Electronic Supplementary Material (ESI) for RSC Advances.

Electronic Supplementary Information

Synthesis of 2,3-Disubstituted Thiophenes from 2-Aryl-3-Nitro-Cyclopropane-1,1-Dicarboxylates and 1,4-Dithiane-2,5-Diol

Thangavel Selvi, Govindhraj Vanmathi and Kannupal Srinivasan*

School of Chemistry, Bharathidasan University, Tiruchirapalli 620 024, Tamil Nadu, India

srinivasank@bdu.ac.in

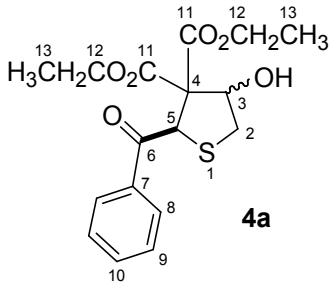
List of Contents

A. EXPERIMENTAL PROCEDURES AND CHARACTERIZATION DATA

General Methods: Melting point was determined by the open capillary tube method and is uncorrected. The NMR spectra were recorded on a *400 MHz* NMR spectrometer. High resolution mass spectra (ESI) were recorded on a Q-TOF mass spectrometer. Low resolution mass spectra (ESI) were recorded on a LC mass spectrometer. Elemental analyses were performed on a CHN analyzer. The IR spectra were recorded on a FT-IR spectrometer. Thin layer chromatography (TLC) was performed on pre-coated alumina sheets and detected under UV light. *S*ilica gel (100-200 mesh) was used for column chromatography.

General procedure for the synthesis of tetrahydrothiophenes 4a-i: To a solution of nitrocyclopropane 1 (1 mmol) in dichloromethane (5 mL) was added $BF_3 \cdot OEt_2$ (0.13 mL; 1 mmol) at room temperature. The reaction mixture was stirred until the starting material disappeared completely (2-24 h; as judged by TLC). To the same reaction flask, 1,4-dithiane-2,5-diol (0.08 mg; 0.5 mmol) and Et_3N (0.28 mL; 2.0 mmol) were added and the reaction mixture was stirred at room temperature. After completion of the reaction (1-6 h), it was quenched with water. The organic layer was separated, washed with water, dried (anhydrous Na_2SO_4) and the solvent was removed under reduced pressure. The crude product 4 was purified by column chromatography using 8-15% ethyl acetate/hexane. (Note: All the products were chromatographically homogeneous diastereomeric mixtures. However, in case of **4d**, the liquid diastereomeric mixture when kept at room temperature for 3-4 days formed crystals of one of the diastereomers. The impure crystals were collected and further recrystallized from $CHCl_3$/MeOH (1:1*v/v*) to obtain the diastereomer **4d** in pure form).

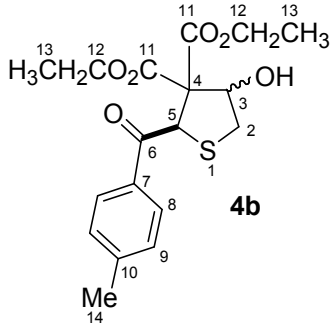
Diethyl 2-benzoyl-4-hydroxy-dihydro-thiophene-3,3-dicarboxylate (4a):



4a

Yellow semisolid; Yield: 292 mg (83%); dr = 1:1.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 7.6 Hz, H8 min), 7.81 (d, *J* = 7.6 Hz, H8 maj), 7.54 (t, *J* = 9.2 Hz, H10 both isomers), 7.45-7.39 (m, H9 both isomers), 5.39 (d, *J* = 10.0 Hz, H3 min), 5.19 (s, H5 min), 5.18-5.15 (m, H3 & H5 maj), 4.26-4.23 (m, H12 both isomers), 4.14-4.07 (m, H12 both isomers), 3.39-3.35 (m, H2 min & -OH both isomers), 3.19 (dd, *J* = 6.4, 10.4 Hz, H2 maj), 3.09 (dd, *J* = 1.6, 12.0 Hz, H2 min), 2.98 (t, *J* = 9.8 Hz, H2 maj), 1.27-1.18 (m, H13 both isomers), 1.11 (t, *J* = 7.2 Hz, H13 min), 1.04 (t, *J* = 7.2 Hz, H13 maj) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 194.3, 169.8, 167.48, 167.48, 166.5, 135.6, 134.6, 133.9, 133.7, 129.1, 128.9, 128.8, 128.7, 77.8, 77.0, 73.5, 65.9, 63.0, 62.5, 62.4, 61.8, 51.4, 49.8, 40.5, 34.7, 14.1, 14.0, 13.9, 13.7 ppm; IR (KBr): 3328 (O-H), 1745 (C=O, ester), 1679 (C=O) cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{20}O_6S$: 353.1053 [M + H^+], found**:** 353.1060.

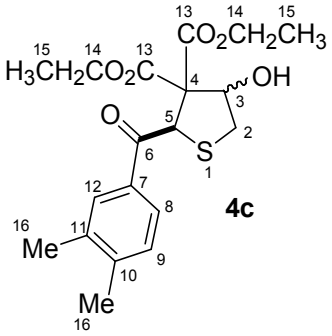
Diethyl 4-hydroxy-2-(4-methyl-benzoyl)-dihydro-thiophene-3,3-dicarboxylate (4b):



Yellow semisolid; Yield: 293 mg (80%); dr = 1:1.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.4 Hz, H8 min), 7.79 (d, *J* = 8.0 Hz, H8 maj), 7.27 (t, *J* = 9.2 Hz, H9 both isomers), 5.67 (d, *J* = 9.6 Hz, H3 min), 5.48 (s, H5 min), 5.26 (brs, H3, H5 maj), 4.33-4.29 (m, H12 both isomers), 4.20-4.12 (m, H12 both isomers), 3.68 (brs, -OH both isomers), 3.43 (dd, *J* = 5.6, 12.0 Hz, H2 min), 3.25 (dd, *J* = 6.4, 10.0 Hz, H2 maj), 3.14 (dd, *J* = 1.2, 11.6 Hz, H2 min), 3.05 (t, *J* = 9.8 Hz, H2 maj), 2.41 (s, H14 min), 2.39 (s, H14 maj), 1.33-1.24 (m, H13 both isomers), 1.17 (t, *J* = 7.0 Hz, H13 min), 1.09 (t, *J* = 7.0 Hz, H13 maj) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.9, 193.9, 169.6, 167.5, 167.4, 166.4, 145.0, 144.7, 132.9, 132.1, 129.51, 129.47, 129.1,

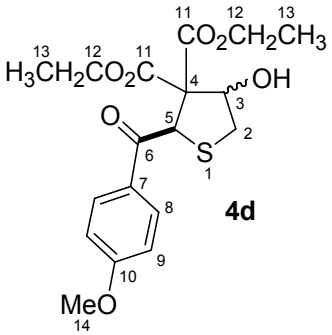
128.7, 77.7, 77.1, 73.3, 66.0, 62.9, 62.3, 62.2, 61.6, 51.2, 49.8, 40.5, 34.9, 21.63, 21.60, 14.0, 13.9, 13.8, 13.7 ppm; MS (ESI): *m/z* 367 [M + H^+]. Anal. calcd. $C_{18}H_{22}O_6S$: C 59.00, H 6.05; found: C 59.16, H 6.08.

Diethyl 2-(3,4-dimethyl-benzoyl)-4-hydroxy-dihydro-thiophene-3,3-dicarboxylate (4c):



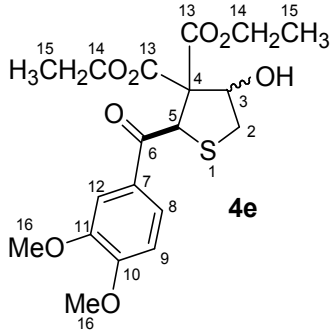
Yellow semisolid; Yield: 323 mg (85%); dr = 1:2.2; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84-7.80 (m, H8 min), 7.76-7.70 (m, H8 maj), 7.66-7.60 (m, H12 both isomers), 7.29-7.19 (m, H9 both isomers), 5.70 (d, *J* = 9.6 Hz, H3 min), 5.46 (s, H5 min), 5.28-5.20 (m, H3 & H5 maj), 4.34-4.29 (m, H14 both isomers), 4.18-4.11 (m, H14 both isomers), 3.56 (s, -OH both isomers), 3.42 (dd, *J* = 5.6, 11.6 Hz, H2 min), 3.23 (dd, *J* = 6.6, 10.2 Hz, H2 maj), 3.14 (dd, *J* = 1.8, 11.8 Hz, H2 min), 3.04 (t, *J* = 10.0 Hz, H2 maj), 2.33 (s, H16 both isomers), 2.32 (s, H16 both isomers), 1.34-1.24 (m, H15 both isomers), 1.18 (t, *J* = 7.2 Hz, H15 min), 1.11 (t, *J* = 7.0 Hz, H15 maj) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.2, 194.2, 171.2, 169.8, 167.6, 166.4, 143.9, 143.5, 137.3, 132.4, 130.2, 130.1, 130.0, 129.7, 126.8, 126.4, 77.7, 77.0, 73.3, 65.8, 62.9, 62.4, 62.3, 61.7, 51.2, 49.7, 40.6, 34.6, 20.10, 20.06, 19.81, 19.77, 14.1, 14.0, 13.9, 13.7 ppm; MS (ESI): *m/z* 381 [M + H^+]. Anal. calcd. $C_{19}H_{24}O_6S$: C 59.98, H 6.36; found: C 60.16, H 6.48.

Diethyl 4-hydroxy-2-(4-methoxy-benzoyl)-dihydro-thiophene-3,3-dicarboxylate (4d):



Yellow semisolid; Yield: 309 mg (81%); dr = 1:1.1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.8 Hz, H8 maj), 7.86 (d, *J* = 8.8 Hz, H8 min), 6.96 (t, *J* = 9.8 Hz, H9 both isomers), 5.77 (d, *J* = 9.6 Hz, H3 min), 5.45 (s, H5 min), 5.26-5.19 (m, H3 & H5 maj), 4.35-4.30 (m, H12 both isomers), 4.20-4.14 (m, H12 both isomers), 3.89 (s, H14 min), 3.88 (s, H14 maj), 3.45-3.41 (m, H2 min & -OH both isomers), 3.25 (dd, *J* = 6.4, 10.0 Hz, H2 maj), 3.16 (d, *J* = 11.6 Hz, H2 min), 3.04 (t, *J* = 9.8 Hz, H2 maj), 1.34-1.26 (m, H13 both isomers), 1.17 (t, *J* = 7.0 Hz, H13 min), 1.10 (t, *J* = 7.0 Hz, H13 maj) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9, 193.1, 169.7, 167.6, 167.5, 166.3, 164.3, 164.0, 132.5, 131.5, 130.9, 130.3, 128.2, 127.4, 77.7, 77.1, 73.4, 66.0, 62.9, 62.3, 62.2, 61.6, 55.6, 55.5, 50.9, 49.6, 40.6, 34.8, 14.1, 13.9, 13.8, 13.7 ppm; HRMS (ESI) calcd for $C_{18}H_{22}O_7S$: 383.1159 [M + H^+], found: 383.1156. Data for pure diastereomer of **4d**: White solid; M.p.: 110-112 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.8 Hz, 2H, H8), 6.95 (d, *J* = 8.8 Hz, 2H, H9), 5.24 (t, *J* = 8.0 Hz, 1H, H3), 5.20 (s, 1H, H5), 4.34-4.29 (m, 2H, H12), 4.18-4.13 (m, 2H, H12), 3.87 (s, 3H, H14), 3.50 (s, 1H, -OH), 3.25 (dd, *J* = 6.4 & 10.0 Hz, 1H, H2), 3.04 (t, *J* = 9.8 Hz, 1H, H2), 1.31 (t, *J* = 7.2 Hz, 3H, H13), 1.10 (t, *J* = 7.2 Hz, 3H, H13) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.1, 169.8, 167.6, 164.1, 131.0, 127.4, 114.1, 77.0, 65.9, 62.4, 61.7, 55.6, 49.5, 34.6, 14.1, 13.7 ppm; HRMS (ESI) calcd for $C_{18}H_{22}O_7S$: 383.1159 [M + H^+], found: 383.1156.

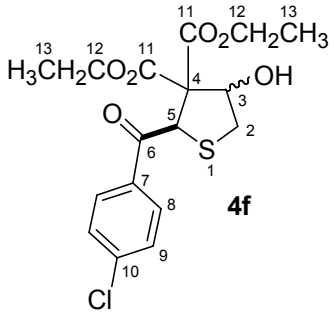
Diethyl 2-(3,4-dimethoxy-benzoyl)-4-hydroxy-dihydro-thiophene-3,3-dicarboxylate (4e):



Yellow semisolid; Yield: 358 mg (87%); dr = 1:1.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (dd, *J* = 1.8, 8.6 Hz, H8 min), 7.57 (d, *J* = 1.9 Hz, H8 maj), 7.49-7.48 (m, H12 both isomers), 6.95-6.90 (m, H9 both isomers), 5.71 (d, *J* = 8.4 Hz, H3 min), 5.49 (s, H5 min), 5.26-5.22 (m, H3 & H5 maj), 4.35-4.30 (m, H14 both isomers), 4.22-4.15 (m, H14 both isomers), 3.97 (s, H16 min), 3.96 (s, H16 maj), 3.95 (s, H16 min), 3.93 (s, H16 maj), 3.55 (brs, -OH both isomers), 3.44

(dd, *J* = 5.5, 11.8 Hz, H2 min), 3.26 (dd, *J* = 6.5, 10.2 Hz, H2 maj), 3.17 (dd, *J* = 1.6, 11.8 Hz, H2 min), 3.02 (t, *J* = 9.9 Hz, H2 maj), 1.35-1.30 (m, H15 both isomers), 1.19 (t, *J* = 7.0 Hz, H15 min), 1.12 (t, *J* = 7.0 Hz, H15 maj) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.8, 193.2, 169.8, 167.6, 167.5, 166.4, 154.2, 153.9, 149.33, 149.30, 128.3, 127.6, 124.0, 123.2, 111.1, 110.7, 110.2, 110.1, 77.8, 77.0, 73.3, 65.9, 62.9, 62.4, 62.3, 61.7, 56.2, 56.1, 56.0, 50.8, 40.6, 34.7, 14.1, 13.9, 13.8, 13.7 ppm; MS (ESI): *m/z* 435.12 [M + Na^+]. Anal. calcd. for $C_{19}H_{24}O_8S$: C 55.33, H 5.87; found: C 55.46, H 5.91.

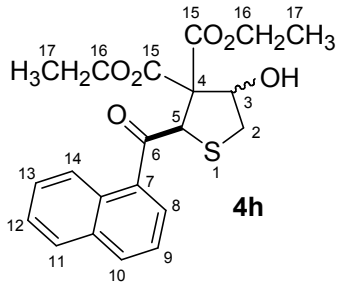
Diethyl 2-(4-chloro-benzoyl)-4-hydroxy-dihydro-thiophene-3,3-dicarboxylate (4f):



4f

Yellow semisolid; Yield: 286 mg (74%); dr = 1:1.1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.4 Hz, H8 min), 7.87 (d, *J* = 8.0 Hz, H8 maj), 7.48-7.44 (m, H9 both isomers), 5.47 (s, H5 maj), 5.41 (brs, H5 min), 5.30-5.26 (m, H3 both isomers), 4.34-4.21 (m, H12 both isomers), 4.19-4.10 (m, H12 both isomers), 3.92 (brs, -OH both isomers) 3.45 (dd, *J* = 5.8, 11.4 Hz, H2 min), 3.32 (dd, *J* = 6.4, 10.0 Hz, H2 maj), 3.16 (d, *J* = 11.6 Hz, H2 min), 3.09 (t, *J* = 9.4 Hz, H2 maj), 1.32-1.24 (m, H13 both isomers), 1.19 (t, *J* = 6.8 Hz, H13 min), 1.11 (t, *J* = 6.8 Hz, H13 maj) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.7, 192.9, 169.1, 167.3, 167.2, 166.3, 140.1, 139.9, 133.9, 133.0, 130.3, 130.0, 129.01, 128.95, 77.6, 77.1, 73.1, 66.3, 62.9, 62.2, 61.8, 61.5, 51.2, 50.0, 40.2, 35.4, 13.9, 13.8, 13.7, 13.6 ppm; HRMS (ESI) calcd for $C_{17}H_{19}ClO_6S$: 387.0664 [M + H^+], found: 387.0672.

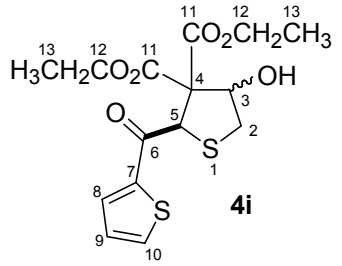
Diethyl 4-hydroxy-2-(naphthalene-1-carbonyl)-dihydro-thiophene-3,3-dicarboxylate (4h):



4h

Yellow semisolid; Yield: 326 mg (81%); dr = 1:1.2; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, *J* = 8.0 Hz, H14 both isomers), 8.03-7.95 (m, H8 min & H10 both isomers), 7.88-7.80 (m, H8 maj & H11 both isomers), 7.62-7.47 (m, H9, H12 & H13 both isomers), 5.71 (d, *J* = 9.6 Hz, H3 min), 5.43-5.34 (m, H3 maj & H5 both isomers), 4.35-4.22 (m, H16 maj & H16 both isomers), 4.18-4.10 (m, H16 min), 3.51 (dd, *J* = 6.0, 11.6 Hz, H2 min), 3.45 (brs, -OH both isomers), 3.33 (dd, *J* = 6.8, 9.2 Hz, H2 maj), 3.23 (d, *J* = 12.0 Hz, H2 min), 3.08 (t, *J* = 9.4 Hz, H2 maj), 1.34-1.29 (m, H17 both isomers), 1.24 (t, *J* = 6.6 Hz, H17 min), 1.14 (t, *J* = 7.0 Hz, H17 maj) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.1, 197.1, 169.8, 167.5, 167.4, 166.7, 135.2, 133.93, 133.87, 133.4, 133.2, 137.0, 130.8, 128.4, 128.3, 128.19, 128.15, 127.9, 127.6, 126.7, 125.83, 125.76, 124.2, 77.8, 77.2, 73.8, 66.4, 62.9, 62.5, 62.0, 55.6, 53.4, 40.4, 34.9, 14.1, 13.9, 13.8 ppm. HRMS (ESI) calcd for $C_{21}H_{22}O_6S$: 403.1210 [M + H^+], found: 403.1206.

Diethyl 4-hydroxy-2-(thiophene-2-carbonyl)-dihydro-thiophene-3,3-dicarboxylate (4i):



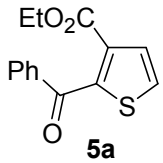
4i

Brown semisolid; Yield: 90 mg (25%); dr = 1:1.1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (t, *J* = 8.4 Hz, H8 both isomers), 7.74-7.68 (t, *J* = 3.6 Hz, H10 both isomers), 7.20-7.16 (m, H9 both isomers), 5.75 (d, *J* = 10.0 Hz, H3 min), 5.31-5.25 (m, H3 maj & H5 min), 5.13 (brs, H5 maj), 4.36-4.29 (m, H12 both isomers), 4.19-4.14 (m, H12 both isomers), 3.60 (s, -OH both isomers),

3.49 (dd, *J* = 5.8, 11.8 Hz, H2 min), 3.30 (dd, *J* = 6.4, 10.4 Hz, H2 maj), 3.18 (dd, *J* = 1.6, 12.0 Hz, H2 min), 3.06 (t, *J* = 9.8 Hz, H2 maj), 1.34-1.29 (m, H13 both isomers), 1.17 (t, *J* = 7.2 Hz, H13 min), 1.10 (t, *J* = 7.0 Hz, H13 maj) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.3, 188.1, 169.2, 167.3, 167.2, 166.0, 142.3, 141.8, 136.3, 135.3, 134.0, 132.9, 128.7, 128.5, 77.5, 77.2, 73.8, 66.3, 63.0, 62.42, 62.38, 61.8, 52.5, 50.8, 40.8, 35.1, 14.0, 13.9, 13.8, 13.7 ppm; MS (ESI): *m/z* 359 [M + H^+]. Anal. calcd. $C_{15}H_{18}O_6S_2$: C 50.26, H 5.06; found: C 50.20, H 5.08.

General procedure for the synthesis of thiophenes 5: To a solution of tetrahydrothiophene **4** (1 mmol) in toluene (5 mL) was added *p*-toluenesulphonic acid (0.172 mg; 1 mmol). The reaction mixture was heated under stirring at 90 ºC for 15-24 h. After completion of the reaction, it was cooled to room temperature and the solvent was removed under reduced pressure. The residue was extracted with ethyl acetate, the organic layer was washed with water, dried (anhydrous Na_2SO_4) and the solvent was removed under reduced pressure. The crude product **5** was purified by column chromatography using 5-10% ethyl acetate/hexane.

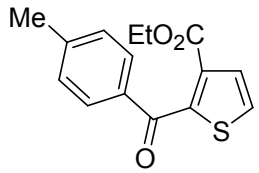
Ethyl 2-benzoyl-thiophene-3-carboxylate (5a):



5a

Yellow oil; Yield: 187 mg (72%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 7.2 Hz, 2H), 7.57 (d, *J* = 7.2 Hz, 1H), 7.51-7.44 (m, 4H), 3.93 (q, *J* = 7.2 Hz, 2H), 0.90 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.7, 162.5, 145.2, 137.8, 134.0, 133.4, 129.3, 129.0, 128.6, 127.8, 61.2, 13.5 ppm; MS (ESI): *m/z* 283.03 [M + Na^+]. Anal. calcd. $C_{14}H_{12}O_3S$: C 64.60, H 4.65; found: C 64.66, H 4.79.

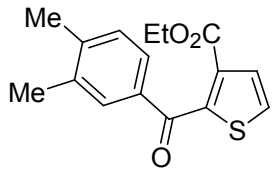
Ethyl 2-(4-methyl-benzoyl)-thiophene-3-carboxylate (5b):



5b

Yellow oil; Yield: 186 mg (68%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 7.6 Hz, 2H), 7.53-7.45 (m, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 3.96 (q, *J* = 7.2 Hz, 2H), 2.41 (s, 3H), 0.94 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.4, 162.5, 145.6, 144.4, 135.2, 133.6, 129.6, 129.3, 128.8, 127.4, 61.1, 21.7, 13.5 ppm; MS (ESI): *m/z* 297.04 [M + Na^+]. Anal. calcd. $C_{15}H_{14}O_3S$: C 65.67, H 5.14; found: C 65.76, H 5.28.

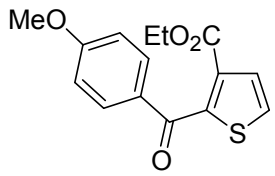
Ethyl 2-(3,4-dimethyl-benzoyl)-thiophene-3-carboxylate (5c):



5c

Brown oil; Yield: 228 mg (79%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (s, 1H), 7.52-7.49 (m, 2H), 7.45 (d, *J* = 4.4 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 3.97 (q, *J* = 7.2 Hz, 2H), 2.32 (s, 3H), 2.29 (s, 3H), 0.95 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.6, 162.6, 145.7, 143.2, 137.0, 135.5, 133.6, 130.3, 129.8, 128.7, 127.39, 127.37, 61.1, 20.1, 19.7, 13.5 ppm; MS (ESI): *m/z* 289 [M + H^+]. Anal. calcd. $C_{16}H_{16}O_3S$: C 66.64, H 5.59; found: C 66.76, H 5.64.

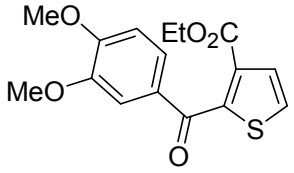
Ethyl 2-(4-methoxy-benzoyl)-thiophene-3-carboxylate (5d):



5d

Yellow oil; Yield: 255 mg (88%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.8 Hz, 2H), 7.50 (d, *J* = 4.8 Hz, 1H), 7.44 (d, *J* = 4.8 Hz, 1H), 6.92 (d, *J* = 8.8 Hz, 2H), 3.99 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 0.96 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.5, 164.0, 162.5, 145.8, 133.2, 131.9, 130.7, 128.7, 127.0, 113.8, 61.1, 55.6, 13.6 ppm; MS (ESI): *m/z* 291 [M + H^+]. Anal. calcd. $C_{15}H_{14}O_4S$: C 62.05, H 4.86; found: C 62.16, H 4.88.

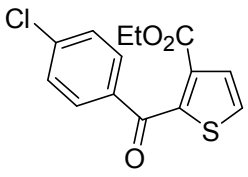
Ethyl 2-(3,4-dimethoxy-benzoyl)-thiophene-3-carboxylate (5e):



5e

Yellow oil; Yield: 259 mg (81%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 1.6 Hz, 1H), 7.49 (d, *J* = 5.2 Hz, 1H), 7.44 (d, *J* = 4.8 Hz, 1H), 7.28 (dd, *J* = 1.6 & 8.4 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 4.00 (q, *J* = 7.2 Hz, 2H), 3.924 (s, 3H), 3.919 (s, 3H), 0.98 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.4, 162.6, 153.8, 149.2, 145.6, 133.5, 130.8, 128.7, 127.1, 125.2, 110.8, 110.0, 61.1, 56.12, 56.05, 13.7 ppm; MS (ESI): *m/z* 321 [M + H^+]. Anal. calcd. $C_{16}H_{16}O_5S$: C 59.99, H 5.03; found: C 60.06, H 5.18.

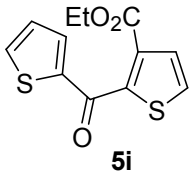
Ethyl 2-(4-chloro-benzoyl)-thiophene-3-carboxylate (5f):



5f

Yellow oil; Yield: 185 mg (63%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.50 (q, *J* = 5.2 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 3.99 (q, *J* = 7.2 Hz, 2H), 0.98 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.6, 162.3, 144.8, 139.9, 136.1, 133.9, 130.7, 129.0, 128.9, 127.9, 61.3, 13.6 ppm; MS (ESI): *m/z* 295.0 [M + H^+]. Anal. calcd. $C_{14}H_{11}ClO_3S$: C 57.05, H 3.76; found: C 57.26, H 3.88.

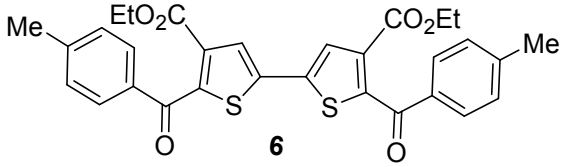
Ethyl 2-(thiophene-2-carbonyl)-thiophene-3-carboxylate (5i):



5i

Yellow oil; Yield: 162 mg (61%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 8.8 Hz, 1H), 7.38-7.32 (m, 3H), 6.98 (d, *J* = 3.6 Hz, 1H), 3.98 (d, *J* = 7.2 Hz, 2H), 0.91 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.5, 162.5, 144.5, 144.4, 135.1, 134.8, 133.8, 128.9, 128.2, 127.3, 61.3, 13.6 ppm; MS (ESI): *m/z* 288.9 [M + Na^+]. Anal. calcd. $C_{12}H_{10}O_3S_2$: C 54.12, H 3.78; found: C 54.36, H 3.90.

Diethyl 5,5'-bis-(4-methyl-benzoyl)-[2,2']bithiophenyl-4,4'-dicarboxylate (6): To a solution of thiophene **5b** (1 mmol) in DMSO (5 mL) was added $PdCl_2(PPh_3)_2$ (0.021 mg; 3 mol%) followed by AgOAc (0.334 mg; 2 mmol) The reaction mixture was heated at 60 °C for 24 h. After completion of the reaction, it was diluted with water. The organic layer was separated, washed with water, dried (anhydrous Na_2SO_4) and the solvent was removed under reduced pressure. The crude product **6** was purified by column chromatography using 10-20% ethyl acetate/hexane.



6

Yellow semisolid; Yield: 142 mg (52%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.62 (s, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 3.99 (q, *J* = 7.2 Hz, 2H), 2.44 (s, 3H), 0.96 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.4, 162.0, 145.0, 144.8, 137.2, 134.9, 134.4, 129.6, 129.4, 126.3, 61.5, 21.8, 13.5 ppm; MS (ESI): *m/z* 547.1 [M + H^+]. Anal. calcd. $C_{30}H_{26}O_6S_2$: C 65.91, H 4.79; found: C 65.98, H 4.92.

B. NMR SPECTRA FOR ALL COMPOUNDS

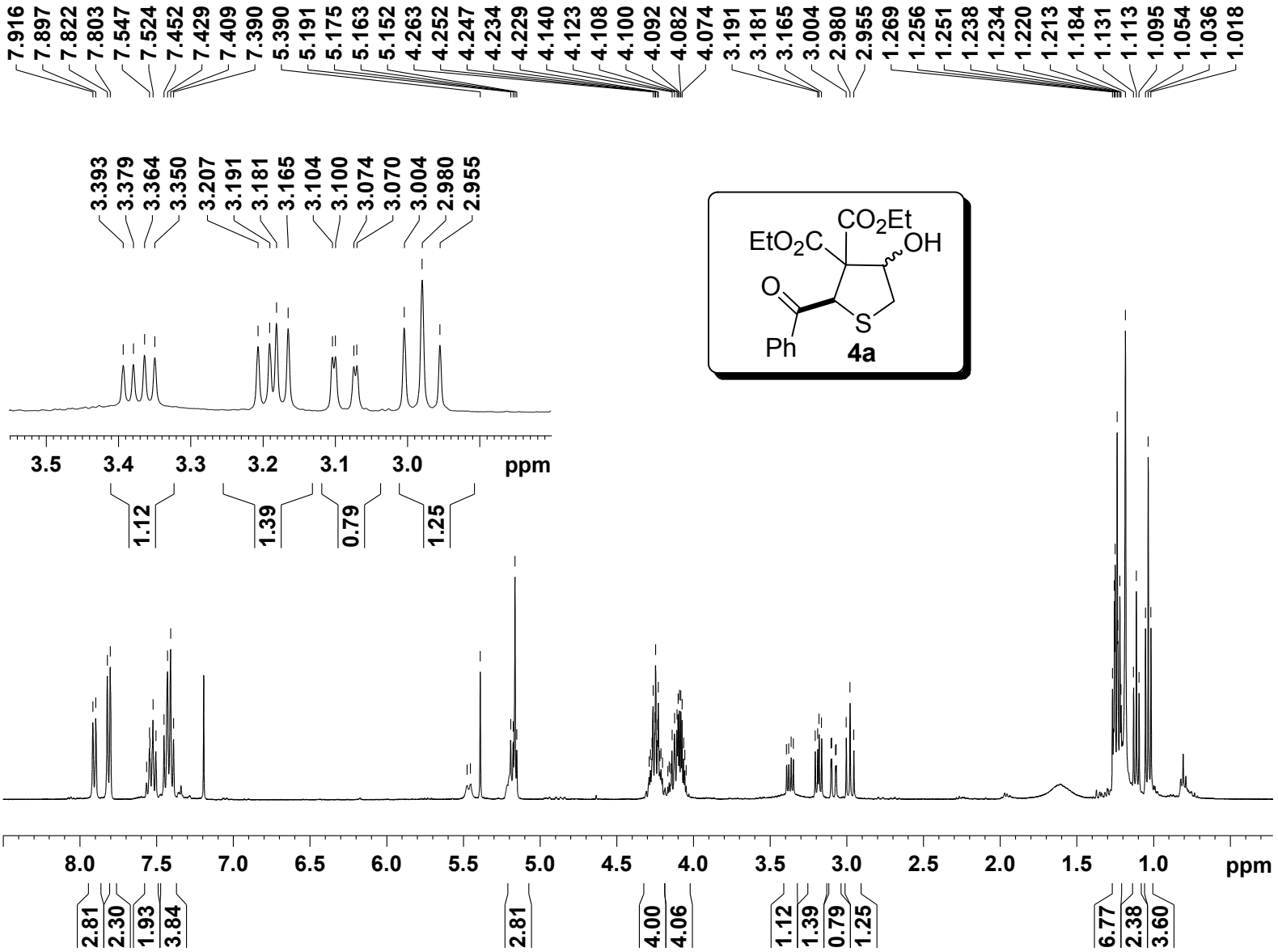


Figure 1. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **4a**

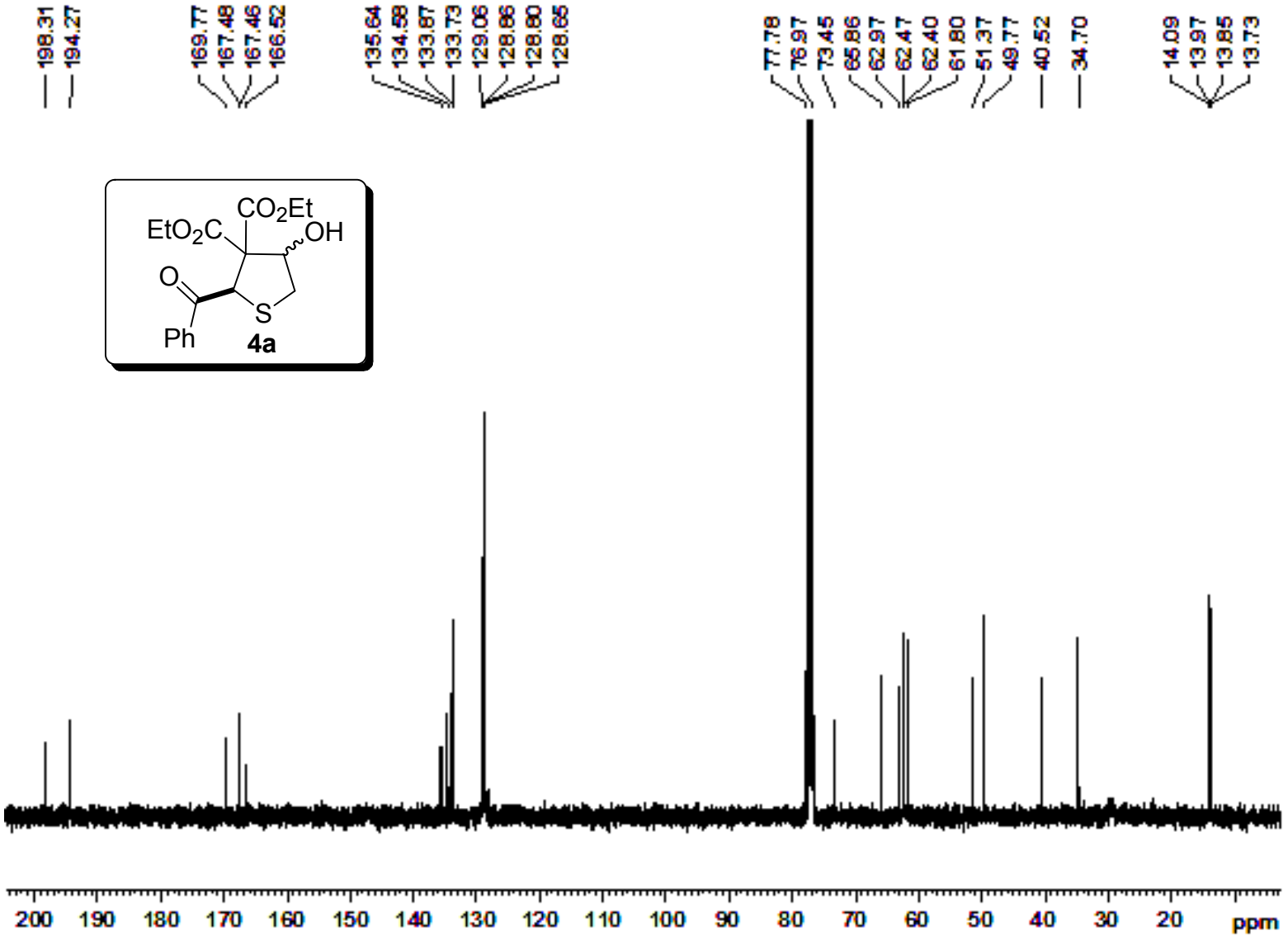


Figure 2. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **4a**

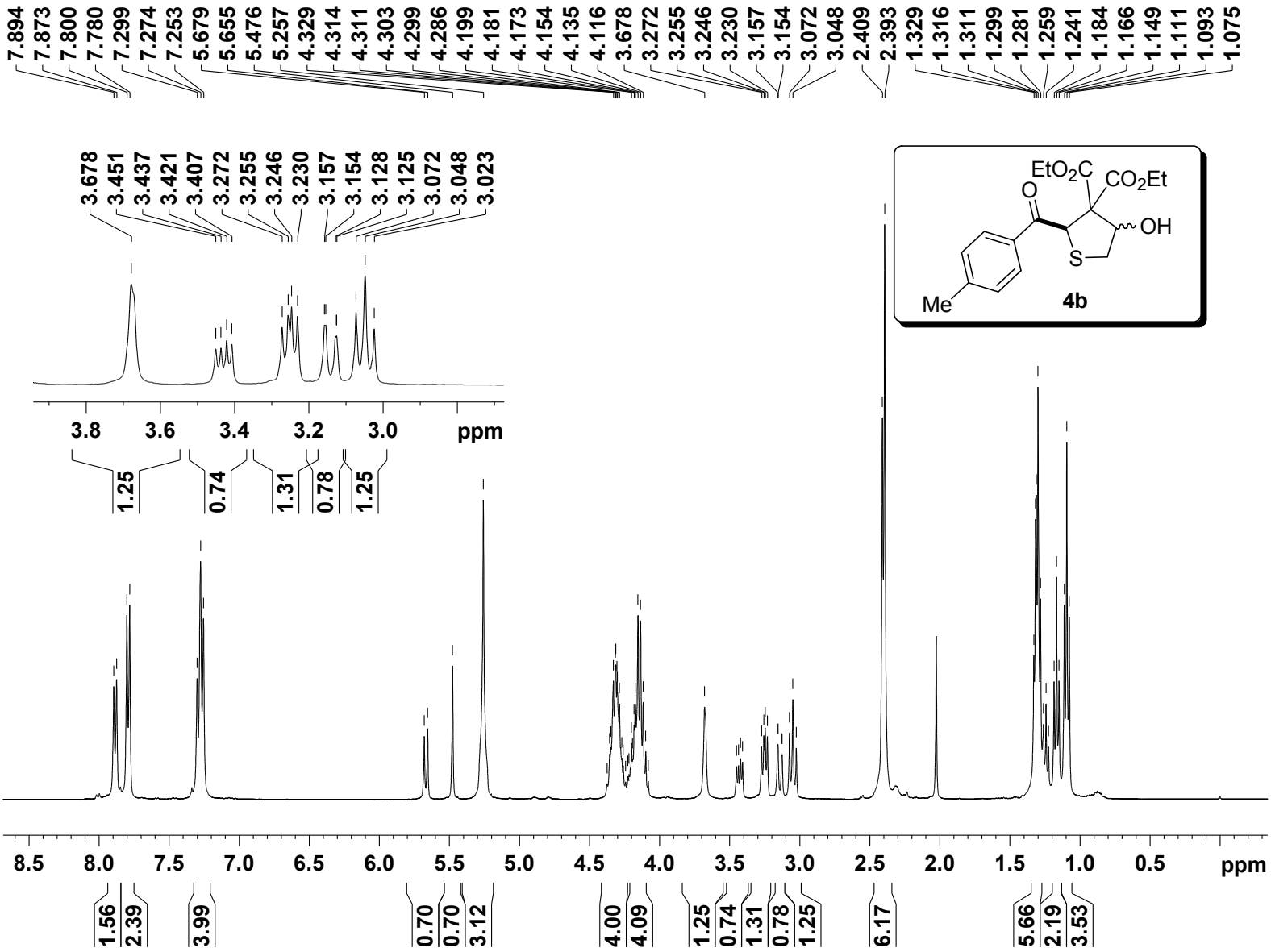


Figure 3. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **4b**

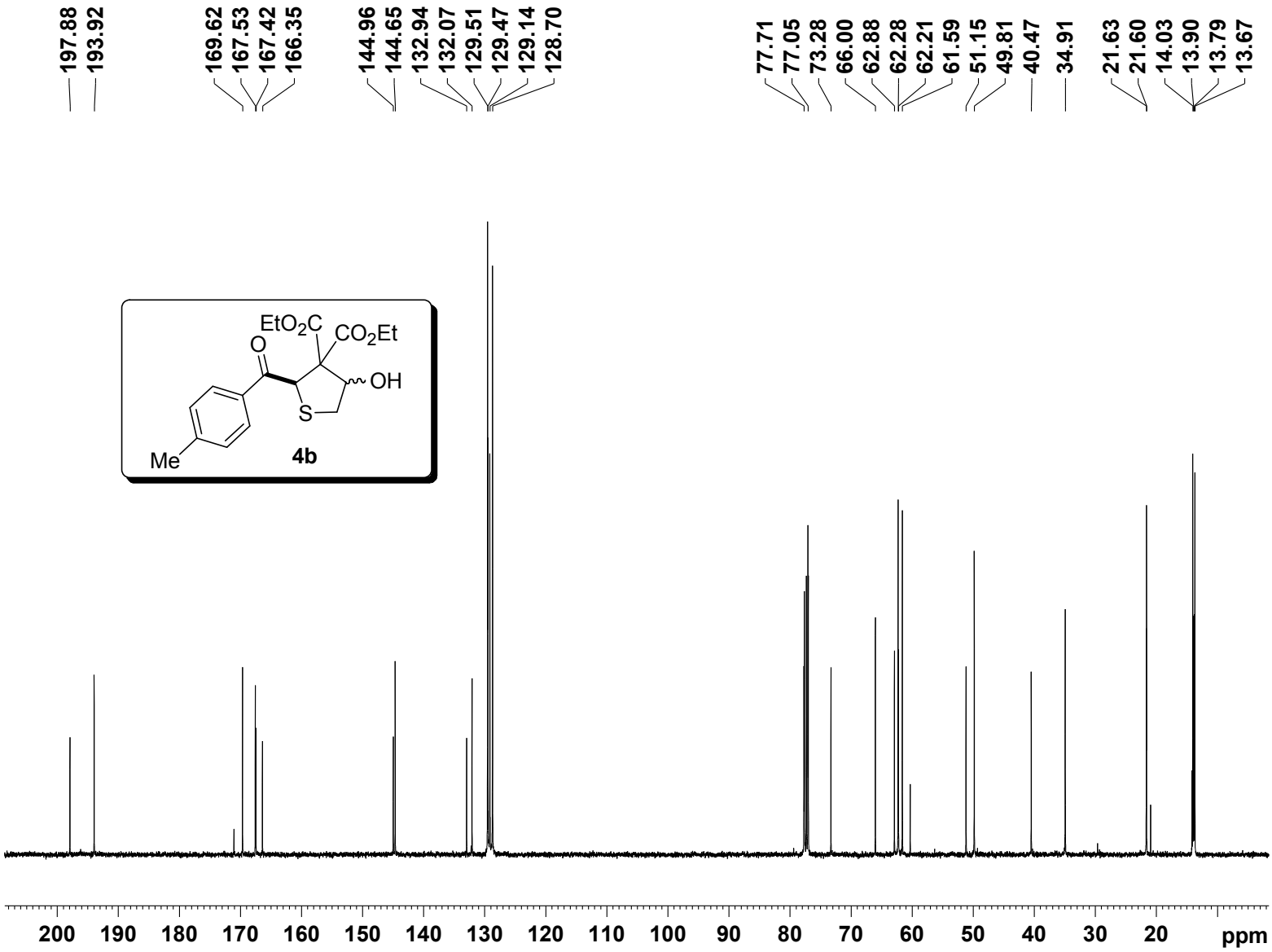


Figure 4. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **4b**

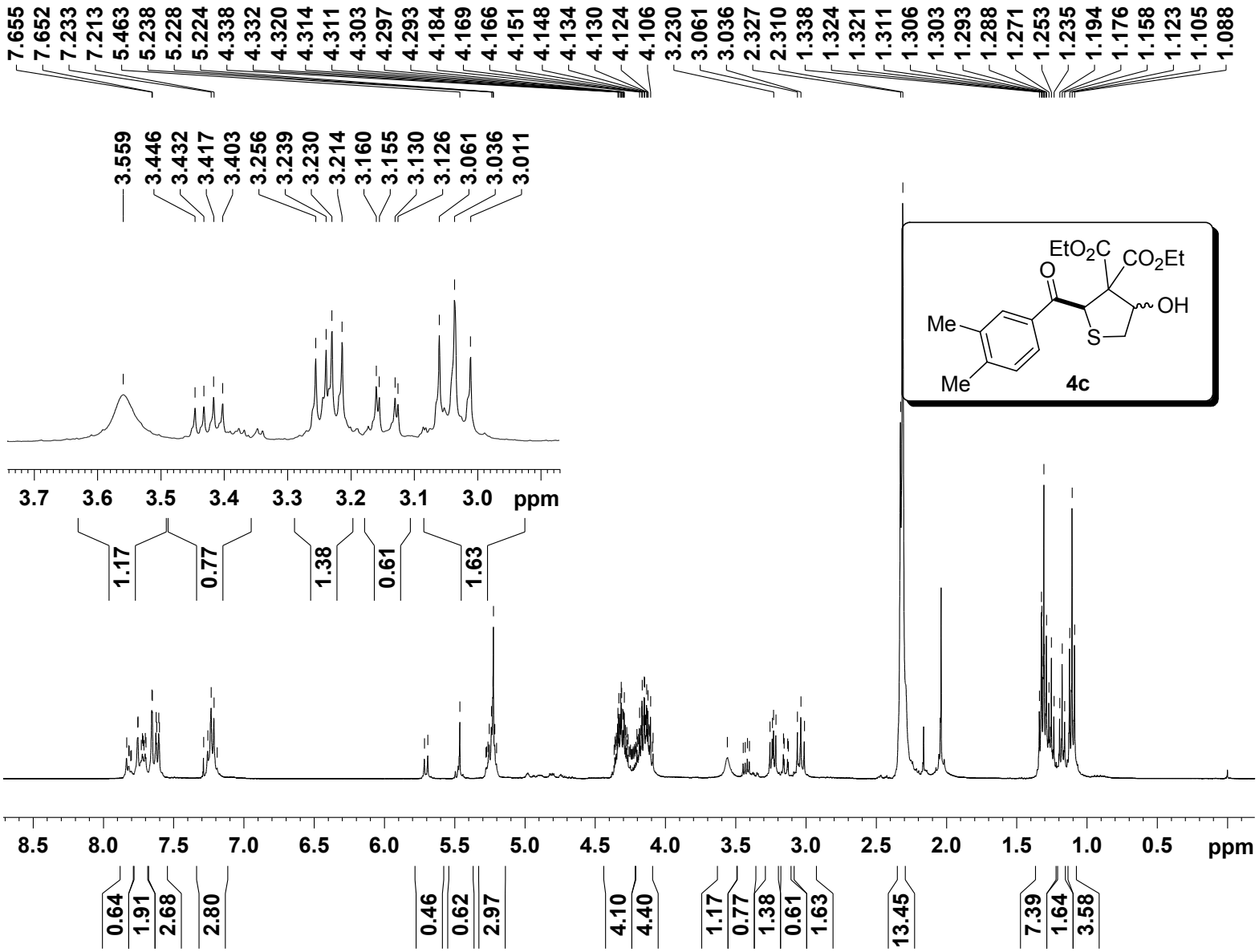


Figure 5. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **4c**

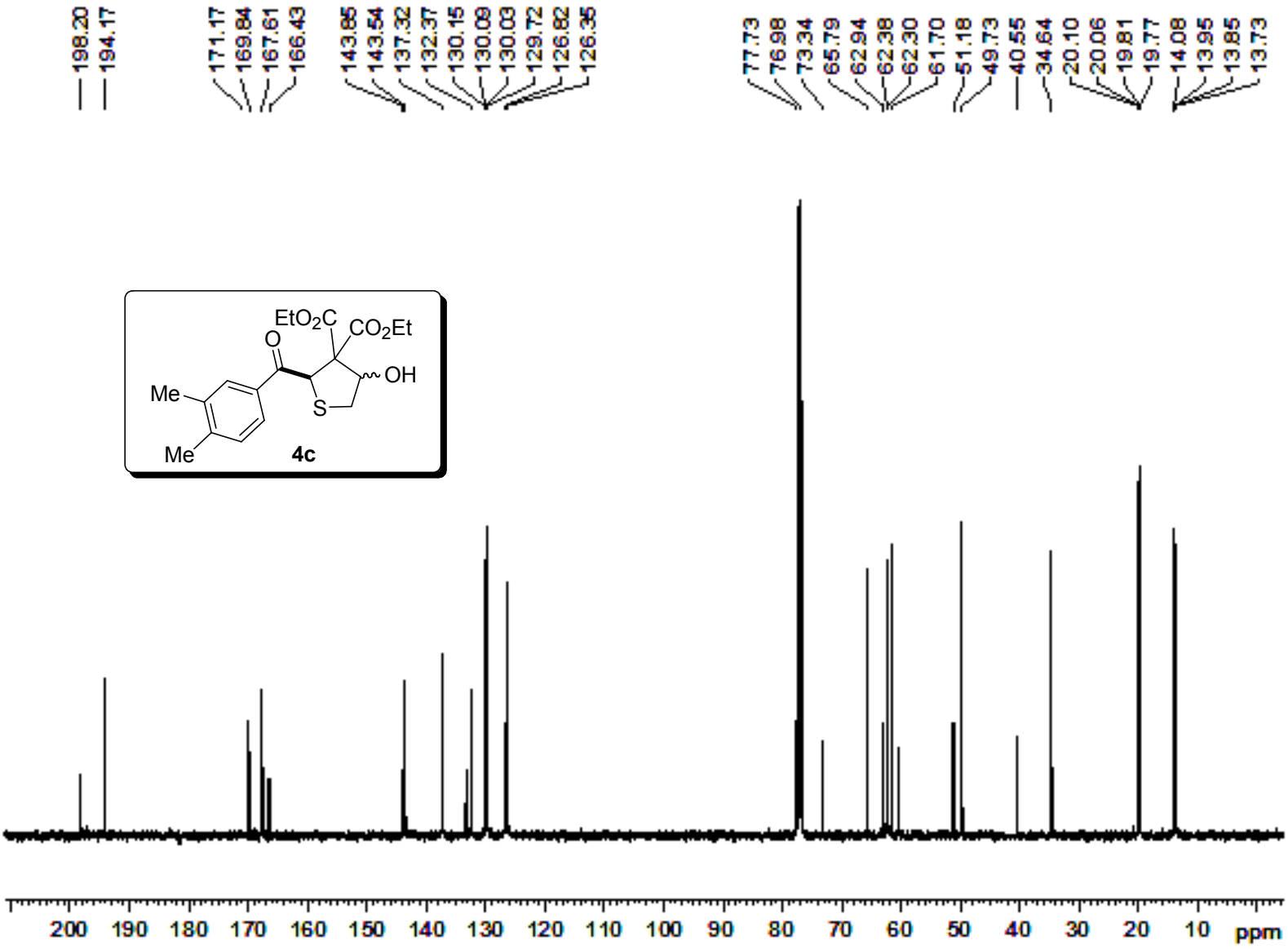


Figure 6. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **4c**

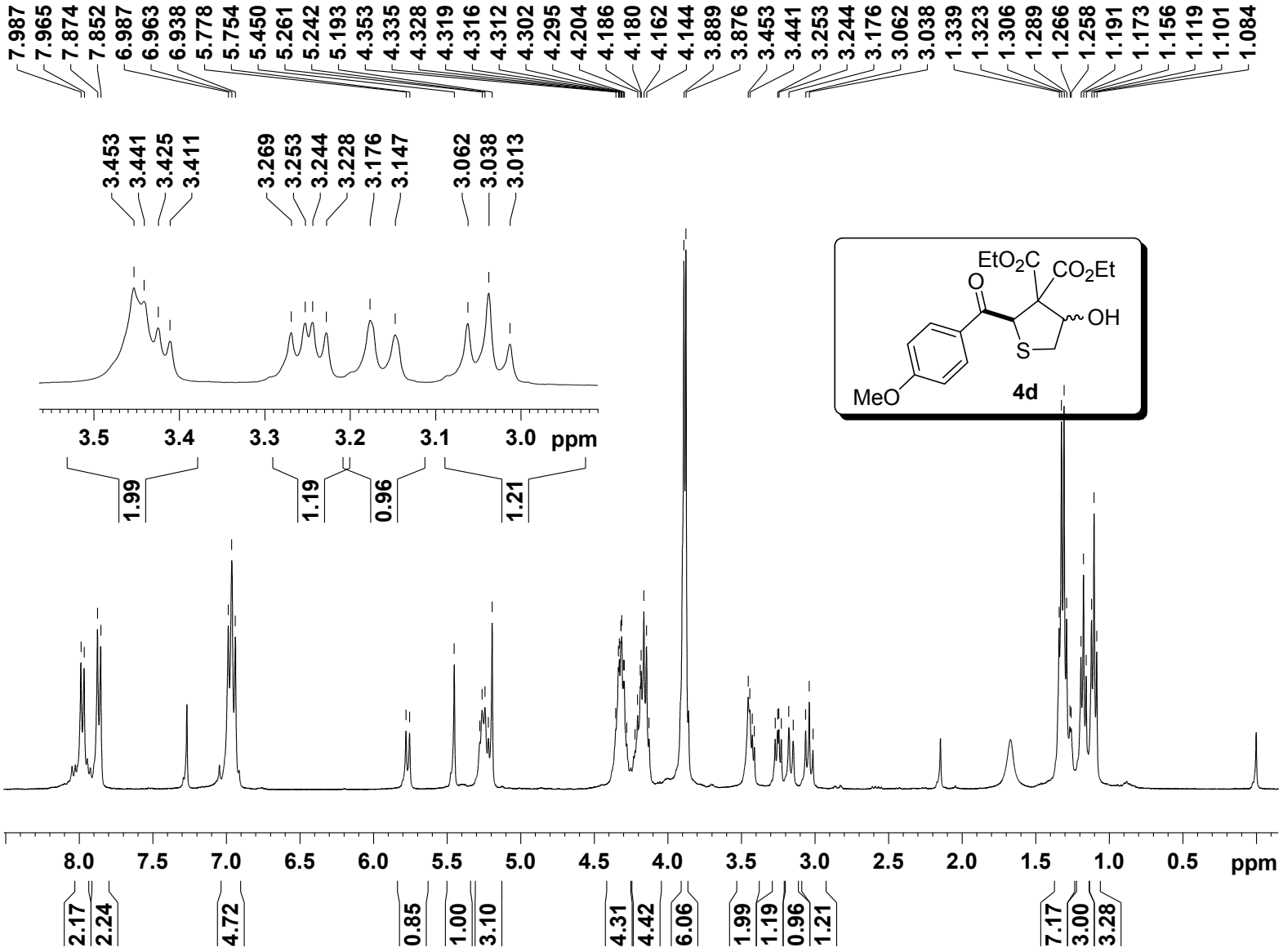


Figure 7. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **4d**

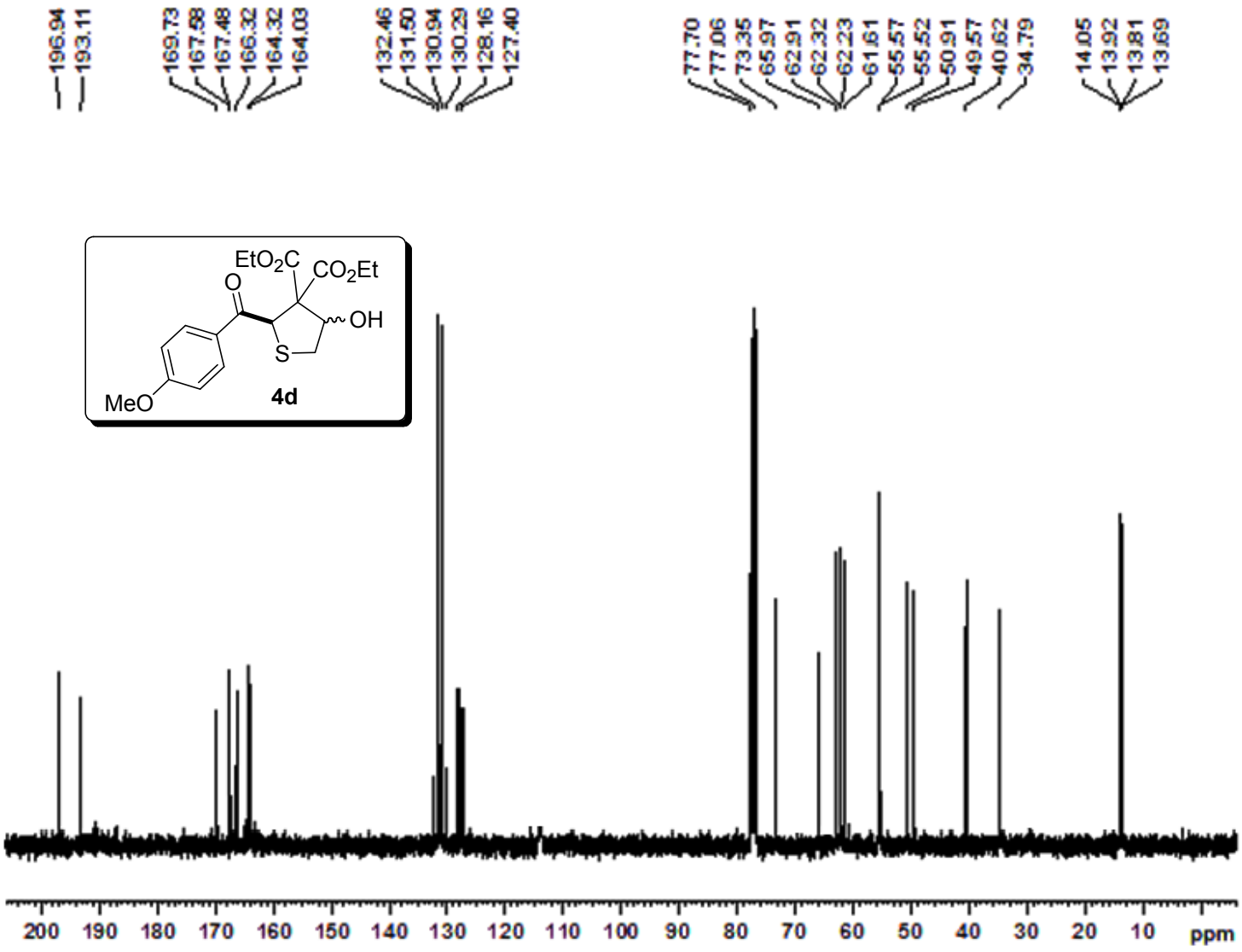


Figure 8. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **4d**

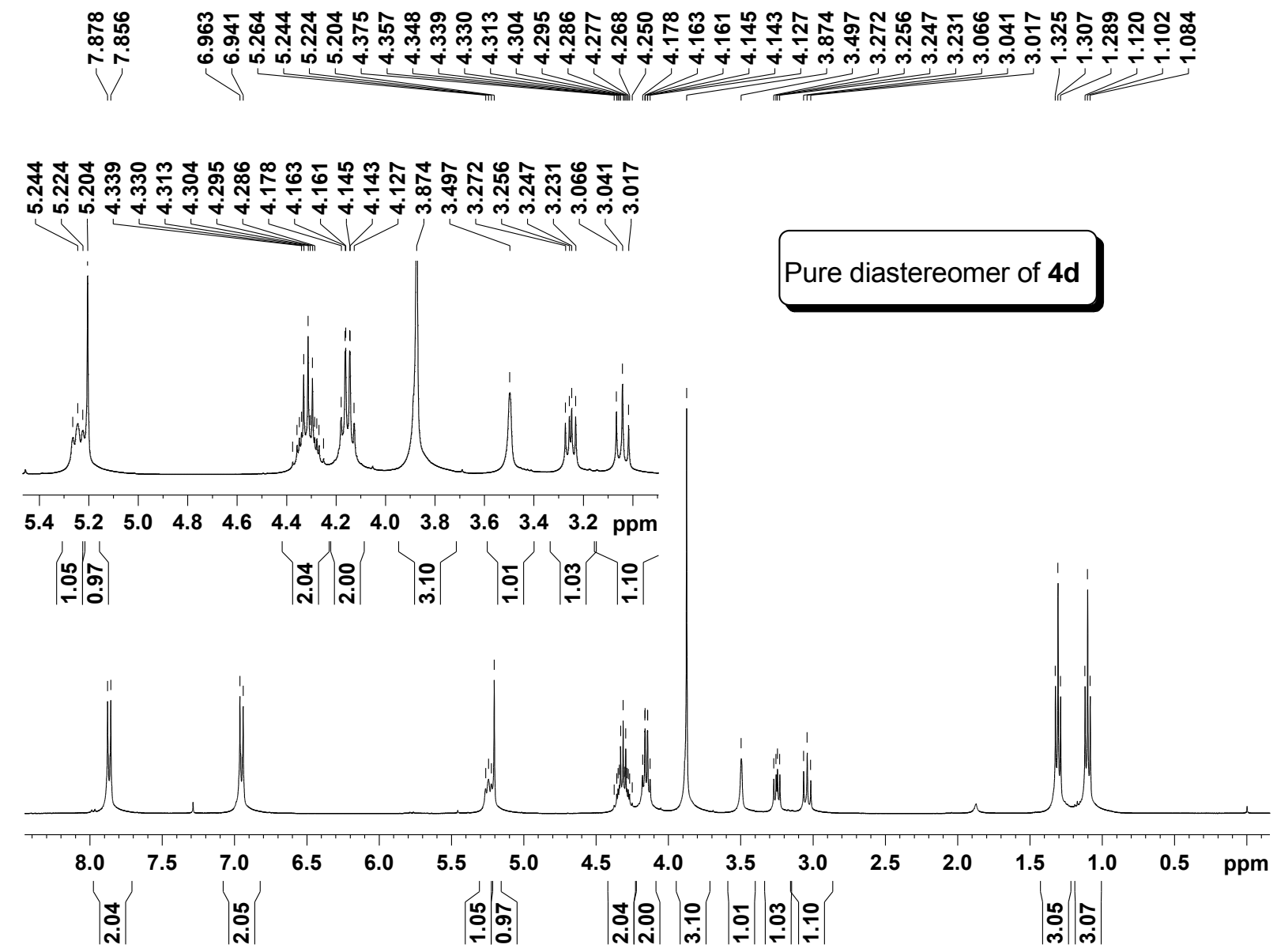


Figure 9. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of pure diastereomer of **4d**

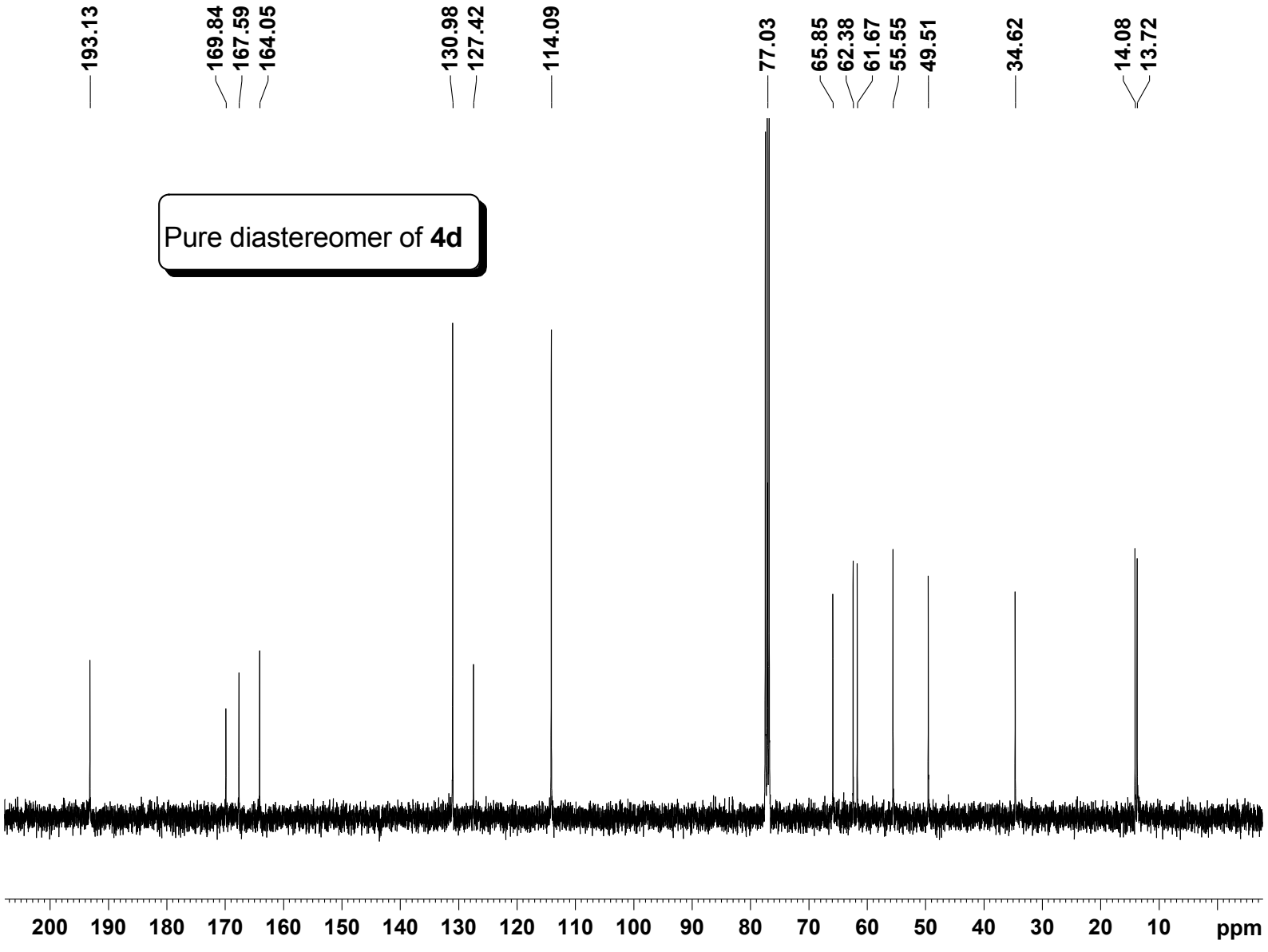


Figure 10. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of pure diastereomer of **4d**

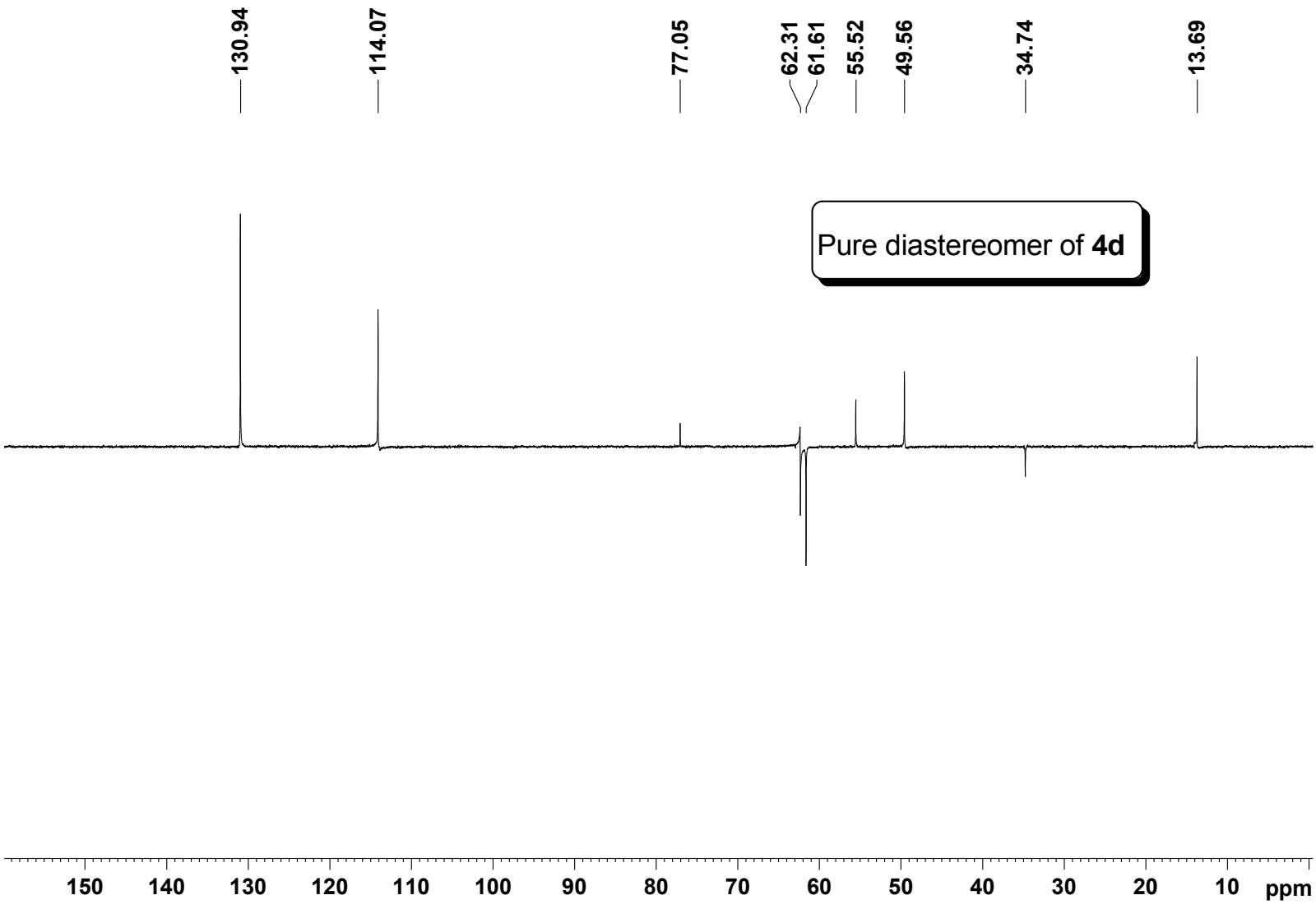


Figure 11. The DEPT-135 spectrum of pure diastereomer of **4d** in $CDCl_3$ solvent

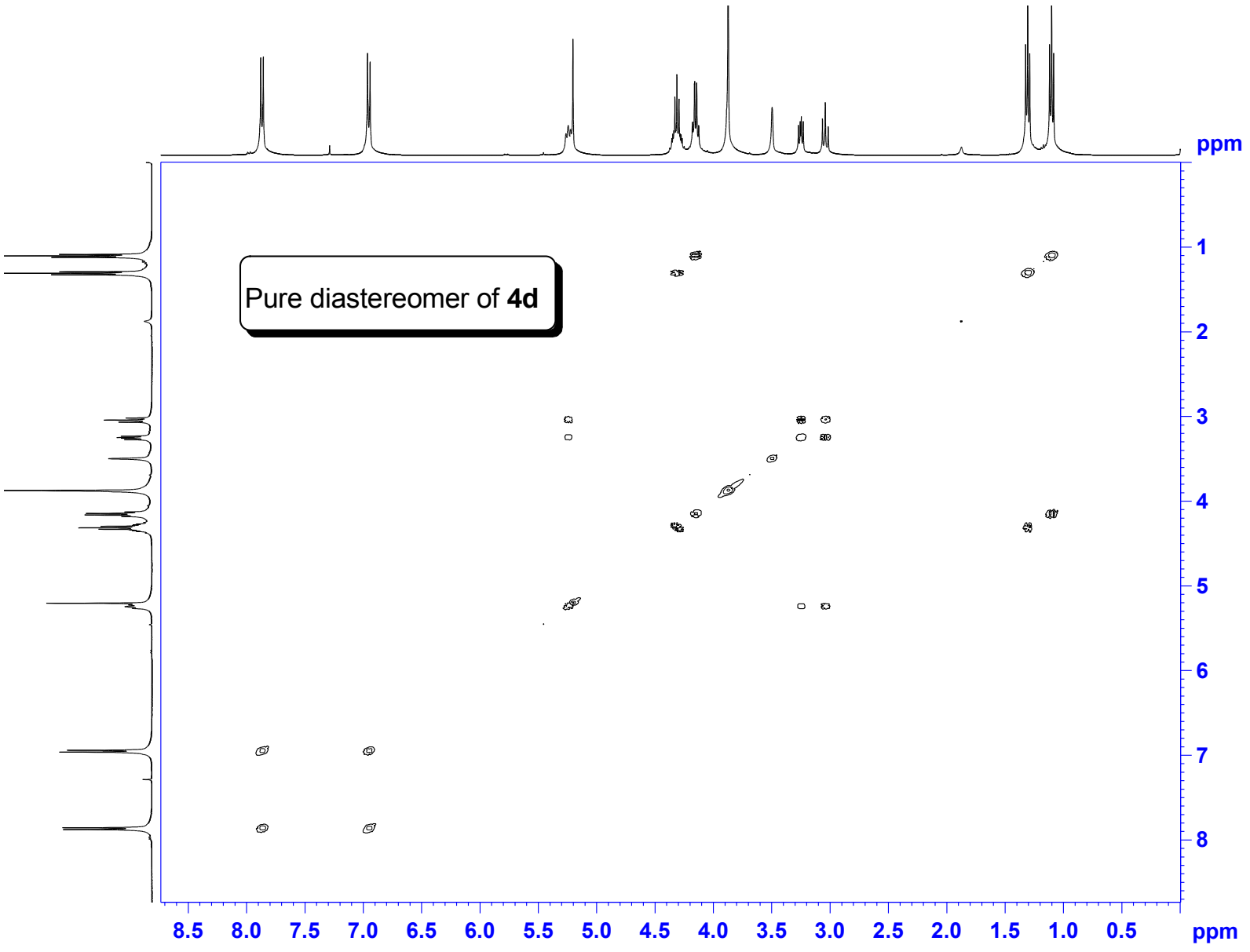


Figure 12. The COSY spectrum of pure diastereomer of **4d** in $CDCl_3$ solvent

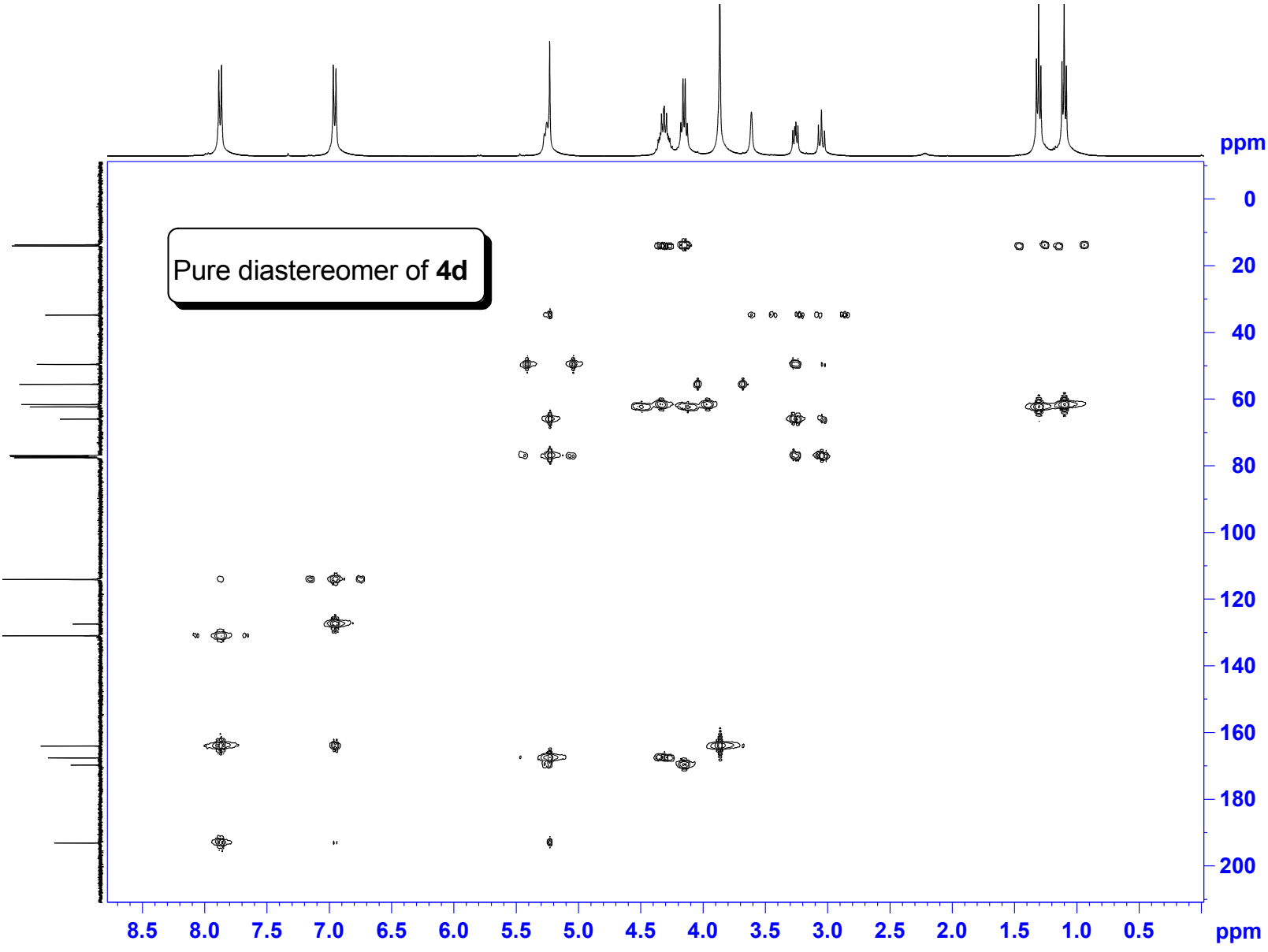


Figure 13. The HMBC spectrum of pure diastereomer of **4d** in $CDCl_3$ solvent

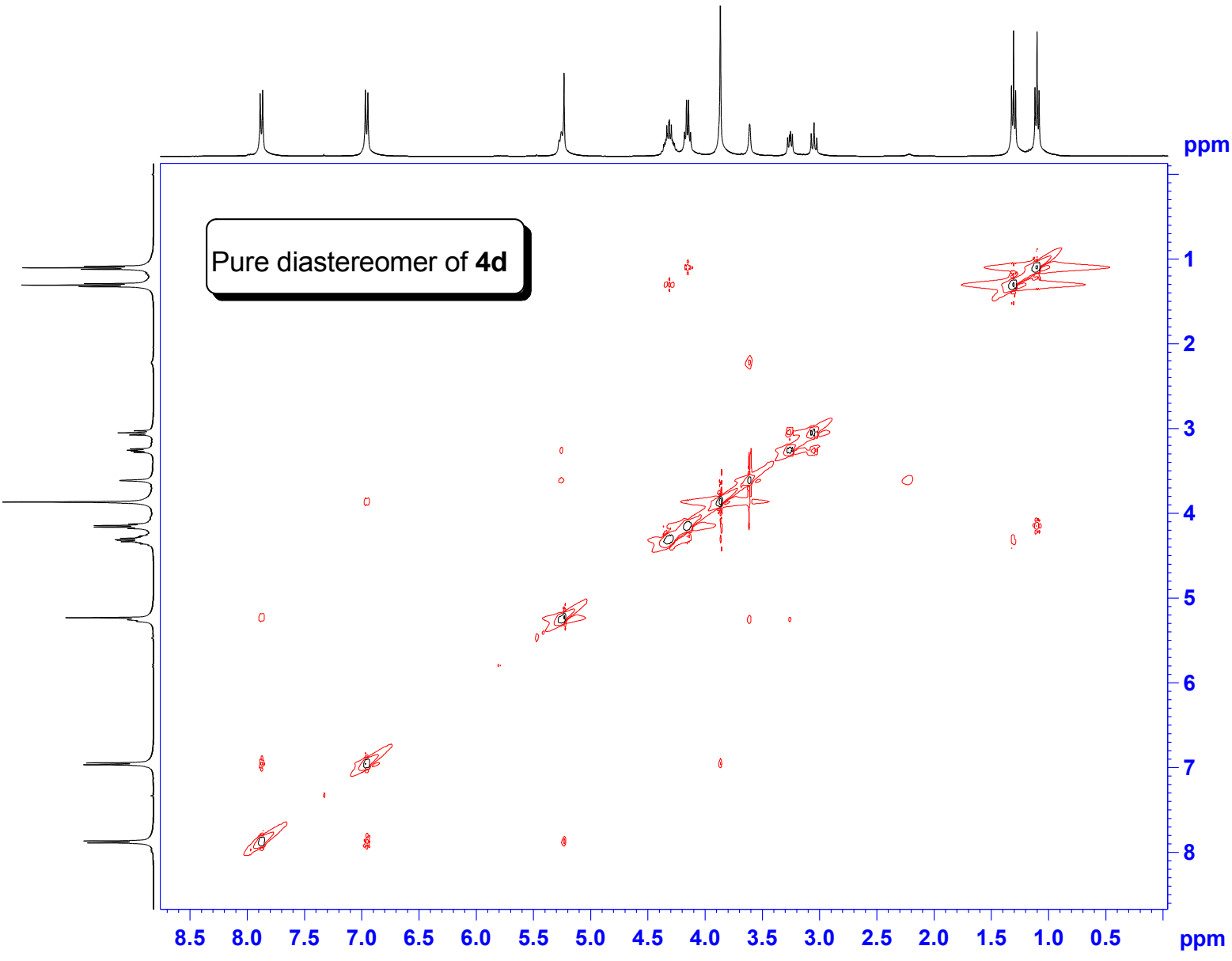


Figure 14. The NOESY spectrum of pure diastereomer of **4d** in $CDCl_3$ solvent

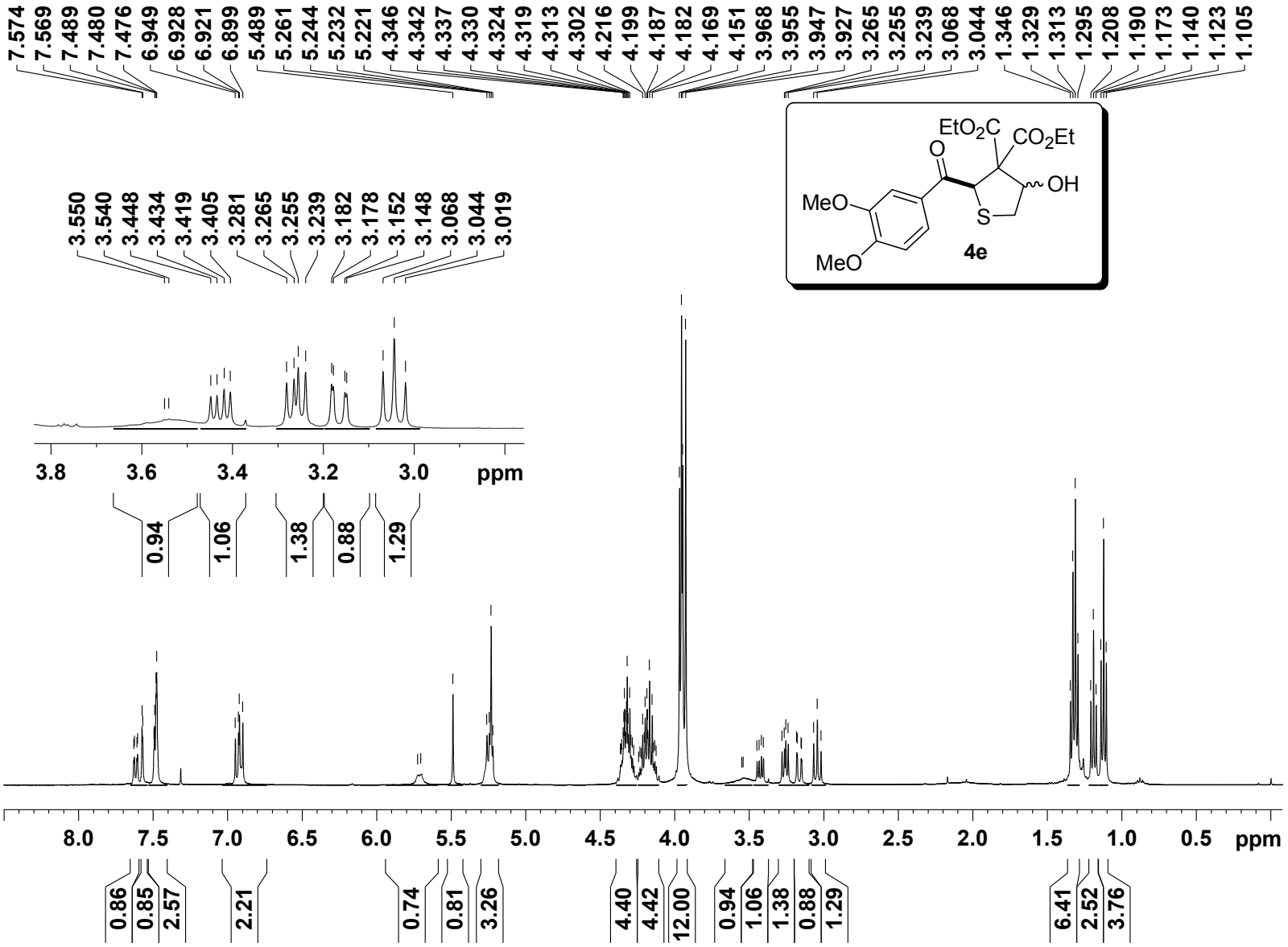


Figure 15. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **4e**

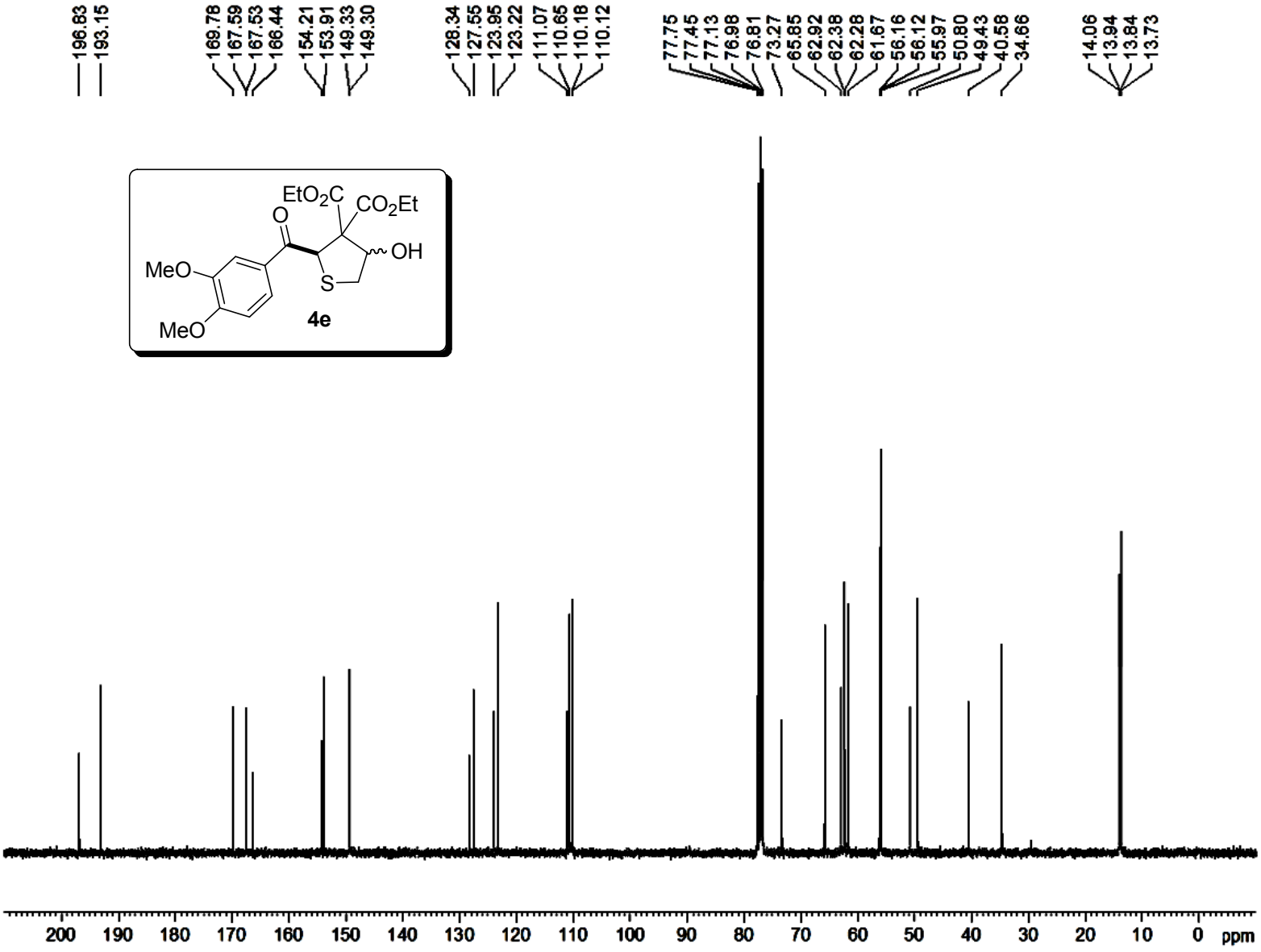


Figure 16. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **4e**

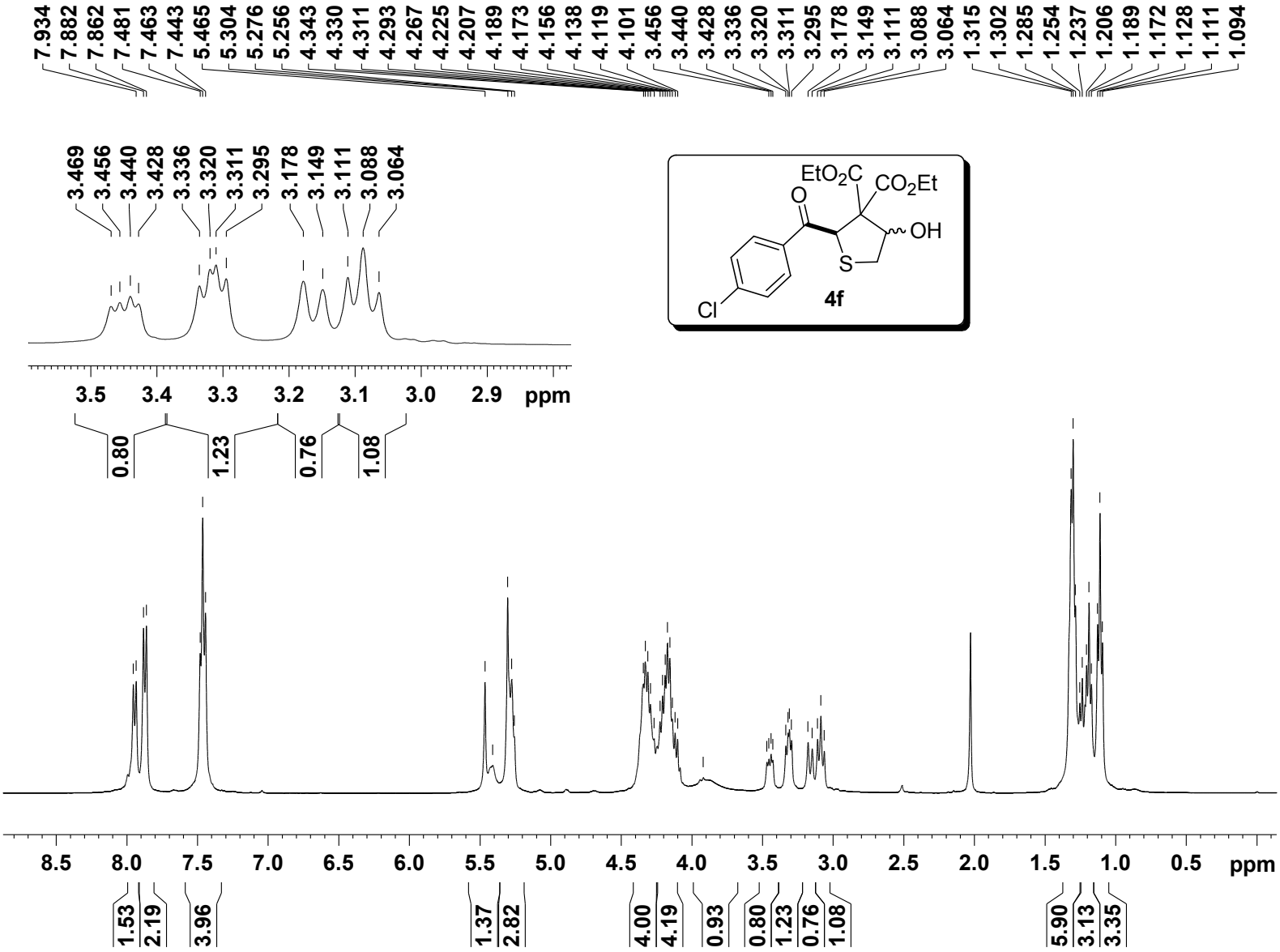


Figure 17. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **4f**

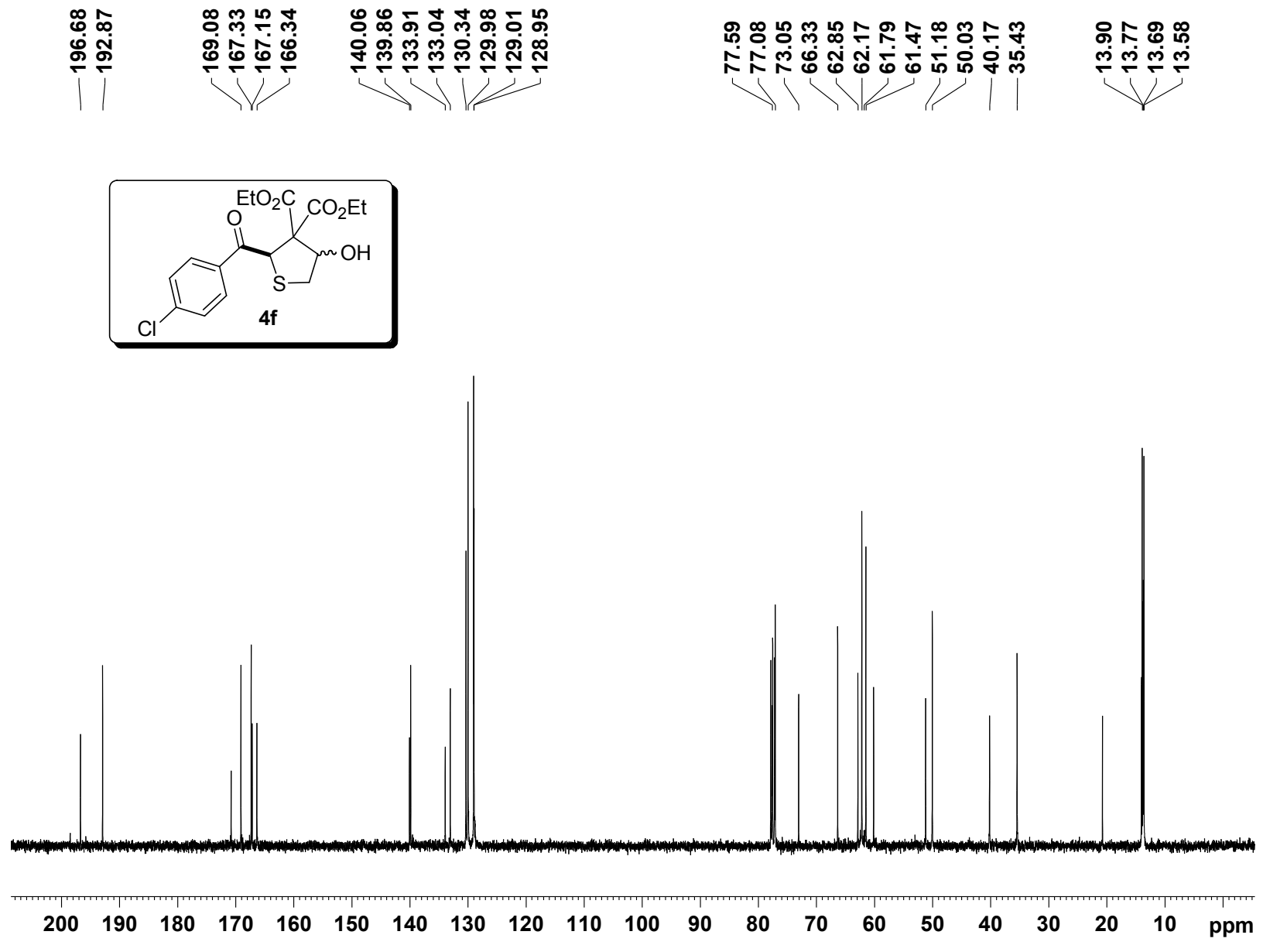


Figure 18. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **4f**

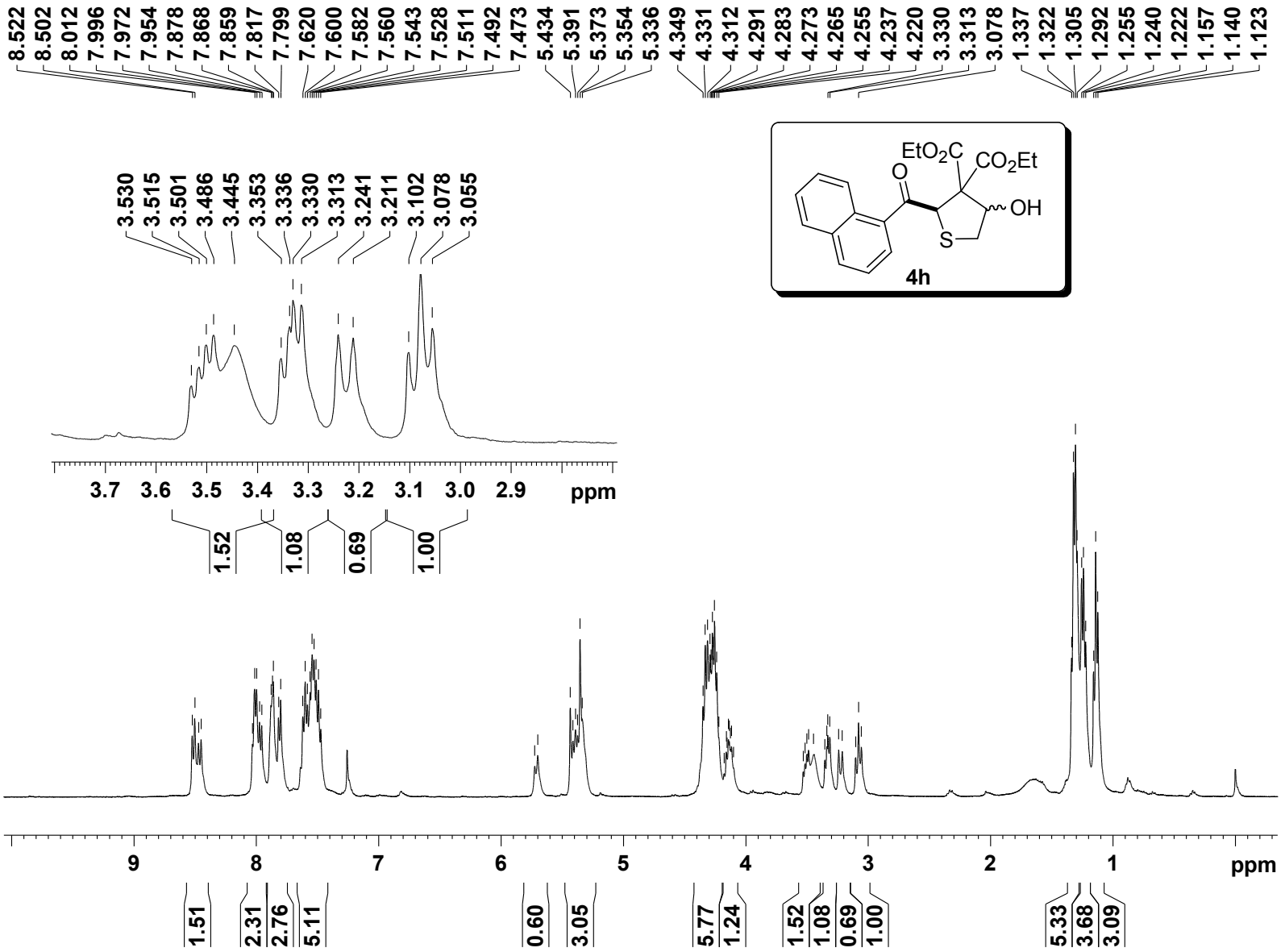


Figure 19. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **4h**

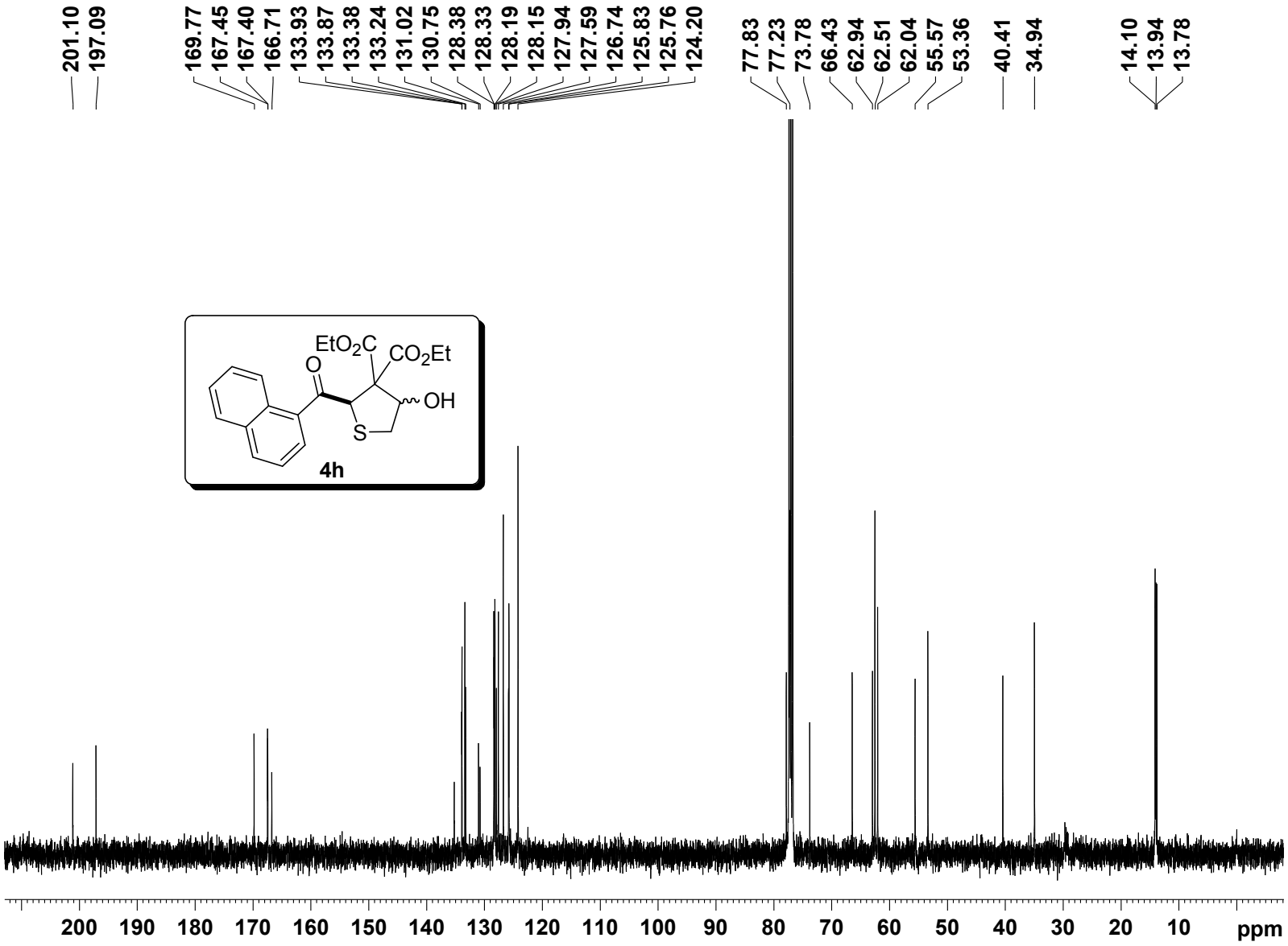


Figure 20. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **4h**

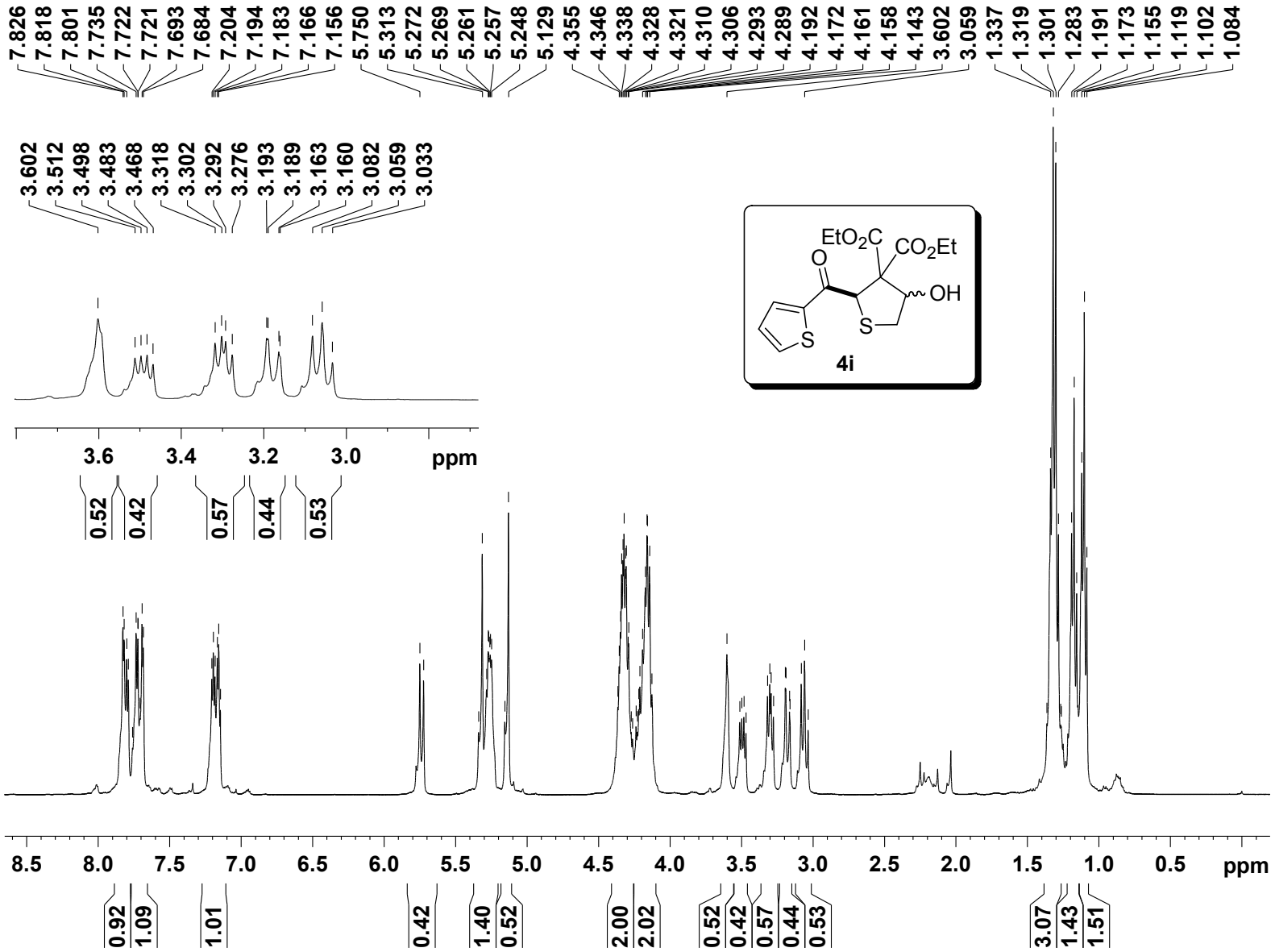


Figure 21. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **4i**

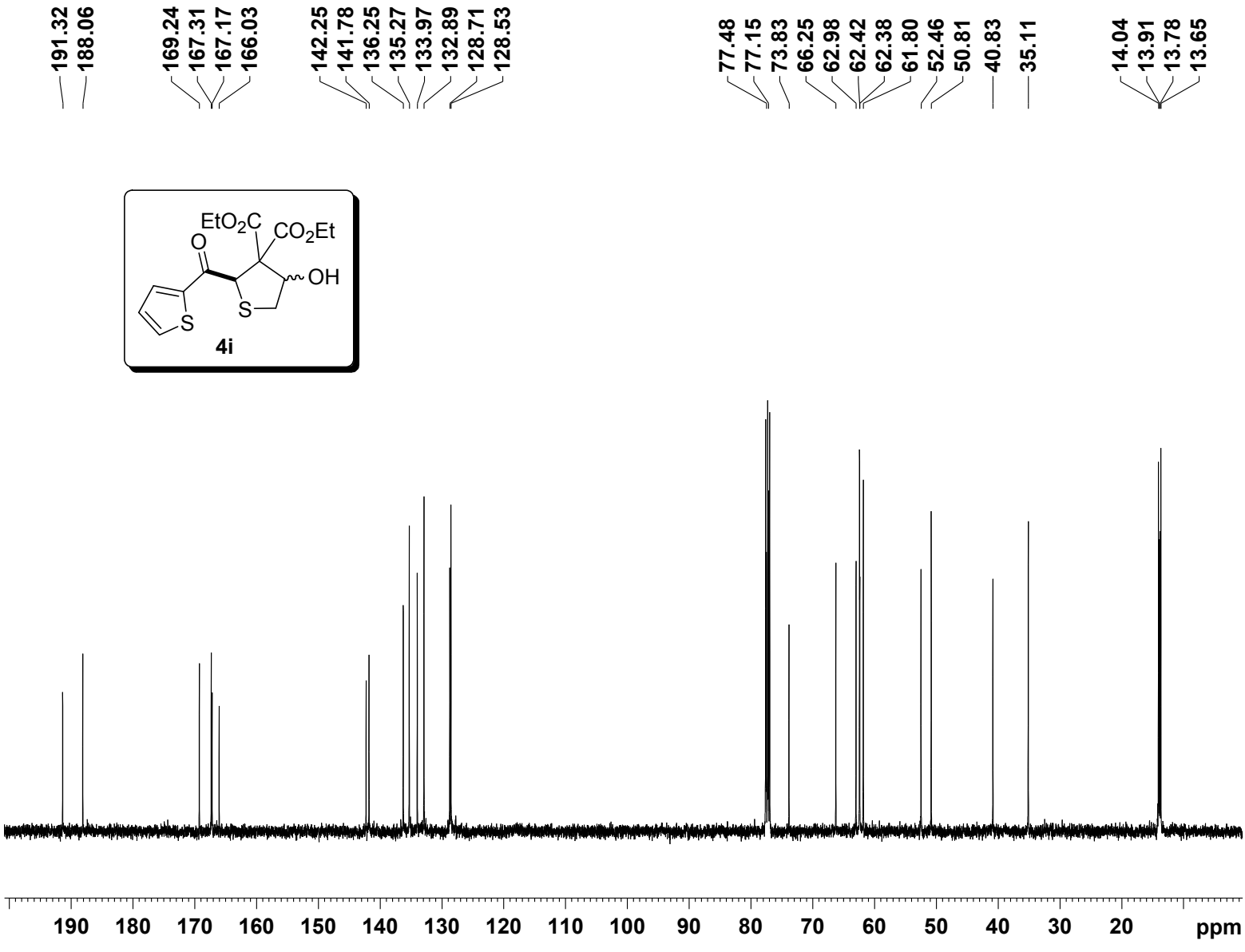


Figure 22. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **4i**

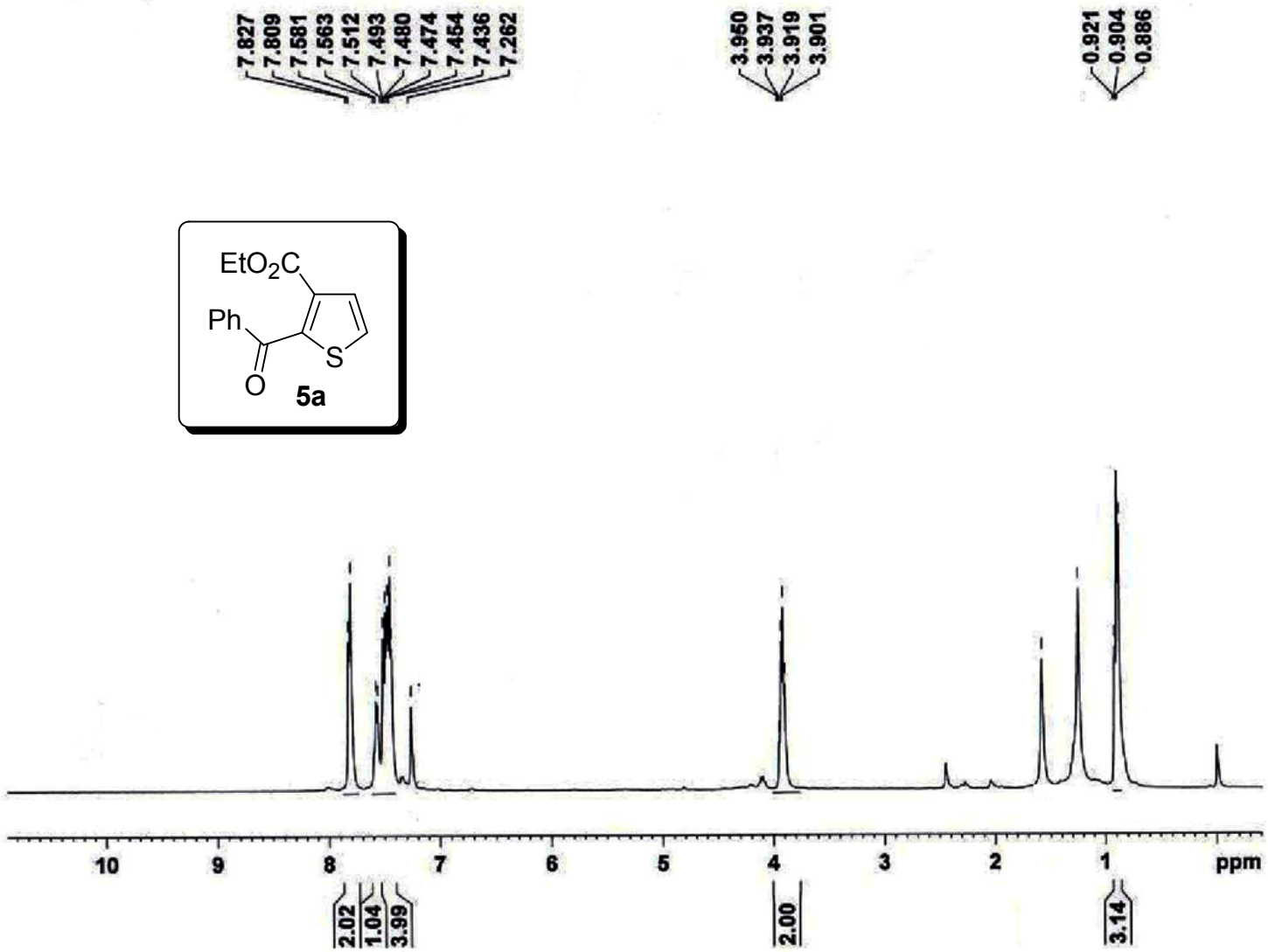


Figure 23. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **5a**

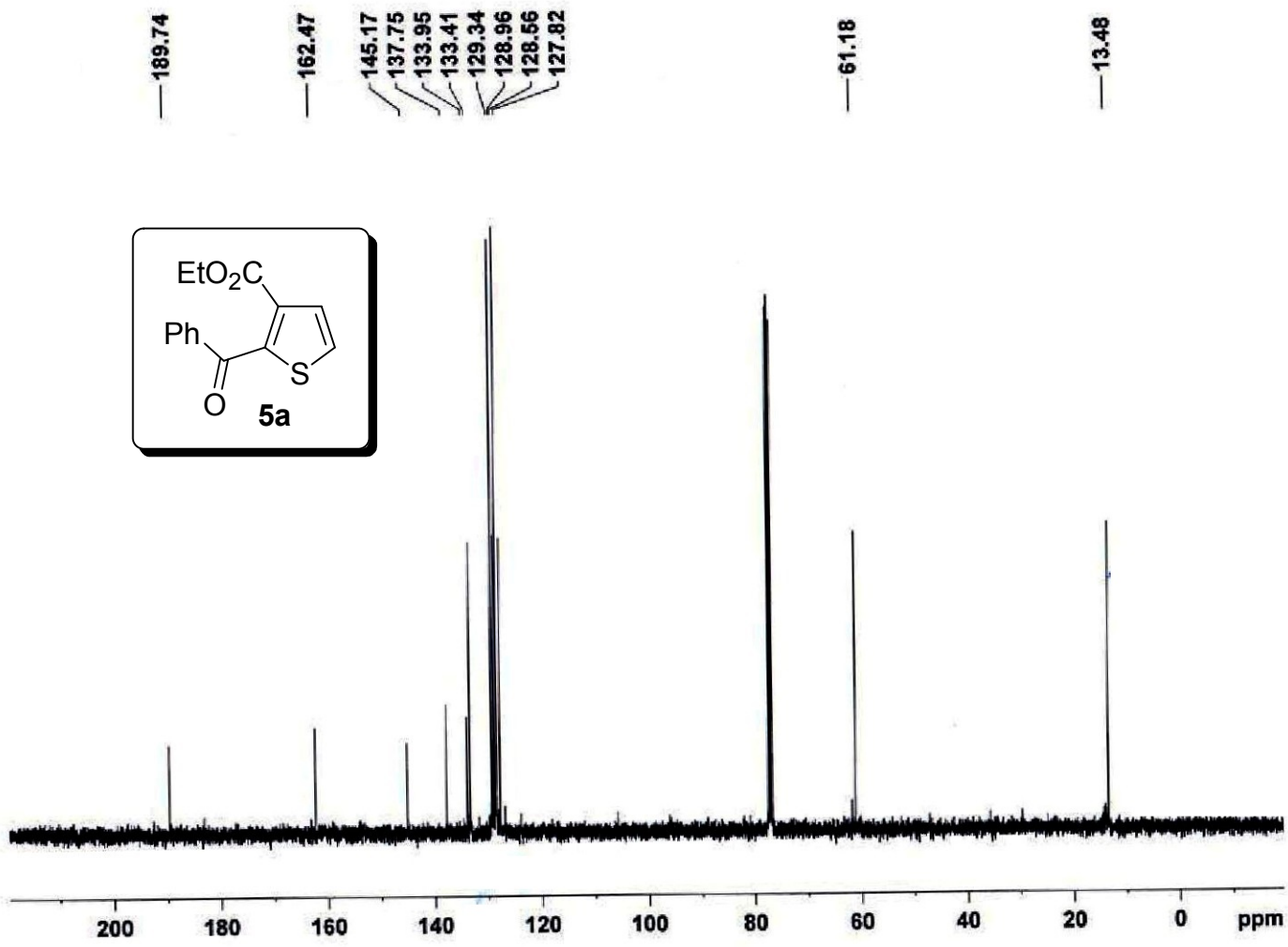


Figure 24. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **5a**

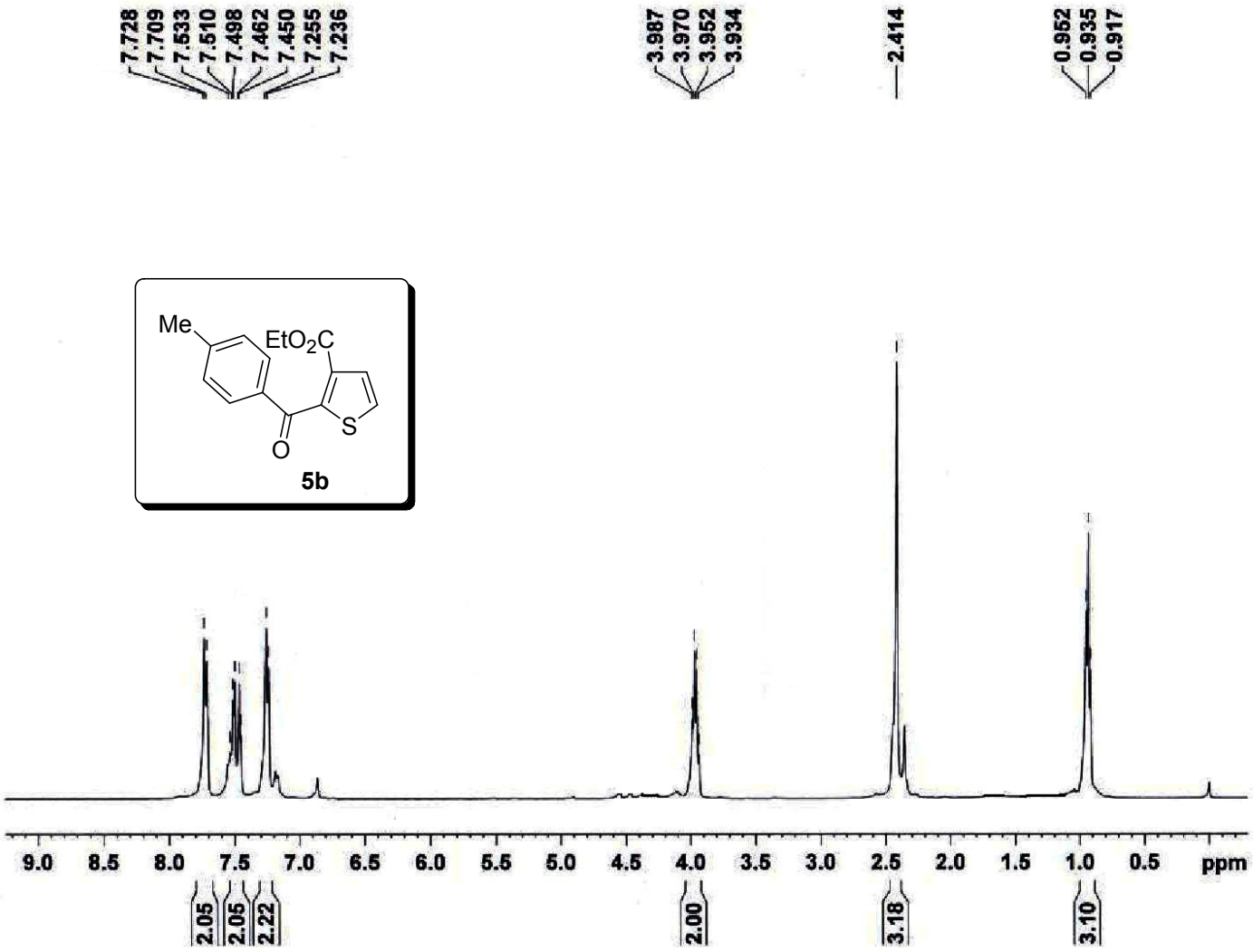


Figure 25. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **5b**

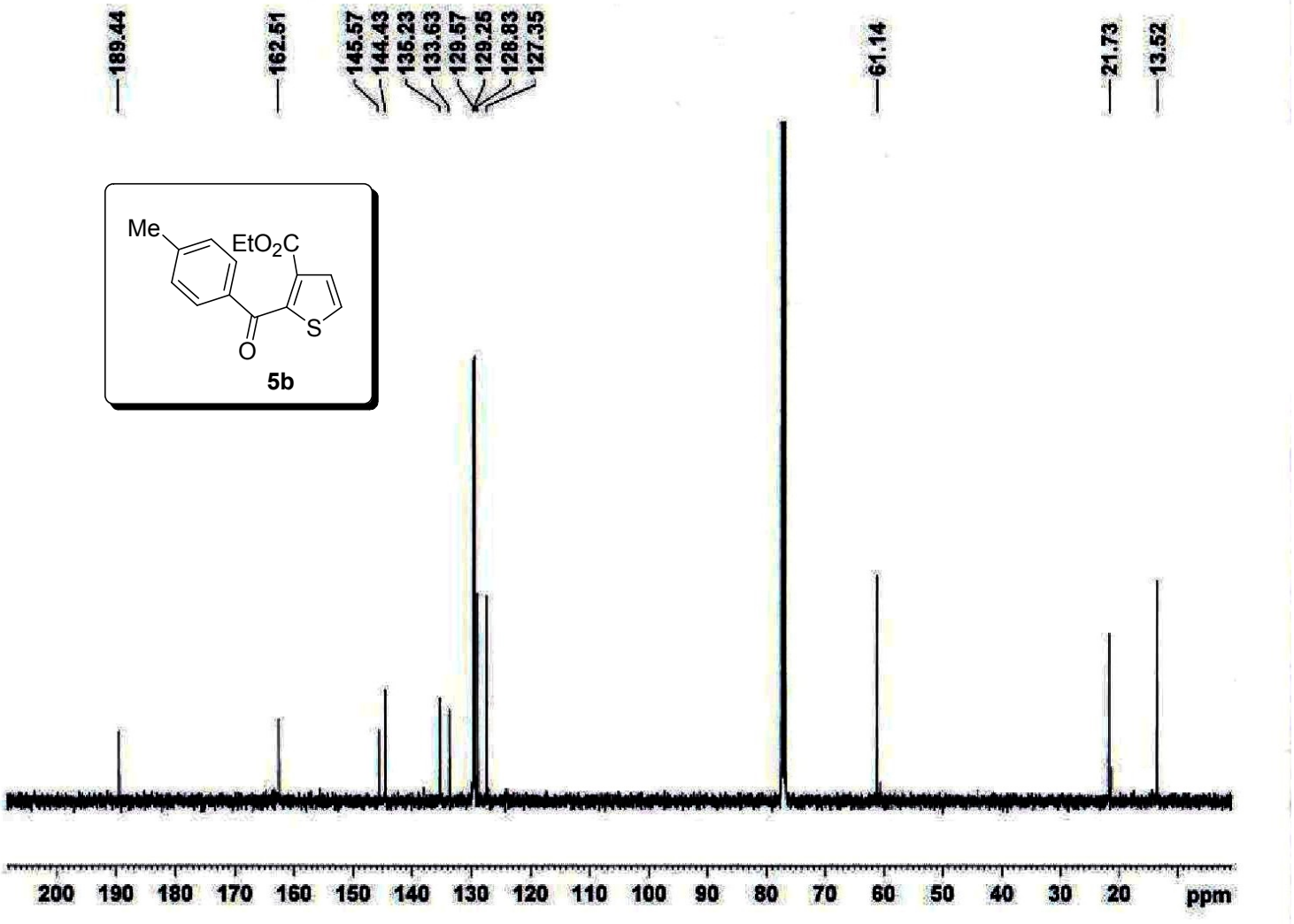


Figure 26. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **5b**

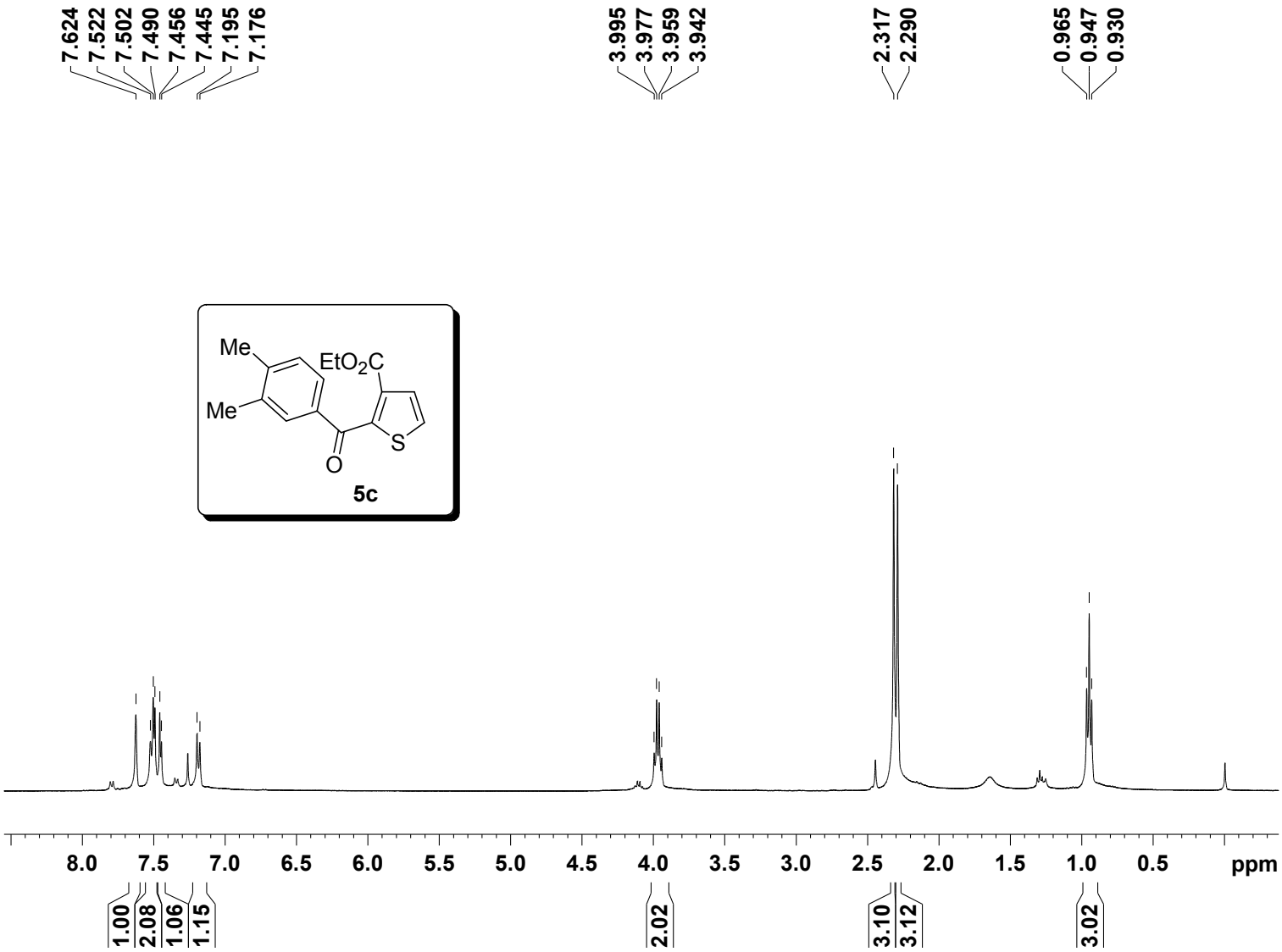


Figure 27. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **5c**

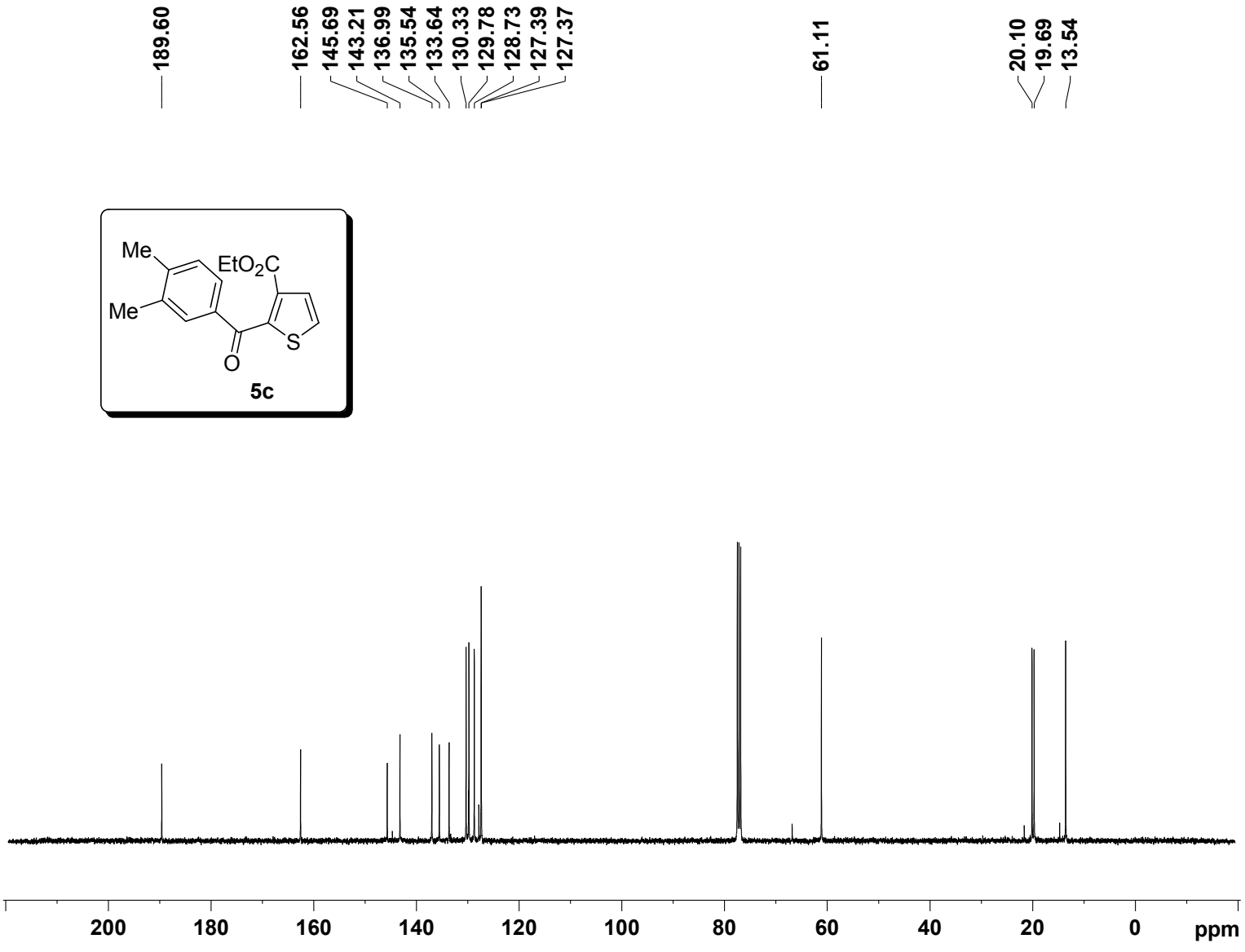


Figure 28. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **5c**

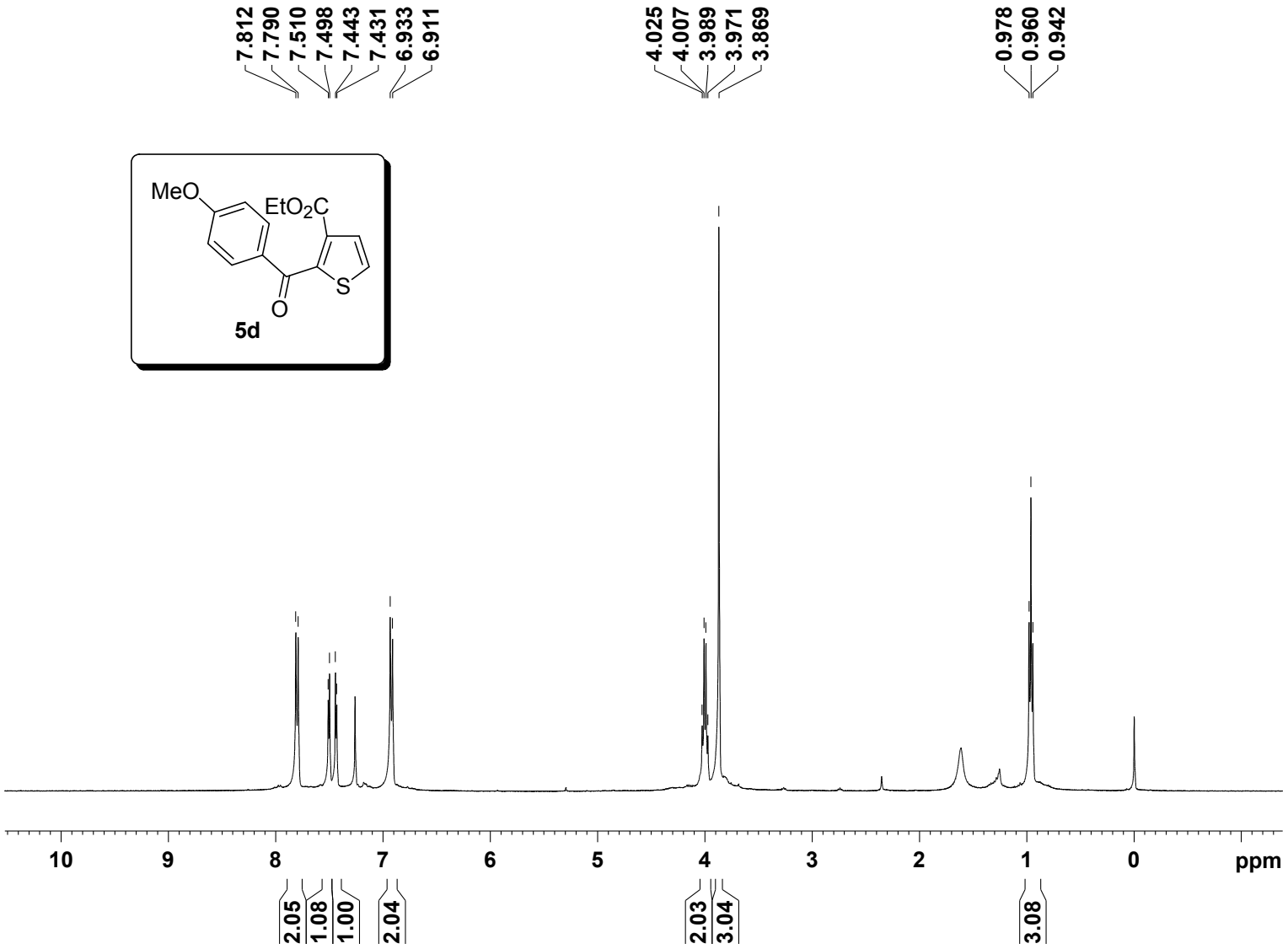


Figure 29. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **5d**

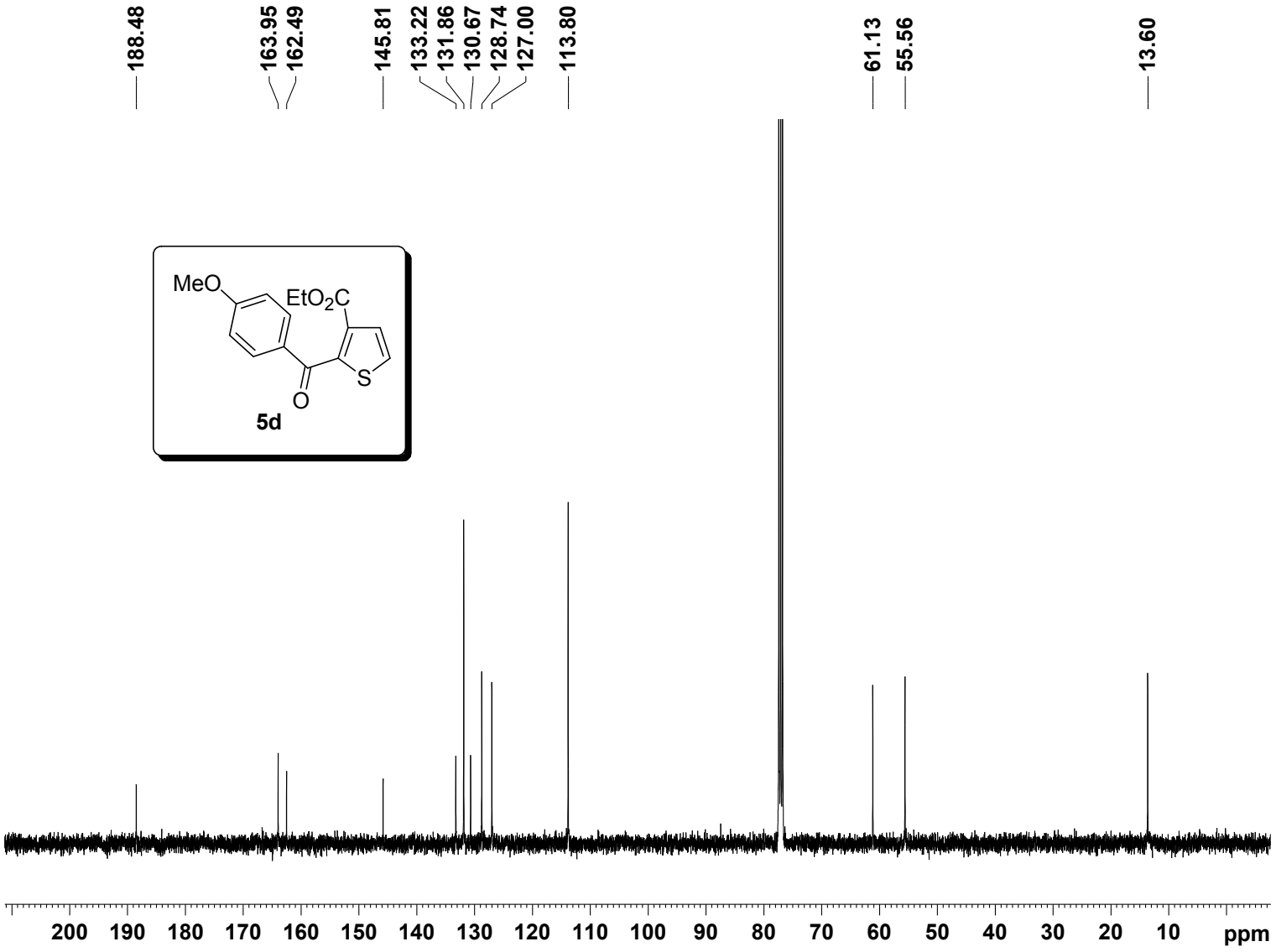


Figure 30. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **5d**

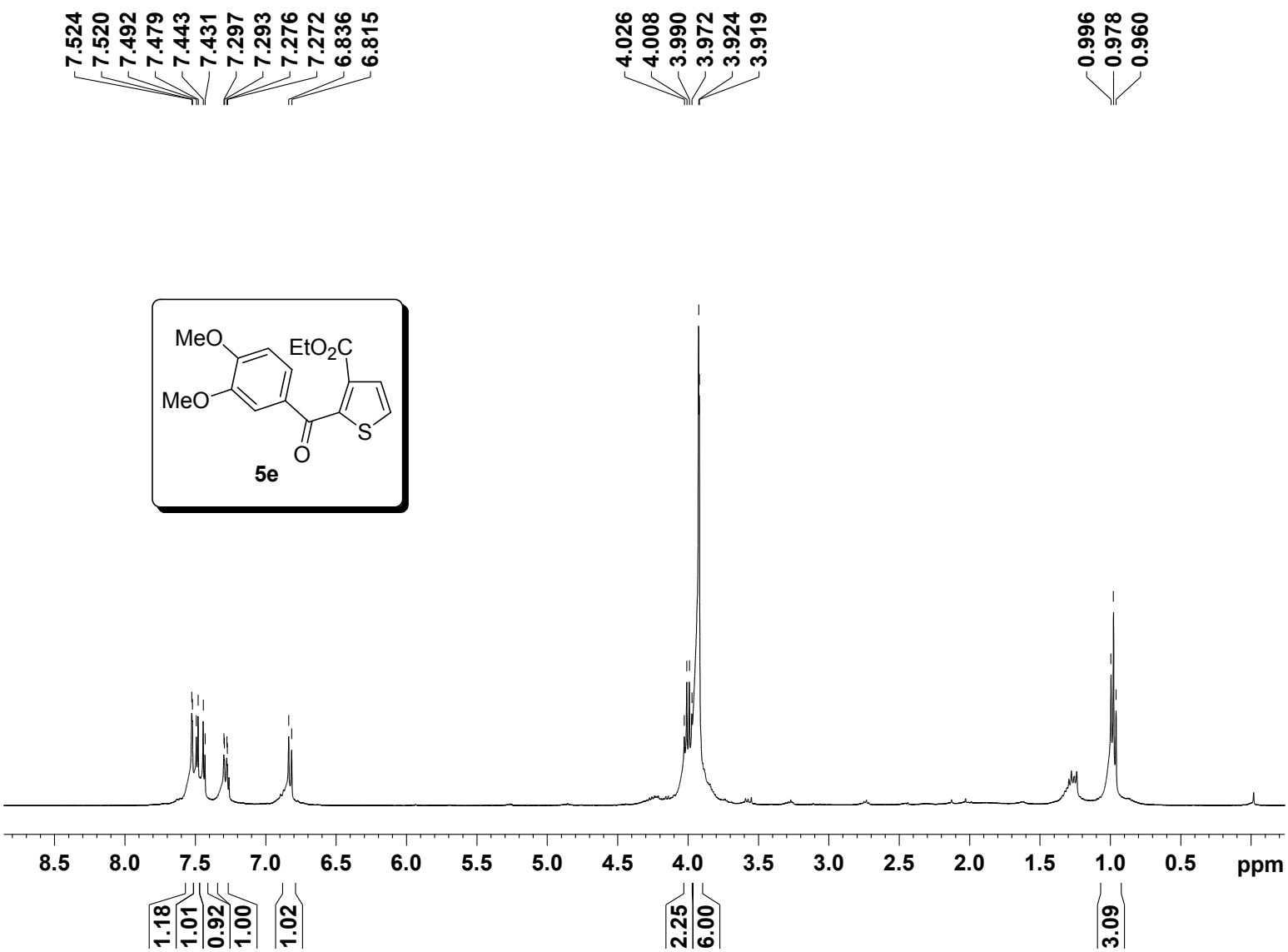


Figure 31. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **5e**

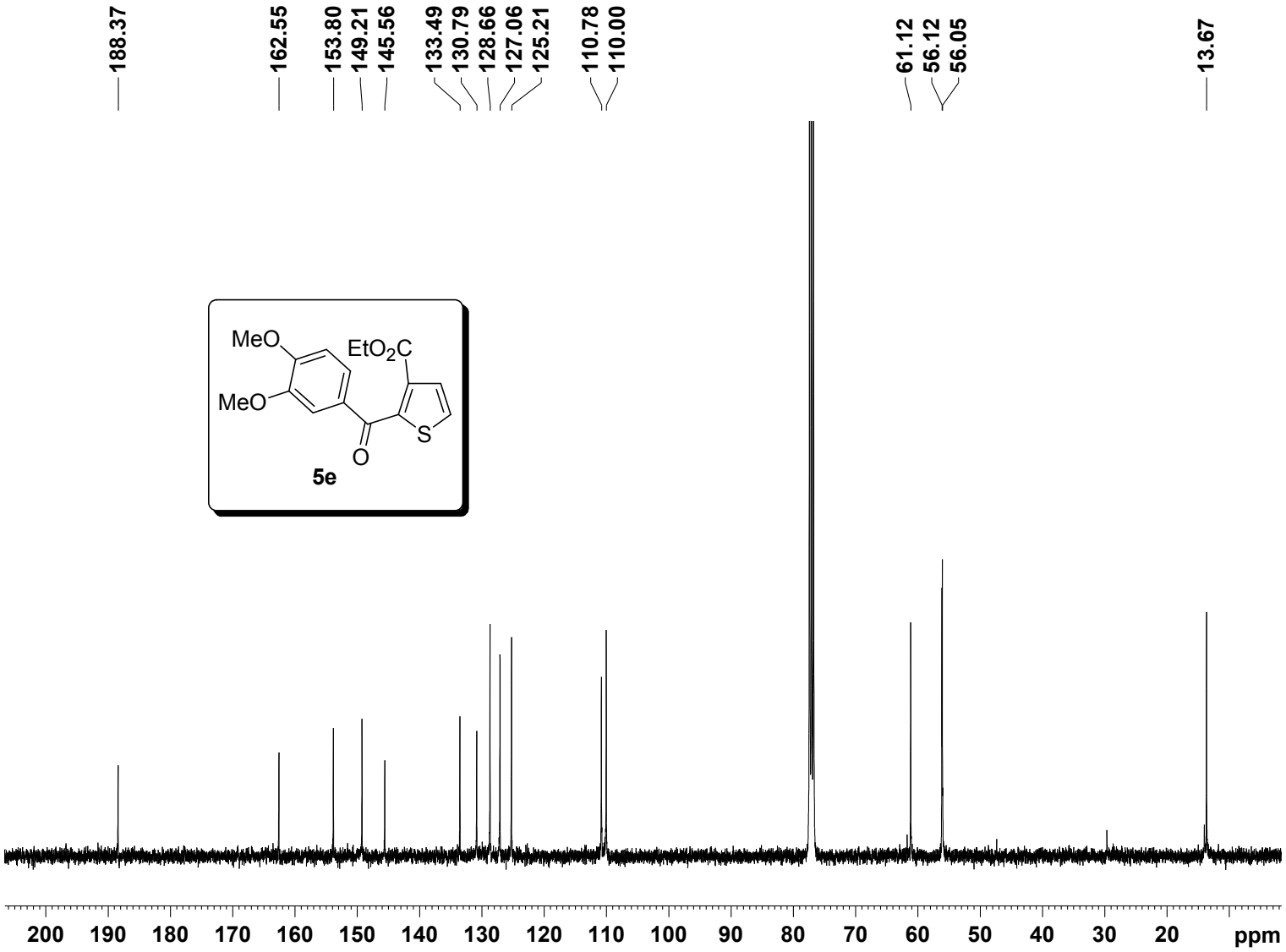


Figure 32. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **5e**

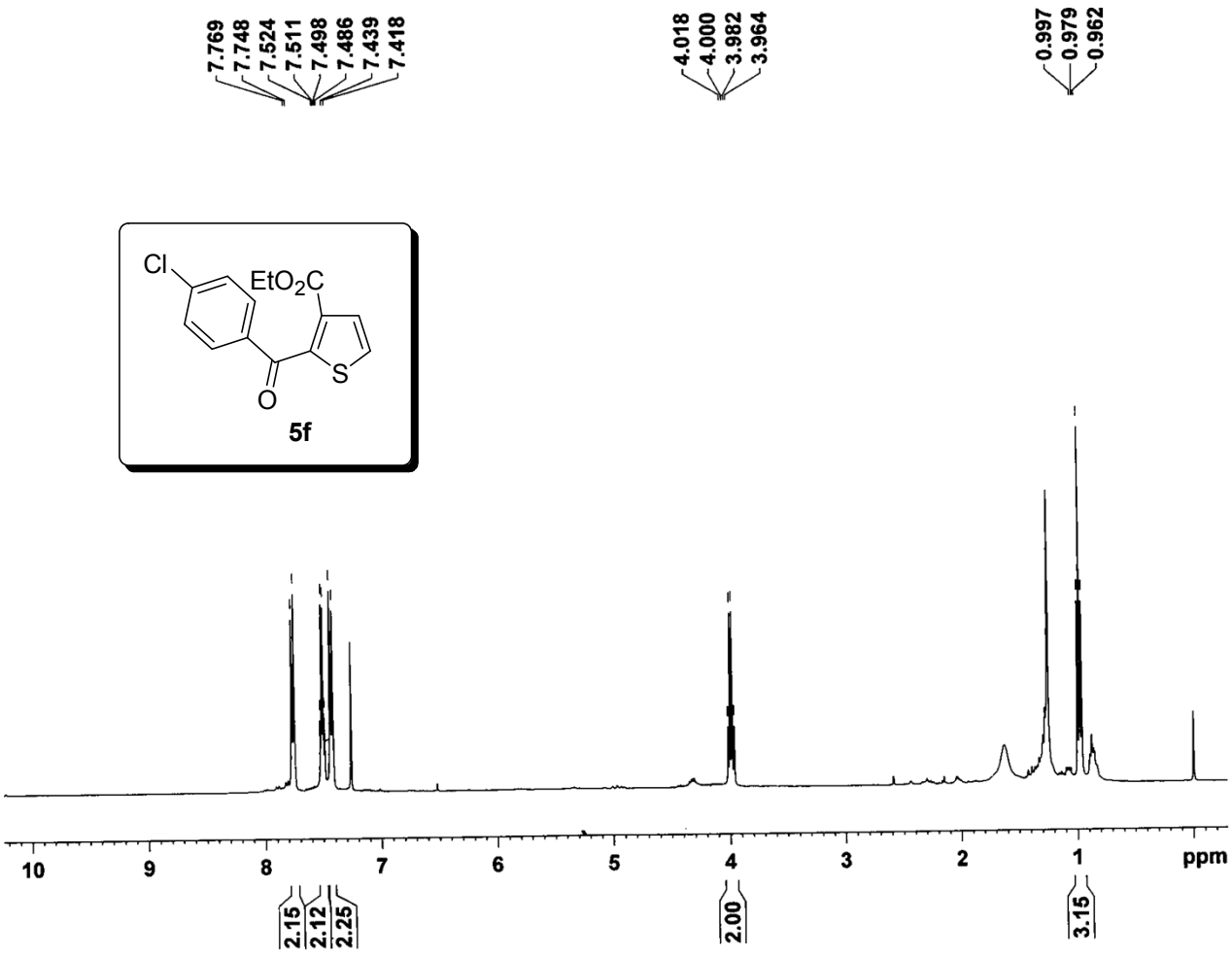


Figure 33. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **5f**

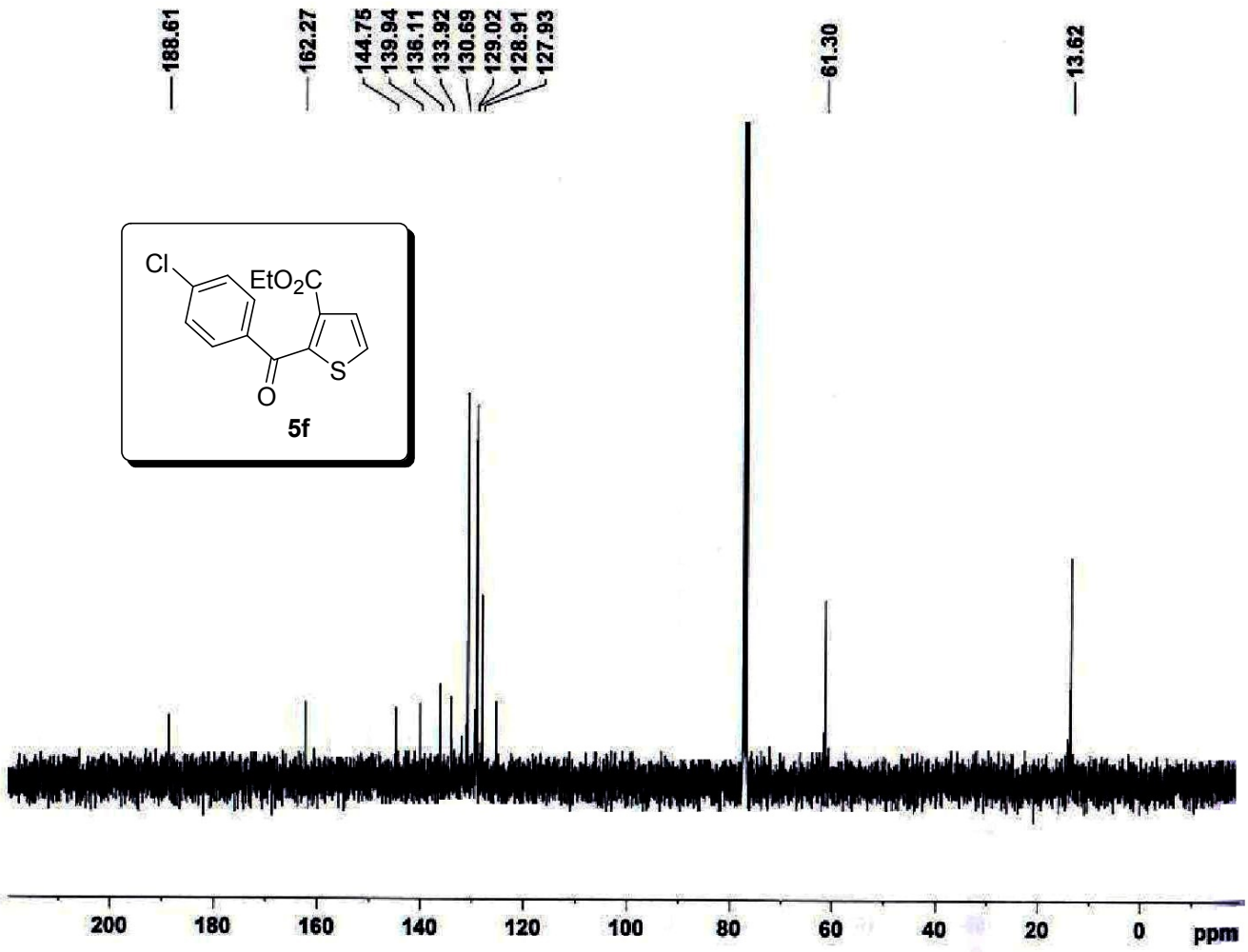


Figure 34. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **5f**

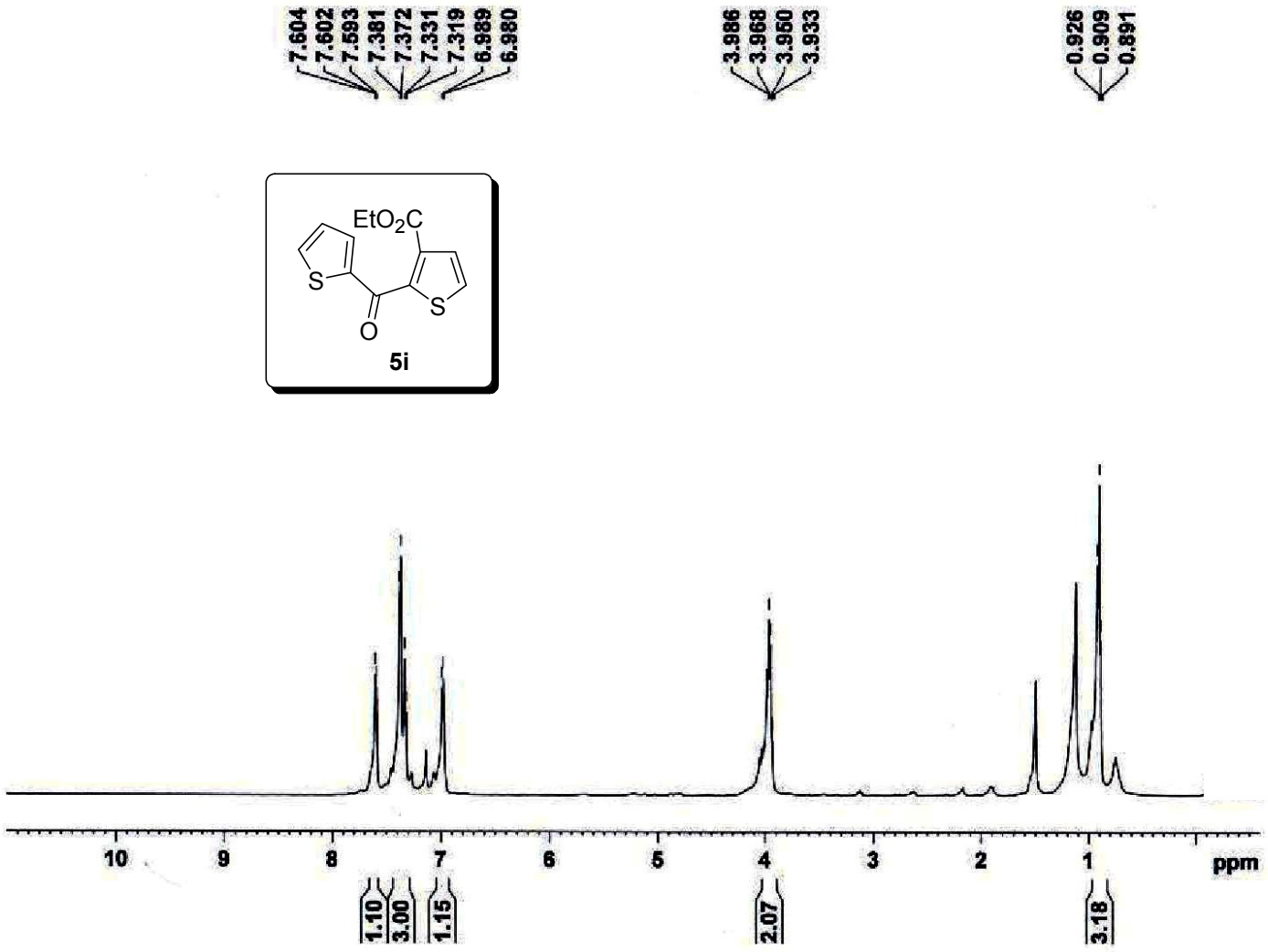


Figure 35. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **5i**

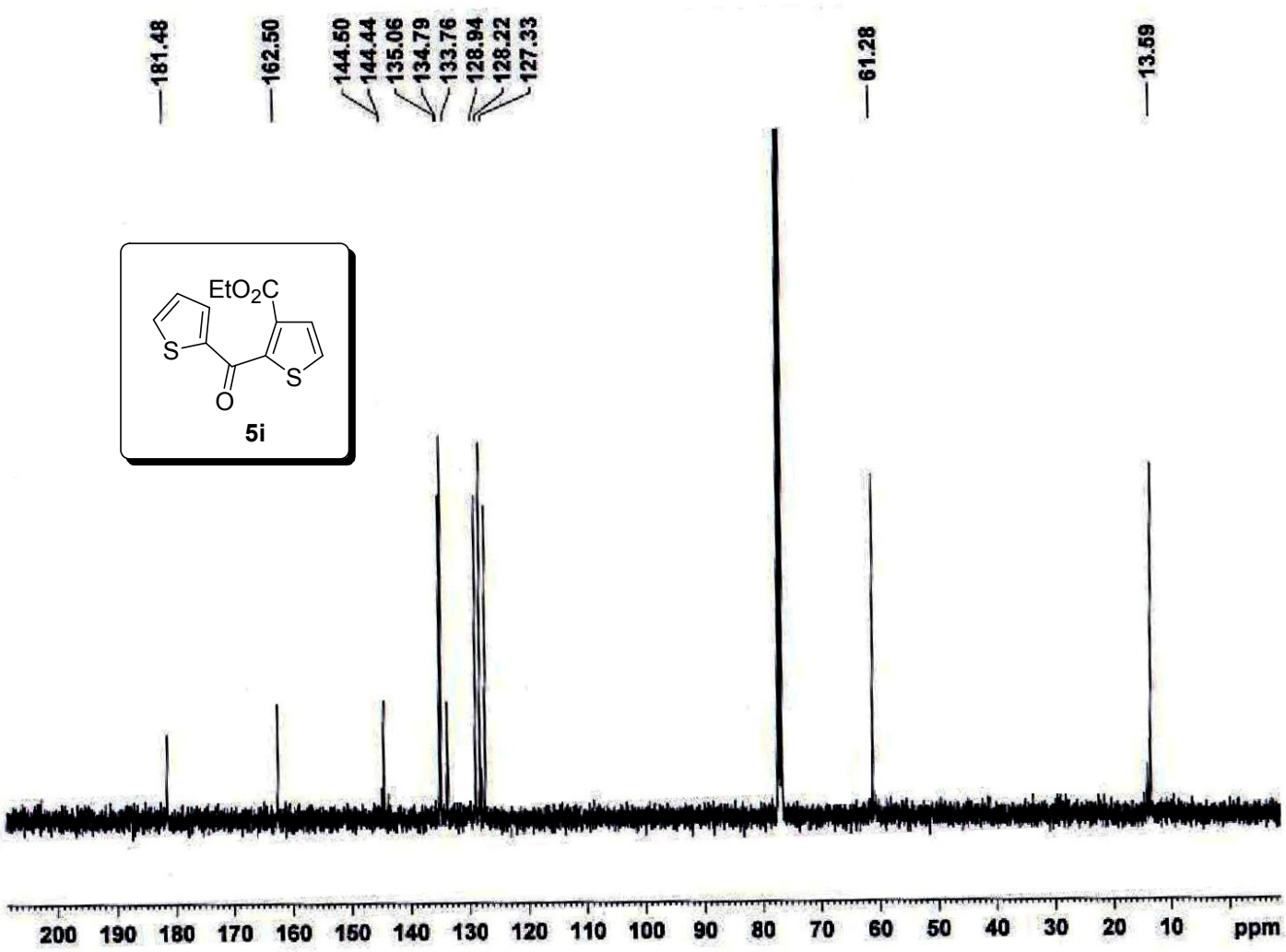


Figure 36. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **5i**

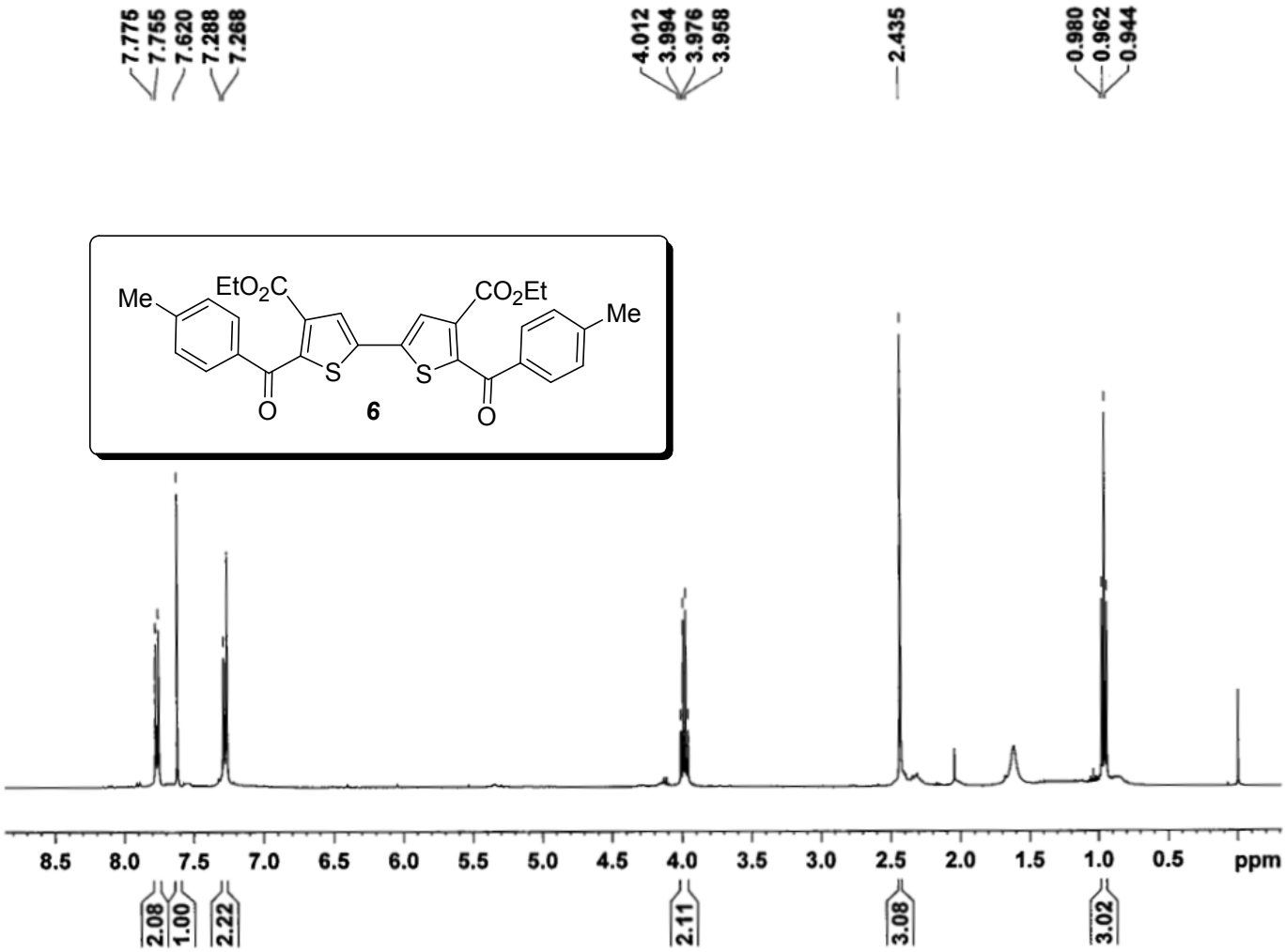


Figure 37. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **6**

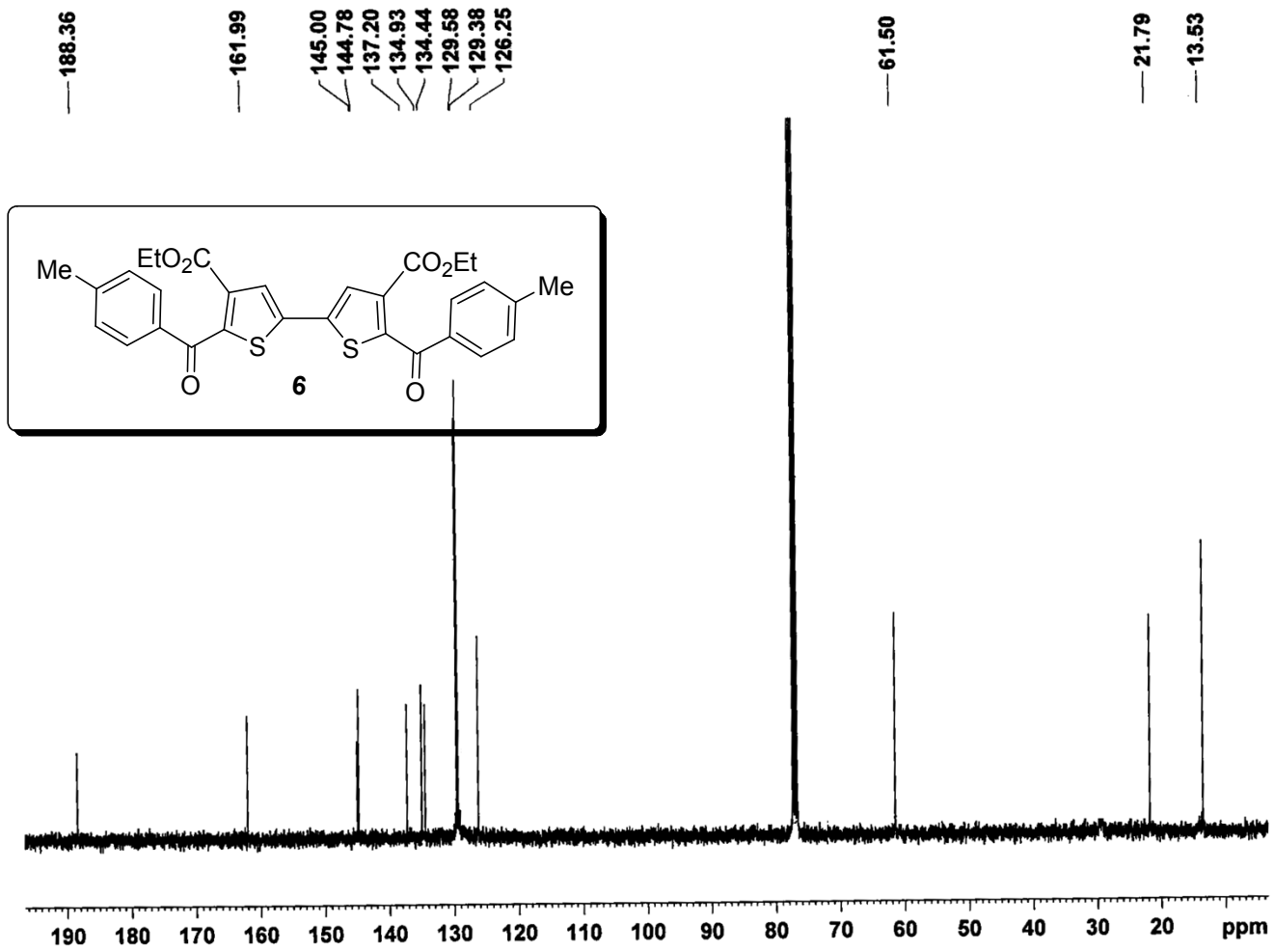


Figure 38. The ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **6**