Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Synthesis of Pyrazolylvinyl Ketones from Furan Derivatives

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Supporting information

General remarks

All commercial products and solvents were used without further purification. All reactions were run under the air unless noted otherwise.

The reactions under microwave irradiation were conducted in Microwave Synthesis Reactor «Biotage® Robot Eight» using sealed microwave reaction vessels. TLC analyses were performed on Merck 60 F254 aluminum plates in combination with UV detection (254 nm). Flash chromatography was performed on silica gel 200-300 mesh using mixture EtOAc/*i*-hexane as eluents. Melting points were determined on a Mel-Temp II Laboratory Devices apparatus; the values are uncorrected. NMR spectra were recorded on a Bruker AV-600 (^{1}H NMR at 600 MHz and ^{13}C NMR at 151 MHz) and Bruker AV-400 (^{1}H NMR at 400 MHz and ^{13}C NMR at 101 MHz) spectrometers. Proton chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ δ = 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets), coupling constants (*J*) and integration. Coupling constants (*J*) are reported in Hertz (Hz). Carbon chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ δ = 77.16 ppm).

IR spectra were measured on PerkinElmer Spectrum BX spectrophotometer (KBr and NaCl plates). HRMS-ESI spectra were recorded at the Chair of Organic Chemistry, Friedrich Alexander University of Erlangen-Nuremberg. LC-MS data were obtained on a BRUKER ESQUIRE 2000 using electrospray ionization (ESI), DAD detector, and a Kinetex C8 analytical column (2.1 mm x 75 mm, 2.6 μm). Single crystals of $C_{22}H_{21}FN_2O$ (**3h**) were crystalized from $CDCl_3$. A suitable crystal was selected and mounted on a loop on a SuperNova, Dual, Cu at zero, Atlas diffractometer. The crystal was kept at 152(1) K during data collection. Using Olex2[1], the structure was solved with the ShelXT[2] structure solution program using Intrinsic Phasing and refined with the ShelXL[3] refinement package using Least Squares minimisation.

General procedure for the synthesis of xanthates S1

NaI (1.5 g, 10 mmol) was added to a stirred solution of commercially available phenacyl bromide (10 mmol) in dry acetone (15 mL) at 20°C, and the mixture was stirred for 10 min. Then the potassium xanthogenate (12 mmol) was added in small portions over a period of 5 min. The resulting mixture was stirred at 20 C for approximately 20 min (the reaction completion was followed by TLC). Acetone was evaporated and the residue was extracted with dichloromethane (3×30 mL), washed with brine, and the solution was dried over Na_2SO_4. Dichloromethane was evaporated under reduced pressure to give products **S1** in good yields.

O-Ethyl S-(2-oxo-2-phenylethyl) carbonodithioate (S1a). Yield 2.28 g (95%). White solid. M. p. 30–32 °C (lit. 31–32 °C).[4] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03–8.00 (m, 2H), 7.63–7.58 (m, 1H), 7.51–7.47 (m, 2H), 4.59 (s, 2H), 4.63–4.58 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 213.3, 192.3, 135.9, 133.8, 128.8, 128.5, 70.7, 43.6, 13.7 ppm. HRMS (ESI) calcd. for $C_{11}H_{12}O_2S_2$ $[M+Na]^+$: 263.0176; found: 263.0172.

S-(2-(4-Bromophenyl)-2-oxoethyl) O-ethyl carbonodithioate (S1b). Yield 3.07 g (97 %). White solid. M. p. 83–84 °C (lit. 84–86 °).[4] ^{1}H NMR (400 MHz, $CDCl_3$): 7.90–7.85 (m, 2H), 7.66–7.63 (m, 2H), 4.64 (q, *J* = 7.1 Hz, 2H), 4.61 (s, 2H), 1.40 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 213.3, 191.6, 134.7, 132.3, 130.1, 129.2, 71.0, 43.5, 13.9 ppm.

O-Ethyl S-(2-(4-fluorophenyl)-2-oxoethyl) carbonodithioate (S1c). Yield 2.48 g (96%). White solid. M. p. 60–62 °C (lit. 58–61 °C).[24] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.08–8.05 (m, 2H), 7.20–7.16 (m, 2H), 4.66–4.63 (m, 4H), 1.40 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 213.2, 190.9, 167.0, 165.3, 131.2, 131.2, 116.0, 115.9, 70.8, 43.4, 13.7 ppm. HRMS (ESI): *m/z* calcd. for $C_{11}H_{11}FO_2S_2$ $[M+H]^+$: 259.0263, found: 259.0252.

O-Ethyl S-(2-(4-methoxyphenyl)-2-oxoethyl) carbonodithioate (S1d). Yield 2.65 g (98%). White solid. M. p. 67–68 °C (lit. 68–69 °C).[5] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03–8.00 (m, 2H), 6.98–6.96 (m, 2H), 4.67–4.61 (m, 4H), 3.89 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 213.5, 190.8, 164.0, 131.0, 128.8, 114.0, 70.6, 55.6, 43.4, 13.8 ppm. HRMS **(ESI)**: *m/z* calcd. for $C_{12}H_{14}O_3S_2$ $[M+Na]^+$: 293.0282, found: 293.0277.

O-Ethyl S-(2-oxo-2-(*p*-tolyl)ethyl) carbonodithioate (S1e). Yield 2.5 g (100%). White solid. M. p. 85–86 °C (lit. 88–89 °C).[6] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.95–7.94 (m, 2H), 7.33–7.31 (m,

2H), 4.68–4.65 (m, 4H), 2.46 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H) ppm.^{13}C NMR (151 MHz, $CDCl_3$): δ = 213.1, 191.6, 144.4, 133.0, 129.2, 128.3, 70.3, 43.2, 21.4, 13.4 ppm. HRMS (ESI): *m/z* calcd. for $C_{12}H_{14}O_2S_2$ $[M+H]^+$: 255.0513, found: 255.0507.

General procedure for the synthesis of furfuryl ketones 1

A solution of xanthogenate **S1** (12.5 mmol) and furan (80 mmol for 2-methylfuran and 2-ethylfuran; 13 mmol for 2-butylfuran and 2-phenylfuran) in DMSO (30 ml) was cooled (5–10°C) and treated with $FeSO_4 \cdot 7H_2O$ (6.25 mmol). Then 34% aqueous H_2O_2 (2.5 ml, 25 mmol) was dropwise added. After adding H_2O_2, the reaction mixture was stirred for 30 min at 5–10°C, then for 2-3 h at room temperature (TLC control). The mixture was poured into water (300 ml), extracted with ethyl acetate (4×50 ml), the combined extracts were washed with saturated aqueous NaCl solution, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was purified by flash chromatography using EtOAc/*i*-Hex as eluent.

2-(5-Methylfuran-2-yl)-1-phenylethan-1-one (1a). Yield 1.6 g (64%). Pale yellow oil.[7] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.04–8.03 (m, 2H), 7.60–7.57 (m, 1H), 7.50–7.47 (m, 2H), 6.12 (d, *J* = 3.0 Hz, 1H), 5.93 (dd, *J* = 3.0, 0.9 Hz, 1H), 4.27 (s, 2H), 2.28 (br. s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.4, 151.7, 146.3, 136.3, 133.3, 128.7, 128.7, 109.1, 106.6, 38.6, 13.6 ppm. IR (NaCl): 1693 (C=O), 1597, 1220, 1021, 784 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{13}H_{12}O_2$ $[M+H]^+$: 201.0916; found: 201.0901.

1-(4-Bromophenyl)-2-(5-methylfuran-2-yl)ethan-1-one (1b). Yield 2.12 g (61%). Pale beige solid. M. p. 58–59 °C (lit. 58–59 °C).[5] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.85 (m, 2H), 7.61–7.59 (m, 2H), 6.08 (d, *J* = 2.9 Hz, 1H), 5.90 (m, 1H), 4.20 (s, 2H), 2.25 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.2, 151.8, 145.8, 135.0, 131.9, 130.1, 128.5, 109.1, 106. 6, 38.6, 13.5 ppm. IR (KBr): 1682 (C=O), 1582, 1220, 1070, 1022, 785 cm^{-1}.

1-(4-Fluorophenyl)-2-(5-methylfuran-2-yl)ethan-1-one (1c). Yield 1.63 g (60%). Brownish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09–8.04 (m, 2H), 7.18–7.12 (m, 2H), 6.11 (d, *J* = 3.0 Hz, 1H), 5.94–5.93 (m, 1H), 4.24 (s, 2H), 2.28 (br. s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.8, 167.1, 164.6, 151.8, 146.1, 131.4, 131.3, 115.9, 115.7, 109.1, 106.6, 38.6, 13.6 ppm. IR (NaCl): 1697 (C=O), 1601, 1235, 1158, 847 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{13}H_{11}FO_2$ $[M]^+$: 218.0743; found: 218.0737.

1-(4-Methoxyphenyl)-2-(5-methylfuran-2-yl)ethanone (1d). Yield 1.67 g (58%). Pale beige solid. M. p. 68–69 °C (lit. 69-70 °C).[5] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (m, 2H), 6.93 (m, 2H), 6.07 (d, *J* = 2.8 Hz, 1H), 5.89 (m, 1H), 4.18 (s, 2H), 3.87 (s, 3H), 2.25 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.9, 163.9, 151.7, 147.0, 131.1, 129.8, 114.0, 108.9, 106.7, 55.6, 38.6, 13.6 ppm. IR (KBr): 1682 (C=O), 1602, 1509, 1333, 1267, 1226, 1184, 1020, 830 cm^{-1}.

2-(5-Ethylfuran-2-yl)-1-phenylethan-1-one (1e). Yield 1.87 g (70%). Brownish oil.[7] ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.02–8.00 (m, 2H), 7.57–7.54 (m, 1H), 7.47–7.45 (m, 2H), 6.10 (d, *J* = 3.1 Hz, 1H), 5.91 (m, 1H), 4.25 (s, 2H), 2.60 (q, *J* = 7.5 Hz, 2H), 1.19 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 195.1, 157.2, 146.0, 136.2, 133.1, 128.4, 128.4, 108.6, 38.4, 21.2, 11.9 ppm. IR (NaCl): 1686 (C=O), 1597, 1219, 1181, 1013, 779 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{14}H_{14}O_2$ $[M+H]^+$: 215.1072; found: 215.1065.

2-(5-Ethylfuran-2-yl)-1-(*p*-tolyl)ethan-1-one (1f). Yield 1.42 g (50%). White solid. M. p. 42–44 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.92–7.90 (m, 2H), 7.26–7.25 (m, 2H), 6.09 (d, *J* = 3.0 Hz, 1H), 5.90 (m, 1H), 4.22 (s, 2H), 2.60 (q, *J* = 7.5 Hz, 2H), 2.40 (s, 3H), 1.19 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.0, 157.4, 146.4, 144.2, 133.8, 129.3, 128.8, 108.7, 104.9, 38.6, 21.7, 21.4, 12.1 ppm. IR (NaCl): 1684 (C=O), 1606, 1223, 1181, 776 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{15}H_{16}O_2$ $[M+H]^+$: 229.1229; found: 229.1220.

2-(5-Ethylfuran-2-yl)-1-(4-fluorophenyl)ethan-1-one (1g). Yield 1.3 g (45%). Brownish oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.06–8.02 (m, 2H), 7.15–7.11 (m, 2H), 6.10 (d, *J* = 3.1 Hz, 1H), 5.91 (d, *J* = 3.1 Hz, 1H), 4.22 (s, 2H), 2.60 (q, *J* = 7.5 Hz, 2H), 1.19 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 193.7, 166.7, 165.0, 157.5, 145.9, 131.4, 131.3, 115.8, 115.7, 108.9, 105.0, 38.7, 21.3, 12.1 ppm. IR (NaCl): 1693 (C=O), 1599, 1233, 1158, 845 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{14}H_{13}FO_2$ $[M]^+$: 232.0900; found: 232.0892.

2-(5-Butylfuran-2-yl)-1-(4-fluorophenyl)ethan-1-one (1h). Yield 1.33 g (41%). Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06–8.01 (m, 2H), 7.14–7.08 (m, 2H), 6.09 (d, *J* = 3.1 Hz, 1H), 5.91 (d, *J* = 3.1 Hz, 1H), 4.22 (s, 2H), 2.56 (t, *J* = 7.6 Hz, 2H), 1.61–1.50 (m, 2H), 1.32 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.8, 167.1, 164.5, 156.3, 145.9, 131.4, 131.3, 115.8, 115.6, 108.8, 105.7, 38.7, 30.1, 27.7, 22.2, 13.8 ppm. MS (ESI): *m/z* calcd. for $C_{16}H_{17}FO_2$ $[M]^+$: 260.1213; found: 260.91.

1-(4-Fluorophenyl)-2-(5-phenylfuran-2-yl)ethan-1-one (1i). Yield 1.75 g (50%). Pale yellow solid. M. p. 84-86 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–7.99 (m, 2H), 7.55–7.52 (m, 2H), 7.30–7.26 (m, 2H), 7.19–7.06 (m, 3H), 6.53 (d, *J* = 3.3 Hz, 1H), 6.25 (dd, *J* = 2.6, 0.7 Hz, 1H), 4.28 (s, 2H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 193.3, 166.8, 165.1, 153.6, 147.6, 131.4, 131.4, 130.7, 128.6, 127.2, 123.6, 115.9, 115.8, 110.5, 106.1, 38.8 ppm. IR (NaCl): 1693 (C=O), 1598, 1505, 1229, 1157, 1022, 843, 760 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{18}H_{13}FO_2$ $[M+H]^+$: 281.0978; found: 281.0971.

General procedure for the synthesis of pyrazoles 3

Hydrazine hydrochloride (2 mmol) and anhydrous NaOAc (4 mmol) were added to a solution of furfuryl ketone **1** (2 mmol) in ethanol (5 mL), and the mixture was stirred for 24 hours at 80 °C (TLC and LC-MS control). Then, the reaction mixture was poured into H_2O (100 mL) and extracted with EtOAc (4 × 25 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The resulting crude product was purified by flash chromatography using EtOAc/*i*-Hex as eluents to give a mixture of (*E*,*Z*)-isomers which was isomerized to give (*E*)-**3**.

Isomerization (*E*,*Z*)-3 → (*E*)-3

Microwave reaction vessel was charged with (*E*,*Z*)-**3** (0.2 mmol), I_2 (0.0034 g, 0.013 mmol) and toluene (5 mL). The reaction mixture was stirred at 140 ºC in a microwave reactor for 2-6 hours.* After completion of the reaction, toluene and iodine were removed under reduced pressure to afford pure (*E*)-**3**.

*For compounds with R^1 = Me the isomerization might be achieved by heating of the reaction mixture with iodine at 80 ºC

(*E*)-(4-(1,3-Diphenyl-1*H*-pyrazol-5-yl)but-3-en-2-one ((*E*)-3a). Yield 0.29 g (50%). Yellow solid. M. p. 110–112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92–7.91 (m, 2H), 7.58–7.35 (m, 9H), 7.09 (s, 1H), 6.74 (dd, *J* = 16.1, 1.4 Hz, 1H), 2.32 (d, *J* = 1.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.9, 151.9, 139.3, 138.4, 131.9, 129.0, 128.5, 128.3, 128.3, 128.2, 127.9, 125.3, 125.1, 103.1, 27.6 ppm. IR (NaCl): 1691 (C=O), 1608, 1502, 1348, 1241, 943 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{19}H_{16}N_2O$ $[M+H]^+$: 289.1341; found: 289.1335.

(*Z*)-(4-(1,3-Diphenyl-1*H*-pyrazol-5-yl)but-3-en-2-one ((*Z*)-3a). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.91 (m, 2H), 7.69 (m, 1H), 7.52–7.40 (m, 8H), 6.54 (d, *J* = 12.7, 1H), 6.23 (d, *J* = 12.7 Hz, 1H), 2.34 (s, 3H) ppm.

(*E*)-4-(3-(4-Bromophenyl)-1-phenyl-1*H*-pyrazol-5-yl)but-3-en-2-one ((*E*)-3b). Yield 0.38 g (53%). Yellow solid. M. p. 108–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69–7.65 (m, 2H), 7.48–7.40 (m, 7H), 7.25 (d, *J* = 16.1 Hz, 1H), 6.95 (s, 1H), 6.63 (d, *J* = 16.1 Hz, 1H), 2.22 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.4, 151.3, 140.0, 138.8, 131.9, 131.9, 129.6, 129.0, 128.9, 128.8, 127.4, 125.6, 122.4, 103.5, 28.2 ppm. IR (NaCl): 1736 (C=O), 1604, 1503, 1447, 1349, 1246, 1145, 983 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{19}H_{15}BrN_2O$ $[M+H]^+$: 367.0446; found: 367.0441.

(*Z*)-4-(3-(4-Bromophenyl)-1-phenyl-1*H*-pyrazol-5-yl)but-3-en-2-one ((*Z*)-3b). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.78 (m, 2H), 7.56 (s, 1H), 7.56–7.26 (m, 7H), 6.52 (d, *J* = 12.7 Hz, 1H), 6.23 (d, *J* = 12.7 Hz, 1H), 2.33 (s, 3H) ppm.

(*E*)-4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-5-yl)but-3-en-2-one ((*E*)-3c). Yield 0.42 g (68%). Yellow solid. M. p. 145–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79–7.76 (m, 2H), 7.46–7.38 (m, 5H), 7.26 (d, *J* = 16.1 Hz, 1H), 7.07–7.01 (m, 2H), 6.93 (s, 1H), 6.63 (d, *J* = 16.1 Hz, 1H), 2.22 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.4, 164.2, 161.7, 151.5, 140.0, 138.8, 129.5, 128.9, 128.9, 127.6, 127.5, 125.6, 115.8, 115.6, 103.4, 28.1 ppm. IR (NaCl): 1741 (C=O), 1622, 1507, 1487, 1377, 1236, 982, 956 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{19}H_{15}FN_2O$ $[M+H]^+$: 307.1247; found: 307.1241.

(*Z*)-4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-5-yl)but-3-en-2-one ((*Z*)-3c). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82–7.80 (m, 2H), 7.57 (s, 1H), 7.45–7.42 (m, 5H), 7.04–7.02 (m, 2H), 6.42 (d, *J* = 12.7 Hz, 1H), 6.14 (d, *J* = 12.7 Hz, 1H), 2.26 (s, 3H) ppm.

(*E*)-4-(3-(4-Methoxyphenyl)-1-phenyl-1*H*-pyrazol-5-yl)but-3-en-2-one ((*E*)-3d)

Yield 0.27 g (42%). Beige solid. M. p. 125–127 °C (EtOAc/Hex = 1:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.83 (m, 2H), 7.58–7.47 (m, 5H), 7.34 (d, *J* = 16.1 Hz, 1H), 7.02–6.98 (m, 3H), 6.73 (d, *J* = 16.1 Hz, 1H), 3.87 (s, 3H), 2.33 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.6, 159.8, 152.2, 139.7, 138.9, 129.5, 129.2, 128.7, 128.6, 127.1, 125.6, 125.1, 114.1, 103.1, 55.4, 28.1 ppm. IR (NaCl): 1667 (C=O), 1652, 1613, 15919, 1498, 1452, 1438, 1426, 1361, 1243, 1179. HRMS (ESI): *m/z* calcd. for $C_{20}H_{18}N_2O_2$ $[M+Na]^+$: 341.1266; found: 341.1255.

(*E*)-1-(1,3-Diphenyl-1*H*-pyrazol-5-yl)pent-1-en-3-one ((*E*)-3e). Yield 0.15 g (50%). Yellow solid. M. p. 98–101 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.89–7.88 (m, 2H), 7.55–7.35 (m, 9H), 7.07 (s, 1H), 6.76 (d, *J* = 16.0 Hz, 1H), 2.62 (q, *J* = 7.3 Hz, 2H), 1.14 (t, *J* = 7.3 Hz, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 200.1, 152.3, 140.0, 139.0, 132.4, 129.5, 128.7, 128.6, 128.6, 128.3, 128.1, 127.8, 125.8, 125.6, 103.4,

34.7, 8.0 ppm. IR (NaCl): 1691 (C=O), 1613, 1498, 765 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{20}H_{18}N_2O$ $[M+H]^+$: 303.1497, found: 303.1494.

(*Z*)-1-(1,3-Diphenyl-1*H*-pyrazol-5-yl)pent-1-en-3-one ((*Z*)-3e). ^1H NMR (600 MHz, $CDCl_3$): δ = 7.94–7.92 (m, 2H), 7.73 (s, 1H), 7.54–7.32 (m, 8H), 6.52 (d, *J* = 12.7 Hz, 1H), 6.22 (d, *J* = 12.7 Hz, 1H), 2.64 (q, *J* = 7.3 Hz, 2H), 1.16 (t, *J* = 7.3 Hz, 3H) ppm.

(*E*)-1-(1-Phenyl-3-(*p*-tolyl)-1*H*-pyrazol-5-yl)pent-1-en-3-one ((*E*)-3f). Yield 0.2 g (32%). Yellow solid. M. p. 129–132 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.78–7.77 (m, 2H), 7.54–7.45 (m, 5H), 7.39 (d, *J* = 16.0 Hz, 1H), 7.26–7.23 (m, 2H), 7.04 (s, 1H), 6.74 (d, *J* = 16.0 Hz, 1H), 2.61 (q, *J* = 7.3 Hz, 2H), 2.39 (s, 3H), 1.14 (t, *J* = 7.3 Hz, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 204.1, 156.4, 143.9, 143.0, 142.2, 133.6, 133.4, 133.4, 132.6, 132.1, 131.7, 129.7, 129.6, 107.3, 38.7, 25.3, 12.0 ppm. IR (NaCl): 1691 (C=O), 1611, 1499, 1443, 1352, 1234, 1185, 956 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{21}H_{20}N_2O$ $[M+H]^+$: 317.1654; found: 317.1657.

(*Z*)-1-(1-Phenyl-3-(*p*-tolyl)-1*H*-pyrazol-5-yl)pent-1-en-3-one ((*Z*)-3f). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.83 (m, 2H), 7.73 (s, 1H), 7.59–7.48 (m, 5H), 7.31–7.27 (m, 2H), 6.54 (d, *J* = 12.8, 1H), 6.23 (d, *J* = 12.8 Hz, 1H), 2.65 (q, *J* = 7.3 Hz, 2H), 2.41 (s, 3H), 1.18 (t, *J* = 7.3 Hz, 3H) ppm.

(*E*)-1-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-5-yl)pent-1-en-3-one ((*E*)-3g). Yield 0.34 g (53%). Yellow solid. M. p. 111–113 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.87–7.84 (m, 2H), 7.55–7.46 (m, 5H), 7.39 (d, *J* = 16.0 Hz, 1H), 7.14–7.10 (m, 2H), 7.01 (s, 1H), 6.74 (d, *J* = 16.0 Hz, 1H), 2.62 (q, *J* = 7.3 Hz, 2H), 1.14 (t, *J* = 7.3 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.2, 164.2, 161.7, 151.4, 140.2, 138.8, 129.6, 128.0, 128.0, 127.6, 127.6, 125.6, 115.8, 115.6, 103.3, 34.8, 8.1 ppm. IR (NaCl): 1669 (C=O), 1609, 1499, 1446, 1231, 1156, 763 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{20}H_{17}FN_2O$ $[M+H]^+$: 321.1403; found: 321.1392.

(*Z*)-1-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-5-yl)pent-1-en-3-one ((*Z*)-3g). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96–7.88 (m, 2H), 7.75 (s, 1H), 7.52–7.48 (m, 5H), 7.12 (m, 2H), 6.49 (d, *J* = 12.8 Hz, 1H), 6.21 (d, *J* = 12.8 Hz, 1H), 2.64 (q, *J* = 7.3 Hz, 2H), 1.15 (t, *J* = 7.3 Hz, 3H) ppm.

(*E*)-1-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-5-yl)hept-1-en-3-one ((*E*)-3h). Yield 0.36 g (52%). White solid. M. p. 121–123 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.77 (m, 2H), 7.47–7.41 (m, 5H), 7.30 (d, *J* = 16.0 Hz, 1H), 7.07–7.03 (m, 2H), 6.95 (s, 1H), 6.67 (d, *J* = 16.0 Hz, 1H), 2.51 (t, *J* = 7.4 Hz,

2H), 1.59–1.50 (m, 2H), 1.29–1.25 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 198.8, 162.7, 161.1, 150.4, 139.1, 137.9, 128.5, 127.7, 127.1, 127.0, 126.5, 126.5, 124.6, 114.7, 114.6, 102.2, 40.3, 25.3, 21.4, 12.8 ppm. IR (NaCl): 1660 (C=O), 1608, 1498, 1447, 1224, 1157, 956 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{22}H_{21}FN_2O$ $[M+H]^+$: 349.1716; found: 349.1703.

(*Z*)-1-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-5-yl)hept-1-en-3-one ((*Z*)-3h). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (m, 2H), 7.74 (s, 1H), 7.71–7.44 (m, 5H), 7.13 (m, 2H), 6.52 (d, *J* = 12.8 Hz, 2H), 6.24 (d, *J* = 12.8 Hz, 1H), 2.61 (t, *J* = 7.0 Hz, 1H), 1.75–1.45 (m, 2H), 1.45–1.28 (m, 2H), 0.95 (t, *J* = 7.3, 3H) ppm.

(*E*)-3-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-5-yl)-1-phenylprop-2-en-1-one ((*E*)-3i). Yield 0.27 g (37%). Yellow solid. M. p. 149-152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = δ 7.94–7.92 (m, 2H), 7.84–7.79 (m, 2H), 7.60 (d, *J* = 15.6 Hz, 1H), 7.53–7.39 (m, 9H), 7.09–7.03 (m, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 188.3, 163.1, 160.6, 150.4, 139.5, 137.9, 136.6, 132.2, 129.3, 128.5, 127.7, 127.4, 126.6, 126.5, 124.7, 123.0, 114.8, 114.6, 102.4 ppm. IR (NaCl): 1662 (C=O), 1597, 1514, 1447, 1225, 1154, 1013, 956, 840, 769, 701 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{24}H_{17}FN_2O$ $[M+H]^+$: 369.1403; found: 369.1390.

(*Z*)-3-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-5-yl)-1-phenylprop-2-en-1-one ((*Z*)-3i). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08–8.00 (m, 2H), 7.86 (m, 2H), 7.65–7.48 (m, 7H), 7.46 (s, 1H), 7.10 (m, 3H), 6.84 (d, *J* = 12.9 Hz, 1H), 6.79 (d, *J* = 12.9 Hz, 1H) ppm.

(*E*)-4-(3-(4-Fluorophenyl)-1-(*p*-tolyl)-1*H*-pyrazol-5-yl)but-3-en-2-one ((*E*)-3j). Yield 0.34 g (53%). Yellow solid. M. p. 133–135 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.86–7.83 (m, 2H), 7.37–7.30 (m, 5H), 7.13–7.10 (m, 2H), 6.99 (s, 1H), 6.70 (d, *J* = 16.1 Hz, 1H), 2.45 (s, 3H), 2.30 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.6, 164.1, 161.7, 151.3, 139.9, 139.0, 136.3, 130.1, 129.1, 128.7, 127.6, 127.5, 125.5, 115.8, 115.6, 103.1, 28.1, 21.2 ppm. IR (NaCl): 1653 (C=O), 1609, 1515, 1448, 1260, 1156, 800 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{20}H_{17}FN_2O$ $[M]^+$: 320.1325, found: 320.1319.

(*Z*)-4-(3-(4-Fluorophenyl)-1-(*p*-tolyl)-1*H*-pyrazol-5-yl)but-3-en-2-one ((*Z*)-3j). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95–7.88 (m, 2H), 7.67 (s, 1H), 7.39 (m, 4H), 7.37–6.99 (m, 2H), 6.52 (d, *J* = 12.7 Hz, 1H), 6.22 (d, *J* = 12.8 Hz, 1H), 2.46 (s, 3H), 2.36 (s, 3H) ppm.

(*E*)-1-(3-(4-Fluorophenyl)-1-*p*-tolyl-1*H*-pyrazol-5-yl)pent-1-en-3-one ((*E*)-3k). Yield 0.35 g (53%). Pale yellow solid. M. p. 163–165 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.86–7.84 (m, 2H), 7.38–7.32 (m, 5H), 7.13–7.10 (m, 2H), 6.99 (s, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 2.61 (q, *J* = 7.3 Hz, 2H), 2.45 (s, 3H), 1.14 (t, *J* = 7.3 Hz, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 200.1, 163.7, 163.1, 151.2, 140.2, 138.9, 136.4, 130.1, 127.8, 127.8, 125.6, 127.5, 125.5, 115.8, 115.6, 102.9, 34.7, 21.2, 8.1 ppm. IR (NaCl): 1669 (C=O), 1610, 1514, 1447, 1231, 1230, 956 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{21}H_{19}FN_2O$ $[M+H]^+$: 335.1560, found: 335.1558.

(*Z*)-1-(3-(4-Fluorophenyl)-1-*p*-tolyl-1*H*-pyrazol-5-yl)pent-1-en-3-one ((*Z*)-3k). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (m, 2H), 7.40–7.29 (m, 5H), 7.17–7.07 (m, 2H), 6.51 (d, *J* = 12.7 Hz, 1H), 6.22 (d, *J* = 12.8 Hz, 1H), 2.62 (q, *J* = 7.3 Hz, 2H), 2.46 (s, 3H), 1.14 (t, *J* = 7.3 Hz, 3H) ppm.

(*E*)-(1-(3-(4-Fluorophenyl)-1-(4-methoxyphenyl)-1*H*-pyrazol-5-yl)pent-1-en-3-one ((*E*)-3l). Yield 0.36 g (52%). Pale yellow solid. M. p. 124–127 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.86–7.82 (m, 2H), 7.40–7.38 (m, 2H), 7.33 (d, *J* = 16.0 Hz, 1H), 7.13–7.09 (m, 2H), 7.04–7.02 (m, 2H), 6.98 (s, 1H), 6.71 (d, *J* = 16.0 Hz, 1H), 3.88 (s, 3H), 2.61 (q, *J* = 7.3 Hz, 2H), 1.13 (t, *J* = 7.3 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.2, 164.1, 161.7, 159.9, 151.1, 140.3, 131.8, 128.1, 127.7, 127.6, 127.5, 127.1, 115.8, 115.6, 114.6, 102.7, 55.7, 34.7, 8.1 ppm. IR (NaCl): 1669 (C=O), 1609, 1514, 1447, 1253, 1156, 837 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{21}H_{19}FN_2O_2$ $[M+H]^+$: 351.1509, found: 351.1511.

(*Z*)-(1-(3-(4-Fluorophenyl)-1-(4-methoxyphenyl)-1*H*-pyrazol-5-yl)pent-1-en-3-one ((*Z*)-3l). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (m, 2H), 7.39–7.11 (m, 5H), 7.03 (m, 2H), 6.48 (d, *J* = 12.8 Hz, 1H), 6.22 (d, *J* = 12.8 Hz, 1H), 3.90 (s, 3H), 2.61 (q, *J* = 7.3 Hz, 2H), 1.13 (t, *J* = 7.3 Hz, 3H) ppm.

(*E*)-3-(3-(4-Fluorophenyl)-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)-1-phenylprop-2-en-1-one (*(E)*-3o). Yield 0.19 g (24%). Yellow solid. M. p. 134–137 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.00–7.99 (m, 2H), 7.89–7.85 (m, 2H), 7.63–7.59 (m, 2H), 7.52–7.50 (m, 3H), 7.44–7.41 (m, 2H), 7.14–7.10 (m, 3H), 7.05–7.03 (m, 2H), 3.89 (s, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 189.4, 163.7, 162.1, 159.9, 151.1, 140.7, 137.7, 133.2, 132.0, 130.4, 128.7, 128.5, 127.6, 127.5, 127.2, 127.0, 123.8, 115.7, 115.6, 114.7, 102.9, 55.7 ppm. IR (NaCl): 1668 (C=O), 1604, 1513, 1448, 1250, 1156, 1024, 958, 751 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{25}H_{19}FN_2O_2$ $[M+H]^+$: 399.1509; found: 399.1497.

(1-(2-Bromophenyl)-2-(2-(5-ethylfuran-2-yl)-1-(4-fluorophenyl)ethylidene)-hydrazine (2n). Yield 0.4 g (50%). Yellow solid. M. p. 76–78 °C (EtOAc/*i*-Hex = 1:7). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.36 (s,

1H), 7.87–7.84 (m, 2H), 7.62–7.60 (m, 1H), 7.44–7.43 (m, 1H), 7.29–7.26 (m, 1H), 7.11–7.06 (m, 2H), 6.76–6.73 (m, 1H), 6.12 (d, *J* = 3.1 Hz, 1H), 5.89 (d, *J* = 3.1 Hz, 1H), 4.07 (s, 2H), 2.61 (q, *J* = 7.6 Hz, 2H), 1.19 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.2, 161.8, 157.8, 146.3, 142.7, 142.7, 142.2, 132.3, 128.5, 127.8, 127.7, 120.9, 115.5, 115.3, 114.7, 108.0, 104.8, 27.1, 21.5, 12.2 ppm. IR (NaCl): 2974, 1602, 1508, 1232, 1158, 1012, 843 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{20}H_{18}BrFN_2O$ $[M+H]^+$: 401.0665; found: 401.0631.

1,2-Bis(2-(5-ethylfuran-2-yl)-1-(4-fluorophenyl)ethylidene)hydrazine (2o). Yield 0.22 g (24%). Yellow solid. M. p. 76–78 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.96–7.94 (m, 2H), 7.09–7.06 (m, 2H), 5.77–5.74 (m, 2H), 4.22 (s, 2H), 2.52 (q, *J* = 7.5 Hz, 2H), 1.13 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$): δ = 164.7, 163.0, 158.0, 156.5, 148.2, 133.4, 129.4, 129.3, 115.4, 115.2, 107.3, 104.7, 28.3, 21.3, 12.1 ppm. IR (NaCl): 1592, 1504, 1458, 1232, 1153, 1020, 840 cm^{-1}. HRMS (ESI): *m/z* calcd. for $C_{28}H_{26}F_2N_2O_2$ $[M+H]^+$: 461.2041; found: 461.2025.

1-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-5-yl)-1-(4-(2-methoxyphenyl)piperazin-1-yl)pentan-3-one (4)

Pyrazolylvinyl ketone **3g** (0.045 g, 0.14 mmol) and 1-(2-methoxyphenyl)piperazine (0.028 mL, 0.16 mmol) were mixed in 4 mL of DCM. Sodium triacetoxyborohydride (0.038 g, 0.18 mmol) was added to the above solution and the mixture was stirred at room temperature under nitrogen for 24 h. The solution was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The resulting crude product was purified by flash chromatography using EtOAc/*i*-Hex as eluents to give **4**. Yield 0.036 g (50%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.75 (m, 4H), 7.52–7.40 (m, 3H), 7.12– 6.81 (m, 6H), 6.52 (s, 1H), 4.56–5.53 (m, 1H), 3.82 (s, 3H), 3.15–2.91 (m, 6H), 2.56–2.44 (m, 6H), 1.04 (t, *J* = 7.3 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 208.69, 150.13, 142.82, 140.99, 129.03, 128.22, 127.47, 127.39, 126.34, 125.62, 123.06, 120.89, 118.14, 115.59, 115.38, 110.94, 102.74, 55.30, 54.80, 50.89, 48.83, 42.99, 36.70, 7.68 ppm. HRMS (ESI): *m/z* calcd. for $C_{31}H_{33}FN_4O_2$ $[M+H]^+$: 513.2666; found: 513.2657.

Figure S1: ^{1}H NMR spectrum of O-ethyl S-(2-oxo-2-phenylethyl) carbonodithioate **S1a** (400 MHz, $CDCl_3$)

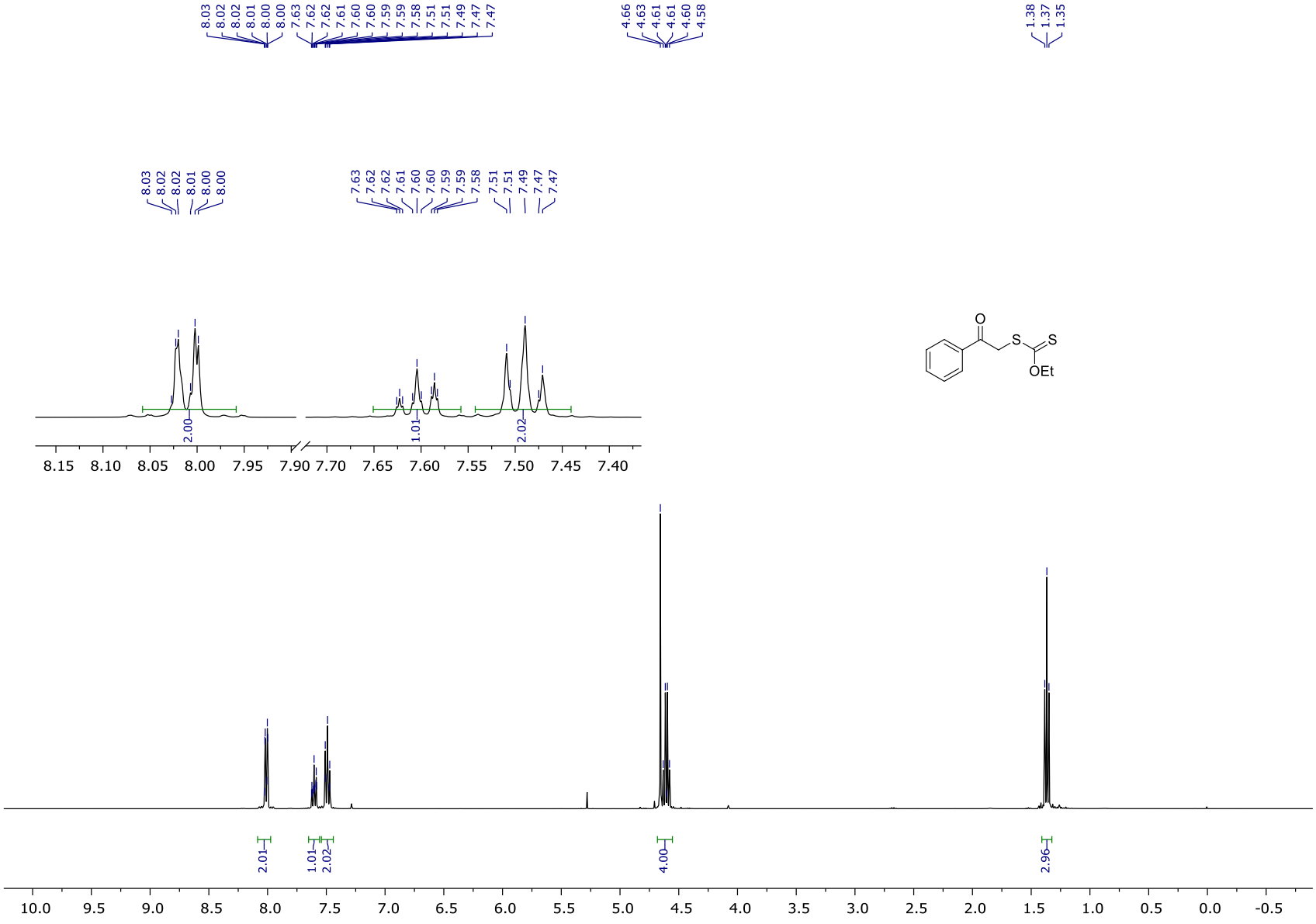


Figure S2: ^{13}C NMR spectrum of O-ethyl S-(2-oxo-2-phenylethyl) carbonodithioate **S1a** (101 MHz, $CDCl_3$)

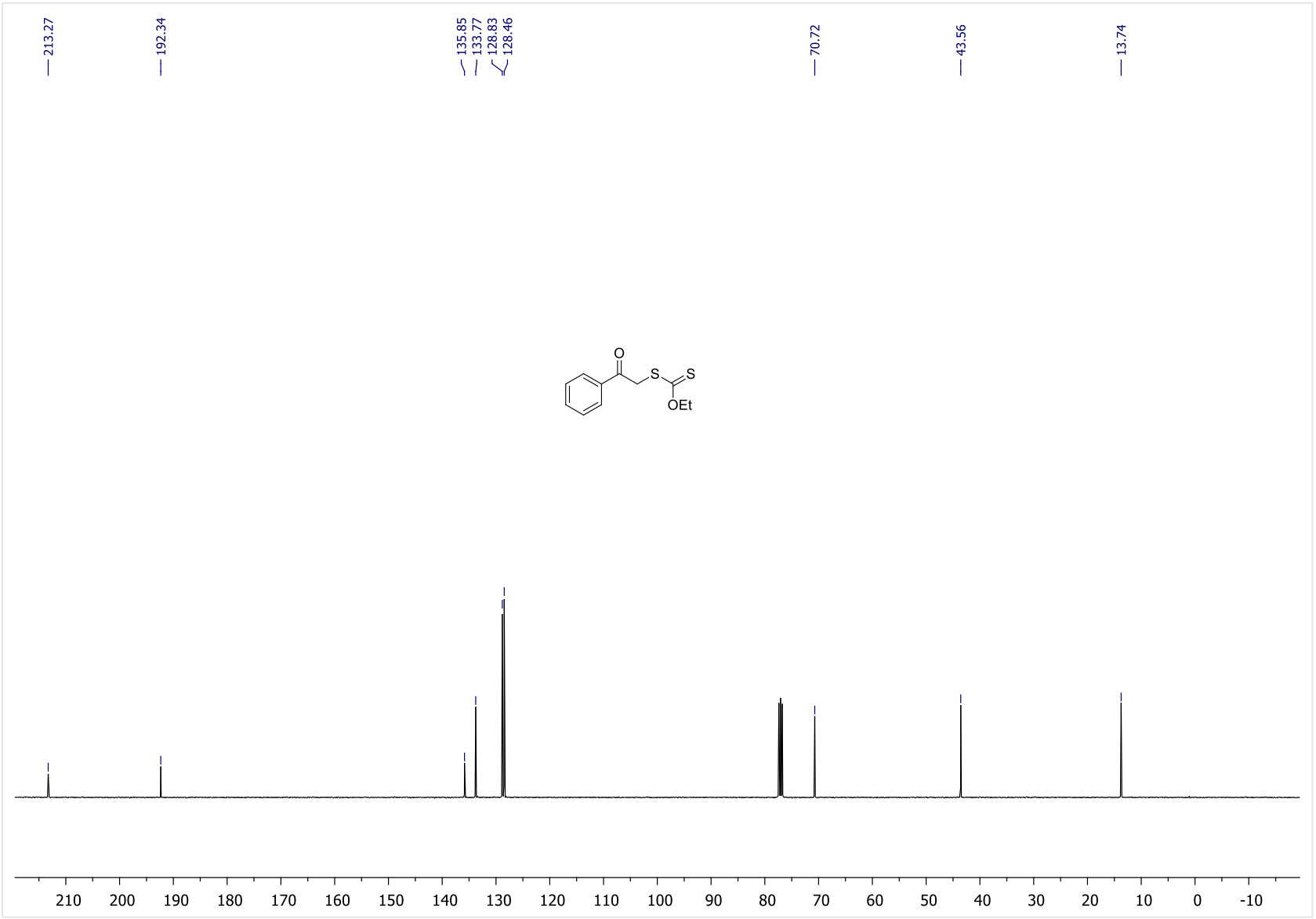


Figure S3: ^{1}H NMR spectrum of S-(2-(4-bromophenyl)-2-oxoethyl) O-ethyl carbonodithioate **S1b** (400 MHz, $CDCl_3$)

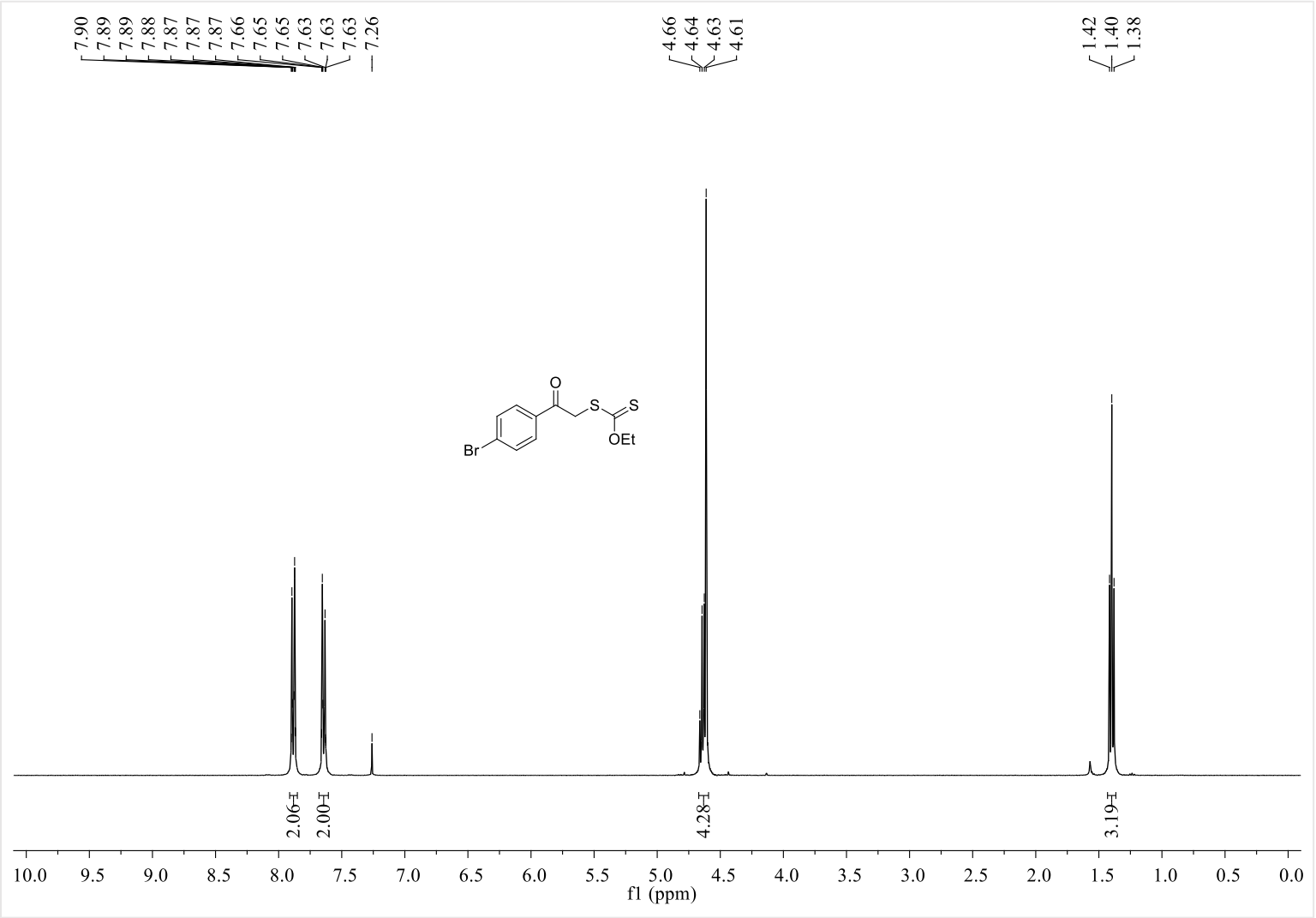


Figure S4: ^{13}C NMR spectrum of S-(2-(4-bromophenyl)-2-oxoethyl) O-ethyl carbonodithioate **S1b** (101 MHz, $CDCl_3$)

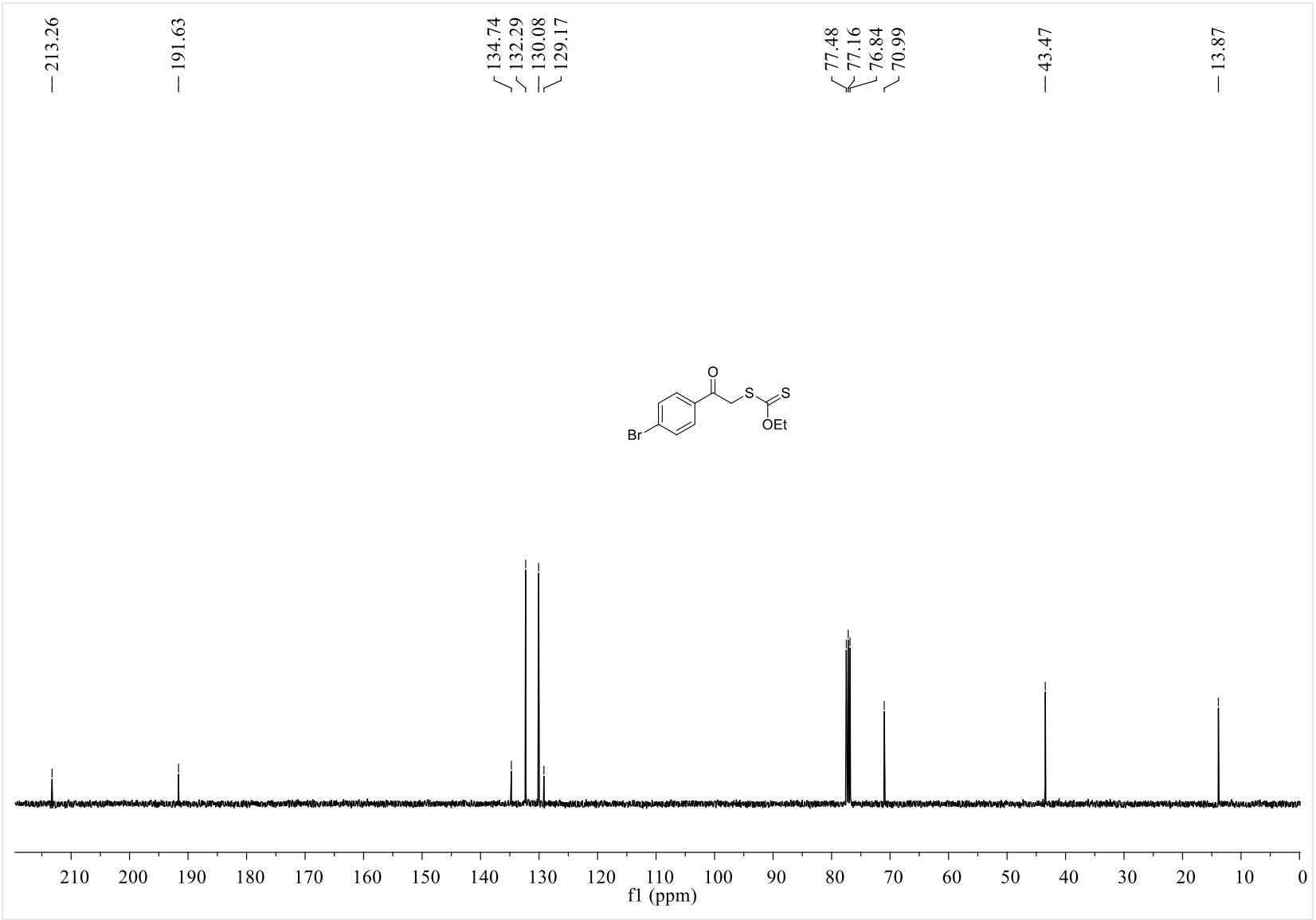


Figure S5: ^{1}H NMR spectrum of O-ethyl S-(2-(4-fluorophenyl)-2-oxoethyl)carbonodithioate **S1c** (600 MHz, $CDCl_3$)

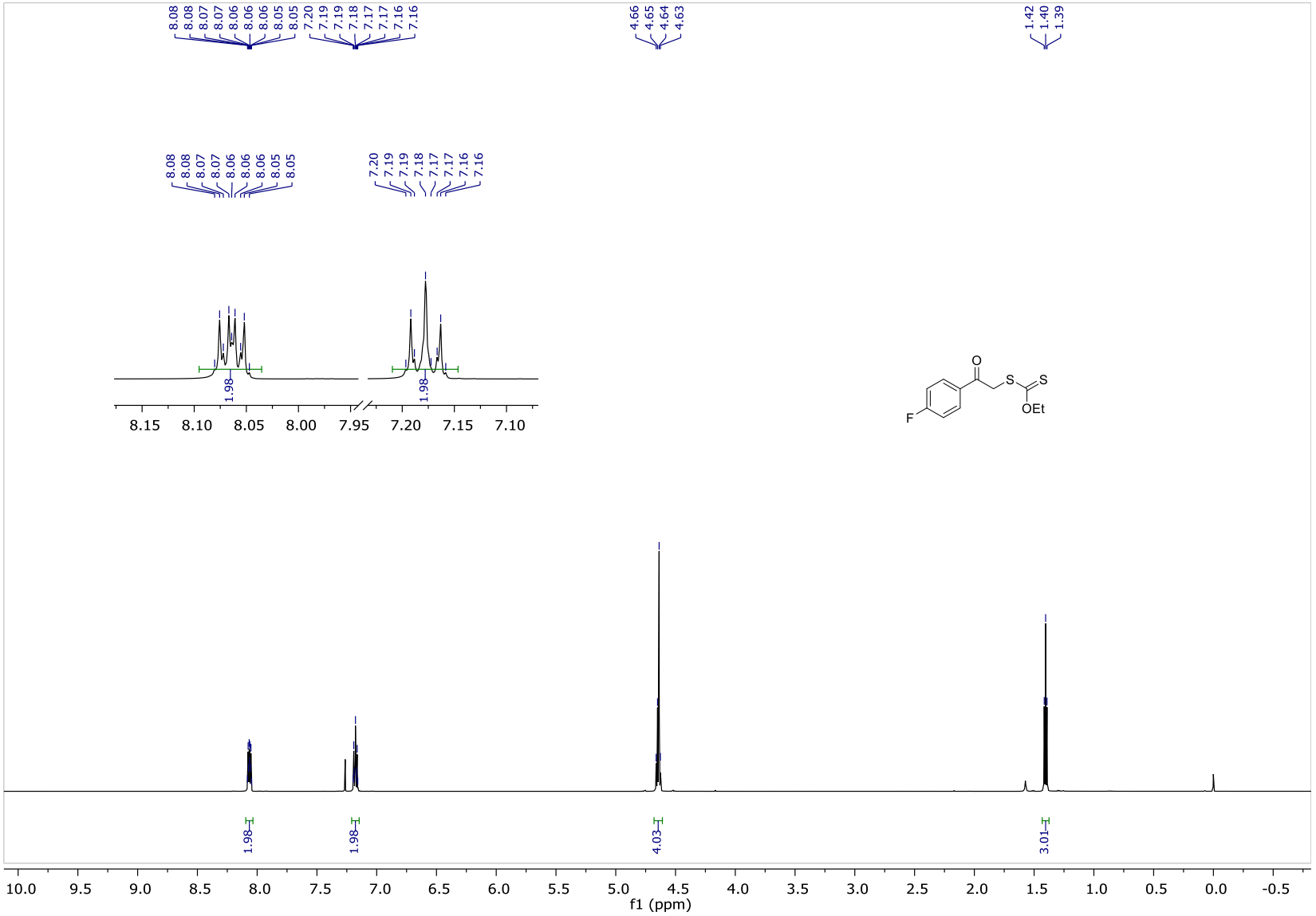


Figure S6: ^{13}C NMR spectrum of O-ethyl S-(2-(4-fluorophenyl)-2-oxoethyl)carbonodithioate **S1c** (151 MHz, $CDCl_3$)

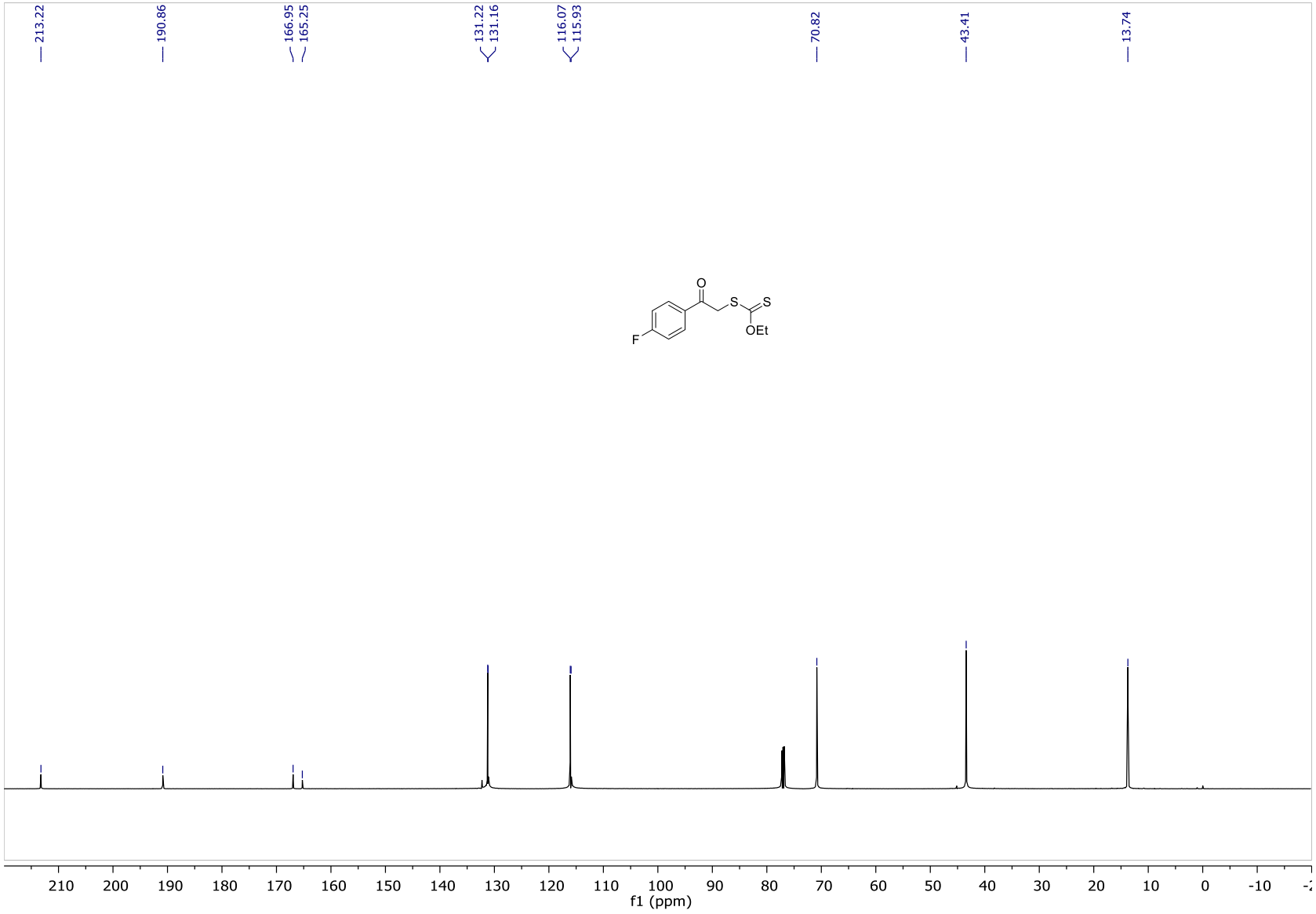


Figure S7: ^{1}H NMR spectrum of O-ethyl S-(2-(4-fluorophenyl)-2-oxoethyl)carbonodithioate **S1d** (400 MHz, $CDCl_3$)

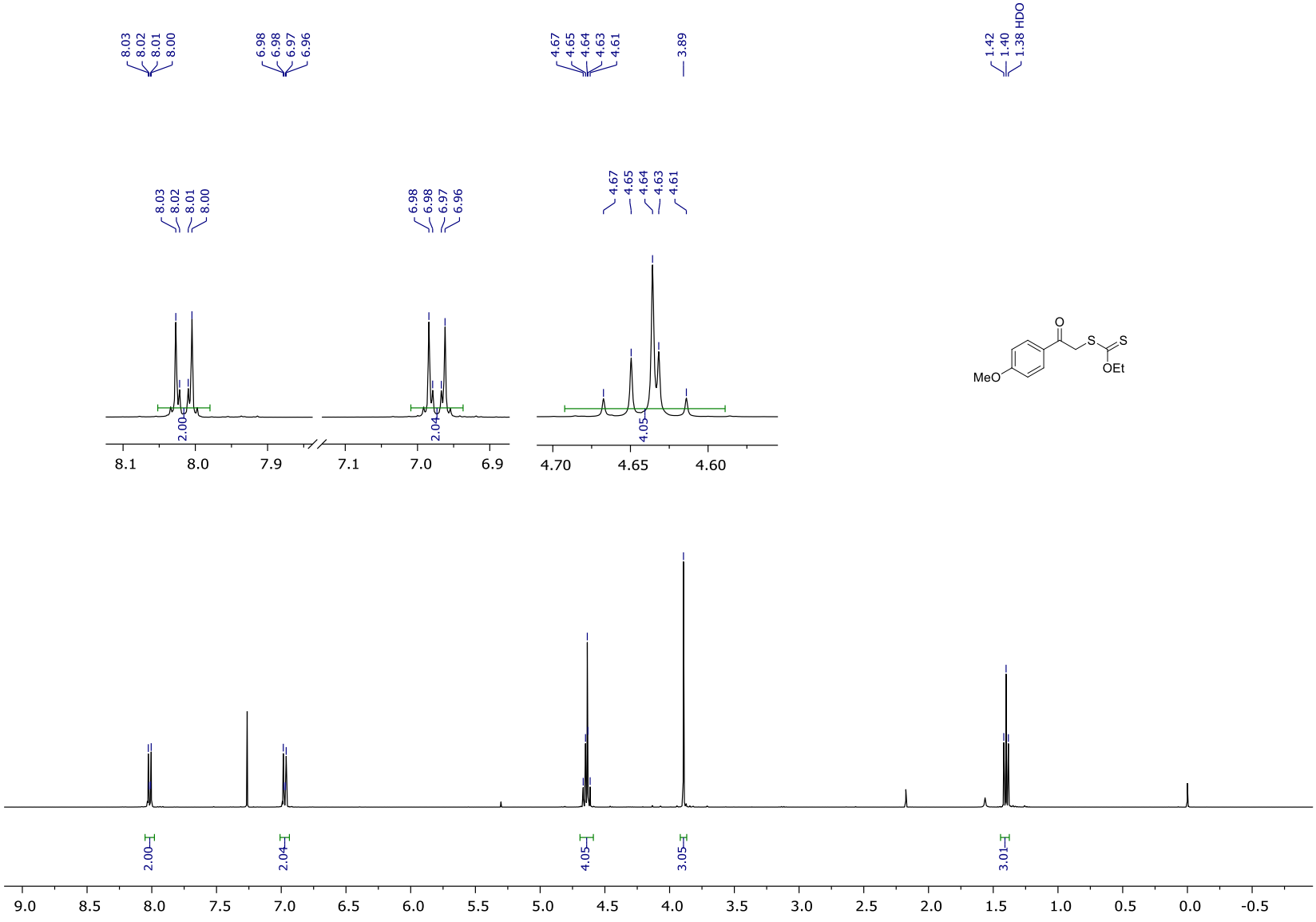


Figure S8: ^{13}C NMR spectrum of O-ethyl S-(2-(4-fluorophenyl)-2-oxoethyl)carbonodithioate **S1d** (101 MHz, $CDCl_3$)

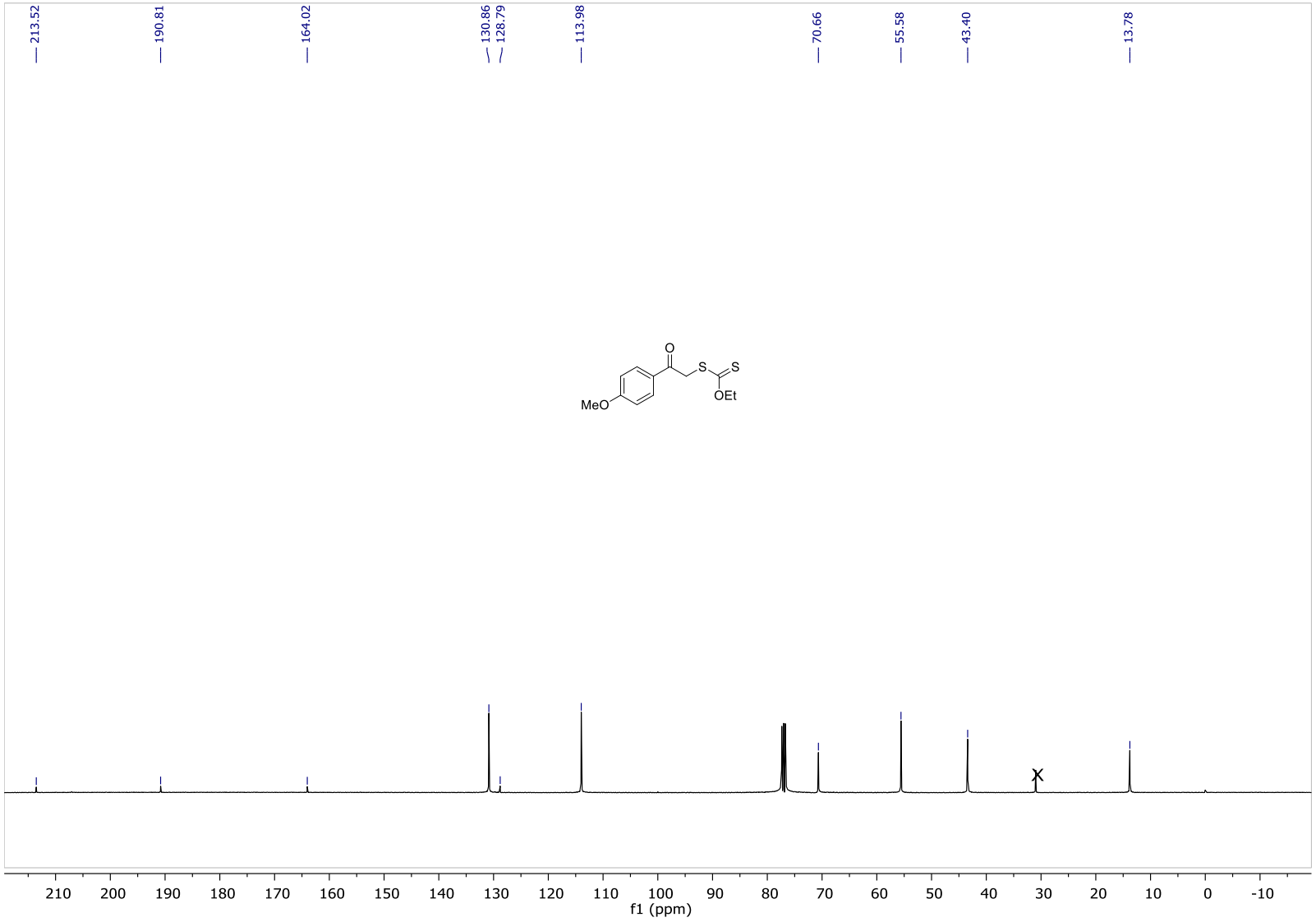


Figure S9: ^{1}H NMR spectrum of O-ethyl S-(2-oxo-2-(*p*-tolyl)ethyl)carbonodithioate **S1e** (600 MHz, $CDCl_3$)

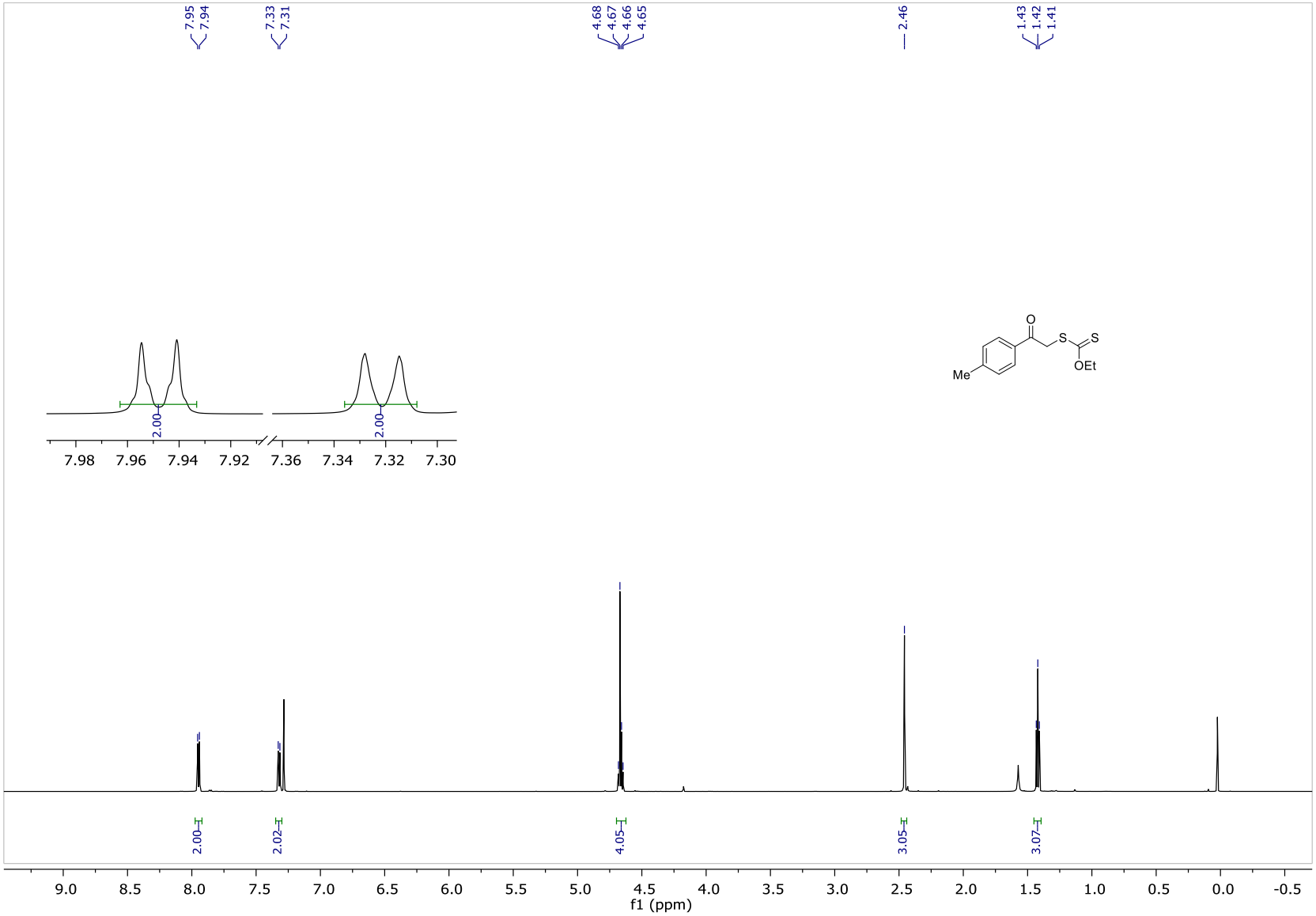


Figure S10: ^{13}C NMR spectrum of O-ethyl S-(2-oxo-2-(*p*-tolyl)ethyl)carbonodithioate **S1e** (151 MHz, $CDCl_3$)

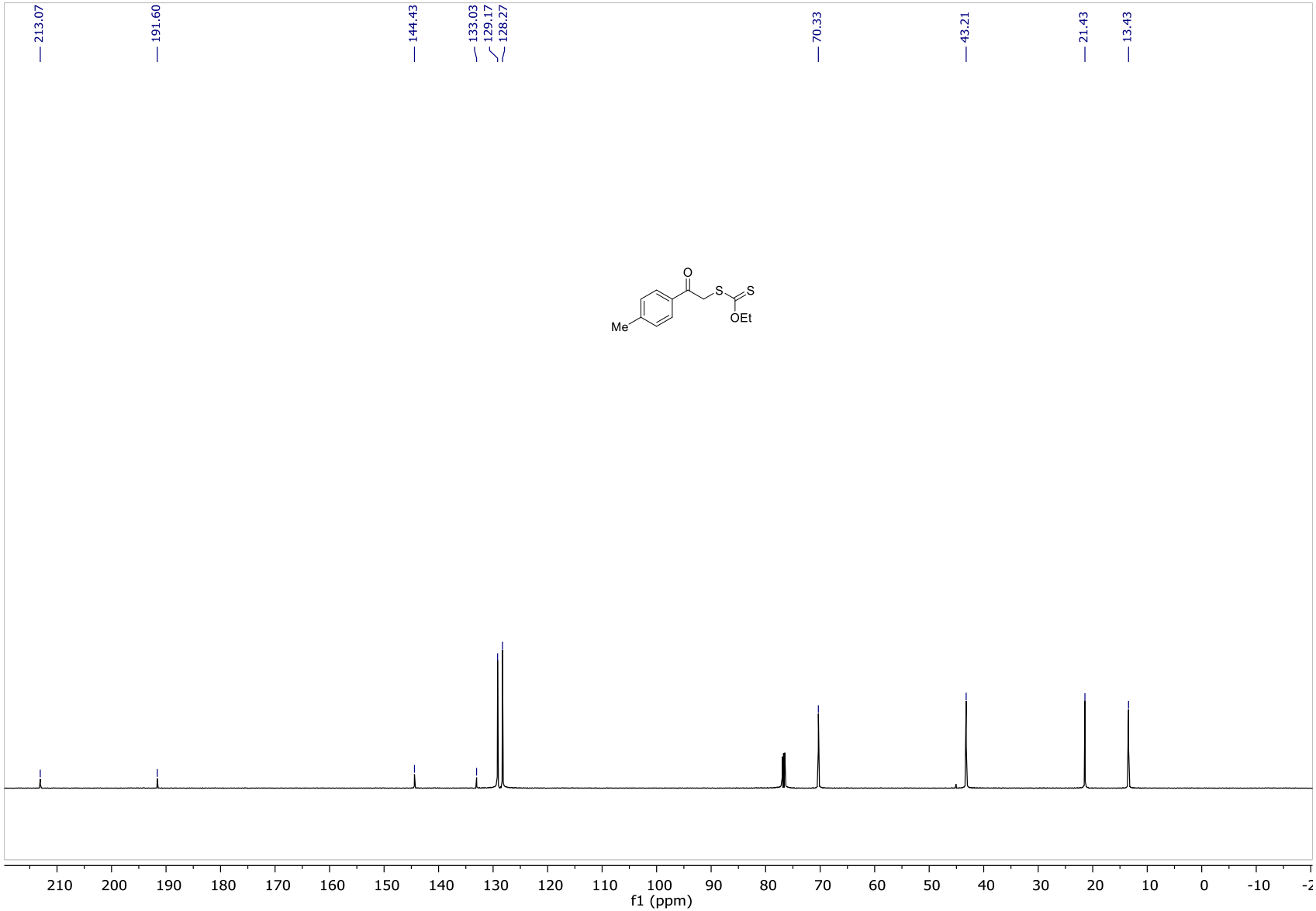


Figure S11: ^{1}H NMR spectrum of compound **1a** (600 MHz, $CDCl_3$)

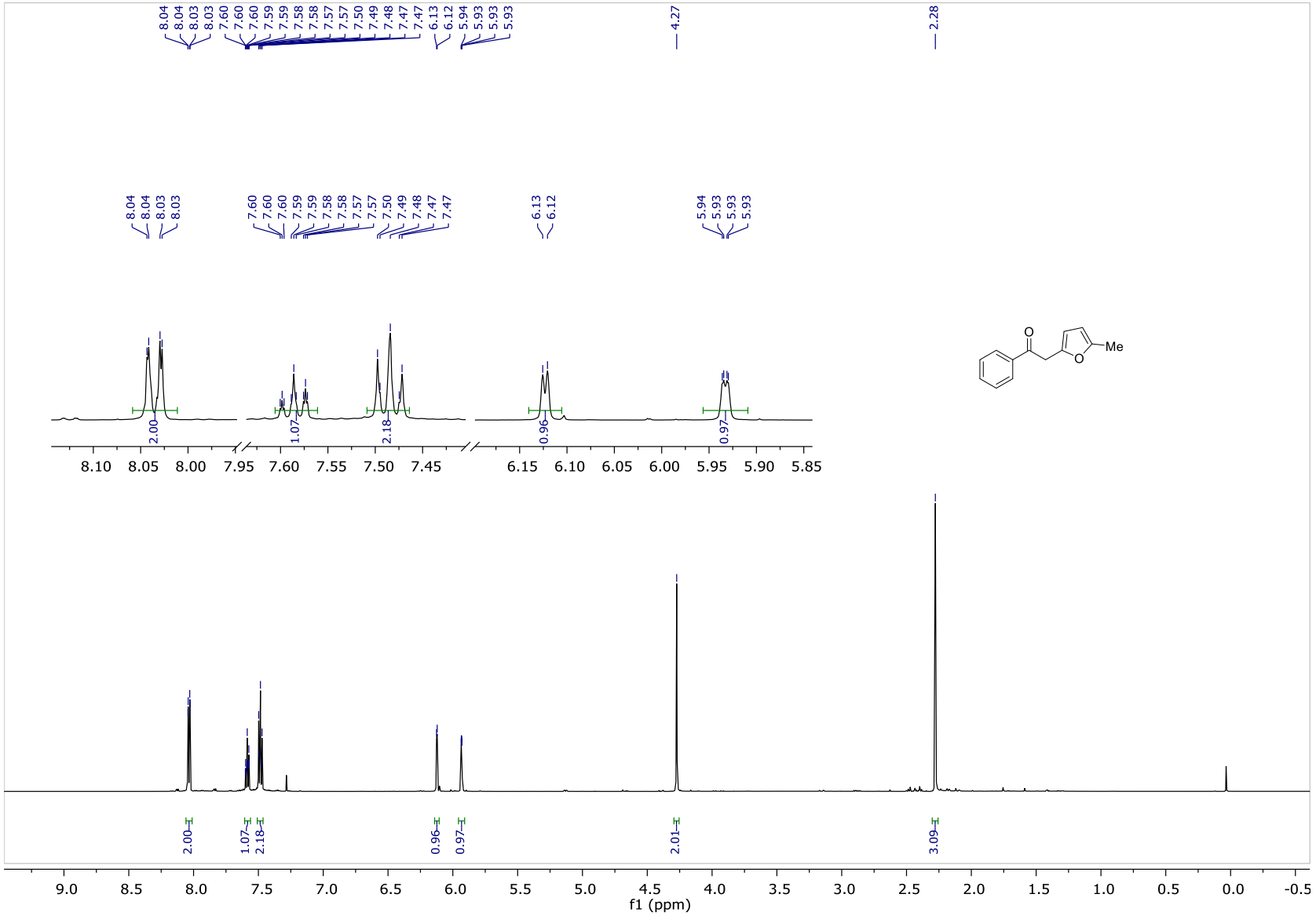


Figure S12: ^{13}C NMR spectrum of compound **1a** (101 MHz, $CDCl_3$)

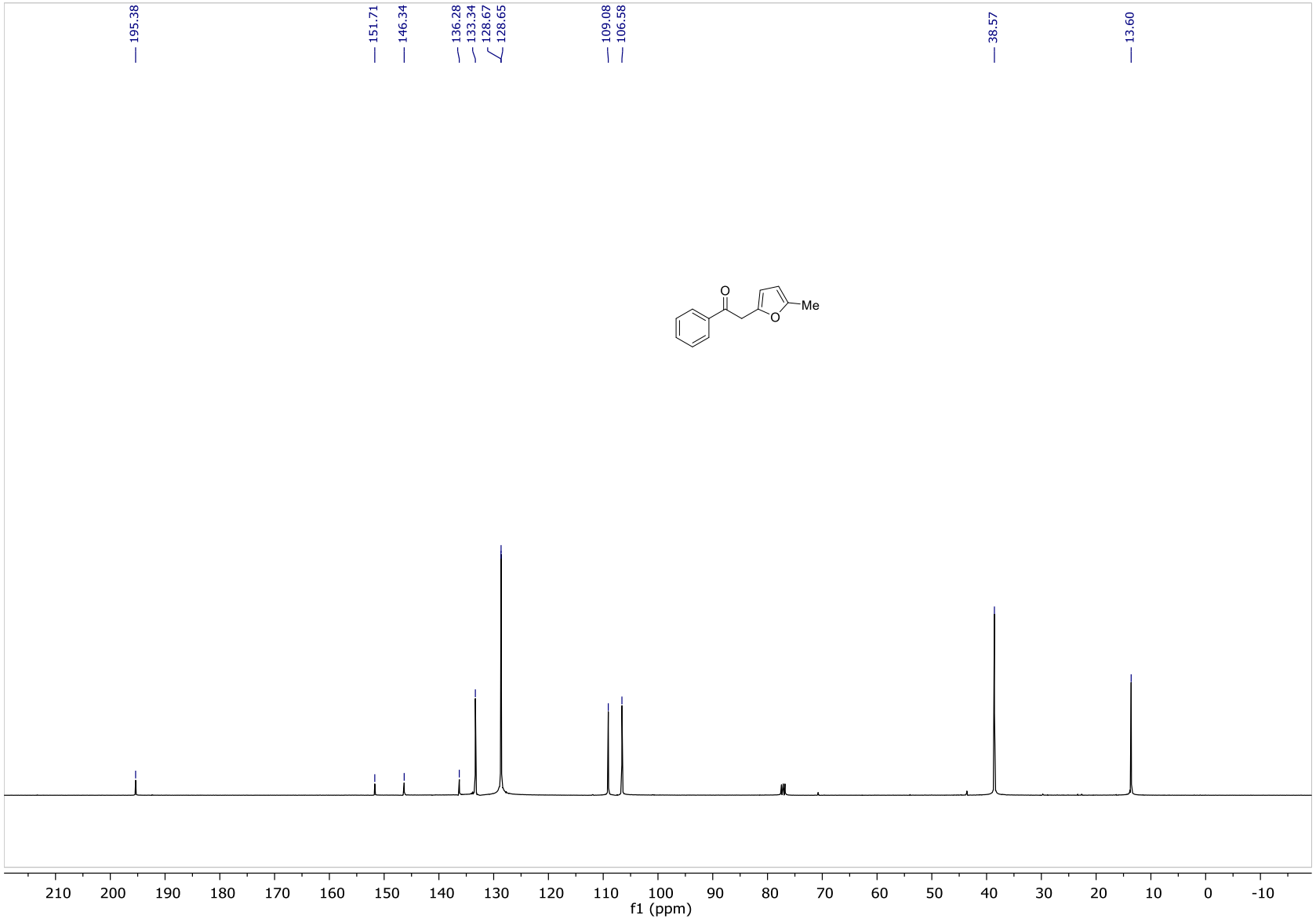


Figure S13: ^{1}H NMR spectrum of compound **1b** (400 MHz, $CDCl_3$)

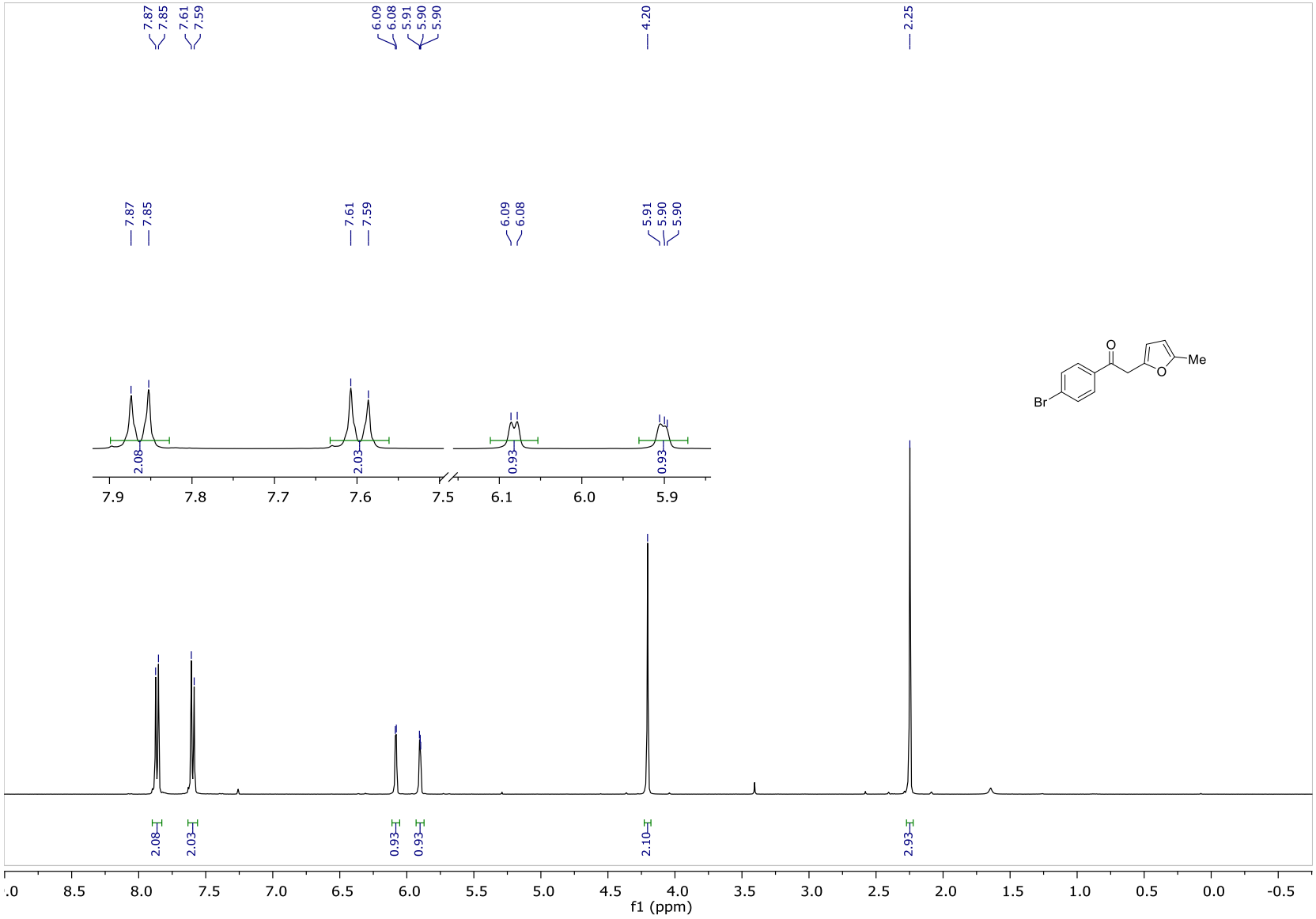


Figure S14: ^{13}C NMR spectrum of compound **1b** (101 MHz, $CDCl_3$)

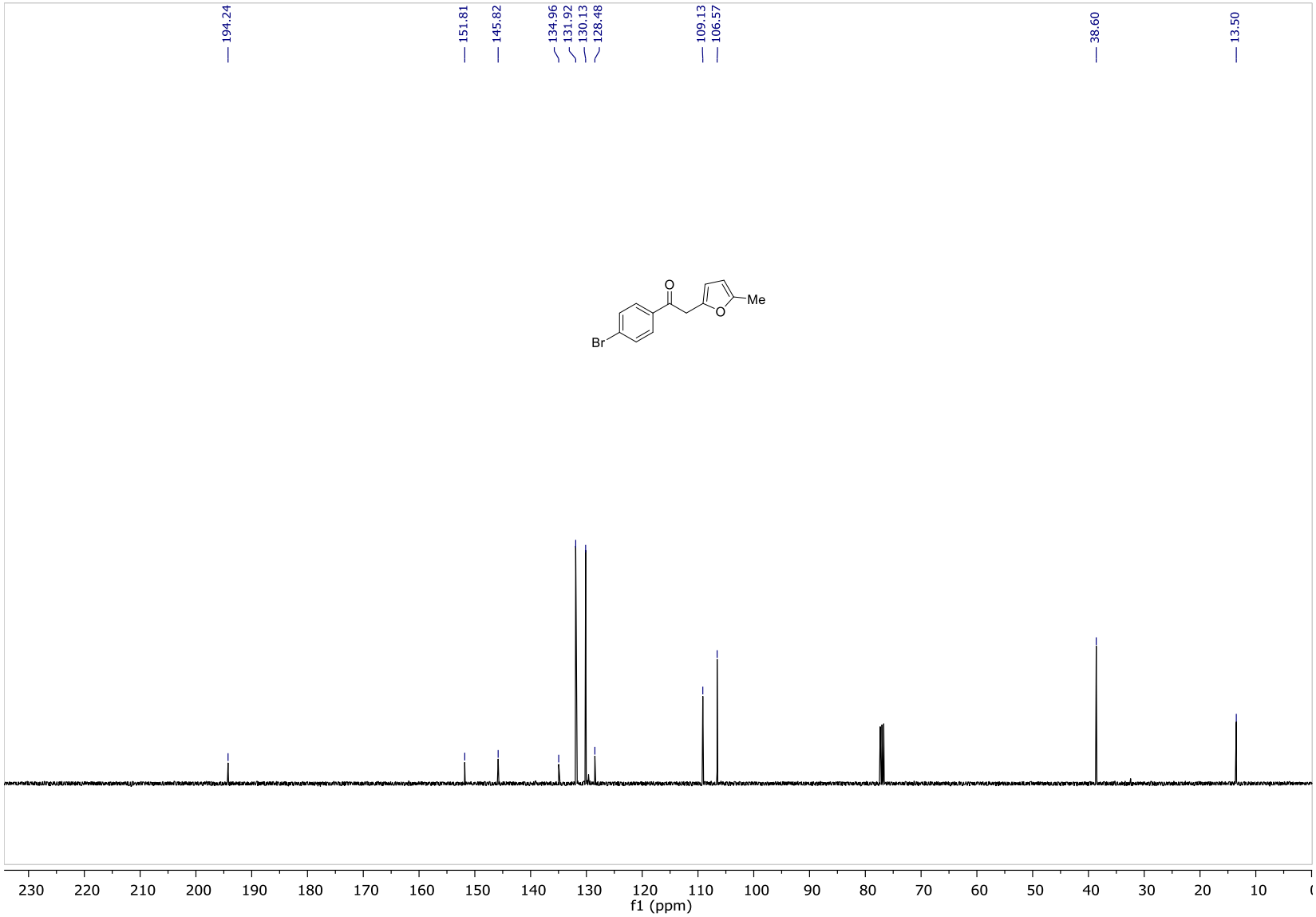


Figure S15: ^{1}H NMR spectrum of compound **1c** (400 MHz, $CDCl_3$)

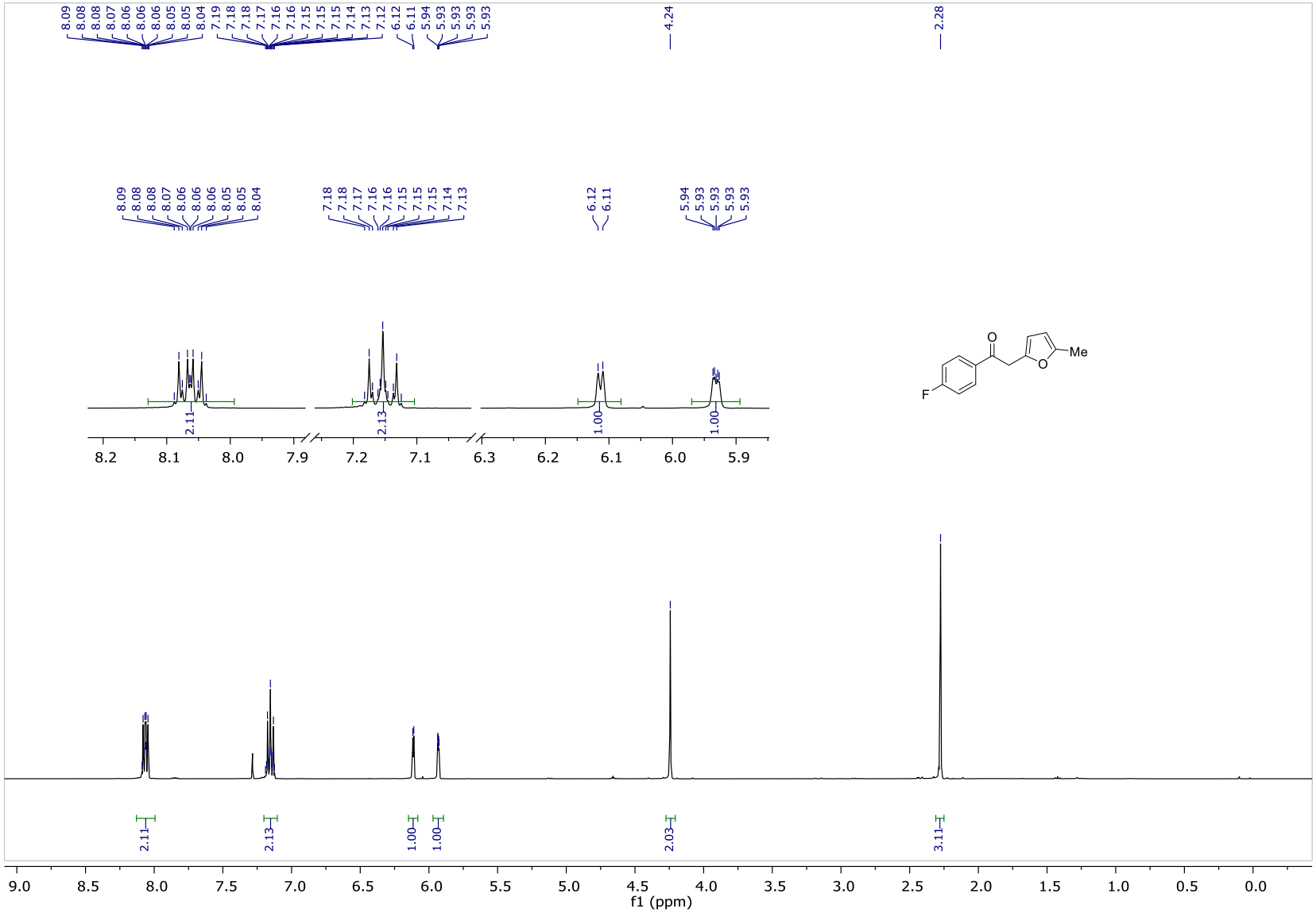


Figure S16: ^{13}C NMR spectrum of compound **1c** (101 MHz, $CDCl_3$)

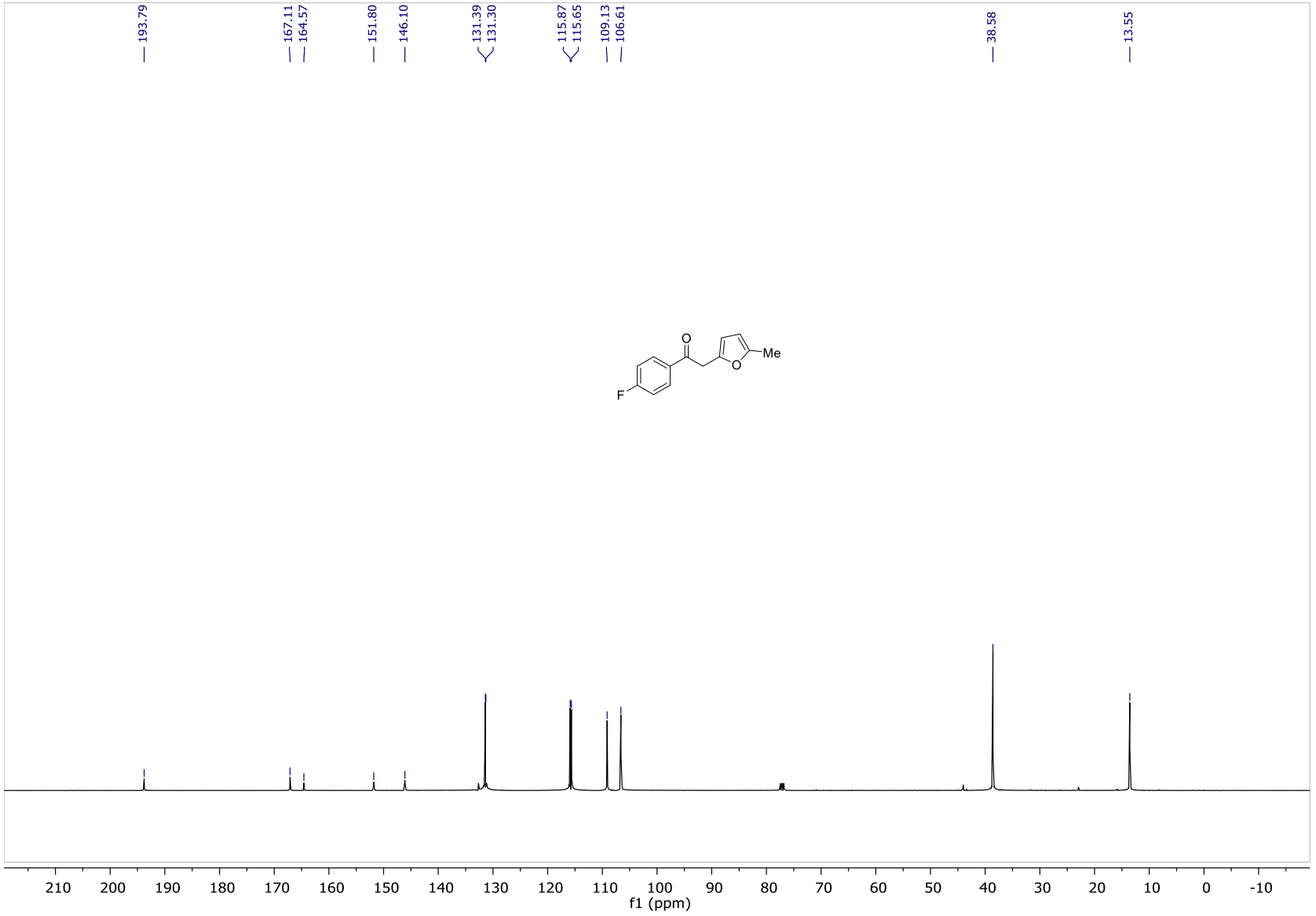


Figure S17: ^{1}H NMR spectrum of compound **1d** (400 MHz, $CDCl_3$)

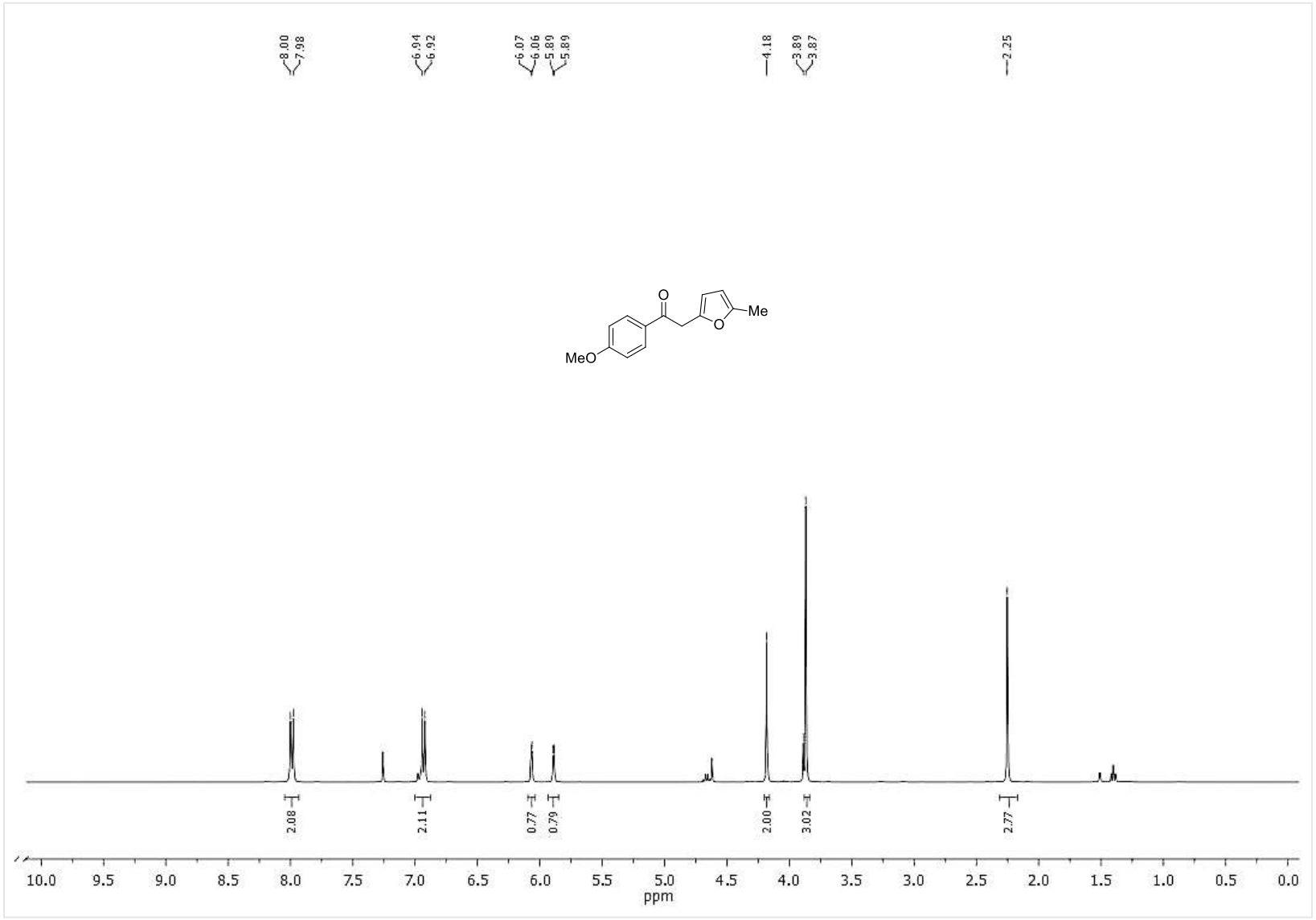


Figure S18: ^{13}C NMR spectrum of compound **1d** (101 MHz, $CDCl_3$)

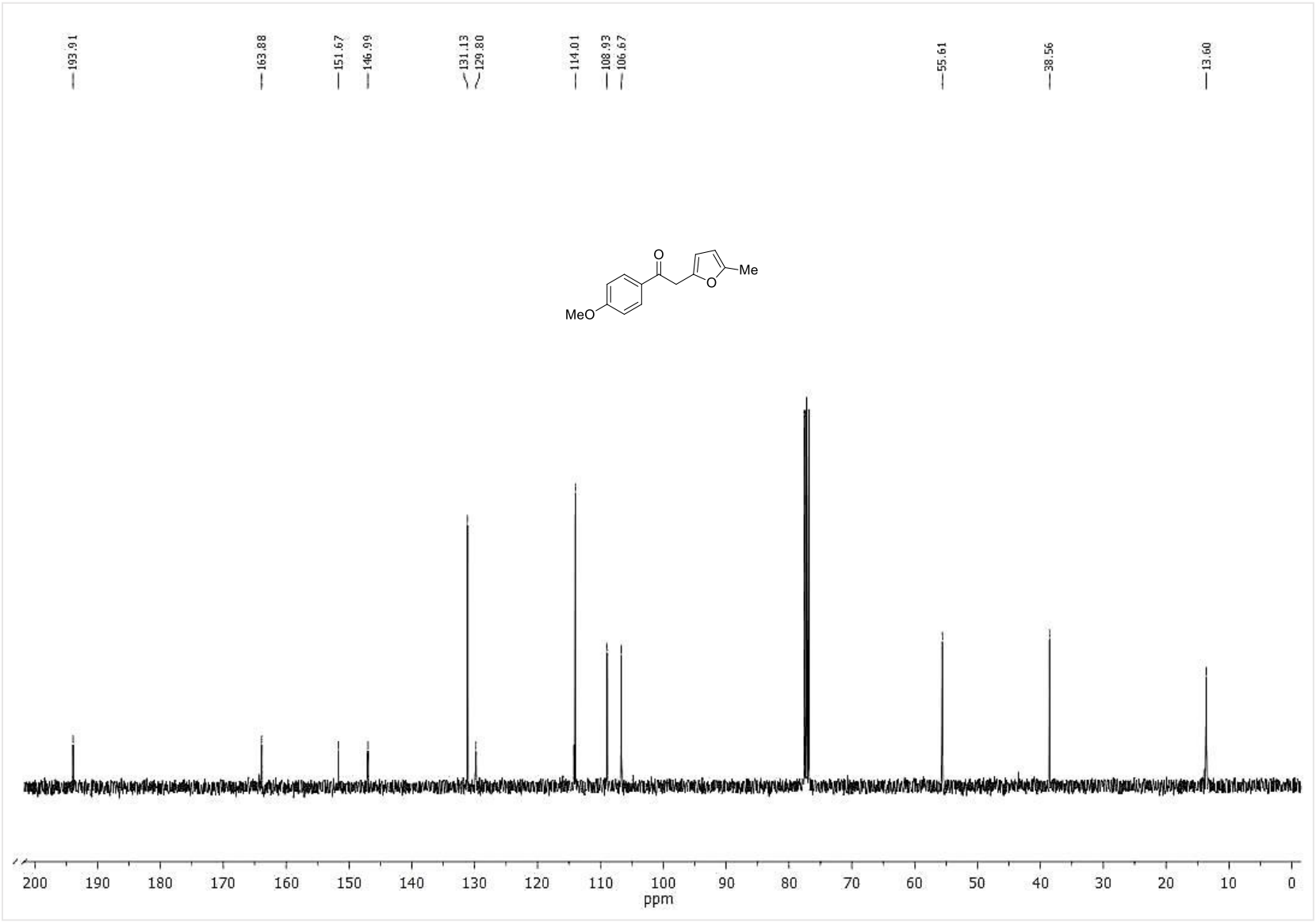


Figure S19: ^{1}H NMR spectrum of compound **1e** (600 MHz, $CDCl_3$)

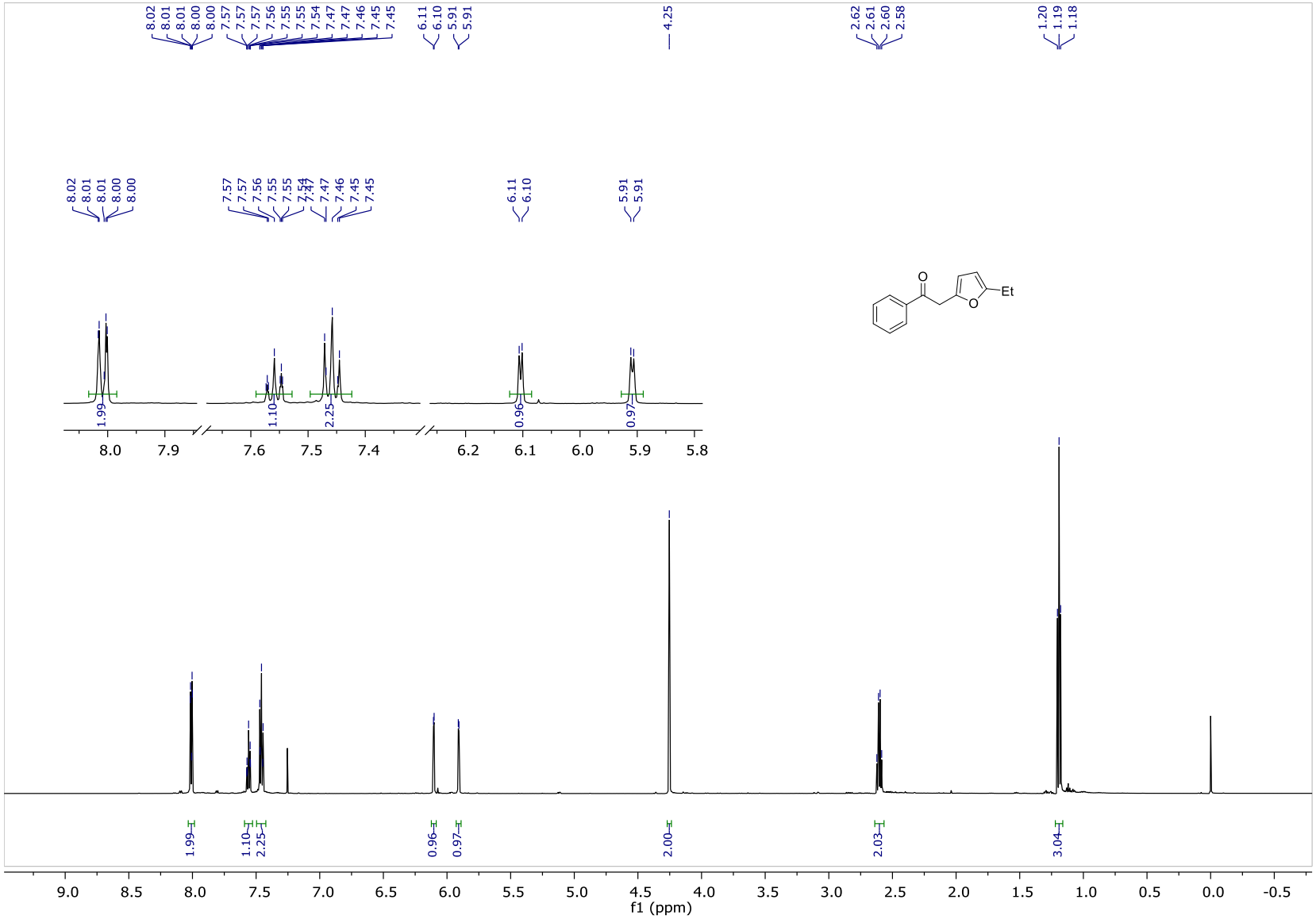


Figure S20: ^{13}C NMR spectrum of compound **1e** (151 MHz, $CDCl_3$)

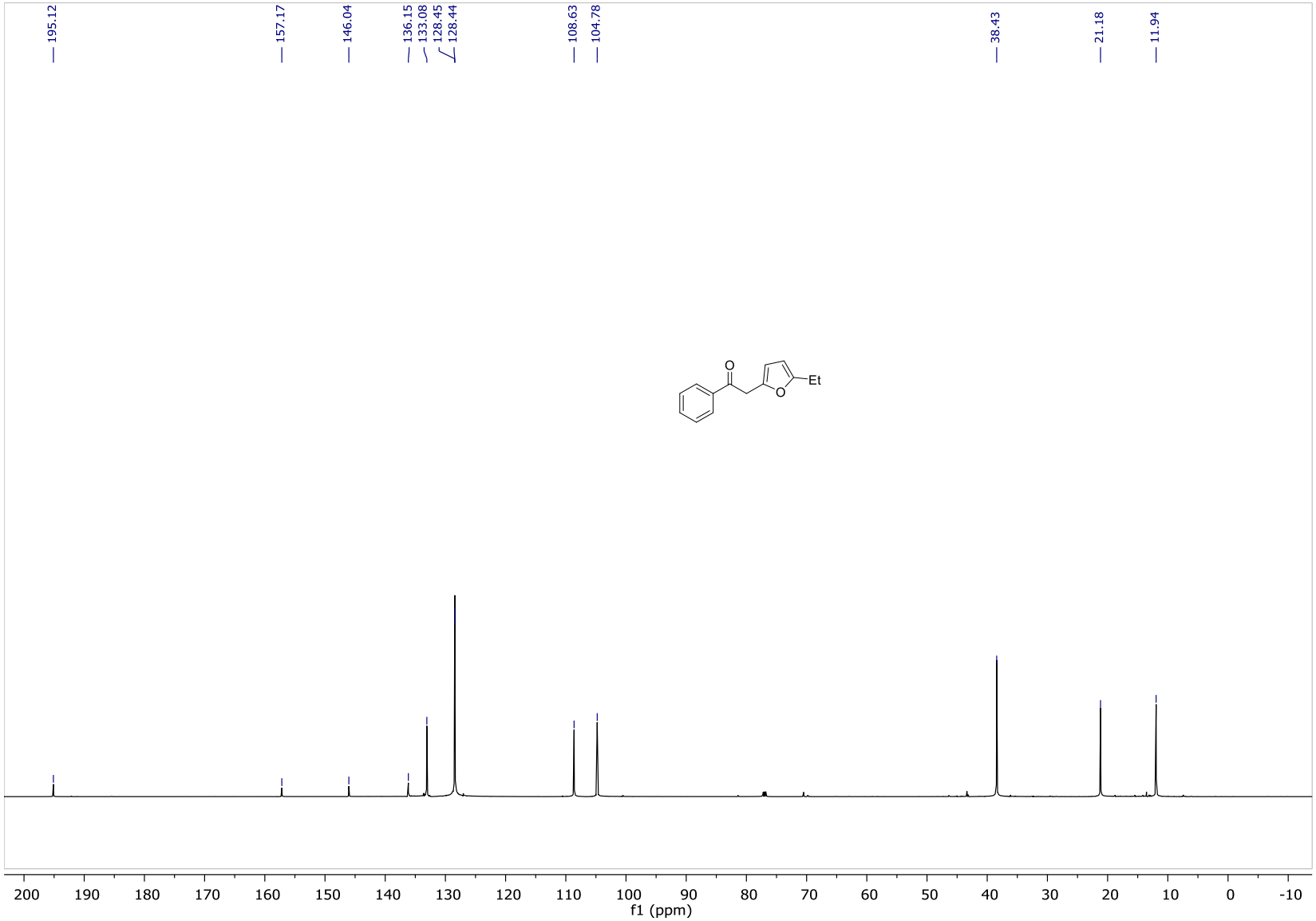


Figure S21: ^{1}H NMR spectrum of compound **1f** (600 MHz, $CDCl_3$)

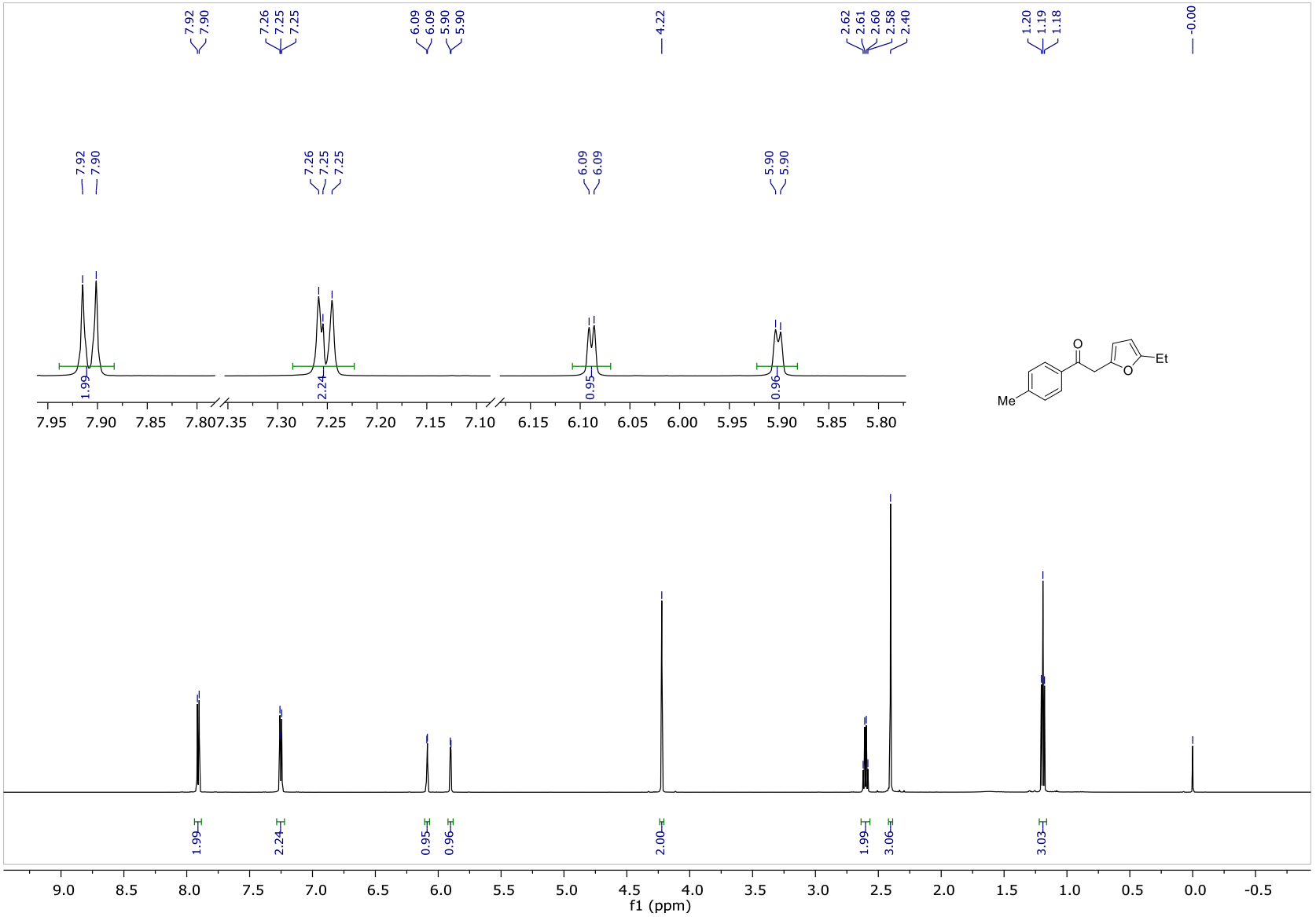


Figure S22: ^{13}C NMR spectrum of compound **1f** (101 MHz, $CDCl_3$)

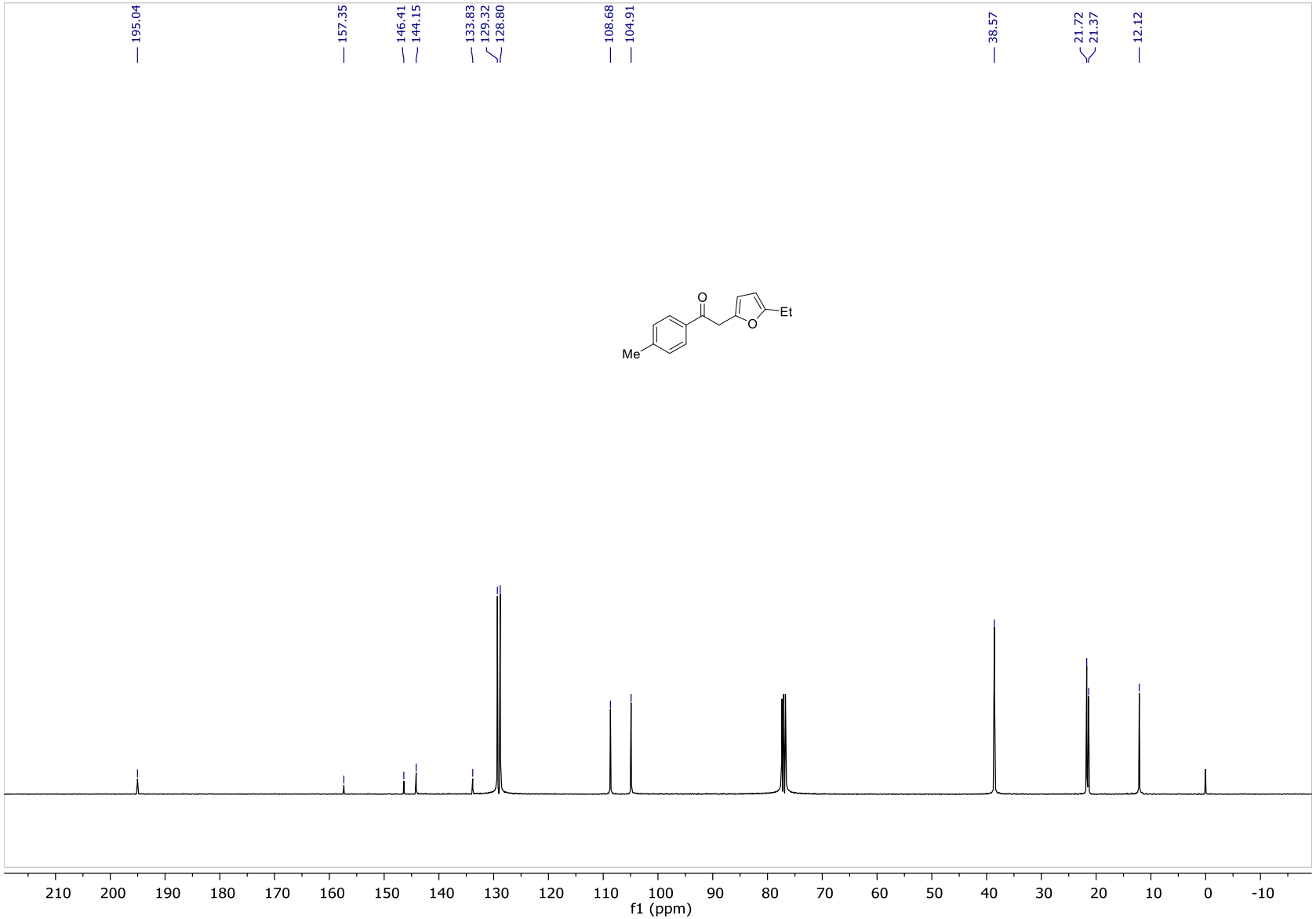


Figure S23: ^{1}H NMR spectrum of compound **1g** (600 MHz, $CDCl_3$)

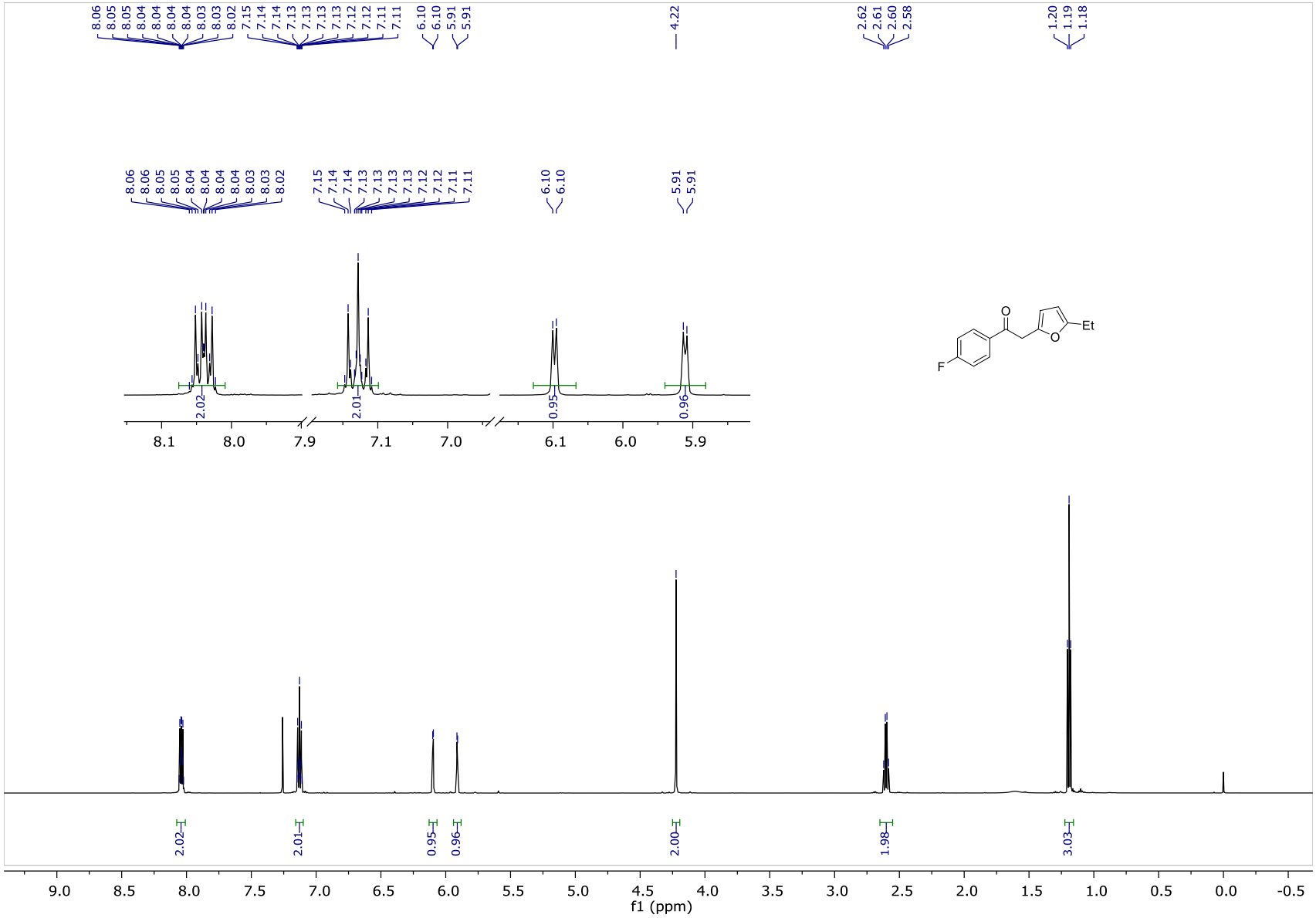


Figure S24: ^{13}C NMR spectrum of compound **1g** (151 MHz, $CDCl_3$)

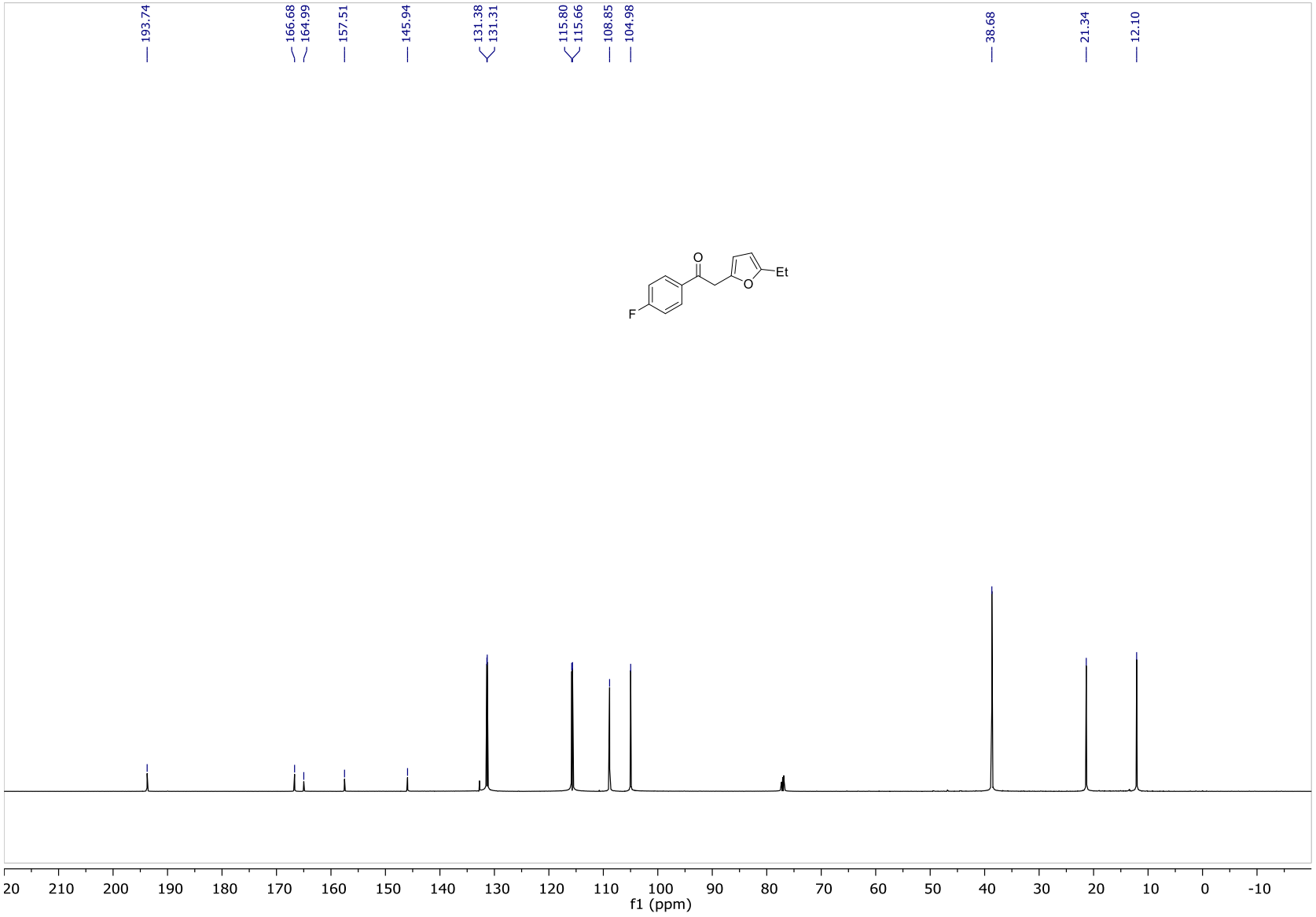


Figure S25: ^{1}H NMR spectrum of compound **1h** (400 MHz, $CDCl_3$)

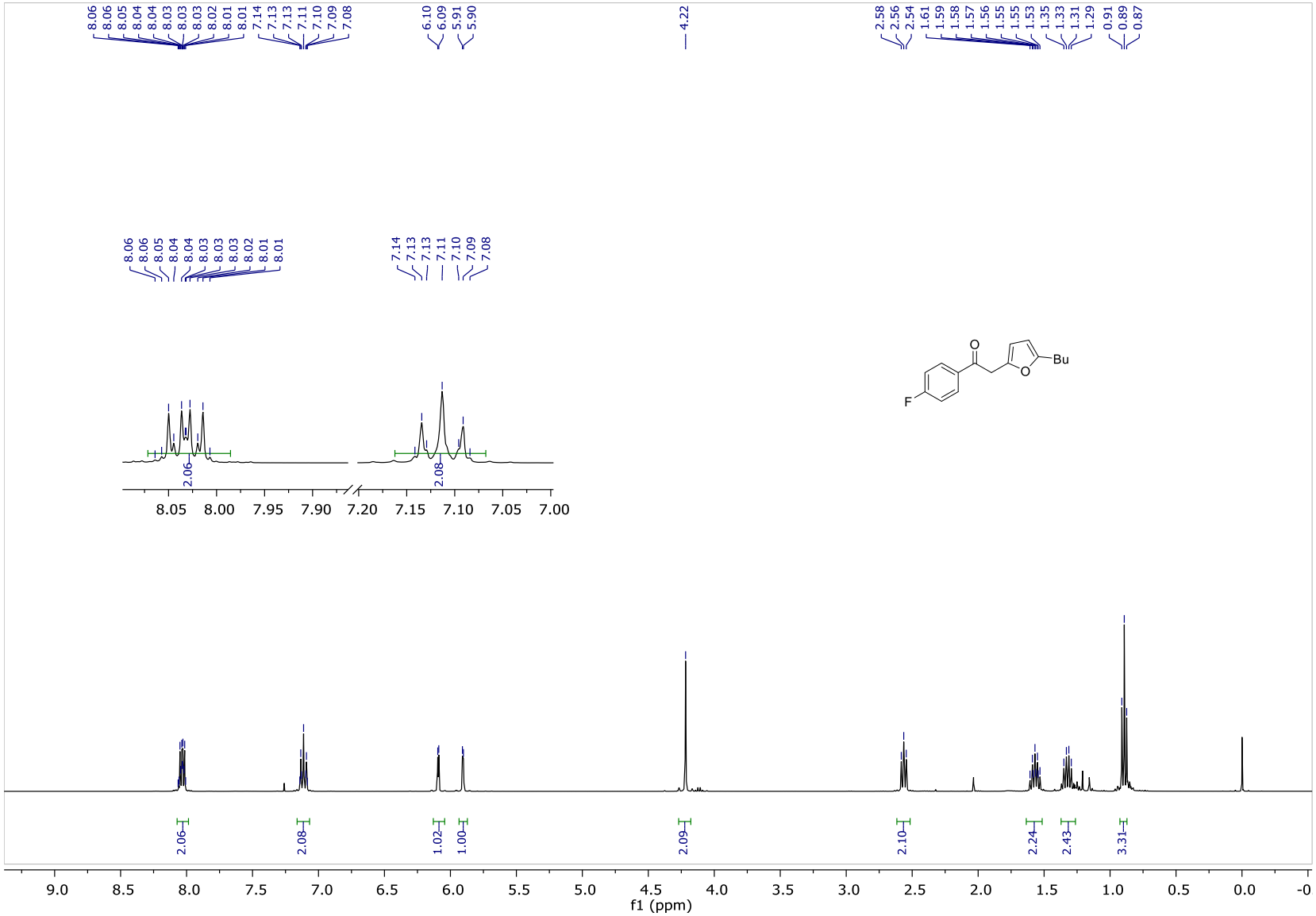


Figure S26: ^{13}C NMR spectrum of compound **1h** (101 MHz, $CDCl_3$)

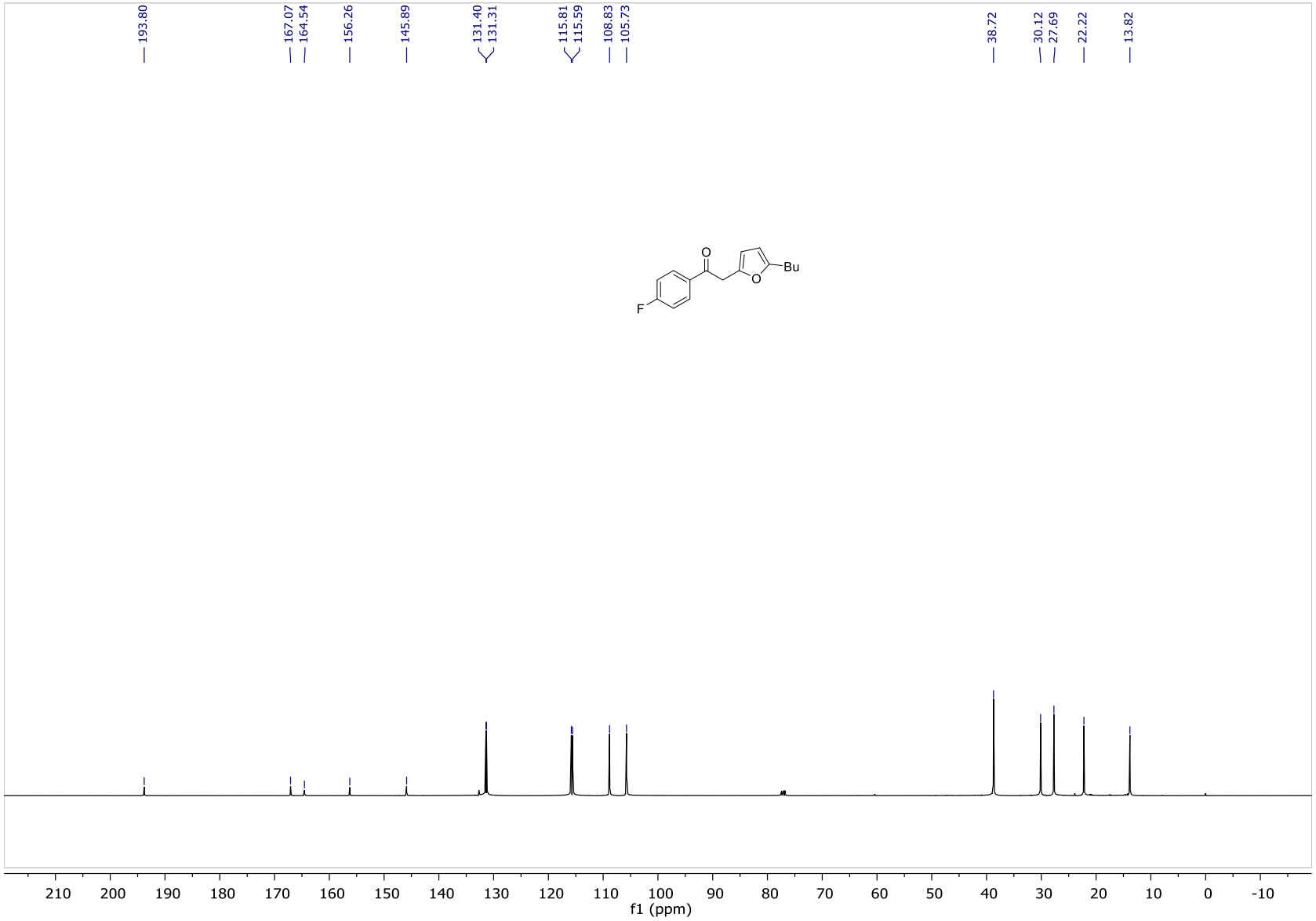


Figure S27: ^{1}H NMR spectrum of compound **1i** (400 MHz, $CDCl_3$)

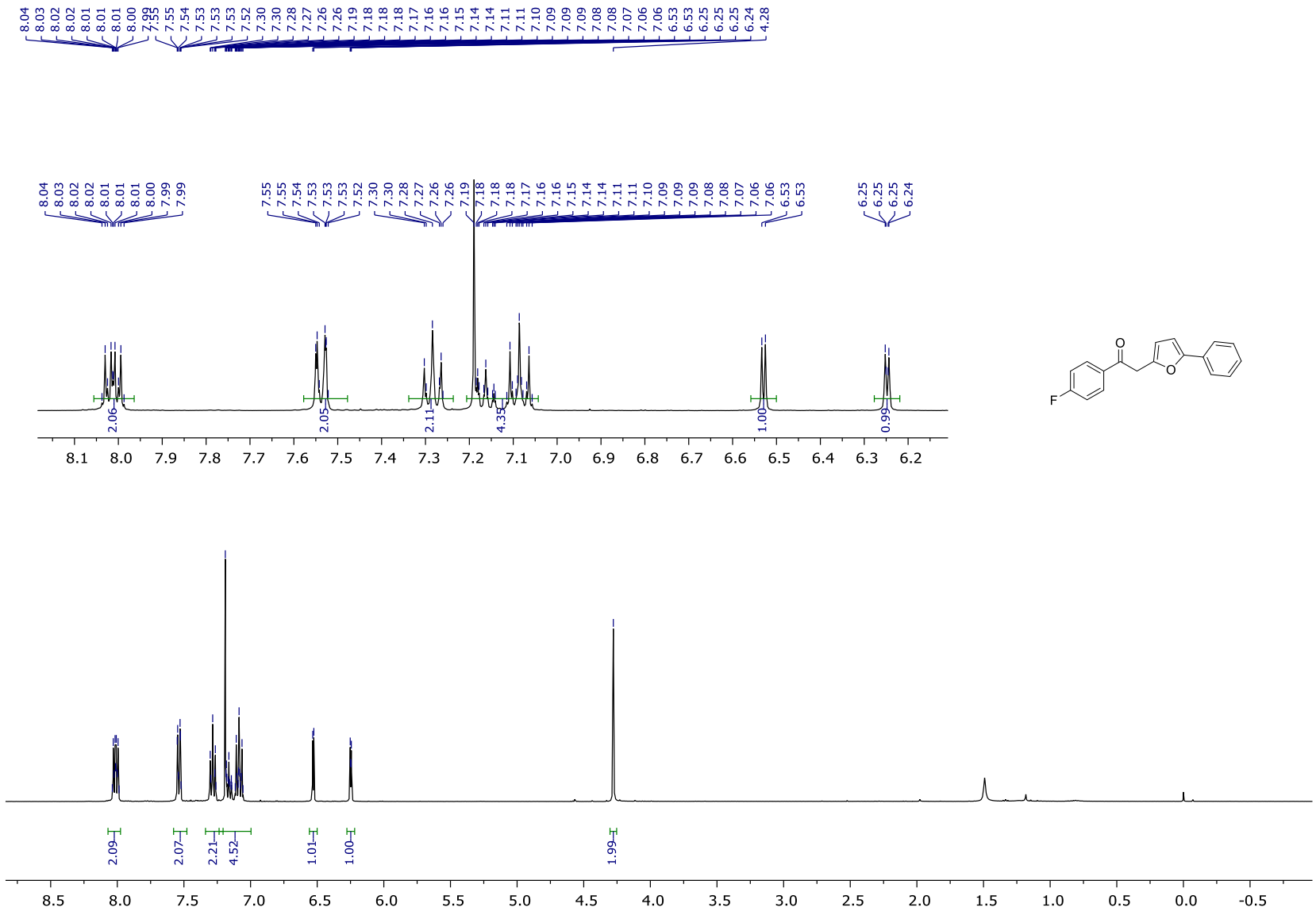


Figure S28: ^{13}C NMR spectrum of compound **1i** (151 MHz, $CDCl_3$)

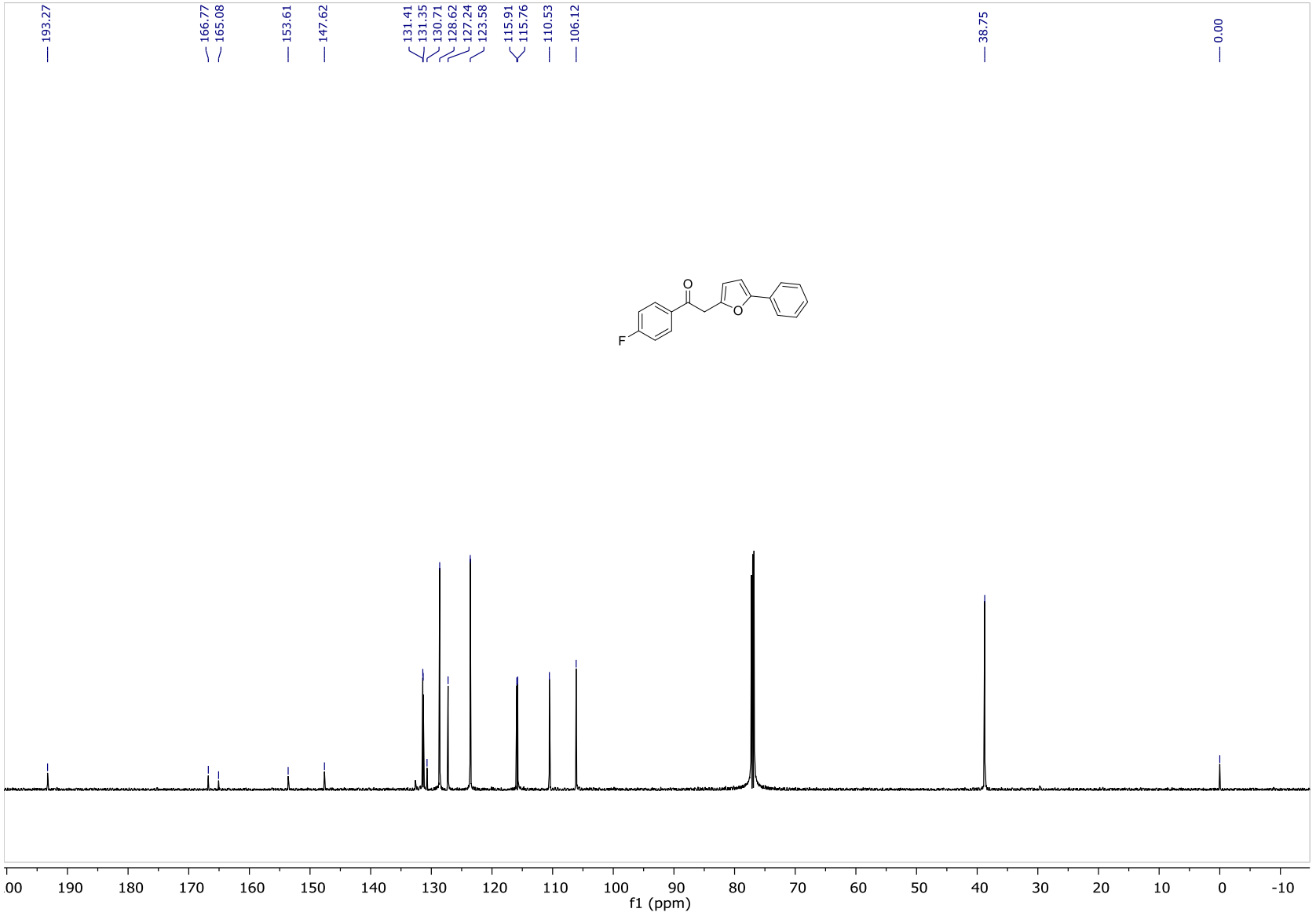


Figure S29: ^{1}H NMR spectrum of compound *(E)*-**3a** (400 MHz, $CDCl_3$)

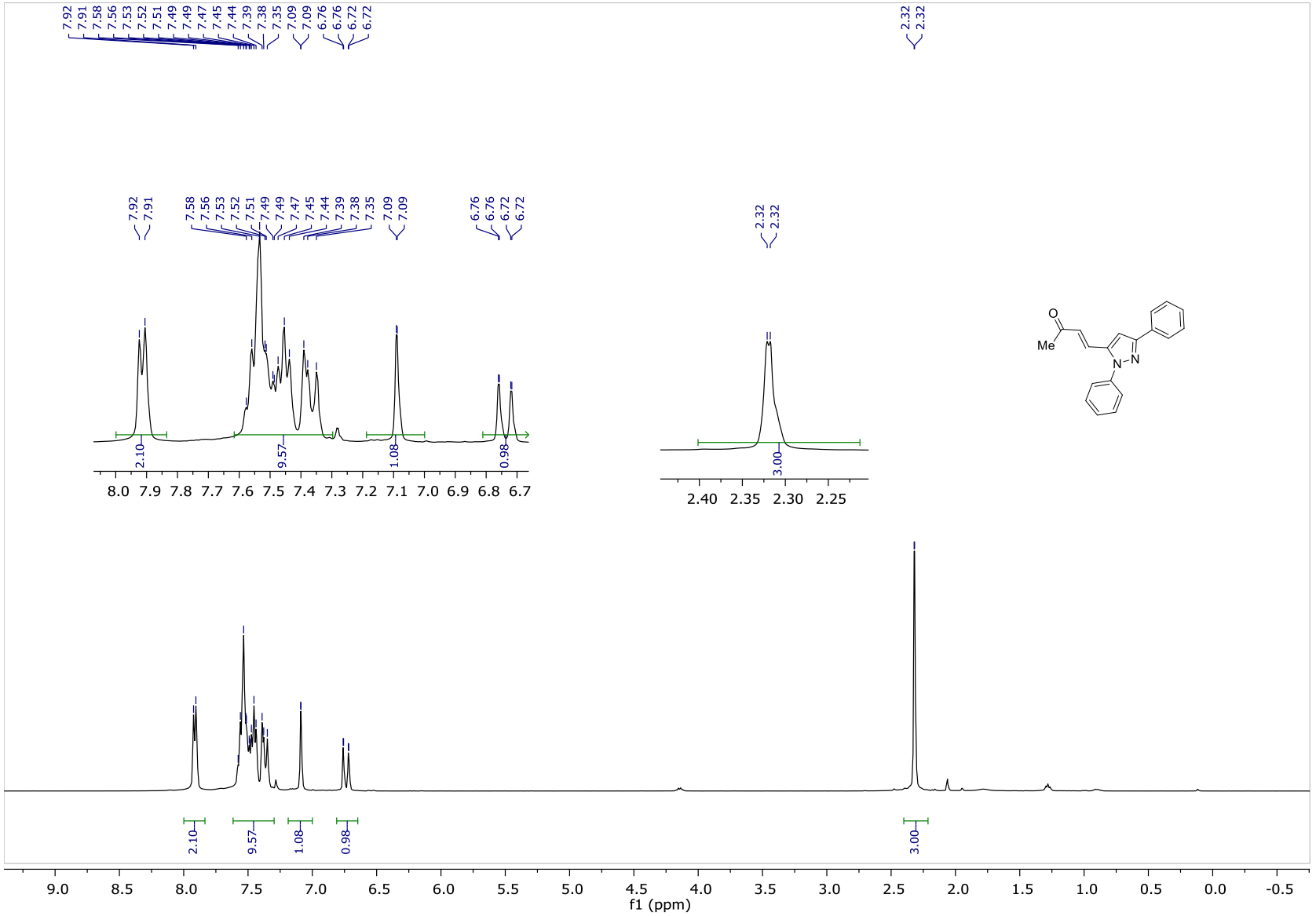


Figure S30: ^{13}C NMR spectrum of compound *(E)*-**3a** (101 MHz, $CDCl_3$)

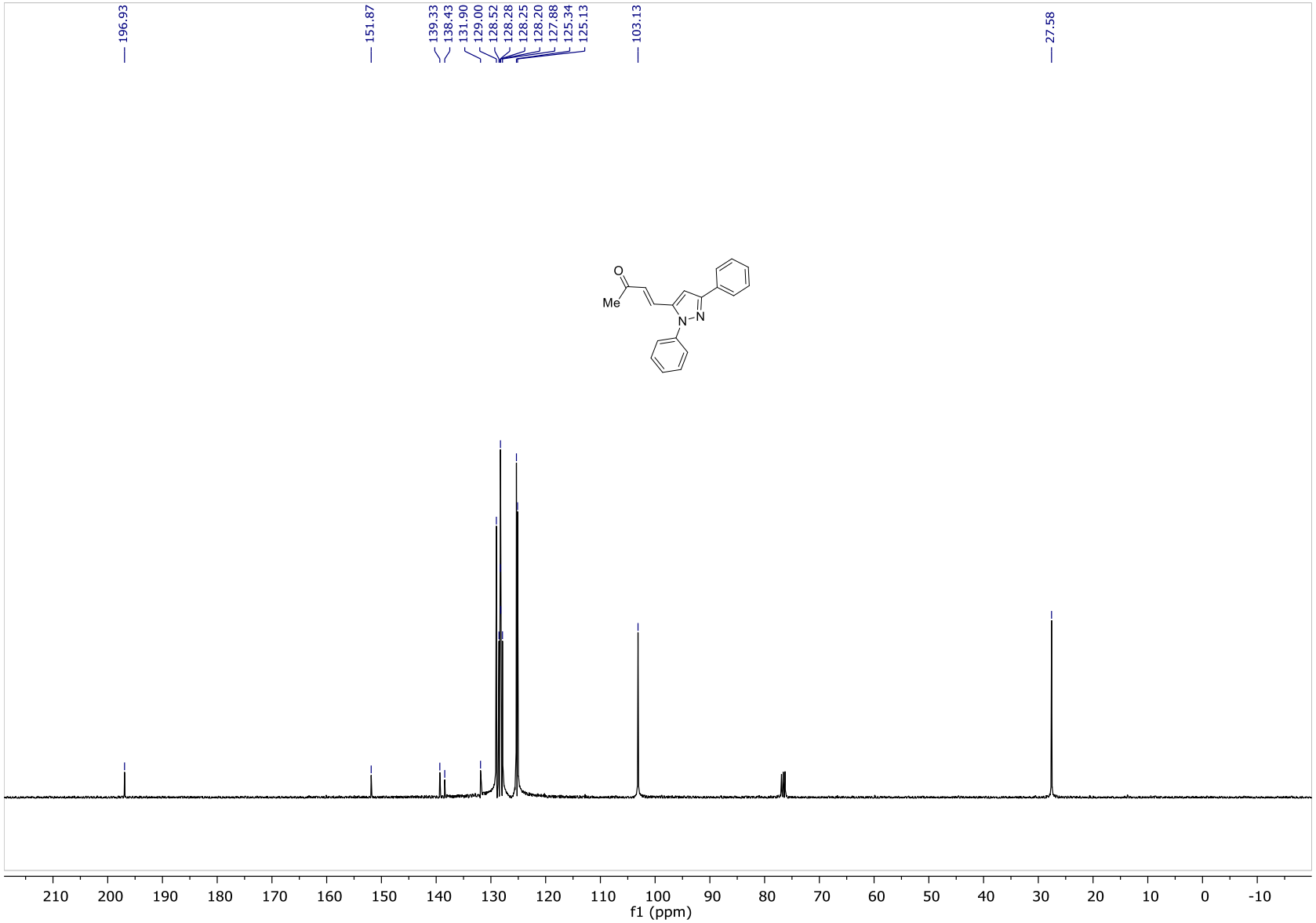


Figure S31: ^{1}H NMR spectrum of compound *(E)*-**3b** (400 MHz, $CDCl_3$)

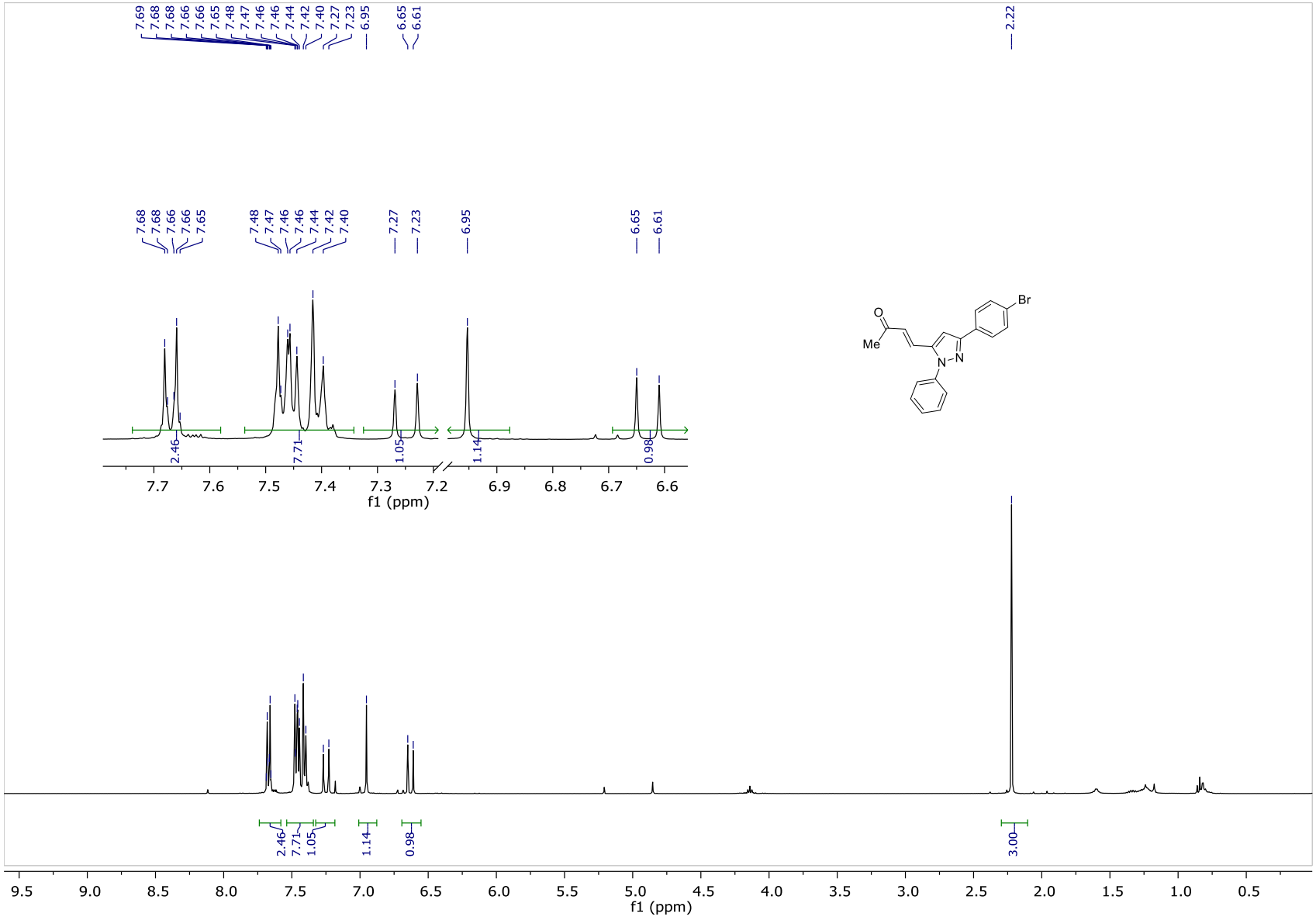


Figure S32: ^{13}C NMR spectrum of compound *(E)*-**3b** (101 MHz, $CDCl_3$)

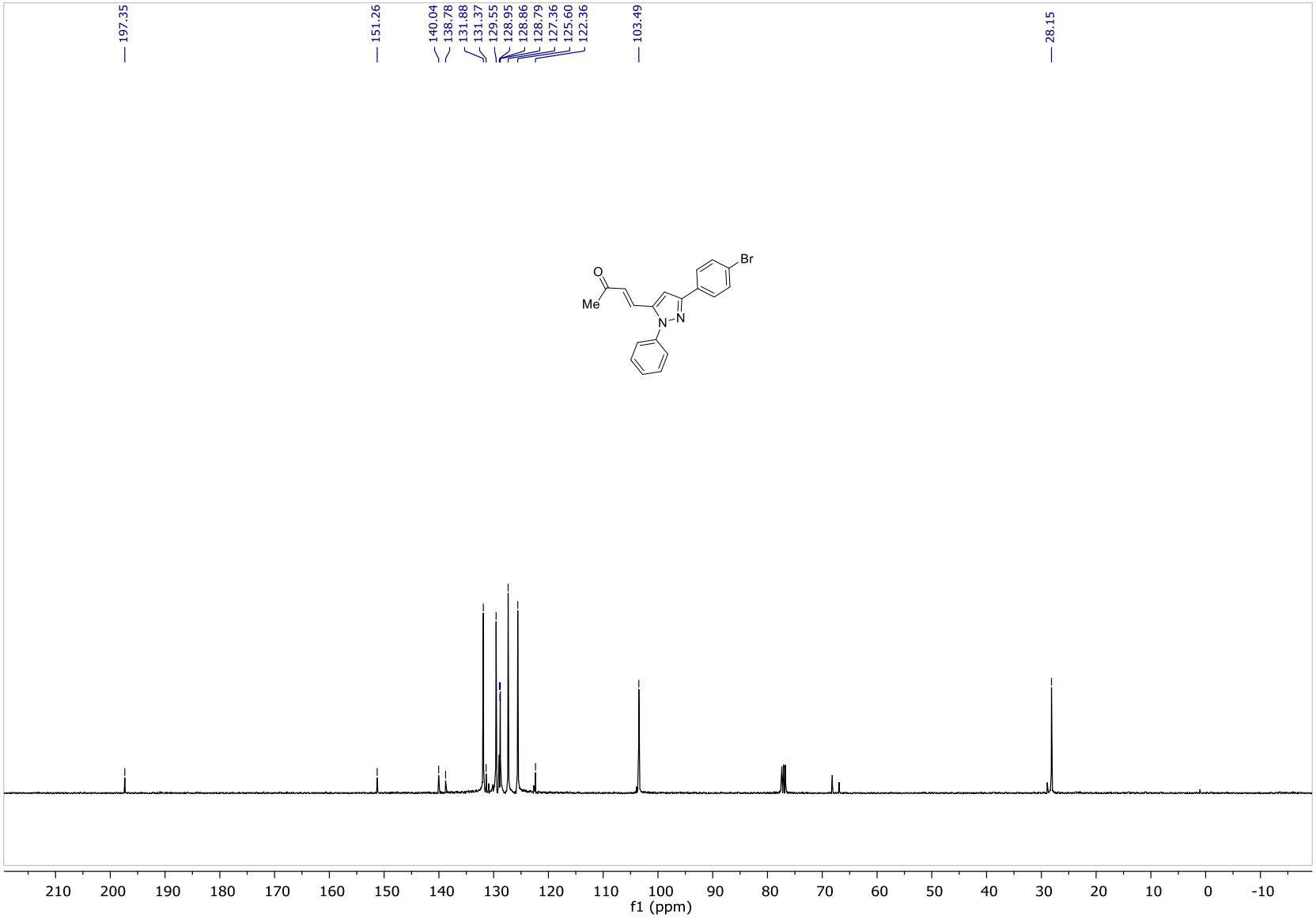


Figure S33: ^{1}H NMR spectrum of compound *(E)*-**3c** (400 MHz, $CDCl_3$)

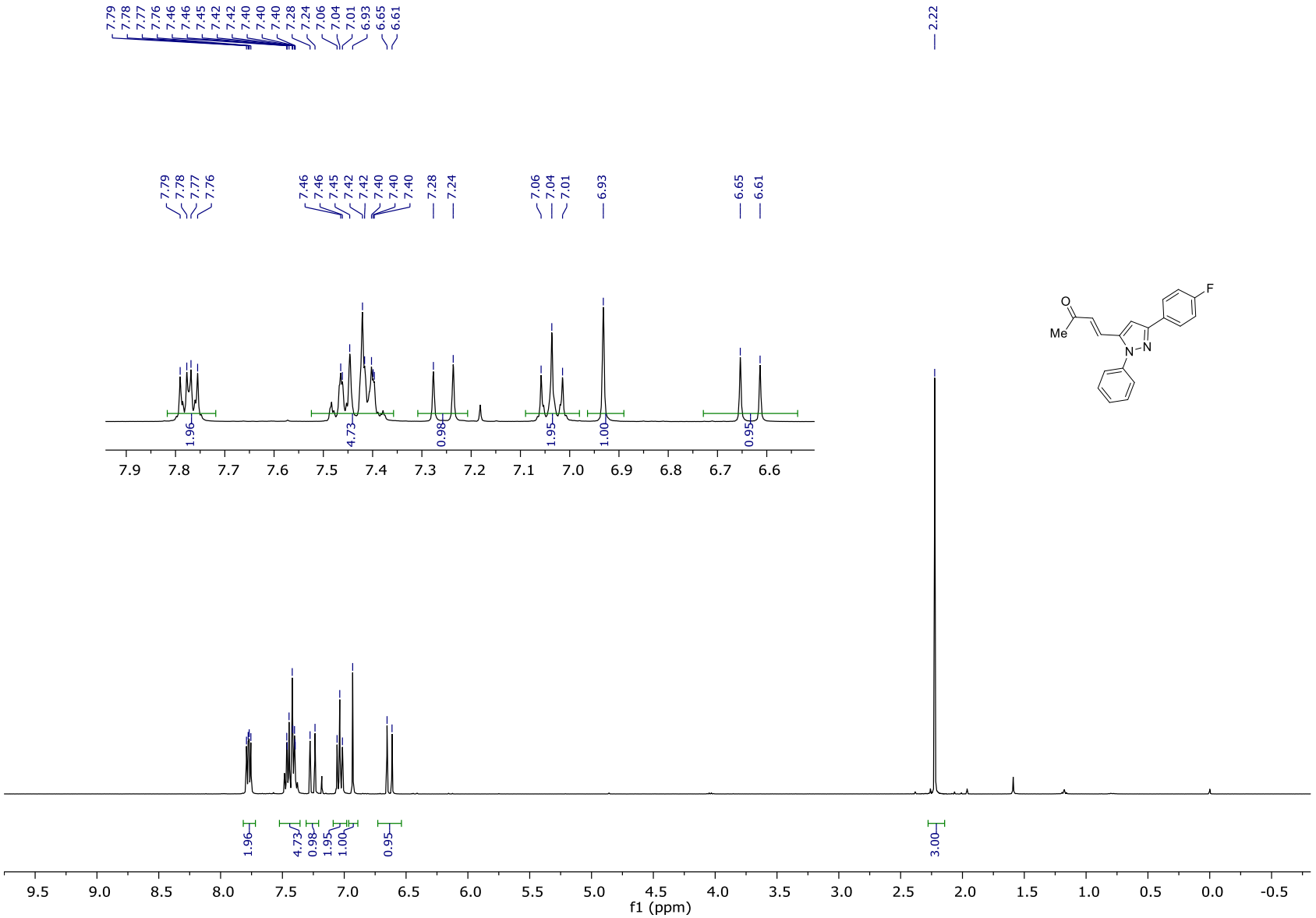


Figure S34: ^{13}C NMR spectrum of compound *(E)*-**3c** (101 MHz, $CDCl_3$)

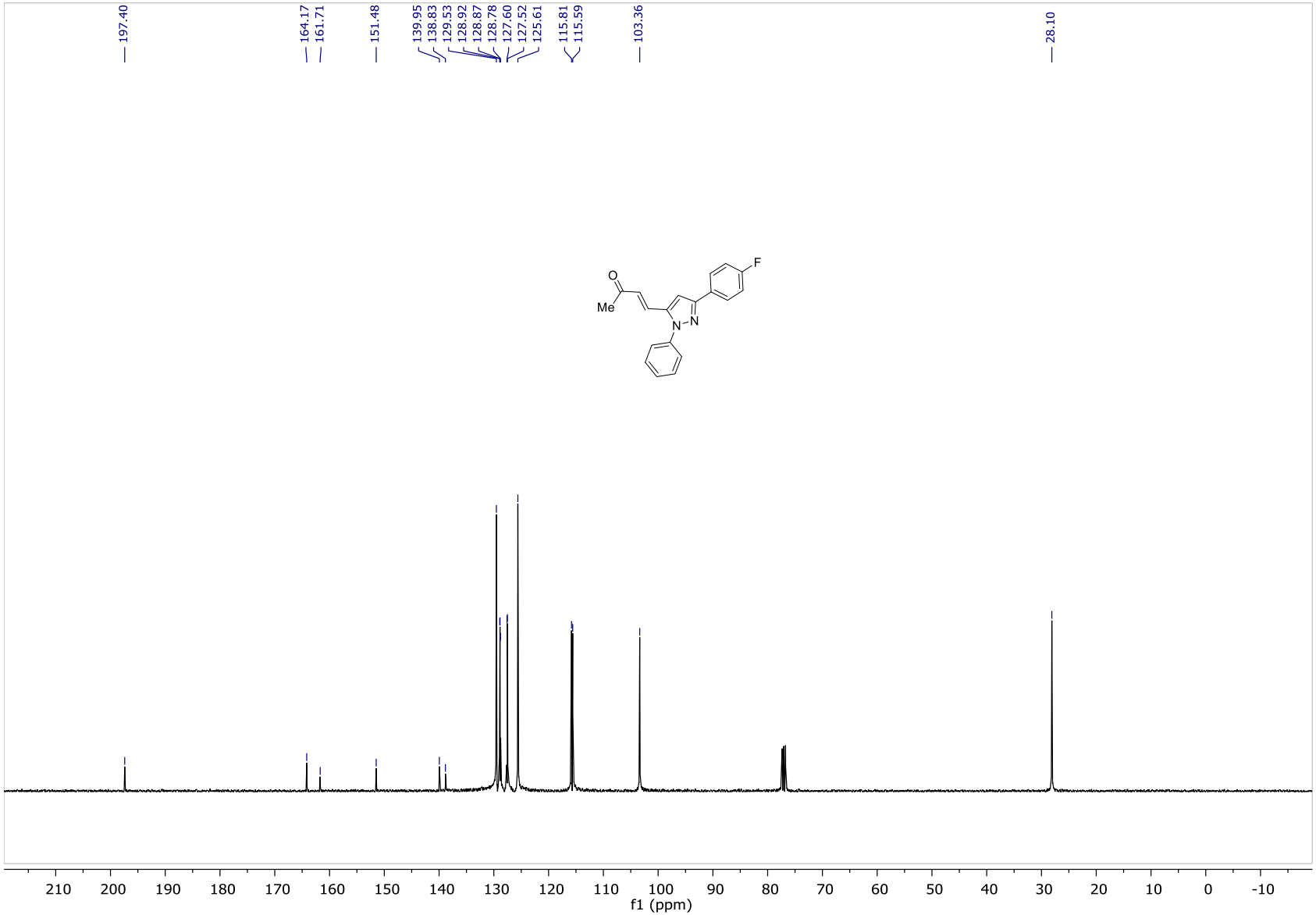


Figure S35: ^{1}H NMR spectrum of compound *(E)*-**3d** (400 MHz, $CDCl_3$)

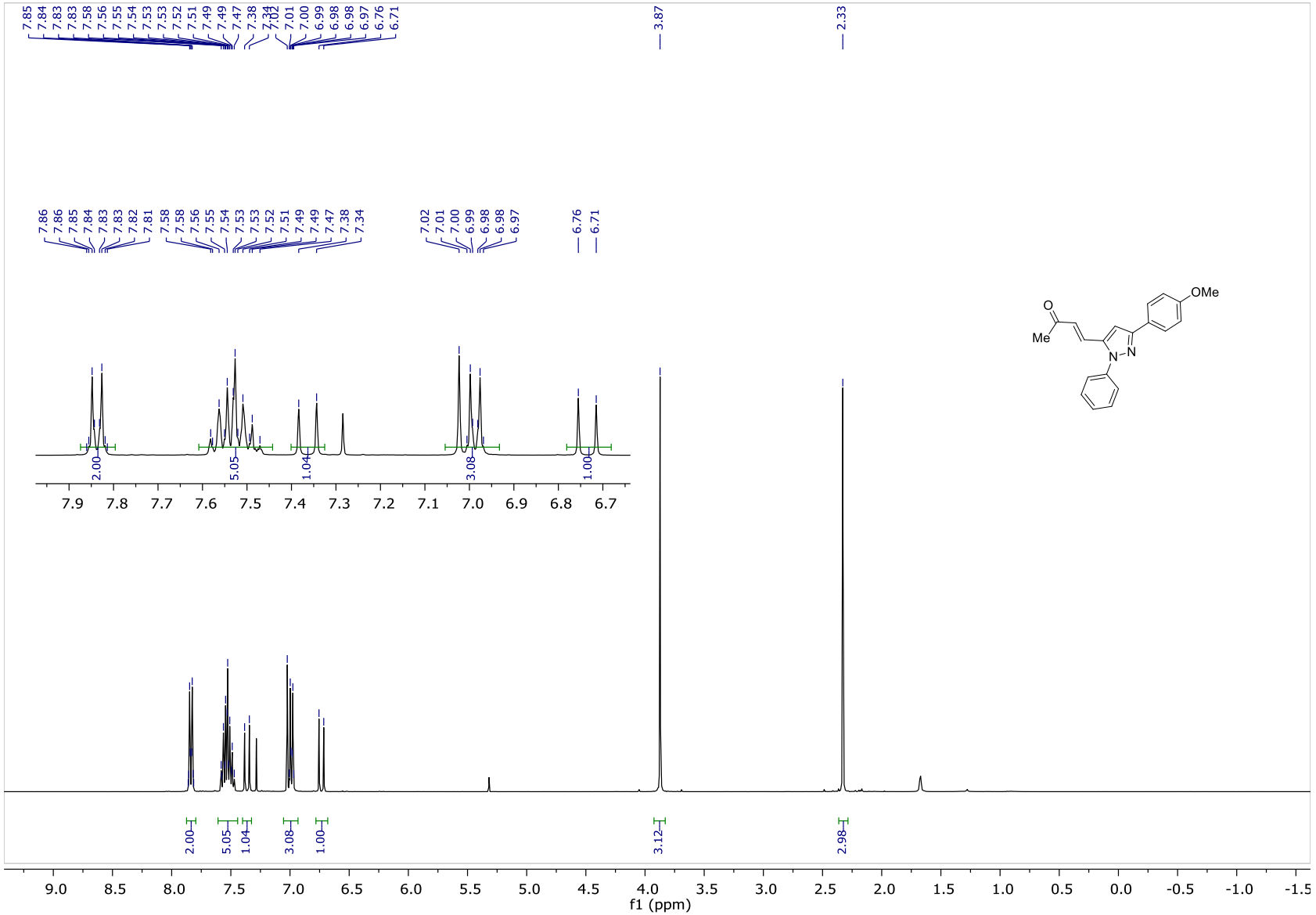


Figure S36: ^{13}C NMR spectrum of compound *(E)*-**3d** (101 MHz, $CDCl_3$)

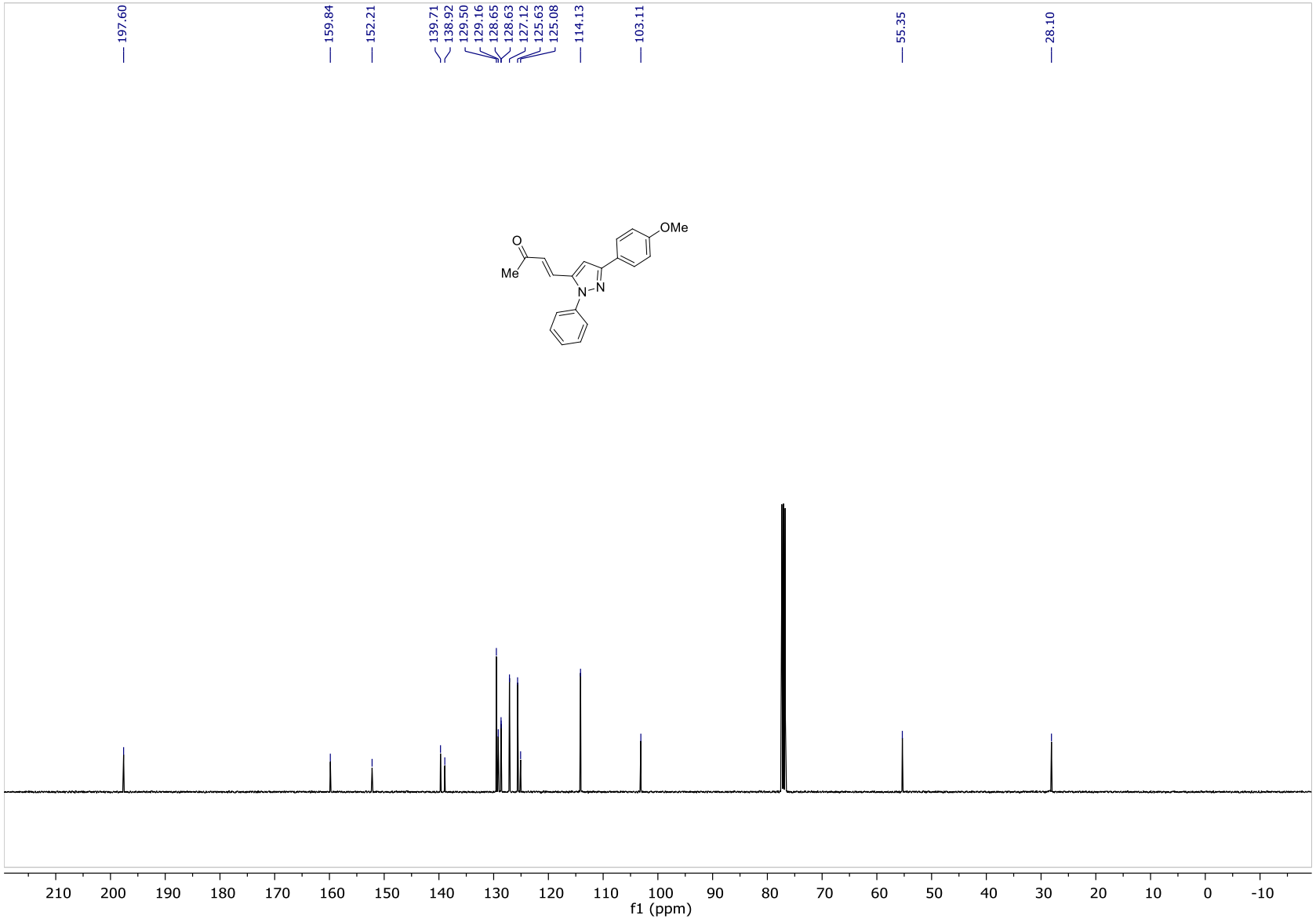


Figure S37: ^{1}H NMR spectrum of compound *(E)*-**3e** (600 MHz, $CDCl_3$)

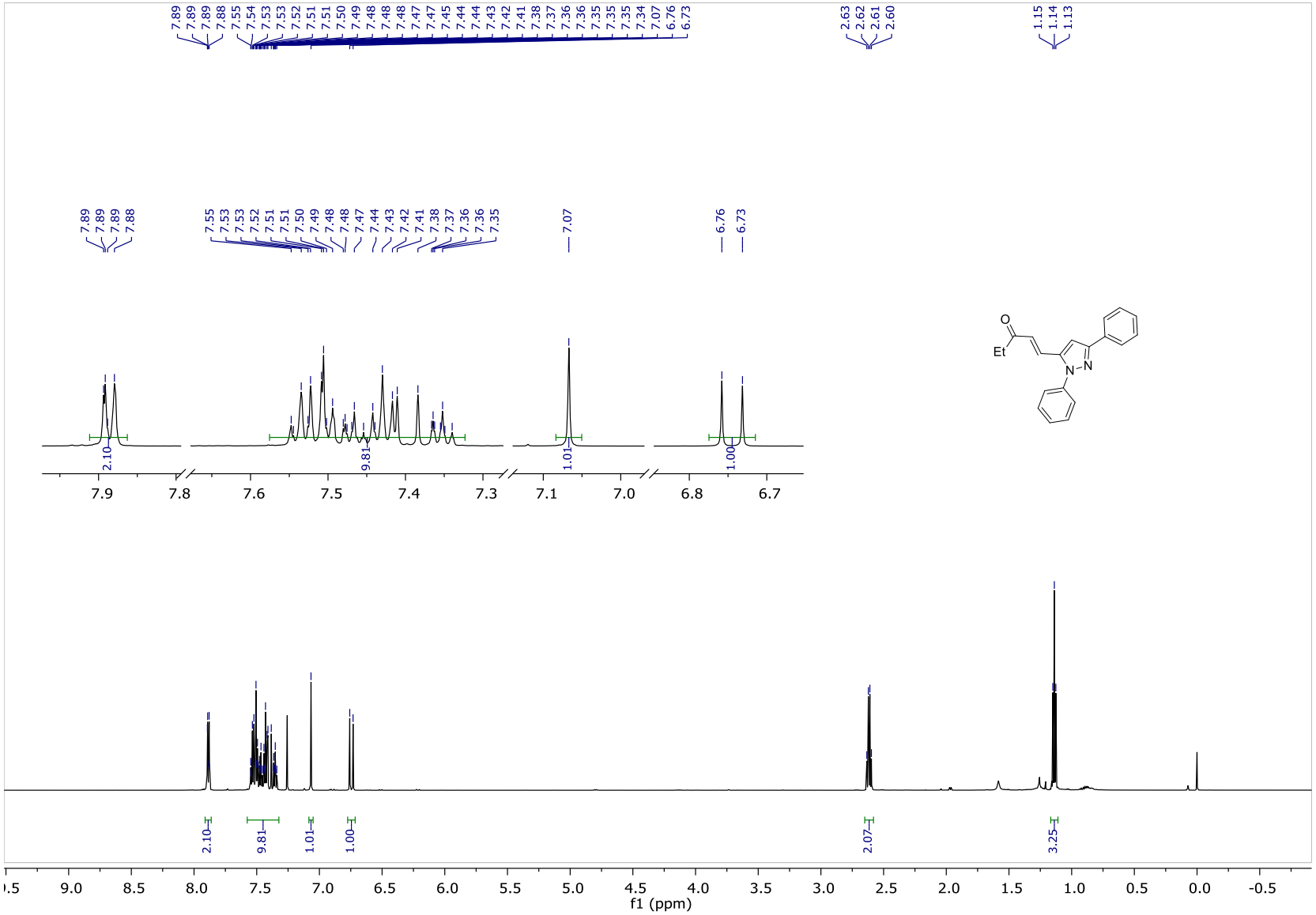


Figure S38: ^{13}C NMR spectrum of compound *(E)*-**3e** (151 MHz, $CDCl_3$)

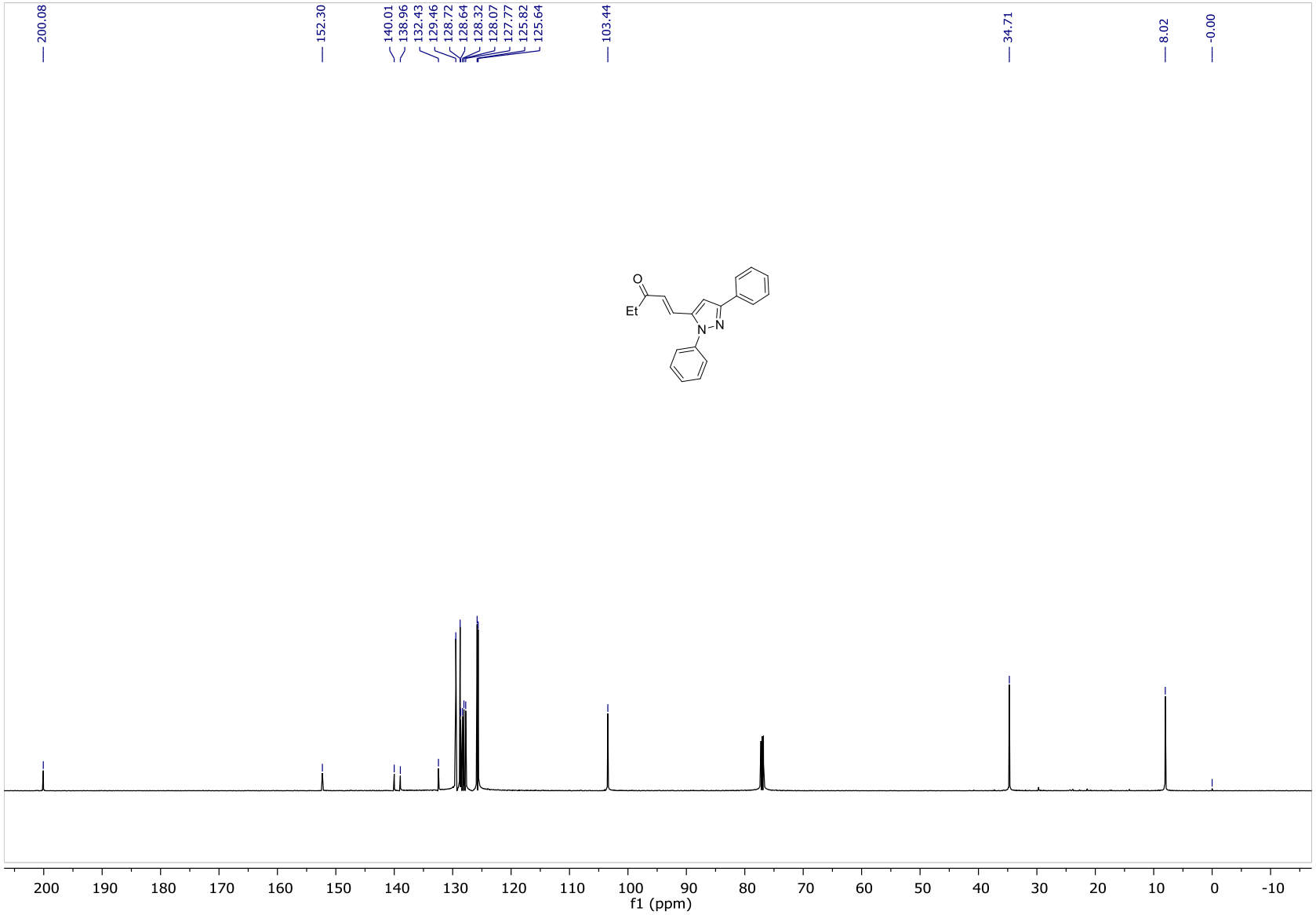


Figure S39: ^{1}H NMR spectrum of compound *(E)*-**3f** (600 MHz, $CDCl_3$)

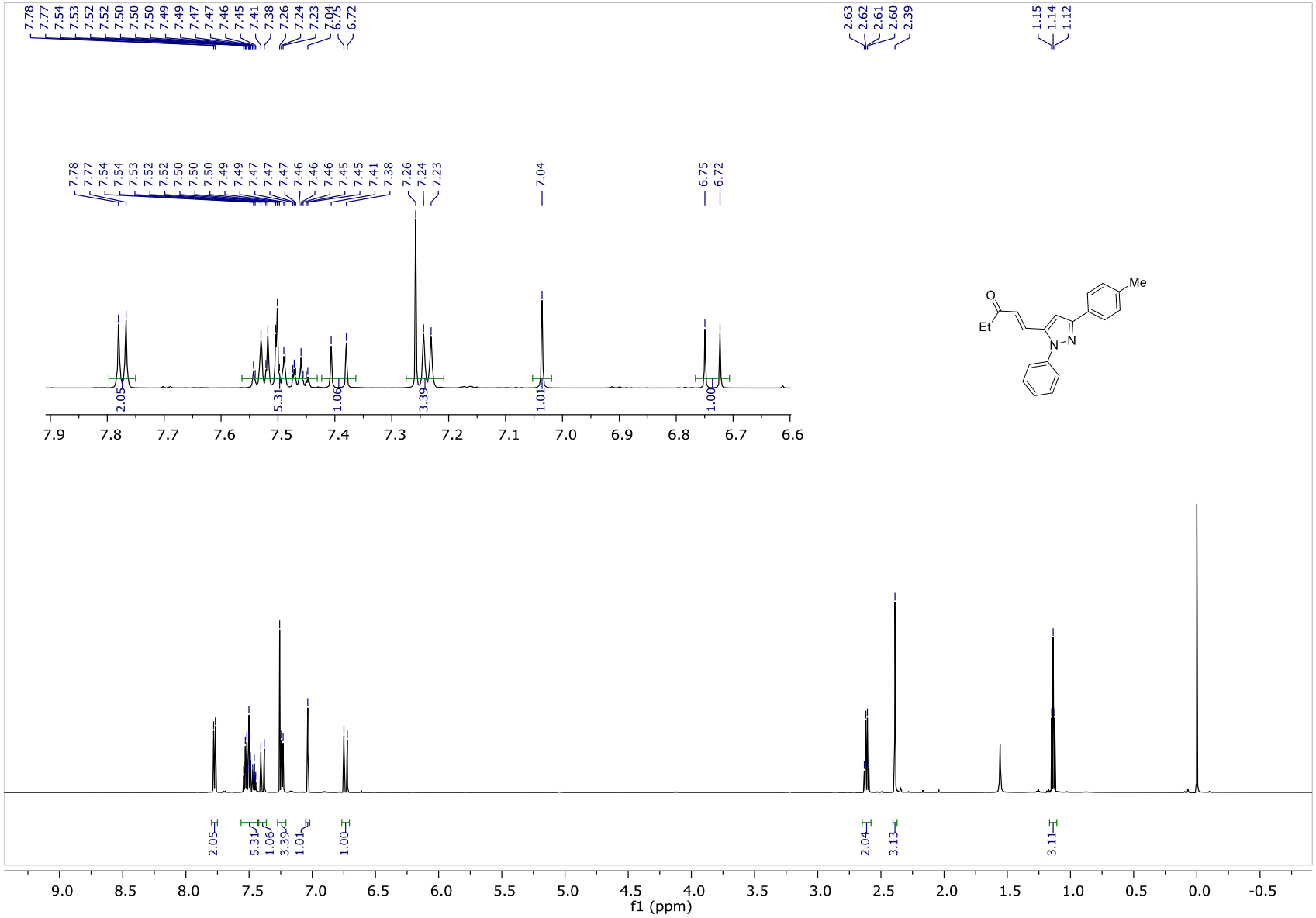


Figure S40: ^{13}C NMR spectrum of compound *(Z)*-**3f** (151 MHz, $CDCl_3$)

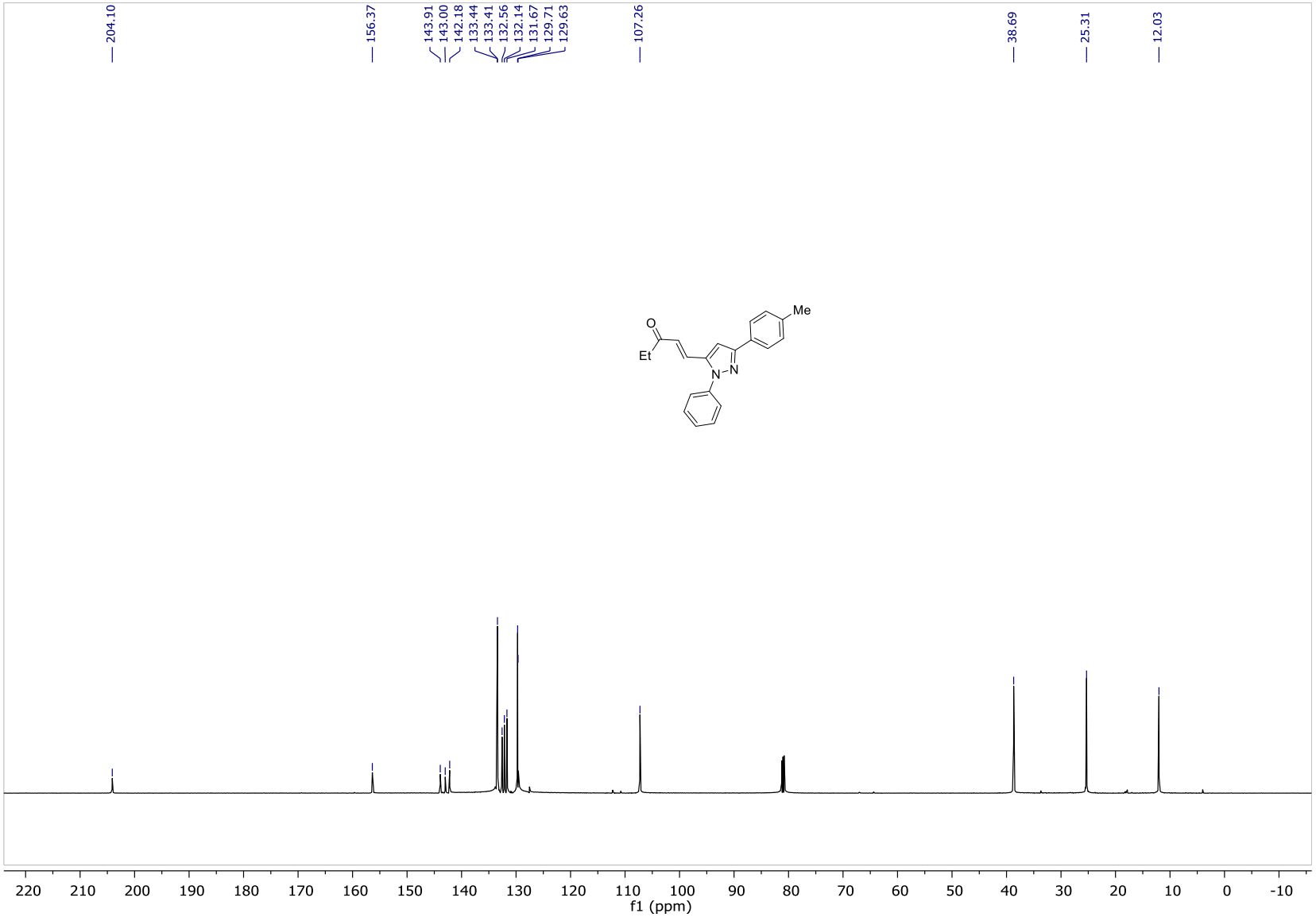


Figure S41: ^{1}H NMR spectrum of compound *(E)*-**3g** (600 MHz, $CDCl_3$)

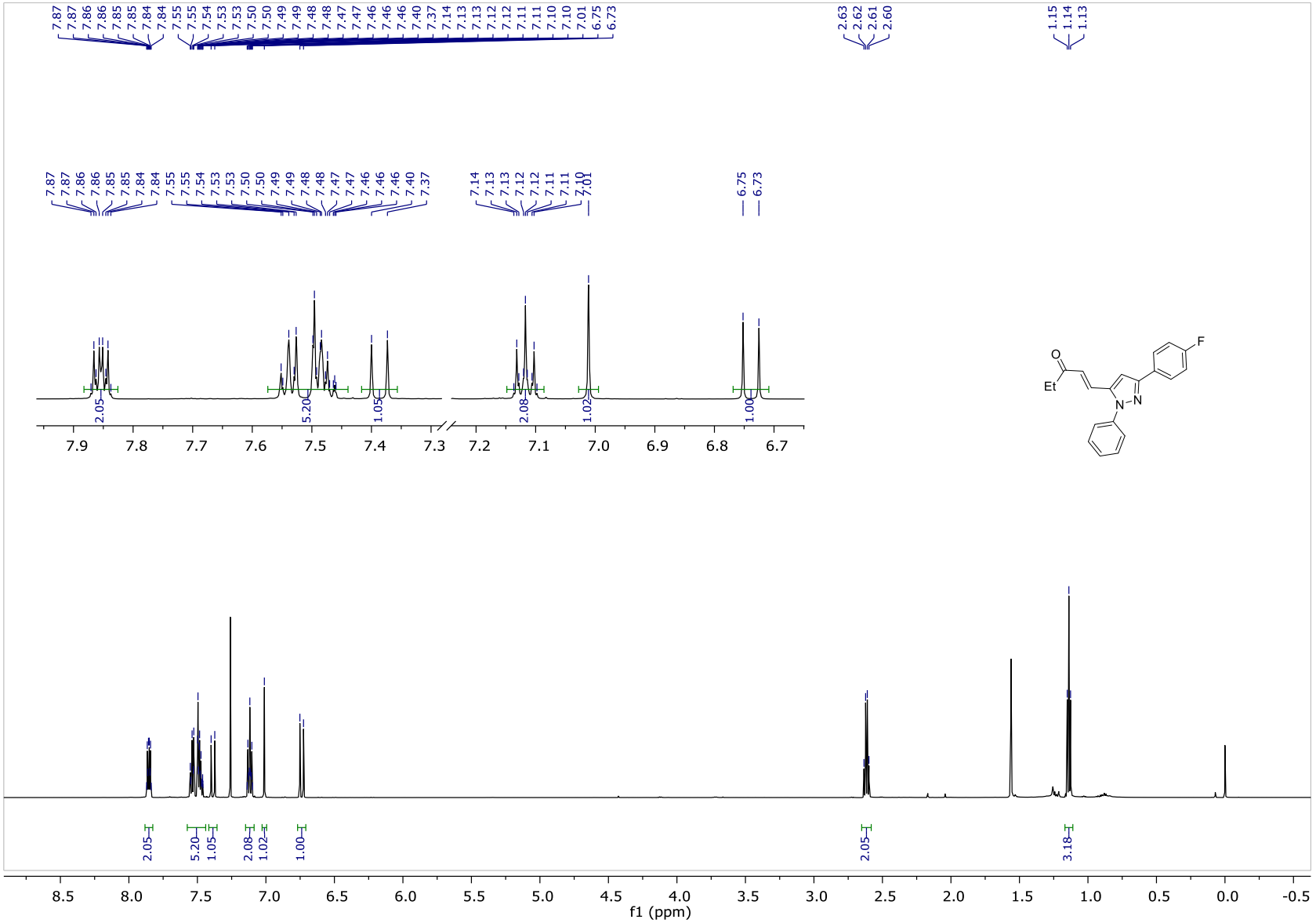


Figure S42: ^{13}C NMR spectrum of compound *(E)*-**3g** (101 MHz, $CDCl_3$)

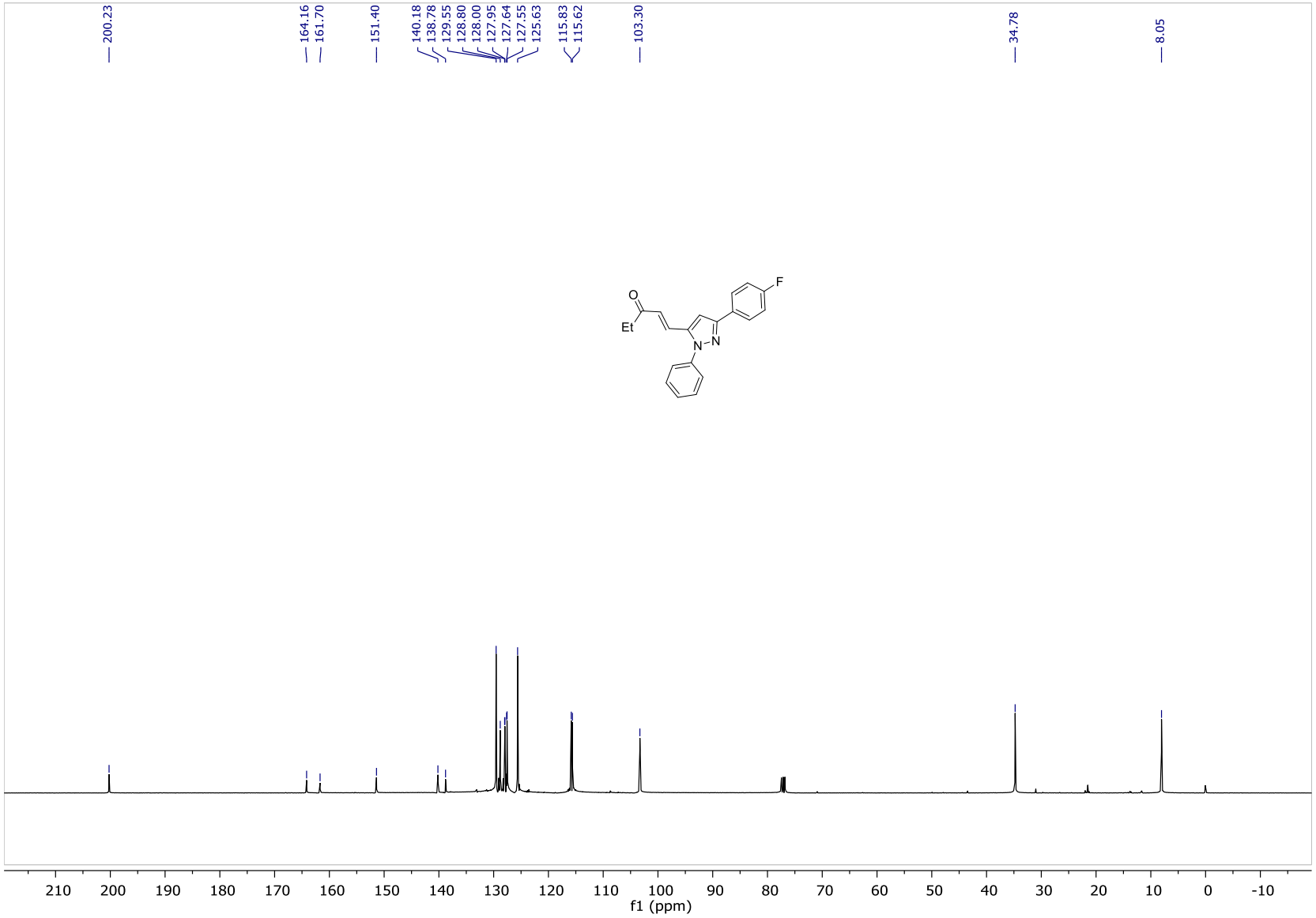


Figure S43: ^{1}H NMR spectrum of compound *(E)*-**3h** (400 MHz, $CDCl_3$)

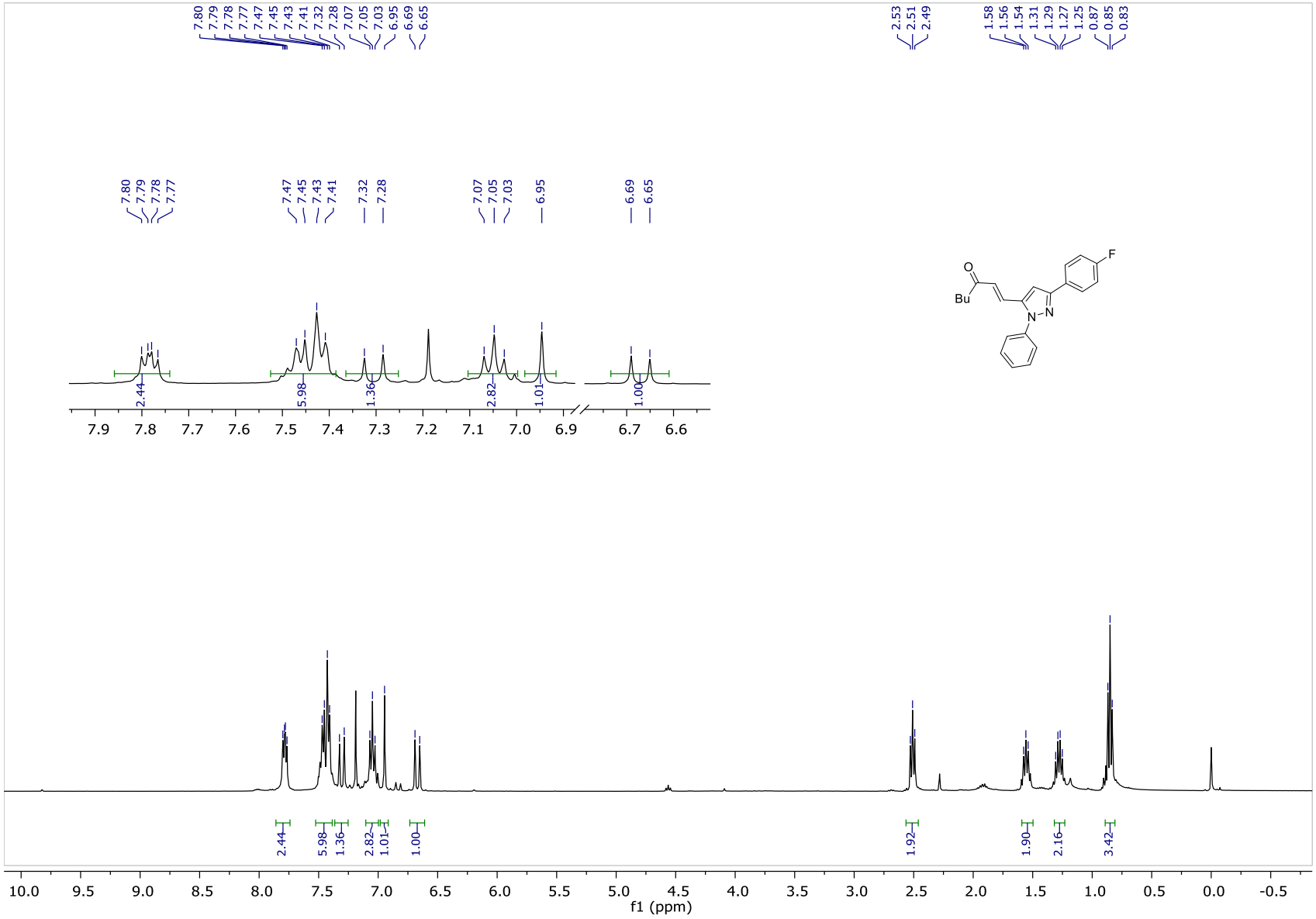


Figure S44: ^{13}C NMR spectrum of compound *(E)*-**3h** (151 MHz, $CDCl_3$)

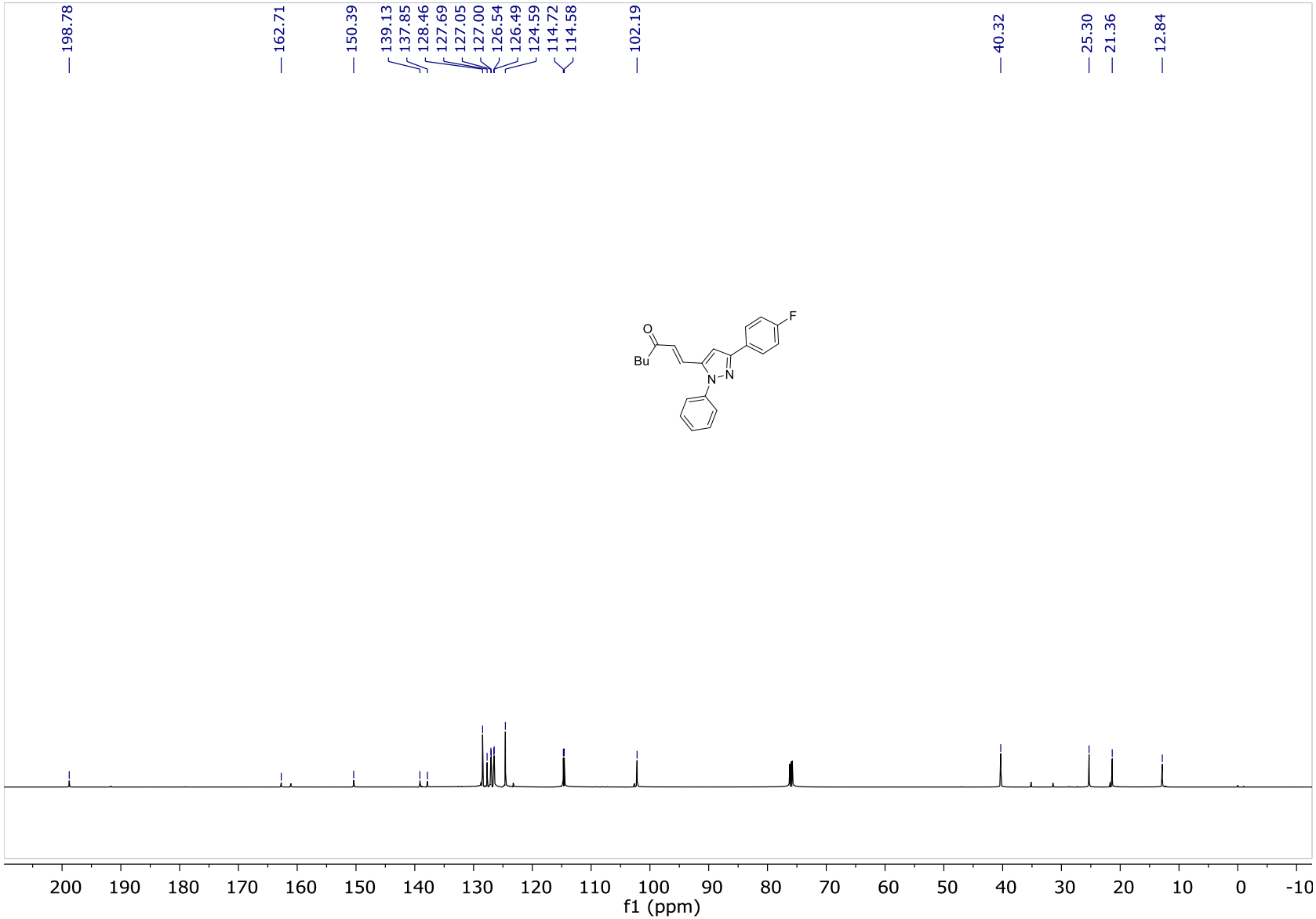


Figure S45: ^{1}H NMR spectrum of compound *(E)*-**3i** (400 MHz, $CDCl_3$)

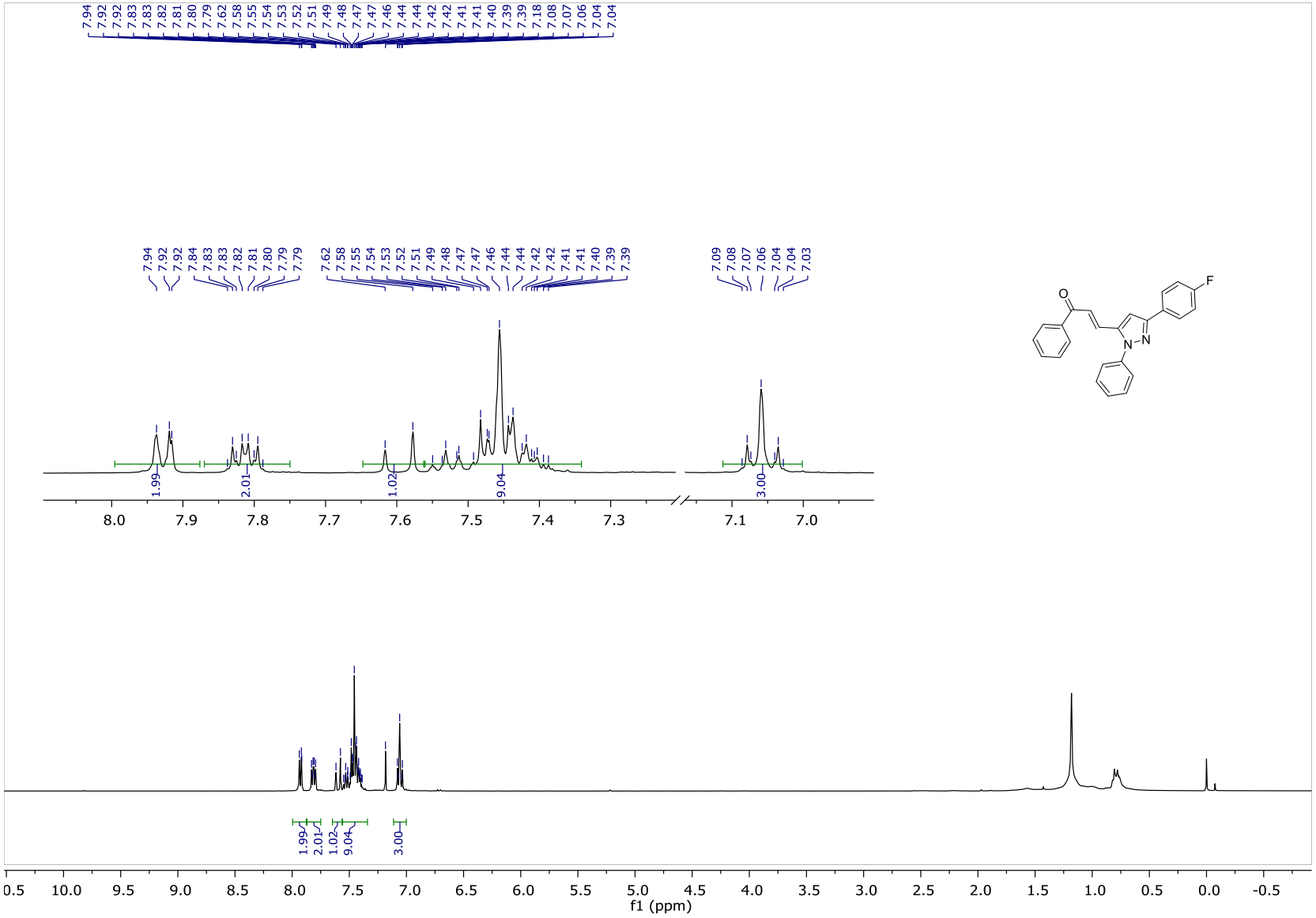


Figure S46: ^{13}C NMR spectrum of compound *(E)*-**3i** (101 MHz, $CDCl_3$)

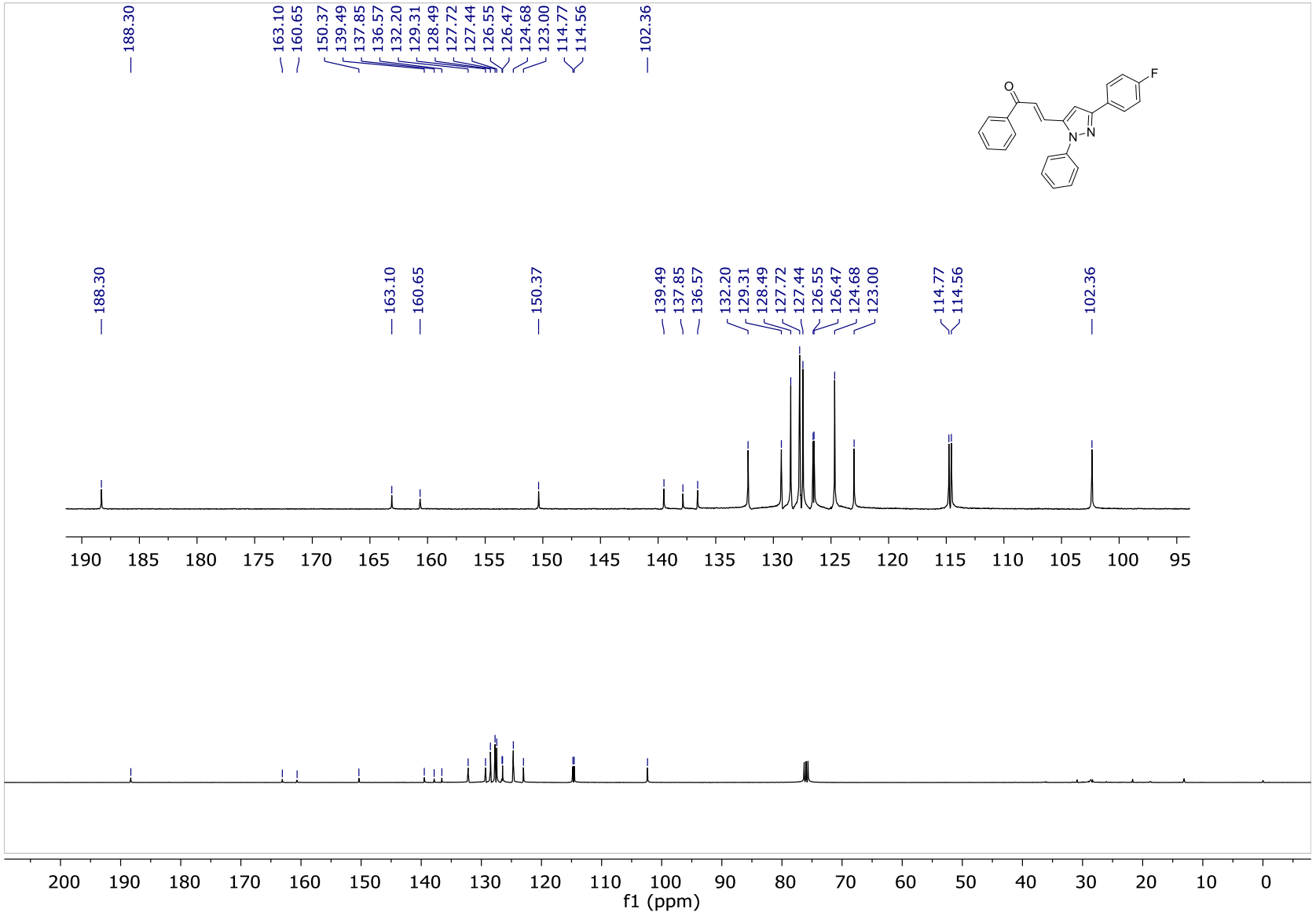


Figure S47: ^{1}H NMR spectrum of compound *(E)*-**3j** (600 MHz, $CDCl_3$)

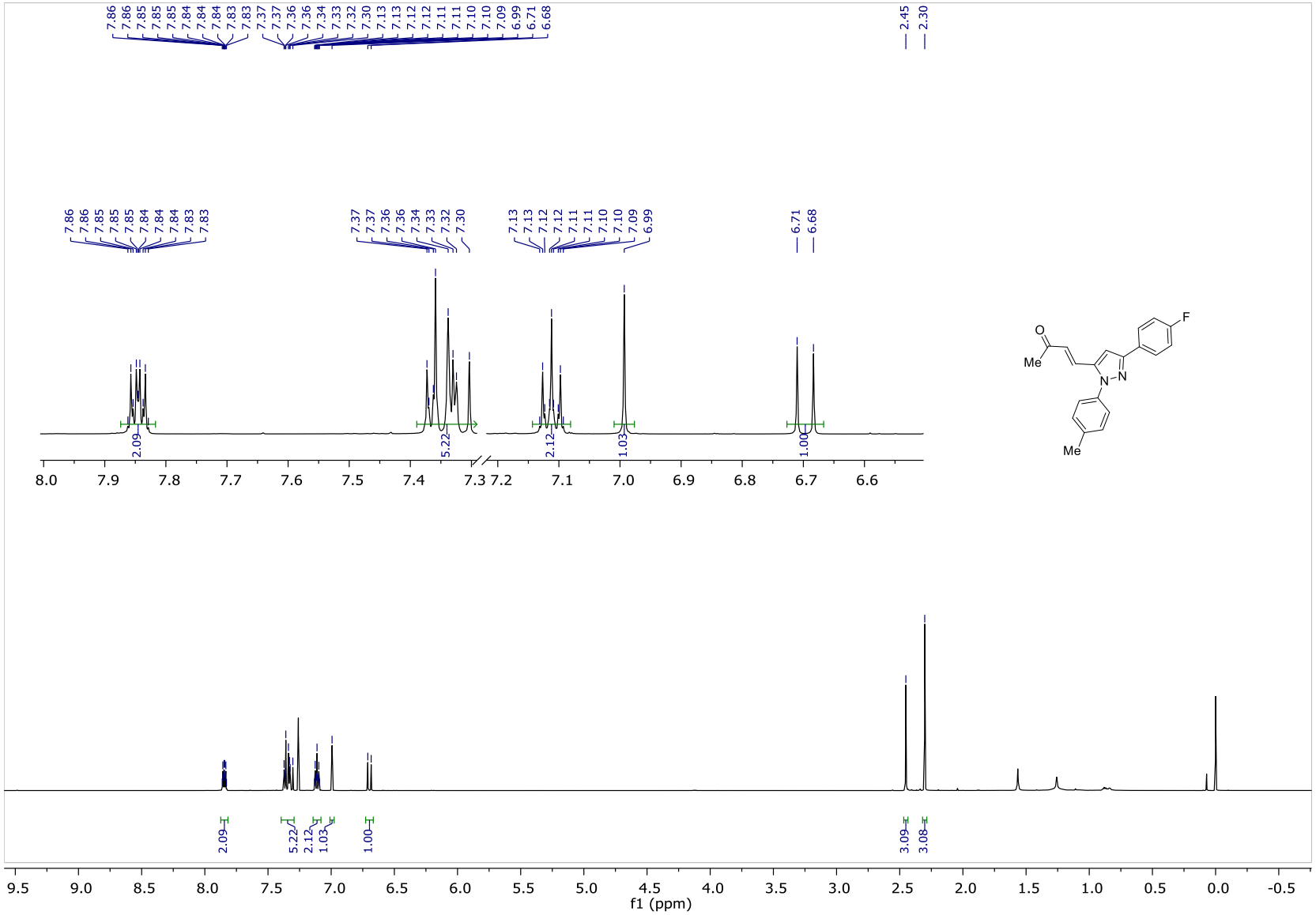


Figure S48: ^{13}C NMR spectrum of compound *(E)*-**3j** (101 MHz, $CDCl_3$)

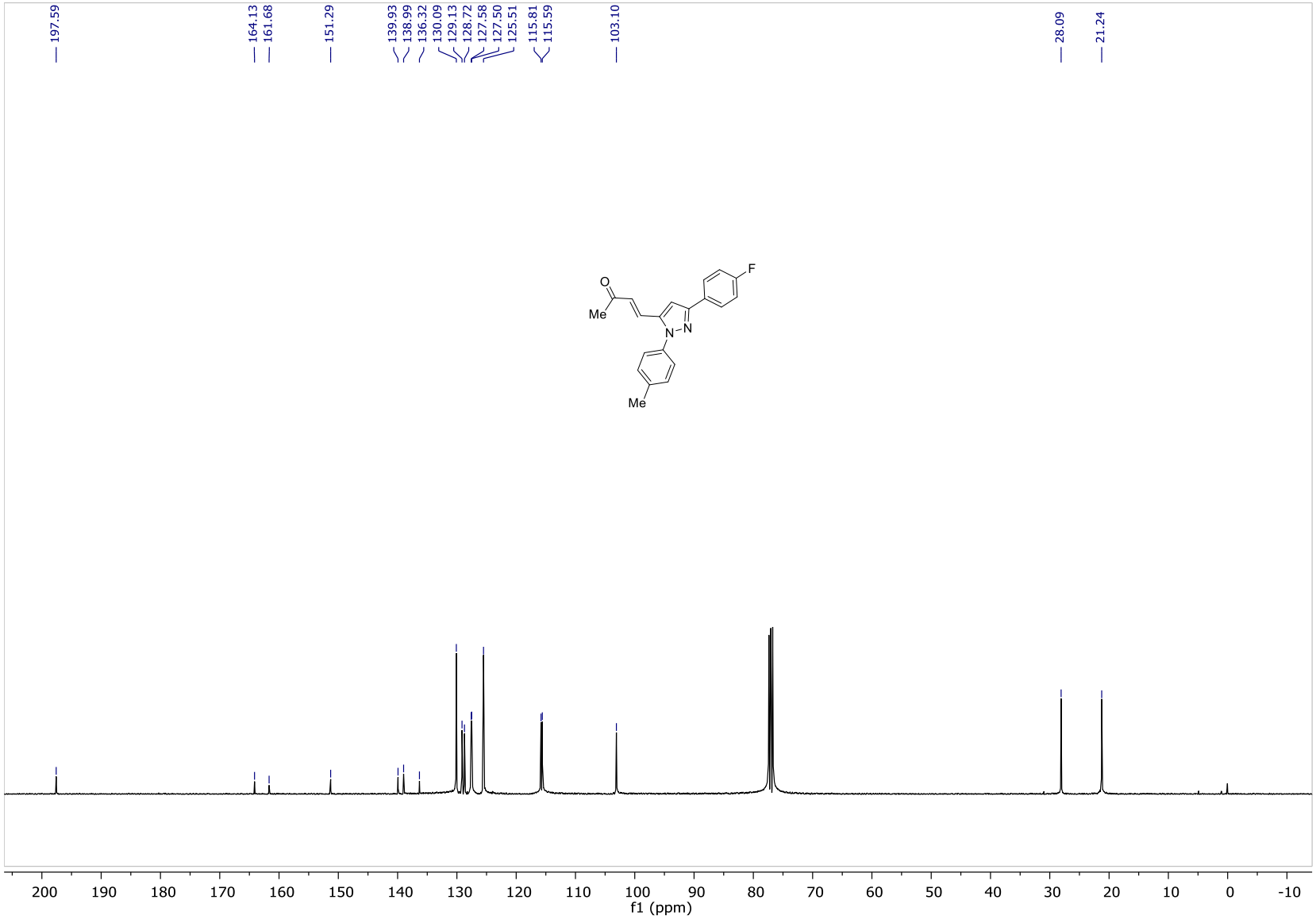


Figure S49: ^{1}H NMR spectrum of compound *(E)*-**3k** (600 MHz, $CDCl_3$)

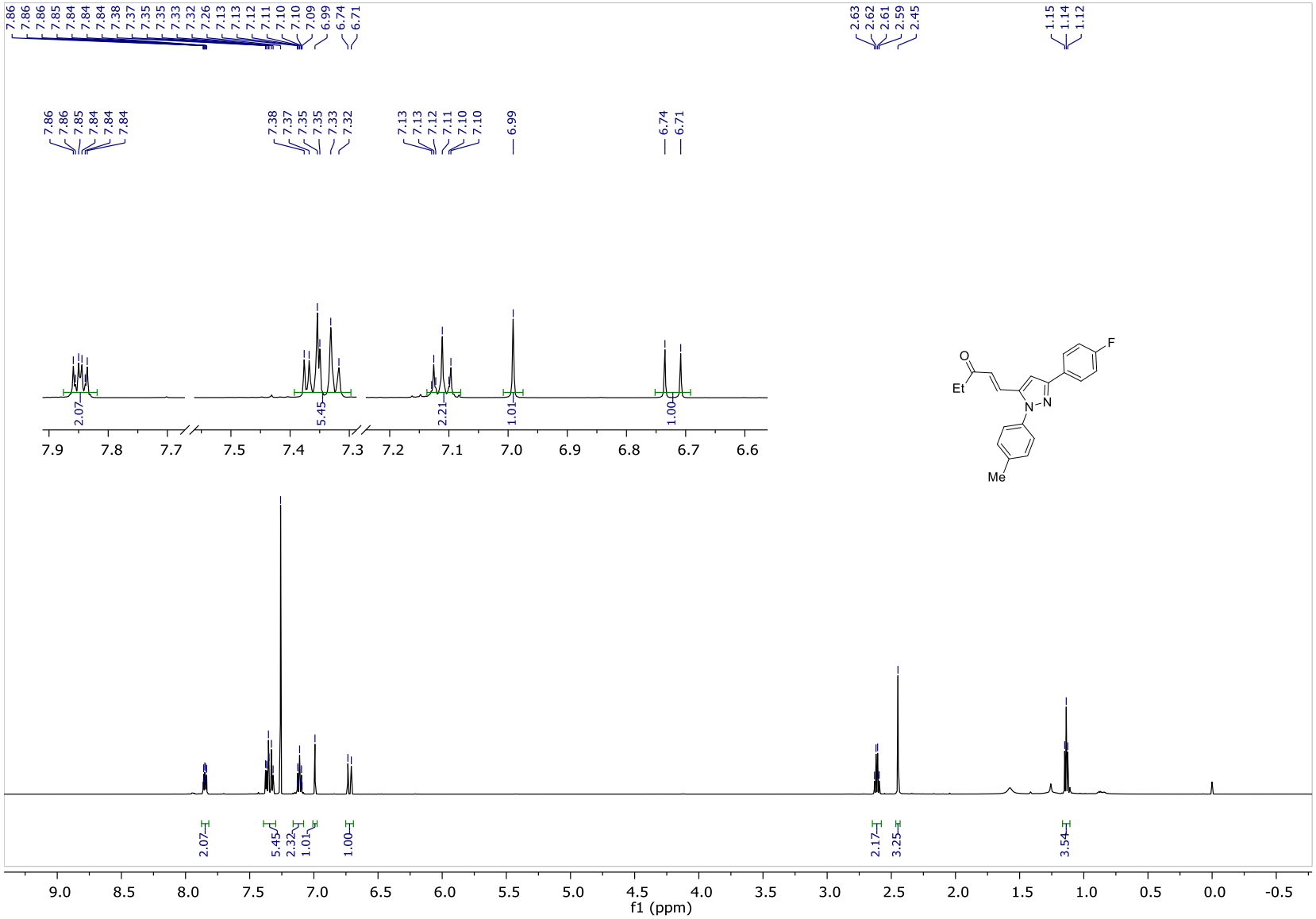


Figure S50: ^{13}C NMR spectrum of compound *(E)*-**3k** (151 MHz, $CDCl_3$)

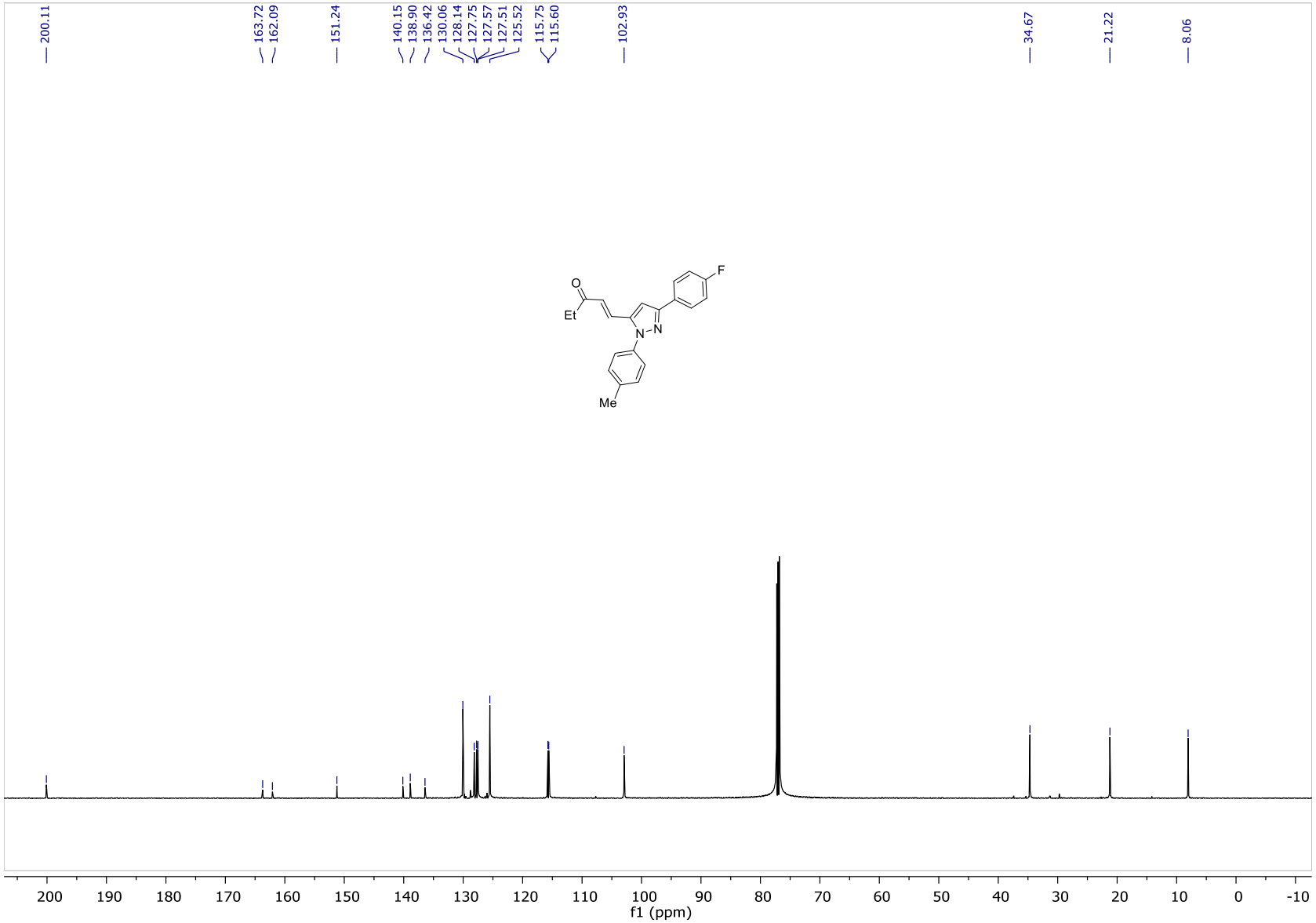


Figure S51: ^{1}H NMR spectrum of compound *(E)*-**3l** (600 MHz, $CDCl_3$)

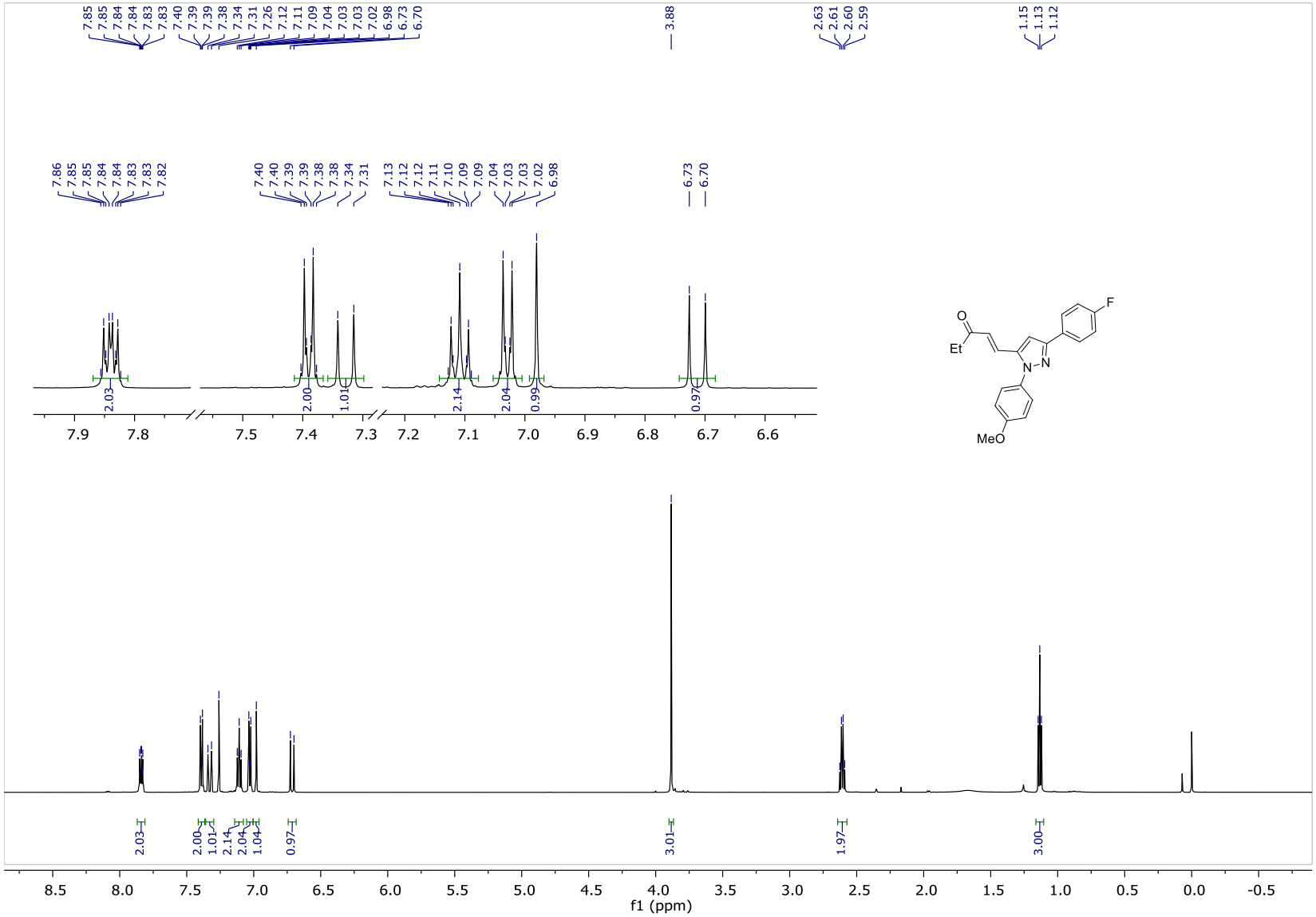


Figure S52: ^{13}C NMR spectrum of compound *(E)*-**3l** (101 MHz, $CDCl_3$)

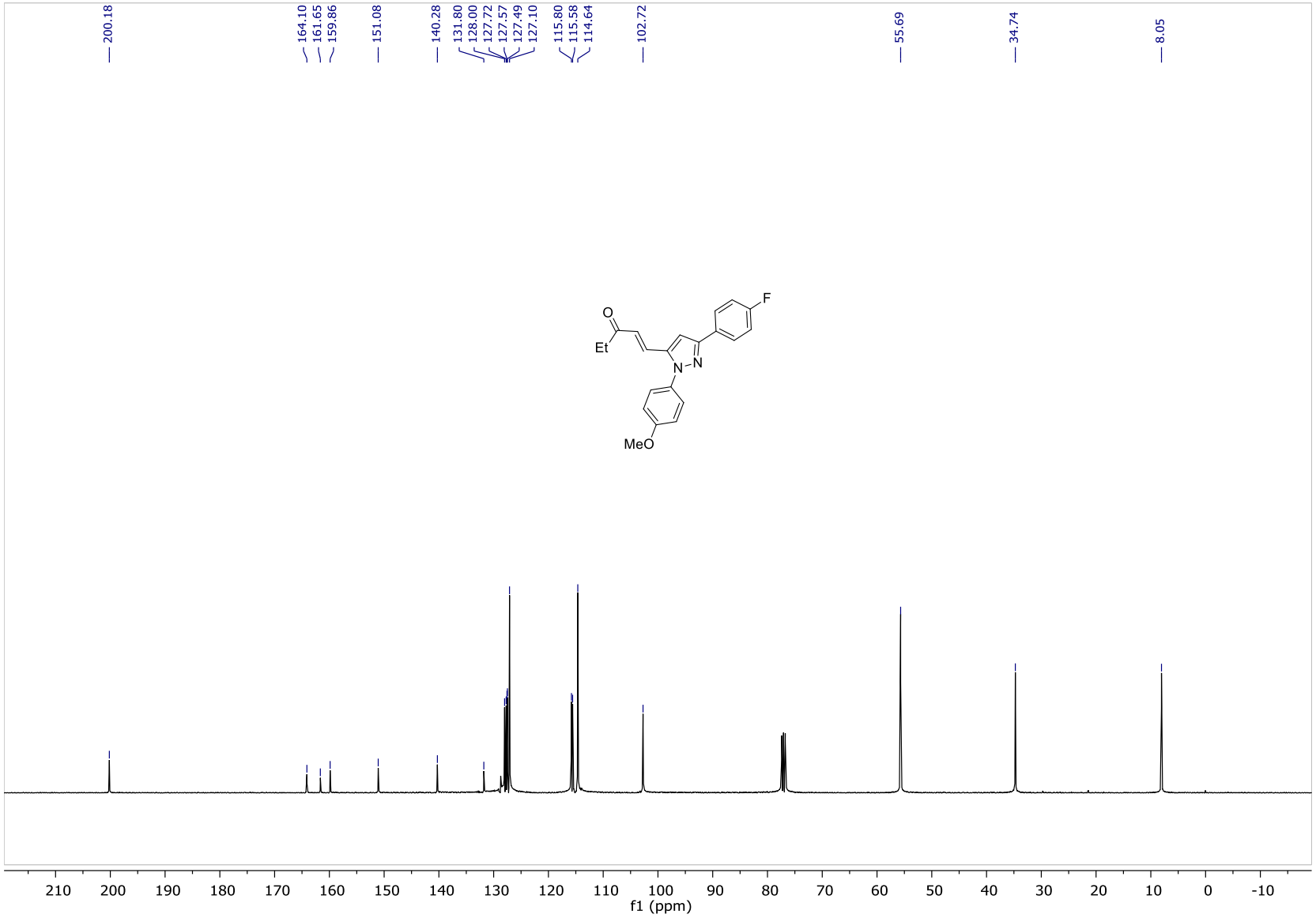


Figure S53: ^{1}H NMR spectrum of compound **3m** (600 MHz, $CDCl_3$)

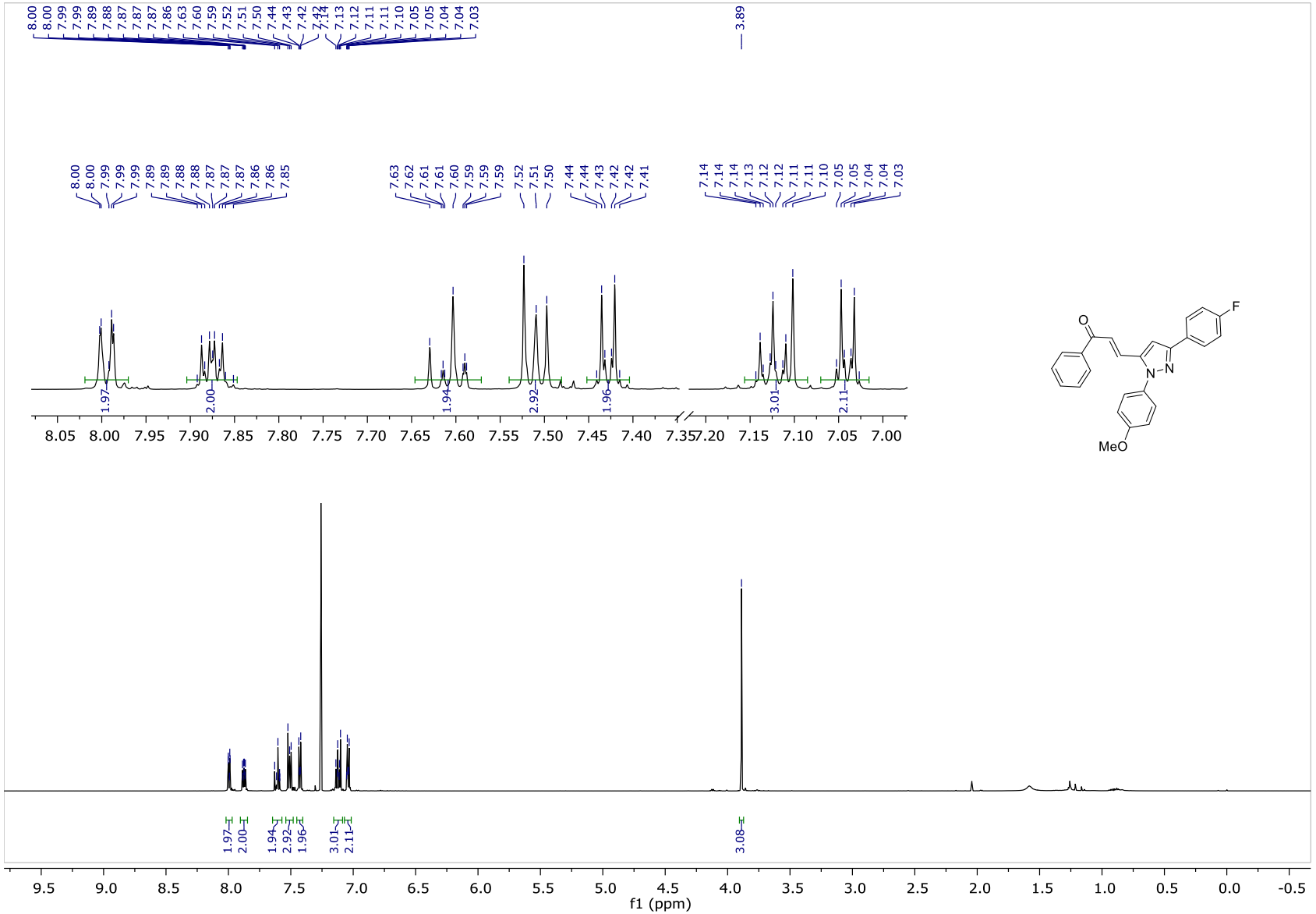


Figure S54: ^{13}C NMR spectrum of compound **3o** (151 MHz, $CDCl_3$)

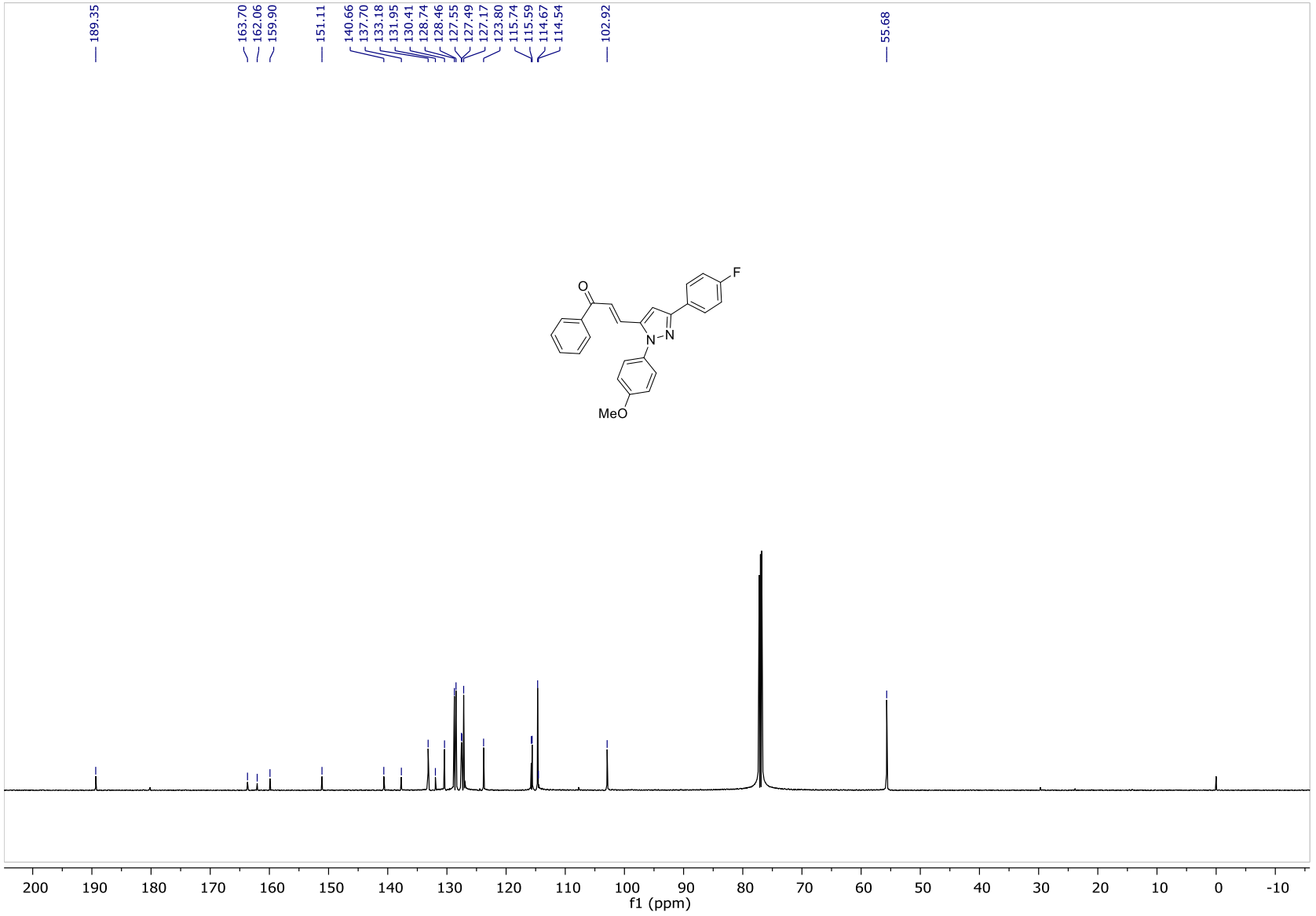


Figure S55: ^{1}H NMR spectrum of compound **2n** (600 MHz, $CDCl_3$)

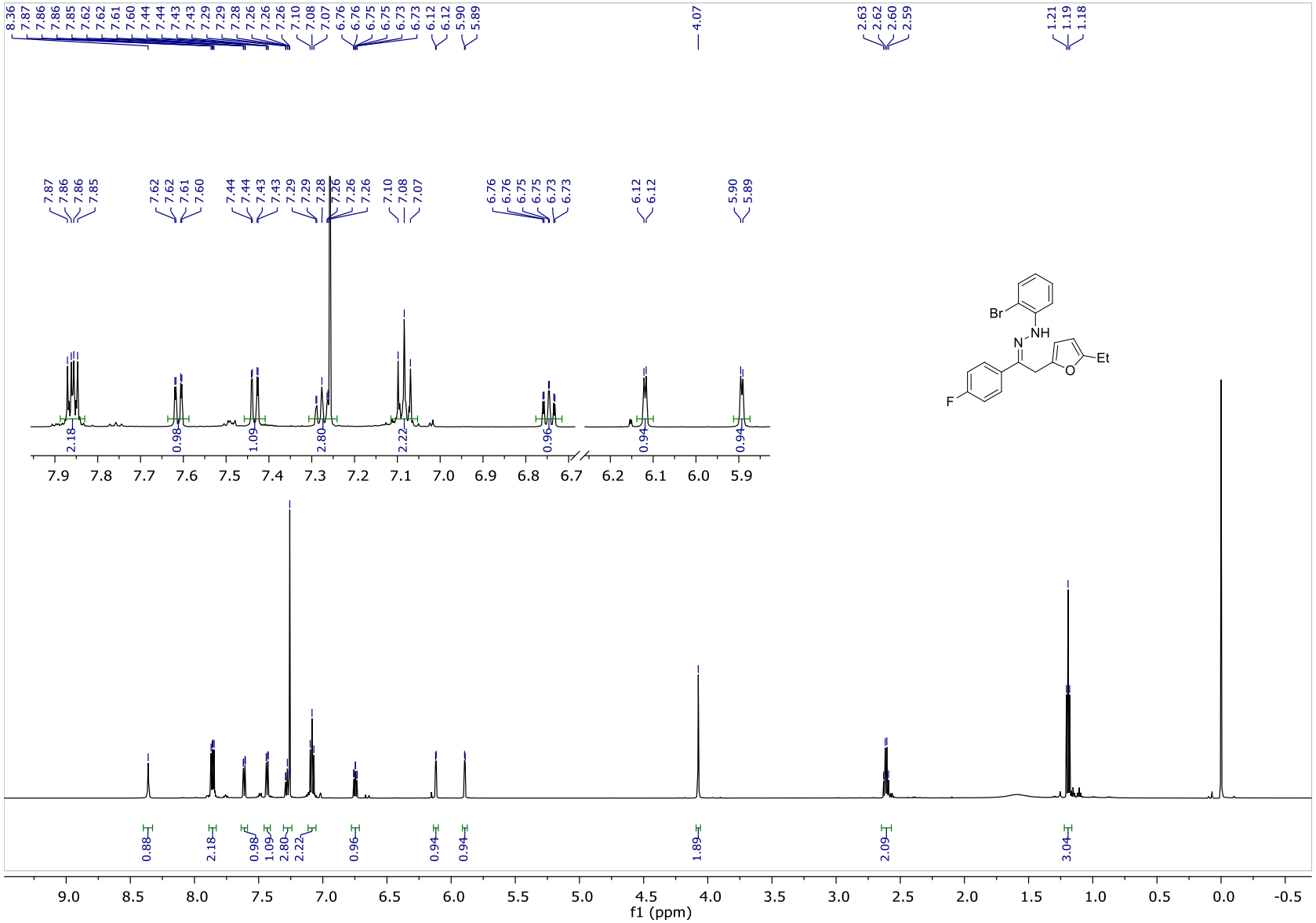


Figure S56: ^{13}C NMR spectrum of compound **2n** (101 MHz, $CDCl_3$)

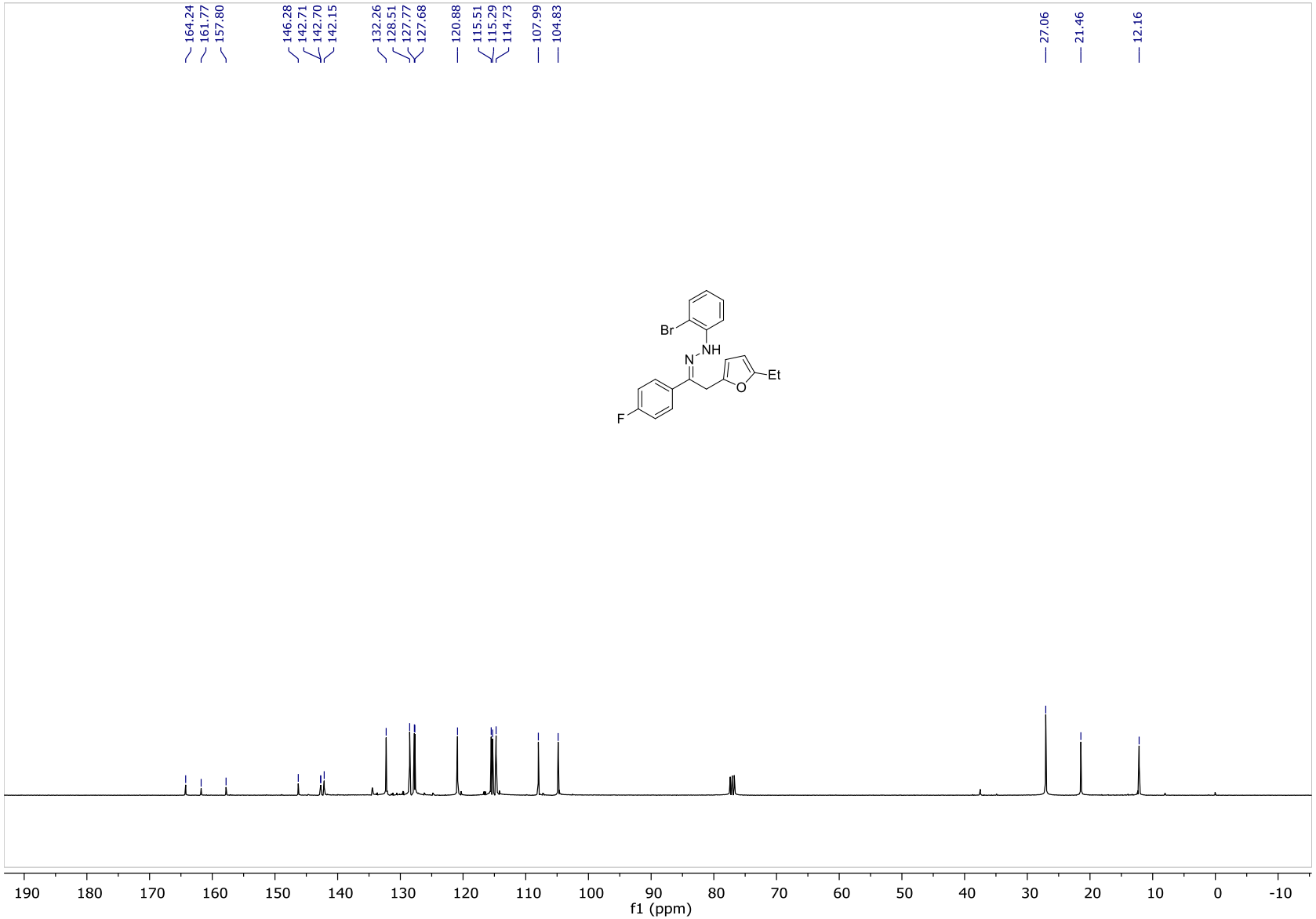


Figure S57: ^{1}H NMR spectrum of compound **2o** (600 MHz, $CDCl_3$)

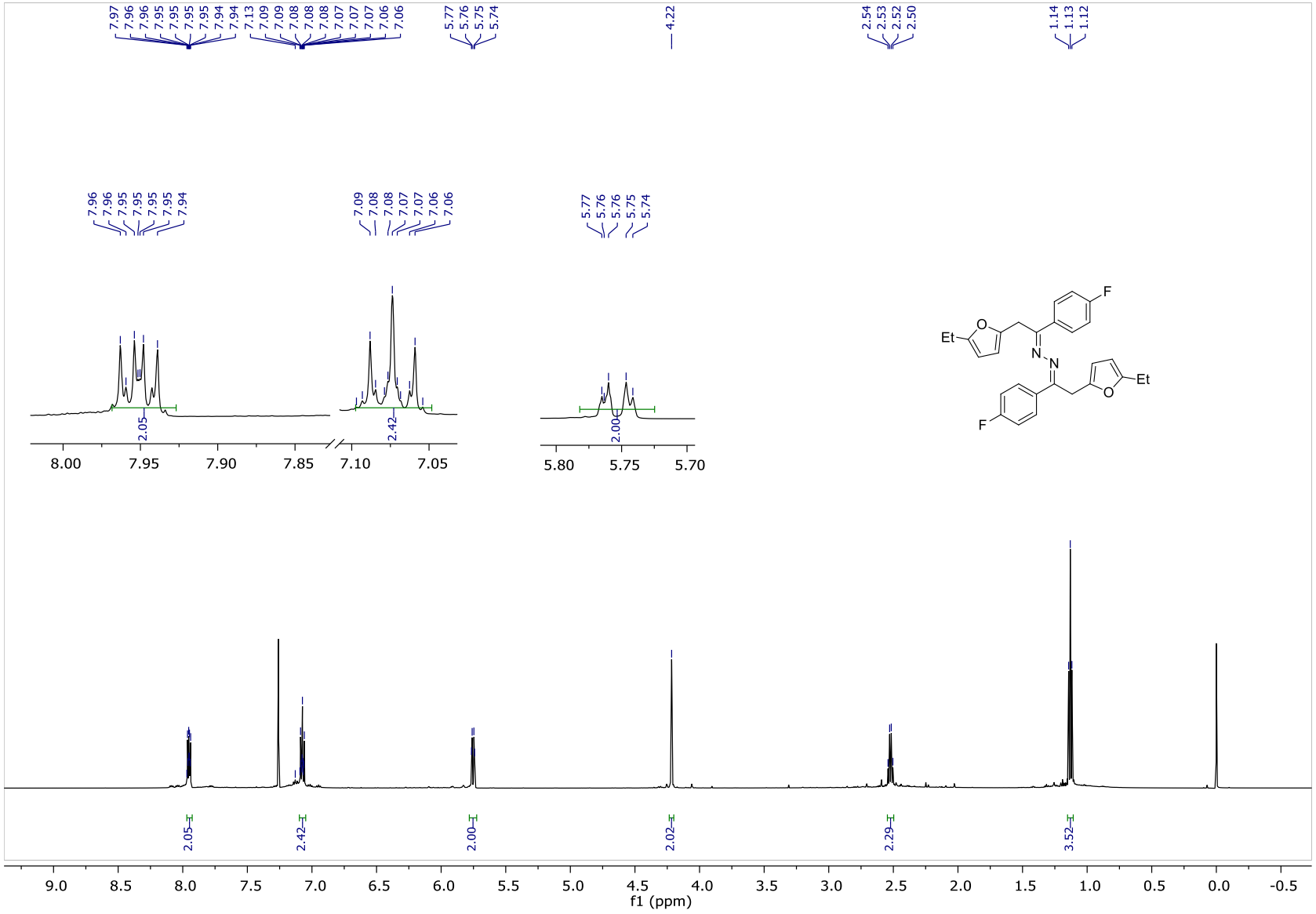


Figure S58: ^{13}C NMR spectrum of compound **2o** (151 MHz, $CDCl_3$)

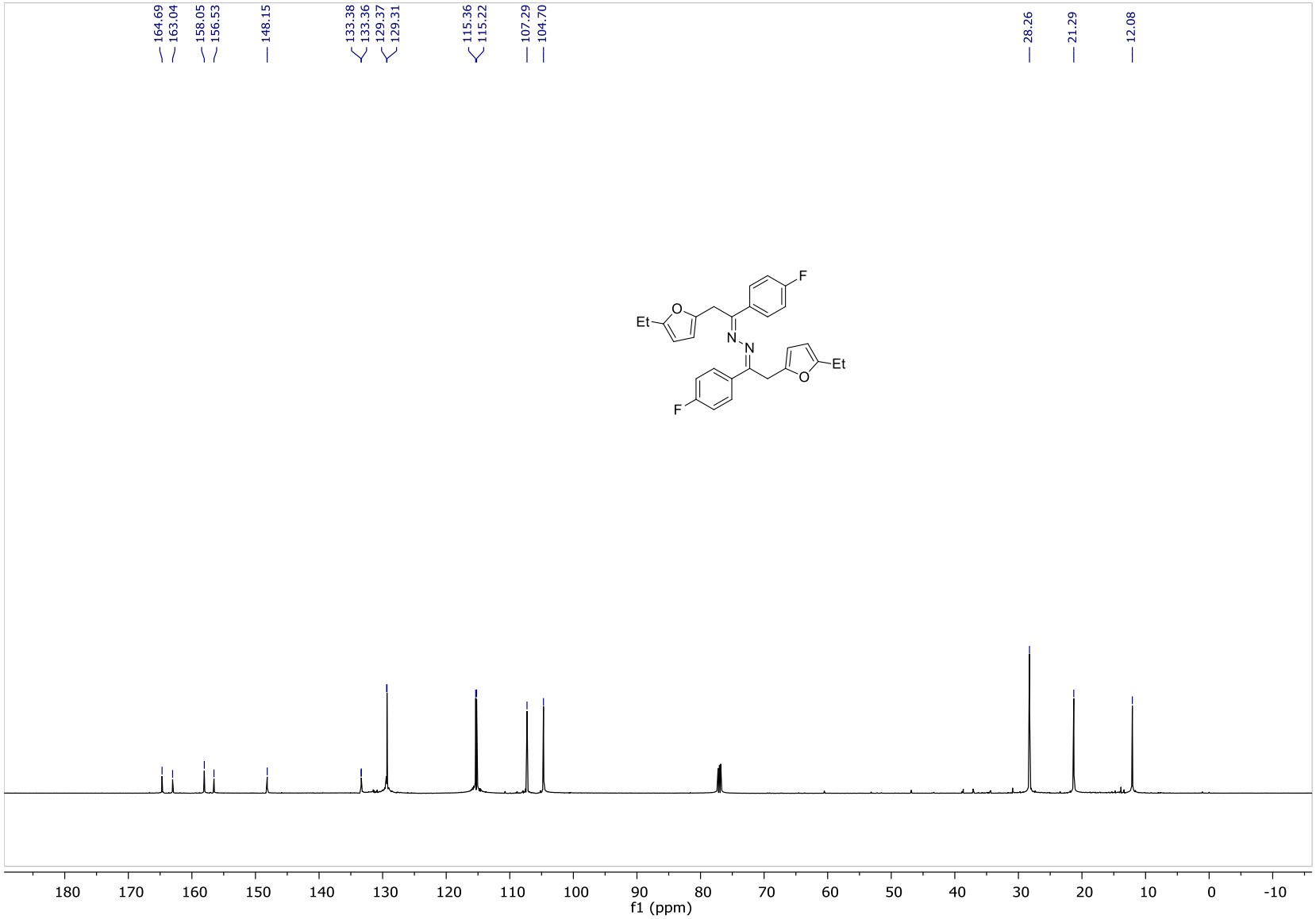


Figure S59: ^{1}H NMR spectrum of compound **4** (400 MHz, $CDCl_3$)

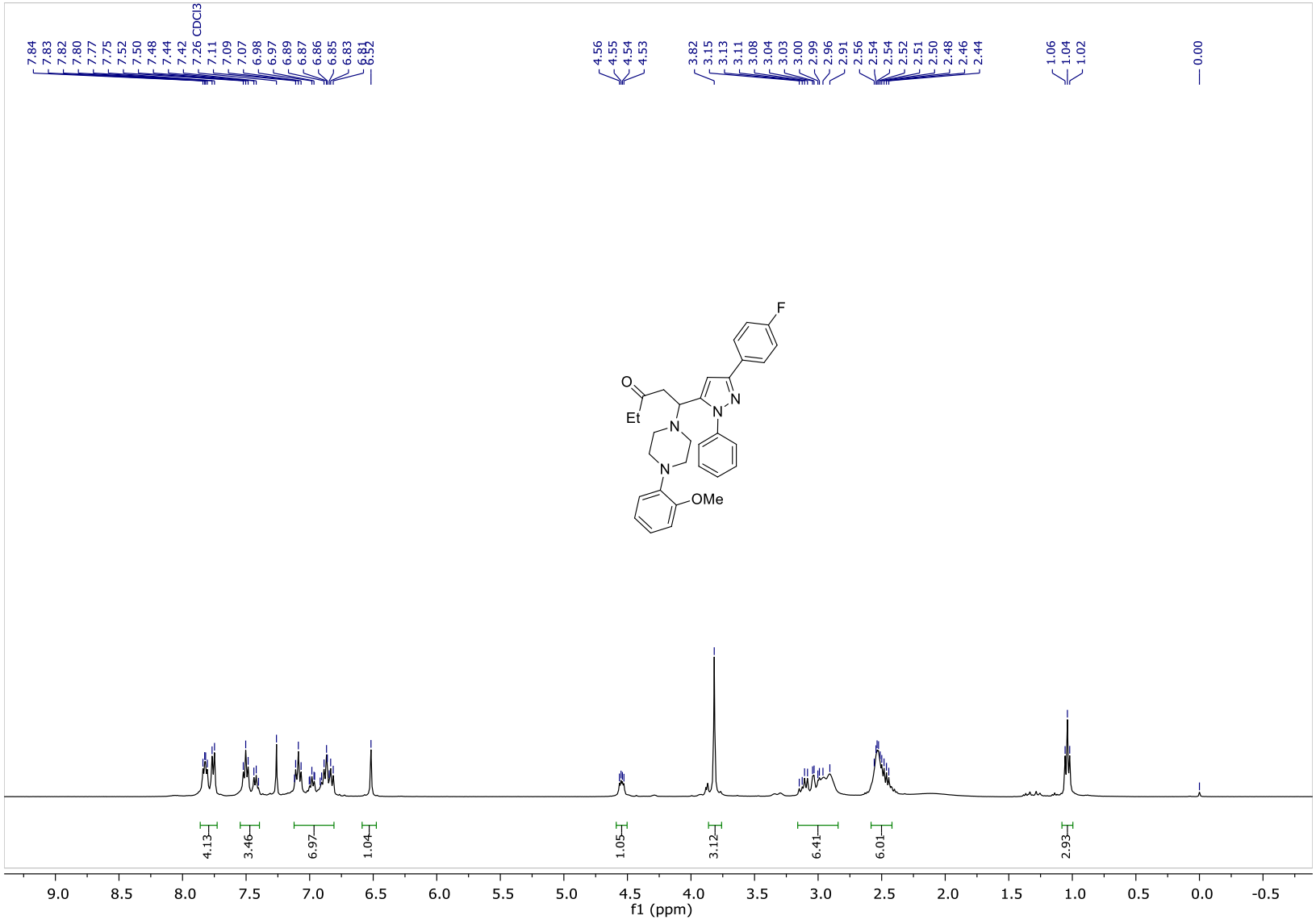


Figure S60: ^{13}C NMR spectrum of compound **4** (101 MHz, $CDCl_3$)

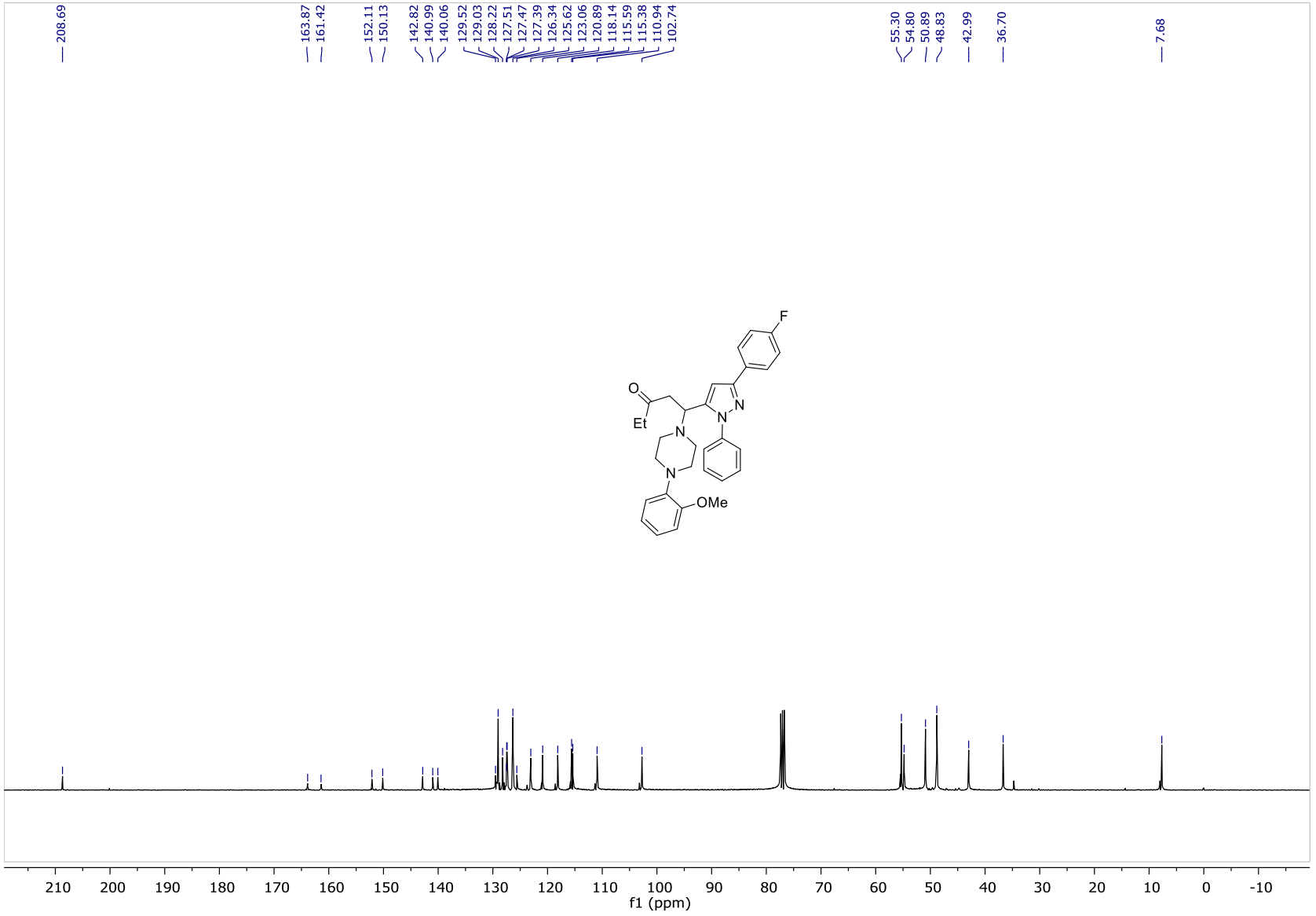


Figure S61: ^{1}H NMR spectrum of compound (*E,Z*)-**3e** (600 MHz, $CDCl_3$)

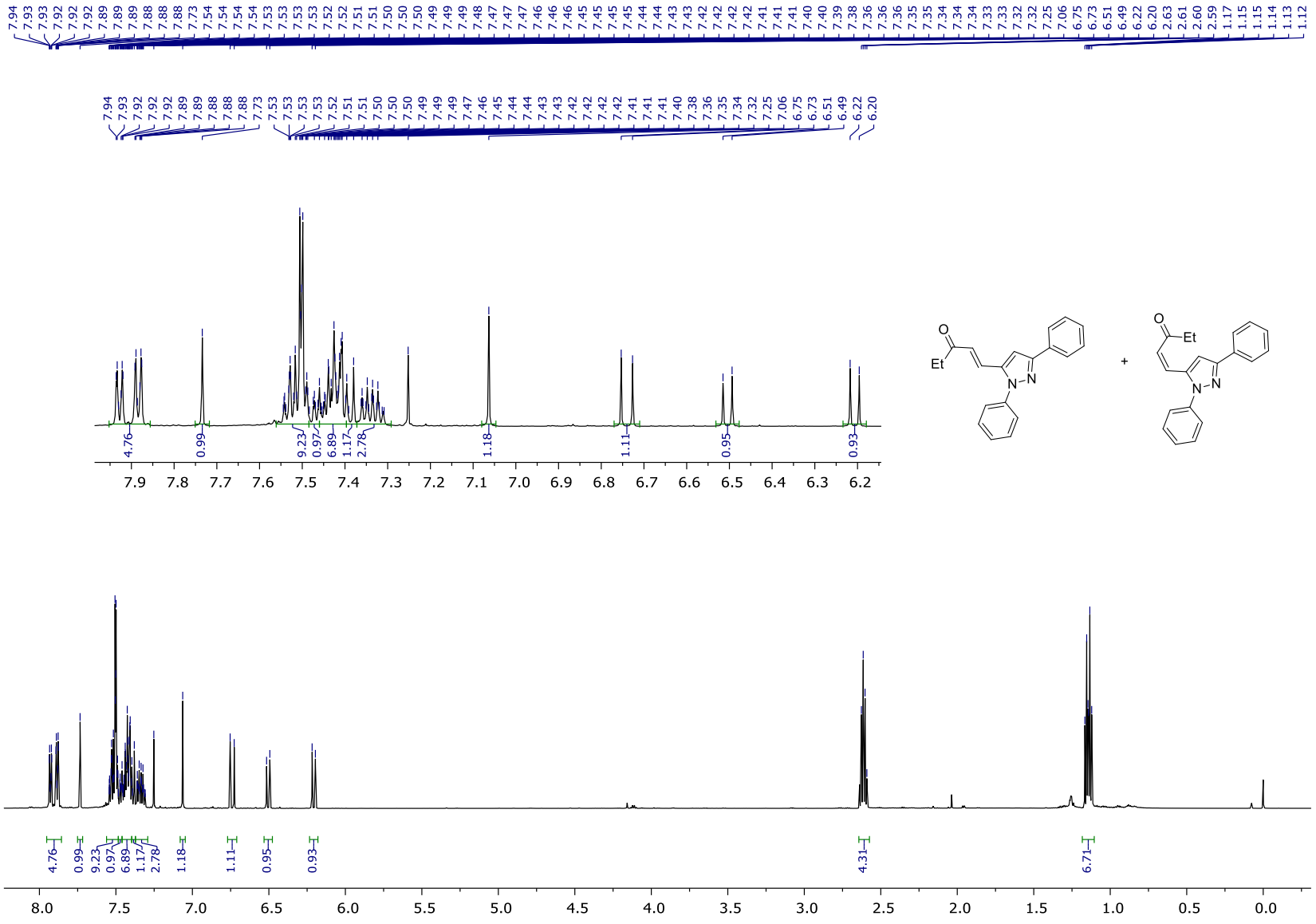


Figure S62: ^{1}H NMR spectra of compounds (*E*)-**3e** [1] and (*E*,*Z*)-**3e** [2] (600 MHz, $CDCl_3$)

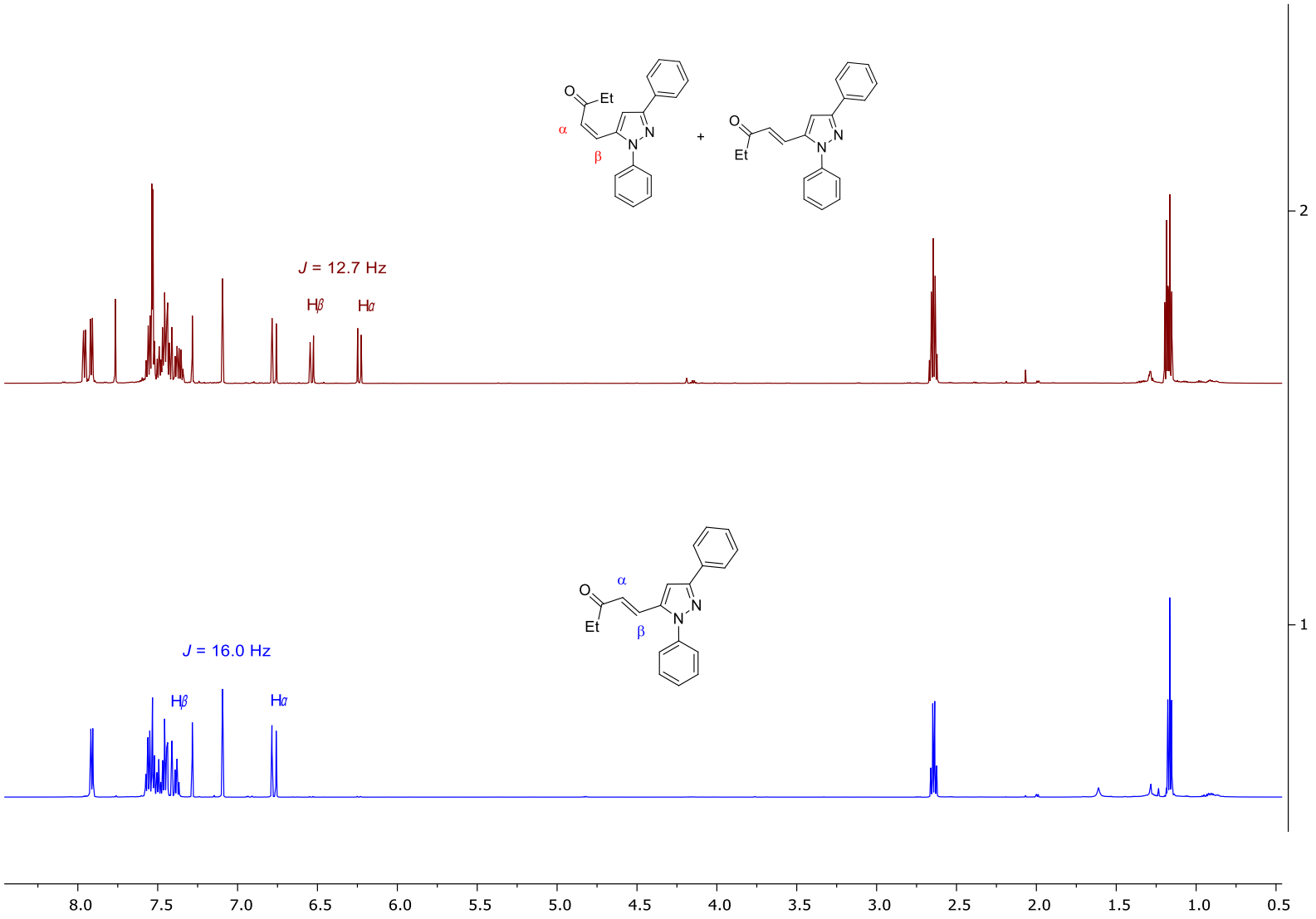


Figure S63: ^{13}C NMR spectra of compounds (*E*)-**3e** [1] and (*E,Z*)-**3e** [2] (151 MHz, $CDCl_3$)

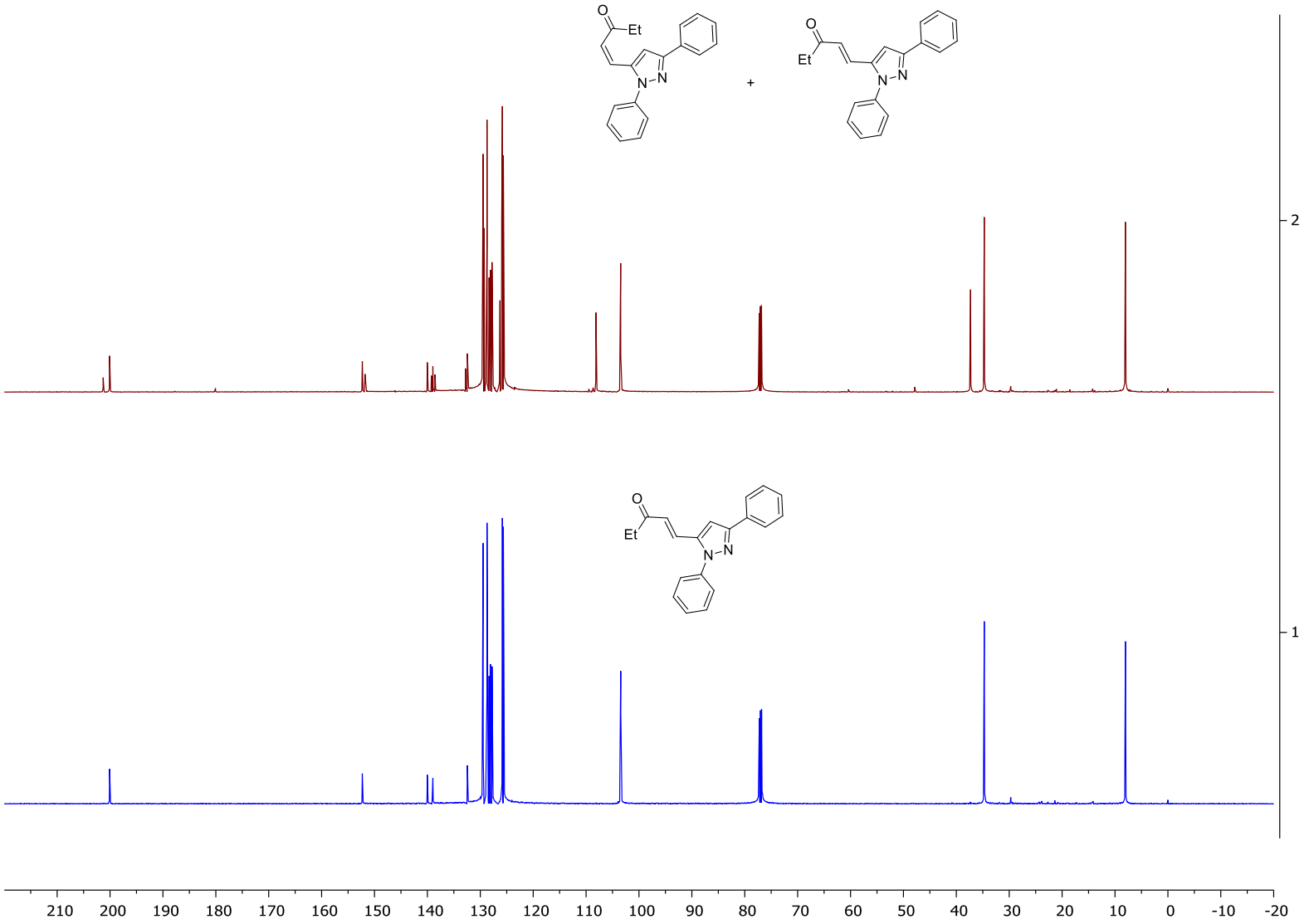


Figure S64: ^{1}H-^{13}C HMBC spectrum of compound *(E)*-**3e** ($CDCl_3$)

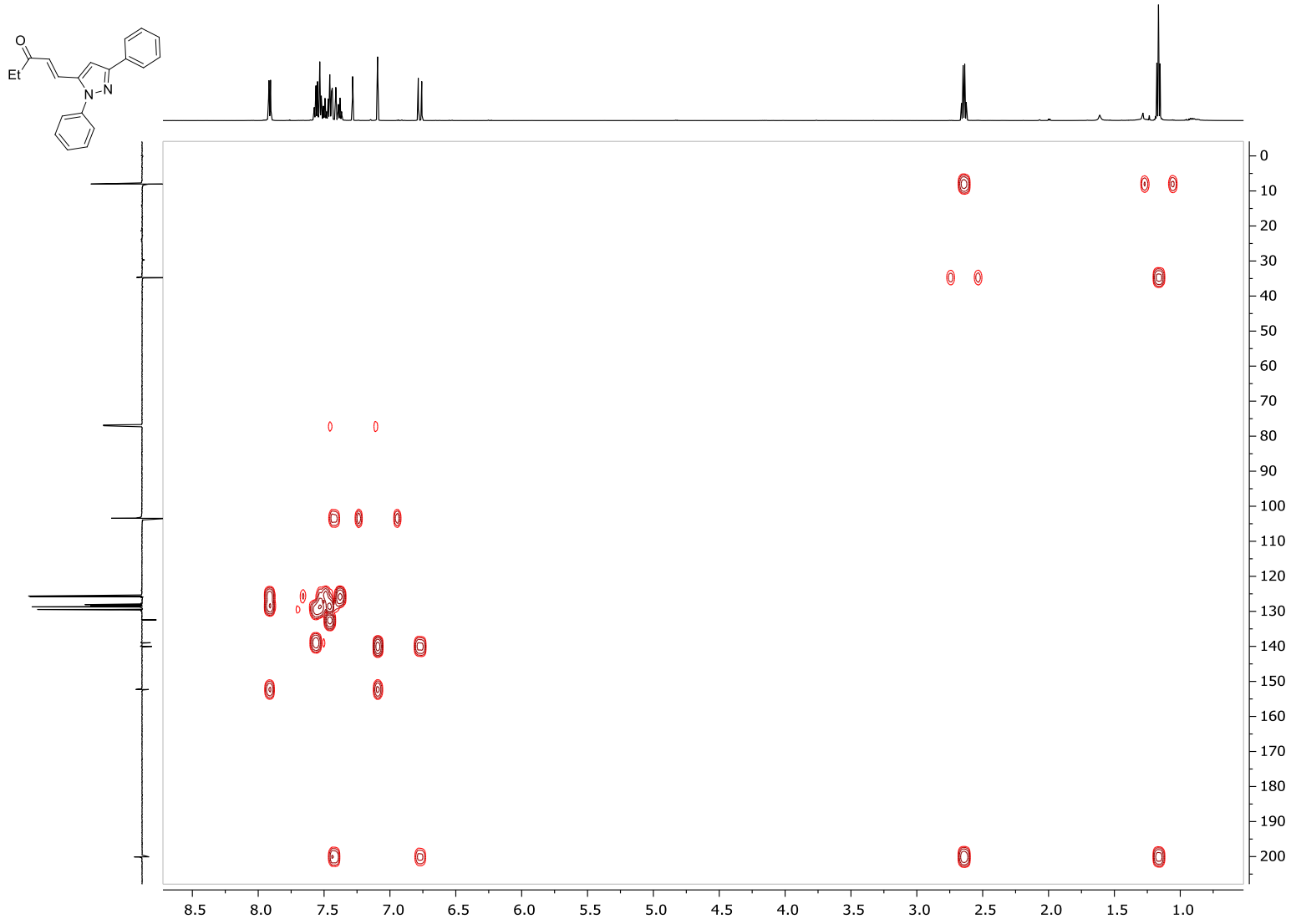


Figure S65: ^{1}H-^{13}C HSQC spectrum of compound *(E)*-**3e** ($CDCl_3$)

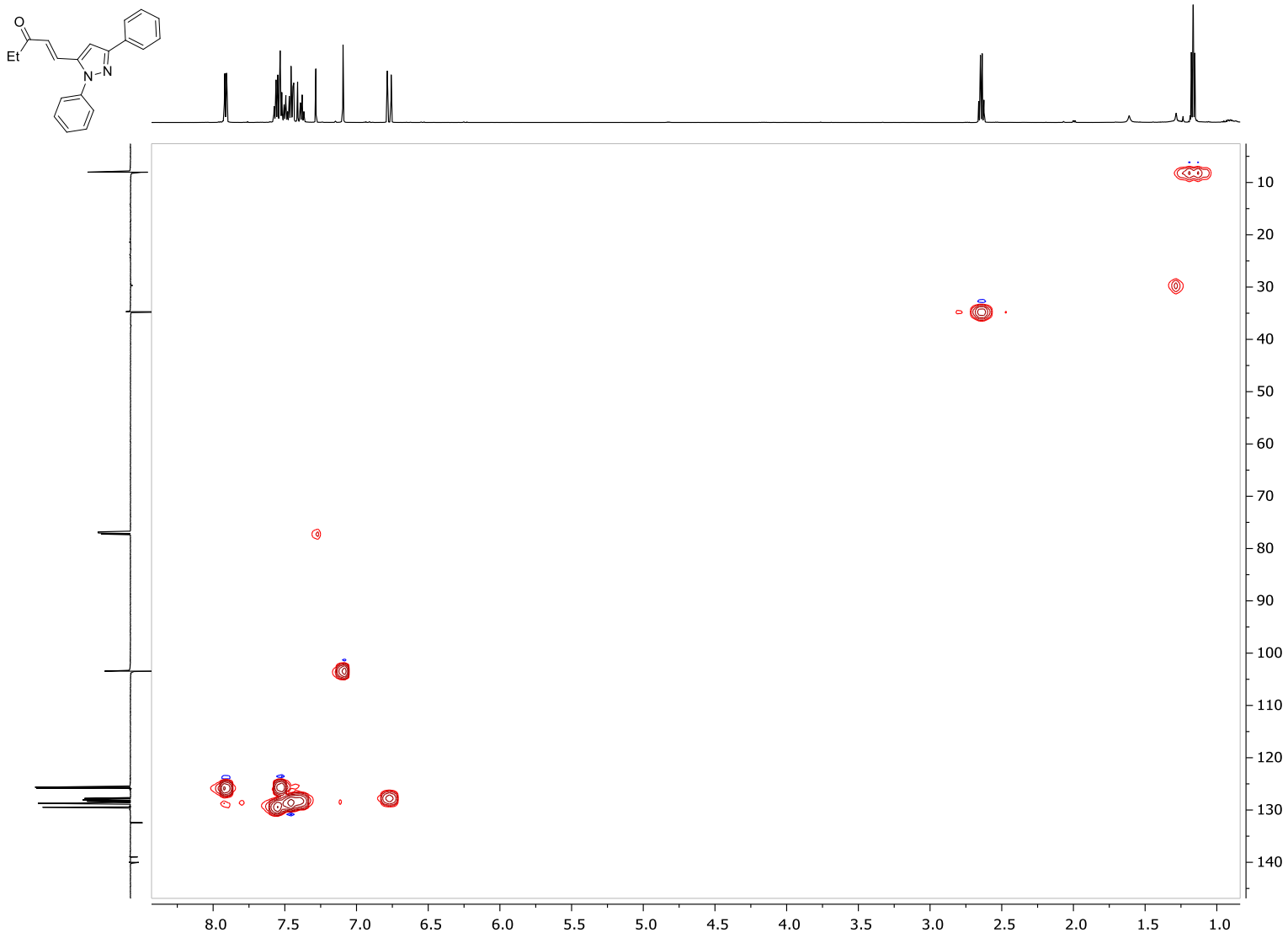


Figure S66: ^{1}H-^{1}H COSY spectrum of compound *(E)*-**3e** ($CDCl_3$)

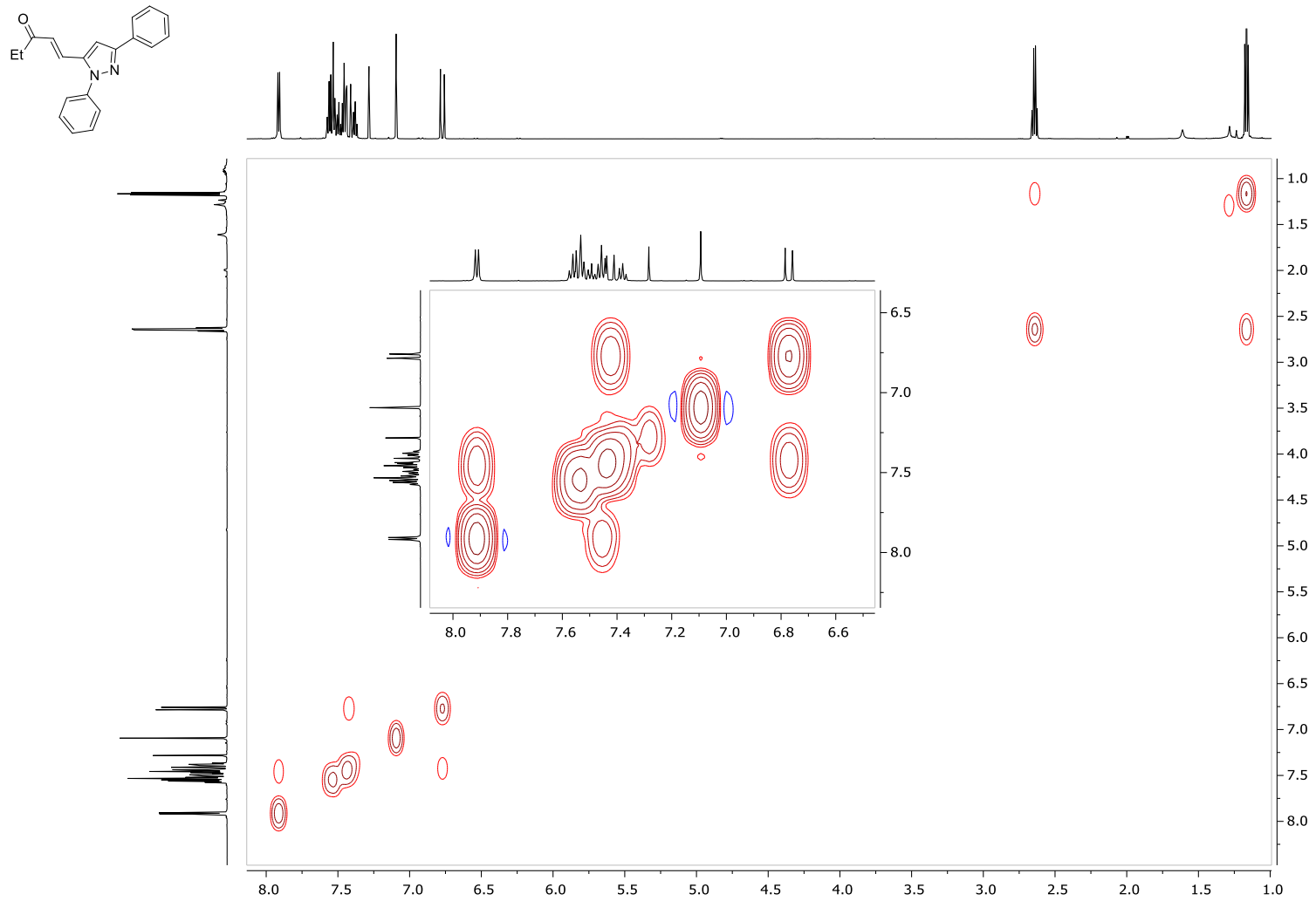
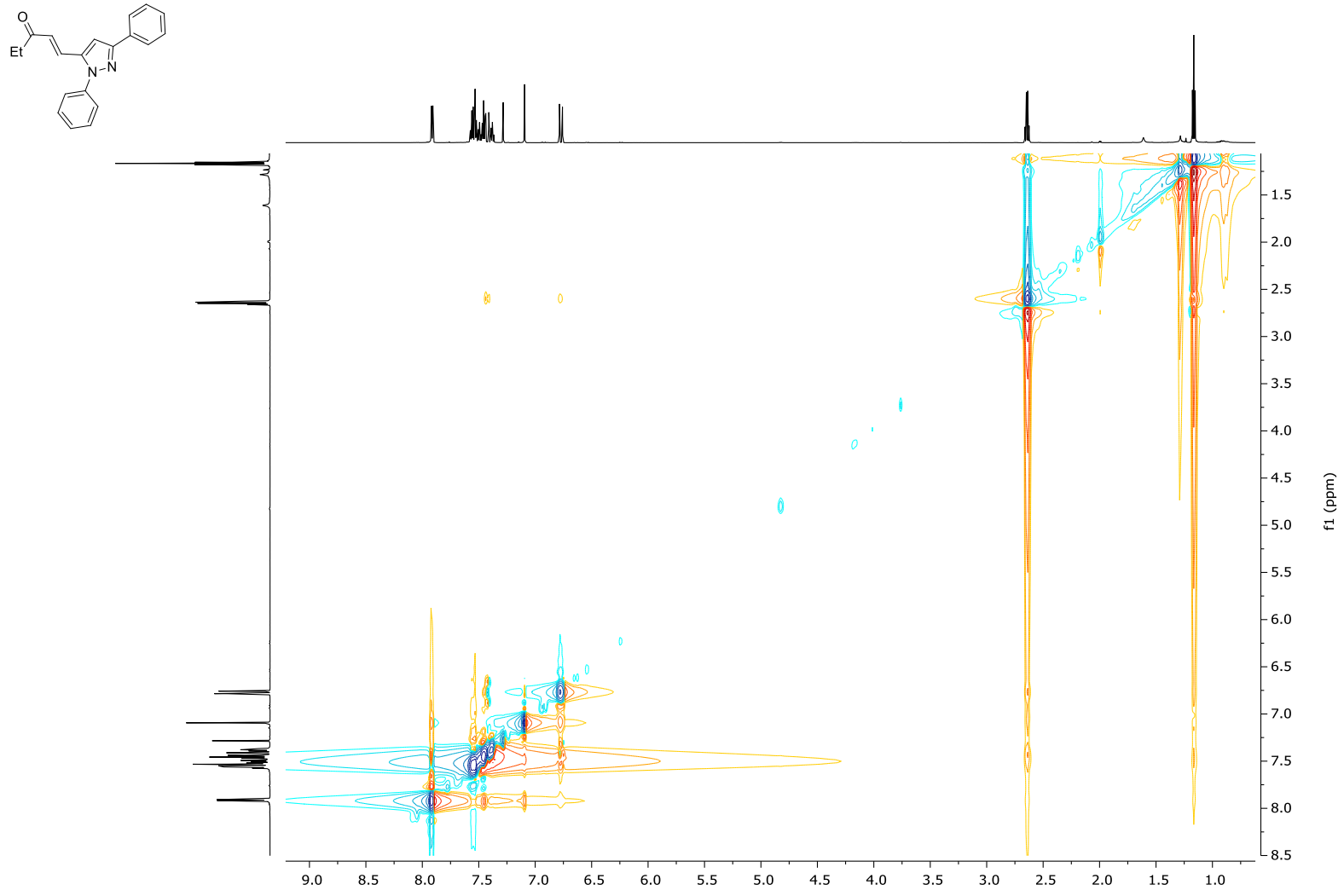


Figure S67: NOESY spectrum of compound *(E)*-**3e** ($CDCl_3$)



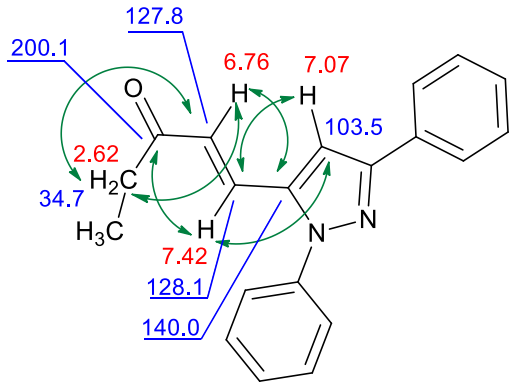


Table S1. Cross peaks in HSQC and HMBC correlation spectra of compound *(E)*-**3e**

^{1}H, δ, ppm	**^{13}C, δ, ppm**	
	HMQC	**HMBC**
7.42 (β-H)	128.1	103.5, 200.1 (C=O)
7.07 (H_{Prz})	103.5	128.1, 140.0
6.76 (α-H)	127.8	34.7, 140.0, 200.1 (C=O)
2.62 (CH_2)	34.7	127.8, 200.1 (C=O)

Figure S68: ^{1}H-^{13}C HMBC spectrum of compound *(E,Z)*-**3e** ($CDCl_3$)

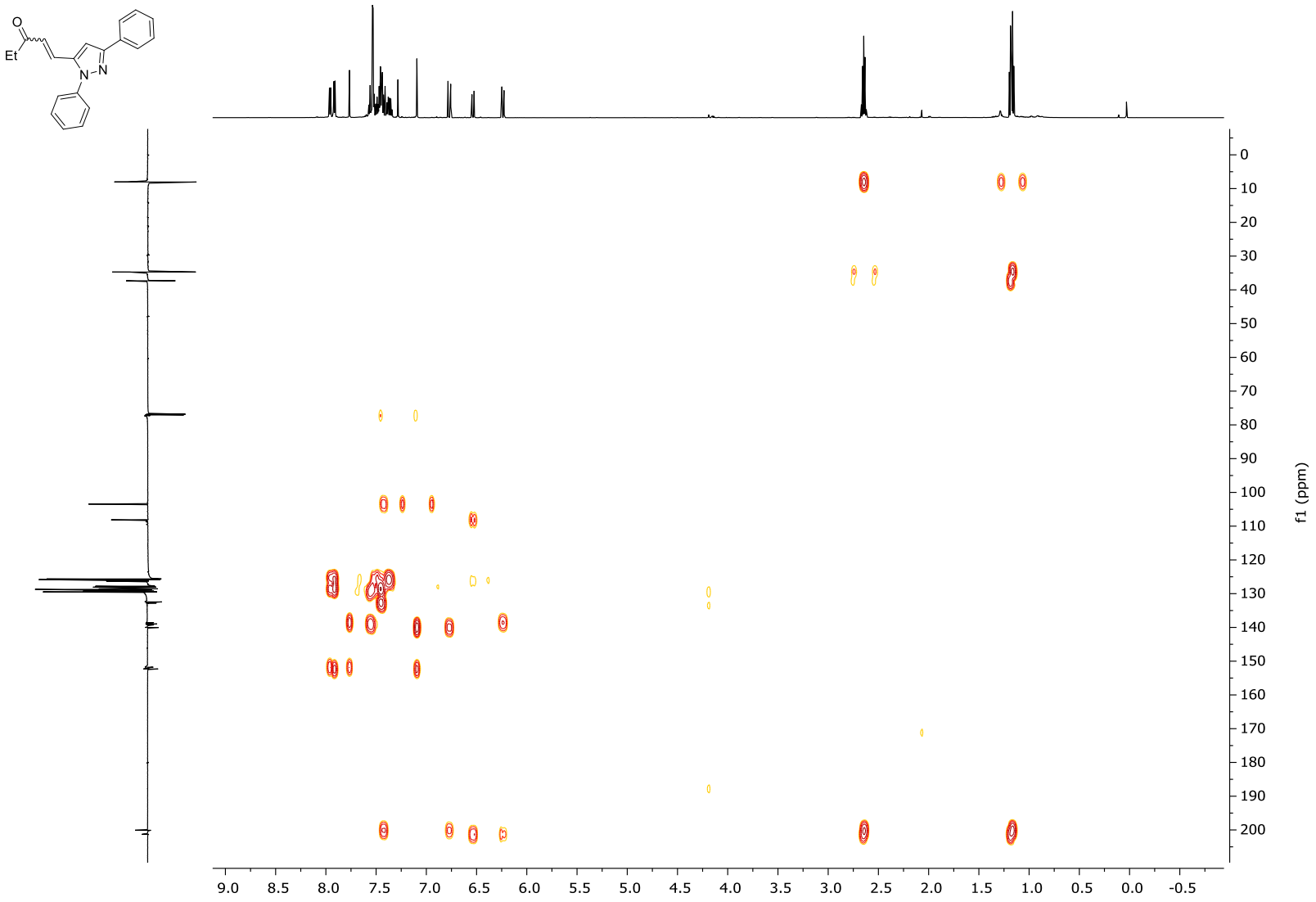


Figure S69: ^{1}H-^{13}C HSQC spectrum of compound *(E,Z)*-**3e** ($CDCl_3$)

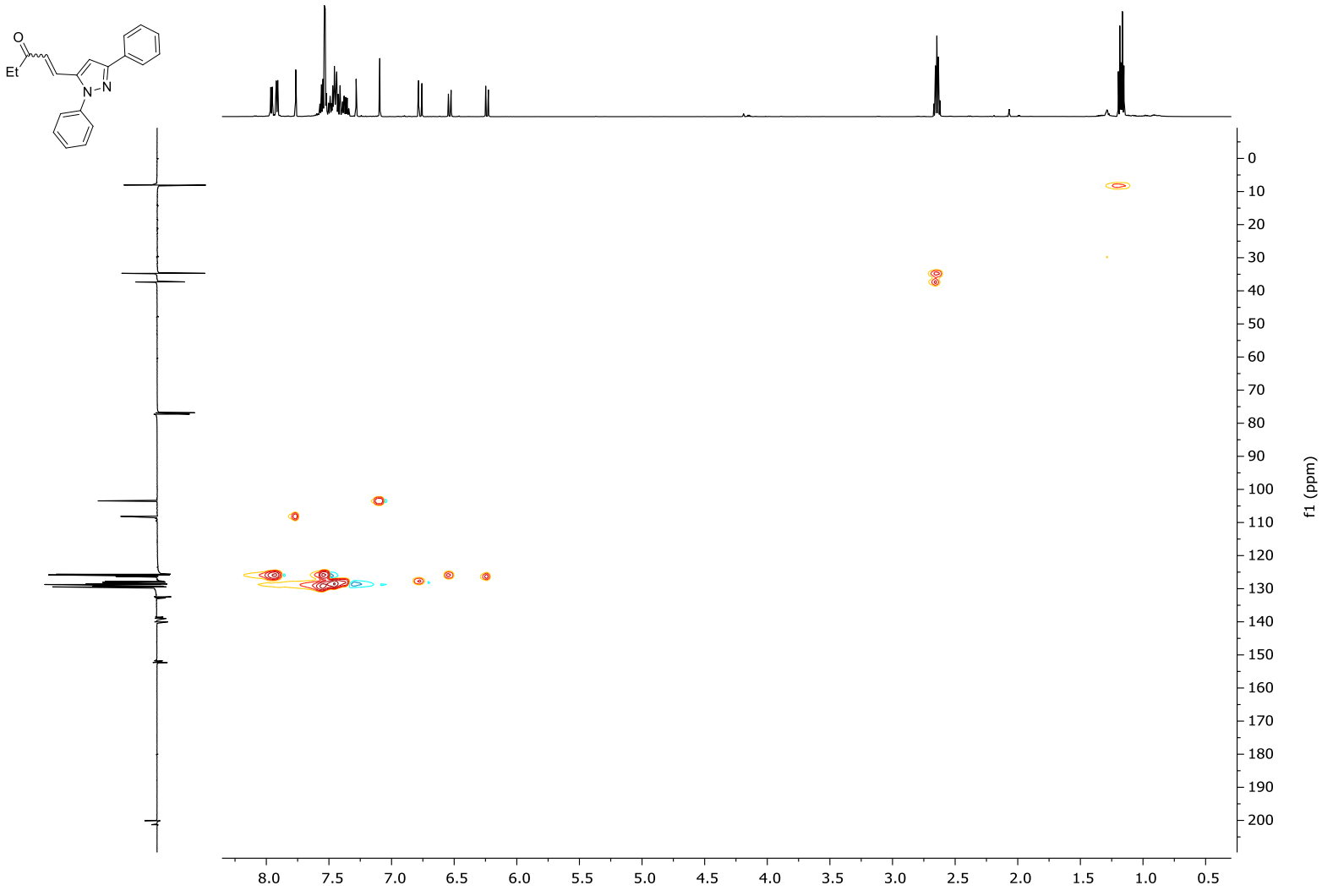
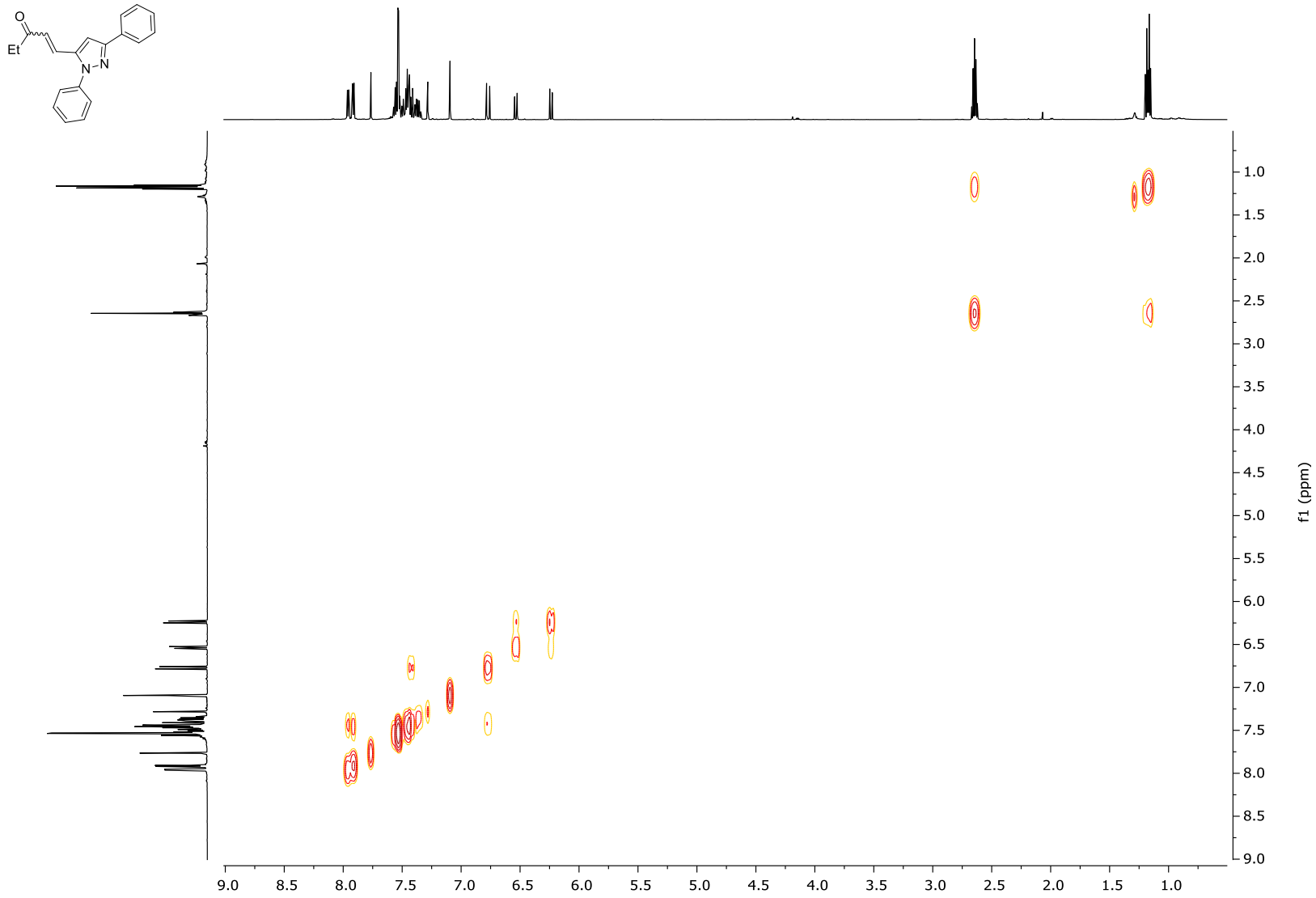


Figure S70: ^{1}H-^{1}H COSY spectrum of compound *(E,Z)*-**3e** ($CDCl_3$)



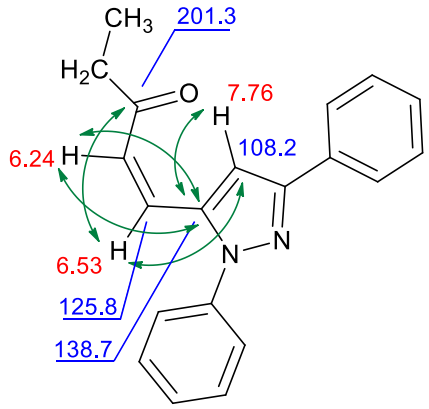


Table S2. Cross peaks in HSQC and HMBC correlation spectra of compound *(Z)*-**3e**

^{1}H, δ, ppm	**^{13}C, δ, ppm**	
	HMQC	**HMBC**
7.76 (H_{Prz})	108.2	138.7, 151.8
6.53 (β-H)	125.8	108.2, 202.3 (C=O)
6.24 (α-H)	126.6	138.7, 202.3 (C=O)

LC-MS data

Figure S71: LC-MS control of reaction **1a→2a→3a** (1h)

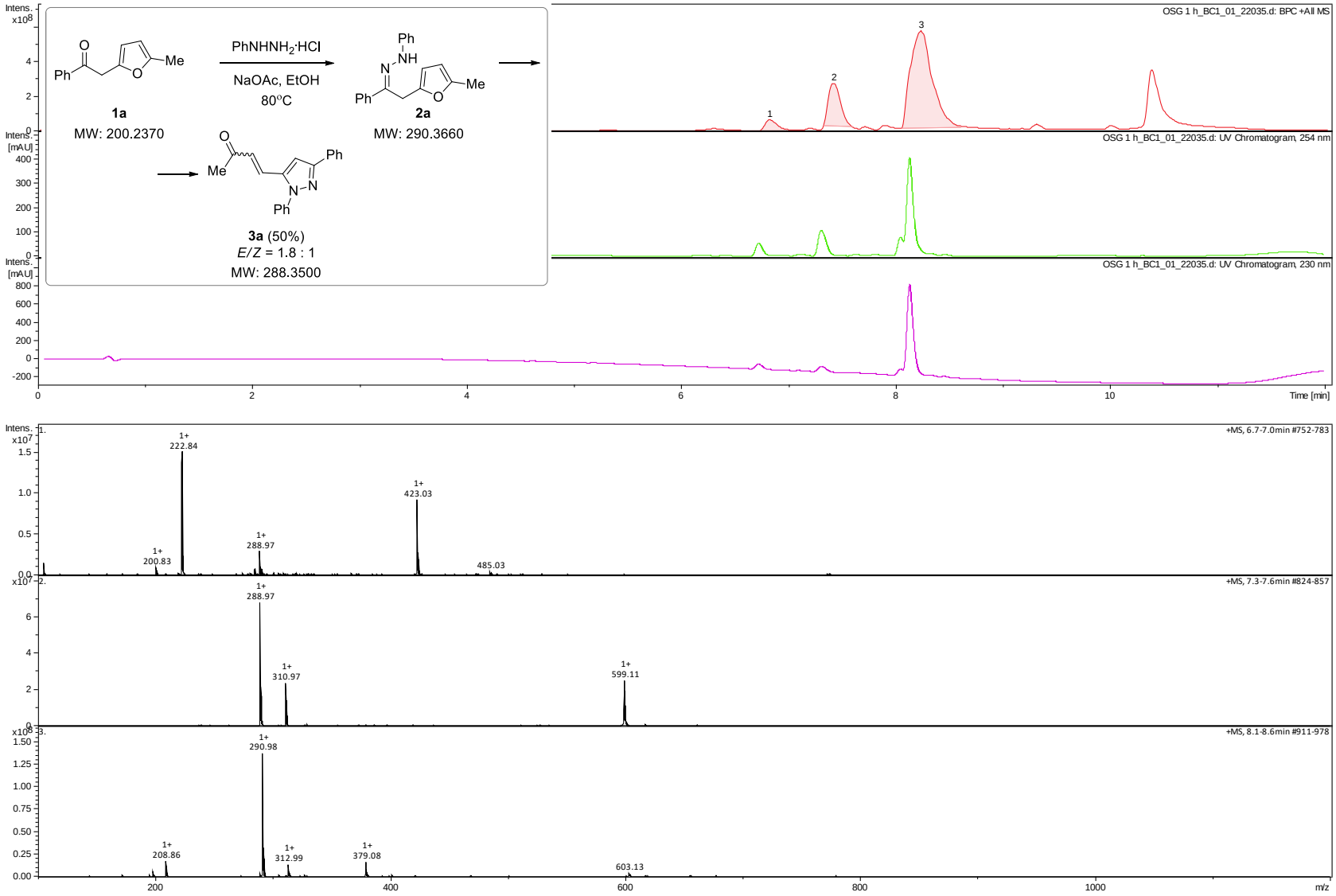


Figure S72: LC-MS control of reaction **1a→2a→3a** (5h)

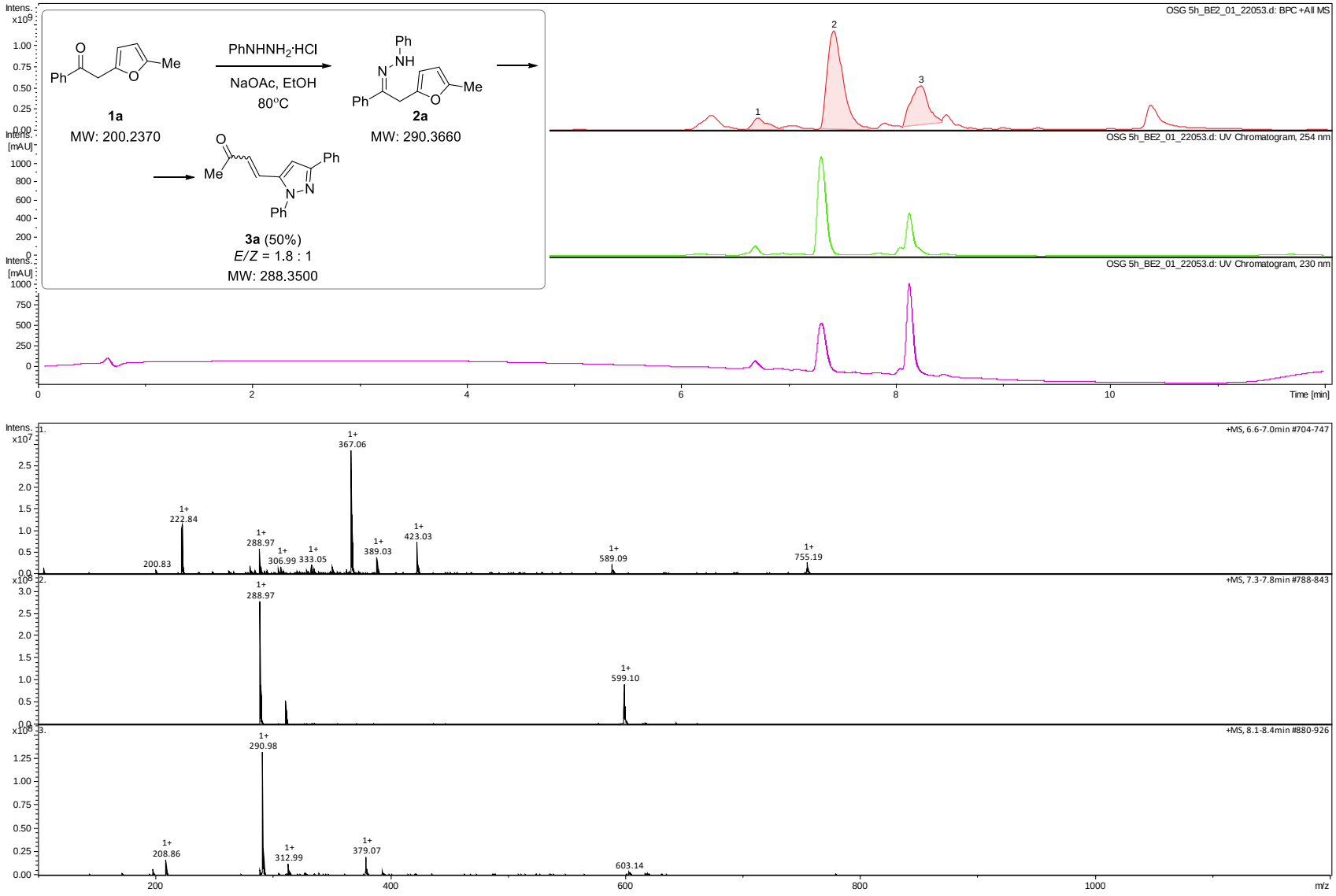
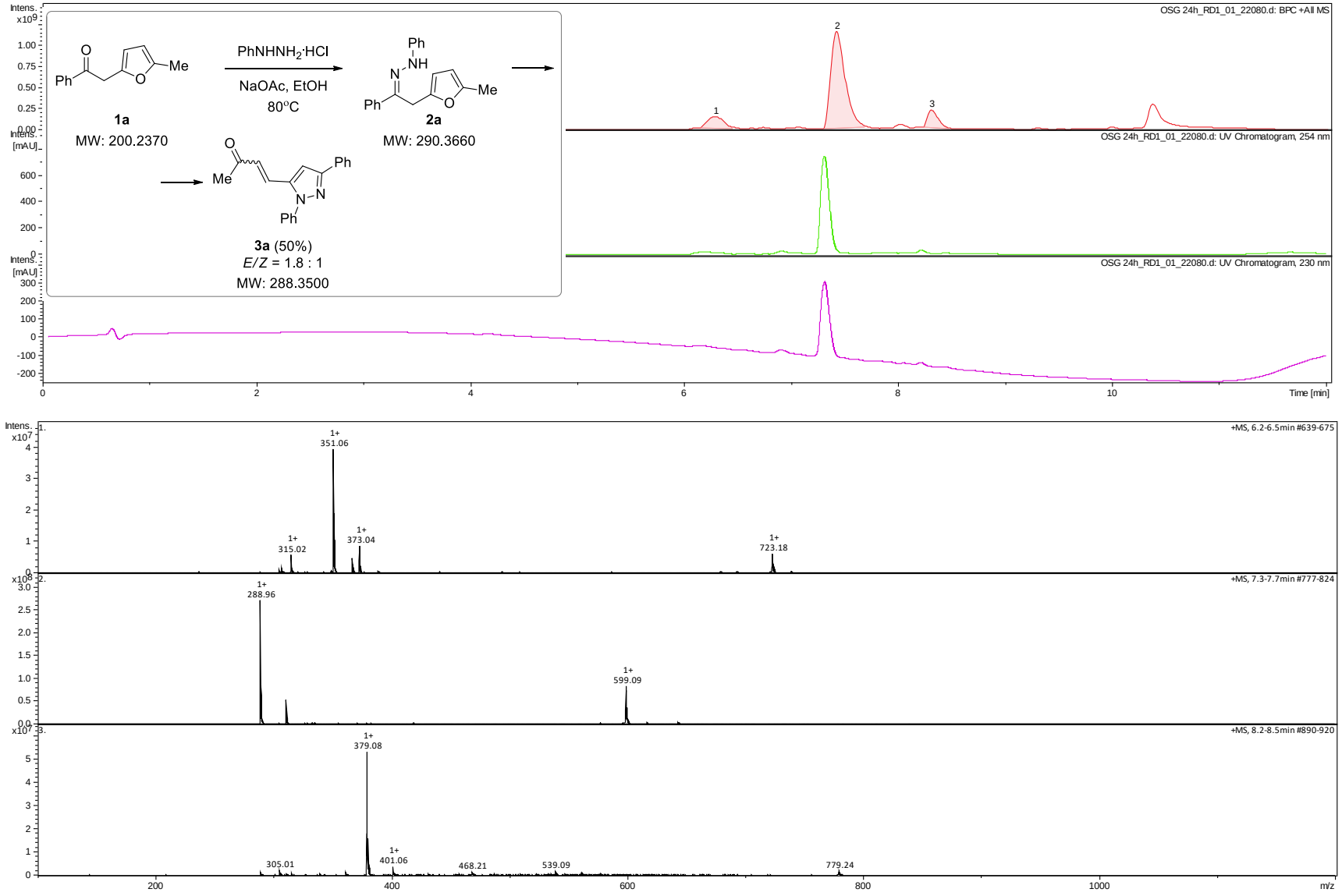


Figure S73: LC-MS control of reaction **1a→2a→3a** (24h)



X-Ray data

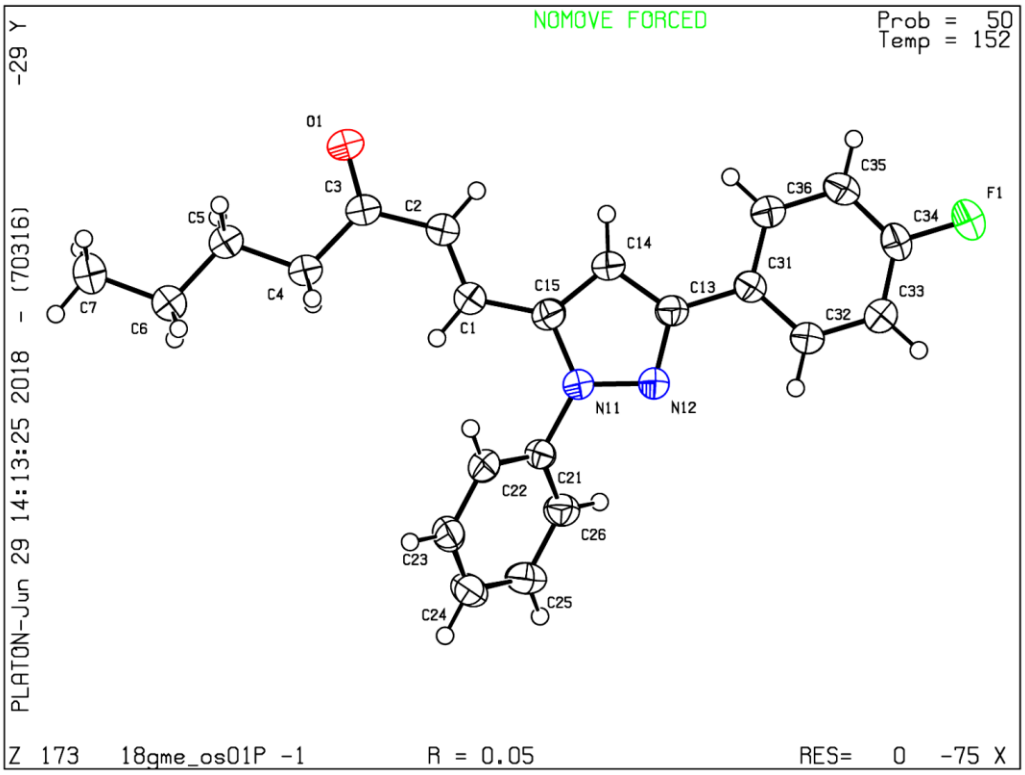


Table S3. Crystal data and structure refinement for **3h**.

Empirical formula	$C_{22}H_{21}FN_2O$
Formula weight	348.41
Temperature/K	152(1)
Crystal system	triclinic
Space group	P-1
a/Å	7.4796(7)
b/Å	8.7825(8)
c/Å	14.3379(14)
α/°	79.991(8)
β/°	78.903(8)
γ/°	89.752(7)
Volume/Å^3	909.76(15)
Z	2
ρ_{calc}g/cm^3	1.272
μ/mm^{-1}	0.690
F(000)	368.0
Crystal size/mm^3	0.312 × 0.259 × 0.226
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	10.232 to 129.636

Index ranges	$-8 \leq h \leq 8, -10 \leq k \leq 9, -13 \leq l \leq 16$
Reflections collected	4868
Independent reflections	2931 [R_{int} = 0.0287, R_{sigma} = 0.0325]
Data/restraints/parameters	2931/0/236
Goodness-of-fit on F^2	1.036
Final R indexes [I>=2σ (I)]	R_1 = 0.0497, wR_2 = 0.1258
Final R indexes [all data]	R_1 = 0.0630, wR_2 = 0.1403
Largest diff. peak/hole / e $Å^{-3}$	0.19/-0.31

Table S4. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **3h**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
C1	6274(3)	6801(2)	7761.9(13)	38.3(5)
F1	-4249.5(17)	2196.8(15)	7221.3(9)	60.8(4)
O1	7751(2)	6179(2)	10010.4(10)	70.2(6)
C2	6325(3)	6355(3)	8691.8(14)	46.7(5)
C3	7798(3)	6745(2)	9167.6(13)	45.4(5)
C4	9316(3)	7863(2)	8616.5(13)	41.2(5)
C5	10712(3)	8179(2)	9204.1(14)	42.8(5)
C6	12134(3)	9405(3)	8657.5(15)	48.7(5)
C7	13495(3)	9752(3)	9266.1(17)	60.5(7)
N11	4670(2)	6852.5(18)	6388.1(10)	36.2(4)
N12	3158(2)	6255.8(18)	6170.5(11)	37.2(4)
C13	2284(2)	5418(2)	7010.3(13)	35.7(4)
C14	3240(3)	5464(2)	7752.7(13)	38.5(5)
C15	4776(3)	6393(2)	7337.0(13)	37.8(4)
C21	5891(2)	7864(2)	5651.6(13)	35.4(4)
C22	6426(3)	9271(2)	5833.7(14)	39.2(5)
C23	7581(3)	10256(2)	5114.5(14)	44.0(5)
C24	8171(3)	9853(2)	4222.4(15)	47.8(5)
C25	7617(3)	8454(2)	4042.8(14)	46.1(5)
C26	6478(3)	7442(2)	4757.7(13)	40.6(5)
C31	526(3)	4611(2)	7074.8(13)	36.5(4)
C32	-386(3)	4838(2)	6299.6(13)	39.4(5)
C33	-1989(3)	4026(2)	6346.3(14)	42.5(5)
C34	-2681(3)	3011(2)	7176.5(15)	45.3(5)
C35	-1858(3)	2788(2)	7967.1(15)	48.2(5)
C36	-242(3)	3594(2)	7911.3(14)	42.6(5)

Table S5. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **3h**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	36.4(10)	42.2(11)	35.3(10)	-3.2(8)	-7.4(8)	-3.5(8)
F1	52.7(8)	67.1(9)	60.0(8)	-3.2(6)	-11.6(6)	-26.0(6)
O1	70.8(11)	97.9(13)	36.5(9)	15.0(8)	-20.3(8)	-35.5(10)
C2	44.2(12)	58.2(13)	35.2(11)	-0.6(9)	-8.3(9)	-12.9(10)
C3	47.5(12)	54.0(13)	32.3(10)	0.3(9)	-9.1(9)	-7.8(10)
C4	42.1(11)	47.2(12)	32.5(10)	-0.5(8)	-8.9(8)	-4.7(9)
C5	42.5(11)	49.3(12)	36.3(10)	-3.6(9)	-10.0(8)	-3.1(9)
C6	46.4(12)	54.5(13)	43.5(11)	-1.8(10)	-10.4(9)	-10.0(10)
C7	49.4(13)	74.3(17)	57.1(14)	-5.8(12)	-13.8(11)	-19.5(12)
N11	36.8(9)	39.7(9)	31.2(8)	-2.0(6)	-8.3(6)	-5.4(7)
N12	37.8(9)	39.2(9)	34.2(8)	-2.6(7)	-9.7(7)	-5.7(7)
C13	38.8(10)	35.2(10)	32.1(9)	-3.2(8)	-6.7(8)	-0.8(8)
C14	39.1(10)	46.0(11)	28.2(9)	-1.1(8)	-6.0(8)	-4.5(8)
C15	38.8(10)	43.0(11)	31.5(10)	-5.5(8)	-7.6(8)	0.6(8)
C21	30.4(9)	40.3(11)	32.8(9)	2.2(8)	-7.3(7)	-2.9(8)
C22	38.6(11)	42.8(11)	37.0(10)	-2.3(8)	-14.0(8)	-0.9(8)
C23	40.1(11)	41.1(11)	49.5(12)	3.8(9)	-15.5(9)	-6.7(9)
C24	36.9(11)	50.4(13)	48.4(12)	9.2(10)	-5.1(9)	-5.4(9)
C25	46.0(12)	49.3(12)	36.9(11)	1.6(9)	-1.1(9)	4.3(9)
C26	44.4(11)	38.7(11)	36.9(10)	-2.1(8)	-7.5(8)	-0.3(8)
C31	37.4(10)	36.9(10)	34.0(10)	-4.3(8)	-5.6(8)	-3.7(8)
C32	40.8(11)	40.5(11)	35.0(10)	-1.5(8)	-7.6(8)	-3.6(8)
C33	43.0(11)	47.4(12)	38.1(10)	-4.9(9)	-12.2(8)	-3.0(9)
C34	40.5(11)	45.9(12)	49.1(12)	-7.2(9)	-8.5(9)	-12.5(9)
C35	52.3(13)	47.5(12)	39.9(11)	2.3(9)	-5.4(9)	-14.0(10)
C36	46.4(11)	44.8(11)	35.5(10)	-0.7(8)	-10.7(8)	-4.8(9)

Table S6. Bond Lengths for **3h**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C2	1.331(3)	C13	C31	1.476(3)
C1	C15	1.448(3)	C14	C15	1.384(3)
F1	C34	1.362(2)	C21	C22	1.383(3)
O1	C3	1.218(2)	C21	C26	1.386(3)
C2	C3	1.473(3)	C22	C23	1.382(3)
C3	C4	1.508(3)	C23	C24	1.376(3)
C4	C5	1.516(3)	C24	C25	1.380(3)

C5	C6	1.517(3)	C25	C26	1.386(3)
C6	C7	1.526(3)	C31	C32	1.398(3)
N11	N12	1.360(2)	C31	C36	1.390(3)
N11	C15	1.368(2)	C32	C33	1.382(3)
N11	C21	1.431(2)	C33	C34	1.370(3)
N12	C13	1.346(2)	C34	C35	1.376(3)
C13	C14	1.398(2)	C35	C36	1.385(3)

Table S7. Bond Angles for **3h**.

Atom	**Atom**	**Atom**	**Angle/°**	**Atom**	**Atom**	**Atom**	**Angle/°**
C2	C1	C15	122.91(18)	C22	C21	N11	119.42(17)
C1	C2	C3	125.45(18)	C22	C21	C26	120.90(17)
O1	C3	C2	119.29(18)	C26	C21	N11	119.64(17)
O1	C3	C4	120.85(17)	C23	C22	C21	119.22(18)
C2	C3	C4	119.84(16)	C24	C23	C22	120.49(19)
C3	C4	C5	113.97(15)	C23	C24	C25	119.97(18)
C4	C5	C6	112.75(16)	C24	C25	C26	120.45(19)
C5	C6	C7	112.36(17)	C21	C26	C25	118.96(19)
N12	N11	C15	112.24(15)	C32	C31	C13	121.01(17)
N12	N11	C21	119.30(14)	C36	C31	C13	120.13(17)
C15	N11	C21	128.45(15)	C36	C31	C32	118.85(18)
C13	N12	N11	104.62(14)	C33	C32	C31	120.81(18)
N12	C13	C14	111.36(16)	C34	C33	C32	118.50(18)
N12	C13	C31	120.97(16)	F1	C34	C33	118.66(18)
C14	C13	C31	127.66(17)	F1	C34	C35	118.77(18)
C15	C14	C13	105.69(16)	C33	C34	C35	122.57(18)
N11	C15	C1	124.30(17)	C34	C35	C36	118.59(18)
N11	C15	C14	106.08(16)	C35	C36	C31	120.63(18)
C14	C15	C1	129.59(17)				

Table S8. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for **3h**.

Atom	***x***	***y***	***z***	**U(eq)**
H1	7242	7402	7368	46
H2	5350	5747	9073	56
H4A	8791	8834	8384	49
H4B	9932	7453	8057	49
H5A	11317	7226	9390	51

H5B	10089	8511	9790	51
H6A	11528	10348	8453	58
H6B	12786	9057	8083	58
H7A	14368	10529	8892	91
H7B	14113	8826	9461	91
H7C	12859	10120	9828	91
H14	2913	4974	8393	46
H22	6014	9551	6433	47
H23	7962	11198	5234	53
H24	8943	10524	3741	57
H25	8010	8188	3438	55
H26	6113	6494	4639	49
H32	92	5545	5746	47
H33	-2583	4164	5826	51
H35	-2375	2110	8527	58
H36	334	3454	8438	51

Crystal structure determination of **3h**

Crystal Data for $C_{22}H_{21}FN_2O$ (*M* =348.41 g/mol): triclinic, space group P-1 (no. 2), *a* = 7.4796(7) Å, *b* = 8.7825(8) Å, *c* = 14.3379(14) Å, α = 79.991(8)°, β = 78.903(8)°, γ = 89.752(7)°, *V* = 909.76(15) Å^3, *Z* = 2, *T* = 152(1) K, μ(CuKα) = 0.690 mm^{-1}, *Dcalc* = 1.272 g/cm^3, 4868 reflections measured (10.232° ≤ 2Θ ≤ 129.636°), 2931 unique (R_{int} = 0.0287, R_{sigma} = 0.0325) which were used in all calculations. The final R_1 was 0.0497 (I > 2σ(I)) and wR_2 was 0.1403 (all data).

Refinement model description
Number of restraints - 0, number of constraints - unknown.
Details:

1. Fixed Uiso
   At 1.2 times of:
   All C(H) groups, All C(H,H) groups
   At 1.5 times of:
   All C(H,H,H) groups
   2.a Secondary CH2 refined with riding coordinates:
   C4(H4A,H4B), C5(H5A,H5B), C6(H6A,H6B)
   2.b Aromatic/amide H refined with riding coordinates:
   C1(H1), C2(H2), C14(H14), C22(H22), C23(H23), C24(H24), C25(H25), C26(H26), C32(H32), C33(H33), C35(H35), C36(H36)
   2.c Idealised Me refined as rotating group:
   C7(H7A,H7B,H7

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