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3-Methylene-2,4-chromandione in situ trapping: Introducing molecular diversity on 4-hydroxycoumarin

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Supplementary Information

General information

All reagents and solvents used for synthesis were commercial and used without further purification. They were supplied by Aldrich, Acros, Lancaster, Alfa Aesar and Fluka. All reactions were performed under hydrogen atmosphere in a 50mL-autoclave using anhydrous solvents, unless otherwise stated. All compounds were characterized by spectroscopic data. NMR spectra were recorded at 293 K, unless stated otherwise using a Bruker ALS or DRX spectrometer (^{1}H: 300 MHz, ^{13}C: 100 MHz and 125 MHz). Shifts are referenced relative to the deuterated solvent (d_6-DMSO) residual peaks. The chemical shifts (δ) are expressed in ppm, and the coupling constants (*J*) are given in Hz. The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad. Electrospray ionization (ESI) mass spectra (MS) and High-Resolution Mass Spectra (HRMS) were recorded in the positive mode using a Bruker MicrOTOF-Q II XL spectrometer. Thin-layer chromatography (TLC) was carried out on aluminum sheets coated with silica gel Merck 60 F254 (0.25 mm). Flash column chromatography was performed with silica gel Merck Si 60 (40–63 μm). Infra-red (IR) spectra were recorded in a SMART iTR-Nicolet iS10 spectrometer using Attenuated Total Reflectance (ATR) and the wave numbers (ν) are expressed in cm^{-1}. Melting points were measured using a Banc Kofler apparatus and noted in ^{o}C.

Method A: General procedure for the preparation of pyrrolidine intermediates

A solution of 4-hydroxycoumarin (1 eq), 4-hydroxythiocoumarin (1 eq) or 4-hydroxyquinolin-2(1*H*)-one in anhydrous dichloromethane [0.5M] was stirred at room temperature in the presence of pyrrolidine (1 eq) and aldehyde (1 eq). After complete conversion, the reaction mixture was concentrated, precipitated in ethyl acetate and filtrated on a sintered glass funnel to yield *ortho*-quinone methide trapped derivative.

4-Hydroxy-3-[phenyl(pyrrolidin-1-yl)methyl]-2*H*-chromen-2-one (1a)

The title compound was prepared from 4-hydroxycoumarin (1 g, 6.17 mmol, 1 eq), benzaldehyde (6.17 mmol, 1 eq) and pyrrolidine (6.17 mmol, 1 eq) to give **1a** (2.04 g, 99%) as a white solid. mp 185-186 °C (EtOAc); IR 3061, 1658, 1658, 1642, 1597, 1532, 1162, 760 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.82-2.05 (m, 4 H, 2 CH_2), 3.01-3.25 (m, 4 H, 2 CH_2), 5.33 (s, 1 H, CH), 7.12-7.19 (m, 2 H, H_{arom}), 7.26-7.35 (m, 3 H, H_{arom}), 7.43 (td, 1 H, *J* = 1.6, *J* = 7.5, H_{arom}), 7.68-7.72 (m, 2 H, H_{arom}), 7.98 (dd, 1 H, *J* = 1.6, *J* = 7.8, H_{arom}), 10.95 (s, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 23.1 (2 CH_2), 53.1 (2 CH_2), 68.1 (CH), 93.9 (C_q), 115.7 (CH), 122.0 (C_q), 122.2 (CH), 124.2 (CH), 127.7 (2 CH), 127.9 (CH), 128.2 (2 CH), 130.6 (CH), 138.8 (C_q), 153.6 (C_q), 162.9 (C_q), 172.7 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 321; $[M+H]^+$ found 322; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{20}H_{20}NO_3$: 322.1438; found: 322.1439.

3-[(1,1'-Biphenyl)-4-yl(pyrrolidin-1-yl)methyl]-4-hydroxy-2*H*-chromen-2-one (1b)

The title compound was prepared from 4-hydroxycoumarin (3.89 g, 24.0 mmol, 1 eq), (1,1'-biphenyl)-4-carbaldehyde (4.37 g, 24.0 mmol, 1 eq) and pyrrolidine (2 mL, 24.0 mmol, 1 eq) to give **1b** (9.02 g, 90%) as a white solid. mp 169-170 °C (EtOAc); IR 3055, 1638, 1600, 1534, 1409, 1061, 753 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.85-2.10 (m, 4 H, 2 CH_2), 3.09-3.32 (m, 4 H, 2 CH_2), 5.38 (s, 1 H, CH), 7.13-7.20 (m, 2 H, H_{arom}), 7.34 (t, 1 H, *J* = 7.3, H_{arom}), 7.44 (t, 3 H, *J* = 7.5, H_{arom}), 7.63 (d, 4 H, *J* = 6.5, H_{arom}), 7.78 (d, 2 H, *J* = 8.3, H_{arom}), 7.88 (dd, 1 H, *J* = 1.5, *J* = 6.3, H_{arom}), 10.87 (s, 1 H, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 23.3 (2 CH_2), 53.3 (2 CH_2), 67.7 (CH), 94.0 (C_q), 115.8 (CH), 122.2 (CH), 122.4 (C_q), 124.4 (CH), 126.7 (2 CH), 126.7 (2 CH), 127.5 (CH), 128.3 (2 CH), 128.9 (2 CH), 130.8 (CH), 138.1 (C_q), 139.7 (C_q), 139.8 (C_q), 153.7 (C_q), 163.0 (C_q),

172.8 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 397; $[M+H]^+$ found 398; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{26}H_{24}NO_3$: 398.1751; found: 398.1744.

4-Hydroxy-3-{[(4-methoxyphenyl)pyrrolidin-1-yl]methyl}-2*H*-chromen-2-one (1c)

The title compound was prepared from 4-hydroxycoumarin (500 mg, 3.08 mmol, 1 eq), 4-methoxybenzaldehyde (408 mg, 3 mmol, 1 eq) and pyrrolidine (219 mg, 3.08 mmol, 1 eq) to give **1c** (1.05 g, 99%) as a white solid. mp 155-156 °C (EtOAc); IR 3390, 3068, 2835, 1644, 1622, 1599, 1523, 1511, 1451, 1032, 750 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 1.82-2.05 (m, 4 H, 2 CH_2), 2.91-3.22 (m, 4 H, 2 CH_2), 3.72 (s, 3 H, CH_3), 5.23 (s, 1 H, CH), 6.89 (d, 2 H, *J* = 8.5, H_{arom}), 7.12-7.20 (m, 2 H, H_{arom}), 7.44 (t, 1 H, *J* = 7.6, H_{arom}), 7.62 (d, 2 H, *J* = 8.6, H_{arom}), 7.87 (d, 1 H, *J* = 7.1, H_{arom}), 10.91 (s, 1 H, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ = 23.2 (2 CH_2), 53.0 (2 CH_2), 55.1 (CH_3), 67.7 (CH), 94.4 (C_q), 113.7 (2 CH), 115.8 (CH), 122.2 (CH), 122.4 (C_q), 124.3 (CH), 129.3 (2 CH), 130.8 (CH), 131.0 (C_q), 153.7 (C_q), 159.0 (C_q), 163.0 (C_q), 172.7 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 351; $[M+H]^+$ found 352; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{21}H_{22}NO_4$: 352.1543; found: 352.1553.

4-Hydroxy-3-{pyrrolidin-1-yl[4-(trifluoromethoxy)phenyl]methyl}-2*H*-chromen-2-one (1d)

The title compound was prepared from 4-hydroxycoumarin (500 mg, 3.08 mmol, 1 eq), 4-(trifluoromethoxy)benzaldehyde (586 mg, 3.08 mmol, 1 eq) and pyrrolidine (219 mg, 3.08 mmol, 1 eq) to give **1d** (1.24 g, 99%) as a white solid. mp 164-165 °C (EtOAc); IR 3087, 1657, 1635, 1601, 1531, 1409, 1252, 1154, 757 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 1.85-2.05 (m, 4 H, 2 CH_2), 3.05-3.25 (m, 4 H, 2 CH_2), 5.41 (s, 1 H, CH), 7.12-7.20 (m, 2 H, H_{arom}), 7.35 (d, 2 H, *J* = 8.5, H_{arom}), 7.44 (td, 1 H, *J* = 1.6, *J* = 7.4, H_{arom}), 7.82 (d, 2 H, *J* = 8.5, H_{arom}), 7.86 (dd, 1 H, *J* = 1.6, *J* = 7.8, H_{arom}), 10.78 (s, 1 H, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 23.3 (2 CH_2), 53.4 (2 CH_2), 67.0 (CH), 93.8 (C_q), 115.9 (CH), 120.0 (C_q, J_1C-F_3 = 256), 121.0 (2 CH), 122.1 (C_q), 122.4 (CH), 124.4 (CH), 129.6 (2 CH), 130.9 (CH), 138.4 (C_q), 147.9 (C_q), 153.7 (C_q), 163.0 (C_q), 172.8 (C_q). ^{19}F NMR (282 MHz, DMSO-d_6) δ = -56.7. MS (ESI, CH_3CN): *m/z* calcd. 405; $[M+H]^+$ found 406; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{21}H_{19}F_3NO_4$: 406.1261; found: 406.1256.

3-{[(4-Bromophenyl)pyrrolidin-1-yl]methyl}-4-hydroxy-2*H*-chromen-2-one (1e)

The title compound was prepared from 4-hydroxycoumarin (3.24 g, 20.0 mmol, 1 eq), 4-bromobenzaldehyde (3.70 g, 20.0 mmol, 1 eq) and pyrrolidine (1.42 g, 20.0 mmol, 1 eq) to give **1e** (7 g, 87%) as a white solid. mp 197-198 °C (EtOAc); IR 3379, 3061, 2961, 2868, 1645, 1600, 1519, 1422, 1320, 1043, 754 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.82-2.05 (m, 4 H, 2 CH_2), 3.00-3.35 (m, 4 H, 2 CH_2), 5.34 (s, 1 H, CH), 7.12-7.19 (m, 2 H, H_{arom}), 7.43 (td, 1 H, *J* = 1.5, *J* = 7.6, H_{arom}), 7.55 (d, 2 H, *J* = 8.5, H_{arom}), 7.66 (d, 2 H, *J* = 8.5, H_{arom}), 7.87 (dd, 1 H, *J* = 1.5, *J* = 7.7, H_{arom}), 10.82 (s, 1 H, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 23.3 (2 CH_2), 53.3 (2 CH_2), 67.3 (CH), 93.7 (C_q), 115.8 (CH), 121.3 (C_q), 122.1 (C_q), 122.4 (CH), 124.4 (CH), 129.9 (2 CH), 130.9 (CH), 131.3 (2 CH), 138.2 (C_q), 153.7 (C_q), 163.0 (C_q), 172.8 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 399; $[M+H]^+$ found 400; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{20}H_{19}BrNO_3$: 400.0543; found: 400.0546.

4-{[(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)pyrrolidin-1-yl]methyl}benzonitrile (1f)

The title compound was prepared from 4-hydroxycoumarin (486 mg, 3 mmol, 1 eq), 4-formylbenzonitrile (393 mg, 3 mmol, 1 eq) and pyrrolidine (213 mg, 3 mmol, 1 eq) to give **1f** (937 mg, 90%) as a white solid. mp 172-173 °C (EtOAc); IR 3083, 2222, 1637, 1600, 1532, 1408, 1060, 759 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ = 1.81-2.09 (m, 4 H, 2 CH_2), 3.07-3.29 (m, 4 H, 2 CH_2), 5.49 (s, 1 H, CH), 7.11-7.20 (m, 2 H, H_{arom}), 7.44 (td, 1 H, *J* = 1.7, *J* = 7.2, H_{arom}), 7.81-7.89 (m, 5 H, H_{arom}), 10.91 (s, 1 H, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ = 23.3 (2 CH_2), 53.5 (2 CH_2), 67.2 (CH), 93.3 (C_q), 110.6 (C_q), 115.9 (CH), 118.7 (C_q), 122.1 (C_q), 122.5 (CH), 124.4 (CH), 128.3 (2 CH), 131.0 (CH), 132.4 (2 CH), 144.0 (C_q), 153.7 (C_q), 163.0 (C_q), 173.9 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 346; $[M+H]^+$ found 347; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{21}H_{19}N_2O_3$: 347.1390; found: 347.1380.

4-Hydroxy-3-{[(4-nitrophenyl)pyrrolidin-1-yl]methyl}-2*H*-chromen-2-one (1g)

The title compound was prepared from 4-hydroxycoumarin (486 mg, 3 mmol, 1 eq), 4-nitrobenzaldehyde (453 mg, 3 mmol, 1 eq) and pyrrolidine (213 mg, 3 mmol, 1 eq) to give **1g** (1.04 g, 94%) as a yellow solid. mp 188-189 °C (EtOAc); IR 3062, 2847, 1641, 1601, 1535, 1513, 1362, 1321, 1065, 604 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ = 1.87-2.09 (m, 4 H, 2 CH_2), 3.10-

3.31 (m, 4 H, 2 CH_2), 5.57 (s, 1 H, CH), 7.12-7.21 (m, 2 H, H_{arom}), 7.44 (td, 1 H, *J* = 1.7, *J* = 7.3, H_{arom}), 7.85 (dd, 1 H, *J* = 1.7, *J* = 7.8, H_{arom}), 7.94 (d, 2 H, *J* = 8.9, H_{arom}), 8.21 (d, 2 H, *J* = 8.9, H_{arom}), 10.72 (s, 1H, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ= 23.4 (2 CH_2), 53.5 (2 CH_2), 66.8 (CH), 93.2 (C_q), 115.9 (CH), 122.1 (C_q), 122.5 (CH), 123.6 (2 CH), 124.4 (CH), 128.6 (2 CH), 131.0 (CH), 145.9 (C_q), 146.9 (C_q), 153.7 (C_q), 163.0 (C_q), 173.0 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 366; $[M+H]^+$ found 367; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{20}H_{19}N_2O_5$: 367.1288; found: 365.1301.

4-Hydroxy-3-{[4-(pyridin-4-yl)phenyl][pyrrolidin-1-yl]methyl}-coumarin (1h)

The title compound was prepared from 4-hydroxycoumarin (486 mg, 3 mmol, 1 eq), 4-(pyridin-4-yl)benzaldehyde (549 mg, 3 mmol, 1 eq) and pyrrolidine (213 mg, 3 mmol, 1 eq) to give **1h** (1.20 g, 99%) as a white solid. mp 152-153 °C (EtOAc); IR 3062, 1785, 1598, 1536, 1406, 1240, 762 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ = 1.89-2.09 (m, 4 H, 2 CH_2), 3.08-3.27 (m, 4 H, 2 CH_2), 5.42 (s, 1 H, CH), 7.12-7.21 (m, 2 H, H_{arom}), 7.44 (td, 1 H, *J* = 1.7, *J* = 8.0, H_{arom}), 7.68 (dd, 2 H, *J* = 1.6, *J* = 6.1, H_{arom}), 7.79-7.89 (m, 5 H, H_{arom}), 8.61 (dd, 2 H, *J* = 1.6, *J* = 6.1, H_{arom}), 10.83 (s, 1 H, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 23.8 (2 CH_2), 53.8 (2 CH_2), 68.0 (CH), 94.3 (C_q), 116.3 (CH), 121.6 (2 CH), 122.6 (C_q), 122.9 (CH), 124.8 (CH), 127.4 (2 CH), 128.9 (2 CH), 131.4 (CH), 137.2 (C_q), 140.4 (C_q), 147.0 (C_q), 150.7 (2 CH), 154.2 (C_q), 163.5 (C_q), 173.3 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 398; $[M+H]^+$ found 399; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{25}H_{23}N_2O_3$: 399.1703; found: 399.1697.

3-[(2,2-Difluorobenzo[*d*][1,3]dioxol-5-yl)(pyrrolidin-1-yl)methyl]-4-hydroxycoumarin (1i)

The title compound was prepared from 4-hydroxycoumarin (486 mg, 3 mmol, 1 eq), 2,2-difluorobenzo[*d*][1,3]dioxole-5-carbaldehyde (558 mg, 3 mmol, 1 eq) and pyrrolidine (213 mg, 3 mmol, 1 eq) to give **1i** (859 mg, 71% yield) as a white solid. mp 157-158 °C (EtOAc); IR 3009, 3068, 1650, 1598, 1526, 1239, 1217, 1144, 757 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.80-2.12 (m, 4 H, 2 CH_2), 3.00-3.27 (m, 4 H, 2 CH_2), 5.38 (s, 1 H, CH), 7.12-7.21 (m, 2 H, H_{arom}), 7.39-7.50 (m, 3 H, H_{arom}), 7.81 (d, 1 H, *J* = 1.4, H_{arom}), 7.87 (dd, 1 H, *J* = 1.6, *J* = 7.8, H_{arom}), 10.69 (s, 1 H, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ = 23.2 (2 CH_2), 53.3 (2 CH_2), 67.3 (CH), 93.8 (C_q), 109.3 (CH), 109.9 (CH), 115.9 (CH), 122.1 (C_q), 122.5 (CH), 124.3 (CH), 124.4 (CH), 131.0 (CH), 131.1 (C_q, J_1C-

F_2 = 253.1), 135.8 (C_q), 142.4 (C_q), 142.6 (C_q), 153.7 (C_q), 163.0 (C_q), 172.8 (C_q). ^{19}F NMR (376 MHz, DMSO-d_6) δ = -48.9 (CF_2). MS (ESI, CH_3CN): *m/z* calcd. 401; $[M+H]^+$ found 402; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{21}H_{18}F_2NO_5$: 402.1148; found: 402.1142.

3-{[(4-Phenoxybenzyl)pyrrolidin-1-yl]methyl}-4-hydroxycoumarin (1j)

The title compound was prepared from 4-hydroxycoumarin (500 mg, 3.1 mmol, 1 eq), 4-phenoxybenzaldehyde (614 mg, 3.1 mmol, 1 eq) and pyrrolidine (220 mg, 3.1 mmol, 1 eq) to give **1j** (892 mg, 70% yield) as a beige power. mp 116-117°C (MeOH); IR 3066, 3060, 1645, 1599, 1531, 1330, 760 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.80-2.12 (m, 4 H, 2 CH_2), 3.10-3.27 (m, 4 H, 2 CH_2), 5.33 (s, 1 H, CH), 6.97-7.02 (m, 4 H, H_{arom}), 7.12-7.21 (m, 3 H, H_{arom}), 7.38 (dd, 2 H, *J* = 7.4, *J* = 8.5, H_{arom}), 7.45 (ddd, 1 H, *J* = 1.7 *J* = 7.3 *J* = 8.2, H_{arom}), 7.72 (d, 2 H, *J* = 8.8, H_{arom}), 7.88 (dd, 1 H, *J* = 1.6, *J* = 7.8, H_{arom}), 10.93 (s, 1 H, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ = 23.2 (2 CH_2), 53.2 (2 CH_2), 67.5 (CH), 94.1 (C_q), 115.9 (CH), 118.3 (2 CH), 118.8 (2 CH), 122.2 (C_q), 122.5 (CH), 123.6 (CH), 124.4 (CH), 129.7 (2 CH), 130.0 (2 CH), 130.9 (CH), 134.0 (C_q), 153.71 (C_q), 156.4 (C_q), 156.5 (C_q), 163.03 (C_q), 172.77 (C_q). HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{26}H_{24}FNO_4$: 414.1700; found: 414.1685.

3-{[(4-Benzylphenyl)pyrrolidin-1-yl]methyl}-4-hydroxycoumarin (1k)

The title compound was prepared from 4-hydroxycoumarin (300 mg, 1.85 mmol, 1 eq), 4-benzylbenzaldehyde (363 mg, 1.85 mmol, 1 eq) and pyrrolidine (107 mg, 1.85 mmol, 1 eq) to give **1k** (663 mg, 87%) as a white solid. mp 138-139 °C (MeOH); IR 3399, 3025, 2847, 1666, 1643, 1596, 1551, 1536, 1036, 758 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.85-2.03 (m, 4 H, 2 CH_2), 3.03-321 (m, 4 H, 2 CH_2), 3.89 (s, 2 H, CH_2), 5.27 (s, 1 H, CH), 7.10-7.28 (m, 9 H, H_{arom}), 7.42 (td, 1 H, *J* = 1.6, *J* = 7.3, H_{arom}), 7.60 (d, 2 H, *J* = 8.2, H_{arom}), 7.85 (dd, 1 H, *J* = 1.6, *J* = 7.8, H_{arom}), 9.96 (s, 1 H_{OH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 23.2 (2 CH_2), 40.8 (CH_2), 53.2 (2 CH_2), 67.8 (CH), 94.1 (C_q), 115.8 (CH), 122.2 (C_q), 122.4 (CH), 124.4 (CH), 126.0 (CH), 127.9 (2 CH), 128.4 (2 CH), 128.7 (2 CH), 128.7 (2 CH), 130.8 (CH), 136.6 (C_q), 141.0 (C_q), 141.1 (C_q), 153.7 (C_q), 163.0 (C_q), 172.7 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 411; $[M+H]^+$ found 412; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{27}H_{26}NO_3$: 412.1907; found: 412.1897.

4-Hydroxy-3-[phenyl(pyrrolidin-1-yl)methyl]quinolin-2(1*H*)-one (1l)

The title compound was prepared from 4-hydroxyquinolin-2(1*H*)-one (500 mg, 3.1 mmol), benzaldehyde (320 μl g, 3.1 mmol), and pyrrolidine (260 μl, 3.1 mmol) to give **1l** (1.01 g, 99% yield) as an orange solid. mp 186-187 °C (EtOAc); IR 3508, 3402, 2957, 2854, 1617, 1572, 1523, 1422, 1171, 794 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ = 1.80-1.99 (m, 4 H, 2 CH_2), 2.75-2.99 (m, 4 H, 2 CH_2), 5.13 (s, 1 H, CH), 7.04 (td, 1 H, *J* = 1.2, *J* = 7.5, H_{arom}), 7.13 (d, 1 H, *J* = 7.7, H_{arom}), 7.23-7.38 (m, 4 H, H_{arom}), 7.60 (dd, 2 H, *J* = 1.6, *J* = 8.7, H_{arom}), 7.85 (dd, 1 H, *J* = 1.2, *J* = 7.9, H_{arom}), 10.62 (s, 1 H_{OH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 23.1 (2 CH_2), 52.4 (2 CH_2), 68.1 (CH), 103.8 (C_q), 114.7 (CH), 118.7 (C_q), 120.0 (CH), 123.5 (CH), 127.8 (CH), 128.2 (2 CH), 128.4 (2 CH), 129.7 (CH), 138.9 (C_q), 140.1 (C_q), 162.6 (C_q), 167.6 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 320; $[M+H]^+$ found 321; HRMS-ESI: calcd for $C_{20}H_{21}N_2O_2$: 321.1598; found: 321.1590.

3-[(1,1'-Biphenyl)-4-yl(pyrrolidin-1-yl)methyl]-4-hydroxyquinolin-2(1*H*)-one (1m)

The title compound was prepared from 4-hydroxyquinolin-2(1*H*)-one (500 mg, 3.1 mmol, 1 eq), (1,1'-biphenyl)-4-carbaldehyde (565 mg, 3.1 mmol, 1 eq) and pyrrolidine (220 mg, 3.1 mmol, 1 eq) to give **1m** (1.21 g, 99%) as a white solid. mp 168-170 °C (MeOH); IR 2972, 1619, 1581, 1526, 1427, 756 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.79-1.97 (m, 4 H, 2 CH_2), 2.75-2.98 (m, 4 H, 2 CH_2), 5.22 (s, 1 H, CH), 7.05 (t, 1 H, *J* = 7.6, H_{arom}), 7.16 (d, 1 H, *J* = 8.1, H_{arom}), 7.31-7.39 (m, 2 H, H_{arom}), 7.43 (t, 2 H, *J* = 7.5, H_{arom}), 7.59-7.62 (m, 4 H, H_{arom}), 7.72 (d, 1 H, *J* = 8.2, H_{arom}), 7.90 (dd, 2 H, *J* = 1.1, *J* = 7.9, H_{arom}), 10.74 (s, 1 H_{OH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 23.1 (2 CH_2), 52.5 (2 CH_2), 67.7 (CH), 103.7 (C_q), 114.8 (CH), 118.9 (C_q), 120.1 (CH), 123.5 (CH), 126.6 (2 CH), 126.7 (2 CH), 127.5 (CH), 128.7 (2 CH), 128.9 (2 CH), 129.8 (CH), 138.9 (C_q), 139.3 (C_q), 139.7 (C_q), 139.8 (C_q), 162.7 (C_q), 167.9 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 396; $[M+H]^+$ found 397; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{26}H_{25}N_2O_2$: 397.1911; found: 397.1901.

4-Hydroxy-3-(phenyl(pyrrolidin-1-yl)methyl)-2*H*-thiochromen-2-one (1n)

The title compound was prepared from 4-hydroxythiocoumarin (534 mg, 3 mmol), benzaldehyde (318 g, 3 mmol), and pyrrolidine (213 mg, 3 mmol) to give **1n** (865 mg, 85%) as a white solid. mp 177-178 °C (EtOAc); IR 3057, 1563, 1501, 1459, 1281, 1053, 766 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ = 1.80-2.05 (m, 4 H, 2 CH_2), 2.89-3.30 (m, 4 H, 2 CH_2), 5.59 (s, 1 H, CH), 7.29-7.42 (m, 6 H, H_{arom}), 7.69 (d, 2 H, *J* = 6.9, H_{arom}), 8.23 (d, 1 H, *J* = 7.4, H_{arom}), 11.06 (s, 1 H, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ = 23.3 (2 CH_2), 53.2 (2 CH_2), 67.6 (CH), 107.9 (C_q), 124.8 (CH), 125.0 (CH), 127.4 (CH), 127.8 (2 CH), 127.9 (CH), 128.3 (2 CH), 129.6 (CH), 130.1 (C_q), 135.8 (C_q), 138.8 (C_q), 175.7 (C_q), 176.2 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 337; $[M+H]^+$ found 338; HRMS-ESI: calcd for $C_{20}H_{20}NO_2S$: 338.1209; found: 338.1203.

3-[(1,1'-Biphenyl)-4-yl(pyrrolidin-1-yl)methyl]-4-hydroxythiocoumarin (1o)

The title compound was prepared from 4-hydroxythiocoumarin (356 mg, 2 mmol, 1 eq), (1,1'-biphenyl)-4-carbaldehyde (364 mg, 2 mmol, 1 eq) and pyrrolidine (142 g, 2 mmol, 1 eq) to give **1o** (690 mg, 83%) as a white solid. mp 137-138 °C (EtOAc); IR 3057, 1736, 1570, 1497, 1450, 1286, 1157, 767, 692 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ = 1.85-2.08 (m, 4 H, 2 CH_2), 3.00-3.30 (m, 4 H, 2 CH_2), 5.66 (s, 1 H, CH), 7.29-7.45 (m, 6 H, H_{arom}), 7.60-7.64 (m, 4 H, H_{arom}), 7.79 (d, 2 H, *J* = 8.3, H_{arom}), 8.26 (dd, 1 H, *J* = 1.6, *J* = 8.4, H_{arom}), 11.00 (s, 1 H, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 23.4 (2 CH_2), 53.3 (2 CH_2), 67.2 (CH), 107.9 (C_q), 124.8 (CH), 125.0 (CH), 126.6 (2 CH), 126.7 (2 CH), 127.4 (CH), 127.5 (CH), 128.4 (2 CH), 128.9 (2 CH), 129.7 (CH), 130.1 (C_q), 135.9 (C_q), 137.9 (C_q), 139.7 (C_q), 139.74 (C_q), 175.7 (C_q), 176.2 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 413; $[M+H]^+$ found 414; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{26}H_{24}NO_2S$: 414.1522; found: 414.1522.

Method B: General procedure for the hetereogeneous hydrogenation

A solution of P-*o*-QM (1 eq), Pd/C (5%) on activated carbon (5 mol% Pd), in anhydrous ethanol [0.1 M] was stirred at room temperature under H_2 (1 atm) for 18 h. After filtration (Millipore Durapore filter 0.1 µm) and removal of the solvent, the crude diluted in ethyl acetate (20 mL), was poured into 1M HCl solution (15 mL). After extraction with ethyl acetate (2 x 80 mL), the combined organic layers were washed with brine (10 mL) and dried over $MgSO_4$. After filtration, the solvent was removed by evaporation providing a powder. The product **2** was washed with methanol and filtered on a sintered glass to yield the hydrogenated compound.

3-Benzyl-4-hydroxycoumarin (2a)

The title compound was prepared from compound **1a** (300 mg, 0.93 mmol, 1 eq), providing **2a** (233 mg, 99%) as a white solid; mp 203-204 °C (MeOH); IR 3035, 1650, 1627, 1604, 1494, 1396, 1260, 1178, 1081, 949 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 3.88 (s, 2 H, CH_2), 7.12-7.18 (m, 1 H, H_{arom}), 7.24 (m, 4 H, H_{arom}), 7.36 (m, 2 H, H_{arom}), 7.61 (td, 1 H, *J* = 1.5, *J* = 7.9, H_{arom}), 7.97 (dd, 1 H, *J* = 1.5, *J* = 8.3, H_{arom}), 11.07 (s, 1H, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ = 29.2 (CH_2), 104.1 (C_q), 116.2 (CH), 116.4 (C_q), 123.4 (CH), 123.9 (CH), 125.9 (CH), 128.1 (2 CH), 128.2 (2 CH), 131.9 (CH), 139.9 (C_q), 152.0 (C_q), 160.7 (C_q), 162.9 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 252; $[M+H]^+$ found 253; HRMS-ESI: calcd for $C_{16}H_{12}NaO_3$: 275.0679; found: 275.0684.

3-([1,1'-Biphenyl]-4-ylmethyl)-4-hydroxycoumarin (2b)

The title compound was prepared from compound **1b** (397 mg, 1 mmol, 1 eq), providing **2b** (244 mg, 74%) as a white solid; mp 221-222 °C (MeOH); IR 3235, 3042, 1666, 1629, 1497, 1392, 1195, 1163, 1109, 1063, 962, 940, 751, 695 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) □ = 3.93 (s, 2 H, CH_2), 7.32-7.46 (m, 7 H, H_{arom}), 7.53-7.62 (m, 5 H, H_{arom}), 7.99 (dd, 1 H, *J* = 1.3, *J* = 7.7, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 28.8 (CH_2), 104.1 (C_q), 116.2 (CH), 116.3 (C_q), 123.4 (CH), 123.9 (CH), 126.5 (2 CH), 126.6 (2 CH), 127.2 (CH), 128.7 (2 CH), 128.9 (2 CH), 131.9 (CH), 137.9 (C_q), 139.1 (C_q), 140.1 (C_q), 152.0 (C_q), 160.6 (C_q), 162.9 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 328; $[M+H]^+$ found 329; HRMS-ESI: *m/z* $[M+Na]^+$ calcd for $C_{22}H_{16}NaO_3$: 351.0992; found: 351.0984.

4-Hydroxy-3-(4-methoxybenzyl)-coumarin (2c)

The title compound was prepared from compound **1c** (300 mg, 0.85 mmol, 1 eq), providing **2c** (251 mg, 99%) as a white solid; mp 184-185 °C (MeOH); IR 3070, 2989, 2955, 1677, 1651, 1621, 1608, 1508, 1430, 1393, 1244, 1220, 1164, 1075, 962, 791, 760 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.69 (s, 3 H, OCH_3), 3.81 (s, 2 H, CH_2), 6.80 (d, 2 H, *J* = 8.6, H_{arom}), 7.16 (d, 2 H, *J* = 8.6, H_{arom}), 7.36 (m, 2 H, H_{arom}), 7.61 (td, 1 H, *J* = 1.5, *J* = 7.8, H_{arom}), 7.97 (dd, 1 H, *J* = 1.5, *J* = 8.0, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 28.2 (CH_2), 55.0 (CH_3), 104.7 (C_q), 113.6 (2 CH), 116.2 (CH), 116.3 (C_q), 123.3 (CH), 123.9 (CH), 129.1 (2 CH), 131.7 (C_q), 131.8 (CH), 151.9 (C_q), 157.5 (C_q), 160.2 (C_q), 162.8 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 282; $[M+H]^+$ found 283; HRMS-ESI: *m/z* $[M+Na]^+$ calcd for $C_{17}H_{14}NaO_4$: 305.0784; found: 305.0779.

4-Hydroxy-3-(4- trifluoromethoxy)-coumarin (2d)

The title compound was prepared from 4-hydroxy-3-{pyrrolidin-1-yl[4-(trifluoromethoxy)phenyl]methyl}-coumarin (**1d**) (405 mg, 1 mmol, 1 eq) to give **2d** (240 mg, 71%) as a white solid. mp 221-222 °C (MeOH); IR 3195, 1660, 1628, 1506, 1395, 1262, 1147, 752 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.90 (s, 2 H, CH_2), 7.24 (d, 2 H, *J* = 7.9, H_{arom}), 7.34-7.38 (m, 4 H, H_{arom}), 7.62 (td, 1 H, *J* = 1.5, *J* = 7.9, H_{arom}), 7.98 (dd, 1 H, *J* = 1.5, *J* = 8.3, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 28.5 (CH_2), 103.7 (C_q), 116.2 (C_q), 116.3 (CH), 120.0 (C_q, J_1C-F_3 = 256.0), 120.9 (2 CH), 123.4 (CH), 124.0 (CH), 129.8 (2 CH), 132.0 (CH), 139.4 (C_q), 146.6 (C_q), 152.1 (C_q), 160.8 (C_q), 162.8 (C_q). ^{19}F NMR (282 MHz, DMSO-d_6) = -56.8. MS (ESI, CH_3CN): *m/z* calcd. 336; $[M+H]^+$ found 337; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{17}H_{11}F_3NaO_4$: 359.0502; found: 359.0502.

4-Hydroxy-3-[4-(pyridin-4-yl)benzyl]-coumarin (2e)

The title compound was prepared from compound **1h** (397 mg, 1 mmol, 1 eq), providing **2e** (230 mg, 69%) as a white solid; mp 289-290 °C (MeOH); IR 3345, 2991, 2729, 1677, 1630, 1604, 1489, 1384, 1239, 1049 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 4.02 (s, 2 H, CH_2), 7.35-7.39 (m, 2 H, H_{arom}), 7.49 (d, 2 H, *J* = 8.4, H_{arom}), 7.62 (td, 1 H, *J* = 1.7, *J* = 7.8, H_{arom}), 7.93 (d, 2 H, *J* = 8.4, H_{arom}), 8.08 (dd, 1 H, *J* = 1.7, *J* = 8.0, H_{arom}), 8.32 (d, 2 H, *J* = 6.8, H_{arom}), 8.90 (d, 2 H, *J* = 6.8,

H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 29.2 (CH_2), 103.6 (C_q), 116.2 (C_q), 116.3 (CH), 123.4 (2 CH), 123.7 (CH), 124.0 (CH), 127.9 (2 CH), 129.4 (2 CH), 132.0 (CH, C_q), 142.3 (2 CH), 144.3 (C_q), 152.1 (C_q), 155.1 (C_q), 161.0 (C_q), 162.9 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 329; $[M+H]^+$ found 330; HRMS-ESI: *m/z* $[M+H]^+$ calcd. for $C_{21}H_{16}NO_3$: 330.1125; found: 330.1136.

4-Hydroxy-3-[(2,2-difluorobenzo[*d*][1,3]dioxol-5-yl)methyl]-coumarin (2f)

The title compound was prepared from 3-[(2,2-difluorobenzo[*d*][1,3]dioxol-5-yl)(pyrrolidin-1-yl)methyl]-4-hydroxycoumarin (**1i**) (401 mg, 1 mmol, 1 eq) to give **2f** (236 mg, 71%) as a white solid. mp 219-220 °C (MeOH); IR 3189, 1663, 1630, 1491, 1396, 1229, 1140, 1113, 751 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ = 3.89 (s, 2 H, CH_2), 7.08 (dd, 1 H, *J* = 1.5, *J* = 8.3, H_{arom}), 7.25-7.27 (m, 2 H, H_{arom}), 7.34-7.38 (m, 2 H, H_{arom}),7.61 (td, 1 H, *J* = 1.4, *J* = 7.9, H_{arom}), 7.98 (dd, 1 H, *J* = 1.4, *J* = 7.0, H_{arom}), 11.75 (s, 1 H_{OH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 28.9 (CH_2), 103.8 (C_q), 109.7 (CH), 109.9 (CH), 116.2 (C_q), 116.3 (CH), 123.4 (CH), 123.8 (CH), 123.9 (CH), 131.2 (C_q, J_1C-F_2 = 251), 132.0 (CH), 136.9 (C_q), 141.0 (C_q), 142.7 (C_q), 152.1 (C_q), 160.8 (C_q), 162.8 (C_q). ^{19}F NMR (282 MHz, DMSO-d_6) δ = -49.2. MS (ESI, CH_3CN): *m/z* calcd. 332; $[M+Na]^+$ found 355; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{17}H_{10}F_2NaO_5$: 355.0389; found: 355.0386.

4-Hydroxy-3-(4-phenoxybenzyl)-coumarin (2g)

The title compound was prepared from 3-{[4-(4-bromophenoxy)phenyl][pyrrolidin-1-yl]methyl}-4-hydroxycoumarin (**1j**) (393 mg, 1 mmol, 1 eq) to give **2g** (186 mg, 66%) as a white solid. mp 170-171 °C (MeOH); IR 3073, 1650, 1621, 1486, 1391, 1229, 1190, 1165, 752 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ = 3.87 (s, 2 H, CH_2), 6.90-6.95 (m, 4 H, H_{arom}), 7.08 (t, 1 H, *J* = 7.3, H_{arom}), 7.25-7.38 (m, 6 H, H_{arom}), 7.61 (td, 1 H, *J* = 1.0, *J* = 7.8, H_{arom}), 7.98 (dd, 1 H, *J* = 1.0, *J* = 8.1, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 28.4 (CH_2), 104.3 (C_q), 116.2 (C_q, CH), 118.1 (2 CH), 118.8 (2 CH), 123.1 (CH), 123.4 (CH), 123.9 (CH), 129.7 (2 CH), 130.0 (2 CH), 131.9 (CH), 135.0 (C_q), 152.0 (C_q), 154.6 (C_q), 157.1 (C_q), 160.5 (C_q), 162.9 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 344; $[M+H]^+$ found 345; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{22}H_{16}NaO_4$: 367.0941; found: 367.0952.

3-(4-Benzylbenzyl)-4-hydroxycoumarin (2h)

The title compound was prepared from 3-{[(4-benzylphenyl)pyrrolidin-1-yl]methyl}-4-hydroxycoumarin (**1k**) (411 mg, 1 mmol, 1 eq) to give **2h** (113 mg, 92%) as a white solid. mp 196-197 °C (MeOH); IR 3178, 2933, 1670, 1629, 1611, 1496, 1396, 1171, 946 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.84 (s, 2 H, CH_2), 3.86 (s, 2 H, CH_2), 7.09-7.18 (m, 7 H, H_{arom}), 7.22-7.26 (m, 2 H, H_{arom}), 7.33-7.37 (m, 2 H, H_{arom}), 7.60 (td, 1 H, *J* = 1.5, *J* = 7.8, H_{arom}), 7.97 (dd, 1 H, *J* = 1.5, *J* = 8.6, H_{arom}), 11.64 (s, 1 H_{OH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 28.7 (CH_2), 40.7 (CH_2), 104.3 (C_q), 116.2 (CH), 116.2 (C_q), 123.4 (CH), 123.9 (CH), 125.9 (CH), 128.2 (2 CH), 128.4 (2 CH), 128.6 (2 CH), 128.6 (2 CH), 131.9 (CH), 137.4 (C_q), 138.8 (C_q), 141.4 (C_q), 152.0 (C_q), 160.4 (C_q), 162.8 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 342; $[M+H]^+$ found 343; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{23}H_{18}NaO_3$: 365.1148; found: 365.1139.

3-Benzylquinoline-2,4-diol (2i)

The title compound was prepared from compound **1l** (1 g, 3.12 mmol, 1 eq), providing **2i** (674 mg, 88%) as a white solid. mp 186-187 °C (MeOH); IR 3148, 1631, 1603, 1556, 1496, 1194, 1099, 781 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.93 (s, 2 H, CH_2), 7.09-7.28 (m, 7 H, H_{arom}), 7.45 (td, 1 H, *J* = 1.2, *J* = 7.6, H_{arom}), 7.93 (dd, 1 H, *J* = 1.2, *J* = 8.1, H_{arom}), 11.4 (s, 1 H_{OH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 28.6 (CH_2), 110.8 (C_q), 115.0 (CH), 115.3 (C_q), 121.1 (CH), 122.8 (CH), 125.5 (CH), 128.0 (2 CH), 128.3 (2 CH), 130.0 (CH), 137.6 (C_q), 140.9 (C_q), 157.7 (C_q), 163.5 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 251; $[M+H]^+$ found 252; HRMS-ESI: calcd. for $C_{16}H_{14}NO_2$: 252.1019; found: 252.1016.

3-[(1,1'-Biphenyl)-4-ylmethyl]-4-hydroxyquinolin-2(1*H*)-one (2j)

The title compound was prepared from 3-[(1,1'-biphenyl)-4-yl(pyrrolidin-1-yl)methyl]-4-hydroxyquinolin-2(1*H*)-one (**1m**) (400 mg, 1.01 mmol, 1 eq) to give **2j** (207 mg, 63%) as a white solid. mp 275-277 °C (MeOH); IR 2989, 1631, 1600, 1558, 1485, 1337, 1271, 754 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.98 (s, 2 H, CH_2), 7.16 (t, 1 H, *J* = 7.8, H_{arom}), 7.28-7.35 (m, 4 H, H_{arom}), 7.40-7.53 (m, 5 H, H_{arom}), 7.58-7.59 (m, 2 H, H_{arom}), 7.94 (d, 1 H, *J* = 7.7, H_{arom}), 10.4 and 11.4 (2 s, $H_{OH,}$ H_{NH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 28.2 (CH_2), 110.8 (C_q), 115.0 (CH), 115.3 (C_q),

121.1 (CH), 122.8 (CH), 126.4 (2 CH), 126.5 (2 CH), 127.1 (CH), 128.8 (2 CH), 128.9 (2 CH), 130.1 (CH), 137.6 (C_q), 137.7 (C_q), 140.2 (C_q), 140.3 (C_q), 157.7 (C_q), 163.5 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 327; $[M+H]^+$ found 328; HRMS-ESI: *m/z* $[M+H]^+$ calcd. for $C_{22}H_{18}NO_2$: 328.1332; found: 328.1327.

3-[(1,1'-Biphenyl)-4-ylmethyl]-4-hydroxythiocoumarin (2k)

The title compound was prepared from 3-[(1,1'-biphenyl)-4-yl(pyrrolidin-1-yl)methyl]-4-hydroxythiocoumarin (**1o**) (590 mg, 1.43 mmol, 1 eq) to give **2k** (after flash chromatography) (116 mg, 23%) as a white solid. mp 186-187 °C (MeOH); IR 3294, 3028, 2921, 1592, 1563, 1544, 1364, 1180, 756 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ = 4.06 (s, 2 H, CH_2), 7.28-7.33 (m, 3 H, H_{arom}), 7.42 (t, 2 H, *J* = 7.5, H_{arom}), 7.48-7.54 (m, 3 H, H_{arom}), 7.57-7.62 (m, 4 H, H_{arom}), 8.26 (d, 1 H, *J* = 7.9, H_{arom}), 11.33 (s, 1 H_{OH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 28.6 (CH_2), 116.5 (C_q), 124.1 (C_q), 125.5 (CH), 126.5 (3 CH), 126.6 (2 CH), 127.2 (CH), 128.7 (2 CH), 128.9 (3 CH), 130.4 (CH), 134.5 (C_q), 137.9 (C_q), 139.1 (C_q), 140.1 (C_q), 162.2 (C_q), 180.0 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 353; $[M+H]^+$ found 354; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{22}H_{17}O_2S$: 345.0944; found: 345.0937; *m/z* $[M+Na]^+$ calcd for $C_{22}H_{16}NaO_2S$: 367.0763; found: 367.0749.

Procedure C: Nucleophilic attack on *o*-QM

A solution of *o*-QM (1 eq) and a nucleophile (1 eq), in acetonitrile [0.25 M] was stirred at 50 °C under argon until complete conversion. After removal of the solvent by evaporation, the crude was diluted in dichloromethane (20 mL), poured into 1M HCl solution (30 mL) and then extracted with dichloromethane (3 x 80 mL). The combined organic layers were then washed with brine (10 mL), dried over $MgSO_4$. After filtration and evaporation a powder is obtained. The product was washed with methanol and filtered on a sintered glass to yield desired compound.

4-Hydroxy-3-[(4-hydroxy-2-oxo-2*H*-thiochromen-3-yl)(phenyl)methyl]-coumarin (3a)

The title compound was prepared from 4-hydroxy-3-[phenyl(pyrrolidin-1-yl)methyl]-coumarin (**1a**) (160 mg, 0.5 mmol, 1 eq) and 4-hydroxythiocoumarin (89 mg, 0.5 mmol, 1 eq) to give after 45 min **3a** (208 mg, 97%) as a white solid. mp 212-213 °C (MeOH); IR 2896, 2593, 1653, 1603, 1515, 1278, 1097, 778 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ = 6.54 (s, 1 H, CH), 7.08-7.14 (m, 3 H, H_{arom}), 7.16-7.22 (m, 2 H, H_{arom}), 7.30-7.43 (m, 3 H, H_{arom}), 7.51-7.56 (m, 2 H, H_{arom}), 7.60 (td, 1 H, *J* = 1.6, *J* = 7.8, H_{arom}), 7.91 (dd, 1 H, *J* = 1.6, *J* = 7.9, H_{arom}), 7.91 (d, 1 H, *J* = 8.2, H_{arom}), 8.47 (s, 2 H_{OH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 35.6 (CH), 103.2 (C_q), 115.9 (CH), 116.8 (C_q), 117.9 (C_q), 123.7 (CH), 123.9 (CH), 124.9 (CH), 125.9 (CH), 126.1 (CH), 126.5 (2 CH), 126.8 (C_q), 127.2 (CH), 128.0 (2 CH), 130.2 (CH), 131.9 (CH), 134.7 (C_q), 140.5 (C_q), 152.2 (C_q), 165.1 (C_q), 165.7 (C_q), 168.6 (C_q), 182.9 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 428; $[M+Na]^+$ found 451; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{25}H_{16}NaO_5S$: 451.0611; found: 451.0605.

3-[(1,1'-Biphenyl)-4-yl(4-hydroxythiocoumanin-3-yl)methyl)-4-hydroxycoumarin (3b)

The title compound was prepared from 3-[(1,1'-biphenyl)-4-yl(pyrrolidin-1-yl)methyl]-4-hydroxycoumarin **1b** (198 mg, 0.5 mmol, 1 eq) and 4-hydroxythiocoumarin (89 mg, 0.5 mmol, 1 eq) to give after 3 h **3b** (228 mg, 90%) as a white solid. mp 205-206 °C (MeOH); IR 3026, 2597, 2360, 1652, 1608, 1562, 1519, 1487, 1280, 752 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ = 6.59 (s, 1 H, CH), 7.19 (d, 2 H, *J* = 7.6, H_{arom}), 7.25-7.48 (m, 6 H, H_{arom}), 7.49-7.58 (m, 4 H, H_{arom}), 7.59-7.65 (m, 3 H, H_{arom}), 7.93 (dd, 1 H, *J* = 1.5, *J* = 7.8, H_{arom}), 8.20 (d, 1 H, *J* = 8.1, H_{arom}), 11.17 (s, 2 H_{OH}).

^{13}C NMR (125 MHz, DMSO-d_6) δ = 35.4 (CH), 103.2 (C_q), 116.0 (CH), 116.8 (C_q), 117.9 (C_q), 123.8 (CH), 124.0 (CH), 124.9 (CH), 126.1 (CH), 126.3 (CH), 126.4 (3 CH), 126.8 (C_q), 127.0 (CH), 127.2 (2 CH), 128.8 (3 CH), 130.3 (CH), 131.9 (CH), 134.8 (C_q), 137.3 (C_q), 139.9 (C_q), 140.1 (C_q), 152.2 (C_q), 165.1 (C_q), 165.7 (C_q), 168.6 (C_q), 182.9 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 504; $[M+H]^+$ found 505; HRMS-ESI: *m/z* $[M+H]^+$ calcd. for $C_{31}H_{21}O_5S$: 505.1104; found: 505.1103.

4-Hydroxy-3-[(4-hydroxy-thiocoumarin-3-yl)(4- methoxyphenyl)methyl]-coumarin (3c)

The title compound was prepared from 4-hydroxy-3-{[(4-methoxyphenyl)pyrrolidin-1-yl]methyl}-coumarin **1c** (175 mg, 0.5 mmol, 1 eq) and 4-hydroxythiocoumarin (89 mg, 0.5 mmol, 1 eq) to give after 3 h **3c** (206 mg, 89%) as a white solid. mp 257-258 °C (MeOH); IR 2832, 2586, 1737, 1650, 1606, 1563, 1509, 1354, 756 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ =3.69 (s, 3 H, CH_3), 6.46 (s, 1 H, CH), 6.78 (d, 2 H, *J* = 8.8 H_{arom}), 7.00 (d, 2 H, *J* = 8.8 H_{arom}), 7.28-7.49 (m, 3 H, H_{arom}), 7.50-7.55 (m, 2 H, H_{arom}), 7.60 (td, 1 H, *J* = 1.5, *J* = 7.7, H_{arom}), 7.91 (dd, 1 H, *J* = 1.5, *J* = 7.9, H_{arom}), 8.18 (d, 1 H, *J* = 8.1, H_{arom}), 10.69 (s, 2 H_{OH}). ^{13}C NMR (75 MHz, DMSO-d_6) δ = 34.9 (CH), 54.9 (CH_3), 103.6 (C_q), 113.4 (2 CH), 116.0 (CH), 117.0 (C_q), 117.8 (C_q), 123.8 (CH), 123.9 (CH), 124.9 (CH), 126.1 (CH), 126.7 (C_q), 127.1 (CH), 127.6 (2 CH), 130.2 (CH), 131.8 (C_q), 131.9 (CH), 134.7 (C_q), 152.2 (C_q), 157.2 (C_q), 165.1 (C_q), 165.5 (C_q), 168.2 (C_q), 183.1 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 458; $[M+H]^+$ found 459; HRMS-ESI: *m/z* $[M+H]^+$ calcd. for $C_{26}H_{19}O_6S$: 459.0897; found: 459.0892.

3-[(4-Bromophenyl)-(4-hydroxythiocoumarin-3-yl)methyl)-4-hydroxycoumarin (3d)

The title compound was prepared from 3-{[(4-bromophenyl)pyrrolidin-1-yl]methyl}-4-hydroxycoumarin **1e** (200 mg, 0.5 mmol, 1 eq) and 4-hydroxythiocoumarin (89 mg, 0.5 mmol, 1 eq) to give after 3 h **3d** (239 mg, 94%) as a white solid. mp 282-283 °C (MeOH); IR 2904, 2595, 1648, 1606, 1561, 1522, 1485, 1283, 745 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 6.49 (s, 1 H, CH), 7.04 (d, 2 H, *J* = 7.0, H_{arom}), 7.28-7.42 (m, 5 H, H_{arom}), 7.38-7.55 (m, 2 H, H_{arom}), 7.57 (td, 1 H, *J* = 1.5, *J* = 7.6, H_{arom}), 7.88 (dd, 1 H, *J* = 1.5, *J* = 7.8, H_{arom}), 8.17 (d, 1 H, *J* = 8.4, H_{arom}), 11.76 (s, 2 H_{OH}). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 35.2 (CH), 102.7 (C_q), 115.8 (CH), 116.5 (C_q), 118.1 (C_q), 118.2 (C_q), 123.6 (CH), 124.0 (CH), 124.7 (CH), 125.9 (CH), 127.2 (CH), 127.3 (C_q), 128.9 (2 CH),

130.1 (CH), 130.7 (2 CH), 131.7 (CH), 134.8 (C_q), 140.8 (C_q), 152.3 (C_q), 164.7 (C_q), 166.1 (C_q), 169.3 (C_q), 182.2 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 507; $[M+H]^+$ found 508; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{25}H_{15}BrNaO_5S$: 528.9716; found: 5289726.

4-[(4-Hydroxycoumarin-3-yl)(4-hydroxy-thiocoumarin-3-yl)methyl]benzonitrile (3e)

The title compound was prepared from 4-{[(4-hydroxy-2-oxo-*2H*-chromen-3-yl)pyrrolidin-1-yl]methyl}benzonitrile **1f** (173 mg, 0.5 mmol, 1 eq) and 4-hydroxythiocoumarin (89 mg, 0.5 mmol, 1 eq) to give after 3 h **3e** (208 mg, 92%) as a white solid. mp 247-248 °C (MeOH); IR 2901, 2559, 2226, 1651, 1606, 1558, 1510, 1329, 755 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ = 6.58 (s, 1 H, CH), 7.22-7.40 (m, 5 H, H_{arom}), 7.45-7.52 (m, 2 H, H_{arom}), 7.57 (td, 1 H, *J* = 1.4, *J* = 7.8, H_{arom}), 7.87 (dd, 1 H, *J* = 1.4, *J* = 7.9, H_{arom}), 8.15 (d, 1 H, *J* = 7.8, H_{arom}), 11.88 (s, 2 H_{OH}). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 36.0 (CH), 102.2 (C_q), 107.8 (C_q), 115.8 (CH), 116.2 (C_q), 118.4 (C_q), 119.2 (C_q), 123.5 (CH), 124.0 (CH), 124.7 (CH), 125.8 (CH), 127.3 (CH), 127.6 (2 CH, C_q), 130.1 (CH), 131.7 (CH), 131.8 (2 CH), 134.9 (C_q), 148.4 (C_q), 152.3 (C_q), 164.4 (C_q), 166.4 (C_q), 170.1 (C_q), 181.7 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 453; $[M+H]^+$ found 454; HRMS-ESI: *m/z* $[M+H]^+$ calcd. for $C_{26}H_{16}NO_5S$: 454.0744; found: 454.0739.

4-Hydroxy-3-[(4-hydroxy-thiocoumarin-3-yl)(4-nitrophenyl)methyl]-coumarin (3f)

The title compound was prepared from 4-hydroxy-3-{[(4-nitrophenyl)pyrrolidin-1-yl]methyl}-coumarin **1g** (183 mg, 0.5 mmol, 1 eq) and 4-hydroxythiocoumarin (89 mg, 0.5 mmol, 1 eq) to give after 3 h **3f** (223 mg, 94%) as a white solid. mp 257-258 °C (MeOH); IR 2899, 2577, 1645, 1604, 1560, 1516, 1346, 761 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ = 6.62 (s, 1 H, CH), 7.25-7.40 (m, 5 H, H_{arom}), 7.45-7.52 (m, 2 H, H_{arom}), 7.57 (td, 1 H, *J* = 1.5, *J* = 7.5, H_{arom}), 7.87 (dd, 1 H, *J* = 1.5, *J* = 7.8, H_{arom}), 8.07 (d, 2 H, *J* = 8.8, H_{arom}), 8.15 (d, 1 H, *J* = 7.8, H_{arom}), 11.57 (s, 2 H_{OH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 36.1 (CH), 102.3 (C_q), 115.8 (CH), 116.3 (C_q), 118.4 (C_q), 123.2 (2 CH), 123.5 (CH), 124.1 (CH), 124.8 (CH), 125.8 (CH), 127.4 (CH), 127.8 (2 CH), 127.8 (C_q), 130.1 (CH), 131.7 (CH), 134.9 (C_q), 145.3 (C_q), 151.2 (C_q), 152.4 (C_q), 164.4 (C_q), 166.5 (C_q), 170.4 (C_q), 181.6 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 473; $[M+H]^+$ found 474; HRMS-ESI: *m/z* $[M+H]^+$ calcd. for $C_{25}H_{16}NO_7S$: 474.0642; found: 474.0630.

3,3'-(Phenylmethylene)bis(4-hydroxycoumarin) (DIM)

The title compound was prepared from 4-hydroxy-3-[phenyl(pyrrolidin-1-yl)methyl]-coumarin (**1a**) (160 mg, 0.5 mmol, 1 eq) and 4-hydroxycoumarin (81 mg, 0.5 mmol, 1 eq) to give after 45 min **DIM** (200 mg, 98%) as a white crystalline solid. mp 231-232 °C (MeOH); IR 3068, 1652, 1602, 725 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 6.36 (s, 1 H, CH), 7.12-7.16 (m, 3 H, H_{arom}), 7.20-7.24 (m, 2 H, H_{arom}), 7.30-7.37 (m, 4 H, H_{arom}), 7.59 (td, 2 H, *J* = 1.5, *J* = 7.8, H_{arom}), 7.90 (dd, 2 H, *J* = 1.5, *J* = 8.0, H_{arom}), 9.62 (s, 2 H_{OH}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 35.9 (CH), 104.1 (2 C_q), 115.9 (2 CH), 118.1 (2 C_q), 123.7 (2 CH), 123.9 (2 CH), 125.5 (CH), 126.7 (2 CH), 128.0 (2 CH), 131.8 (2 CH), 140.1 (C_q), 152.2 (2 C_q), 164.8 (2 C_q), 165.5 (2 C_q). MS (ESI, CH_3CN): *m/z* calcd. 412; $[M+Na]^+$ found 435; HRMS-ESI: *m/z* $[M+Na]^+$ calcd for $C_{25}H_{16}NaO_6$: 435.0839; found: 435.0820.

2-Amino-5-oxo-4-phenyl-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (4a)

The title compound was prepared from 4-hydroxy-3-[phenyl(pyrrolidin-1-yl)methyl]-coumarin (**1a**) (160 mg, 0.5 mmol, 1 eq) and malononitrile (33 mg, 0.5 mmol, 1 eq), to give after 45 min **4a** (155 mg, 98% yield) as a white solid. mp 257-258 °C (MeOH); IR 3369, 3284, 3256, 3177, 2197, 1705, 1672, 1602, 1491, 1377, 1056, 705 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 4.45 (s, 1 H, CH), 7.21-7.33 (m, 5 H, H_{arom}), 7.41-7.50 (m, 4 H, H_{arom}, H_{NH2}), 7.70 (td, 1 H, *J* = 1.5, *J* = 7.8, H_{arom}), 7.90 (dd, 1 H, *J* = 1.5, *J* = 8.1, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 37.0 (CH), 58.0 (C_q), 104.0 (C_q), 113.0 (C_q), 116.6 (CH), 119.2 (C_q), 122.5 (CH), 124.7 (CH), 127.1 (CH), 127.6 (2 CH), 128.5 (2 CH), 132.9 (CH), 143.3 (C_q), 152.1 (C_q), 153.4 (C_q), 158.0 (C_q), 159.5 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 316; $[M+Na]^+$ found 339; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{19}H_{12}N_2NaO_3$: 339.0740; found: 339.0740.

4-[(1,1'-Biphenyl)-4-yl]-2-amino-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (4b)

The title compound was prepared from 3-[(1,1'-biphenyl)-4-yl(pyrrolidin-1-yl)methyl]-4-hydroxycoumarin (**1b**) (198 mg, 0.5 mmol, 1 eq) and malononitrile (33 mg, 0.5 mmol, 1 eq), to give after 3 h compound **4b** (128 mg, 65% yield) as a white solid. mp 235-236 °C (MeOH); IR 3405, 3320, 3185, 2192, 1705, 1670, 1604, 1380, 1057, 756 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ = 4.51 (s, 1 H, CH), 7.30-7.39 (m, 3 H, H_{arom}), 7.40-7.52 (m, 6 H, H_{arom}, H_{NH2}),7.55-7.68 (m, 4 H,

H_{arom}), 7.71 (td, 1 H, *J* = 1.1, *J* = 7.8, H_{arom}), 7.89 (dd, 1 H, *J* = 1.1, *J* = 7.9, H_{arom}). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 36.6 (CH), 57.8 (C_q), 103.9 (C_q), 113.0 (C_q), 116.6 (CH), 119.2 (C_q), 122.5 (CH), 124.7 (CH), 126.6 (2 CH), 126.9 (2 CH), 127.4 (CH), 128.2 (2 CH), 128.9 (2 CH), 132.9 (CH), 139.1 (C_q), 139.8 (C_q), 142.5 (C_q), 152.1 (C_q), 153.4 (C_q), 158.0 (C_q), 159.6 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 392; $[M+H]^+$ found 393; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{25}H_{16}N_2NaO_3$: 415.1053; found: 415.1039.

2-Amino-4-(4-methoxyphenyl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (4c)

The title compound was prepared from 4-hydroxy-3-{[(4-methoxyphenyl)pyrrolidin-1-yl]methyl}-coumarin (**1c**) (176 mg, 0.5 mmol, 1 eq) and malononitrile (33 mg, 0.5 mmol, 1 eq), to give after 3 h compound **4c** (138 mg, 80% yield) as a white solid. mp 239-240 °C (MeOH); IR 3366, 3252, 3187, 2207, 1705, 1670, 1606, 1510, 1379, 1051, 750 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ = 3.71 (s, 3 H, CH_3), 4.39 (s, 1 H, CH), 6.86 (d, 2 H, *J* = 8.7, H_{arom}), 7.17 (d, 2 H, *J* = 8.7, H_{arom}), 7.37 (s, 2 H, H_{NH2}), 7.41-7.52 (m, 2 H, H_{arom}), 7.70 (td, 1 H, *J* = 1.5, *J* = 7.8, H_{arom}), 7.89 (dd, 1 H, *J* = 1.5, *J* = 7.8, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 36.2 (CH), 55.0 (CH_3), 58.2 (C_q), 104.3 (C_q), 113.0 (C_q), 113.9 (2 CH), 116.6 (CH), 119.3 (C_q), 122.4 (CH), 124.7 (CH), 128.8 (2 CH), 132.9 (CH), 135.4 (C_q), 152.1 (C_q), 153.1 (C_q), 157.9 (C_q), 158.3 (C_q), 159.5 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 346; $[M+Na]^+$ found 369; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{20}H_{14}N_2NaO_4$: 369.0846; found: 369.0829.

2-Amino-5-oxo-4-(4-(trifluoromethoxy)phenyl)-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (4d)

The title compound was prepared from 4-hydroxy-3-{pyrrolidin-1-yl[4-(trifluoromethoxy)phenyl]methyl}-coumarin **1d** (202 mg, 0.5 mmol, 1 eq) and malononitrile (33 mg, 0.5 mmol, 1 eq), to give after 3 h compound **4d** (128 mg, 64% yield) as a white solid. mp 232-233 °C (MeOH); IR 3403, 3323, 3196, 2198, 1709, 1672, 1639, 1607, 1380, 1250, 1168, 768 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ = 4.54 (s, 1 H, CH), 7.30 (d, 2 H, *J* = 8.1, H_{arom}), 7.38-7.52 (m, 6 H, H_{arom}, H_{NH2}), 7.71 (td, 1 H, *J* = 1.4, *J* = 7.8, H_{arom}), 7.90 (dd, 1 H, *J* = 1.4, *J* = 7.9, H_{arom}). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 36.4 (CH), 57.5 (C_q), 103.5 (C_q), 112.9 (C_q), 116.6 (CH), 119.1 (C_q),

120.1 (C_q, J_1C-F_3 = 256), 121.0 (2 CH), 122.5 (CH), 124.7 (CH), 129.6 (2 CH), 133.0 (CH), 142.6 (C_q), 147.3 (C_q), 152.2 (C_q), 153.6 (C_q), 158.0 (C_q), 159.5 (C_q). ^{19}F NMR (282 MHz, DMSO-d_6) δ = -56.8. MS (ESI, CH_3CN): *m/z* calcd. 400; $[M+H]^+$ found 401; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{20}H_{11}F_3N_2NaO_4$: 423.0563; found: 423.0554.

2-Amino-4-(4-bromophenyl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (4e)

The title compound was prepared from 3-{[(4-bromophenyl)pyrrolidin-1-yl]methyl}-4-hydroxycoumarin (**1e**) (200 mg, 0.5 mmol, 1 eq) and malononitrile (33 mg, 0.5 mmol, 1 eq), to give after 3 h compound **4e** (137 mg, 69% yield) as a light yellow solid. mp 255-256 °C (MeOH); IR 3381, 3312, 3189, 2193, 1706, 1670, 1605, 1376, 1053, 758 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 4.47 (s, 1 H, CH), 7.24 (d, 2 H, *J* = 8.4, H_{arom}), 7.42-7.58 (m, 6 H, H_{arom}, H_{NH2}), 7.71 (td, 1 H, *J* = 1.2, *J* = 7.9, H_{arom}), 7.89 (dd, 1 H, *J* = 1.2, *J* = 7.8, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 36.5 (CH), 57.4 (C_q), 103.4 (C_q), 112.9 (C_q), 116.6 (CH), 119.1 (C_q), 120.2 (C_q), 122.5 (CH), 124.7 (CH), 130.0 (2 CH), 131.4 (2 CH), 133.0 (CH), 142.8 (C_q), 152.2 (C_q), 153.6 (C_q), 157.9 (C_q), 159.6 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 394; $[M+H]^+$ found 395; HRMS-ESI: *m/z* $[M+H]^+$ calcd. for $C_{19}H_{12}BrN_2O_3$: 395.0026; found: 395.0019.

2-Amino-4-(4-cyanophenyl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (4f)

The title compound was prepared from 4-{[(4-hydroxy-2-oxo-2H-chromen-3-yl)pyrrolidin-1-yl]methyl}benzonitrile **1f** (173 mg, 0.5 mmol, 1 eq) and malononitrile (33 mg, 0.5 mmol, 1 eq), to give after 3 h compound **4f** (128 mg, 75% yield) as a white solid. mp 288-289 °C (MeOH); IR 3432, 3319, 3194, 3061, 2234, 2196, 1715, 1674, 1597, 1369, 1054, 761 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 4.59 (s, 1 H, CH), 7.41-7.57 (m, 6 H, H_{arom}, H_{NH2}), 7.72 (td, 1 H, *J* = 1.4, *J* = 7.8, H_{arom}), 7.78 (d, 2 H, *J* = 8.3, H_{arom}), 7.89 (dd, 1 H, *J* = 1.4, *J* = 7.9, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 37.0 (CH), 56.9 (C_q), 102.9 (C_q), 109.9 (C_q) 112.9 (C_q), 116.6 (CH), 118.7 (C_q), 119.0 (C_q), 122.6 (CH), 124.7 (CH), 128.9 (2 CH), 132.5 (2 CH), 133.1 (CH), 148.8 (C_q), 152.3 (C_q), 153.9 (C_q), 158.0 (C_q), 159.6 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 341; $[M+H]^+$ found 342; HRMS-ESI: *m/z* $[M+Na]^+$ calcd. for $C_{20}H_{11}N_3NaO_3$: 364.0693; found: 364.0676.

2-Amino-4-(4-nitrophenyl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (4g)

The title compound was prepared from 4-hydroxy-3-{[(4-nitrophenyl)pyrrolidin-1-yl]methyl}-coumarin (**1g**) (183 mg, 0.5 mmol, 1 eq) and malononitrile (33 mg, 0.5 mmol, 1 eq), to give after 3 h compound **4g** (130 mg, 72% yield) as a light yellow solid. mp 266-267 °C (MeOH); IR 3480, 3427, 3368, 3332, 3193, 3070, 2194, 1715, 1669, 1604, 1502, 1344, 1053, 764 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 4.67 (s, 1 H, CH), 7.43-7.65 (m, 6 H, H_{arom}, H_{NH2}), 7.73 (td, 1 H, *J* = 1.3, *J* = 7.9, H_{arom}), 7.91 (dd, 1 H, *J* = 1.3, *J* = 7.8, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 36.8 (CH), 56.7 (C_q), 102.8 (C_q), 112.9 (C_q), 116.7 (CH), 118.9 (C_q), 122.6 (CH), 123.7 (2 CH), 124.8 (CH), 129.2 (2 CH), 133.2 (CH), 146.6 (C_q), 150.8 (C_q), 152.3 (C_q), 153.9 (C_q), 158.1 (C_q), 159.6 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 361; $[M+H]^+$ found 362; HRMS-ESI: *m/z* $[M+H]^+$ calcd. for $C_{19}H_{12}N_3O_5$: 362.0771; found: 362.0759.

2-Amino-5-oxo-4-phenyl-4,5-dihydrothiopyrano[3,2-*c*]chromene-3-carbonitrile (4h)

The title compound was prepared from 4-hydroxy-3-(phenyl(pyrrolidin-1-yl)methyl)-thiocoumarin **1n** (168 mg, 0.5 mmol, 1 eq) and malononitrile (33 mg, 0.5 mmol, 1 eq), to give after 96 h compound **4h** (43 mg, 25% yield) as a white solid. mp 272-273 °C (MeOH); IR 3403, 3310, 3269, 3188, 2206, 1673, 1584, 1554, 1361, 1260, 745 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ = 4.61 (s, 1 H, CH), 7.12-7.31 (m, 5 H, H_{arom}), 7.44 (s, 2 H, H_{NH2}), 7.69-7.78 (m, 3 H, H_{arom}), 8.38 (d, 1 H, *J* = *J* = 7.7, H_{arom}). ^{13}C NMR (125 MHz, DMSO-d_6) δ = 36.9 (CH), 57.8 (C_q), 114.4 (C_q), 119.2 (C_q), 120.7 (C_q), 125.8 (CH), 126.0 (CH), 127.0 (CH), 127.1 (CH), 127.2 (2 CH), 128.6 (2 CH), 131.2 (CH), 134.5 (C_q), 143.8 (C_q), 154.8 (C_q), 158.5 (C_q), 181.7 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 332; $[M+H]^+$ found 333; HRMS-ESI: *m/z* $[M+H]^+$ calcd. for $C_{19}H_{13}N_2O_2S$: 333.00692; found: 333.0689.

3-{[(4-Bromophenyl)thio][phenyl]methyl}-4-hydroxycoumarin (5a)

The title compound was prepared from 4-hydroxy-3-[phenyl(pyrrolidin-1-yl)methyl]-coumarin **1a** (160 mg, 0.5 mmol), 4-bromothiophenol (94 mg, 0.5 mmol) to give **5a** (127 mg, 57% yield) as a white solid. mp 164-165 °C (MeOH); IR 3195, 1672, 1620, 1567, 1473, 1496, 1450, 1400, 1189, 718 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 6.02 (s, 1 H, CH), 7.15-7.43 (m, 7 H, H_{arom}), 7.48 (d, 2

H, *J* = 8.4, H_{arom}), 7.57 (d, 2 H, *J* = 7.6, H_{arom}), 7.63 (t, 1 H, *J* = 7.2, H_{arom}), 8.03 (d, 1 H, *J* = 7.5, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 47.1 (CH), 106.2 (C_q), 115.9 (C_q), 116.4 (CH), 119.3 (C_q), 123.8 (CH), 124.1 (CH), 126.9 (CH), 127.6 (2 CH), 128.1 (2 CH), 131.1 (2 CH), 131.9 (2 CH), 132.5 (CH), 136.9 (C_q), 139.9 (C_q), 152.1 (C_q), 160.6 (C_q), 161.1 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 438; $[M-H]^-$ found 437; HRMS-ESI: calcd for $C_{22}H_{14}BrO_3S$: 436.9853; found: 436.9858.

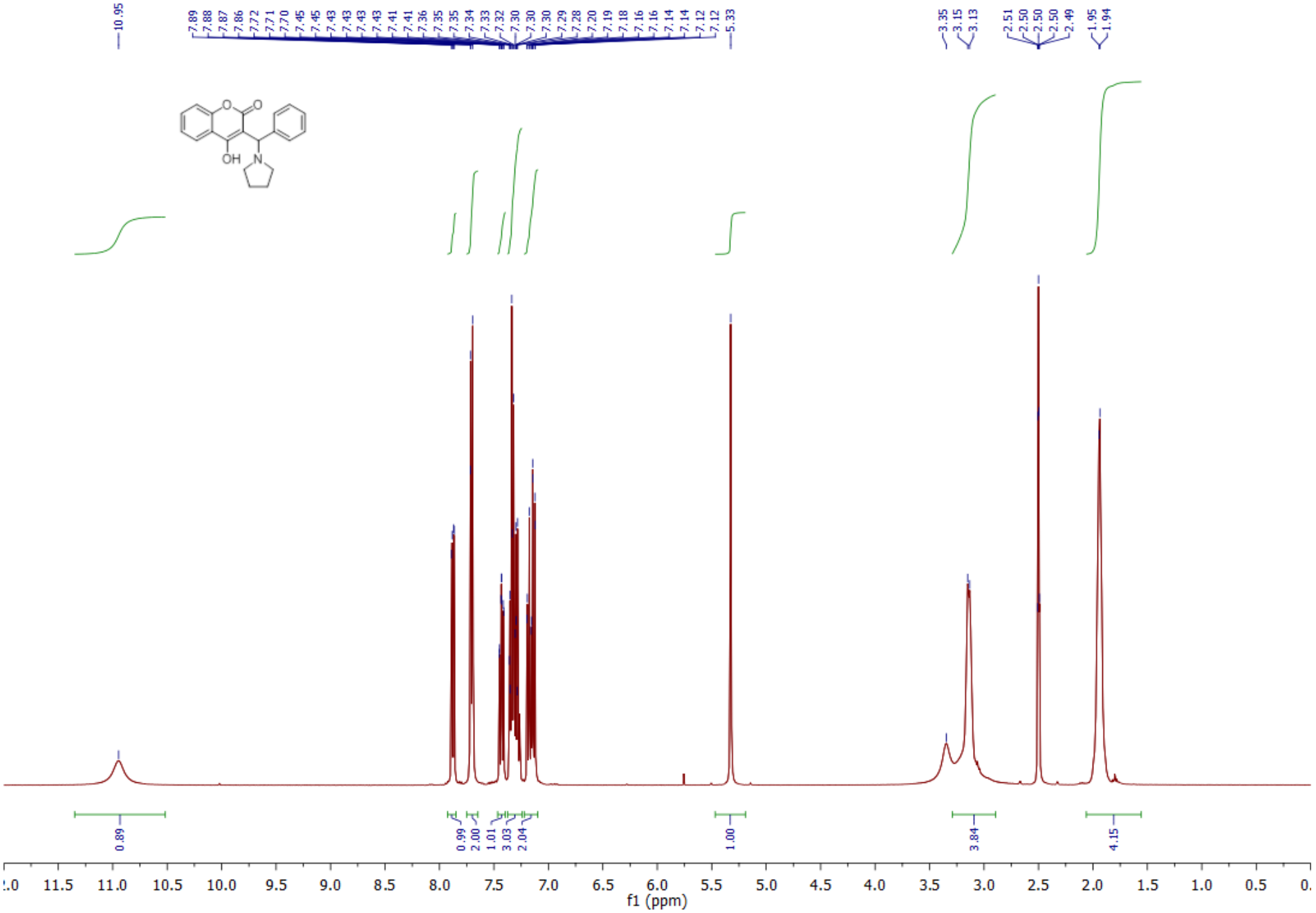
3-{[1,1'-Biphenyl]-4-yl[(4-bromophenyl)thio]methyl}-4-hydroxycoumarin (5b)

The title compound was prepared from 3-[(1,1'-Biphenyl)-4-yl(pyrrolidin-1-yl)methyl]-4-hydroxycoumarin **1b** (198 mg, 0.5 mmol), 4-bromothiophenol (94 mg, 0.5 mmol) to give **5b** (196 mg, 76% yield) as a white solid. mp 165-166 °C (MeOH); IR 3076, 1692, 1620, 1573, 1489, 1473, 1246, 749 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 6.07 (s, 1 H, CH), 7.27-7.55 (m, 9 H, H_{arom}), 7.56-7.64 (m, 7 H, H_{arom}), 8.04 (d, 1 H, *J* = 7.7, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 46.8 (CH), 106.1 (C_q), 115.9 (C_q), 116.4 (CH), 119.3 (C_q), 123.8 (CH), 124.1 (CH), 126.5 (2 CH), 126.6 (2 CH), 127.4 (CH), 128.2 (2 CH), 128.9 (2 CH), 131.0 (2 CH), 131.9 (2 CH), 132.6 (CH), 136.9 (C_q), 138.8 (C_q), 139.2 (C_q), 139.7 (C_q), 152.2 (C_q), 160.7 (C_q), 161.2 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 514; $[M-H]^-$ found 513; HRMS-ESI: calcd for $C_{28}H_{18}BrO_3S$: 513.0166; found: 513.0169.

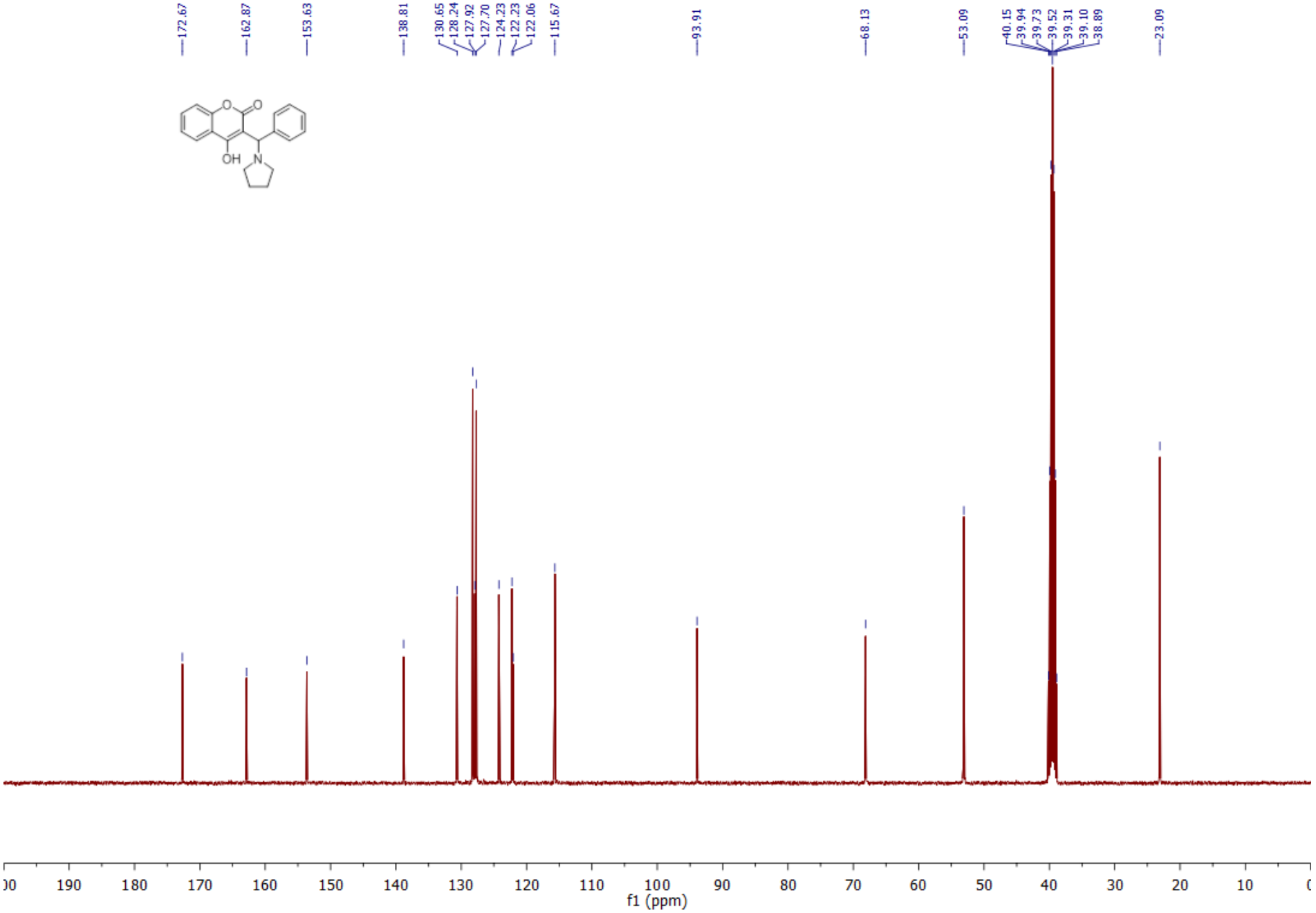
3-{[4-Bromophenyl][(4-bromophenyl)thio]methyl}-4-hydroxycoumarin (5c)

The title compound was prepared from 3-{[(4-bromophenyl)pyrrolidin-1-yl]methyl}-4-hydroxycoumarin **1e** (200 mg, 0.5 mmol), 4-bromothiophenol (94 mg, 0.5 mmol) to give **5c** (179 mg, 69% yield) as a white solid. mp 165-166 °C (MeOH); IR 3185, 1669, 1623, 1557, 1494, 1485, 1395, 1191, 750 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 5.97 (s, 1 H, CH), 7.28 (d, 2 H, *J* = 8.3, H_{arom}), 7.32-7.42 (m, 2 H, H_{arom}), 7.44-7.58 (m, 6 H, H_{arom}), 7.63 (t, 1 H, *J* = 7.5, H_{arom}), 8.02 (d, 1 H, *J* = 7.8, H_{arom}). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 46.6 (CH), 105.7 (C_q), 115.9 (C_q), 116.4 (CH), 119.5 (C_q), 120.0 (C_q), 123.8 (CH), 124.1 (CH), 129.9 (2 CH), 131.0 (2 CH), 131.2 (2 CH), 131.9 (2 CH), 132.6 (CH), 136.5 (C_q), 139.4 (C_q), 152.2 (C_q), 160.9 (C_q), 161.1 (C_q). MS (ESI, CH_3CN): *m/z* calcd. 515; $[M-H]^-$ found 4514; HRMS-ESI: calcd for $C_{22}H_{13}Br_2O_3S$: 514.8958; found: 514.8953.

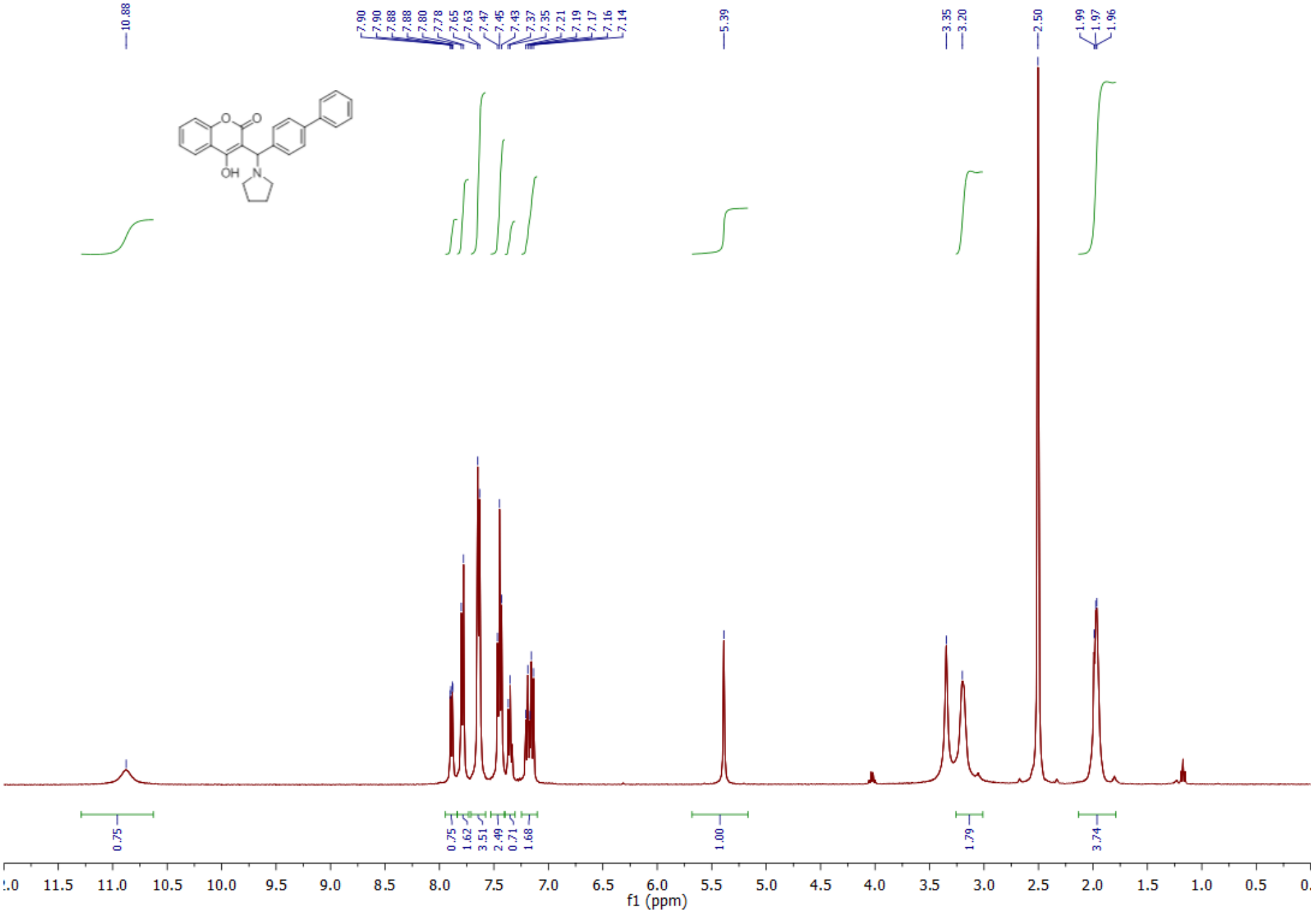
^{1}H NMR (400 MHz, d_6-DMSO): compound **1a**



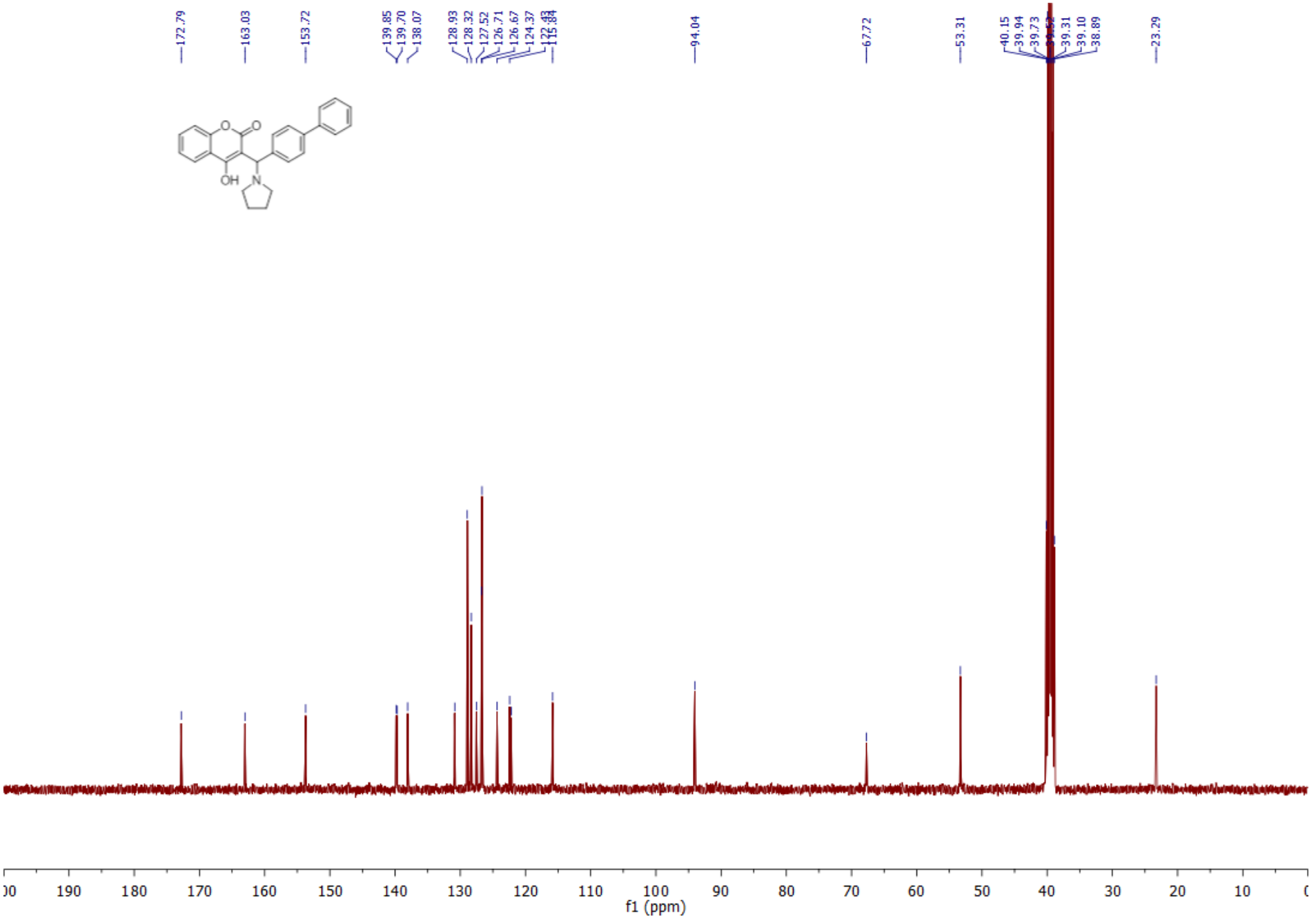
^{13}C NMR (100 MHz, d_6-DMSO): compound **1a**



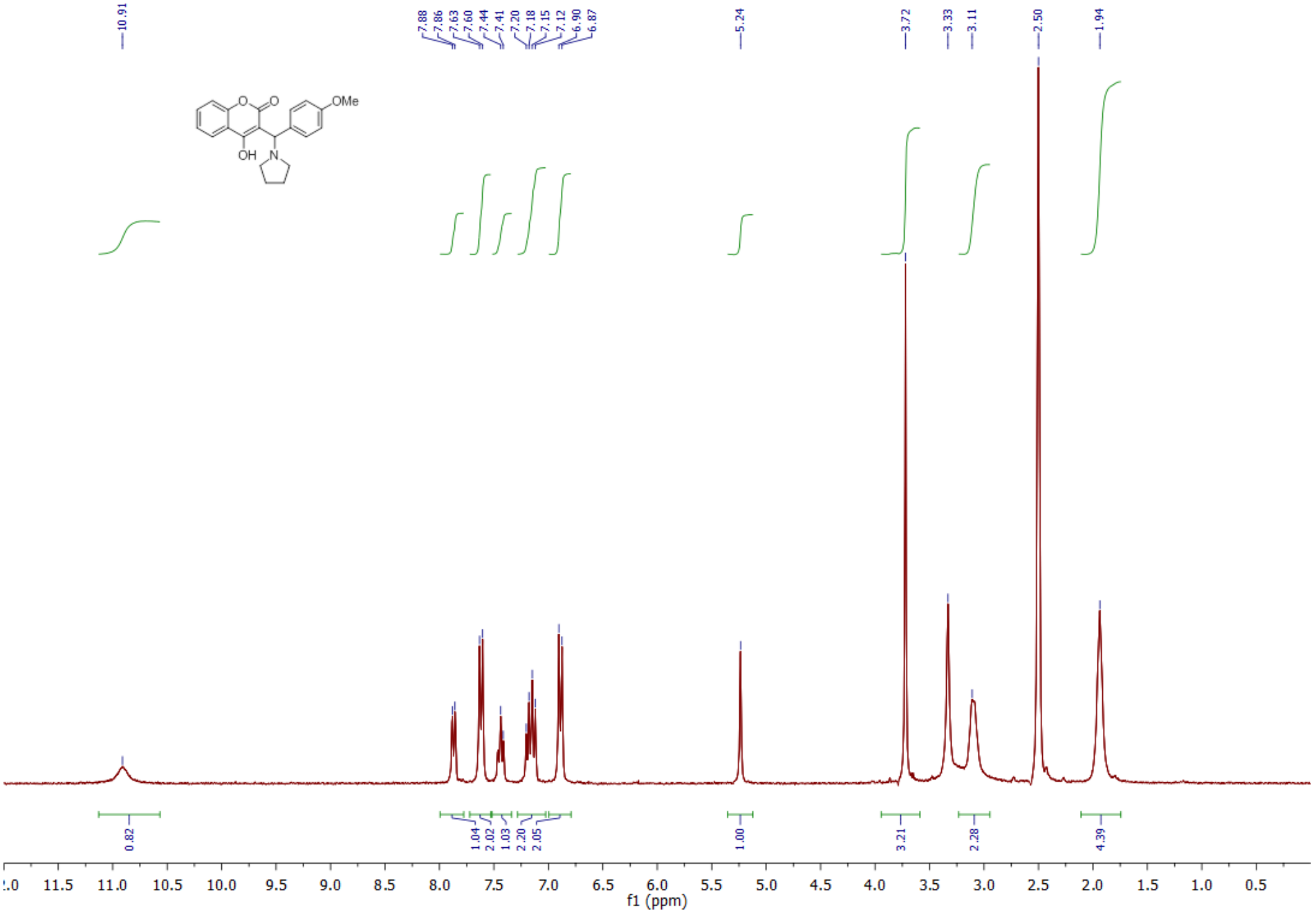
^{1}H NMR (400 MHz, d_6-DMSO): compound **1b**



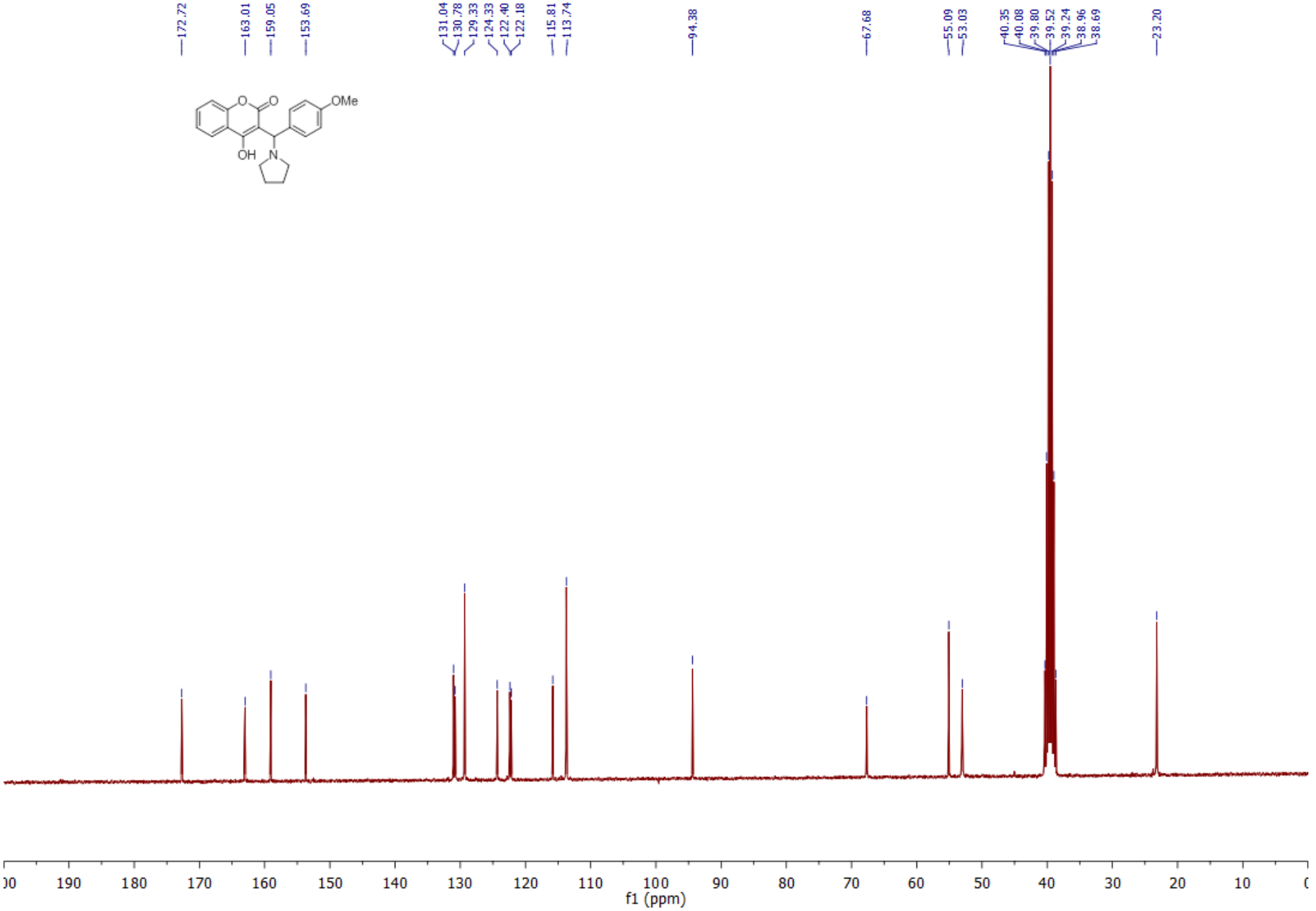
^{13}C NMR (100 MHz, d_6-DMSO): compound **1b**



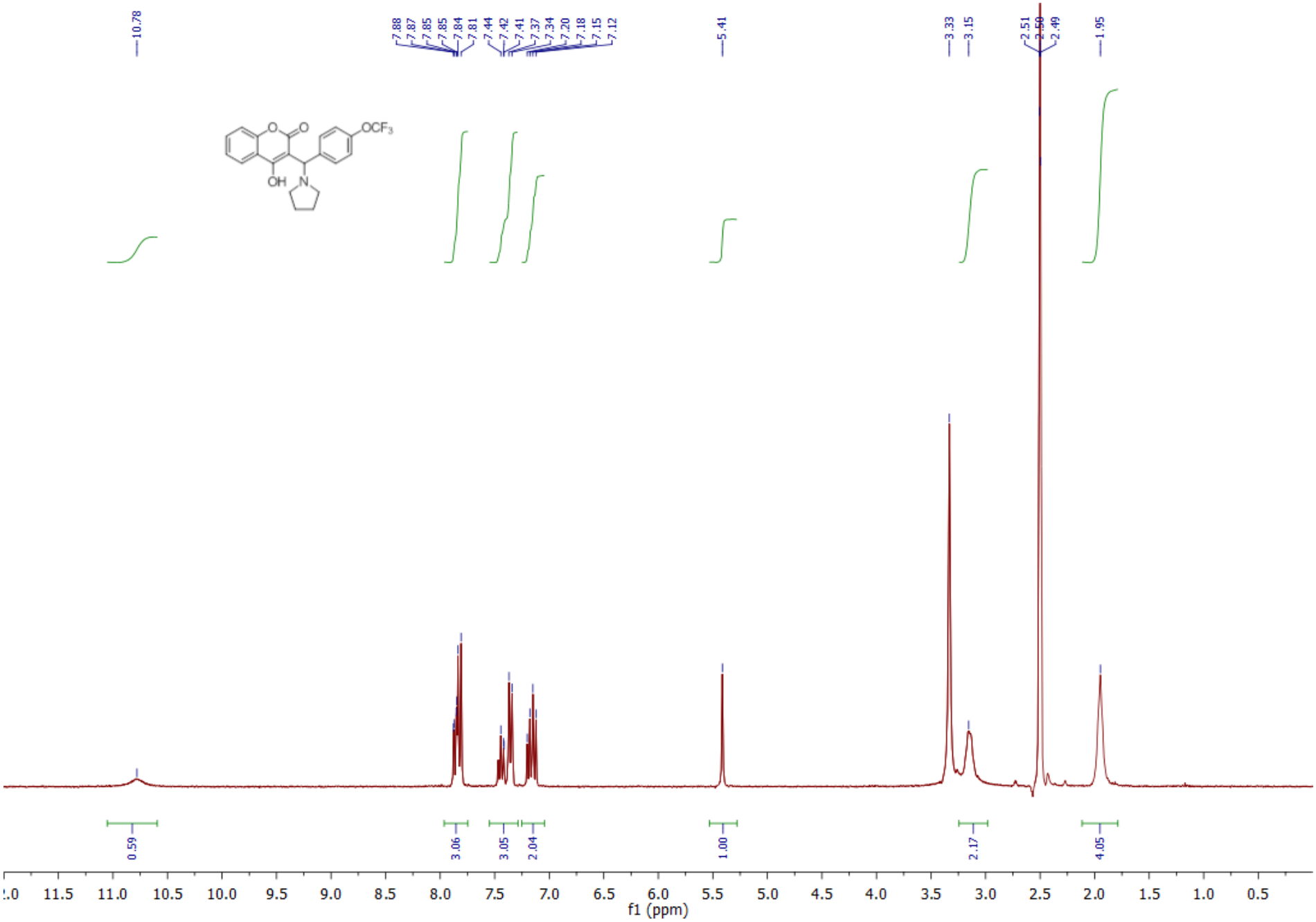
^{1}H NMR (300 MHz, d_6-DMSO): compound **1c**



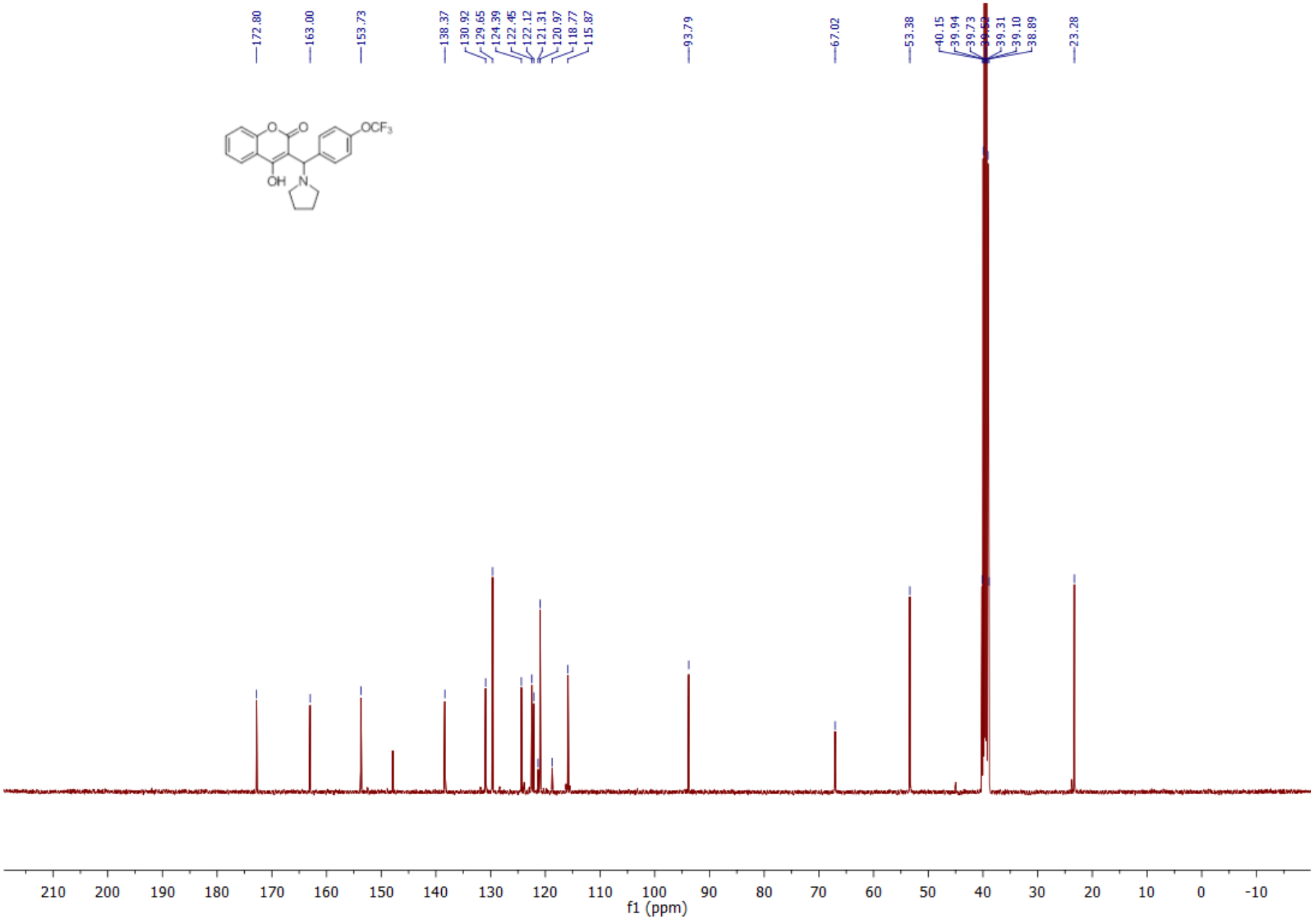
^{13}C NMR (75 MHz, d_6-DMSO): compound **1c**



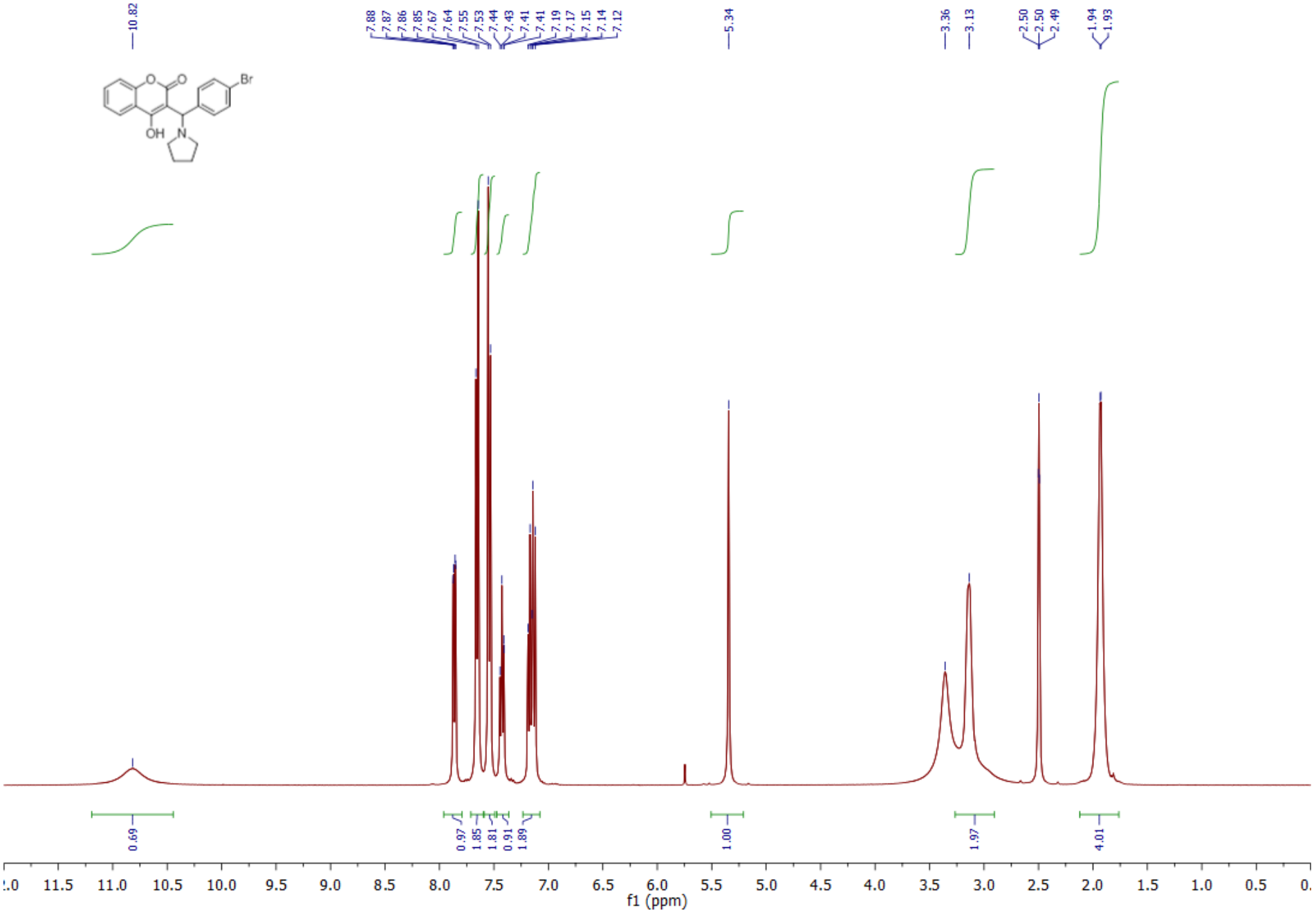
^{1}H NMR (400 MHz, d_6-DMSO): compound **1d**



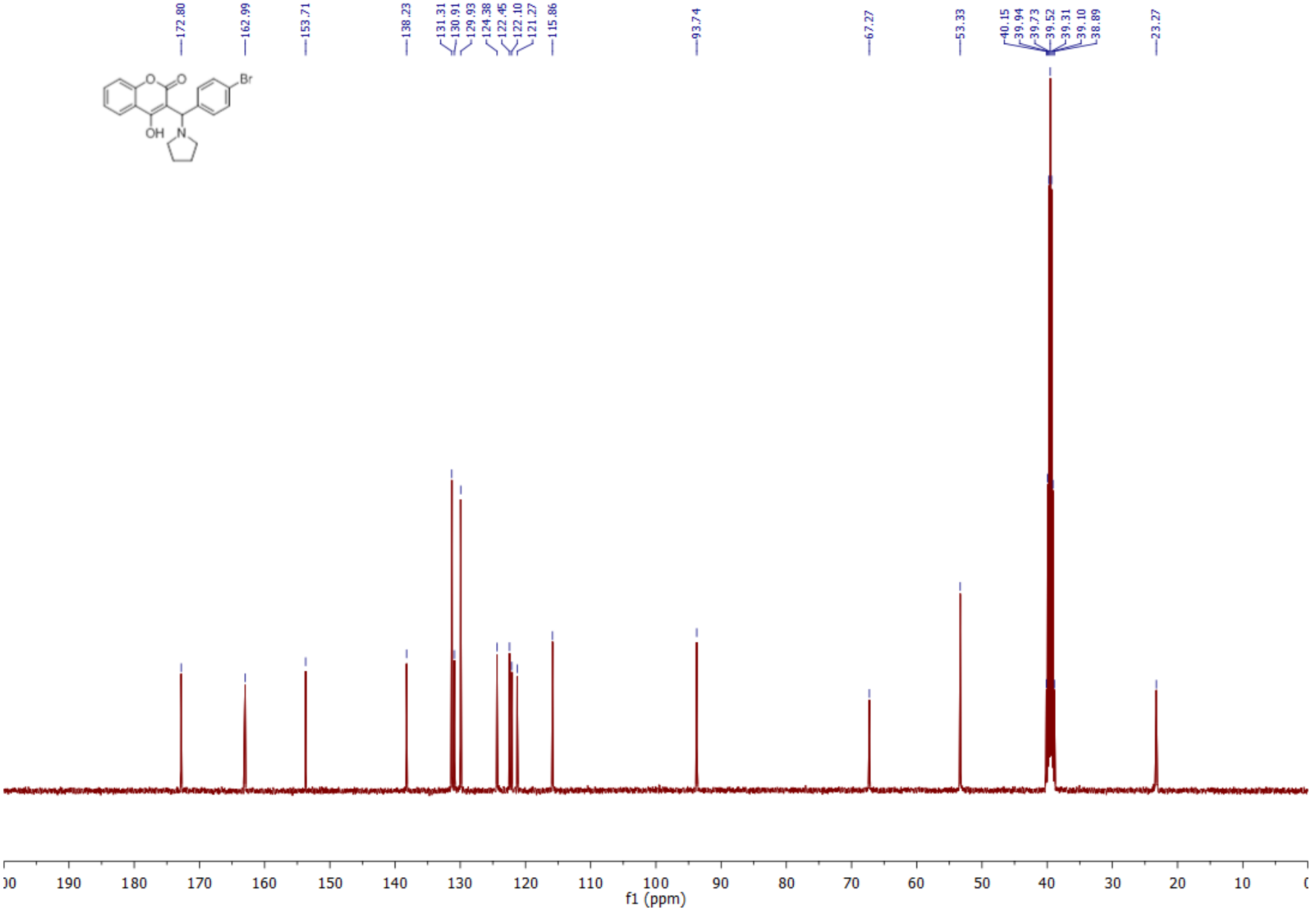
^{13}C NMR (100 MHz, d_6-DMSO): compound **1d**



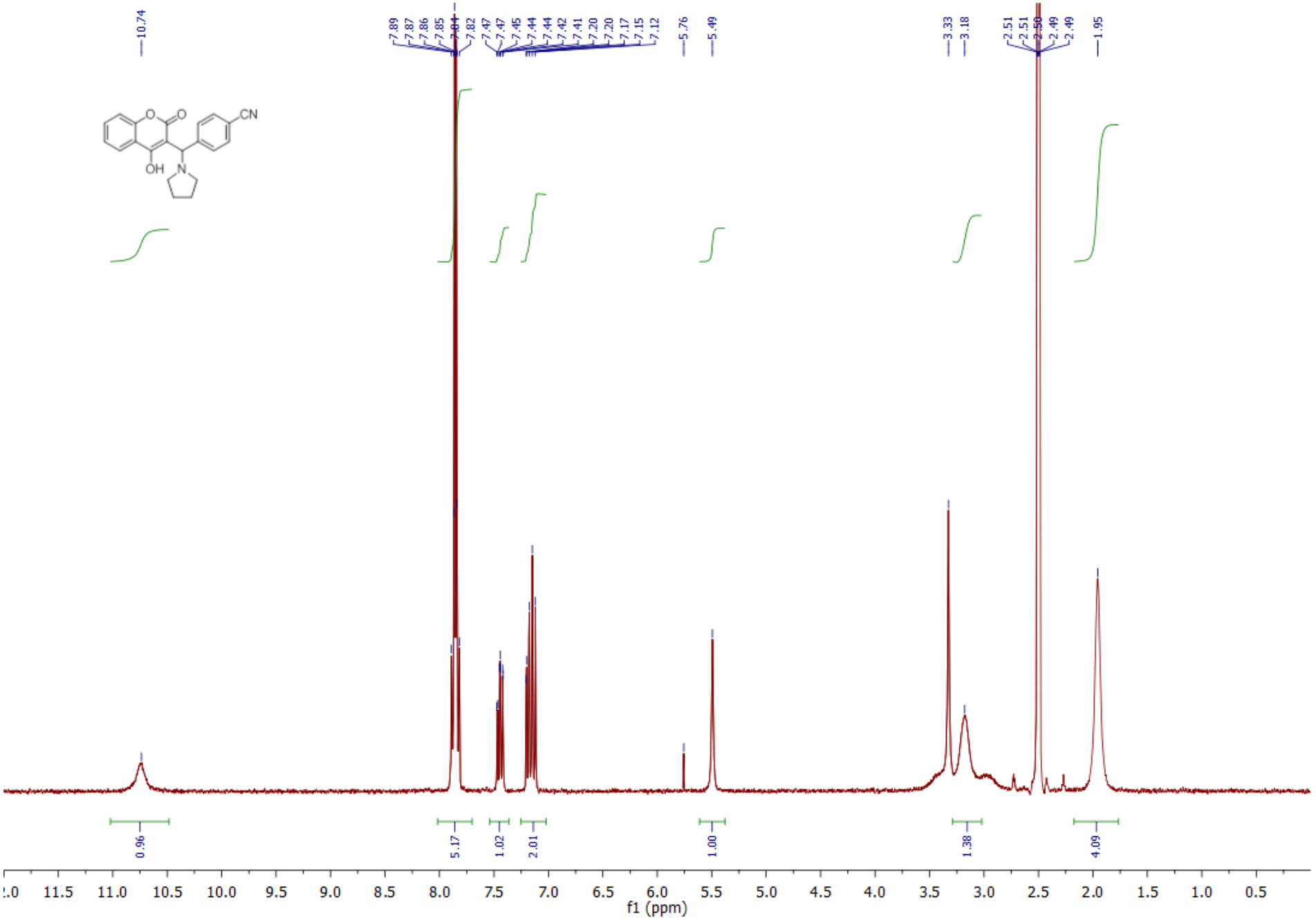
^{1}H NMR (400 MHz, d_6-DMSO): compound **1e**



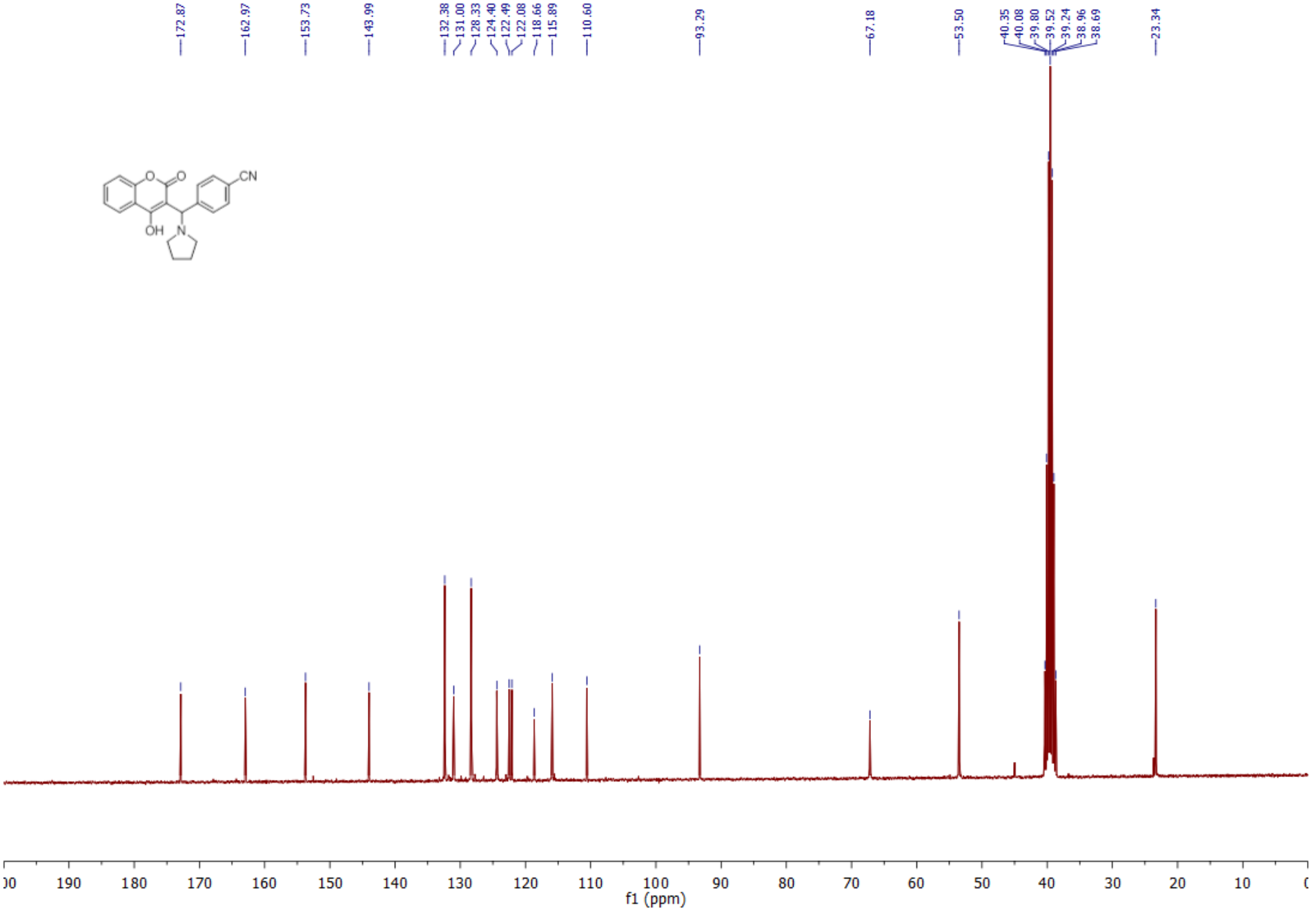
^{13}C NMR (100 MHz, d_6-DMSO): compound **1e**



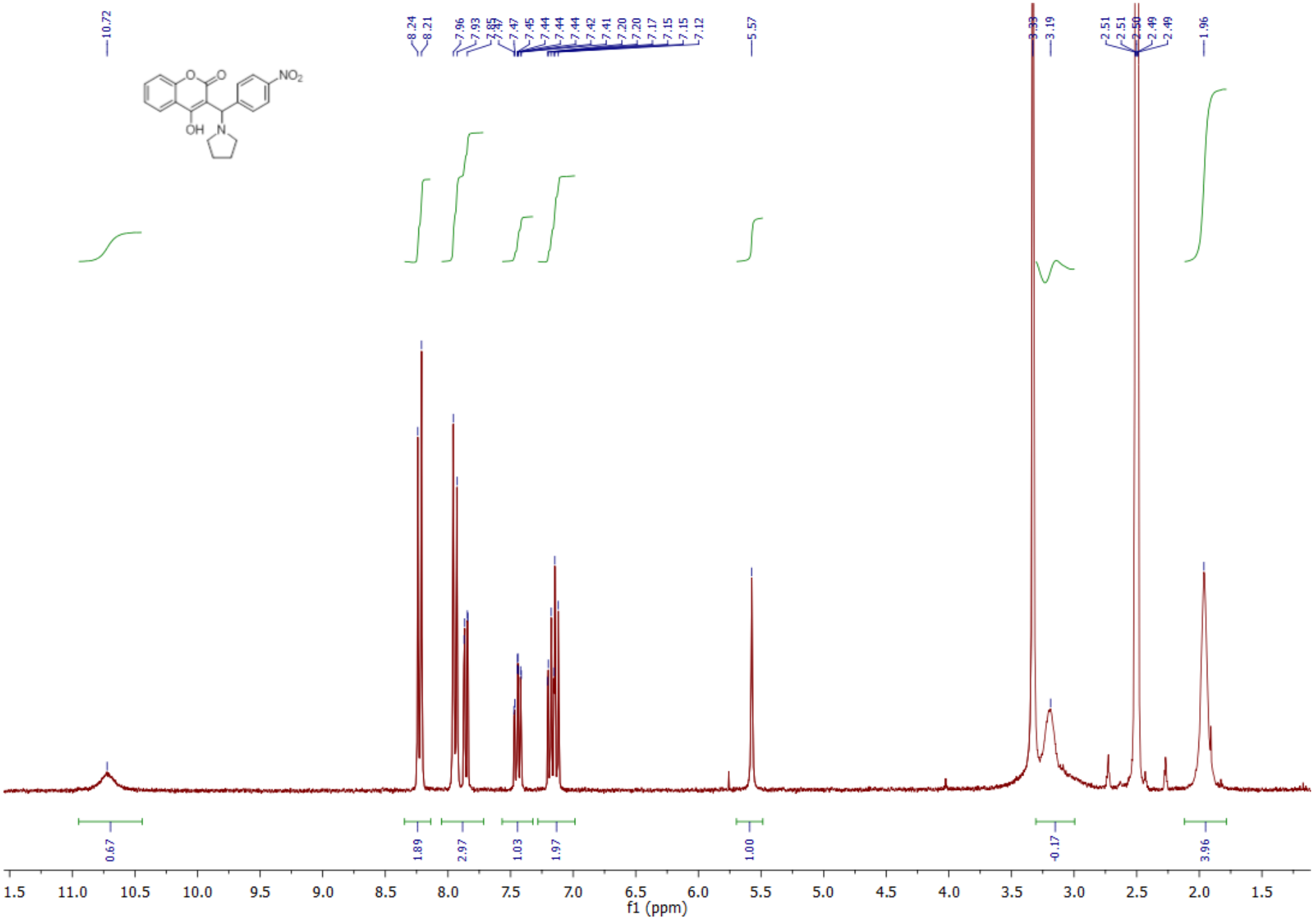
^{1}H NMR (300 MHz, d_6-DMSO): compound **1f**



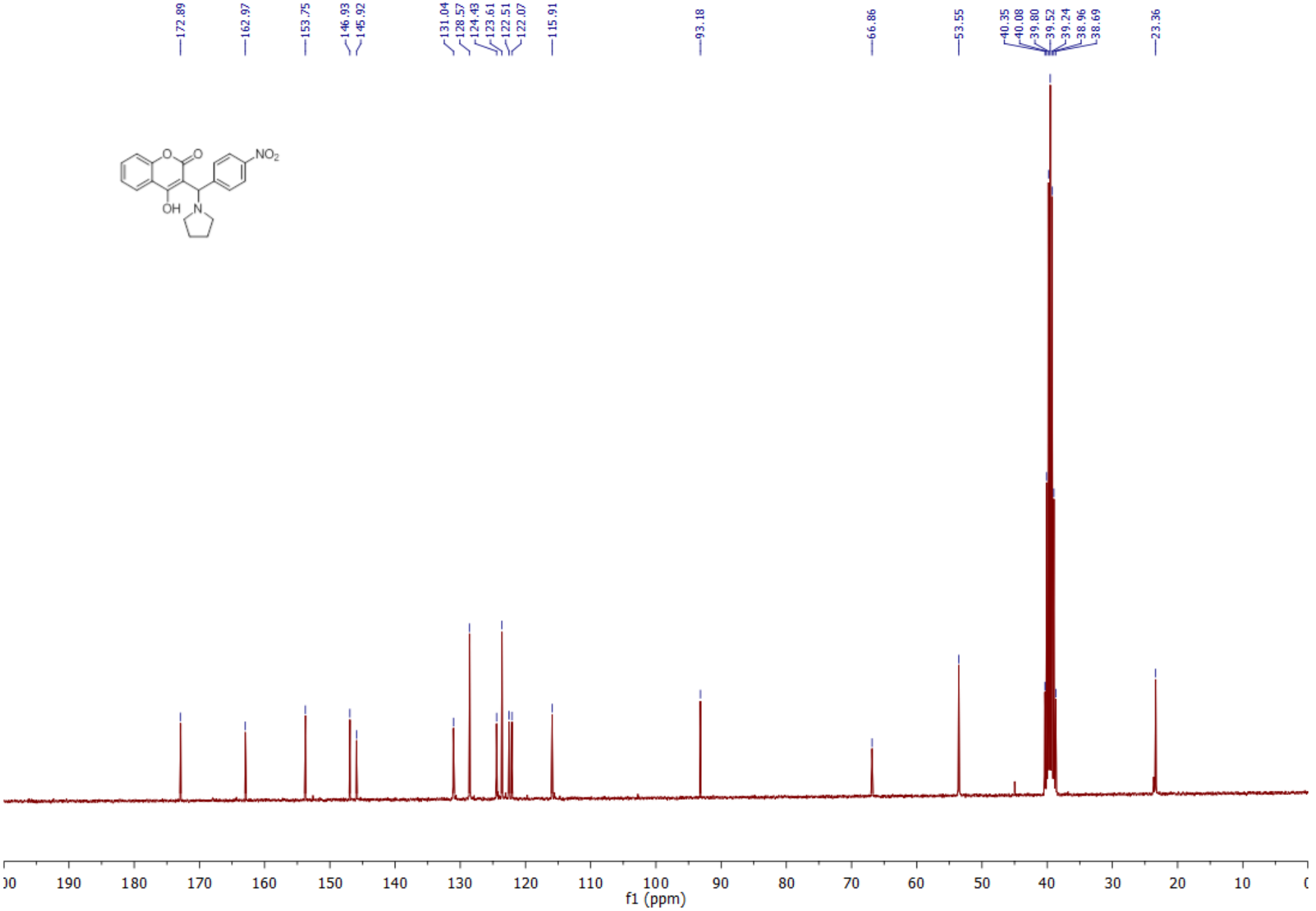
^{13}C NMR (75 MHz, d_6-DMSO): compound **1f**



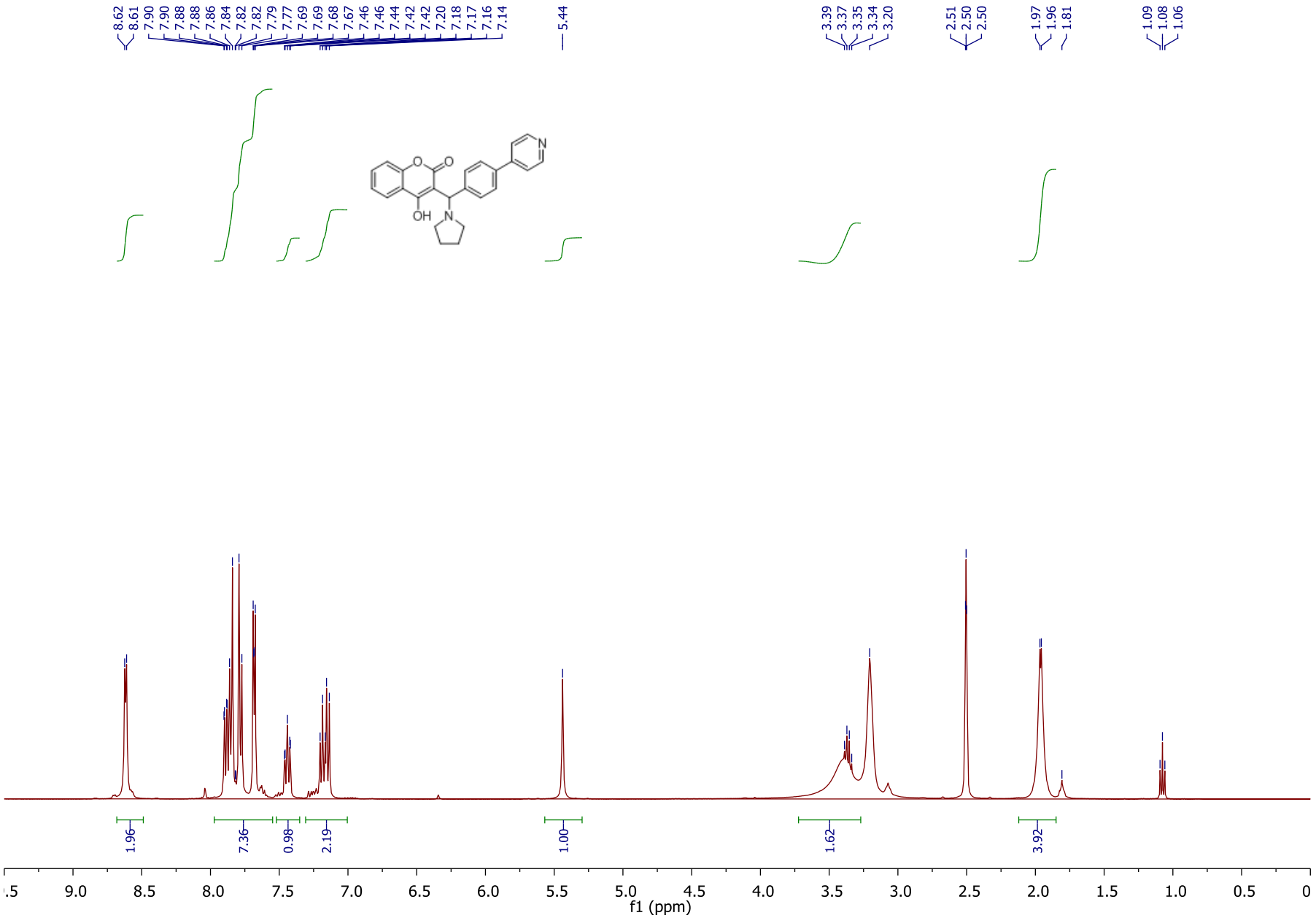
^{1}H NMR (300 MHz, d_6-DMSO): compound **1g**



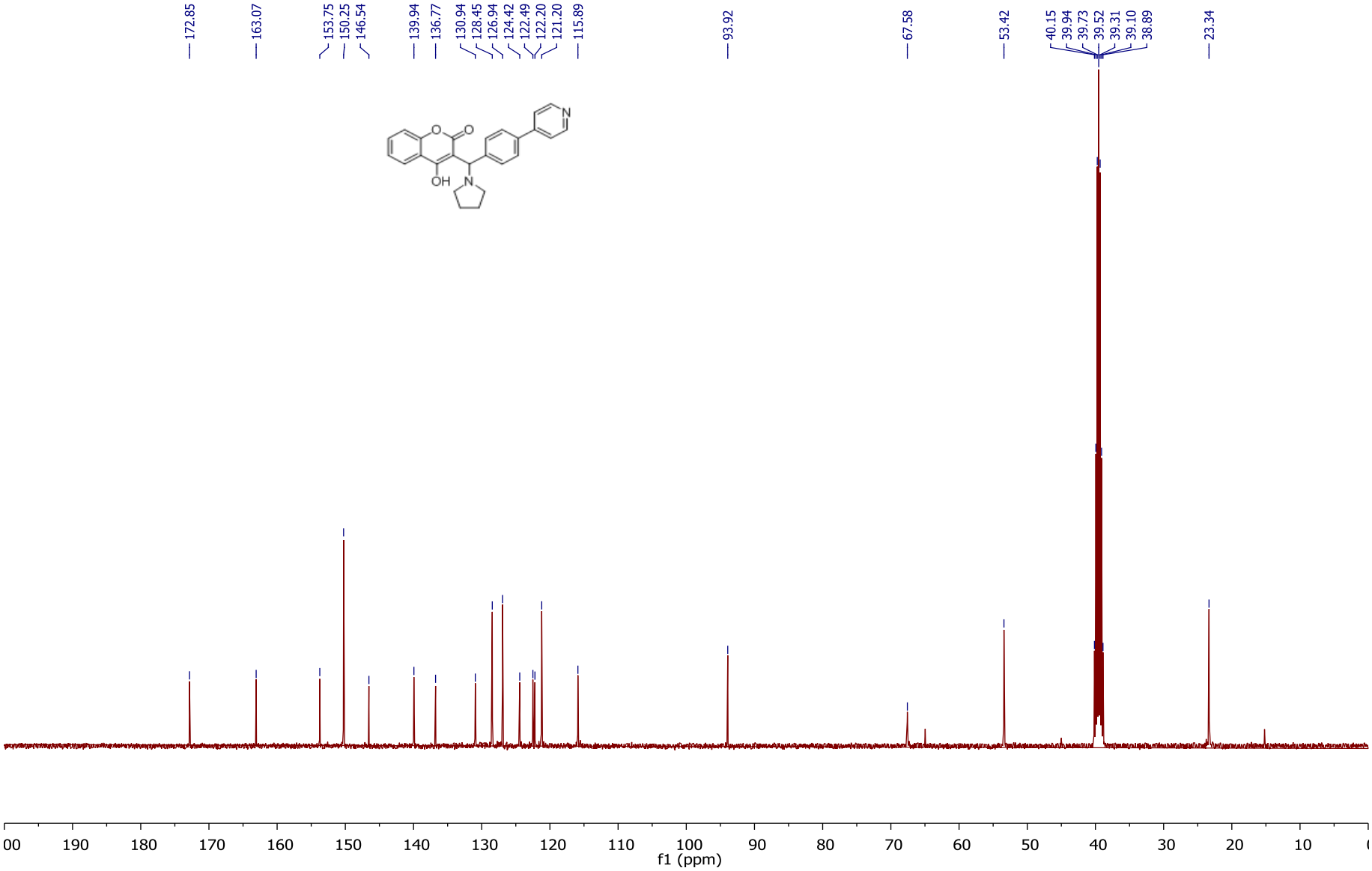
^{13}C NMR (75 MHz, d_6-DMSO): compound **1g**



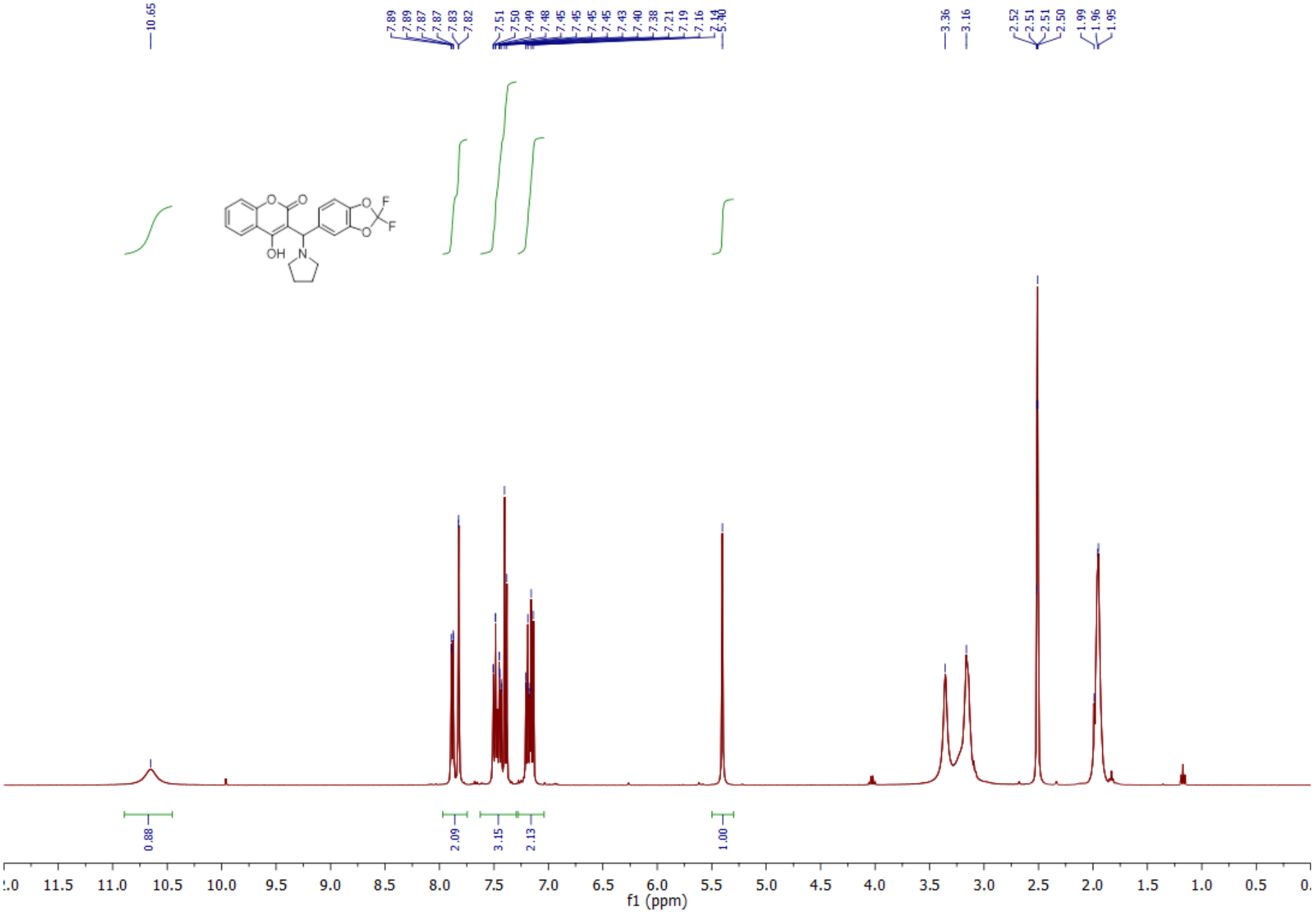
^{1}H NMR (300 MHz, d_6-DMSO): compound **1h**



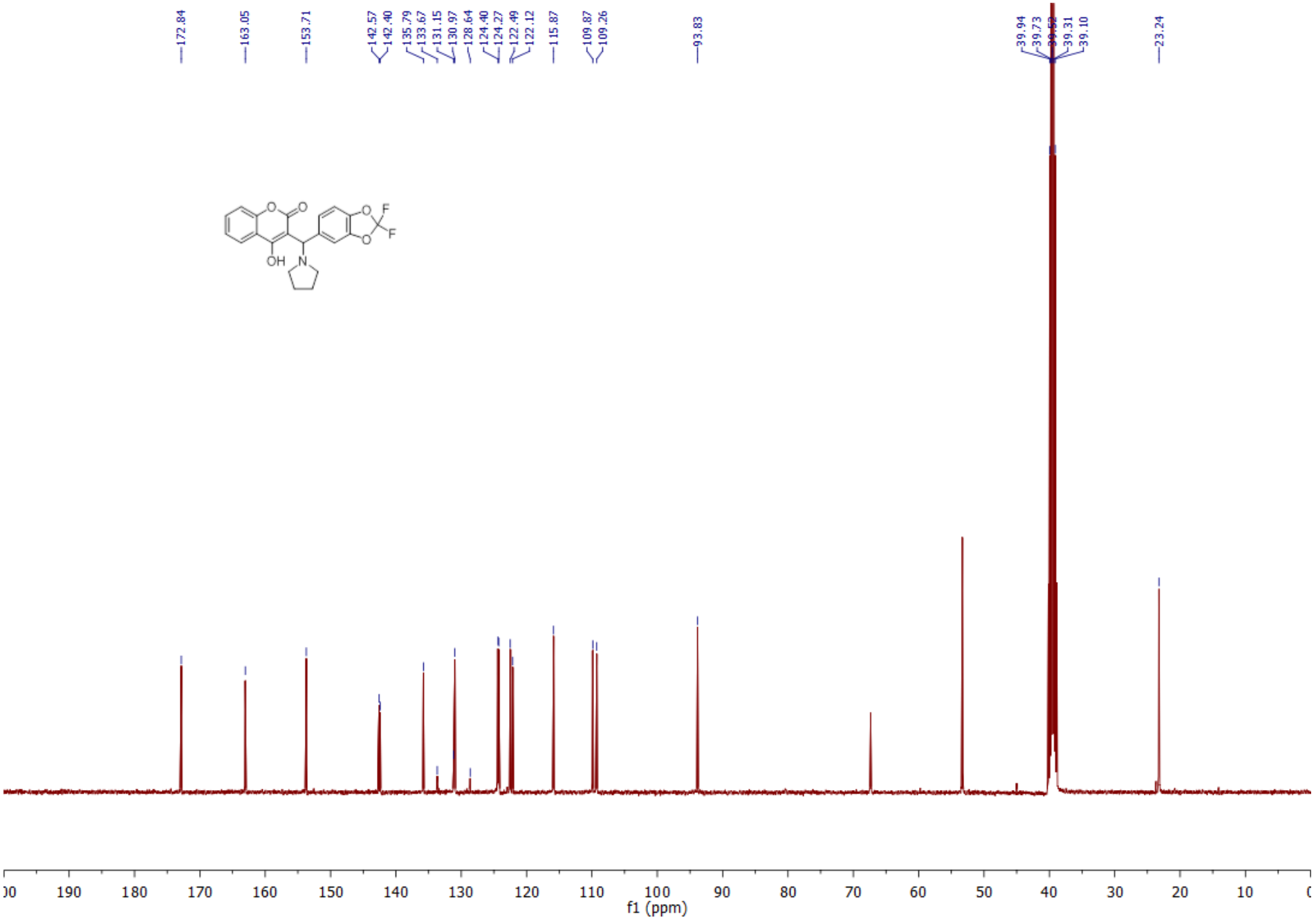
^{13}C NMR (100 MHz, d_6-DMSO): compound **1h**



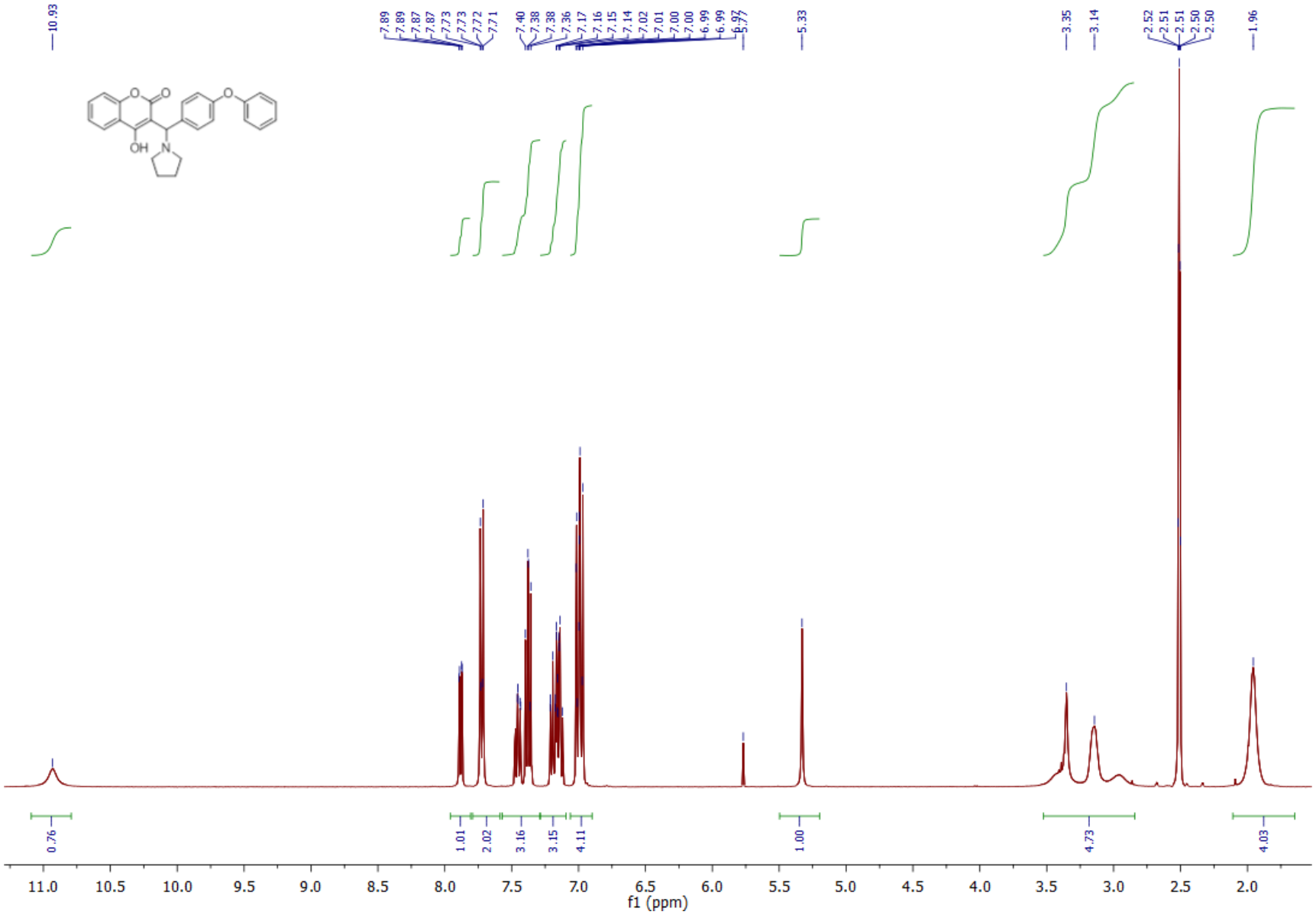
^{1}H NMR (400 MHz, d_6-DMSO): compound **1i**



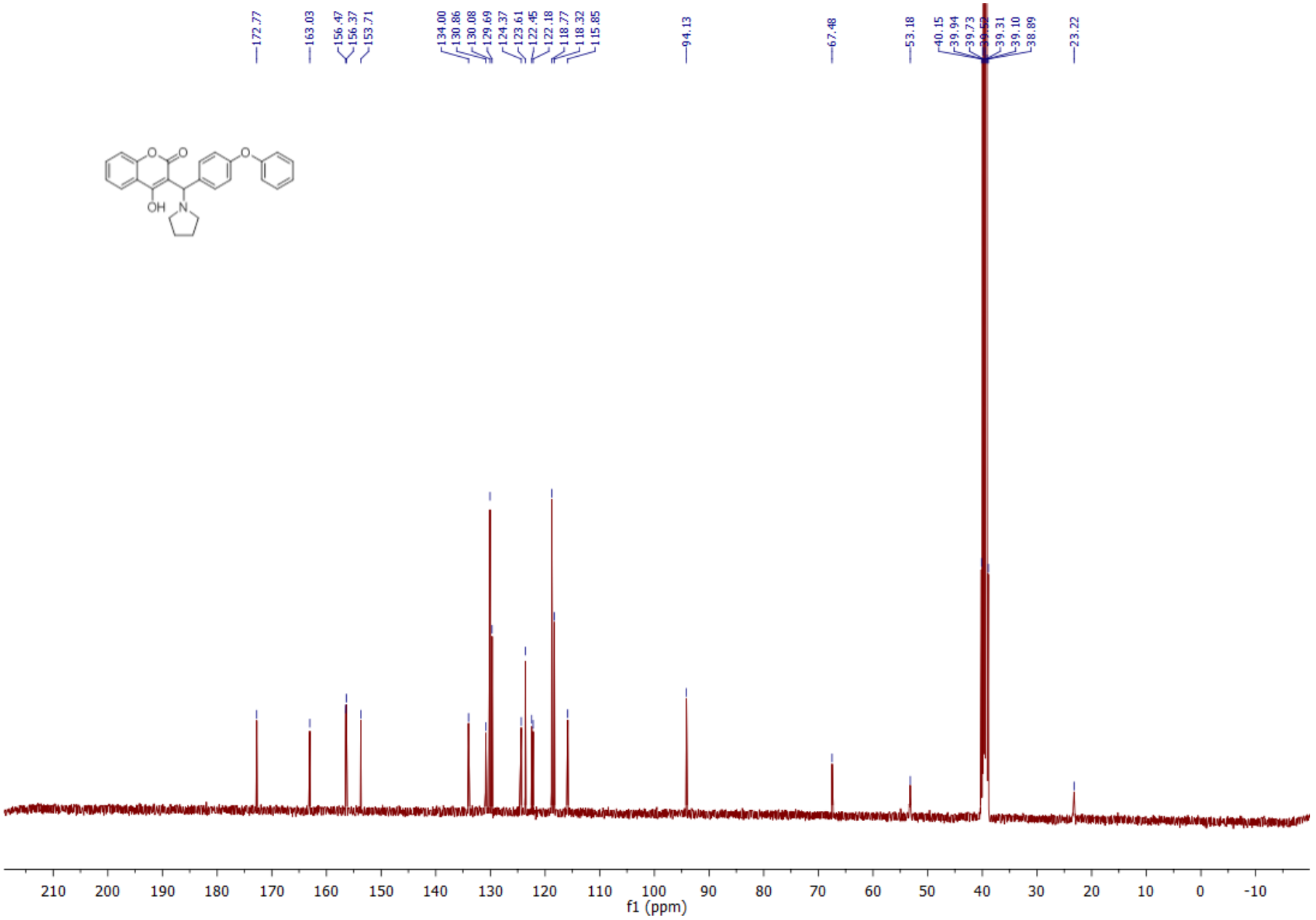
^{13}C NMR (75 MHz, d_6-DMSO): compound **1i**



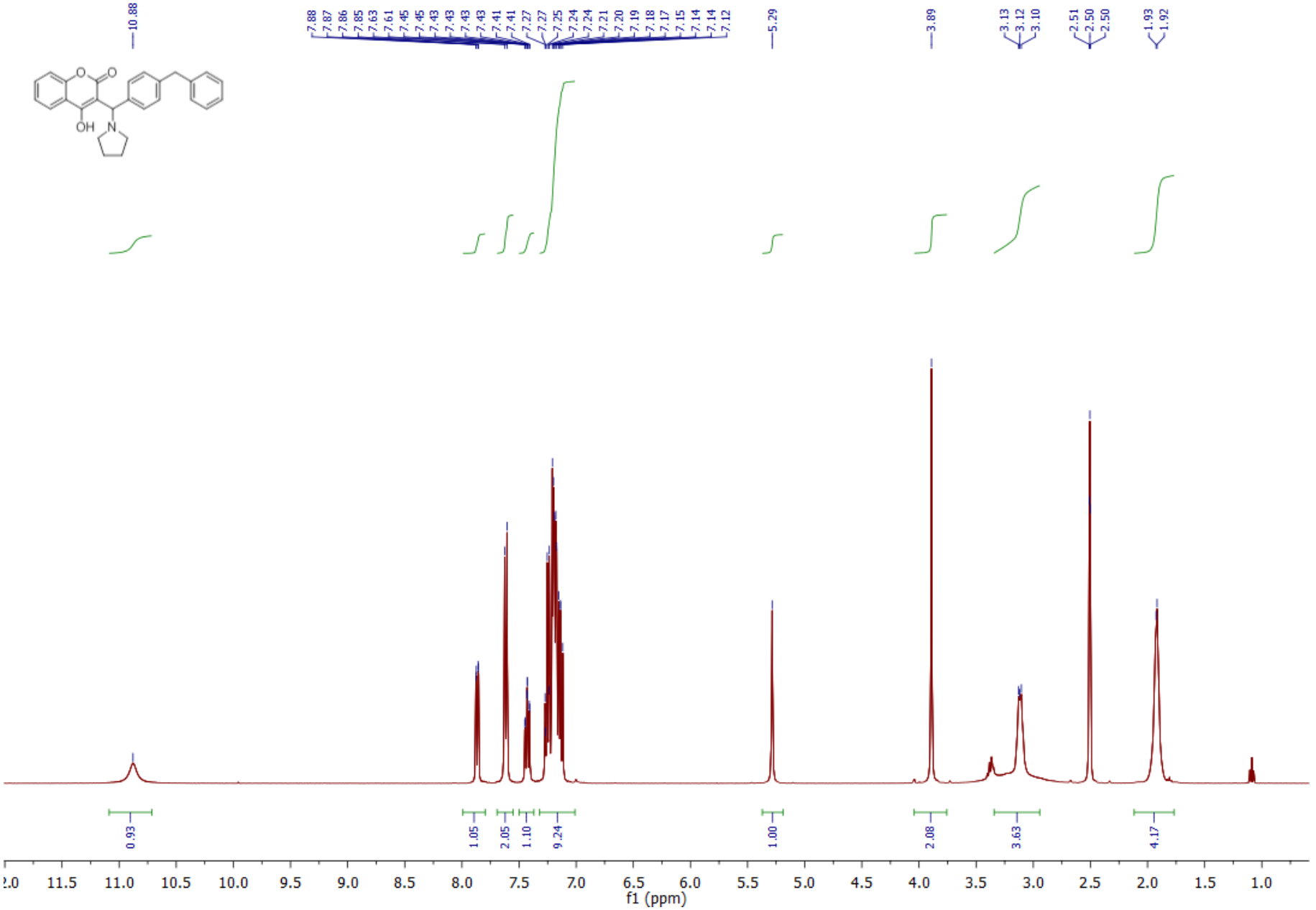
^{1}H NMR (400 MHz, d_6-DMSO): compound **1j**



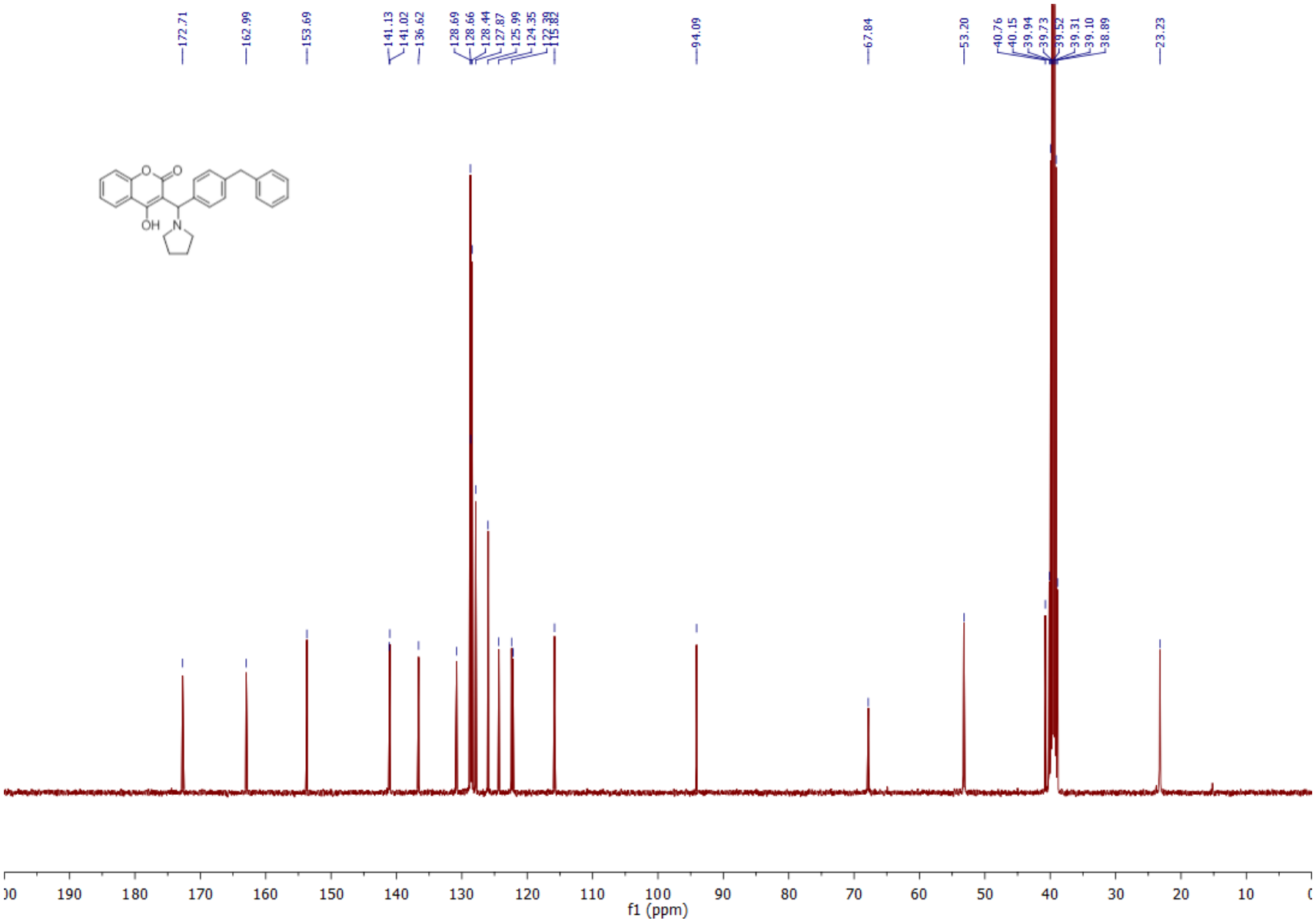
^{13}C NMR (75 MHz, d_6-DMSO): compound **1j**



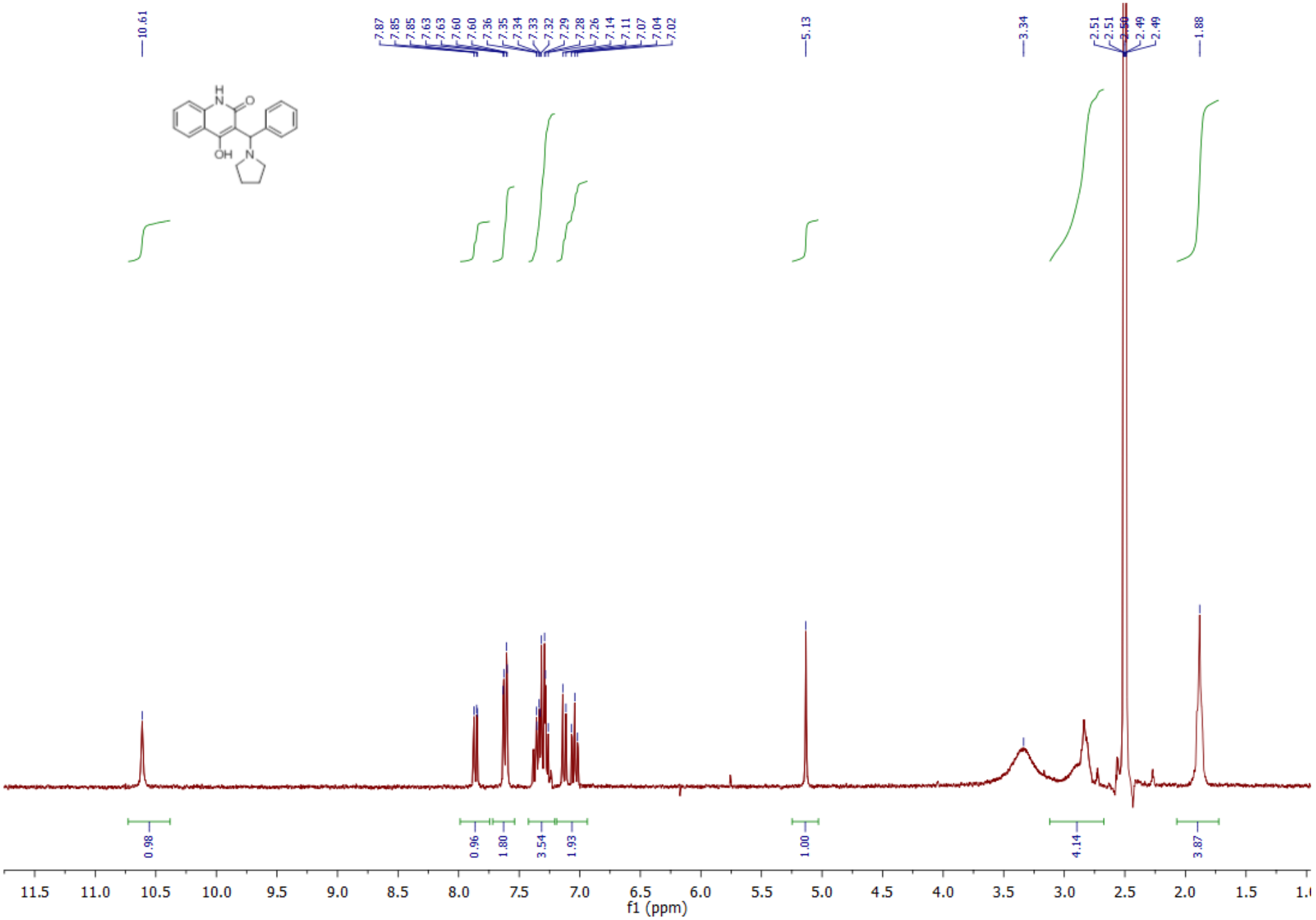
^{1}H NMR (400 MHz, d_6-DMSO): compound **1k**



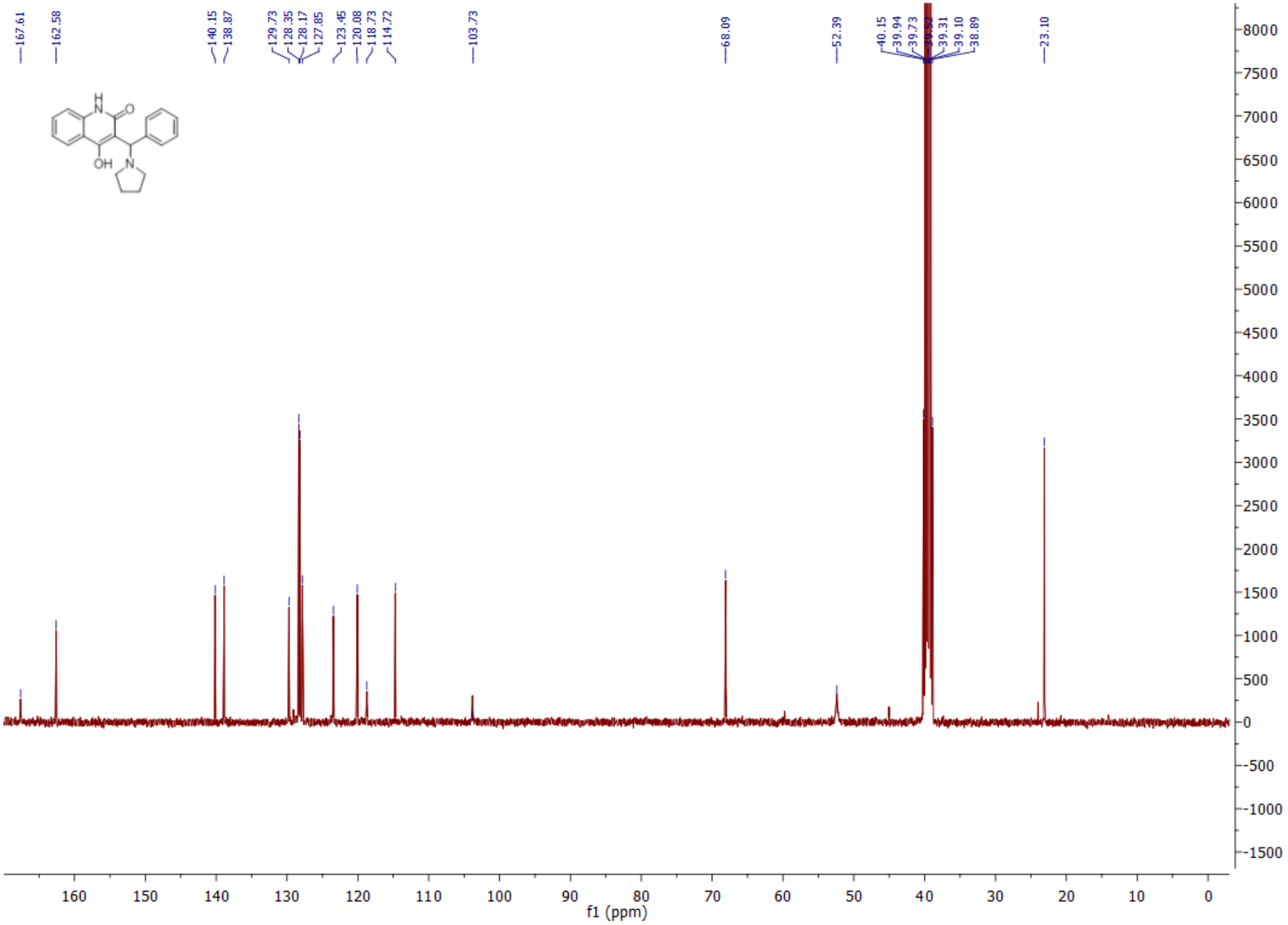
^{13}C NMR (75 MHz, d_6-DMSO): compound **1k**



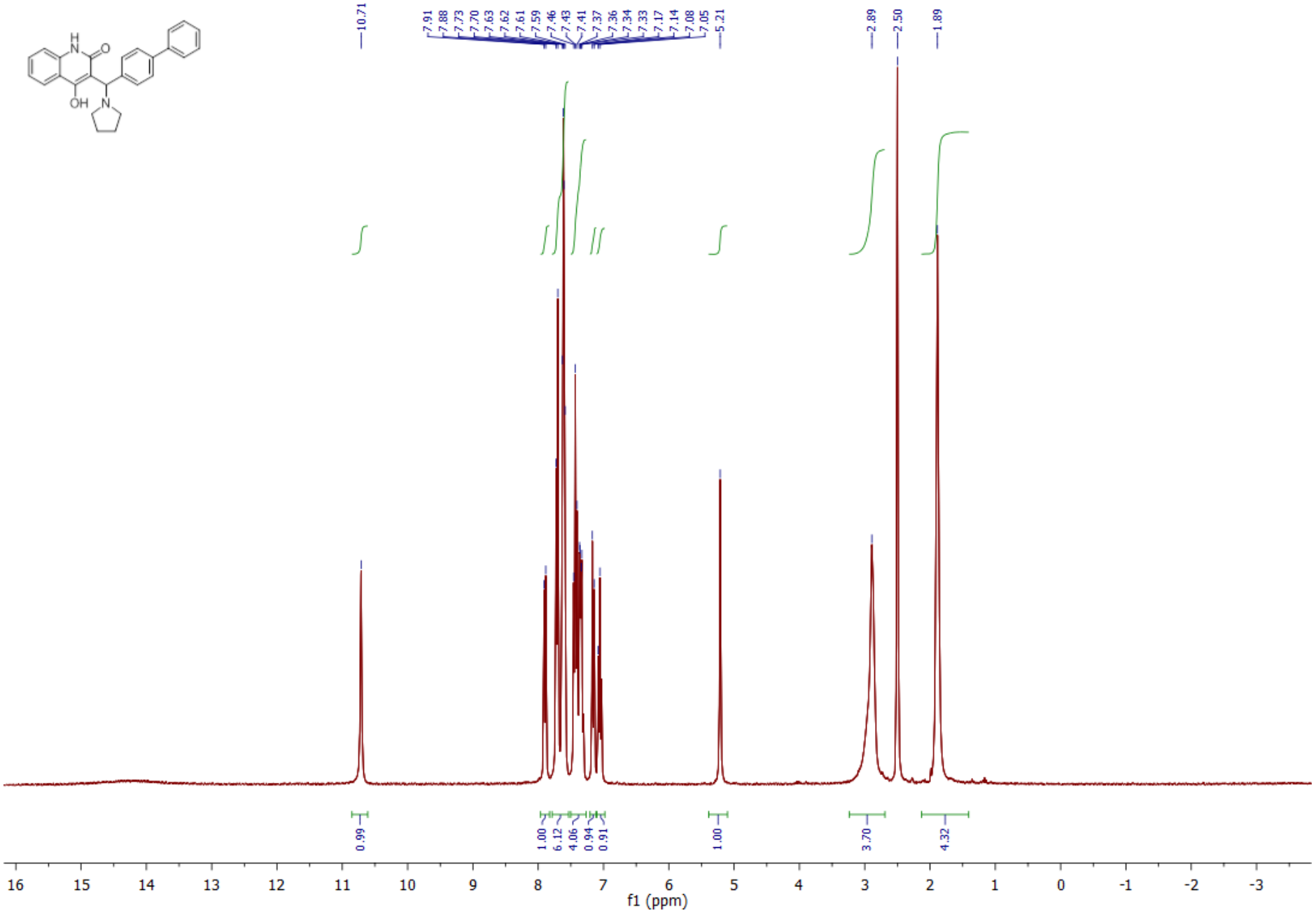
^{1}H NMR (300 MHz, d_6-DMSO): compound **1l**



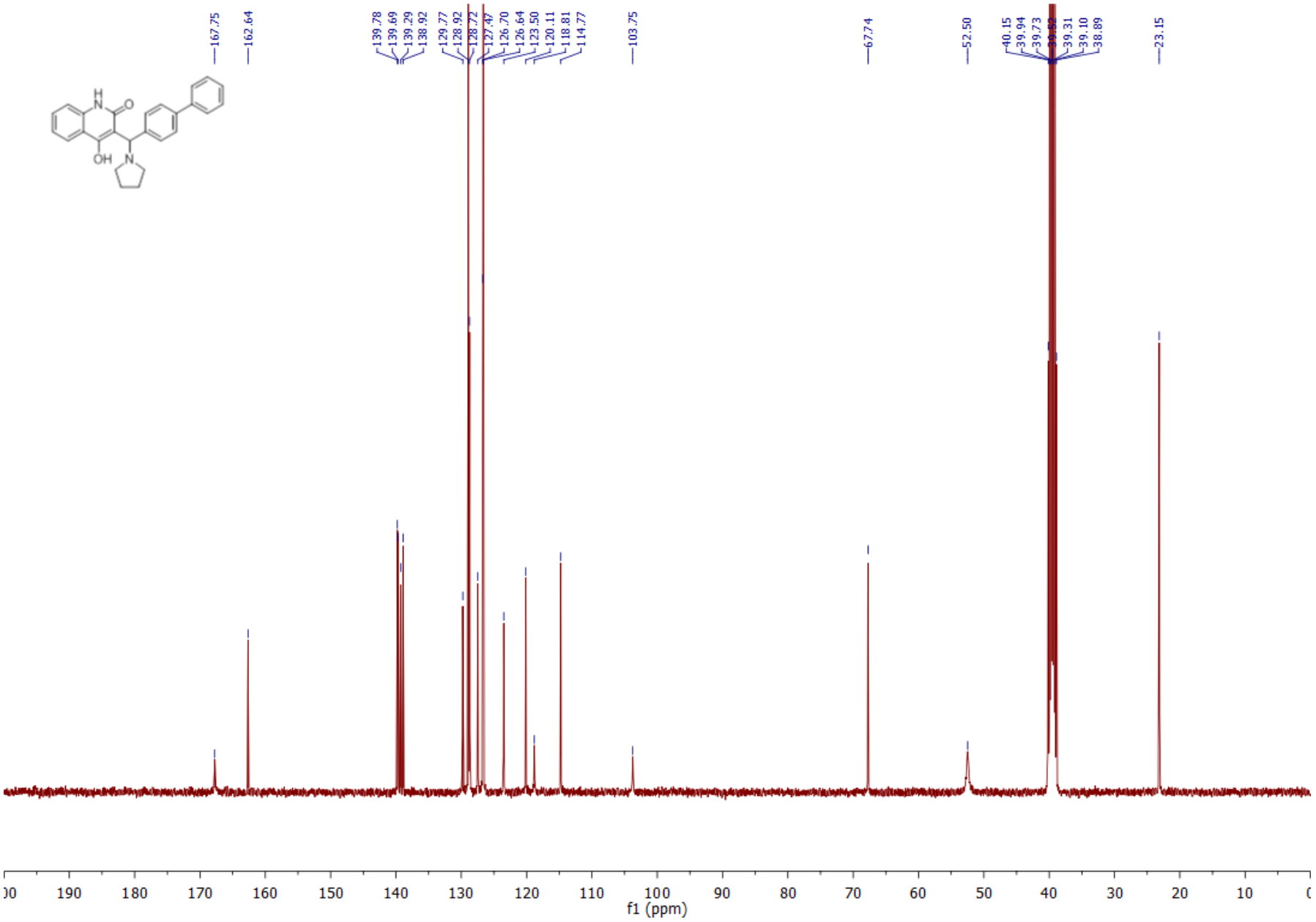
^{13}C NMR (100 MHz, d_6-DMSO): compound **1l**



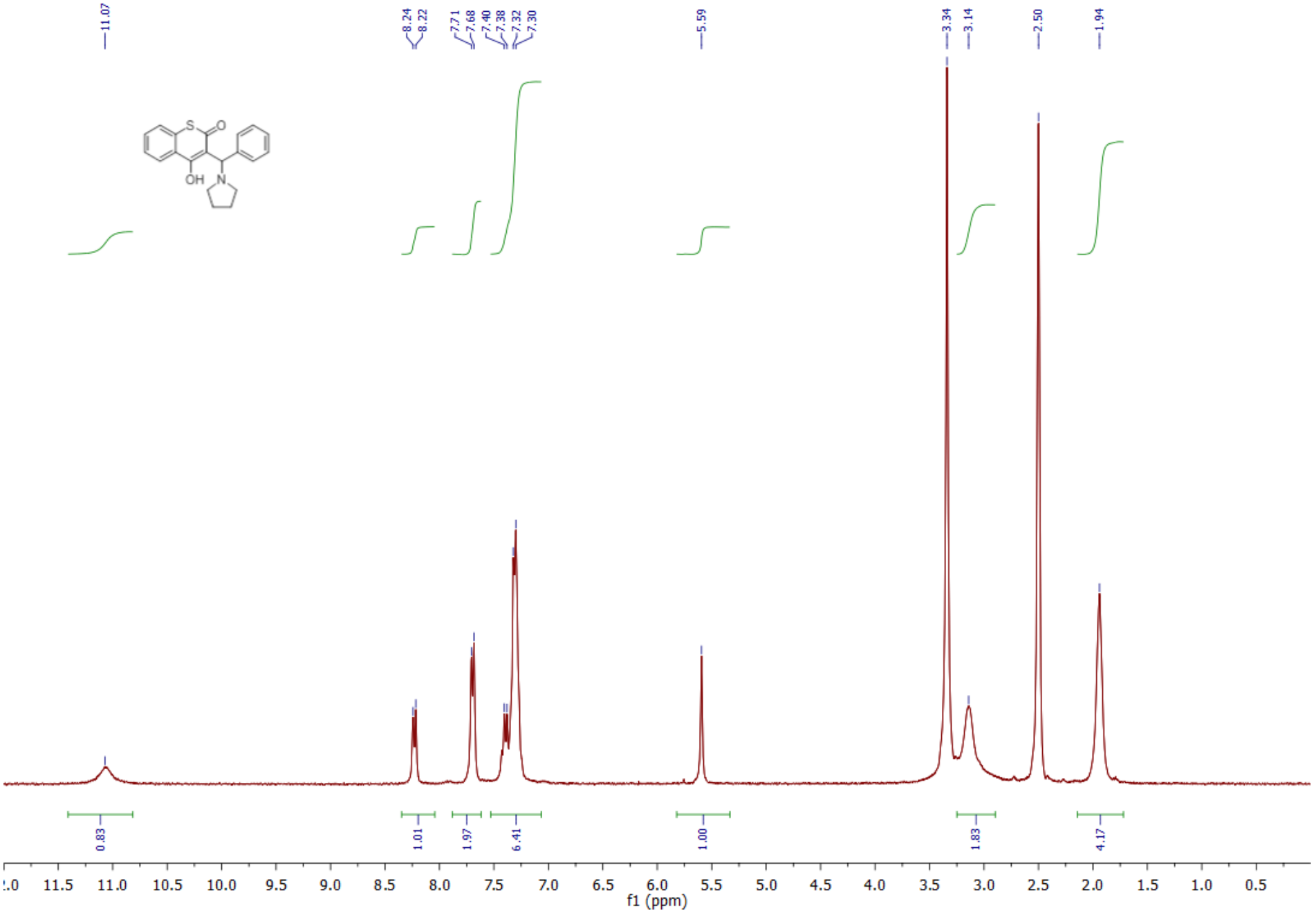
^{1}H NMR (300 MHz, d_6-DMSO): compound **1m**



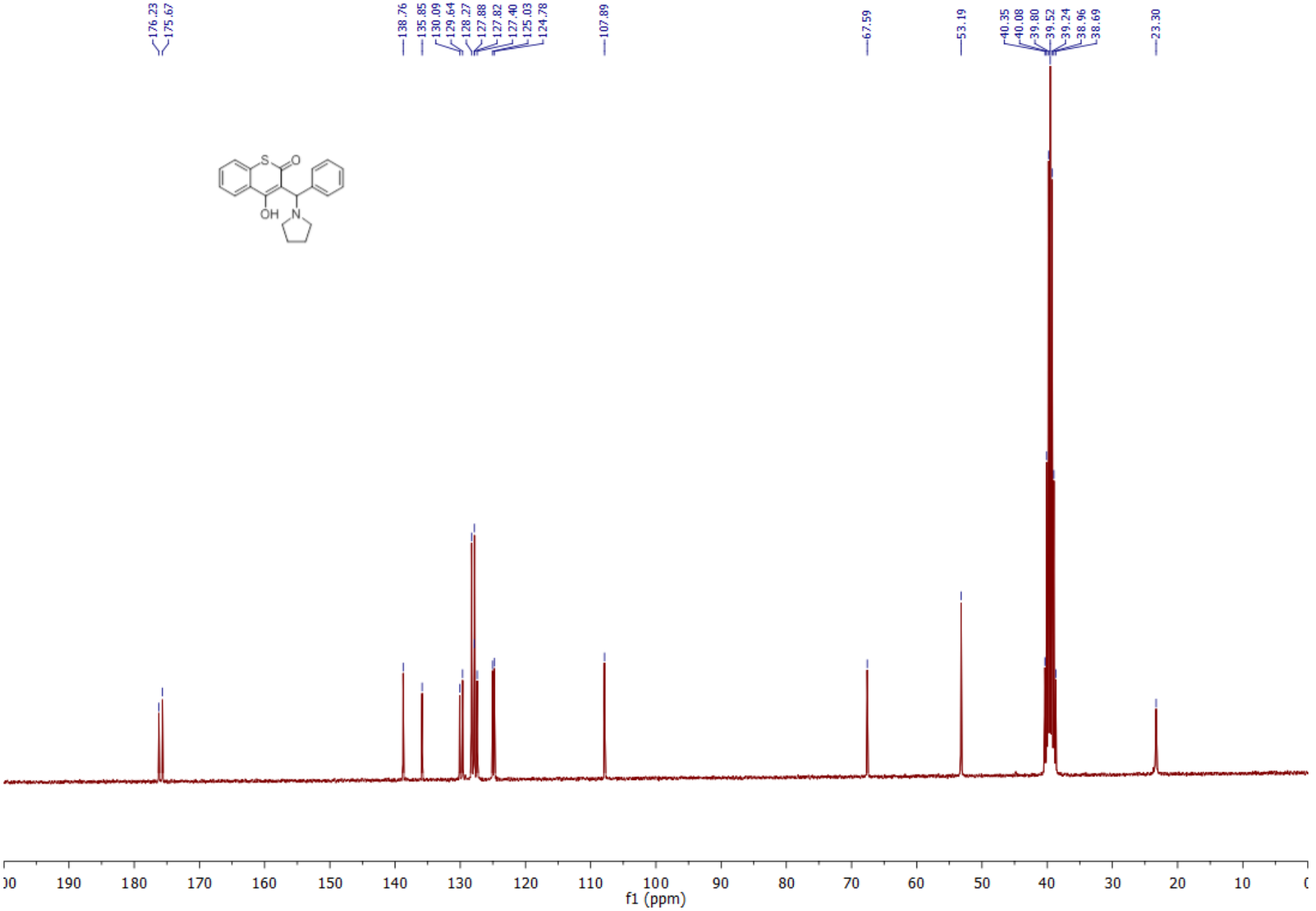
^{13}C NMR (100 MHz, d_6-DMSO): compound **1m**



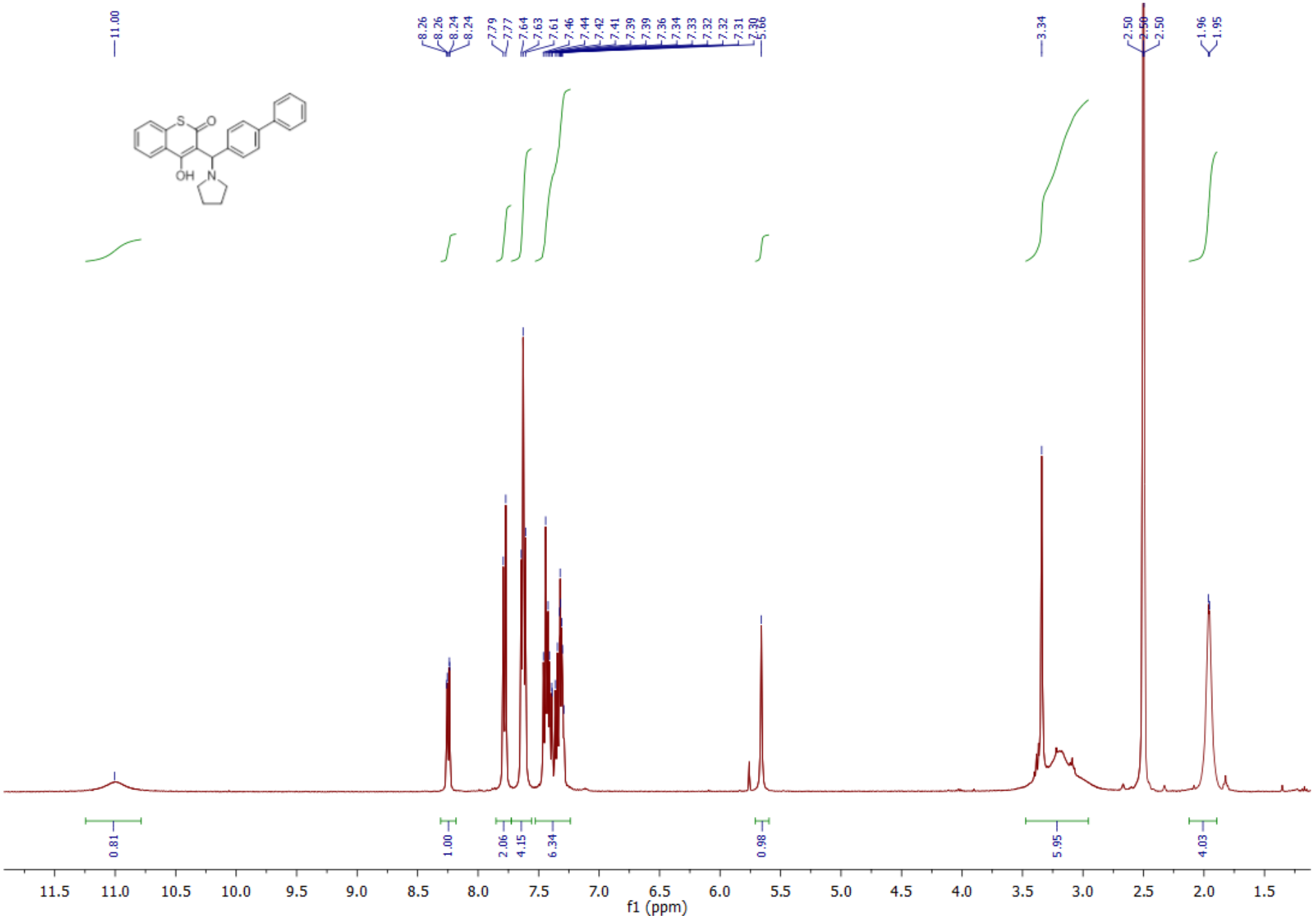
^{1}H NMR (300 MHz, d_6-DMSO): compound **1n**



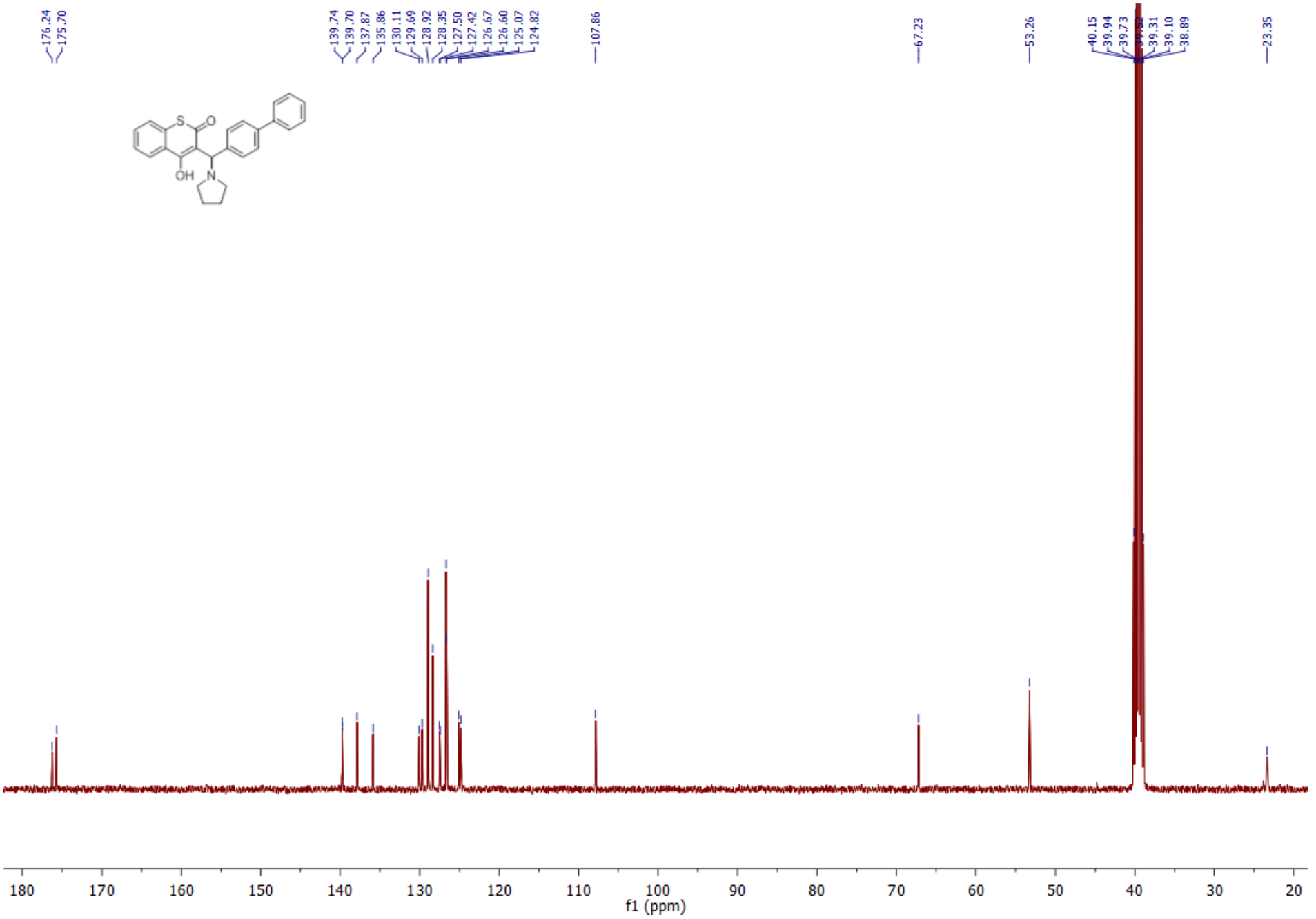
^{13}C NMR (75 MHz, d_6-DMSO): compound **1n**



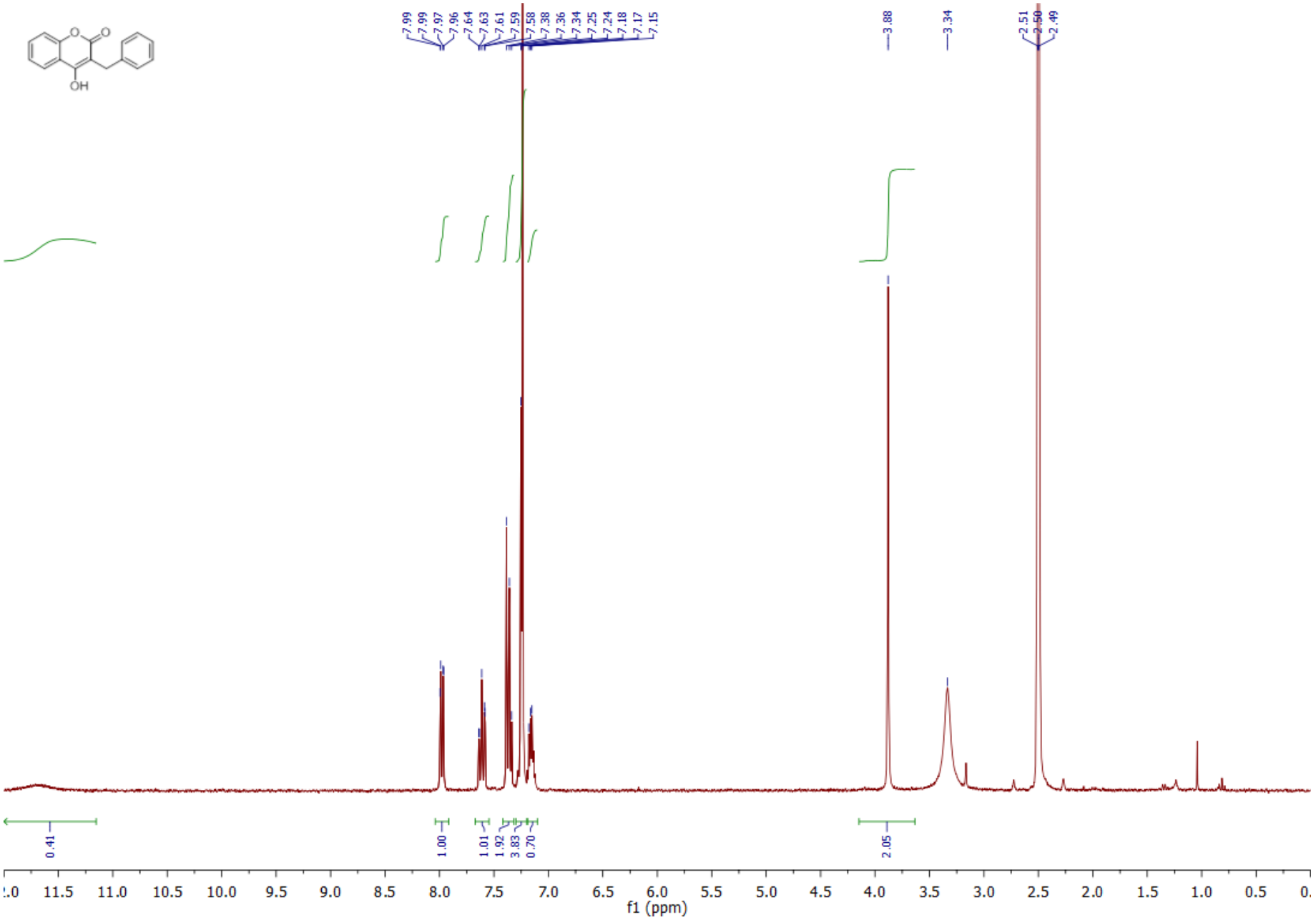
^{1}H NMR (300 MHz, d_6-DMSO): compound **1o**



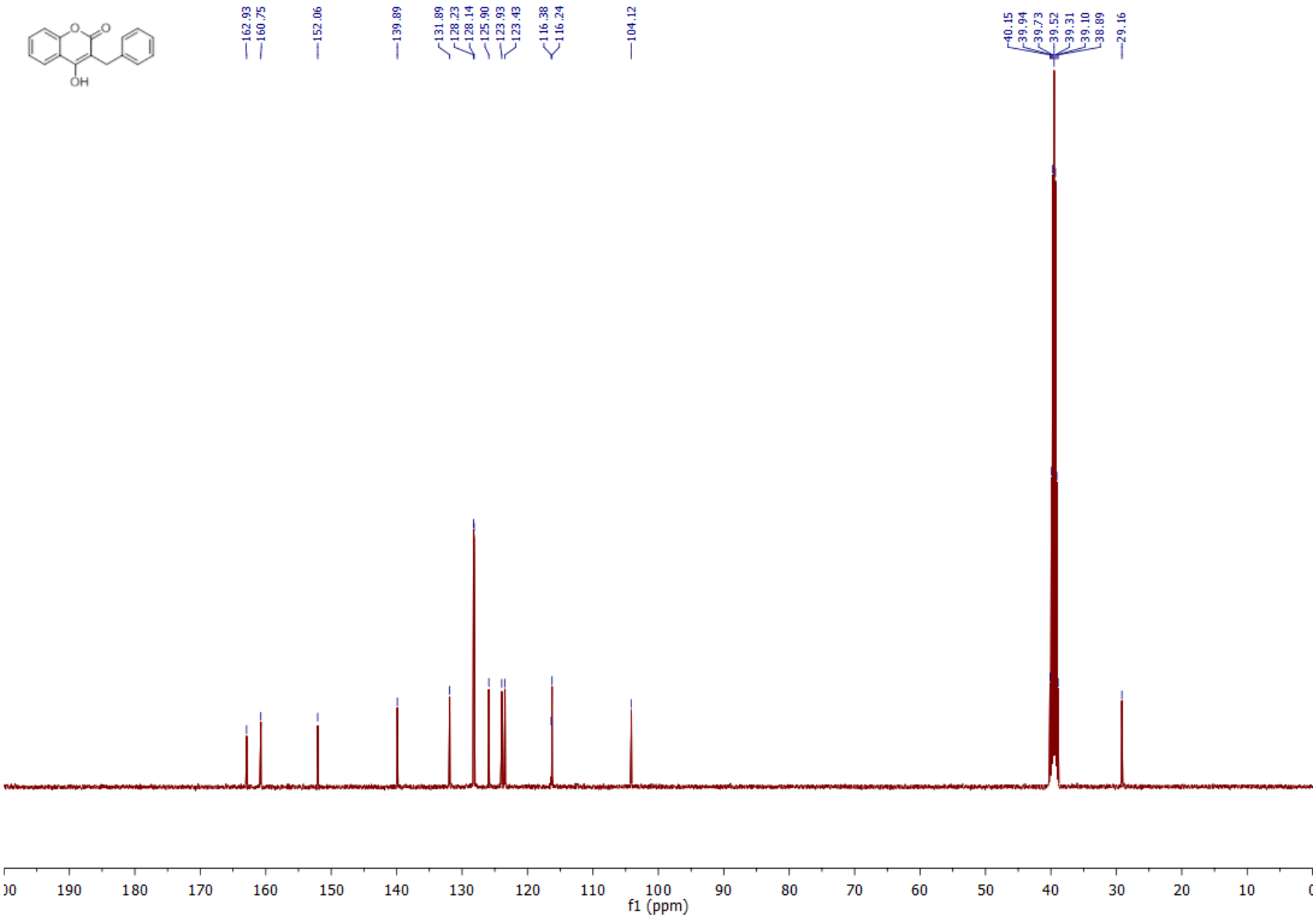
^{13}C NMR (100 MHz, d_6-DMSO): compound **1o**



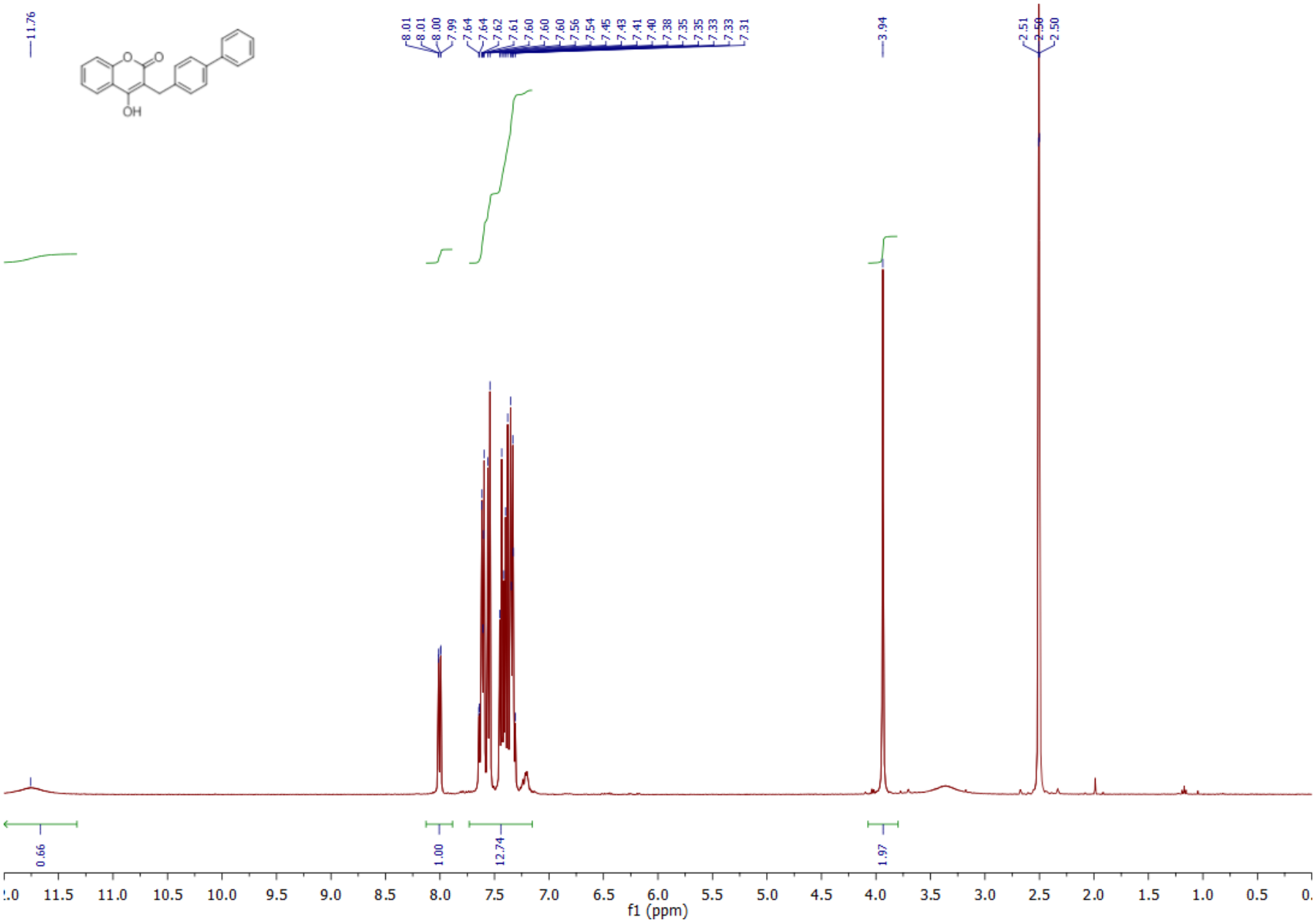
^{1}H NMR (300 MHz, d_6-DMSO): compound **2a**



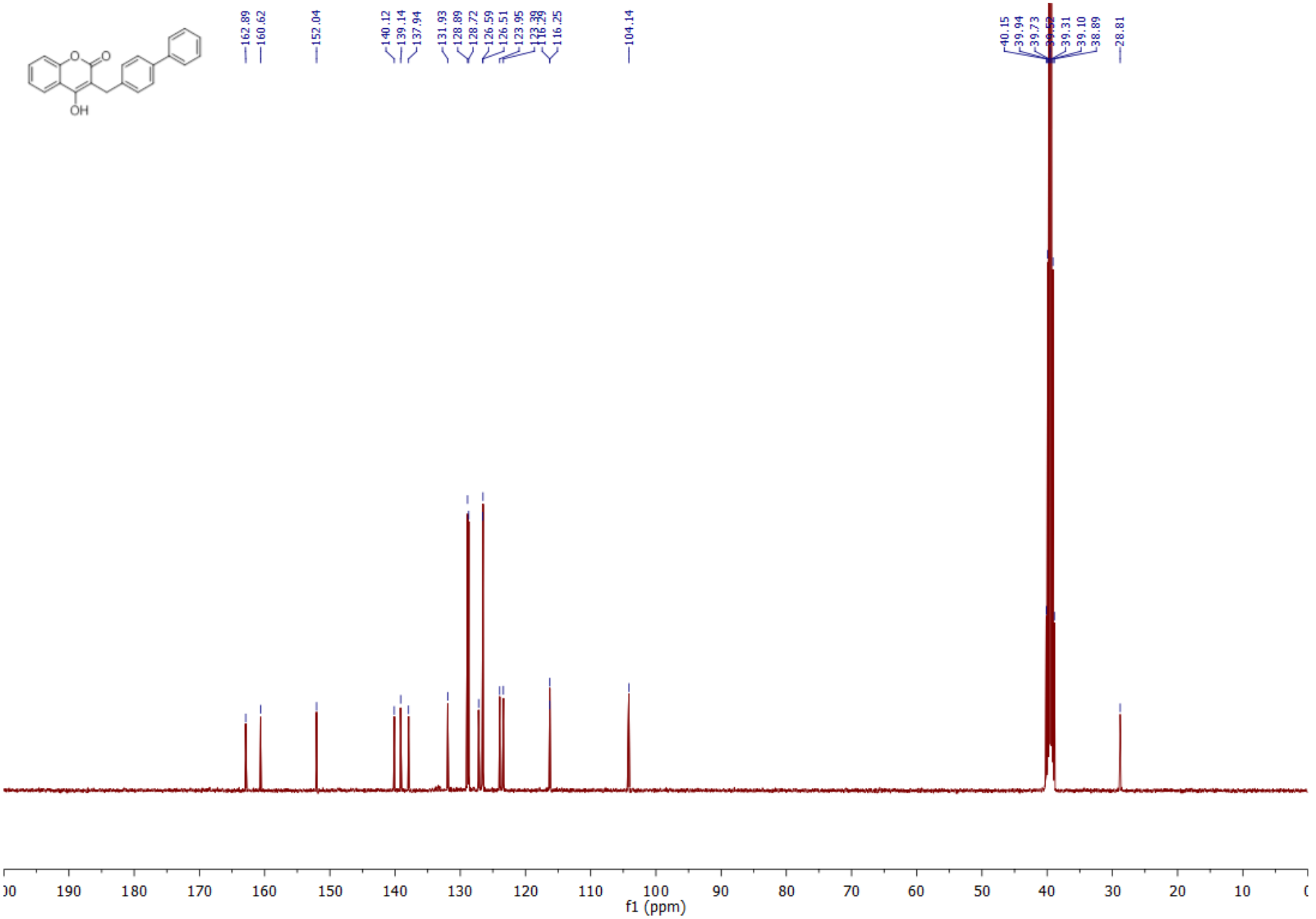
^{13}C NMR (75 MHz, d_6-DMSO): compound **2a**



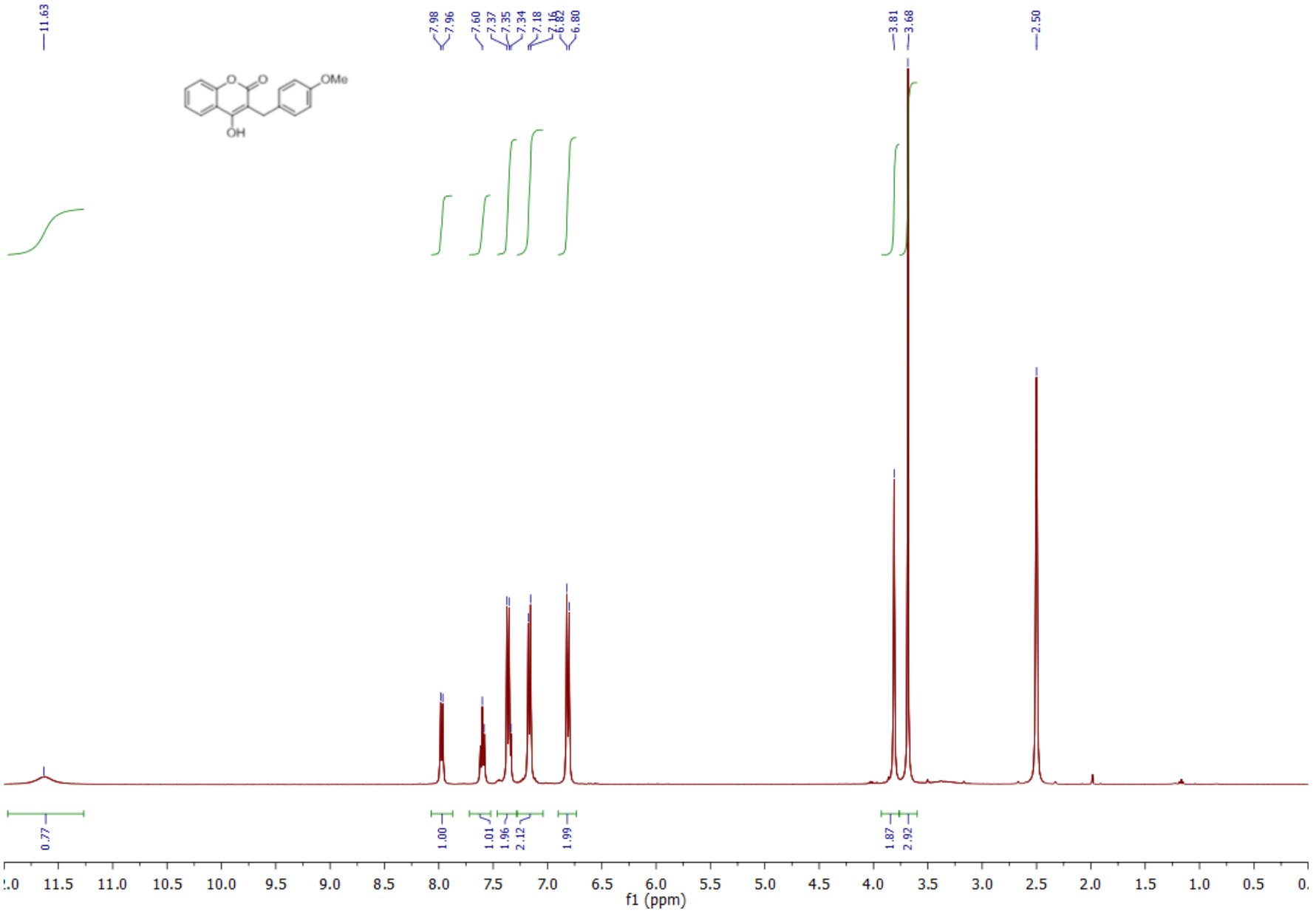
^{1}H NMR (400 MHz, d_6-DMSO): compound **2b**



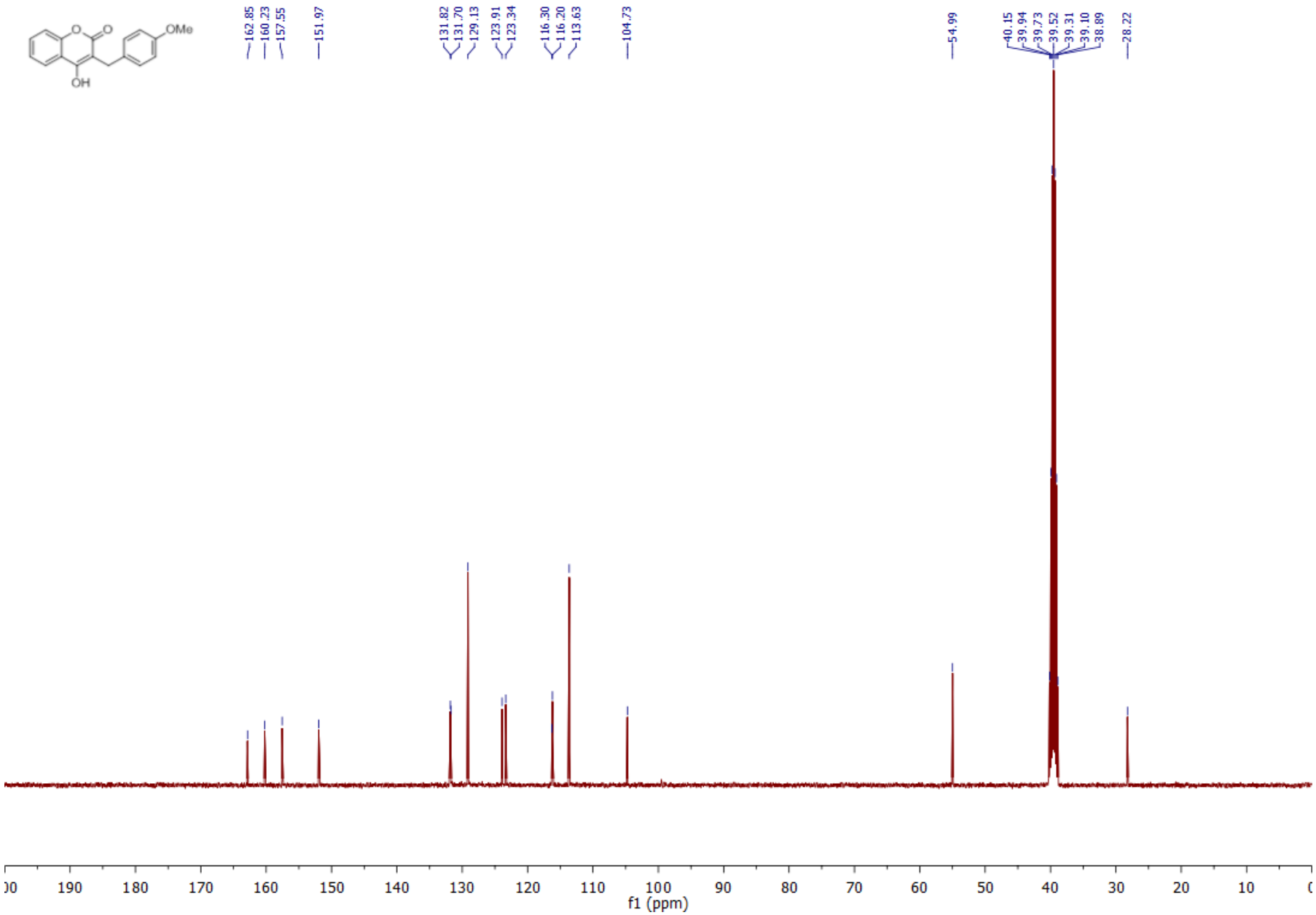
^{13}C NMR (100 MHz, d_6-DMSO): compound **2b**



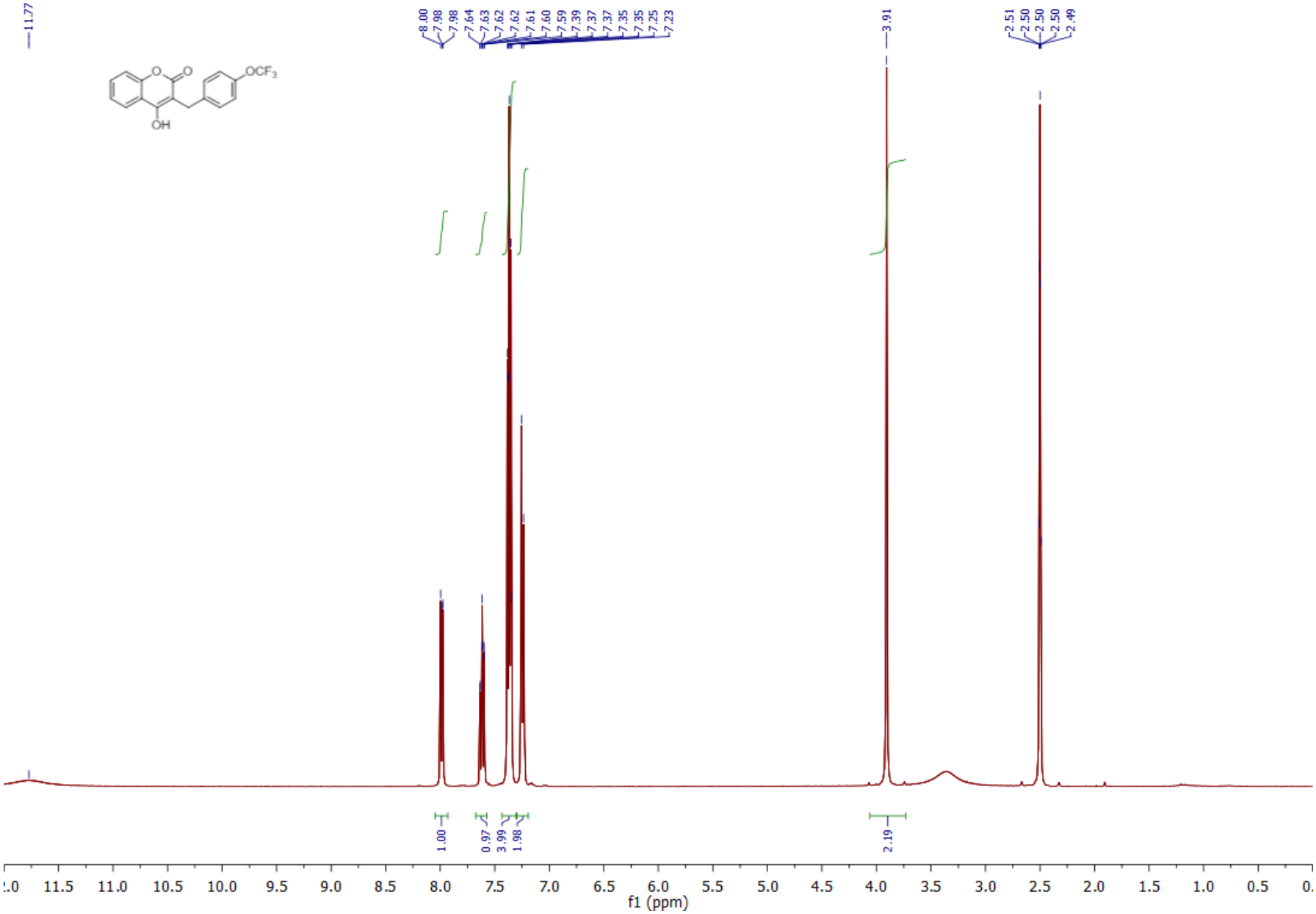
^{1}H NMR (400 MHz, d_6-DMSO): compound **2c**



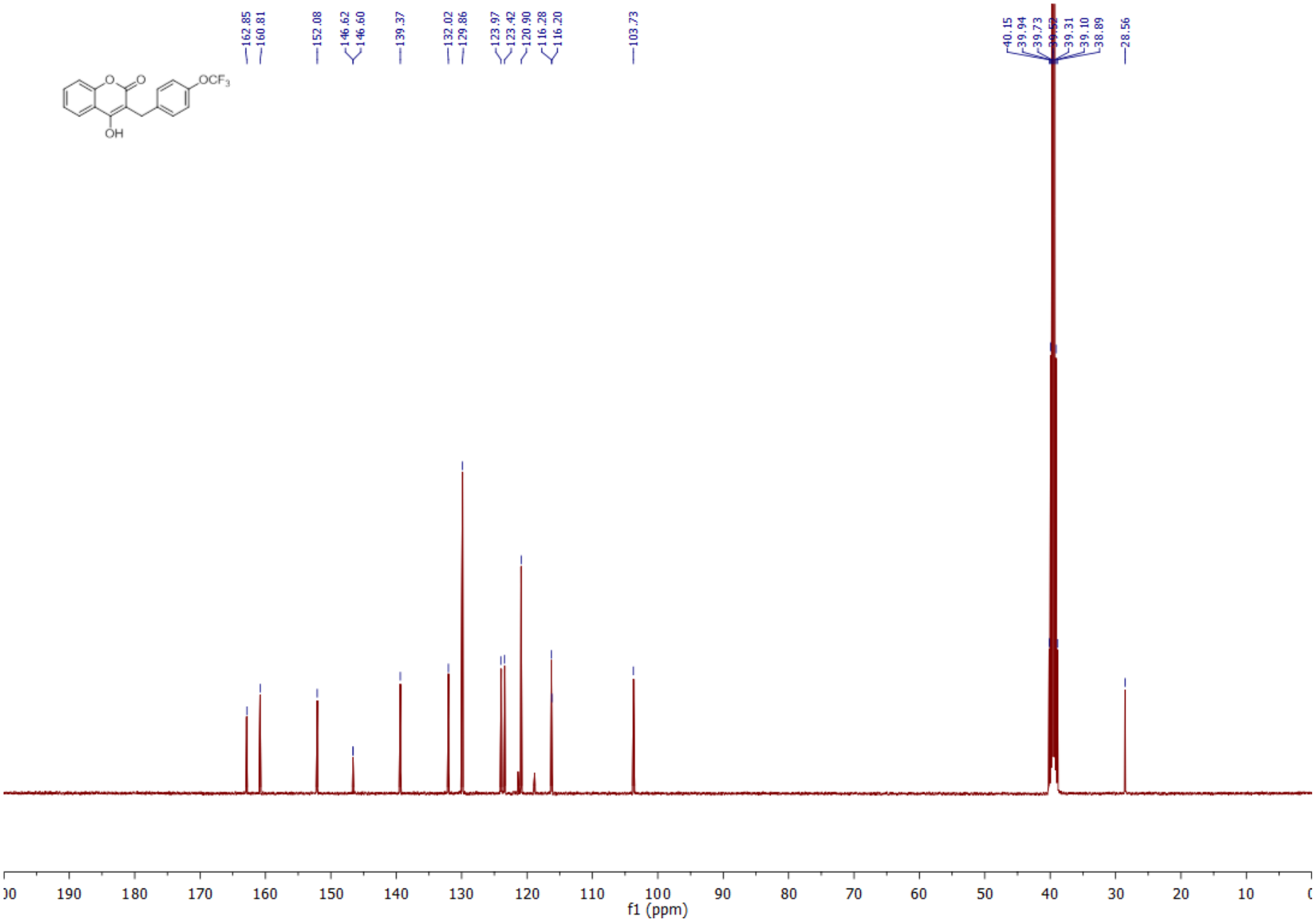
^{13}C NMR (100 MHz, d_6-DMSO): compound **2c**



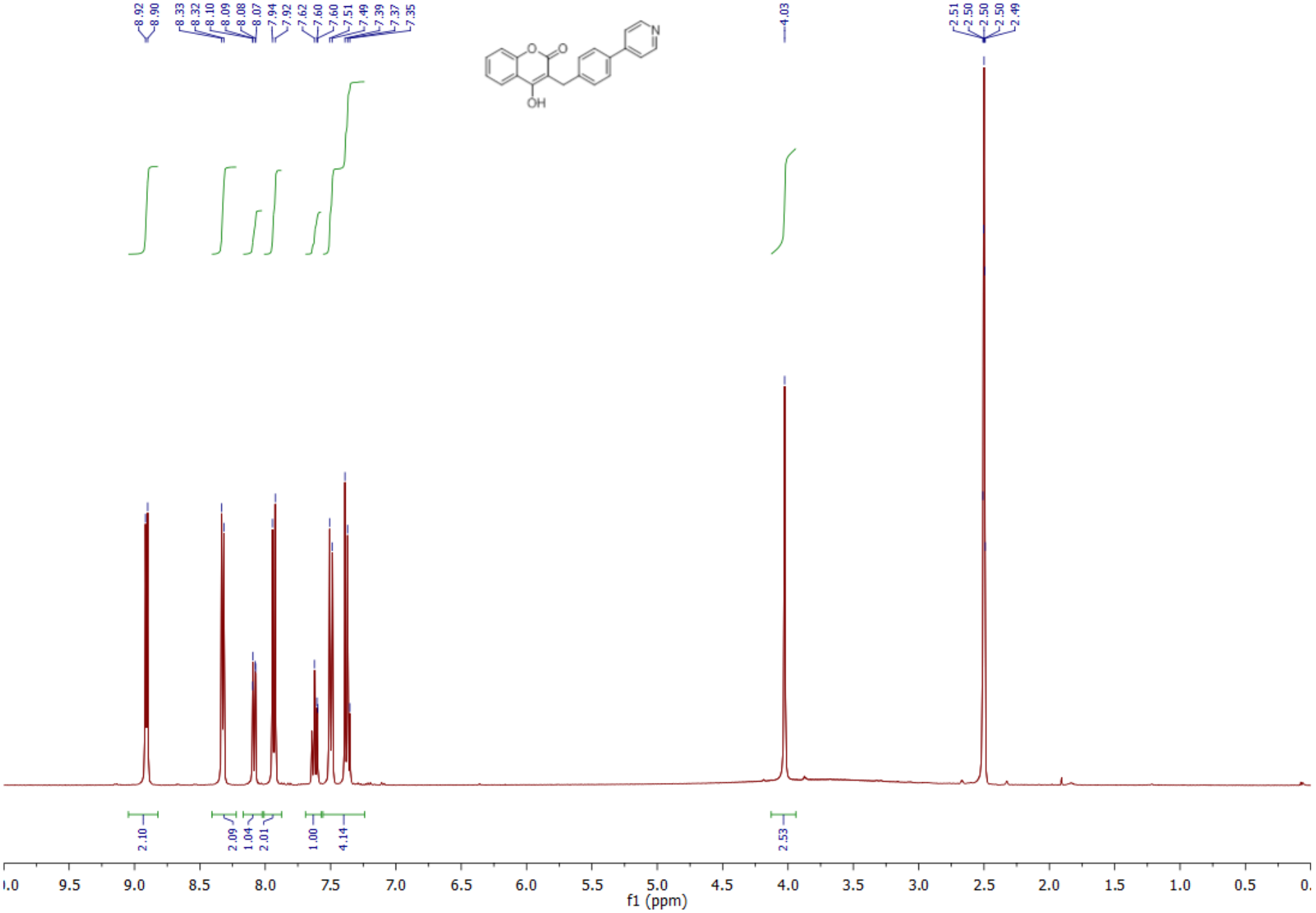
^{1}H NMR (400 MHz, d_6-DMSO): compound **2d**



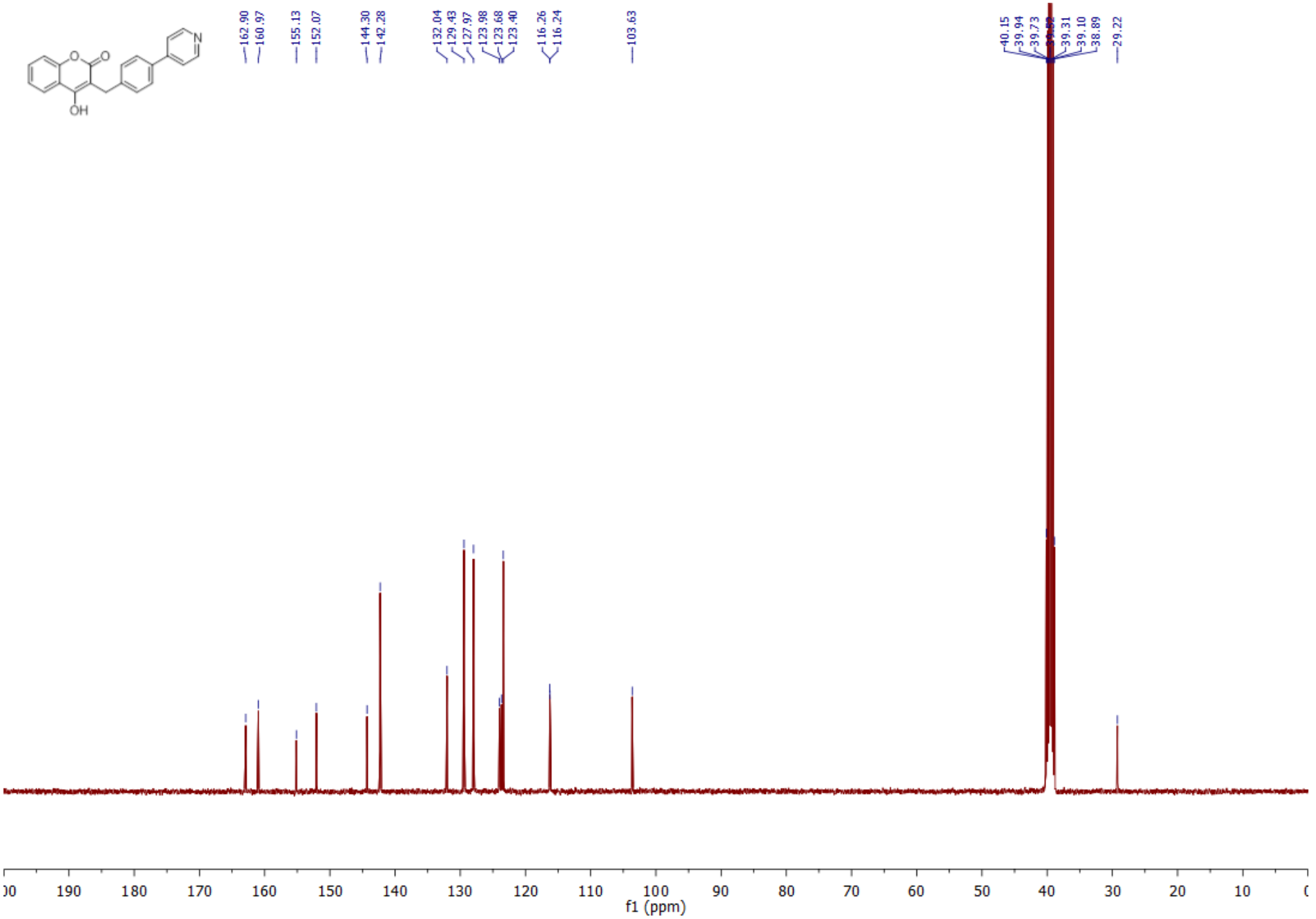
^{13}C NMR (100 MHz, d_6-DMSO): compound **2d**



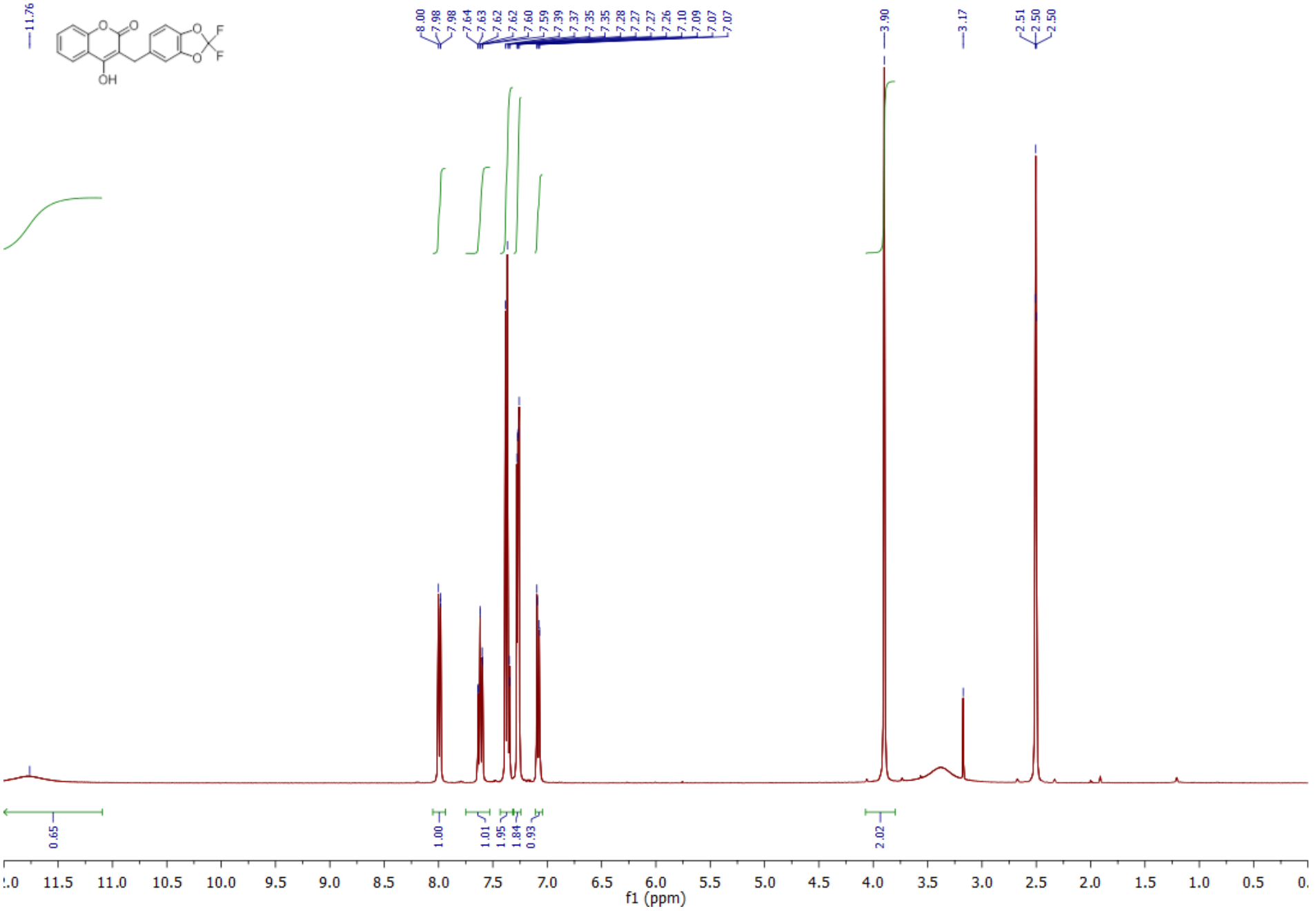
^{1}H NMR (400 MHz, d_6-DMSO): compound **2e**



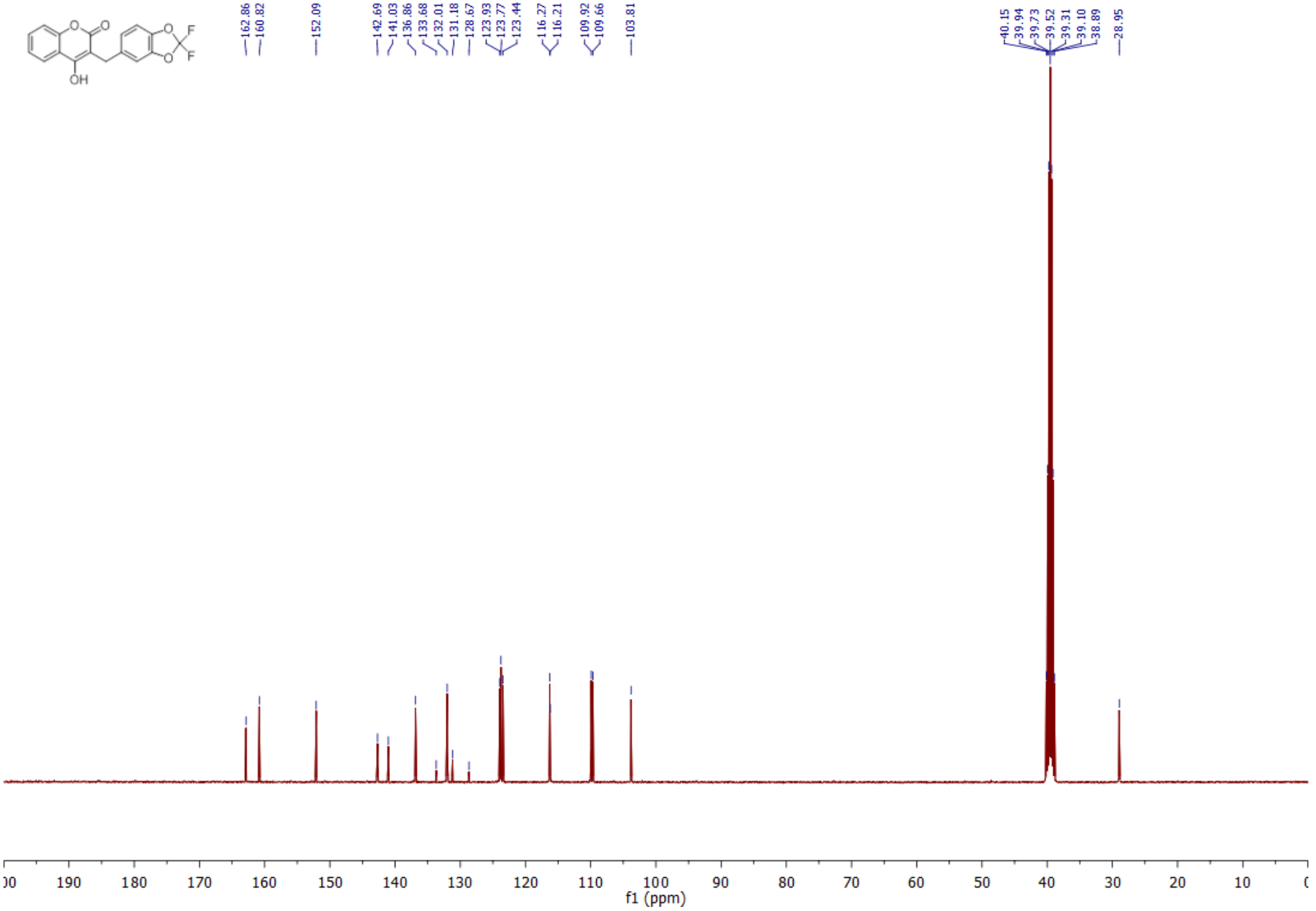
^{13}C NMR (100 MHz, d_6-DMSO): compound **2e**



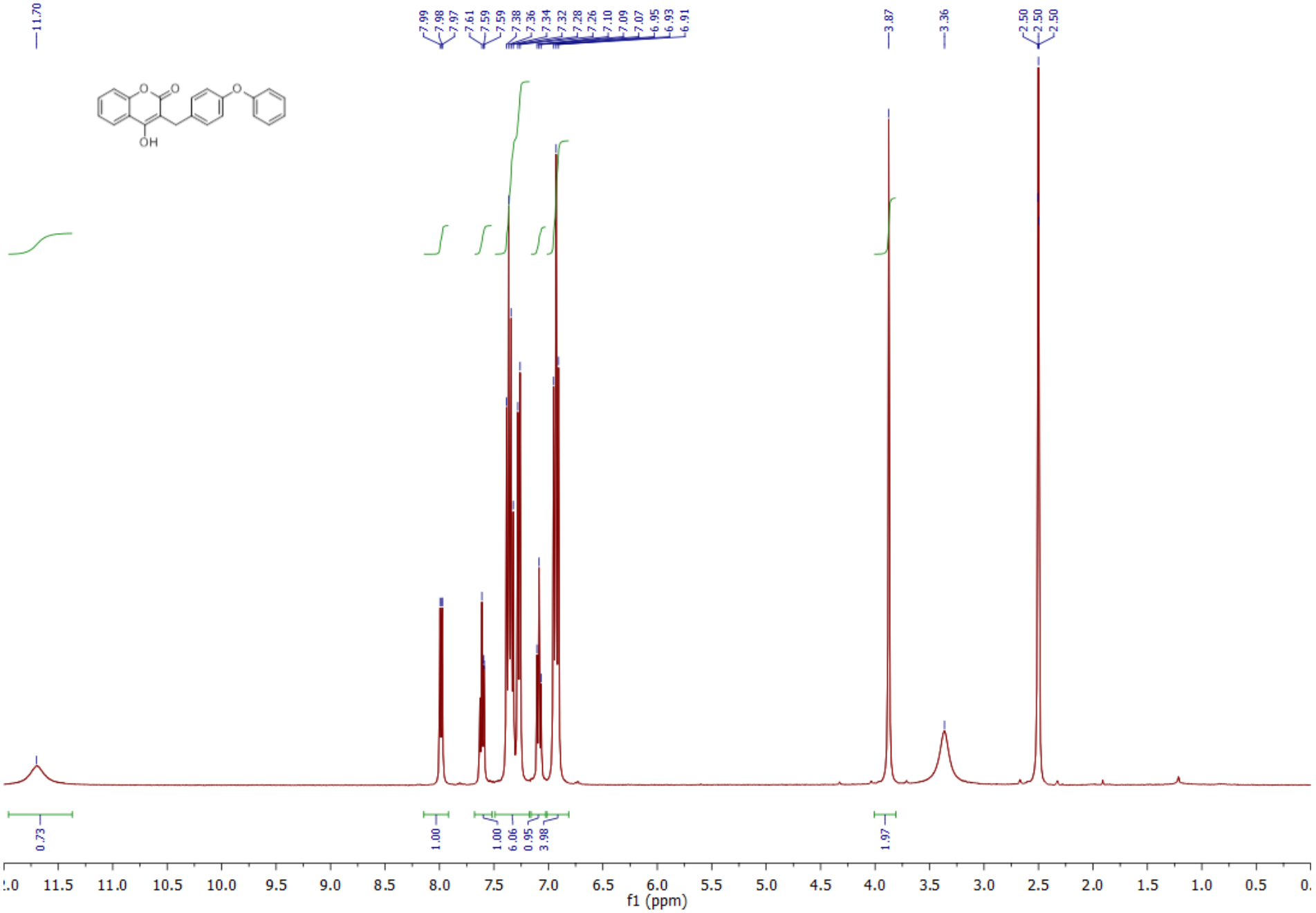
^{1}H NMR (400 MHz, d_6-DMSO): compound **2f**



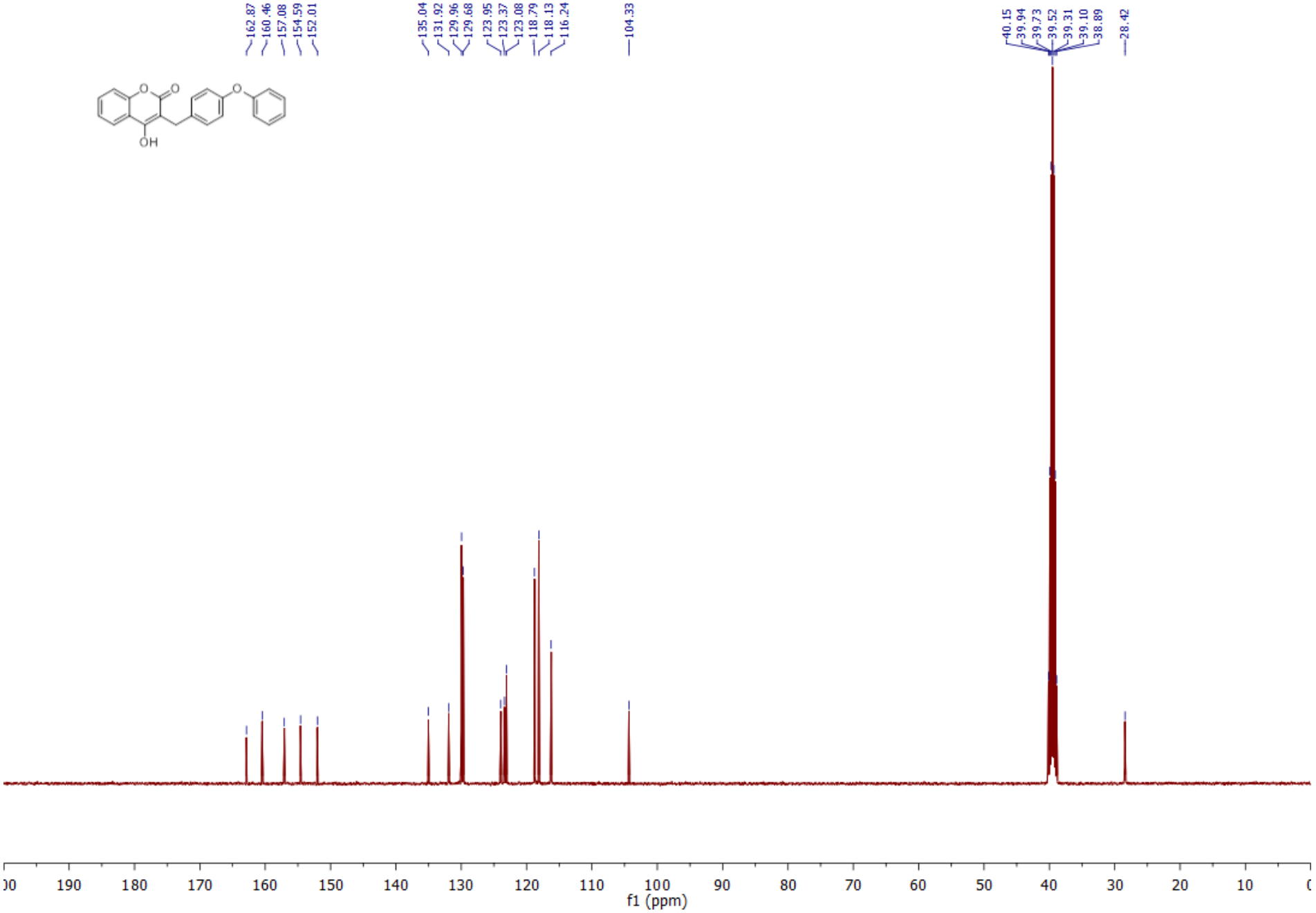
^{13}C NMR (100 MHz, d_6-DMSO): compound **2f**



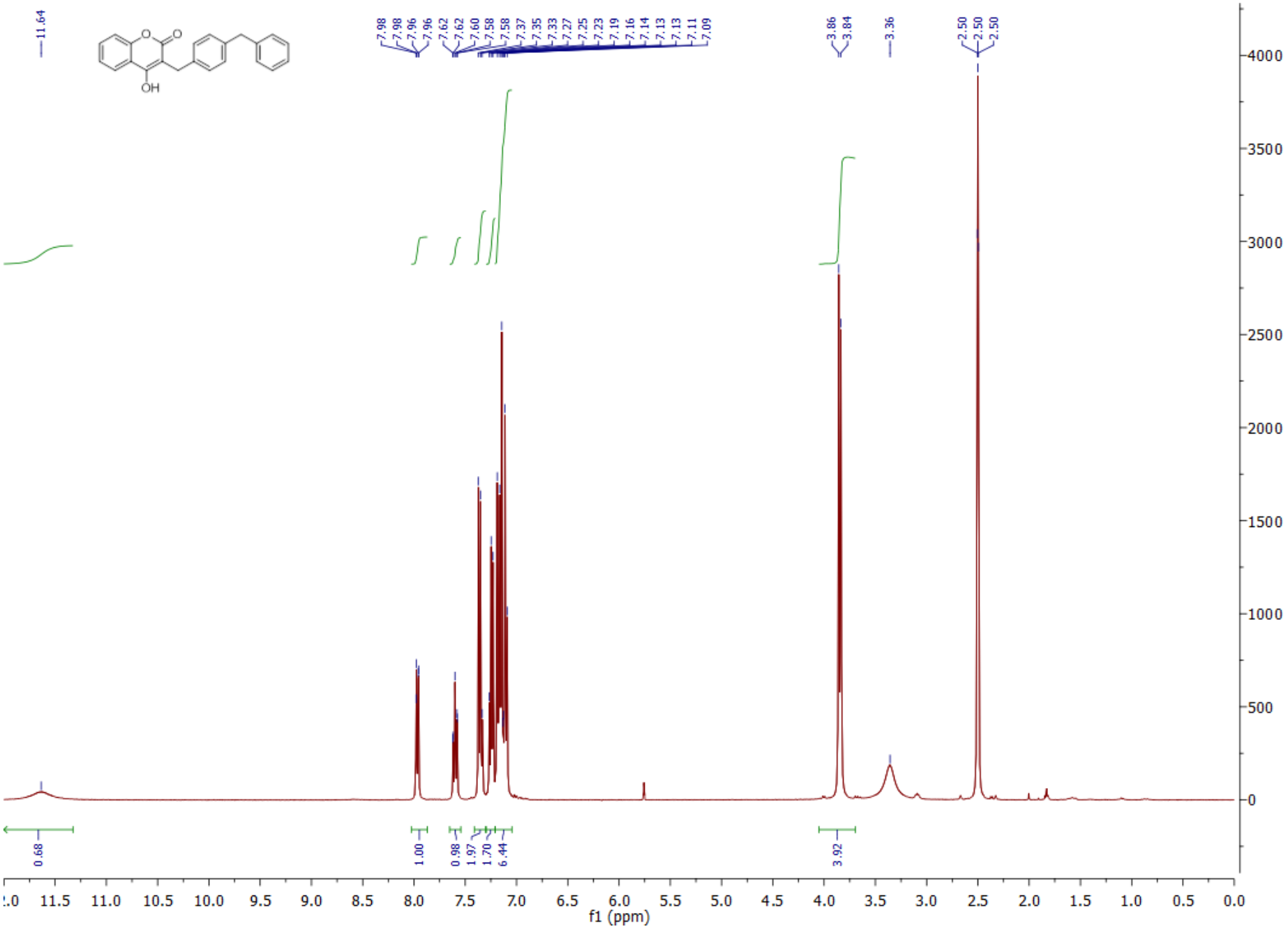
^{1}H NMR (400 MHz, d_6-DMSO): compound **2g**



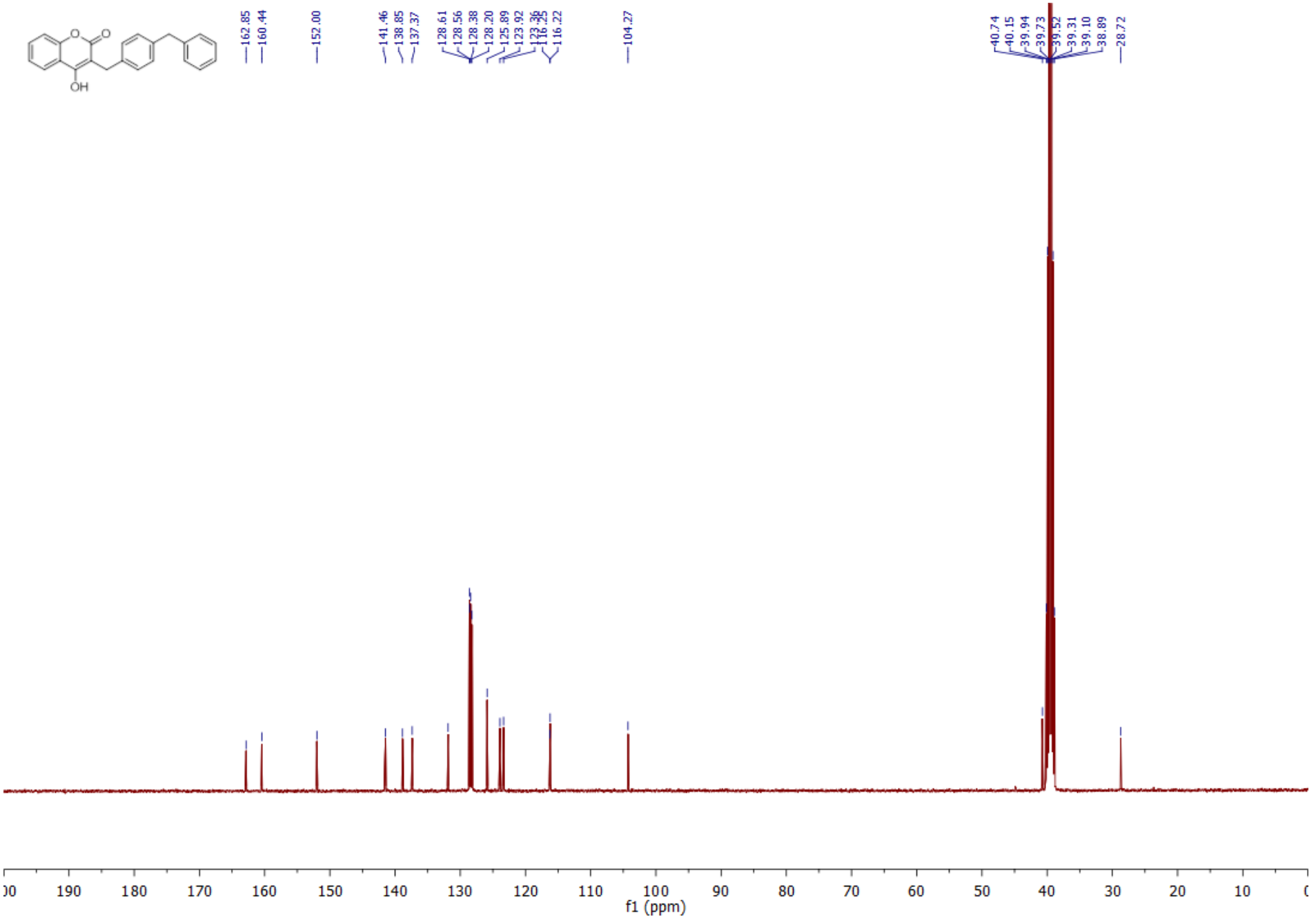
^{13}C NMR (100 MHz, d_6-DMSO): compound **2g**



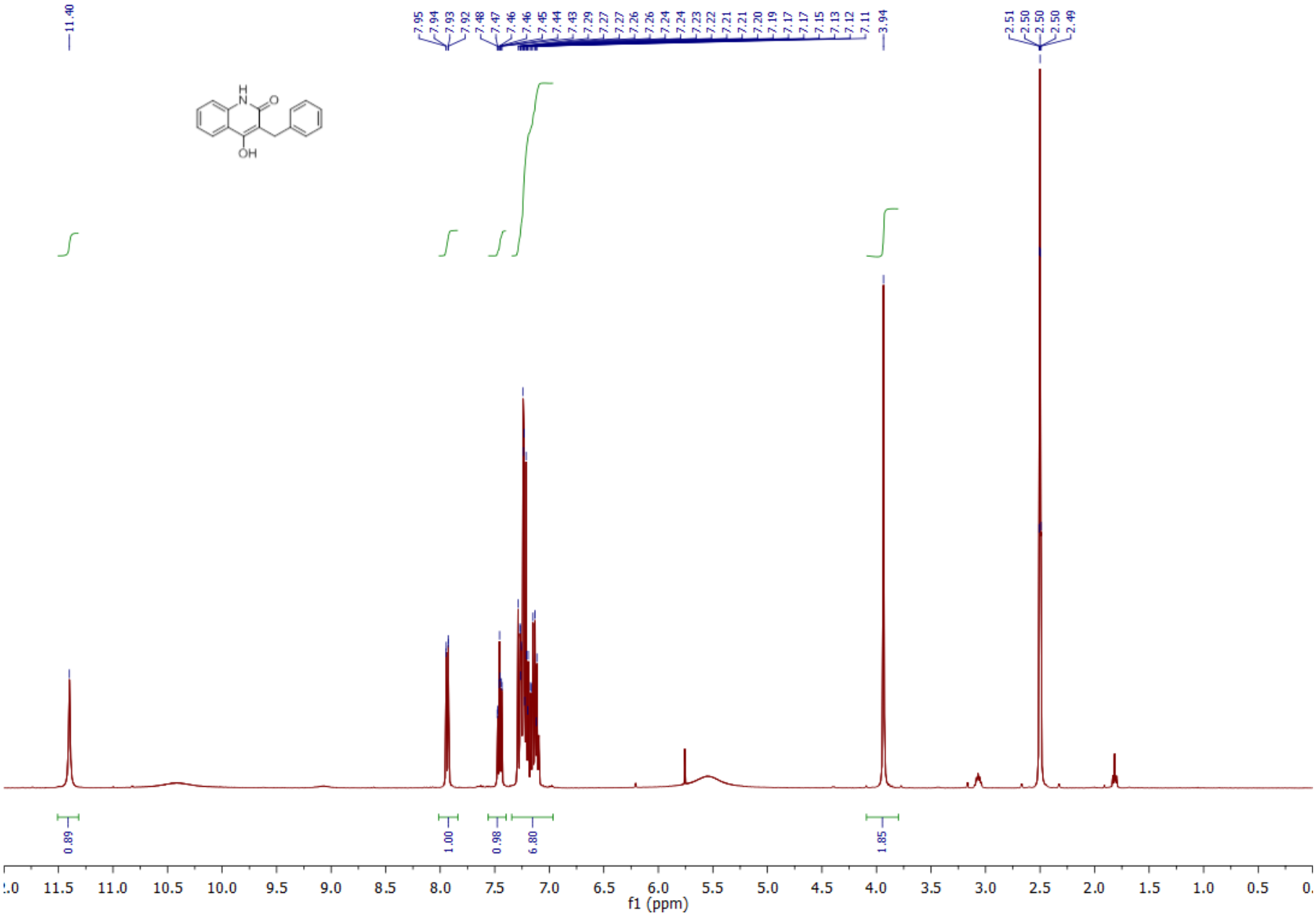
^{1}H NMR (400 MHz, d_6-DMSO): compound **2h**



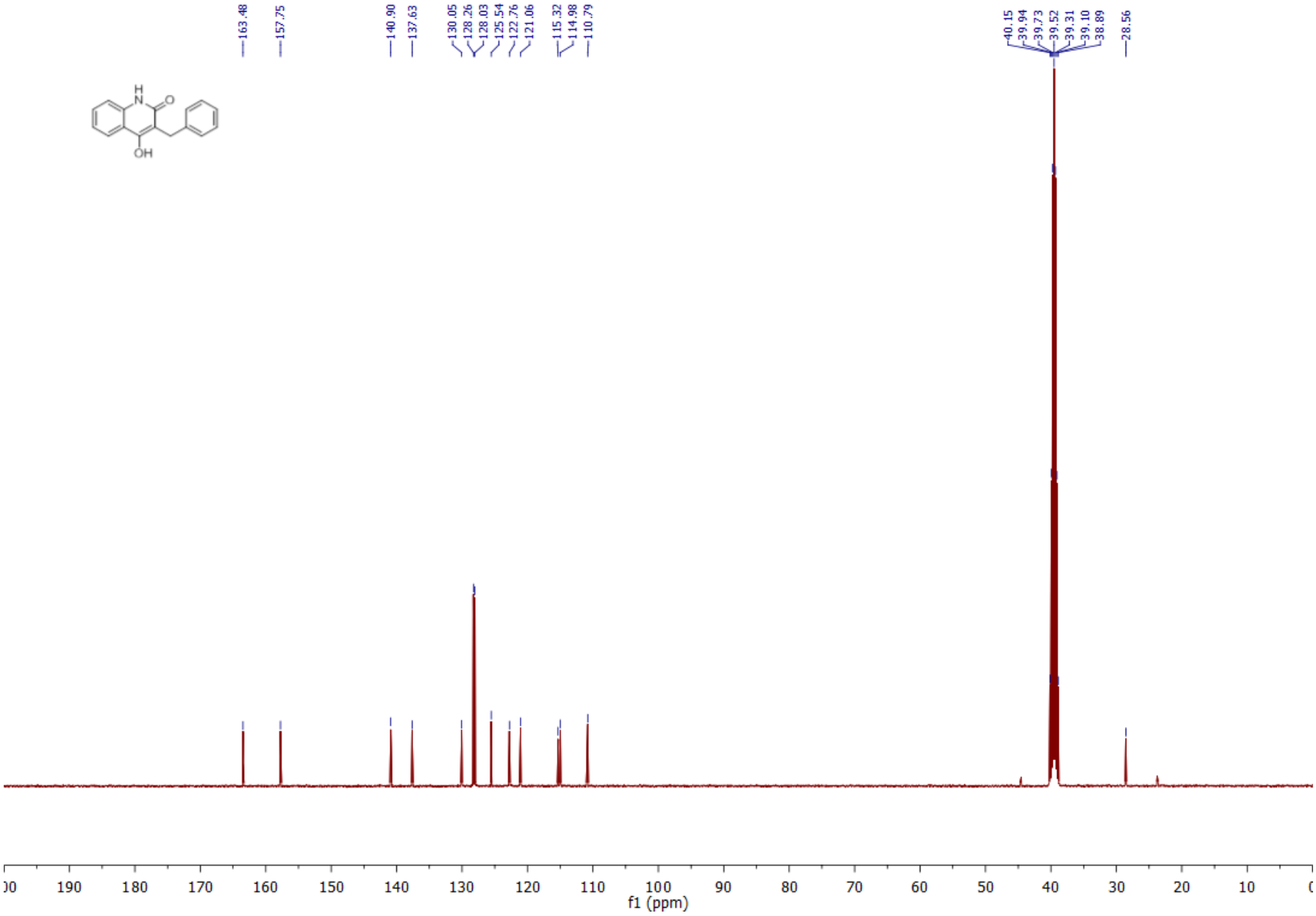
^{13}C NMR (100 MHz, d_6-DMSO): compound **2h**



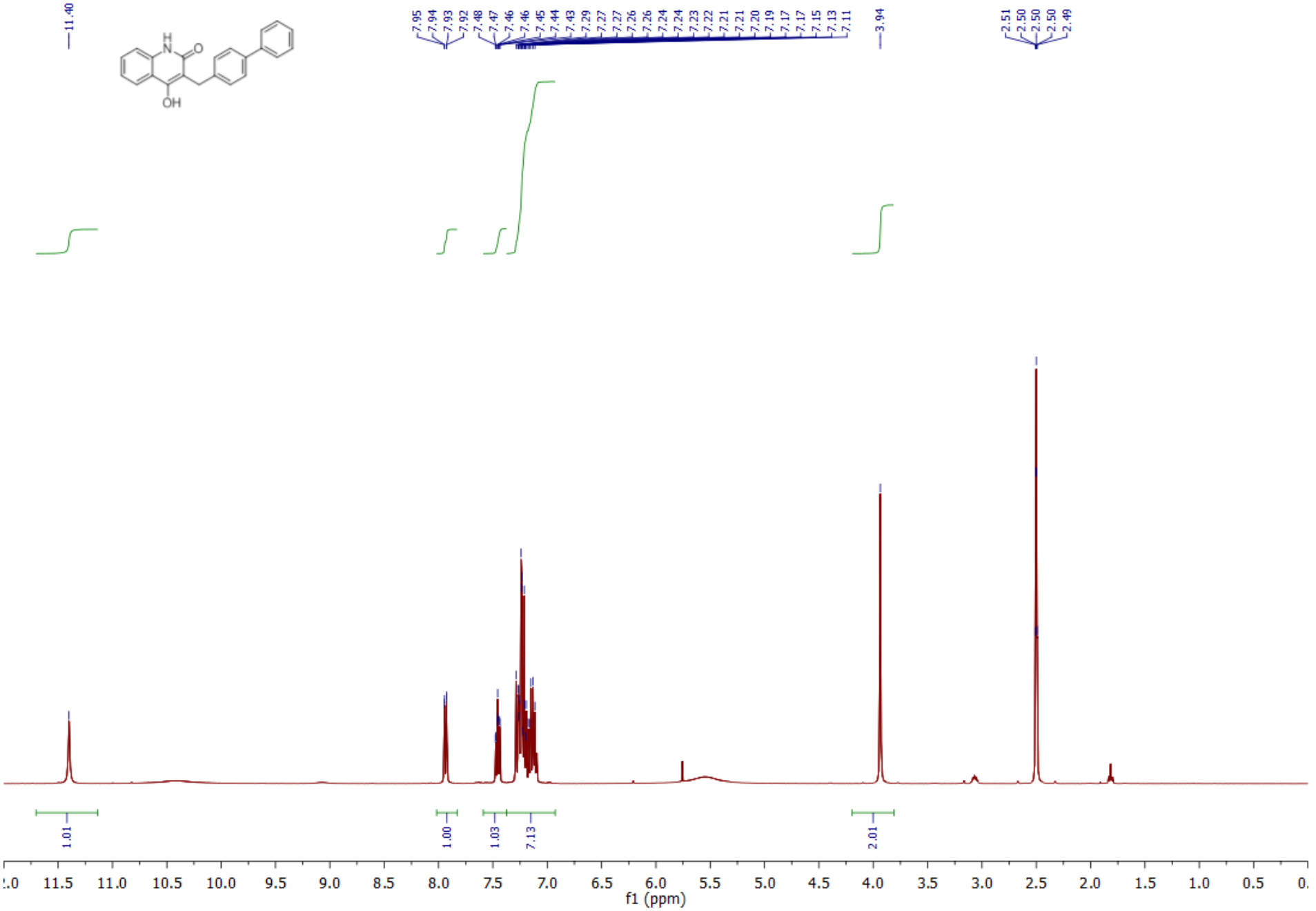
^{1}H NMR (400 MHz, d_6-DMSO): compound **2i**



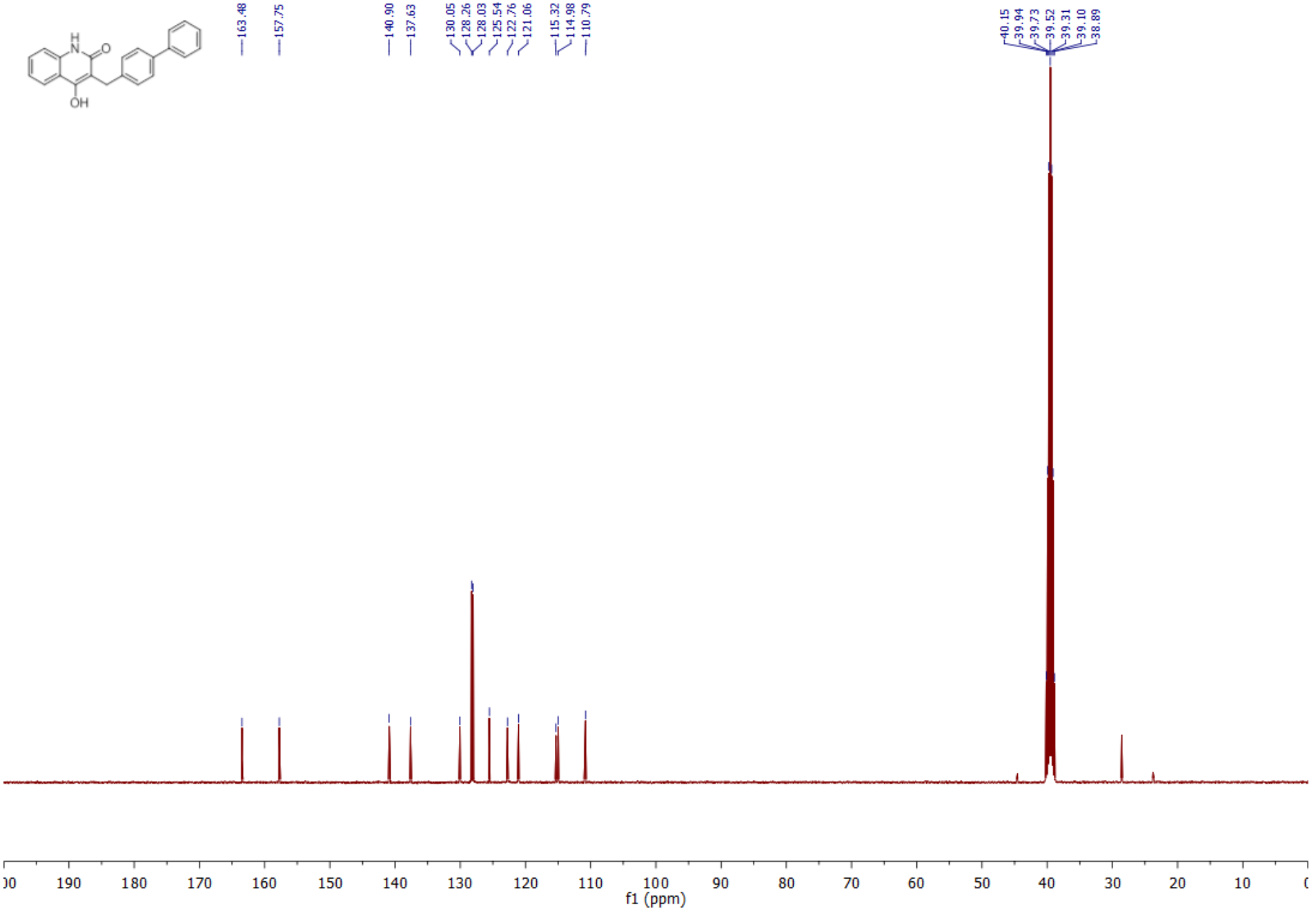
^{13}C NMR (100 MHz, d_6-DMSO): compound **2i**



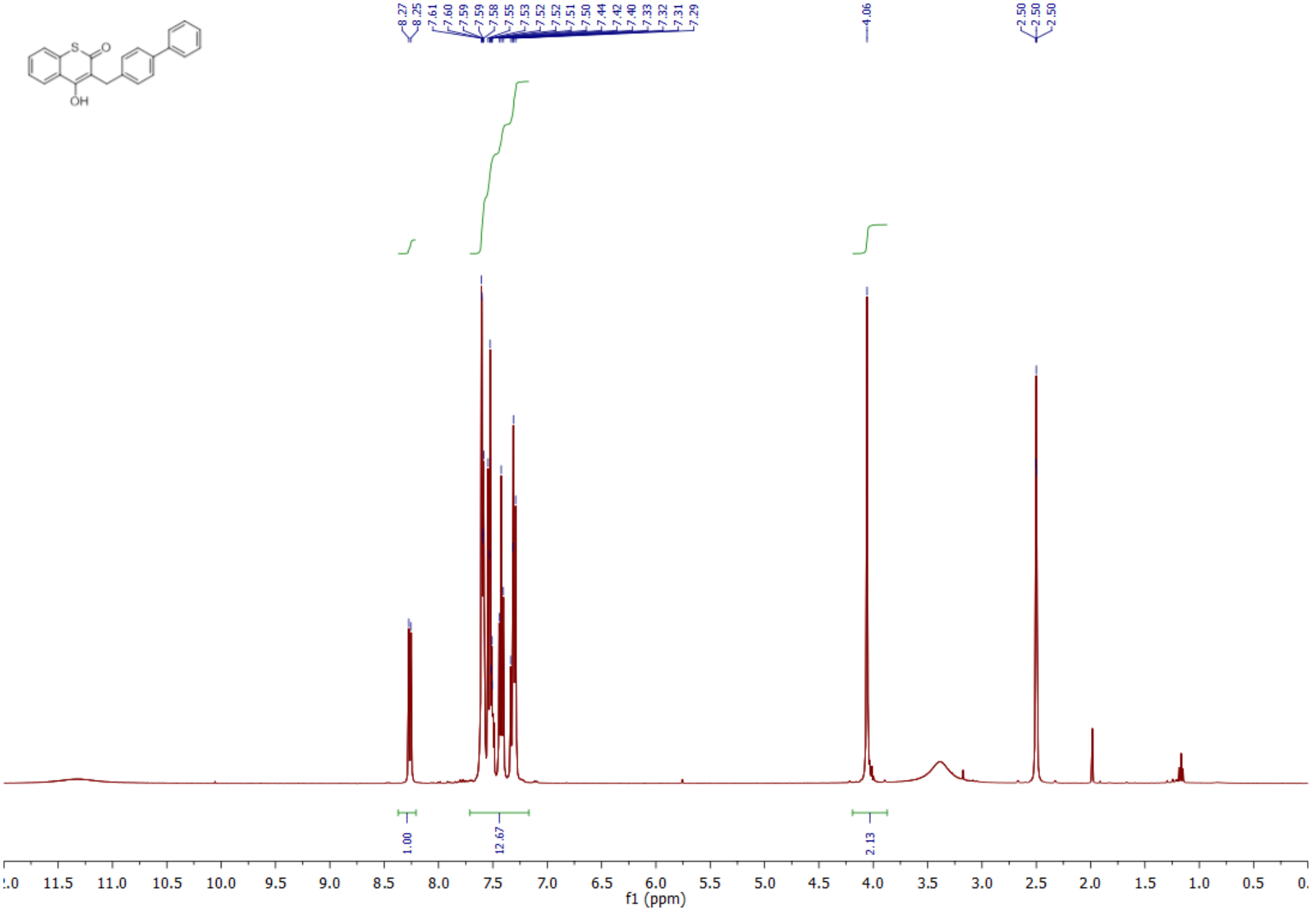
^{1}H NMR (400 MHz, d_6-DMSO): compound **2j**



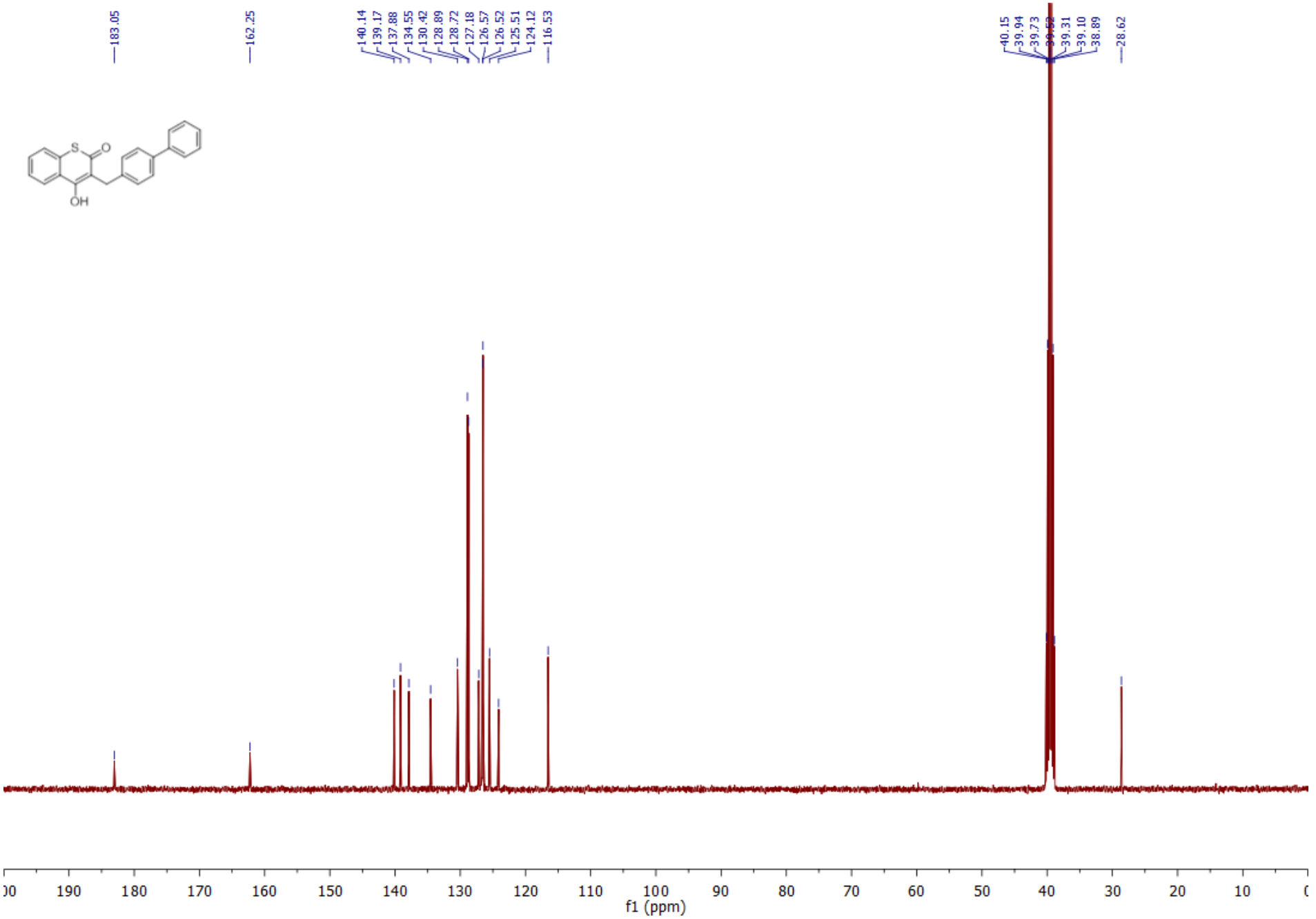
^{13}C NMR (100 MHz, d_6-DMSO): compound **2j**



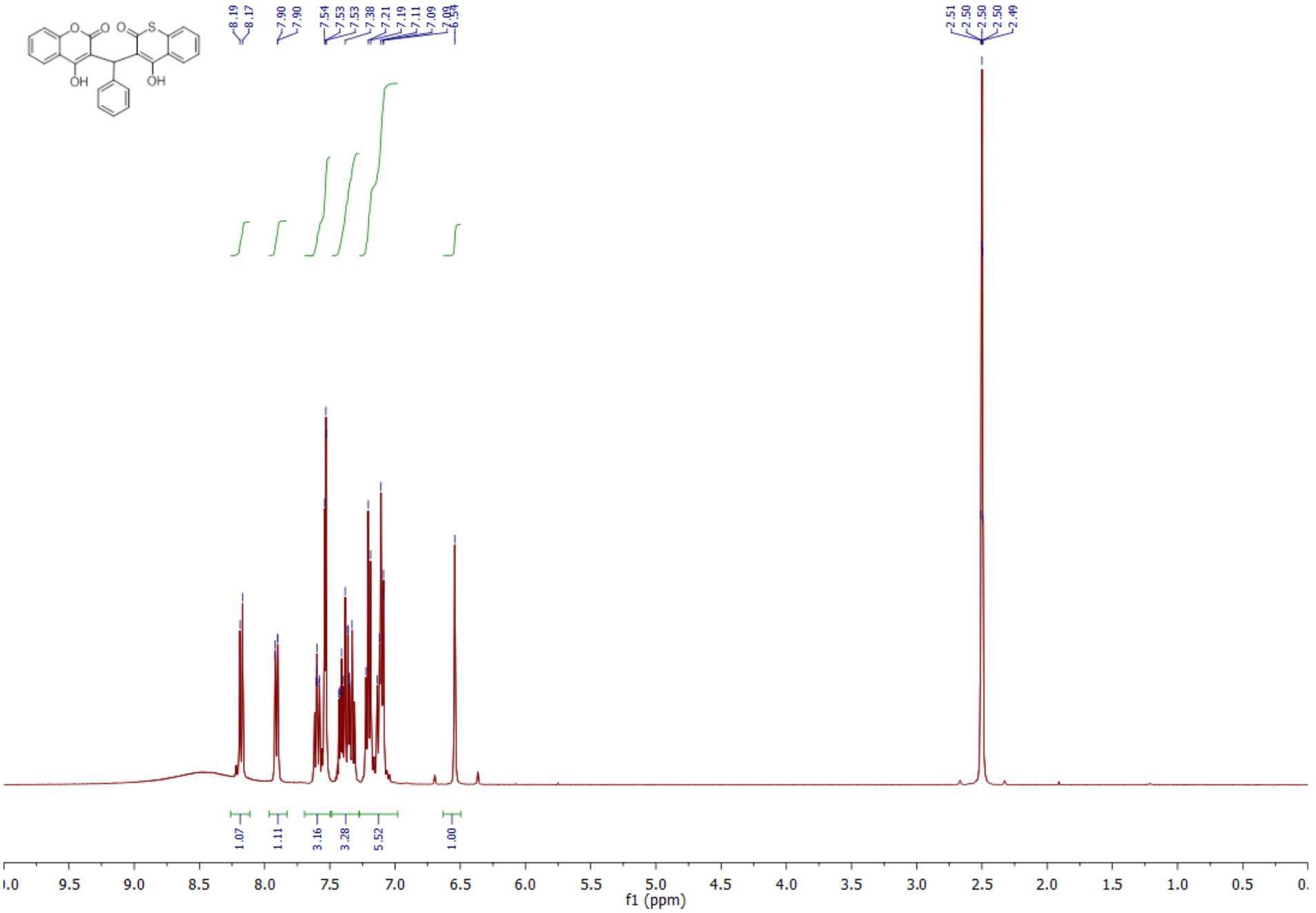
^{1}H NMR (400 MHz, d_6-DMSO): compound **2k**



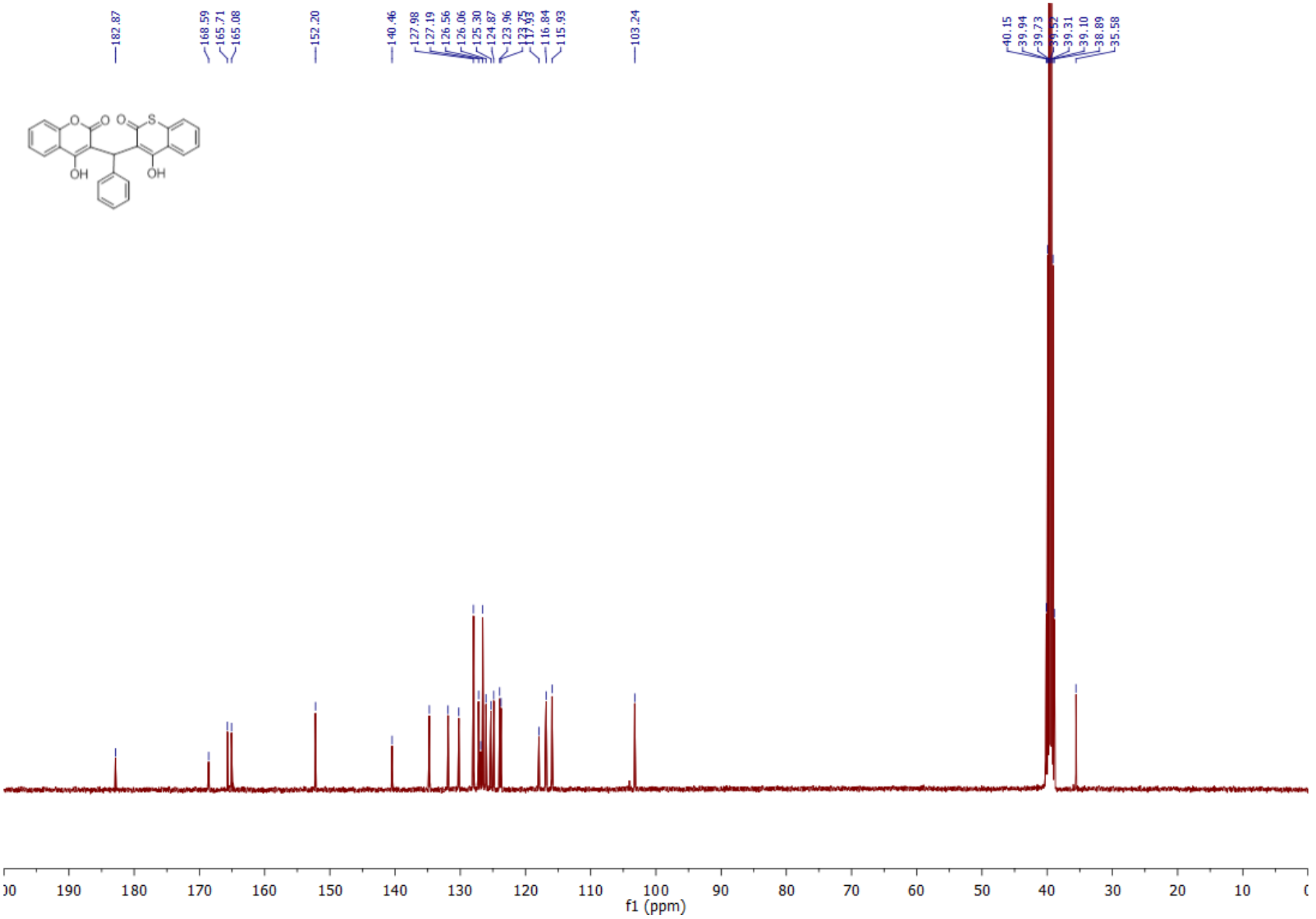
^{13}C NMR (100 MHz, d_6-DMSO): compound **2k**



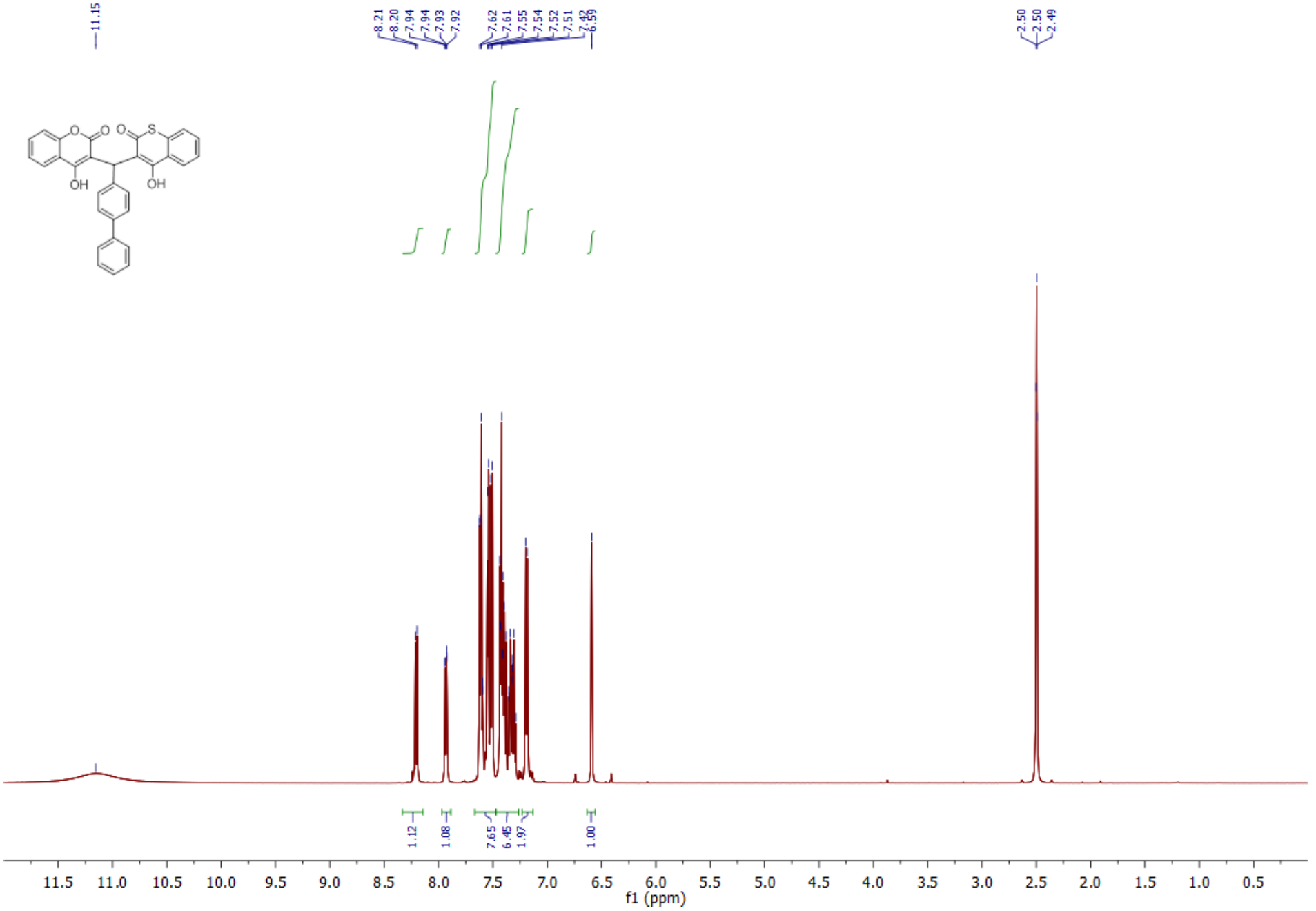
^{1}H NMR (400 MHz, d_6-DMSO): compound **3a**



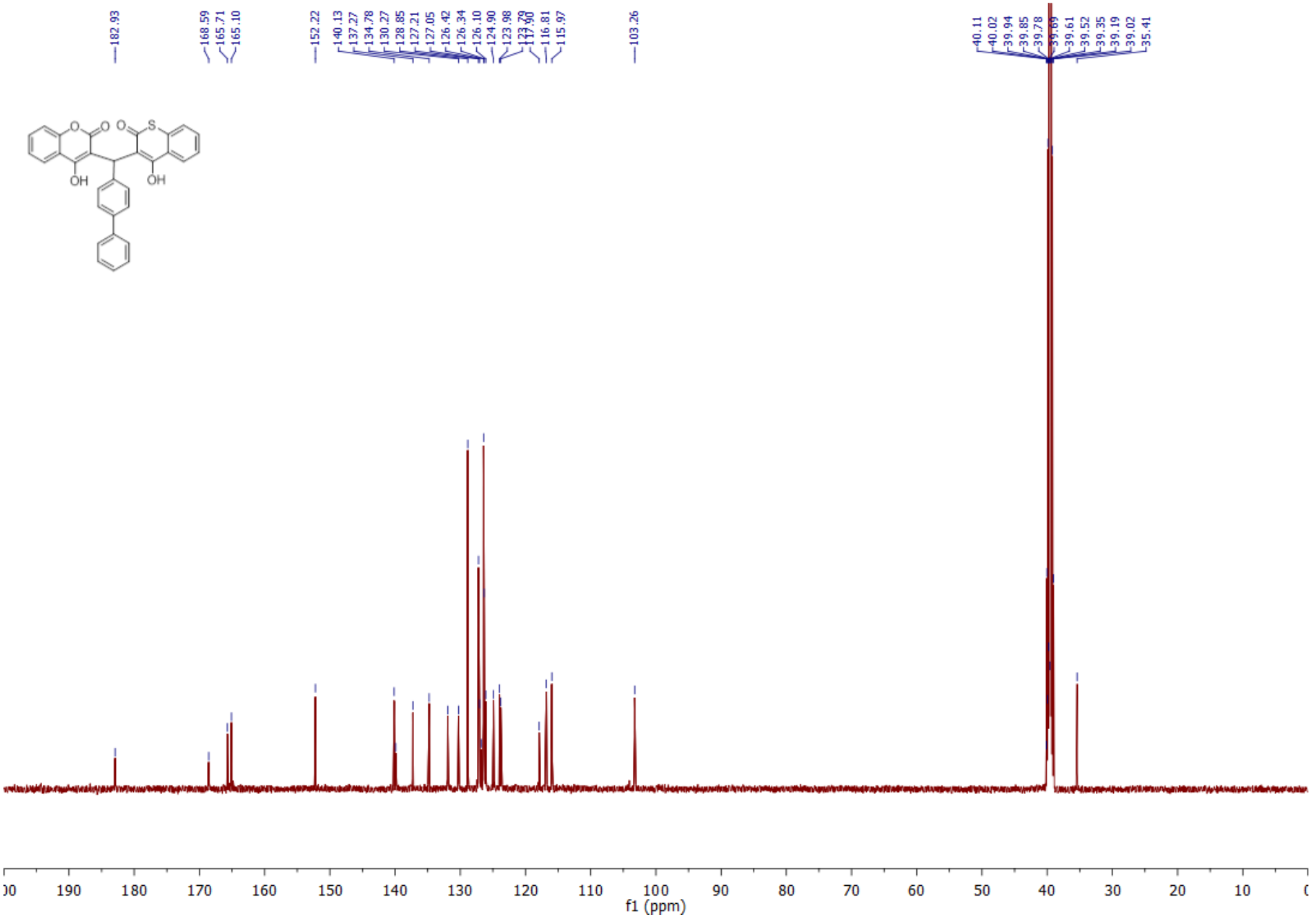
^{13}C NMR (100 MHz, d_6-DMSO): compound **3a**



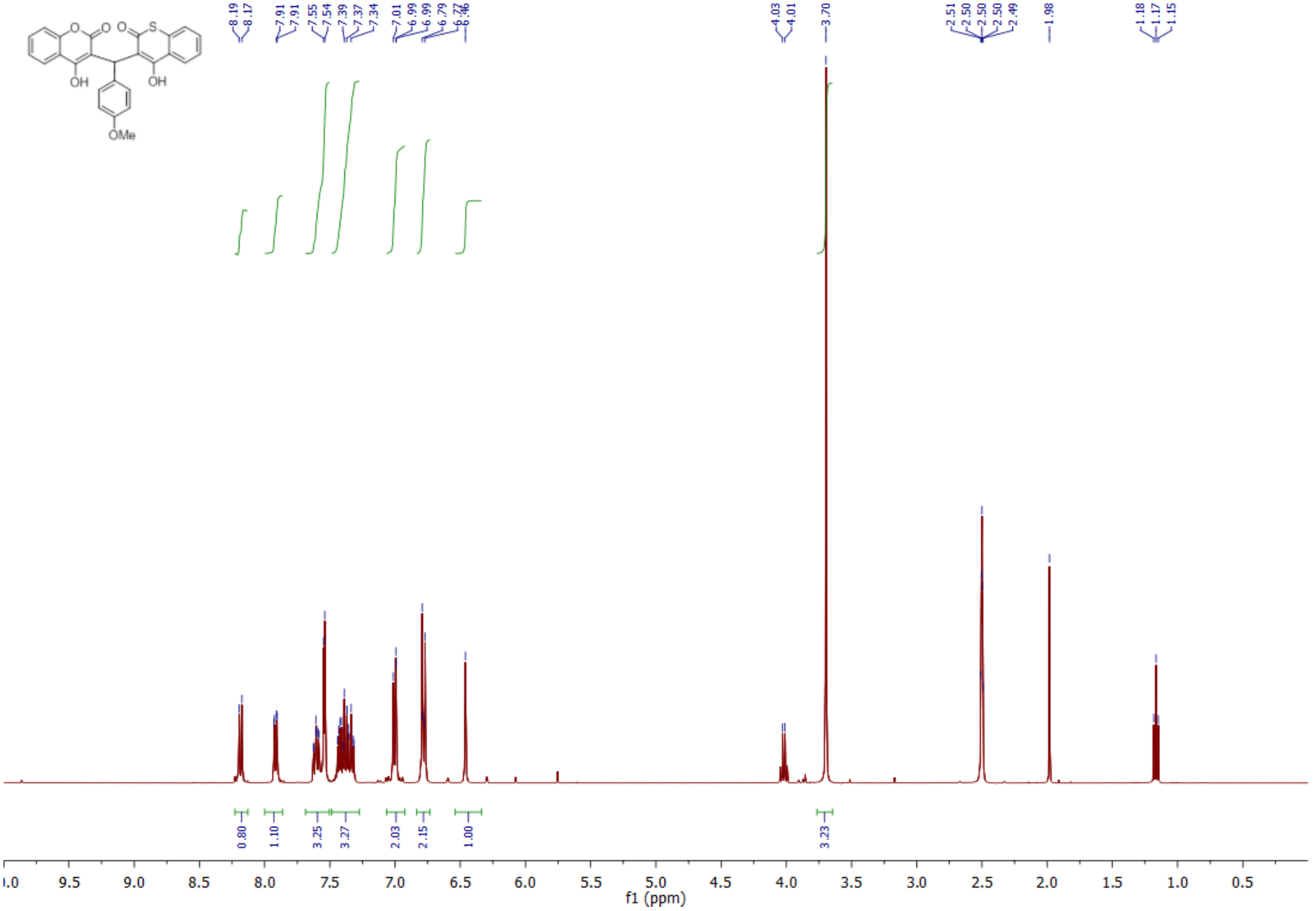
^{1}H NMR (500 MHz, d_6-DMSO): compound **3b**



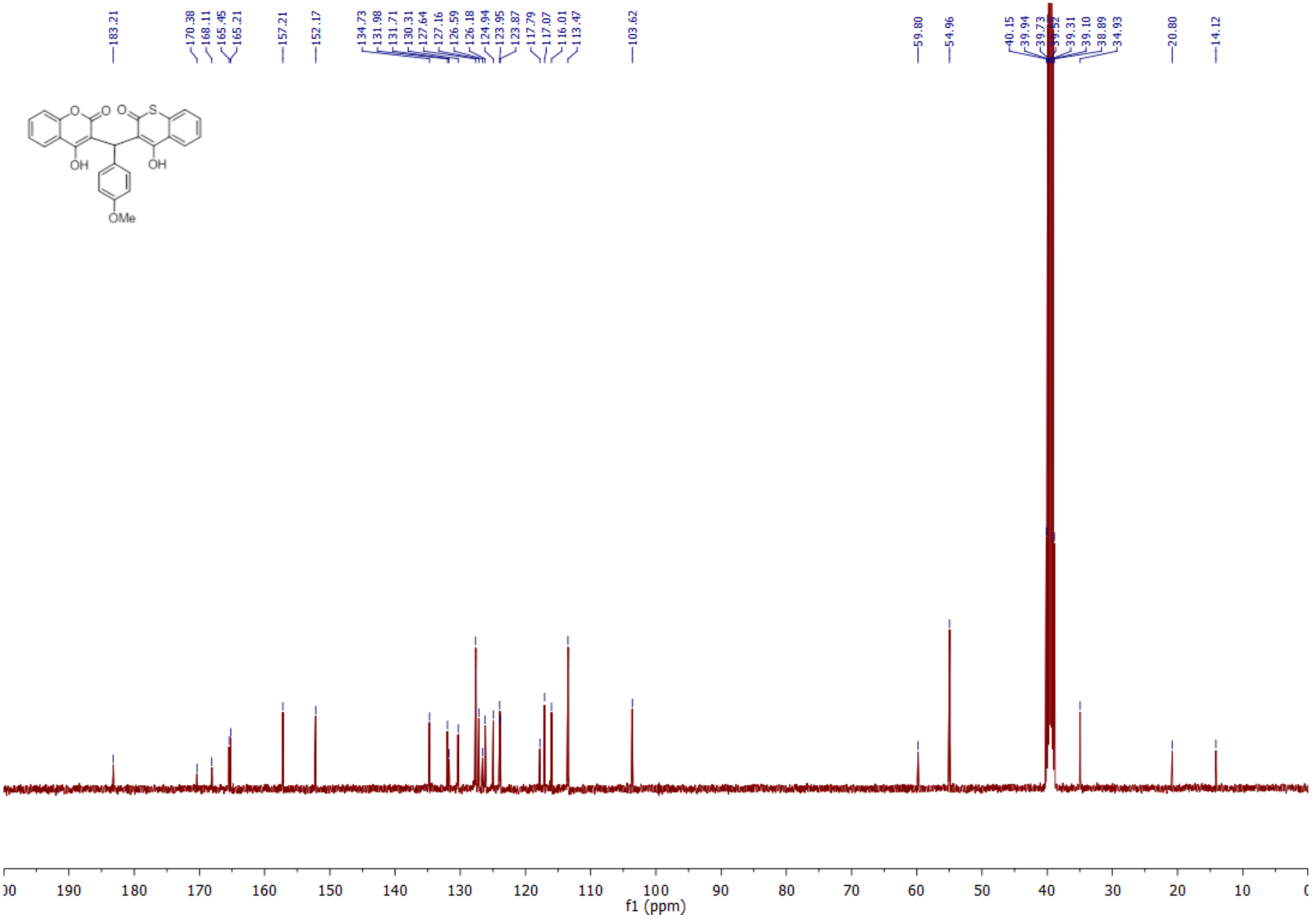
^{13}C NMR (125 MHz, d_6-DMSO): compound **3b**



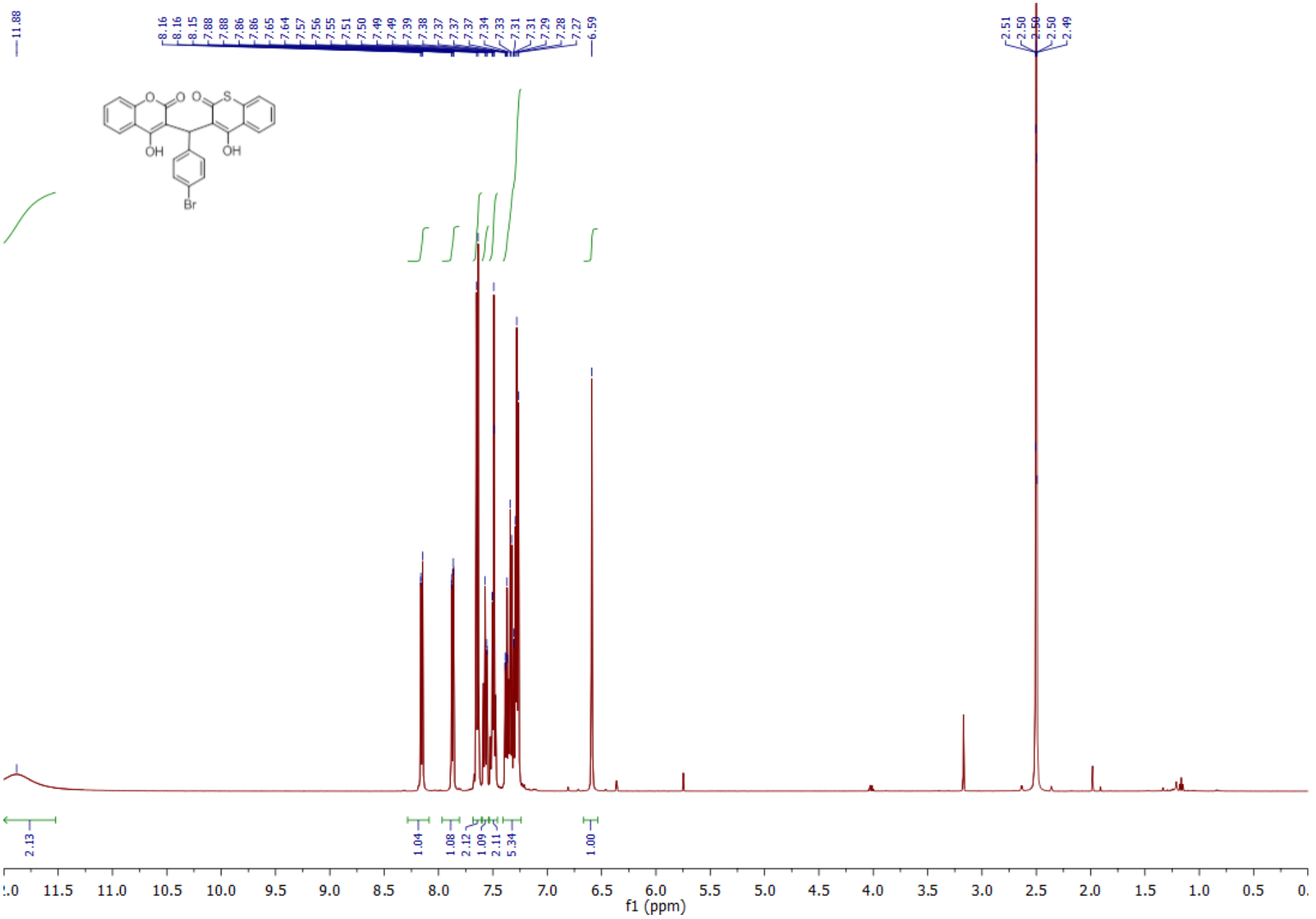
^{1}H NMR (400 MHz, d_6-DMSO): compound **3c**



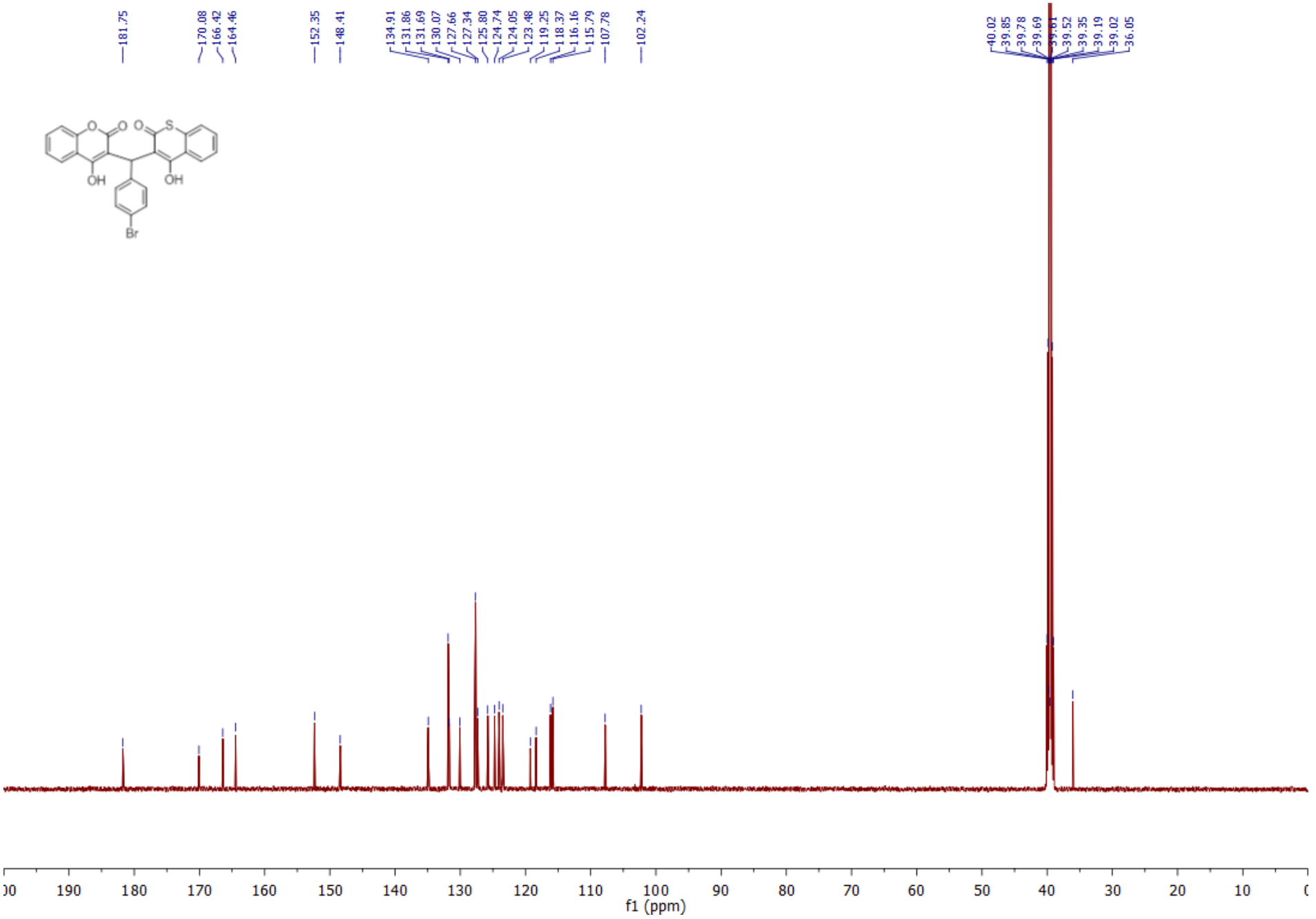
^{13}C NMR (100 MHz, d_6-DMSO): compound **3c**



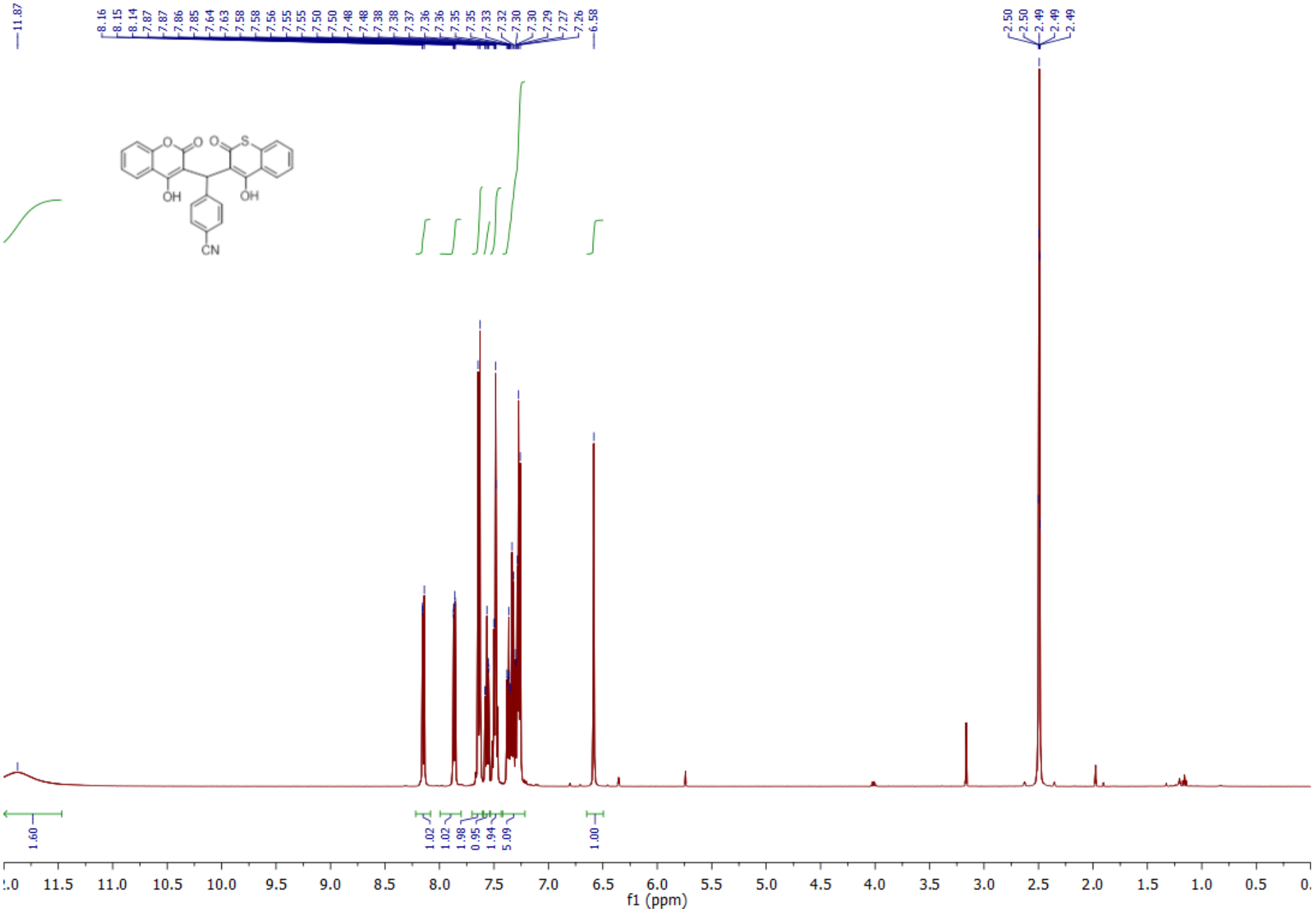
^{1}H NMR (500 MHz, d_6-DMSO): compound **3d**



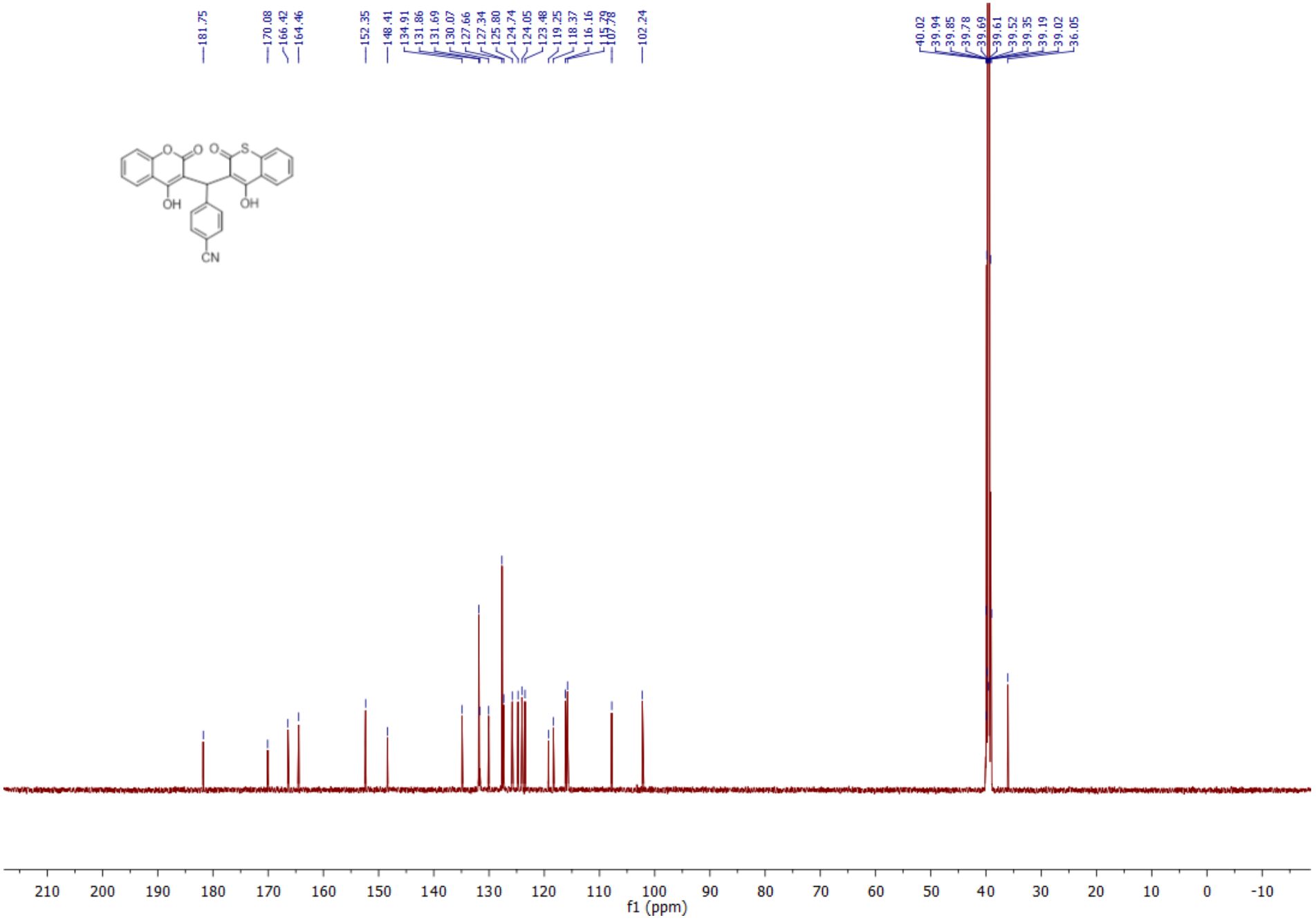
^{13}C NMR (125 MHz, d_6-DMSO): compound **3d**



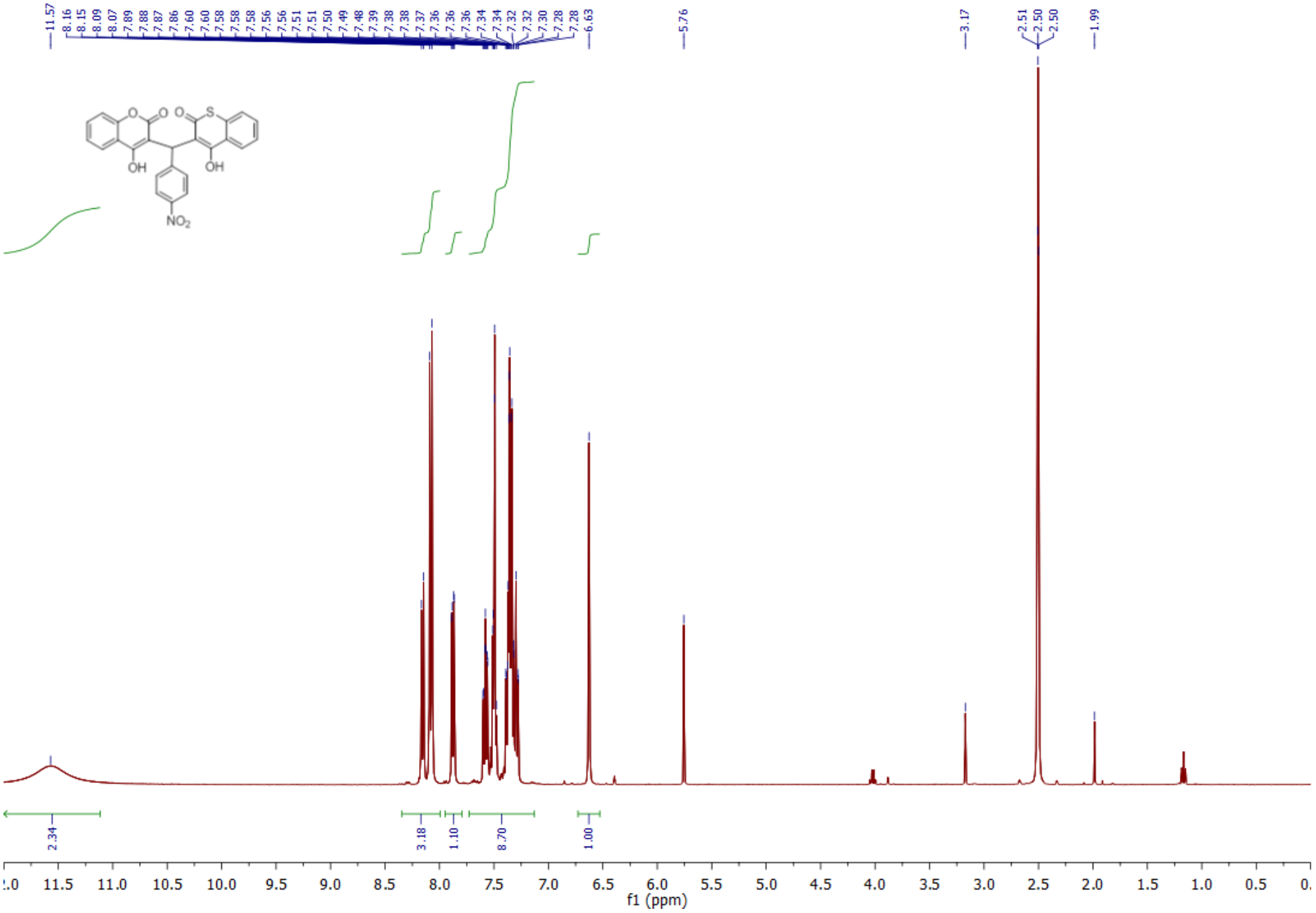
^{1}H NMR (500 MHz, d_6-DMSO): compound **3e**



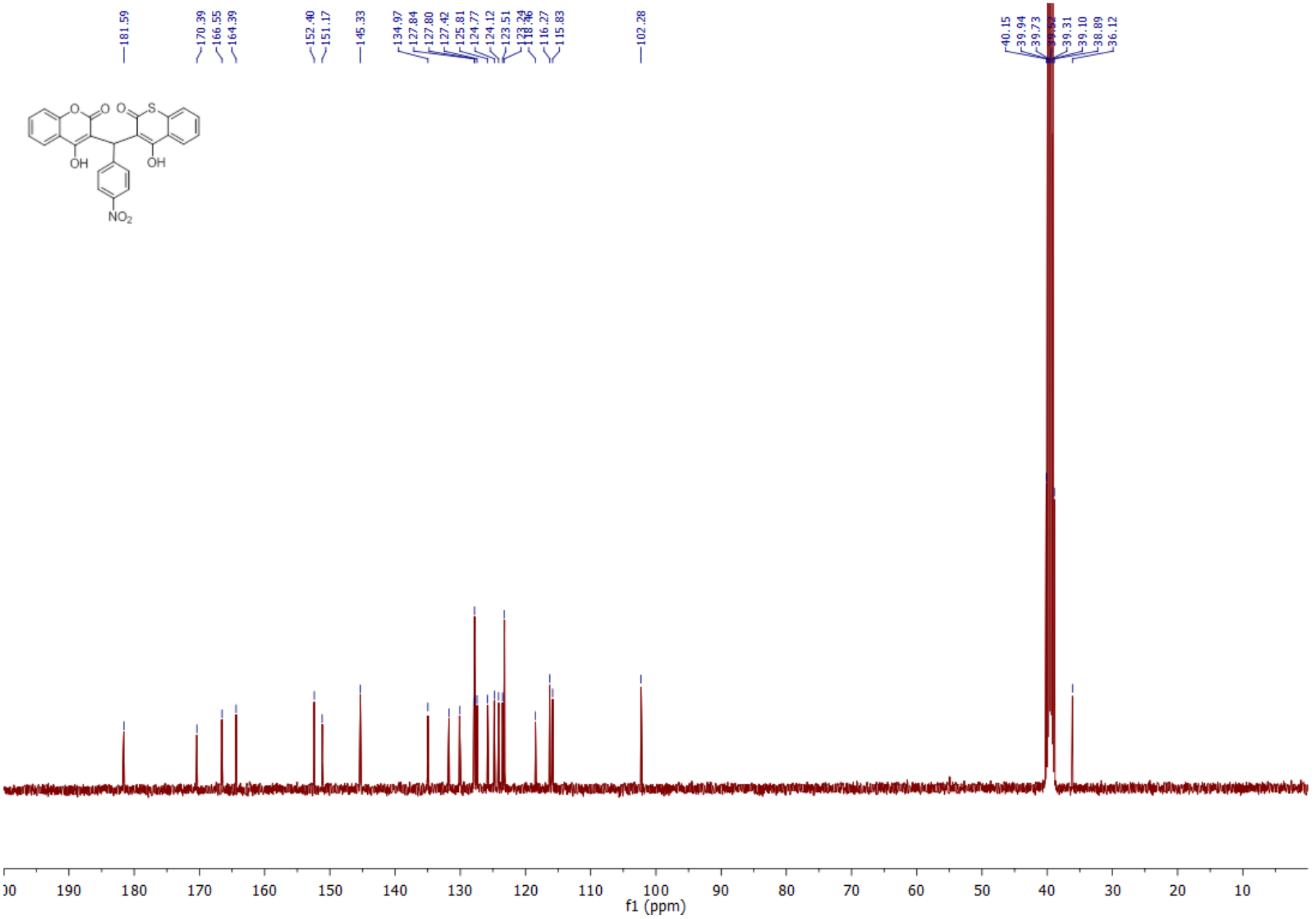
^{13}C NMR (125 MHz, d_6-DMSO): compound **3e**



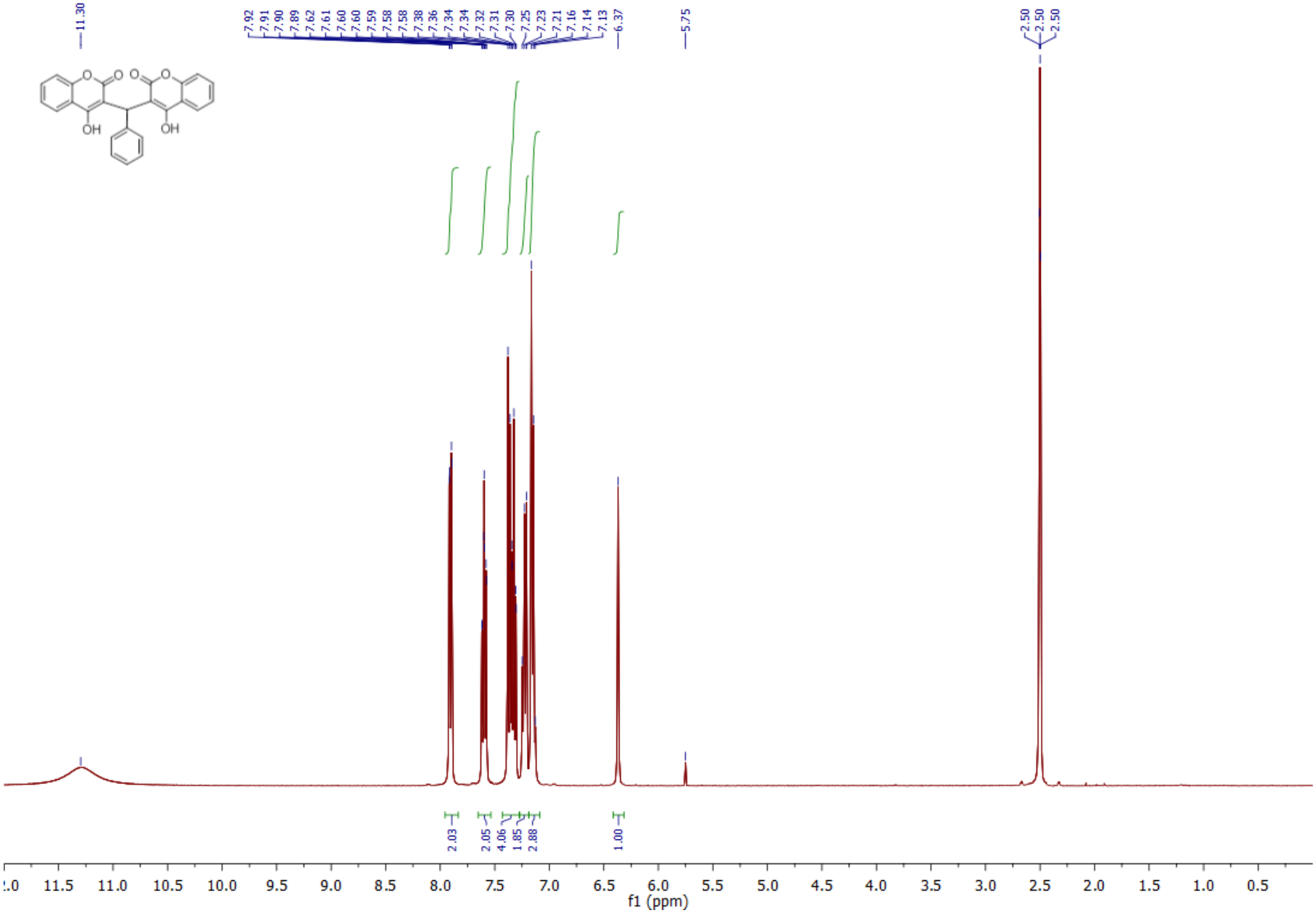
^{1}H NMR (400 MHz, d_6-DMSO): compound **3f**



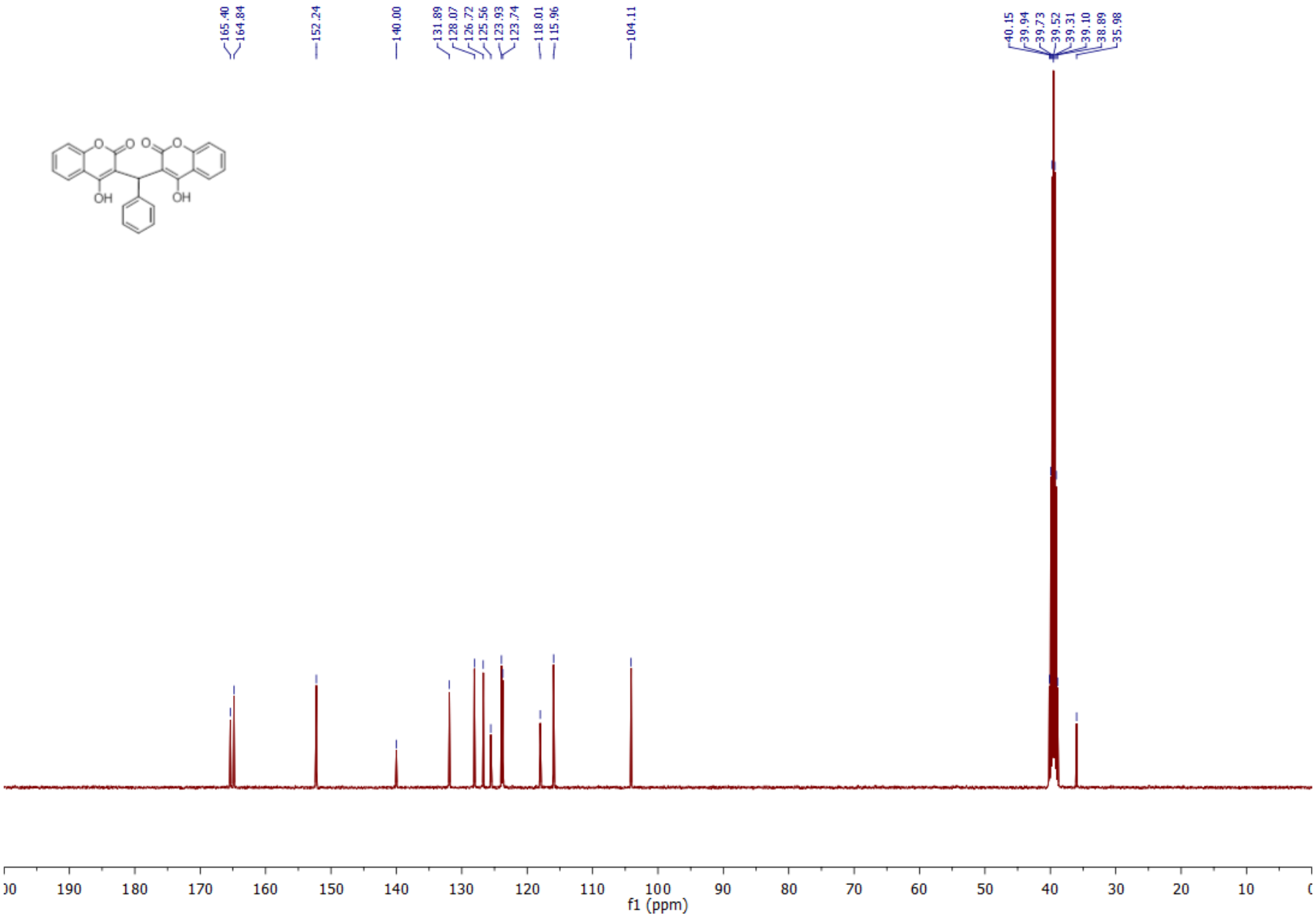
^{13}C NMR (100 MHz, d_6-DMSO): compound **3f**



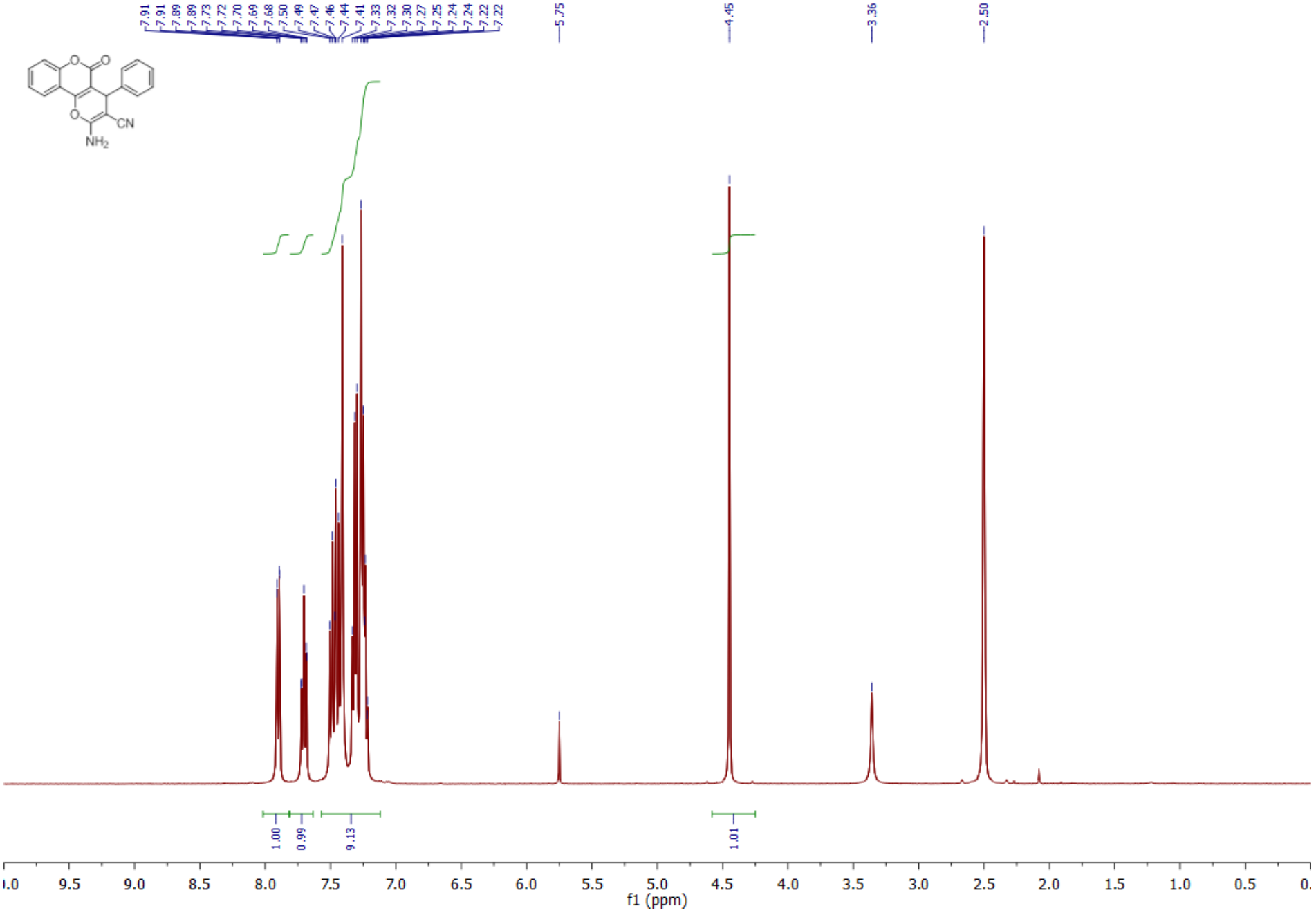
^{1}H NMR (400 MHz, d_6-DMSO): compound **DIM**



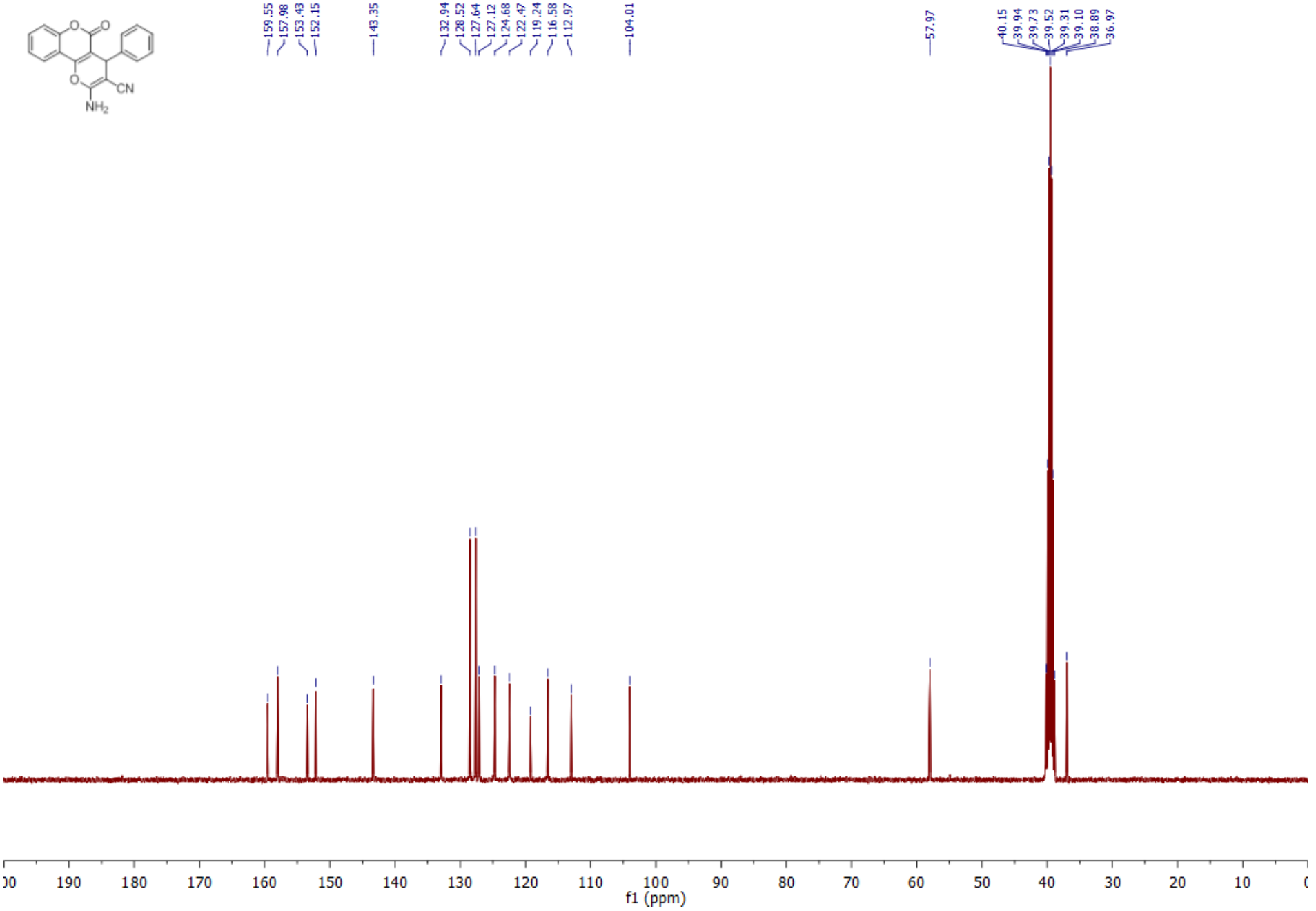
^{13}C NMR (100 MHz, d_6-DMSO): compound **DIM**



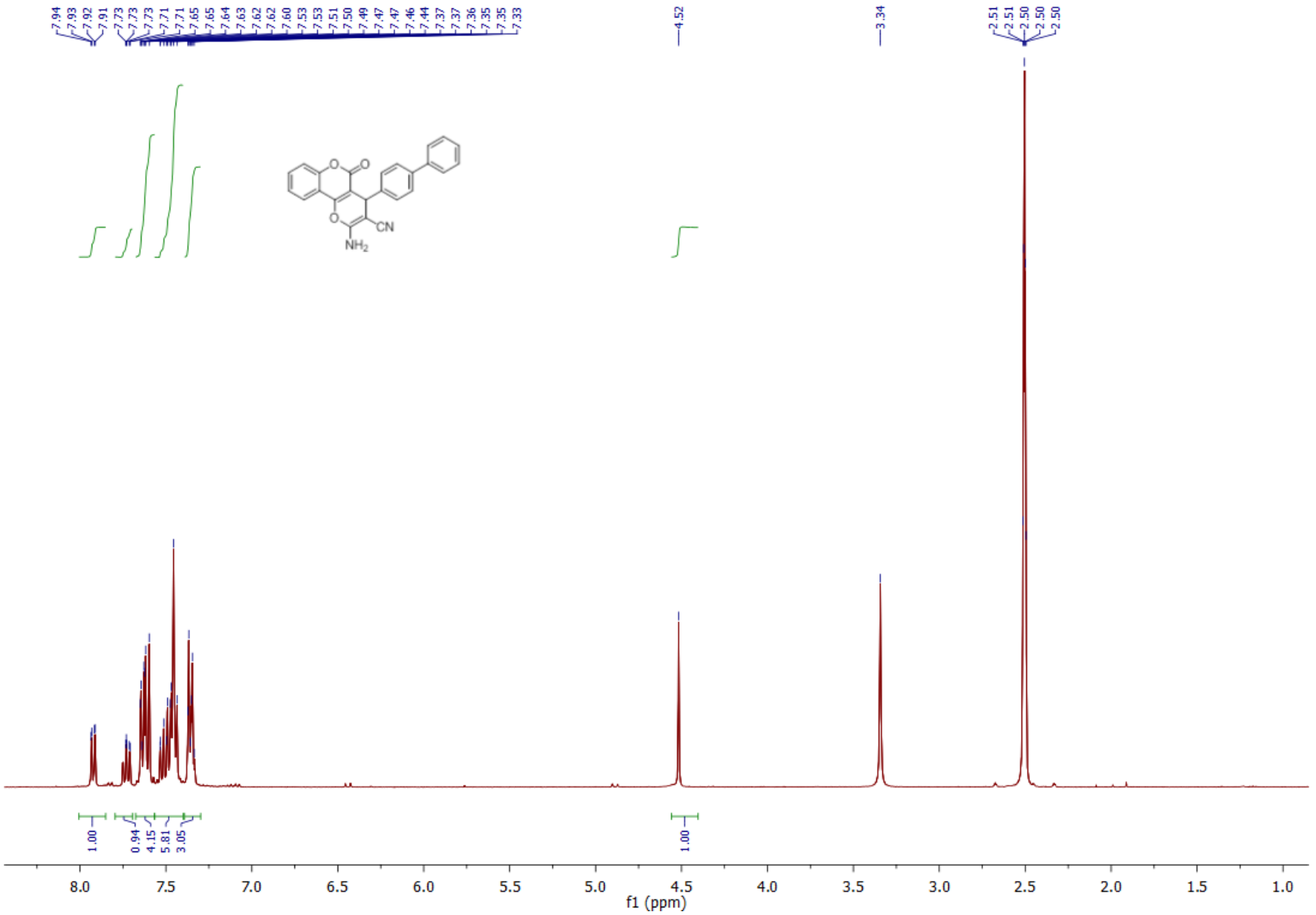
^{1}H NMR (400 MHz, d_6-DMSO): compound **4a**



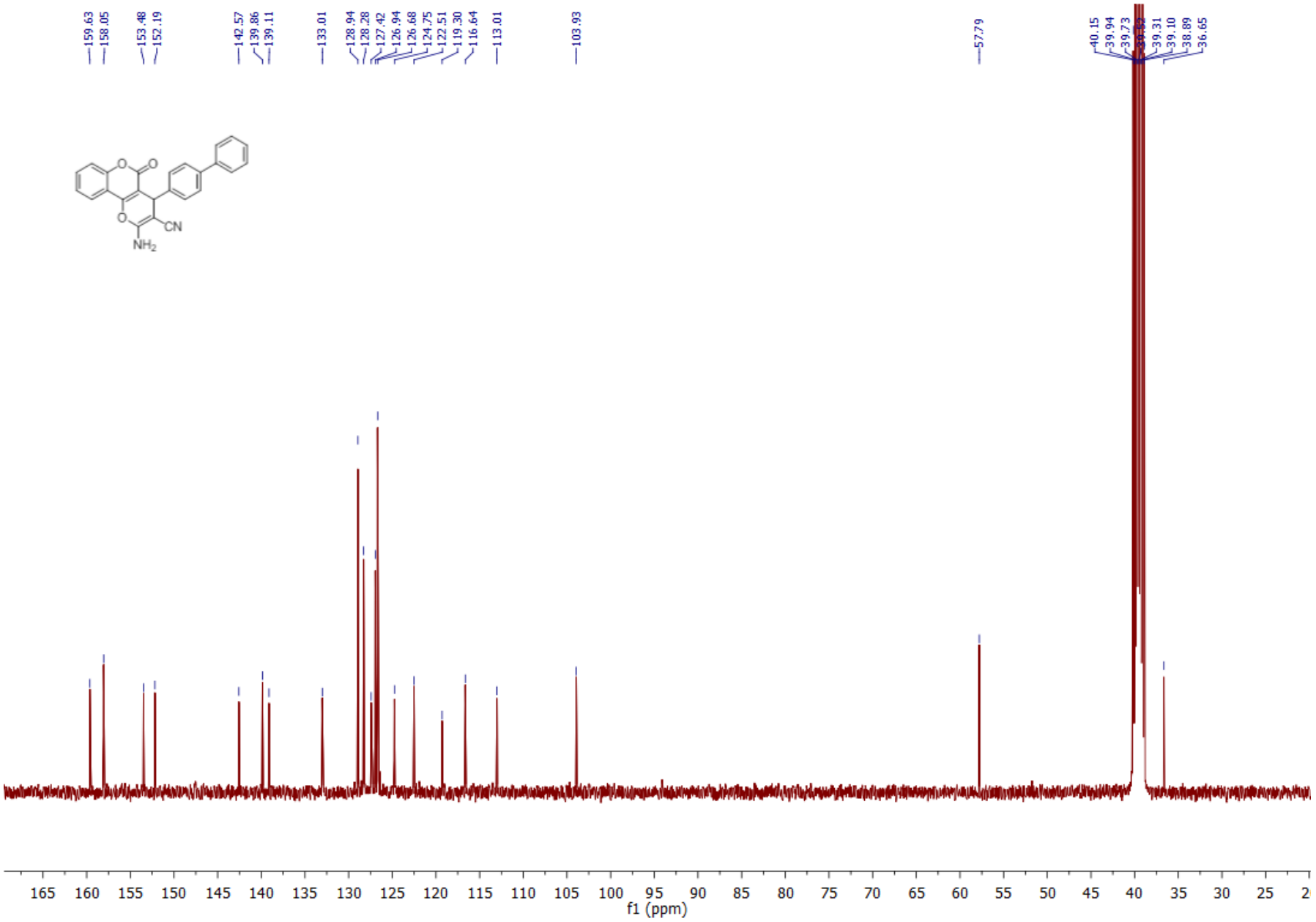
^{13}C NMR (100 MHz, d_6-DMSO): compound **4a**



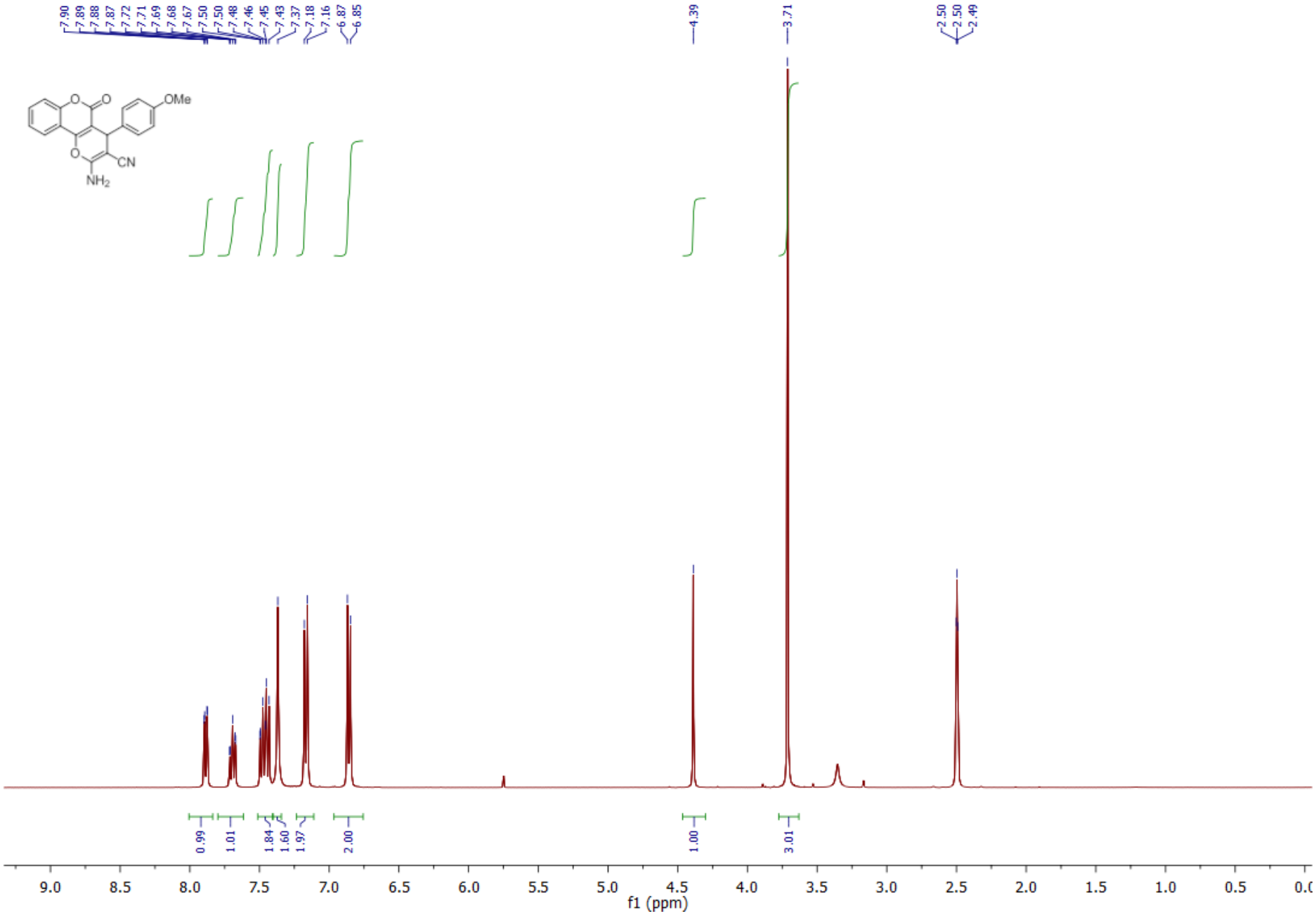
^{1}H NMR (400 MHz, d_6-DMSO): compound **4b**



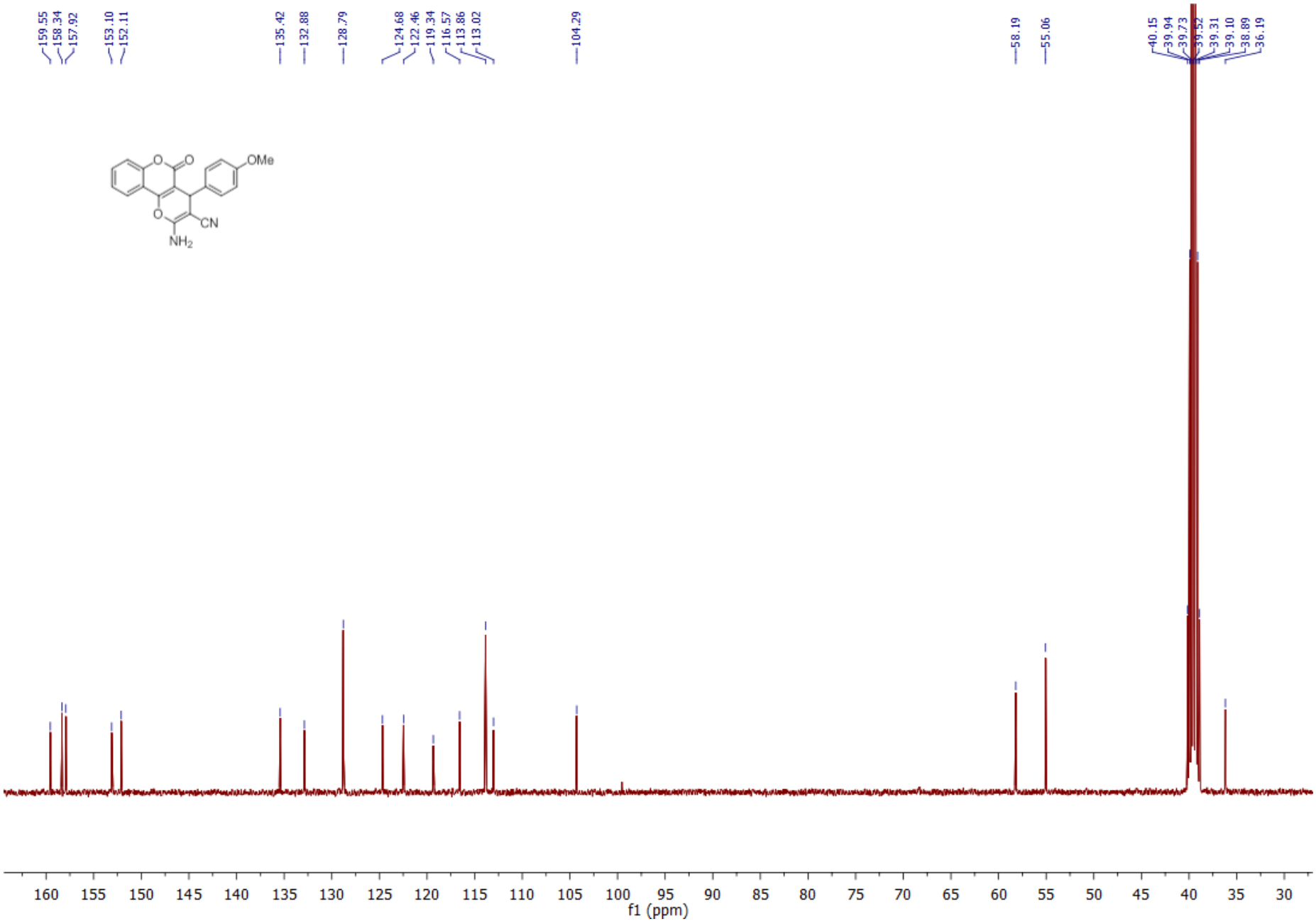
^{13}C NMR (100 MHz, d_6-DMSO): compound **4b**



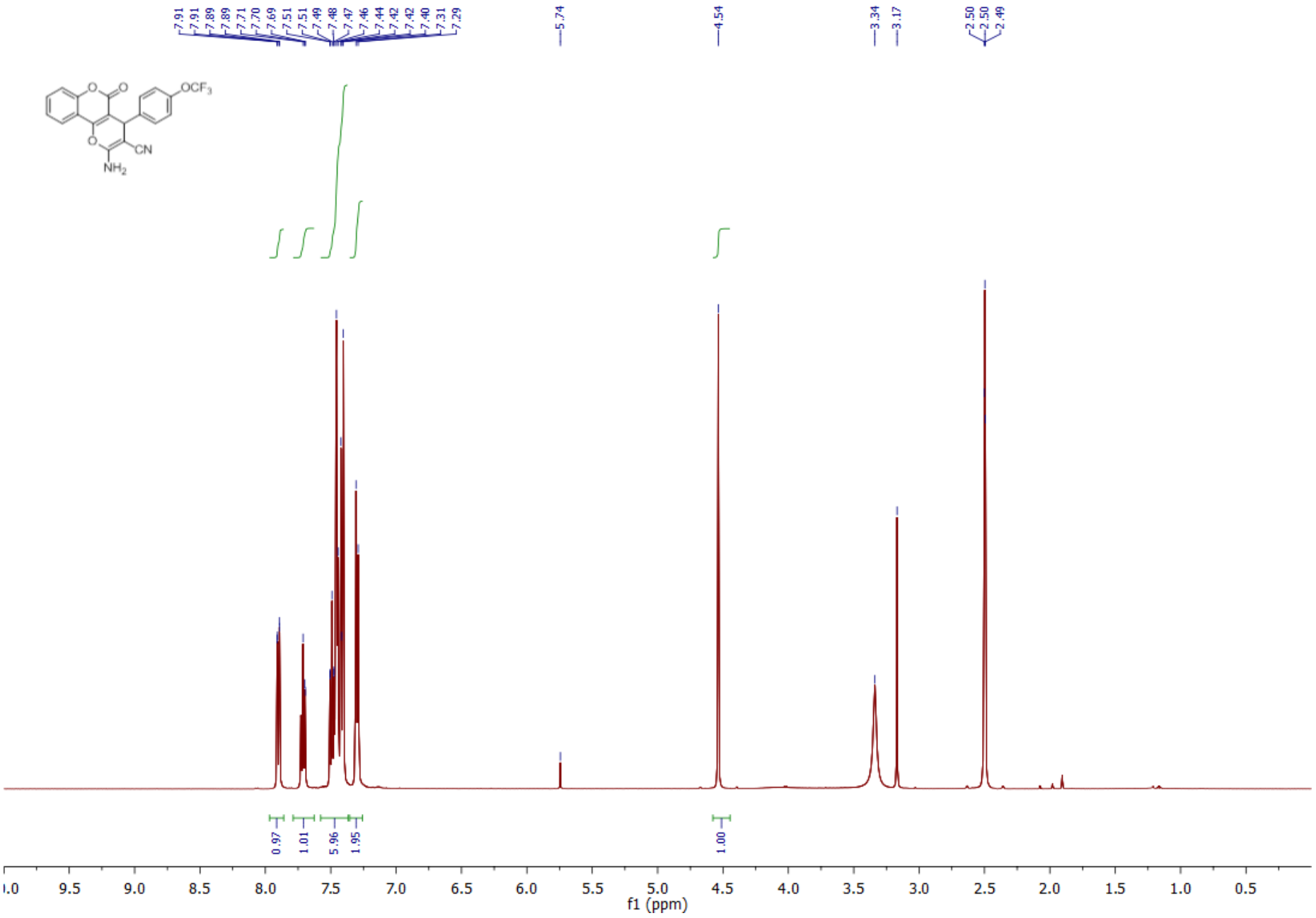
^{1}H NMR (400 MHz, d_6-DMSO): compound **4c**



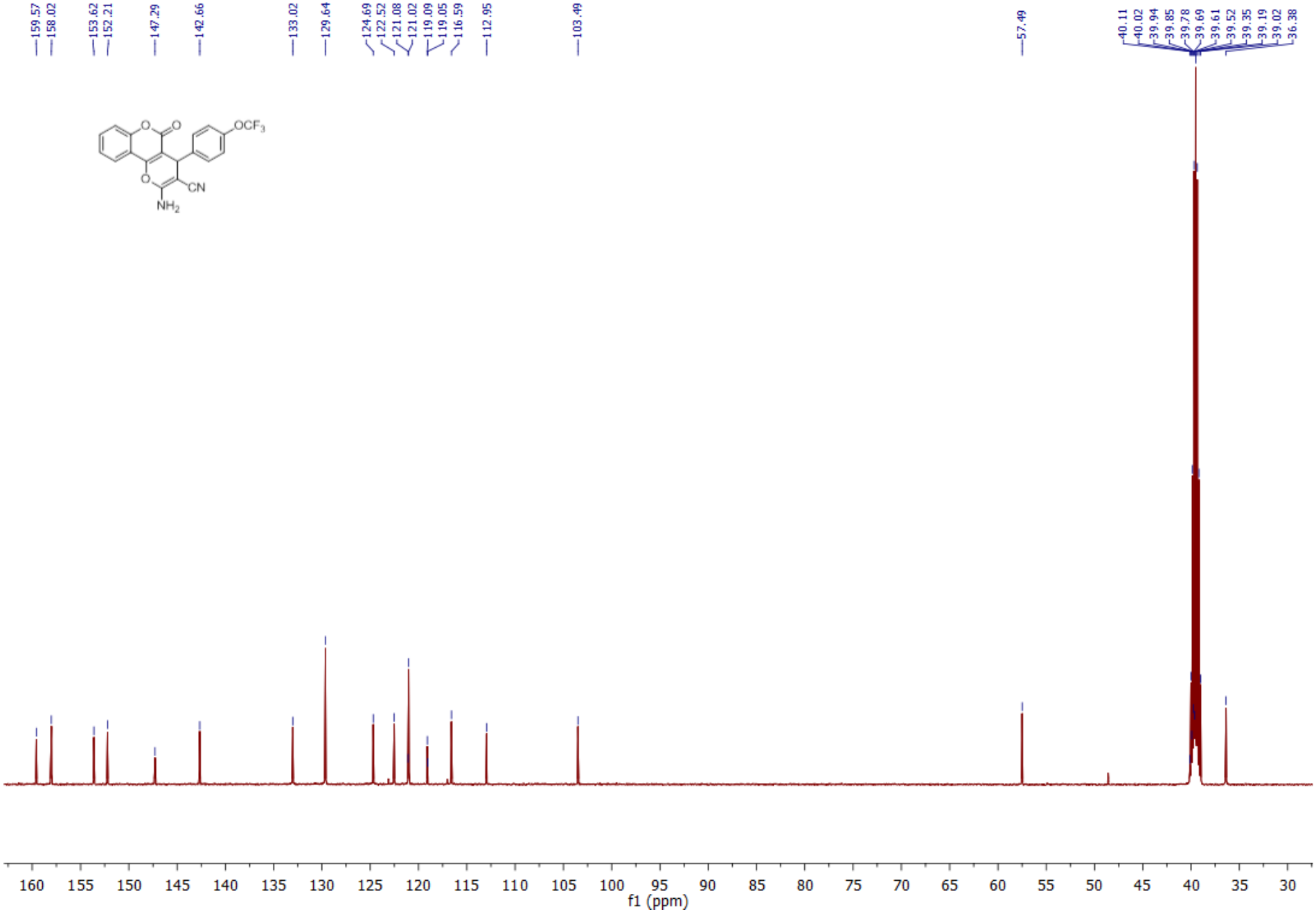
^{13}C NMR (100 MHz, d_6-DMSO): compound **4c**



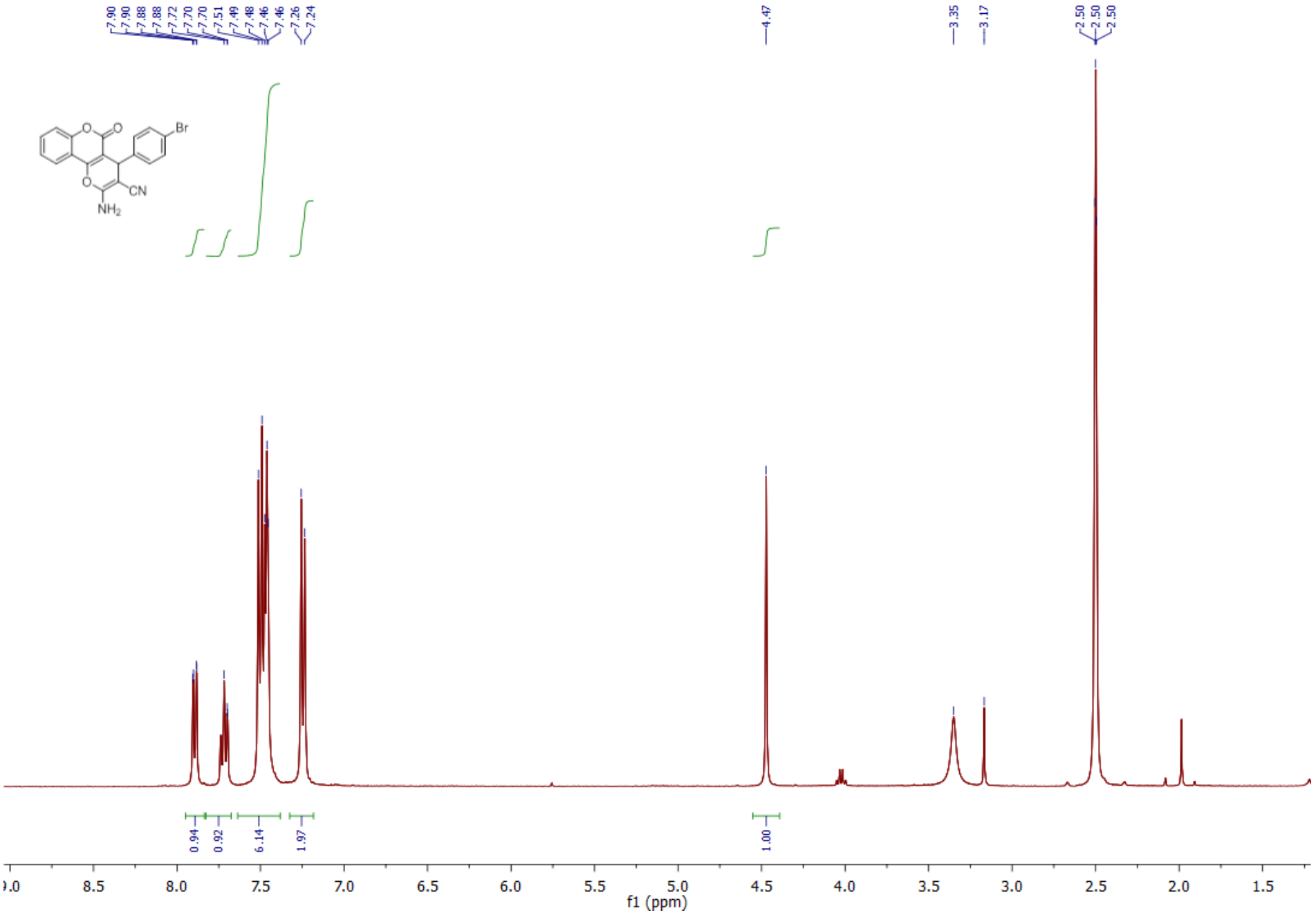
^{1}H NMR (500 MHz, d_6-DMSO): compound **4d**



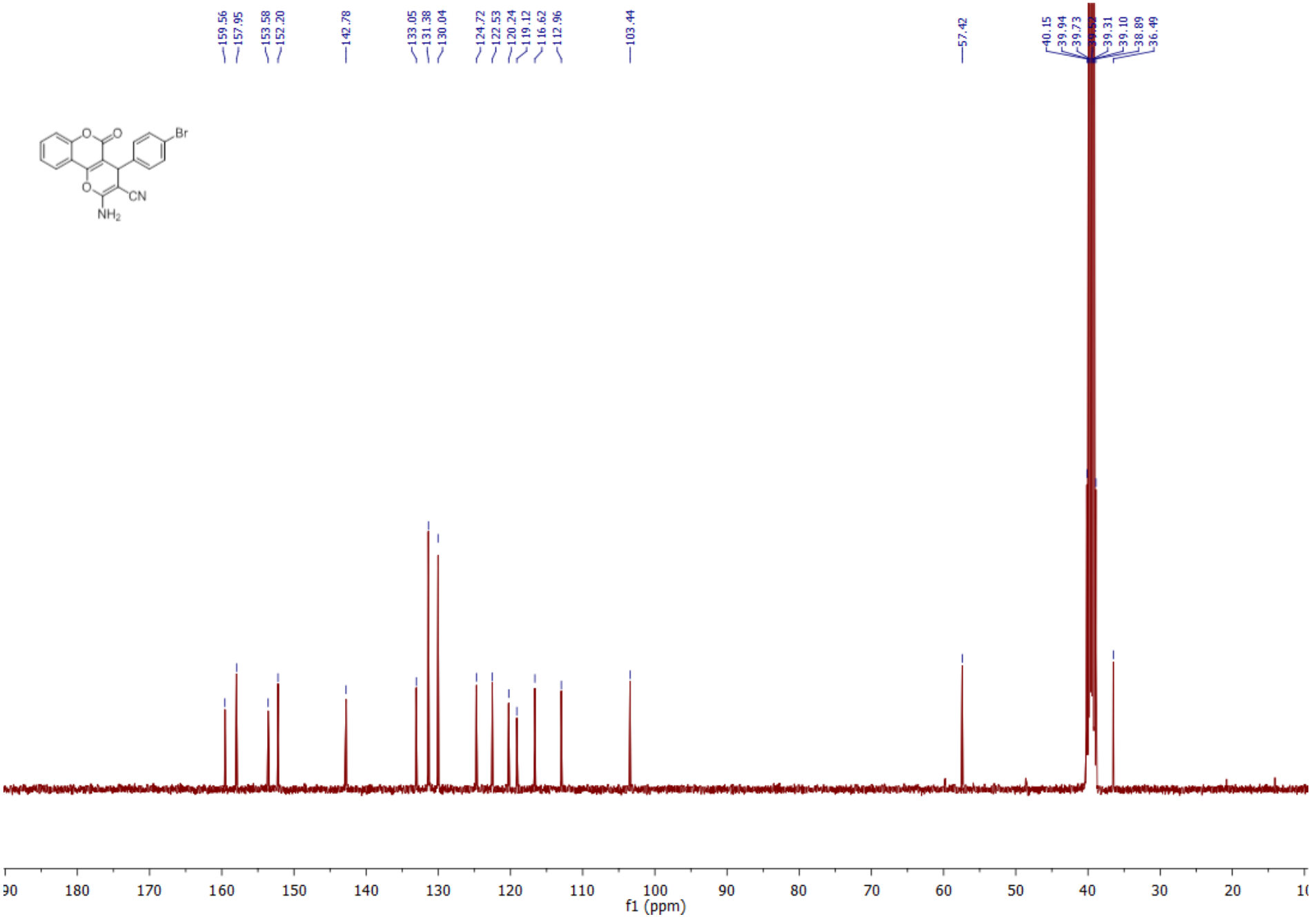
^{13}C NMR (125 MHz, d_6-DMSO): compound **4d**



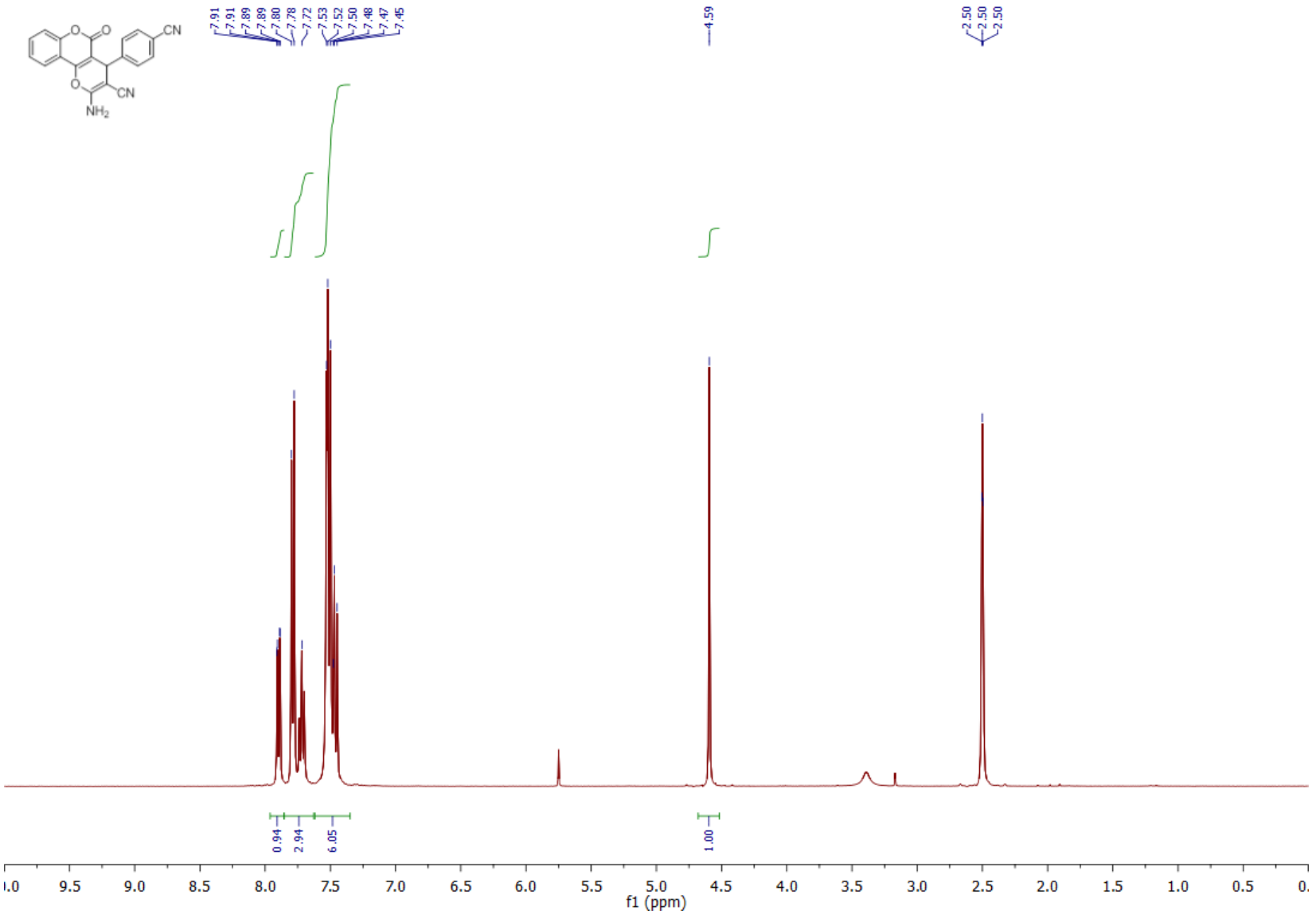
^{1}H NMR (400 MHz, d_6-DMSO): compound **4e**



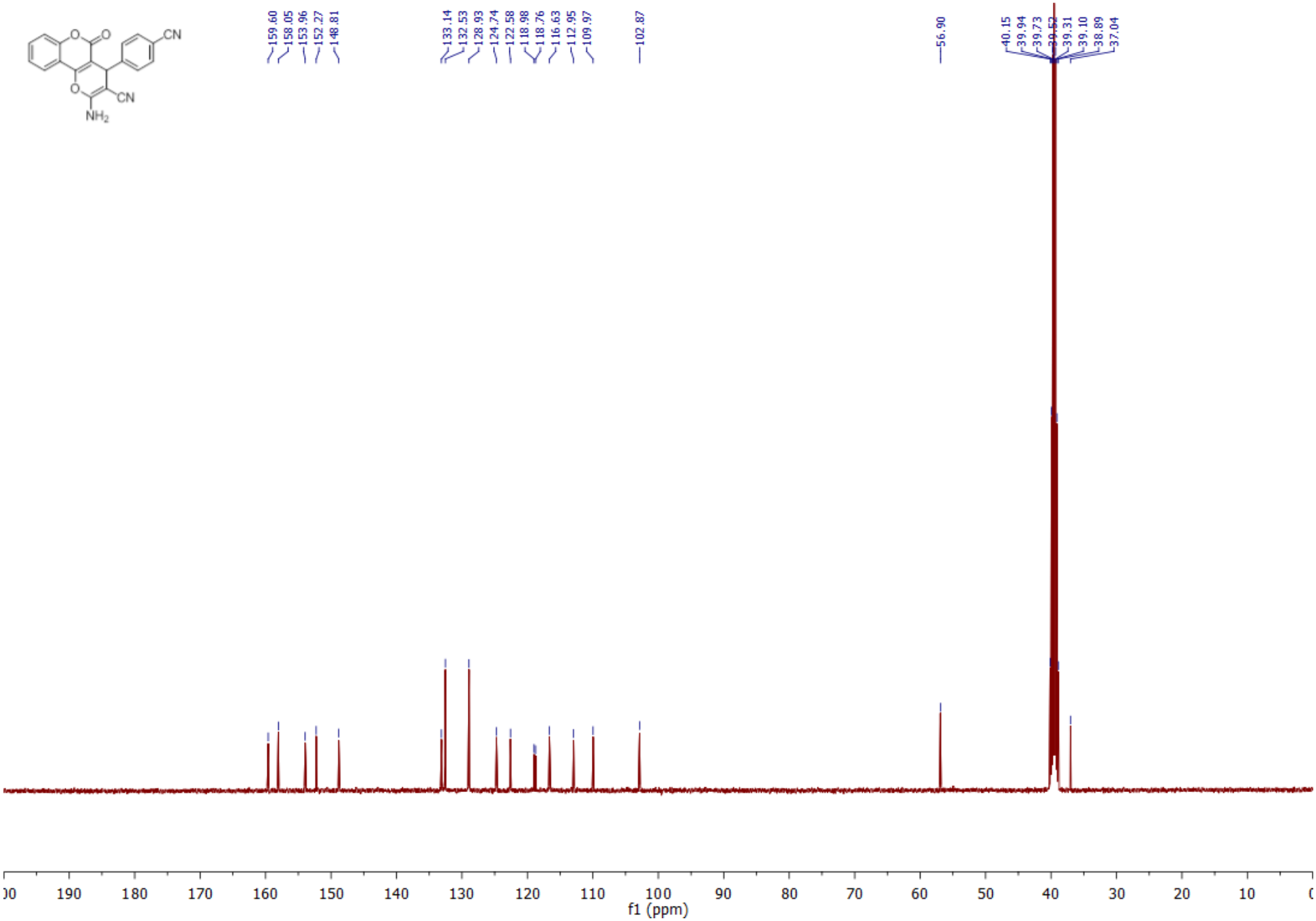
^{13}C NMR (100 MHz, d_6-DMSO): compound **4e**



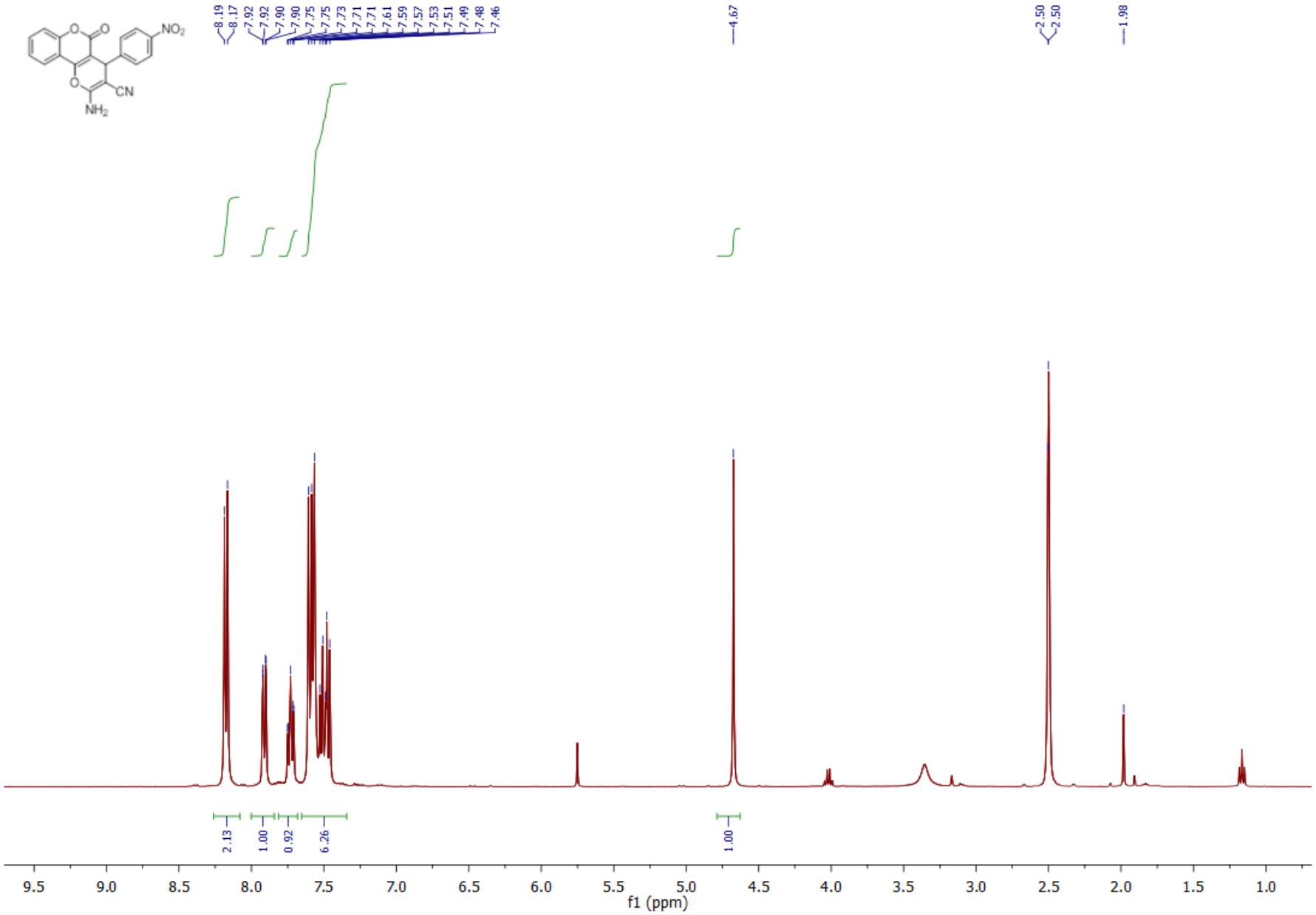
^{1}H NMR (400 MHz, d_6-DMSO): compound **4f**



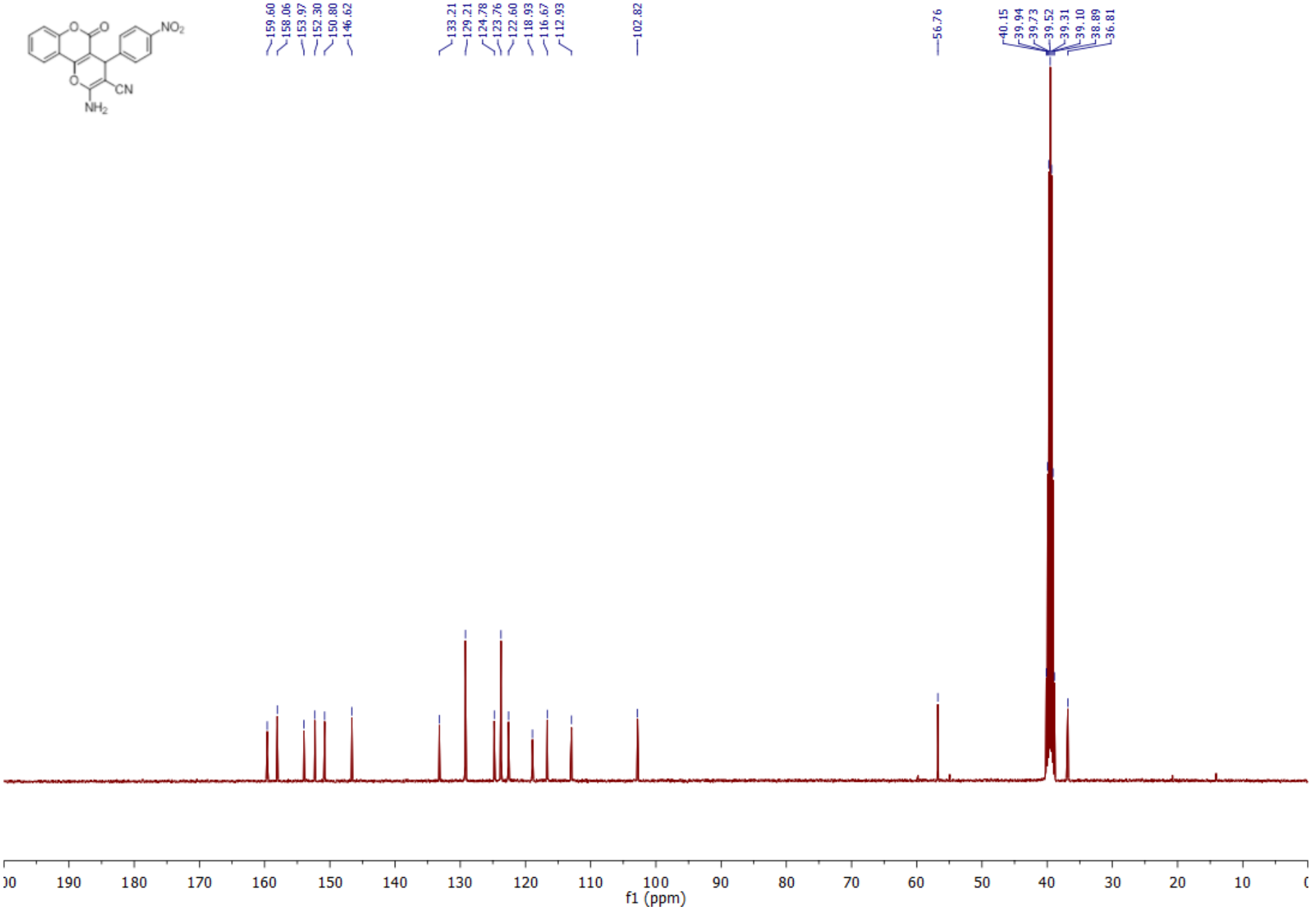
^{13}C NMR (100 MHz, d_6-DMSO): compound **4f**



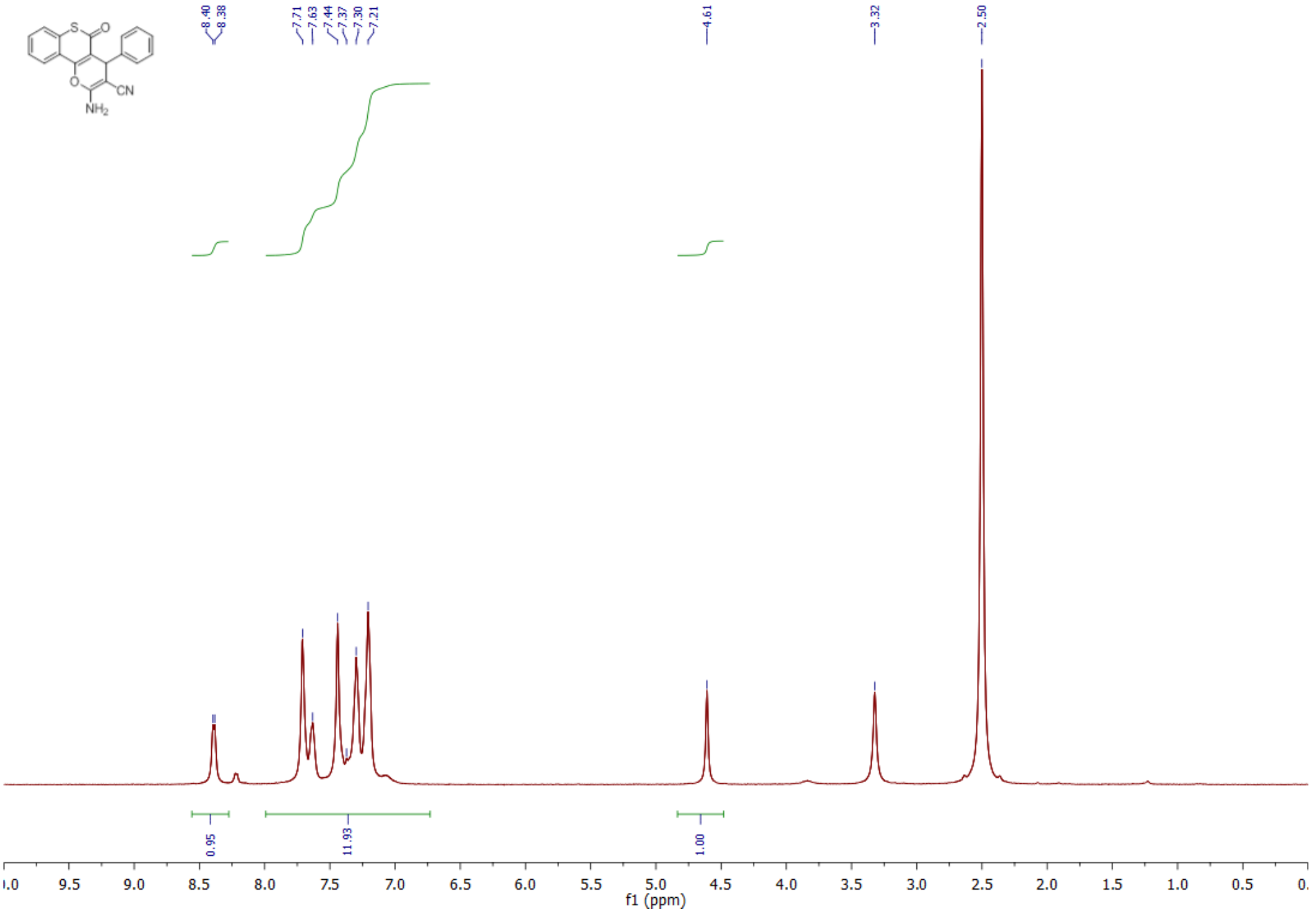
^{1}H NMR (400 MHz, d_6-DMSO): compound **4g**



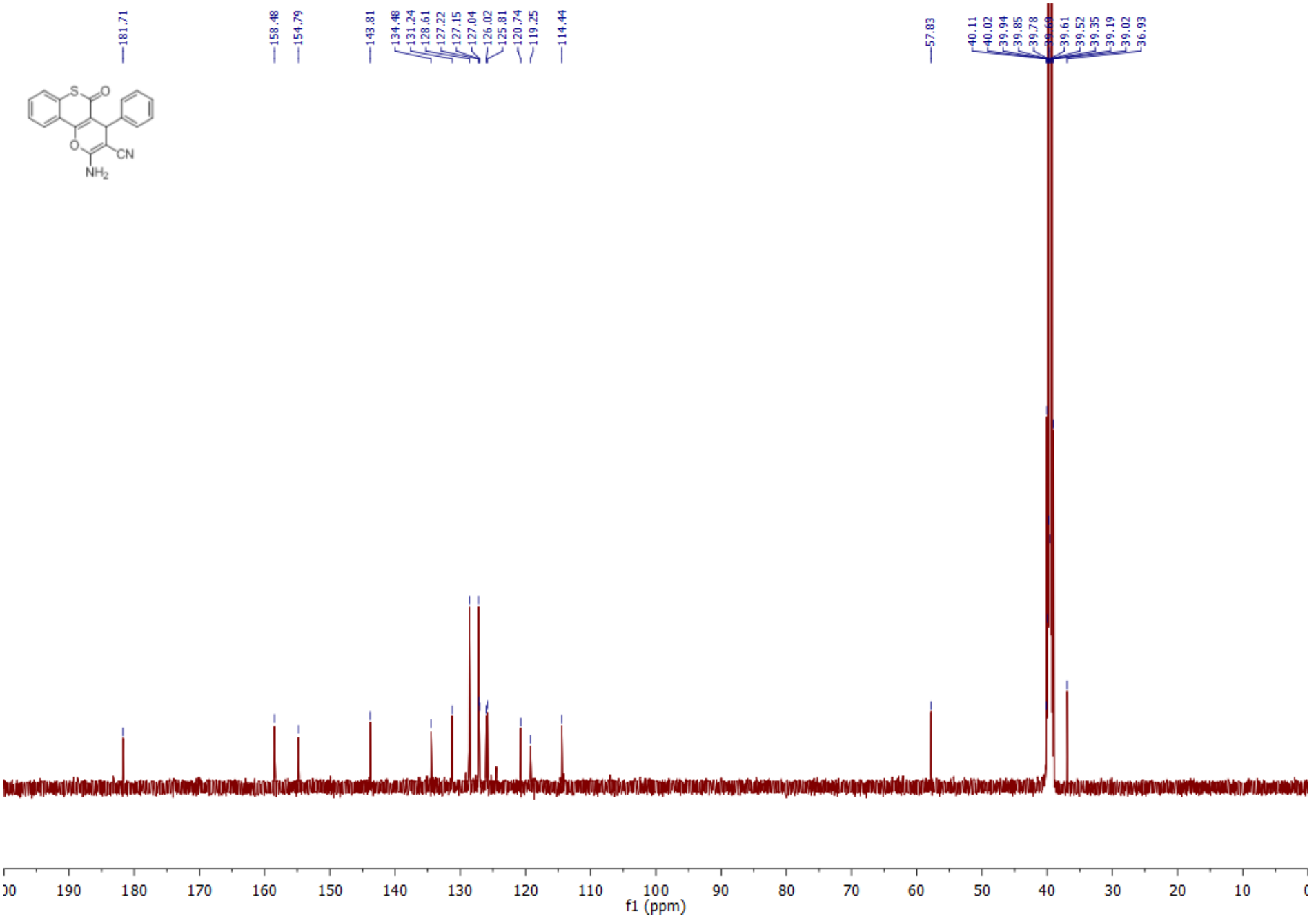
^{13}C NMR (100 MHz, d_6-DMSO): compound **4g**



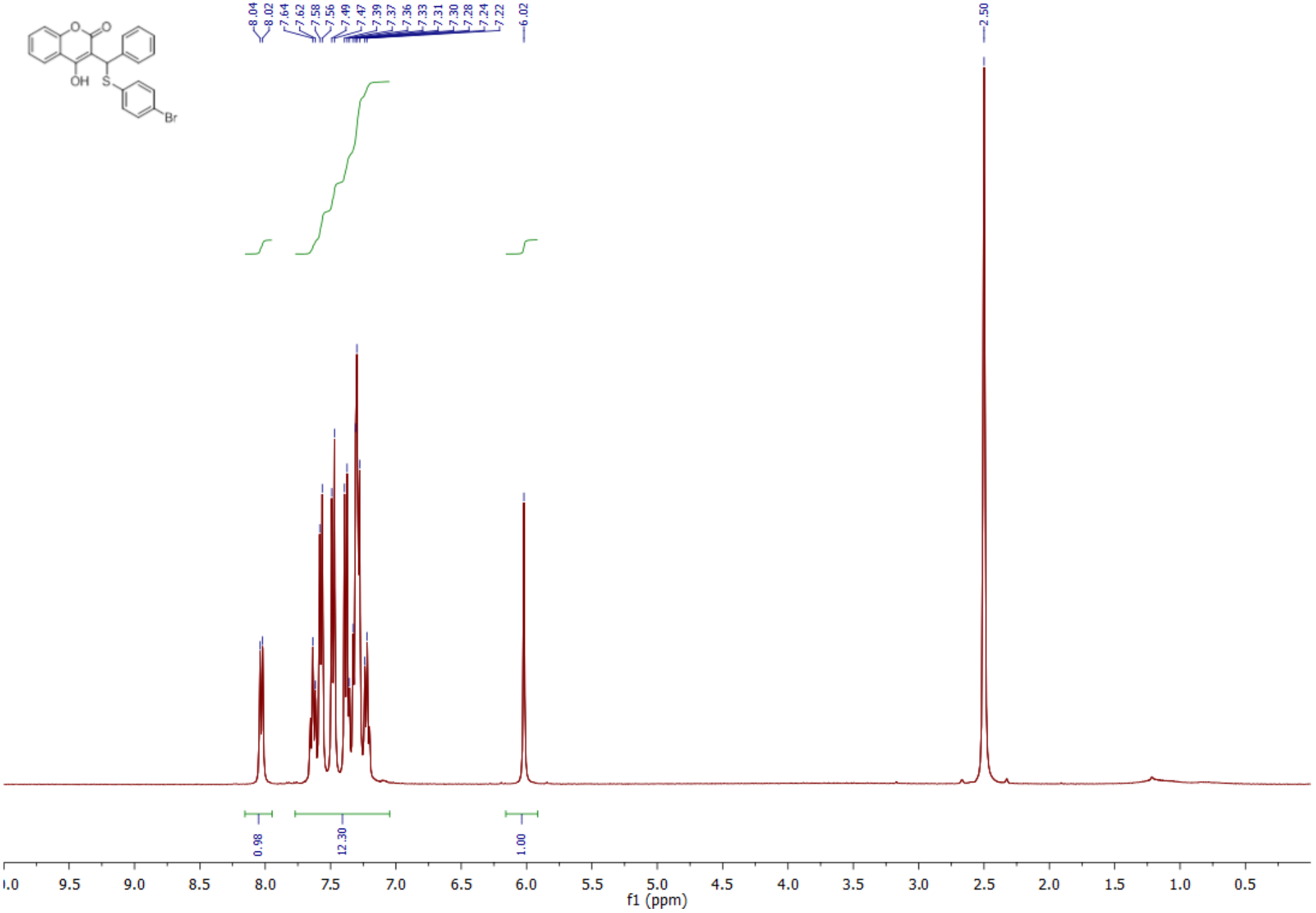
^{1}H NMR (500 MHz, d_6-DMSO): compound **4h**



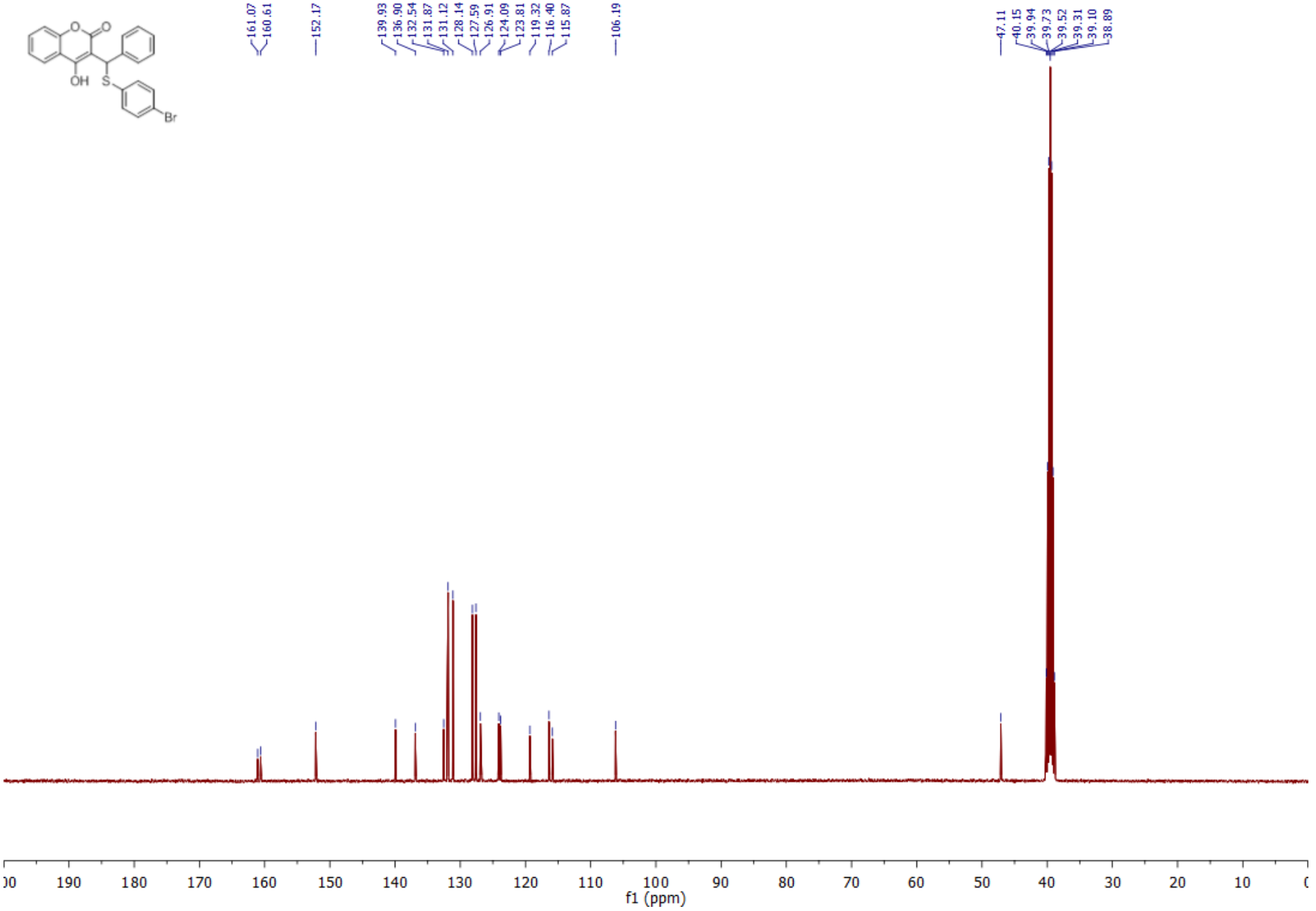
^{13}C NMR (125 MHz, d_6-DMSO): compound **4h**



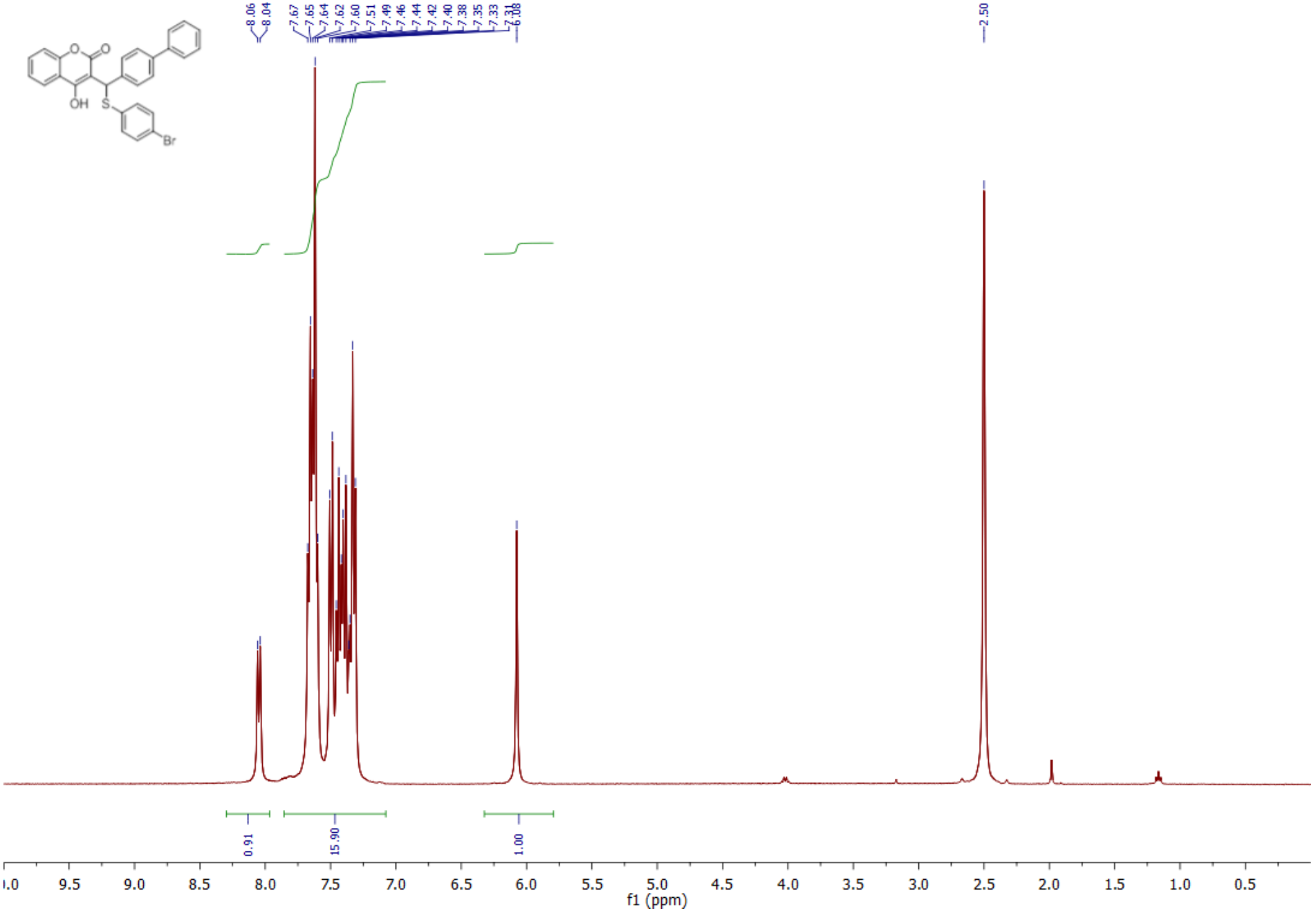
^{1}H NMR (400 MHz, d_6-DMSO): compound **5a**



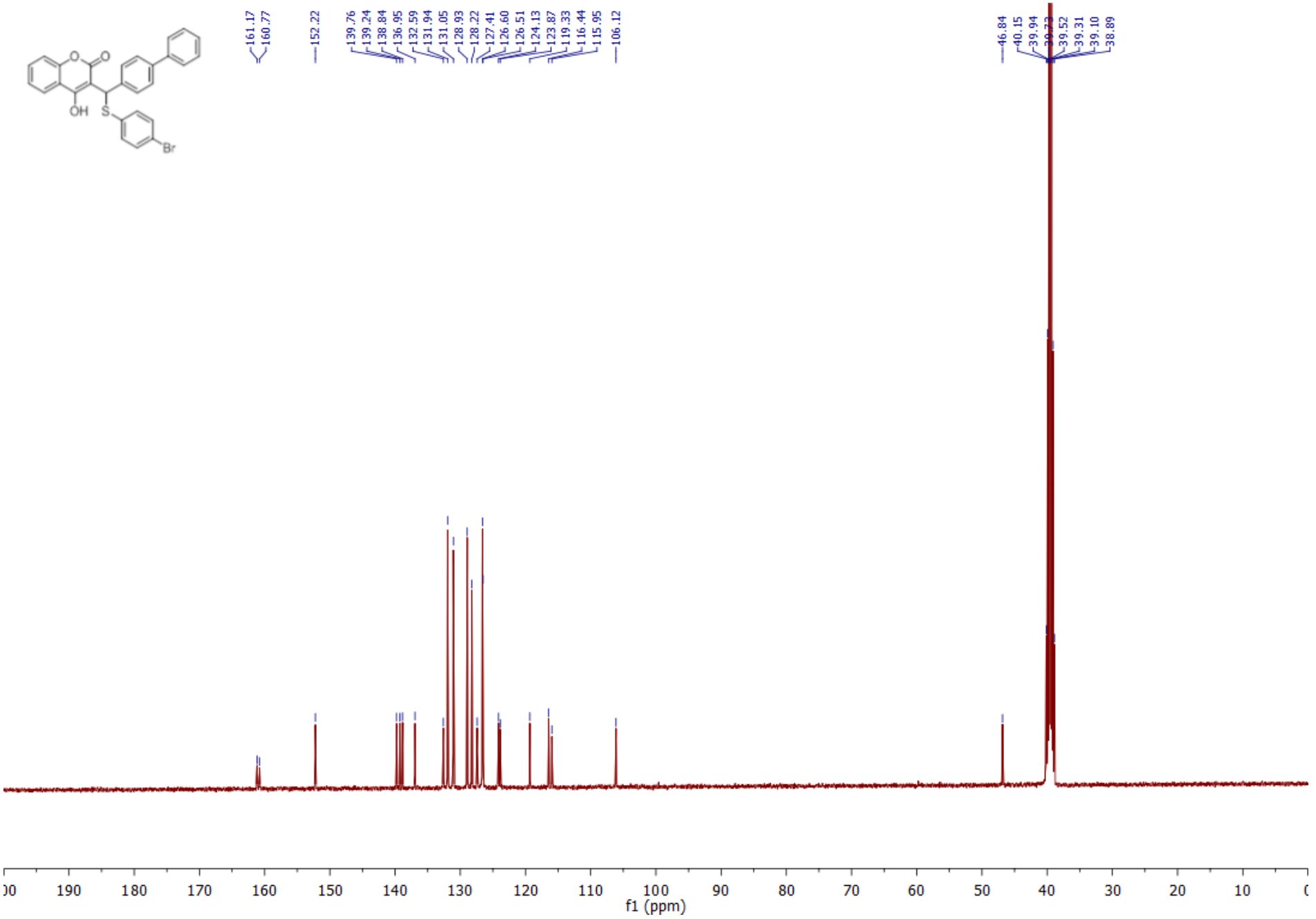
^{13}C NMR (100 MHz, d_6-DMSO): compound **5a**



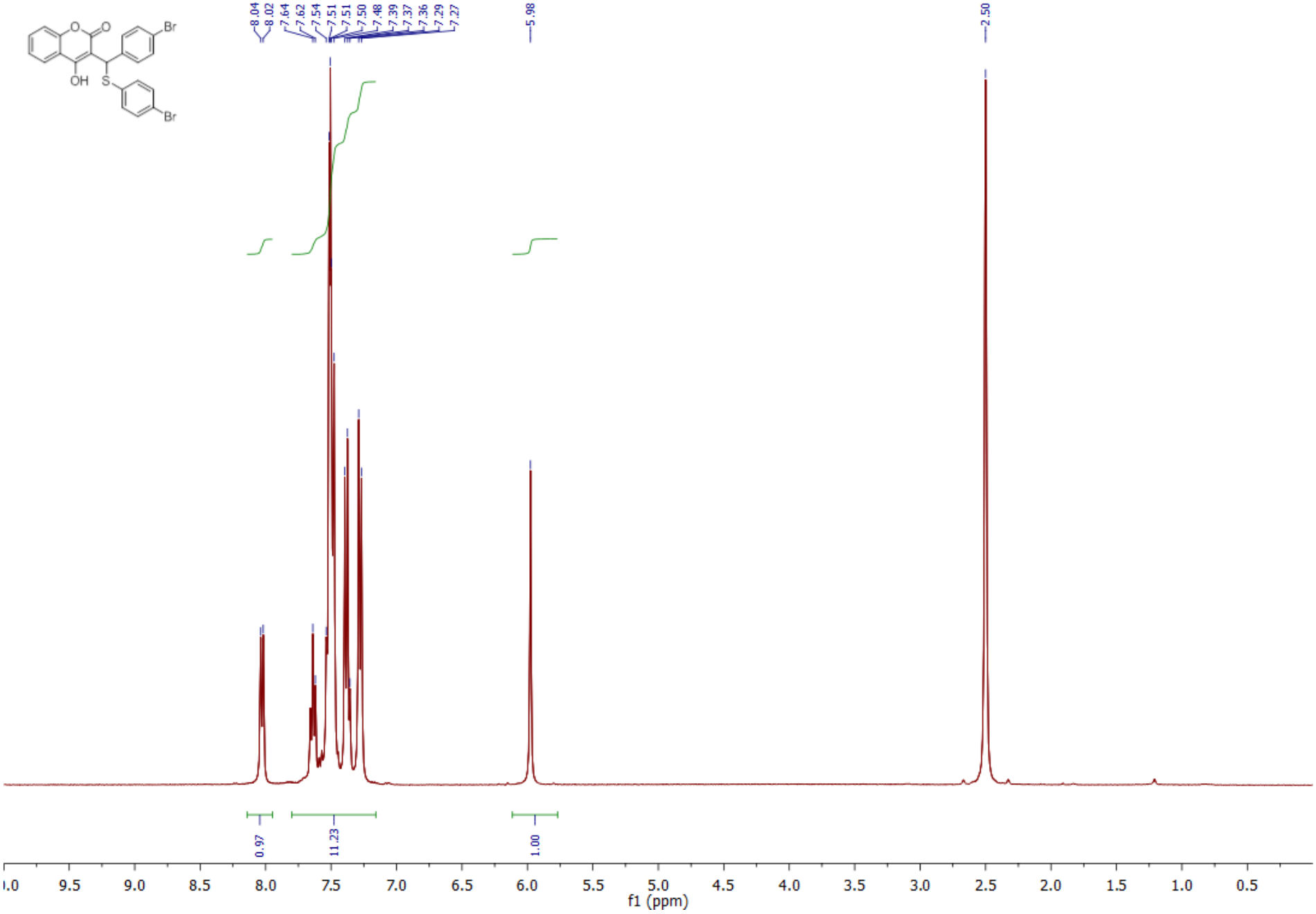
^{1}H NMR (400 MHz, d_6-DMSO): compound **5b**



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



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



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