α-C–H/N–H Annulation of Alicyclic Amines via Transient Imines: Preparation of Polycyclic Lactams

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Supporting Information

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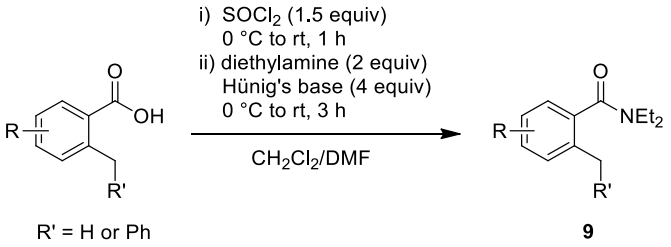
General Information: Starting materials and reagents were purchased from commercial sources and used as received unless stated otherwise. Anhydrous THF, diethyl ether and dichloromethane were dried using a JC Meyer solvent system. All liquid amines and trifluoroacetophenone were distilled prior to use. Benzophenone was recrystallized from hexanes/EtOAc. Lithium chloride (LiCl) solution (0.5 M in anhydrous THF) was purchased from Sigma-Aldrich and used as received. *n*-BuLi solution in hexanes, *s*-BuLi solution in cyclohexane were purchased from commercial sources and freshly titrated using *N*-pivaloyl-*o*-toluidine prior to use.[1] Purification of reaction products was carried out by flash column chromatography using Sorbent Technologies Standard Grade silica gel (60 Å, 230–400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60 F254 plates or SORBTECH 0.25 mm neutral alumina w/UV254 plates. Visualization was accomplished with UV light or Dragendorff-Munier stains, followed by heating. Melting points were recorded on a Thomas Hoover capillary melting point apparatus and are uncorrected. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Varian Unity Inova 500 MHz and chemical shifts are reported in ppm using the solvent as an internal standard ($CDCl_3$ at 7.26 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) spectra were recorded on a Varian Unity Inova 500 MHz and chemical shifts are reported in ppm using the solvent as an internal standard ($CDCl_3$ at 77.0 ppm). High resolution mass spectra (HRMS) were obtained from an Agilent 6230 ESI-TOF instrument. Accurate mass data (ESI) was obtained from Agilent 1260 Infinity II LC/MSD using MassWorks 5.0 from CERNO bioscience.[2] *o*-Toluamides **9d**,[3] **9l**,[4] **9n**,[5] **9y**,[6] 2-methyl-1-naphthoic acid[7], *o*-benzylbenzoic acid[8] were prepared according to literature procedures and their published characterization data matched our own in all respects.

Scheme S1: Synthesis of *N,N*-Diethyl-*o*-Toluamides 9a, 9c, 9e-g, 9k, 9m, 9o, 9p-q and *o*-Benzyl *N,N*-Diethylbenzamide 9z.

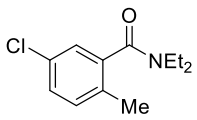


General Procedure A for the Synthesis of *N,N*-Diethyl-*o*-Toluamide from *o*-Toluic acid and *o*-Benzyl *N,N*-Diethylbenzamide from *o*-Benzylbenzoic Acid:

To a stirred solution of *o*-toluic acid (5 mmol, 1 equiv) or *o*-benzylbenzoic acid (5 mmol, 1 equiv) in dry CH_2Cl_2 (14 mL) and DMF (1 mL) was added dropwise thionyl chloride (7.5 mmol, 1.5 equiv, 0.55 mL) at 0 °C under nitrogen. The mixture was then allowed to warm up to room temperature and stir for 1 hour. This mixture was then added dropwise to a stirred solution of diethylamine (10 mmol, 2 equiv, 1.04 mL) and Hünig's base (20 mmol, 4 equiv, 3.49 mL) in dry CH_2Cl_2 (20 mL) cooled at 0 °C. The resulting mixture was then allowed to warm up to room temperature again and stir for 3 hours. The mixture was washed with water (50 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with 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.

New compounds are characterized below.

5-Chloro-*N*,*N*-diethyl-2-methylbenzamide



9f

Following general procedure A, compound **9f** was obtained from 5-chloro-*o*-toluic acid (853 mg) as a brown oil in 95% yield (1.07 g). Hexanes/EtOAc 50/50 v/v was used as the eluent for silica gel chromatography.

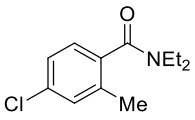
Characterization data:

R_f = 0.26 in hexanes/EtOAc 70:30 v/v.

^{1}H NMR (500 MHz, $CDCl_3$): 7.21 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.14–7.09 (comp, 2H), 3.90–3.20 (m, 2H), 3.20–3.00 (m, 2H), 2.23 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.03 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (125 MHz, $CDCl_3$): 169.2, 138.5, 132.3, 131.6, 131.5, 128.5, 125.4, 42.6, 38.8, 18.2, 13.9, 12.8.

HRMS (ESI-TOF): Calculated for $C_{12}H_{17}ClNO$ $[M + H]^+$: 226.0993, Found: 226.0997.

4-Chloro-*N*,*N*-diethyl-2-methylbenzamide



9g

Following general procedure A, compound **9g** was obtained from 4-chloro-*o*-toluic acid (853 mg) as a brown solid in 95% yield (1.07 g). Hexanes/EtOAc 50/50 v/v was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.25 in hexanes/EtOAc 30:70 v/v.

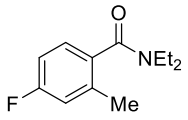
m.p.: 53–55 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.17–7.11 (comp, 2H), 7.05 (d, *J* = 8.1 Hz, 1H), 3.90–3.15 (m, 2H), 3.06 (q, *J* = 6.9 Hz, 2H), 2.22 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): 169.6, 135.9, 135.5, 133.9, 130.1, 126.6, 125.8, 42.5, 38.7, 18.5, 13.9, 12.7.

HRMS (ESI-TOF): Calculated for $C_{12}H_{17}ClNO$ $[M + H]^+$: 226.0993, Found: 226.0999.

***N,N*-Diethyl-4-fluoro-2-methylbenzamide**



9k

Following general procedure A, compound **9k** was obtained from 4-fluoro-*o*-toluic acid (771 mg) as a brown solid in 92% yield (0.96 g). Hexanes/EtOAc 50/50 v/v was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.22 in hexanes/EtOAc 70:30 v/v.

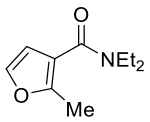
m.p.: 71–72 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.12 (dd, *J* = 8.2, 5.8 Hz, 1H), 6.93–6.85 (comp, 2H), 3.55 (br s, 2H), 3.10 (q, *J* = 7.1 Hz, 2H), 2.27 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.1, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): 170.0, 162.4 (d, J_{C-F} = 247.1 Hz), 136.8 (d, J_{C-F} = 8.0 Hz), 133.2 (d, J_{C-F} = 3.4 Hz), 127.2 (d, J_{C-F} = 8.6 Hz), 117.0 (d, J_{C-F} = 21.4 Hz), 112.7 (d, J_{C-F} = 21.5 Hz), 42.6, 38.8, 18.9 (d, J_{C-F} = 1.6Hz), 14.0, 12.8.

HRMS (ESI-TOF): Calculated for $C_{12}H_{17}FNO$ $[M + H]^+$: 210.1289, Found: 210.1308.

***N*,*N*-Diethyl-2-methylfuran-3-carboxamide**



9q

Following general procedure A, compound **9q** was obtained from 2-methylfuran-3-carboxylic acid (631 mg) as an orange oil in 90% yield (815 mg). Hexanes/EtOAc 50/50 v/v was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.22 in hexanes/EtOAc 70:30 v/v.

^{1}H NMR (500 MHz, $CDCl_3$): 7.15 (d, *J* = 1.9 Hz, 1H), 6.25 (d, *J* = 1.9 Hz, 1H), 3.34 (br s, 4H), 2.27 (s, 3H), 1.12–1.06 (comp, 6H).
^{13}C NMR (125 MHz, $CDCl_3$): 165.6, 152.5, 139.9, 116.3, 109.4, 42.6, 39.1, 14.1, 12.53, 12.52.

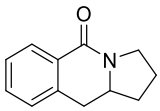
HRMS (ESI-TOF): Calculated for $C_{10}H_{16}NO_2$ $[M + H]^+$: 182.1181, Found: 182.1174.

General Procedure B for the Synthesis of Polycyclic Lactams:

To a stirred solution of diisopropylamine (0.75 mmol, 1.5 equiv, 105 μL) in dry THF (1 mL) was added dropwise *n*-BuLi in hexanes (0.75 mmol, 1.5 equiv) at −78 °C under nitrogen. The mixture was allowed to stir at the same temperature for 20 minutes followed by the addition of LiCl solution in dry THF (0.5 M, 0.75 mmol, 1.5 mL), and the mixture was allowed to stir at −78 °C for another 10 minutes. To this at −78 °C was then added dropwise a solution of the corresponding *N*,*N*-diethyl-*o*-toluamide (0.5 mmol, 1 equiv) in dry THF (1.5 mL) via cannula, and the resulting dark red solution was allowed to stir at −78 °C for 30 minutes for the formation of lithiated *o*-toluamide. To a separate dry round-bottom flask charged with the corresponding cyclic amine (1 mmol, 2 equiv) was added dry ether (1 mL). The solution was cooled to −78 °C and *n*-BuLi in hexanes (1 mmol, 2 equiv) was added dropwise. The mixture was allowed to stir at the same temperature for 5 minutes, and a solution of trifluoroacetophenone (1 mmol, 2 equiv, 140 μL) in dry ether (1.5 mL) was then added dropwise via cannula. The mixture was allowed to stir at −78 °C for another 5 minutes to give the corresponding cyclic imine ether solution. The imine solution was then taken up by syringe and added in one portion to the stirred lithiated *o*-toluamide solution at −78 °C. The resulting mixture was allowed to stir at −78 °C for 2 hours followed by quenching with 1 M HCl aqueous solution (3 mL) at the same temperature. The reaction mixture was then allowed to warm up to room temperature and stir for 30 minutes. The crude mixture was washed with 0.5 M HCl aqueous solution (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography.

Note: for basic products **10p**, **10w** and **10x**, the crude mixture was washed with sat. $NaHCO_3$ aqueous solution instead of 0.5 M HCl aqueous solution.

2,3,10,10a-Tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**10a**

Following general procedure B, compound (±)-**10a** was obtained from *o*-toluamide **9a** (95.7 mg) and pyrrolidine (84 μL) as a white solid in 70% yield (65.2 mg). Hexanes containing EtOAc (20–50%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.27 in hexanes/EtOAc 40:60 v/v.

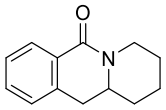
m.p.: 106–107 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.03 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.38 (app td, *J* = 7.4, 1.5 Hz, 1H), 7.33–7.29 (m, 1H), 7.18–7.13 (m, 1H), 3.85–3.72 (comp, 2H), 3.62 (ddd, *J* = 12.3, 9.9, 7.5 Hz, 1H), 3.00 (dd, *J* = 15.3, 4.0 Hz, 1H), 2.84–2.74 (m, 1H), 2.31–2.23 (m, 1H), 2.12–2.01 (m, 1H), 1.92–1.77 (m, 1H), 1.71 (app tdd, J = 12.0, 10.2, 7.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 163.2, 137.4, 131.4, 130.2, 127.5, 127.03, 126.95, 56.8, 44.7, 34.9, 33.6, 23.0

HRMS (ESI-TOF): Calculated for $C_{12}H_{14}NO$ $[M + H]^+$: 188.1070, Found: 188.1073.

1,2,3,4,11,11a-Hexahydro-6*H*-pyrido[1,2-*b*]isoquinolin-6-one



(±)-**10b**

Following general procedure B, compound (±)-**10b** was obtained from *o*-toluamide **9a** (95.6 mg) and piperidine (99 μL) as a white solid in 58% yield (58.2 mg). Hexanes containing EtOAc (10–20%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.70 in hexanes/EtOAc 40:60 v/v.

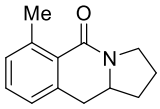
m.p.: 94–96 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.12–8.06 (m, 1H), 7.38 (app td, *J* = 7.5, 1.5 Hz, 1H), 7.30 (app t, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 7.4 Hz, 1H), 4.73–4.15 (m, 1H), 3.59–3.49 (m, 1H), 3.04 (dd, *J* = 16.1, 5.3 Hz, 1H), 2.81 (dd, *J* = 16.1, 9.3 Hz, 1H), 2.67 (app td, *J* = 13.3, 3.2 Hz, 1H), 1.88–1.73 (comp, 3H), 1.58–1.39 (comp, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): 165.0, 136.5, 131.6, 128.5, 128.3, 126.8, 126.7, 55.1, 43.5, 34.6, 33.1, 24.7, 23.6.

HRMS (ESI-TOF): Calculated for $C_{13}H_{16}NO$ $[M + H]^+$: 202.1226, Found: 202.1231.

6-Methyl-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**10c**

Following general procedure B with the modification that the *ortho*-lithiation step was performed at −40 °C for 30 minutes, compound (±)-**10c** was obtained from *o*-toluamide **9c** (102.7 mg) and pyrrolidine (84 μL) as a yellow solid in 52% yield (51.8 mg). Hexanes containing EtOAc (10–40%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.50 in hexanes/EtOAc 40:60 v/v.

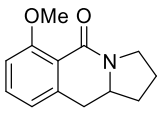
m.p.: 56–59 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.22 (app t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.5 Hz, 1H), 3.81–3.59 (m, 3H), 2.93 (dd, *J* = 15.0, 3.6 Hz, 1H), 2.76 (app t, *J* = 14.1 Hz, 1H), 2.70 (s, 3H), 2.27 (app dtd, *J* = 12.2, 6.2, 2.0 Hz, 1H), 2.06 (app dtt, *J* = 11.5, 6.9, 2.2 Hz, 1H), 1.84 (app tddd, *J* = 12.2, 10.0, 8.6, 6.4 Hz, 1H), 1.69 (app tdd, *J* = 11.9, 9.6, 6.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 164.2, 140.2, 138.7, 130.8, 130.4, 128.5, 125.0, 56.2, 45.0, 36.5, 33.7, 23.3, 21.8.

HRMS (ESI-TOF): Calculated for $C_{13}H_{16}NO$ $[M + H]^+$: 202.1226, Found: 202.1225.

6-Methoxy-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**10d**

Following general procedure B with the modification that the *ortho*-lithiation step was performed at −40 °C for 30 minutes, compound (±)-**10d** was obtained from *o*-toluamide **9d** (110.7 mg) and pyrrolidine (84 μL) as a white solid in 50% yield (54.6 mg). EtOAc containing MeOH (0–5%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.33 in EtOAc/methanol 95:5 v/v.

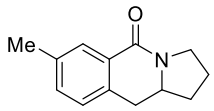
m.p.: 131–133 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.28 (app t, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.72 (d, *J* = 7.4 Hz, 1H), 3.88 (s, 3H), 3.76–3.66 (comp, 2H), 3.60 (ddd, *J* = 12.0, 10.2, 7.1 Hz, 1H), 2.89 (dd, *J* = 15.0. 3.5 Hz, 1H), 2.71 (app t, *J* = 14.1 Hz, 1H), 2.26–2.20 (m, 1H), 2.06–1.97 (m, 1H), 1.85–1.73 (m, 1H), 1.65 (app tdd, *J* = 11.8, 9.6, 6.8 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 162.1, 159.5, 140.5, 131.9, 119.3, 119.1, 110.9, 56.2, 56.0, 44.9, 36.5, 33.5, 23.3.

HRMS (ESI-TOF): Calculated for $C_{13}H_{15}NO_2Na$ $[M + Na]^+$: 240.0995, Found: 240.0991.

7-Methyl-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**10e**

Following general procedure B, compound (±)-**10e** was obtained from *o*-toluamide **9e** (102.7 mg) and pyrrolidine (84 μL) as a white solid in 71% yield (71.2 mg). Hexanes containing EtOAc (20–50%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.35 in hexanes/EtOAc 40:60 v/v.

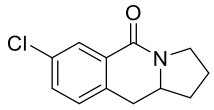
m.p.: 129–130 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.86–7.83 (m, 1H), 7.20–7.16 (m, 1H), 7.04 (d, *J* = 7.6, 1H), 3.81–3.71 (comp, 2H), 3.61 (ddd, *J* = 12.2, 9.9, 7.5 Hz, 1H), 2.95 (dd, *J* = 15.1, 4.0 Hz, 1H), 2.74 (t, *J* = 14.2 Hz, 1H), 2.35 (s, 3H), 2.29–2.22 (m, 1H), 2.06 (app dtt, *J* = 12.6, 7.2, 1.9 Hz, 1H), 1.83 (app tddd, *J* = 12.3, 9.8, 9.0, 6.5 Hz, 1H), 1.70 (app tdd, *J* = 11.9, 10.1, 7.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 163.4, 136.6, 134.4, 132.1, 129.9, 127.9, 126.9, 57.0, 44.7, 34.6, 33.5, 23.0, 21.0.

HRMS (ESI-TOF): Calculated for $C_{13}H_{16}NO$ $[M + H]^+$: 202.1226, Found: 202.1222.

7-Chloro-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**10f**

Following general procedure B, compound (±)-**10f** was obtained from *o*-toluamide **9f** (112.9 mg) and pyrrolidine (84 μL) as a white solid in 67% yield (74.2 mg). Hexanes containing EtOAc (20–50%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.35 in hexanes/EtOAc 40:60 v/v.

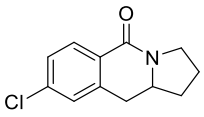
m.p.: 109–112 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.96 (d, *J* = 2.3 Hz, 1H), 7.30 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 1H), 3.80–3.68 (comp, 2H), 3.57 (ddd, *J* = 12.3, 9.9, 7.6 Hz, 1H), 2.97 (dd, *J* = 15.4, 4.0 Hz, 1H), 2.76–2.67 (m, 1H), 2.29–2.23 (m, 1H), 2.05 (app dtt, *J* = 14.5, 7.2, 2.0 Hz, 1H), 1.88–1.77 (m, 1H), 1.68 (app tdd, *J* = 12.0, 10.2, 7.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 161.8, 135.7, 132.9, 131.7, 131.2, 128.5, 127.4, 56.8, 44.7, 34.2, 33.4, 22.9.

HRMS (ESI-TOF): Calculated for $C_{12}H_{13}ClNO$ $[M + H]^+$: 222.0680, Found: 222.0686.

8-Chloro-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**10g**

To a stirred solution of diisopropylamine (3 mmol, 1.5 equiv, 0.42 mL) in dry THF (2 mL) was added dropwise *n*-BuLi in hexanes (3 mmol, 1.5 equiv) at −78 °C under nitrogen. The mixture was allowed to stir at the same temperature for 20 minutes, followed by the addition of LiCl solution in dry THF (0.5 M, 3 mmol, 6 mL), and the mixture was allowed to stir at −78 °C for another 10 minutes. To this at −78 °C was then added dropwise a solution of 4-chloro-*N*,*N*-diethyl-2-methylbenzamide **9g** (2 mmol, 1 equiv, 451.4 mg) in dry THF (6 mL) via cannula, and the resulting dark red solution was allowed to stir at −78 °C for 30 minutes. To a separate dry round-bottom flask charged with pyrrolidine (4 mmol, 2 equiv, 0.33 mL) was added dry ether (2 mL). The solution was cooled to −78 °C and *n*-BuLi in hexanes (4 mmol, 2 equiv) was added dropwise. The mixture was allowed to stir at the same temperature for 5 minutes, and a solution of trifluoroacetophenone (4 mmol, 2 equiv, 0.56 mL) in dry ether (3 mL) was then added dropwise via cannula. The mixture was allowed to stir at −78 °C for another 5 minutes to give the corresponding cyclic imine ether solution. The imine solution was then taken up by syringe and added in one portion to the stirred lithiated *o*-toluamide solution at −78 °C. The resulting mixture was allowed to stir at −78 °C for 2 hours followed by quenching with 1 M aqueous HCl (10 mL) at the same temperature. The reaction mixture was then allowed to warm up to room temperature and stirred for 30 minutes. The crude mixture was washed with 0.5 M aqueous HCl (60 mL) and extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography. Compound (±)-**10g** was obtained as a white solid in 72% yield (317.7 mg). Hexanes containing EtOAc (20–50%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.33 in hexanes/EtOAc 40:60 v/v.

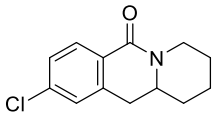
m.p.: 161–162 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.97 (d, *J* = 8.3 Hz, 1H), 7.31–7.25 (m, 1H), 7.16 (s, 1H), 3.87–3.71 (comp, 2H), 3.66–3.57 (m, 1H), 2.98 (dd, *J* = 15.4, 3.9 Hz, 1H), 2.78 (t, *J* = 14.3 Hz, 1H), 2.33–2.25 (m, 1H), 2.13–2.04 (m, 1H), 1.92–1.79 (m, 1H), 1.77–1.68 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 162.3, 139.2, 137.3, 129.0, 128.7, 127.2, 127.1, 56.7, 44.7, 34.7, 33.5, 22.9.

HRMS (ESI-TOF): Calculated for $C_{12}H_{13}ClNO$ $[M + H]^+$: 222.0680, Found: 222.0682.

9-Chloro-1,2,3,4,11,11a-hexahydro-6*H*-pyrido[1,2-*b*]isoquinolin-6-one



(±)-**10h**

Following general procedure B, compound (±)-**10h** was obtained from *o*-toluamide **9g** (112.9 mg) and piperidine (99 μL) as a white solid in 62% yield (73.2 mg). Hexanes containing EtOAc (10−30%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.50 in hexanes/EtOAc 60:40 v/v.

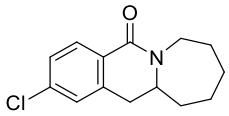
m.p.: 148–149 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.00 (d, *J* = 8.4 Hz, 1H), 7.27–7.21 (m, 1H), 7.09 (s, 1H), 4.68–4.61 (m, 1H), 3.56–3.46 (m, 1H), 3.00 (dd, *J* = 16.2, 5.3 Hz, 1H), 2.76 (dd, *J* = 16.2, 9.2 Hz, 1H), 2.65 (app td, *J* = 12.9, 3.2 Hz, 1H), 1.86–1.72 (comp, 3H), 1.55–1.37 (comp, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): 164.1, 138.2, 137.6, 130.0, 127.04, 126.96, 126.7, 54.9, 43.5, 34.2, 33.0, 24.6, 23.5.

HRMS (ESI-TOF): Calculated for $C_{13}H_{15}ClNO$ $[M + H]^+$: 236.0837, Found: 236.0853.

2-Chloro-8,9,10,11,11a,12-hexahydroazepino[1,2-*b*]isoquinolin-5(7*H*)-one



(±)-**10i**

Following general procedure B, compound (±)-**10i** was obtained from *o*-toluamide **9g** (112.9 mg) and azepane (113 μL) as a white solid in 68% yield (85.3 mg). Hexanes containing EtOAc (10–30%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.4 in hexanes/EtOAc 60:40 v/v.

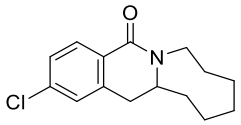
m.p.: 84–86 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.95 (d, *J* = 8.3 Hz, 1H), 7.24 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.11 (s, 1H), 4.47 (app dt, *J* = 13.8, 55.3 Hz, 1H), 3.73 (app dq, *J* = 9.8, 4.9 Hz, 1H), 3.17 (dd, *J* = 15.8, 5.6 Hz, 1H), 2.93 (ddd, *J* = 14.1, 9.4, 4.8 Hz, 1H), 2.71 (dd, *J* = 15.9, 4.3 Hz, 1H), 1.96–1.85 (m, 1H), 1.71–1.43 (comp, 7H).

^{13}C NMR (125 MHz, $CDCl_3$): 162.8, 138.4, 137.4, 129.6, 127.5, 127.4, 127.0, 57.0, 46.0, 33.8, 33.5, 27.8, 26.2, 25.9.

HRMS (ESI-TOF): Calculated for $C_{14}H_{17}ClNO$ $[M + H]^+$: 250.0993, Found: 250.0999.

2-Chloro-7,8,9,10,11,12,12a,13-octahydro-5*H*-azocino[1,2-*b*]isoquinolin-5-one



(±)-**10j**

Following general procedure B, compound (±)-**10j** was obtained from *o*-toluamide **9g** (112.9 mg) and azocane (126 μL) as a white solid in 70% yield (92.5 mg). Hexanes containing EtOAc (10–30%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.3 in hexanes/EtOAc 70:30 v/v.

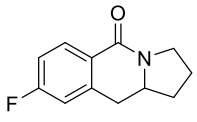
m.p.: 120–122 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.92 (d, *J* = 8.3 Hz, 1H), 7.27–7.21 (m, 1H), 7.10 (s, 1H), 4.42 (ddd, *J* = 13.9, 6.2, 3.9 Hz, 1H), 3.74–3.67 (m, 1H), 3.20 (dd, *J* = 15.7, 5.4 Hz, 1H), 2.92 (ddd, *J* = 13.5, 9.3, 3.3 Hz, 1H), 2.63 (dd, *J* = 15.7, 3.4 Hz, 1H), 1.94–1.83 (m, 1H), 1.76–1.35 (comp, 9H).

^{13}C NMR (125 MHz, $CDCl_3$): 163.0, 138.6, 137.3, 129.5, 128.1, 127.4, 127.0, 56.8, 48.0, 34.6, 32.9, 26.5, 26.1, 25.6, 24.4.

HRMS (ESI-TOF): Calculated for $C_{15}H_{19}ClNO$ $[M + H]^+$: 264.1150, Found: 264.1153.

8-Fluoro-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**10k**

Following general procedure B, compound (±)-**10k** was obtained from *o*-toluamide **9k** (104.6 mg) and pyrrolidine (84 μL) as a white solid in 78% yield (80.2 mg). Hexanes containing EtOAc (30–60%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.25 in hexanes/EtOAc 40:60 v/v.

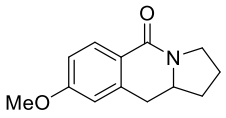
m.p.: 128–129 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.03 (dd, *J* = 8.6, 5.9 Hz, 1H), 6.98 (app tdd, *J* = 8.5, 2.6, 1.0 Hz, 1H), 6.87–6.83 (m, 1H), 3.86–3.78 (m, 1H), 3.74 (ddd, *J* = 11.7, 9.1, 2.3 Hz, 1H), 3.60 (ddd, *J* = 12.2, 9.9, 7.5 Hz, 1H), 2.98 (dd, *J* = 15.4, 4.0 Hz, 1H), 2.83–2.75 (m, 1H), 2.31–2.24 (m, 1H), 2.08 (app dtt, *J* = 12.6, 7.3, 2.0 Hz, 1H), 1.91–1.79 (m, 1H), 1.71 (app tdd, *J* = 12.0, 10.2, 7.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 165.5, 162.9 (d, $J_{C\text{-}F}$ = 139.2 Hz), 140.2 (d, $J_{C\text{-}F}$ = 8.8 Hz), 130.1 (d, $J_{C\text{-}F}$ = 9.4 Hz), 126.5 (d, $J_{C\text{-}F}$ = 2.7 Hz), 114.1 (d, $J_{C\text{-}F}$ = 12.2 Hz), 113.9 (d, $J_{C\text{-}F}$ = 12.7 Hz), 56.8, 44.7, 34.9 (d, $J_{C\text{-}F}$ = 1.5 Hz), 33.5, 23.0.

HRMS (ESI-TOF): Calculated for $C_{12}H_{13}FNO$ $[M + H]^+$: 206.0976, Found: 206.0983.

8-Methoxy-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**10l**

Following general procedure B, compound (±)-**10l** was obtained from *o*-toluamide **9l** (110.7 mg) and pyrrolidine (84 μL) as a white solid in 67% yield (73.2 mg). Hexanes/EtOAc 40/60 to 20/80 v/v was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.25 in hexanes/EtOAc 20:80 v/v.

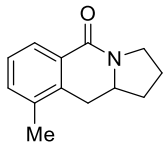
m.p.: 89–91 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.99 (d, *J* = 8.6 Hz, 1H), 6.82 (app ddd, *J* = 8.7, 2.5, 0.9 Hz, 1H), 6.67–6.65 (m, 1H), 3.83 (s, 3H), 3.82–3.71 (comp, 2H), 3.60 (ddd, *J* = 12.1, 9.8, 7.7 Hz, 1H), 2.95 (dd, *J* = 15.2, 4.0 Hz, 1H), 2.82–2.75 (m, 1H), 2.30–2.23 (m, 1H), 2.07 (app dtt, *J* = 14.5, 7.3, 2.0 Hz, 1H), 1.85 (app tddd, *J* = 12.3, 9.7, 9.0, 6.6 Hz, 1H), 1.71 (app tdd, *J* = 11.9, 10.2, 7.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 163.3, 162.1, 139.6, 129.5, 123.1, 112.5, 112.0, 56.9, 55.3, 44.6, 35.3, 33.6, 23.1.

HRMS (ESI-TOF): Calculated for $C_{13}H_{15}NONa$ $[M + Na]^+$: 240.0995, Found: 240.0989.

9-Methyl-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**10m**

Following general procedure B, compound (±)-**10m** was obtained from *o*-toluamide **9m** (102.6 mg) and pyrrolidine (84 μL) as a white solid in 82% yield (82.0 mg). Hexanes containing EtOAc (30–60%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.27 in hexanes/EtOAc 40:60 v/v.

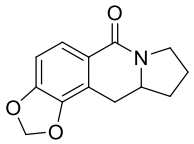
m.p.: 94–96 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.88 (d, *J* = 7.5 Hz, 1H), 7.22 (d, *J* = 7.0 Hz, 1H), 7.17 (app t, *J* = 7.6 Hz, 1H), 3.75–3.66 (comp, 2H), 3.58 (ddd, *J* = 12.2, 9.7, 7.5 Hz, 1H), 3.09 (dd, *J* = 15.6, 4.1 Hz, 1H), 2.52–2.45 (m, 1H), 2.31–2.21 (comp, 4H), 2.03 (app dtt, *J* = 11.2, 7.1, 2.0 Hz, 1H), 1.81 (app ttd, *J* = 12.1, 9.3, 6.3 Hz, 1H), 1.70 (app tdd, *J* = 11.9, 10.1, 6.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 163.3, 135.8, 134.4, 132.9, 130.0, 126.2, 125.3, 56.1, 44.6, 33.6, 31.3, 22.8, 19.1.

HRMS (ESI-TOF): Calculated for $C_{13}H_{15}NONa$ $[M + Na]^+$: 224.1046, Found: 224.1034.

9,10,10a,11-Tetrahydro-[1,3]dioxolo[4,5-*f*]pyrrolo[1,2-*b*]isoquinolin-6(8*H*)-one



(±)-**10n**

To a stirred solution of *N,N,N',N'*-tetramethylethylenediamine (0.75 mmol, 1.5 equiv, 112 μL) in dry THF (1 mL) was added dropwise *s*-BuLi in cyclohexane (0.75 mmol, 1.5 equiv) at −78 °C under nitrogen. The resulting mixture was allowed to stir at the same temperature for 10 minutes. To this at −78 °C was then added dropwise a solution of *o*-toluamide **9n** (0.5 mmol, 1 equiv, 117.7 mg) in dry THF (1.5 mL) via cannula, and the resulting dark red solution was allowed to stir at −78 °C for 30 minutes for the formation of lithiated *o*-toluamide. The following procedures are the same as general procedure B. Compound (±)-**10n** was obtained as a white solid in 43% yield (50.2 mg). Hexanes containing EtOAc (30–60%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.30 in hexanes/EtOAc 40:60 v/v.

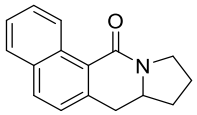
m.p.: 161–163 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.63 (d, *J* = 8.1 Hz, 1H), 6.75 (dd, *J* = 8.1, 0.9 Hz, 1H), 6.01 (d, *J* = 1.3 Hz, 1H), 6.00 (d, *J* = 1.4 Hz, 1H), 3.80–3.71 (comp, 2H), 3.59 (ddd, *J* = 12.2, 9.8, 7.6 Hz, 1H), 3.13 (dd, *J* = 15.5, 4.0 Hz, 1H), 2.59–2.46 (m, 1H), 2.31–2.25 (m, 1H), 2.10–2.03 (m, 1H), 1.90–1.79 (m, 1H), 1.73 (app tdd, *J* = 11.9, 10.1, 6.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 162.9, 149.9, 143.7, 124.6, 122.6, 118.5, 106.7, 101.6, 56.5, 44.8, 33.6, 28.2, 23.0.

HRMS (ESI-TOF): Calculated for $C_{13}H_{13}NO_3Na$ $[M + Na]^+$: 254.0788, Found: 254.0764.

7a,8,9,10-Tetrahydrobenzo[h]pyrrolo[1,2-*b*]isoquinolin-12(7*H*)-one



(±)-**10o**

Following general procedure B, compound (±)-**10o** was obtained from 2-methyl-1-naphthamide **9o** (120.7 mg) and pyrrolidine (84 μL) as a white solid in 36% yield (42.2 mg). Hexanes containing EtOAc (10–30%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.45 in hexanes/EtOAc 50:50 v/v.

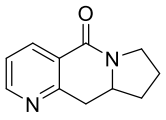
m.p.: 141–142 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 9.46–9.43 (m, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.84–7.81 (m, 1H), 7.60 (ddd, *J* = 8.6, 6.8, 1.4 Hz, 1H), 7.49 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 1H), 3.94–3.74 (comp, 3H), 3.09 (dd, *J* = 15.4, 4.1 Hz, 1H), 3.00 (dd, *J* = 15.3, 13.2 Hz, 1H), 2.36 (app dtd, *J* = 12.2, 6.1, 2.0 Hz, 1H), 2.19–2.11 (m, 1H), 1.93 (app tddd, *J* = 12.1, 9.9, 8.5, 6.3 Hz, 1H), 1.80 (app tdd, *J* = 11.9, 9.5, 6.8 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 164.0, 137.9, 133.2, 132.1, 131.6, 128.0, 127.5, 126.7, 125.6, 125.4, 125.3, 55.8, 45.2, 36.7, 33.6, 23.5.

HRMS (ESI-TOF): Calculated for $C_{16}H_{15}NONa$ $[M + Na]^+$: 260.1046, Found: 260.1066.

8,9,9a,10-Tetrahydropyrrolo[1,2-*g*][1,6]naphthyridin-5(7*H*)-one



(±)-**10p**

Following general procedure B, compound (±)-**10p** was obtained from 2-methylnicotinamide **9p** (96.1 mg) and pyrrolidine (84 μL) as a white solid in 55% yield (51.8 mg). EtOAc containing methanol (0–5%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.15 in EtOAc/methanol 95:5 v/v.

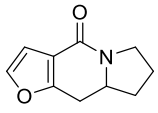
m.p.: 103–105 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.57 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.29 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.28 (app ddd, *J* = 7.7, 4.9, 1.0 Hz, 1H), 3.97–3.89 (m, 1H), 3.77 (ddd, *J* = 11.7, 9.1, 2.2 Hz, 1H), 3.62 (ddd, *J* = 12.3, 9.8, 7.6 Hz, 1H), 3.28 (dd, *J* = 15.9, 4.1 Hz, 1H), 2.96 (dd, *J* = 15.7, 13.6 Hz, 1H), 2.38–2.32 (m, 1H), 2.12 (app dtt, *J* = 12.6, 7.2, 1.9 Hz, 1H), 1.95–1.84 (m, 1H), 1.77 (app tdd, *J* = 12.0, 10.2, 6.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 162.0, 157.7, 151.6, 135.3, 125.7, 122.4, 56.4, 44.7, 37.7, 33.6, 23.0.

HRMS (ESI-TOF): Calculated for $C_{11}H_{13}N_2O$ $[M + H]^+$: 189.1022, Found: 189.1023.

7,8,8a,9-Tetrahydrofuro[3,2-*f*]indolizin-4(6*H*)-one



(±)-**10q**

Following general procedure B with the modification that the *ortho*-lithiation step was performed at −40 °C for 30 minutes, compound (±)-**10q** was obtained from *o*-toluamide **9q** (90.2 mg) and pyrrolidine (84 μL) as a white solid in 51% yield (45.2 mg). Hexanes containing EtOAc (10–20%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.25 in hexanes/EtOAc 80:20 v/v.

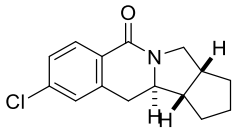
m.p.: 116–117 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.28 (app dd, *J* = 2.0, 1.0 Hz, 1H), 6.68 (m, 1H), 3.97 (app ddt, *J* = 13.6, 10.5, 5.4 Hz, 1H), 3.69 (ddd, *J* = 11.7, 9.1, 2.4 Hz, 1H), 3.46 (ddd, *J* = 11.8, 9.5, 7.7 Hz, 1H), 3.02 (dd, *J* = 16.1, 5.4 Hz, 1H), 2.75–2.67 (m, 1H), 2.27–2.21 (m, 1H), 2.10–2.03 (m, 1H), 1.86 (app ttd, *J* = 12.1, 9.3, 6.4 Hz, 1H), 1.75 (app tdd, *J* = 11.8, 10.2, 7.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 161.5, 158.0, 142.6, 116.9, 107.9, 58.1, 43.4, 32.8, 29.2, 23.3.

HRMS (ESI-TOF): Calculated for $C_{10}H_{12}NO$ $[M + H]^+$: 178.0863, Found: 178.0866.

***trans*-9-Chloro-1,2,3,3a,4,11,11a,11b-octahydro-6*H*-cyclopenta[3,4]pyrrolo[1,2-*b*]isoquinolin-6-one**



(±)-**10r**

Following general procedure B, compound (±)-**10r** was obtained from *o*-toluamide **9g** (112.9 mg) and *cis*-octahydrocyclopenta[c]pyrrole (111.2 mg) as a white solid in 70% yield (90.2 mg) and > 20:1 diastereomeric ratio. Hexanes containing EtOAc (20–40%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.25 in hexanes/EtOAc 70:30 v/v.

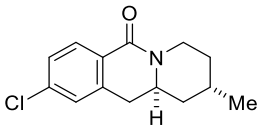
m.p.: 169–171 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.93 (d, *J* = 8.3 Hz, 1H), 7.25 (app ddd, *J* = 8.2, 2.1, 1.0 Hz, 1H), 7.14–7.12 (m, 1H), 4.08 (dd, *J* = 12.5, 8.5 Hz, 1H), 3.44 (ddd, *J* = 12.8, 8.2, 4.2 Hz, 1H), 3.22 (dd, *J* = 12.7, 4.9 Hz, 1H), 2.95 (dd, *J* = 15.5, 4.2 Hz, 1H), 2.83–2.73 (comp, 2H), 2.50 (app qd, *J* =8.2, 2.2 Hz, 1H), 1.85–1.65 (comp, 4H), 1.61–1.53 (m, 1H), 1.44 (app dq, *J* = 12.6, 6.3 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 162.1, 139.2, 137.3, 129.1, 128.3, 127.11, 127.06, 62.4, 51.6, 50.8, 41.6, 34.4, 32.0, 29.6, 25.3.

HRMS (ESI-TOF): Calculated for $C_{15}H_{17}ClNO$ $[M + H]^+$: 262.0993, Found: 262.0994.

***trans*-9-Chloro-2-methyl-1,2,3,4,11,11a-hexahydro-6*H*-pyrido[1,2-*b*]isoquinolin-6-one**



(±)-**10s**

Following general procedure B, compound (±)-**10s** was obtained from *o*-toluamide **9g** (112.9 mg) and 4-methyl-piperidine (118 μL) as a white solid in 70% yield (87.2 mg) and > 20:1 diastereomeric ratio. Hexanes containing EtOAc (5–20%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.50 in hexanes/EtOAc 70:30 v/v.

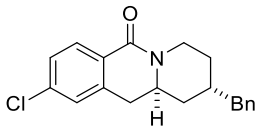
m.p.: 151–152 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.02 (d, *J* = 8.3 Hz, 1H), 7.27 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.12–7.11 (m, 1H), 4.33 (ddd, *J* = 13.8, 5.1, 3.4 Hz, 1H), 3.82–3.74 (m, 1H), 3.08 (ddd, *J* = 13.8, 12.4, 3.7 Hz, 1H), 2.91 (dd, *J* = 16.1, 4.9 Hz, 1H), 2.77 (dd, *J* = 16.1, 10.3 Hz, 1H), 2.17–2.06 (m, 1H), 1.84 (app ddt, *J* = 13.7, 12.4, 5.1 Hz, 1H), 1.73 (ddd, *J* = 13.5, 11.5, 5.0 Hz, 1H), 1.67–1.60 (m, 1H), 1.58–1.50 (m, 1H), 1.08 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): 164.2, 138.3, 137.5, 129.9, 127.2, 127.1, 126.6, 49.2, 38.3, 37.7, 34.5, 29.8, 24.7, 17.1.

HRMS (ESI-TOF): Calculated for $C_{14}H_{17}ClNO$ $[M + H]^+$: 250.0993, Found: 250.0998.

***trans*-2-Benzyl-9-chloro-1,2,3,4,11,11a-hexahydro-6*H*-pyrido[1,2-*b*]isoquinolin-6-one**



(±)-**10t**

Following general procedure B, compound (±)-**10t** was obtained from *o*-toluamide **9g** (112.9 mg) and 4-benzyl-piperidine (176 μL) as a white solid in 67% yield (109.8 mg) and > 20:1 diastereomeric ratio. Hexanes containing EtOAc (10–20%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.40 in hexanes/EtOAc 70:30 v/v.

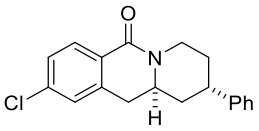
m.p.: 102–104 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.04 (d, *J* = 8.3 Hz, 1H), 7.33–7.26 (comp, 3H), 7.24–7.19 (m, 1H), 7.17–7.13 (comp, 2H), 7.13–7.09 (m, 1H), 4.34 (ddd, *J* = 13.9, 5.1, 3.6 Hz, 1H), 3.85 (app tt, *J* = 10.8, 4.4 Hz, 1H), 3.19 (ddd, *J* = 13.9, 12.2, 3.8 Hz, 1H), 2.87 (dd, *J* = 16.1, 4.8 Hz, 1H), 2.81–2.70 (comp, 3H), 2.28–2.19 (m, 1H), 1.87–1.61 (comp, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): 164.4, 140.1, 138.3, 137.6, 129.9, 128.7, 128.4, 127.2, 127.1, 126.7, 126.0, 49.4, 37.9, 37.3, 35.8, 34.7, 32.1, 27.5.

HRMS (ESI-TOF): Calculated for $C_{20}H_{21}ClNO$ $[M + H]^+$: 326.1306, Found: 326.1323.

***trans*-9-Chloro-2-phenyl-1,2,3,4,11,11a-hexahydro-6*H*-pyrido[1,2-*b*]isoquinolin-6-one**



(±)-**10u**

Following general procedure B, compound (±)-**10u** was obtained from *o*-toluamide **9g** (112.9 mg) and 4-phenyl-piperidine (161.3 mg) as a white solid in 30% yield (46.5 mg) and > 20:1 diastereomeric ratio. Hexanes containing EtOAc (10–20%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.45 in hexanes/EtOAc 70:30 v/v.

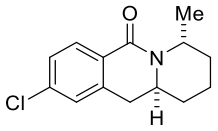
m.p.: 128–130 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.02 (d, *J* = 8.3 Hz, 1H), 7.36–7.27 (comp, 5H), 7.25–7.19 (m, 1H), 7.14 (s, 1H), 4.31 (app dt, *J* = 13.7, 5.1 Hz, 1H), 3.92 (app tt, *J* = 10.1, 4.5 Hz, 1H), 3.31 (ddd, *J* = 14.3, 9.4, 5.3 Hz, 1H), 3.27–3.20 (m, 1H), 2.96–2.84 (comp, 2H), 2.30 (app dt, *J* = 14.2, 4.1 Hz, 1H), 2.22–2.10 (comp, 2H), 2.04 (ddd, *J* = 14.0, 10.5, 5.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 164.1, 143.4, 138.2, 137.7, 129.9, 128.6, 127.4, 127.3, 127.2, 126.8, 126.2, 50.1, 38.7, 36.4, 34.6, 34.4, 28.7.

HRMS (ESI-TOF): Calculated for $C_{19}H_{19}ClNO$ $[M + H]^+$: 312.1150, Found: 312.1152.

***trans*-9-Chloro-4-methyl-1,2,3,4,11,11a-hexahydro-6*H*-pyrido[1,2-*b*]isoquinolin-6-one**



(±)-**10v**

Following general procedure B, compound (±)-**10v** was obtained from *o*-toluamide **9g** (112.9 mg) and 2-methyl-piperidine (118 μL) as a white solid in 28% yield (35.5 mg) and > 20:1 diastereomeric ratio. Hexanes containing EtOAc (5–20%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.45 in hexanes/EtOAc 75:25 v/v.

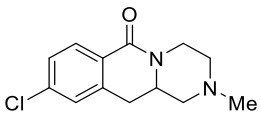
m.p.: 130–132 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.04 (d, *J* = 8.3 Hz, 1H), 7.32–7.27 (m, 1H), 7.15–7.10 (m, 1H), 5.02–4.94 (m, 1H), 3.76–3.68 (m, 1H), 2.94 (dd, *J* = 16.0, 4.8 Hz, 1H), 2.82 (dd, *J* = 16.0, 10.9 Hz, 1H), 1.95–1.88 (m, 1H), 1.80–1.61 (comp, 4H), 1.49–1.37 (m, 1H), 1.19 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): 163.9, 138.1, 137.6, 130.1, 127.7, 127.1, 126.5, 49.6, 45.3, 35.0, 33.7, 29.7, 17.8, 15.6.

HRMS (ESI-TOF): Calculated for $C_{14}H_{17}ClNO$ $[M + H]^+$: 250.0993, Found: 250.1009.

***trans*-9-Chloro-2-methyl-1,2,3,4,11,11a-hexahydro-6*H*-pyrazino[1,2-*b*]isoquinolin-6-one**



(±)-**10w**

Following general procedure B, compound (±)-**10w** was obtained from *o*-toluamide **9g** (112.9 mg) and 4-methyl-piperazine (111 μL) as a yellow solid in 88% yield (110.5 mg). EtOAc containing methanol (2–10%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.20 in EtOAc/methanol 90:10 v/v.

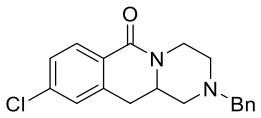
m.p.: 136–137 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.98 (d, *J* = 8.5 Hz, 1H), 7.23 (d, *J* = 8.3 Hz, 1H), 7.08 (s, 1H), 4.48–4.41 (m, 1H), 3.75–3.64 (m, 1H), 2.97–2.74 (comp, 5H), 2.28 (s, 3H), 2.11–2.01 (m, 1H), 1.91 (app t, *J* = 10.8 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 164.1, 137.9, 137.8, 130.0, 127.2, 126.72, 126.67, 61.4, 54.0, 52.9, 45.8, 42.0, 31.5.

HRMS (ESI-TOF): Calculated for $C_{13}H_{16}ClN_2O$ $[M + H]^+$: 251.0946, Found: 251.0947.

***trans*-2-Benzyl-9-chloro-1,2,3,4,11,11a-hexahydro-6*H*-pyrazino[1,2-*b*]isoquinolin-6-one**



(±)-**10x**

Following general procedure B, compound (±)-**10x** was obtained from *o*-toluamide **9g** (112.9 mg) and 4-benzyl-piperazine (176.3 mg) as a yellow solid in 72% yield (116.7 mg). Hexanes containing EtOAc (10–30%) was used as the eluent for silica gel chromatography.

Characterization data:

R_f = 0.20 in hexanes/EtOAc 70:30 v/v.

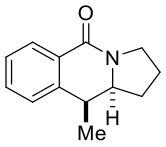
m.p.: 120–122 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.03 (d, *J* = 8.4 Hz, 1H), 7.35–7.32 (comp, 4H), 7.31–7.25 (comp, 2H), 7.12–7.09 (m, 1H), 4.53–4.50 (m, 1H), 3.74 (app tdd, *J* = 10.1, 7.4, 3.3 Hz, 1H), 3.60 (d, *J* = 13.0 Hz, 1H), 3.51 (d, *J* = 13.0 Hz, 1H), 3.03–2.94 (comp, 3H), 2.83–2.79 (comp, 2H), 2.18 (app td, *J* = 12.9, 3.3 Hz, 1H), 1.99 (app t, *J* = 11.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 164.2, 138.0, 137.9, 137.4, 130.0, 129.0, 128.3, 127.31, 127.28) 126.77, 126.75, 62.6, 59.3, 53.1, 52.2, 42.1, 31.6.

HRMS (ESI-TOF): Calculated for $C_{19}H_{20}ClN_2O$ $[M + H]^+$: 327.1259, Found: 327.1268.

10-Methyl-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**10y**

To a stirred solution of *N,N,N',N'*-tetramethylethylenediamine (1 mmol, 2 equiv, 150 μL) in dry THF (1 mL) was added dropwise *s*-BuLi in cyclohexane (1 mmol, 2 equiv) at −78 °C under nitrogen. The resulting mixture was allowed to stir at the same temperature for 10 minutes. To this was then added dropwise a solution of *o*-ethyl-benzamide **9y** (0.5 mmol, 1 equiv, 102.6 mg) in dry THF (1.5 mL) via cannula, and the resulting dark red solution was allowed to stir at −78 °C for 1 hour for the formation of lithiated *o*-ethyl-benzamide. The following procedures are the same as general procedure B with the modification that 3 equiv of 1-pyrroline was generated to react with lithiated *o*-ethyl-benzamide. Compound (±)-**10y** was obtained as a white solid in 56% yield (56.3 mg) as a 2:1 (*cis*/*trans*) mixture of two diastereomers. Hexanes containing EtOAc (20–50%) was used as the eluent for silica gel chromatography.

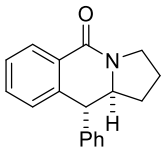
Characterization data:

$\mathbf{R_f}$ = 0.35 in hexanes/EtOAc 40:60 v/v.

^{1}H NMR (500 MHz, $CDCl_3$, due to overlapping peaks, integration values of the diastereomers are reported together): 8.06 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.03 (dd, *J* = 7.7, 1.4 Hz, 2H), 7.45 (app td, *J* = 7.6, 1.5 Hz, 1H), 7.40 (app td, *J* = 7.5, 1.4 Hz, 2H), 7.35–7.27 (comp, 4H), 7.19–7.16 (m, 2H), 3.97 (ddd, *J* = 10.3, 6.2, 4.0 Hz, 2H), 3.85–3.77 (comp, 3H), 3.63 (ddd, *J* = 12.2, 10.2, 7.5 Hz, 1H), 3.58–3.51 (m, 2H), 3.47–3.40 (m, 1H), 3.01 (qd, *J* = 7.1, 3.9 Hz, 2H), 2.83 (dq, *J* = 13.3, 6.8 Hz, 1H), 2.37–2.31 (m, 1H), 2.12–2.00 (comp, 5H), 1.98–1.77 (comp, 5H), 1.72 (app tdd, *J* = 12.2, 10.3, 6.8 Hz, 1H), 1.39 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 7.1 Hz, 6H).
^{13}C NMR (125 MHz, $CDCl_3$): 163.2, 163.0, 144.5, 141.7, 131.63, 131.61, 130.3, 128.9, 127.7, 127.5, 126.9, 126.8, 126.7, 123.8, 62.6, 59.3, 45.2, 45.1, 38.3, 36.0, 33.0, 28.6, 23.3, 22.8, 15.6, 14.1.

HRMS (ESI-TOF): Calculated for $C_{13}H_{16}NO$ $[M + H]^+$: 202.1226, Found: 202.1233.

***trans*-10-Phenyl-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one**



(±)-**10z**

Following general procedure B with the modification that the reaction was allowed to warm up to room temperature over 30 min after 1-pyrroline was added to *ortho*-lithiated amide. Compound (±)-**10z** was obtained from *o*-toluamide **9z** (133.7 mg) and pyrrolidine (84 μL) as a white solid in 80% yield (106.0 mg) and > 20:1 diastereomeric ratio. Hexanes containing EtOAc (20–50%) was used as the eluent for silica gel chromatography. The relative configuration of compound (±)-**10z** was determined by the comparison with reported characterization data[9] of the corresponding benzoindolizidine which was obtained by the $LiAlH_4$ reduction of (±)-**10z** according to procedures described for the synthesis of compound (±)-**12**.

Characterization data:

R_f = 0.30 in hexanes/EtOAc 50:50 v/v.

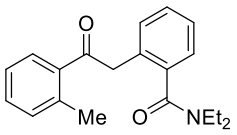
m.p.: 185–187 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.14–8.10 (m, 1H), 7.43–7.37 (m, 2H), 7.37–7.27 (comp, 3H), 7.27–7.23 (m, 2H), 6.70–6.67 (m, 1H), 4.05–3.94 (comp, 2H), 3.87 (ddd, *J* = 11.7, 8.9, 2.1 Hz, 1H), 3.69 (ddd, *J* = 12.3, 9.8, 7.5 Hz, 1H), 2.06–1.98 (m, 1H), 1.90–1.83 (m, 1H), 1.82–1.63 (comp, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): 162.9, 141.4, 139.1, 131.5, 130.3, 129.2, 128.9, 127.53, 127.49, 126.9, 126.6, 62.5, 52.0, 45.4, 32.8, 22.6.

HRMS (ESI-TOF): Calculated for $C_{18}H_{17}NONa$ $[M + Na]^+$: 286.1202, Found: 286.1186.

***N*,*N*-Diethyl-2-(2-oxo-2-(o-tolyl)ethyl)benzamide**



11

To a stirred solution of diisopropylamine (0.75 mmol, 1.5 equiv, 105 μL) in dry THF (1 mL) was added dropwise *n*-BuLi in hexanes (0.75 mmol, 1.5 equiv) at −78 °C under nitrogen, and the mixture was allowed to stir at the same temperature for 20 minutes. To this at −78 °C was then added dropwise a solution of the *o*-toluamide **9a** (0.5 mmol, 1 equiv, 95.7 mg) in dry THF (1.5 mL) via cannula, and the resulting dark red solution was allowed to stir at −78 °C for 30 minutes for the formation of lithiated *o*-toluamide. To a separate dry round-bottom flask charged with pyrrolidine (1 mmol, 2 equiv, 84 μL) was added dry ether (1 mL). The solution was cooled to −78 °C and *n*-BuLi in hexanes (1 mmol, 2 equiv) was added dropwise. The mixture was allowed to stir at the same temperature for 5 minutes, and a solution of benzophenone (1 mmol, 2 equiv, 182.2 mg) in dry ether (1.5 mL) was then added dropwise via cannula. The mixture was allowed to stir at −78 °C for another 5 minutes to give pyrroline ether solution. The pyrroline solution was then taken up by syringe and added in one portion to the stirred lithiated *o*-toluamide solution at −78 °C. The resulting mixture was allowed to stir at −78 °C for 2 hours followed by quenching with 1 M HCl aqueous solution (3 mL) at the same temperature. The reaction mixture was then allowed to warm up to room temperature and stir for 30 minutes. The crude mixture was washed with 0.5 M HCl aqueous solution (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography using hexanes containing EtOAc (5–20%) as the eluent. Compound **11** was obtained as a yellow oil in 15% yield (11.7 mg). Compound (±)-**10a** was also obtained as a white solid in 34% yield (31.5 mg).

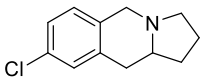
Characterization data for 11:

R_f = 0.70 in hexanes/EtOAc 40:60 v/v.

^{1}H NMR (500 MHz, $CDCl_3$): 7.78 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.40–7.33 (comp, 2H), 7.32–7.21 (comp, 5H), 4.35 (br s, 2H), 3.49 (br s, 2H), 3.17 (br s, 2H), 2.47 (s, 3H), 1.11–1.05 (comp, 6H).
^{13}C NMR (125 MHz, $CDCl_3$): 201.0, 170.6, 138.3, 137.43, 137.40, 132.0, 131.9, 131.5, 131.4, 128.9, 128.8, 126.7, 125.8, 125.7, 45.4, 43.0, 38.6, 21.4, 13.9, 12.6.

Accurate Mass (ESI): Calculated for $C_{20}H_{24}NO_2$ $[M + H]^+$ 310.1802, Found: 310.1738, Spectral Accuracy: 99.1%.

8-Chloro-1,2,3,5,10,10a-hexahydropyrrolo[1,2-*b*]isoquinoline



(±)-**12**

To a suspension of $LiAlH_4$ (1.2 mmol, 4 equiv, 45.5 mg) in dry THF (1.5 mL) was added dropwise a solution of lactam (±)-**10g** (0.3 mmol, 1 equiv, 66.5 mg) in dry THF (1.5 mL) at 0 °C. The mixture was heated under reflux in an oil bath for 5 hours. The reaction mixture was then allowed to cool to room temperature and quenched with aqueous ammonia solution (1 mL) at 0 °C. The resulting mixture was filtered through a short pad of celite and washed with EtOAc (6 x 10 mL). Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography using EtOAc containing methanol (2–5%) as the eluent. Compound (±)-**12** was obtained as a white solid in 80% yield (49.8 mg).

Characterization data:

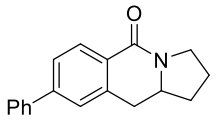
$\mathbf{R_f}$ = 0.30 in EtOAc/methanol 90:10 v/v.

m.p.: 78–79 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.12–7.05 (comp, 2H), 6.97 (d, *J* = 8.7 Hz, 1H), 4.08 (d, *J* = 14.7 Hz, 1H), 3.35 (d, *J* = 14.7 Hz, 1H), 3.26 (app td, *J* = 8.7, 2.3 Hz, 1H), 2.93 (dd, *J* = 16.1, 3.8 Hz, 1H), 2.67 (dd, *J* = 16.1, 10.8 Hz, 1H), 2.35–2.20 (comp, 2H), 2.08 (dddd, *J* = 12.5, 10.0, 6.8, 4.2 Hz, 1H), 1.96–1.86 (m, 1H), 1.85–1.76 (m, 1H), 1.53 (app tdd, *J* = 11.7, 9.5, 6.4 Hz, 1H).
^{13}C NMR (125 MHz, $CDCl_3$): 136.7, 133.4, 131.5, 128.6, 127.8, 125.8, 60.3, 55.3, 54.6, 35.8, 30.8, 21.5.

HRMS (ESI-TOF): Calculated for $C_{12}H_{15}ClN$ $[M + H]^+$: 208.0888, Found: 208.0879.

8-Phenyl-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**13**

A dry 10 mL reaction vial was charged with a stir bar, lactam (±)-**10g** (0.2 mmol, 1 equiv, 44.3 mg), phenylboronic acid (0.3 mmol, 1.5 equiv, 36.6 mg), SPhos (14 μmol, 7 mol%, 5.8 mg), $Pd(OAc)_2$ (6 μmol, 3 mol%, 1.4 mg) and K_3PO_4 (0.4 mmol, 2 equiv, 84.9 mg). The reaction vial was then sealed with a septum-lined cap. The vial was evacuated (via a needle connected to a Schlenk line) and then purged with nitrogen, and this process was repeated three times. Dry toluene (1 mL) was added and the mixture was heated in an oil bath and allowed to stir under nitrogen at 100 °C for 14 hours. The reaction mixture was allowed to cool to room temperature and then filtered through a short pad of celite and washed with EtOAc (6 x 10 mL). Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography using hexanes containing EtOAc (20–50%) as the eluent. Compound (±)-**13** was obtained as a white solid in 93% yield (49.0 mg).

Characterization data:

R_f = 0.35 in hexanes/EtOAc 40:60 v/v.

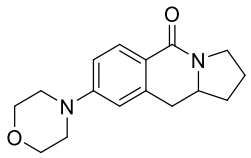
m.p.: 125–128 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.10 (d, *J* = 8.0 Hz, 1H), 7.63–7.57 (m, 2H), 7.56–7.52 (m, 1H), 7.47–7.40 (m, 2H), 7.40–7.33 (comp, 2H), 3.90–3.73 (comp, 2H), 3.64 (ddd, *J* = 12.2, 9.9, 7.6 Hz, 1H), 3.06 (dd, *J* = 15.2, 3.9 Hz, 1H), 2.84 (app t, *J* = 14.3 Hz, 1H), 2.32–2.26 (m, 1H), 2.13–2.05 (m, 1H), 1.92–1.80 (m, 1H), 1.73 (app tdd, *J* = 12.0, 10.1, 7.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): 163.1, 144.1, 140.1, 137.9, 129.0, 128.8, 128.0, 127.8, 127.1, 125.73, 125.71, 56.9, 44.7, 35.1, 33.6, 23.0.

HRMS (ESI-TOF): Calculated for $C_{18}H_{17}NONa$ $[M + Na]^+$: 286.1202, Found: 286.1187.

8-Morpholino-2,3,10,10a-tetrahydropyrrolo[1,2-*b*]isoquinolin-5(1*H*)-one



(±)-**14**

A dry 10 mL reaction vial was charged with a stir bar, lactam (±)-**10g** (0.2 mmol, 1 equiv, 44.3 mg), CyJohnPhos (12 μmol, 6 mol%, 4.2 mg), $Pd(OAc)_2$ (6 μmol, 3 mol%, 1.4 mg) and K_3PO_4 (0.3 mmol, 1.5 equiv, 63.7 mg). The reaction vial was then sealed with a septum-lined cap. The vial was evacuated (via a needle connected to a Schlenk line) and then purged with nitrogen, and this process was repeated three times. Dry 1,2-dimethoxyethane (1 mL) and morpholine (0.24 mmol, 1.2 equiv, 21 μL) were successively added, and the mixture was heated in an oil bath and allowed to stir at 100 °C for 20 hours. The reaction mixture was allowed to cool to room temperature and then filtered through a short pad of celite and washed with EtOAc (6 x 10 mL). Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography using EtOAc containing methanol (0–5%) as the eluent. Compound (±)-**14** was obtained as a white solid in 77% yield (42.0 mg).

Characterization data:

R_f = 0.40 in EtOAc/methanol 95:5 v/v.

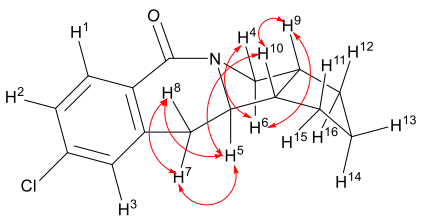
m.p.: 168–170 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 7.91 (d, *J* = 8.6 Hz, 1H), 6.79 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.62–6.57 (m, 1H), 3.85–3.80 (comp, 4H), 3.80–3.69 (comp, 2H), 3.58 (ddd, *J* = 12.0, 9.7, 7.6 Hz, 1H), 3.25–3.18 (comp, 4H), 2.90 (dd, *J* = 15.22, 4.0 Hz, 1H), 2.75 (app t, *J* = 14.2 Hz, 1H), 2.27–2.21 (m, 1H), 2.08–2.00 (m, 1H), 1.82 (app ttd, *J* = 12.3, 9.4, 6.4 Hz, 1H), 1.68 (app tdd, *J* = 11.9, 10.1, 7.0 Hz, 1H).
^{13}C NMR (125 MHz, $CDCl_3$): 163.4, 153.2, 139.0, 128.9, 121.4, 112.9, 112.4, 66.6, 56.8, 48.1, 44.5, 35.5, 33.6, 23.0.

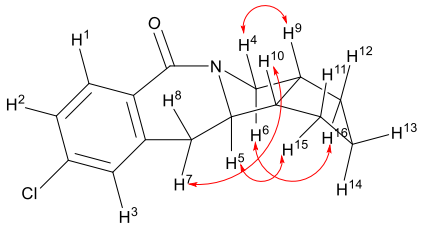
HRMS (ESI-TOF): Calculated for $C_{16}H_{21}N_2O_2$ $[M + H]^+$: 273.1598, Found: 273.1598.

2D-NMR Analysis for Compound (±)-10r, Selected Interactions

GCOSY



NOESY

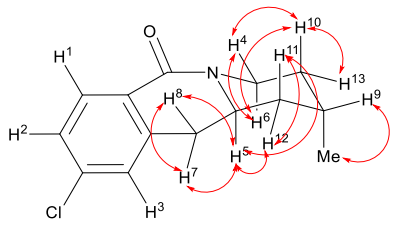


^{1}H NMR shifts

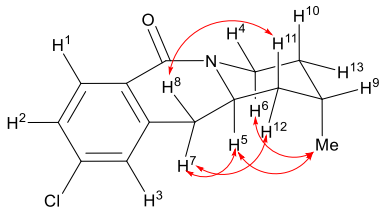
Protons	Chemical shifts (ppm)
H^{1}	7.93
H^{2}	7.25
H^{3}	7.14–7.12
H^{4}	4.08
H^{5}	3.44
H^{6}	3.22
H^{7}	2.95
$H^{8,9}$	2.83–2.73
H^{10}	2.50
$H^{11\text{-}14}$	1.85–1.65
H^{15}	1.61–1.53
H^{16}	1.44

2D-NMR Analysis for Compound (±)-10s, Selected Interactions

GCOSY



NOESY

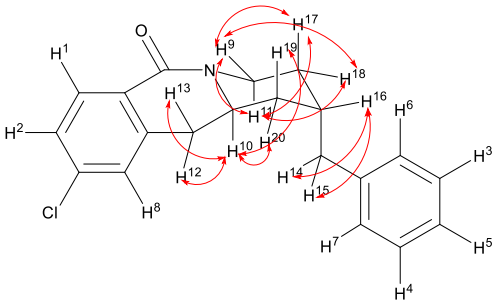


^{1}H NMR shifts

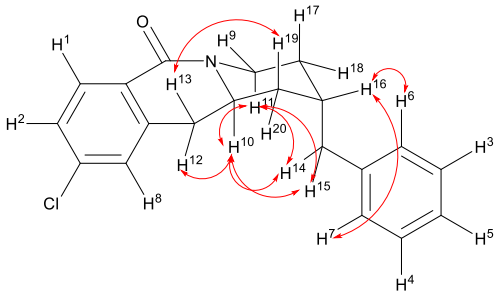
Protons	Chemical shifts (ppm)
H^{1}	8.02
H^{2}	7.27
H^{3}	7.12–7.11
H^{4}	4.33
H^{5}	3.82–3.74
H^{6}	3.08
H^{7}	2.91
H^{8}	2.77
H^{9}	2.17–2.06
H^{10}	1.84
H^{11}	1.73
H^{12}	1.67–1.60
H^{13}	1.58–1.50
Me	1.08

2D-NMR Analysis for Compound (±)-10t, Selected Interactions

GCOSY



NOESY

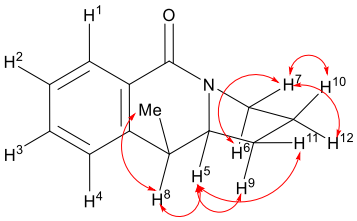


^{1}H NMR shifts

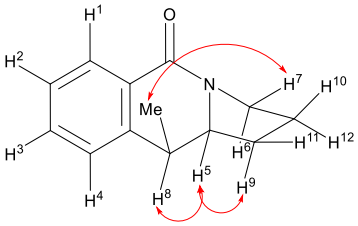
Protons	Chemical shifts (ppm)
H^{1}	8.04
H^{2-4}	7.33–7.26
H^{5}	7.24–7.19
$H^{6,7}$	7.17–7.13
H^{8}	7.13–7.09
H^{9}	4.34
H^{10}	3.85
H^{11}	3.19
H^{12}	2.87
H^{13-15}	2.81–2.70
H^{16}	2.28–2.19
H^{17-20}	1.87–1.61

2D-NMR Analysis for the Major Diastereomer of Compound (±)-10y, Selected Interactions

GCOSY (major)



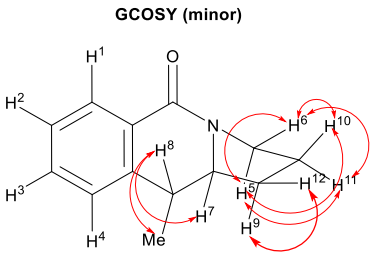
NOESY (major)

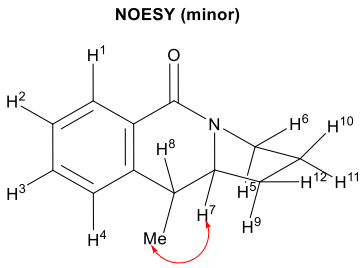


^{1}H NMR shifts of major diastereomer

Protons	Chemical shifts (ppm)
H^{1}	8.03
H^{2}	7.40
H^{3}	7.35–7.27
H^{4}	7.19–7.16
H^{5}	3.97
H^{6}	3.85–3.77
H^{7}	3.58–3.51
H^{8}	3.01
$H^{9\text{-}12}$	2.12–1.77
Me	1.07

2D-NMR Analysis for the Minor Diastereomer of Compound (±)-10y, Selected Interactions





^{1}H NMR shifts of minor diastereomer

Protons	Chemical shifts (ppm)
H^{1}	8.06
H^{2}	7.45
$H^{3,4}$	7.35–7.27
H^{5}	3.85–3.77
H^{6}	3.63
H^{7}	3.47–3.40
H^{8}	2.83
H^{9}	2.37–2.31
$H^{10,11}$	2.12–1.77
H^{12}	1.72
Me	1.39

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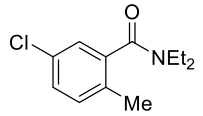
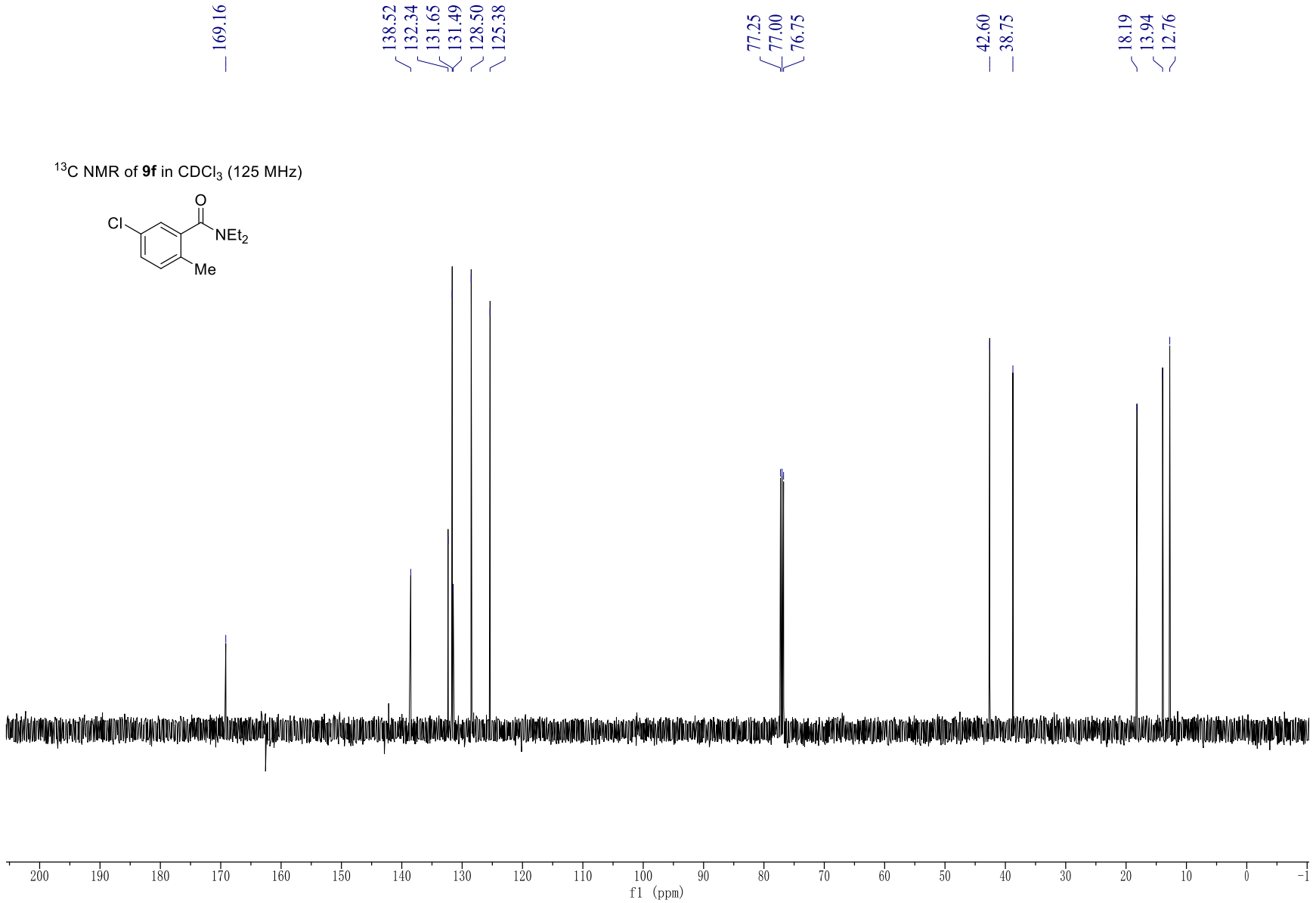
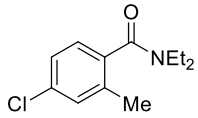
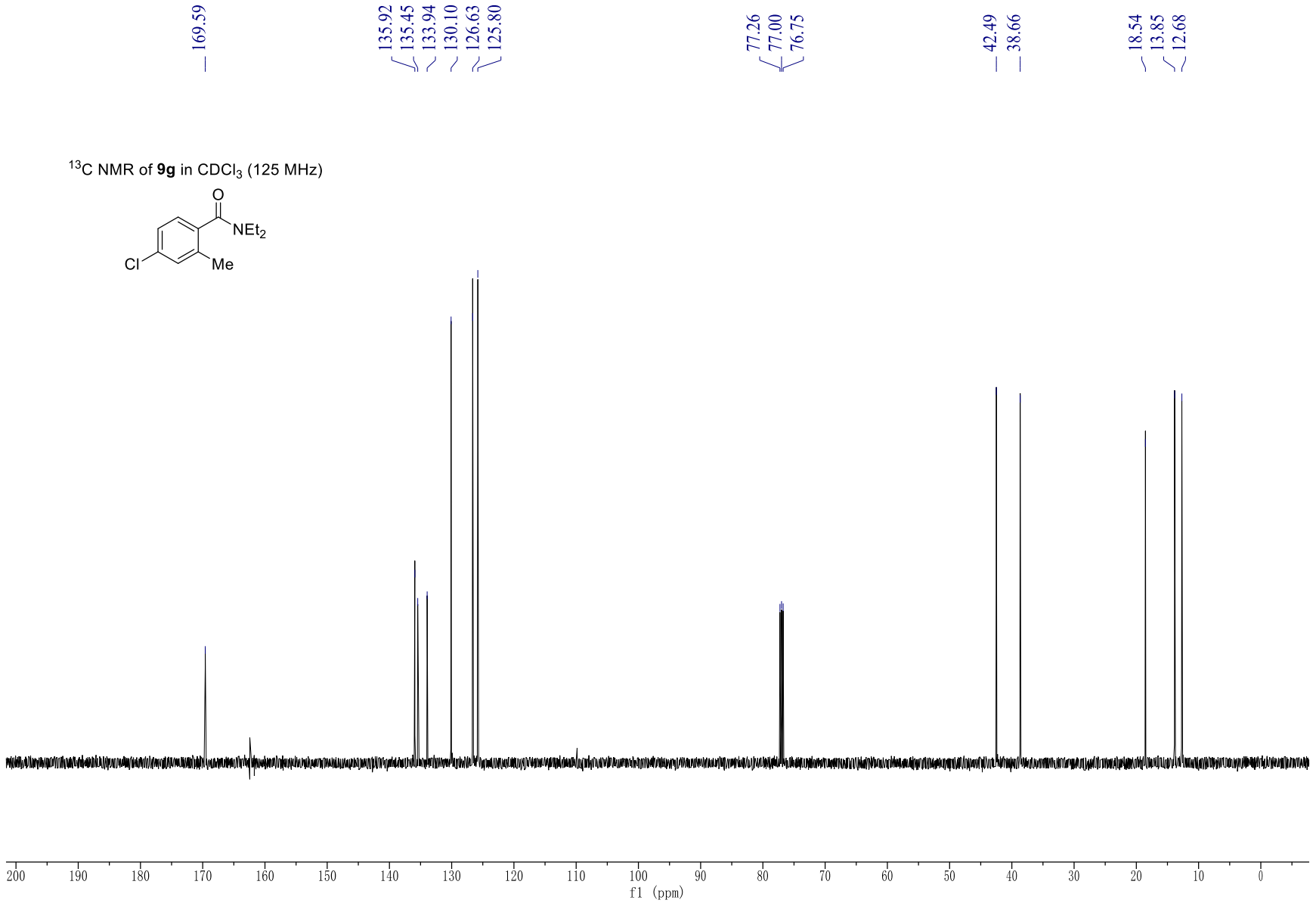
^{1}H NMR of **9f** in $CDCl_3$ (500 MHz)

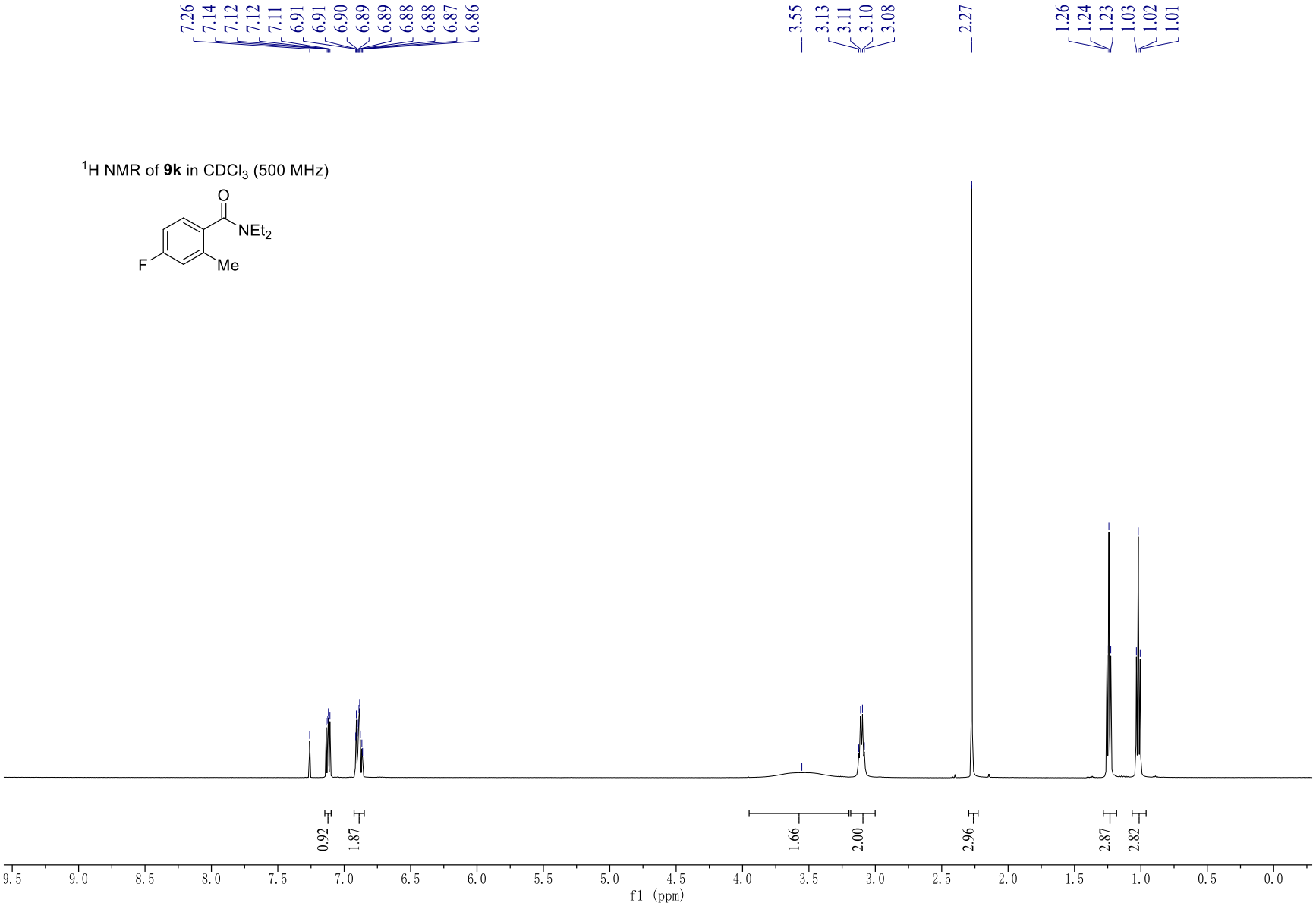



169.16
138.52
132.34
131.65
131.49
128.50
125.38
77.25
77.00
76.75
42.60
38.75
18.19
13.94
12.76
13C NMR of 9f in CDCl3 (125 MHz)
O
Cl
NEt2
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

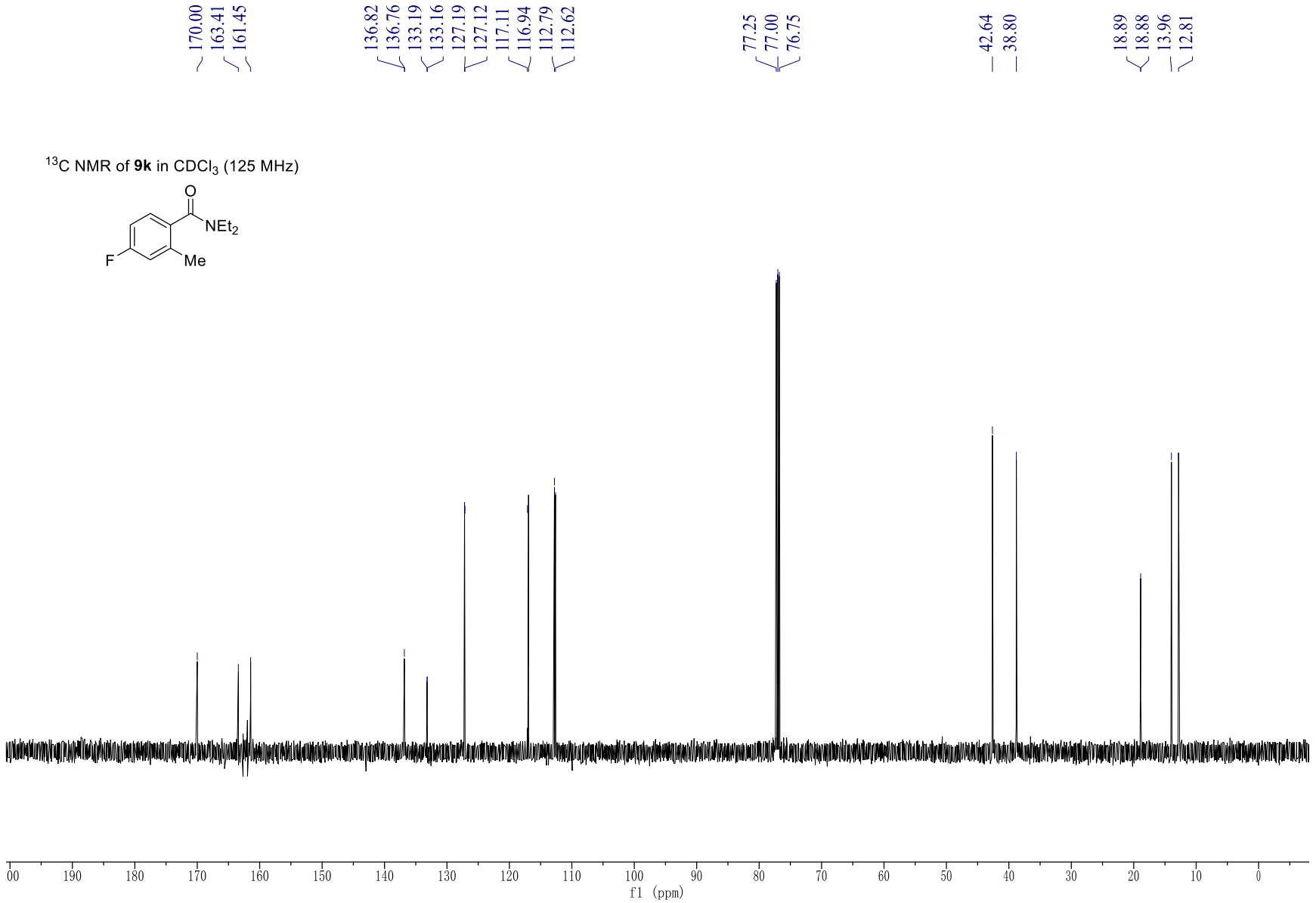
^{1}H NMR of **9g** in $CDCl_3$ (500 MHz)




169.59
135.92
135.45
133.94
130.10
126.63
125.80
77.26
77.00
76.75
42.49
38.66
18.54
13.85
12.68
13C NMR of 9g in CDCl3 (125 MHz)
O
NEt2
Cl
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

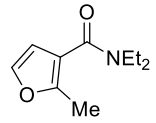


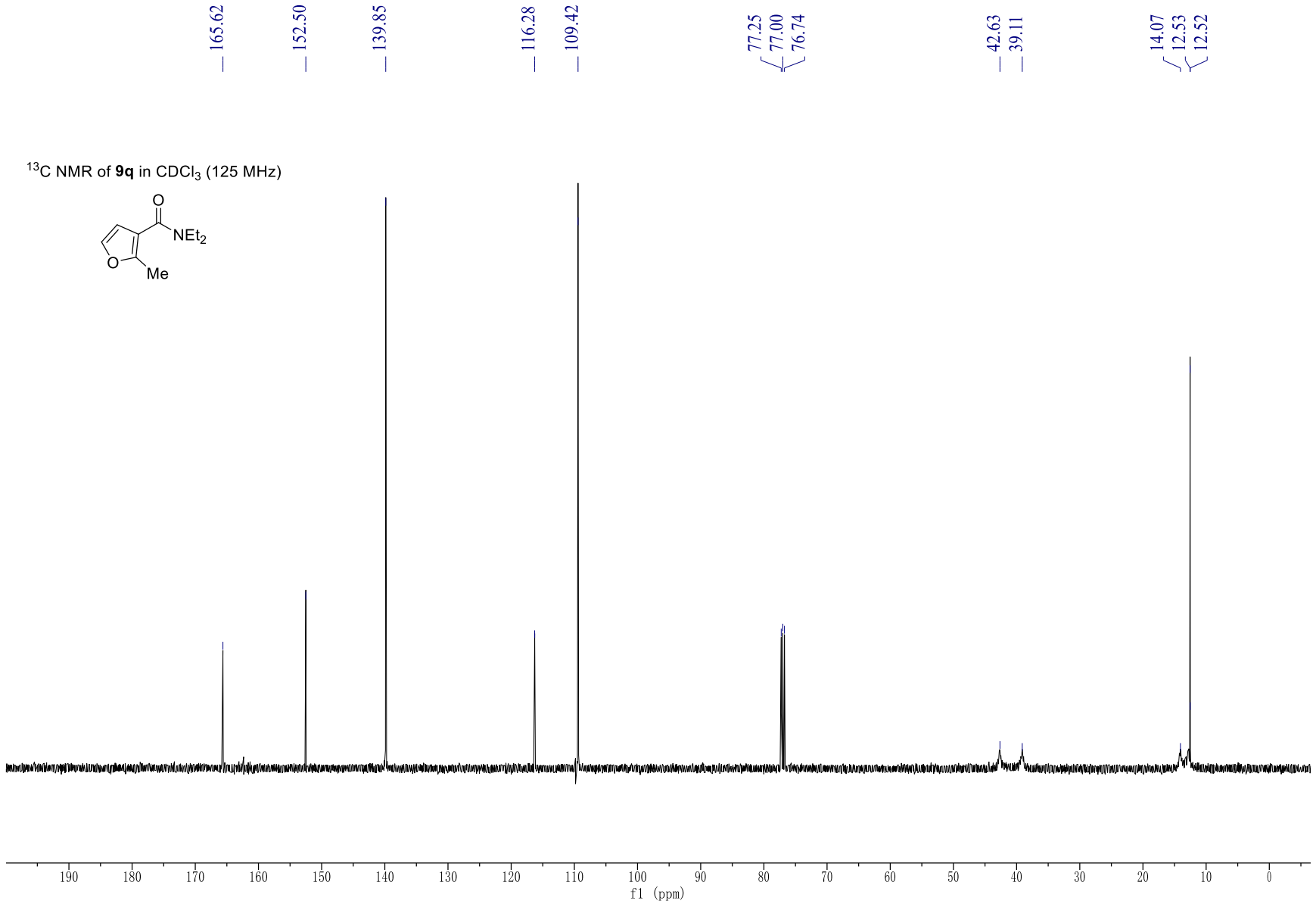
^{1}H NMR of **9k** in $CDCl_3$ (500 MHz)

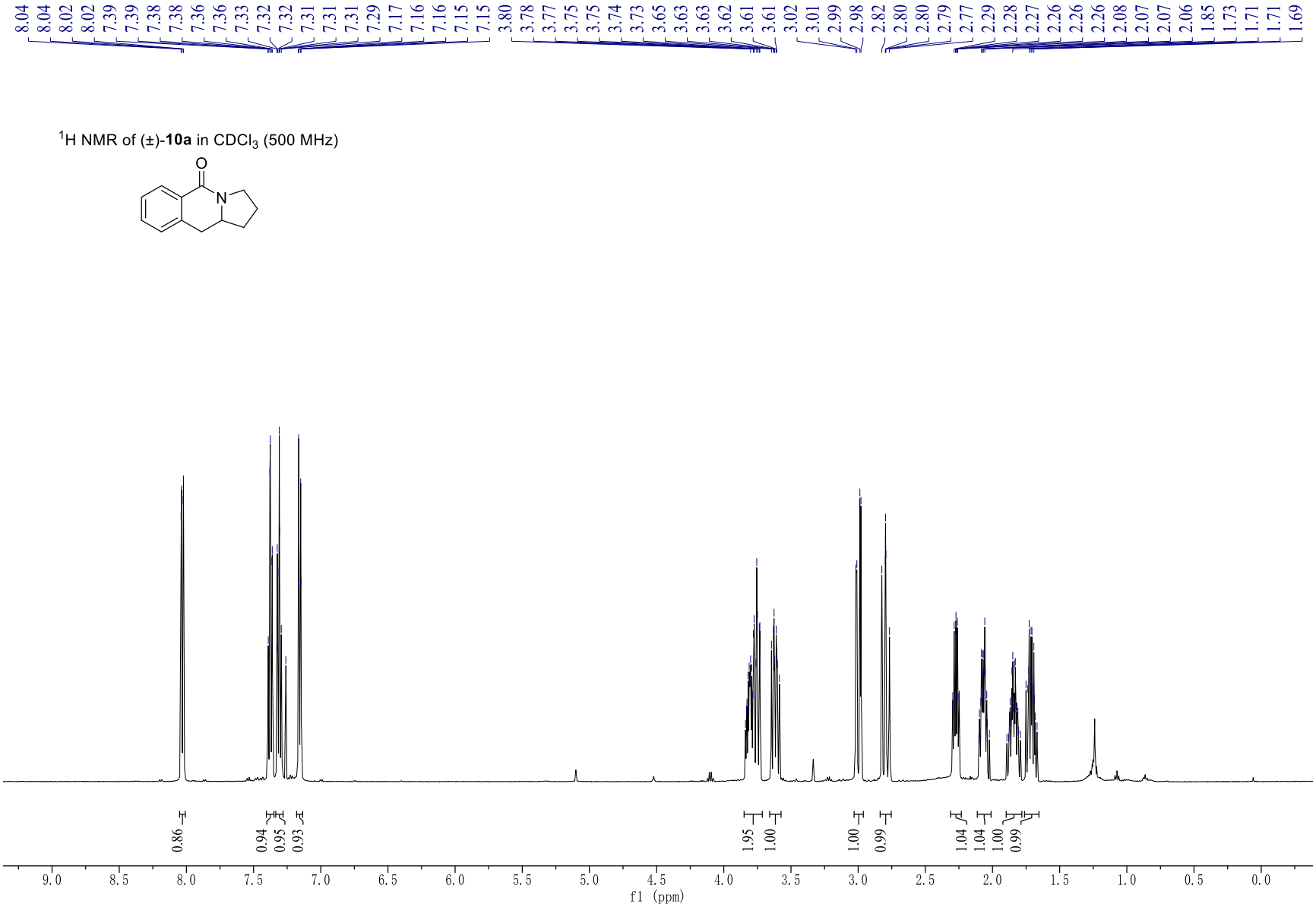


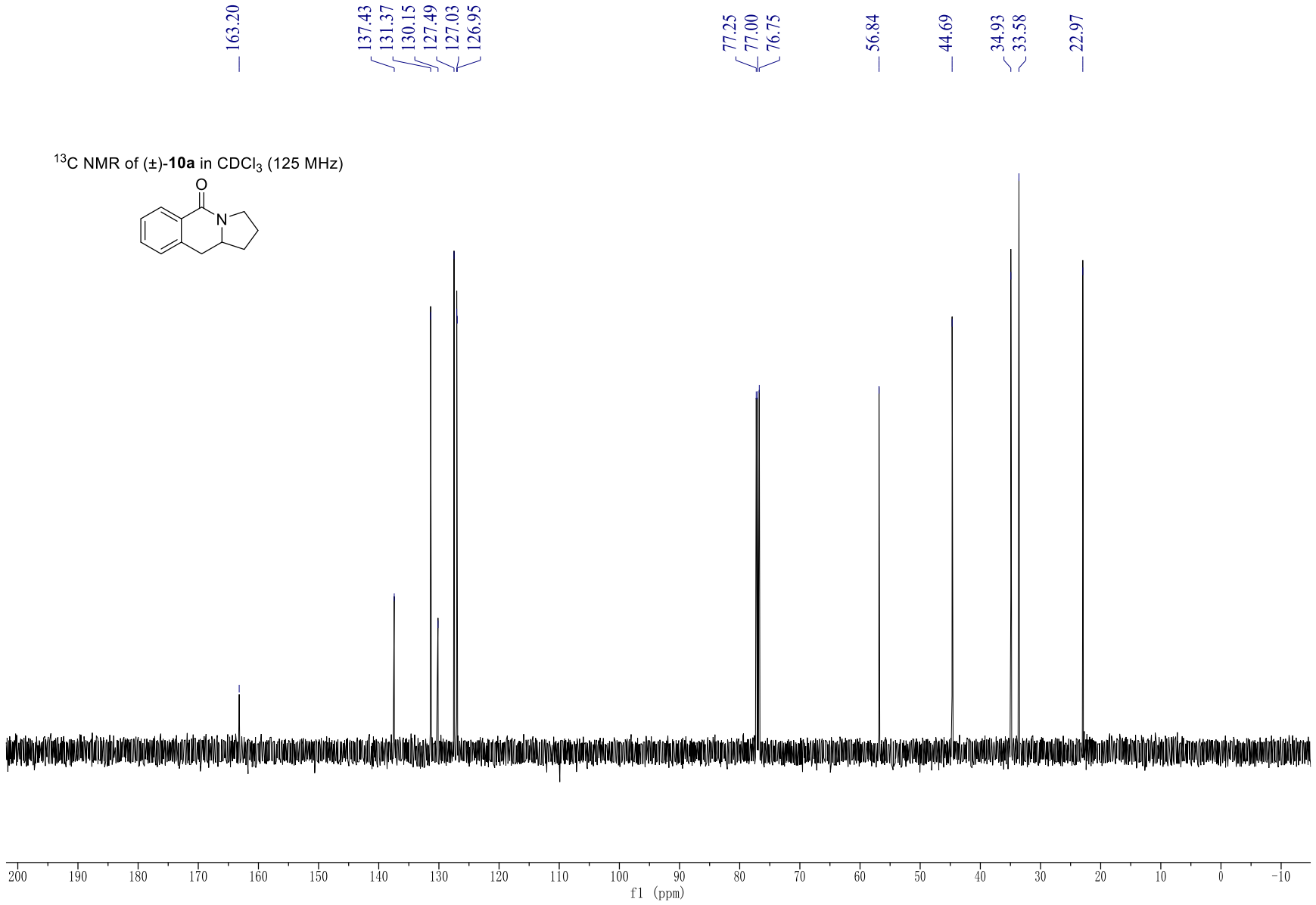
^{13}C NMR of **9k** in $CDCl_3$ (125 MHz)

^{1}H NMR of **9q** in $CDCl_3$ (500 MHz)

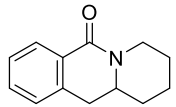


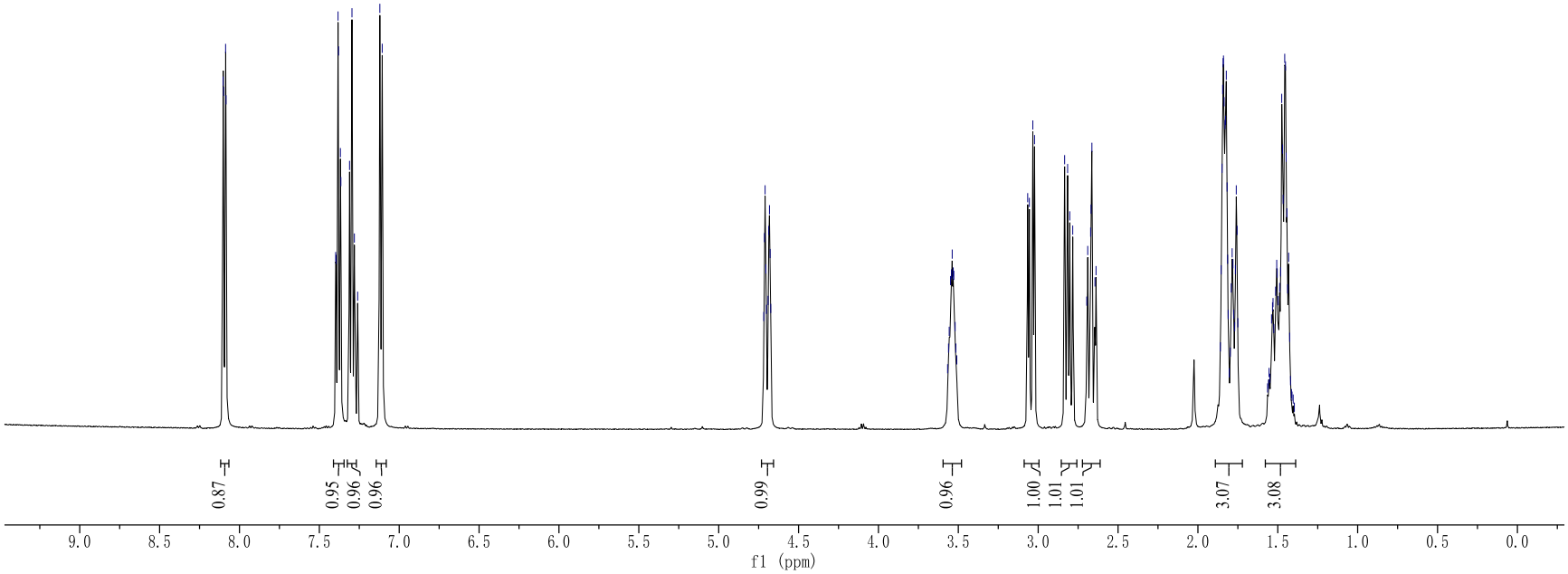

165.62
152.50
139.85
116.28
109.42
77.25
77.00
76.74
42.63
39.11
14.07
12.53
12.52
13C NMR of 9q in CDCl3 (125 MHz)
O
NEt2
O
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

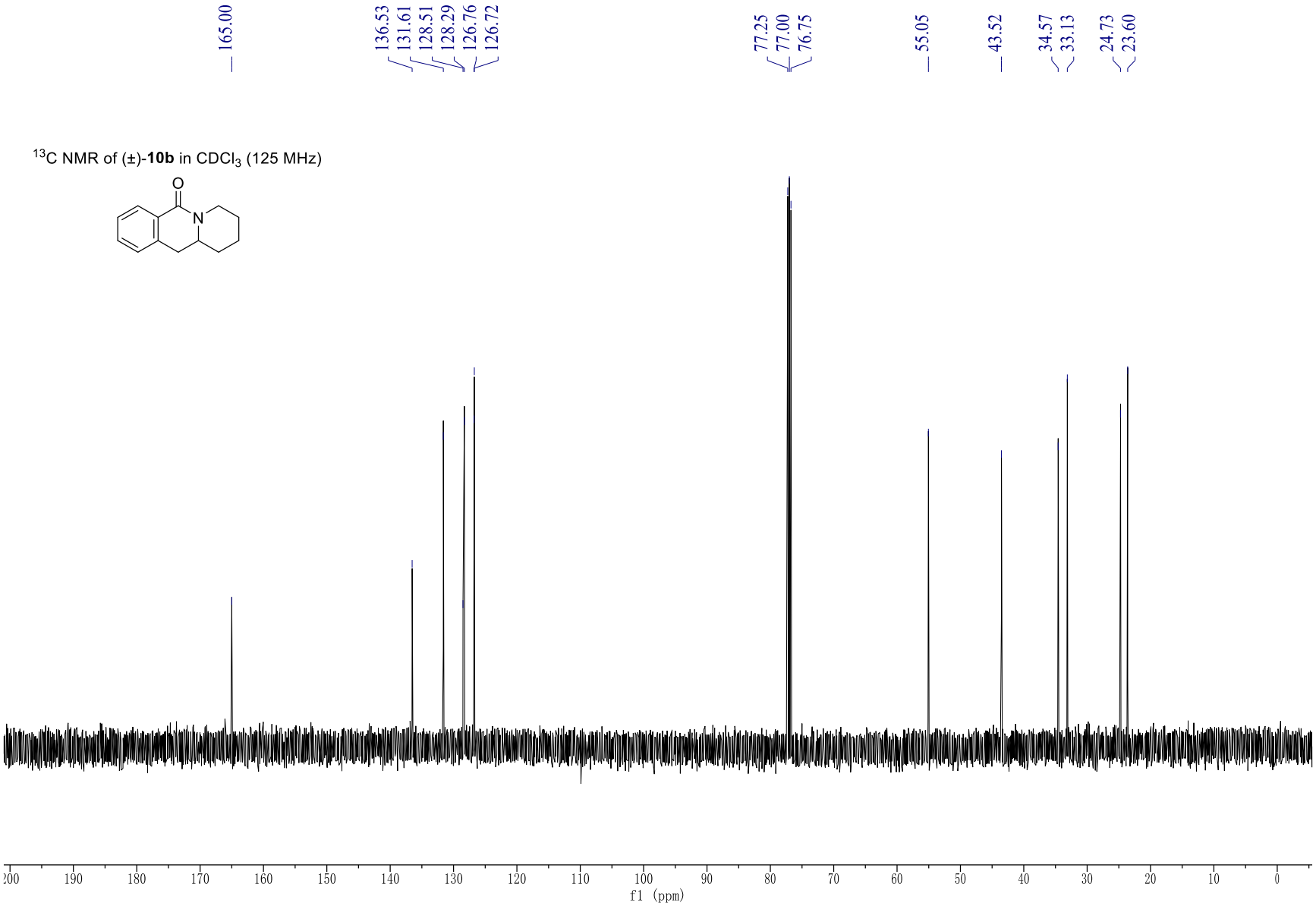

8.04 8.04 8.02 8.02 7.39 7.39 7.38 7.38 7.36 7.36 7.33 7.32 7.32 7.31 7.31 7.31 7.29 7.17 7.16 7.16 7.15 7.15
3.80 3.78 3.77 3.75 3.75 3.74 3.73 3.65 3.63 3.63 3.62 3.61 3.61
3.02 3.01 2.99 2.98
2.82 2.80 2.80 2.79 2.77 2.29 2.28 2.27 2.26 2.26 2.26 2.08 2.07 2.07 2.06 1.85 1.73 1.71 1.71 1.69
^{1}H NMR of (±)-**10a** in $CDCl_3$ (500 MHz)
O
N
0.86
0.94
0.95
0.93
1.95
1.00
1.00
0.99
1.04
1.04
1.00
0.99
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
f1 (ppm)


163.20
137.43
131.37
130.15
127.49
127.03
126.95
77.25
77.00
76.75
56.84
44.69
34.93
33.58
22.97
^{13}C NMR of (±)-**10a** in $CDCl_3$ (125 MHz)
O
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

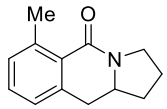
^{1}H NMR of (±)-**10b** in $CDCl_3$ (500 MHz)

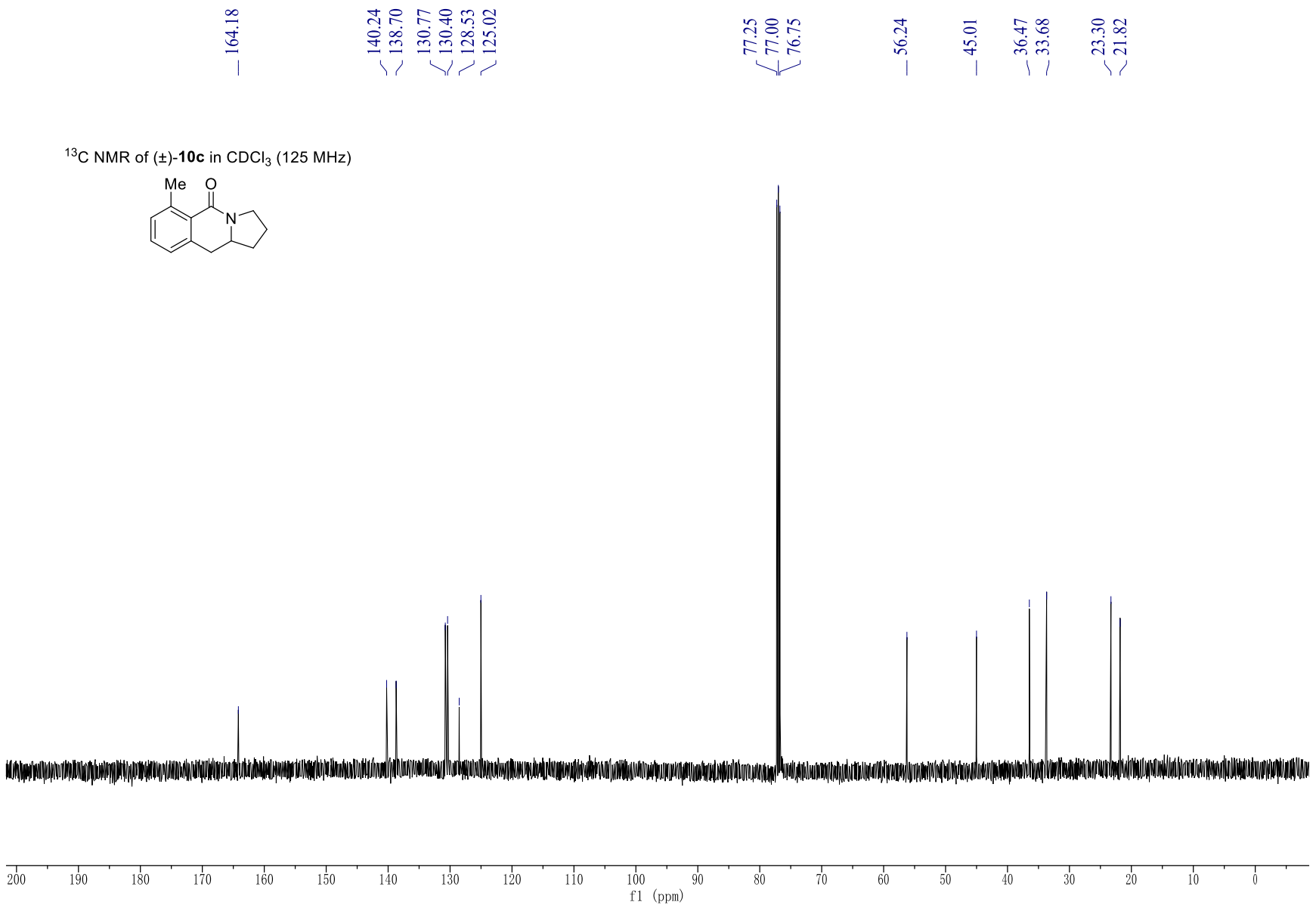





165.00
136.53
131.61
128.51
128.29
126.76
126.72
77.25
77.00
76.75
55.05
43.52
34.57
33.13
24.73
23.60
^{13}C NMR of (±)-**10b** in $CDCl_3$ (125 MHz)
O
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

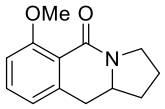
^{1}H NMR of (±)-**10c** in $CDCl_3$ (500 MHz)

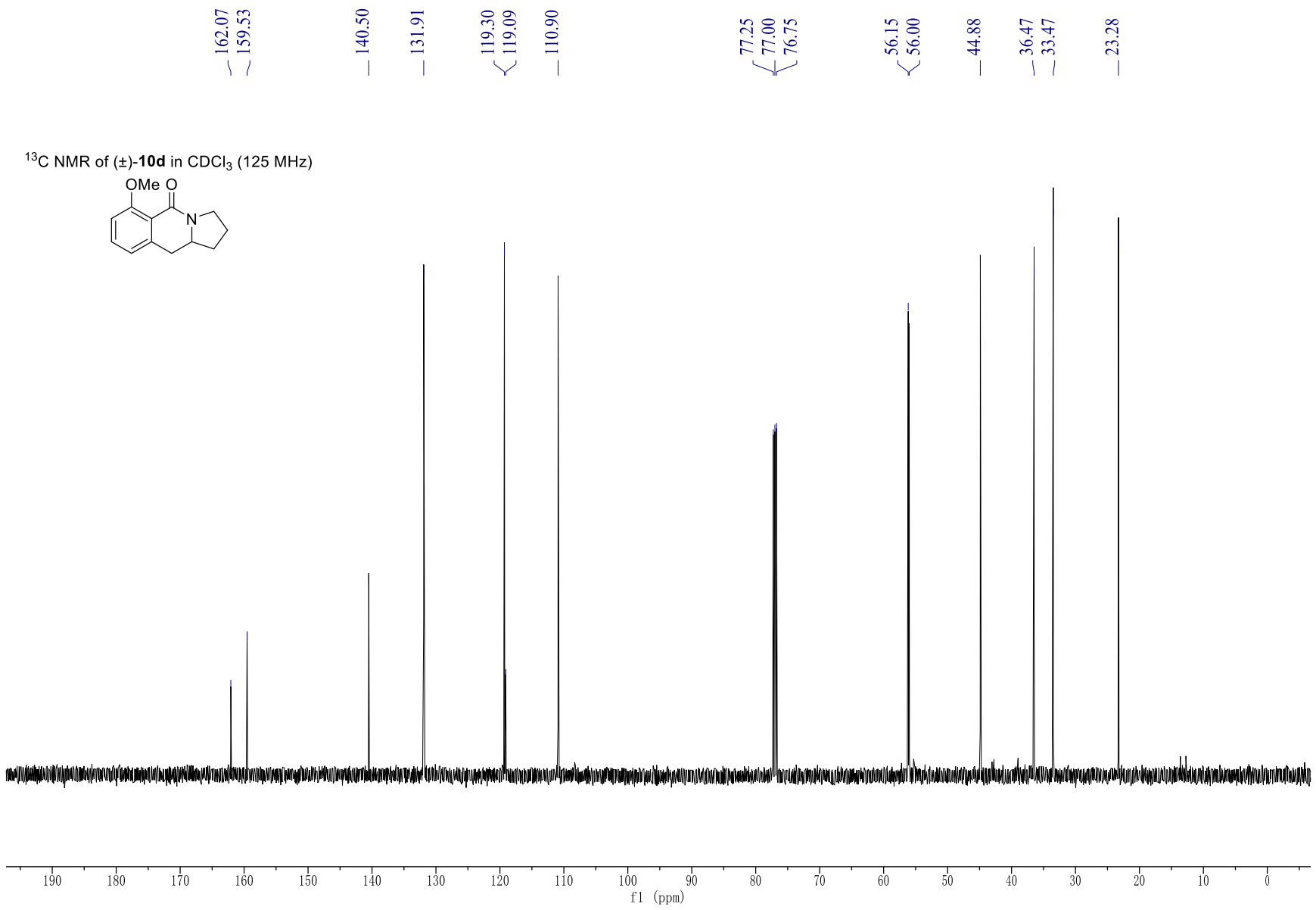


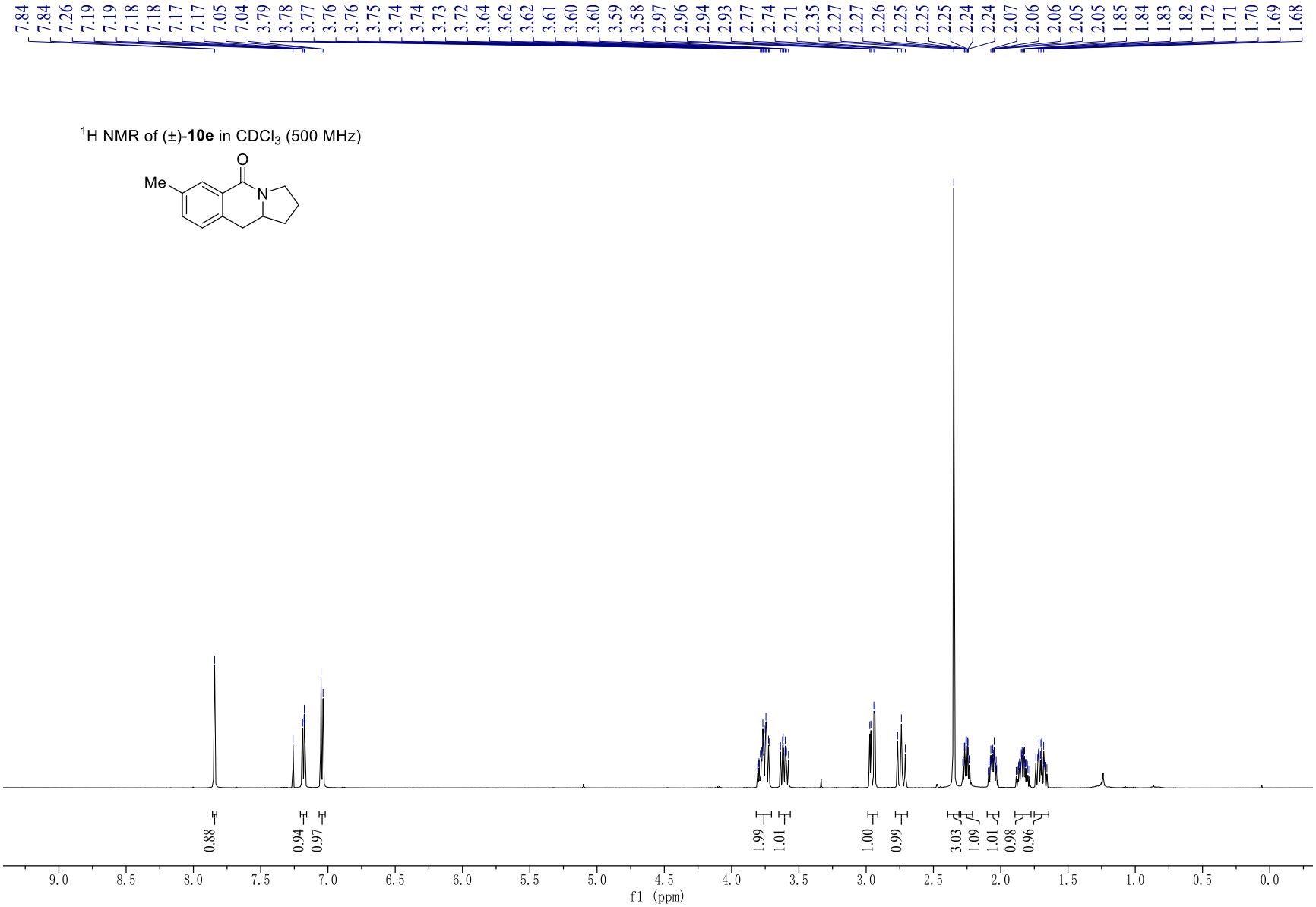


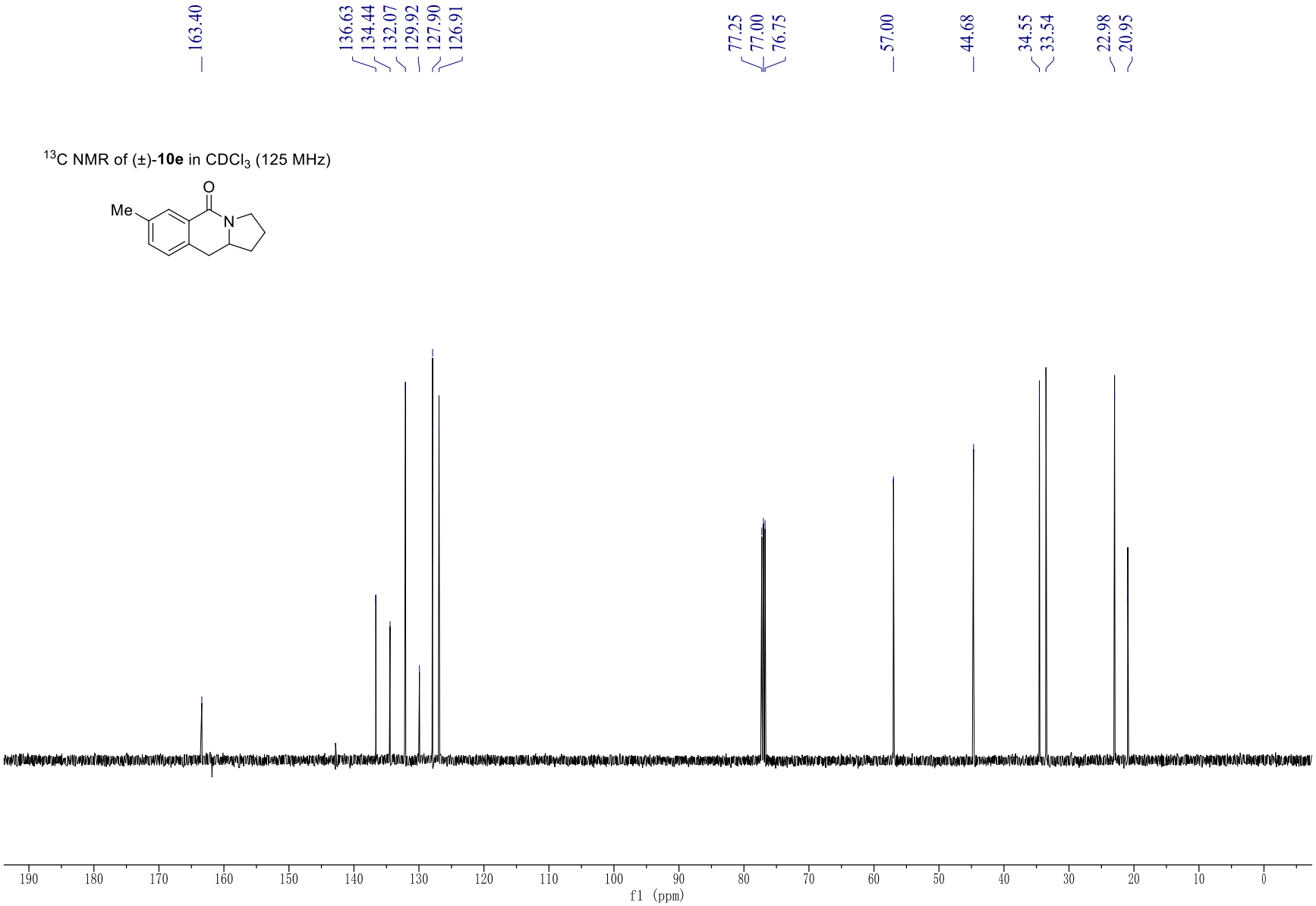
^{13}C NMR of (±)-**10c** in $CDCl_3$ (125 MHz)

^{1}H NMR of (±)-**10d** in $CDCl_3$ (500 MHz)



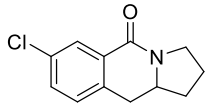

162.07
159.53
140.50
131.91
119.30
119.09
110.90
77.25
77.00
76.75
56.15
56.00
44.88
36.47
33.47
23.28
^{13}C NMR of (±)-**10d** in $CDCl_3$ (125 MHz)
OMe O
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

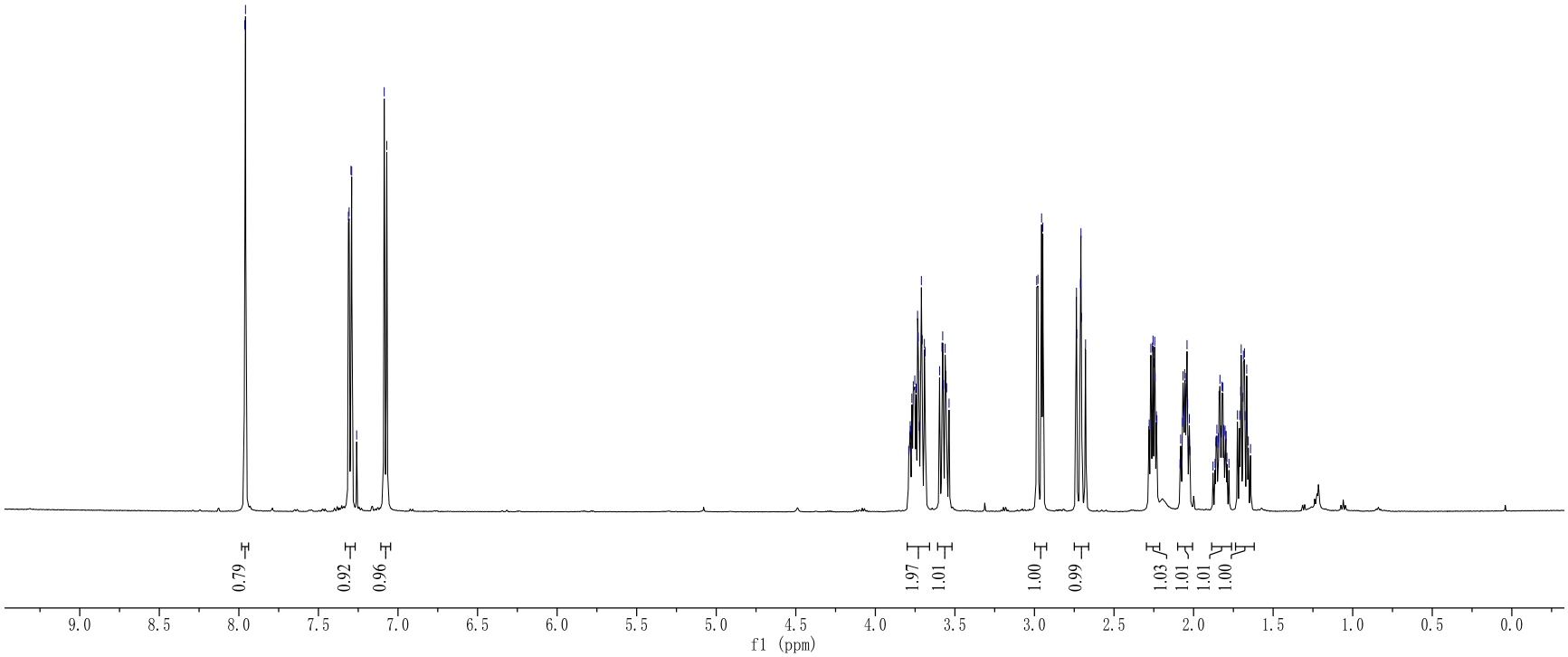

7.84 7.84 7.26 7.19 7.19 7.18 7.18 7.17 7.17 7.05 7.04 3.79 3.78 3.77 3.76 3.76 3.75 3.74 3.74 3.73 3.72 3.64 3.62 3.62 3.61 3.60 3.60 3.59 3.58 2.97 2.96 2.94 2.93 2.77 2.74 2.71 2.35 2.27 2.27 2.26 2.25 2.25 2.25 2.24 2.24 2.07 2.06 2.06 2.05 2.05 1.85 1.84 1.83 1.82 1.72 1.71 1.70 1.69 1.68
^{1}H NMR of (±)-**10e** in $CDCl_3$ (500 MHz)
O
Me
N
0.88 0.94 0.97 1.99 1.01 1.00 0.99 3.03 1.09 1.01 0.98 0.96
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
f1 (ppm)

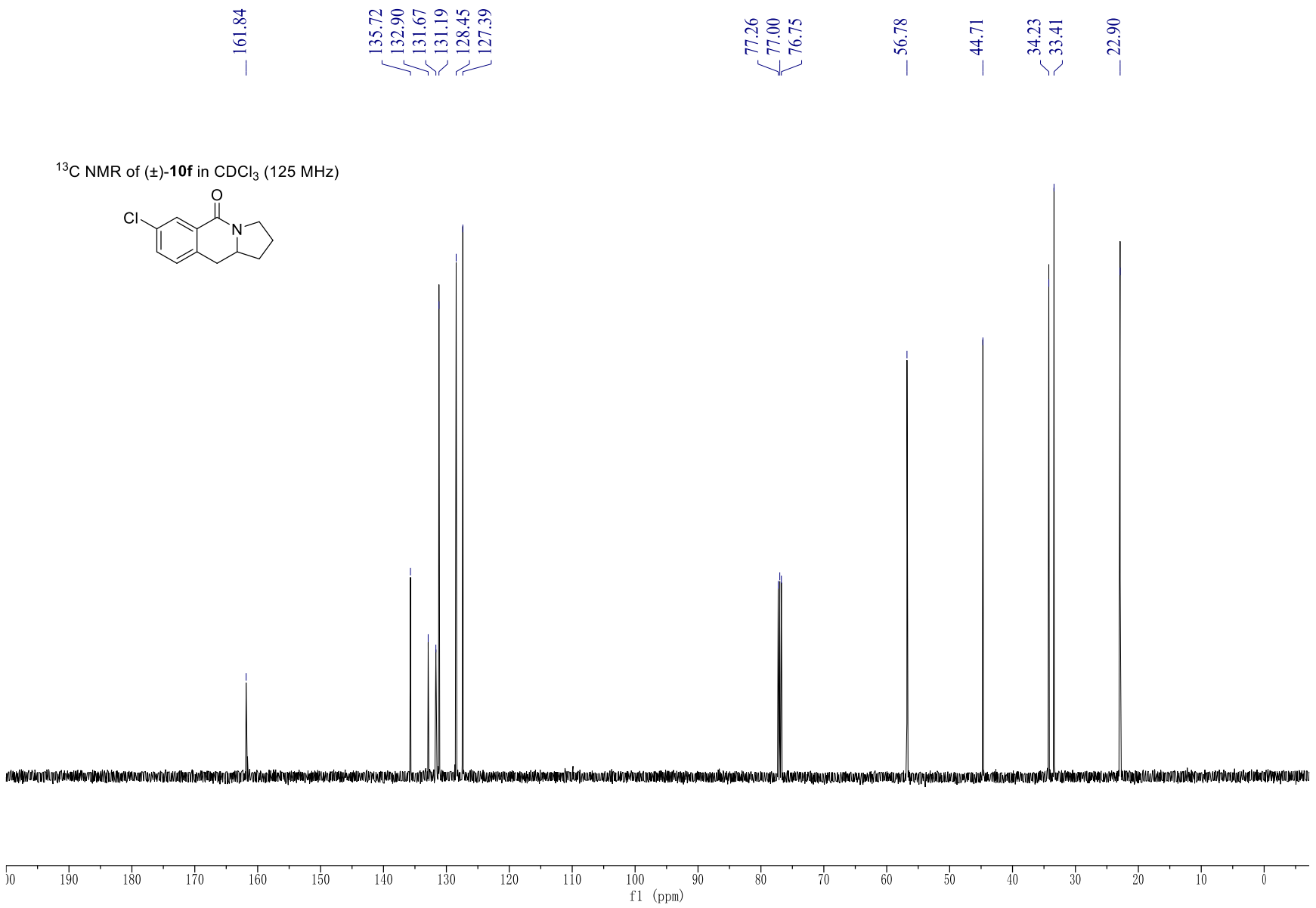


^{13}C NMR of (±)-**10e** in $CDCl_3$ (125 MHz)

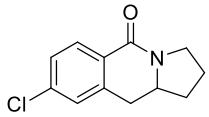
^{1}H NMR of (±)-**10f** in $CDCl_3$ (500 MHz)

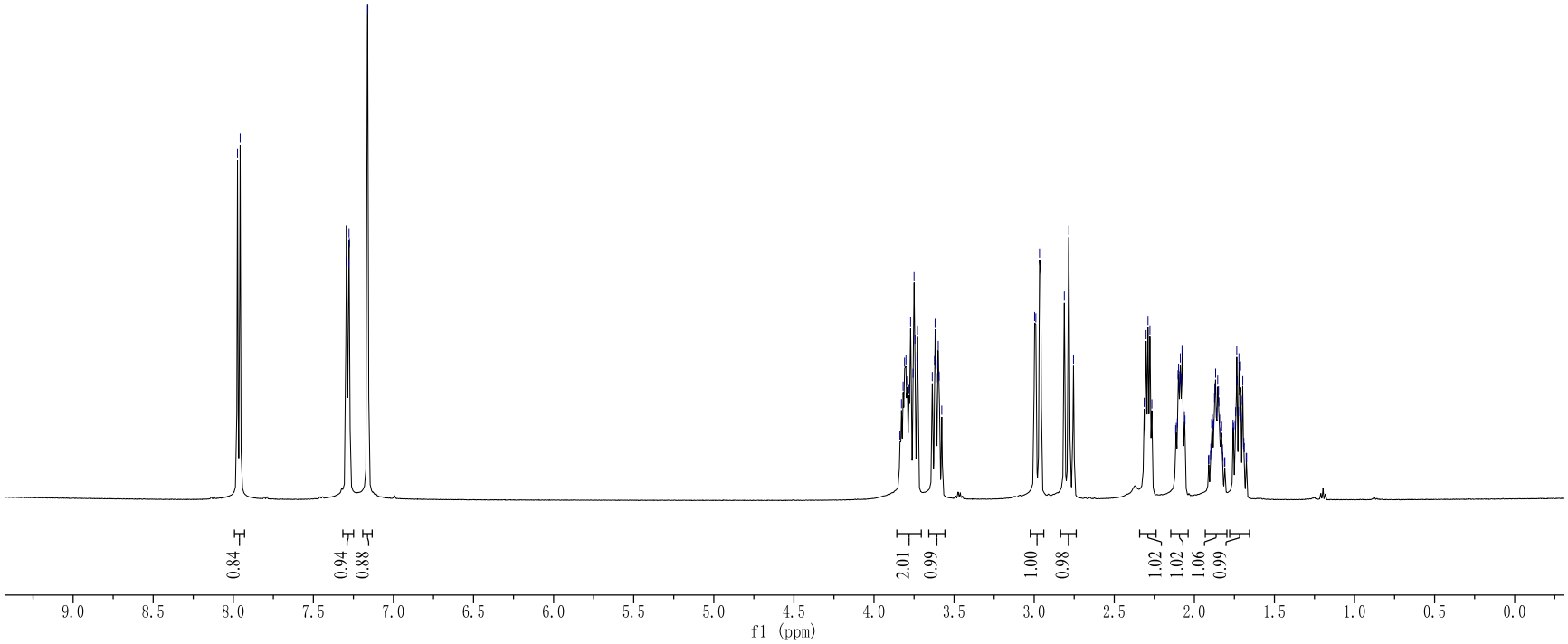


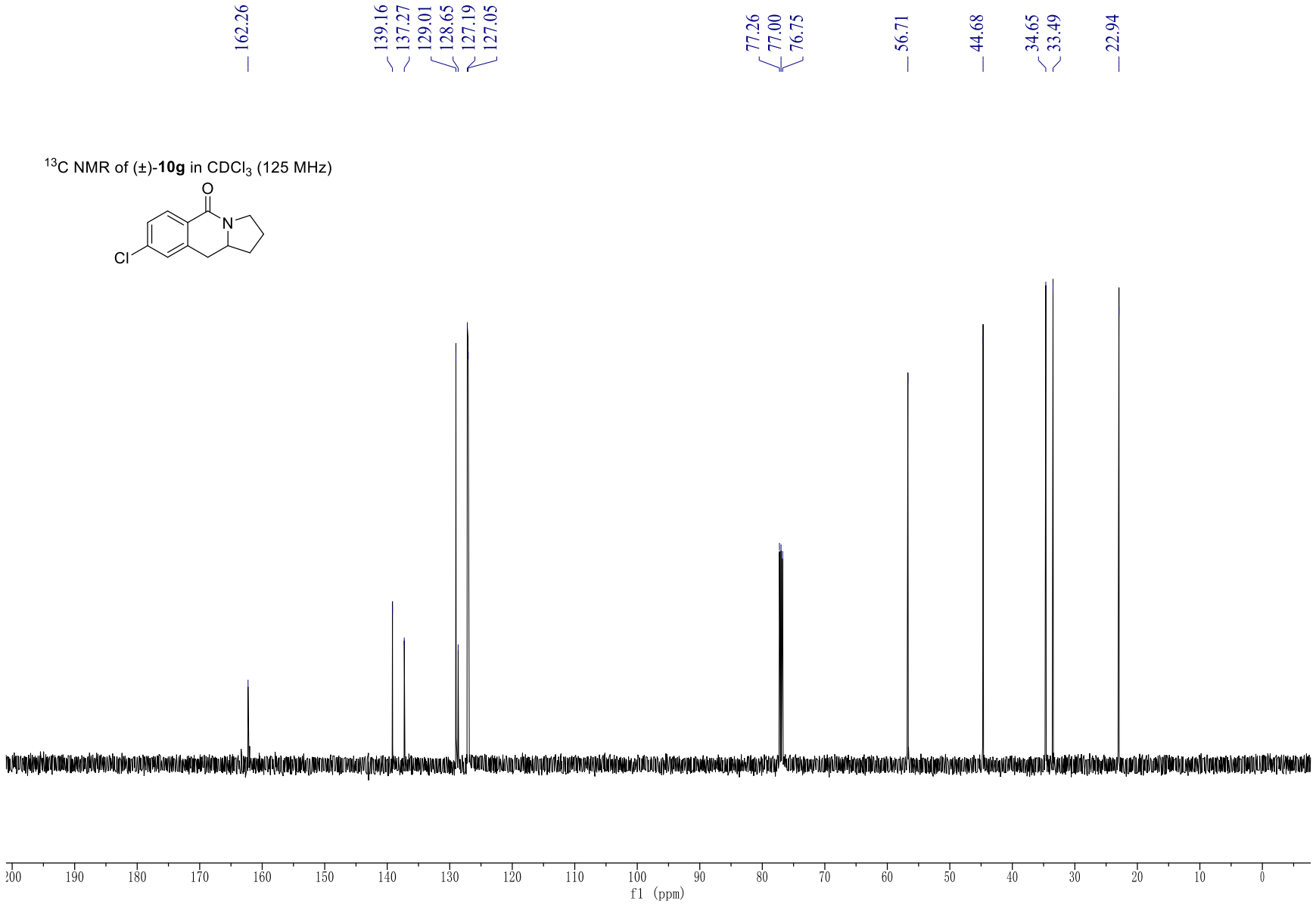



161.84
135.72
132.90
131.67
131.19
128.45
127.39
77.26
77.00
76.75
56.78
44.71
34.23
33.41
22.90
^{13}C NMR of (±)-**10f** in $CDCl_3$ (125 MHz)
Cl
O
N
f1 (ppm)

^{1}H NMR of (±)-**10g** in $CDCl_3$ (500 MHz)

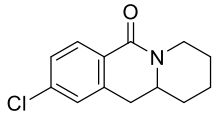


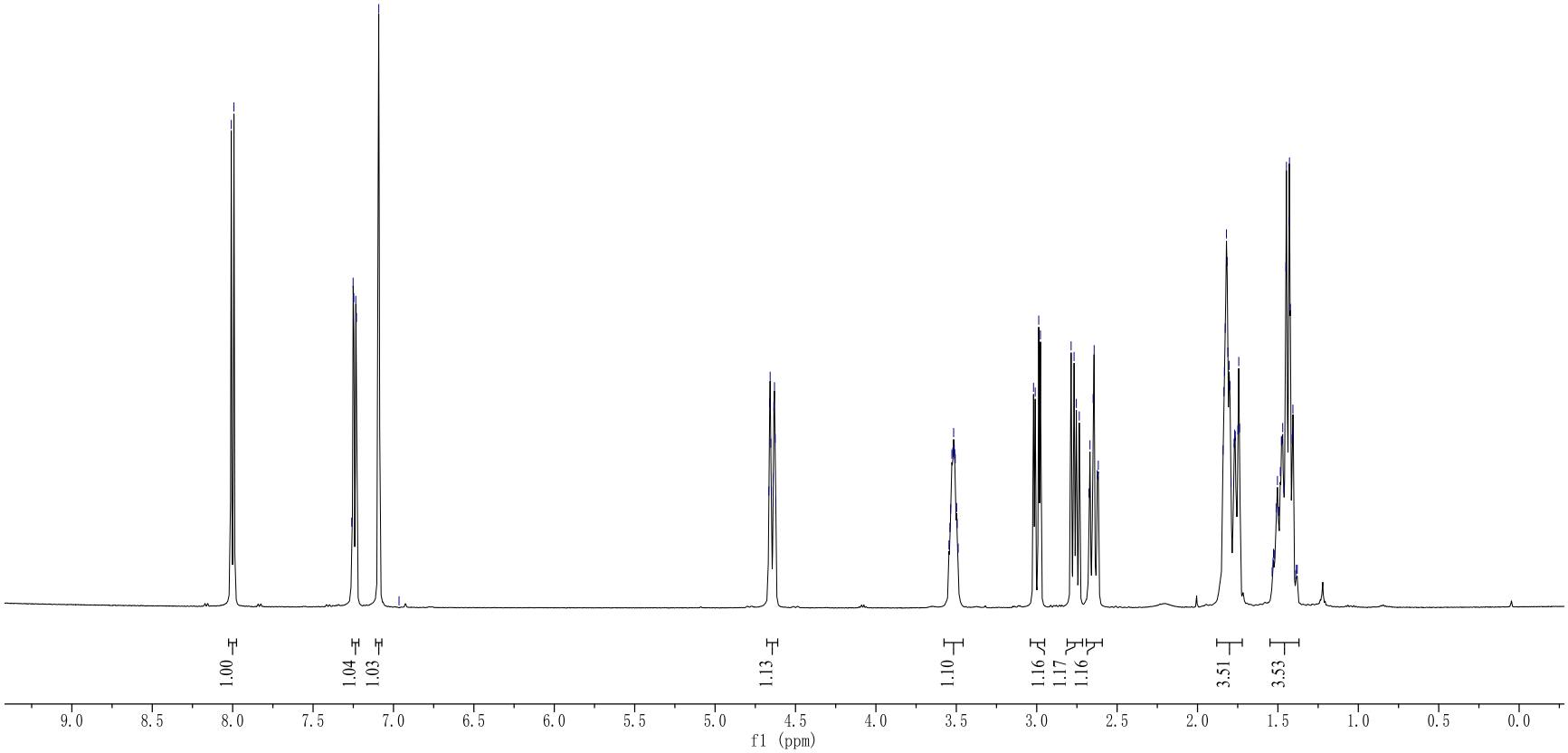


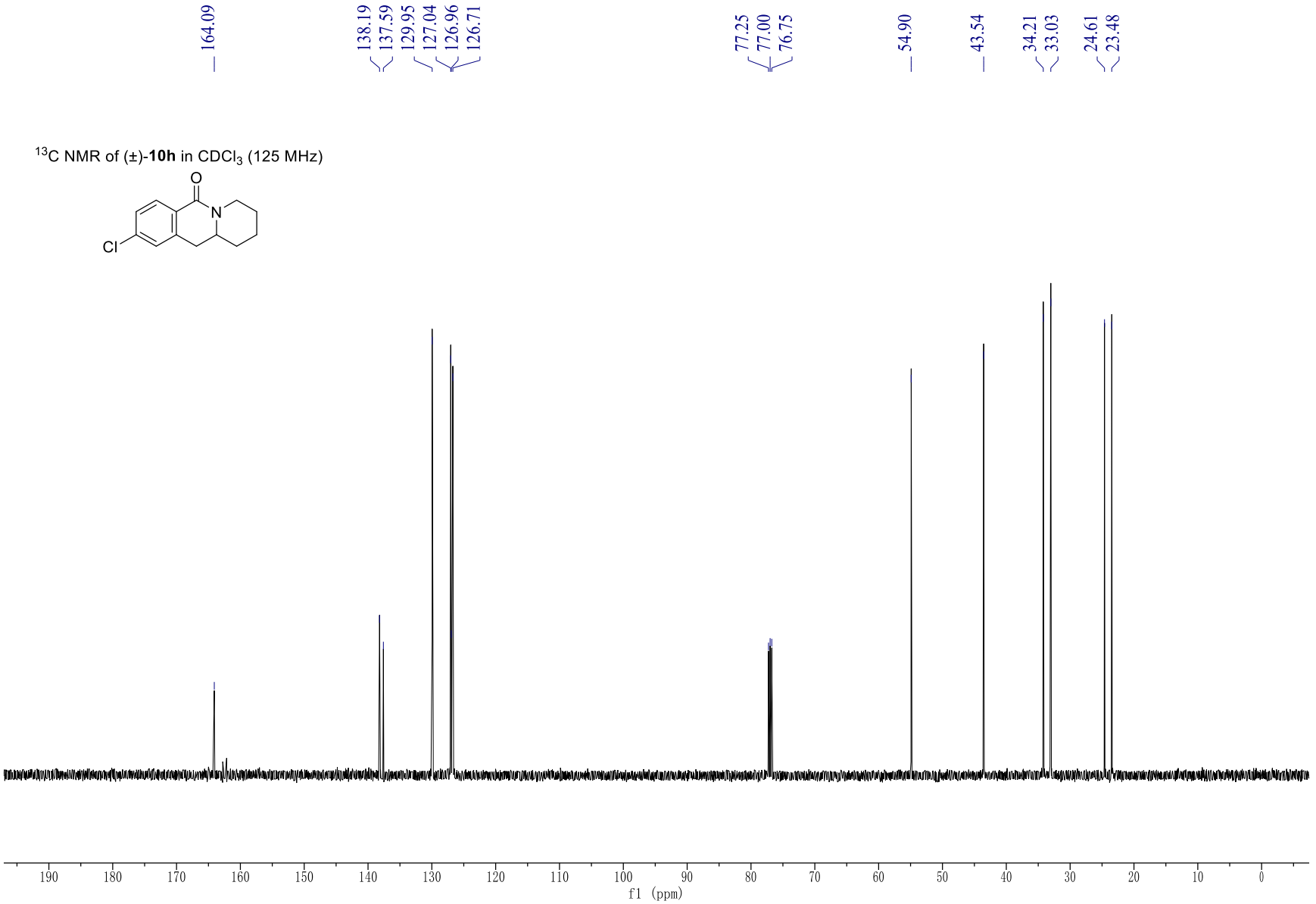


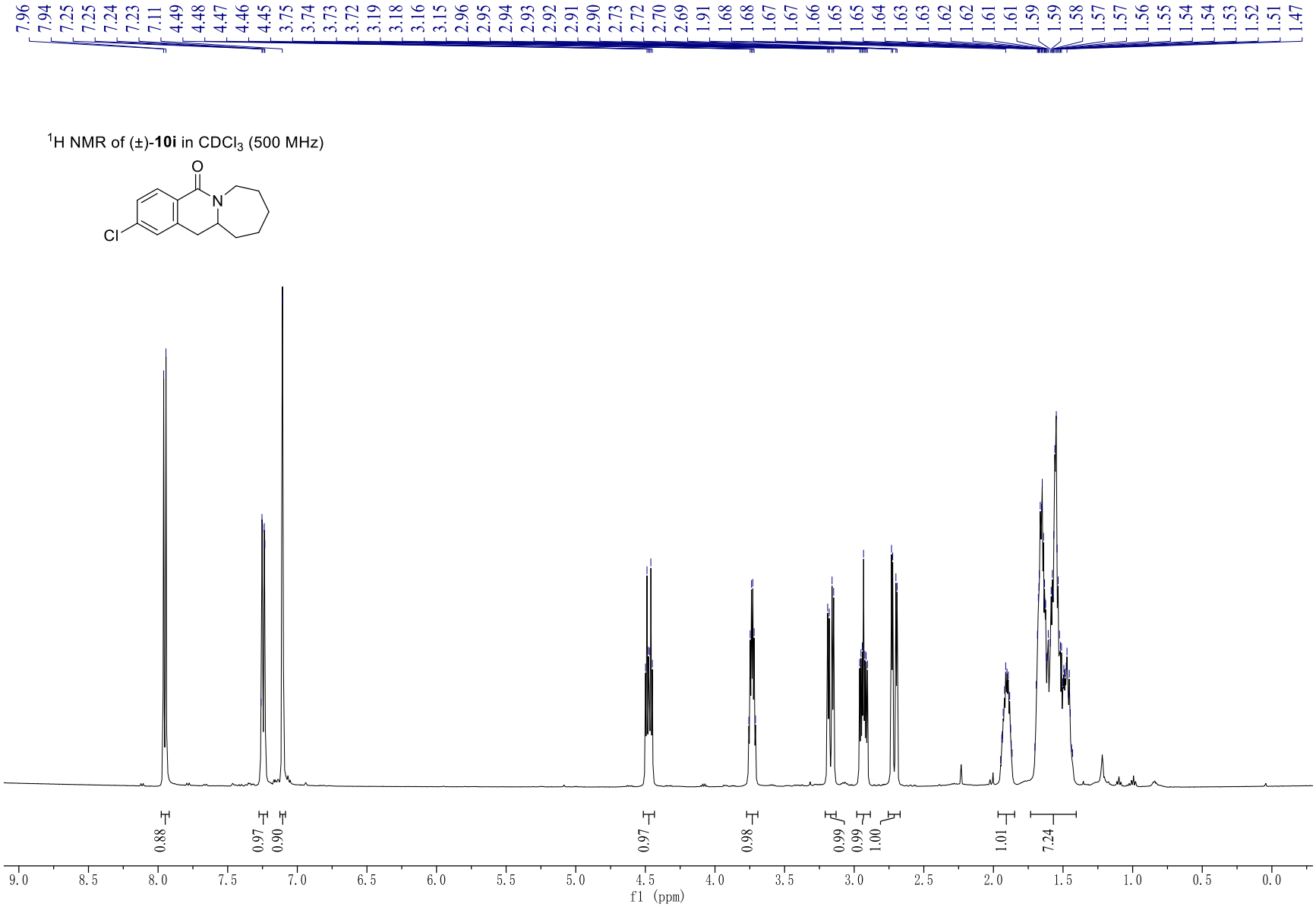
^{13}C NMR of (±)-**10g** in $CDCl_3$ (125 MHz)

^{1}H NMR of (±)-**10h** in $CDCl_3$ (500 MHz)

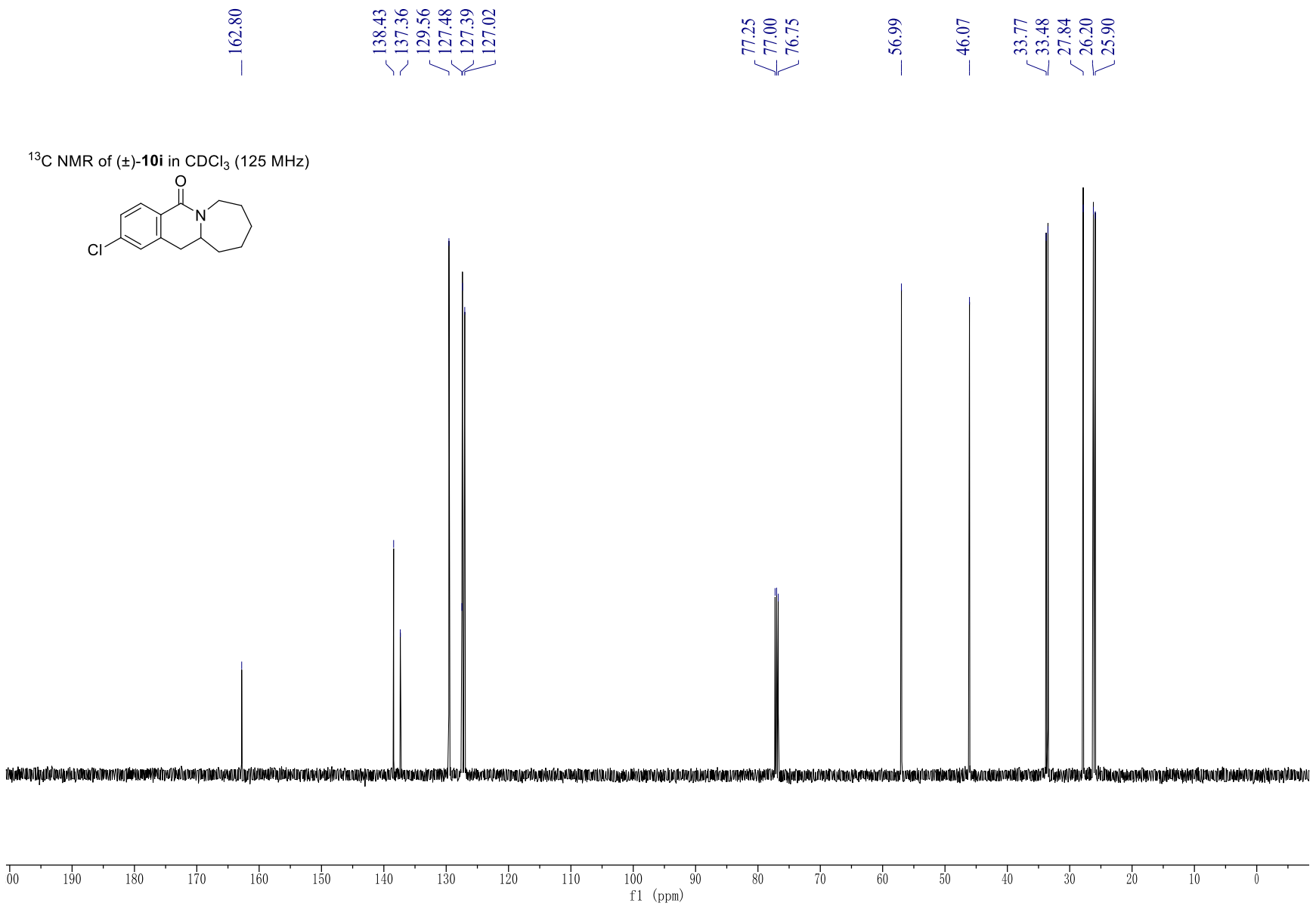


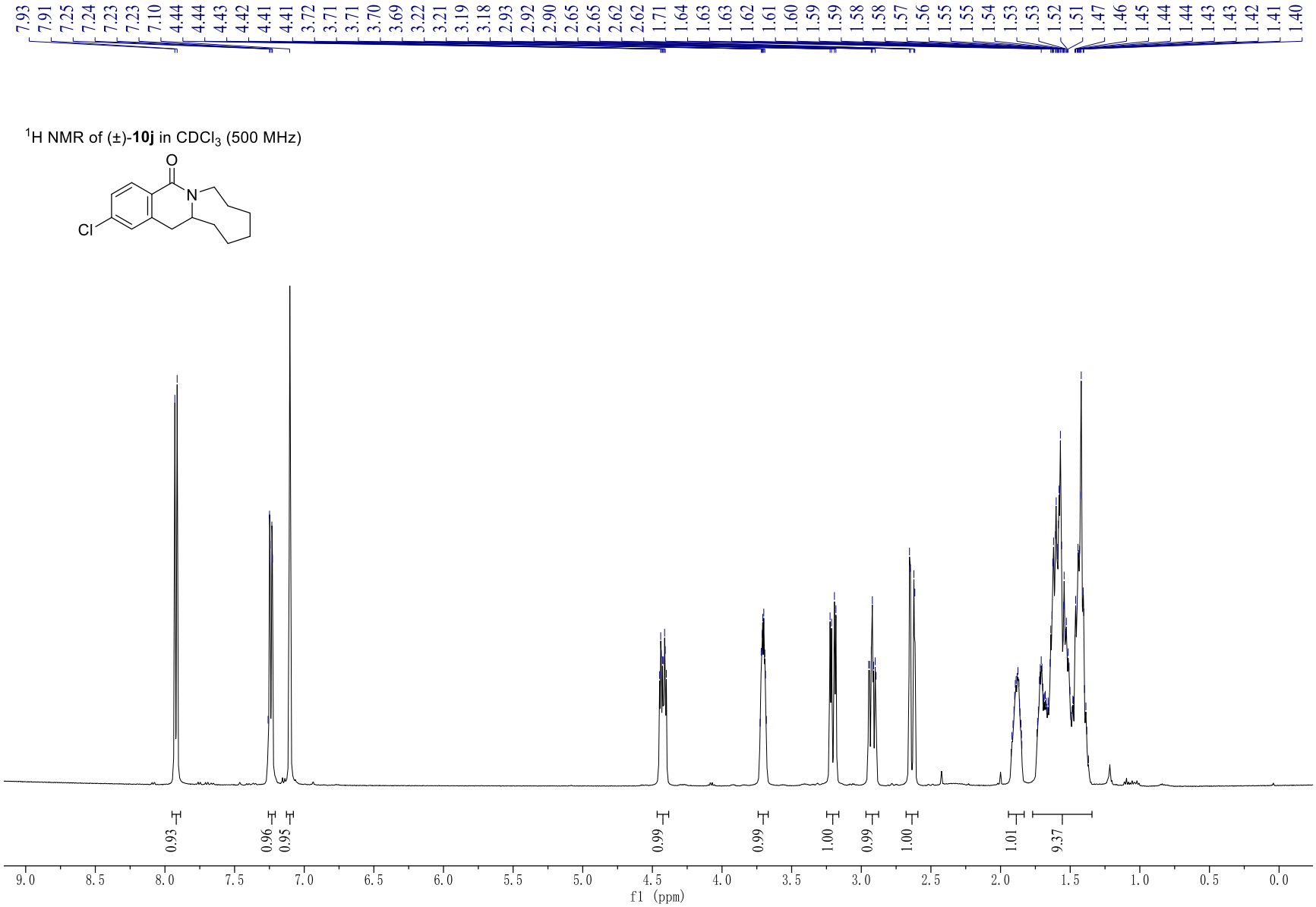


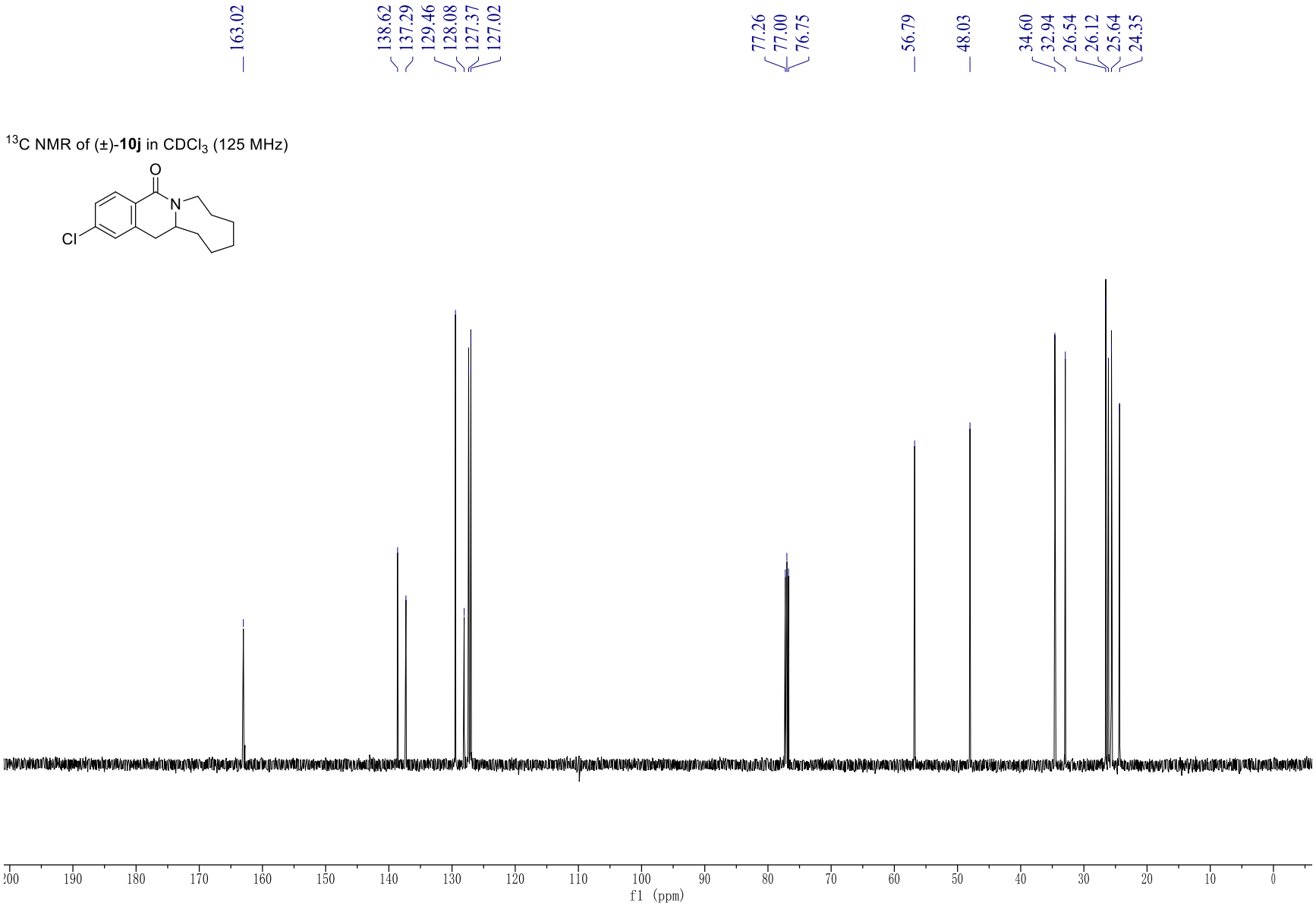

164.09
138.19
137.59
129.95
127.04
126.96
126.71
77.25
77.00
76.75
54.90
43.54
34.21
33.03
24.61
23.48
^{13}C NMR of (±)-**10h** in $CDCl_3$ (125 MHz)
O
N
Cl
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



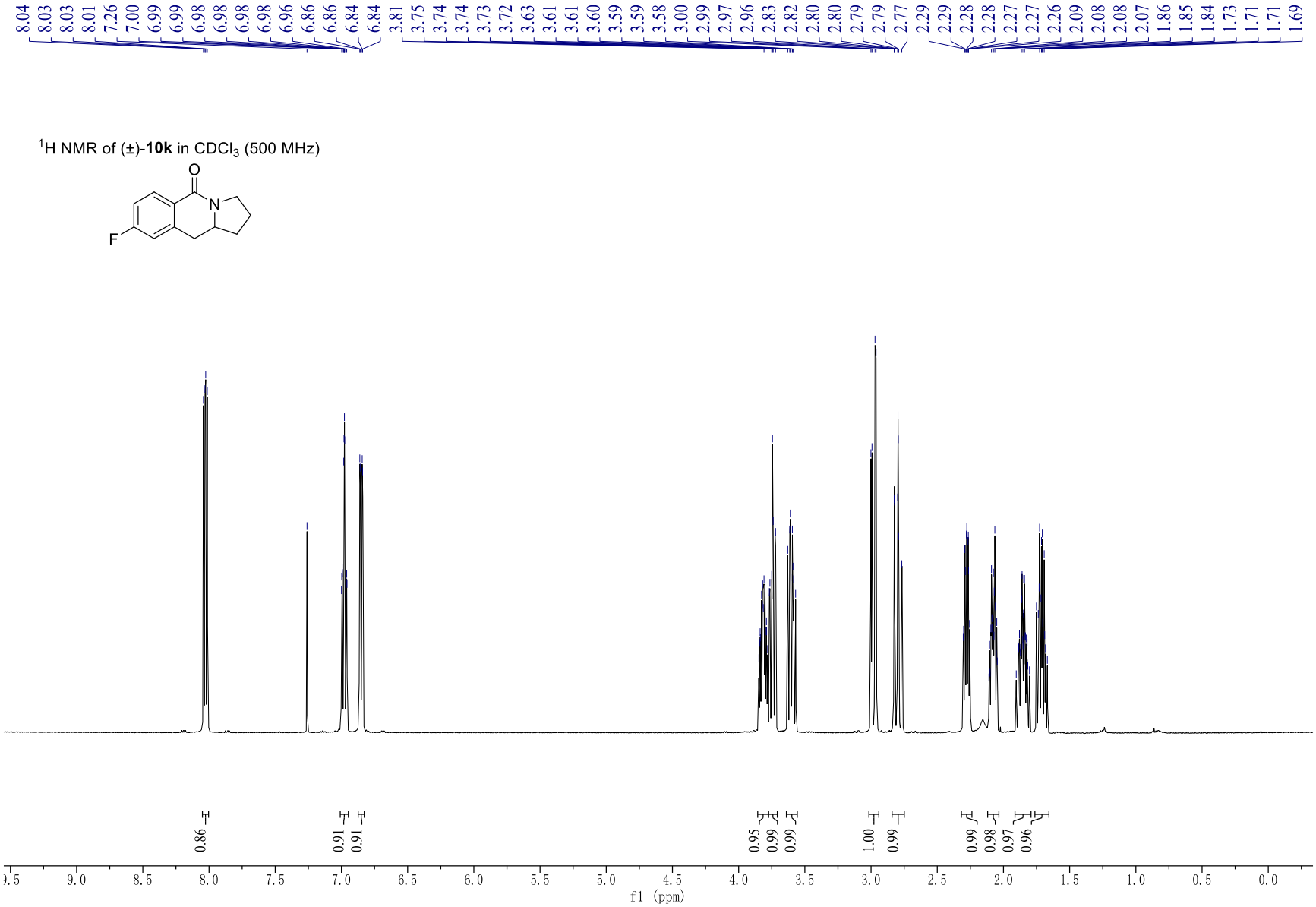
^{1}H NMR of (±)-**10i** in $CDCl_3$ (500 MHz)

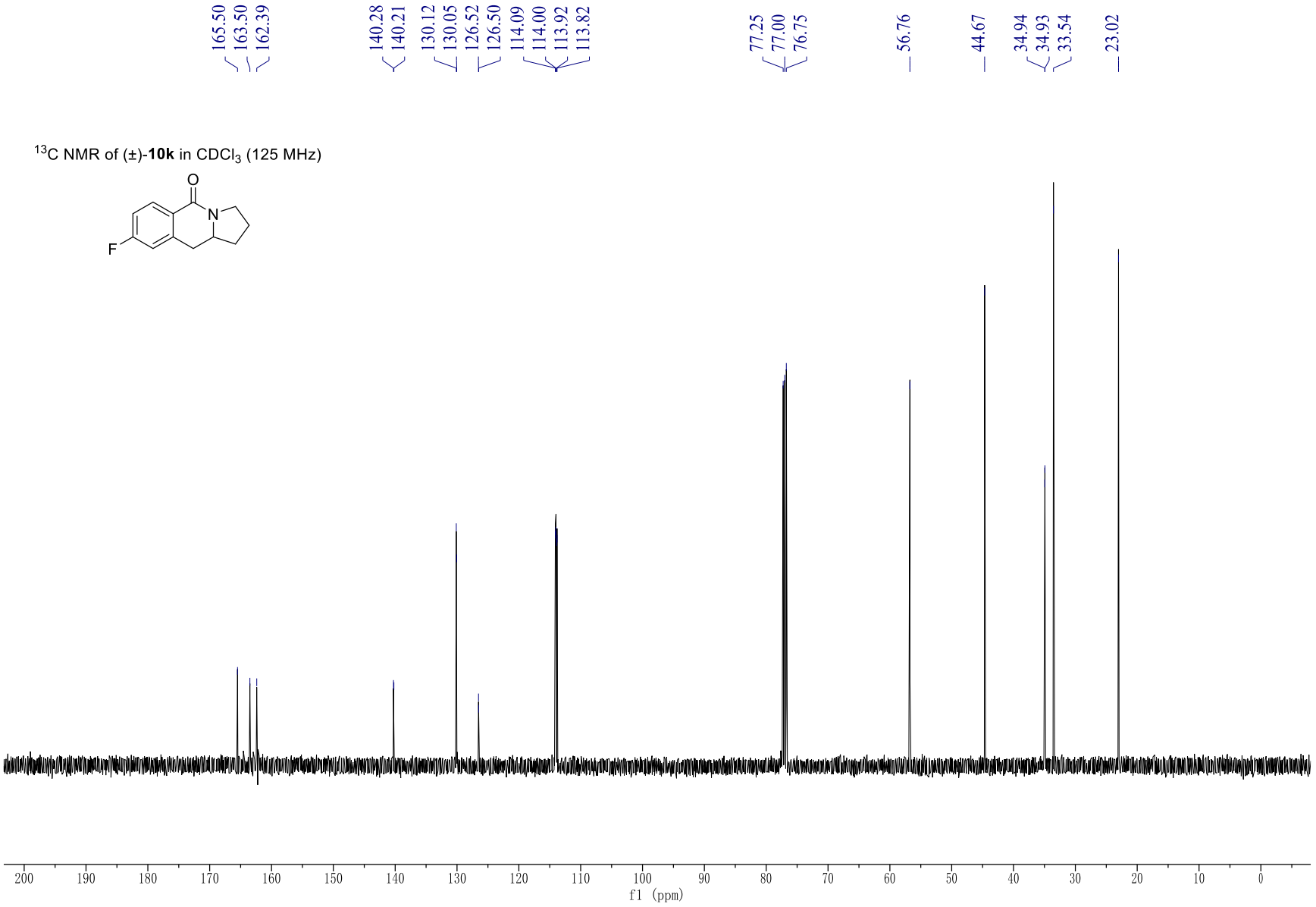

162.80
138.43
137.36
129.56
127.48
127.39
127.02
77.25
77.00
76.75
56.99
46.07
33.77
33.48
27.84
26.20
25.90
13C NMR of (±)-10i in CDCl3 (125 MHz)
O
N
Cl
f1 (ppm)


7.93 7.91 7.25 7.24 7.23 7.23 7.10 4.44 4.44 4.43 4.42 4.41 4.41 3.72 3.71 3.71 3.70 3.69 3.22 3.21 3.19 3.18 2.93 2.92 2.90 2.65 2.65 2.62 2.62 1.71 1.64 1.63 1.63 1.62 1.61 1.60 1.59 1.59 1.58 1.58 1.57 1.56 1.55 1.55 1.54 1.53 1.53 1.52 1.51 1.47 1.46 1.45 1.44 1.44 1.43 1.43 1.42 1.41 1.40
^{1}H NMR of (±)-**10j** in $CDCl_3$ (500 MHz)
O
N
Cl
0.93
0.96
0.95
0.99
0.99
1.00
0.99
1.00
1.01
9.37
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
f1 (ppm)

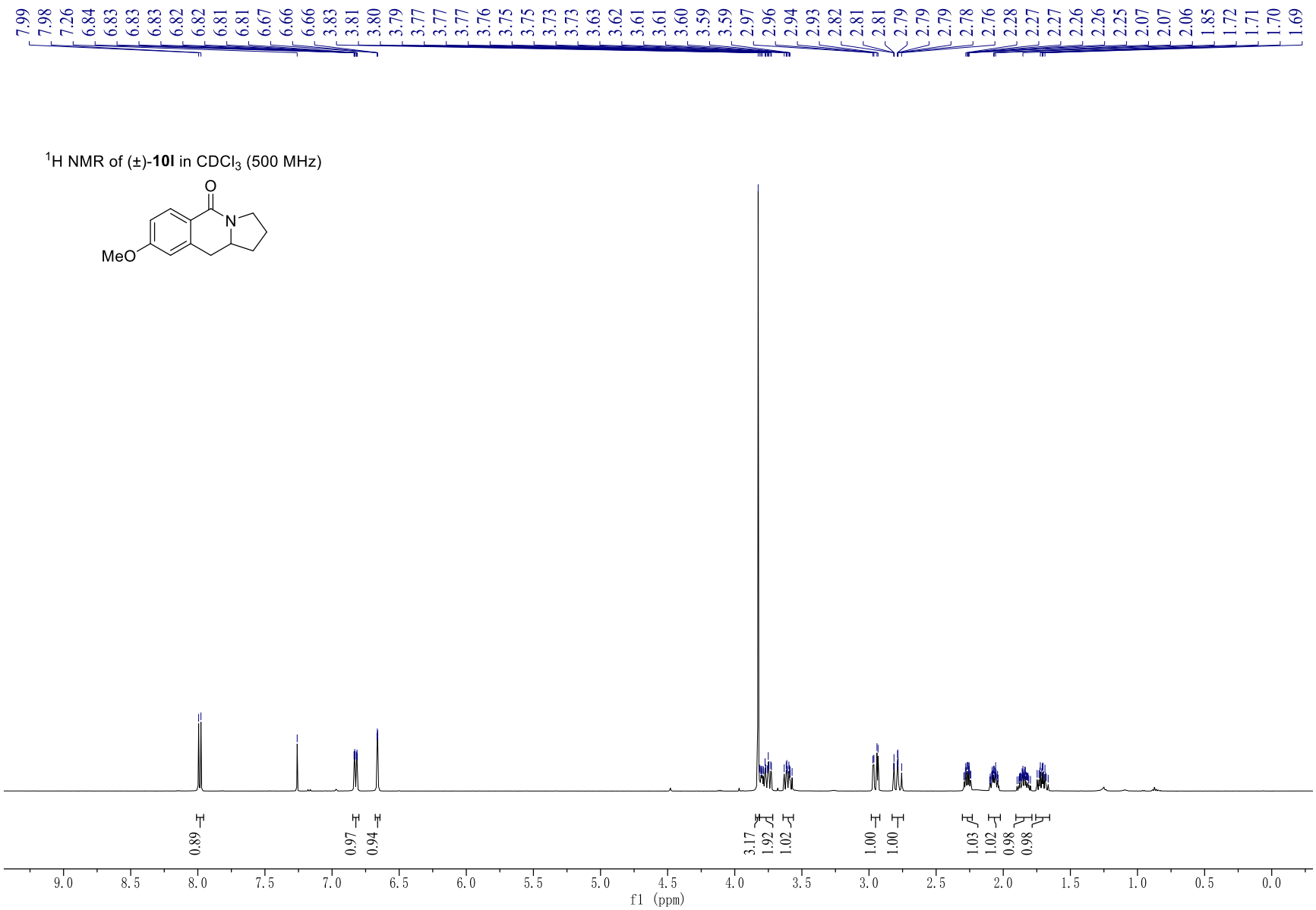


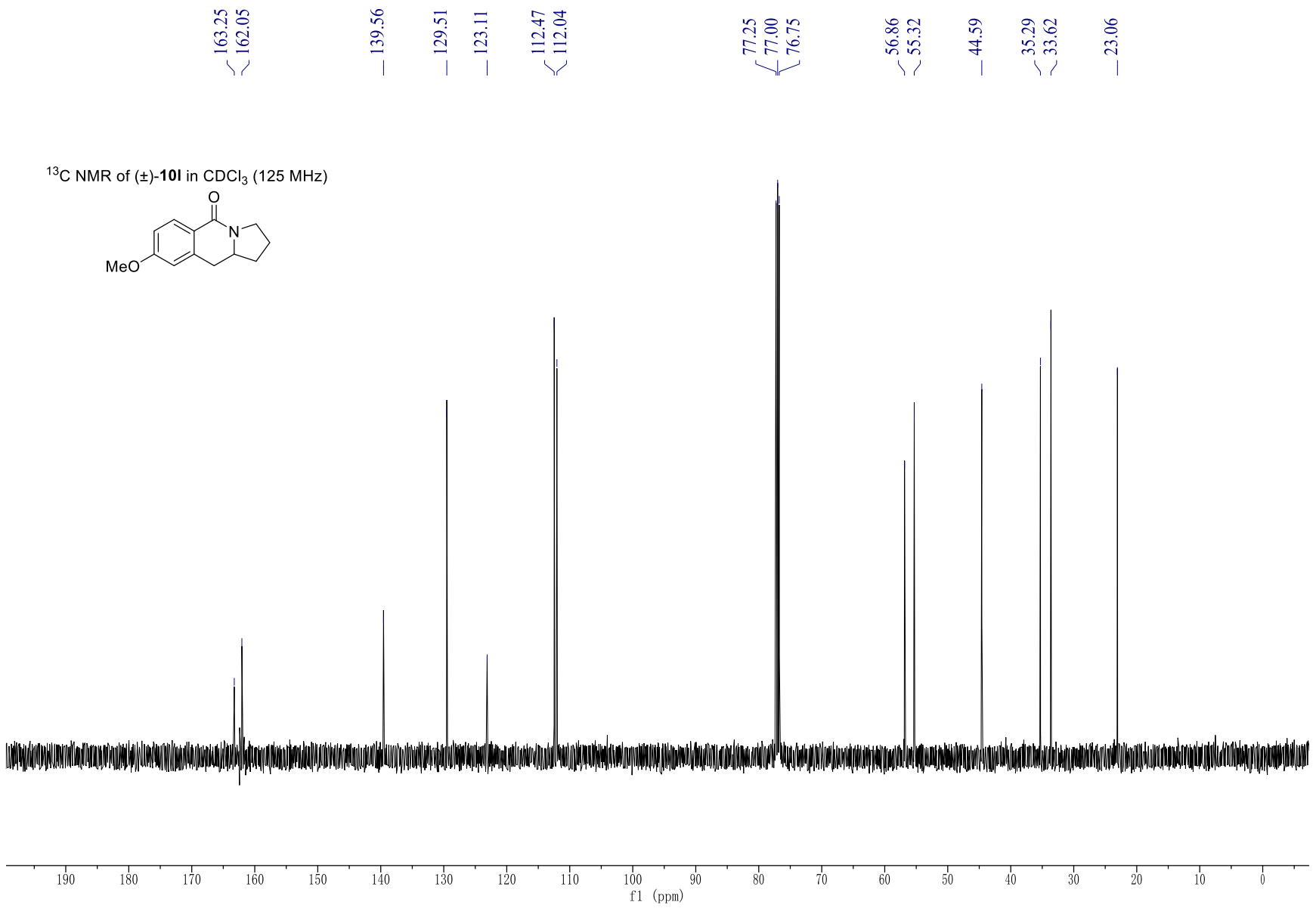
^{13}C NMR of (±)-**10j** in $CDCl_3$ (125 MHz)

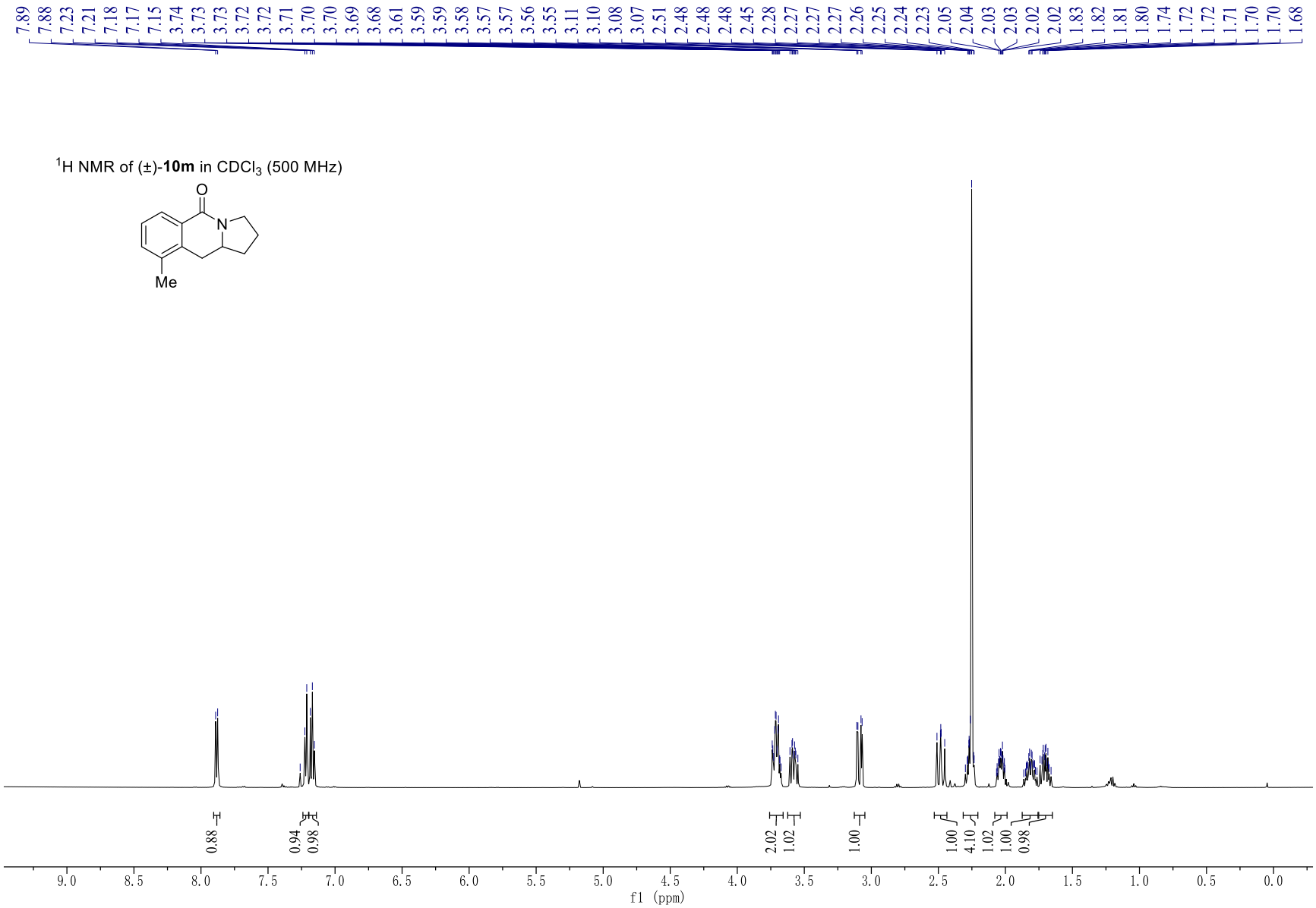

8.04 8.03 8.03 8.01 7.26 7.00 6.99 6.99 6.98 6.98 6.98 6.98 6.96 6.86 6.86 6.84 6.84
3.81 3.75 3.74 3.74 3.73 3.72 3.63 3.61 3.61 3.60 3.59 3.59 3.58 3.00 2.99 2.97 2.96 2.83 2.82 2.80 2.80 2.79 2.79 2.77
2.29 2.29 2.28 2.28 2.27 2.27 2.26 2.09 2.08 2.08 2.07 1.86 1.85 1.84 1.73 1.71 1.71 1.69
^{1}H NMR of (±)-**10k** in $CDCl_3$ (500 MHz)
O
N
F
0.86 0.91 0.91 0.95 0.99 0.99 1.00 0.99 0.99 0.98 0.97 0.96
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
f1 (ppm)

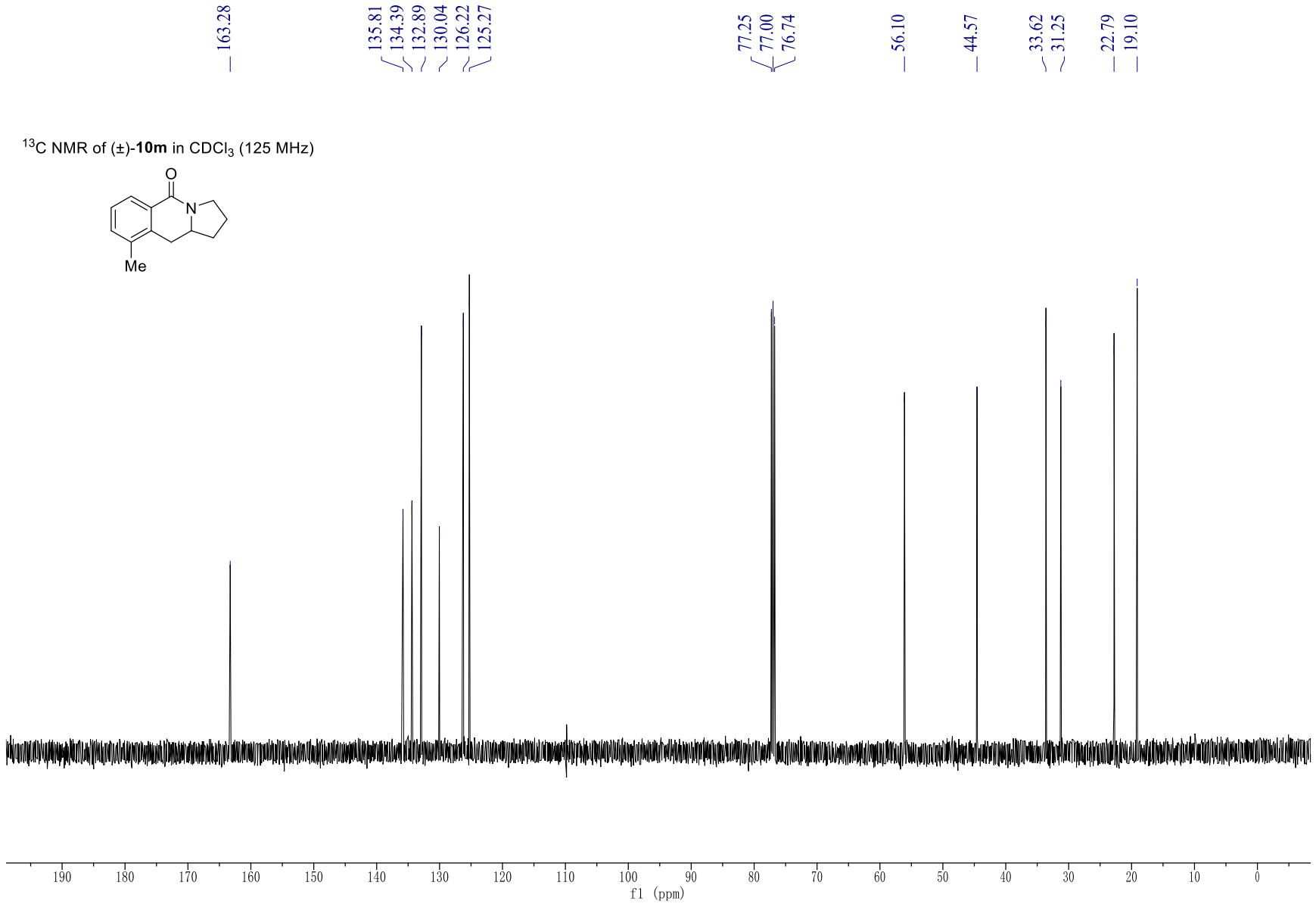


^{13}C NMR of (±)-**10k** in $CDCl_3$ (125 MHz)

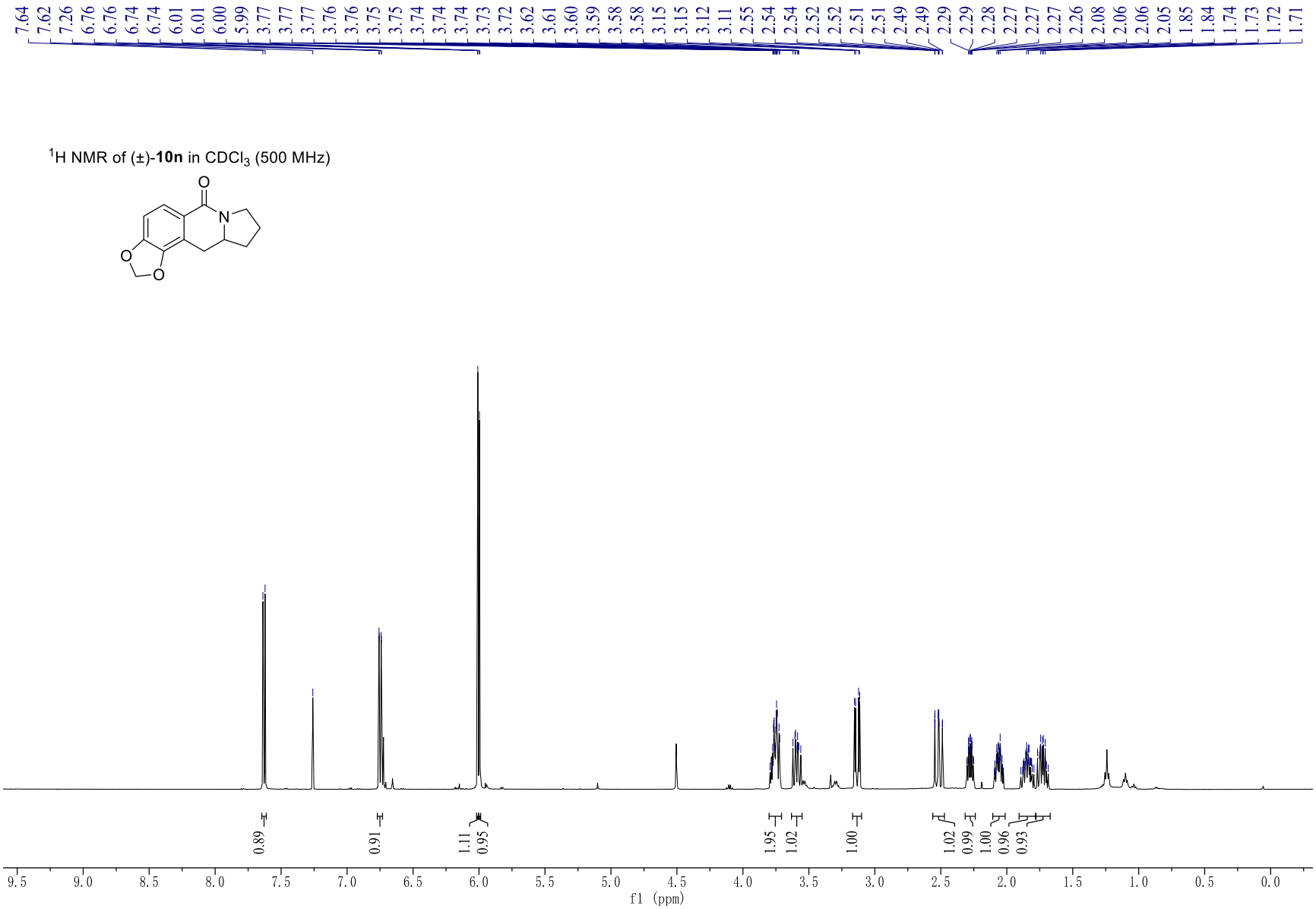

7.99
7.98
7.26
6.84
6.83
6.83
6.83
6.82
6.82
6.81
6.81
6.67
6.66
6.66
3.83
3.81
3.80
3.79
3.77
3.77
3.77
3.76
3.75
3.75
3.73
3.73
3.63
3.62
3.61
3.61
3.60
3.59
3.59
2.97
2.96
2.94
2.93
2.82
2.81
2.81
2.79
2.79
2.79
2.78
2.76
2.28
2.27
2.27
2.26
2.26
2.25
2.07
2.07
2.06
1.85
1.72
1.71
1.70
1.69
1H NMR of (±)-10l in CDCl3 (500 MHz)
O
N
MeO
0.89
0.97
0.94
3.17
1.92
1.02
1.00
1.00
1.03
1.02
0.98
0.98
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
f1 (ppm)


163.25
162.05
139.56
129.51
123.11
112.47
112.04
77.25
77.00
76.75
56.86
55.32
44.59
35.29
33.62
23.06
^{13}C NMR of (±)-**10l** in $CDCl_3$ (125 MHz)
O
N
MeO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.89
7.88
7.23
7.21
7.18
7.17
7.15
3.74
3.73
3.73
3.72
3.72
3.71
3.70
3.70
3.69
3.68
3.61
3.59
3.59
3.58
3.57
3.57
3.56
3.55
3.11
3.10
3.08
3.07
2.51
2.48
2.48
2.48
2.45
2.28
2.27
2.27
2.27
2.26
2.25
2.24
2.23
2.05
2.04
2.03
2.03
2.02
2.02
1.83
1.82
1.81
1.80
1.74
1.72
1.72
1.71
1.70
1.70
1.68
^{1}H NMR of (±)-**10m** in $CDCl_3$ (500 MHz)
O
N
Me
0.88
0.94
0.98
2.02
1.02
1.00
1.00
4.10
1.02
1.00
0.98
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
f1 (ppm)

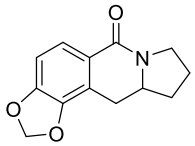


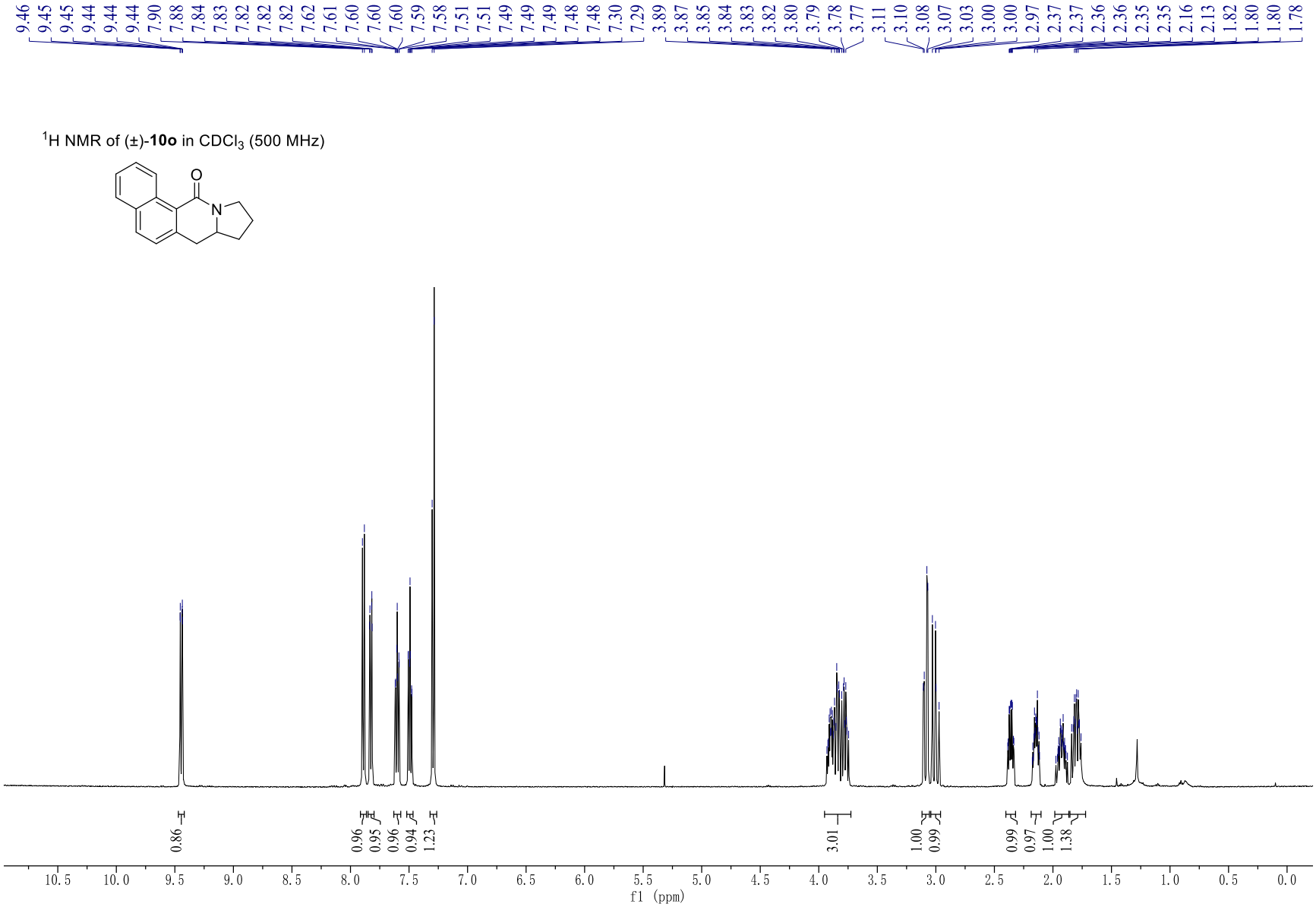
^{13}C NMR of (±)-**10m** in $CDCl_3$ (125 MHz)

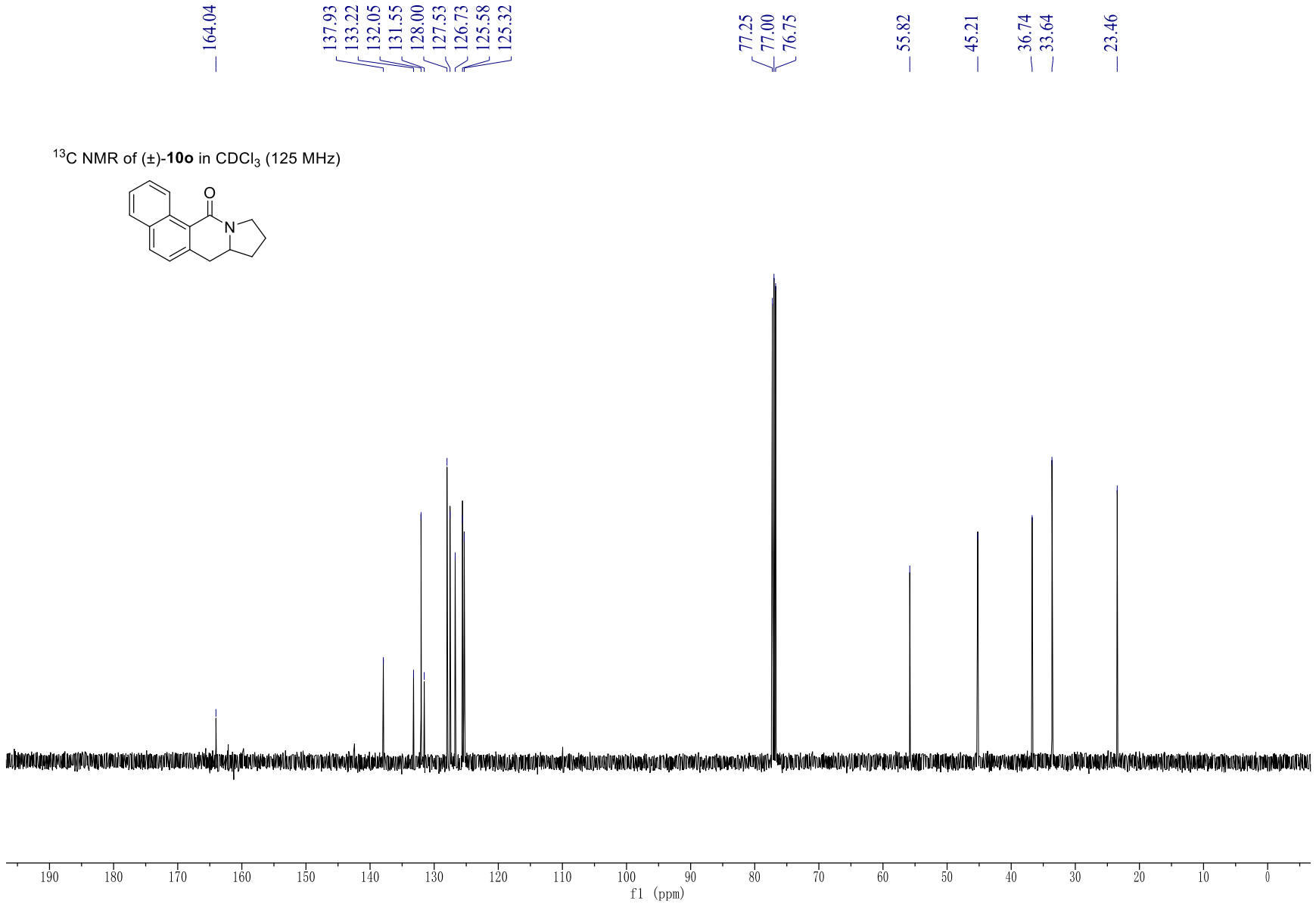


^{1}H NMR of (±)-**10n** in $CDCl_3$ (500 MHz)

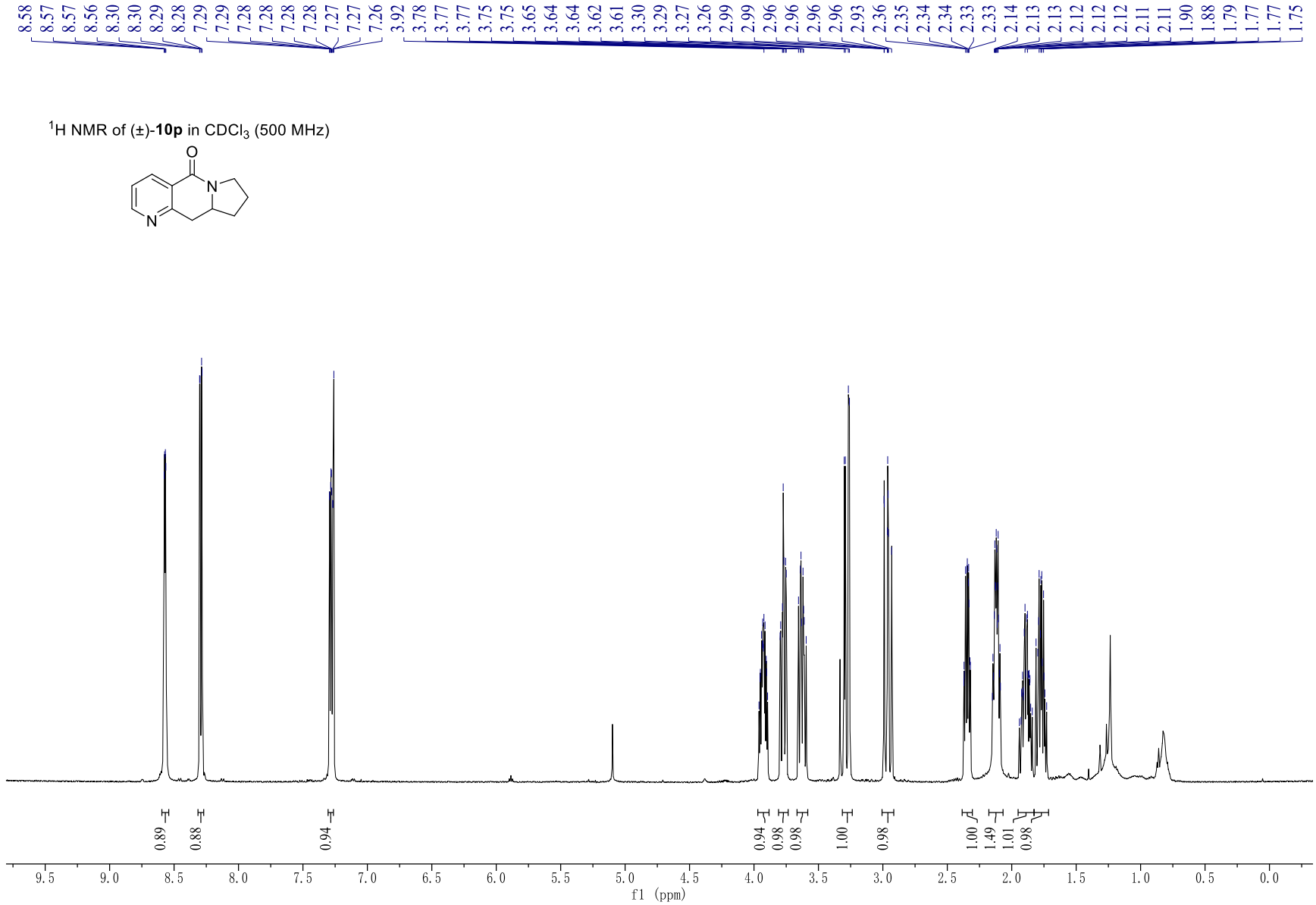
^{13}C NMR of (±)-**10n** in $CDCl_3$ (125 MHz)

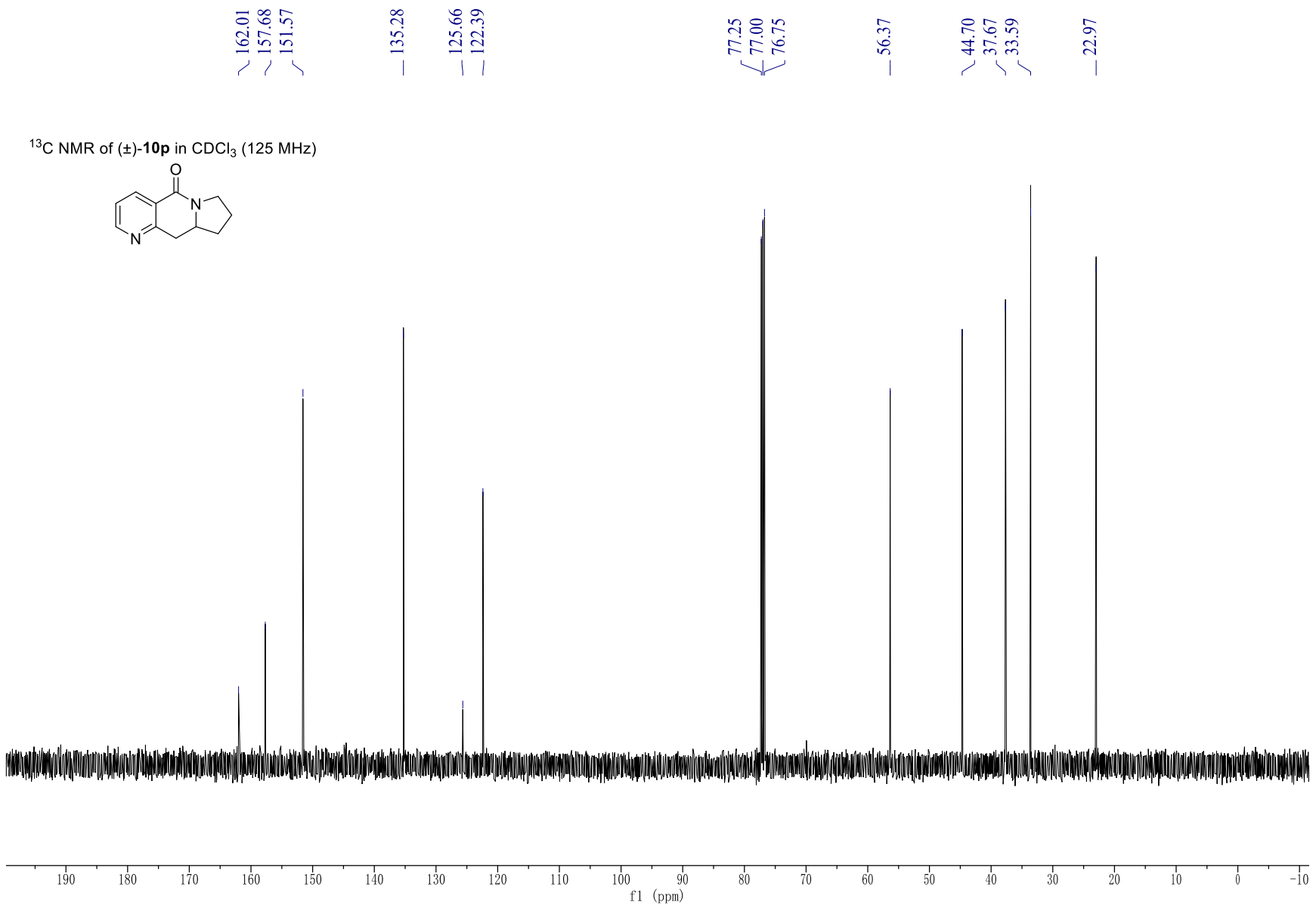



9.46 9.45 9.45 9.44 9.44 9.44 7.90 7.88 7.84 7.83 7.82 7.82 7.82 7.62 7.61 7.60 7.60 7.60 7.59 7.58 7.51 7.51 7.49 7.49 7.49 7.48 7.48 7.30 7.29
3.89 3.87 3.85 3.84 3.83 3.82 3.80 3.79 3.78 3.77
3.11 3.10 3.08 3.07 3.03 3.00 3.00 2.97 2.37 2.37 2.36 2.36 2.35 2.35 2.16 2.13 1.82 1.80 1.80 1.78
^{1}H NMR of (±)-**10o** in $CDCl_3$ (500 MHz)
O
N
0.86
0.96 0.95 0.96 0.94 1.23
3.01
1.00 0.99
0.99 0.97 1.00 1.38
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
f1 (ppm)

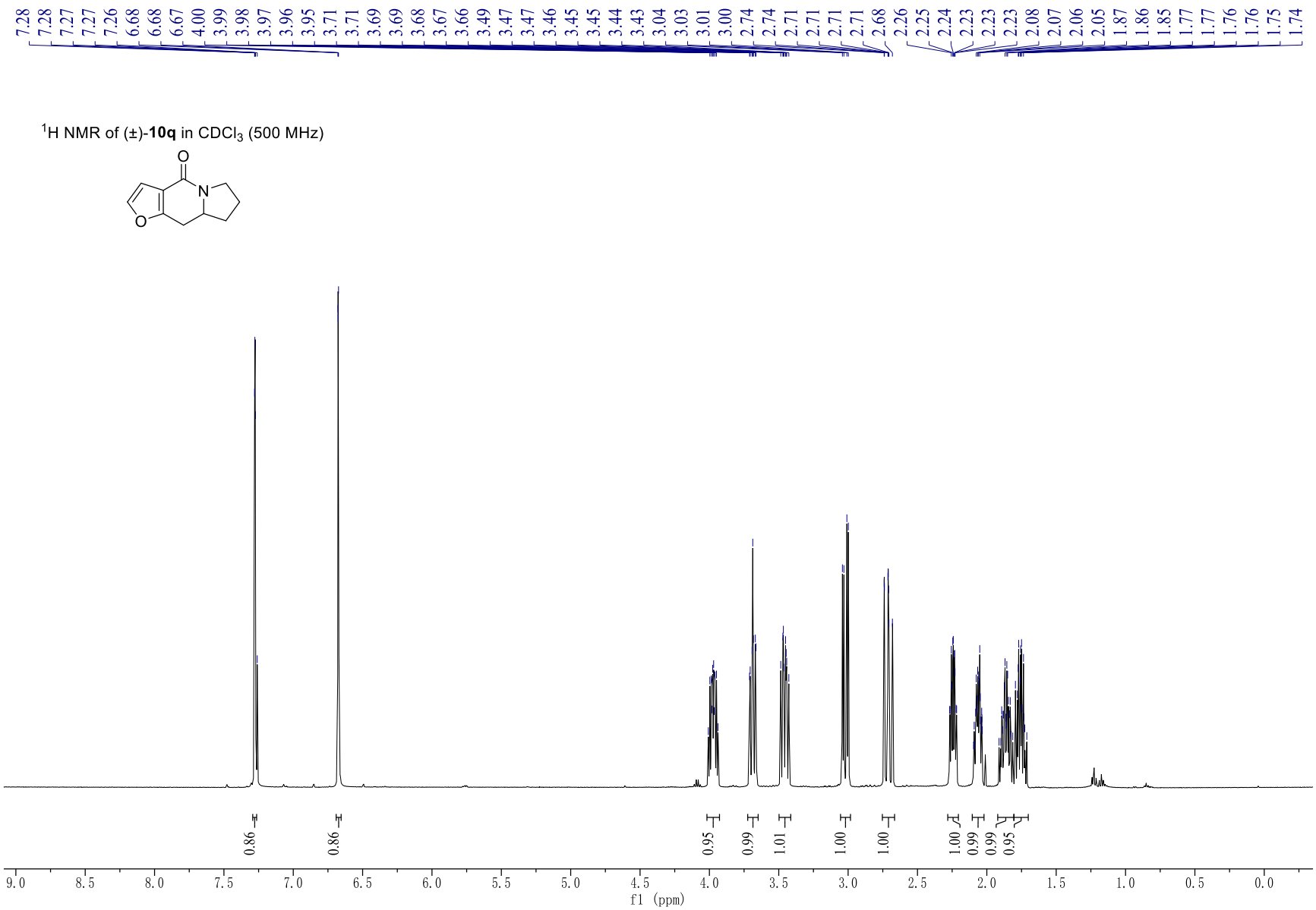


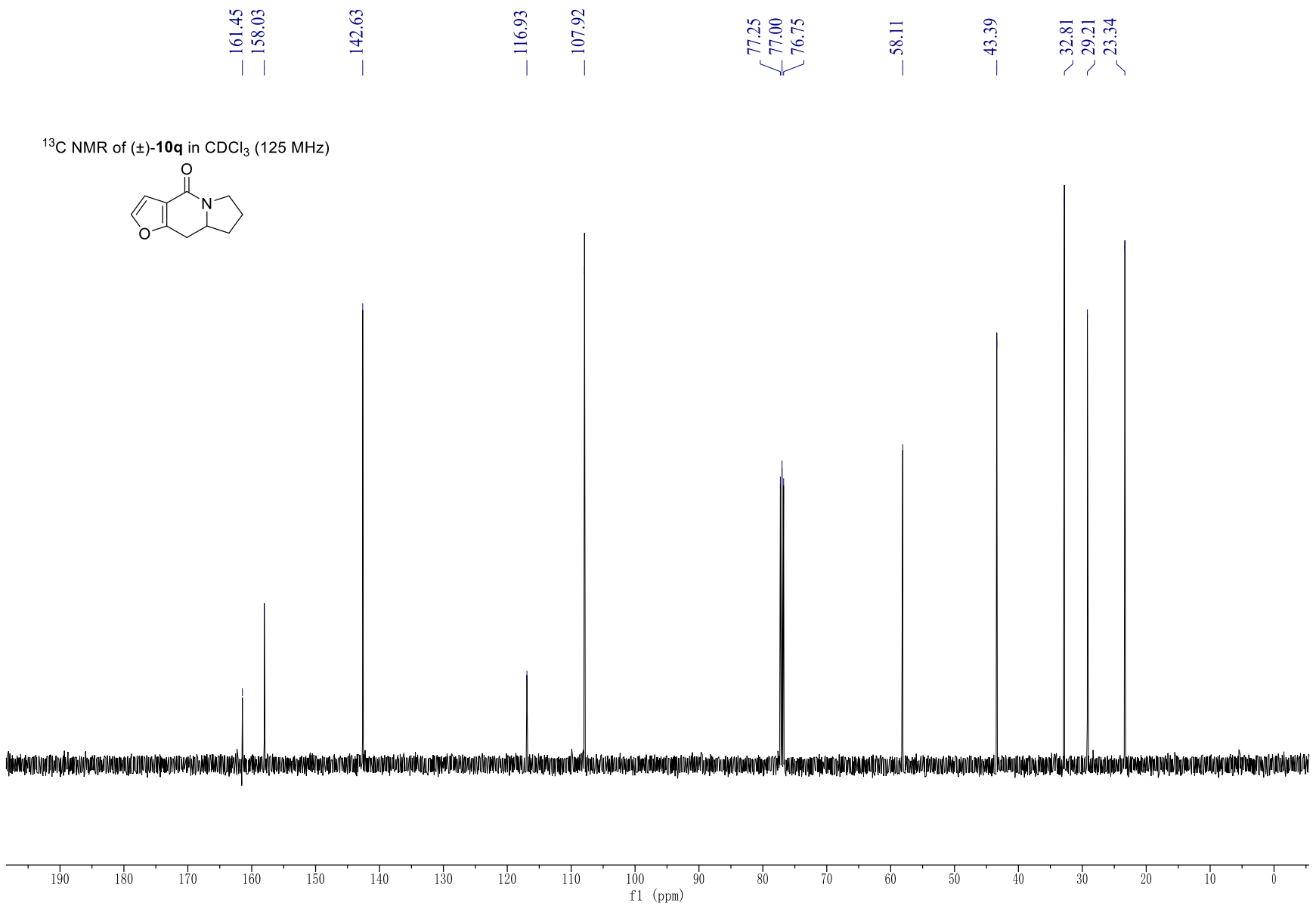
^{13}C NMR of (±)-**10o** in $CDCl_3$ (125 MHz)


8.58 8.57 8.57 8.56 8.30 8.30 8.29 8.28 7.29 7.29 7.28 7.28 7.28 7.28 7.27 7.27 7.26
3.92 3.78 3.77 3.77 3.75 3.75 3.65 3.64 3.64 3.62 3.61 3.30 3.29 3.27 3.26 2.99 2.99 2.96 2.96 2.96 2.96 2.93 2.36 2.35 2.34 2.34 2.33 2.33 2.14 2.13 2.13 2.12 2.12 2.12 2.11 2.11 1.90 1.88 1.79 1.77 1.77 1.75
^{1}H NMR of (±)-**10p** in $CDCl_3$ (500 MHz)
O
N
N
0.89 0.88 0.94 0.94 0.98 0.98 1.00 0.98 1.00 1.49 1.01 0.98
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
f1 (ppm)

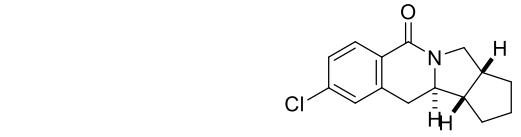


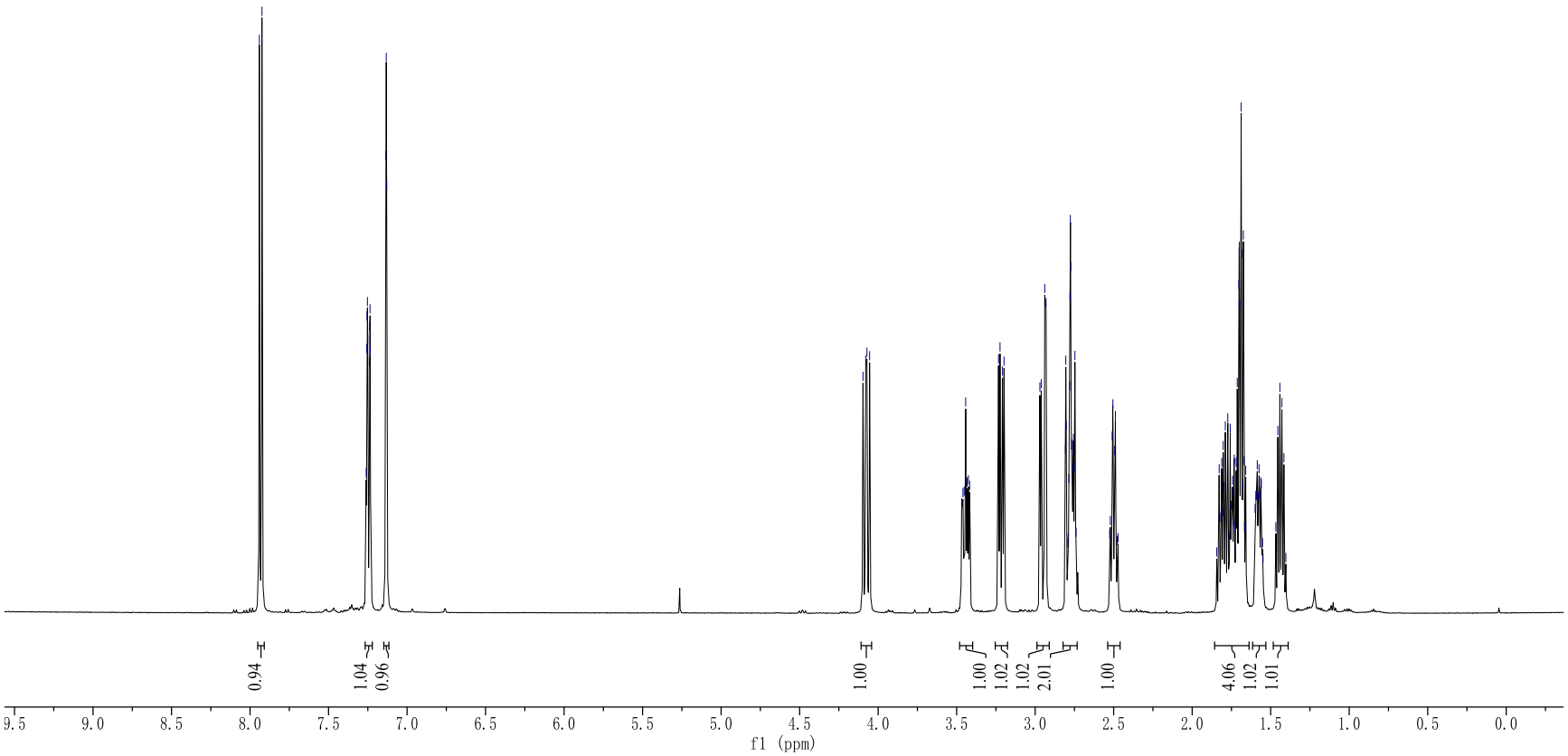
^{13}C NMR of (±)-**10p** in $CDCl_3$ (125 MHz)

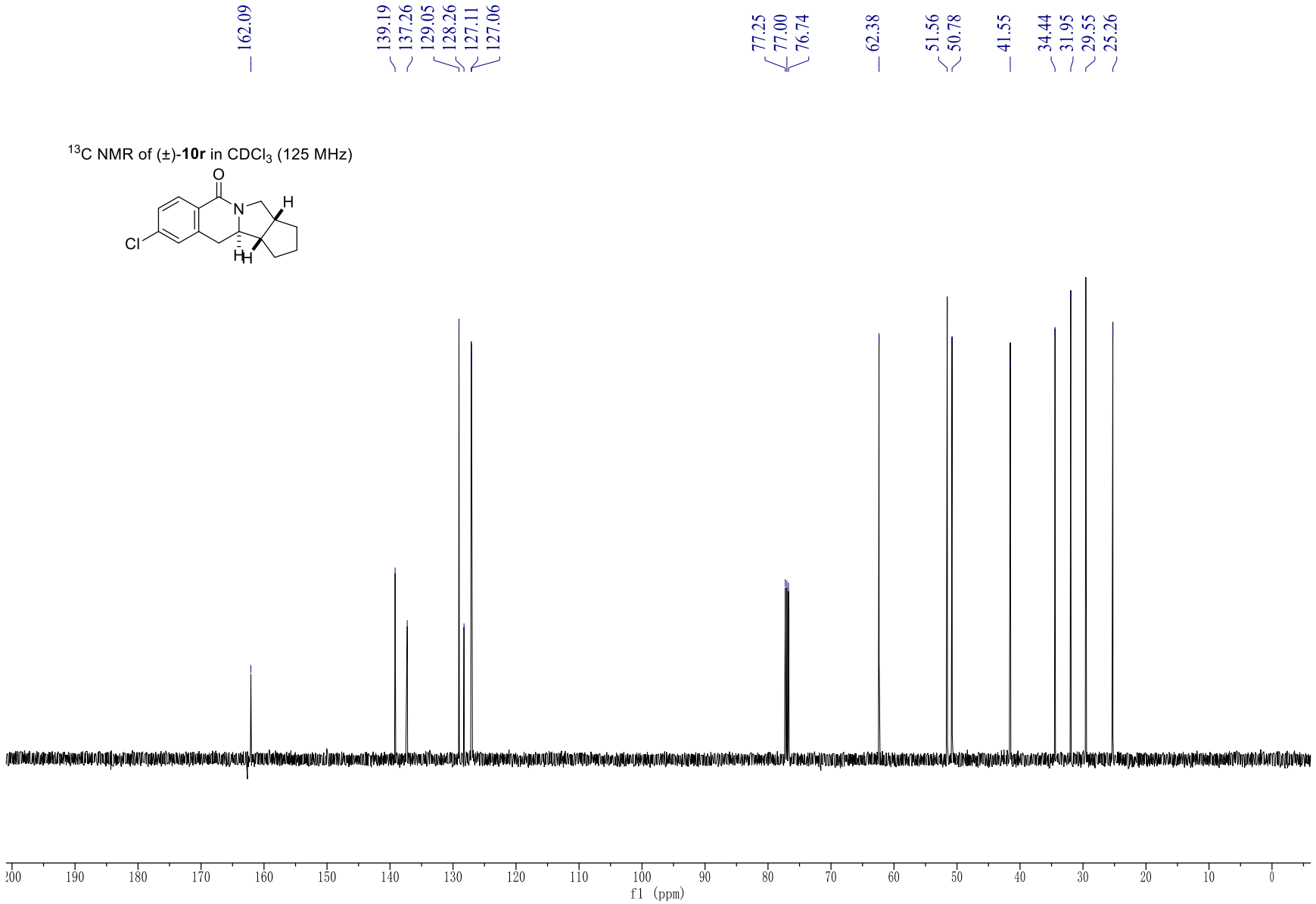

7.28 7.28 7.27 7.27 7.26 6.68 6.68 6.67 4.00 3.99 3.98 3.97 3.96 3.95 3.71 3.71 3.69 3.69 3.68 3.67 3.66 3.49 3.47 3.47 3.46 3.45 3.45 3.44 3.43 3.04 3.03 3.01 3.00 2.74 2.74 2.71 2.71 2.71 2.71 2.68 2.26 2.25 2.24 2.23 2.23 2.23 2.08 2.07 2.06 2.05 1.87 1.86 1.85 1.77 1.77 1.76 1.76 1.75 1.74
^{1}H NMR of (±)-**10q** in $CDCl_3$ (500 MHz)
O
N
O
0.86
0.86
0.95
0.99
1.01
1.00
1.00
1.00
0.99
0.99
0.95
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
f1 (ppm)


161.45
158.03
142.63
116.93
107.92
77.25
77.00
76.75
58.11
43.39
32.81
29.21
23.34
^{13}C NMR of (±)-**10q** in $CDCl_3$ (125 MHz)
O
N
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H NMR of (±)-**10r** in $CDCl_3$ (500 MHz)

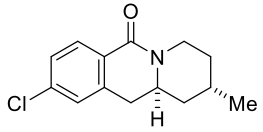


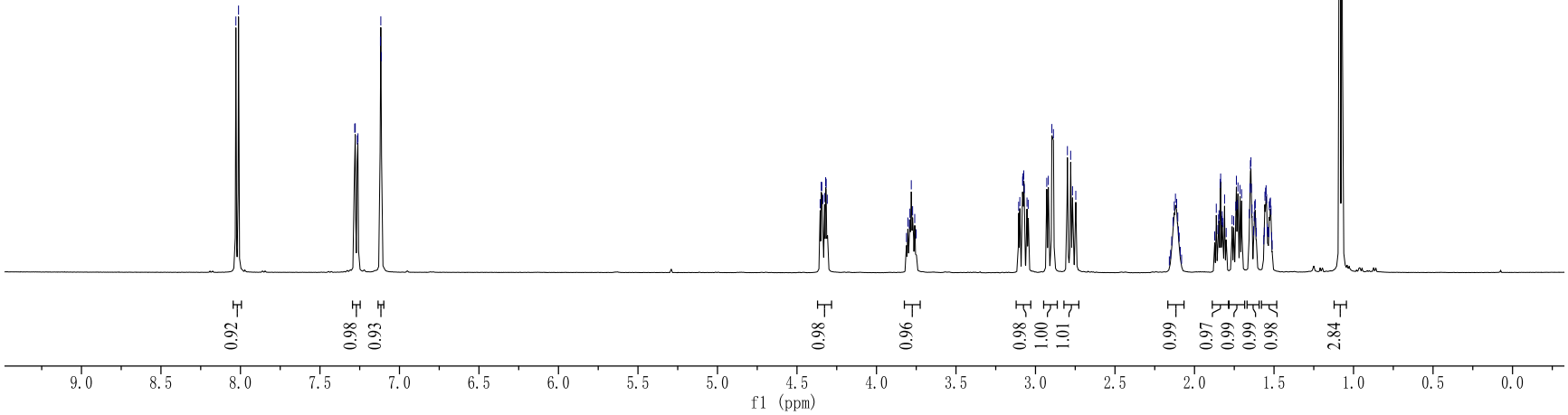


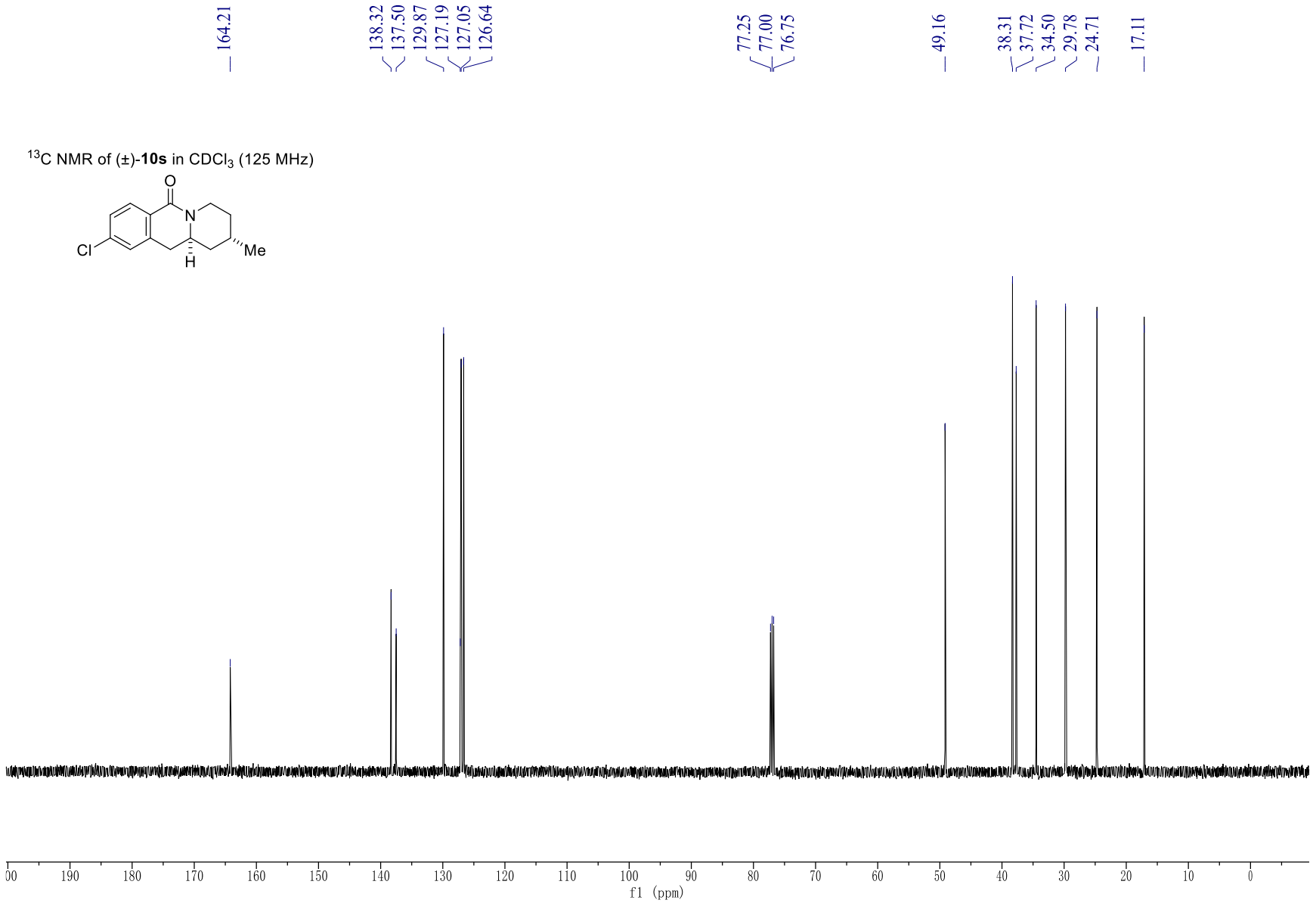

162.09
139.19
137.26
129.05
128.26
127.11
127.06
77.25
77.00
76.74
62.38
51.56
50.78
41.55
34.44
31.95
29.55
25.26
^{13}C NMR of (±)-**10r** in $CDCl_3$ (125 MHz)
O
N
H
Cl
H
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

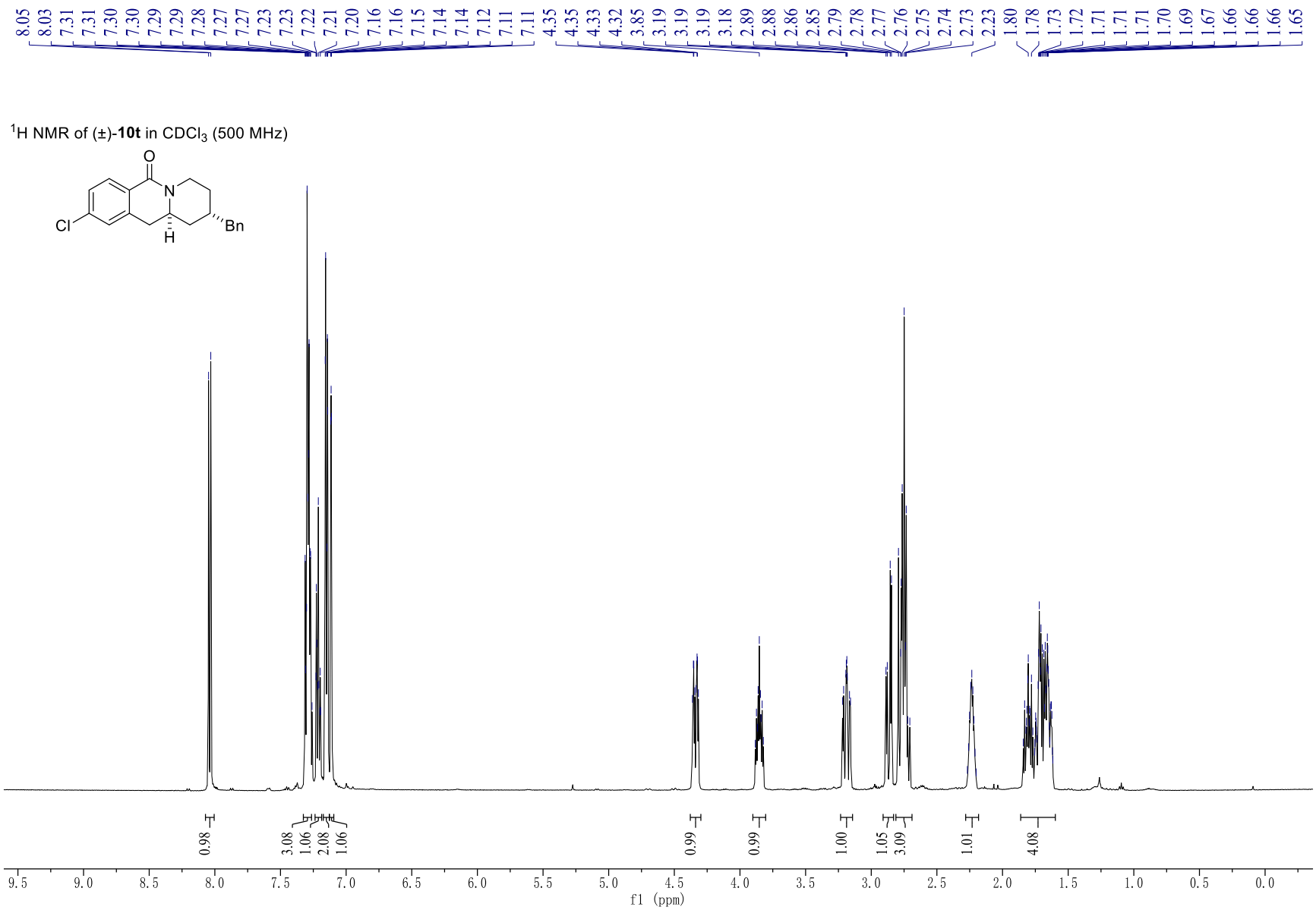
8.03 8.01 7.28 7.28 7.27 7.26 7.12 7.12 7.11 4.35 4.35 4.34 4.34 4.33 4.32 4.32 4.31 3.78 3.10 3.08 3.08 3.08 3.07 3.07 3.05 3.05 2.93 2.92 2.90 2.89 2.80 2.78 2.77 2.75 2.12 2.11 1.84 1.84 1.81 1.74 1.73 1.73 1.71 1.70 1.65 1.65 1.65 1.64 1.62 1.62 1.56 1.55 1.55 1.55 1.53 1.53 1.52 1.09 1.07

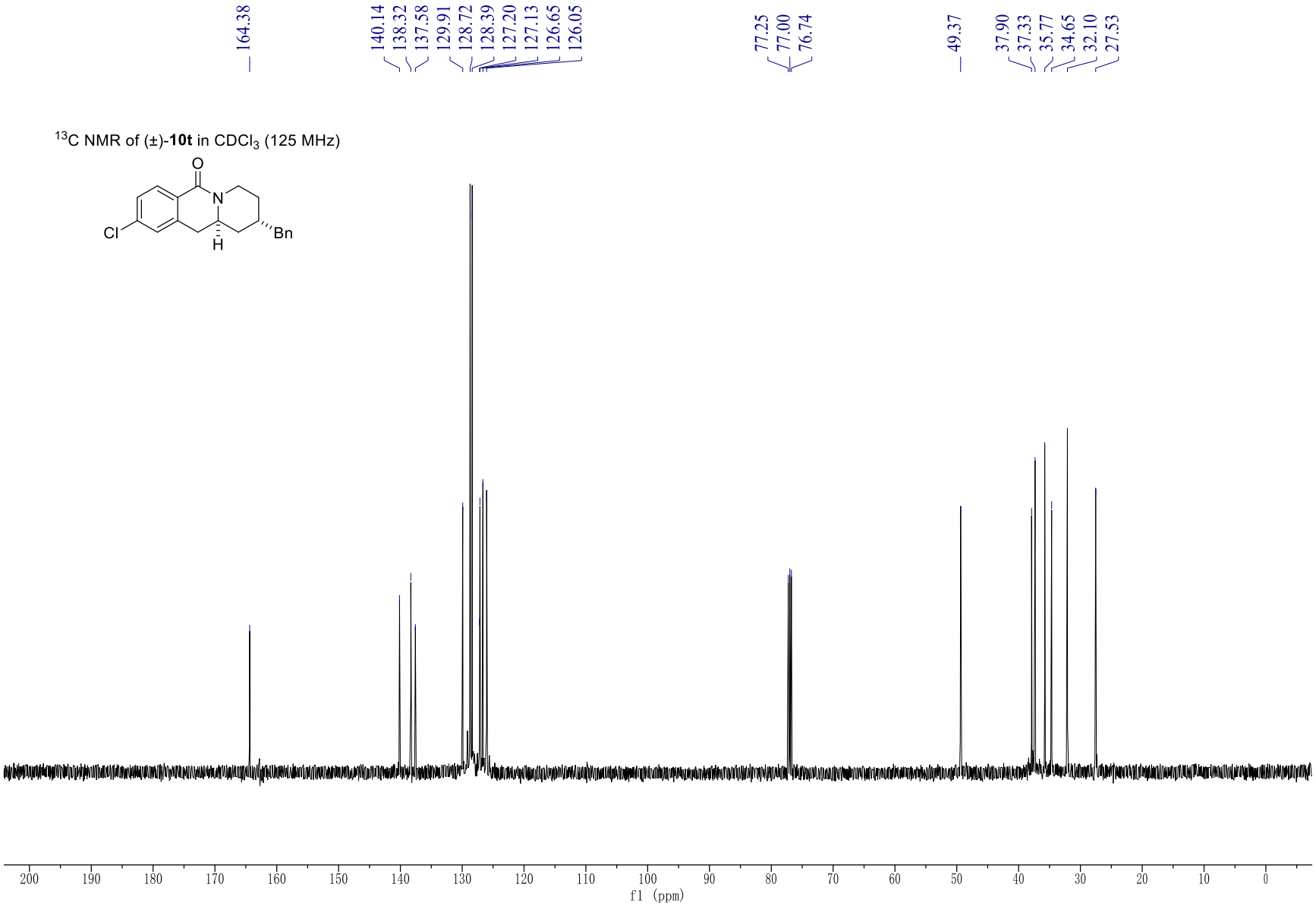
^{1}H NMR of (±)-**10s** in $CDCl_3$ (500 MHz)

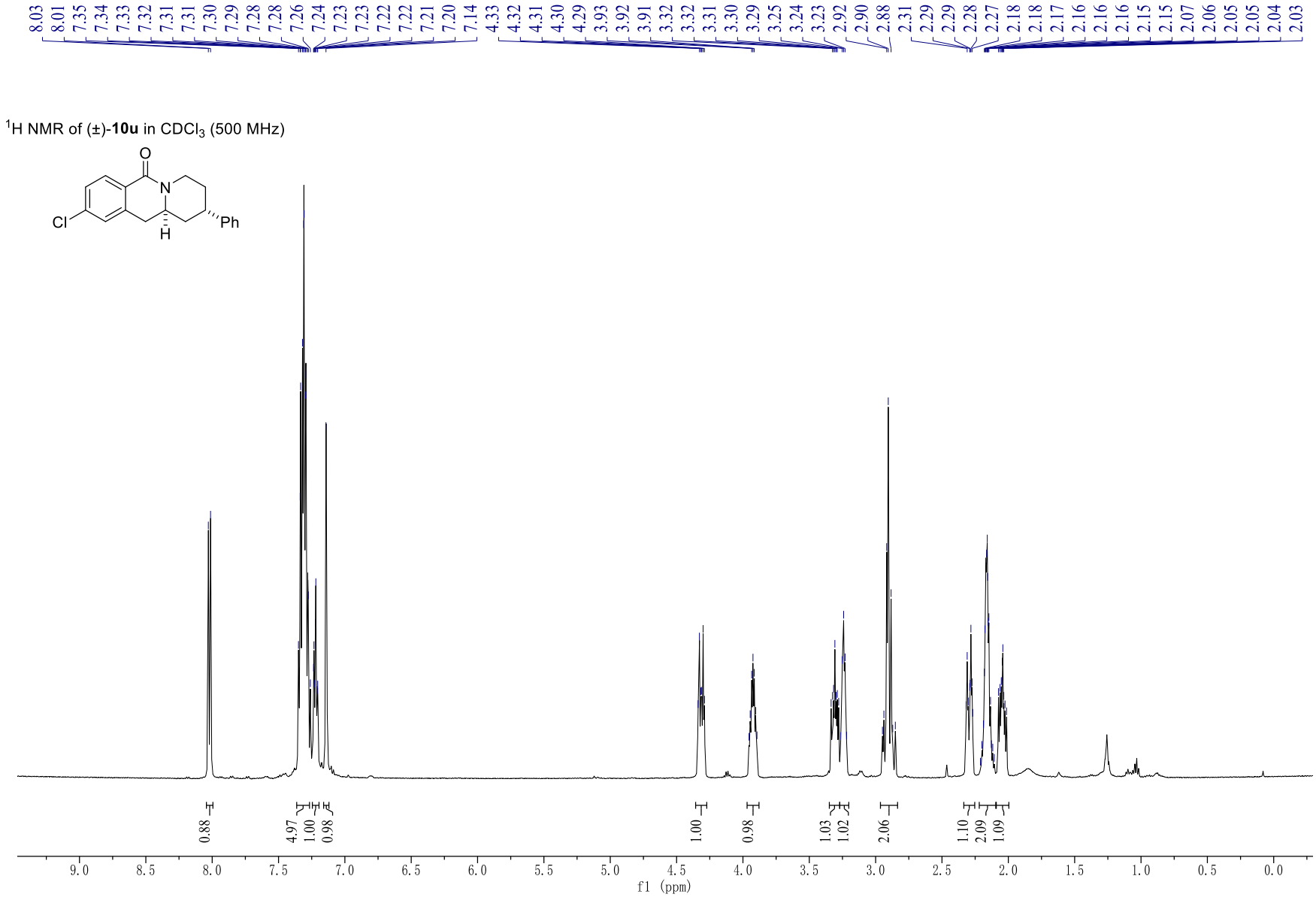




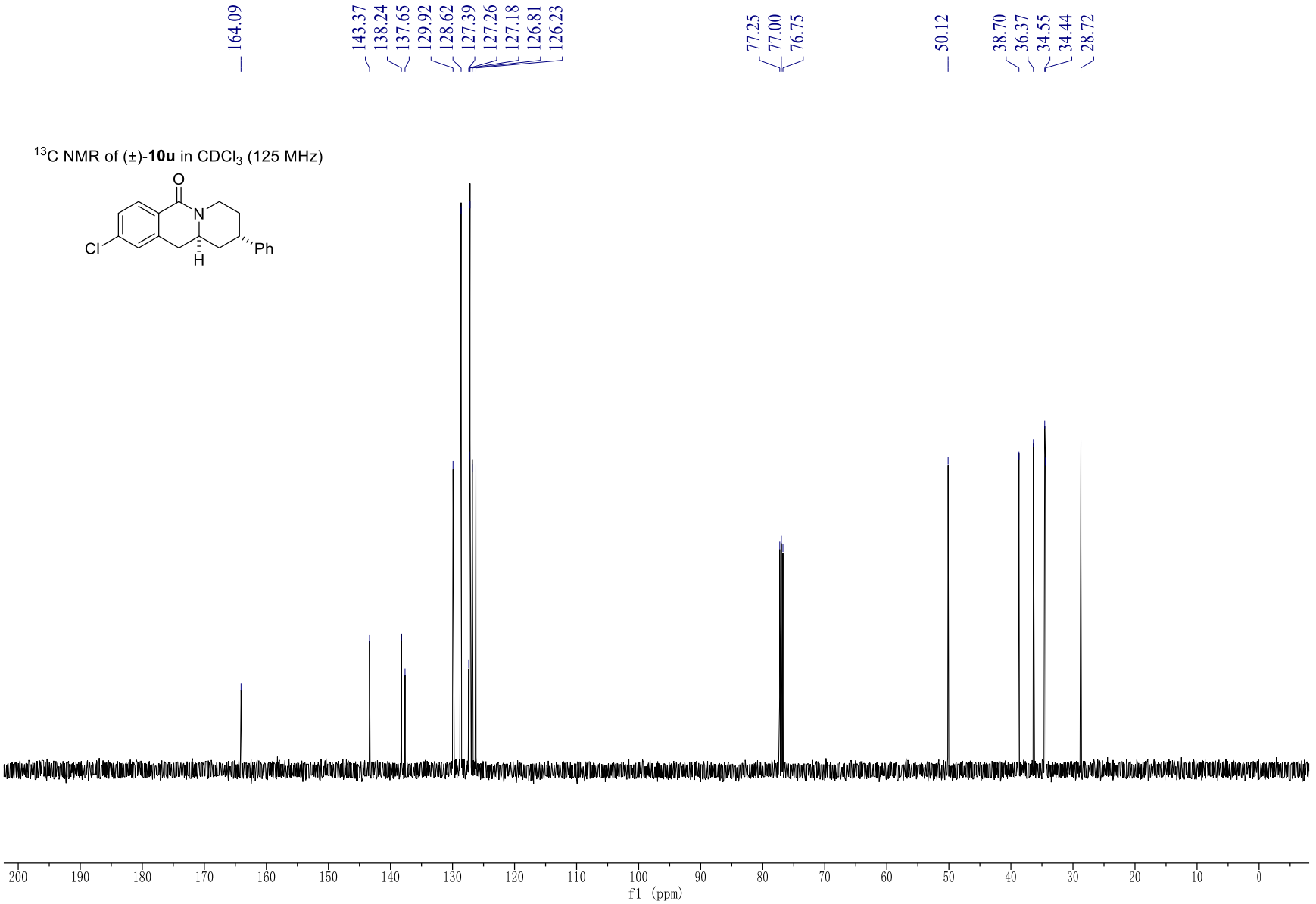

164.21
138.32
137.50
129.87
127.19
127.05
126.64
77.25
77.00
76.75
49.16
38.31
37.72
34.50
29.78
24.71
17.11
^{13}C NMR of (±)-**10s** in $CDCl_3$ (125 MHz)
O
N
Cl
H
Me
f1 (ppm)


8.05 8.03 7.31 7.31 7.30 7.30 7.29 7.29 7.28 7.27 7.27 7.23 7.23 7.22 7.21 7.20 7.16 7.16 7.15 7.14 7.14 7.12 7.11 7.11
4.35 4.35 4.33 4.32 3.85 3.19 3.19 3.19 3.18 2.89 2.88 2.86 2.85 2.79 2.78 2.77 2.76 2.75 2.74 2.73 2.23 1.80 1.78 1.73 1.72 1.71 1.71 1.71 1.70 1.69 1.67 1.66 1.66 1.66 1.65
1H NMR of (±)-10t in CDCl3 (500 MHz)
O
N
Cl
Bn
H
0.98 3.08 1.06 2.08 1.06 0.99 0.99 1.00 1.05 3.09 1.01 4.08
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
f1 (ppm)


164.38
140.14
138.32
137.58
129.91
128.72
128.39
127.20
127.13
126.65
126.05
77.25
77.00
76.74
49.37
37.90
37.33
35.77
34.65
32.10
27.53
^{13}C NMR of (±)-**10t** in $CDCl_3$ (125 MHz)
O
N
Cl
H
Bn
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

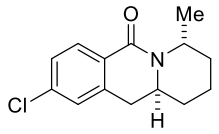


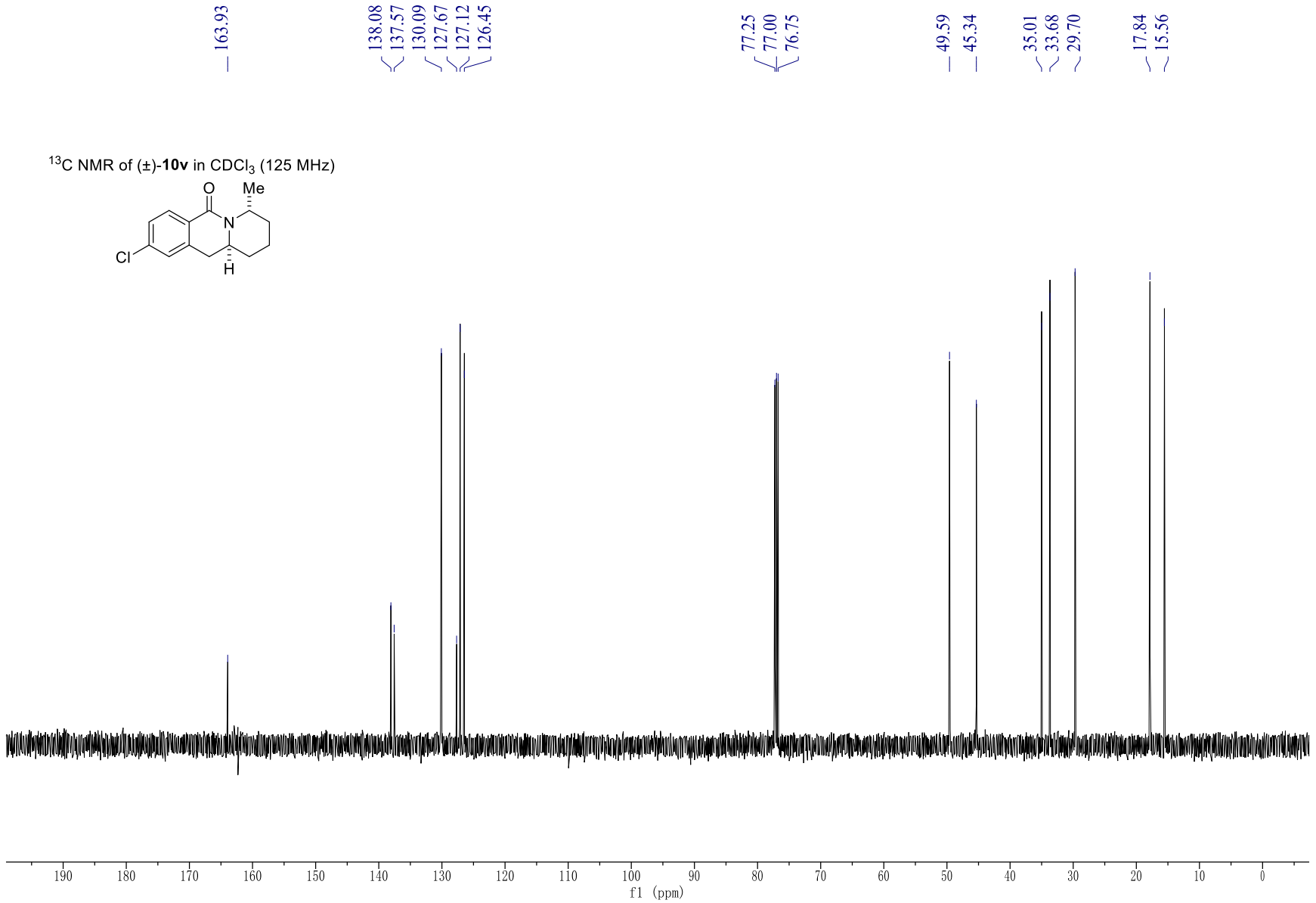
^{1}H NMR of (±)-**10u** in $CDCl_3$ (500 MHz)


164.09
143.37
138.24
137.65
129.92
128.62
127.39
127.26
127.18
126.81
126.23
77.25
77.00
76.75
50.12
38.70
36.37
34.55
34.44
28.72
^{13}C NMR of (±)-**10u** in $CDCl_3$ (125 MHz)
O
N
Cl
H
Ph
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

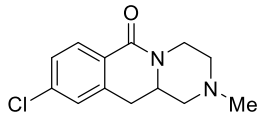
8.05 8.03 7.30 7.30 7.30 7.30 7.29 7.28 7.28 7.14 7.14 7.13 4.99 4.98 4.98 2.96 2.95 2.93 2.92 2.85 2.85 2.85 2.83 2.83 2.82 2.82 2.79 1.93 1.93 1.92 1.90 1.90 1.90 1.90 1.90 1.75 1.75 1.75 1.74 1.74 1.74 1.73 1.72 1.71 1.71 1.70 1.70 1.70 1.69 1.69 1.69 1.68 1.68 1.68 1.67 1.67 1.66 1.66 1.20 1.18

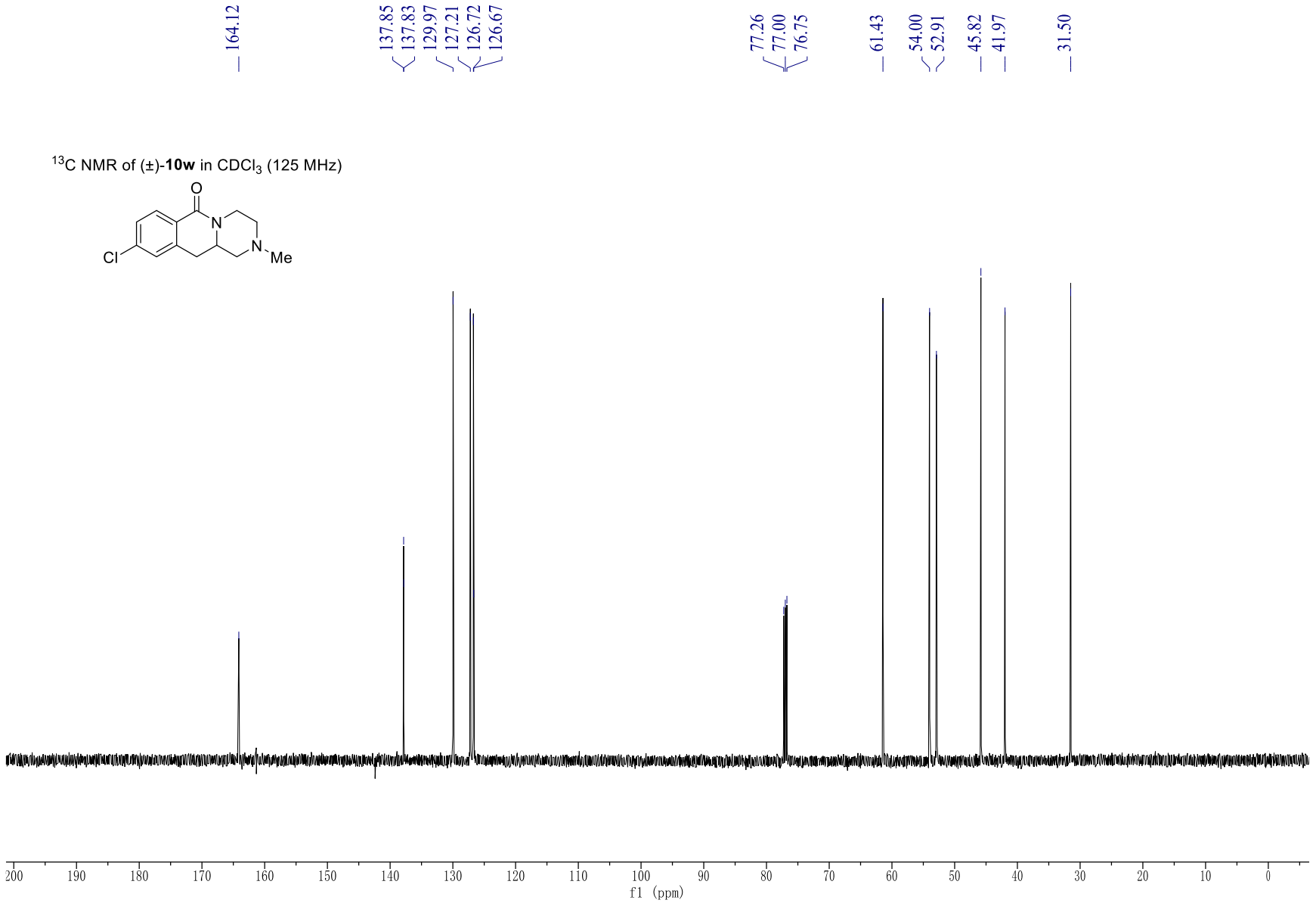
^{1}H NMR of (±)-**10v** in $CDCl_3$ (500 MHz)



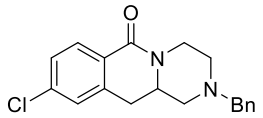

163.93
138.08
137.57
130.09
127.67
127.12
126.45
77.25
77.00
76.75
49.59
45.34
35.01
33.68
29.70
17.84
15.56
13C NMR of (±)-10v in CDCl3 (125 MHz)
O
Me
N
Cl
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

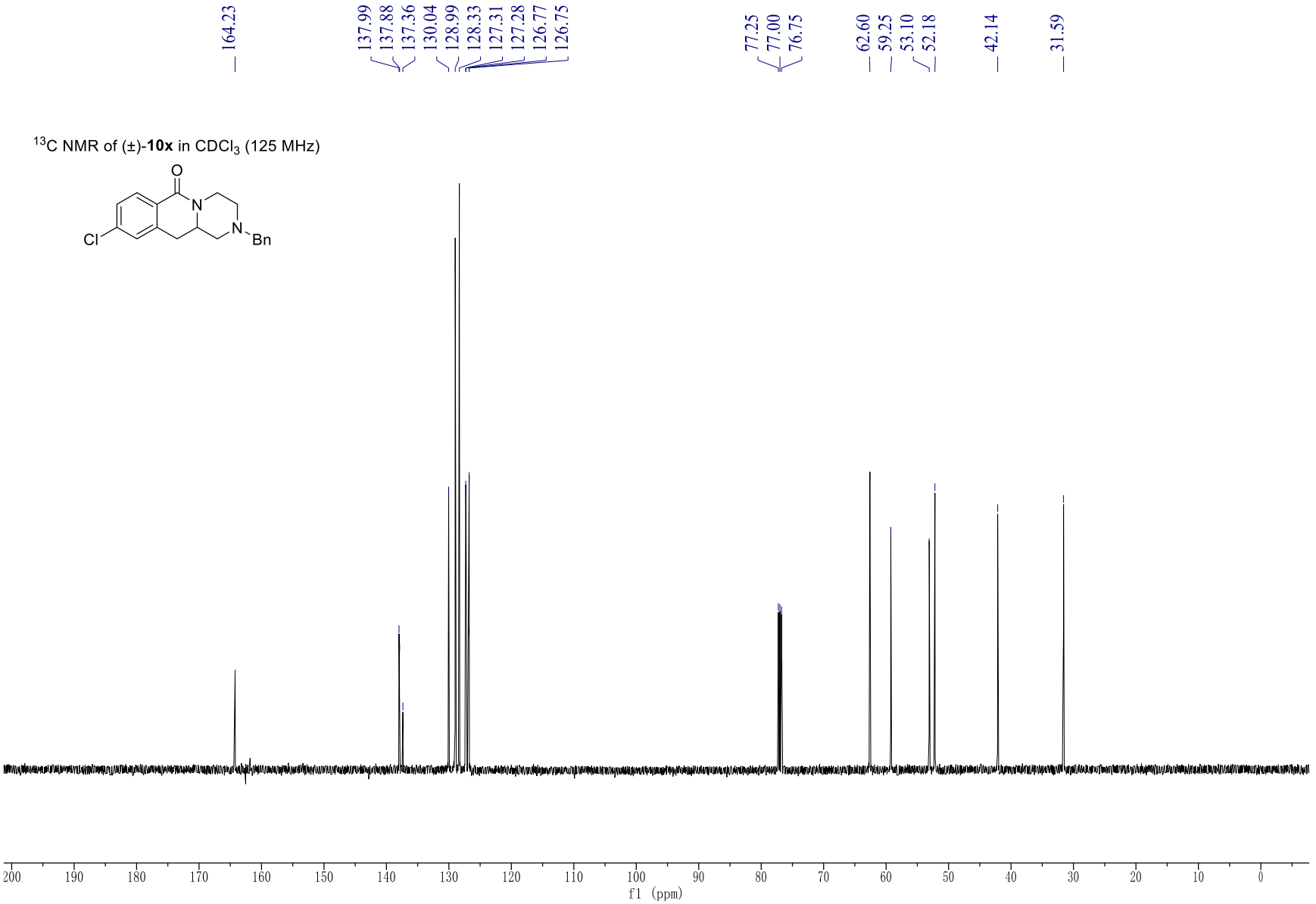
^{1}H NMR of (±)-**10w** in $CDCl_3$ (500 MHz)



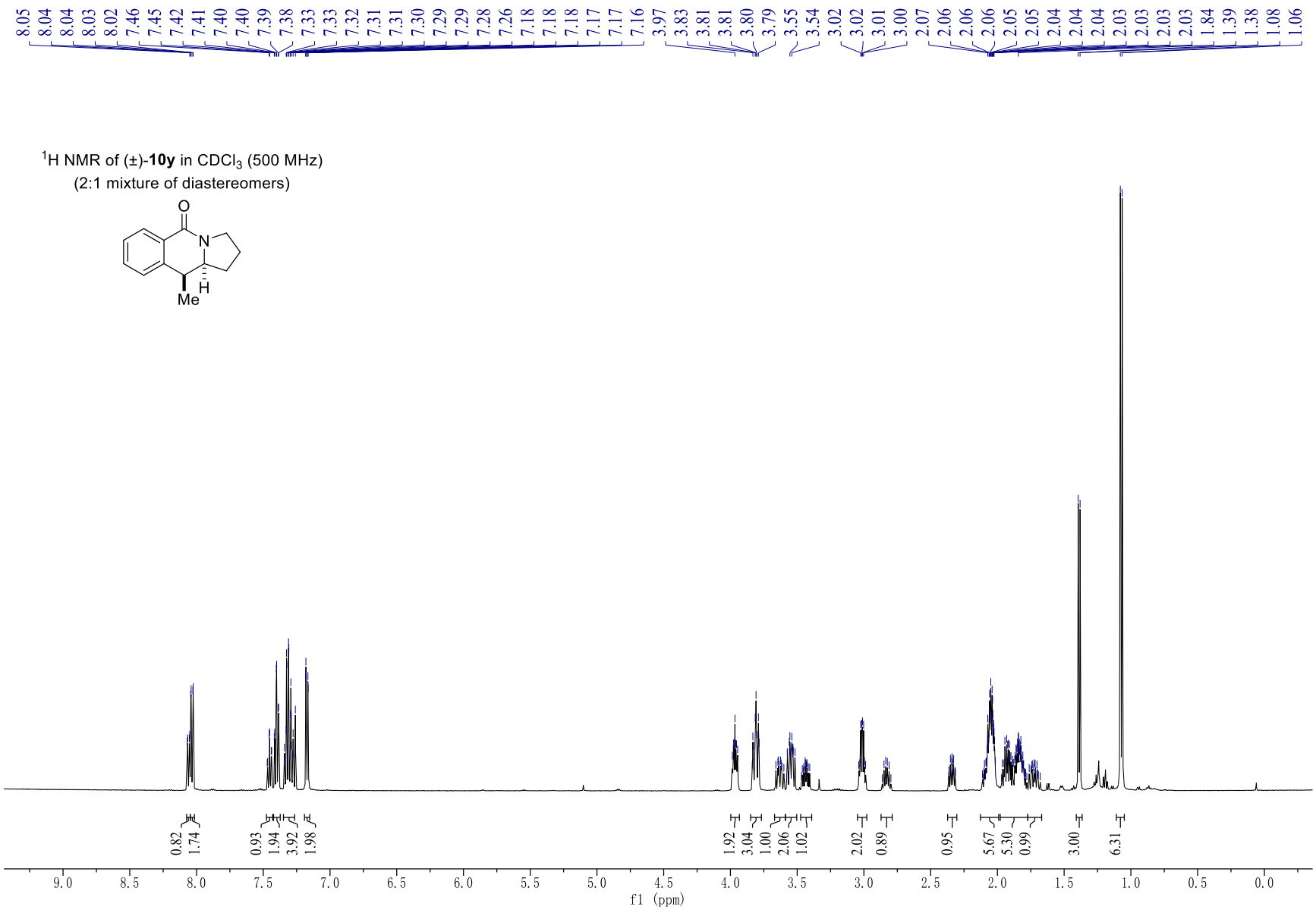

164.12
137.85
137.83
129.97
127.21
126.72
126.67
77.26
77.00
76.75
61.43
54.00
52.91
45.82
41.97
31.50
^{13}C NMR of (±)-**10w** in $CDCl_3$ (125 MHz)
O
N
N
Me
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

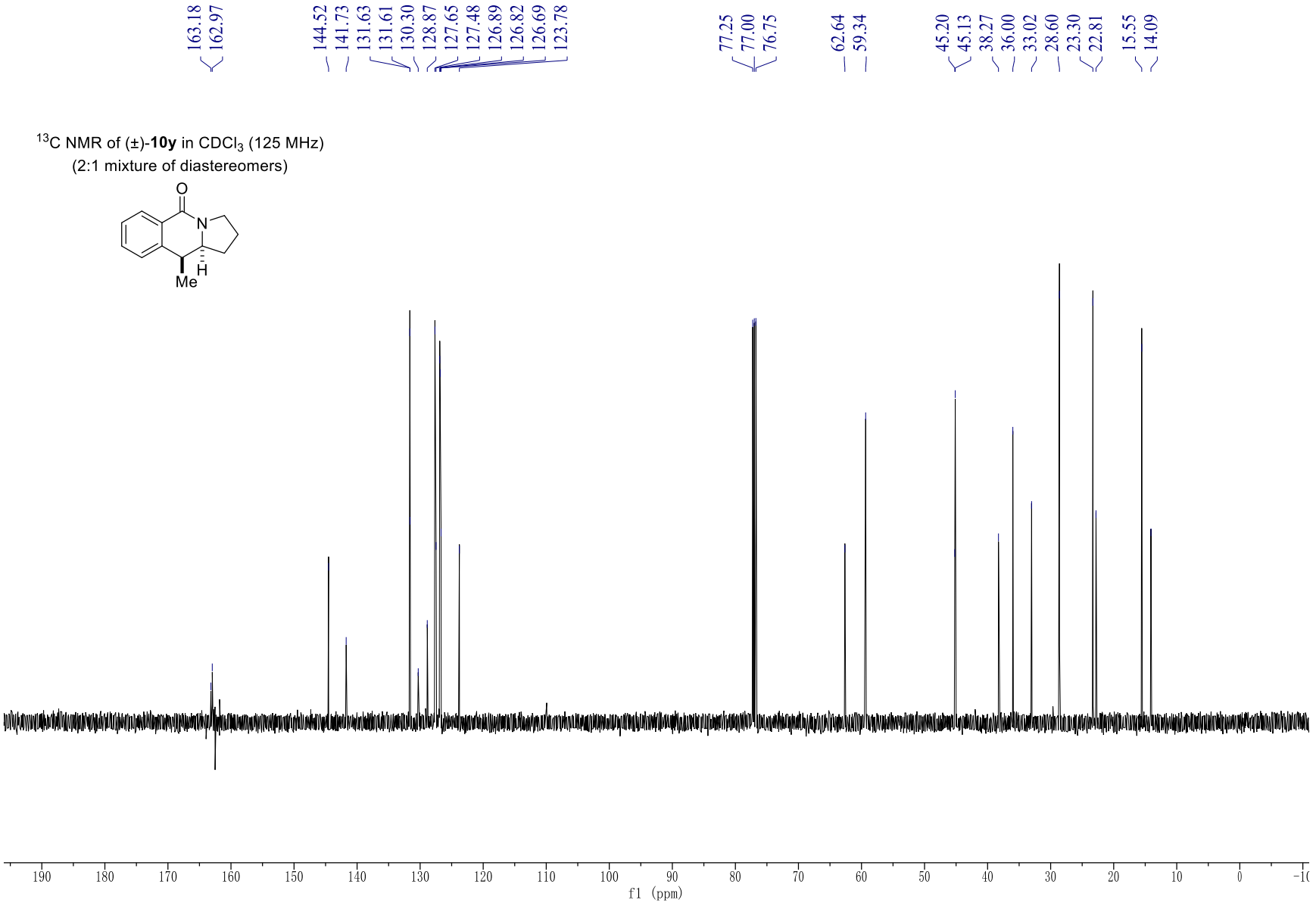
^{1}H NMR of (±)-**10x** in $CDCl_3$ (500 MHz)



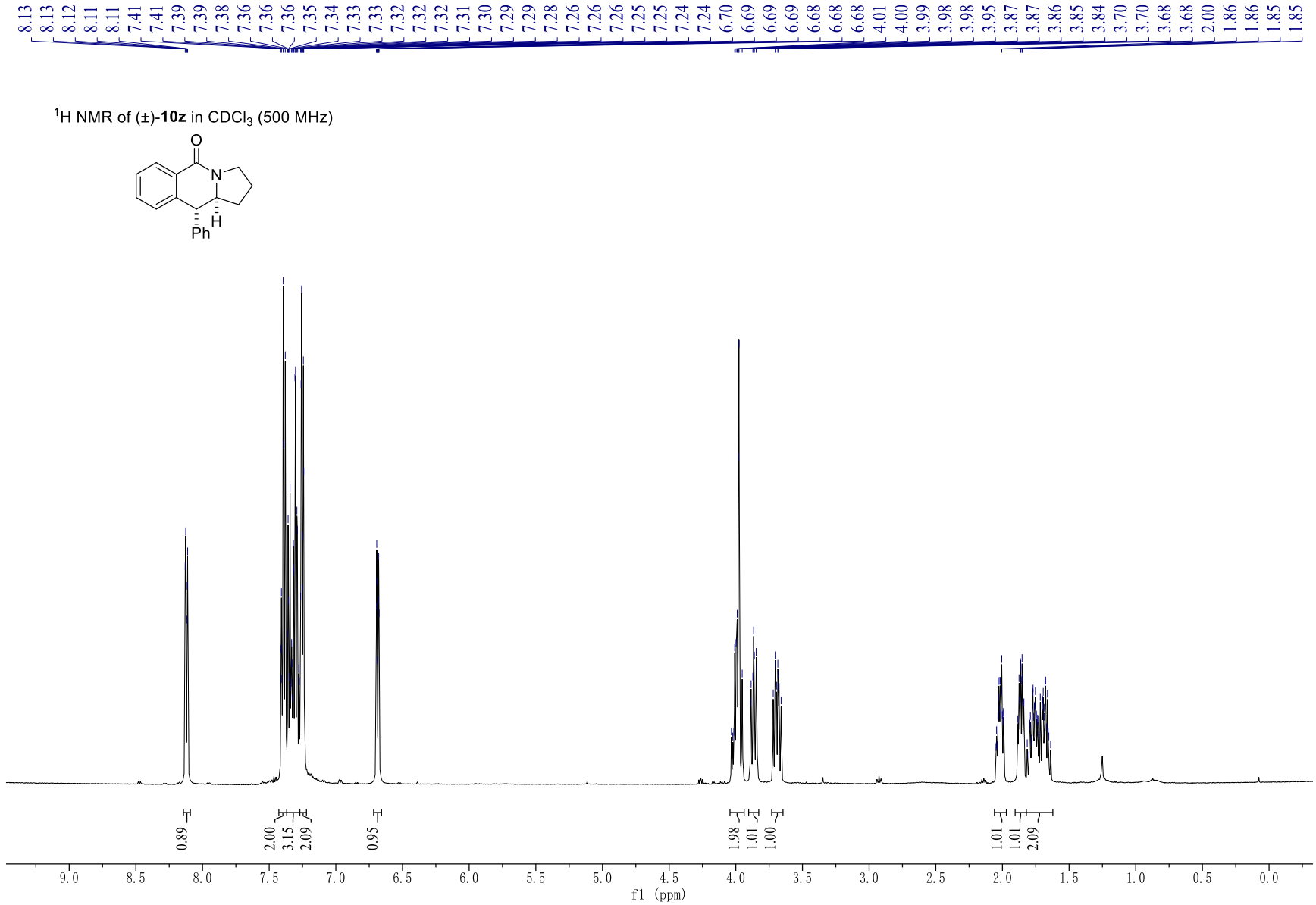


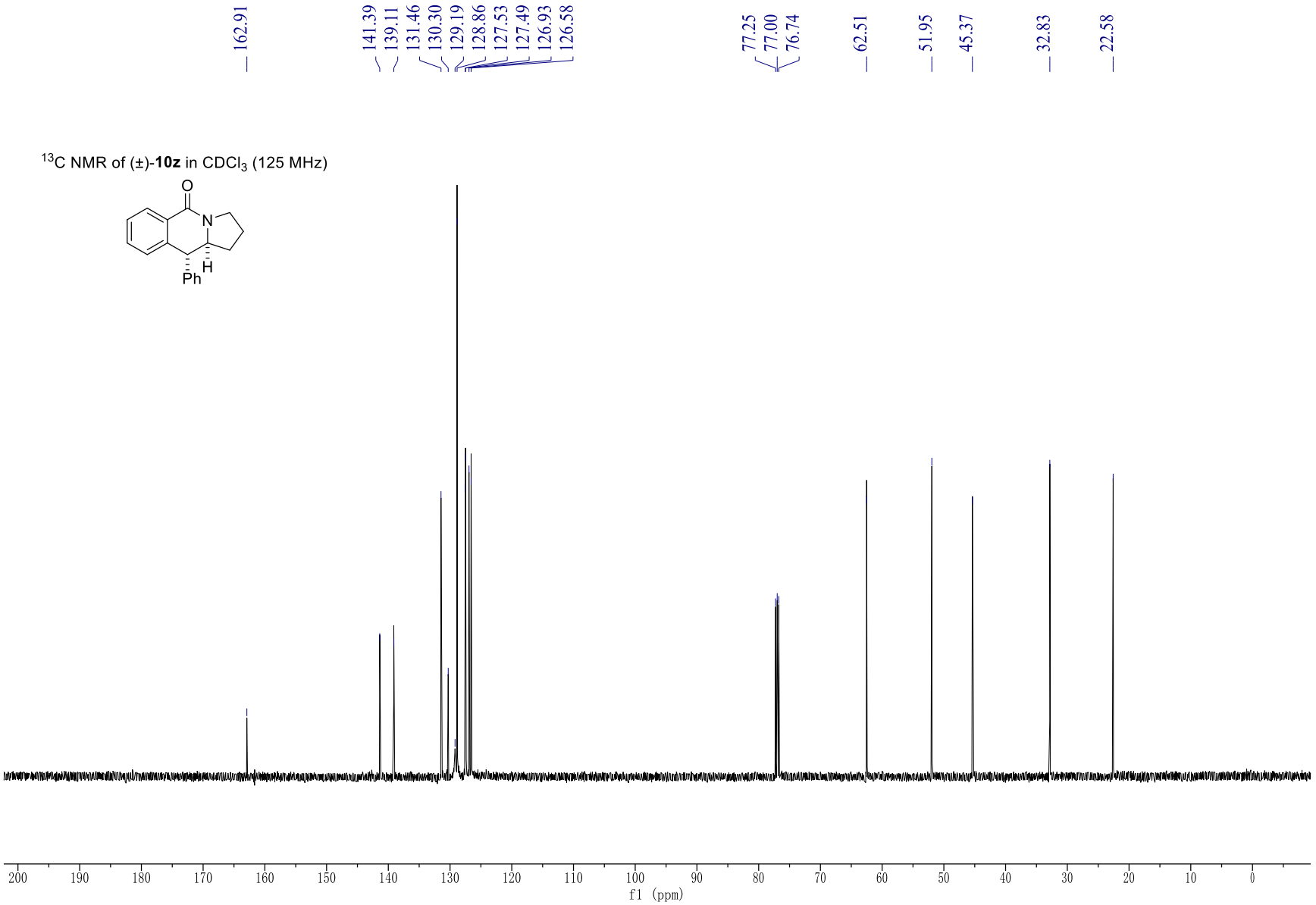
^{13}C NMR of (±)-**10x** in $CDCl_3$ (125 MHz)


8.05 8.04 8.04 8.03 8.02 7.46 7.45 7.42 7.41 7.40 7.40 7.39 7.38 7.33 7.33 7.32 7.31 7.31 7.30 7.29 7.29 7.28 7.26 7.18 7.18 7.18 7.17 7.17 7.16
3.97 3.83 3.81 3.81 3.80 3.79 3.55 3.54 3.02 3.02 3.01 3.00 2.07 2.06 2.06 2.06 2.05 2.05 2.04 2.04 2.04 2.03 2.03 2.03 2.03 1.84 1.39 1.38 1.08 1.06
^{1}H NMR of (±)-**10y** in $CDCl_3$ (500 MHz)
(2:1 mixture of diastereomers)
O
N
H
Me
0.82 1.74 0.93 1.94 3.92 1.98 1.92 3.04 1.00 2.06 1.02 2.02 0.89 0.95 5.67 5.30 0.99 3.00 6.31
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
f1 (ppm)

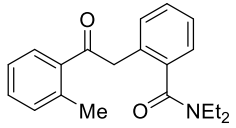


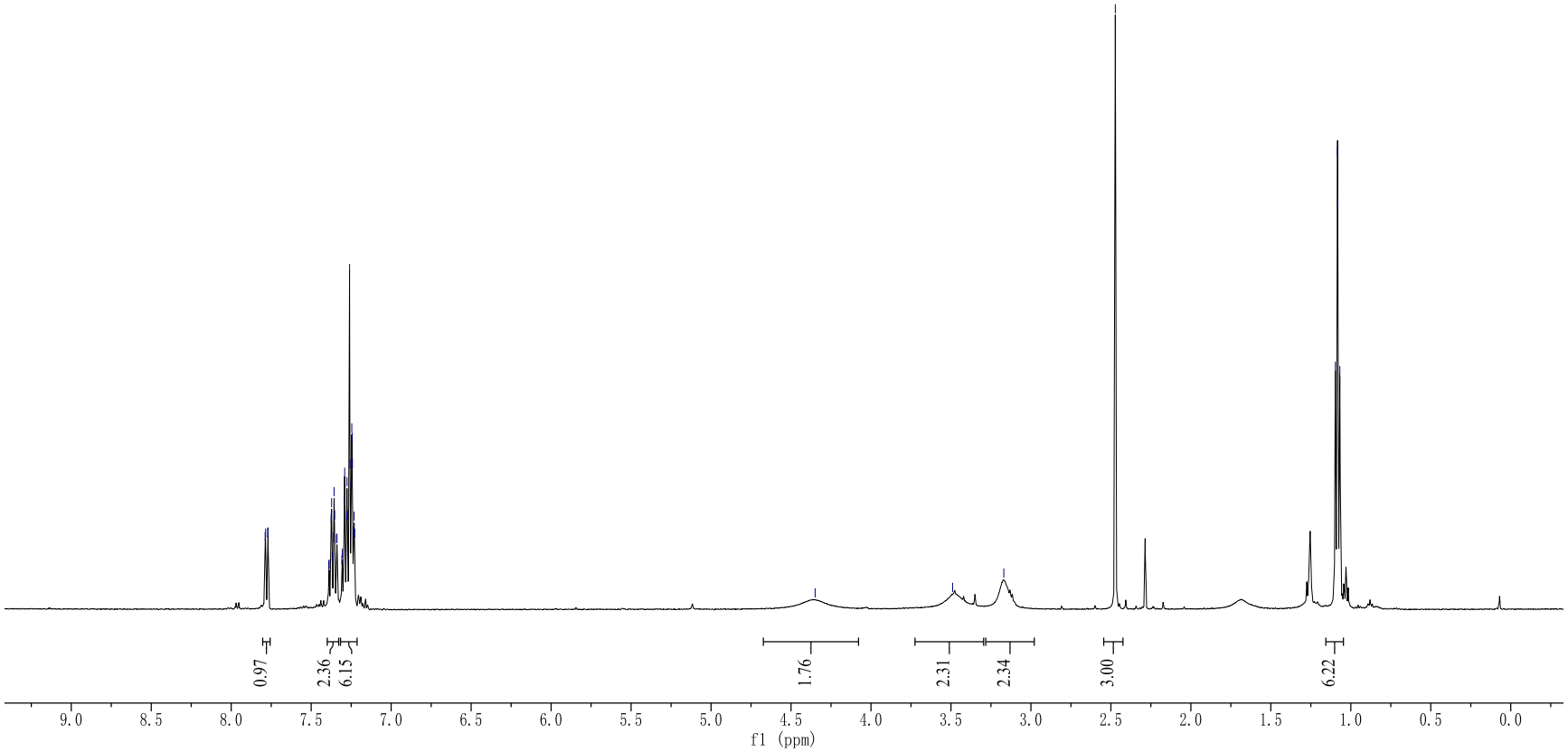
^{13}C NMR of (±)-**10y** in $CDCl_3$ (125 MHz)
(2:1 mixture of diastereomers)

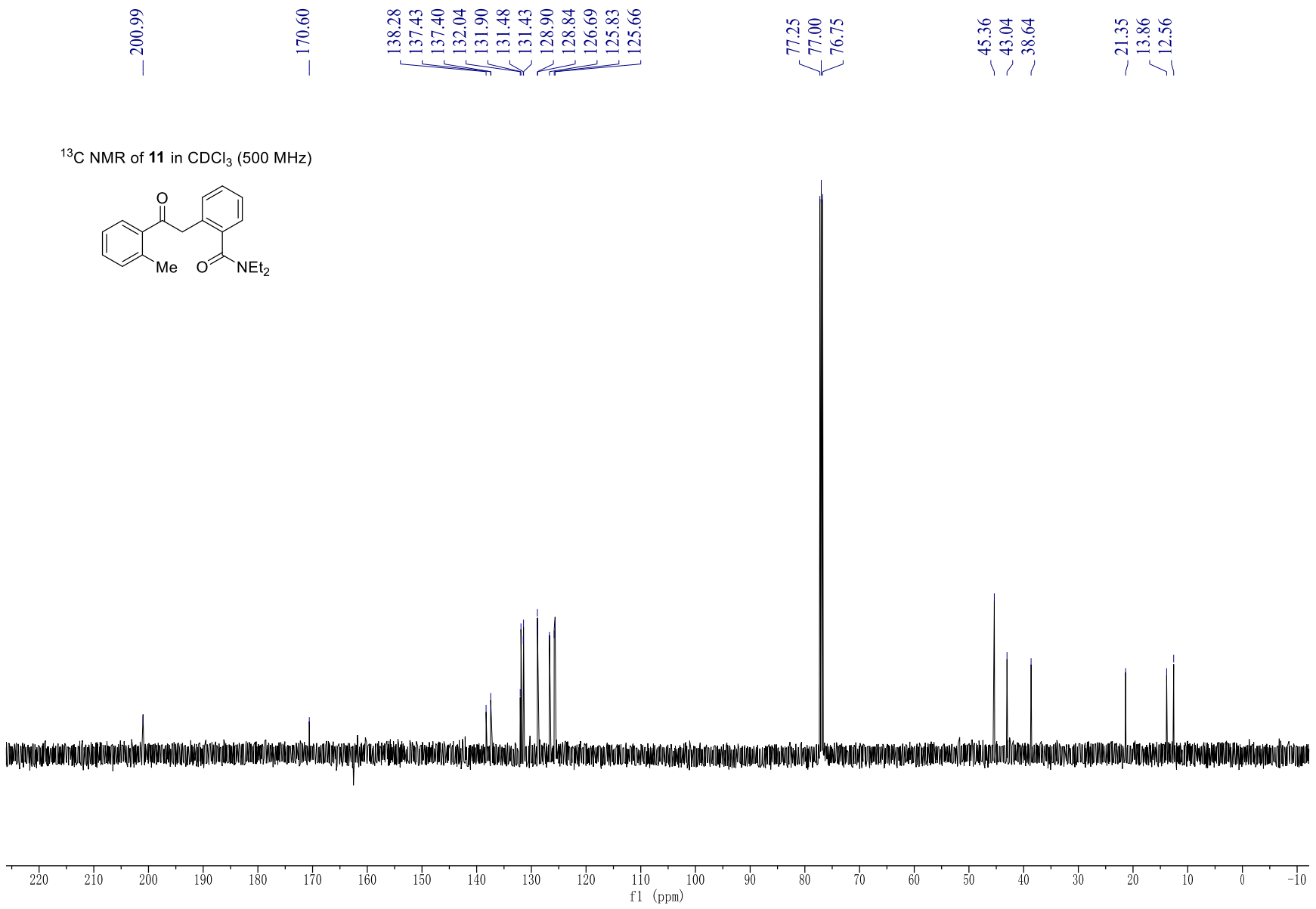

8.13 8.13 8.12 8.11 8.11 7.41 7.41 7.39 7.39 7.38 7.36 7.36 7.36 7.35 7.34 7.33 7.33 7.32 7.32 7.32 7.31 7.30 7.29 7.29 7.28 7.26 7.26 7.26 7.25 7.25 7.24 7.24 6.70 6.69 6.69 6.69 6.68 6.68 6.68 4.01 4.00 3.99 3.98 3.98 3.95 3.87 3.87 3.86 3.85 3.84 3.70 3.70 3.68 3.68 2.00 1.86 1.86 1.85 1.85
^{1}H NMR of (±)-**10z** in $CDCl_3$ (500 MHz)
O
N
H
Ph
0.89 2.00 3.15 2.09 0.95 1.98 1.01 1.00 1.01 1.01 2.09
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
f1 (ppm)


162.91
141.39
139.11
131.46
130.30
129.19
128.86
127.53
127.49
126.93
126.58
77.25
77.00
76.74
62.51
51.95
45.37
32.83
22.58
13C NMR of (±)-10z in CDCl3 (125 MHz)
O
N
H
Ph
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

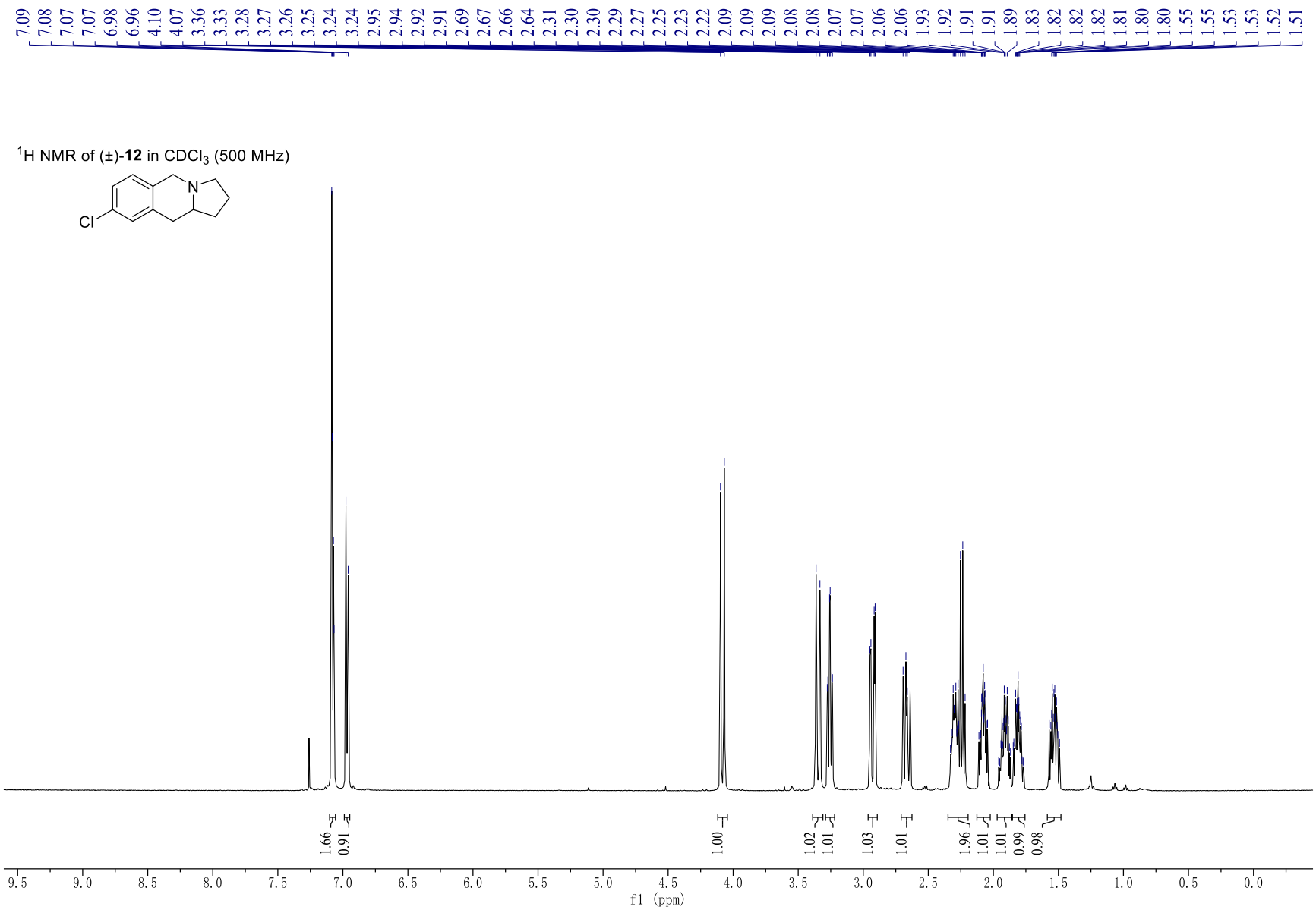
^{1}H NMR of **11** in $CDCl_3$ (500 MHz)

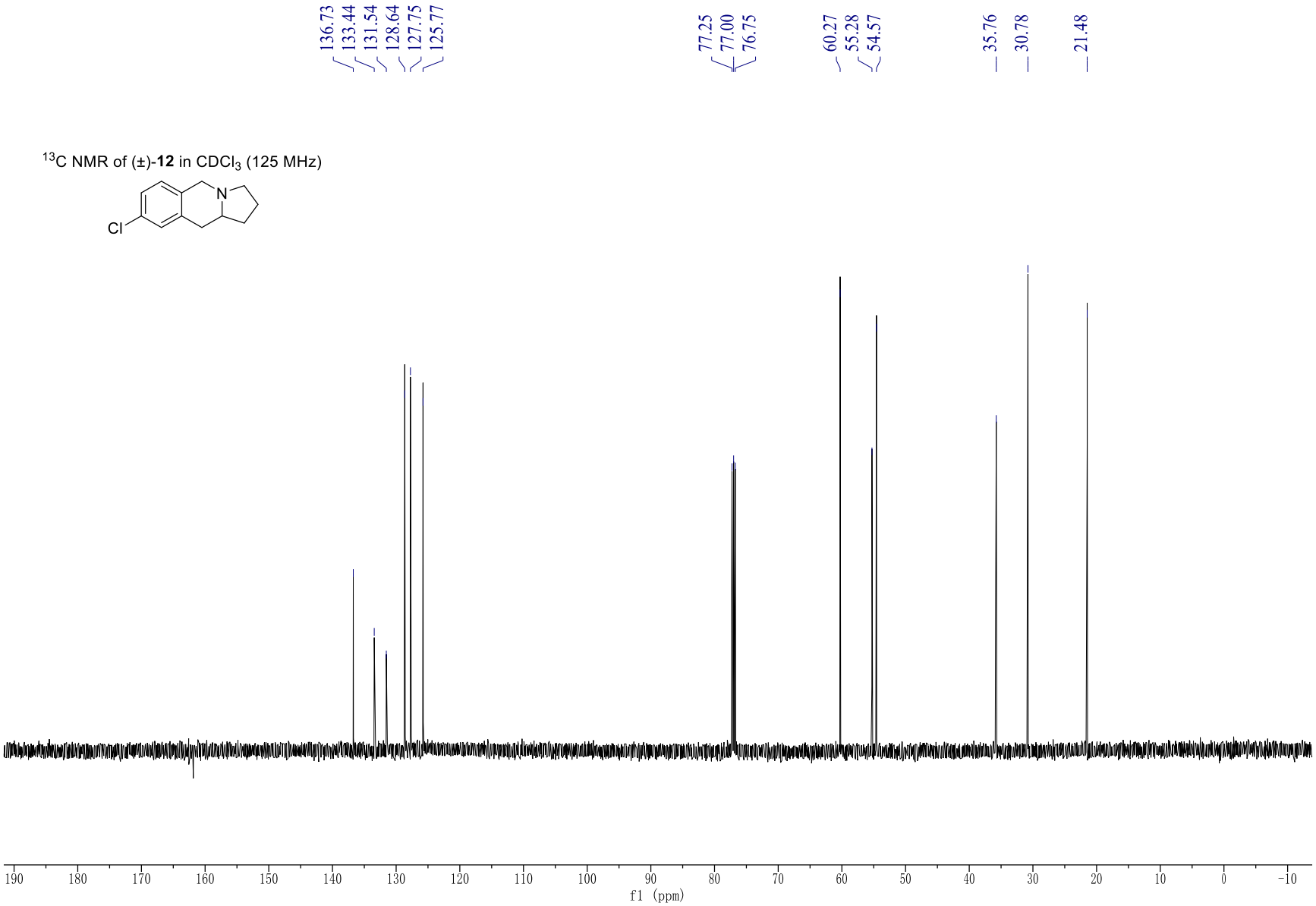


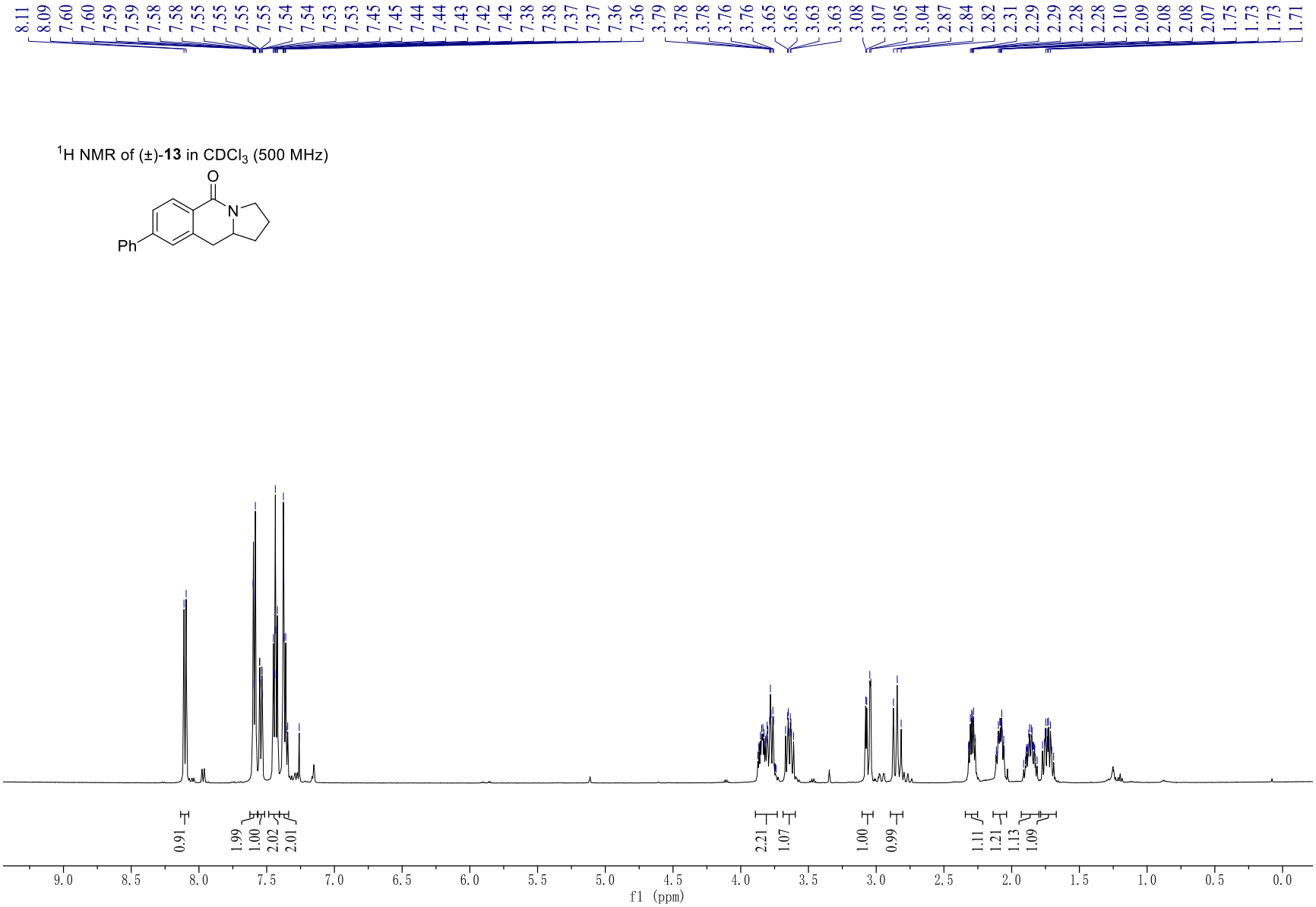




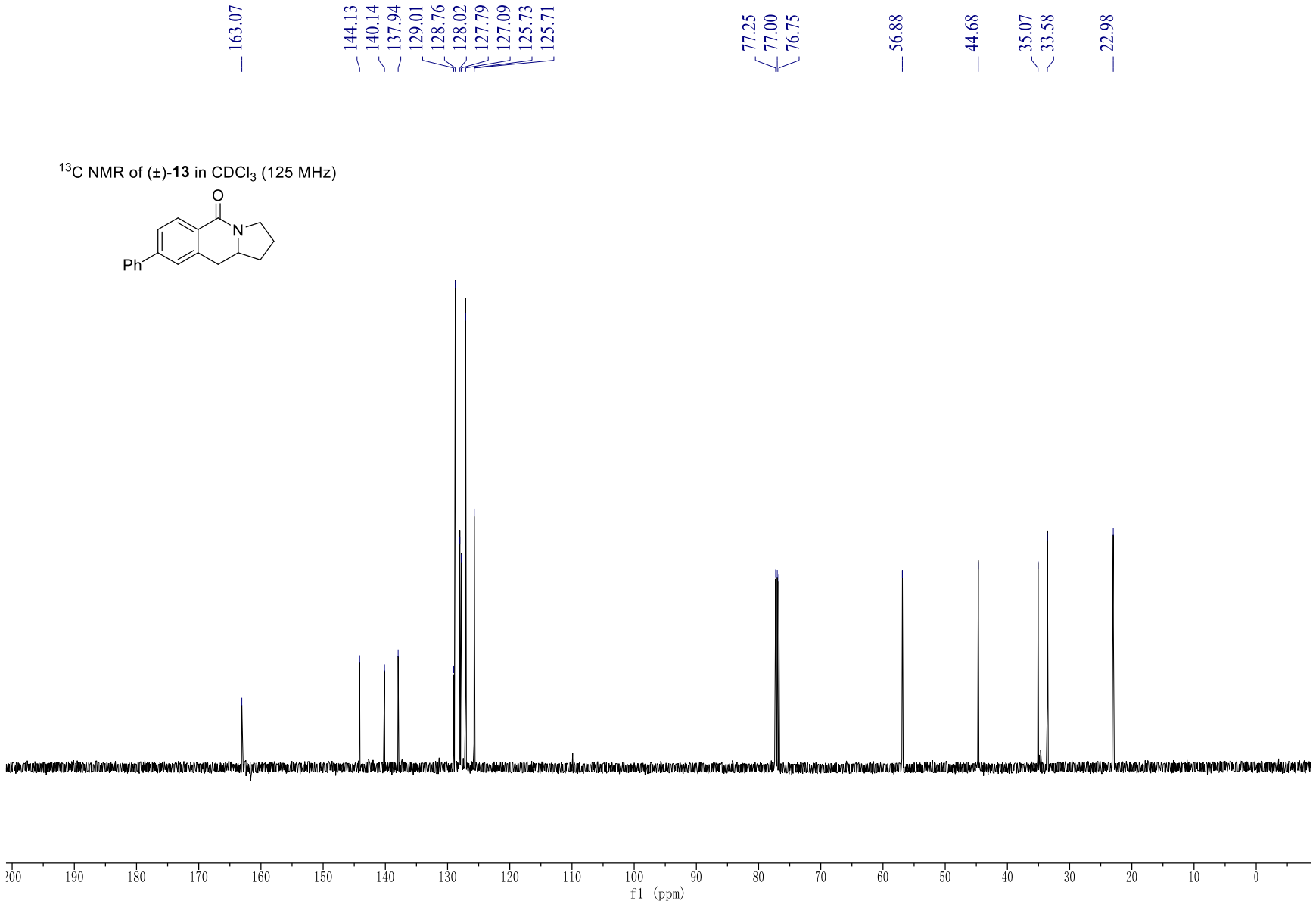
^{13}C NMR of **11** in $CDCl_3$ (500 MHz)


7.09 7.08 7.07 7.07 6.98 6.96 4.10 4.07 3.36 3.33 3.28 3.27 3.26 3.25 3.24 3.24 2.95 2.94 2.92 2.91 2.69 2.67 2.66 2.64 2.31 2.30 2.30 2.29 2.27 2.25 2.23 2.22 2.09 2.09 2.09 2.08 2.08 2.07 2.07 2.06 2.06 1.93 1.92 1.91 1.91 1.89 1.83 1.82 1.82 1.82 1.81 1.80 1.80 1.55 1.55 1.53 1.53 1.52 1.51
1H NMR of (±)-12 in CDCl3 (500 MHz)
Cl
N
1.66
0.91
1.00
1.02
1.01
1.03
1.01
1.96
1.01
1.01
0.99
0.98
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
f1 (ppm)

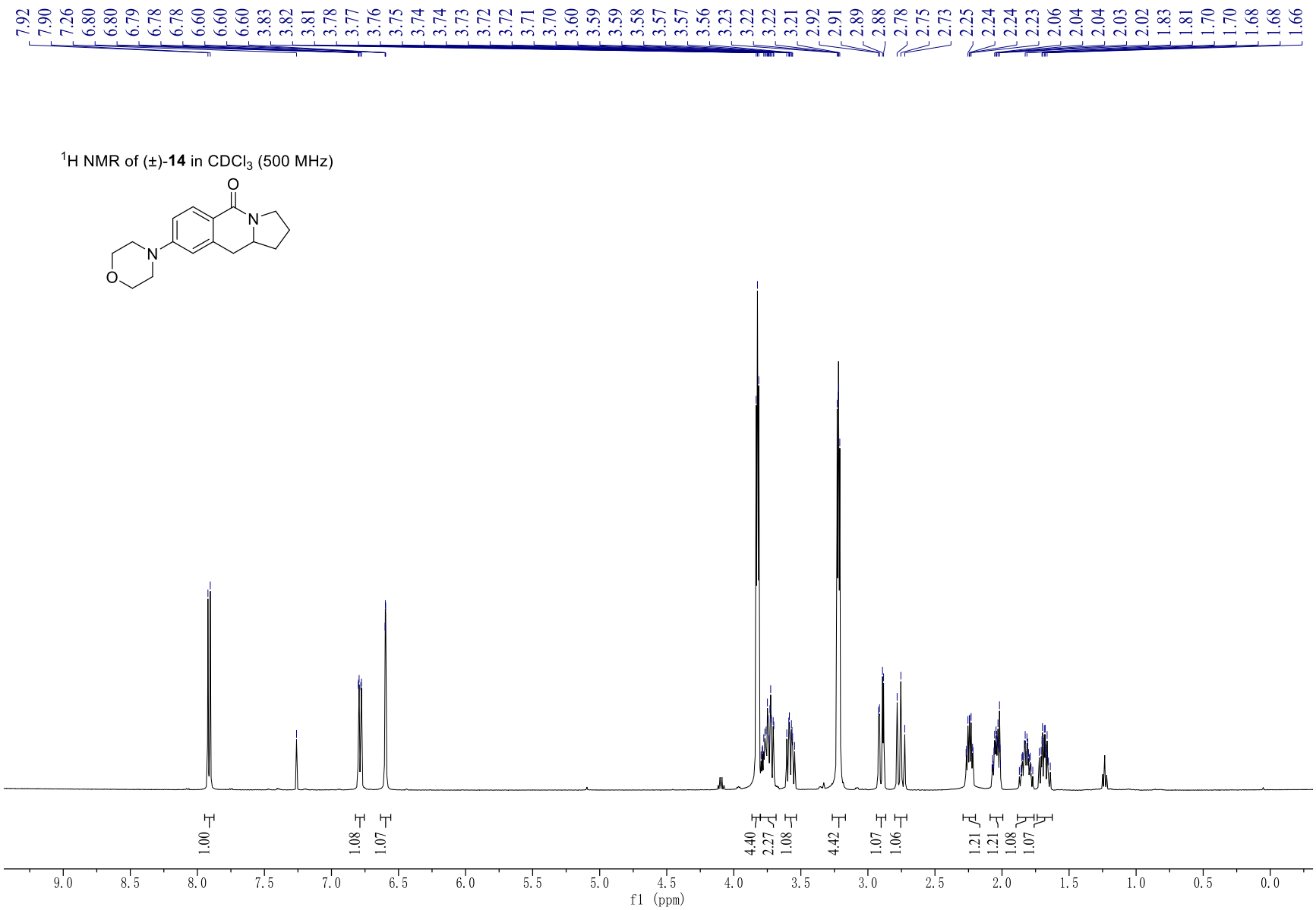

136.73
133.44
131.54
128.64
127.75
125.77
77.25
77.00
76.75
60.27
55.28
54.57
35.76
30.78
21.48
^{13}C NMR of (±)-**12** in $CDCl_3$ (125 MHz)
N
Cl
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

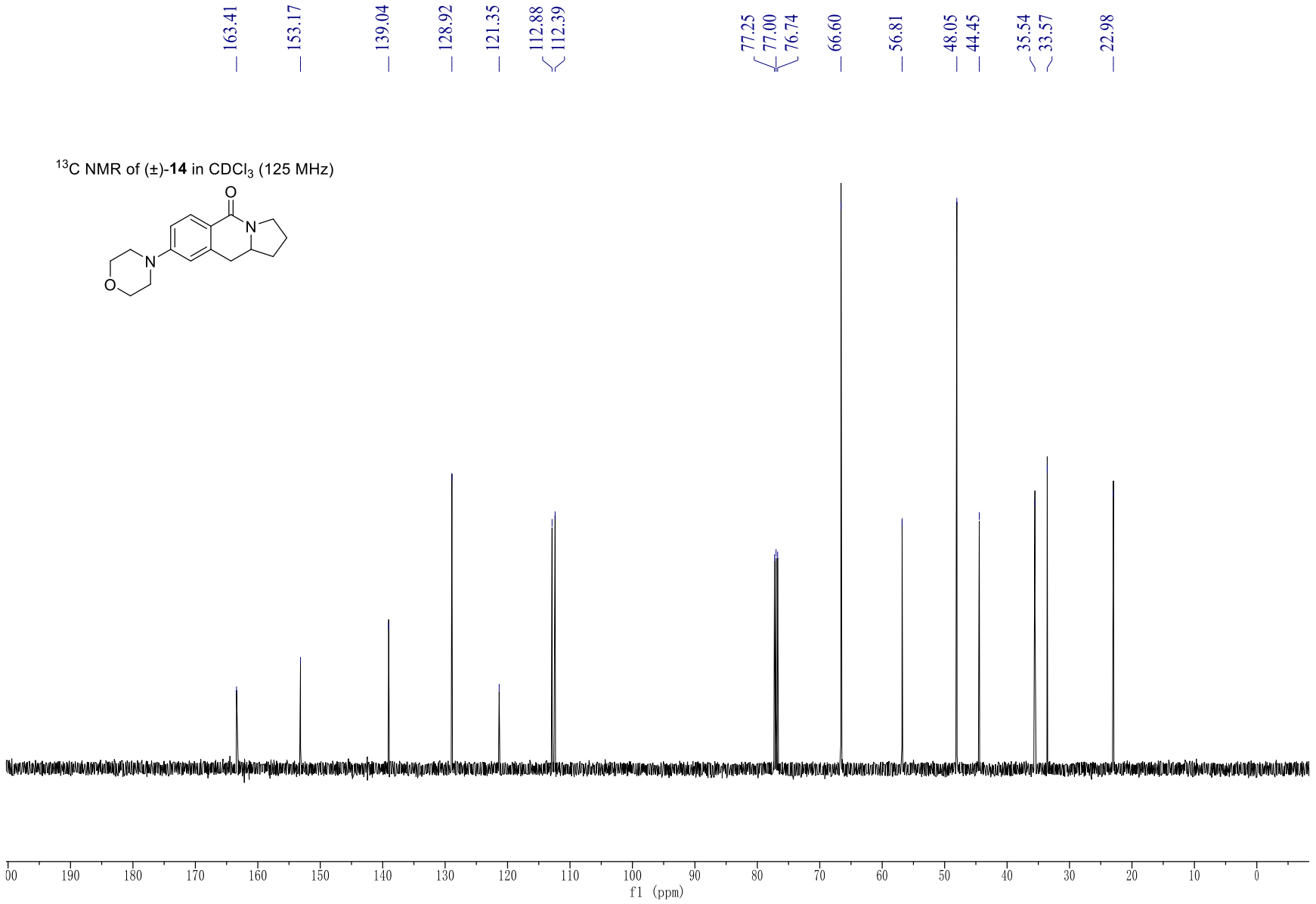


^{1}H NMR of (±)-**13** in $CDCl_3$ (500 MHz)

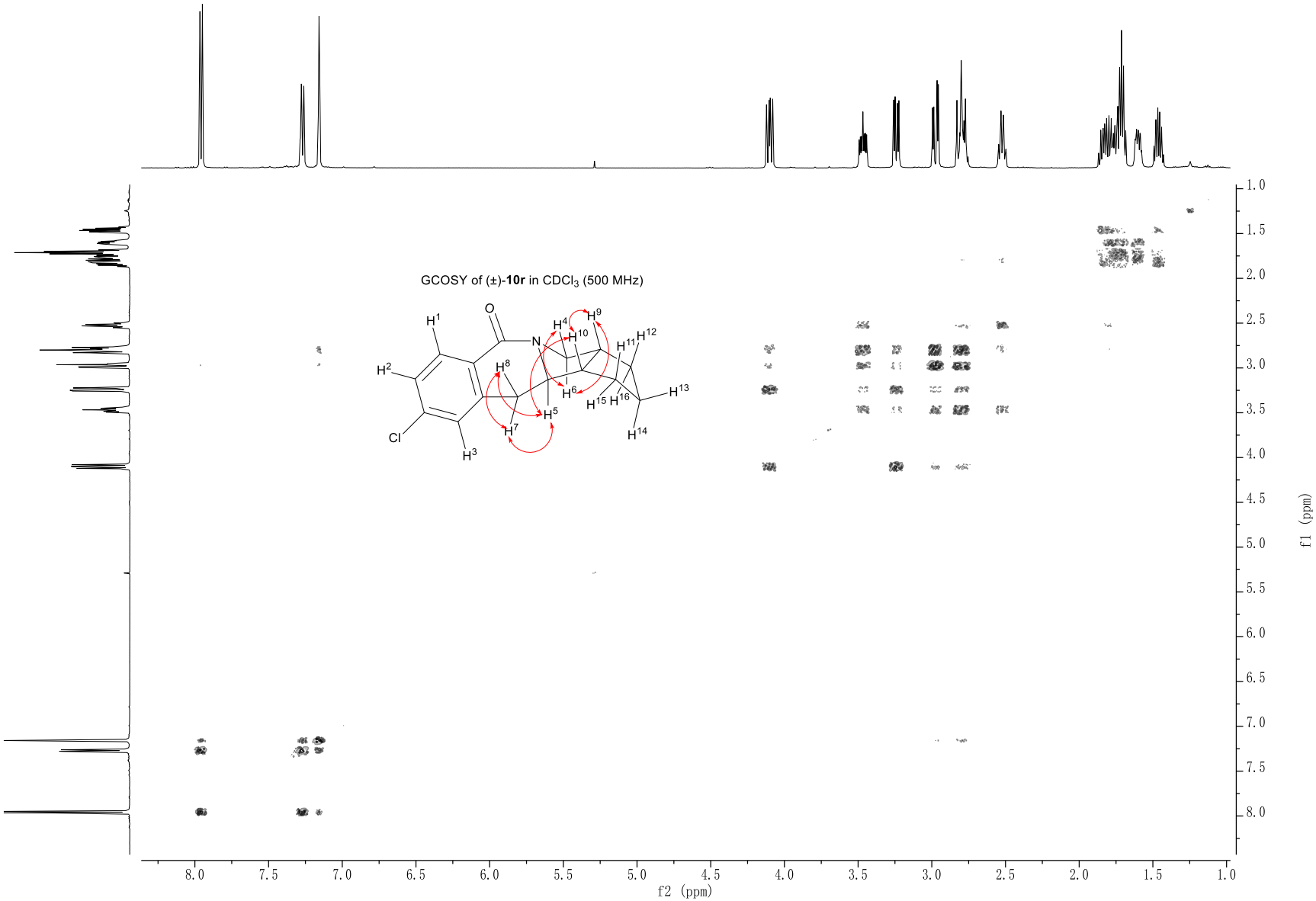


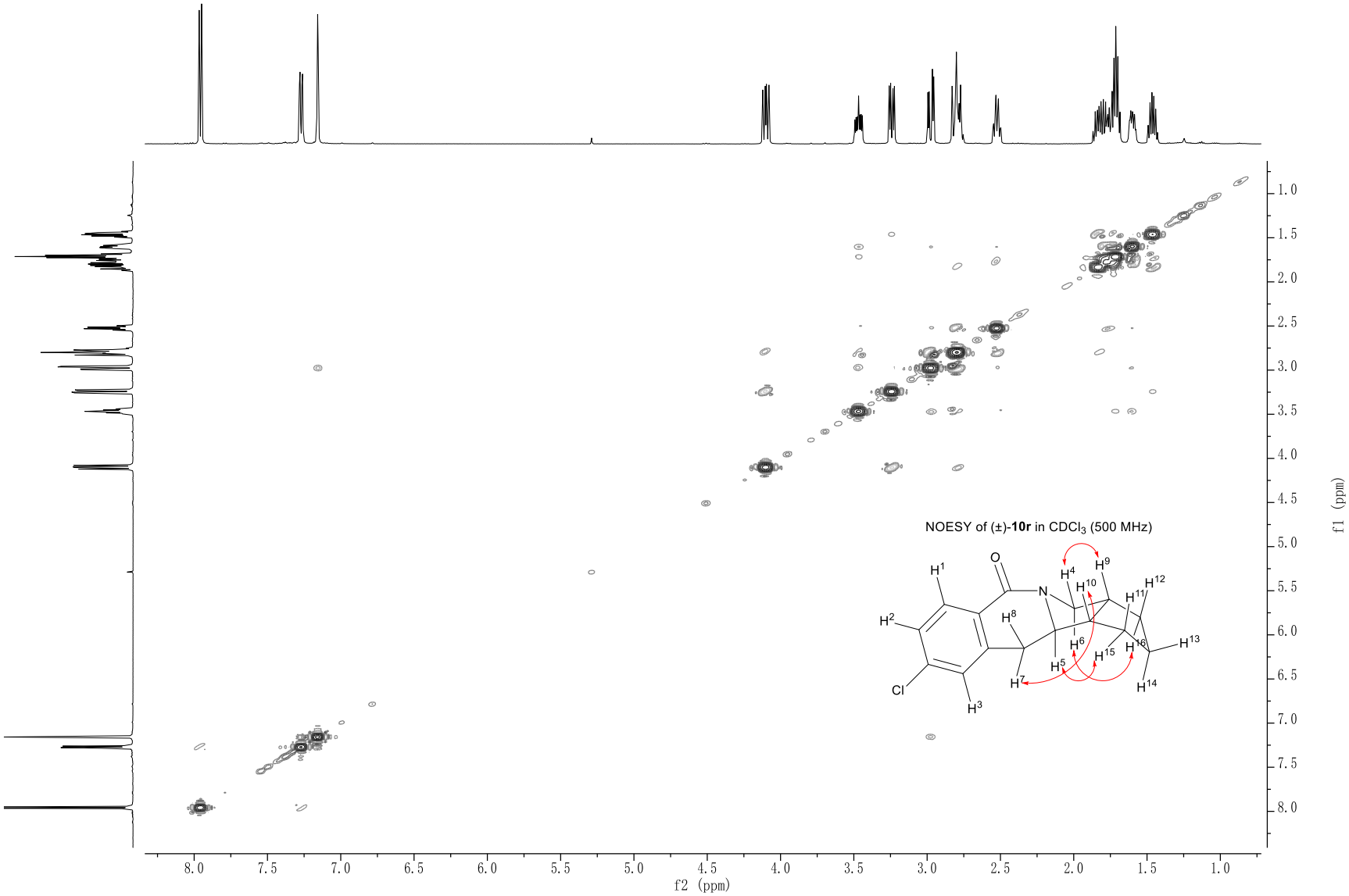
^{13}C NMR of (±)-**13** in $CDCl_3$ (125 MHz)

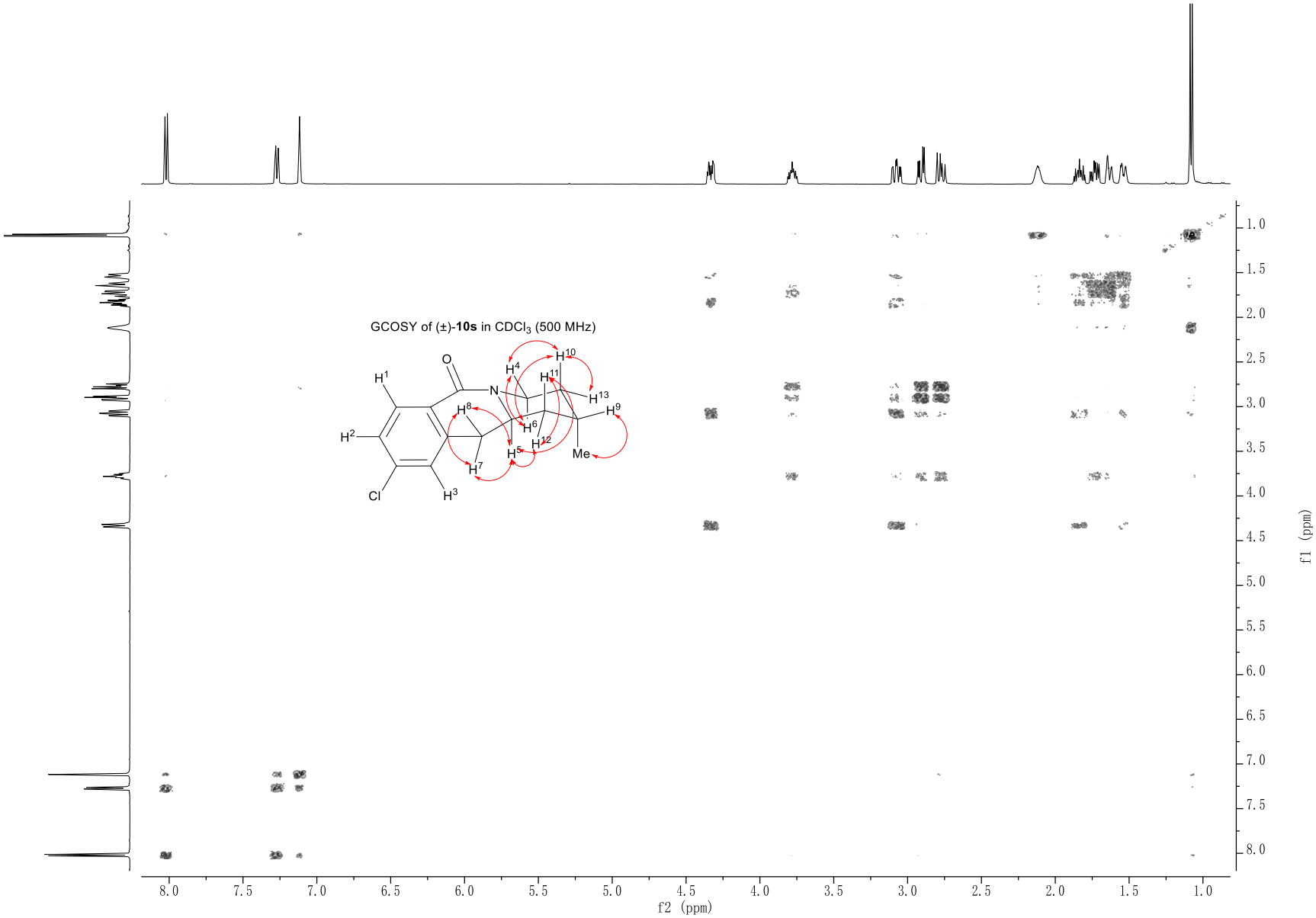

7.92 7.90 7.26 6.80 6.80 6.79 6.78 6.78 6.60 6.60 6.60 3.83 3.82 3.81 3.78 3.77 3.76 3.75 3.74 3.74 3.73 3.72 3.72 3.71 3.70 3.60 3.59 3.59 3.58 3.57 3.57 3.56 3.23 3.22 3.22 3.21 2.92 2.91 2.89 2.88 2.78 2.75 2.73 2.25 2.24 2.24 2.23 2.06 2.04 2.04 2.03 2.02 1.83 1.81 1.70 1.70 1.68 1.68 1.66
1H NMR of (±)-14 in CDCl3 (500 MHz)
O
N
N
O
1.00
1.08
1.07
4.40
2.27
1.08
4.42
1.07
1.06
1.21
1.21
1.08
1.07
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
f1 (ppm)

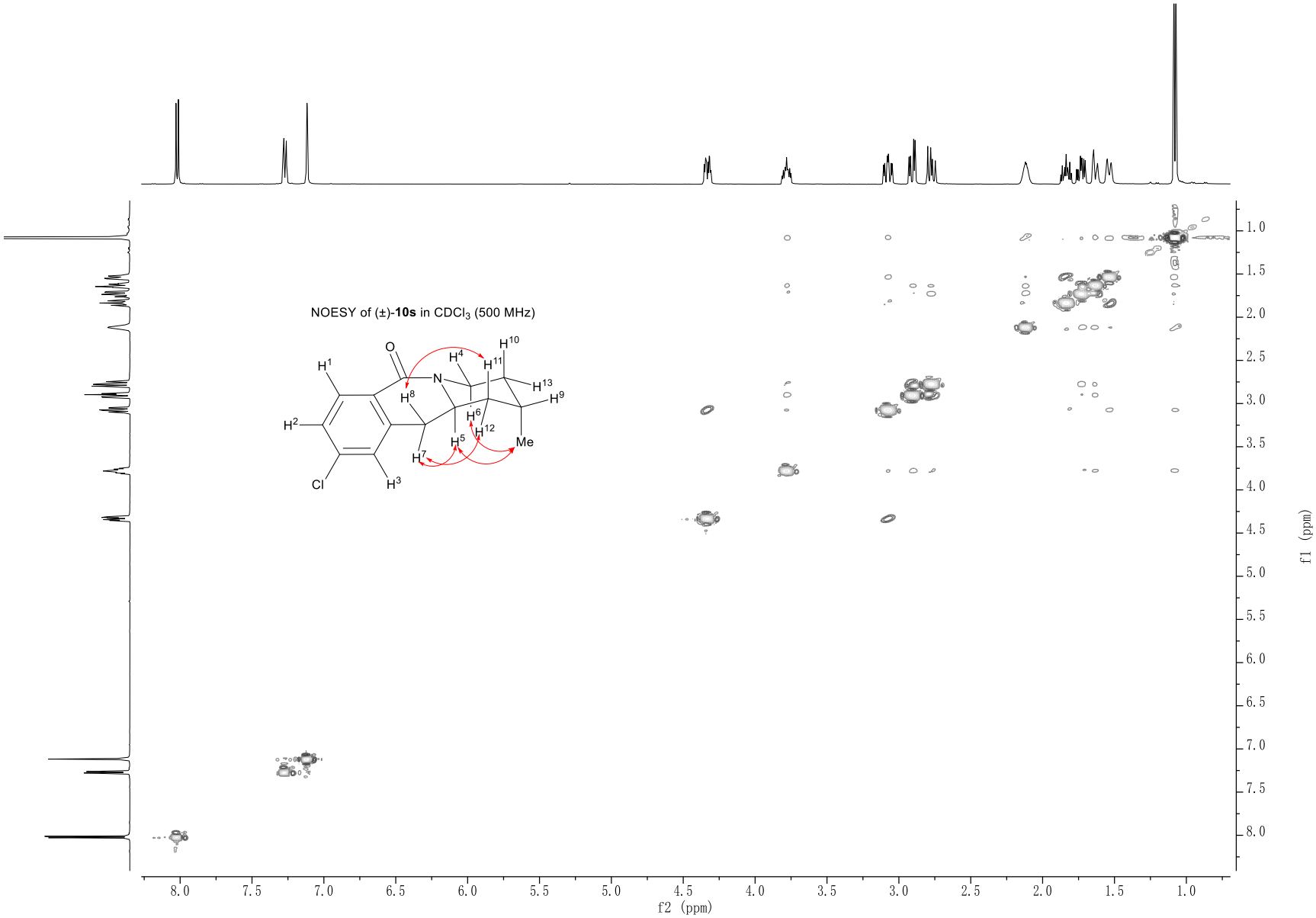


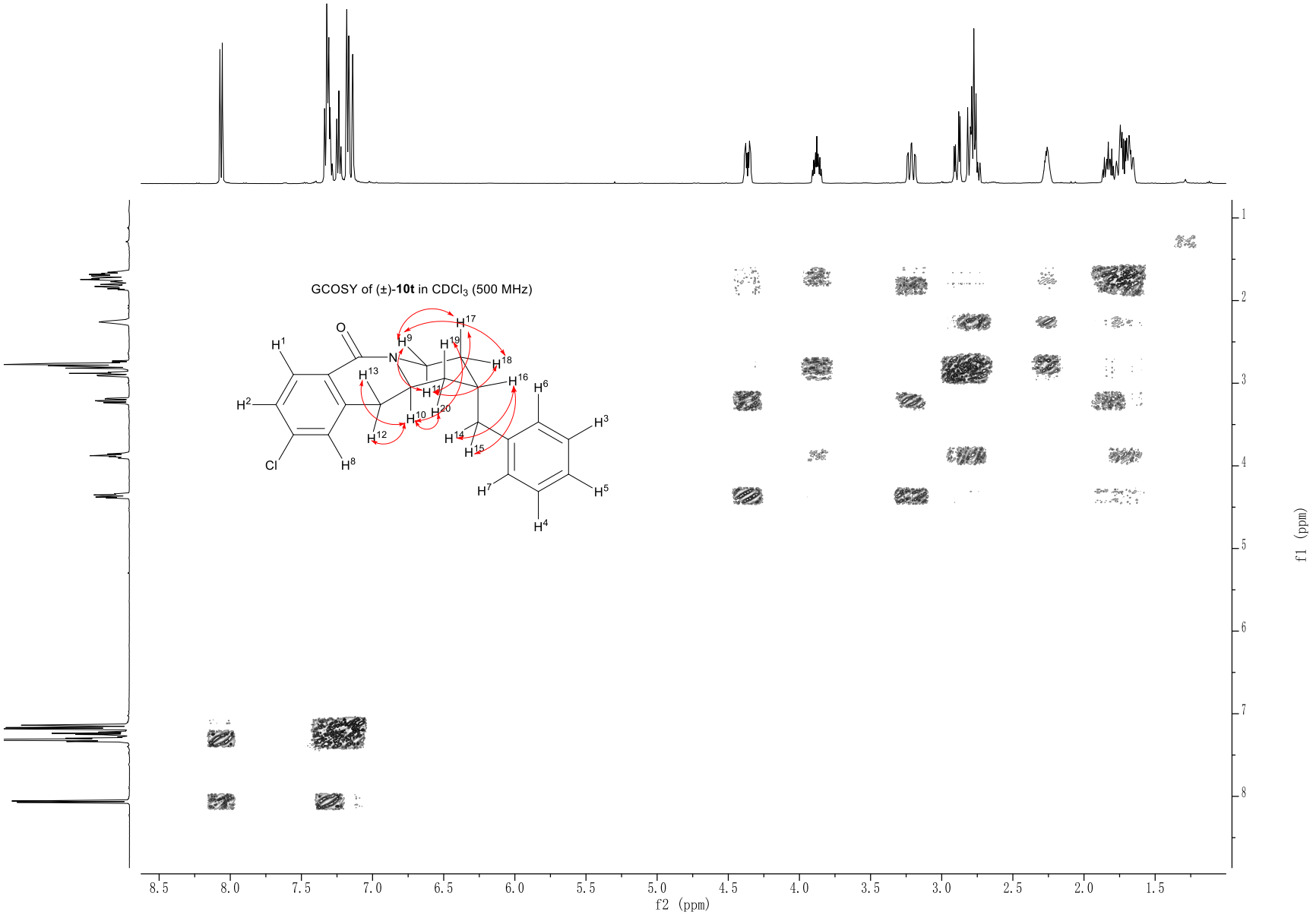
^{13}C NMR of (±)-**14** in $CDCl_3$ (125 MHz)

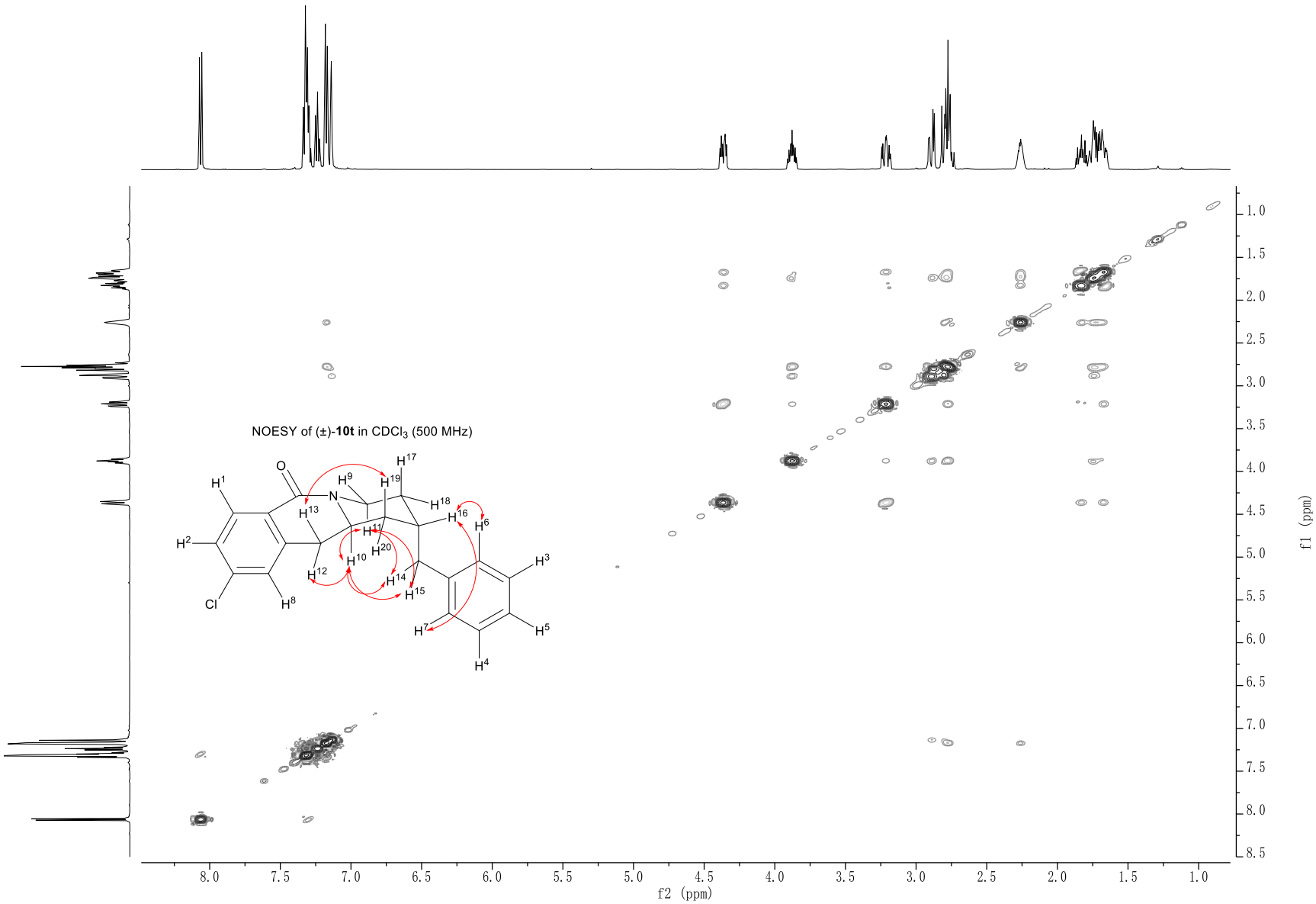

GCOSY of (±)-10r in CDCl3 (500 MHz)
O
N
Cl
H1
H2
H3
H4
H5
H6
H7
H8
H9
H10
H11
H12
H13
H14
H15
H16
f2 (ppm)
f1 (ppm)

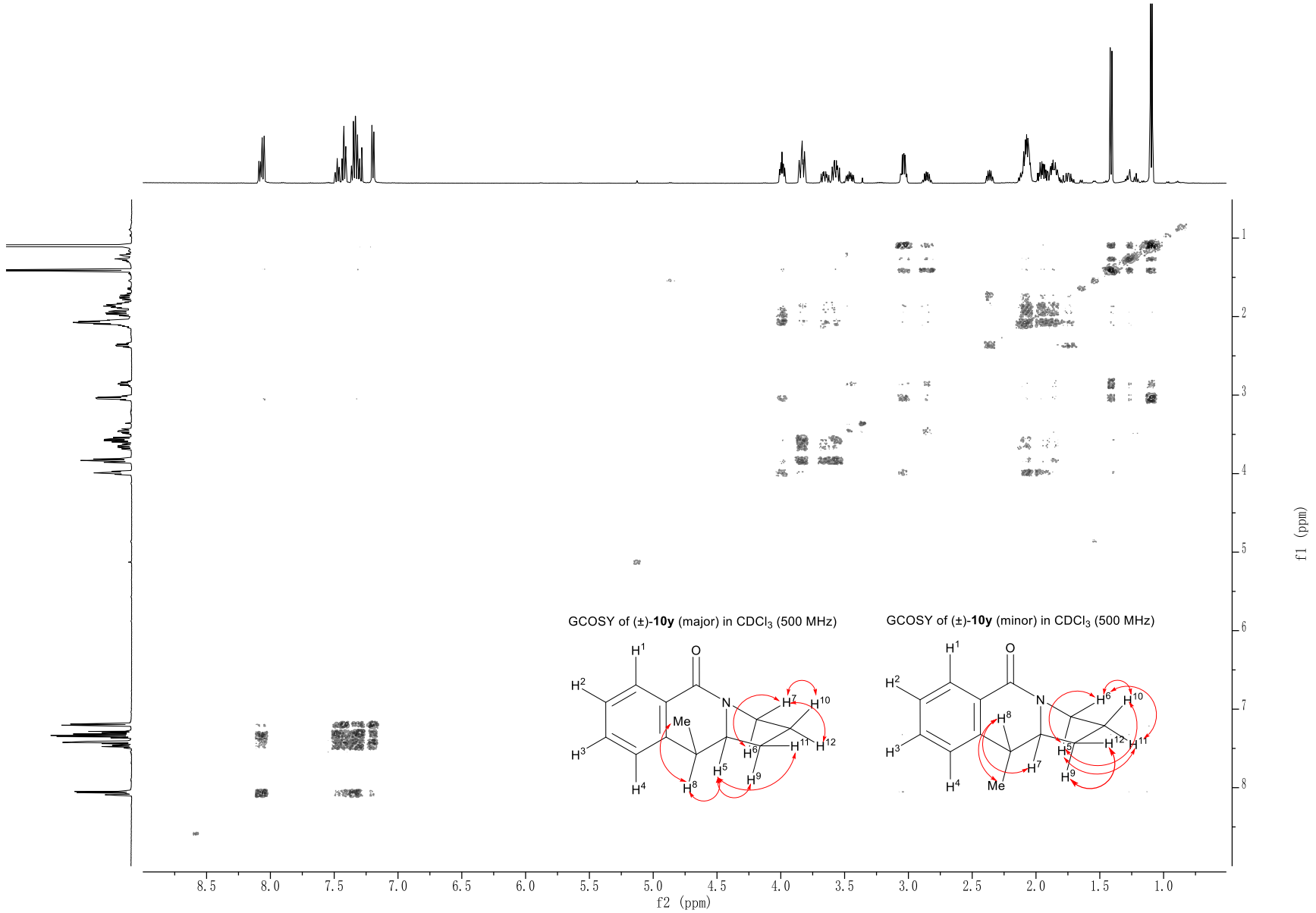

NOESY of (±)-10r in CDCl3 (500 MHz)
f2 (ppm)
f1 (ppm)

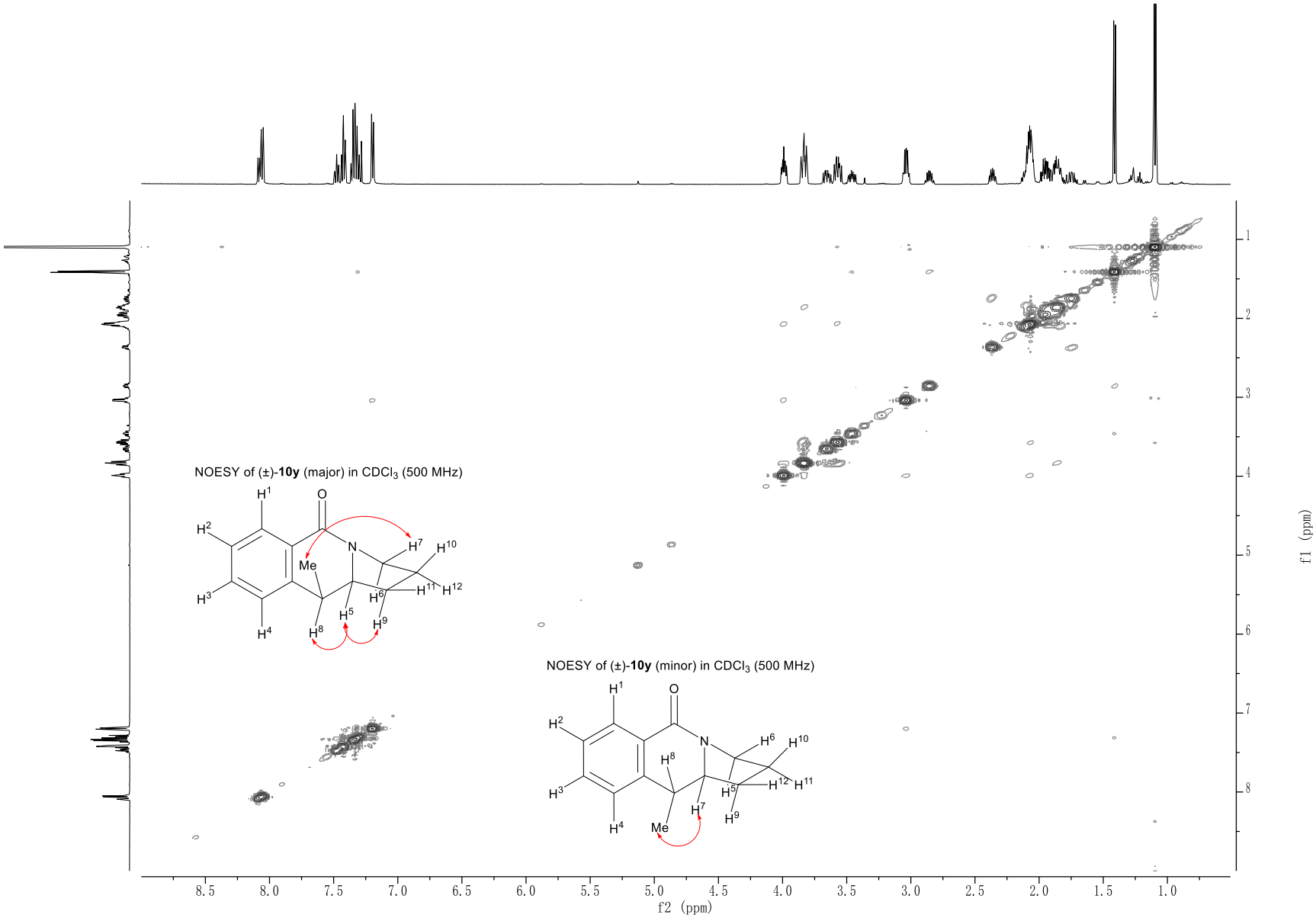

GCOSY of (±)-10s in CDCl3 (500 MHz)
O
N
H1
H2
H3
Cl
H4
H5
H6
H7
H8
H9
H10
H11
H12
H13
Me
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
f1 (ppm)


NOESY of (±)-10s in CDCl3 (500 MHz)
O
H1
H4
H10
H11
N
H13
H9
H8
H2
H6
H12
H5
Me
H7
Cl
H3
f2 (ppm)
f1 (ppm)


GCOSY of (±)-10t in CDCl3 (500 MHz)
O
N
Cl
H1
H2
H3
H4
H5
H6
H7
H8
H9
H10
H11
H12
H13
H14
H15
H16
H17
H18
H19
H20
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
f2 (ppm)
1
2
3
4
5
6
7
8
f1 (ppm)


NOESY of (±)-10t in CDCl3 (500 MHz)
O
H1
H9
H17
H19
N
H18
H13
H16
H6
H2
H11
H20
H10
H3
H12
H14
H15
Cl
H8
H7
H5
H4
f2 (ppm)
f1 (ppm)


GCOSY of (±)-10y (major) in CDCl3 (500 MHz)
GCOSY of (±)-10y (minor) in CDCl3 (500 MHz)
f2 (ppm)
f1 (ppm)


NOESY of (±)-10y (major) in CDCl3 (500 MHz)
NOESY of (±)-10y (minor) in CDCl3 (500 MHz)
f2 (ppm)
f1 (ppm)