Redox-Annulations of Cyclic Amines with 2-(2-oxoethyl)malonates

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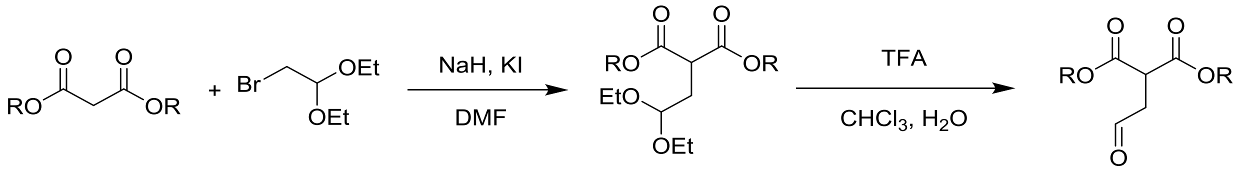
Supporting Information

General Information: Reagents and solvents were purchased from commercial sources and were purified by distillation or recrystallization prior to use. Purification of reaction products was carried out by flash column chromatography using EM Reagent silica gel 60 (230–400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60 F_{254} plates. Visualization was accomplished with UV light, and potassium permanganate, Dragendorff-Munier, and anisaldehyde stains, followed by heating. Melting points were recorded on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis Series FT-Infrared spectrophotometer. Microwave reactions were carried out in a CEM Discover reactor. Silicon carbide (SiC) passive heating elements were purchased from Anton Paar. Proton nuclear magnetic resonance spectra (^{1}H-NMR) were recorded on a Varian VNMRS-500 MHz instrument and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm, $(CD_3)_2SO$ at 2.50 ppm). Data are reported as app = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = complex, br = broad; coupling constant(s) in Hz. Proton-decoupled carbon nuclear magnetic resonance spectra (^{13}C-NMR) were recorded on a Varian VNMRS-500 MHz instrument and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.16 ppm, $(CD_3)_2SO$ at 39.52 ppm). Mass spectra were recorded on a Finnigan LCQ-DUO mass spectrometer or on a Finnigan 2001 Fourier Transform Ion Cyclotron Resonance Mass Spectrometer. Products **1a**,[1] **1b**,[2] **1f**[3] and **1h**[4] were previously reported and their published characterization data matched our own in all regards. Ratios of diastereomeric products were determined by ^{1}H-NMR analysis of the crude reaction mixture.

General Procedure A for the synthesis of the 2-(2-oxoethyl)malonate:



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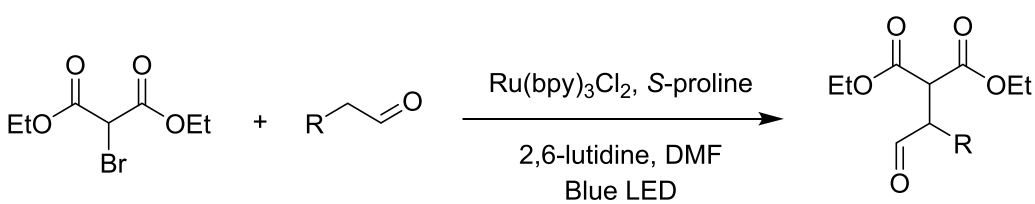
Following a modified literature procedure,[1] to an ice-cooled suspension of NaH (1.08 g, 60 wt% in mineral oil, 27.0 mmol, 1.8 equiv) in dry DMF (25 mL) was slowly added diethyl malonate (3.28 mL, 22.5 mmol, 1.5 equiv). The reaction mixture was stirred for 1 h at the same temperature, followed by slow addition of KI (0.45 g, 3.0 mmol, 0.2 equiv) and bromoacetaldehyde diethyl acetal (2.33 mL, 15.0 mmol, 1 equiv). Subsequently, the reaction mixture was heated at 100 °C for 24 h, cooled to 0 °C, diluted with Et_2O (75 mL), and quenched by slow addition of saturated aqueous NH_4Cl solution (10 mL). The organic layer was separated and washed with saturated aqueous NH_4Cl solution (2 × 10 mL), H_2O (2 × 25 mL), brine (25 mL), then dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue was used directly in the next step.

Compound **8** (4.14 g, 15 mmol) was treated with TFA/H_2O/$CHCl_3$ (3/1/3, 0.4 M) at 0 °C for 50 min. The mixture was poured into ice-cooled 1M K_2CO_3 (75 mL) and CH_2Cl_2 (125 mL), followed by slow addition of solid K_2CO_3 until the pH reached 7.5. The organic phase was washed with water (50 mL) and brine (50 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography.

General Procedure B for the synthesis of the 2-(1-alkyl-2-oxoethyl)malonate:



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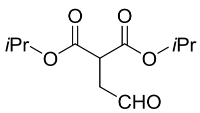
Following a modified literature procedure,[4] an oven-dried 8 mL vial equipped with a Teflon septum and magnetic stir bar was charged with tris-(2,2´-bipyridyl)ruthenium(II) chloride hexahydrate (11 mg, 15 µmol, 0.005 equiv), diethyl 2-bromomalonate (717 mg, 3 mmol, 1.0 equiv), and *S*-proline (69 mg, 0.6 mmol, 0.2 equiv). The vial was purged with a stream of nitrogen and 3 mL of dry DMF was added via syringe, followed by the corresponding aldehyde (6 mmol, 2.0 equiv) and 2,6-lutidine (0.35 mL, 6 mmol, 2.0 equiv). The vial was then sealed and placed approximately 8 cm from a 15 W fluorescent lamp. After the reaction was completed as indicated by TLC, the mixture was poured into a separatory funnel containing 5 mL of Et_2O and 5 mL of H_2O. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 5 mL) and the combined organic layers were washed with brine (20 mL) and dried over anhydrous

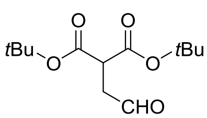
Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography.

New compounds were characterized as below:

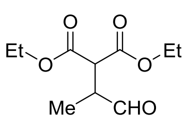
Diisopropyl 2-(2-oxoethyl)malonate 1c: Following the general procedure A, product **1c** was obtained from diisopropyl malonate and bromoacetaldehyde diethyl acetal as a yellow oil in 40% yield (over 2 steps) (1.38 g), (R_f = 0.57 in hexane/EtOAc 70:30 v/v); IR (film) 3443, 2989, 2737, 2354, 2092, 1756, 1639, 1468, 1451, 1406, 1376, 1321, 1273, 1170, 1100, 1050, 978, 900, 873, 820; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.77 (s, 1H), 5.05 (hept, *J* = 6.3 Hz, 2H), 3.80 (t, *J* = 7.0 Hz, 1H), 3.05 (dd, *J* = 6.9, 0.6 Hz, 2H), 1.26 (d, *J* = 6.3 Hz, 6H), 1.24 (d, *J* = 6.3 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.4, 168.1, 69.6, 46.3, 42.4, 21.73, 21.67; *m/z* (ESI–MS) 230.9 $[M + H]^+$.



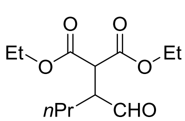
Di-*tert*-butyl 2-(2-oxoethyl)malonate 1d: Following the general procedure A, product **1d** was obtained from di-*tert*-butyl malonate and bromoacetaldehyde diethyl acetal as a yellow oil in 32% yield (over 2 steps) (1.24 g), (R_f = 0.42 in hexane/EtOAc 70:30 v/v); IR (film) 3440, 3004, 2980, 2930, 2852, 2729, 2092, 1725, 1640, 1478, 1458, 1394, 1370, 1283, 1255, 1163, 1144, 1034, 973, 893, 847, 738; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.76 (s, 1H), 3.69 (t, *J* = 7.0 Hz, 1H), 2.96 (dd, *J* = 7.0, 0.8 Hz, 2H), 1.46 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 167.9, 82.2, 48.0, 42.5, 28.0; *m/z* (ESI–MS) 258.9 $[M + H]^+$.



Diethyl 2-(1-oxopropan-2-yl)malonate 1e: Following the general procedure B, product **1e** was obtained from diethyl 2-bromomalonate and propionaldehyde as a yellow oil in 42% yield (270 mg), (R_f = 0.26 in hexane/Ether 70:30 v/v); IR (film) 3451, 2990, 2937, 2731, 2085, 1761, 1643, 1465, 1391, 1371, 1158, 1086, 1026, 950, 923, 862, 813; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.71 (d, *J* = 0.7 Hz, 1H), 4.26–4.14 (comp, 4H), 3.68 (d, *J* = 8.1 Hz, 1H), 3.17–3.09 (m, 1H), 1.26 (comp, 6H), 1.20 (d, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.1, 168.09, 168.07, 62.0, 61.9, 52.9, 45.4, 14.2, 14.1, 11.6; *m/z* (ESI–MS) 217.0 $[M + H]^+$.



Diethyl 2-(1-oxopentan-2-yl)malonate 1g: Following the general procedure B, product **1g** was obtained from diethyl 2-bromomalonate and valeraldehyde as a yellow oil in 55% yield (402 mg), (R_f = 0.34 in hexane/Ether 70:30 v/v); IR (film) 3440, 3059, 2987, 2964, 2934, 2869, 2364, 2339, 1783, 1731, 1644, 1466, 1371, 1311, 1266, 1183, 1158, 1100, 1035, 955, 903, 858, 739, 703; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.75 (d, *J* = 1.2 Hz, 1H), 4.25–4.12 (comp, 4H), 3.71 (d, *J* = 8.5 Hz, 1H), 3.09 (dddd, *J* = 9.0, 8.1, 5.0, 1.2 Hz, 1H), 1.72–1.63 (m, 1H), 1.54 (app ddt, *J* = 14.0, 10.6, 5.3 Hz, 1H), 1.47–1.35 (m, 1H), 1.35–1.26 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.6, 168.2, 168.1, 61.9, 61.9, 51.9, 50.2, 29.3, 20.0, 14.2, 14.14, 14.08; *m/z* (ESI–MS) 244.9 $[M + H]^+$.



General Procedure C for the redox-annulation of malonate aldehyde with secondary amines:

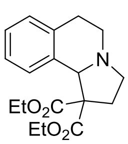
To a mixture of the malonate aldehyde **1** (0.5 mmol, 1 equiv), benzoic acid (12 mg, 0.1 mmol, 0.2 equiv), and 4 Å MS (100 mg) in toluene (0.1 M, 5 mL) was added the amine (1.0 mmol, 2 equiv). The mixture was heated under reflux until **1** was consumed as judged by TLC analysis. The reaction mixture was then allowed to cool to room temperature, diluted with EtOAc (20 mL), and washed with saturated aqueous $NaHCO_3$ (3 x 20 mL). The combined aqueous layers were extracted with EtOAc (2 x 10 mL) and the combined organic layers washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue was purified by silica gel chromatography.

General Procedure D for the redox-annulation of malonate aldehyde with amino acids:

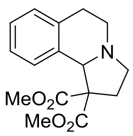
A solution of amino acid (2 mmol, 4 equiv), 4 Å MS (100 mg) and AcOH (0.57 mL, 10 mmol, 20 equiv) in mesitylene (4 mL) was heated under reflux. **1a** (101 mg, 0.5 mmol, 0.5 M solution in mesitylene) was delivered through the top of the reflux condenser over 1 hour via syringe pump. The reaction was then kept under reflux for a further 0.5 hours at which time **1a** was consumed as judged by TLC analysis. Subsequently, the reaction mixture was allowed to cool to room temperature, diluted with EtOAc (20 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 20 mL). The combined aqueous layers were extracted with EtOAc (2 x 10 mL) and the combined organic layers washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue was purified by silica gel chromatography.

New compounds were characterized as below:

Diethyl 2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-**2a:** To a mixture of **1a** (404.4 mg, 2 mmol, 1 equiv), benzoic acid (48.8 mg, 0.4 mmol, 0.2 equiv) and 4 Å MS (500 mg) in toluene (0.1 M, 20 mL) were added 1,2,3,4-tetrahydroisoquinoline (0.51 mL, 4 mmol, 2 equiv). The resulting mixture was heated under reflux for 1 h. The reaction mixture was then allowed to cool to room temperature, diluted with EtOAc (40 mL), and washed with saturated $NaHCO_3$ (2 x 40 mL). The combined aqueous layers were extracted with EtOAc (2 x 40 mL), and the combined organic layers washed with brine (80 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue was purified by silica gel chromatography. Product (±)-**2a** was obtained as a yellow oil in 70% yield (445 mg), (R_f = 0.29 in hexane/EtOAc 20:80 v/v); IR (film) 3427, 3054, 2985, 2837, 2306, 1720, 1649, 1612, 1504, 1466, 1369, 1266, 1231, 1191, 1123, 1097, 1038, 896, 738, 704; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.44 (dd, *J* = 6.7, 1.8 Hz, 1H), 7.15–7.02 (comp, 3H), 4.76 (s, 1H), 4.35 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.27 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.76 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.59 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.29–3.16 (comp, 2H), 2.95–2.77 (comp, 4H), 2.67 (ddd, *J* = 11.1, 6.3, 4.8 Hz, 1H), 2.43–2.33 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.84 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 171.2, 135.2, 133.6, 128.3, 128.2, 126.6, 125.2, 68.2, 65.6, 61.8, 61.3, 53.6, 46.4, 34.4, 29.0, 14.2, 13.6; *m/z* (ESI–MS) 318.2 $[M + H]^+$.

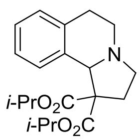


Dimethyl 2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-2b:



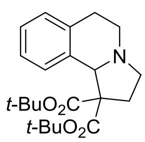
Following the general procedure C, **1b** and 1,2,3,4-tetrahydroisoquinoline were heated at reflux for 2 h. Product (±)-**2b** was obtained as a yellow oil in 78% yield (113 mg), (R_f = 0.37 in hexane/EtOAc 20:80 v/v); IR (KBr) 2950, 2845, 2777, 2376, 1730, 1651, 1556, 1488, 1431, 1336, 1247, 1237, 1219, 1124, 1083, 1068, 1028, 923, 815, 765, 748, 693, 663, 643, 610, 495; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.41–7.38 (m, 1H), 7.15–7.06 (comp, 3H), 4.75 (s, 1H), 3.85 (s, 3H), 3.28–3.20 (comp, 5H), 2.96–2.78 (comp, 4H), 2.68 (ddd, *J* = 11.3, 6.5, 4.8 Hz, 1H), 2.46–2.36 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 171.6, 135.3, 133.5, 128.4, 127.8, 126.7, 125.2, 68.4, 65.7, 53.7, 53.0, 52.2, 46.6, 34.4, 28.9; *m/z* (ESI–MS) 290.1 $[M + H]^+$

Diisopropyl 2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-2c:



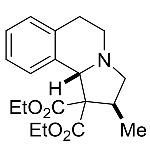
Following the general procedure C, **1c** and 1,2,3,4-tetrahydroisoquinoline were heated at reflux for 2 h. Product (±)-**2c** was obtained as a yellow oil in 56% yield (96 mg), (R_f = 0.35 in hexane/EtOAc 20:80 v/v); IR (film) 2982, 2932, 2870, 1717, 1655, 1494, 1454, 1374, 1264, 1219, 1184, 1145, 1107, 949, 936, 830, 759, 745, 660, 488, 423; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.51–7.44 (m, 1H), 7.12–7.02 (comp, 3H), 5.17 (app hept, *J* = 6.3 Hz, 1H), 4.71 (s, 1H), 4.57 (app hept, *J* = 6.3 Hz, 1H), 3.26–3.16 (comp, 2H), 2.92–2.77 (comp, 4H), 2.64 (ddd, *J* = 11.2, 6.4, 4.8 Hz, 1H), 2.35–2.27 (m, 1H), 1.30 (d, *J* = 6.3 Hz, 3H), 1.29 (d, *J* = 6.3 Hz, 3H), 0.91 (d, *J* = 6.3 Hz, 3H), 0.71 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 170.6, 135.2, 133.8, 128.6, 128.2, 126.5, 125.2, 69.1, 69.0, 68.1, 65.3, 53.3, 46.5, 34.5, 29.2, 21.8, 21.6, 21.2, 21.0; *m/z* (ESI–MS) 346.1 $[M + H]^+$.

Di-tert-butyl 2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-2d:



Following the general procedure C, **1d** and 1,2,3,4-tetrahydroisoquinoline were heated at reflux for 2 h. Product (±)-**2d** was obtained as a yellow oil in 50% yield (94 mg), (R_f = 0.38 in hexane/EtOAc 20:80 v/v); IR (film) 3054, 2982, 2933, 2303, 1720, 1651, 1495, 1478, 1455, 1423, 1369, 1266, 1150, 1122, 1100, 1083, 1037, 909, 896, 841, 739; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.54–7.47 (m, 1H), 7.13–7.07 (comp, 2H), 7.07–7.03 (m, 1H), 4.70 (s, 1H), 3.25–3.11 (comp, 2H), 2.95–2.76 (comp, 4H), 2.63 (ddd, *J* = 11.1, 6.1, 5.0 Hz, 1H), 2.23–2.14 (m, 1H), 1.52 (s, 9H), 1.02 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 170.2, 135.3, 133.9, 129.6, 128.2, 126.5, 125.2, 81.6, 81.4, 67.6, 66.2, 53.2, 46.4, 34.4, 29.2, 28.1, 27.4; *m/z* (ESI–MS) 374.1 $[M + H]^+$.

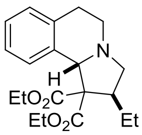
Diethyl (2*S*,10*bS*)-2-methyl-2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-2e:



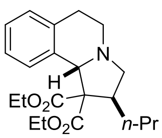
Following the general procedure C, **1e** and 1,2,3,4-tetrahydroisoquinoline were heated at reflux for 2 h. Product (±)-**2e** was obtained in 30% yield (40 mg), (3.8:1 mixture of diastereomers). The major diastereomer was isolated as a yellow oil, (R_f = 0.15 in hexane/EtOAc 90:10 v/v); IR (film) 3054, 2985, 2929, 2872, 2799, 2684, 2305, 1721, 1493, 1422, 1368, 1265, 1200, 1126, 1108, 1080, 1035, 893, 739, 704; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37–7.32 (m, 1H), 7.12–7.01 (comp, 3H), 4.89 (s, 1H), 4.34 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.23 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.74 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.54–3.43 (comp, 2H), 3.31 (m, 1H), 3.13–3.05 (m, 1H), 2.86 (ddd, *J* = 15.5, 7.6, 4.7 Hz, 1H), 2.75–2.60 (comp, 2H), 2.57 (dd, *J* = 10.0, 7.4 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.07 (d, *J* = 7.1 Hz, 3H), 0.76 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

170.9, 170.8, 135.6, 133.7, 129.2, 128.2, 126.5, 124.9, 68.6, 67.3, 61.3, 61.0, 47.2, 38.3, 28.5, 16.2, 14.3, 13.4; *m/z* (ESI–MS) 332.1 [M + H]$^+$.

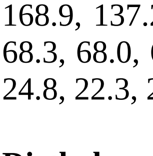
Diethyl (2*S*,10*bS*)-2-ethyl-2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-**2f:** Following the general procedure C, **1f** and 1,2,3,4-tetrahydroisoquinoline were heated at reflux for 1 h. Product (±)-**2f** was obtained as a yellow oil in 30% yield (51 mg), (3.1:1 mixture of diastereomers). The major diastereomer was isolated as a yellow oil, (R_f = 0.18 in hexane/EtOAc 90:10 v/v); IR (film) 3416, 3054, 2987, 2924, 2854, 2684, 2411, 2305, 1721, 1640, 1422, 1265, 1196, 1046, 896, 742, 705; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34–7.28 (m, 1H), 7.13–7.01 (comp, 3H), 4.79 (s, 1H), 4.35 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.21 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.76 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.54 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.44 (dd, *J* = 10.1, 7.0 Hz, 1H), 3.21–3.06 (comp, 2H), 2.88 (ddd, *J* = 16.1, 7.9, 4.8 Hz, 1H), 2.72 (app dt, *J* = 16.0, 5.3 Hz, 1H), 2.60 (ddd, *J* = 11.9, 7.7, 4.5 Hz, 1H), 2.56 (dd, *J* = 10.1, 8.1 Hz, 1H), 1.58 (m, 1H), 1.33–1.19 (comp, 4H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.76 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 170.9, 135.4, 133.8, 129.1, 128.3, 126.5, 124.8, 68.3, 68.1, 61.3, 61.0, 59.2, 47.4, 45.3, 29.0, 23.8, 14.2, 13.4, 12.5; *m/z* (ESI–MS) 346.3 [M + H]$^+$.



Diethyl (2*S*,10*bS*)-2-propyl-2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-**2g:** Following the general procedure C, **1g** and 1,2,3,4-tetrahydroisoquinoline were heated at reflux for 1 h. Product (±)-**2g** was obtained as a yellow oil in 42% yield (75 mg), (3.7:1 mixture of diastereomers) (R_f = 0.24 in hexane/EtOAc 90:10 v/v); IR (film) 3054, 2986, 2959, 2932, 2873, 2687, 2516, 2411, 2305, 1720, 1651, 1546, 1421, 1368, 1266, 1198, 1033, 896, 745; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.52–7.44 (m, 0.48H), 7.34–7.29 (m, 0.99H), 7.24–6.96 (comp, 4.33H), 5.17 (s, 0.30H), 4.81 (s, 1H), 4.34 (app dtd, *J* = 10.9, 7.2, 3.7 Hz, 1.47H), 4.23 (dq, *J* = 10.8, 7.2 Hz, 1.08H), 4.16 (app dtd, *J* = 17.8, 7.1, 4.0 Hz, 0.38H), 4.13–4.00 (m, 0.40H), 3.75 (dq, *J* = 10.7, 7.1 Hz, 1.08H), 3.64–3.46 (comp, 1.74H), 3.41 (dd, *J* = 10.1, 7.0 Hz, 1.01H), 3.23 (app dddd, *J* = 16.9, 13.2, 9.2, 6.0 Hz, 1.42H), 3.15–3.05 (comp, 1.48H), 3.04–2.94 (m, 0.47H), 2.95–2.82 (comp, 1.55H), 2.77–2.64 (comp, 1.36H), 2.65–2.53 (comp, 2.06H), 2.47–2.38 (m, 0.44H), 1.90–1.72 (comp, 1.70H), 1.53–1.14 (comp, 10.12H), 0.98–0.85 (comp, 3.95H), 0.82 (t, *J* = 7.1 Hz, 0.78H), 0.76 (t, *J* = 7.1 Hz, 2.77H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 171.0, 170.9, 168.9, 137.2, 136.5, 135.4, 133.8, 129.2, 128.4, 128.3, 127.2, 126.5, 126.0, 125.8, 124.8, 69.1, 68.3, 68.0, 66.0, 61.7, 61.3, 61.0, 60.8, 59.5, 56.6, 47.3, 46.8, 45.6, 43.4, 33.0, 31.4, 30.4, 28.9, 24.8, 22.3, 21.2, 14.3, 14.3, 14.2, 13.6, 13.4; *m/z* (ESI–MS) 360.2 [M + H]$^+$.

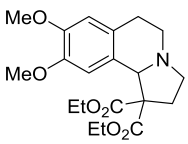


Diethyl (2*S*,10*bS*)-2-benzyl-2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-**2h:** Following the general procedure C, **1h** and 1,2,3,4-tetrahydroisoquinoline were heated at reflux for 1 h. Product (±)-**2h** was obtained as a yellow oil in 75% yield (152 mg), (1.6:1 mixture of diastereomers) (R_f = 0.26 in hexane/EtOAc 90:10 v/v); IR (film) 3417, 3054, 2985, 2937, 2684, 2305, 1721, 1651, 1495, 1455, 1422, 1368, 1266, 1200, 1160, 1125, 1096, 1061, 1031, 896, 740, 704; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.54–7.50 (m, 0.67H), 7.36 (app dd, *J* = 6.9, 2.2 Hz, 1.02H), 7.34–7.19 (comp, 8.18H), 7.15–7.02 (comp, 4.82H), 5.22 (s, 0.63H), 4.96 (s, 1.00H), 4.44–4.34 (comp, 2.34H), 4.22 (dq, *J* = 10.8, 7.1 Hz, 1.27H), 3.80 (dq, *J* = 10.7, 7.1 Hz, 1.16H), 3.71–3.53 (comp, 3.56H), 3.35–3.28 (comp, 1.28H), 3.15 (dd, *J* = 10.3, 6.8 Hz, 1.14H), 3.07–2.94 (comp,

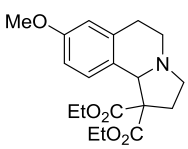


3.90H), 2.89–2.78 (comp, 2.43H), 2.71–2.54 (comp, 3.88H), 2.49–2.39 (comp, 1.79H), 1.42 (t, *J* = 7.1 Hz, 1.88H), 1.31 (t, *J* = 7.1 Hz, 2.98H), 0.90 (t, *J* = 7.1 Hz, 1.89H), 0.80 (t, *J* = 7.1 Hz, 2.84H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 170.8, 170.7, 168.7, 140.9, 139.7, 137.2, 136.3, 135.6, 133.7, 129.1, 129.0, 128.8, 128.57, 128.55, 128.4, 128.3, 127.3, 126.5, 126.4, 126.3, 126.1, 125.8, 124.9, 68.7, 68.04, 67.96, 66.3, 61.9, 61.5, 61.1, 61.0, 58.8, 56.1, 47.6, 47.2, 46.7, 44.7, 36.8, 35.7, 28.6, 24.7, 14.3, 14.2, 13.6, 13.4; *m/z* (ESI–MS) 408.1 $[M + H]^+$.

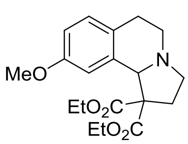
Diethyl 8,9-dimethoxy-2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-**2i:** Following the general procedure C, **1a** and 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline were heated at reflux for 1 h. Product (±)-**2i** was obtained as a yellow oil in 75% yield (141 mg), (R_f = 0.30 in MeOH/EtOAc 1:99 v/v); IR (film) 3439, 2937, 2835, 2256, 1724, 1651, 1612, 1518, 1465, 1367, 1267, 1228, 1122, 1097, 1061, 1019, 955, 865, 774, 734, 701; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.04 (s, 1H), 6.54 (s, 1H), 4.68 (s, 1H), 4.37–4.22 (comp, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 3.80–3.76 (m, 1H), 3.62 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.24–3.15 (comp, 2H), 2.95–2.79 (comp, 2H), 2.78–2.70 (comp, 2H), 2.64 (ddd, *J* = 10.9, 5.8, 4.8 Hz, 1H), 2.38 (ddd, *J* = 13.0, 6.3, 2.6 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 171.3, 147.7, 146.6, 127.5, 125.4, 111.2, 110.8, 67.9, 65.8, 61.7, 61.3, 55.82, 55.81, 53.6, 46.3, 34.3, 28.5, 14.2, 13.6; *m/z* (ESI–MS) 378.1 $[M + H]^+$.



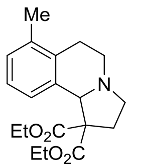
Diethyl 8-methoxy-2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-**2j:** Following the general procedure C, **1a** and 6-methoxy-1,2,3,4-tetrahydroisoquinoline were heated at reflux for 1 h. Product (±)-**2j** was obtained as a yellow oil in 62% yield (108 mg), (R_f = 0.40 in MeOH/EtOAc 1:99 v/v); IR (film) 3416, 3054, 2987, 2679, 2306, 1726, 1641, 1608, 1504, 1446, 1422, 1369, 1266, 1161, 1226, 1095, 1035, 896, 738, 705; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39–7.35 (m, 1H), 6.67 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.60 (d, *J* = 2.6 Hz, 1H), 4.70 (s, 1H), 4.34 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.27 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.84–3.78 (m, 1H), 3.76 (s, 3H), 3.63 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.27–3.18 (comp, 2H), 2.93–2.77 (comp, 4H), 2.65 (ddd, *J* = 11.1, 6.1, 4.9 Hz, 1H), 2.40–2.33 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 171.3, 158.2, 136.7, 129.5, 125.8, 112.6, 111.7, 67.9, 65.7, 61.8, 61.3, 55.3, 53.7, 46.4, 34.3, 29.4, 14.2, 13.7; *m/z* (ESI–MS) 348.1 $[M + H]^+$.



Diethyl 9-methoxy-2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-**2k:** Following the general procedure C, **1a** and 7-methoxy-1,2,3,4-tetrahydroisoquinoline were heated at reflux for 1 h. Product (±)-**2k** was obtained as a yellow oil in 77% yield (134 mg), (R_f = 0.37 in MeOH/EtOAc 1:99 v/v); IR (KBr) 3440, 3056, 2984, 2939, 2837, 2305, 2068, 1717, 1651, 1613, 1505, 1465, 1443, 1369, 1318, 1266, 1231, 1193, 1123, 1097, 1058, 1036, 895, 860, 734; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.05 (d, *J* = 2.7 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.69 (dd, *J* = 8.4, 2.7 Hz, 1H), 4.71 (s, 1H), 4.38–4.23 (comp, 2H), 3.84–3.72 (comp, 4H), 3.65 (m, 1H), 3.21 (comp, 2H), 2.94–2.71 (comp, 4H), 2.70–2.60 (m, 1H), 2.44–2.34 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.85 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 171.2, 157.2, 134.6, 129.1, 127.4, 113.4, 112.7, 68.4, 65.8, 61.8, 61.3, 55.3, 53.6, 46.7, 34.4, 28.1, 14.2, 13.5; *m/z* (ESI–MS) 348.2 $[M + H]^+$.

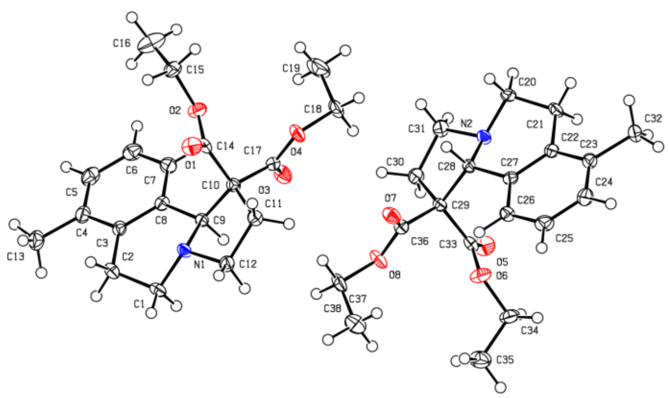


Diethyl 7-methyl-2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-**2l:**



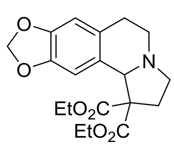
Following the general procedure C, **1a** and 5-methyl-1,2,3,4-tetrahydroisoquinoline were heated at reflux for 1 h. Product (±)-**2l** was obtained as a yellow solid in 68% yield (112 mg), (R_f = 0.22 in hexane/EtOAc 70:30 v/v); mp = 69–72 °C; IR (KBr) 2986, 2922, 2807, 2744, 1720, 1651, 1584, 1476, 1387, 1367, 1303, 1264, 1243, 1207, 1178, 1129, 1114, 1083, 1066, 1026, 937, 870, 859; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.32–7.28 (m, 1H), 7.02–6.96 (comp, 2H), 4.71 (s, 1H), 4.34 (dq, *J* = 10.7, 7.2 Hz, 1H), 4.27 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.78 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.61 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.27–3.19 (comp, 2H), 2.93–2.82 (comp, 2H), 2.82–2.73 (m, 1H), 2.71–2.63 (comp, 2H), 2.43–2.34 (m, 1H), 2.20 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.84 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 171.3, 135.5, 133.6, 133.3, 128.0, 125.9, 124.8, 68.7, 65.6, 61.8, 61.3, 53.7, 46.4, 34.5, 26.6, 19.6, 14.2, 13.6; *m/z* (ESI–MS) 332.1 $[M + H]^+$.

X-ray quality crystals of (±)-**2l** were obtained from hexane/diethyl ether through slow diffusion at room temperature.



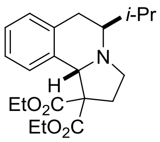
The requisite CIF has been submitted to the journal and deposited with the CCDC (deposition # 1562033).

Diethyl 2,3,6,11*b*-tetrahydro-[1,3]dioxolo[4,5-*g*]pyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-**2m:**



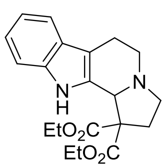
Following the general procedure C, **1a** and 5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*]isoquinoline were heated at reflux for 1 h. Product (±)-**2m** was obtained as a yellow solid in 83% yield (150 mg), (R_f = 0.33 in MeOH/EtOAc 1:99 v/v); IR (film) 3435, 3058, 2983, 1721, 1651, 1505, 1485, 1385, 1368, 1341, 1265, 1220, 1155, 1122, 1039, 932, 861, 787, 735, 703; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.97 (s, 1H), 6.52 (s, 1H), 5.85(3) (d, *J* = 1.4 Hz, 1H), 5.84(7) (d, *J* = 1.4 Hz, 1H), 4.66 (s, 1H), 4.33 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.25 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.82 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.73 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.24–3.13 (comp, 2H), 2.92–2.82 (comp, 2H), 2.80–2.68 (comp, 2H), 2.61 (ddd, *J* = 10.9, 5.9, 4.9 Hz, 1H), 2.38–2.28 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 171.2, 146.3, 145.3, 128.8, 126.4, 108.5, 108.0, 100.7, 68.3, 65.6, 61.8, 61.3, 53.6, 46.3, 34.3, 29.1, 14.2, 13.6; *m/z* (ESI–MS) 362.1 $[M + H]^+$.

Diethyl (5*S*,10*bS*)-5-isopropyl-2,3,6,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,1(5*H*)-dicarboxylate (±)-**2n:**



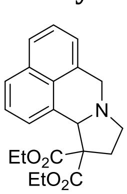
Following the general procedure C, **1a** and 3-isopropyl-1,2,3,4-tetrahydroisoquinoline were heated at reflux for 1 h. Product (±)-**2n** was obtained as a yellow oil in 69% yield (124 mg), (1.5:1 mixture of diastereomers) (R_f = 0.50 in hexane/ether 70:30 v/v); IR (film) 3432, 2960, 2787, 1728, 1644, 1492, 1454, 1387, 1367, 1344, 1264, 1220, 1187, 1144, 1102, 1061, 1025, 862, 751, 433; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.44–7.39 (m, 1.00H), 7.35 (app dt, *J* = 7.2, 1.4 Hz, 0.66H), 7.11–6.98 (comp, 5.14H), 5.16 (s, 1.00H), 4.62 (s, 0.68H), 4.37–4.22 (comp, 3.49H), 3.73 (qd, *J* = 7.1, 2.5 Hz, 1.37H), 3.62 (dq, *J* = 10.7, 7.1 Hz, 1.04H), 3.49–3.41 (comp, 2.09H), 3.23 (ddd, *J* = 8.2, 7.2, 5.9 Hz, 0.70H), 3.02 (ddd, *J* = 9.4, 7.1, 4.4 Hz, 1.05H), 2.82 (dd, *J* = 15.4, 4.4 Hz, 1.03H), 2.73 (dd, *J* = 16.0, 11.5 Hz, 1H), 2.67–2.60 (comp, 1.76H), 2.59–2.49 (comp, 3.74H), 2.44 (ddd, *J* = 11.3, 6.1, 3.0 Hz, 0.70H), 2.32–2.20 (comp, 1.78H), 1.95 (dhept, *J* = 13.3, 6.5 Hz, 0.71H), 1.53 (dhept, *J* = 8.5, 6.7 Hz, 1.02H), 1.32 (app dt, *J* = 9.4, 7.1 Hz, 5.21H), 0.99 (d, *J* = 6.8 Hz, 2.15H), 0.95 (app dd, *J* = 6.7, 2.7 Hz, 5.36H), 0.83 (app dt, *J* = 15.5, 7.1 Hz, 5.29H), 0.77 (d, *J* = 6.7 Hz, 3.20H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 172.2, 171.0, 170.5, 136.5, 135.2, 135.2, 134.8, 128.6, 128.5, 128.0, 127.2, 126.4, 126.1, 125.2, 125.1, 69.0, 65.9, 64.2, 63.9, 62.9, 61.7, 61.6, 61.04, 60.98, 60.4, 52.0, 46.2, 33.7, 33.5, 30.0, 28.9, 27.7, 26.5, 20.5, 20.3, 18.5, 17.1, 14.2, 13.6, 13.5; *m/z* (ESI–MS) 360.3 $[M + H]^+$.

Diethyl 2,3,5,6,11,11b-hexahydro-1*H*-indolizino[8,7-*b*]indole-1,1-dicarboxylate (±)-**2o:**



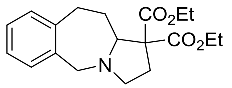
Following the general procedure C, **1a** and 2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole were heated at reflux for 1 h. Product (±)-**2o** was obtained as a yellow oil in 60% yield (108 mg), (R_f = 0.22 in hexane/EtOAc 50:50 v/v); IR (KBr) 3404, 3057, 2980, 2923, 2804, 2360, 2343, 1726, 1654, 1489, 1467, 1452, 1383, 1371, 1302, 1276, 1244, 1217, 1198, 1159, 1135, 1097, 1074, 1016, 937, 857; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.58 (br s, 1H), 7.50–7.46 (m, 1H), 7.33 (app dt, *J* = 8.1, 0.9 Hz, 1H), 7.14 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.07 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 4.42–4.27 (comp, 3H), 3.89–3.79 (comp, 2H), 3.35–3.25 (comp, 2H), 2.94–2.83 (comp, 3H), 2.78 (m, 1H), 2.68 (ddd, *J* = 11.1, 8.3, 4.6 Hz, 1H), 2.35–2.25 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.75 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.8, 136.0, 130.9, 126.8, 121.6, 119.0, 118.3, 110.9, 110.1, 65.1, 63.6, 62.1, 61.7, 51.9, 48.2, 31.5, 21.6, 14.2, 13.6; *m/z* (ESI–MS) 357.1 $[M + H]^+$

Diethyl 9,10-dihydro-7*H*-benzo[*de*]pyrrolo[2,1-*a*]isoquinoline-11,11(11*aH*)-dicarboxylate (±)-**2p:**

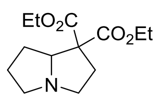


Following the general procedure C, **1a** and 2,3-dihydro-1*H*-benzo[*de*]isoquinoline were heated at reflux for 1 h. Product (±)-**2p** was obtained as a yellow solid in 55% yield (97 mg), (R_f = 0.40 in hexane/EtOAc 20:80 v/v); IR (film) 3054, 2987, 2306, 1728, 1661, 1591, 1548, 1422, 1371, 1341, 1266, 1151, 1098, 1023, 896, 738, 705; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.73–7.66 (comp, 2H), 7.63 (app dt, *J* = 7.2, 1.2 Hz, 1H), 7.38 (comp, 2H), 7.19 (dd, *J* = 7.0, 1.1 Hz, 1H), 4.70 (s, 1H), 4.42–4.36 (comp, 2H), 4.35–4.29 (m, 1H), 3.87 (d, *J* = 14.1 Hz, 1H), 3.75 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.62 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.40 (ddd, *J* = 10.0, 7.6, 1.4 Hz, 1H), 2.97 (ddd, *J* = 12.9, 10.6, 7.7 Hz, 1H), 2.87 (app td, *J* = 10.2, 7.4 Hz, 1H), 2.54 (ddd, *J* = 12.9, 7.4, 1.4 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.67 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 171.1, 133.1, 132.8, 131.8, 128.0, 126.8, 126.3, 125.3, 125.1, 123.8, 122.4, 69.7, 64.7, 61.9, 61.4, 53.5, 53.4, 34.0, 14.2, 13.5; *m/z* (ESI–MS) 354.1 $[M + H]^+$.

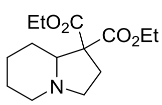
Diethyl 2,3,5,10,11,11*a*-hexahydro-1*H*-benzo[e]pyrrolo[1,2-*a*]azepine-1,1-dicarboxylate (±)-**4:** A 10 mL microwave reaction tube was charged with a 10 x 8 mm SiC passive heating element, **1a** (101 mg, 0.5 mmol, 1 equiv), 2,3,4,5-tetrahydro-1*H*-benzo[*c*]azepine (147 mg, 1 mmol, 2 equiv), benzoic acid (12 mg, 0.1 mmol, 0.2 equiv) 4 Å MS (100 mg), and toluene (2 mL). The reaction tube was sealed with a Teflon-lined snap cap and heated in a microwave reactor at 200 °C (200 W, 70–100 psi) for 20 minutes. After cooling with compressed air flow, the reaction mixture was diluted with EtOAc (20 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 20 mL). The combined aqueous layers were extracted with EtOAc (2 x 10 mL) and the combined organic layers were washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography. Product (±)-**4** was obtained as a yellow oil in 54% yield (89 mg), (R_f = 0.50 in hexane/EtOAc 70:30 v/v); IR (KBr) 3443, 3054, 2982, 2687, 2305, 2093, 1723, 1640, 1441, 1422, 1368, 1266, 1193, 1148, 1097, 1015, 975, 896, 734, 700; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.17–7.05 (comp, 4H), 4.31–4.06 (comp, 4H), 3.80 (d, *J* = 13.9 Hz, 1H), 3.69 (d, *J* = 13.8 Hz, 1H), 3.23 (dd, *J* = 11.3, 2.3 Hz, 1H), 3.12 (app td, *J* = 8.6, 2.3 Hz, 1H), 2.98–2.90 (m, 1H), 2.82 (ddd, *J* = 14.7, 7.1, 1.7 Hz, 1H), 2.69 (ddd, *J* = 13.4, 9.4, 8.4 Hz, 1H), 2.51 (ddd, *J* = 9.5, 8.8, 8.1 Hz, 1H), 2.22–2.12 (comp, 2H), 1.38 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 170.3, 142.4, 138.6, 129.9, 128.9, 127.4, 126.3, 74.2, 63.8, 61.53, 61.51, 59.5, 53.9, 34.2, 31.4, 29.6, 14.3, 14.2; *m/z* (ESI–MS) 332.2 $[M + H]^+$.



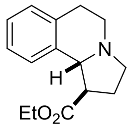
Diethyl hexahydro-1*H*-pyrrolizine-1,1-dicarboxylate (±)-**5:** Following the general procedure D, **1a** and *L*-proline were heated at reflux for 1.5 h. Product (±)-**5** was obtained as a yellow oil in 81% yield (103 mg), (R_f = 0.43 in hexane/EtOAc 20:80 v/v); IR (film) 3417, 3055, 2982, 2875, 2307, 1727, 1466, 1447, 1421, 1390, 1368, 1266, 1189, 1112, 1072, 1022, 976, 896, 863, 738, 704; ^{1}H NMR ($CDCl_3$, 500 MHz) 4.30–4.09 (comp, 5H), 3.12 (ddd, *J* = 9.8, 7.0, 2.9 Hz, 1H), 2.98 (ddd, *J* = 11.1, 8.8, 6.1 Hz, 1H), 2.77 (ddd, *J* = 11.4, 7.2, 4.5 Hz, 1H), 2.59–2.45 (comp, 2H), 2.12 (ddd, *J* = 13.1, 6.1, 4.5 Hz, 1H), 1.93–1.80 (comp, 2H), 1.83–1.69 (m, 1H), 1.40–1.28 (m, 1H), 1.24 (app td, *J* = 7.1, 0.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 170.4, 68.4, 63.8, 61.7, 61.5, 55.6, 52.8, 32.6, 28.8, 26.5, 14.2, 14.2; *m/z* (ESI–MS) 256.1 $[M + H]^+$.



Diethyl hexahydroindolizine-1,1(5*H*)-dicarboxylate (±)-**6:** Following the general procedure D, **1a** and piperidine-2-carboxylic acid were heated at reflux for 1.5 h. Product (±)-**6** was obtained as a yellow solid in 69% yield (93 mg), (R_f = 0.28 in hexane/EtOAc 20:80 v/v); mp = 34–36 °C; IR (KBr) 3458, 2935, 2858, 2786, 2731, 2360, 1732, 1645, 1469, 1445, 1384, 1366, 1320, 1250, 1210, 1187, 1148, 1119, 1080, 1019, 943, 862; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.22–4.06 (comp, 4H), 3.12–3.03 (comp, 2H), 2.64 (ddd, *J* = 13.4, 9.5, 8.4 Hz, 1H), 2.43 (dd, *J* = 11.1, 2.5 Hz, 1H), 2.08 (app dt, *J* = 9.3, 8.6 Hz, 1H), 1.98 (ddd, *J* = 13.3, 8.5, 1.7 Hz, 1H), 1.90 (app ddd, *J* = 12.0, 10.8, 3.1 Hz, 2H), 1.78–1.72 (m, 1H), 1.58–1.39 (comp, 2H), 1.28–1.16 (comp, 7H), 1.09 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 170.5, 69.1, 61.7, 61.3, 61.1, 53.8, 53.4, 31.2, 28.0, 24.8, 24.3, 14.2, 14.0; *m/z* (ESI–MS) 270.1 $[M + H]^+$.



Ethyl (1*R*,10*bR*)-1,2,3,5,6,10*b*-hexahydropyrrolo[2,1-*a*]isoquinoline-1-carboxylate (±)-7:

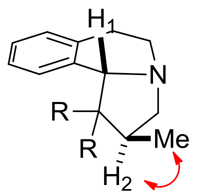


Following a modified literature procedure,[5] a 10 mL round-bottom flask was charged with (±)-**2a** (63 mg, 0.2 mmol), LiCl (42 mg, 1 mmol, 5 equiv) in H_2O (0.2 mL), and DMSO (2 mL). The mixture was heated at reflux for 12 h. The reaction was allowed to cool to room temperature and poured into a separatory funnel containing 5 mL of Et_2O and 5 mL of H_2O. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with brine (20 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography. Product (±)-**7** was obtained as a yellow oil in 60% yield (29 mg), (R_f = 0.45 in hexane/EtOAc 20:80 v/v); IR (film) 3425, 2926, 2854, 2794, 1728, 1651, 1493, 1454, 1374, 1293, 1248, 1193, 1105, 1035, 935, 860, 735; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.19–7.07 (comp, 4H), 4.26 (comp, 2H), 3.99 (d, *J* = 8.4 Hz, 1H), 3.14–2.99 (comp, 3H), 2.96 (ddd, *J* = 10.7, 8.4, 6.2 Hz, 1H), 2.88–2.81 (comp, 2H), 2.77 (ddd, *J* = 11.2, 8.8, 4.9 Hz, 1H), 2.31 (m, 1H), 2.08 (dddd, *J* = 12.8, 8.1, 6.2, 3.5 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 137.4, 134.3, 128.8, 126.6, 126.1, 125.9, 66.3, 61.0, 53.2, 49.2, 48.0, 29.1, 28.4, 14.4; *m/z* (ESI–MS) 246.1 $[M + H]^+$

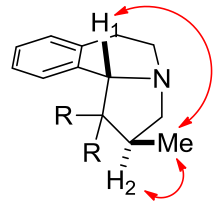
.

2D-NMR Analysis for (±)-2e, Selected Interactions (in $CDCl_3$)

GCOSY



NOESY



R=COOEt

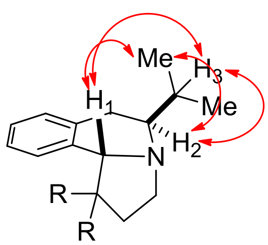
R=COOEt

Proton assigned for the major product

Protons	Chemical Shifts (ppm)
H_1	4.89
H_2	3.31
Me	1.07

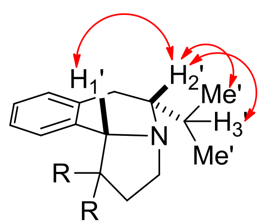
2D-NMR Analysis for (±)-2n, Selected Interactions (in $CDCl_3$)

NOESY for major



R=COOEt

NOESY for minor



R=COOEt

Proton assigned for the major product

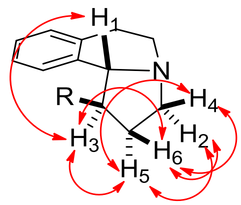
Protons	Chemical Shifts (ppm)
H_1	5.17
H_2	2.67–2.60
H_3	1.53
Me	0.77

Proton assigned for the minor product

Protons	Chemical Shifts (ppm)
$H_{1'}$	4.62
$H_{2'}$	2.59–2.49
$H_{3'}$	1.94
Me’	0.99

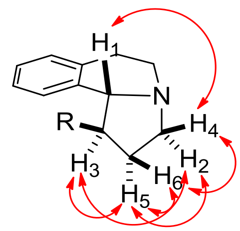
2D-NMR Analysis for (±)-7, Selected Interactions (in DMSO-*d*6)

GCOSY



R=COOEt

NOESY



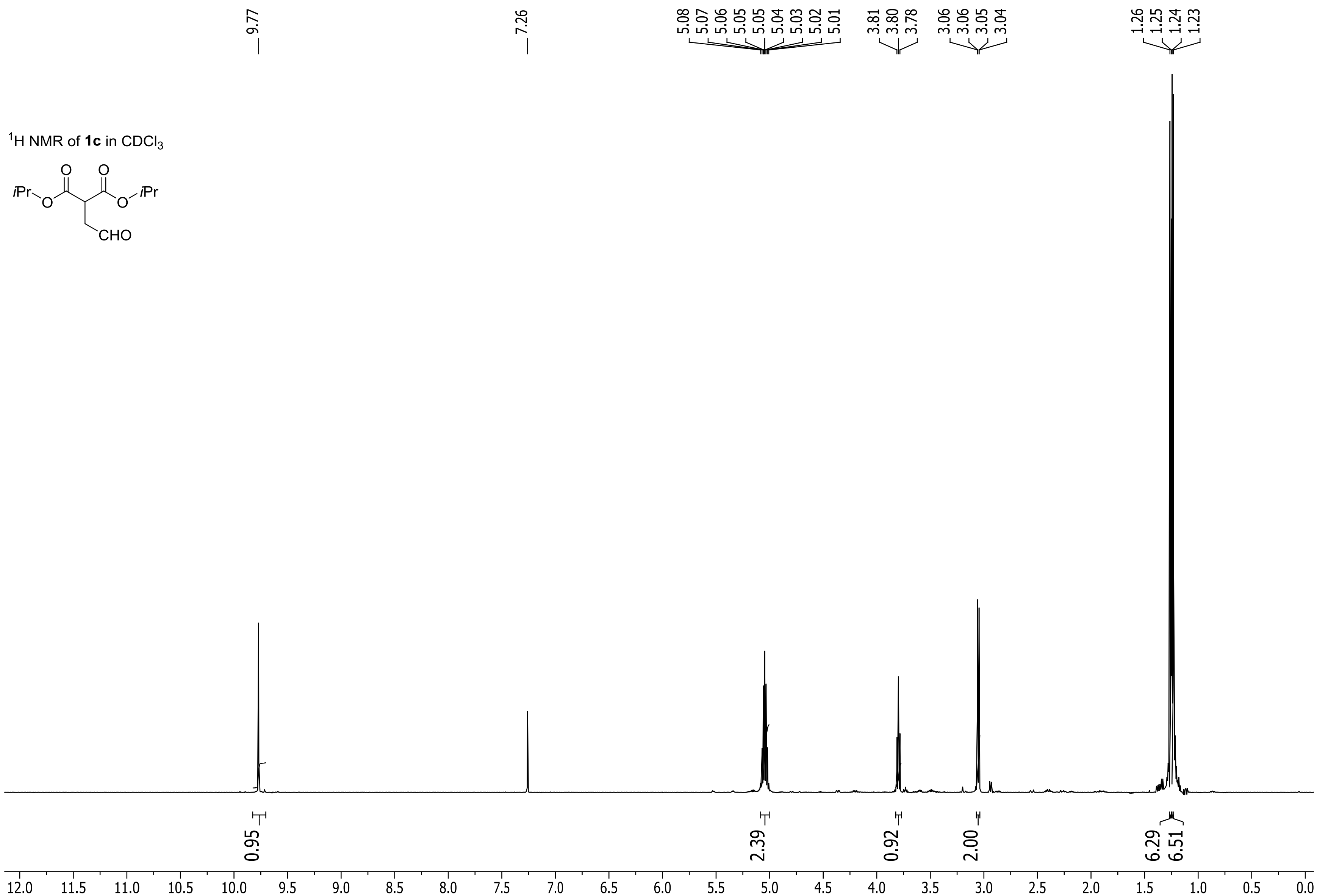
R=COOEt

Proton assigned for the major product

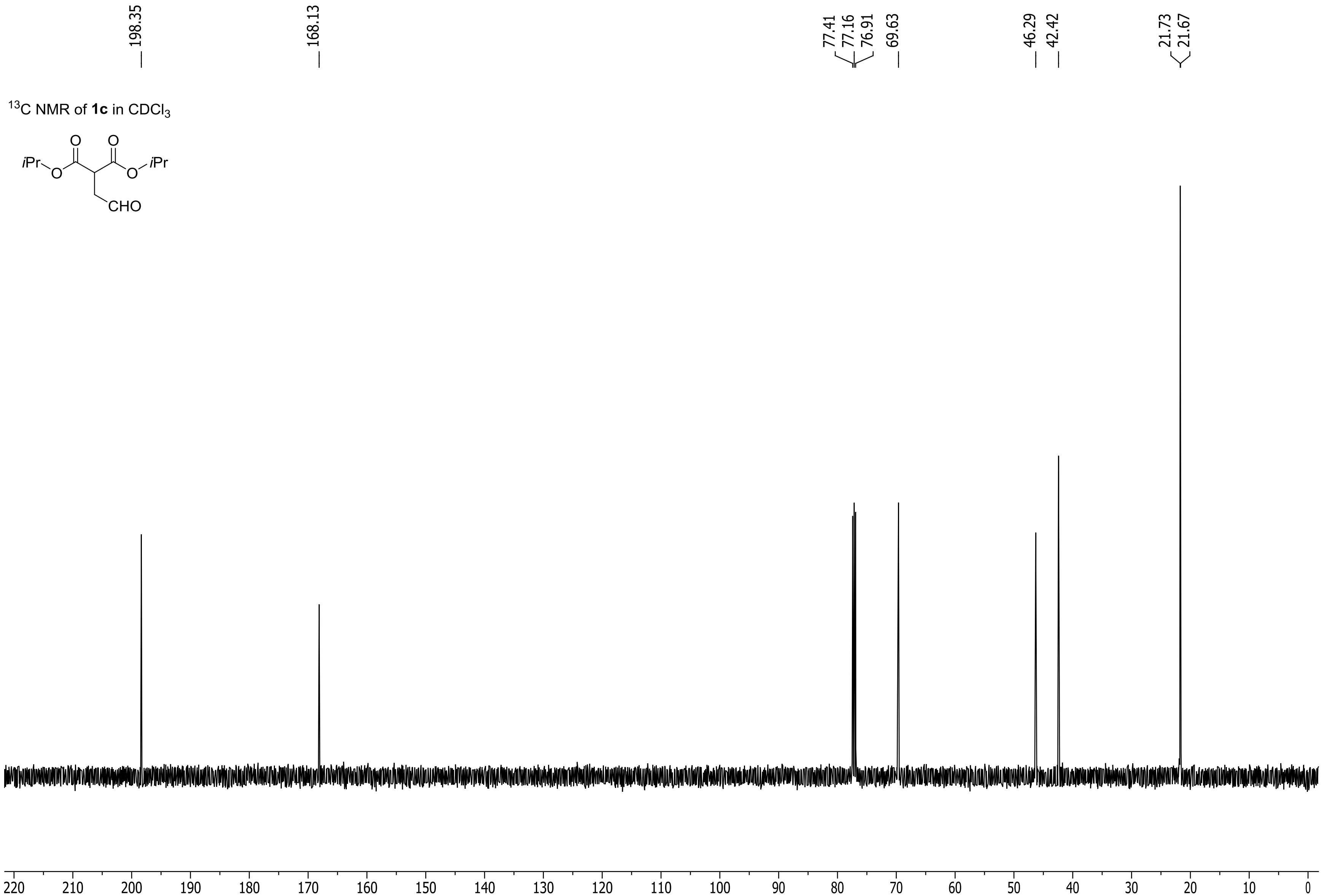
Protons	Chemical Shifts (ppm)
H_1	3.80
H_2	3.03–2.97
H_3	2.75
H_4	2.72–2.66
H_5	2.27–2.17
H_6	1.91

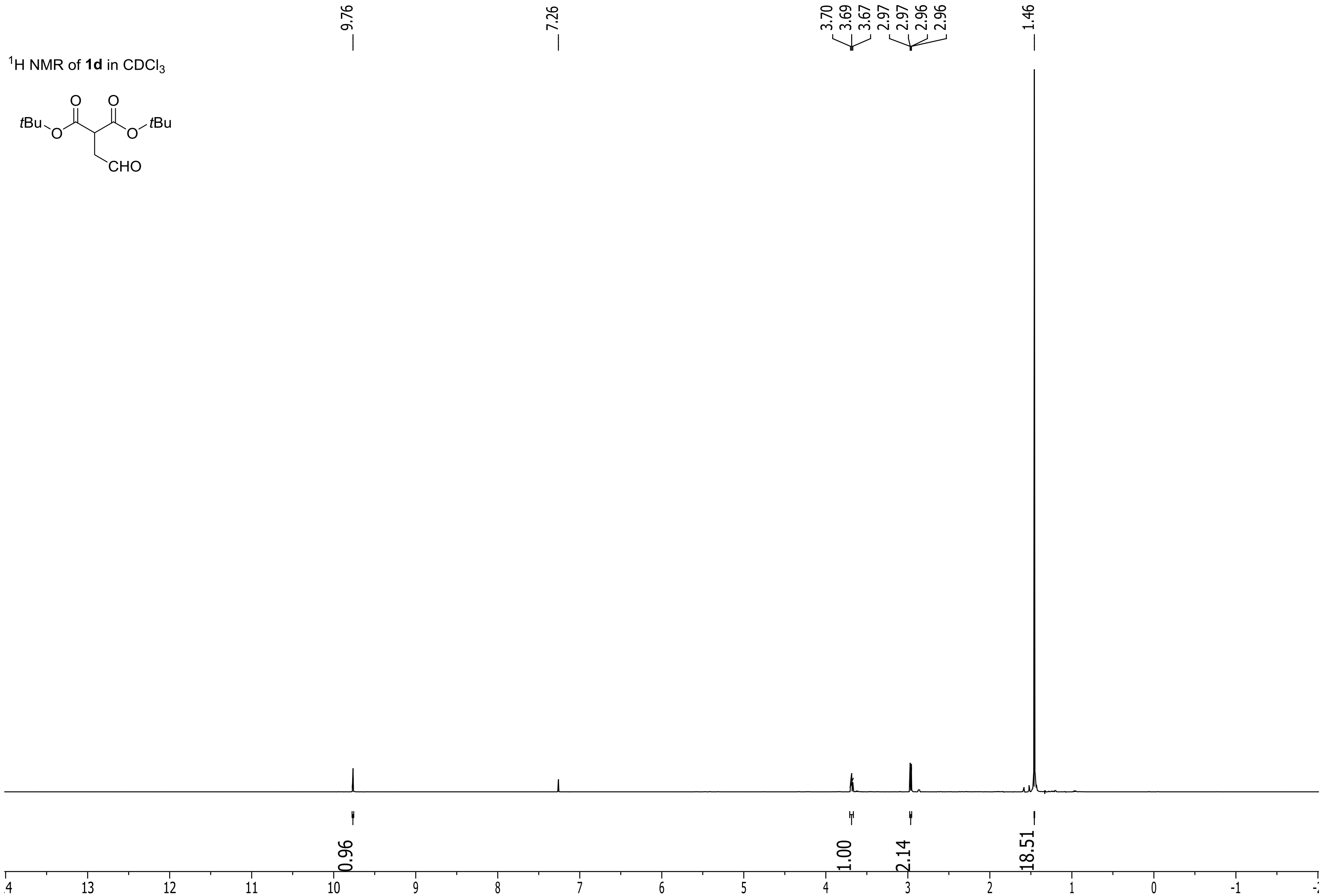
References:

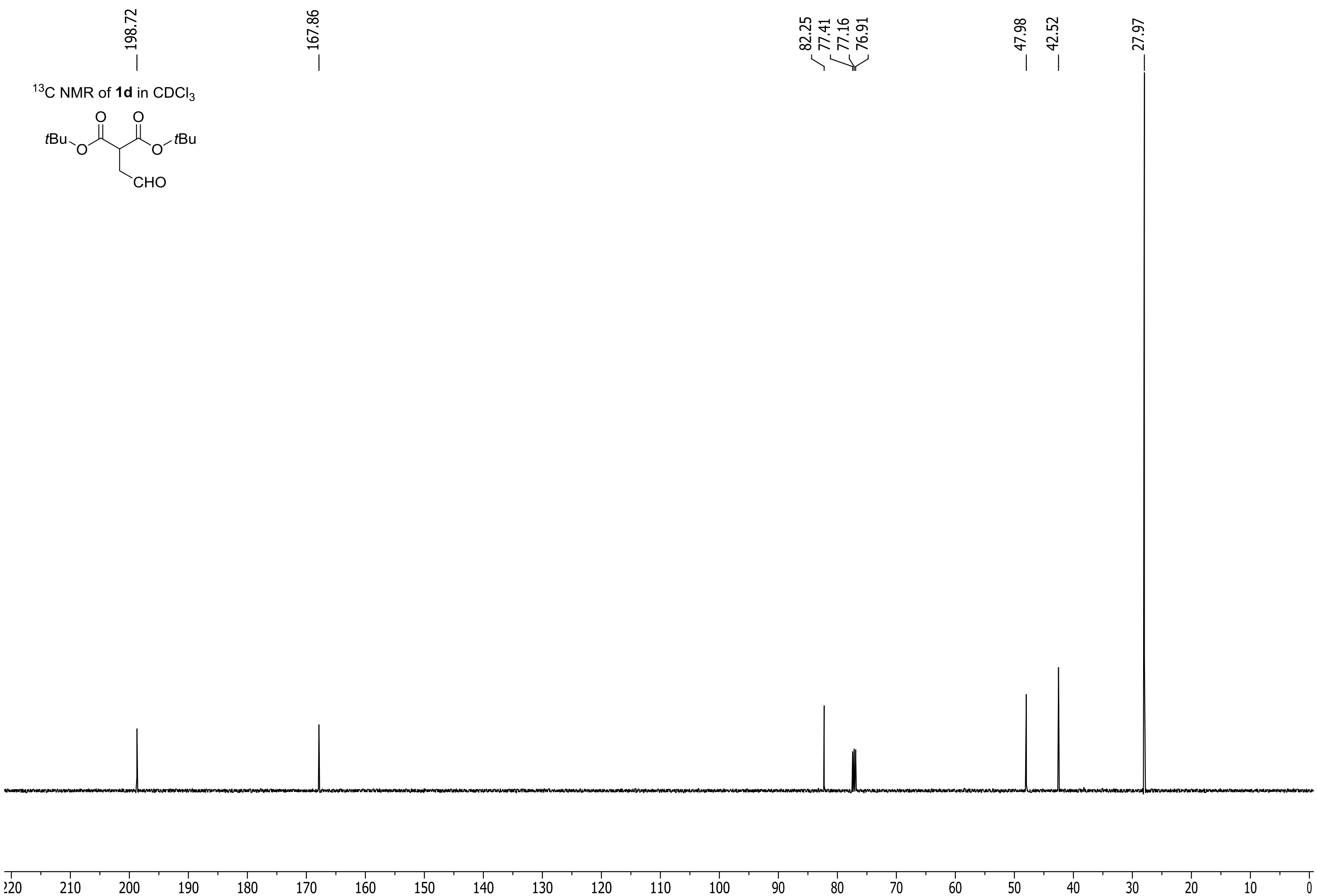
(1) Groth, T.; Meldal, M. *J. Comb. Chem*. **2001**, *3*, 34.
(2) Robinson, E. R.; Frost, A. B. Elías-Rodríguez P.; Smith, A. D. *Synthesis*, **2017**, 409.
(3) Silvi, M.; Arceo, E.; Jurberg, I. D.; Cassani, C.; Melchiorre, P. *J. Am. Chem. Soc*. **2015**, *137*, 6120.
(4) Nicewicz, D.; MacMillan, D. *Science* **2008**, *322*, 77.
(5) Krapcho, A.; Weimaster, J. *J. Org. Chem*. **1980**, *45*, 4105.



^{1}H NMR of **1c** in CDCl$_3$
iPr
O
O
O
O
iPr
CHO
9.77
7.26
5.08
5.07
5.06
5.05
5.05
5.04
5.03
5.02
5.01
3.81
3.80
3.78
3.06
3.06
3.05
3.04
1.26
1.25
1.24
1.23
0.95
2.39
0.92
2.00
6.29
6.51
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

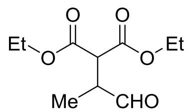

198.35
168.13
77.41
77.16
76.91
69.63
46.29
42.42
21.73
21.67
^{13}C NMR of **1c** in $CDCl_3$
O
O
*i*Pr
O
O
*i*Pr
CHO
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

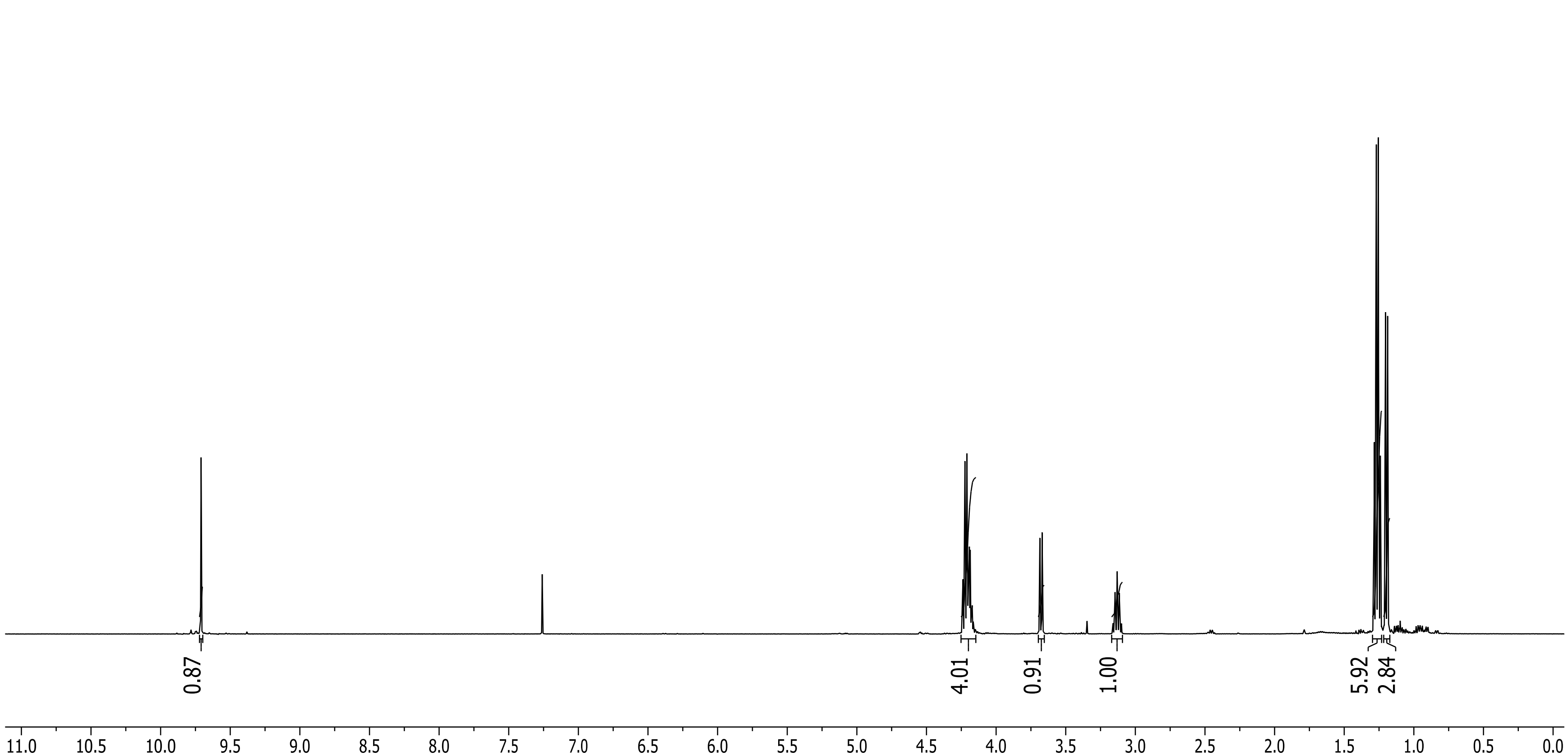

[1]H NMR of 1d in CDCl3
tBu
O
O
O
O
tBu
CHO
9.76
7.26
3.70
3.69
3.67
2.97
2.97
2.96
2.96
1.46
0.96
1.00
2.14
18.51
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1

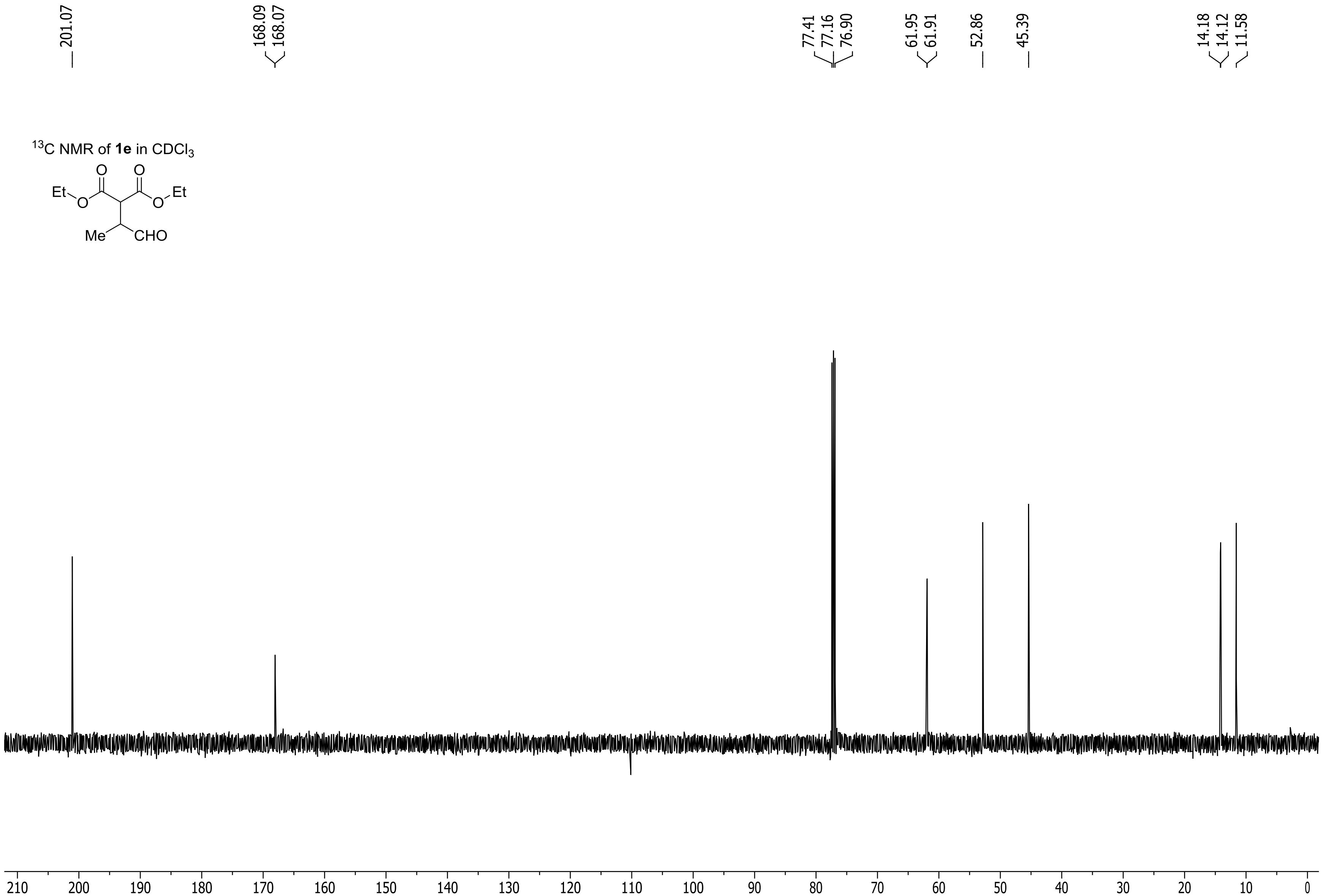


^{13}C NMR of **1d** in $CDCl_3$
tBu
O
O
O
O
tBu
CHO
198.72
167.86
82.25
77.41
77.16
76.91
47.98
42.52
27.97
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

^{1}H NMR of **1e** in $CDCl_3$






201.07
168.09
168.07
77.41
77.16
76.90
61.95
61.91
52.86
45.39
14.18
14.12
11.58
13C NMR of 1e in CDCl3
O
O
Et
O
O
Et
Me
CHO
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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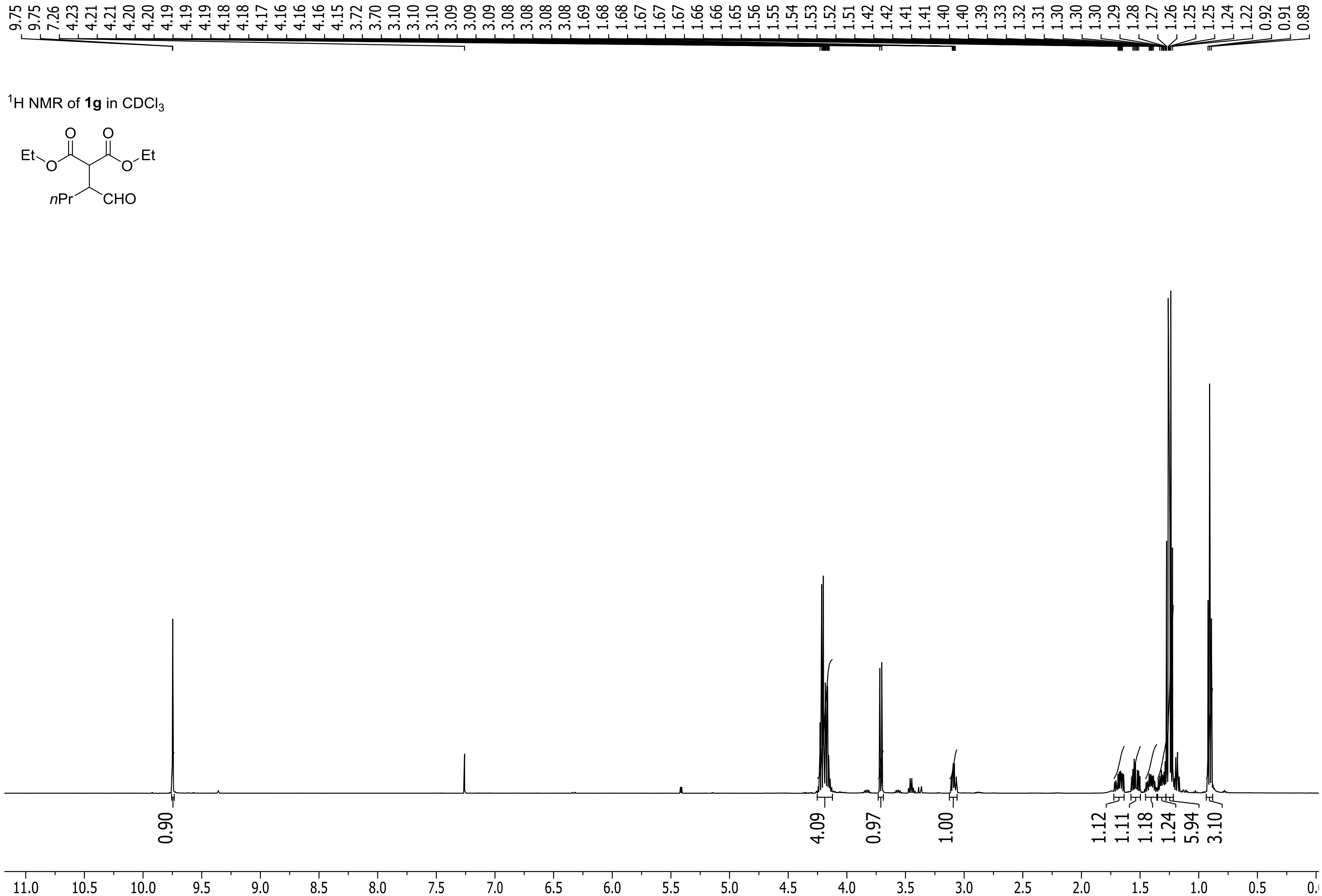
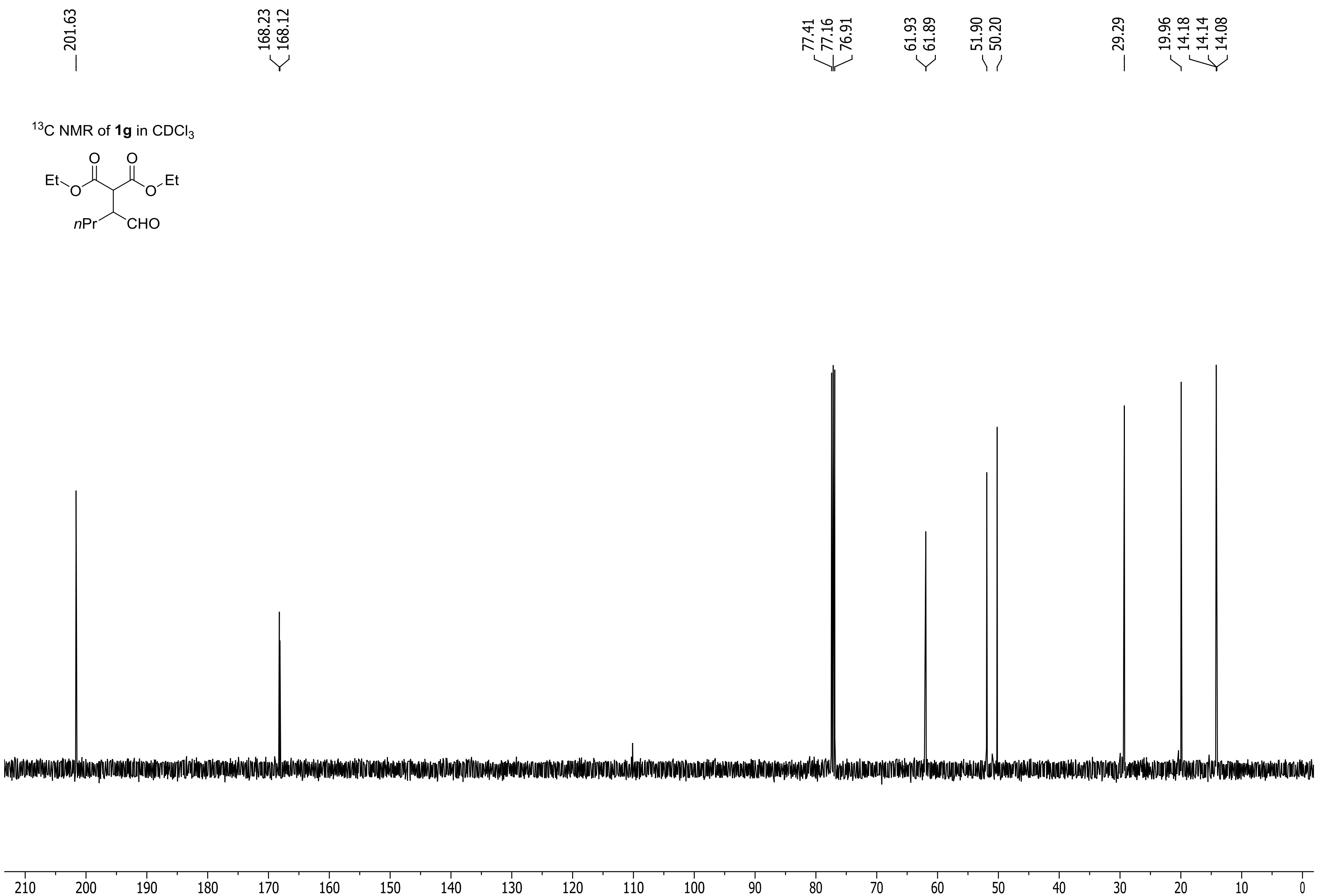
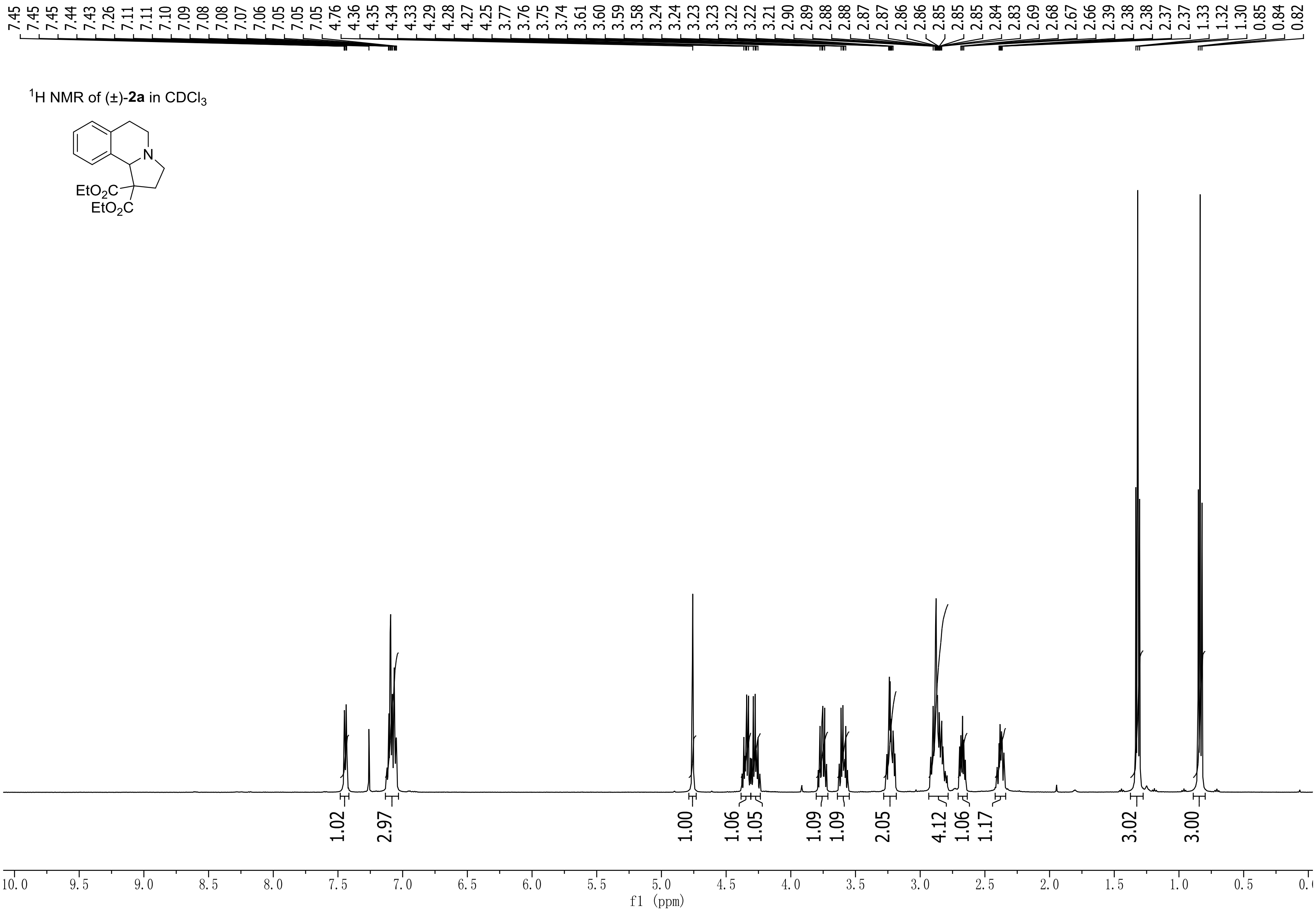
40
30
20
10
0



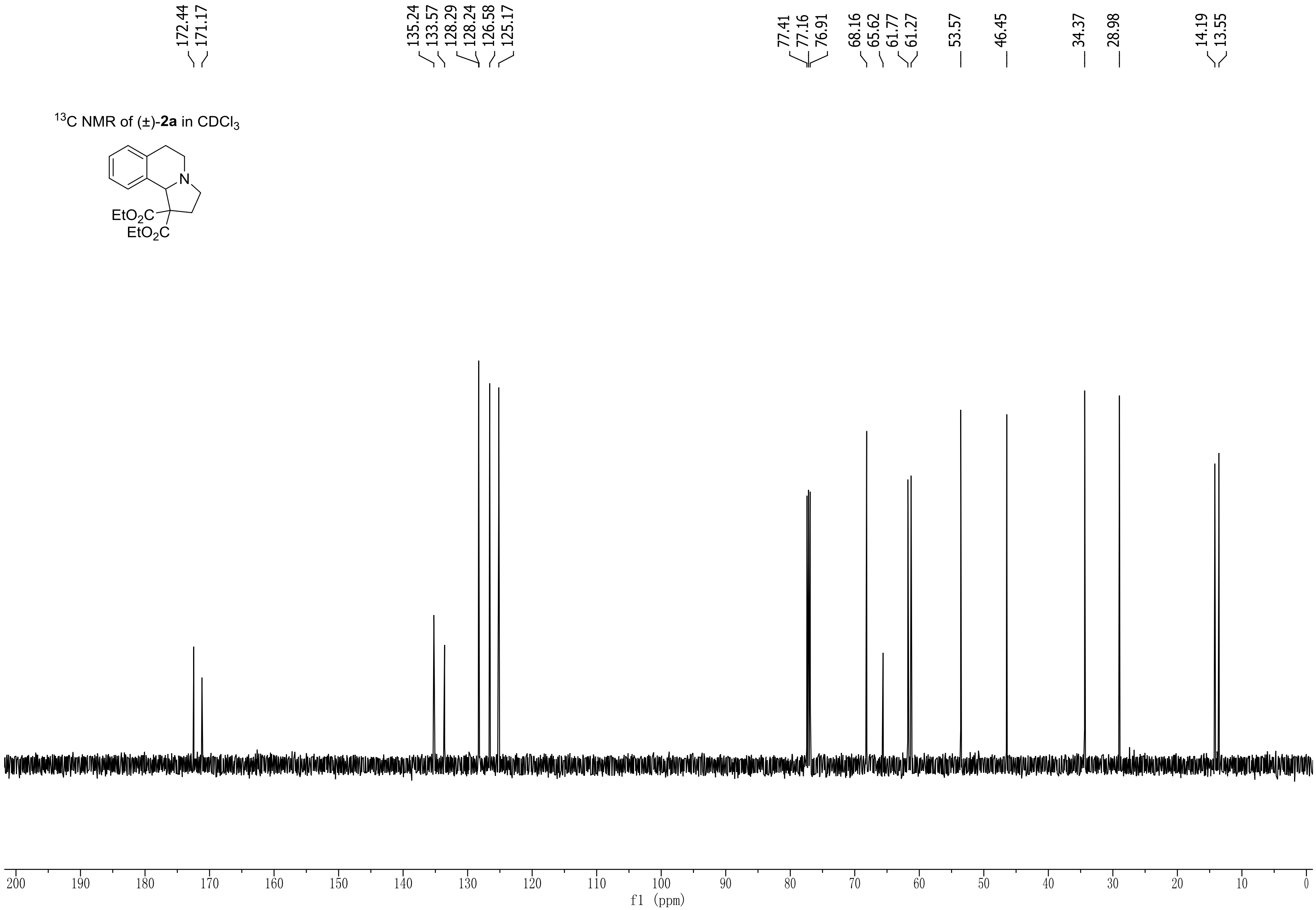
9.75 9.75 7.26 4.23 4.21 4.21 4.20 4.20 4.19 4.19 4.19 4.18 4.18 4.17 4.16 4.16 4.16 4.15 3.72 3.70 3.10 3.10 3.10 3.09 3.09 3.09 3.08 3.08 3.08 3.08 1.69 1.68 1.68 1.67 1.67 1.67 1.66 1.66 1.65 1.56 1.55 1.54 1.53 1.52 1.51 1.42 1.42 1.41 1.41 1.40 1.40 1.39 1.33 1.32 1.31 1.30 1.30 1.30 1.29 1.28 1.27 1.26 1.25 1.25 1.24 1.22 0.92 0.91 0.89
^{1}H NMR of **1g** in $CDCl_3$
Et
O
O
O
O
Et
nPr
CHO
0.90
4.09
0.97
1.00
1.12
1.11
1.18
1.24
5.94
3.10
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

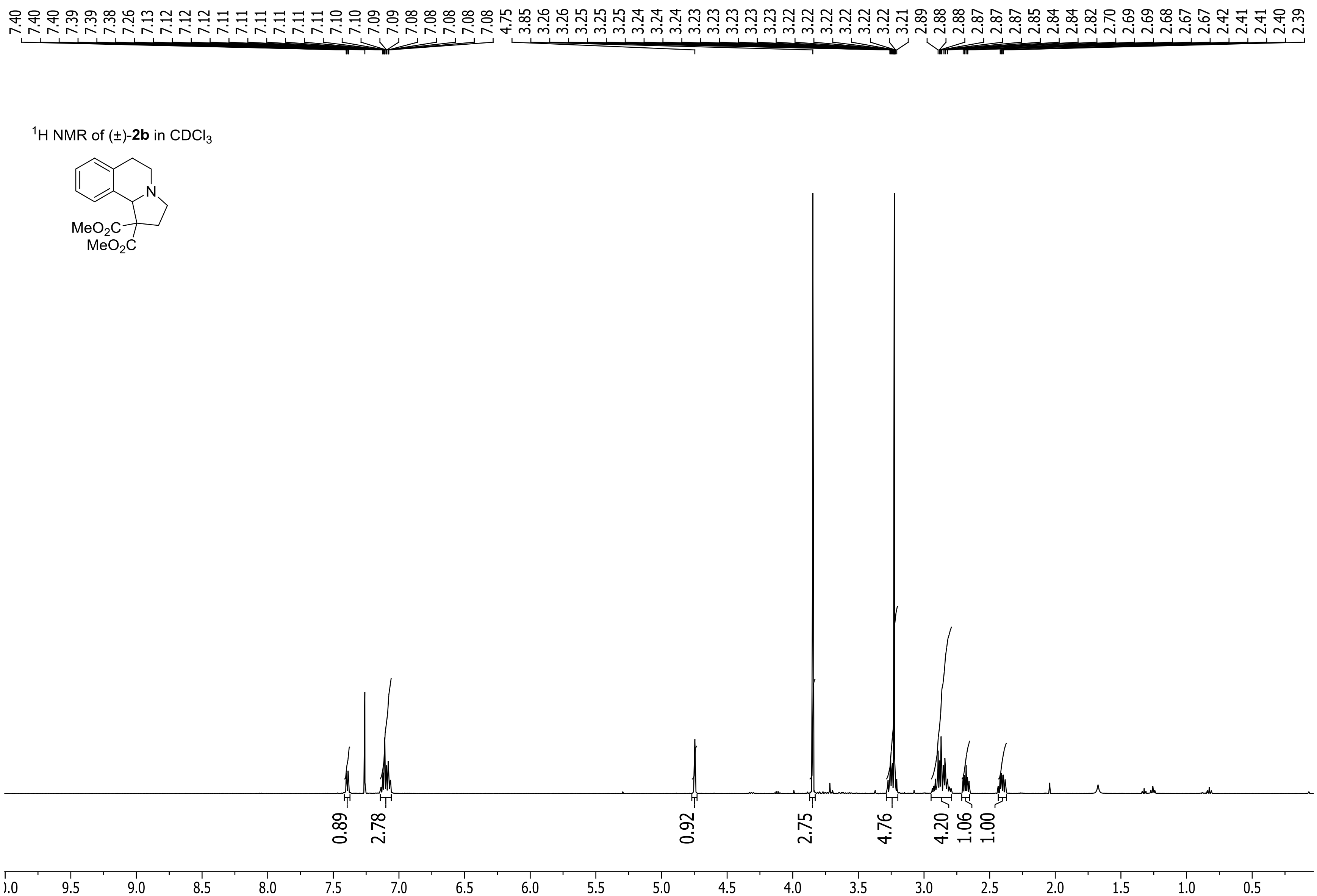

201.63
168.23
168.12
77.41
77.16
76.91
61.93
61.89
51.90
50.20
29.29
19.96
14.18
14.14
14.08
^{13}C NMR of **1g** in $CDCl_3$
Et
O
O
O
O
Et
*n*Pr
CHO
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

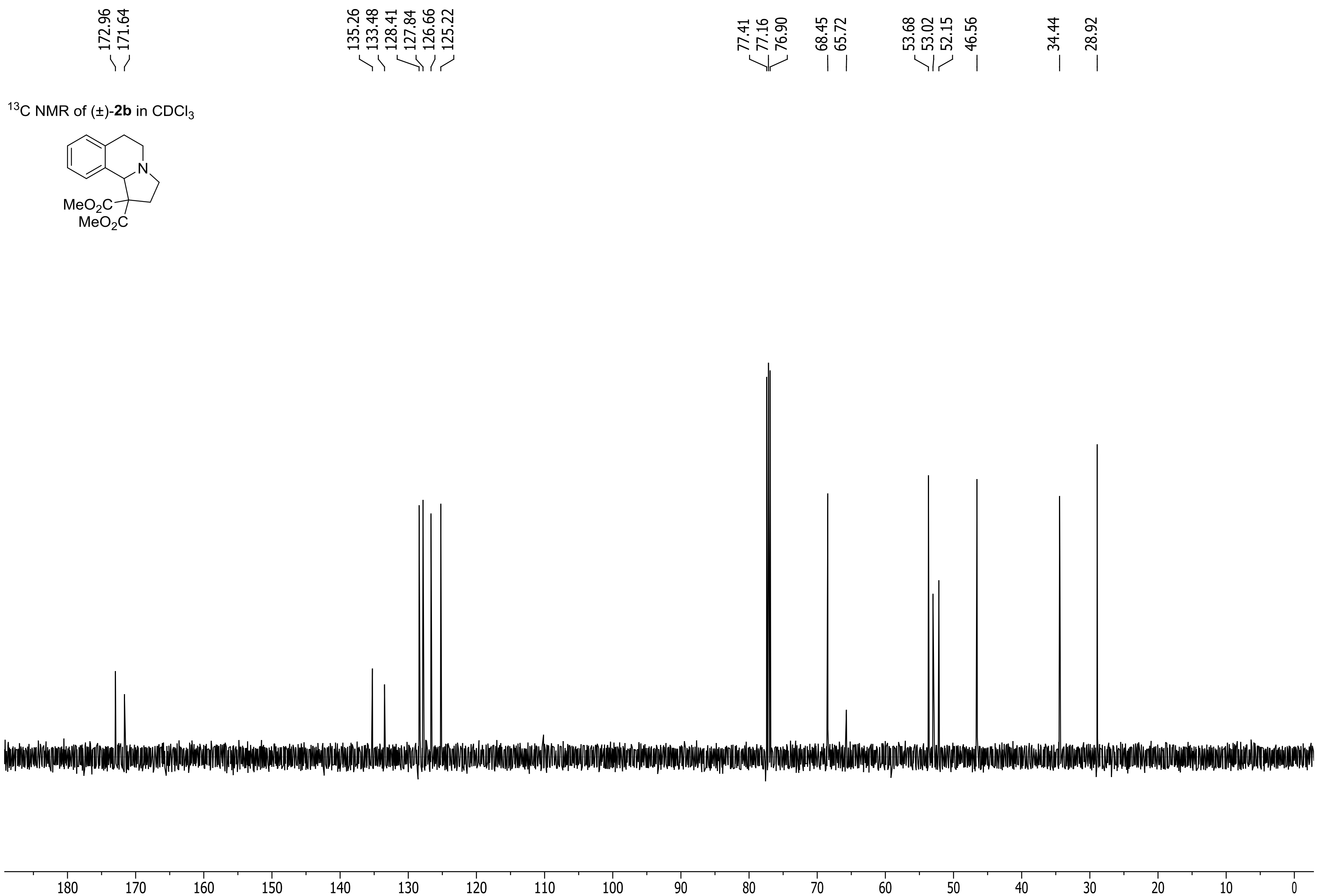
^{1}H NMR of (±)-**2a** in $CDCl_3$



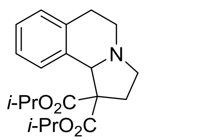
^{13}C NMR of (±)-**2a** in $CDCl_3$

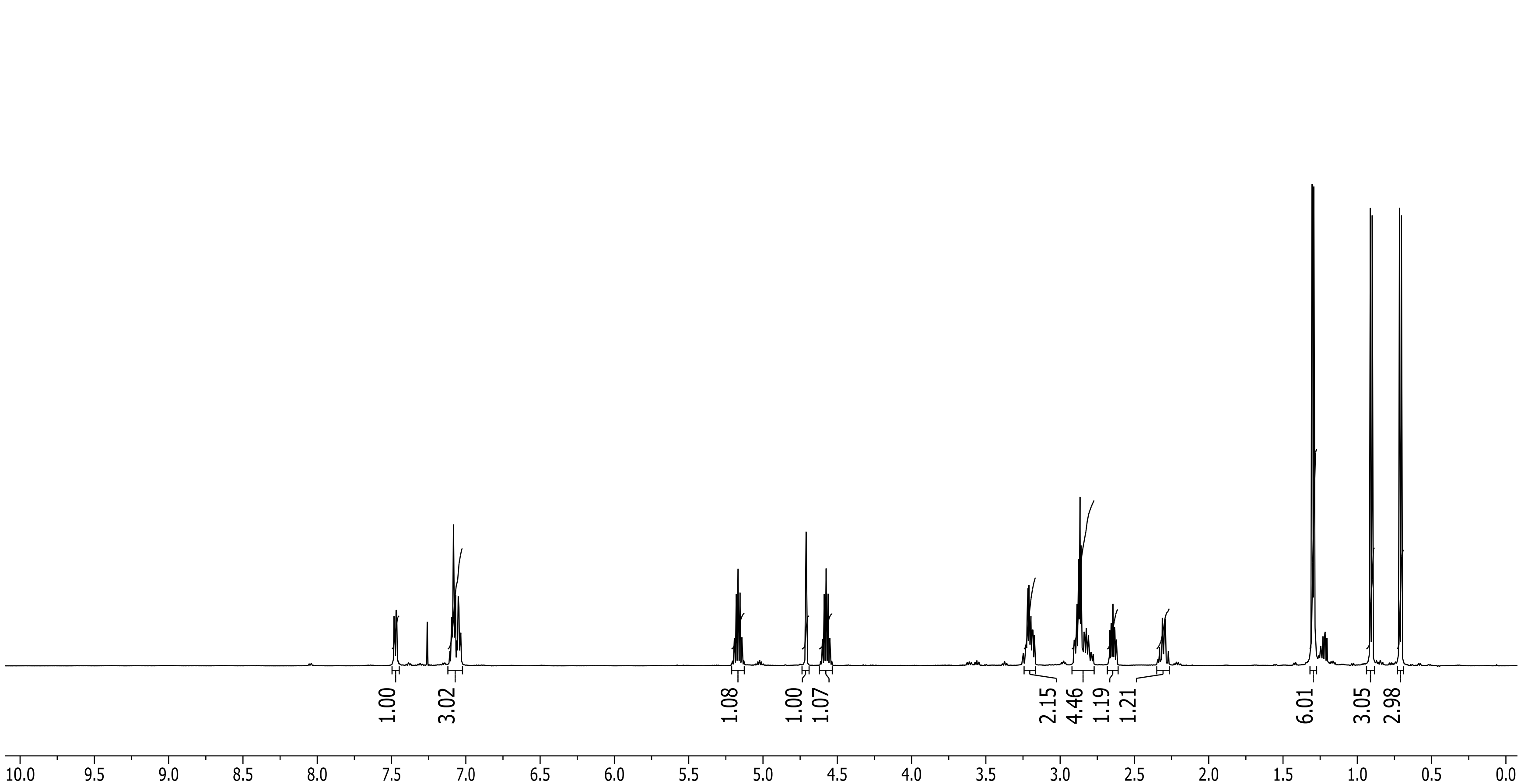



7.40 7.40 7.40 7.39 7.39 7.38 7.26 7.13 7.12 7.12 7.12 7.11 7.11 7.11 7.11 7.11 7.11 7.10 7.10 7.09 7.09 7.08 7.08 7.08 7.08 7.08 4.75 3.85 3.26 3.26 3.25 3.25 3.25 3.24 3.24 3.24 3.23 3.23 3.23 3.23 3.23 3.22 3.22 3.22 3.22 3.22 3.22 3.21 2.89 2.88 2.88 2.87 2.87 2.87 2.85 2.84 2.84 2.82 2.70 2.69 2.69 2.68 2.67 2.67 2.42 2.41 2.41 2.40 2.39
1H NMR of (±)-2b in CDCl3
N
MeO2C
MeO2C
0.89 2.78 0.92 2.75 4.76 4.20 1.06 1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

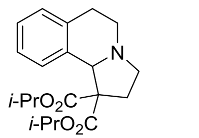

172.96
171.64
135.26
133.48
128.41
127.84
126.66
125.22
77.41
77.16
76.90
68.45
65.72
53.68
53.02
52.15
46.56
34.44
28.92
13C NMR of (±)-2b in CDCl3
N
MeO2C
MeO2C
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

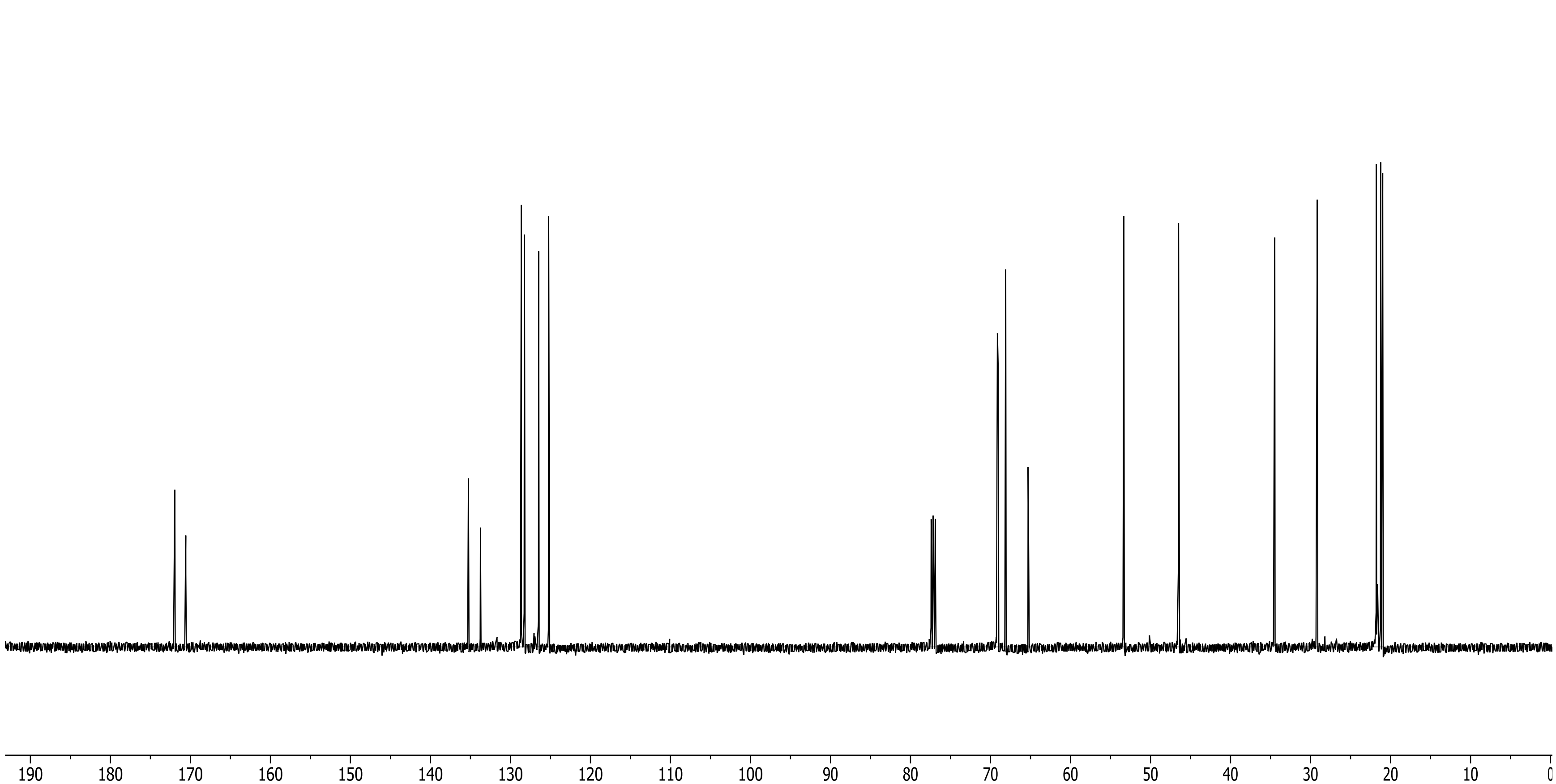
^{1}H NMR of (±)-**2c** in $CDCl_3$

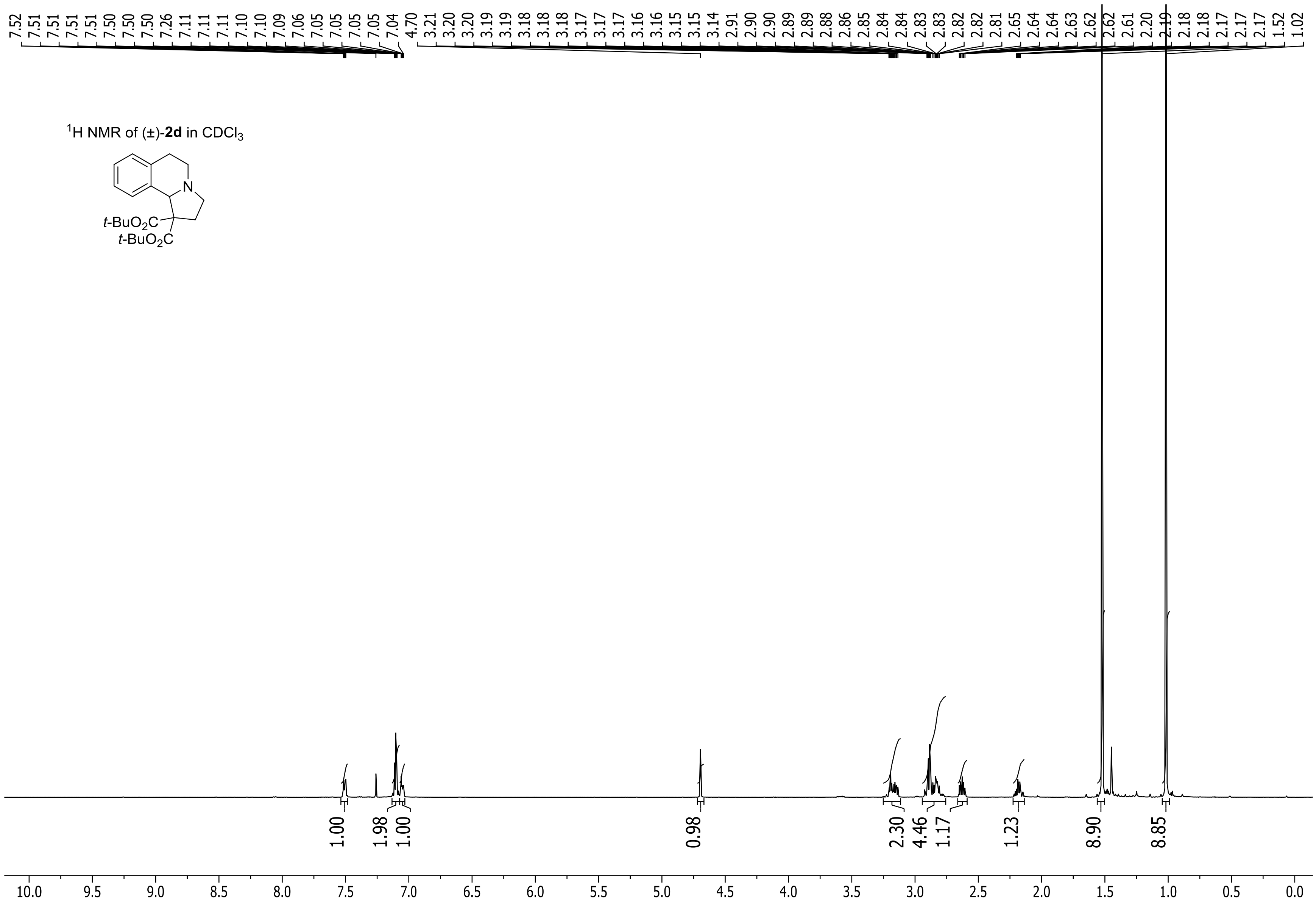




^{13}C NMR of (±)-**2c** in $CDCl_3$

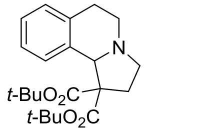


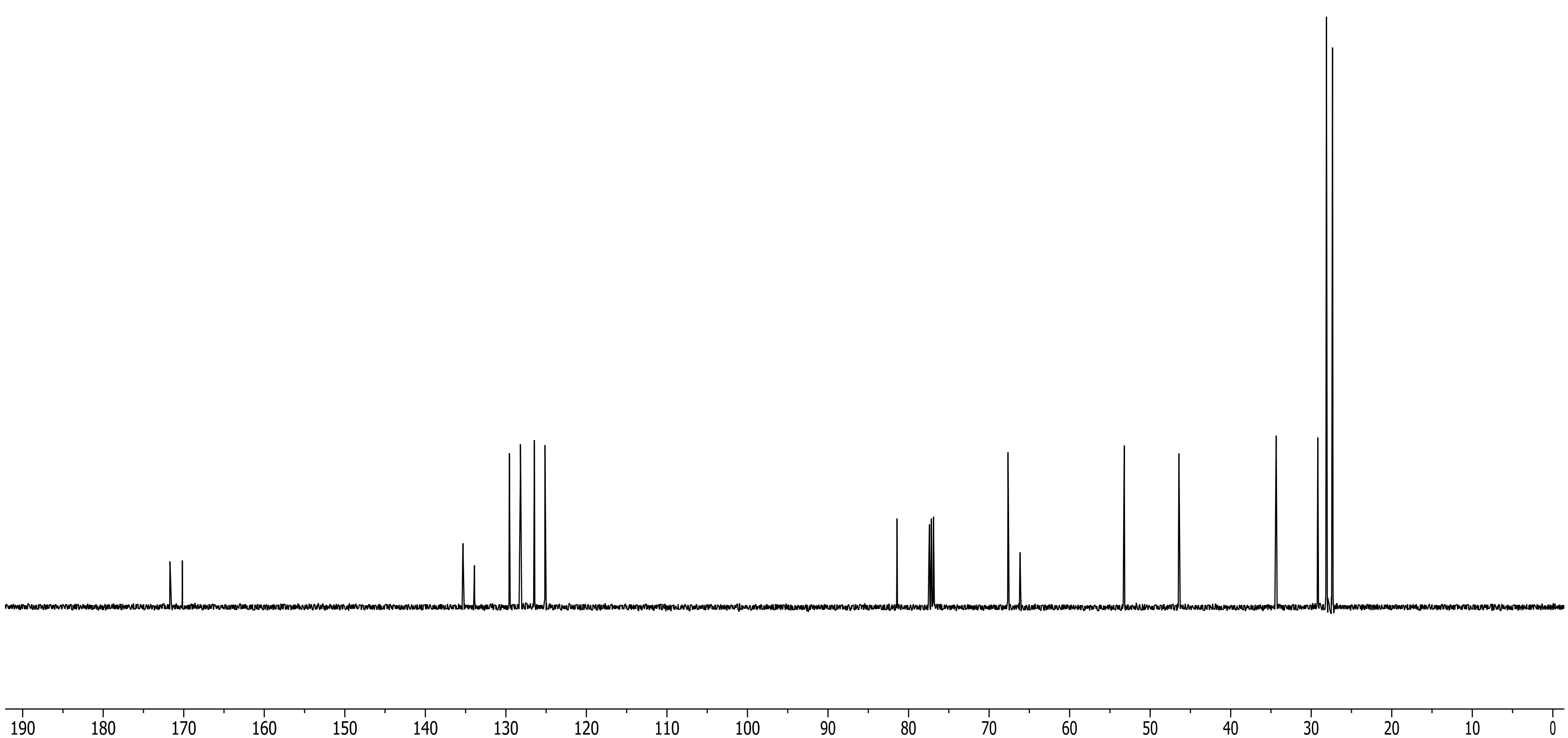


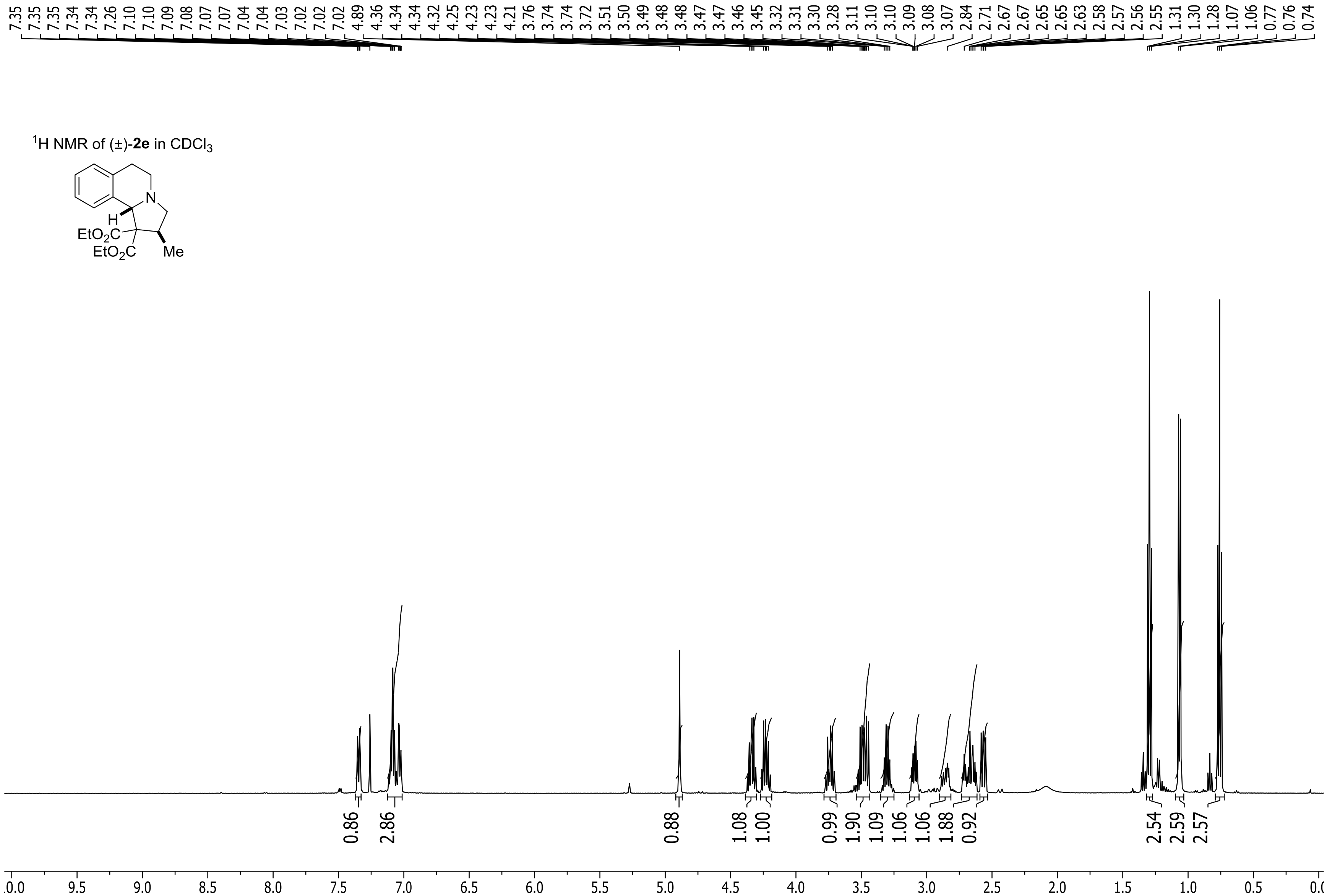


7.52 7.51 7.51 7.51 7.51 7.50 7.50 7.50 7.26 7.11 7.11 7.11 7.10 7.10 7.09 7.06 7.05 7.05 7.05 7.04 4.70 3.21 3.20 3.20 3.19 3.19 3.18 3.18 3.18 3.17 3.17 3.17 3.16 3.16 3.15 3.15 3.14 2.91 2.90 2.90 2.89 2.89 2.88 2.86 2.85 2.84 2.84 2.83 2.83 2.82 2.82 2.81 2.65 2.64 2.64 2.63 2.62 2.62 2.61 2.20 2.19 2.18 2.18 2.17 2.17 2.17 1.52 1.02
¹H NMR of (±)-2d in CDCl₃
N
t-BuO₂C
t-BuO₂C
1.00 1.98 1.00 0.98 2.30 4.46 1.17 1.23 8.90 8.85
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

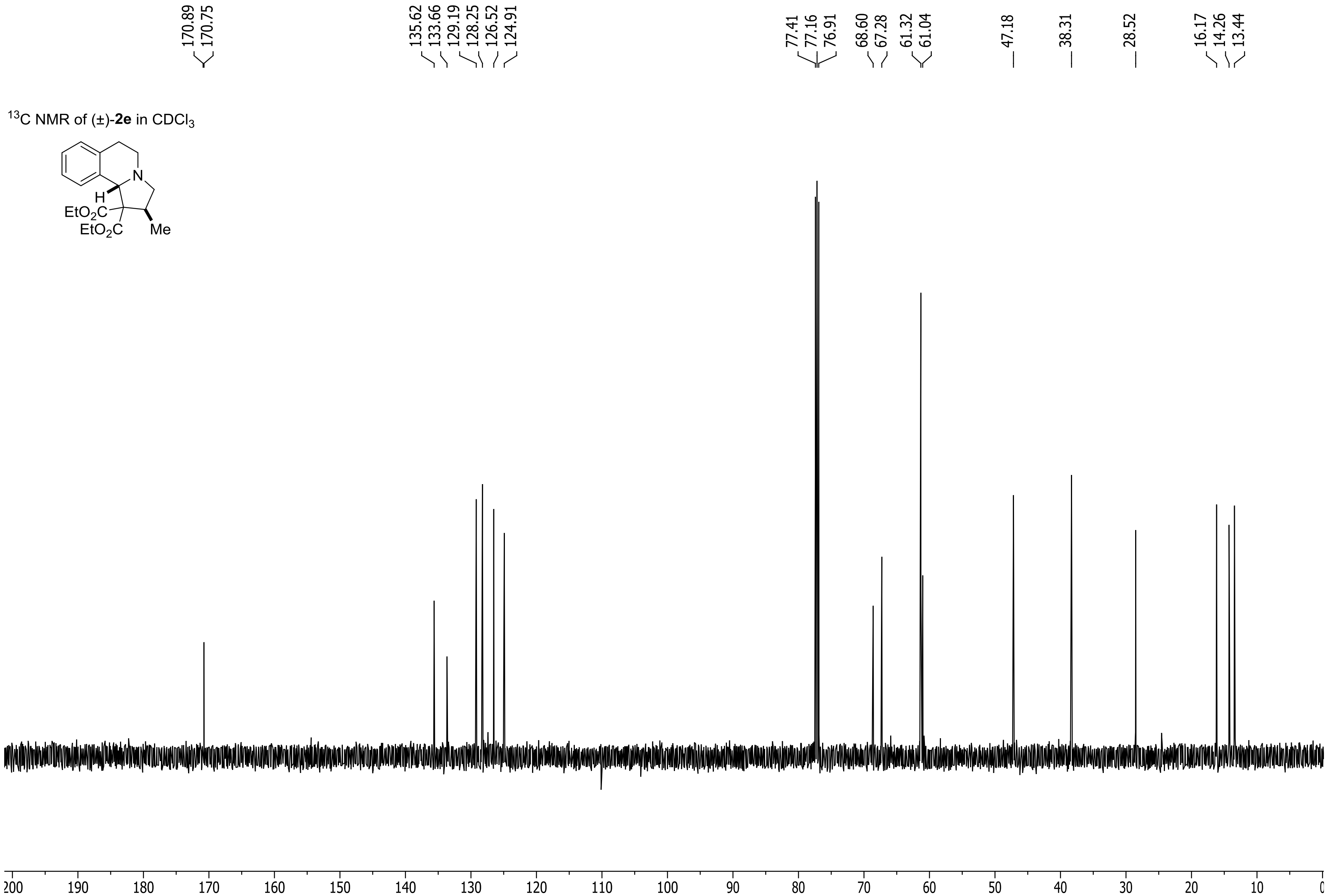
^{13}C NMR of (±)-**2d** in $CDCl_3$



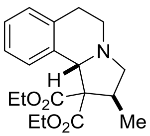


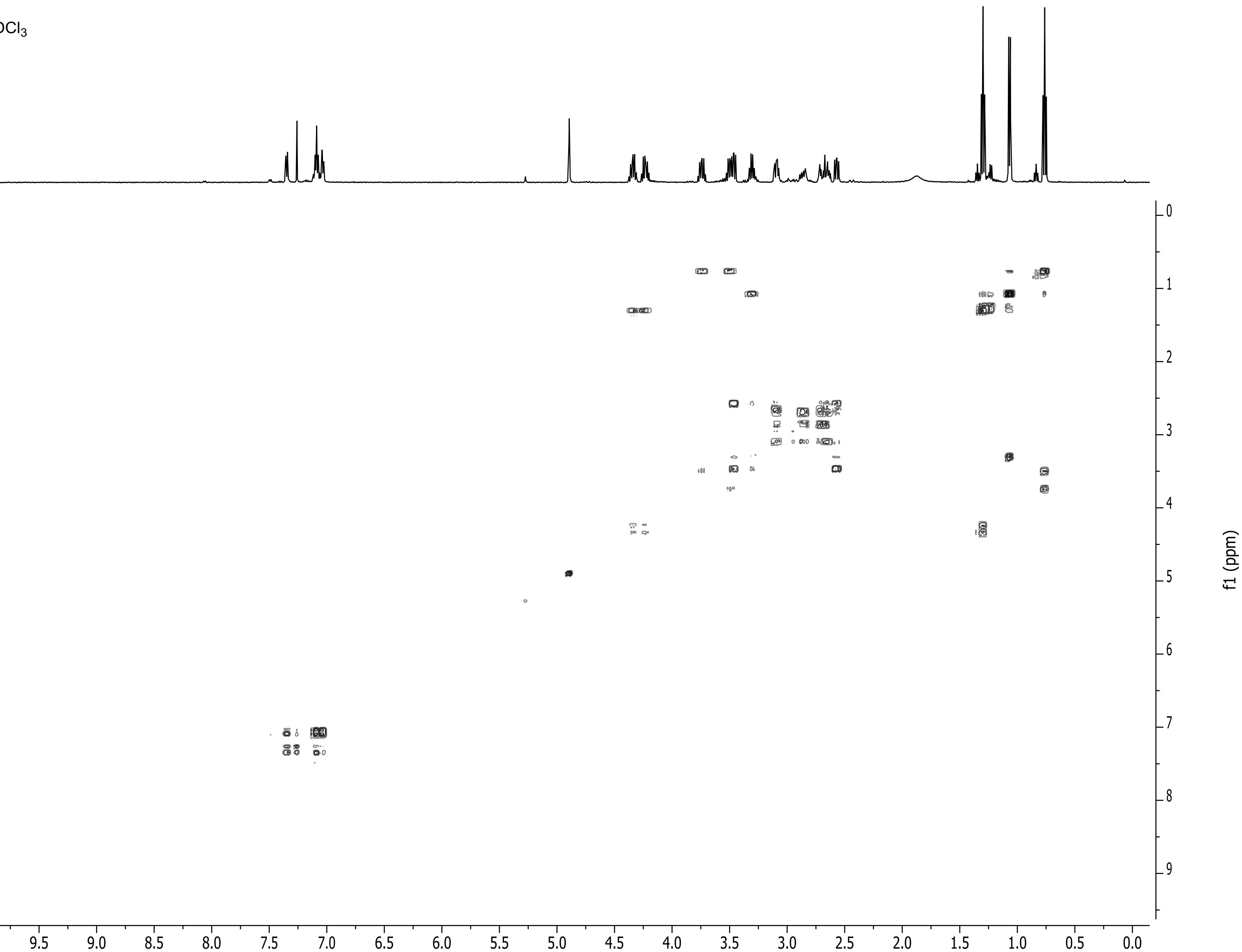

^{1}H NMR of (±)-**2e** in $CDCl_3$
EtO$_2$C
EtO$_2$C
H
N
Me

^{13}C NMR of (±)-**2e** in $CDCl_3$

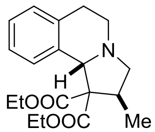


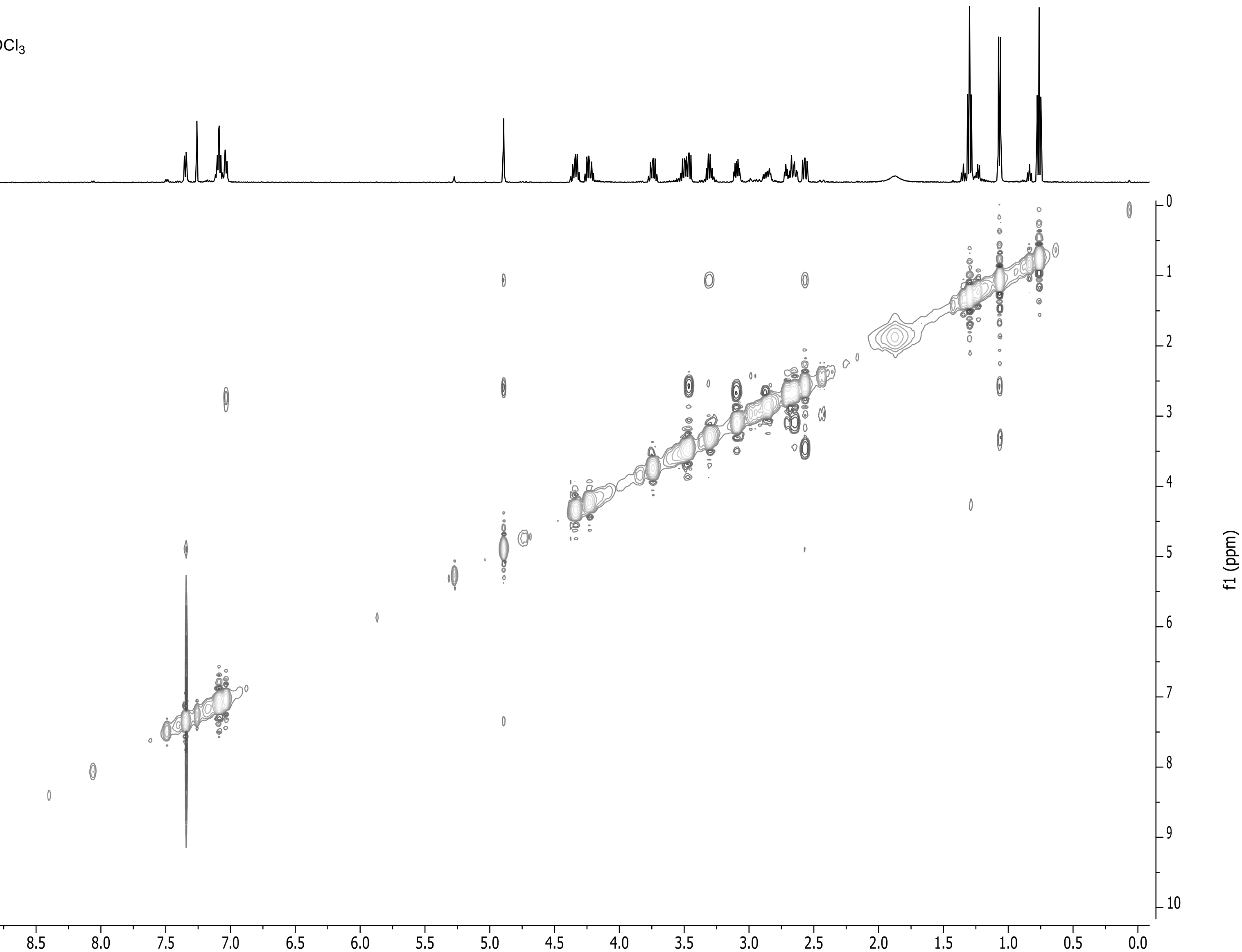
GCOSY of (±)-**2e** in $CDCl_3$

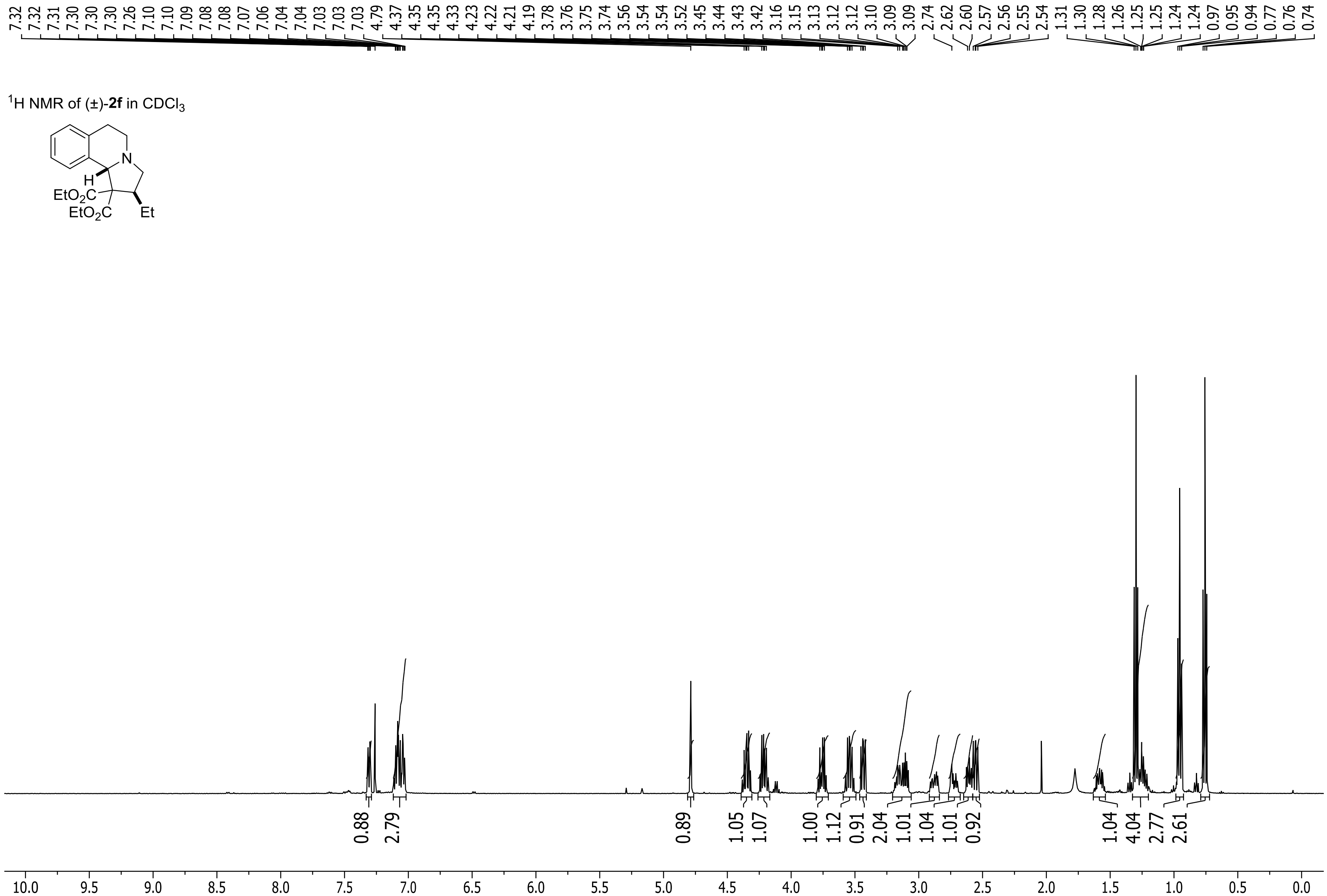




NOESY of (±)-**2e** in $CDCl_3$

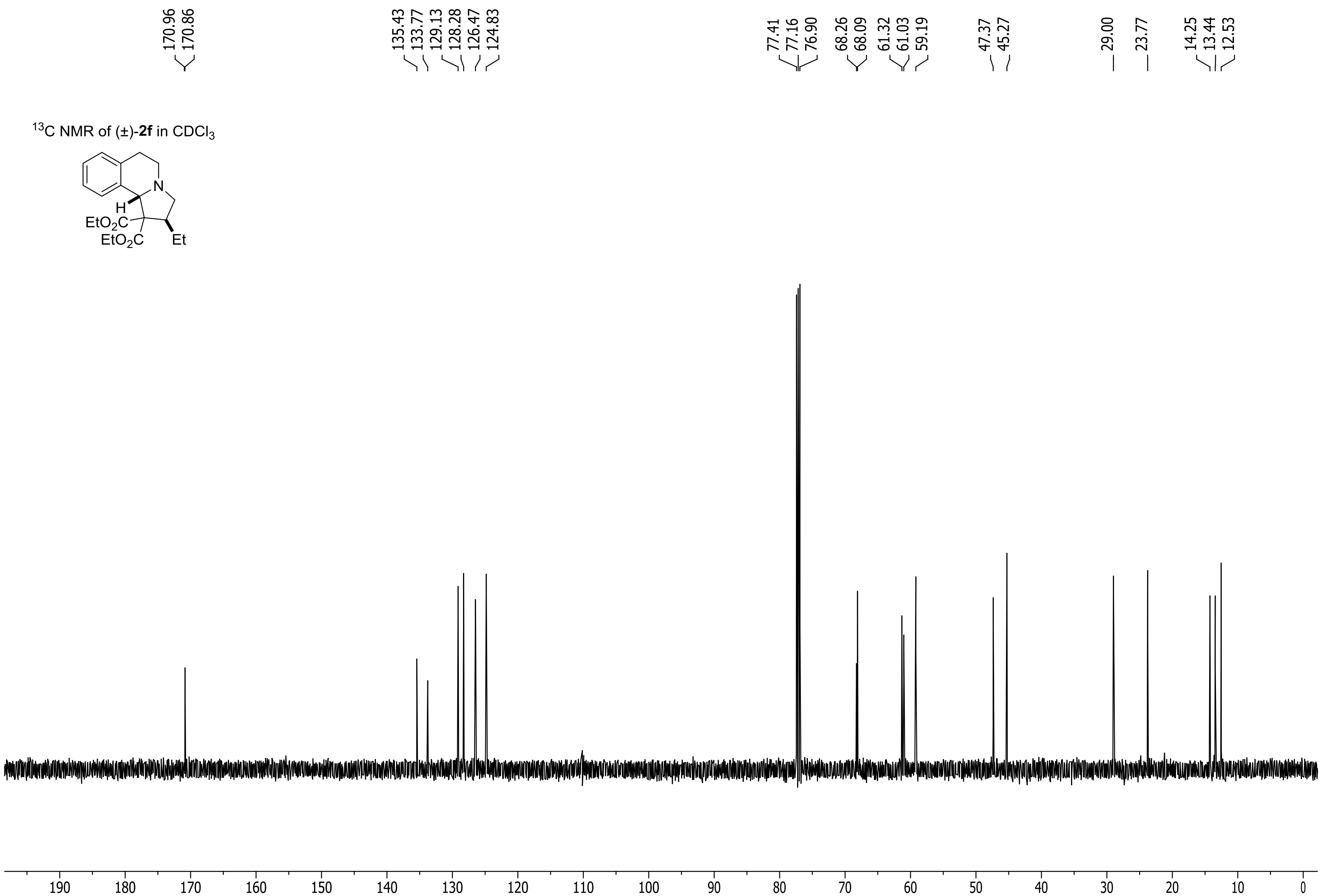




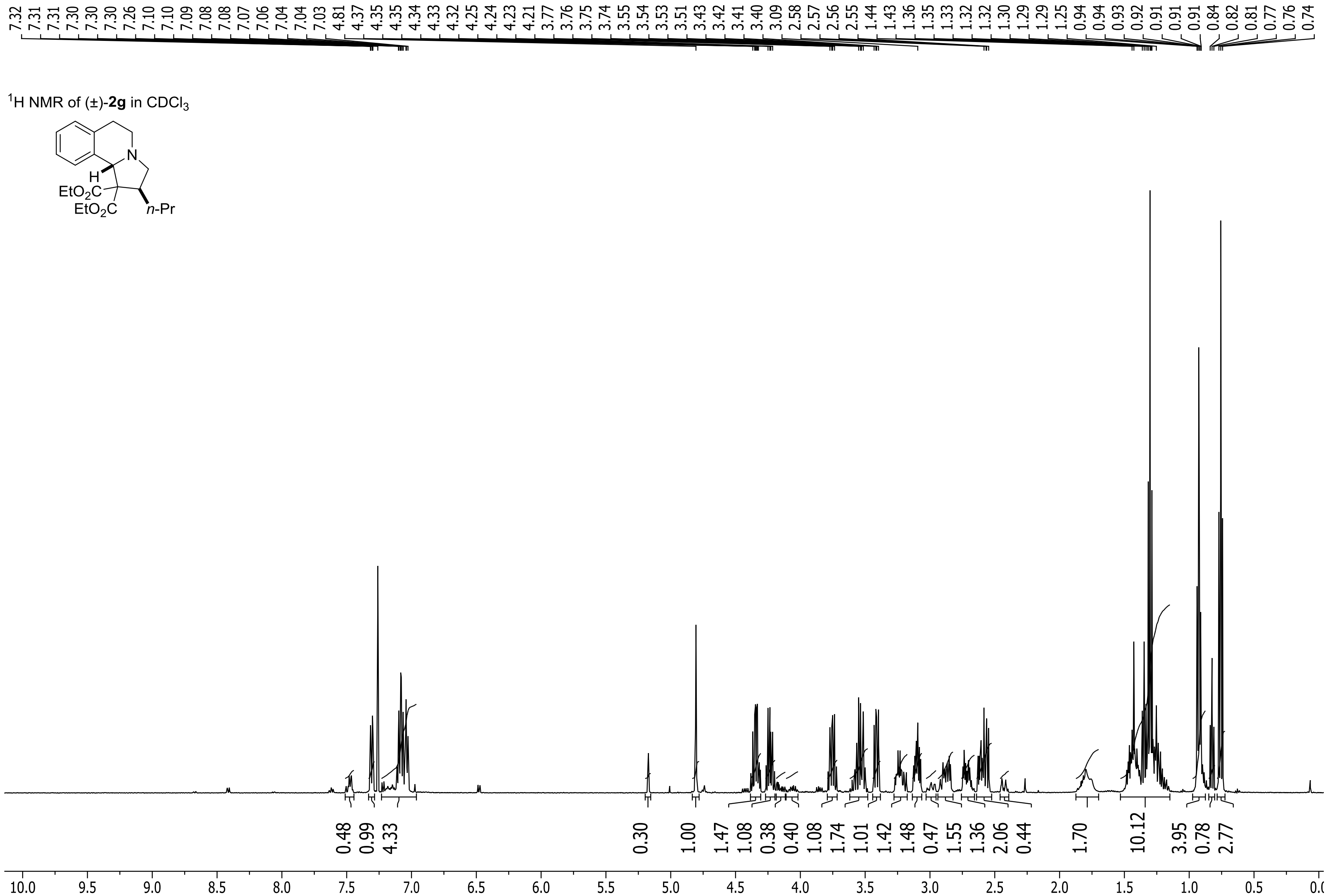


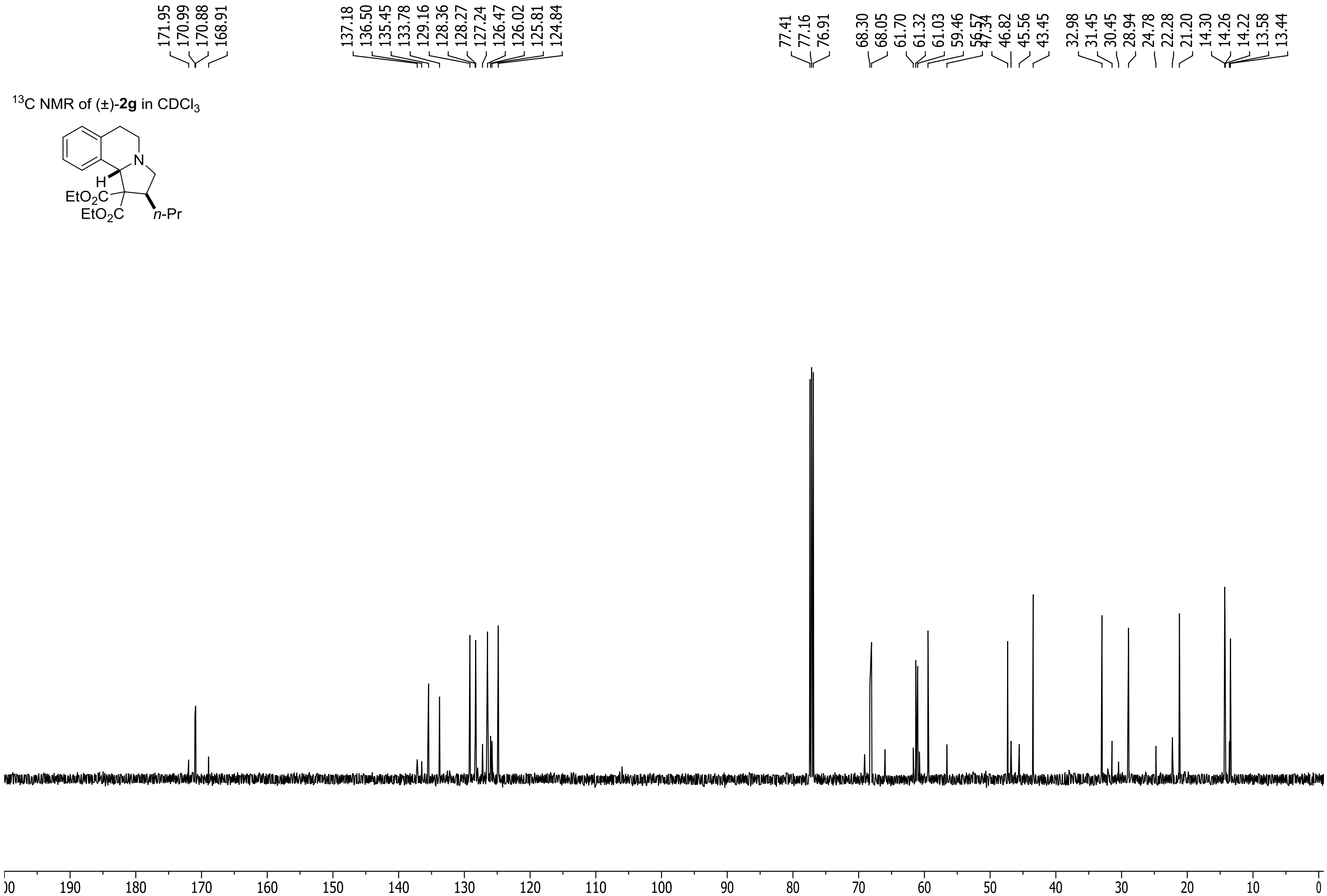
7.32 7.32 7.31 7.30 7.30 7.30 7.26 7.10 7.10 7.09 7.08 7.08 7.07 7.06 7.04 7.04 7.03 7.03 7.03 4.79 4.37 4.35 4.35 4.33 4.23 4.22 4.21 4.19 3.78 3.76 3.75 3.74 3.56 3.54 3.54 3.52 3.45 3.44 3.43 3.42 3.16 3.15 3.13 3.12 3.12 3.10 3.09 3.09 2.74 2.62 2.60 2.57 2.56 2.55 2.54 1.31 1.30 1.28 1.26 1.25 1.25 1.24 1.24 0.97 0.95 0.94 0.77 0.76 0.74
¹H NMR of (±)-2f in CDCl₃
N
H
EtO₂C
EtO₂C
Et
0.88 2.79 0.89 1.05 1.07 1.00 1.12 0.91 2.04 1.01 1.04 1.01 0.92 1.04 4.04 2.77 2.61
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

^{13}C NMR of (±)-**2f** in $CDCl_3$

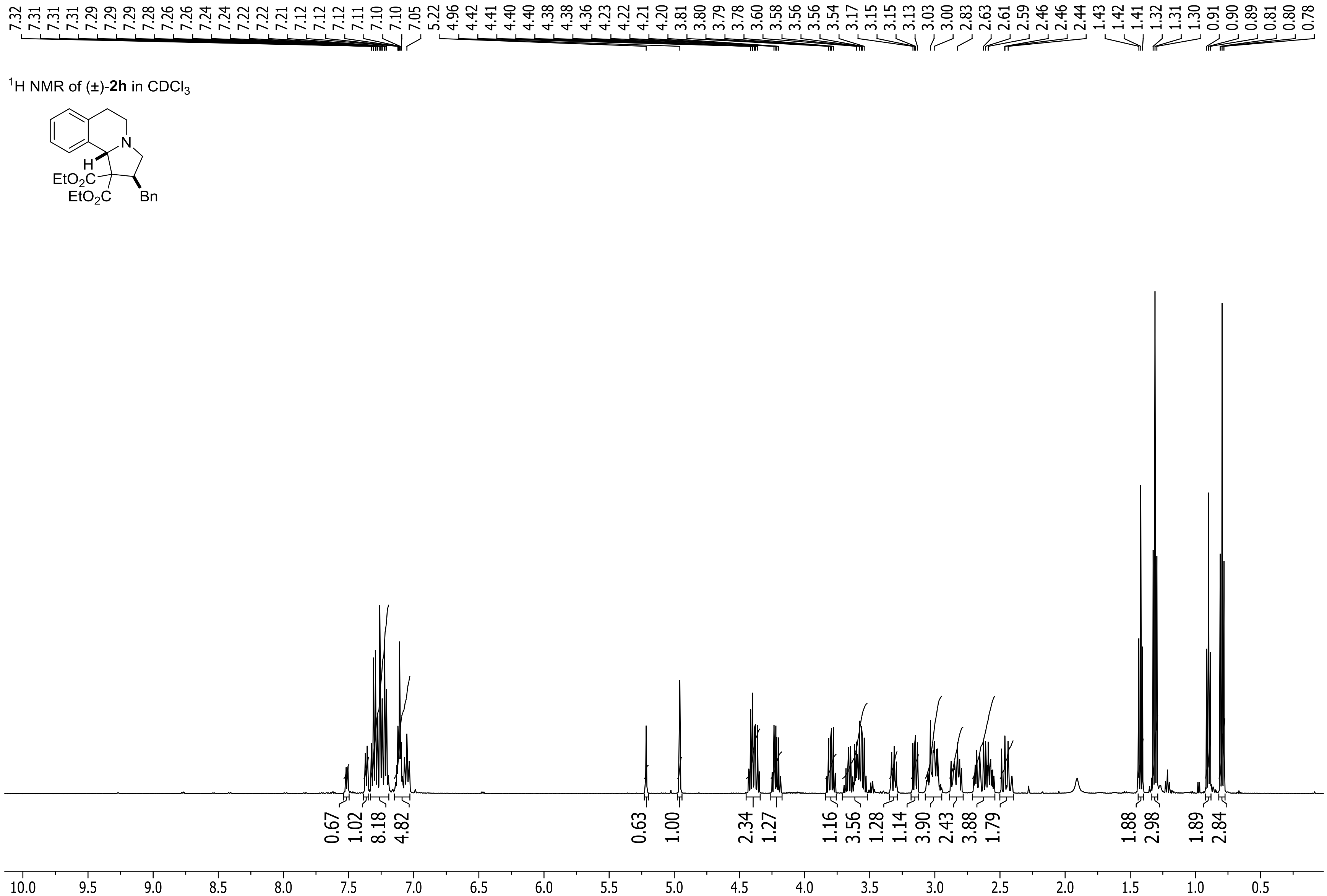


^{1}H NMR of (±)-**2g** in $CDCl_3$



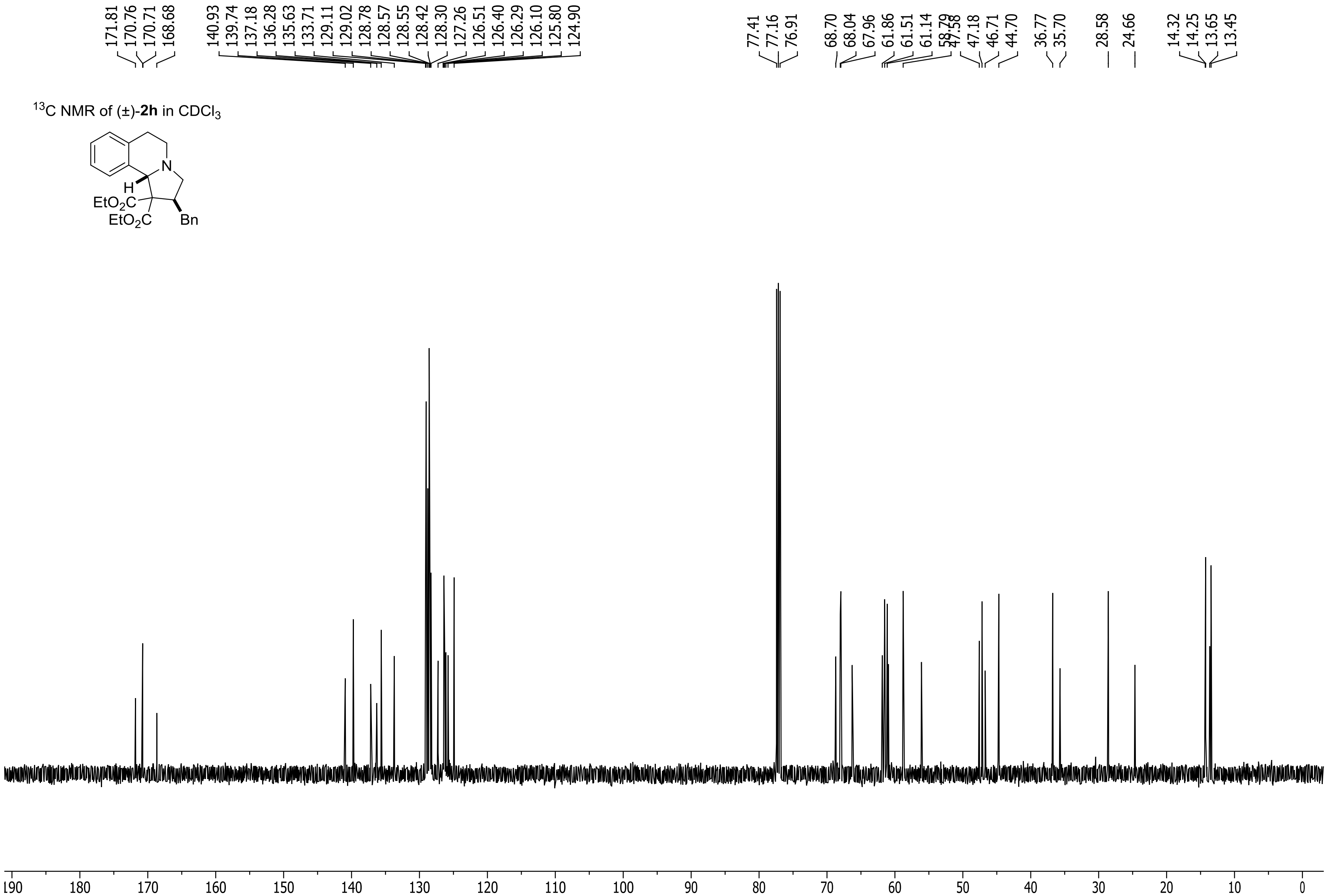


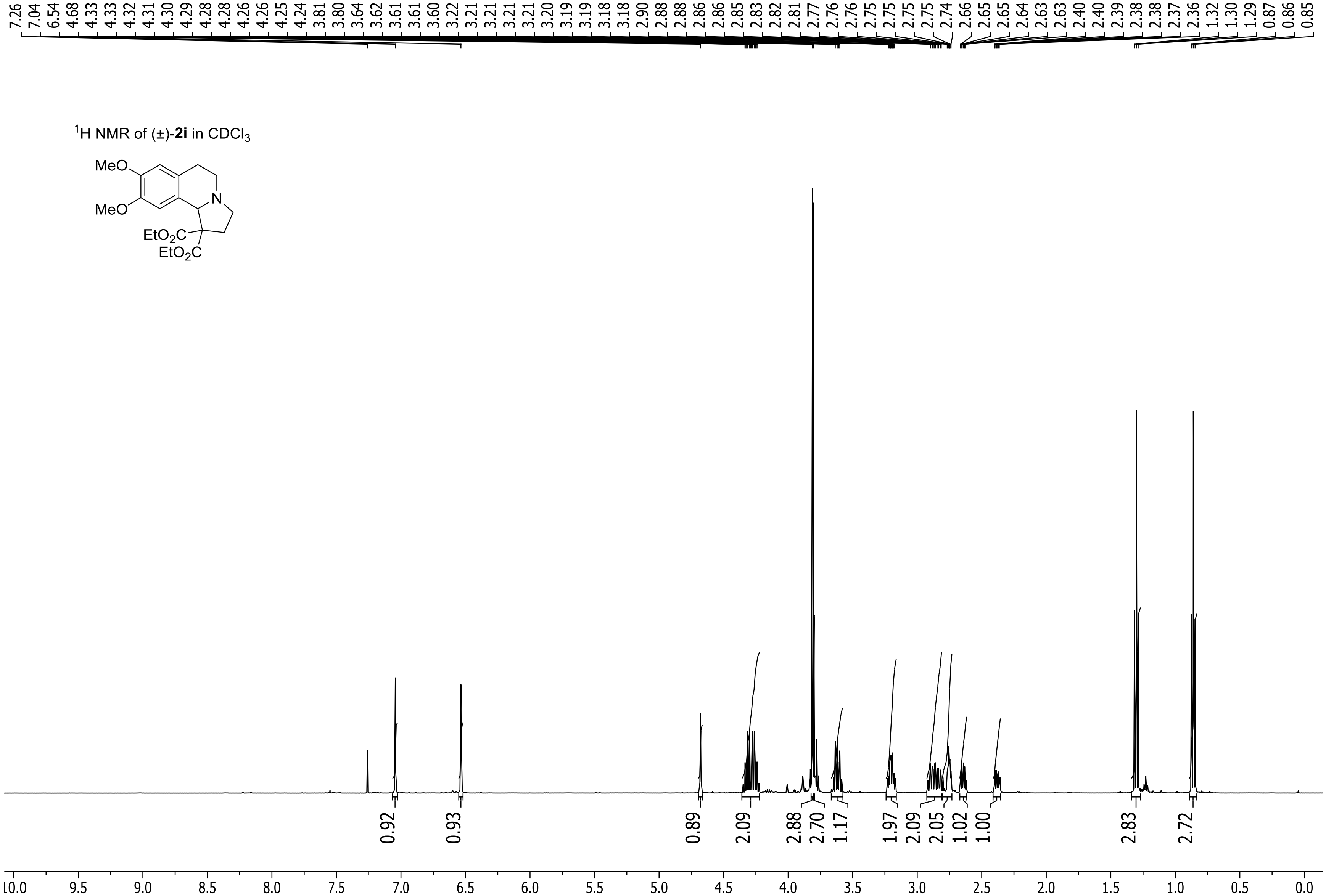
^{13}C NMR of (±)-**2g** in CDCl$_3$
EtO$_2$C
EtO$_2$C
H
N
n-Pr
171.95
170.99
170.88
168.91
137.18
136.50
135.45
133.78
129.16
128.36
128.27
127.24
126.47
126.02
125.81
124.84
77.41
77.16
76.91
68.30
68.05
61.70
61.32
61.03
59.46
56.57
47.34
46.82
45.56
43.45
32.98
31.45
30.45
28.94
24.78
22.28
21.20
14.30
14.26
14.22
13.58
13.44



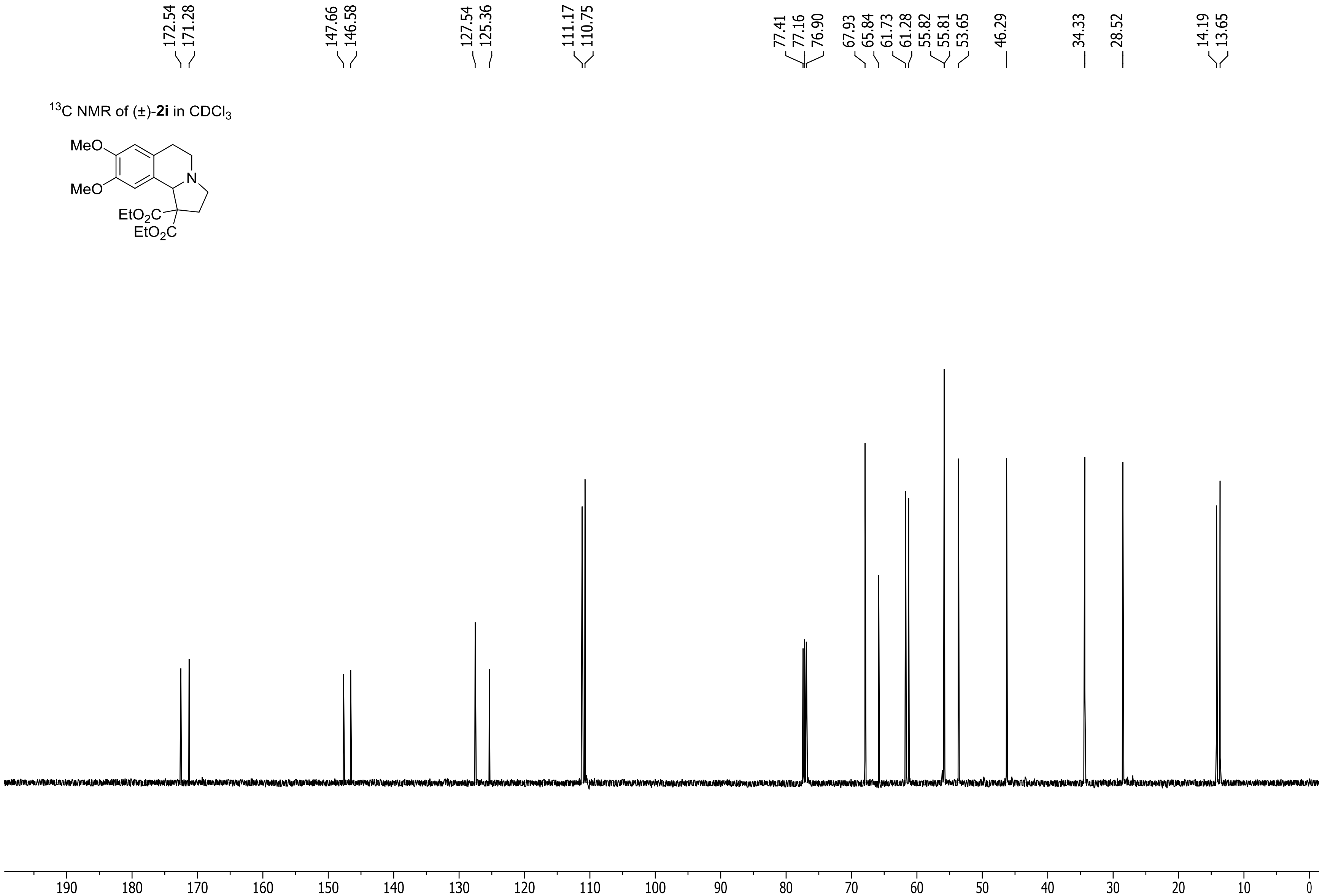
^1H NMR of (±)-**2h** in $CDCl_3$

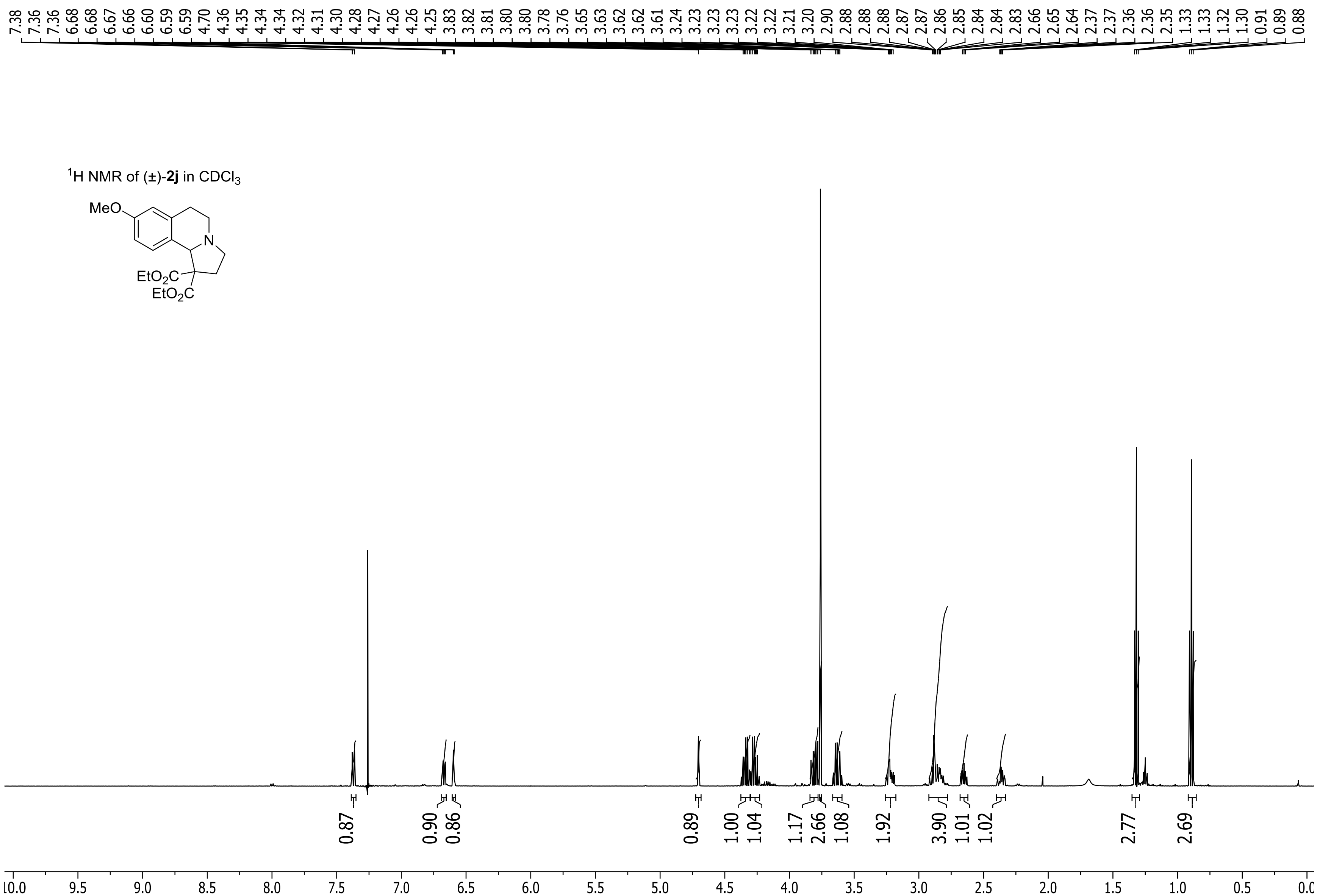
^{13}C NMR of (±)-**2h** in $CDCl_3$

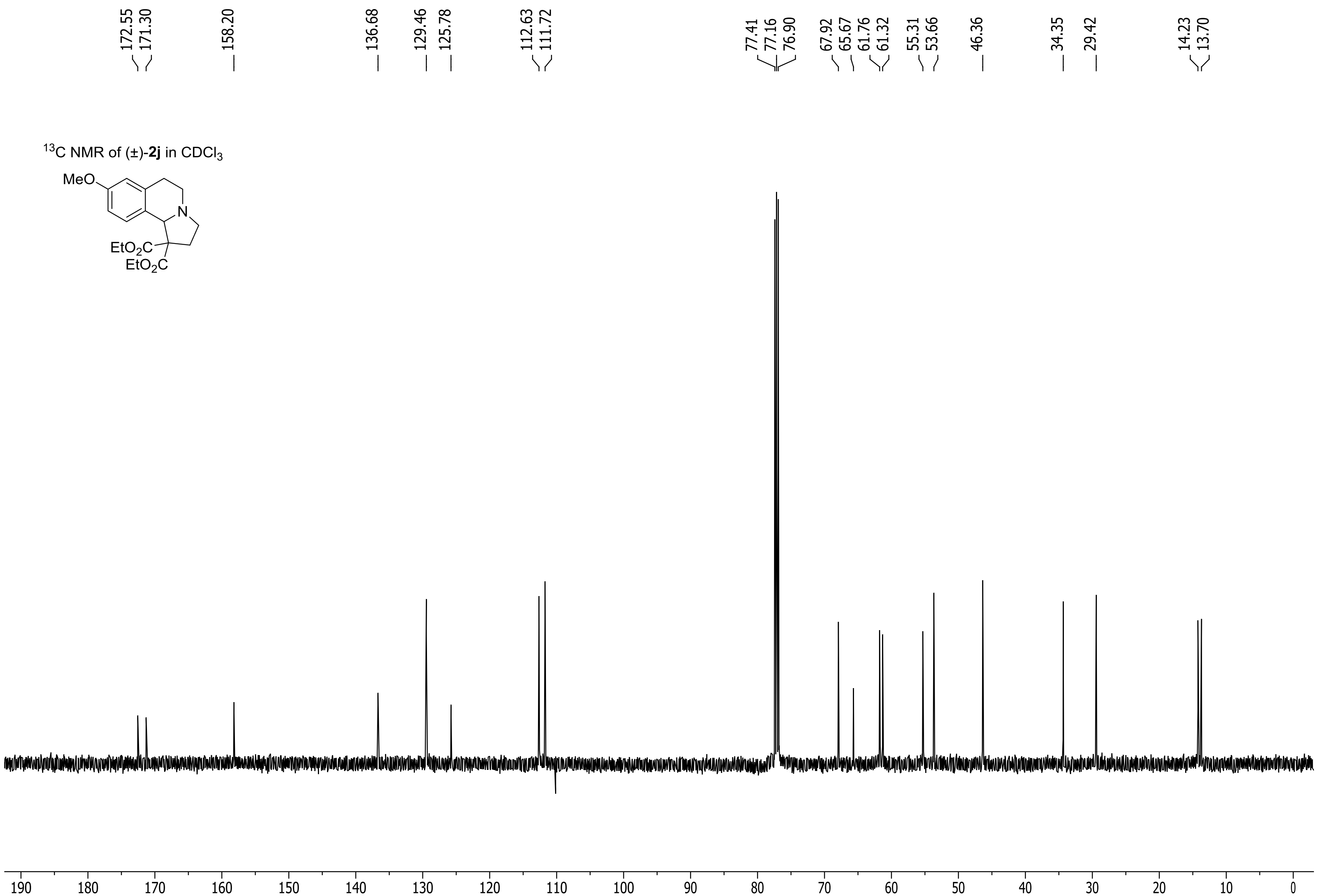



7.26 7.04 6.54 4.68 4.33 4.33 4.32 4.31 4.30 4.29 4.28 4.28 4.26 4.26 4.25 4.24 3.81 3.80 3.64 3.62 3.61 3.61 3.60 3.22 3.21 3.21 3.21 3.21 3.20 3.19 3.19 3.18 3.18 2.90 2.88 2.88 2.86 2.86 2.85 2.83 2.82 2.81 2.77 2.76 2.76 2.75 2.75 2.75 2.75 2.74 2.66 2.65 2.65 2.64 2.63 2.63 2.40 2.40 2.39 2.38 2.38 2.37 2.36 1.32 1.30 1.29 0.87 0.86 0.85
1H NMR of (±)-2i in CDCl3
MeO
MeO
N
EtO2C
EtO2C
0.92
0.93
0.89
2.09
2.88
2.70
1.17
1.97
2.09
2.05
1.02
1.00
2.83
2.72
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

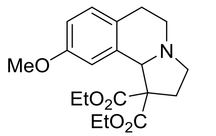
^{13}C NMR of (±)-**2i** in $CDCl_3$

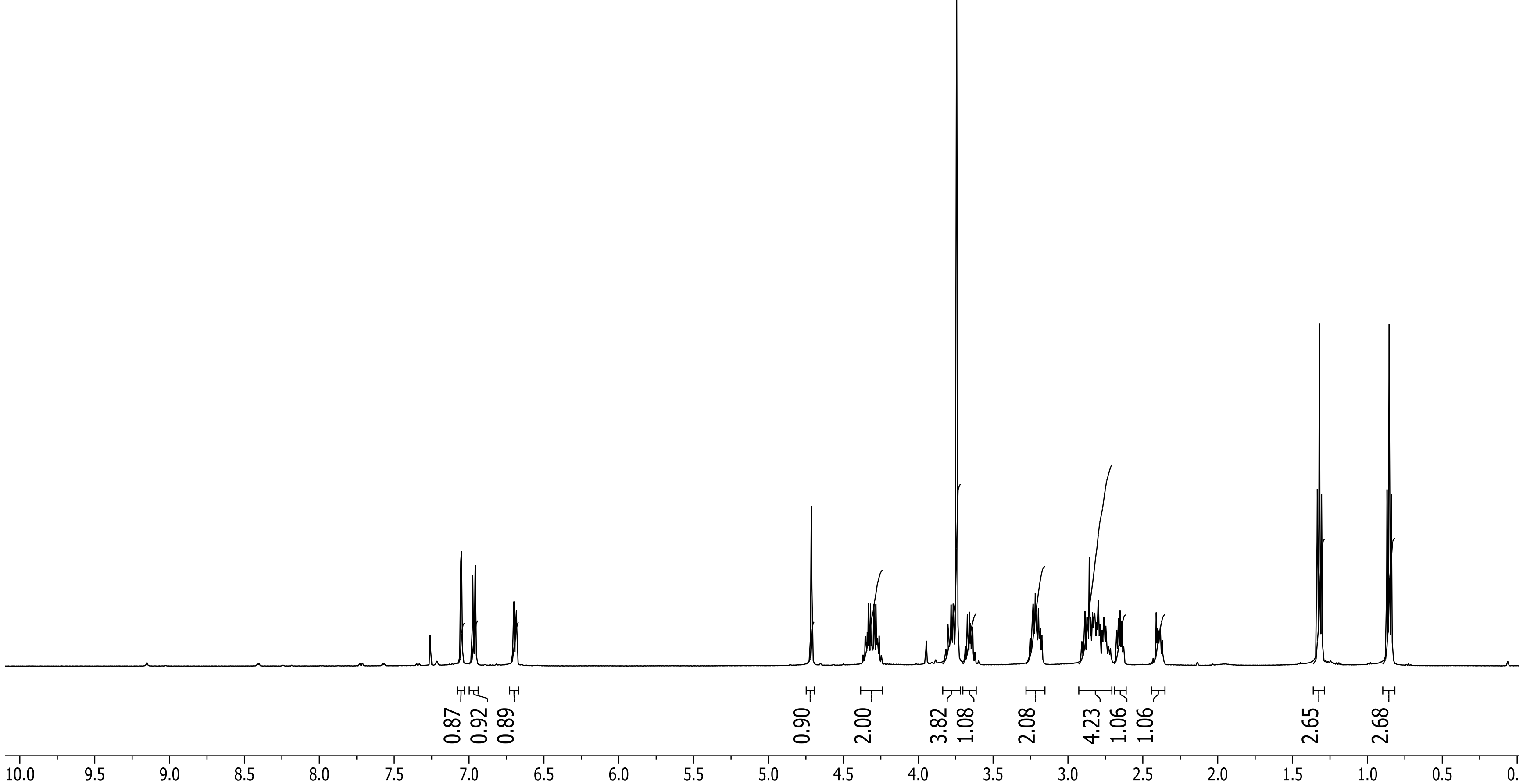


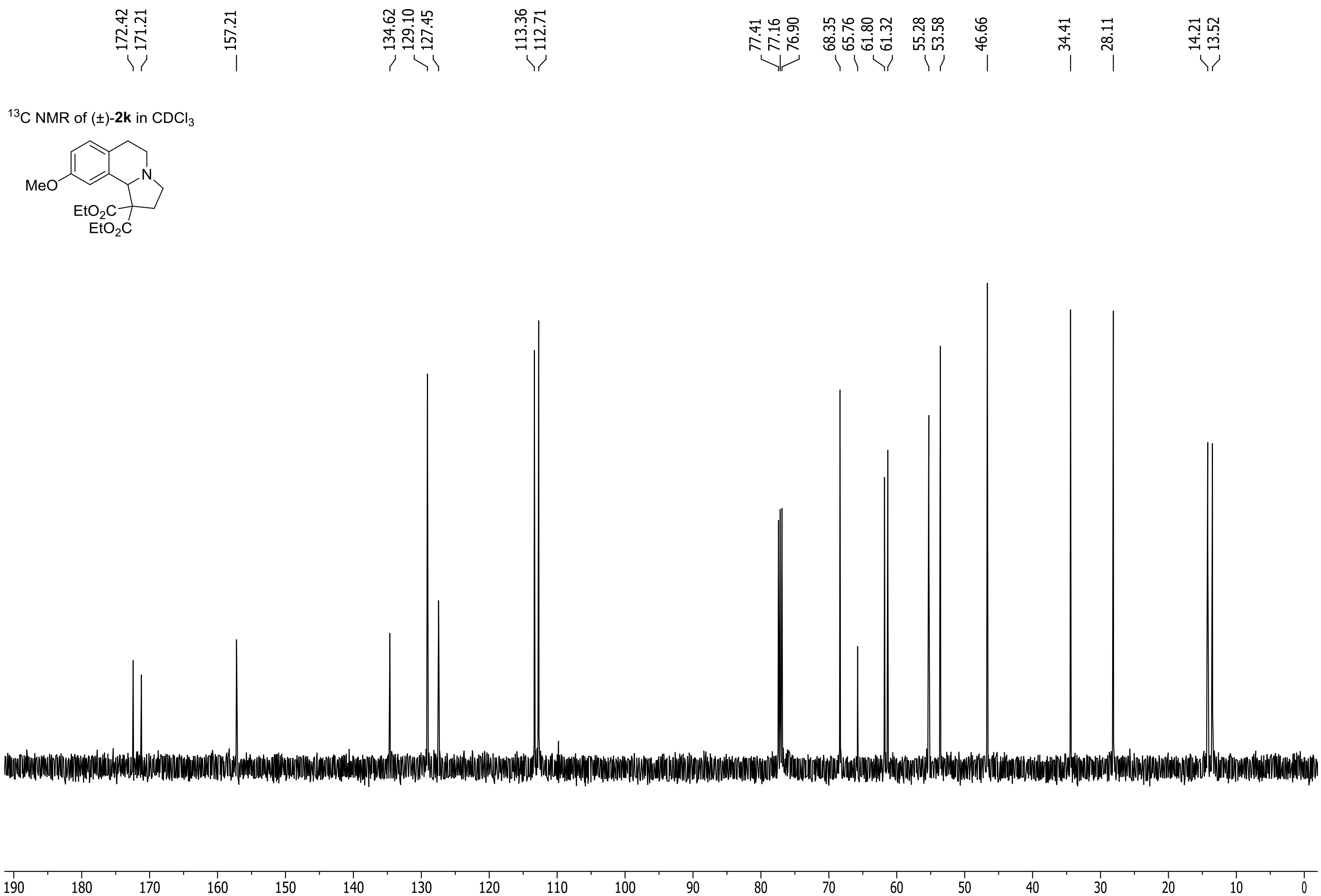

1H NMR of (±)-2j in CDCl3
MeO
N
EtO2C
EtO2C
0.87
0.90
0.86
0.89
1.00
1.04
1.17
2.66
1.08
1.92
3.90
1.01
1.02
2.77
2.69
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0


13C NMR of (±)-2j in CDCl3
MeO
N
EtO2C
EtO2C
172.55
171.30
158.20
136.68
129.46
125.78
112.63
111.72
77.41
77.16
76.90
67.92
65.67
61.76
61.32
55.31
53.66
46.36
34.35
29.42
14.23
13.70
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

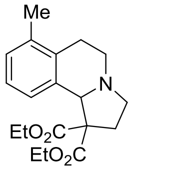
^{1}H NMR of (±)-**2k** in $CDCl_3$

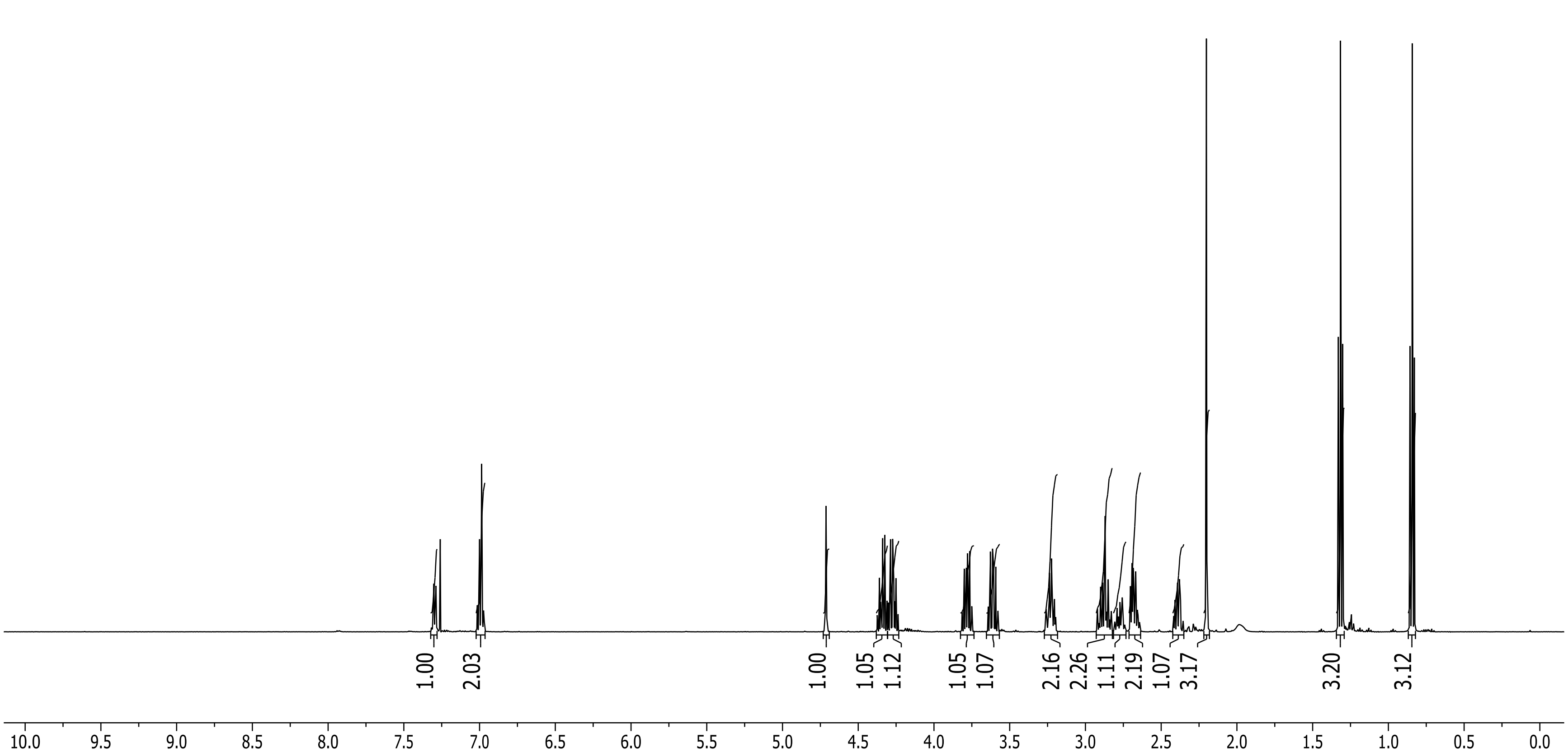




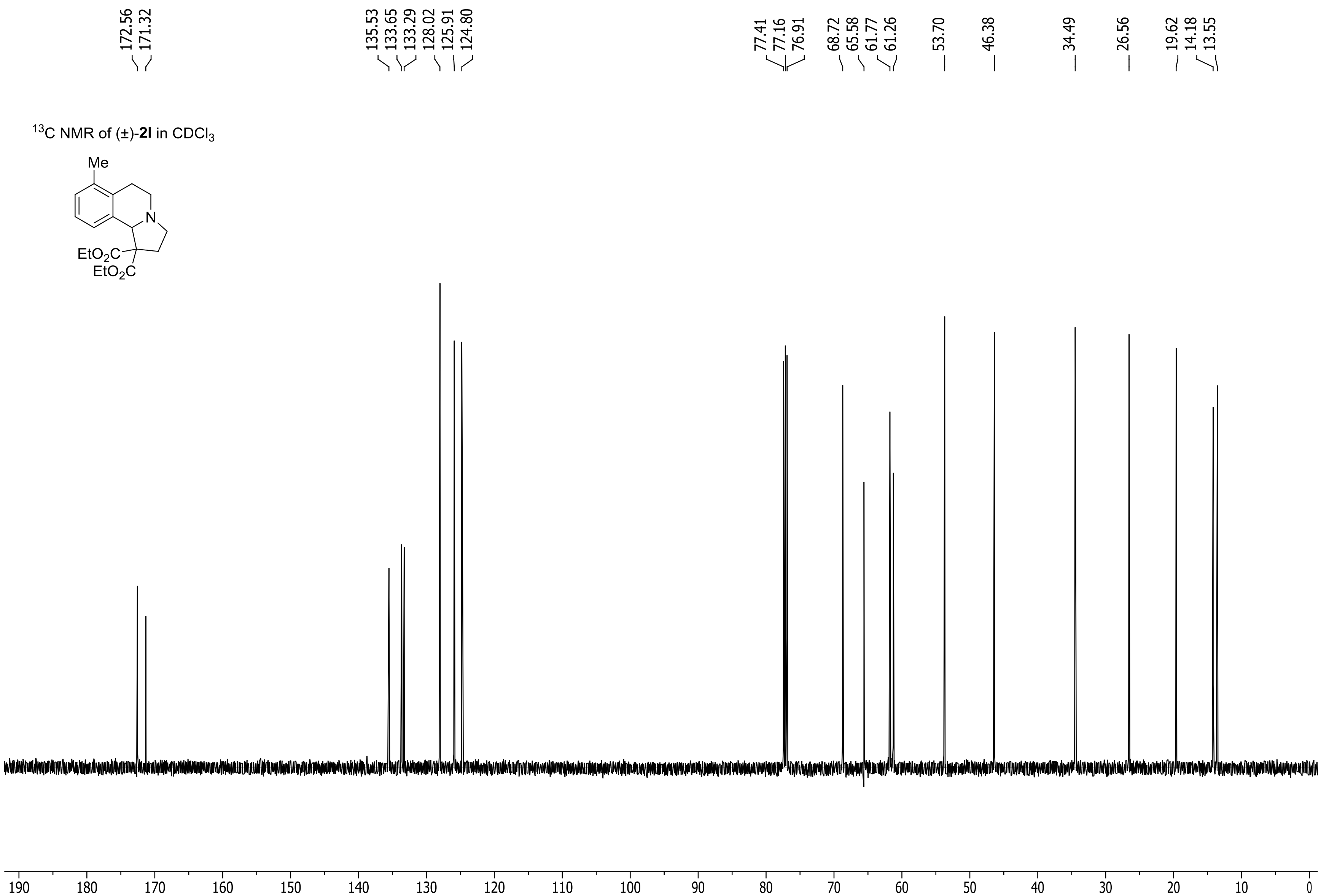

13C NMR of (±)-2k in CDCl3
172.42
171.21
157.21
134.62
129.10
127.45
113.36
112.71
77.41
77.16
76.90
68.35
65.76
61.80
61.32
55.28
53.58
46.66
34.41
28.11
14.21
13.52
MeO
N
EtO2C
EtO2C
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

[1]H NMR of (±)-**2l** in $CDCl_3$

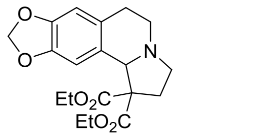


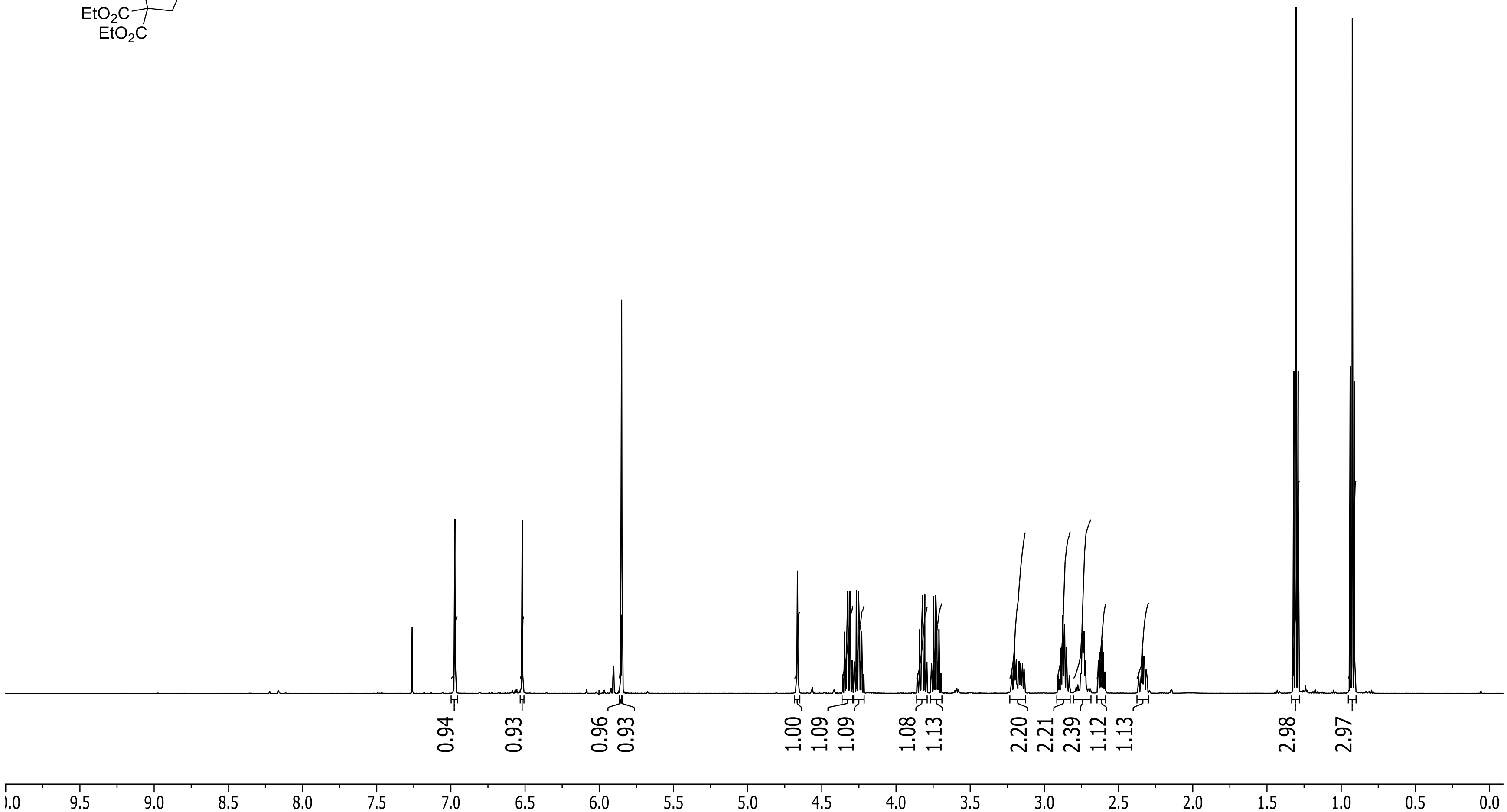


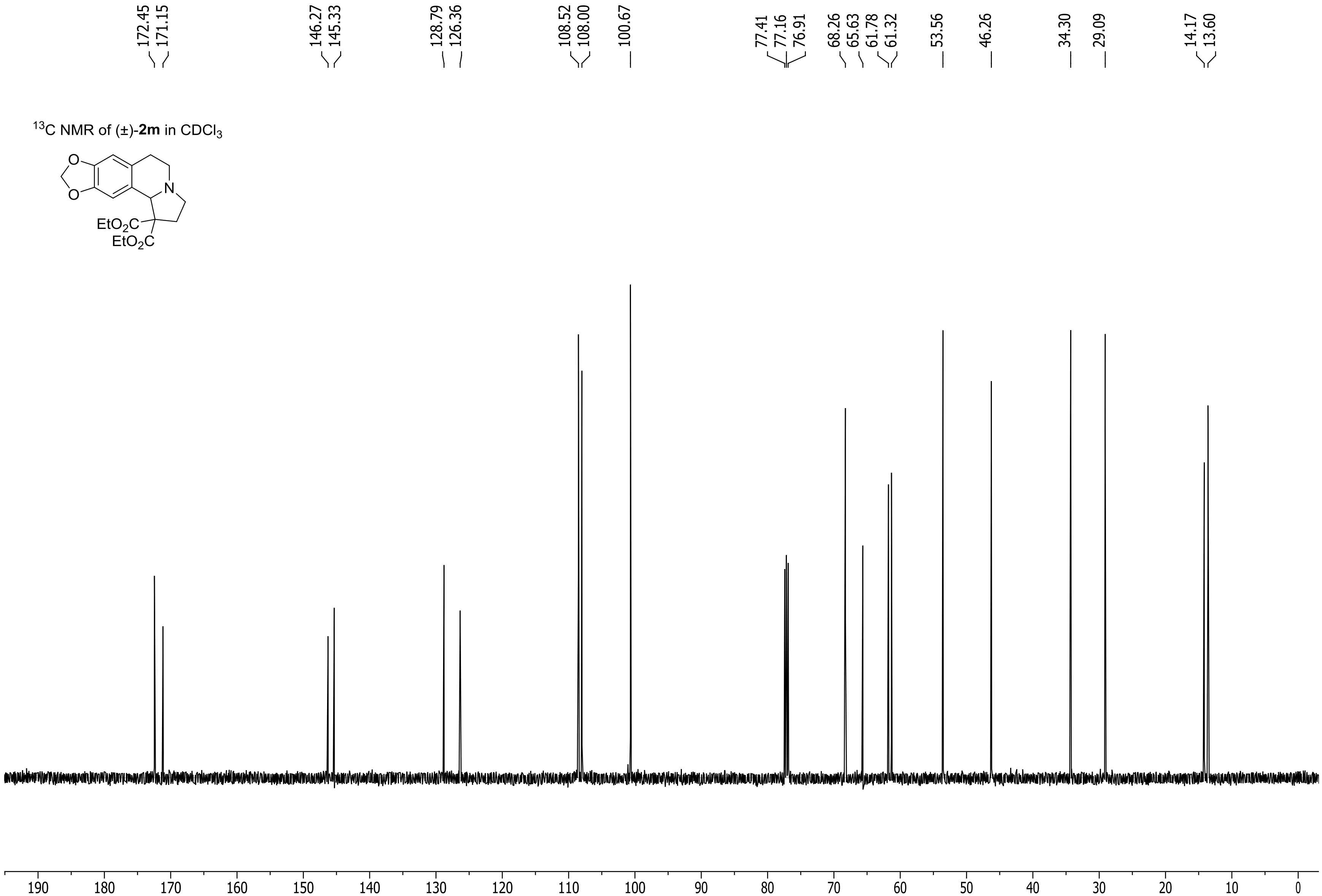
^{13}C NMR of (±)-**2l** in $CDCl_3$



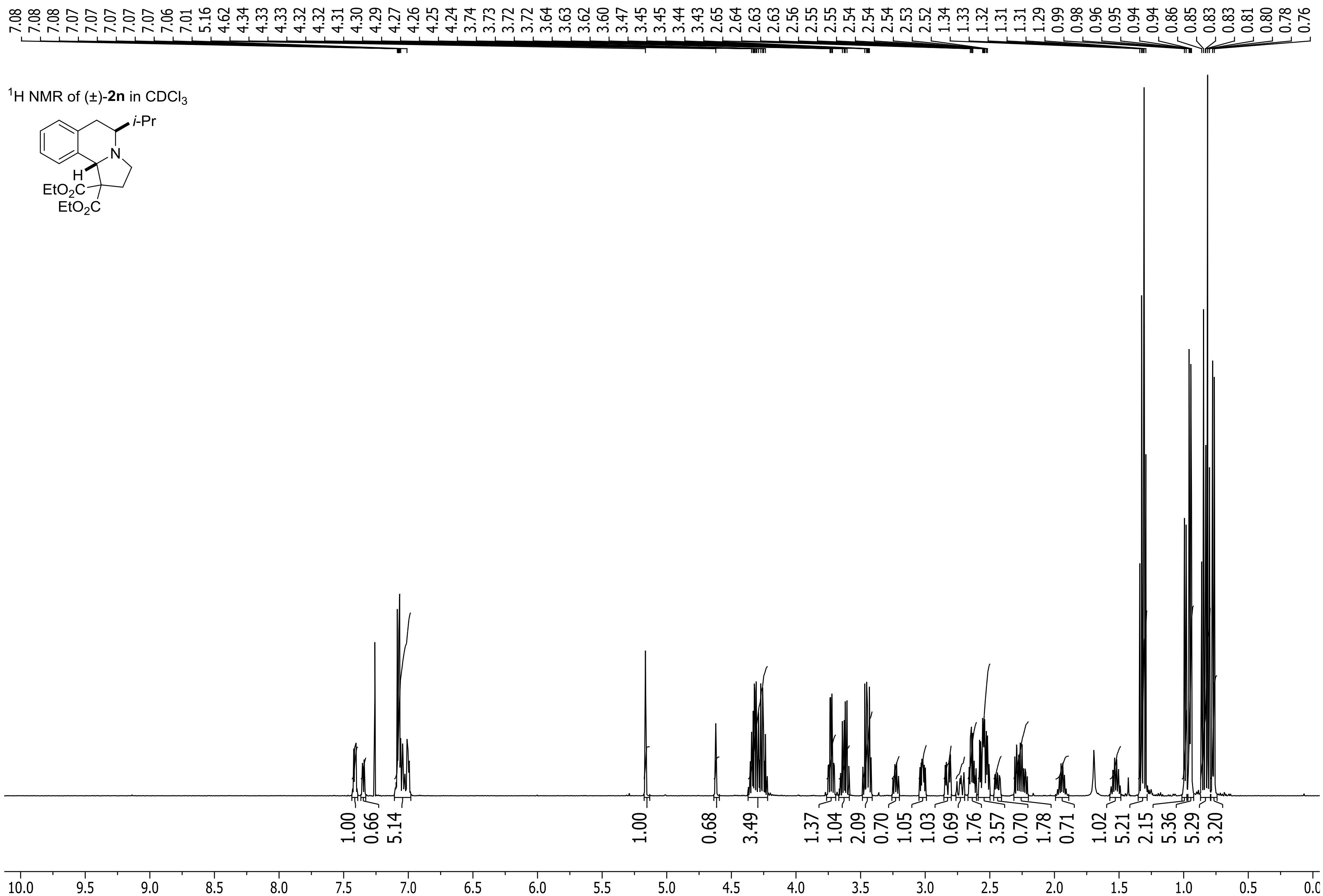
^{1}H NMR of (±)-**2m** in $CDCl_3$



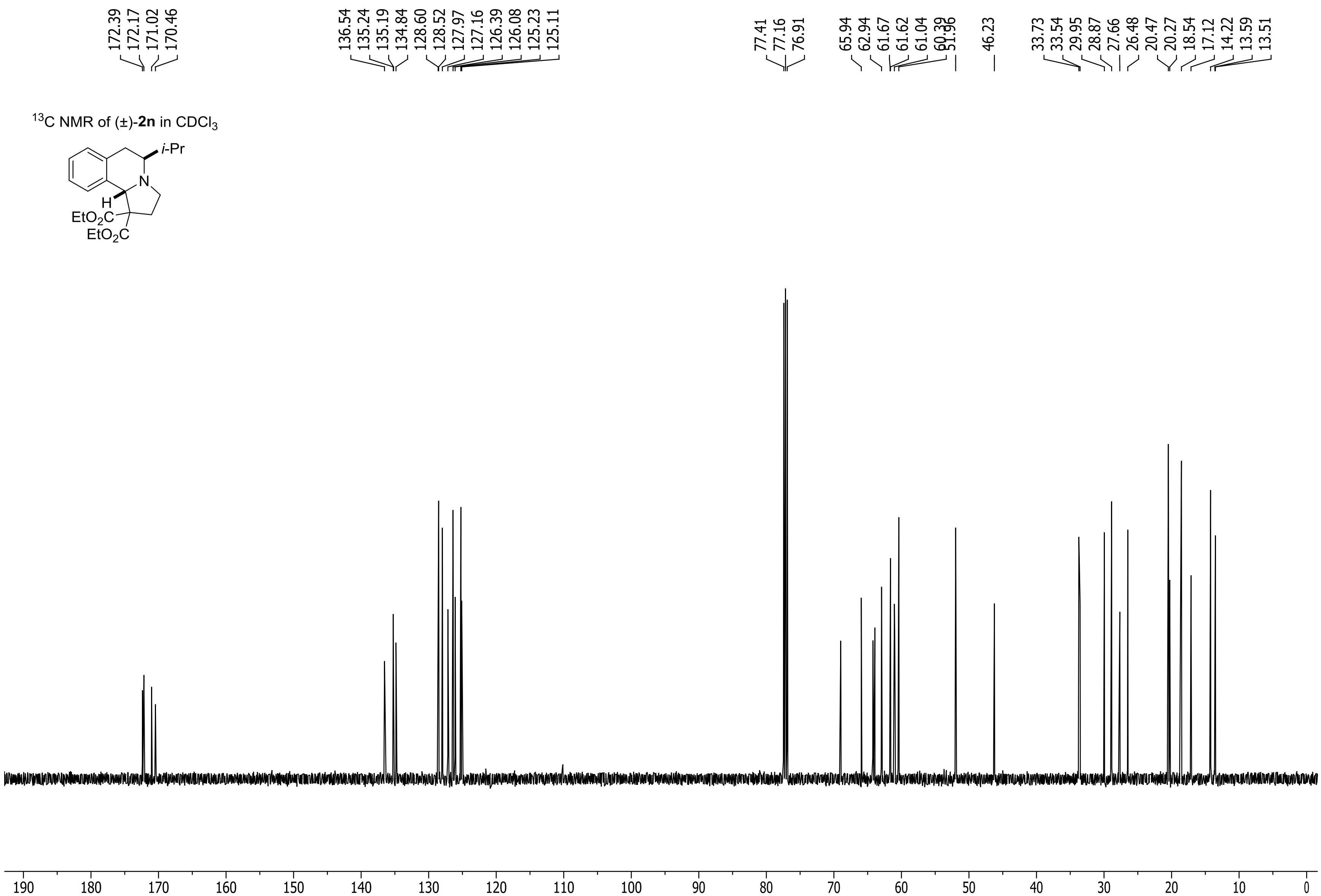




13C NMR of (±)-2m in CDCl3
EtO2C
EtO2C
O
O
N
172.45
171.15
146.27
145.33
128.79
126.36
108.52
108.00
100.67
77.41
77.16
76.91
68.26
65.63
61.78
61.32
53.56
46.26
34.30
29.09
14.17
13.60
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

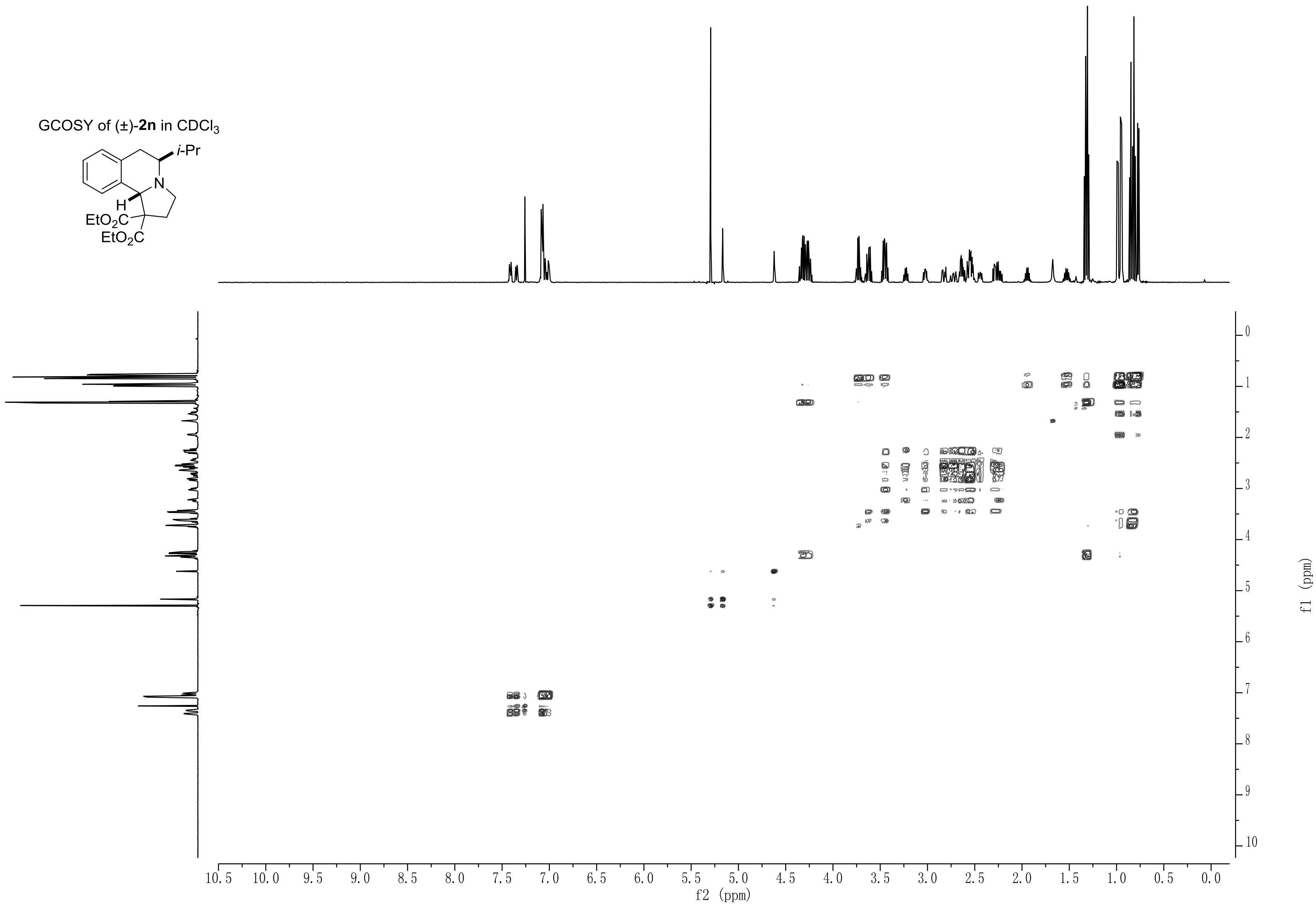


1H NMR of (±)-2n in CDCl3
i-Pr
N
H
EtO2C
EtO2C
7.08 7.08 7.08 7.07 7.07 7.07 7.07 7.07 7.06 7.01 5.16 4.62 4.34 4.33 4.33 4.32 4.32 4.31 4.30 4.29 4.27 4.26 4.25 4.24 3.74 3.73 3.72 3.72 3.64 3.63 3.62 3.60 3.47 3.45 3.45 3.44 3.43 2.65 2.64 2.63 2.63 2.56 2.55 2.55 2.54 2.54 2.54 2.53 2.52 1.34 1.33 1.32 1.31 1.31 1.29 0.99 0.98 0.96 0.95 0.94 0.94 0.86 0.85 0.83 0.83 0.81 0.80 0.78 0.76
1.00 0.66 5.14 1.00 0.68 3.49 1.37 1.04 2.09 0.70 1.05 1.03 0.69 1.76 3.57 0.70 1.78 0.71 1.02 5.21 2.15 5.36 5.29 3.20
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

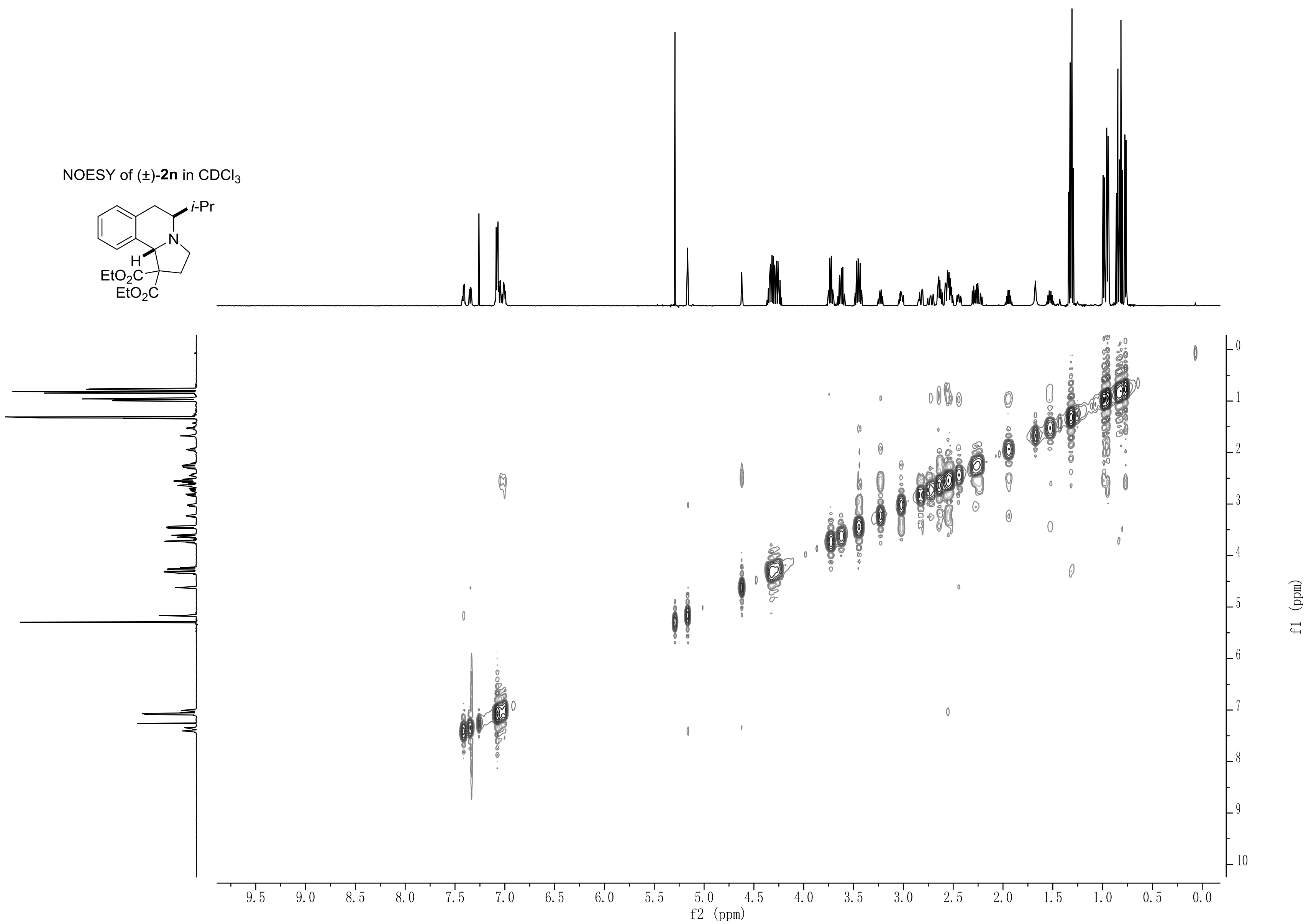


^{13}C NMR of (±)-**2n** in $CDCl_3$

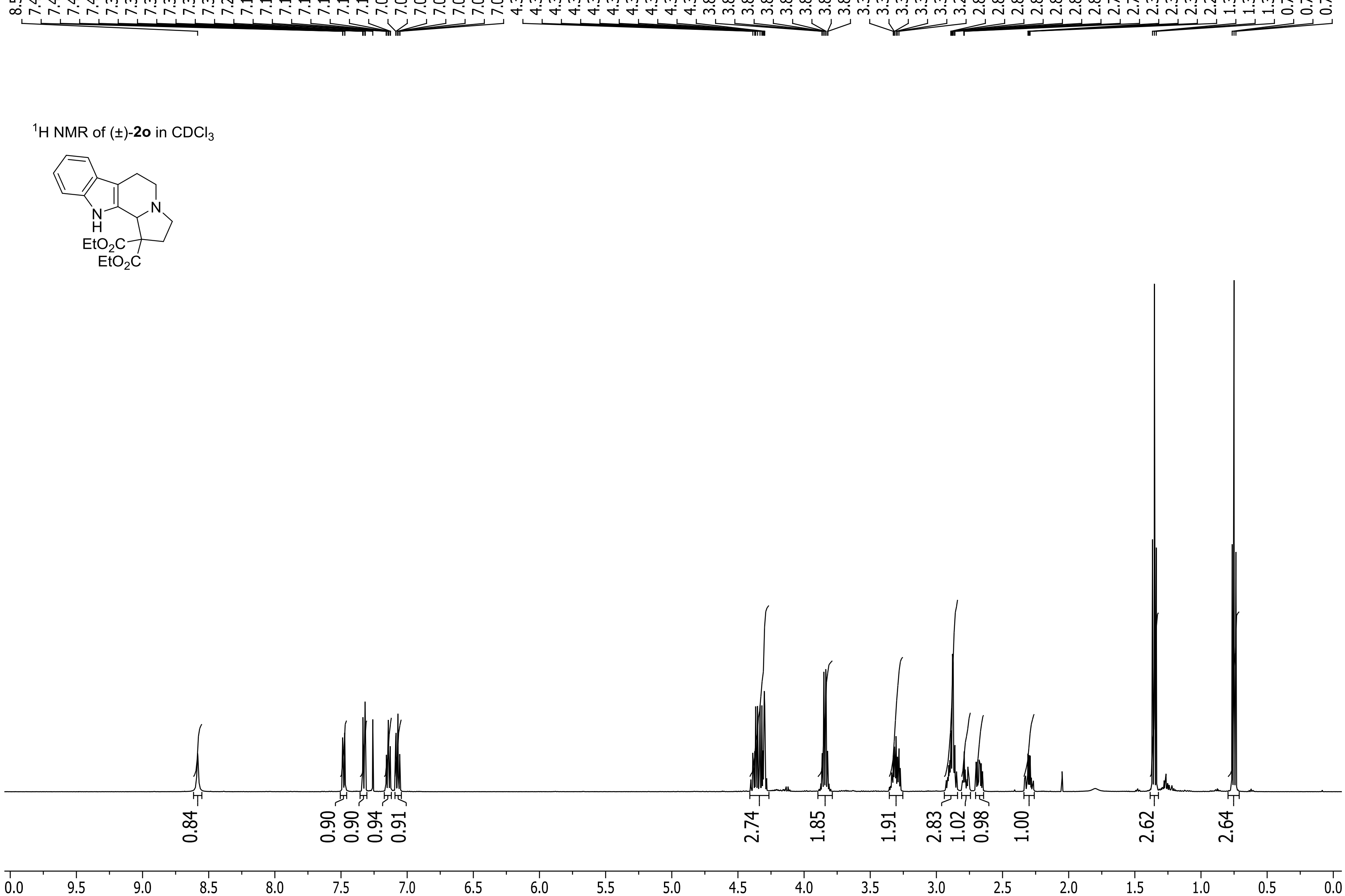
GCOSY of (±)-**2n** in $CDCl_3$



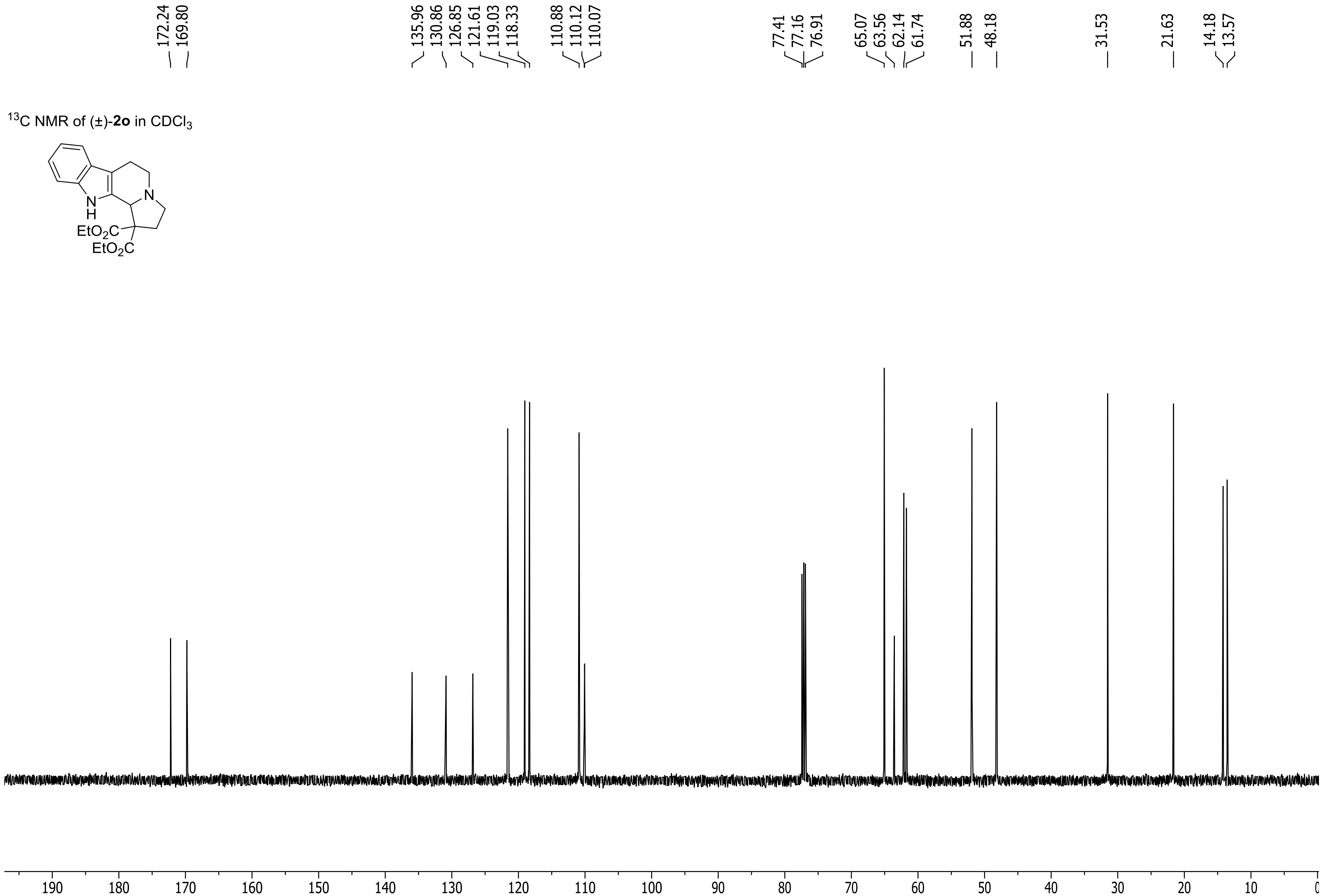
NOESY of (±)-**2n** in $CDCl_3$

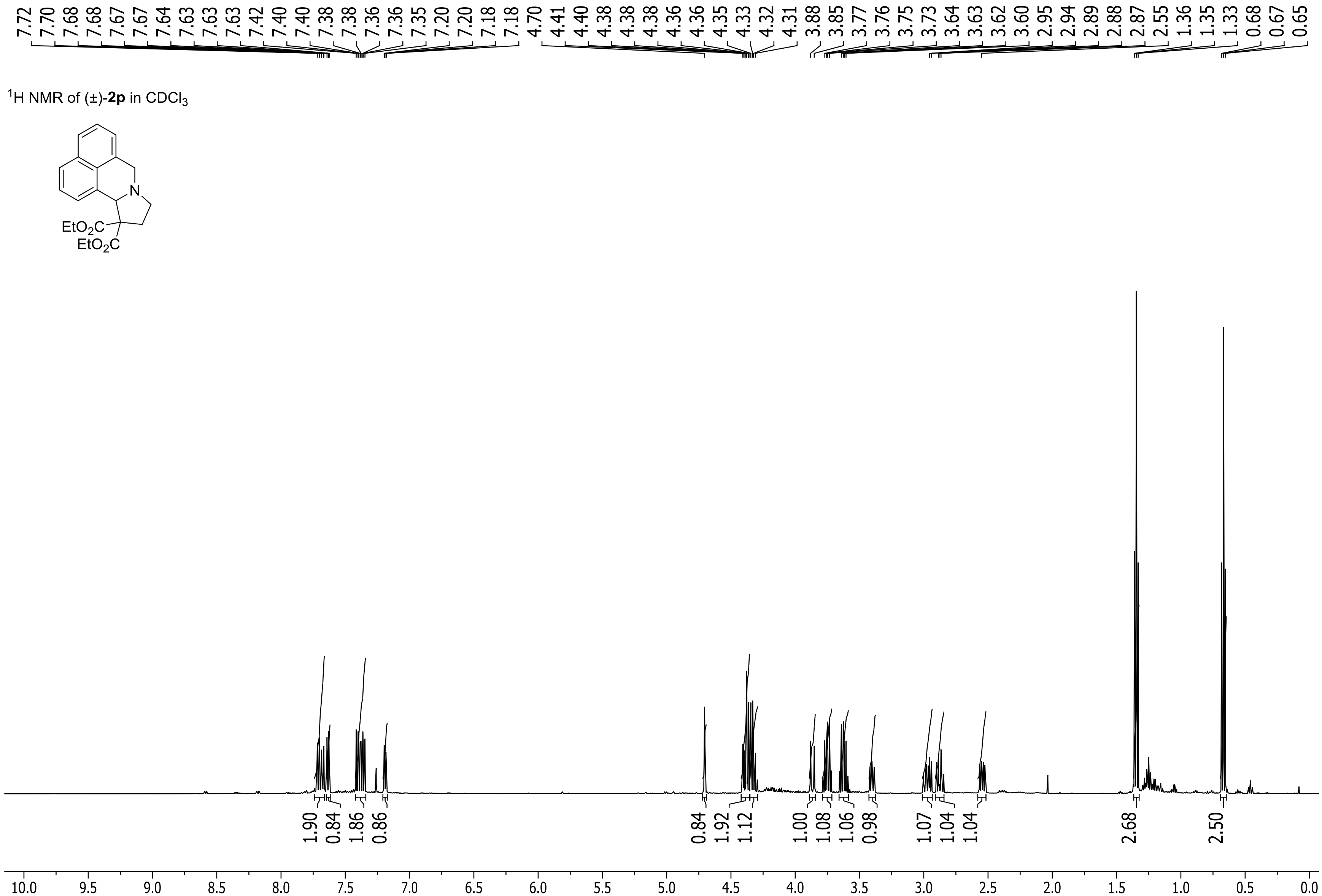


^{1}H NMR of (±)-**2o** in $CDCl_3$

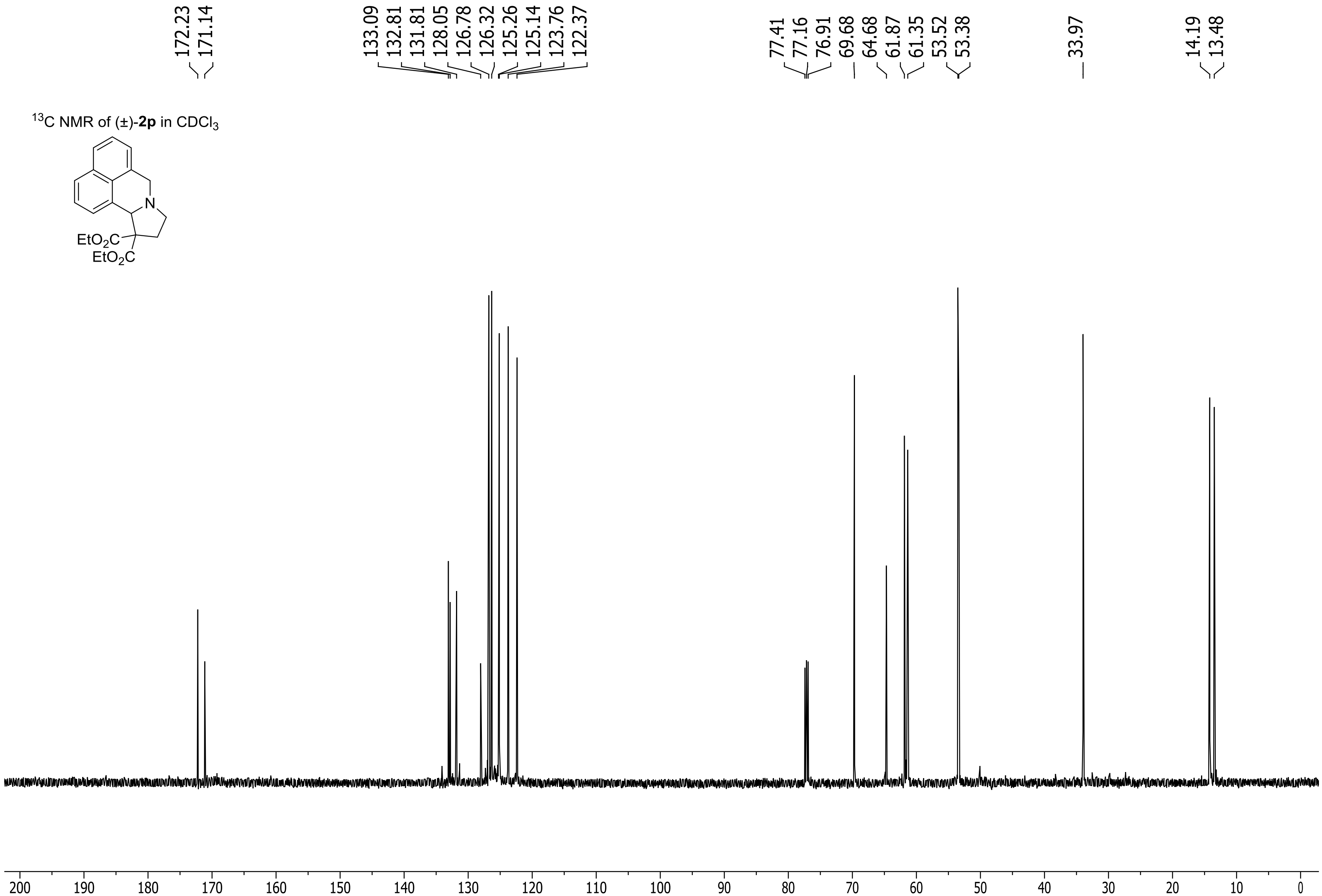


^{13}C NMR of (±)-**2o** in $CDCl_3$

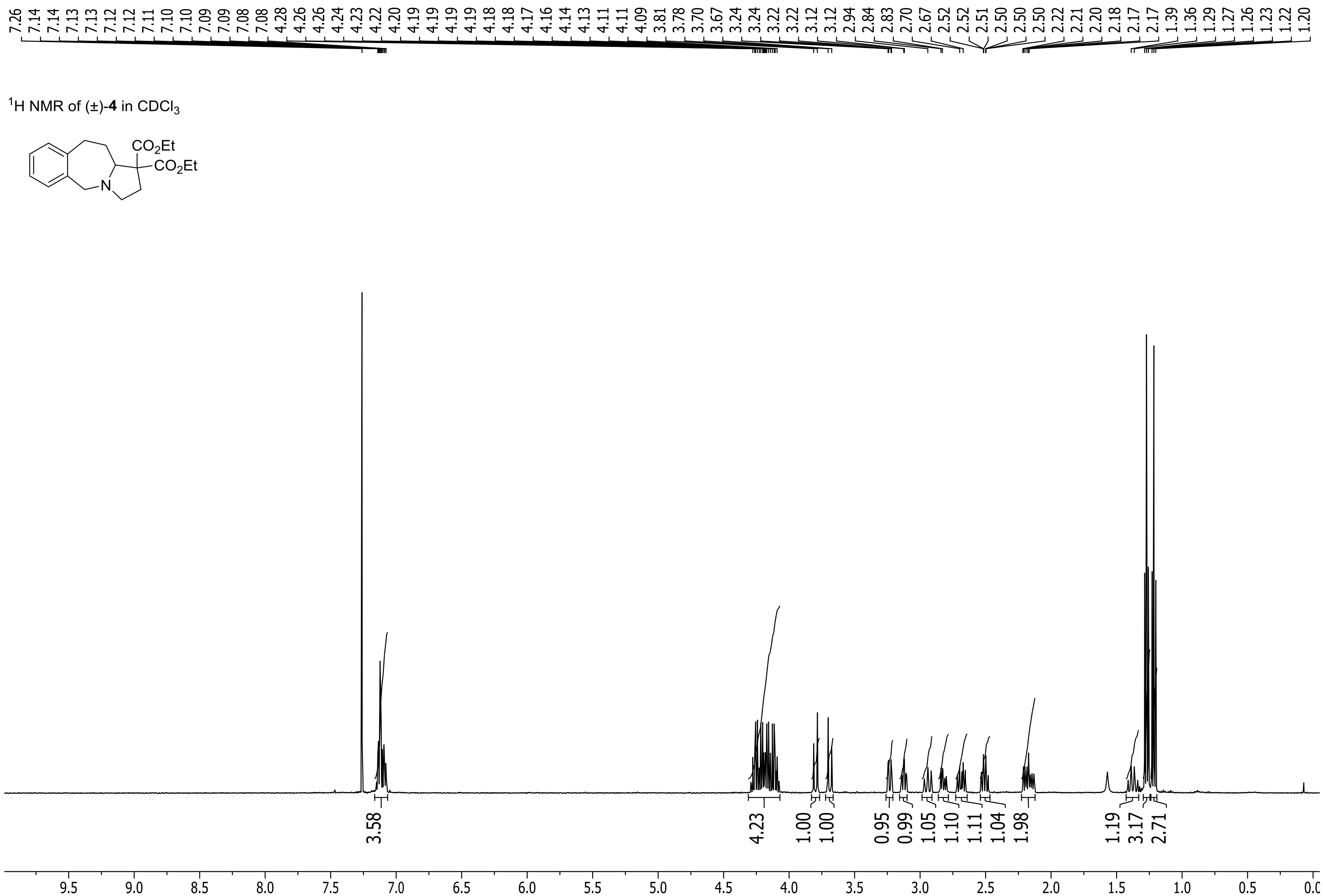


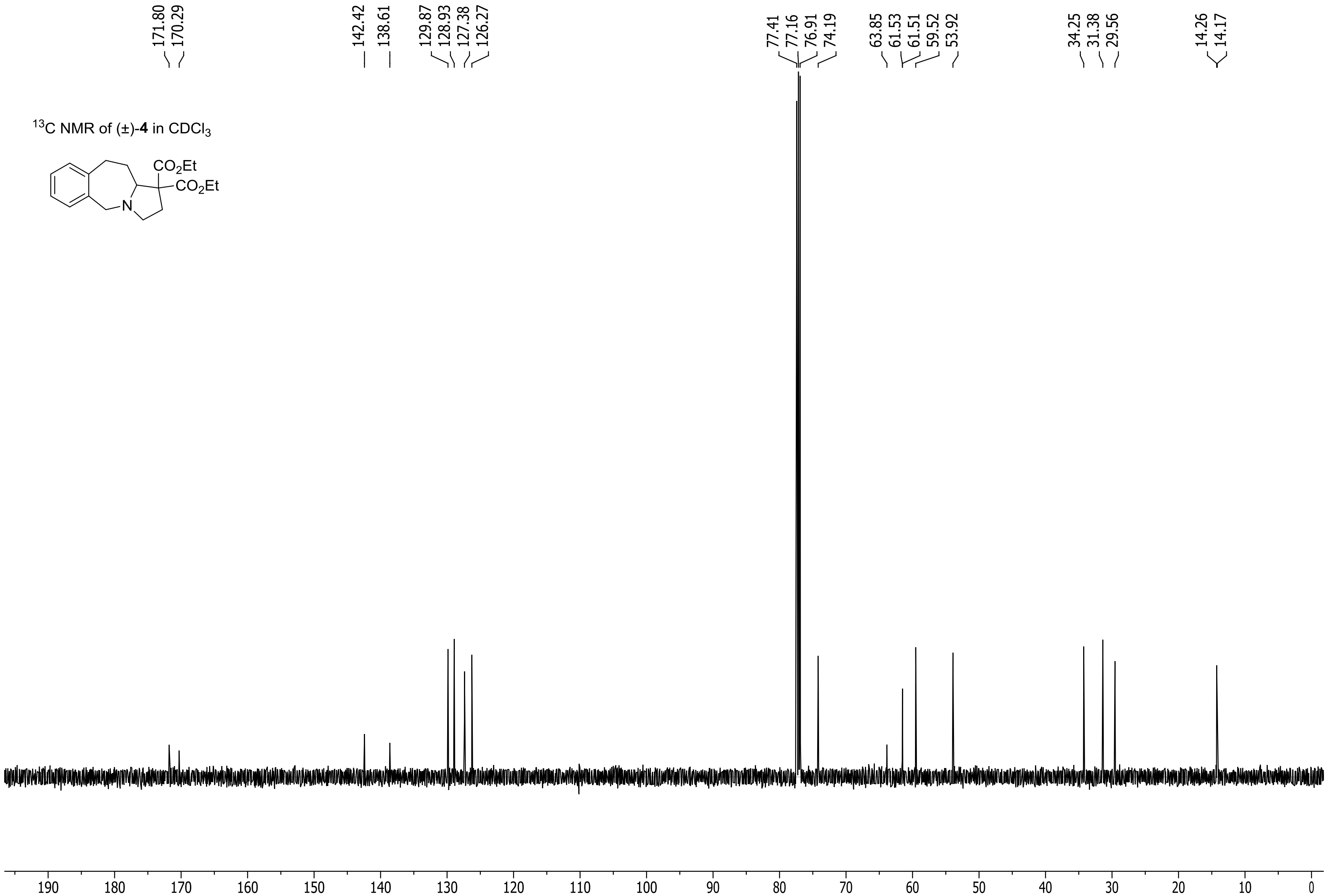


^{1}H NMR of (±)-**2p** in $CDCl_3$

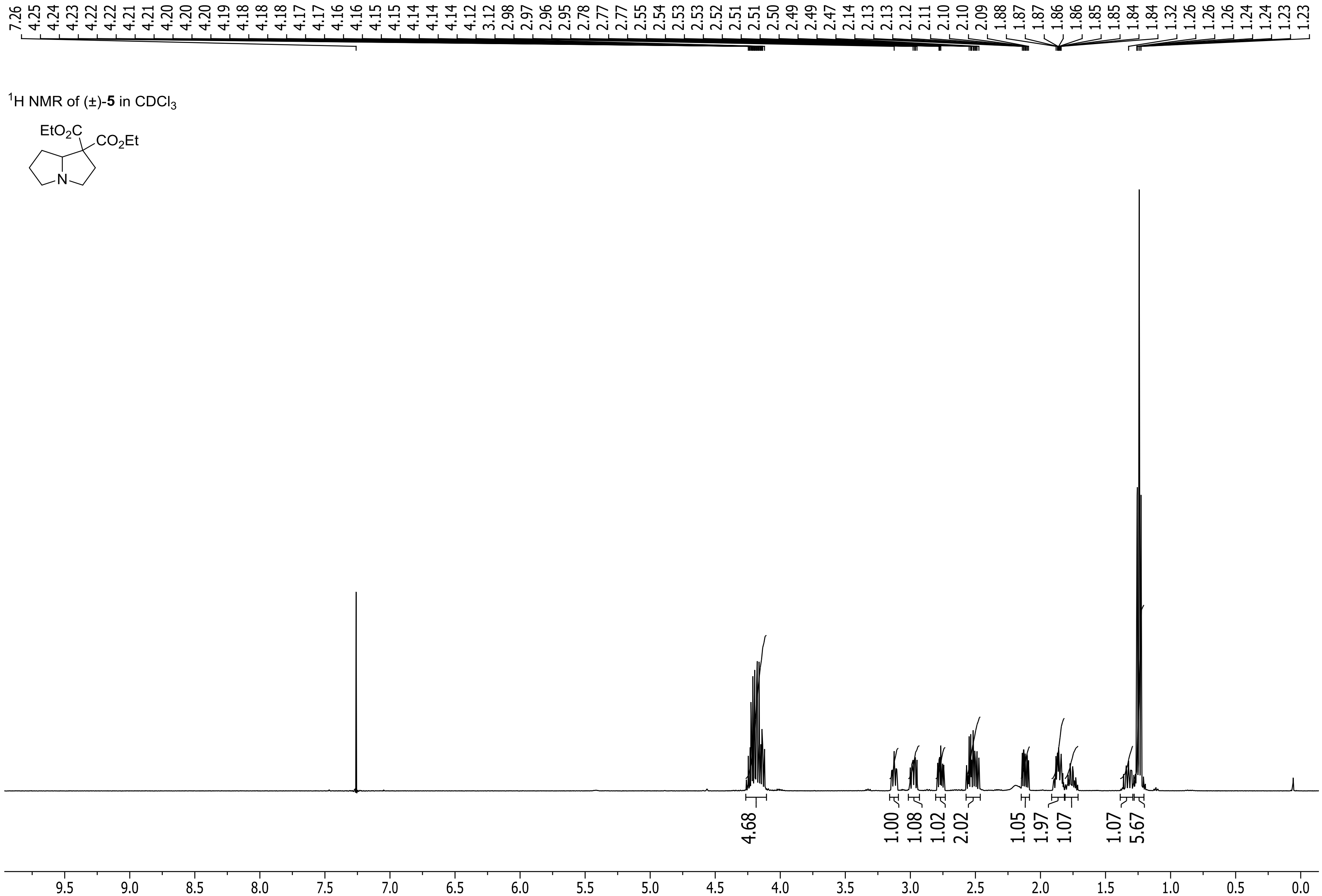

172.23
171.14
133.09
132.81
131.81
128.05
126.78
126.32
125.26
125.14
123.76
122.37
77.41
77.16
76.91
69.68
64.68
61.87
61.35
53.52
53.38
33.97
14.19
13.48
13C NMR of (±)-2p in CDCl3
N
EtO2C
EtO2C
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

^{1}H NMR of (±)-**4** in $CDCl_3$

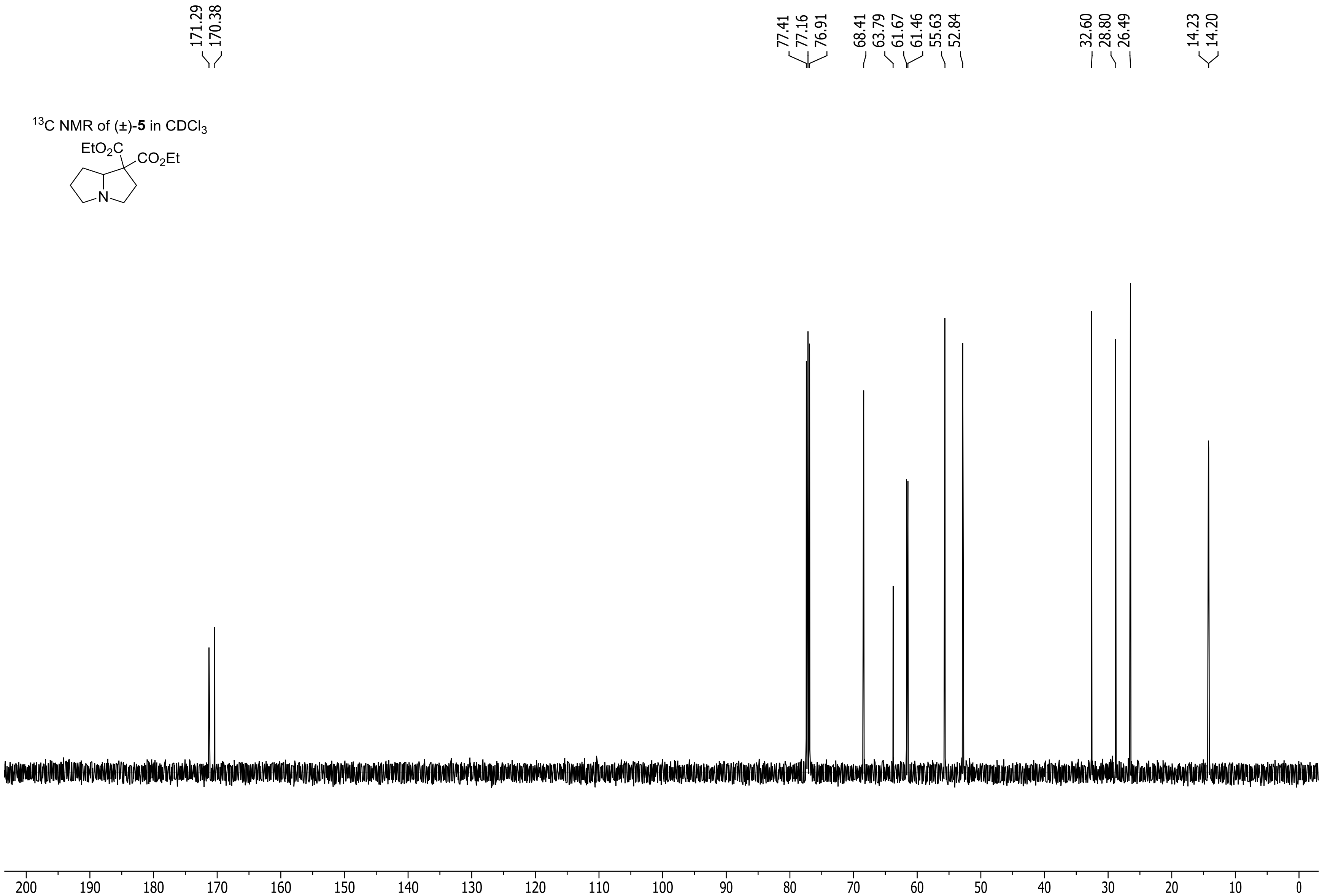




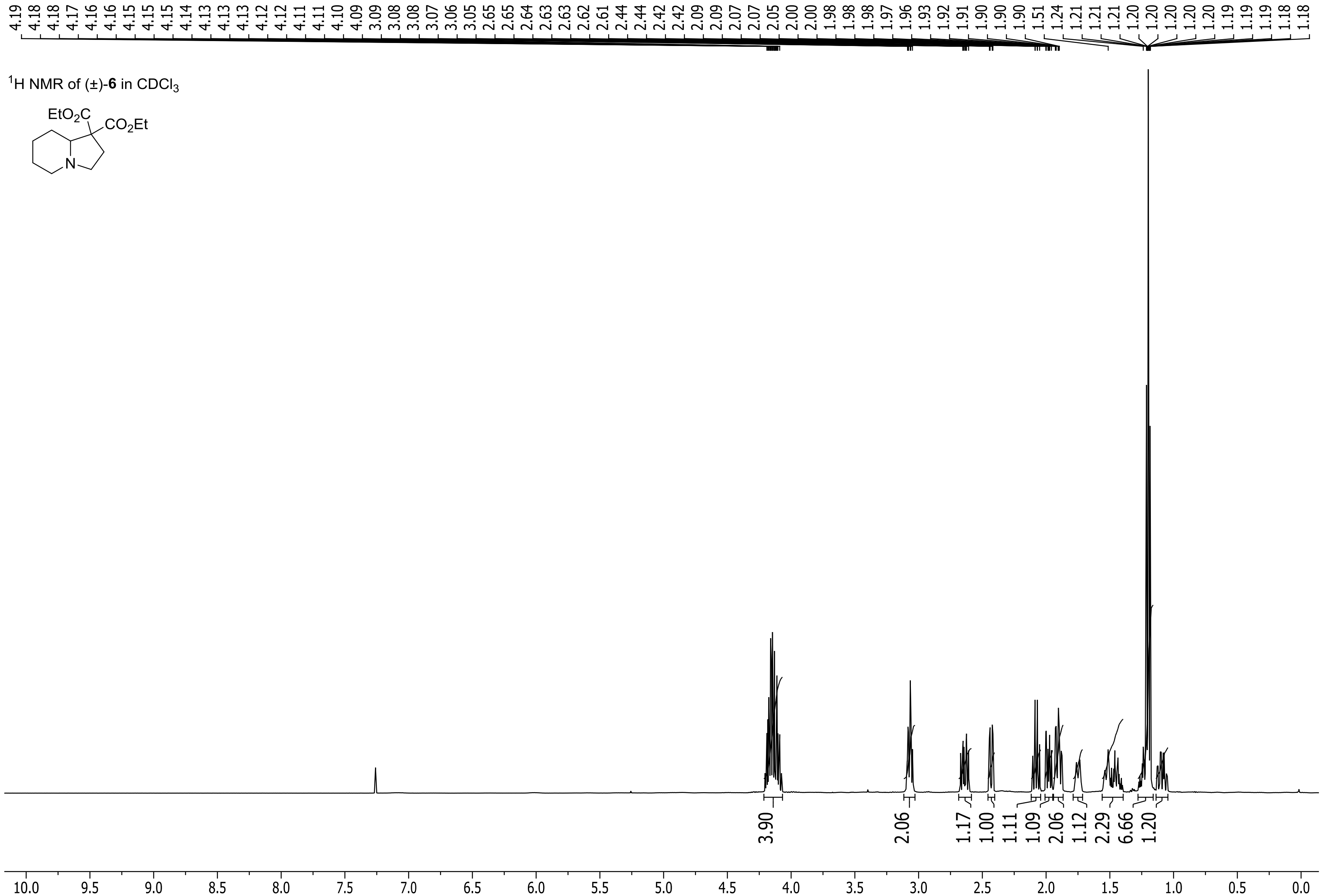
^{13}C NMR of (±)-**4** in $CDCl_3$
CO_2Et
CO_2Et
N
171.80
170.29
142.42
138.61
129.87
128.93
127.38
126.27
77.41
77.16
76.91
74.19
63.85
61.53
61.51
59.52
53.92
34.25
31.38
29.56
14.26
14.17
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

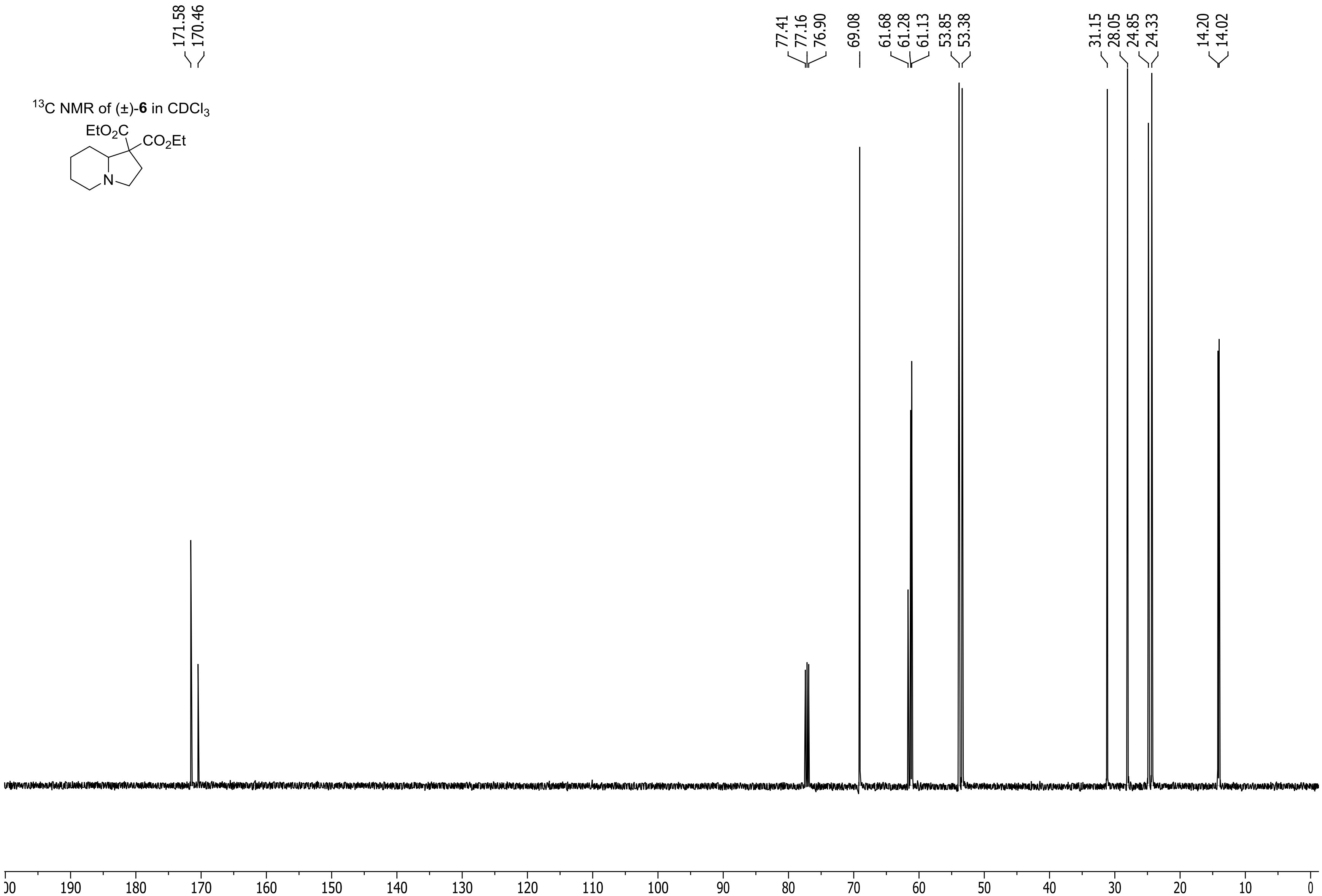


^{1}H NMR of (±)-**5** in $CDCl_3$
EtO_2C
CO_2Et
N
7.26 4.25 4.24 4.23 4.22 4.22 4.21 4.21 4.20 4.20 4.19 4.18 4.18 4.18 4.17 4.17 4.16 4.16 4.15 4.15 4.14 4.14 4.14 4.12 3.12 2.98 2.97 2.96 2.95 2.78 2.77 2.77 2.55 2.54 2.53 2.53 2.52 2.51 2.51 2.50 2.49 2.49 2.47 2.14 2.13 2.13 2.12 2.11 2.10 2.10 2.09 1.88 1.87 1.87 1.86 1.86 1.85 1.85 1.84 1.84 1.32 1.26 1.26 1.26 1.24 1.24 1.23 1.23
4.68 1.00 1.08 1.02 2.02 1.05 1.97 1.07 1.07 5.67
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

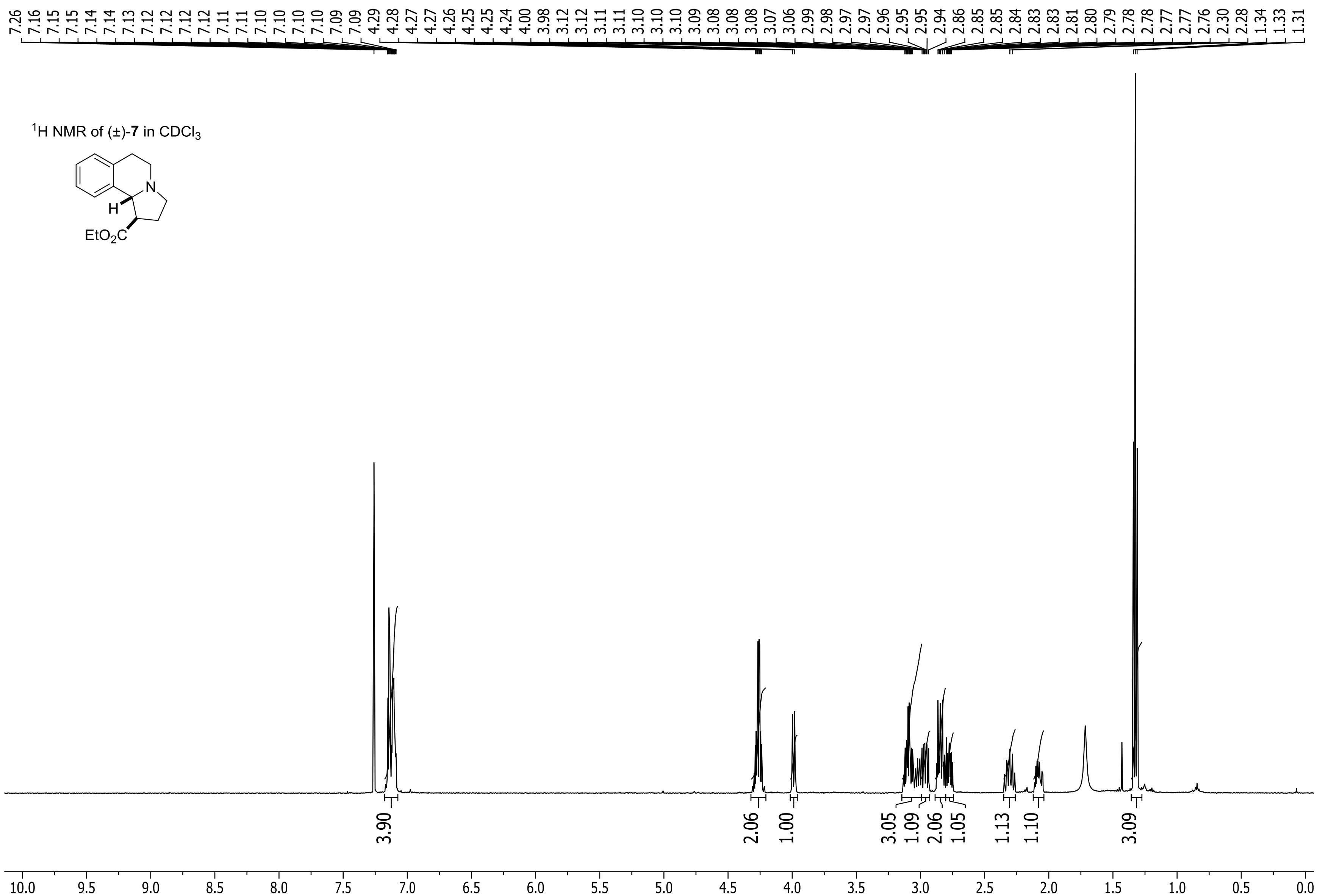


^{13}C NMR of (±)-**5** in $CDCl_3$
EtO_2C
CO_2Et
N
171.29
170.38
77.41
77.16
76.91
68.41
63.79
61.67
61.46
55.63
52.84
32.60
28.80
26.49
14.23
14.20
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


4.19 4.18 4.18 4.17 4.16 4.16 4.15 4.15 4.15 4.14 4.13 4.13 4.13 4.12 4.12 4.11 4.11 4.10 4.09 3.09 3.08 3.08 3.07 3.06 3.05 2.65 2.65 2.64 2.63 2.63 2.62 2.61 2.44 2.44 2.42 2.42 2.09 2.09 2.07 2.07 2.05 2.00 2.00 1.98 1.98 1.98 1.97 1.96 1.93 1.92 1.91 1.90 1.90 1.90 1.51 1.24 1.21 1.21 1.21 1.20 1.20 1.20 1.20 1.20 1.19 1.19 1.19 1.18 1.18
[1]H NMR of (±)-**6** in $CDCl_3$
EtO_2C
CO_2Et
N
3.90 2.06 1.17 1.00 1.11 1.09 2.06 1.12 2.29 6.66 1.20
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

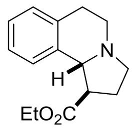


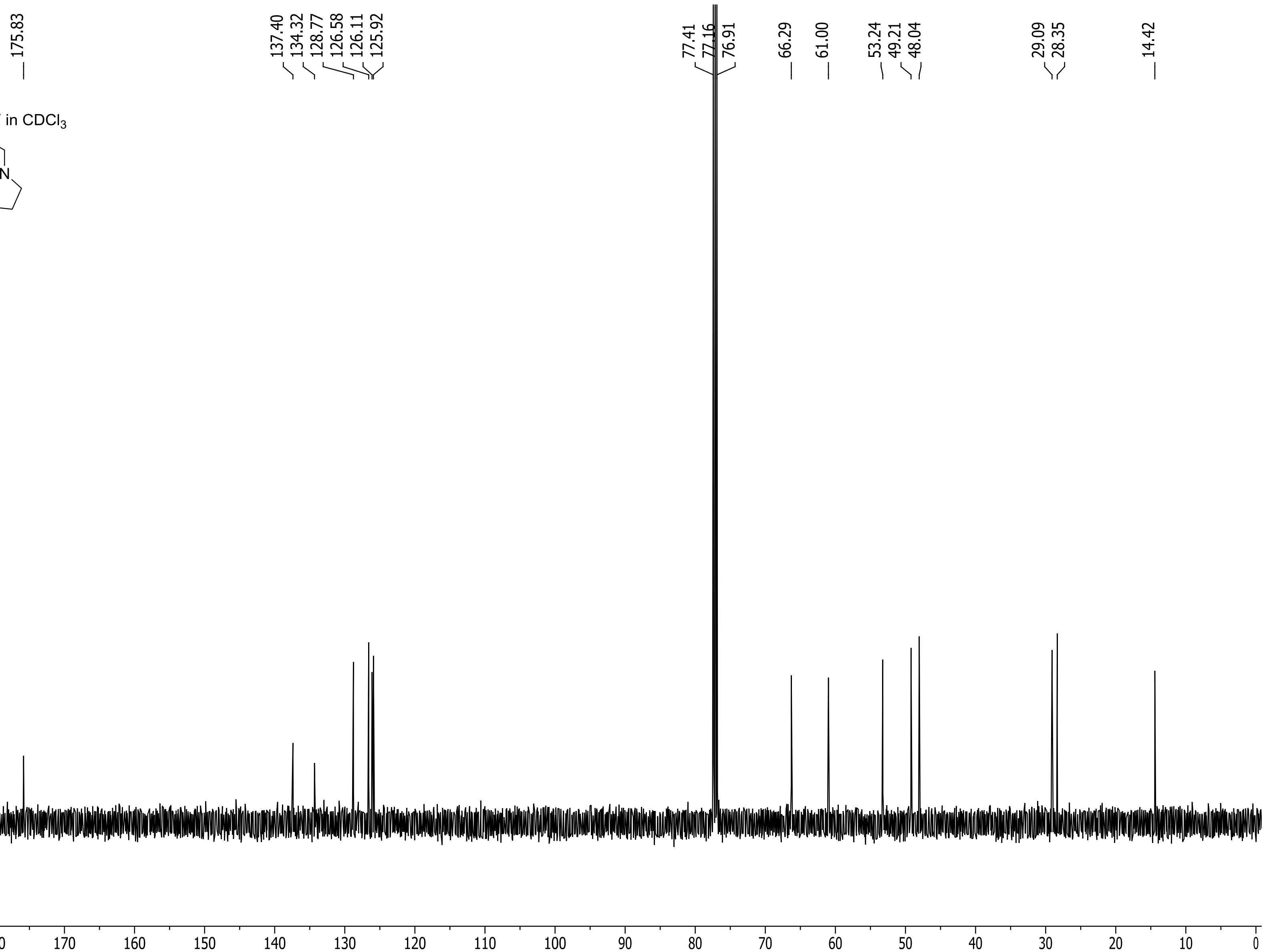
171.58
170.46
77.41
77.16
76.90
69.08
61.68
61.28
61.13
53.85
53.38
31.15
28.05
24.85
24.33
14.20
14.02
^{13}C NMR of (±)-**6** in $CDCl_3$
EtO_2C
CO_2Et
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0



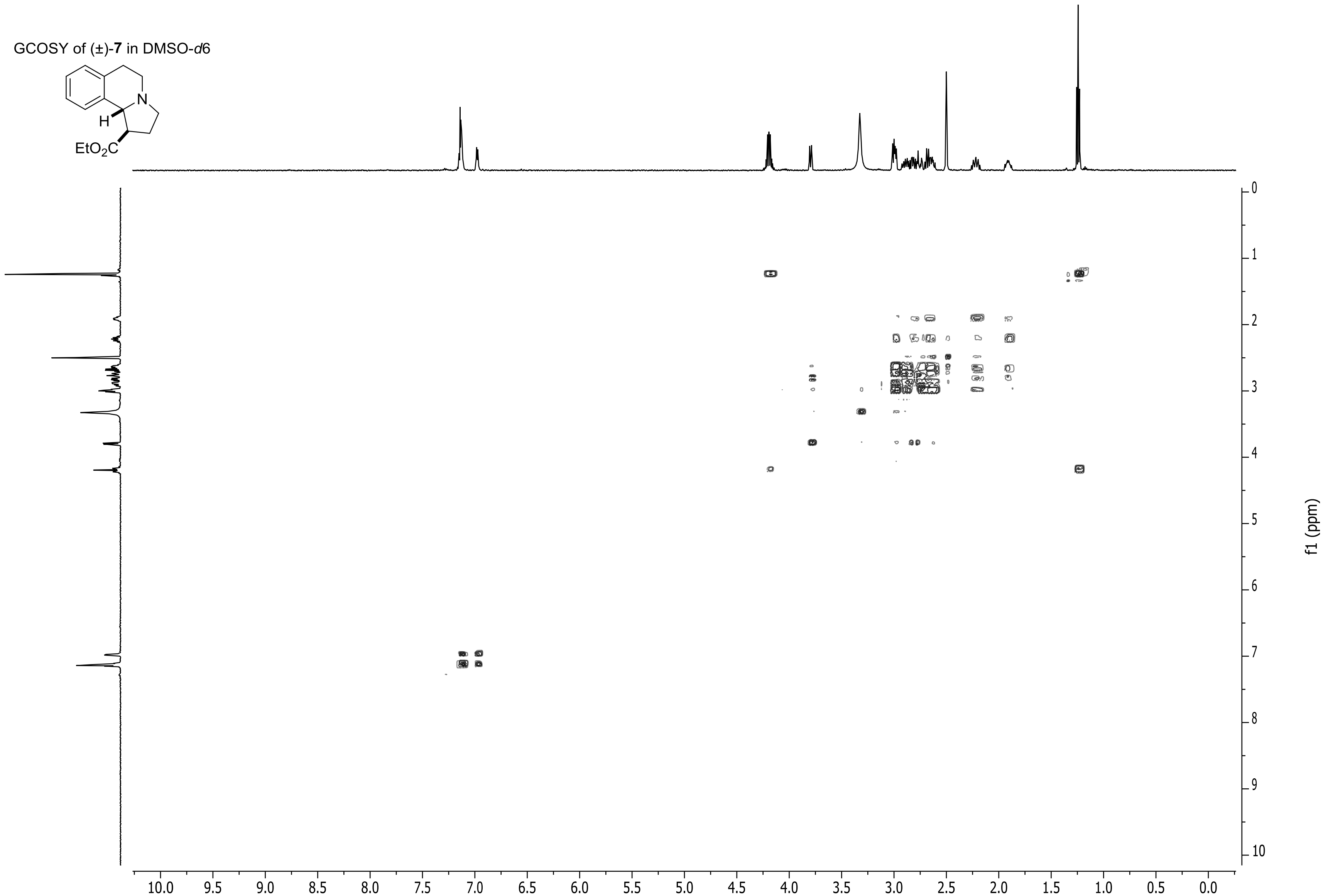
7.26 7.16 7.15 7.15 7.14 7.14 7.13 7.12 7.12 7.12 7.12 7.11 7.11 7.10 7.10 7.10 7.10 7.09 7.09 4.29 4.28 4.27 4.27 4.26 4.25 4.25 4.24 4.00 3.98 3.12 3.12 3.11 3.11 3.10 3.10 3.10 3.09 3.08 3.08 3.08 3.07 3.06 2.99 2.98 2.97 2.97 2.96 2.95 2.95 2.94 2.86 2.85 2.85 2.84 2.83 2.83 2.81 2.80 2.79 2.78 2.78 2.77 2.77 2.76 2.30 2.28 1.34 1.33 1.31
^{1}H NMR of (±)-**7** in $CDCl_3$
N
H
EtO_2C
3.90
2.06
1.00
3.05
1.09
2.06
1.05
1.13
1.10
3.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

^{13}C NMR of (±)-**7** in $CDCl_3$





GCOSY of (±)-**7** in DMSO-*d*6



NOESY of (±)-**7** in DMSO-*d*6