ELECTRONIC SUPPORTING INFORMATION (ESI) for

Constructing spirooxindoles from non-oxindole precursors: a one-pot nitro-reduction/double lactamization approach to spiro[indoline-3,3'-quinoline]-2,2'-diones

Raju Chouhan, Abhijit Gogoi and Sajal Kumar Das*

Department of Chemical Sciences, Tezpur University

Napaam, Tezpur, Dist-Sonitpur, Assam-784028, INDIA

Correspondence to: sajalkd@tezu.ernet.in

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1. General Information

***Reagents and Solvents*:** Unless otherwise stated, all commercially available reagents and solvents were employed for reactions as received without further purification. Dry solvents refer to solvents freshly distilled over appropriate drying agents prior to use. All dry reactions were carried out in oven-dried glassware and under nitrogen (N_2) atmosphere sealed with rubber septa (Aldrich). Commercially available solvents were used for column chromatography without any further purification.

***Purification of Synthesized Compounds*:** All reactions and fractions from column chromatography were monitored by thin-layer chromatography (TLC). Commercial aluminum sheets pre-coated (0.2mm layer thickness) with silica gel 60 F_{254} were used for this purpose. Visualization of TLC plates was performed by UV fluorescence at 254 nm and/or by staining with I_2 vapor or by immersion in an ethanolic vanillin solution or by immersion in a $KMnO_4$ solution followed by heating. Product purification by column chromatography was executed using silica gel (100–200 mesh) procured from Merck.

***Spectroscopy and Spectrometry*:** NMR spectra were recorded on JEOL 400 MHz and Bruker 400 MHz spectrometers. Chemical shifts (δ) are quoted in parts per million (ppm) and are referenced to residual $CHCl_3$ (7.26 or 7.27 ppm) or DMSO (2.50 ppm) for ^1H NMR spectra and for ^{13}C spectra, δ values were referenced to $CDCl_3$ (77.00 or 77.16 ppm) or DMSO-d_6 (39.52 ppm) as the solvents. Coupling constants (*J*) are quoted in Hertz (Hz), rounded to the nearest 0.1 Hz. The ^1H NMR spectra are reported as follows: ppm (multiplicity, coupling constants, and number of protons). Multiplicities in ^1H NMR are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), triplet of doublets (td), multiplet (m) and broad (br). All spectra were recorded at 25 ^oC. Spectra were analyzed using Mestrelab MestReNova 14.1 software. Low-resolution mass spectra (LRMS) were recorded on an Agilent 6125 SQ LCMS system.

***CHN content*:** The organic content (wt % C, H, N) in the synthesized compounds was determined by combustion analysis using a PerkinElmer 20 CHN analyzer.

Stereochemical Notation and Naming of Compounds: Relative stereochemistry is indicated by solid bold (—) and hatched bold (⋯) bonds according to the Maehr convention. Compound

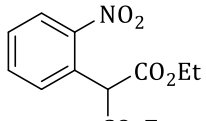
names were given following IUPAC nomenclature and are generated using ChemDraw 19.0 software.

2. Experimental Details and Characterization Data

General Procedure A for the synthesis of 2-(2-nitrophenyl)malonates (2a–f):

A mixture of 2-nitrofluorobemnezene (1.0 mmol, 1 equiv), diethyl malonate (400 mg, 2.5 mmol, 2.5 equiv) and K_2CO_3 (346 mg, 2.5 mmol, 2.5 equiv) in DMF (5 mL) was heated at 100 °C for 1.5 h. The crude reaction mixture was diluted with H_2O (20 mL) and extracted with EtOAc (25 × 3 mL). The combined organic extracts were then washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure. Purification of the crude product using a silica gel column chromatography delivered the corresponding diethyl 2-(2-nitrophenyl)malonate in pure form.

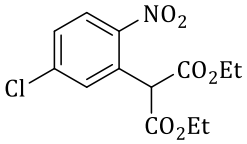
Diethyl 2-(2-nitrophenyl)malonate (2a)



2a

Following the **General Procedure A**, compound **2a** was prepared from **1a** (141 mg, 1.0 mmol) and diethyl malonate (400 mg, 2.5 mmol). Purification of the crude product through silica gel chromatography (using 2–10% EtOAc in hexanes as eluents) afforded product **2a** as a yellow liquid (253 mg, 90% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08 (d, *J* = 7.3 Hz, 1H), 7.66 (t, *J* = 7.3 Hz, 1H), 7.59–7.47 (m, 2H), 5.30 (s, 1H), 4.27 (q, *J* = 7.1 Hz, 4H), 1.29 (t, *J* = 7.1 Hz, 6H). The spectral data are in full agreement with the literature data.[1]

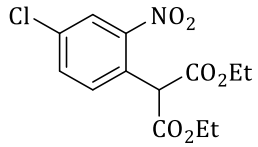
Diethyl 2-(5-chloro-2-nitrophenyl)malonate (2b)



2b

Following the **General Procedure A**, compound **2b** was prepared from **1b** (175 mg, 1.0 mmol) and diethyl malonate (400 mg, 2.5 mmol). Purification of the crude product through silica gel chromatography (using 2–10% EtOAc in hexanes as eluents) afforded product **2b** as a yellow liquid (275 mg, 87% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05 (d, *J* = 8.7 Hz, 1H), 7.55–7.40 (m, 2H), 5.30 (s, 1H), 4.30 (q, *J* = 7.1 Hz, 4H), 1.31 (t, *J* = 7.1 Hz, 6H). The spectral data are in full agreement with the literature data.[2]

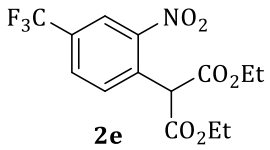
Diethyl 2-(4-chloro-2-nitrophenyl)malonate (2d)



2d

Following the **General Procedure A**, compound **2e** was prepared from **1d** (176 mg, 1.0 mmol) and diethyl malonate (400 mg, 2.5 mmol). Purification of the crude product through silica gel chromatography (using 2–10% EtOAc in hexanes as eluents) afforded product **2d** as a yellow liquid (290 mg, 91% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05 (d, *J* = 2.2 Hz, 1H), 7.62 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.49 (d, *J* = 8.5 Hz, 1H), 5.24 (s, 1H), 4.26 (q, *J* = 7.1 Hz, 4H), 1.28 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.0, 149.2, 135.3, 133.7, 132.7, 127.8, 125.9, 62.6, 54.0, 14.1.

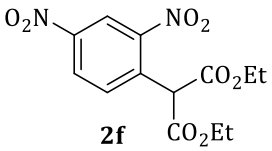
Diethyl 2-(2-nitro-4-(trifluoromethyl)phenyl)malonate (2e)



2e

Following the **General Procedure A**, compound **2e** was prepared from **1e** (209 mg, 1.0 mmol) and diethyl malonate (400 mg, 2.5 mmol). Purification of the crude product through silica gel chromatography (using 5–15% EtOAc in hexanes as eluents) afforded product **2e** as a yellow liquid (318 mg, 91% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.32 (d, *J* = 2.0 Hz, 1H), 7.89 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 5.34 (s, 1H), 4.28 (dq, *J* = 7.3, 2.0 Hz, 4H), 1.29 (t, *J* = 7.2 Hz, 6H). The spectral data are in full agreement with the literature data.[3]

Diethyl 2-(2,4-dinitrophenyl)malonate (2f)



2f

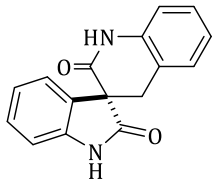
Following the **General Procedure A**, compound **2f** was prepared from **1f** (186 mg, 1.0 mmol) and diethyl malonate (400 mg, 2.5 mmol). Purification of the crude product through silica gel chromatography (using 5–15% EtOAc in hexanes as eluents) afforded product **2f** as a yellow liquid (287 mg, 88% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.88 (d, *J* = 2.4 Hz, 1H), 8.47 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.82 (d, *J* = 8.8 Hz, 1H), 5.36 (s, 1H), 4.29 (dq, *J* = 7.0, 2.6 Hz, 4H), 1.29 (t, *J* = 7.2 Hz, 6H). The spectral data are in agreement with the literature data.[3]

General Procedure B for the synthesis of spirooxindoles (5a–s):

To a solution of **2** (0.5 mmol, 1.0 equiv) in DMF (4 mL) were added K_2CO_3(173 mg, 1.25 mmol, 2.5 equiv) and **3** (0.55 mmol, 1.1 equiv) sequentially. The resulting mixture was stirred for 6 h at room temperature. The reaction mixture was then diluted with H_2O (10 mL) and extracted with EtOAc (10 x 3 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in *vacuo* and the resulting residue was passed through a short pad of silica gel furnishing **4** in essentially pure form.

A mixture of **4** and Fe-powder (>100 mesh, 8.0 equiv) in AcOH (4 mL) was heated to 115°C for 30 min. During this time, the color of the reaction mixture changed from black to tan. The reaction mixture was cooled, diluted with H_2O (10 mL), poured slowly into saturated aq. $NaHCO_3$ (25 mL), and extracted with EtOAc (20 × 2 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography to afford the corresponding spirooxindoles **5** in pure form.

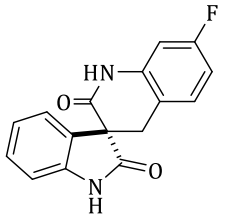
1',4'-Dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5a)



5a

Product **5a** was synthesized according to **General Procedure B**, starting from **2a** (141 mg, 0.5 mmol) and **3a** (118 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5a** as a white solid (90 mg, 68%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.68 (s, 1H), 10.67 (s, 1H), 7.26 (t, *J* = 7.7 Hz, 1H), 7.19 (td, *J* = 7.7, 1.3 Hz, 2H), 7.02–6.99 (m, 2H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.77 (td, *J* = 7.6, 1.1 Hz, 1H), 6.45 (d, *J* = 7.5 Hz, 1H), 3.45 (d, *J* = 15.9 Hz, 1H), 2.98 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.8, 167.2, 142.2, 137.6, 130.0, 129.0, 128.7, 127.9, 122.8, 122.6, 121.6, 120.7, 115.0, 110.0, 54.5, 34.0. LRMS (ESI$^+$) *m/z* 265.1 [M + H]$^+$. Anal. calcd. for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60; found: C, 72.87; H, 4.62; N, 10.55.

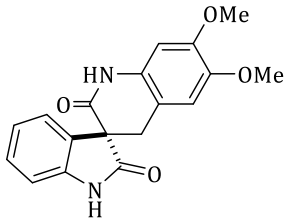
7'-Fluoro-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5b)



5b

Product **5b** was synthesized according to **General Procedure B**, starting from **2a** (141 mg, 0.5 mmol) and **3b** (129 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5b** as a white solid (92 mg, 65%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.79 (s, 1H), 10.71 (s, 1H), 7.26–7.19 (m, 2H), 6.89 (d, J = 7.6 Hz, 1H), 6.86–6.77 (m, 3H), 6.53 (d, J = 7.5 Hz, 1H), 3.39 (d, J = 16.0 Hz, 1H), 3.03 (d, J = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.5, 167.2, 161.6 (d, J = 241.6 Hz), 142.2, 139.1 (d, J = 11.1 Hz), 130.2, 129.7, 129.1, 122.7, 121.7, 116.9 (d, J = 2.9 Hz), 110.0, 109.0 (d, J = 21.3 Hz), 102.14 (d, J = 25.8 Hz), 54.3, 33.3. LRMS (ESI$^+$) m/z 283.1 [M + H]$^+$. Anal. calcd. for $C_{16}H_{11}FN_2O_2$: C, 68.08; H, 3.93; N, 9.92; found: C, 68.28; H, 3.97; N, 9.81.

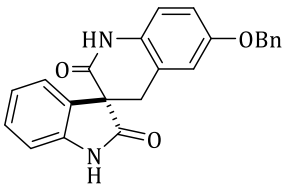
6',7'-Dimethoxy-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5c)



5c

Product **5c** was synthesized according to **General Procedure B**, starting from **2a** (141 mg, 0.5 mmol) and **3c** (152 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5c** as a white solid (99 mg, 61%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.65 (s, 1H), 10.42 (s, 1H), 7.19 (t, J = 7.7 Hz, 1H), 6.89 (d, J = 7.7 Hz, 1H), 6.85 (s, 1H), 6.78 (t, J = 7.6 Hz, 1H), 6.65 (s, 1H), 6.49 (d, J = 7.4 Hz, 1H), 3.76 (s, 3H), 3.69 (s, 3H), 3.42 (d, partially merged with water peak at δ = 3.38), 2.85 (d, J = 15.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.0, 167.0, 148.3, 144.4, 142.1, 130.8, 130.2, 129.0, 122.7, 121.6, 112.8, 111.7, 109.9, 100.2, 55.9, 54.6, 33.7. LRMS (ESI$^+$) m/z 325.1 [M + H]$^+$. Anal. calcd. for $C_{18}H_{16}N_2O_4$: C, 66.66; H, 4.97; N, 8.64; found: C, 66.77; H, 5.06; N, 8.68.

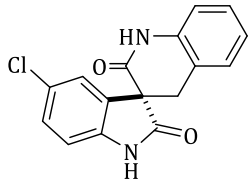
6'-(Benzyloxy)-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5d)



5d

Product **5d** was synthesized according to **General Procedure B**, starting from **2a** (141 mg, 0.5 mmol) and **3d** (177 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5d** as a white solid (117 mg, 63%). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.71 (s, 1H), 10.57 (s, 1H), 7.45–7.30 (m, 5H), 7.20 (t, *J* = 7.7 Hz, 1H), 6.94 (s, 3H), 6.90 (d, *J* = 7.7 Hz, 1H), 6.78 (t, *J* = 7.6 Hz, 1H), 6.48 (d, *J* = 7.6 Hz, 1H), 5.03 (s, 2H), 3.42 (d, merged with water peak, 1H), 2.94 (d, *J* = 16.1 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 176.0, 166.9, 154.1, 142.2, 137.1, 131.2, 130.1, 129.1, 128.5, 127.9, 122.7, 122.1, 121.7, 115.9, 115.3, 114.0, 110.0, 69.6, 54.4, 34.2. LRMS (ESI$^+$) *m*/*z* 371.1 [M + H]$^+$. Anal. calcd. for $C_{23}H_{18}N_2O_3$: C, 74.58; H, 4.90; N, 7.56; found: C, 74.45; H, 4.98; N, 7.50.

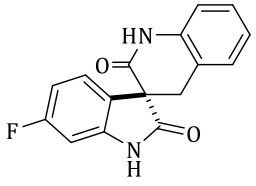
5-Chloro-1',4'-dihydro-2'H-spiro[indoline-3,3'-quinoline]-2,2'-dione (5e)



5e

Product **5e** was synthesized according to **General Procedure B**, starting from **2b** (158 mg, 0.5 mmol) and **3a** (118 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5e** as a white solid (96 mg, 64%). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.83 (s, 1H), 10.76 (s, 1H), 7.29–7.26 (m, 2H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.04–6.98 (m, 2H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.49 (d, *J* = 2.2 Hz, 1H), 3.40 (d, *J* = 12.9 Hz, 2H, merged with water peak), 3.13 (d, *J* = 16.3 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 175.4, 166.5, 141.3, 137.4, 131.9, 128.9, 128.7, 128.0, 125.4, 122.9, 122.8, 120.4, 115.1, 111.4, 54.7, 33.7. LRMS (ESI$^+$) *m*/*z* 299.1 [M + H]$^+$. Anal. calcd. for $C_{16}H_{11}ClN_2O_2$: C, 64.33; H, 3.71; N, 9.38; found: C, 64.47; H, 3.76; N, 9.45.

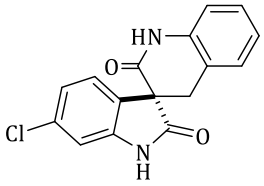
6-Fluoro-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5f)



5f

Product **5f** was synthesized according to **General Procedure B**, starting from **2c** (150 mg, 0.5 mmol) and **3a** (118 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5f** as a white solid (92 mg, 65%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.84 (s, 1H), 10.70 (s, 1H), 7.26 (t, J = 7.7 Hz, 1H), 7.20 (d, J = 7.3 Hz, 1H), 7.00 (t, J = 7.9 Hz, 2H), 6.72 (dd, J = 9.2, 2.5 Hz, 1H), 6.61 (ddd, J = 9.8, 8.3, 2.5 Hz, 1H), 6.45 (dd, J = 8.4, 5.5 Hz, 1H), 3.43 (d, J = 15.9 Hz, 1H), 3.02 (d, J = 16.3 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.1, 167.0, 162.6 (d, J = 242.9 Hz), 143.9 (d, J = 12.5 Hz), 137.5, 128.7, 128.0, 125.9 (d, J = 2.7 Hz), 124.0, 122.9, 120.5, 115.1, 107.7 (d, J = 22.8 Hz), 98.23 (d, J = 27.0 Hz), 54.1, 33.8. LRMS (ESI$^+$) m/z 283.1 [M + H]$^+$. Anal. calcd. for $C_{16}H_{11}FN_2O_2$: C, 68.08; H, 3.93; N, 9.92; found: C, 68.29; H, 3.89; N, 9.98.

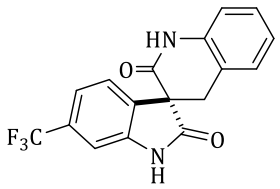
6-Chloro-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5g)



5g

Product **5g** was synthesized according to **General Procedure B**, starting from **2d** (158 mg, 0.5 mmol) and **3a** (118 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5g** as a white solid (94 mg, 63%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.85 (s, 1H), 10.73 (s, 1H), 7.26 (t, J = 7.7 Hz, 1H), 7.20 (d, J = 6.4 Hz, 1H), 7.03–6.98 (m, 2H), 6.91–6.85 (m, 2H), 6.46 (d, J = 8.0 Hz, 1H), 3.43 (d, J = 15.9 Hz, 1H), 3.04 (d, J = 16.1 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.7, 166.7, 143.8, 137.4, 133.4, 128.8, 128.7, 128.4, 124.1, 122.9, 121.4, 120.4, 115.1, 110.0, 54.2, 33.7. LRMS (ESI$^+$) m/z 299.1 [M + H]$^+$. Anal. calcd. for $C_{16}H_{11}ClN_2O_2$: C, 64.33; H, 3.71; N, 9.38; found: C, 64.42; H, 3.78; N, 9.32.

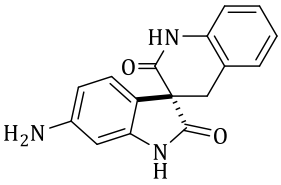
6-(Trifluoromethyl)-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5h)



5h

Product **5h** was synthesized according to **General Procedure B**, starting from **2e** (192 mg, 0.5 mmol) and **3a** (118 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5h** as a white solid (108 mg, 65%). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.98 (s, 1H), 10.80 (s, 1H), 7.27 (t, *J* = 7.7 Hz, 1H), 7.23–7.20 (m, 2H), 7.12 (d, *J* = 1.7 Hz, 1H), 7.04–7.00 (m, 2H), 6.72 (d, *J* = 7.8 Hz, 1H), 3.45 (d, *J* = 16.0 Hz, 1H), 3.13 (d, *J* = 16.1 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 175.5, 166.3, 143.2, 137.4, 134.3, 129.5 (q, *J* = 31.7 Hz), 128.7, 128.0, 124.0 (q, *J* = 272.3 Hz), 123.5, 123.0, 120.3, 118.8 (d, *J* = 4.5 Hz), 115.1, 106.0 (d, *J* = 4.0 Hz), 54.6, 33.6. LRMS (ESI$^+$) *m*/*z* 333.1 [M + H]$^+$. Anal. calcd. for $C_{17}H_{11}F_3N_2O_2$: C, 61.45; H, 3.34; N, 8.43; found: C, 61.52; H, 3.38; N, 8.33.

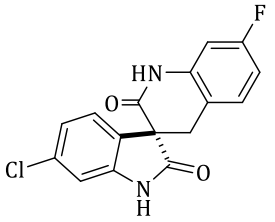
6-Amino-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5i)



5i

Product **5i** was synthesized according to **General Procedure B**, starting from **2f** (163 mg, 0.5 mmol) and **3a** (118 mg, 0.55 mmol). It should be noted that 12 equiv (instead of 8 equiv) of Fe-powder was used in the double cyclization step. Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5i** as a brown semi solid (91 mg, 65%). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.49 (s, 1H), 10.41 (s, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 6.98–6.96 (m, 2H), 6.18–6.16 (m, 1H), 6.04–6.04 (m, 1H), 5.91 (d, *J* = 8.2 Hz, 1H), 5.17 (br. s, 2H), 3.41 (d, *J* = 15.8 Hz, 1H, partially merged with water peak), 2.81 (d, *J* = 15.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 176.9, 168.3, 149.9, 143.1, 137.8, 128.8, 127.9, 123.0, 122.8, 121.2, 117.0, 115.0, 106.6, 96.4, 54.1, 34.5. LRMS (ESI$^+$) *m*/*z* 280.1 [M + H]$^+$. Anal. calcd. for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.05; found: C, 68.93; H, 4.75; N, 15.09.

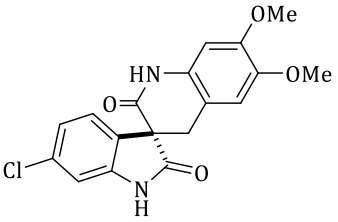
6-Chloro-7'-fluoro-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5j)



5j

Product **5j** was synthesized according to **General Procedure B**, starting from **2d** (158 mg, 0.5 mmol) and **3b** (129 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5j** as a white solid (100 mg, 63%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.86 (s, 1H), 10.84 (s, 1H), 7.23 (dd, *J* = 8.3, 6.1 Hz, 1H), 6.91–6.88 (m, 2H), 6.84 (td, *J* = 8.7, 2.6 Hz, 1H), 6.78 (dd, *J* = 10.0, 2.6 Hz, 1H), 6.56 (d, *J* = 7.9 Hz, 1H), 3.37 (d, merged with water peak 1H), 3.08 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.4, 166.7, 161.6 (d, *J* = 241.3 Hz), 143.8, 140.0 (d, *J* = 11.0 Hz), 133.5, 130.2, 128.6, 124.2, 121.5, 116.6 (d, *J* = 2.9 Hz), 110.1, 109.2 (d, *J* = 21.4 Hz), 102.2 (d, *J* = 25.9 Hz), 54.1, 33.1. LRMS (ESI$^+$) *m*/*z* 317.0 [M + H]$^+$. Anal. calcd. for $C_{16}H_{10}ClFN_2O_2$: C, 60.68; H, 3.18; N, 8.85; found: C, 60.57; H, 3.22; N, 8.92.

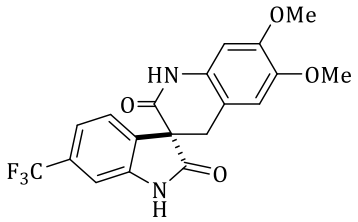
6-Chloro-6',7'-dimethoxy-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5k)



5k

Product **5k** was synthesized according to **General Procedure B**, starting from **2d** (158 mg, 0.5 mmol) and **3c** (152 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5k** as a white solid (124 mg, 69%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.82 (s, 1H), 10.48 (s, 1H), 6.91–6.86 (m, 2H), 6.84 (s, 1H), 6.64 (s, 1H), 6.48 (d, *J* = 8.0 Hz, 1H), 3.75 (s, 3H), 3.69 (s, 3H), 3.37 (s, 1H, merged with water peak), 2.89 (d, *J* = 15.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.9, 166.5, 148.4, 144.4, 143.7, 133.3, 130.7, 129.0, 124.1, 121.4, 112.7, 111.3, 110.0, 100.2, 55.8, 55.5, 54.4, 33.5. LRMS (ESI$^+$) *m*/*z* 359.1 [M + H]$^+$. Anal. calcd. for $C_{18}H_{15}ClN_2O_4$: C, 60.26; H, 4.21; N, 7.81; found: C, 60.43; H, 4.27; N, 7.75.

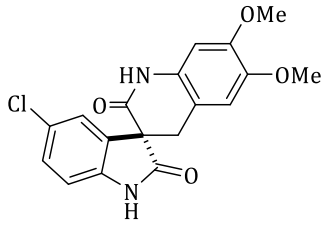
6',7'-Dimethoxy-6-(trifluoromethyl)-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5l)



5l

Product **5l** was synthesized according to **General Procedure B**, starting from **2e** (192 mg, 0.5 mmol) and **3c** (152 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5l** as a white solid (125 mg, 64%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.97 (s, 1H), 10.57 (s, 1H), 7.22 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.13 (d, *J* = 1.7 Hz, 1H), 6.85 (s, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.67 (s, 1H), 3.76 (s, 3H), 3.69 (s, 3H), 3.42 (d, *J* = 15.6 Hz, 1H, partially merged with water peak), 2.97 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.8, 166.2, 148.5, 144.6, 143.2, 134.5, 130.7, 129.7 (q, *J* = 31.8 Hz), 124.0 (q, *J* = 272.2 Hz) 123.6, 118.9, 111.3, 106.1, 100.4, 55.9, 55.6, 54.8, 33.4. LRMS (ESI$^+$) *m*/*z* 393.1 [M + H]$^+$. Anal. calcd. for $C_{19}H_{15}F_3N_2O_4$: C, 58.17; H, 3.85; N, 7.14; found: C, 58.39; H, 3.75; N, 7.23.

5-Chloro-6',7'-dimethoxy-1',4'-dihydro-2'H-spiro[indoline-3,3'-quinoline]-2,2'-dione (5m)

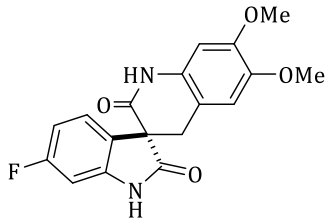


5m

Product **5m** was synthesized according to **General Procedure B**, starting from **2b** (158 mg, 0.5 mmol) and **3c** (152 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5m** as a white solid (118 mg, 66%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.79 (s, 1H), 10.49 (s, 1H), 7.28 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 6.86 (s, 1H), 6.65 (s, 1H), 6.50 (d, *J* = 2.2 Hz, 1H), 3.76 (s, 3H), 3.70 (s, 4H), 3.35 (d, merged with water peak, 1H), 2.97 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.5, 166.2, 148.4, 144.4, 141.2, 132.1, 130.6, 128.8, 125.4, 122.7, 112.7, 111.4, 111.2, 100.2, 55.8, 55.5, 54.8,

33.4. LRMS (ESI$^+$) *m*/*z* 359.1 [M + H]$^+$. Anal. calcd. for $C_{18}H_{15}ClN_2O_4$: C, 60.26; H, 4.21; N, 7.81; found: C, 60.19; H, 4.27; N, 7.85.

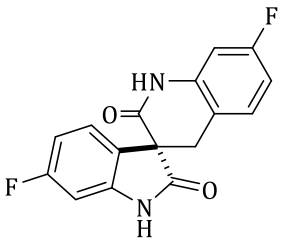
6-Fluoro-6',7'-dimethoxy-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5n)



5n

Product **5n** was synthesized according to **General Procedure B**, starting from **2c** (150 mg, 0.5 mmol) and **3c** (152 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5n** as a white solid (116 mg, 68%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.82 (s, 1H), 10.45 (s, 1H), 6.85 (s, 1H), 6.71 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.65–6.60 (m, 2H), 6.47 (dd, *J* = 8.3, 5.4 Hz, 1H), 3.75 (s, 3H), 3.69 (s, 3H), 3.35 (d, merged with water peak, 1H,), 2.87 (d, *J* = 15.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.3, 166.8, 162.6 (d, *J* = 242.9 Hz), 148.3, 144.4, 143.9 (d, *J* = 12.5 Hz), 130.7, 126.1 (d, *J* = 2.6 Hz), 124.1 (d, *J* = 10.2 Hz), 112.7, 111.5, 107.8 (d, *J* = 22.3 Hz), 100.2, 98.2 (d, *J* = 27.0 Hz) 55.8, 55.5, 54.2, 33.6. LRMS (ESI$^+$) *m*/*z* 343.1 [M + H]$^+$. Anal. calcd. for $C_{18}H_{15}FN_2O_4$: C, 63.16; H, 4.42; N, 8.18; found: C, 63.26; H, 4.47; N, 8.11.

6,7'-Difluoro-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5o)

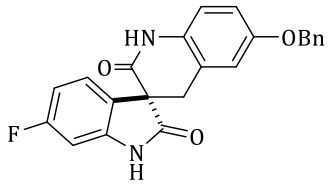


5o

Product **5o** was synthesized according to **General Procedure B**, starting from **2c** (150 mg, 0.5 mmol) and **3b** (129 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5o** as a white solid (98 mg, 65%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.88 (s, 1H), 10.83 (s, 1H), 7.25–7.22 (m, 1H), 6.86–6.77 (m, 2H), 6.72 (dd, *J* = 9.2,

2.5 Hz, 1H), 6.64 (ddd, *J* = 10.2, 8.3, 2.5 Hz, 1H), 6.55 (dd, *J* = 8.3, 5.5 Hz, 1H), 3.37 (d, *J* = 16.2 Hz, 2H), 3.06 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.9, 167.0, 163.4 (d, *J* = 103.0 Hz), 161.0 (d, *J* = 101.6 Hz), 144.0 (d, *J* = 12.5 Hz), 139.0 (d, *J* = 11.0 Hz), 130.3, 125.6 (d, *J* = 3.0 Hz), 124.3 (d, *J* = 10.1 Hz), 116.7 (d, *J* = 3.0 Hz), 109.2 (d, *J* = 21.3 Hz), 107.9 (d, *J* = 22.1 Hz), 102.3 (d, *J* = 25.7 Hz), 98.3 (d, *J* = 27.3 Hz), 54.0, 33.2. LRMS (ESI$^+$) *m/z* 301.1 [M + H]$^+$. Anal. calcd. for $C_{16}H_{10}F_2N_2O_2$: C, 64.00; H, 3.36; N, 9.33; found: C, 64.18; H, 3.47; N, 9.39.

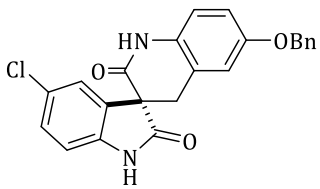
6'-(Benzyloxy)-6-fluoro-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5p)



5p

Product **5p** was synthesized according to **General Procedure B**, starting from **2c** (150 mg, 0.5 mmol) and **3d** (177 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5p** as a white solid (118 mg, 61%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.84 (s, 1H), 10.58 (s, 1H), 7.45–7.30 (m, 5H), 6.96–6.91 (m, 3H), 6.72 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.62 (ddd, *J* = 9.8, 8.3, 2.4 Hz, 1H), 6.48 (dd, *J* = 8.3, 5.5 Hz, 1H), 5.03 (s, 2H), 3.43 (d, 1H, merged with water peak), 2.97 (d, *J* = 16.1 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.2, 166.6, 162.6 (d, *J* = 243.0 Hz), 154.2, 144.0 (d, *J* = 12.0 Hz), 137.1, 131.1, 128.5, 128.4, 127.8, 126.0 (d, *J* = 2.8 Hz), 124.1, 121.9, 116.0, 115.3 (d, *J* = 6.2 Hz), 114.0, 107.8 (d, *J* = 22.0 Hz), 98.23 (d, *J* = 27.7 Hz), 69.6, 54.0, 34.1. LRMS (ESI$^+$) *m/z* 389.1 [M + H]$^+$. Anal. calcd. for $C_{23}H_{17}FN_2O_3$: C, 71.13; H, 4.41; N, 7.21; found: C, 71.29; H, 4.33; N, 7.14.

6'-(Benzyloxy)-5-chloro-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (5q)

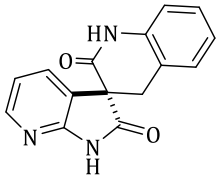


5q

Product **5q** was synthesized according to **General Procedure B**, starting from **2b** (158 mg, 0.5 mmol) and **3d** (177 mg, 0.55 mmol). Purification of the crude product on silica gel using a

gradient of 0–10% MeOH/CH_2Cl_2 afforded **5q** as a white solid (130 mg, 64%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.80 (s, 1H), 10.60 (s, 1H), 7.45–7.42 (m, 2H), 7.40–7.36 (m, 2H), 7.34–7.32 (m, 1H), 7.28 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.94–6.90 (m, 4H), 6.53 (d, *J* = 2.2 Hz, 1H), 5.05 (s, 2H), 3.38 (d, *J* = 16.2 Hz, 1H), 3.08 (d, *J* = 16.1 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.9, 166.5, 154.6, 141.8, 137.6, 132.5, 131.5, 128.94, 128.90, 128.3, 125.9, 123.3, 122.2, 116.5, 115.9, 114.6, 111.9, 70.0, 55.1, 34.4. LRMS (ESI$^+$) *m/z* 405.1 [M + H]$^+$. Anal. calcd. for $C_{23}H_{17}FN_2O_3$: C, 68.24; H, 4.23; N, 6.92; found: C, 68.05; H, 4.26; N, 6.88.

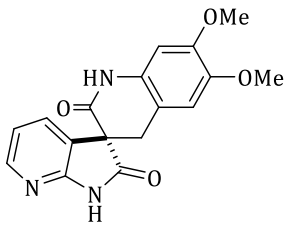
1',4'-dihydro-2'*H*-spiro[pyrrolo[2,3-b]pyridine-3,3'-quinoline]-2,2'(1*H*)-dione-dione (5r)



5r

Product **5r** was synthesized according to **General Procedure B**, starting from **2g** (141 mg, 0.5 mmol) and **3a** (118 mg, 0.55 mmol). Purification of the crude product on silica gel using a gradient of 0–10% MeOH/CH_2Cl_2 afforded **5r** as a white solid (80 mg, 60%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.86 (s, 1H), 10.70 (s, 1H), 7.96 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.25–7.14 (m, 4H), 6.97–6.92 (m, 2H), 3.41 (d, *J* = 16.5 Hz, 1H), 3.21 (d, *J* = 16.5 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.4, 165.8, 151.4, 142.1, 137.4, 137.3, 128.0, 127.3, 123.8, 122.5, 120.4, 116.2, 114.9, 55.2, 32.7. LRMS (ESI$^+$) *m/z* 266.1 [M + H]$^+$. Anal. calcd. for $C_{15}H_{11}N_3O_2$: C, 67.92; H, 4.18; N, 15.84; found: C, 67.79; H, 4.15; N, 15.88.

6',7'-Dimethoxy-1',4'-dihydro-2-spiro[pyrrolo[2,3-*b*]pyridine-3,3'-quinoline]-2,2'(1*H*)-dione (5s)

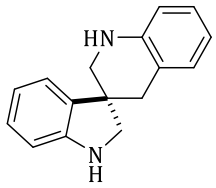


5s

Product **5s** was synthesized according to **General Procedure B**, starting from **2g** (141 mg, 0.5 mmol) and **3c** (152 mg, 0.55 mmol). Purification of the crude product on silica gel using a

gradient of 0–10% MeOH/CH_2Cl_2 afforded **5s** as a white solid (109 mg, 67%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.82 (s, 1H), 10.44 (s, 1H), 7.97 (dd, *J* = 4.51, 1.92 Hz, 1H), 7.24–7.18 (m, 2H), 6.79 (s, 1H), 6.58 (s, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.17–3.07 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.0, 165.9, 152.1, 148.4, 144.6, 142.5, 137.7, 131.2, 124.2, 116.6, 112.9, 111.9, 100.7, 56.3, 56.0, 55.7, 33.0. LRMS (ESI$^+$) *m/z* 326.1 [M + H]$^+$. Anal. calcd. for $C_{17}H_{15}N_3O_4$: C, 62.76; H, 4.65; N, 12.92; found: C, 62.87; H, 4.61; N, 12.97.

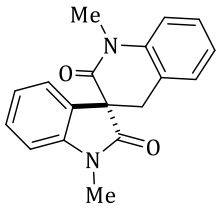
1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline] (6a)



6a

To a stirred suspension of $LiAlH_4$ (22 mg, 0.9 mmol, 3.0 equiv) in anhydrous THF (2 mL) at 0 °C was added a solution of **5a** (79 mg, 0.3 mmol, 1.0 equiv) in anhydrous THF (2mL) under nitrogen atmosphere. The resulting mixture was stirred at rt for 5 h. After completion the reaction mixture was quenched with drop wise addition of ice-cold water (0.5 mL) and 20% aqueous NaOH solution (0.5 mL) subsequently at 0 °C. and then extracted with ethyl acetate (5 x 3 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated and purified through silica gel column chromatography using a gradient of 0–7% MeOH/CH_2Cl_2 to afford **6a** as a semi solid (55 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (td, *J* = 7.64, 1.34 Hz, 1H), 7.05–6.97 (m, 2H), 6.93 (dd, *J* = 7.48, 1.31 Hz, 1H), 6.80–6.68 (m, 2H), 6.64 (td, *J* = 7.40, 1.24 Hz, 1H), 6.55 (dd, *J* = 7.95, 1.20 Hz, 1H), 3.56 (d, *J* = 9.31 Hz, 1H), 3.36–3.31 (m, 2H), 3.22 (dd, *J* = 11.29, 2.18 Hz, 1H), 3.11 (d, *J* = 16.13 Hz, 1H), 2.82 (dd, *J* = 16.16, 2.13 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.6, 143.8, 134.5, 130.2, 128.3, 127.2, 123.4, 119.8, 119.3, 117.3, 113.9, 110.1, 57.1, 49.9, 42.9, 38.2. LRMS (ESI$^+$) *m/z* 326.1 [M + H]$^+$. Anal. Calcd. For $C_{17}H_{15}N_3O_4$: C, 62.76; H, 4.65; N, 12.92; found: C, 62.76; H, 4.65; N, 12.92.

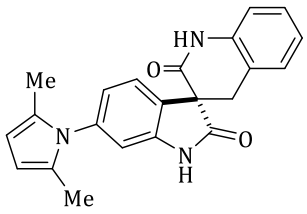
1,1'-Dimethyl-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (6b)



6b

To a stirred solution of **5a** (78 mg, 0.3 mmol, 1 equiv) in anhydrous DMF (2 mL) at 0 °C was added NaH (22 mg, 0.9 mmol, 3 equiv) under nitrogen atmosphere. Next, a solution of methyl iodide (107 mg, 0.8 mmol, 2.5 equiv) was added to it and the resulting mixture was stirred at rt for 4 h. The reaction was quenched with saturated aqueous NH_4Cl (2 mL) at 0 °C and then extracted with ethyl acetate (5 x 3 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated and purified through silica gel column chromatography using a gradient of 0–7% MeOH/CH_2Cl_2 to afford **6b** as a semi solid (61 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.36 (m, 1H), 7.25–7.21 (m, 1H), 7.16–7.07 (m, 3H), 6.84 (dt, *J* = 7.8, 0.8 Hz, 1H), 6.75 (td, *J* = 7.6, 1.0 Hz, 1H), 6.34 (ddd, *J* = 7.5, 1.3, 0.6 Hz, 1H), 3.81 (d, *J* = 15.6 Hz, 1H), 3.42 (s, 3H), 3.28 (s, 3H), 2.83 (d, *J* = 15.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 167.1, 143.8, 140.1, 129.3, 129.1, 128.9, 128.3, 123.6, 123.1, 122.9, 122.6, 114.8, 108.7, 55.1, 34.5, 30.3, 26.8. LRMS (ESI$^+$) *m/z* 293.1 $[M + H]^+$. Anal. calcd. for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58; found: C, 73.81; H, 5.57; N, 9.52.

6-(2,5-dimethyl-1*H*-pyrrol-1-yl)-1',4'-dihydro-2'*H*-spiro[indoline-3,3'-quinoline]-2,2'-dione (6c)



6c

A mixture of **5i** (70 mg, 0.25 mmol) and hexane-2,5-dione (30 mg, 0.26 mmol) was stirred at rt for 2 h. The mixture was concentrated under reduced pressure to obtain the crude product which was purified by silica gel column chromatography using a solvent gradient of 0–5% MeOH/CH_2Cl_2 to obtain **6c** as a brown solid (67 mg, 75%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.82 (s, 1H), 10.73 (s, 1H), 7.29–7.25 (m, 2H), 7.04–7.00 (m, 2H), 6.71 (d, *J* = 1.9 Hz, 1H), 6.68 (dd, *J* = 7.9, 2.0 Hz, 1H), 6.55 (d, *J* = 7.9 Hz, 1H), 5.75 (s, 2H), 3.48 (d, *J* = 16.1 Hz, 1H, partially

merged with water peak), 3.09 (d, *J* = 16.1 Hz, 1H), 1.93 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.9, 166.9, 143.0, 139.0, 137.5, 129.1, 128.8, 128.1, 127.7, 123.2, 123.0, 121.3, 120.6, 115.2, 112.7 (d, *J* = 4.3 Hz), 109.7, 106.1, 54.5, 33.7, 13.0. LRMS (ESI$^+$) *m/z* 358.2 $[M + H]^+$. Anal. calcd. for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76; found: C, 74.10; H, 5.44; N, 11.85.

3. X-Ray Crystallography Data

X-ray reflections were collected on a Bruker APEX-II, CCD diffractometer using Mo Kα (λ = 0.71073 Å) radiation. Data reduction was performed using Bruker SAINT Software.[5a] Intensities for absorption were corrected using SADABS-2014/2. Structure was solved in Olex2-1.5-alpha software[5b] using SHELXT 2018/2 and refined using 'SHELXL 2018/3 with anisotropic displacement parameters for non-H atoms. A check of the final CIF file using PLATON did not show any missed symmetry.[5c,d] The crystallographic parameters for the structure are summarized in table SI-1

Table SI-1: Crystallographic data of **5a**

Crystal Data	ag453_a
Formula unit	C_{16} H_{12} N_2 O_2
Formula wt.	264.28
Crystal system	triclinic
T [K]	296
a [Å]	5.713(2)
b [Å]	9.479(4)
c [Å]	12.310(5)
α [°]	102.192(10)
β [°]	96.254(10)
γ [°]	105.998(9)
Volume [Å^3]	616.4(4)
Space group	*P -1*
Z	2
D_{calc} [g cm^{-3}]	1.424
μ/mm^{-1}	0.096

Reflns. Collected	3210
Observed reflns.	2172
R_1 [I>2σ(I)], wR_2	0.0534 (2172), 0.1432(3210)
GOOF	1.020
Instrument	Bruker APEX-II CCD
X-ray	MoK\a
CCDC Reference No.	**2364972**

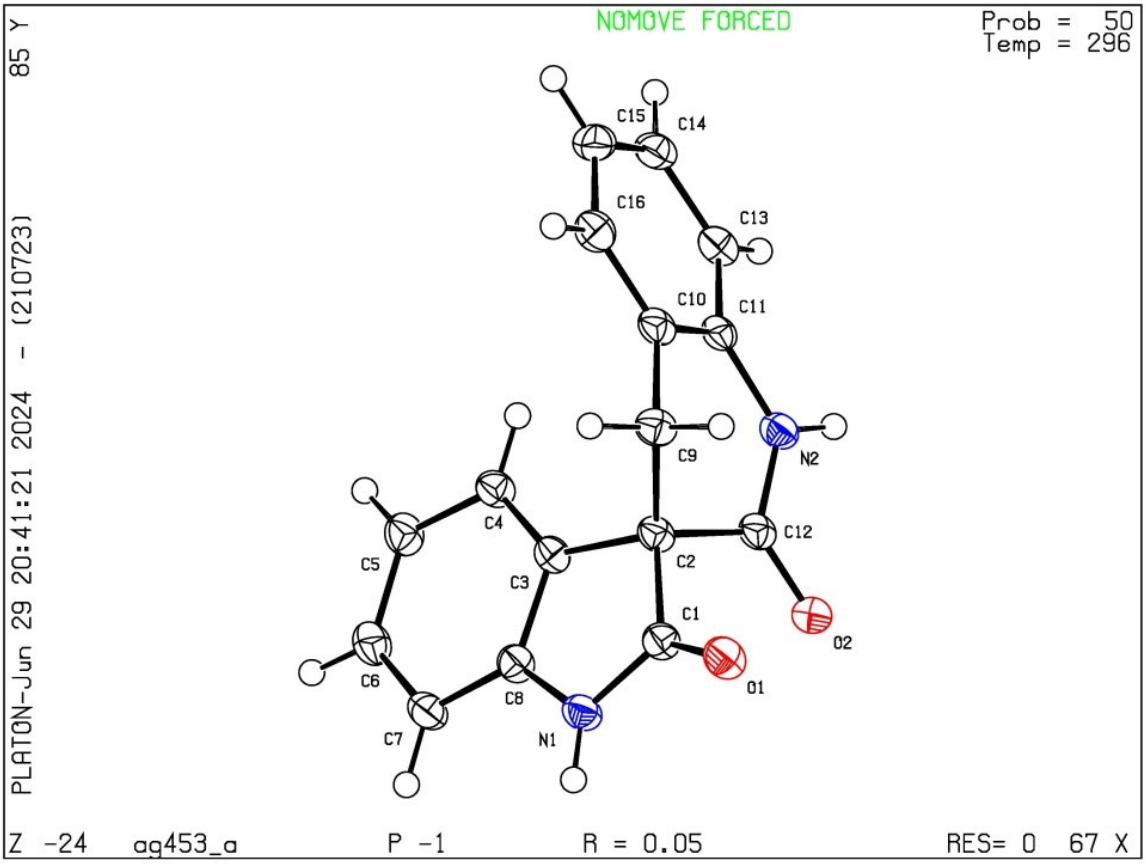


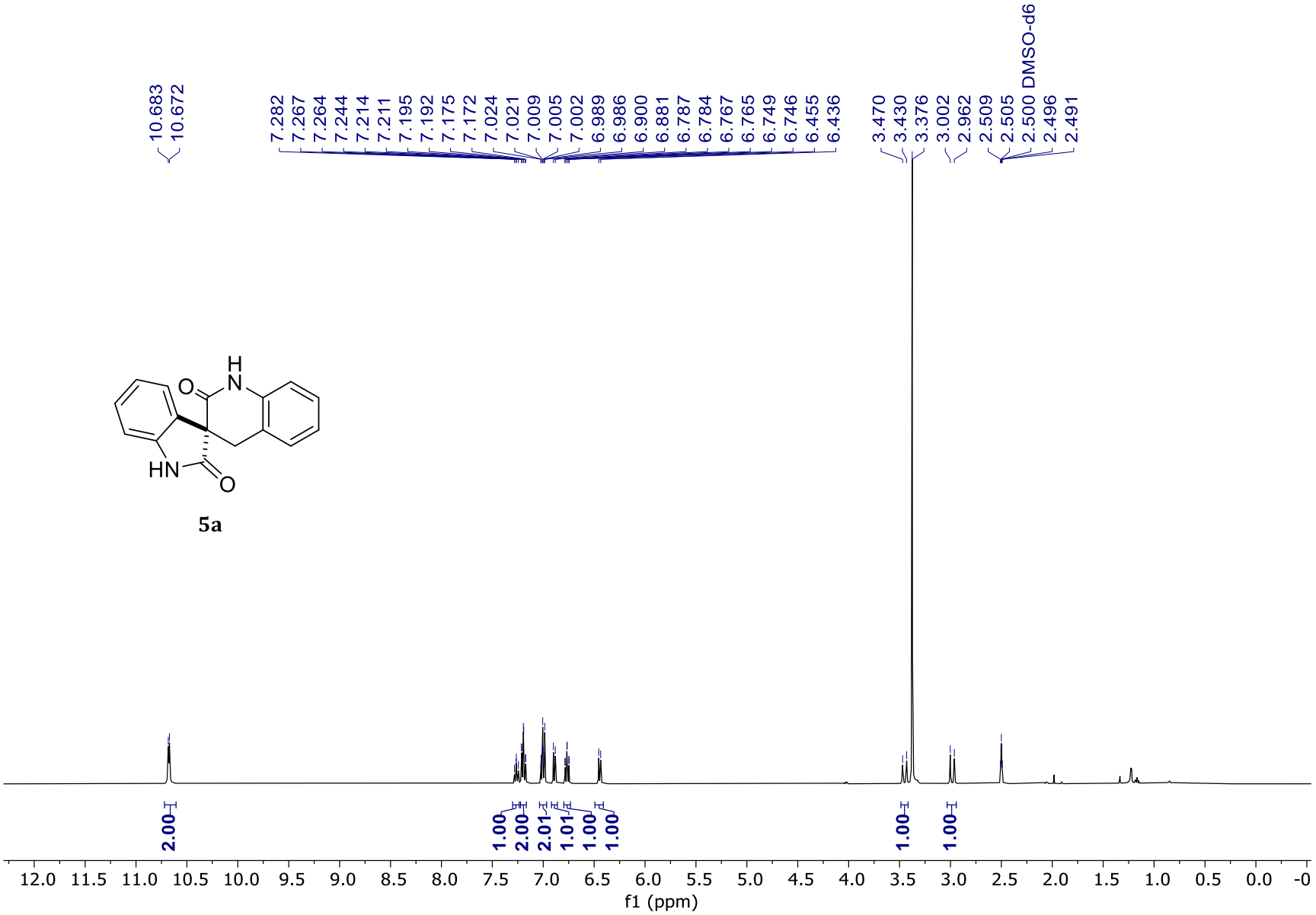
Figure SI-1. ORTEP diagram of **5a** with 50% probability ellipsoid.

4. References

1. M. Ueno, M. Yonemoto, M. Hashimoto, A. E. H. Wheatley, H. Naka and Y. Kondo, *Chem. Commun*., 2007, 2264–2266.

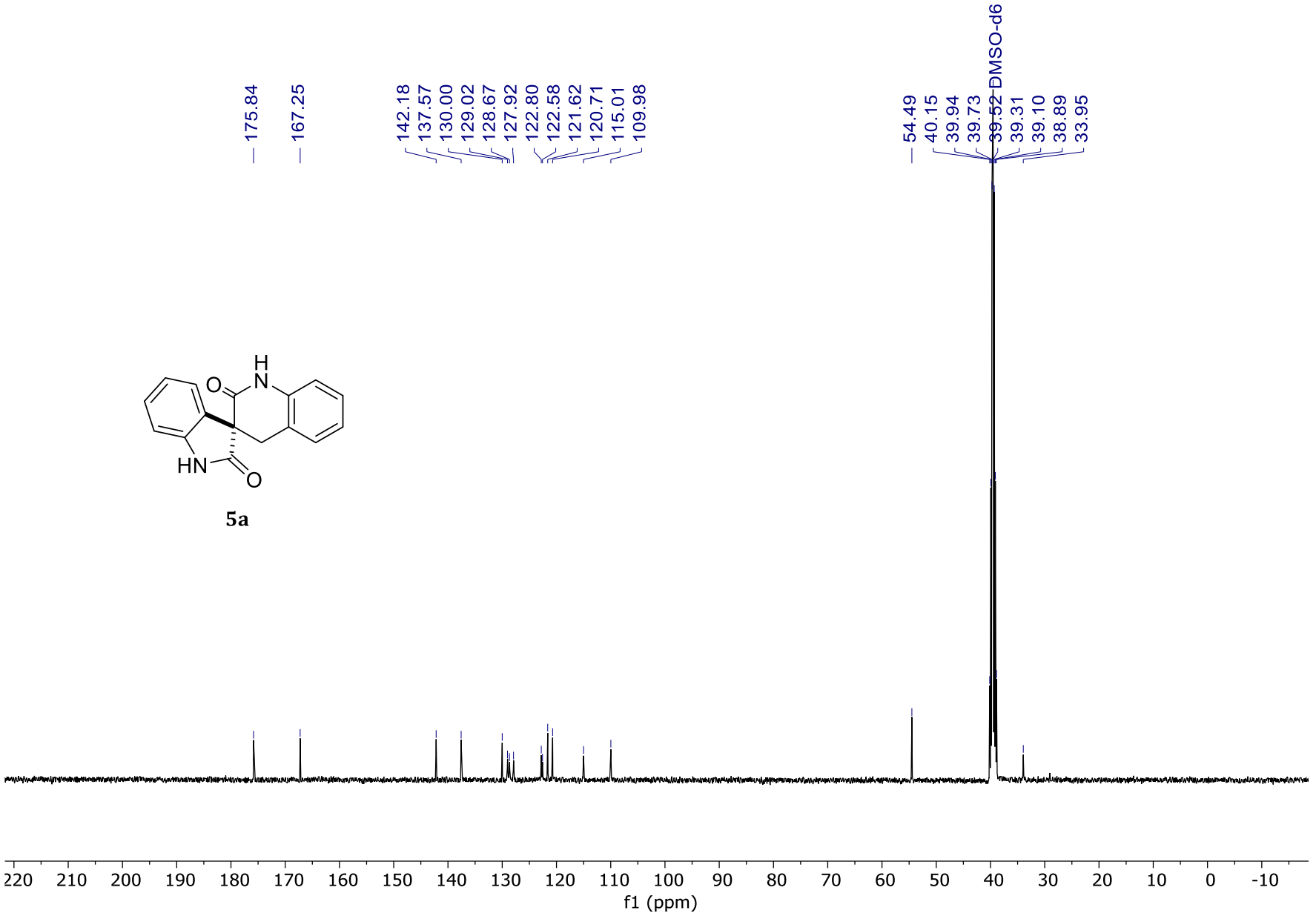
2. K. R. Batler *et al*., Substituted Pyrazoles, Pharmaceutical Composition Based on Thereof, Using Pharmaceutical Composition and Method for Inhibition of Cathepsin S Activity. RU 2 317 988 C2, 2006.
3. C. Stuart, M. Neil, W. Simon, L. Graham, P. Michael and G. S. J. Miguel, Spiroindoline for treating or preventing respiratory syncytial virus infection (RSV). US Patent US-10106539-B2, 2018.
4. S. Mondal, G. Dolai and B. Mandal, *ACS Omega*, 2023, **8**, 1401–1409.
5. (a) SAINT Plus, Bruker AXS Inc.: Madison, WI, **2008**; BRUKER AXS (v 6.14); (b) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. OLEX2: A complete structure solution, refinement and analysis program. *J. Appl. Cryst*., **2009**, *42*, 339–341. (c) PLATON, A Multipurpose Crystallographic Tool; Spek, A. L. Utrecht University: Utrecht, Netherland, 2002; (d) Spek, A. L. *J. Appl. Crystallogr.* **2003**, *36*, 7–13.

5. Copies of ^{1}H and ^{13}C NMR spectra of compounds

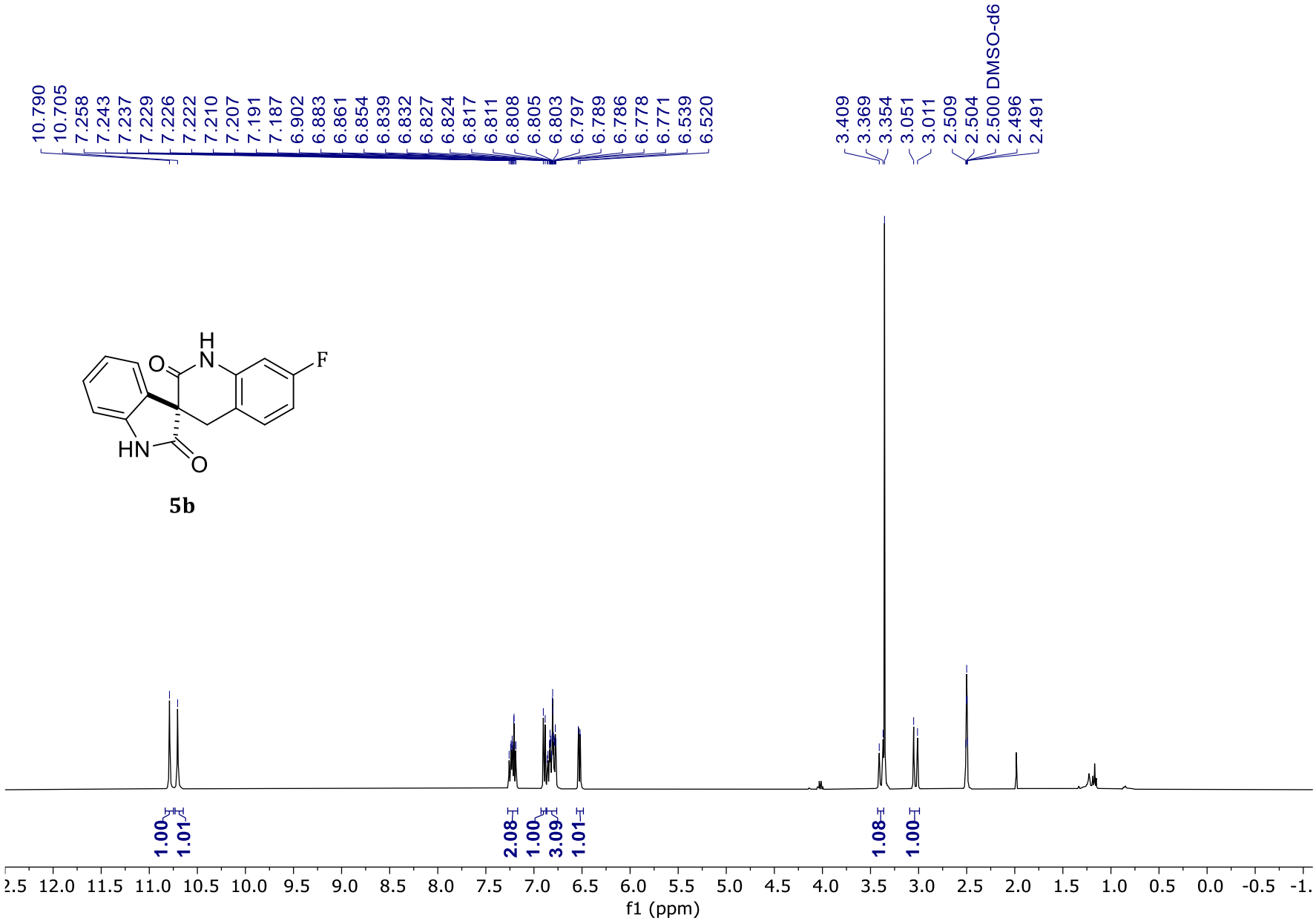


5a

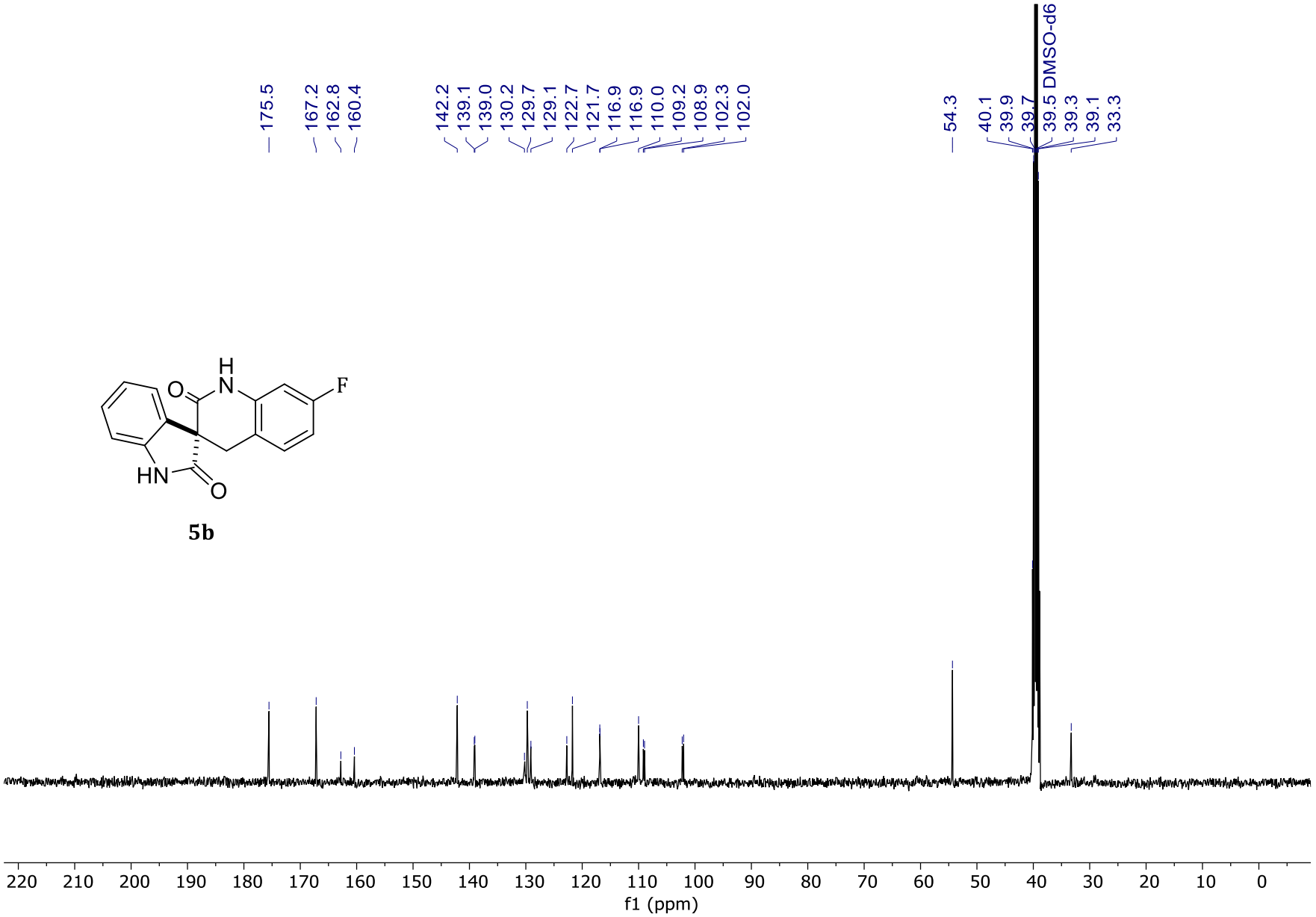
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5a**.



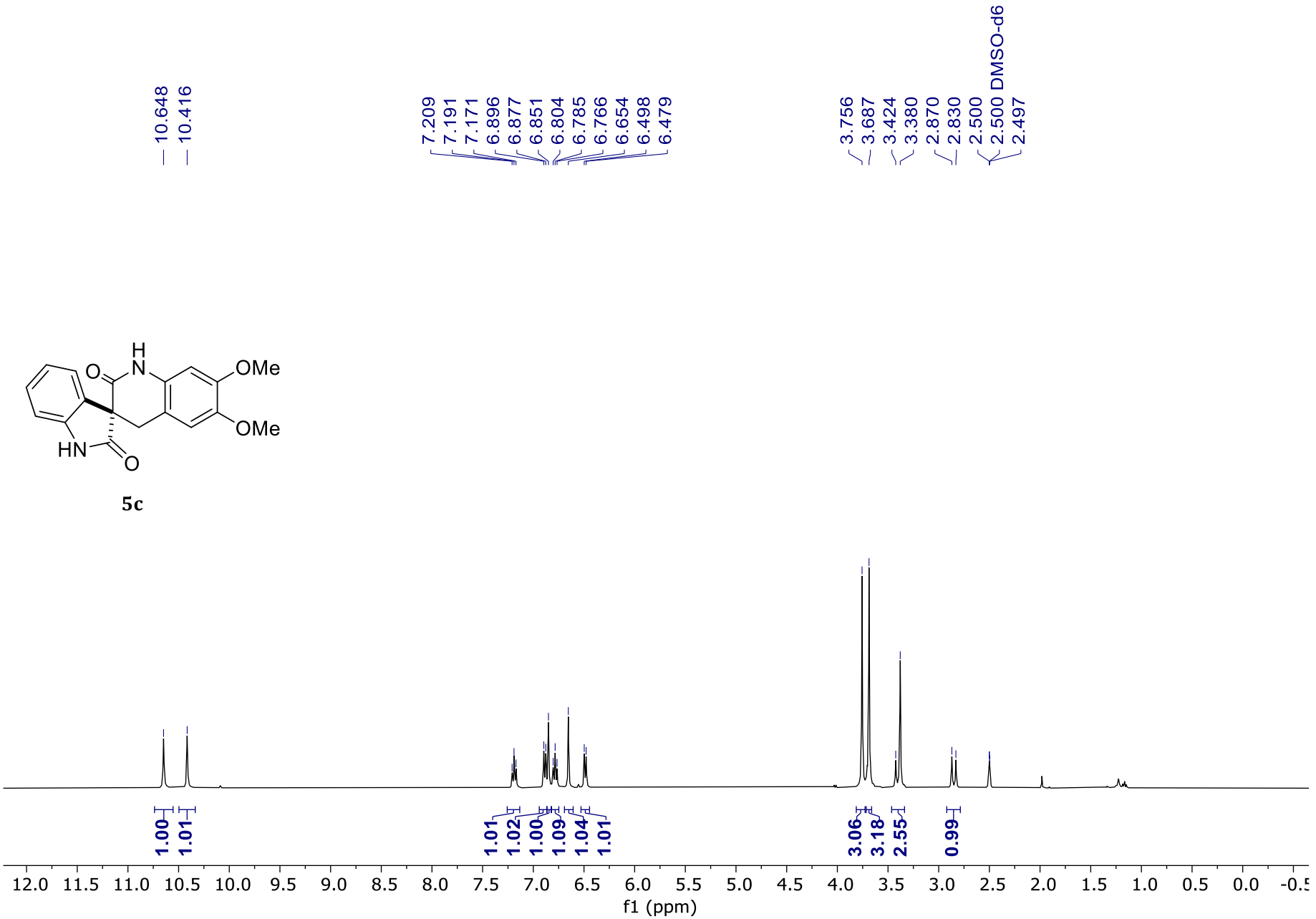
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5a**.



^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5b**.

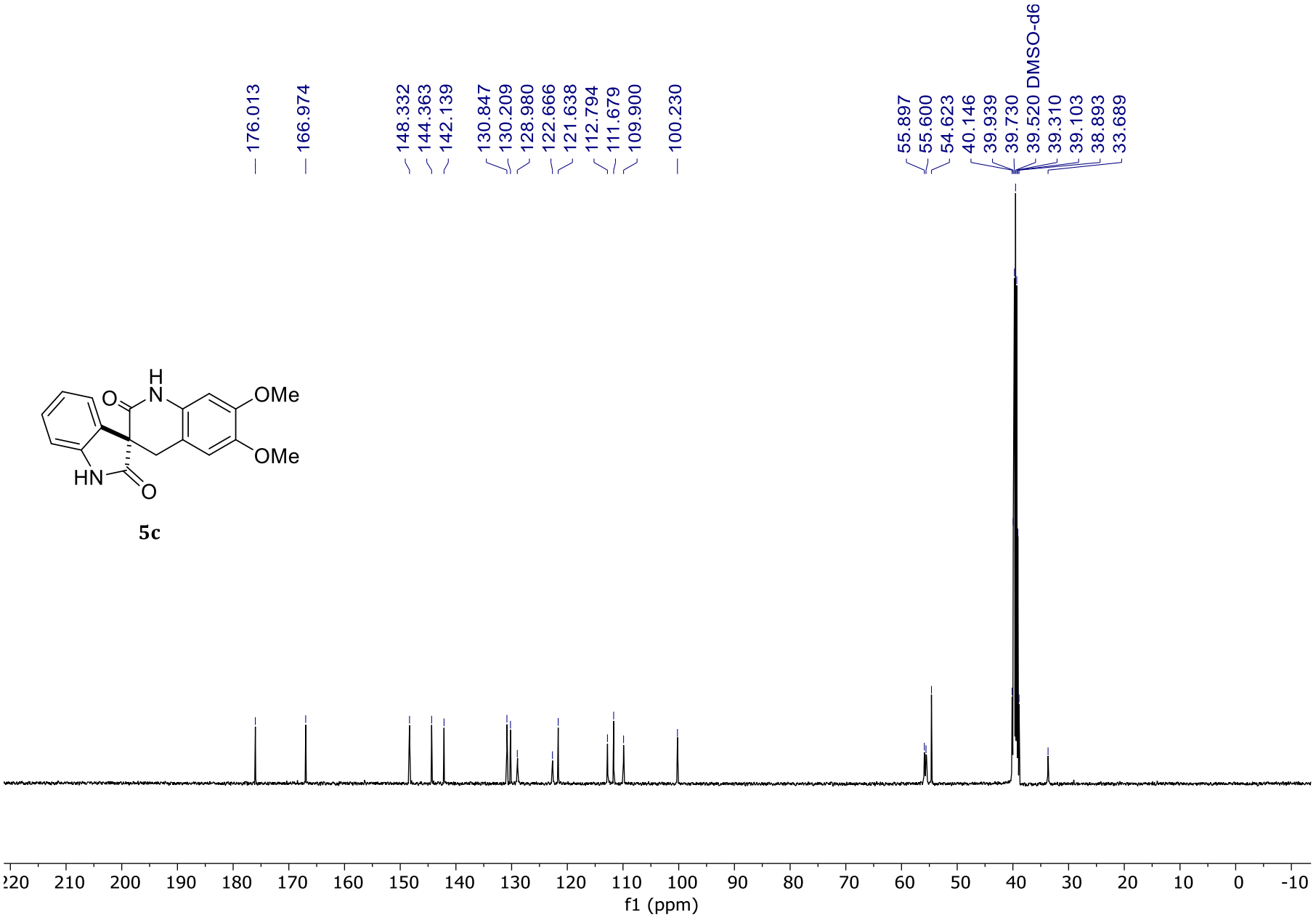


^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5b**.



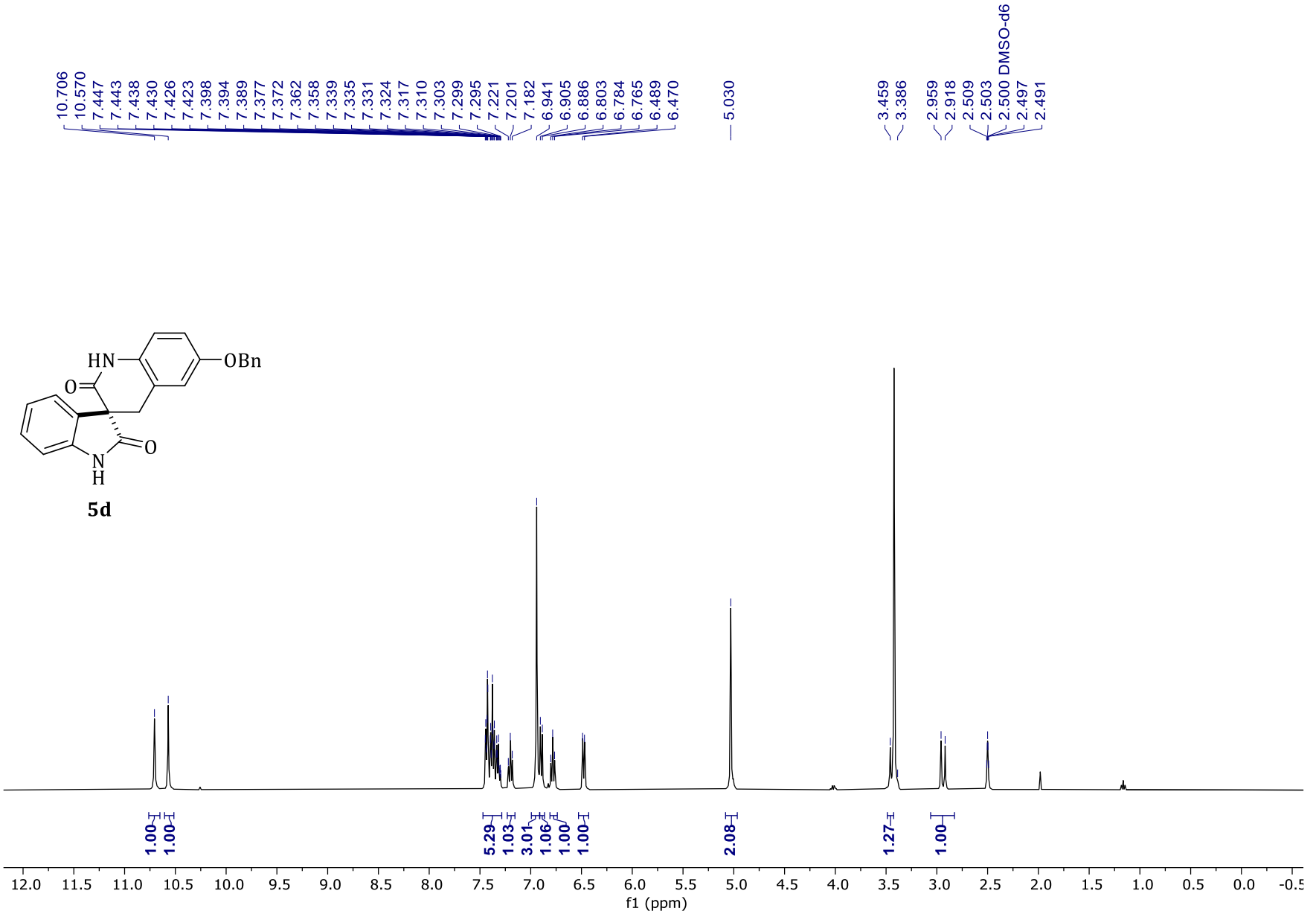
5c

^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5c**.

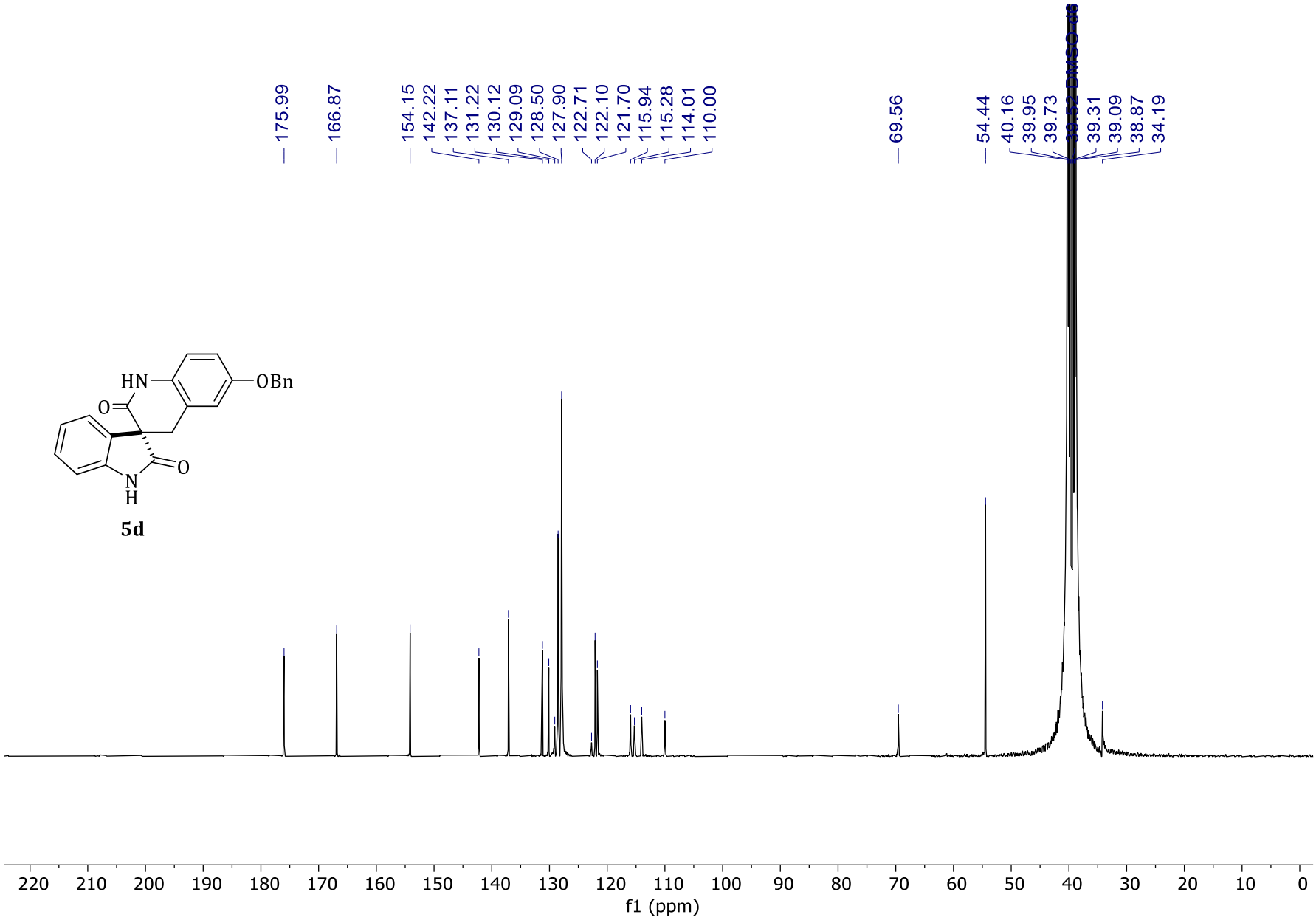


5c

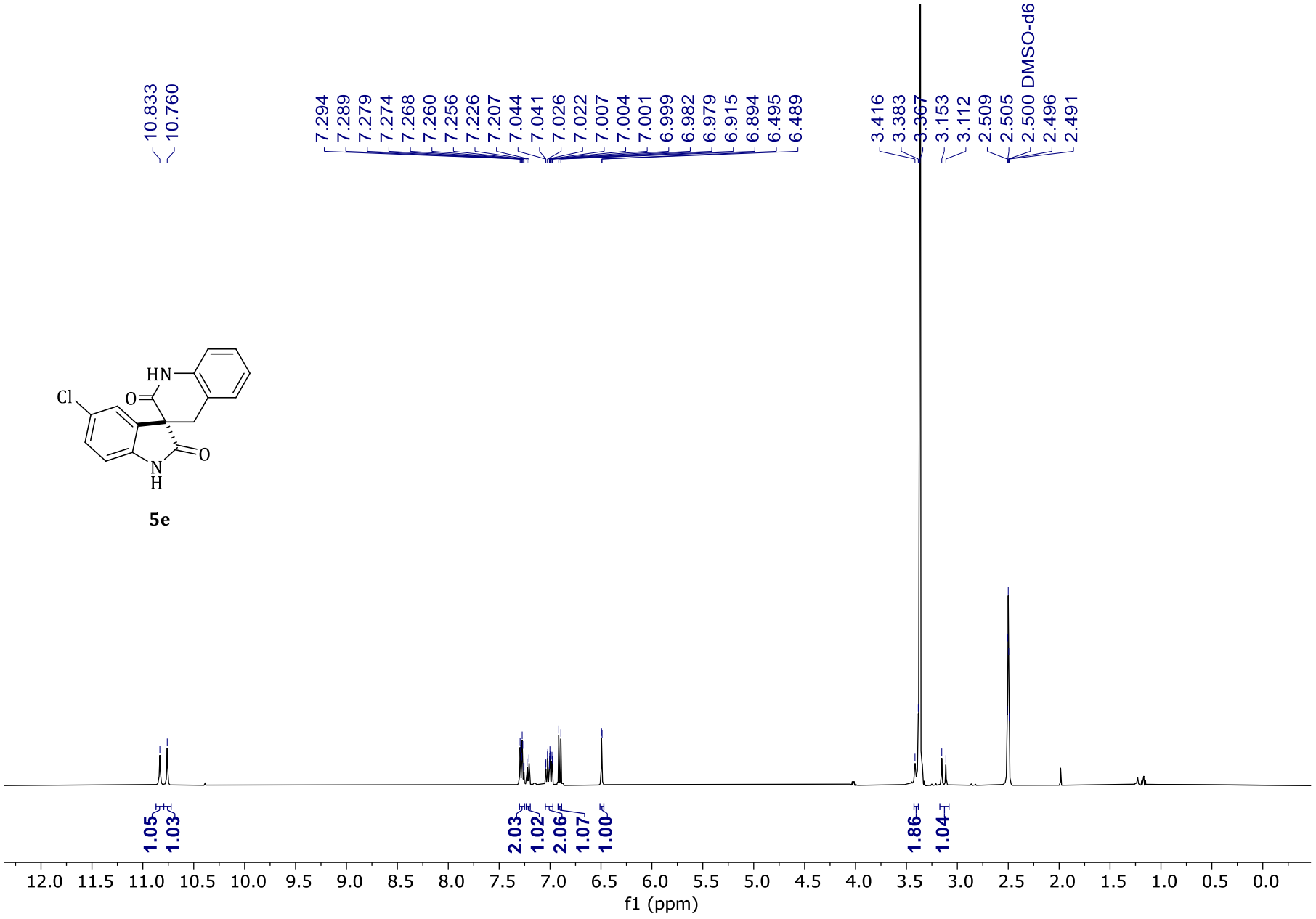
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5c**.



^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5d.**

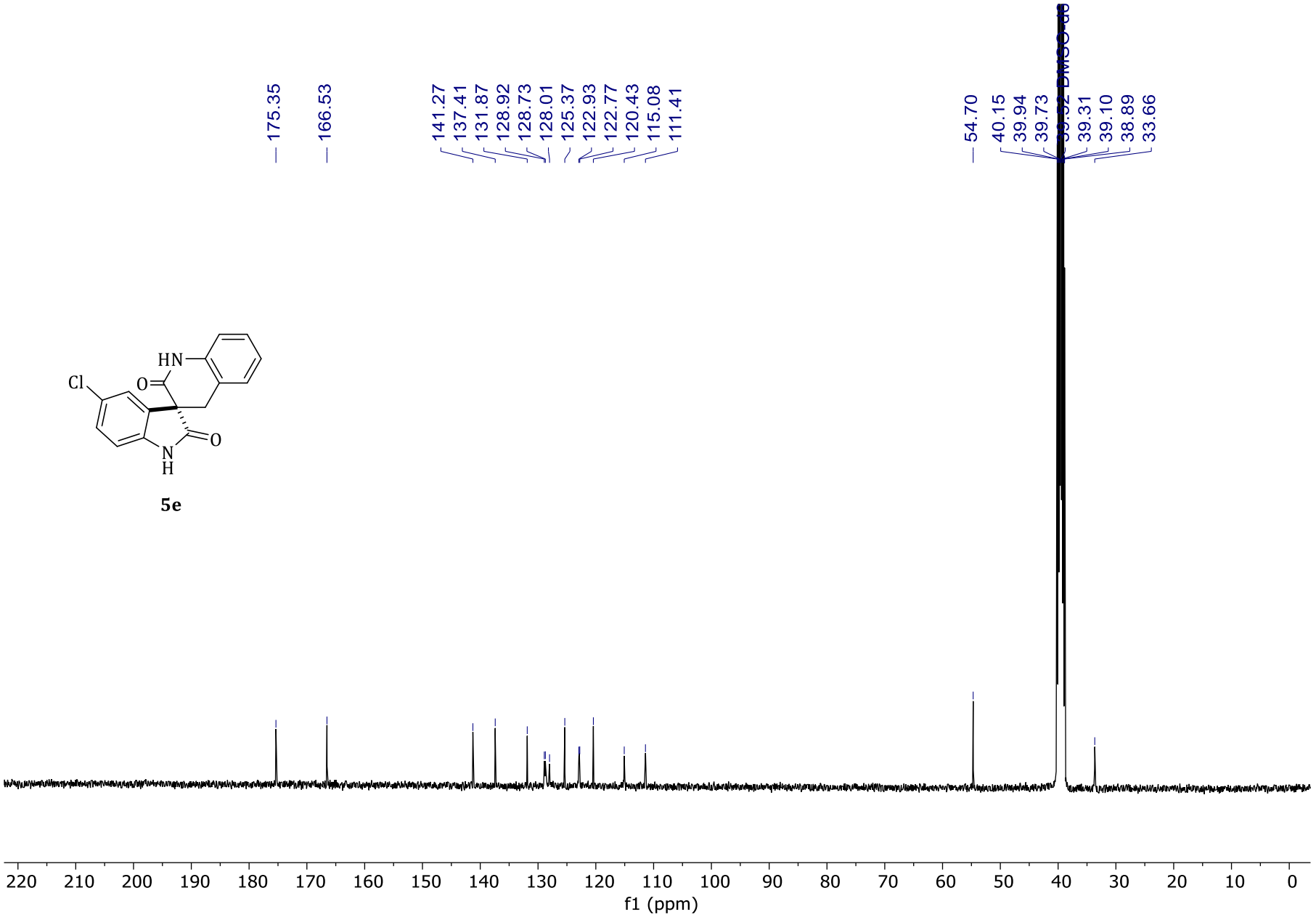


^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5d.**



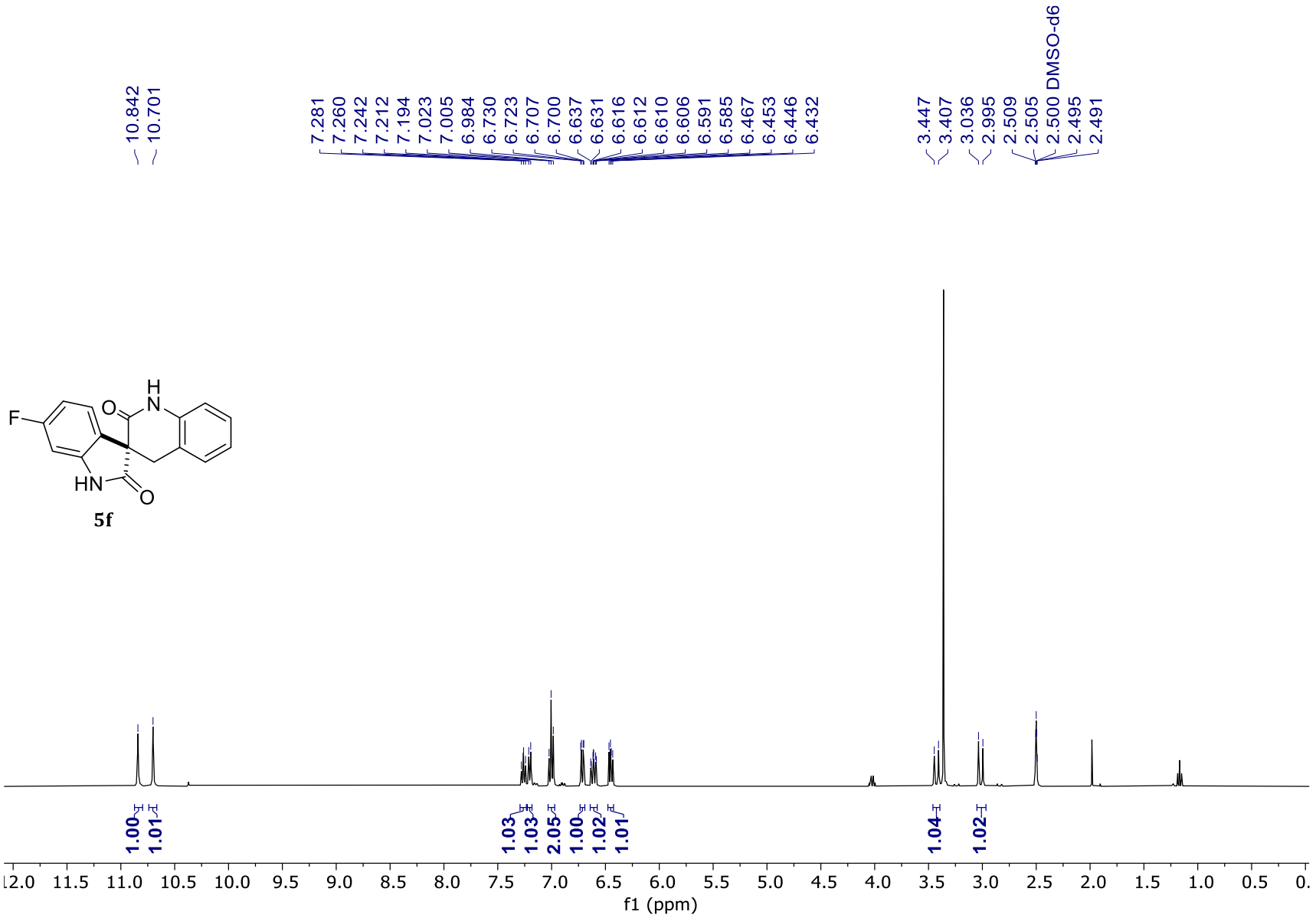
5e

^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5e**.

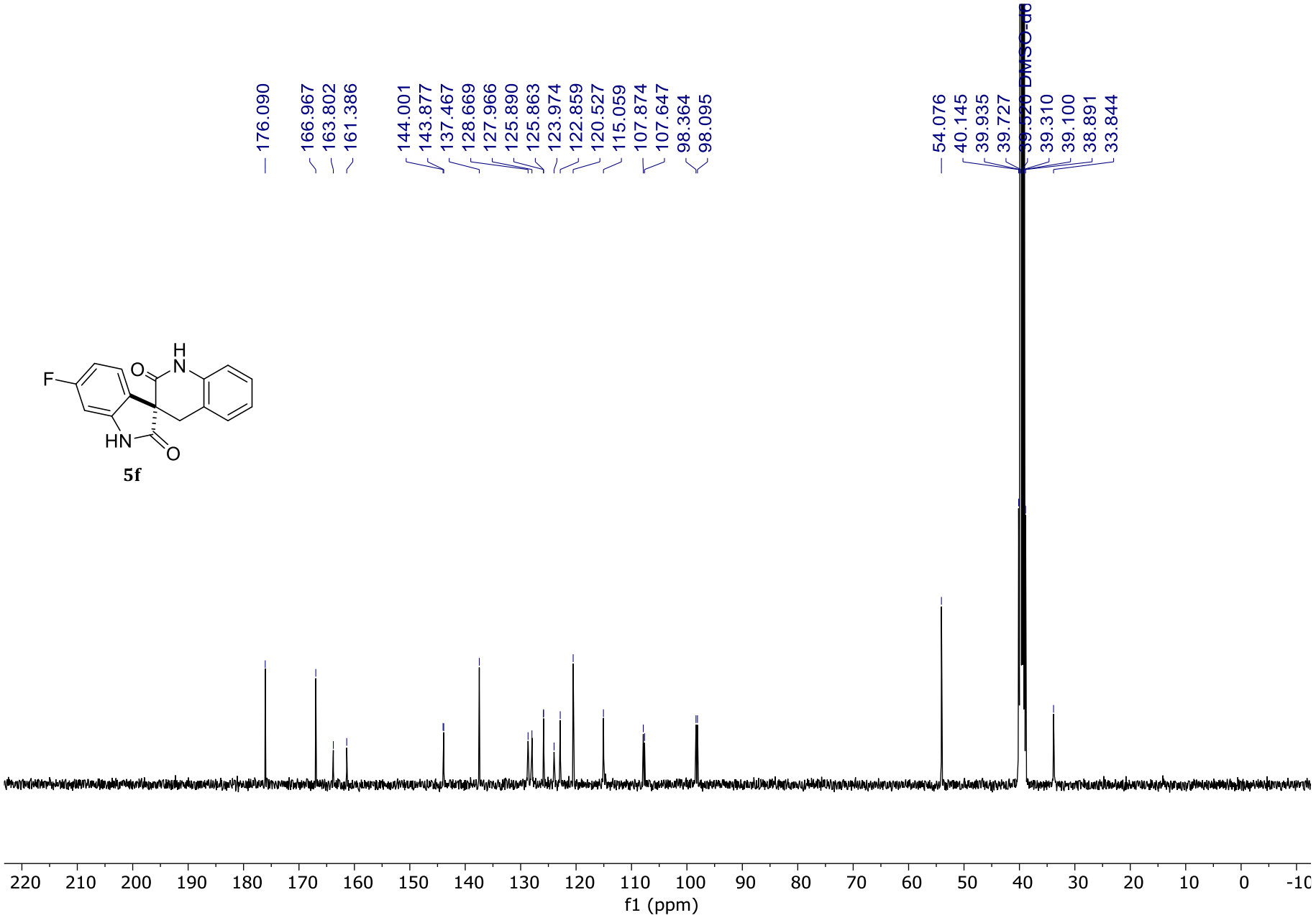


5e

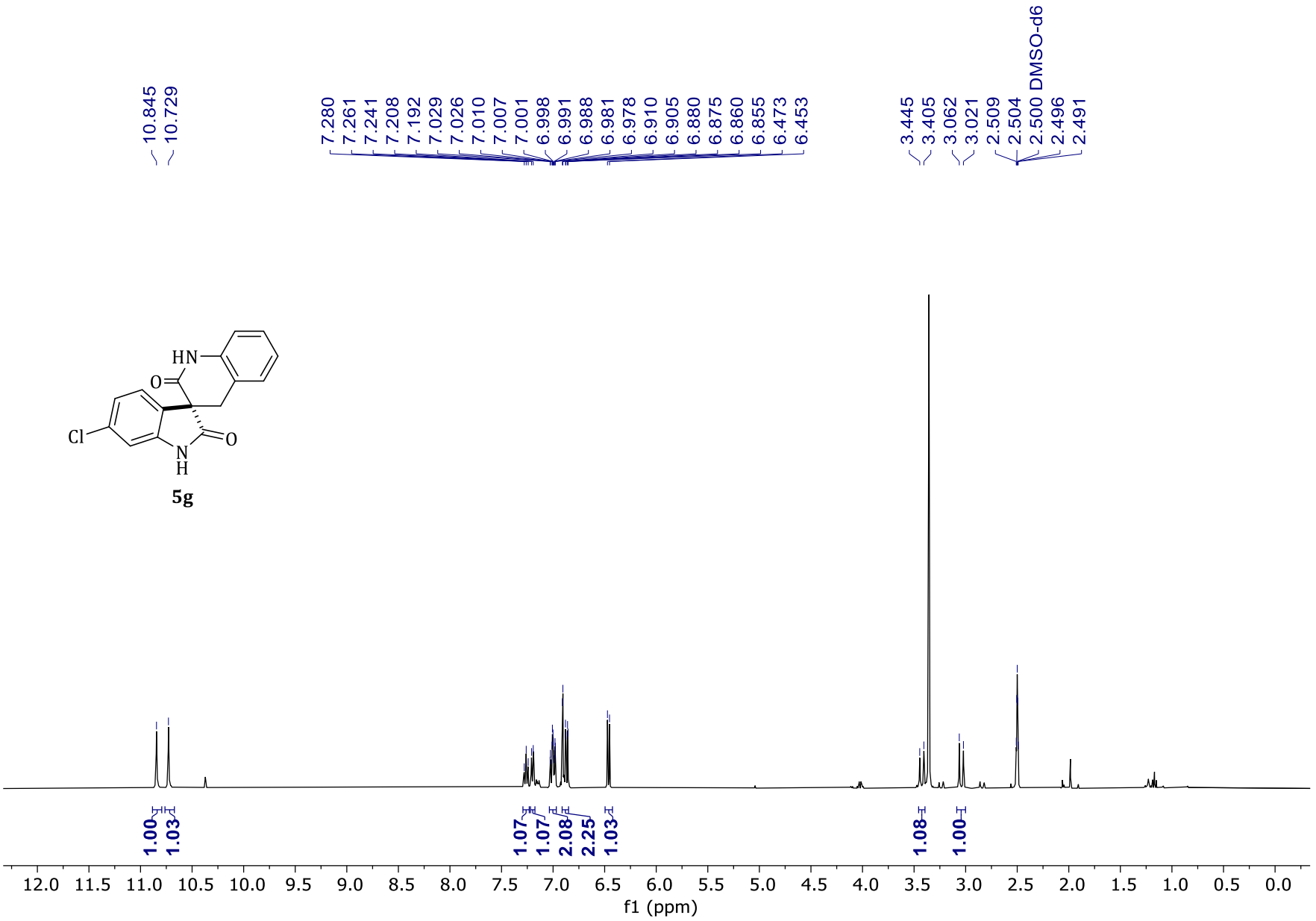
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5e.**



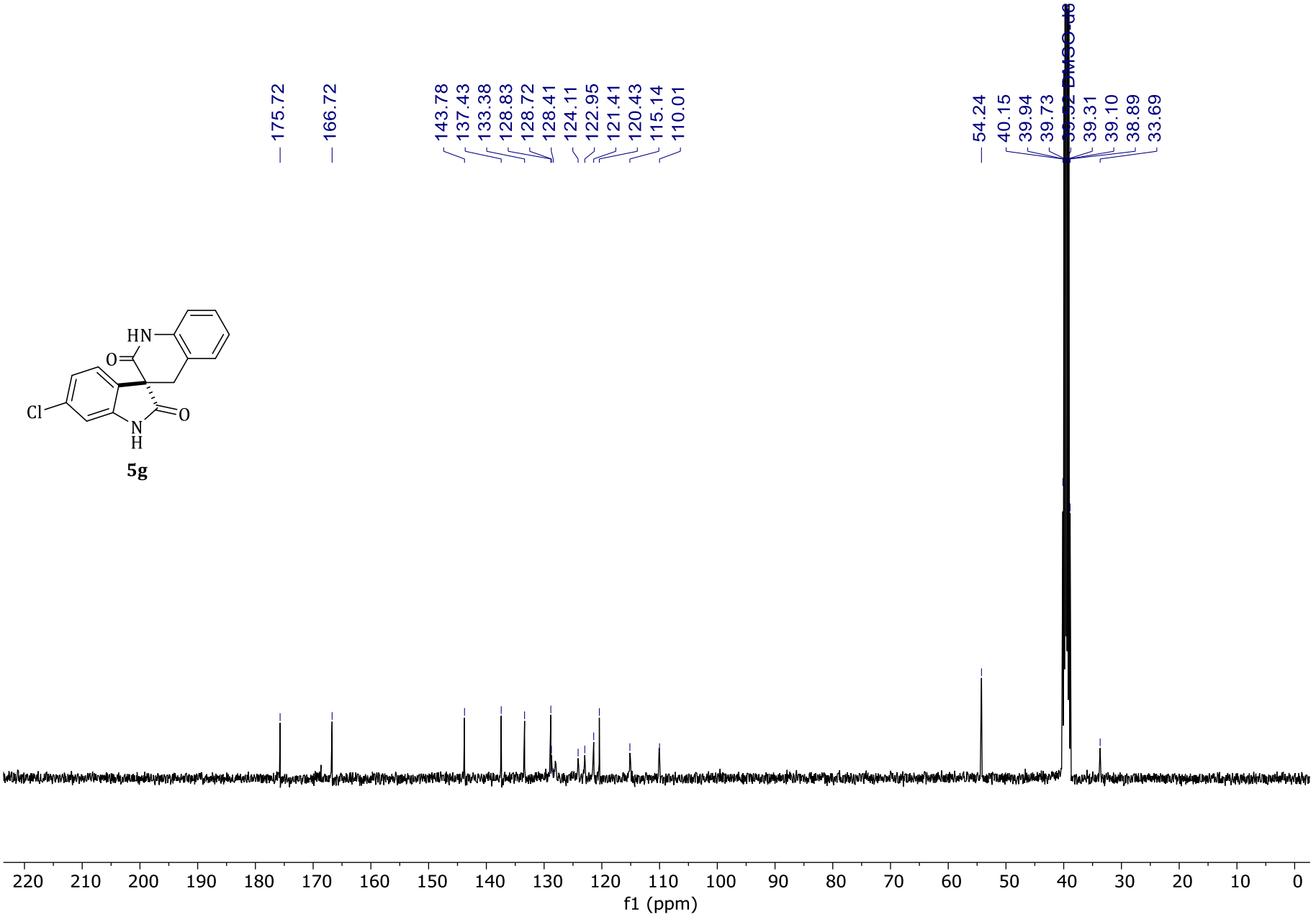
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5f**.



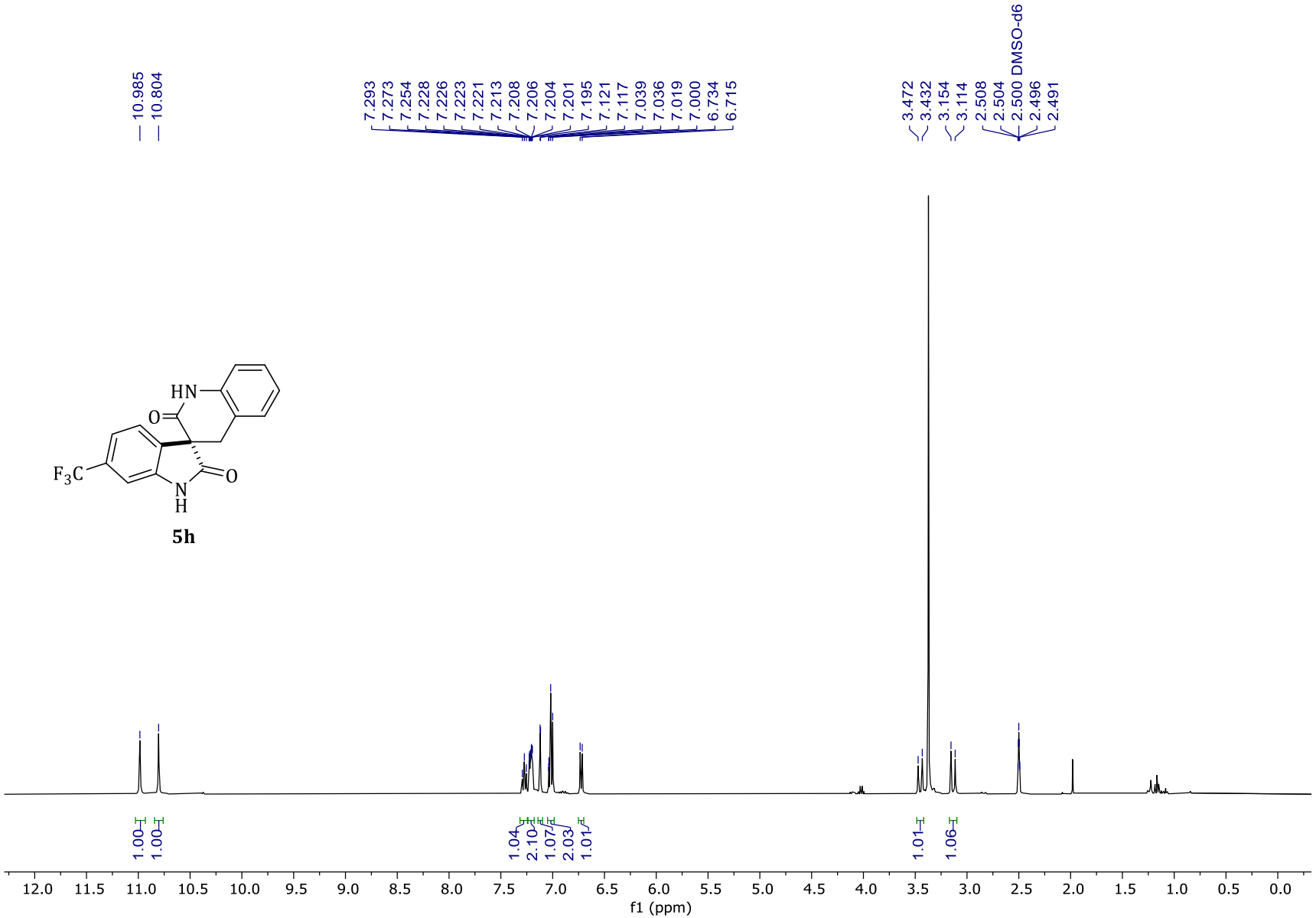
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5f**.



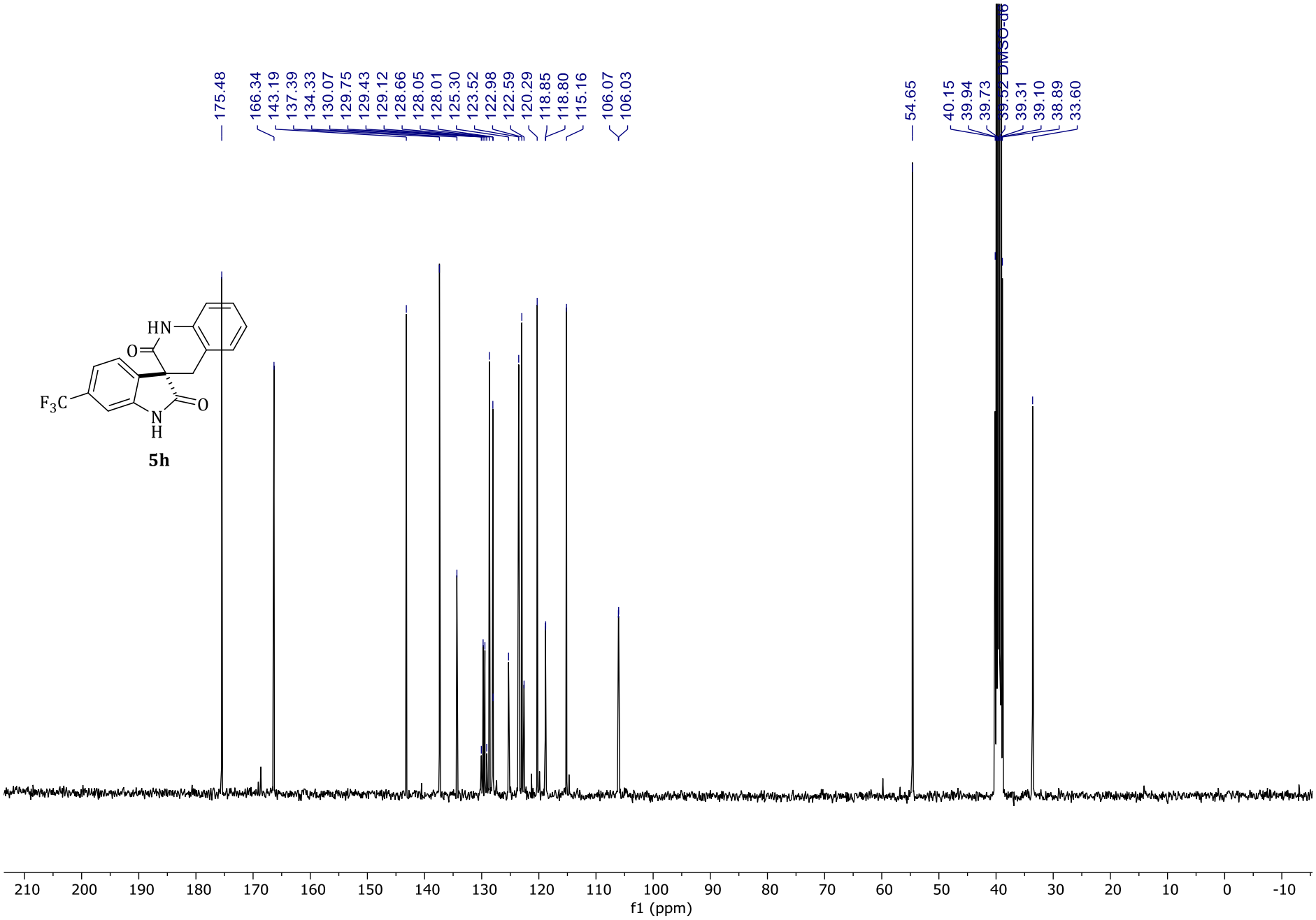
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5g**.



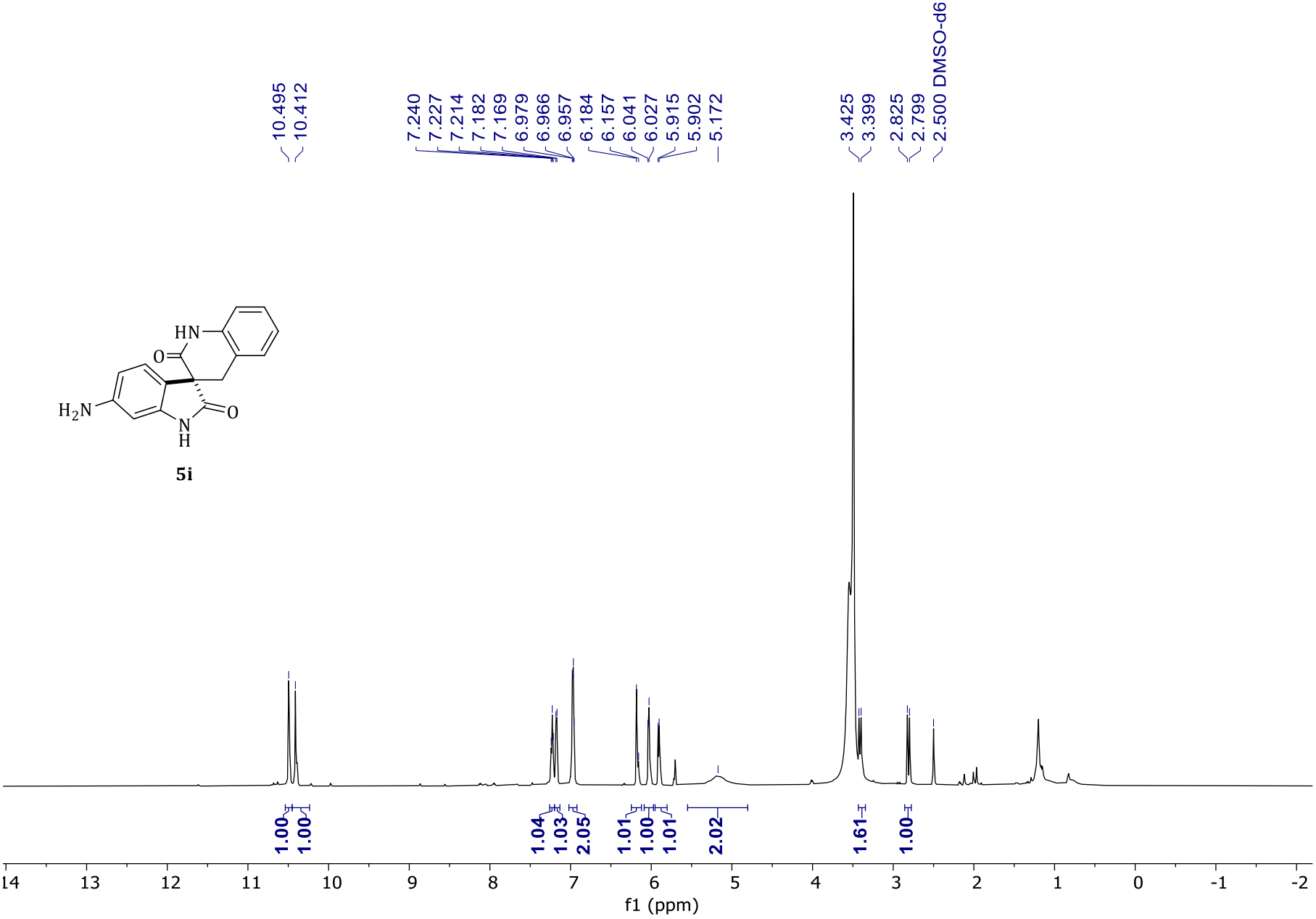
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5g**.



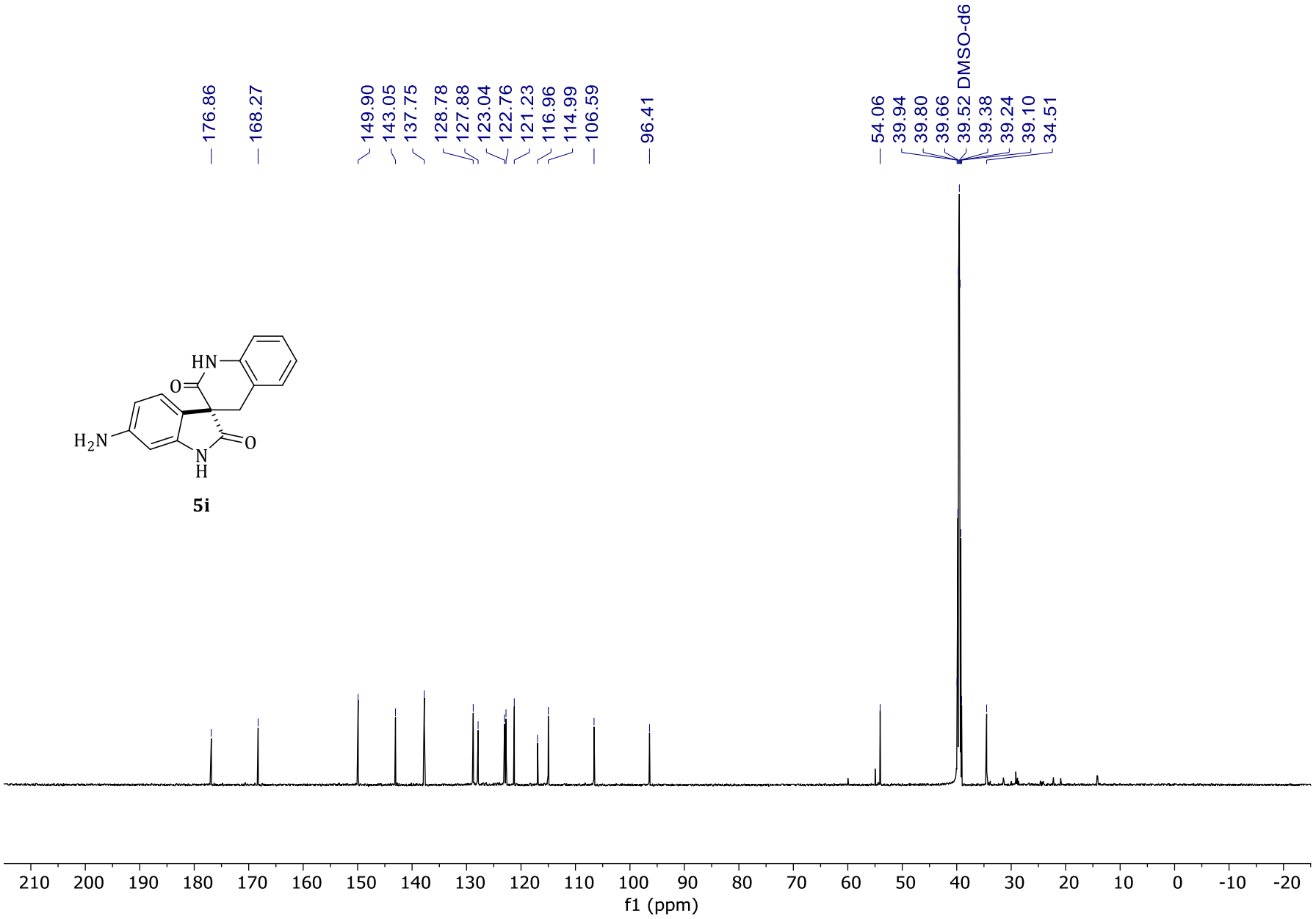
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5h**.



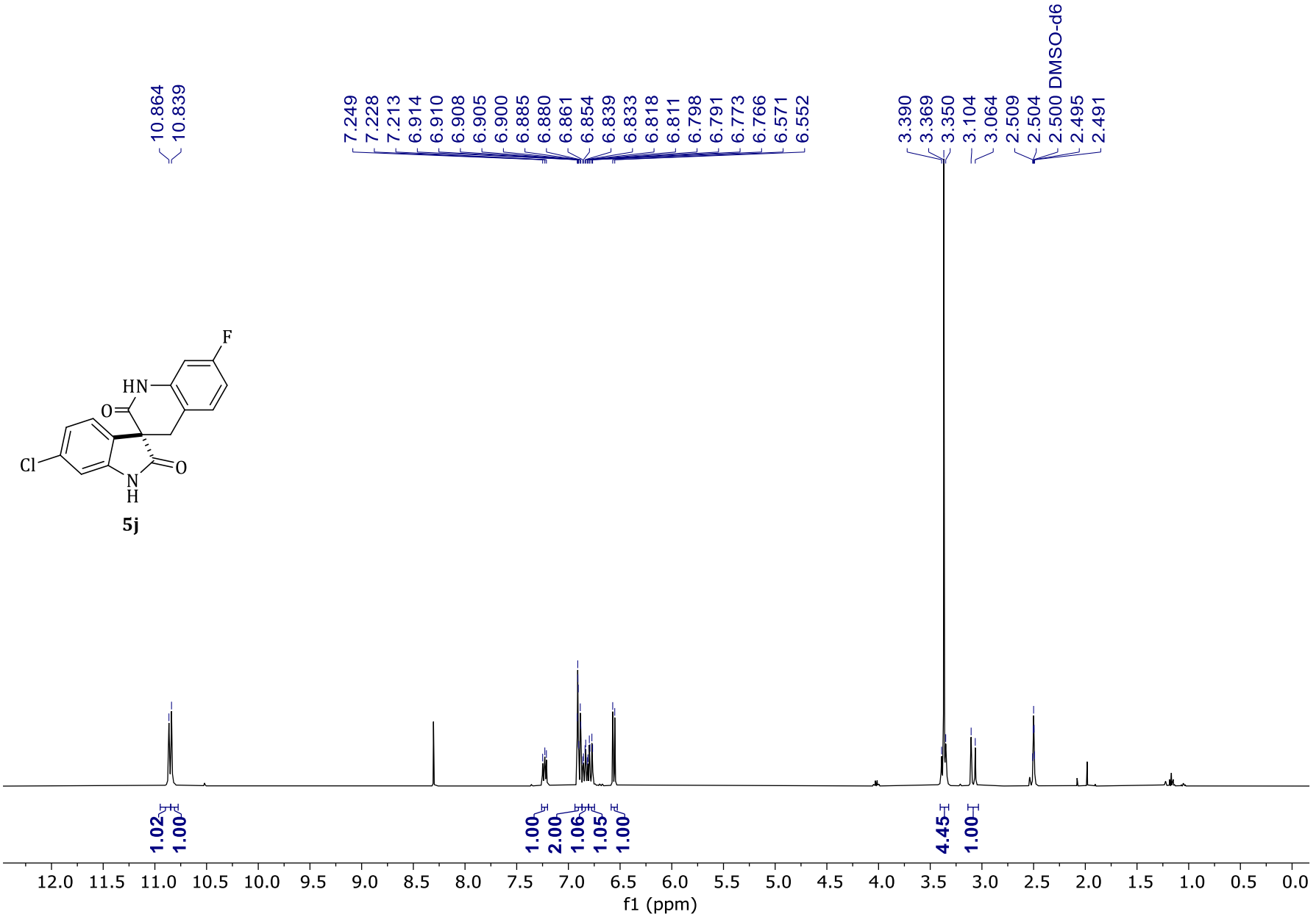
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5h**.



^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5i.**

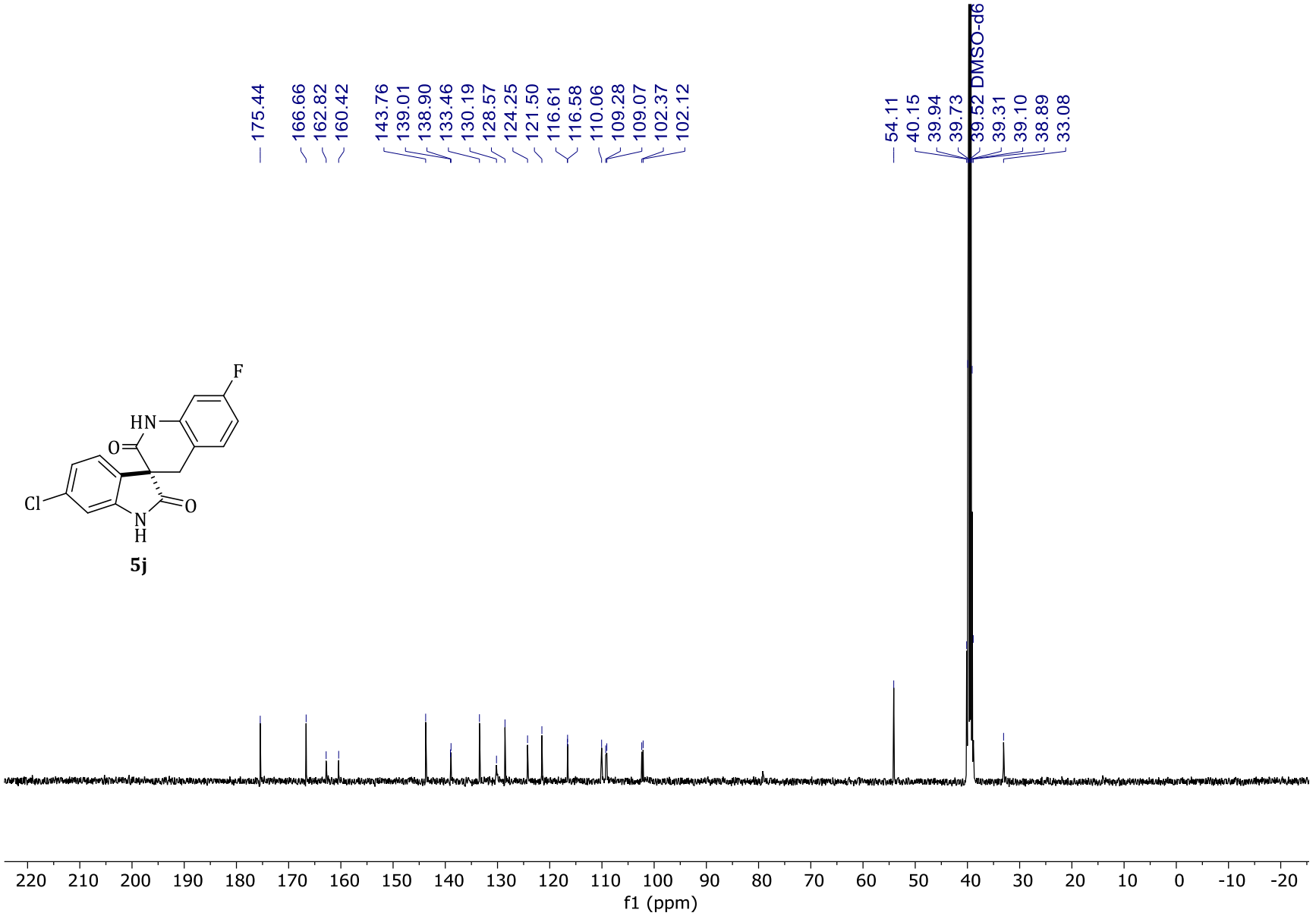


^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5i.**



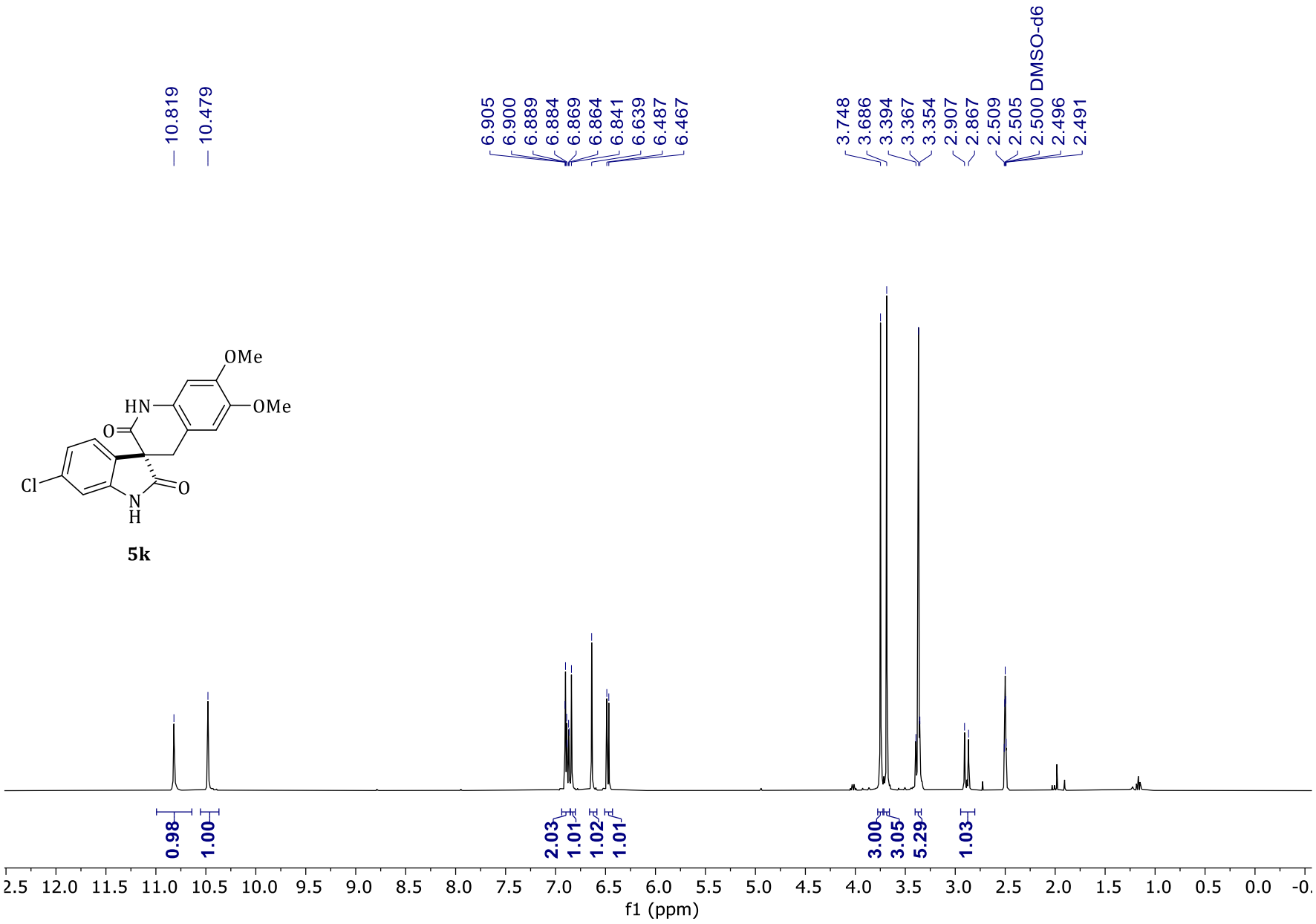
5j

^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5j**.



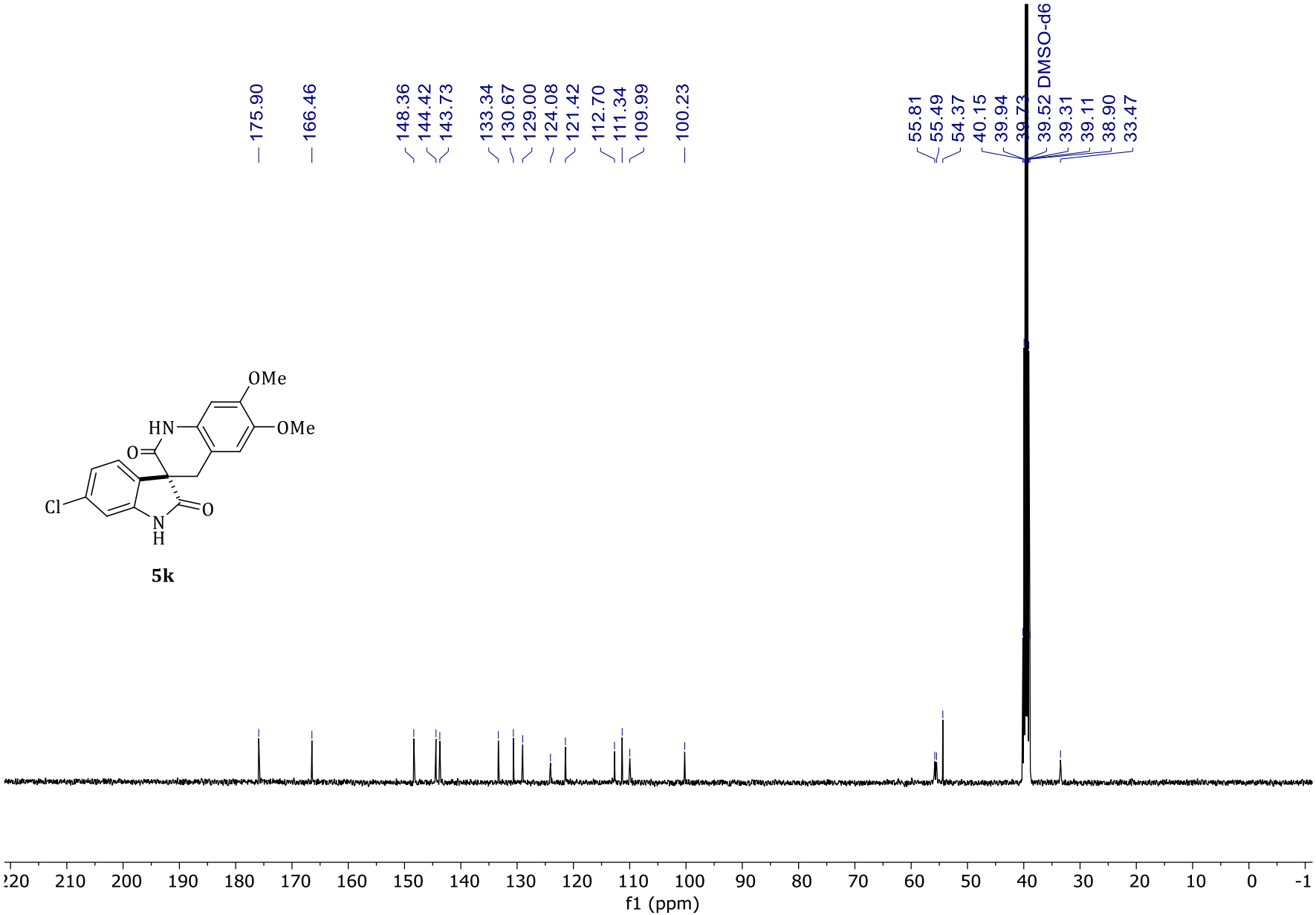
5j

^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5j.**



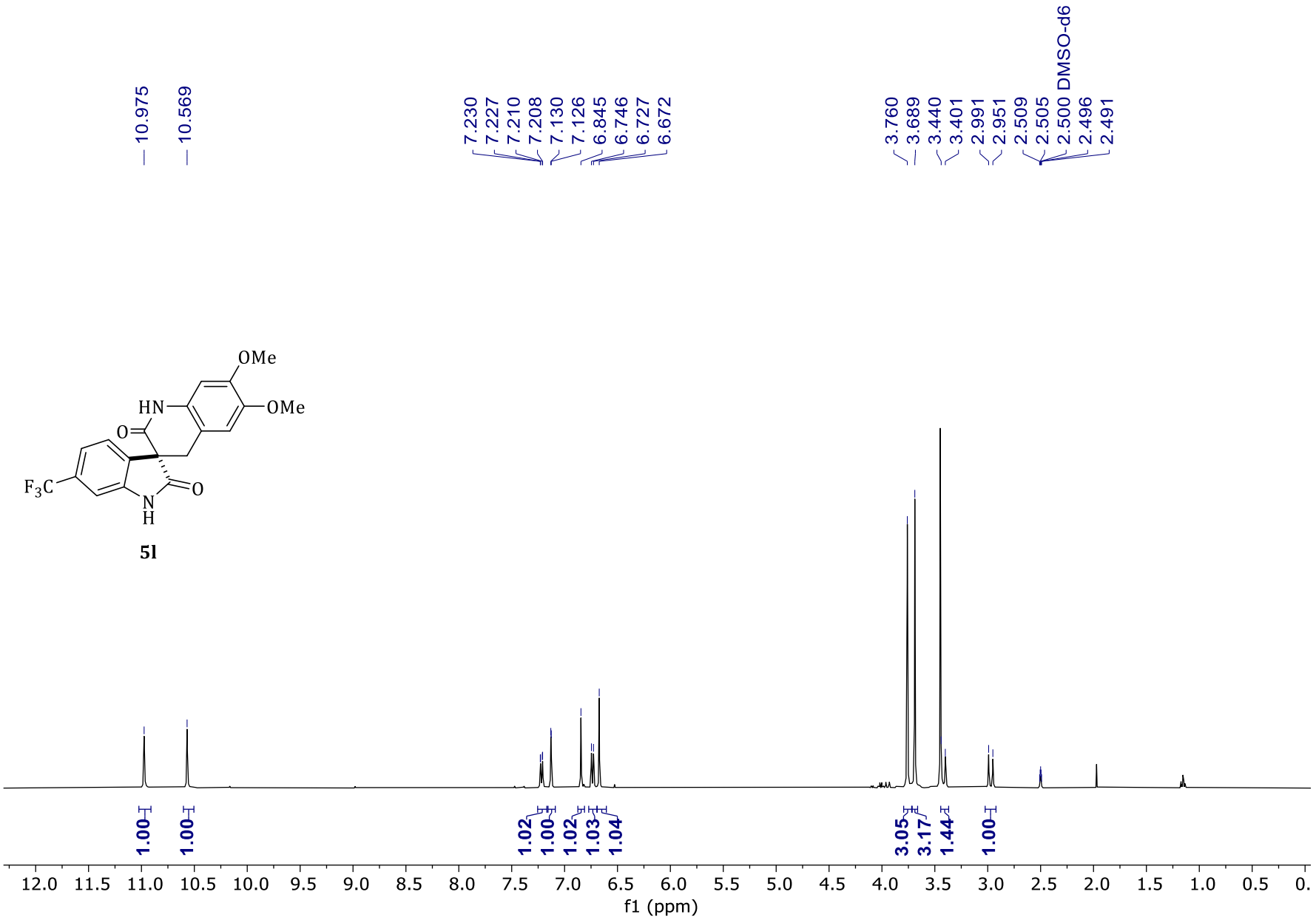
5k

^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5k.**

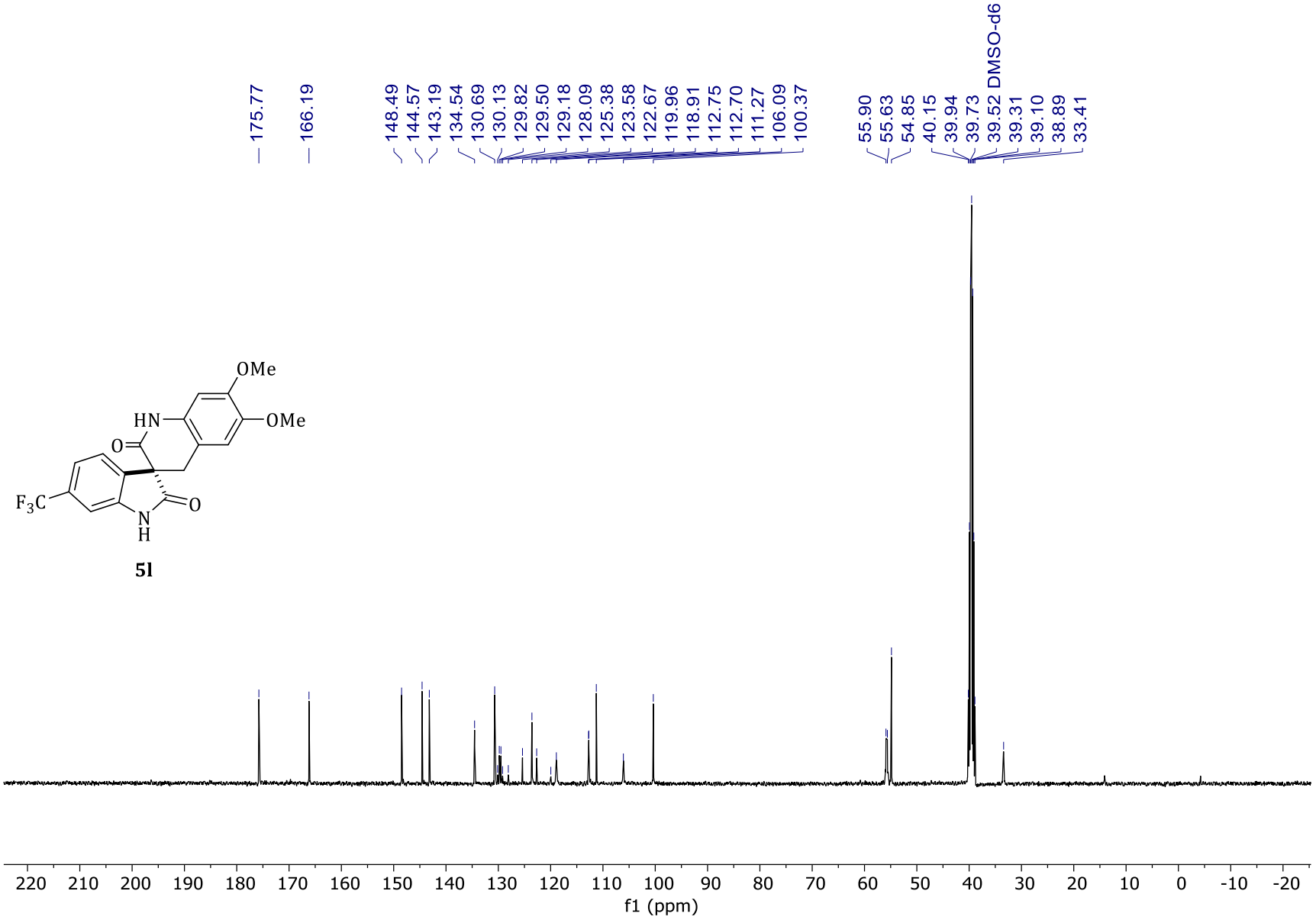


5k

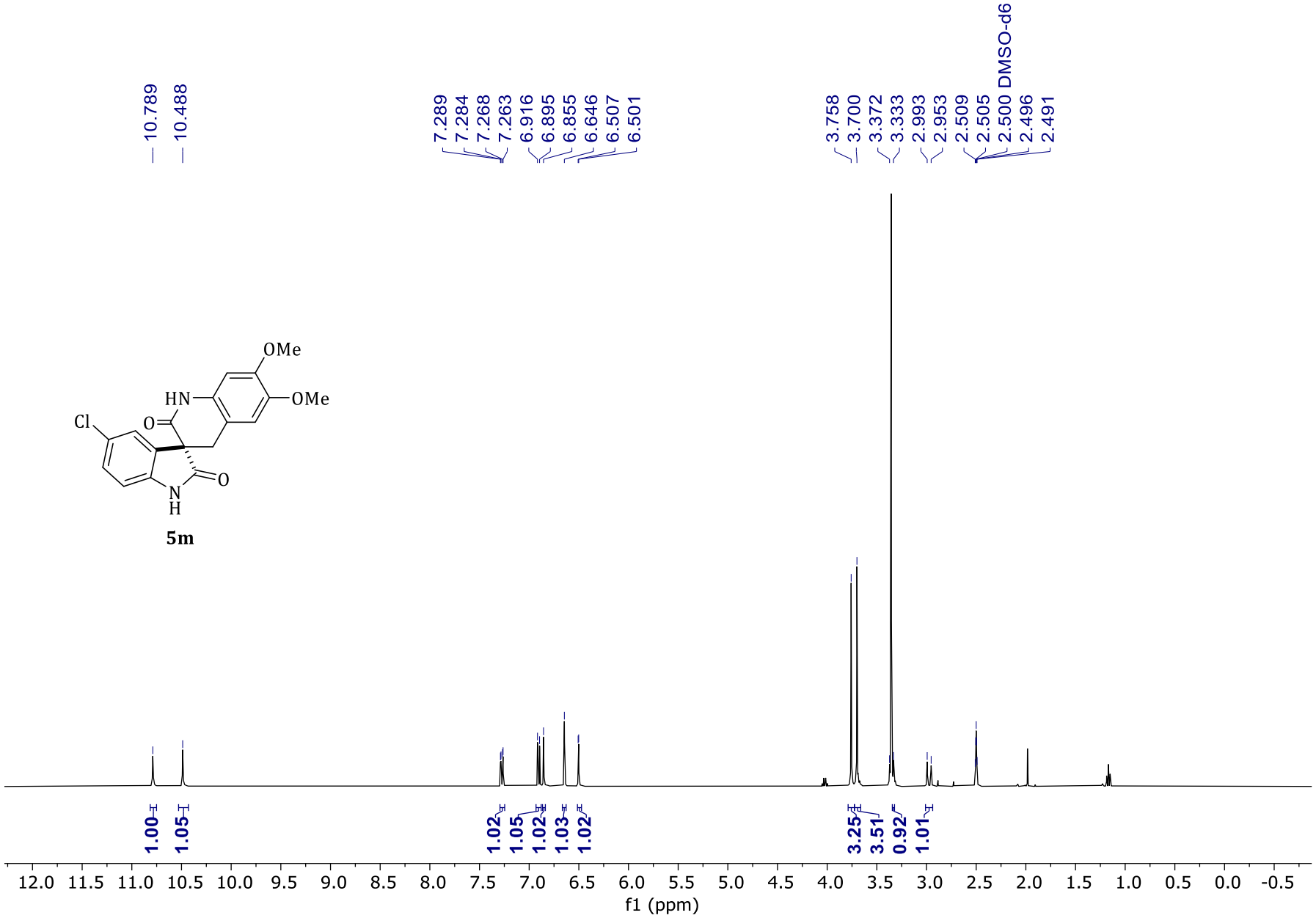
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5k.**



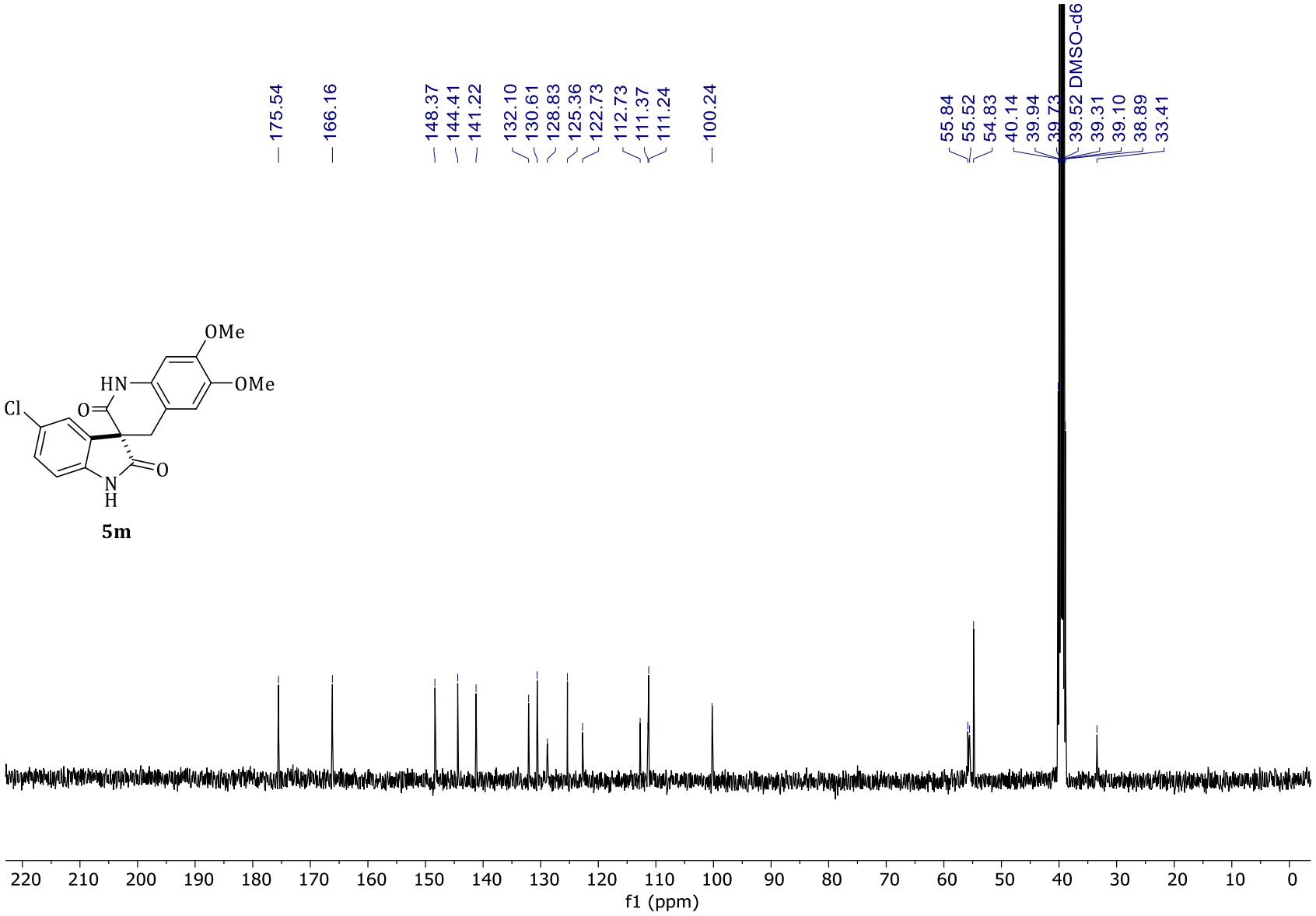
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5l.**



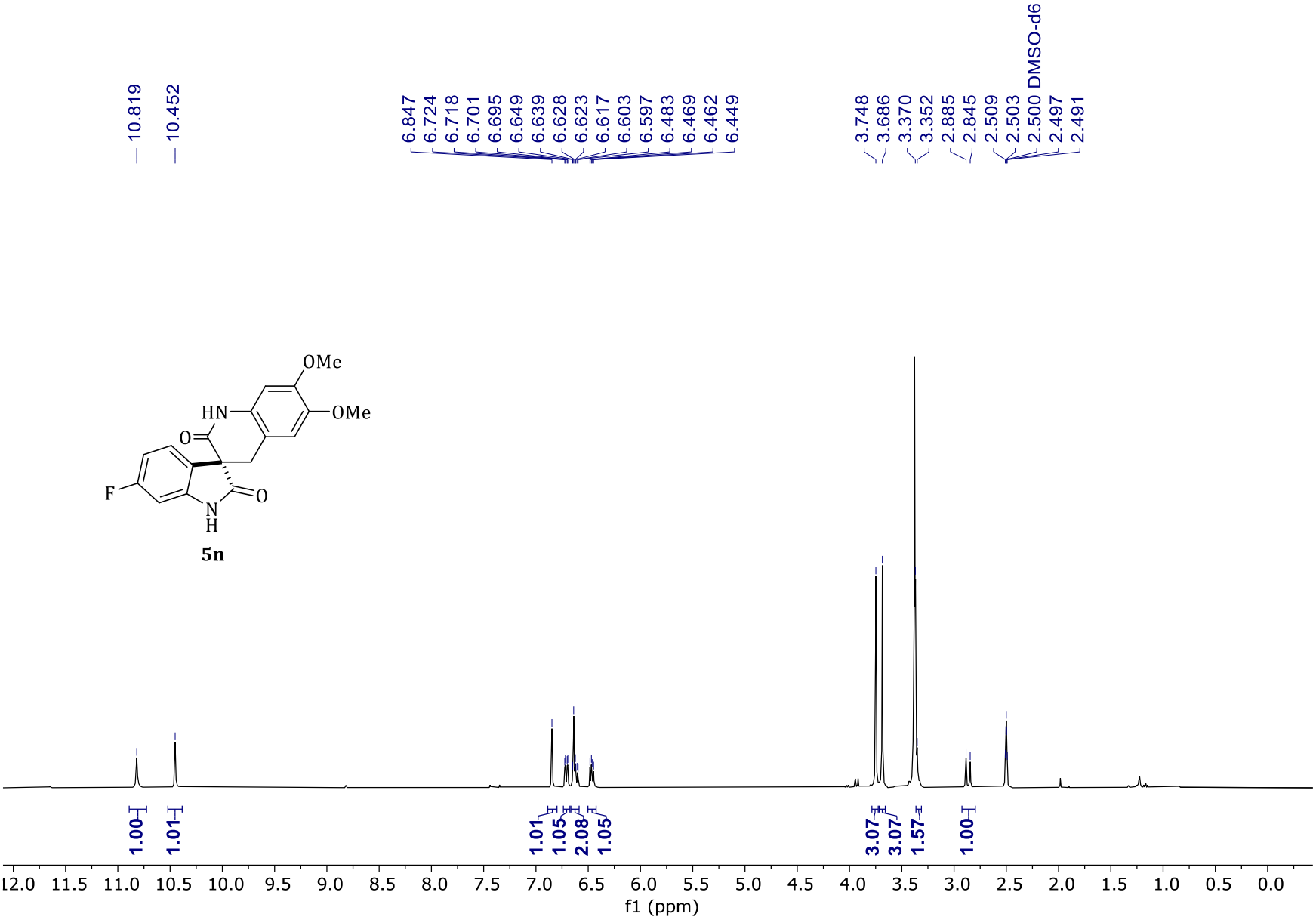
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5l.**



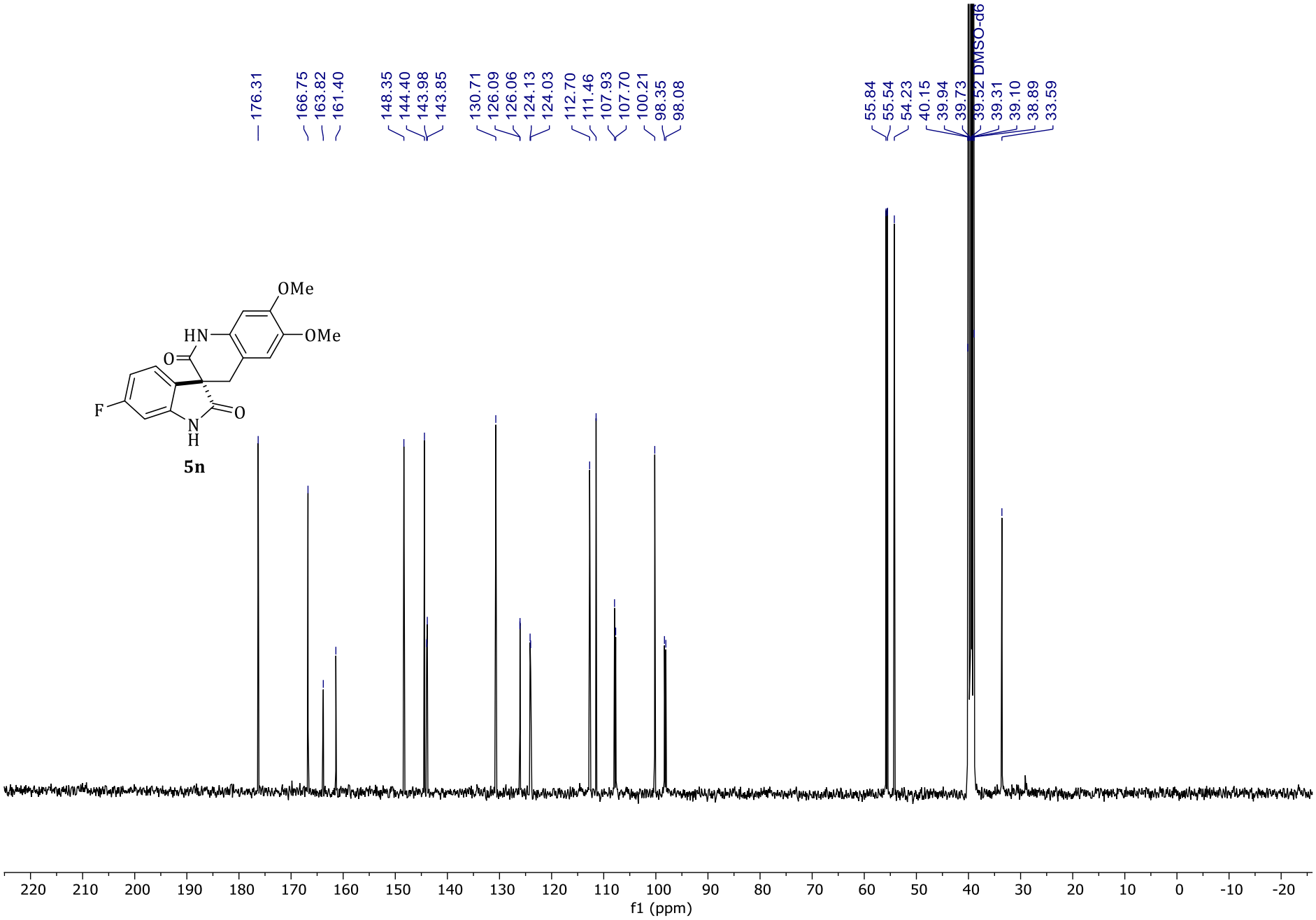
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5m.**



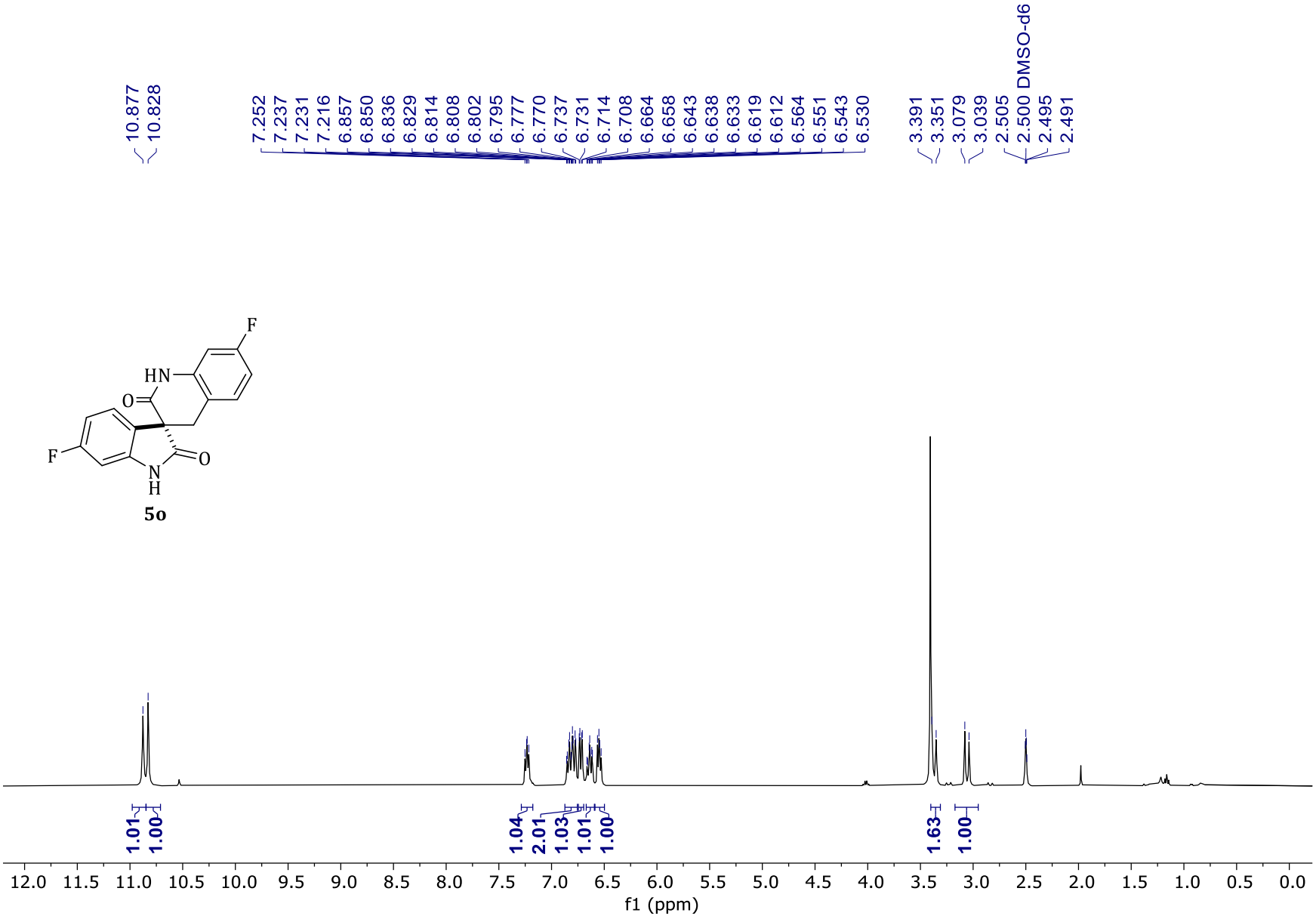
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5m.**



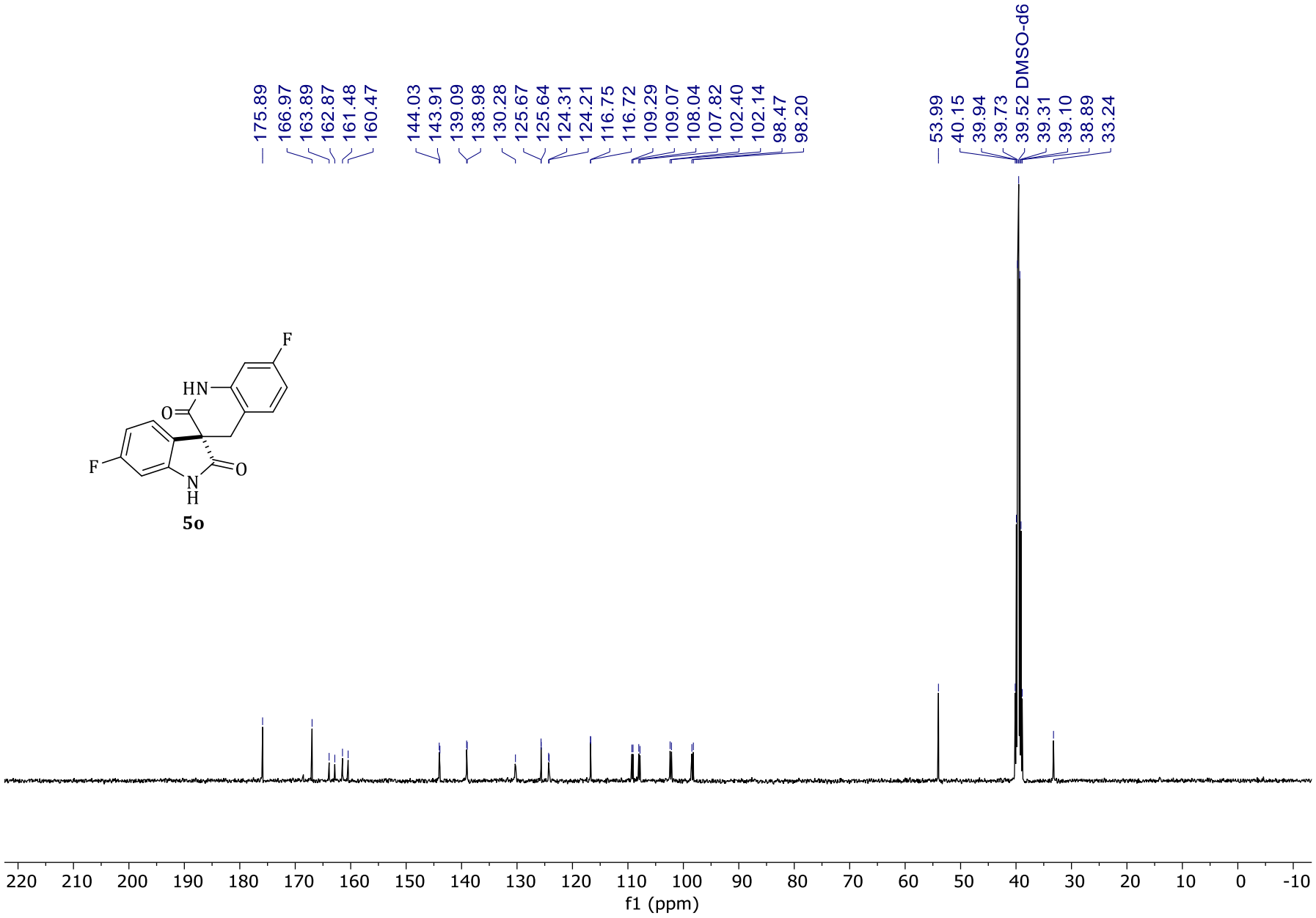
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5n.**



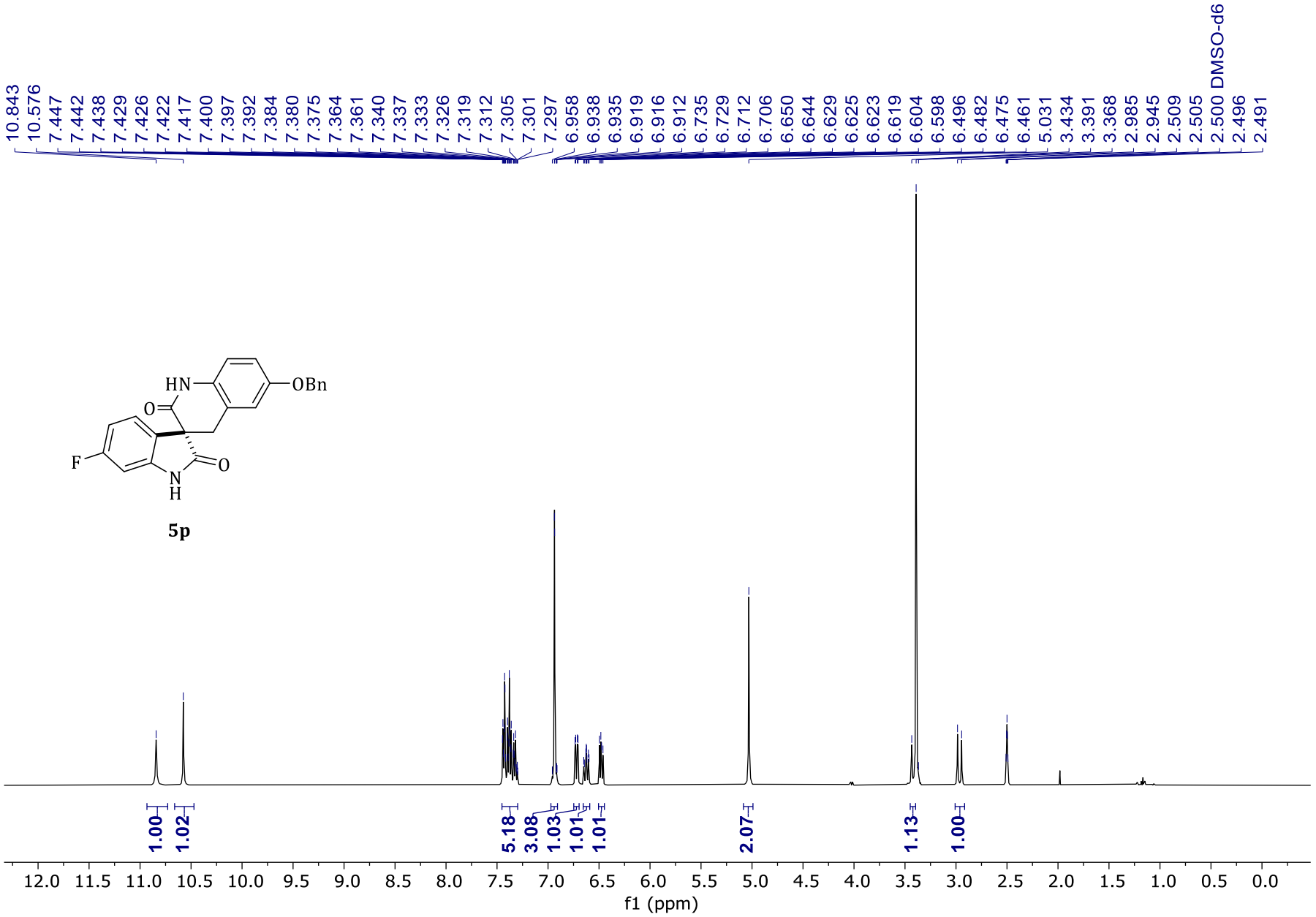
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5n.**



^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5o.**

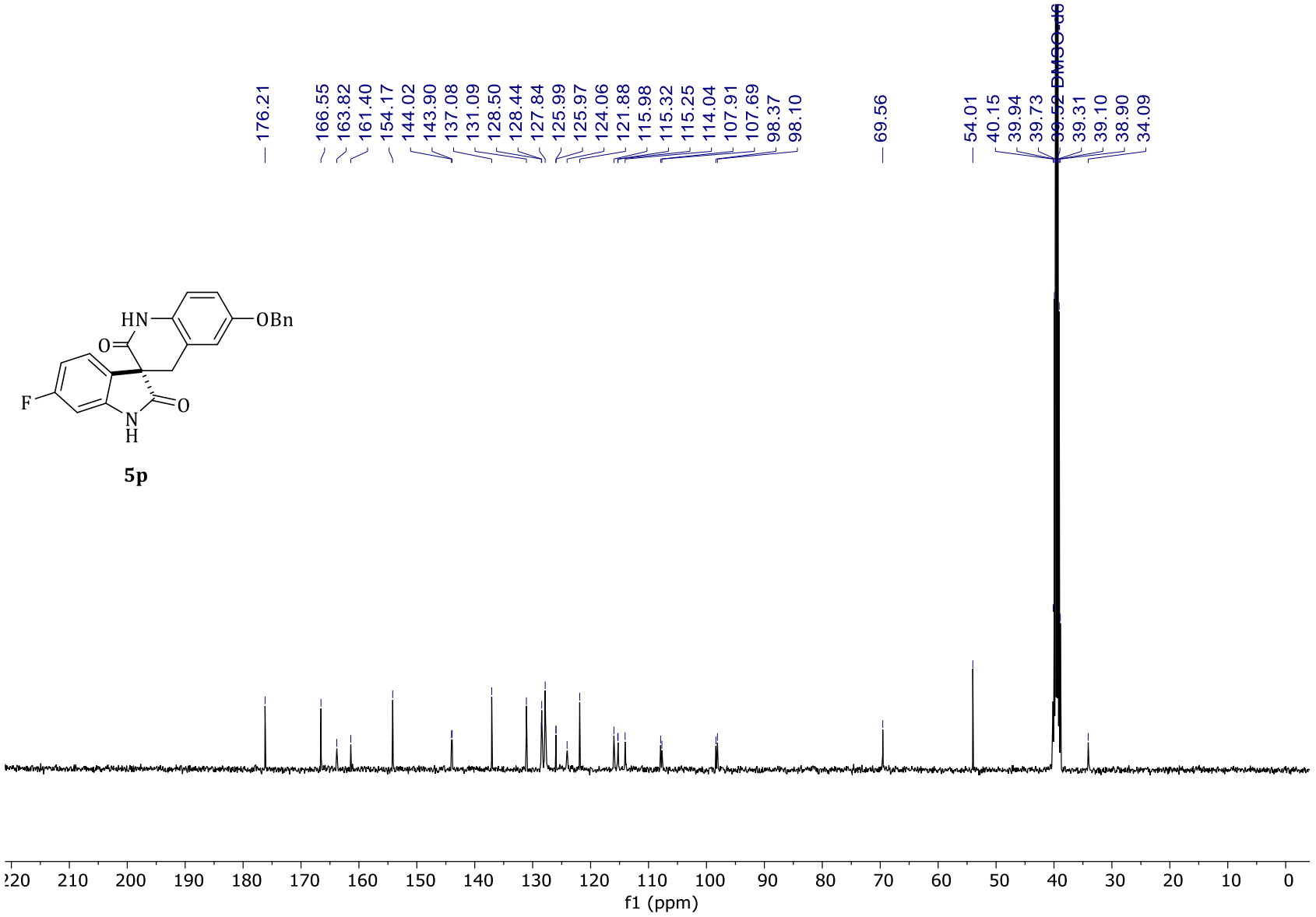


^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5o**.

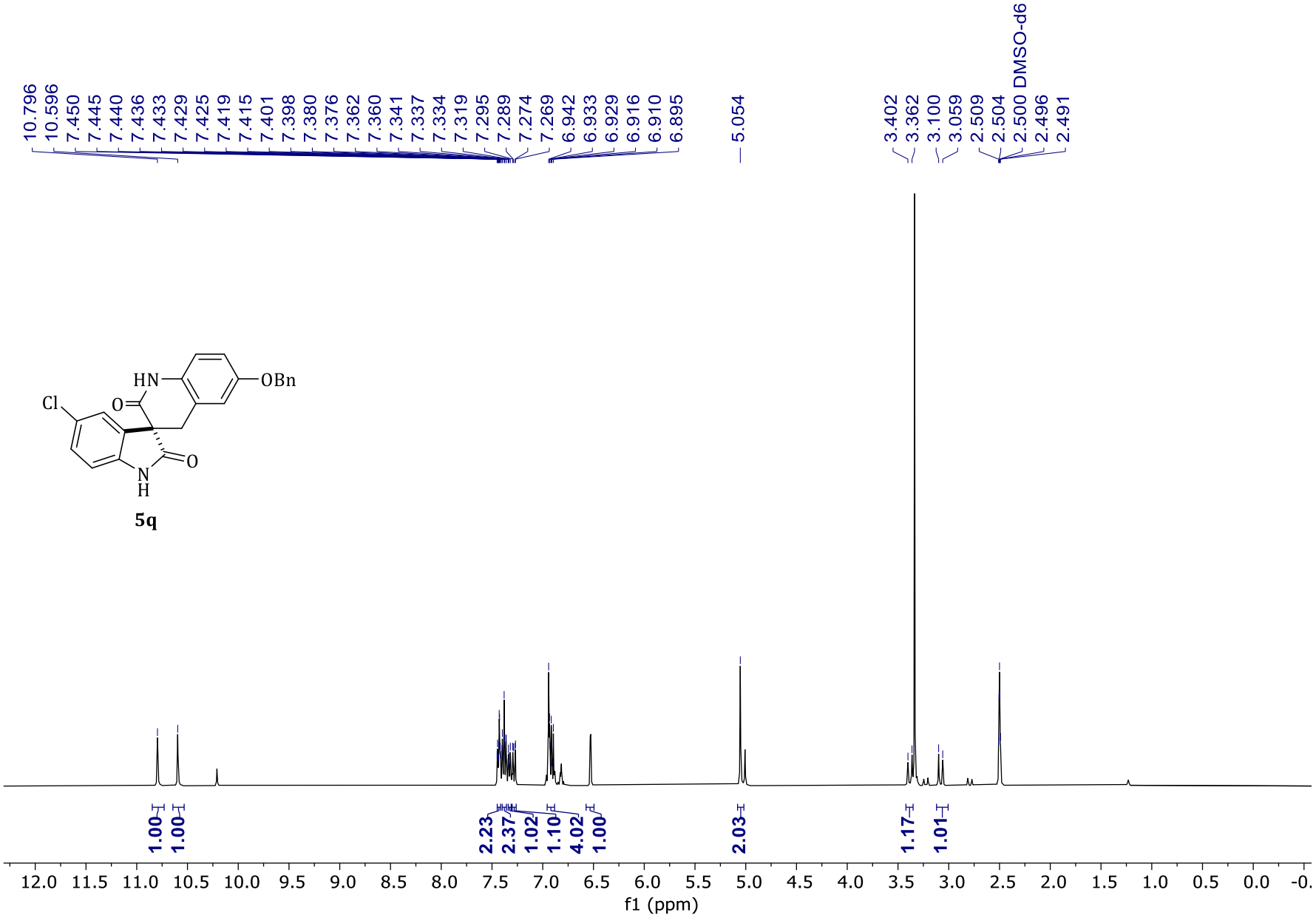


5p

^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5p.**

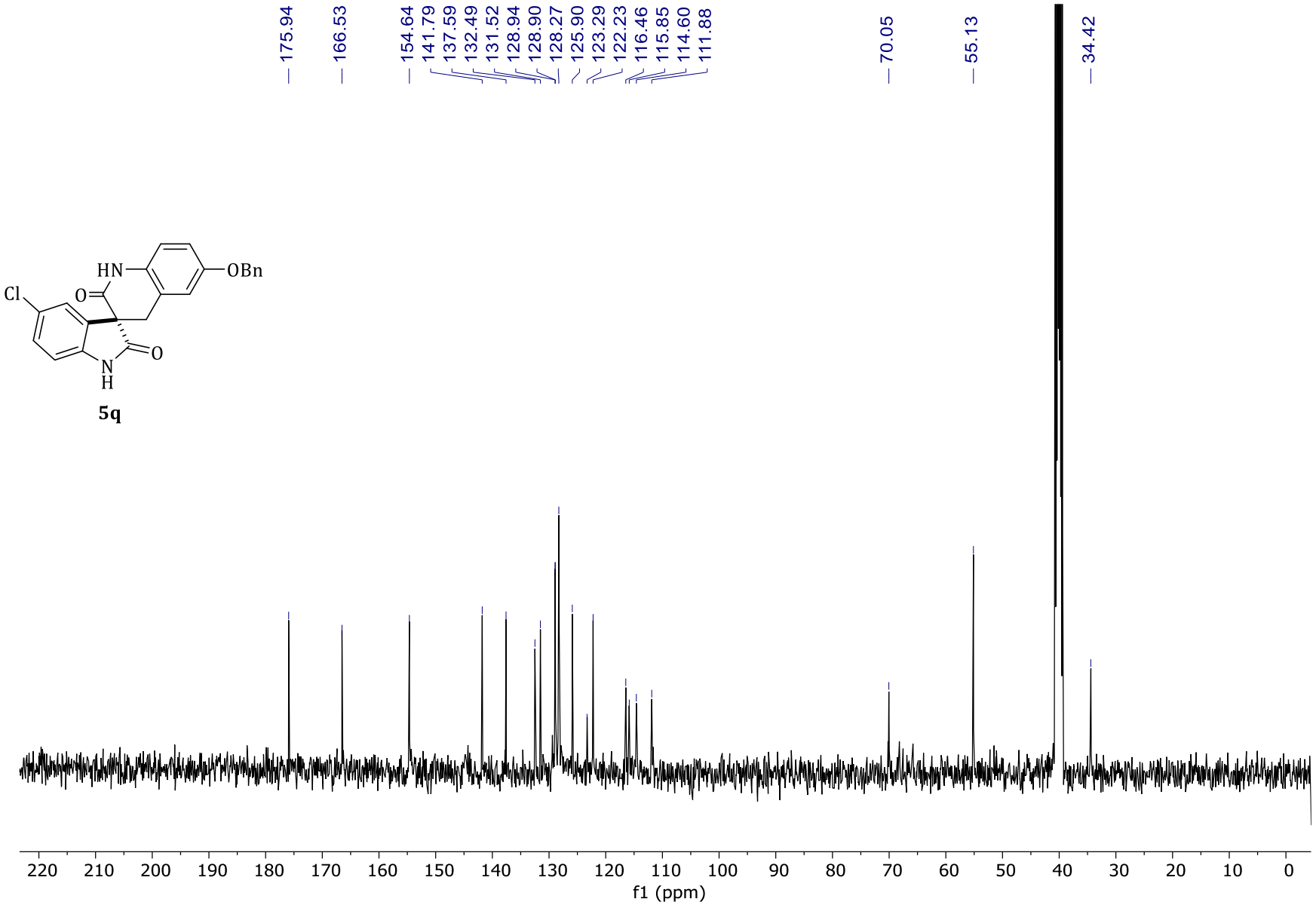


^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5p.**

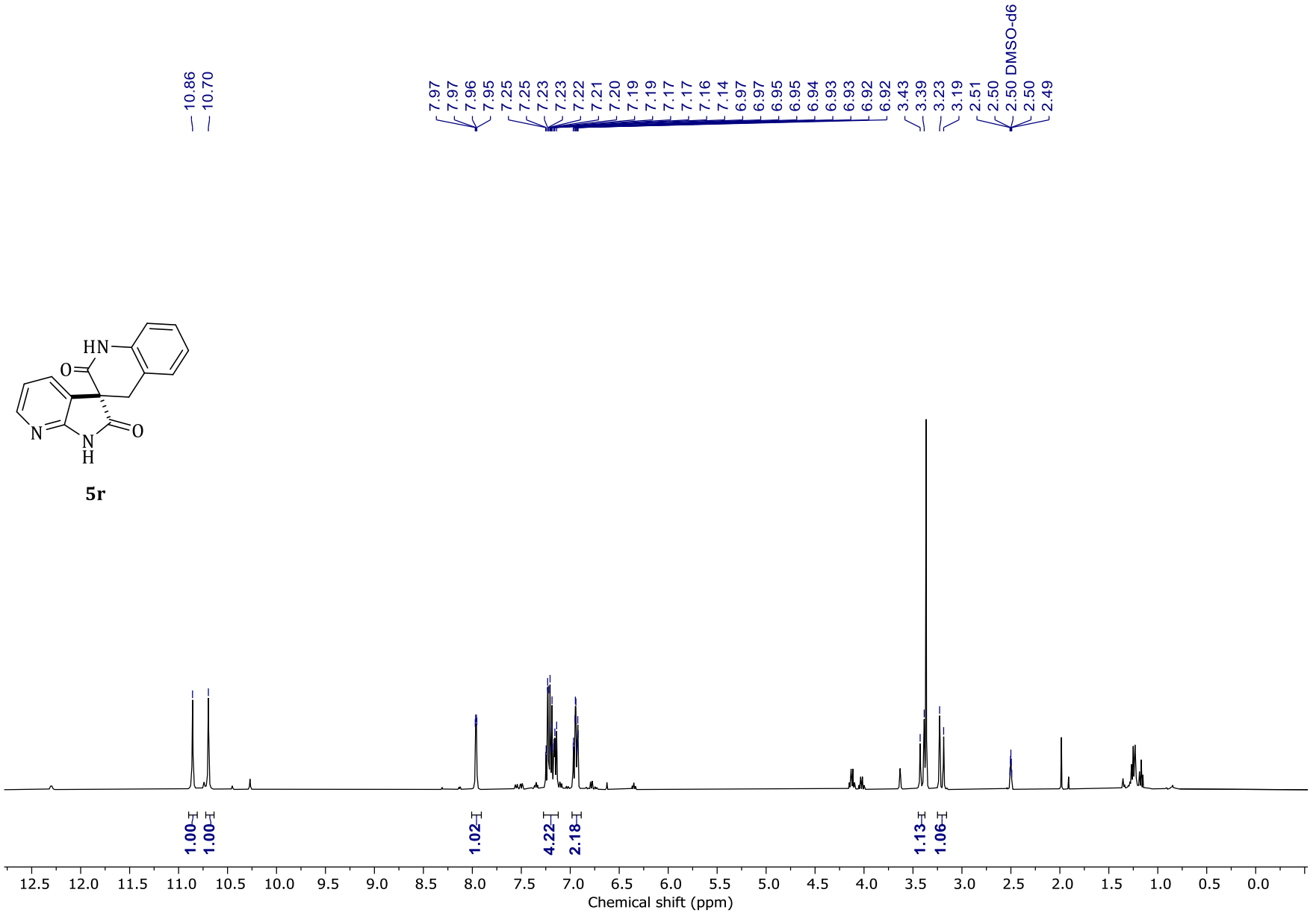


5q

^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5q.**

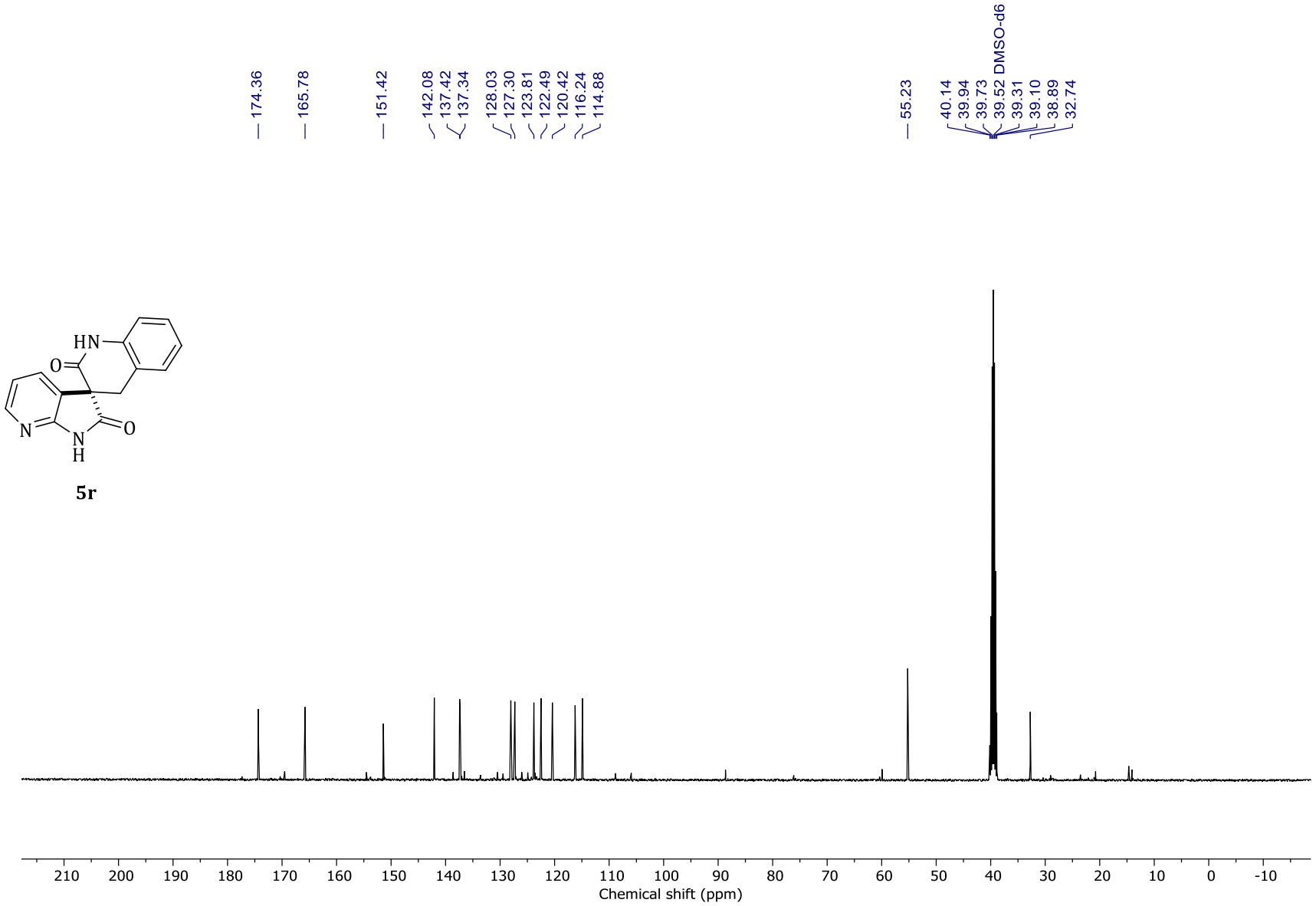


^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5q.**



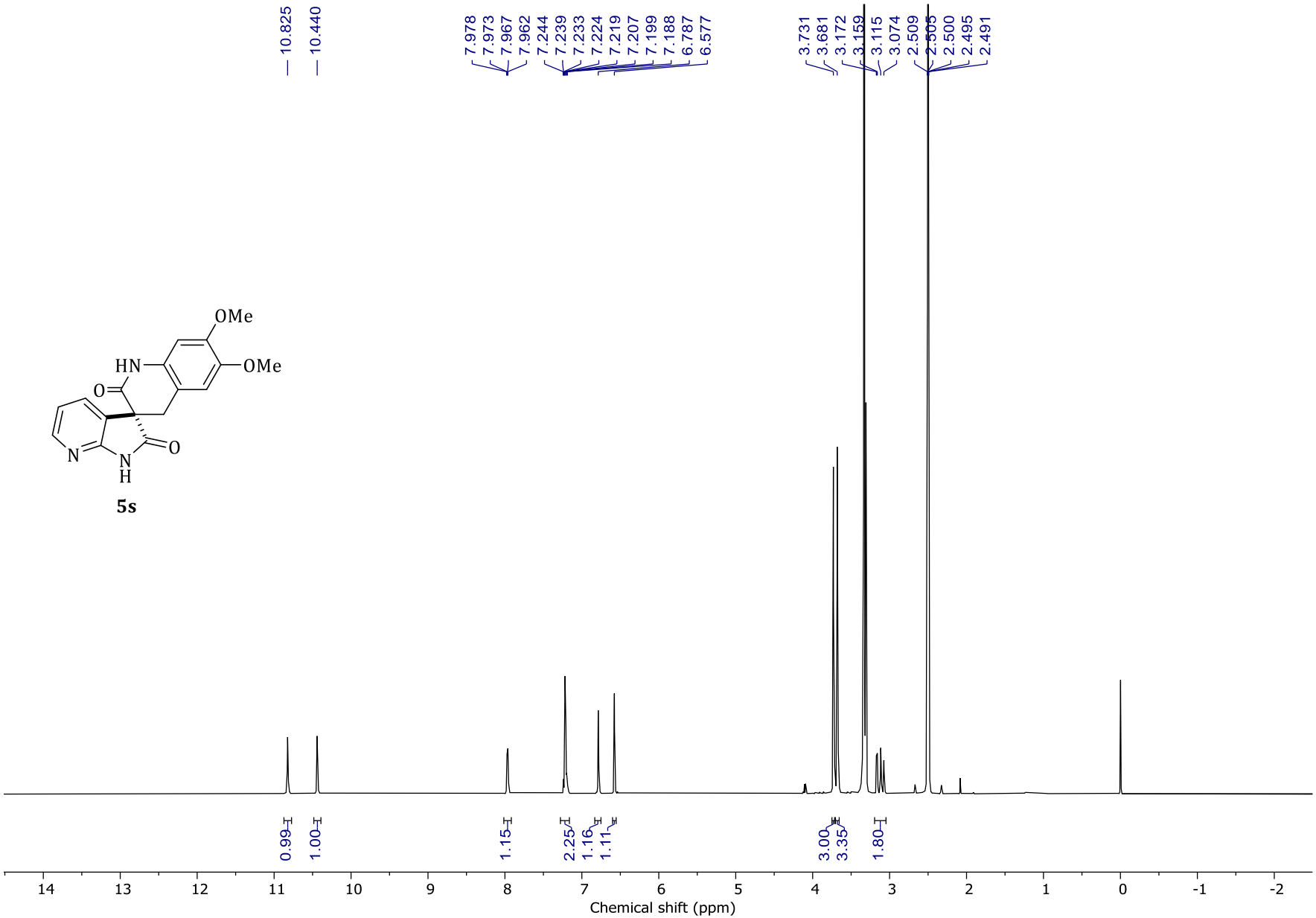
5r

^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5r.**

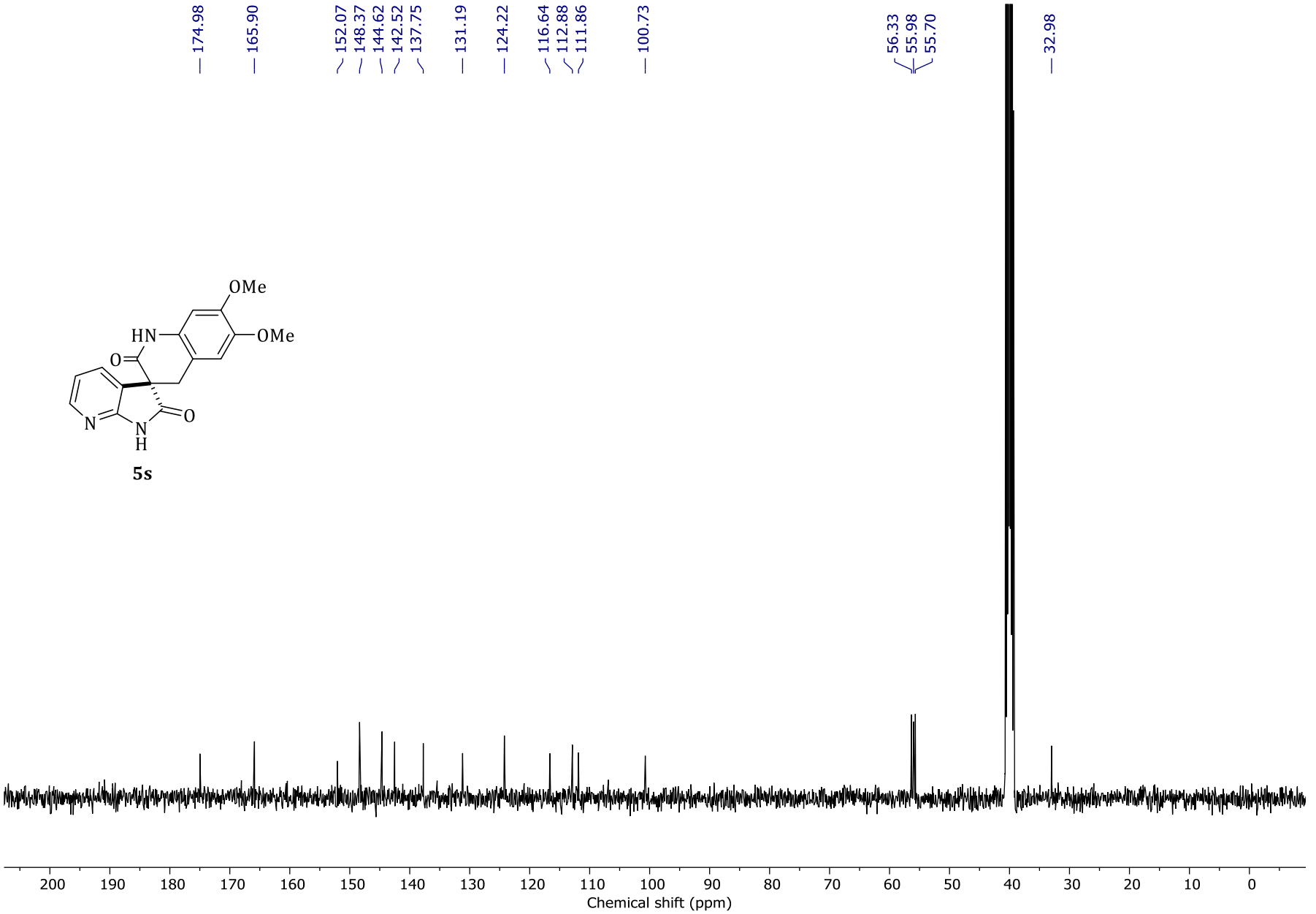


5r

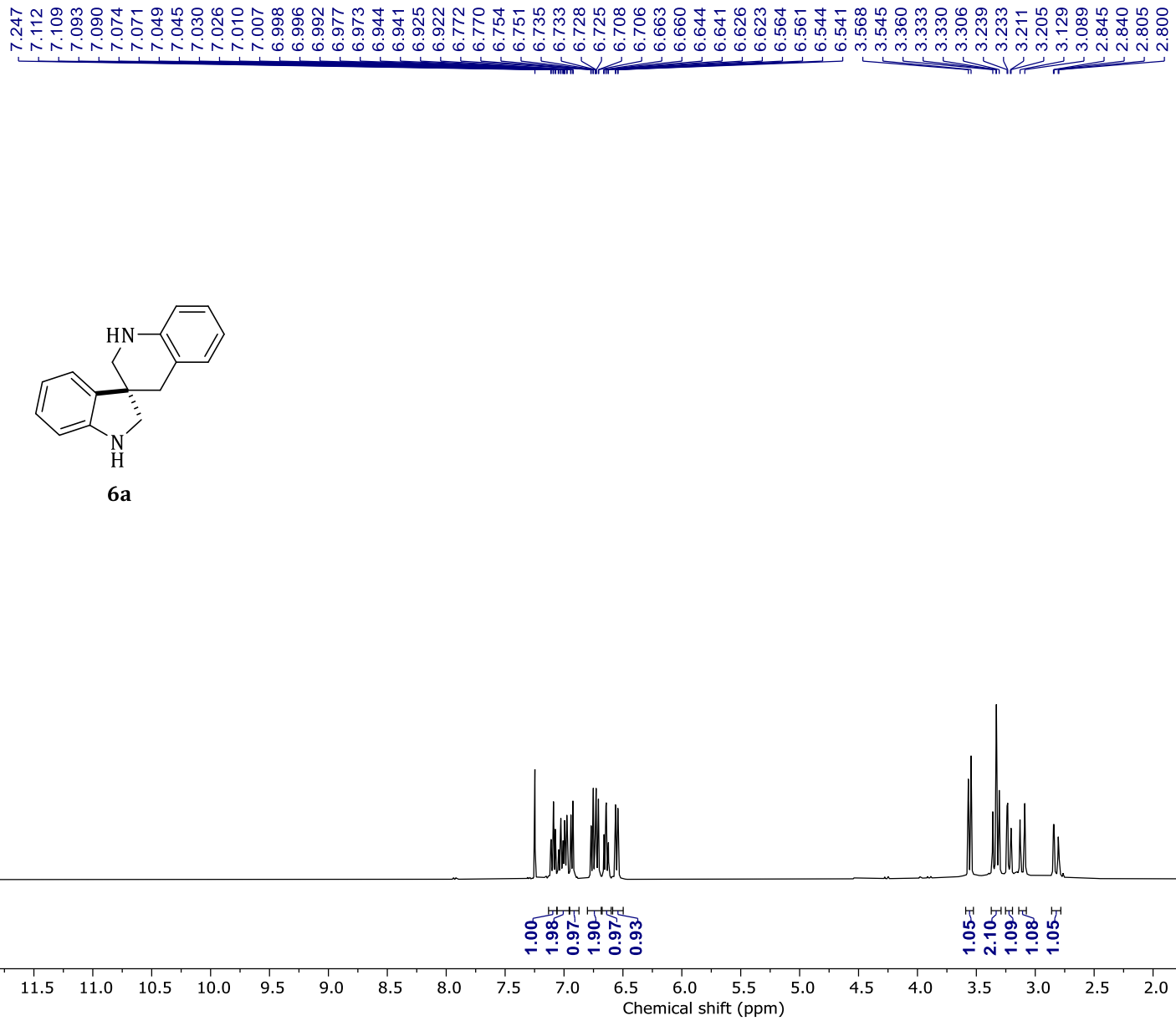
^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5r.**



^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **5s.**

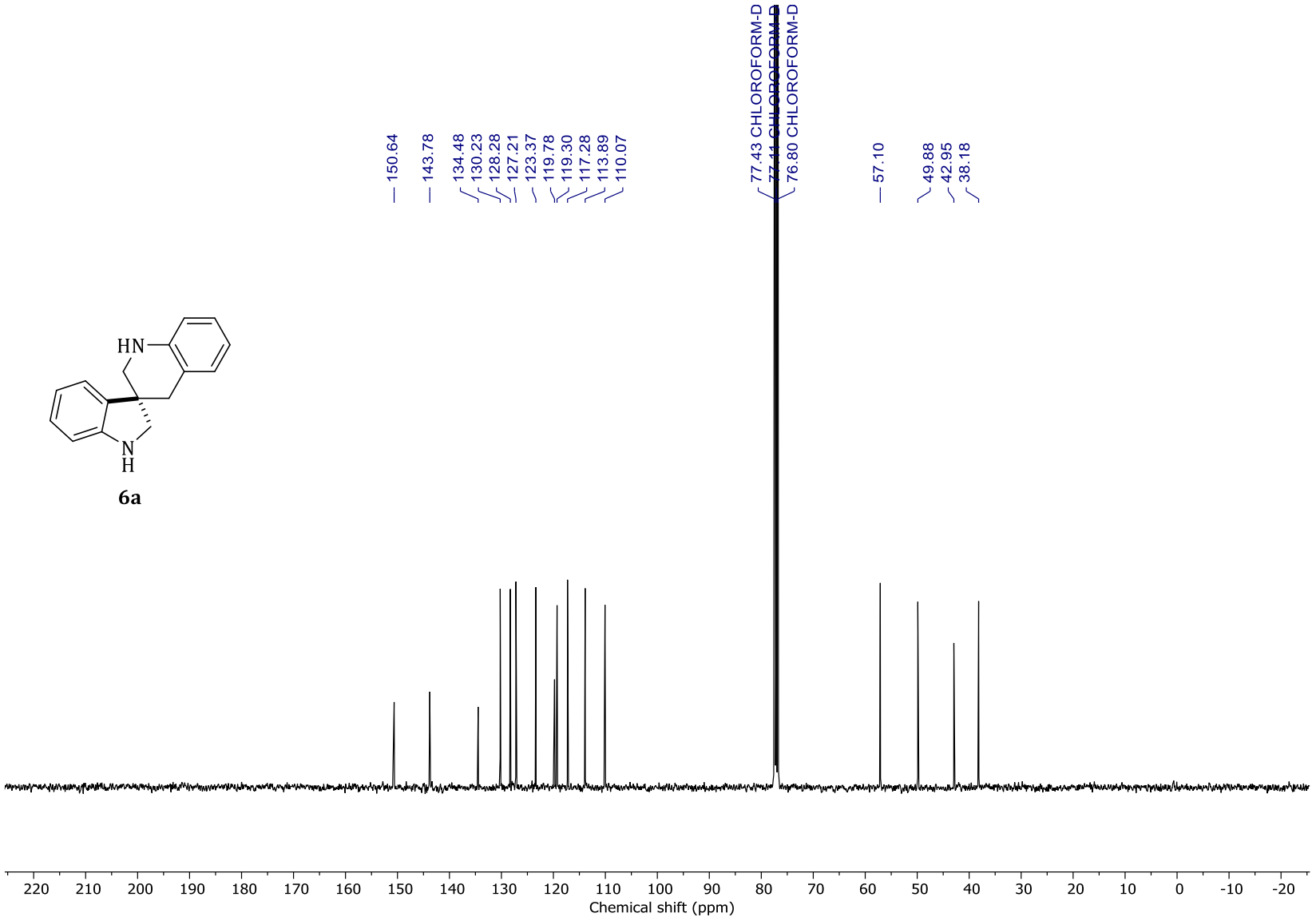


^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **5s.**

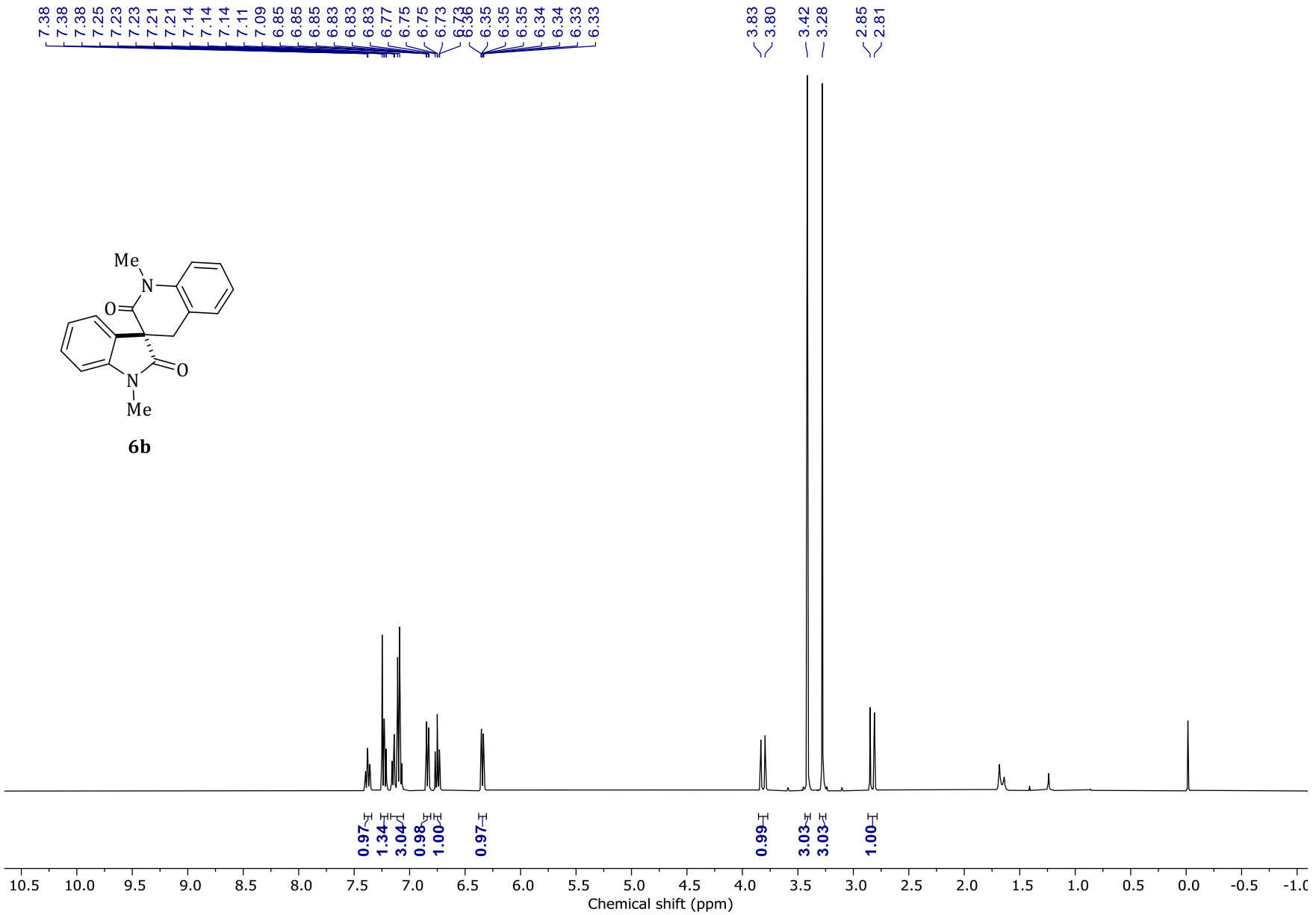


6a

^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **6a.**

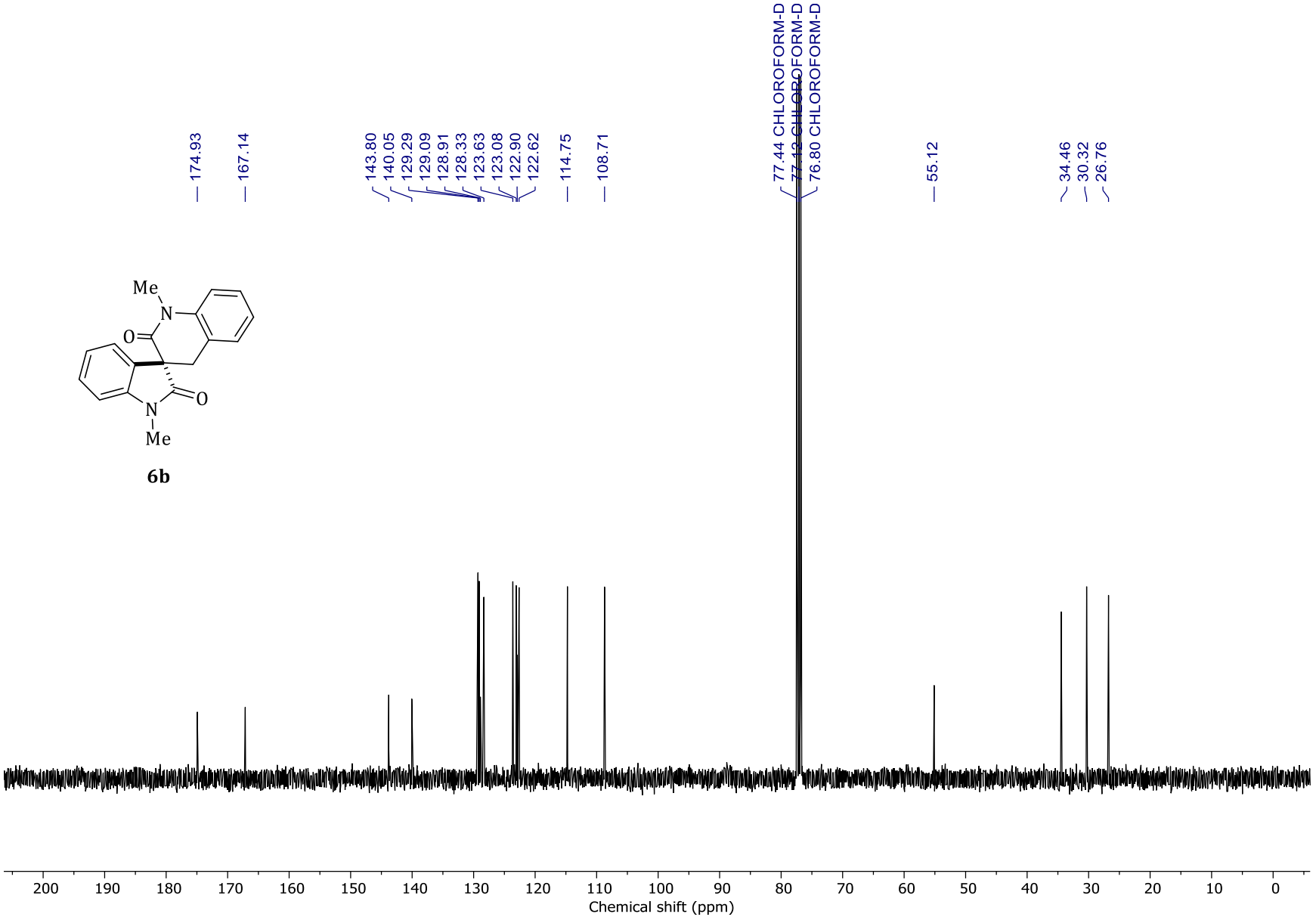


^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound **6a.**

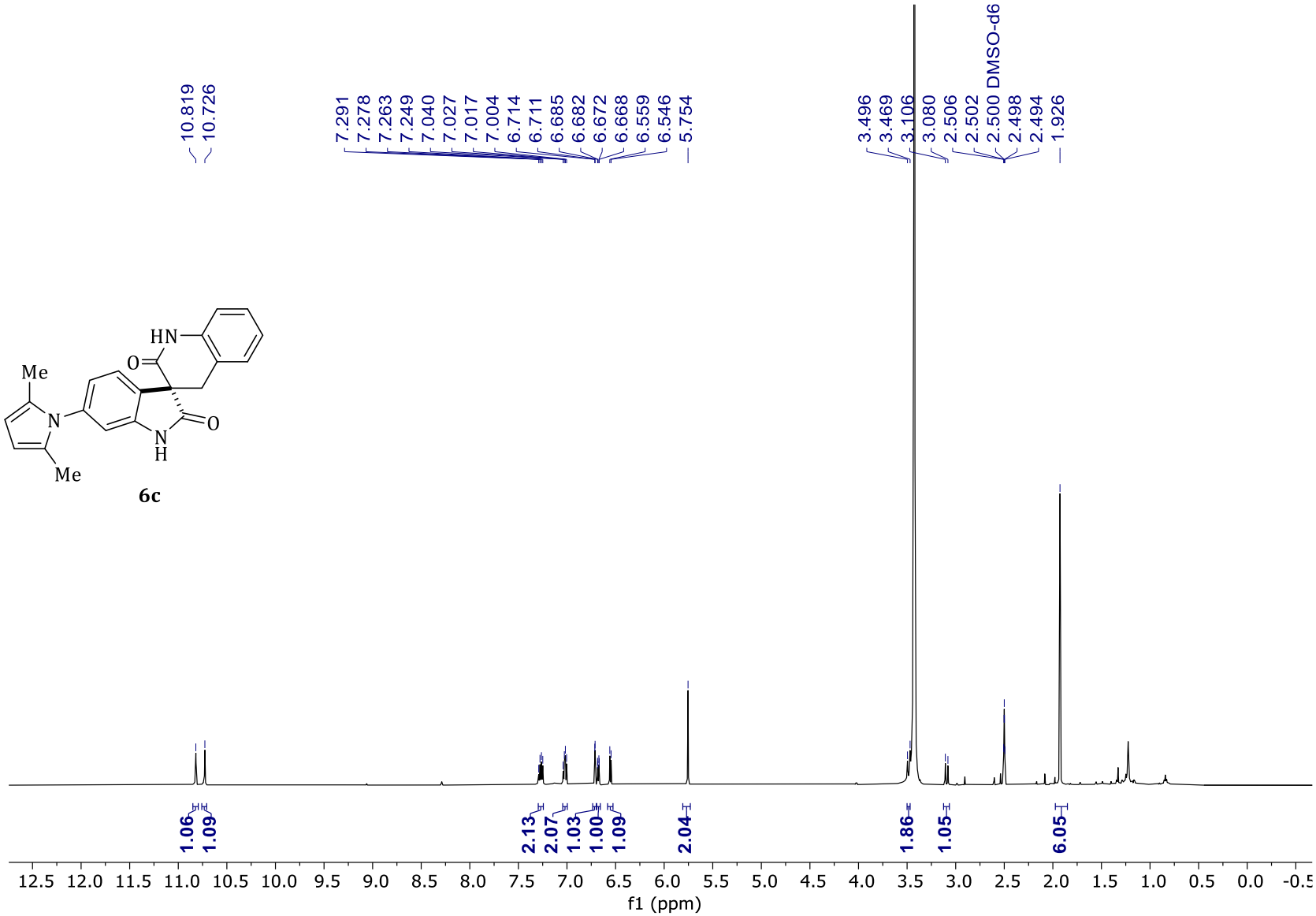


6b

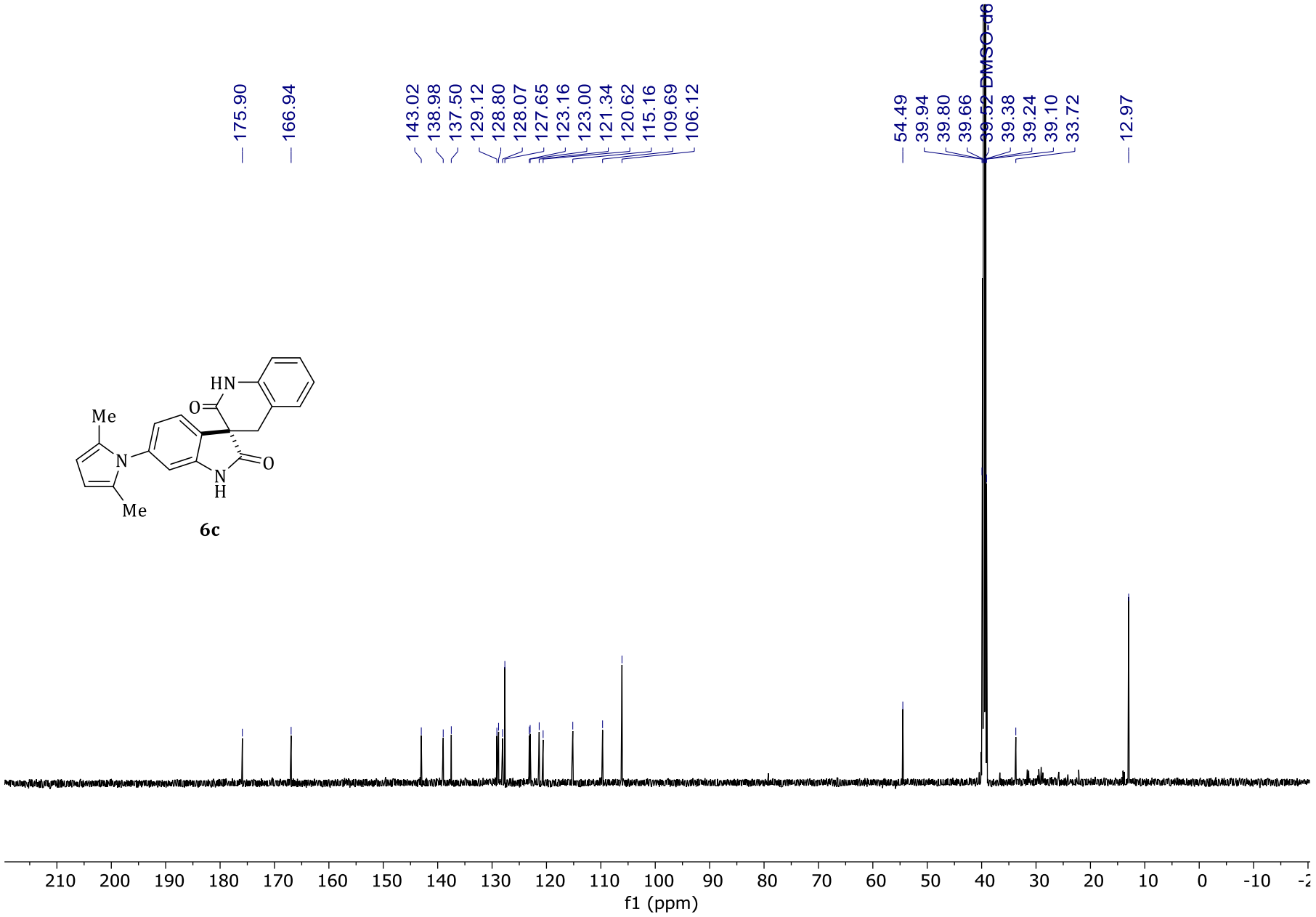
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **6b.**



^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of compound **6b.**



^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **6c.**



^{13}C NMR (DMSO-d_6, 100 MHz) spectrum of compound **6c.**