Supplementary Information

Scaffold hybridization strategy towards potent hydroxamate-based inhibitors of *Flaviviridae* viruses and *Trypanosoma* species

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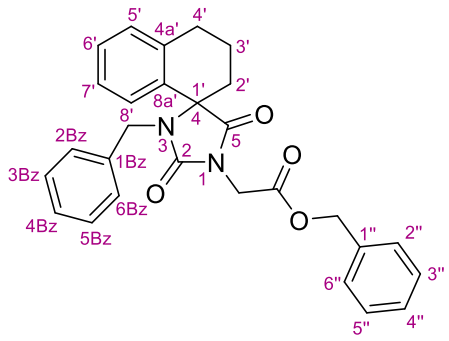
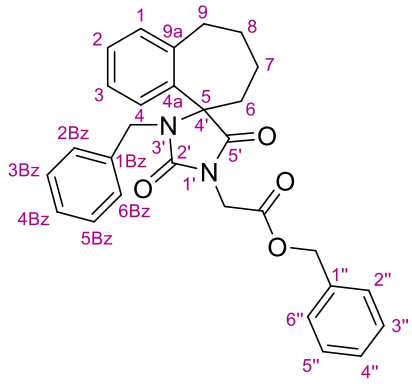


Benzyl 2-(3-benzyl-2,5-dioxo-3',4'-dihydro-2'*H*-spiro[imidazolidine-4,1'-naphthalen]-1-yl)acetate (8b)

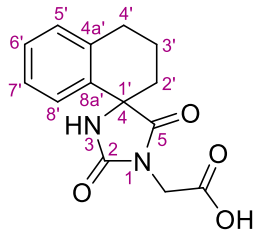
Prepared by *N*-alkylation of benzyl ester **8** (600 mg, 1.65 mmol) in dry DMF (7.3 mL) by using NaH (79 mg, 1.98 mmol, 60% dispersion in mineral oil) and benzyl bromide (339 mg, 1.98 mmol) as described in the main manuscript for the preparation of *N*-benzylated derivatives. The reaction mixture was diluted with 80 mL ice-water and extracted with AcOEt (3 × 60 mL). The combined organic extracts were washed with H_2O (3 × 100 mL) and brine (2 × 100 mL), dried with anh. Na_2SO_4 and evaporated *in vacuo*. The pale-yellow viscous oily residue was purified by column chromatography on silica gel using CH_2Cl_2 to afford the title compound **8b** as a glass solid, which was further crystallized to a white crystalline solid upon treatment with *n*-pentane-dry Et_2O (5:1) (440 mg, 59%); mp 125-127 °C (from AcOEt/*n*-pentane), R_f = 0.81 (CH_2Cl_2/AcOEt 8:1). ^{1}H NMR (600.11 MHz, $CDCl_3$) δ (ppm) 1.70 (dddt, 1H, J_1=13.4 Hz, J_2=6.4 Hz, J_3=5.0 Hz, J_4=3.3 Hz, $H_{3'}$), 1.84 (ddd, 1H, J_1=13.7 Hz, J_2=11.4 Hz, J_3=3.3 Hz, $H_{2'}$), 2.05 (dddd, 1H, J_1=13.8 Hz, J_2=6.5 Hz, J_3=3.1 Hz, J_4=1.2 Hz, $H_{2'}$), 2.29 (ddddd, 1H, J_1=13.3 Hz, J_2=11.3 Hz, J_3=9.9 Hz, J_4=5.0 Hz, J_5=3.1 Hz, $H_{3'}$), 2.73 (ddd, 1H, J_1=16.2 Hz, J_2=9.9 Hz, J_3=5.1 Hz, $H_{4'}$), 2.83 (dt, 1H, J_1=16.7 Hz, J_2=5.0 Hz, $H_{4'}$), 3.81 (d, 1H, J=16.1 Hz, NC*H*HPh), 4.38-4.49 (q, AB, 2H, J_{AB}=17.3 Hz, NCH_2COO), 4.88 (d, 1H, J=16.1 Hz, NCH*H*Ph), 5.19-5.27 (q, AB, 2H, J_{AB}=12.2 Hz, OCH_2Ph), 7.06-7.12 (m, 2H, $H_{7'}$, $H_{8'}$), 7.17-7.20 (m, 2H, $H_{5'}$, $H_{6'}$), 7.22-7.29 (complex m, 5H, H_{2Bz}, H_{3Bz}, H_{4Bz}, H_{5Bz}, H_{6Bz}), 7.34-7.41 (m, 5H, $H_{2''}$, $H_{3''}$, $H_{4''}$, $H_{5''}$, $H_{6''}$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ (ppm) 19.3 ($C_{3'}$), 29.1 ($C_{4'}$), 32.4 ($C_{2'}$), 40.0 (N*C*H$_2$COO), 44.4 (N*C*H$_2$Ph), 67.3 ($C_{1'}$/C_4), 67.8 (COO*C*H$_2$Ph), 126.8 ($C_{8'}$), 127.1 ($C_{7'}$), 127.6 (C_{4Bz}), 127.7 (C_{2Bz}, C_{6Bz}), 128.6 ($C_{2''}$, $C_{6''}$), 128.7 ($C_{3''}$, $C_{4''}$, $C_{5''}$), 128.8 (C_{3Bz}, C_{5Bz}), 128.9 ($C_{6'}$), 130.1 ($C_{5'}$), 130.5 ($C_{8a'}$), 135.1 ($C_{1''}$), 137.6 (C_{1Bz}), 139.9 ($C_{4a'}$), 156.3 (C_2=O), 167.3 (*C*OOCH$_2$Ph), 175.1 (C_5=O). Found: C, 74.08; H, 5.80; N, 6.11. Calc. for $C_{28}H_{26}N_2O_4$: C, 73.99; H, 5.77; N, 6.16%



Benzyl 2-(3'-benzyl-2',5'-dioxo-6,7,8,9-tetrahydrospiro[benzo[7]annulene-5,4'-imidazolidin]-1'-yl)acetate (9b)

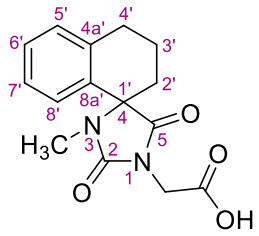
A stirred solution of benzyl ester **9** (550 mg, 1.45 mmol) in dry DMF (8 mL) was treated with NaH (70 mg, 1.74 mmol, 60% dispersion in mineral oil) and benzyl bromide (298 mg, 1.74 mmol), by employing the *N*-alkylation reaction previously described. The reaction mixture was quenched with 80 mL ice-water and extracted with AcOEt (3 × 60 mL). The organic layer was washed with H_2O (3 × 100 mL) and brine (2 × 100 mL), dried over anh. Na_2SO_4 and evaporated *in vacuo*. The yellowish oily residue was purified by column chromatography on silica gel using *n*-hexane/AcOEt 6:1 to afford the title compound **9b** as a colorless viscous oil, which was further crystallized to a white crystalline solid by treatment with *n*-pentane under ice-cooling (490 mg, 72%); mp 112-114 °C (from AcOEt/*n*-pentane), R_f = 0.27 (*n*-hexane/AcOEt 5:1). ^{1}H NMR (600.11 MHz, $CDCl_3$) δ (ppm) 1.57 (ddq, 1H, J_1=14.4 Hz, J_2=8.1 Hz, J_3=4.2 Hz, H_7), 1.67-1.75 (m, 1H, H_8), 1.78-1.87 (complex m, 2H, H_7, H_8), 2.02 (ddd, 1H, J_1=14.8 Hz, J_2=8.9 Hz, J_3=2.8 Hz, H_6), 2.06 (ddd, 1H, J_1=14.6 Hz, J_2=7.1 Hz, J_3=2.7 Hz, H_6), 2.83 (ddd, 1H, J_1=14.7 Hz, J_2=8.4 Hz, J_3=4.6 Hz, H_9), 3.09 (ddd, 1H, J_1=14.5 Hz, J_2=7.8 Hz, J_3=4.1 Hz, H_9), 3.87 (d, 1H, J=16.0 Hz, NC*H*HPh), 4.37-4.46 (q, AB, 2H, J_{AB}=17.3 Hz, NCH_2COO), 4.96 (d, 1H, J=16.0 Hz, NCH*H*Ph), 5.17-5.24 (q, AB, 2H, J_{AB}=12.1 Hz, OCH_2Ph), 7.08 (dd, 1H, J_1=7.9 Hz, J_2=1.3 Hz, H_4), 7.12 (td, 1H, J_1=7.6 Hz, J_2=1.5 Hz, H_3), 7.15 (dd, 1H, J_1=7.5 Hz, J_2=1.0 Hz, H_1), 7.22 (td, 1H, J_1=7.3 Hz, J_2=1.6 Hz, H_2), 7.22-7.29 (m, 5H, H_{2Bz}, H_{3Bz}, H_{4Bz}, H_{5Bz}, H_{6Bz}), 7.32-7.39 (m, 5H, $H_{2''}$, $H_{3''}$, $H_{4''}$, $H_{5''}$, $H_{6''}$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ (ppm) 19.9 (C_7), 25.7 (C_8), 32.6 (C_9), 32.8 (C_6), 40.0 (N*C*H$_2$COO), 44.7 (N*C*H$_2$Ph), 67.8 (O*C*H$_2$Ph), 73.0 (C_5/$C_{4'}$), 127.4 (C_3), 127.6 (C_4), 127.9 (C_{2Bz}, C_{6Bz}), 128.5 ($C_{2''}$, $C_{6''}$), 128.66 (C_{3Bz}, C_{4Bz}, C_{5Bz}), 128.69 ($C_{4''}$), 128.8 ($C_{3''}$, $C_{5''}$), 129.2 (C_2), 131.8 (C_1), 134.1 (C_{4a}), 135.0 ($C_{1''}$), 137.7 (C_{1Bz}), 142.1 (C_{9a}), 155.7 ($C_{2'}$=O), 167.3 (*C*OOCH$_2$Ph), 175.2 ($C_{5'}$=O). Found: C, 74.40; H, 6.00; N, 6.03. Calc. for $C_{29}H_{28}N_2O_4$: C, 74.34; H, 6.02; N, 5.98%

Ib Synthesis of carboxylic acids 11, 11a, 11b, 12, 12a, 12b



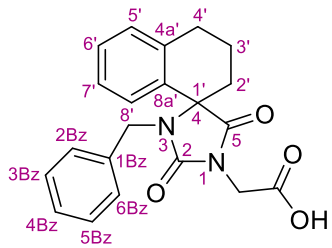
2-(2,5-dioxo-3',4'-dihydro-2'*H*-spiro[imidazolidine-4,1'-naphthalen]-1-yl)acetic acid (11)

Following the general hydrogenolysis procedure for the preparation of carboxylic acids described in the main manuscript, benzyl ester **8** (350 mg, 0.96 mmol) in a mixture of 19 mL EtOH/AcOEt (3:1) provided the target compound **11** as a white crystalline solid (260 mg, almost quantitative yield); mp 214-216 °C (from AcOEt/*n*-pentane), R_f = 0.05 (AcOEt). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.86 (dtt, 1H, J_1=13.3 Hz, J_2=6.7 Hz, J_3=2.7 Hz, $H_{3'}$), 1.94 (ddd, 1H, J_1=13.6 Hz, J_2=7.7 Hz, J_3=2.7 Hz, $H_{2'}$), 2.05 (ddd, 1H, J_1=13.4 Hz, J_2=5.7 Hz, J_3=3.0 Hz, $H_{3'}$), 2.10 (ddd, 1H, J_1=11.0 Hz, J_2=9.2 Hz, J_3=2.8 Hz, $H_{2'}$), 2.97 (t, 2H, J=6.2 Hz, $H_{4'}$), 4.09-4.17 (q, AB, 2H, J_{AB}=17.4 Hz, NCH_2COOH), 7.15-7.20 (m, 2H, $H_{5'}$, $H_{7'}$), 7.22-7.26 (m, 2H, $H_{6'}$, $H_{8'}$), 8.94 (s, 1H, H_3), 13.15 (br s, 1H, NCH$_2$COO*H*); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.4 ($C_{3'}$), 28.4 ($C_{4'}$), 33.6 ($C_{2'}$), 39.2 (N*C*H$_2$COOH), 62.4 ($C_{1'}$/C_4), 126.5 ($C_{7'}$), 127.3 ($C_{8'}$), 128.2 ($C_{6'}$), 129.2 ($C_{5'}$), 134.0 ($C_{8a'}$), 137.8 ($C_{4a'}$), 155.1 (C_2=O), 168.9 (NCH$_2$*C*OOH), 176.0 (C_5=O). Found: C, 61.38; H, 5.21; N, 10.19. Calc. for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.15; N, 10.21%



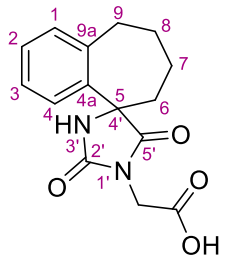
2-(3-methyl-2,5-dioxo-3',4'-dihydro-2'*H*-spiro[imidazolidine-4,1'-naphthalen]-1-yl)acetic acid (11a)

It was prepared by hydrogenolysis of benzyl ester **8a** (250 mg, 0.66 mmol) in a mixture of EtOH/AcOEt 3:1 (13 mL) following the general procedure previously described. Evaporation of the solvents gave the corresponding carboxylic acid **11a** as a white crystalline solid (190 mg, almost quantitative yield); mp > 250 °C (from AcOEt/*n*-pentane), R_f = 0.09 (AcOEt). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.87 (dddd, 1H, J_1=13.4 Hz, J_2=6.2 Hz, J_3=4.9 Hz, J_4=3.3 Hz, $H_{3'}$), 2.02 (ddd, 1H, J_1=13.3 Hz, J_2=6.0 Hz, J_3=2.9 Hz, $H_{2'}$), 2.15 (ddd, 1H, J_1=13.5 Hz, J_2=11.4 Hz, J_3=3.1 Hz, $H_{2'}$), 2.25 (ddddd, 1H, J_1=13.4 Hz, J_2=11.3 Hz, J_3=9.8 Hz, J_4=5.4 Hz, J_5=3.3 Hz, $H_{3'}$), 2.63 (s, 3H, NCH_3), 2.80 (ddd, 1H, J_1=16.7 Hz, J_2=9.9 Hz, J_3=4.7 Hz, $H_{4'}$), 2.84 (dt, 1H, J_1=16.7 Hz, J_2=4.8 Hz, $H_{4'}$), 3.09-3.61 (br s, NCH$_2$COO*H*, under DMSO-water peak), 4.08-4.18 (q, AB, 2H, J_{AB}=17.5 Hz, NCH_2COOH), 7.04 (dd, 1H, J_1=7.8 Hz, J_2=1.3 Hz, $H_{8'}$), 7.21 (td, 1H, J_1=7.4 Hz, J_2=1.7 Hz, $H_{7'}$), 7.24 (dd, 1H, J_1=7.6 Hz, J_2=1.5 Hz, $H_{5'}$), 7.27 (td, 1H, J_1=7.3 Hz, J_2=1.7 Hz, $H_{6'}$); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.8 ($C_{3'}$), 25.0 (N*C*H$_3$), 28.2 ($C_{4'}$), 29.9 ($C_{2'}$), 39.2 (N*C*H$_2$COOH), 65.0 ($C_{1'}$/C_4), 126.2 ($C_{8'}$), 126.7 ($C_{7'}$), 128.4 ($C_{6'}$), 129.7 ($C_{5'}$), 130.5 ($C_{8a'}$), 139.5 ($C_{4a'}$), 154.8 (C_2=O), 168.7 (NCH$_2$*C*OOH), 174.6 (C_5=O). Found: C, 62.44; H, 5.55; N, 9.78. Calc. for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72%



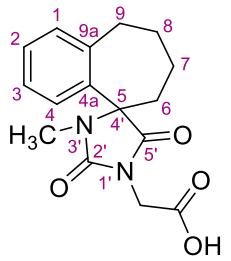
2-(3-benzyl-2,5-dioxo-3',4'-dihydro-2'*H*-spiro[imidazolidine-4,1'-naphthalen]-1-yl)acetic acid (11b)

A mixture of benzyl ester **8b** (380 mg, 0.84 mmol) and 10% Pd on charcoal (46 mg) in EtOH/AcOEt 3:1 (17 ml) was hydrogenated following the general procedure for the preparation of carboxylic acids, to give the title compound **11b** as a foamy solid. Crystallization upon treatment with *n*-pentane (0 °C) afforded a white crystalline solid (305 mg, almost quantitative yield); mp 143-145 °C (from AcOEt/*n*-pentane-dry Et$_2$O), R_f = 0.20 (AcOEt). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.67 (ddt, 1H, J_1=10.3 Hz, J_2=7.2 Hz, J_3=4.2 Hz, $H_{3'}$), 1.91 (ddd, 1H, J_1=13.9 Hz, J_2=11.0 Hz, J_3=3.2 Hz, $H_{2'}$), 2.02 (ddd, 1H, J_1=13.8 Hz, J_2=6.8 Hz, J_3=3.0 Hz, $H_{2'}$), 2.11 (qt, 1H, J_1=12.5 Hz, J_2=3.3 Hz, $H_{3'}$), 2.69-2.81 (m, 2H, $H_{4'}$), 3.85 (d, 1H, J=16.5 Hz, NC*H*HPh), 4.16-4.25 (q, AB, 2H, J_{AB}=17.5 Hz, NCH_2COOH), 4.66 (d, 1H, J=16.5 Hz, NCH*H*Ph), 7.10 (d, 1H, J=7.7 Hz, $H_{8'}$), 7.16 (t, 1H, J=7.4 Hz, $H_{7'}$), 7.21 (t, 4H, J=7.0 Hz, $H_{5'}$, H_{2Bz}, H_{4Bz}, H_{6Bz}), 7.24-7.30 (m, 3H, $H_{6'}$, H_{3Bz}, H_{5Bz}), 13.34 (br s, 1H, NCH$_2$COO*H*); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.7 ($C_{3'}$), 28.2 ($C_{4'}$), 31.3 ($C_{2'}$), 39.7 (N*C*H$_2$COOH), 43.5 (N*C*H$_2$Ph), 66.2 ($C_{1'}$/C_4), 126.5 ($C_{8'}$), 126.6 ($C_{7'}$), 127.0 (C_{4Bz}), 127.1 (C_{2Bz}, C_{6Bz}), 128.3 (C_{3Bz}, C_{5Bz}), 128.5 ($C_{6'}$), 129.7 ($C_{5'}$), 130.8 ($C_{8a'}$), 137.7 (C_{1Bz}), 139.6 ($C_{4a'}$), 155.7 (C_2=O), 168.8 (NCH$_2$*C*OOH), 174.5 (C_5=O). Found: C, 69.29; H, 5.43; N, 7.72. Calc. for $C_{21}H_{20}N_2O_4$: C, 69.22; H, 5.53; N, 7.69%



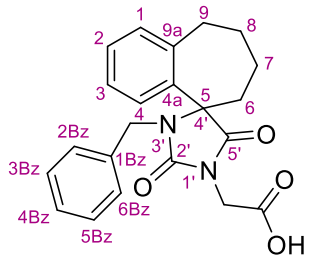
2-(2',5'-dioxo-6,7,8,9-tetrahydrospiro[benzo[7]annulene-5,4'-imidazolidin]-1'-yl)acetic acid (12)

Following the general hydrogenolysis procedure for the synthesis of carboxylic acids described in the main manuscript, benzyl ester **9** (360 mg, 0.95 mmol) in a mixture of 19 mL EtOH/AcOEt (3:1) yielded the target compound **12** as a white crystalline solid (270 mg, almost quantitative yield); mp 216-218 °C (from AcOEt/*n*-pentane-dry Et_2O), R_f = 0.05 (AcOEt). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.63 (dtt, 1H, J_1=13.1 Hz, J_2=8.1 Hz, J_3=4.7 Hz, H_8), 1.78 (ddd, 1H, J_1=14.7 Hz, J_2=7.4 Hz, J_3=4.0 Hz, H_8), 1.83 (ddddd, 1H, J_1=13.5 Hz, J_2=10.8 Hz, J_3=7.3 Hz, J_4=5.6 Hz, J_5=2.5 Hz, H_7), 1.86-1.91 (complex m, 1H, H_7), 1.93 (ddd, 1H, J_1=13.8 Hz, J_2=6.3 Hz, J_3=2.8 Hz, H_6), 2.11 (ddd, 1H, J_1=13.4 Hz, J_2=10.7 Hz, J_3=2.9 Hz, H_6), 2.98 (ddd, 1H, J_1=14.9 Hz, J_2=8.7 Hz, J_3=3.1 Hz, H_9), 3.02 (ddd, 1H, J_1=14.9 Hz, J_2=7.8 Hz, J_3=3.3 Hz, H_9), 3.11-3.67 (br s, 1H, NCH_2COOH, under DMSO-water peak), 4.12 (s, 2H, NCH_2COOH), 7.15 (td, 1H, J_1=7.3 Hz, J_2=2.0 Hz, H_3), 7.18 (dd, 1H, J_1=7.5 Hz, J_2=1.8 Hz, H_1), 7.19 (td, 1H, J_1=6.8 Hz, J_2=1.4 Hz, H_2), 7.22 (dd, 1H, J_1=7.6 Hz, J_2=1.2 Hz, H_4), 9.00 (s, 1H, $H_{3'}$); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 23.7 (C_7), 26.5 (C_8), 34.2 (C_9), 35.8 (C_6), 39.2 (NCH_2COOH), 68.1 ($C_5/C_{4'}$), 126.2 (C_3), 127.7 (C_4), 128.1 (C_2), 131.2 (C_1), 137.7 (C_{4a}), 142.2 (C_{9a}), 155.0 ($C_{2'}$=O), 168.8 (NCH_2COOH), 175.6 ($C_{5'}$=O). Found: C, 62.43; H, 5.68; N, 9.80. Calc. for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72%



2-(3'-methyl-2',5'-dioxo-6,7,8,9-tetrahydrospiro[benzo[7]annulene-5,4'-imidazolidin]-1'-yl)acetic acid (12a)

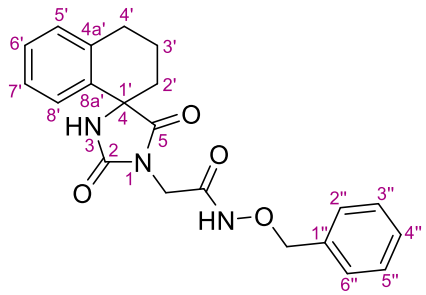
It was prepared by hydrogenolysis of the corresponding benzyl ester **9a** (350 mg, 0.89 mmol) in a mixture of 18 mL EtOH/AcOEt (3:1) following the general procedure for the preparation of carboxylic acids. After removal of the solvent under reduced pressure, the title compound **12a** was obtained as a white crystalline solid (265 mg, almost quantitative yield); mp > 250 °C (from AcOEt/*n*-pentane-dry Et_2O), R_f = 0.05 (AcOEt). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.63-1.74 (m, 2H, H_7, H_8), 1.84 (dddd, 1H, J_1=10.7 Hz, J_2=8.0 Hz, J_3=5.4 Hz, J_4=3.2 Hz, H_8), 1.89 (dddd, 1H, J_1=13.5 Hz, J_2=10.8 Hz, J_3=7.3 Hz, J_4=5.6 Hz, H_7), 2.11 (ddd, 1H, J_1=14.6 Hz, J_2=7.5 Hz, J_3=2.0 Hz, H_6), 2.31 (ddd, 1H, J_1=14.6 Hz, J_2=10.4 Hz, J_3=1.9 Hz, H_6), 2.74 (s, 3H, CH_3), 2.88 (ddd, 1H, J_1=14.8 Hz, J_2=7.9 Hz, J_3=4.0 Hz, H_9), 3.19 (ddd, 1H, J_1=14.5 Hz, J_2=8.9 Hz, J_3=4.0 Hz, H_9), 4.06-4.16 (q, AB, 2H, J_{AB}=17.5 Hz, NCH_2COOH), 7.03-7.07 (m, 1H, H_4), 7.21-7.28 (complex m, 3H, H_1, H_2, H_3), 13.21 (br s, 1H, NCH_2COOH); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 20.3 (C_7), 25.2 (NCH_3), 25.5 (C_8), 31.7 (C_6), 32.1 (C_9), 70.7 (NCH_2COOH), 68.1 ($C_5/C_{4'}$), 126.8 (C_3), 127.8 (C_4), 128.6 (C_2), 131.4 (C_1), 134.2 (C_{4a}), 141.7 (C_{9a}), 154.2 ($C_{2'}$=O), 168.7 (NCH_2COOH), 174.4 ($C_{5'}$=O). Found: C, 63.60; H, 5.96; N, 9.35. Calc. for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27%



2-(3'-benzyl-2',5'-dioxo-6,7,8,9-tetrahydrospiro[benzo[7]annulene-5,4'-imidazolidin]-1'-yl)acetic acid (12b)

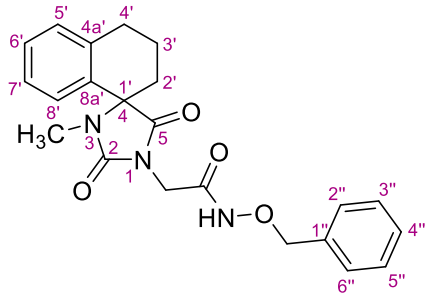
A mixture of benzyl ester **9b** (450 mg, 0.96 mmol) and 10% Pd on charcoal (54 mg) in EtOH/AcOEt 3:1 (19 ml) was hydrogenated following the general procedure described for the preparation of carboxylic acids to afford the title compound **12b** as a glass solid. Crystallization upon treatment with *n*-pentane (0 °C) yielded **12b** as a white crystalline solid (360 mg, almost quantitative yield); mp 167-169 °C (from AcOEt/*n*-pentane), R_f = 0.44 (AcOEt). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.51-1.60 (m, 1H, H_7), 1.62-1.75 (complex m, 3H, H_7, H_8), 2.01 (ddd, 1H, J_1=14.8 Hz, J_2=8.0 Hz, J_3=1.2 Hz, H_6), 2.11 (ddd, 1H, J_1=14.6 Hz, J_2=10.0 Hz, J_3=2.0 Hz, H_6), 2.89 (ddd, 1H, J_1=13.8 Hz, J_2=8.3 Hz, J_3=4.7 Hz, H_9), 2.95 (ddd, 1H, J_1=14.3 Hz, J_2=6.5 Hz, J_3=4.4 Hz, H_9), 3.15-3.48 (br s, NCH_2COOH, under DMSO-water peak), 3.99 (d, 1H, J=16.3 Hz, $NCHPh$), 4.15-4.22 (q, AB, 2H, J_{AB}=17.4 Hz, NCH_2COOH), 4.73 (d, 1H, J=16.3 Hz, $NCHPh$), 7.11 (dd, 1H, J_1=8.0 Hz, J_2=1.1 Hz, H_4), 7.17 (td, 1H, J_1=7.4 Hz, J_2=1.6 Hz, H_3), 7.18 (d, 1H, J_1=7.7 Hz, H_1), 7.20 (td, 1H, J_1=7.5 Hz, J_2=1.5 Hz, H_2), 7.21-7.26 (m, 5H, H_{2Bz}, H_{3Bz}, H_{4Bz}, H_{5Bz}, H_{6Bz}); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 19.0 (C_7), 25.0 (C_8), 31.4 (C_6), 31.5 (C_9), 39.4 (NCH_2COOH), 43.6 (NCH_2Ph), 71.8 ($C_5/C_{4'}$), 126.9 (C_3), 127.1 (C_{4Bz}), 127.3 (C_{2Bz}, C_{6Bz}), 128.2 (C_{3Bz}, C_{5Bz}), 128.7 (C_4), 128.8 (C_2), 131.2 (C_1), 134.3 (C_{4a}), 137.7 (C_{1Bz}), 141.5 (C_{9a}), 155.0 ($C_{2'}$=O), 168.8 (NCH_2COOH), 174.8 ($C_{5'}$=O). Found: C, 69.89; H, 5.91; N, 7.43. Calc. for $C_{22}H_{22}N_2O_4$: C, 69.83; H, 5.86; N, 7.40%

Ic Synthesis of *N*-(phenylmethoxy)acetamides 14, 14a, 14b, 15, 15a, 15b



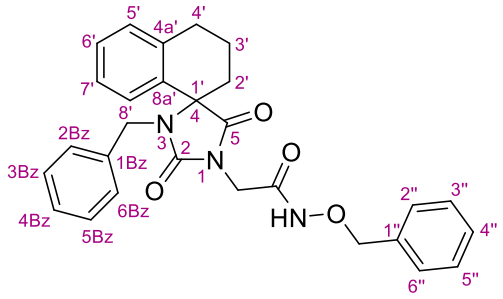
N-(phenylmethoxy)-2-(2,5-dioxo-3',4'-dihydro-2'*H*-spiro[imidazolidine-4,1'-naphthalen]-1-yl)acetamide (14)

The *N*-benzyloxy precursor **14** was prepared from carboxylic acid **11** (200 mg, 0.73 mmol) in dry THF (9 mL) upon treatment with CDI (143 mg, 0.88 mmol), *O*-benzylhydroxylamine hydrochloride (140 mg, 0.88 mmol) and TEA (135 mg, 1.33 mmol), following the amidation procedure described in the main manuscript (Method B). After removal of the solvent under vacuum, the reaction mixture was poured into 15 mL ice-water and extracted with AcOEt (4 x 15 mL). The combined organic phases were washed with H_2O (3 × 25 mL) and brine (2 × 25 mL), dried with anh. Na_2SO_4 and evaporated under reduced pressure. The resulting colorless viscous oil was chromatographed on silica gel using CH_2Cl_2/AcOEt 20:1, 10:1 and AcOEt as eluents to afford the corresponding *O*-benzyl hydroxamate **14** as a glass solid. The product was treated with *n*-pentane under ice-cooling to give a white crystalline solid (232 mg, 84%); mp 146-148 °C (from AcOEt/*n*-pentane-dry Et_2O), R_f = 0.07 (CH_2Cl_2/AcOEt 8:1). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.86 (ddtd, 1H, J_1=13.6 Hz, J_2=10.0 Hz, J_3=6.8 Hz, J_4=2.4 Hz, $H_{3'}$), 1.96 (ddd, 1H, J_1=13.1 Hz, J_2=7.4 Hz, J_3=2.7 Hz, $H_{2'}$), 2.02-2.09 (m, 1H, $H_{3'}$), 2.12 (ddd, 1H, J_1=13.3 Hz, J_2=10.5 Hz, J_3=2.8 Hz, $H_{2'}$), 2.80 (t, 2H, J=6.2 Hz, $H_{4'}$), 3.94-4.06 (q, AB, 1.6H, J_{AB}=16.2 Hz, NCH_2CO), 4.29 (br s, 0.3H, NCH_2CO), 4.83, 4.88 (s + s, 2H, OCH_2Ph), 7.17 (d, 1H, J=7.6 Hz, $H_{5'}$), 7.21 (t, 1H, J=7.6 Hz, $H_{7'}$), 7.25 (t, 1H, J=7.2 Hz, $H_{6'}$), 7.34 (d, 1H, J=7.7 Hz, $H_{8'}$), 7.36-7.49 (m, 5H, $H_{2''}$, $H_{3''}$, $H_{4''}$, $H_{5''}$, $H_{6''}$), 8.92 (s, 1H, H_3), 11.03 (s, 0.15H, CON*H*OCH$_2$Ph), 11.40 (s, 0.75H, CON*H*OCH$_2$Ph); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.4 ($C_{3'}$), 28.4 ($C_{4'}$), 33.6 ($C_{2'}$), 37.8 (N*C*H$_2$CO), 62.4 ($C_{1'}$/C_4), 77.0 (O*C*H$_2$Ph), 126.4 ($C_{7'}$), 127.5 ($C_{8'}$), 128.0 ($C_{6'}$), 128.3 ($C_{3''}$, $C_{4''}$, $C_{5''}$), 128.8 ($C_{2''}$, $C_{6''}$), 129.1 ($C_{5'}$), 134.0 ($C_{8a'}$), 135.8 ($C_{1''}$), 137.6 ($C_{4a'}$), 155.2 (C_2=O), 163.7 (*C*ONHOCH$_2$Ph), 176.1 (C_5=O). Found: C, 66.53; H, 5.55; N, 11.00. Calc. for $C_{21}H_{21}N_3O_4$: C, 66.48; H, 5.58; N, 11.08%



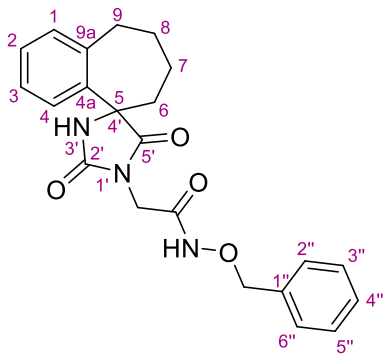
N-(phenylmethoxy)-2-(3-methyl-2,5-dioxo-3',4'-dihydro-2'*H*-spiro[imidazolidine-4,1'-naphthalen]-1-yl)acetamide (14a)

Carboxylic acid **11a** (160 mg, 0.55 mmol) was treated with CDI (107 mg, 0.66 mmol), *O*-benzylhydroxylamine hydrochloride (105 mg, 0.66 mmol) and TEA (101 mg, 1.00 mmol) in 7 mL dry THF as described for the synthesis of *O*-benzyl hydroxamates (Method B). The reaction was worked up in exactly the same way described in the main manuscript and the resulting oily residue was purified by column chromatography on silica gel using CH_2Cl_2/AcOEt 20:1 and AcOEt as eluents to give the corresponding *O*-benzyl hydroxamate **14a** as a glass solid. Crystallization of this material upon treatment with a *n*-pentane-dry Et_2O mixture (5:1) afforded a white crystalline solid (120 mg, 55%); mp melted gradually from 139 °C to145 °C (from AcOEt/*n*-pentane-dry Et_2O), R_f = 0.45 (CH_2Cl_2/AcOEt 8:1). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.87 (~dq, 1H, J_1=12.7 Hz, J_2=6.6, 5.7 Hz, $H_{3'}$), 2.06 (br d, 1H, J=12.8 Hz, $H_{2'}$), 2.14 (td, 1H, J_1=12.3 Hz, J_2=3.0 Hz, $H_{2'}$), 2.25 (ddt, 1H, J_1=14.9 Hz, J_2=10.9 Hz, J_3=5.2 Hz, $H_{3'}$), 2.63 (s, 3H, NCH_3), 2.82 (dq, 2H, J_1=16.5 Hz, J_2=8.9 Hz, $H_{4'}$), 3.92-4.06 (q, AB, 1.55H, J_{AB}=16.3 Hz, NCH_2CO), 4.20-4.32 (q, AB, 0.3H, J_{AB}=16.6 Hz, NCH_2CO), 4.80, 4.86 (s + s, 2H, OCH_2Ph), 7.11 (dd, 1H, J_1=7.4 Hz, J_2=1.6 Hz, $H_{8'}$), 7.17-7.31 (complex m, 3H, $H_{5'}$, $H_{6'}$, $H_{7'}$), 7.33-7.48 (complex m, 5H, $H_{2''}$, $H_{3''}$, $H_{4''}$, $H_{5''}$, $H_{6''}$), 11.01 (s, 0.1H, CON*H*OCH$_2$Ph), 11.38 (s, 0.7H, CON*H*OCH$_2$Ph); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.8 ($C_{3'}$), 25.0 (N*C*H$_3$), 28.2 ($C_{4'}$), 30.0 ($C_{2'}$), 38.2 (N*C*H$_2$CO), 65.0 ($C_{1'}$/C_4), 77.0 (O*C*H$_2$Ph), 126.4 ($C_{8'}$), 126.6 ($C_{7'}$), 128.3 ($C_{3''}$, $C_{4''}$, $C_{5''}$, $C_{6'}$), 128.8 ($C_{2''}$, $C_{6''}$), 129.6 ($C_{5'}$), 130.5 ($C_{8a'}$), 135.7 ($C_{1''}$), 139.4 ($C_{3a'}$), 154.9 (C_2=O), 163.5 (*C*ONHOCH$_2$Ph), 174.8 (C_5=O). Found: C, 67.25; H, 5.82; N, 10.74. Calc. for $C_{22}H_{23}N_3O_4$: C, 67.16; H, 5.89; N, 10.68%



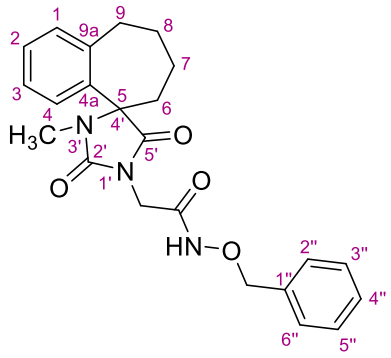
N-(phenylmethoxy)-2-(3-benzyl-2,5-dioxo-3',4'-dihydro-2'*H*-spiro[imidazolidine-4,1'-naphthalen]-1-yl)acetamide (14b)

Using the general procedure described for the preparation of *N*-(phenylmethoxy)acetamides (Method B), the carboxylic acid precursor **11b** (230 mg, 0.63 mmol) was treated with CDI (123 mg, 0.76 mmol), *O*-benzylhydroxylamine hydrochloride (121 mg, 0.76 mmol) and TEA (116 mg, 1.15 mmol) in dry THF (8 mL). After removal of the solvent under reduced pressure, the reaction mixture was quenched with 15 mL ice-water and extracted with AcOEt (4 x 15 mL). The combined organic phases were washed with H_2O (3 × 25 mL) and brine (2 × 25 mL), dried with anh. Na_2SO_4 and evaporated *in vacuo*. The resulting colorless oil was chromatographed on silica gel using CH_2Cl_2, CH_2Cl_2/AcOEt 20:1, 10:1 and AcOEt as eluents to afford the corresponding *O*-benzyl hydroxamate **14b** as a foamy solid. The title compound was crystallized to a white crystalline solid after treatment with *n*-pentane under ice-cooling (180 mg, 61%); mp 121-123 °C (from AcOEt/*n*-pentane-dry Et_2O), R_f= 0.44 (CH_2Cl_2/AcOEt 8:1). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.67 (dt, 1H, J_1=17.3 Hz, J_2=6.0 Hz, $H_{3'}$), 1.92 (ddd, 1H, J_1=13.9 Hz, J_2=10.9 Hz, J_3=3.1 Hz, $H_{2'}$), 2.07 (td, 2H, J_1=14.1 Hz, J_2=4.2 Hz, $H_{2'}$, $H_{3'}$), 2.75 (dq, 2H, J_1=11.0 Hz, J_2=5.4 Hz, $H_{4'}$), 3.85 (d, 1H, J=16.5 Hz, NC*H*HPh), 4.00-4.12 (q, AB, 1.55H, J_{AB}=16.2 Hz, NCH_2CO), 4.29-4.38 (q, AB, 0.3H, J_{AB}=16.5 Hz, NCH_2CO), 4.65 (d, 1H, J=16.4 Hz, NCH*H*Ph), 4.82, 4.88 (s + s, 2H, OCH_2Ph), 7.14-7.19 (m, 2H, $H_{7'}$, $H_{8'}$), 7.19-7.24 (m, 4H, $H_{5'}$, $H_{6'}$, H_{2Bz}, H_{6Bz}), 7.24-7.30 (m, 3H, H_{3Bz}, H_{4Bz}, H_{5Bz}), 7.33-7.49 (m, 5H, $H_{2''}$, $H_{3''}$, $H_{4''}$, $H_{5''}$, $H_{6''}$), 11.06 (s, 0.15H, CON*H*OCH$_2$Ph), 11.43 (s, 0.7H, CON*H*OCH$_2$Ph); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.7 ($C_{3'}$), 28.2 ($C_{4'}$), 31.4 ($C_{2'}$), 38.4 (N*C*H$_2$CO), 43.5 (N*C*H$_2$Ph), 66.2 ($C_{1'}$/C_4), 77.1 (O*C*H$_2$Ph), 126.6 ($C_{8'}$), 126.8 ($C_{7'}$), 127.0, 127.1 (C_{2Bz}, C_{6Bz}), 128.25 (C_{3Bz}, C_{4Bz}, C_{5Bz}), 128.37 ($C_{3''}$, $C_{4''}$, $C_{5''}$), 128.44 ($C_{6'}$), 128.8 ($C_{2''}$, $C_{6''}$), 129.6 ($C_{5'}$), 130.8 ($C_{8a'}$), 135.8 ($C_{1''}$), 137.7 (C_{1Bz}), 139.5 ($C_{4a'}$), 155.8 (C_2=O), 163.6 (*C*ONHOCH$_2$Ph), 174.8 (C_5=O). Found: C, 71.55; H, 5.87; N, 8.99. Calc. for $C_{28}H_{27}N_3O_4$: C, 71.62; H, 5.80; N, 8.95%



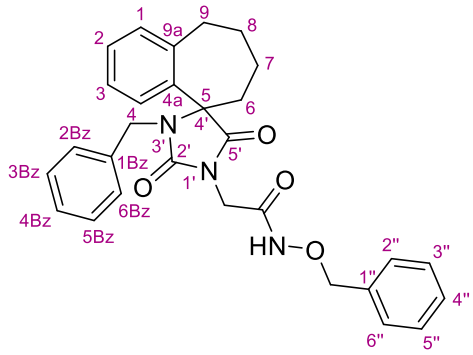
N-(phenylmethoxy)-2-(2',5'-dioxo-6,7,8,9-tetrahydrospiro[benzo[7]annulene-5,4'-imidazolidin]-1'-yl)acetamide (15)

Prepared from carboxylic acid **12** (230 mg, 0.80 mmol) upon treatment with EDCI·HCl (184 mg, 0.96 mmol), HOBt (162 mg, 0.96 mmol, 80% monohydrate), *O*-benzylhydroxylamine hydrochloride (153 mg, 0.96 mmol) and TEA (470 mg, 4.64 mmol) in dry CH_2Cl_2/dry DMF 4:1 (8 mL) following the general procedure for the synthesis of *O*-benzyl hydroxamates (Method A). After removal of CH_2Cl_2 under reduced pressure, the reaction mixture was poured into 15 mL ice-water and extracted with AcOEt (4 × 15 mL). The combined organic layers were washed with H_2O (3 × 35 mL) and brine (2 × 35 mL), dried over Na_2SO_4 and concentrated to dryness *in vacuo*. The yellowish solid was chromatographed on silica gel column using CH_2Cl_2, CH_2Cl_2/AcOEt 8:1, 2:1 and then AcOEt as eluents to give the desired compound **15** as a white crystalline solid (205 mg, 65%); mp 203-205 °C (from AcOEt/*n*-pentane), R_f = 0.17 (CH_2Cl_2/AcOEt 8:1). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.64 (dtt, 1H, J_1=11.9 Hz, J_2=7.9 Hz, J_3=3.3 Hz, H_8), 1.74-1.92 (complex m, 3H, H_7, H_8), 1.96 (ddd, 1H, J_1=13.9 Hz, J_2=6.6 Hz, J_3=2.9 Hz, H_6), 2.12 (ddd, 1H, J_1=14.3 Hz, J_2=10.7 Hz, J_3=3.4 Hz, H_6), 3.00 (dt, 2H, J_1=8.6 Hz, J_2=3.8 Hz, H_9), 3.97 (s, 1.5H, NCH_2CO), 4.27 (s, 0.35H, NCH_2CO), 4.81, 4.87 (s + s, 2H, OCH_2Ph), 7.13-7.23 (m, 3H, H_1, H_2, H_3), 7.27 (dd, 1H, J_1=7.9 Hz, J_2=1.6 Hz, H_4), 7.33-7.48 (complex m, 5H, $H_{2''}$, $H_{3''}$, $H_{4''}$, $H_{5''}$, $H_{6''}$), 8.96 (s, 1H, $H_{3'}$), 11.41 (s, 0.6H, CON*H*OCH$_2$Ph); ^{13}C NMR (50.32 MHz, DMSO-d_6) δ (ppm) 23.8 (C_7), 26.5 (C_8), 34.3 (C_9), 35.8 (C_6), 38.0, 38.3 (N*C*H$_2$CO), 68.1 (C_5/$C_{4'}$), 77.0, 78.6 (O*C*H$_2$Ph), 126.3 (C_3), 128.0 (C_4), 128.1 (C_2), 128.4 ($C_{3''}$, $C_{4''}$, $C_{5''}$), 128.9 ($C_{2''}$, $C_{6''}$), 131.2 (C_1), 135.8 ($C_{1''}$), 137.8 (C_{4a}), 142.2 (C_{9a}), 155.1 ($C_{2'}$=O), 163.6 (*C*ONHOCH$_2$Ph), 175.8 ($C_{5'}$=O). Found: C, 67.21; H, 5.95; N, 10.70. Calc. for $C_{22}H_{23}N_3O_4$: C, 67.16; H, 5.89; N, 10.68%



N-(phenylmethoxy)-2-(3'-methyl-2',5'-dioxo-6,7,8,9-tetrahydrospiro[benzo[7]annulene-5,4'-imidazolidin]-1'-yl)acetamide (15a)

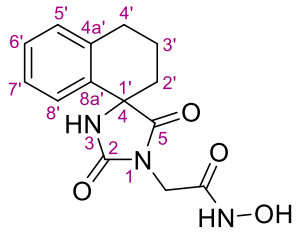
The *N*-benzyloxy precursor **15a** was prepared from carboxylic acid **12a** (212 mg, 0.70 mmol) in dry THF (9 mL) upon treatment with CDI (136 mg, 0.84 mmol), *O*-benzylhydroxylamine hydrochloride (134 mg, 0.84 mmol) and TEA (129 mg, 1.27 mmol), following the amidation procedure described in the main manuscript (Method B). After removal of the solvent *in vacuo*, the reaction mixture was quenched with 15 mL ice-water and extracted with AcOEt (4 x 15 mL). The combined organic phases were washed with H_2O (3 × 25 mL) and brine (2 × 25 mL), dried over anh. Na_2SO_4 and evaporated under reduced pressure. The colorless viscous oily residue was purified by column chromatography on silica gel using CH_2Cl_2/AcOEt 20:1 and AcOEt as eluents to give the corresponding *O*-benzylhydroxamate **15a** as a glass solid. Crystallization of this material upon treatment with a *n*-pentane-dry Et_2O mixture (10:1) gave a white crystalline solid (157 mg, 55%); mp 71-73 °C (from AcOEt/*n*-pentane), R_f = 0.18 (CH_2Cl_2/AcOEt 8:1). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.63-1.75 (complex m, 2H, H_7, H_8), 1.78-1.95 (complex m, 2H, H_7, H_8), 2.12 (dd, 1H, J_1=13.7 Hz, J_2=7.2 Hz, H_6), 2.32 (dd, 1H, J_1=13.3 Hz, J_2=11.1 Hz, H_6), 2.74 (s, 3H, NCH_3), 2.89 (ddd, 1H, J_1=14.5 Hz, J_2=7.9 Hz, J_3=3.8 Hz, H_9), 3.17 (ddd, 1H, J_1=13.8 Hz, J_2=8.5 Hz, J_3=4.1 Hz, H_9), 3.90-4.02 (q, AB, 1.6H, J_{AB}=16.3 Hz, NCH_2CO), 4.19-4.30 (q, AB, 0.3H, J_{AB}=16.7 Hz, NCH_2CO), 4.79, 4.85 (s + s, 2H, OCH_2Ph), 7.11 (dd, 1H, J_1=7.3 Hz, J_2=1.9 Hz, H_4), 7.19-7.29 (m, 3H, H_1, H_2, H_3), 7.30-7.46 (complex m, 5H, $H_{2''}$, $H_{3''}$, $H_{4''}$, $H_{5''}$, $H_{6''}$), 11.01 (s, 0.1H, CON*H*OCH$_2$Ph), 11.38 (s, 0.7H, CON*H*OCH$_2$Ph); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 20.2 (C_7), 25.1 (N*C*H$_3$), 25.5 (C_8), 31.6 (C_6), 32.1 (C_9), 38.3 (N*C*H$_2$CO), 70.7 (C_5/$C_{4'}$), 77.0 (O*C*H$_2$Ph), 126.8 (C_3), 128.1 (C_4), 128.3 ($C_{3''}$, $C_{4''}$, $C_{5''}$), 128.5 (C_2), 128.7 ($C_{2''}$, $C_{6''}$), 131.3 (C_1), 134.3 (C_{4a}), 135.7 ($C_{1''}$), 141.6 (C_{9a}), 154.3 ($C_{2'}$=O), 163.4 (*C*ONHOCH$_2$Ph), 174.6 ($C_{5'}$=O). Found: C, 67.88; H, 6.23; N, 10.25. Calc. for $C_{23}H_{25}N_3O_4$: C, 67.80; H, 6.18; N, 10.31%



N-(phenylmethoxy)-2-(3'-benzyl-2',5'-dioxo-6,7,8,9-tetrahydrospiro[benzo[7]annulene-5,4'-imidazolidin]-1'-yl)acetamide (15b)

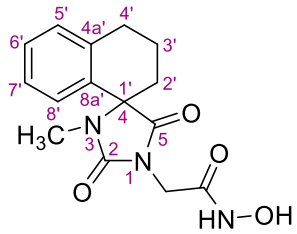
Carboxylic acid **12b** (300 mg, 0.79 mmol) in 8 mL dry CH_2Cl_2/dry DMF (4:1) was treated with EDCI·HCl (182 mg, 0.95 mmol), HOBt (160 mg, 0.95 mmol, 80% monohydrate), *O*-benzylhydroxylamine hydrochloride (152 mg, 0.95 mmol) and TEA (463 mg, 4.58 mmol) as previously described for the preparation of *N*-benzyloxy analogues (Method A). After removal of CH_2Cl_2 under reduced pressure, ice-water (15 mL) was added, and the mixture was extracted with AcOEt (4 × 15 mL). The combined organic layers were washed with H_2O (3 × 35 mL) and brine (2 × 35 mL), dried with anh. Na_2SO_4 and evaporated under reduce pressure. The viscous oily residue was purified by column chromatography on silica gel eluting first with CH_2Cl_2/AcOEt 30:1, 15:1, 8:1 and then 4:1 to give the corresponding *O*-benzyl hydroxamate **15b** as a glass solid. The title compound was crystallized to a white crystalline solid upon treatment with *n*-pentane under ice-cooling (180 mg, 47%); mp 64-66 °C (from AcOEt/*n*-pentane), R_f = 0.49 (CH_2Cl_2/AcOEt 8:1). ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.56 (~dq, 1H, J_1=12.7 Hz, J_2=6.4, 5.8 Hz, H_7), 1.62-1.77 (complex m, 3H, H_7, H_8), 2.03 (dd, 1H, J_1=14.6 Hz, J_2=7.5 Hz, H_6), 2.12 (dd, 1H, J_1=14.7 Hz, J_2=10.1 Hz, H_6), 2.86-2.97 (m, 2H, H_9), 3.99 (d, 1H, J=16.3 Hz, NC*H*HPh), 4.01-4.10 (q, AB, 1.5H, J_{AB}=16.2 Hz, NCH_2COO), 4.34 (br s, 0.3H, NCH_2COO), 4.72 (d, 1H, J=16.3 Hz, NCH*H*Ph), 4.82, 4.88 (s + s, 2H, OCH_2Ph), 7.15-7.22 (m, 6H, H_1, H_3, H_4, H_{2Bz}, H_{4Bz}, H_{6Bz}), 7.22-7.27 (m, 3H, H_2, H_{3Bz}, H_{5Bz},), 7.34-7.48 (m, 5H, $H_{2''}$, $H_{3''}$, $H_{4''}$, $H_{5''}$, $H_{6''}$), 11.06 (s, 0.15H, CON*H*OCH$_2$Ph), 11.43 (s, 0.7H, CON*H*OCH$_2$Ph); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.9 (C_7), 24.9 (C_8), 31.3 (C_6), 31.5 (C_9), 38.4 (N*C*H$_2$CO), 43.6 (N*C*H$_2$Ph), 71.8 (C_5/$C_{4'}$), 77.0 (O*C*H$_2$Ph), 126.9 (C_3), 127.0 (C_{4Bz}), 127.3 (C_{2Bz}, C_{6Bz}), 128.1 (C_{3Bz}, C_{5Bz}), 128.3 ($C_{3''}$, $C_{4''}$, $C_{5''}$), 128.7 (C_4), 128.8 ($C_{2''}$, $C_{6''}$), 129.0 (C_2), 131.1 (C_1), 134.3 (C_{4a}), 135.8 ($C_{1''}$), 137.7 (C_{1Bz}), 141.4 (C_{9a}), 155.1 ($C_{2'}$=O), 163.5 (*C*OOCH$_2$Ph), 175.0 ($C_{5'}$=O). Found: C, 72.10; H, 6.08; N, 8.77. Calc. for $C_{29}H_{29}N_3O_4$: C, 72.03; H, 6.05; N, 8.69%

Id Synthesis of *N*-(hydroxy)acetamides 17, 17a, 17b, 18, 18a, 18b



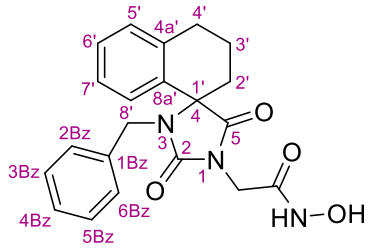
N-hydroxy-2-(2,5-dioxo-3',4'-dihydro-2'*H*-spiro[imidazolidine-4,1'-naphthalen]-1-yl)acetamide (17)

The *N*-benzyloxy precursor **14** (170 mg, 0.45 mmol) was subjected to catalytic hydrogenation in a mixture of EtOH/AcOEt 3:1 (18 mL) according to the procedure described in the main manuscript for the synthesis of hydroxamate analogues. Concentration to dryness under reduced pressure afforded the title compound **17** as a white foamy solid, which strongly binds the aforementioned solvents. Removal of the entrapped solvents upon drying under high vacuum gave the target compound **17** as a glass solid which was crystallized on standing (130 mg, almost quantitative yield); mp 180-183 °C (from AcOEt/*n*-pentane), R_f = 0.47 (AcOEt). This compound appeared in the ^{1}H and ^{13}C NMR spectra as a mixture of *E*/*Z* conformers. ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.85 (dqt, 1H, J_1=17.0 Hz, J_2=6.4 Hz, J_3=2.4 Hz, $H_{3'}$), 1.95 (ddd, 1H, J_1=12.9 Hz, J_2=7.1 Hz, J_3=2.4 Hz, $H_{2'}$), 2.01-2.07 (complex m, 1H, $H_{2'}$), 2.10 (ddd, 1H, J_1=13.2 Hz, J_2=10.7 Hz, J_3=2.9 Hz, $H_{3'}$), 2.74-2.83 (m, 2H, $H_{4'}$), 3.92-4.02 (q, AB, 1.45H, J_{AB}=16.0 Hz, NCH_2CO, *E*-isomer), 4.21-4.31 (q, AB, 0.45H, J_{AB}=17.3 Hz, NCH_2CO, *Z*-isomer), 7.16 (d, 1H, *J*=7.8 Hz, $H_{5'}$), 7.17 (t, 1H, *J*=7.8 Hz, $H_{7'}$), 7.24 (td, 1H, J_1=7.4 Hz, J_2=1.4 Hz, $H_{6'}$), 7.35 (d, 0.5H, *J*=7.6 Hz, $H_{8'}$), 7.40 (d, 0.2H, *J*=7.6 Hz, $H_{8'}$), 8.87, 8.89 (s + s, 1H, H_3), 8.98 (s, 0.6H, CH_2CONHO*H*, *E*-isomer), 9.35 (s, 0.2H, NCH_2CONHO*H*, *Z*-isomer), 10.30 (s, 0.2H, NCH_2CON*H*OH, *Z*-isomer), 10.73 (s, 0.6H, CH_2CON*H*OH, *E*-isomer); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.4 ($C_{3'}$), 28.4 ($C_{4'}$), 33.5, 33.7 ($C_{2'}$), 38.0 (N*C*H_2CO, *E*-isomer), 38.5 (N*C*H_2CO, *Z*-isomer), 62.3 ($C_{1'}$/C_4), 126.4 ($C_{7'}$), 127.6 ($C_{8'}$), 128.0 ($C_{6'}$), 129.0 ($C_{5'}$), 134.1 ($C_{8a'}$), 137.6 ($C_{4a'}$), 155.3 (C_2=O, *E*-isomer), 155.5 (C_2=O, *Z*-isomer), 163.4 (NCH_2*C*O, *E*-isomer), 168.9 (NCH_2*C*O, *Z*-isomer), 176.2 (C_5=O, *E*-isomer), 176.4 (C_5=O, *Z*-isomer). Found: C, 58.23; H, 5.27; N, 14.60. Calc. for $C_{14}H_{15}N_3O_4$: C, 58.13; H, 5.23; N, 14.53%



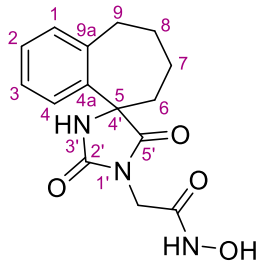
N-hydroxy-2-(3-methyl-2,5-dioxo-3',4'-dihydro-2'*H*-spiro[imidazolidine-4,1'-naphthalen]-1-yl)acetamide (17a)

A solution of the *O*-benzyl hydroxamate **14a** (90 mg, 0.23 mmol) in EtOH/AcOEt 3:1 (9 mL) was hydrogenated as described for the preparation of acetohydroxamic acids. Evaporation of the solvents *in vacuo* yielded the title compound **17a** as a white foamy solid, which strongly binds the above-mentioned solvents. Removal of the entrapped solvents upon drying under high vacuum and treatment with *n*-pentane at 0 °C gave **17a** as a white crystalline solid (68 mg, almost quantitative yield); mp 179-181 °C (from AcOEt/*n*-pentane-dry Et_2O), R_f = 0.52 (AcOEt). This compound exhibited distinct peaks attributed to each of the two *E*/*Z* conformers in the ^{1}H and ^{13}C NMR spectra. ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.86 (ddtd, 1H, J_1=13.4 Hz, J_2=6.2 Hz, J_3=4.9 Hz, J_4=3.3 Hz, $H_{3'}$), 2.05 (ddd, 1H, J_1=13.2 Hz, J_2=6.1 Hz, J_3=2.9 Hz, $H_{2'}$), 2.14 (ddd, 1H, J_1=14.2 Hz, J_2=11.2 Hz, J_3=3.1 Hz, $H_{2'}$), 2.23 (ddddd, 1H, J_1=13.4 Hz, J_2=11.3 Hz, J_3=9.8 Hz, J_4=5.4 Hz, J_5=3.3 Hz, $H_{3'}$), 2.62 (s, 3H, NCH_3), 2.79 (ddd, 1H, J_1=16.7 Hz, J_2=9.9 Hz, J_3=4.7 Hz, $H_{4'}$), 2.84 (dt, 1H, J_1=16.7 Hz, J_2=4.8 Hz, $H_{4'}$), 3.92-4.03 (q, AB, 1.45H, J_{AB}=16.0 Hz, NCH_2CO, *E*-isomer), 4.20-4.31 (q, AB, 0.45H, J_{AB}=17.4 Hz, NCH_2CO, *Z*-isomer), 7.10-7.18 (complex m, 1H, $H_{8'}$), 7.20 (td, 1H, J_1=7.4 Hz, J_2=1.5 Hz, $H_{7'}$), 7.22 (dd, 1H, J_1=7.5 Hz, J_2=2.0 Hz, $H_{5'}$), 7.26 (td, 1H, J_1=7.3 Hz, J_2=1.3 Hz, $H_{6'}$), 8.97 (s, 0.6H, CH_2CONHO*H*, *E*-isomer), 9.35 (s, 0.2H, NCH_2CONHO*H*, *Z*-isomer), 10.31 (s, 0.2H, NCH_2CON*H*OH, *Z*-isomer), 10.72 (s, 0.6H, CH_2CON*H*OH, *E*-isomer); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.8 ($C_{3'}$), 25.0 (N*C*H_3), 28.3 ($C_{4'}$), 30.0, 30.1 ($C_{2'}$), 38.3 (N*C*H_2CO, *E*-isomer), 38.8 (N*C*H_2CO, *Z*-isomer), 65.0 ($C_{1'}$/C_4), 126.5 ($C_{8'}$), 126.6 ($C_{7'}$), 128.3 ($C_{6'}$), 129.6 ($C_{5'}$), 130.6 ($C_{8a'}$), 139.4 ($C_{4a'}$), 155.0 (C_2=O, *E*-isomer), 155.1 (C_2=O, *Z*-isomer), 163.2 (NCH_2*C*O, *E*-isomer), 168.7 (NCH_2*C*O, *Z*-isomer), 174.9 (C_5=O, *E*-isomer), 175.0 (C_5=O, *Z*-isomer). Found: C, 59.49; H, 5.70; N, 13.81. Calc for $C_{15}H_{17}N_3O_4$: C, 59.40; H, 5.65; N, 13.85%



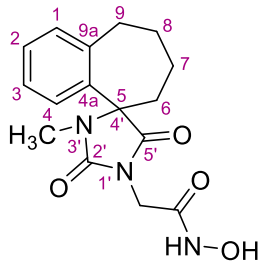
N-hydroxy-2-(3-benzyl-2,5-dioxo-3',4'-dihydro-2'*H*-spiro[imidazolidine-4,1'-naphthalen]-1-yl)acetamide (17b)

A solution of the appropriate *O*-benzyl hydroxamate **14b** (150 mg, 0.32 mmol) in a mixture of EtOH/AcOEt (3:1, 13 mL) was hydrogenated following the general procedure described for the synthesis of acetohydroxamic acids. Evaporation of the solvents under reduced pressure yielded the title compound **17b** as a glass solid, which strongly binds the aforementioned solvents. Removal of the entrapped solvents upon drying under high vacuum and treatment with *n*-pentane under ice-cooling gave **17b** as a white crystalline solid (120 mg, almost quantitative yield); mp 173-175 °C (melted gradually from 168 °C) (from AcOEt/*n*-pentane), R_f = 0.53 (AcOEt). In the ^{1}H and ^{13}C NMR spectra of this compound, double set of characteristic peaks are distinguished for each of the two *E*/*Z* conformers. ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.61-1.69 (m, 1H, $H_{3'}$), 1.90 (ddd, 1H, J_1=13.9 Hz, J_2=11.0 Hz, J_3=3.1 Hz, $H_{2'}$), 2.05 (ddd, 1H, J_1=13.7 Hz, J_2=7.2 Hz, J_3=2.9 Hz, $H_{2'}$), 2.06-2.13 (complex m, 1H, $H_{3'}$), 2.74 (dt, 1H, J_1=11.1 Hz, J_2=5.5 Hz, $H_{4'}$), 3.84 (d, 1H, J=16.5 Hz, NC*H*HPh), 4.00-4.10 (q, AB, 1.5H, J_{AB}=16.1 Hz, NCH_2CO, *E*-isomer), 4.28-4.39 (q, AB, 0.45H, J_{AB}=17.3 Hz, NCH_2CO, *Z*-isomer), 4.65 (dd, 1H, J_1=16.6 Hz, J_2=4.8 Hz, NCH*H*Ph), 7.15 (td, 1H, J_1=7.4 Hz, J_2=1.4 Hz, $H_{7'}$), 7.17-7.23 (m, 5H, $H_{5'}$, $H_{6'}$, H_{2Bz}, H_{4Bz}, H_{6Bz}), 7.23-7.29 (complex m, 3H, $H_{8'}$, H_{3Bz}, H_{5Bz}), 9.02 (s, 0.65H, CH_2CONHO*H*, *E*-isomer), 9.40 (s, 0.2H, NCH_2CONHO*H*, *Z*-isomer), 10.35 (s, 0.2H, NCH_2CON*H*OH, *Z*-isomer), 10.78 (s, 0.65H, CH_2CON*H*OH, *E*-isomer); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.7 ($C_{3'}$), 28.2 ($C_{4'}$), 31.4, 31.5 ($C_{2'}$), 38.4 (N*C*H_2CO, *E*-isomer), 39.0 (N*C*H_2CO, *Z*-isomer), 43.5 (N*C*H_2Ph), 66.1 ($C_{1'}$/C_4), 126.6 ($C_{7'}$), 126.8 ($C_{8'}$), 126.97 (C_{4Bz}), 127.04 (C_{2Bz}, C_{6Bz}), 128.2 (C_{3Bz}, C_{5Bz}), 128.4 ($C_{6'}$), 129.5 ($C_{5'}$), 130.9 ($C_{8a'}$), 137.8 (C_{1Bz}), 139.5 ($C_{4a'}$), 155.9 (C_2=O, *E*-isomer), 156.0 (C_2=O, *Z*-isomer), 163.2 (NCH_2*C*O, *E*-isomer), 168.7 (NCH_2*C*O, *Z*-isomer), 174.8 (C_5=O, *E*-isomer), 175.1 (C_5=O, *Z*-isomer). Found: C, 66.53; H, 5.60; N, 11.18. Calc. for $C_{21}H_{21}N_3O_4$: C, 66.48; H, 5.58; N, 11.08%



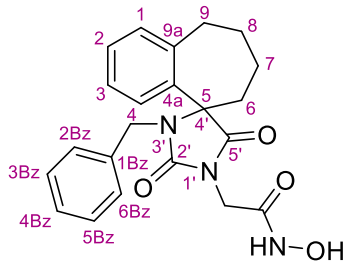
N-(hydroxy)-2-(2',5'-dioxo-6,7,8,9-tetrahydrospiro[benzo[7]annulene-5,4'-imidazolidin]-1'-yl)acetamide (18)

The *N*-benzyloxy precursor **15** (160 mg, 0.41 mmol) was subjected to catalytic hydrogenation in a mixture of EtOH/AcOEt 3:1 (16 mL) according to the procedure described in the main manuscript for the synthesis of hydroxamate analogues. Concentration to dryness under reduced pressure gave the title compound **18** as a white foamy solid, which strongly binds the aforementioned solvents. Removal of the entrapped solvents upon drying under high vacuum gave the hydrogenolysis product as a glass solid which was crystallized on standing (123 mg, almost quantitative yield); mp 184-186 °C (from AcOEt/*n*-pentane-dry Et_2O), R_f = 0.16 (AcOEt). This compound appeared in the ^{1}H and ^{13}C NMR spectra as a mixture of *E*/*Z* conformers. ^{1}H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.63 (ddt, 1H, J_1=13.5 Hz, J_2=8.1 Hz, J_3=4.9 Hz, H_8), 1.74-1.91 (complex m, 3H, H_7, H_8), 1.95 (ddd, 1H, J_1=14.1 Hz, J_2=6.4 Hz, J_3=3.1 Hz, H_6), 2.11 (ddd, 1H, J_1=14.2 Hz, J_2=10.8 Hz, J_3=3.4 Hz, H_6), 2.99 (dd, 2H, J_1=7.1 Hz, J_2=4.6 Hz, H_9), 3.96 (s, 1.3H, NCH_2CO, *E*-isomer), 4.00 (s, 0.3H, NCH_2CO, *E*-isomer), 4.25 (s, 0.4H, NCH_2CO, *Z*-isomer), 7.15 (td, 1H, J_1=7.0 Hz, J_2=1.9 Hz, H_3), 7.18 (d, 1H, J=6.9 Hz, H_1), 7.20 (td, 1H, J_1=7.1 Hz, J_2=1.3 Hz, H_2), 7.28 (dd, 0.6H, J_1=7.7 Hz, J_2=1.4 Hz, H_4), 7.31 (dd, 0.15H, J=7.8 Hz, H_4), 8.89 (s, 0.15H, $H_{3'}$), 8.92, 8.93 (s + s, 0.85H, $H_{3'}$), 8.97 (s, 0.6H, CH_2CONHO*H*, *E*-isomer), 9.35 (s, 0.2H, NCH_2CONHO*H*, *Z*-isomer), 10.30 (s, 0.2H, NCH_2CON*H*OH, *Z*-isomer), 10.74 (s, 0.6H, NCH_2CON*H*OH, *E*-isomer); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 23.69, 23.73 (C_7), 26.48, 26.51 (C_8), 34.2, 34.3 (C_9), 35.65, 35.73 (C_6), 37.9 (N*C*H_2CO, *E*-isomer), 38.4 (N*C*H_2CO, *Z*-isomer), 39.8 (N*C*H_2CO, *E*-isomer), 68.0, 68.1 (C_5/$C_{4'}$), 126.2 (C_3), 128.02 (C_2), 128.05 (C_4), 131.1 (C_1), 137.88, 137.94 (C_{4a}), 142.2 (C_{9a}), 155.2 ($C_{2'}$=O, *E*-isomer), 155.4 ($C_{2'}$=O, *Z*-isomer), 163.3, 167.7 (NCH_2*C*O, *E*-isomer), 168.8 (NCH_2*C*O, *Z*-isomer), 175.9 ($C_{5'}$=O, *E*-isomer), 176.0 ($C_{5'}$=O, *Z*-isomer). Found: C, 59.46; H, 5.68; N, 13.93. Calc. for $C_{15}H_{17}N_3O_4$: C, 59.40; H, 5.65; N, 13.85%



N-(hydroxy)-2-(3'-methyl-2',5'-dioxo-6,7,8,9-tetrahydrospiro[benzo[7]annulene-5,4'-imidazolidin]-1'-yl)acetamide (18a)

A solution of the *O*-benzyl hydroxamate **15a** (115 mg, 0.28 mmol) in EtOH/AcOEt 3:1 (11 mL) was hydrogenated in the presence of Pd/C (14 mg) as described for the preparation of final compounds. Concentration to dryness yielded the acetohydroxamic acid **18a** as a white foamy solid, which strongly binds the above-mentioned solvents. Removal of the entrapped solvents upon drying under high vacuum and treatment with *n*-pentane/dry Et_2O at 0 °C gave **18a** as a white crystalline solid (88 mg, almost quantitative yield); mp gradual degradation from 90 to 110 °C (from AcOEt/*n*-pentane), R_f = 0.31 (AcOEt). This compound exhibited distinct peaks attributed to each of the two *E*/*Z* conformers in the ^1H and ^{13}C NMR spectra. ^1H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.64-1.75 (m, 2H, H_7, H_8), 1.83 (dddd, 1H, J_1=13.9 Hz, J_2=10.2 Hz, J_3=5.0 Hz, J_4=2.5 Hz, H_8), 1.89 (dddd, 1H, J_1=13.2 Hz, J_2=10.2 Hz, J_3=6.7 Hz, J_4=2.1 Hz, H_7), 2.12 (ddd, 1H, J_1=14.9 Hz, J_2=7.7 Hz, J_3=2.4 Hz, H_6), 2.31 (ddd, 1H, J_1=14.8 Hz, J_2=10.6 Hz, J_3=2.1 Hz, H_6), 2.73 (s, 3H, NCH_3), 2.90 (ddd, 1H, J_1=14.4 Hz, J_2=8.1 Hz, J_3=3.9 Hz, H_9), 3.15 (ddd, 1H, J_1=14.3 Hz, J_2=8.4 Hz, J_3=4.1 Hz, H_9), 3.90-4.01 (q, AB, 1.5H, J_{AB}=16.0 Hz, NCH_2CO, *E*-isomer), 4.19-4.29 (q, AB, 0.45H, J_{AB}=17.4 Hz, NCH_2CO, *Z*-isomer), 7.10-7.18 (m, 1H, H_4), 7.20-7.27 (complex m, 3H, H_1, H_2, H_3), 8.94 (s, 0.6H, CH_2CONHO*H*, *E*-isomer), 9.33 (s, 0.2H, NCH_2CONHO*H*, *Z*-isomer), 10.28 (s, 0.2H, NCH_2CON*H*OH, *Z*-isomer), 10.70 (s, 0.55H, NCH_2CON*H*OH, *E*-isomer); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 20.1 (C_7), 25.1 (N*C*H_3), 25.5 (C_8), 31.5, 31.6 (C_6), 32.1 (C_9), 38.3 (N*C*H_2CO, *E*-isomer), 38.8 (N*C*H_2CO, *Z*-isomer), 39.8 (N*C*H_2CO, *E*-isomer), 70.6 (C_5/$C_{4'}$), 126.8 (C_3), 128.1, 128.2 (C_4), 128.5 (C_2), 131.3 (C_1), 134.4 (C_{4a}), 141.6 (C_{9a}), 154.4 ($C_{2'}$=O, *E*-isomer), 154.5 ($C_{2'}$=O, *Z*-isomer), 163.1 (NCH_2*C*O, *E*-isomer), 168.6 (NCH_2*C*O, *Z*-isomer), 174.7 ($C_{5'}$=O, *E*-isomer), 174.8 ($C_{5'}$=O, *Z*-isomer). Found: C, 60.60; H, 6.09; N, 13.30. Calc. for $C_{16}H_{19}N_3O_4$: C, 60.56; H, 6.04; N, 13.24%

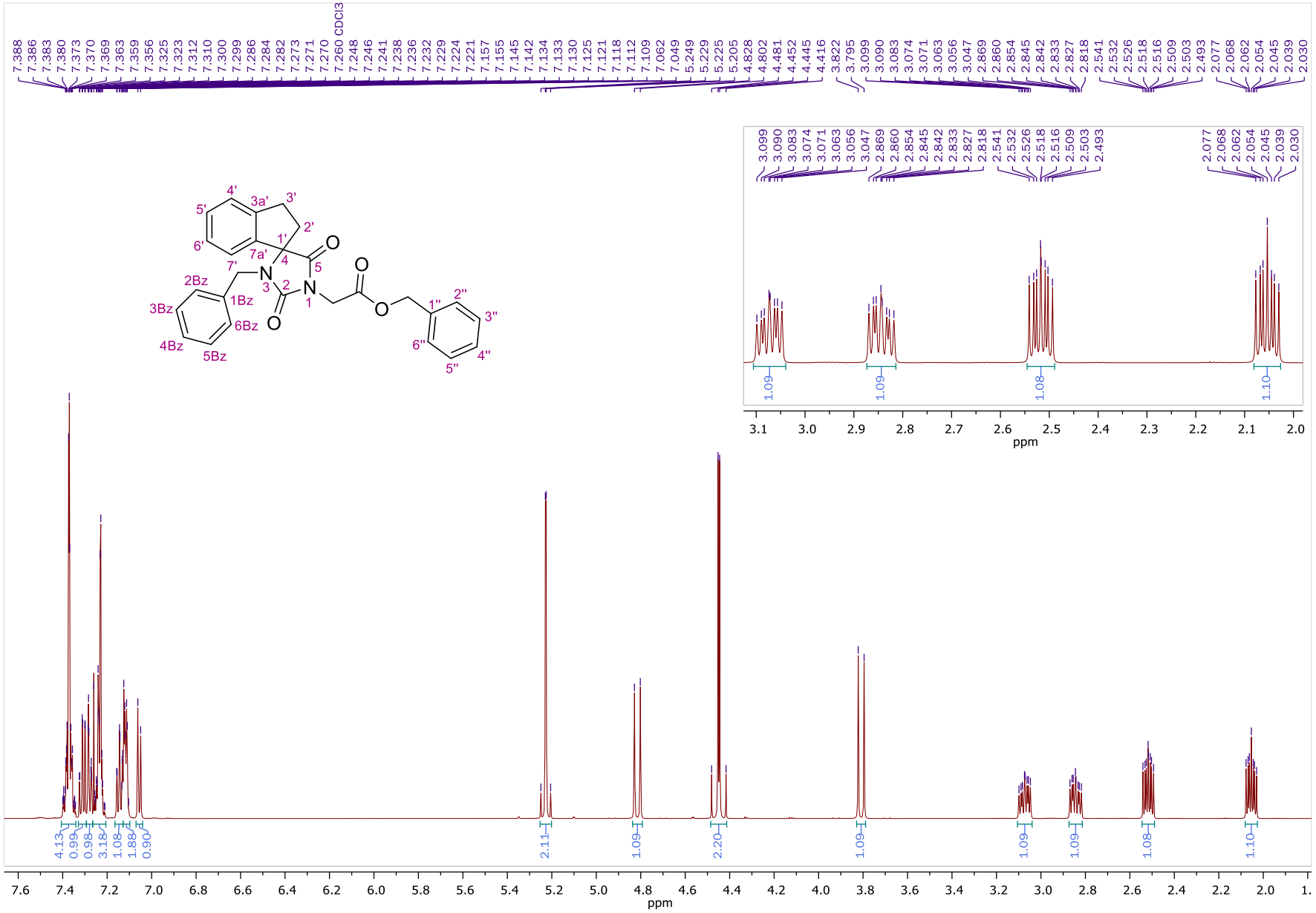


N-hydroxy-2-(3'-benzyl-2',5'-dioxo-6,7,8,9-tetrahydrospiro[benzo[7]annulene-5,4'-imidazolidin]-1'-yl)acetamide (18b)

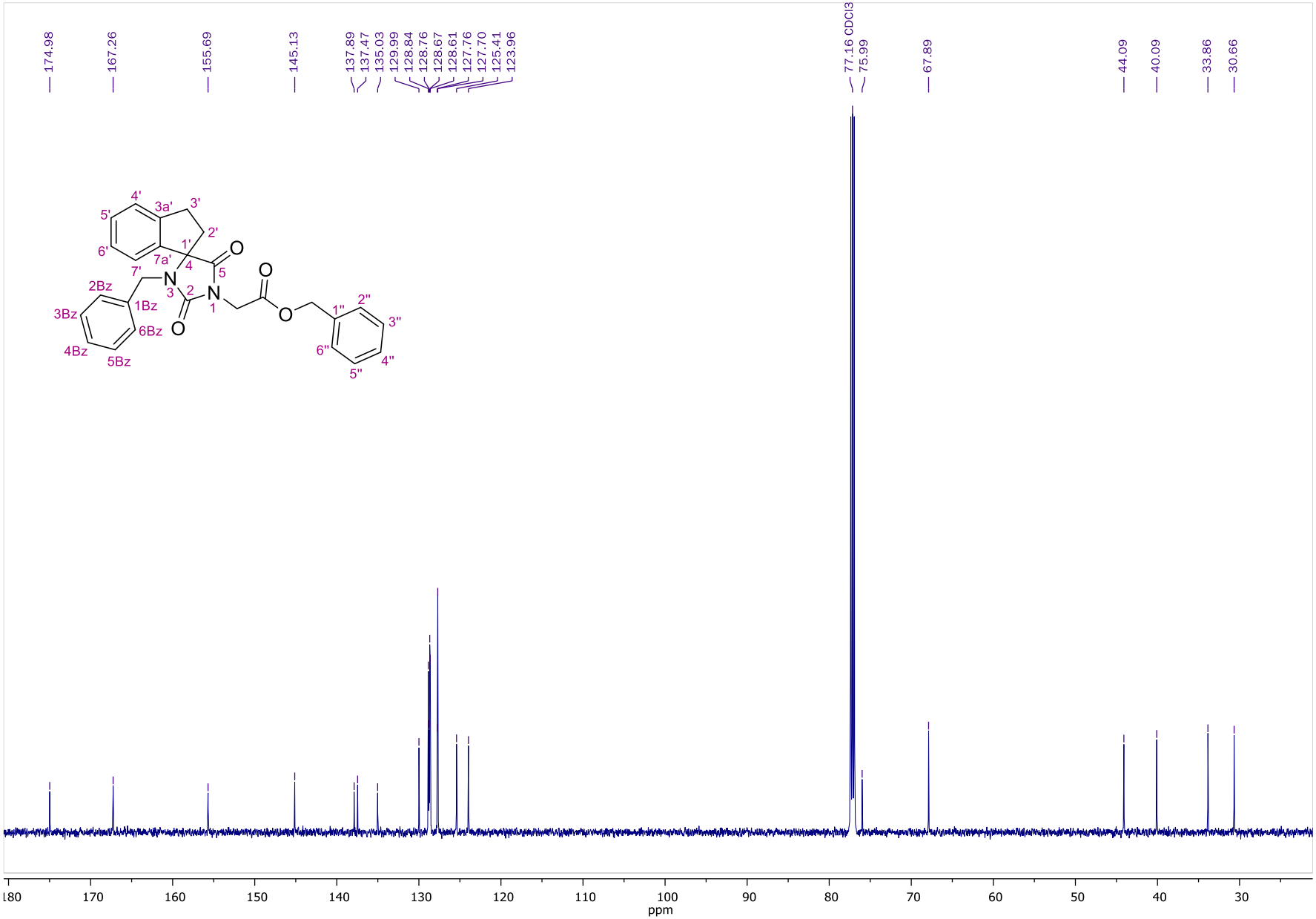
The *N*-benzyloxy precursor **15b** (145 mg, 0.3 mmol) was subjected to catalytic hydrogenolysis in a mixture of EtOH/AcOEt 3:1 (12 mL) according to the procedure described in the main manuscript for the synthesis of hydroxamate analogues. Concentration to dryness of the solvents under reduced pressure yielded the desired compound **18b** as a white foamy solid, which strongly binds the solvents. Removal of the entrapped solvents upon drying under high vacuum and treatment with *n*-pentane at 0 °C gave **18b** as a white crystalline solid (118 mg, almost quantitative yield); mp 167-169 °C (from AcOEt/*n*-pentane), R_f = 0.46 (AcOEt). In the ^1H and ^{13}C NMR spectra of this compound, double set of characteristic peaks are distinguished for each of the two (*E*/*Z*) conformers. ^1H NMR (600.11 MHz, DMSO-d_6) δ (ppm) 1.52-1.60 (m, 1H, H_7), 1.61-1.76 (complex m, 3H, H_7, H_8), 2.02 (ddd, 1H, J_1=14.9 Hz, J_2=7.7 Hz, J_3=1.8 Hz, H_6), 2.10 (ddd, 1H, J_1=14.8 Hz, J_2=9.9 Hz, J_3=2.3 Hz, H_6), 2.86-2.95 (m, 2H, H_9), 3.98 (d, 1H, *J*=16.4 Hz, NC*H*HPh), 4.01-4.09 (q, AB, 1.5H, J_{AB}=16.1 Hz, NCH_2CO, *E*-isomer), 4.29-4.38 (q, AB, 0.5H, J_{AB}=17.4 Hz, NCH_2CO, *Z*-isomer), 4.71 (dd, 1H, J_1=16.4 Hz, J_2=5.3 Hz, NCH*H*Ph), 7.14-728 (m, 9H, H_1, H_2, H_3, H_4, H_{2Bz}, H_{3Bz}, H_{4Bz}, H_{5Bz}, H_{6Bz}), 9.03 (s, 0.6H, CH_2CONHO*H*, *E*-isomer), 9.40 (s, 0.2H, NCH_2CONHO*H*, *Z*-isomer), 10.35 (s, 0.2H, NCH_2CON*H*OH, *Z*-isomer), 10.79 (s, 0.6H, NCH_2CON*H*OH, *E*-isomer); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ (ppm) 18.8 (C_7), 25.0 (C_8), 31.2 (C_6), 31.5 (C_9), 38.4 (N*C*H_2CO, *E*-isomer), 39.1 (N*C*H_2CO, *Z*-isomer), 43.6 (N*C*H_2Ph), 71.7 (C_5/$C_{4'}$), 126.9 (C_3), 127.0 (C_{4Bz}), 127.3 (C_{2Bz}, C_{6Bz}), 128.1 (C_{3Bz}, C_{5Bz}), 128.7 (C_4), 129.1 (C_2), 131.1 (C_1), 134.4 (C_{4a}), 137.7 (C_{1Bz}), 141.4 (C_{9a}), 155.2 ($C_{2'}$=O, *E*-isomer), 155.4 ($C_{2'}$=O, *Z*-isomer), 163.3 (NCH_2*C*ONHOH, *E*-isomer), 168.7 (NCH_2*C*ONHOH, *Z*-isomer), 175.2 ($C_{5'}$=O, *E*-isomer), 175.5 ($C_{5'}$=O, *Z*-isomer). Found: C, 67.10; H, 5.95; N, 10.69. Calc. for $C_{22}H_{23}N_3O_4$: C, 67.16; H, 5.89; N, 10.68%

II Copies of NMR spectra

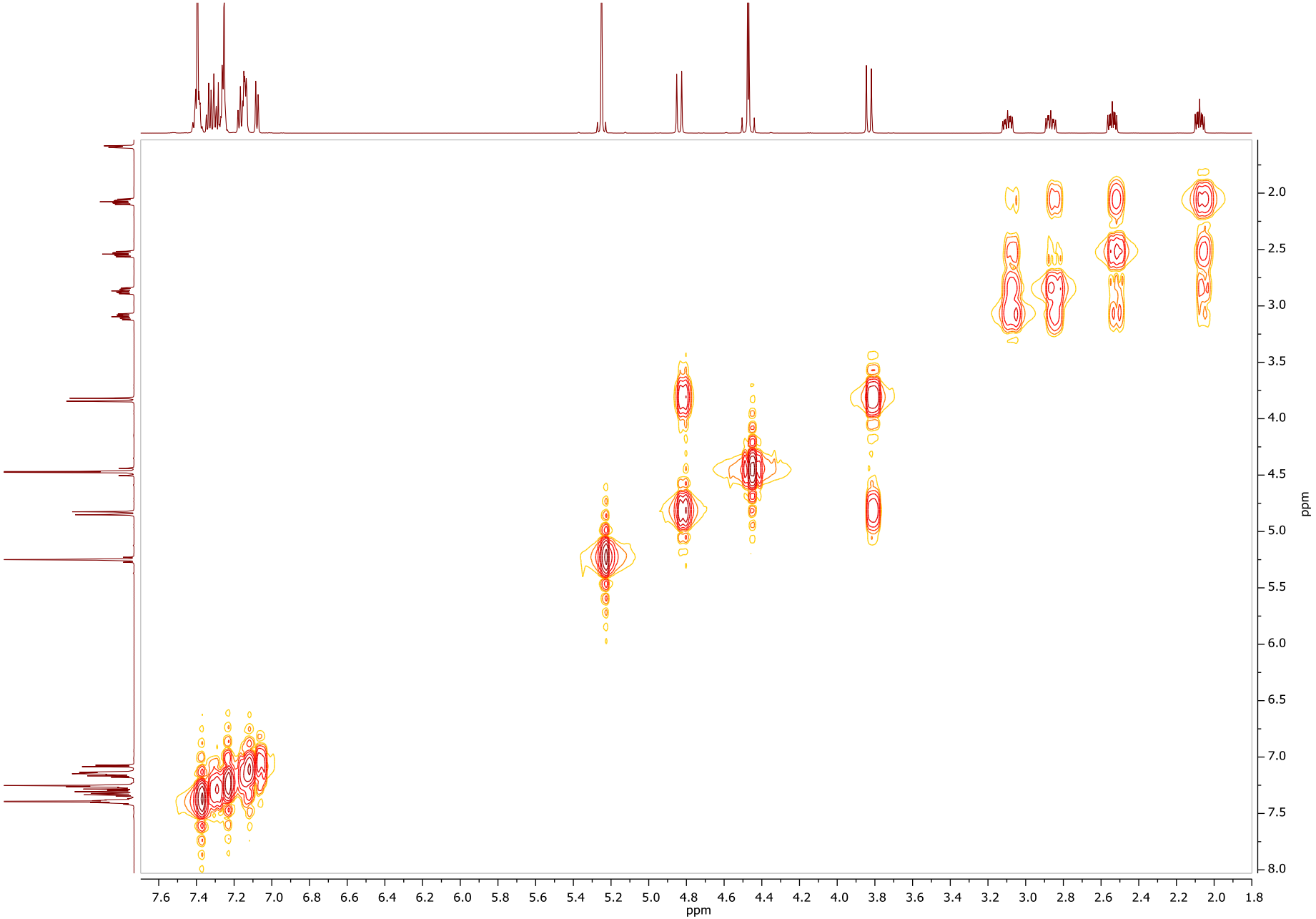
^{1}H NMR of **7b** (600.11 MHz, $CDCl_3$)



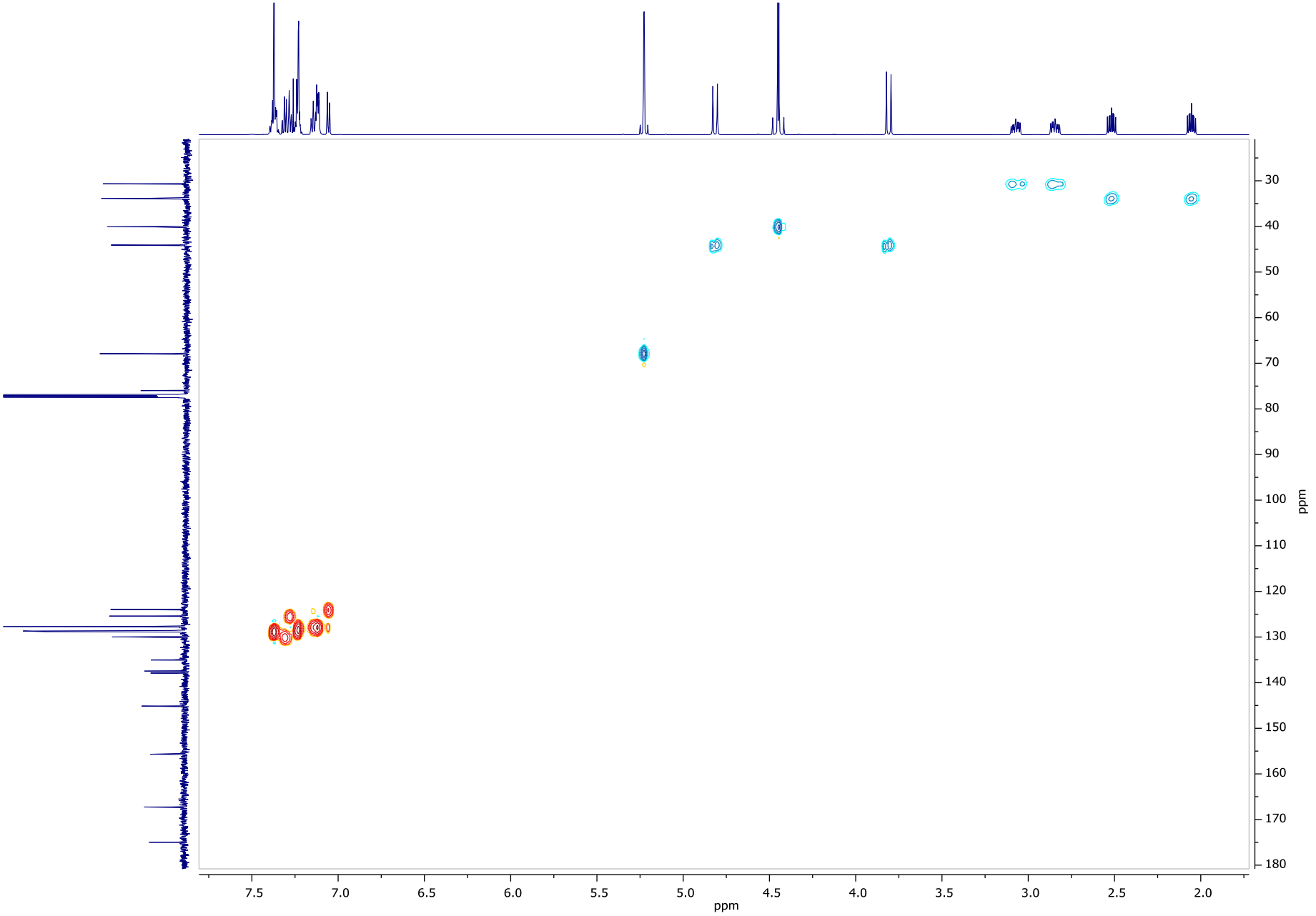
^{13}C NMR of **7b** (150.9 MHz, $CDCl_3$)



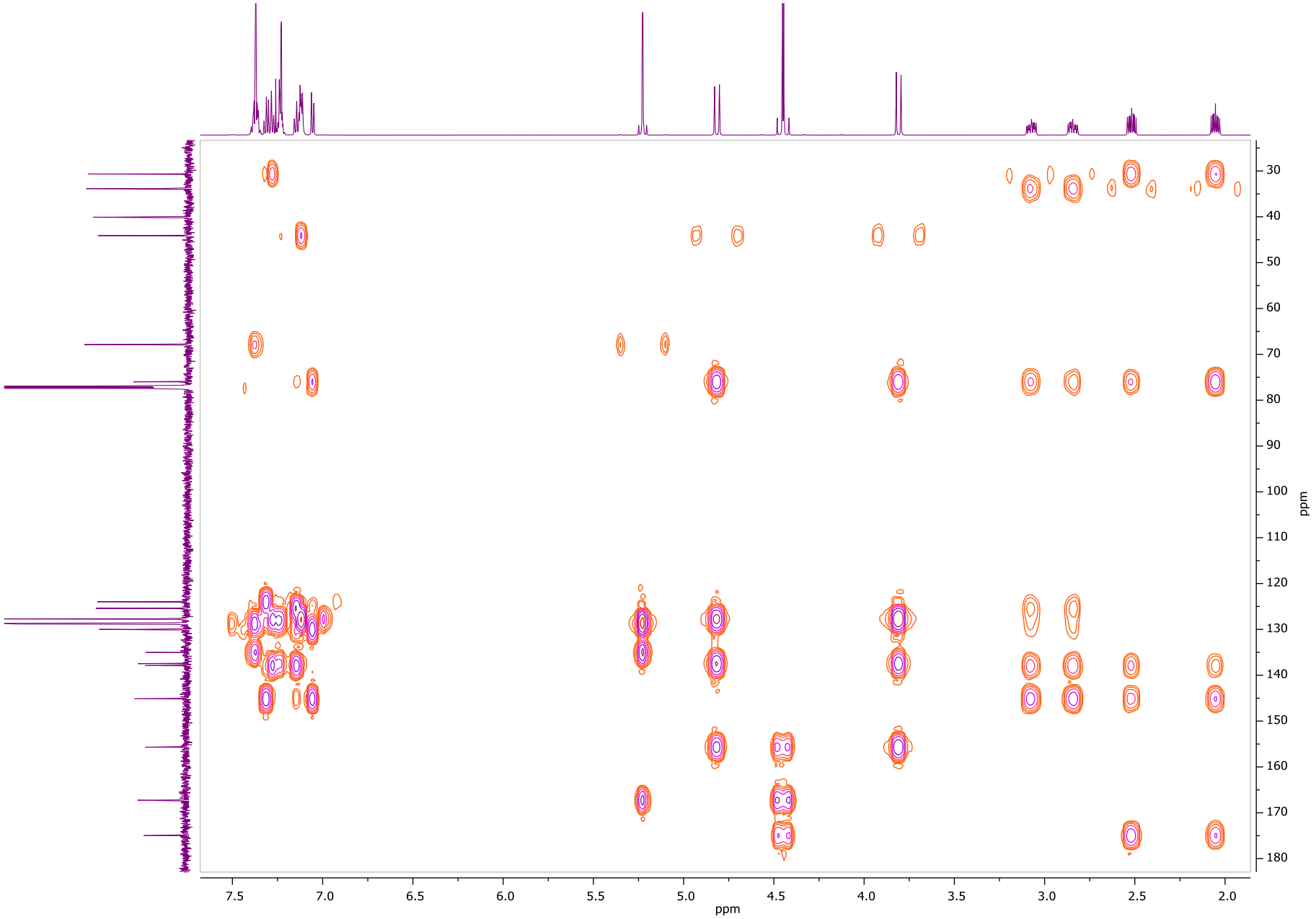
COSY NMR of **7b** (600.11 MHz, $CDCl_3$)



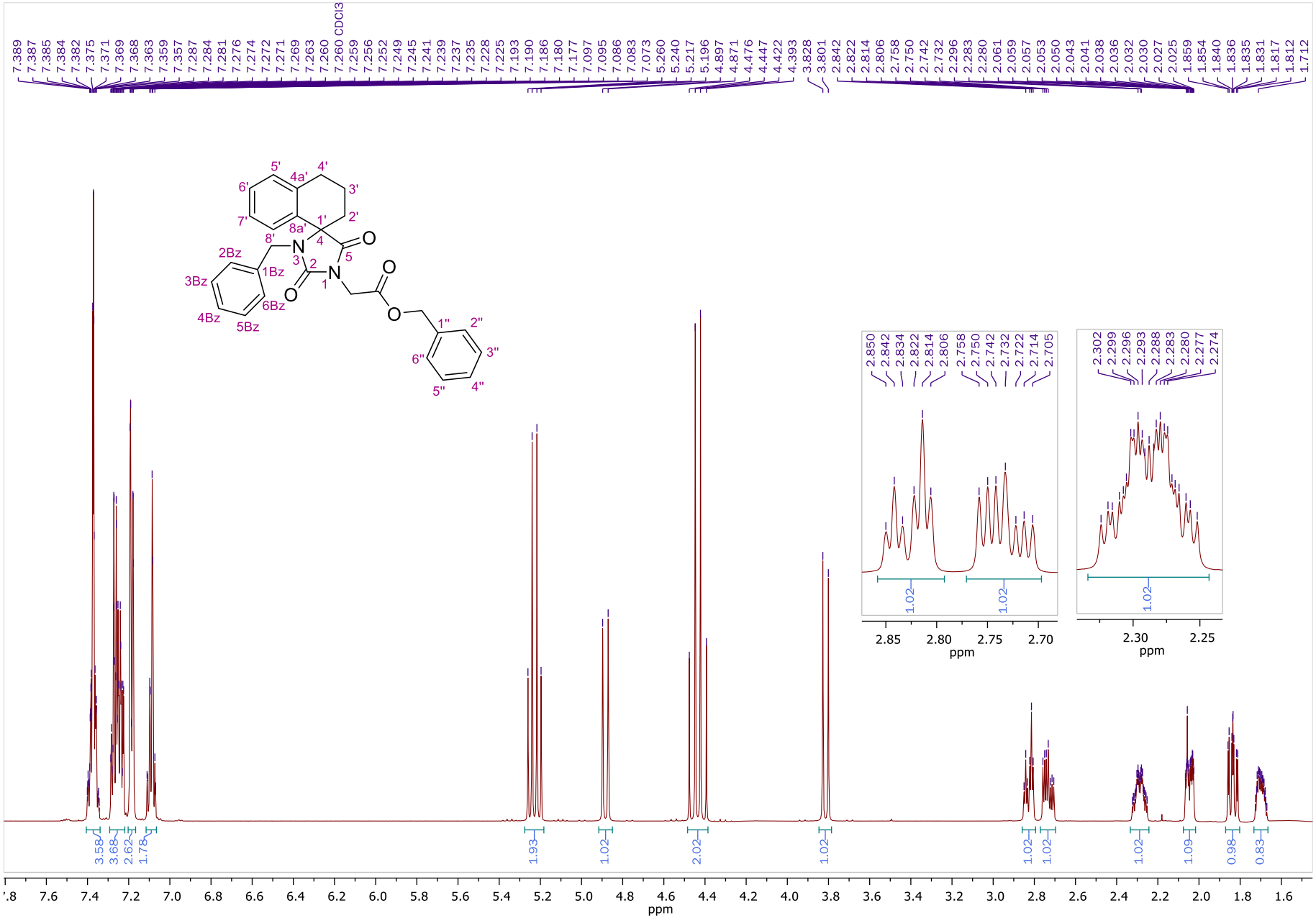
HSQC-DEPT NMR of **7b** (600.11 MHz, $CDCl_3$)



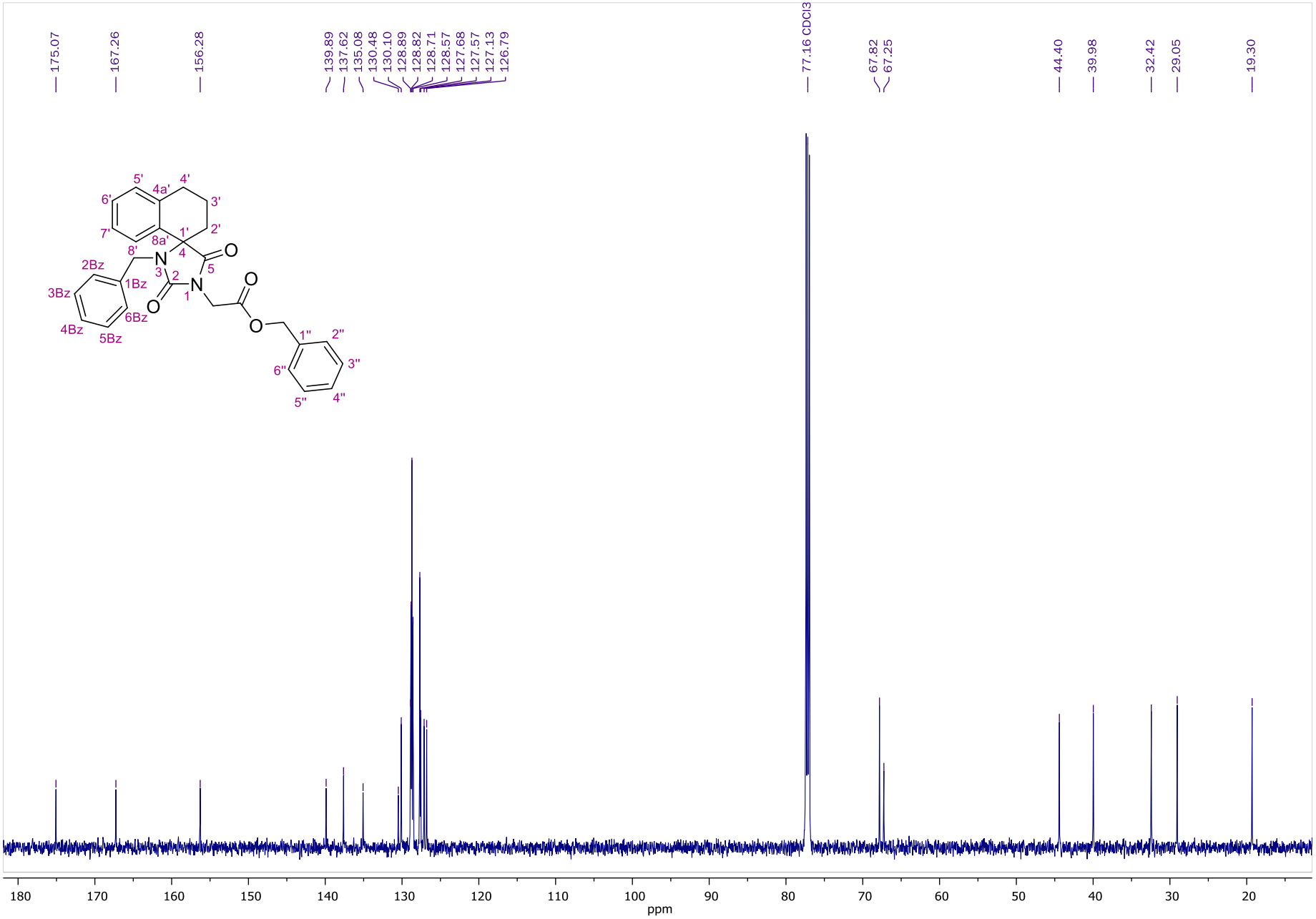
HMBC NMR of **7b** (600.11 MHz, $CDCl_3$)



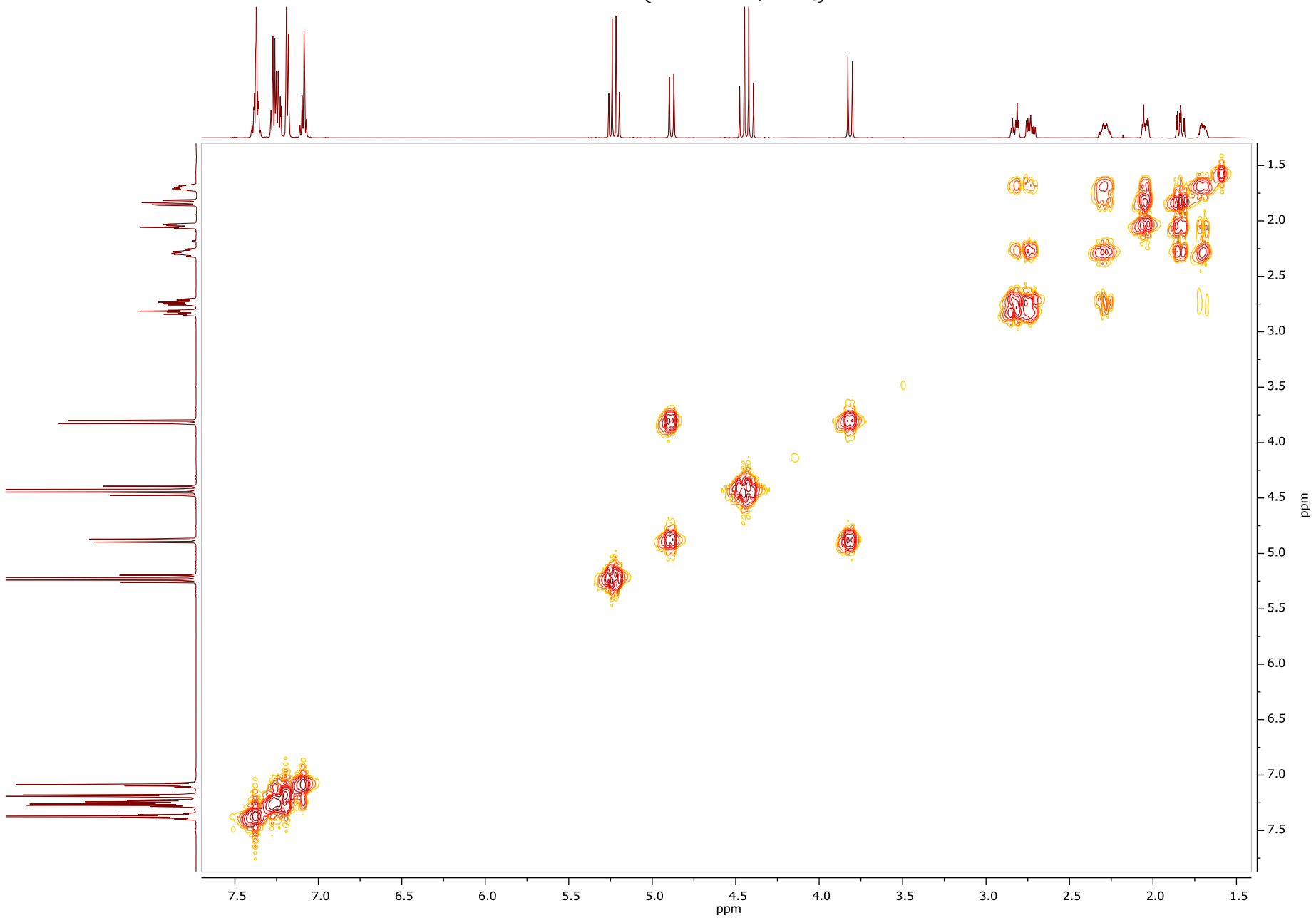
^{1}H NMR of **8b** (600.11 MHz, $CDCl_3$)



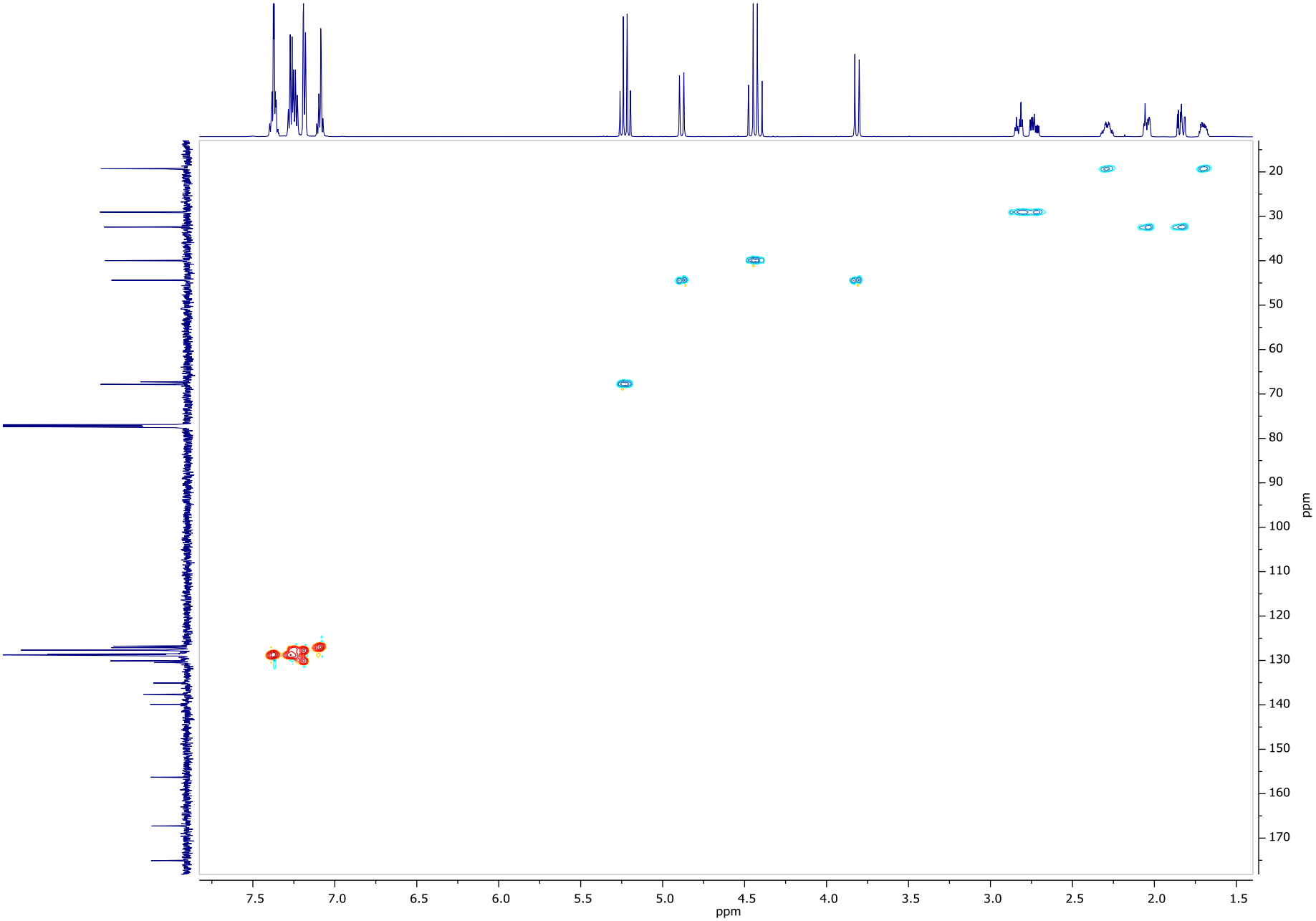
^{13}C NMR of **8b** (150.9 MHz, $CDCl_3$)



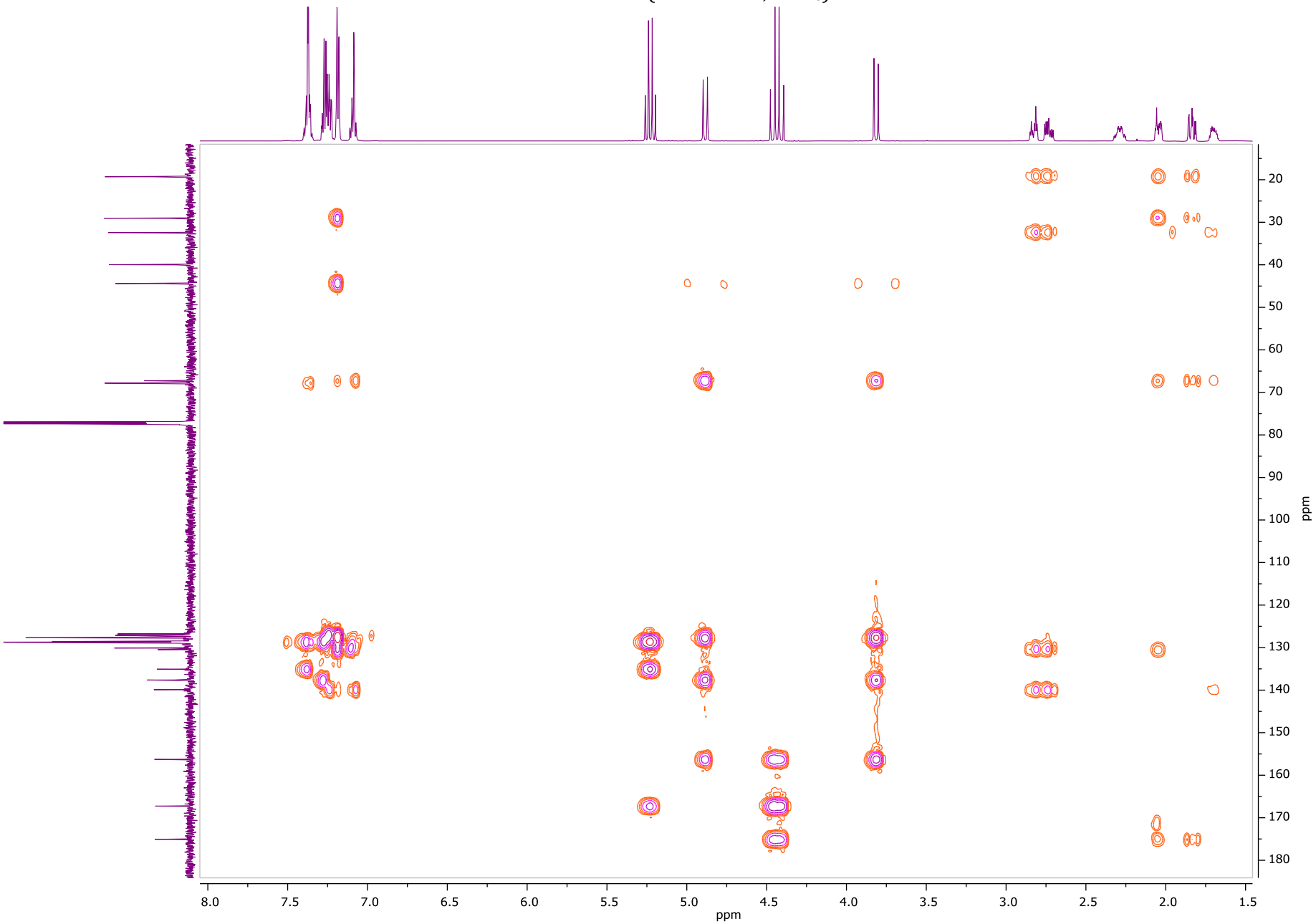
COSY NMR of **8b** (600.11 MHz, $CDCl_3$)



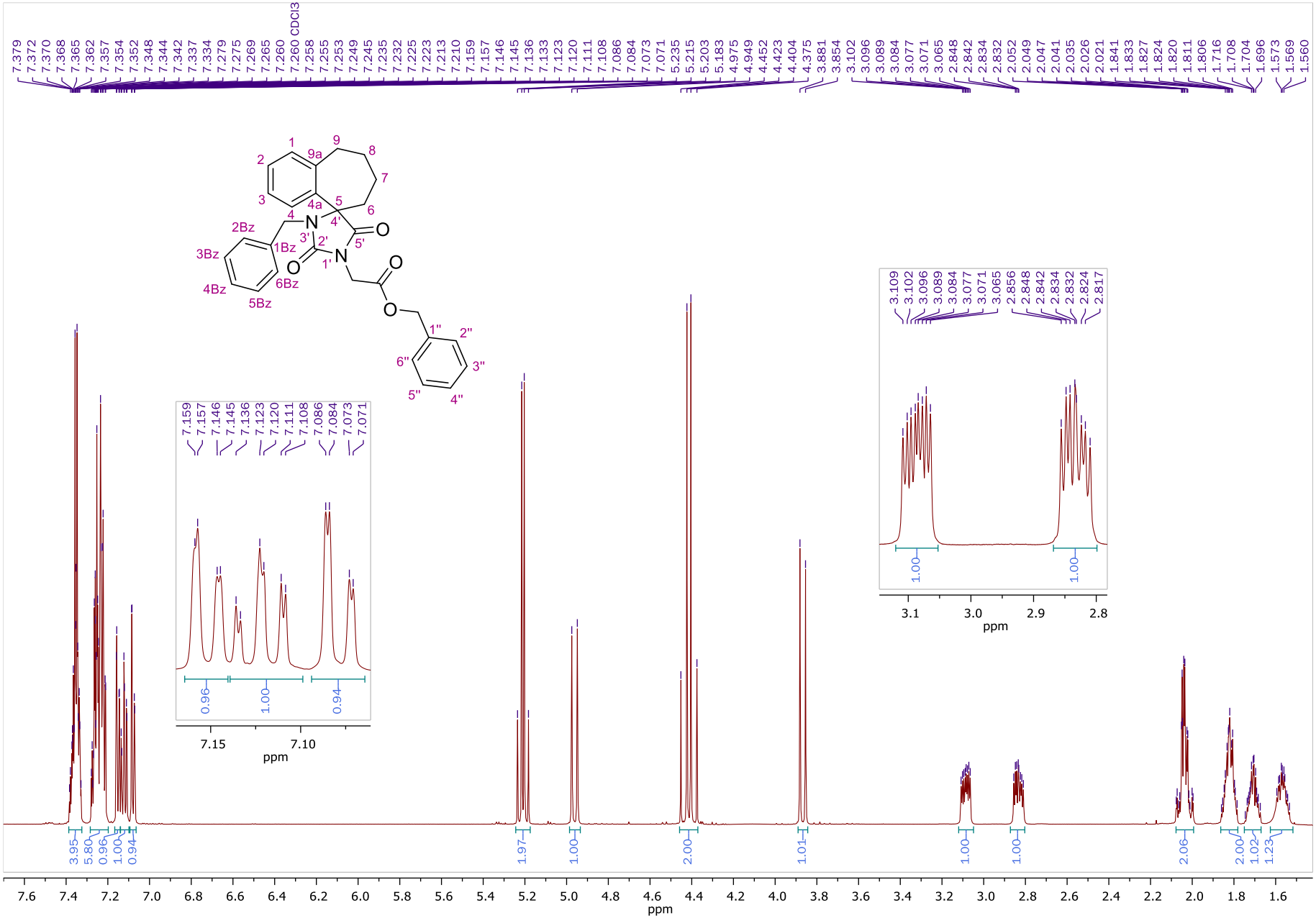
HSQC-DEPT NMR of **8b** (600.11 MHz, $CDCl_3$)



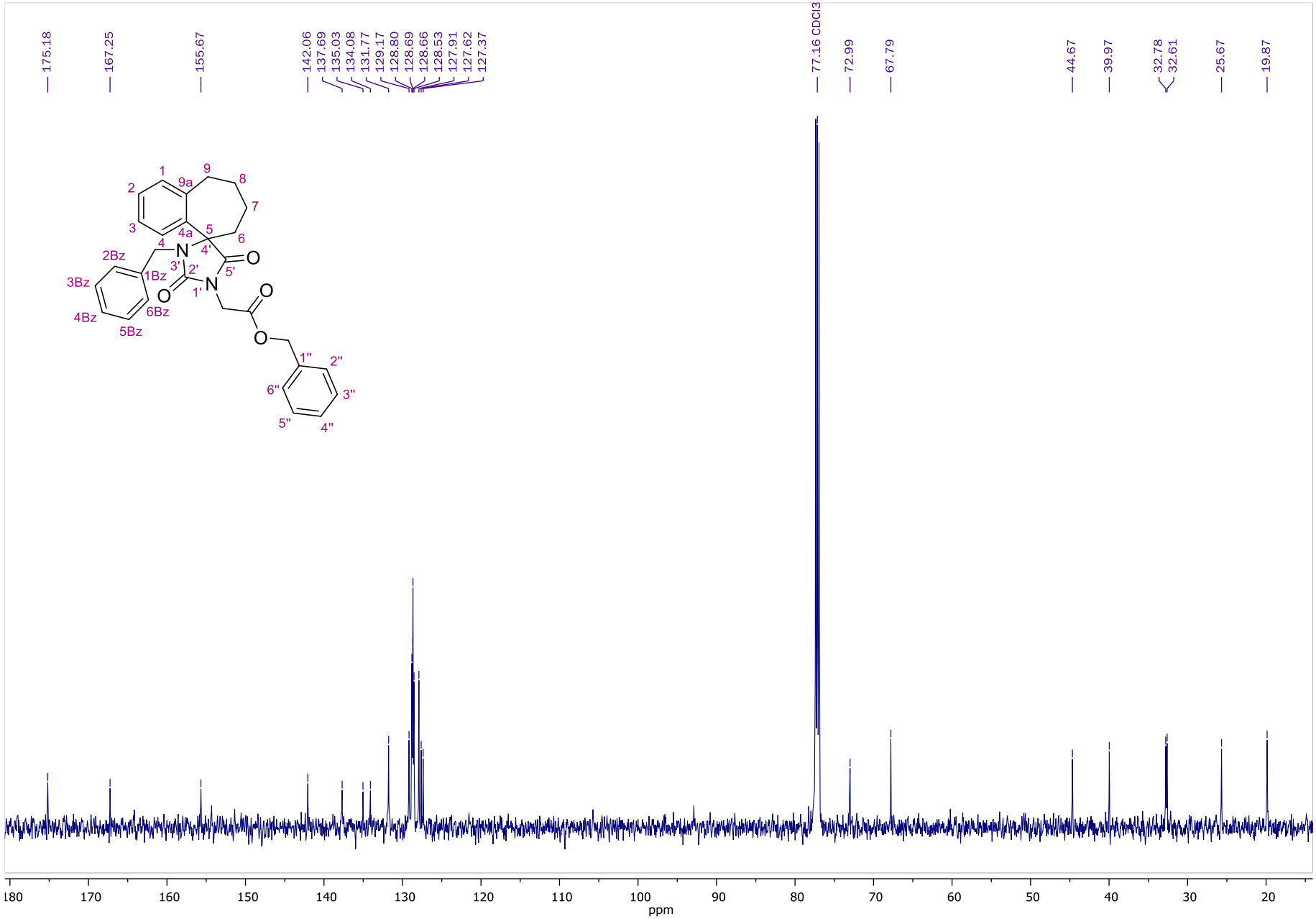
HMBC NMR of **8b** (600.11 MHz, $CDCl_3$)



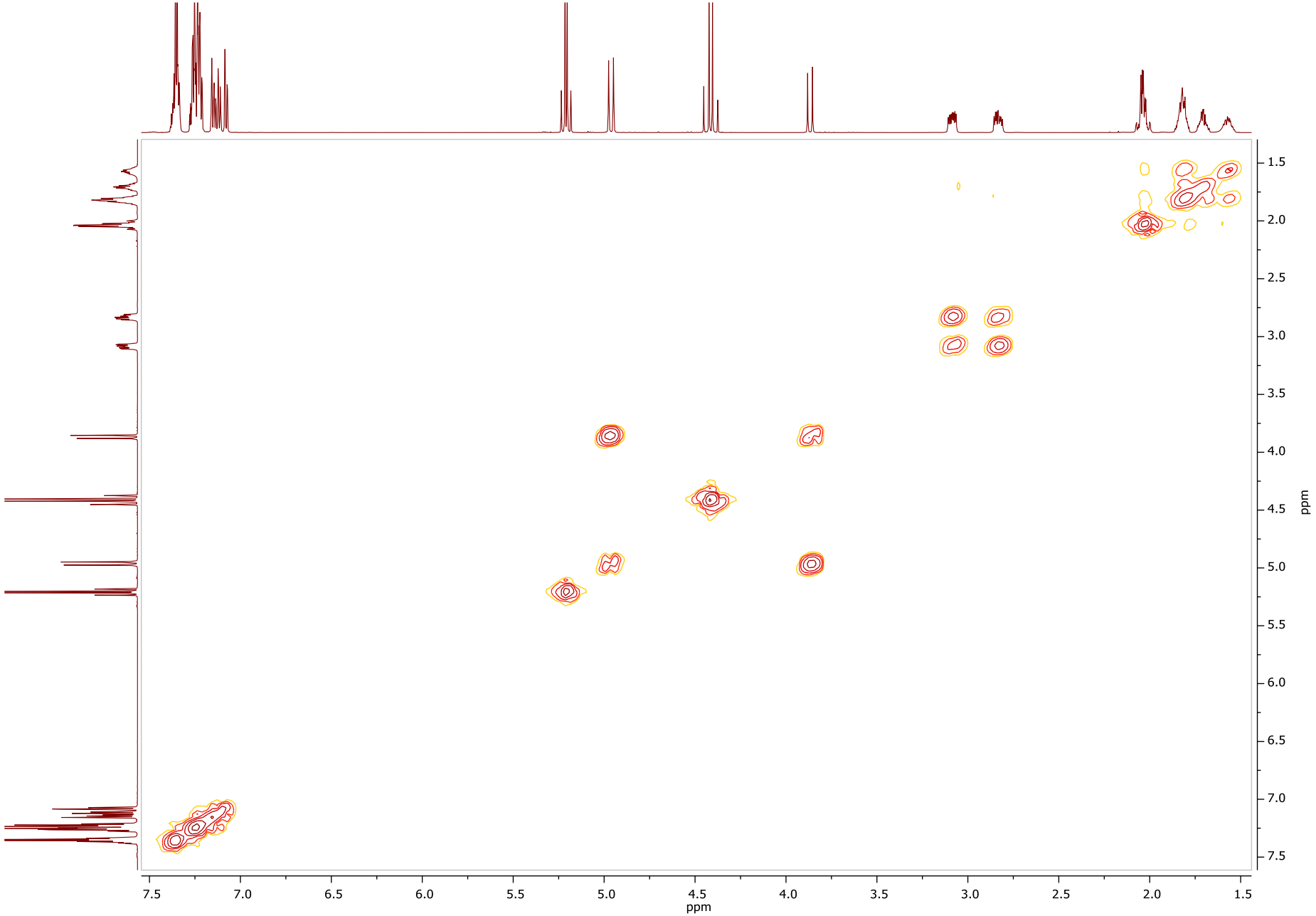
^{1}H NMR of **9b** (600.11 MHz, $CDCl_3$)



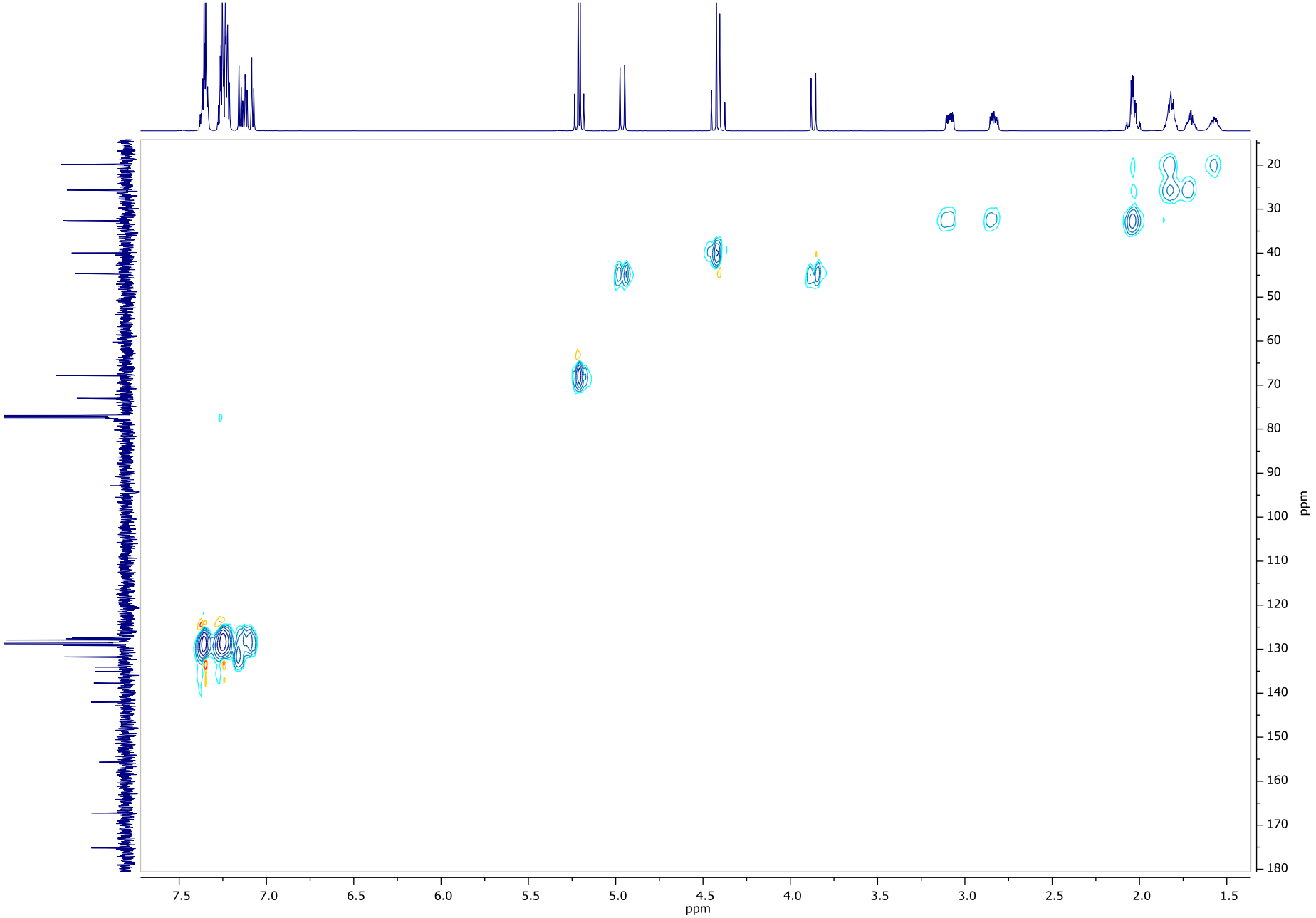
^{13}C NMR of **9b** (150.9 MHz, $CDCl_3$)



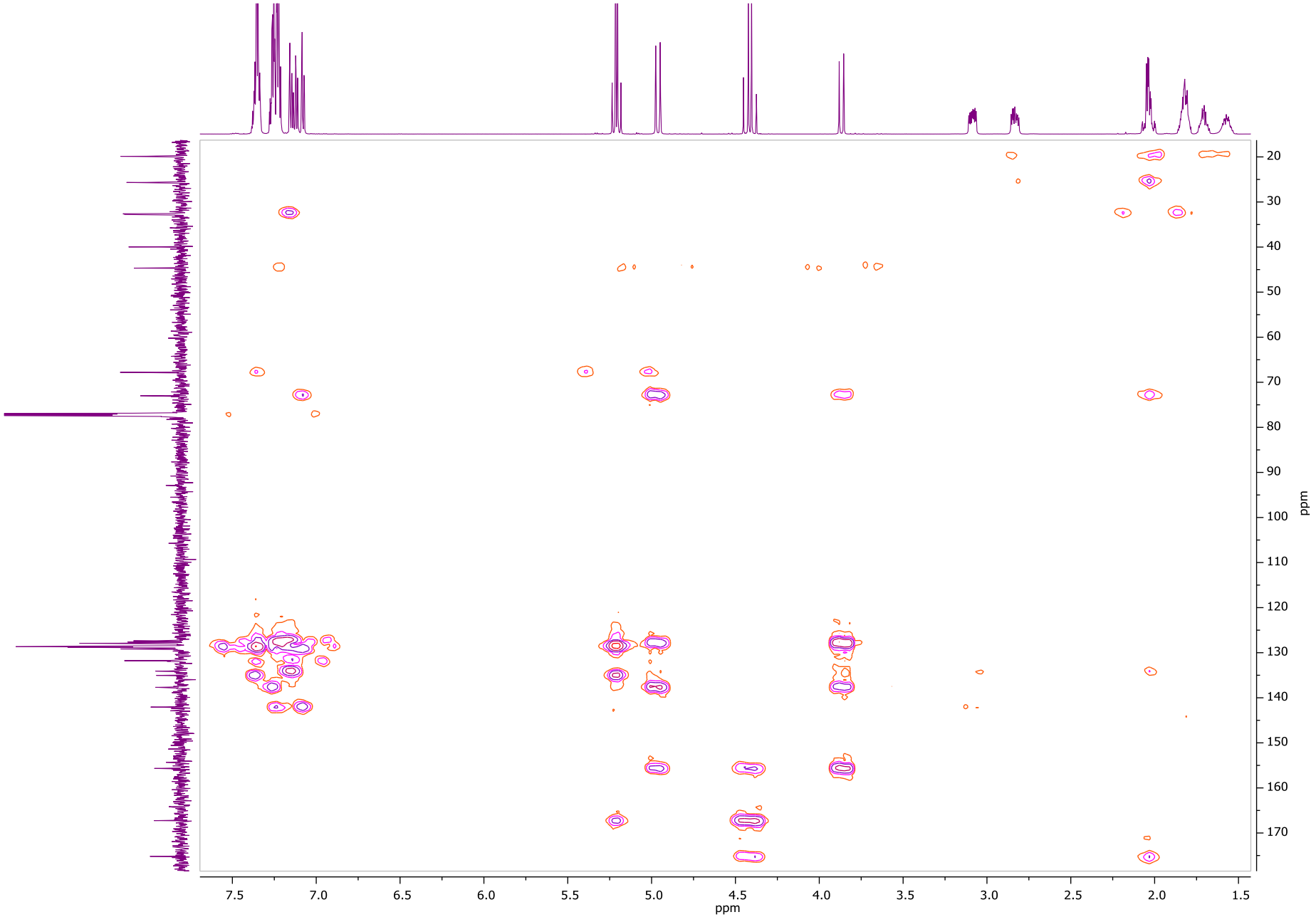
COSY NMR of **9b** (400.13 MHz, $CDCl_3$)



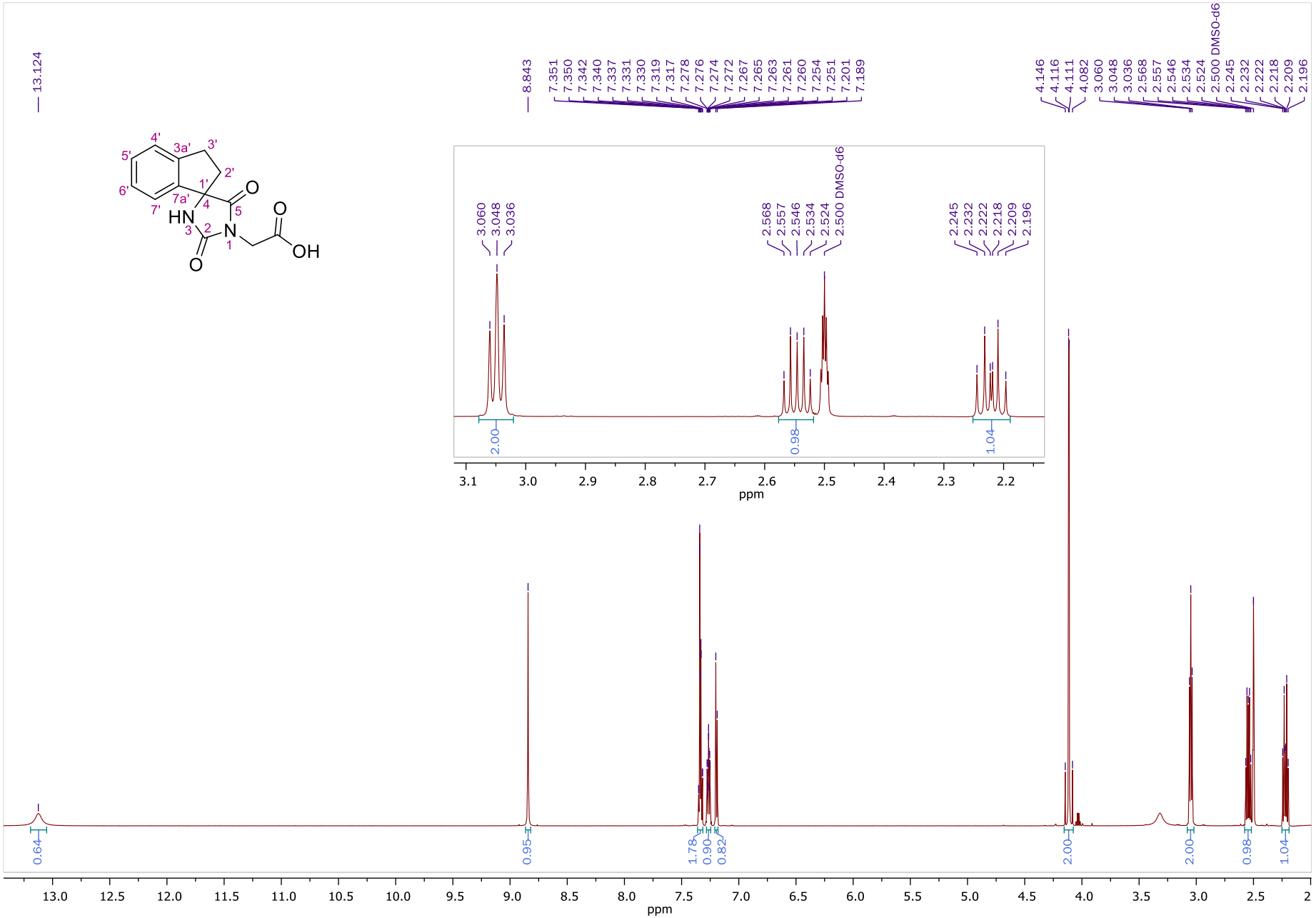
HSQC NMR of **9b** (400.13 MHz, $CDCl_3$)



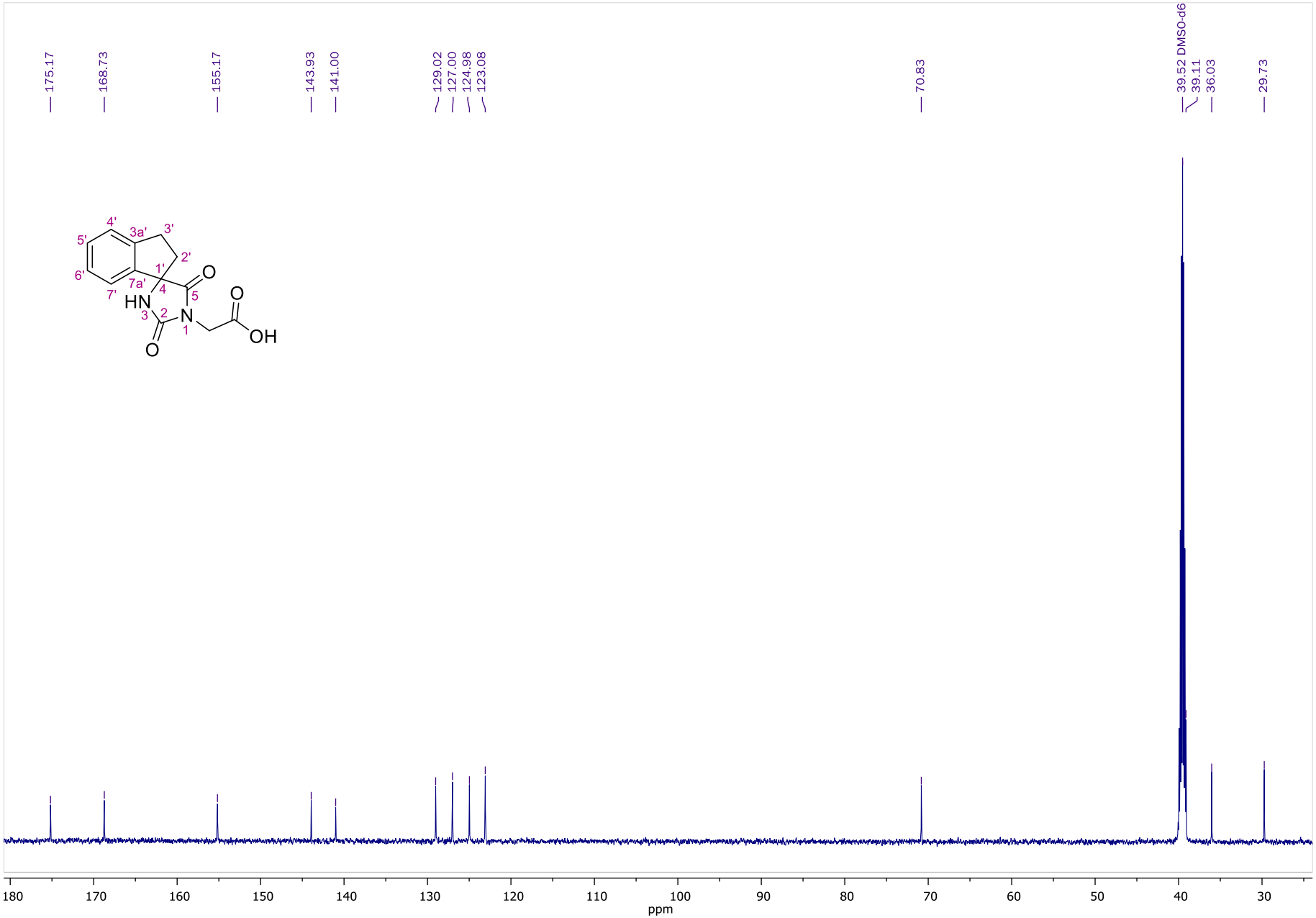
HMBC NMR of **9b** (400.13 MHz, $CDCl_3$)



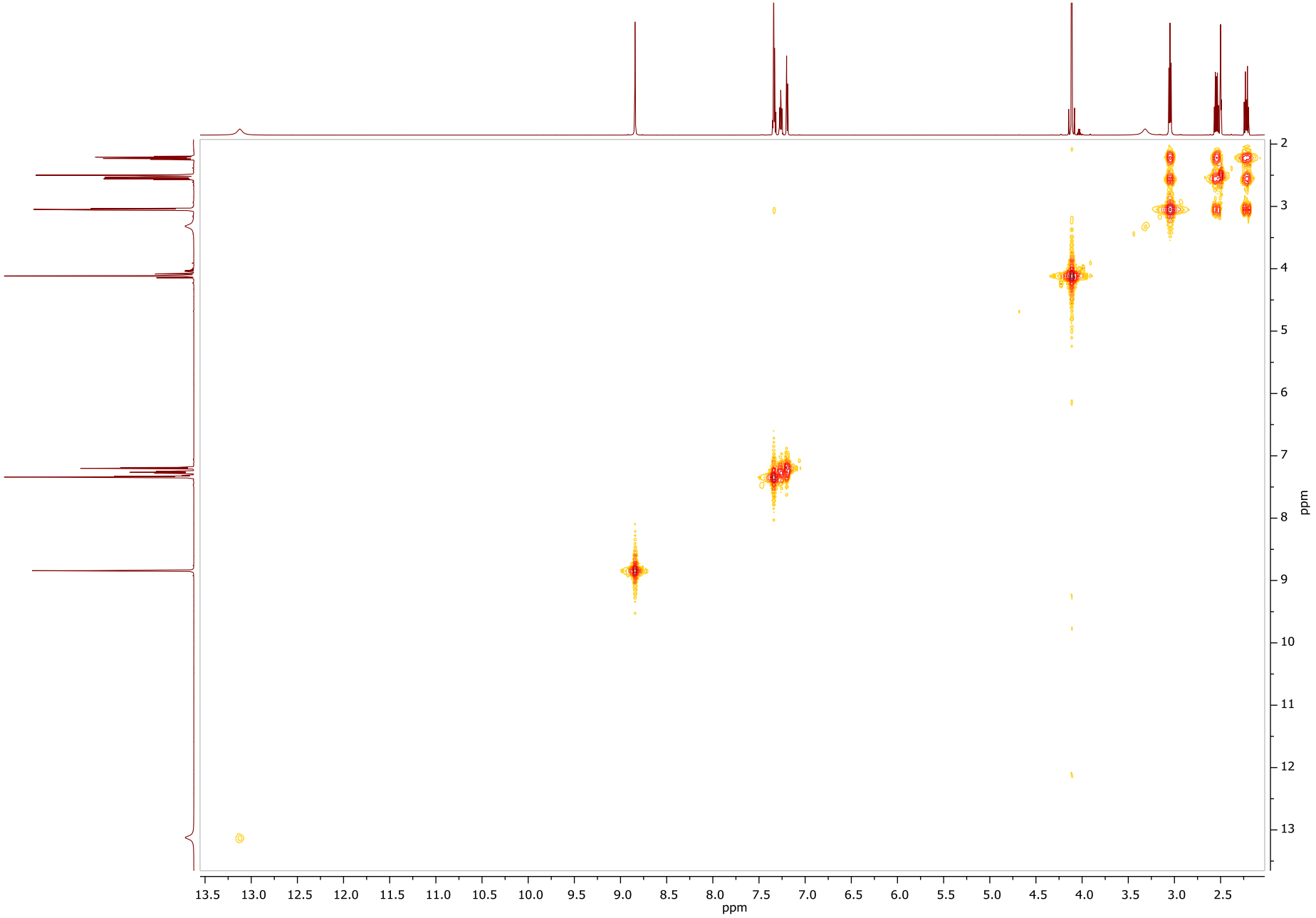
^{1}H NMR of **10** (600.11 MHz, DMSO-d_6)



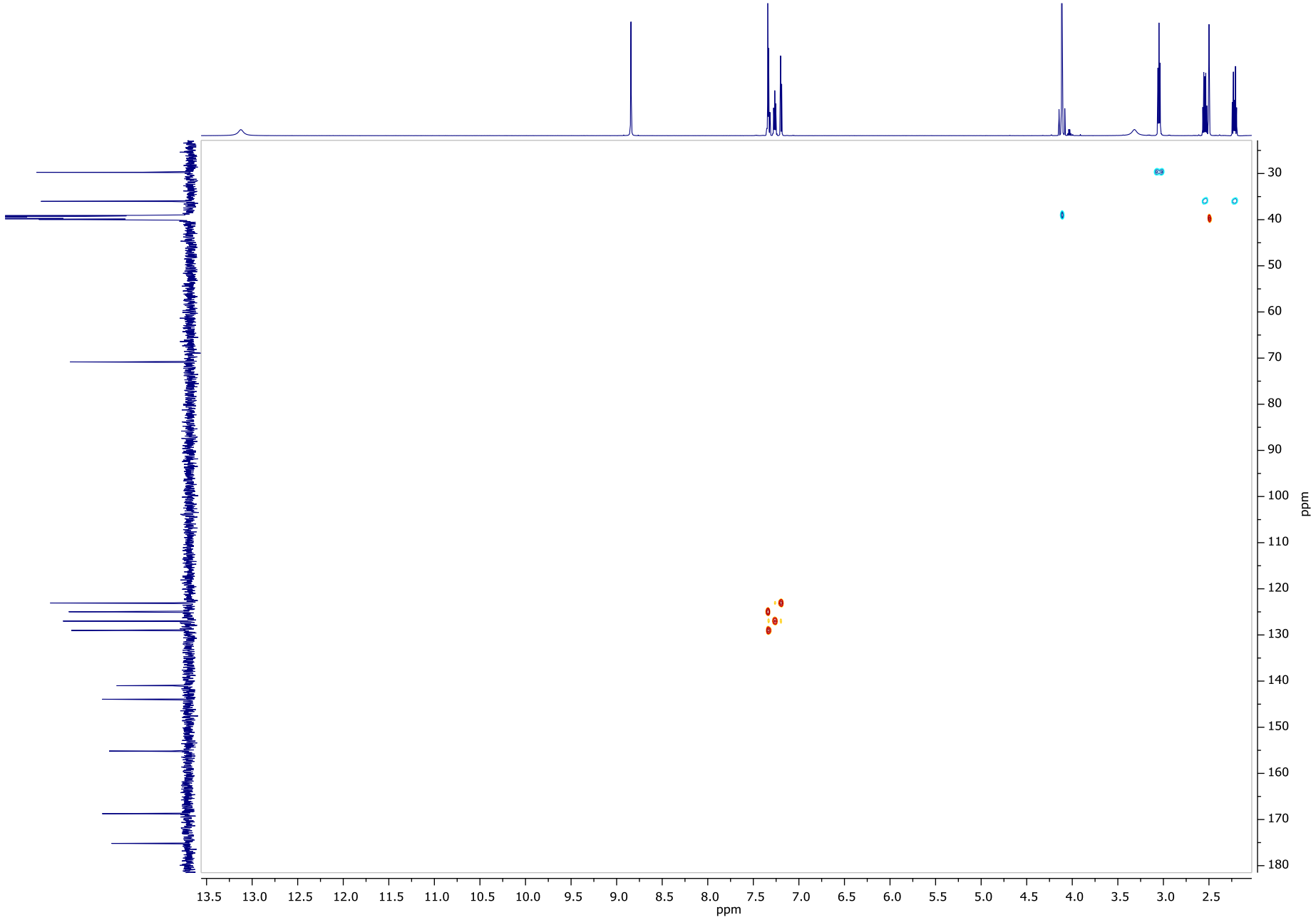
^{13}C NMR of **10** (150.9 MHz, DMSO-d_6)



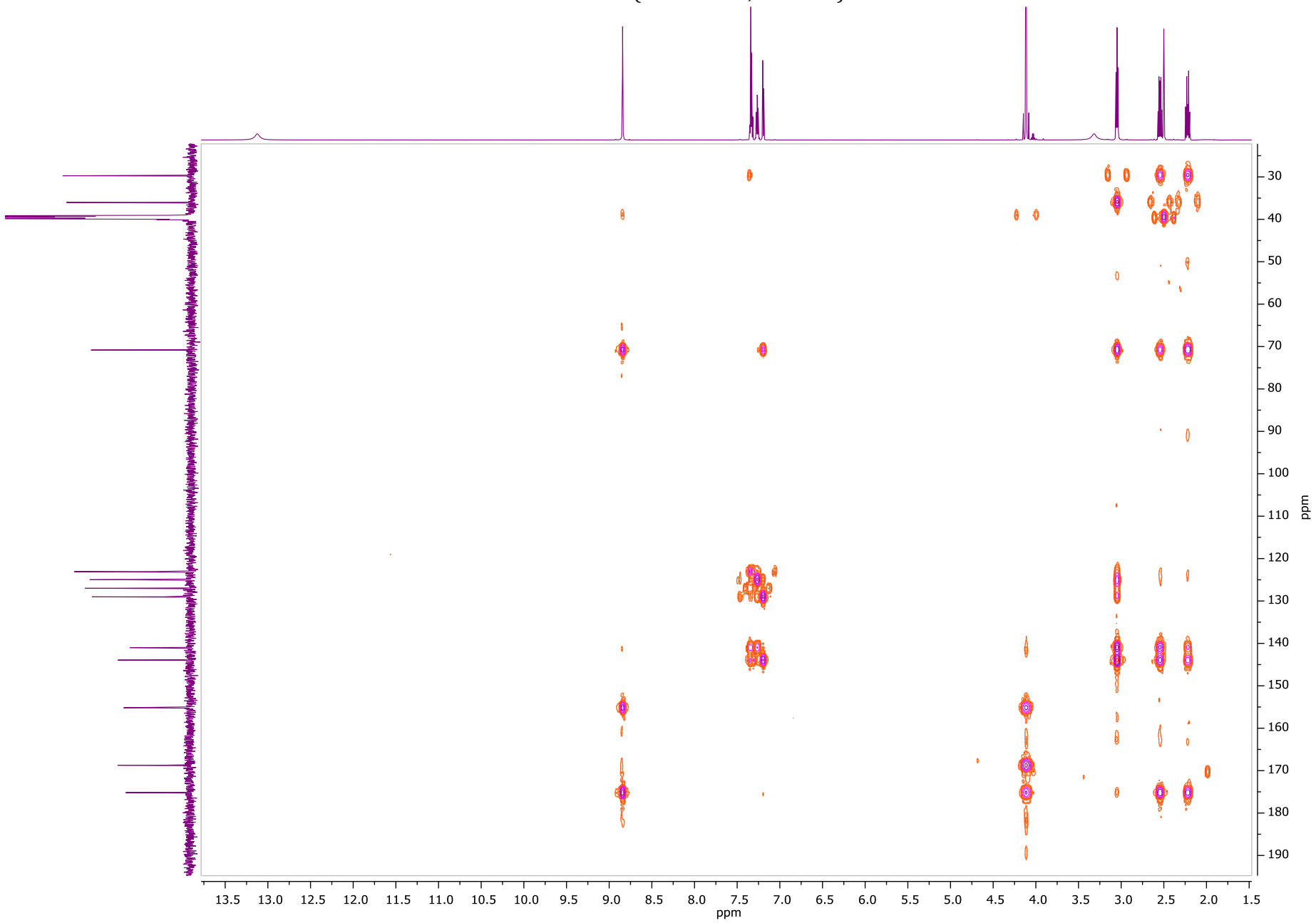
COSY NMR of **10** (600.11 MHz, DMSO-d_6)



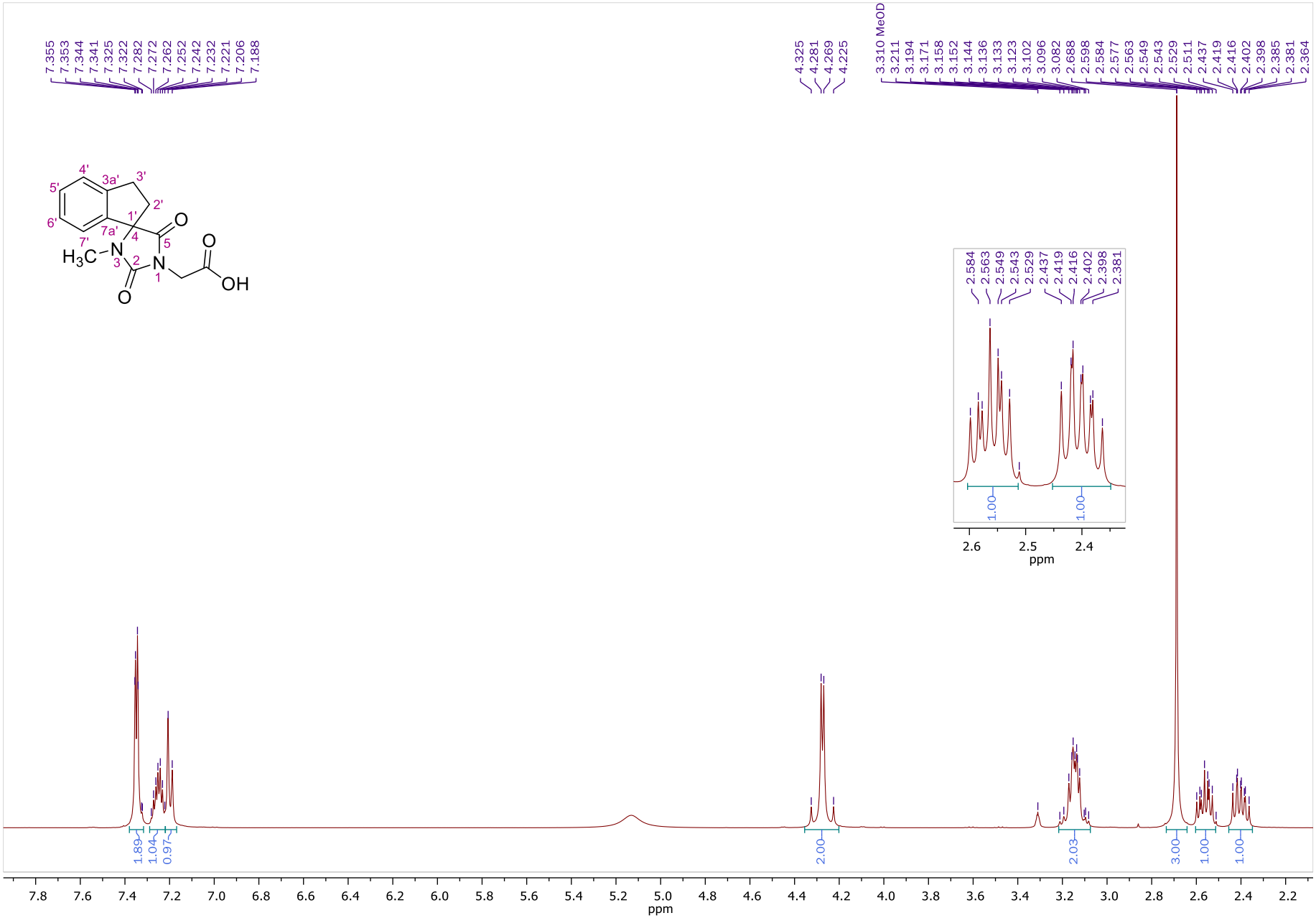
HSQC-DEPT NMR of **10** (600.11 MHz, DMSO-d_6)



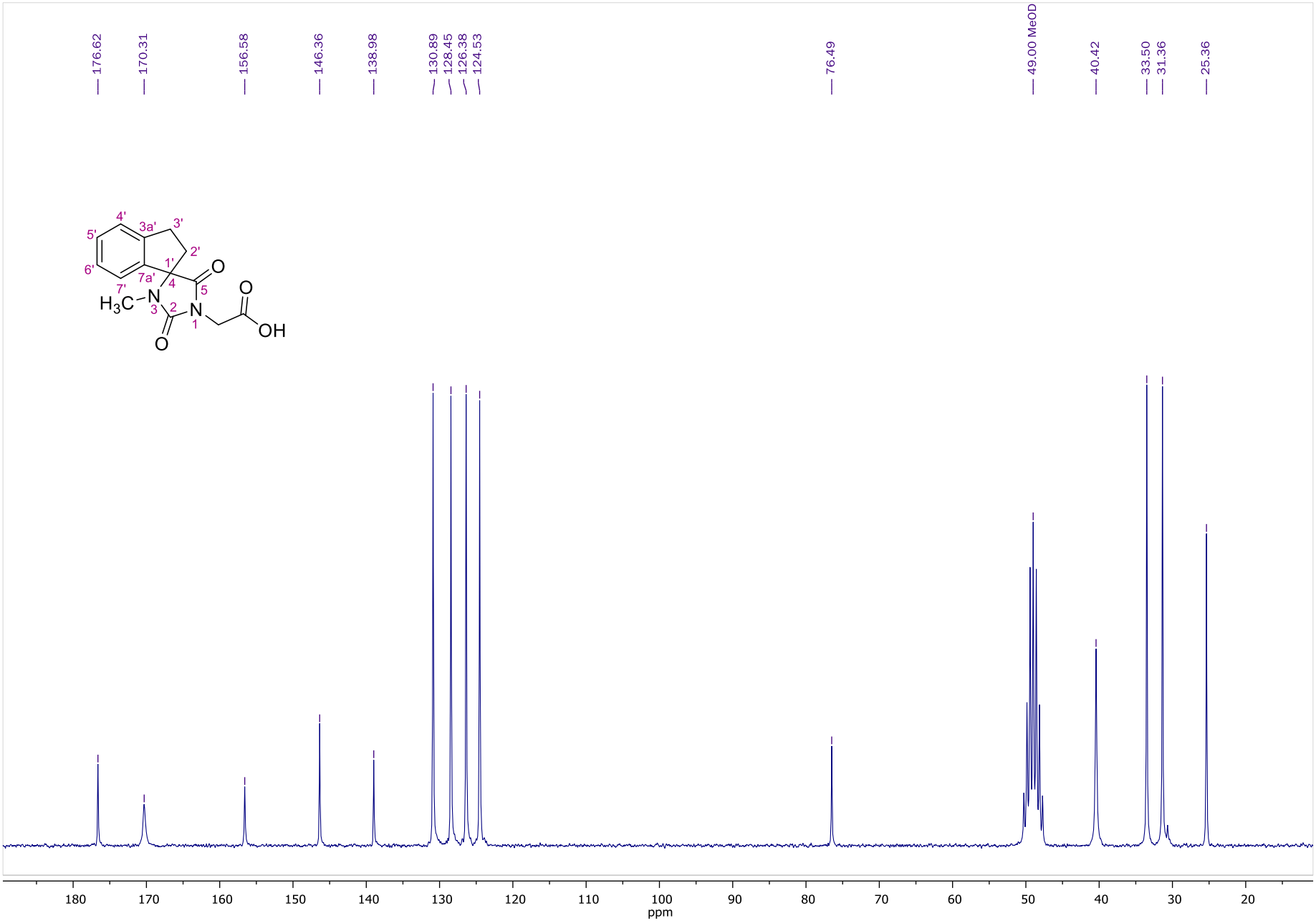
HMBC NMR of **10** (600.11 MHz, DMSO-d_6)



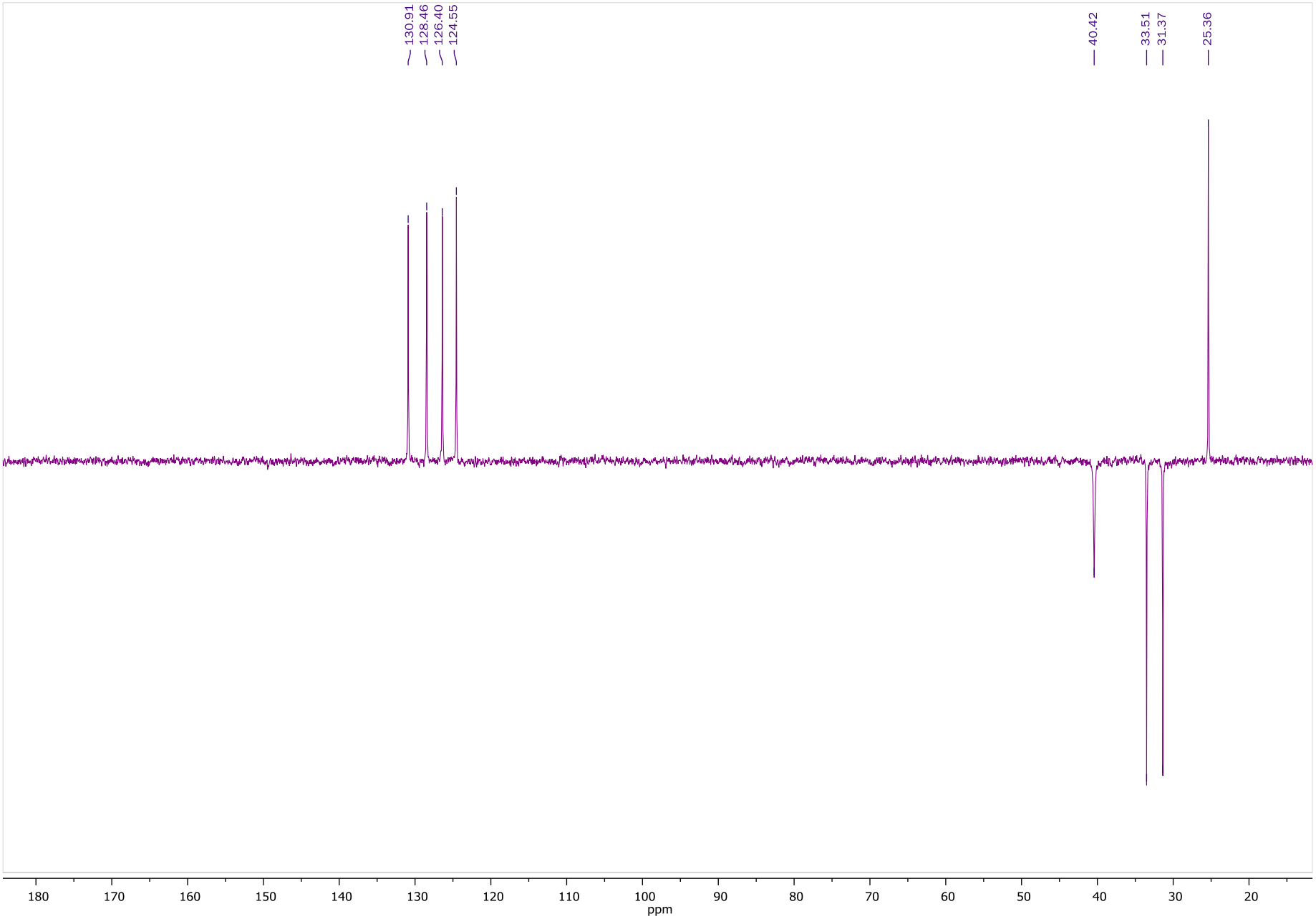
^{1}H NMR of **10a** (400.13 MHz, MeOD-d_4)



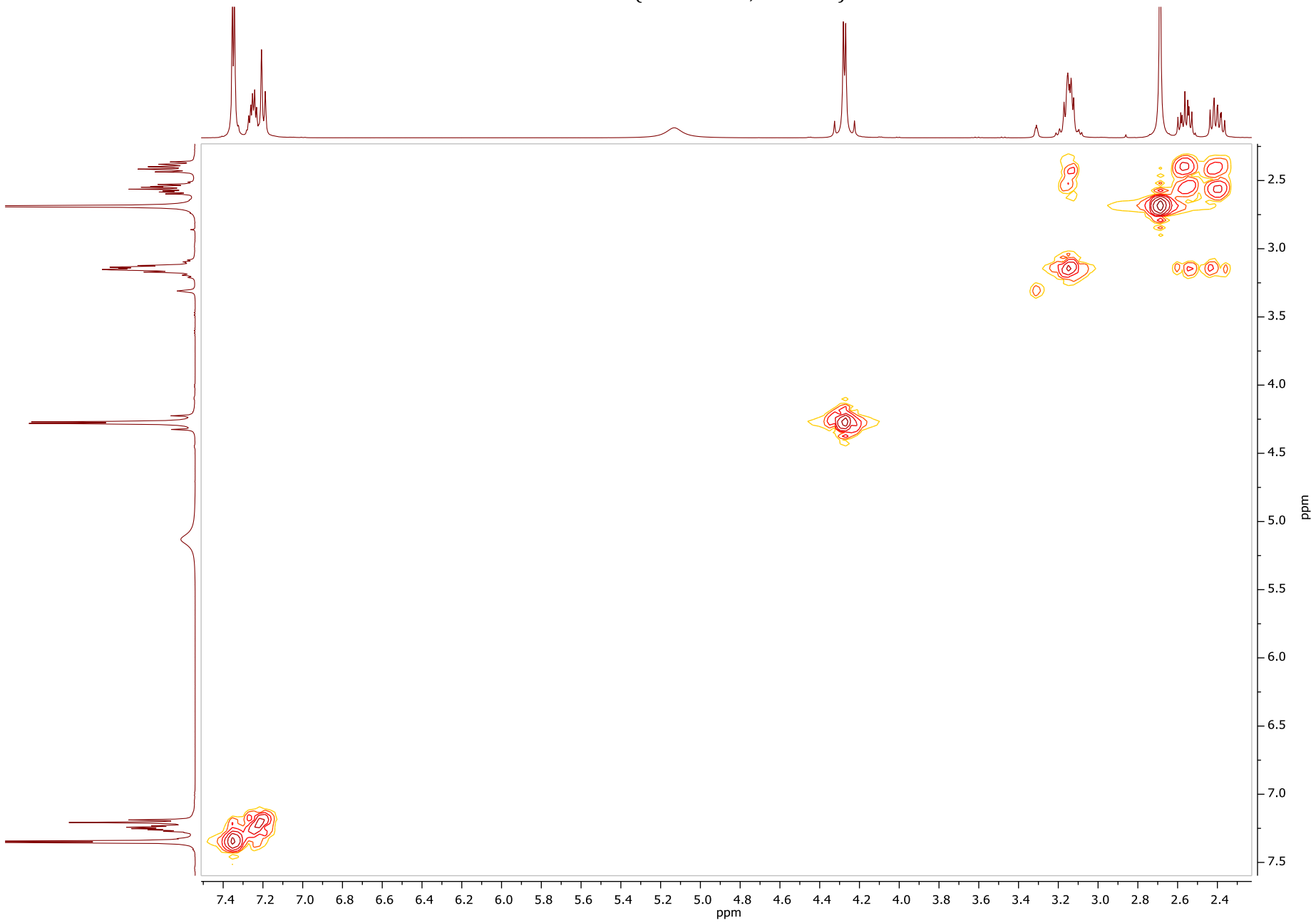
^{13}C NMR of **10a** (50.32 MHz, MeOD-d_4)



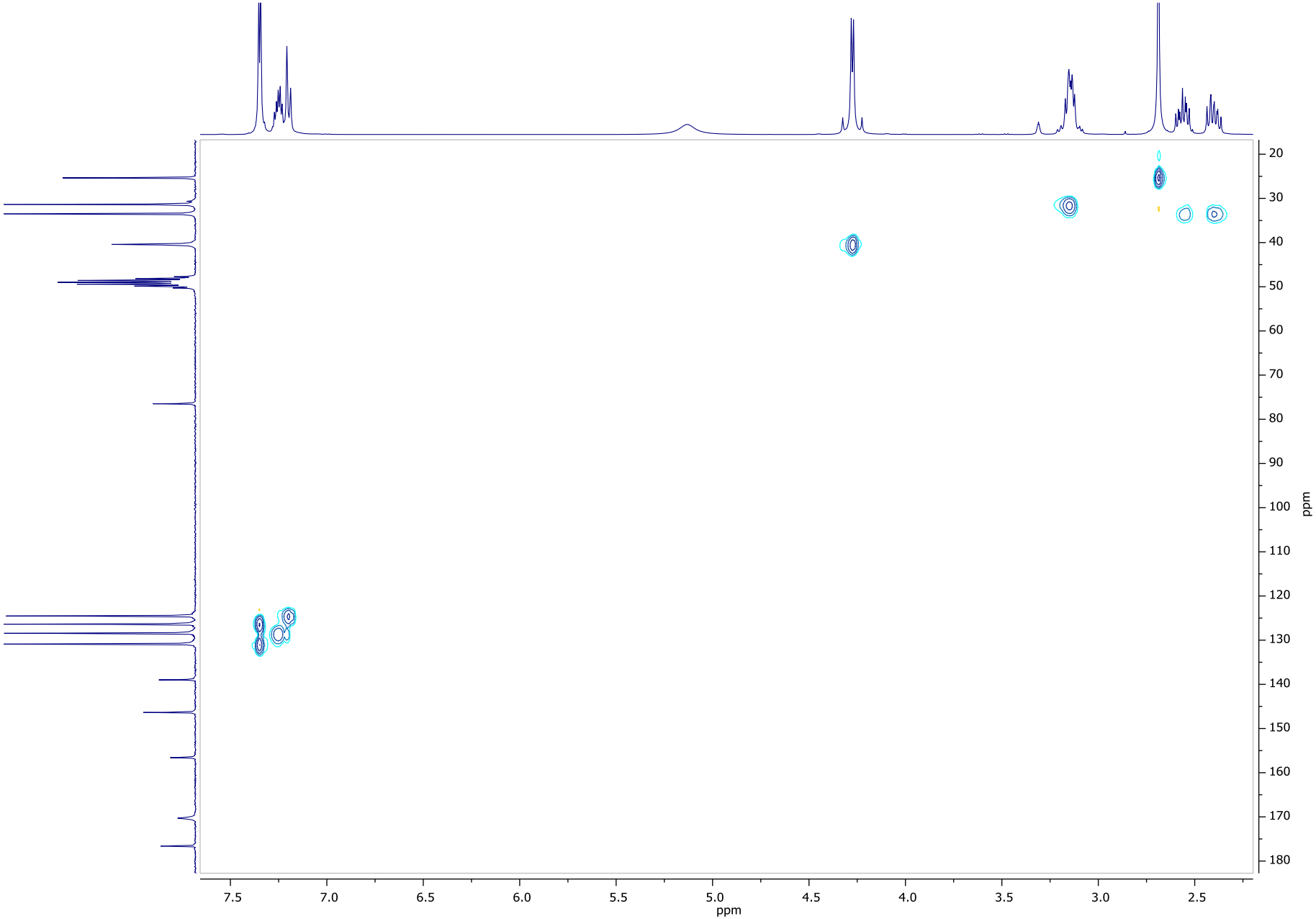
DEPT NMR of **10a** (50.32 MHz, MeOD-d_4)



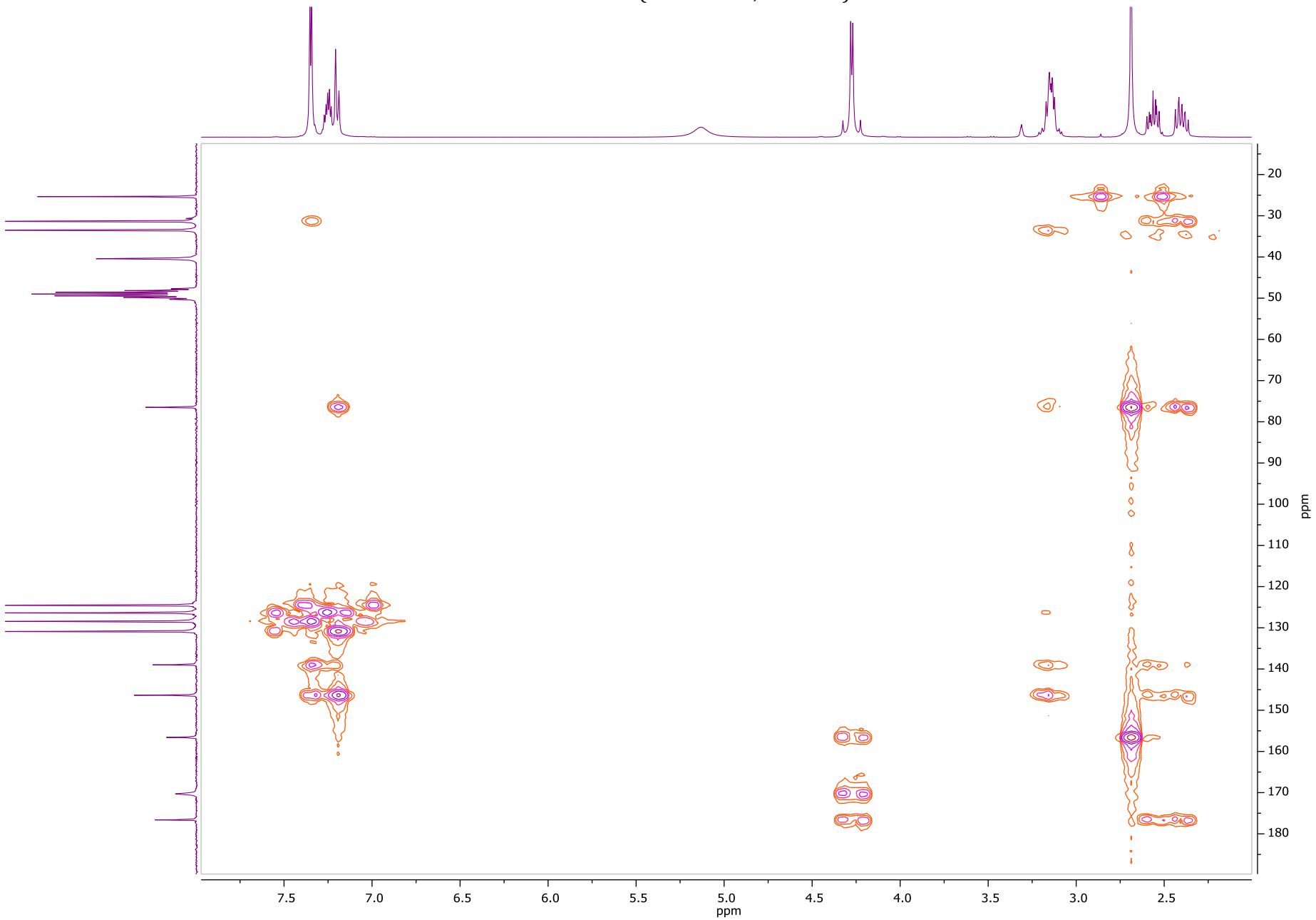
COSY NMR of **10a** (400.13 MHz, MeOD-d_4)



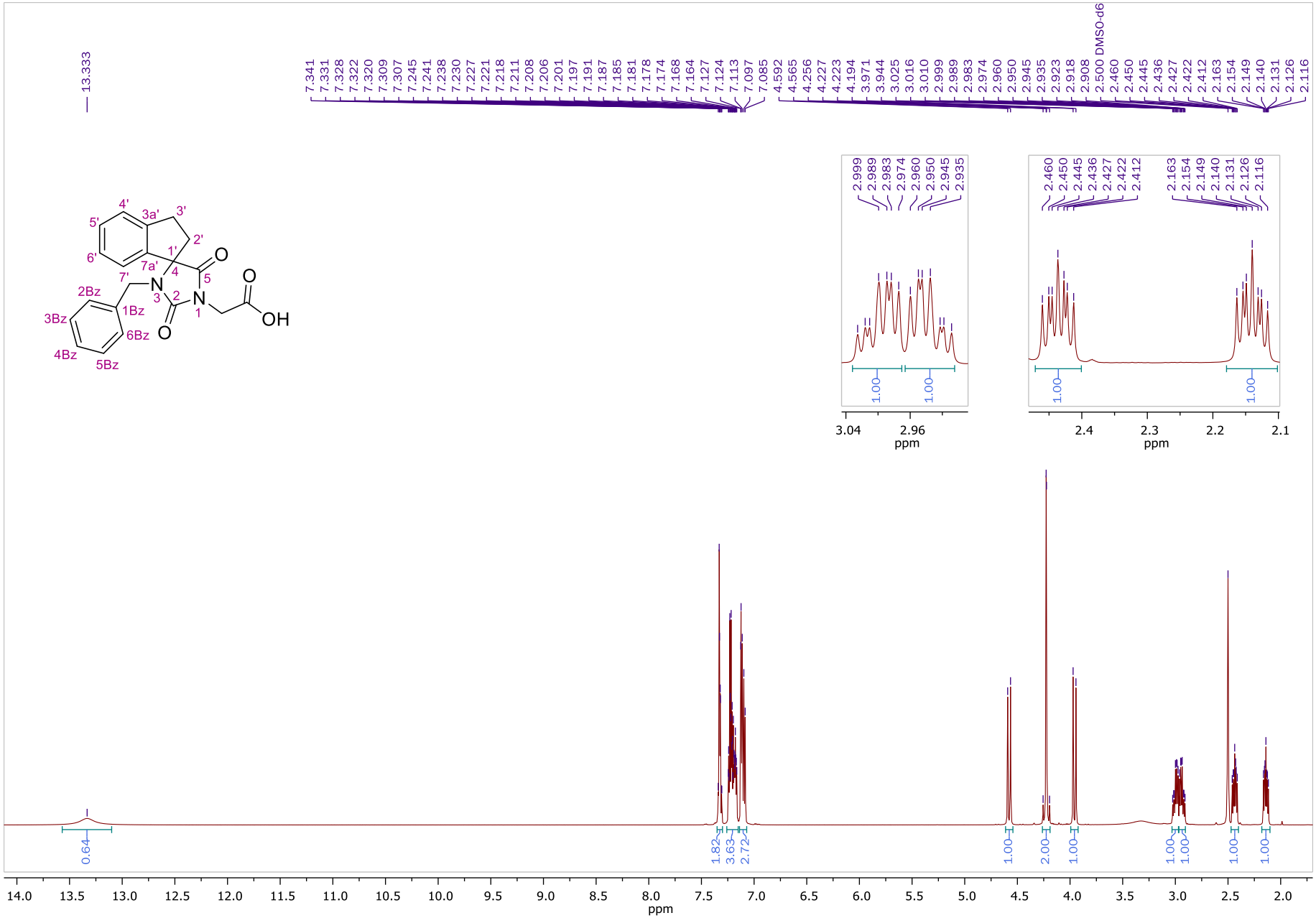
HSQC NMR of **10a** (400.13 MHz, MeOD-d_4)



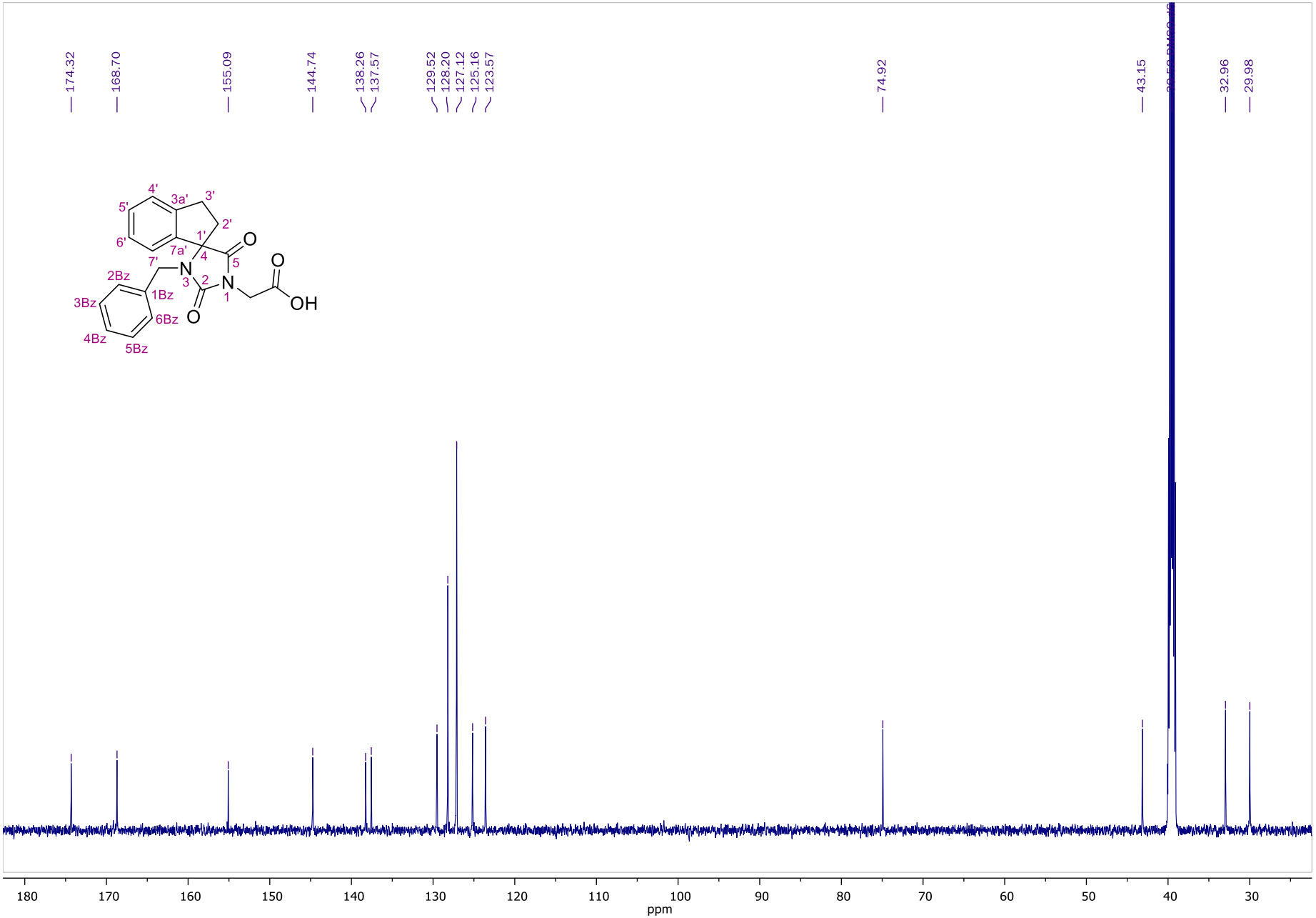
HMBC NMR of **10a** (400.13 MHz, MeOD-d_4)



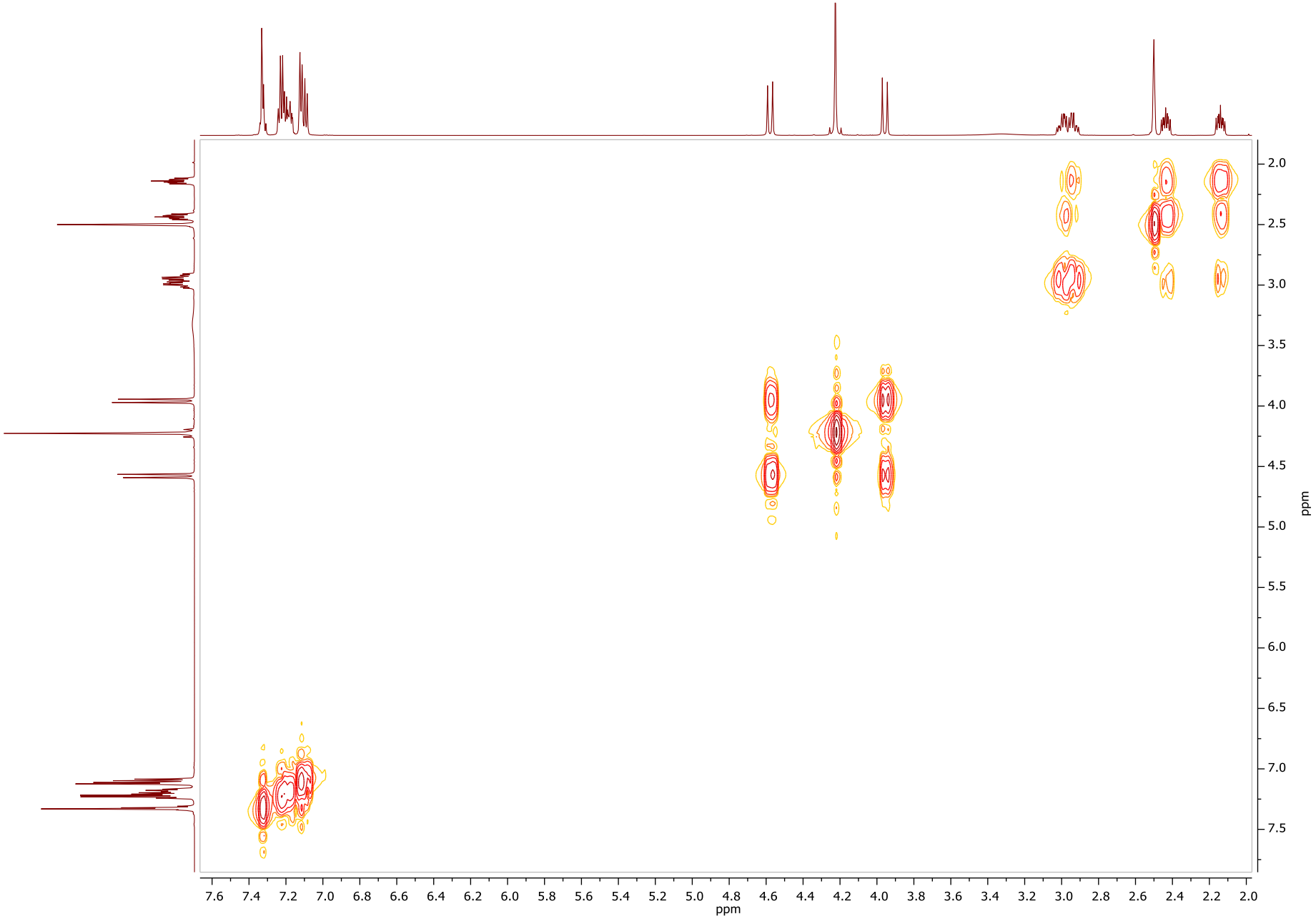
^{1}H NMR of **10b** (600.11 MHz, DMSO-d_6)



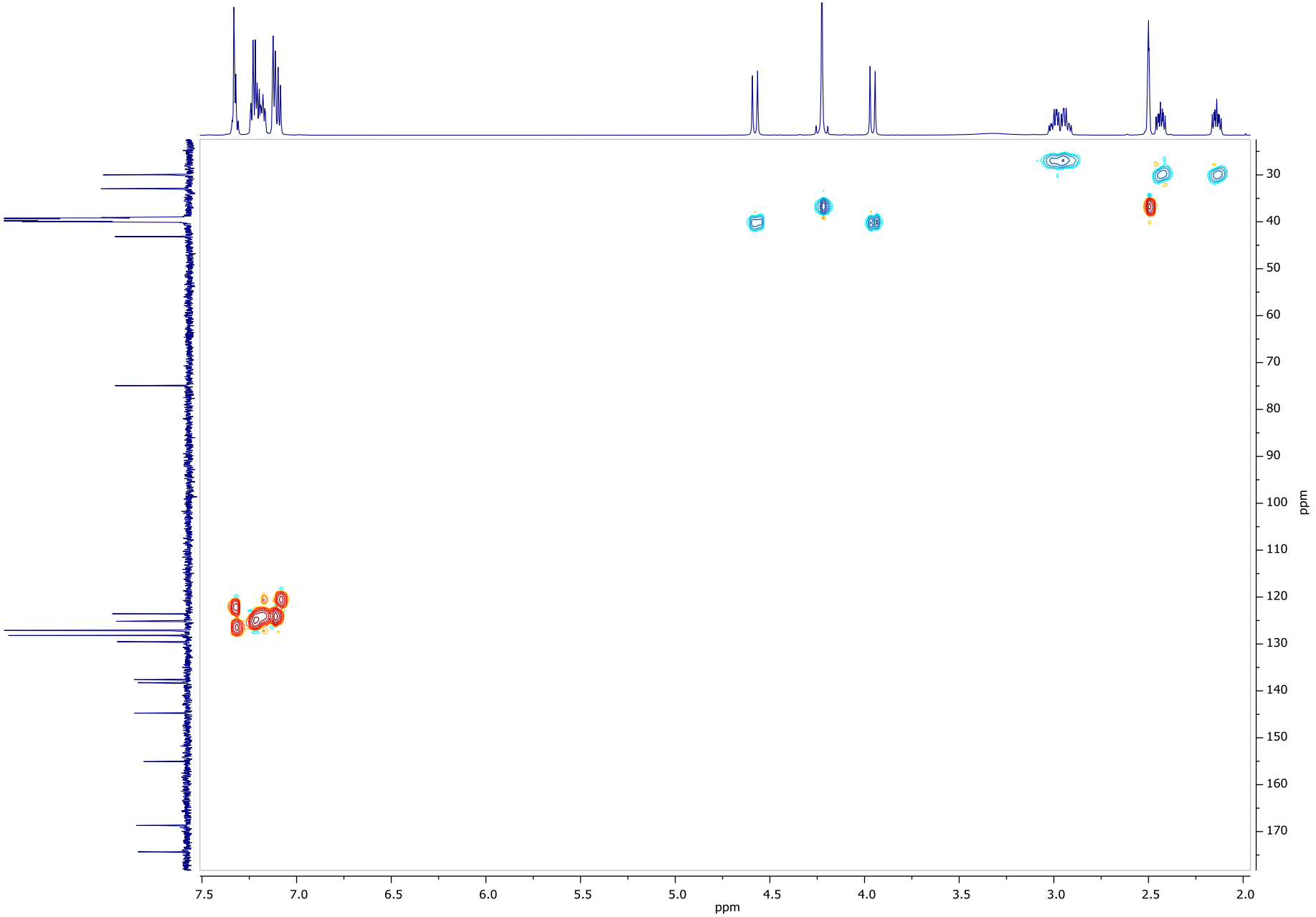
^{13}C NMR of **10b** (150.9 MHz, DMSO-d_6)



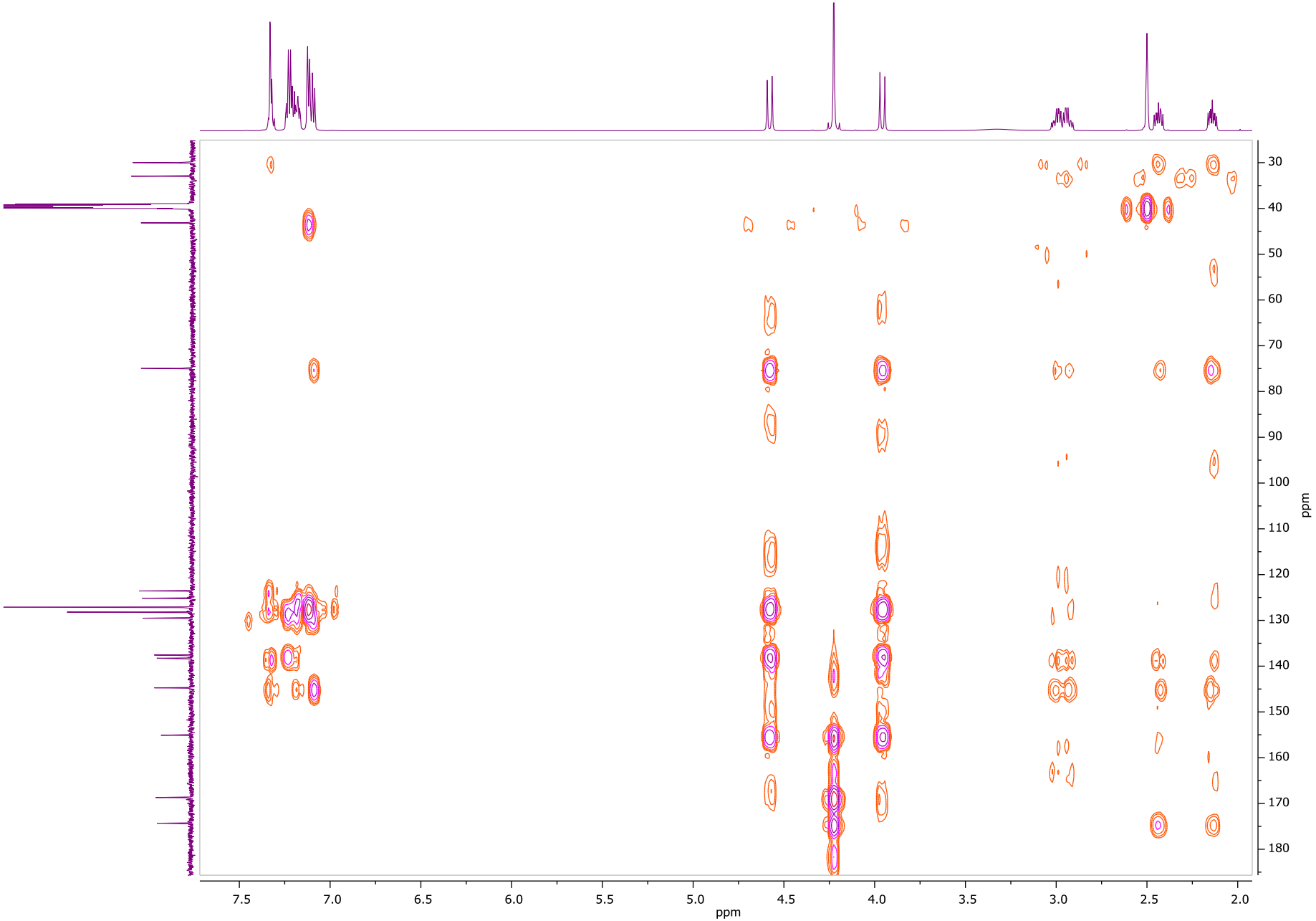
COSY NMR of **10b** (600.11 MHz, DMSO-d_6)



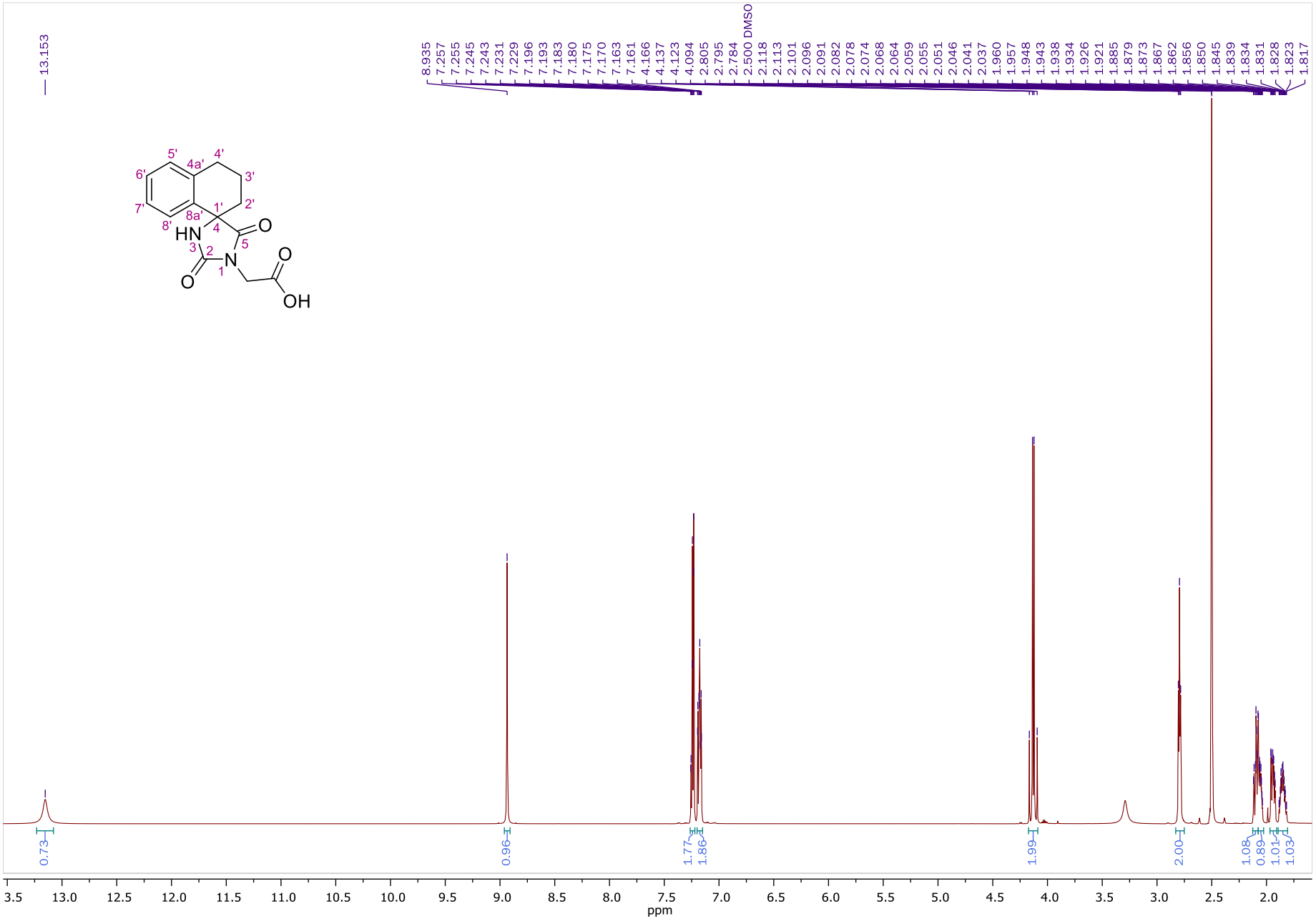
HSQC-DEPT NMR of **10b** (600.11 MHz, DMSO-d_6)



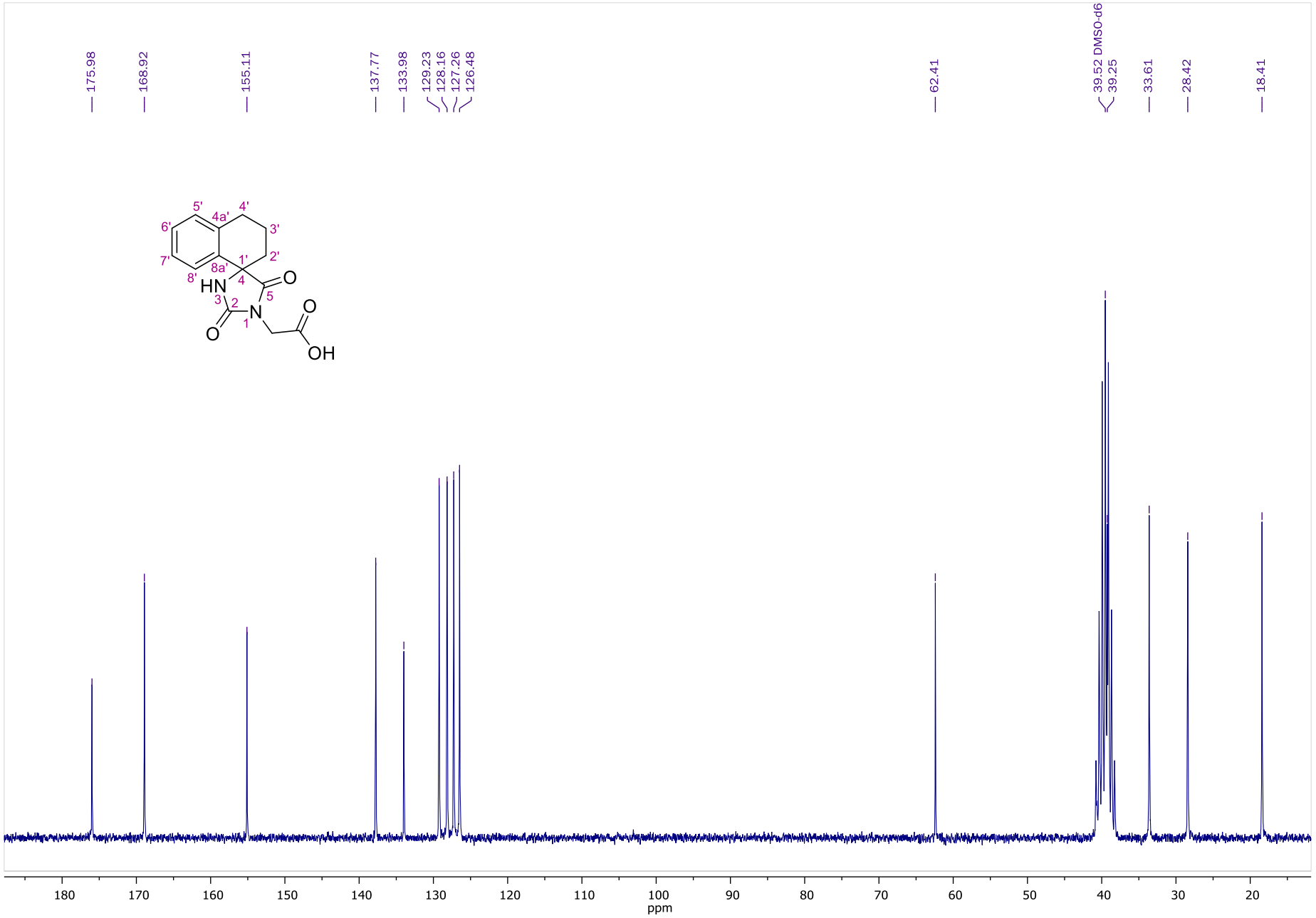
HMBC NMR of **10b** (600.11 MHz, DMSO-d_6)



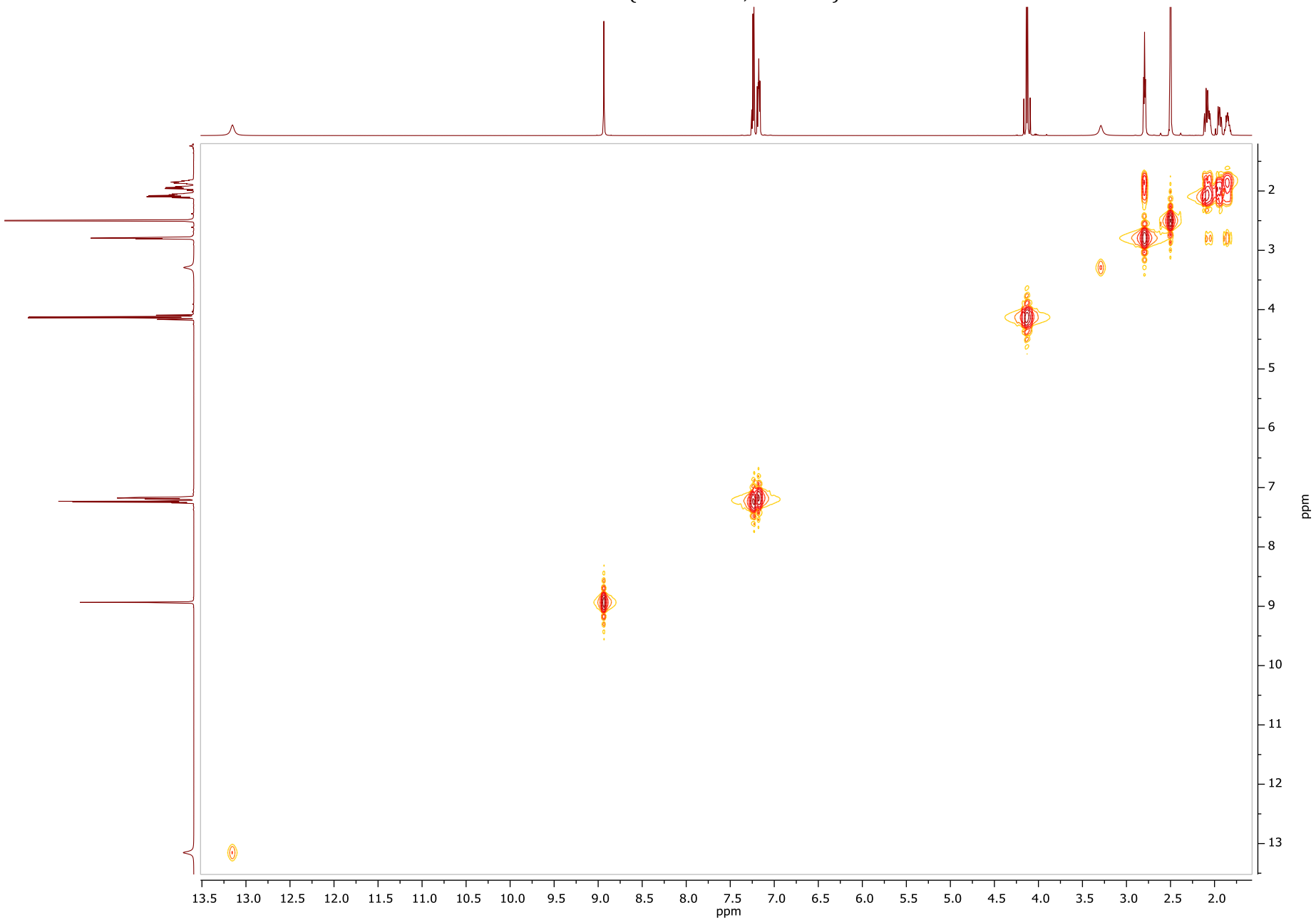
^{1}H NMR of **11** (600.11 MHz, DMSO-d_6)



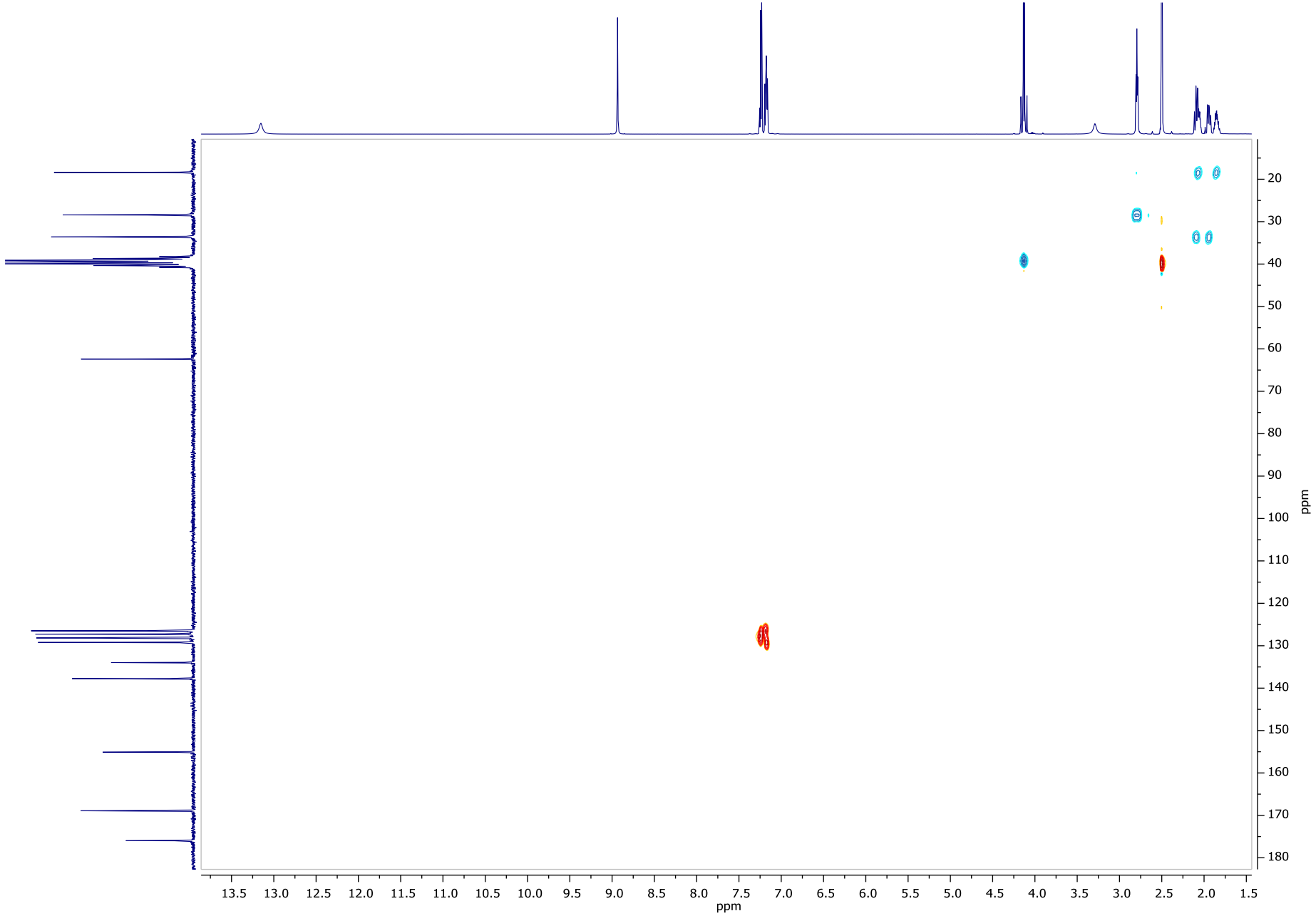
^{13}C NMR of **11** (150.9 MHz, DMSO-d_6)



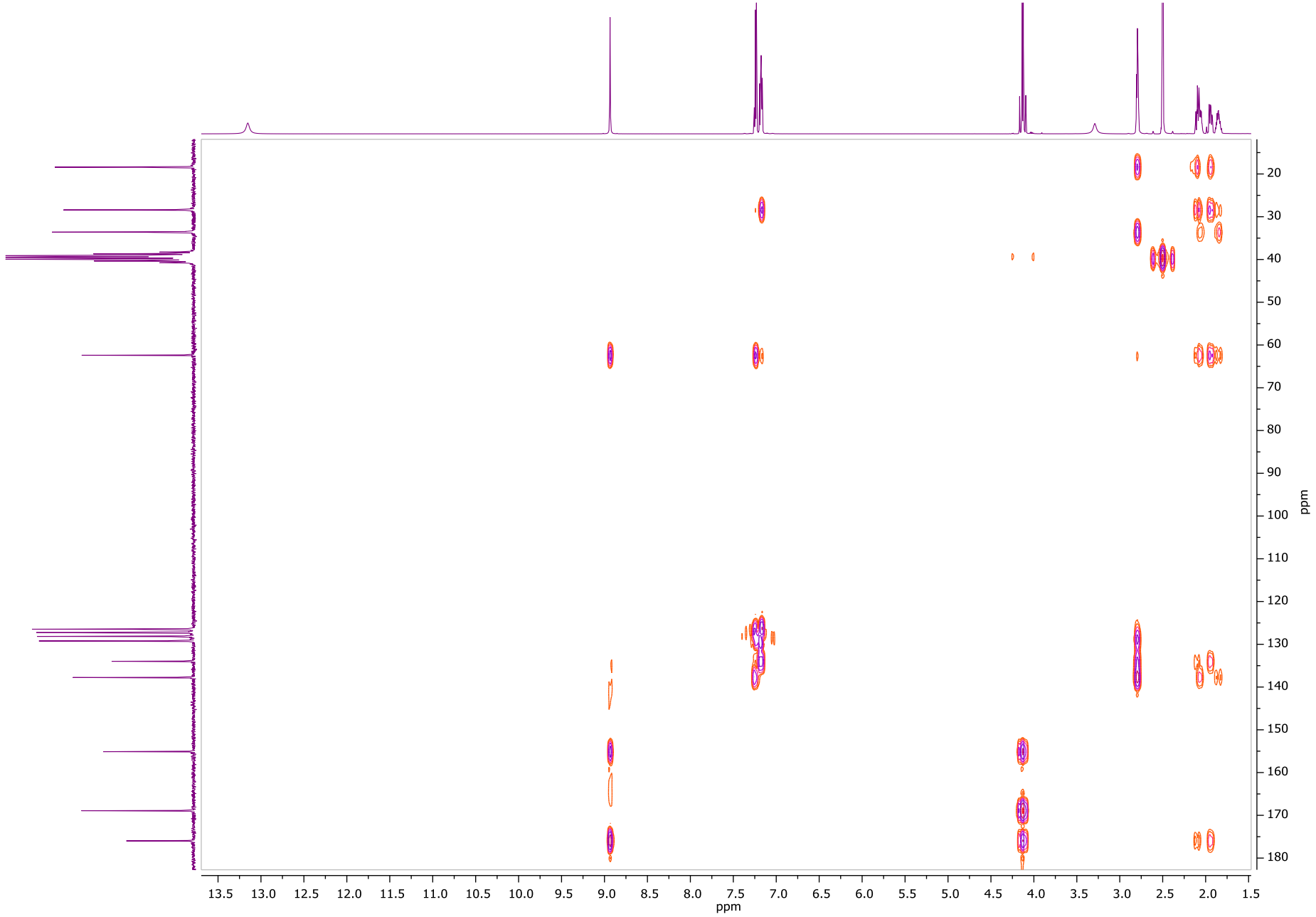
COSY NMR of **11** (600.11 MHz, DMSO-d_6)



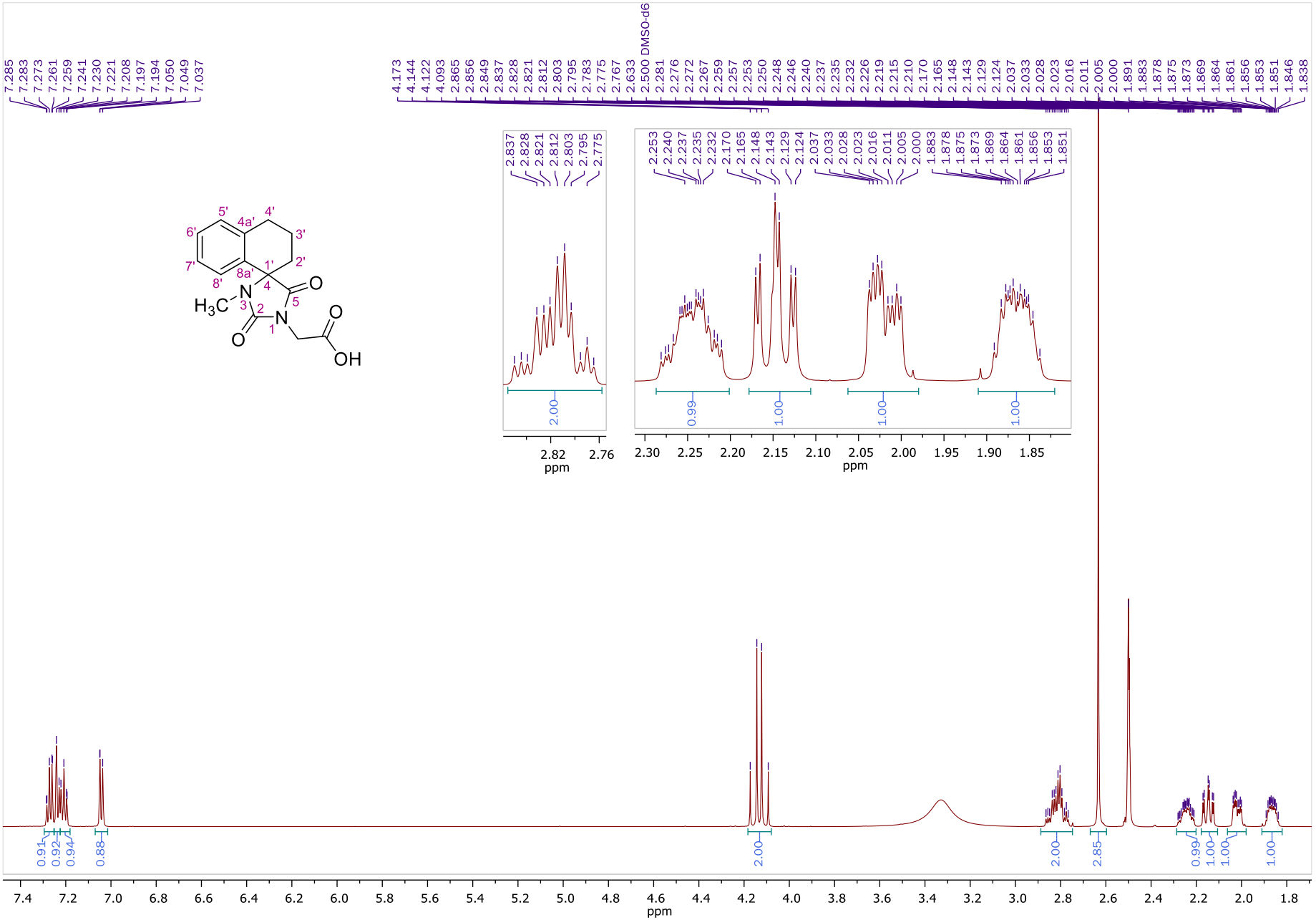
HSQC-DEPT NMR of **11** (600.11 MHz, DMSO-d_6)



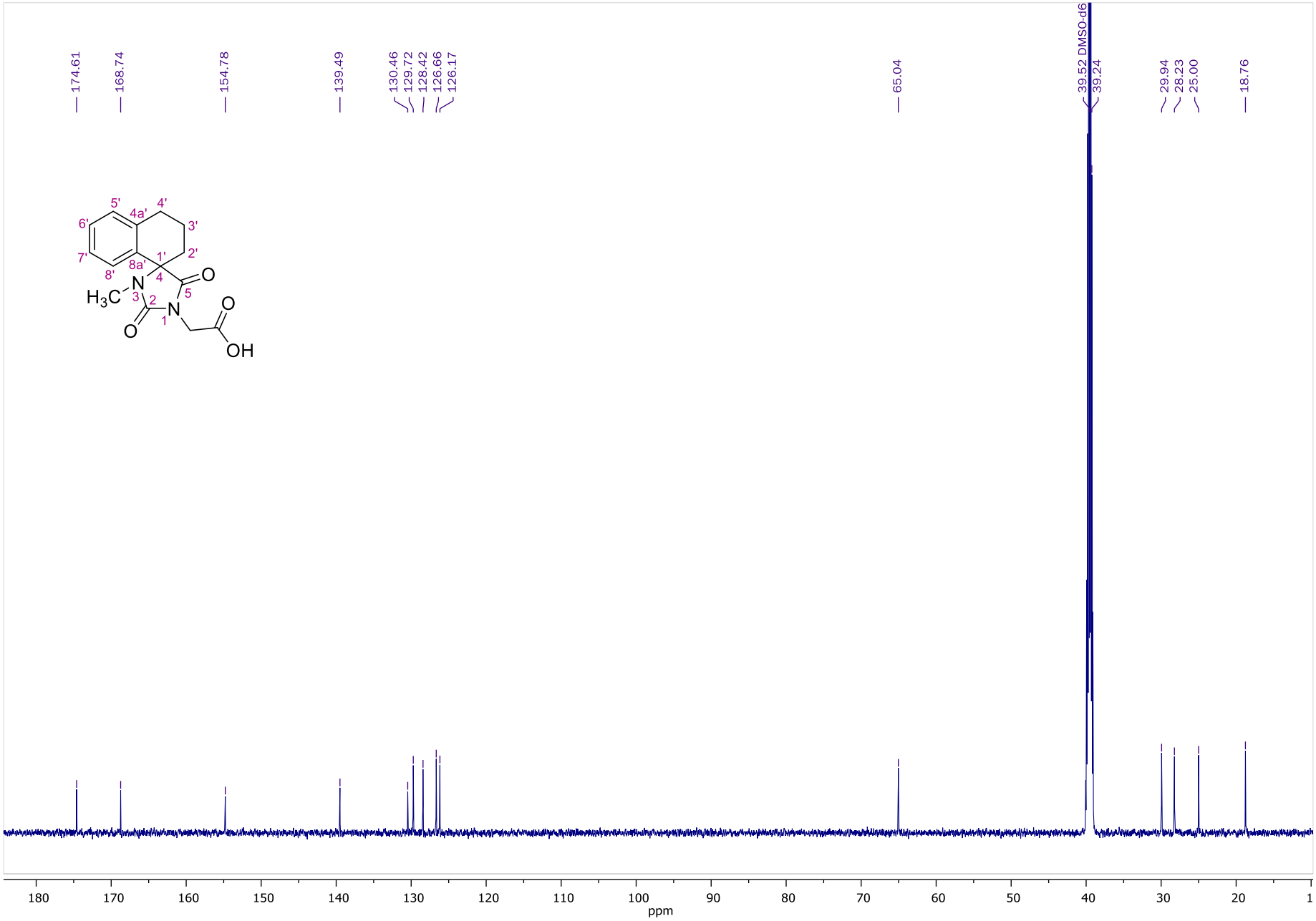
HMBC NMR of **11** (600.11 MHz, DMSO-d_6)



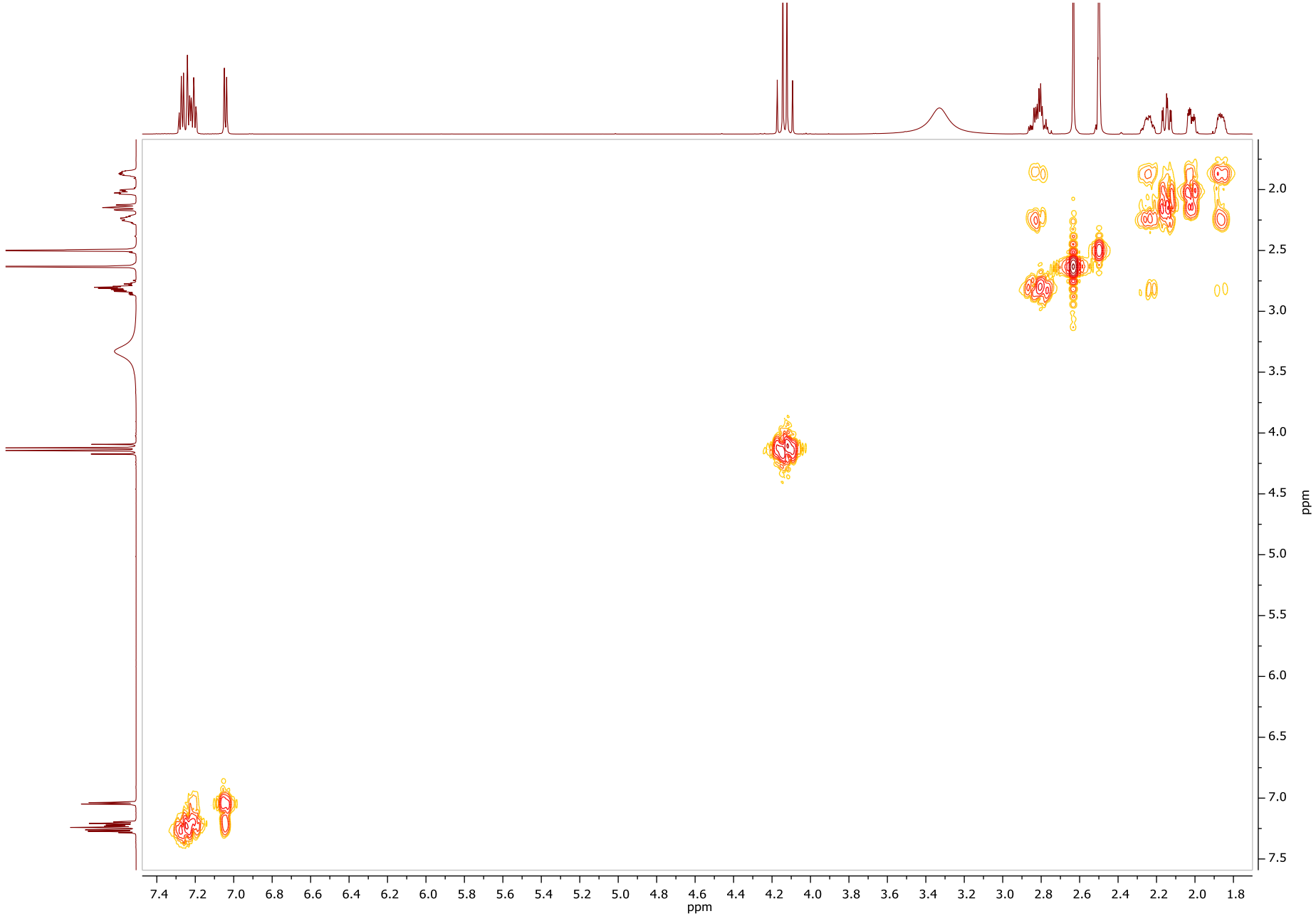
^{1}H NMR of **11a** (600.11 MHz, DMSO-d_6)



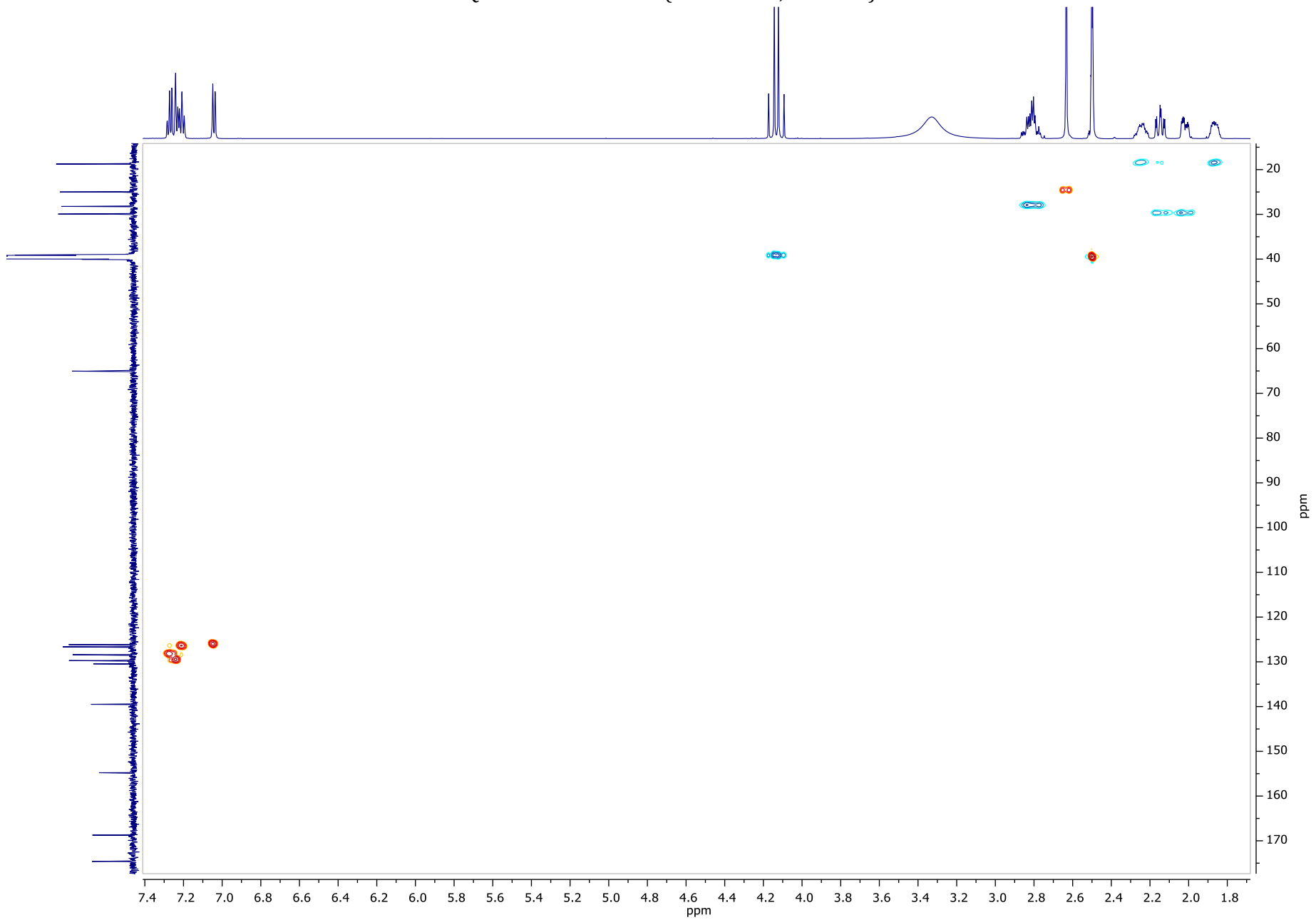
^{13}C NMR of **11a** (150.9 MHz, DMSO-d_6)



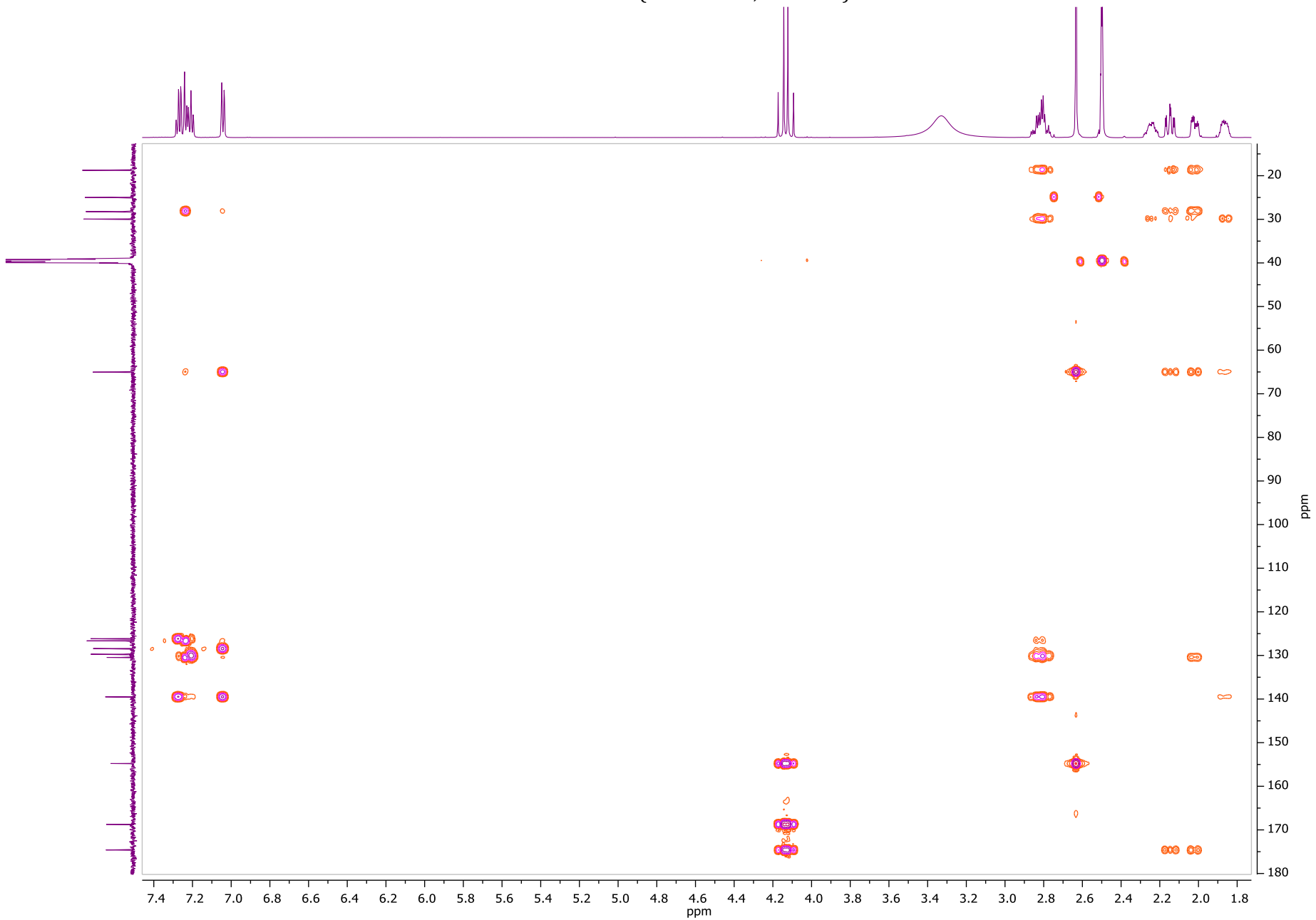
COSY NMR of **11a** (600.11 MHz, DMSO-d_6)



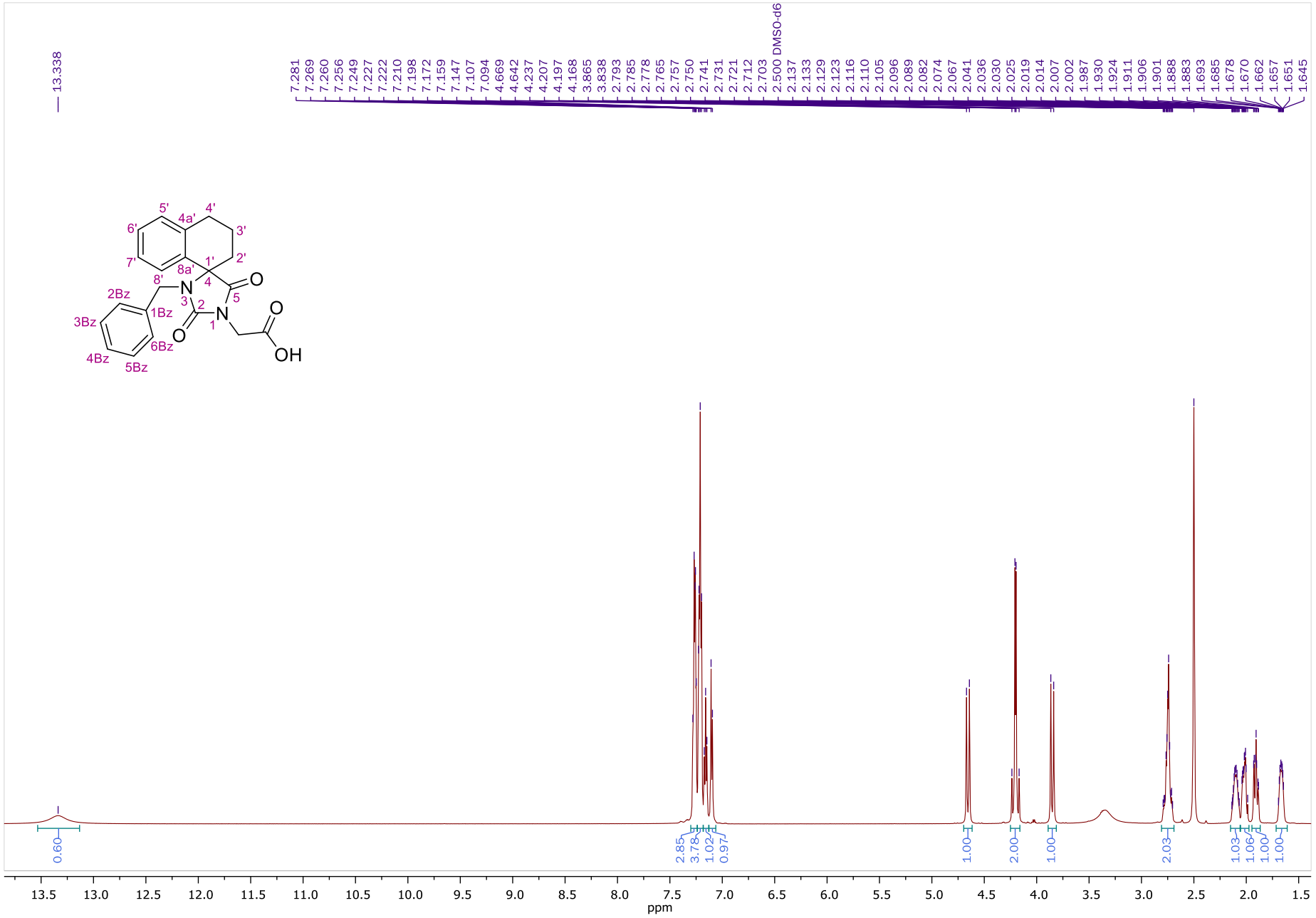
HSQC-DEPT NMR of **11a** (600.11 MHz, DMSO-d_6)



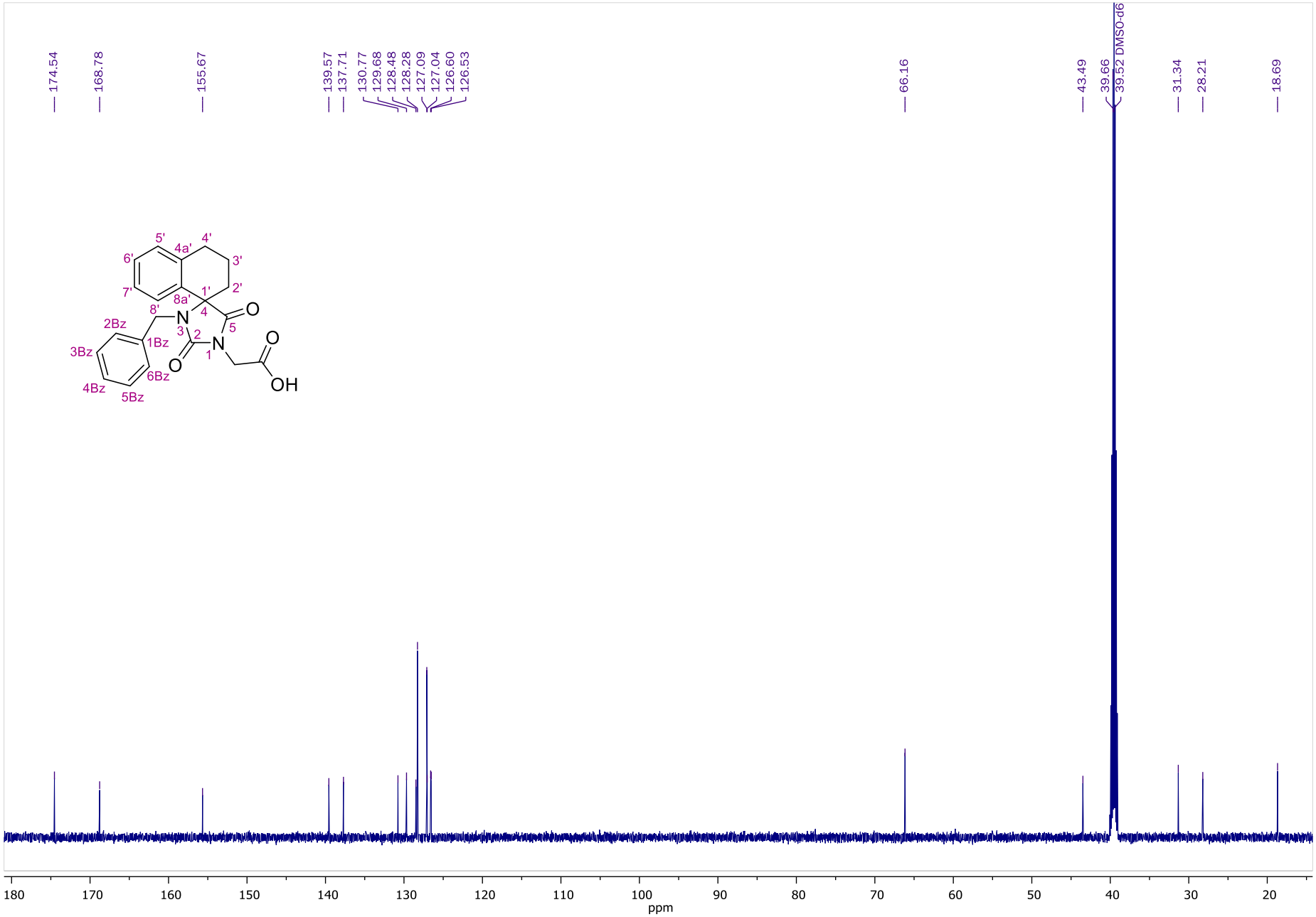
HMBC NMR of **11a** (600.11 MHz, DMSO-d_6)



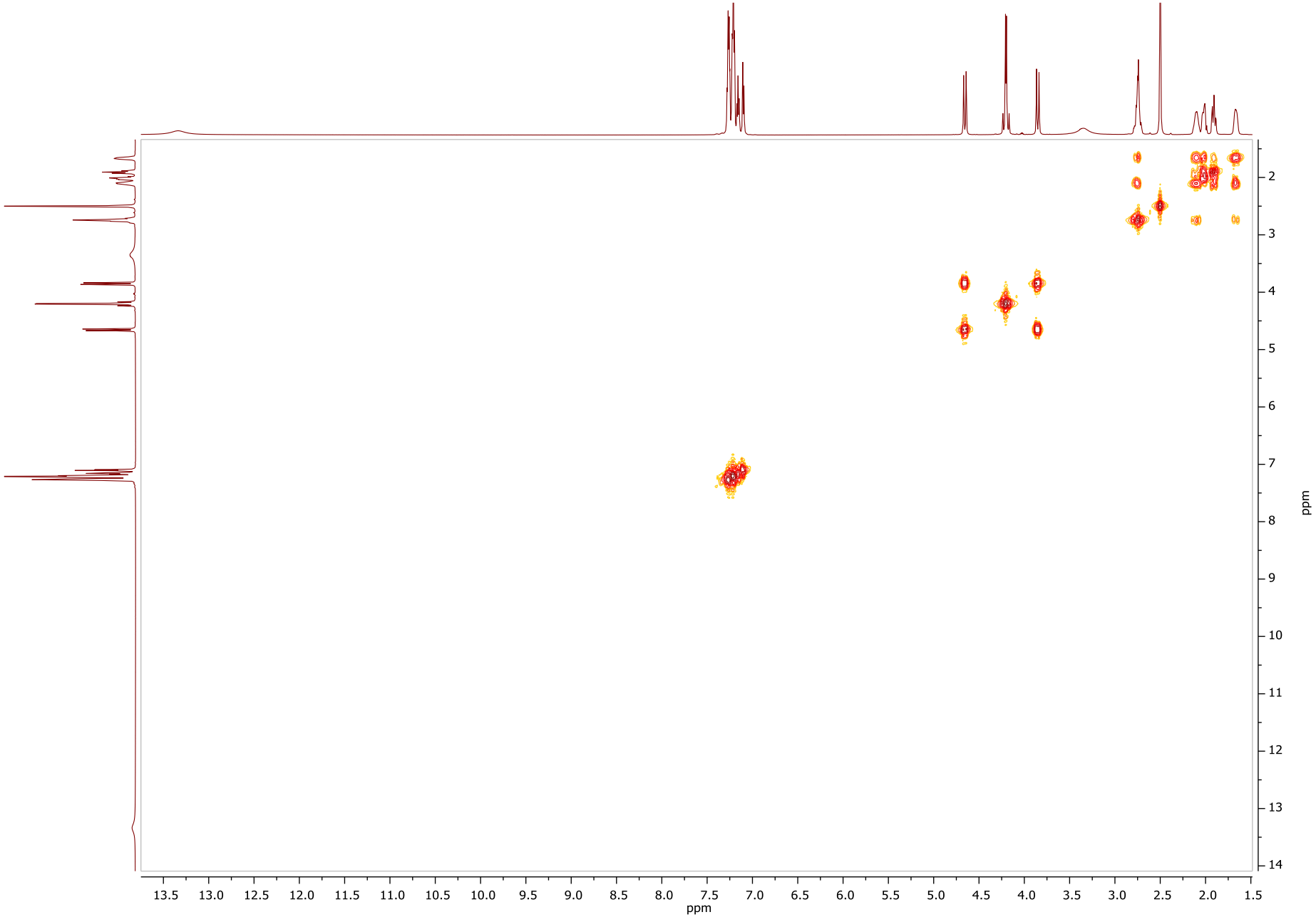
^{1}H NMR of **11b** (600.11 MHz, DMSO-d_6)



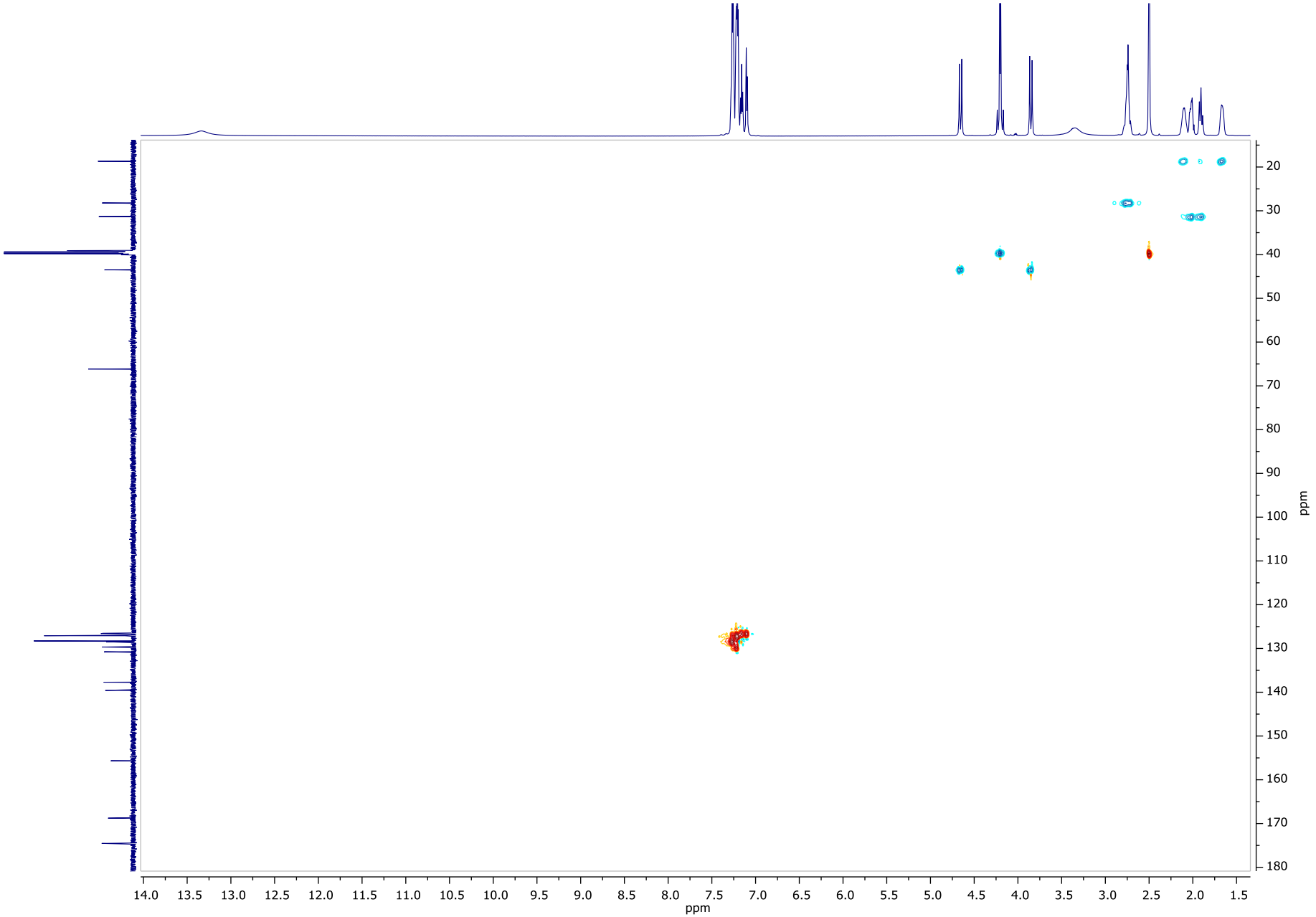
^{13}C NMR of **11b** (150.9 MHz, DMSO-d_6)



COSY NMR of **11b** (600.11 MHz, DMSO-d_6)

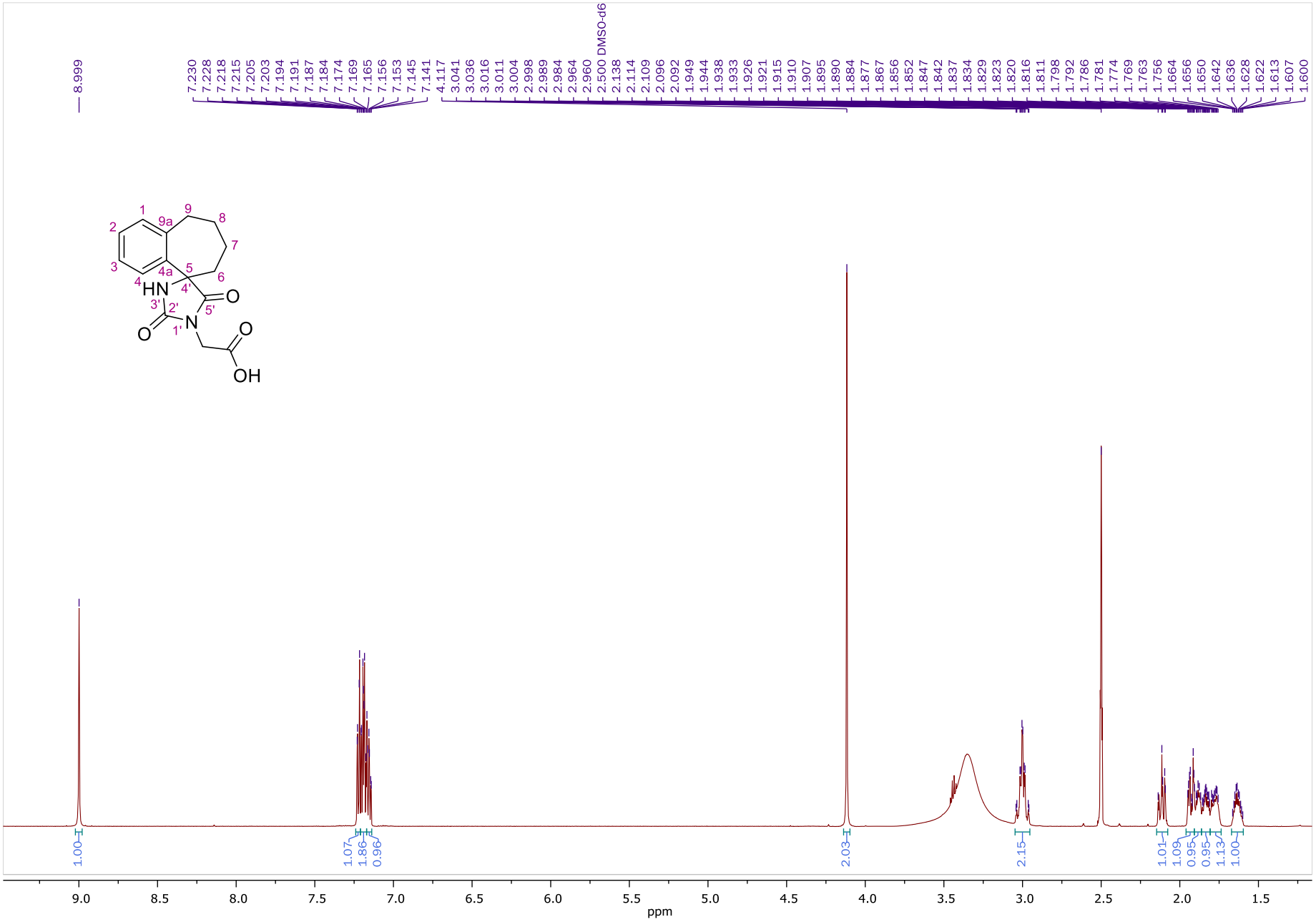


HSQC-DEPT NMR of **11b** (600.11 MHz, DMSO-d_6)

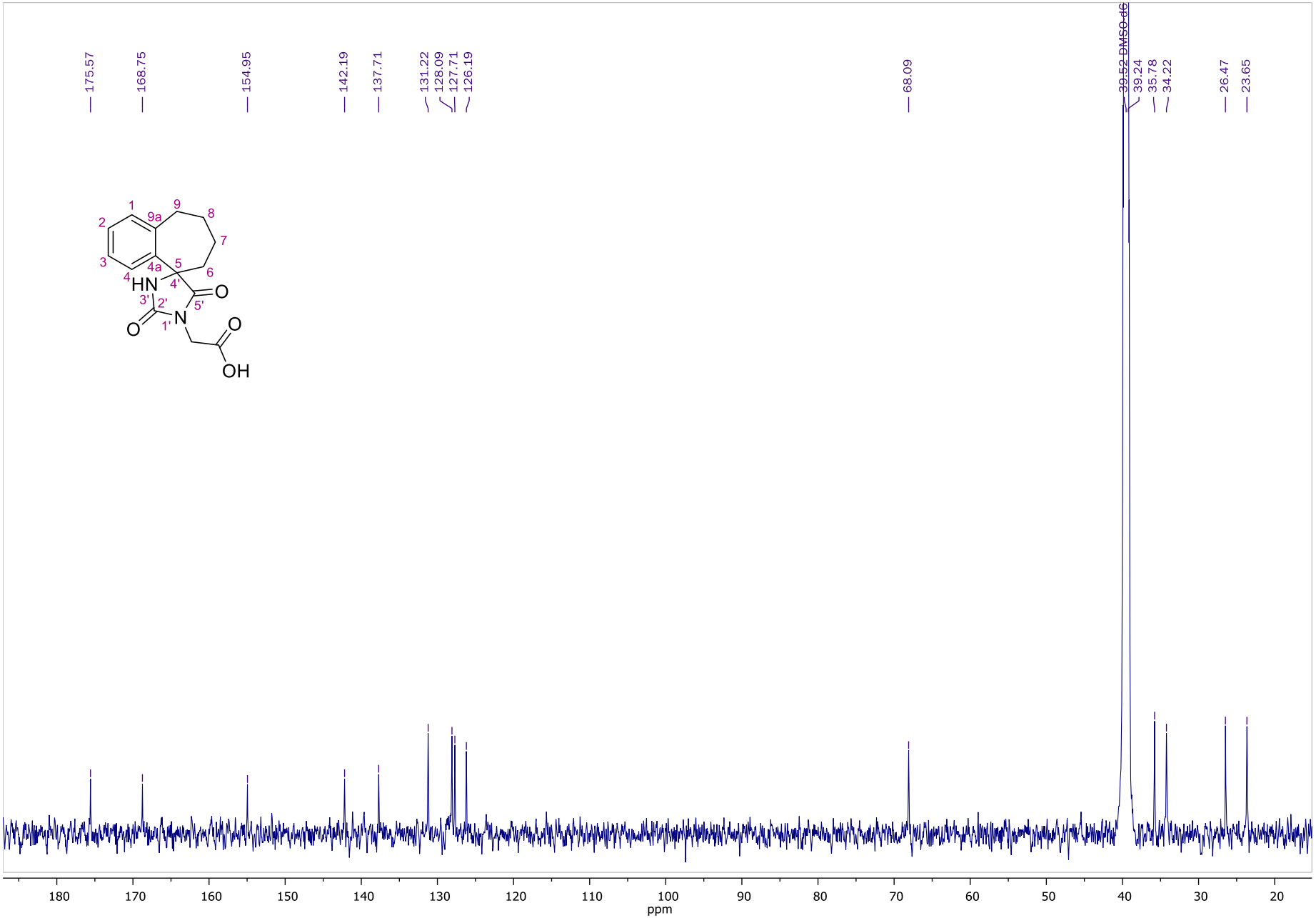


HMBC NMR of **11b** (600.11 MHz, DMSO-d_6)

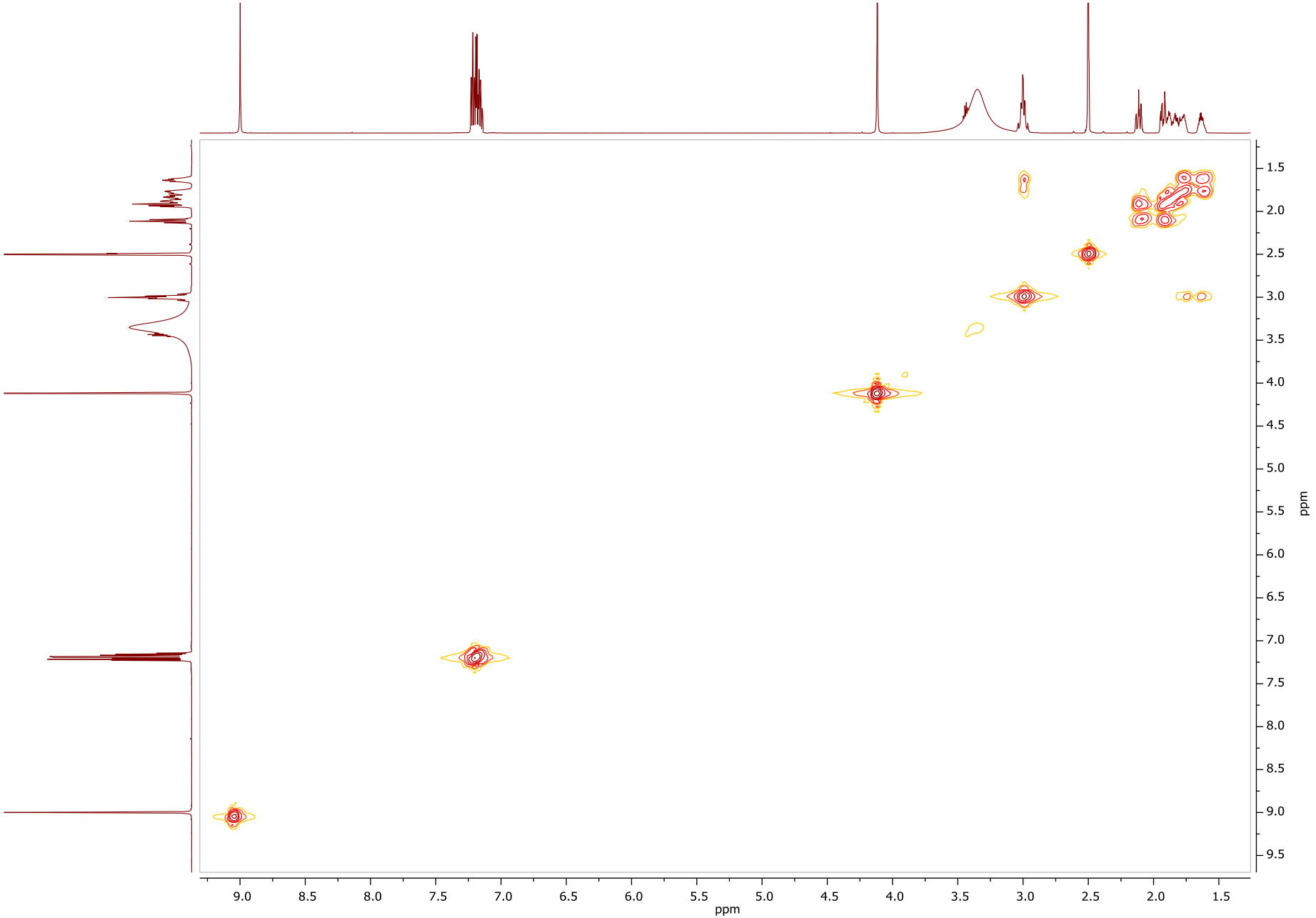
^{1}H NMR of **12** (600.11 MHz, DMSO-d_6)



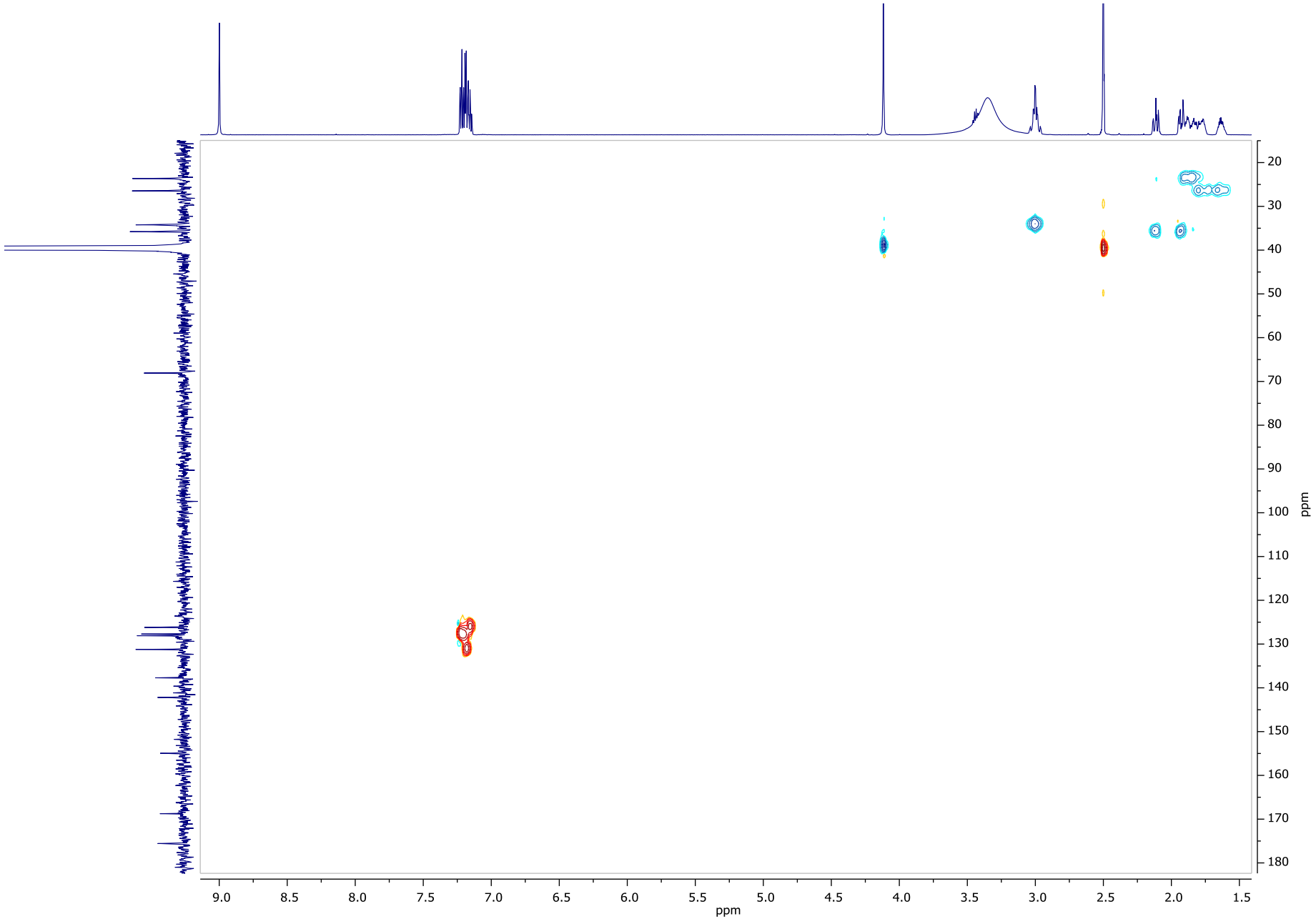
^{13}C NMR of **12** (150.9 MHz, DMSO-d_6)



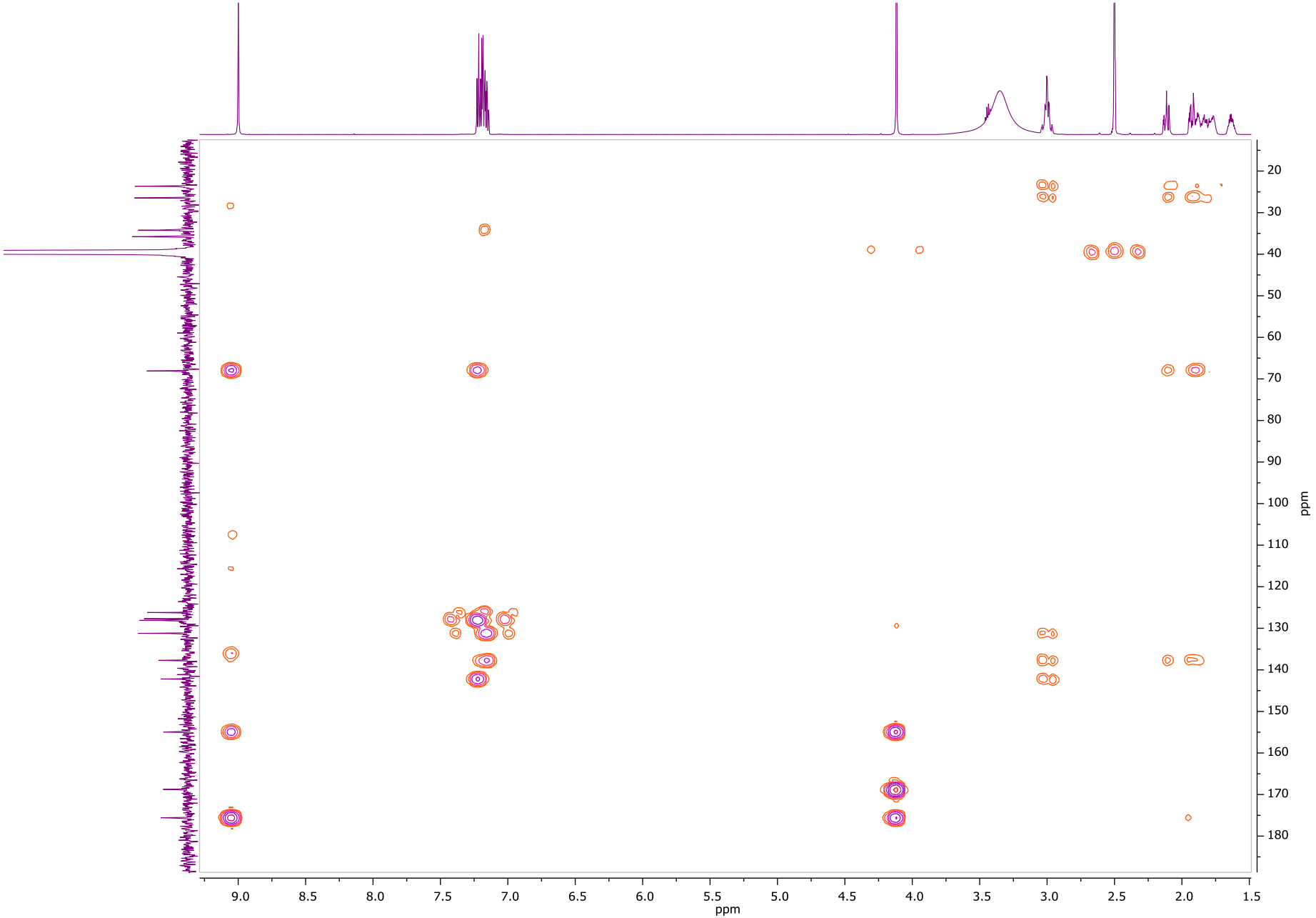
COSY NMR of **12** (400.13 MHz, DMSO-d_6)



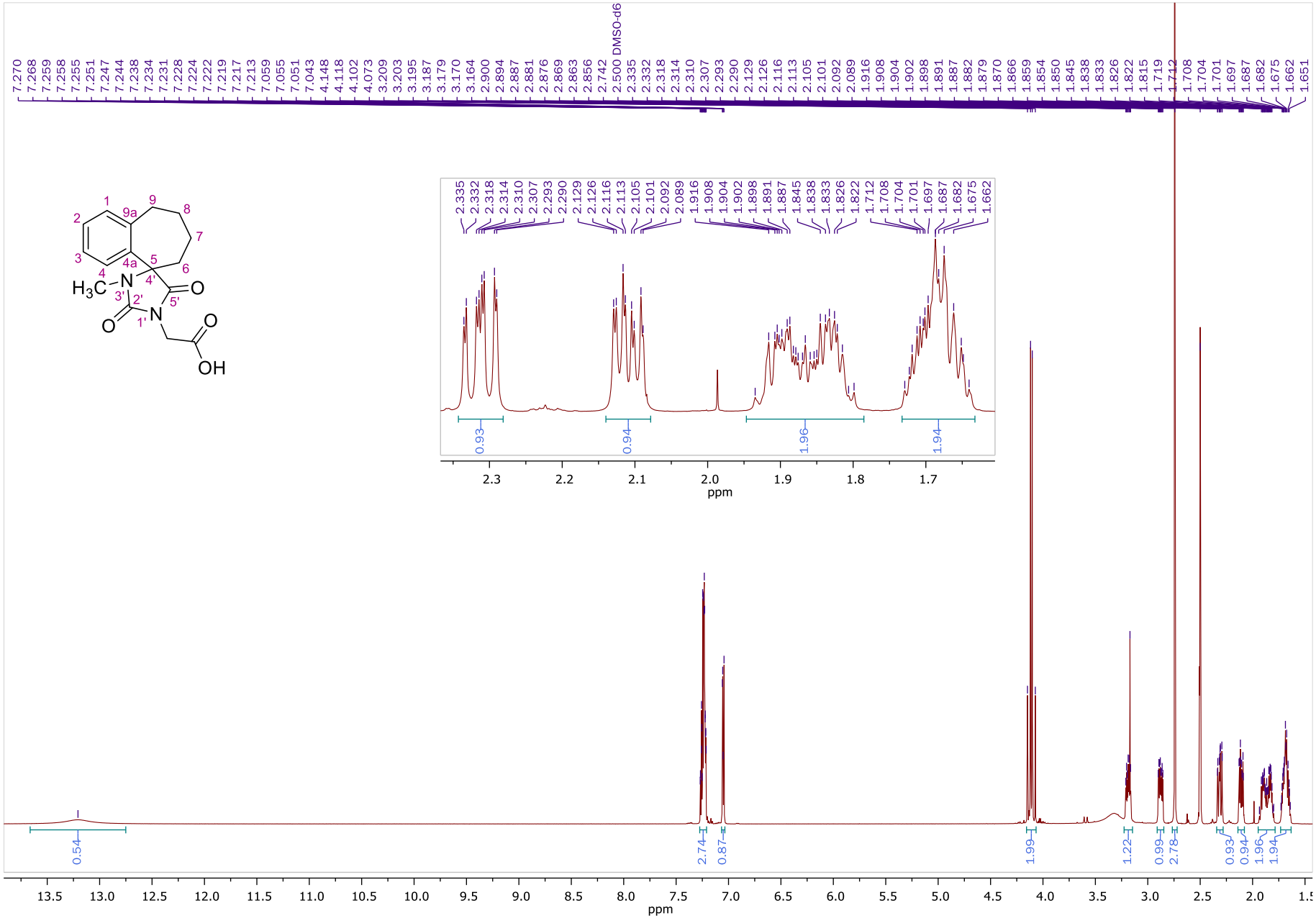
HSQC-DEPT NMR of **12** (600.11 MHz, DMSO-d_6)



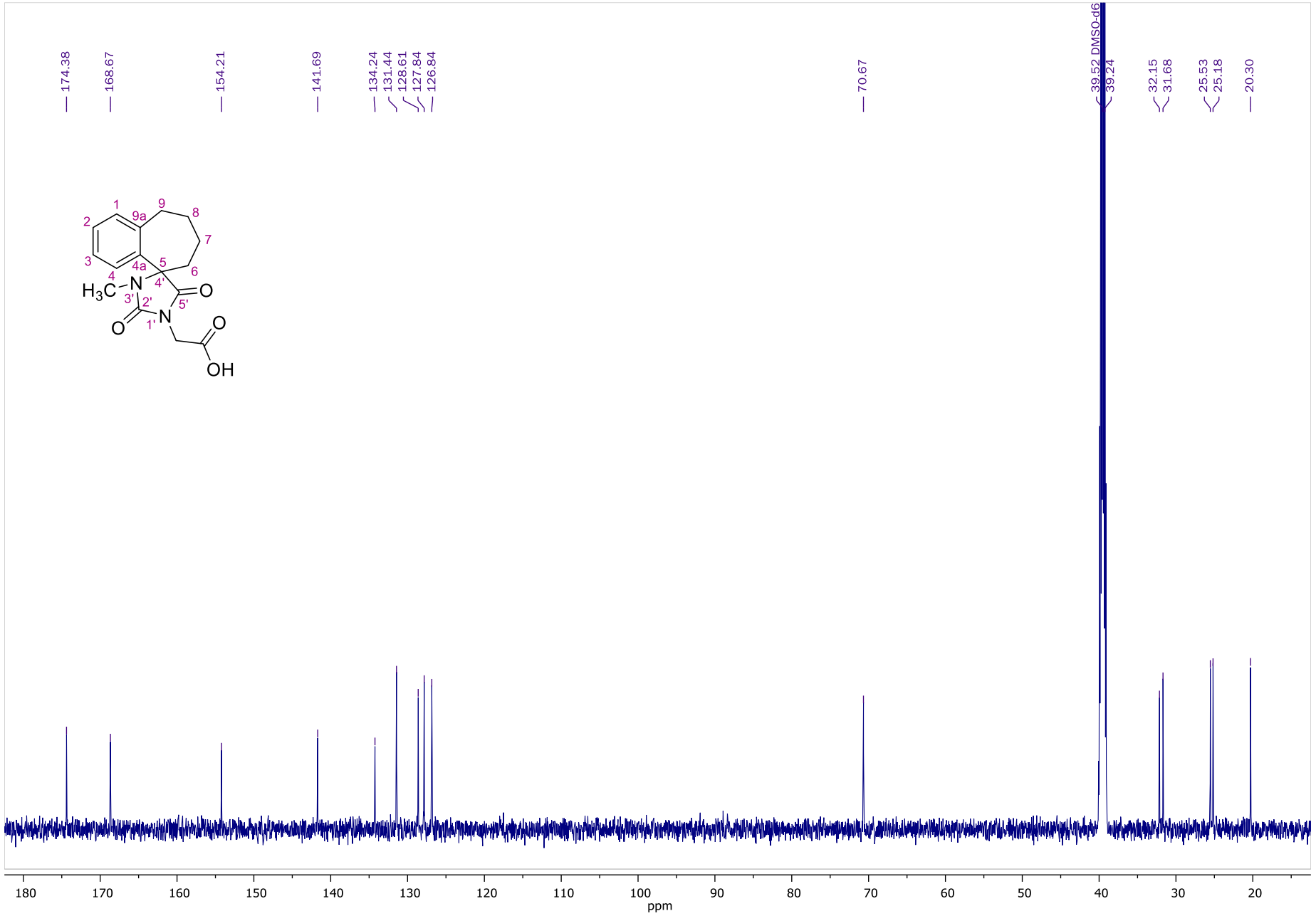
HMBC NMR of **12** (400.13 MHz, DMSO-d_6)



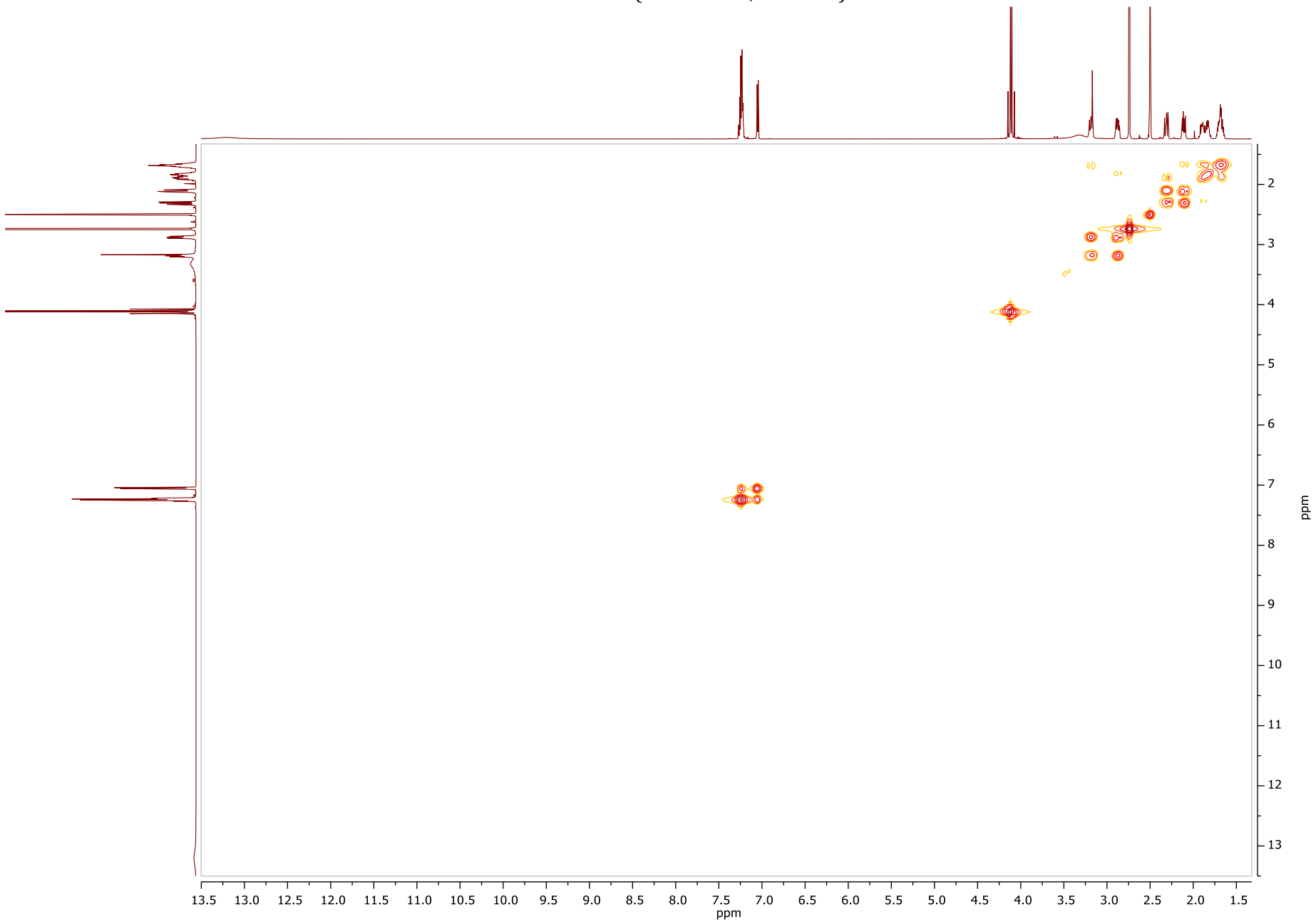
^{1}H NMR of **12a** (600.11 MHz, DMSO-d_6)



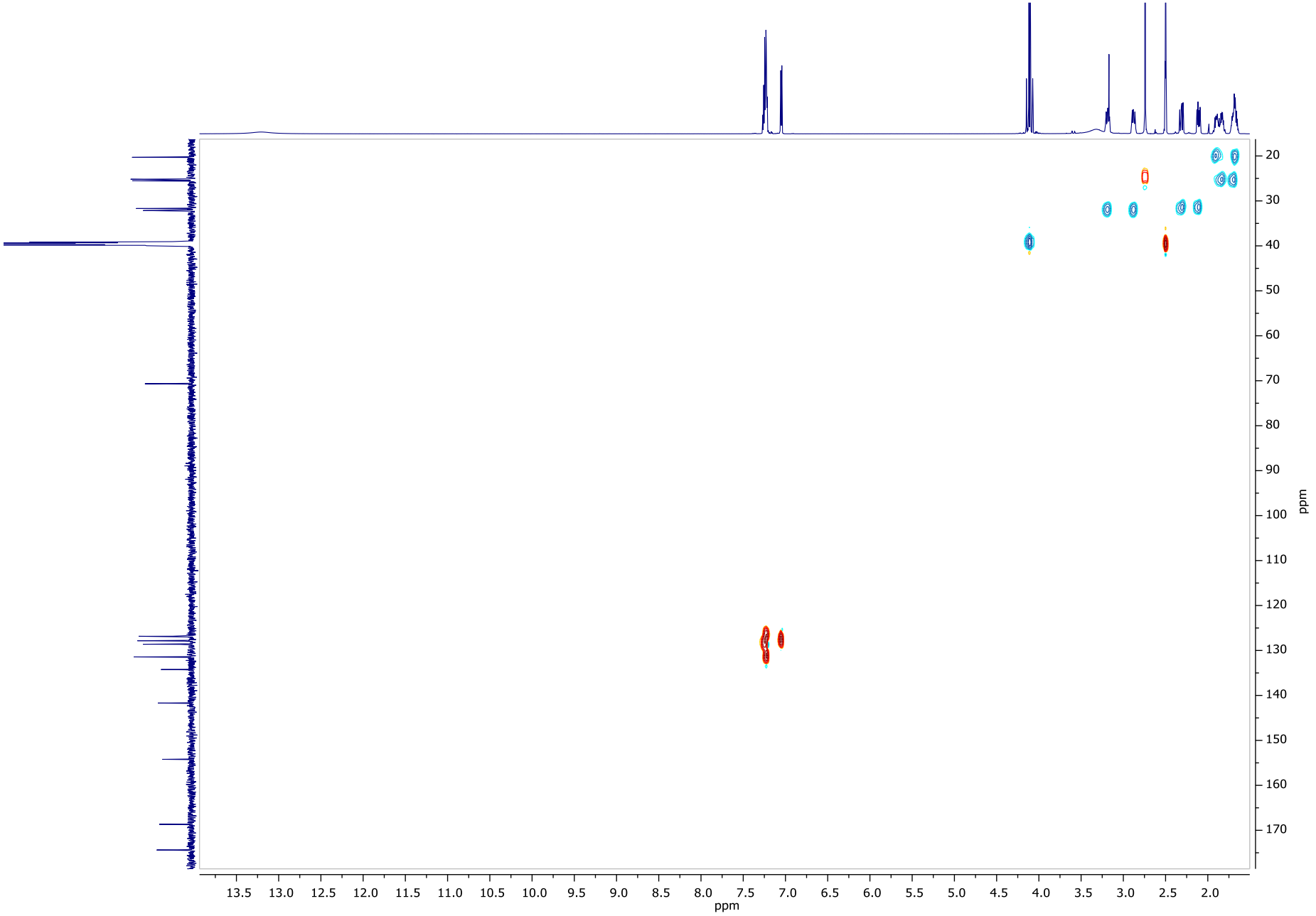
^{13}C NMR of **12a** (150.9 MHz, DMSO-d_6)



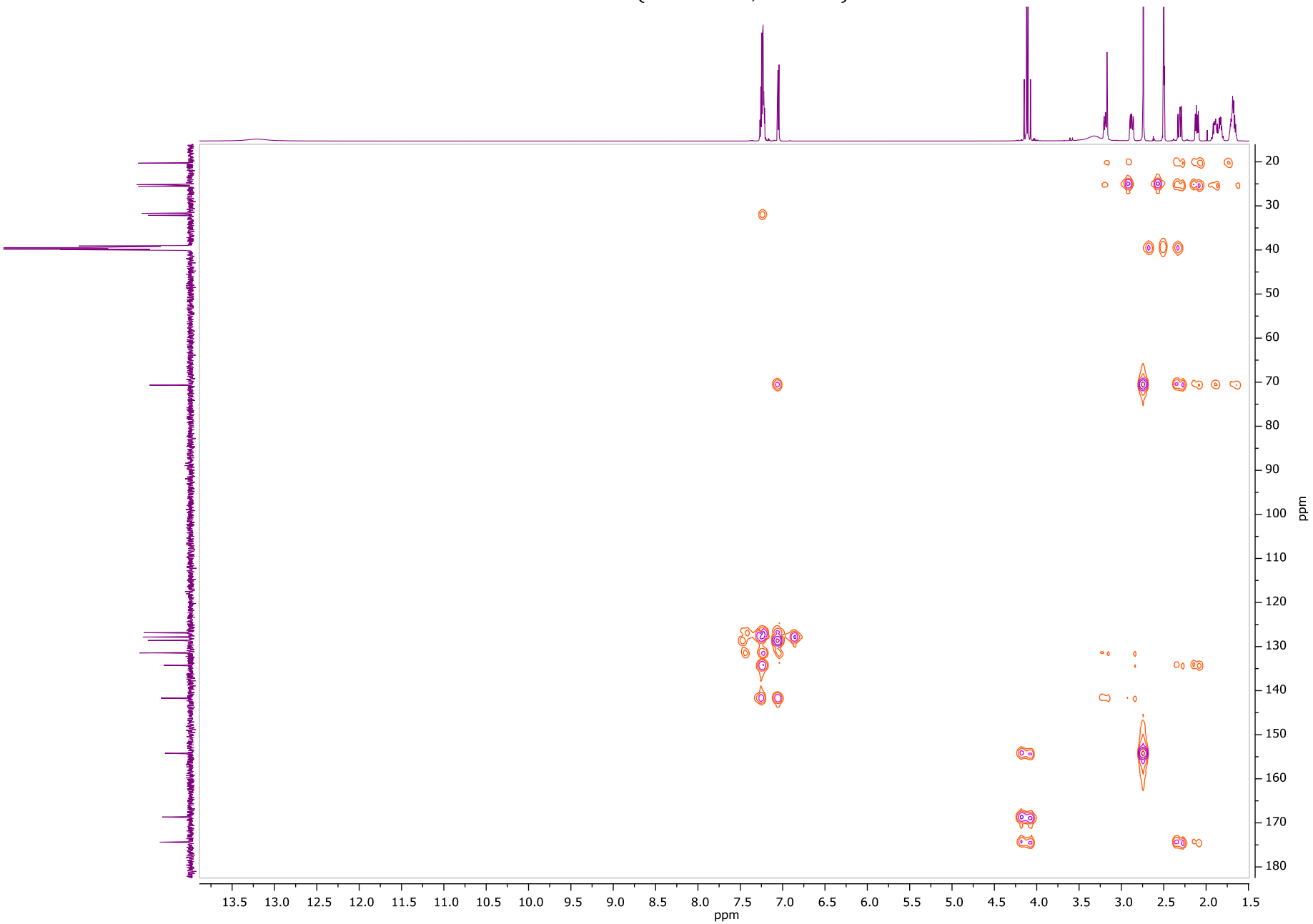
COSY NMR of **12a** (400.13 MHz, DMSO-d_6)



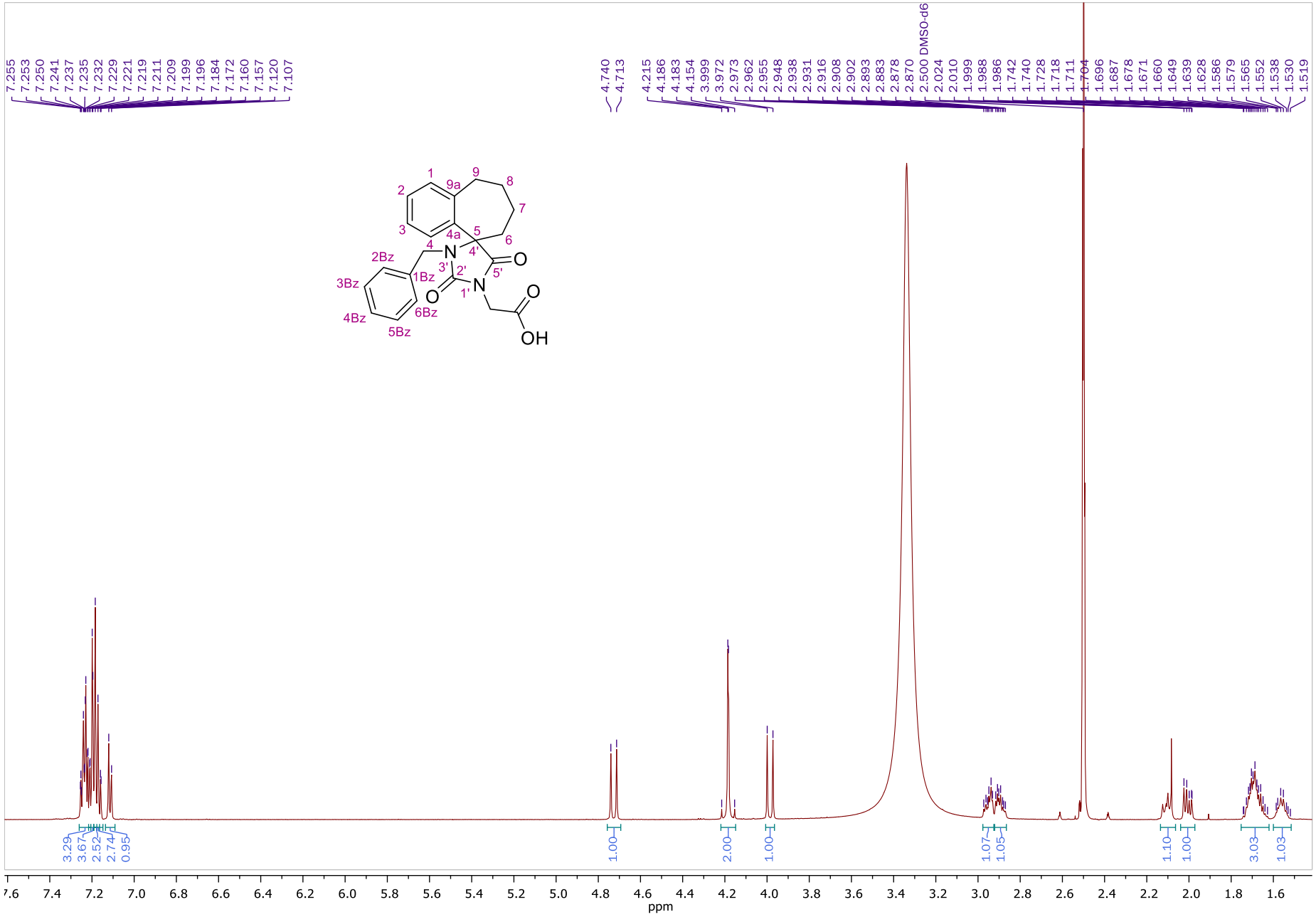
HSQC-DEPT NMR of **12a** (600.11 MHz, DMSO-d_6)



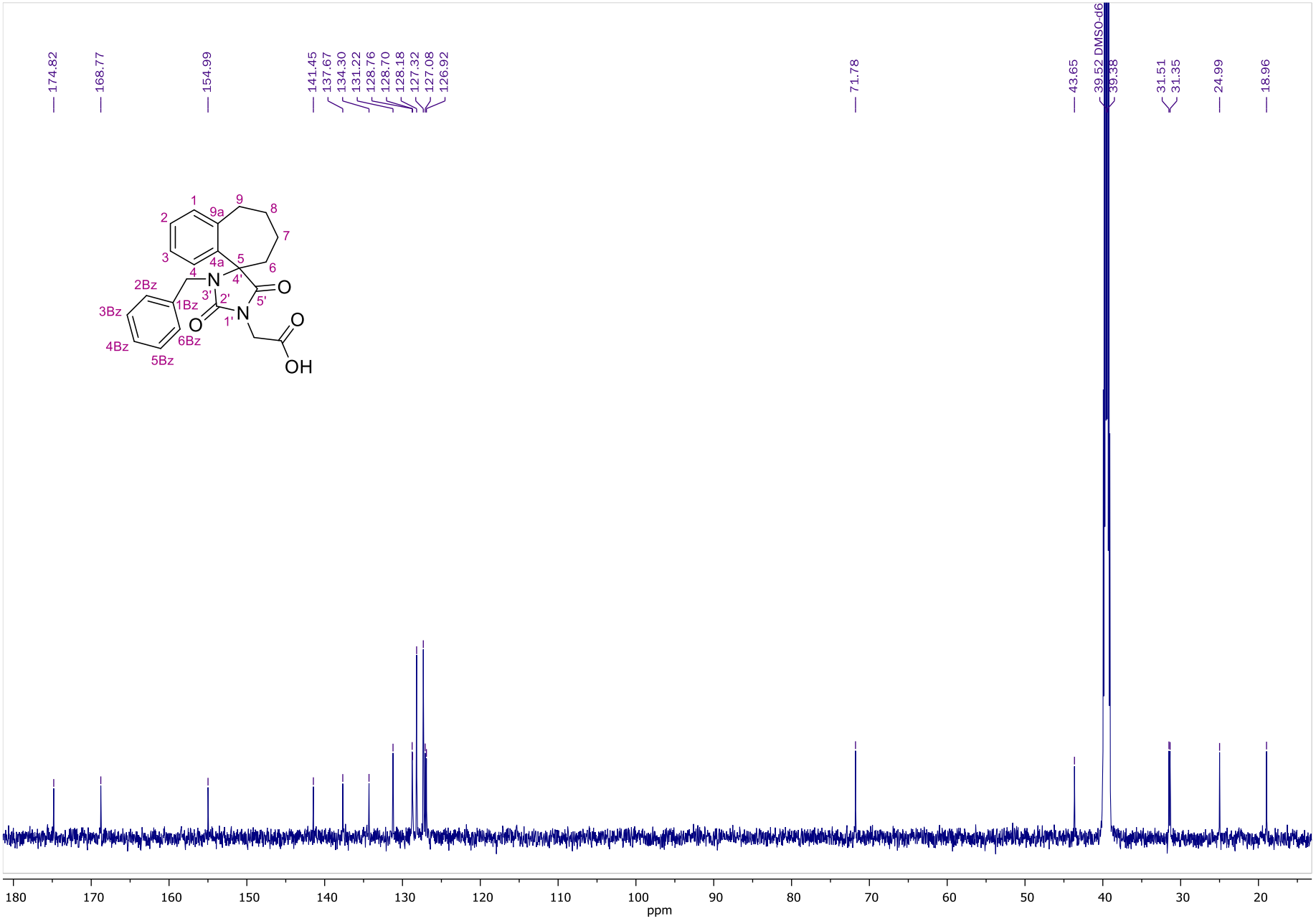
HMBC NMR of **12a** (400.13 MHz, DMSO-d_6)



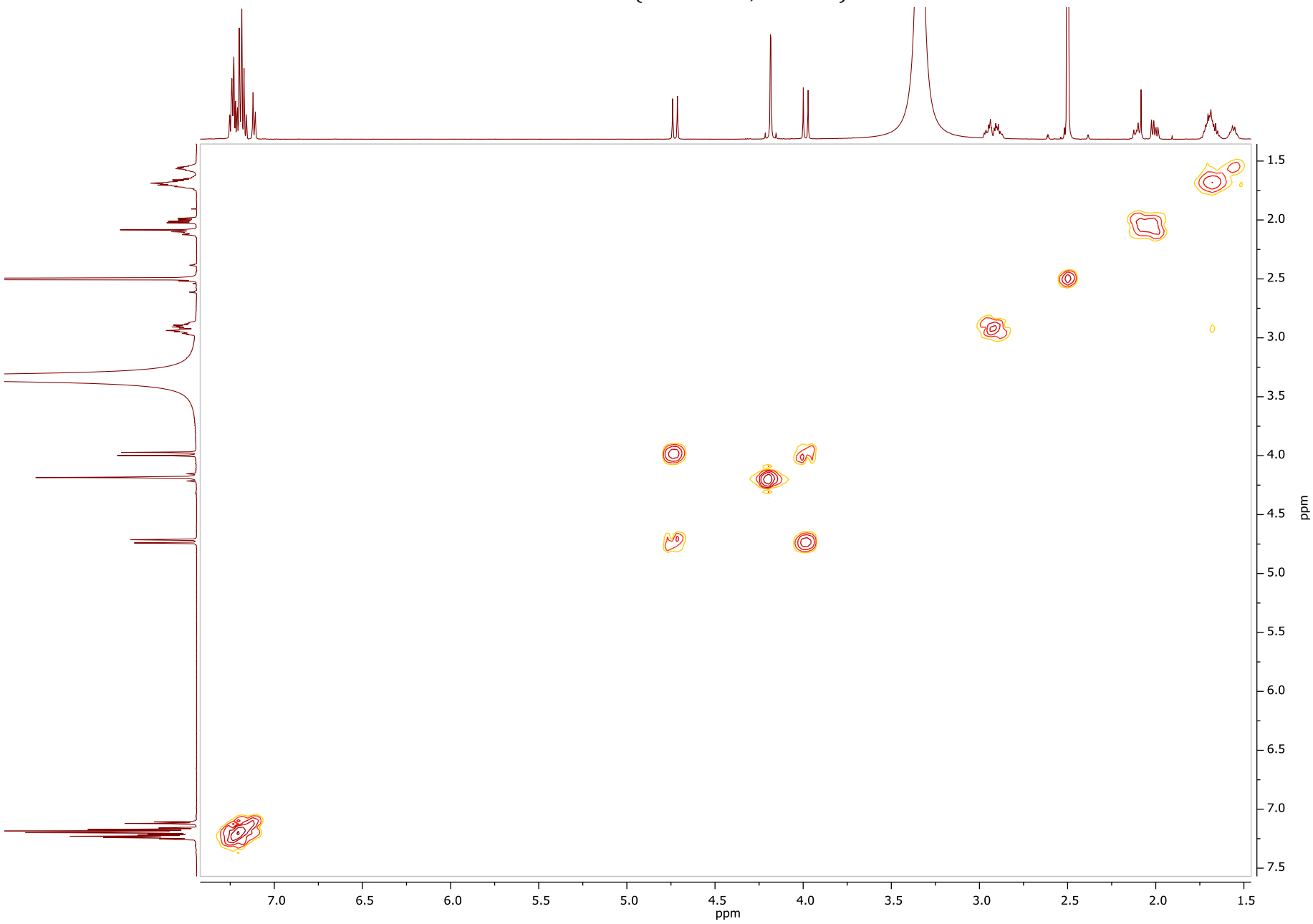
^{1}H NMR of **12b** (600.11 MHz, DMSO-d_6)



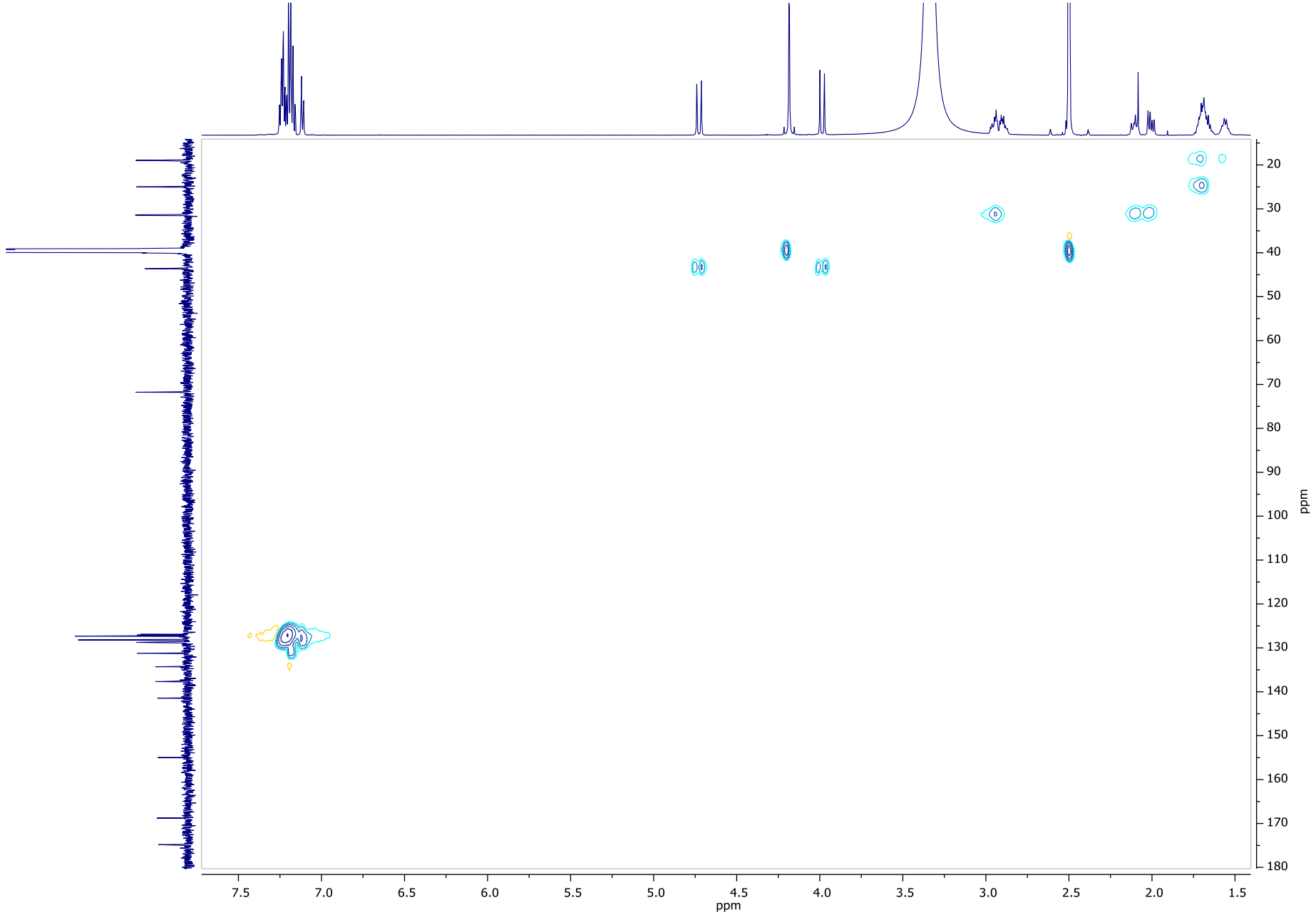
^{13}C NMR of **12b** (150.9 MHz, DMSO-d_6)



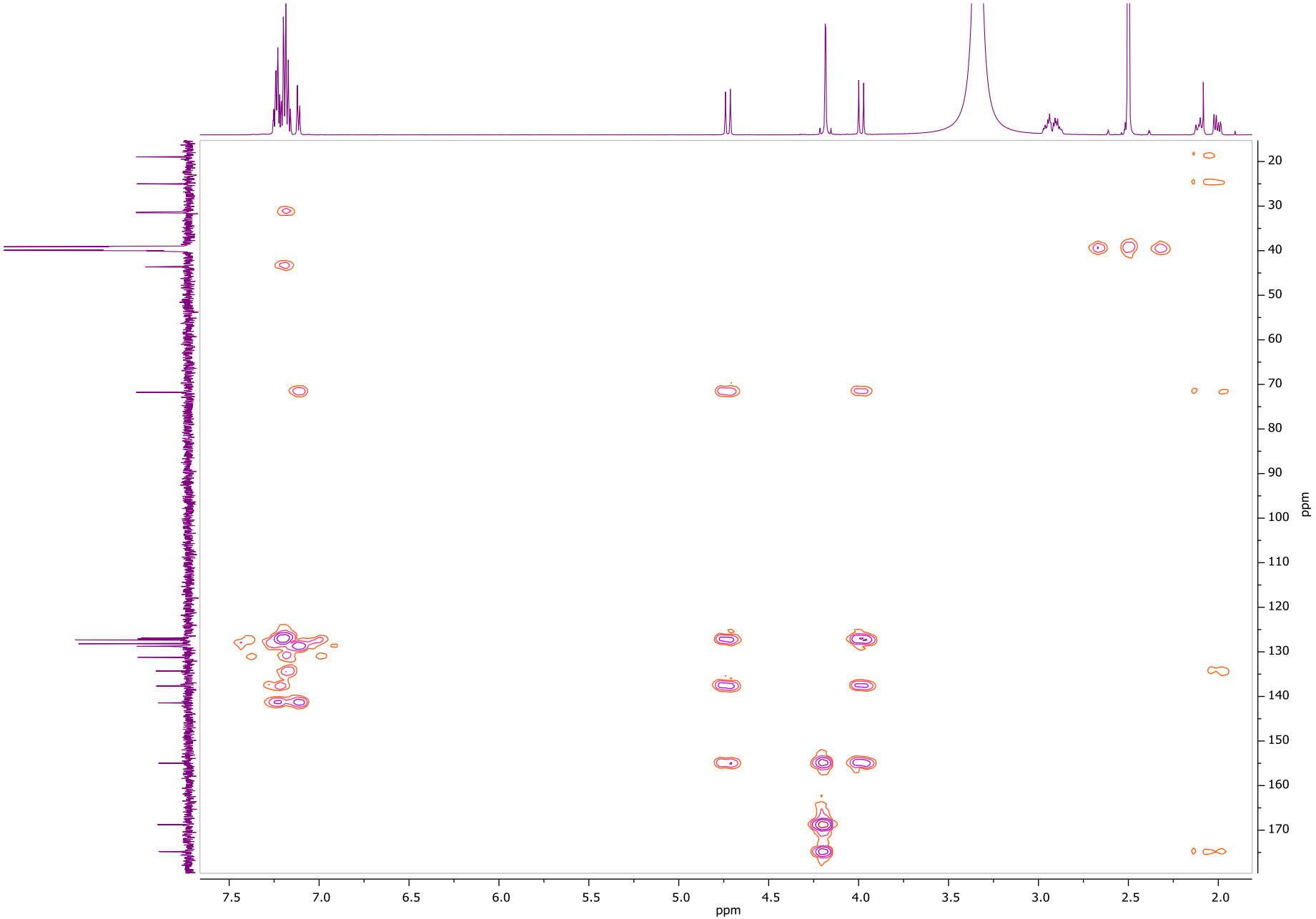
COSY NMR of **12b** (400.13 MHz, DMSO-d_6)



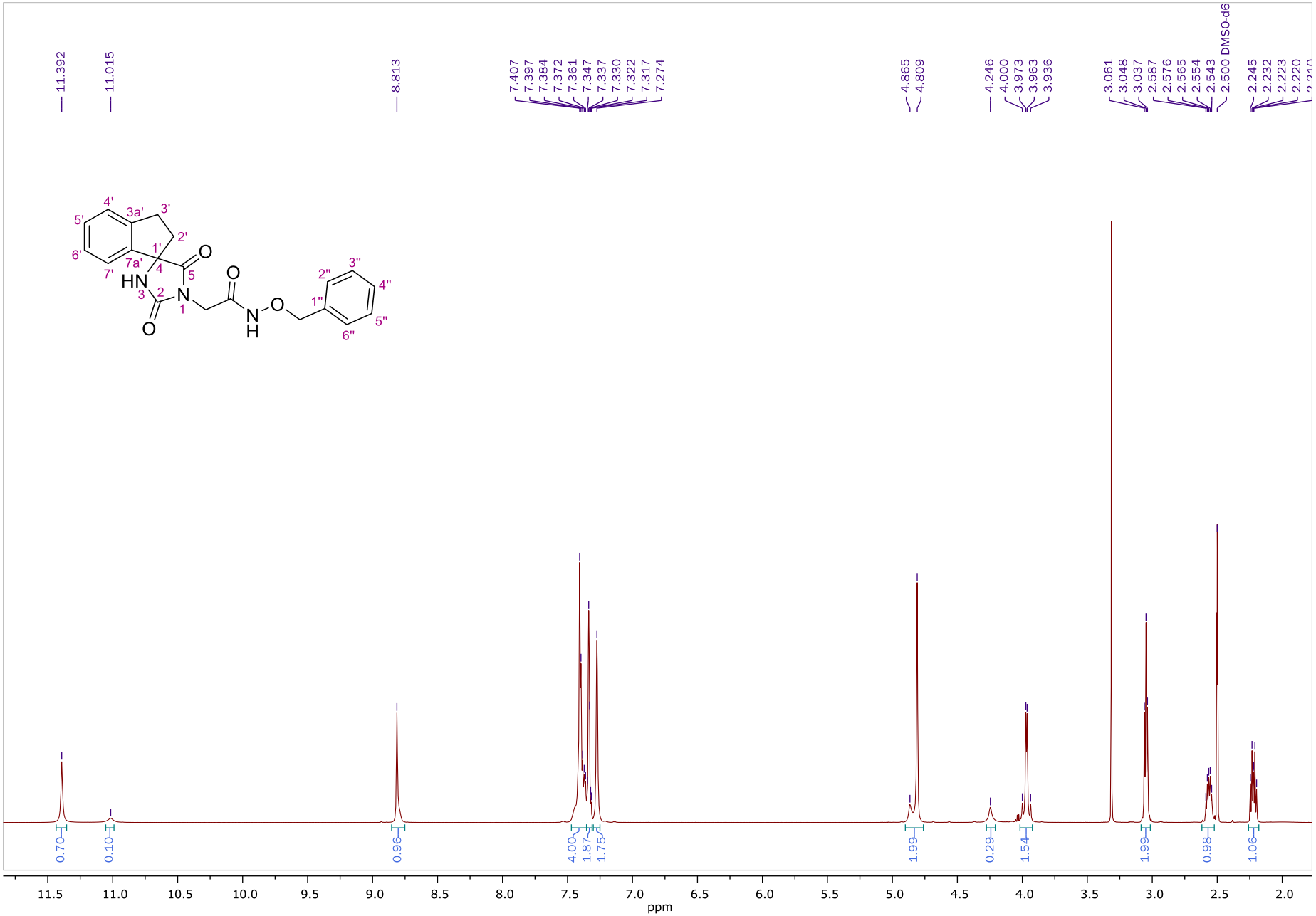
HSQC NMR of **12b** (400.13 MHz, DMSO-d_6)



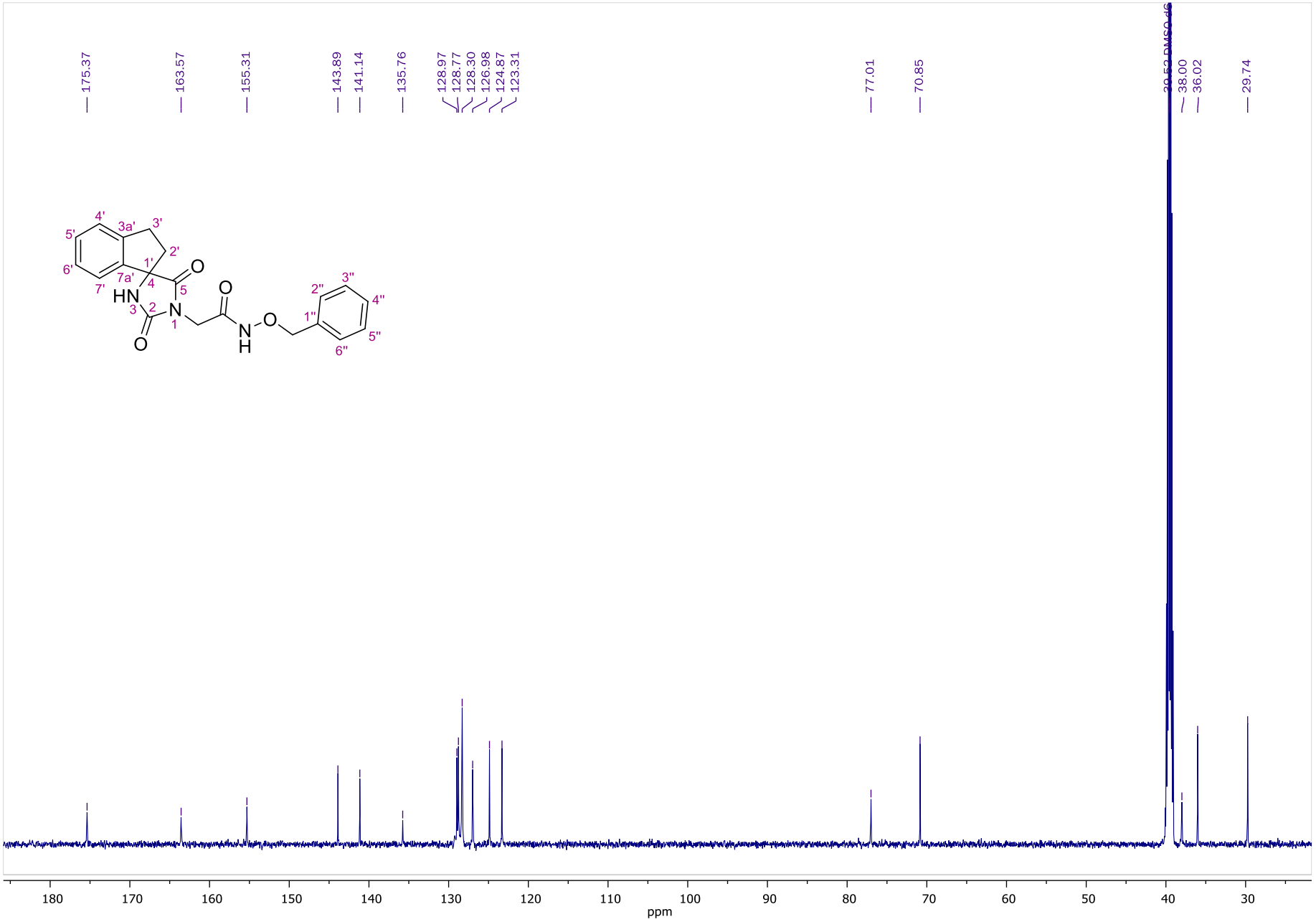
HMBC NMR of **12b** (400.13 MHz, DMSO-d_6)



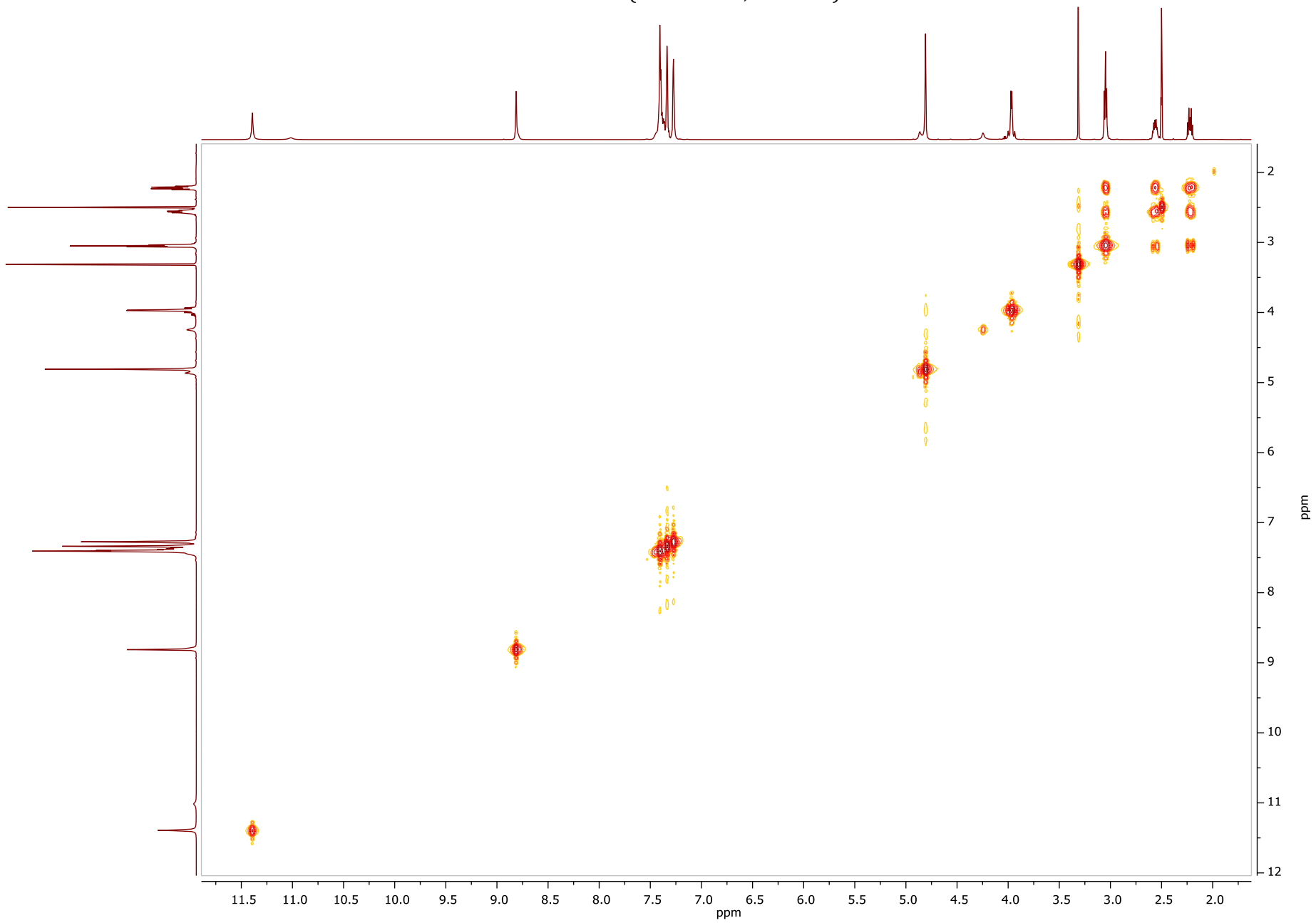
^{1}H NMR of **13** (600.11 MHz, DMSO-d_6)



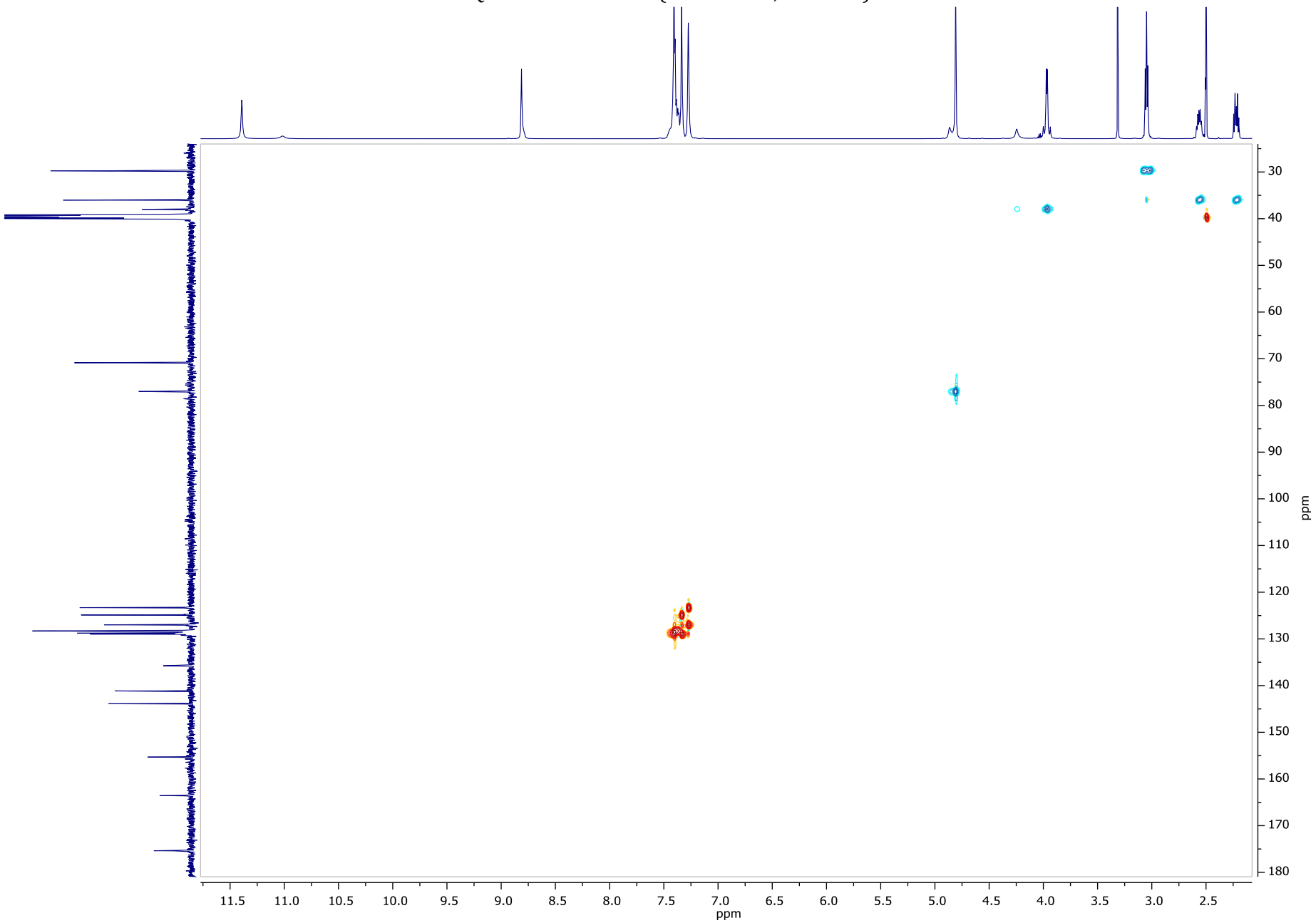
^{13}C NMR of **13** (150.9 MHz, DMSO-d_6)



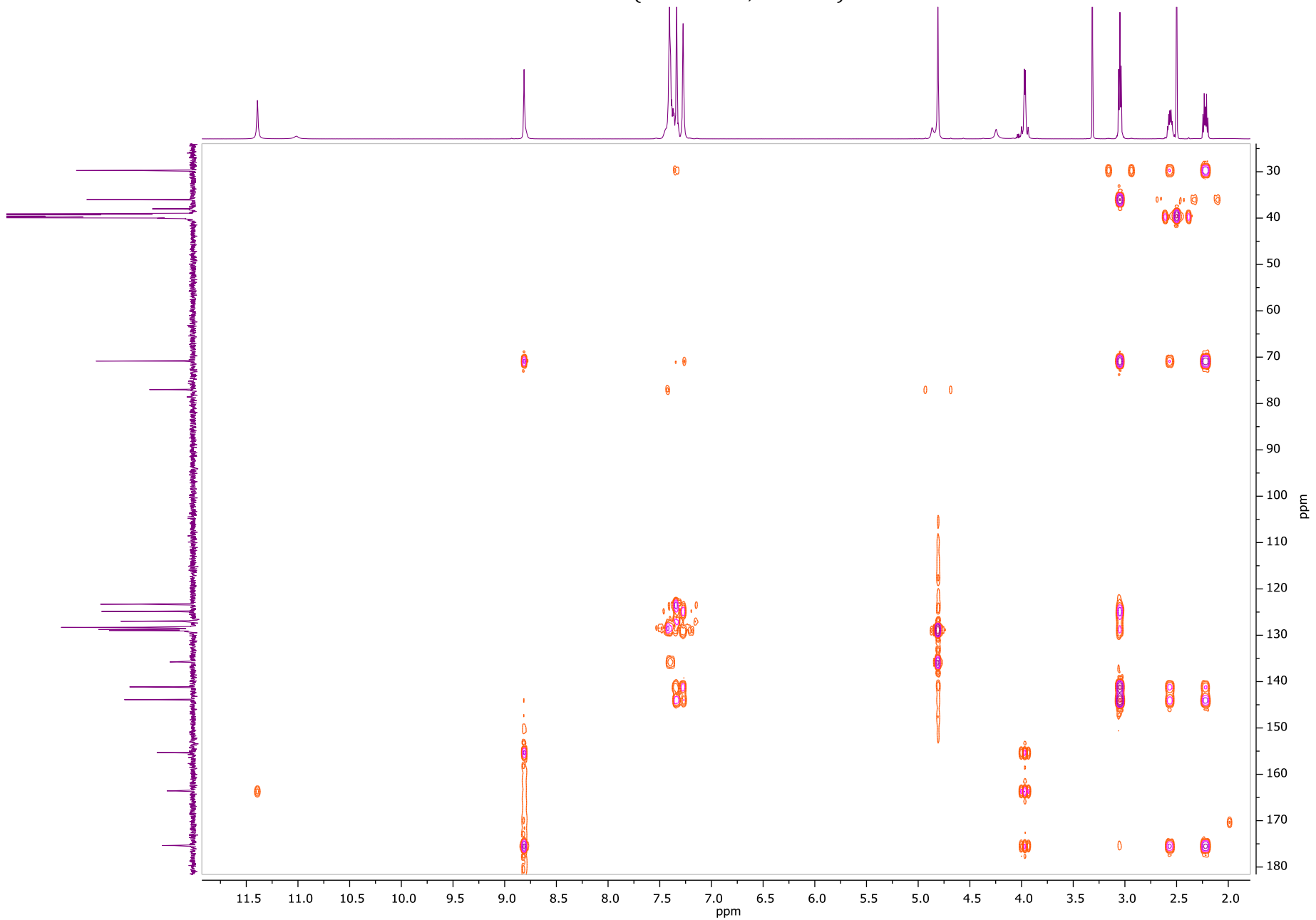
COSY NMR of **13** (600.11 MHz, DMSO-d_6)



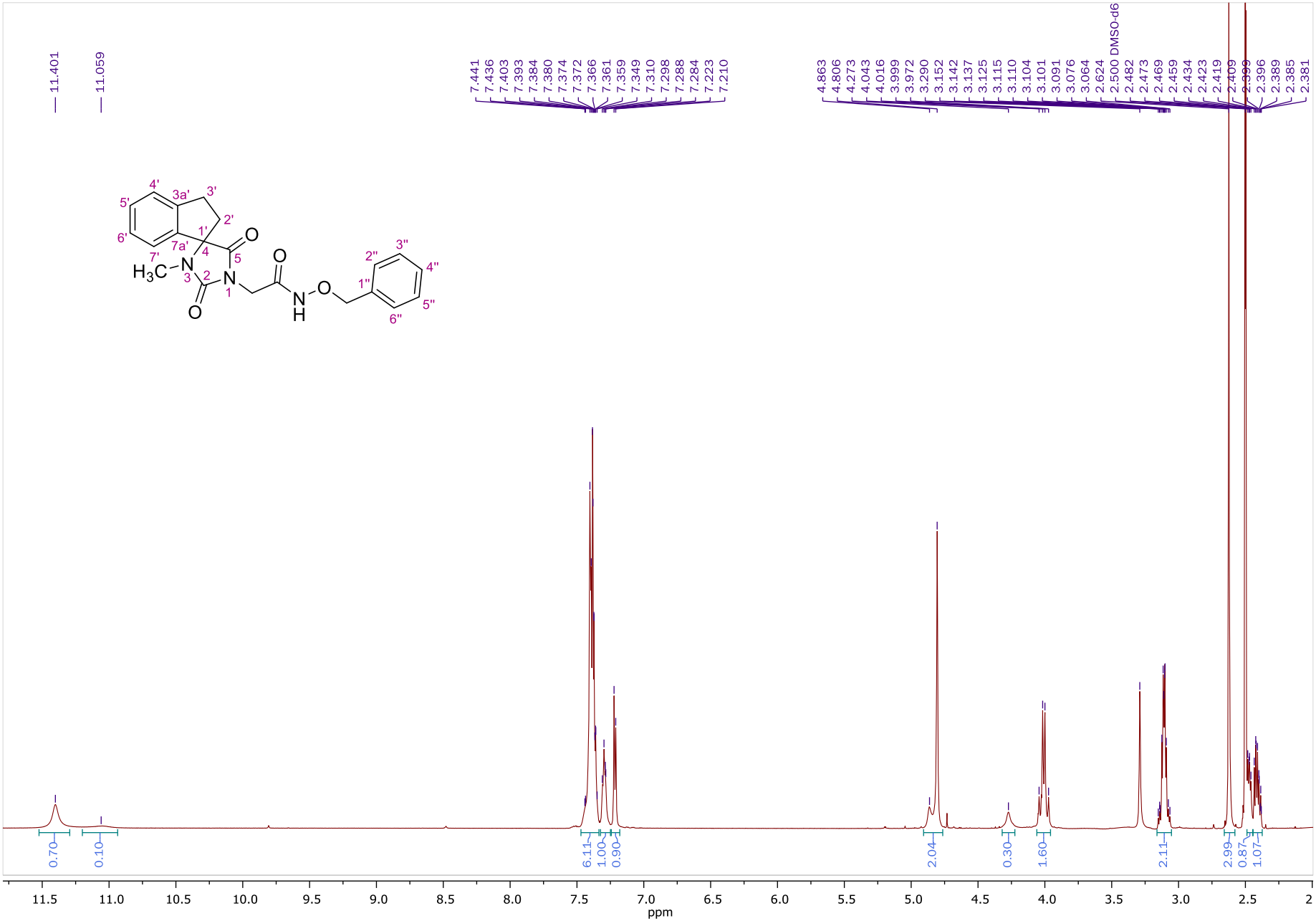
HSQC-DEPT NMR of **13** (600.11 MHz, DMSO-d_6)



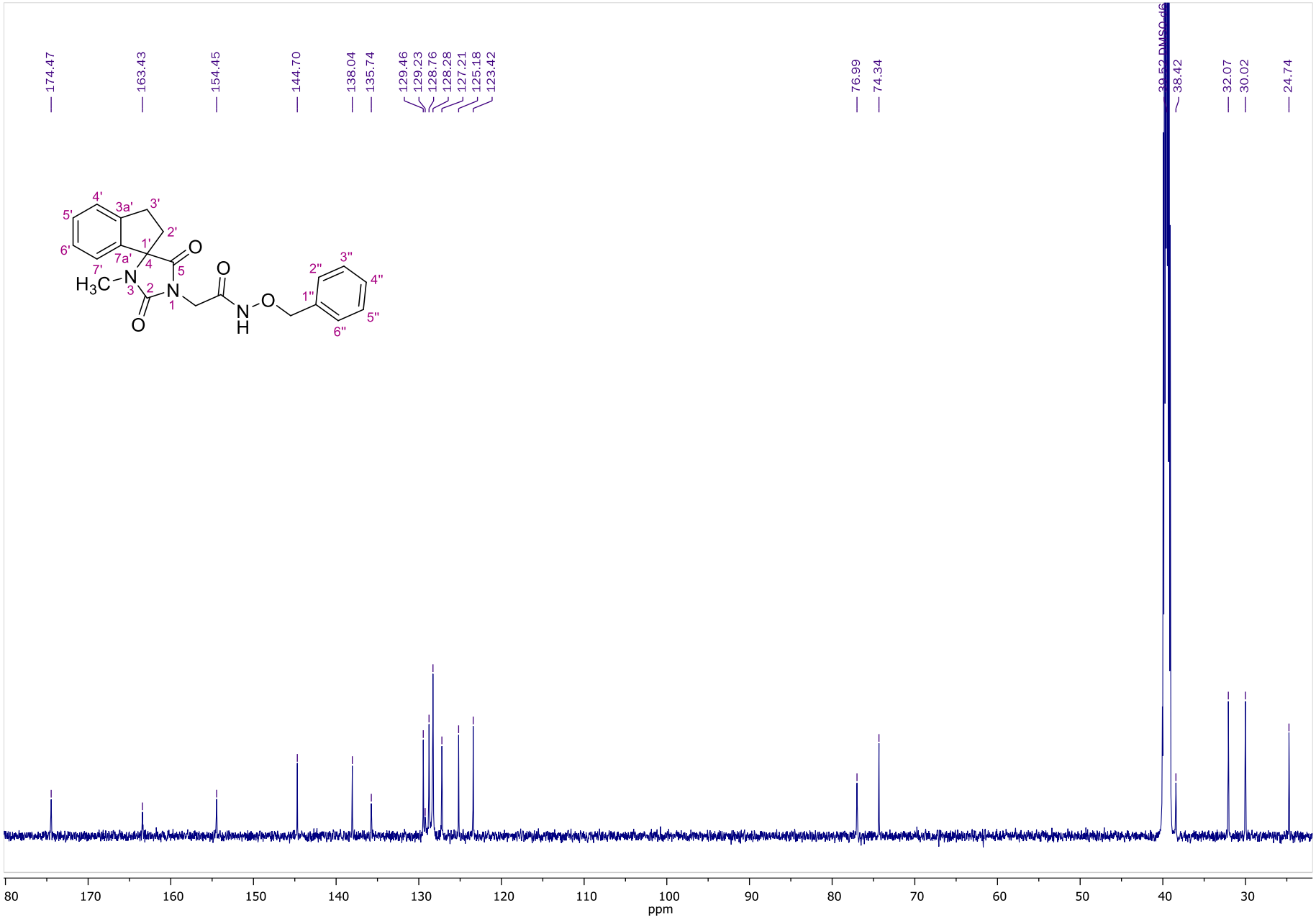
HMBC NMR of **13** (600.11 MHz, DMSO-d_6)



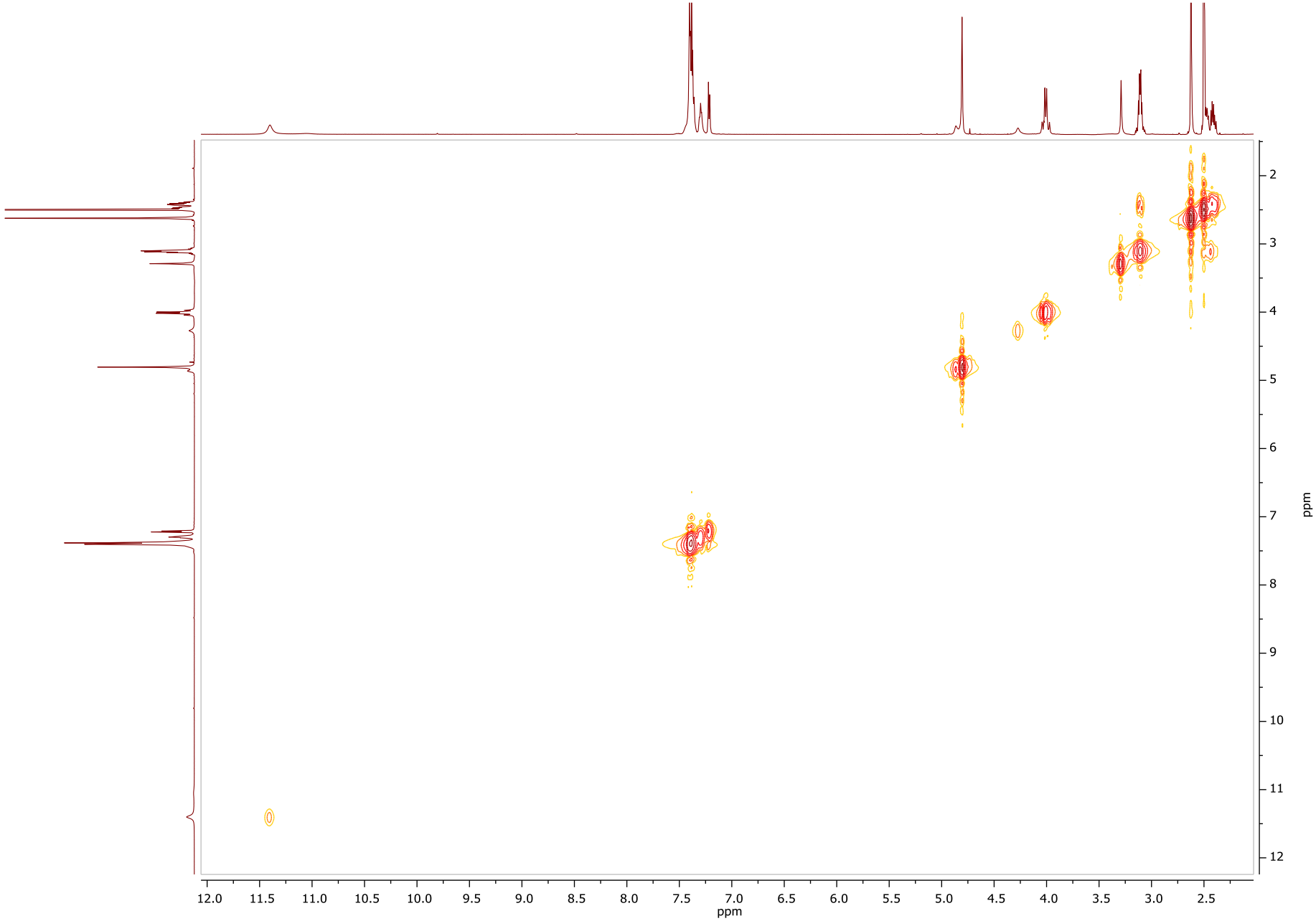
^{1}H NMR of **13a** (600.11 MHz, DMSO-d_6)



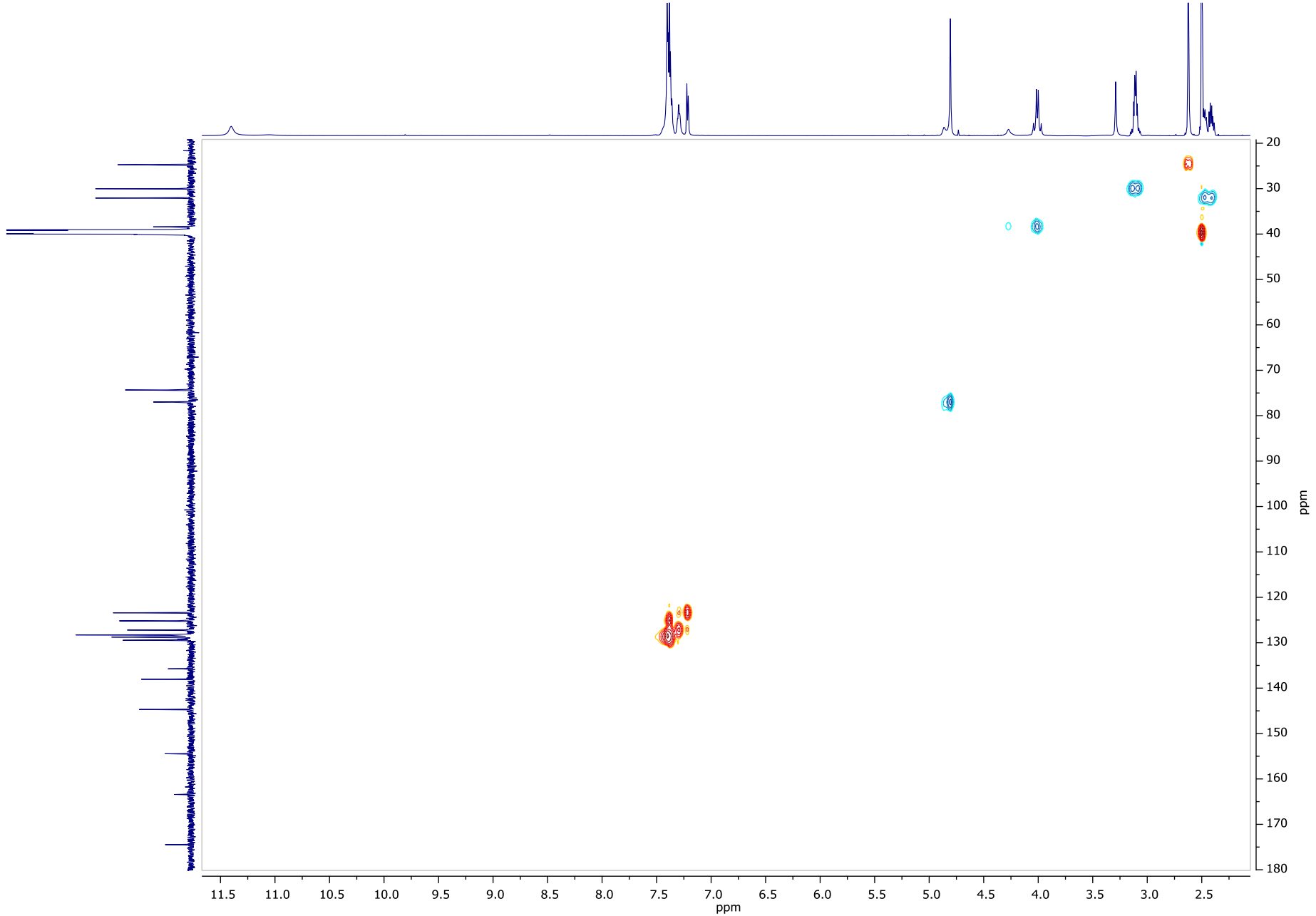
^{13}C NMR of **13a** (150.9 MHz, DMSO-d_6)



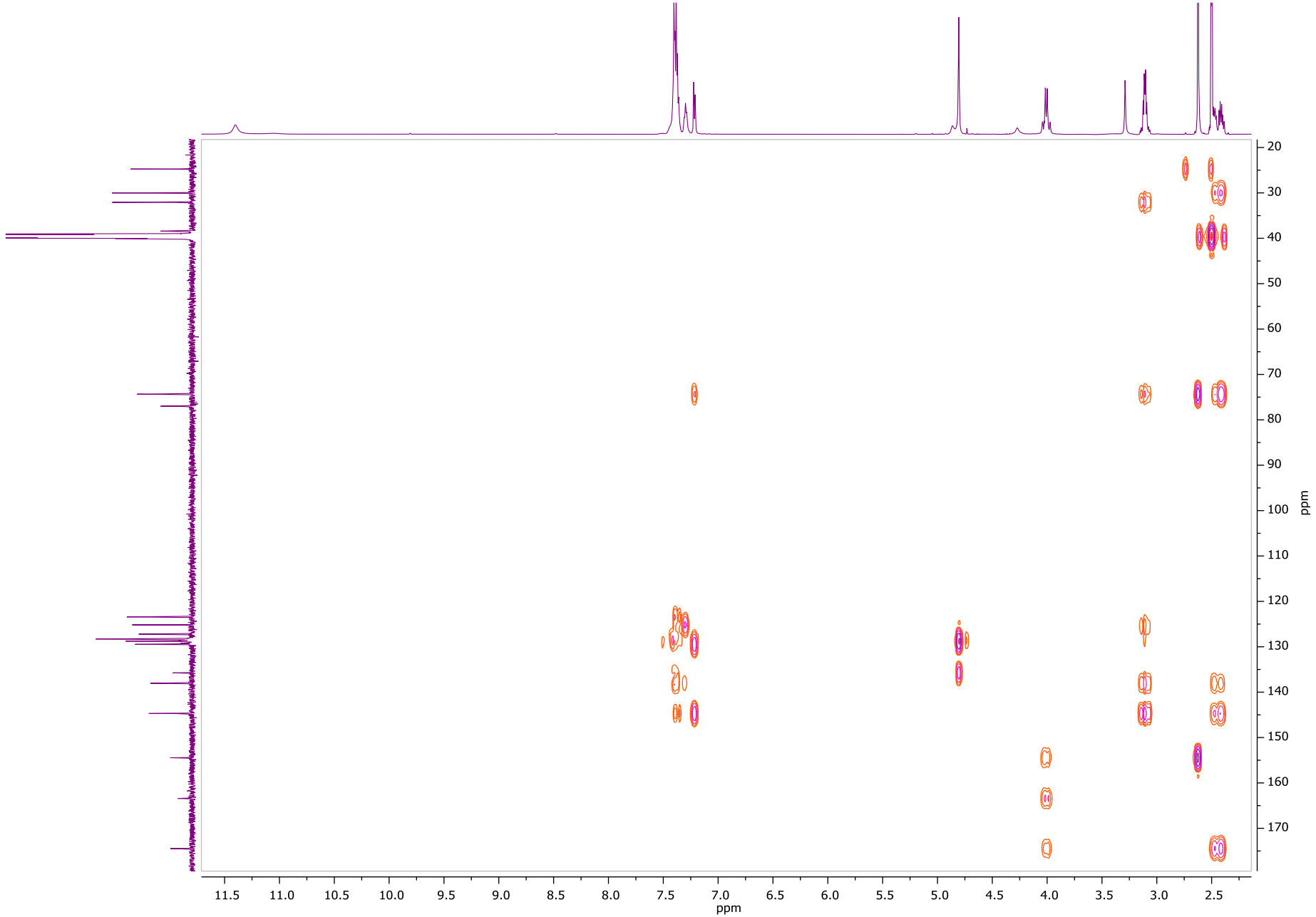
COSY NMR of **13a** (600.11 MHz, DMSO-d_6)



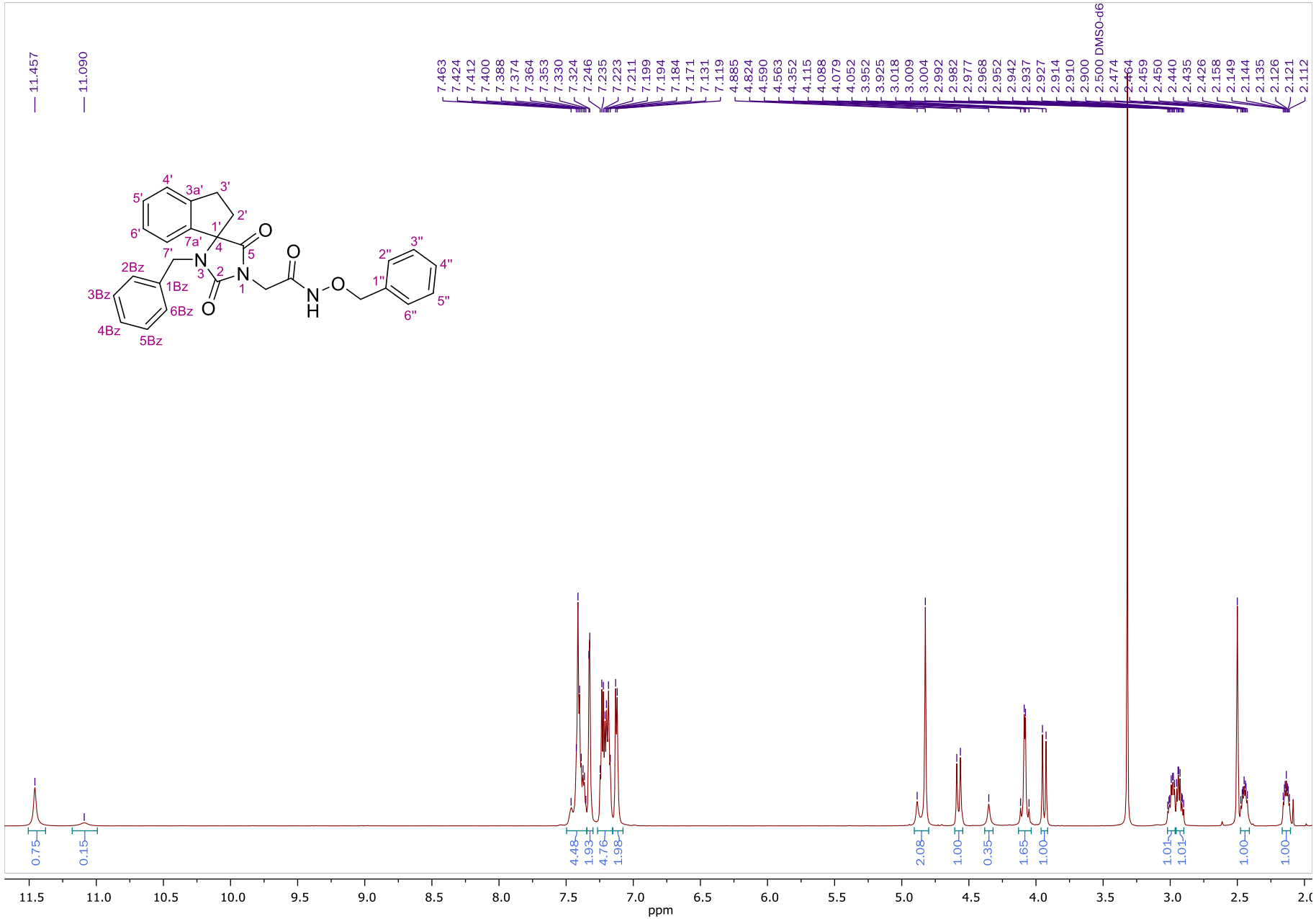
HSQC-DEPT NMR of **13a** (600.11 MHz, DMSO-d_6)



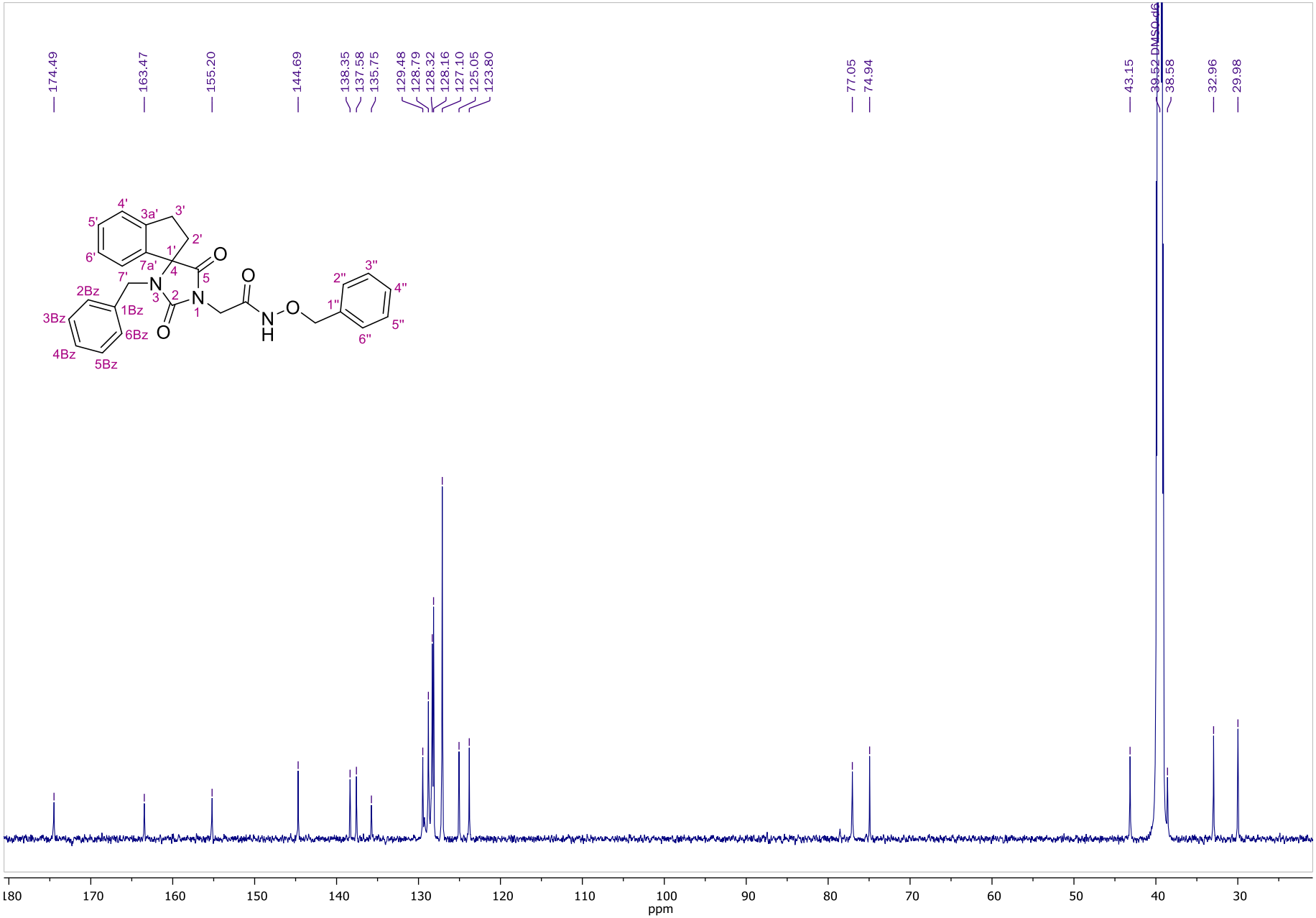
HMBC NMR of **13a** (600.11 MHz, DMSO-d_6)



^{1}H NMR of **13b** (600.11 MHz, DMSO-d_6)

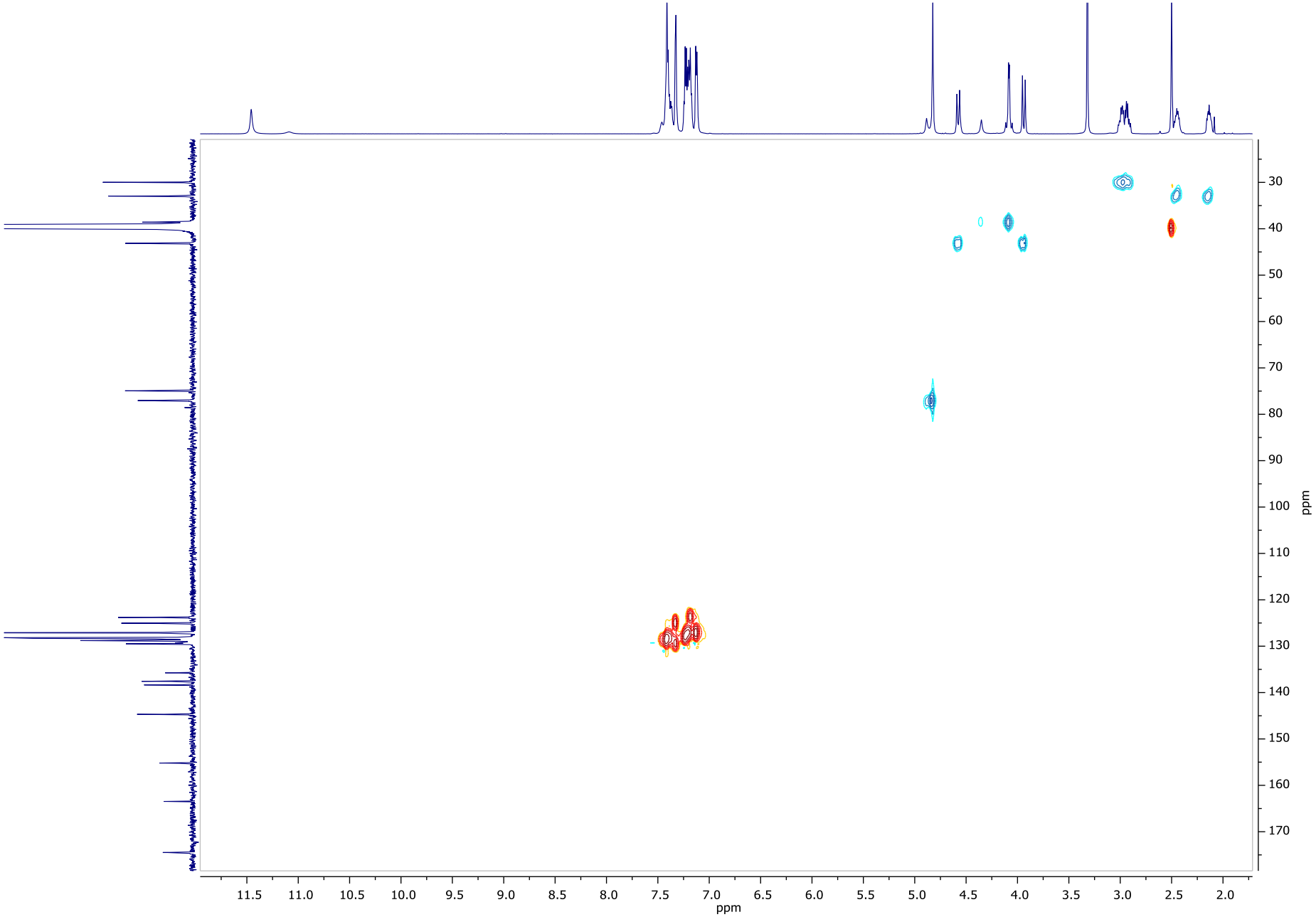


^{13}C NMR of **13b** (150.9 MHz, DMSO-d_6)



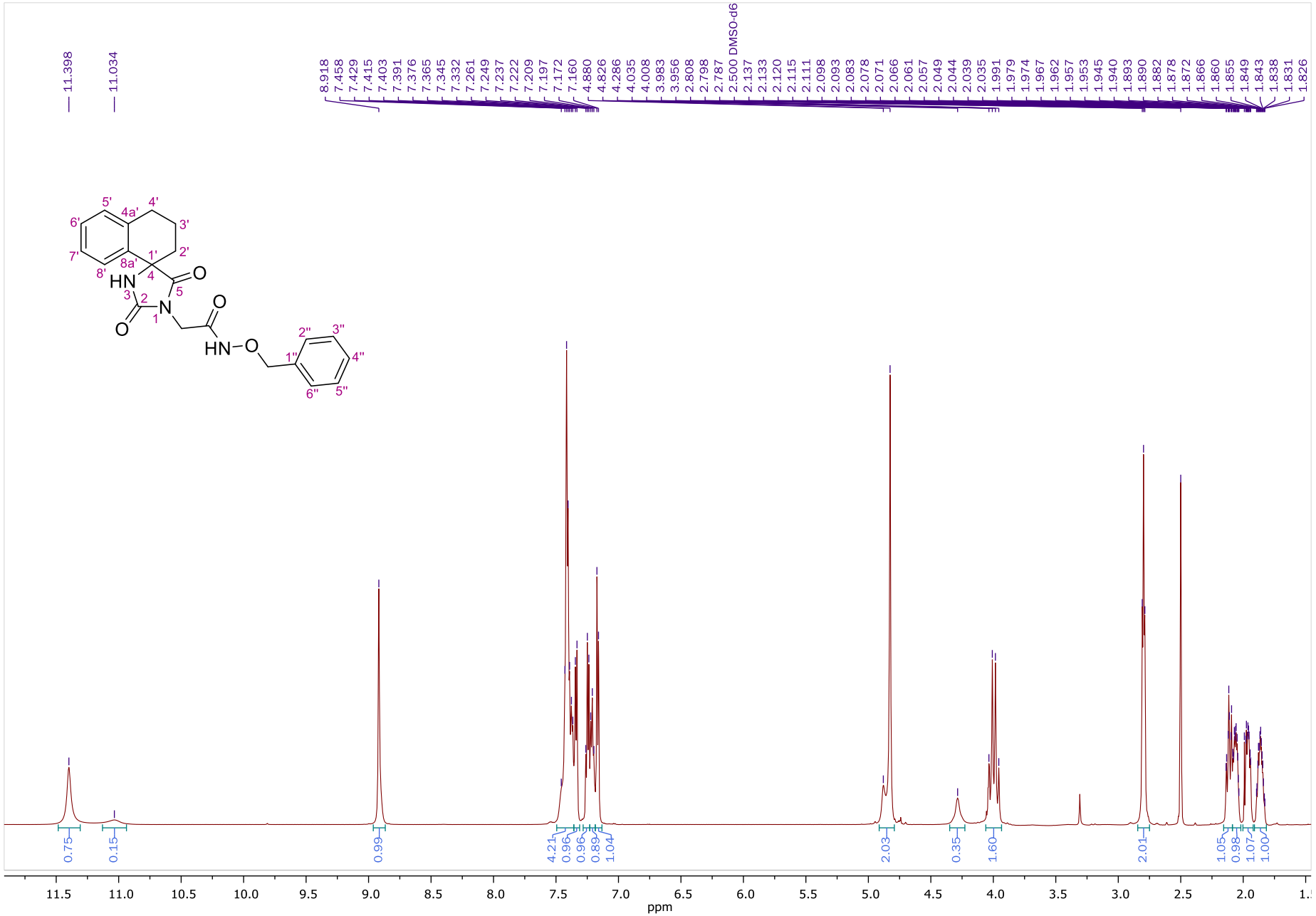
COSY NMR of **13b** (600.11 MHz, DMSO-d_6)

HSQC-DEPT NMR of **13b** (600.11 MHz, DMSO-d_6)

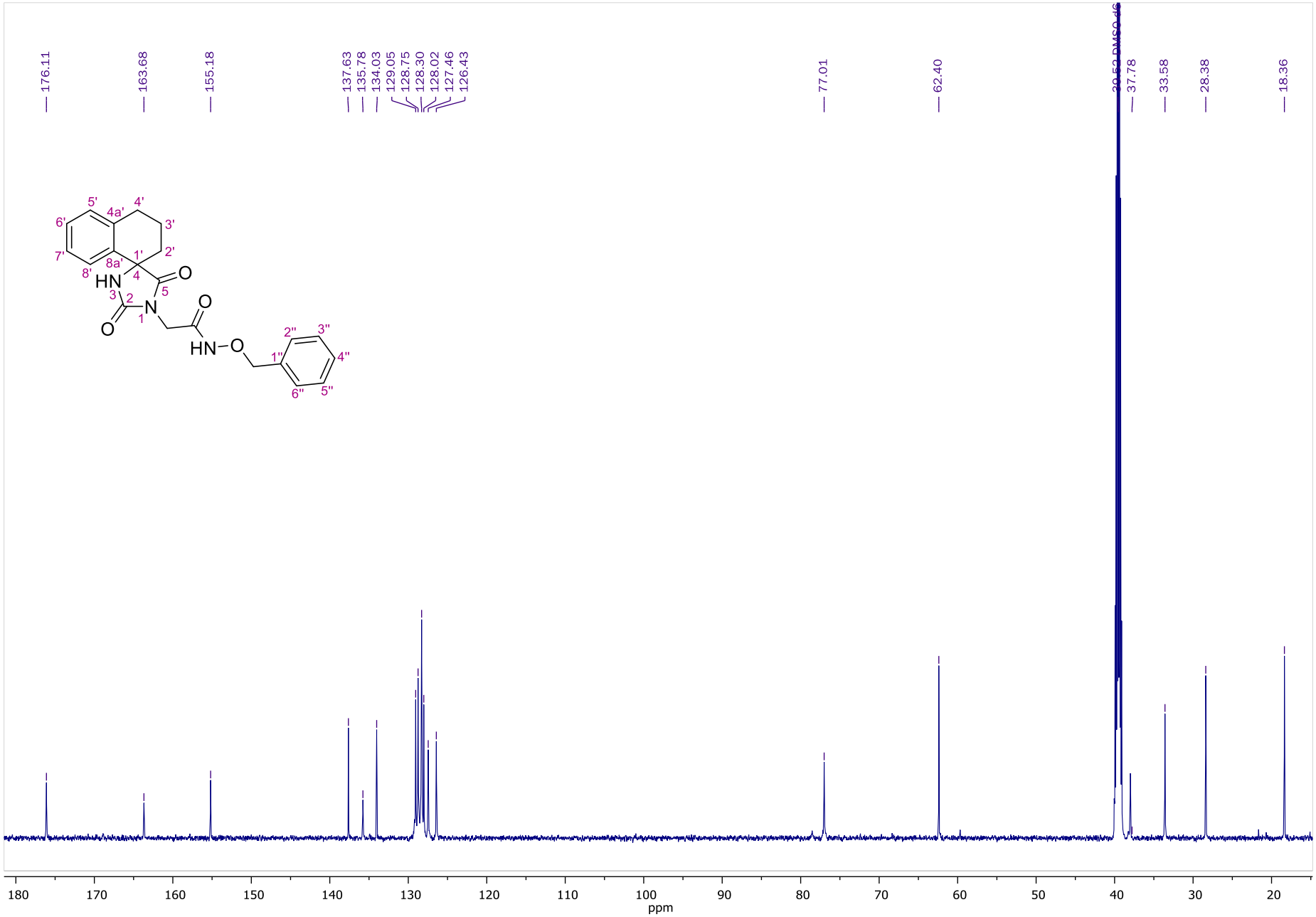


HMBC NMR of **13b** (600.11 MHz, DMSO-d_6)

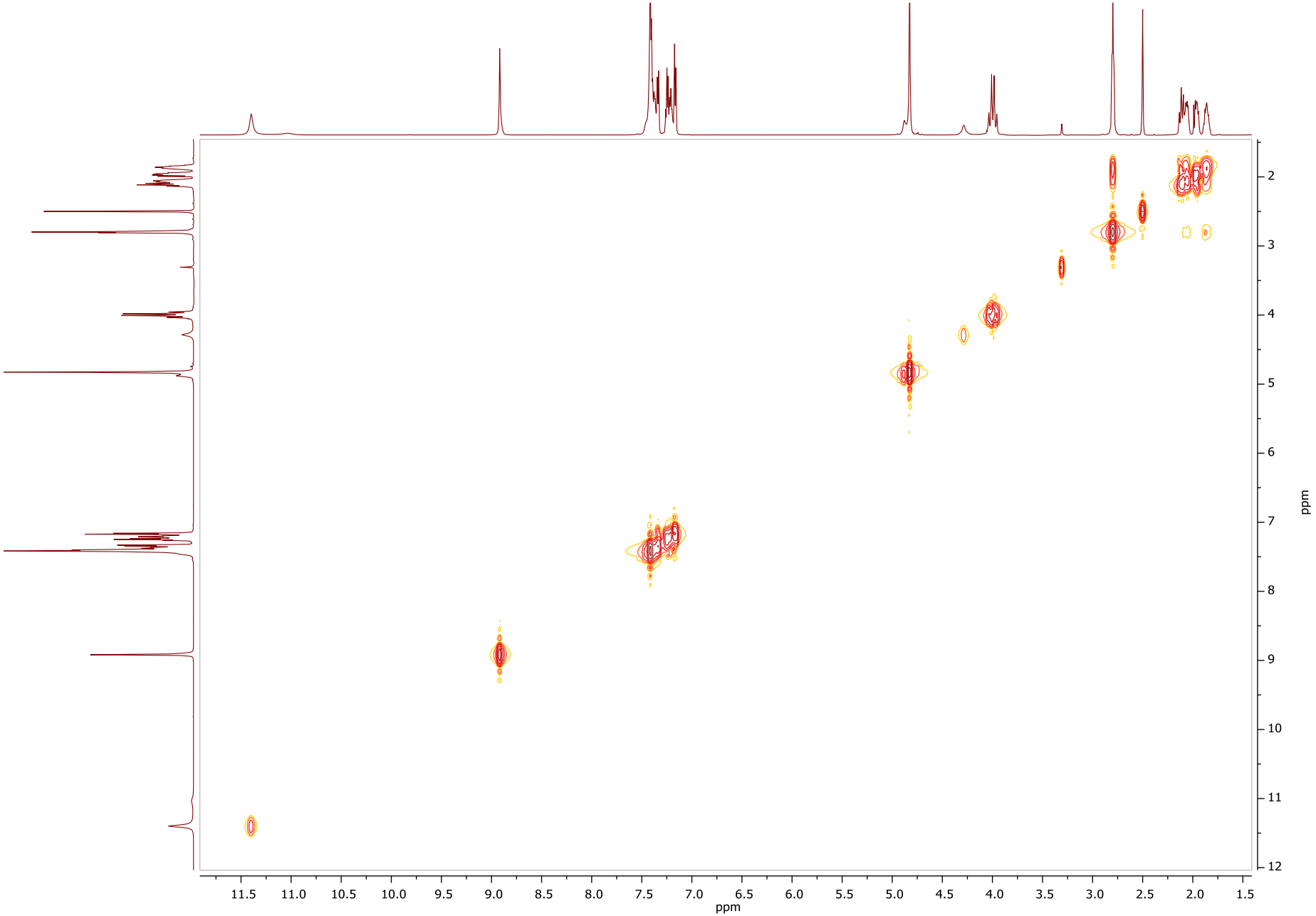
^{1}H NMR of **14** (600.11 MHz, DMSO-d_6)



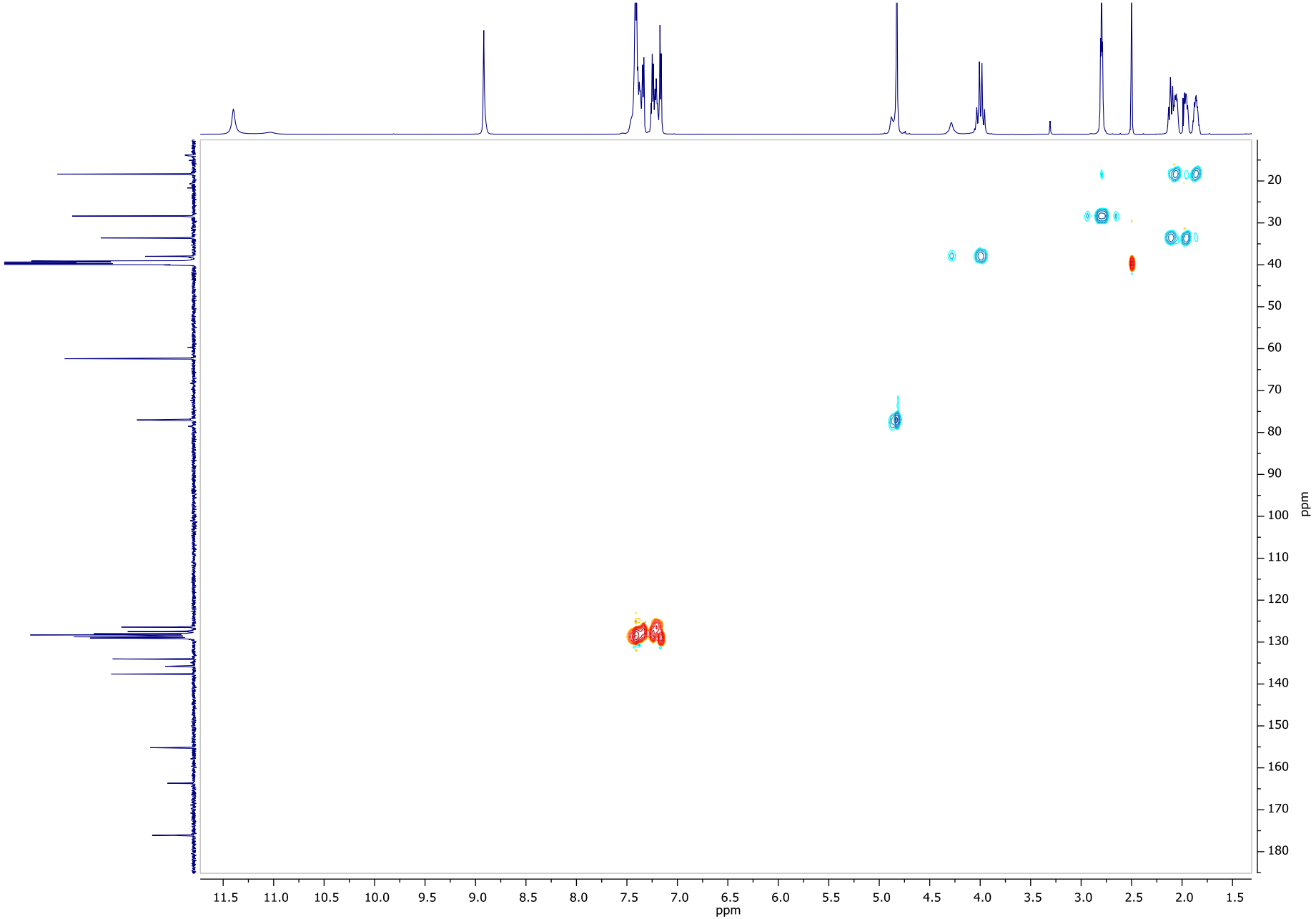
^{13}C NMR of **14** (150.9 MHz, DMSO-d_6)



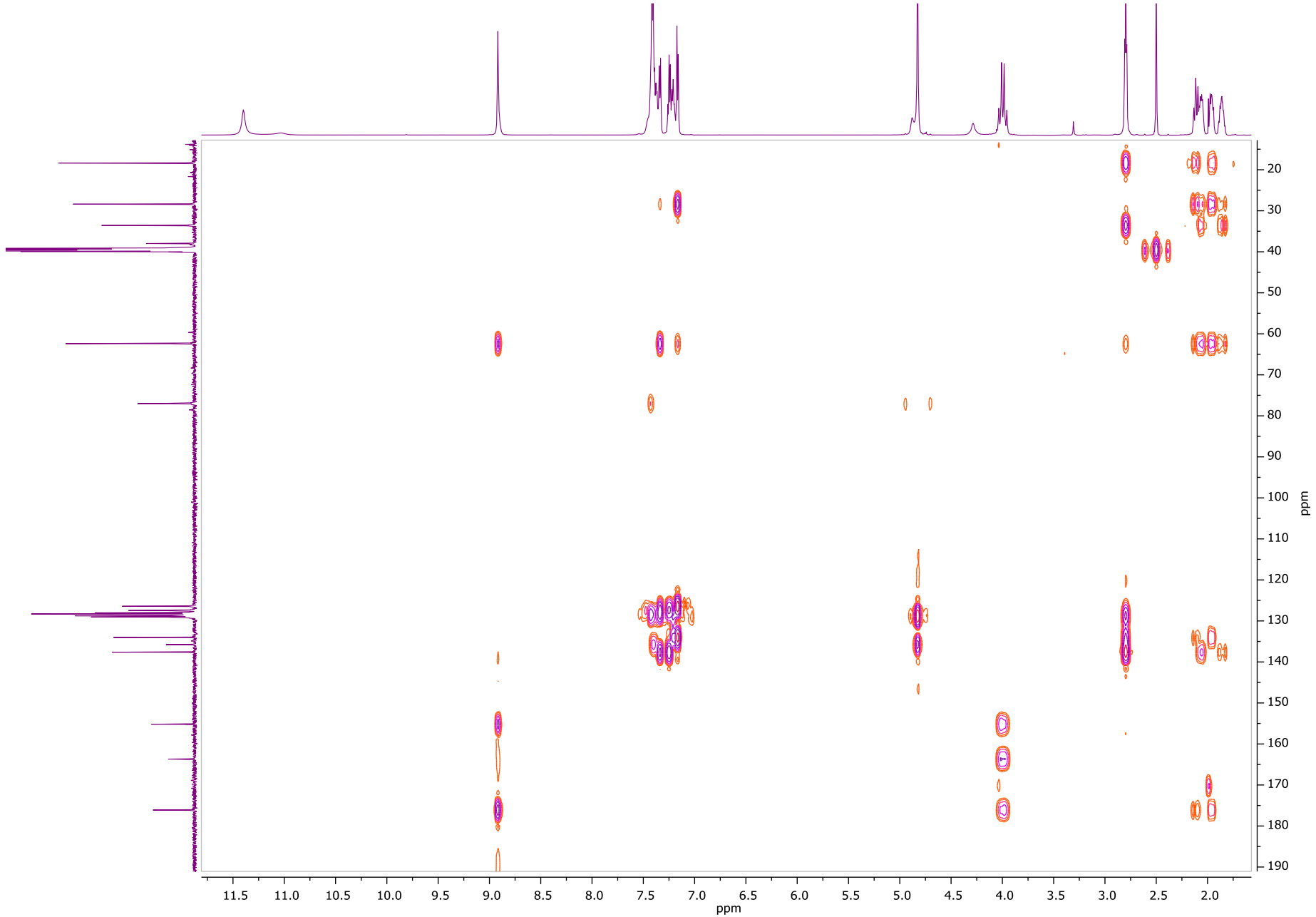
COSY NMR of **14** (600.11 MHz, DMSO-d_6)



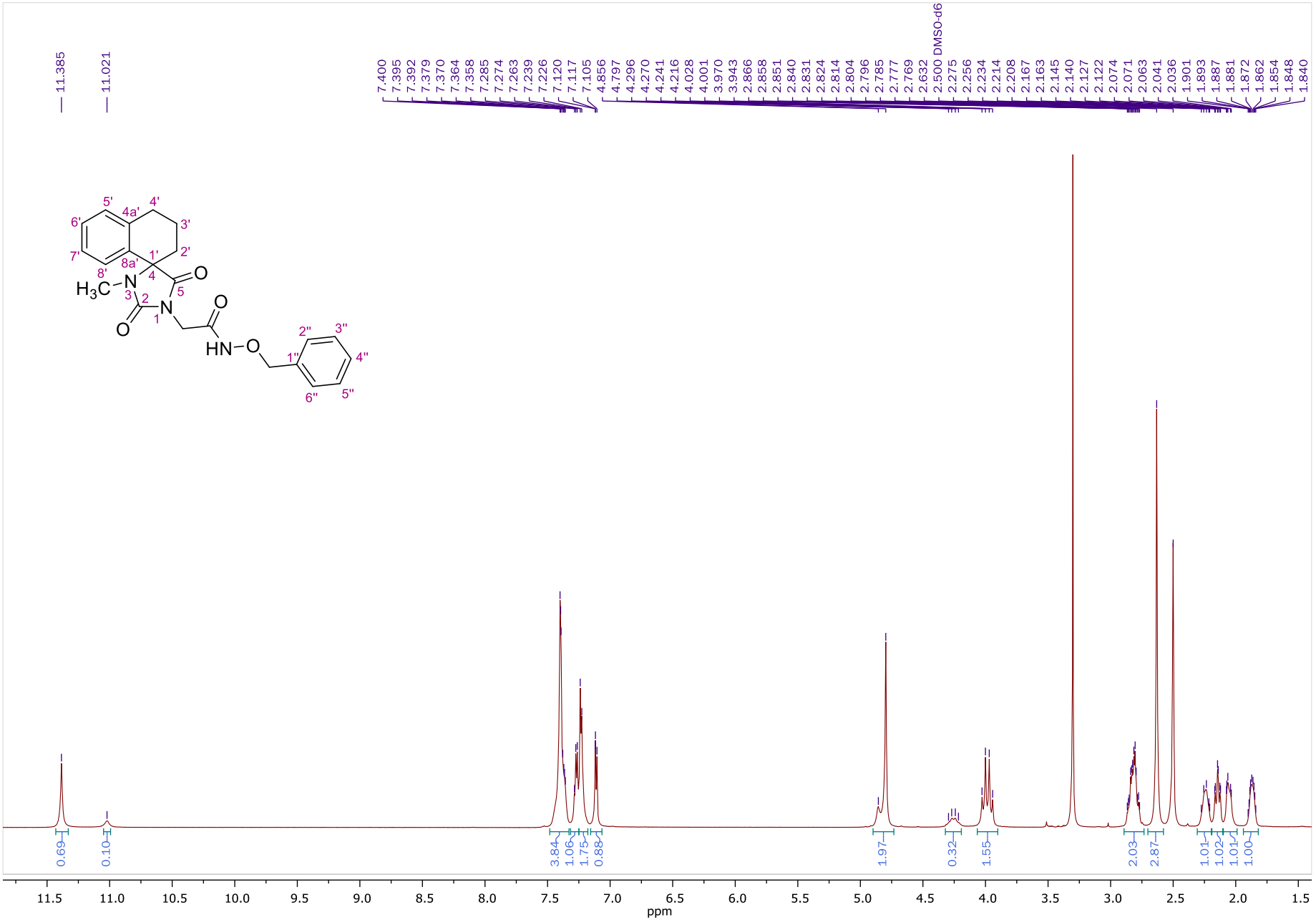
HSQC-DEPT NMR of **14** (600.11 MHz, DMSO-d_6)



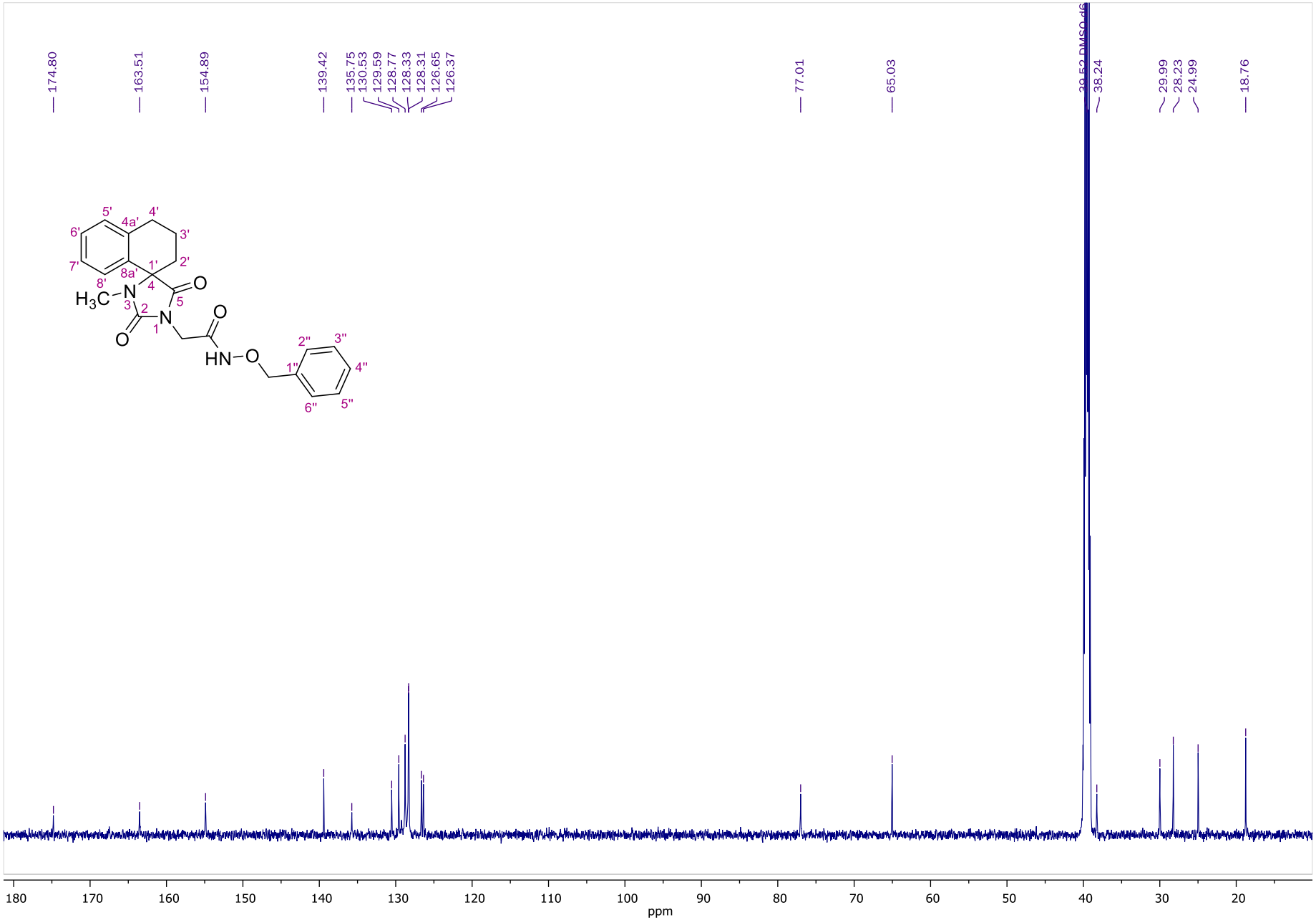
HMBC NMR of **14** (600.11 MHz, DMSO-d_6)



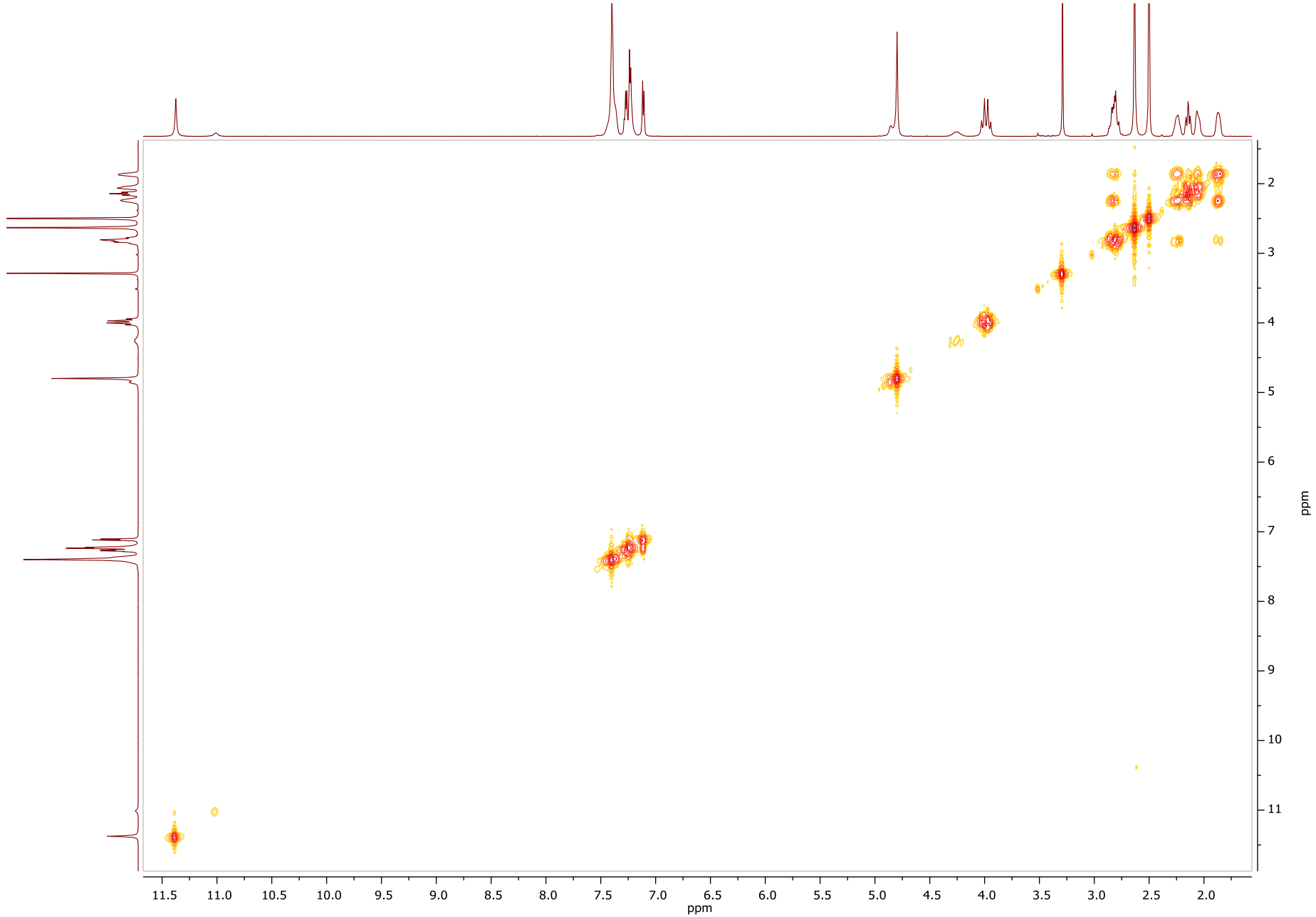
^{1}H NMR of **14a** (600.11 MHz, DMSO-d_6)



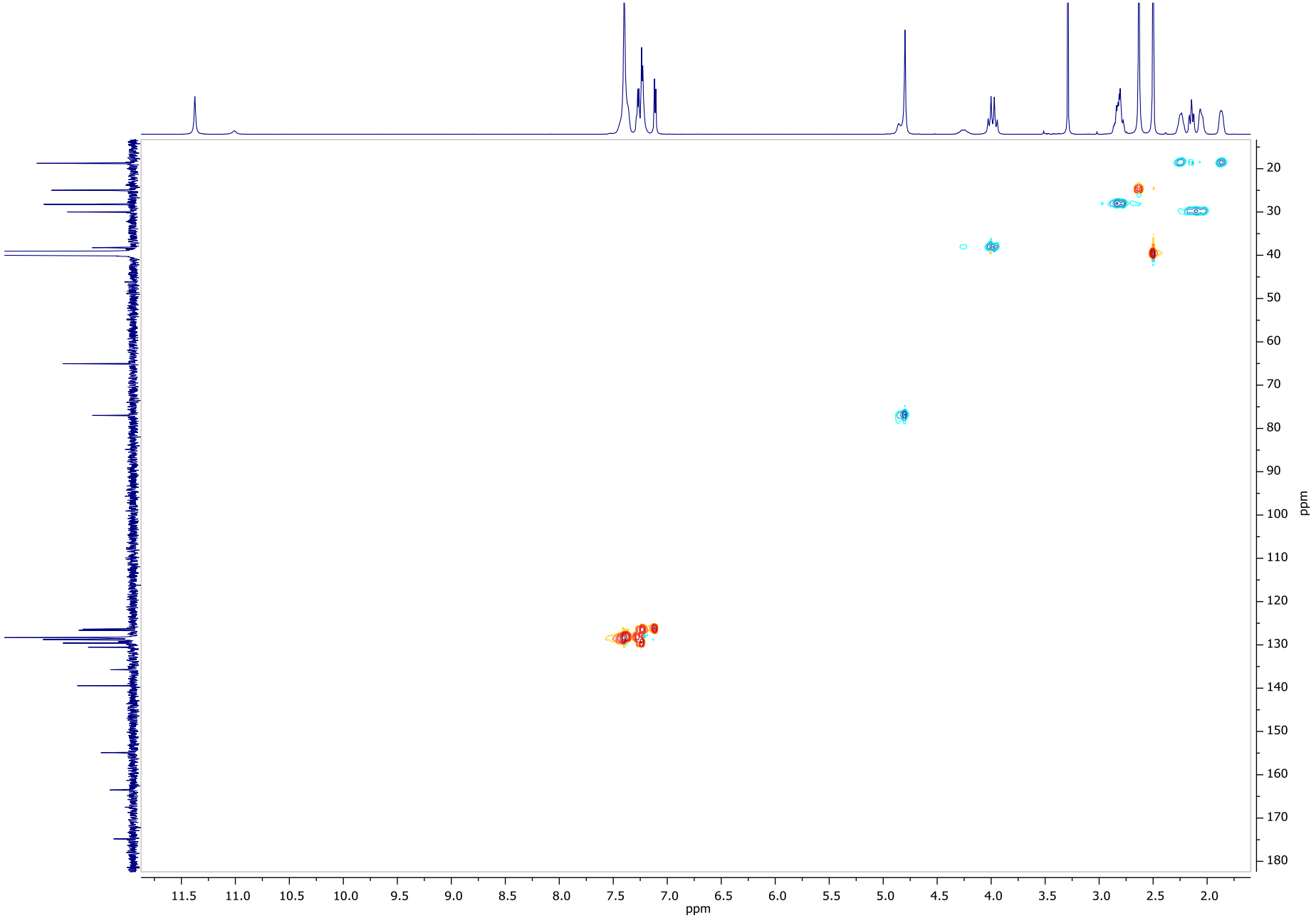
^{13}C NMR of **14a** (150.9 MHz, DMSO-d_6)



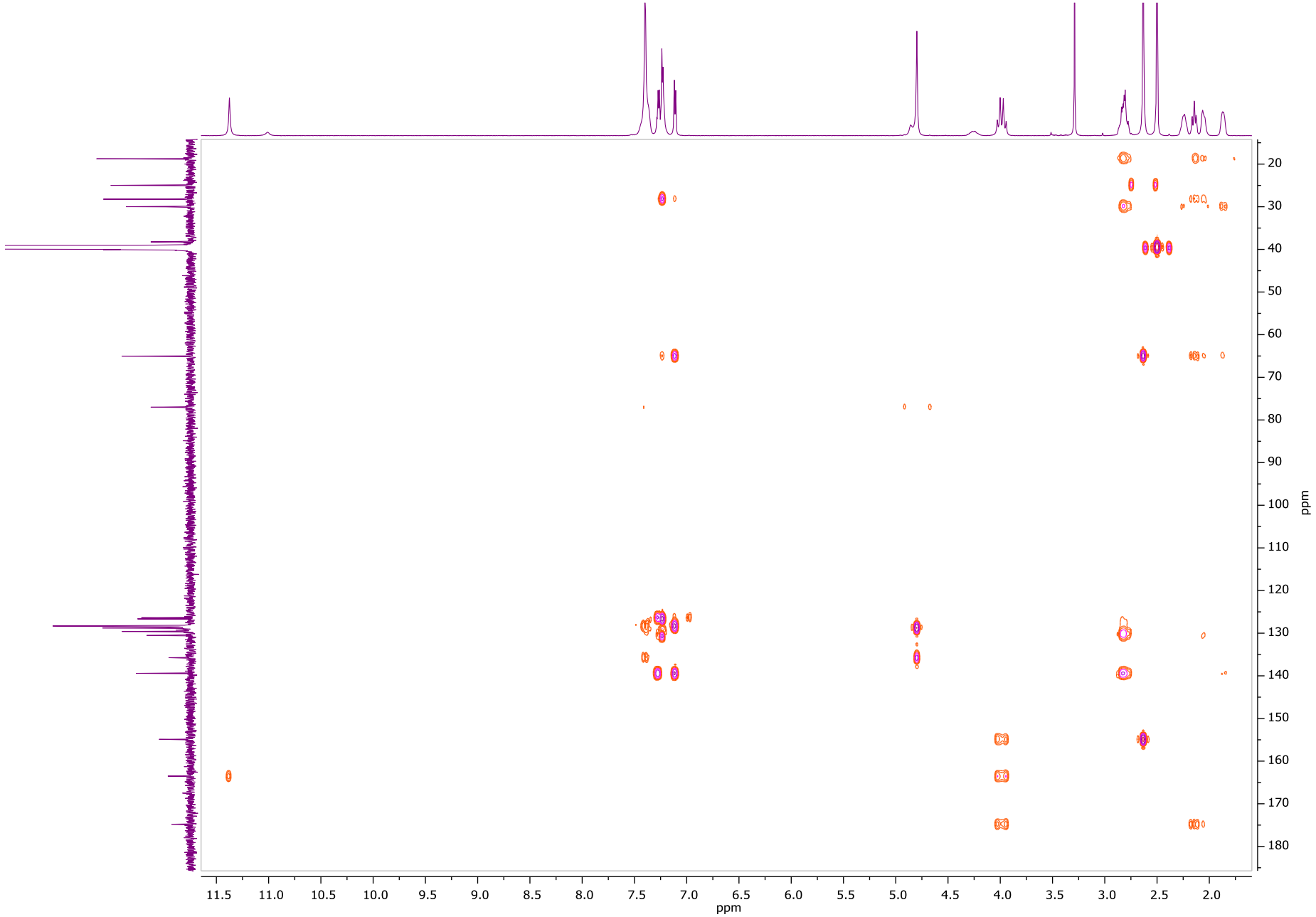
COSY NMR of **14a** (600.11 MHz, DMSO-d_6)



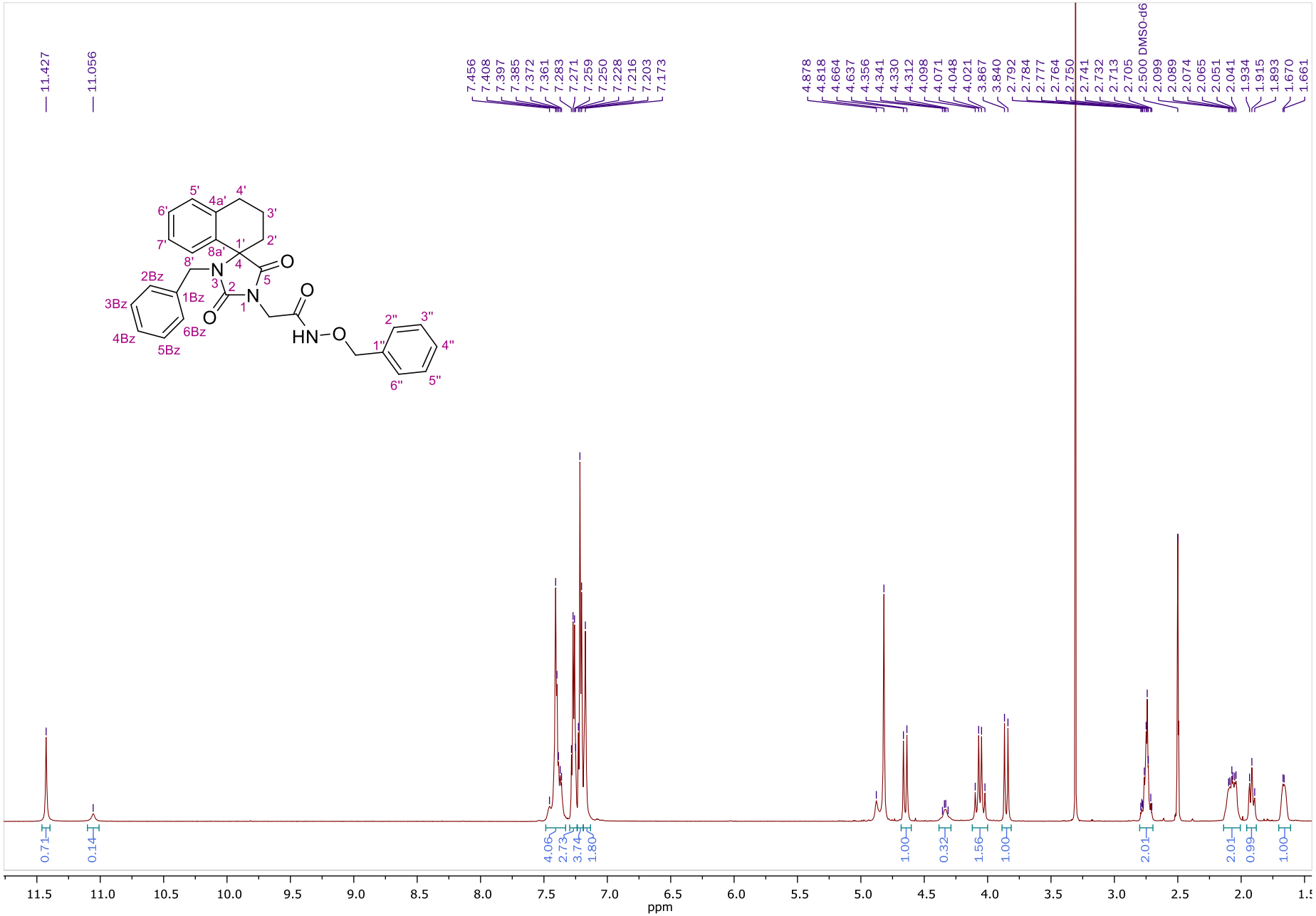
HSQC-DEPT NMR of **14a** (600.11 MHz, DMSO-d_6)



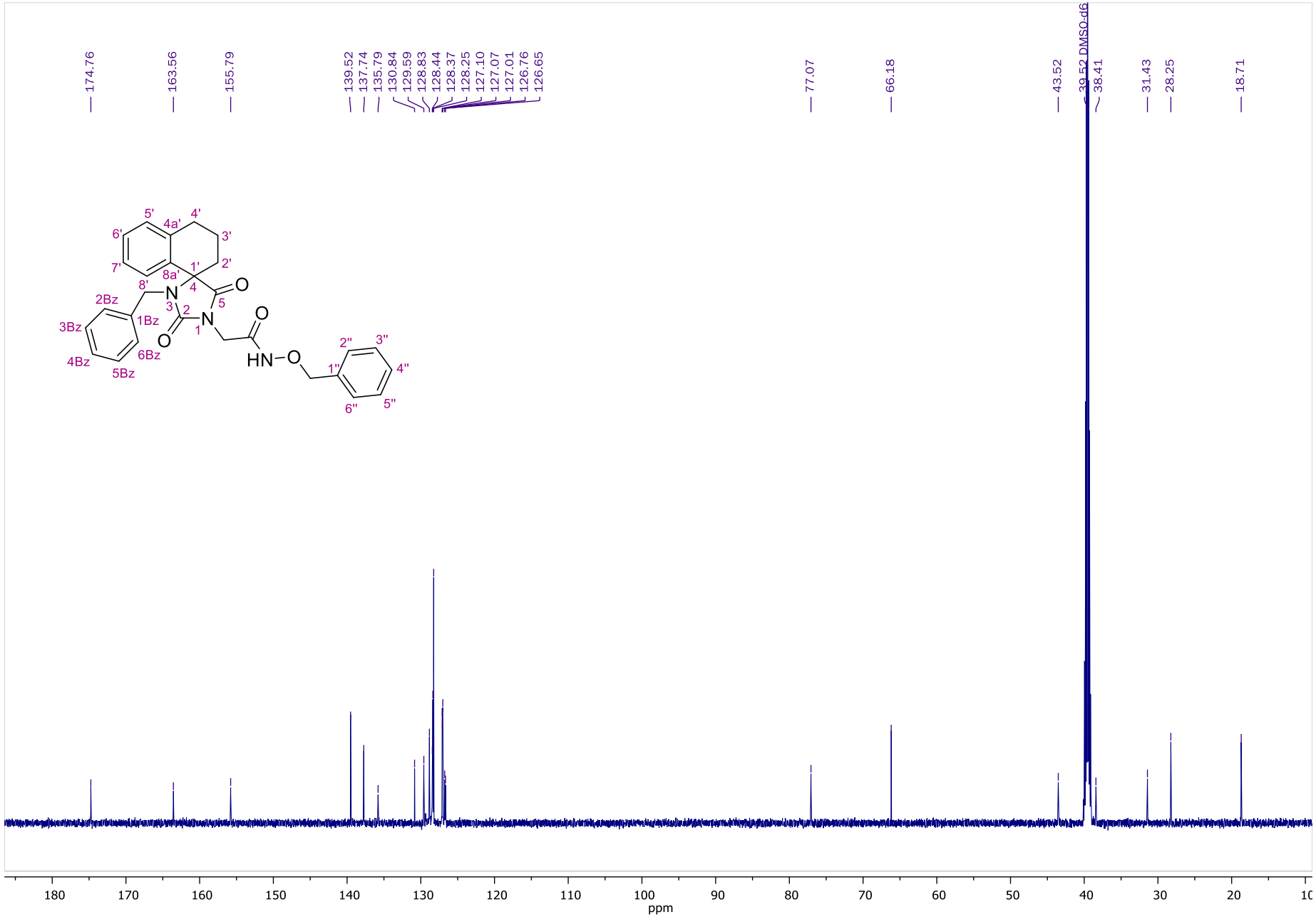
HMBC NMR of **14a** (600.11 MHz, DMSO-d_6)



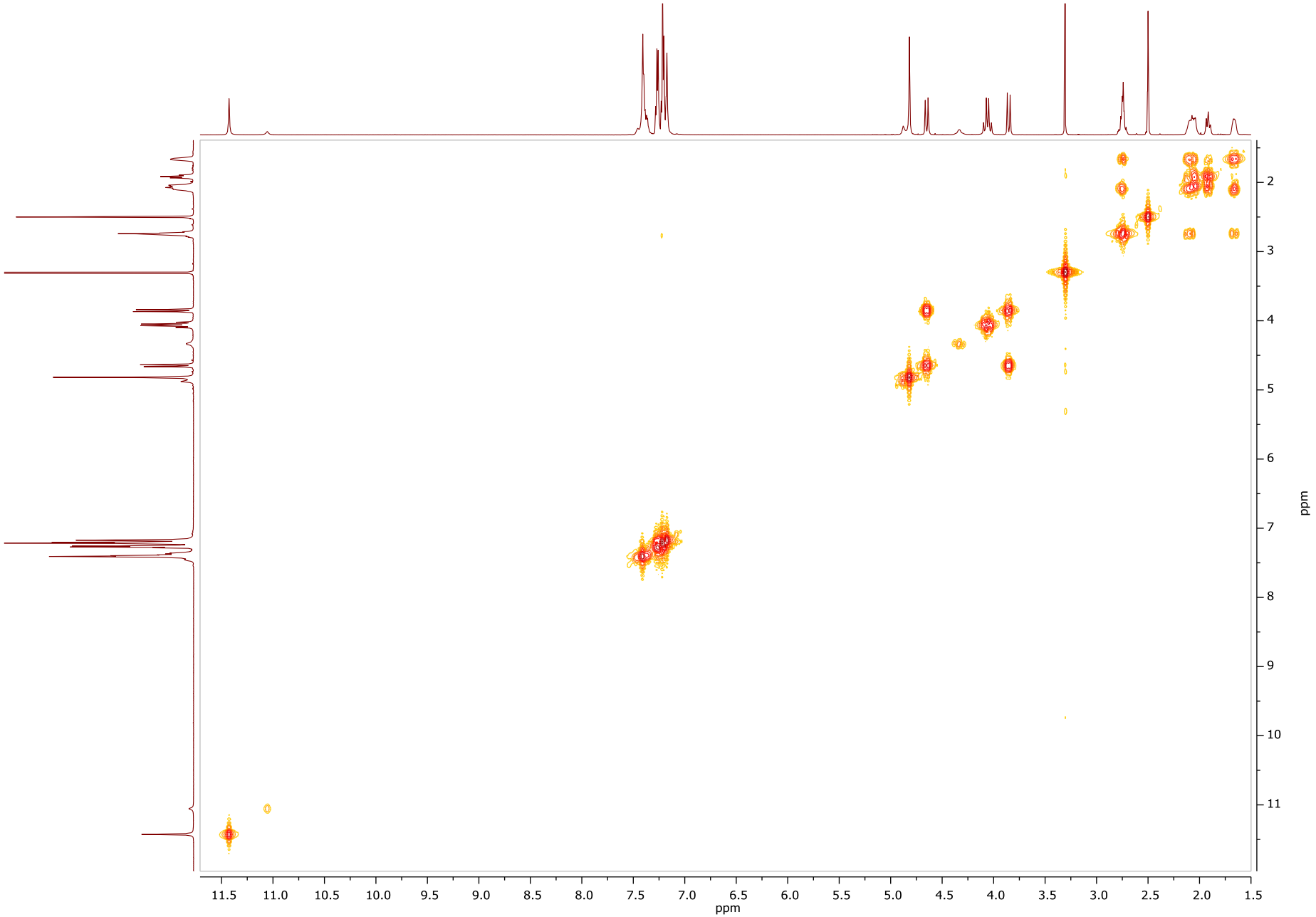
^{1}H NMR of **14b** (600.11 MHz, DMSO-d_6)



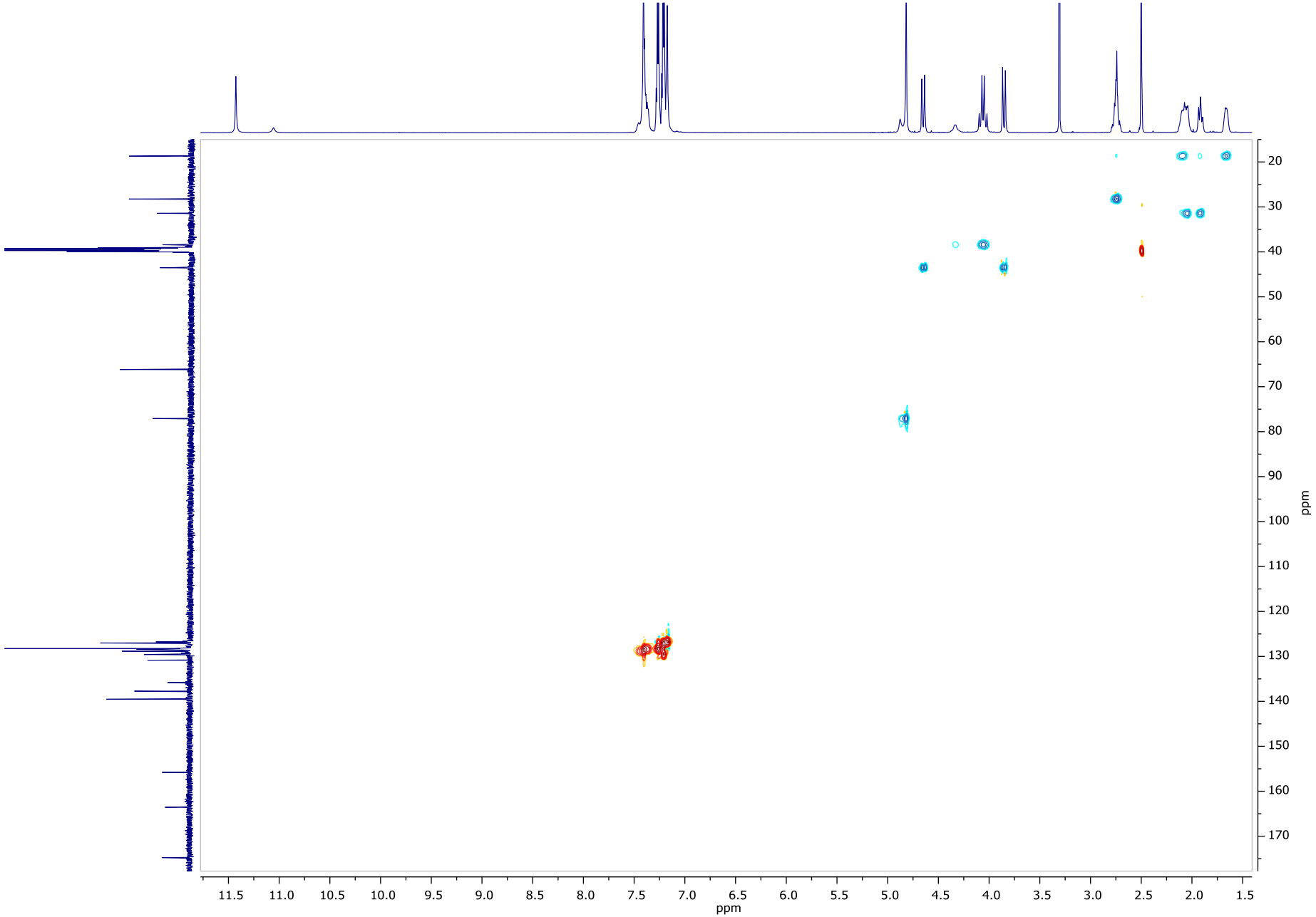
^{13}C NMR of **14b** (150.9 MHz, DMSO-d_6)



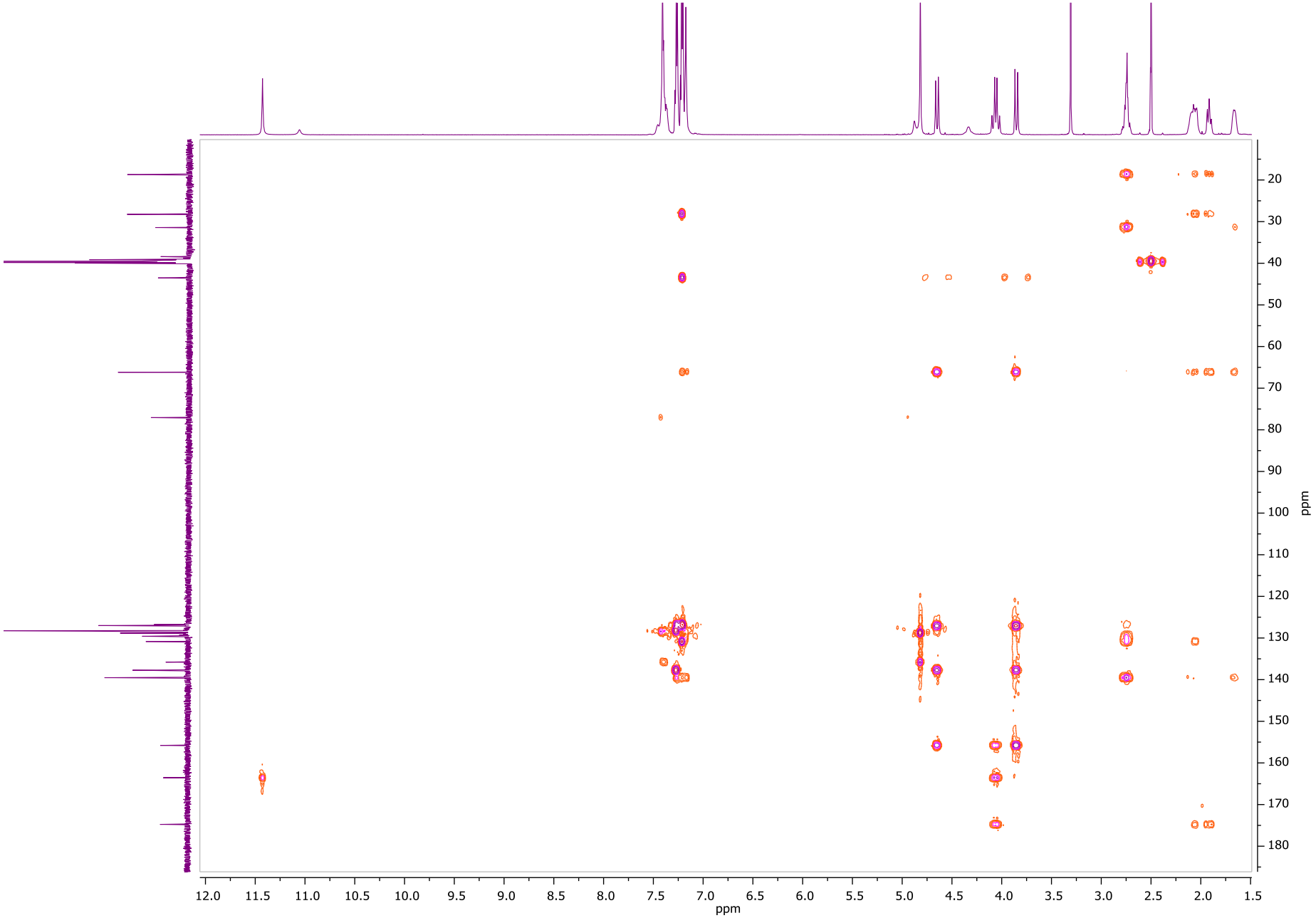
COSY NMR of **14b** (600.11 MHz, DMSO-d_6)



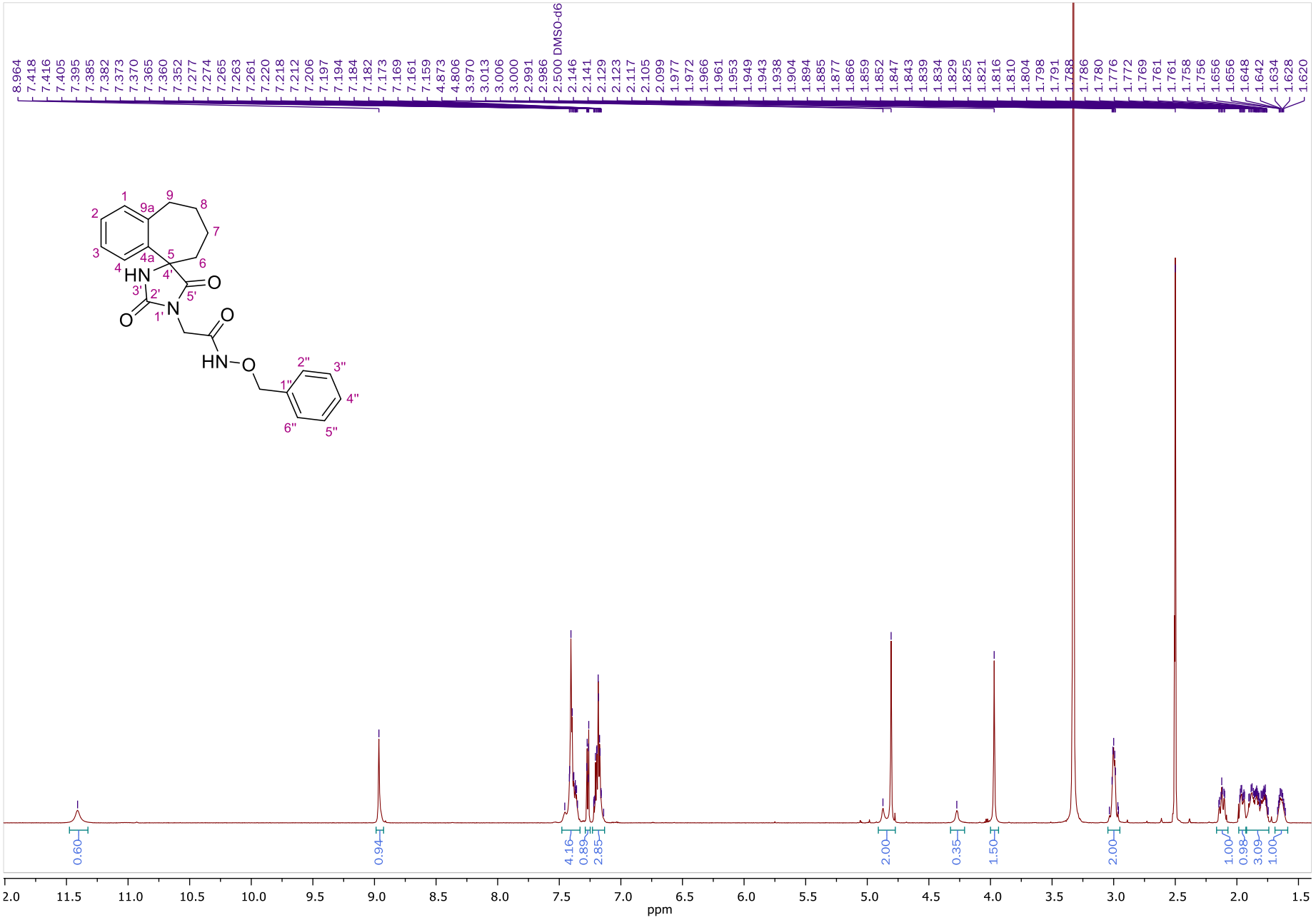
HSQC-DEPT NMR of **14b** (600.11 MHz, DMSO-d_6)



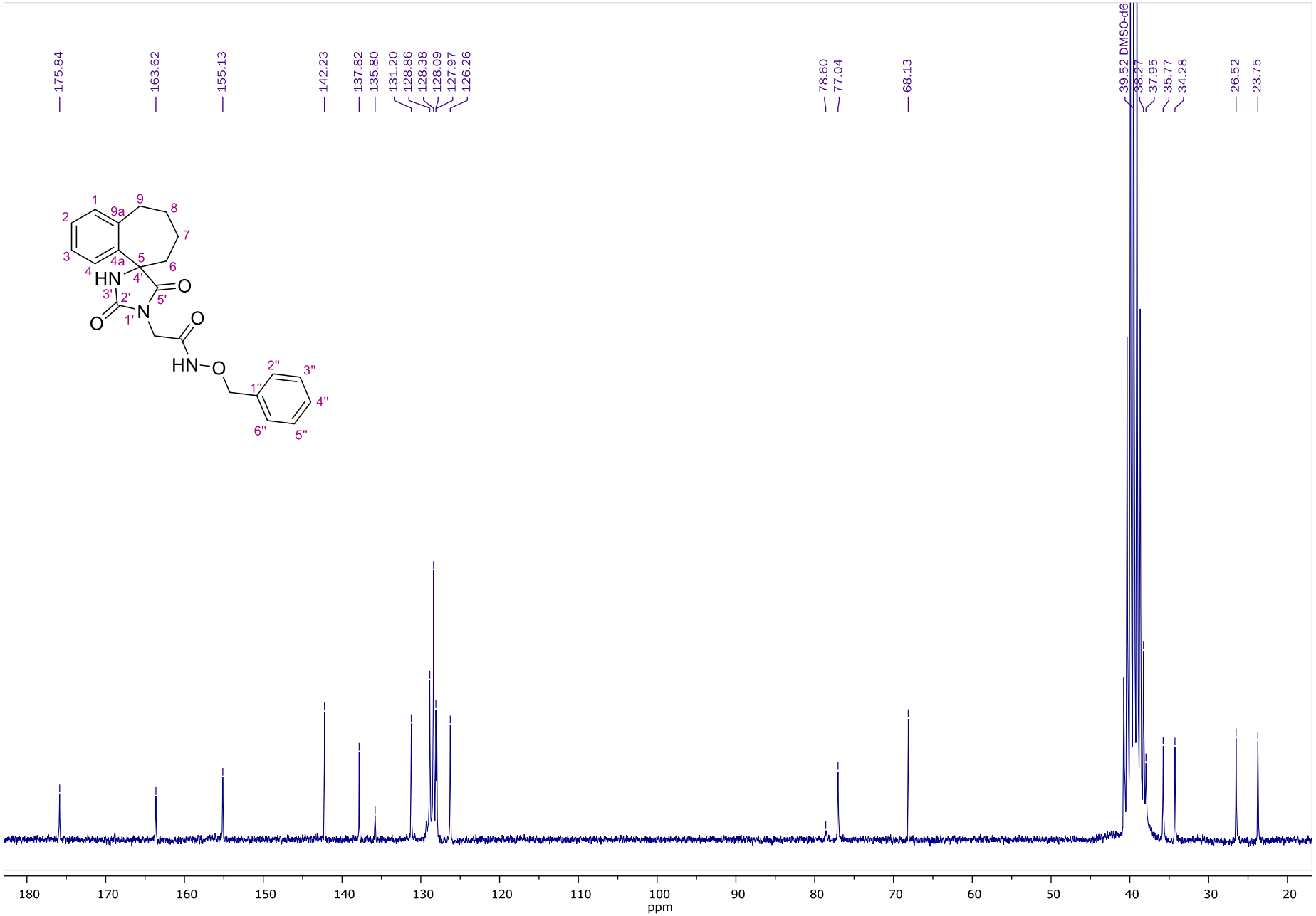
HMBC NMR of **14b** (600.11 MHz, DMSO-d_6)



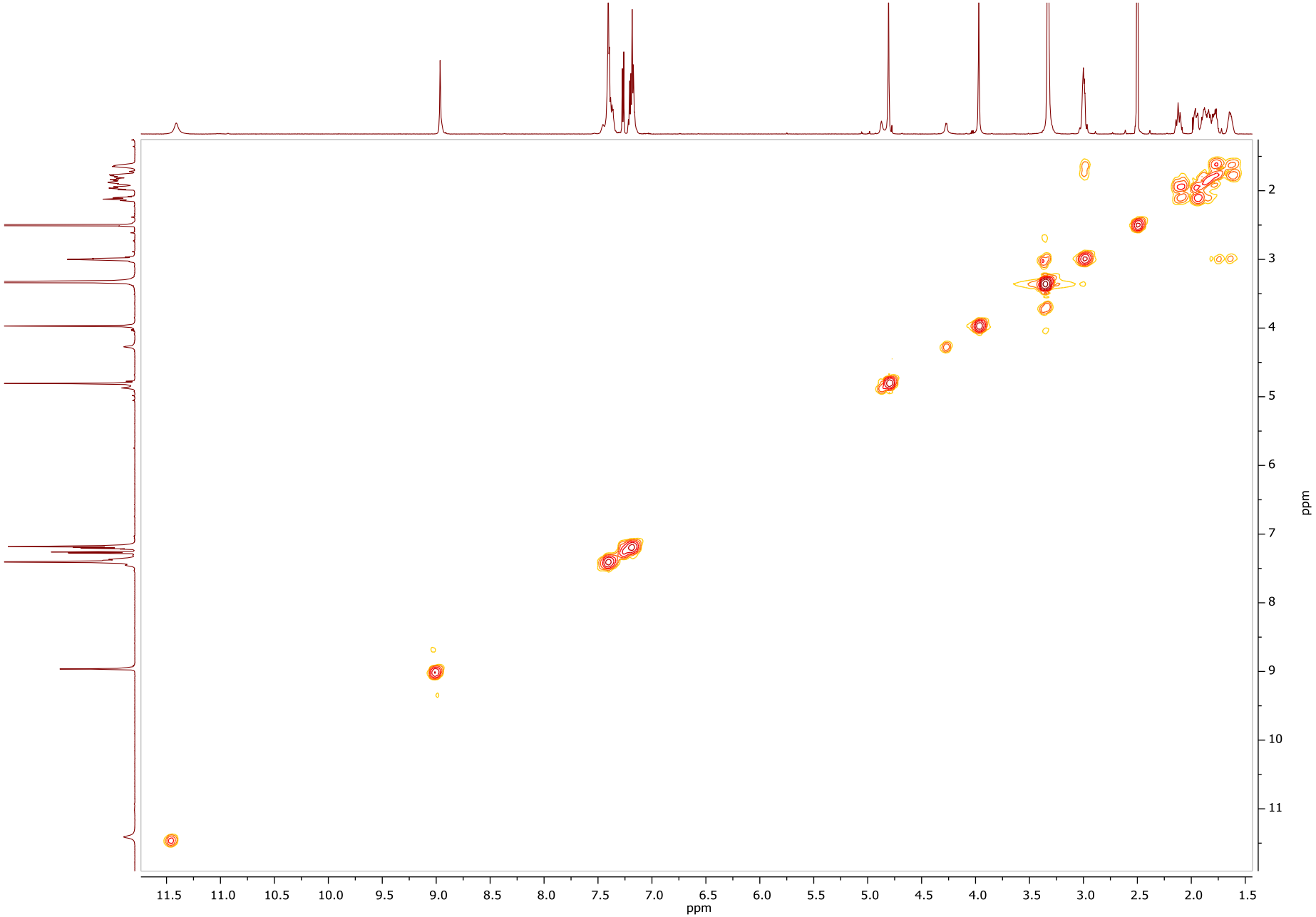
^{1}H NMR of **15** (600.11 MHz, DMSO-d_6)



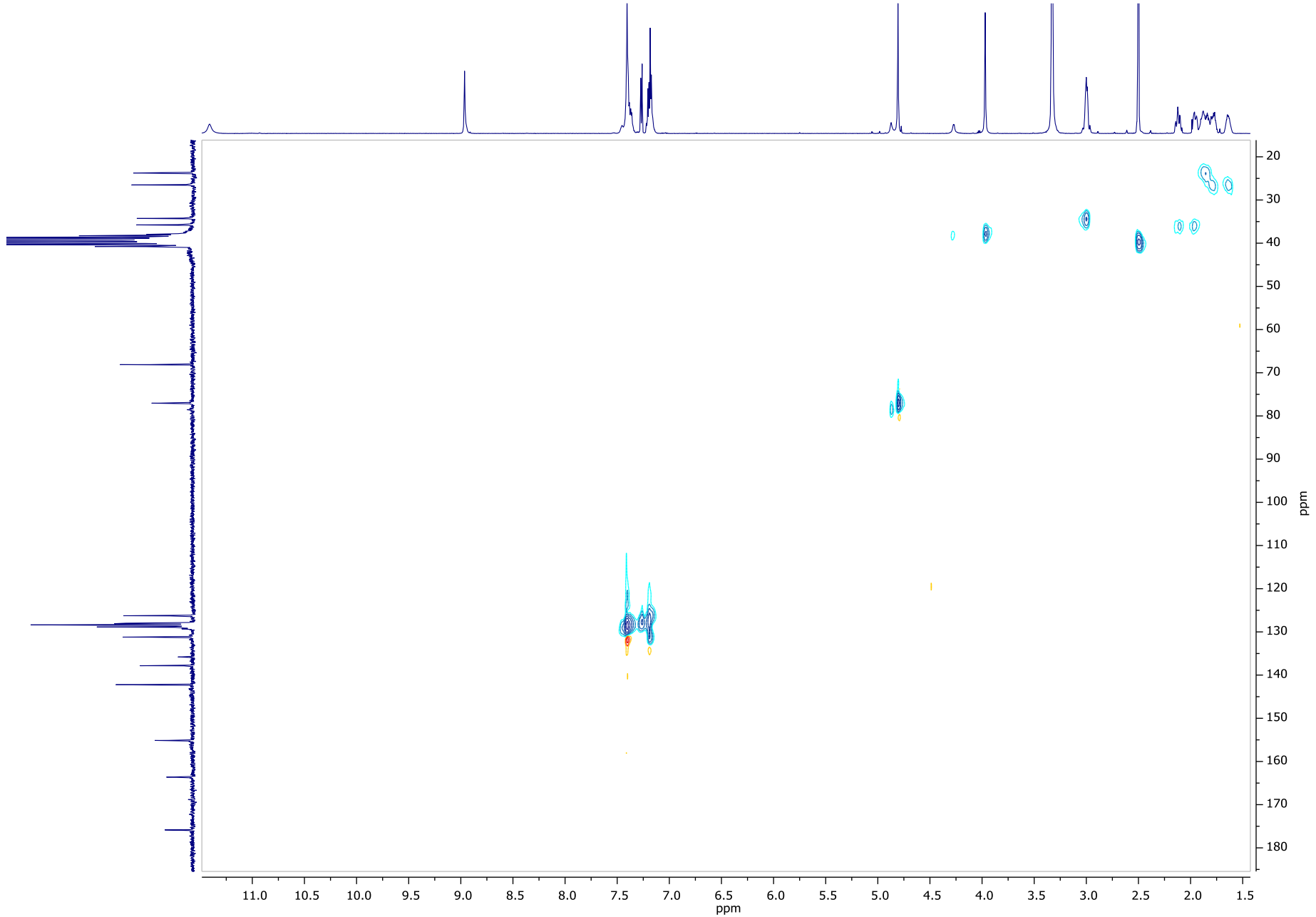
^{13}C NMR of **15** (50.32 MHz, DMSO-d_6)



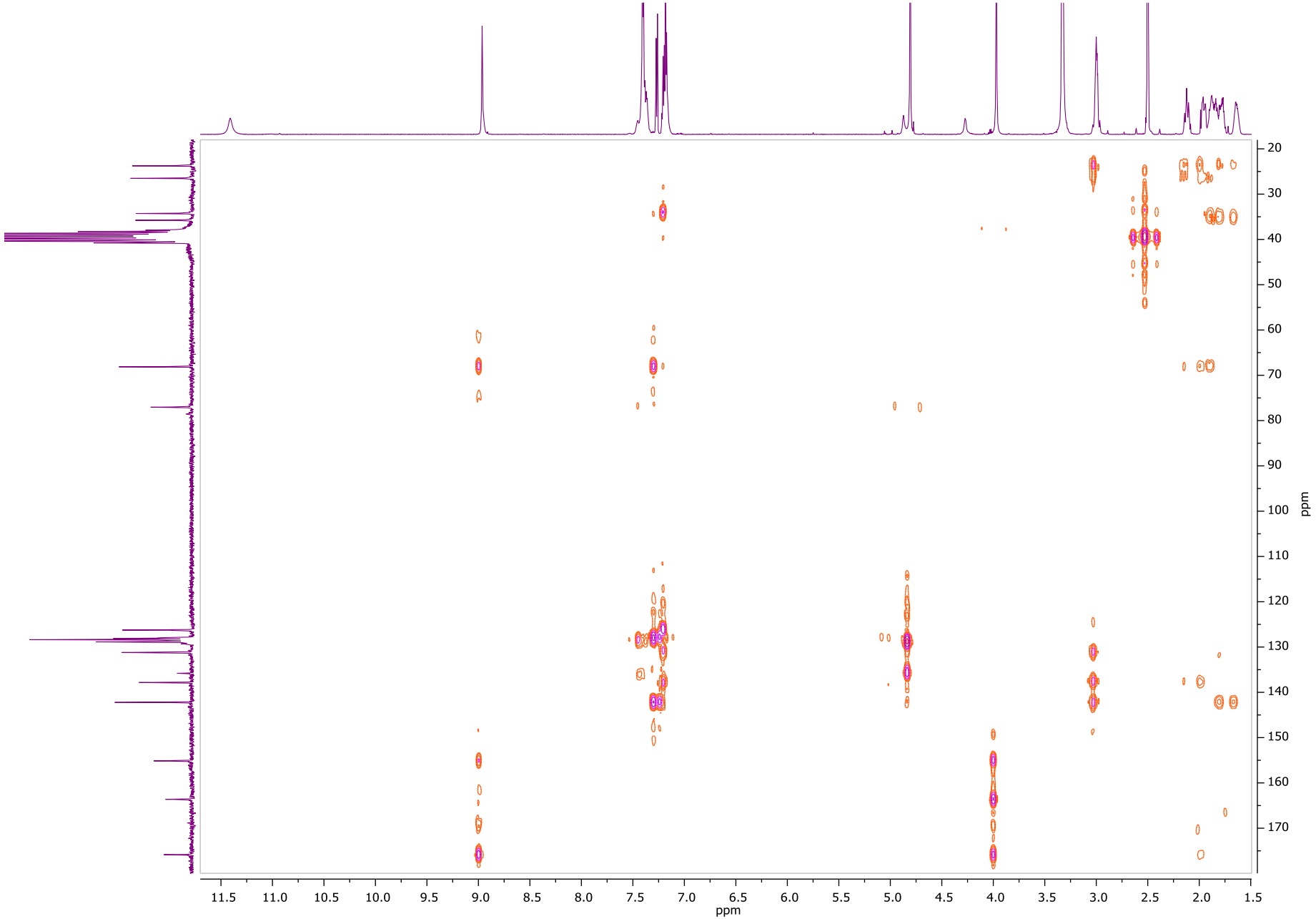
COSY NMR of **15** (400.13 MHz, DMSO-d_6)



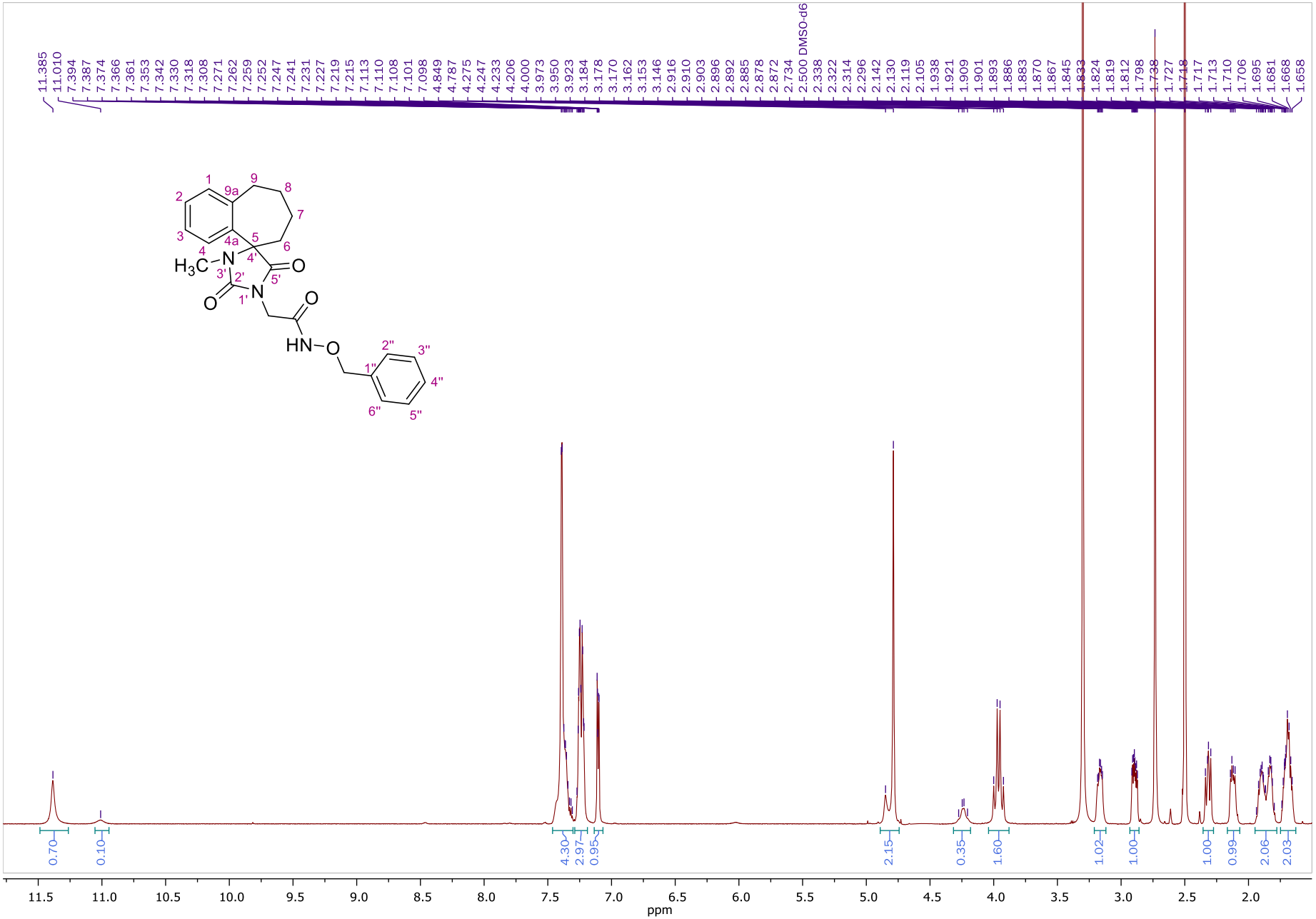
HSQC NMR of **15** (400.13 MHz, DMSO-d_6)



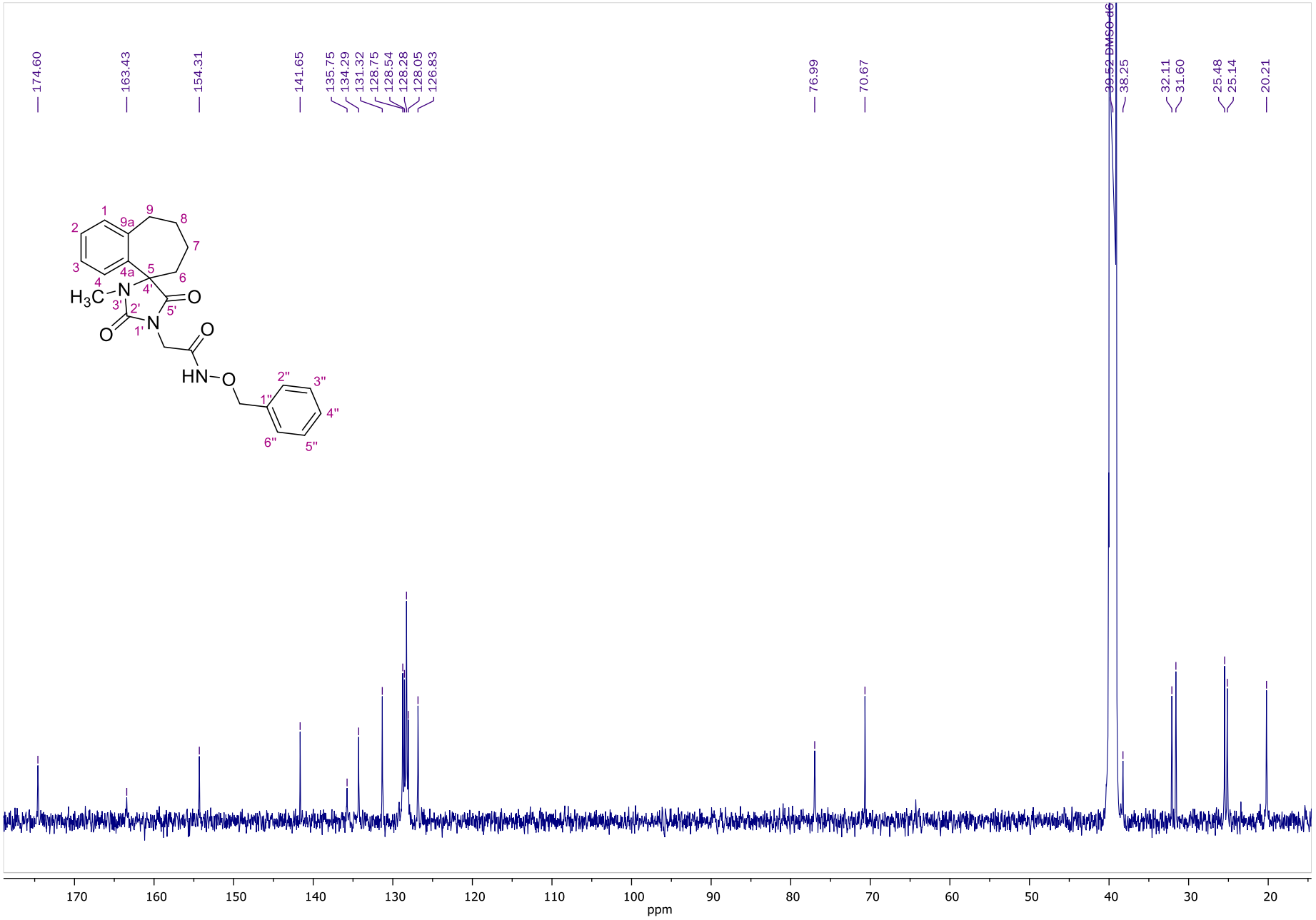
HMBC NMR of **15** (600.11 MHz, DMSO-d_6)



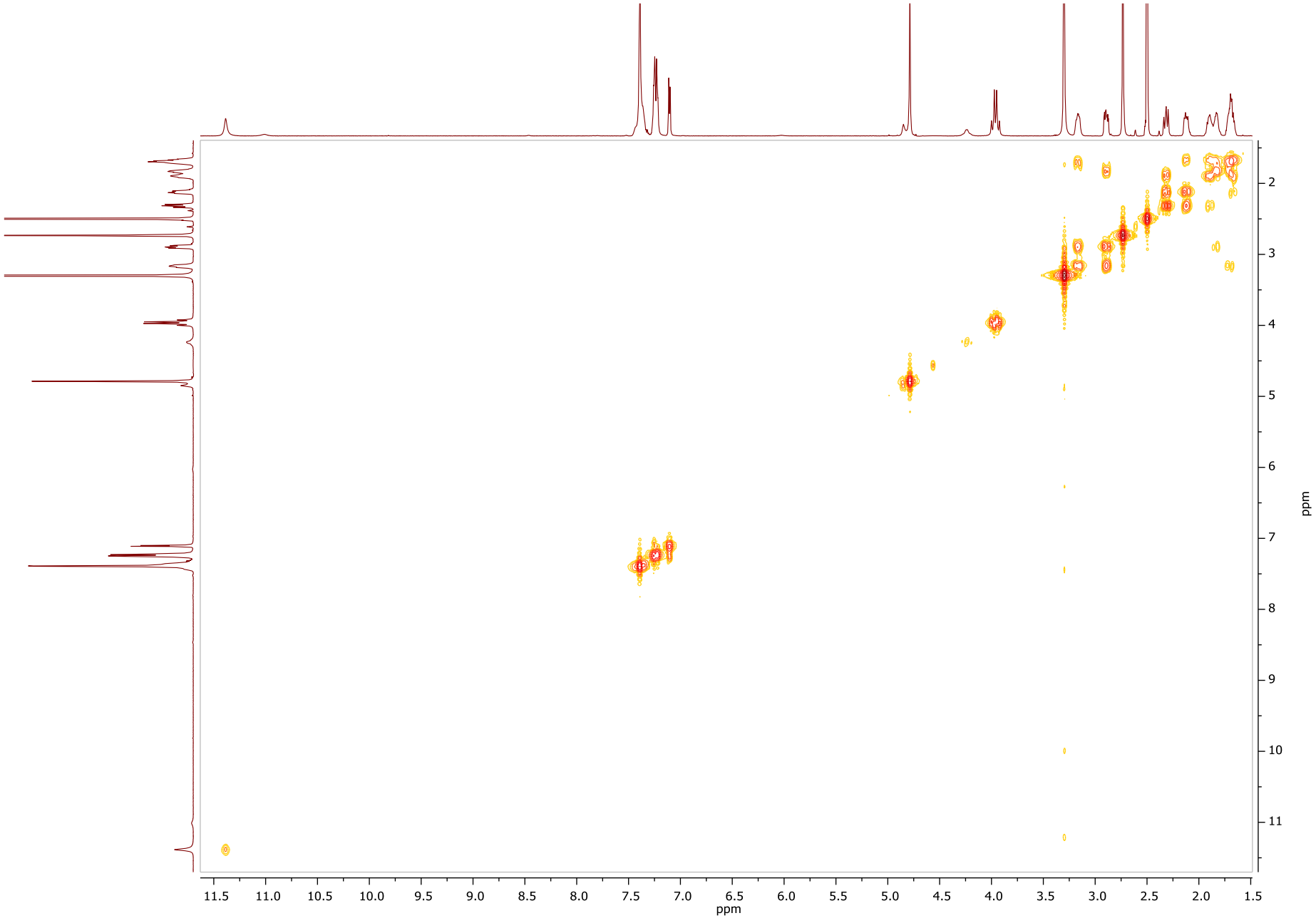
^{1}H NMR of **15a** (600.11 MHz, DMSO-d_6)



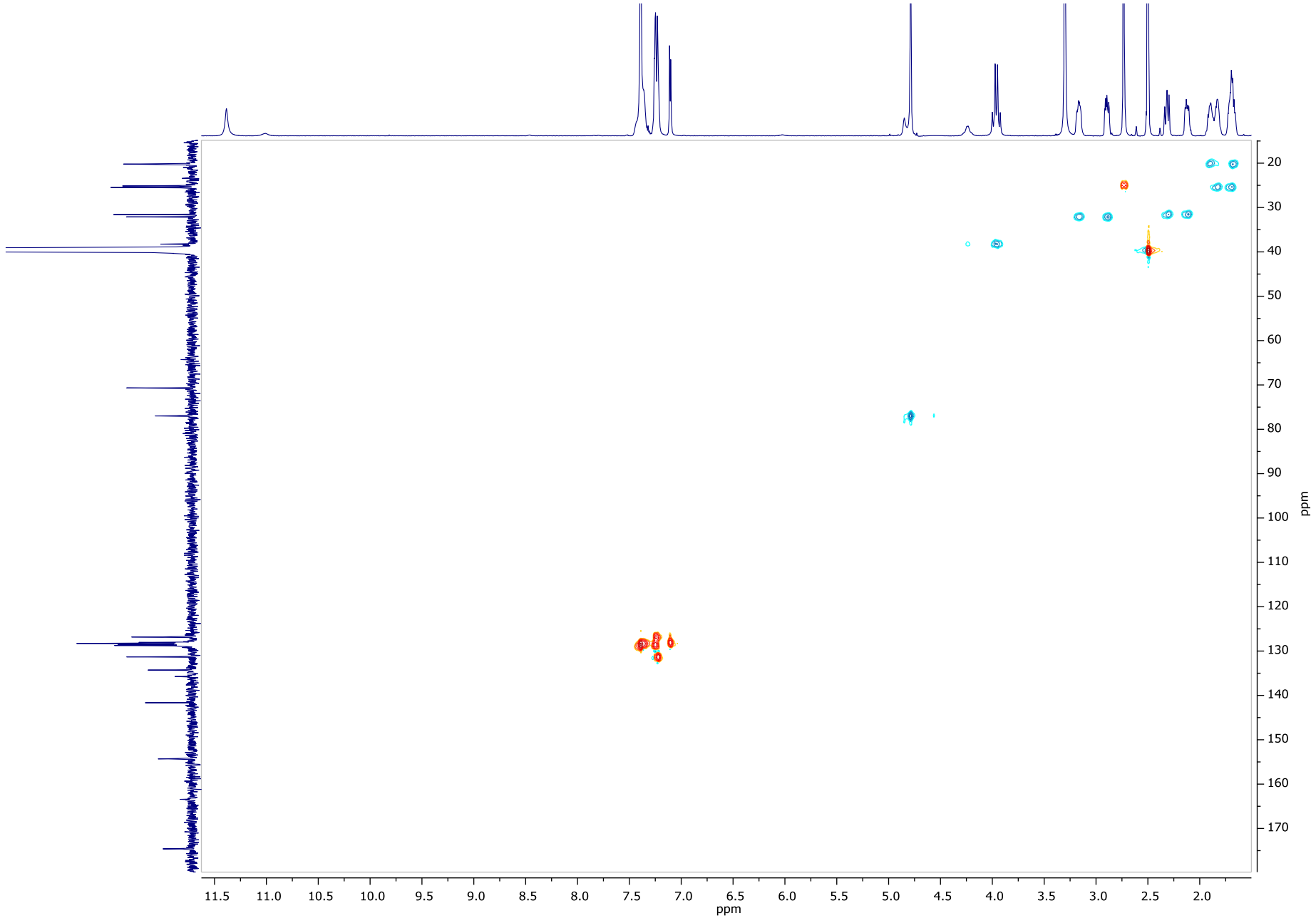
^{13}C NMR of **15a** (150.9 MHz, DMSO-d_6)



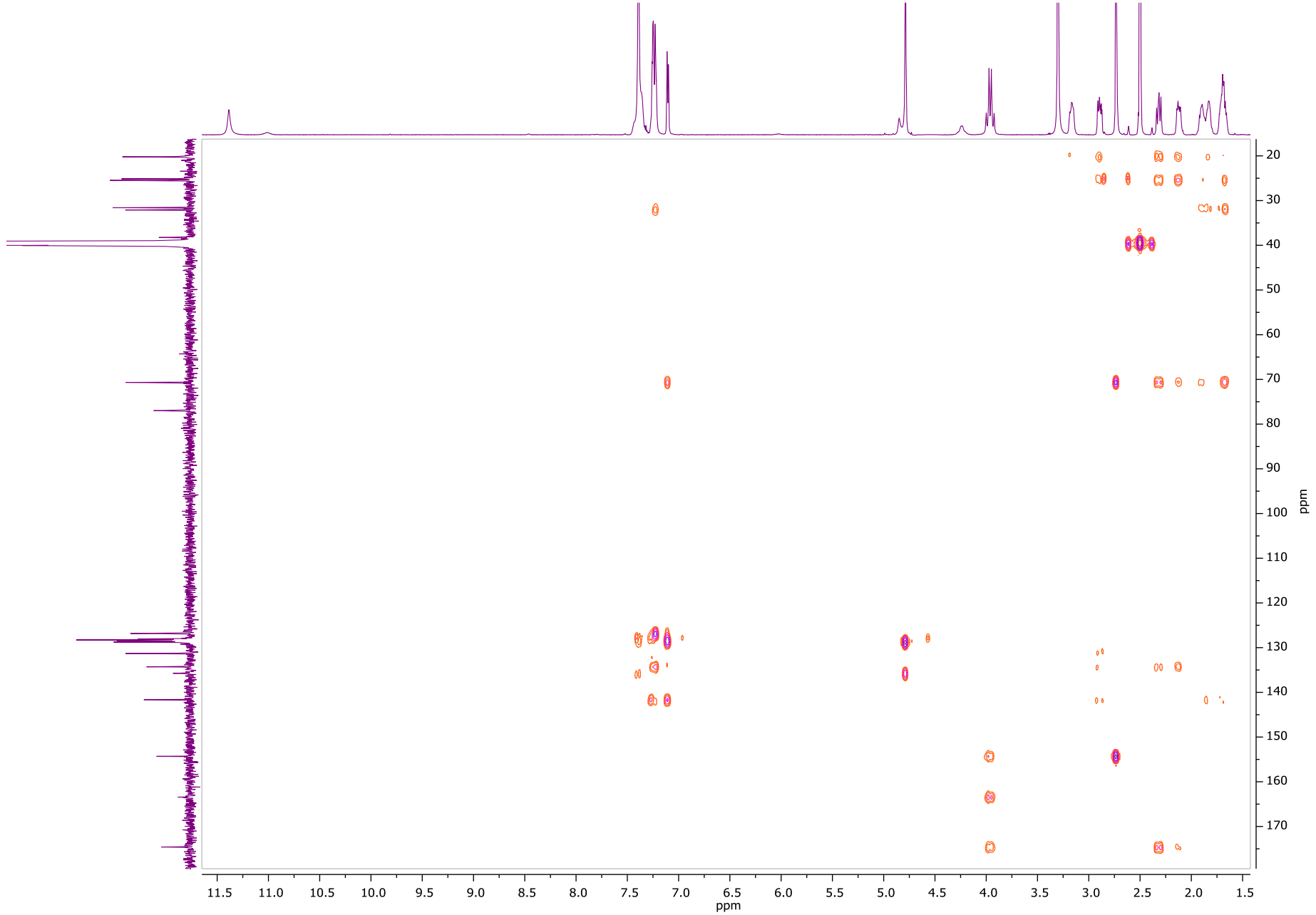
COSY NMR of **15a** (600.11 MHz, DMSO-d_6)



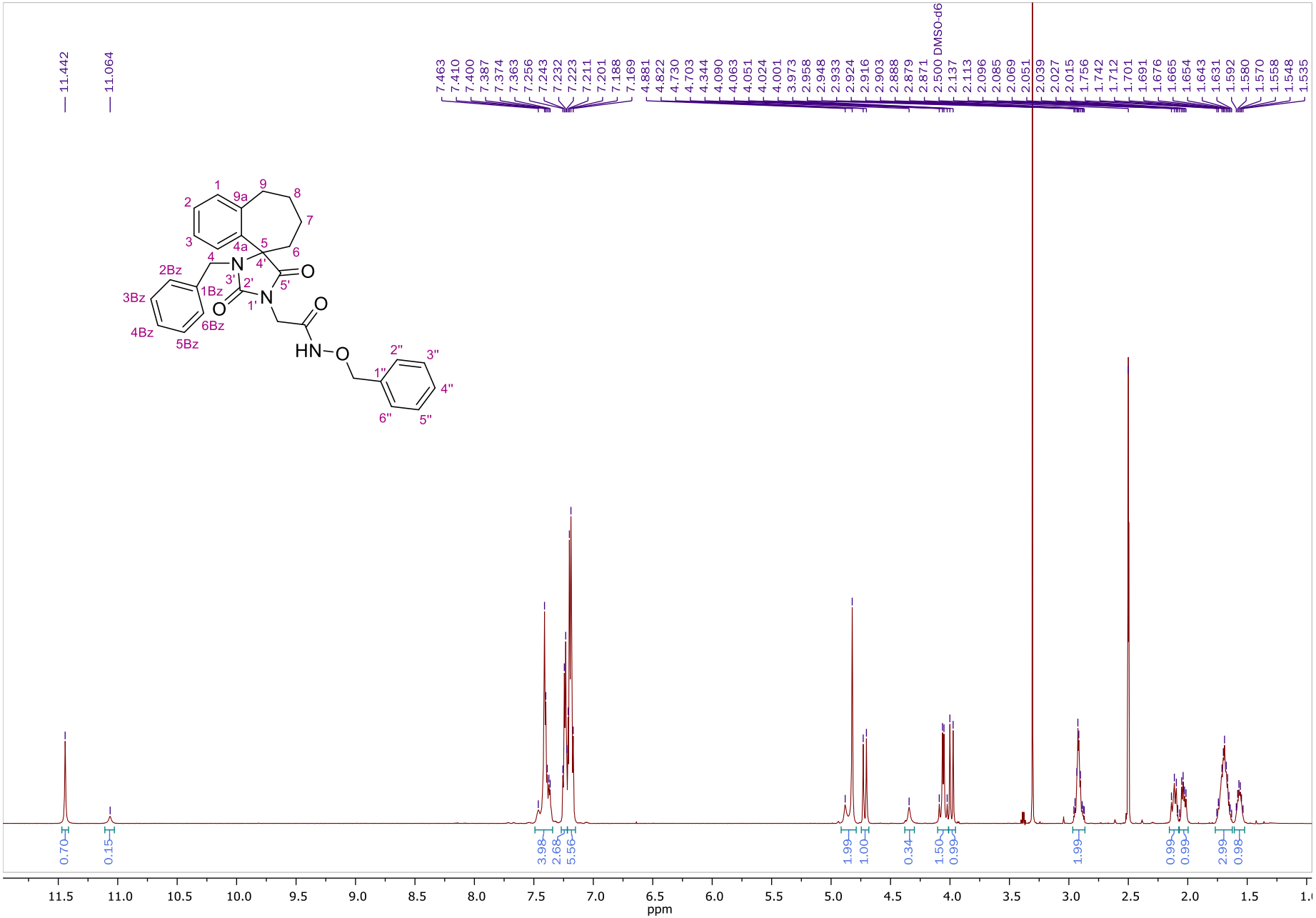
HSQC-DEPT NMR of **15a** (600.11 MHz, DMSO-d_6)



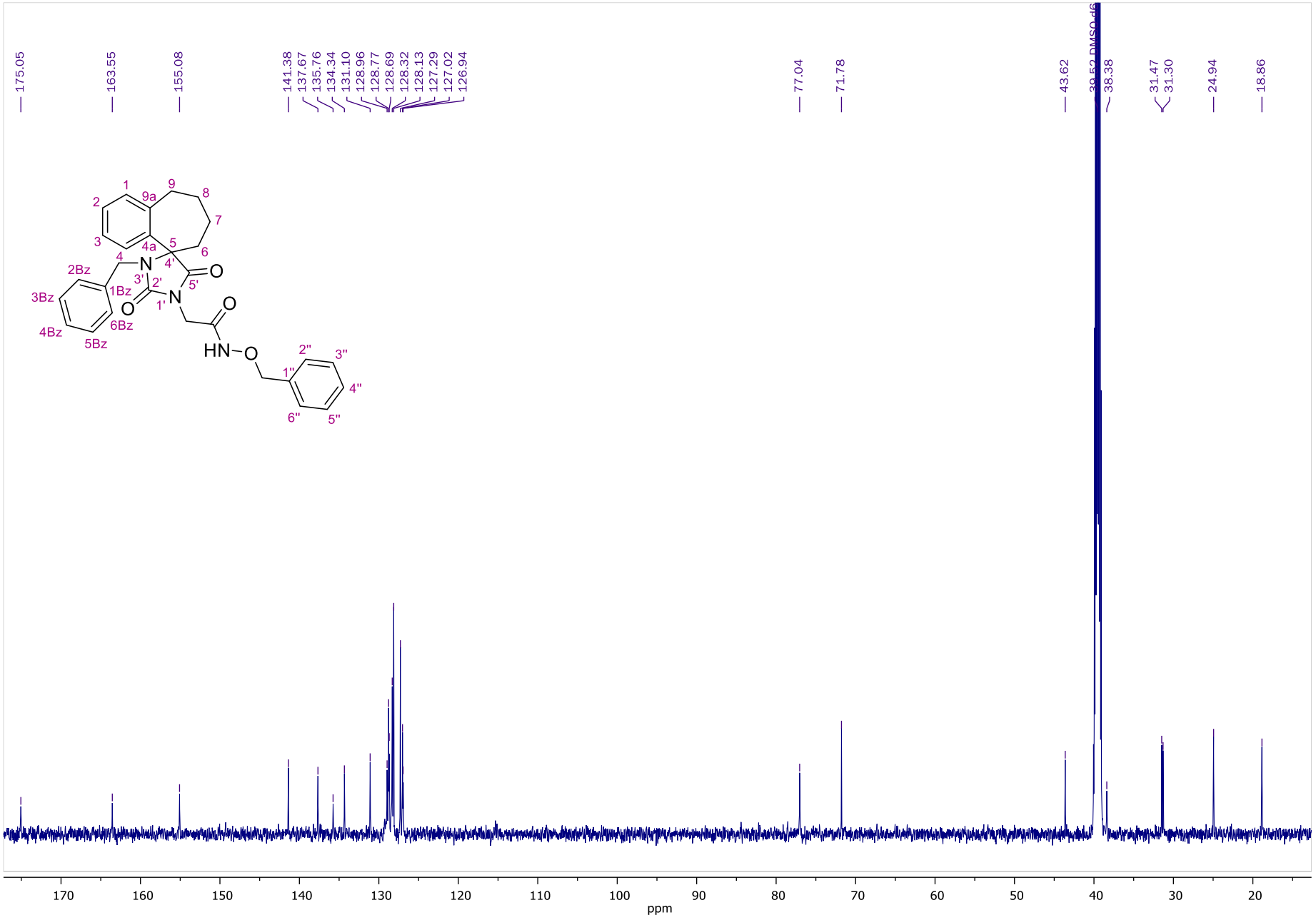
HMBC NMR of **15a** (600.11 MHz, DMSO-d_6)



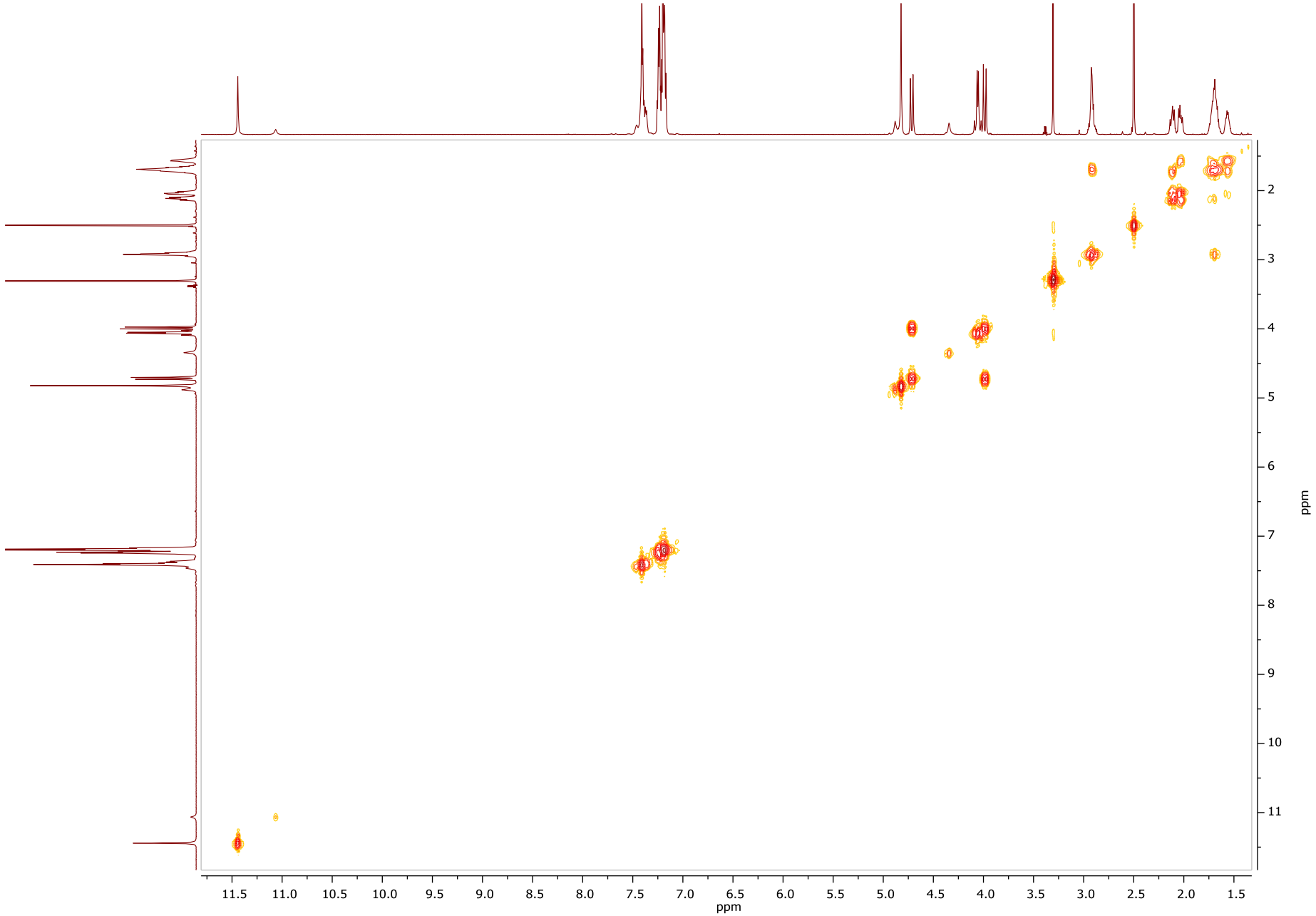
^{1}H NMR of **15b** (600.11 MHz, DMSO-d_6)



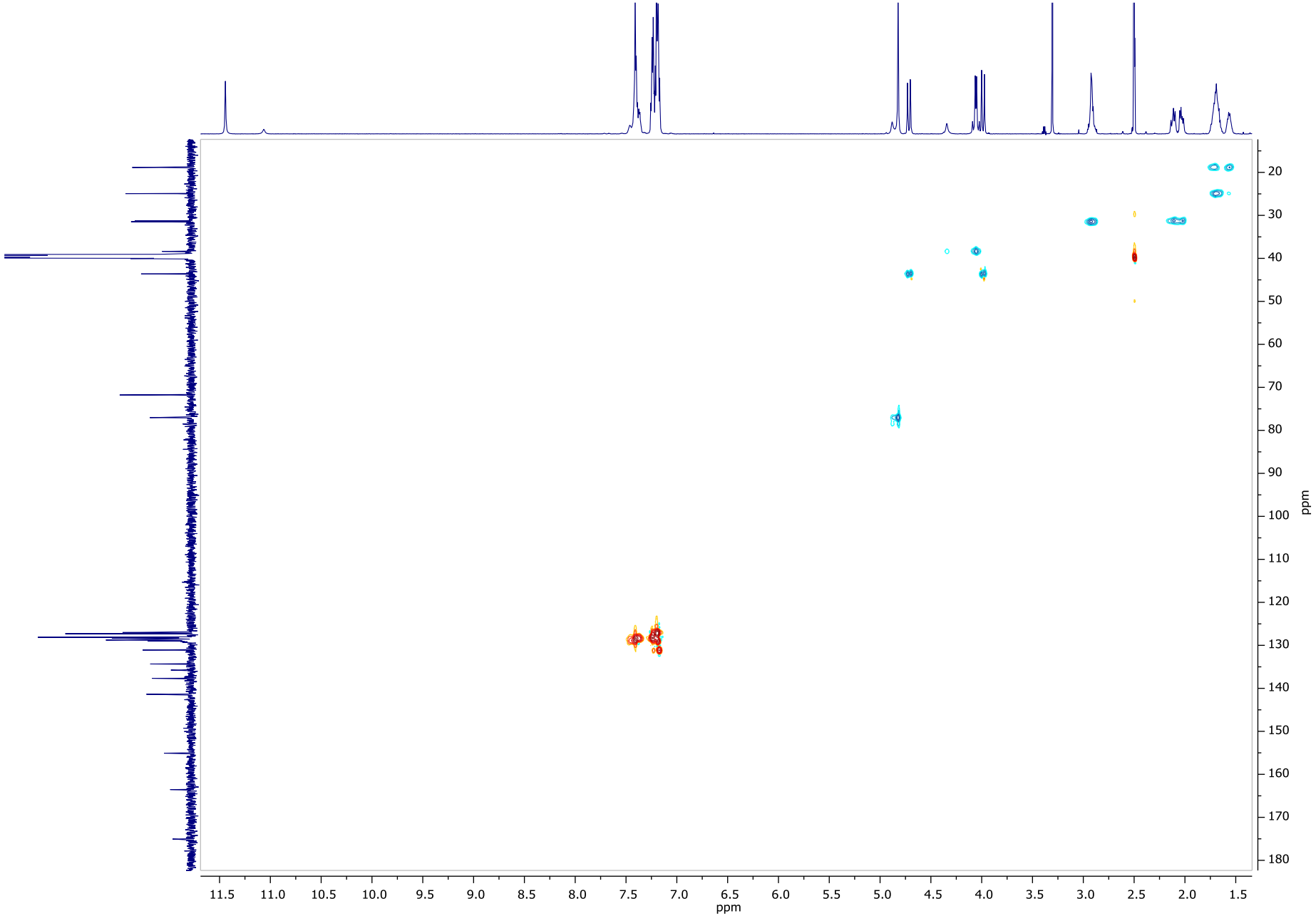
^{13}C NMR of **15b** (150.9 MHz, DMSO-d_6)



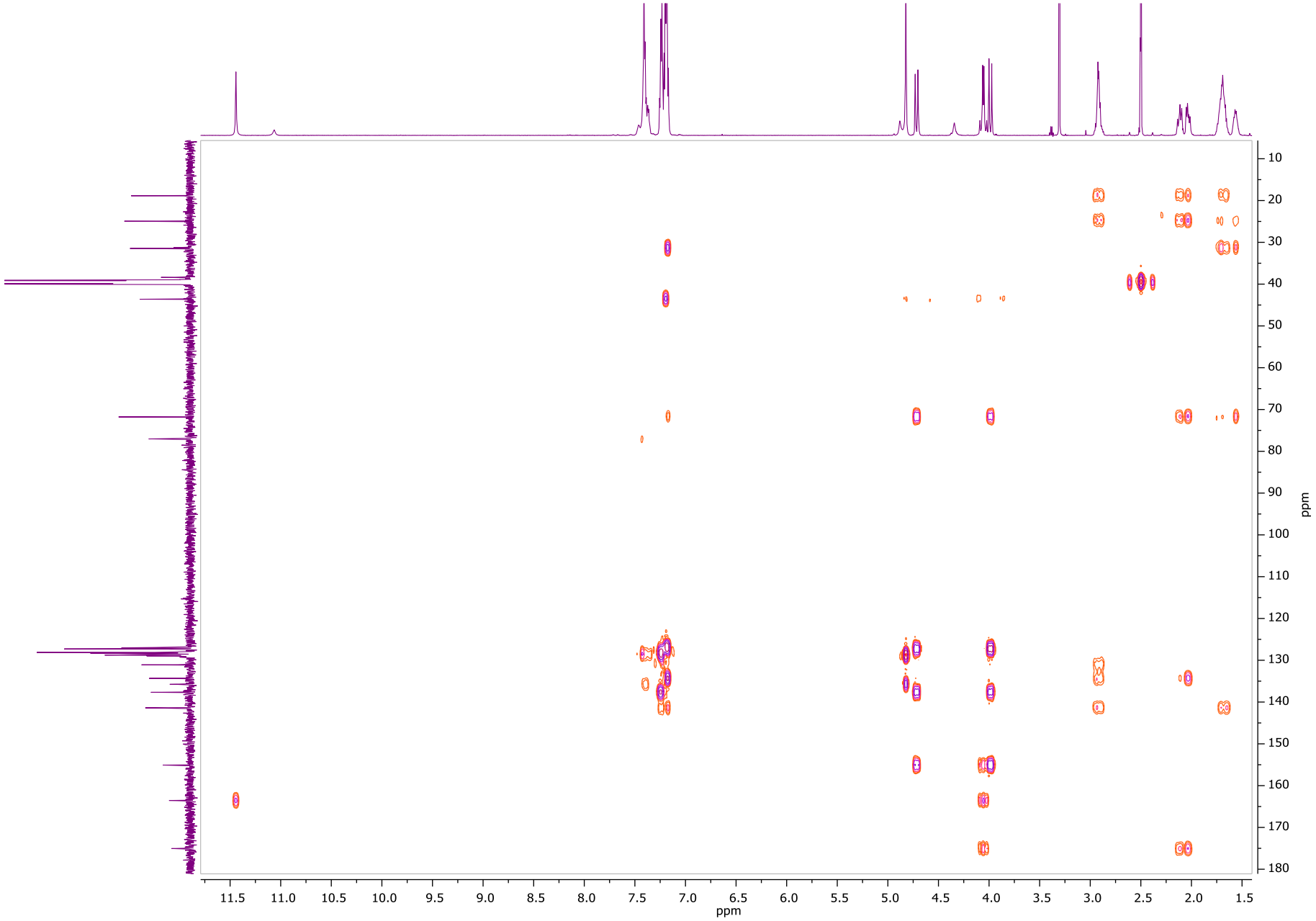
COSY NMR of **15b** (600.11 MHz, DMSO-d_6)



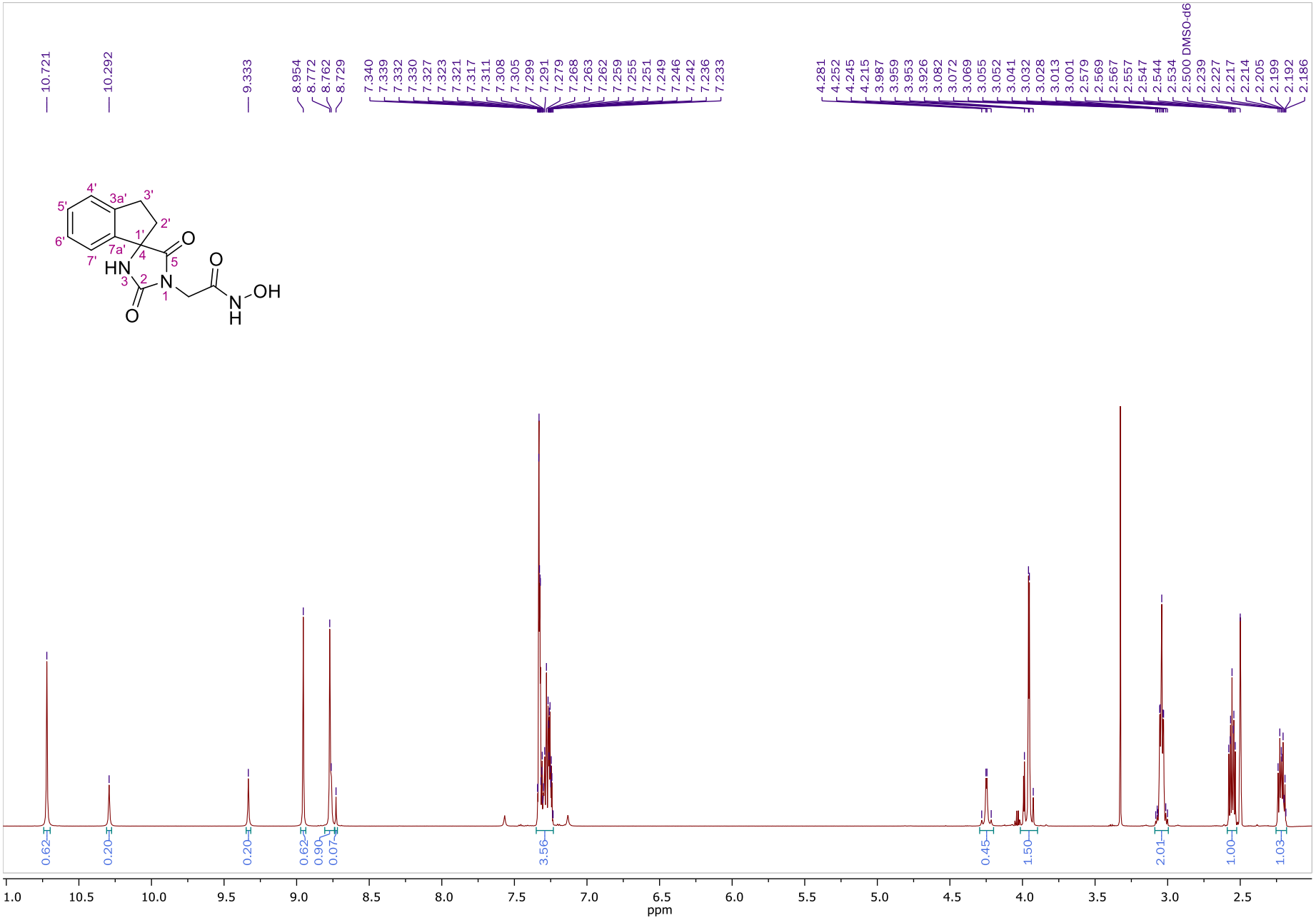
HSQC-DEPT NMR of **15b** (600.11 MHz, DMSO-d_6)



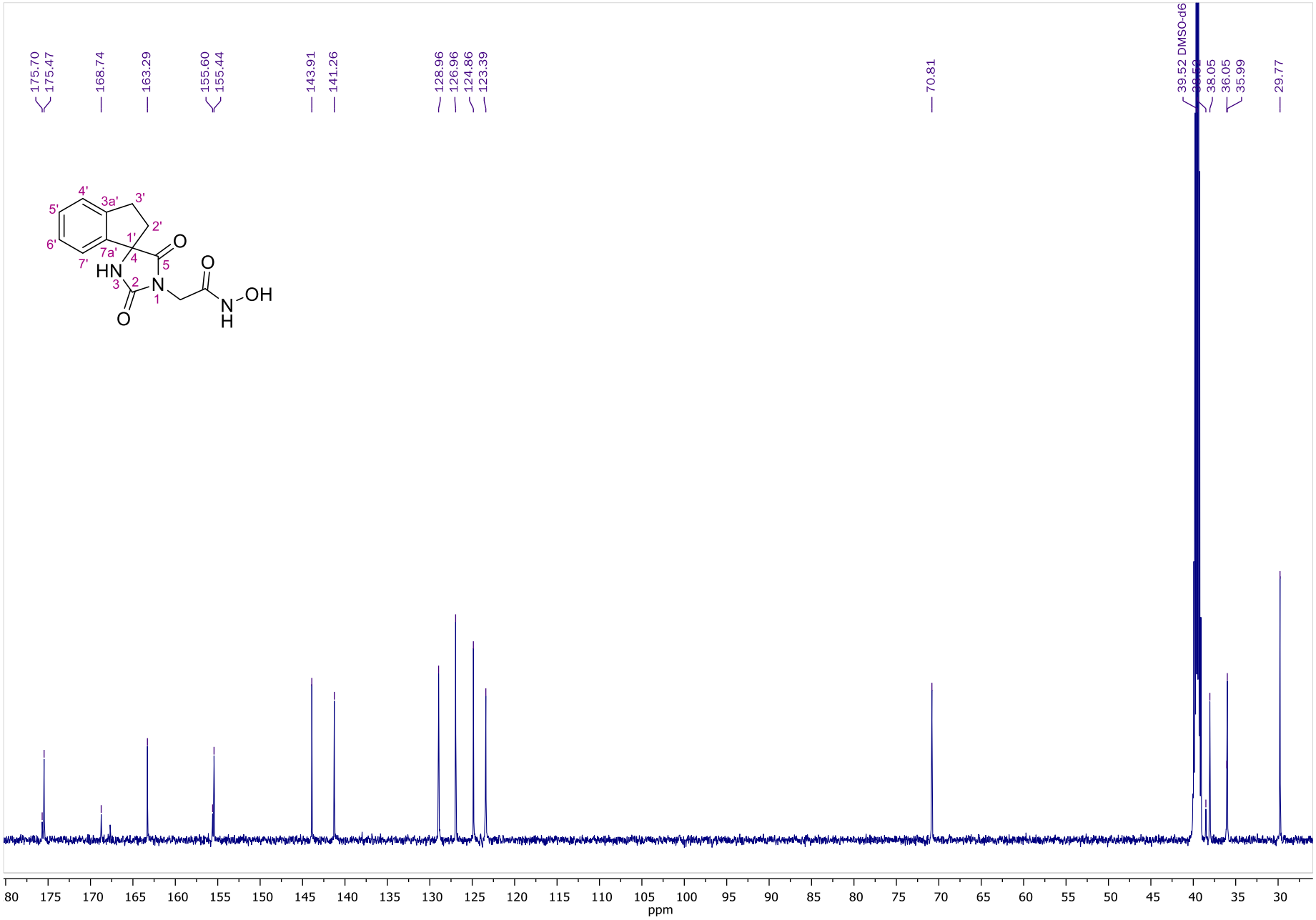
HMBC NMR of **15b** (600.11 MHz, DMSO-d_6)



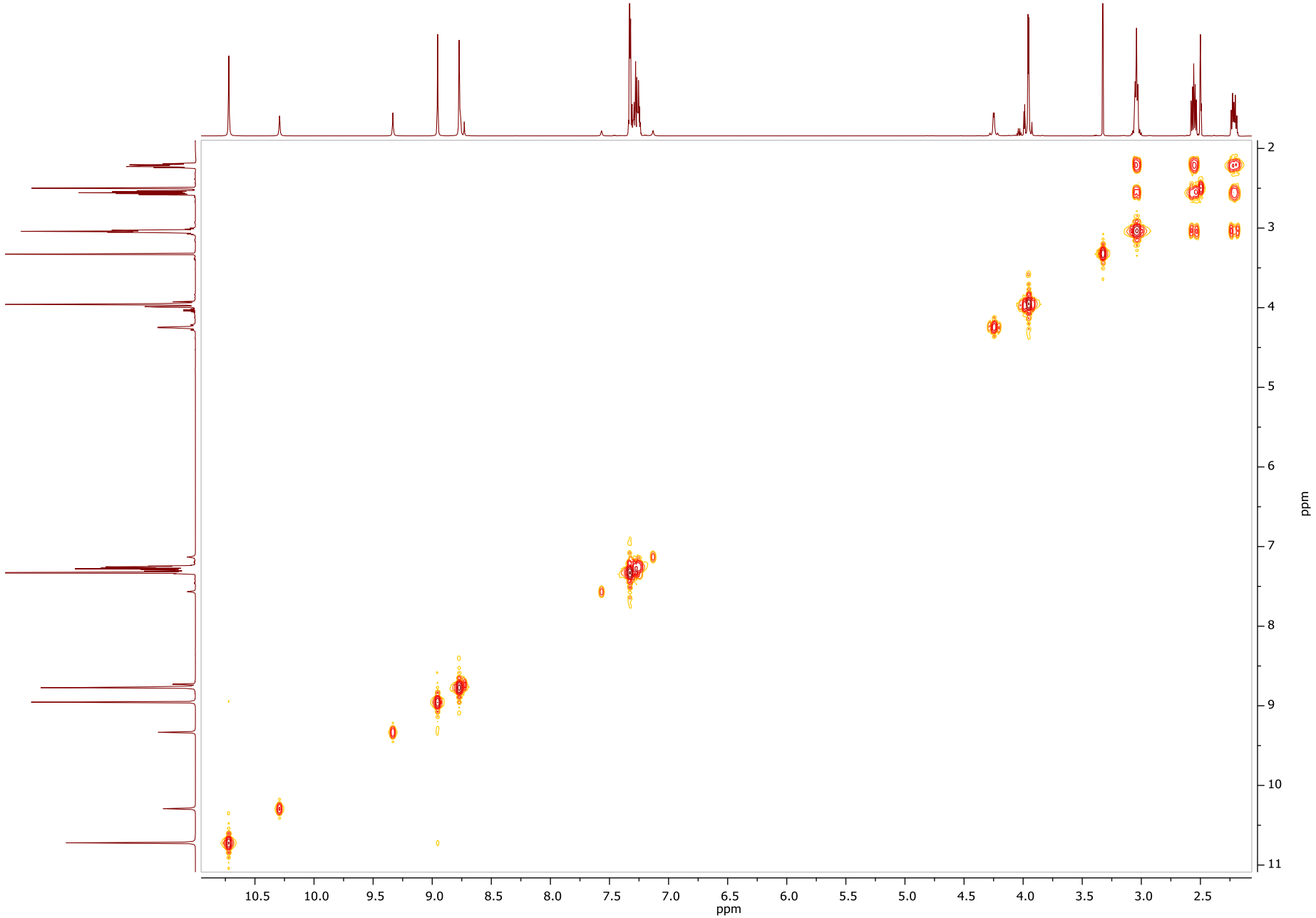
^{1}H NMR of **16** (600.11 MHz, DMSO-d_6)



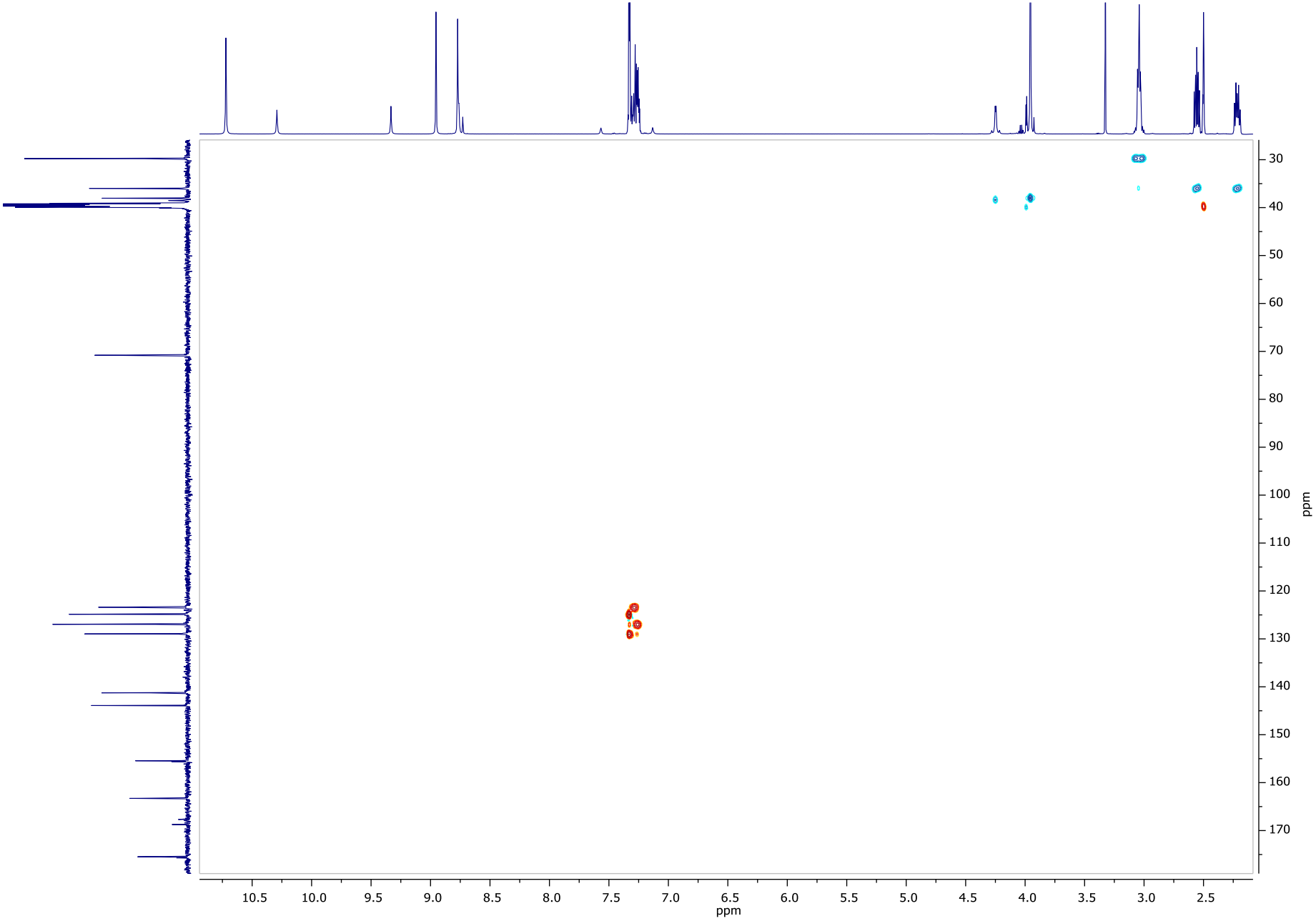
^{13}C NMR of **16** (150.9 MHz, DMSO-d_6)



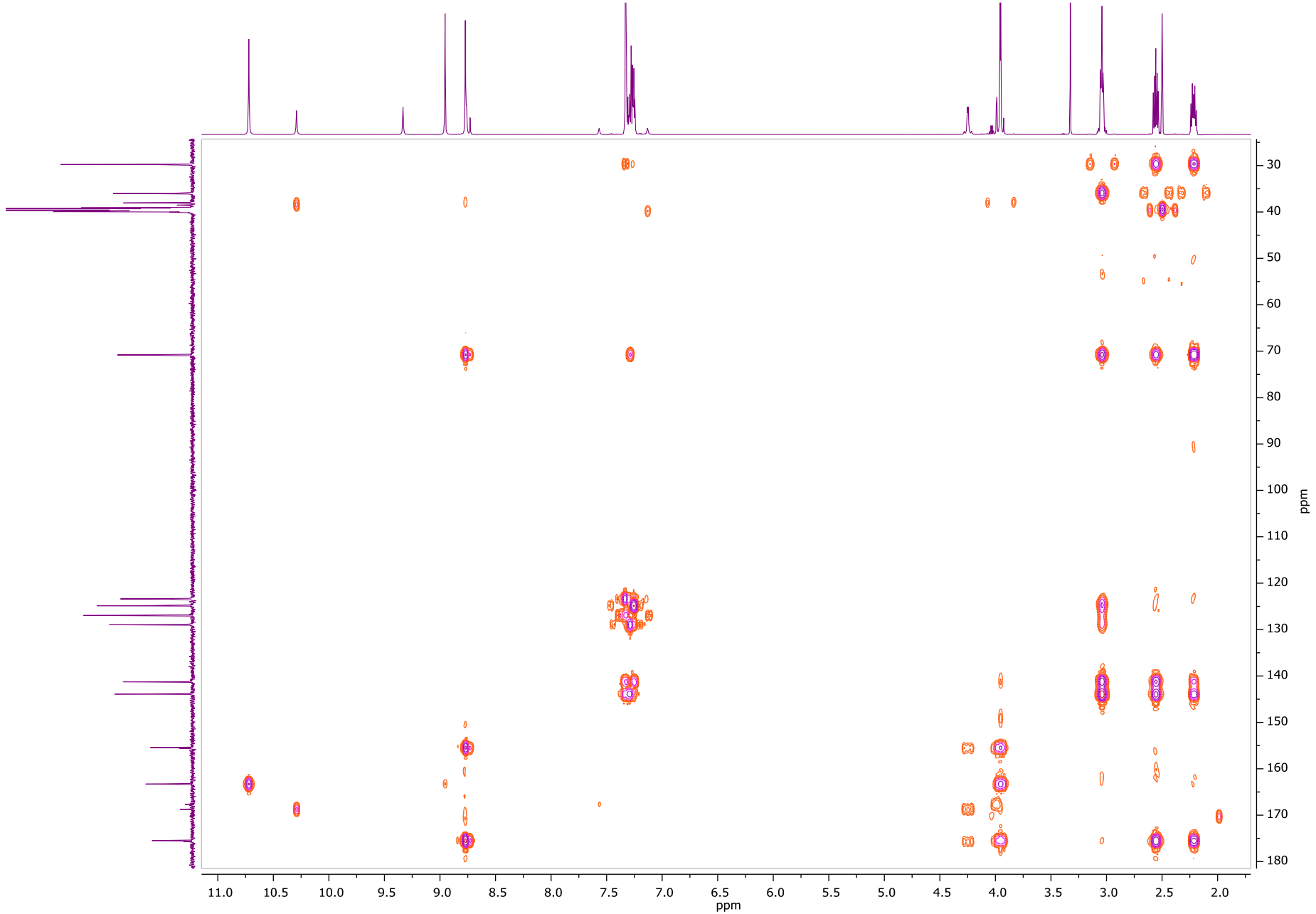
COSY NMR of **16** (600.11 MHz, DMSO-d_6)



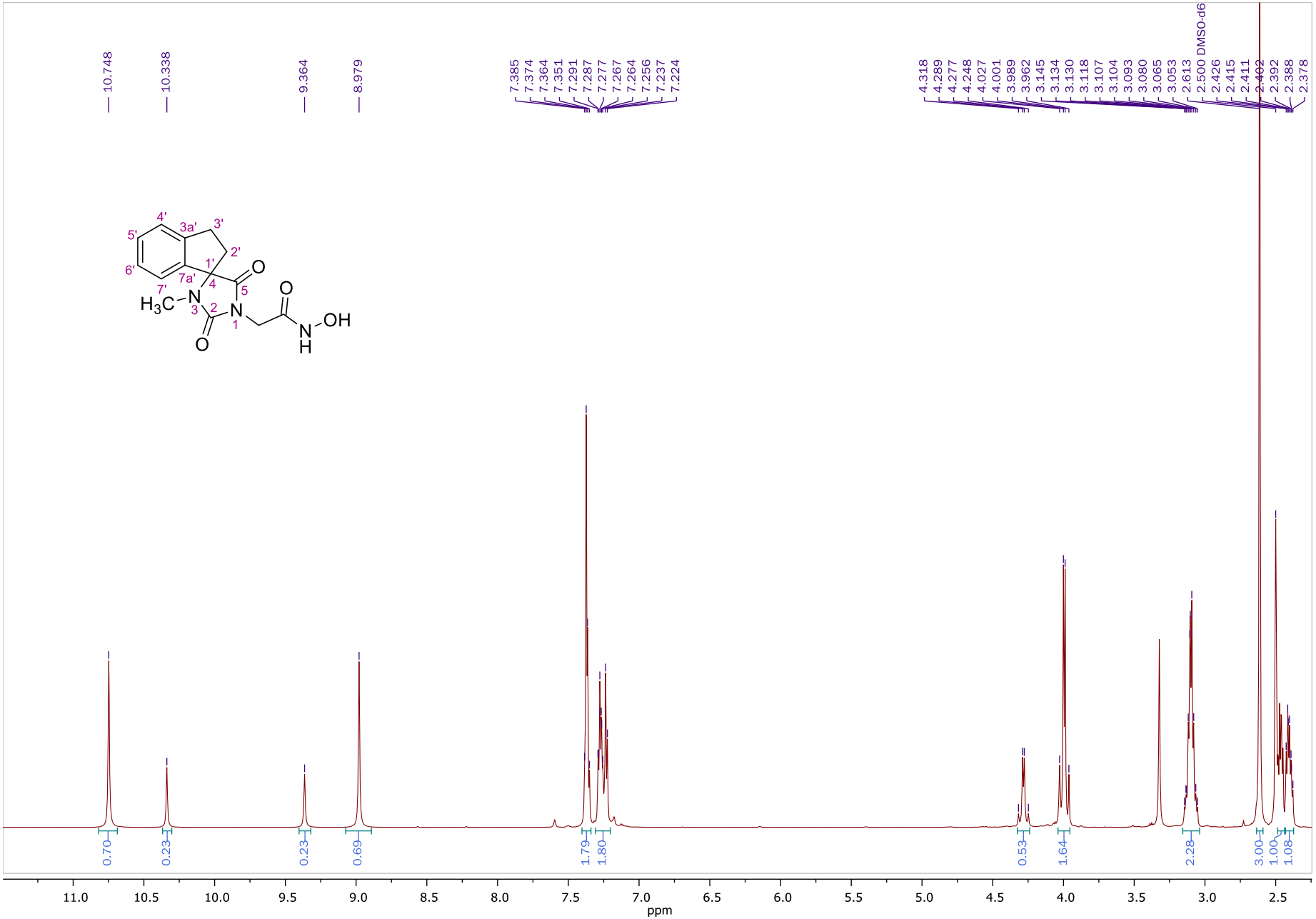
HSQC-DEPT NMR of **16** (600.11 MHz, DMSO-d_6)



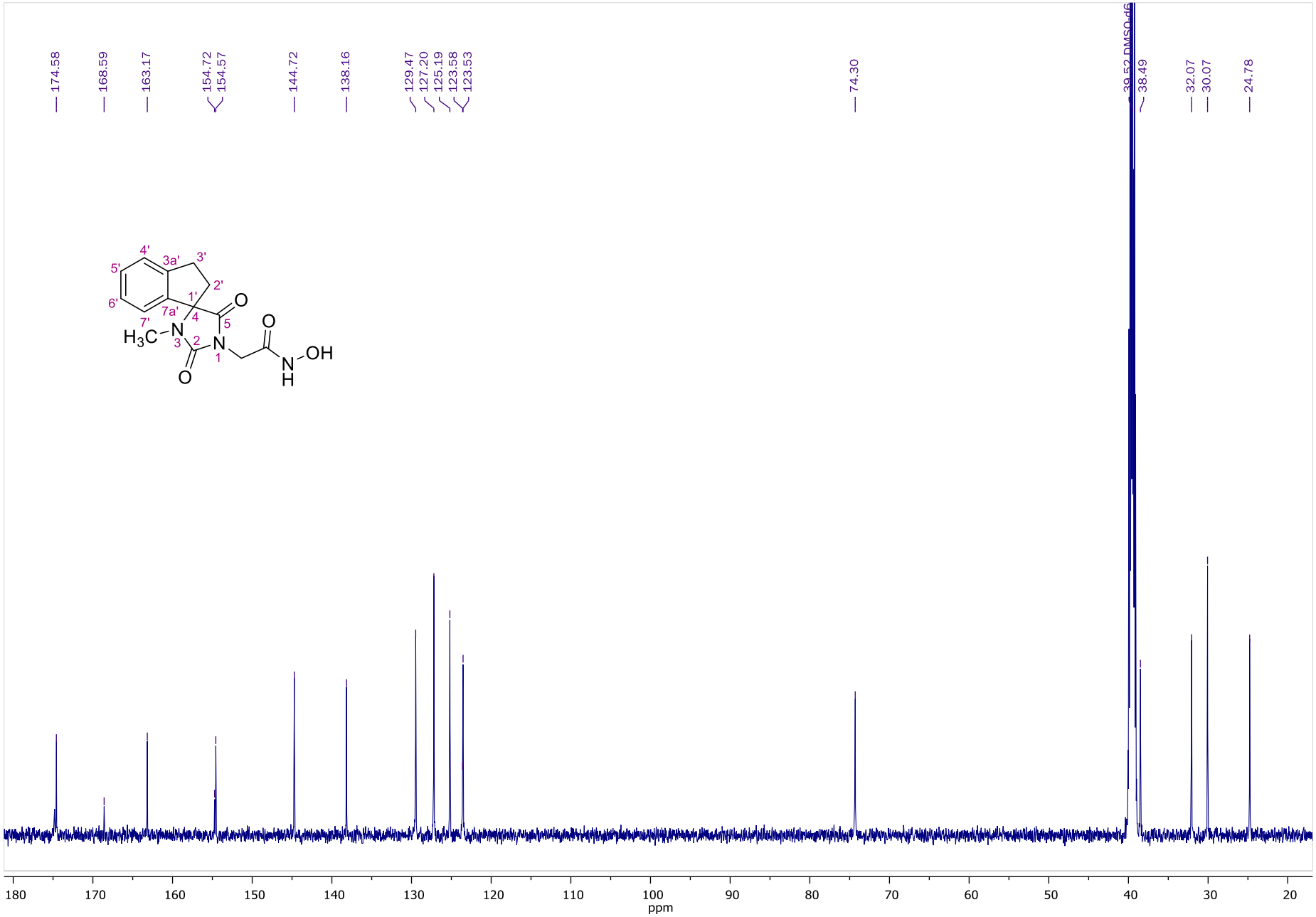
HMBC NMR of **16** (600.11 MHz, DMSO-d_6)



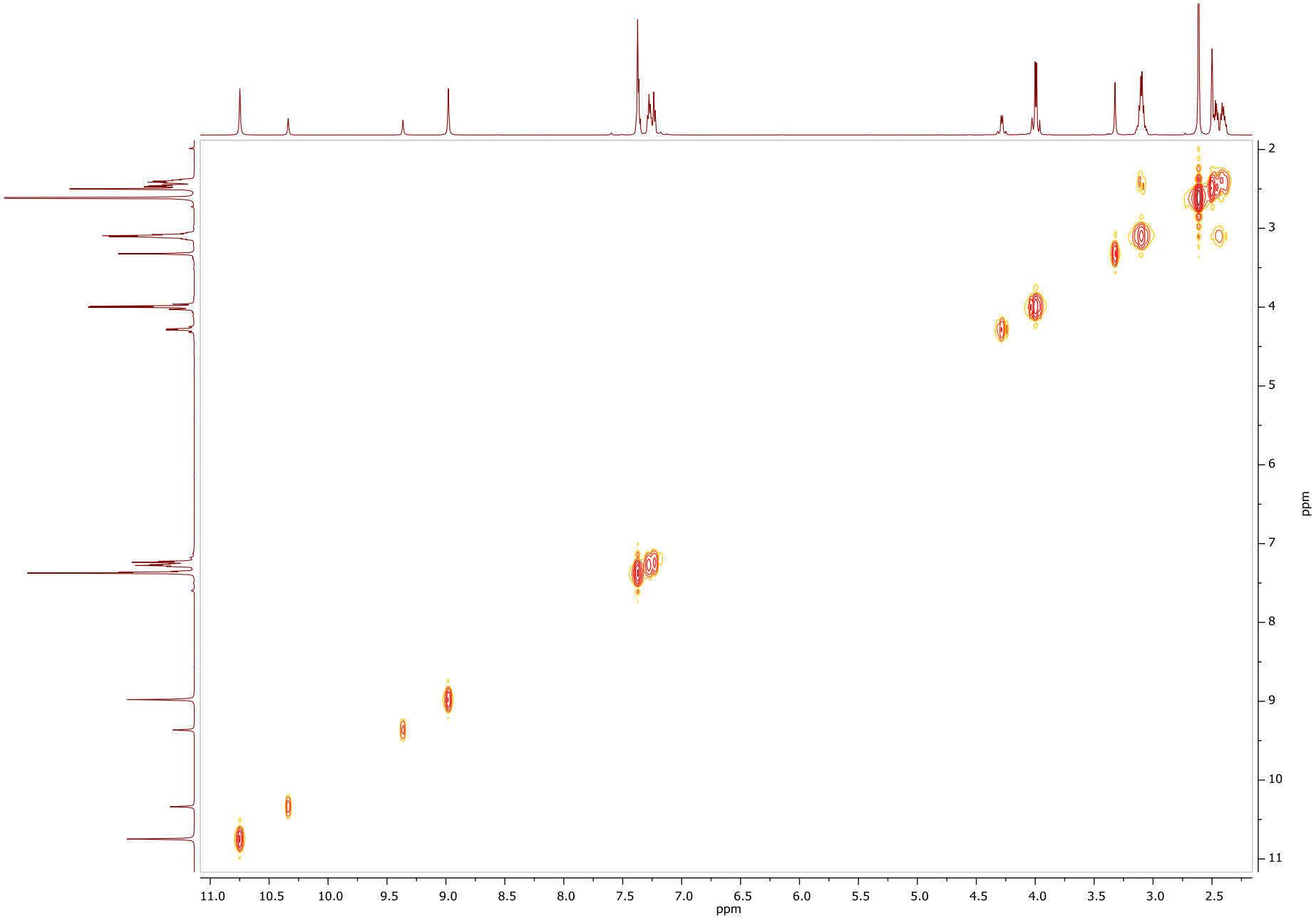
^{1}H NMR of **16a** (600.11 MHz, DMSO-d_6)



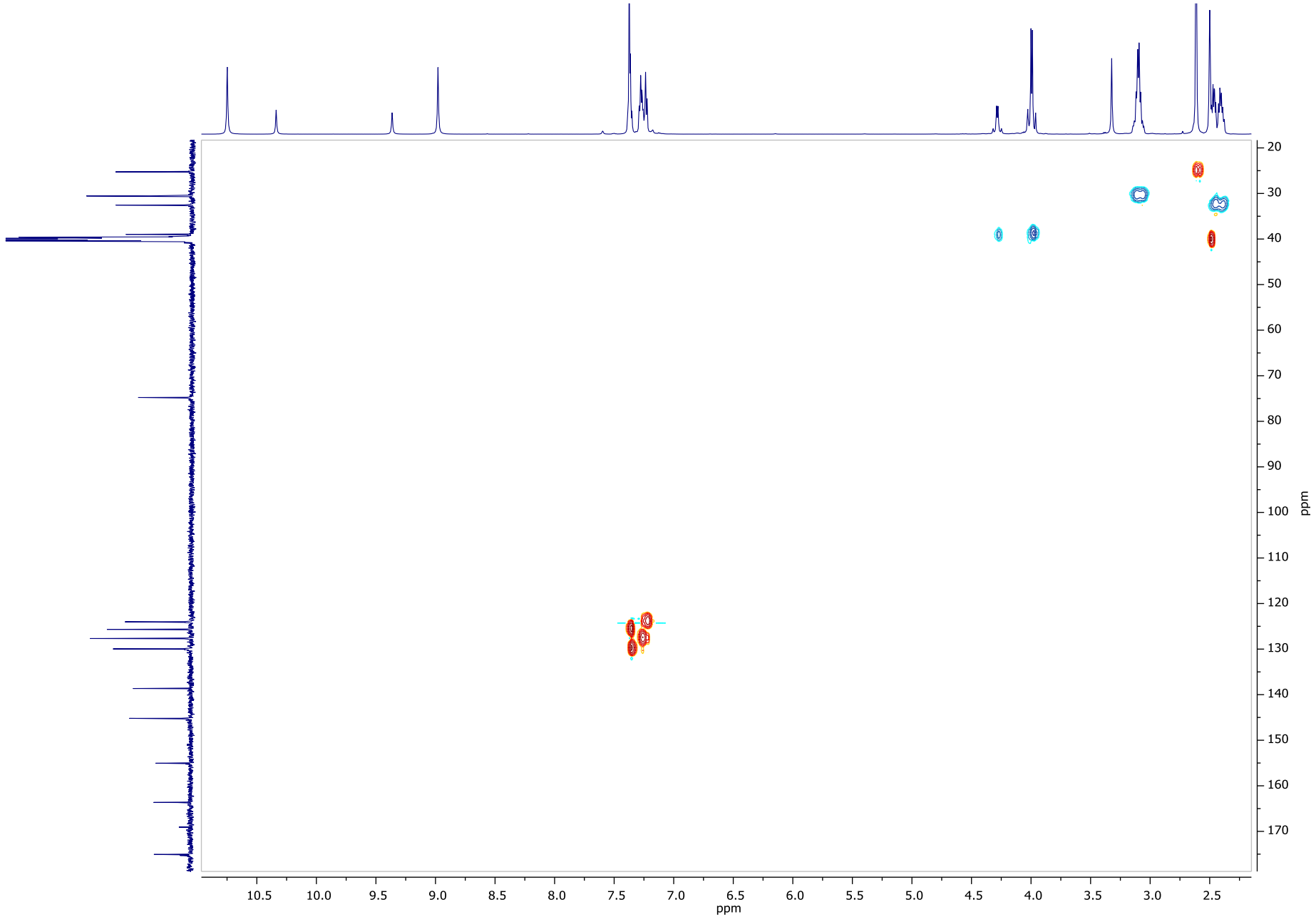
^{13}C NMR of **16a** (150.9 MHz, DMSO-d_6)



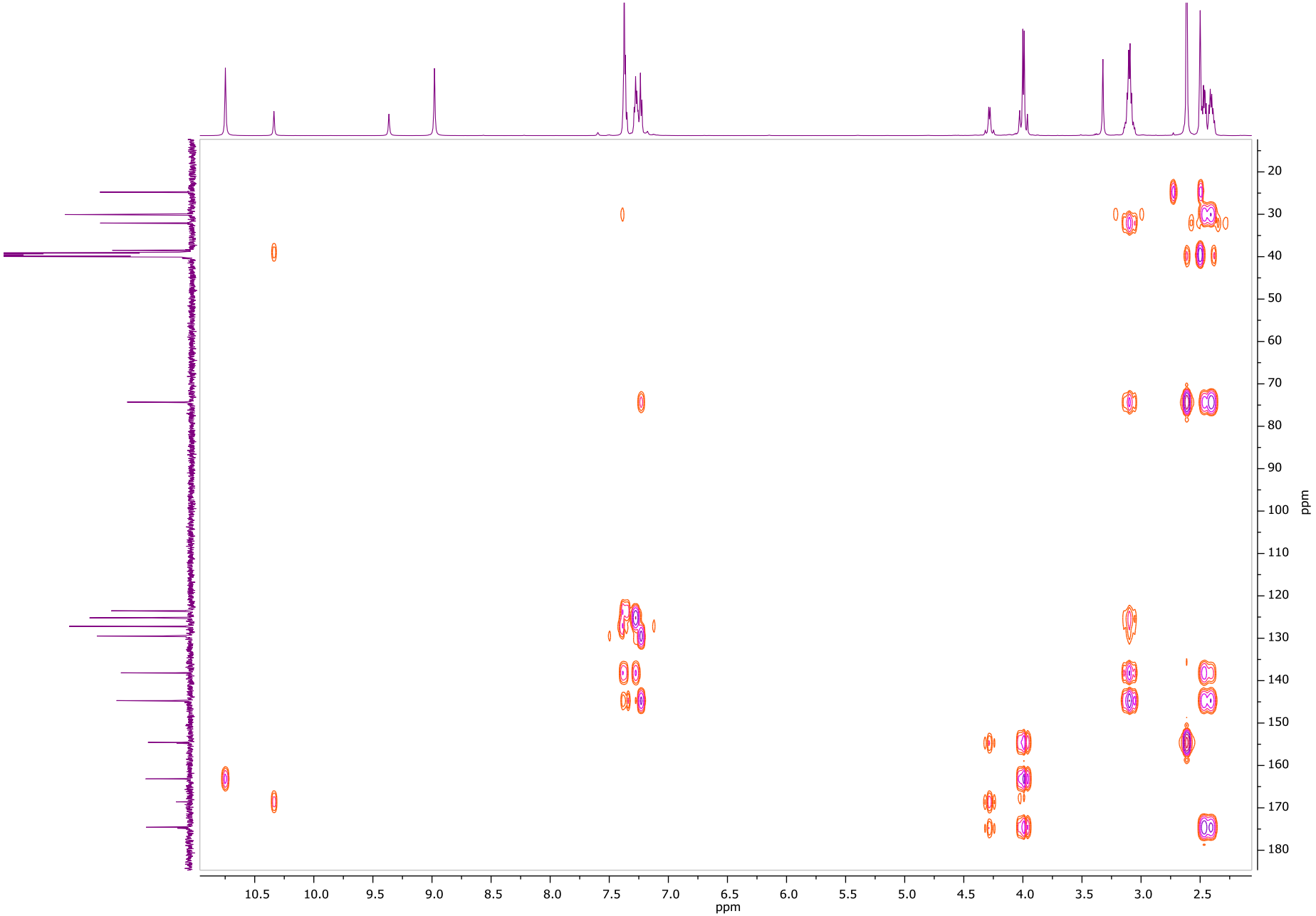
COSY NMR of **16a** (600.11 MHz, DMSO-d_6)



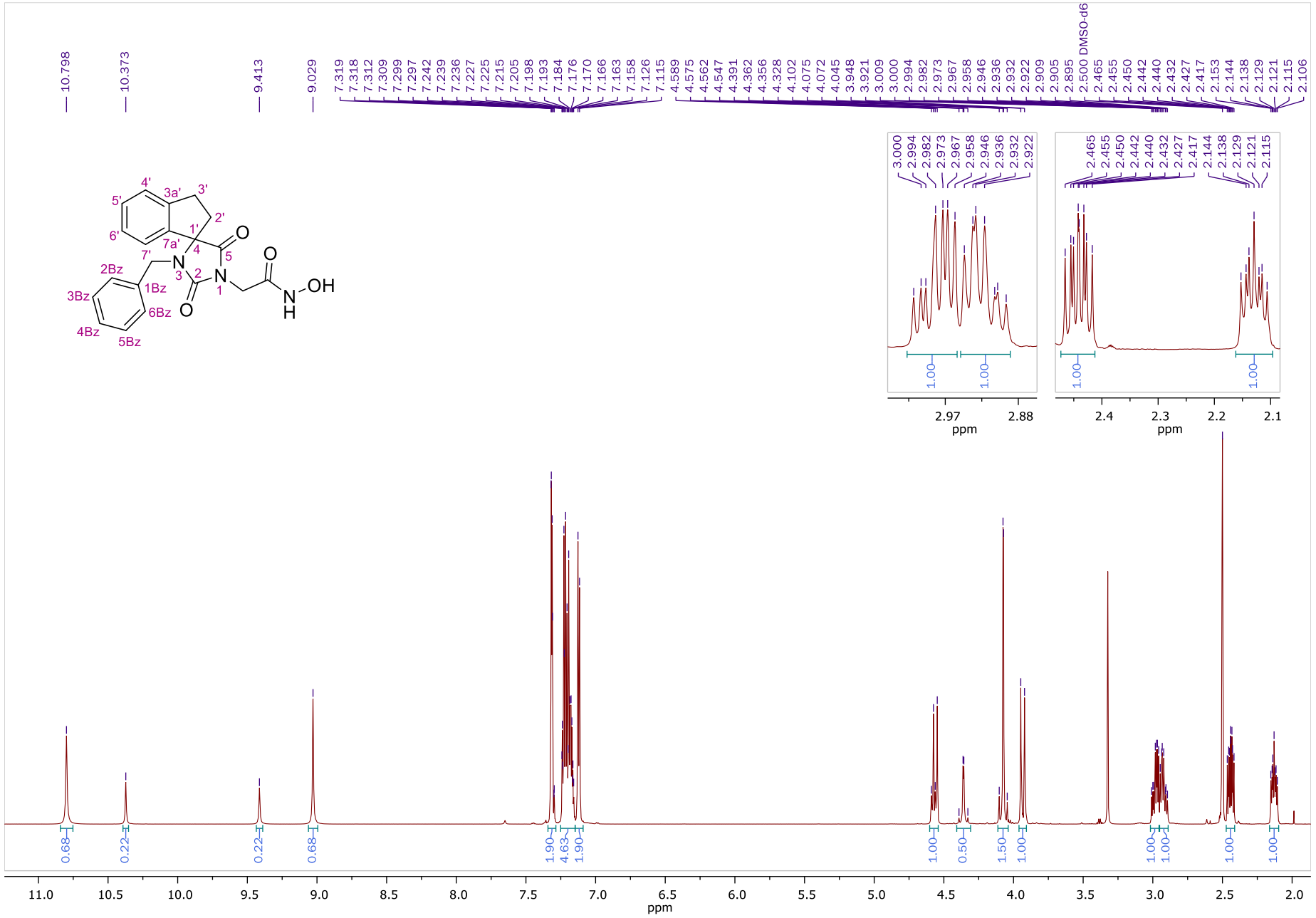
HSQC-DEPT NMR of **16a** (600.11 MHz, DMSO-d_6)



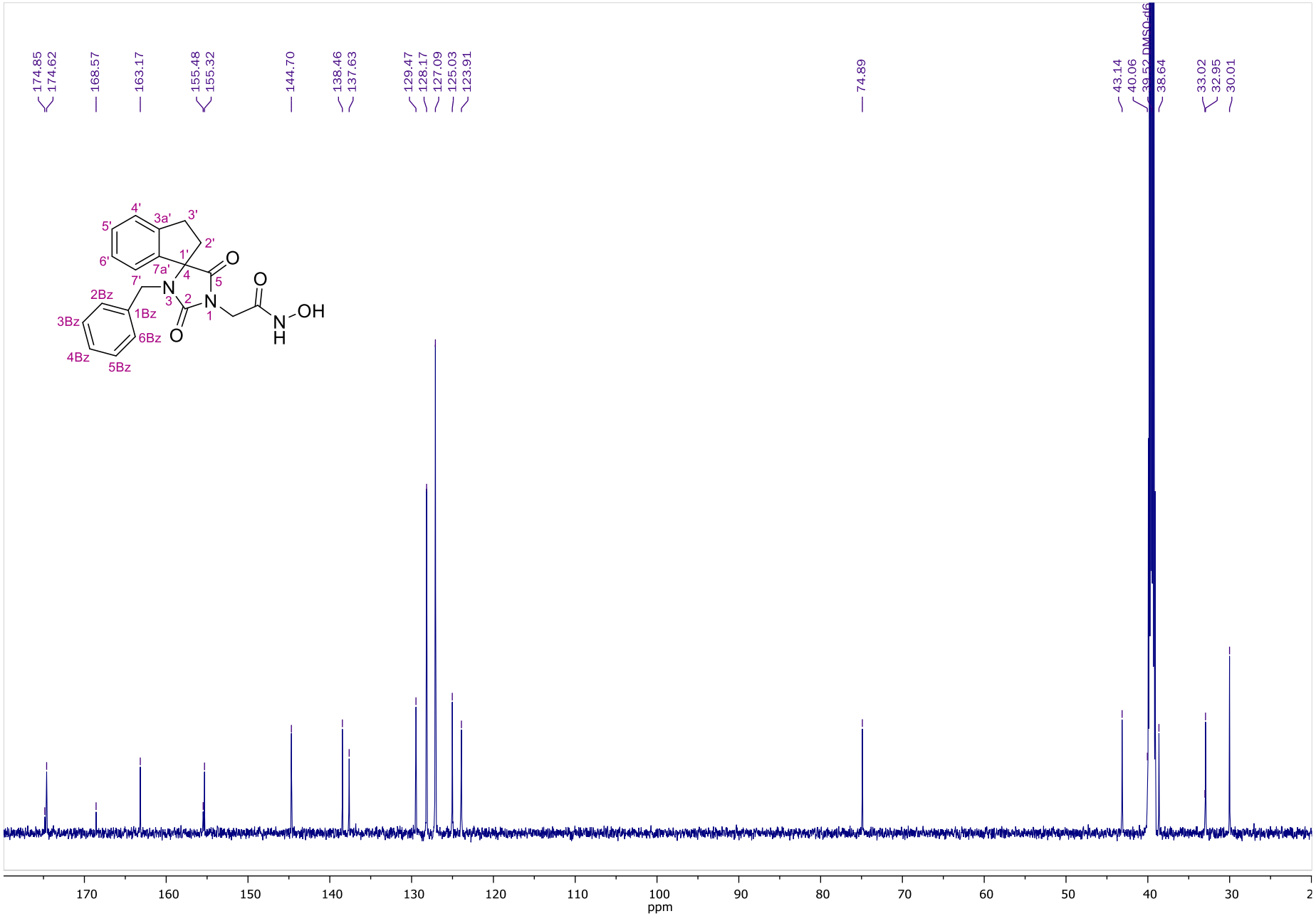
HMBC NMR of **16a** (600.11 MHz, DMSO-d_6)



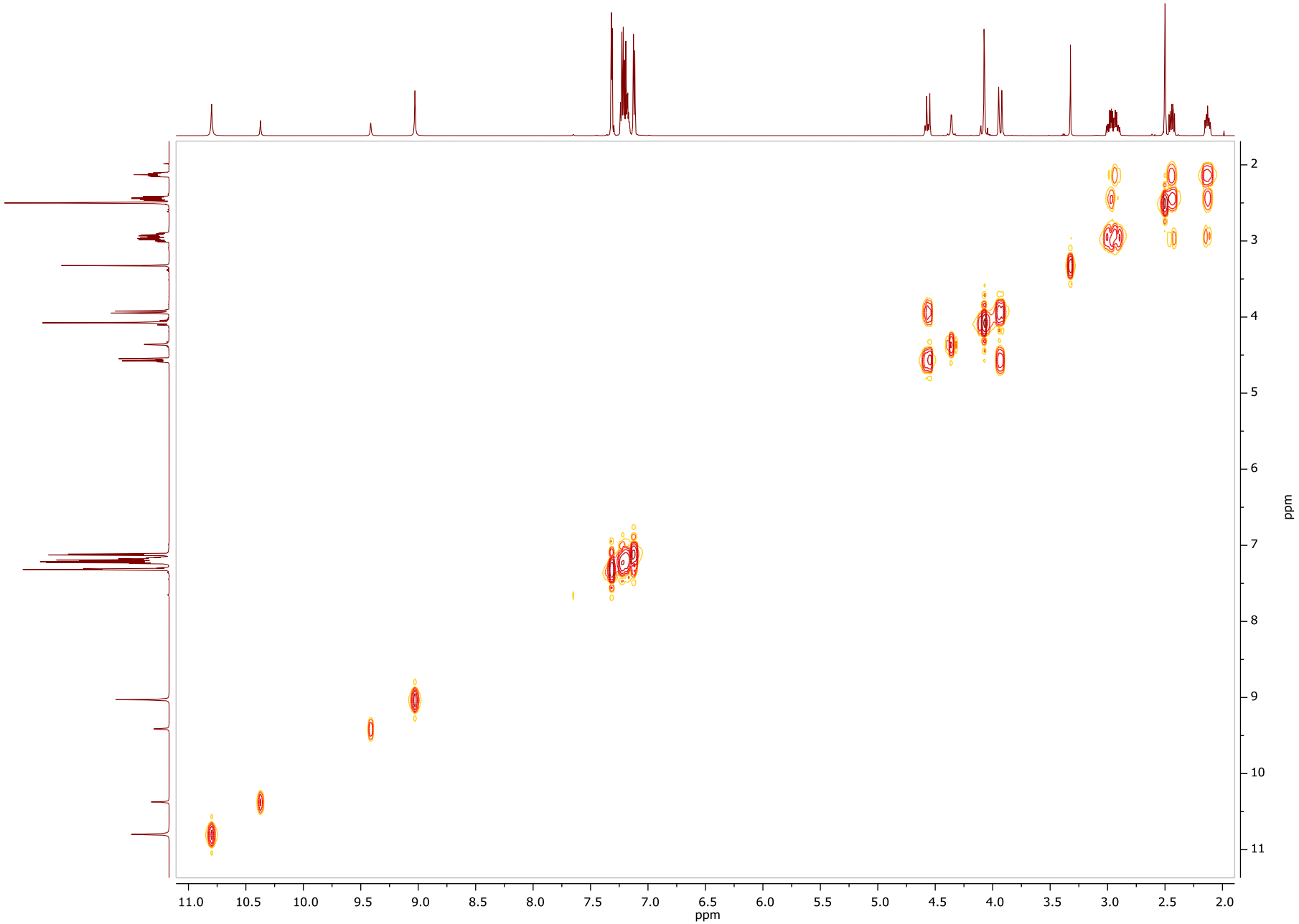
^{1}H NMR of **16b** (600.11 MHz, DMSO-d_6)



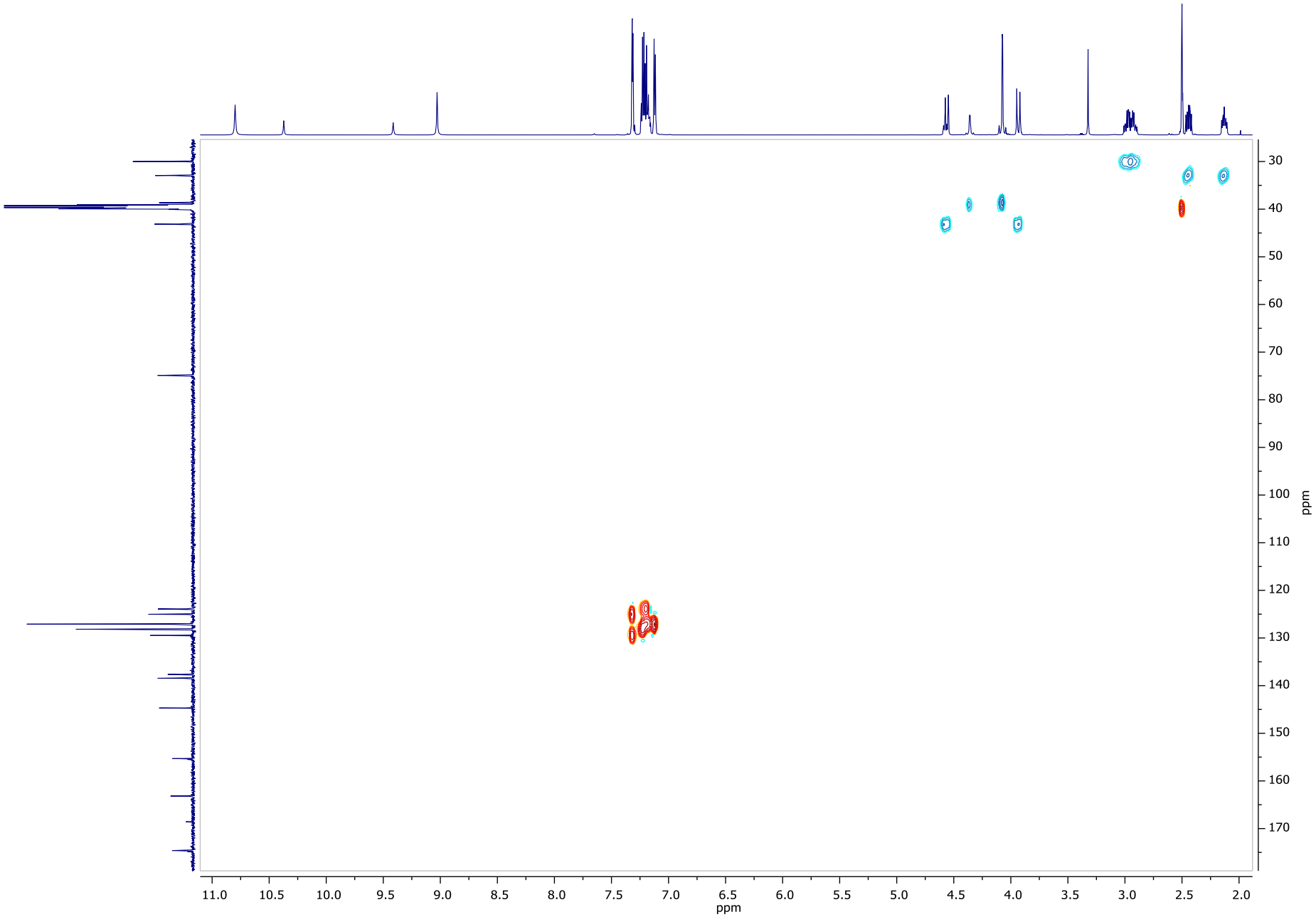
^{13}C NMR of **16b** (150.9 MHz, DMSO-d_6)



COSY NMR of **16b** (600.11 MHz, DMSO-d_6)

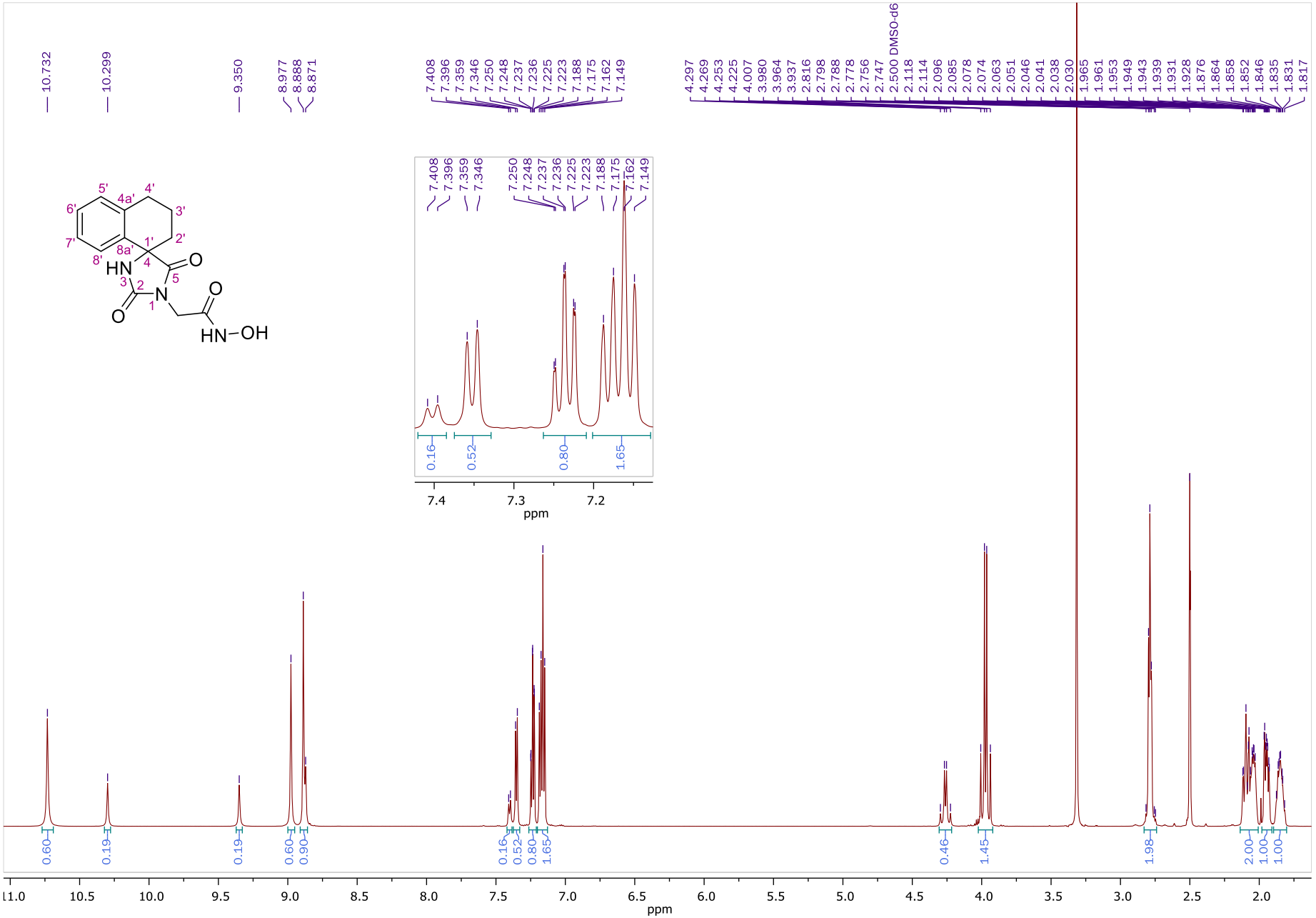


HSQC-DEPT NMR of **16b** (600.11 MHz, DMSO-d_6)

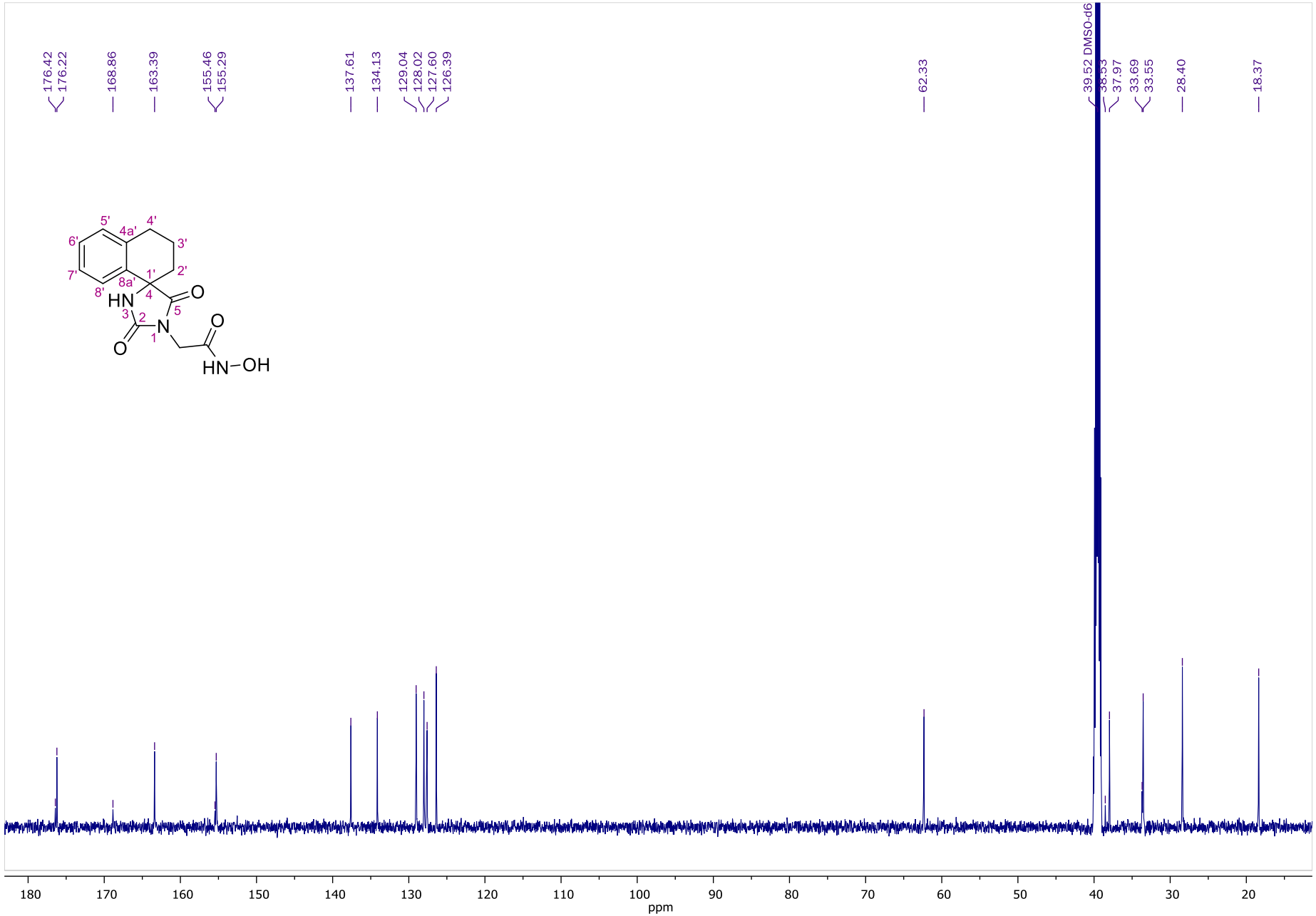


HMBC NMR of **16b** (600.11 MHz, DMSO-d_6)

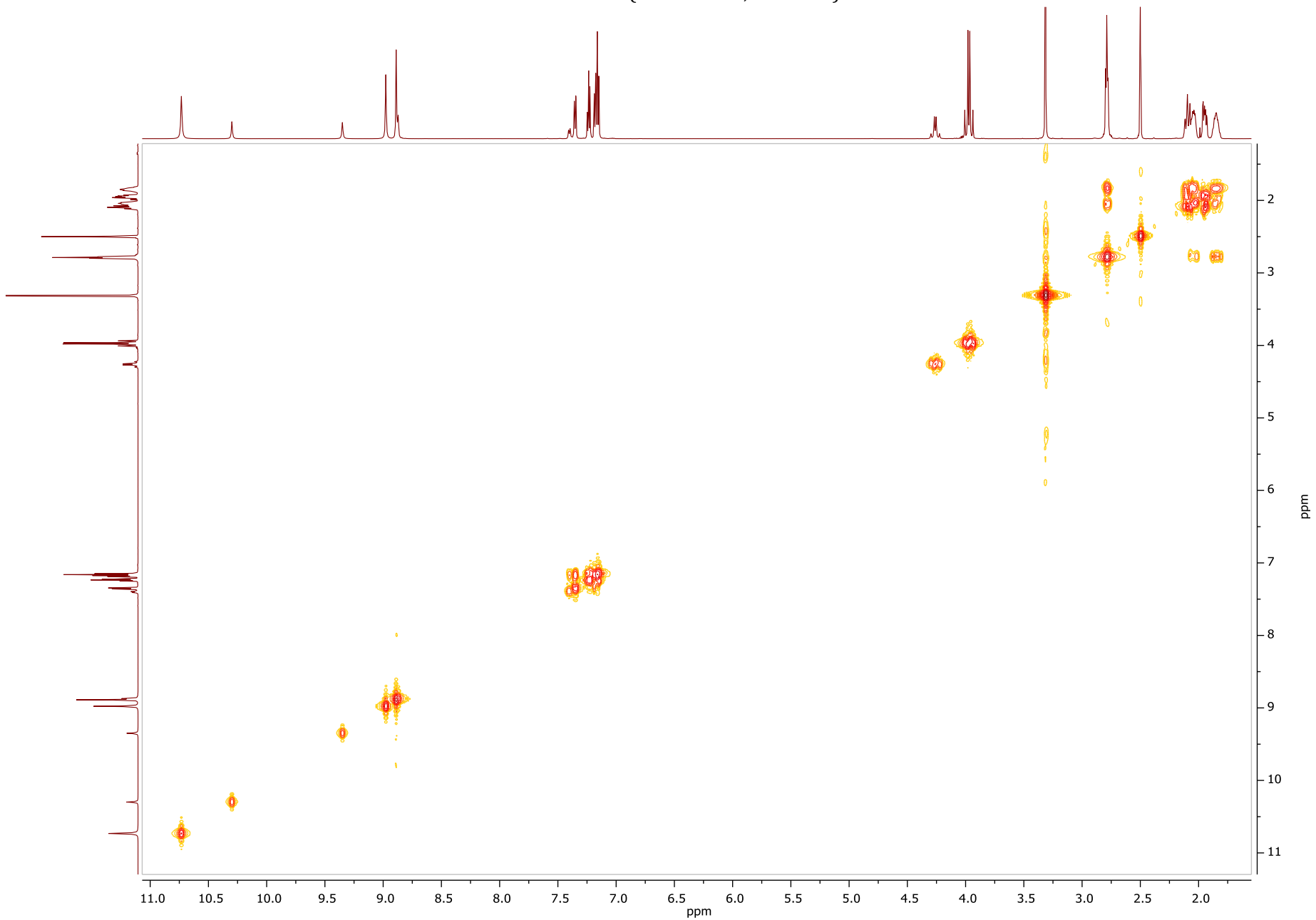
^{1}H NMR of **17** (600.11 MHz, DMSO-d_6)



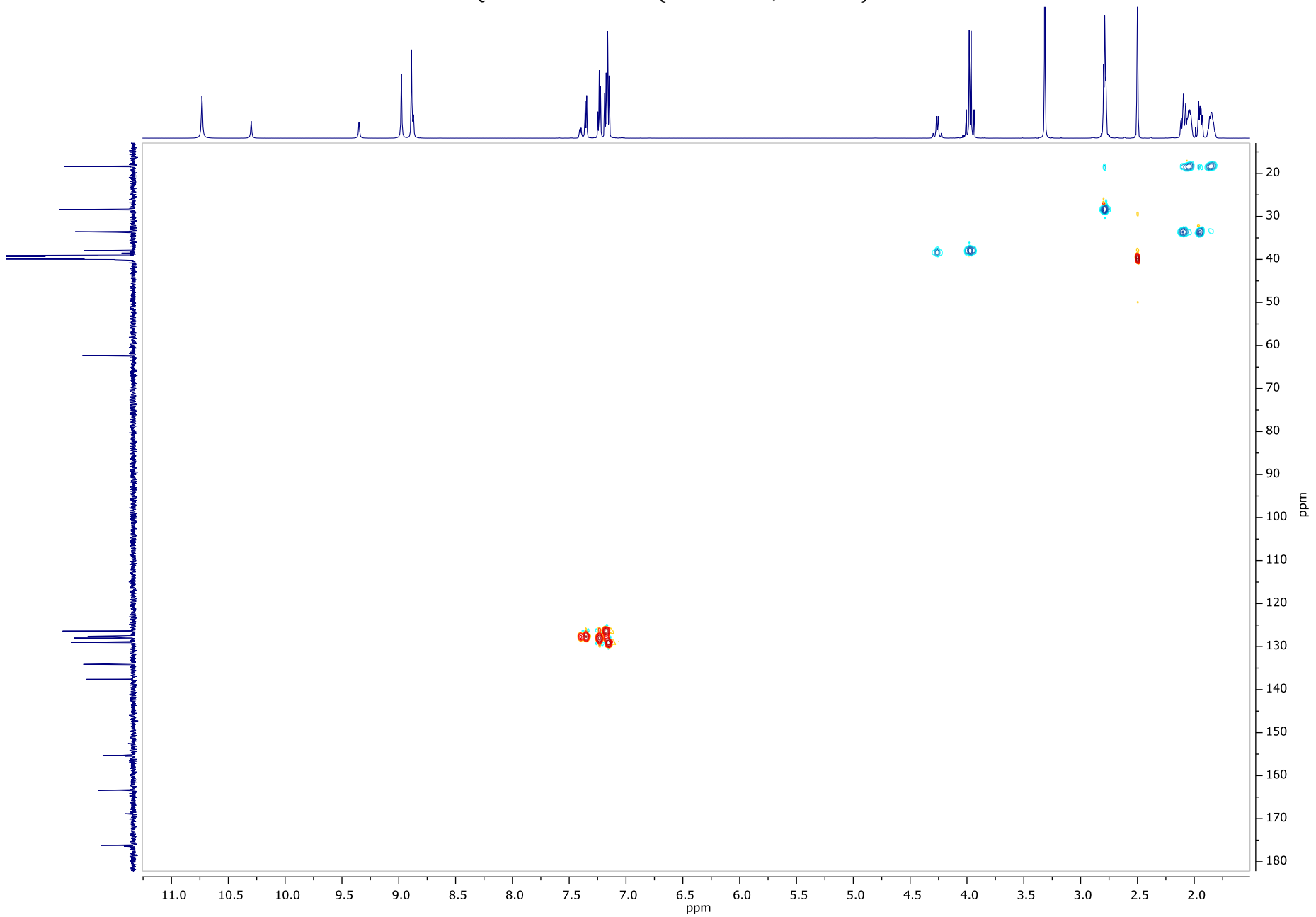
^{13}C NMR of **17** (150.9 MHz, DMSO-d_6)



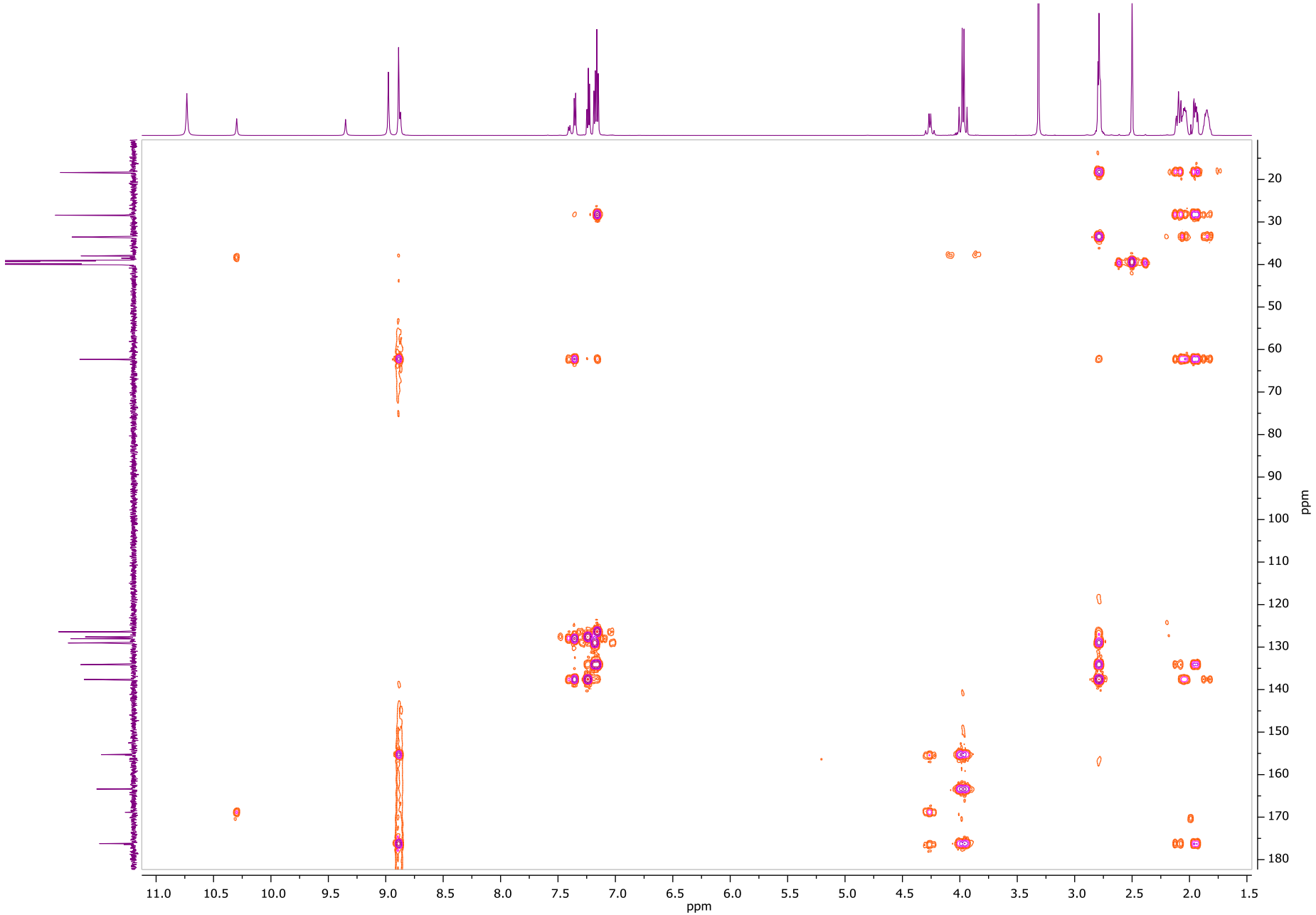
COSY NMR of **17** (600.11 MHz, DMSO-d_6)



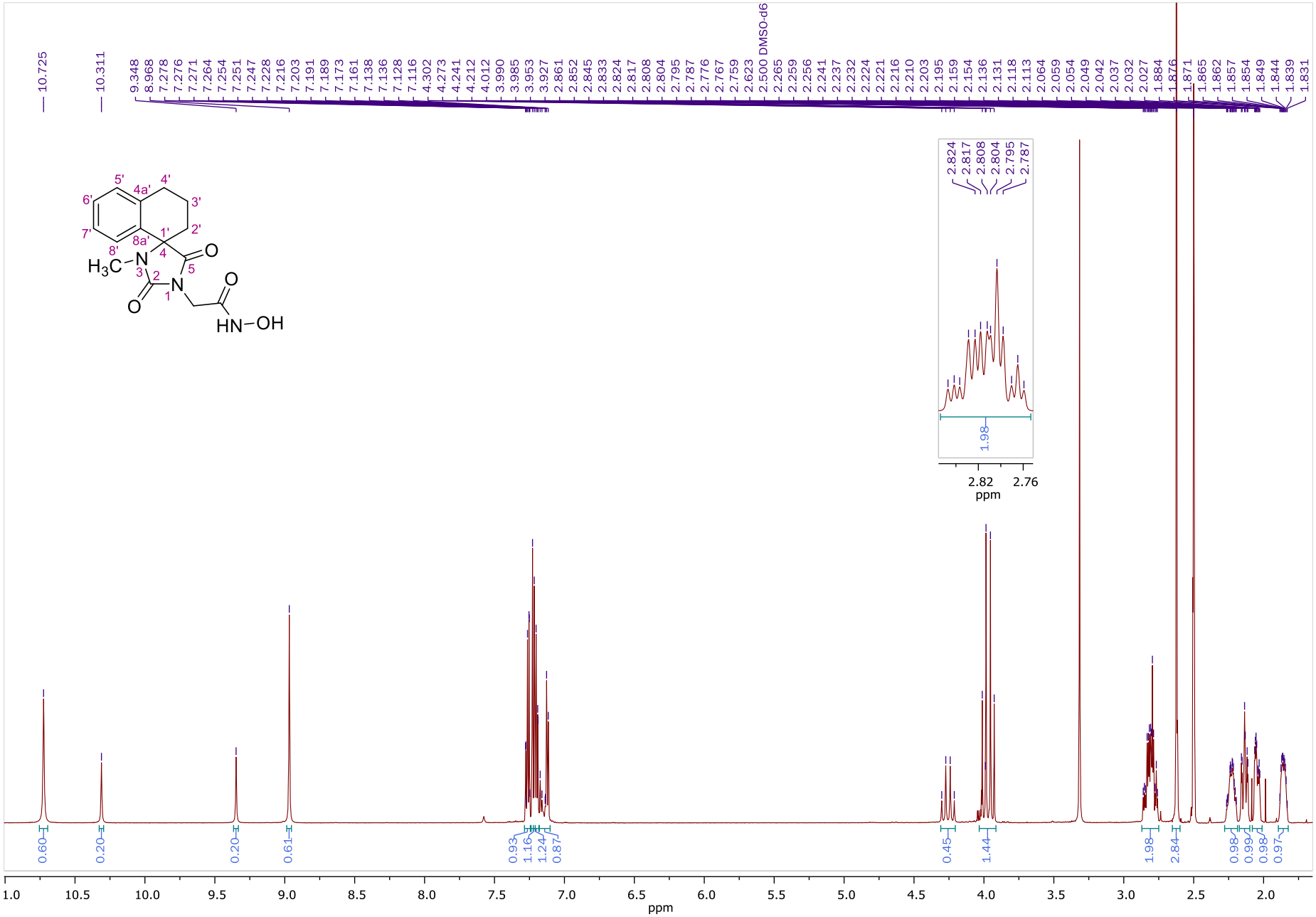
HSQC-DEPT NMR of **17** (600.11 MHz, DMSO-d_6)



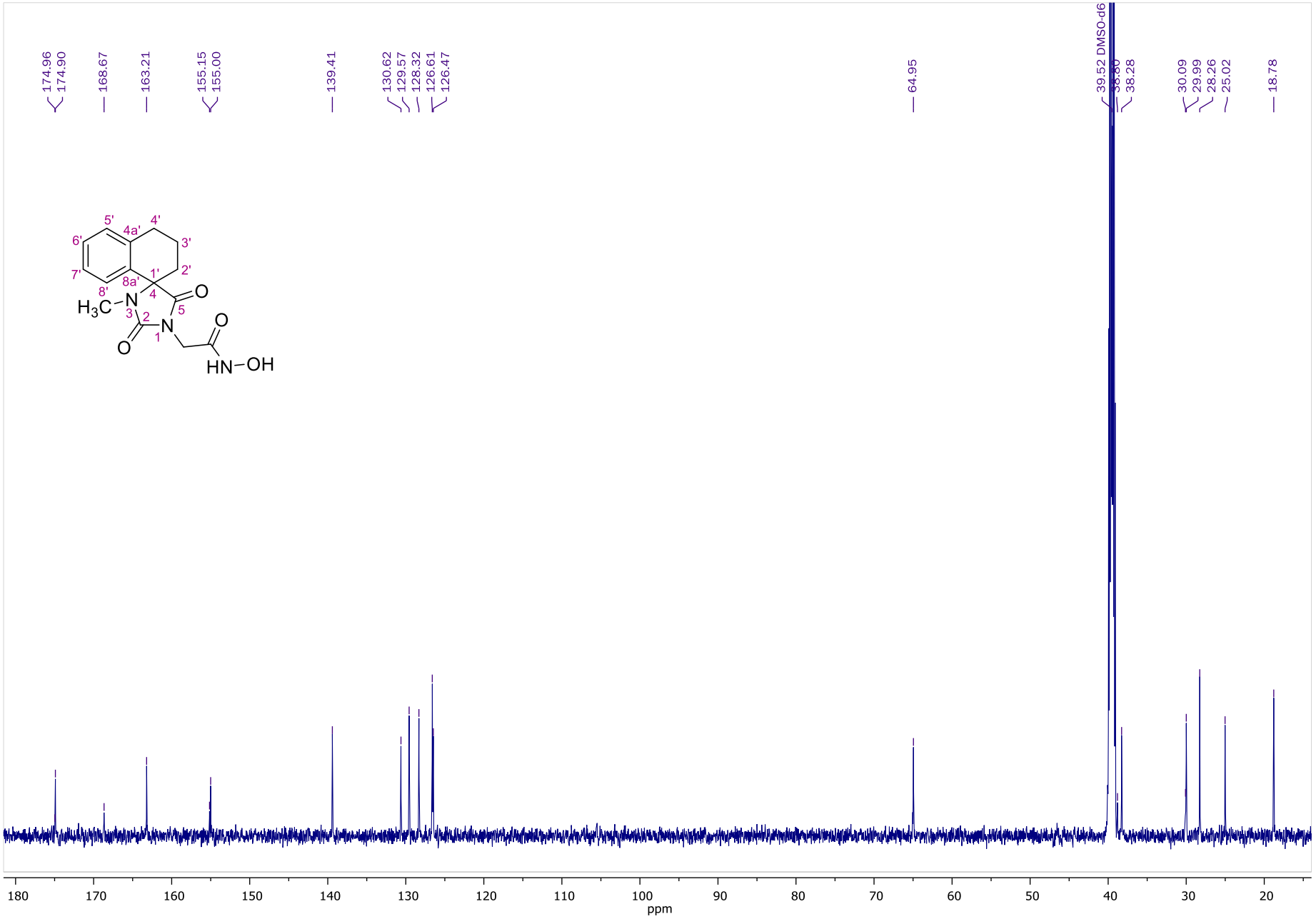
HMBC NMR of **17** (600.11 MHz, DMSO-d_6)



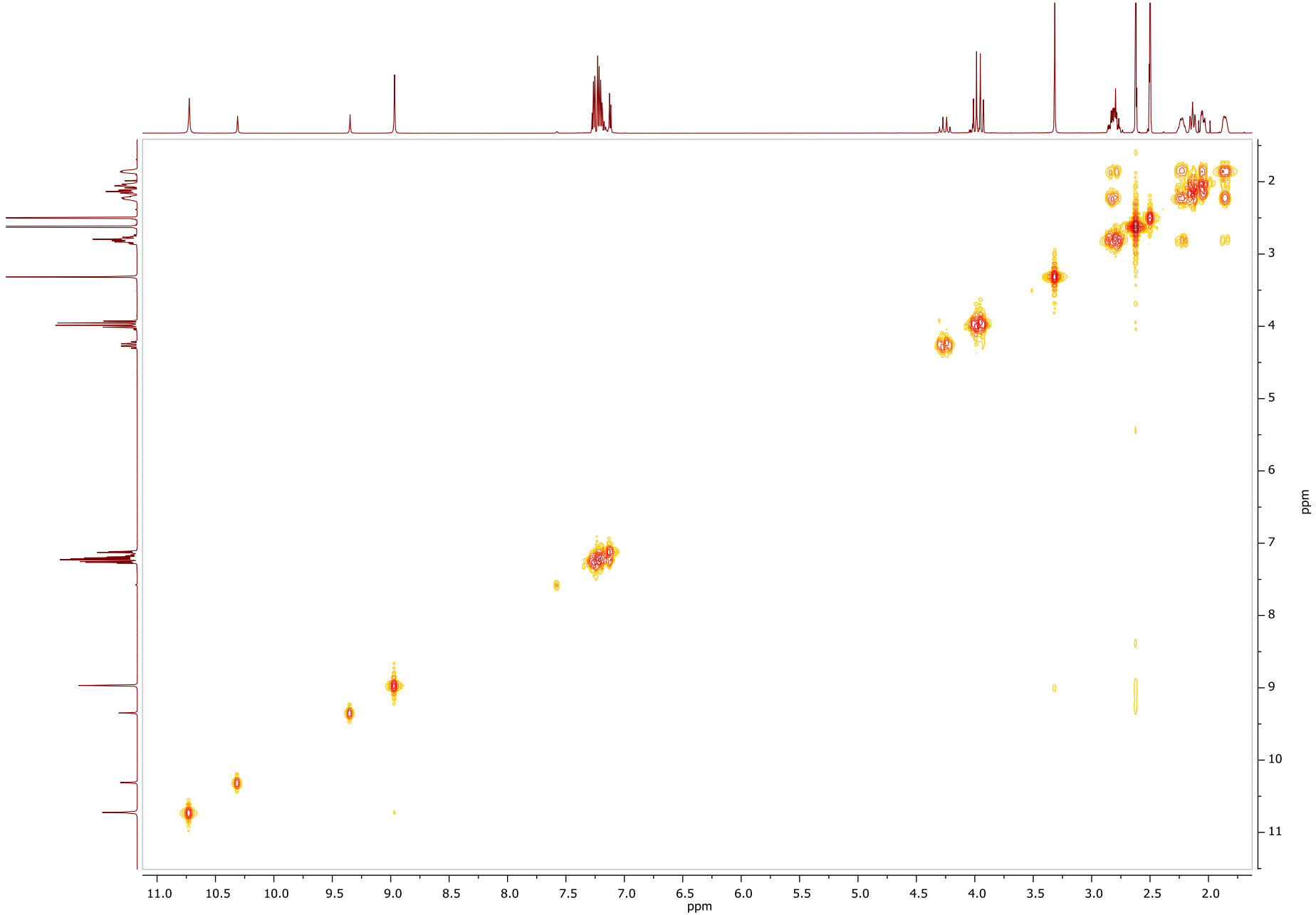
^{1}H NMR of **17a** (600.11 MHz, DMSO-d_6)



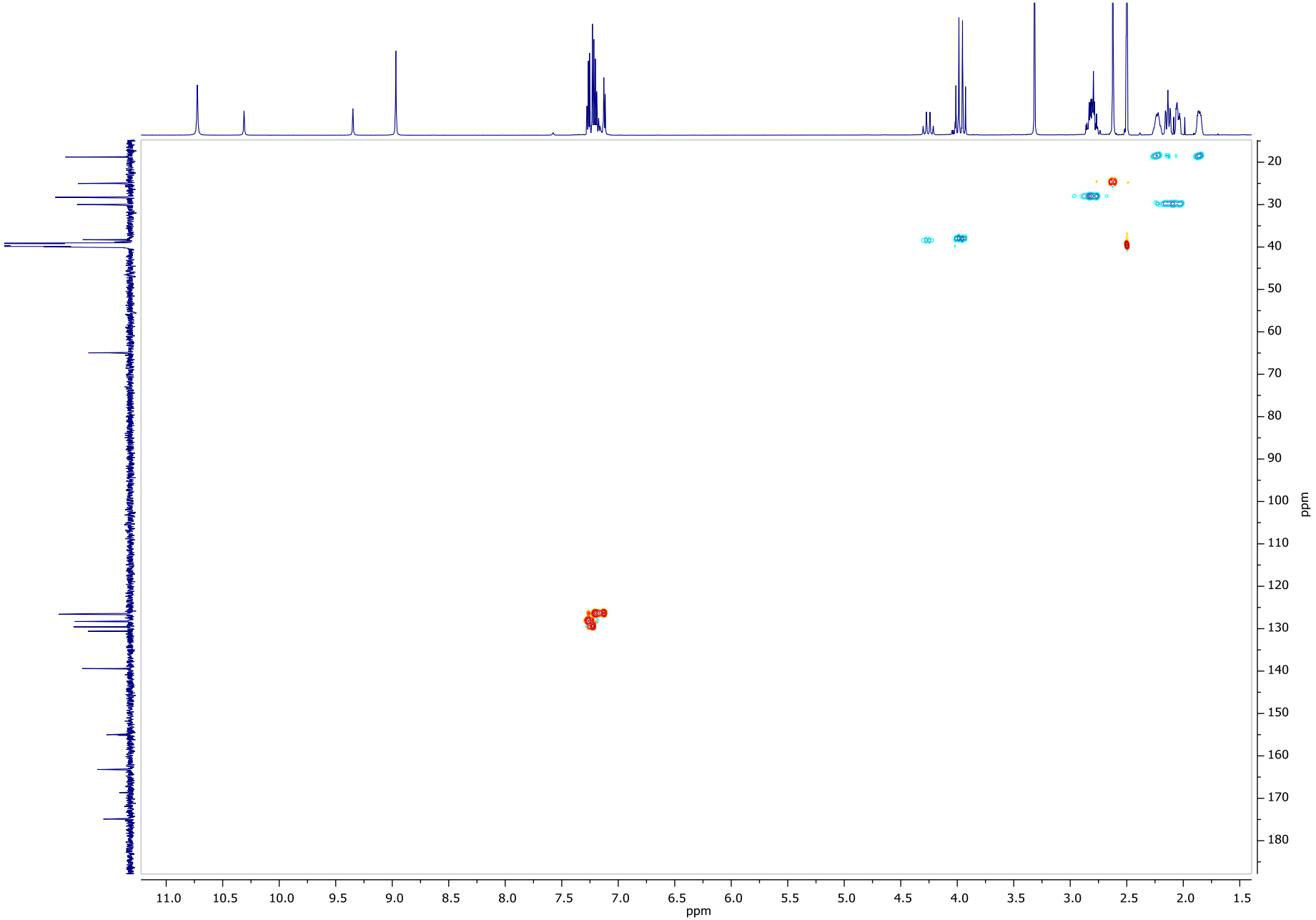
^{13}C NMR of **17a** (150.9 MHz, DMSO-d_6)



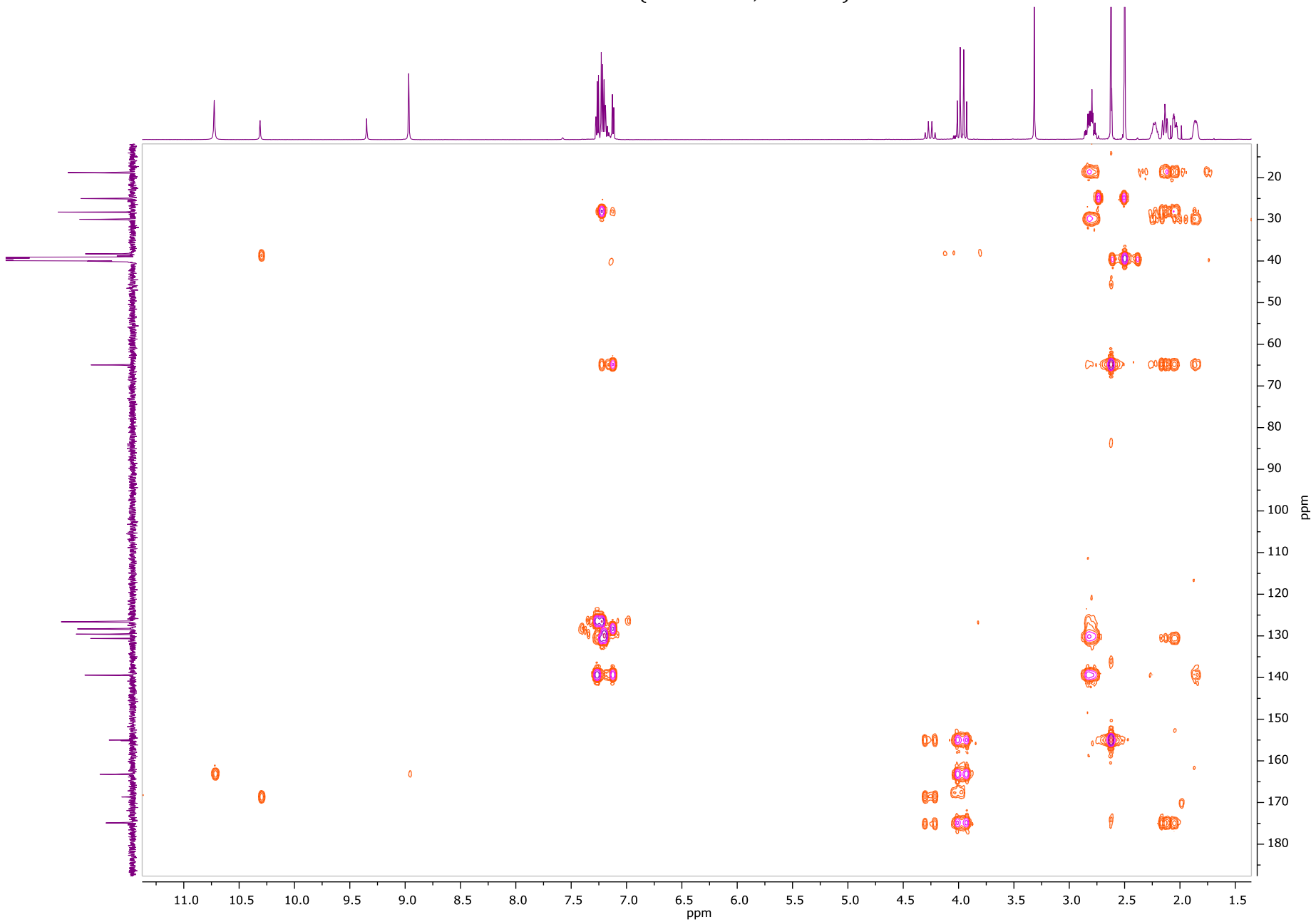
COSY NMR of **17a** (600.11 MHz, DMSO-d_6)



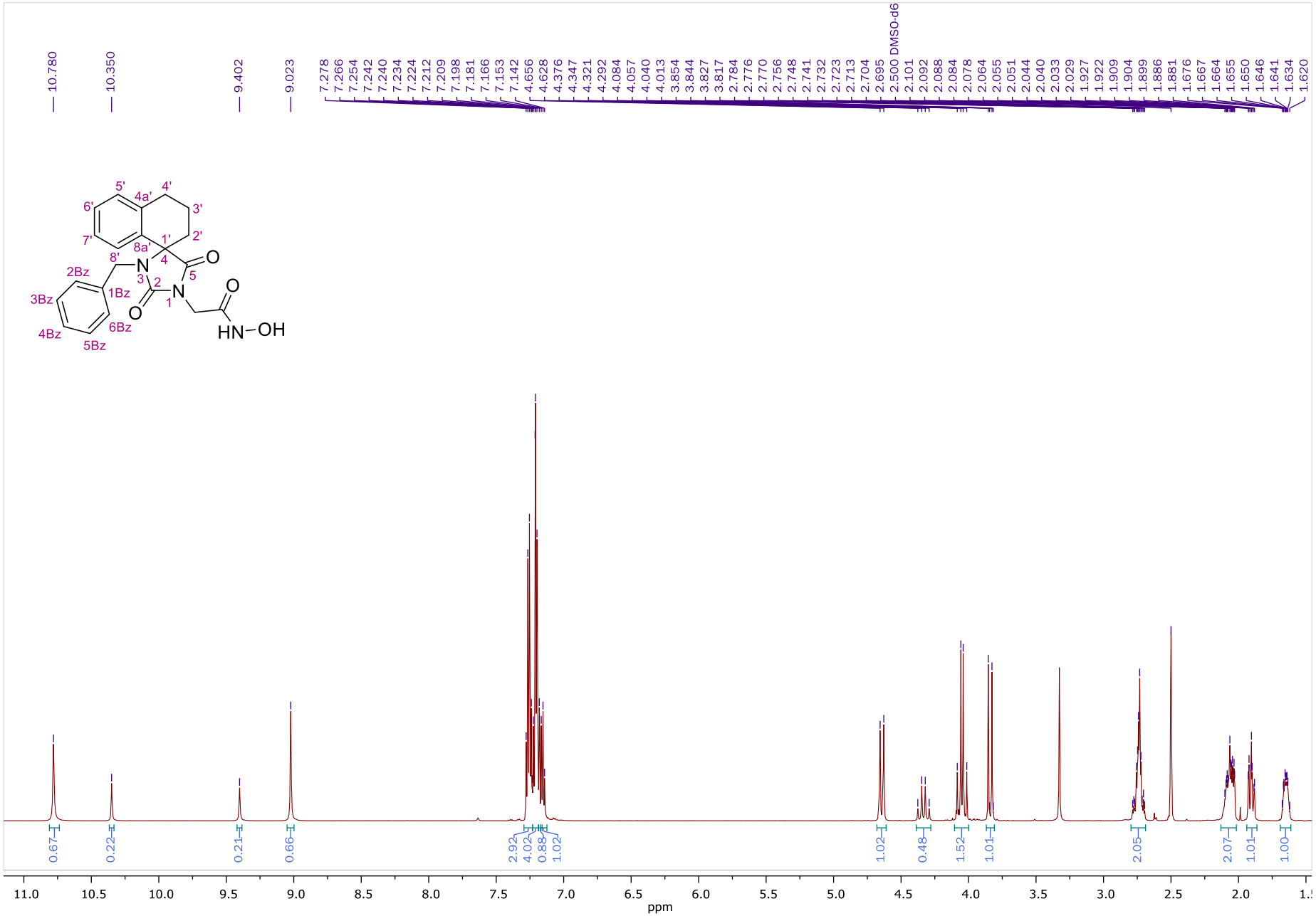
HSQC-DEPT NMR of **17a** (600.11 MHz, DMSO-d_6)



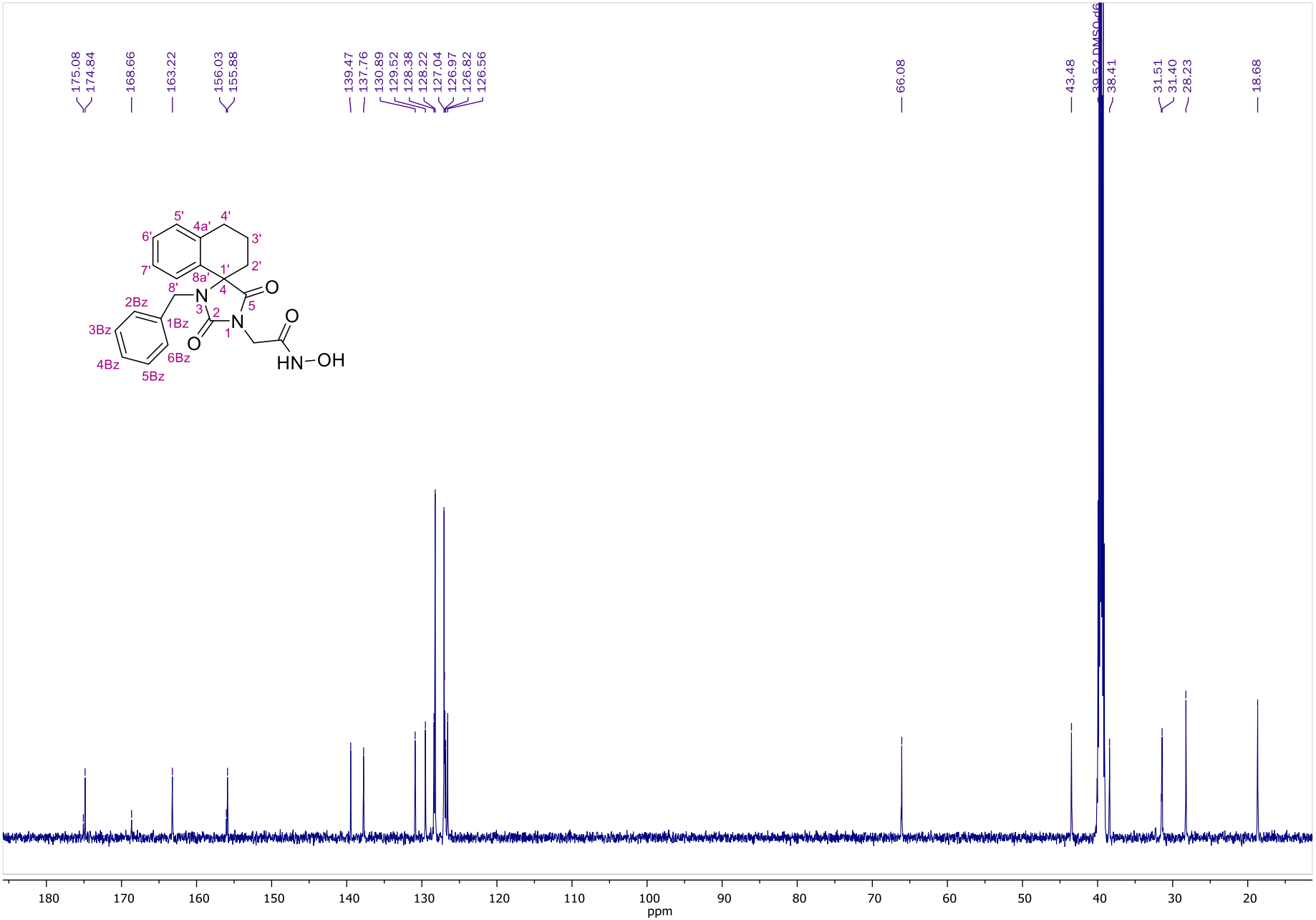
HMBC NMR of **17a** (600.11 MHz, DMSO-d_6)



^{1}H NMR of **17b** (600.11 MHz, DMSO-d_6)

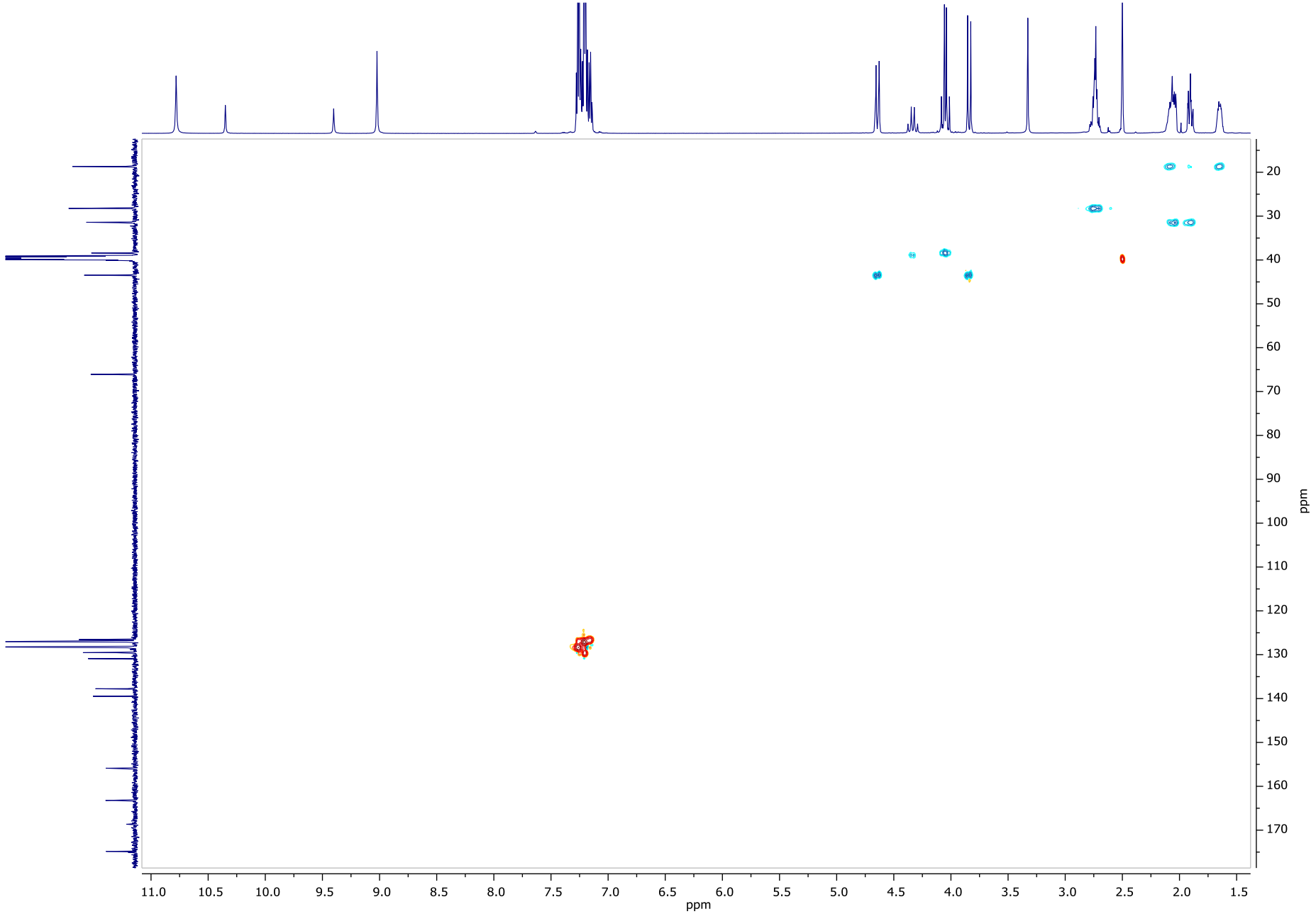


^{13}C NMR of **17b** (150.9 MHz, DMSO-d_6)



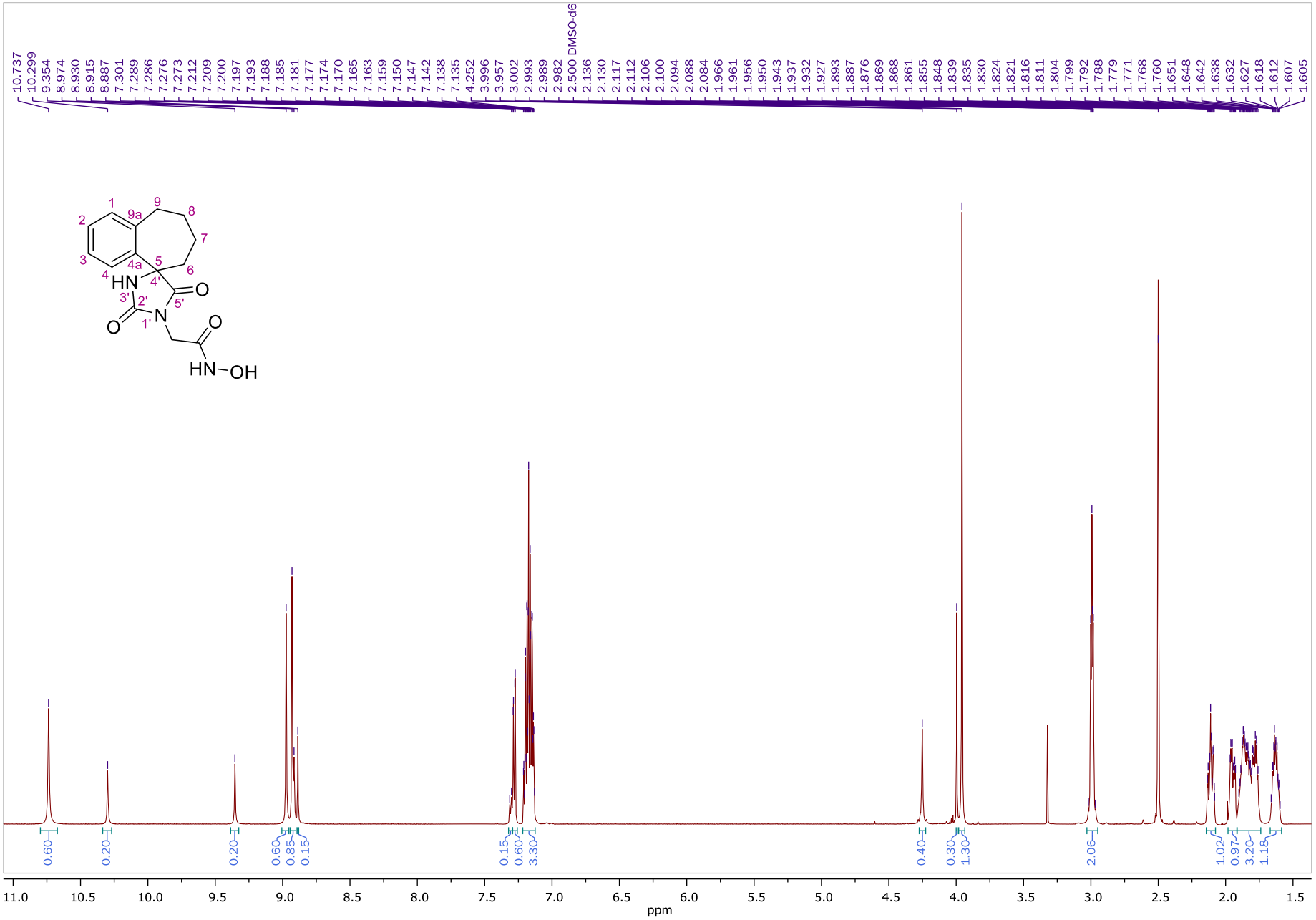
COSY NMR of **17b** (600.11 MHz, DMSO-d_6)

HSQC-DEPT NMR of **17b** (600.11 MHz, DMSO-d_6)

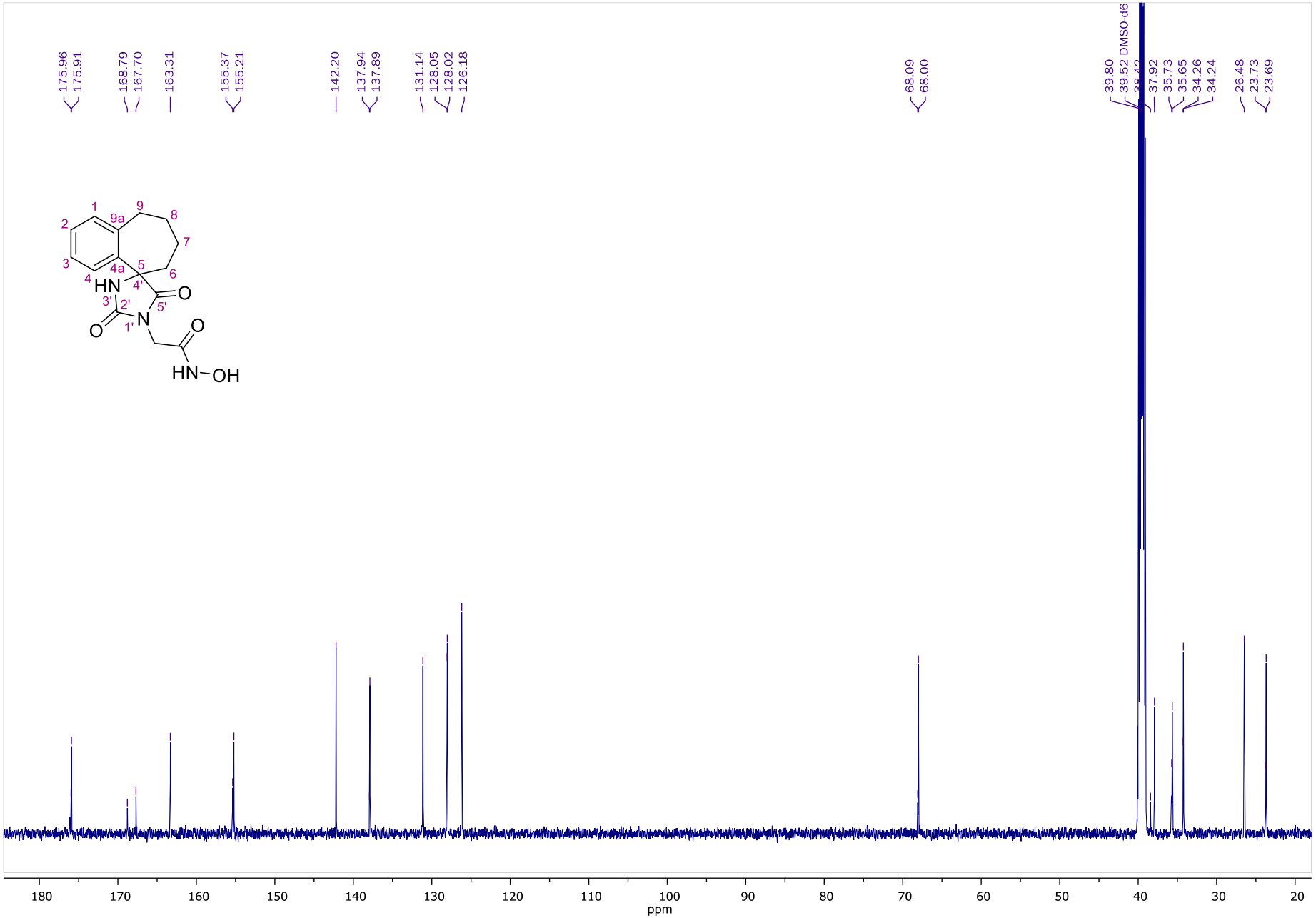


HMBC NMR of **17b** (600.11 MHz, DMSO-d_6)

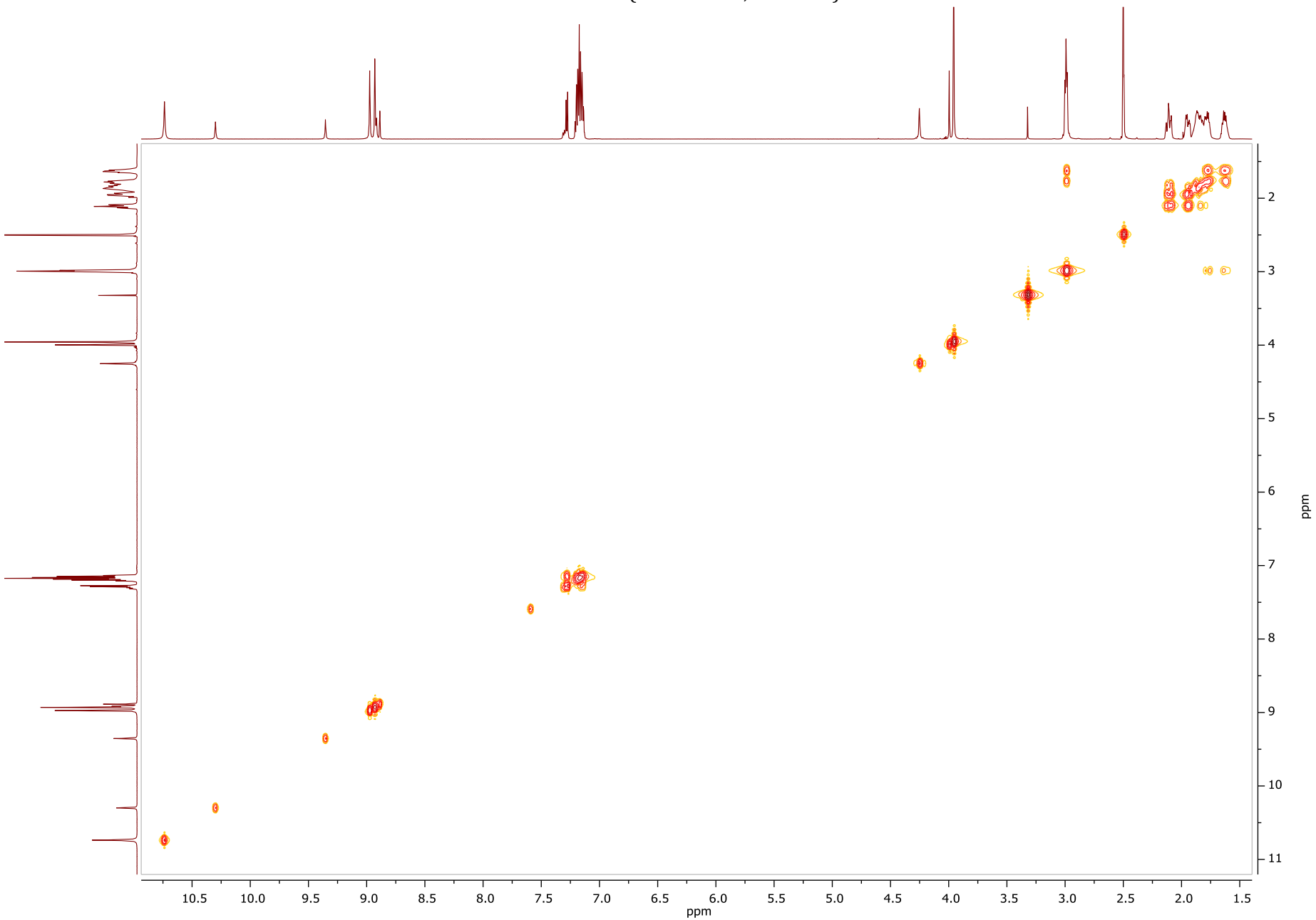
^{1}H NMR of **18** (600.11 MHz, DMSO-d_6)



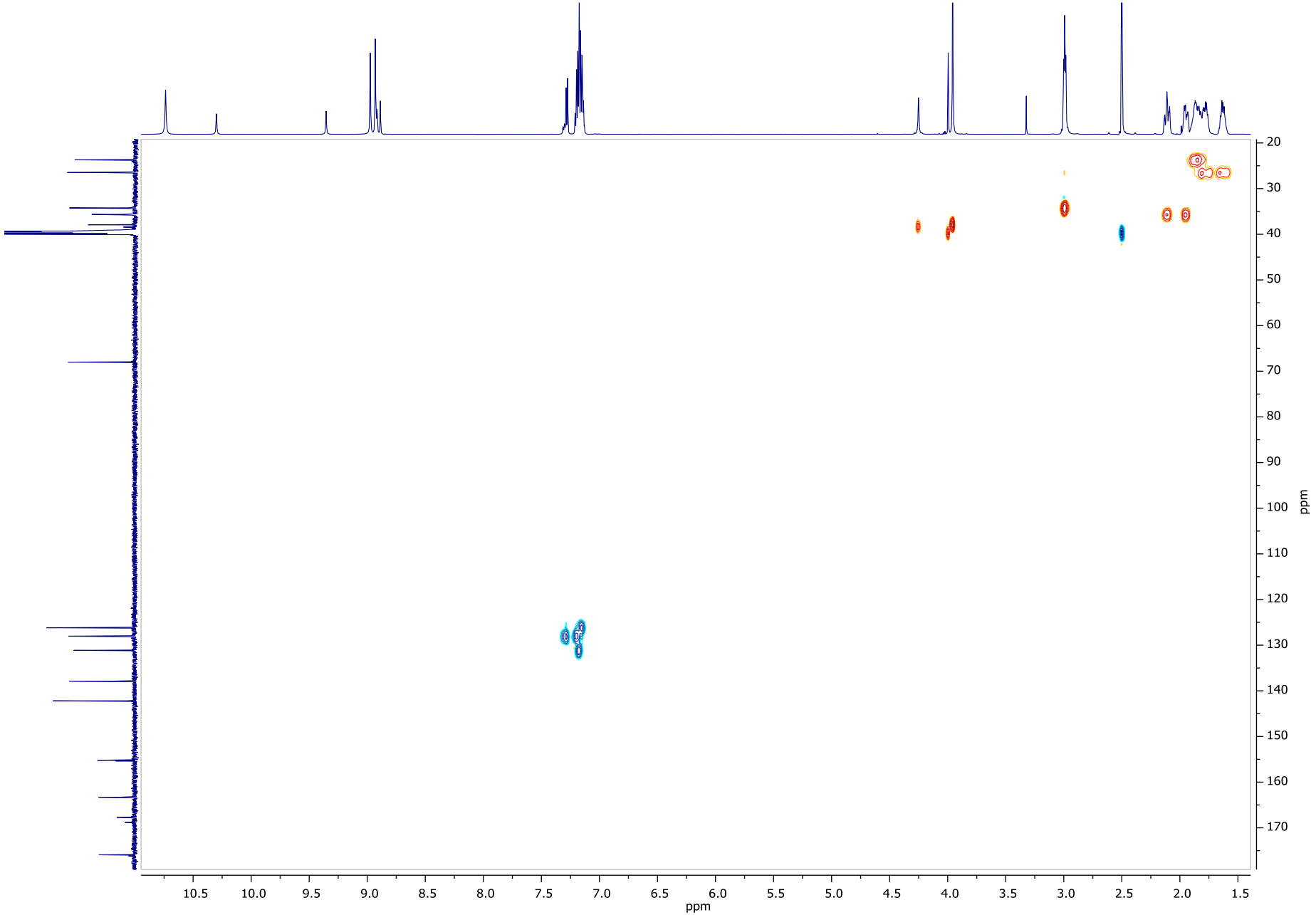
^{13}C NMR of **18** (150.9 MHz, DMSO-d_6)



COSY NMR of **18** (600.11 MHz, DMSO-d_6)

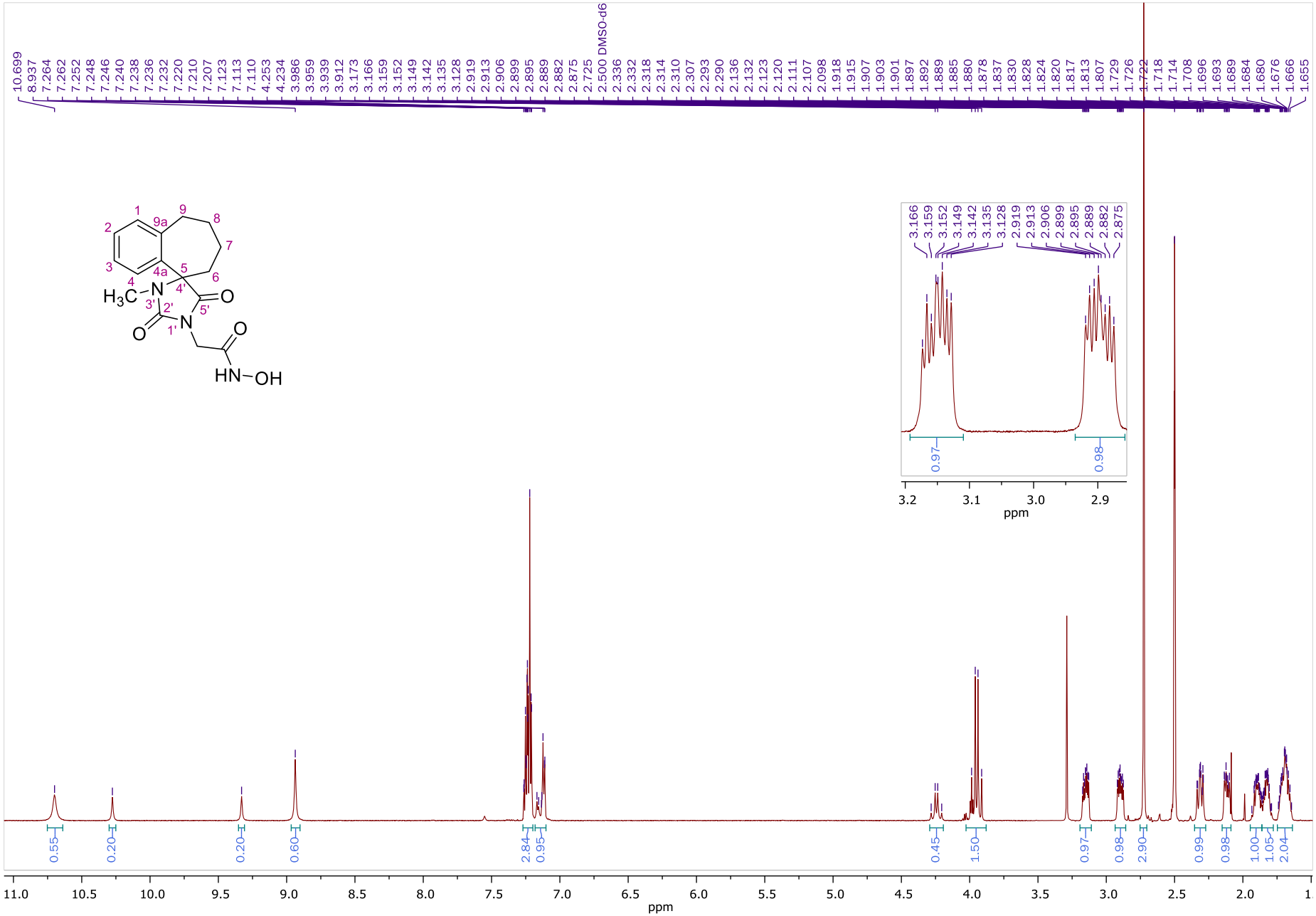


HSQC-DEPT NMR of **18** (600.11 MHz, DMSO-d_6)

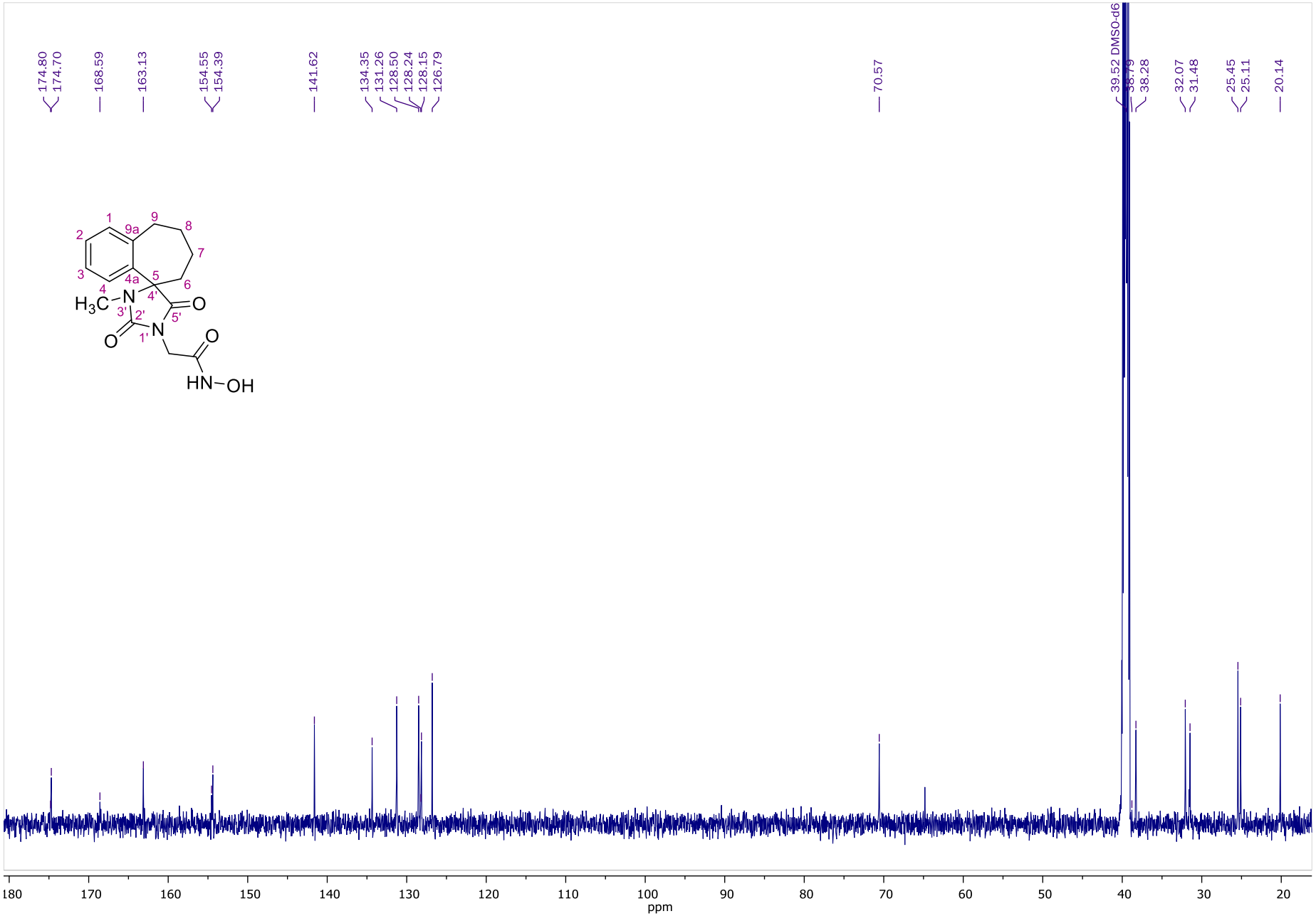


HMBC NMR of **18** (600.11 MHz, DMSO-d_6)

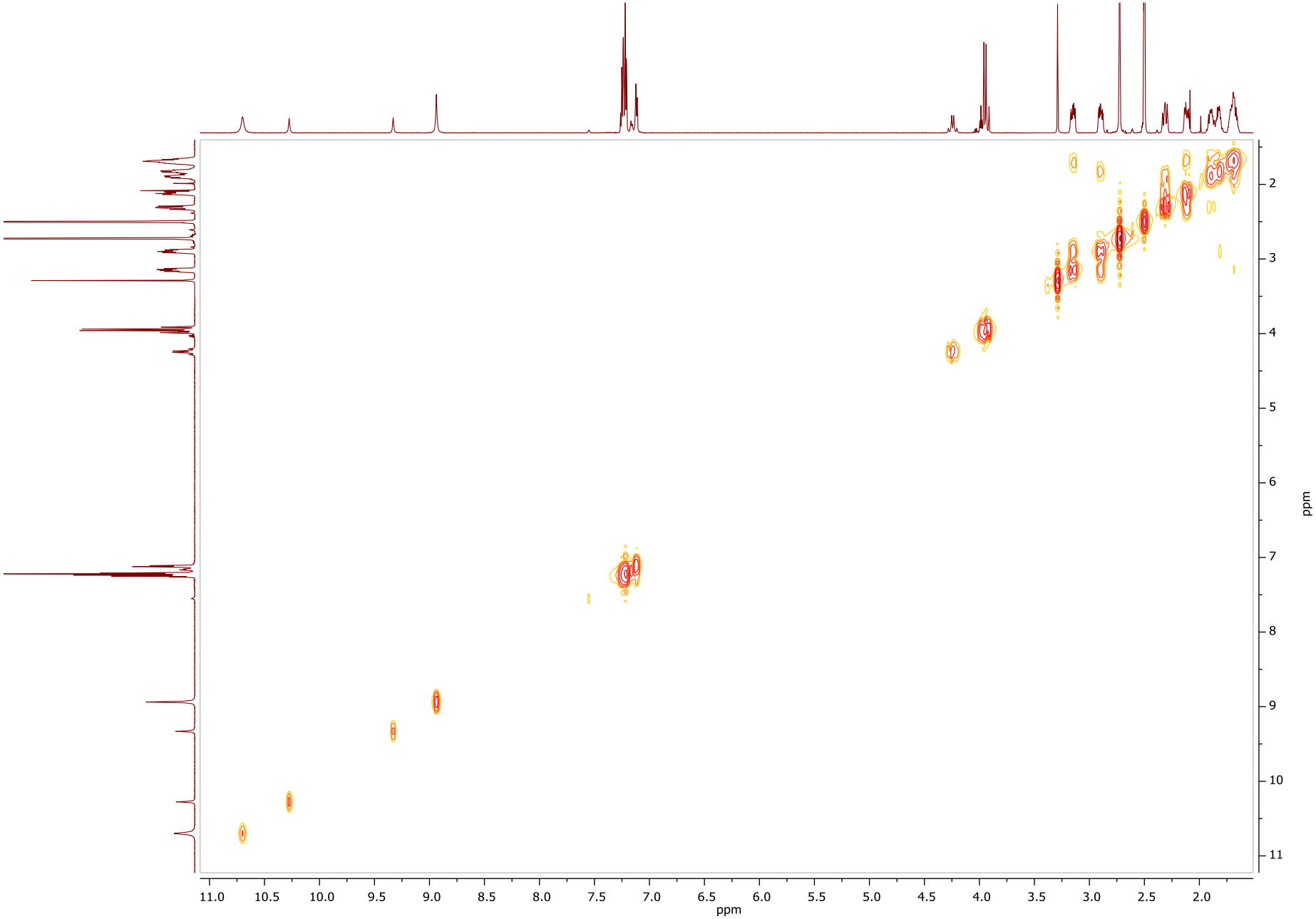
^{1}H NMR of **18a** (600.11 MHz, DMSO-d_6)



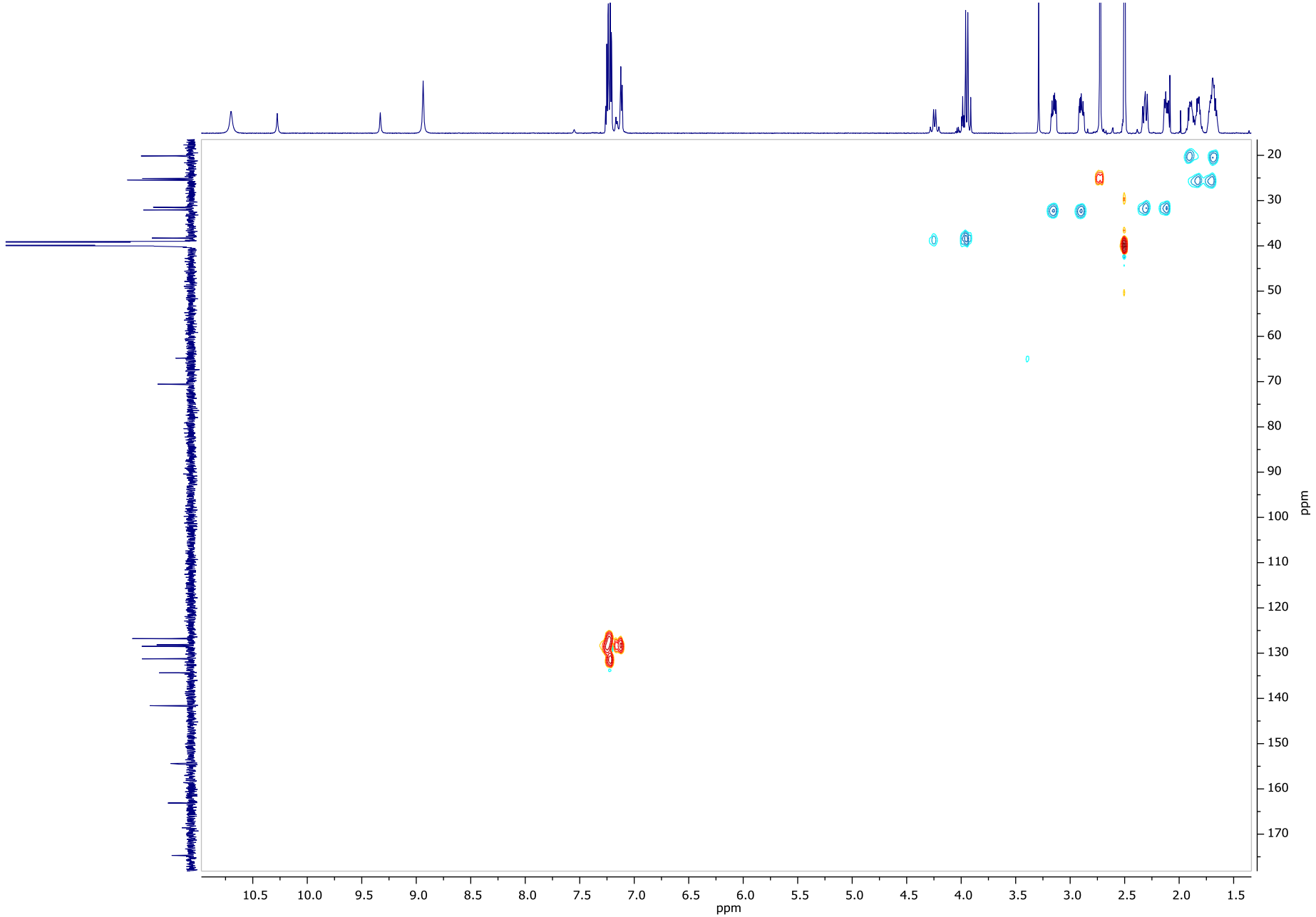
^{13}C NMR of **18a** (150.9 MHz, DMSO-d_6)



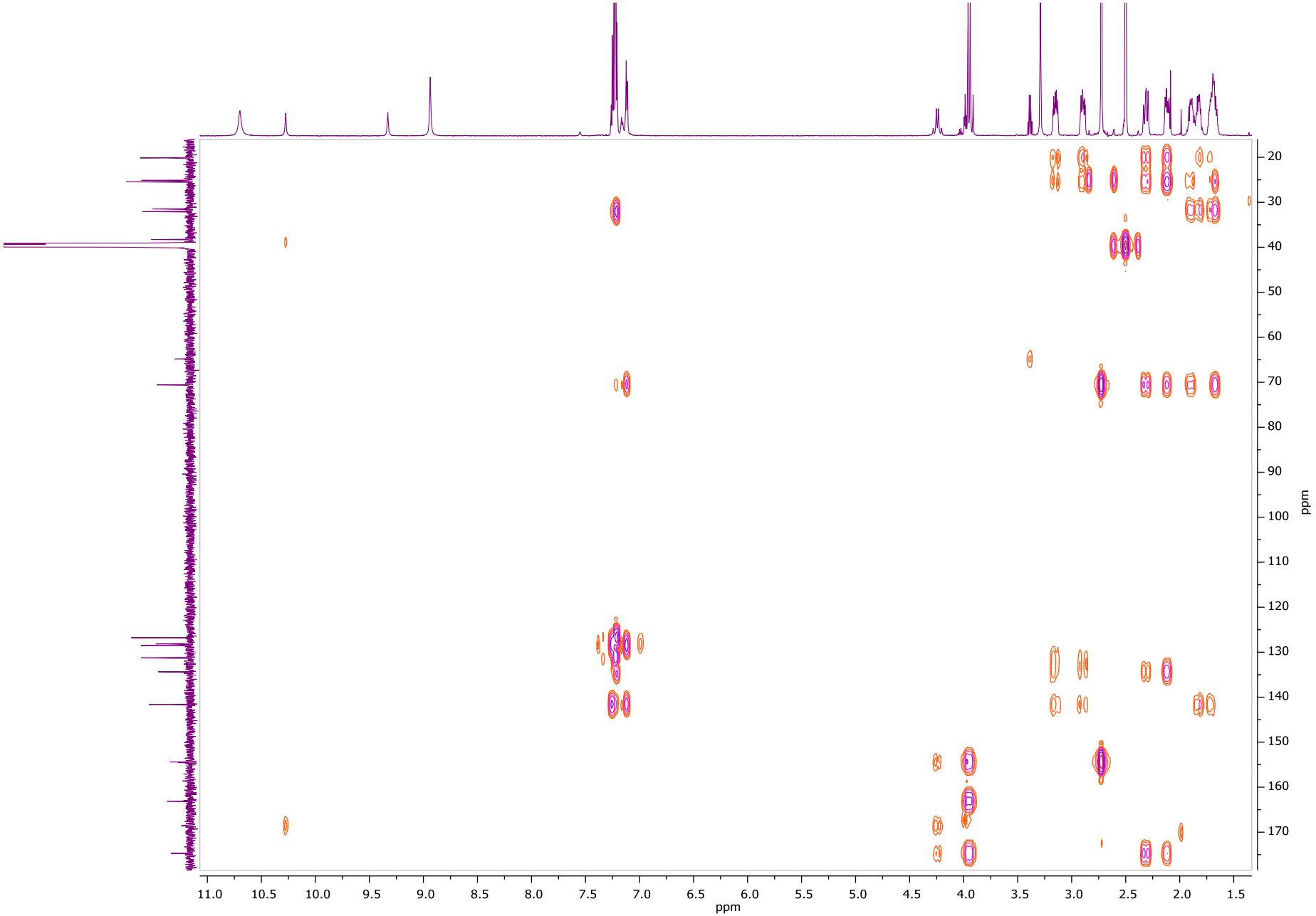
COSY NMR of **18a** (600.11 MHz, DMSO-d_6)



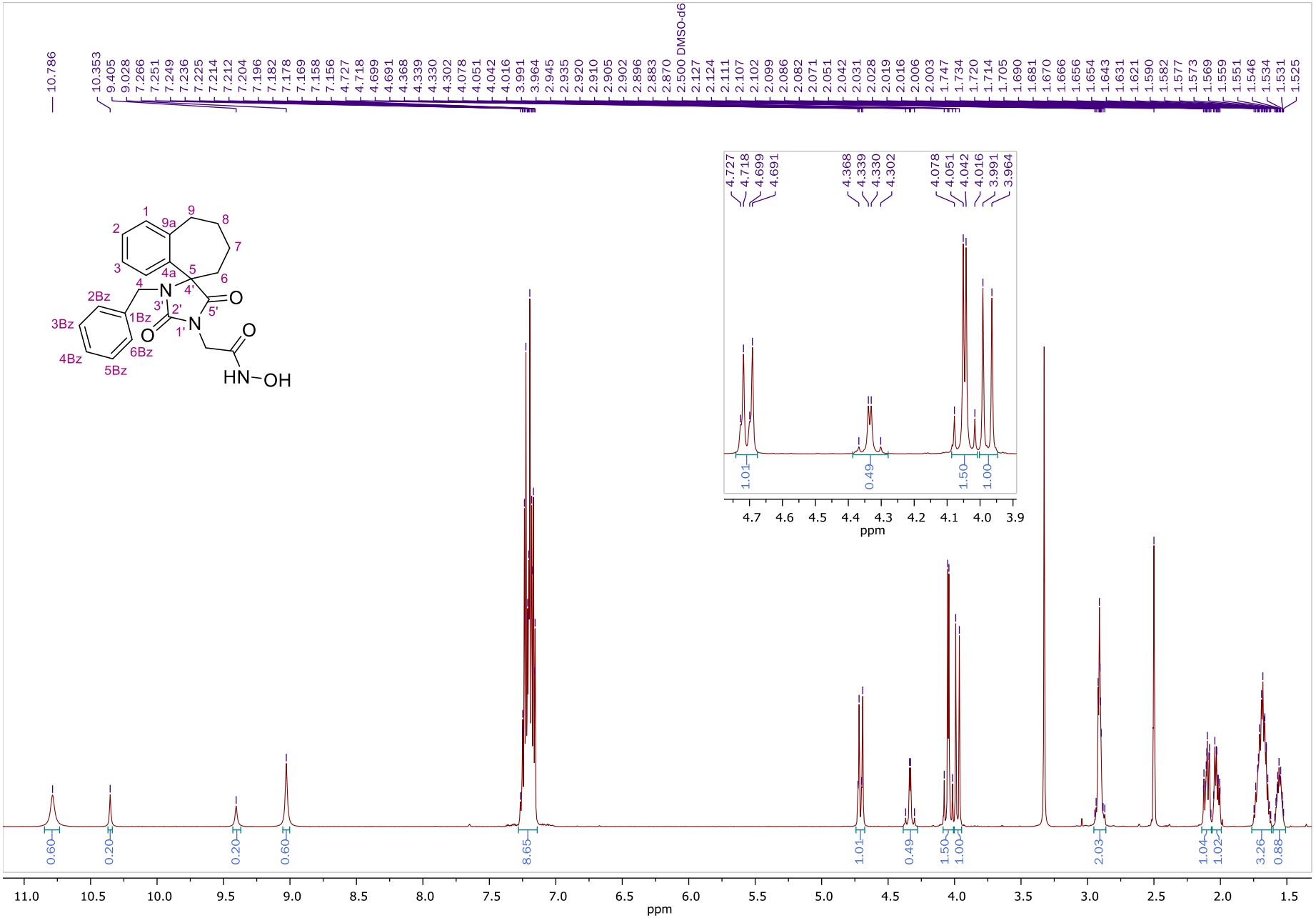
HSQC-DEPT NMR of **18a** (600.11 MHz, DMSO-d_6)



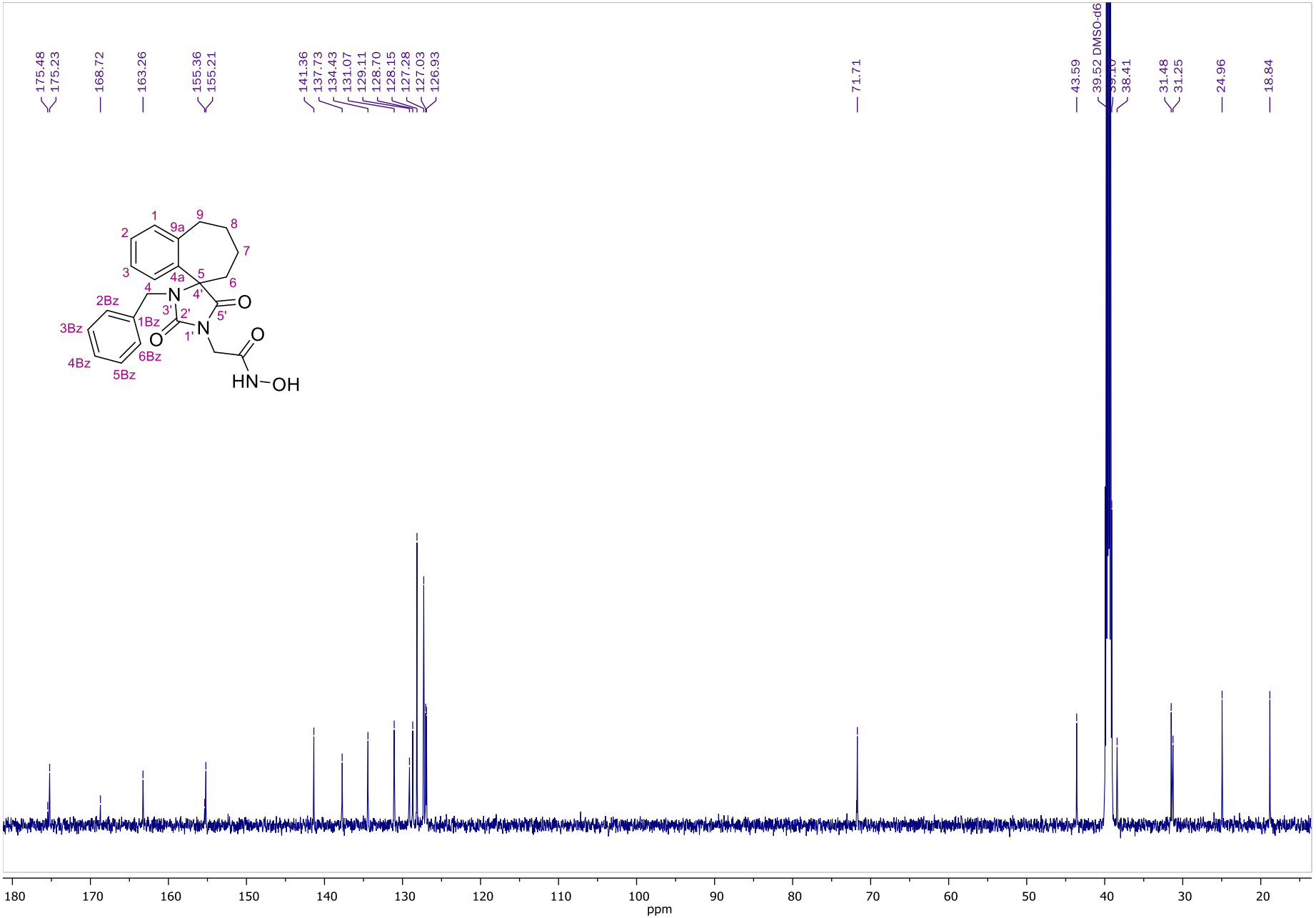
HMBC NMR of **18a** (600.11 MHz, DMSO-d_6)



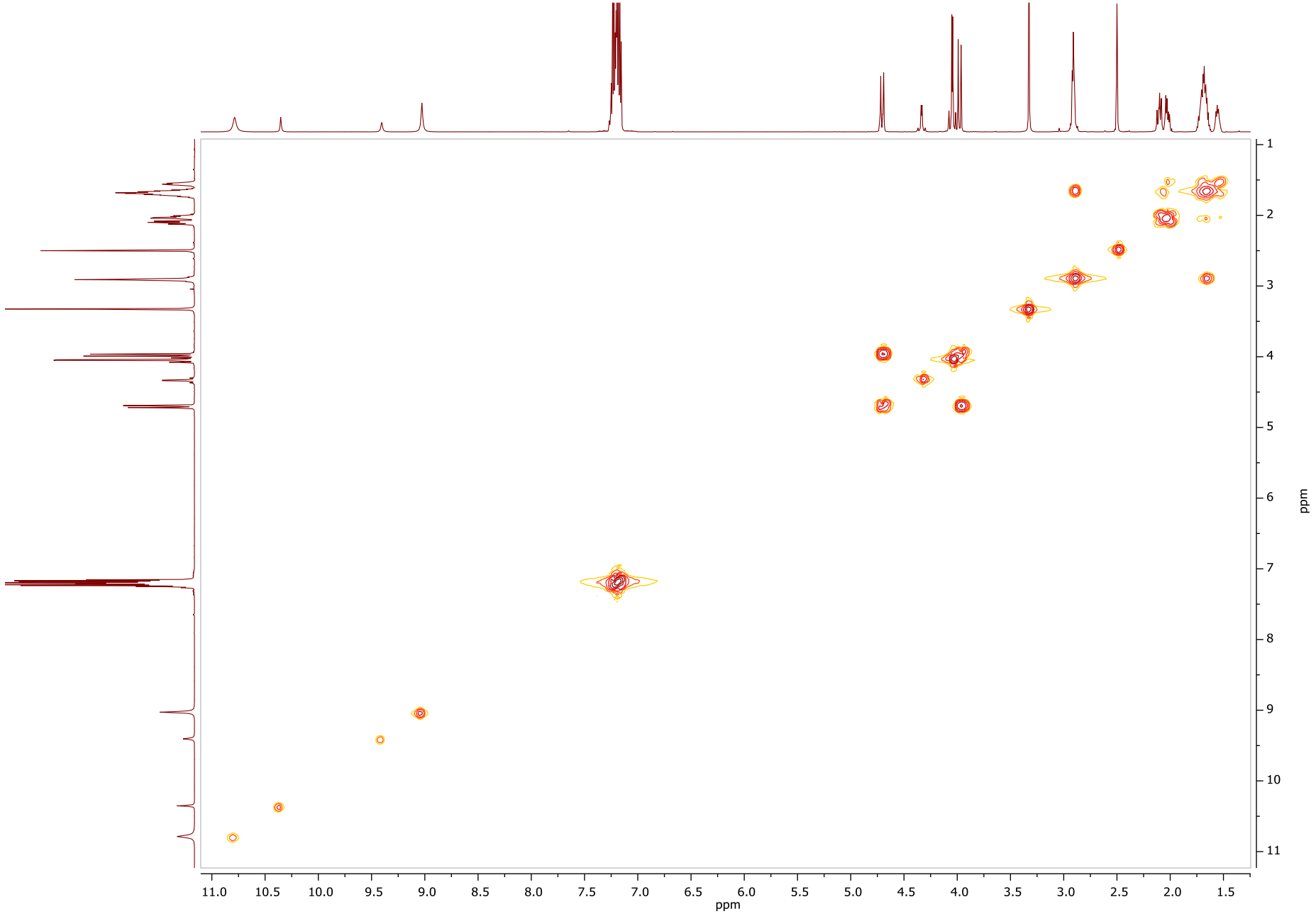
^{1}H NMR of **18b** (600.11 MHz, DMSO-d_6)



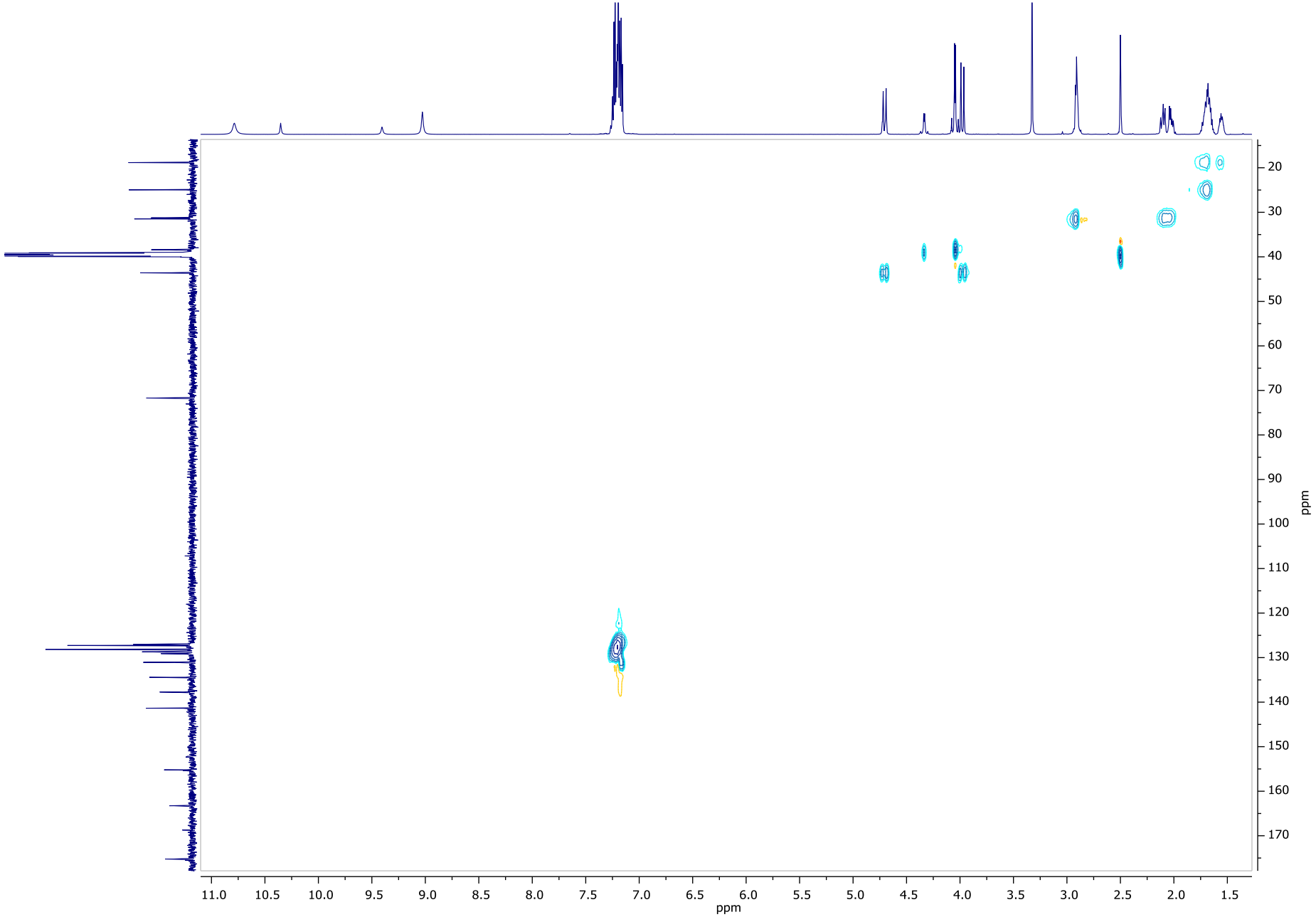
^{13}C NMR of **18b** (150.9 MHz, DMSO-d_6)



COSY NMR of **18b** (400.13 MHz, DMSO-d_6)



HSQC NMR of **18b** (400.13 MHz, DMSO-d_6)



HMBC NMR of **18b** (400.13 MHz, DMSO-d_6)