Supporting Information

A Biomimetic Approach to Lycogarubin C, Lynamicin D and Related Analogues

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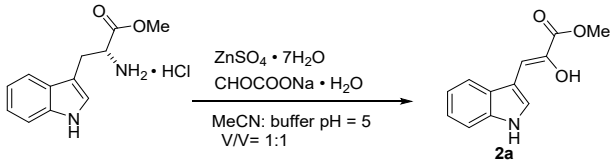
Column chromatographic purifications were performed on SDZF silica gel 160. ^{1}H, ^{13}C and ^{19}F NMR spectra were obtained on a Bruker NMR spectrometer at 600 MHz, 150 MHz and 565 MHz, respectively, referenced internally based on the residual solvent signal. The data reported for the ^{1}H NMR spectra are as follows: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; and m, multiplet), coupling constant in hertz, and number of protons. The data reported for the ^{13}C spectra are given as chemical shift (δ, ppm). The data reported for the ^{19}F spectra are given as chemical shift (δ, ppm). High-resolution mass spectra (HRMS) were obtained on an Agilent mass spectrometer by electrospray ionization-time of flight (ESI-TOF) analysis. Melting points were measured with a melting point instrument without correction. All the chemical reagents and solvents were purchased from commercial sources and used as received.

1. Experimental and spectroscopic data for compounds **2a-d**, **3e-i**, **2e-i**, **1a-z** and **II**: **Page S2-16**.

1.1 Synthesis of compounds **2a-d**

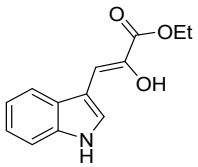


2a

To a solution of *L*-tryptophan methyl ester hydrochloride (6.0 g, 23.56 mmol) in 70 mL of MeCN and 70 mL of buffer (pH=5, containing 6.6 g sodium acetate and 1.2 mL acetic acid) were added $ZnSO_4 \cdot 7H_2O$ (3.39 g, 11.78 mmol), $CHOCOONa \cdot H_2O$ (4.16 g, 28.27 mmol). The resulting mixture was stirred at room temperature for 5 h. Then H_2O was added to the reaction, the mixture was extracted with ethyl acetate, the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column silica gel chromatography (PE/EA=5:1) to give **2a** as a white solid (3.7 g, yield 72%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.46 (s, 1H), 9.02 (d, J = 1.5 Hz, 1H), 7.92 (d, J = 2.6 Hz, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.45-7.40 (m, 1H), 7.15 (t, J = 7.4 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 6.85 (s, 1H), 3.80 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.2, 137.3, 135.6, 127.6, 126.4, 121.8, 119.5, 118.1, 111.7, 109.5, 104.9, 52.1. The NMR data is consistent with literature values.[1]

Compounds **2b-c** were also prepared from commercially available *L*-tryptophan ethyl ester hydrochloride (537 mg, 2.0 mmol) and *L*-tryptophan benzyl ester hydrochloride (661 mg, 2.0 mmol) following above procedure. Compound **2d** was prepared from 1-Me *L*-tryptophan methyl ester hydrochloride[2] (537 mg, 2.0 mmol).

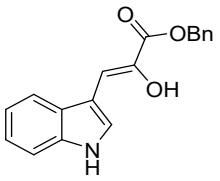
Ethyl (*Z*)-2-hydroxy-3-(1*H*-indol-3-yl)acrylate (2b)



Purification by flash column silica gel chromatography (PE/EA=4:1) to give **2b** as a white solid (380 mg, yield 82%). m.p. 140.1-141.4 °C. IR (KBr) 3382, 1683, 1645, 1398, 1337, 1227, 771, 753 cm^{-1}. H NMR (600 MHz, DMSO-d_6) δ 11.45 (s, 1H), 8.96 (s, 1H), 7.90 (d, J = 2.6 Hz, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.44-7.39 (m, 1H), 7.14 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.08 (ddd, J = 8.0, 7.0, 1.1 Hz, 1H), 6.82 (s, 1H), 4.25 (q, J = 7.1 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150MHz, DMSO-d_6) δ 164.7, 137.5, 135.6, 127.6, 126.4, 121.8, 119.5, 118.2, 111.7, 109.6, 104.6, 60.7, 14.3. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{13}NO_3Na$ 254.0787; found 254.0778.

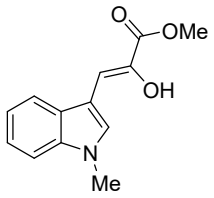
Benzyl (*Z*)-2-hydroxy-3-(1*H*-indol-3-yl)acrylate (2c)

Purification by flash column silica gel chromatography (PE/EA=4:1) to give **2c** as a white solid (530 mg,



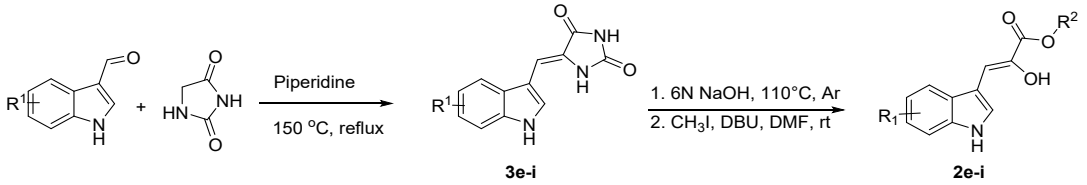
yield 90%). m.p.161.3-162.5 °C. IR (KBr) 3450, 3384, 1674, 1516, 1388, 1275, 1206, 768, 750 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 11.46 (s, 1H), 9.04 (s, 1H), 7.92 (d, J = 2.6 Hz, 1H), 7.70 (dd, J = 8.0, 1.0 Hz, 1H), 7.50-7.45 (m, 2H), 7.44-7.39 (m, 3H), 7.38-7.33 (m, 1H), 7.14 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.07 (ddd, J = 8.0, 7.0, 1.1 Hz, 1H), 6.91-6.88 (m, 1H), 5.31 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.6, 137.2, 136.4, 135.6, 128.5, 128.0, 127.9, 127.8, 126.3, 121.8, 119.5, 118.1, 111.7, 109.5, 105.3, 66.0. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{15}NO_3Na$ 316.0944; found 316.0932.

Methyl (*Z*)-2-hydroxy-3-(1-methyl-1*H*-indol-3-yl)acrylate (2d)



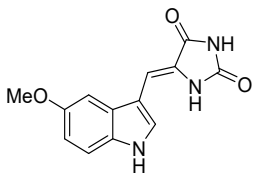
Purification by flash column silica gel chromatography (PE/EA=5:1) to give **2d** as white solid (402 mg, 87%). m.p. 184.1-184.9 °C. IR (KBr) 1698, 1646, 1558, 1506, 1472, 1232, 732 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 9.10 (s, 1H), 7.89 (s, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.45 (d, J = 8.2 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 7.4 Hz, 1H), 6.82 (s, 1H), 3.82 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.2, 137.4, 136.2, 131.7, 126.9, 122.0, 119.8, 118.4, 110.1, 108.8, 104.6, 52.1, 32.8. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{13}NO_3Na$ 254.0787; found 254.0775.

1.2 Synthesis of compounds **2e-i**



Indole-3-carboxaldehyde fragment (27.83 mmol) and hydantoin (2.79 g, 27.83 mmol) was dissolved in 15.0 mL piperidine. The mixture was refluxed at 150 °C using an oil bath and stirred for 5 h. After cooling to room temperature, the mixture was concentrated under reduced pressure. The residues were filtered and washed with methanol, dichloromethane and ethyl acetate to give **3**.

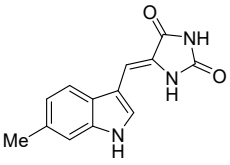
(*Z*)-5-((5-Methoxy-1*H*-indol-3-yl)methylene)imidazolidine-2,4-dione (3e)



5.6 g, yellow solid, yield 78%. m.p. 313.2-314.3 °C. IR (KBr) 3255, 1732, 1691, 1523, 1385, 1028, 755, 658 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 11.68 (s, 1H), 11.02 (s, 1H), 10.07 (s, 1H), 8.10-8.07 (m, 1H), 7.32-7.26 (m, 2H), 6.83-6.77 (m, 2H),

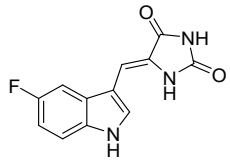
3.81 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.4, 155.3, 154.4, 130.7, 127.6, 127.2, 123.1, 112.7, 108.4, 102.4, 99.7, 55.4. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{11}N_3O_3Na$ 280.0692; found 280.0679.

(*Z*)-5-((6-Methyl-1*H*-indol-3-yl)methylene)imidazolidine-2,4-dione (3f)



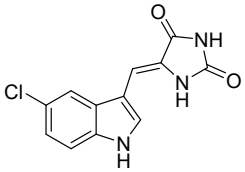
6.0 g, yellow solid, yield 90%. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.66 (s, 1H), 10.28(s, 2H), 8.05 (s, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.21 (s, 1H), 6.95 (dd, J = 8.2, 1.5 Hz, 1H), 6.72 (s, 1H), 2.40 (s, 3H). The NMR data is consistent with literature values.[3]

(*Z*)-5-((5-Fluoro-1*H*-indol-3-yl)methylene)imidazolidine-2,4-dione (3g)



5.5 g, yellow solid, yield 80%. m.p. 315.2-314.5 °C. IR (KBr) 3261, 1736, 1688, 1487, 1168, 1086, 684, 657 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.90 (s, 1H), 11.06 (s, 1H), 10.12 (s, 1H), 8.17(s, 1H), 7.58 (dd, *J* = 9.9, 2.5 Hz, 1H), 7.42 (dd, *J* = 8.8, 4.5 Hz, 1H), 7.02 (td, *J* = 9.1, 2.5 Hz, 1H), 6.73 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.7, 158.1 (d, *J* = 233.8 Hz), 155.7, 132.8, 128.9, 127.9 (d, *J* = 10.0 Hz), 124.2, 113.4 (d, *J* = 9.9 Hz), 110.9 (d, *J* = 26.1 Hz), 109.2 (d, *J* = 4.4 Hz), 103.8 (d, *J* = 23.7 Hz), 102.1. ^{19}F NMR (565 MHz, DMSO-d_6) δ -122.9. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{12}H_8N_3O_2FNa$ 268.0492; found 268.0480.

(*Z*)-5-((5-Chloro-1*H*-indol-3-yl)methylene)imidazolidine-2,4-dione (3h)



5.4 g, yellow solid, yield 74%. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.98 (s, 1H), 11.06 (s, 1H), 10.14 (s, 1H), 8.16 (s, 1H), 7.85 (d, *J* = 2.0 Hz, 1H), 7.44 (d, *J* = 8.6 Hz, 1H), 7.18 (dd, *J* = 8.6, 2.1 Hz, 1H), 6.73 (s, 1H). The NMR data is consistent with literature values.[4]

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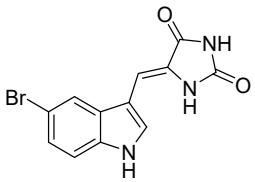
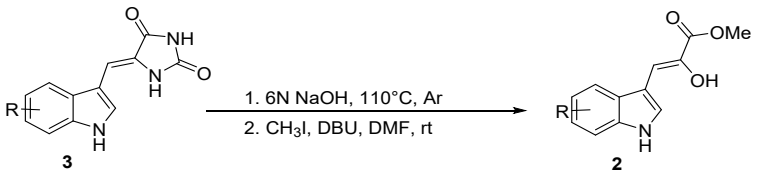
(*Z*)-5-((5-Bromo-1*H*-indol-3-yl)methylene)imidazolidine-2,4-dione (3i)



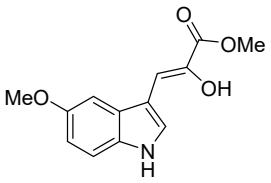
6.1 g, yellow solid, yield 71%. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.99 (s, 1H), 10.46 (s, 2H), 8.15 (s, 1H), 7.99 (s, 1H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.29 (d, *J* = 8.6 Hz, 1H), 6.73 (s, 1H)·. The NMR data is consistent with literature values.[5]



3 2

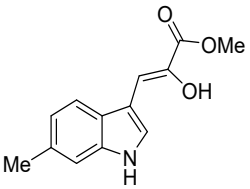
The mixtures of compound **3** (19.11 mmol) and 20% aq. NaOH (40 mL) was stirred at 110 °C for 4 h under argon atmosphere, the solution was cooled to room temperature, diluted with water, and extracted with ethyl ether. The aqueous phase was then acidified with 6 M HCl to pH 2.0 and extracted with ethyl acetate. The organic layers were combined, dried over anhydrous sodium sulfate, filtered and concentrated in vacuum to give the crude acid which was used directly in next step. The crude acid was dissolved in DMF (5.0 mL), DBU (0.77 mL, 5.6 mmol) and methyl iodide (0.43 mL, 6.94 mmol) were added under ice-cooling and the mixture was stirred at room temperature for 3 h. The reaction mixture was diluted by ethyl acetate, the organic layer was washed with 1 M HCl aqueous solution, H_2O and saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified by flash column silica gel chromatography to give **2e-i.**

Methyl (*Z*)-2-hydroxy-3-(5-methoxy-1*H*-indol-3-yl) acrylate (2e).



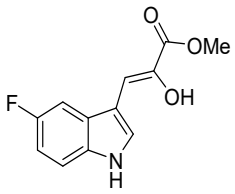
Purification by flash column silica gel chromatography (PE/EA=5:1) to give **2e** as a white solid (504 mg, yield 10% for 2 steps). m.p. 163.5-164.7 °C. IR (KBr) 3378, 1675, 1486, 1317, 1214, 1023, 810, 703 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 11.30 (s, 1H), 8.90 (s, 1H), 7.87 (s, 1H), 7.30 (d, J = 8.7 Hz, 1H), 7.22 (d, J = 2.4 Hz, 1H), 6.84 (s, 1H), 6.77 (dd, J = 8.7, 2.5 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.2, 153.9, 136.8, 130.6, 128.2, 126.9, 112.4, 112.0, 109.5, 105.4, 99.9, 55.4, 52.0. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{13}NO_4$ Na 270.0736; Found 270.0726.

Methyl (*Z*)-2-hydroxy-3-(6-methyl-1*H*-indol-3-yl)acrylate (2f).



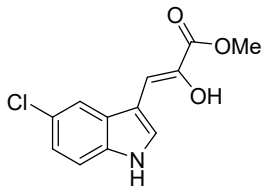
Purification by flash column silica gel chromatography (PE/EA=4:1) to give **2f** as a white solid (1.53 g, yield 34% for 2 steps). m.p. 167.6-168.4 °C. IR (KBr) 3402, 1698, 1442, 1336, 1243, 977, 806, 769 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 11.29 (s, 1H), 8.93 (s, 1H), 7.81 (d, J = 2.6 Hz, 1H), 7.59 (s, 1H), 7.20 (s, 1H), 6.91 (dd, J = 8.2, 1.5 Hz, 1H), 6.80 (s, 1H), 3.79 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.2, 137.1, 136.0, 130.9, 127.1, 124.4, 121.3, 117.9, 111.5, 109.5, 105.2, 52.0, 21.3. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{13}NO_3Na$ 254.0787; found 254.0778.

Methyl (*Z*)-3-(5-fluoro-1*H*-indol-3-yl)-2-hydroxyacrylate (2g).



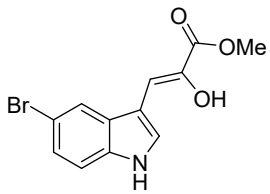
Purification by flash column silica gel chromatography (PE/EA=5:1) to give **2g** as a white solid (514 mg, yield 11% for 2 steps). m.p. 136.4-136.9 °C. IR (KBr) 3406, 1698, 1457, 1318, 1257, 1116, 851, 769 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 11.53 (s, 1H), 9.02 (s, 1H), 7.95 (d, J = 2.7 Hz, 1H), 7.55 (dd, J = 10.1, 2.6 Hz, 1H), 7.41 (dd, J = 8.8, 4.6 Hz, 1H), 6.98 (td, J = 9.1, 2.6 Hz, 1H), 6.79 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.1, 158.1, 156.6, 137.3, 132.3, 129.5, 126.8 (d, J = 10.1 Hz), 112.7 (d, J = 9.8 Hz), 109.9, 104.8, 103.5 (d, J = 23.6 Hz), 52.1. ^{19}F NMR (565 MHz, DMSO-d_6) δ -119.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{10}NO_3FNa$ 258.0536; found 258.0529.

Methyl (*Z*)-3-(5-chloro-1*H*-indol-3-yl)-2-hydroxyacrylate (2h)



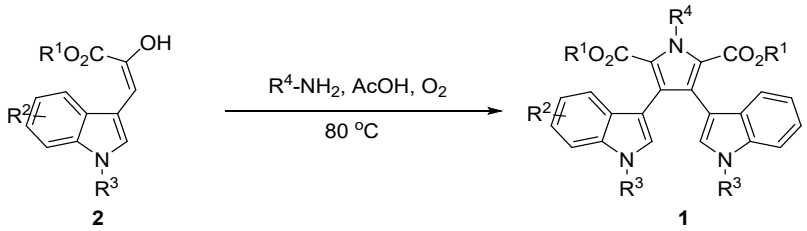
Purification by flash column silica gel chromatography (PE/EA=5:1) to give **2h** as a white solid (605 mg, yield 14% for 2 steps). m.p. 160.8-161.7 °C. IR (KBr) 3406, 1690, 1444, 1307, 1224, 977, 802, 769 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 11.62 (s, 1H), 9.11 (s, 1H), 7.94 (s, 1H), 7.83 (d, J = 2.1 Hz, 1H), 7.43 (d, J = 8.6 Hz, 1H), 7.14 (dd, J = 8.6, 2.1 Hz, 1H), 6.81 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.1, 137.7, 134.1, 129.1, 127.5, 124.2, 121.7, 117.9, 113.3, 109.6, 104.5, 52.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{10}NO_3ClNa$ 274.0241; found 274.0231.

Methyl (*Z*)-3-(5-bromo-1*H*-indol-3-yl)-2-hydroxyacrylate (2i).



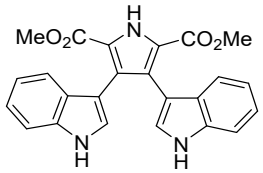
Purification by flash column silica gel chromatography (PE/EA=5:1) to give **2i** as a white solid (674 mg, yield 12% for 2 steps). m.p. 164.8-165.5 °C. IR (KBr) 3408, 1694, 1443, 1306, 1260, 1100, 859, 797 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 11.62 (s, 1H), 9.09 (s, 1H), 7.97 (d, J = 1.9 Hz, 1H), 7.92 (d, J = 2.7 Hz, 1H), 7.38 (d, J = 8.6 Hz, 1H), 7.25 (dd, J = 8.5, 1.9 Hz, 1H), 6.80 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.1, 137.7, 134.4, 128.9, 128.1, 124.2, 120.9, 113.7, 112.2, 109.5, 104.4, 52.1. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{12}H_{10}NO_3BrNa$ 317.9736; Found 317.9726.

1.3 Synthesis of compounds **1a-z**.



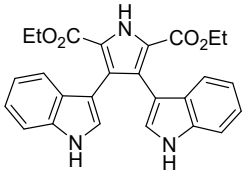
To a solution of compound **2** (0.46 mmol) in 3.0 mL acetic acid was added amine (0.23 mmol for aniline substrates/0.92 mmol for other amines), and the reaction mixture was stirred at 80 °C under O_2 for 3-12 h. The reaction mixture was concentrated under reduce pressure. H_2O and ethyl acetate were added to the residues. The organic phase was washed with 5% $NaHCO_3$ solution, saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The obtained crude products was purified by flash column silica gel chromatography to give compound **1**.

Dimethyl 3,4-di(1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate: lycogarubin C (1a)



Purification by flash column silica gel chromatography (PE/EA=3:1) to give lycogarubin C (**1a**) as a yellow solid (60 mg, yield 63 %). m.p. 146.3-146.9 °C. IR (KBr) 3403, 1705, 1519, 1455, 1271, 1242, 1061, 742 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 12.20 (s, 1H), 10.86 (s, 2H), 7.24 (d, J = 8.1 Hz, 2H), 7.05-7.00 (m, 4H), 6.95 (t, J = 7.5 Hz, 2H), 6.77 (t, J = 7.4 Hz, 2H), 3.59 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.6, 135.5, 127.5, 125.1, 124.5, 122.7, 120.4, 119.1, 118.3, 111.1, 107.6, 51.1. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{19}N_3O_4Na$ 436.1267; Found 436.1254.

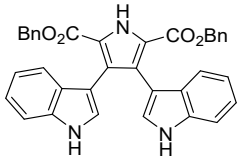
Diethyl 3,4-di(1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1b)



Purification by flash column silica gel chromatography (PE/EA=3:1) to give **1b** as a yellow solid (64 mg, yield 63%). m.p. 119.3-120.4 °C. IR (KBr) 3392, 1715, 1699, 1683, 1267, 1233, 1097, 743cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 12.20 (s, 1H), 10.85 (s, 2H), 7.24 (d, J = 8.1 Hz, 2H), 7.07-7.02 (m, 4H), 6.95 (t, J = 7.6 Hz, 2H), 6.79 (t, J = 7.5 Hz, 2H), 4.01 (q, J = 7.1 Hz, 4H), 0.88 (t, J = 7.1 Hz, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.3, 135.4, 127.7, 125.0, 124.2, 123.1, 120.3, 119.2, 118.2, 111.0, 107.8, 59.7, 13.5. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{26}H_{23}N_3O_4Na$ 464.1580; found 464.1573.

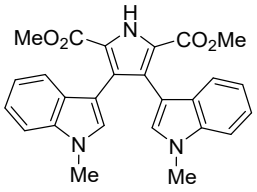
Dibenzyl 3,4-di(1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1c)

Purification by flash column silica gel chromatography (PE/EA=3:1) to give **1c** as a yellow solid (74 mg,



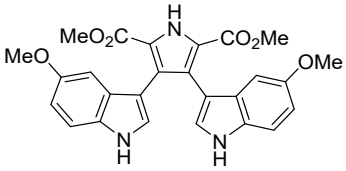
yield 57%). m.p. 102.7-103.4 °C. IR (KBr) 3408, 1698, 1683, 1455, 1268, 1239, 1097, 741 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.62 (s, 2H), 7.27 (d, *J* = 14.7 Hz, 2H), 7.24-7.18 (m, 2H), 7.18-7.13 (m, 6H), 7.11-7.06 (m, 2H), 6.96 (t, *J* = 7.5 Hz, 2H), 6.87-6.83 (m, 4H), 6.60 (s, 2H), 5.13 (s, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.7, 135.6, 135.4, 128.3, 128.0, 127.9, 125.4, 124.3, 123.0, 121.7, 120.1, 119.6, 111.0, 108.8, 66.6. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{36}H_{27}N_3O_4Na$ 588.1893; found 588.1887.

Dimethyl 3,4-bis(1-methyl-1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1d)



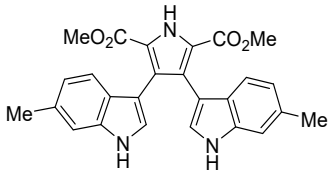
Purification by flash column silica gel chromatography (PE/EA=5:1) to give **1d** as a yellow solid (84 mg, yield 83%). m.p 226.1-227.3 °C. IR (KBr) 3392, 1715, 1699, 1456, 1267, 1233, 1097, 743 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 12.29 (s, 1H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.09 (s, 2H), 7.01 (dd, *J* = 8.2, 6.6 Hz, 4H), 6.80 (t, *J* = 7.5 Hz, 2H), 3.64 (s, 6H), 3.58 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.5, 136.0, 129.5, 127.8, 124.0, 122.8, 120.6, 119.4, 118.5, 109.4, 106.7, 51.2, 32.3. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{26}H_{23}N_3O_4Na$ 464.1580; found 464.1577.

Dimethyl 3,4-bis(5-methoxy-1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1e)



Purification by flash column silica gel chromatography (PE/EA=3:1) to give **1e** as a yellow solid (52 mg, yield 47%). m.p. 234.2-235.4 °C. IR (KBr) 3452, 1726, 1698, 1481, 1247, 1210, 1060, 912 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 12.14 (s, 1H), 10.73 (s, 2H), 7.10 (d, *J* = 8.7 Hz, 2H), 7.03 (d, *J* = 2.6 Hz, 2H), 6.54 (dd, *J* = 8.7, 2.5 Hz, 2H), 6.38 (d, *J* = 2.6 Hz, 2H), 3.64 (s, 6H), 3.30 (s, 6H). ^{13}C NMR (150 MHz, DMSO-*d6*) δ 160.6, 152.8, 130.5, 127.4, 126.1, 124.4, 122.3, 111.7, 110.8, 107.4, 100.6, 54.6, 51.2. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{26}H_{23}N_3O_6Na$ 496.1479; found 496.1469.

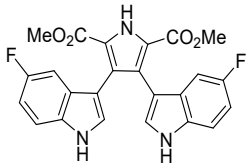
Dimethyl 1-benzyl-3,4-bis(6-methyl-1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1f).



Purification by flash column silica gel chromatography (PE/EA=3:1) to give **1f** as a yellow solid (35 mg, yield 34%). m.p. 149.2-149.9 °C. IR (KBr) 3405, 1704, 1454, 1276, 1243, 1098, 800, 782 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 12.14 (s, 1H), 10.69 (s, 2H), 7.02 (s, 2H), 6.92-6.86 (m, 4H),

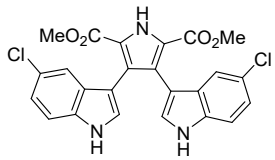
6.60 (d, *J* = 8.1 Hz, 2H), 3.58 (s, 6H), 2.31 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.6, 135.9, 129.2, 125.4, 124.6, 124.4, 122.6, 120.1, 118.9, 111.0, 107.4, 51.1, 21.3. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{26}H_{23}N_3O_4Na$ 464.1586; found 464.1564.

Dimethyl 3,4-bis(5-fluoro-1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1g).



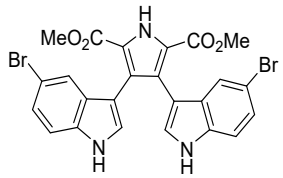
Purification by flash column silica gel chromatography (PE/EA=3:1) to give **1g** as a yellow solid (69 mg, yield 66 %). m.p. 144.3-145.7 °C. IR (KBr) 3419, 1715, 1698, 1487, 1271, 1243, 1055, 796 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.26 (s, 1H), 11.01 (s, 2H), 7.24 (dd, *J* = 8.8, 4.6 Hz, 2H), 7.17 (d, *J* = 2.6 Hz, 2H), 6.78 (td, *J* = 9.0, 2.6 Hz, 2H), 6.65 (dd, *J* = 10.3, 2.6 Hz, 2H), 3.63 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.5, 157.5, 155.9, 132.2, 127.9-127.4 (m), 124.0, 122.6, 112.0 (d, *J* = 9.9 Hz), 108.6 (d, *J* = 26.2 Hz), 107.8 (d, *J* = 5.0 Hz), 103.7 (d, *J* = 23.3 Hz), 51.3. ^{19}F NMR (565 MHz, DMSO-d_6) δ -125.6. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ $C_{24}H_{17}N_3O_4F_2Na$ 472.1079; found 472.1069.

Dimethyl 3,4-bis(5-chloro-1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate：lynamicin D (1h).



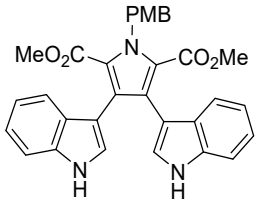
Purification by flash column silica gel chromatography (PE/EA=3:1) to give lynamicin D (**1h**) as a yellow solid (52 mg, yield 47 %). m.p. 153.7-154.6 °C. IR (KBr) 3419, 1715, 1698, 1457, 1260, 1234, 1050, 796 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.94 (s, 2H) 7.15 (s, 2H), 6.95-6.92 (m, 4H), 6.73 (d, *J* = 2.7 Hz, 2H), 3.73 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.7, 133.9, 128.5, 125.9, 125.3, 124.7, 122.5, 121.9, 119.4, 112.1, 108.2, 51.9. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{24}H_{17}N_3O_4Na$ 504.0488; Found 504.0475.

Dimethyl 3,4-bis(5-bromo-1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1i).



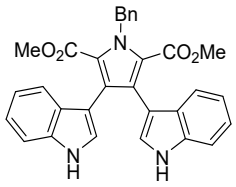
Purification by flash column silica gel chromatography (PE/EA=3:1) to give **1d** as yellow solid (95 mg, yield 72%). m.p. 244.3-245.1 °C. IR (KBr) 3450, 1705, 1558, 1456, 1258, 1236, 1097, 580 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.37 (s, 1H), 11.13 (s, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 2.5 Hz, 2H), 7.08 (d, *J* = 1.9 Hz, 2H), 7.05 (dd, *J* = 8.5, 1.9 Hz, 2H), 3.62 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.4, 134.1, 129.0, 126.9, 123.6, 122.9, 122.7, 121.4, 113.1, 111.1, 107.2, 51.2. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{24}H_{17}N_3O_4Br_2Na$ 591.9478; Found 591.9468.

Dimethyl 3,4-di(1*H*-indol-3-yl)-1-(4-methoxybenzyl)-1*H*-pyrrole-2,5-dicarboxylate (1j).



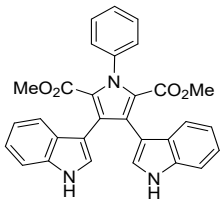
Purification by flash column silica gel chromatography (PE/EA=3:1) to give **1j** as a yellow solid (75 mg, yield 61%). m.p. 201.3-202.4 °C. IR (KBr) 3402, 1715, 1694, 1457, 1263, 1227, 1095, 749 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 7.59 (s, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.13 (dd, *J* = 8.4, 4.0 Hz, 4H), 7.09 (t, *J* = 7.5 Hz, 2H), 7.00 (t, *J* = 7.4 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.48 (s, 2H), 6.06 (s, 2H), 3.77 (s, 3H), 3.36 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.5, 158.7, 135.5, 131.2, 128.2, 127.9, 125.8, 124.6, 124.0, 121.5, 119.6, 119.5, 114.0, 111.0, 109.6, 55.3, 51.6, 49.2. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{32}H_{27}N_3O_5Na$ 556.1842; found 556.1830.

Dimethyl 1-benzyl-3,4-di(1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1k).



Purification by flash column silica gel chromatography (PE/EA=4:1) to give **1k** (80 mg, yield 70 %) as a yellow solid. m.p. 96.1-97.2 °C. IR (KBr) 3407, 1714, 1455, 1436, 1269, 1203, 1010, 742 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 7.56 (s, 2H), 7.34 (ddd, *J* = 20.0, 10.0, 5.1 Hz, 4H), 7.30-7.24 (m, 1H), 7.19 (d, *J* = 7.6 Hz, 2H), 7.16-7.08 (m, 4H), 7.03 (t, *J* = 7.5 Hz, 2H), 6.48 (s, 2H), 6.16 (s, 2H), 3.35 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.4, 139.1, 135.5, 128.7, 128.2, 127.1, 126.4, 126.0, 124.7, 124.0, 121.5, 119.67, 119.61, 111.0, 109.6, 51.6, 49.9. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{31}H_{25}N_3O_4Na$ 526.1737; found 526.1727

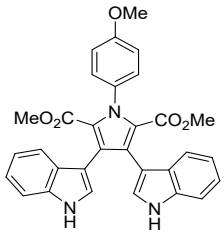
Dimethyl 3,4-di(1*H*-indol-3-yl)-1-phenyl-1*H*-pyrrole-2,5-dicarboxylate (1l)



Purification by flash column silica gel chromatography (PE/EA=2:1) to give **1l** as a yellow solid (40 mg, yield 35%). m.p 184.3-185.7 °C. IR (KBr) 3426, 1716, 1689, 1496, 1465, 1220, 1003, 742 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 10.95 (d, *J* = 2.5 Hz, 2H), 7.46 (dq, *J* = 21.0, 7.3 Hz, 5H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.13-7.07 (m, 4H), 6.97 (t, *J* = 7.5 Hz, 2H), 6.81 (t, *J* = 7.5 Hz, 2H), 3.20 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 161.2, 139.3, 135.5, 128.4, 128.1, 127.4, 127.3, 126.3, 125.1, 123.6, 120.6, 118.8, 118.5, 111.3, 107.2, 51.3. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{30}H_{24}N_3O_4$ 490.1761; found 490.1759.

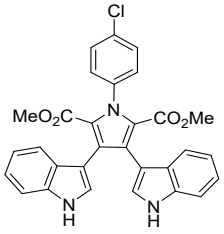
Dimethyl 3,4-di(1*H*-indol-3-yl)-1-(4-methoxyphenyl)-1*H*-pyrrole-2,5-dicarboxylate (1m).

Purification by flash column silica gel chromatography (PE/EA=4:1) to give **1m** as a yellow solid (65 mg, yield 54 %). m.p 170.5-171.2 °C. IR (KBr) 3429, 1716, 1513, 1455, 1254, 1132, 836, 762 cm^{-1}. ^1H NMR



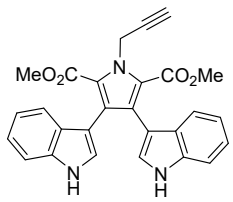
(600 MHz, DMSO-d_6) δ 10.94 (s, 2H), 7.35 (d, J = 8.8 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.12-7.06 (m, 4H), 7.02-6.95 (m, 4H), 6.81 (ddd, J = 8.0, 7.0, 1.0 Hz, 2H), 3.82 (s, 3H), 3.21 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 161.3, 158.7, 135.5, 131.9, 128.6, 127.4, 126.6, 125.0, 123.3, 120.6, 118.7, 118.5, 113.4, 111.3, 107.3, 55.3, 51.3. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{31}H_{25}N_3O_5Na$ 542.1686; found 542.1672.

Dimethyl 1-(4-chlorophenyl)-3,4-di(1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1n).



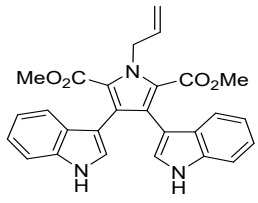
Purification by flash column silica gel chromatography (PE/EA=2:1) to give **1n** as a yellow solid (25 mg, yield 27%). m.p 213.1-214.5 °C. IR (KBr) 3499, 1719, 1559, 1493, 1436, 1219, 1093, 748 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.95 (d, J = 2.5 Hz, 2H), 7.53 (d, J = 8.5 Hz, 2H), 7.49 (d, J = 8.5 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 2.5 Hz, 2H), 6.98 (t, J = 7.5 Hz, 2H), 6.80 (s, 2H), 3.22 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 161.0, 138.3, 135.5, 132.6, 129.4, 128.3, 127.3, 126.3, 125.1, 124.1, 120.6, 118.7, 118.6, 111.3, 107.1, 51.3. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{30}H_{23}N_3O_4Cl$ 524.1372; found 524.1368.

Dimethyl 3,4-di(1*H*-indol-3-yl)-1-(prop-2-yn-1-yl)-1*H*-pyrrole-2,5-dicarboxylate (1o).



Purification by flash column silica gel chromatography (PE/EA=4:1) to give **1o** as a yellow solid (82 mg, yield 78 %). m.p 232.4-233.3 °C. IR (KBr) 3418, 1713, 1697, 1456, 1271, 1209, 1106, 744 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.89 (s, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.02 (d, J = 7.5 Hz, 4H), 6.97 (t, J = 7.5 Hz, 2H), 6.82 (t, J = 7.5 Hz, 2H), 5.54 (d, J = 2.5 Hz, 2H), 3.42 (s, 6H), 3.35 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 161.6, 135.4, 127.4, 125.0, 124.8, 124.6, 120.5, 118.5, 118.4, 111.3, 107.4, 79.8, 74.8, 51.5, 36.0. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{27}H_{21}N_3O_4Na$ 474.1424; found 474.1412.

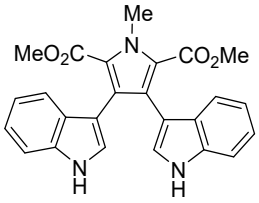
Dimethyl 1-allyl-3,4-di(1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1p).



Purification by flash column silica gel chromatography (PE/EA=4:1) to give **1p** as a yellow solid (50 mg, yield 48 %). m.p. 161.7-162.5 °C. IR (KBr) 3401, 1693, 1456, 1430, 1272, 1207, 1095, 739 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68 (s, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H), 7.13-7.08 (m, 2H), 7.00 (t, J = 7.5 Hz, 2H),

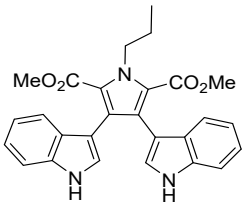
6.56 (s, 2H), 6.12 (ddt, *J* = 17.1, 10.3, 5.1 Hz, 1H), 5.52 (d, *J* = 4.0 Hz, 2H), 5.18 (d, *J* = 10.2 Hz, 1H), 5.09 (d, *J* = 17.0 Hz, 1H), 3.41 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.4, 135.5, 135.4, 128.3, 125.6, 124.4, 123.8, 121.5, 119.7, 119.6, 116.0, 111.0, 109.8, 51.6, 48.9. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{27}H_{23}N_3O_4Na$ 476.1580; found 476.1578.

Dimethyl 3,4-di(1*H*-indol-3-yl)-1-methyl-1*H*-pyrrole-2,5-dicarboxylate (1q).



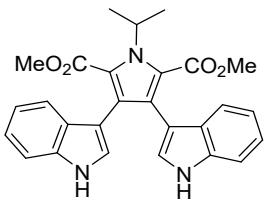
Purification by flash column silica gel chromatography (PE/EA=4:1) to give **1q** as a yellow solid (51 mg, yield 51%). m.p 224.3-225.1 °C. IR (KBr) 3378, 1675, 1652, 1486, 1317, 1234, 1023, 810 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (s, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.13-7.07 (m, 2H), 7.00 (t, *J* = 7.5 Hz, 2H), 6.58 (s, 2H), 4.25 (s, 3H), 3.43 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.5, 135.5, 128.3, 126.3, 124.0, 123.8, 121.5, 119.8, 119.6, 110.9, 110.0, 51.5, 35.4. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{25}H_{21}N_3O_4Na$ 450.1424; found 450.1409.

Dimethyl 3,4-di(1*H*-indol-3-yl)-1-propyl-1*H*-pyrrole-2,5-dicarboxylate (1r).



Purification by flash column silica gel chromatography (PE/EA=4:1) to give **1r** as a yellow solid (70 mg, yield 66%). m.p 151.3-152.6 °C. IR (KBr) 3395, 1716, 1698, 1456, 1210 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (s, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.10 (t, *J* = 7.5 Hz, 2H), 7.01 (t, *J* = 7.7 Hz, 2H), 6.46 (s, 2H), 4.78-4.72 (m, 2H), 3.40 (s, 6H), 1.94 (q, *J* = 7.5 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.5, 135.5, 128.3, 125.5, 124.1, 123.8, 121.5, 119.7, 119.5, 111.0, 109.9, 51.5, 48.7, 25.5, 11.3. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{27}H_{25}N_3O_4Na$ 478.1737; found 478.1733.

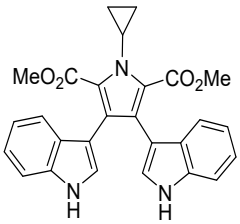
Dimethyl 3,4-di(1*H*-indol-3-yl)-1-isopropyl-1*H*-pyrrole-2,5-dicarboxylate (1s).



Purification by flash column silica gel chromatography (PE/EA=4:1) to give **1s** as a yellow solid (40 mg, yield 38%). m.p 193.7-194.4 °C. IR (KBr) 3396, 1715, 1690, 1436, 1268, 1215, 1010, 744 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 (s, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.11-7.06 (m, 2H), 6.98 (t, *J* = 7.5 Hz, 2H), 6.57-6.54 (m, 2H), 5.35 (m, 1H), 3.43 (s, 6H), 1.72 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.6, 135.5, 128.2, 126.0, 124.0, 123.3, 121.5, 119.8, 119.5, 110.9, 109.7, 51.8, 51.5, 22.3. HRMS

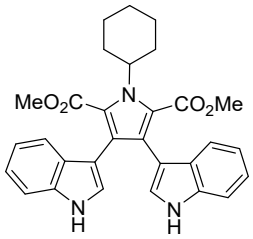
(ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{27}H_{25}N_3O_4Na$ 478.1737; found 478.1726.

Dimethyl 1-cyclopropyl-3,4-di(1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1t)



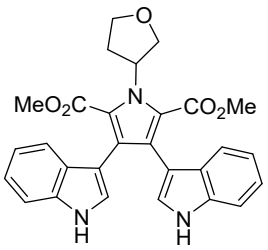
Purification by flash column silica gel chromatography (PE/EA=3:1) to give **1t** as a yellow solid (56 mg, yield 53%). m.p 175.4-176.8 °C. IR (KBr) 3422, 1706, 1454, 1416, 1259, 1215, 1009, 746 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 7.63 (s, 2H), 7.28-7.18 (m, 2H), 7.14-7.03 (m, 4H), 6.95 (t, *J* = 7.4 Hz, 2H), 6.57 (s, 2H), 3.84 (tt, *J* = 7.4, 4.0 Hz, 1H), 3.57 (s, 6H), 1.10 (d, *J* = 6.9 Hz, 2H), 0.86 (d, *J* = 6.9 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) 162.3, 135.5, 127.8, 127.5, 124.4, 122.8, 121.5, 119.8, 119.4, 111.0, 108.9, 51.8, 31.4, 9.4. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{24}N_3O_4$ 454.1761; found 454.1761.

Dimethyl 1-cyclohexyl-3,4-di(1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1u)



Purification by flash column silica gel chromatography (PE/EA=3:1) to give **1u** as a yellow solid (51 mg, yield 44%). m.p 154.2-155.1 °C. IR (KBr) 3428, 1704, 1407, 1358, 1240, 1207, 1108, 742 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 7.55 (s, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 7.08 (t, *J* = 7.5 Hz, 2H), 6.97 (t, *J* = 7.5 Hz, 2H), 6.48 (s, 2H), 4.91-4.82 (m, 1H), 3.43 (s, 6H), 2.26 (qd, *J* = 12.3, 3.6 Hz, 2H), 2.20-2.17 (m, 2H), 1.92 (dt, *J* = 13.6, 3.3 Hz, 2H), 1.72 (d, *J* = 13.0 Hz, 1H), 1.46 (qt, *J* = 13.1, 3.6 Hz, 2H), 1.31 - 1.20 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.6, 135.5, 128.2, 126.3, 124.0, 123.3, 121.5, 119.9, 119.5, 110.9, 109.7, 60.2, 51.8, 32.4, 26.7, 25.4. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{30}H_{30}N_3O_4$ 496.2231; found 496.2278.

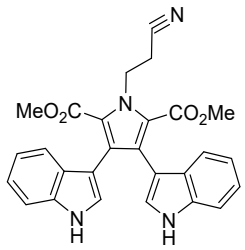
Dimethyl -3,4-di(1*H*-indol-3-yl)-1-(tetrahydrofuran-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1v)



Purification by flash column silica gel chromatography (PE/EA=2:1) to give **1v** as a yellow solid (64 mg, yield 57%). m.p 110.8-111.5 °C. IR (KBr) 3408, 1714, 1508, 1456, 1434, 1219, 1097, 743 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 7.71 (s, 2H), 7.32-7.24 (m, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.12-7.05 (m, 2H), 6.98 (t, *J* = 7.5 Hz, 2H), 6.59 (s, 2H), 5.87-5.78 (m, 1H), 4.32-4.14 (m, 3H), 3.91 (d, *J* = 8.0 Hz, 1H), 3.45 (s, 6H), 2.69-2.51 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.2, 135.5, 128.0, 126.5, 124.1, 124.0,

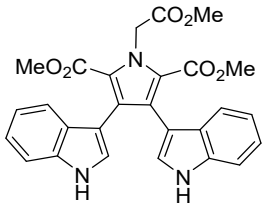
121.6, 119.8, 119.6, 111.0, 109.4, 71.7, 68.5, 58.3, 52.0, 32.9. (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{28}H_{26}N_3O_5$ 484.1867; found 484.1865.

Dimethyl 1-(2-cyanoethyl)-3,4-di(1*H*-indol-3-yl)-1*H*-pyrrole-2,5-dicarboxylate (1w).



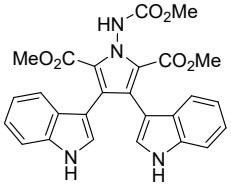
Purification by flash column silica gel chromatography (PE/EA=1:1) to give **1w** as a yellow solid (76 mg, yield 70%). m.p 185.3-186.2 °C. IR (KBr) 3404, 1705, 1683, 1436, 1258, 1232, 1200, 742 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 10.87 (s, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 7.00-6.93 (m, 4H), 6.83 (t, J = 7.5 Hz, 2H), 4.94 (s, 2H), 3.36 (s, 6H), 3.18 (t, J = 6.7 Hz, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 161.8, 135.4, 127.6, 124.9, 124.8, 124.6, 120.5, 118.5, 118.5, 118.4, 111.3, 107.7, 51.4, 42.1, 19.5. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{27}H_{22}N_4O_4Na$ 489.1533; found 489.1521.

Dimethyl 3,4-di(1*H*-indol-3-yl)-1-(2-methoxy-2-oxoethyl)-1*H*-pyrrole-2,5-dicarboxylate (1x).



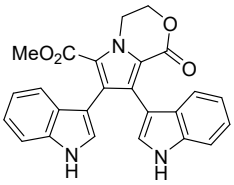
Purification by flash column silica gel chromatography (PE/EA=2:1) to give **1x** as a yellow solid (40 mg, yield 36%). m.p. 112.4-113.3 °C. IR (KBr) 3419, 1715, 1698, 1456, 1273, 1239, 1210, 668 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 10.88 (s, 2H), 7.25 (d, J = 8.1 Hz, 2H), 7.03 (d, J = 8.0 Hz, 2H), 7.00-6.94 (m, 4H), 6.82 (t, J = 7.5 Hz, 2H), 5.51 (s, 2H), 3.75 (s, 3H), 3.33 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.3, 161.7, 135.4, 127.6, 125.2, 124.8, 124.4, 120.5, 118.5, 118.5, 111.3, 107.7, 52.1, 51.4, 48.5. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{27}H_{23}N_3O_6Na$ 508.1479; found 508.1476.

Dimethyl 3,4-di(1*H*-indol-3-yl)-1-((methoxycarbonyl)amino)-1*H*-pyrrole-2,5-dicarboxylate (1y).



Purification by flash column silica gel chromatography (PE/EA=1:1) to give **1y** as a yellow solid (50 mg, yield 44%). m.p 157.3-158.4 °C. IR (KBr) 3403, 1715, 1683, 1506, 1456, 1257, 1223, 744 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 10.93 (d, J = 2.5 Hz, 2H), 10.71 (s, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.03- 6.94 (m, 6H), 6.81 (t, J = 7.5 Hz, 2H), 3.73 (s, 3H), 3.42 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.1, 156.3, 135.5, 127.2, 125.1, 124.8, 121.8, 120.6, 118.6, 118.5, 111.4, 106.9, 52.5, 51.4. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{22}N_4O_6$ 509.1431; found 509.1429.

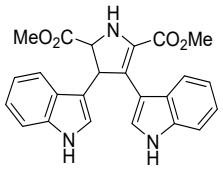
Methyl 7,8-di(1*H*-indol-3-yl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-6-carboxylate (1z).



Purification by flash column silica gel chromatography (PE/EA=2:1) to give **1z** as a yellow solid (65 mg, yield 66%). m.p 248.1-249.5 °C. IR (KBr) 3404, 1699, 1683, 1456, 1238, 1207, 1105, 743 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 10.91 (s, 2H), 7.26 (t, J = 8.8 Hz, 2H), 7.06 (t, J = 7.4 Hz, 2H), 7.03-6.93 (m, 4H), 6.82 (t, J = 7.5 Hz, 1H),6.77 (t, J = 7.5 Hz, 1H), 4.71 (m, 4H), 3.47 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 161.1, 157.4, 135.5, 135.5, 127.5, 127.0, 125.8, 125.2, 125.0, 124.3, 123.0, 120.5, 120.4, 119.9, 119.7, 118.7, 118.5, 118.3, 111.3, 111.1, 107.4, 107.1, 65.7, 51.4, 43.2. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{19}N_3O_4Na$ 448.1267; found 448.1257.

1.4 Synthesis of compound II (dimethyl 3,4-di(1*H*-indol-3-yl)-2,3-dihydro-1*H*-pyrrole-2,5-dicarboxylate).

To a solution of compound **2a** (100 mg, 0.46 mmol) in 3.0 mL acetic acid NH_4HCO_3 (73 mg, 0.92 mmol) was added, and the reaction mixture was stirred at 80 °C under Ar for 3 h. The reaction mixture was concentrated under reduce pressure. H_2O and ethyl acetate were added to the residues. The organic phase was washed with 5% $NaHCO_3$ solution, saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude products were purified by flash column silica gel chromatography (PE/EA=4:1-2:1) to give compound **II** (white solid, 21 mg, 22% yield). Compounds **2a** (32 mg) and **1a** (9 mg, 10%) were also isolated in the purification.



m.p. 145.1-146.9 °C. IR (KBr) 3396, 1739, 1463, 1435, 1259, 1010, 931, 743 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 11.39 (s, 1H), 10.95 (s, 1H), 7.70 (d, J = 7.5 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.24-7.20 (m, 1H), 7.11-6.99 (m, 4H), 6.91 (ddd, J = 8.1, 6.9, 1.0 Hz, 1H), 6.86 (d, J = 2.5 Hz, 1H), 5.48 (s, 1H), 5.46 (s, 1H), 4.25 (t, J = 1.8 Hz, 1H), 3.82 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 171.3, 165.4, 140.0, 135.7, 135.5, 128.1, 126.8, 126.6, 124.7, 121.7, 120.8, 119.3, 118.8, 118.5, 117.5, 114.3, 111.4, 110.9, 107.7, 103.4, 58.3, 52.7, 52.3, 41.4. ^1H NMR (600 MHz, CD_3OD) δ 7.69-7.64 (m, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 8.1 Hz, 1H), 7.21-7.18 (m, 1H), 7.16 (s, 1H), 7.10-7.06 (m, 2H), 7.05-7.01 (m, 1H), 6.94 (td, J = 7.5, 1.0 Hz, 1H), 6.88 (s, 1H), 5.51 (d, J = 2.0 Hz, 1H), 4.15 (d, J = 2.0 Hz, 1H), 3.85 (s, 3H), 3.68 (s, 3H). ^{13}C NMR (150MHz, CD_3OD) δ 172.9, 167.6, 141.3, 137.4, 129.9, 128.6, 128.2, 125.8, 122.9, 122.1, 120.4, 119.9, 119.7, 118.5, 116.0, 112.1, 111.7, 109.6, 105.8, 60.4, 53.1, 52.7, 43.1. HRMS (ESI-TOF) *m/z*: $[M +Na]^+$ Calcd for $C_{24}H_{21}N_3O_4Na$ 438.1424; Found 438.1414.

References:

(1) Nishizawa, T.; Grüschow, S.; Jayamaha, D.-H. E.; Nishizawa-Harada, C.; Sherman, D. H. *J. Am. Chem. Soc.* **2006**, 128, 724-725.

(2) 1-Me *L*-tryptophan methyl ester hydrochloride was prepared through methyl esterification of commercially available 1-Me *L*-tryptophan. Yang, W. B.; Huang, L.; Yu, Y.; Daniel Pflästerer, D.; Rominger, F.; Hashmi A. S. K. *Chem-Eur. J.* **2014**. 20, 3927-3931.

(3) Moriya, T.; Hagio, K.; Yoneda, N. *Chem. Pharm. Bull.* **1980**, 28, 1891-1893.

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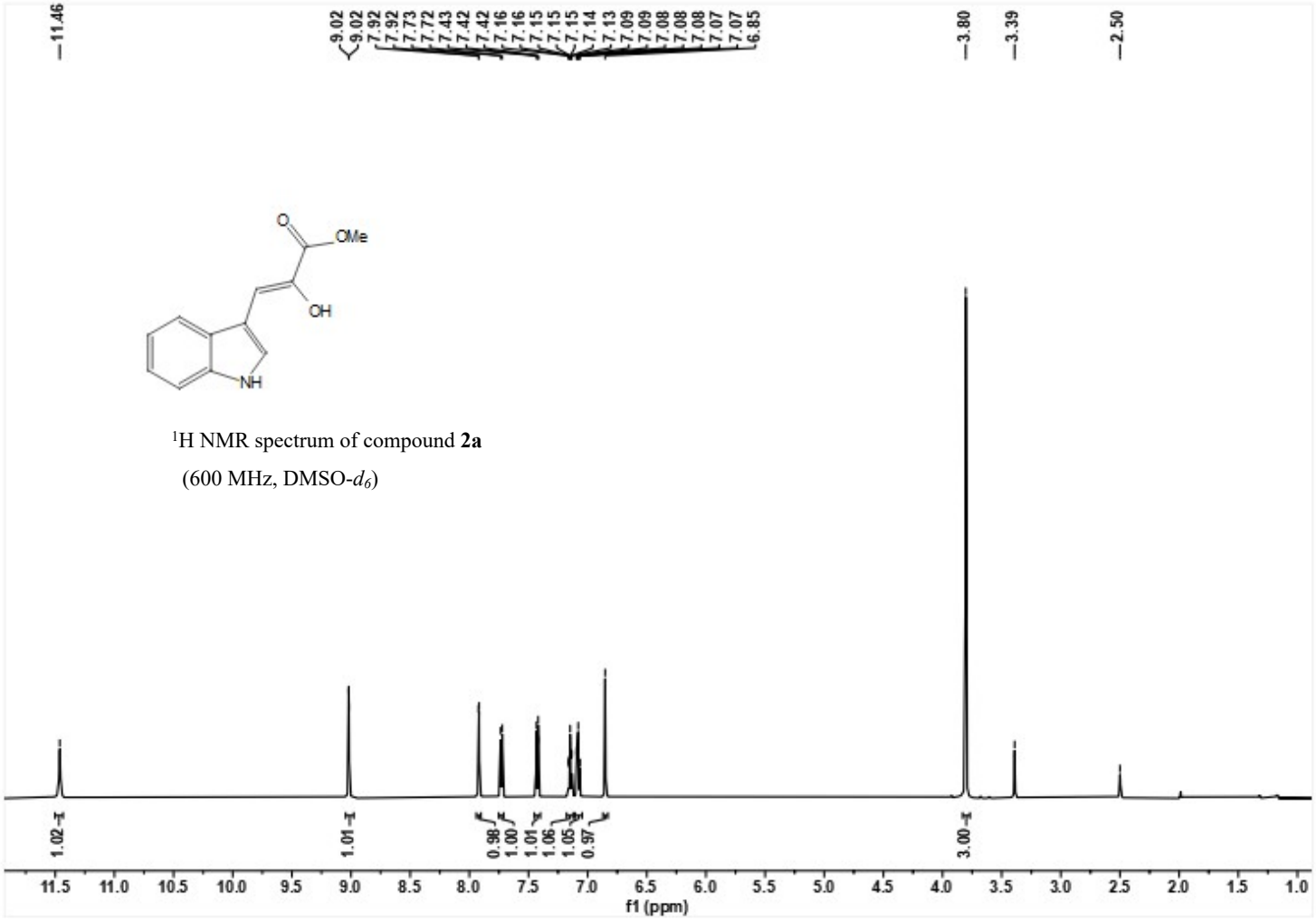
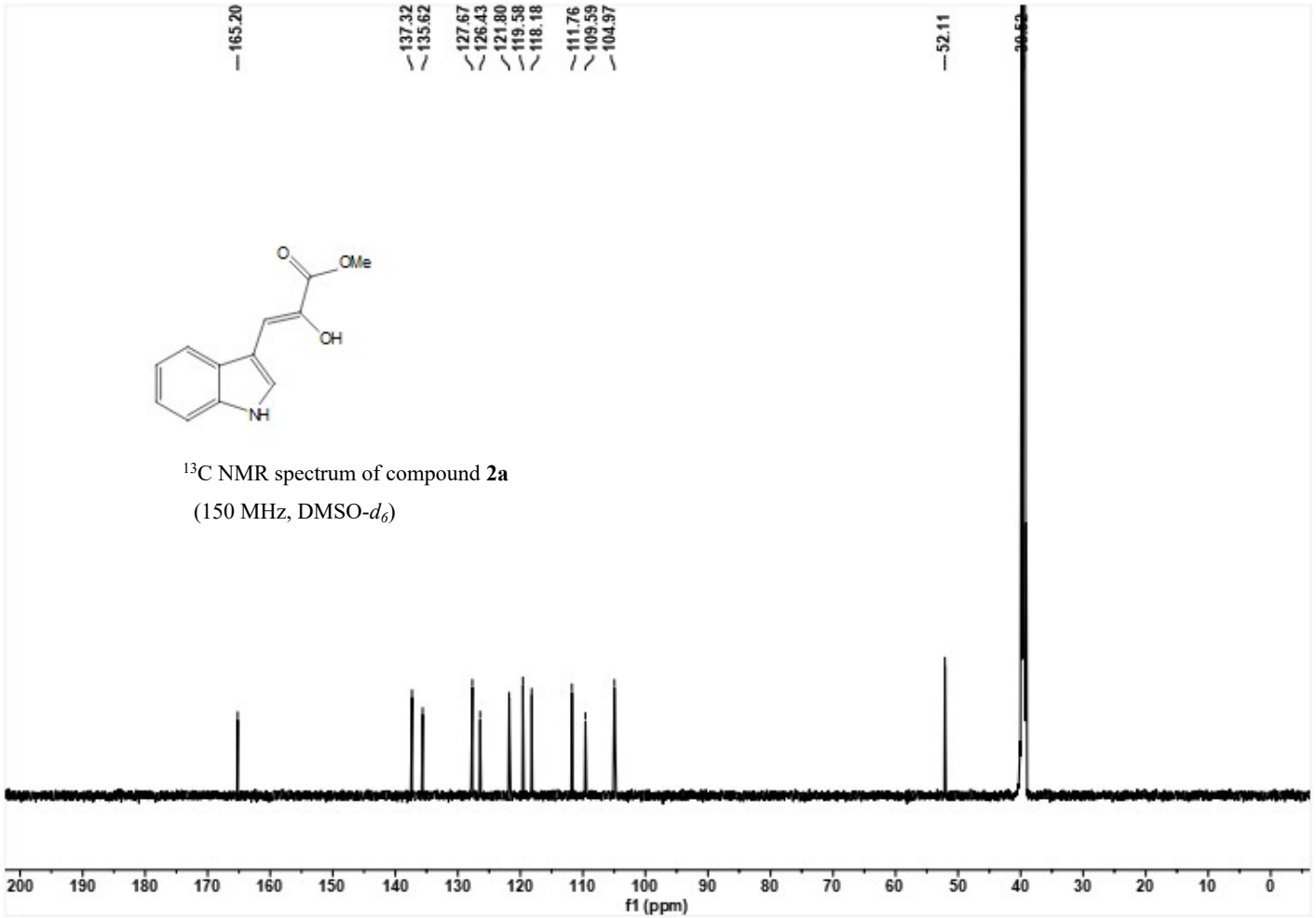
(5) Angelova, V. T.; Pencheva, T.; Buyukliev, R; Yovkova, E. K.; Valkova, I.; Momekov, G; Vulcheva, V. *Russ. J. Bioorg. Chem.* **2021**, 47, 122–133.

2.NMR spectra for compounds **2a-d**, **3e-i**, **2e-i**, **1a-z** and **II**: **Page S17-103**.



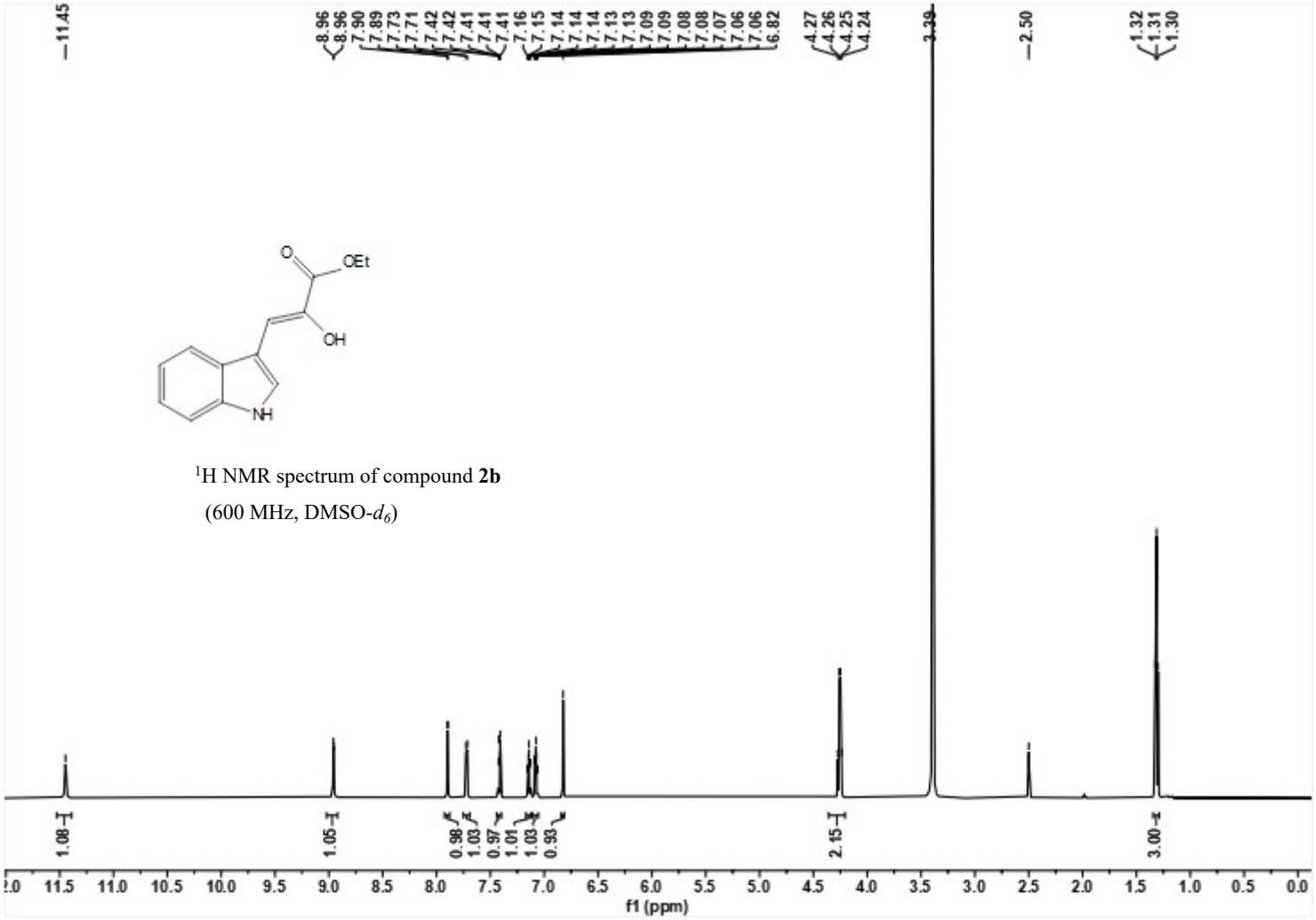
^{1}H NMR spectrum of compound **2a**

(600 MHz, DMSO-d_6)



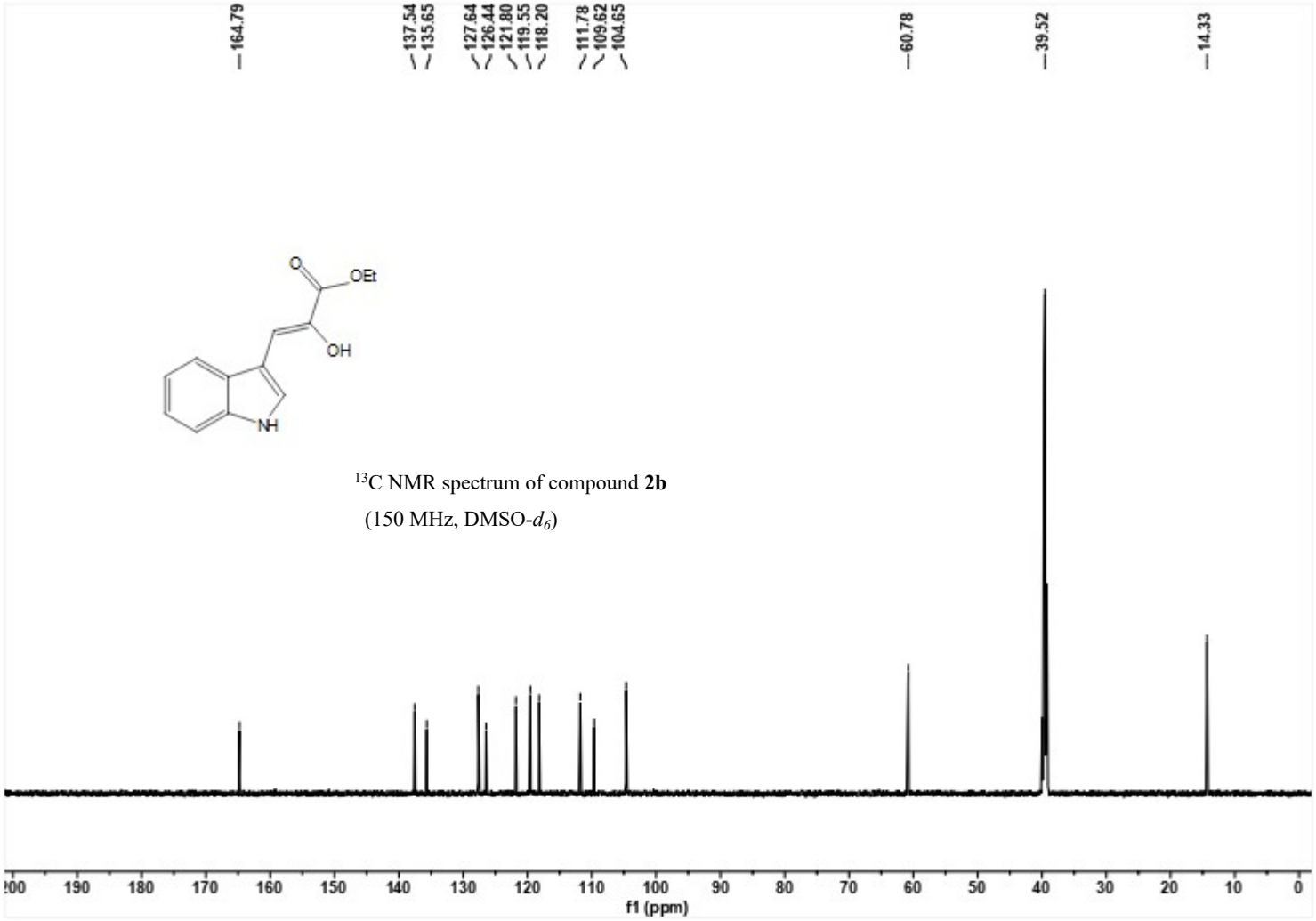
^{13}C NMR spectrum of compound **2a**

(150 MHz, DMSO-d_6)



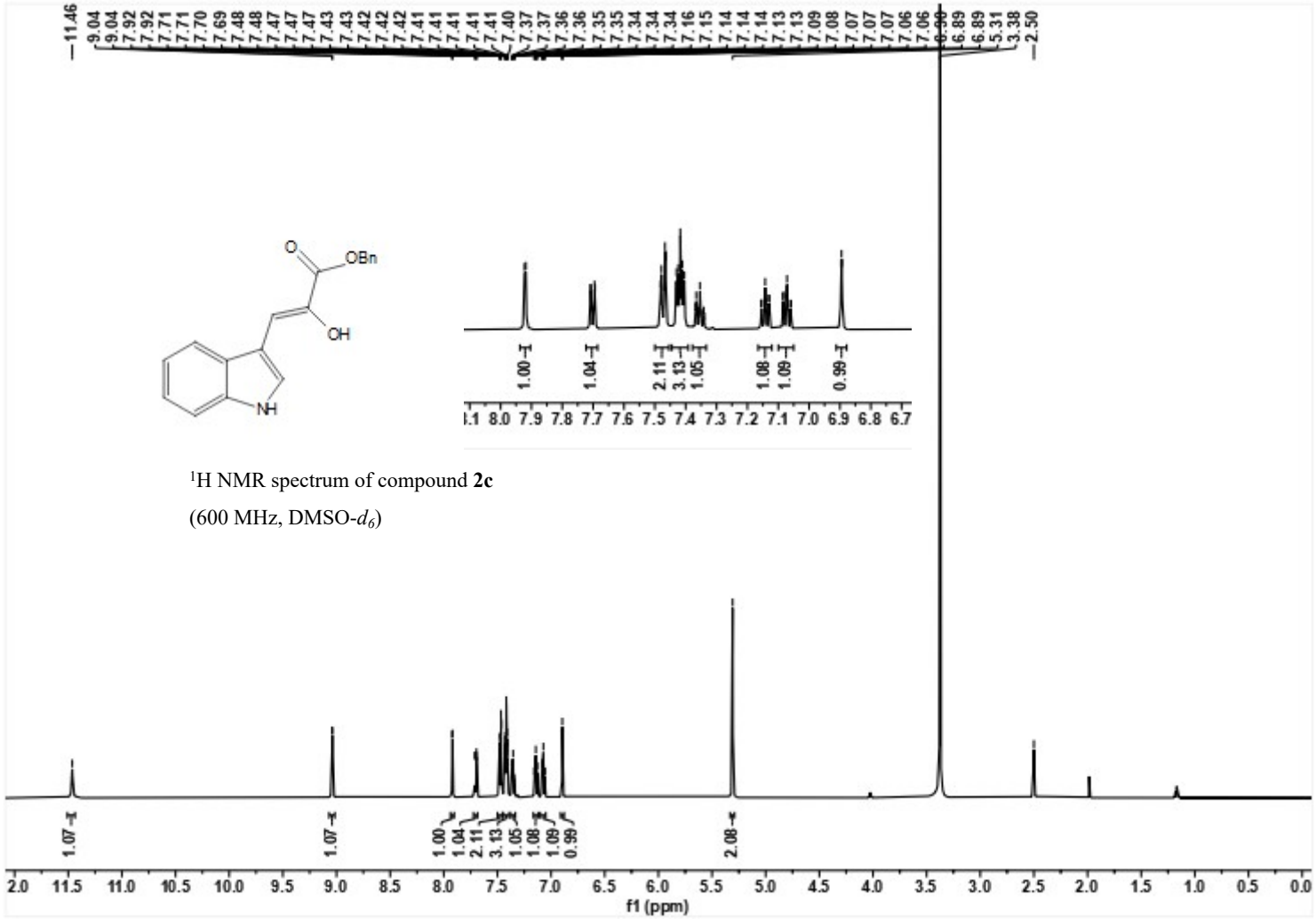
^{1}H NMR spectrum of compound **2b**

(600 MHz, DMSO-d_6)



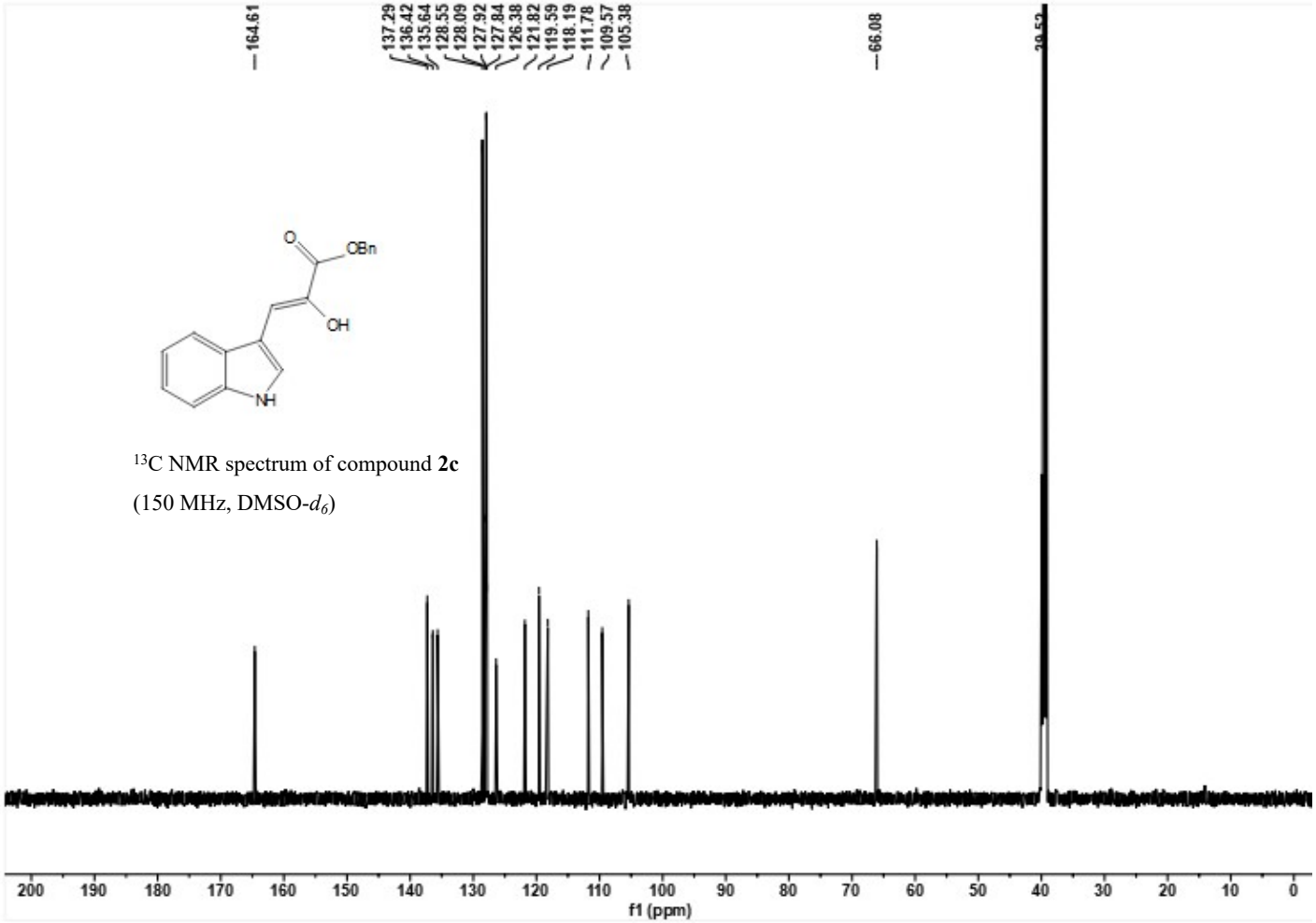
^{13}C NMR spectrum of compound **2b**

(150 MHz, DMSO-d_6)



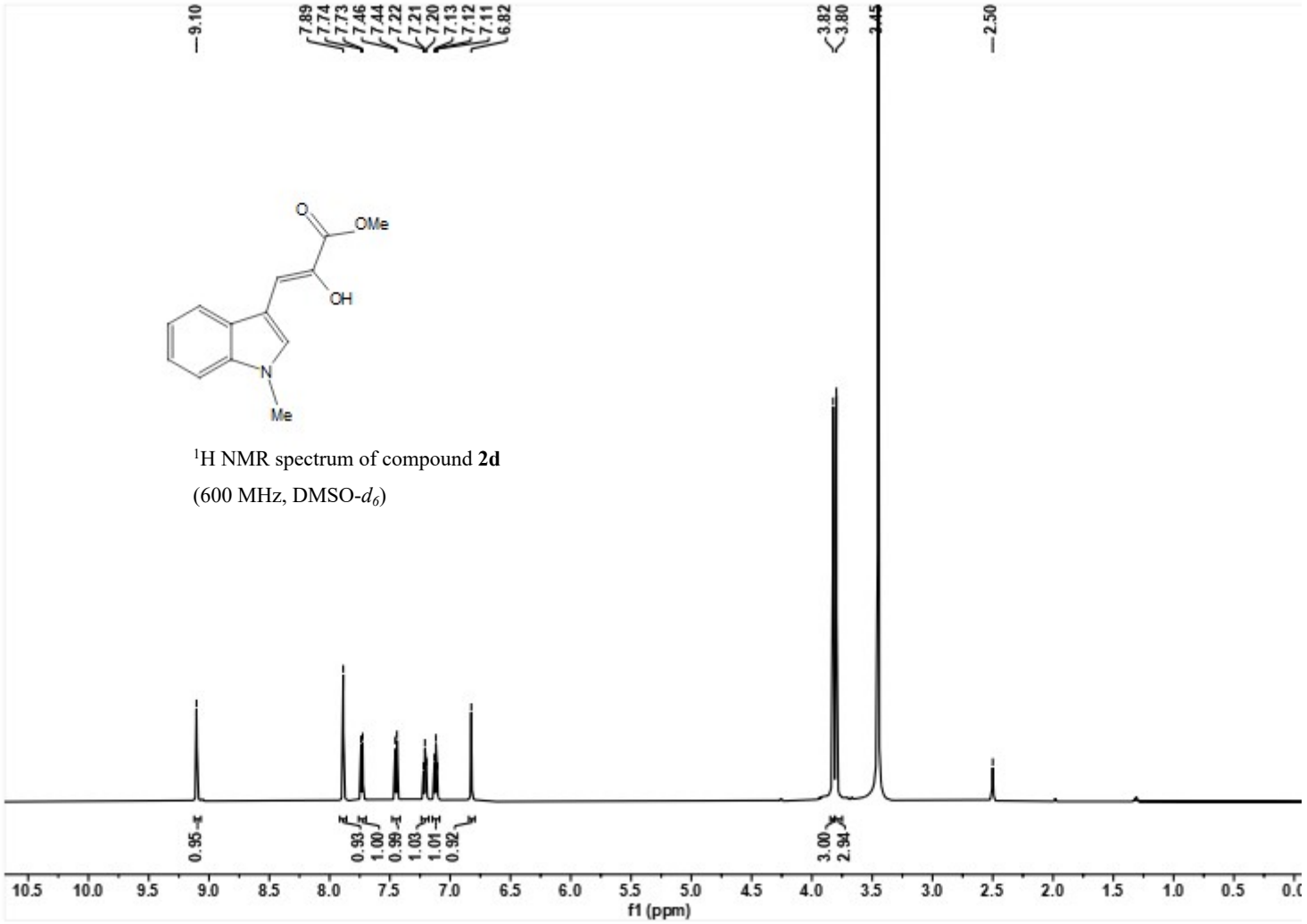
^{1}H NMR spectrum of compound **2c**

(600 MHz, DMSO-d_6)

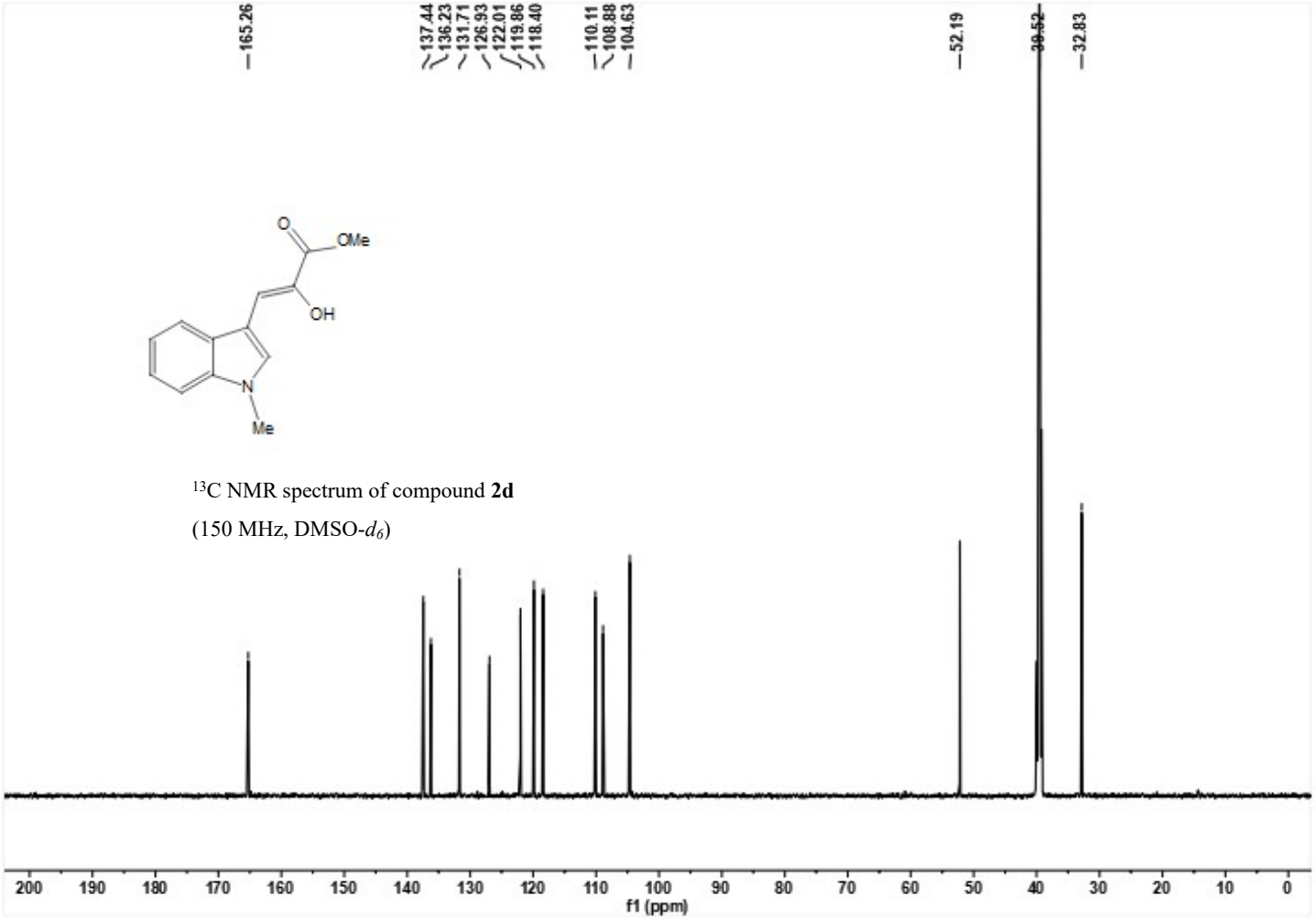


^{13}C NMR spectrum of compound **2c**

(150 MHz, DMSO-d_6)

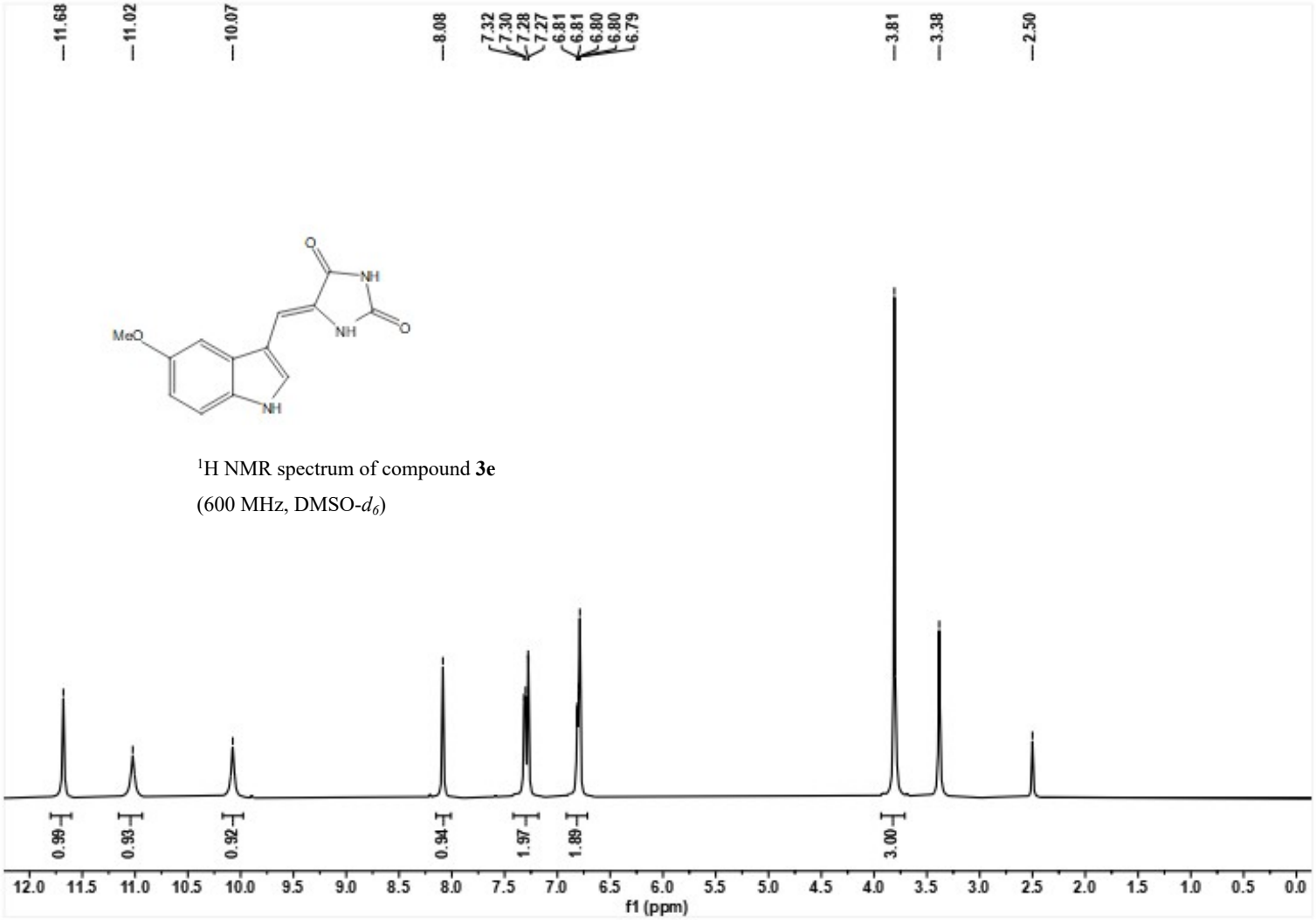


^{1}H NMR spectrum of compound **2d**
(600 MHz, DMSO-d_6)

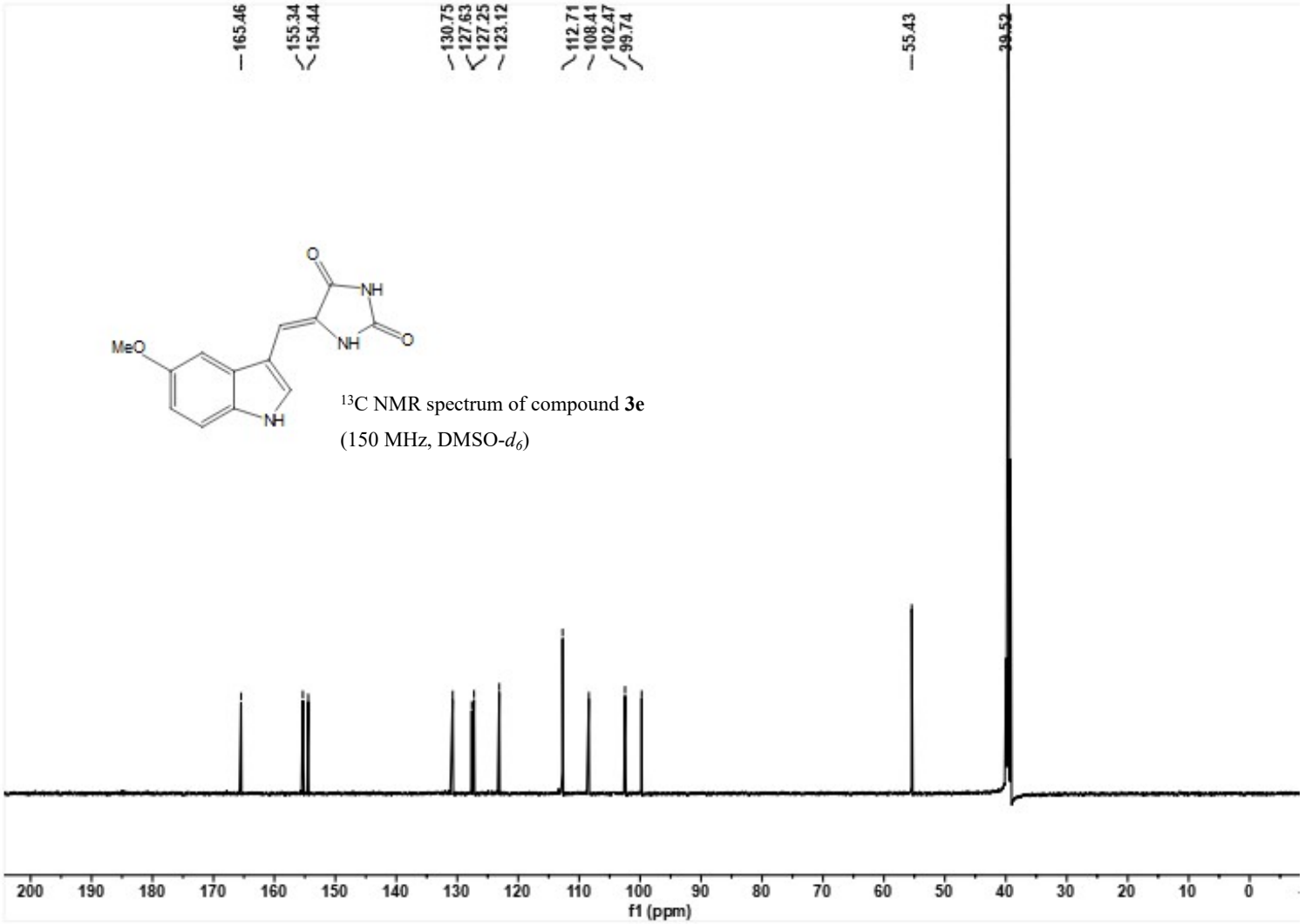


^{13}C NMR spectrum of compound **2d**

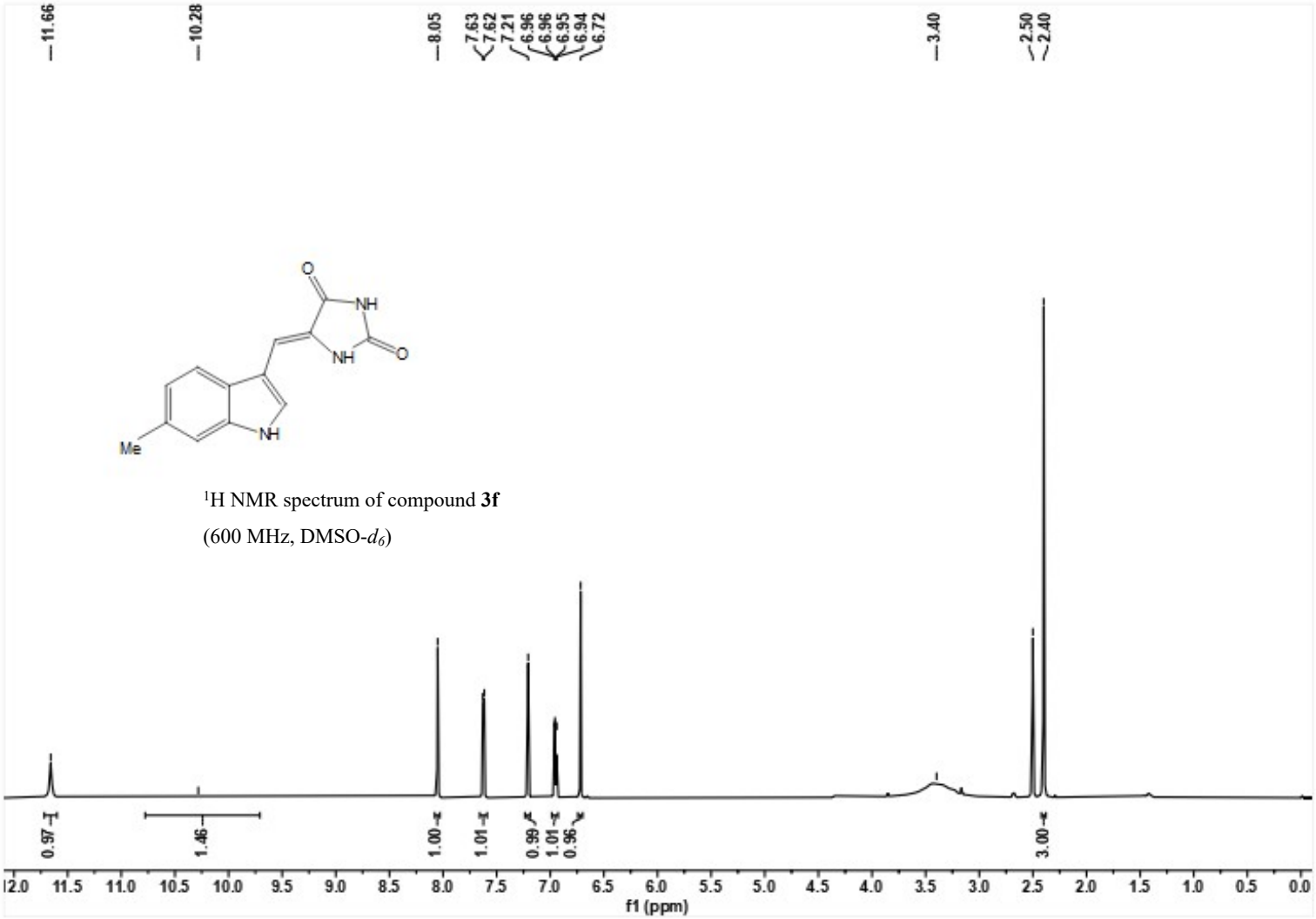
(150 MHz, DMSO-d_6)



^{1}H NMR spectrum of compound **3e**
(600 MHz, DMSO-d_6)

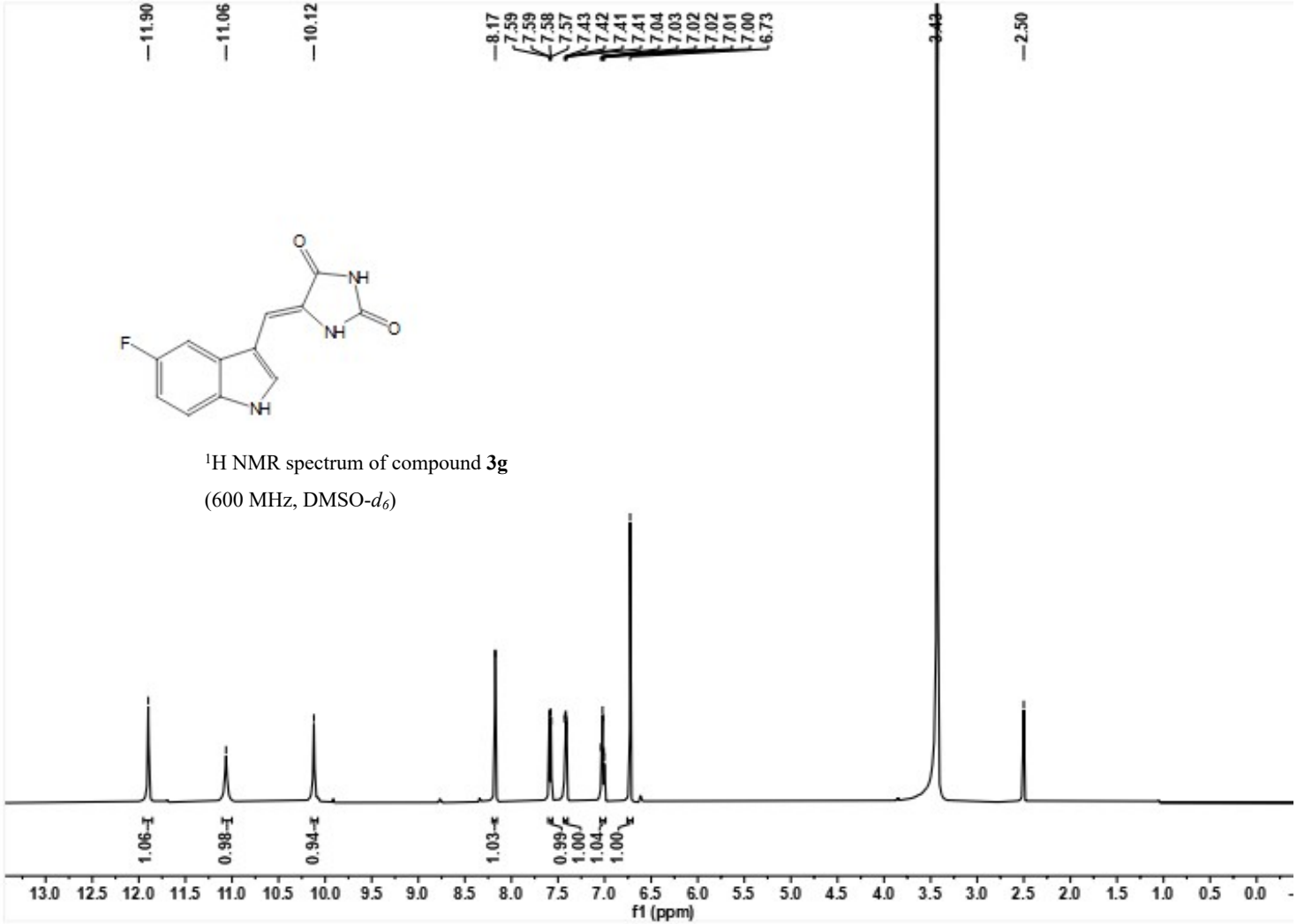


^{13}C NMR spectrum of compound **3e**
(150 MHz, DMSO-d_6)



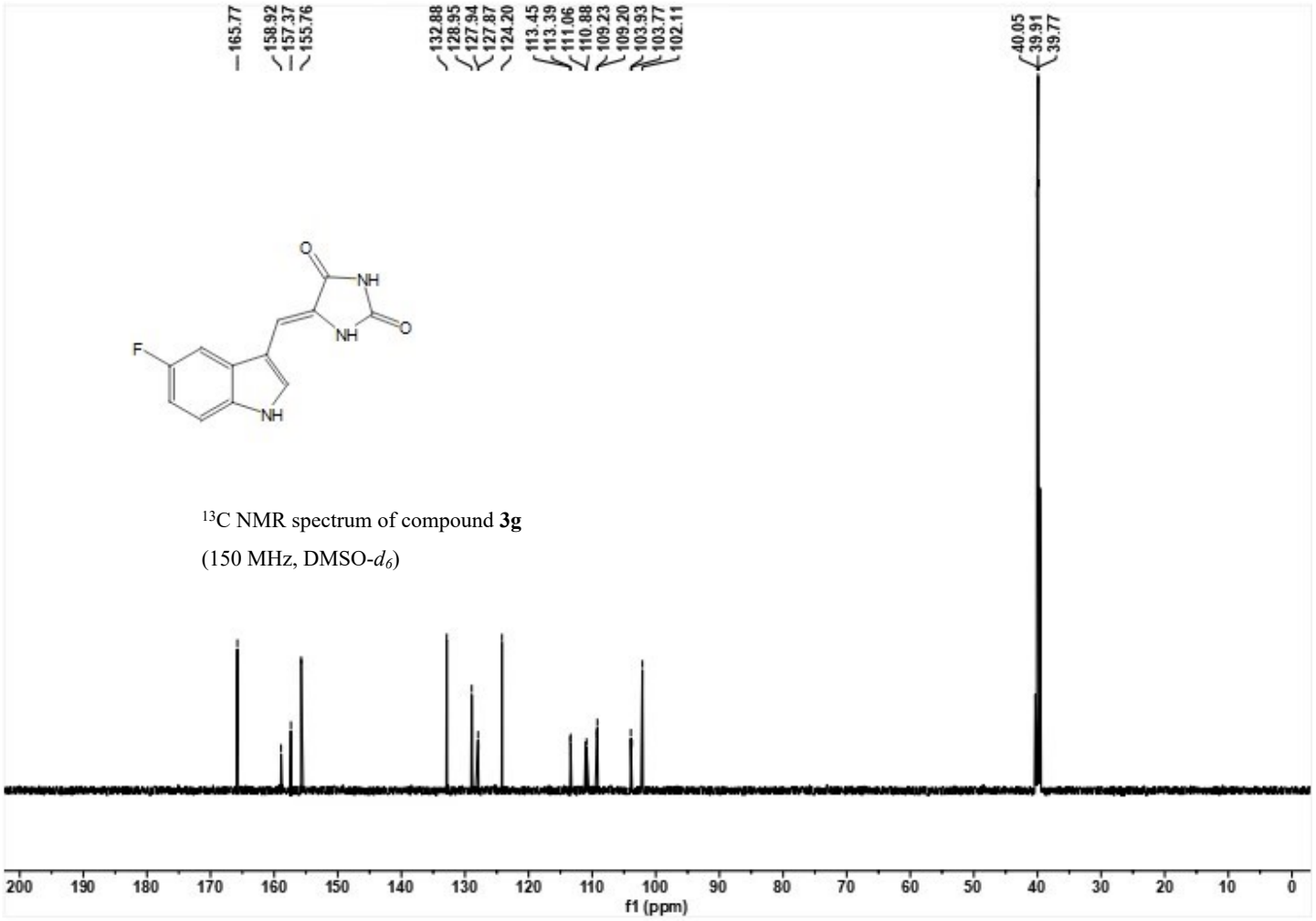
^{1}H NMR spectrum of compound **3f**

(600 MHz, DMSO-d_6)



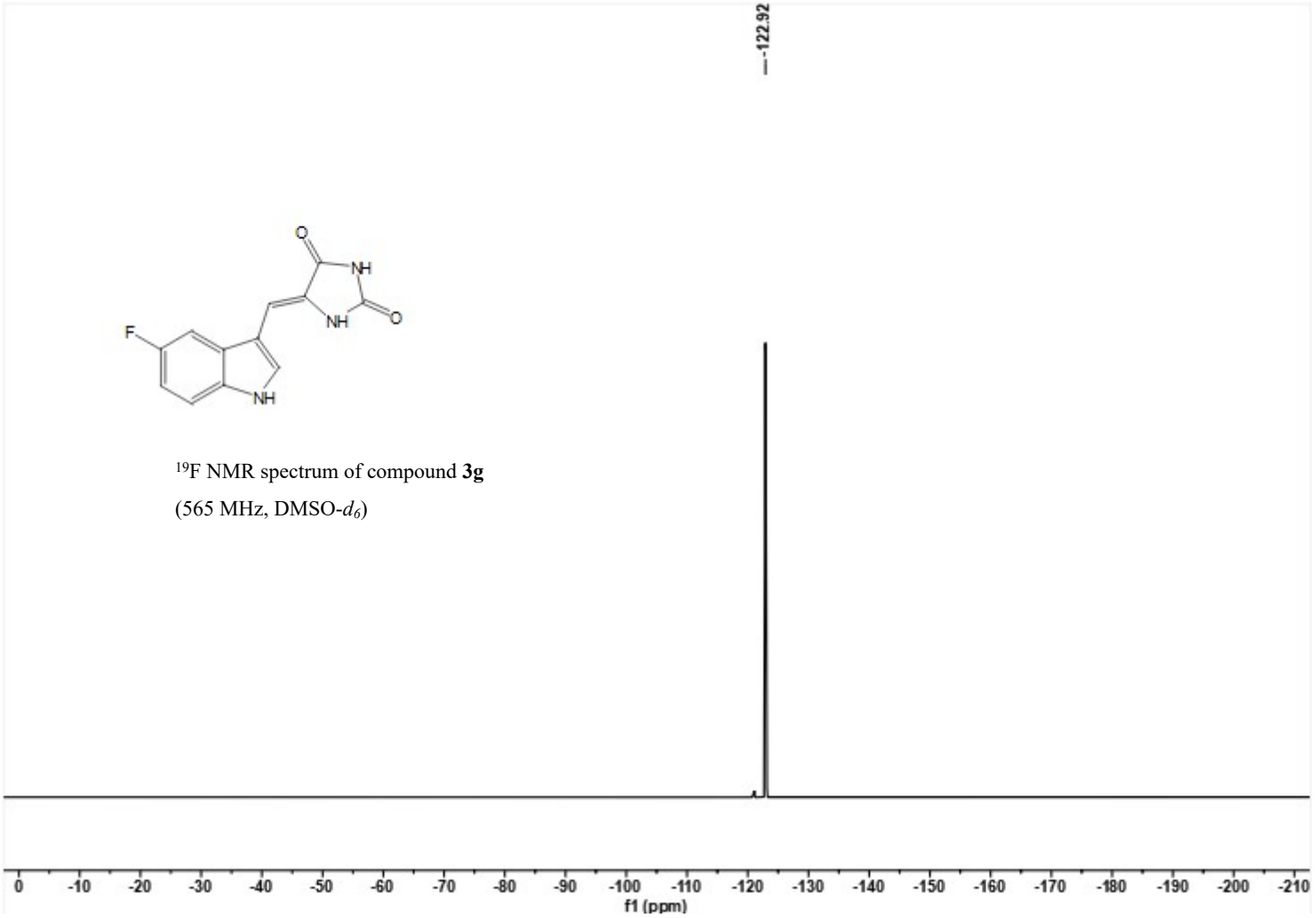
^{1}H NMR spectrum of compound **3g**

(600 MHz, DMSO-d_6)



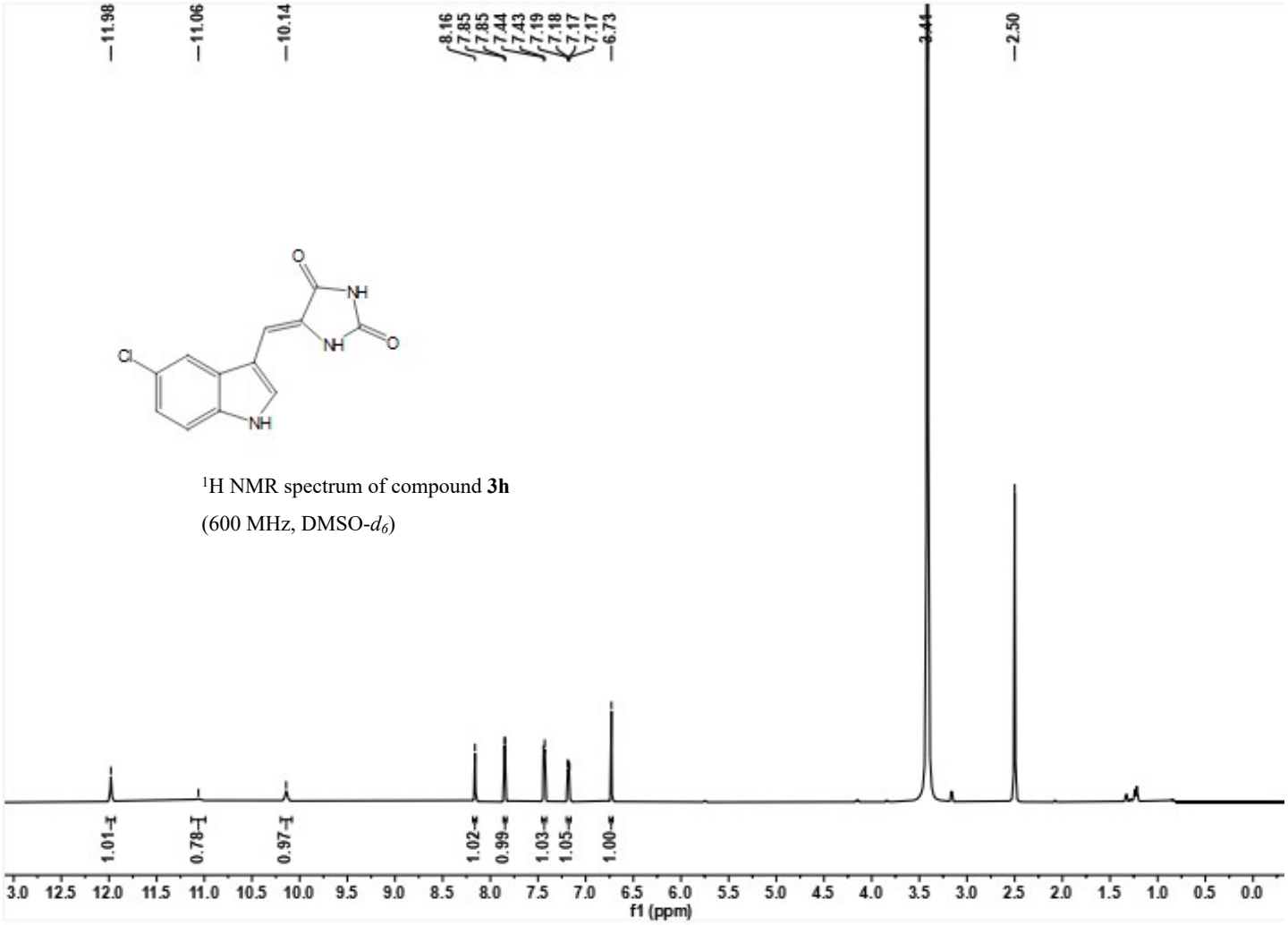
^{13}C NMR spectrum of compound **3g**

(150 MHz, DMSO-d_6)



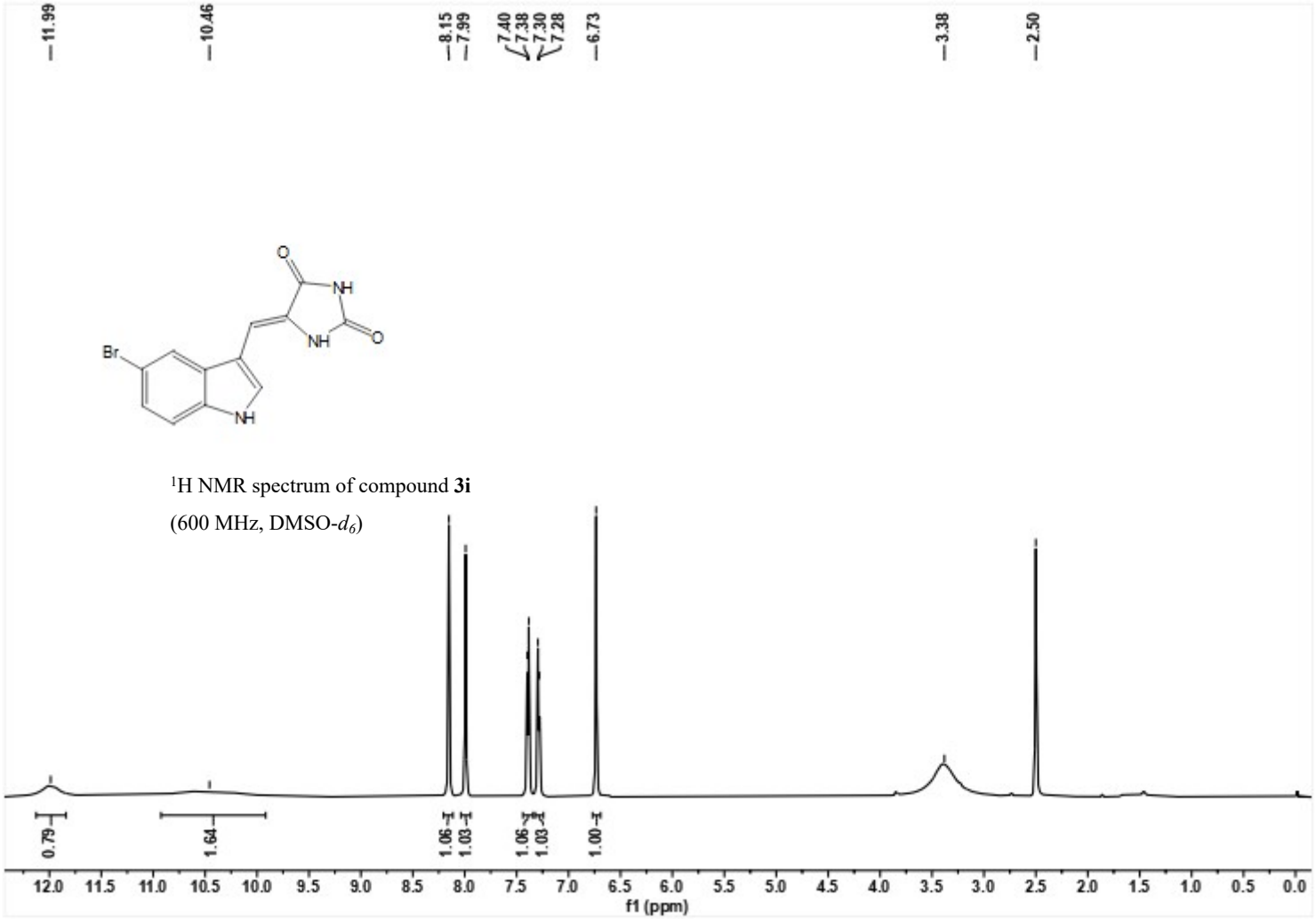
^{19}F NMR spectrum of compound **3g**

(565 MHz, DMSO-d_6)



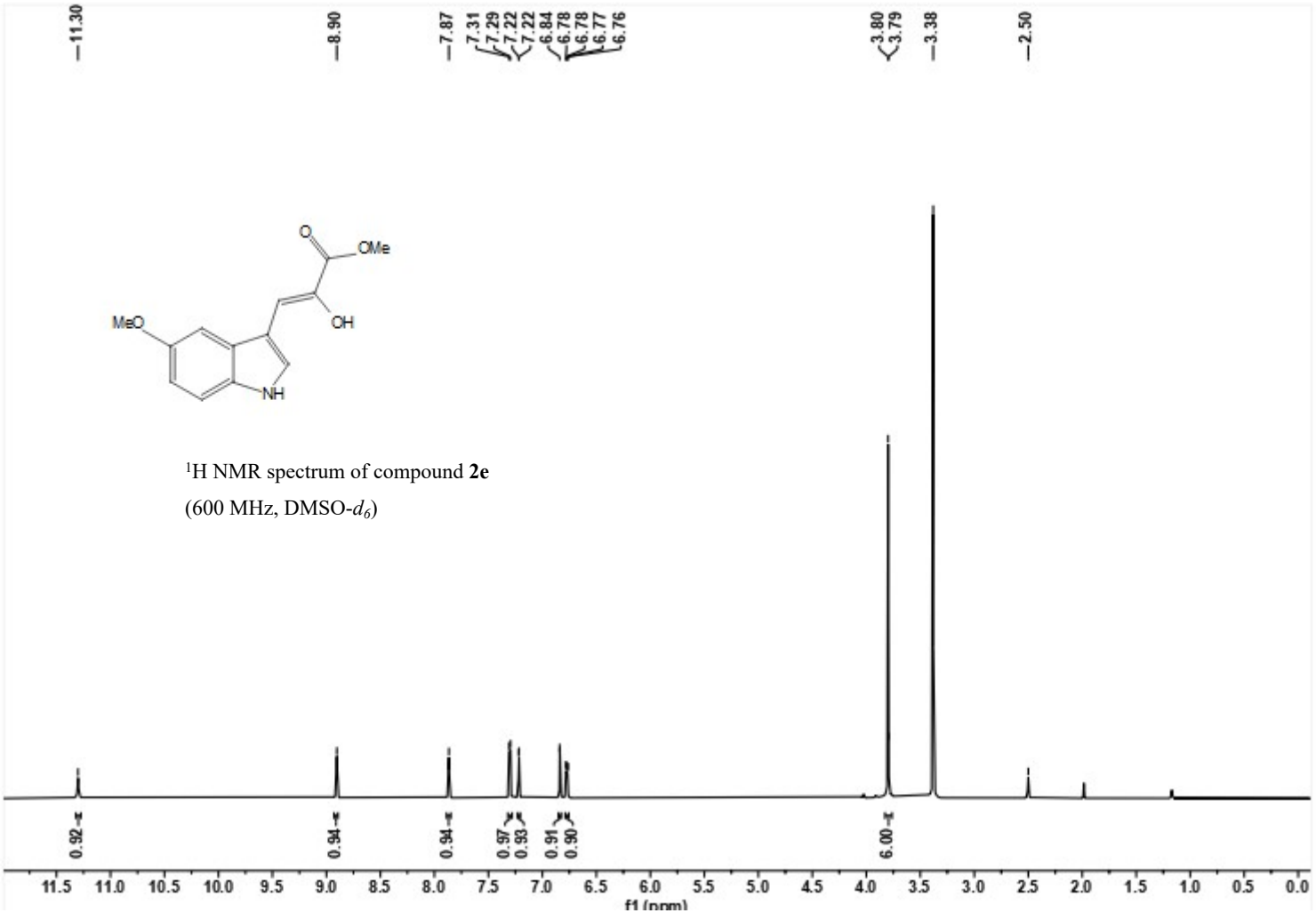
^{1}H NMR spectrum of compound **3h**

(600 MHz, DMSO-d_6)



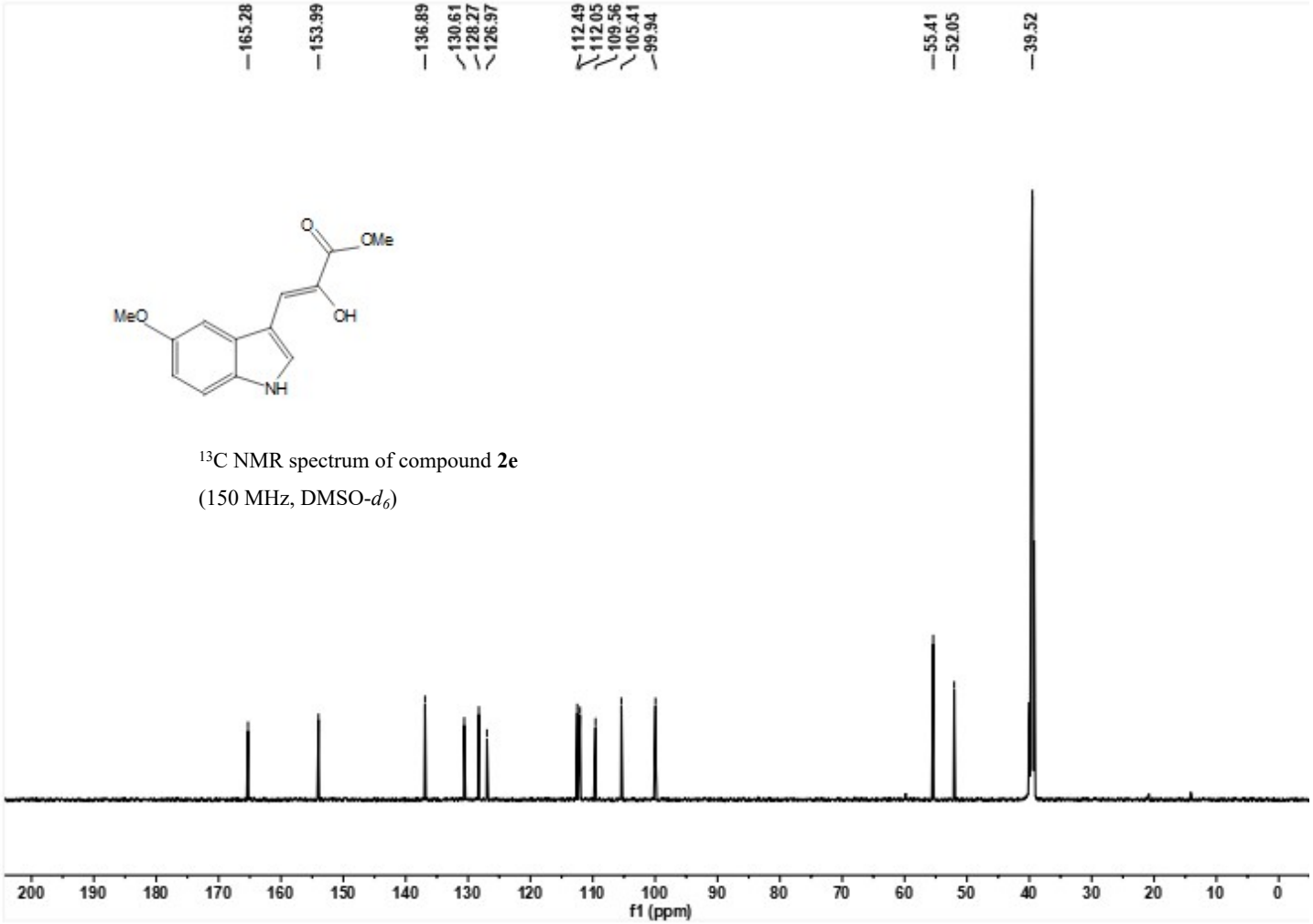
^{1}H NMR spectrum of compound **3i**

(600 MHz, DMSO-d_6)



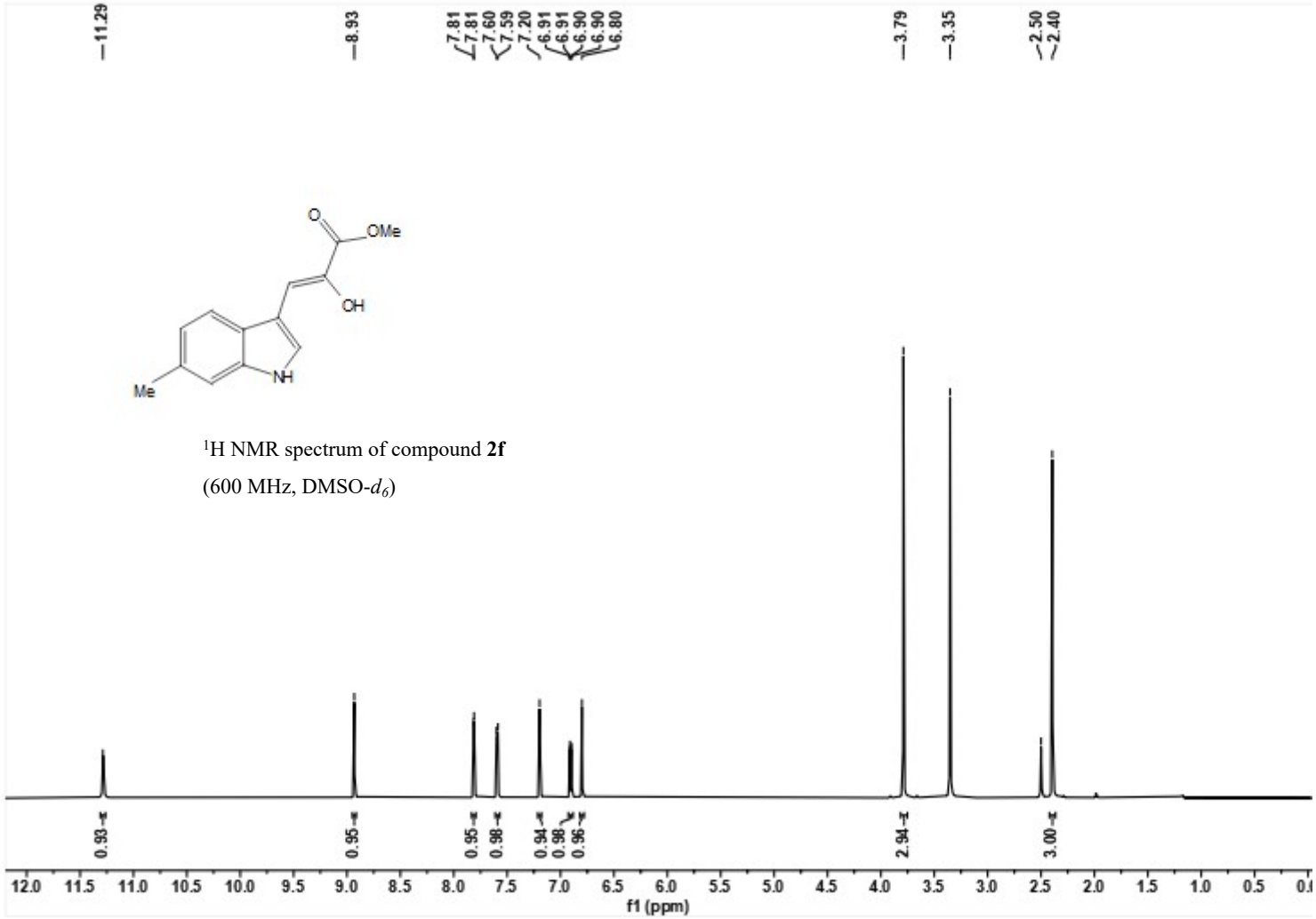
^{1}H NMR spectrum of compound **2e**

(600 MHz, DMSO-d_6)



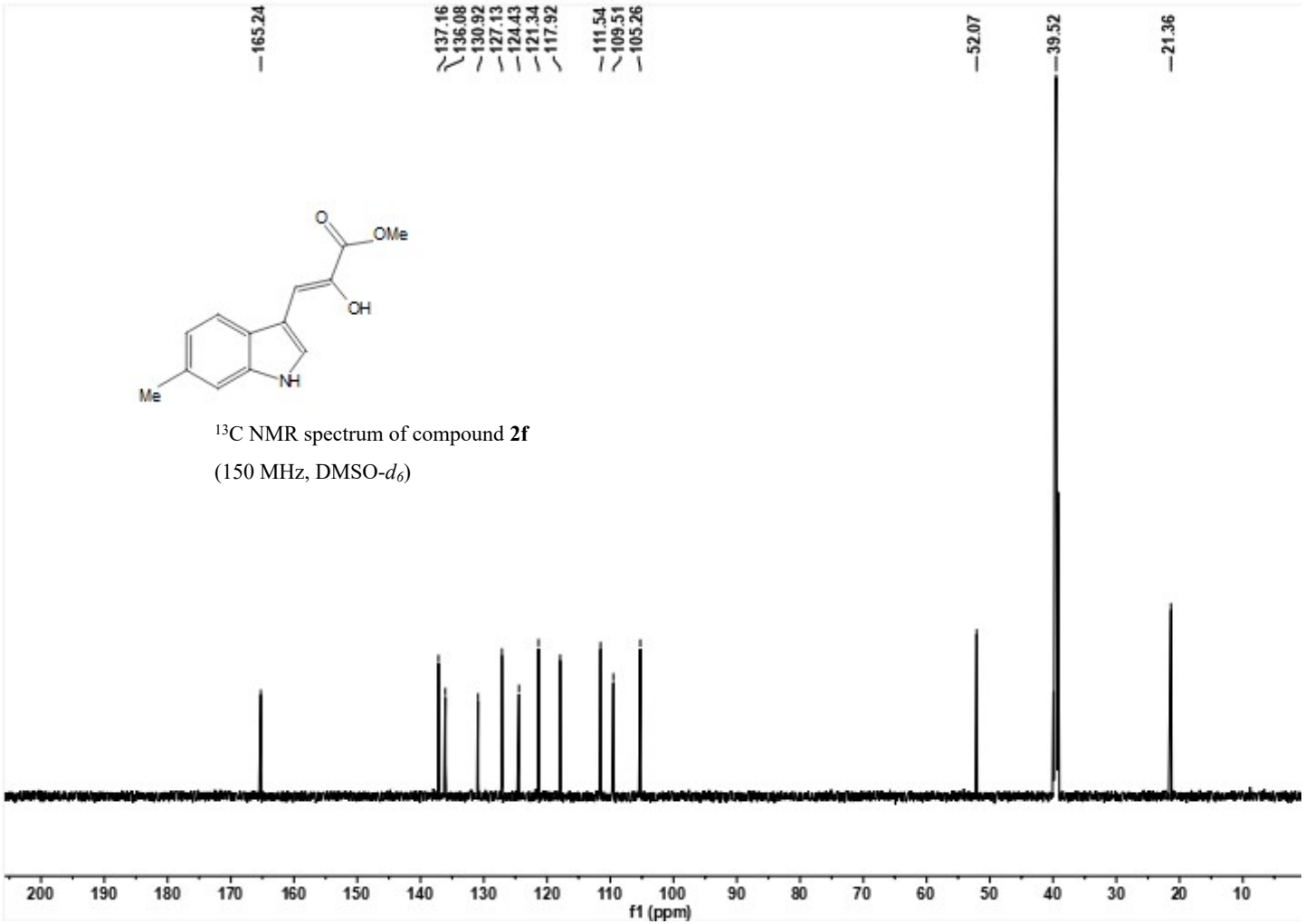
^{13}C NMR spectrum of compound **2e**

(150 MHz, DMSO-d_6)



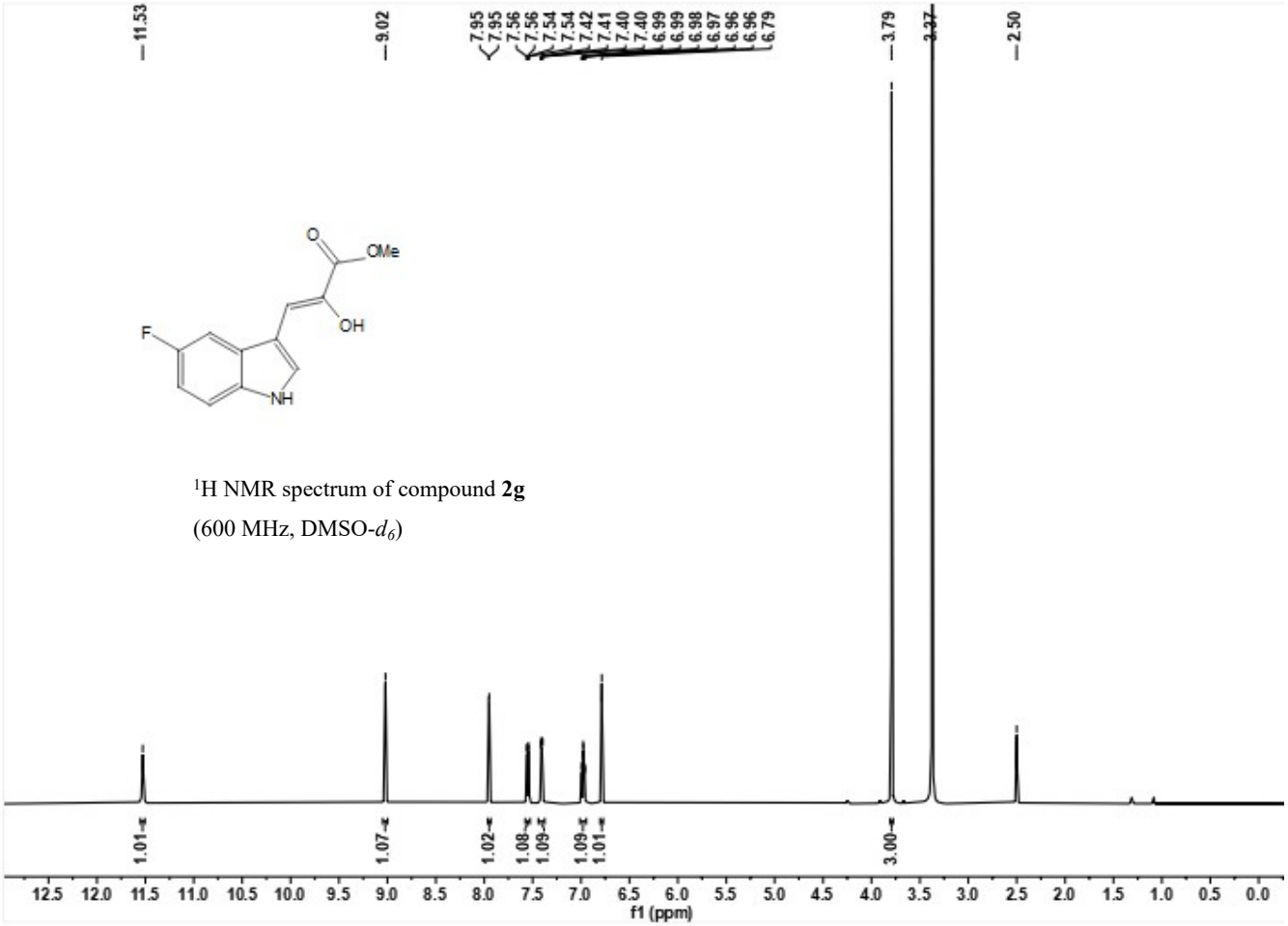
^{1}H NMR spectrum of compound **2f**

(600 MHz, DMSO-d_6)



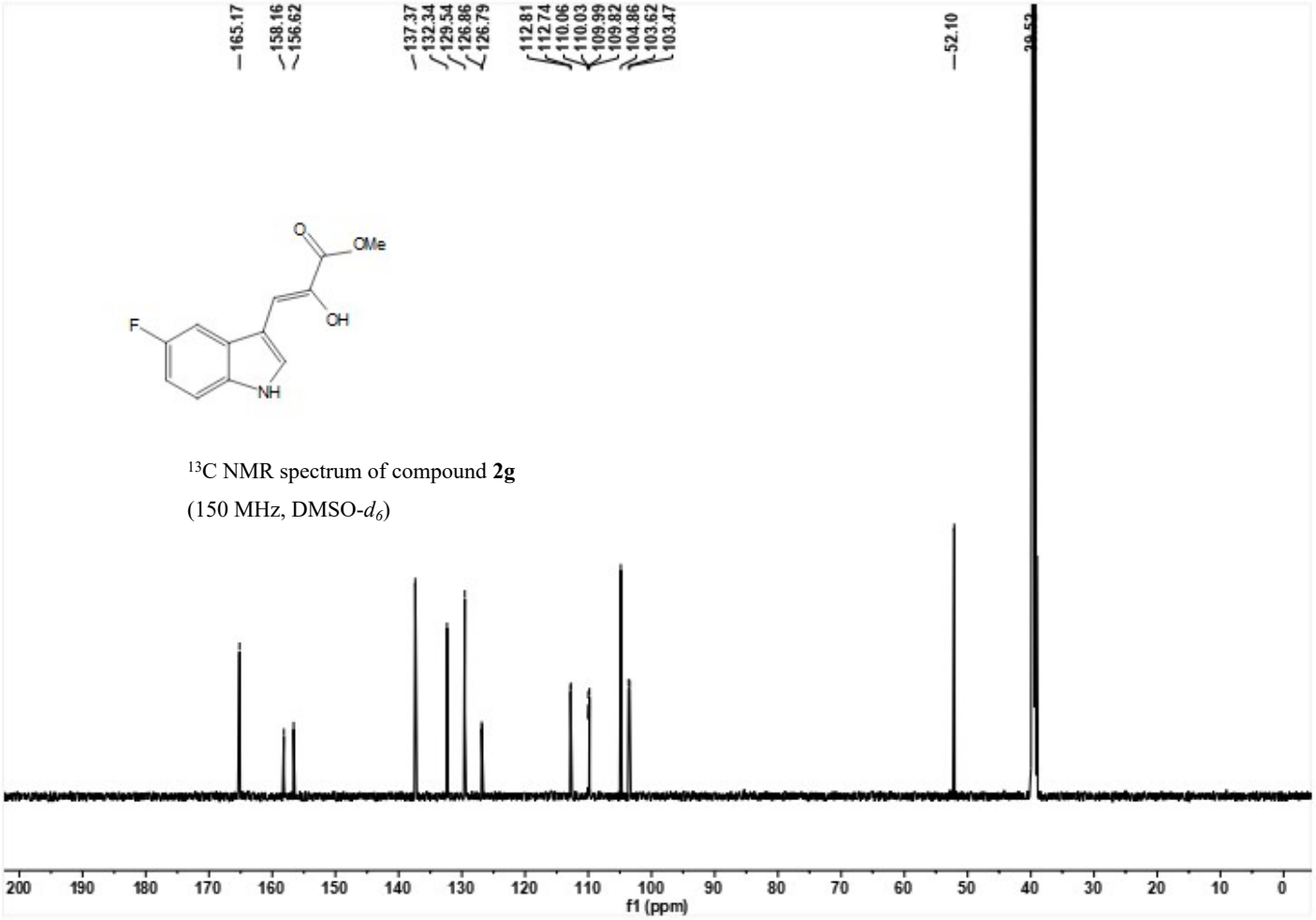
^{13}C NMR spectrum of compound **2f**

(150 MHz, DMSO-d_6)



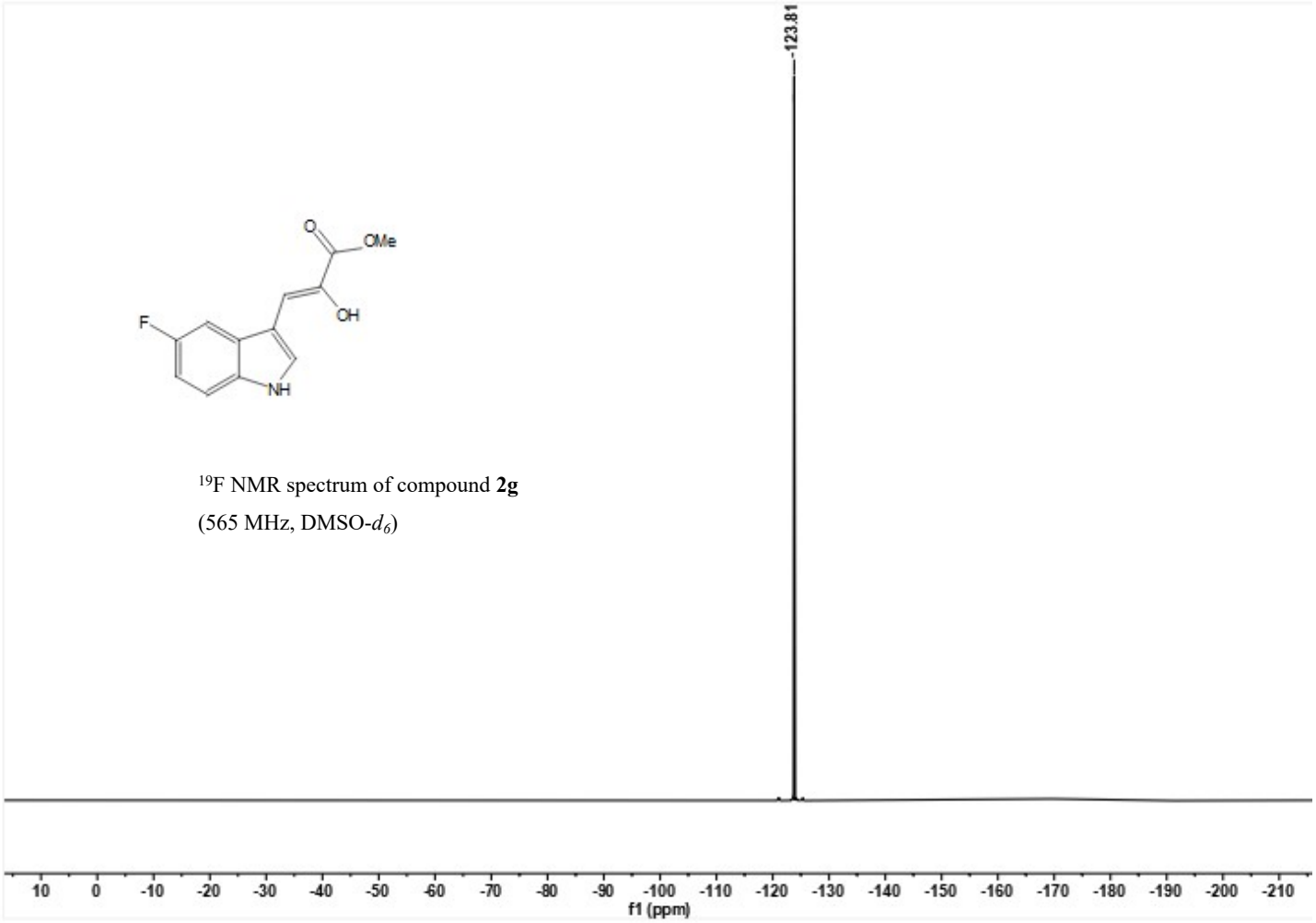
^{1}H NMR spectrum of compound **2g**

(600 MHz, DMSO-d_6)



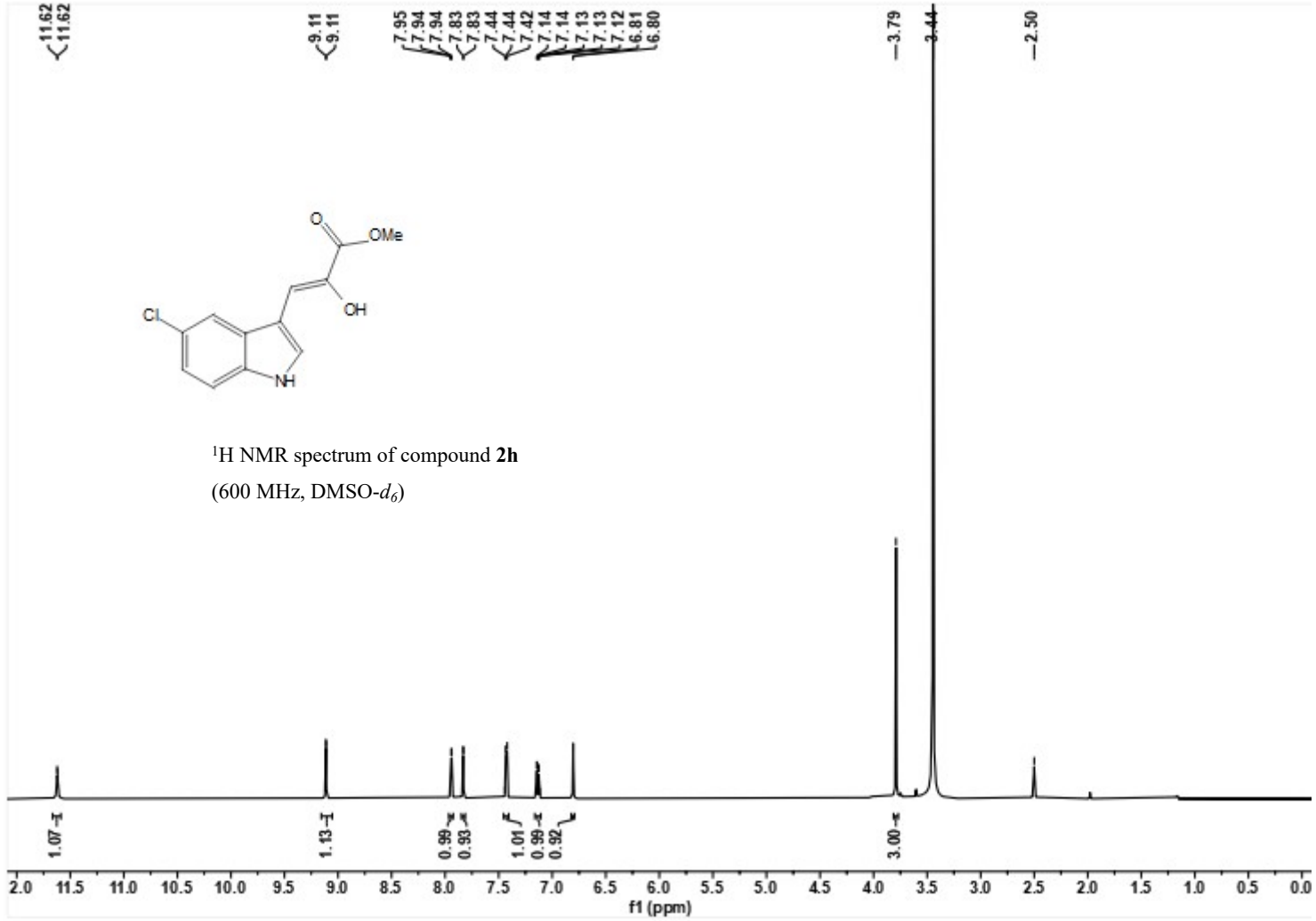
^{13}C NMR spectrum of compound **2g**

(150 MHz, DMSO-d_6)



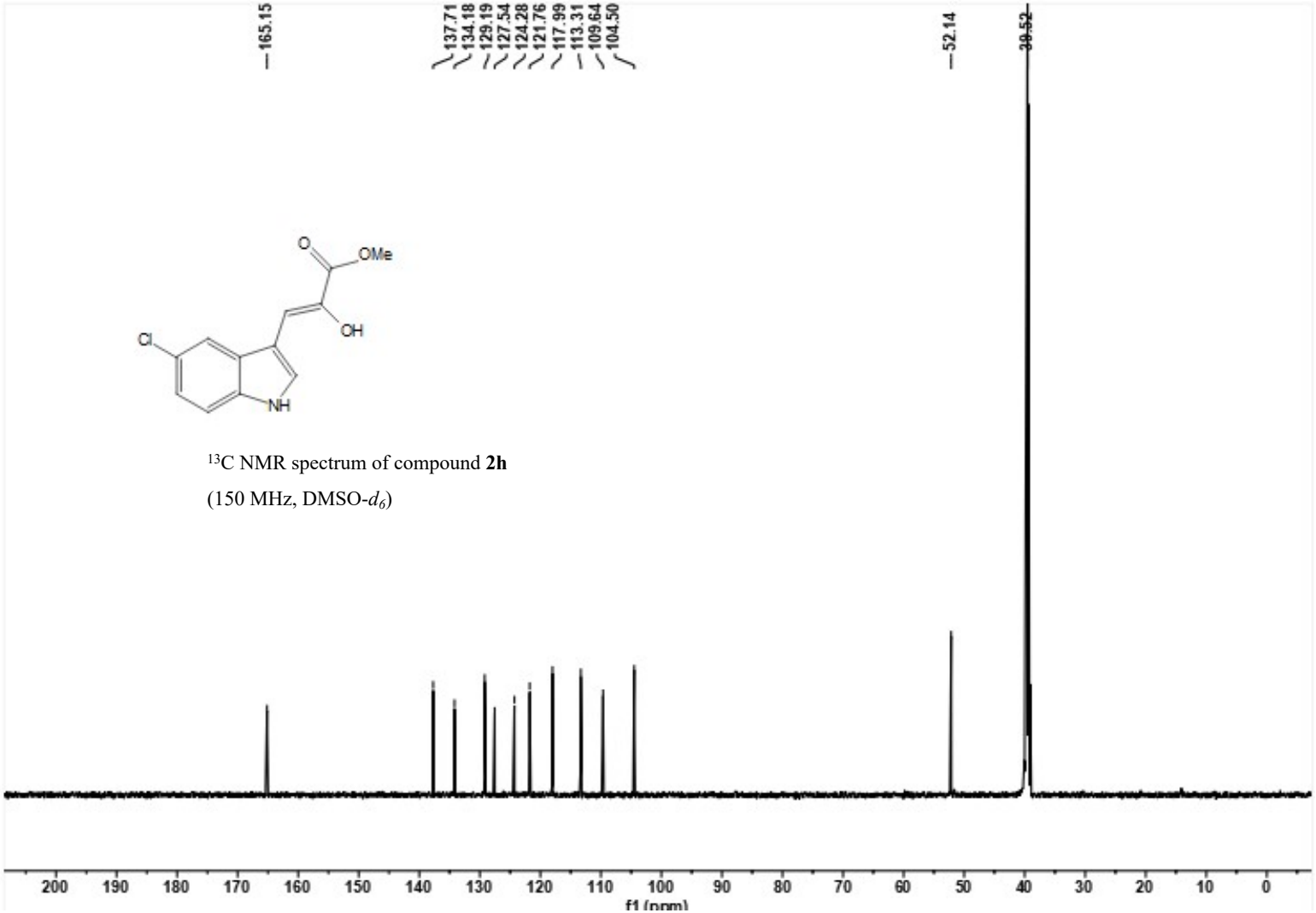
^{19}F NMR spectrum of compound **2g**

(565 MHz, DMSO-d_6)



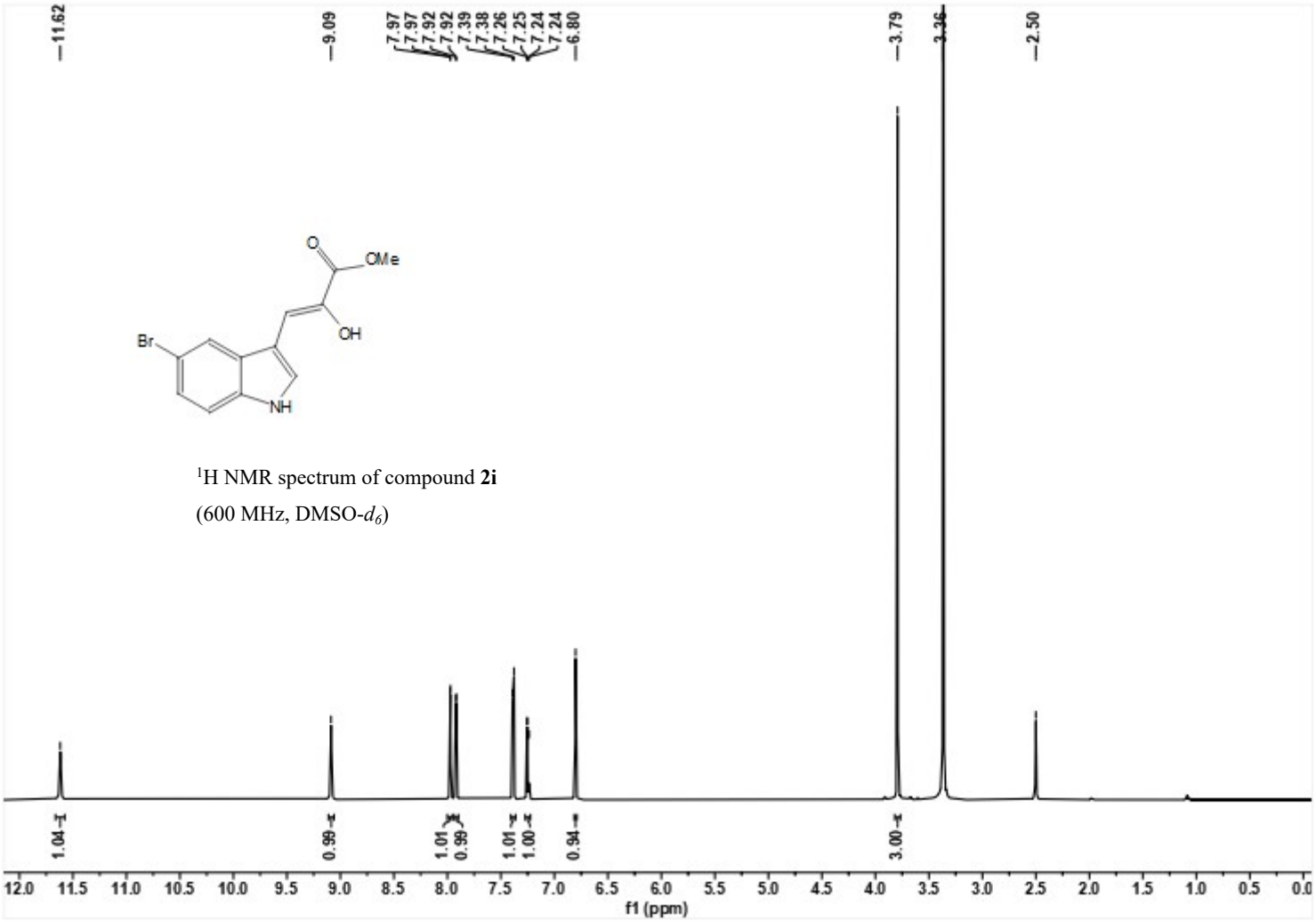
^{1}H NMR spectrum of compound **2h**

(600 MHz, DMSO-d_6)



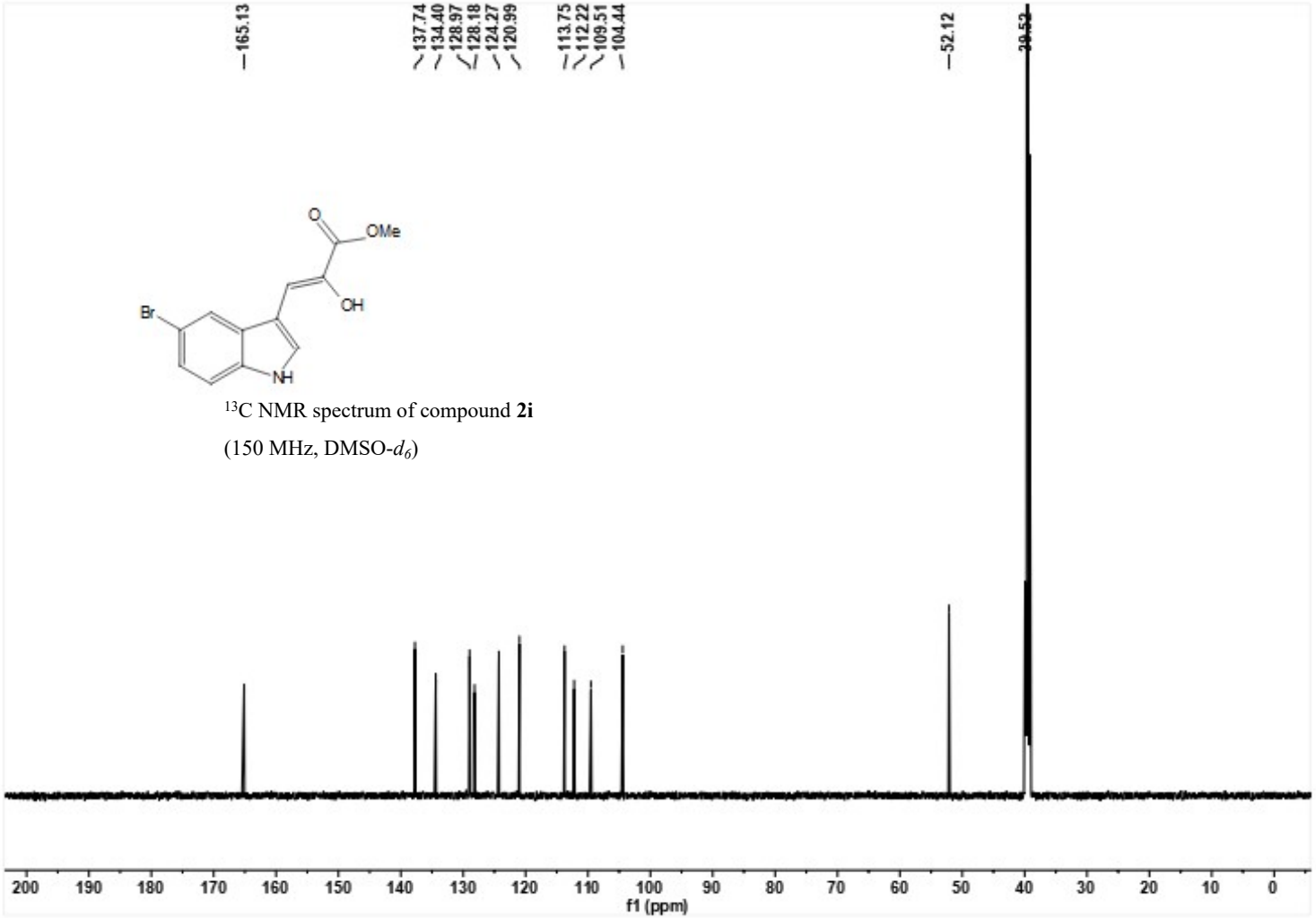
^{13}C NMR spectrum of compound **2h**

(150 MHz, DMSO-d_6)



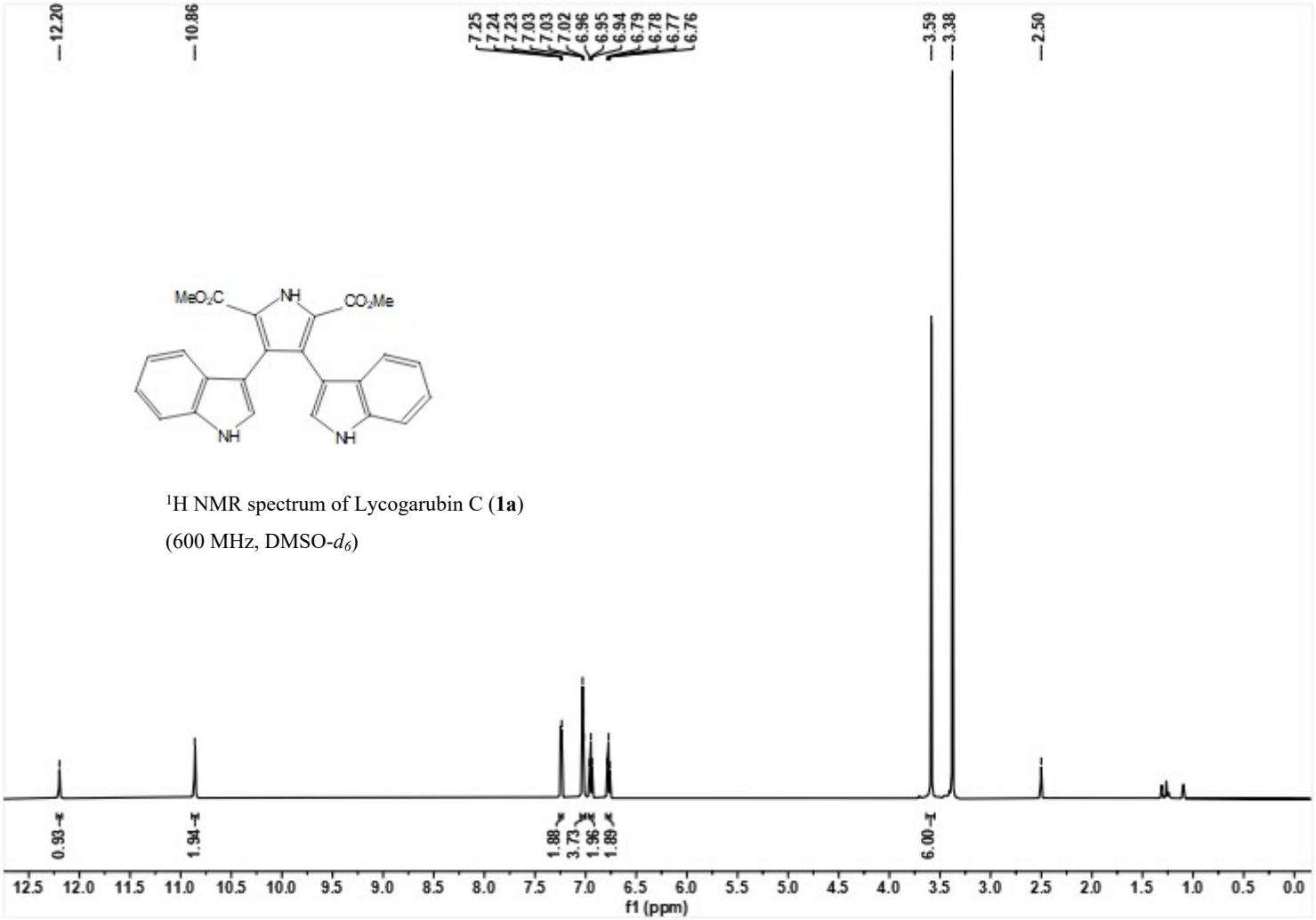
^{1}H NMR spectrum of compound **2i**

(600 MHz, DMSO-d_6)



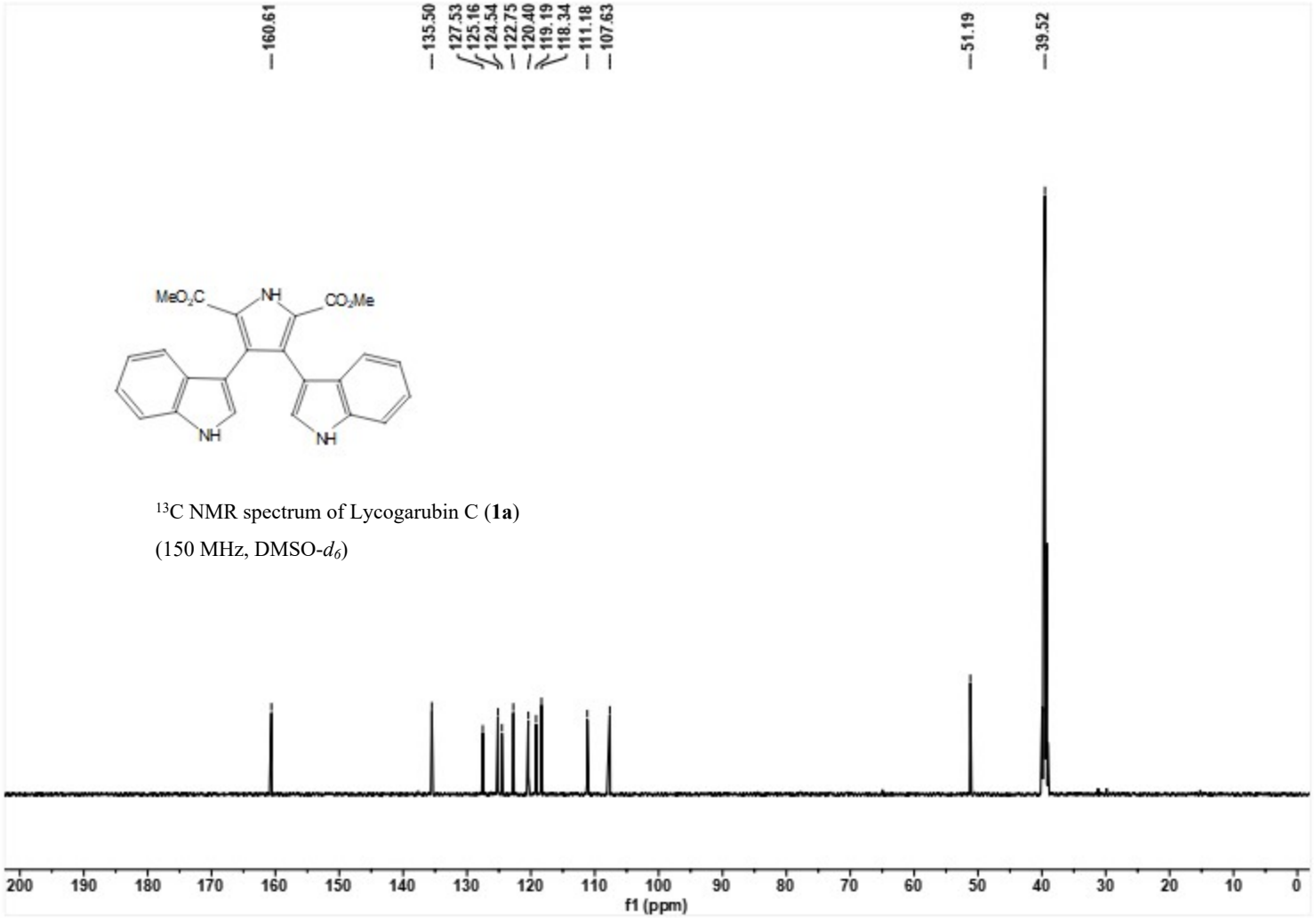
^{13}C NMR spectrum of compound **2i**

(150 MHz, DMSO-d_6)



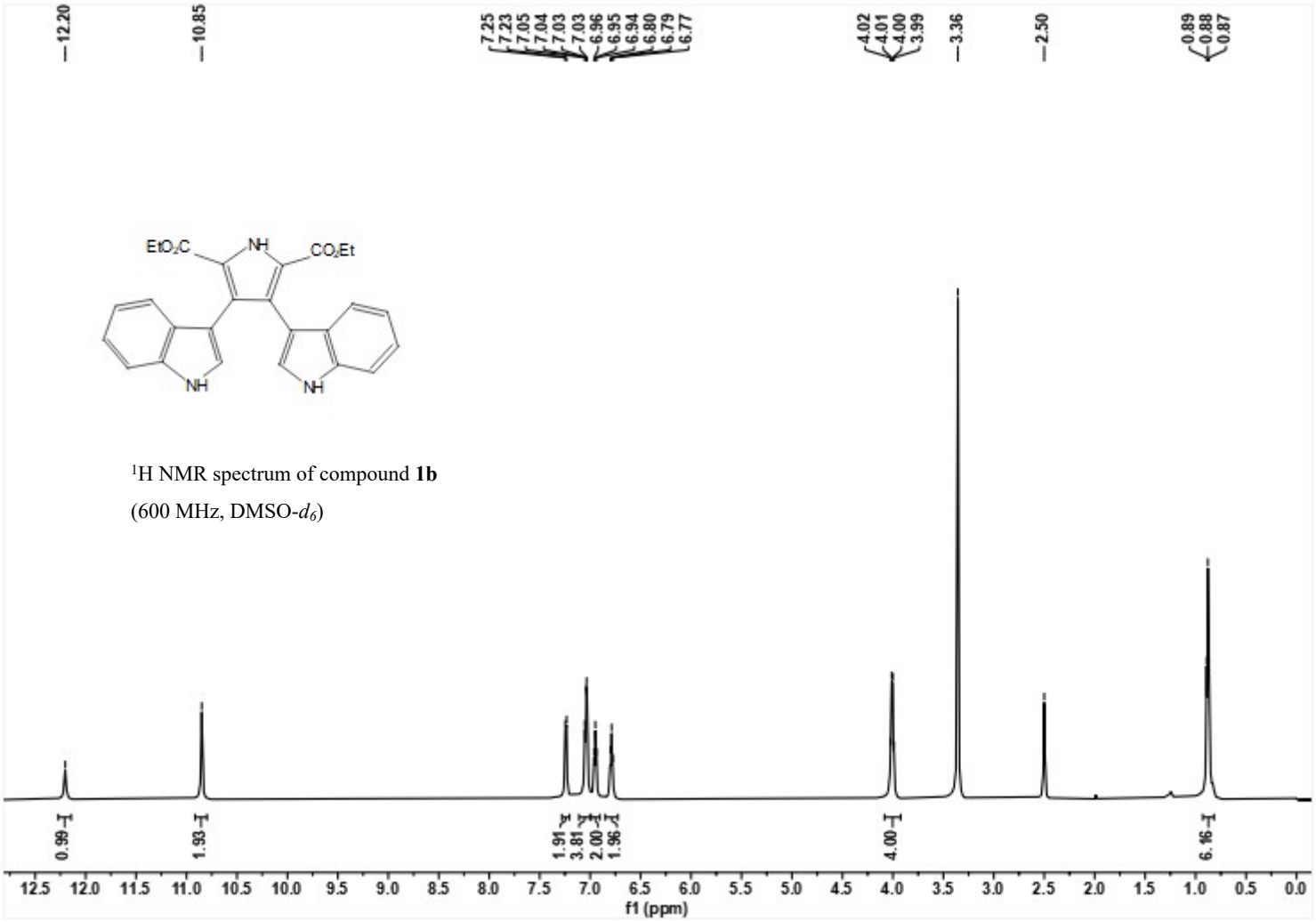
^{1}H NMR spectrum of Lycogarubin C (**1a**)

(600 MHz, DMSO-d_6)



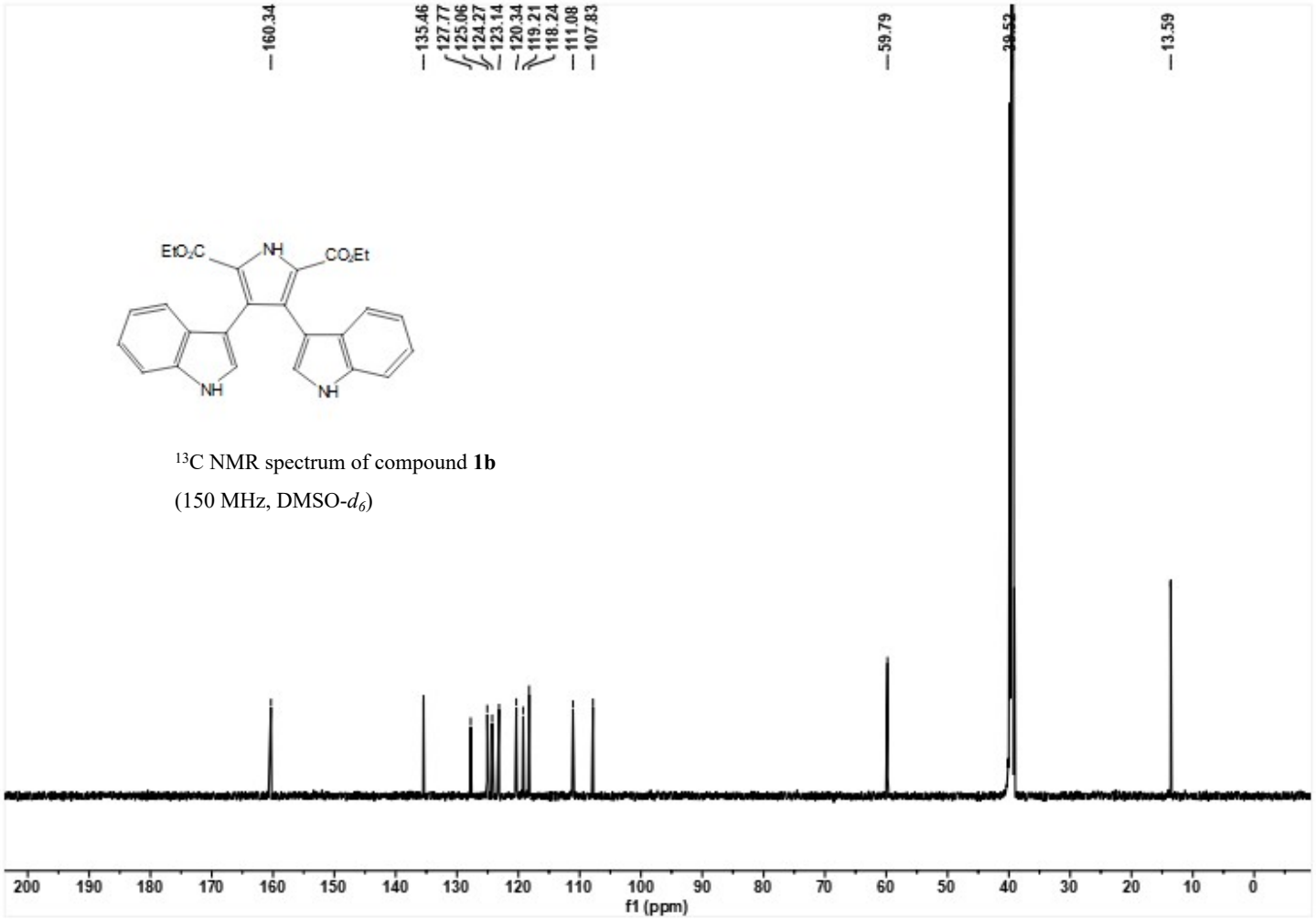
^{13}C NMR spectrum of Lycogarubin C (**1a**)

(150 MHz, DMSO-d_6)



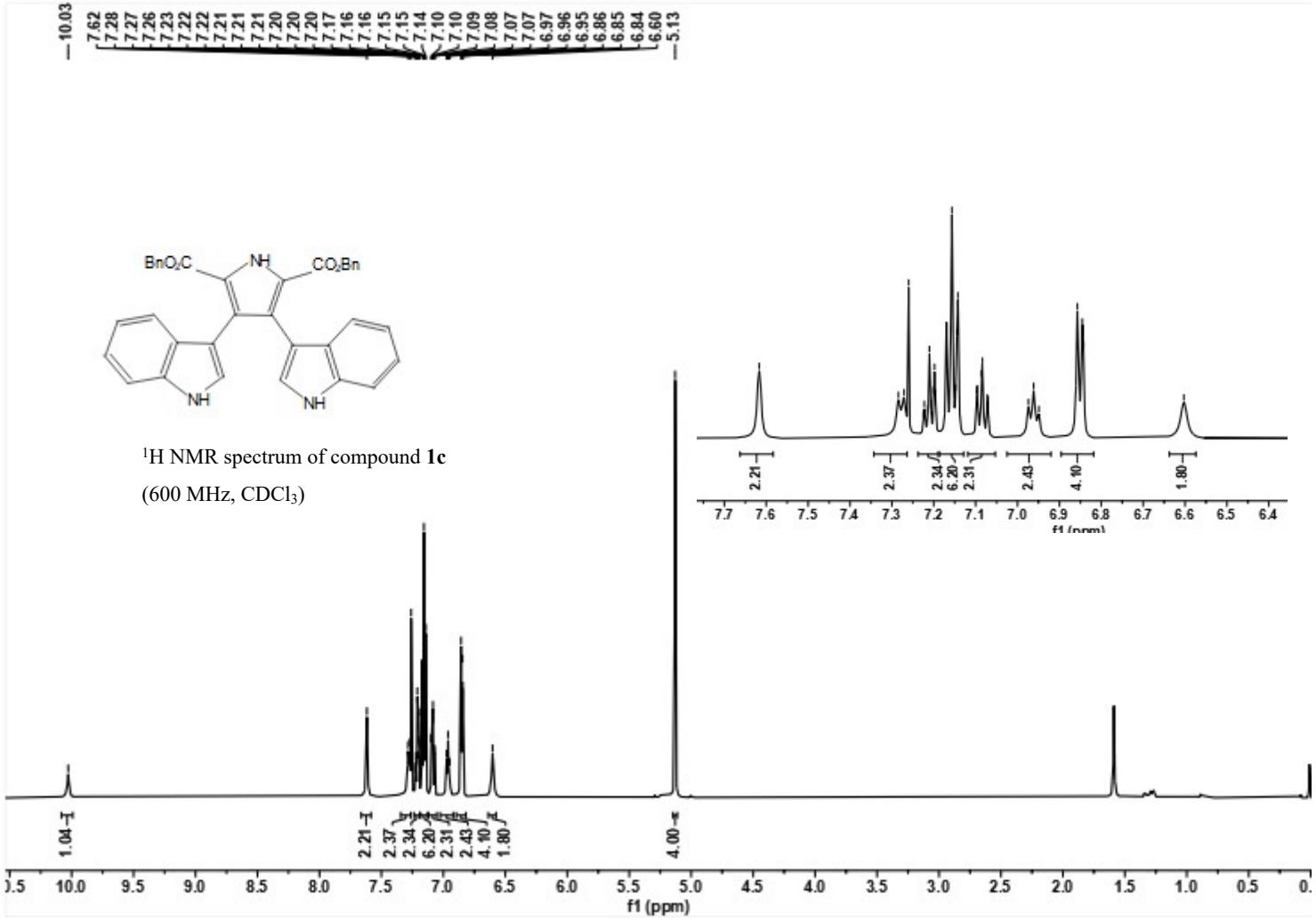
^{1}H NMR spectrum of compound **1b**

(600 MHz, DMSO-d_6)



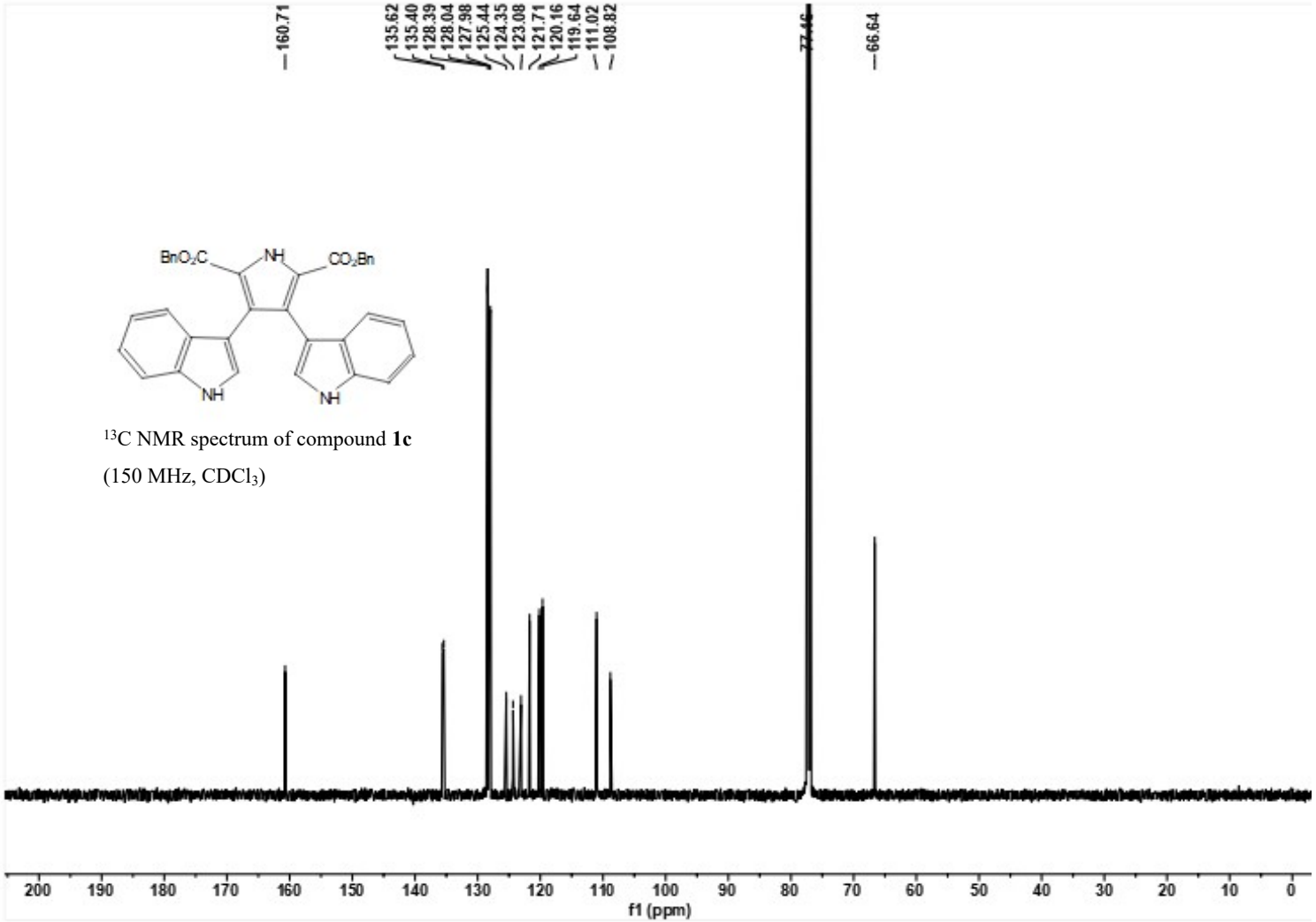
^{13}C NMR spectrum of compound **1b**

(150 MHz, DMSO-d_6)



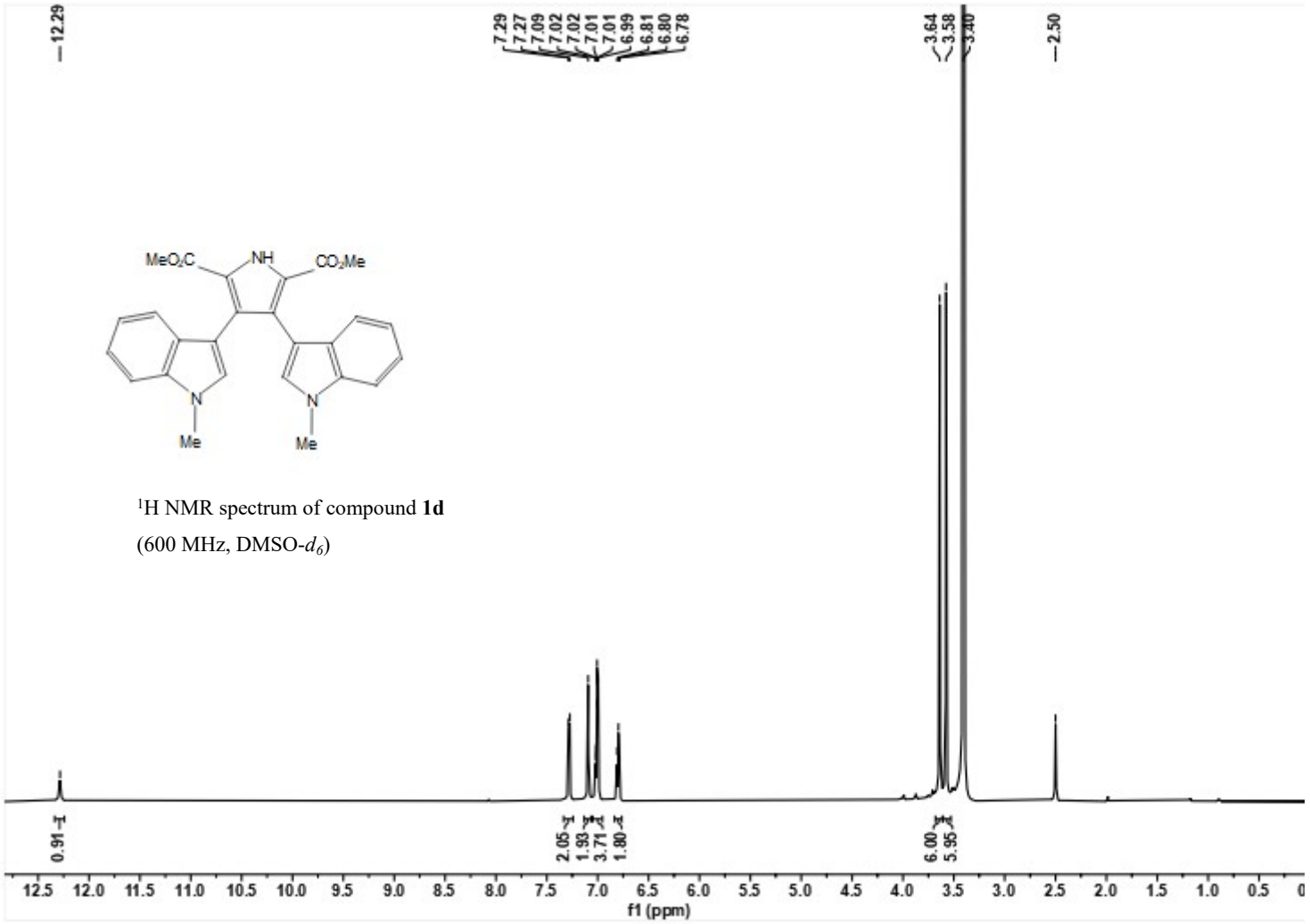
^{1}H NMR spectrum of compound **1c**

(600 MHz, $CDCl_3$)

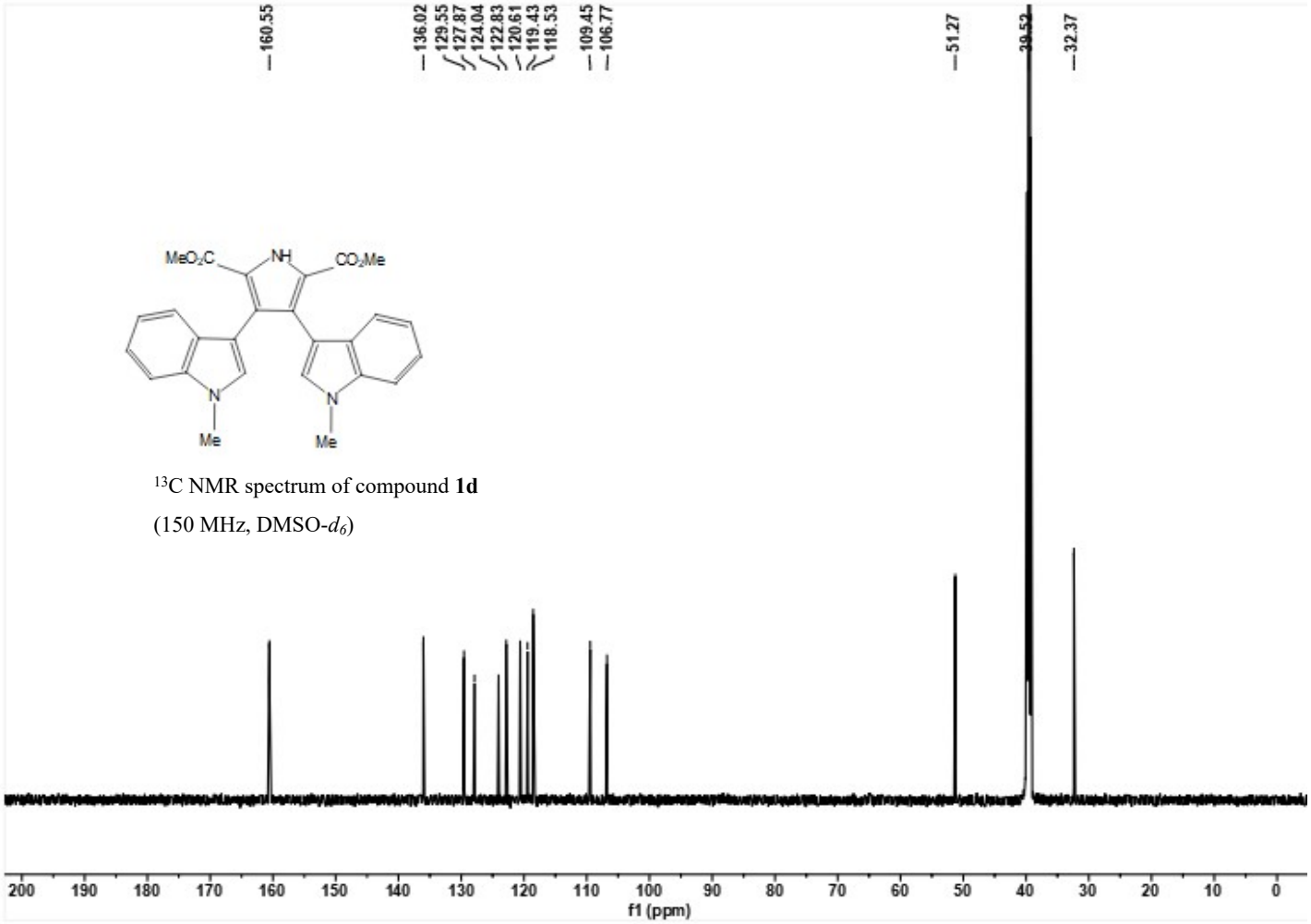


^{13}C NMR spectrum of compound **1c**

(150 MHz, $CDCl_3$)

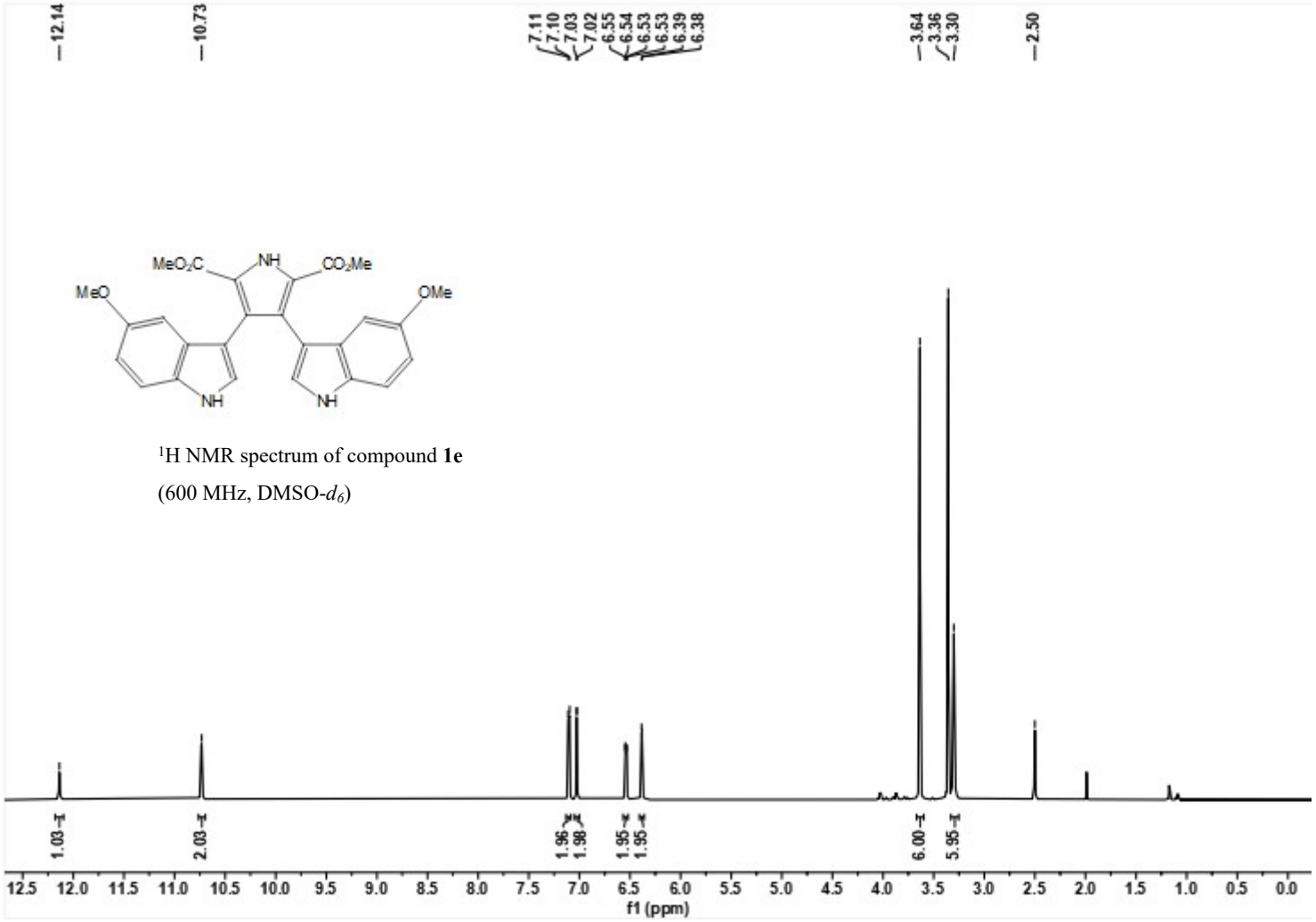


^{1}H NMR spectrum of compound **1d**
(600 MHz, DMSO-d_6)



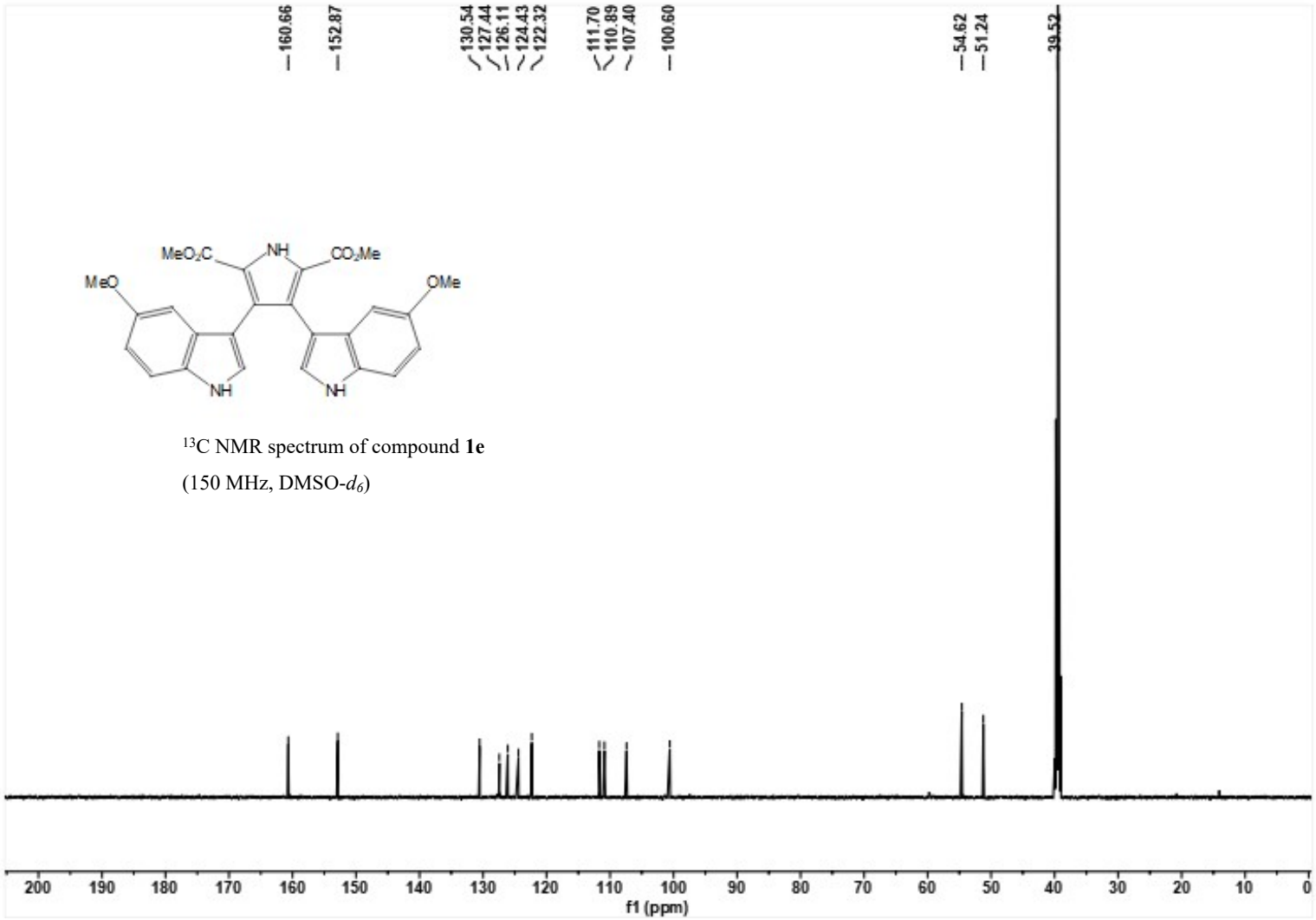
^{13}C NMR spectrum of compound **1d**

(150 MHz, DMSO-d_6)



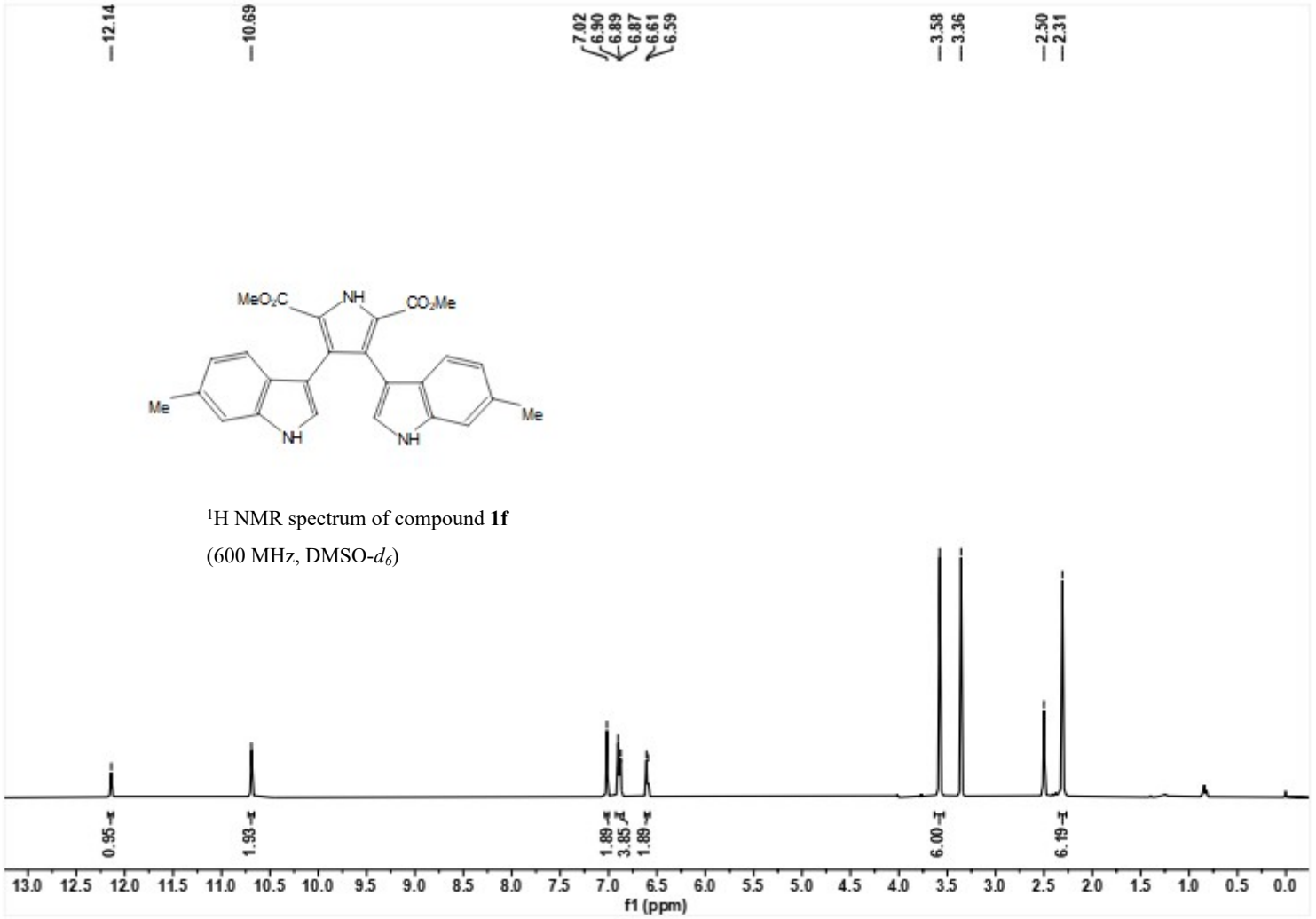
^{1}H NMR spectrum of compound **1e**

(600 MHz, DMSO-d_6)



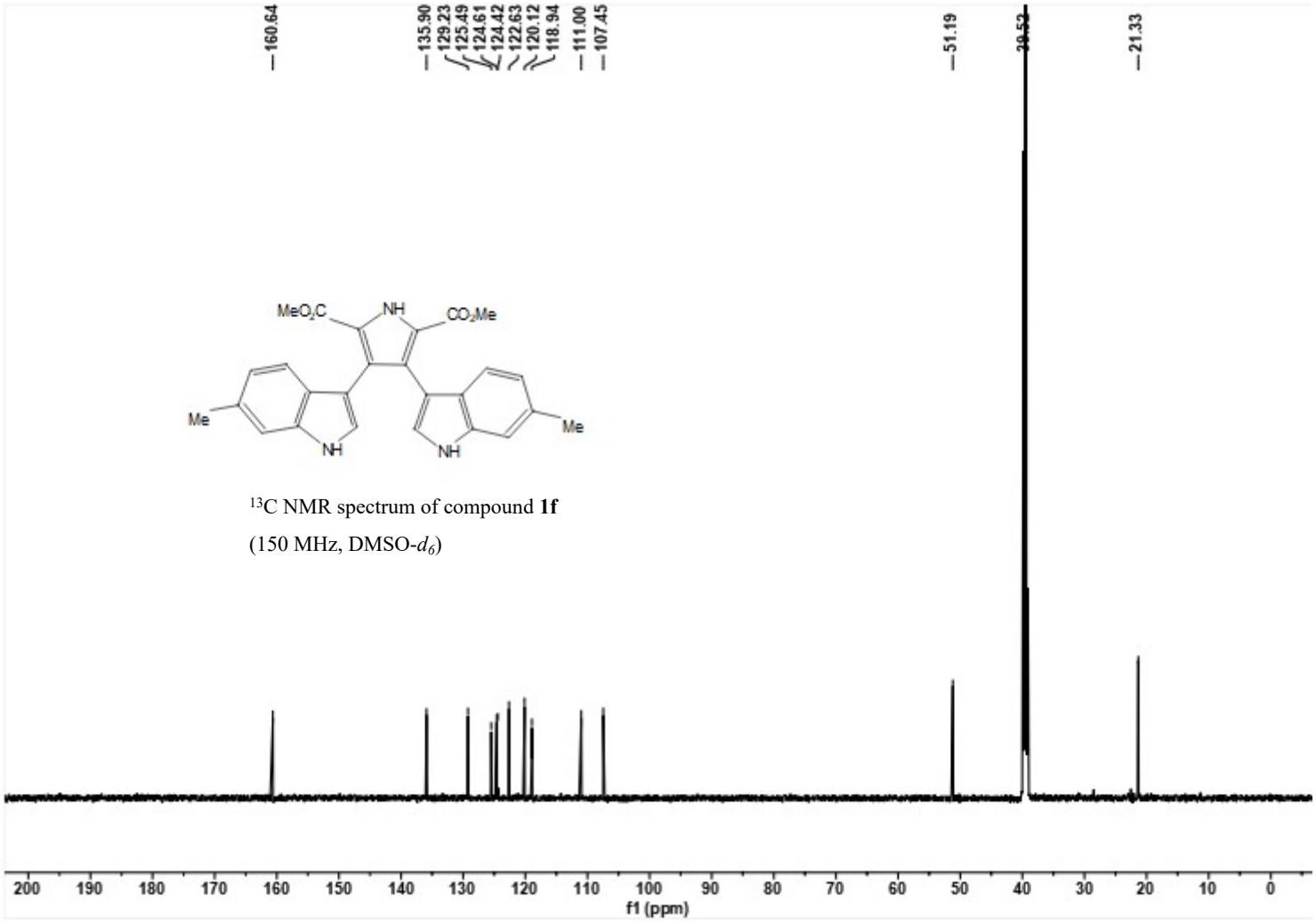
^{13}C NMR spectrum of compound **1e**

(150 MHz, DMSO-d_6)



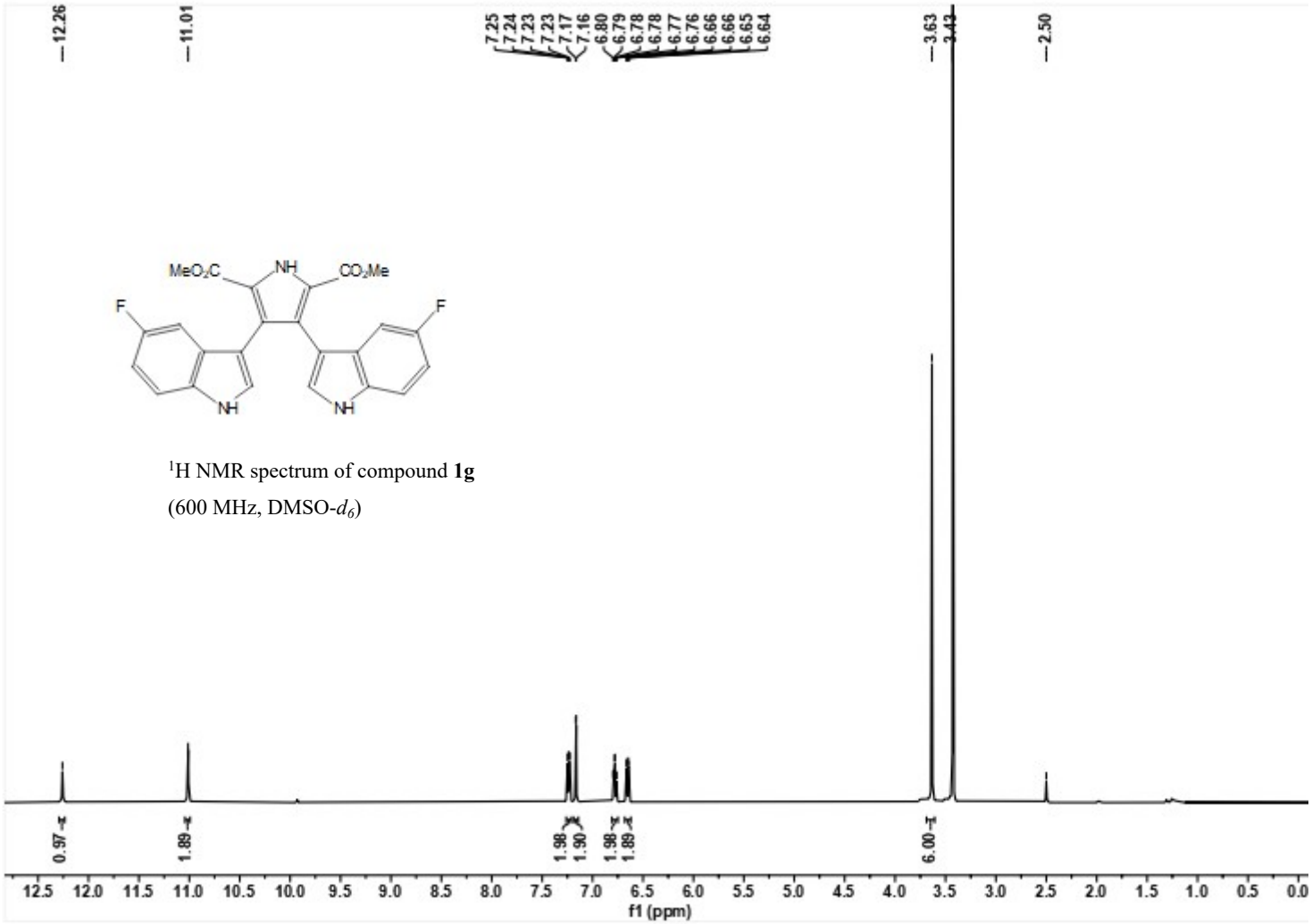
^{1}H NMR spectrum of compound **1f**

(600 MHz, DMSO-d_6)



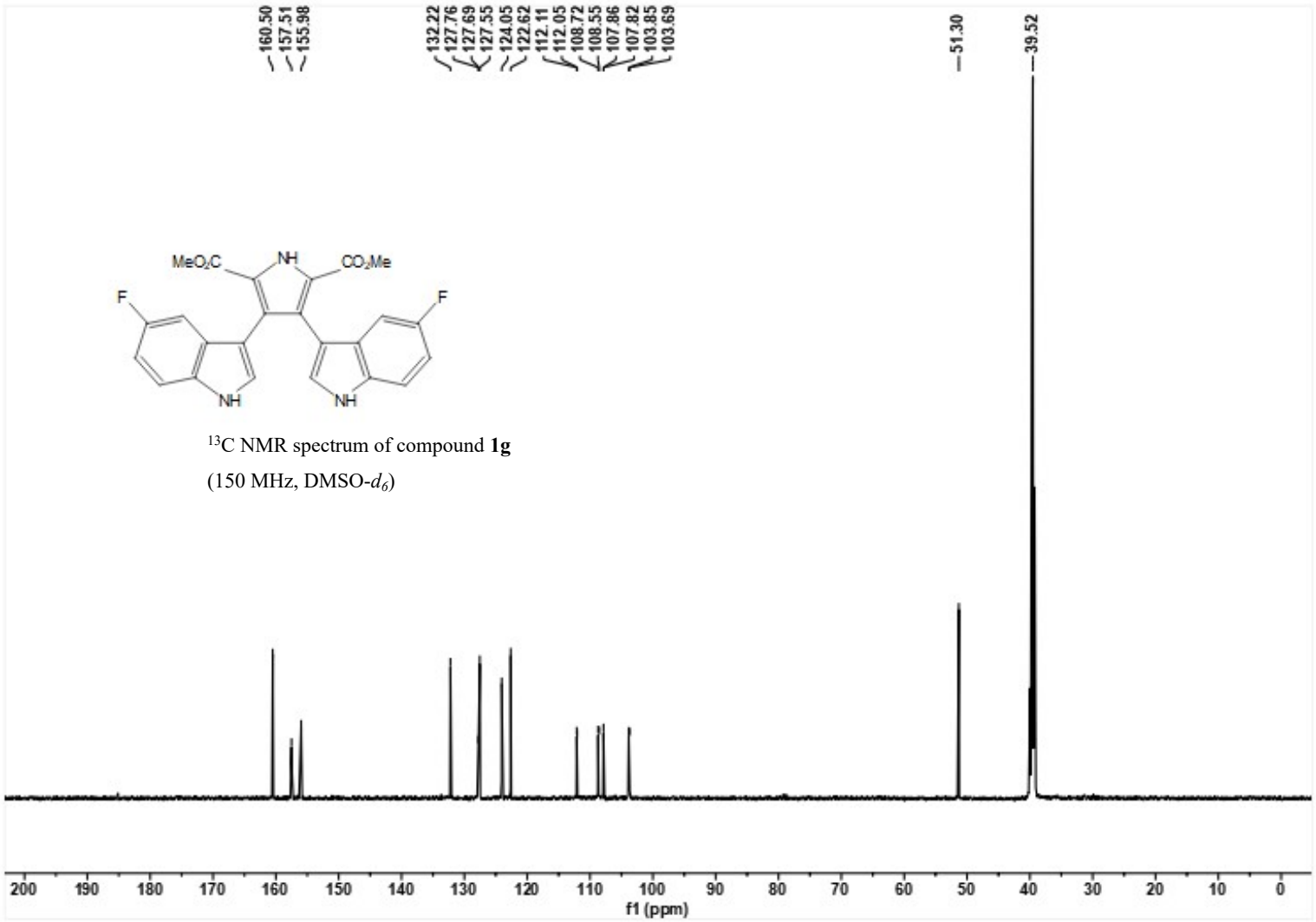
^{13}C NMR spectrum of compound **1f**

(150 MHz, DMSO-d_6)



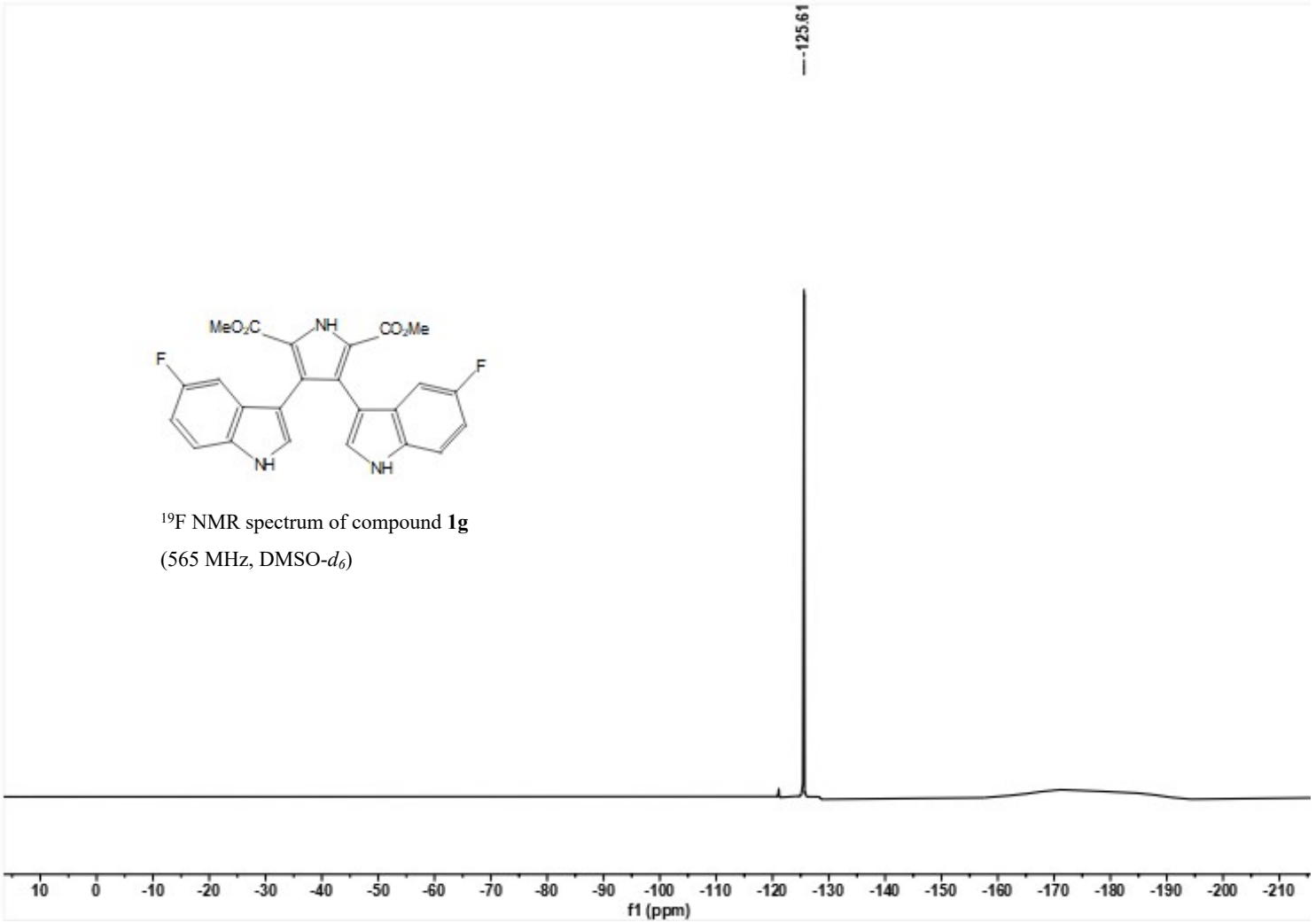
^{1}H NMR spectrum of compound **1g**

(600 MHz, DMSO-d_6)



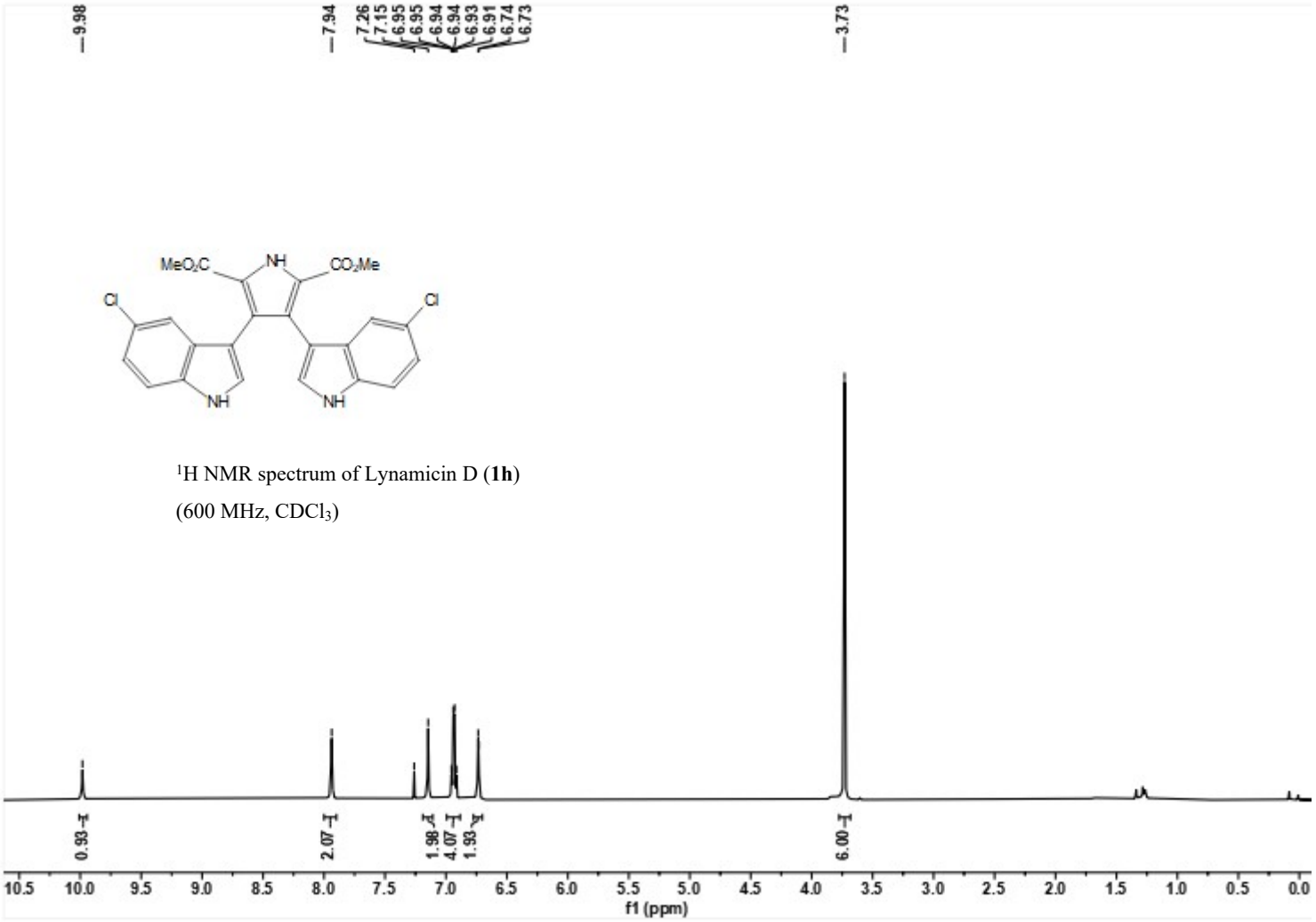
^{13}C NMR spectrum of compound **1g**

(150 MHz, DMSO-d_6)



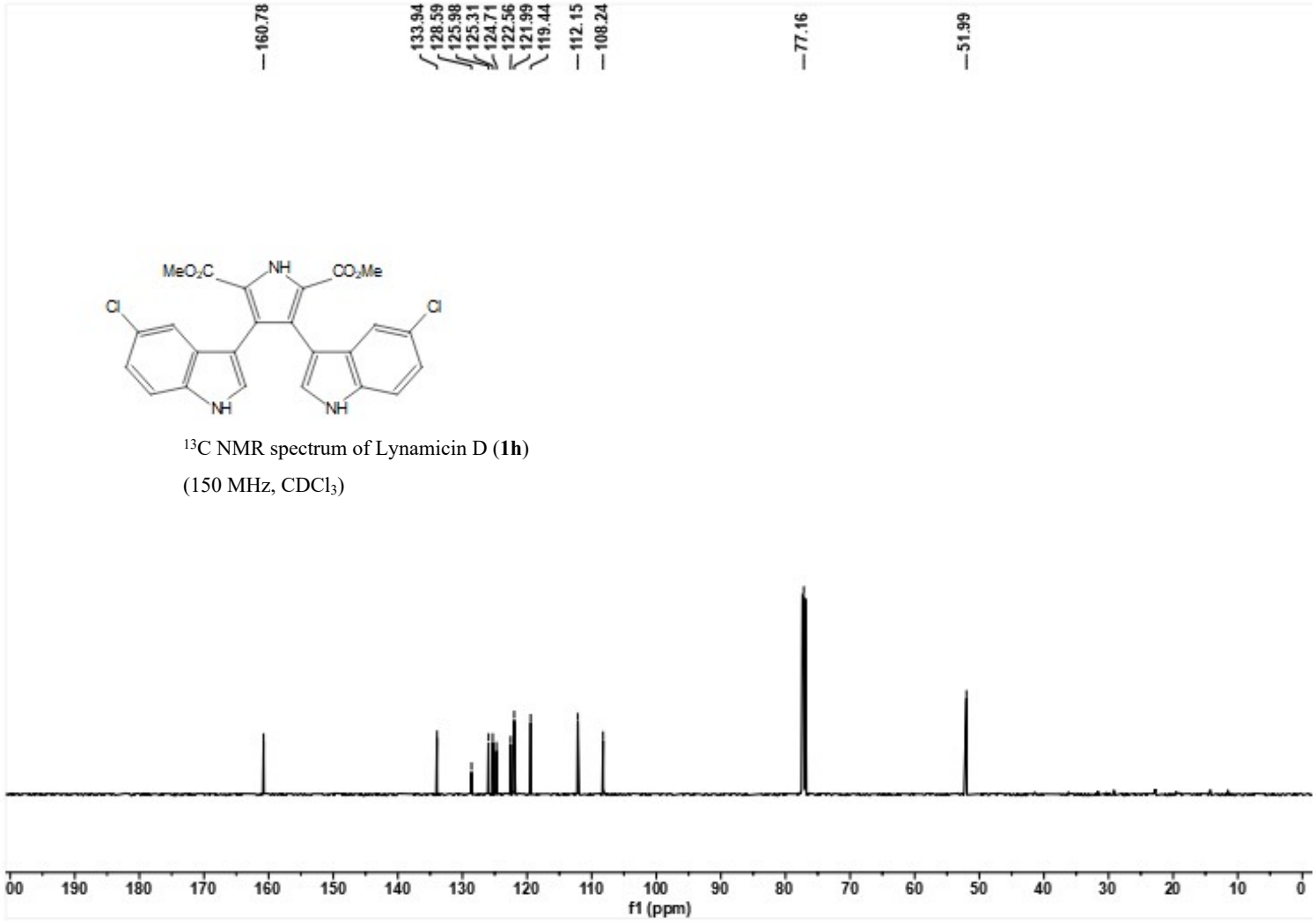
^{19}F NMR spectrum of compound **1g**

(565 MHz, DMSO-d_6)



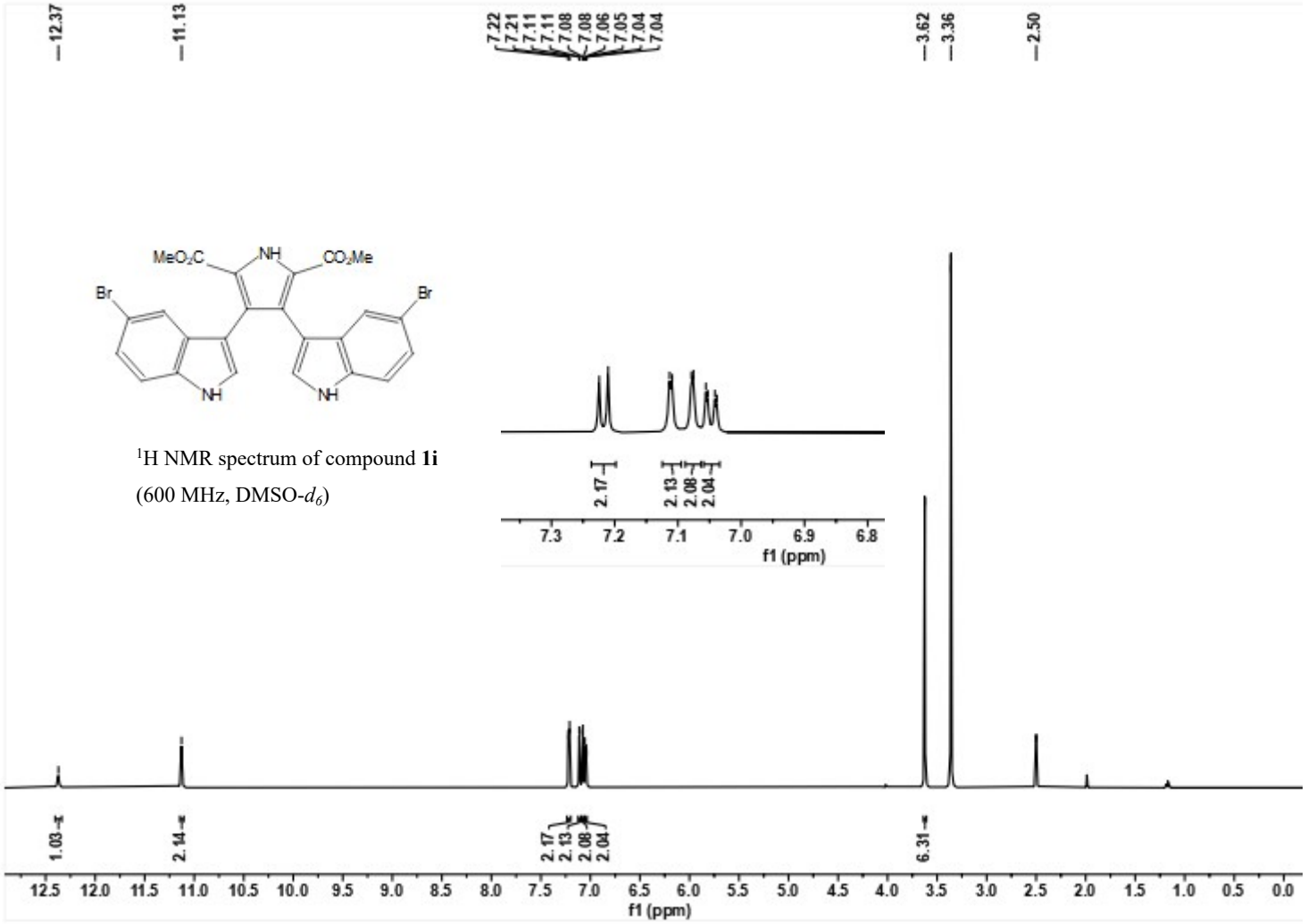
^{1}H NMR spectrum of Lynamicin D (**1h**)

(600 MHz, $CDCl_3$)

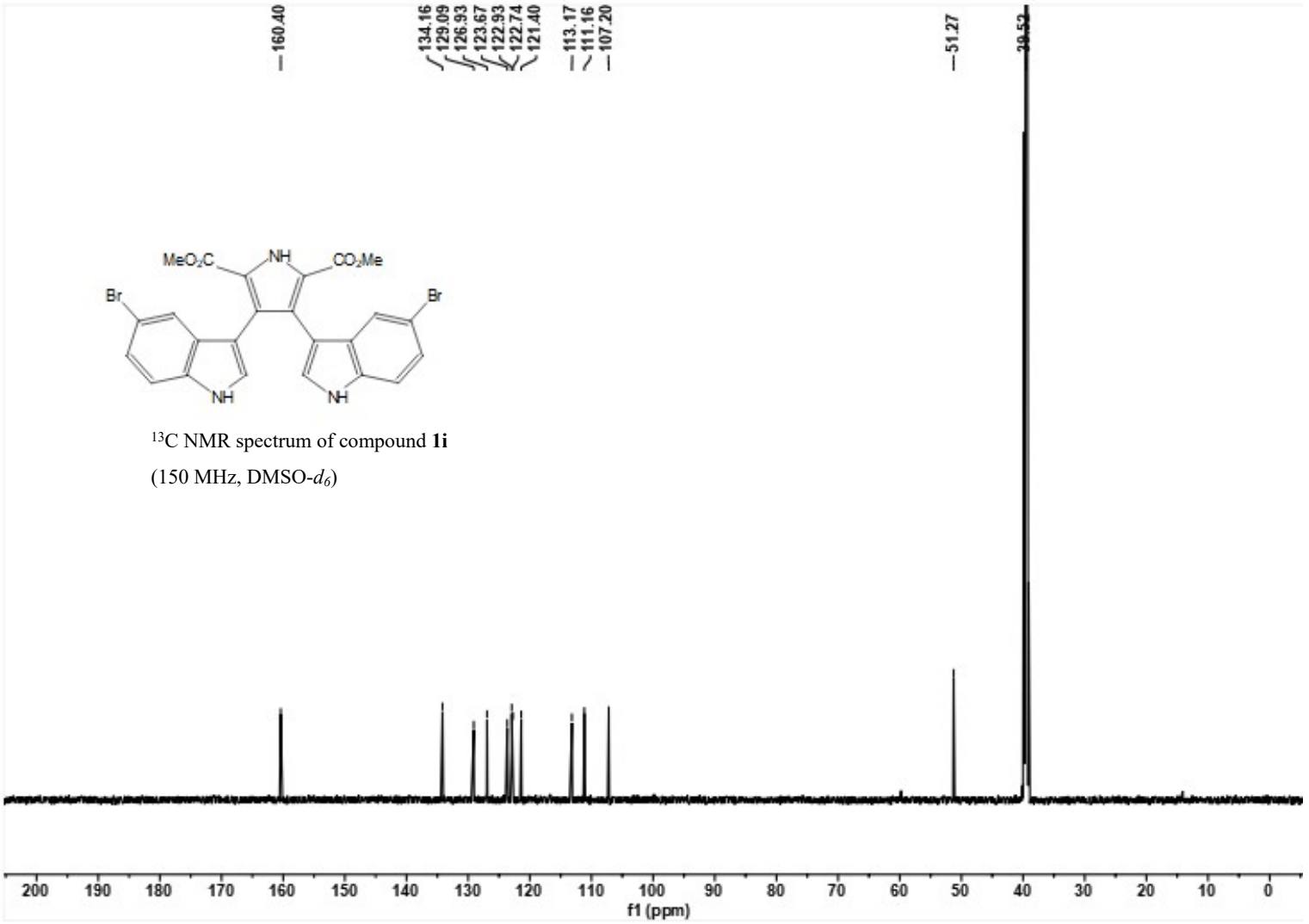


^{13}C NMR spectrum of Lynamicin D (**1h**)

(150 MHz, $CDCl_3$)

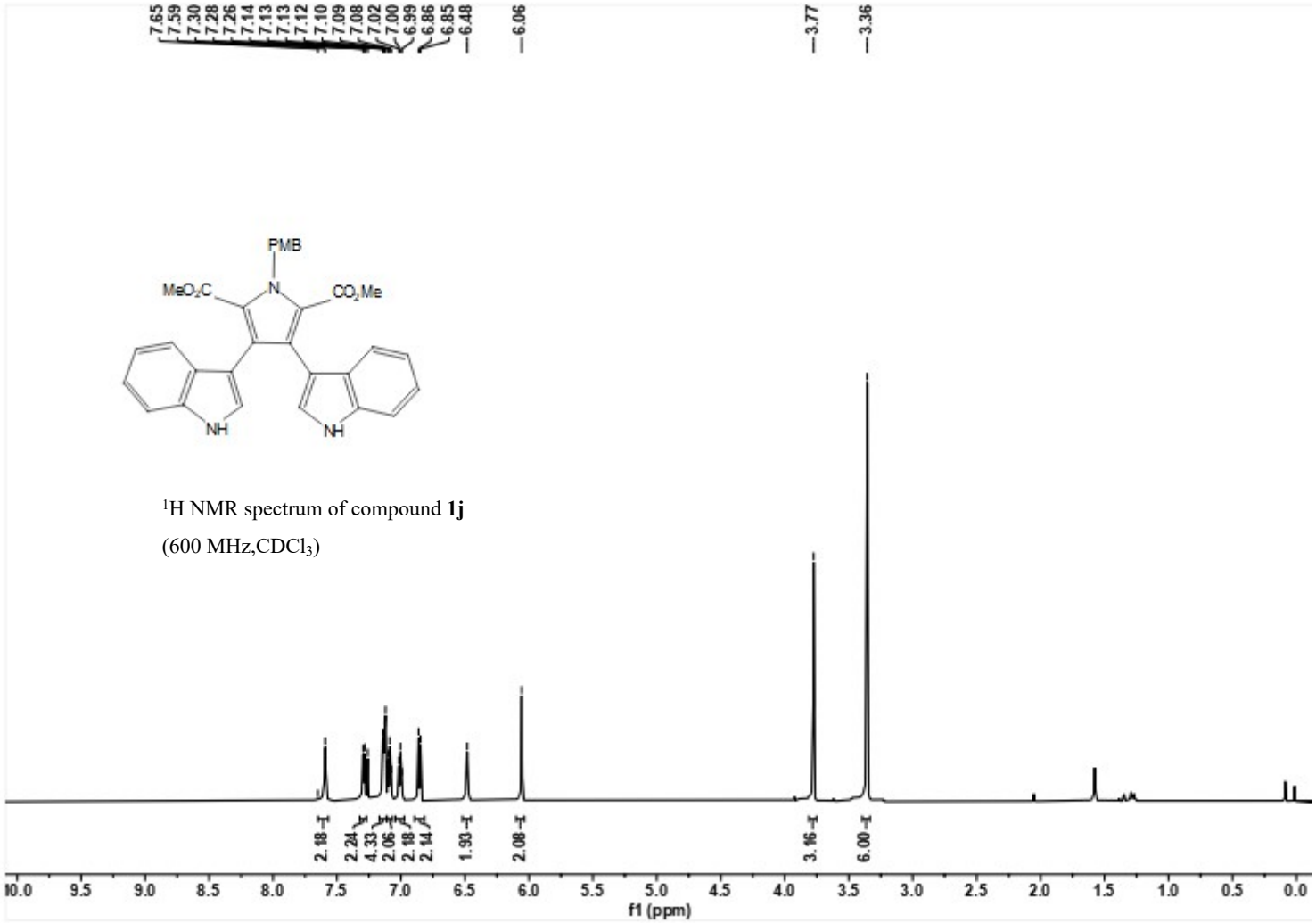


^{1}H NMR spectrum of compound **1i**
(600 MHz, DMSO-d_6)



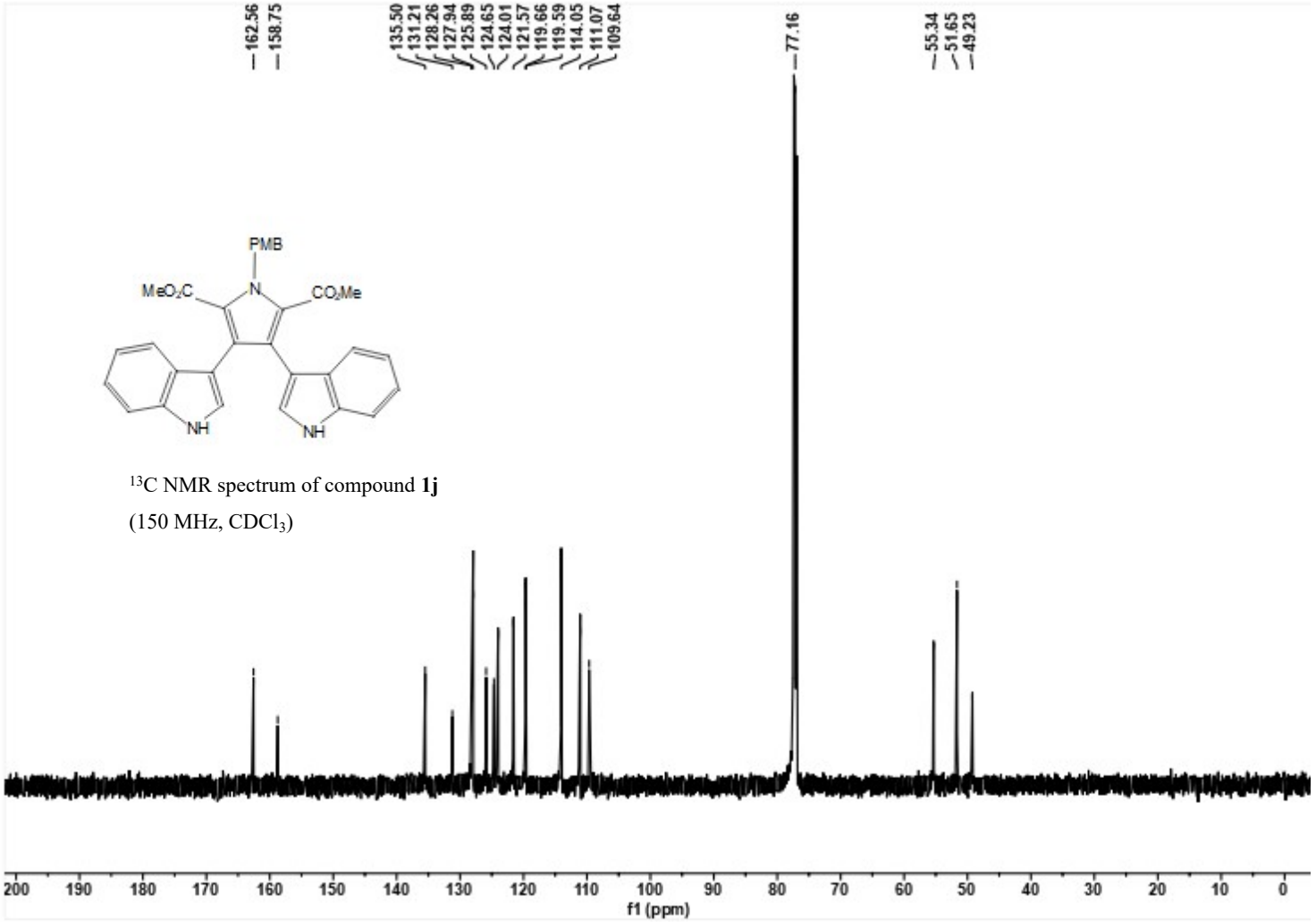
^{13}C NMR spectrum of compound **1i**

(150 MHz, DMSO-d_6)



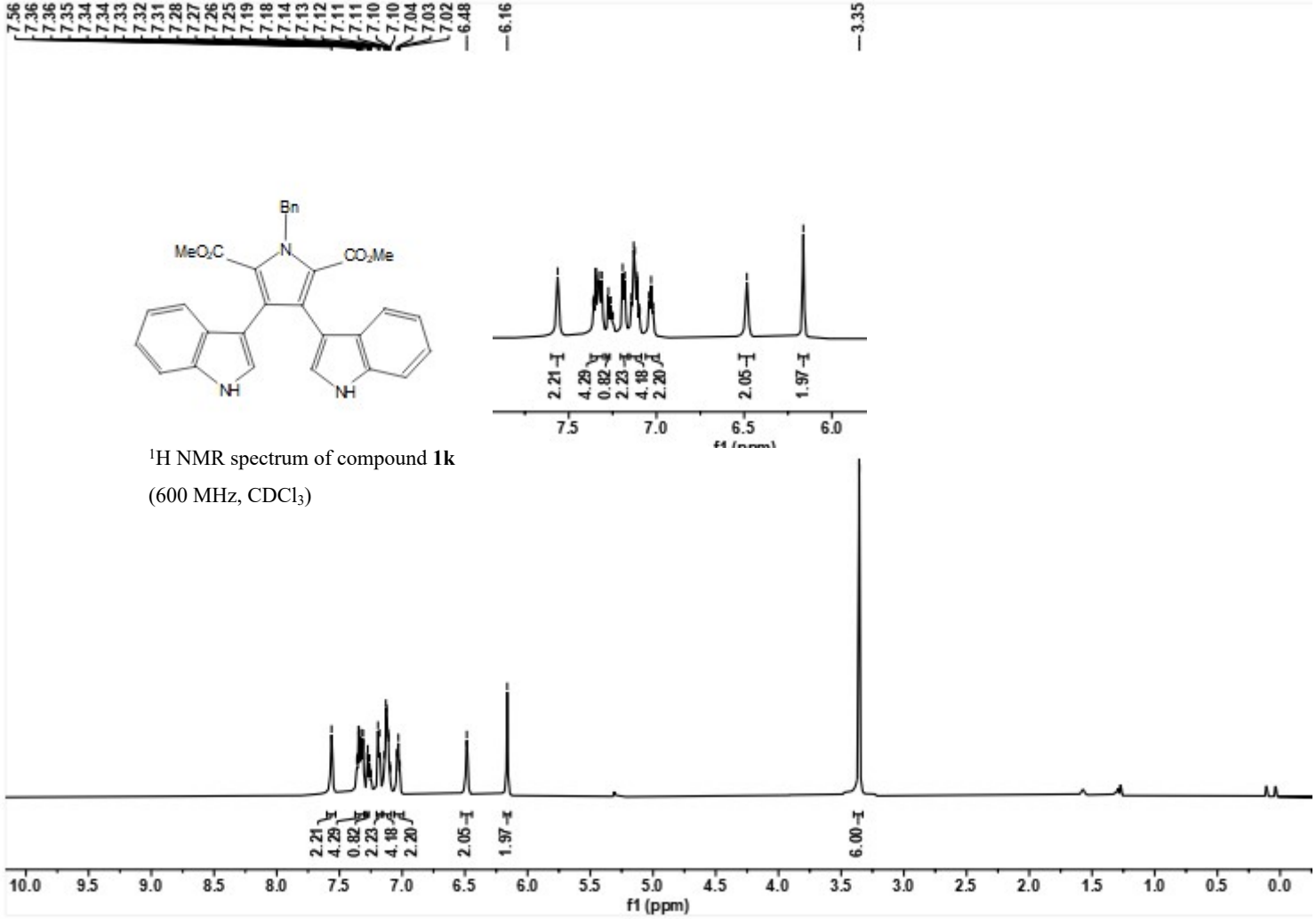
^{1}H NMR spectrum of compound **1j**

(600 MHz,$CDCl_3$)

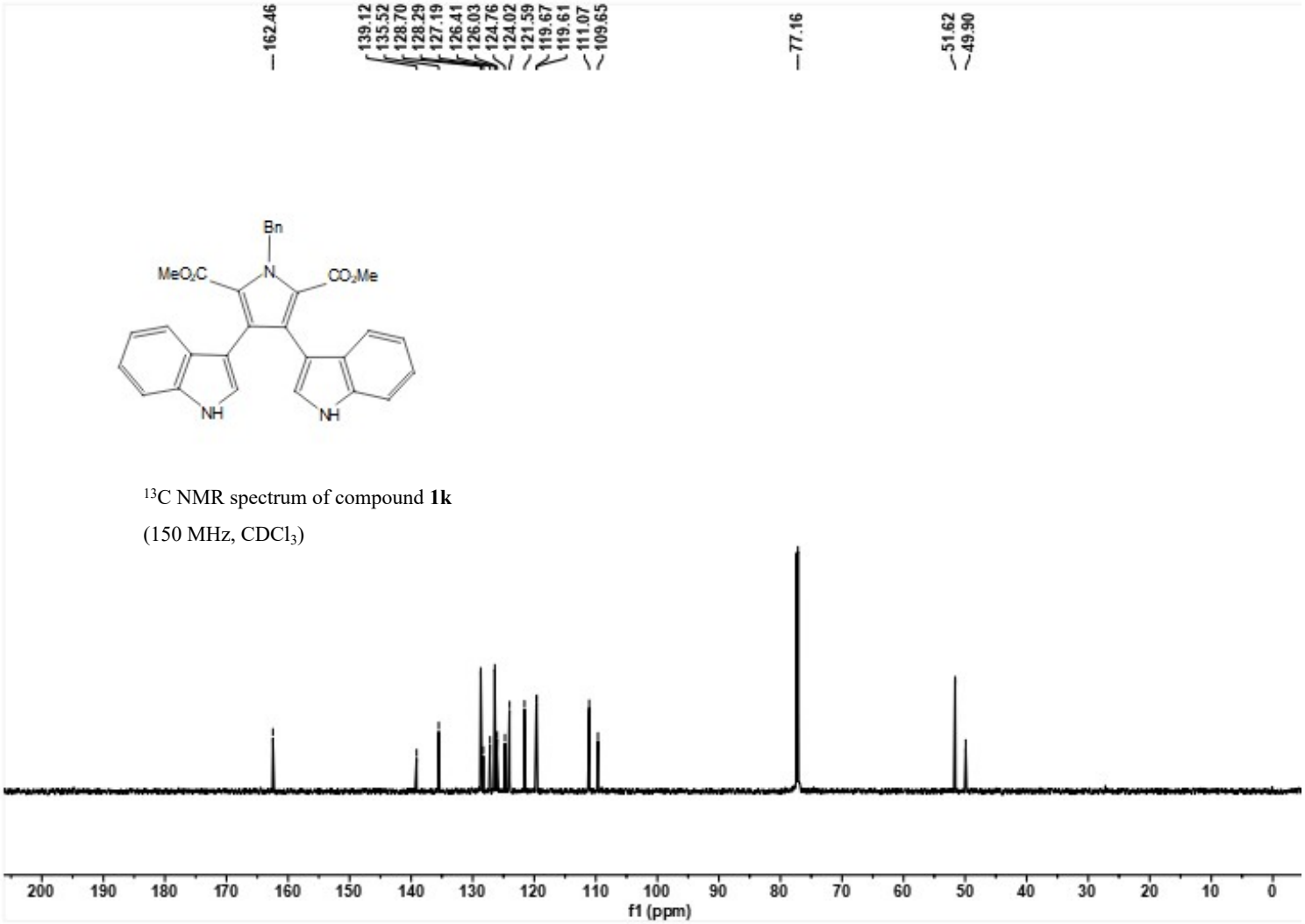


^{13}C NMR spectrum of compound **1j**

(150 MHz, $CDCl_3$)

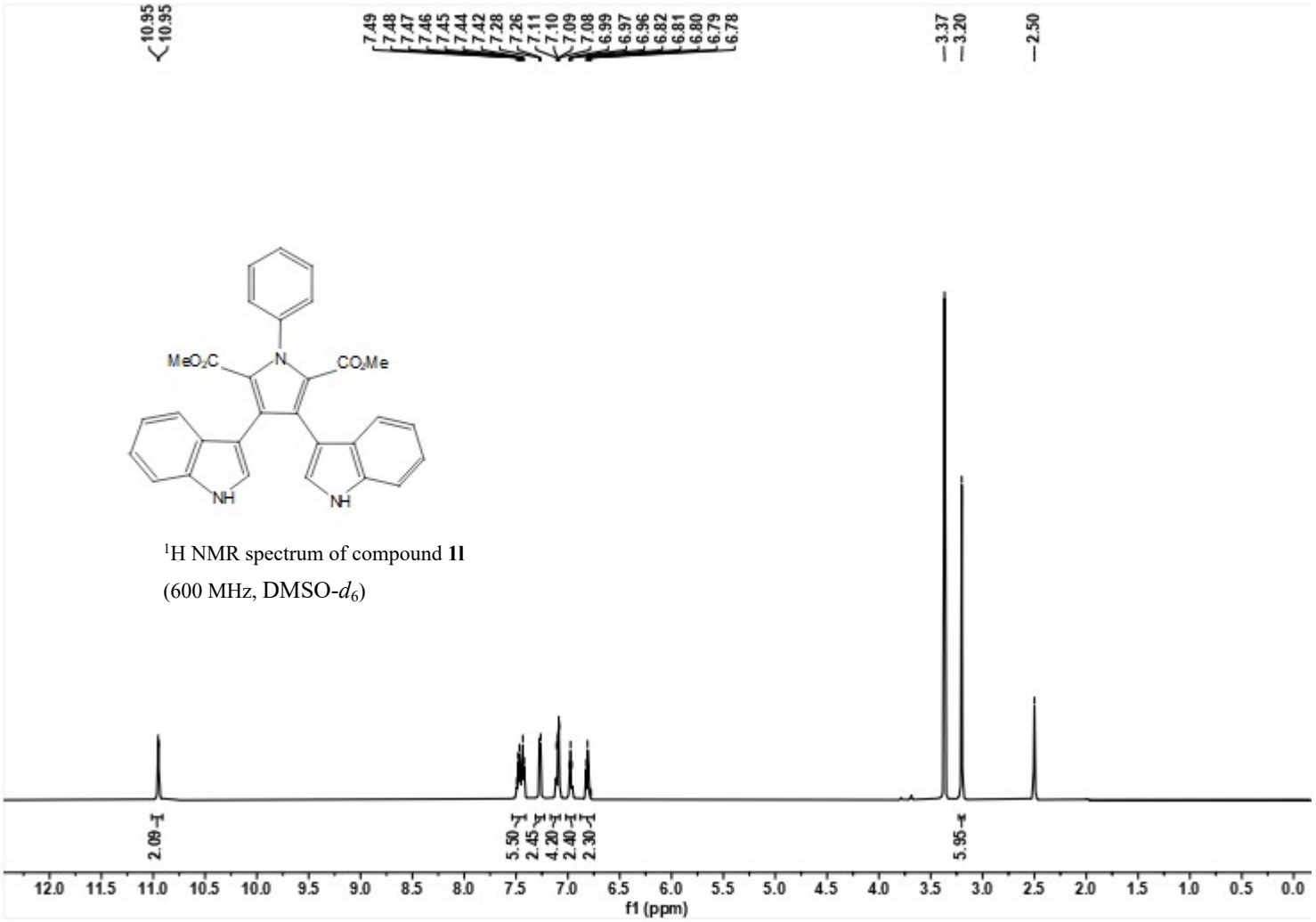


^{1}H NMR spectrum of compound **1k**
(600 MHz, $CDCl_3$)

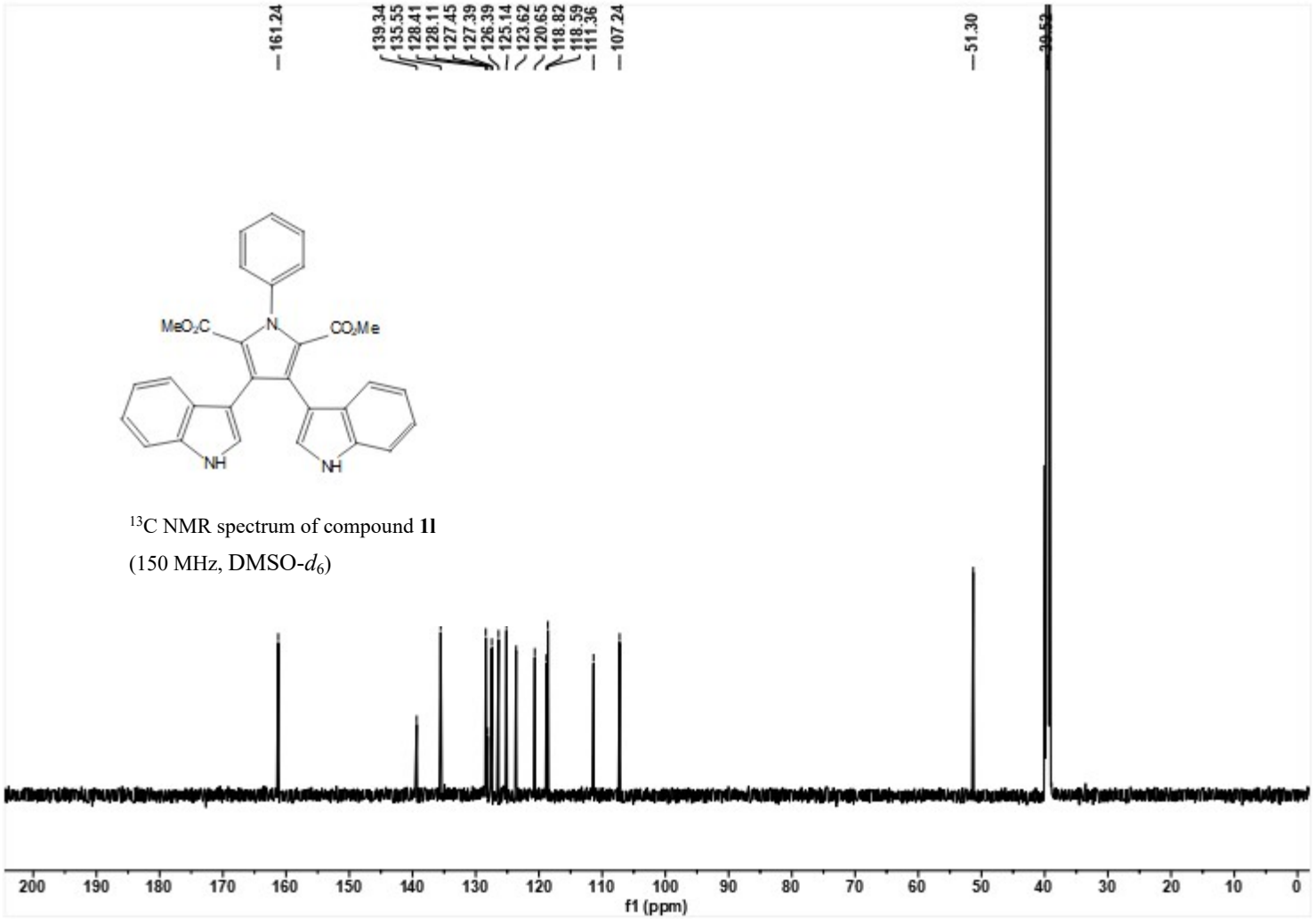


^{13}C NMR spectrum of compound **1k**

(150 MHz, $CDCl_3$)

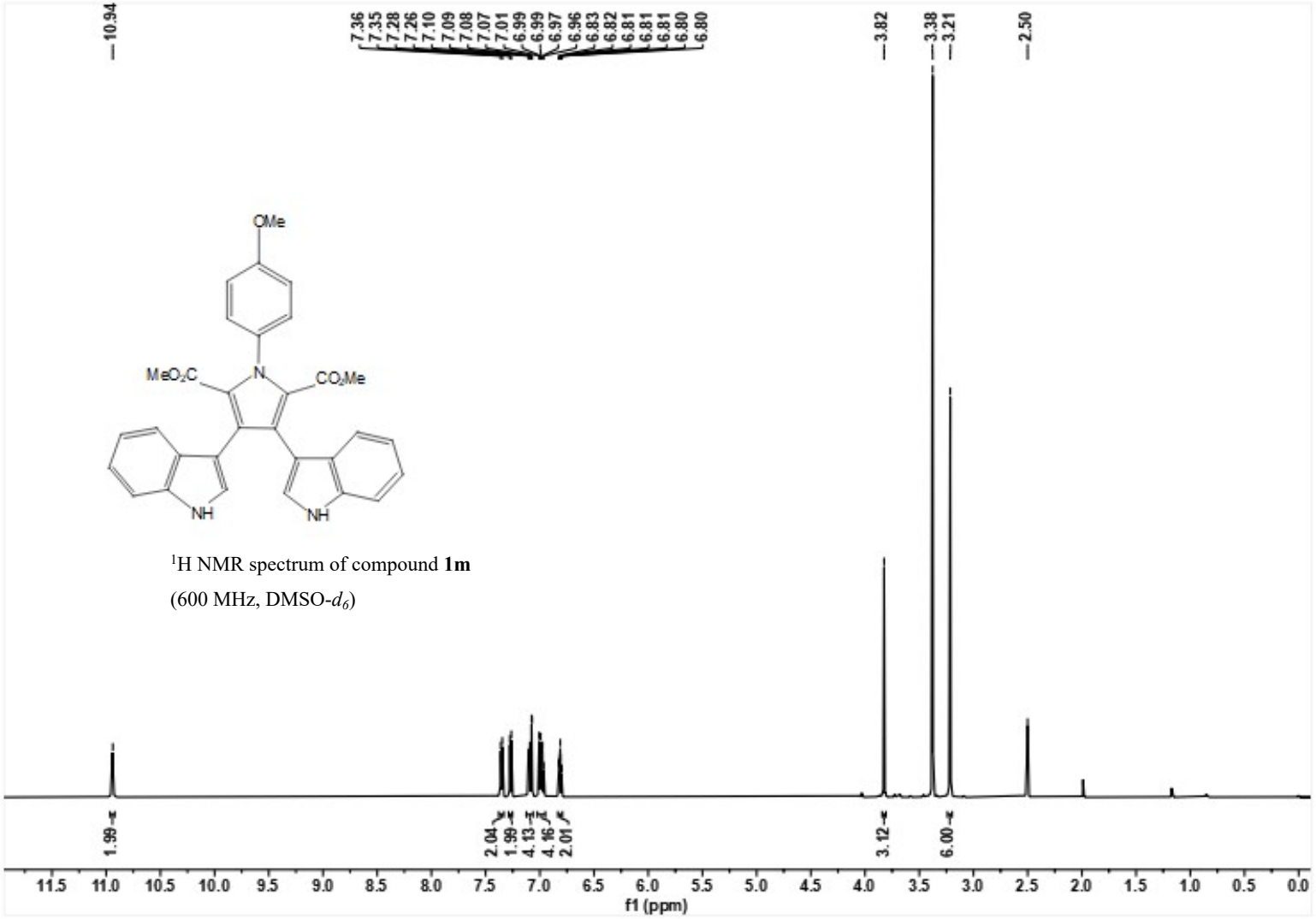


^{1}H NMR spectrum of compound **1l**
(600 MHz, DMSO-d_6)



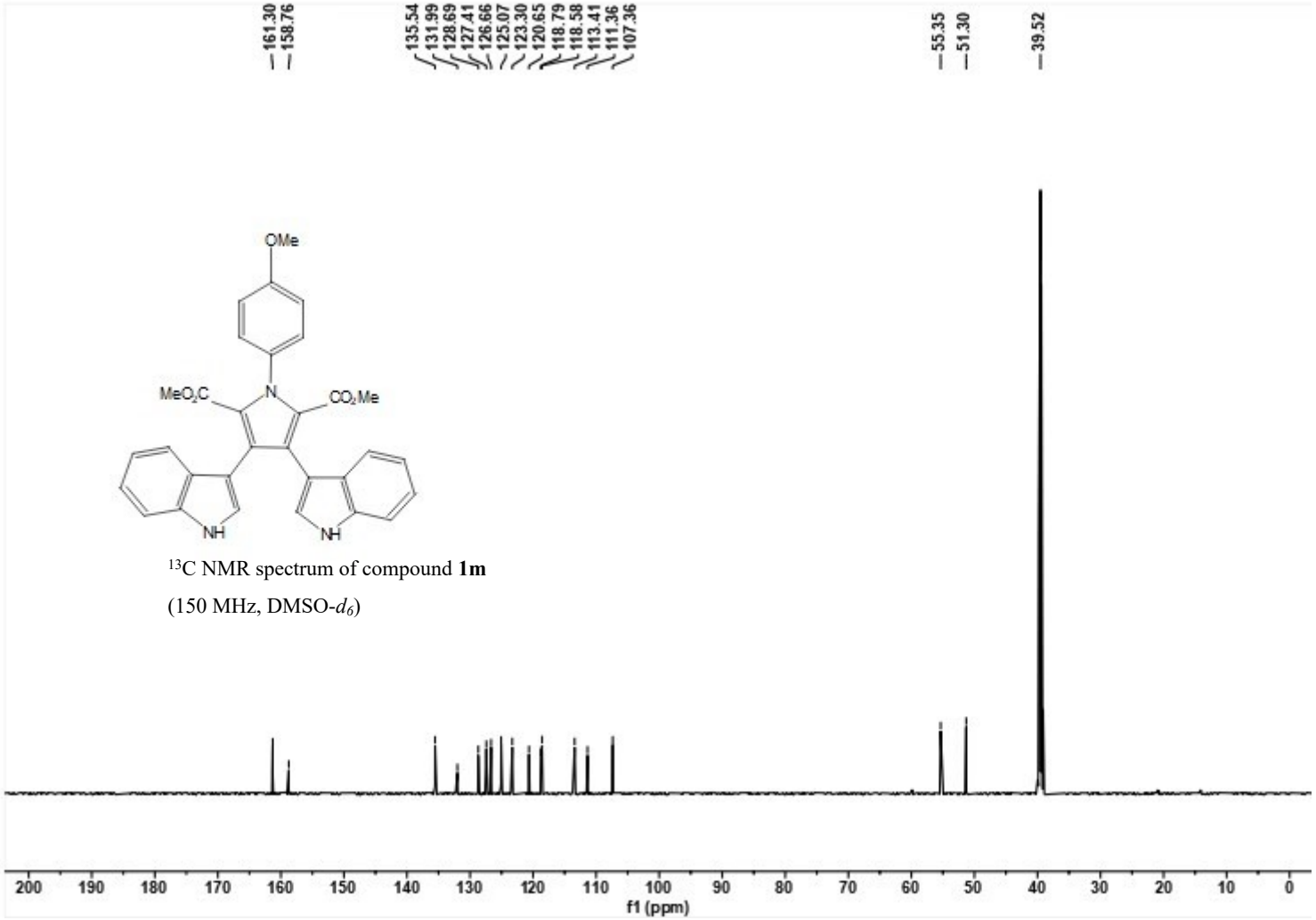
^{13}C NMR spectrum of compound **1l**

(150 MHz, DMSO-d_6)



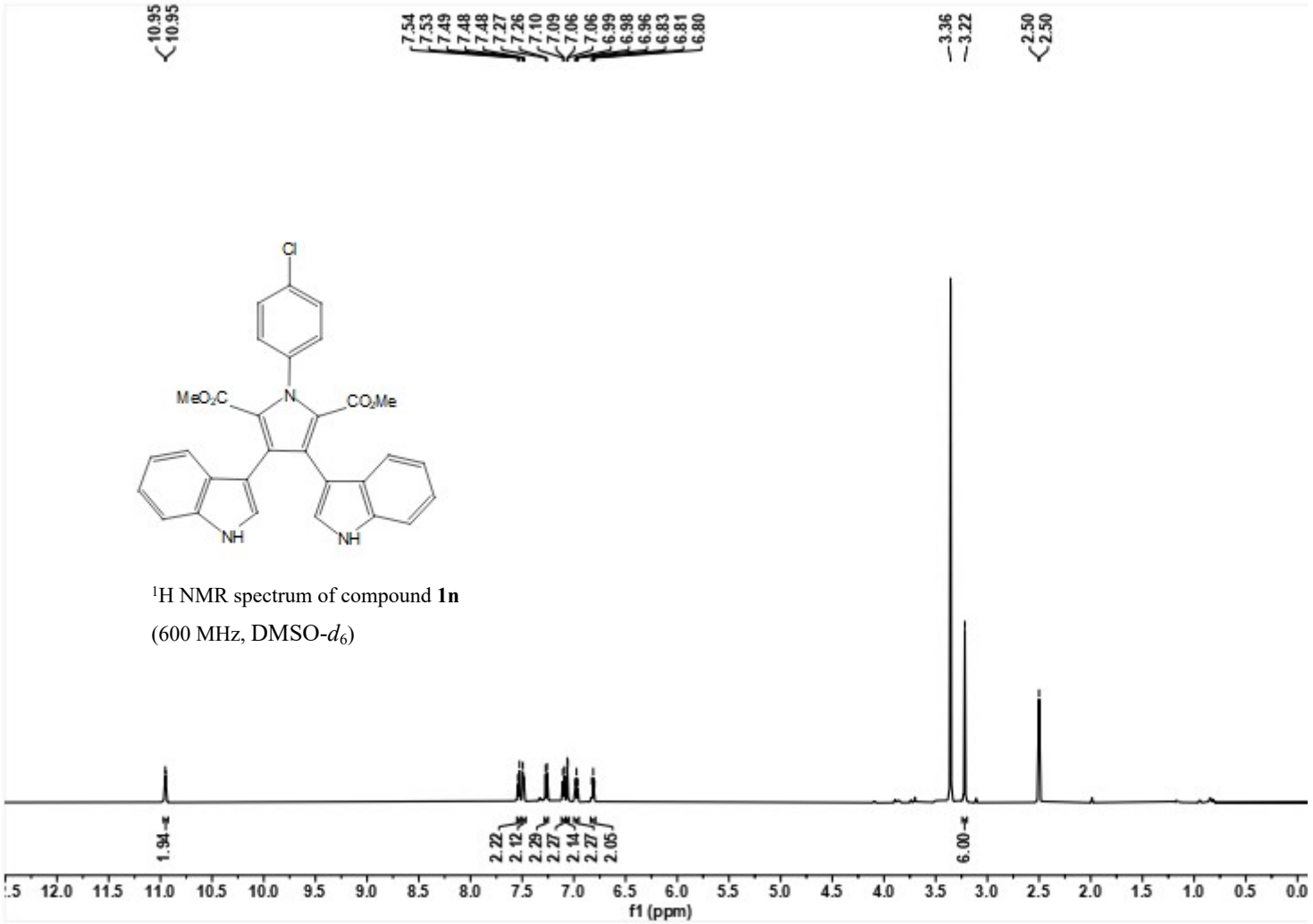
^{1}H NMR spectrum of compound **1m**

(600 MHz, DMSO-d_6)



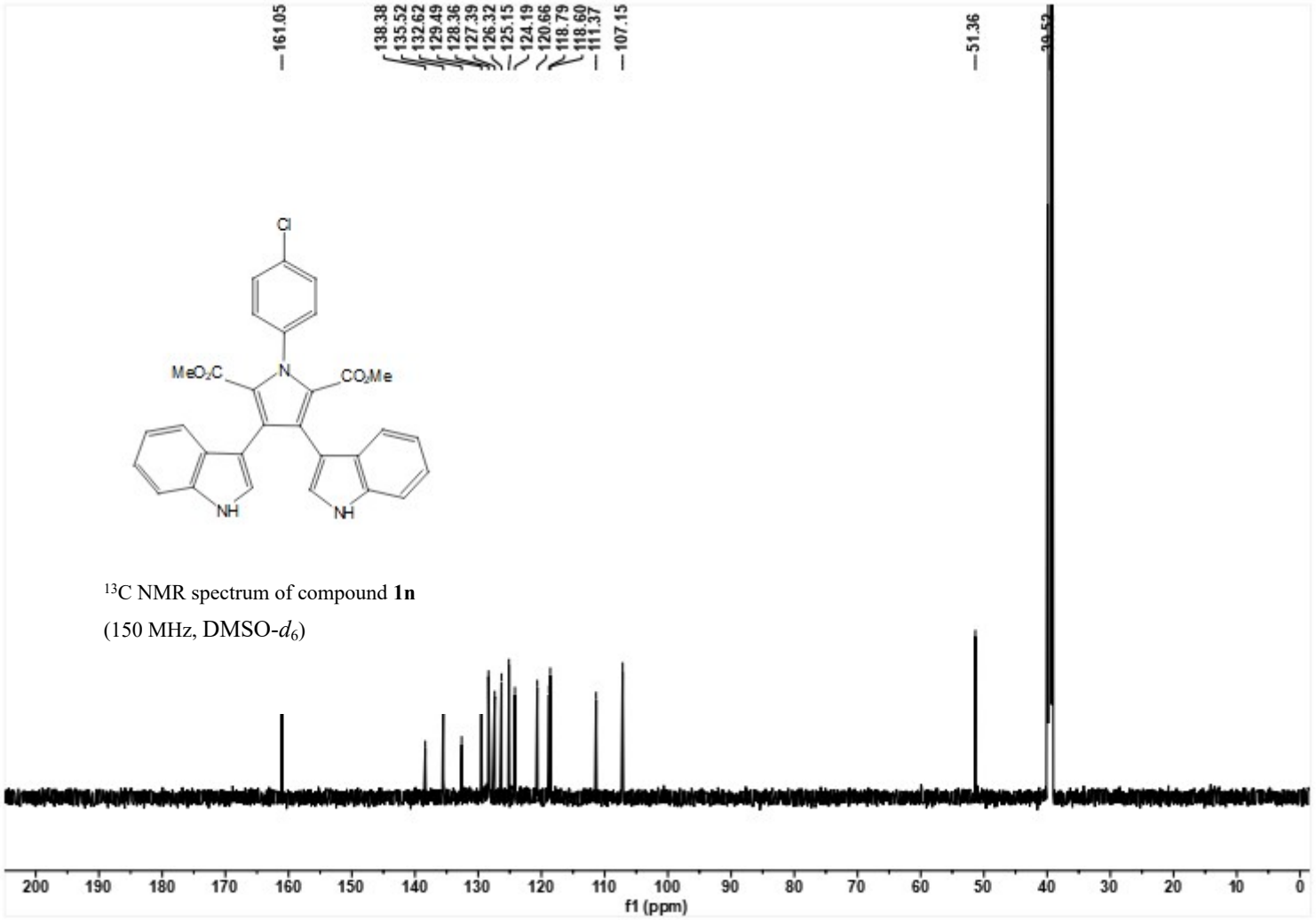
^{13}C NMR spectrum of compound **1m**

(150 MHz, DMSO-d_6)



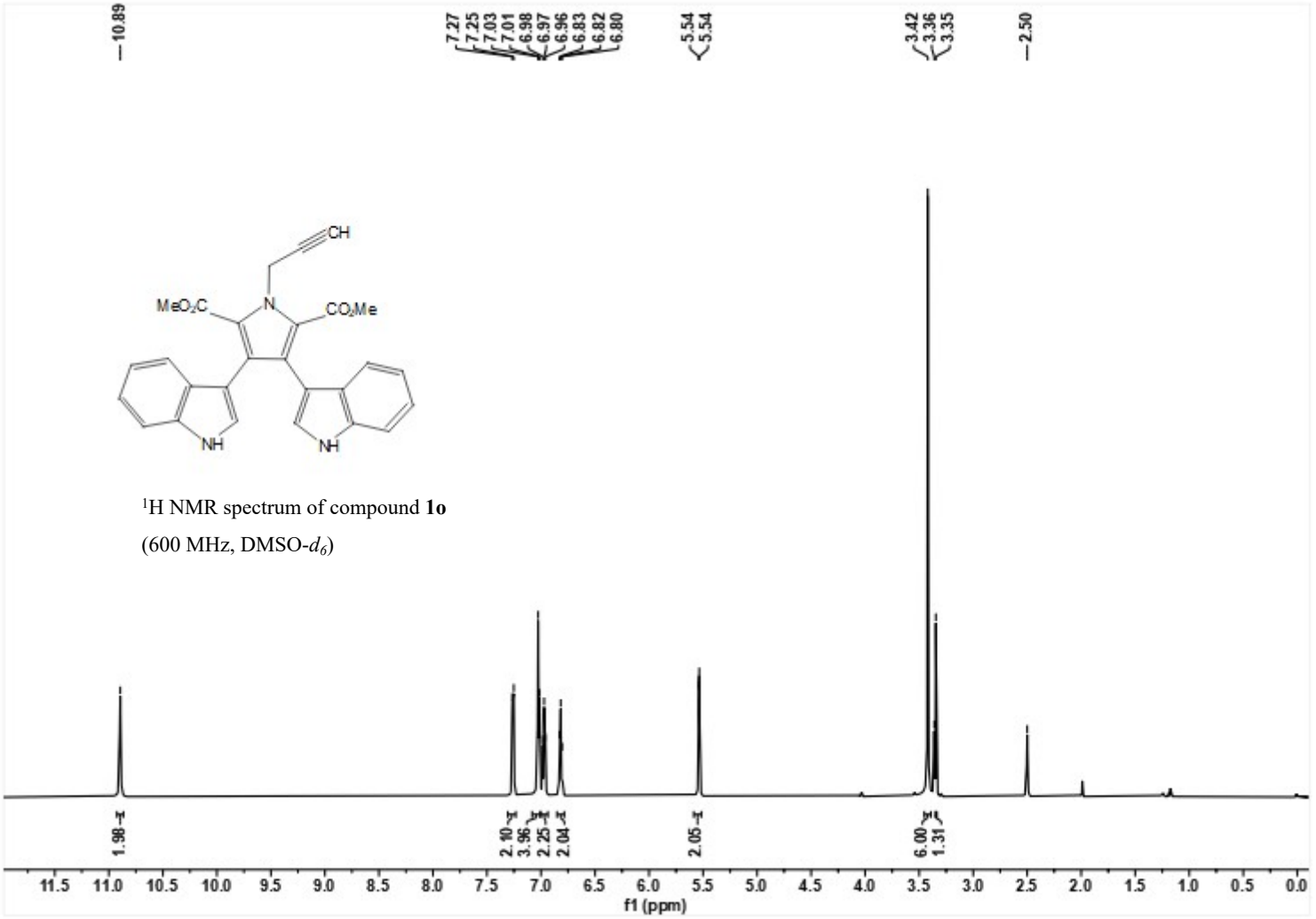
^{1}H NMR spectrum of compound **1n**

(600 MHz, DMSO-d_6)



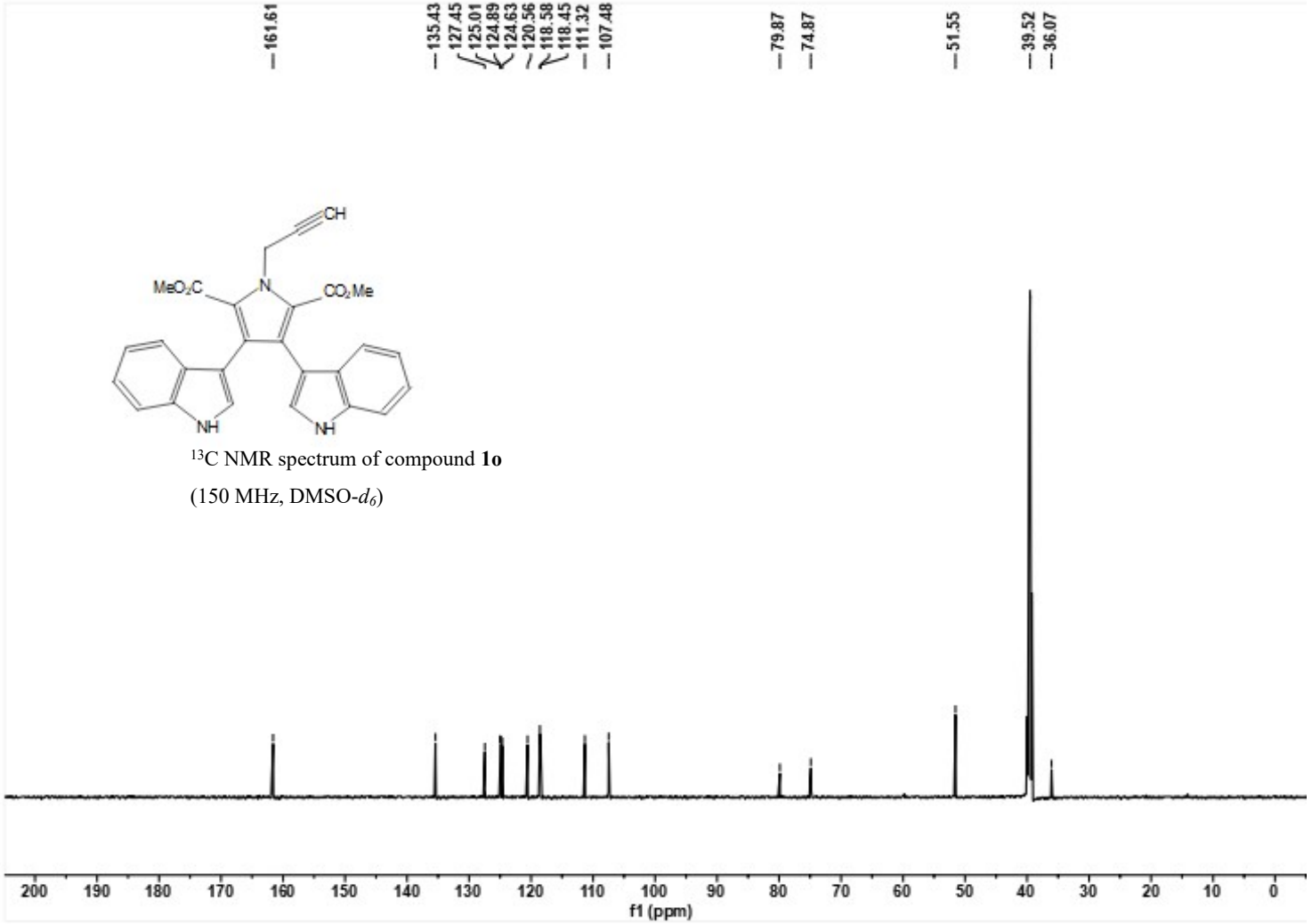
^{13}C NMR spectrum of compound **1n**

(150 MHz, DMSO-d_6)



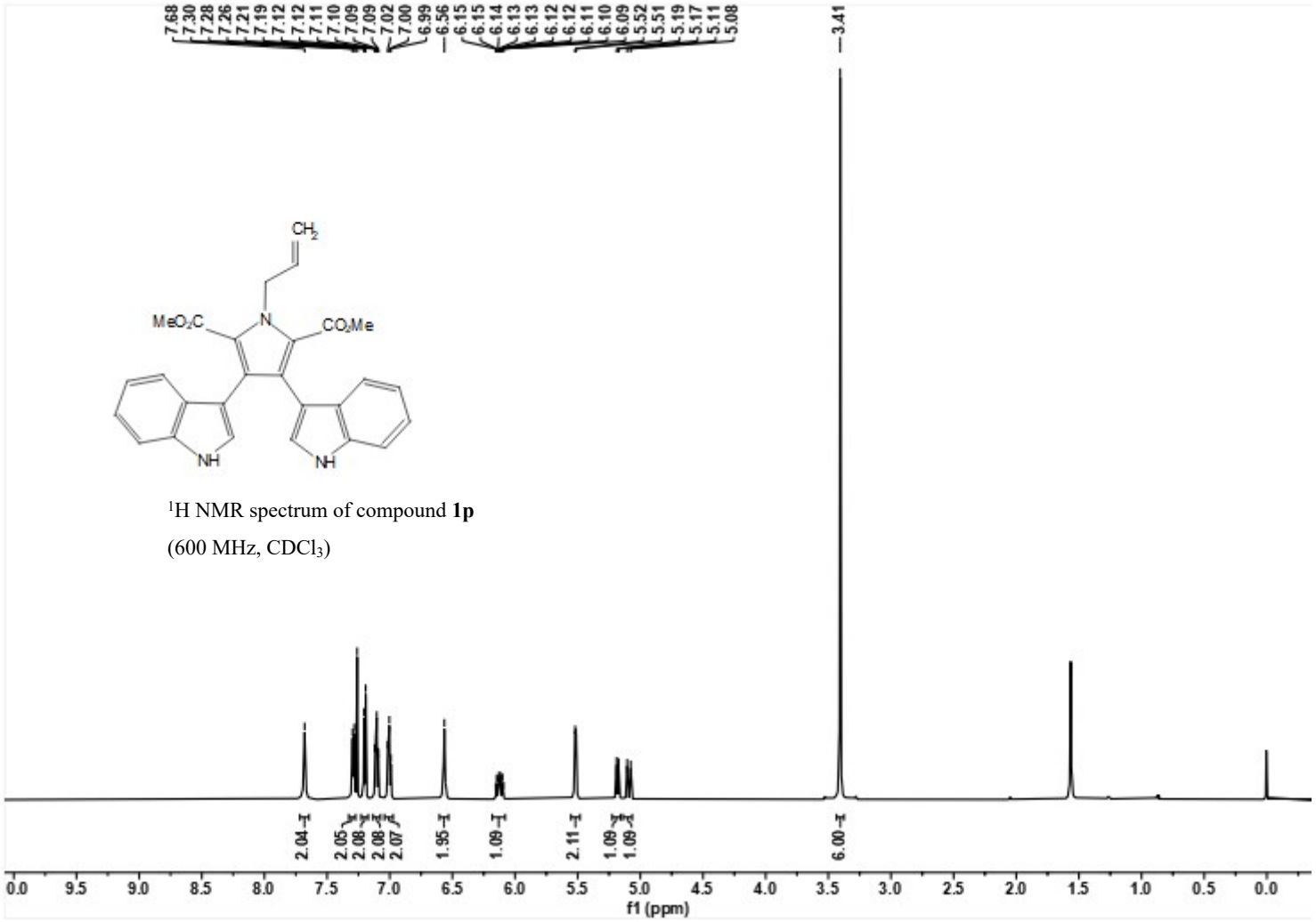
^{1}H NMR spectrum of compound **1o**

(600 MHz, DMSO-d_6)



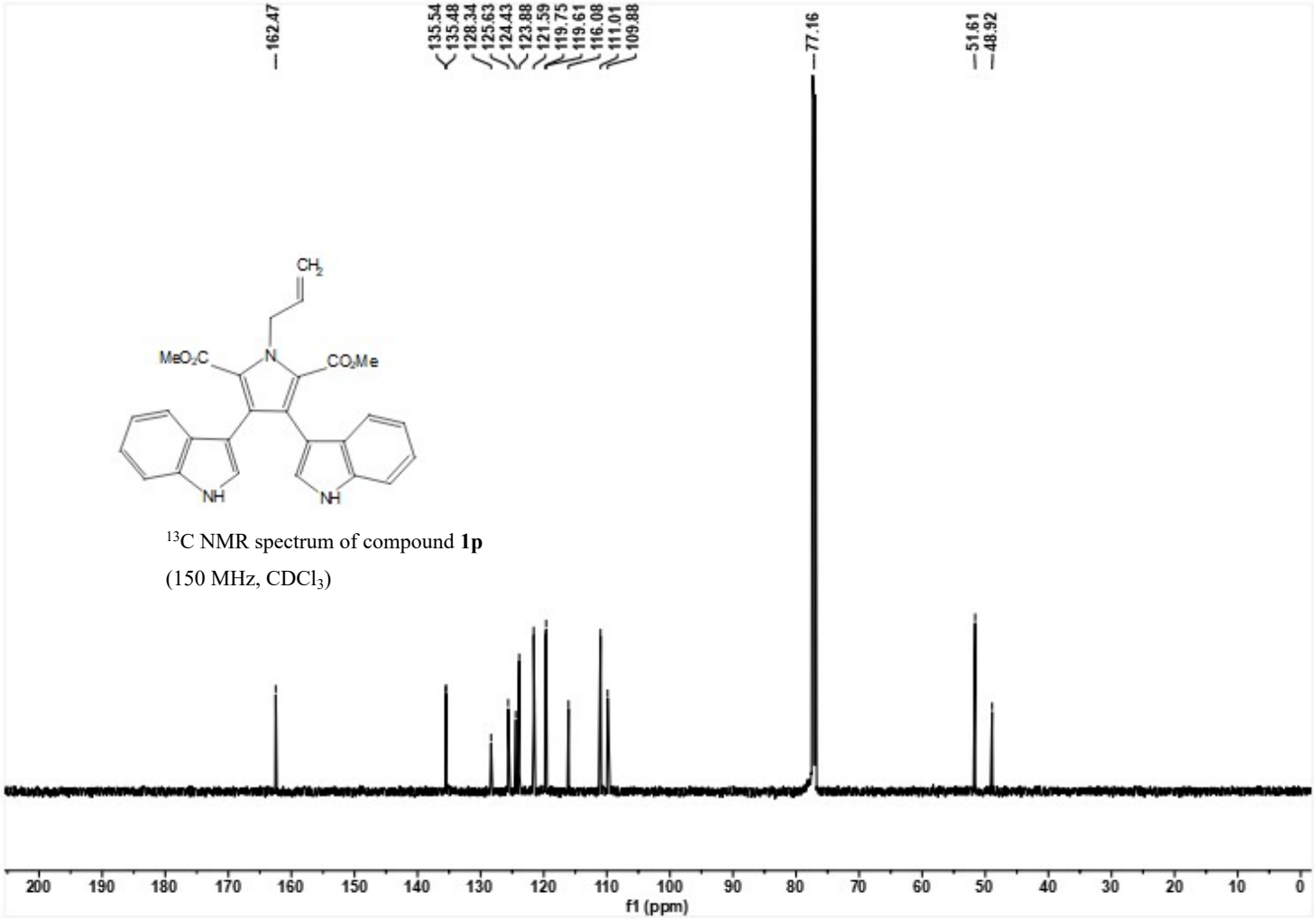
^{13}C NMR spectrum of compound **1o**

(150 MHz, DMSO-d_6)



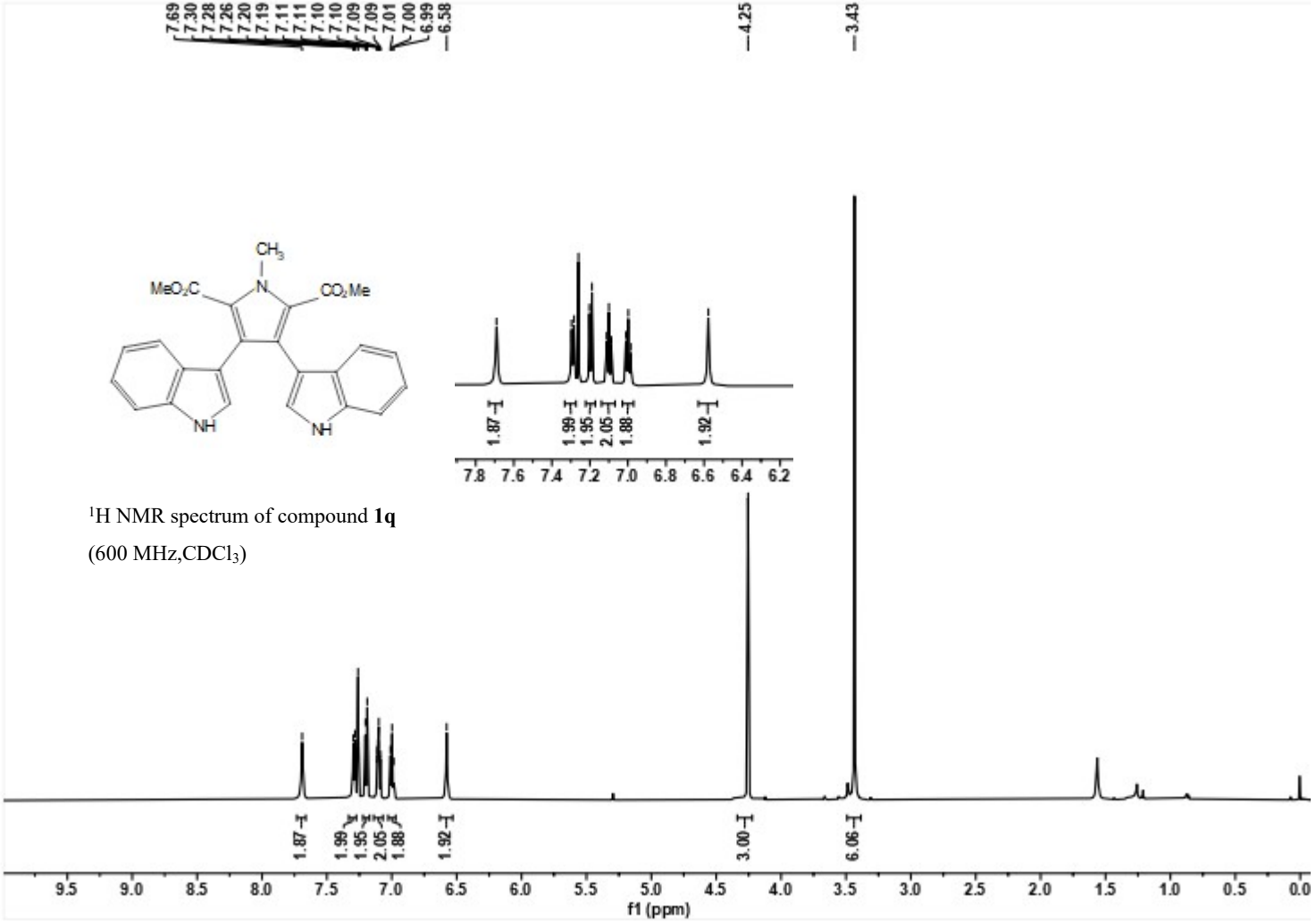
^{1}H NMR spectrum of compound **1p**

(600 MHz, $CDCl_3$)



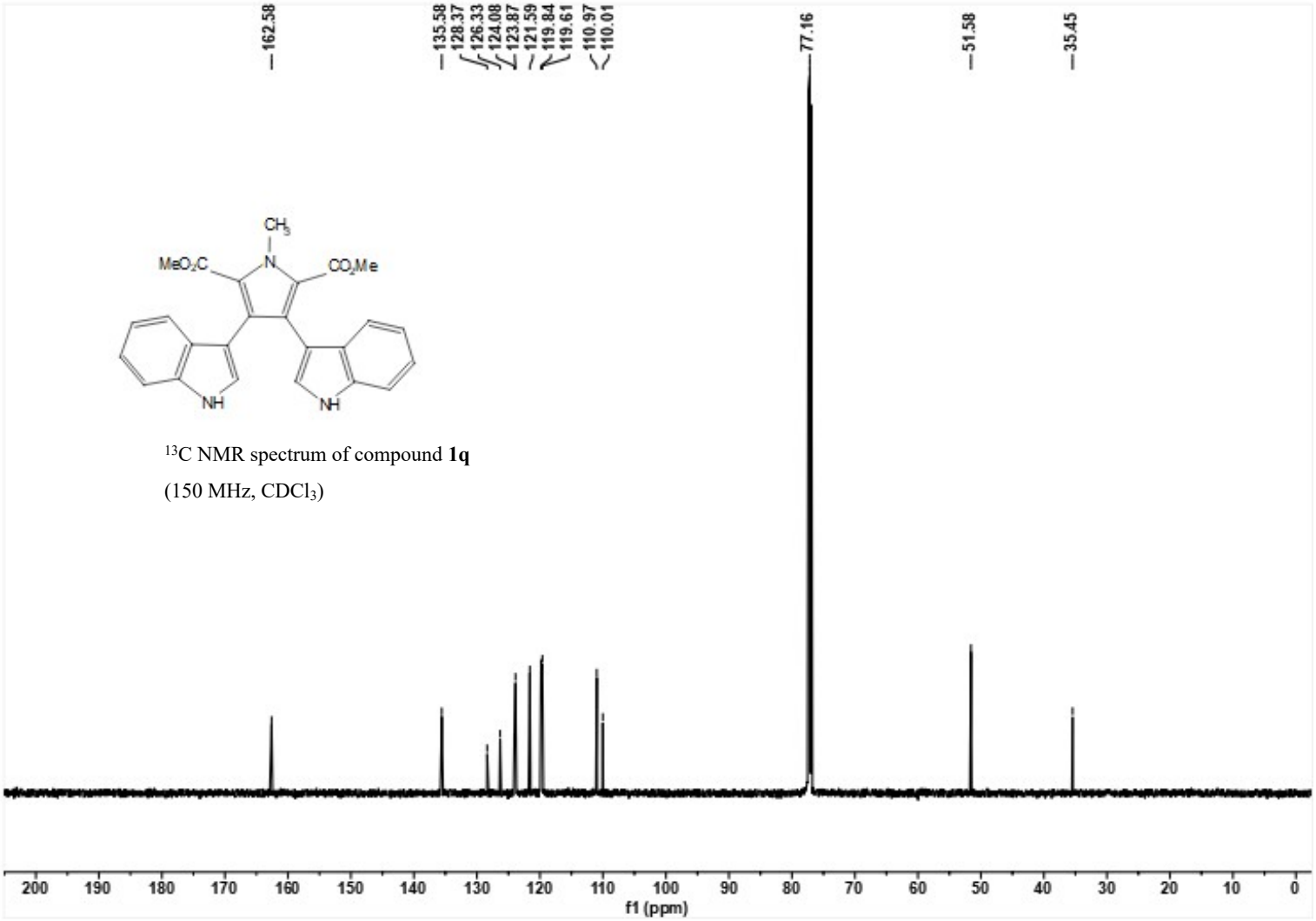
^{13}C NMR spectrum of compound **1p**

(150 MHz, $CDCl_3$)



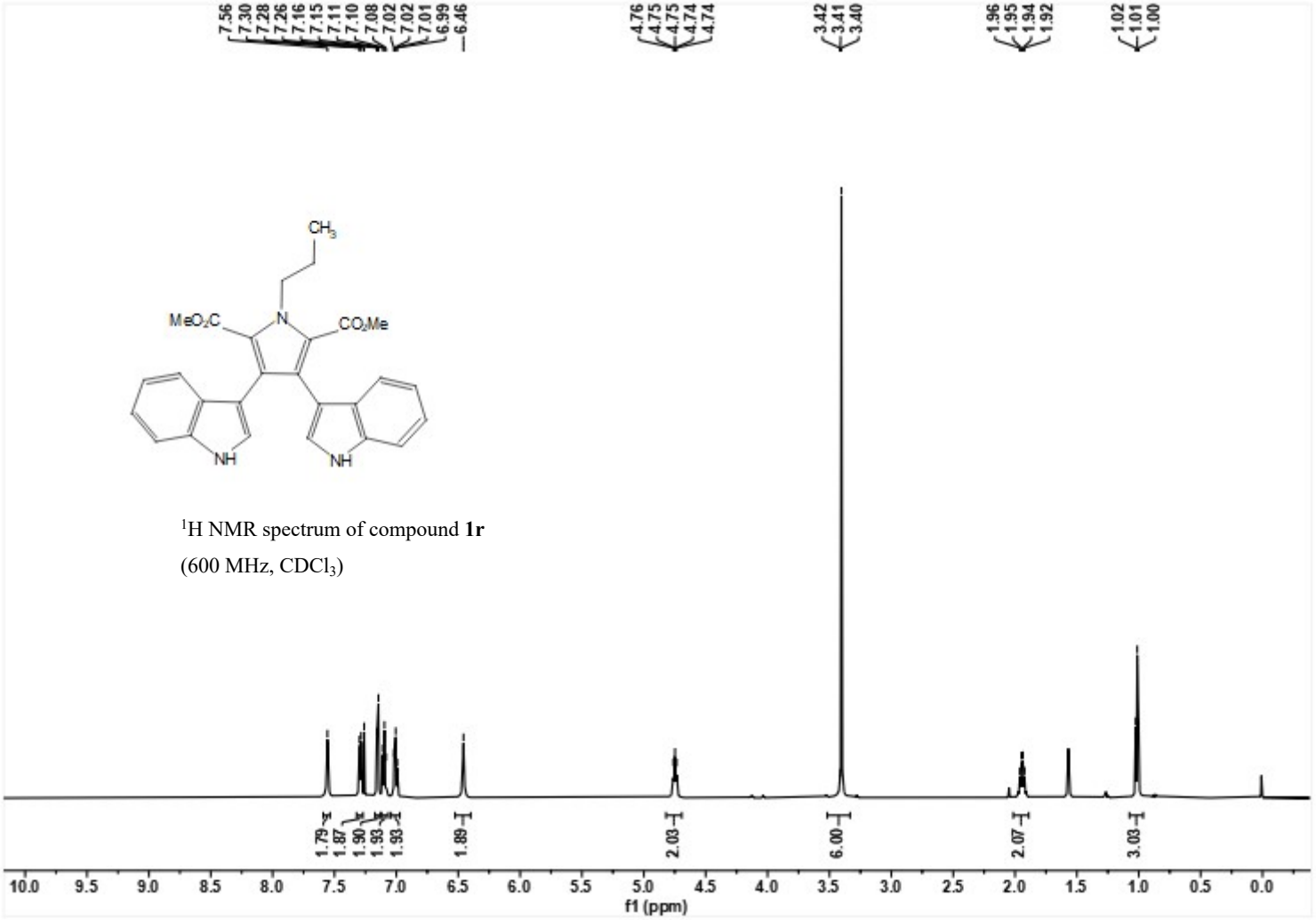
^{1}H NMR spectrum of compound **1q**

(600 MHz,$CDCl_3$)



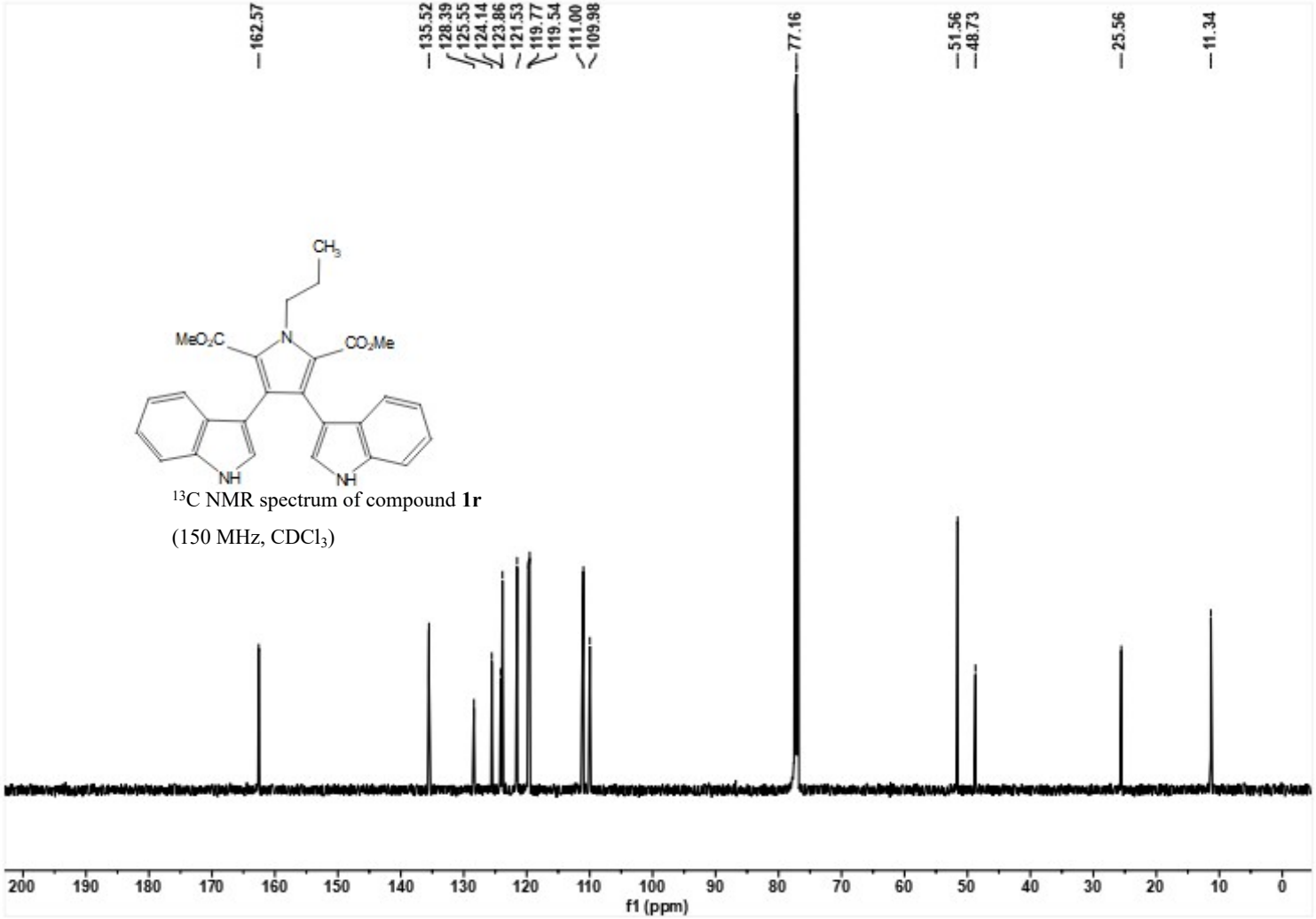
^{13}C NMR spectrum of compound **1q**

(150 MHz, $CDCl_3$)



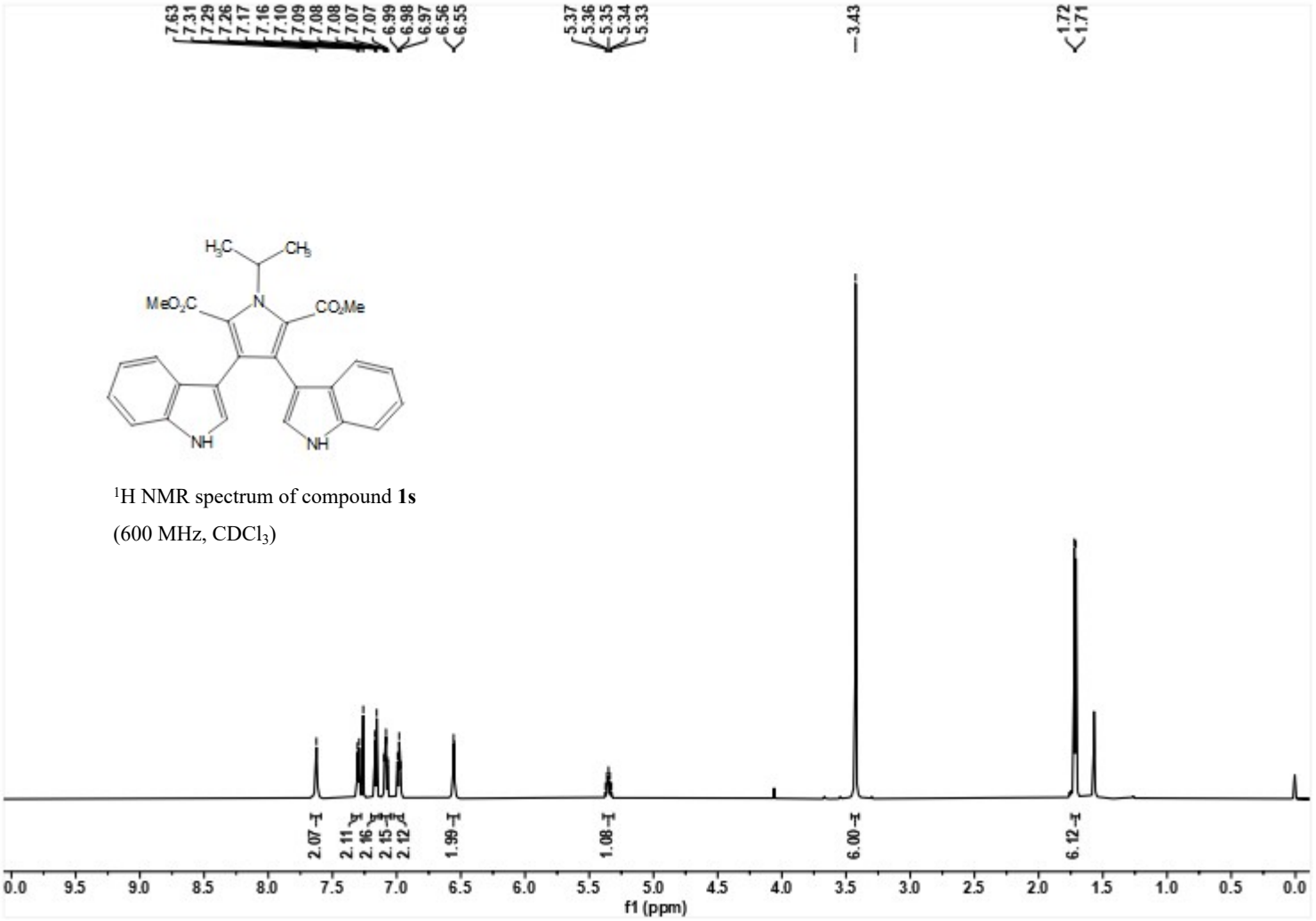
^{1}H NMR spectrum of compound **1r**

(600 MHz, $CDCl_3$)



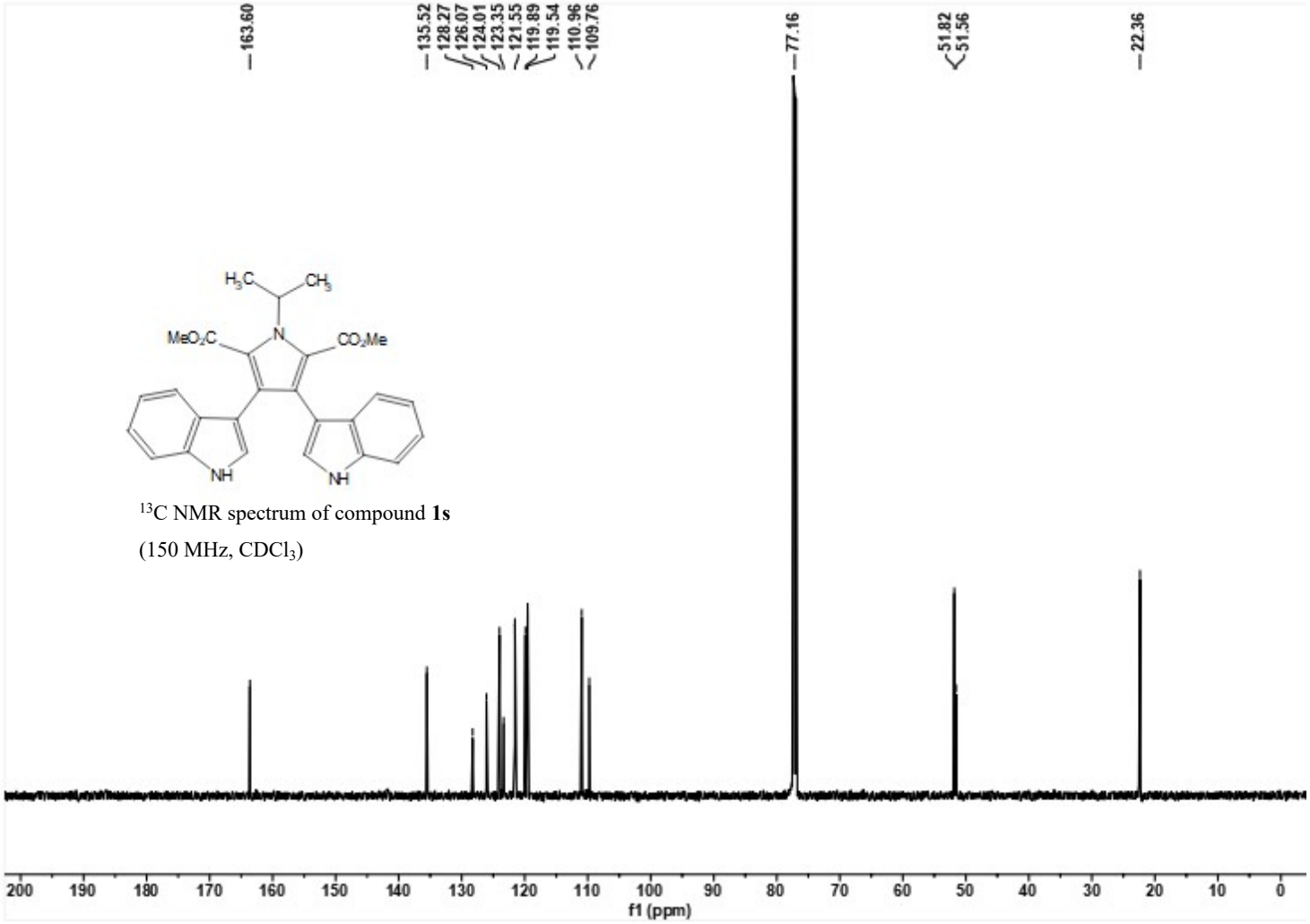
^{13}C NMR spectrum of compound **1r**

(150 MHz, $CDCl_3$)



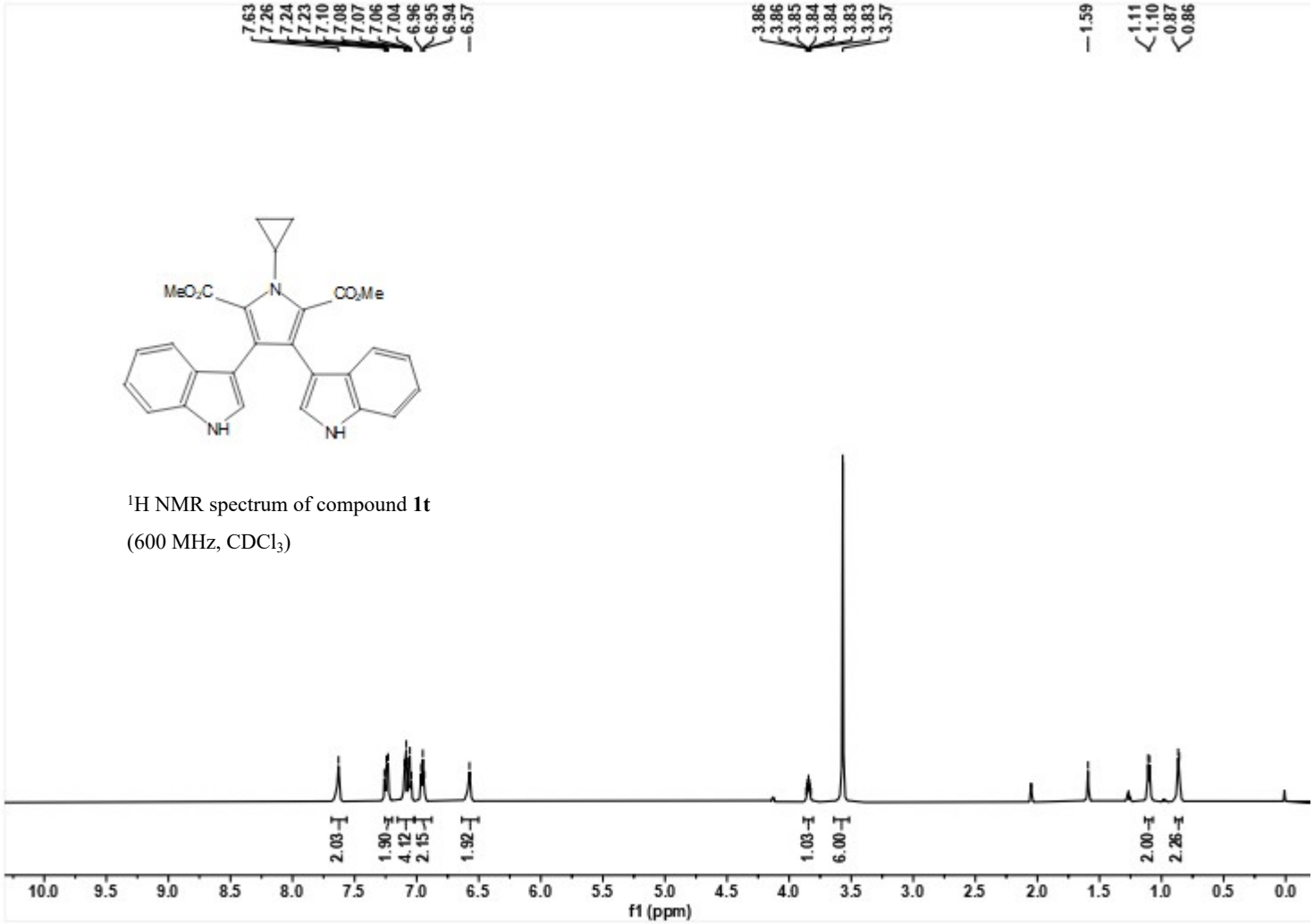
^{1}H NMR spectrum of compound **1s**

(600 MHz, $CDCl_3$)



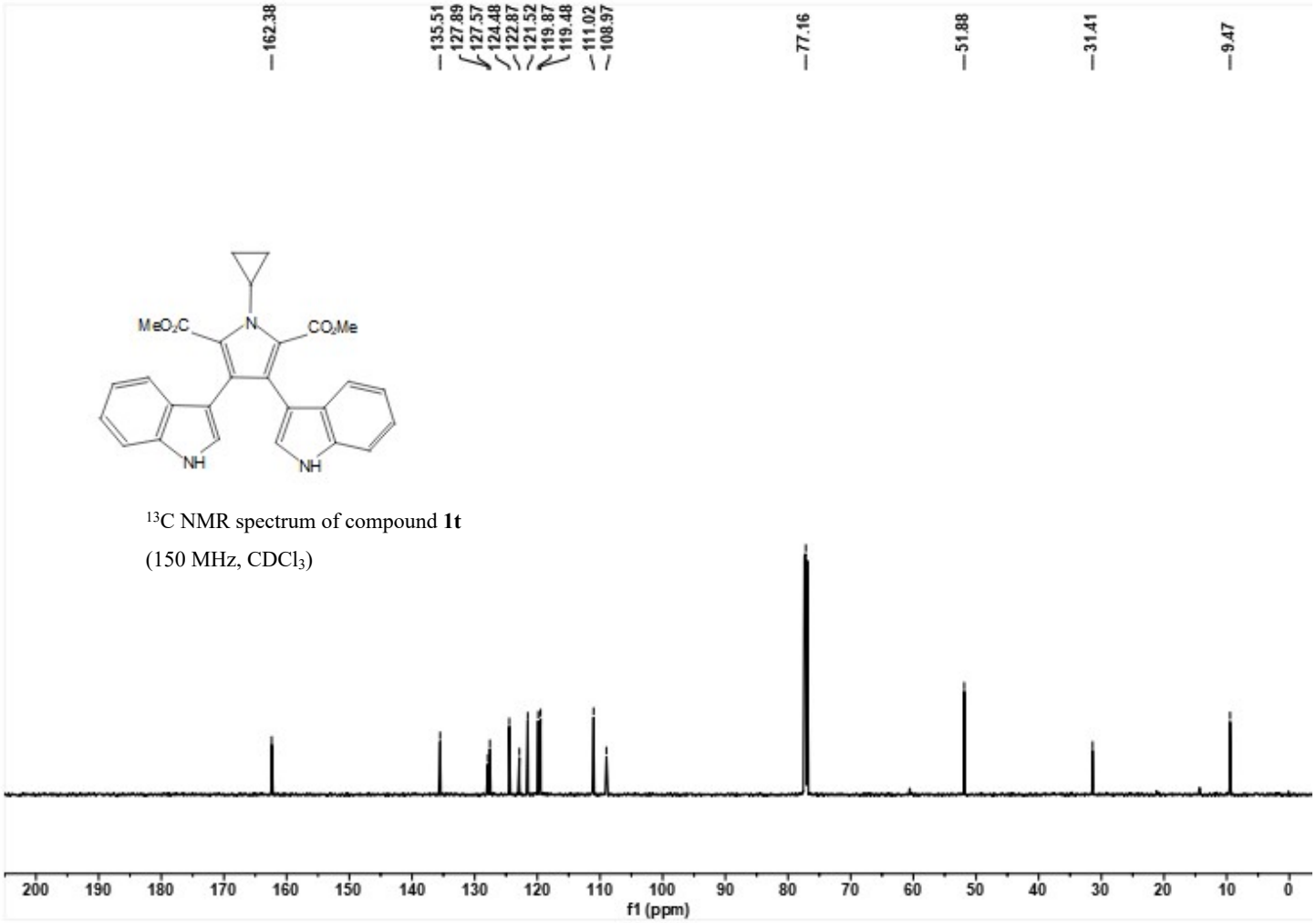
^{13}C NMR spectrum of compound **1s**

(150 MHz, $CDCl_3$)



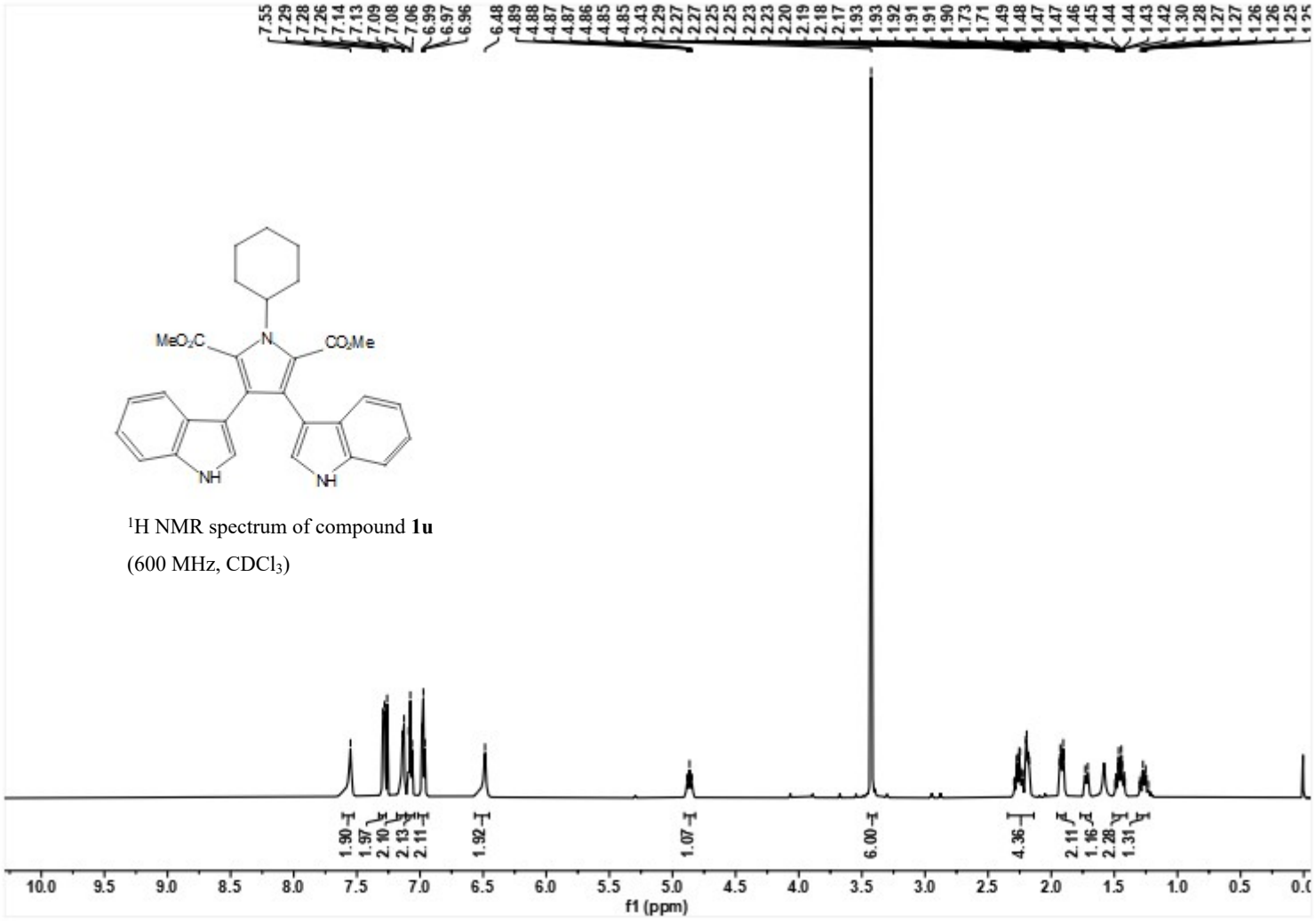
^{1}H NMR spectrum of compound **1t**

(600 MHz, $CDCl_3$)



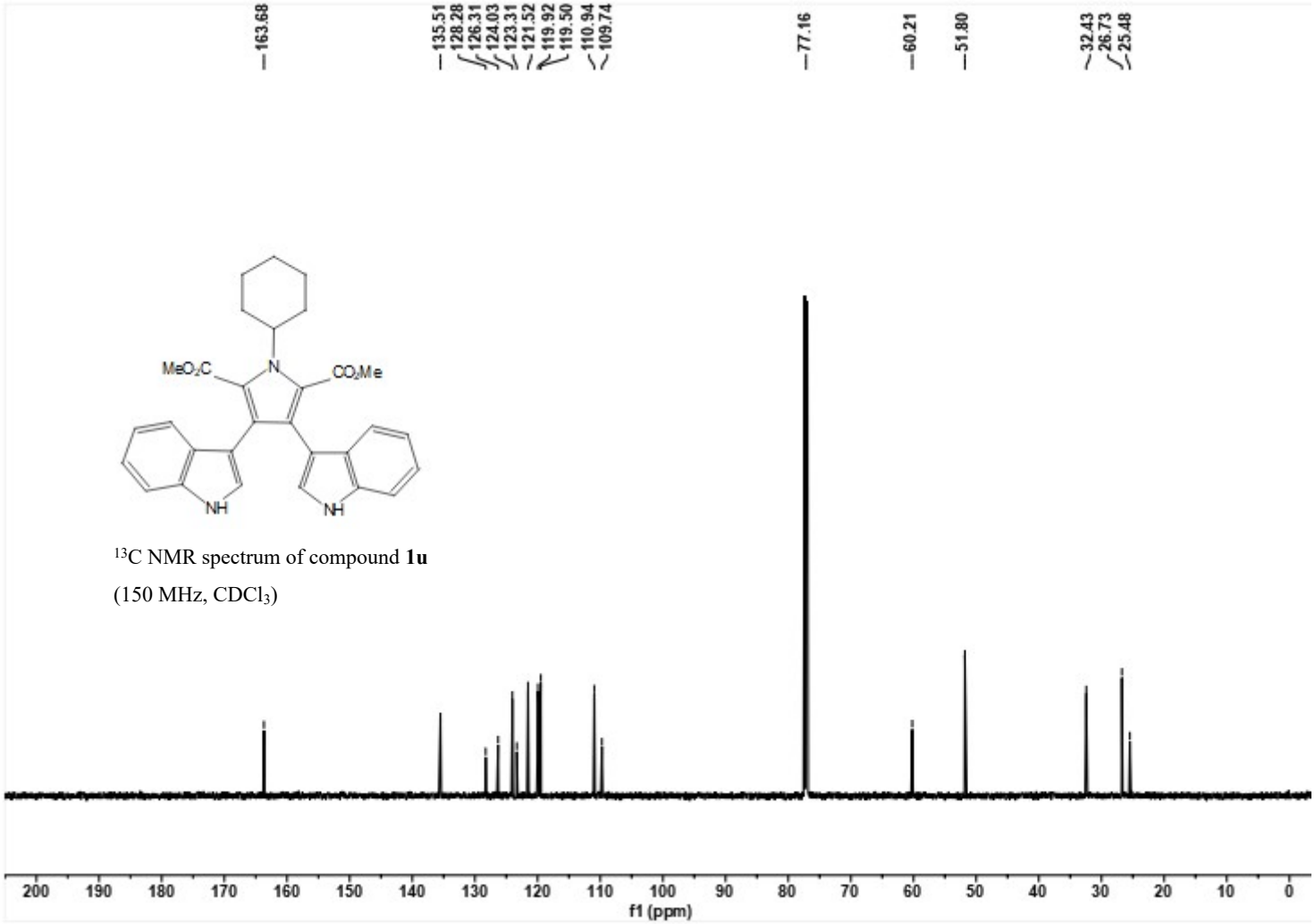
^{13}C NMR spectrum of compound **1t**

(150 MHz, $CDCl_3$)



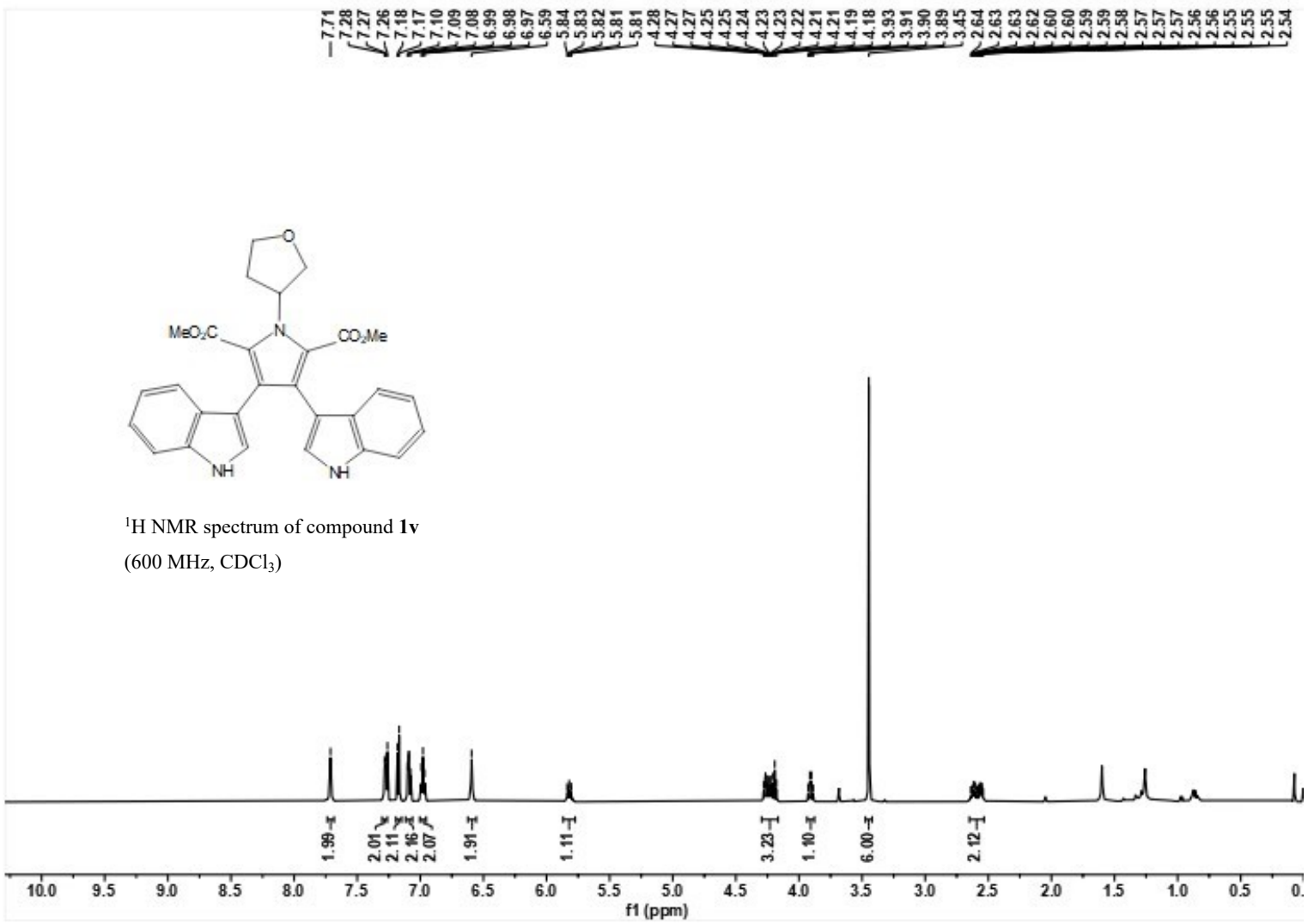
^{1}H NMR spectrum of compound **1u**

(600 MHz, $CDCl_3$)



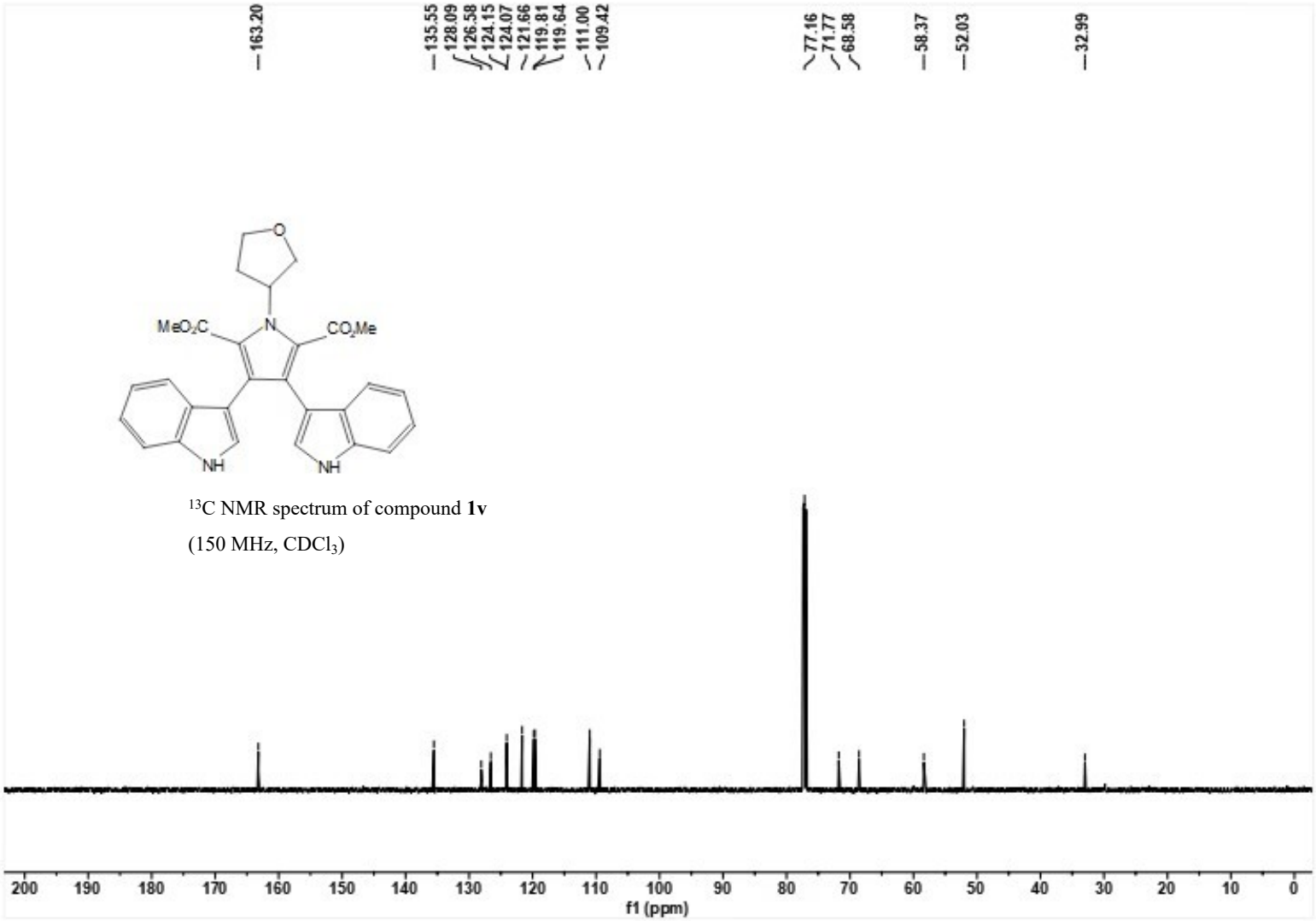
^{13}C NMR spectrum of compound **1u**

(150 MHz, $CDCl_3$)



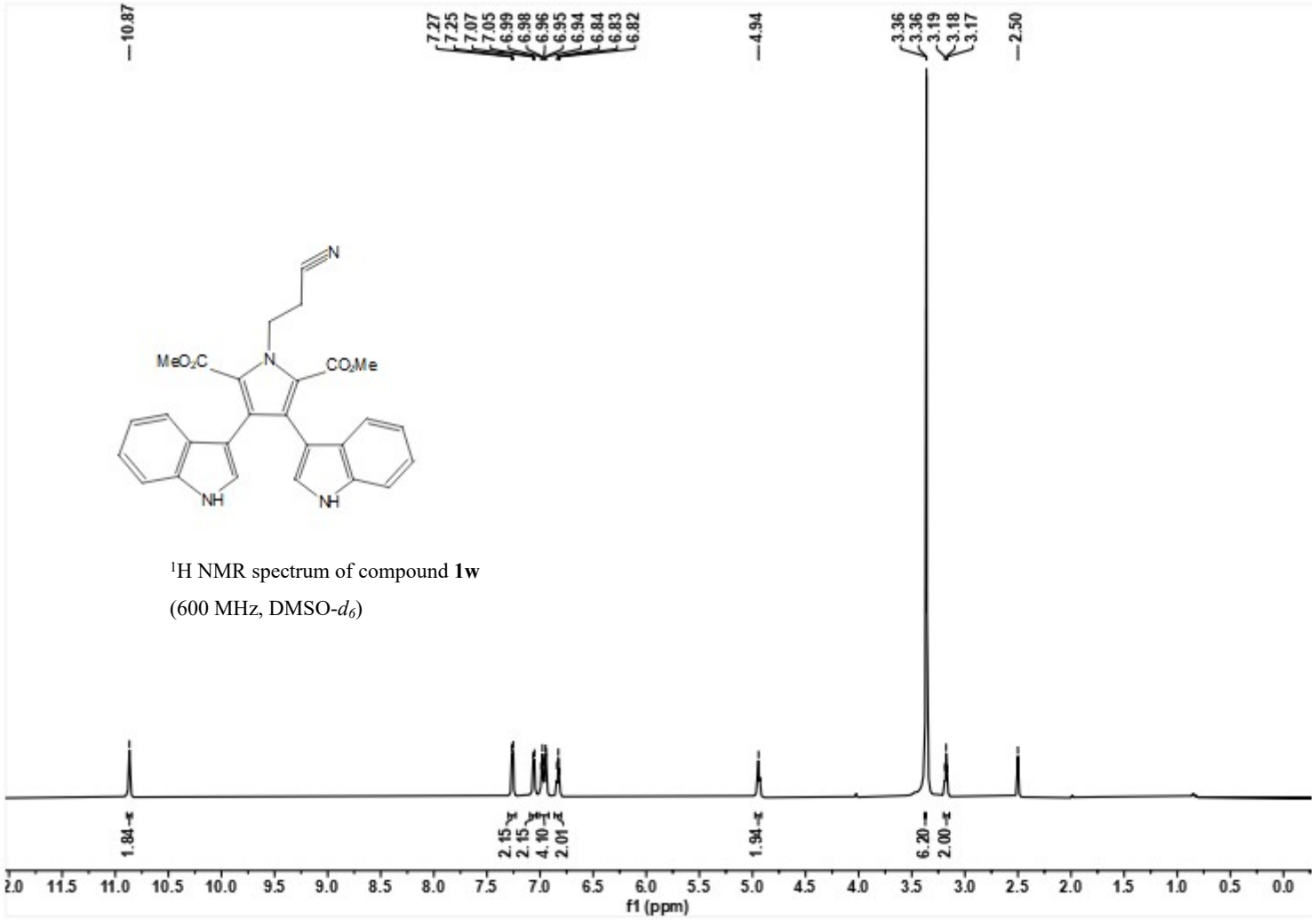
^{1}H NMR spectrum of compound **1v**

(600 MHz, $CDCl_3$)



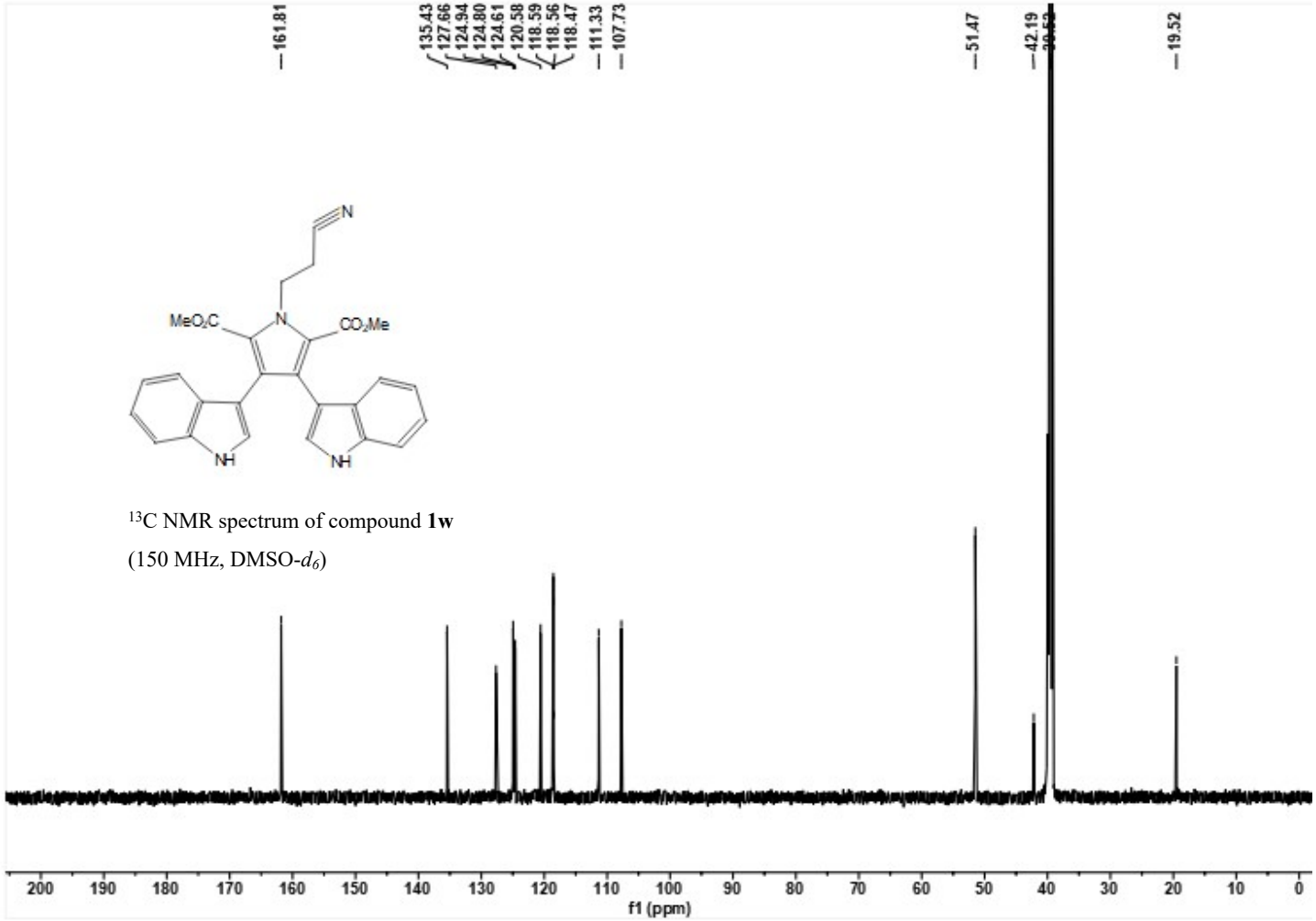
^{13}C NMR spectrum of compound **1v**

(150 MHz, $CDCl_3$)



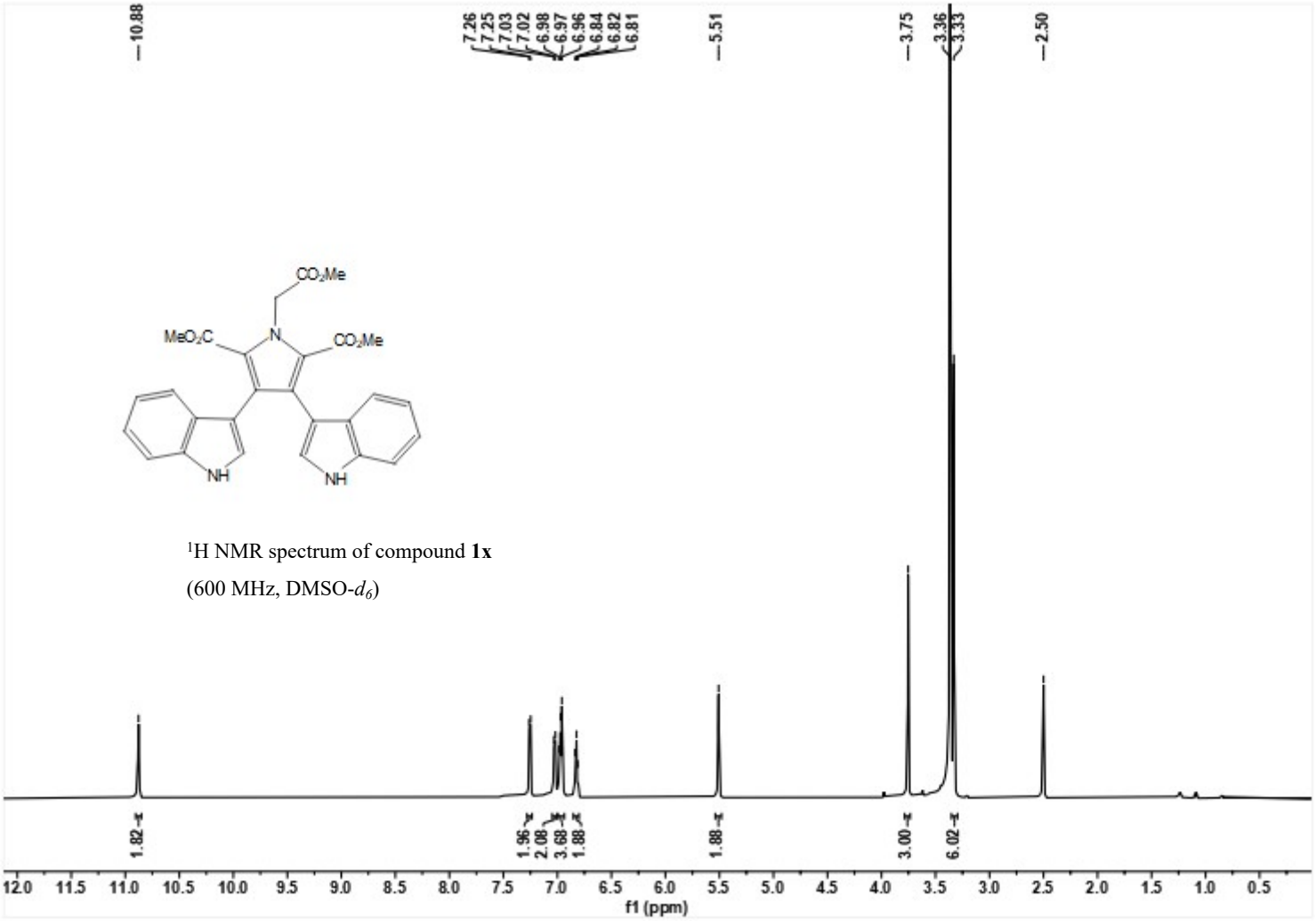
^{1}H NMR spectrum of compound **1w**

(600 MHz, DMSO-d_6)



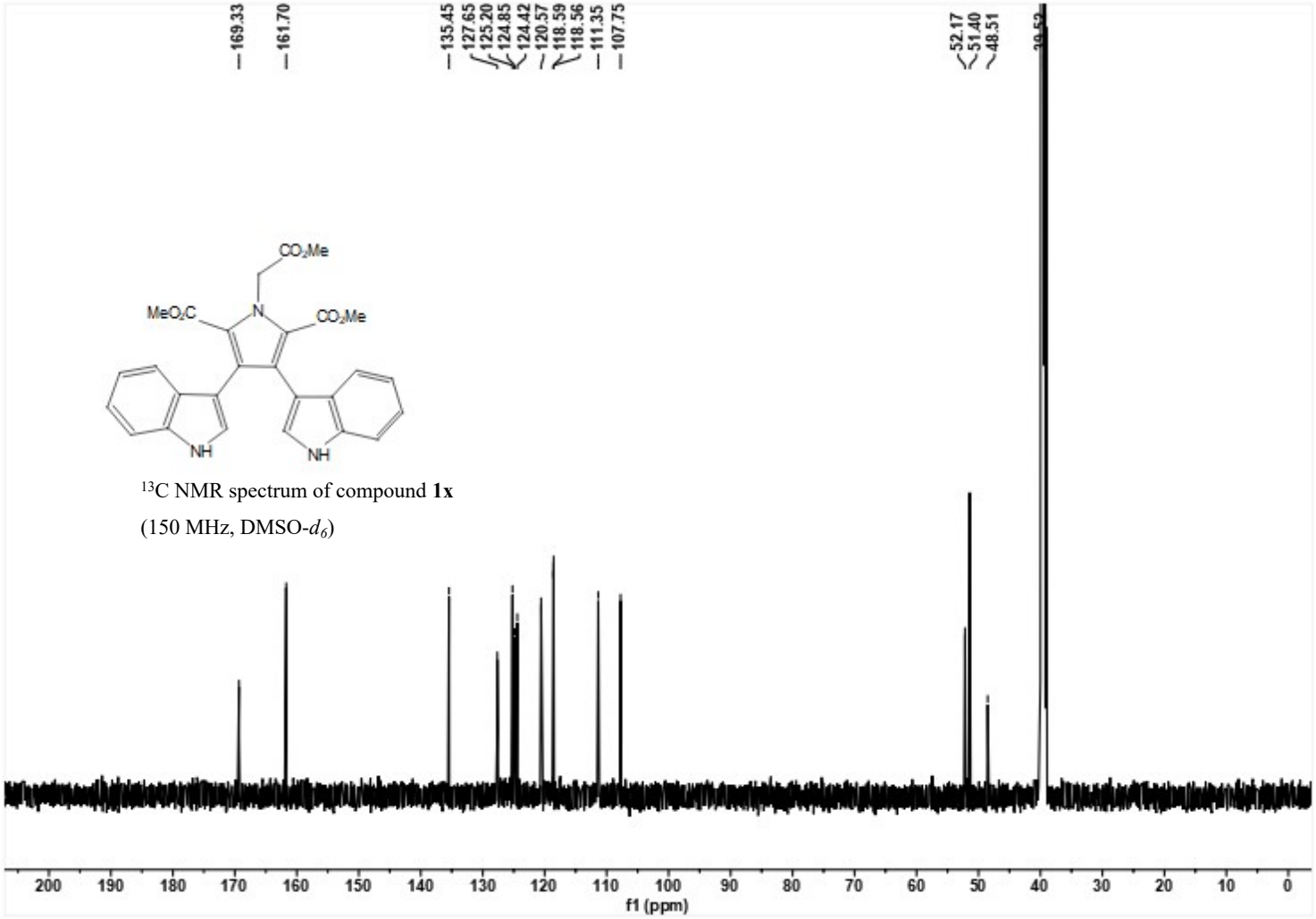
^{13}C NMR spectrum of compound **1w**

(150 MHz, DMSO-d_6)



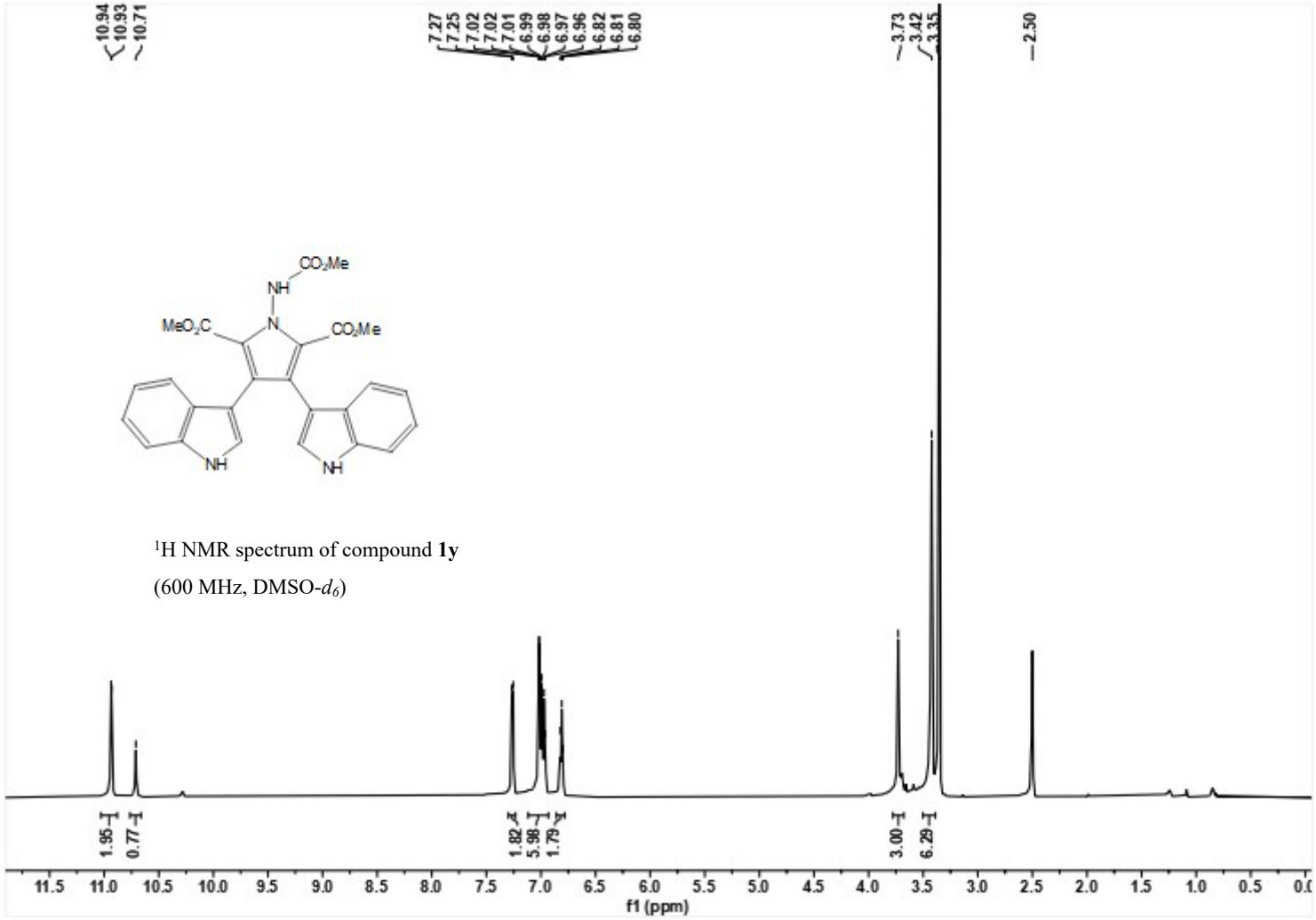
^{1}H NMR spectrum of compound **1x**

(600 MHz, DMSO-d_6)



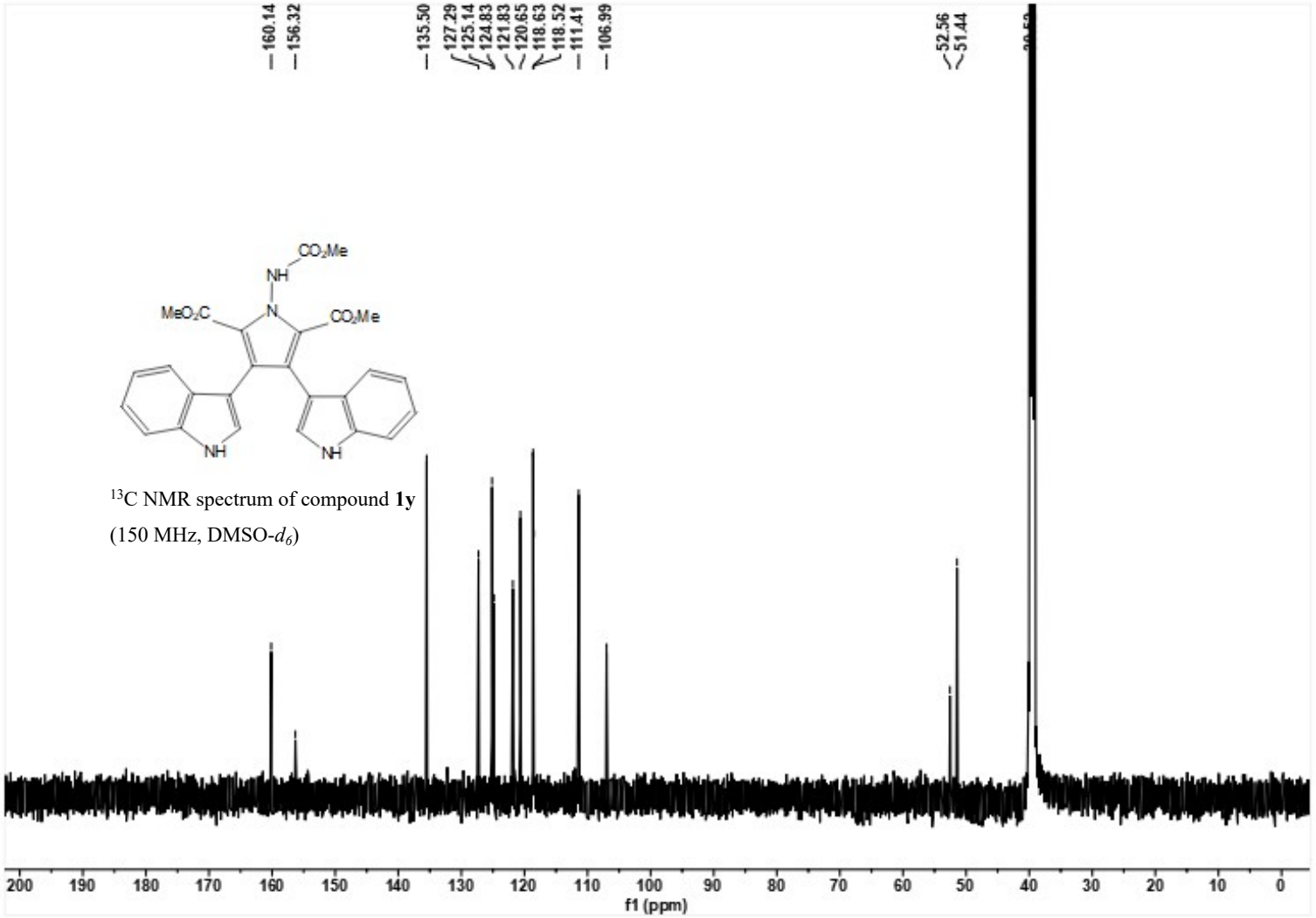
^{13}C NMR spectrum of compound **1x**

(150 MHz, DMSO-d_6)

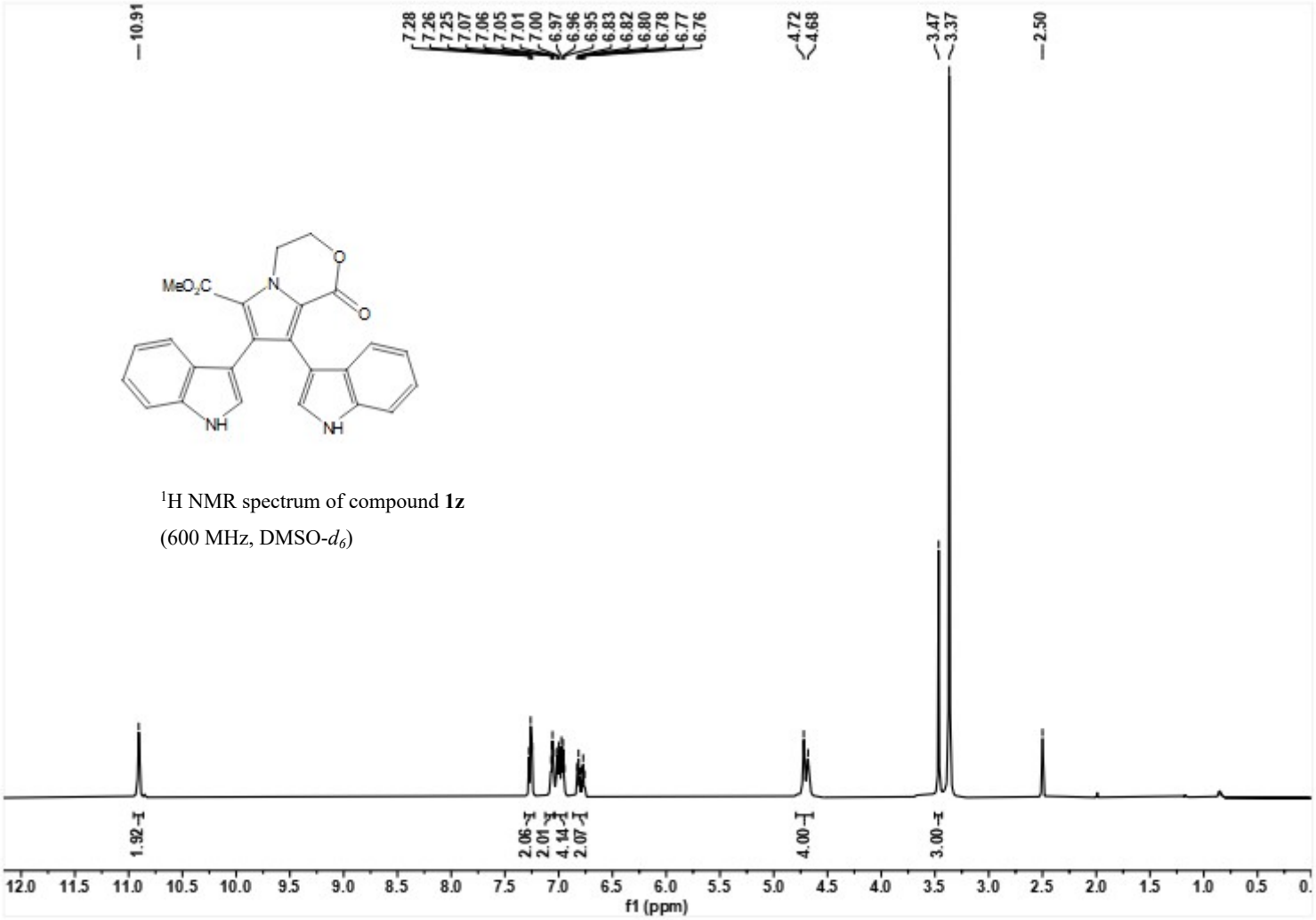


^{1}H NMR spectrum of compound **1y**

(600 MHz, DMSO-d_6)

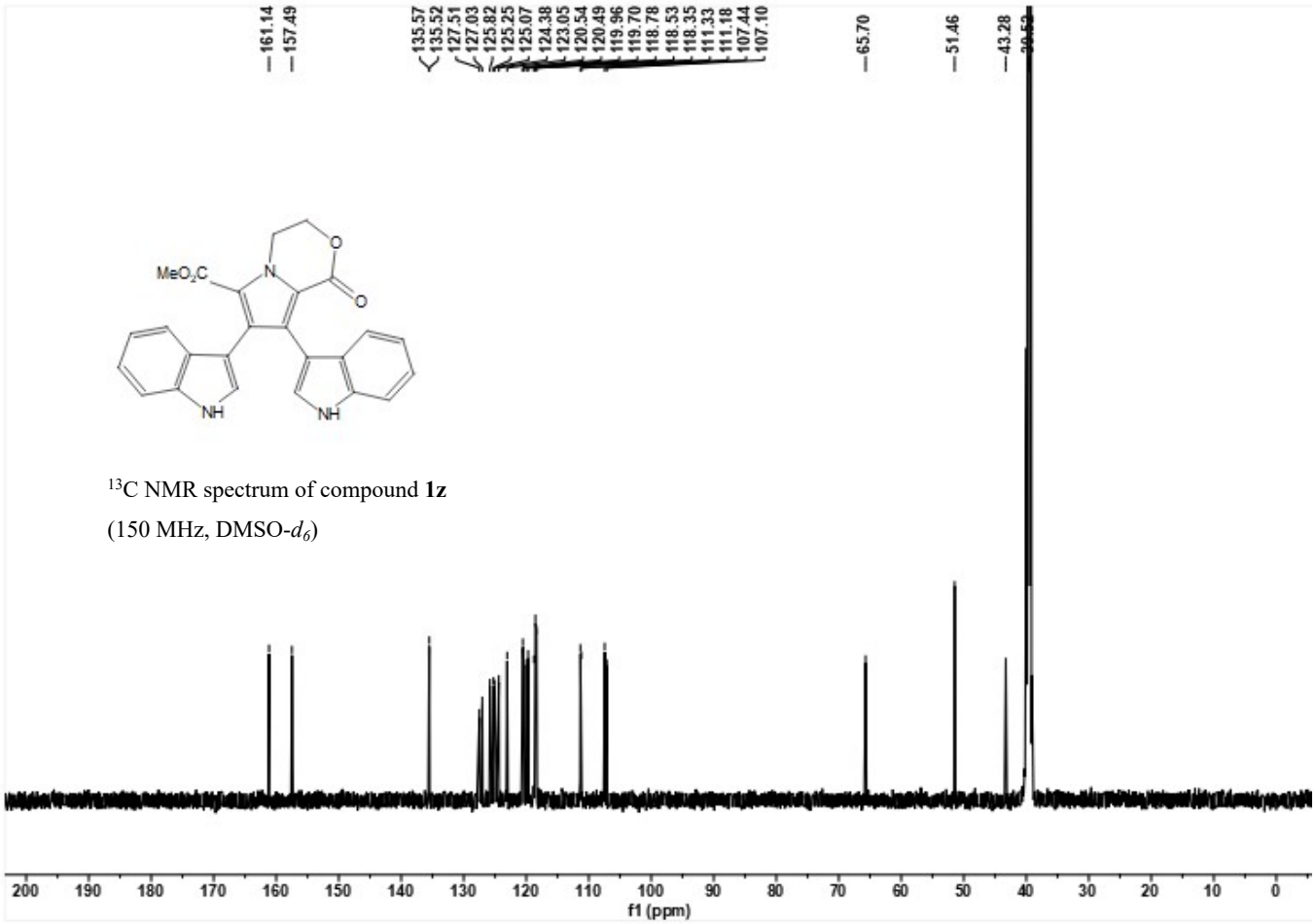


^{13}C NMR spectrum of compound **1y**
(150 MHz, DMSO-d_6)



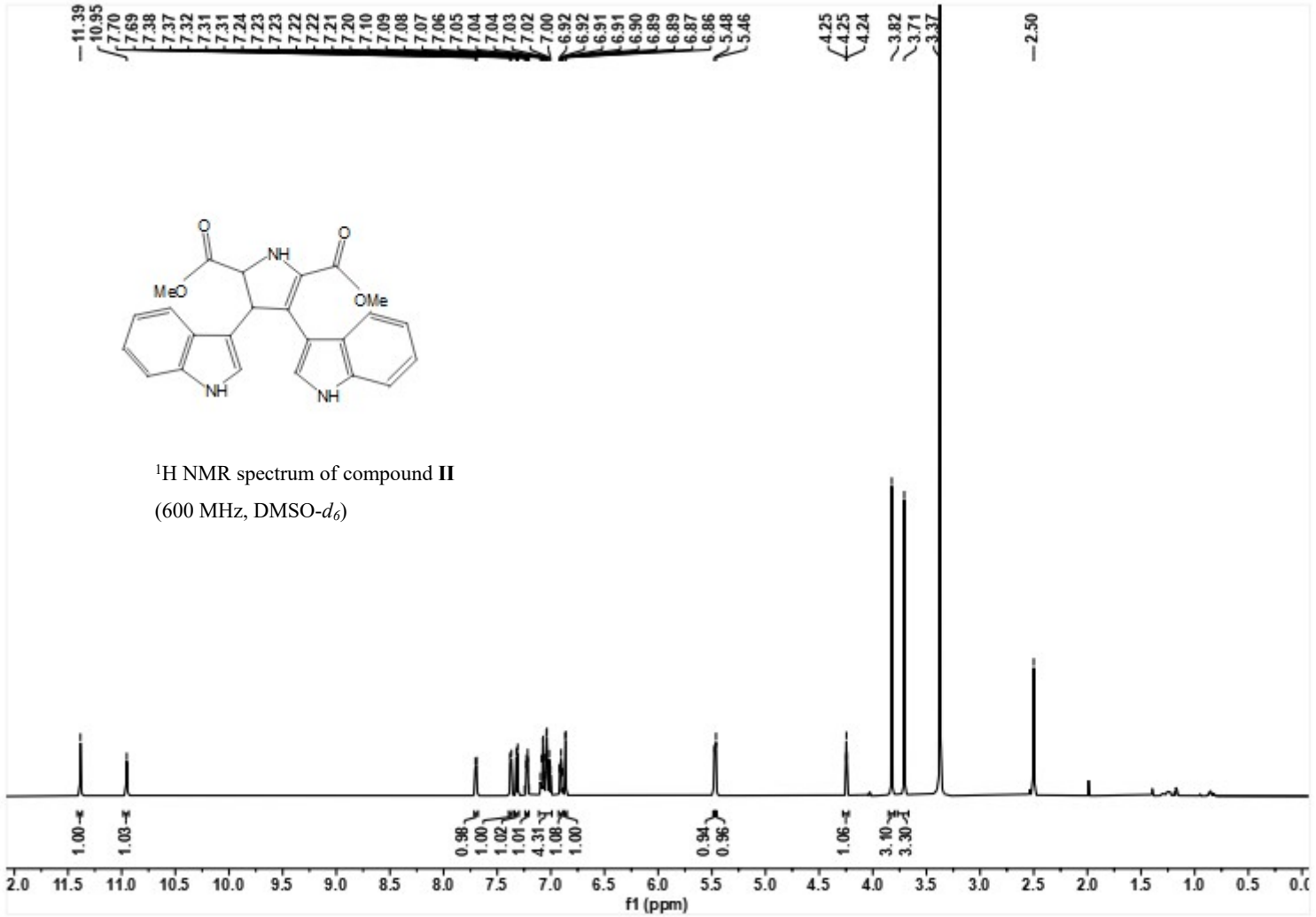
^{1}H NMR spectrum of compound **1z**

(600 MHz, DMSO-d_6)



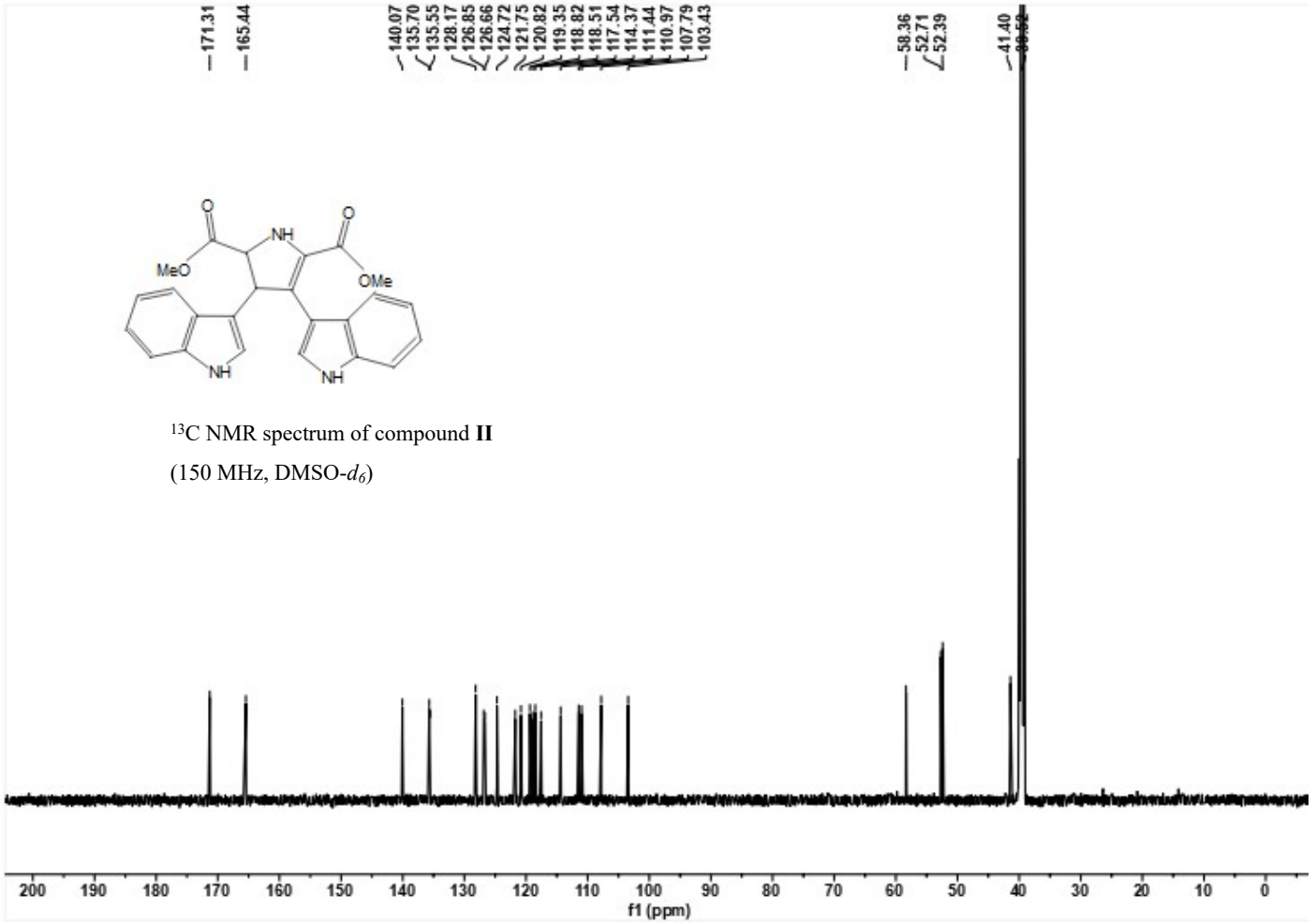
^{13}C NMR spectrum of compound **1z**

(150 MHz, DMSO-d_6)



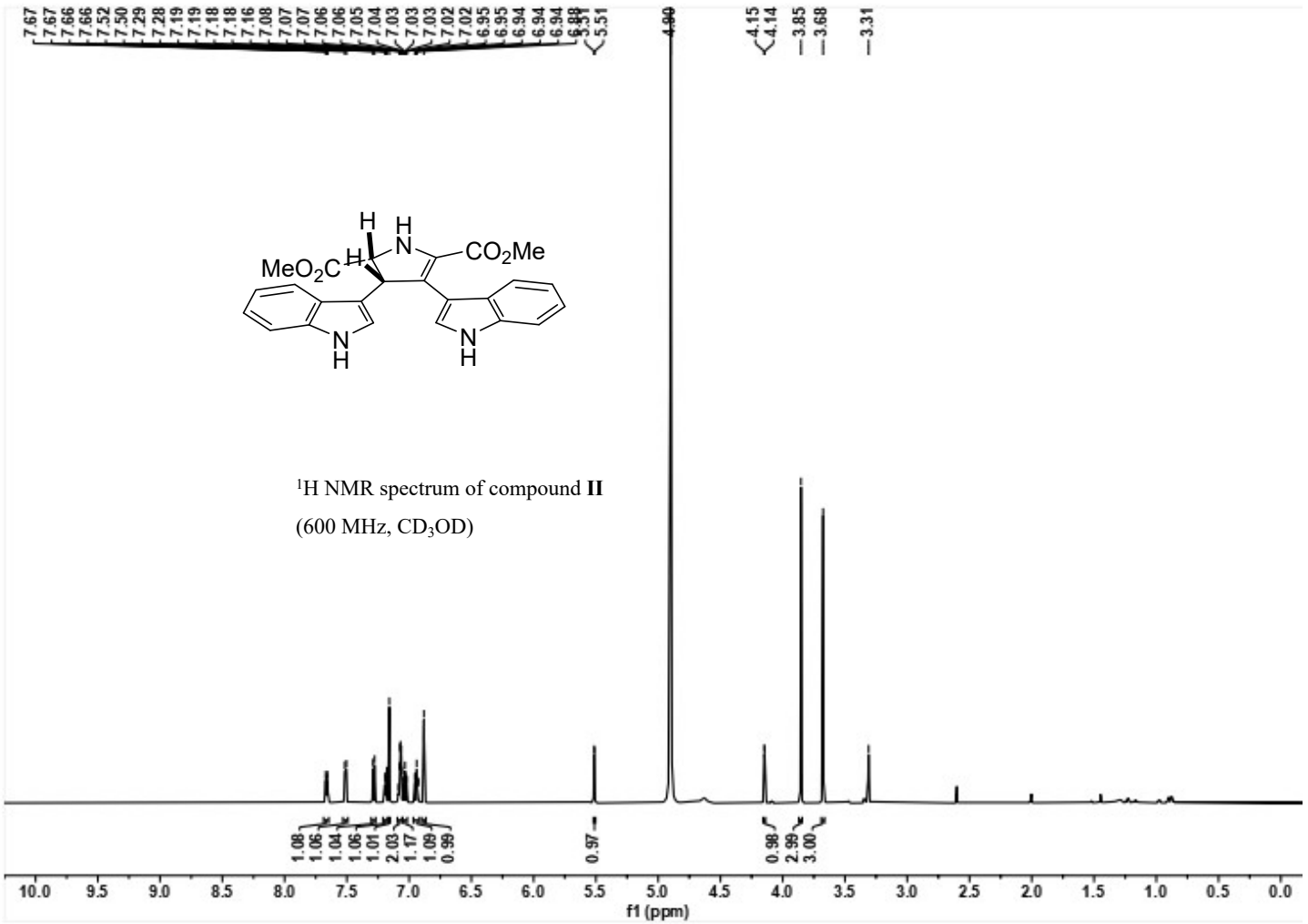
^{1}H NMR spectrum of compound **II**

(600 MHz, DMSO-d_6)



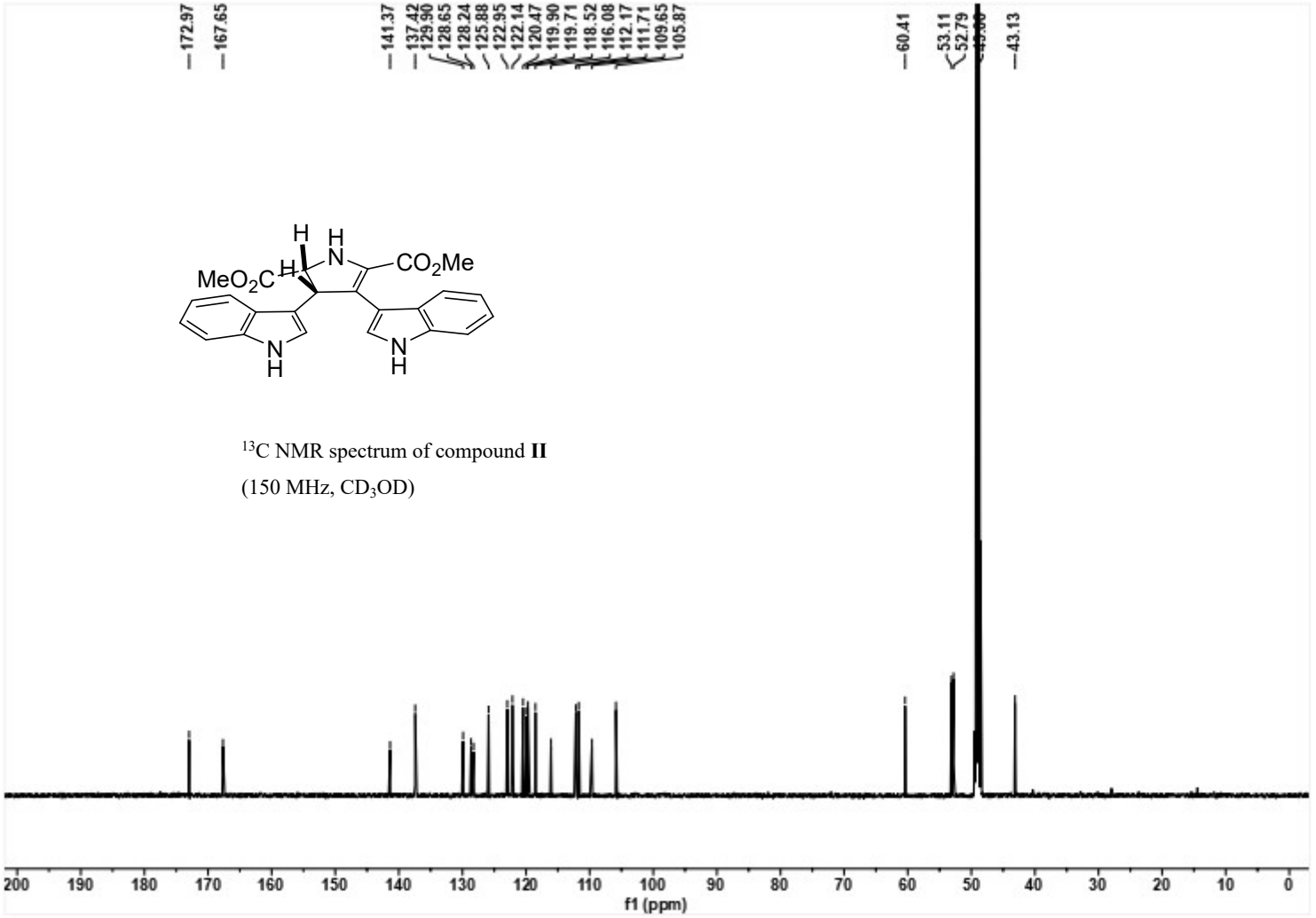
^{13}C NMR spectrum of compound **II**

(150 MHz, DMSO-d_6)



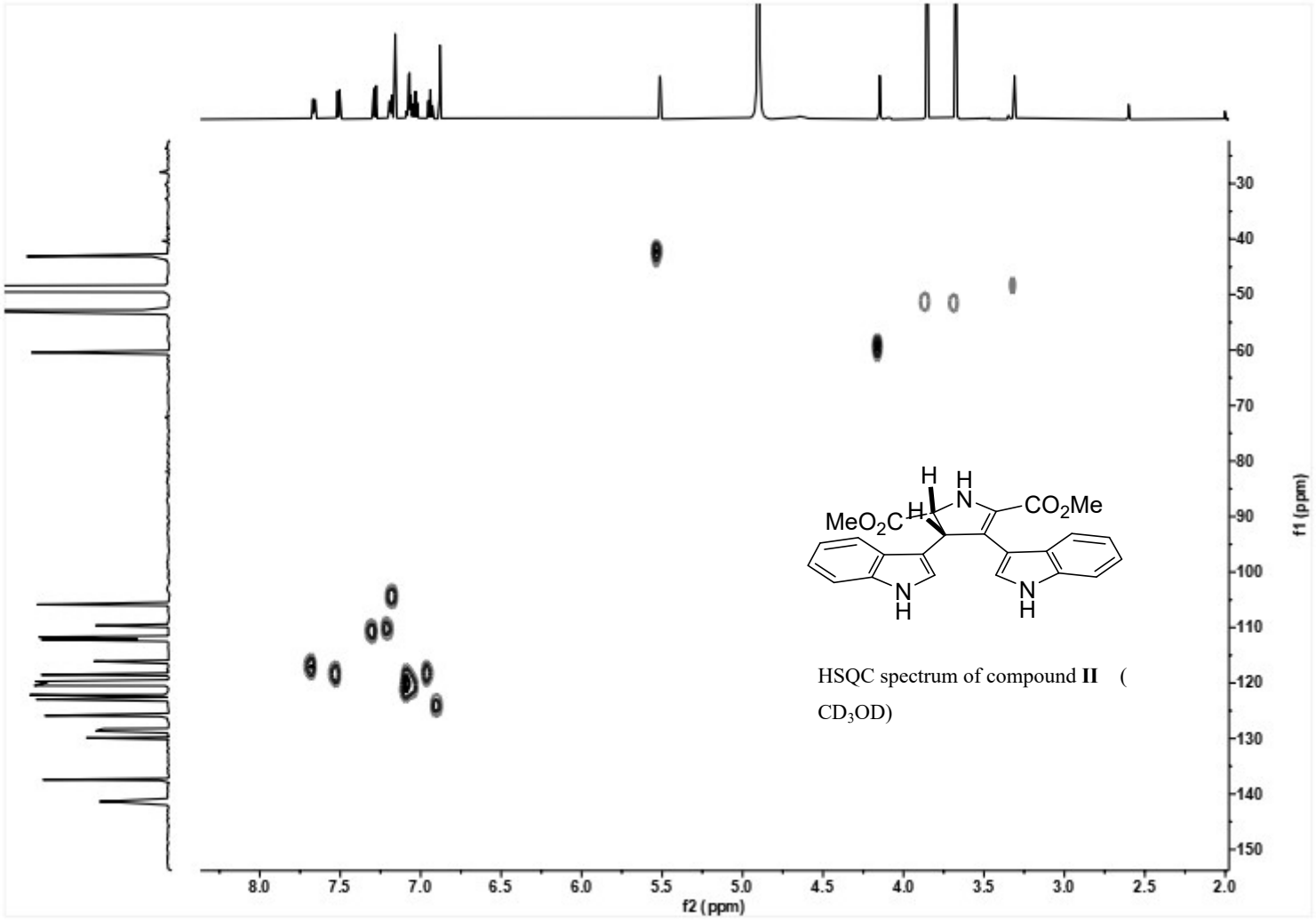
^{1}H NMR spectrum of compound **II**

(600 MHz, CD_3OD)

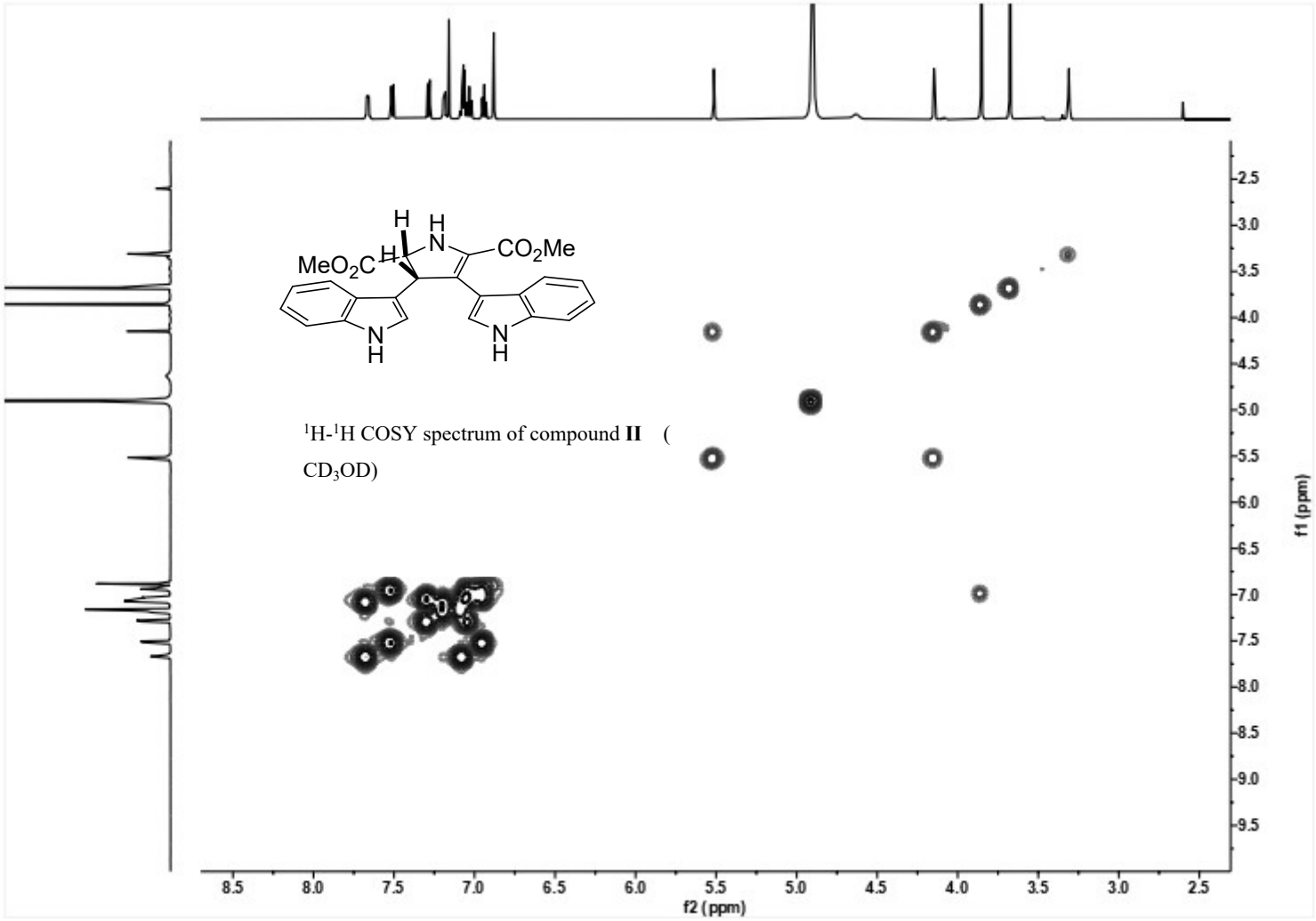


^{13}C NMR spectrum of compound **II**

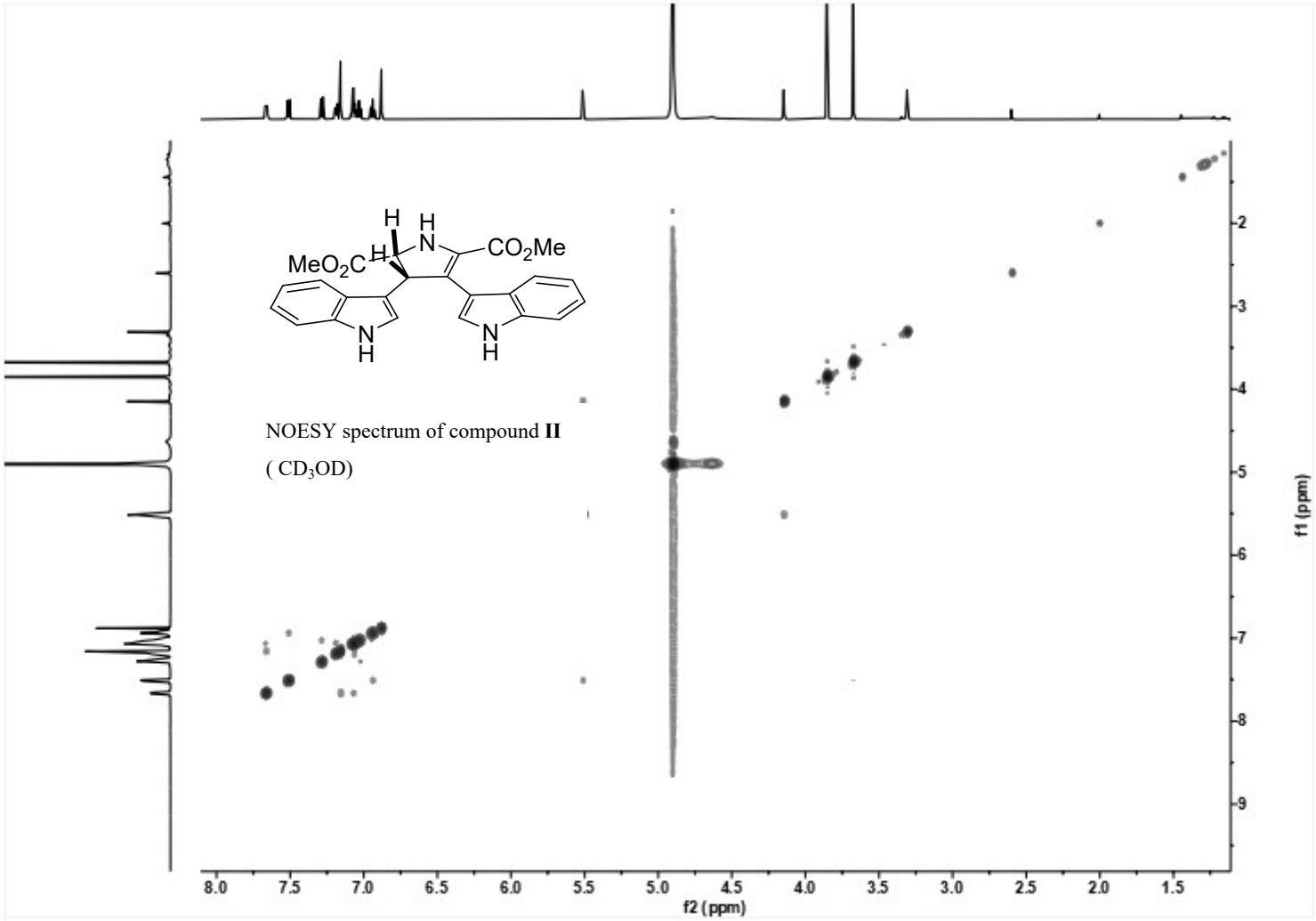
(150 MHz, CD_3OD)



HSQC spectrum of compound **II** (CD_3OD)



^{1}H-^{1}H COSY spectrum of compound **II** (CD_3OD)



NOESY spectrum of compound **II**

(CD_3OD)