Electronic Supplementary Material (ESI) for RSC Advances

Supporting Information

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Experimental Section

Chemistry

General Remarks

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 (300 MHz, ^{1}H; 75 MHz ^{13}C) and 400 (400 MHz, ^{1}H; 100 MHz ^{13}C) instruments. The chemical shifts are reported in parts per million relative to tetramethylsilane using the residual solvent signal as internal reference. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), qt (quintet), m (multiplet) and b (broad). Coupling constants, *J*, are reported in Hertz. Mass spectra were recorded by using a Kratos MS50TC and a Kratos Mach III data system. The ion source temperature was 150-250 °C as required. High resolution EI-mass spectra were performed with a resolution of 10000. The low resolution spectra were obtained with a HP5989A MS instrument. For thin layer chromatography, analytical TLC plates (Alugram SIL G/UV_{254} and 70-230 mesh silica gel (E.M.Merck)) were used. Visualization was accomplished with UV (254).

Microwave Irradiation Experiments

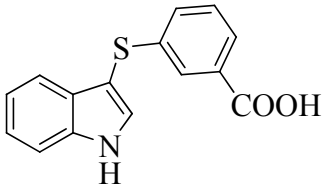
All microwave irradiation experiments were carried out in a dedicated CEM-Discover monomode microwave apparatus (CEM Corporation P.O. Box 200 Matthews, NC 28106), operating at a frequency of 2.45 GHz with maximum irradiation power of 300 W. Reaction mixtures were efficiently stirred with a magnetic stirrer. The reactions were carried out in a sealed 10 mL glass vial. The temperature of the reactions was measured by infrared.

General procedure for the thioarylation of the indoles

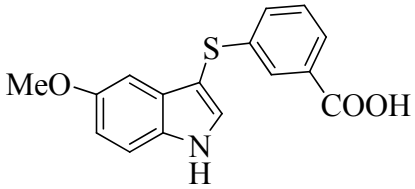
A mixture of the indole **1** (0.2 mmol), mercaptobenzoic acid (**3**) (0.2 mmol) and anhydrous $FeCl_3$ (7 mg, 20 mol %) in acetonitrile (2 mL) was irradiated at a ceiling temperature of 140 °C and a maximum power of 150 W for 30 min. The progress of the reaction was monitored by TLC and CI-

MS. After complete conversion the reaction mixture was cooled by compressed air and brought to r.t.. The $FeCl_3$ was filtered off on Celite, the acetonitrile was evaporated under reduced pressure and the resulted crude product was purified by column chromatography over silica gel (heptane-EtOAc 8:2 containing acetic acid (0.1 %)) yielding the desired products **3a-d** in 90-96 % yield.

A mixture of the indole **1** (0.2 mmol), mercaptobenzoic acid (**3**) (0.2 mmol) and anhydrous $FeCl_3$ (7 mg, 20 mol %) in acetonitrile (2 mL) was irradiated at a ceiling temperature of 140 °C and a maximum power of 150 W for 30 min. The progress of the reaction was monitored by TLC and CI-MS. After complete conversion the reaction mixture was cooled by compressed air and brought to r.t.. The $FeCl_3$ was filtered off on Celite, the acetonitrile was evaporated under reduced pressure and the resulted crude product was purified by column chromatography over silica gel (heptane-EtOAc 8:2 containing acetic acid (0.1 %)) yielding the desired products **3a-d** in 90-96 % yield.

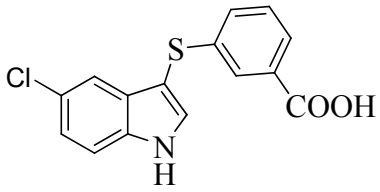


3-(1 *H*-Indol-3-ylthio) benzoic acid (3a) It was obtained as a brown oil (92 % yield). ^{1}H NMR (300 MHz, DMSO): 11.76 (bs, 1H), 7.82-7.81 (m, 1H), 7.62 (d, 1H, J = 7.35 Hz), 7.54-7.49 (m, 2H), 7.40-7.25 (m, 3H), 7.19 (t, 1H, J = 7.35 Hz). 7.07 (t, 1H, J = 7.35 Hz). ^{13}C NMR (75 MHz, DMSO): 166.7, 140.0, 136.7, 132.7, 131.5, 129.3, 129.0, 128.4, 125.7, 122.2, 118.1, 112.4, 98.4. HRMS (EI): calcd. for $C_{15}H_{11}NO_2S$: 269.0510; found: 269.0527.

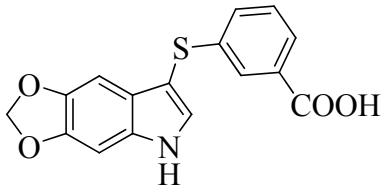


3-(5-Methoxy-1*H*-indol-3-ylthio)benzoic acid (3b) It was obtained as a yellow oil (96 % yield). ^{1}H NMR (300 MHz, DMSO): 11.98 (bs, 1H), 7.92-7.91 (m, 1H), 7.65 (d, 1H, J = 7.53 Hz), 7.55-7.52 (m, 2H), 7.39-7.34 (m, 2H), 7.29-7.27 (m, 1H), 7.22-7.19 (m, 1H). ^{13}C NMR (75 MHz, DMSO): 166.7, 139.5, 135.2, 134.6, 131.5, 129.7, 129.4, 129.2,

125.9, 125.6, 125.0, 122.3, 117.1, 114.1, 98.3. HRMS (EI): calcd. for $C_{16}H_{13}NO_3S$: 299.0616, found: 299.0627.



3-(5-Chloro-1*H*-indol-3-ylthio)benzoic acid (3c) It was obtained as a dark orange oil (90 % yield). ^{1}H NMR (300 MHz, DMSO): 11.63 (bs, 1H), 7.65 (d, 1H, J = 2.64 Hz), 7.63 (d, 1H, J = 7.53 Hz), 7.54 (s, 1H), 7.42-7.25 (m, 3H), 6.84-6.82 (m, 2H), 3.68 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 166.3, 154.3, 140.2, 136.1, 132.1, 131.5, 131.4, 131.1, 129.8, 129.2, 128.4, 127.3, 125.4, 99.4, 97.8, 55.2. HRMS (EI): calcd. for $C_{15}H_{10}ClNO_2S$: 303.0121; found: 303.0148.



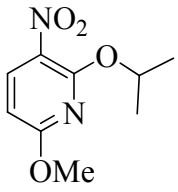
3-(5*H*-[1-3]Dioxolo-[4,5-f]indol-7-ylthio)benzoic (3d) It was obtained as a yellow oil (91 % yield). ^{1}H NMR (300 MHz, DMSO): 11.54 (bs, 1H), 7.64-7.60 (m, 2H), 7.53 (s, 1H), 7.33 (t, 1H, J = 7.71 Hz), 7.26-7.24 (m, 1H), 7.01 (s, 1H), 6.74 (s, 1H), 5.95 (s, 2H). ^{13}C NMR (75 MHz, DMSO): 166.8, 144.8, 143.2, 140.0, 131.4, 130.9, 129.3, 129.0, 125.7, 125.5, 122.6, 100.5, 96.5, 98.5, 93.0, 54.9. HRMS (EI): calcd. for $C_{16}H_{11}NO_4S$: 313.0409; found: 313.0384.

Compounds **5a,b** were prepared and characterized in accordance with the published procedure.[1]

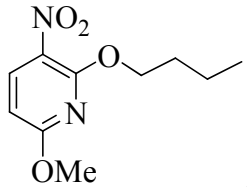
General procedure for the synthesis of compounds 7a,b

A mixture of the 6-chloro-2-alkoxy-3-nitropyridine (**5**) (0.5 mmol) and anhydrous NaOMe (28 mg, 0.525 mmol,) was refluxed for 2 h in dry MeOH (6 mL). The progress of the reaction was monitored by TLC and CI-MS. After complete conversion the mixture was cooled to r.t. and the

MeOH was evaporated under reduced pressure. The organic residue was washed with H_2O, extracted with EtOAc and the extract was dried on Na_2SO_4. The crude compound was purified by column chromatography over silica gel (heptane-EtOAc 8:2) giving the desired products **7a,b** in 72-80 % yield.



2-Isopropoxy-6-methoxy-3-nitropyridine (7a) It was obtained as a dark brown oil (80 % yield). ^{1}H NMR (300 MHz, DMSO): 8.38 (d, 1H, *J* = 8.67 Hz), 6.52 (d, 1H, *J* = 8.85 Hz), 5.49-5.41 (m, 1H), 3.95 (s, 3H), 1.39 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 164.8, 155.9, 139.0, 126.3, 102.4, 71.0, 54.5, 21.6. HRMS (EI): calcd. for $C_9H_{12}N_2O_4$: 212.0797; found: 212.0801.

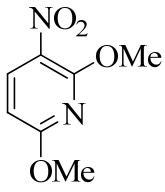


2-Butoxy-6-methoxy-3-nitropyridine (7b) It was obtained as a light brown oil (72 % yield). ^{1}H NMR (300 MHz, DMSO): 8.40 (d, 1H, *J* = 8.85 Hz), 6.54 (d, 1H, *J* = 8.67 Hz), 4.49 (t, 2H, *J* = 6.42 Hz), 3.96 (s, 3H), 1.77-1.70 (m, 2H), 1.49-1.42 (m, 2H), 0.94 (t, 3H, *J* = 7.35 Hz). ^{13}C NMR (75 MHz, DMSO): 153.1, 149.2, 125.1, 124.4, 99.5, 64.6, 52.9, 30.7, 18.7, 13.7. HRMS (EI): calcd. for $C_{10}H_{14}N_2O_4$: 226.0954; found: 226.0960.

Procedure for the synthesis of compound 7c

Compound **7c** was obtained using a slightly modified procedure which consisted of directly refluxing the commercially available 2,6-dichloro-3-nitropyridine (**6**) (96 mg, 5 mmol) with anhydrous NaOMe (80 mg, 12.5 mmol) for 2 h in dry MeOH (6 mL). The progress of the reaction was monitored by TLC and CI-MS. After complete conversion the reaction mixture was cooled to r.t., the MeOH was evaporated under reduced pressure and the organic residue was washed with

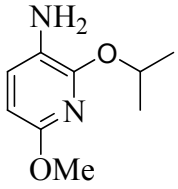
H_2O and extracted with EtOAc. The extract was dried on Na_2SO_4 and the crude product was purified by column chromatography over silica gel (heptane-EtOAc 8:2) giving the desired product **7c** in 93 % yield.



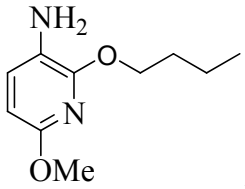
2,6-Dimethoxy-3-nitropyridine (7c) It was obtained as a yellow solid (93 % yield)., m.p. 89-90 °C ^{1}H NMR (300 MHz, DMSO): 8.42 (d, 1H, *J* = 8.67 Hz), 6.56 (d, 1H, *J* = 8.55 Hz), 4.06 (s, 3H), 3.99 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 164.9, 139.1, 126.2, 102.7, 54.6 (x 2). HRMS (EI): calcd. for $C_7H_8N_2O_4$: 184.0484; found: 184.0481.

General method for the synthesis of compounds 8a-c

A mixture of compound **7** (0.2 mmol) and 5 % Pd/C (5 mol %) in MeOH (5 mL) was agitated at r.t. under 25 psi hydrogen for 2 h. The catalyst was removed by filtration on Celite and the filtrate was evaporated to dryness to give the pure products (75-82%).

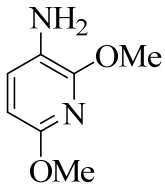


2-Isopropoxy-6-methoxypyridin-3-amine (8a) It was obtained as a dark brown oil (82% yield). ^{1}H NMR (300 MHz, $CDCl_3$): 6.93 (d, 1H, *J* = 8.22 Hz), 6.13 (d, 1H, *J* = 8.22 Hz), 5.33-4-25 (m, 1H), 3.81 (s, 3H), 1.37 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 155.4, 150.4, 126.0, 124.0, 99.6, 68.5, 53.7, 22.6. HRMS (EI): calcd. for $C_9H_{14}N_2O_2$ 182.1055; found: 182.1057.



2-Butoxy-6-methoxypyridin-3-amine (8b) It was obtained as a brown oil (75% yield). ^{1}H NMR (300 MHz, DMSO): 6.94 (d, 1H, *J* = 8.1 Hz), 6.13 (d, 1H, *J* = 8.1 Hz), 4.25 (t, 2H,

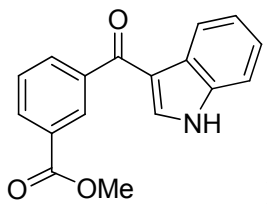
J = 6.39 Hz), 3.70 (s, 3H), 1.74-1.65 (m, 2H), 1.49-1.37 (m, 2H), 0.93 (t, 3H, *J* = 7.35 Hz). ^{13}C NMR (75 MHz, DMSO): 153.1, 149.2, 125.1, 124.4, 99.5, 64.6, 52.9, 30.7, 18.7, 13.7. HRMS (EI): calcd. for $C_{10}H_{16}N_2O_2$ 196.1212; found: 196.1218.



2,6-Dimethoxypyridin-3-amine (8c) It was obtained as a dark brown oil (80% yield). ^{1}H NMR (300 MHz, $CDCl_3$): 6.96 (d, 1H, *J* = 7.89 Hz), 6.16 (d, 1H, *J* = 7.89 Hz), 3.97 (s, 3H), 3. 84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 153.1, 149.4, 125.1, 124.4, 99.5, 53.0, 52.6. HRMS (EI): calcd. for $C_7H_{10}N_2O_2$ 154.0742; found: 154.0724.

General procedure for the synthesis of compound 10

To perform the Friedel-Crafts acylation, the commercially available *mono*-methyl isophtalate (**9**) was converted to the corresponding acid chloride in accordance with the published procedure.[30] To a DCM (2 mL) solution of indole (**1a**) (54 mg, 0.46 mmol) was added diethylalluminum chloride (0.38 mL, 0.7 mmol, 1.8 M in toluene) at 0°C. The mixture was stirred at 0°C for 30 min and then the acid chloride derivative of compound **9** (81 mg, 0.69 mmol) in DCM (2 mL) was added drop wise. The resulting solution was stirred at 0°C for 2 h and then brought to r.t.. A pH 7 phosphate buffer was added to quench the reaction and the mixture was extracted with EtOAc. The combined organic layers were concentrated under vacuum and the residue was purified by column chromatography over silica gel (heptane-EtOAc 9:1) yielding the desired compound in 63%.

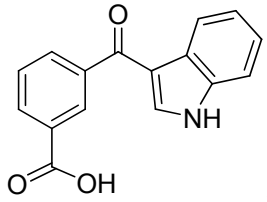


Methyl 3-(1*H*-indol-3-carbonyl)benzoate (10) It was obtained as a white solid (63 % yield)., m. p. 209-210 °C, ^{1}H NMR (300 MHz, DMSO): 12.15 (bs, 1H), 8.29 (s, 1H), 8.24 (d, 1H, *J* = 8.49 Hz), 8.17 (d, 1H, *J* = 7.71 Hz), 8.06 (d, 1H, *J* = 7.53 Hz), 7.98 (s, 1H), 7.71 (t,

1H, *J* = 7.71 Hz), 7.53 (d, 1H, *J* = 6.78 Hz), 7.31-7.25 (m, 2H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 188.9, 165.8, 140.7, 136.7, 136.1, 132.9, 131.4, 129.7, 129.1, 128.7, 126.0, 123.3, 122.1, 121.3, 114.7, 112.3, 52.3. HRMS (EI): calcd. for $C_{17}H_{13}NO_3$ 279.0895; found: 279.0907.

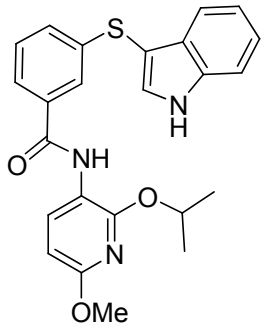
General procedure for the synthesis of compound 11

A suspension of the ester **10** (50 mg, 0.178 mmol) in NaOH (5 mL, 2M) was refluxed until no more starting material was observed (TLC and CI-MS monitoring). The mixture was neutralized with HCl (1 M) and extracted with EtOAc. The organic layers were combined and concentrated under vacuum. The crude product **11** (40 mg) was directly used without further purification.



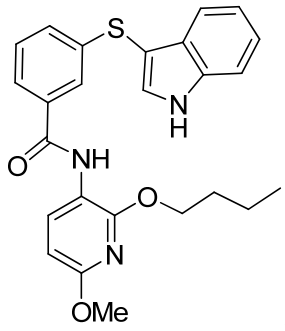
3-(1*H*-Indol-3-carbonyl)benzoic acid (11) It was obtained as a white solid (85% yield). ^{1}H NMR (300 MHz, DMSO): 12.12 (bs, 1H), 8.28-8.23 (m, 2H), 8.17-8.14 (m, 1H), 8.04-7.97 (m, 2H), 7.68-7.64 (m, 1H), 7.55-7.52 (m, 1H), 7.27-7.25 (m, 2H). HRMS (EI): calcd. for $C_{16}H_{11}NO_3$ 265.0739; found 265.0747.

General procedure for the formation of the amides CAB1-13 A mixture of thioether **3** (0.25 mmol), 3-aminopyridine **8** (0.325 mmol), EDC.HCl (0.325 mmol), HOAt (0.325 mmol,) and *N*-methyl-morpholine (0.325 mmol,) in DCM (2 mL) was irradiated at a ceiling temperature of 80 °C and a maximum power of 80 W for 20 min. The progress of the reaction was monitored by TLC and CI-MS. After completion of the reaction the mixture was cooled by compressed air and brought to r.t.. The mixture was washed with $KHSO_4$, $NaHCO_3$ and H_2O. The combined extracts were dried on Na_2SO_4 and concentrated under vacuum. The resulting crude product was purified by column chromatography over silica gel (heptane-EtOAc 8:2) giving the desired products **CAB1-13** in 50-80 % yields.



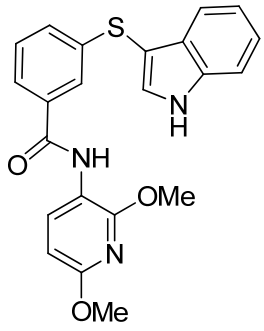
3-(1*H*-Indol-3-ylthio)-*N*-(2-isopopoxy-6-methoxypyridin-3-yl)benzamide

(CAB1) It was obtained as a brown oil (75 % yield). ^{1}H NMR (400 MHz, DMSO): 11.75 (bs, 1H), 9.36 (bs, 1H), 7.81, (s, 1H), 7.76 (d, 1H, *J* = 8.04 Hz), 7.61 (s, 2H), 7.50 (d, 1H, *J* = 8.28 Hz), 7.40 (d, 1H, *J* = 8.04 Hz), 7.34 (t, 1H, *J* = 8.04 Hz), 7.21-7.15 (m, 2H), 7.07 (t, 1H, *J* = 7.08 Hz), 6.34 (d, 1H, *J* = 8.32 Hz), 5.20-5.17 (m, 1H) 3.82 (s, 3H), 1.28 (d, 6H, *J* = 6.28). ^{13}C NMR (100 MHz, DMSO):165.4, 159.8, 155.4, 140,4 138.2, 137.2, 135.5, 133.1, 129.4, 128.9, 128.6, 124.9, 124.3, 122.6, 120.7, 118.6, 114.1, 112.9, 100.3, 99.1, 69.1, 53.7, 22.3. HRMS (EI): calcd. for $C_{24}H_{23}N_3O_3S$: 433.1460, found: 433.1462.

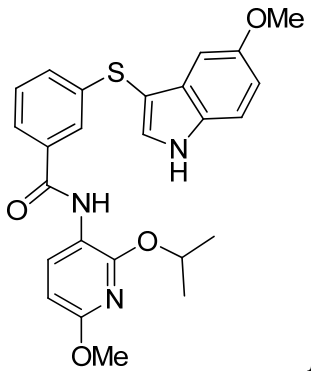


3-(1*H*-Indol-3-ylthio)-*N*-(2-butoxy-6-methoxypyridin-3-yl)benzamide

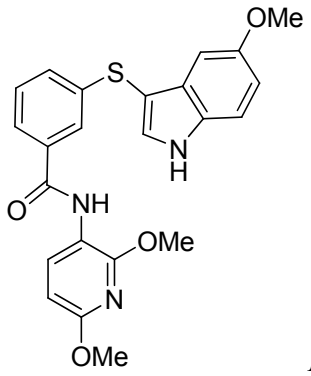
(CAB2). It was obtained as a brown oil (54 % yield). ^{1}H NMR (300 MHz, DMSO): 11.75 (bs, 1H), 9.49 (bs, 1H), 7.81 (s, 1H), 7.73 (d, 1H, *J* = 8.28 Hz), 7.64 (m, 2H), 7.50 (d, 1H, *J* = 7.92 Hz), 7.40 (d, 1H, *J* = 7.71 Hz), 7.33 (m, 1H), 7.19-7.07 (m, 4H), 6.36 (d, 1H, *J* = 8.28 Hz), 4.29 (t, 2H, *J* = 6.39 Hz), 3.83 (s, 3H), 1.68-1.63 (m, 2H), 1.41-1.37 (m, 2H), 0.89 (m, 3H). ^{13}C NMR (75 MHz, DMSO): 164.9, 159.5, 155.6, 139.9, 138.1, 136.7, 134.9, 132.6, 128.9, 128.4, 128.1, 124.4, 123.8, 122.1, 120.1, 118.1, 113.4, 112.3, 100.0, 98.6, 65.3, 53.3, 30.5, 18.6, 13.6. HRMS (EI): calcd. for $C_{24}H_{22}ClN_3O_3S$: 447.1617; found: 447.1623.



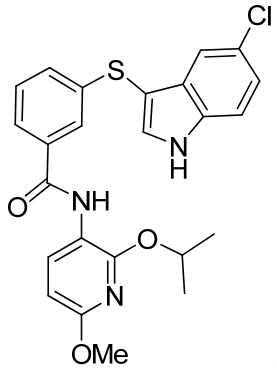
3-(1*H*-Indol-3-ylthio)-*N*-(2,6-dimethoxypyridin-3-yl)benzamide (CAB3) It was obtained as a brown oil (65 % yield). ^{1}H NMR (300 MHz, DMSO):11.76 (bs, 1H), 9.58 (bs, 1H), 7.82 (d, 1H, *J* = 2.07 Hz), 7.74 (d, 1H, *J* = 8.1 Hz), 7.67-7.65 (m,2H), 7.51 (d, 1H, *J* = 7.92 Hz), 7.41 (d, 1H, *J* = 7.74 Hz), 7,32 (t, 1H, *J* = 7.74 Hz), 7.30-7.16 (m, 2H), 7.97 (t, 1H, *J* = 7.53 Hz), 6.38 (d, 1H, *J* = 8.28 Hz), 3.87 (s, 3H), 3.85, (s, 3H).^{13}C NMR (75 MHz, DMSO): 164.8, 159.6, 155.7, 139.8, 138.2, 136.7, 134.6, 132.6, 128.8, 128.4, 124.5, 123.9, 122.2, 120.2, 118.1, 113.3, 112.4, 105.8, 100.1, 98.6, 153.3, 53.2. HRMS (EI): calcd. for $C_{22}H_{19}N_3O_3S$: 405.1147; found: 405.1136.



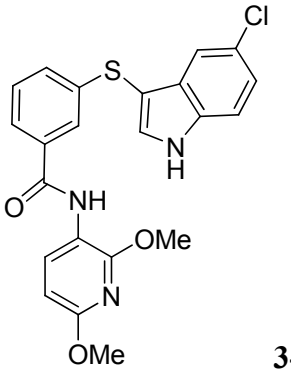
***N*-(2-isopropoxy-6-methoxypyridin-3-yl)-3-(5-methoxy-1*H*-indol-3-ylthio)benzamide (CAB4)** It was obtained as a brown oil (70 % yield). ^{1}H NMR (300 MHz, DMSO):11.63 (bs, 1H), 9.38 (bs, 1H), 7.77-7.74 (m, 2H), 7.64-7.61 (m, 2H), 7.40 (d, 1H, *J* = 9.42 Hz), 7.34 (t, 1H, *J* = 8.1 Hz), 7.15 (d, 1H, *J* = 7.92 Hz), 6-85-6.82 (m, 2H), 6.34 (d, 1H, *J* = 8.31 Hz), 5.23-5.14 (m, 1H), 3.82 (s, 3H), 3.69 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 164.9, 159.3, 154.9, 154.3, 140.0, 137.8, 135.0, 133.1, 131.6, 129.3, 128.9, 124.2, 123.7, 113.6, 113.2, 112.3, 99.8, 99.5, 97.9, 68.6, 55.2, 53.2, 30.6, 21.8. HRMS (EI): calcd. for $C_{25}H_{25}N_3O_4S$: 463.1566; found: 463.1548.



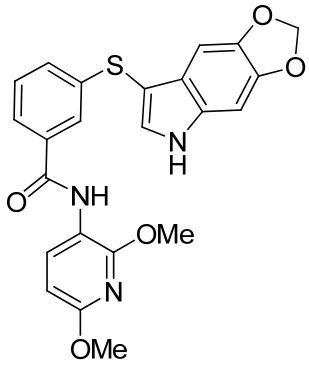
***N*-(2,6-dimethoxypyridin-3-yl)-3-(5-methoxy-1*H*-indol-3-ylthio)benzamide (CAB5)** It was obtained as a brown oil (50 % yield). ^{1}H NMR (300 MHz, DMSO): 11.62 (bs, 1H), 9.57 (bs, 1H), 7.75-7.73 (m, 2H), 7.66 (m, 2H), 7.40 (d, 1H, *J* = 9.42 Hz), 7.33 (t, 1H, *J* = 7.89 Hz), 7.13 (d, 1H, *J* = 8.1 Hz), 6.84-6.82 (m, 2H), 6.38 (d, 1H, *J* = 8.28 Hz), 3.87 (s, 3H), 3.85 (s, 3H), 3.68 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 165.3, 160.1, 154.8, 156.2, 140.5, 138.6, 135.2, 133.6, 132.1, 129.8, 129.3, 128.5, 124.9, 124.3, 113.9, 113.7, 112.8, 100.6, 100.1, 98.5, 55.7, 53.8, 53.7. HRMS (EI): calcd. for $C_{23}H_{21}N_3O_4S$: 435.1253; found: 435.1250.



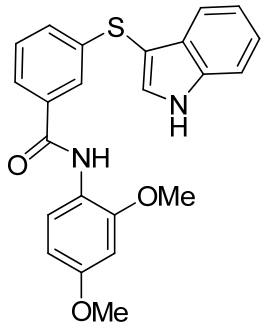
3-(5-Chloro-1*H*-indol-3-ylthio)-*N*-(2-isopropoxy-6-methoxypyridin-3-yl)benzamide (CAB6) It was obtained as a brown oil (65 %yield). ^{1}H NMR (300 MHz, DMSO):11.96 (bs, 1H), 9.39 (bs, 1H), 7.41 (d, 1H, *J* = 2.43 Hz), 7.75 (d, 1H, *J* = 8.23 Hz), 7.64 (d, 1H, *J* = 7.89 Hz), 7.59 (m, 1H), 7.53 (d, 1H, *J* = 8.67 Hz), 7.39-7.35 (m, 2H), 7.22-7.16 (m, 2H), 6.34 (d, 1H, *J* = 8.38 Hz), 5.22-5.14 (m, 1H), 3.81 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 159.9, 139.8, 138.2, 135.7, 135.0, 130.3, 129.5, 128.7, 125.5, 124.9, 124.5, 122.8, 117.6, 114.6, 114.1, 100.3, 99.1, 69.1, 53.7, 22.3. HRMS (EI): calcd. for $C_{24}H_{22}ClN_3O_3S$: 467.1070; found: 467.1086.



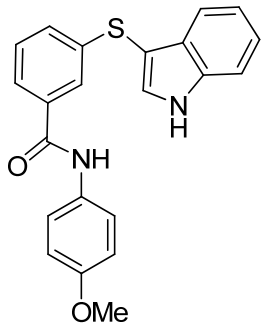
3-(5-Chloro-1*H*-indol-3-ylthio)-*N*-(2,6-dimethoxypyridin-3-yl)benzamide (CAB7) It was obtained as a brown oil (62 % yield). ^{1}H NMR (300 MHz, DMSO): 11.97 (bs, 1H), 9.60 (bs, 1H), 7.92 (d, 1H, *J* = 2.64 Hz), 7.74 (d, 1H, *J* = 8.28 Hz), 7.69-7.65 (m, 2H), 7.53 (d, 1H, *J* = 8.67 Hz), 7.35 (m, 2H), 7.22-7.14 (m, 2H), 6.38 (d, 1H, *J* = 8.28 Hz), 3.87 (s, 3H), 3.86 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 164.7, 159.6, 155.8, 139.3, 136.9, 135.2, 134.7, 134.5, 129.7, 129.0, 128.2, 125.0, 124.6, 124.1, 122.3, 117.1, 114.1, 113.3, 100.1, 98.6, 53.3, 53.2. HRMS (EI): calcd. for $C_{22}H_{18}ClN_3O_3S$: 439.0757; found: 439.0764.



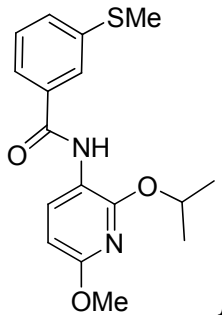
3-(5*H*-[1,3Dioxolo[4,5-f]indol-7-ylthio)-*N*-(2,6-dimethoxypyridin-3-yl)benzamide (CAB8) It was obtained as a yellow oil (55 % yield). ^{1}H NMR (400 MHz, DMSO): 11.53 (bs, 1H), 9.55 (bs, 1H), 7.75 (d, 1H, *J* = 8.32 Hz), 7.67-7.60 (m, 1H), 7.34 (t, 1H, *J* = 7.8 Hz), 7.15 (d, 1H, *J* = 8.3 Hz), 7.02 (s, 1H), 6.76 (s, 1H), 6.39 (d, 1H, *J* = 8.32), 5.95 (s, 2H), 3.88 (s, 3H), 3.86 (s, 3H). ^{13}C NMR(100 MHz, DMSO): 165.3, 160.1, 156.2, 145.3, 143.6, 140.3, 138.6, 135.2, 131.9, 129.3, 125.0, 124.4, 123.2, 113.9, 101.0, 100.6, 99.3, 97.0, 93.5, 65.3, 53.8, 53.7. HRMS (EI): calcd. for $C_{25}H_{23}N_3O_5S$: 449.1045; found: 449.1056.



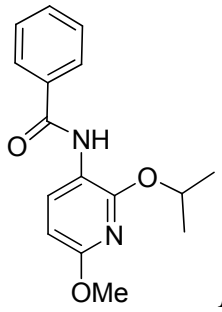
3-(1*H*-indol-3-ylthio)-*N*-(2,4-dimethoxyphenyl)benzamide (CAB9) It was obtained as a brown oil (73 % yield). ^{1}H NMR (300 MHz, DMSO): 11.74 (bs, 1H), 9.31 (bs, 1H), 7.81 (s, 1H), 7.63 (m, 2H), 7.52-7.49 (m,1H), 7.45-7.39 (m, 2H), 7.32 (m, 1H), 7.19-7.16 (m, 2H), 7.08 (m, 1H), 6.62-6.59 (m, 1H), 6.50 (d, 1H, J = 8.1 Hz), 3.76 (s, 6H). ^{13}C NMR (75 MHz, DMSO): 164.4, 157.8, 153.2, 139.8, 136.7, 135.1, 132.6, 128.8, 128.4, 128.0, 126.1, 124.3, 123.8, 122.1, 120.1, 119.5, 118.1, 112.3, 104.1, 98.8, 98.6, 55.6, 55.2. HRMS (EI): calcd. for $C_{23}H_{20}N_2O_3S$: 404.1195; found: 404.1203.



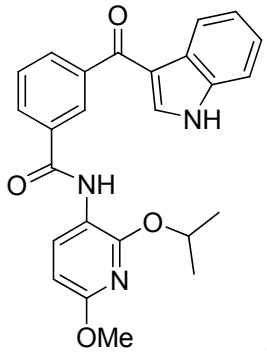
3-(1*H*-Indol-3-ylthio)-*N*–(4-methoxyphenyl)benzamide (CAB10) It was obtained as a brown oil (60 % yield). ^{1}H NMR (300 MHz, DMSO):11.75 (bs, 1H), 10.10 (bs, 1H), 7.81(s, 1H), 7.65-7.60 (m, 4H), 7.50 (d, 1H, J = 7.92 Hz), 7.40 (d, 1H, J = 7.92Hz), 7.32 (t,, 1H, J = 7.71 Hz), 7,19 (t, 1H, J = 7.14 Hz), 7.13-7.04 (m, 2H), 6.89 (d, 2H, J = 8.85 Hz), 3.73 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 164.5, 155.5, 139.8, 136.7, 135.6, 132.6, 132.0, 128.8, 127.9, 124.4, 123.9, 122.1, 121.9, 120.1, 118.1, 113.6, 112.4, 98.6, 55.1. HRMS (EI): calcd. for $C_{22}H_{18}N_2O_2S$: 374.1089; found: 374.1072.



***N*-(2-Isopropoxy-6-methoxypyridin-3-yl)-3-(methylthio)benzamide (CAB11)** It was obtained as a purple oil (84 % yield). ^{1}H NMR (300 MHz, DMSO): 9.48 (bs, 1H), 7.81-7.77 (m, 2H), 7.68 (s, 1H), 7.46 (m, 2H), 6.37 (d, 1H, J = 8.28 Hz), 5.26-5.17 (m, 1H), 3.83 (s, 3H), 2.54 (s, 3H), 1.33 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 164.9, 159.4, 155.0, 138.7, 138.0, 135.0, 128.9, 128.6, 124.4, 123.9, 113.6, 99.9, 68.6, 53.2, 21.9, 14.4. HRMS (EI): calcd. for $C_{17}H_{20}N_2O_3S$: 332.1195; found: 332.1170.



***N*-(2,6-dimethoxypyridin-3-yl)benzamide (CAB12)** It was obtained as a brown oil (80% yield). ^{1}H NMR (300 MHz, DMSO): 9.59 (bs, 1H), 7.96 (d, 2H, J = 7.14 Hz), 7.80 (d, 1H, J = 8.28 Hz), 7.57 (d, 1H, J = 7.17 Hz), 7.53-7.48 (m, 2H), 6.41 (d, 1H, J = 8.28 Hz), 3.90 (s, 3H), 3.87 (s, 3H). ^{13}C NMR (75 MHz, DMSO): 165.3, 159.6, 155.8, 138.2, 134.0, 131.5, 128.3, 127.5, 113.6, 113.5, 100.1, 71.7, 53.3, 53.2. calcd. for $C_{14}H_{14}N_2O_3$: 258.1004; found: 258.1010.



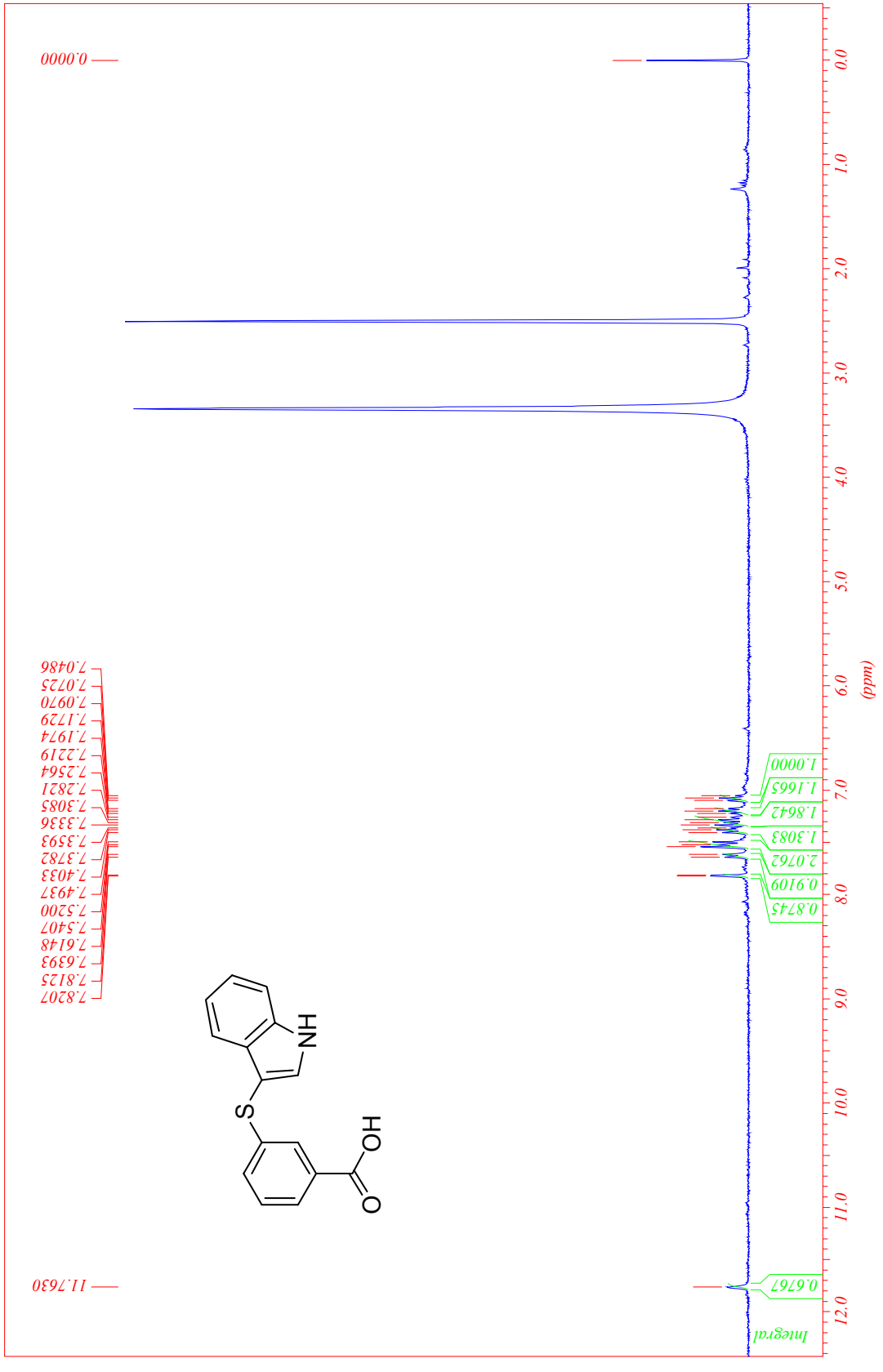
3-(1*H*-indole-3-carbonyl)-N-(2-isopropoxy-6-methoxypyridin-3-yl)benzamide (CAB13) It was obtained as white solid (51 % yield)., m. p. 162-163 °C ^{1}H NMR

(400 MHz, $CDCl_3$): 9.67 (bs, 1H), 8.57 (d, 1H, J = 11.28 Hz), 8.41-8.38 (m, 1H), 8.28 (s, 1H), 8.23 (s, 1H), 8.02-7.95 (m, 2H), 7.59 (t, 1H, J = 10.32 Hz), 7.53 (d, 1H, J = 3.76 Hz), 7.42-7.39 (m, 1H), 7.31-7.28 (m, 2H), 6.32 (d, 1H, J = 11.32 Hz), 5.39-5.31 (m, 1H), 3.87 (s, 3H), 1.37 (d, 6H, J = 8.28 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): 190.3, 164.8, 158.6, 151.5, 141.3, 136.6, 135.0, 134.4, 131.9, 131.6, 129.3, 127.1, 126.2, 124.0, 122.8, 122.2, 116.5, 115.0, 111.7, 100.1, 69.6, 53.6, 22.2. HRMS (EI): calcd. for $C_{25}H_{23}N_3O_4$: 429.1689; found: 429.1693.

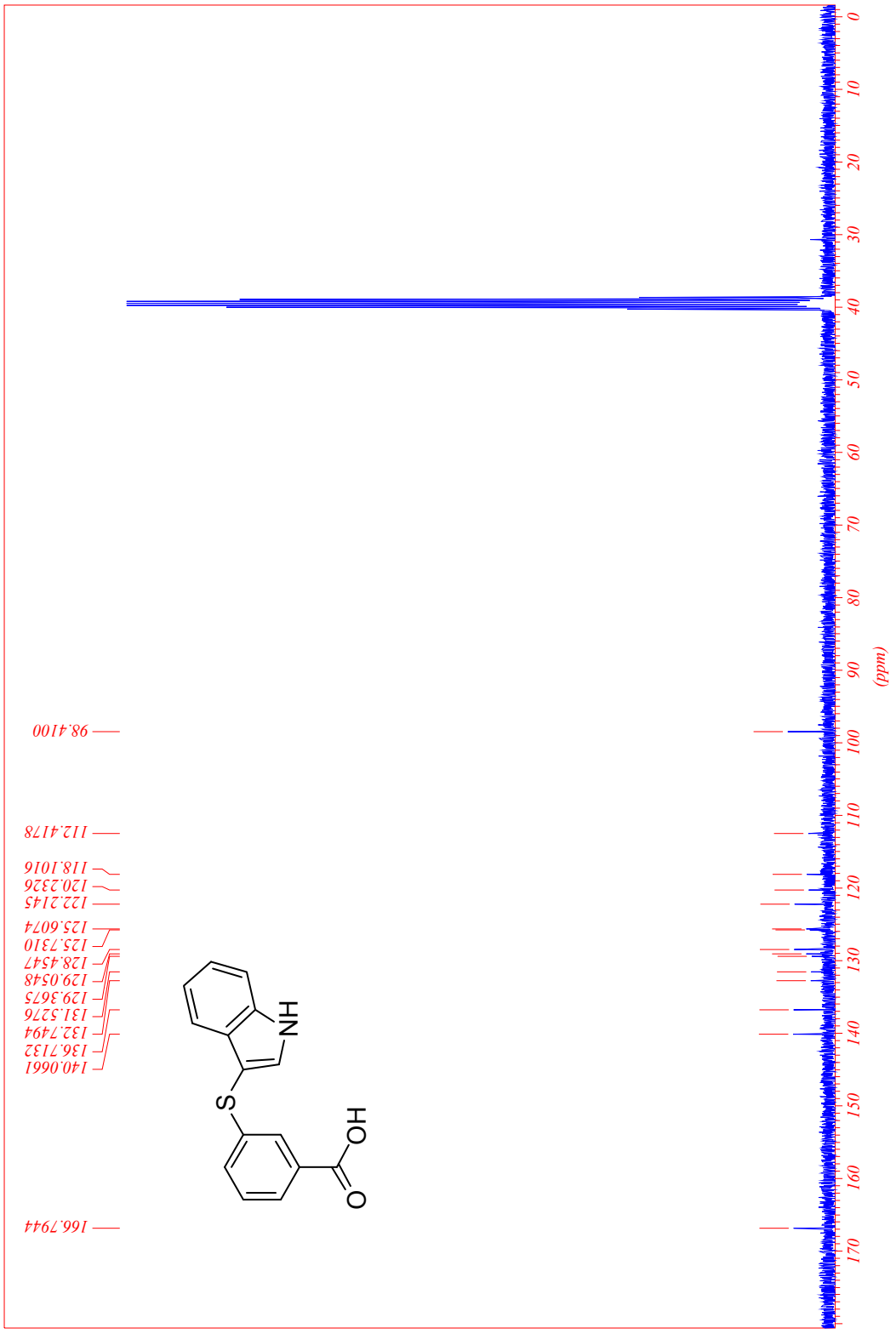
Reference

[1] B. K.Sing, C. Cavalluzzo, M. De Maeyer, Z. Debyser, V. S. Parmar, E. Van der Eycken *Synthesis*, **2009**, 2725-2728.

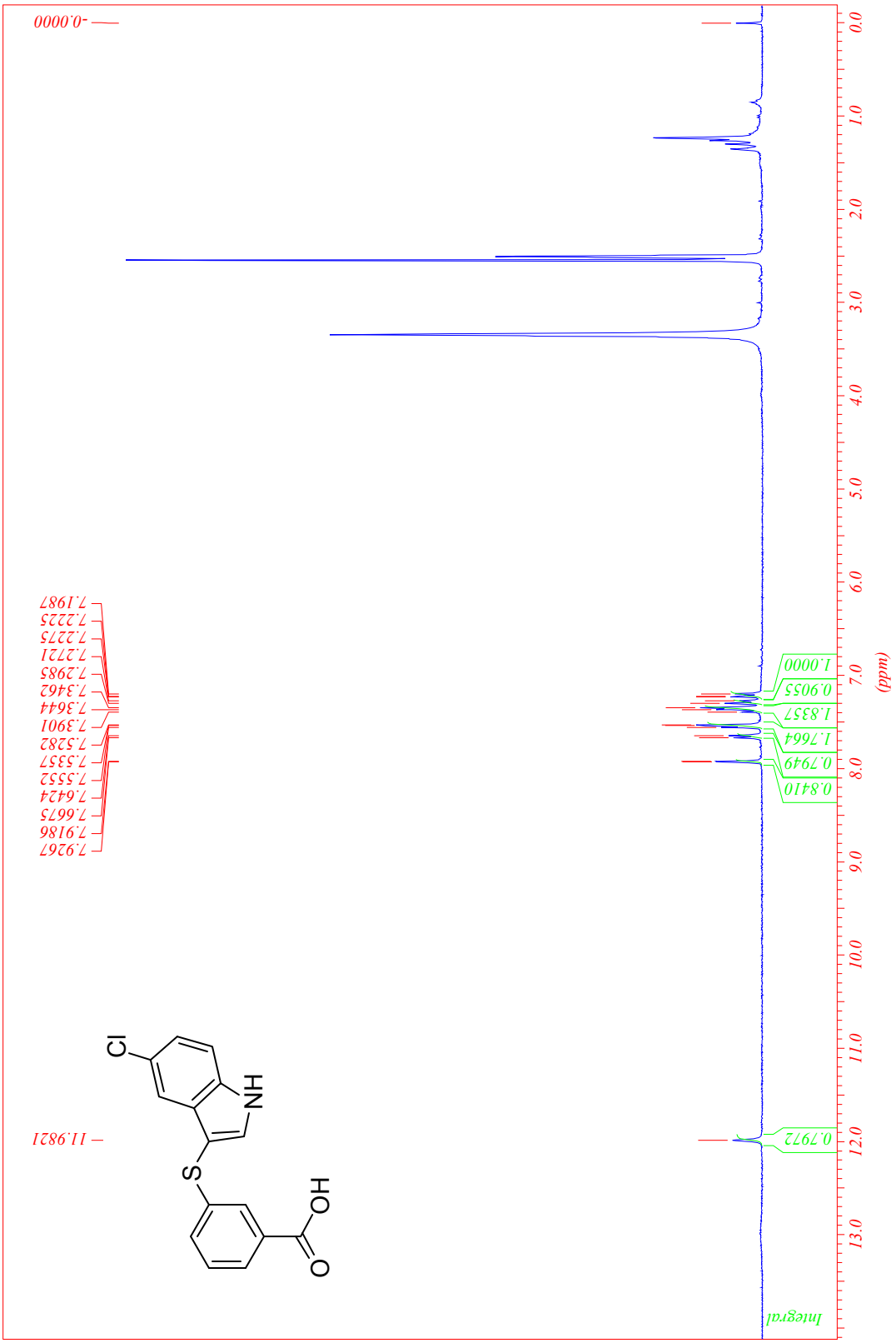
^{1}H NMR spectra of compound **3a** (300 MHz, DMSO)



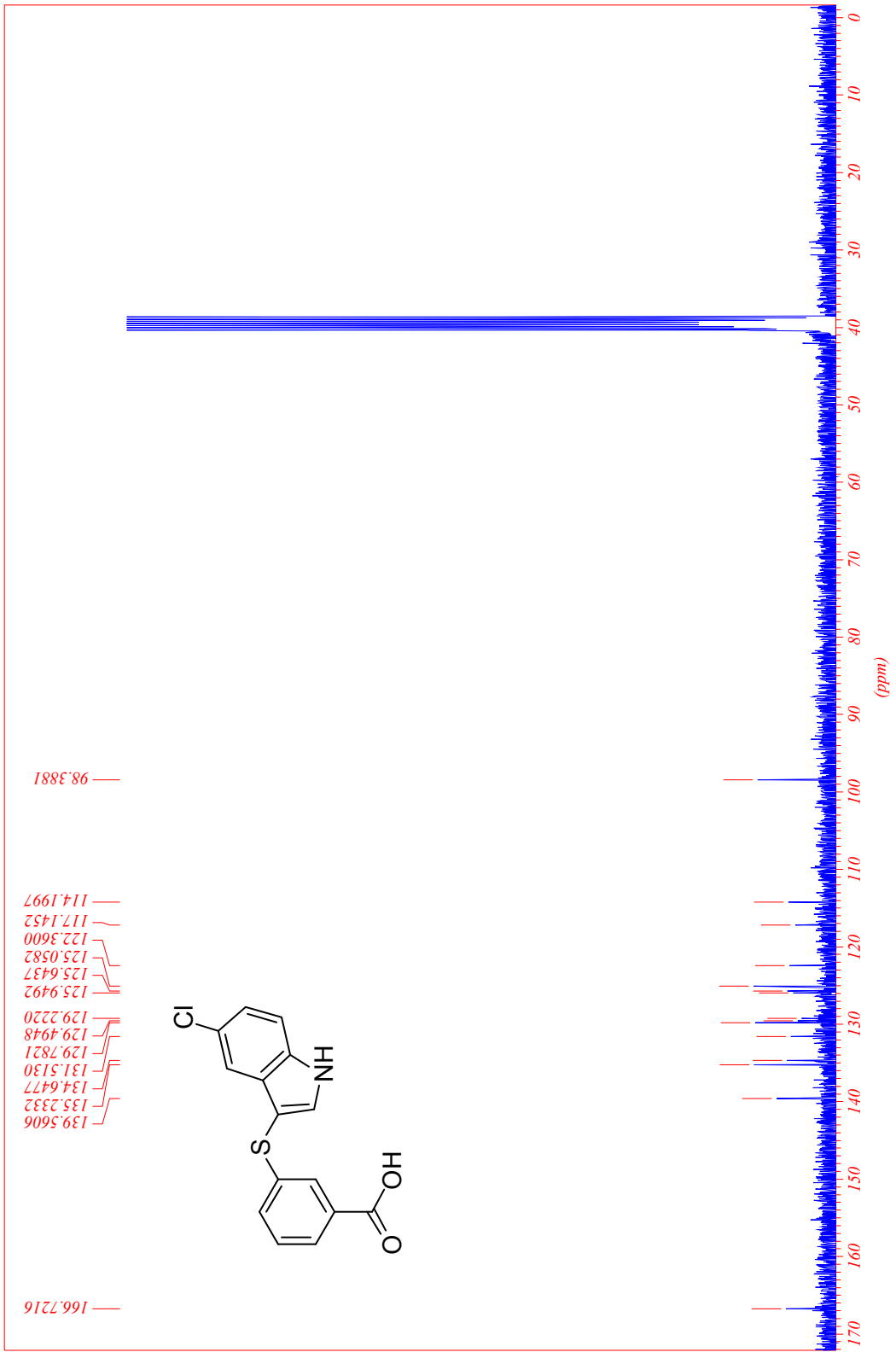
^{13}C NMR spectra of compound **3a** (75 MHz, DMSO)



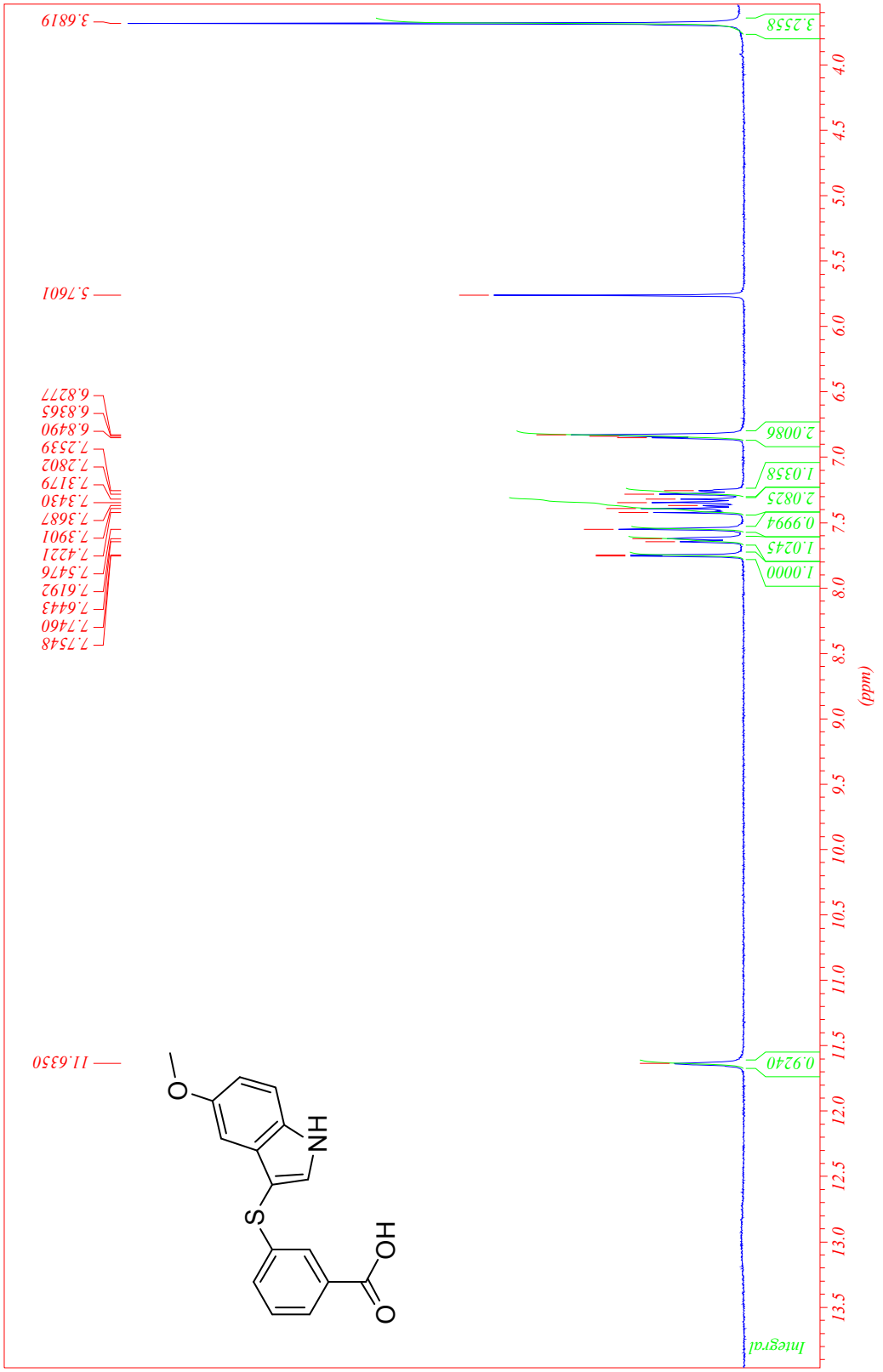
^{1}H NMR spectra of compound **3b** (300 MHz, DMSO)



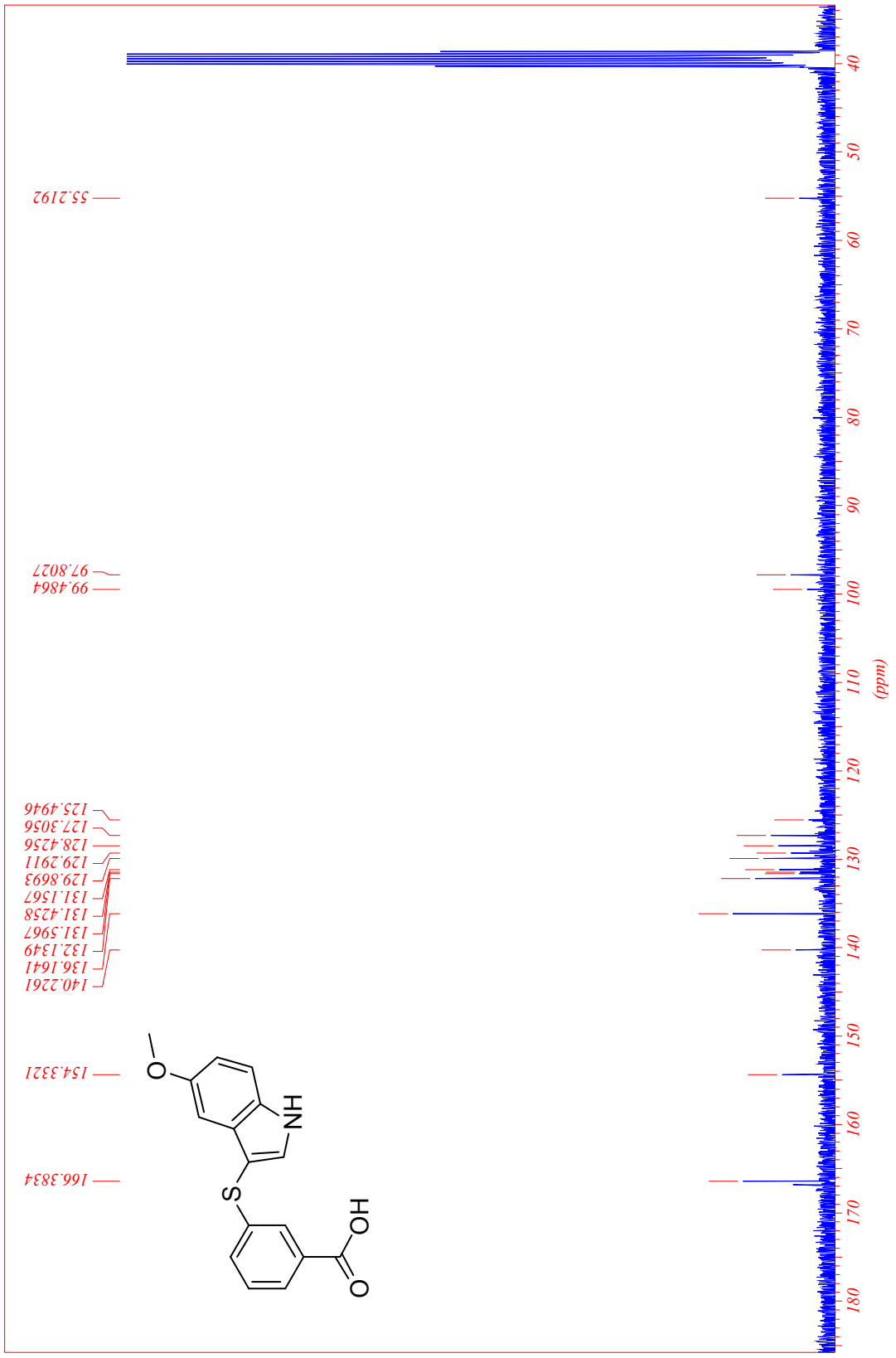
^{13}C NMR spectra of compound **3b** (75 MHz, DMSO)



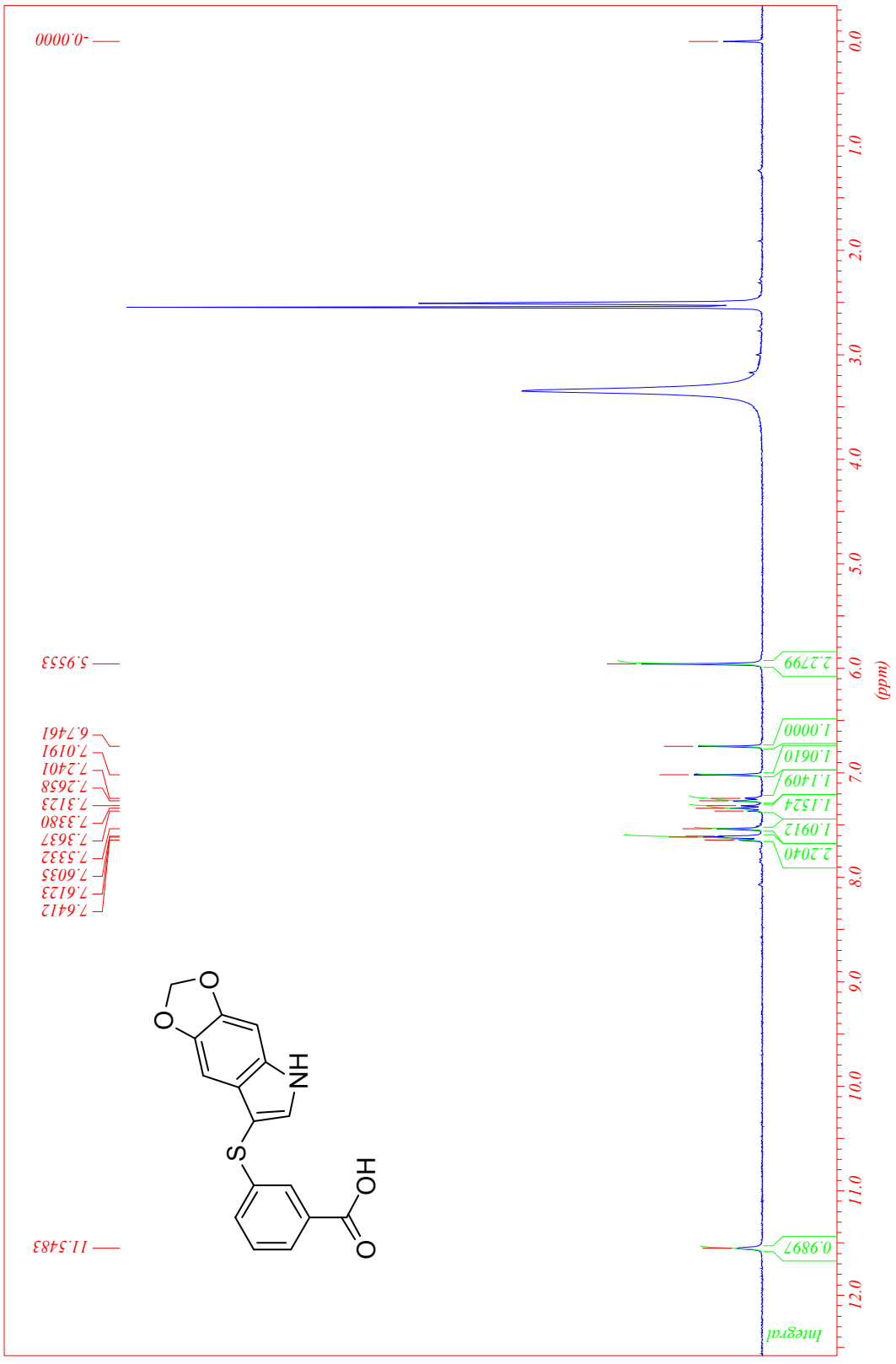
^{1}H NMR spectra of compound **3c** (300 MHz, DMSO)



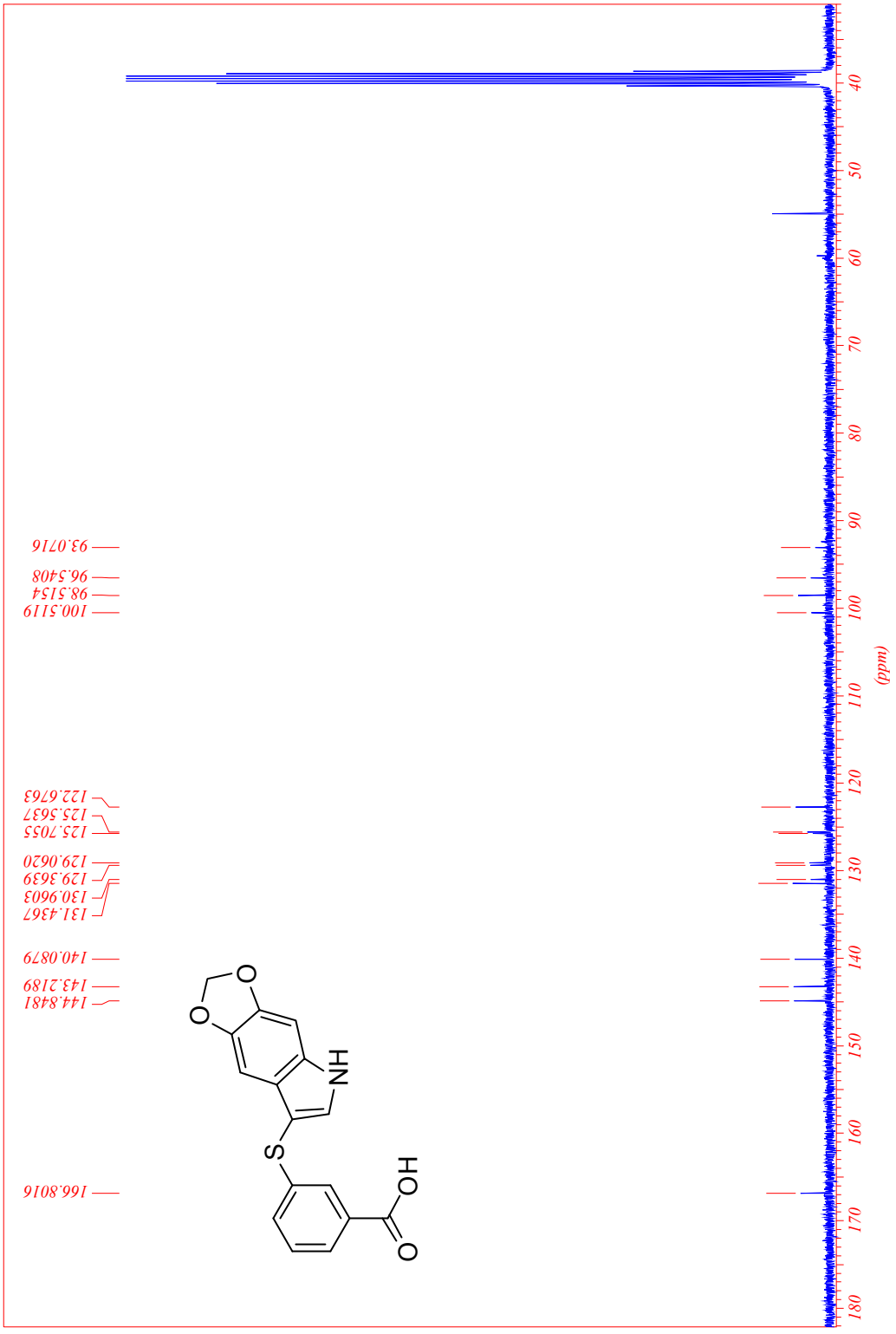
^{13}C NMR spectra of compound **3c** (75 MHz, DMSO)



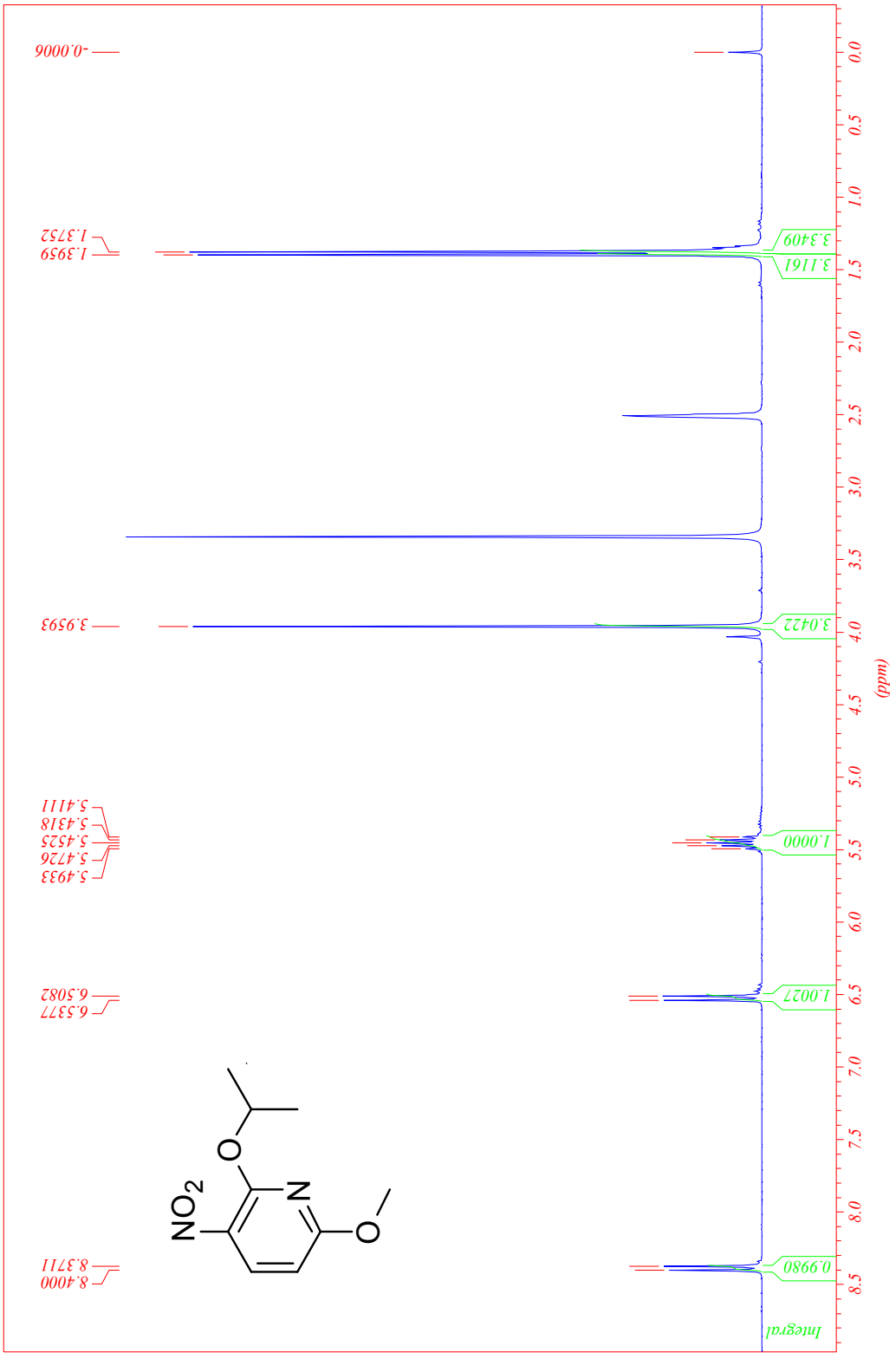
^{1}H NMR spectra of compound **3d** (300 MHz, DMSO)



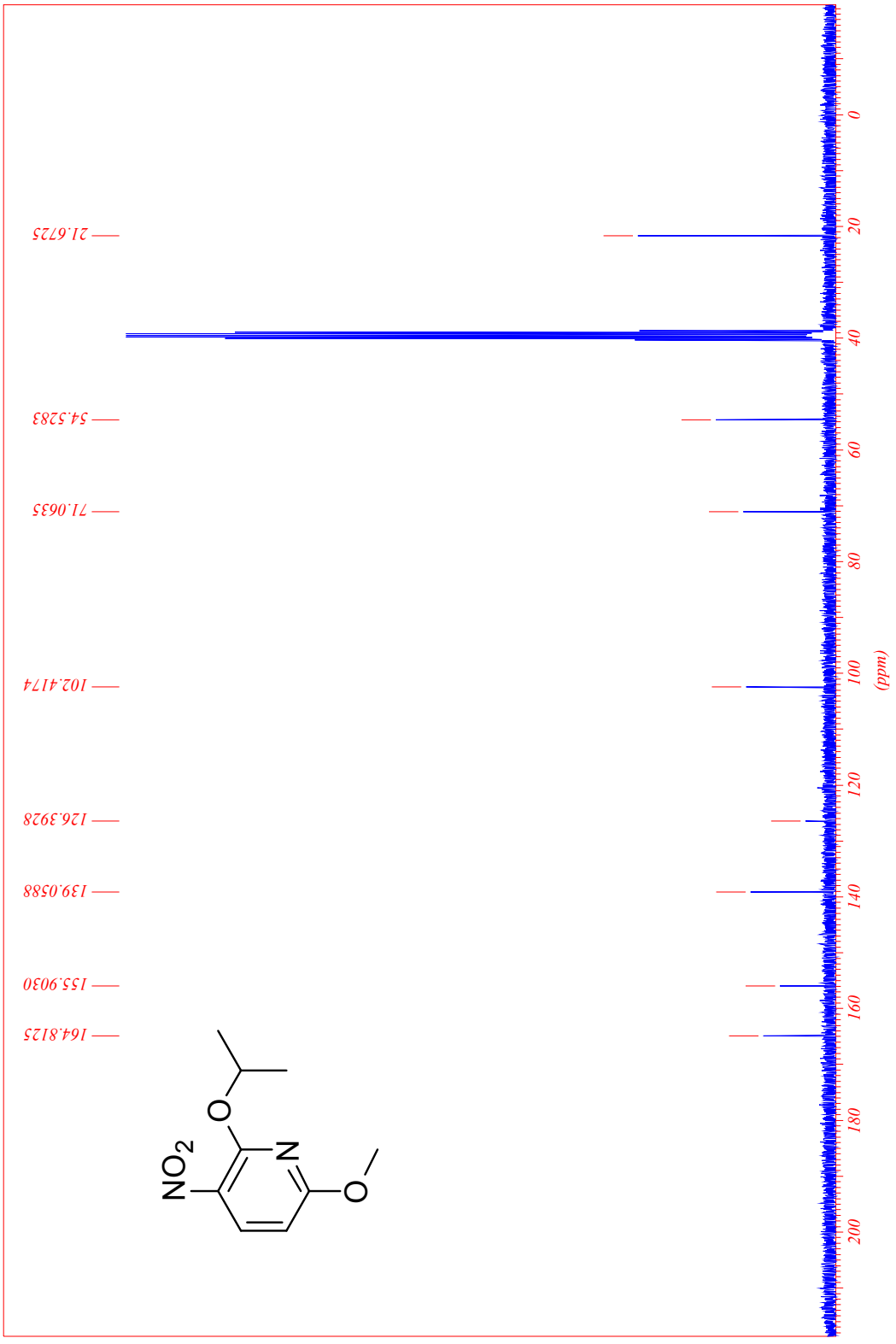
^{13}C NMR spectra of compound **3d** (75 MHz, DMSO)



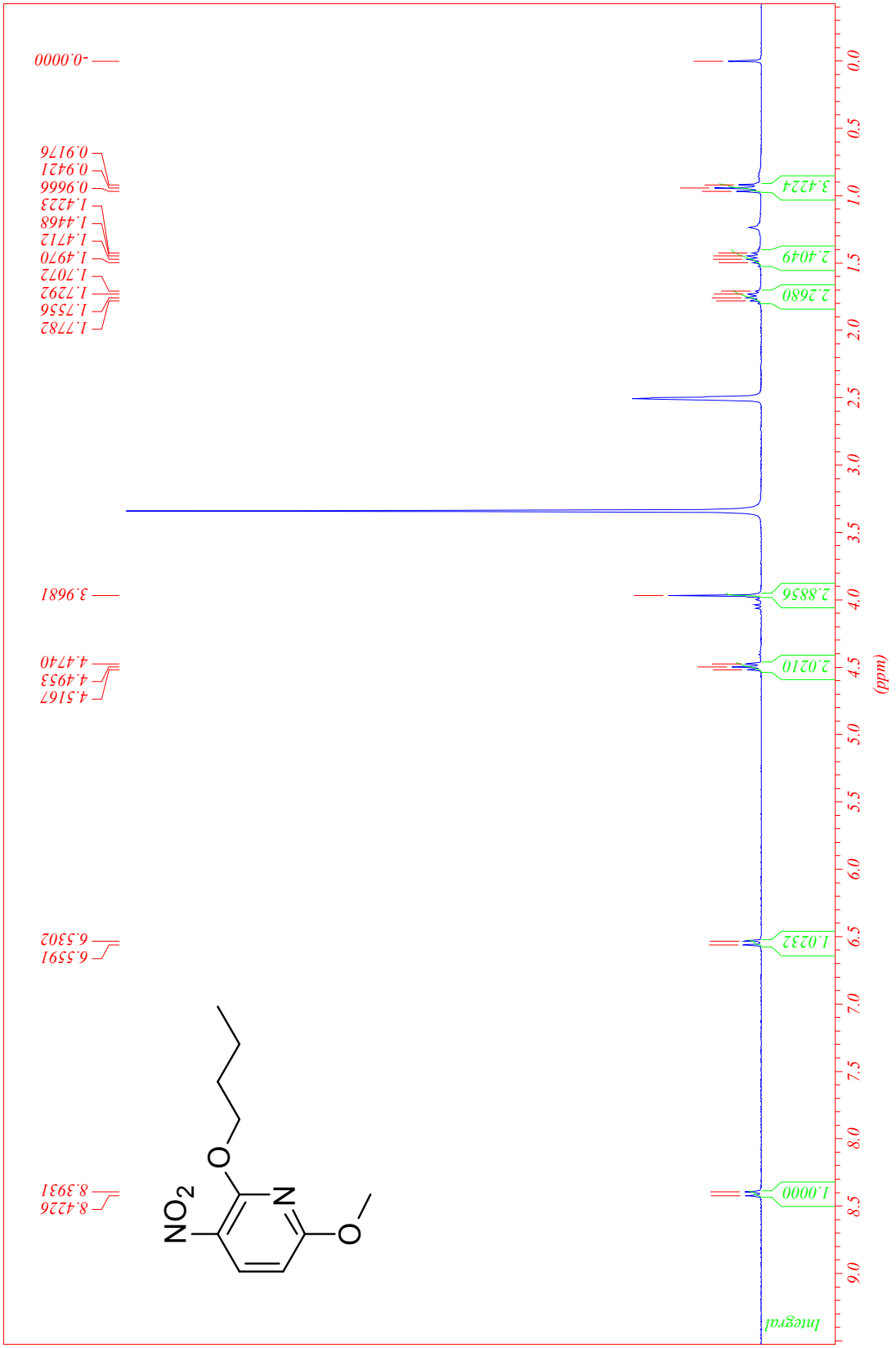
^{1}H NMR spectra of compound **7a** (300 MHz, DMSO)



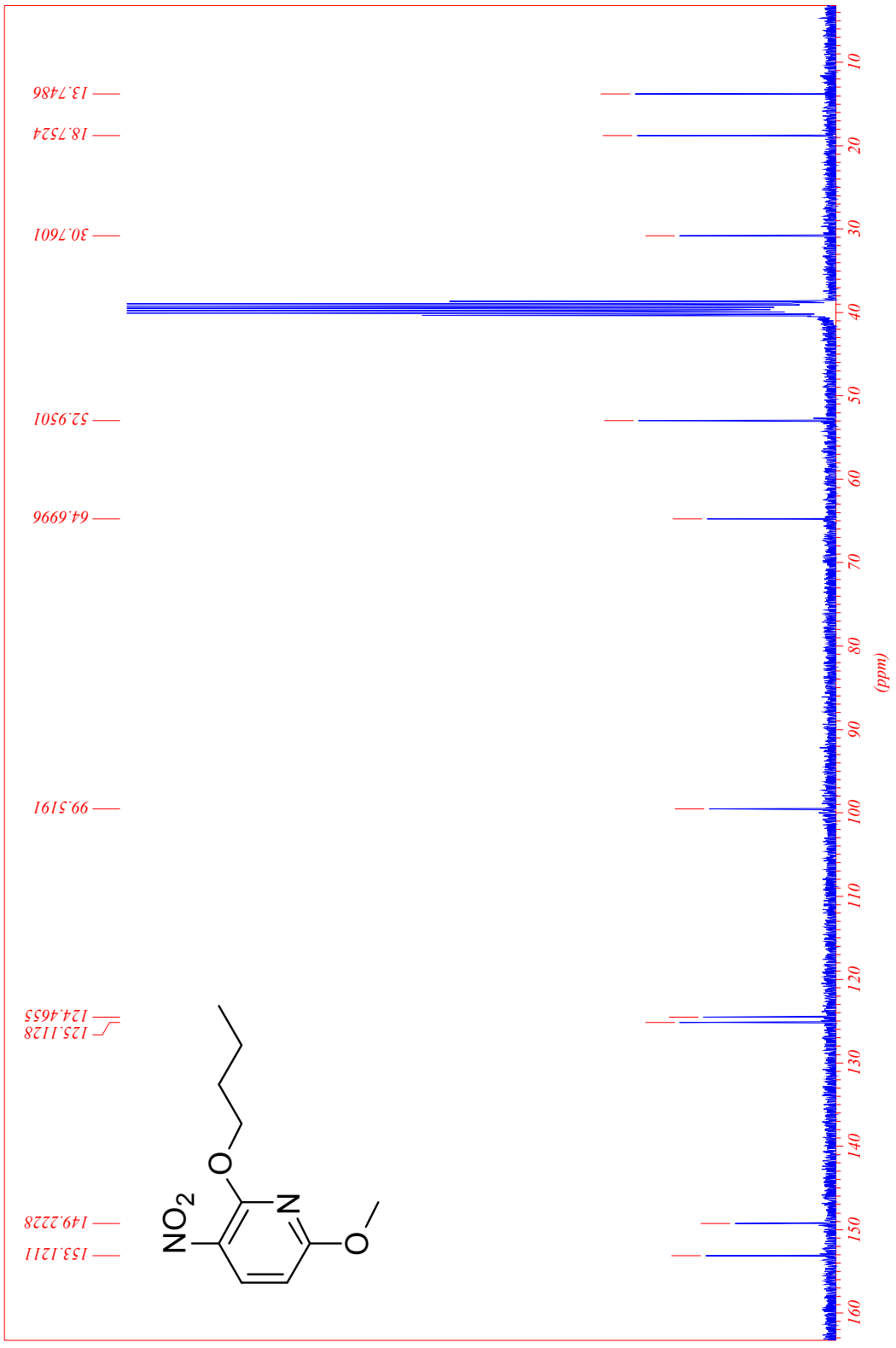
^{13}C NMR spectra of compound **7a** (75 MHz, DMSO)



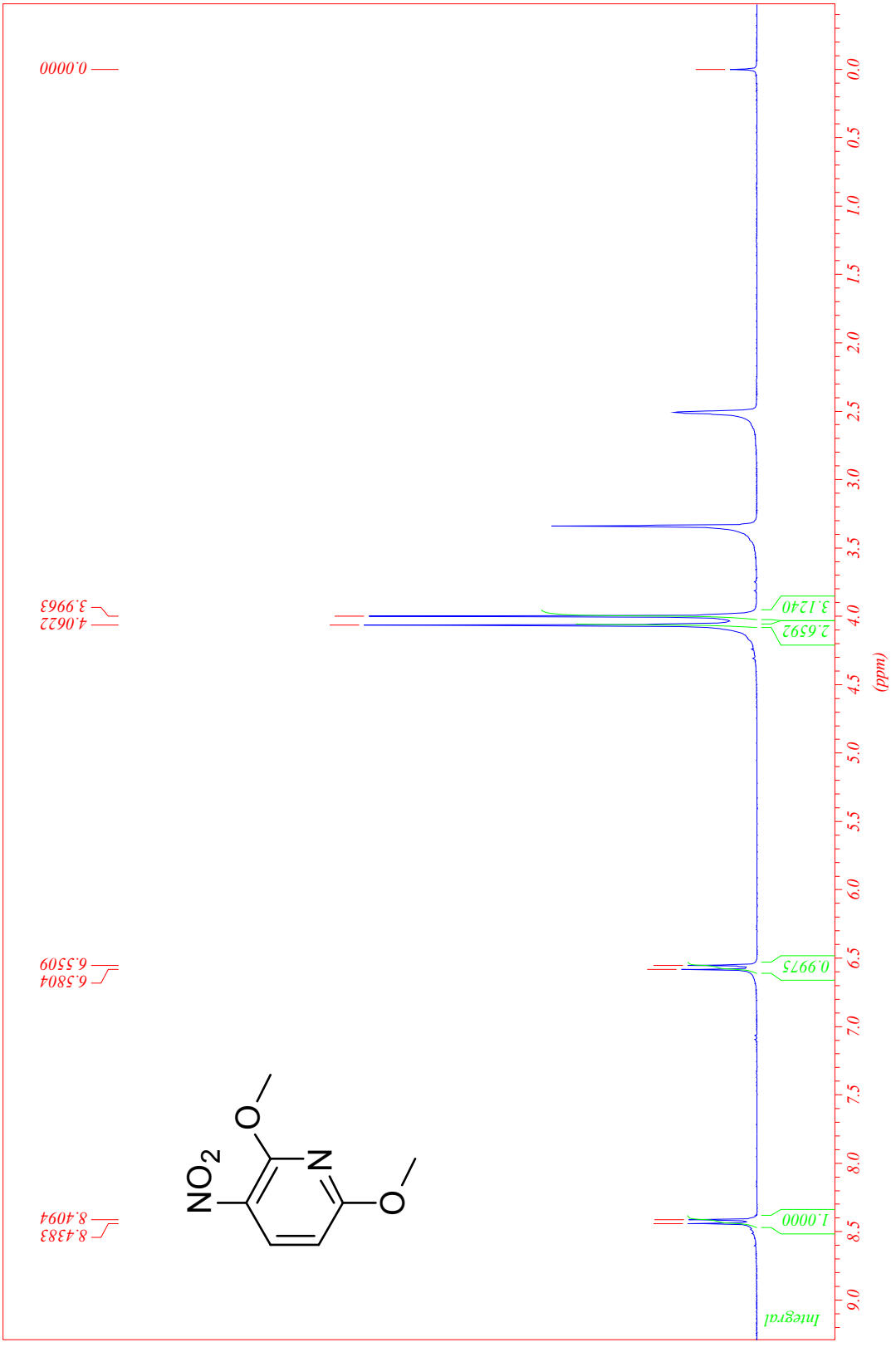
^{1}H NMR spectra of compound **7b** (300 MHz, DMSO)



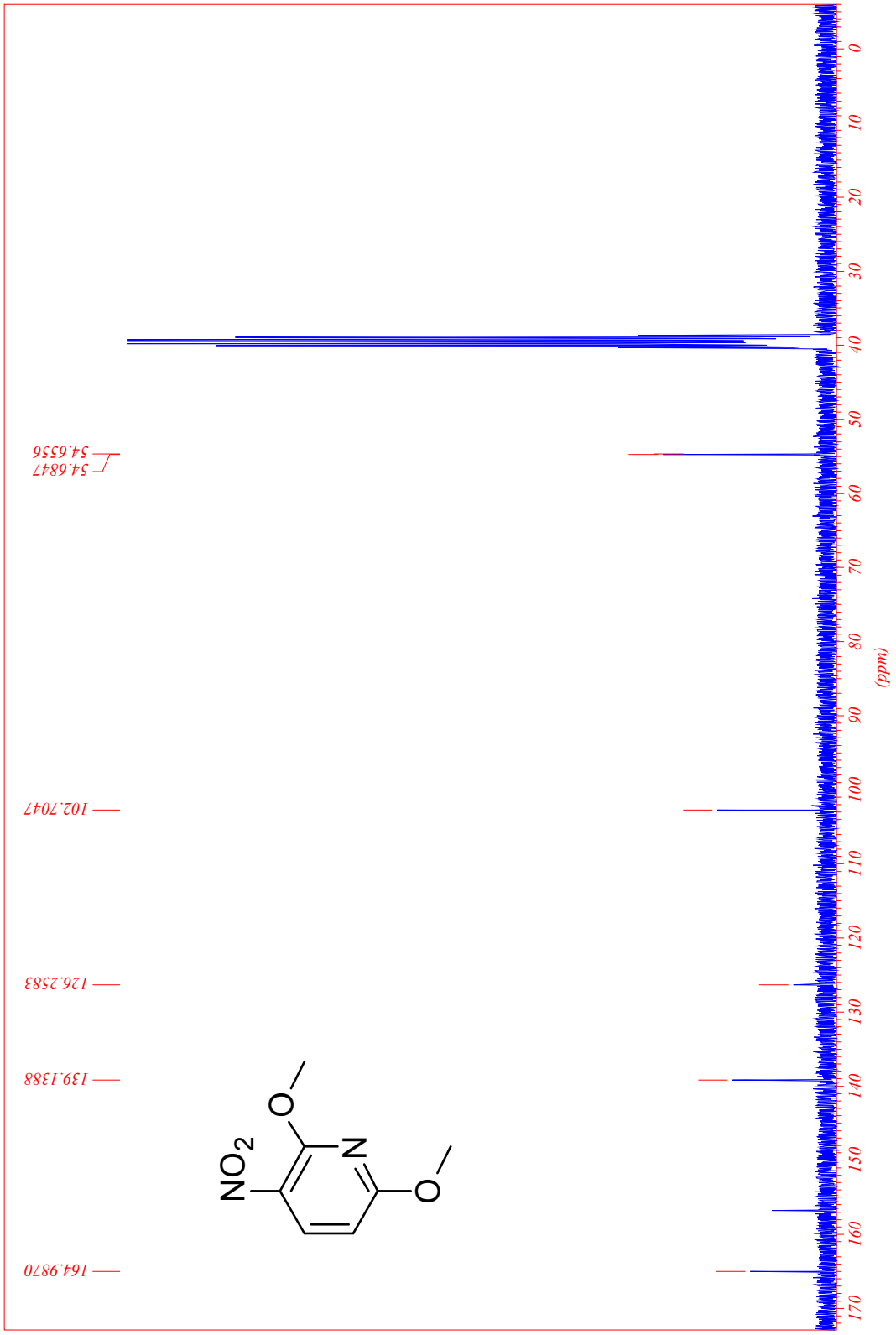
^{13}C NMR spectra of compound **7b** (75 MHz, DMSO)



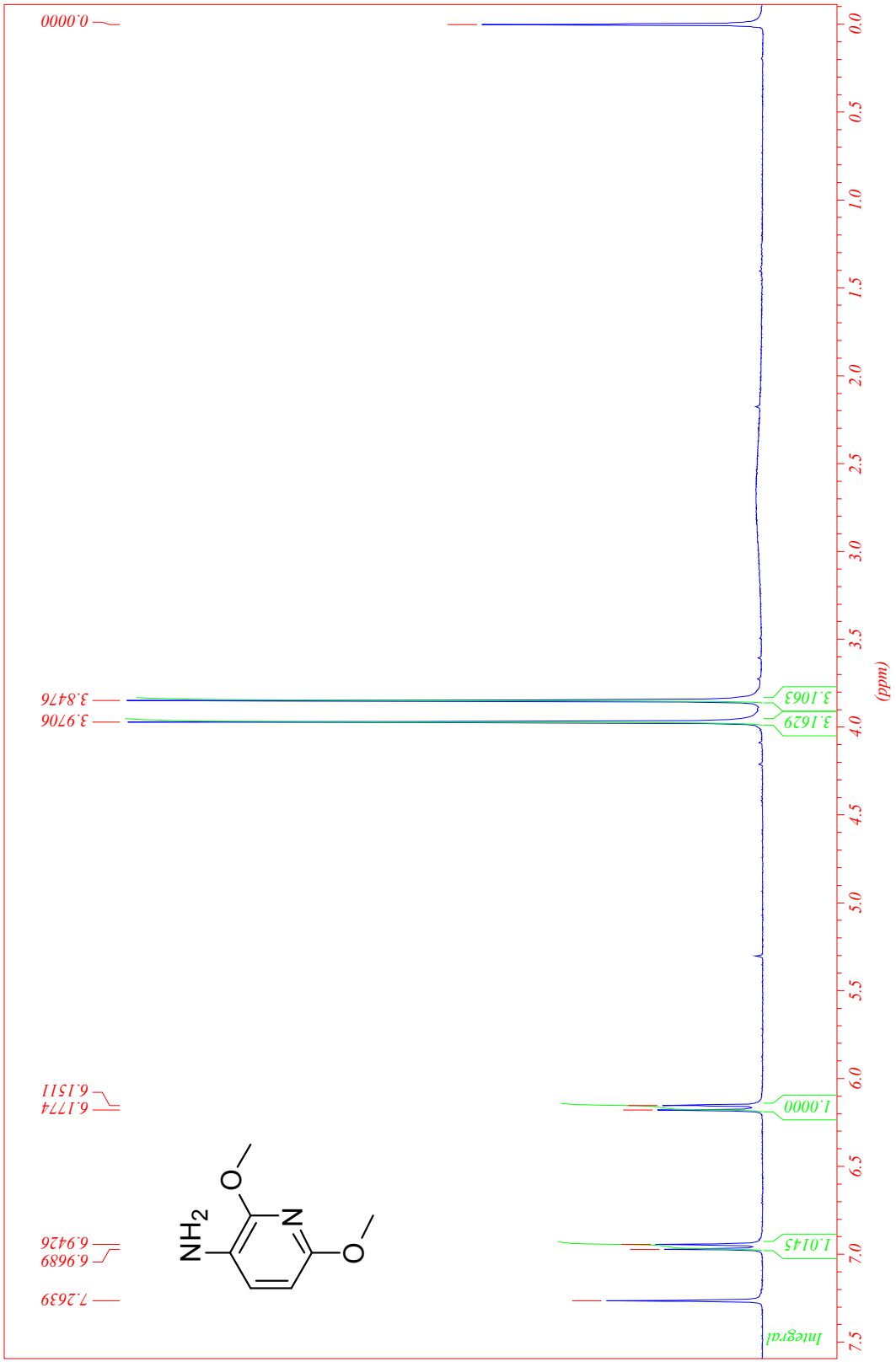
^{1}H NMR spectra of compound **7c** (300 MHz, DMSO)



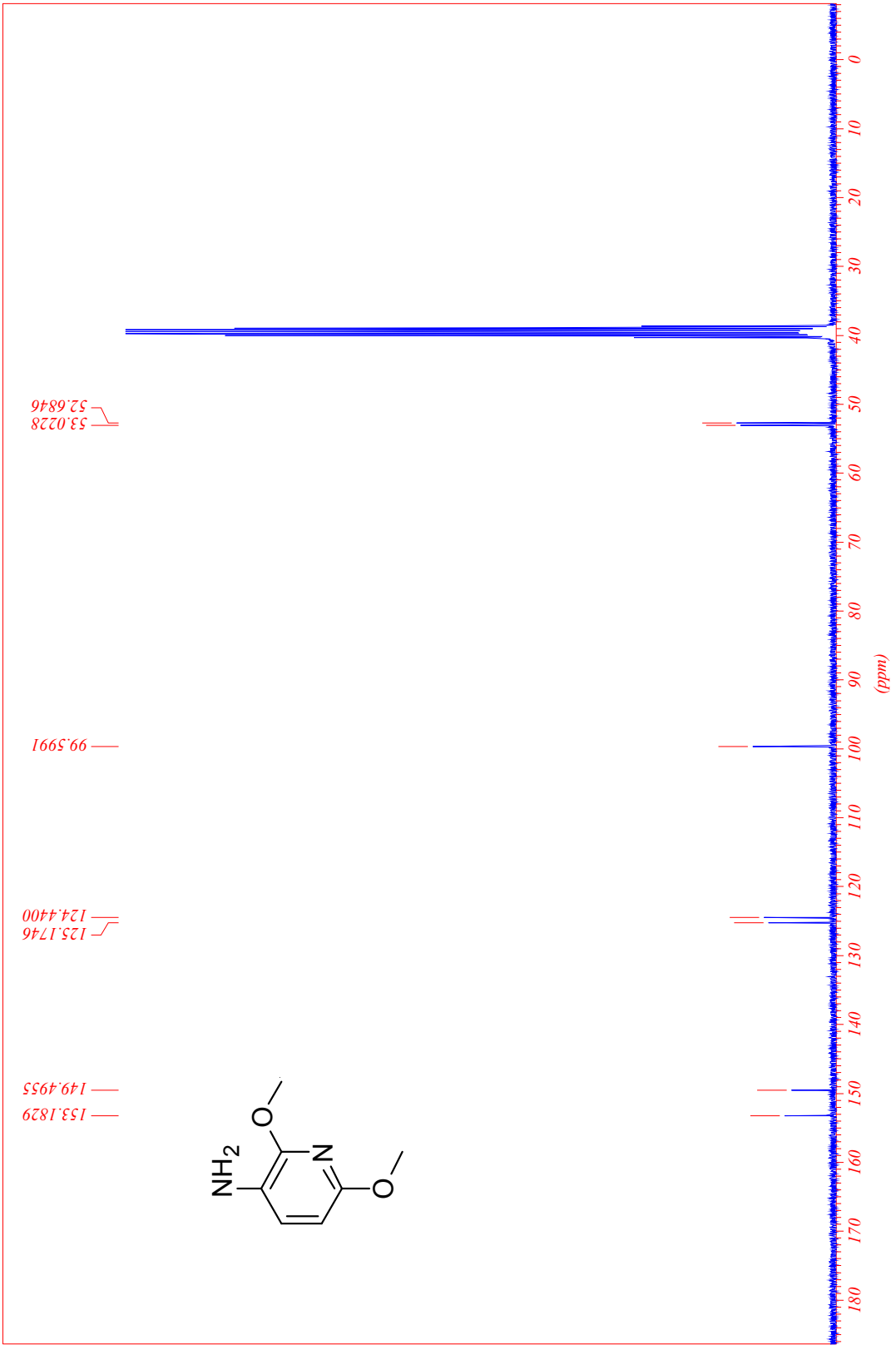
^{13}C NMR spectra of compound **7c** (75 MHz, DMSO)



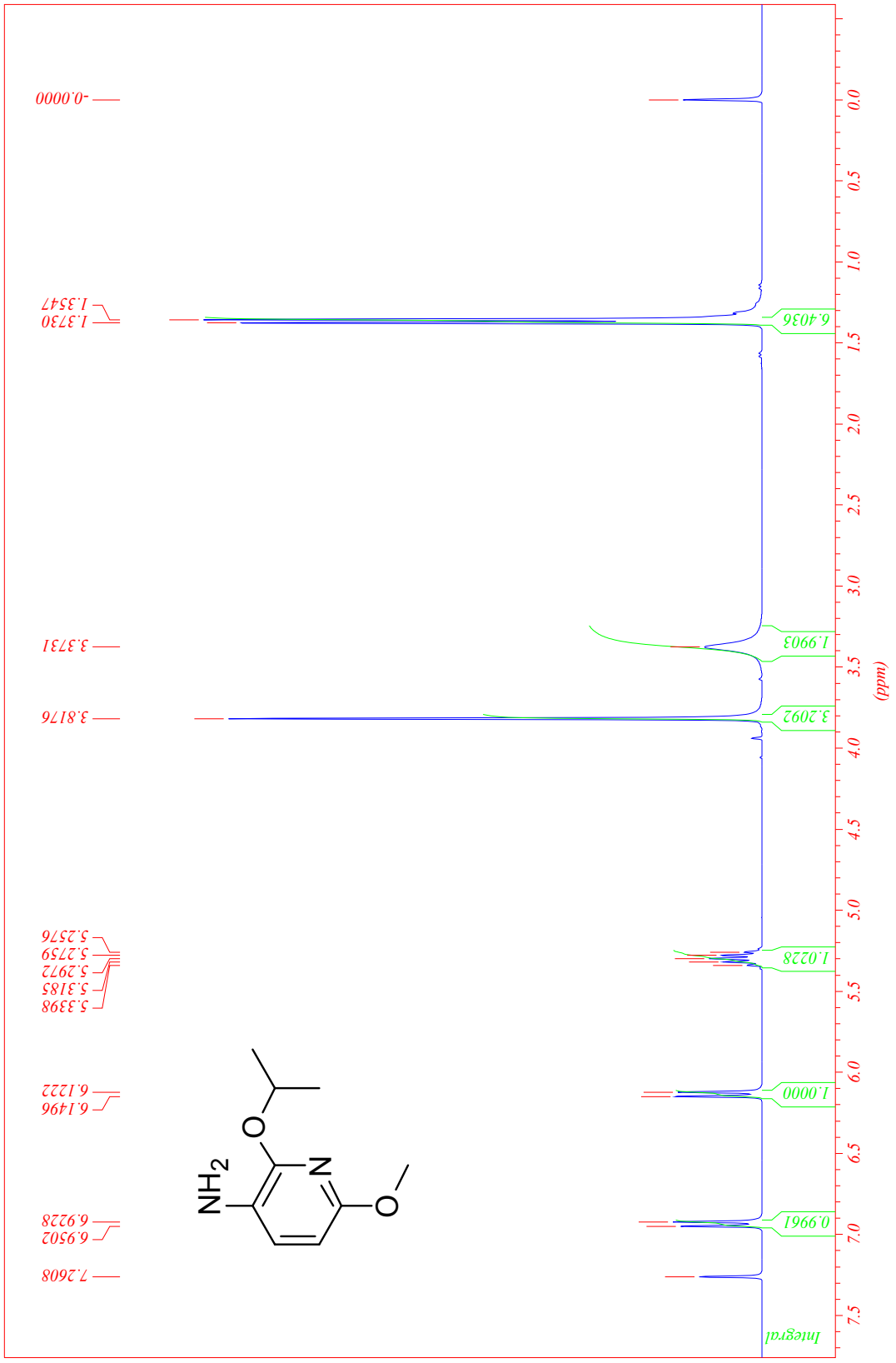
^{1}H NMR spectra of compound **8c** (300 MHz, DMSO)



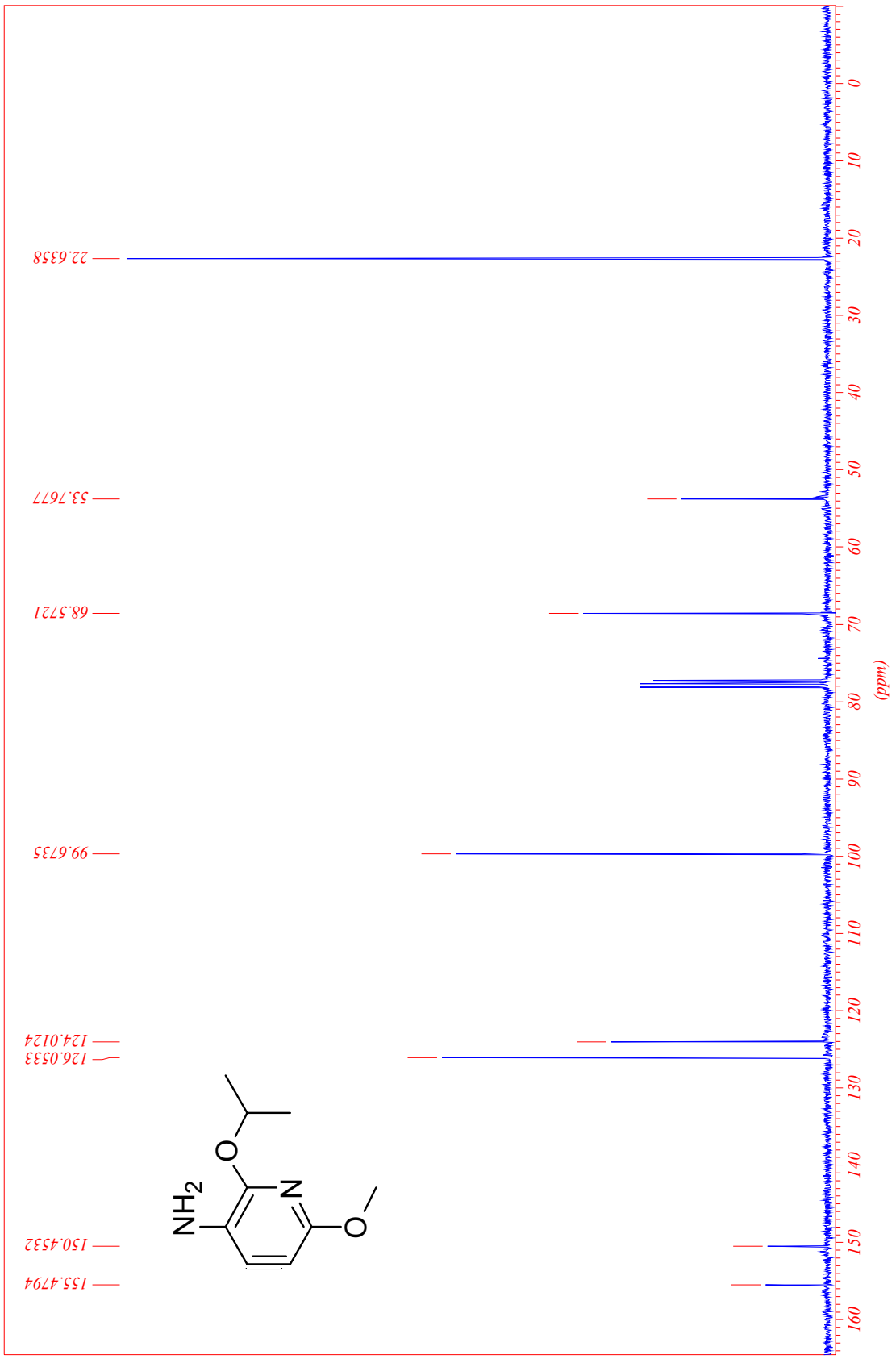
^{13}C NMR spectra of compound **8c** (75 MHz, DMSO)



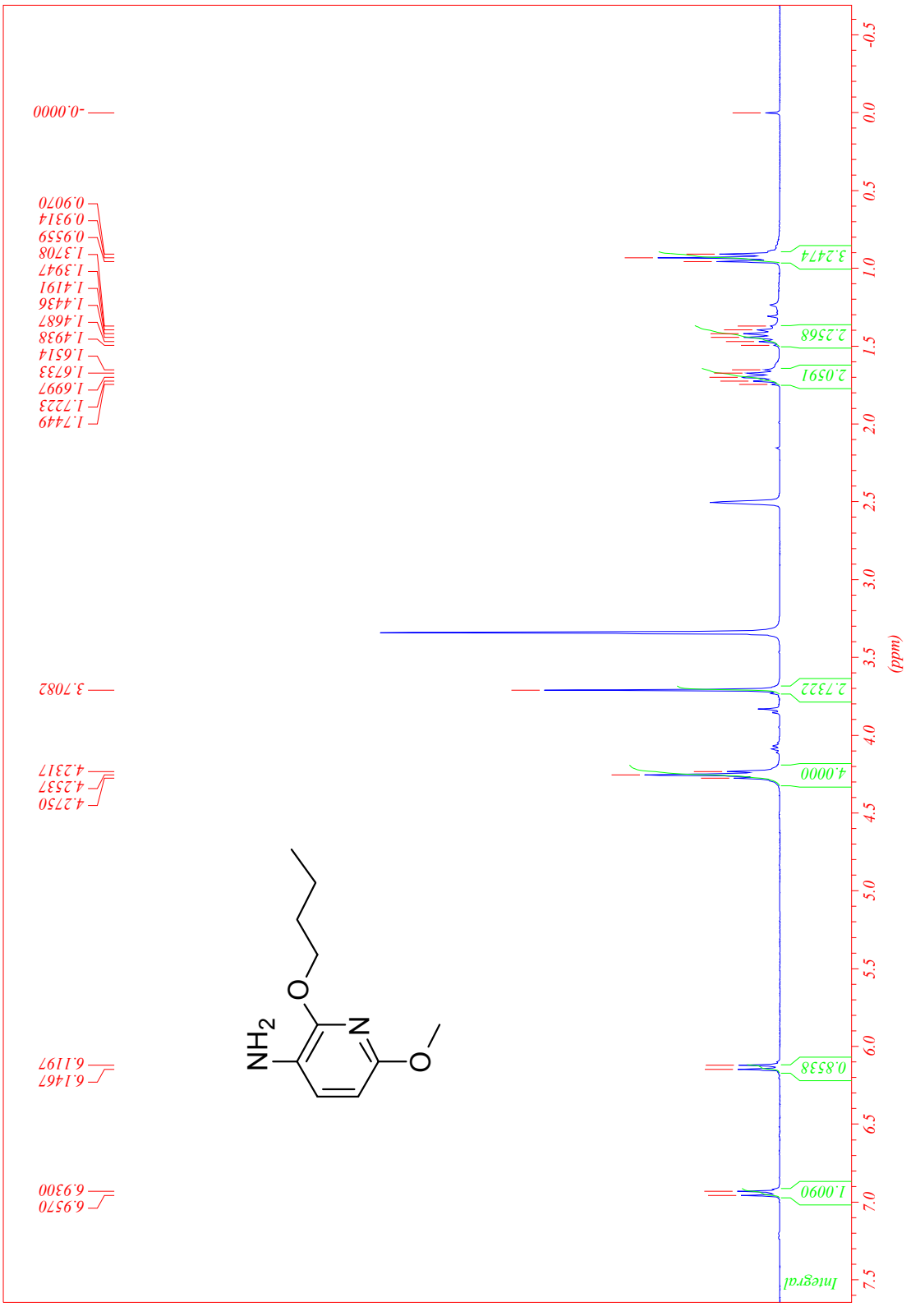
^{1}H NMR spectra of compound **8a** (300 MHz, $CDCl_3$)



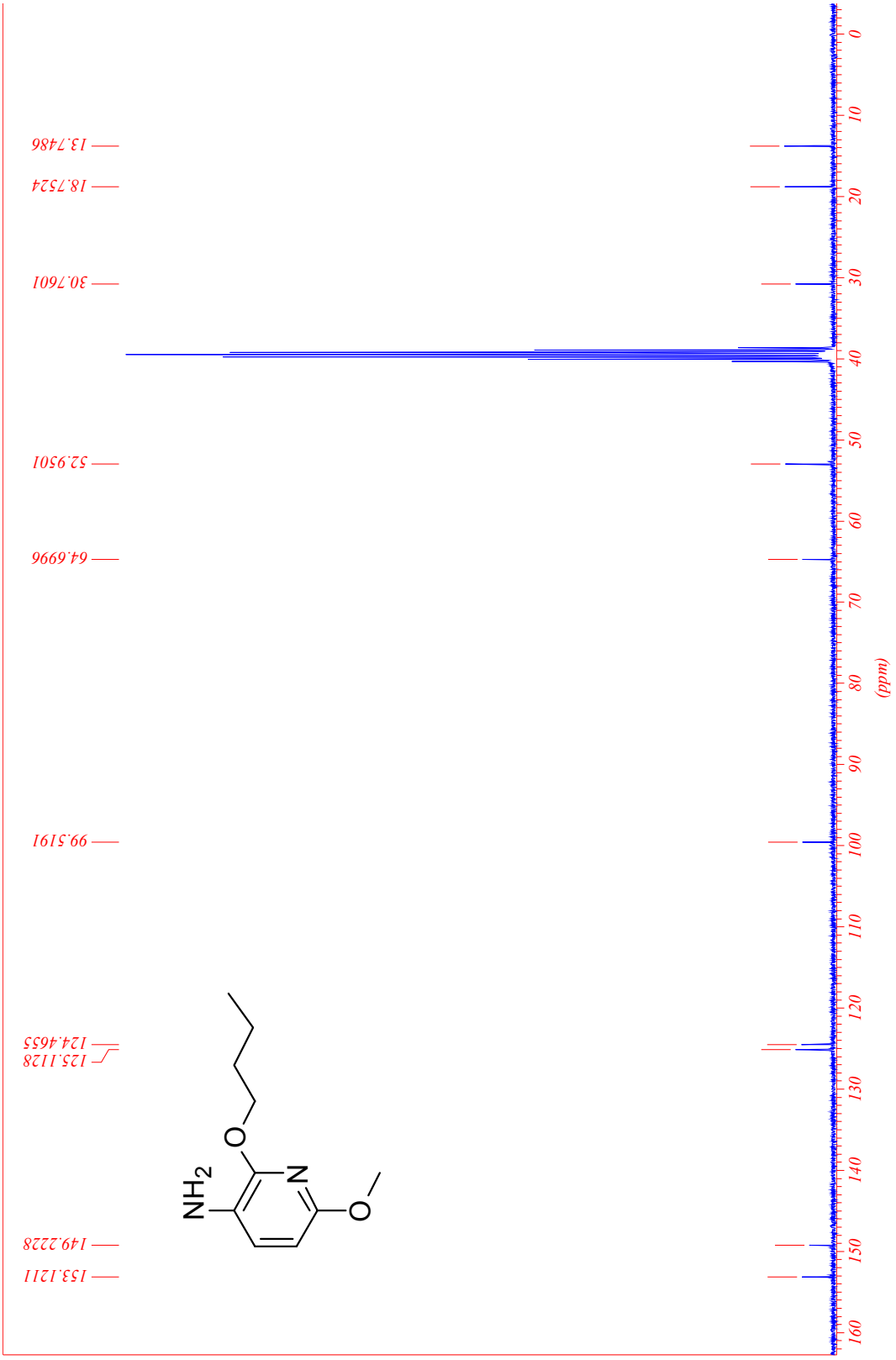
^{13}C NMR spectra of compound **8a** (75 MHz, $CDCl_3$)



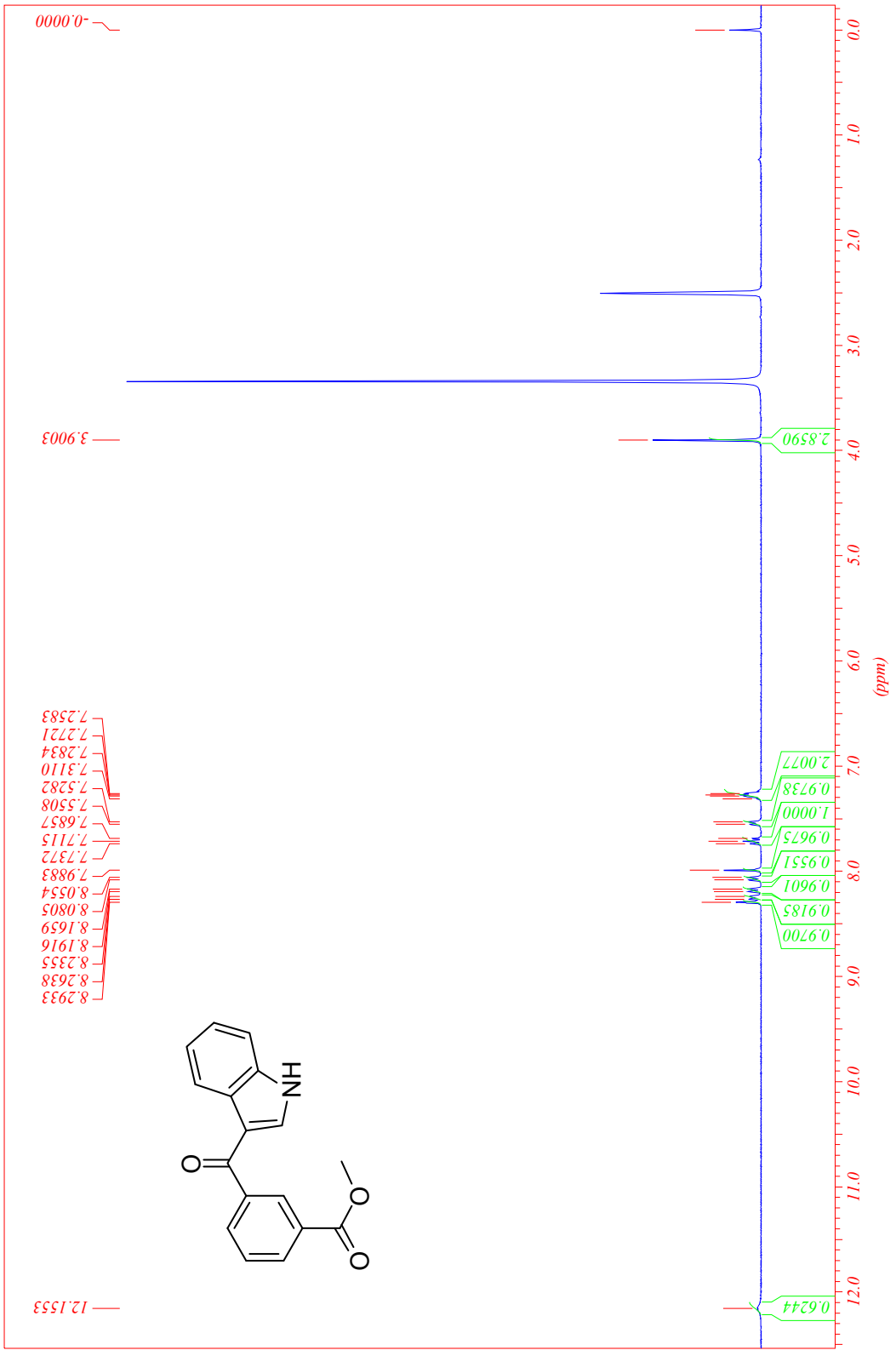
^{1}H NMR spectra of compound **8b** (300 MHz, DMSO)



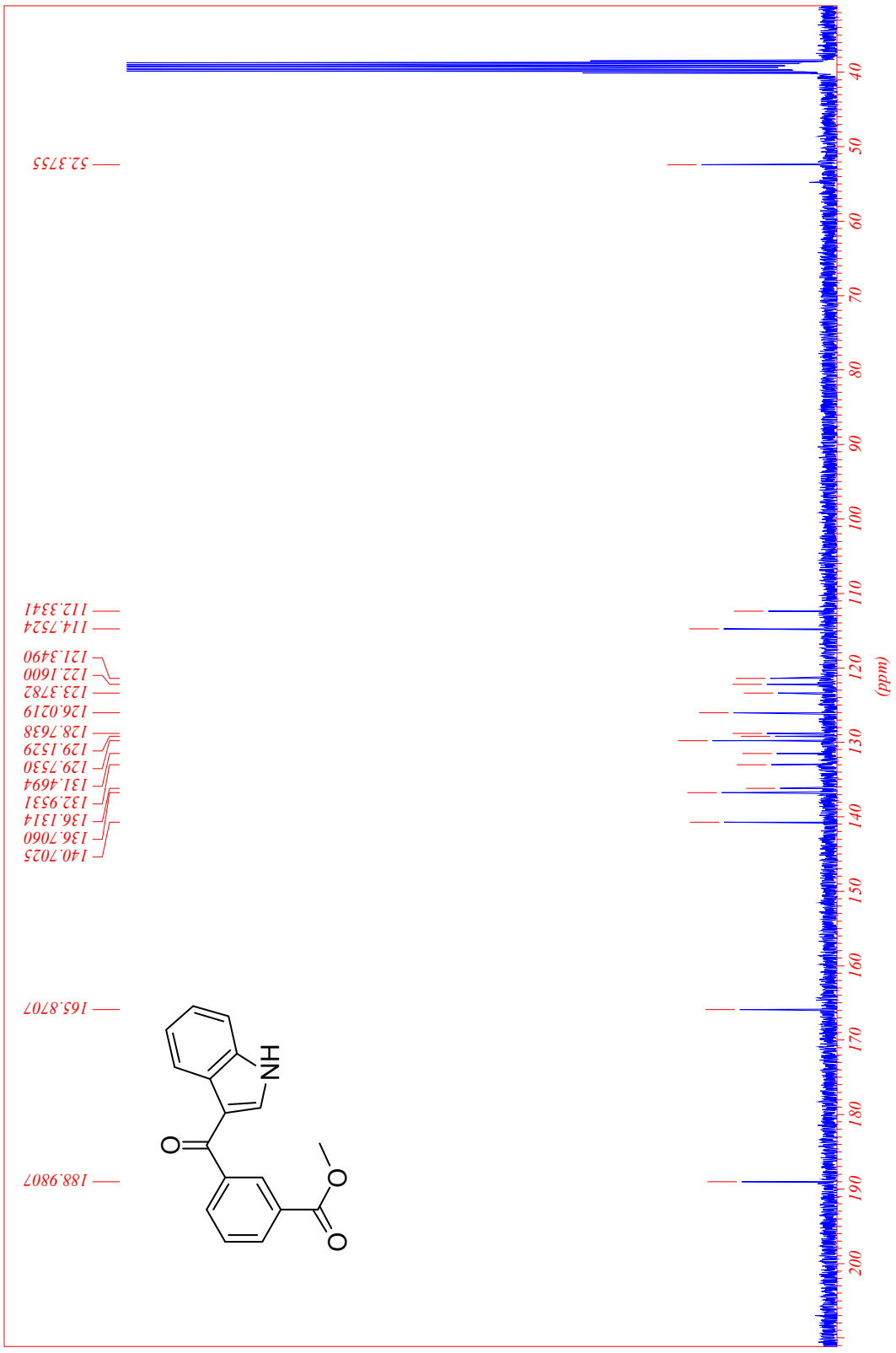
^{13}C NMR spectra of compound **8b** (75 MHz, DMSO)



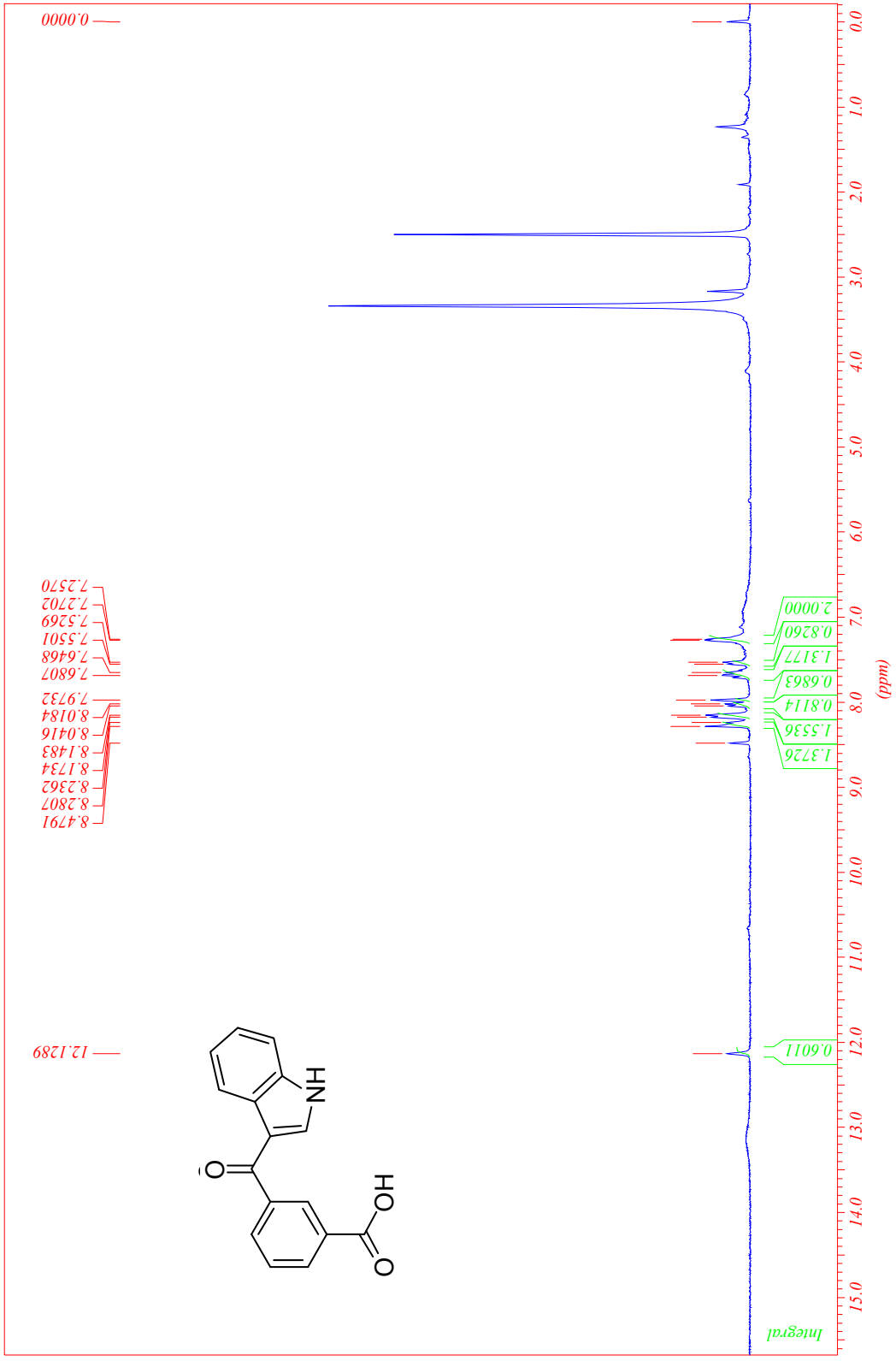
^{1}H NMR spectra of compound **10** (300 MHz, DMSO)



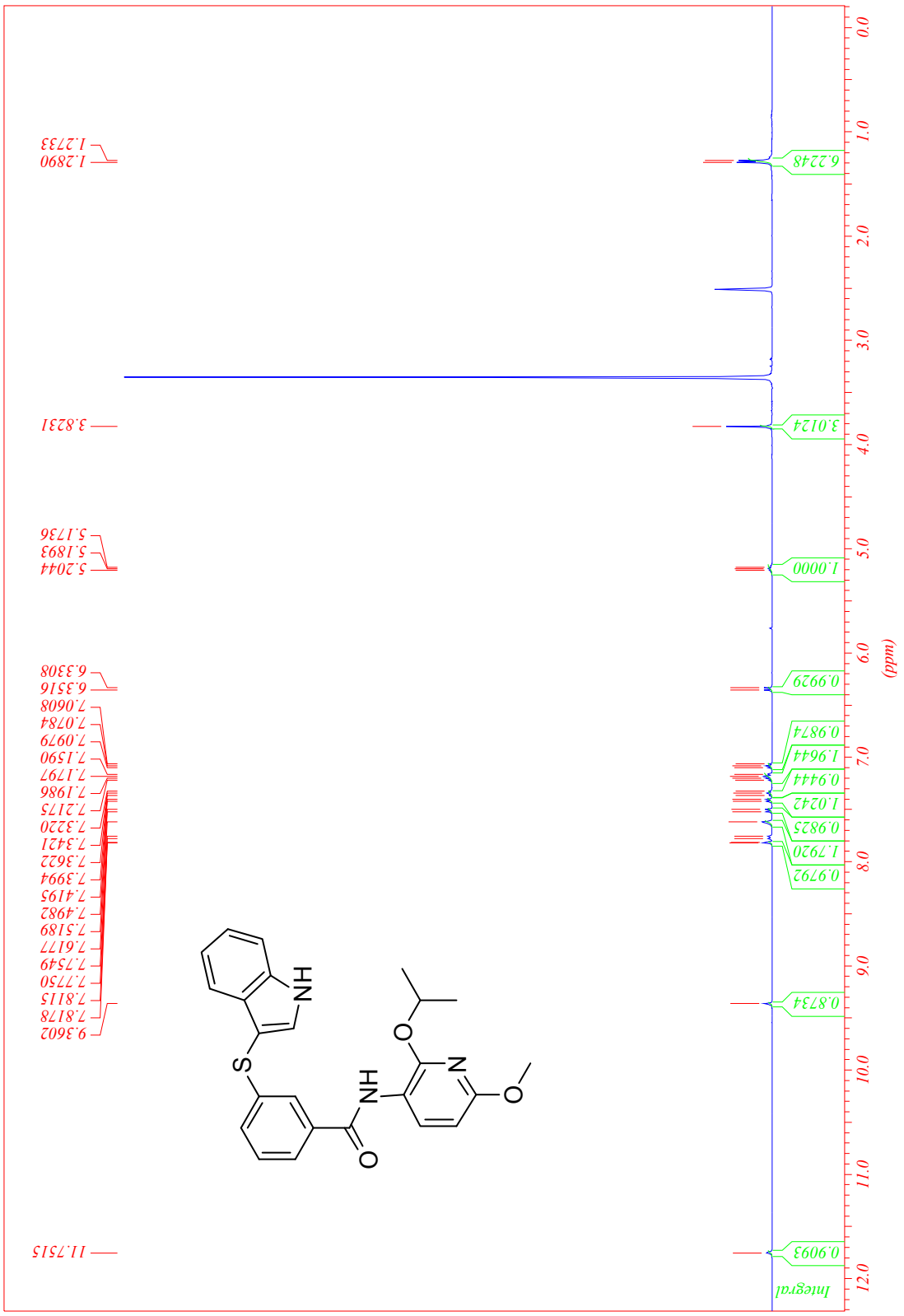
^{13}C NMR spectra of compound **10** (75 MHz, DMSO)



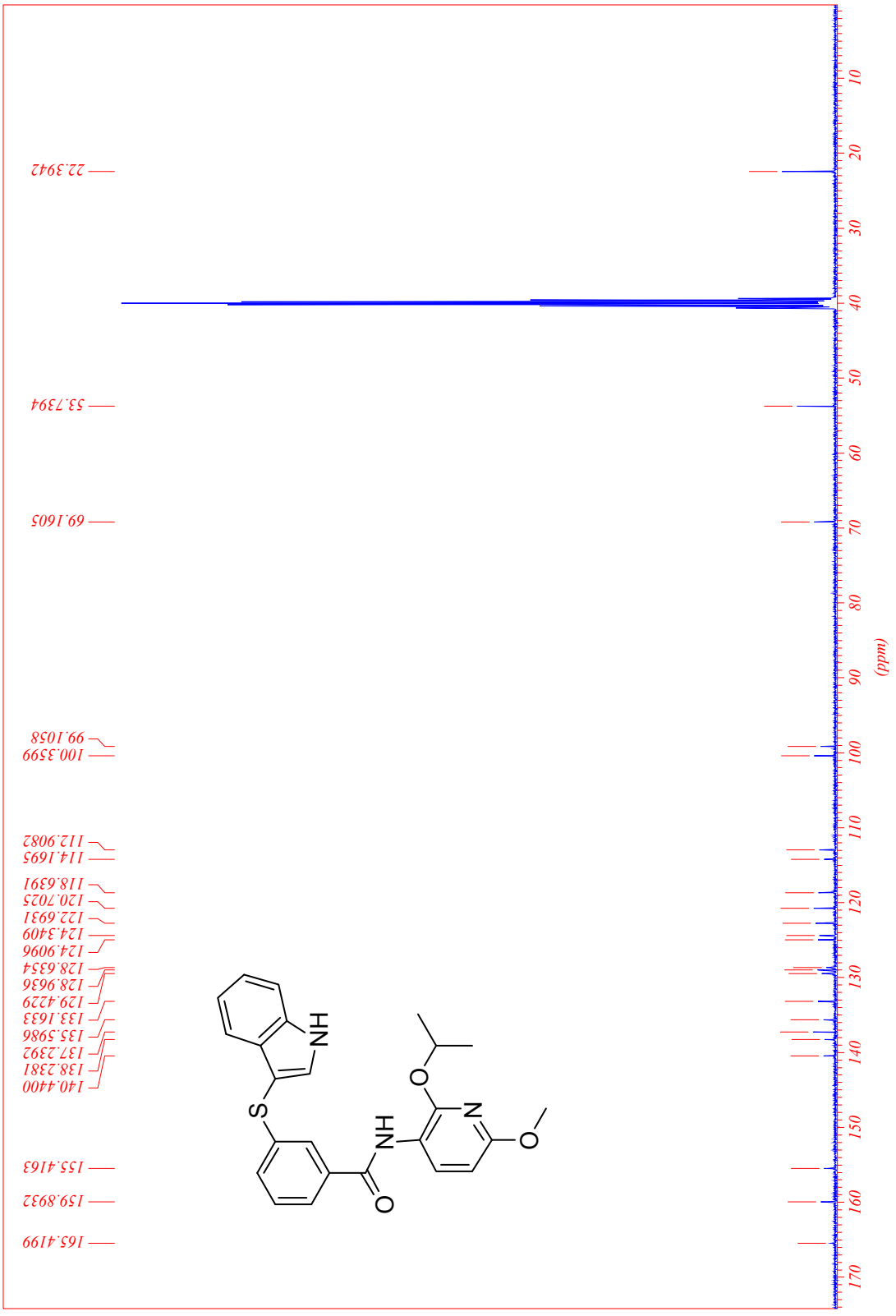
^{1}H NMR spectra of compound **11** (300 MHz, DMSO)



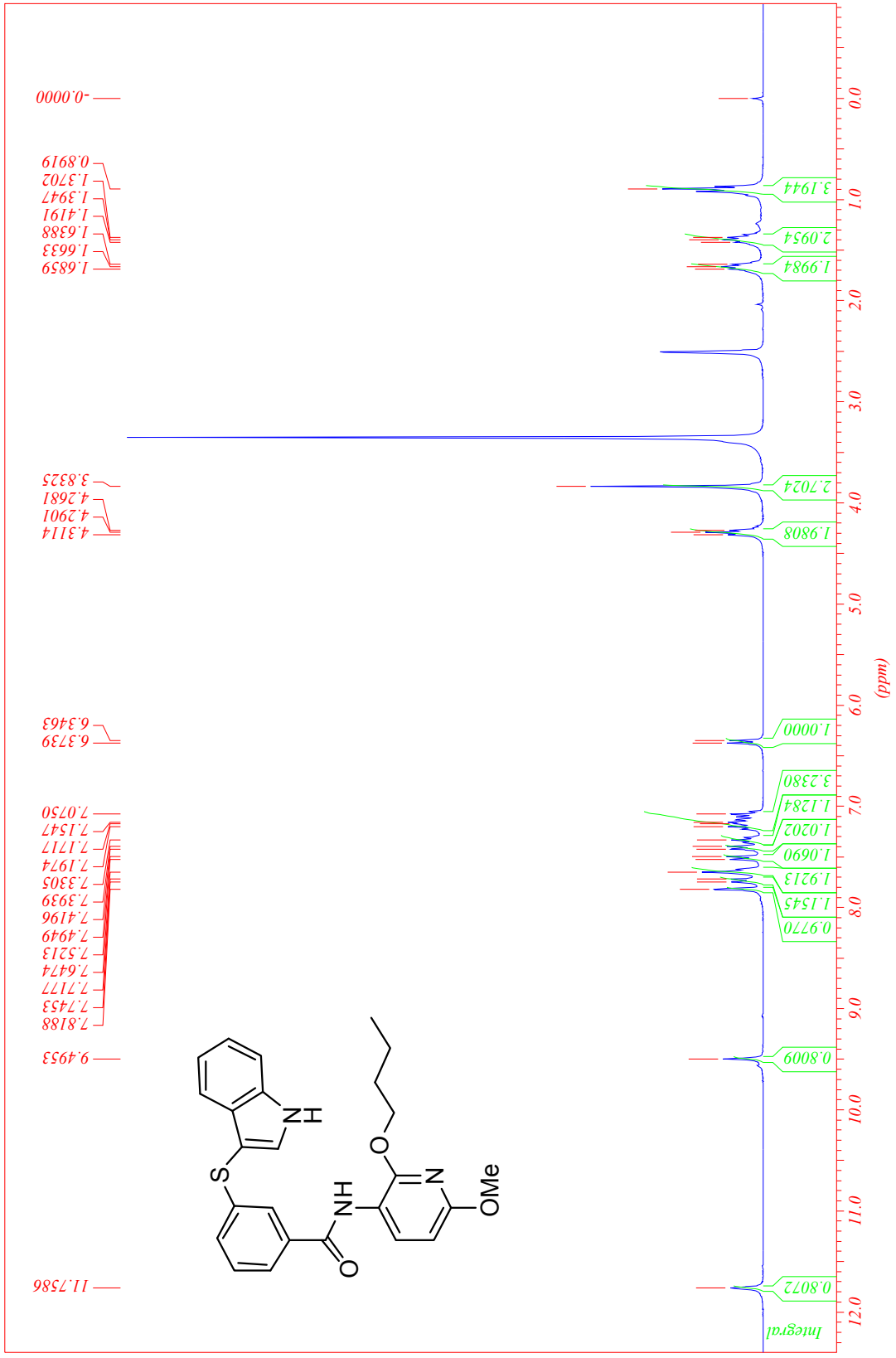
^{1}H NMR spectra of compound **CAB1** (400 MHz, DMSO)



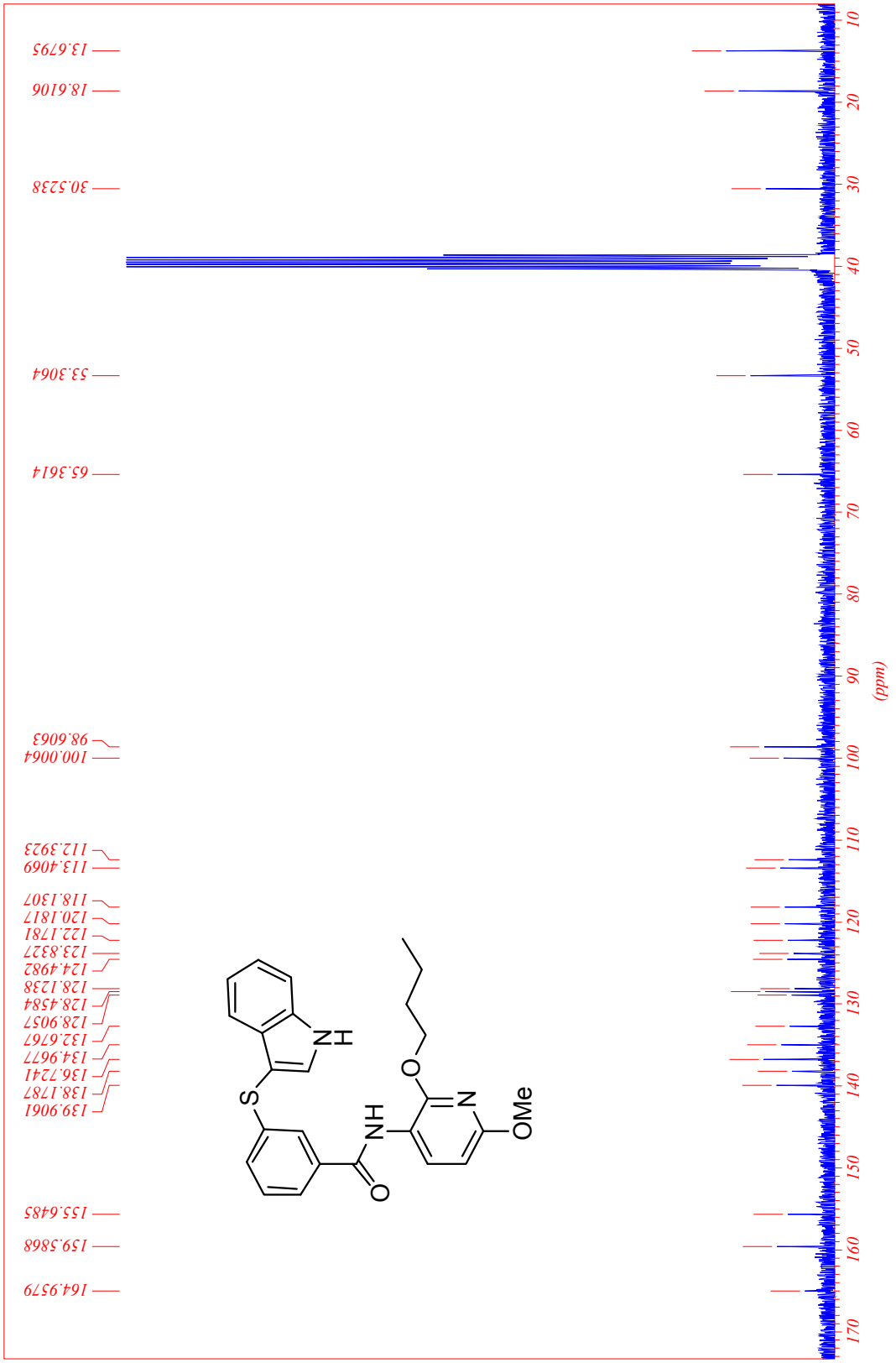
^{13}C NMR spectra of compound **CAB1** (100 MHz, DMSO)



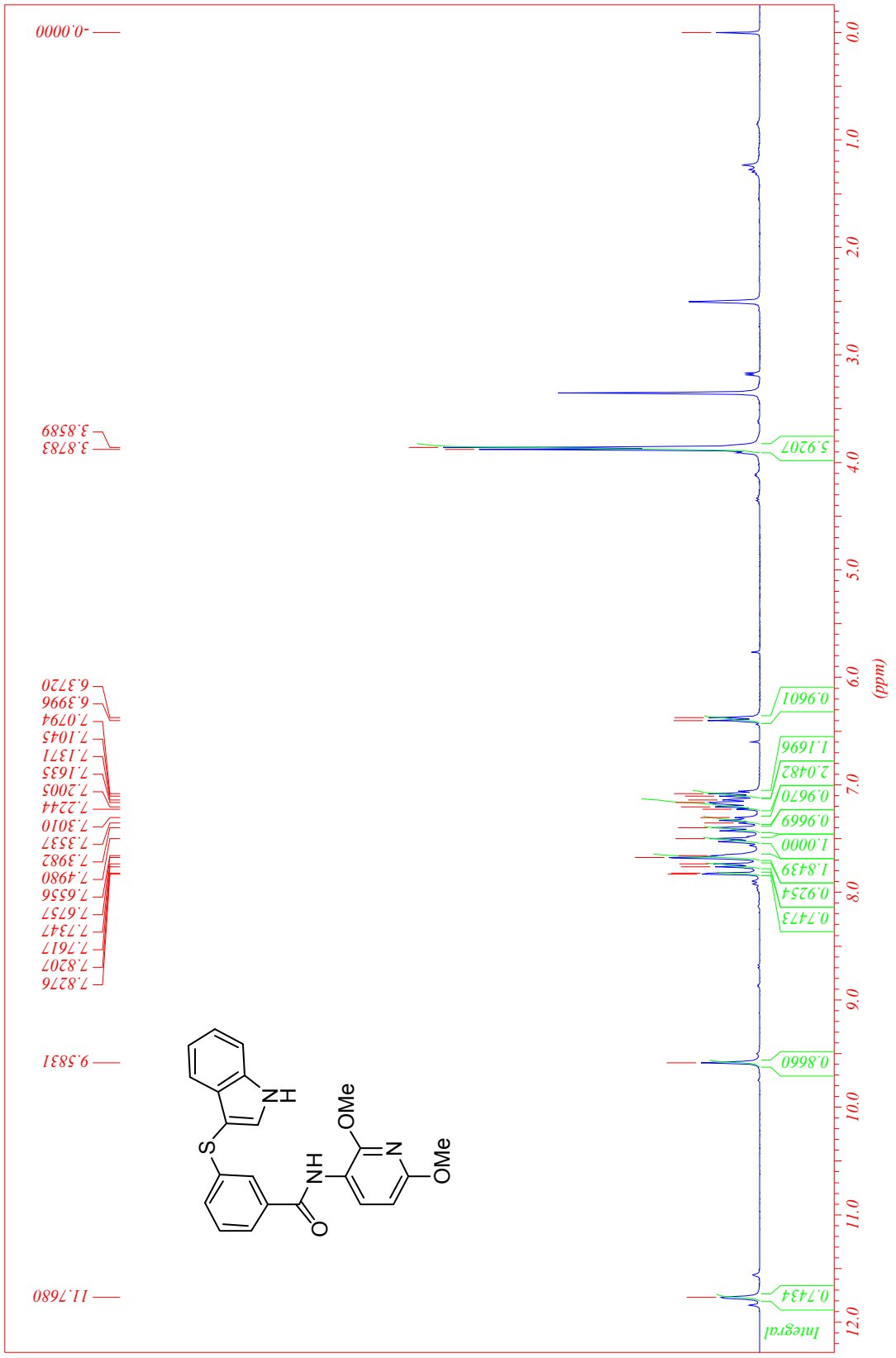
^{1}H NMR spectra of compound **CAB2** (300 MHz, DMSO)



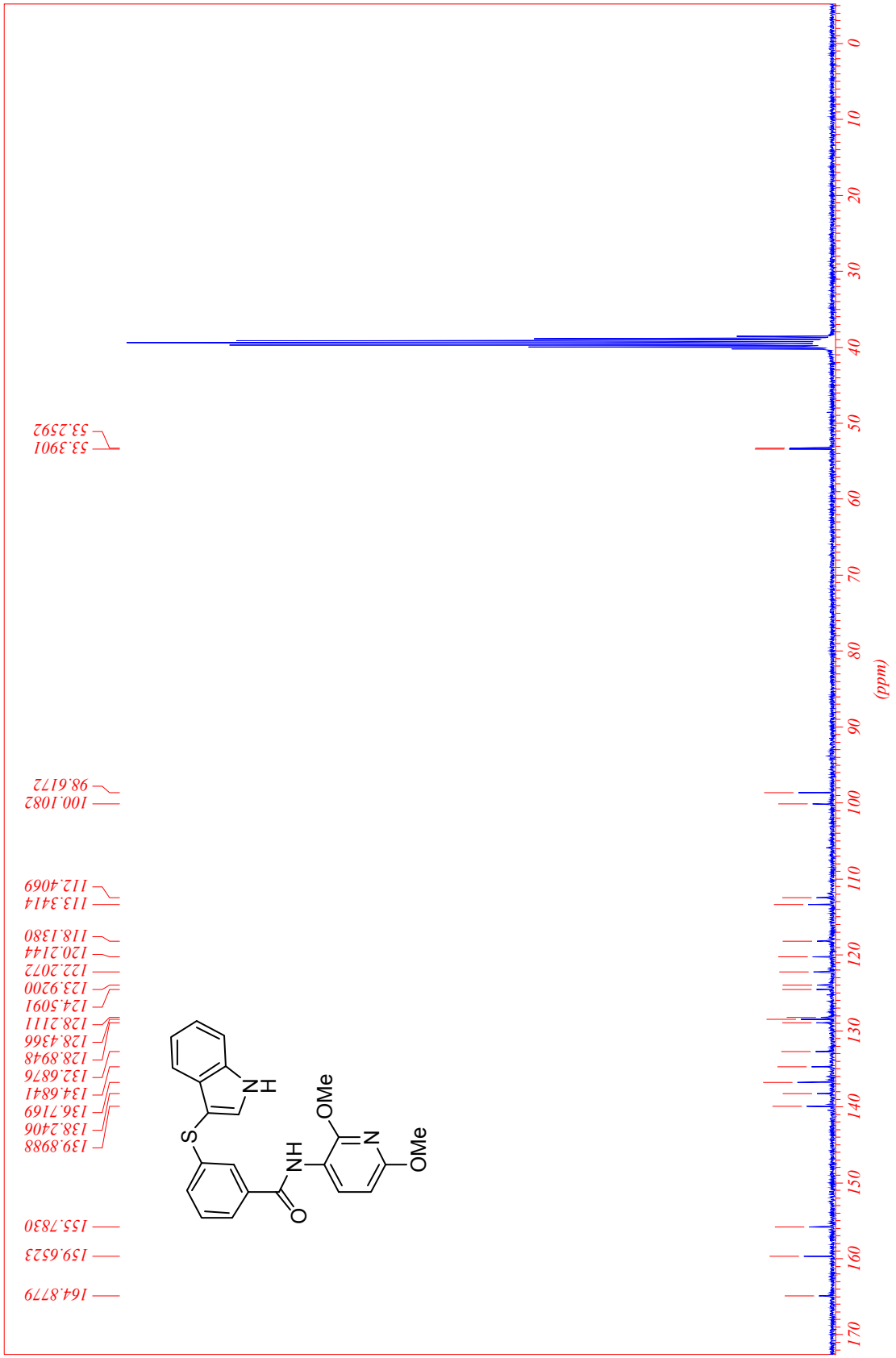
^{13}C NMR spectra of compound **CAB2** (75 MHz, DMSO)



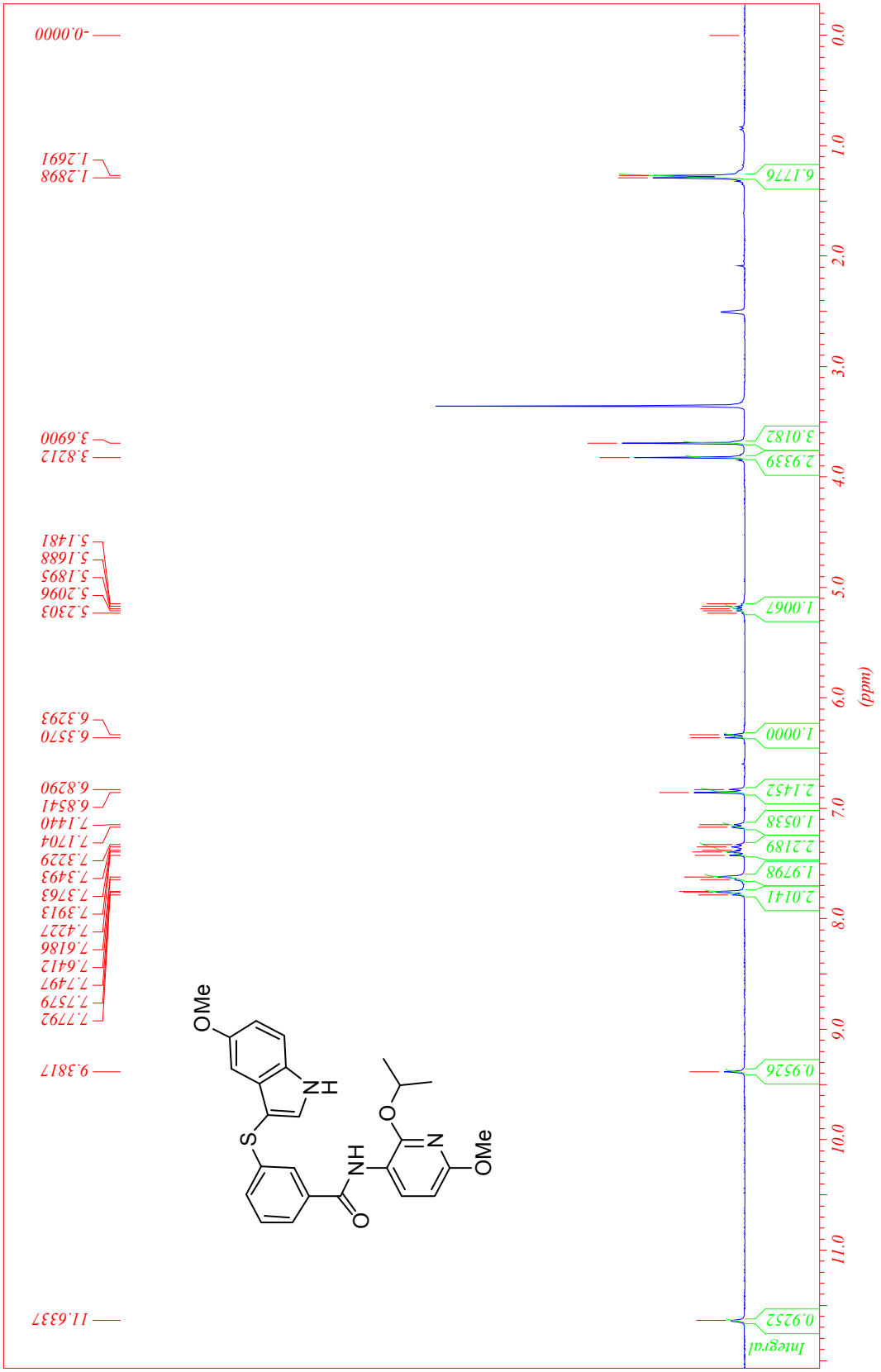
^{1}H NMR spectra of compound **CAB3** (300 MHz, DMSO)



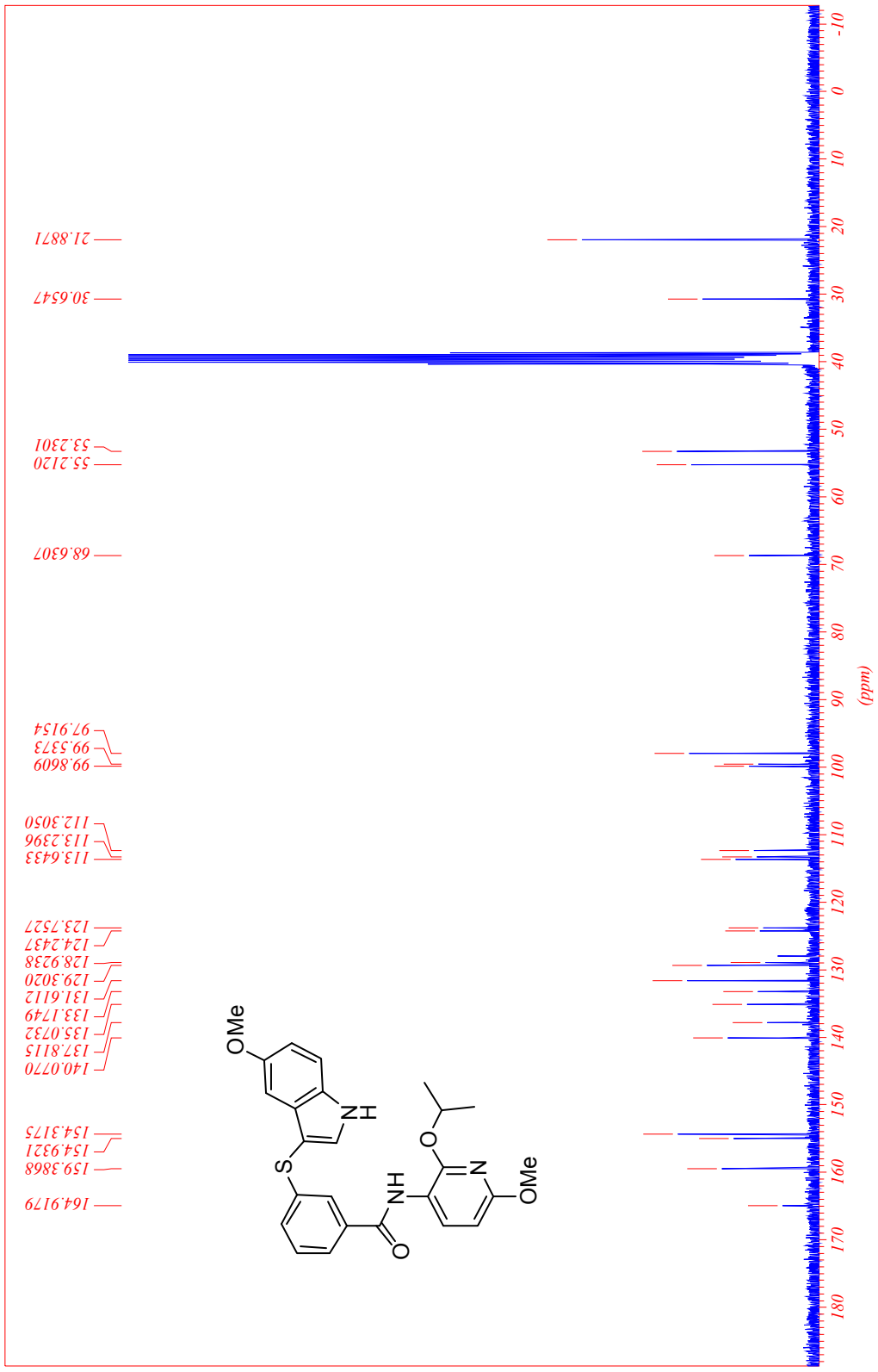
^{13}C NMR spectra of compound **CAB3** (75 MHz, DMSO)



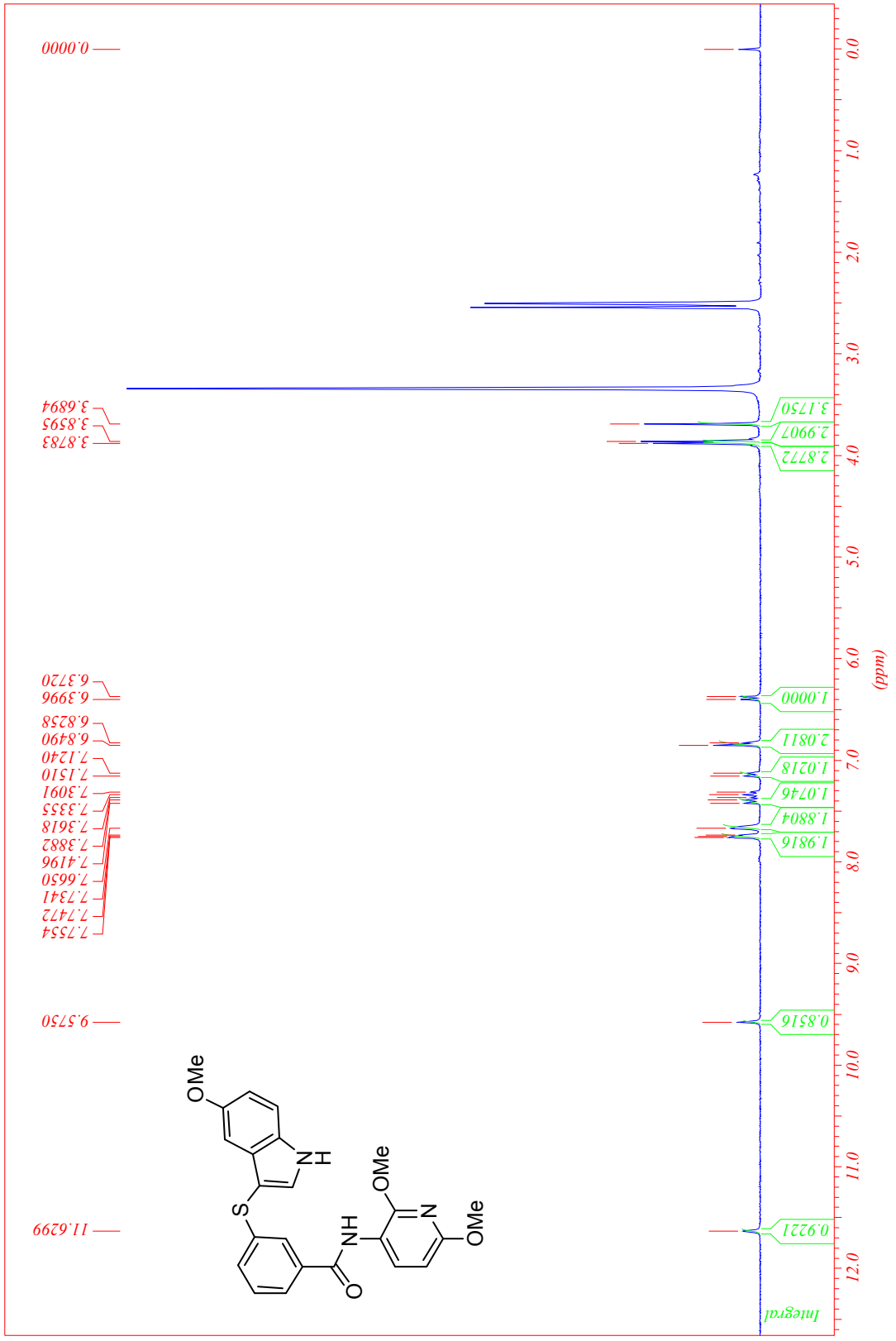
^{1}H NMR spectra of compound **CAB4** (300 MHz, DMSO)



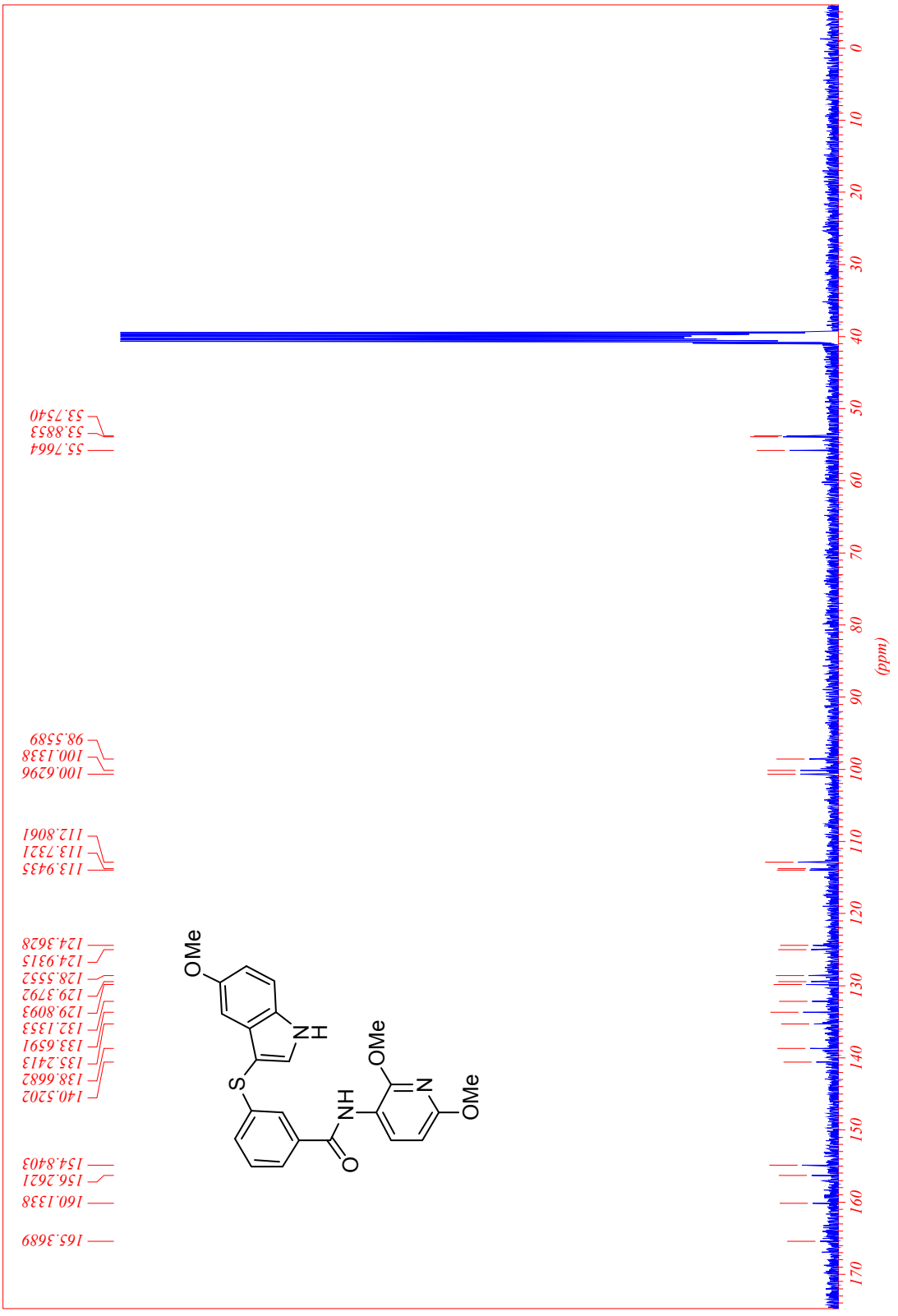
^{13}C NMR spectra of compound **CAB4** (75 MHz, DMSO)



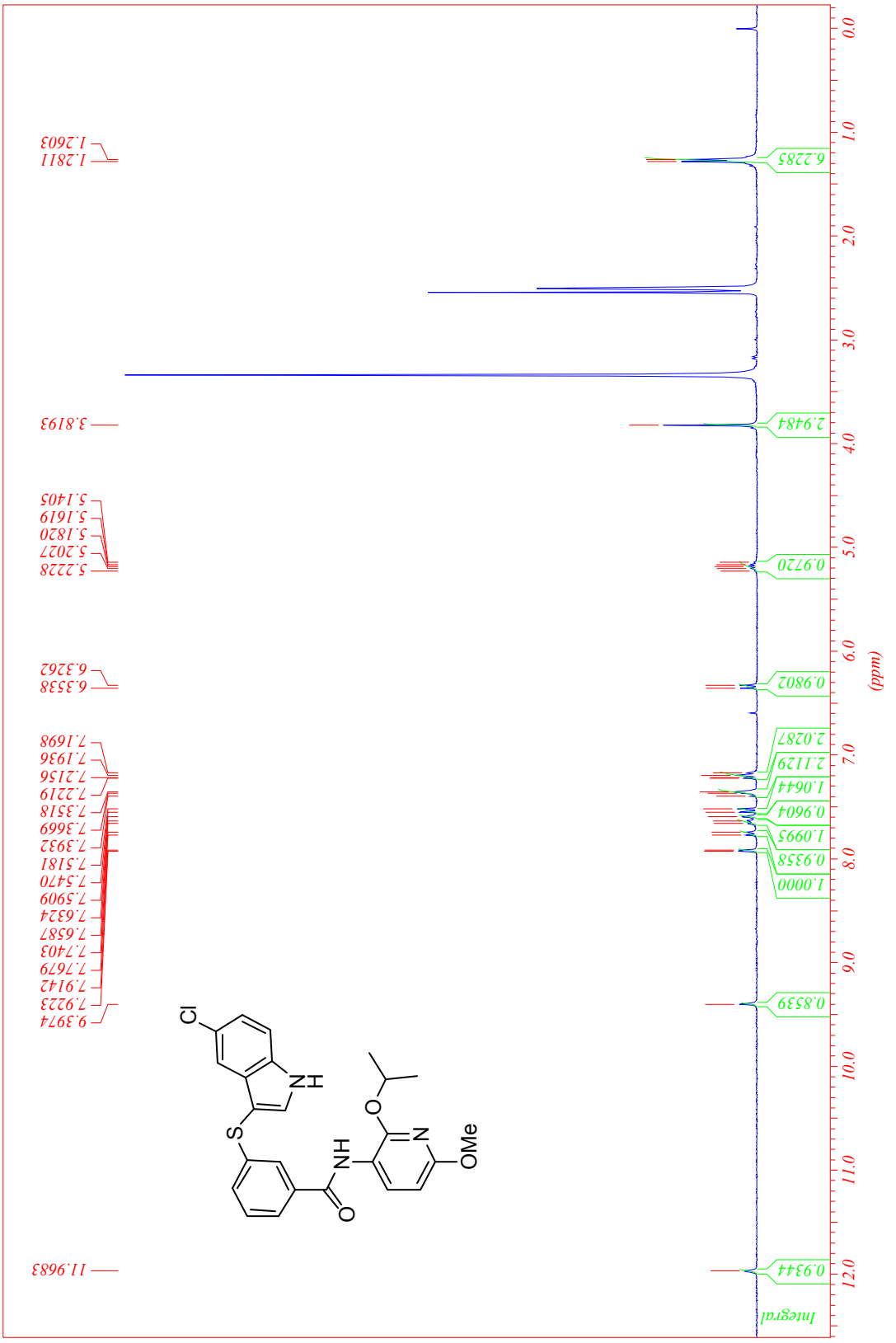
^{1}H NMR spectra of compound **CAB5** (300 MHz, DMSO)

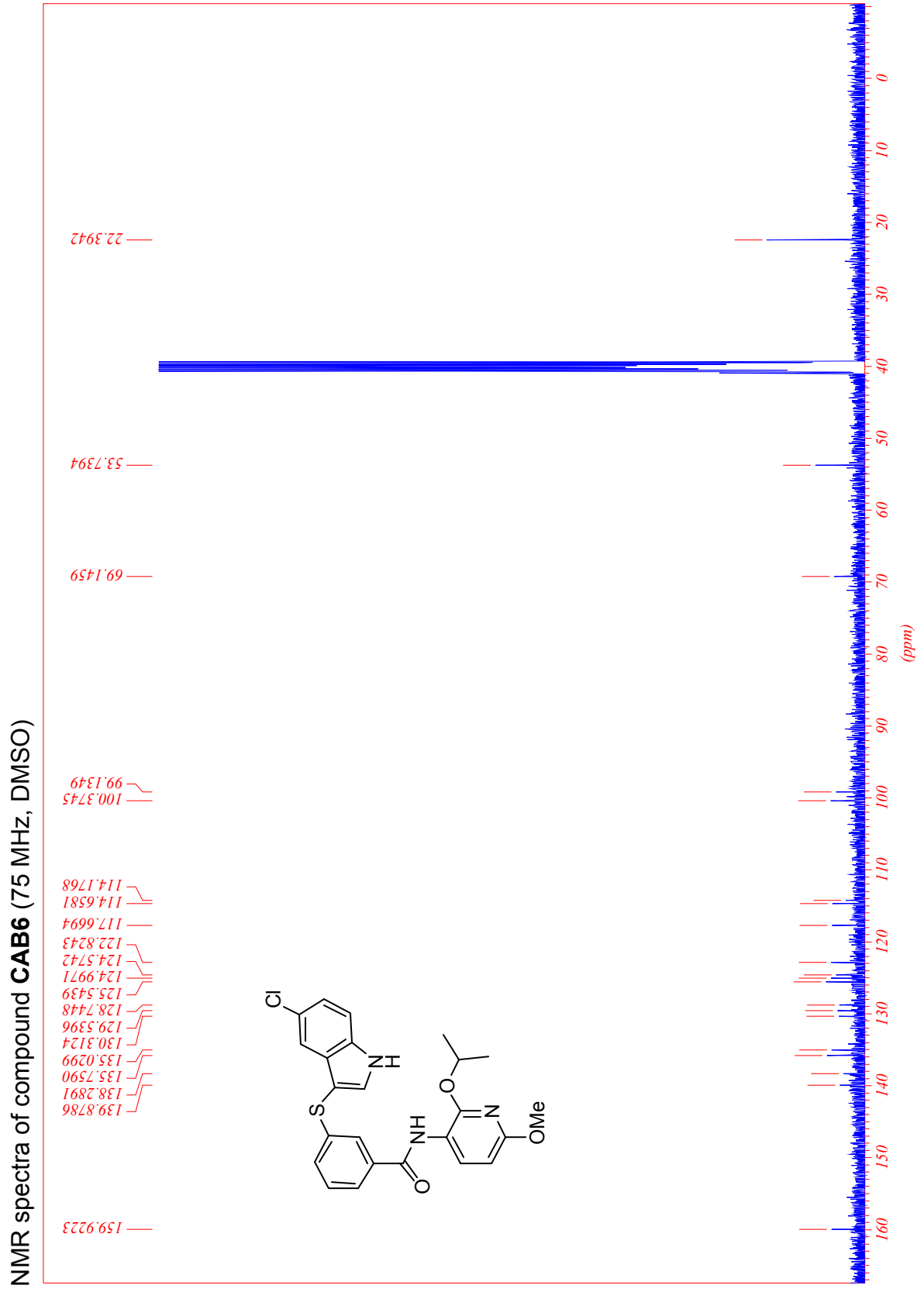


^{13}C NMR spectra of compound **CAB5** (75 MHz, DMSO)

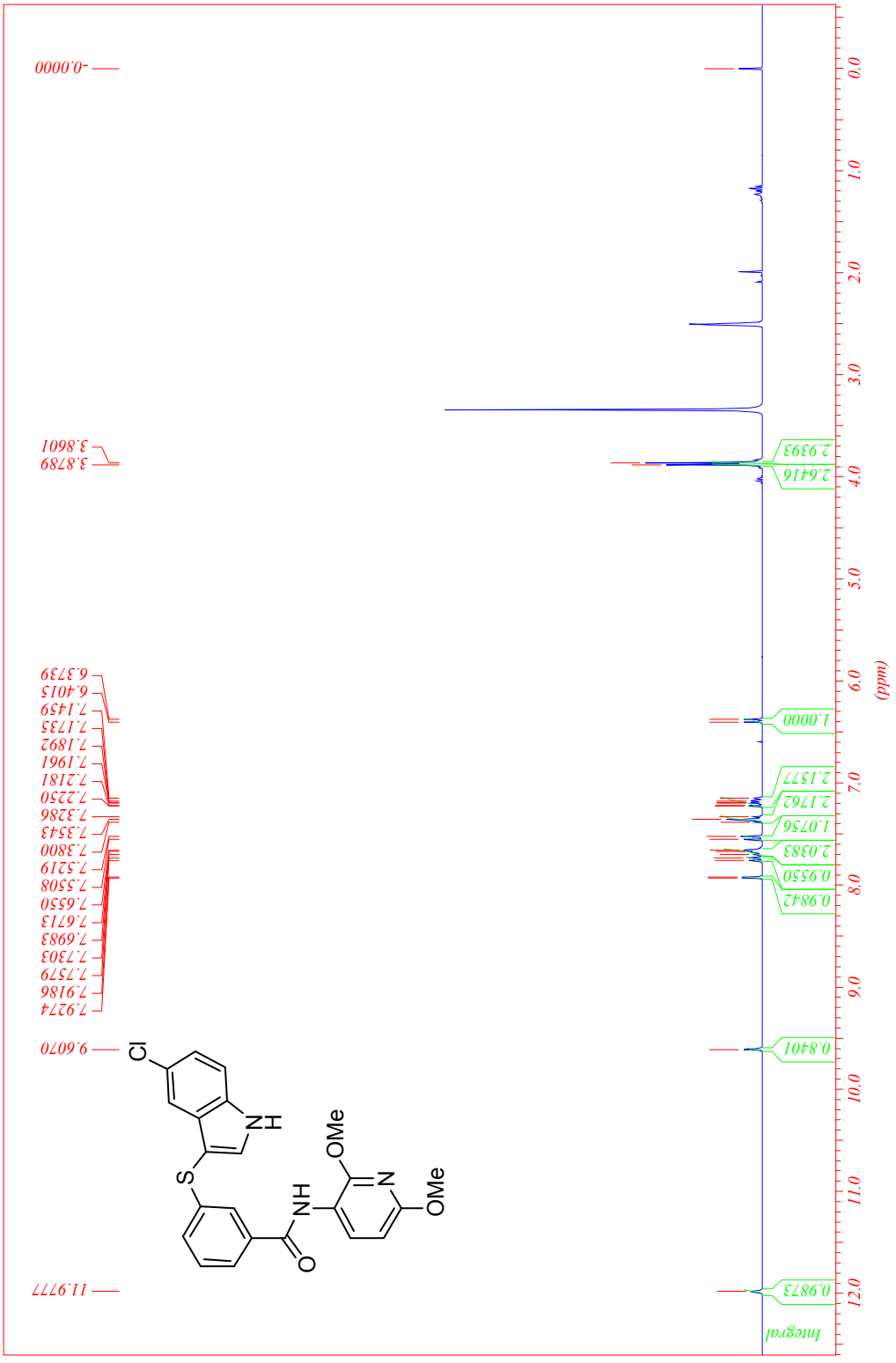


^{1}H NMR spectra of compound **CAB6** (300 MHz, DMSO)

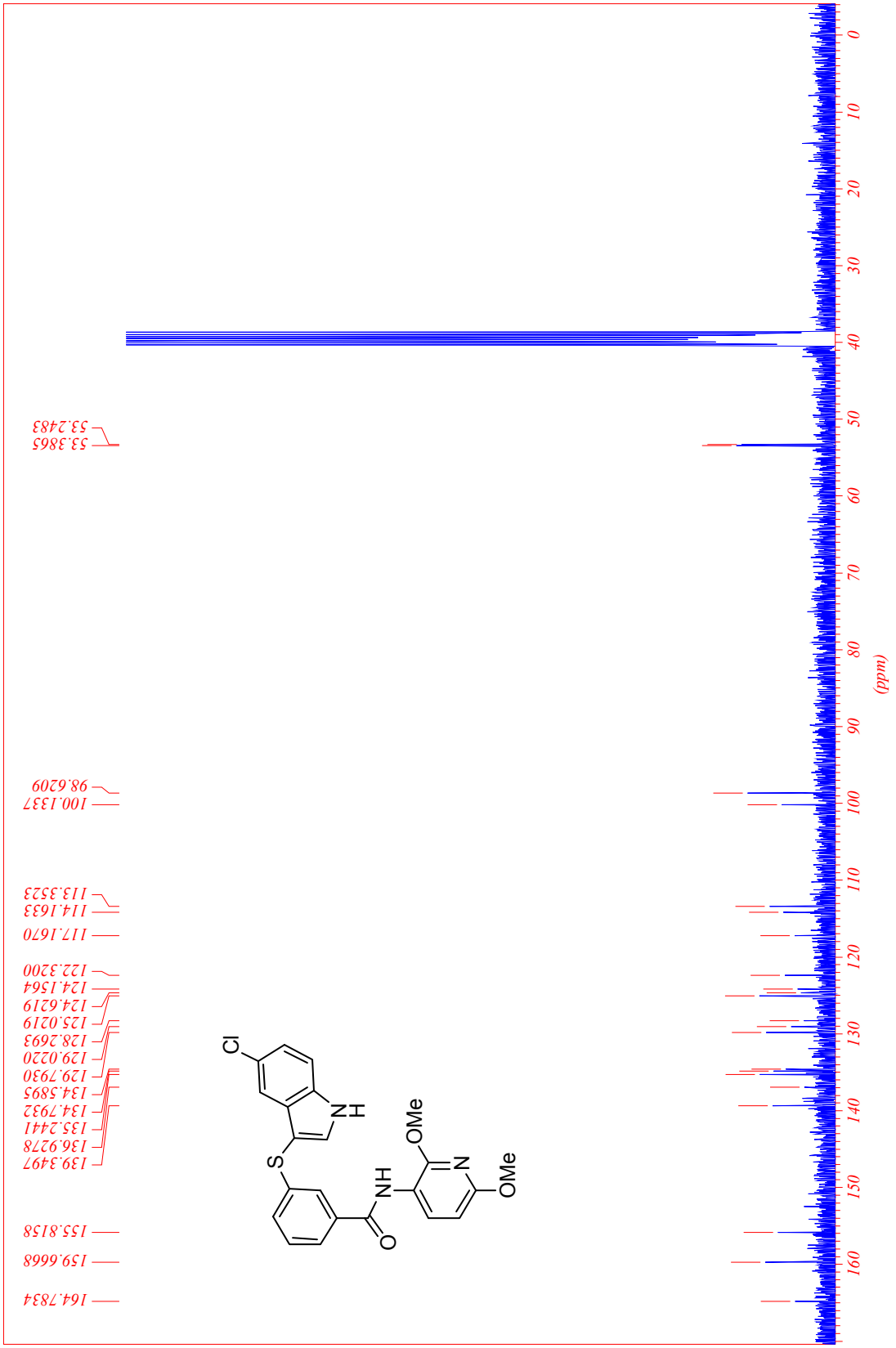




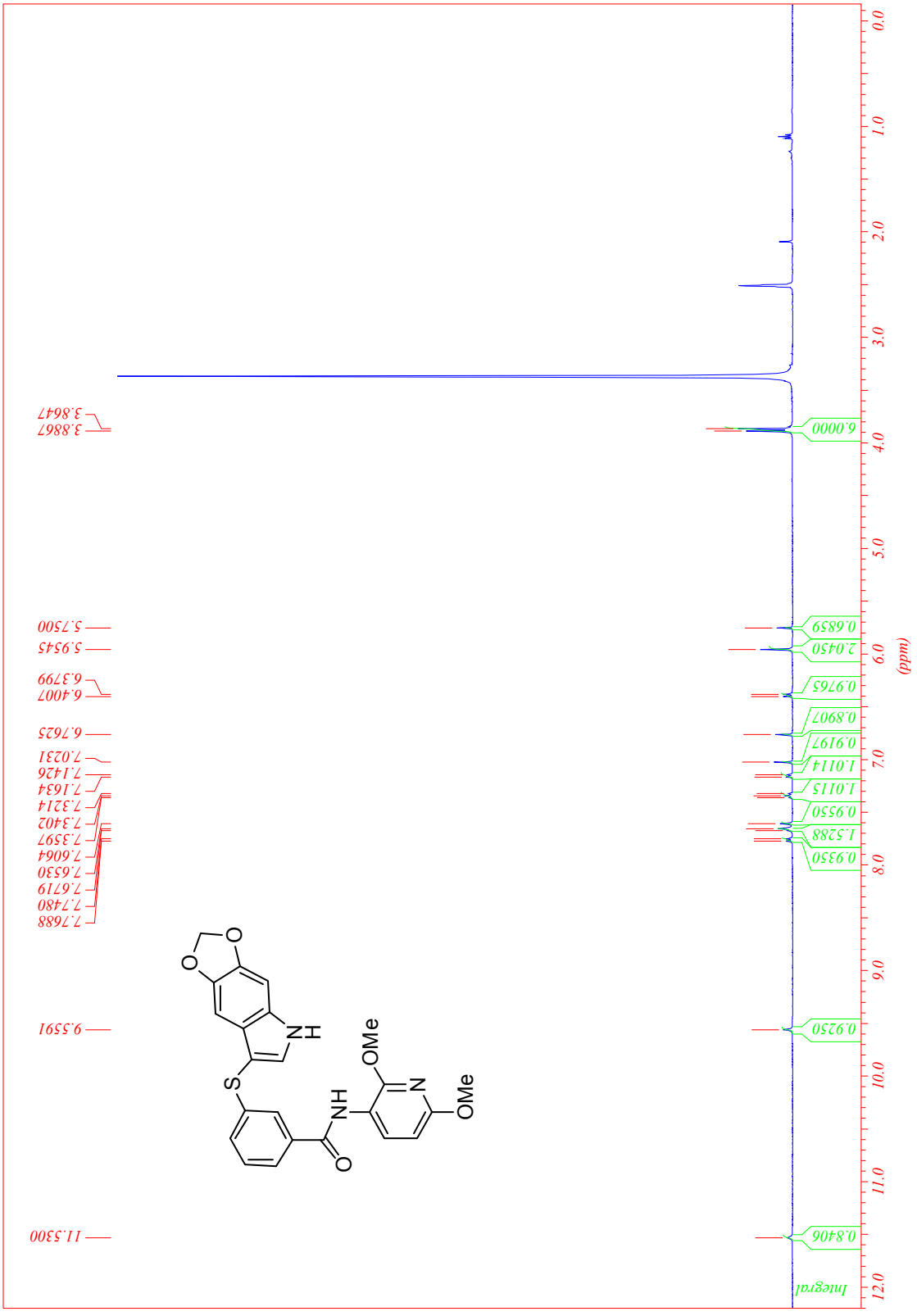
^{1}H NMR spectra of compound **CAB7** (300 MHz,DMSO)



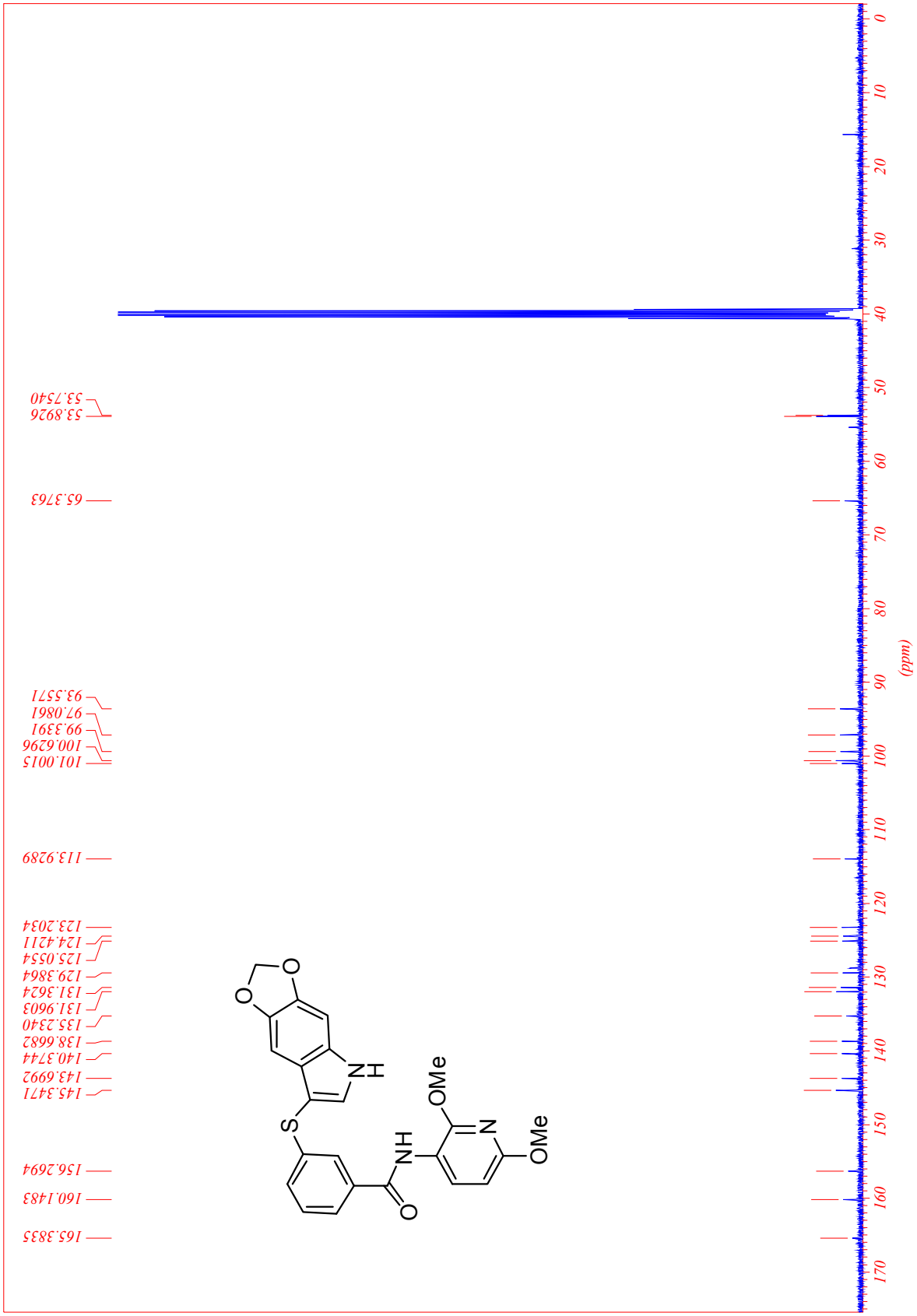
^{13}C NMR spectra of compound **CAB7** (75 MHz, DMSO)



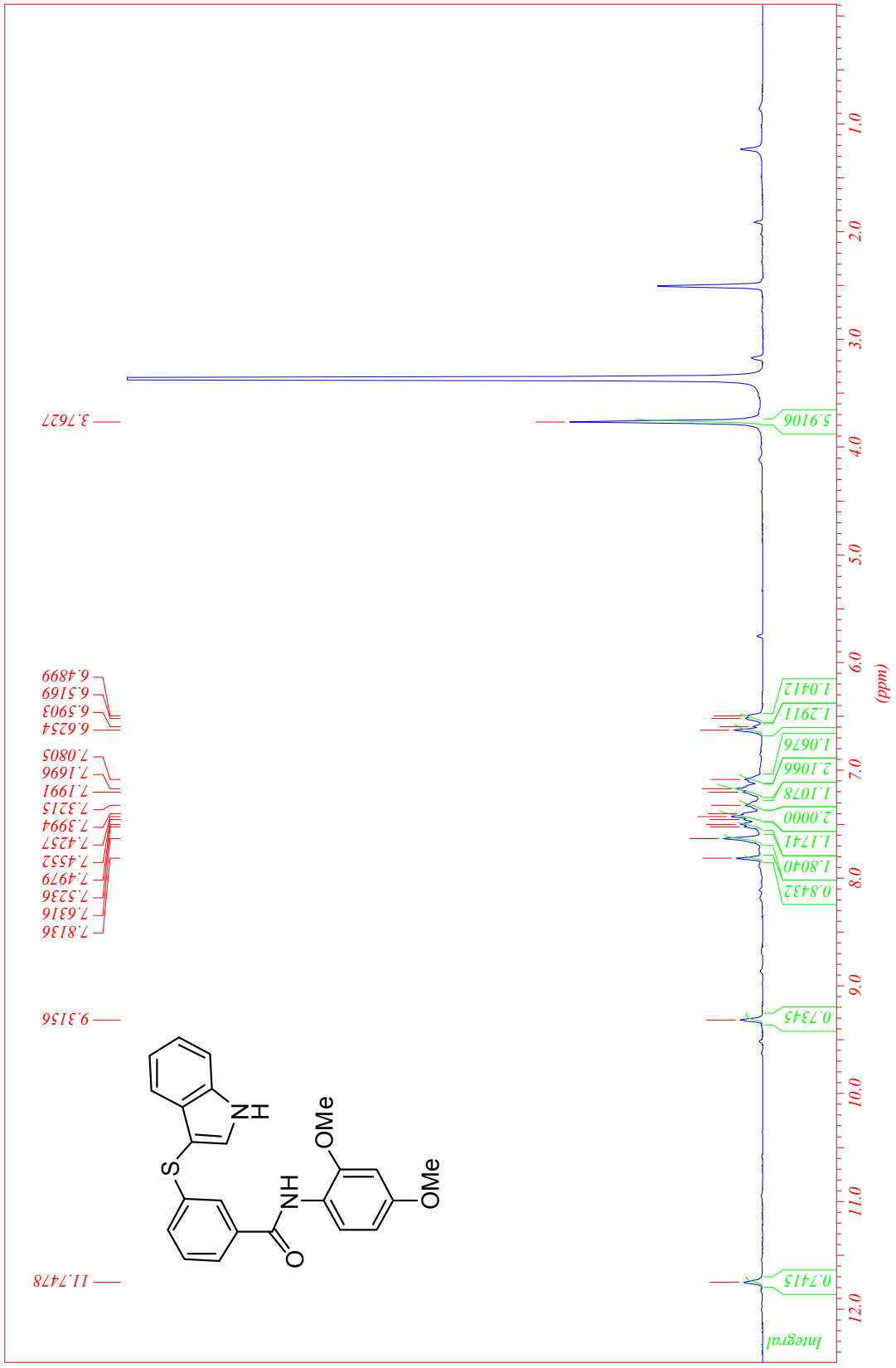
^{1}H NMR spectra of compound **CAB8** (400 MHz, DMSO)



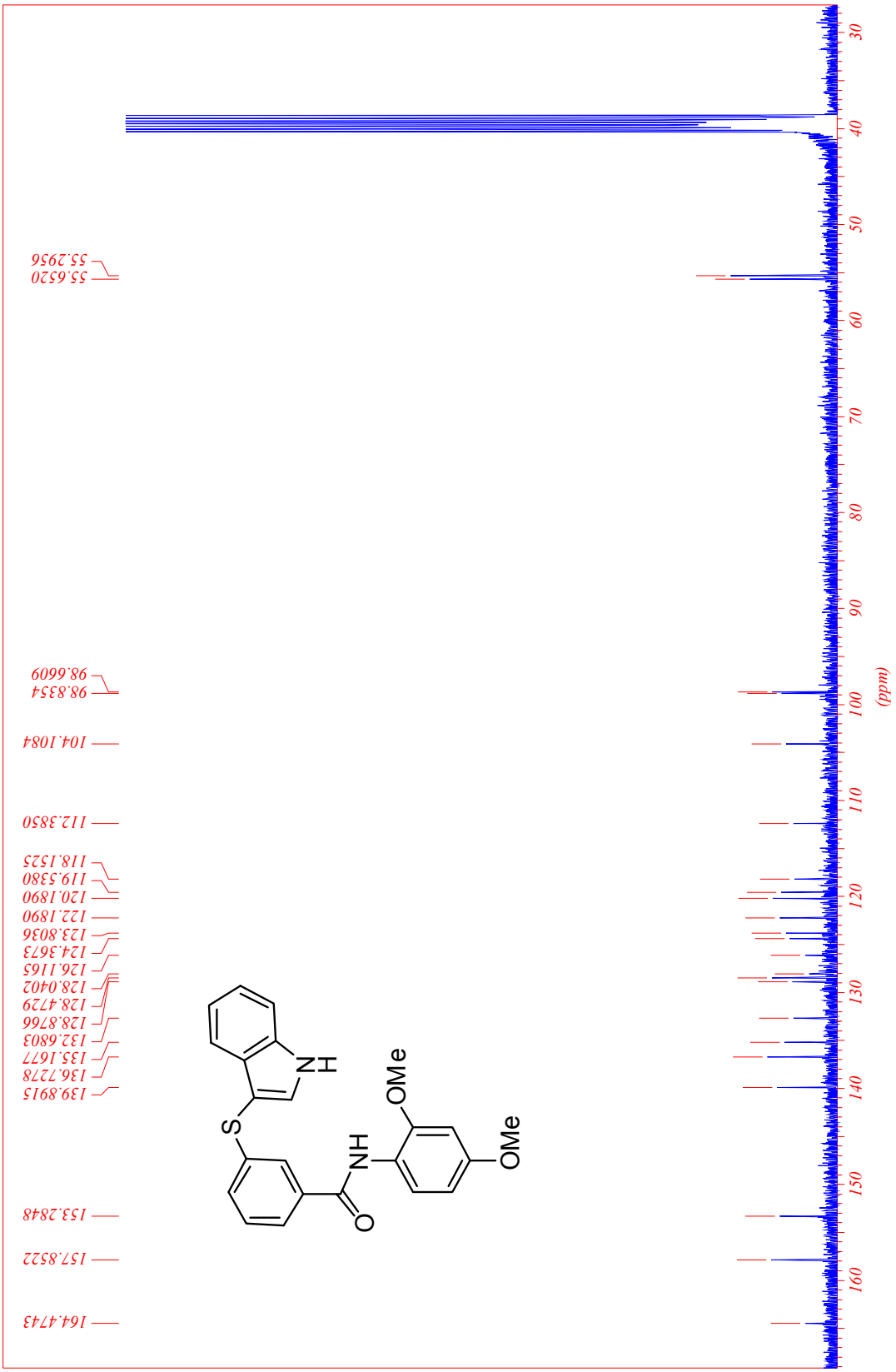
^{13}C NMR spectra of compound **CAB8** (75 MHz, DMSO)



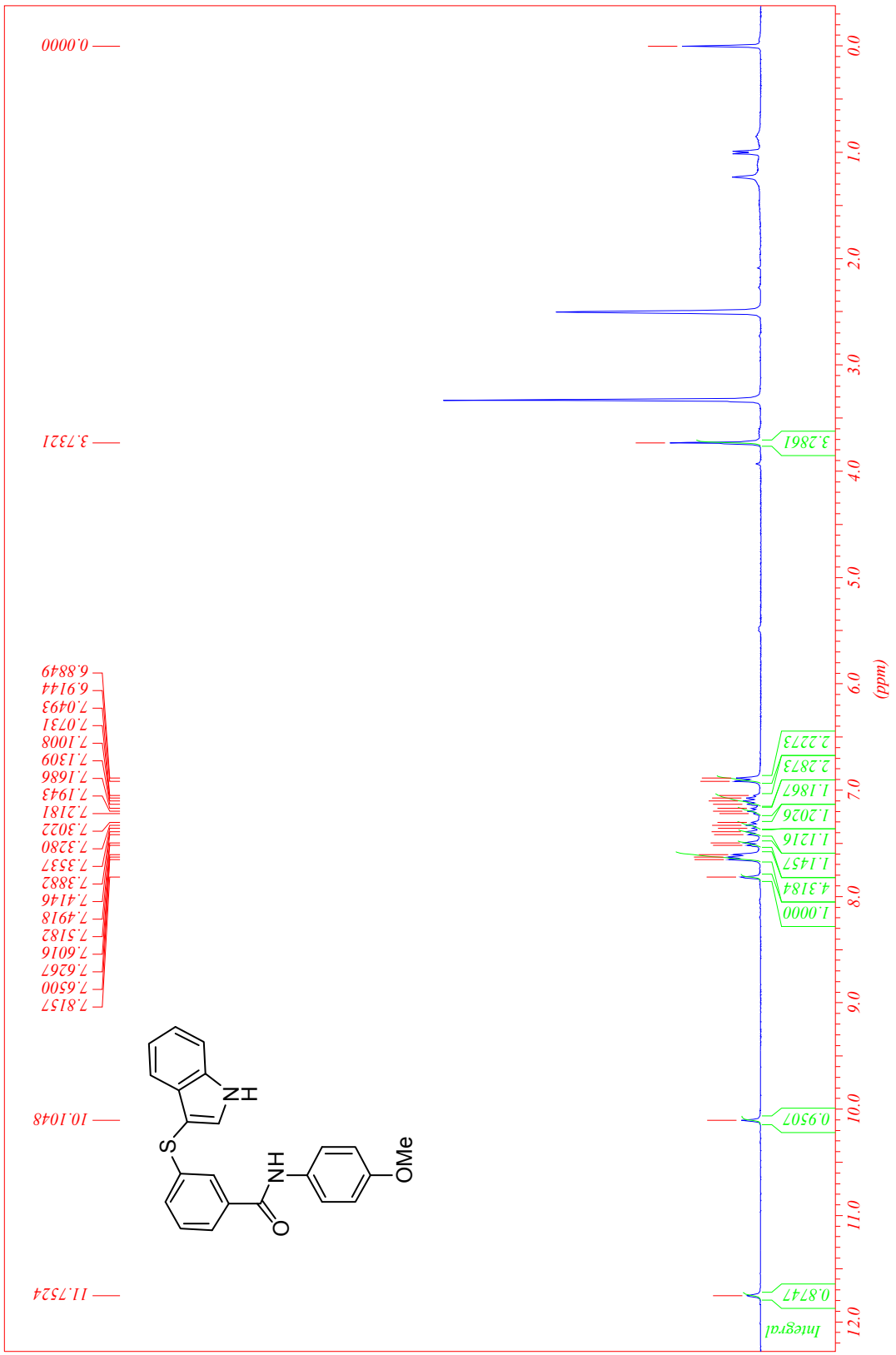
^{1}H NMR spectra of compound **CAB9** (300 MHz, DMSO)



^{13}C NMR spectra of compound **CAB9** (75 MHz, DMSO)

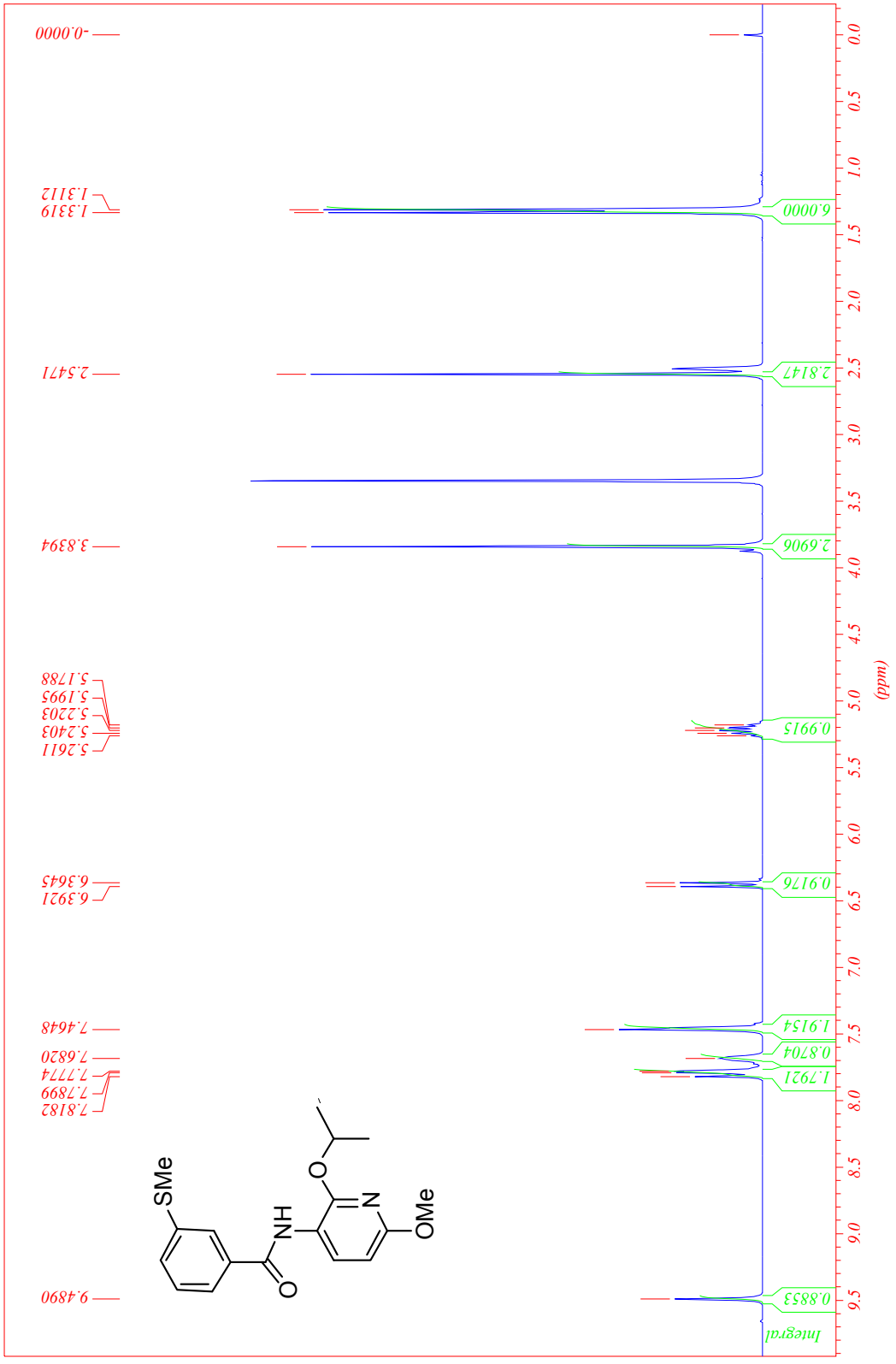


^{1}H NMR spectra of compound **CAB10** (300 MHz, DMSO)

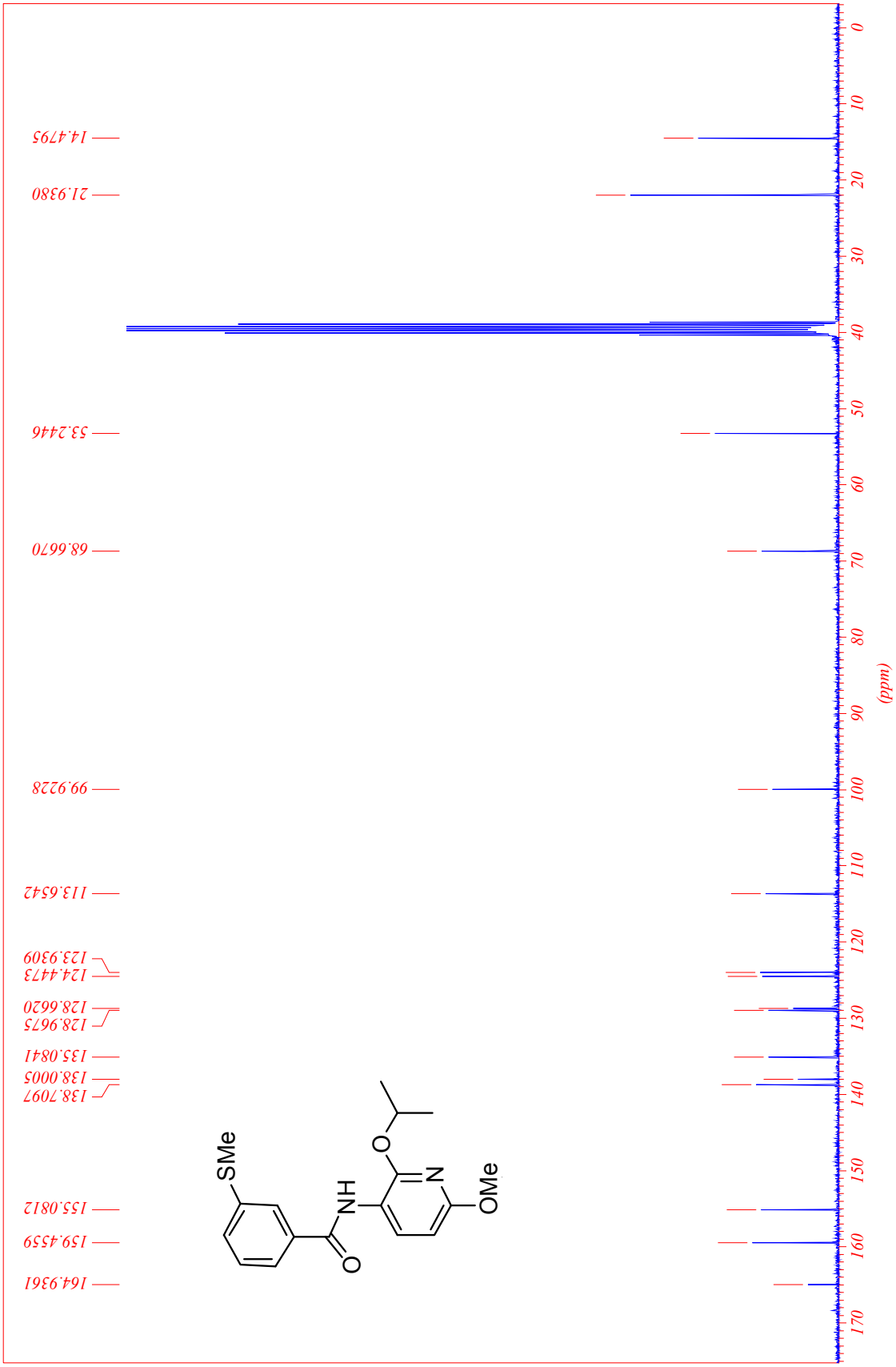


^{13}C NMR spectra of compound **CAB10** (75 MHz, DMSO)

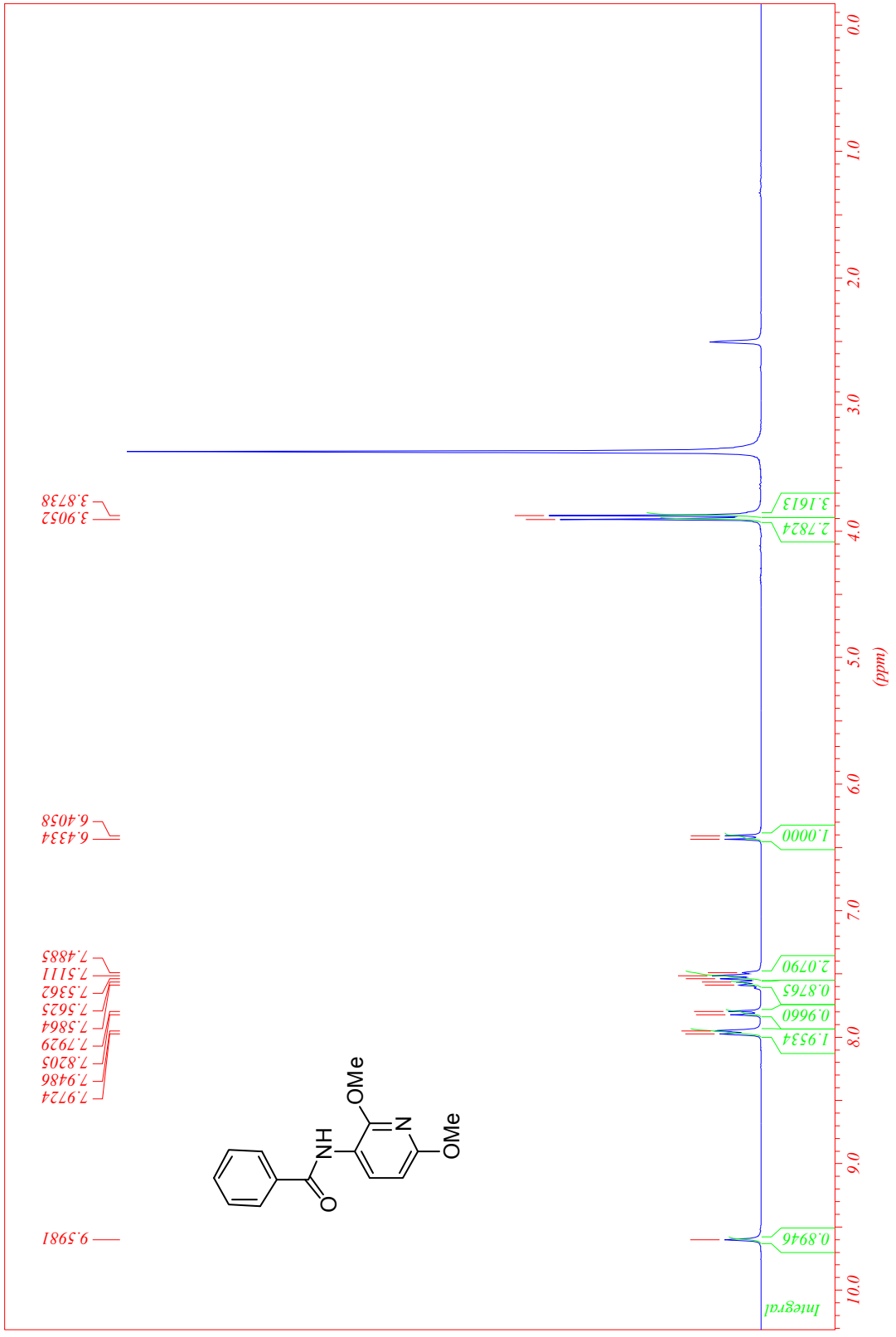
^{1}H NMR spectra of compound **CAB11** (300 MHz, DMSO)



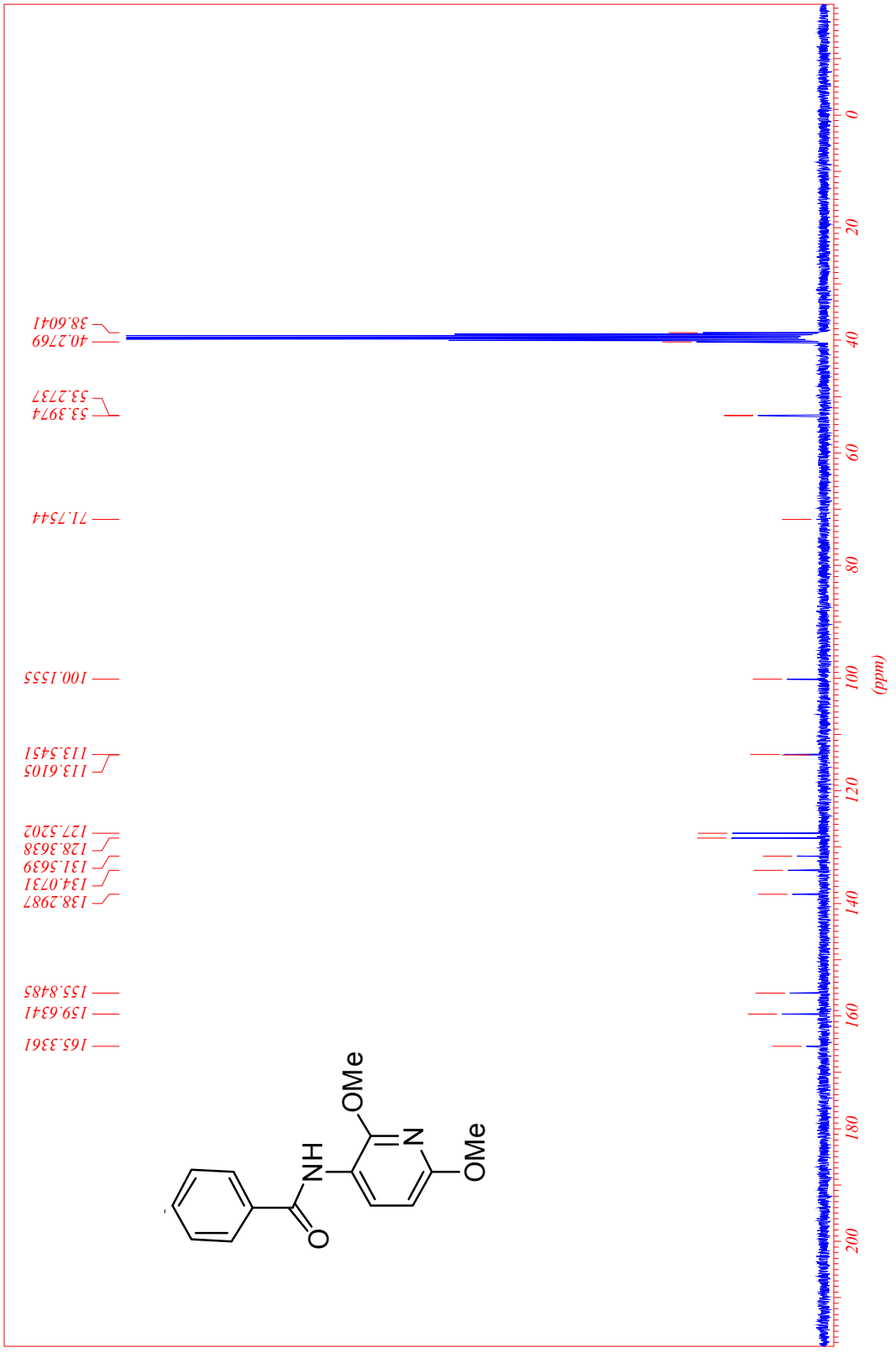
^{13}C NMR spectra of compound **CAB11** (75 MHz, DMSO)



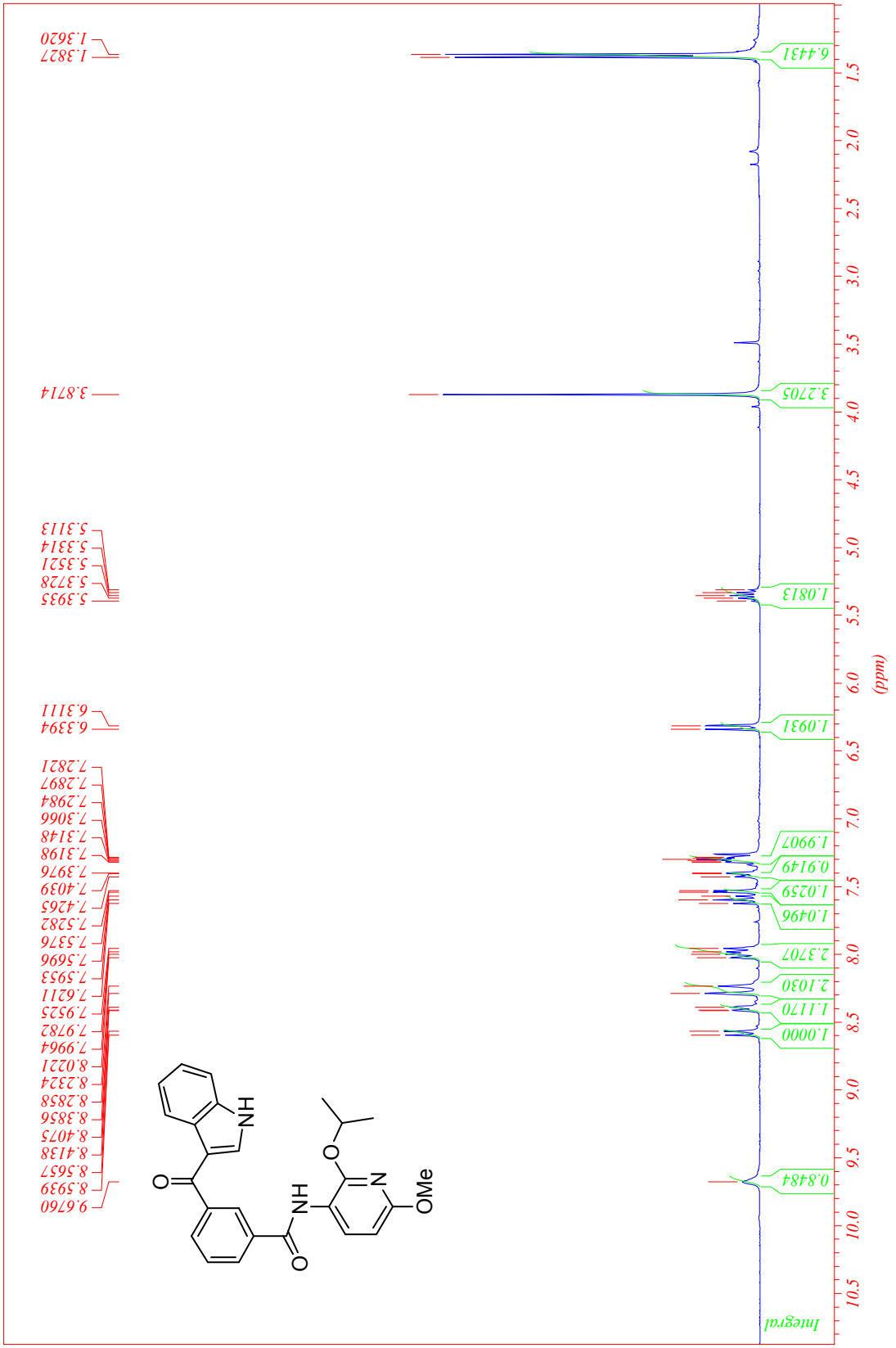
^{1}H NMR spectra of compound **CAB12** (300 MHz, DMSO)



^{13}C NMR spectra of compound **CAB12** (75 MHz, DMSO)



^{1}H NMR spectra of compound **CAB13** (400 MHz, DMSO)



^{13}C NMR spectra of compound **CAB13** (100 MHz, DMSO)