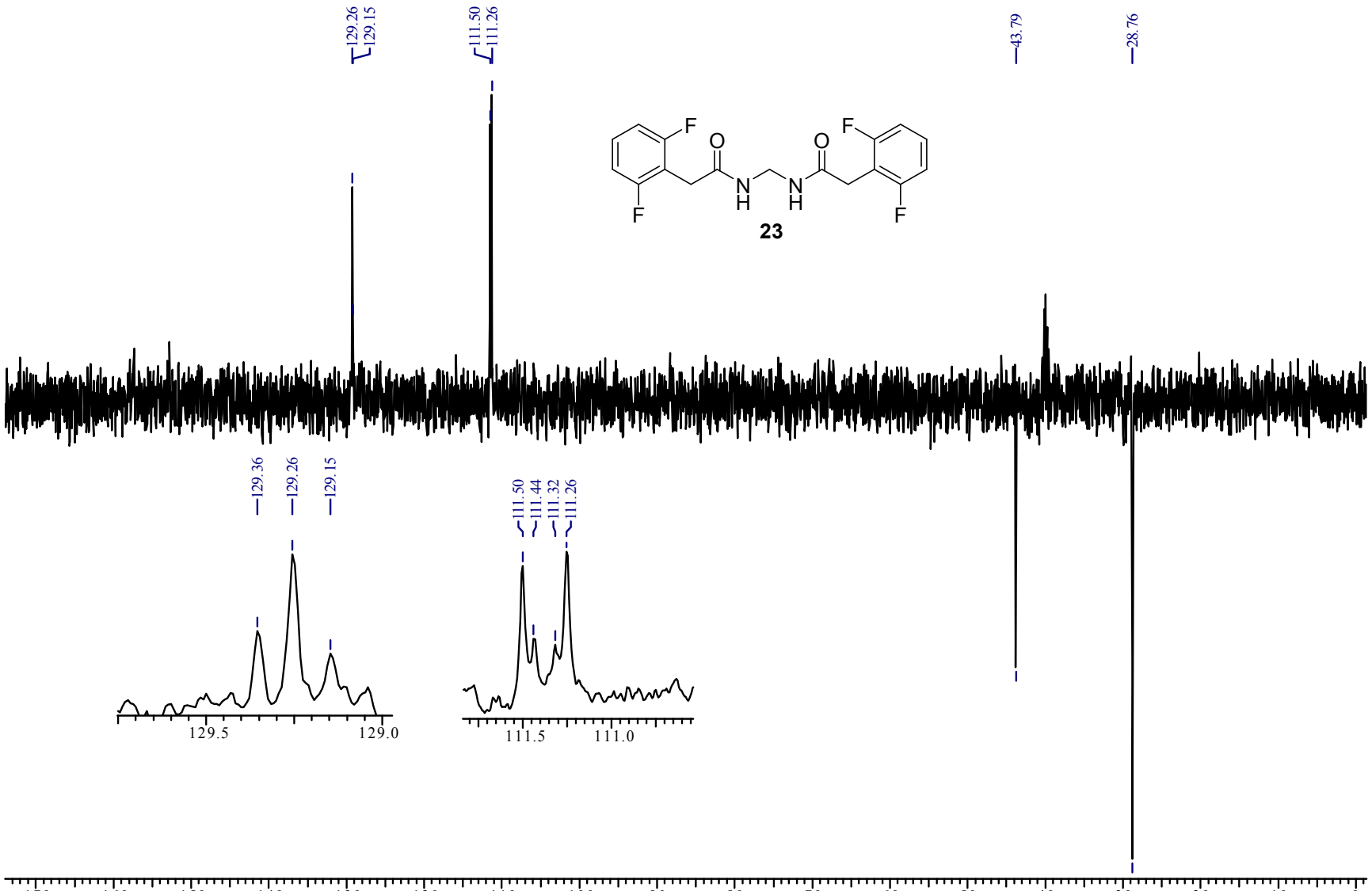
^{1}H NMR, 400 MHz



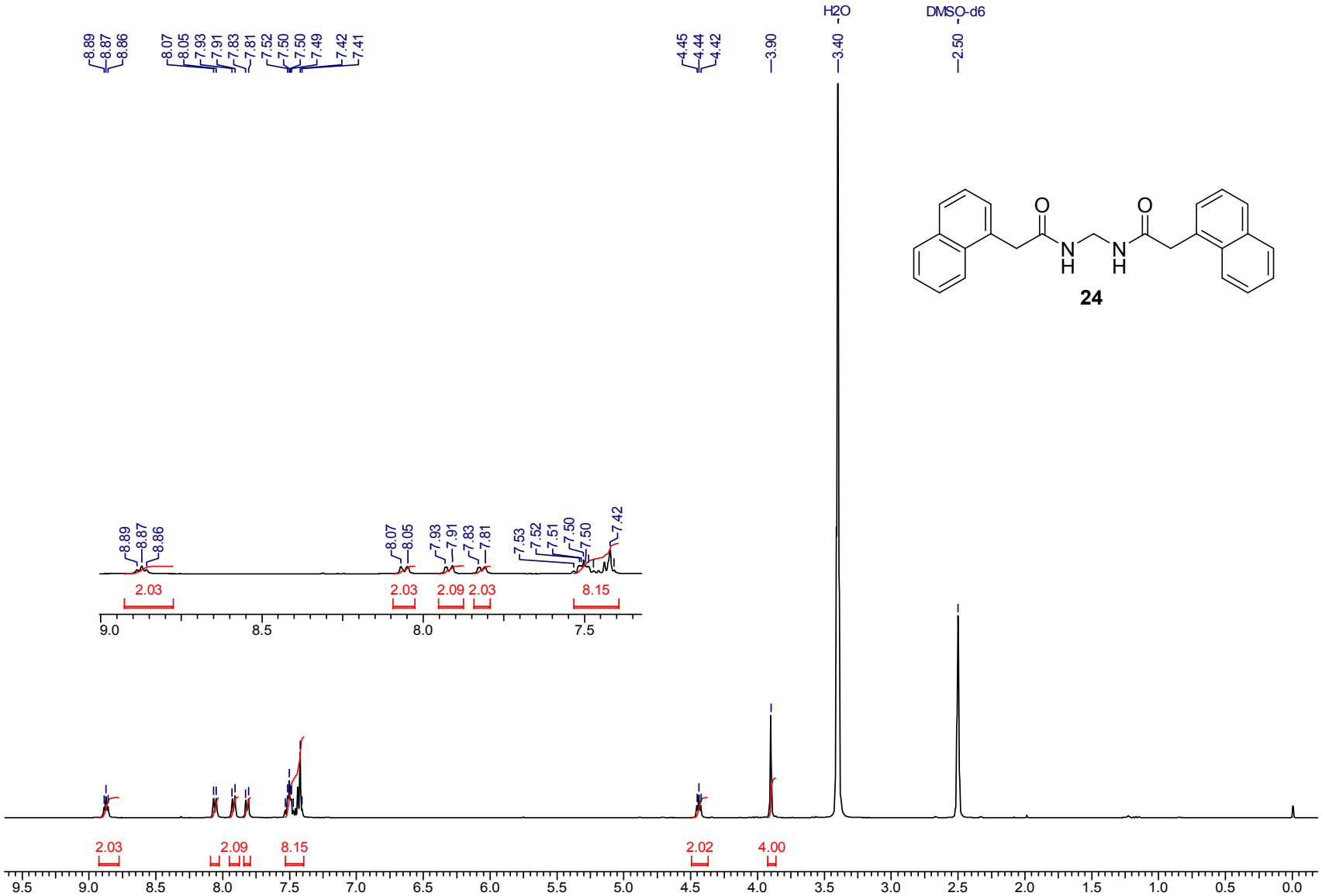
^{13}C NMR, 100 MHz



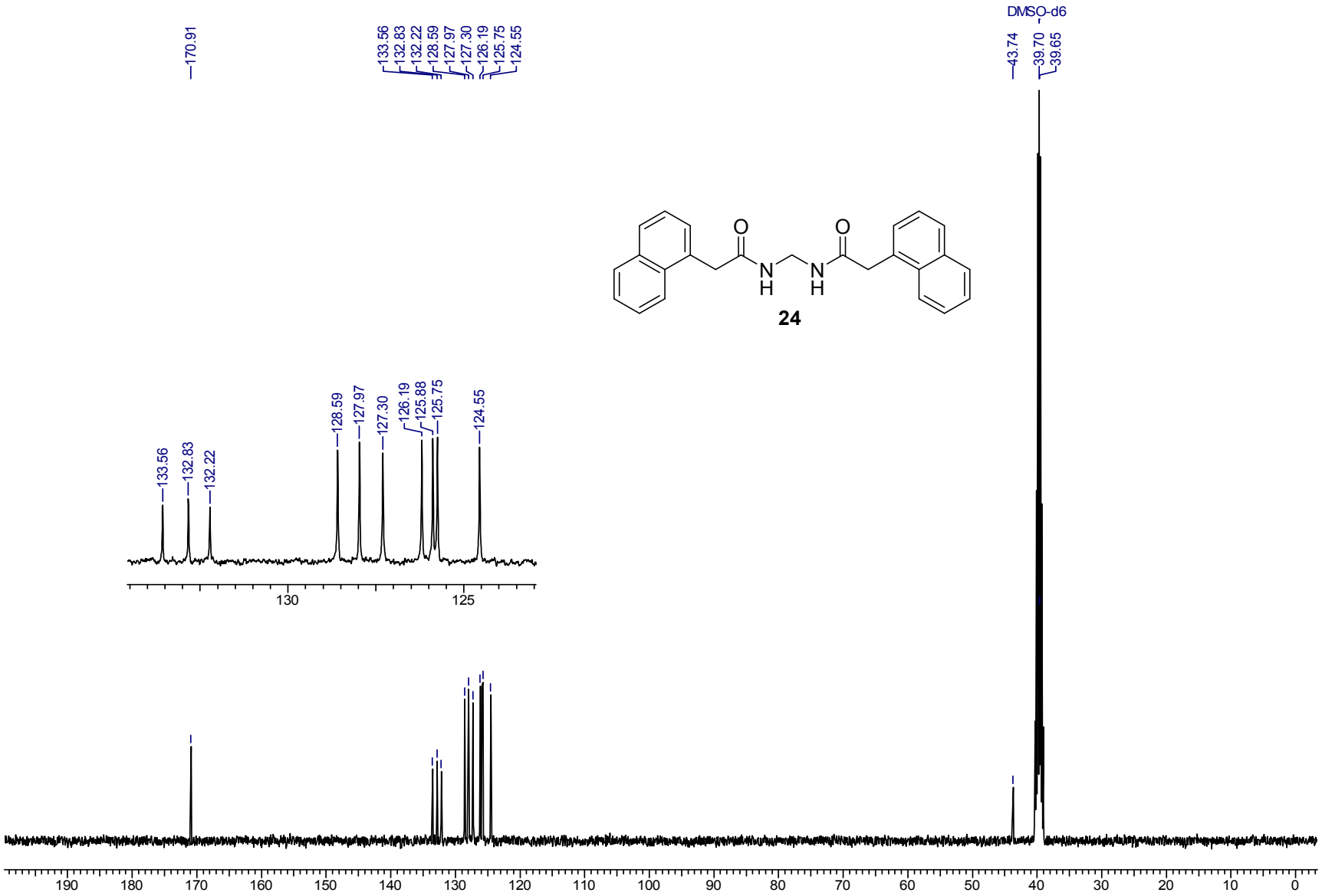
DEPT NMR, 100 MHz



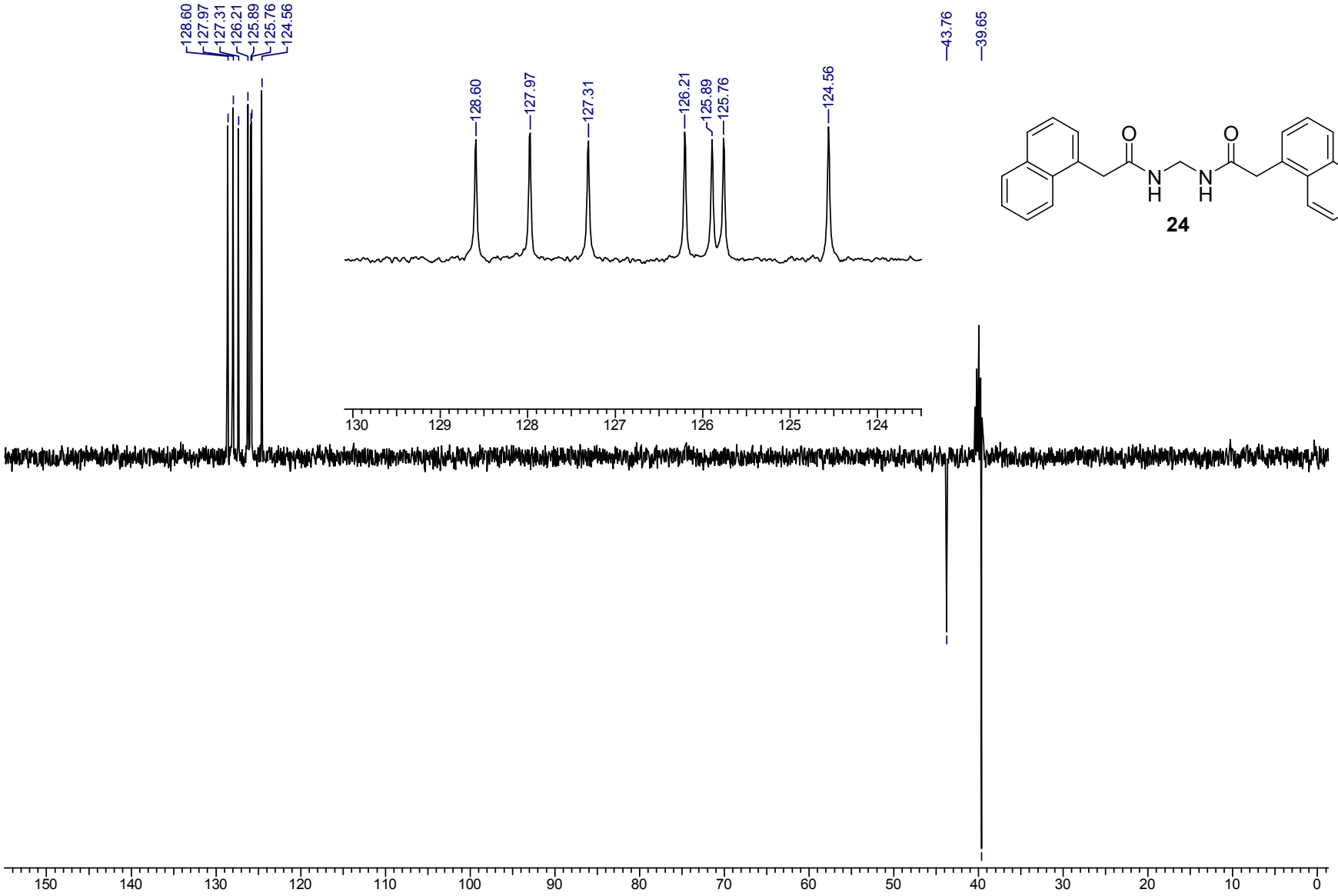
^{1}H NMR, 400 MHz



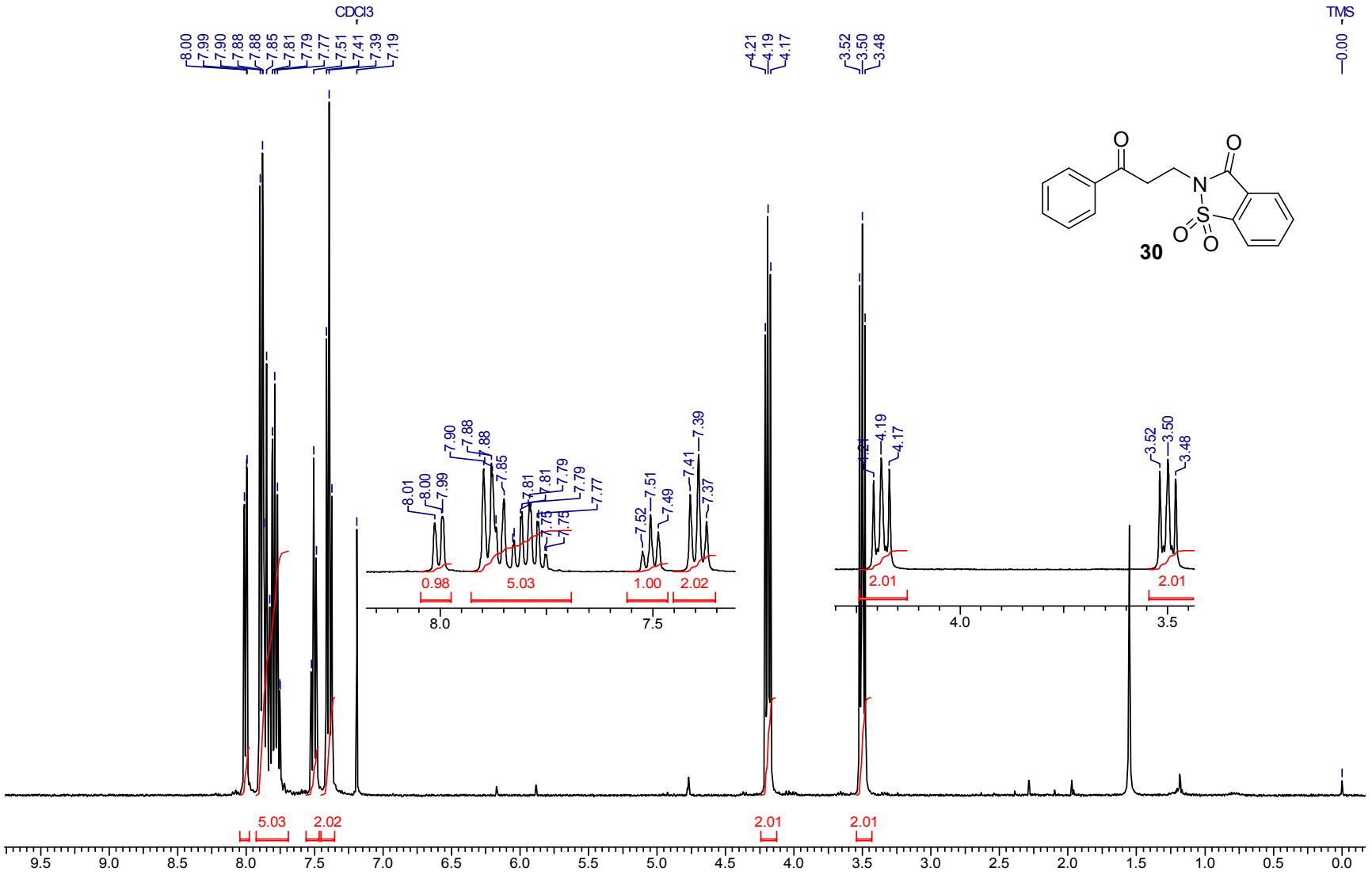
^{13}C NMR, 100 MHz



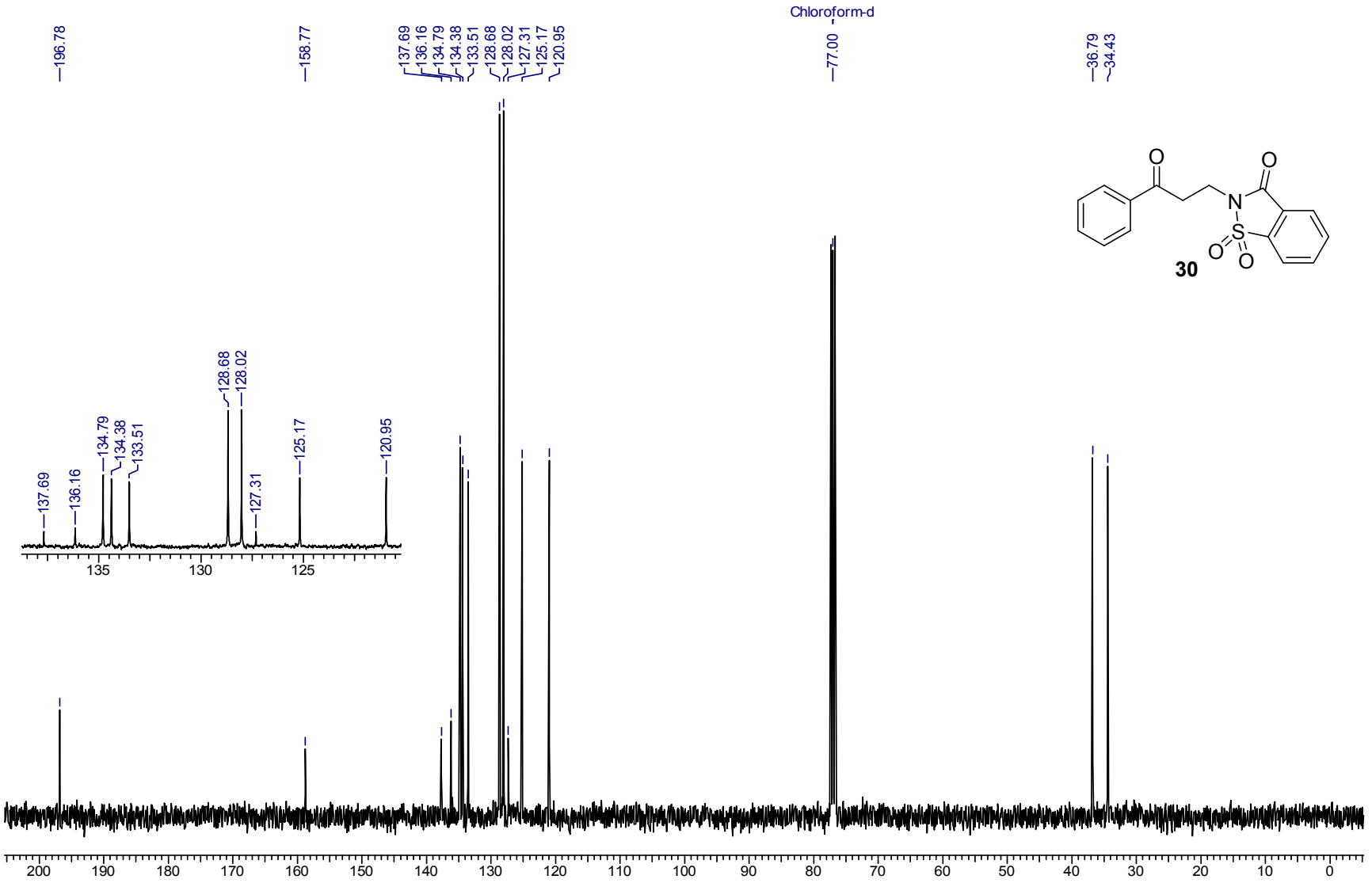
DEPT NMR, 100 MHz



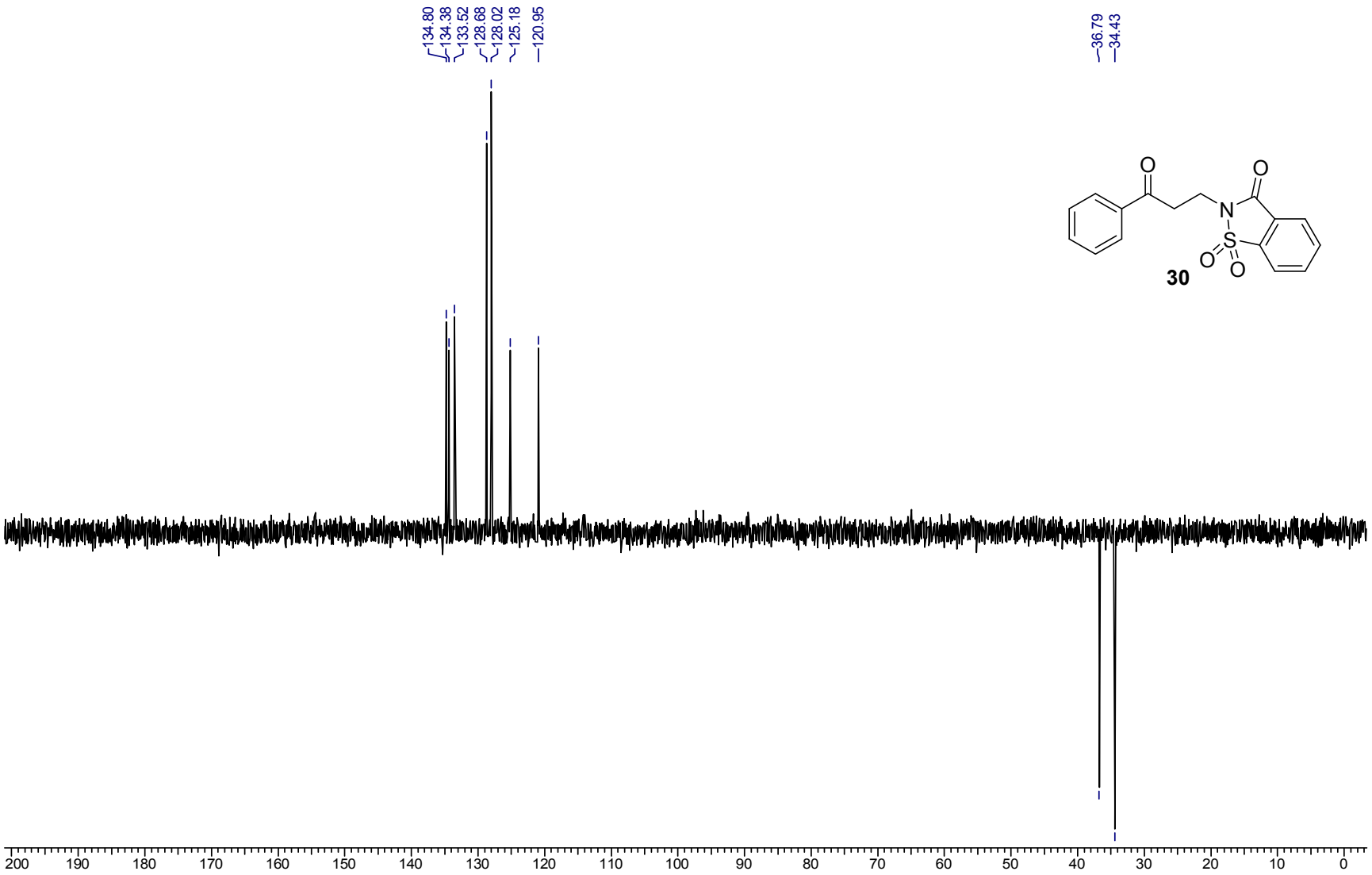
^{1}H NMR, 400 MHz



^{13}C NMR, 100 MHz



DEPT NMR, 100 MHz



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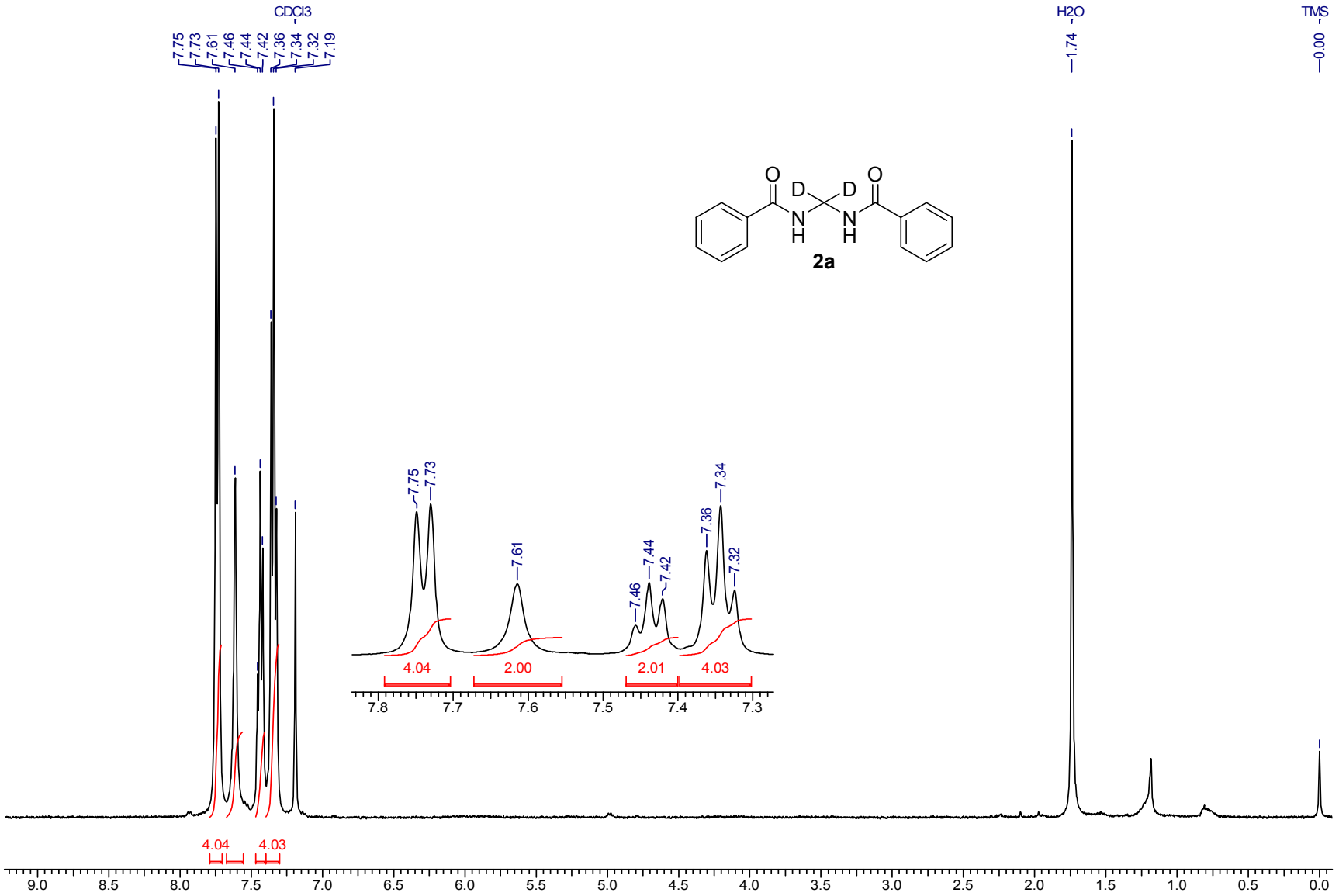
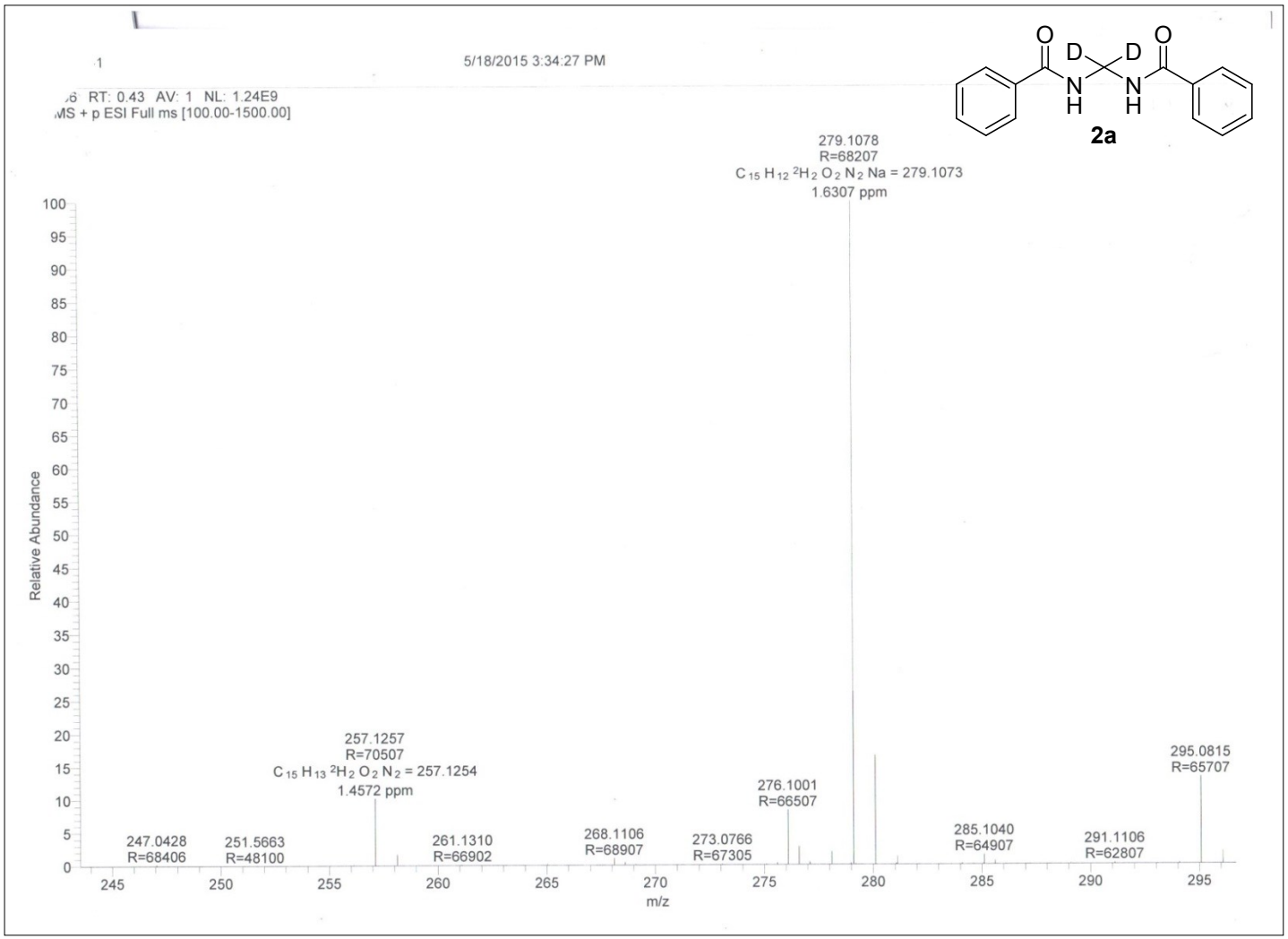
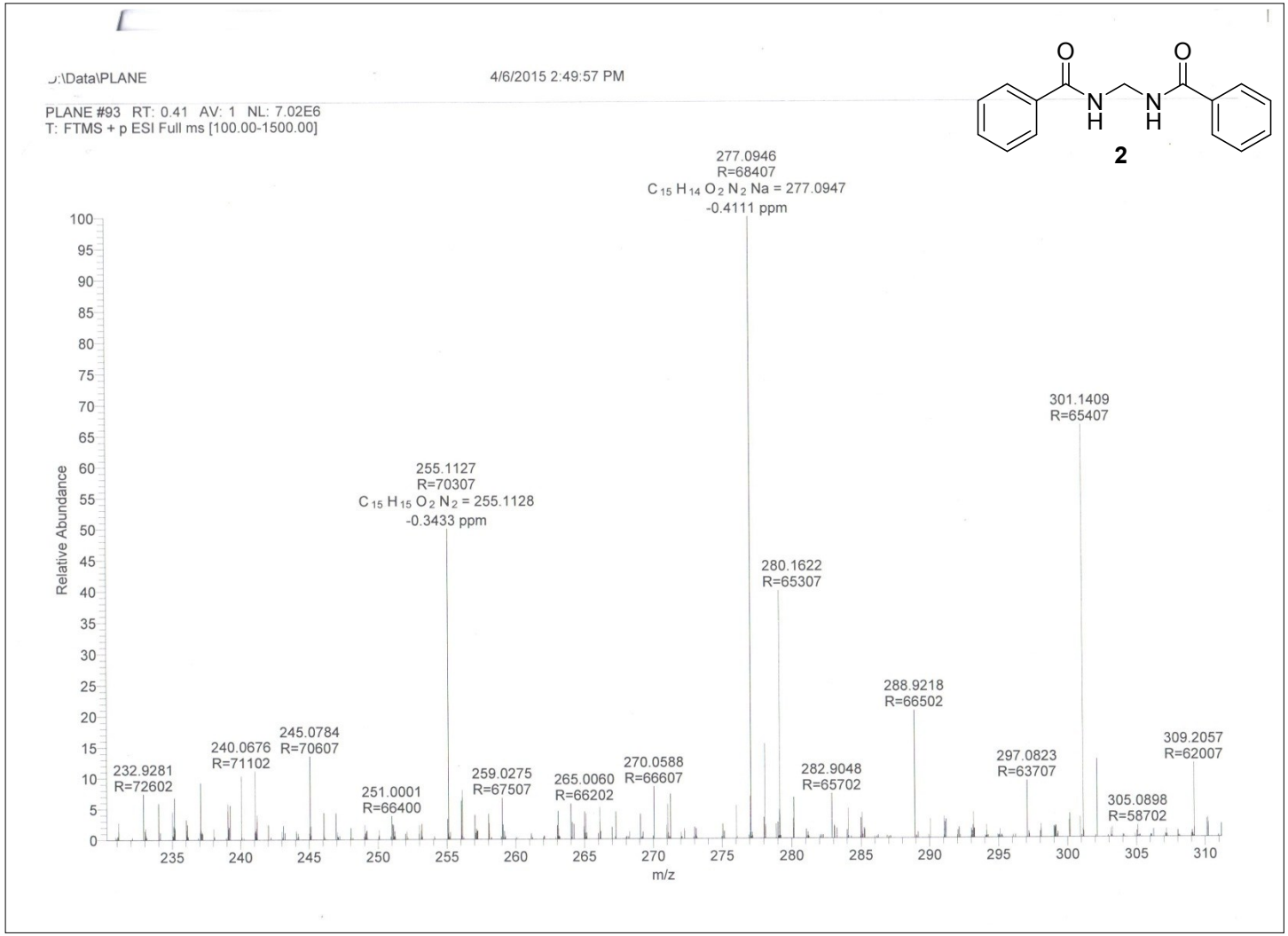


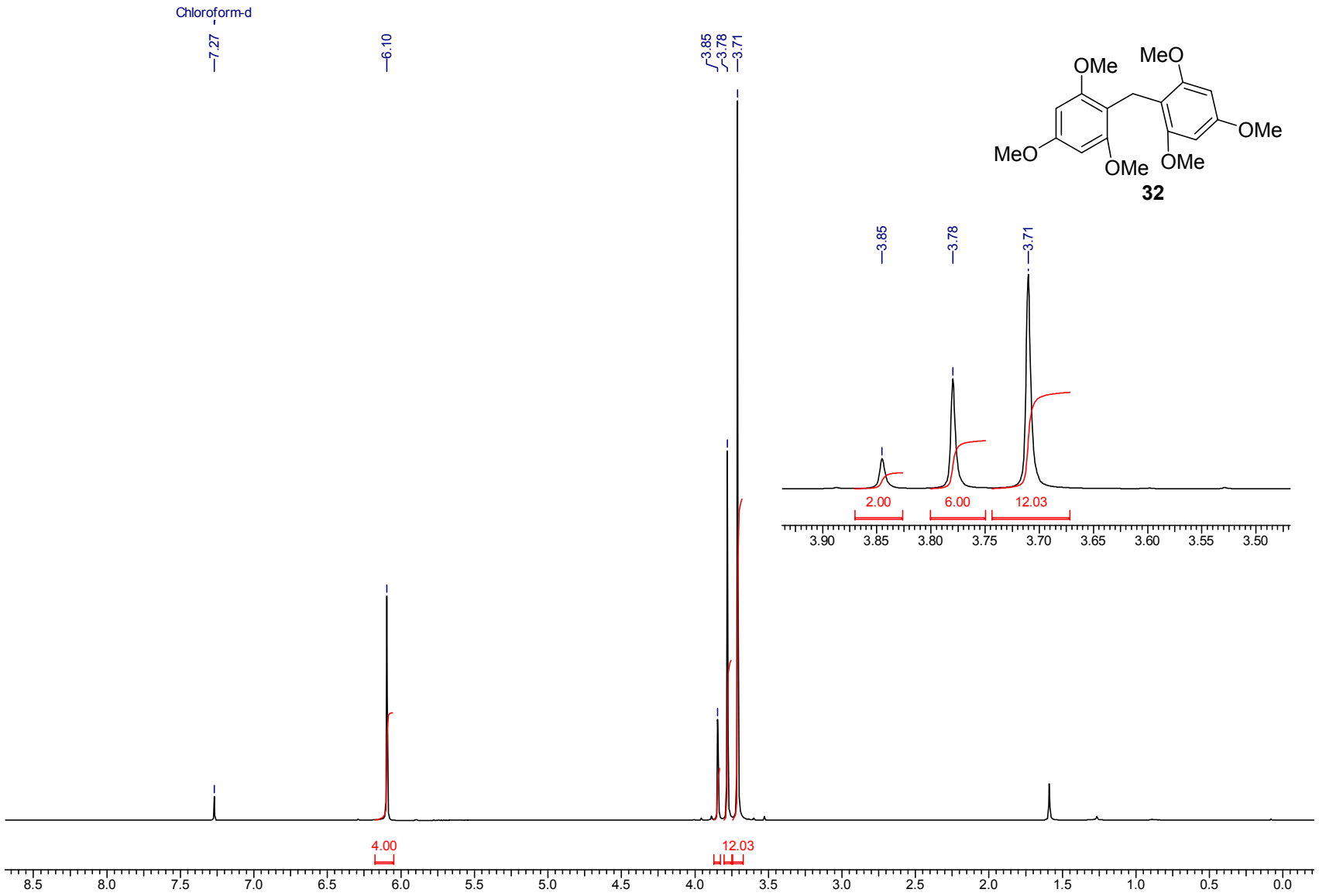
HRMS-ESI


5/18/2015 3:34:27 PM
RT: 0.43 AV: 1 NL: 1.24E9
MS + p ESI Full ms [100.00-1500.00]
2a
279.1078
R=68207
C 15 H 12 2H 2 O 2 N 2 Na = 279.1073
1.6307 ppm
257.1257
R=70507
C 15 H 13 2H 2 O 2 N 2 = 257.1254
1.4572 ppm
247.0428
R=68406
251.5663
R=48100
261.1310
R=66902
268.1106
R=68907
273.0766
R=67305
276.1001
R=66507
285.1040
R=64907
291.1106
R=62807
295.0815
R=65707
Relative Abundance
m/z

HRMS-ESI

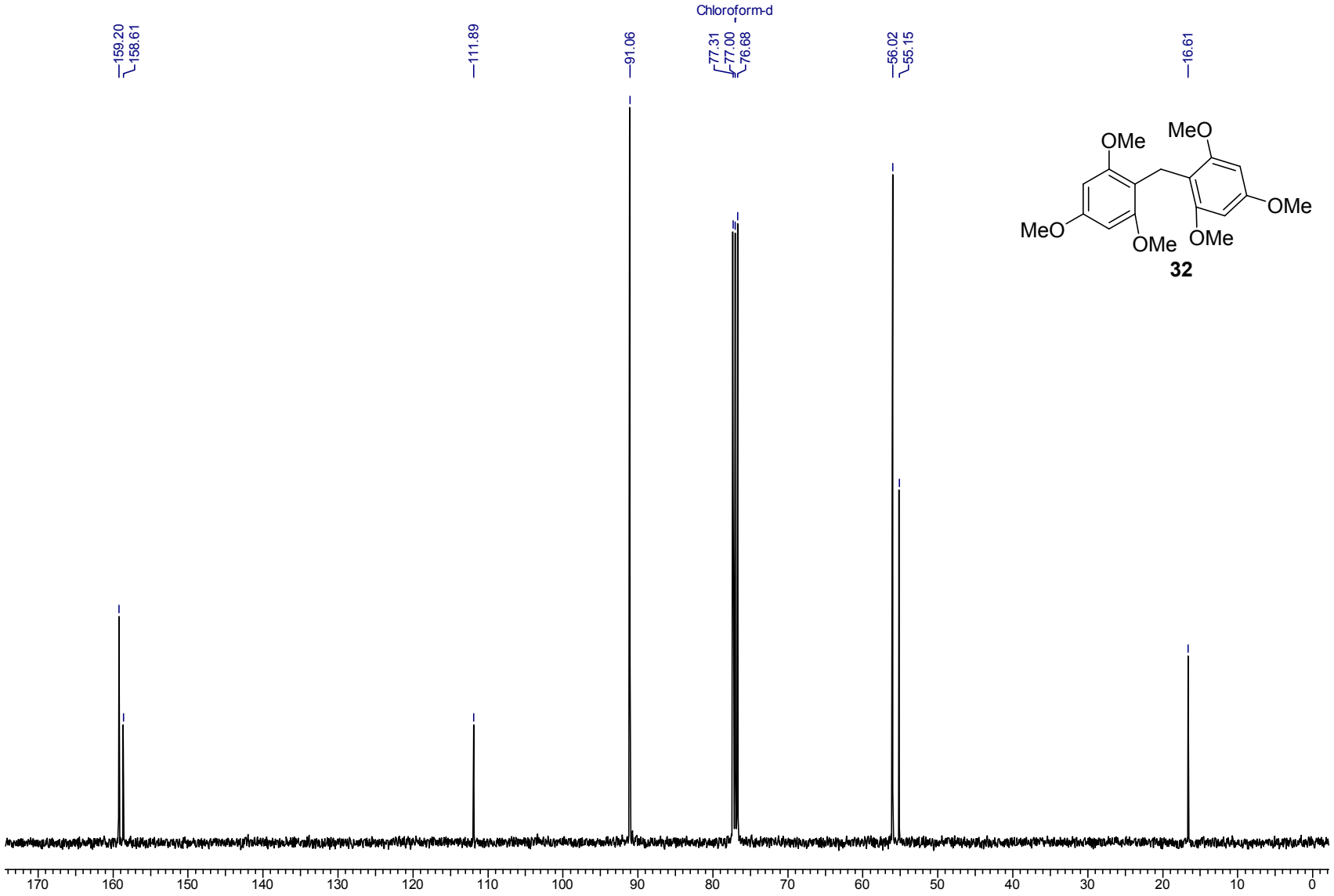

D:\Data\PLANE
4/6/2015 2:49:57 PM
PLANE #93 RT: 0.41 AV: 1 NL: 7.02E6
T: FTMS + p ESI Full ms [100.00-1500.00]
2
277.0946
R=68407
C 15 H 14 O 2 N 2 Na = 277.0947
-0.4111 ppm
255.1127
R=70307
C 15 H 15 O 2 N 2 = 255.1128
-0.3433 ppm
301.1409
R=65407
280.1622
R=65307
288.9218
R=66502
309.2057
R=62007
297.0823
R=63707
305.0898
R=58702
282.9048
R=65702
270.0588
R=66607
265.0060
R=66202
259.0275
R=67507
245.0784
R=70607
240.0676
R=71102
232.9281
R=72602
251.0001
R=66400
Relative Abundance
m/z

^{1}H NMR, 400 MHz

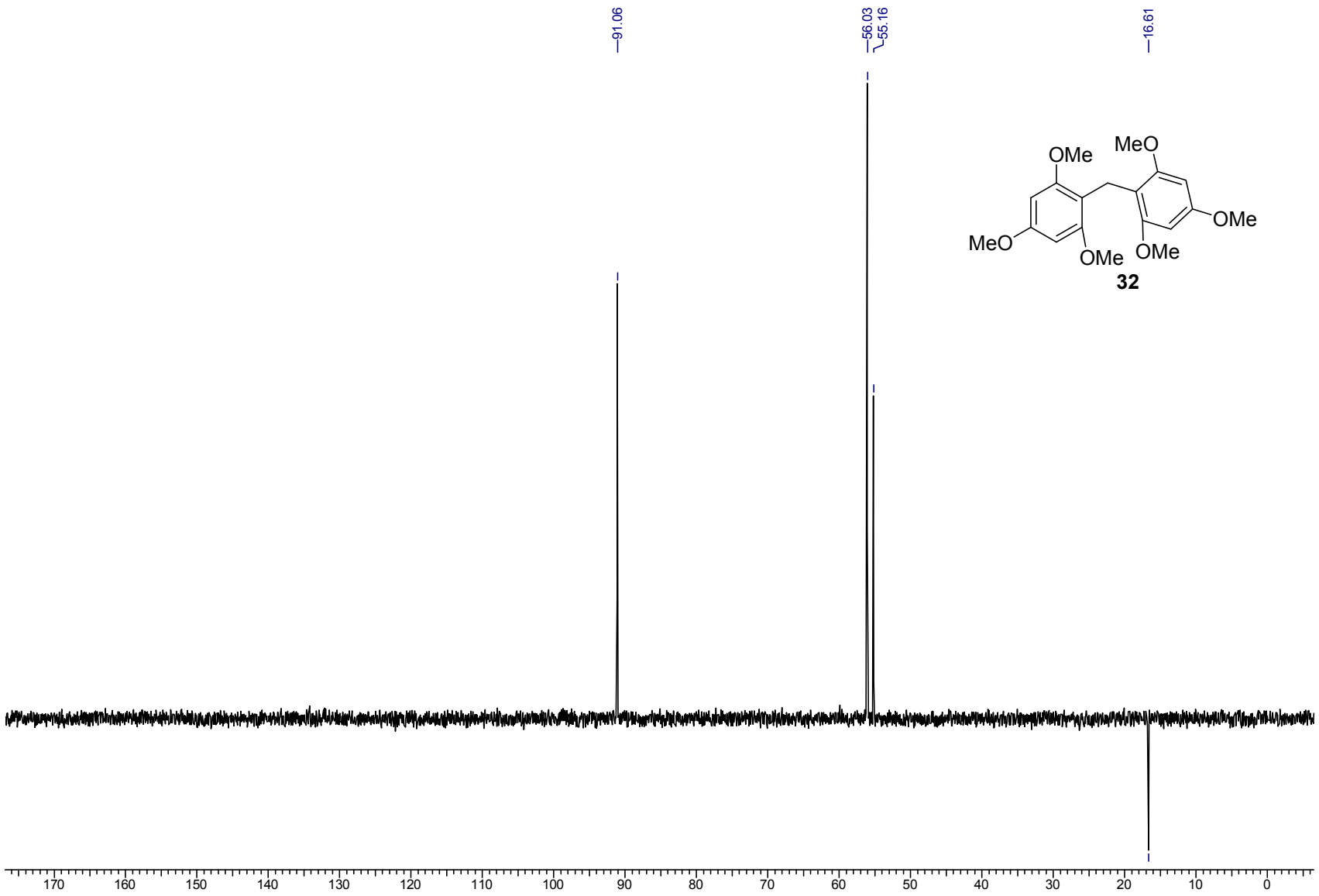


32

^{13}C NMR, 100 MHz

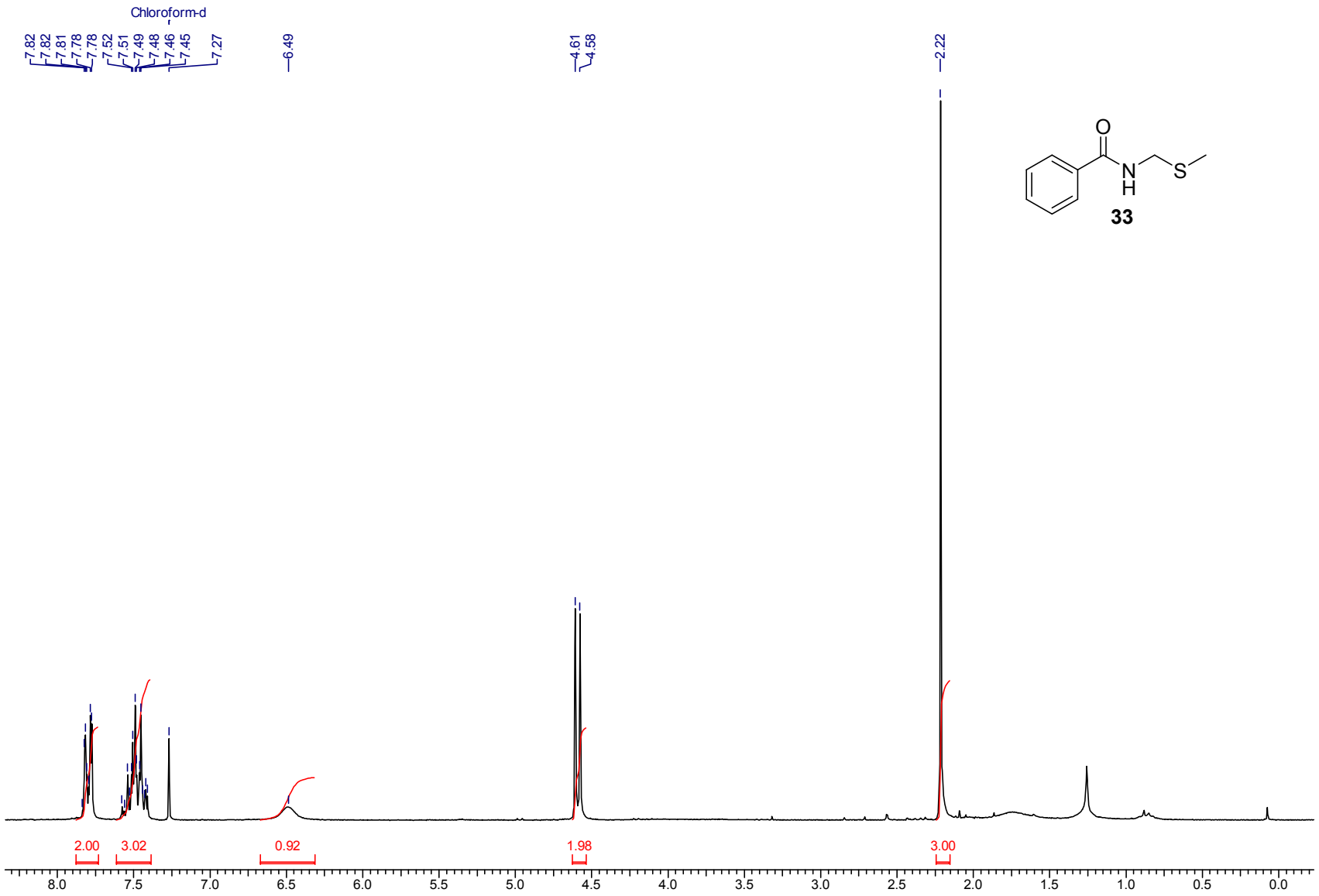


DEPT NMR, 100 MHz

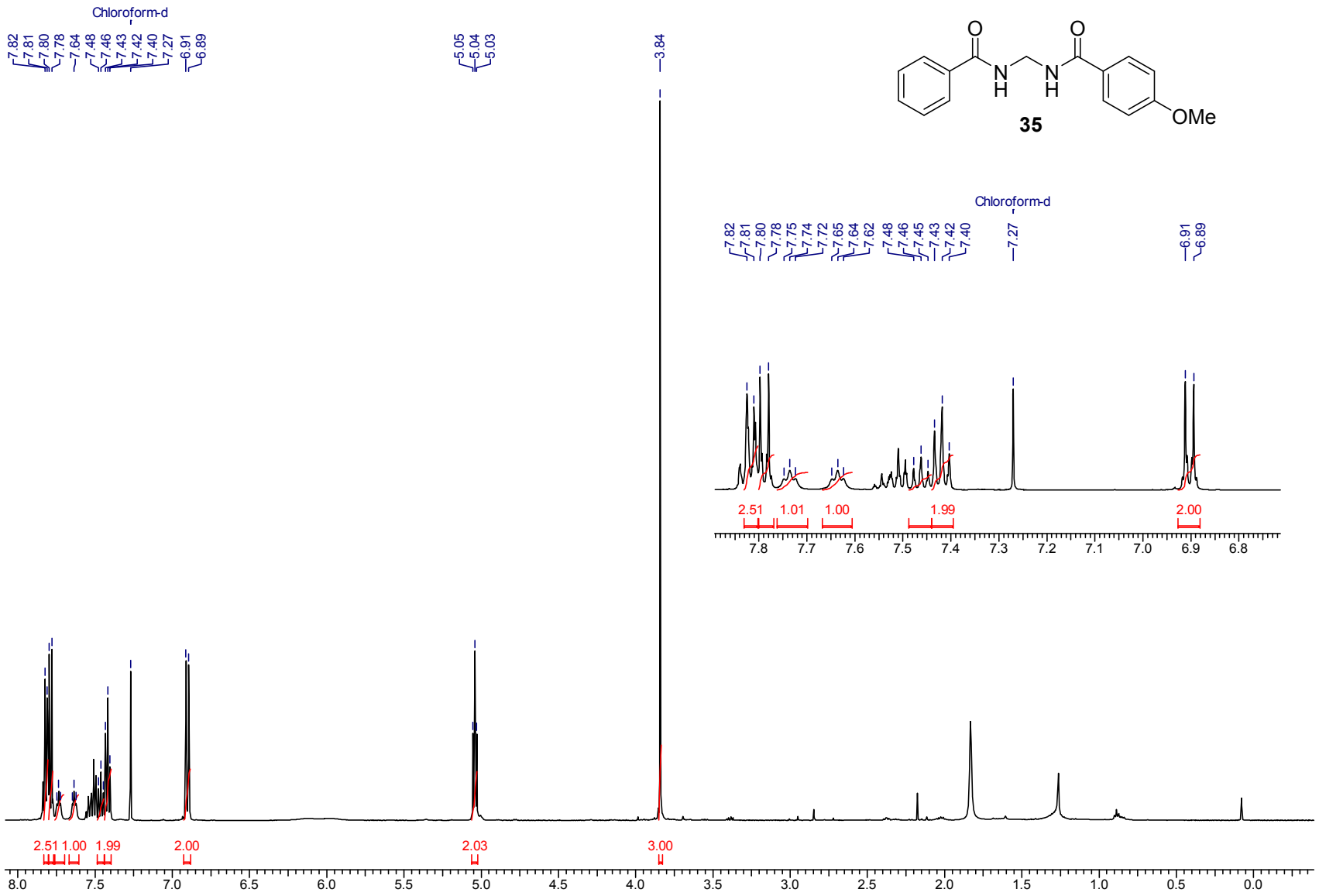


32

^{1}H NMR, 200 MHz

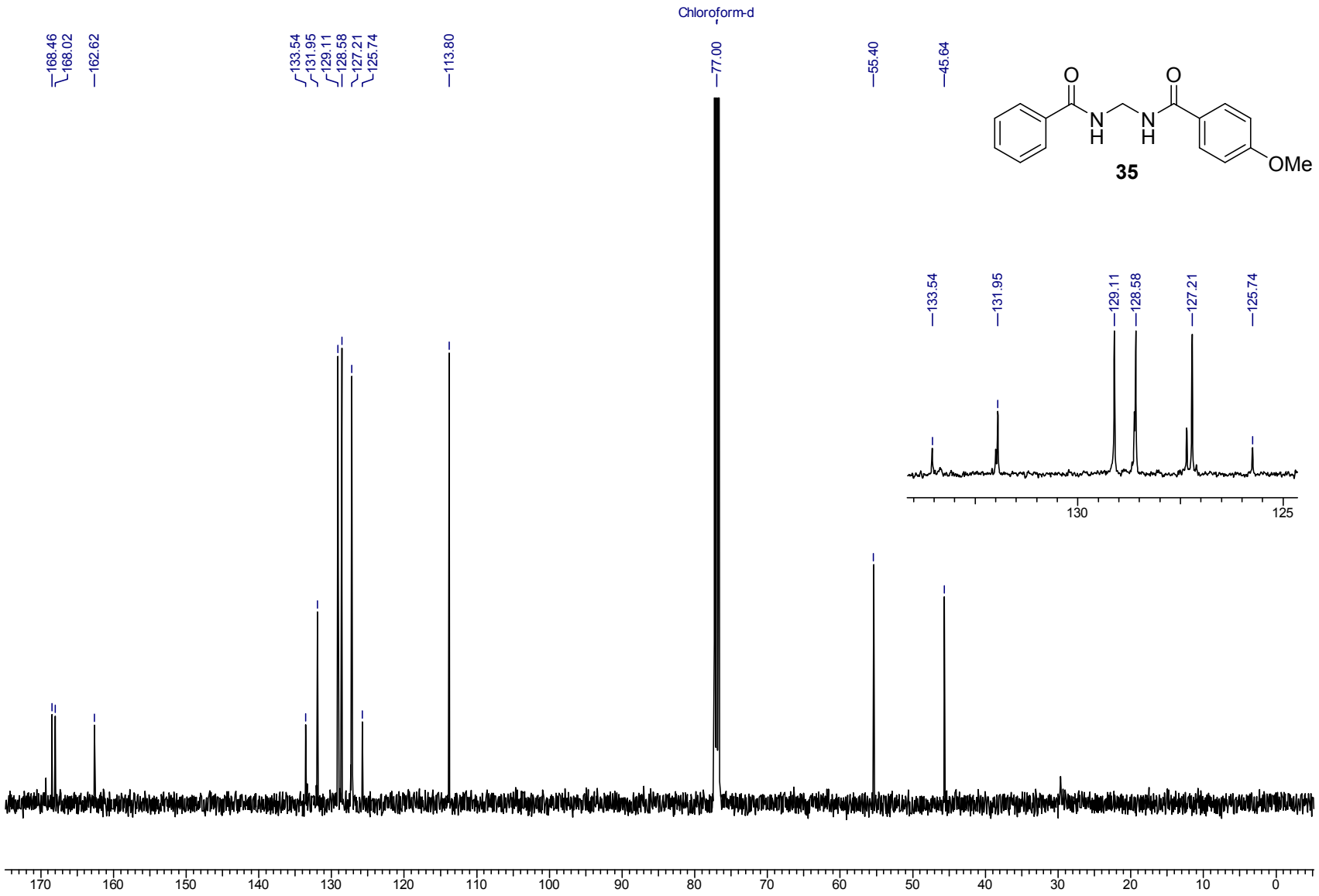


^{1}H NMR, 500 MHz



35

^{13}C NMR, 125 MHz



DEPT NMR, 125 MHz