Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

A palladium-catalyzed intramolecular carbonylative annulation reaction to 4,5-fused tricyclic 2-quinolones

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Table of Contexts

General information

All reagents were obtained from commercial suppliers unless otherwise stated. Tetrahydrofuran (THF) was distilled from potassium sodium alloys; Dichloromethane was distilled from calcium hydride. Flasks were flame-dried under vacuum and cooled under a stream of nitrogen or argon.

Visualization was achieved under a UV lamp (254 nm and 365 nm), and by developing the plates with phosphomolybdic acid or *p*-methoxybezaldehyde in ethanol. Flash column chromatography was performed using silica gel (200-300 mesh) with solvents distilled prior to use.

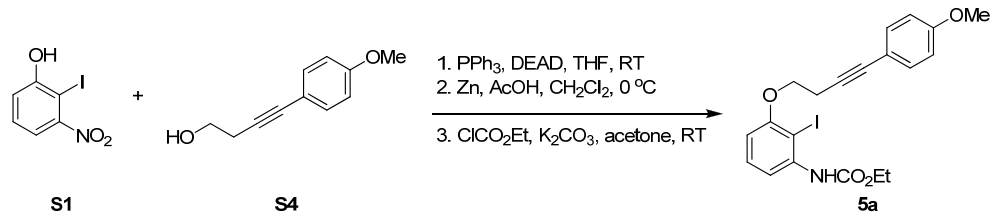
^{1}H NMR were recorded 400 MHz NMR spectrometer, ^{13}C NMR at 100 MHz NMR spectrometer unless otherwise stated. The following abbreviations are used for the multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, quint: quintet, m: multiplet, br s: broad singlet for proton spectra and carbon spectra. Coupling constants (*J*) are reported in Hertz (Hz). Infrared spectra were recorded with a thin layer of the product on a KBr disk.

High resolution mass spectral (HRMS) data were obtained with an ionization mode of ESI.

The following abbreviations are used: **EtOAc**; ethyl acetate; **THF**: tetrahydrofuran; **PE**: petroleum ether; **DCM**: dichloromethane; **PPh_3**: triphenylphosphine; **Et_3N**: triethylamine. **DEAD**: diethyl azodicarboxylate; **DMF**: *N*,*N*-dimethylformamide;

Preparation of starting materials.

Compound 5a



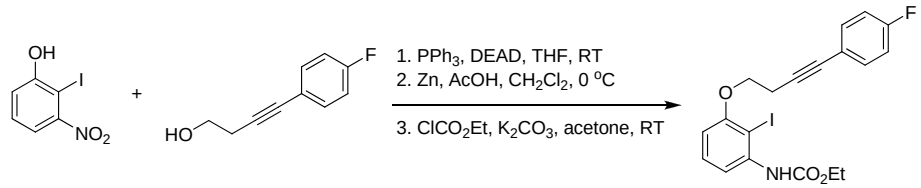
S1 **S4** **5a**

To a stirred solution of **S1** (795 mg, 3.0 mmol) and alcohol **S4** (633 mg, 3.6 mmol) in THF (30 mL) was added PPh_3 (1.18 g, 4.5 mmol). The mixture was cooled down to 0 °C and DEAD (1.14 mL, 2.2 M in THF, 4.5 mmol) was added dropwisely. The solution was warmed to room temperature and kept stirring until completion of the reaction. Then water was added and the mixture was extracted with EtOAc, dried over Na_2SO_4 and filtered. The filtrate was evaporated under reduced pressure and the resulting residue was used in the next step without purification.

To a stirred solution of the crude product in DCM (38 mL) was added activated zinc dust (11.7 g, 180 mmol). The solution was cooled down to 0 °C and HOAc (1.4 mL, 25 mmol) was added dropwisely. After stirred for 10 min at 0 °C, the mixture was filtered through a pad of celite and the celite was washed with EtOAc. The filtrate was neutralized with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4 and filtered. The filtrate was evaporated under reduced pressure and the resulting residue was used in the next step without purification.

To a stirred solution of the crude product and K_2CO_3 (2.07 g, 15 mmol) in acetone (30 mL) was added $ClCO_2Et$ (1.4 equiv). The mixture was stirred at room temperature until completion of the reaction. The mixture was washed with water and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and filtered. The filtrate was evaporated under reduced pressure and the resulting residue was purified by flash column chromatography (PE/EtOAc, 20 : 1) to afford compound **5a** as a yellowish solid in 46% overall yield. M.P. 97-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 8.4 Hz, 2H), 7.26-7.29 (m, 1H), 7.18 (br s, 1H), 6.82 (d, J = 8.4 Hz, 2H), 6.58 (d, J = 8.0, 1H), 4.20-4.27 (m, 4H), 3.80 (s, 3H), 2.95 (t, J = 7.2 Hz, 2H), 1.34 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, $CDCl_3$) δ 159.2, 157.3, 153.4, 139.9, 132.9, 129.6, 115.4, 113.8, 112.7, 107.0, 83.9, 81.9, 67.7, 61.4, 55.1, 20.4, 14.4; IR(KBr): 3384, 2941, 1750, 1596, 1459, 1205, 1044, 766, 536 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{21}INO_4$ $(M + H)^+$ 466.0510, found 466.0511.

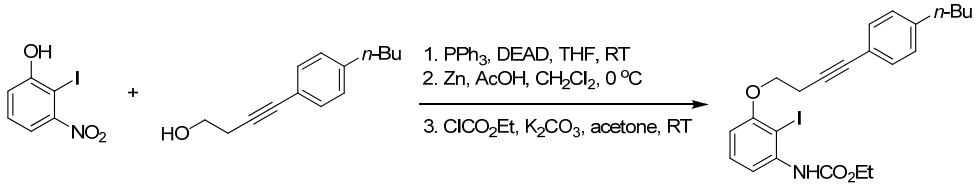
Compound 5b



S1 **S5** **5b**

Compound **5b** was prepared in 46% overall yield following the same procedure as described for the synthesis of **5a**. Purification by FCC (PE/EtOAc, 30 : 1), white solid. M.P. 135-136 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.0 Hz, 1H), 7.38-7.41 (m, 2H), 7.27 (t, J = 8.0 Hz, 1H), 7.18 (s, 1H), 6.98 (t, J = 8.8 Hz, 2H), 6.58 (d, J = 8.0, 1H), 4.21-4.28 (m, 4H), 2.95 (t, J = 7.2 Hz, 2H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 161.1, 157.4, 153.5, 140.1, 133.54, 133.46, 129.8, 119.52, 119.49, 115.6, 115.4, 113.0, 107.2, 85.3, 82.0, 81.2, 67.7, 61.5, 20.5, 14.5; IR(KBr): 3376, 2925, 1738, 1508, 1455, 1210, 1051, 771, 535 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{18}FINO_3$ $(M + H)^+$ 454.0310, found 454.0310.

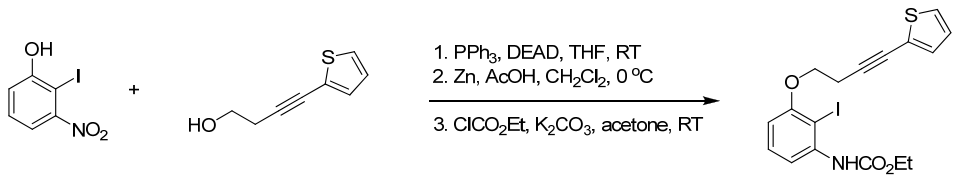
Compound 5c



S1 **S6** **5c**

Compound **5c** was prepared in 29% overall yield following the same procedure as described for the synthesis of **5a**. Purification by FCC (PE/EtOAc, 30 : 1), white solid. M.P. 100-101 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.27 (t, J = 8.0 Hz, 1H), 7.20 (s, 1H), 7.11 (d, J = 8.0 Hz, 2H), 6.57 (d, J = 8.0 Hz, 1H), 4.20-4.28 (m, 4H), 2.96 (t, J = 7.2 Hz, 2H), 2.59 (t, J = 7.6 Hz, 2H), 1.54-1.62 (m, 2H), 1.32-1.36 (m, 5H), 0.93 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 153.3, 142.8, 139.9, 131.4, 129.6, 128.2, 120.4, 112.7, 107.0, 84.7, 82.2, 81.8, 67.6, 61.4, 35.4, 33.3, 22.2, 20.4, 14.4, 13.9; IR(KBr): 3383, 2953, 1750, 1520, 1207, 1045, 765, 540 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{27}INO_3$ $(M + H)^+$ 492.1030, found 492.1032.

Compound 5d

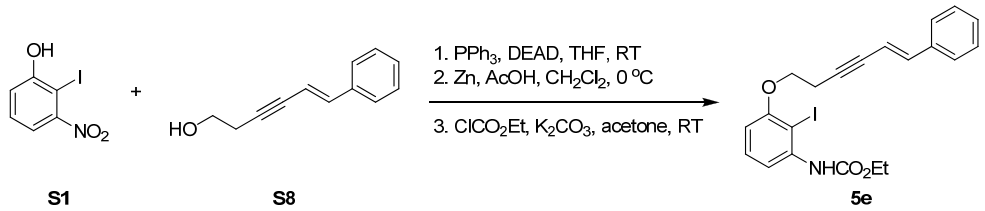


S1 **S7** **5d**

Compound **5d** was prepared in 40% overall yield following the same procedure as described for the synthesis of **5a**. Purification by FCC (PE/EtOAc, 20 : 1), white solid. M.P. 89-90 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.4 Hz, 1H), 7.27 (t, J = 8.4 Hz, 1H), 7.16-7.21 (m, 3H), 6.95 (m,1H), 6.57(d, J = 8.4 Hz, 1H), 4.21-4.27 (m, 4H), 2.99 (t, J = 7.2 Hz, 2H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 157.3, 153.5, 140.1, 131.6, 129.7, 126.8, 126.4, 123.5, 112.9, 107.2, 89.7, 82.0, 75.5, 67.5, 61.5, 20.7, 14.5; IR(KBr): 3383, 2946, 1738, 1521, 1456, 1208, 1049, 770, 544 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{17}INO_3S$ $(M + H)^+$ 441.9968, found 441.9963.

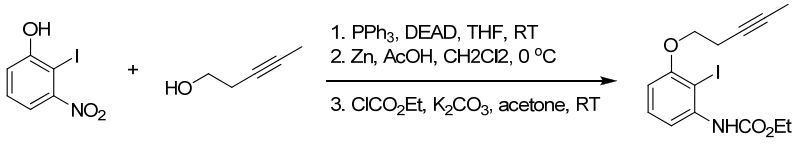
Compound 5e



S1 **S8** **5e**

Compound **5e** was prepared in 26% overall yield following the same procedure as described for the synthesis of **5a**. Purification by FCC (PE/EtOAc, 30 : 1), white solid. M.P. 104-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.26-7.38 (m, 6H), 7.18(s, 1H), 6.92 (d, *J* = 16.4 Hz, 1H), 6.57 (dd, *J* = 8.0, 0.8 Hz, 1H), 6.15 (dt, *J* = 8.4, 2.0 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 4.19 (t, *J* = 7.2 Hz, 2H), 2.93 (dt, *J* = 7.2, 2.0 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 153.5, 141.0, 140.0, 136.3, 129.7, 128.7, 128.5, 126.1, 112.8, 108.2, 107.1, 87.9, 81.4, 67.7, 61.5, 20.7, 14.5; IR(KBr): 3386, 2942, 1742, 1593, 1460, 1210, 1052, 766, 537 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}INO_3Na$ $(M + Na)^+$ 484.0380, found 484.0392.

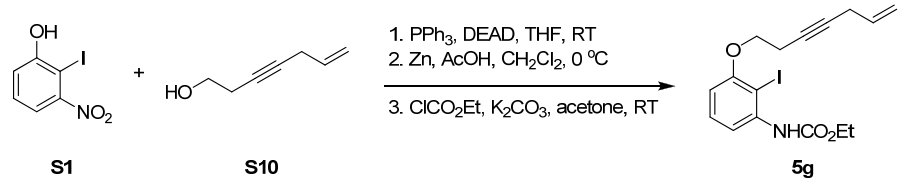
Compound 5f



S1 **S9** **5f**

Compound **5f** was prepared in 35% overall yield following the same procedure as described for the synthesis of **5a**. Purification by FCC (PE/EtOAc, 20 : 1), white solid. M.P. 113-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 1H), 7.26 (t, *J* = 8.4 Hz, 1H), 7.17 (s, 1H), 6.54 (dd, *J* = 8.4, 0.8 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.10 (t, *J* = 7.2 Hz, 2H), 2.68 (m, 2H), 1.80 (t, *J* = 2.4 Hz, 3H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 153.5, 140.0, 129.7, 112.7, 107.1, 81.9, 77.6, 74.7, 68.1, 61.5, 19.7, 14.5, 3.51; IR(KBr): 3388, 2954, 1744, 1520, 1458, 1206, 1051, 767, 513 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}INO_3SiNa$ $(M + Na)^+$ 396.0067, found 396.0069.

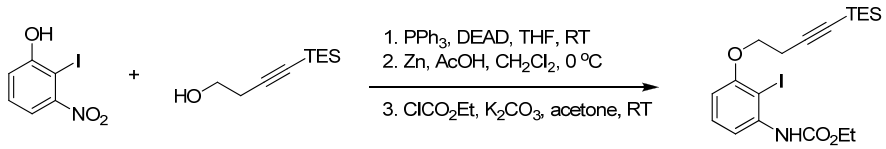
Compound 5g



S1 **S10** **5g**

Compound **5g** was prepared in 26% overall yield following the same procedure as described for the synthesis of **5a**. Purification by FCC (PE/EtOAc, 20 : 1), yellow solid. M.P. 75-76 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 1H), 7.26 (t, J = 8.4 Hz, 1H), 7.17 (s, 1H), 6.54 (d, J = 8.4 Hz, 1H), 5.82 (m, 1H), 5.33 (ddd, J = 16.8, 3.2, 1.6 Hz, 1H), 5.10 (dd, J = 10.0, 1.6 Hz, 1H), 4.24 (q, J = 7.2 Hz, 2H), 4.13 (t, J = 7.2 Hz, 2H), 2.95-2.97 (m, 2H), 2.73-2.78 (m, 2H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 153.3, 139.9, 132.8, 129.6, 115.9, 112.7, 107.0, 81.9, 78.6, 78.1, 68.0, 61.4, 23.0, 19.8, 14.4; IR(KBr): 3372, 2950, 1733, 1527, 1457, 1215, 1052, 767, 560 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{19}INO_3$ $(M + H)^+$ 400.0404, found 400.0409.

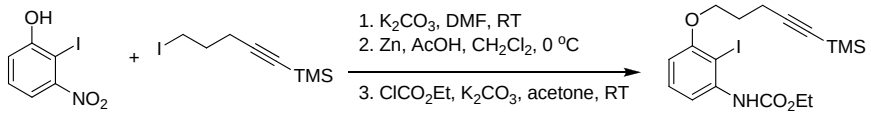
Compound 5h



S1 **S11** **5h**

Compound **5h** was prepared in 61% overall yield following the same procedure as described for the synthesis of **5a**. Purification by FCC (PE/EtOAc, 15 : 1), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 8.0 Hz, 1H), 7.17 (s, 1H), 6.53 (d, J = 8.0 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 4.13 (t, J = 7.2 Hz, 2H), 2.79 (t, J = 7.2 Hz, 2H), 1.32 (t, J = 7.2 Hz, 3H), 0.98 (t, J = 8.0 Hz, 9H), 0.58 (q, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 153.3, 139.9, 129.6, 112.7, 106.9, 103.3, 83.7, 81.8, 67.7, 61.4, 20.8, 14.4, 7.4, 4.3; IR(KBr): 3384, 2954, 2177, 1743, 1593, 1461, 1210, 1049 727, 558 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{29}INO_3Si$ $(M + H)^+$ 474.0956, found 474.0956.

Compound 5i



S1 **S12** **5i**

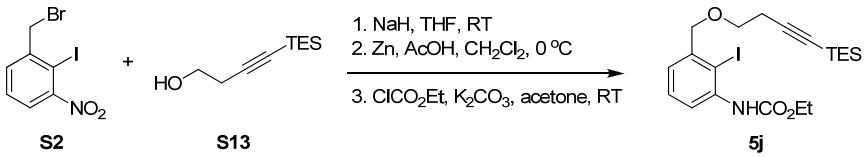
To a stirred solution of **S1** (265 mg, 1 mmol) and K_2CO_3 (414 mg, 3 mmol) in DMF (5 mL) was added the iodide **S12** (532 mg, 2 mmol). The mixture was stirred at room temperature until completion of the reaction. The mixture was washed with water and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and filtered. The filtrate was evaporated under reduced pressure and the resulting residue was used in the next step without purification.

To a stirred solution of the crude product in DCM (12 mL) was added activated zinc dust (3.9 g, 60 mmol). The solution was cooled down to 0 ºC and HOAc (0.46 mL, 8.0 mmol) was added dropwisely. After stirred for 10 min at 0 ºC, the mixture was filtered through a pad of celite and the celite was washed with EtOAc. The filtrate was neutralized with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4 and filtered. The filtrate was evaporated under reduced pressure and the resulting residue was used in the next

step without purification.

To a stirred solution of the crude product and K_2CO_3 (690 mg, 5 mmol) in acetone (10 mL) was added $ClCO_2Et$ (1.4 equiv). The mixture was stirred at room temperature until completion of the reaction. The mixture was washed with water and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and filtered. The filtrate was evaporated under reduced pressure and the resulting residue was purified by flash column chromatography (PE/EtOAc, 60 : 1) to afford compound **5i** as a yellow oil in 85% overall yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.4 Hz, 1H), 7.25 (t, J = 8.4 Hz, 1H), 7.16 (s, 1H), 6.53 (dd, J = 8.4, 0.8 Hz, 1H), 4.24 (q, J = 7.2 Hz, 2H), 4.10 (t, J = 6.0 Hz, 2H), 2.52 (t, J = 7.2 Hz, 2H), 2.00-2.07 (m, 2H), 1.33 (t, J = 7.2 Hz, 3H), 0.14 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 153.4, 139.8, 129.7, 112.5, 106.7, 106.1, 85.2, 81.8, 67.6, 61.4, 28.2, 16.8, 14.5, 0.1; IR(KBr): 3384, 2958, 2175, 1743, 1593, 1461, 1210, 1054, 843, 770 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{25}INO_3Si$ $(M + H)^+$ 446.0643, found 446.0650.

Compound 5j



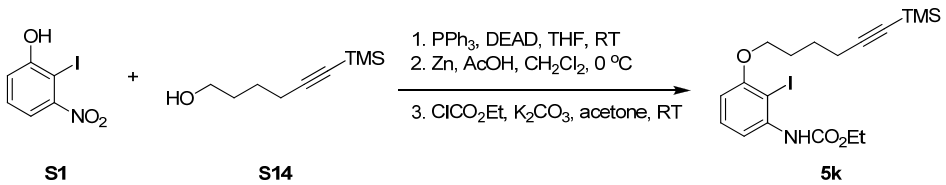
To a suspension of NaH (80 mg, 60%, 2 mmol) in anhydrous THF (10 mL) under an argon atmosphere was added the alcohol **S13** (1 mmol) at room temperature. The mixture was stirred for 20 min, and **S2** (184 mg, 1 mmol) was added. The solution was stirred until completion of the reaction. The mixture was diluted with water and extracted with EtOAc. The combined organic phases were dried over Na_2SO_4 and filtered. The filtrate was evaporated under reduced pressure and the resulting residue was purified by flash column chromatography.

To a stirred solution of the crude product in DCM (12 mL) was added activated zinc dust (3.9 g, 60 mmol). The solution was cooled down to 0 ^{o}C and HOAc (0.46 mL, 8.0 mmol) was added dropwisely. After stirred for 10 min at 0 ^{o}C, the mixture was filtered through a pad of celite and the celite was washed with EtOAc. The filtrate was neutralized with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4 and filtered. The filtrate was evaporated under reduced pressure and the resulting residue was used in the next step without purification.

To a stirred solution of the crude product and K_2CO_3 (690 mg, 5 mmol) in acetone (10 mL) was added $ClCO_2Et$ (1.4 equiv). The mixture was stirred at room temperature until completion of the reaction. The mixture was washed with water and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and filtered. The filtrate was evaporated under reduced pressure and the resulting residue was purified by flash column chromatography (PE/EtOAc, 20 : 1) to afford compound **5i**jas a yellow oil in 46% overall yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.0 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 7.09 (s, 1H), 4.52 (s, 2H), 4.24 (q, J = 7.2 Hz, 2H), 3.69 (t, J = 7.2 Hz,

2H), 2.61 (t, *J* = 7.2 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H), 0.98 (t, *J* = 8.0 Hz, 9H), 0.58 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 141.1, 138.5, 128.8, 123.8, 119.8, 104.5, 93.0, 83.1, 77.5, 69.2, 61.5, 21.3, 14.5, 7.4, 4.4; IR(KBr): 3388, 2955, 2175, 1742, 1520, 1464, 1208, 782, 728 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{31}INO_3Si$ $(M + H)^+$ 488.1112, found 488.1125.

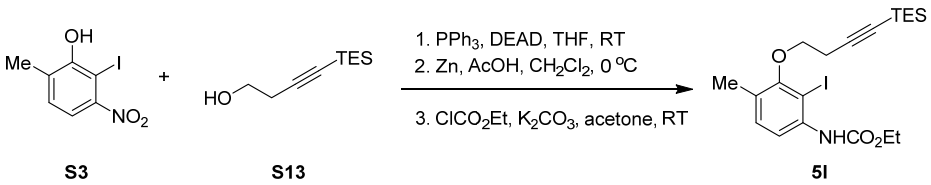
Compound 5k



S1 **S14** **5k**

Compound **5j** was prepared in 40% overall yield following the same procedure as described for the synthesis of **5a**. Purification by FCC (PE/EtOAc, 20 : 1), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.24 (t, *J* = 8.0 Hz, 1H), 7.16 (s, 1H), 6.50 (dd, *J* = 8.0, 0.8 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.04 (t, *J* = 6.0 Hz, 2H), 2.33 (t, *J* = 7.2 Hz, 2H), 1.91-1.98 (m, 2H), 1.74-1.81 (m, 2H), 1.33 (t, *J* = 7.2 Hz, 3H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 153.4, 139.8, 129.6, 112.3, 106.9, 106.6, 84.9, 81.7, 68.7, 61.4, 28.1, 25.2, 19.5, 14.5, 0.1; IR(KBr): 3384, 2956, 2173, 1743, 1593, 1461, 1210, 1049, 843, 771 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{27}INO_3Si$ $(M + H)^+$ 460.0799, found 460.0806.

Compound 5l



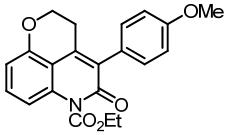
S3 **S13** **5l**

Compound **5j** was prepared in 46% overall yield following the same procedure as described for the synthesis of **5a**. Purification by FCC (PE/EtOAc, 20 : 1), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.4 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.93 (t, *J* = 7.2 Hz, 2H), 2.83 (t, *J* = 7.2 Hz, 2H), 2.33 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H), 0.98 (t, *J* = 8.0 Hz, 9H), 0.58 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 153.6, 137.7, 131.6, 126.7, 116.3, 103.7, 88.3, 83.7, 70.4, 61.5, 21.6, 16.4, 14.5, 7.4, 4.4; IR(KBr): 3389, 2955, 2176, 1741, 1519, 1462, 1212, 1029, 727 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{31}INO_3Si$ $(M + H)^+$ 488.1112, found 488.1113.

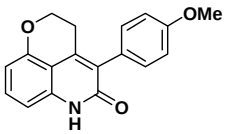
General procedure for synthesis of compound 7:

To a stirred solution of compound **5** (140 mg, 0.3 mmol) in anhydrous DMF (30 mL) was added PPh_3 (0.06 mmol), pyridine (1.5 mmol) and LiCl (0.3 mmol) under argon atmosphere. After discharging oxygen with argon for 0.5 h, $Pd(OAc)_2$ (0.03 mmol) was added under argon. The vial was purged with CO for 2

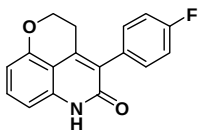
min and then connected to a balloon of CO. The solution was heated at 100 ºC for 24 h. The mixture was cooled down to room temperature, diluted with EtOAc, washed with brine, dried and filtered. The filtrate was evaporated under reduced pressure. The residue was treated with 5 mL of 1 M ethanolic NaOH at room temperature for 1 h. The mixture was diluted with EtOAc, washed with brine, dried and filtered. The filtrate was evaporated under reduced pressure and the resulting residue was purified by flash column chromatography to give compound **7**.



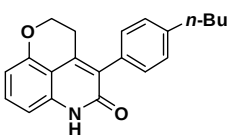
Compound **6a**: (without treated with ethanolic NaOH) Isolated as a white solid. FCC (PE/EtOAc, 10:1). M.P. 223-224 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, J = 8.4 Hz, 1H), 7.27 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.0 Hz, 1H), 6.66 (d, J = 8.0 Hz, 1H), 4.57 (q, J = 7.2 Hz, 2H), 4.24 (t, J = 6.0 Hz, 2H), 3.84 (s, 3H), 2.94 (t, J = 6.0 Hz, 2H), 1.46 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 159.3, 155.0, 153.0, 139.8, 136.2, 131.6, 131.4, 126.7, 125.2, 113.7, 110.1, 108.0, 105.9, 65.7, 65.5, 55.3, 27.8, 13.9; IR(KBr): 2959, 1770, 1653, 1472, 1235, 1023, 857 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NO_5$ $(M + H)^+$ 366.1336, found 366.1335.



Compound 7a: Isolated as a white solid in 95% yield; FCC (PE/EtOAc, 1:1). M.P. 218-219 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.57 (br s, 1H), 7.30-7.36 (m, 3H), 7.00 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.0 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 4.26 (t, J = 6.0 Hz, 2H), 3.87 (s, 3H), 2.95 (t, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 159.1, 154.5, 140.1, 138.1, 131.6, 131.1, 126.1, 113.7, 108.6, 108.4, 107.8, 65.7, 55.3, 27.9; IR(KBr): 3432, 2896, 1643, 1438, 1255, 1102, 913, 833 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{16}NO_3$ $(M + H)^+$ 294.1125, found 294.1124.

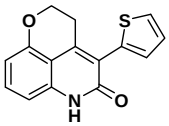


Compound 7b: Isolated as a white solid in 90% yield; FCC (PE/EtOAc, 3:1 to 3:2). M.P. 240-241 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.34 (br s, 1H), 7.33-7.38 (m, 3H), 7.17 (t, J = 8.8 Hz, 2H), 6.82 (d, J = 8.0 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 4.26 (t, J = 6.0 Hz, 2H), 2.92 (t, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 162.7, 161.2, 154.7, 140.6, 138.2, 132.2, 132.1, 131.5, 129.84, 129.81, 126.4, 115.4, 115.2, 108.8, 108.3, 107.7, 65.6, 27.9; IR(KBr): 3433, 2897, 1649, 1513, 1439, 1223, 1106, 911, 845 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{13}FNO_2$ $(M + H)^+$ 282.0925, found 282.0933.

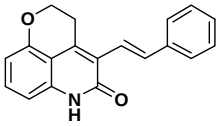


Compound 7c: Isolated as a white solid in 67% yield; FCC (PE/EtOAc, 3:1 to 1:1). M.P. 151-152 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.97 (br s, 1H), 7.27-7.33 (m, 5H), 6.86 (d, J = 8.0 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 4.24 (t, J = 5.6 Hz, 2H), 2.94 (t, J = 6.0 Hz, 2H), 2.68 (t, J = 8.0 Hz, 2H), 1.63-1.71 (m, 2H), 1.38-1.47 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 154.3, 142.4, 140.1, 138.2, 131.2, 131.0, 130.2, 128.1, 127.2, 108.4,

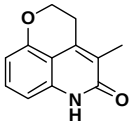
108.1, 65.7, 35.5, 33.5, 27.9, 22.5, 14.0; IR(KBr): 2955, 2930, 2859, 1758, 1532, 1480, 1099, 838, 738 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{22}NO_2$ $(M + H)^+$ 320.1245, found 320.1244.



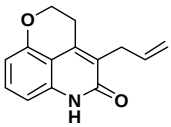
Compound 7d: Isolated as a yellow solid in 80% yield; FCC (PE/EtOAc, 3:1 to 3:2). M.P. 240-241 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.16 (br s, 1H), 7.53 (d, J = 4.8 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.15-7.19 (m, 2H), 6.97 (d, J = 8.0 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 4.29 (t, J = 5.6 Hz, 2H), 3.21 (t, J = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 154.7, 140.7, 137.9, 134.4 131.7, 129.3, 127.4, 126.1, 120.4, 108.9, 108.5, 107.8, 65.6, 28.3; IR(KBr): 3439, 2856, 2242, 1650, 1438, 1257, 1108, 909, 703 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{12}NO_2S$ $(M + H)^+$ 270.0583, found 270.0589.



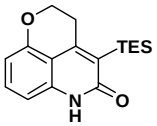
Compound 7e: Isolated as a yellow solid in 63% yield; FCC (PE/EtOAc, 4:1). M.P. 253-254 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.23 (br s, 1H), 7.75 (d, J = 16.4 Hz, 1H), 7.58 (d, J = 7.6 Hz, 2H), 7.33-7.40 (m, 3H), 7.24-7.31 (m, 2H), 6.91 (d, J = 8.0 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 4.37 (t, J = 5.6 Hz, 2H), 3.28 (t, J = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 154.5, 139.4, 137.9, 137.4, 135.4, 131.2, 128.7, 128.0, 126.7, 120.7, 108.7, 107.6, 65.4, 27.1; IR(KBr): 3423, 2925, 1651, 1438, 1225, 1107, 896, 776 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{16}NO_2$ $(M + H)^+$ 290.1176, found 290.1184.



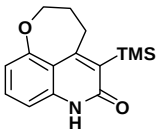
Compound 7f: Isolated as a white solid in 52% yield; FCC (PE/EtOAc, 1:1). M.P. 242-243 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.33 (br s, 1H), 7.32 (t, J = 8.0 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 4.36 (t, J = 5.6 Hz, 2H), 3.03 (t, J = 5.6 Hz, 2H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 138.8, 137.4, 130.3, 122.8, 108.5, 108.4, 107.7, 65.4, 26.8, 11.5; IR(KBr): 2921, 1643, 1435, 1253, 1116, 1024, 795 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{12}NO_2$ $(M + H)^+$ 202.0863, found 202.0868.



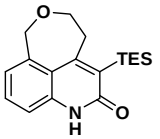
Compound 7g: Isolated as a yellow solid in 51% yield; FCC (PE/EtOAc, 3:1 to 3:3). M.P. 143-144 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.82 (br s, 1H), 7.33 (t, J = 8.0 Hz, 1H), 6.92 (dd, J = 8.0, 4.0 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 5.95 (m, 1H), 5.03-5.08 (m, 2H), 4.34 (t, J = 6.0 Hz, 2H), 3.48 (d, J = 6.0 Hz, 2H), 3.04 (t, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 153.9, 140.1, 137.9, 134.7, 130.6, 124.1, 115.2, 108.40, 108.35, 108.0, 65.4, 29.8, 26.3; IR(KBr): 2905, 1646, 1440, 1253, 1106, 915, 799 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{14}NO_2$ $(M + H)^+$ 228.1019, found 228.1026.



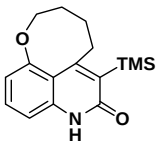
Compound 7h: Isolated as a white solid in 55% yield; FCC (PE/EtOAc, 5:1). M.P. 122-123 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.47 (br s, 1H), 7.34 (t, J = 8.4 Hz, 1H), 6.99 (d, J = 8.4 Hz, 1H), 6.63 (d, J = 8.4 Hz, 1H), 4.33 (t, J = 5.6 Hz, 2H), 3.15 (t, J = 5.6 Hz, 2H), 1.01 (s, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 154.5, 152.1, 139.8, 131.5, 124.1, 108.7, 108.1, 107.6, 65.9, 30.1, 7.9, 5.1; IR(KBr): 3435, 2952, 1637, 1435, 1247, 1104. 998, 735 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{24}NO_2Si$ $(M + H)^+$ 302.1571, found 302.1575.



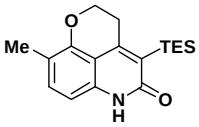
Compound 7i: Isolated as a white solid in 79% yield; FCC (PE/EtOAc, 5:1). M.P. 202-203 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.17 (br s, 1H), 7.29 (t, J = 8.0 Hz, 1H), 6.97 (dd, J = 8.0, 1.6 Hz, 1H), 6.75 (dd, J = 8.0, 0.8 Hz, 1H), 4.24 (t, J = 7.2 Hz, 2H), 3.19 (t, J = 6.4 Hz, 2H), 2.17-2.24 (m, 2H), 0.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 160.0, 158.8, 140.5, 130.4, 129.5, 115.3, 113.3, 110.4, 72.6, 31.4, 28.7, 2.1; IR(KBr): 3425, 2949, 1642, 1590, 1423, 1233, 1091, 841 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{20}NO_2Si$ $(M + H)^+$ 274.1258, found 274.1257.



Compound 7j: Isolated as a white solid in 67% yield; FCC (PE/EtOAc, 10:1 to 5:1). M.P. 112-113 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.73 (br s, 1H), 7.28-7.37 (m, 2H), 6.95 (d, J = 6.8 Hz, 1H), 4.96 (s, 2H), 4.15 (t, J = 5.6 Hz, 2H), 3.34 (t, J = 5.6 Hz, 2H), 1.02 (s, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 159.5, 140.1, 139.4, 129.4, 129.0, 122.4, 121.1, 115.7, 69.6, 68.6, 34.4, 8.0, 5.5; IR(KBr): 3433, 2954, 1639, 1463, 1354, 1217, 999, 729 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{26}NO_2Si$ $(M + H)^+$ 316.1727, found 316.1728.

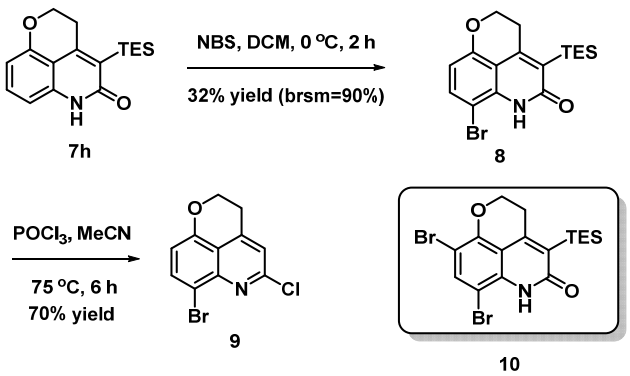


Compound 7k: Isolated as a white solid in 62% yield; FCC (PE/EtOAc, 15:1 to 5:1). M.P. 178-179 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.55 (br s, 1H), 7.40 (t, J = 8.0 Hz, 1H), 7.16 (d, J = 8.0 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 4.37-4.42 (m, 1H), 3.97-3.99 (m, 2H), 2.17-2.24 (m, 2H), 3.16 (m, 1H), 2.02 (m, 1H), 1.64-1.74 (m, 2H), 1.44 (m, 1H), 0.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 159.4, 155.4, 140.0, 131.3, 131.1, 119.0, 117.2, 112.5, 75.8, 32.3, 27.9, 22.9, 2.5; IR(KBr): 3424, 2920, 1638, 1587, 1421, 1230, 1087, 849 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{22}NO_2Si$ $(M + H)^+$ 288.1414, found 288.1413.



Compound 7l Isolated as a white solid in 60% yield; FCC (PE/EtOAc, 5:1). M.P. 167-168 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.18 (br s, 1H), 7.24 (d, J = 8.0 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 4.35 (t, J = 6.0 Hz, 2H), 3.14 (t, J = 6.0 Hz, 2H), 2.23 (s, 3H), 1.00 (s, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 151.8, 137.9, 133.4, 117.1, 108.6, 106.7, 65.8, 30.3, 15.1, 7.9, 5.2; IR(KBr): 3733, 2953, 1639, 1418, 1242, 1003, 727 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{26}NO_2Si$ $(M + H)^+$ 316.1727, found 316.1736.

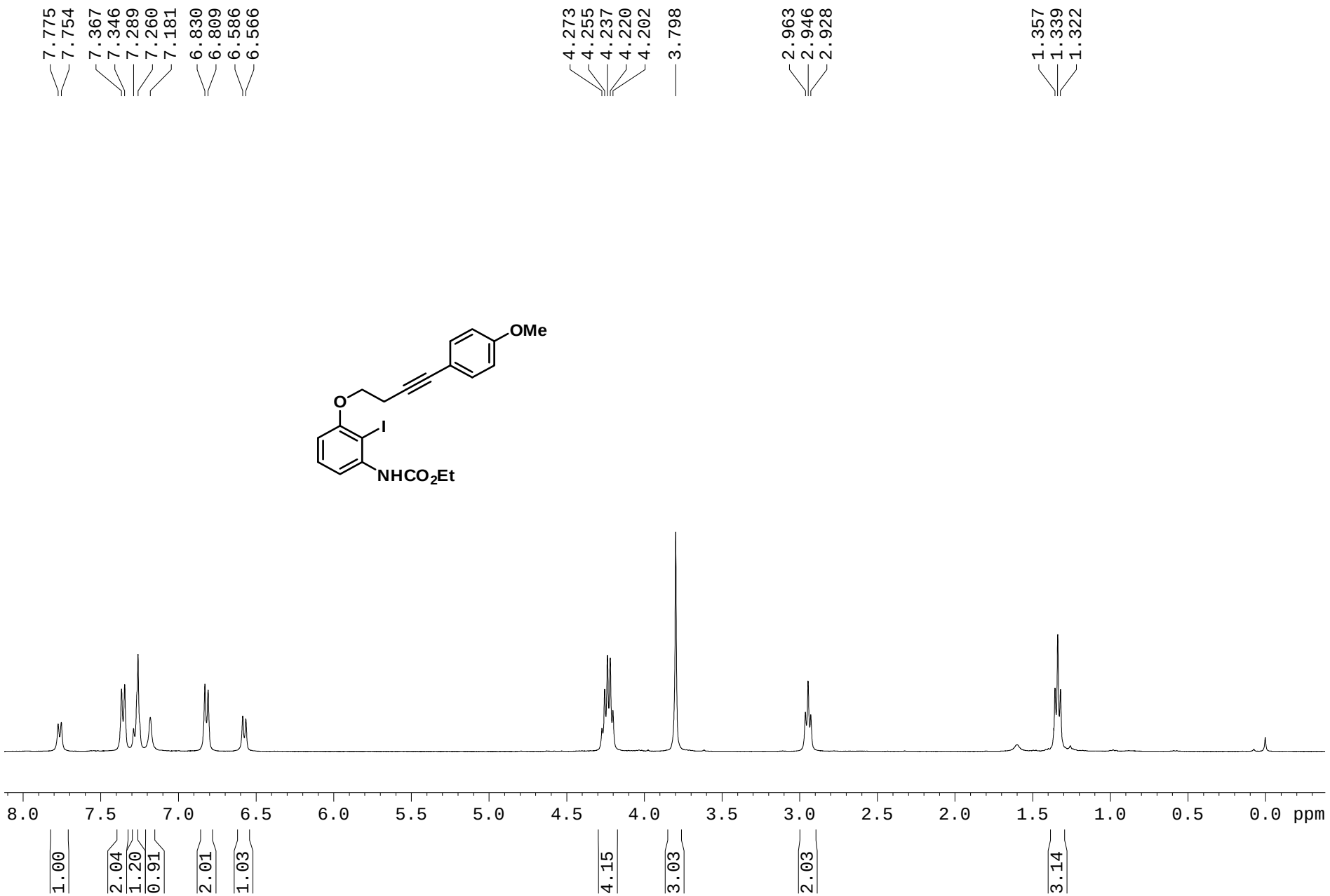
Synthesis of compound 9



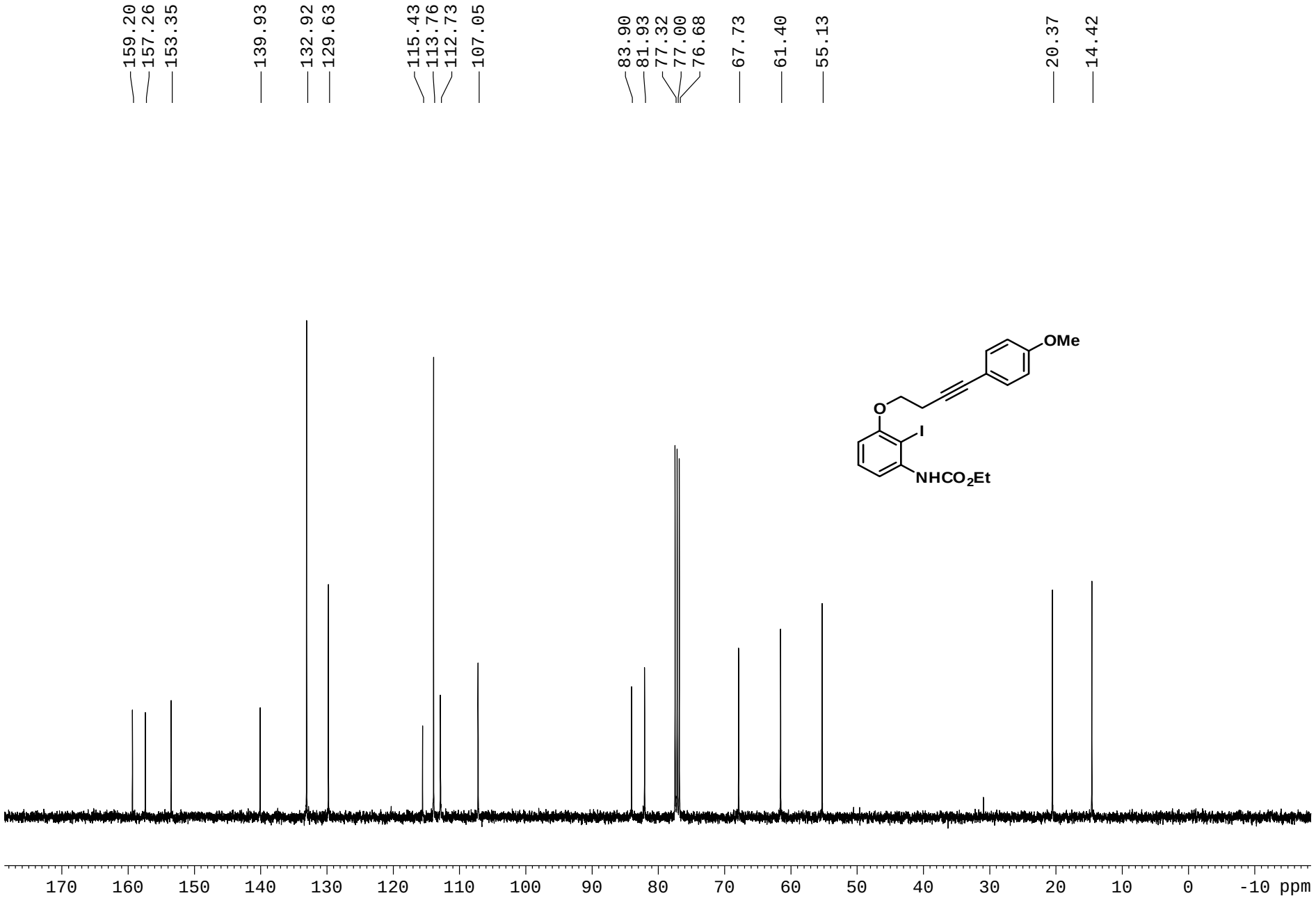
To a solution of compound **7h** (30 mg, 0.10 mmol) in DCM (4 mL) at 0 °C was added NBS (18 mg, 0.10 mmol). After stirring at 0 °C for 2 h, the reaction mixture was extracted with EtOAc and dried over Na_2SO_4. Purification by FCC (PE/EtOAc, 8 : 1) gave compound **8** (13 mg, 32%) as yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (br s, 1H), 7.49 (d, J = 8.4 Hz, 1H), 6.57 (d, J = 8.4 Hz, 1H), 4.31 (t, J = 6.0 Hz, 2H), 3.12 (t, J = 6.0 Hz, 2H), 0.96 (s, 15H). The ^{1}H NMR showed that the reaction also provided trace of compound **10**, and compound **8** and **10** (ratio is 10:1) could not be separated by FCC.

To a solution of compound **8** (12 mg, 0.032 mmol) in MeCN (0.6 mL) was added $POCl_3$ (0.06 ml, 0.64 mmol). After stirring at 75 °C for 6 h, the residue was diluted with EtOAc, neutralized with saturated aqueous $NaHCO_3$ solution, extracted with EtOAc and dried over Na_2SO_4. Purification by FCC (PE/EtOAc, 7 : 1) gave compound **9** (6.4 mg, 70%) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.02 (d, J = 8.4 Hz, 1H), 7.51 (s, H), 7.00 (d, J = 8.4 Hz, 1H), 4.43 (t, J = 5.6 Hz, 1H), 3.28 (t, J = 5.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.0, 151.0, 145.9, 143.9, 134.6, 119.1, 116.9, 111.9, 111.8, 65.5, 27.3; HRMS (ESI) *m/z* calcd for $C_{11}H_8NOClBr$ $(M + H)^+$ 283.9478, found 283.9475.

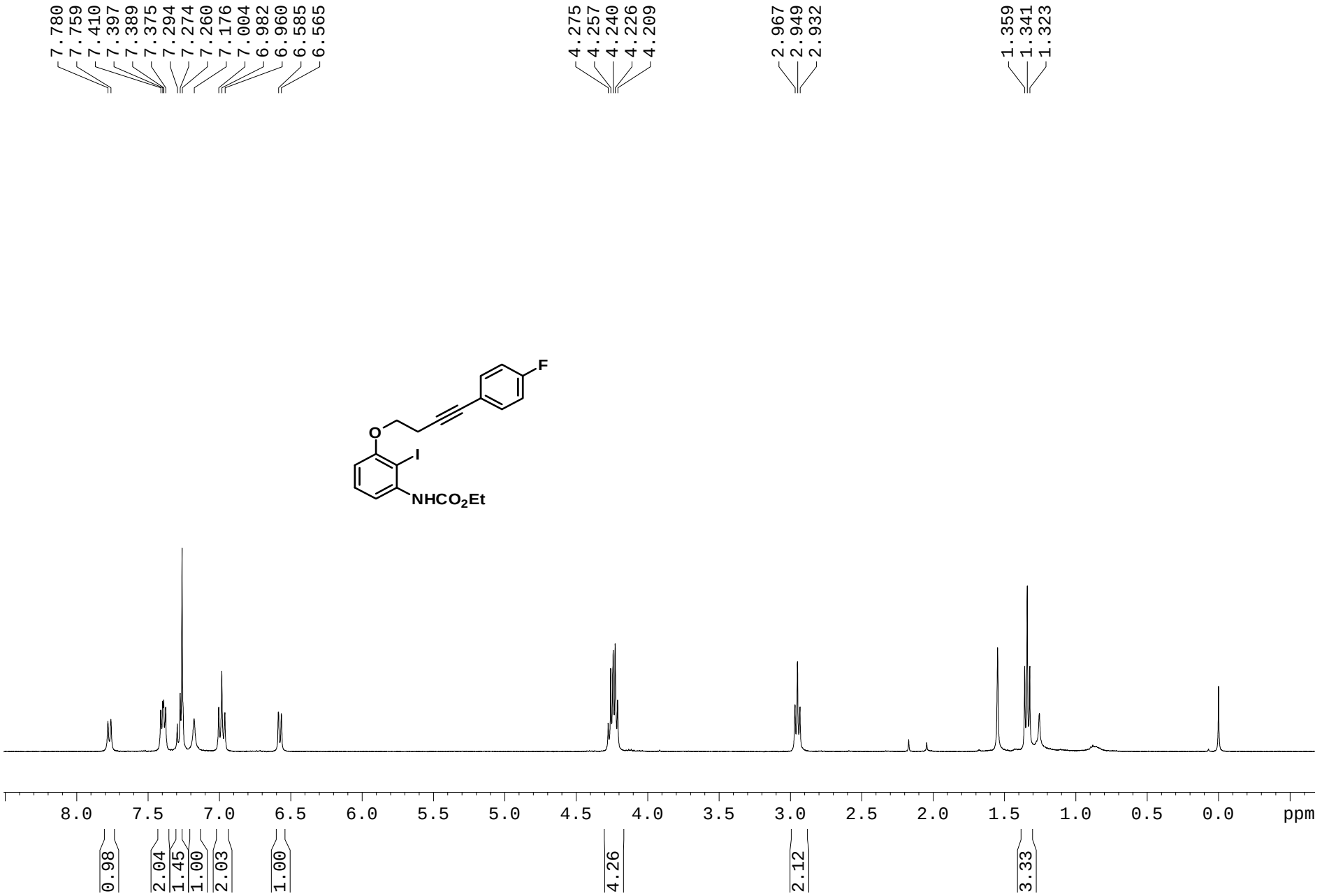
^{1}H NMR of compound 5a ($CDCl_3$, 400 MHz)



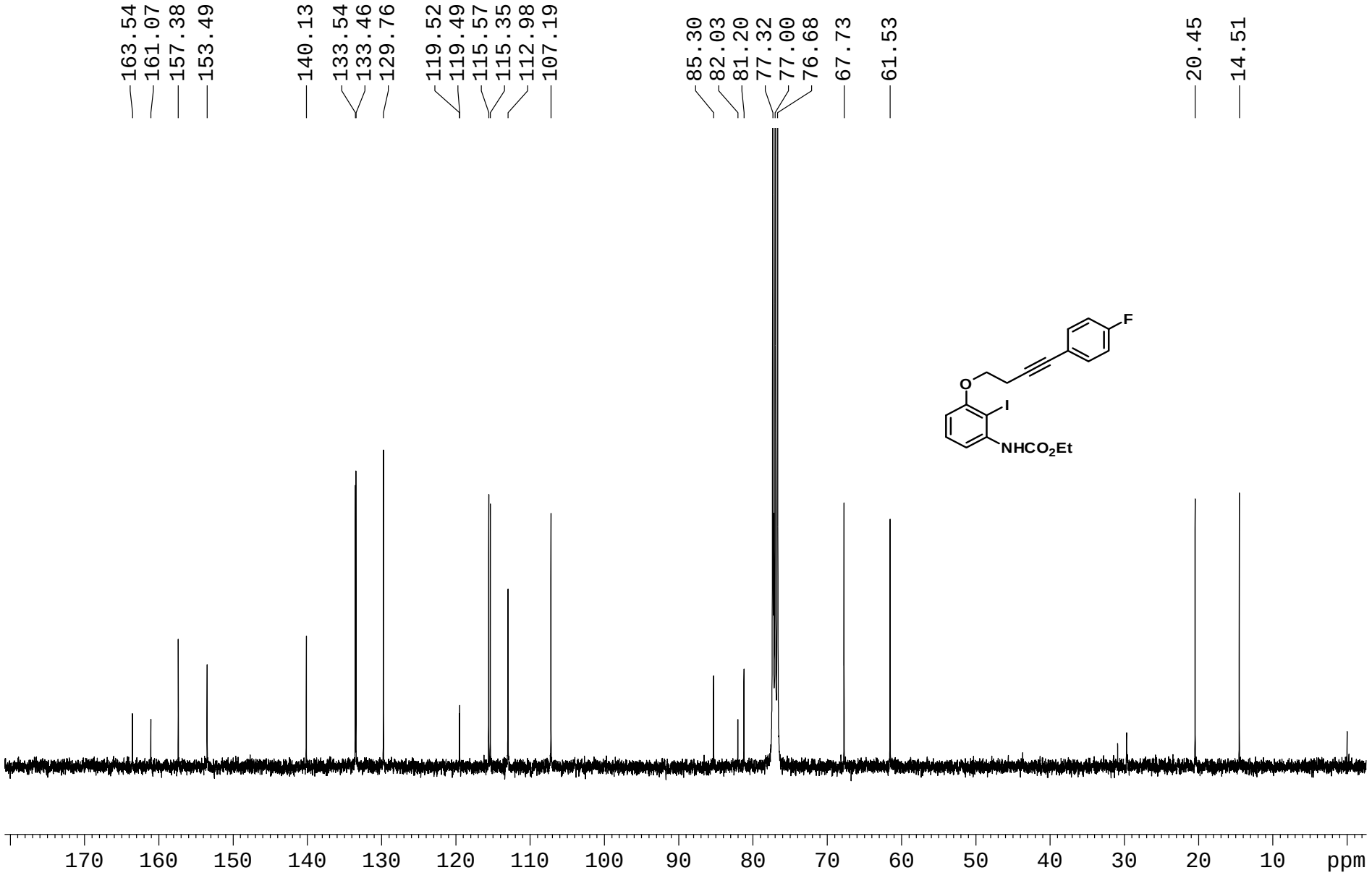
^{13}C NMR of compound 5a ($CDCl_3$, 100 MHz)



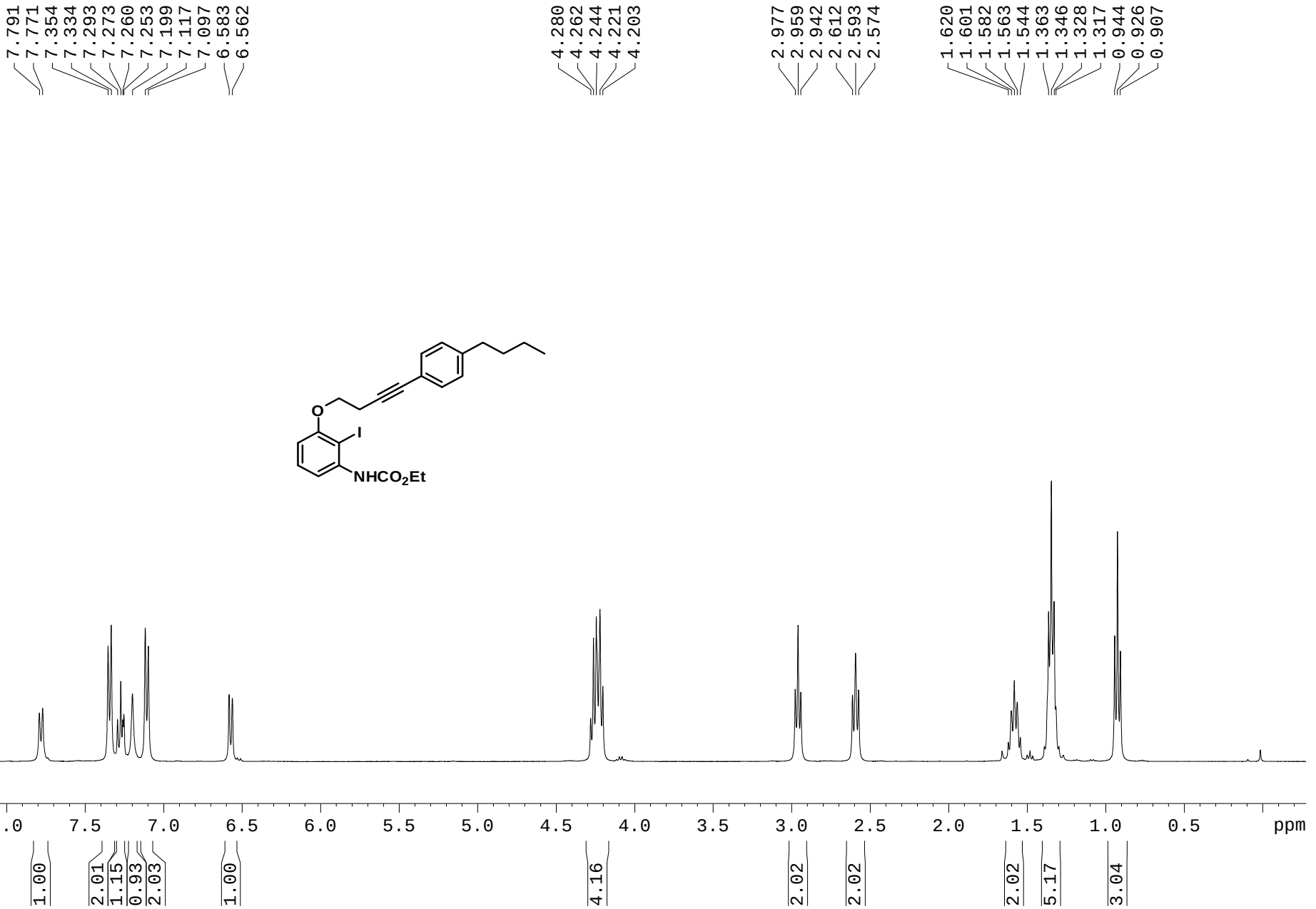
^{1}H NMR of compound 5b ($CDCl_3$, 400 MHz)



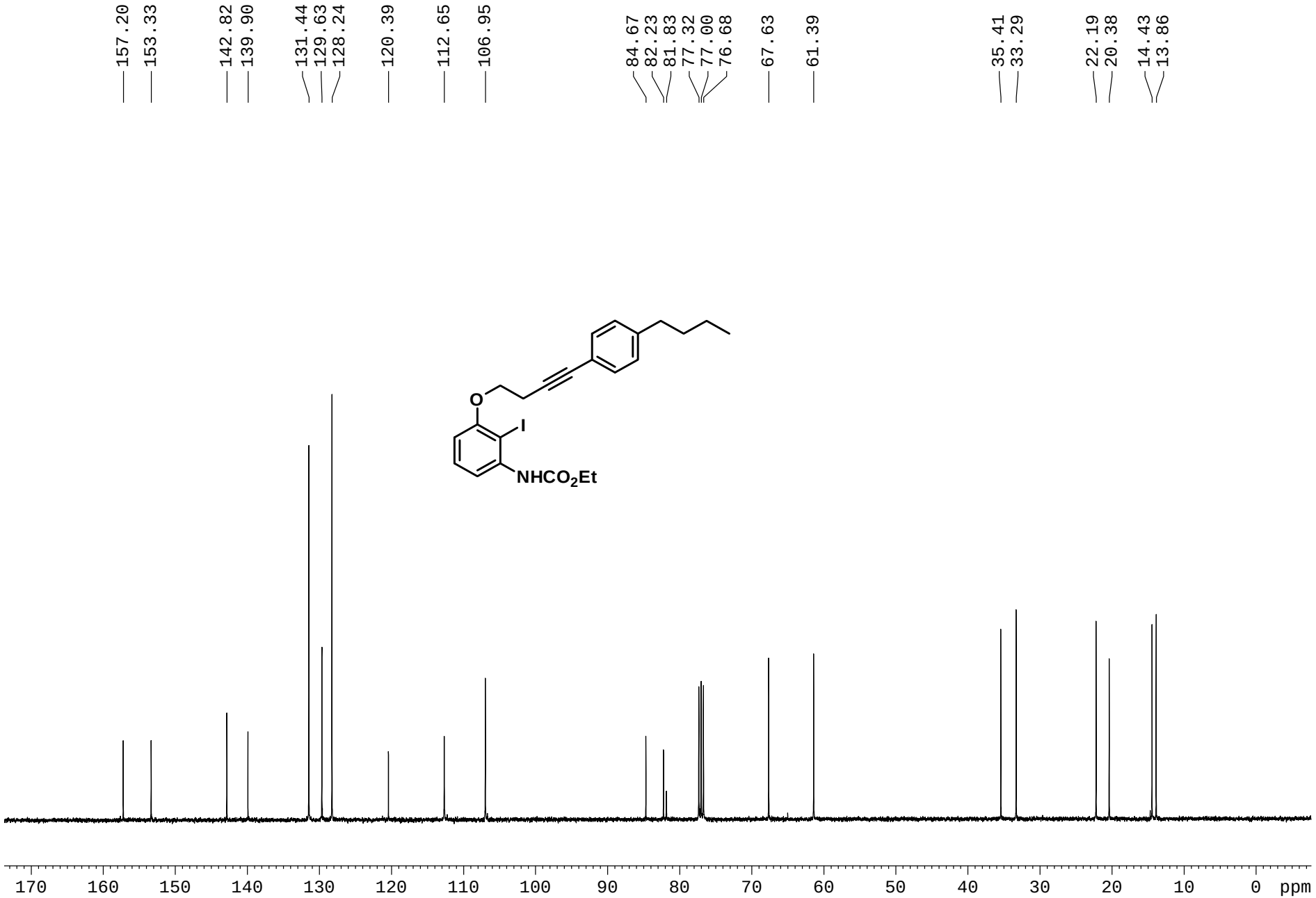
^{13}C NMR of compound 5b ($CDCl_3$, 100 MHz)



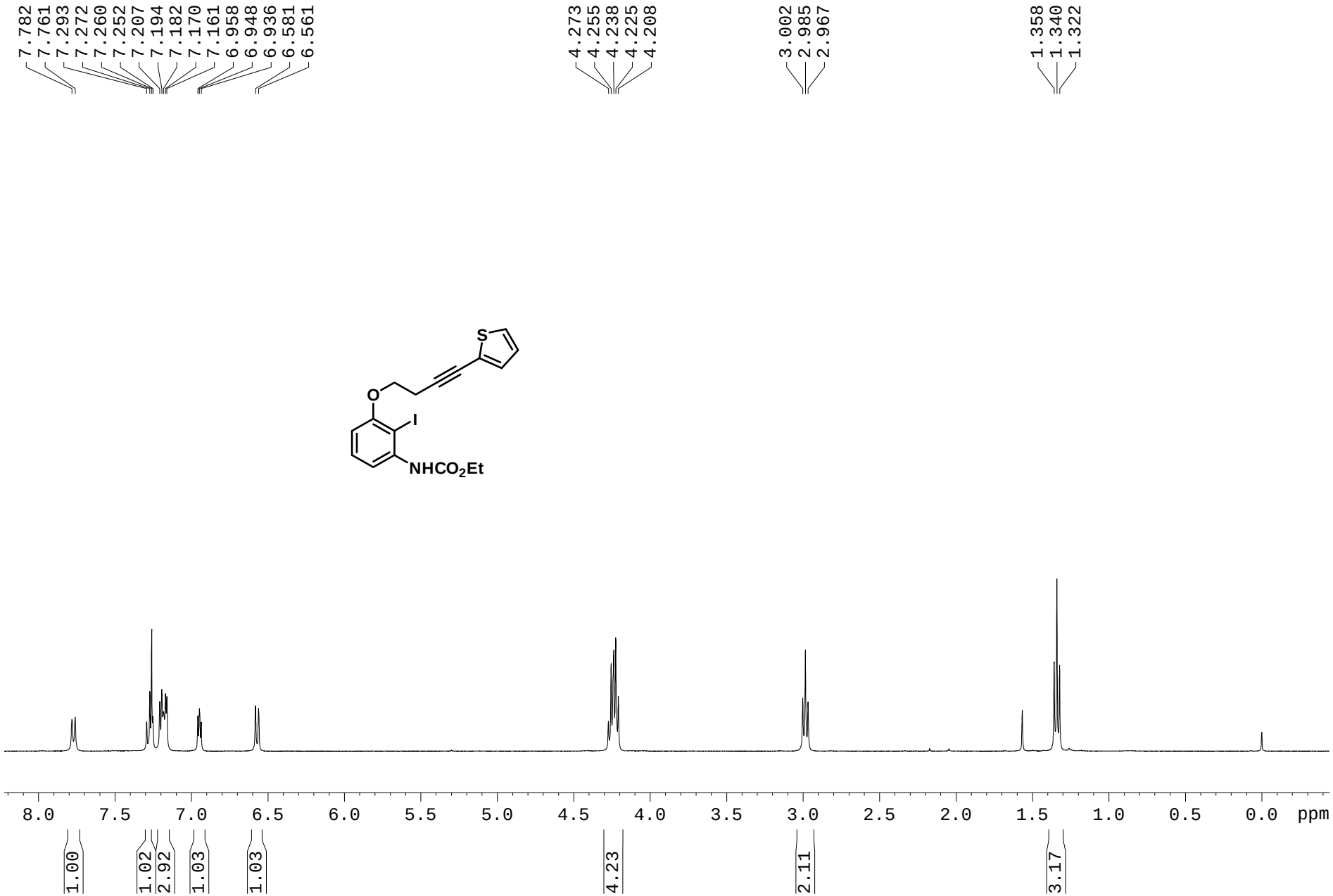
^{1}H NMR of compound 5c ($CDCl_3$, 400 MHz)



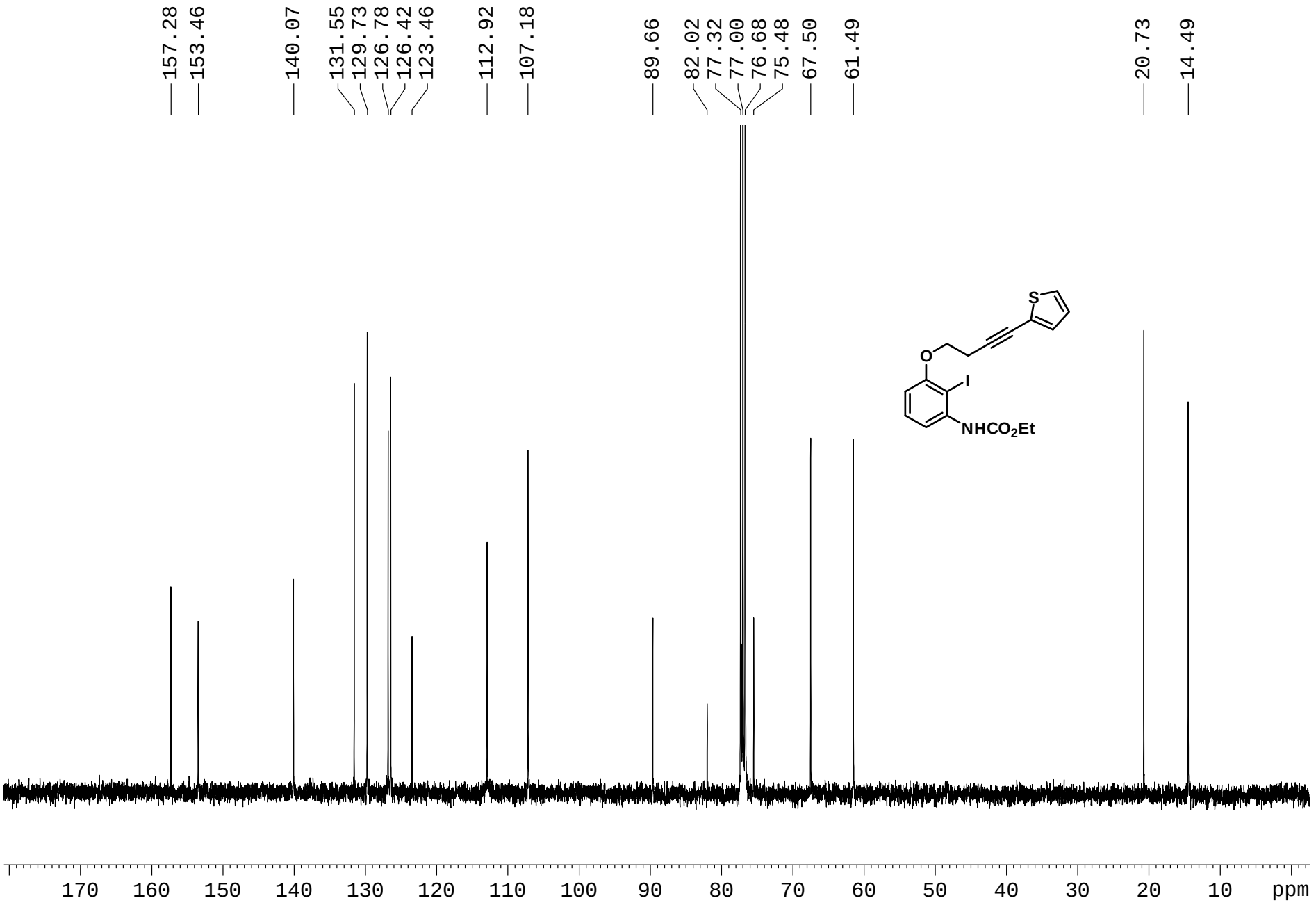
^{13}C NMR of compound 5c ($CDCl_3$, 100 MHz)



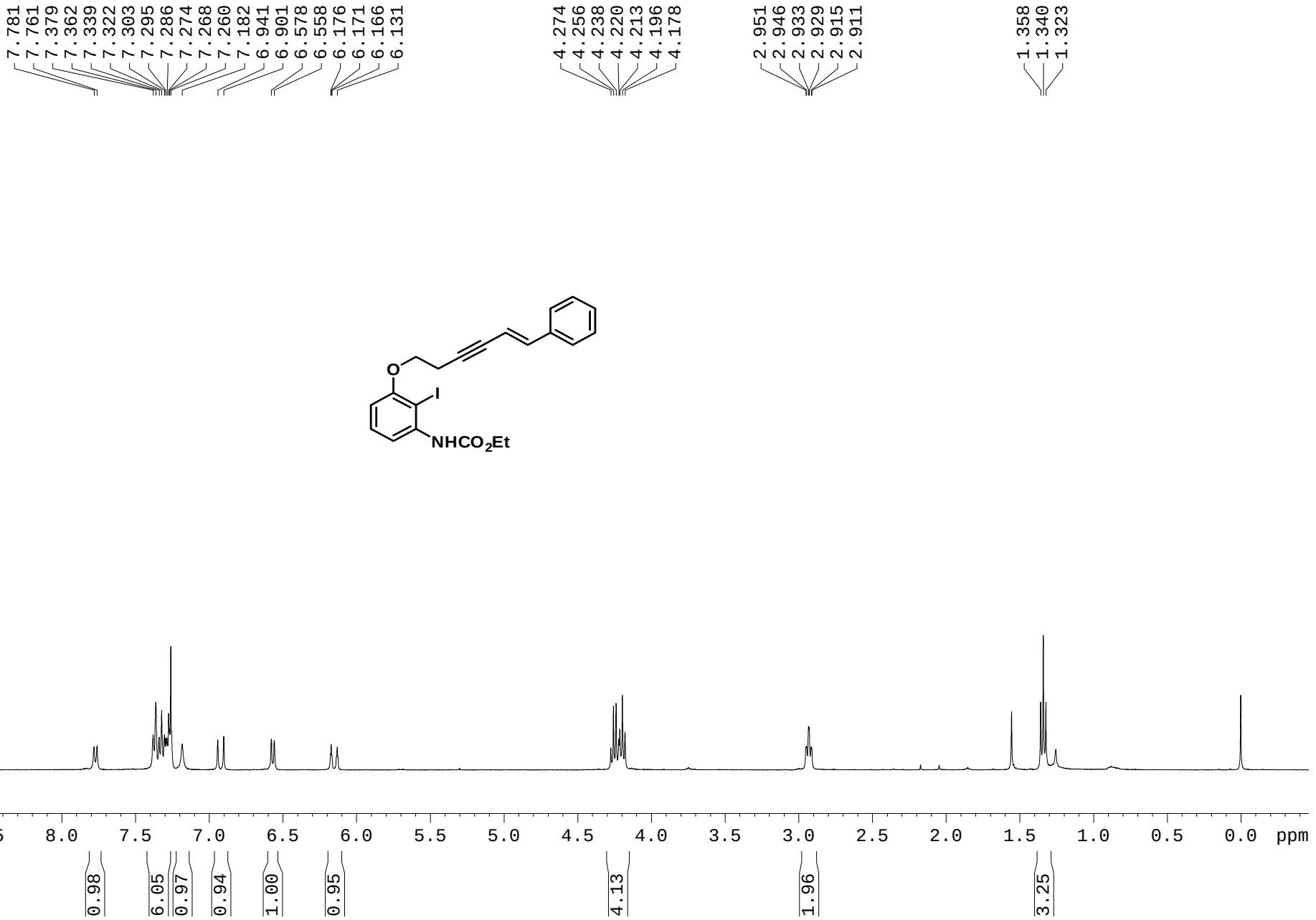
^{1}H NMR of compound 5d ($CDCl_3$, 400 MHz)



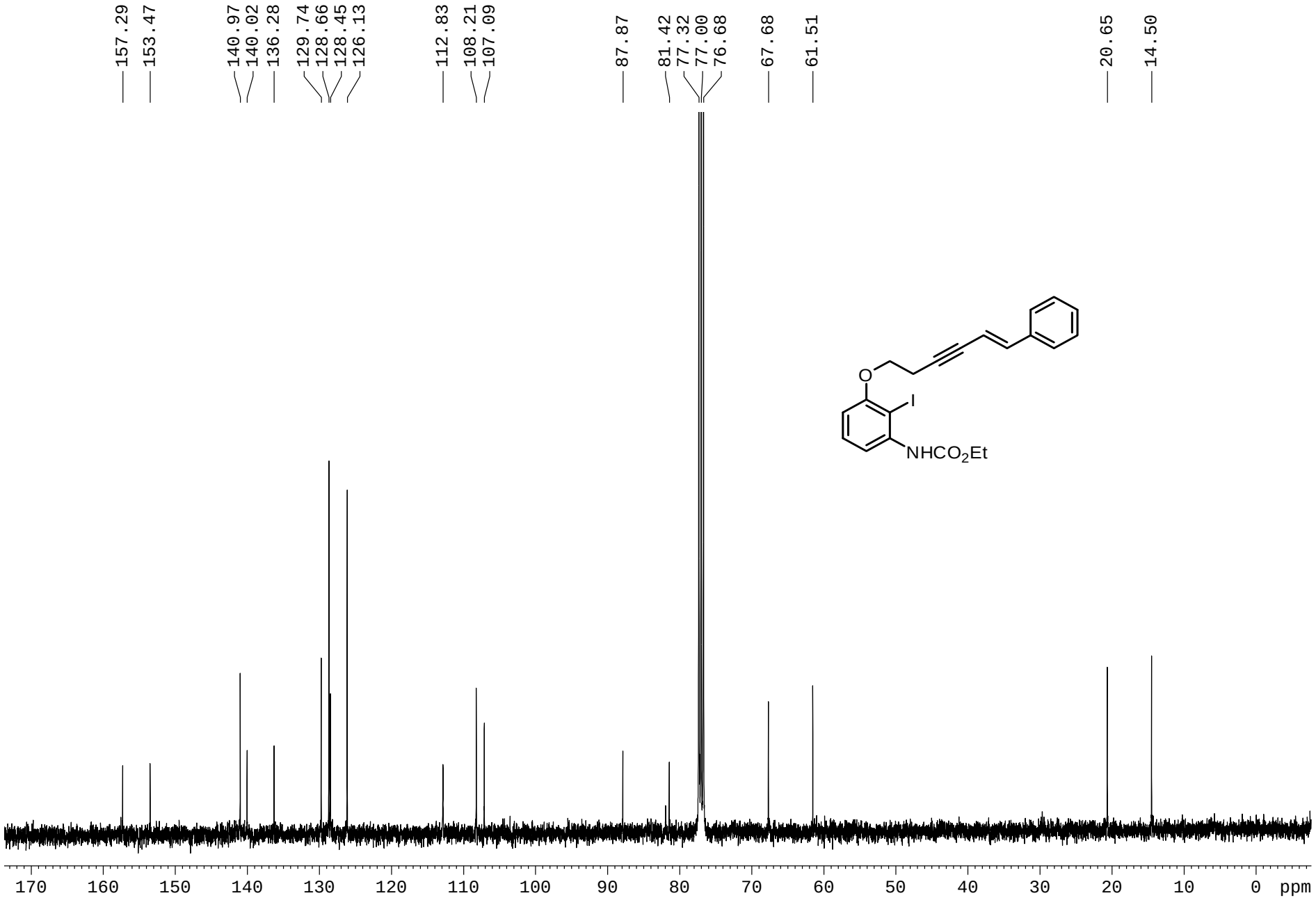
^{13}C NMR of compound 5d ($CDCl_3$, 100 MHz)



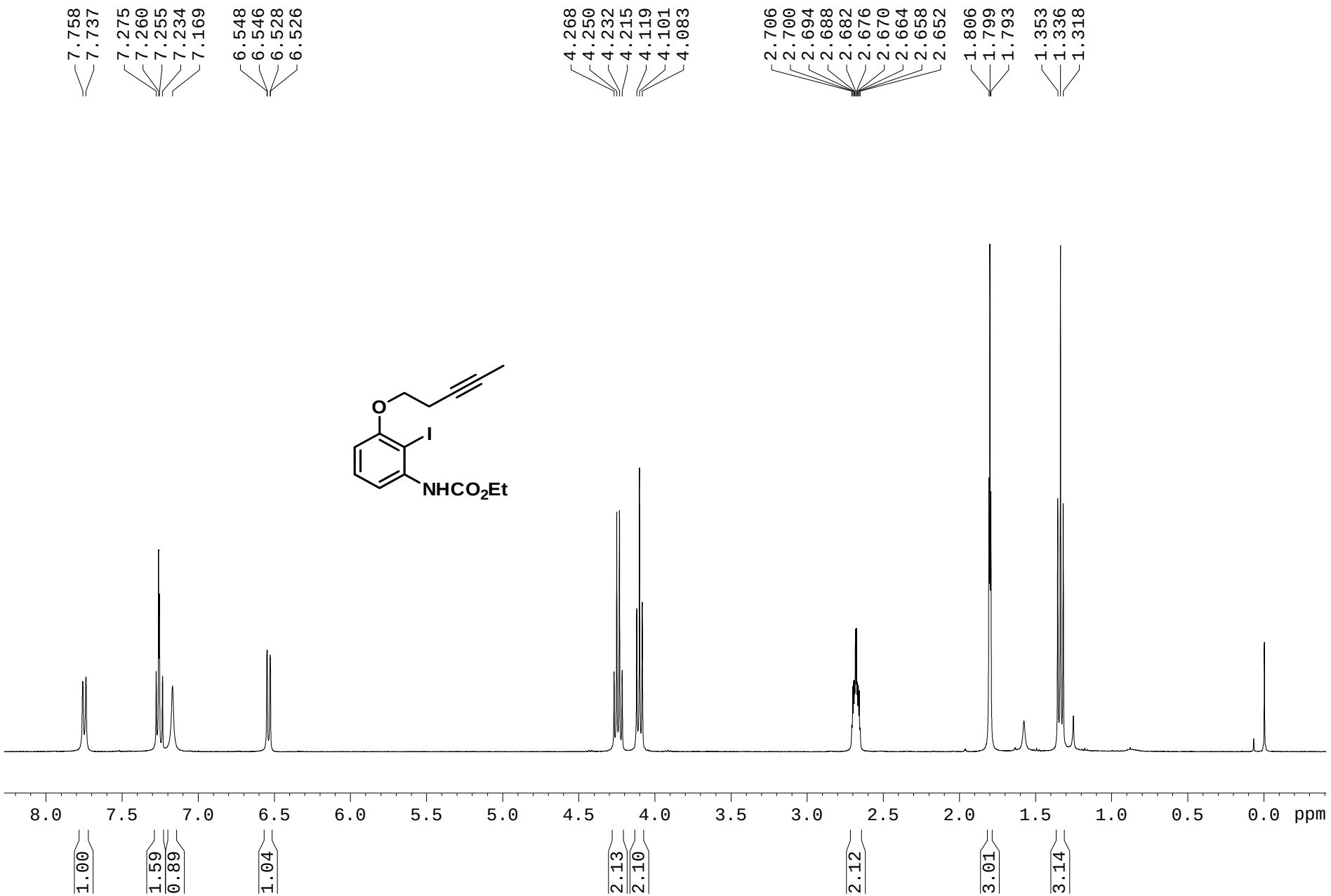
^{1}H NMR of compound 5e ($CDCl_3$, 400 MHz)



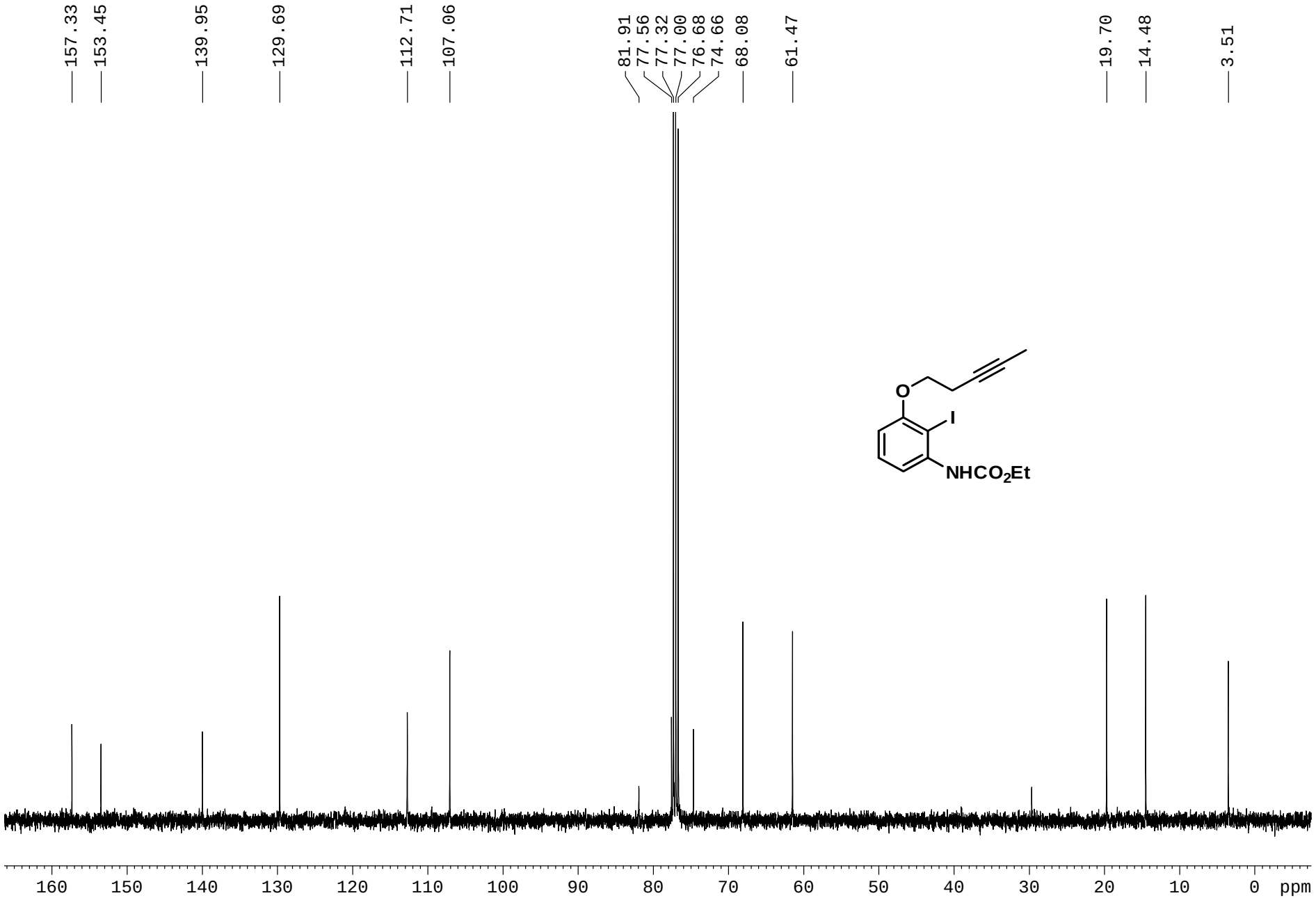
^{13}C NMR of compound 5e ($CDCl_3$, 100 MHz)



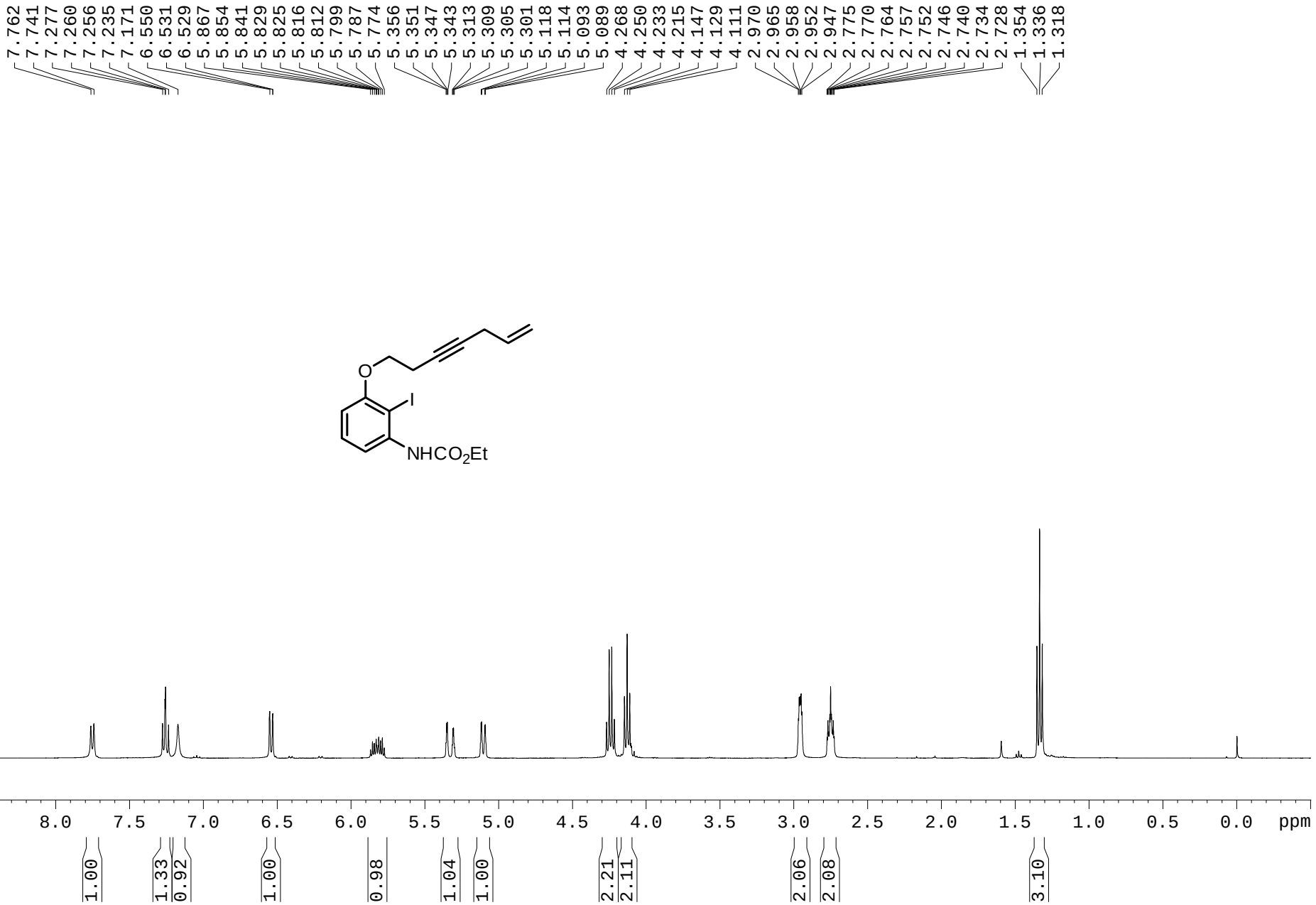
^{1}H NMR of compound 5f ($CDCl_3$, 400 MHz)



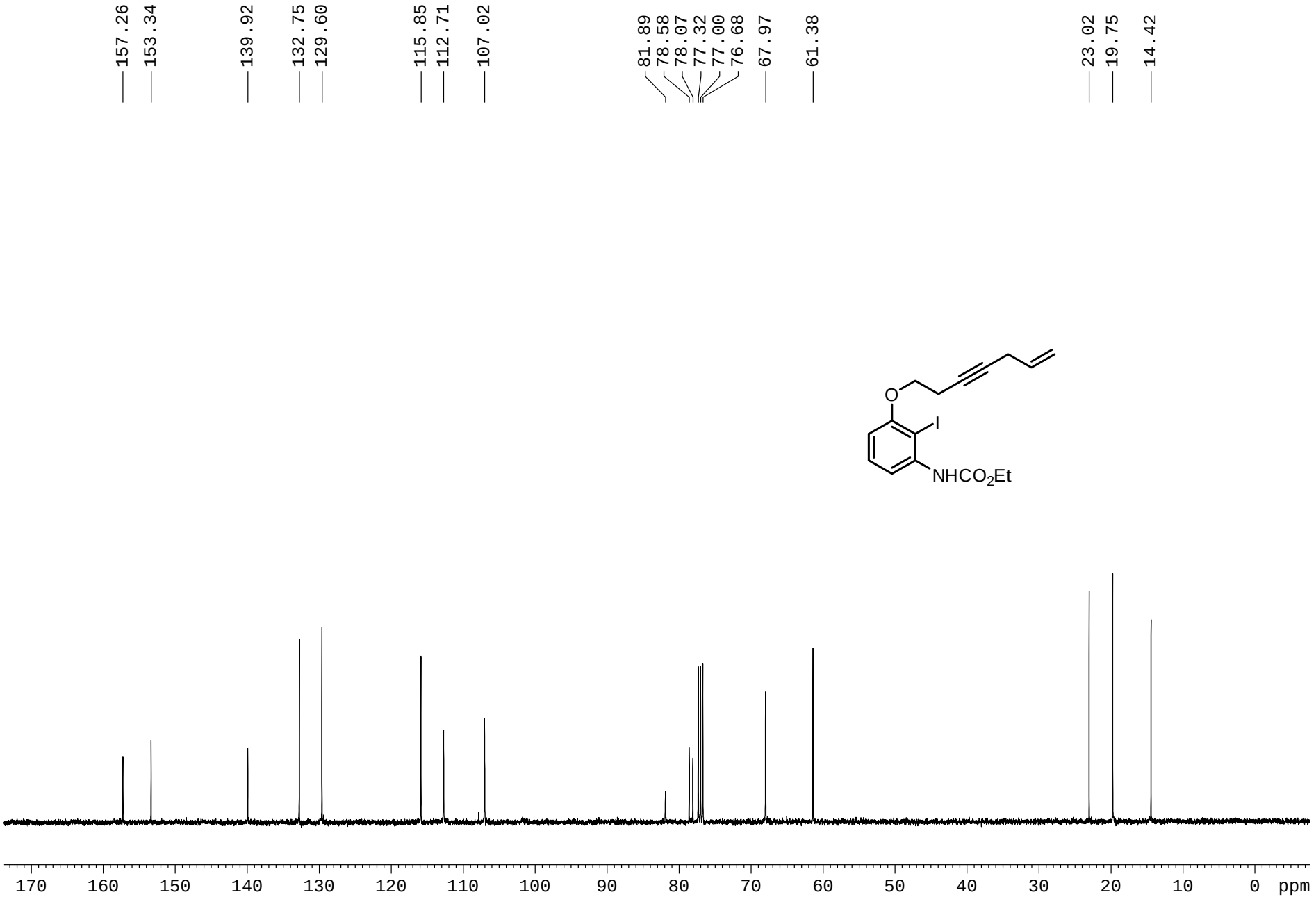
^{13}C NMR of compound 5f ($CDCl_3$, 100 MHz)



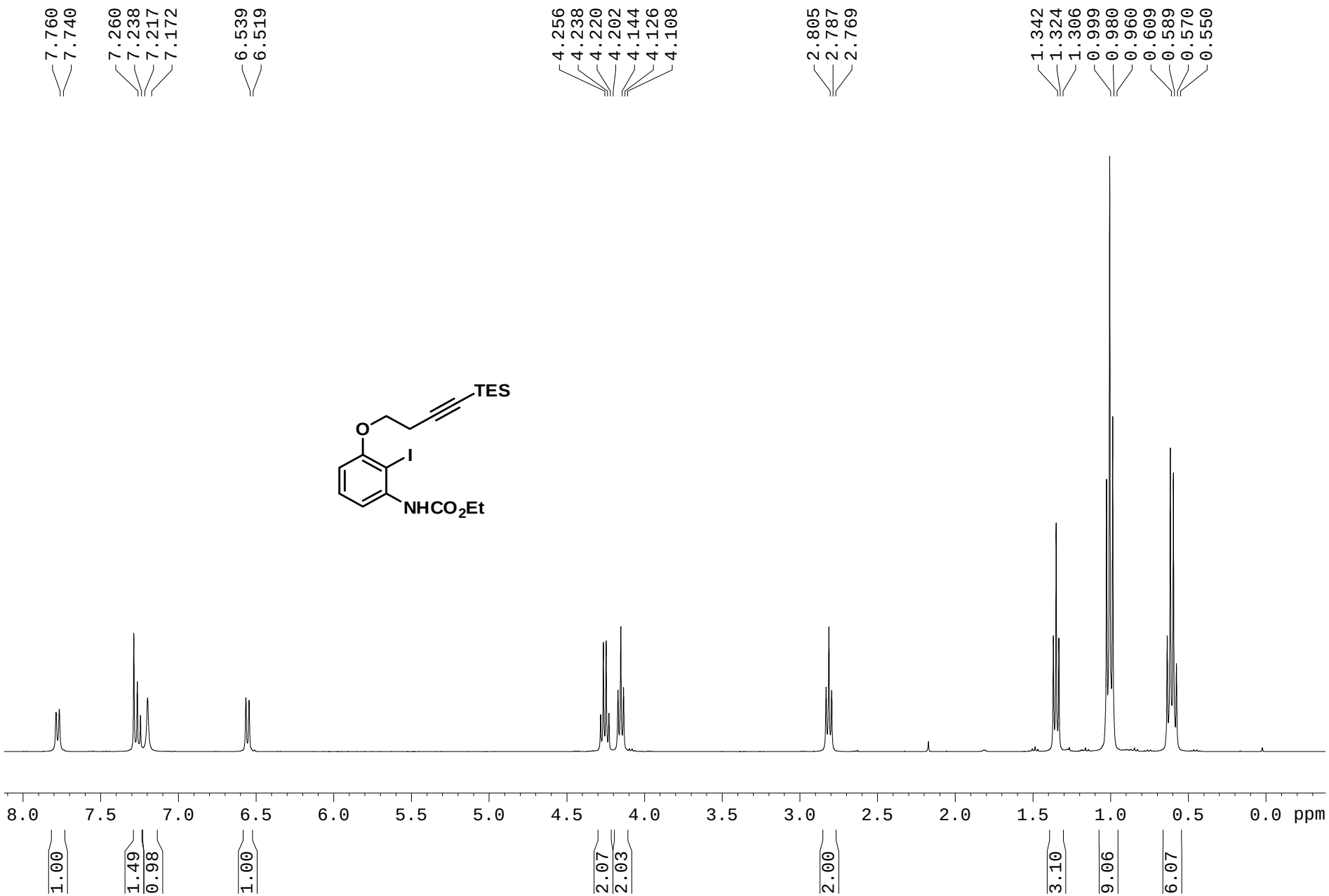
^{1}H NMR of compound 5g ($CDCl_3$, 400 MHz)



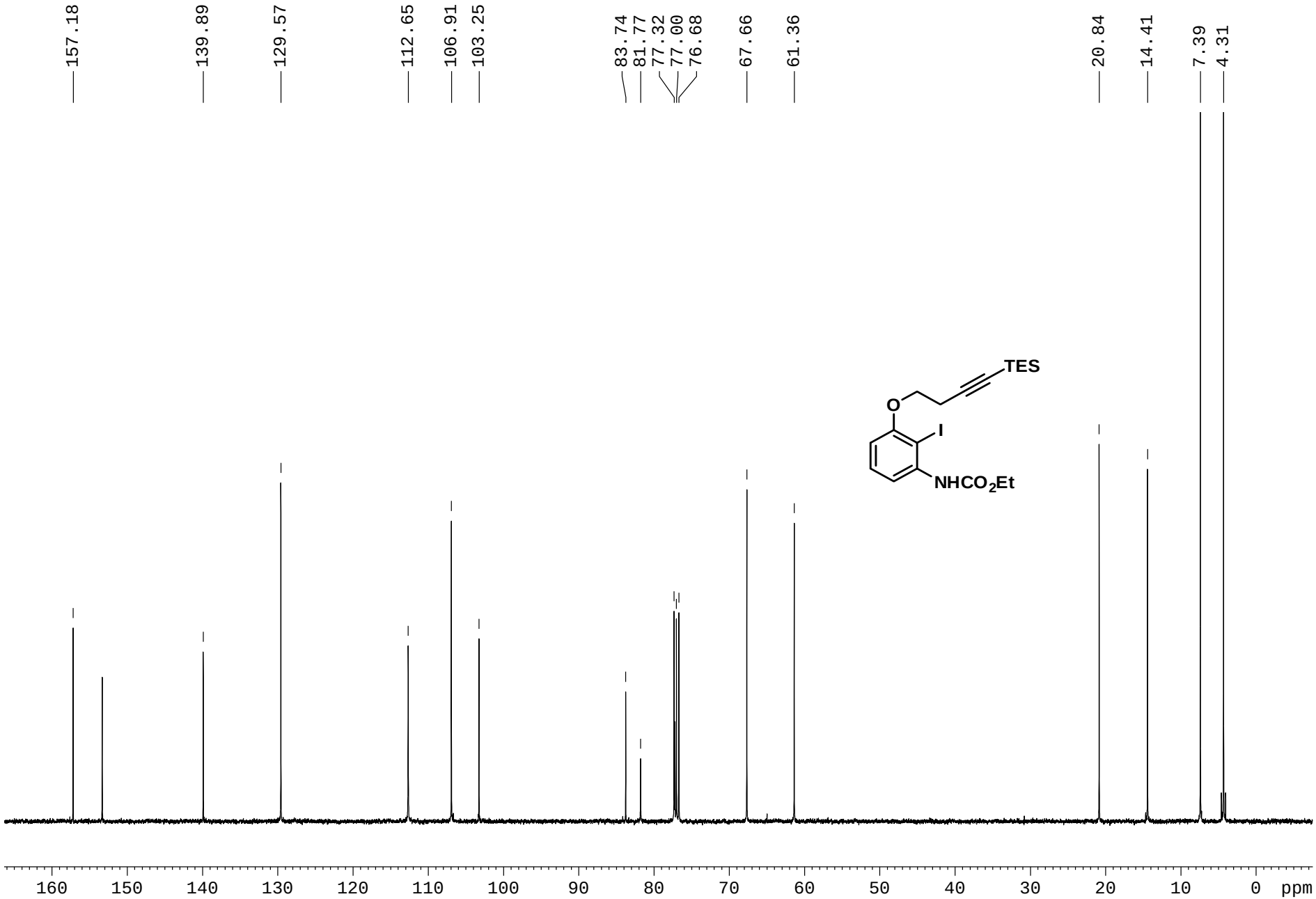
^{13}C NMR of compound 5g ($CDCl_3$, 100 MHz)



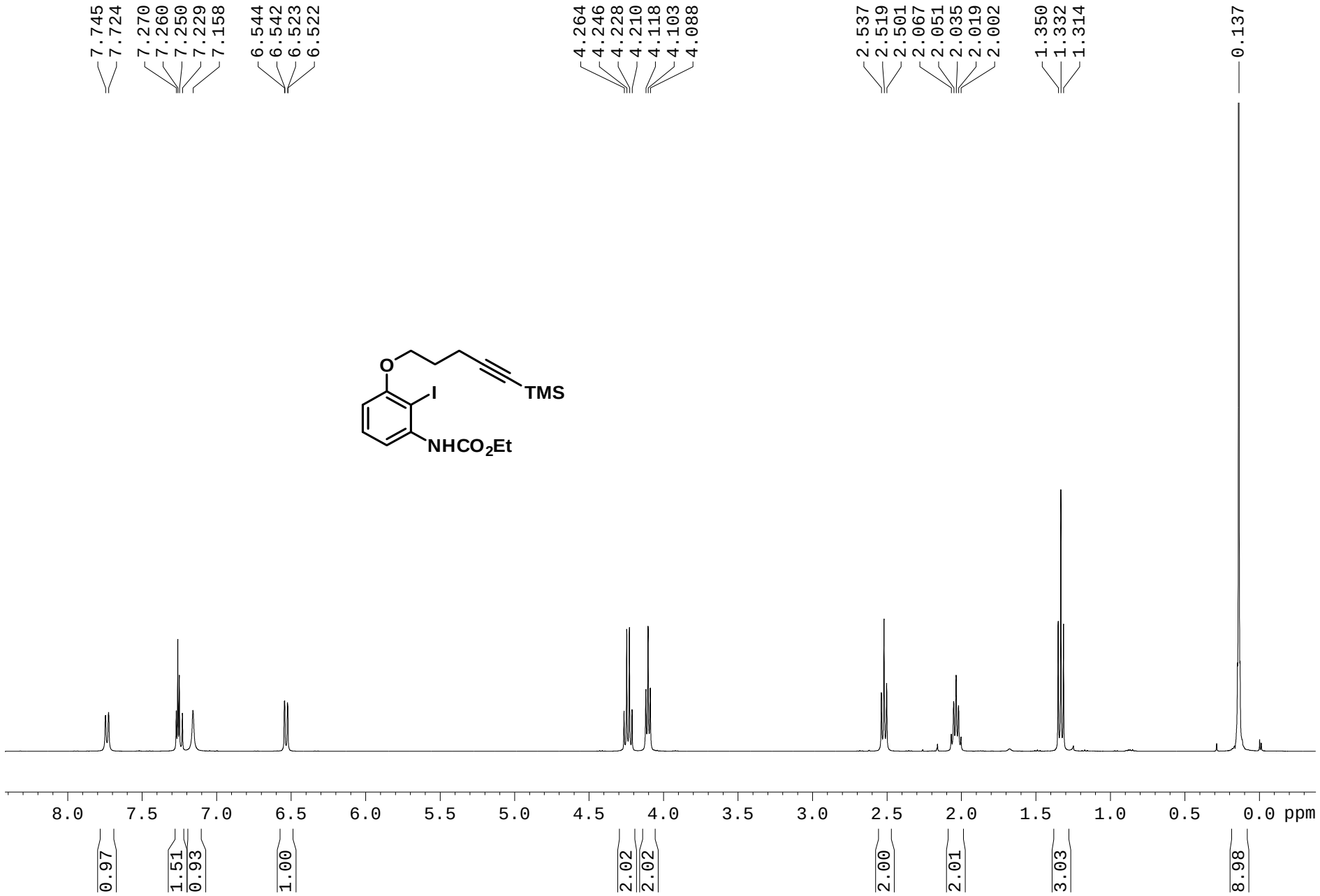
^{1}H NMR of compound 5h ($CDCl_3$, 400 MHz)



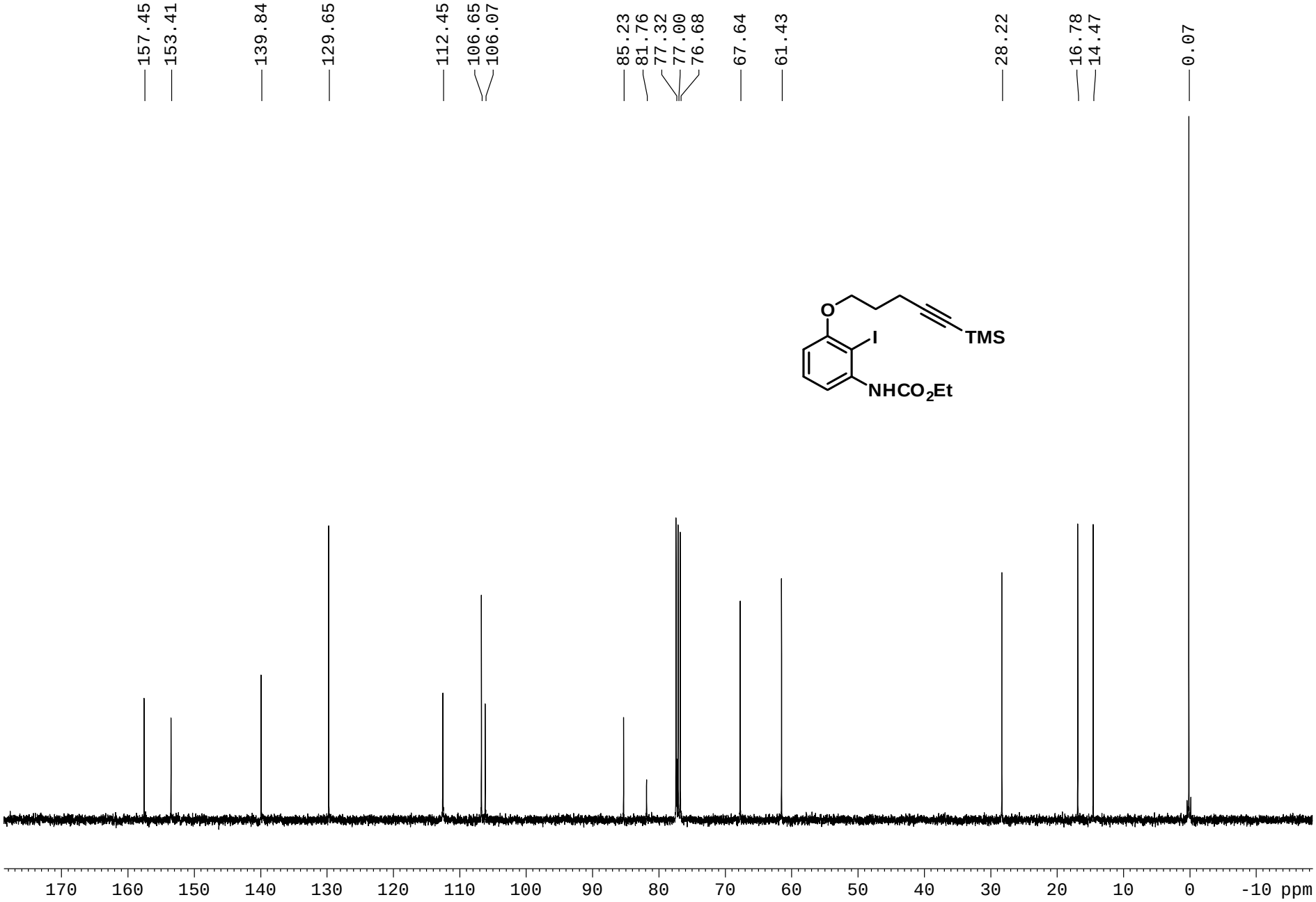
^{13}C NMR of compound 5h ($CDCl_3$, 100 MHz)



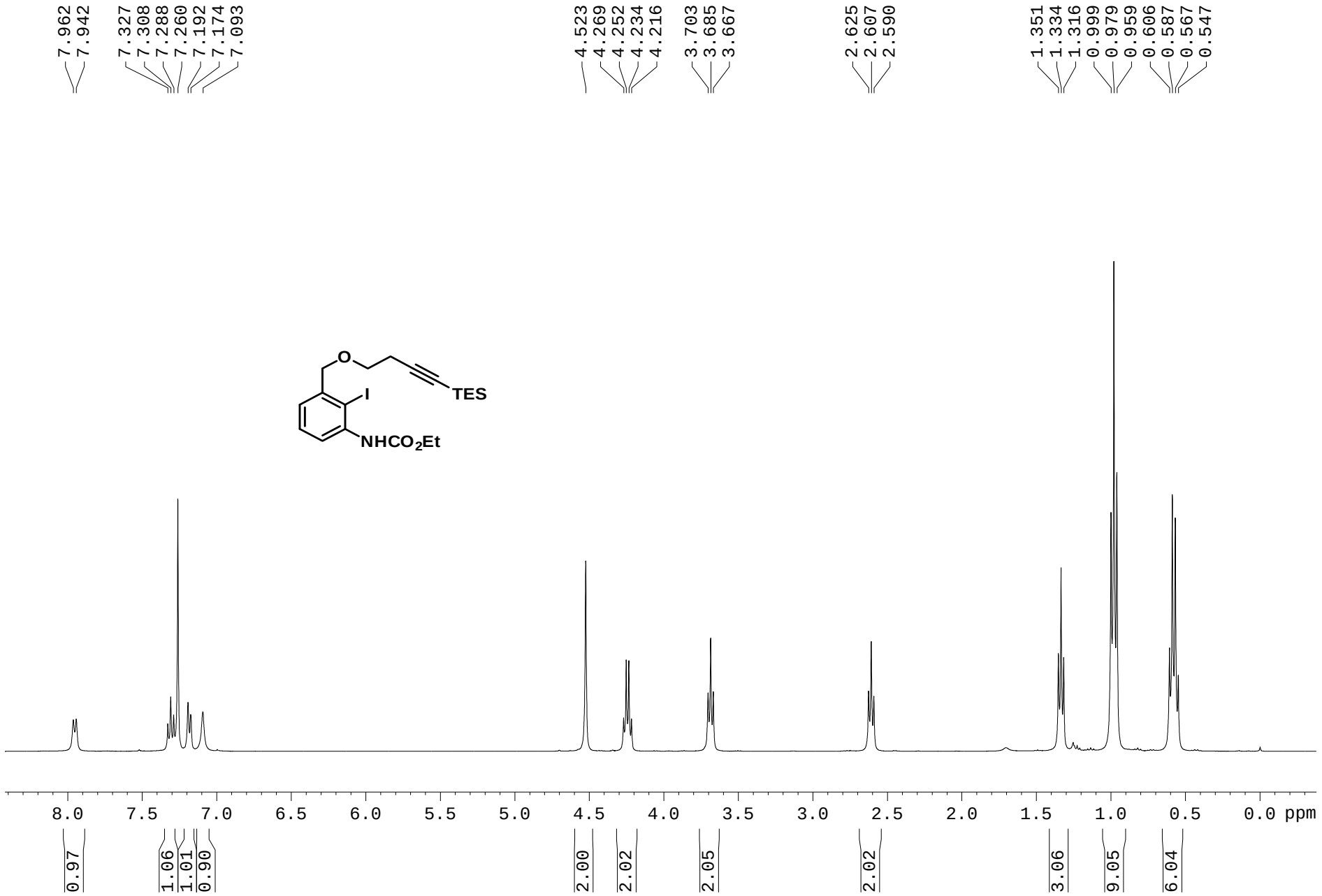
^{1}H NMR of compound 5i ($CDCl_3$, 600 MHz)



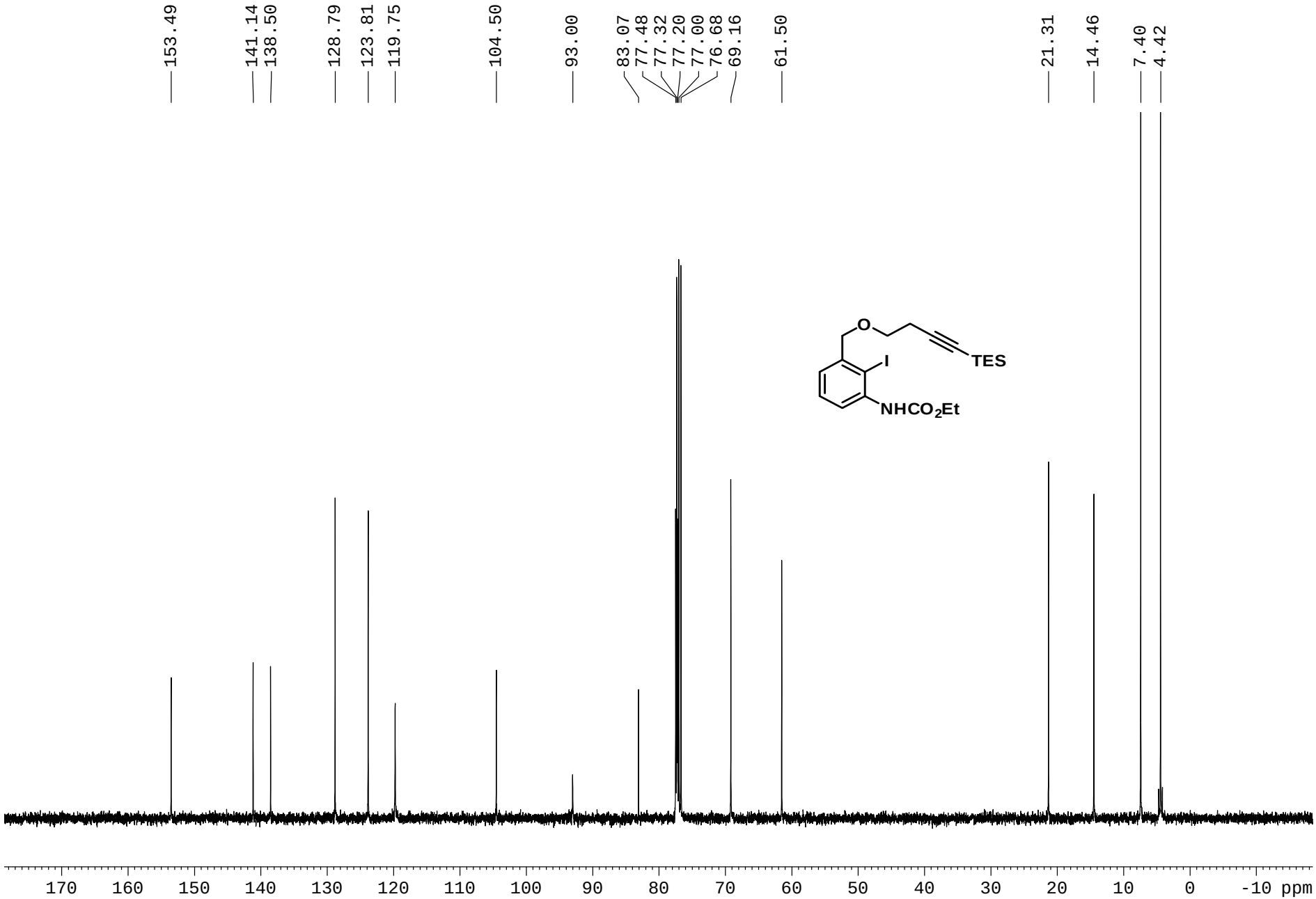
^{13}C NMR of compound 5i ($CDCl_3$, 100 MHz)



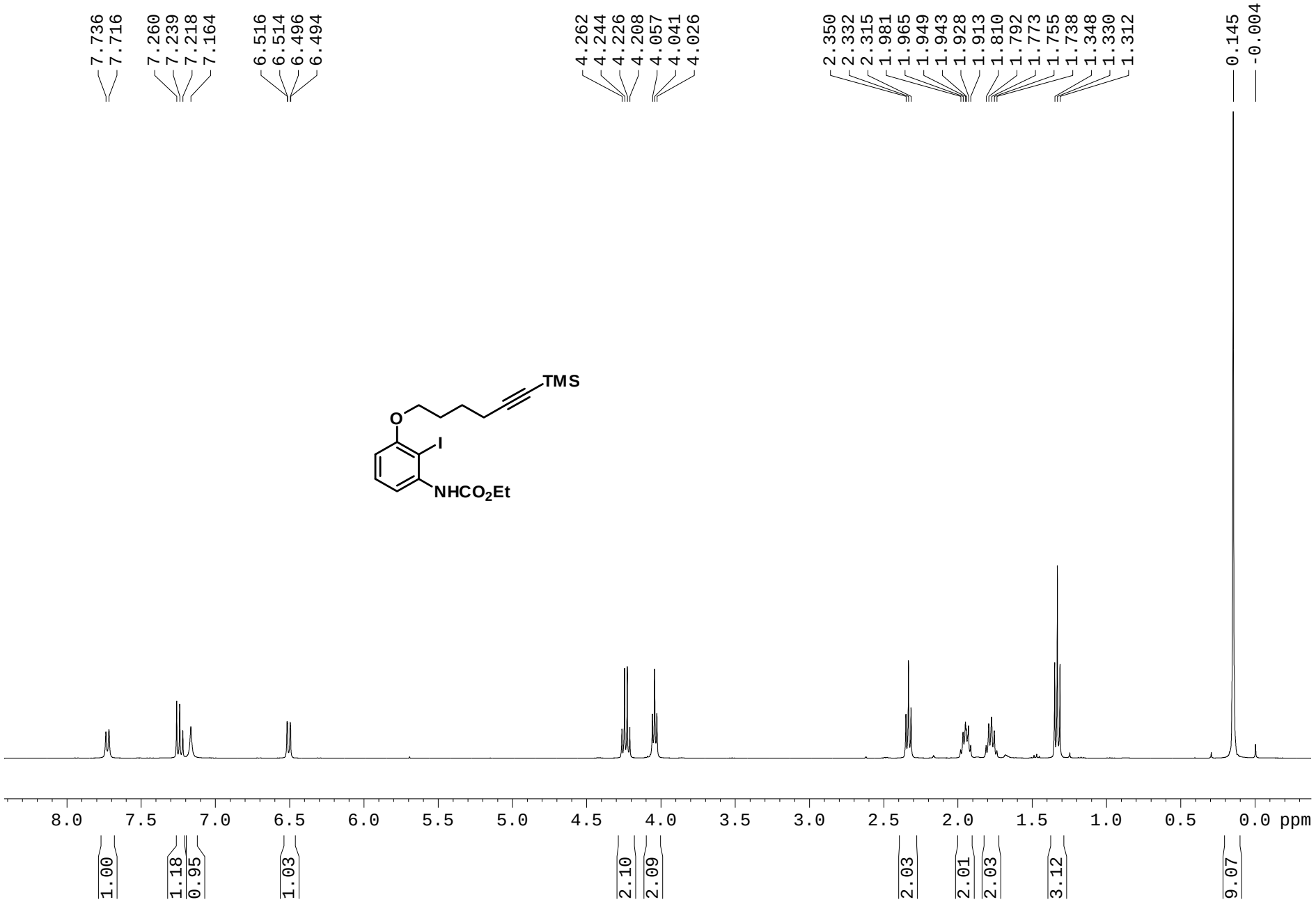
^{1}H NMR of compound 5j ($CDCl_3$, 400 MHz)



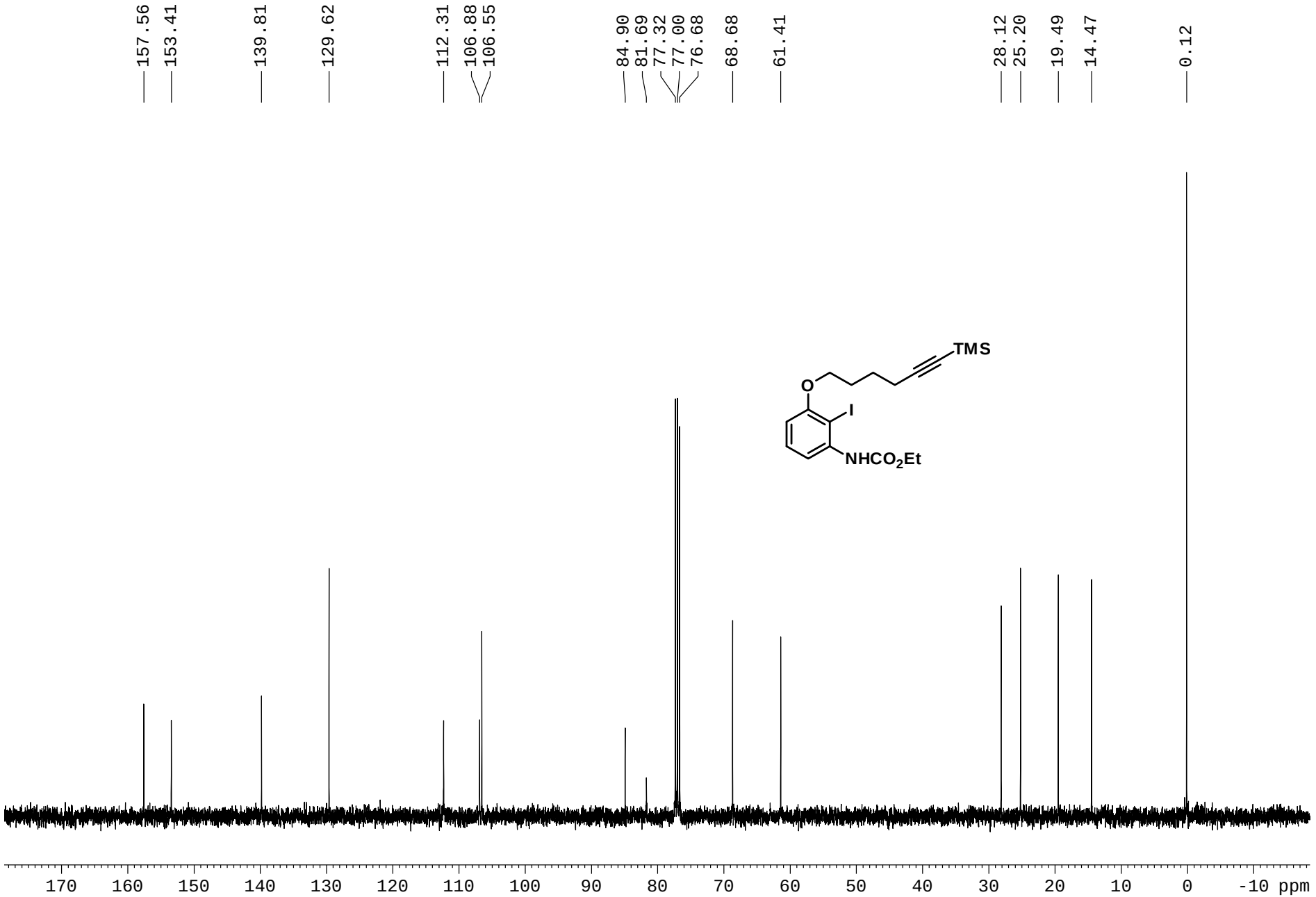
^{13}C NMR of compound 5j ($CDCl_3$, 100 MHz)



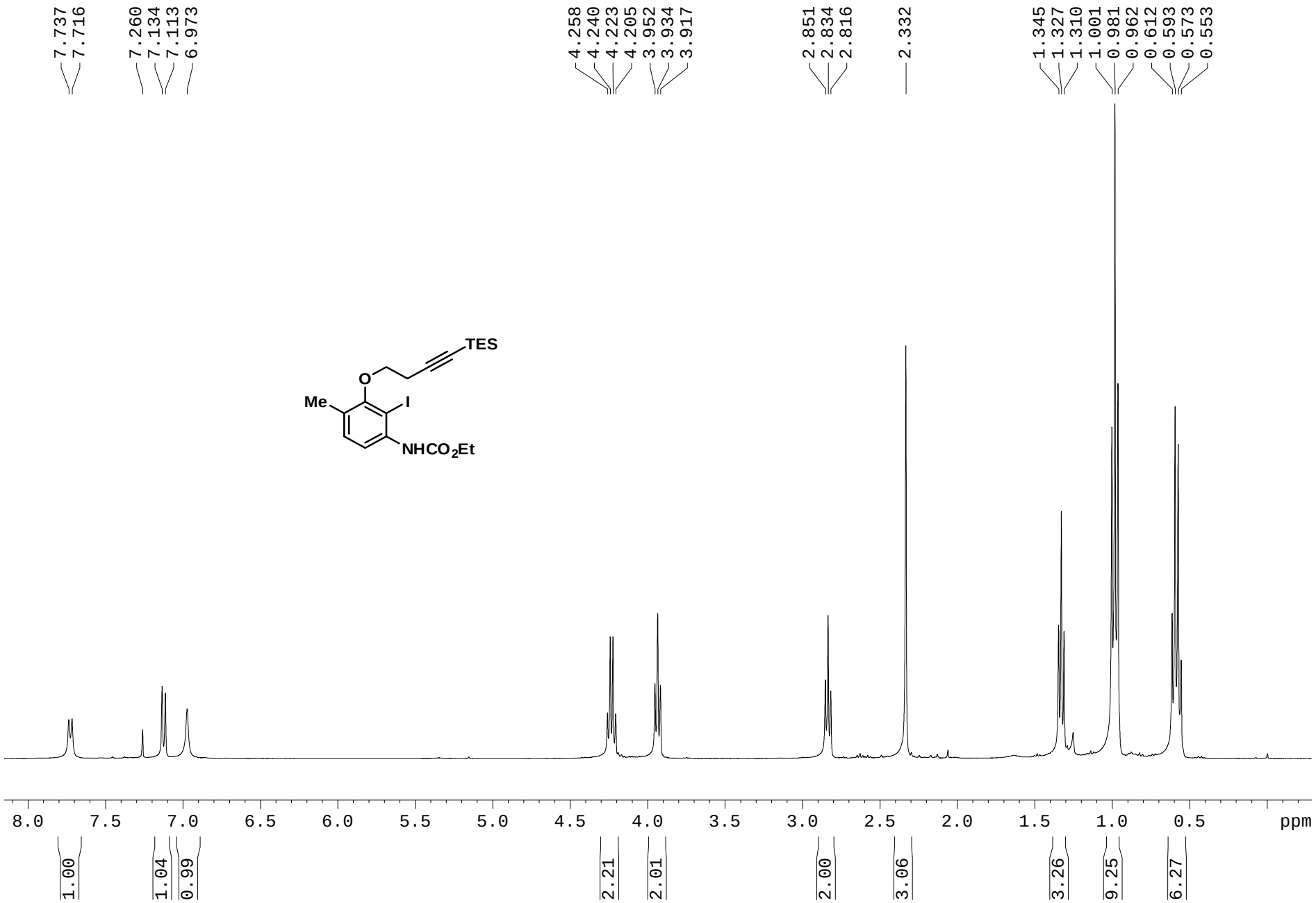
^{1}H NMR of compound 5k ($CDCl_3$, 400 MHz)



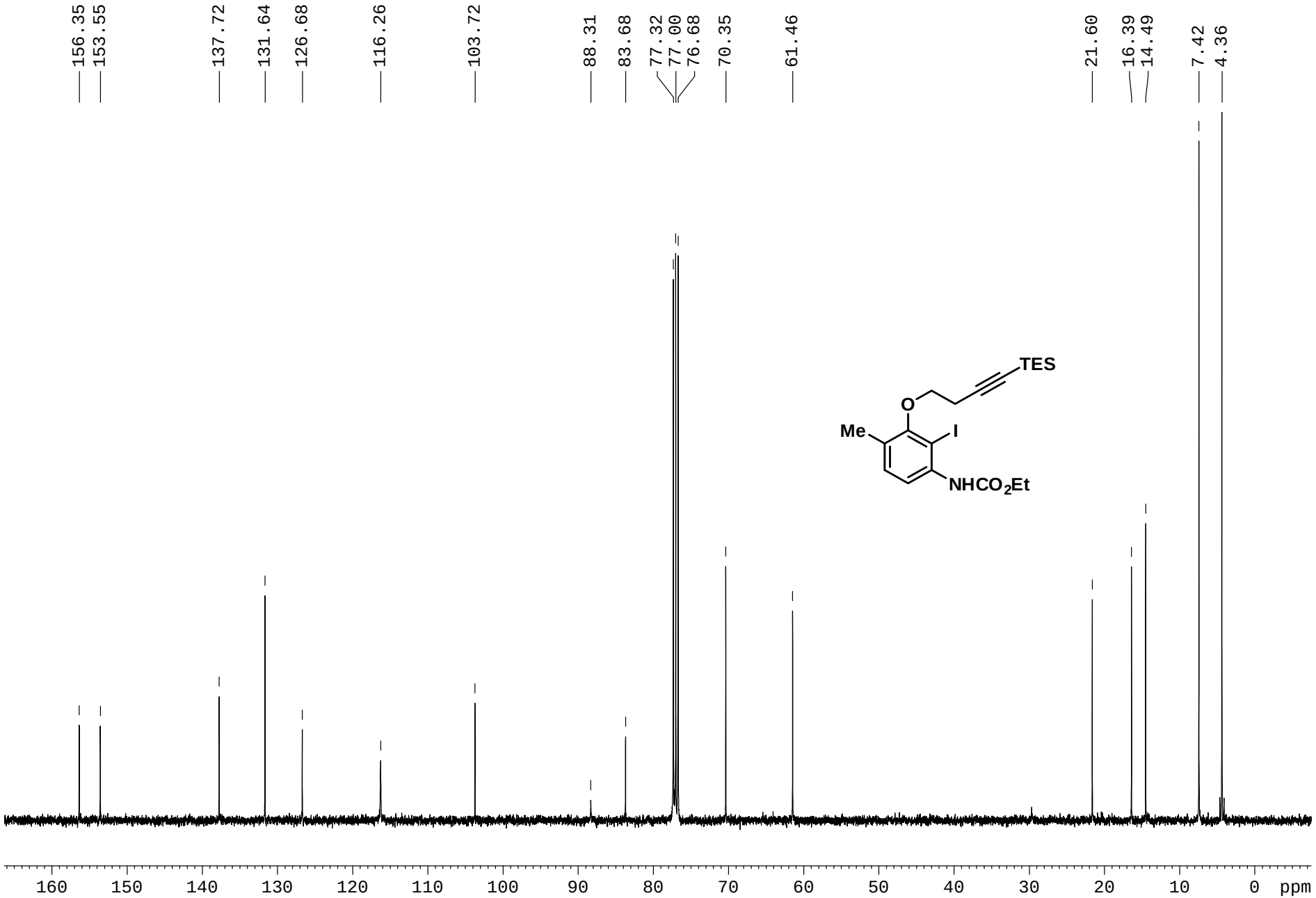
^{13}C NMR of compound 5k ($CDCl_3$, 100 MHz)



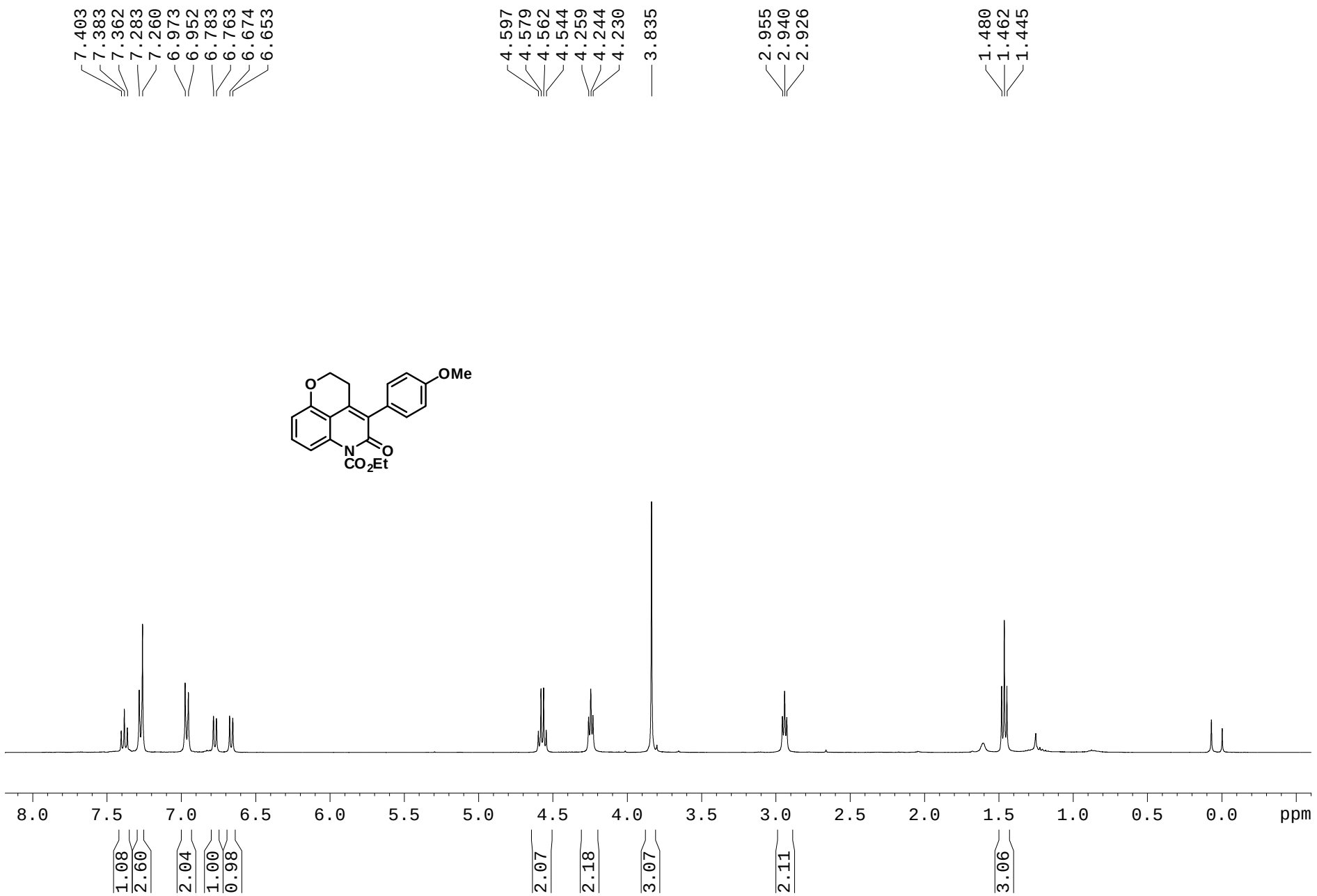
^{1}H NMR of compound 5l ($CDCl_3$, 400 MHz)



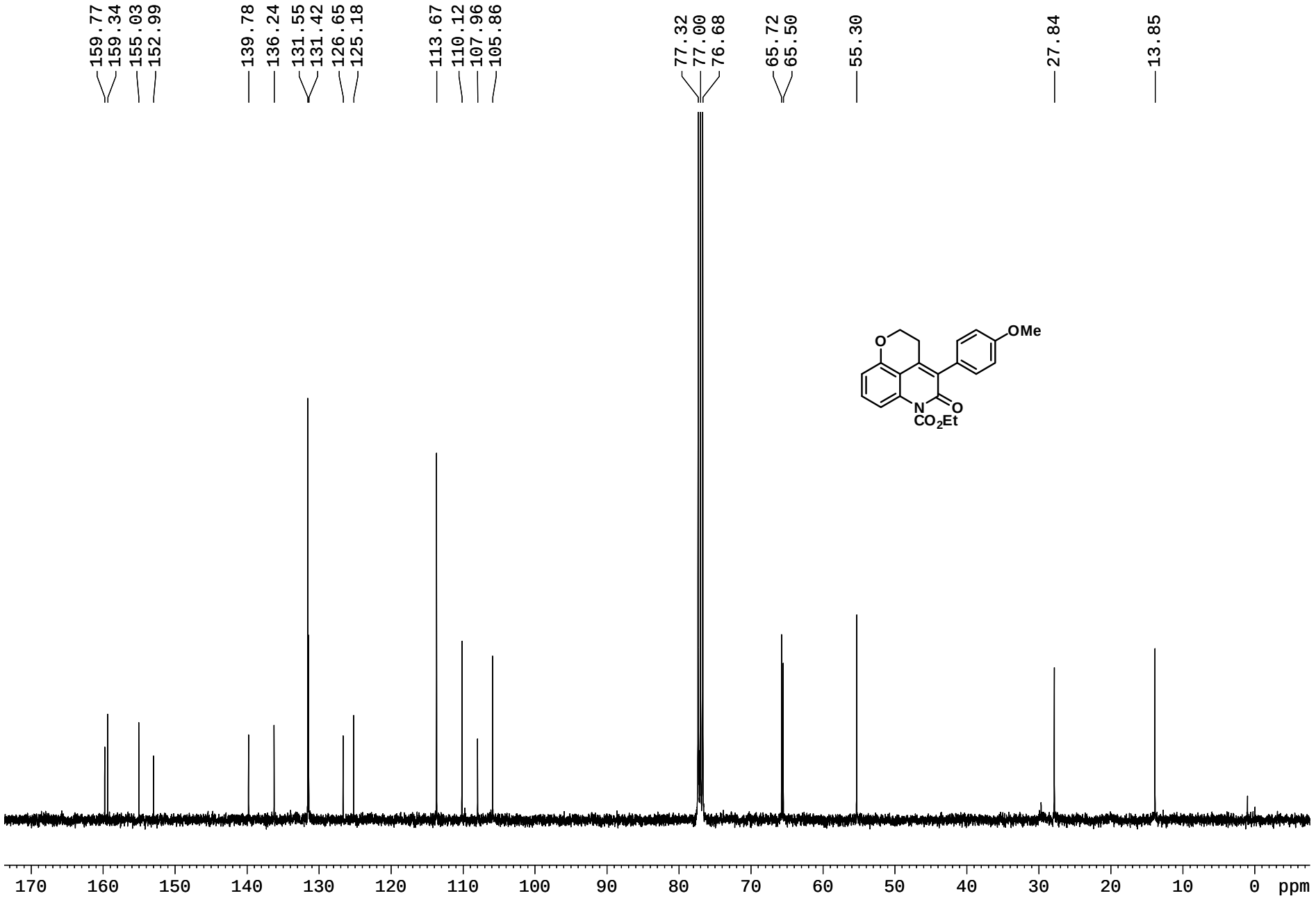
^{13}C NMR of compound 5l ($CDCl_3$, 100 MHz)



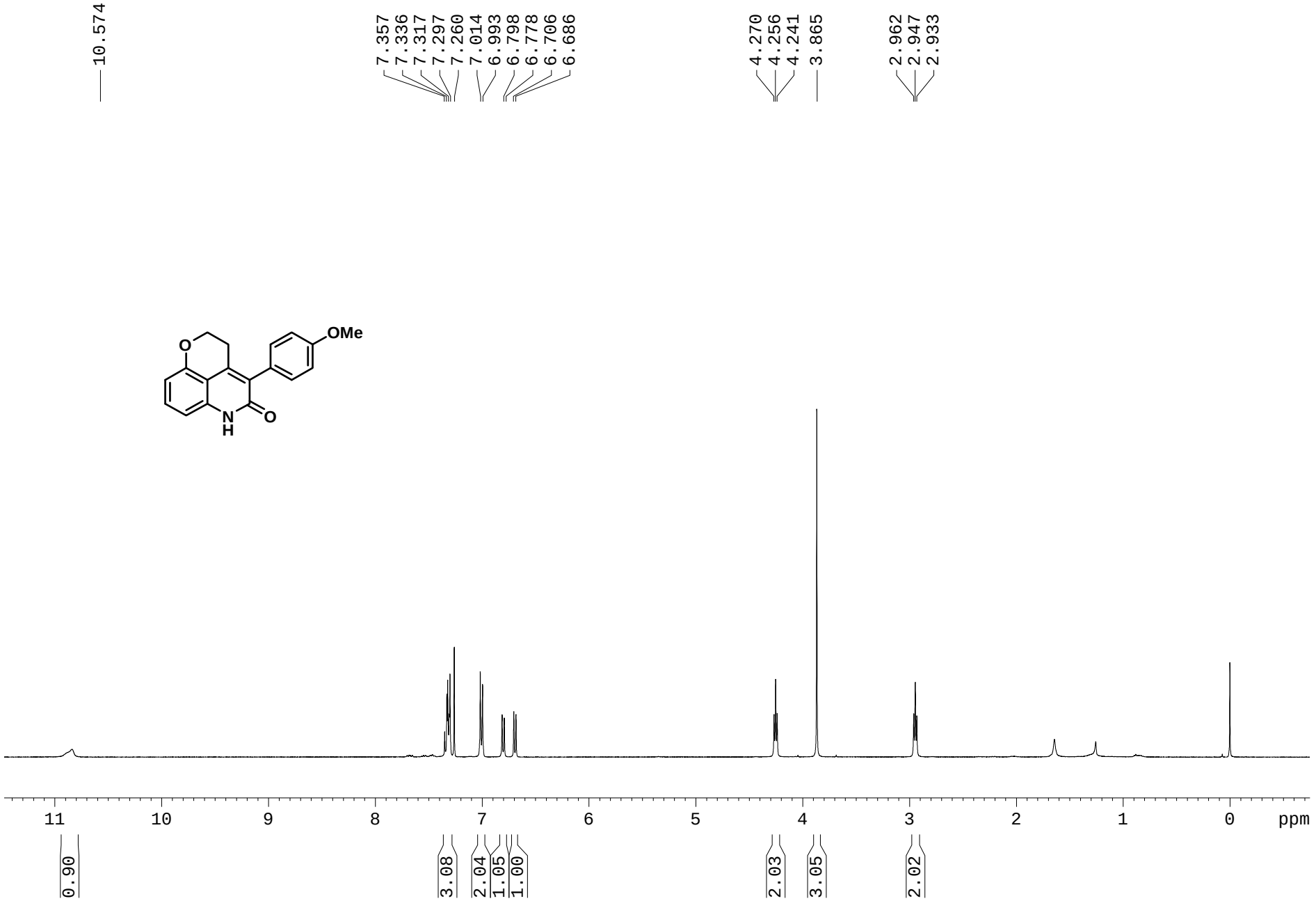
^{1}H NMR of compound 6a ($CDCl_3$, 400 MHz)



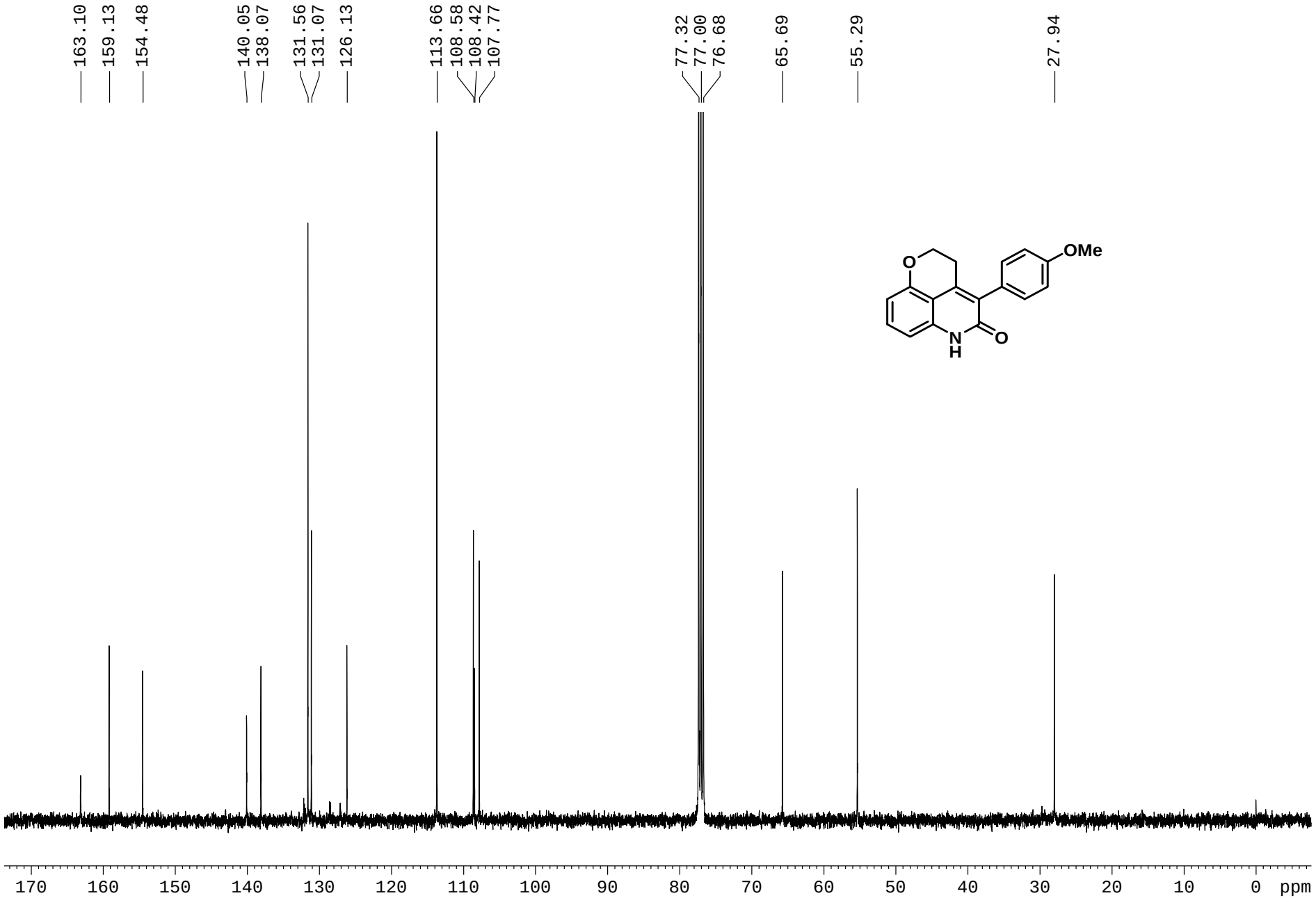
^{13}C NMR of compound 6a ($CDCl_3$, 100 MHz)



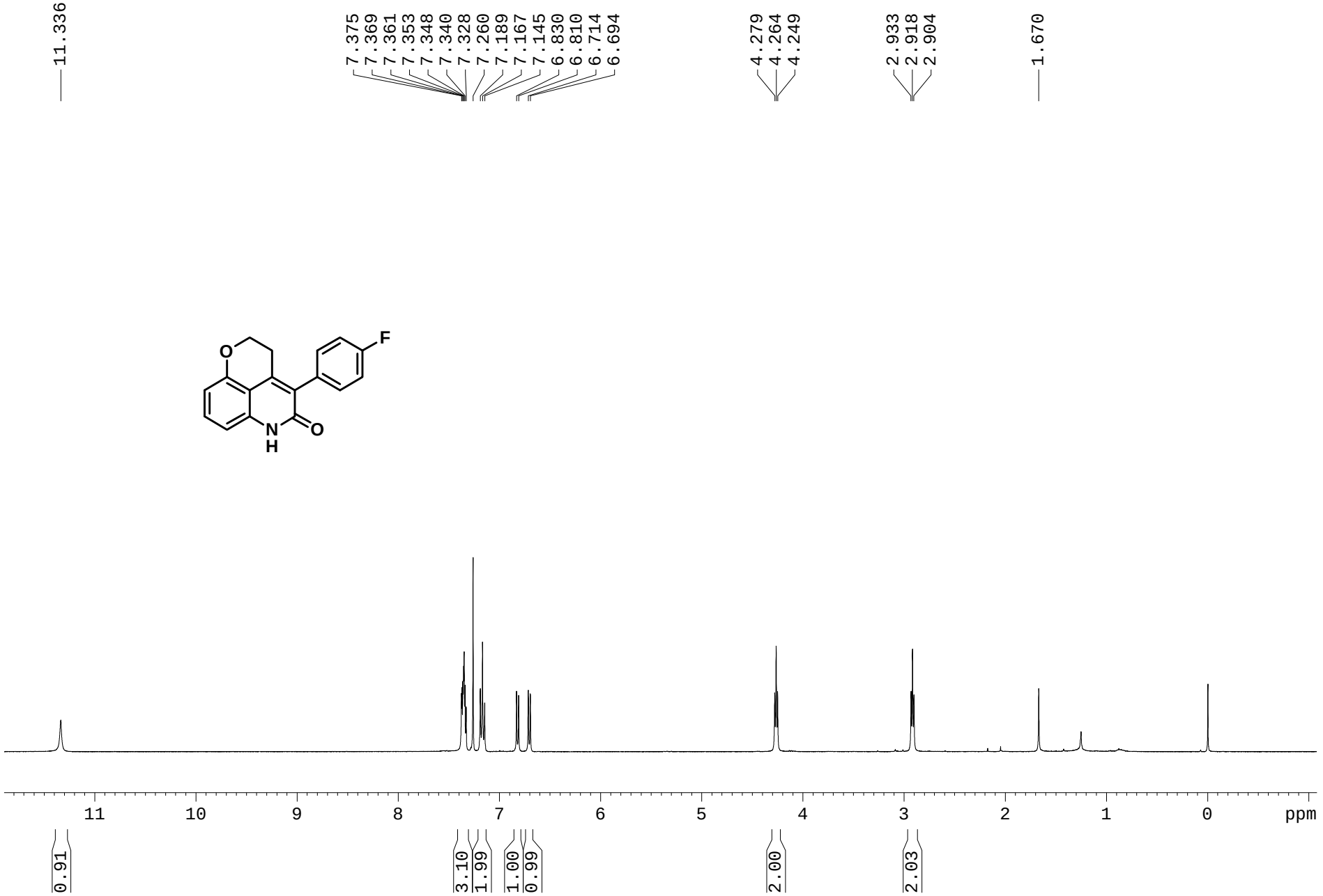
^{1}H NMR of compound 7a ($CDCl_3$, 400 MHz)



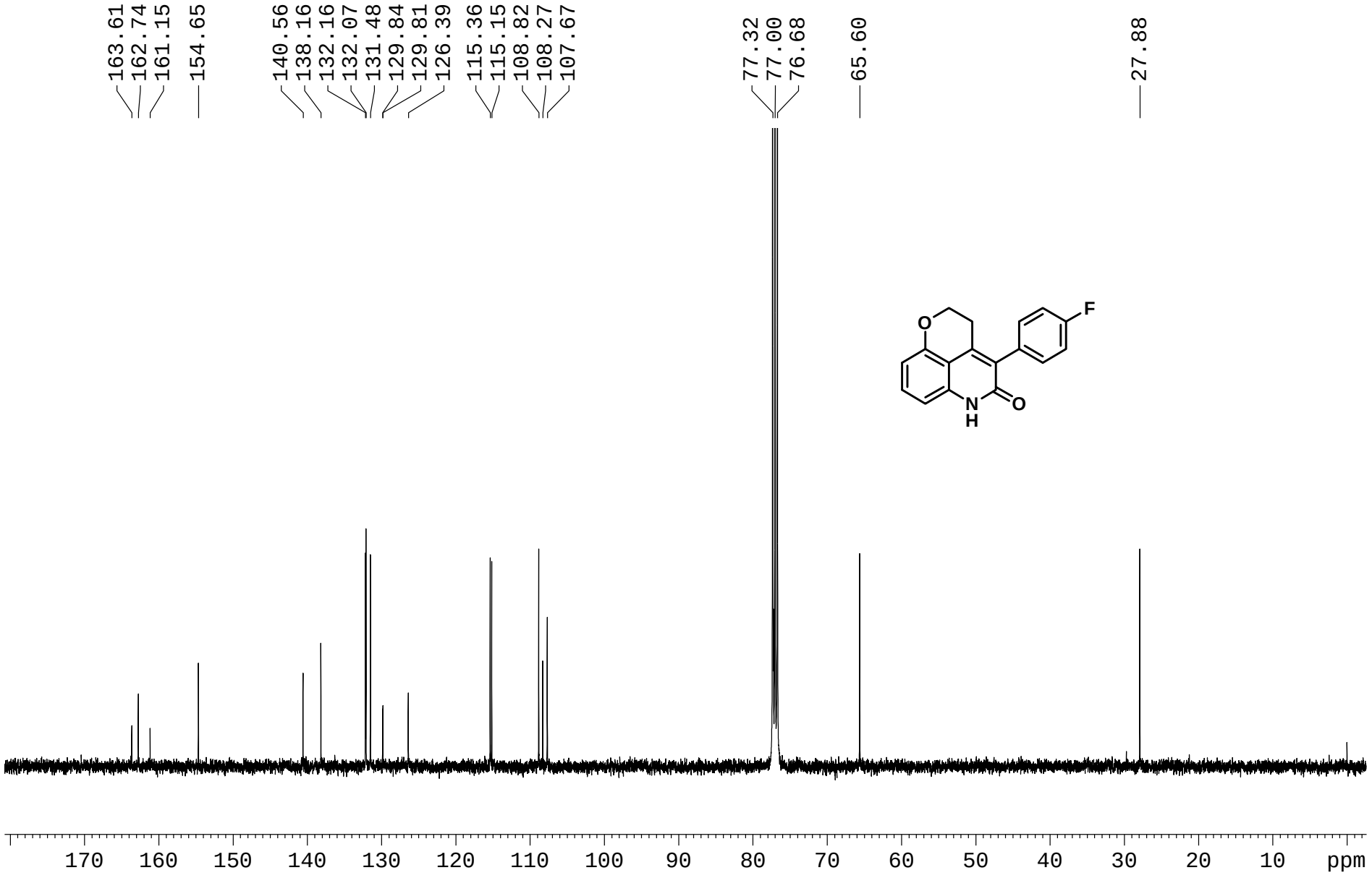
^{13}C NMR of compound 7a ($CDCl_3$, 100 MHz)



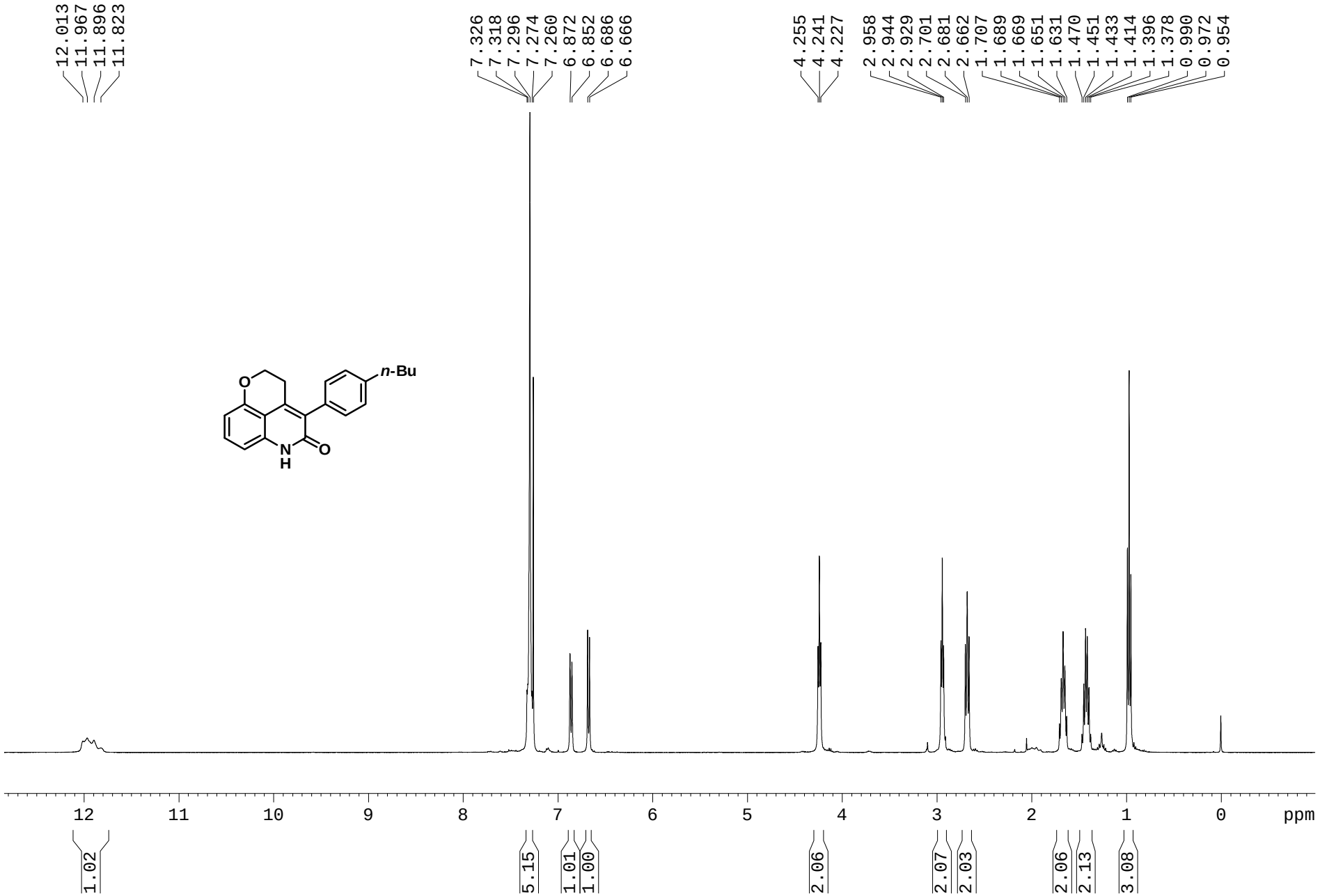
^{1}H NMR of compound 7b ($CDCl_3$, 400 MHz)



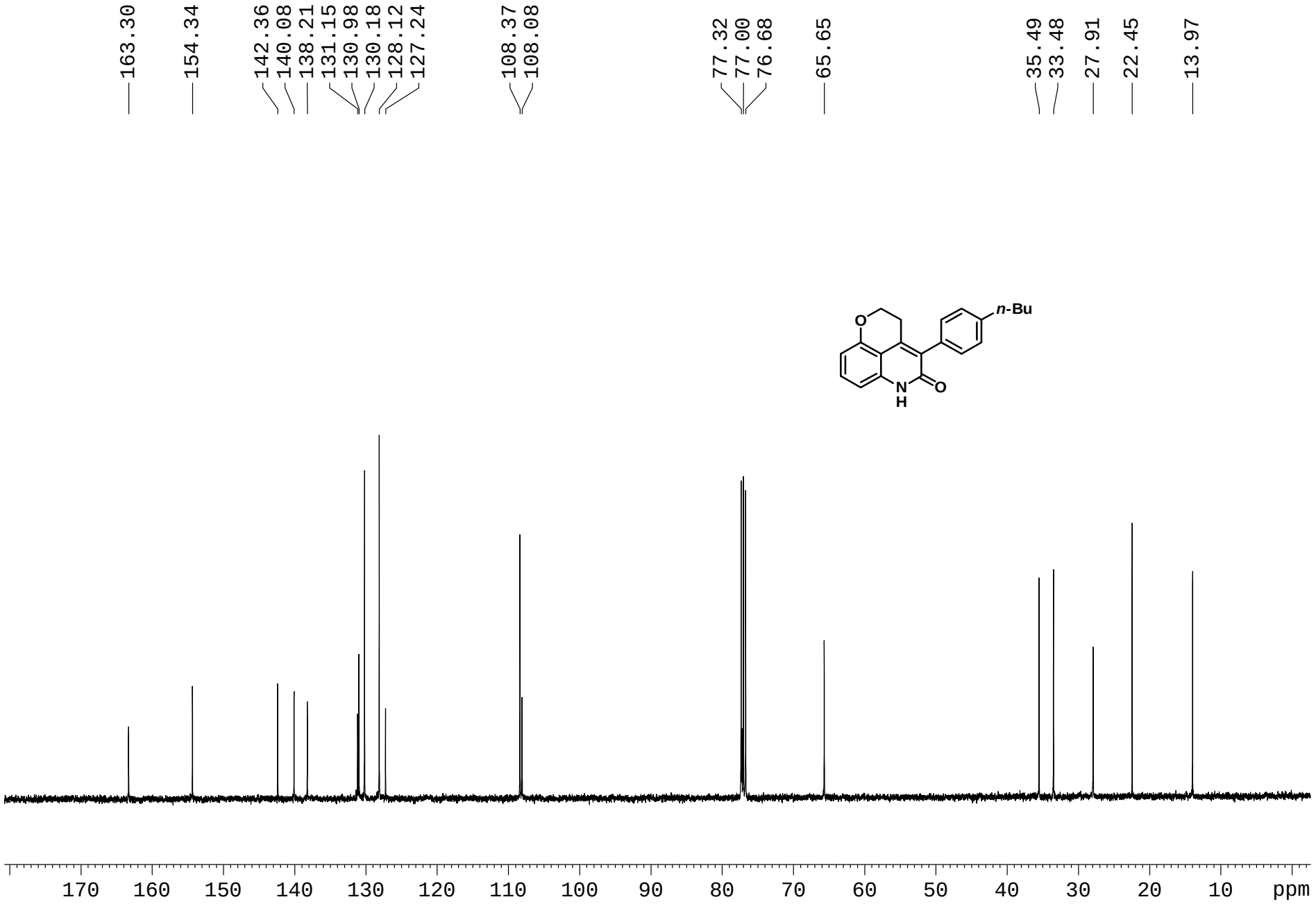
^{13}C NMR of compound 7b ($CDCl_3$, 100 MHz)



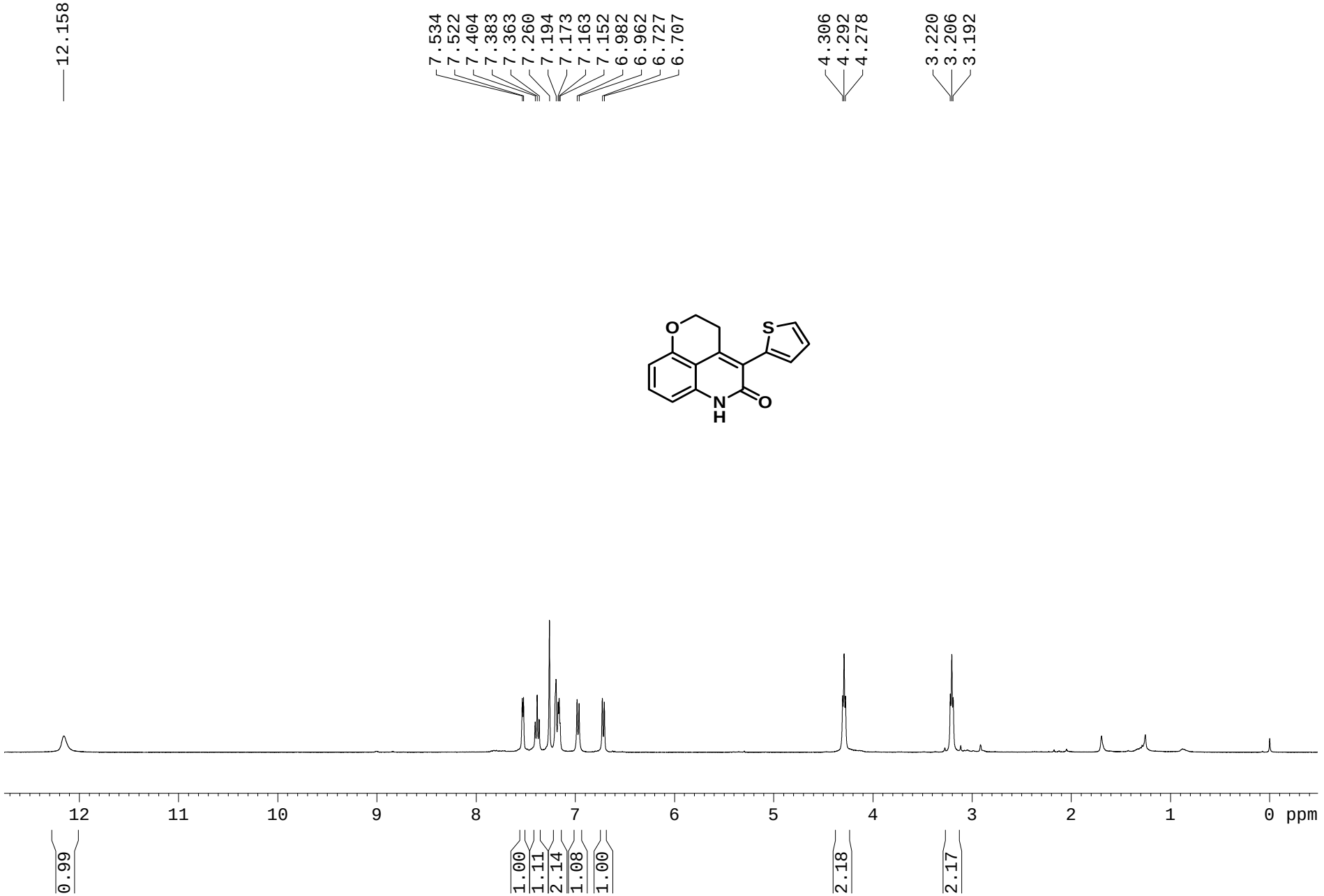
^{1}H NMR of compound 7c ($CDCl_3$, 400 MHz)



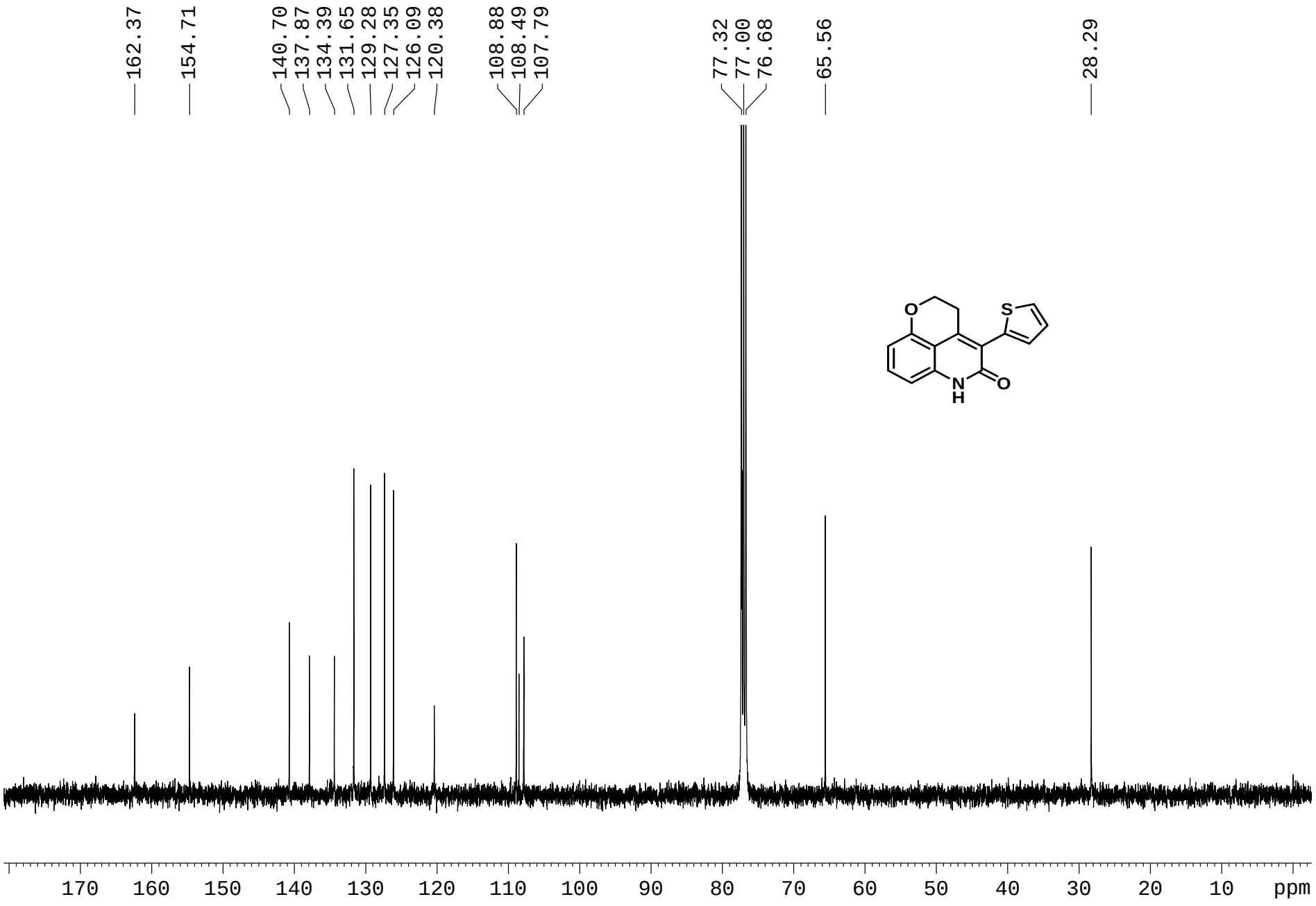
^{13}C NMR of compound 7c ($CDCl_3$, 100 MHz)



^{1}H NMR of compound 7d ($CDCl_3$, 400 MHz)



^{13}C NMR of compound 7d ($CDCl_3$, 100 MHz)



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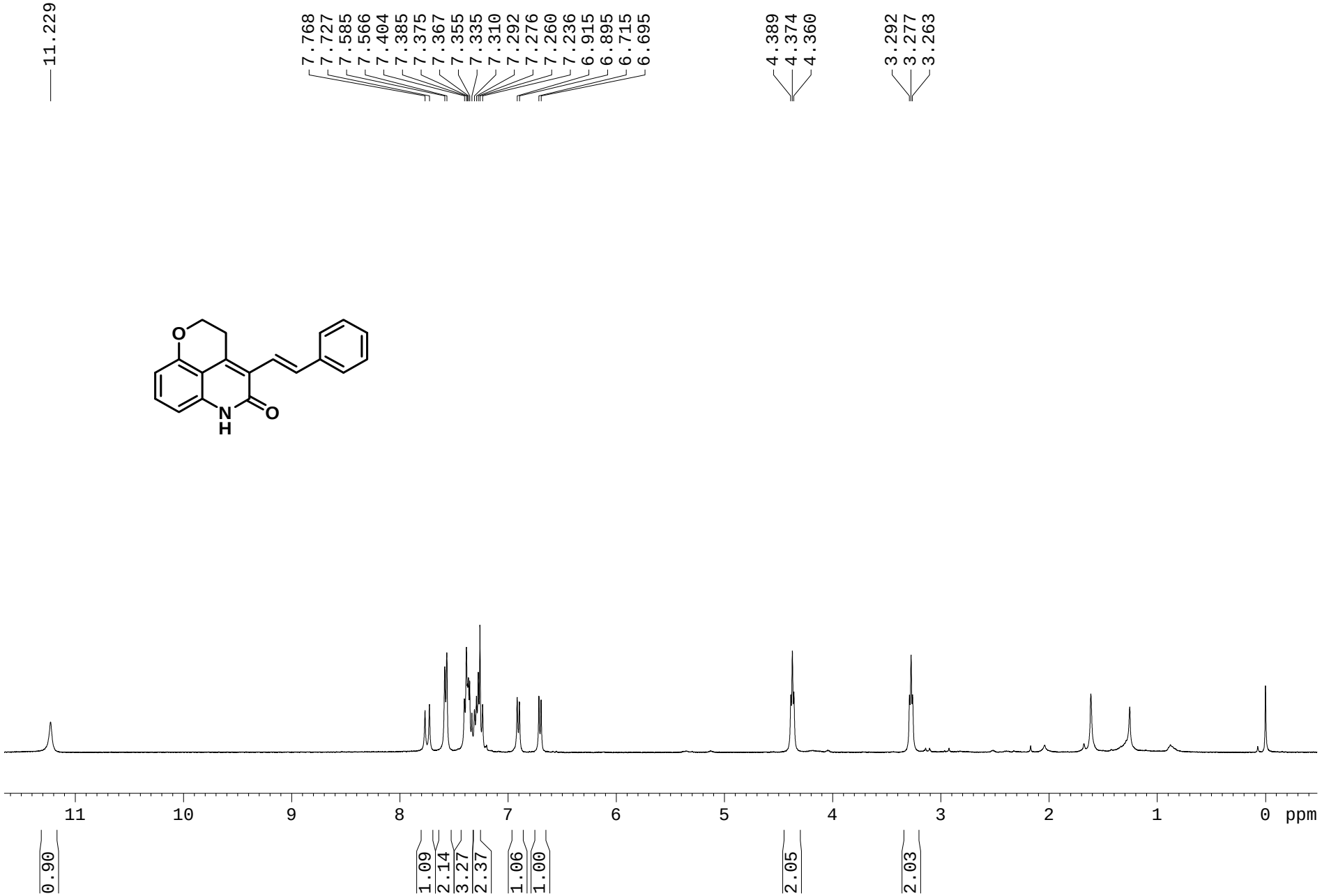
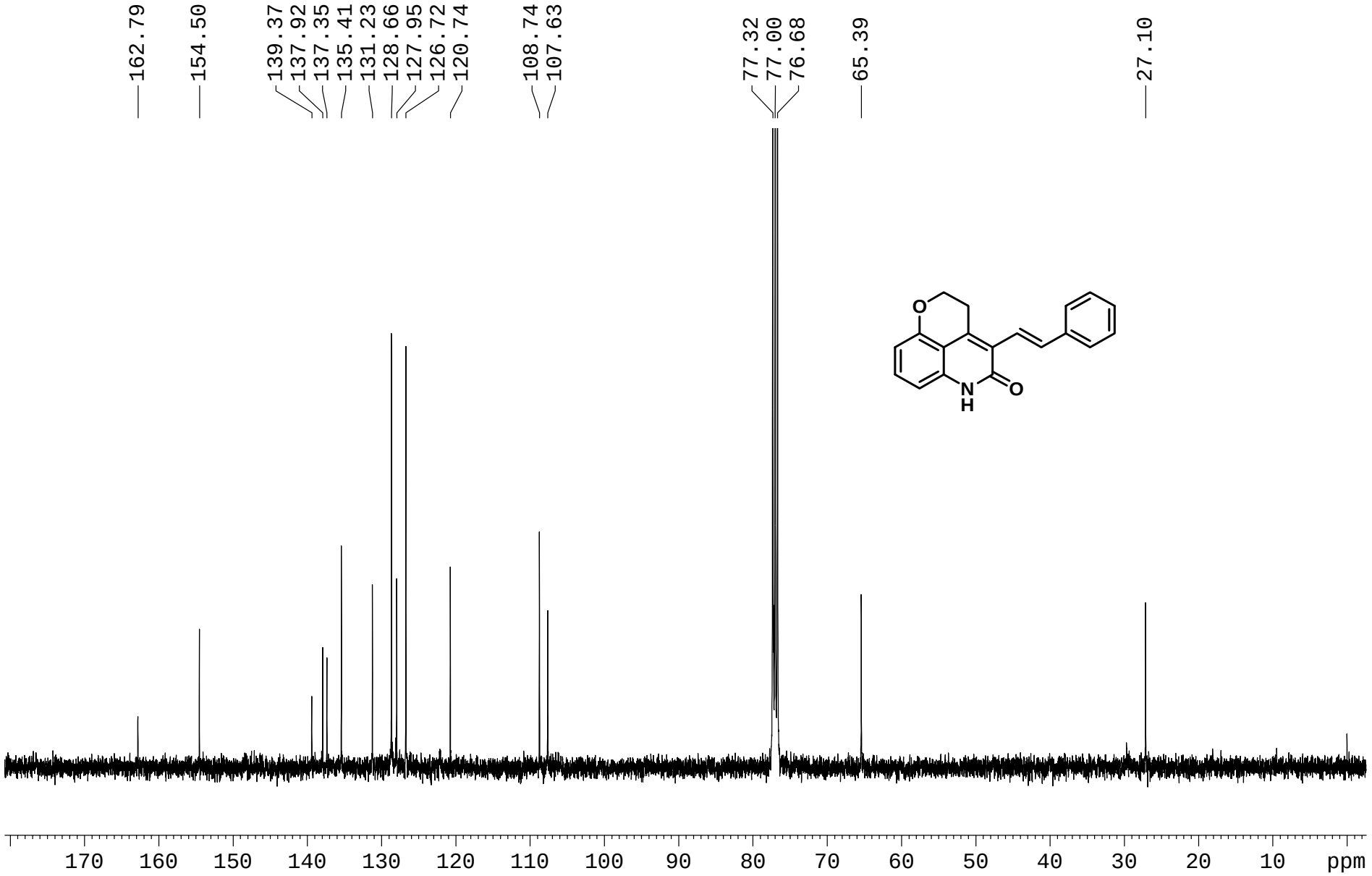
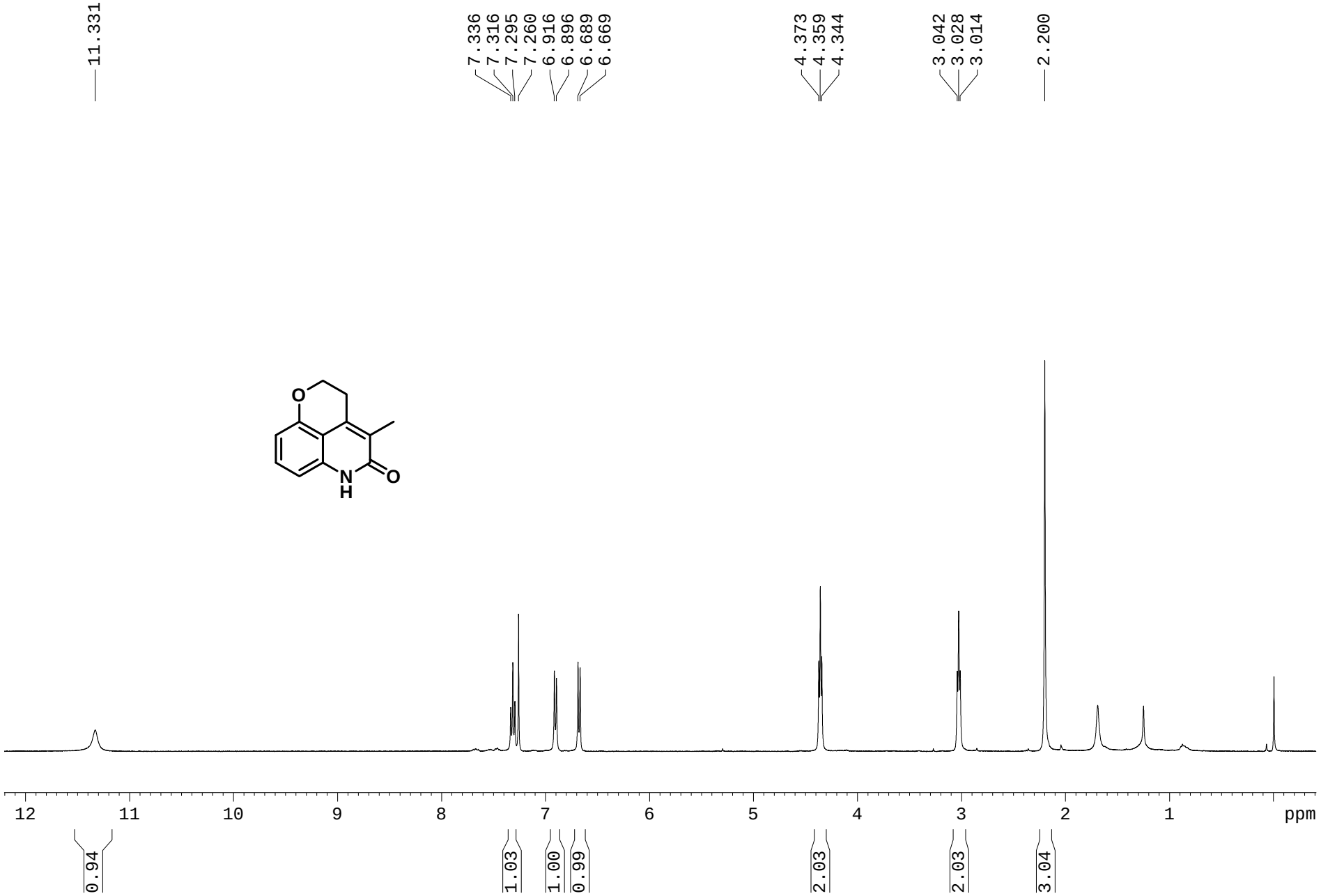


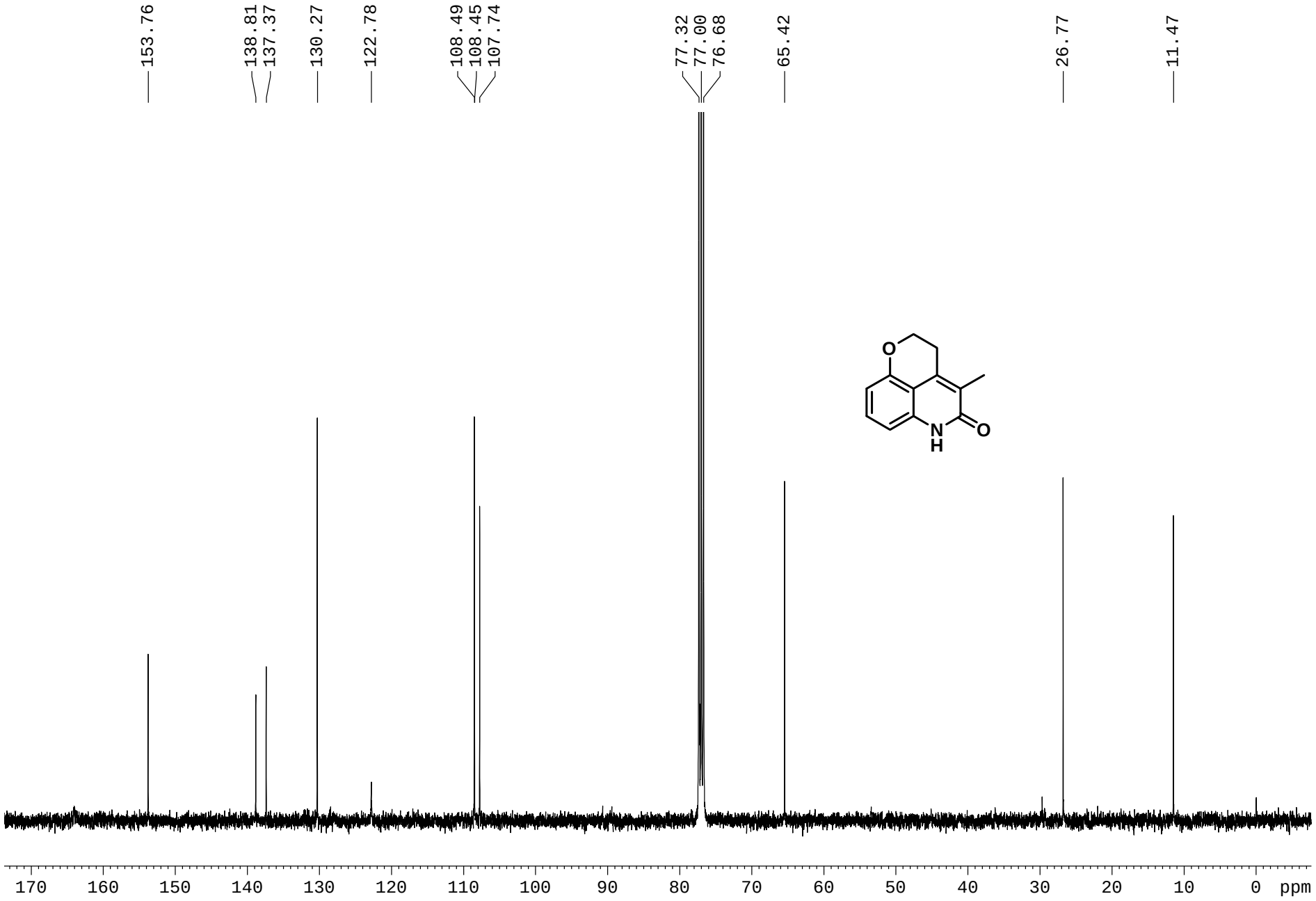
^{13}C NMR of compound 7e ($CDCl_3$, 100 MHz)



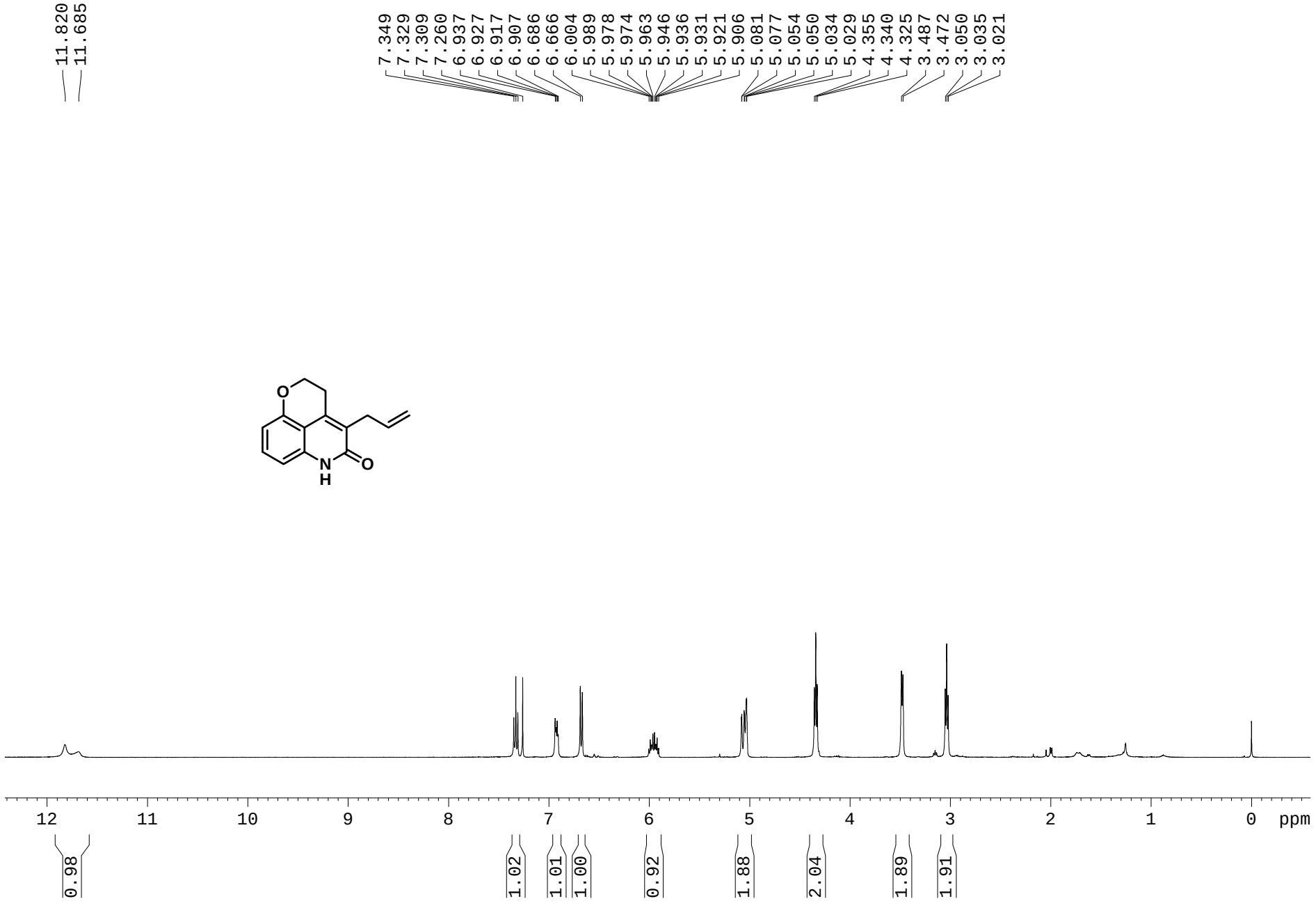
^{1}H NMR of compound 7f ($CDCl_3$, 400 MHz)



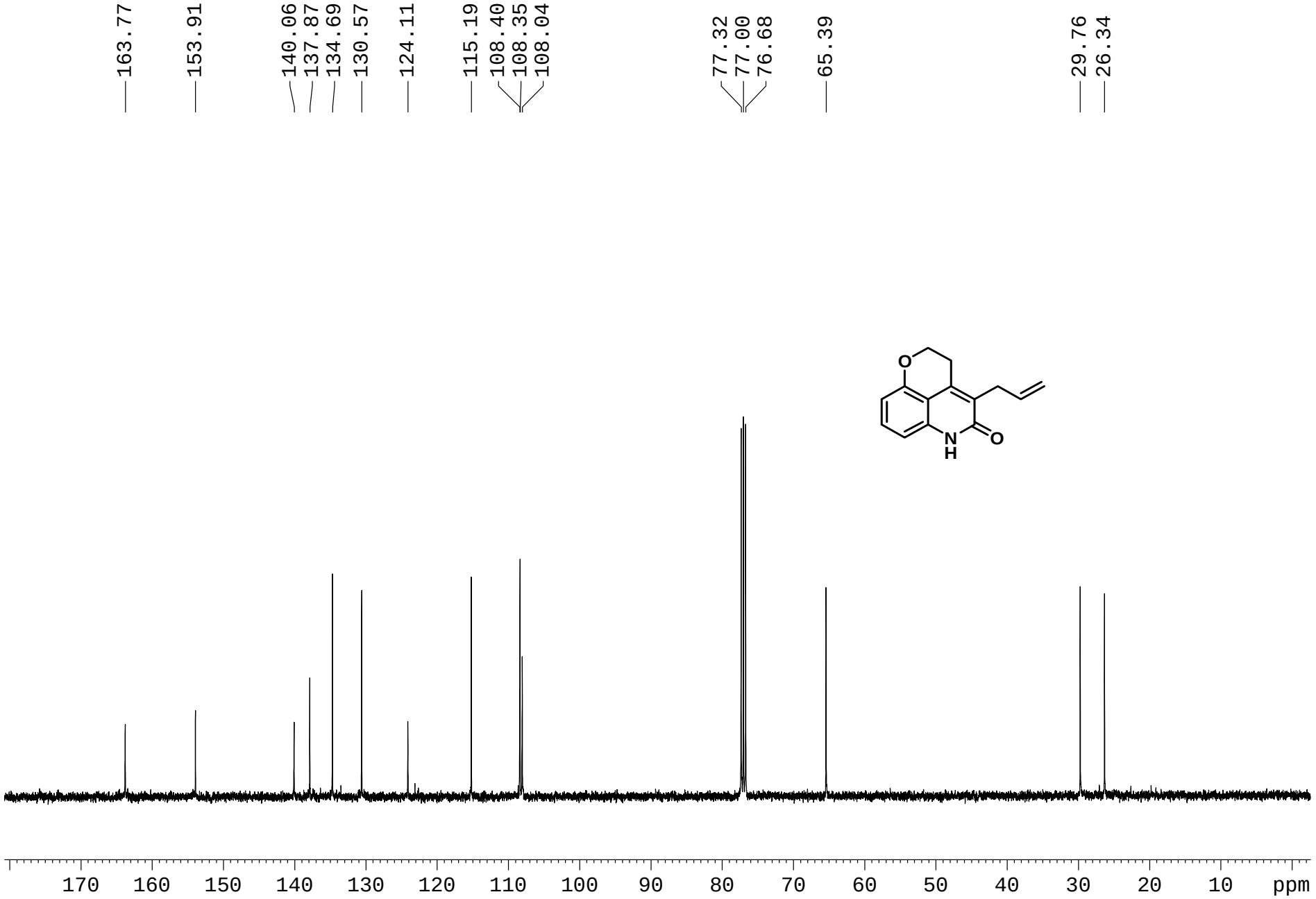
^{13}C NMR of compound 7f ($CDCl_3$, 100 MHz)



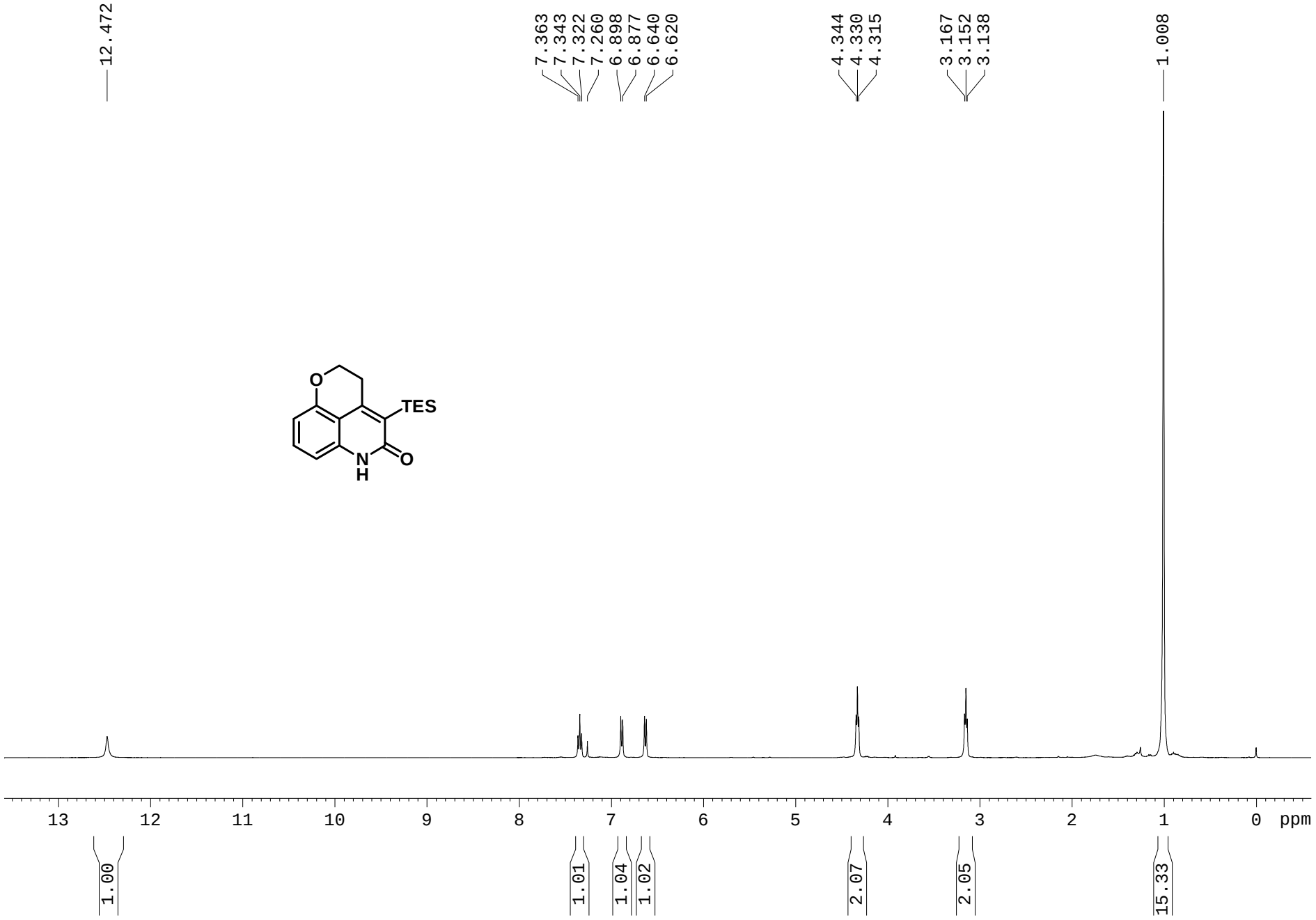
^{1}H NMR of compound 7g ($CDCl_3$, 400 MHz)



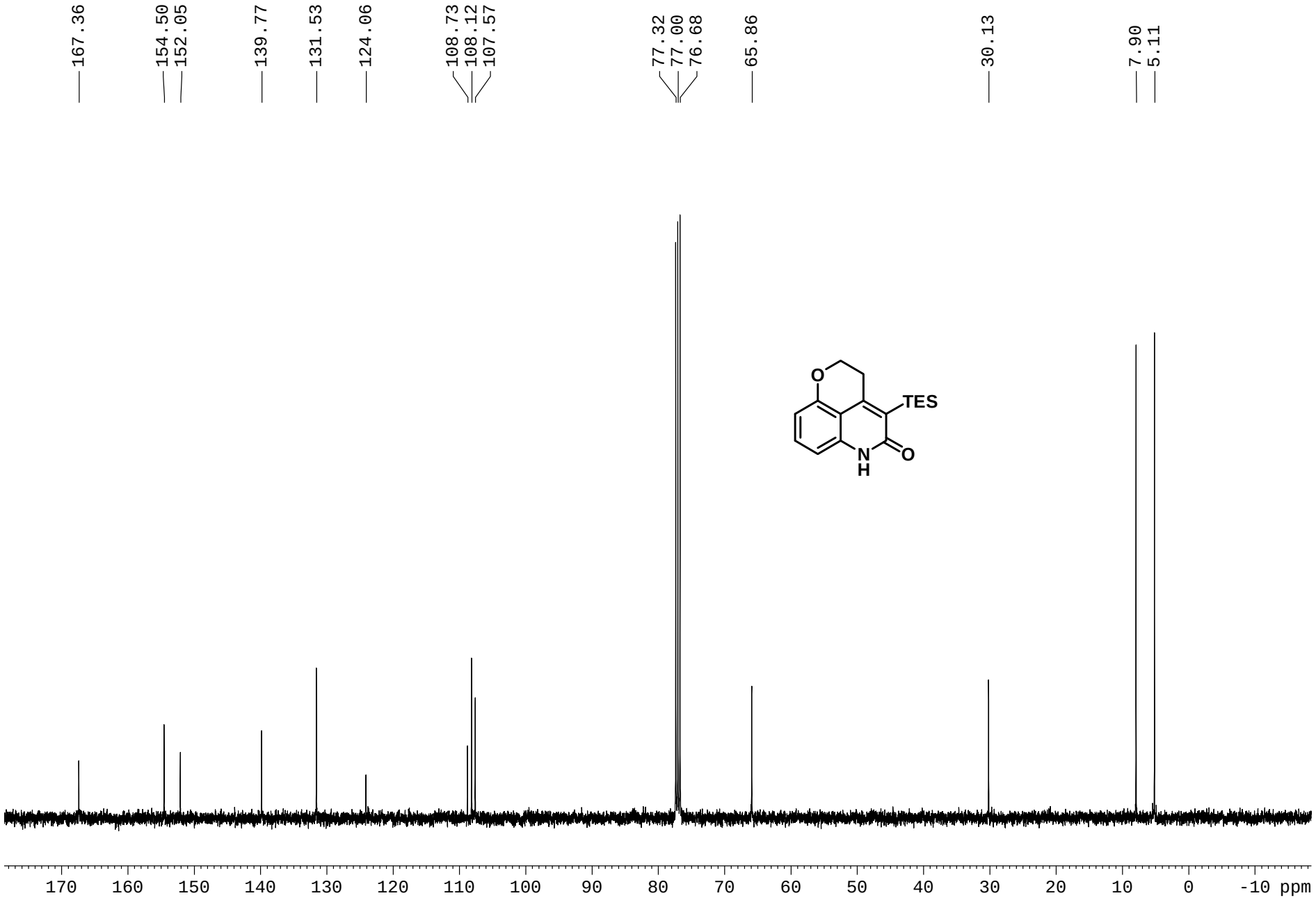
^{13}C NMR of compound 7g ($CDCl_3$, 100 MHz)



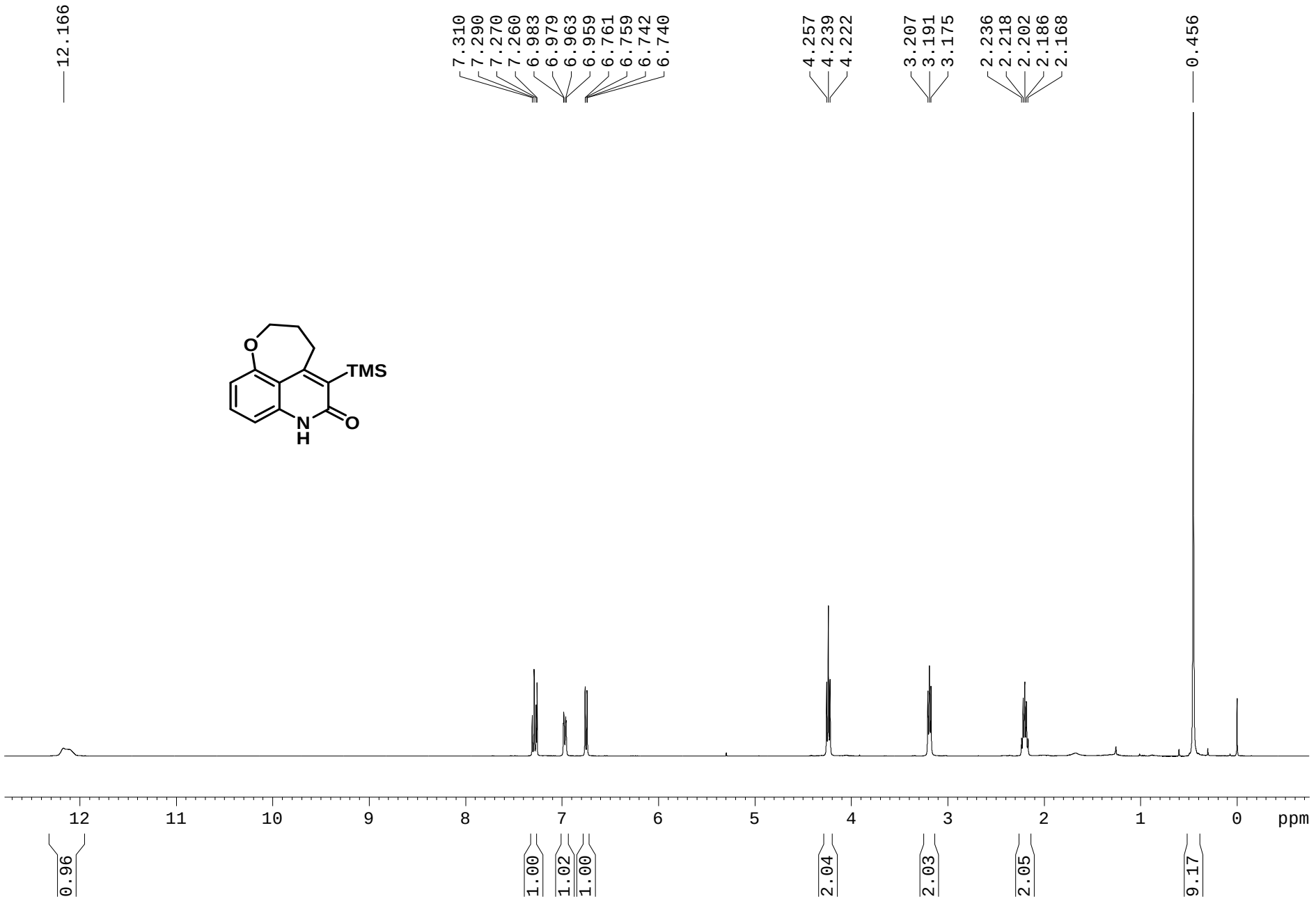
^{1}H NMR of compound 7h ($CDCl_3$, 400 MHz)



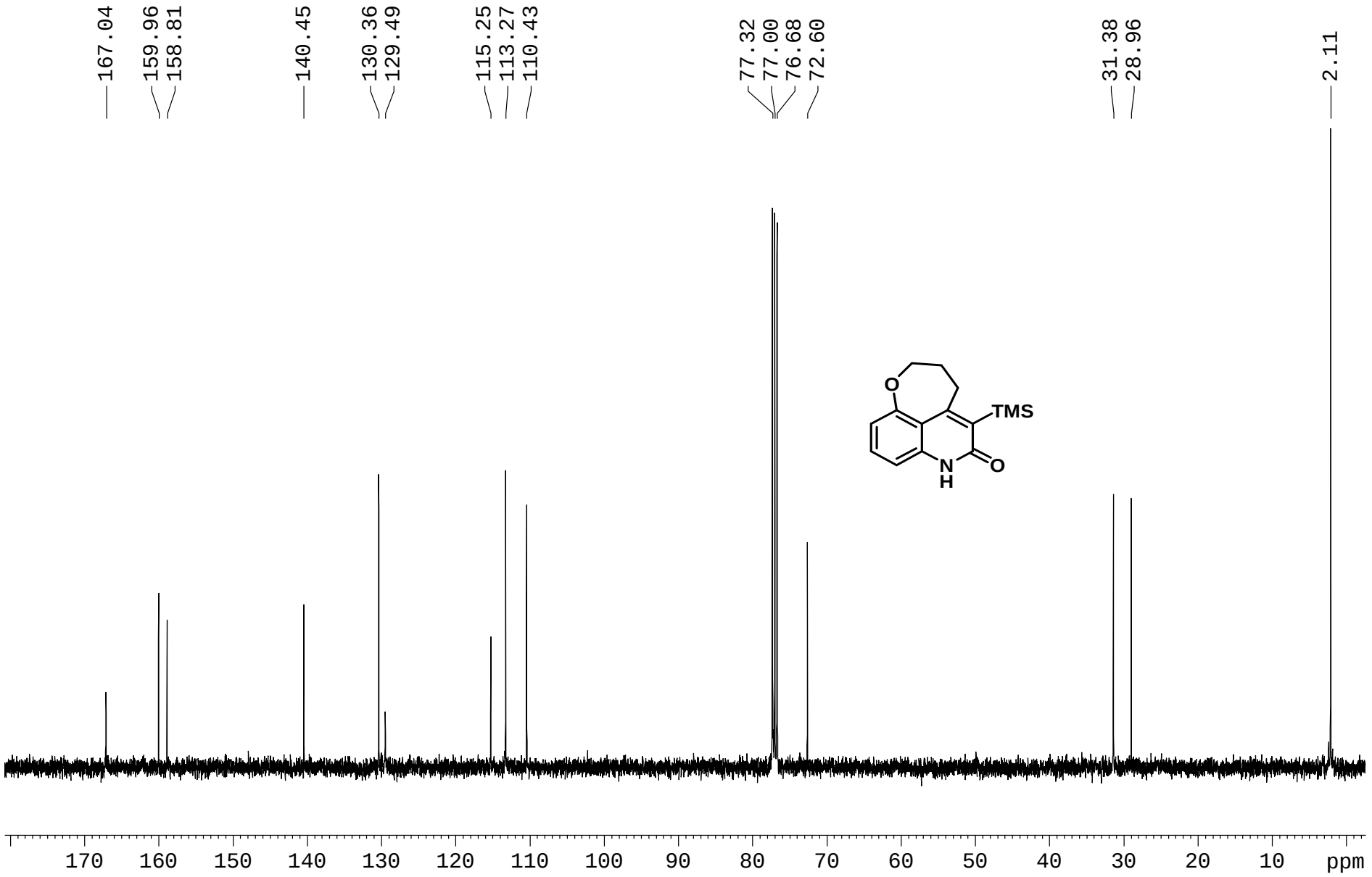
^{13}C NMR of compound 7h ($CDCl_3$, 100 MHz)



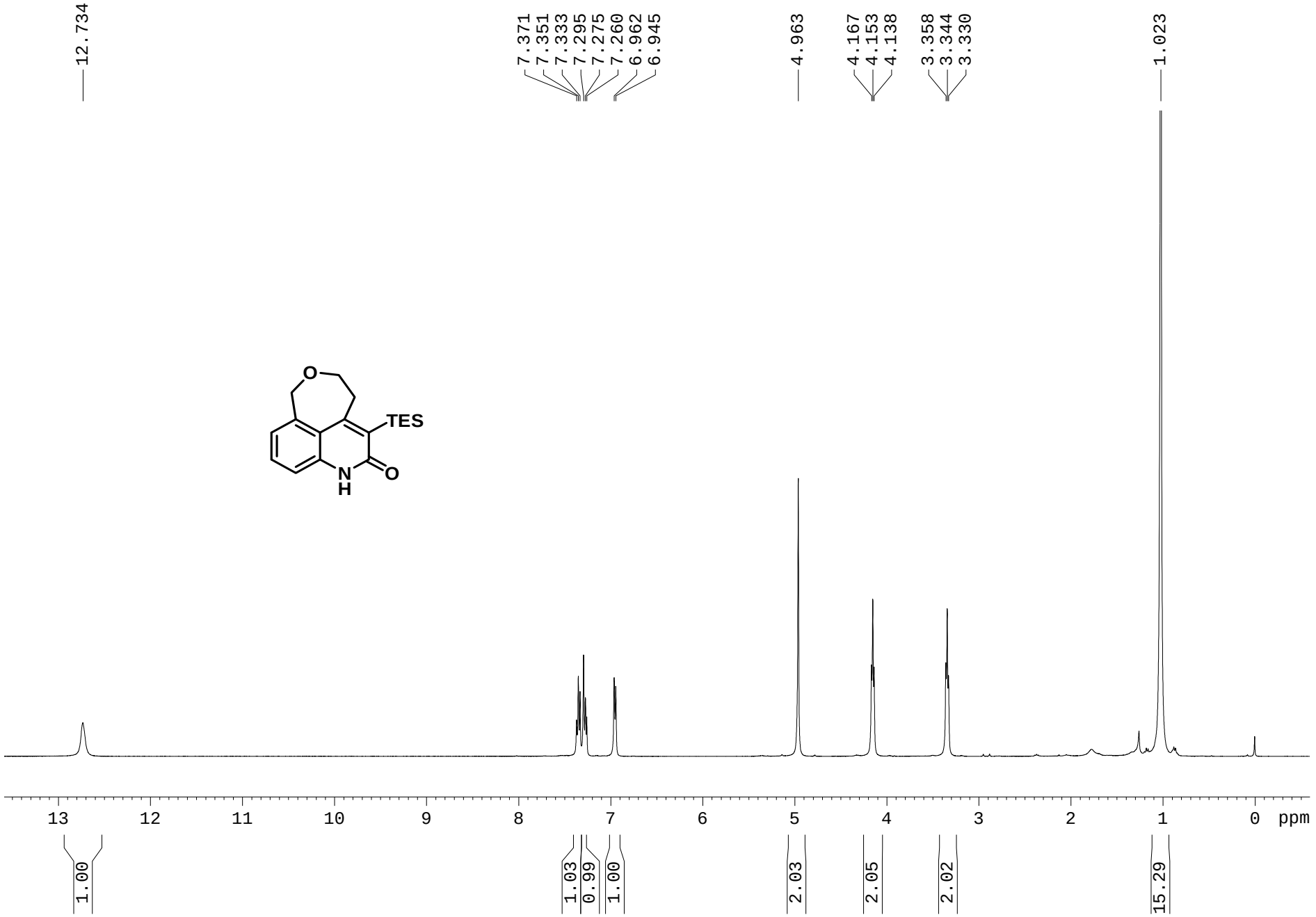
^{1}H NMR of compound 7i ($CDCl_3$, 400 MHz)



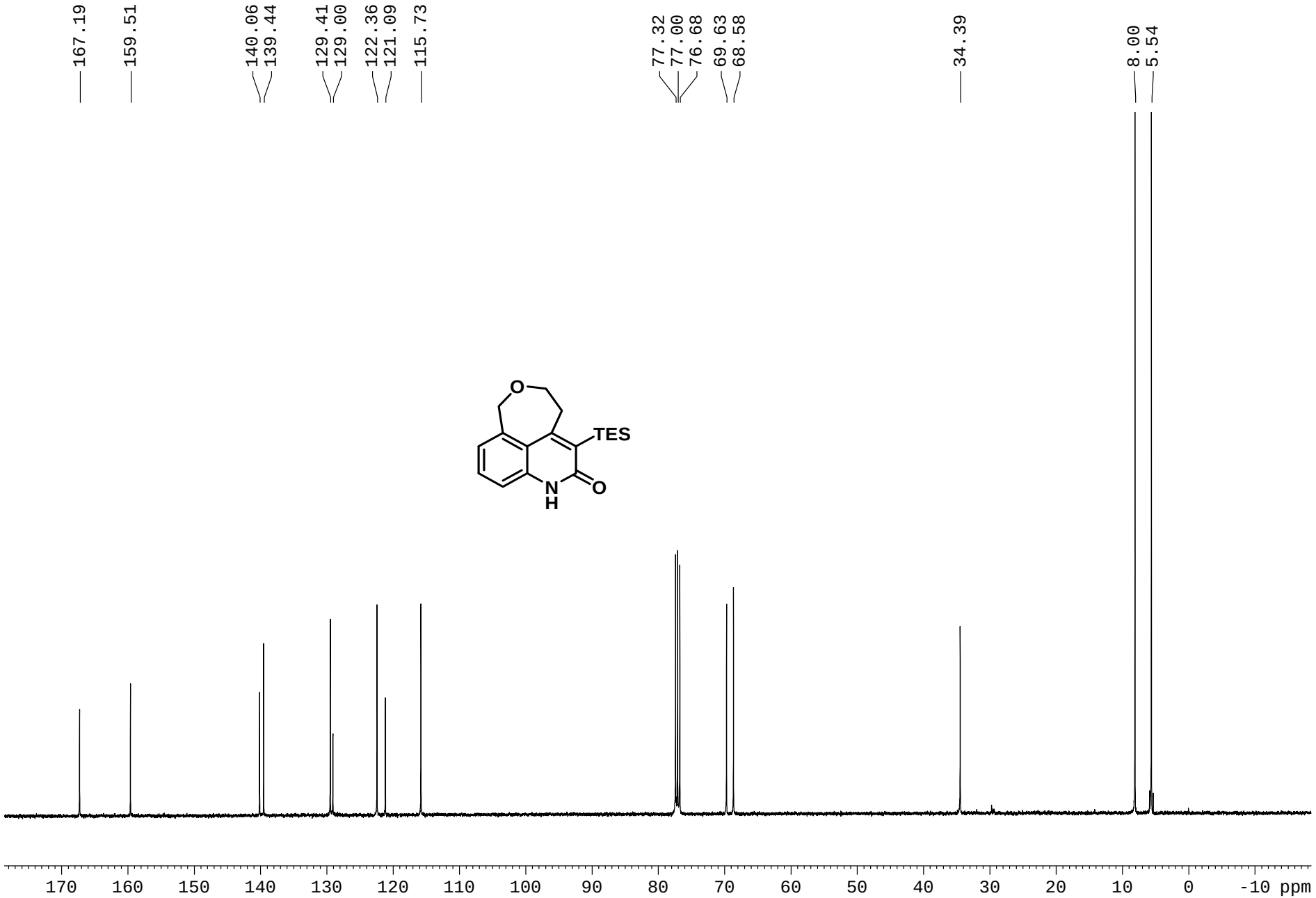
^{13}C NMR of compound 7*i* ($CDCl_3$, 100 MHz)



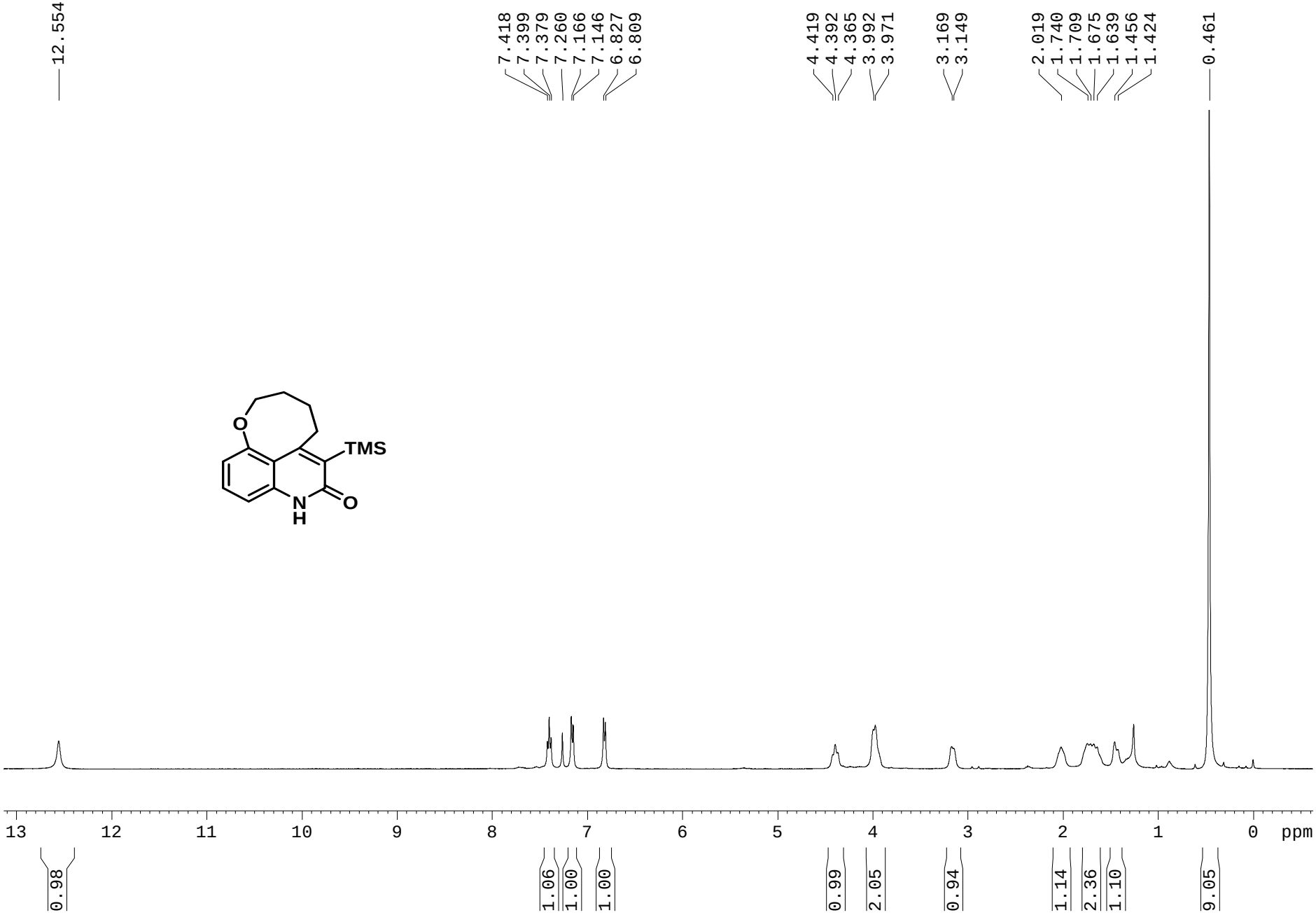
^{1}H NMR of compound 7j ($CDCl_3$, 400 MHz)



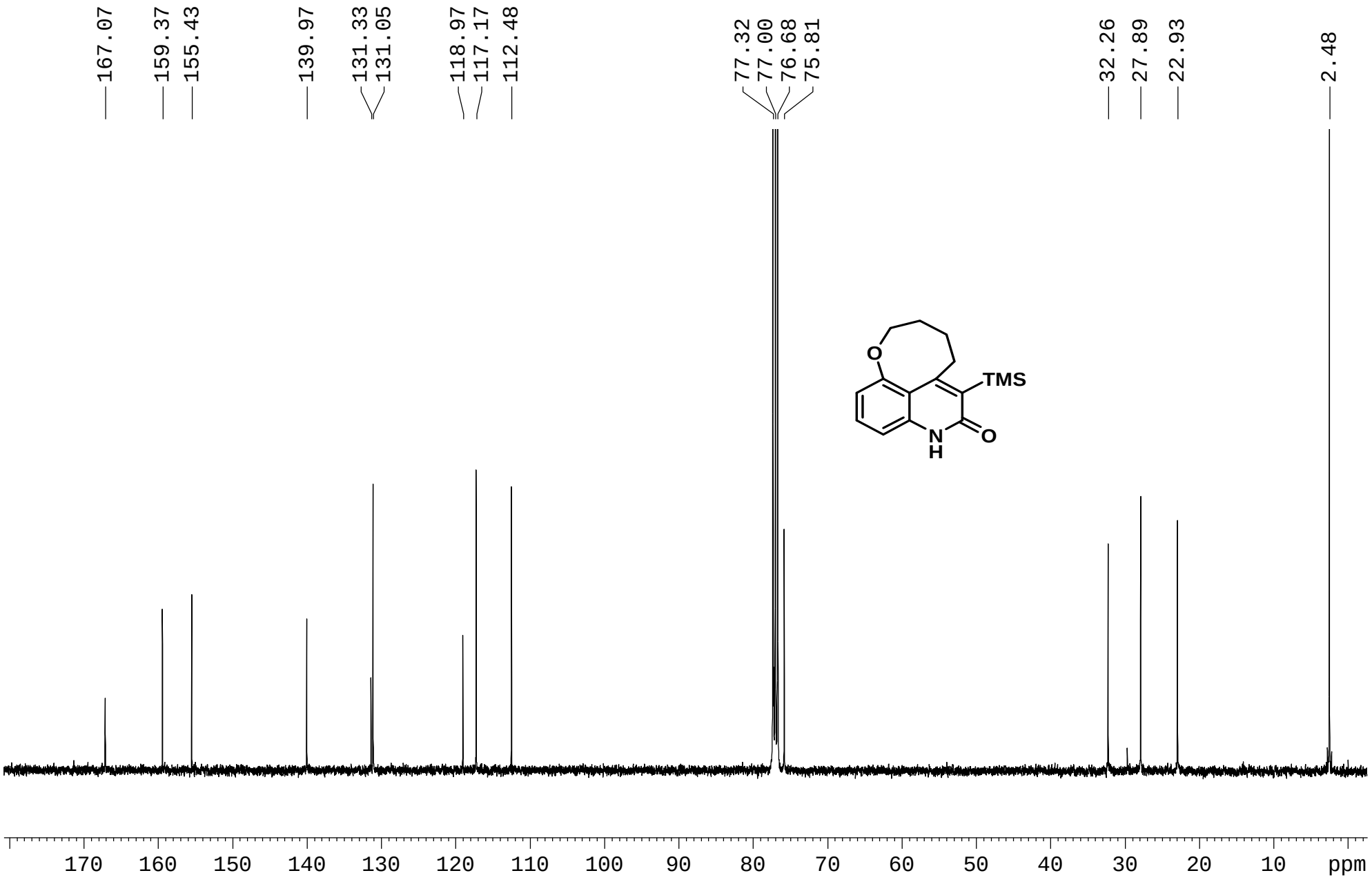
^{13}C NMR of compound 7j ($CDCl_3$, 100 MHz)



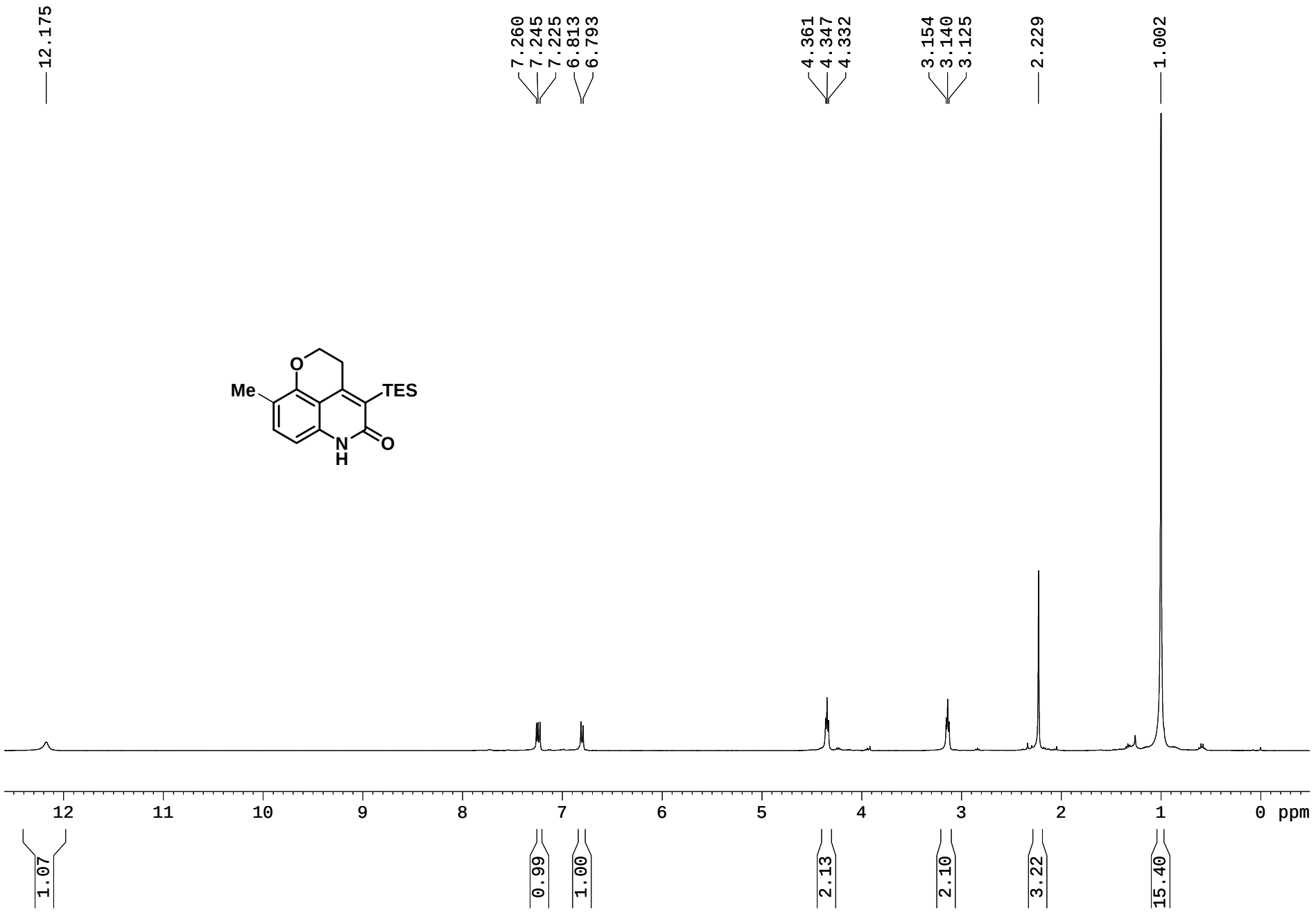
^{1}H NMR of compound 7k ($CDCl_3$, 400 MHz)



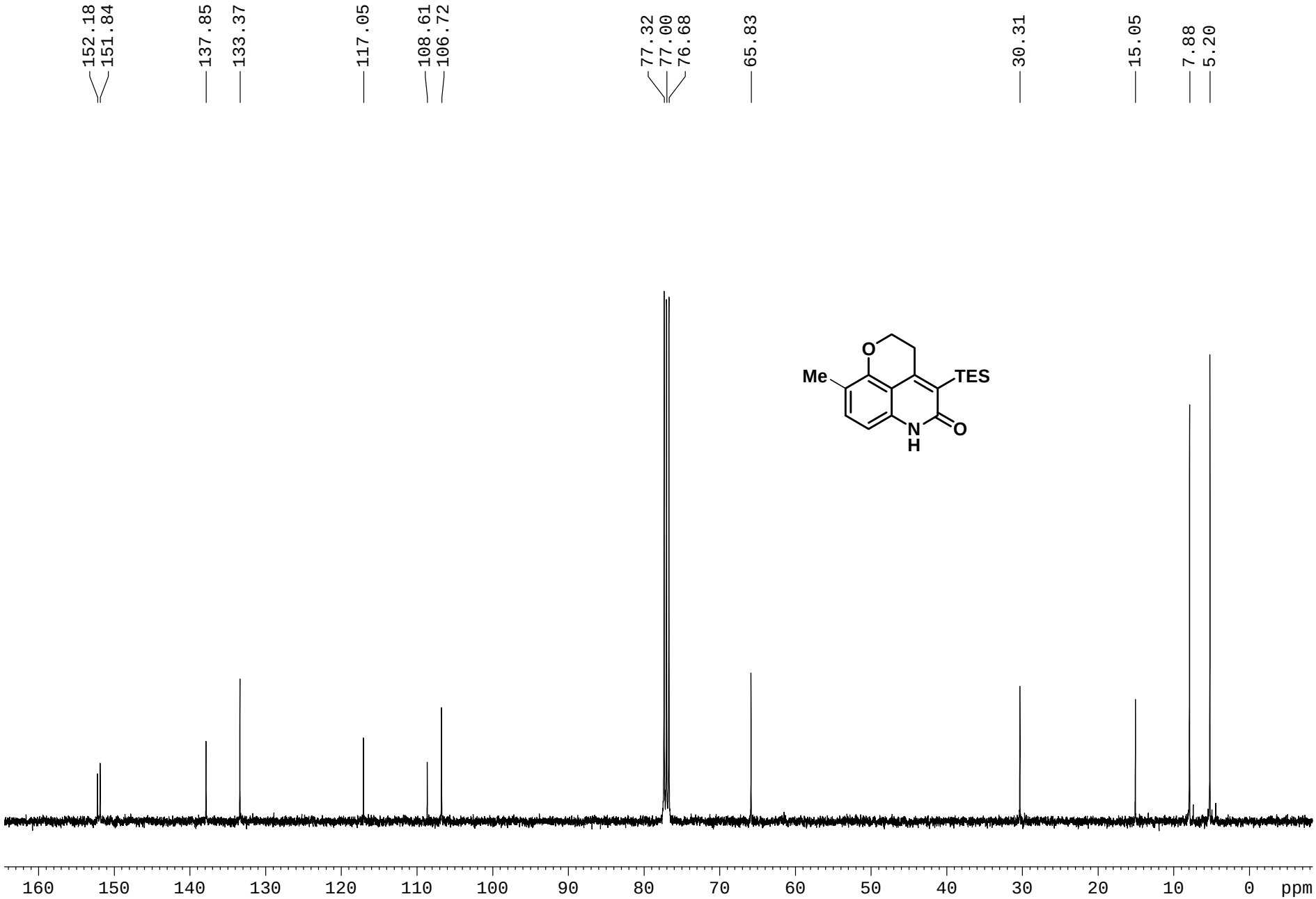
^{13}C NMR of compound 7k ($CDCl_3$, 100 MHz)



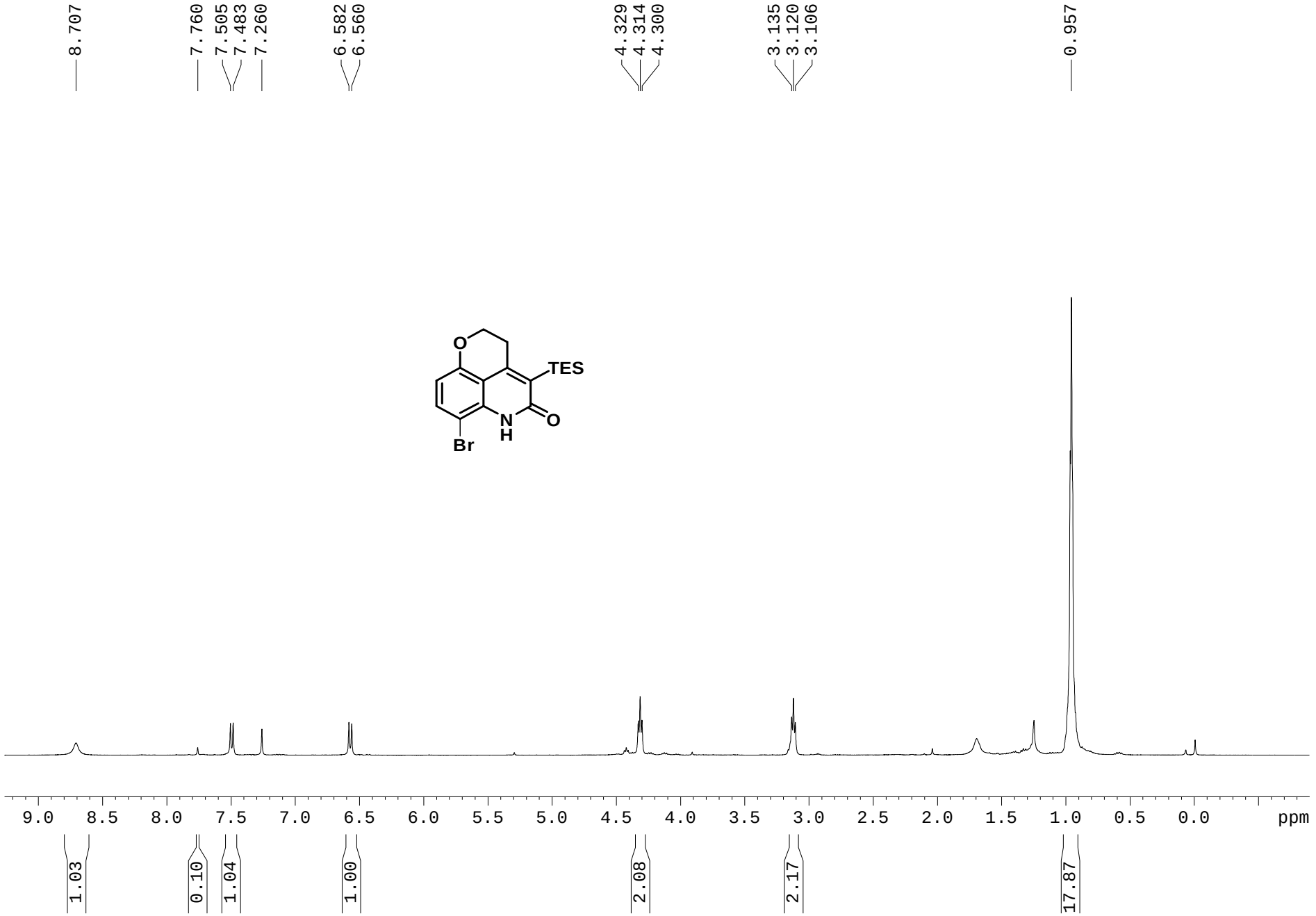
^{1}H NMR of compound 7l ($CDCl_3$, 400 MHz)



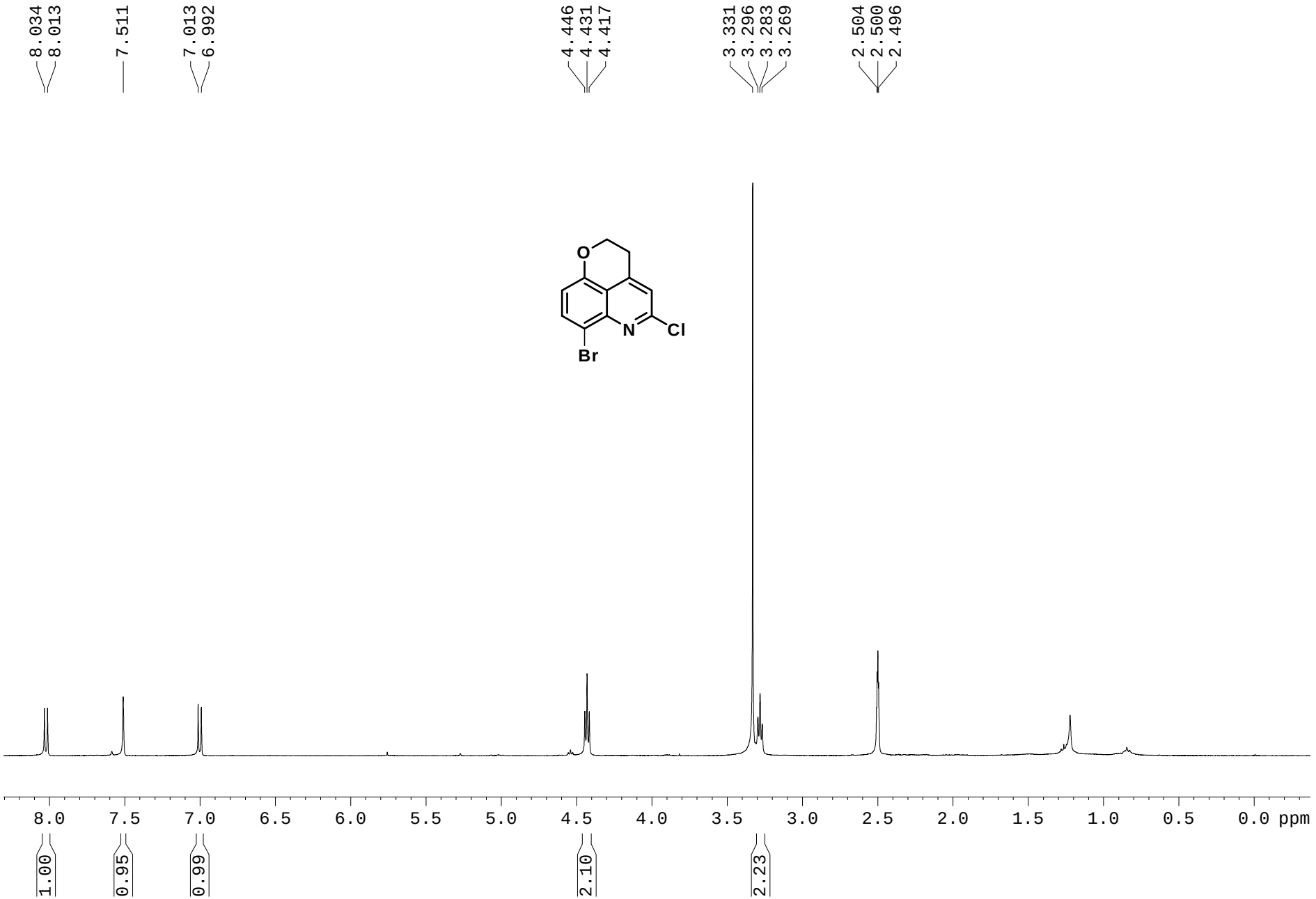
^{13}C NMR of compound 7l ($CDCl_3$, 100 MHz)



^{1}H NMR of compound 8 ($CDCl_3$, 400 MHz)



^{1}H NMR of compound 9 (DMSO-d_6, 400 MHz)



^{13}C NMR of compound 9 (DMSO-d_6, 100 MHz)