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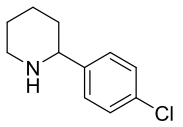
General Information: Starting materials and reagents were purchased from commercial sources and used as received unless stated otherwise. Anhydrous diethyl ether and tetrahydrofuran was dried using a JC Meyer solvent system. All liquid amines, liquid bromobenzenes, thiophene, trifluoroacetophenone, and phenyl *t*-butyl ketone were distilled prior to use. *n*-BuLi solution in hexanes and PhLi solution in dibutyl ether 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. Visualization was accomplished with UV light, Dragendorff-Munier stains or $KMnO_4$ stains, followed by heating. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on Varian Unity Inova 300 MHz, Varian Unity Inova 500 MHz, Bruker 600 MHz and Bruker 400 MHz instrument 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 300 MHz, Varian Unity Inova 500 MHz, Bruker 600 MHz and Bruker 400 MHz instrument and chemical shifts are reported in ppm using the solvent as an internal standard ($CDCl_3$ at 77.16 ppm). High resolution mass spectra (HRMS) were obtained from an Agilent 6230 ESI-TOF instrument. Cyclic 2-arylamines were prepared according to reported procedures by our group.[2] β-Keto acids were synthesized according to reported literature procedures.[3] Amine **4o** was previously reported[4] and their published characterization data matched our own in all respects. In cases where more than one product diastereomer was obtained, dr values shown are based on the corresponding amounts of the two individual diastereomers obtained after separation via a single silica gel column chromatographic purification under the conditions provided. Separation of diastereomers was readily achieved for all products with the exception of (±)-**4c**, (±)-**4d** and (±)-**6m** which were isolated as mixtures of two diastereomers, and dr values of (±)-**4c**, (±)-**4d** and (±)-**6m** were determined by ^{1}H-NMR of the mixture after isolation. Both diastereomers were fully characterized for all products with drs lower than 5:1.

Synthesis of 2-aryl amines

2-(4-Chlorophenyl)piperidine



(±)-**7a**

To a solution of piperidine (296 μL, 3 mmol, 1 equiv) in anhydrous ether (6 mL) cooled to –78 °C was slowly added *n*-BuLi in hexanes (3 mmol, 1 equiv) under the protection of nitrogen, and the resulting solution was stirred at the same temperature for 5 min. To this was then added via cannula a solution of trifluoroacetophenone (522 mg, 3 mmol, 1 equiv) in anhydrous ether (3 mL). The resulting mixture was stirred at –78 °C for 10 min, followed by the addition of 4-chlorophenyl lithium solution (4.5 mmol, 1.5 equiv) in one portion. The reaction mixture was stirred at that temperature for 2 hours and then brought to room temperature over 2 hours. The reaction mixture was then cooled back down to –78 °C and quenched via the addition of MeOH (1.5 mL). The resulting mixture was diluted with ether (20 mL) and washed with water (20 mL). The aqueous layer was then extracted with ether (3 x 20 mL) and the combined organic layers washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography to yield 54% (317 mg) of the desired product.

Preparation of 4-chlorophenyl lithium solution: To a solution of 1-bromo-4-chlorobenzene (862 mg, 4.5 mmol, 1.5 equiv to the amine) in anhydrous ether (6 mL) cooled at –78 °C was added *n*-BuLi in hexanes (4.5 mmol, 1.5 equiv to the amine) dropwise under the protection of nitrogen. The resulting mixture was stirred at the same temperature for 30 min, then warmed up to room temperature over 30 min to give the corresponding aryllithium in ether solution.

Characterization data:

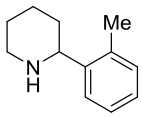
R_f = 0.30 in EtOAc/MeOH/*i*-$PrNH_2$ 90:9:1 v/v/v.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.45–7.14 (comp, 4H), 3.63–3.52 (m, 1H), 3.27–3.13 (m, 1H), 2.80 (app td, *J* = 11.7, 2.8 Hz, 1H), 2.23–1.97 (m, 1H), 1.97–1.85 (m, 1H), 1.78 (dd, *J* = 8.2, 1.5 Hz, 1H), 1.72–1.64 (m, 1H), 1.62–1.39 (comp, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 143.9, 132.7, 128.6, 128.2, 61.7, 47.8, 35.1, 25.8, 25.4.

HRMS (ESI–TOF): Calculated for $C_{11}H_{14}NCl$ $[M + H]^+$: 196.0888, Found: 196.0875.

2-(o-Tolyl)piperidine



(±)-**7b**

To a solution of piperidine (296 μL, 3 mmol, 1 equiv) in anhydrous ether (6 mL) cooled to –78 °C was slowly added *n*-BuLi in hexanes (3 mmol, 1 equiv) under the protection of nitrogen, and the resulting solution was stirred at the same temperature for 5 min. To this was then added via cannula a solution of trifluoroacetophenone (522 mg, 3 mmol, 1 equiv) in anhydrous ether (3 mL). The resulting mixture was stirred at –78 °C for 10 min, followed by the addition of 2-methylphenyl lithium solution (4.5 mmol, 1.5 equiv) in one portion. The reaction mixture was stirred at that temperature for 2 hours and then brought to room temperature over 2 hours. The reaction was then cooled back down to –78 °C and quenched via the addition of MeOH (1.5 mL). The resulting mixture was diluted with ether (20 mL) and washed with water (20 mL). The aqueous layer was then extracted with ether (3 x 20 mL) and the combined organic layers washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography to yield 50% (263 mg) of the desired product.

Preparation of 2-methylphenyl lithium solution: To a solution of 1-bromo-2-methylbenzene (770 mg, 4.5 mmol, 1.5 equiv to the amine) in anhydrous ether (6 mL) cooled at –78 °C was added *n*-BuLi in hexanes (4.5 mmol, 1.5 equiv to the amine) dropwise under the protection of nitrogen. The resulting mixture was stirred at the same temperature for 30 min, then warmed up to room temperature over 30 min to give the corresponding aryllithium in ether solution.

Characterization data:

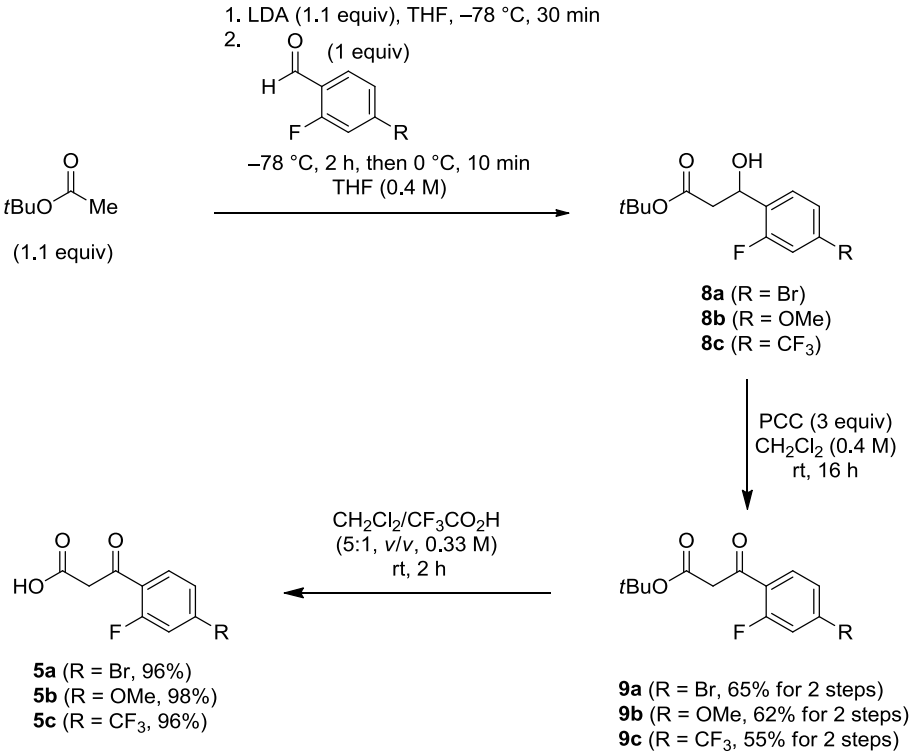
$\mathbf{R_f}$ = 0.22 in EtOAc/MeOH/*i*-$PrNH_2$ 90:9:1 v/v/v.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 7.7 Hz, 1H), 7.20 (ddd, *J* = 8.1, 5.4, 3.4 Hz, 1H), 7.16–7.08 (comp, 2H), 3.87–3.76 (m, 1H), 3.31–3.14 (m, 1H), 2.81 (app td, *J* = 11.8, 2.9 Hz, 1H), 2.49–2.09 (comp, 4H), 1.99–1.84 (m, 1H), 1.79–1.74 (m, 1H), 1.72–1.64 (m, 1H), 1.64–1.39 (comp, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 143.2, 134.8, 130.3, 126.7, 126.4, 125.9, 58.3, 48.1, 33.7, 26.0, 25.7, 19.3.

HRMS (ESI–TOF): Calculated for $C_{12}H_{17}N$ $[M + H]^+$: 176.1434, Found: 176.1423.

Synthesis of β-ketoacids



General procedure A for the preparation of 8

To a solution of diisopropylamine (11 mmol, 1.1 equiv) in anhydrous THF (30 mL) cooled to –78 °C was slowly added *n*-BuLi in hexanes (11 mmol, 1.1 equiv) under the protection of nitrogen, and the resulting solution was stirred at the same temperature for 10 min. To this was then added a solution of the *t*BuOAc (11 mmol, 1.1 equiv) in anhydrous THF (10 mL). The resulting mixture was stirred at –78 °C for 30 min, followed by the addition of a solution of corresponding aldehyde (10 mmol, 1 equiv) in anhydrous THF (10 mL). The resulting mixture was stirred at the same temperature for 2 h and then the reaction vessel was taken into an ice bath and stirred for 10 min. To this was added saturated NH_4Cl aqueous solution (30 mL). The aqueous layer was extracted with EtOAc (2 x 50 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure to provide the crude β-keto alcohol which was used in next step without further purification.

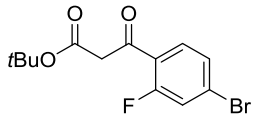
General procedure B for the preparation of 9

To the solution of the crude β-keto alcohol in CH_2Cl_2 (40 mL), pyridinium chlorochromate (30 mmol, 3 equiv) was added at room temperature. The resulting mixture was stirred at the same temperature for 16 h. Celite (10 g) was added to the reaction mixture and stirring was continued for another 1 h. The resulting heterogeneous mixture was filtered through a Celite pad. The filtrate was concentrated in vacuo and the residue purified by flash chromatography to provide β-keto *t*-butyl ester.

General procedure C for the preparation of 5

To the solution of the corresponding β-keto *t*-butyl ester (3 mmol) in CH_2Cl_2 (15 mL) cooled to 0 °C was slowly added trifluoroacetic acid (3 mL). Subsequently, the reaction vessel was removed from the ice bath and the reaction mixture stirred at room temperature for 2 h. Volatiles were then removed under reduced pressure to provide the corresponding β-keto acid which was used without further purification.

***tert*-Butyl 3-(4-bromo-2-fluorophenyl)-3-oxopropanoate (9a)**



9a

Following general procedures A and B, compound **9a** was obtained from 4-bromo-2-fluorobenzaldehyde (2.03 g, 10 mmol) as a clear crystalline solid in 65% yield (2.05 g) over 2 steps.

Characterization data:

$\mathbf{R_f}$ = 0.28 in hexane/EtOAc 95:5 v/v.

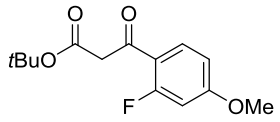
^{1}H-NMR (400 MHz, $CDCl_3$) of 3:1 mixture of enol/keto form: δ = 12.87 (s, 0.75H, **enol**), 7.81 (t, *J* = 8.1 Hz, 0.25H, **keto**), 7.72 (t, *J* = 8.2 Hz, 1H, 0.75H, **enol**), 7.44–7.17 (comp, 2H), 5.73 (s, 0.75H, **enol**), 3.87 (s, 0.5H, **keto**), 1.54 (s, 7H, **enol**), 1.44 (s, 2H, **keto**).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 189.4, 172.98, 166.21, 164.47, 164.43, 162.77, 161.41, 160.20, 158.84, 131.86, 131.84, 130.04, 130.01, 128.73, 128.63, 128.14, 128.10, 127.63, 127.59, 124.84, 124.74, 123.59, 123.47, 120.95, 120.85, 120.18, 119.97, 119.91, 119.71, 94.40, 94.25, 81.91, 81.46, 50.78, 50.70, 28.15, 27.76.

HRMS (ESI–TOF): Calculated for $C_{13}H_{14}BrFO_3$ $[M + Na]^+$: 339.0003, Found: 339.0009.

Note : For the ^{13}C-NMR, all peak values are listed. Signals are greater in number than expected due to the presence of keto and enol forms and carbon-fluorine coupling, complicating assignment.

***tert*-Butyl 3-(2-fluoro-4-methoxyphenyl)-3-oxopropanoate (9b)**



9b

Following general procedures A and B, compound **9b** was obtained from 2-fluoro-4-methoxybenzaldehyde (1.54 g, 10 mmol) as a clear crystalline solid in 62% yield (1.66 g).

Characterization data:

$\mathbf{R_f}$ = 0.28 in hexane/EtOAc 90:10 v/v.

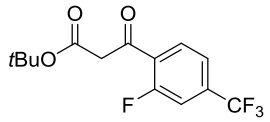
^{1}H-NMR (400 MHz, $CDCl_3$) of keto form (13:1 mixture of keto/enol was observed) : δ = 7.80 (t, *J* = 8.8 Hz, 1H), 6.66 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.51 (dd, *J* = 13.4, 2.5 Hz, 1H), 3.78–3.67 (comp, 5H), 1.35 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 188.91, 188.88, 166.62, 166.59, 165.12, 165.00, 164.71, 162.17, 131.98, 131.93, 117.36, 117.23, 110.72, 110.69, 101.41, 101.14, 81.30, 55.61, 50.53, 50.46, 28.02, 27.61.

HRMS (ESI–TOF): Calculated for $C_{10}H_9FO_4$ $[M + H]^+$: 213.0558, Found: 213.0587.

Note : For the ^{13}C-NMR, all peak values are listed. Signals are greater in number than expected due to the presence of keto and enol forms and carbon-fluorine coupling, complicating assignment.

***tert*-Butyl 3-(2-fluoro-4-(trifluoromethyl)phenyl)-3-oxopropanoate (9c)**



9c

Following general procedures A and B, compound **9c** was obtained from 2-fluoro-4-(trifluoromethyl)benzaldehyde (1.92 g, 10 mmol) as a clear crystalline solid in 55% yield (1.68 g).

Characterization data:

$\mathbf{R_f}$ = 0.30 in hexane/EtOAc 95:5 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$) of 1:1 mixture of enol/keto form: δ = 12.84 (s, 0.5H, **enol**), 8.03 (t, *J* = 7.6 Hz, 0.5H, **keto**), 7.97 (t, *J* = 7.6 Hz, 0.5H, **enol**), 7.54–7.28 (comp, 2H), 5.78 (s, 0.5H, **enol**), 3.90 (comp, 1H, **keto**), 1.53 (s, 4.5H, **enol**), 1.41 (s, 4.5H, **keto**).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 189.71, 189.68, 172.87, 166.09, 166.08, 163.81, 163.77, 162.70, 161.39, 160.16, 158.83, 136.69, 136.60, 136.36, 136.27, 136.02, 133.82, 133.74, 133.49, 133.40, 133.07, 131.89, 131.86, 130.00, 129.98, 127.58, 127.45, 126.93, 126.69, 125.38, 125.28, 124.25, 124.22, 123.97, 123.95, 121.54, 121.52, 121.44, 121.40, 121.37, 121.33, 121.26, 121.24, 121.08, 121.04, 121.00, 120.97, 118.55, 114.38, 114.34, 114.31, 114.11, 114.07, 113.98, 113.94, 113.90, 113.86, 113.67, 113.63, 113.59, 95.58, 95.44, 82.26, 81.86, 77.32, 77.00, 76.68, 50.84, 50.77, 28.14, 27.76.

HRMS (ESI–TOF): Calculated for $C_{10}H_6F_4O_3$ $[M + Na]^+$: 273.0145, Found: 273.0120.

Note : For the ^{13}C-NMR, all peak values are listed. Signals are greater in number than expected due to the presence of keto and enol forms and carbon-fluorine coupling, complicating assignment.

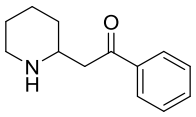
General procedure D for the decarboxylative alkylation of transient imines:

To a solution of the amine (1 mmol, 1 equiv) in anhydrous ether (1.5 mL) cooled to –78 °C was slowly added *n*-BuLi in hexanes (1 mmol, 1 equiv) under the protection of nitrogen. After stirring for 5 min at the same temperature, a solution of the corresponding ketone oxidant in anhydrous ether (1 mL) was added. The resulting mixture was stirred at –78 °C for 5 min. To this was then added a solution of trifluoroacetic acid (1.05 mmol, 1.05 equiv) in anhydrous THF (1 mL). The resulting mixture was stirred at –78 °C for 5 min, followed by the addition of a solution of the corresponding β-keto acid (1.5 mmol, 1.5 equiv) in anhydrous THF (1.5 mL). Subsequently, the reaction vessel was removed from the low temperature bath and the reaction mixture stirred at room temperature for 2 h. The reaction mixture was then cooled to 0 °C and quenched via the addition of 4 mL of saturated $NaHCO_3$ solution. An additional amount of saturated $NaHCO_3$ solution (10 mL) was then added and the resulting mixture was extracted with ether (2 x 20 mL). The combined organic layers washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography.

General procedure E for the decarboxylative alkylation/S_NAr reaction of transient imines:

To a solution of the amine (1 mmol, 1 equiv) in anhydrous ether (1.5 mL) cooled to –78 °C was slowly added *n*-BuLi in hexanes (1 mmol, 1 equiv) under the protection of nitrogen. After stirring for 5 min at the same temperature, a solution of trifluoroacetophenone (1.05 mmol, 1.05 equiv) in anhydrous ether (1 mL) was added. The resulting mixture was stirred at –78 °C for 5 min. To this was then added a solution of trifluoroacetic acid (1.05 mmol, 1.05 equiv) in anhydrous THF (1 mL). The resulting mixture was stirred at –78 °C for 5 min, followed by the addition of a solution of the corresponding β-keto acid (1.5 mmol, 1.5 equiv) in anhydrous THF (1.5 mL). Subsequently, the reaction vessel was removed from the low temperature bath and the reaction mixture stirred at room temperature for 2 h. To this was then added K_2CO_3 (2 mmol, 2 equiv) and DMF (5 mL) and the resulting mixture was stirred at 110 °C for 6 h. The reaction mixture was then allowed to cool to room temperature and water (20 mL) was added. The resulting mixture was extracted with EtOAc (2 x 20 mL) and the combined organic layers washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography.

1-Phenyl-2-(piperidin-2-yl)ethan-1-one



(±)-**4a**

Following general procedure D, compound (±)-**4a** was obtained from piperidine (99 μL, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol) as a colorless oil in 76% yield (154 mg). EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data:

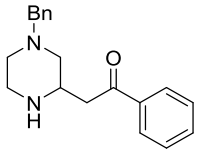
$\mathbf{R_f}$ = 0.27 in CH_2Cl_2/MeOH 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.01–7.86 (m, 2H), 7.61–7.49 (m, 1H), 7.47–7.39 (m, 2H), 3.11 (app ddt, *J* = 12.3, 6.2, 3.3 Hz, 1H), 3.08–2.98 (comp, 3H), 2.71 (app td, *J* = 11.7, 2.9 Hz, 1H), 2.35 (s, 1H), 1.90–1.74 (m, 1H), 1.74–1.58 (comp, 2H), 1.51–1.34 (comp, 2H), 1.36–1.20 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 199.7, 137.2, 133.3, 128.7, 128.2, 53.0, 47.0, 45.8, 32.9, 26.1, 24.9.

HRMS (ESI–TOF): Calculated for $C_{13}H_{17}NO$ $[M + H]^+$: 204.1383, Found: 204.1392.

2-(4-Benzylpiperazin-2-yl)-1-phenylethan-1-one



(±)-**4b**

Following general procedure D, compound (±)-**4b** was obtained from 1-benzylpiperazine (174 μL, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol) as a viscous oil in 51% yield (150 mg). EtOAc containing MeOH (1-15%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data:

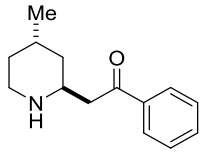
$\mathbf{R_f}$ = 0.28 in EtOAc/MeOH/*i*-$PrNH_2$ 90:9:1 v/v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.92 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.65–7.51 (m, 1H), 7.49–7.39 (m, 2H), 7.34–7.28 (comp, 4H), 7.28–7.21 (m, 1H), 3.55–3.39 (comp, 3H), 3.17–3.05 (comp, 2H), 3.03–2.94 (comp, 2H), 2.92–2.55 (comp, 3H), 2.21 (ddd, *J* = 11.1, 8.4, 5.4 Hz, 1H), 2.03 (app t, *J* = 10.3 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.9, 138.0, 136.9, 133.5, 129.2, 128.8, 128.4, 128.2, 127.2, 63.3, 58.7, 53.2, 51.3, 45.4, 42.4.

HRMS (ESI–TOF): Calculated for $C_{19}H_{22}N_2O$ $[M + H]^+$: 295.1805, Found: 295.1816.

2-((2S*,4S*)-4-Methylpiperidin-2-yl)-1-phenylethan-1-one



(±)-**4c**

Following general procedure D, compound (±)-**4c** was obtained from 4-methylpiperidine (118.3 μL, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol) as a colorless oil in 70% yield (152 mg) and 2:1 diastereomeric ratio. EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography. The two diastereomers were obtained as an inseparable mixture.

Characterization data:

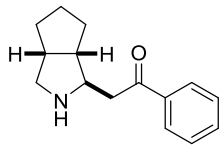
$\mathbf{R_f}$ = 0.22 in CH_2Cl_2/MeOH 90:10 v/v.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.89–7.81 (comp, 2H), 7.49–7.40 (comp, 1H), 7.38–7.28 (comp, 2H), 3.41 (app dt, *J* = 8.4, 4.3 Hz, 0.67H), 3.21–2.47 (comp, 4H), 2.38 (comp, 1.33H), 1.89–1.77 (m, 0.67H), 1.72–1.27 (comp, 3H), 1.23–1.12 (m, 0.66H), 1.09–0.70 (comp, 3.66H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 199.5, 199.3, 136.9, 136.9, 133.0, 132.9, 128.4, 127.9, 52.4, 47.3, 46.4, 45.5, 43.4, 41.2, 40.5, 38.4, 34.5, 32.6, 31.2, 25.9, 22.4, 19.4.

HRMS (ESI–TOF): Calculated for $C_{14}H_{19}NO$ $[M + H]^+$: 218.1539, Found: 218.1531.

2-((1R*,3aR*,6aS*)-Octahydrocyclopenta[c]pyrrol-1-yl)-1-phenylethan-1-one



(±)-**4d**

Following general procedure D, compound (±)-**4c** was obtained from octahydrocyclopenta[c]pyrrole (111 mg, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol) as a colorless oil in 58% yield (133 mg) and 8:1 diastereomeric ratio. EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography. The two diastereomers were obtained as an inseparable mixture.

Characterization data:

$\mathbf{R_f}$ = 0.21 in CH_2Cl_2/MeOH 90:10 v/v.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.04–7.89 (comp, 2H), 7.62–7.48 (comp, 1H), 7.46–7.37 (comp, 2H), 3.42 (d, *J* = 6.4 Hz, 0.11H), 3.32–2.81 (comp, 3.88H), 2.74–2.57 (comp, 1H), 2.54–2.30 (comp, 2H), 2.21 (app ddt, *J* = 9.9, 7.6, 3.8 Hz, 0.88H), 1.96 (m, 0.11H), 1.75–1.01 (comp, 6H).
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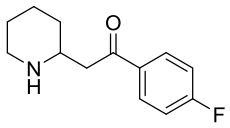
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 199.9, 137.1, 133.1, 133.1, 128.6, 128.1, 128.0, 61.6, 57.3, 53.6, 53.3, 46.5, 44.4, 43.1, 42.8, 40.5, 34.9, 31.7, 30.7, 28.1, 25.2.

HRMS (ESI–TOF): Calculated for $C_{15}H_{19}NO$ $[M + H]^+$: 230.1539, Found: 230.1535.

1-(4-Fluorophenyl)-2-(piperidin-2-yl)ethan-1-one



(±)-**4e**

Following general procedure D, compound (±)-**4e** was obtained from piperidine (99 μL, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-(4-fluorophenyl)-3-oxopropanoic acid (273.2 mg, 1.5 mmol) as a colorless oil in 61% yield (135 mg). EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data:

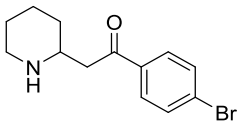
$\mathbf{R_f}$ = 0.17 in EtOAc/MeOH/*i*-$PrNH_2$ 80:19:1 v/v/v.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.91 (ddd, *J* = 8.7, 5.4, 1.7 Hz, 2H), 7.05 (app td, *J* = 8.7, 1.7 Hz, 2H), 3.06 (dddd, *J* = 10.6, 7.4, 4.7, 2.7 Hz, 1H), 3.01–2.89 (comp, 3H), 2.68–2.57 (comp, 2H), 1.76–1.70 (m, 1H), 1.65–1.52 (comp, 2H), 1.45–1.27 (comp, 2H), 1.22 (app tdd, *J* = 12.3, 10.7, 3.7 Hz, 1H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 198.0, 165.9 ($J_{C\text{-}F}$ = 254.9 Hz), 133.6 ($J_{C\text{-}F}$ = 3.0 Hz), 130.8 ($J_{C\text{-}F}$ = 9.4 Hz), 115.8 ($J_{C\text{-}F}$ = 21.9 Hz), 52.8, 46.8, 45.5, 32.7, 25.9, 24.7.

HRMS (ESI–TOF): Calculated for $C_{13}H_{16}NOF$ $[M + H]^+$: 222.1289, Found: 222.1297.

1-(4-Bromophenyl)-2-(piperidin-2-yl)ethan-1-one



(±)-**4f**

Following general procedure D, compound (±)-**4f** was obtained from piperidine (99 μL, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-(4-bromophenyl)-3-oxopropanoic acid (364.5 mg, 1.5 mmol) as a colorless oil in 58% yield (164 mg). EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data:

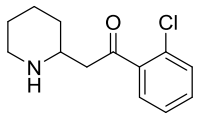
$\mathbf{R_f}$ = 0.15 in EtOAc/MeOH/*i*-$PrNH_2$ 80:19:1 v/v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 8.6 Hz, 2H), 3.12 (dddd, *J* = 10.0, 7.3, 4.8, 2.6 Hz, 1H), 3.07–2.93 (comp, 3H), 2.80 (s, 1H), 2.70 (app td, *J* = 11.8, 2.8 Hz, 1H), 1.92–1.72 (m, 1H), 1.68–1.56 (comp, 2H), 1.53–1.20 (comp, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.5, 135.8, 132.0, 129.7, 128.6, 52.9, 46.9, 45.5, 32.6, 25.9, 24.7.

HRMS (ESI–TOF): Calculated for $C_{13}H_{16}NOBr(79)$ $[M + H]^+$: 282.0488, Found: 282.0497.

1-(2-Chlorophenyl)-2-(piperidin-2-yl)ethan-1-one



(±)-**4g**

Following general procedure D, compound (±)-**4g** was obtained from piperidine (99 μL, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-(2-chlorophenyl)-3-oxopropanoic acid (297.9 mg, 1.5 mmol) as a colorless oil in 46% yield (110 mg). EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data:

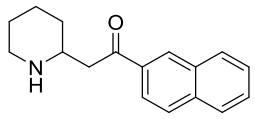
$\mathbf{R_f}$ = 0.21 in CH_2Cl_2/MeOH 95:5 v/v.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.42 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.36–7.30 (comp, 2H), 7.30–7.20 (m, 1H), 3.83 (s, 1H), 3.22–2.88 (comp, 4H), 2.67 (app td, *J* = 11.7, 3.0 Hz, 1H), 1.89–1.53 (comp, 3H), 1.53–0.99 (comp, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 202.3, 139.1, 131.8, 130.9, 130.6, 128.8, 126.9, 52.9, 49.4, 46.6, 32.0, 25.4, 24.3.

HRMS (ESI–TOF): Calculated for $C_{13}H_{16}NOCl$ $[M + H]^+$: 238.0993, Found: 238.1002.

1-(Naphthalen-2-yl)-2-(piperidin-2-yl)ethan-1-one



(±)-**4h**

Following general procedure D, compound (±)-**4h** was obtained from piperidine (99 μL, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-(naphthalen-2-yl)-3-oxopropanoic acid (321 mg, 1.5 mmol) as a colorless solid in 53% yield (134 mg). EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data:

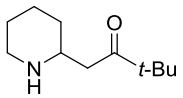
$\mathbf{R_f}$ = 0.27 in CH_2Cl_2/MeOH 90:10 v/v.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.51–8.35 (m, 1H), 7.99 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.92 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.86–7.79 (comp, 2H), 7.59–7.49 (comp, 2H), 3.27–3.09 (comp, 3H), 3.09–3.01 (comp, 2H), 2.72 (app td, *J* = 11.7, 2.8 Hz, 1H), 1.88–1.76 (m, 1H), 1.69 (app ddt, *J* = 12.5, 4.2, 2.4 Hz, 1H), 1.61 (app ddt, *J* = 12.5, 4.2, 2.7 Hz, 1H), 1.54–1.22 (comp, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 199.3, 135.6, 134.3, 132.4, 129.8, 129.6, 128.5, 128.4, 127.7, 126.7, 123.7, 53.0, 46.8, 45.5, 32.6, 25.9, 24.7.

HRMS (ESI–TOF): Calculated for $C_{17}H_{19}NO$ $[M + H]^+$: 254.1539, Found: 254.1551.

3,3-Dimethyl-1-(piperidin-2-yl)butan-2-one



(±)-**4i**

Following general procedure D, compound (±)-**4i** was obtained from piperidine (99 μL, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 4,4-dimethyl-3-oxopentanoic acid (216.2 mg, 1.5 mmol) as a colorless oil in 45% yield (83 mg). EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data:

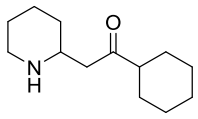
$\mathbf{R_f}$ = 0.16 in EtOAc/MeOH/*i*-$PrNH_2$ 80:19:1 v/v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.04–2.96 (m, 1H), 2.96–2.86 (m, 1H), 2.65 (app td, *J* = 11.7, 2.8 Hz, 1H), 2.59–2.43 (comp, 3H), 1.79–1.68 (m, 1H), 1.64–1.49 (comp, 2H), 1.47–1.27 (comp, 2H), 1.23–1.12 (m, 1H), 1.10 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 215.9, 52.6, 46.9, 44.3, 43.8, 32.5, 26.5, 25.9, 24.8.

HRMS (ESI–TOF): Calculated for $C_{11}H_{21}NO$ $[M + H]^+$: 184.1696, Found: 184.1705.

1-Cyclohexyl-2-(piperidin-2-yl)ethan-1-one



(±)-**4j**

Following general procedure D, compound (±)-**4j** was obtained from piperidine (99 μL, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-cyclohexyl-3-oxopropanoic acid (255 mg, 1.5 mmol) as a colorless oil in 40% yield (84 mg). CH_2Cl_2 containing MeOH (0-10%) was used as the eluent for silica gel chromatography.

Characterization data:

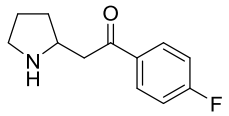
$\mathbf{R_f}$ = 0.37 in CH_2Cl_2/MeOH 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.99–2.90 (m, 1H), 2.90–2.80 (m, 1H), 2.59 (app td, *J* = 11.7, 2.8 Hz, 1H), 2.48–2.38 (comp, 3H), 2.30–2.17 (m, 1H), 1.85–1.64 (comp, 5H), 1.63–1.43 (comp, 3H), 1.41–0.99 (comp, 8H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 213.8, 52.4, 51.2, 47.6, 46.8, 32.5, 28.4, 28.4, 25.9, 25.8, 25.6, 25.6, 24.7.

HRMS (ESI–TOF): Calculated for $C_{13}H_{23}NO$ $[M + H]^+$: 210.1852, Found: 210.1864.

1-(4-Fluorophenyl)-2-(pyrrolidin-2-yl)ethan-1-one



(±)-**4k**

Following general procedure D, compound (±)-**4k** was obtained from pyrrolidine (82 μL, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-(4-fluorophenyl)-3-oxopropanoic acid (273.2 mg, 1.5 mmol) as a colorless oil in 45% yield (93 mg). EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data:

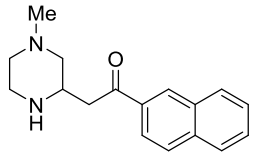
$\mathbf{R_f}$ = 0.21 in EtOAc/MeOH/*i*-$PrNH_2$ 80:19:1 v/v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.12–7.79 (m, 2H), 7.18–6.93 (m, 2H), 3.64–3.47 (m, 1H), 3.19–3.05 (comp, 2H), 3.01 (ddd, *J* = 10.0, 7.7, 5.2 Hz, 1H), 2.91 (ddd, *J* = 10.0, 8.2, 6.9 Hz, 1H), 2.38 (s, 1H), 1.99 (dddd, *J* = 12.0, 8.6, 6.9, 4.7 Hz, 1H), 1.89–1.67 (comp, 2H), 1.40 (dddd, *J* = 12.3, 9.4, 8.2, 7.3 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.1, 165.8 ($J_{C\text{-}F}$ = 254.6 Hz), 133.6 ($J_{C\text{-}F}$ = 3.0 Hz), 130.8 ($J_{C\text{-}F}$ = 9.3 Hz), 115.8 ($J_{C\text{-}F}$ = 21.8 Hz), 54.5, 46.3, 45.3, 31.4, 24.8.

HRMS (ESI–TOF): Calculated for $C_{12}H_{14}NOF$ $[M + H]^+$: 208.1132, Found: 208.1149.

2-(4-Methylpiperazin-2-yl)-1-(naphthalen-2-yl)ethan-1-one



(±)-**4l**

Following general procedure D, compound (±)-**4l** was obtained from 1-methylpiperazine (111 μL, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-(naphthalen-2-yl)-3-oxopropanoic acid (321 mg, 1.5 mmol) as a colorless oil in 48% yield (129 mg). EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data:

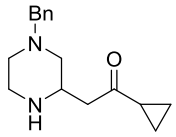
$\mathbf{R_f}$ = 0.27 in CH_2Cl_2/MeOH 90:10 v/v

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.48–8.40 (m, 1H), 7.98 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.93 (ddd, *J* = 7.6, 1.4, 0.7 Hz, 1H), 7.88–7.82 (comp, 2H), 7.69–7.49 (comp, 2H), 3.49 (dddd, *J* = 9.7, 7.7, 4.8, 3.0 Hz, 1H), 3.37–3.31 (s, 1H), 3.29–3.11 (comp, 2H), 3.06–2.97 (comp, 2H), 2.82 (ddd, *J* = 11.1, 2.9, 1.4 Hz, 1H), 2.77–2.70 (m, 1H), 2.30 (s, 3H), 2.20–2.10 (m, 1H), 2.06–1.95 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.6, 135.8, 134.2, 132.5, 130.0, 129.7, 128.7, 128.6, 127.8, 126.9, 123.7, 60.8, 55.2, 51.3, 46.4, 45.3, 42.5.

HRMS (ESI–TOF): Calculated for $C_{17}H_{20}N_2O$ $[M + H]^+$: 269.1648, Found: 269.1660.

2-(4-Benzylpiperazin-2-yl)-1-cyclopropylethan-1-one



(±)-**4m**

Following general procedure D, compound (±)-**4m** was obtained from 1-benzylpiperazine (176 μL, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-cyclopropyl-3-oxopropanoic acid (192 mg, 1.5 mmol) as a colorless oil in 46% yield (119 mg). CH_2Cl_2 containing MeOH (0-10%) was used as the eluent for silica gel chromatography.

Characterization data:

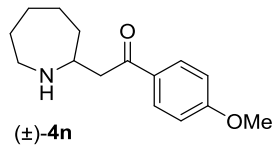
$\mathbf{R_f}$ = 0.575 in CH_2Cl_2/MeOH 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.37–7.16 (comp, 5H), 3.48 (comp, 2H), 3.34–3.13 (comp, 2H), 2.96–2.87 (comp, 2H), 2.80–2.55 (comp, 4H), 2.13 (app dtd, *J* = 10.2, 7.0, 2.1 Hz, 1H), 1.97–1.76 (comp, 2H), 1.07–0.94 (comp, 2H), 0.91–0.76 (comp, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 209.5, 138.0, 129.1, 128.2, 127.0, 63.1, 58.5, 53.2, 50.9, 47.0, 45.2, 21.0, 11.0, 10.8.

HRMS (ESI–TOF): Calculated for $C_{16}H_{22}N_2O$ $[M + H]^+$: 259.1805, Found: 259.1816.

2-(Azepan-2-yl)-1-(4-methoxyphenyl)ethan-1-one



(±)-**4n**

Following general procedure D, compound (±)-**4n** was obtained from azepane (113 μL, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-(4-methoxyphenyl)-3-oxopropanoic acid (291 mg, 1.5 mmol) as a colorless oil in 36% yield (89 mg). EtOAc containing MeOH (5-20%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data:

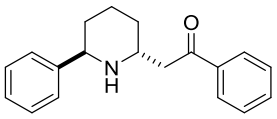
$\mathbf{R_f}$ = 0.21 in EtOAc/MeOH/*i*-$PrNH_2$ 80:19:1 v/v/v.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 3.81 (s, 3H), 3.38–3.24 (m, 1H), 3.11–2.91 (comp, 3H), 2.81–2.66 (m, 1H), 1.87–1.77 (m, 1H), 1.74–1.36 (comp, 8H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.1, 163.5, 130.4, 130.3, 113.7, 55.5(4), 55.4(8), 47.0, 45.7, 36.4, 30.6, 27.3, 25.5.

HRMS (ESI–TOF): Calculated for $C_{15}H_{21}NO_2$ $[M + H]^+$: 248.1645, Found: 248.1654.

1-Phenyl-2-((2R*,6R*)-6-phenylpiperidin-2-yl)ethan-1-one



(±)-**4p**

Following general procedure D, compound (±)-**4p** was obtained from 2-phenylpiperidine (161 mg, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol) as a colorless oil in 64% yield (178.5 mg) and 10:1 diastereomeric ratio. CH_2Cl_2 followed by hexanes containing EtOAc (30-90%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

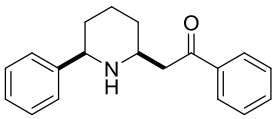
$\mathbf{R_f}$ = 0.28 in hexane/EtOAc 30:70 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.99 (dd, *J* = 7.5, 1.7 Hz, 2H), 7.63–7.54 (m, 1H), 7.52–7.40 (comp, 4H), 7.33 (app t, *J* = 7.5 Hz, 2H), 7.27–7.16 (m, 1H), 4.05 (dd, *J* = 7.9, 3.8 Hz, 1H), 3.79 (app dq, *J* = 9.1, 4.5 Hz, 1H), 3.46 (dd, *J* = 16.6, 8.9 Hz, 1H), 3.13 (dd, *J* = 16.6, 4.3 Hz, 1H), 2.58 (s, 1H), 1.99–1.63 (comp, 5H), 1.58 (app dt, *J* = 12.9, 4.7 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 200.0, 144.6, 137.1, 133.3, 128.7, 128.4, 128.1, 126.8, 54.5, 48.6, 41.3, 33.1, 30.4, 20.4.

HRMS (ESI–TOF): Calculated for $C_{19}H_{21}NO$ $[M + H]^+$: 280.1696, Found: 280.1694.

1-phenyl-2-((2S*,6R*)-6-phenylpiperidin-2-yl)ethan-1-one



(±)-**4p'**

To a solution of 2-phenylpiperidine (161 mg, 1 mmol, 1 equiv) in anhydrous ether (1.5 mL) cooled to –78 °C was slowly added *n*-BuLi in hexanes (1 mmol, 1 equiv) under the protection of nitrogen. After stirring for 5 min at the same temperature, a solution of trifluoroacetophenone (296 mg, 1.7 mmol, 1.7 equiv) in anhydrous ether (1 mL) was added. The resulting mixture was stirred at –78 °C for 5 min. To this was then added a solution of trifluoroacetic acid (1.05 mmol, 1.05 equiv) in anhydrous THF (1 mL). The resulting mixture was stirred at –78 °C for 5 min, followed by the addition of a solution of 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol, 1.5 equiv) in anhydrous THF (1.5 mL). Subsequently, the reaction vessel was removed from the low temperature bath and the reaction mixture stirred at room temperature for 2 h. Solvent was then evaporated and MeOH (5 mL) was added to the reaction mixture which was then stirred at room temperature for 22.5 h. Solvent was then evaporated and 10 mL of ether was added to the flask. The reaction mixture was then cooled to 0 °C and quenched via the addition of 4 mL of saturated $NaHCO_3$ solution. An additional amount of saturated $NaHCO_3$ solution (10 mL) was then added and the resulting mixture was extracted with ether (2 x 20 mL). The combined organic layers were washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography to yield compound (±)-**4p'** as a colorless oil in 65% yield (182 mg) and 13:1 diastereomeric ratio. CH_2Cl_2 followed by hexanes containing EtOAc (30-90%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

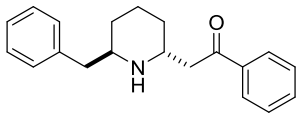
$\mathbf{R_f}$ = 0.4 in hexane/EtOAc 30:70 v/v.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.95 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.60–7.53 (m, 1H), 7.45 (dd, *J* = 8.2, 7.3 Hz, 2H), 7.41–7.35 (m, 2H), 7.31 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.25–7.17 (m, 1H), 3.76 (dd, *J* = 11.0, 2.5 Hz, 1H), 3.37 (app dtd, *J* = 11.2, 6.1, 2.6 Hz, 1H), 3.17–3.10 (comp, 2H), 2.42 (s, 1H), 2.00–1.86 (m, 1H), 1.81 (ddd, *J* = 11.9, 3.2, 1.6 Hz, 1H), 1.72 (app dtd, *J* = 12.9, 2.7, 1.2 Hz, 1H), 1.65–1.46 (comp, 2H), 1.38 (app tdd, *J* = 12.7, 11.1, 3.9 Hz, 1H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 199.5, 145.4, 137.1, 133.3, 128.7, 128.4, 128.1, 127.1, 126.9, 62.1, 53.5, 45.7, 34.3, 32.2, 25.3.

HRMS (ESI–TOF): Calculated for $C_{19}H_{21}NO$ $[M + H]^+$: 280.1696, Found: 280.1706.

2-((2R*,6R*)-6-Benzylpiperidin-2-yl)-1-phenylethan-1-one



(±)-**4q**

Following general procedure D, compound (±)-**4q** was obtained from 2-benzylpiperidine (175 mg, 1 mmol), trifluoroacetophenone (183 mg, 1.05 mmol), and 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol) as a colorless oil in 79% yield (231 mg) and 6:1 diastereomeric ratio. CH_2Cl_2 followed by hexanes containing EtOAc (70%) followed by EtOAc containing MeOH (1-10%) and 1% *i*-$PrNH_2$ was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

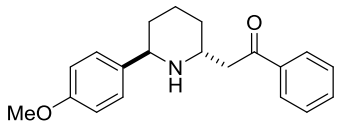
R_f = 0.21 in hexane/EtOAc 30:70 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.96–7.88 (m, 2H), 7.58 (app ddt, *J* = 8.7, 6.7, 1.2 Hz, 1H), 7.47 (dd, *J* = 8.2, 7.1 Hz, 2H), 7.35–7.26 (m, 2H), 7.25–7.22 (m, 1H), 7.21–7.14 (m, 2H), 3.83–3.61 (m, 1H), 3.30–3.11 (comp, 2H), 3.11–2.95 (m, 1H), 2.87–2.74 (comp, 2H), 2.48 (s, 1H), 1.83 (app dq, *J* = 12.6, 3.9 Hz, 1H), 1.79–1.69 (comp, 2H), 1.68–1.57 (m, 1H), 1.52–1.38 (comp, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 199.6, 139.4, 137.2, 133.2, 129.3, 128.7, 128.6, 128.1, 126.3, 53.0, 47.7, 42.8, 40.9, 31.1, 30.3, 19.8.

HRMS (ESI–TOF): Calculated for $C_{20}H_{23}NO$ $[M + H]^+$: 294.1852, Found: 294.1863.

2-((2R*,6R*)-6-(4-Methoxyphenyl)piperidin-2-yl)-1-phenylethan-1-one



(±)-**4r**

Following general procedure D, compound (±)-**4r** was obtained from 2-(4-methoxyphenyl)piperidine (191 mg, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol) as a colorless oil in 66% yield (204 mg) and > 20:1 diastereomeric ratio. CH_2Cl_2 followed by hexanes containing EtOAc (50-100%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

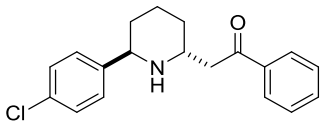
$\mathbf{R_f}$ = 0.21 in hexane/EtOAc 30:70 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.06–7.89 (m, 2H), 7.64–7.53 (m, 1H), 7.52–7.42 (m, 2H), 7.36–7.29 (m, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 3.98 (dd, *J* = 8.0, 3.6 Hz, 1H), 3.81–2.71 (comp, 4H), 3.43 (dd, *J* = 16.5, 9.0 Hz, 1H), 3.12 (dd, *J* = 16.5, 4.3 Hz, 1H), 2.25 (s, 1H), 1.96–1.80 (comp, 2H), 1.78–1.62 (comp, 3H), 1.55 (app dt, *J* = 12.8, 4.6 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 200.1, 158.4, 137.2, 136.9, 133.2, 128.7, 128.1, 127.9, 113.8, 55.3, 53.9, 48.7, 41.4, 33.3, 30.5, 20.5.

HRMS (ESI–TOF): Calculated for $C_{20}H_{23}NO_2$ $[M + H]^+$: 310.1802, Found: 310.1810.

2-((2R*,6R*)-6-(4-Chlorophenyl)piperidin-2-yl)-1-phenylethan-1-one



(±)-**4s**

Following general procedure D, compound (±)-**4s** was obtained from 2-(4-chlorophenyl)piperidine (195.6 mg, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol) as a colorless oil in 54% yield (170 mg) and > 20:1 diastereomeric ratio. CH_2Cl_2 followed by hexanes containing EtOAc (30-100%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

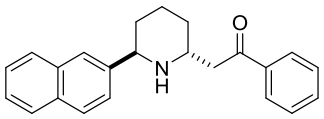
$\mathbf{R_f}$ = 0.40 in hexane/EtOAc 30:70 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.99 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.64–7.56 (m, 1H), 7.52–7.45 (m, 2H), 7.41–7.32 (m, 2H), 7.32–7.25 (m, 2H), 4.09–3.97 (m, 1H), 3.75 (app dq, *J* = 9.0, 4.5 Hz, 1H), 3.43 (dd, *J* = 16.6, 9.2 Hz, 1H), 3.13 (dd, *J* = 16.6, 4.1 Hz, 1H), 2.41 (s, 1H), 1.90–1.80 (comp, 2H), 1.79–1.64 (comp, 3H), 1.62–1.47 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 200.0, 143.2, 137.1, 133.3, 132.3, 128.8, 128.5, 128.3, 128.1, 53.9, 48.6, 41.4, 33.1, 30.5, 20.3.

HRMS (ESI–TOF): Calculated for $C_{19}H_{20}NOCl$ $[M + H]^+$: 314.1306, Found: 314.1321.

2-((2R*,6R*)-6-(Naphthalen-2-yl)piperidin-2-yl)-1-phenylethan-1-one



(±)-**4t**

Following general procedure D, compound (±)-**4t** was obtained from 2-(naphthalen-2-yl)piperidine (211 mg, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol) as a colorless oil in 46% yield (151.3 mg) and > 20:1 diastereomeric ratio. CH_2Cl_2 followed by hexanes containing EtOAc (30-90%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

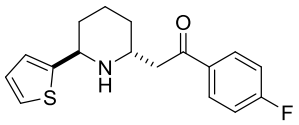
$\mathbf{R_f}$ = 0.22 in hexane/EtOAc 30:70 v/v.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.06–7.96 (m, 2H), 7.90 (s, 1H), 7.87–7.76 (dd, *J* = 9.0, 5.9 Hz, 3H), 7.66–7.37 (m, 6H), 4.21 (dd, *J* = 8.3, 3.6 Hz, 1H), 3.86 (app dq, *J* = 8.9, 4.2 Hz, 1H), 3.49 (dd, *J* = 16.6, 9.0 Hz, 1H), 3.16 (dd, *J* = 16.6, 4.2 Hz, 1H), 2.50 (s, 1H), 2.02–1.80 (comp, 3H), 1.80–1.69 (comp, 2H), 1.61 (dt, *J* = 12.2, 4.4 Hz, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 200.0, 142.2, 137.2, 133.6, 133.3, 132.6, 128.7, 128.1, 128.0, 127.6, 125.9, 125.5, 125.1, 54.6, 48.8, 41.4, 33.3, 30.5, 20.5.

HRMS (ESI–TOF): Calculated for $C_{23}H_{23}NO$ $[M + H]^+$: 330.1852, Found: 330.1842.

1-(4-Fluorophenyl)-2-((2R*,6R*)-6-(thiophen-2-yl)piperidin-2-yl)ethan-1-one



(±)-**4u**

Following general procedure D, compound (±)-**4u** was obtained from 2-(thiophen-2-yl)piperidine (167 mg, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-(4-fluorophenyl)-3-oxopropanoic acid (273.2 mg, 1.5 mmol) as a colorless oil in 55% yield (166 mg) and > 20:1 diastereomeric ratio. Hexanes containing EtOAc (30-100%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

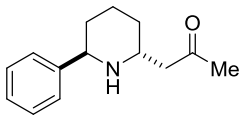
$\mathbf{R_f}$ = 0.41 in hexane/EtOAc 30:70 v/v.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.99 (dd, *J* = 8.9, 5.4 Hz, 2H), 7.19 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.16–7.05 (comp, 3H), 6.97 (dd, *J* = 5.1, 3.5 Hz, 1H), 4.42–4.36 (m, 1H), 3.63 (app dq, *J* = 8.3, 4.2 Hz, 1H), 3.17 (dd, *J* = 16.9, 8.7 Hz, 1H), 3.04 (dd, *J* = 16.9, 4.1 Hz, 1H), 2.58–2.51 (m, 1H), 1.98–1.88 (comp, 2H), 1.74–1.63 (comp, 3H), 1.45–1.35 (m, 1H).

^{13}C-NMR (150 MHz, $CDCl_3$): δ = 198.1, 165.9 ($J_{C\text{-}F}$ = 255 Hz), 148.8, 133.5 ($J_{C\text{-}F}$ = 3.1 Hz), 130.8 ($J_{C\text{-}F}$ = 9.4 Hz), 126.8, 124.0, 123.9, 115.8 ($J_{C\text{-}F}$ = 21.9 Hz), 51.9, 47.5, 43.6, 32.5, 31.5, 20.1.

HRMS (ESI–TOF): Calculated for $C_{17}H_{18}NOSF$ $[M + H]^+$: 304.1166, Found: 304.1179.

1-((2R*,6R*)-6-Phenylpiperidin-2-yl)propan-2-one



(±)-**4v**

Following general procedure D, compound (±)-**4v** was obtained from 2-phenylpiperidine (161 mg, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-oxobutanoic acid (153.1 mg, 1.5 mmol) as a colorless oil in 52% yield (113 mg) and > 20:1 diastereomeric ratio. CH_2Cl_2 containing MeOH (0-10%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

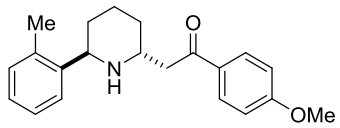
R_f = 0.51 in CH_2Cl_2/MeOH 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.47–7.38 (m, 2H), 7.35–7.29 (m, 2H), 7.25–7.19 (m, 1H), 3.98 (dd, *J* = 8.3, 3.7 Hz, 1H), 3.58 (app dq, *J* = 9.2, 4.6 Hz, 1H), 2.91 (dd, *J* = 16.8, 9.1 Hz, 1H), 2.68–2.40 (comp, 2H), 2.17 (s, 3H), 1.90–1.81 (m, 1H), 1.80–1.69 (comp, 2H), 1.68–1.58 (comp, 2H), 1.49–1.37 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 208.7, 144.3, 128.5, 126.9, 126.8, 54.4, 48.2, 46.6, 32.8, 30.8, 30.3, 20.3.

HRMS (ESI–TOF): Calculated for $C_{14}H_{19}NO$ $[M + H]^+$: 218.1539, Found: 218.1544.

1-(4-Methoxyphenyl)-2-((2R*,6R*)-6-(o-tolyl)piperidin-2-yl)ethan-1-one



(±)-**4w**

Following general procedure D, compound (±)-**4w** was obtained from 2-(o-tolyl)piperidine (175.4 mg, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-(4-methoxyphenyl)-3-oxopropanoic acid (291 mg, 1.5 mmol) as a colorless oil in 65% yield (210 mg) and > 20:1 diastereomeric ratio. CH_2Cl_2 followed by followed by hexanes containing EtOAc (50-90%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

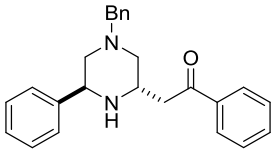
$\mathbf{R_f}$ = 0.31 in hexane/EtOAc 30:70 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.9 Hz, 2H), 7.65–7.50 (m, 1H), 7.23–7.16 (m, 1H), 7.15–7.06 (comp, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 4.24–4.11 (m, 1H), 3.91 (app ddt, *J* = 9.5, 4.8, 2.4 Hz, 1H), 3.86 (s, 3H), 3.55 (dd, *J* = 16.0, 8.9 Hz, 1H), 3.11 (dd, *J* = 16.0, 4.6 Hz, 1H), 2.31 (s, 3H), 2.07 (s, 1H), 2.02–1.88 (m, 1H), 1.86–1.69 (comp, 3H), 1.69–1.44 (comp, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.5, 163.6, 143.2, 135.0, 130.4, 130.3, 130.2, 126.6, 126.3, 126.1, 113.8, 55.5, 50.0, 49.8, 39.3, 33.1, 29.6, 20.8, 19.2.

HRMS (ESI–TOF): Calculated for $C_{21}H_{25}NO_2$ $[M + H]^+$: 324.1958, Found: 324.1973.

2-((2S*,6S*)-4-Benzyl-6-phenylpiperazin-2-yl)-1-phenylethan-1-one



(±)-**4x**

Following general procedure D, compound (±)-**4x** was obtained from 1-benzyl-3-phenylpiperazine (252 mg, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-oxo-3-phenylpropanoic acid (246.2 mg, 1.5 mmol) as a colorless oil in 58% yield (215 mg) and > 20:1 diastereomeric ratio. CH_2Cl_2 followed by followed by hexanes containing EtOAc (10-50%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

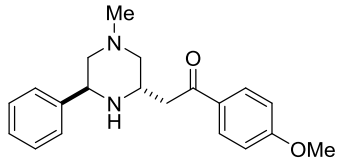
R_f = 0.67 in hexane/EtOAc 30:70 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.09–7.99 (m, 2H), 7.66–7.58 (m, 1H), 7.52 (dd, *J* = 8.4, 7.0 Hz, 2H), 7.48–7.44 (m, 2H), 7.42–7.31 (comp, 6H), 7.29 (dt, *J* = 5.5, 2.2 Hz, 2H), 4.24 (dd, *J* = 9.3, 3.2 Hz, 1H), 3.85 (app dq, *J* = 8.0, 3.6 Hz, 1H), 3.70 (dd, *J* = 17.1, 8.1 Hz, 1H), 3.63–3.50 (comp, 2H), 3.42 (dd, *J* = 17.1, 4.9 Hz, 1H), 2.91 (ddd, *J* = 10.9, 3.2, 1.4 Hz, 1H), 2.71 (app dt, *J* = 11.1, 2.2 Hz, 1H), 2.59 (dd, *J* = 11.1, 3.5 Hz, 1H), 2.44 (s, 1H), 2.29 (app t, *J* = 10.1 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 200.1, 142.6, 138.3, 137.2, 133.2, 128.9, 128.7, 128.3, 128.3, 128.1, 127.3, 127.3, 127.1, 63.1, 60.8, 57.2, 54.4, 49.0, 40.2.

HRMS (ESI–TOF): Calculated for $C_{25}H_{26}N_2O$ $[M + H]^+$: 371.2118, Found: 371.2125.

1-(4-Methoxyphenyl)-2-((2S*,6S*)-4-methyl-6-phenylpiperazin-2-yl)ethan-1-one



(±)-**4y**

Following general procedure D, compound (±)-**4y** was obtained from 1-methyl-3-phenylpiperazine (176 mg, 1 mmol), trifluoroacetophenone (296 mg, 1.7 mmol), and 3-(4-methoxyphenyl)-3-oxopropanoic acid (291 mg, 1.5 mmol) as a colorless oil in 60% yield (195 mg) and > 20:1 diastereomeric ratio. CH_2Cl_2 followed by followed by EtOAc containing MeOH (1-10%) and *i*-$PrNH_2$ (1%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

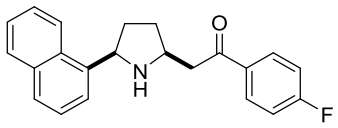
$\mathbf{R_f}$ = 0.58 in CH_2Cl_2/MeOH 90:10 v/v

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.9 Hz, 2H), 7.46–7.33 (m, 2H), 7.33–7.26 (m, 2H), 7.26–7.19 (m, 1H), 6.92 (d, *J* = 8.9 Hz, 2H), 4.17 (dd, *J* = 9.5, 3.1 Hz, 1H), 3.86 (s, 3H), 3.81 (app ddt, *J* = 8.1, 4.8, 2.9 Hz, 1H), 3.61 (dd, *J* = 17.1, 8.4 Hz, 1H), 3.29 (dd, *J* = 17.1, 4.7 Hz, 1H), 2.82 (ddd, *J* = 11.1, 3.1, 1.5 Hz, 1H), 2.63 (ddd, *J* = 11.2, 2.9, 1.5 Hz, 1H), 2.54–2.31 (comp, 2H), 2.27 (s, 3H), 2.13 (app t, *J* = 10.2 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.5, 163.7, 142.6, 130.5, 130.3, 128.4, 127.4, 127.2, 113.8, 63.3, 59.4, 55.6, 54.2, 48.9, 46.7, 39.9.

HRMS (ESI–TOF): Calculated for $C_{20}H_{24}N_2O_2$ $[M + H]^+$: 325.1911, Found: 325.1926.

1-(4-Fluorophenyl)-2-((2S*,5R*)-5-(naphthalen-1-yl)pyrrolidin-2-yl)ethan-1-one



(±)-**4z**

Following general procedure D, compound (±)-**4z** was obtained from 2-(naphthalen-1-yl)pyrrolidine (197 mg, 1 mmol), tert-butylphenylketone (243 mg, 1.5 mmol), and 3-(4-fluorophenyl)-3-oxopropanoic acid (273.2 mg, 1.5 mmol) as a colorless oil in 66% yield (220 mg) and 1.1:1 diastereomeric ratio. CH_2Cl_2 followed by followed by hexanes containing EtOAc (30-90%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

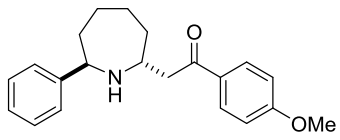
$\mathbf{R_f}$ = 0.19 in hexane/EtOAc 50:50 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.35–7.97 (comp, 3H), 7.86 (app dt, *J* = 7.9, 1.9 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.60–7.33 (comp, 3H), 7.16 (t, *J* = 8.6 Hz, 2H), 5.02 (app t, *J* = 7.6 Hz, 1H), 3.96–3.80 (m, 1H), 3.41–3.15 (comp, 2H), 2.63–2.41 (m, 1H), 2.38–2.07 (comp, 2H), 1.77 (app tdd, *J* = 12.0, 6.0, 3.5 Hz, 1H), 1.69–1.54 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.4, 165.9 ($J_{C\text{-}F}$ = 255.3 Hz), 141.4, 133.9, 133.7 ($J_{C\text{-}F}$ = 3.1 Hz), 131.3, 130.9 ($J_{C\text{-}F}$ = 9.3 Hz), 128.9, 127.1, 125.7(5), 125.7(1), 125.4, 123.6, 122.8, 115.8 ($J_{C\text{-}F}$ = 21.8 Hz), 58.1, 54.3, 46.0, 33.0, 31.0.

HRMS (ESI–TOF): Calculated for $C_{22}H_{20}NFO$ $[M + H]^+$: 334.1602, Found: 334.1614.

1-(4-Methoxyphenyl)-2-((2R*,7R*)-7-phenylazepan-2-yl)ethan-1-one



(±)-**4aa**

Following general procedure D, compound (±)-**4aa** was obtained from 2-phenylazepane (175 mg, 1 mmol), tert-butylphenylketone (243 mg, 1.5 mmol), and 3-(4-methoxyphenyl)-3-oxopropanoic acid (291 mg, 1.5 mmol) as a colorless oil in 42% yield (136 mg) and 11:1 diastereomeric ratio. CH_2Cl_2 followed by followed by hexanes containing EtOAc (30-90%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

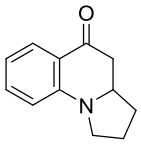
R_f = 0.19 in hexane/EtOAc 50:50 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 8.9 Hz, 2H), 7.35–7.24 (comp, 4H), 7.23–7.17 (m, 1H), 6.89 (d, *J* = 8.9 Hz, 2H), 3.98 (dd, *J* = 10.8, 2.6 Hz, 1H), 3.86 (s, 3H), 3.68 (app dtd, *J* = 7.1, 3.6, 1.6 Hz, 1H), 3.16 (dd, *J* = 15.6, 7.1 Hz, 1H), 3.00 (dd, *J* = 15.6, 5.9 Hz, 1H), 2.12–1.94 (comp, 4H), 1.93–1.86 (m, 1H), 1.79 (ddd, *J* = 13.2, 11.6, 9.7 Hz, 1H), 1.65–1.41 (comp, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.3, 163.5, 147.2, 130.5, 130.4, 128.4, 126.5, 126.4, 113.7, 58.5, 55.1, 52.5, 46.1, 38.4, 36.7, 29.1, 27.3.

HRMS (ESI–TOF): Calculated for $C_{21}H_{25}NO_2$ $[M + H]^+$: 324.1958, Found: 324.1972.

2,3,3a,4-Tetrahydropyrrolo[1,2-a]quinolin-5(1H)-one



(±)-**6a**

Following general procedure E, compound (±)-**6a** was obtained from pyrrolidine (82 μL, 1 mmol) and 3-(2-fluorophenyl)-3-oxopropanoic acid (273 mg, 1.5 mmol) as a pale yellow solid in 60% yield (112 mg). Hexanes containing EtOAc (5-10%) was used as the eluent for silica gel chromatography.

Characterization data:

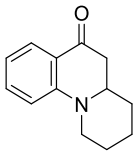
$\mathbf{R_f}$ = 0.19 in hexane/EtOAc 90:10 v/v.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.83 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.36 (ddd, *J* = 8.5, 7.1, 1.7 Hz, 1H), 6.66 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 6.55 (d, *J* = 8.4 Hz, 1H), 3.61 (dddd, *J* = 15.3, 10.3, 5.3, 3.4 Hz, 1H), 3.53–3.44 (m, 1H), 3.28 (app td, *J* = 9.7, 3.5 Hz, 1H), 2.76 (dd, J = 15.8, 3.5 Hz, 1H), 2.51–2.41 (m, 1H), 2.28–2.13 (comp, 2H), 2.02–1.88 (m, 1H), 1.80–1.69 (m, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 194.0, 150.1, 135.6, 128.1, 118.4, 116.0, 112.9, 58.2, 46.2, 43.8, 32.9, 23.1.

HRMS (ESI–TOF): Calculated for $C_{12}H_{13}NO$ $[M + H]^+$: 188.1070, Found: 188.1061.

1,2,3,4,4a,5-Hexahydro-6H-pyrido[1,2-a]quinolin-6-one



(±)-**6b**

Following general procedure E, compound (±)-**6b** was obtained from piperidine (99 μL, 1 mmol) and 3-(2-fluorophenyl)-3-oxopropanoic acid (273 mg, 1.5 mmol) as a pale yellow solid in 72% yield (145 mg). Hexanes containing EtOAc (7%) was used as the eluent for silica gel chromatography.

Characterization data:

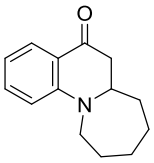
$\mathbf{R_f}$ = 0.25 in hexane/EtOAc 90:10 v/v.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.93 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.41 (ddd, *J* = 8.8, 7.0, 1.8 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 6.78 (app t, *J* = 7.0 Hz, 1H), 4.02–3.92 (m, 1H), 3.29 (app tt, *J* = 11.4, 3.7 Hz, 1H), 2.76–2.49 (comp, 3H), 1.94–1.33 (comp, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 193.8, 152.8, 135.4, 127.9, 121.0, 117.8, 113.9, 57.8, 47.4, 45.4, 32.2, 24.8, 23.5.

HRMS (ESI–TOF): Calculated for $C_{13}H_{15}NO$ $[M + H]^+$: 202.1226, Found: 202.1217.

6a,7,8,9,10,11-Hexahydroazepino[1,2-a]quinolin-5(6H)-one



(±)-**6c**

Following general procedure E, compound (±)-**6c** was obtained from azepane (113 μL, 1 mmol) and 3-(2-fluorophenyl)-3-oxopropanoic acid (273 mg, 1.5 mmol) as a pale yellow solid in 50% yield (108 mg). Hexanes containing EtOAc (5-10%) was used as the eluent for silica gel chromatography.

Characterization data:

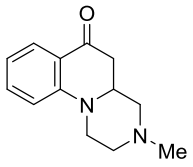
$\mathbf{R_f}$ = 0.18 in hexane/EtOAc 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.82 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.32 (ddd, *J* = 8.7, 7.0, 1.8 Hz, 1H), 6.65–6.55 (comp, 2H), 3.95 (ddd, *J* = 15.4, 6.3, 2.5 Hz, 1H), 3.69–3.58 (m, 1H), 3.26 (ddd, *J* = 15.3, 11.0, 5.5 Hz, 1H), 2.96 (dd, *J* = 16.0, 6.1 Hz, 1H), 2.49 (dd, *J* = 16.0, 3.2 Hz, 1H), 2.14–1.99 (m, 1H), 1.95–1.82 (m, 1H), 1.72–1.43 (comp, 5H), 1.40–1.22 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 193.6, 149.5, 135.7, 127.8, 118.1, 115.2, 112.4, 60.7, 49.3, 43.1, 31.4, 26.7, 25.8, 25.4.

HRMS (ESI–TOF): Calculated for $C_{14}H_{17}NO$ $[M + H]^+$: 216.1383, Found: 216.1375.

3-Methyl-1,2,3,4,4a,5-hexahydro-6H-pyrazino[1,2-a]quinolin-6-one



(±)-**6d**

Following general procedure E, compound (±)-**6d** was obtained from 1-methylpiperazine (111 μL, 1 mmol) and 3-(2-fluorophenyl)-3-oxopropanoic acid (273 mg, 1.5 mmol) as a slightly brown oil in 47% yield (102 mg). EtOAc containing MeOH (5-10%) was used as the eluent for silica gel chromatography.

Characterization data:

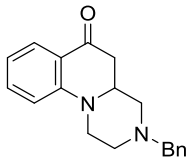
$\mathbf{R_f}$ = 0.17 in EtOAc/MeOH 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.96 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.45 (ddd, *J* = 8.8, 7.1, 1.8 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 6.86 (ddd, *J* = 8.0, 7.1, 0.9 Hz, 1H), 3.79 (app dt, *J* = 11.8, 2.6 Hz, 1H), 3.56–3.45 (m, 1H), 3.01 (app ddt, *J* = 11.3, 3.5, 2.2 Hz, 1H), 2.96–2.84 (comp, 2H), 2.65–2.51 (comp, 2H), 2.37 (s, 3H), 2.38–2.24 (m, 1H), 2.15–2.05 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 192.9, 152.4, 135.5, 127.9, 121.0, 118.5, 113.5, 61.0, 55.9, 54.5, 46.0, 45.9, 42.5.

HRMS (ESI–TOF): Calculated for $C_{13}H_{16}N_2O$ $[M + H]^+$: 217.1335, Found: 217.1337.

3-Benzyl-1,2,3,4,4a,5-hexahydro-6H-pyrazino[1,2-a]quinolin-6-one



(±)-**6e**

Following general procedure E, compound (±)-**6e** was obtained from 1-benzylpiperazine (174 μL, 1 mmol) and 3-(2-fluorophenyl)-3-oxopropanoic acid (273 mg, 1.5 mmol).as a slightly brown oil in 46% yield (135 mg). Hexanes containing EtOAc (20%) was used as the eluent for silica gel chromatography.

Characterization data:

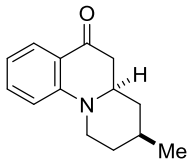
$\mathbf{R_f}$ = 0.15 in hexane/EtOAc 80:20 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.33 (ddd, *J* = 8.8, 7.0, 1.8 Hz, 1H), 7.27–7.14 (comp, 5H), 6.82–6.69 (comp, 2H), 3.65 (app dt, *J* = 11.9, 2.7 Hz, 1H), 3.49 (s, 2H), 3.47–3.33 (m, 1H), 3.02–2.71 (comp, 3H), 2.49–2.40 (comp, 2H), 2.27 (app td, *J* = 11.7, 3.4 Hz, 1H), 2.04 (app t, *J* = 10.8 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 193.0, 152.5, 135.4, 129.1, 128.4, 127.9, 127.4, 121.0, 118.5, 113.4, 62.6, 58.8, 56.0, 52.3, 46.1, 42.5.

HRMS (ESI–TOF): Calculated for $C_{19}H_{20}N_2O$ $[M + H]^+$: 293.1648, Found: 293.1635.

(3S*,4aR*)-3-Methyl-1,2,3,4,4a,5-hexahydro-6H-pyrido[1,2-a]quinolin-6-one



(±)-**6f**

Following general procedure E, compound (±)-**6f** was obtained from 4-methylpiperidine (118 μL, 1 mmol) and 3-(2-fluorophenyl)-3-oxopropanoic acid (273 mg, 1.5 mmol) as a pale yellow solid in 51% yield (110 mg) and 4:1 diastereomeric ratio. Hexanes containing EtOAc (5%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

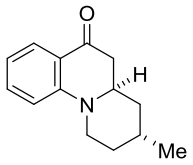
$\mathbf{R_f}$ = 0.28 in hexane/EtOAc 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.93 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.41 (ddd, *J* = 8.8, 7.0, 1.8 Hz, 1H), 6.93 (d, *J* = 8.6 Hz, 1H), 6.79 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 3.96 (ddd, *J* = 12.4, 4.5, 2.5 Hz, 1H), 3.31 (app tt, *J* = 11.7, 3.7 Hz, 1H), 2.75–2.62 (comp, 2H), 2.56 (dd, *J* = 16.4, 12.0 Hz, 1H), 1.87–1.70 (comp, 2H), 1.67–1.52 (m, 1H), 1.35 (app tdd, *J* = 13.0, 11.8, 4.4 Hz, 1H), 1.30–1.19 (m, 1H), 0.98 (d, *J* = 6.5 Hz, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 193.8, 152.7, 135.4, 127.9, 121.0, 117.8, 114.0, 57.4, 47.3, 45.3, 40.7, 33.2, 30.1, 21.8.

HRMS (ESI–TOF): Calculated for $C_{14}H_{17}NO$ $[M + H]^+$: 216.1383, Found: 216.1387.

(3R*,4aR*)-3-Methyl-1,2,3,4,4a,5-hexahydro-6H-pyrido[1,2-a]quinolin-6-one



(±)-**6f'**

From the reaction shown on the previous page, the minor diastereomer was isolated as a pale yellow solid.

Characterization data of the minor diastereomer:

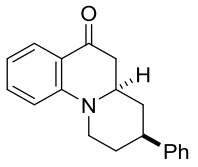
$\mathbf{R_f}$ = 0.26 in hexane/EtOAc 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.94 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.42 (ddd, *J* = 8.8, 7.0, 1.8 Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 1H), 6.80 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 3.71 (ddd, *J* = 12.5, 5.1, 2.6 Hz, 1H), 3.53 (app tt, *J* = 11.9, 3.8 Hz, 1H), 2.91 (app td, *J* = 12.9, 3.3 Hz, 1H), 2.66–2.47 (comp, 2H), 2.18–2.06 (m, 1H), 1.99 (app tt, *J* = 13.3, 4.8 Hz, 1H), 1.83 (ddd, *J* = 13.3, 11.8, 4.7 Hz, 1H), 1.70–1.57 (comp, 2H), 1.08 (d, *J* = 7.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 193.9, 153.0, 135.4, 128.0, 121.0, 117.8, 113.8, 51.9, 45.5, 41.6, 38.0, 30.2, 24.7, 16.4.

HRMS (ESI–TOF): Calculated for $C_{14}H_{17}NO$ $[M + H]^+$: 216.1383, Found: 216.1385.

(3S*,4aR*)-3-Phenyl-1,2,3,4,4a,5-hexahydro-6H-pyrido[1,2-a]quinolin-6-one



(±)-**6g**

Following general procedure E, compound (±)-**6g** was obtained from 4-phenylpiperidine (161 mg, 1 mmol) and 3-(2-fluorophenyl)-3-oxopropanoic acid (273 mg, 1.5 mmol) as a pale yellow solid in 56% yield (155 mg) and 6:1 diastereomeric ratio. Hexanes containing EtOAc (7%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

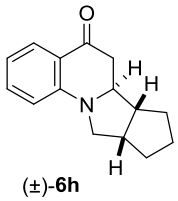
$\mathbf{R_f}$ = 0.23 in hexane/EtOAc 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.98 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.45 (ddd, *J* = 8.8, 6.9, 1.8 Hz, 1H), 7.34 (app t, *J* = 7.5 Hz, 2H), 7.29–7.17 (comp, 3H), 6.99 (d, *J* = 8.6 Hz, 1H), 6.84 (app t, *J* = 7.4 Hz, 1H), 4.15–4.05 (m, 1H), 3.44 (app tt, *J* = 11.7, 3.6 Hz, 1H), 2.84 (app td, *J* = 12.5, 3.1 Hz, 1H), 2.79–2.58 (comp, 3H), 2.07 (app dt, *J* = 13.2, 3.0 Hz, 1H), 2.02–1.85 (comp, 2H), 1.84–1.70 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 193.4, 152.4, 144.7, 135.4, 128.5, 127.9, 126.5, 121.0, 118.0, 113.9, 57.5, 47.4, 45.1, 41.2, 39.7, 32.1

HRMS (ESI–TOF): Calculated for $C_{19}H_{19}NO$ $[M + H]^+$: 278.1539, Found: 278.1529.

(6aS*,6bR*,9aS*)-6,6a,6b,7,8,9,9a,10-Octahydro-5H-cyclopenta[3,4]pyrrolo[1,2-a]quinolin-5-one



(±)-**6h**

Following general procedure E, compound (±)-**6h** was obtained from octahydrocyclopenta[c]pyrrole (111 mg, 1 mmol) and 3-(2-fluorophenyl)-3-oxopropanoic acid (273 mg, 1.5 mmol) as a pale yellow solid in 67% yield (152 mg) and > 20:1 d.r diastereomeric ratio. Hexanes containing EtOAc (5%) was used as the eluent for silica gel chromatography.

Characterization data of the major diastereomer:

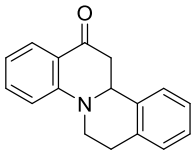
$\mathbf{R_f}$ = 0.31 in hexane/EtOAc 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 7.9 Hz, 1H), 7.35 (app t, *J* = 7.8 Hz, 1H), 6.70 (app t, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 8.3 Hz, 1H), 3.87 (app t, *J* = 9.4 Hz, 1H), 3.10 (ddd, *J* = 14.9, 8.5, 3.4 Hz, 1H), 2.98–2.86 (m, 1H), 2.78 (dd, *J* = 16.1, 3.5 Hz, 1H), 2.66 (dd, *J* = 9.9, 6.7 Hz, 1H), 2.56–2.42 (comp, 2H), 1.79–1.43 (comp, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 194.2, 150.8, 135.3, 127.9, 119.3, 116.9, 113.5, 65.2, 54.1, 50.4, 44.0, 41.6, 32.0, 29.5, 25.2.

HRMS (ESI–TOF): Calculated for $C_{15}H_{17}NO$ $[M + H]^+$: 228.1383, Found: 228.1384.

6,7,11b,12-Tetrahydro-13H-isoquinolino[2,1-a]quinolin-13-one



(±)-**6i**

Following general procedure E, compound (±)-**6i** was obtained from 1,2,3,4-tetrahydroisoquinoline (125 μL, 1 mmol) and 3-(2-fluorophenyl)-3-oxopropanoic acid (273 mg, 1.5 mmol) as a yellow solid in 62% yield (154 mg). Hexanes containing EtOAc (5%) was used as the eluent for silica gel chromatography.

Characterization data:

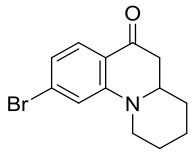
$\mathbf{R_f}$ = 0.27 in hexane/EtOAc 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.03 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.48 (ddd, *J* = 8.7, 7.1, 1.8 Hz, 1H), 7.33–7.16 (comp, 4H), 7.03 (d, *J* = 8.5 Hz, 1H), 6.85 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 4.74 (dd, *J* = 13.9, 3.0 Hz, 1H), 4.14 (ddd, *J* = 11.7, 4.8, 2.5 Hz, 1H), 3.29–3.17 (m, 1H), 3.17–3.06 (comp, 2H), 2.94 (app dt, *J* = 15.0, 2.6 Hz, 1H), 2.81 (dd, *J* = 16.6, 13.8 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 193.8, 152.2, 135.4, 135.4, 133.9, 128.6, 128.2, 126.7, 126.6, 125.5, 120.7, 117.7, 113.1, 57.6, 46.7, 42.2, 29.3.

HRMS (ESI–TOF): Calculated for $C_{17}H_{15}NO$ $[M + H]^+$: 250.1226, Found: 250.1220.

9-Bromo-1,2,3,4,4a,5-hexahydro-6H-pyrido[1,2-a]quinolin-6-one



(±)-**6j**

Following general procedure E, compound (±)-**6j** was obtained from piperidine (99 μL, 1 mmol) and 3-(4-bromo-2-fluorophenyl)-3-oxopropanoic acid (391.5 mg, 1.5 mmol) as a pale yellow solid in 60% yield (168 mg). Hexanes containing EtOAc (7%) was used as the eluent for silica gel chromatography.

Characterization data:

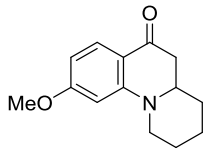
$\mathbf{R_f}$ = 0.21 in hexane/EtOAc 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.4 Hz, 1H), 7.07 (d, *J* = 1.6 Hz, 1H), 6.88 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.86 (app ddt, *J* = 12.5, 4.2, 2.0 Hz, 1H), 3.30 (app tt, *J* = 11.4, 3.8 Hz, 1H), 2.74–2.63 (comp, 2H), 2.53 (dd, *J* = 16.5, 11.6 Hz, 1H), 1.91–1.80 (comp, 2H), 1.80–1.72 (m, 1H), 1.72–1.35 (comp, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 192.8, 153.1, 130.8, 129.3, 121.0, 119.6, 116.8, 57.6, 47.5, 45.0, 32.0, 24.6, 23.2.

HRMS (ESI–TOF): Calculated for $C_{13}H_{14}NOBr(79)$ $[M + H]^+$: 280.0332, Found: 280.0336.

9-Methoxy-1,2,3,4,4a,5-hexahydro-6H-pyrido[1,2-a]quinolin-6-one



(±)-**6k**

Following general procedure E, compound (±)-**6k** was obtained from piperidine (99 μL, 1 mmol) and 3-(2-fluoro-4-methoxyphenyl)-3-oxopropanoic acid (318 mg, 1.5 mmol) as a yellow solid in 61% yield (142 mg). Hexanes containing EtOAc (15%) was used as the eluent for silica gel chromatography.

Characterization data:

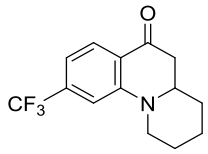
$\mathbf{R_f}$ = 0.13 in hexane/EtOAc 85:15 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.7 Hz, 1H), 6.36–6.29 (comp, 2H), 3.88–3.81 (m, 1H), 3.80 (s, 3H), 3.24 (app tq, *J* = 11.5, 4.0, 3.5 Hz, 1H), 2.68–2.56 (comp, 2H), 2.48 (dd, *J* = 16.5, 11.6 Hz, 1H), 1.86–1.30 (comp, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 192.2, 165.5, 154.4, 130.0, 115.3, 104.6, 98.0, 57.7, 55.2, 47.3, 45.0, 32.2, 24.6, 23.3.

HRMS (ESI–TOF): Calculated for $C_{14}H_{17}NO_2$ $[M + H]^+$: 232.1332, Found: 232.1323.

9-(Trifluoromethyl)-1,2,3,4,4a,5-hexahydro-6H-pyrido[1,2-a]quinolin-6-one



(±)-**6l**

Following general procedure E, compound (±)-**6l** was obtained from piperidine (99 μL, 1 mmol) and 3-(2-fluoro-4-(trifluoromethyl)phenyl)-3-oxopropanoic acid (375 mg, 1.5 mmol) as a bright yellow solid in 61% yield (165 mg). Hexanes containing EtOAc (7%) was used as the eluent for silica gel chromatography.

Characterization data:

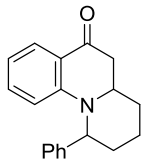
$\mathbf{R_f}$ = 0.24 in hexane/EtOAc 90:10 v/v.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, J = 9.1 Hz, 1H), 7.16 (s, 1H), 6.98 (d, J = 8.2 Hz, 1H), 3.98 (app ddt, J = 12.7, 4.3, 1.9 Hz, 1H), 3.35 (app ddt, J = 15.1, 11.5, 3.3 Hz, 1H), 2.80–2.68 (comp, 2H), 2.59 (dd, J = 16.5, 11.7 Hz, 1H), 1.94–1.37 (comp, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 192.8, 152.3, 136.3 (q, $J_{C\text{-}F}$ = 31.7 Hz), 128.7, 123.7 (q, $J_{C\text{-}F}$ = 271.3 Hz), 122.6, 113.7 (q, $J_{C\text{-}F}$ = 3.7 Hz), 110.9 (q, $J_{C\text{-}F}$ = 4.0 Hz), 57.6, 47.4, 45.0, 32.0, 24.6, 23.2.

HRMS (ESI–TOF): $C_{14}H_{14}NOF_3$ $[M + H]^+$: 270.1100, Found: 270.1096.

1-Phenyl-1,2,3,4,4a,5-hexahydro-6H-pyrido[1,2-a]quinolin-6-one



(±)-**6m**

To a solution of the 2-phenylpiperidine (161 mg, 1 mmol, 1 equiv) in anhydrous ether (1.5 mL) cooled to –78 °C was slowly added *n*-BuLi in hexanes (400 μL, 1 mmol, 1 equiv) under the protection of nitrogen, and the resulting solution was stirred at the same temperature for 5 min. To this was then added a solution of trifluoroacetophenone (296 mg, 1.7 mmol, 1.7 equiv) in anhydrous ether (1 mL). The resulting mixture was stirred at –78 °C for 5 min. To this was then added a solution of trifluoroacetic acid (1.05 mmol, 1.05 equiv) in anhydrous THF (1 mL). The resulting mixture was stirred at –78 °C for 5 min, followed by the addition of a solution of 3-(2-fluorophenyl)-3-oxopropanoic acid (273 mg, 1.5 mmol, 1.5 equiv) in anhydrous THF (1.5 mL) via cannula. Subsequently, the reaction vessel was taken out of the low temperature bath and the reaction mixture stirred at room temperature for 2 h. To this was then added K_2CO_3 (2 mmol, 2 equiv) and DMF (5 mL). The resulting mixture was refluxed for 16 h. The reaction mixture was then allowed to cool to room temperature and water (20 mL) was added. The resulting mixture was extracted with EtOAc (2 x 20 mL) and the combined organic layers washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography to provide compound (±)-**6m** as a yellow solid in 48% yield (133 mg, inseparable 1:1 d.r. mixture).

Characterization data:

$\mathbf{R_f}$ = 0.20 in hexane/EtOAc 90:10 v/v.

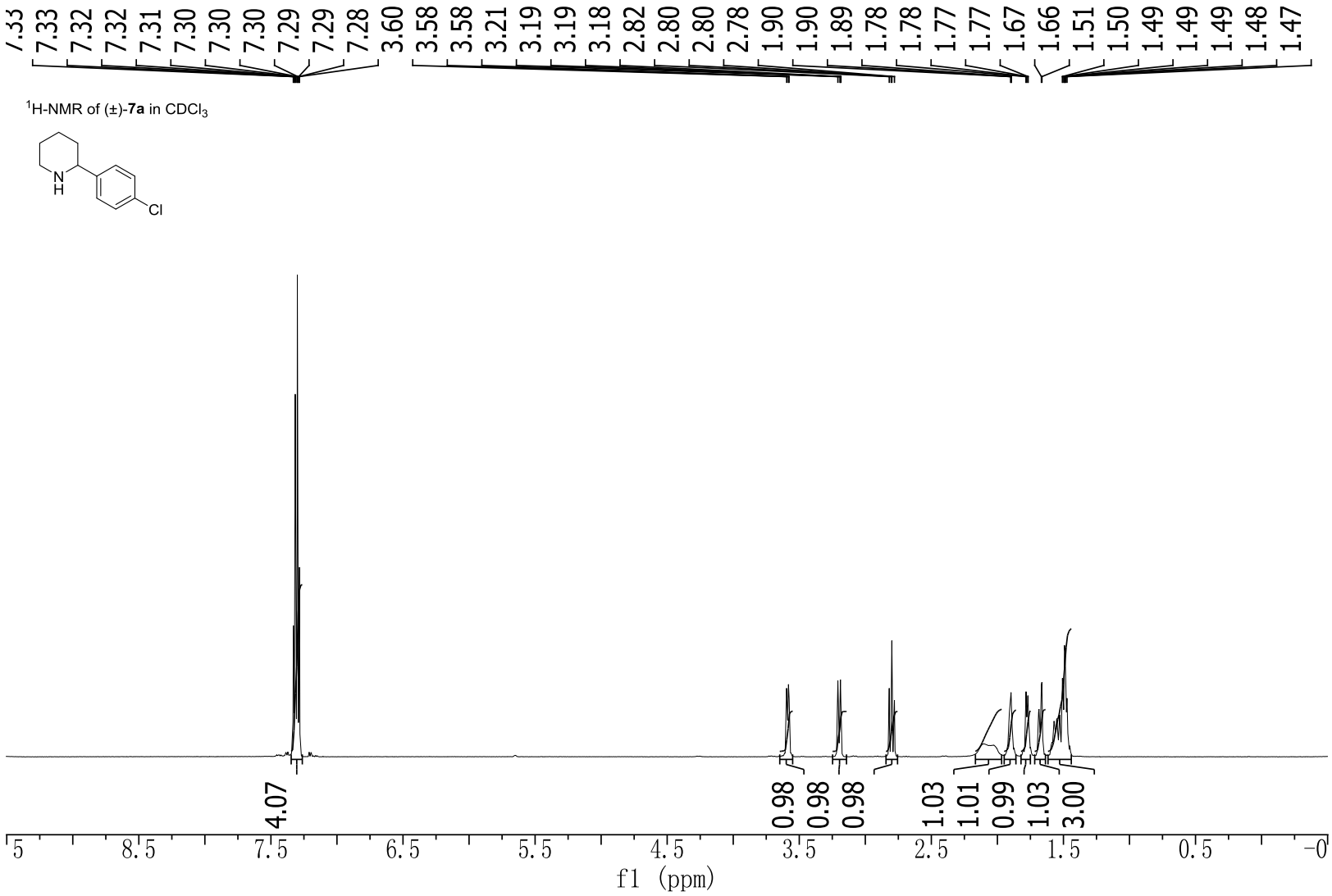
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.97 (dd, J = 7.9, 1.9 Hz, 1H), 7.48–7.42 (m, 1H,), 7.40–7.19 (comp, 4.5 H), 7.15 (ddd, J = 8.8, 7.0, 1.9 Hz, 0.5H), 6.77–6.66 (m, 1.5 H), 6.54 (d, J = 8.6 Hz, 0.5H), 5.31–5.25 (m, 0.5H), 4.48 (dd, J = 8.2, 5.1 Hz, 0.5H), 4.01 (tt, J = 11.2, 3.9 Hz, 0.5H), 3.72 (ddt, J = 12.8, 11.5, 4.1 Hz, 0.5H), 2.86–2.69 (comp, 1.5H), 2.62 (dd, J = 16.0, 11.0 Hz, 0.5H), 2.37–2.25 (m, 1H), 2.15 (dddd, J = 13.6, 12.4, 5.4, 3.5 Hz, 0.5H), 2.03–1.93 (m, 0.5H), 1.90–1.44 (comp, 4H).

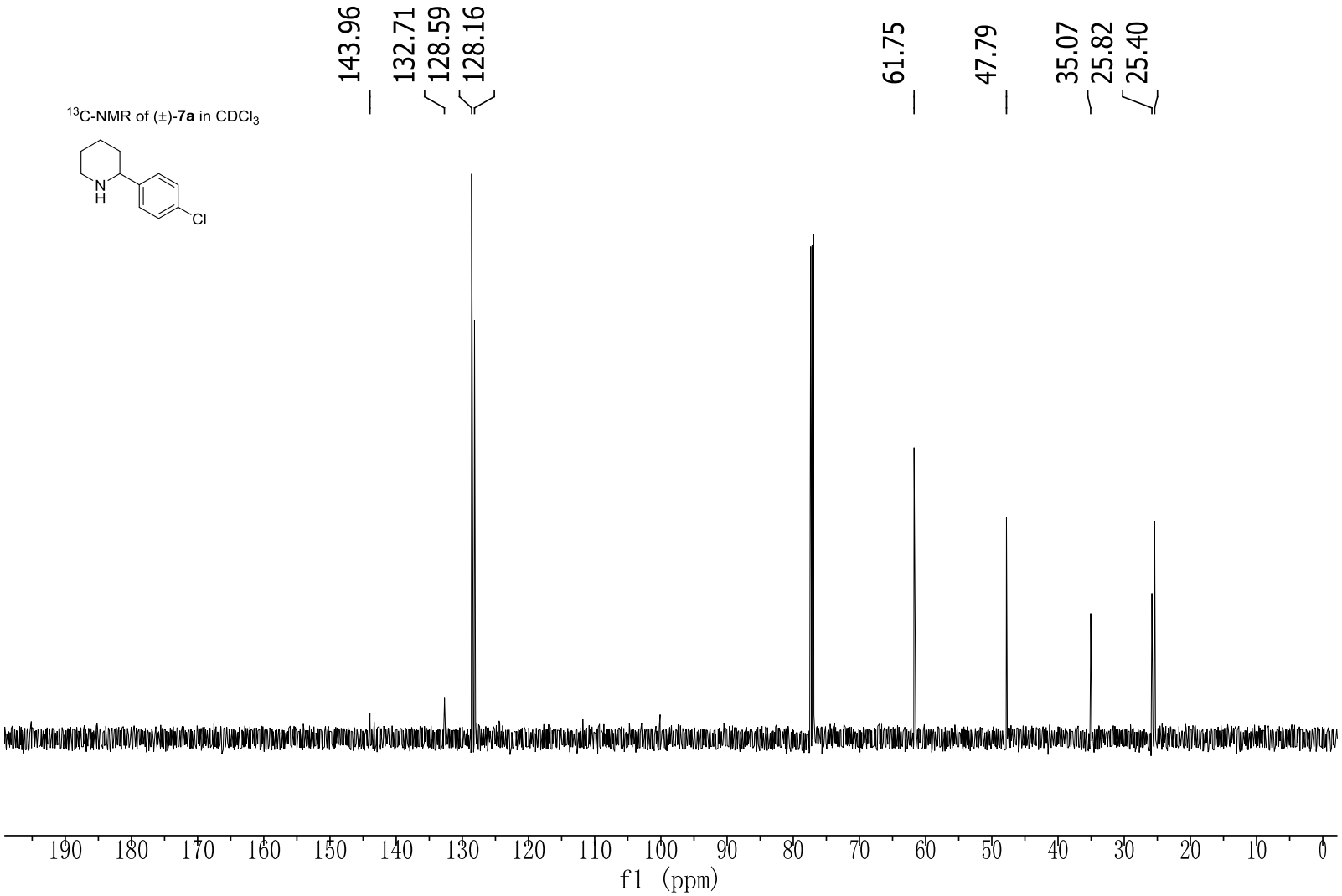
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 194.2, 193.3, 152.8, 151.2, 144.6, 140.7, 135.4, 134.5, 128.8, 128.4, 127.7, 127.5, 127.2, 126.7, 126.4, 125.3, 121.6, 119.9, 117.5, 116.7, 115.8, 114.0, 60.6, 56.3, 55.3, 53.3, 46.8, 45.0, 33.8, 31.9, 31.2, 30.4, 18.9, 18.0.

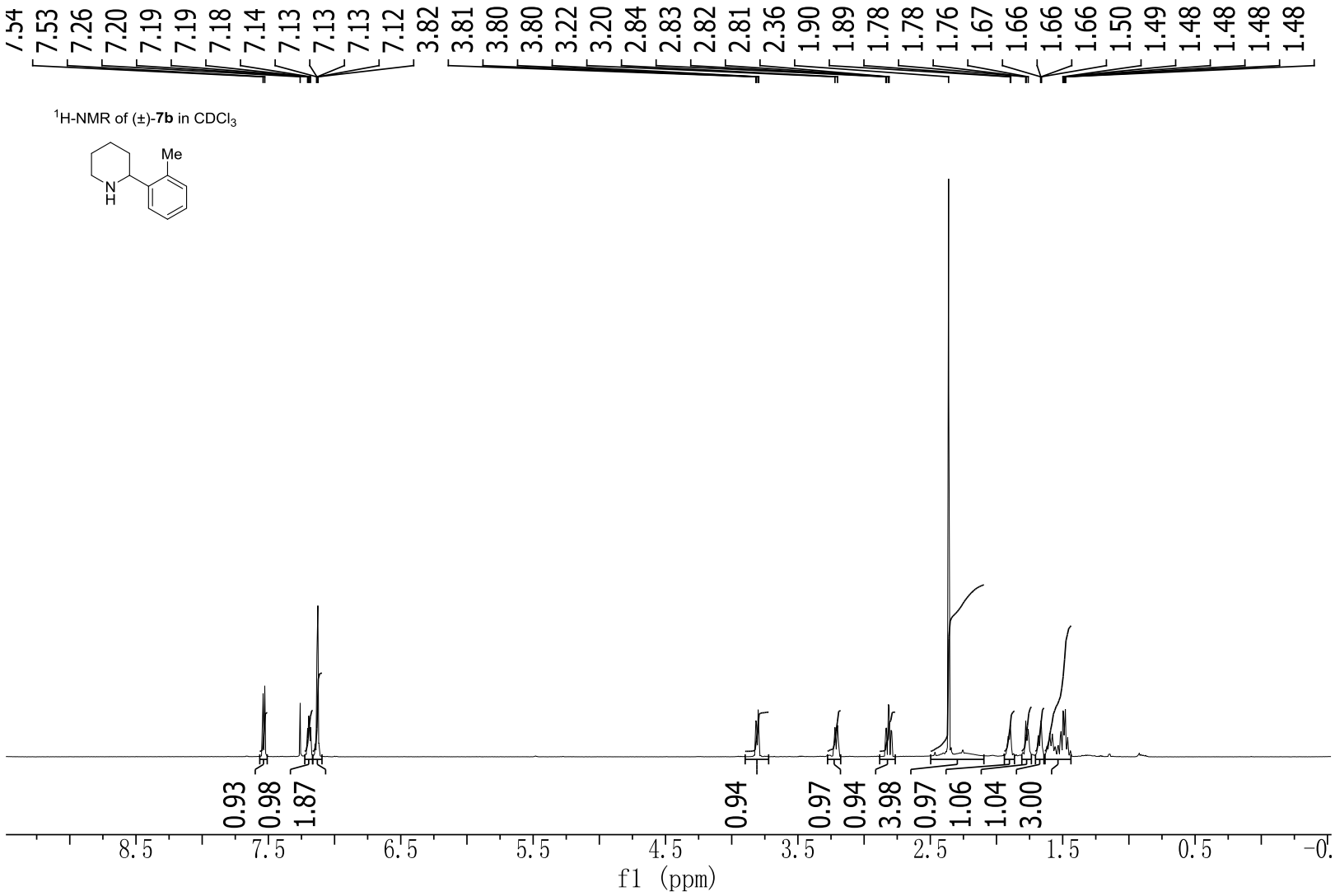
HRMS (ESI–TOF): Calculated for $C_{19}H_{19}NO$ $[M + H]^+$: 278.1539, Found: 278.1552.

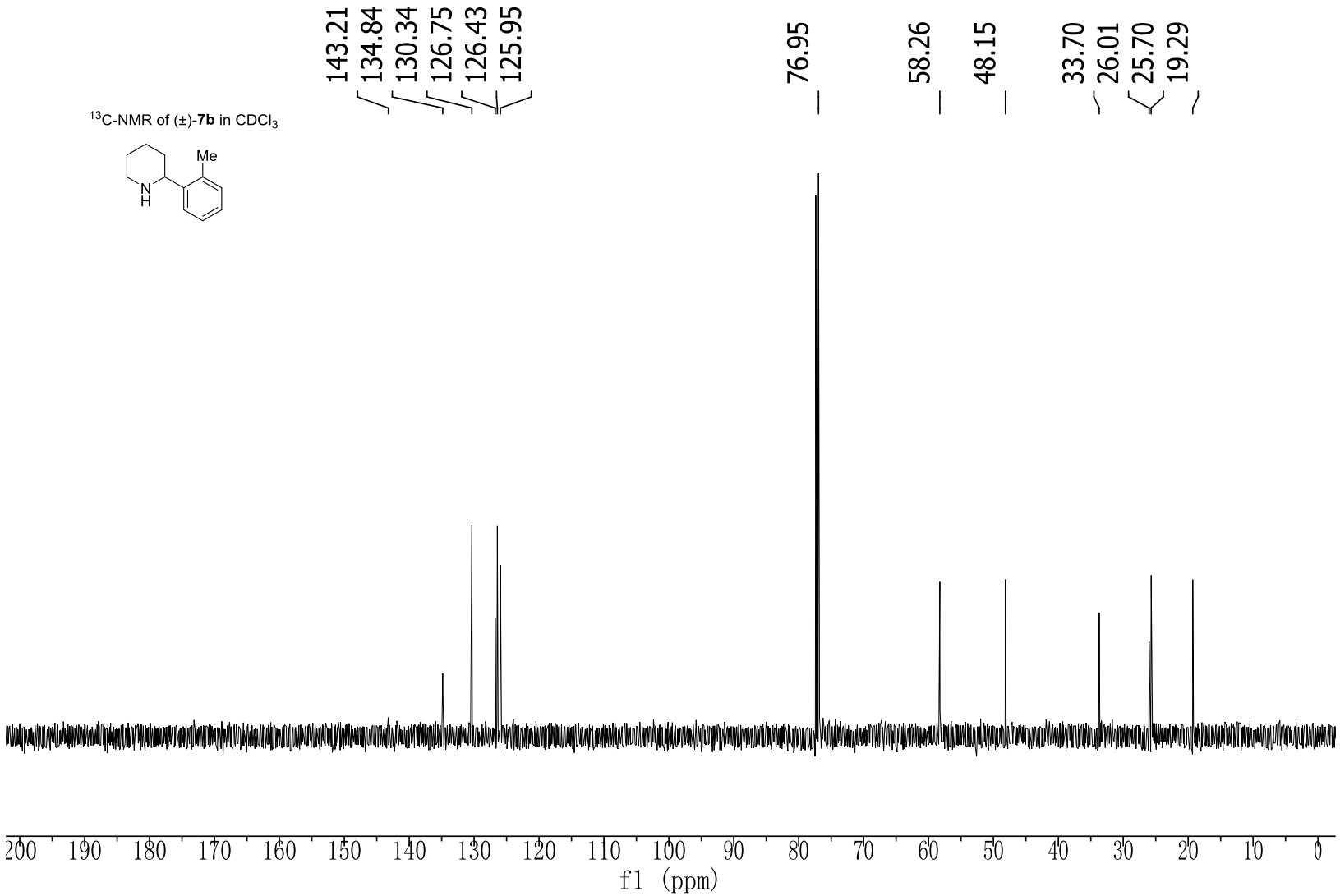
References

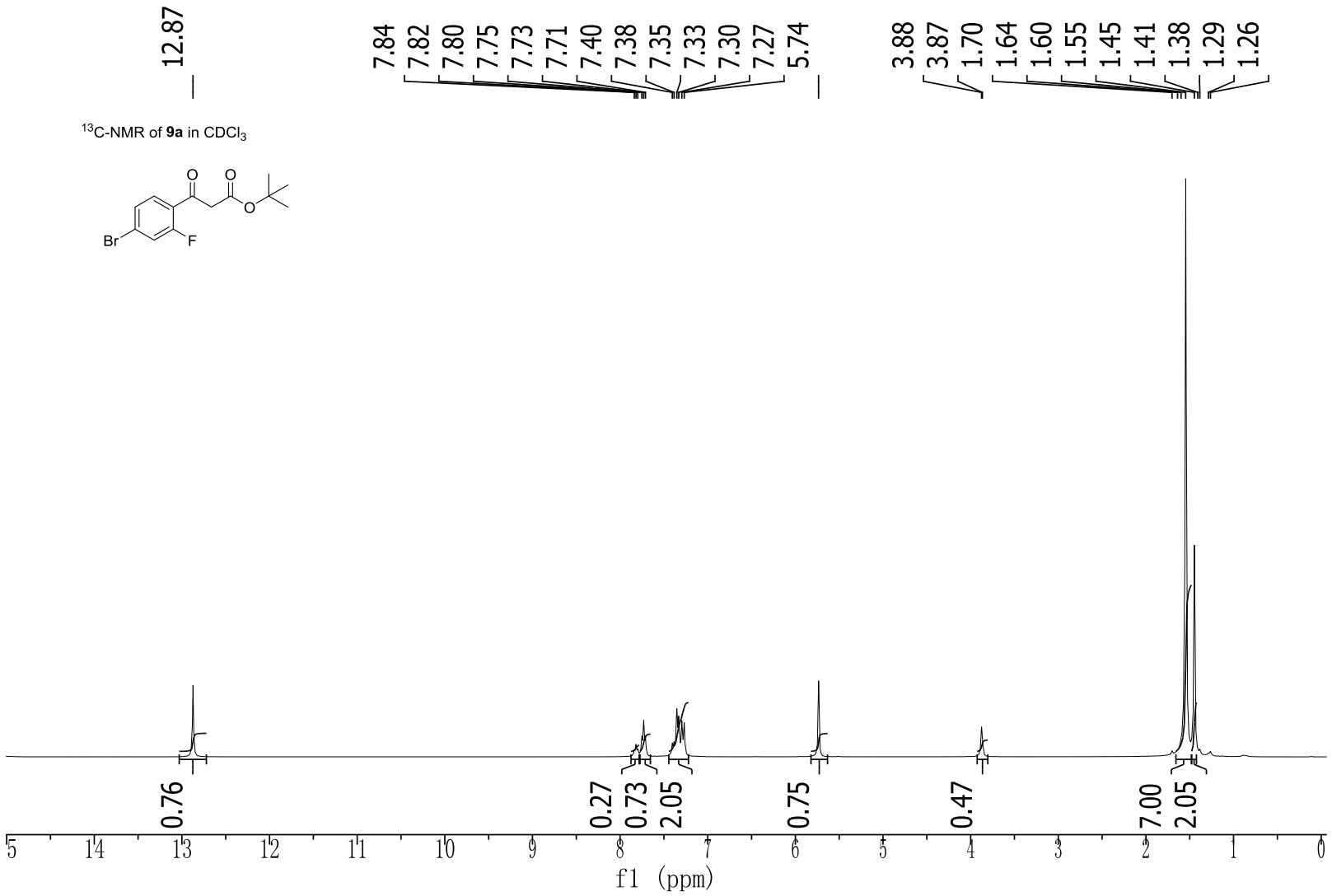
1 J. Suffert, *J. Org. Chem*., **1989**, *54*, 509.
2 W. Chen, L. Ma, A. Paul, D. Seidel, *Nat. Chem*., **2018**, *10*, 165.
3 D. A. Evans, S. Mito, D. Seidel, *J. Am. Chem. Soc*., **2007**, *129*, 11583.
4 B. Schweitzer-Chaput, M. Klussmann, *Eur. J. Org. Chem*., **2013**, *4*, 666.


7.33
7.32
7.32
7.31
7.30
7.30
7.30
7.29
7.29
7.28
3.60
3.58
3.58
3.21
3.19
3.19
3.18
2.82
2.80
2.80
2.78
1.90
1.90
1.89
1.78
1.78
1.77
1.77
1.67
1.66
1.51
1.50
1.49
1.49
1.49
1.48
1.47
1H-NMR of (±)-7a in CDCl3
N
H
Cl
4.07
0.98
0.98
0.98
1.03
1.01
0.99
1.03
3.00
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

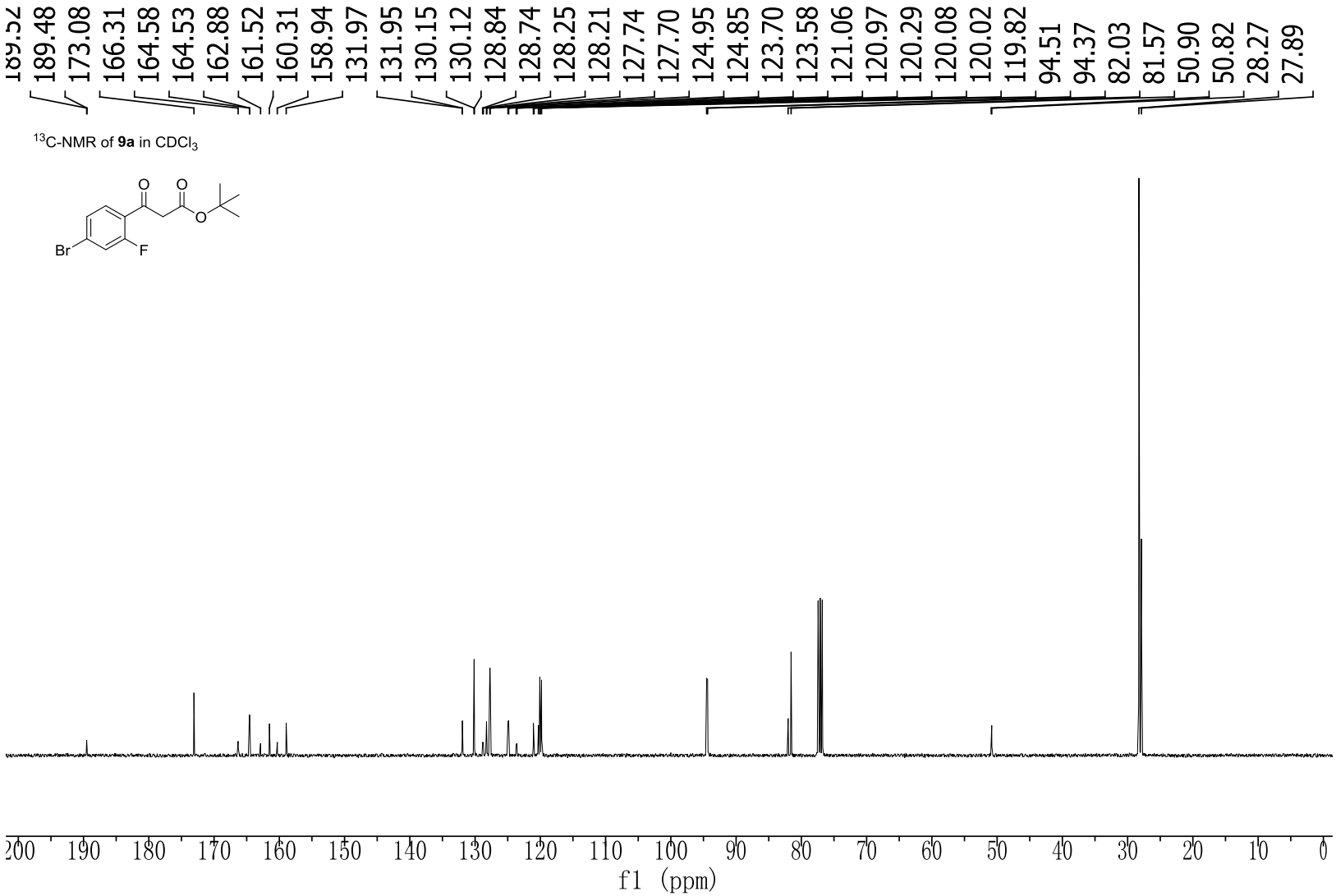

143.96
132.71
128.59
128.16
61.75
47.79
35.07
25.82
25.40
^{13}C-NMR of (±)-**7a** in $CDCl_3$
N
H
Cl
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.54
7.53
7.26
7.20
7.19
7.19
7.18
7.14
7.13
7.13
7.13
7.12
3.82
3.81
3.80
3.80
3.22
3.20
2.84
2.83
2.82
2.81
2.36
1.90
1.89
1.78
1.78
1.76
1.67
1.66
1.66
1.66
1.50
1.49
1.48
1.48
1.48
1.48
1H-NMR of (±)-7b in CDCl3
Me
N
H
0.93
0.98
1.87
0.94
0.97
0.94
3.98
0.97
1.06
1.04
3.00
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.
f1 (ppm)

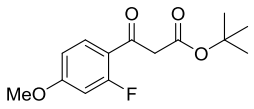

143.21
134.84
130.34
126.75
126.43
125.95
76.95
58.26
48.15
33.70
26.01
25.70
19.29
^{13}C-NMR of (±)-**7b** in $CDCl_3$
Me
N
H
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

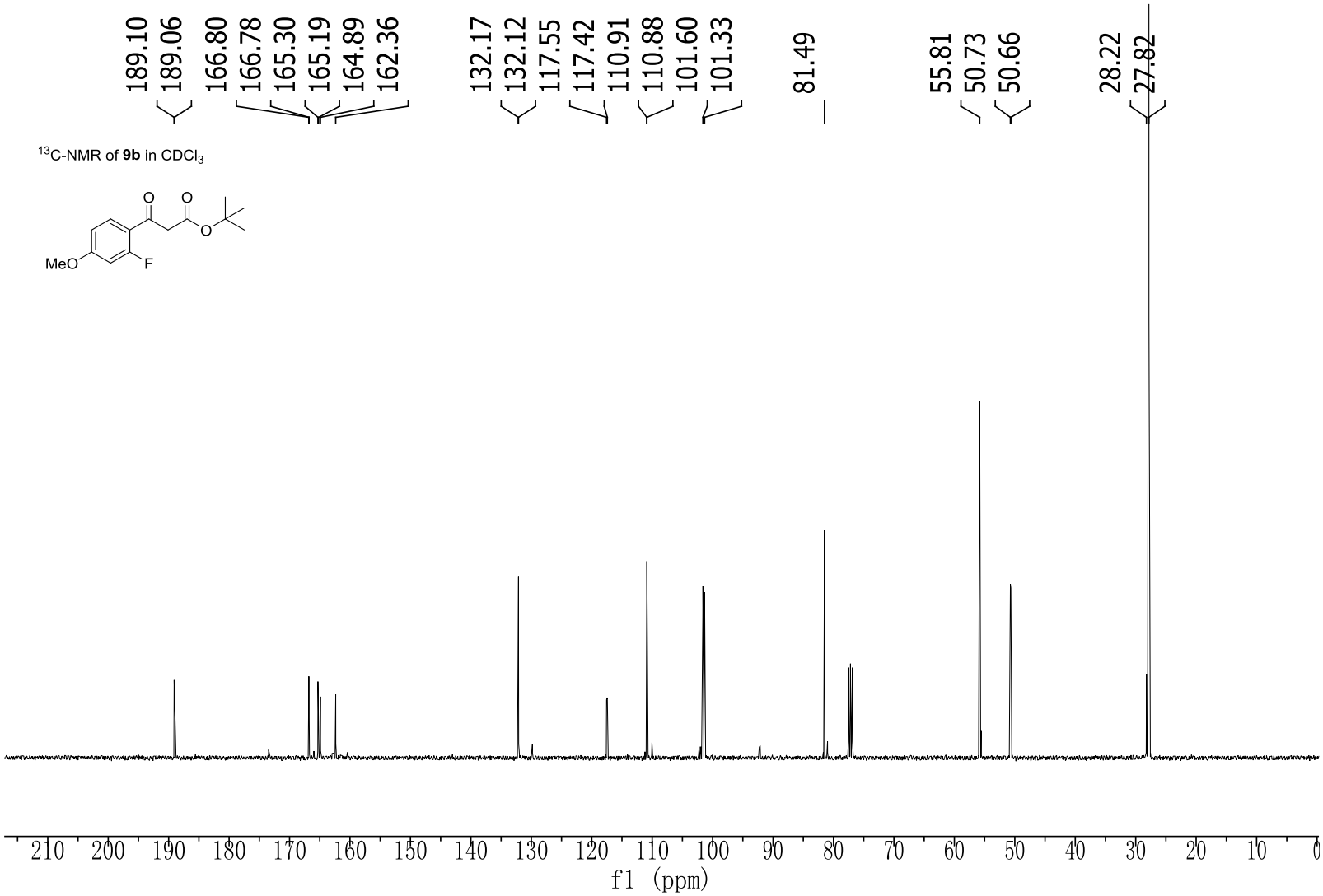


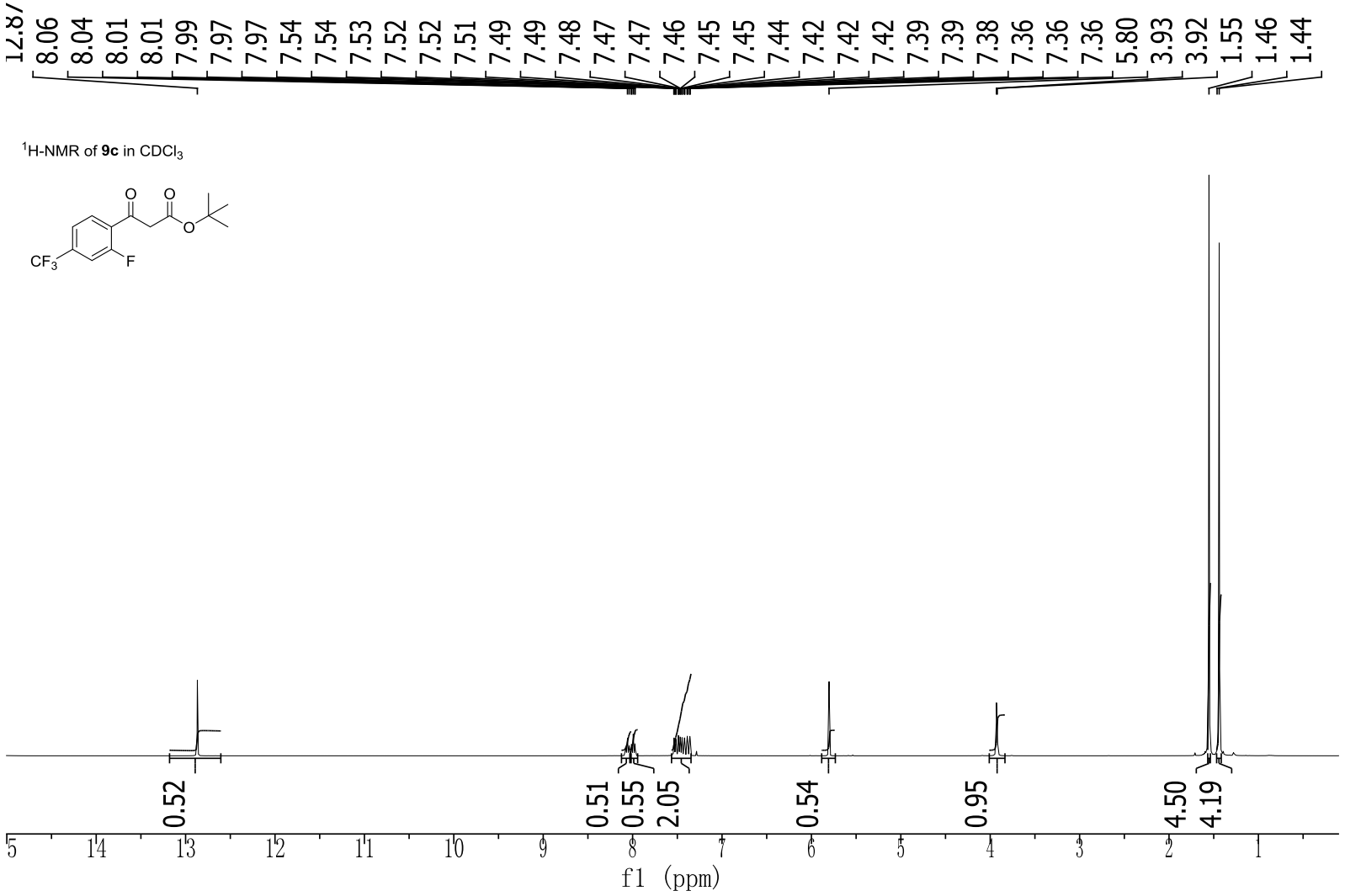
^{13}C-NMR of **9a** in $CDCl_3$


189.52
189.48
173.08
166.31
164.58
164.53
162.88
161.52
160.31
158.94
131.97
131.95
130.15
130.12
128.84
128.74
128.25
128.21
127.74
127.70
124.95
124.85
123.70
123.58
121.06
120.97
120.29
120.08
120.02
119.82
94.51
94.37
82.03
81.57
50.90
50.82
28.27
27.89
^{13}C-NMR of **9a** in $CDCl_3$
O
O
O
Br
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

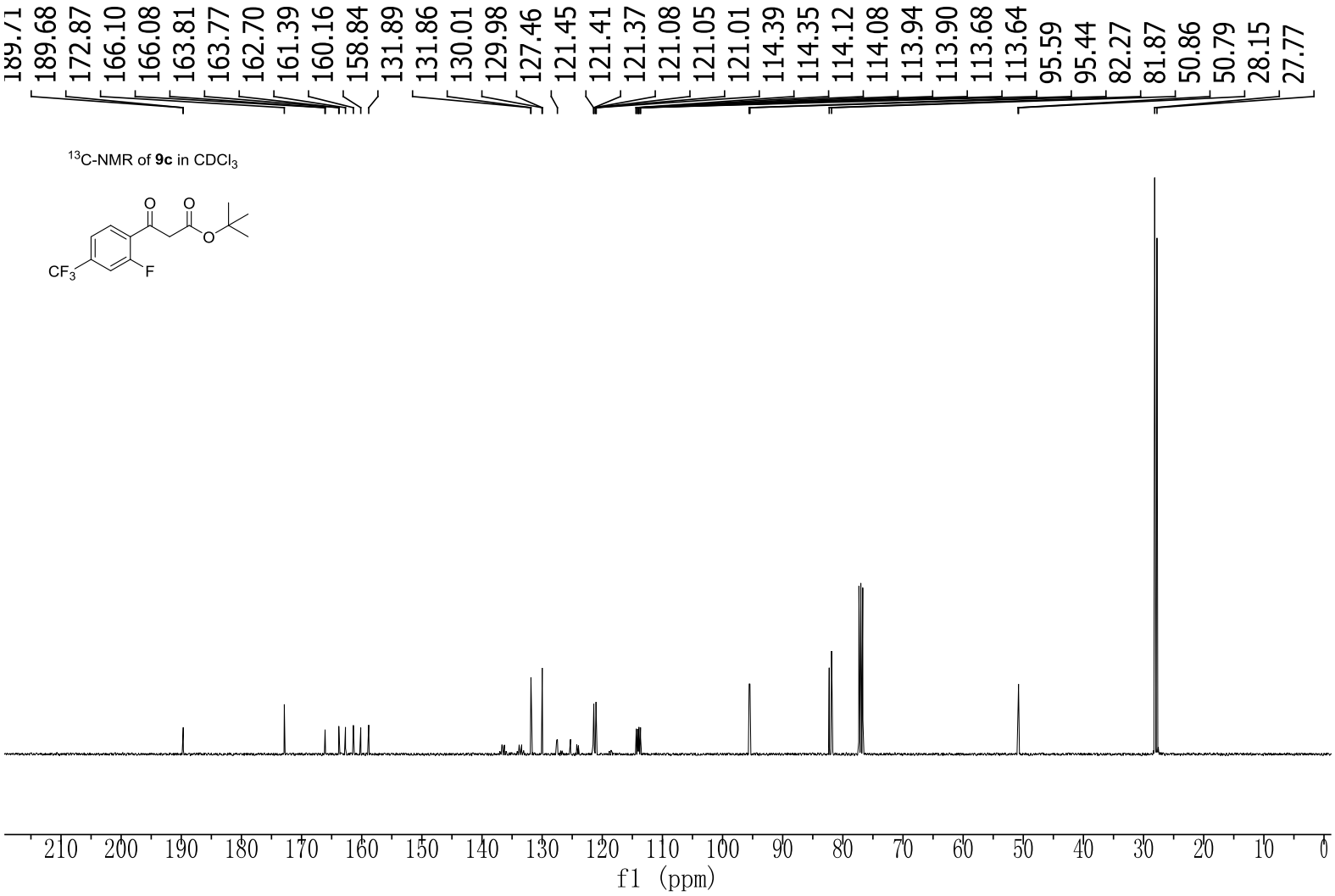
^{1}H-NMR of **9b** in $CDCl_3$

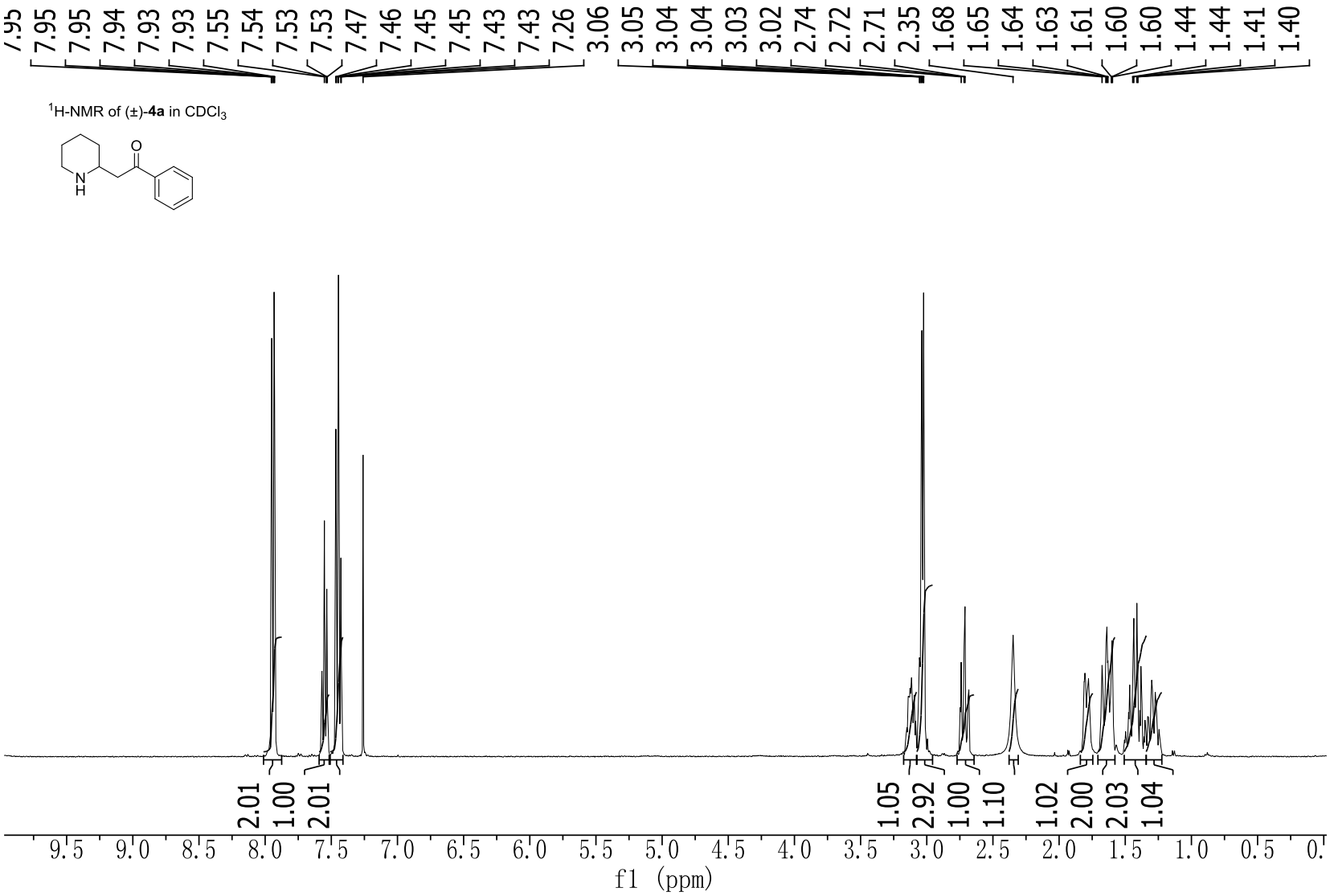


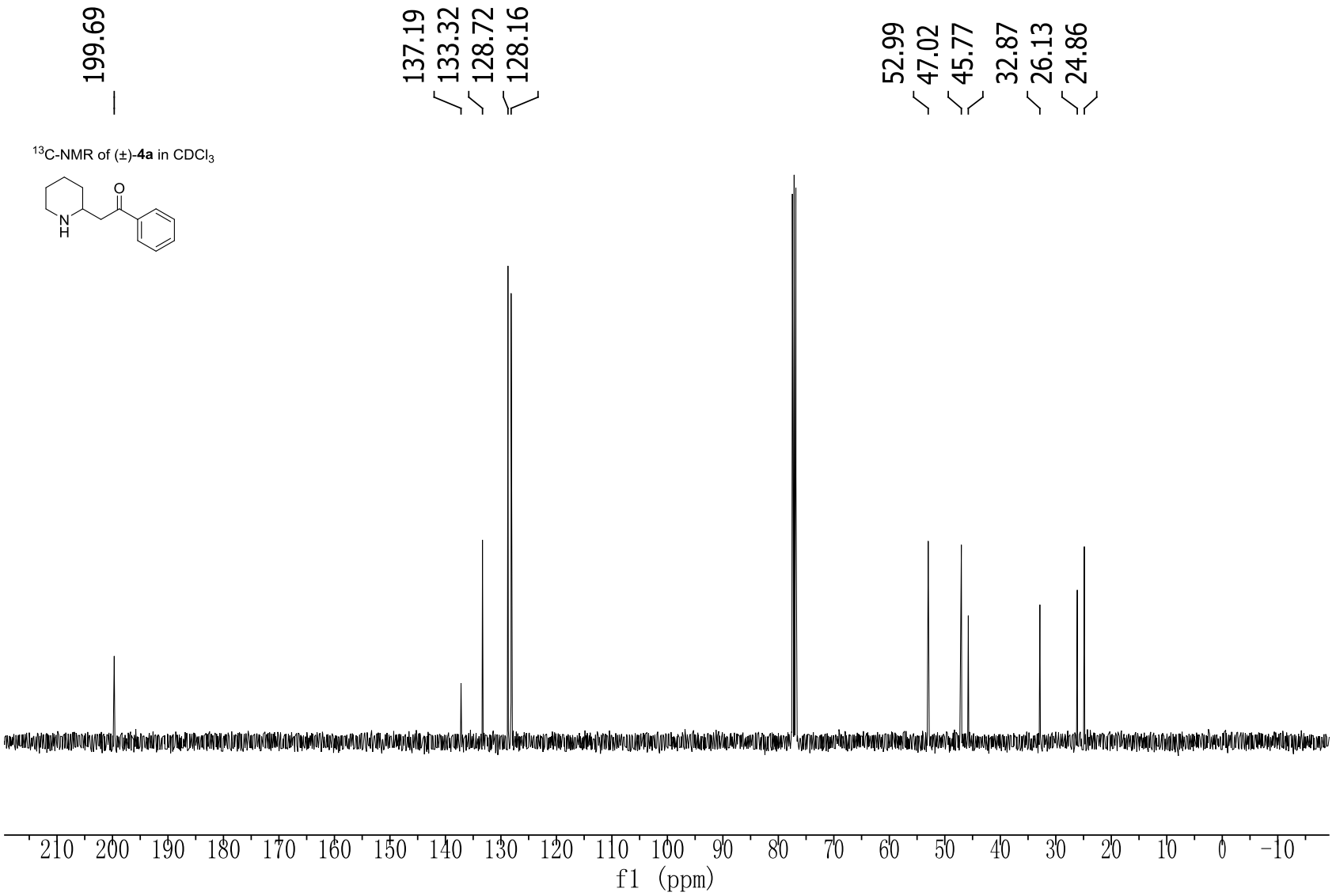

189.10
189.06
166.80
166.78
165.30
165.19
164.89
162.36
132.17
132.12
117.55
117.42
110.91
110.88
101.60
101.33
81.49
55.81
50.73
50.66
28.22
27.82
13C-NMR of 9b in CDCl3
O
O
O
MeO
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

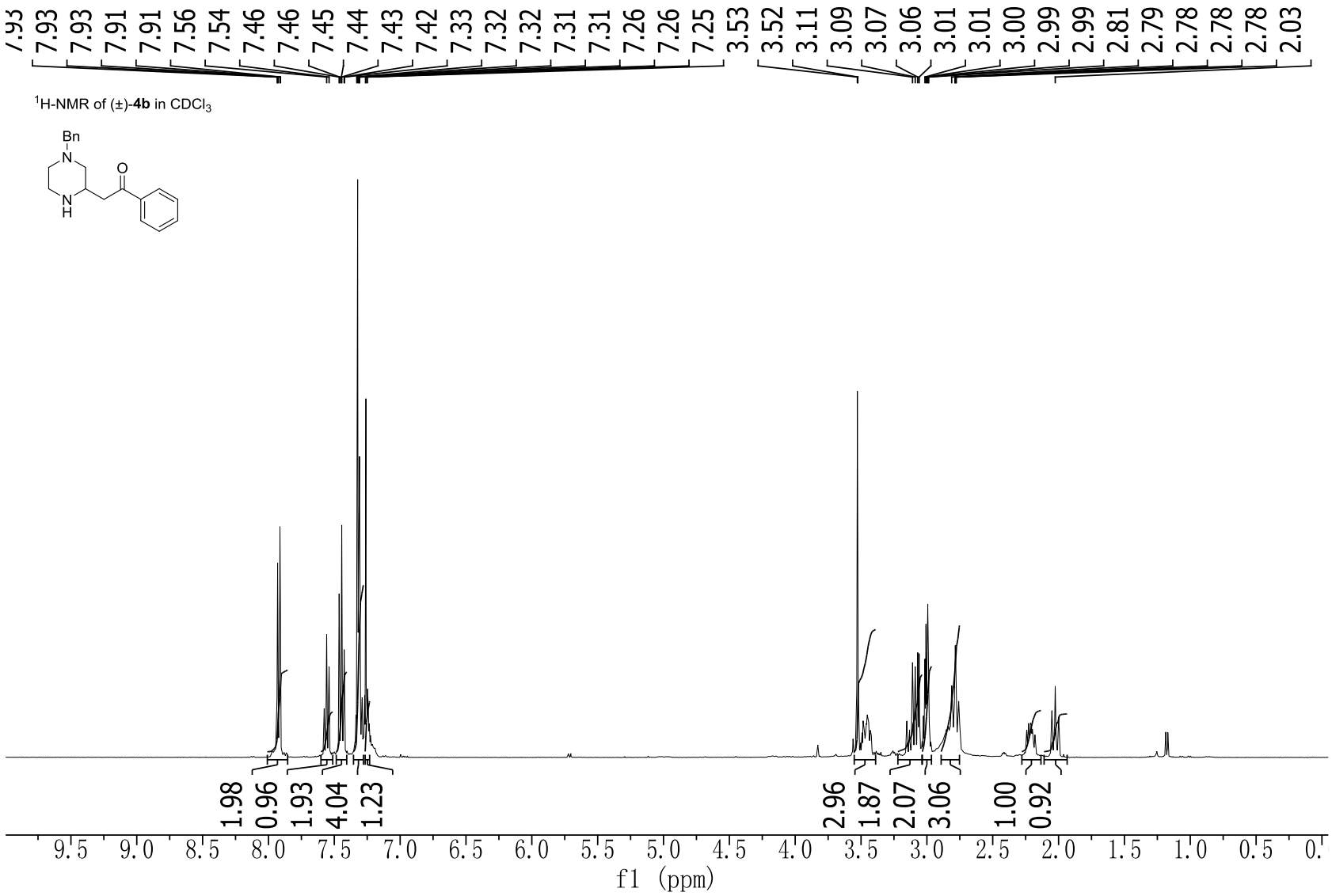


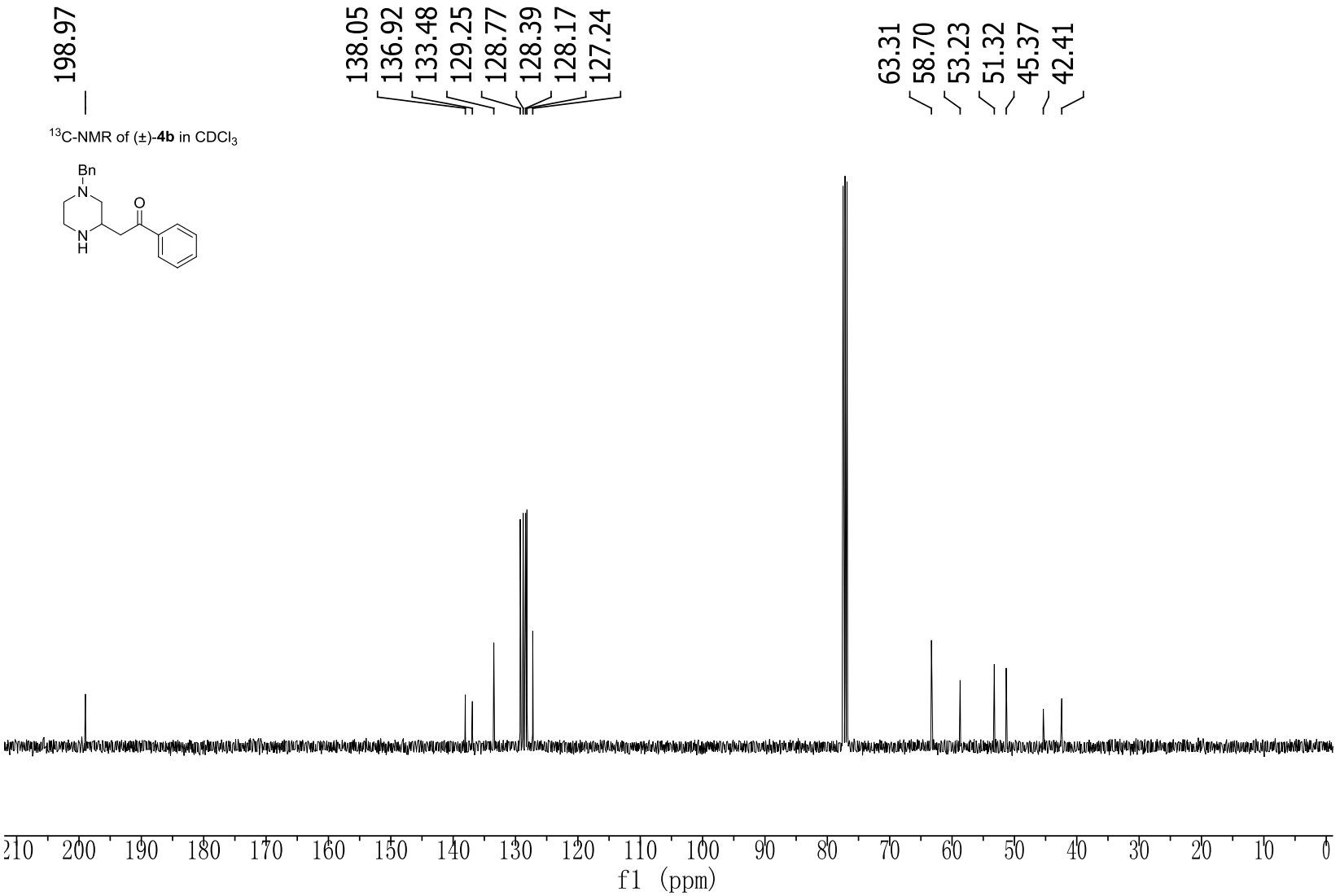
^{1}H-NMR of **9c** in $CDCl_3$


189.71
189.68
172.87
166.10
166.08
163.81
163.77
162.70
161.39
160.16
158.84
131.89
131.86
130.01
129.98
127.46
121.45
121.41
121.37
121.08
121.05
121.01
114.39
114.35
114.12
114.08
113.94
113.90
113.68
113.64
95.59
95.44
82.27
81.87
50.86
50.79
28.15
27.77
13C-NMR of 9c in CDCl3
O
O
O
CF3
F
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

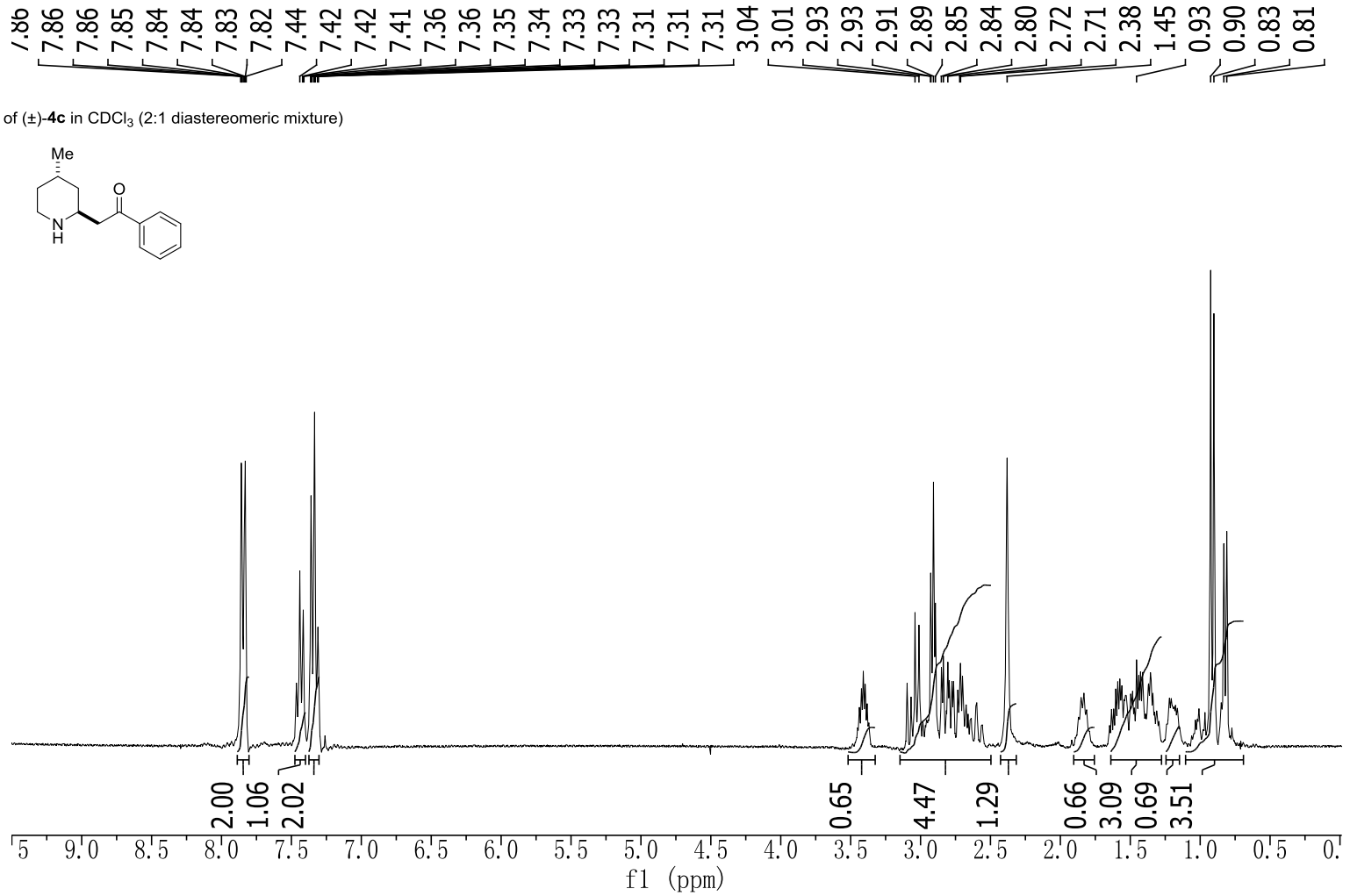

7.95
7.95
7.94
7.93
7.93
7.55
7.54
7.53
7.53
7.47
7.46
7.45
7.45
7.43
7.43
7.26
3.06
3.05
3.04
3.04
3.03
3.02
2.74
2.72
2.71
2.35
1.68
1.65
1.64
1.63
1.61
1.60
1.60
1.44
1.44
1.41
1.40
1H-NMR of (±)-4a in CDCl3
O
N
H
2.01
1.00
2.01
1.05
2.92
1.00
1.10
1.02
2.00
2.03
1.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

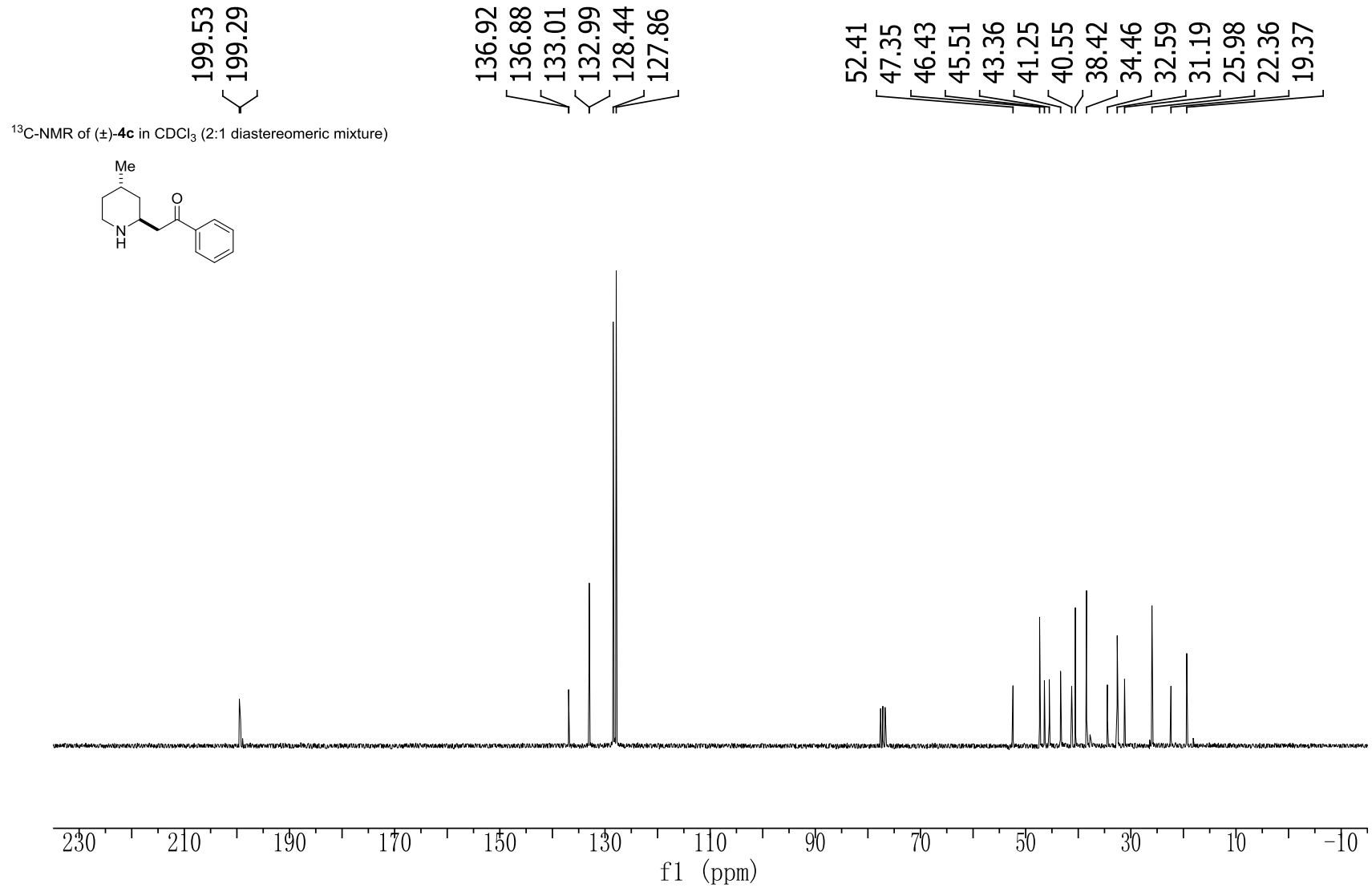

199.69
137.19
133.32
128.72
128.16
52.99
47.02
45.77
32.87
26.13
24.86
13C-NMR of (±)-4a in CDCl3
O
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.93 7.93 7.91 7.91 7.56 7.54 7.46 7.46 7.45 7.44 7.43 7.42 7.33 7.32 7.32 7.31 7.31 7.26 7.26 7.25 3.53 3.52 3.11 3.09 3.07 3.06 3.01 3.01 3.00 2.99 2.99 2.81 2.79 2.78 2.78 2.78 2.03
1H-NMR of (±)-4b in CDCl3
Bn
N
O
N
H
1.98 0.96 1.93 4.04 1.23 2.96 1.87 2.07 3.06 1.00 0.92
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.
f1 (ppm)

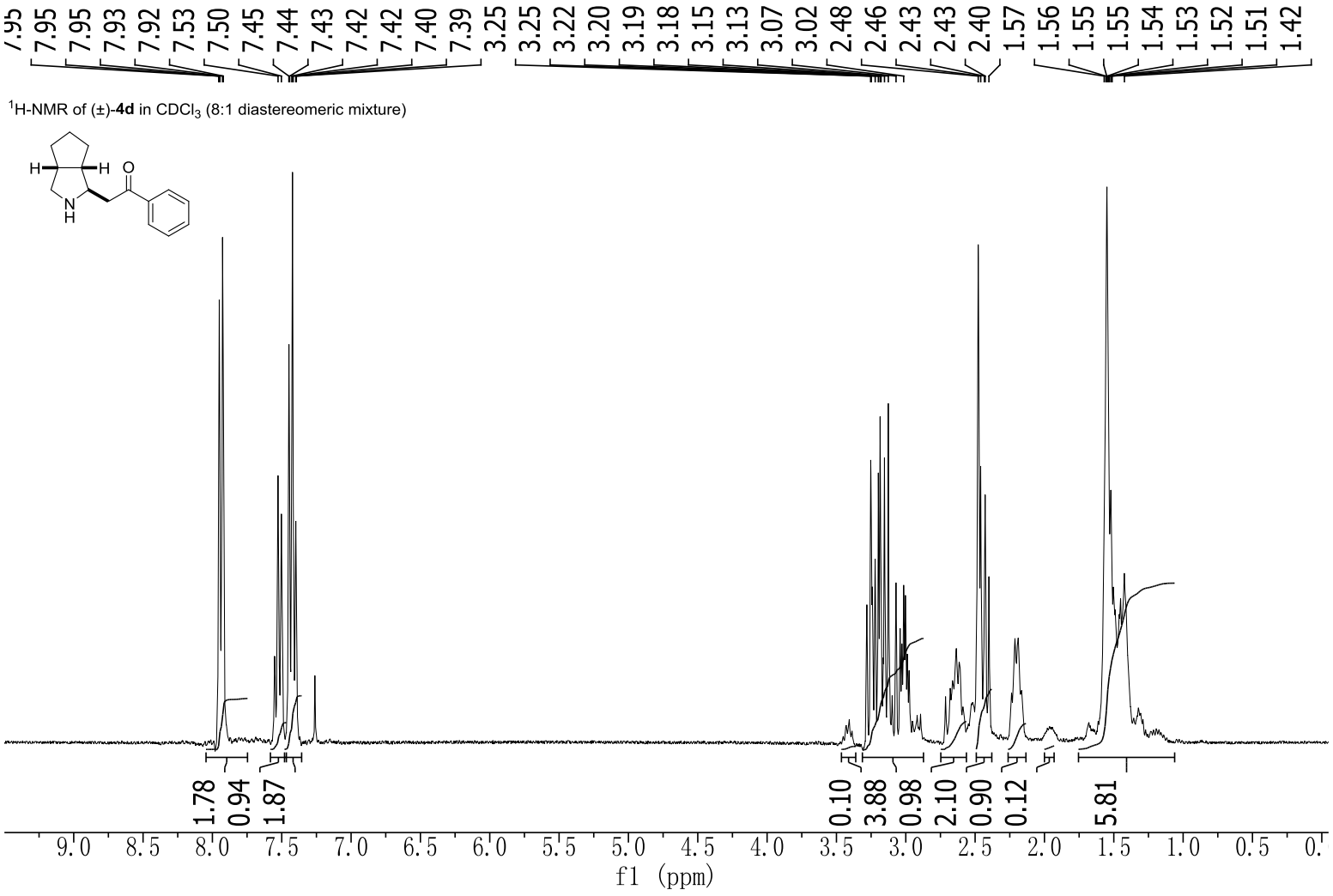

198.97
138.05
136.92
133.48
129.25
128.77
128.39
128.17
127.24
63.31
58.70
53.23
51.32
45.37
42.41
13C-NMR of (±)-4b in CDCl3
Bn
N
O
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

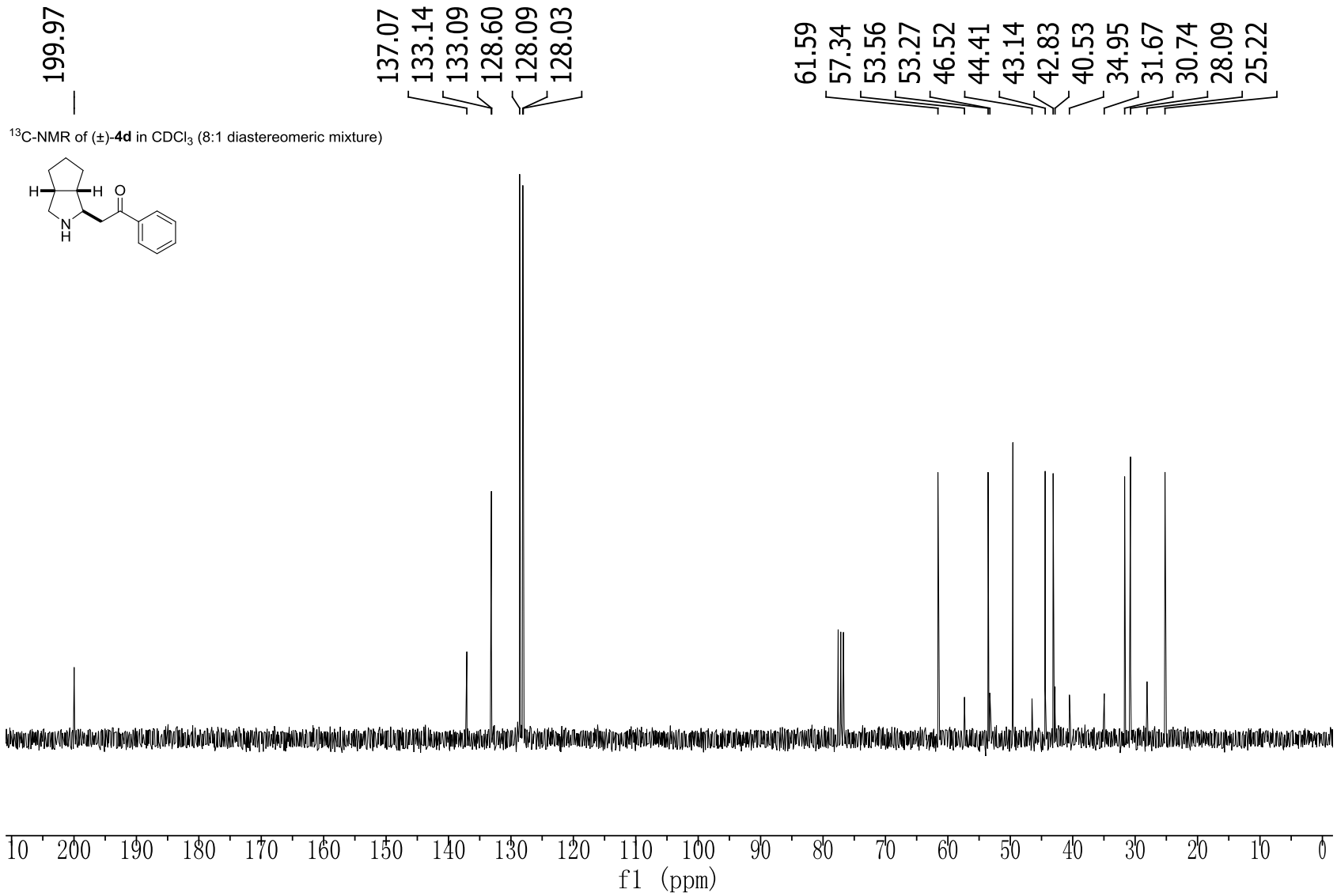
^{1}H-NMR of (±)-**4c** in $CDCl_3$ (2:1 diastereomeric mixture)



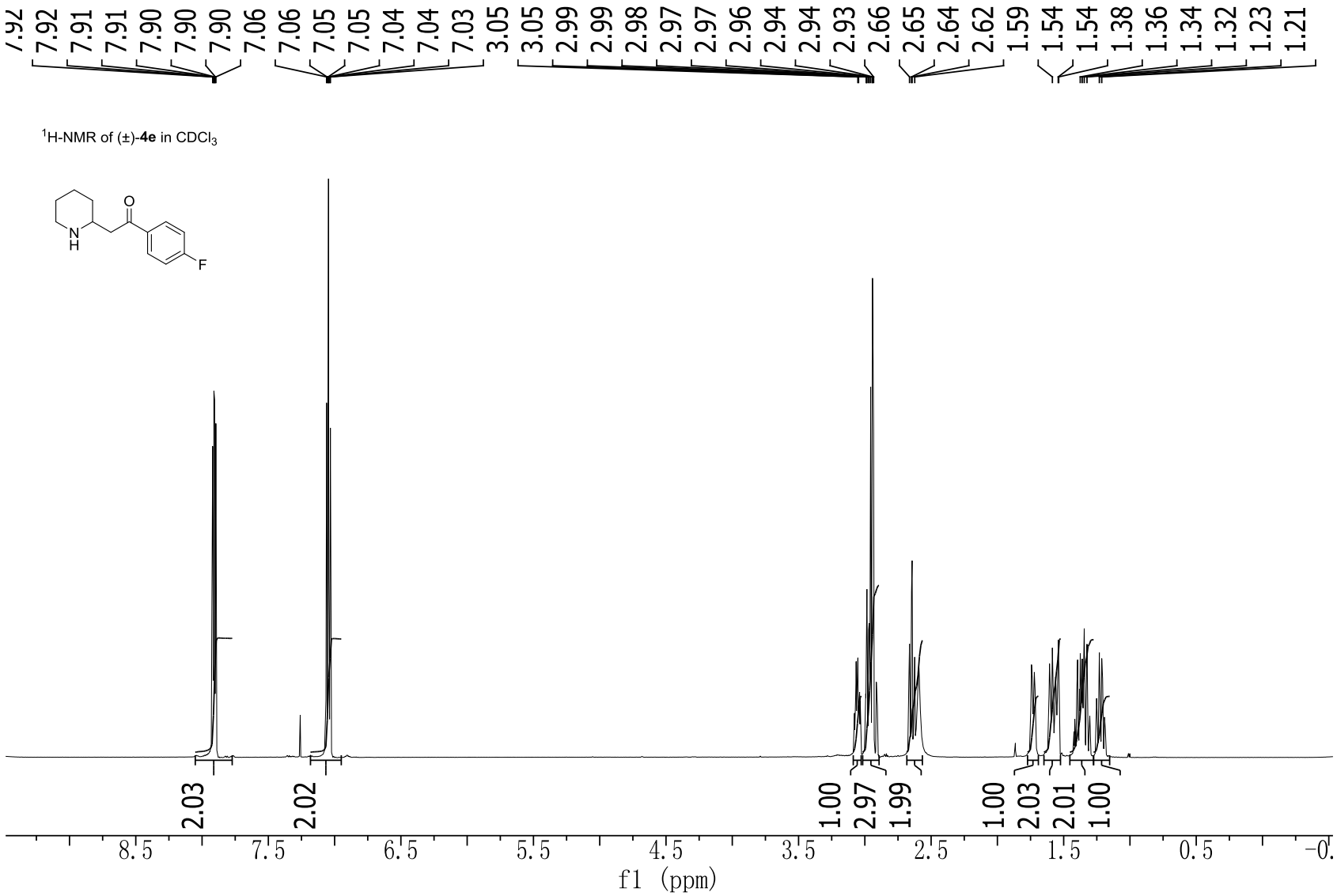


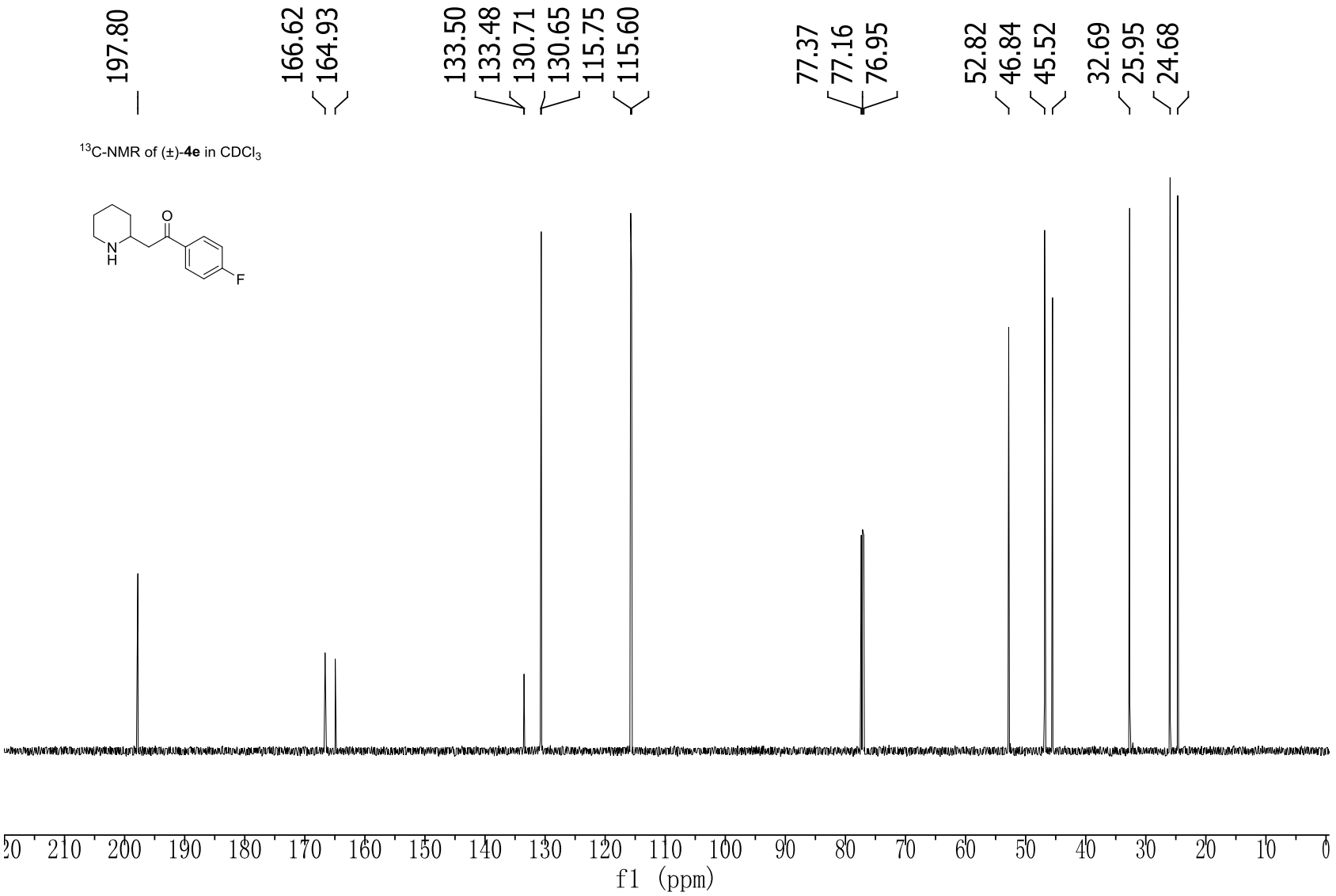
^{13}C-NMR of (±)-**4c** in $CDCl_3$ (2:1 diastereomeric mixture)

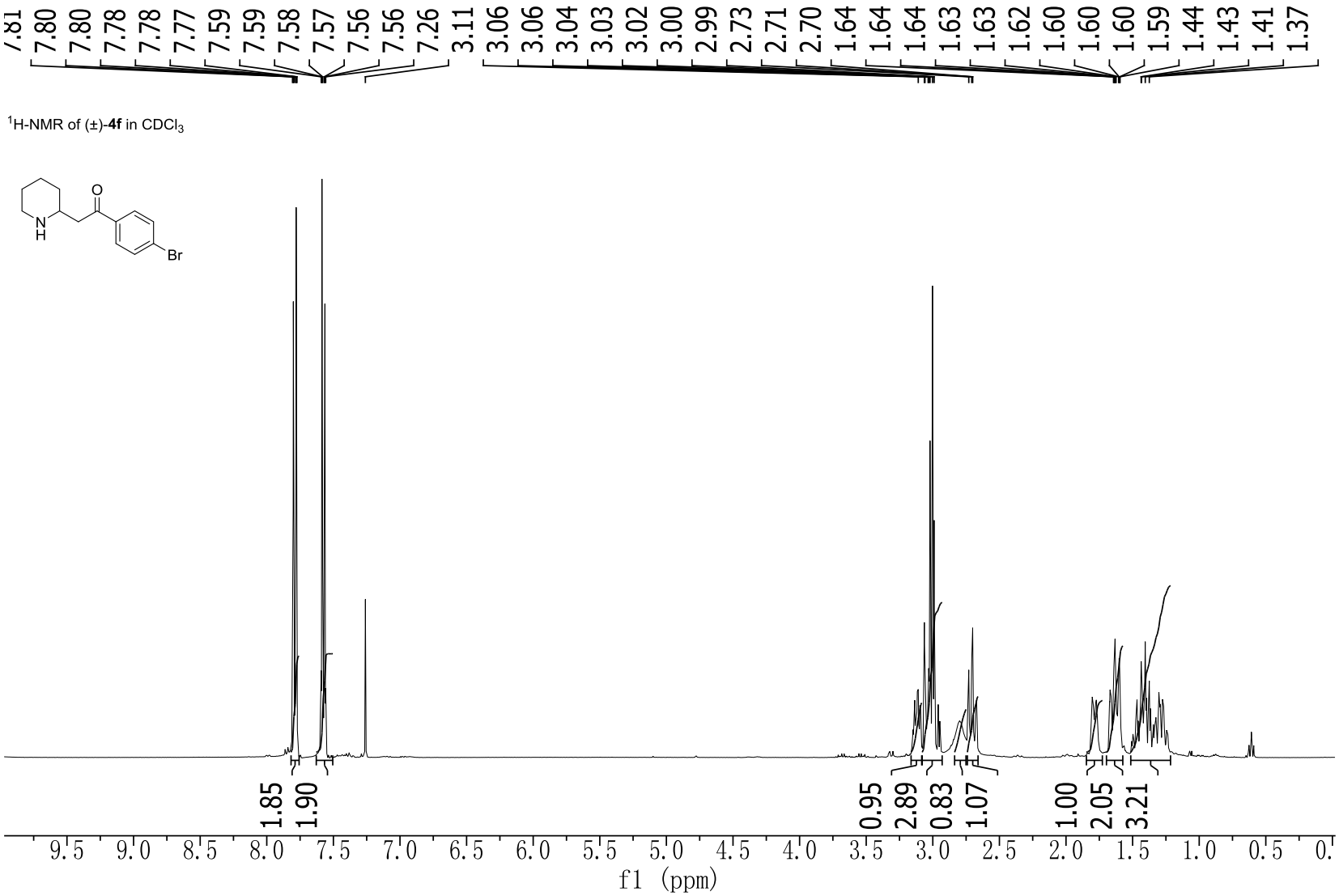

7.95 7.95 7.93 7.92 7.53 7.50 7.45 7.44 7.43 7.42 7.42 7.40 7.39 3.25
3.25 3.22 3.20 3.19 3.18 3.15 3.13 3.07 3.02 2.48 2.46 2.43 2.43 2.40 1.57 1.56 1.55 1.55 1.54 1.53 1.52 1.51 1.42
1H-NMR of (±)-4d in CDCl3 (8:1 diastereomeric mixture)
H
H
O
N
H
1.78 0.94 1.87 0.10 3.88 0.98 2.10 0.90 0.12 5.81
9.0 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.
f1 (ppm)



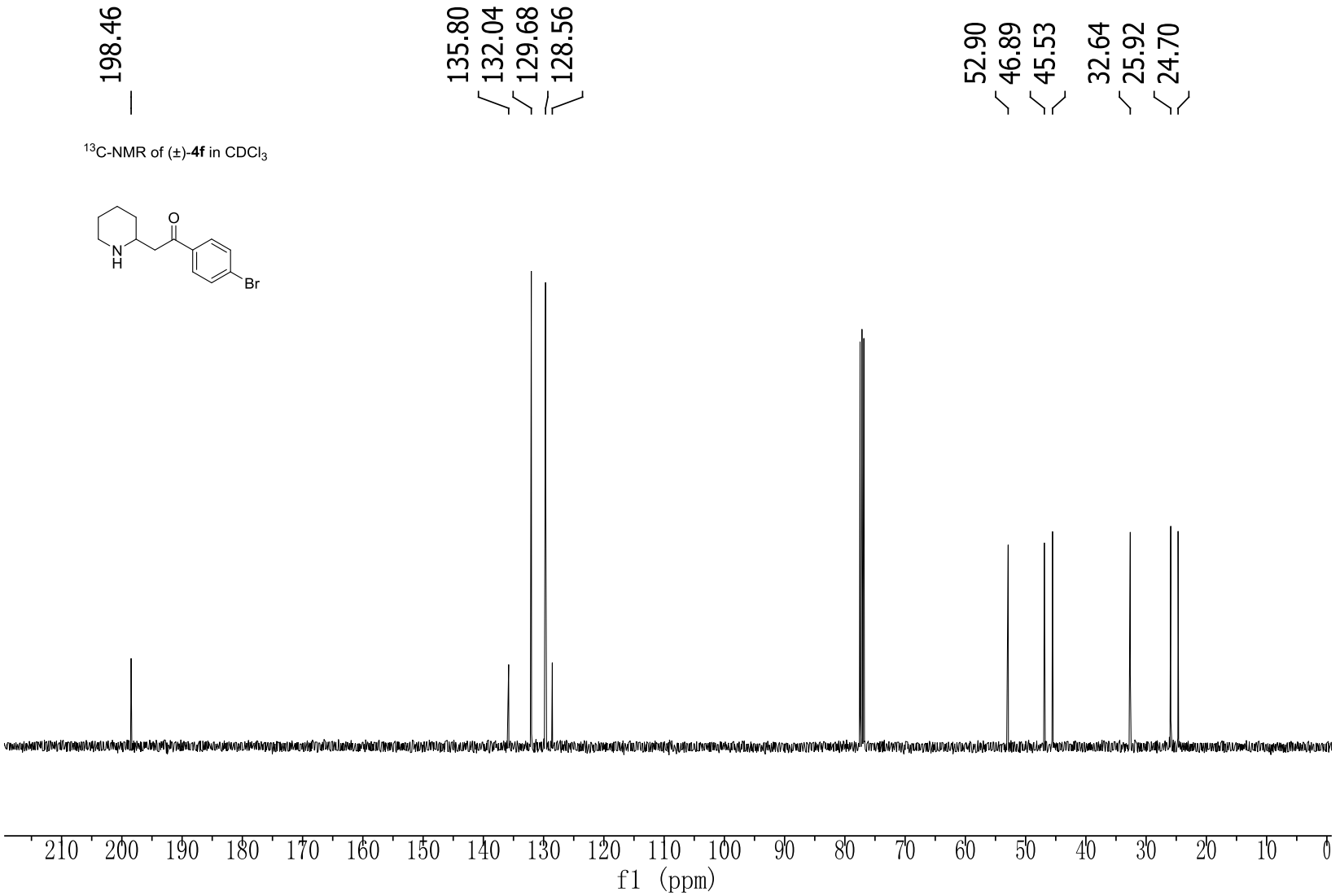
^{13}C-NMR of (±)-**4d** in $CDCl_3$ (8:1 diastereomeric mixture)


7.92
7.92
7.91
7.91
7.90
7.90
7.90
7.06
7.06
7.05
7.05
7.04
7.04
7.03
3.05
3.05
2.99
2.99
2.98
2.97
2.97
2.96
2.94
2.94
2.93
2.66
2.65
2.64
2.62
1.59
1.54
1.54
1.38
1.36
1.34
1.32
1.23
1.21
1H-NMR of (±)-4e in CDCl3
O
N
H
F
2.03
2.02
1.00
2.97
1.99
1.00
2.03
2.01
1.00
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.
f1 (ppm)

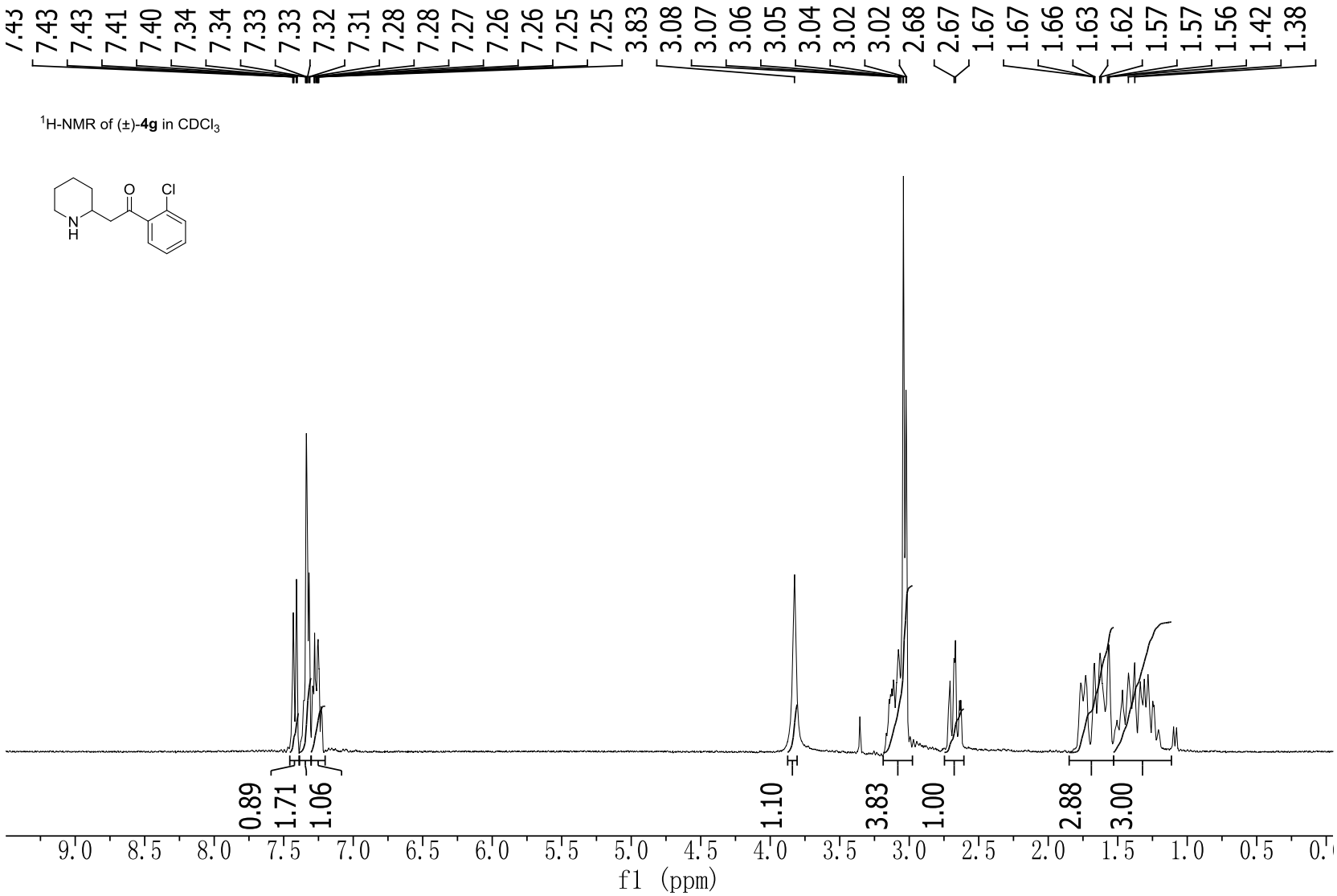

197.80
166.62
164.93
133.50
133.48
130.71
130.65
115.75
115.60
77.37
77.16
76.95
52.82
46.84
45.52
32.69
25.95
24.68
13C-NMR of (±)-4e in CDCl3
O
N
H
F
f1 (ppm)



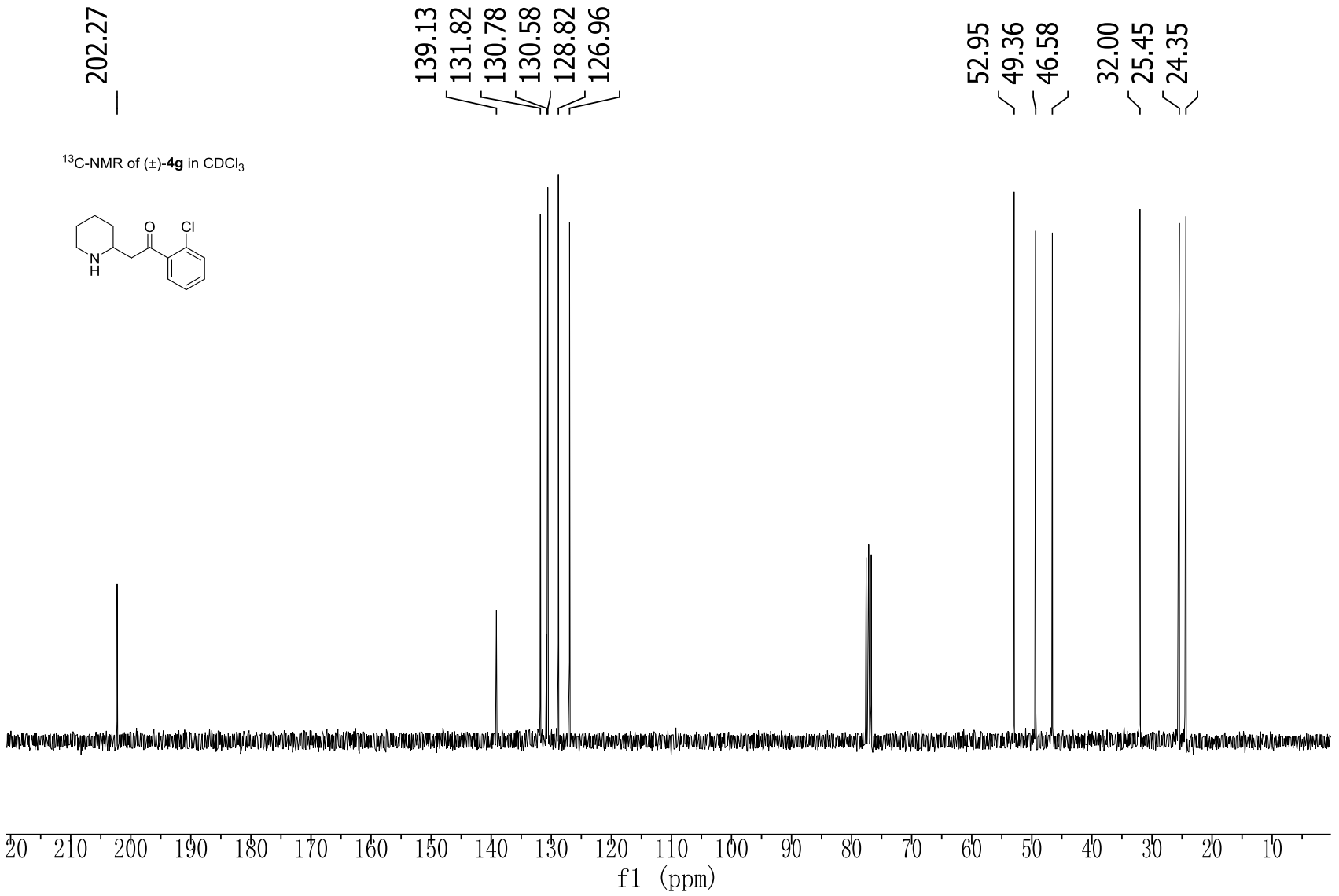
^{1}H-NMR of (±)-**4f** in $CDCl_3$

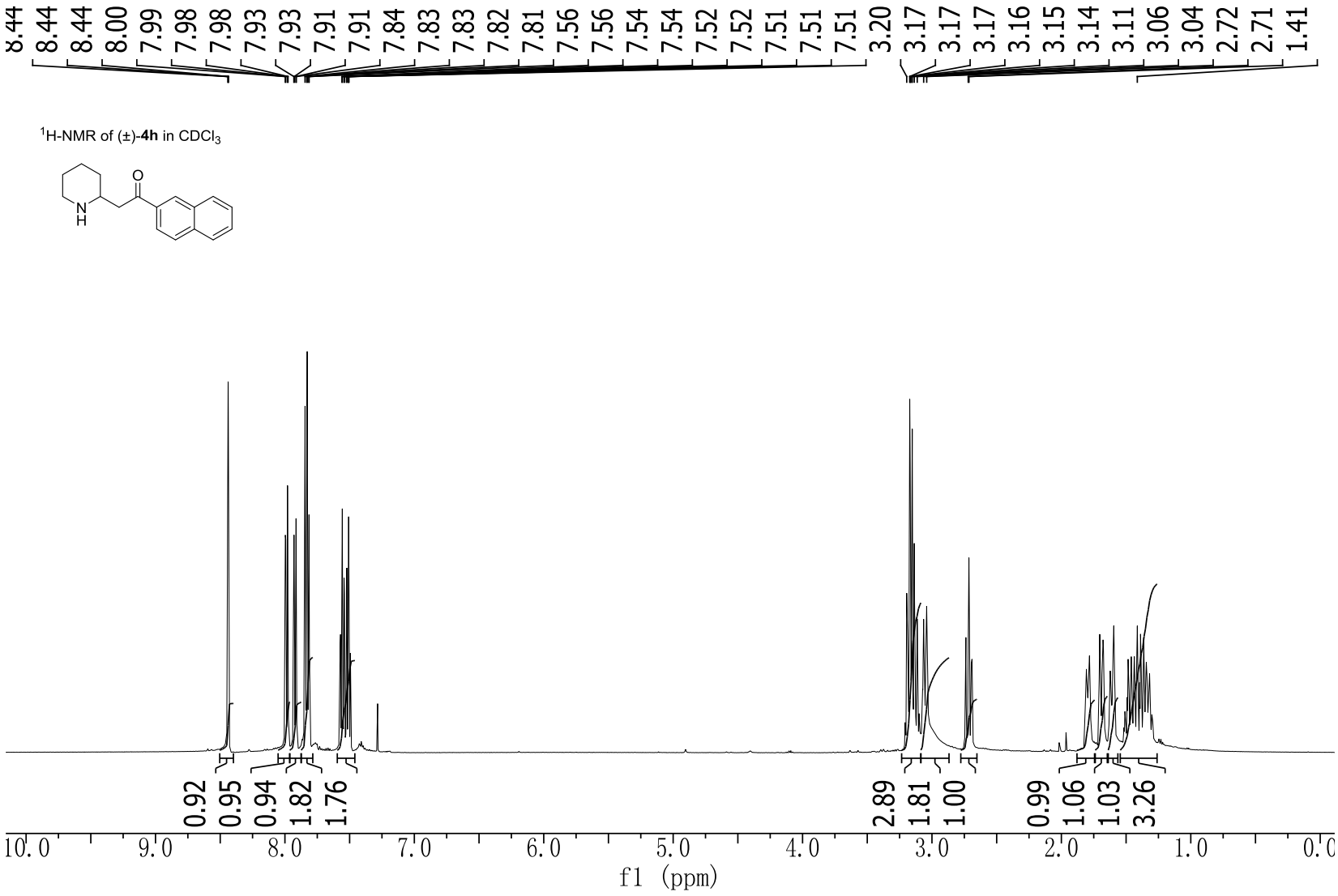


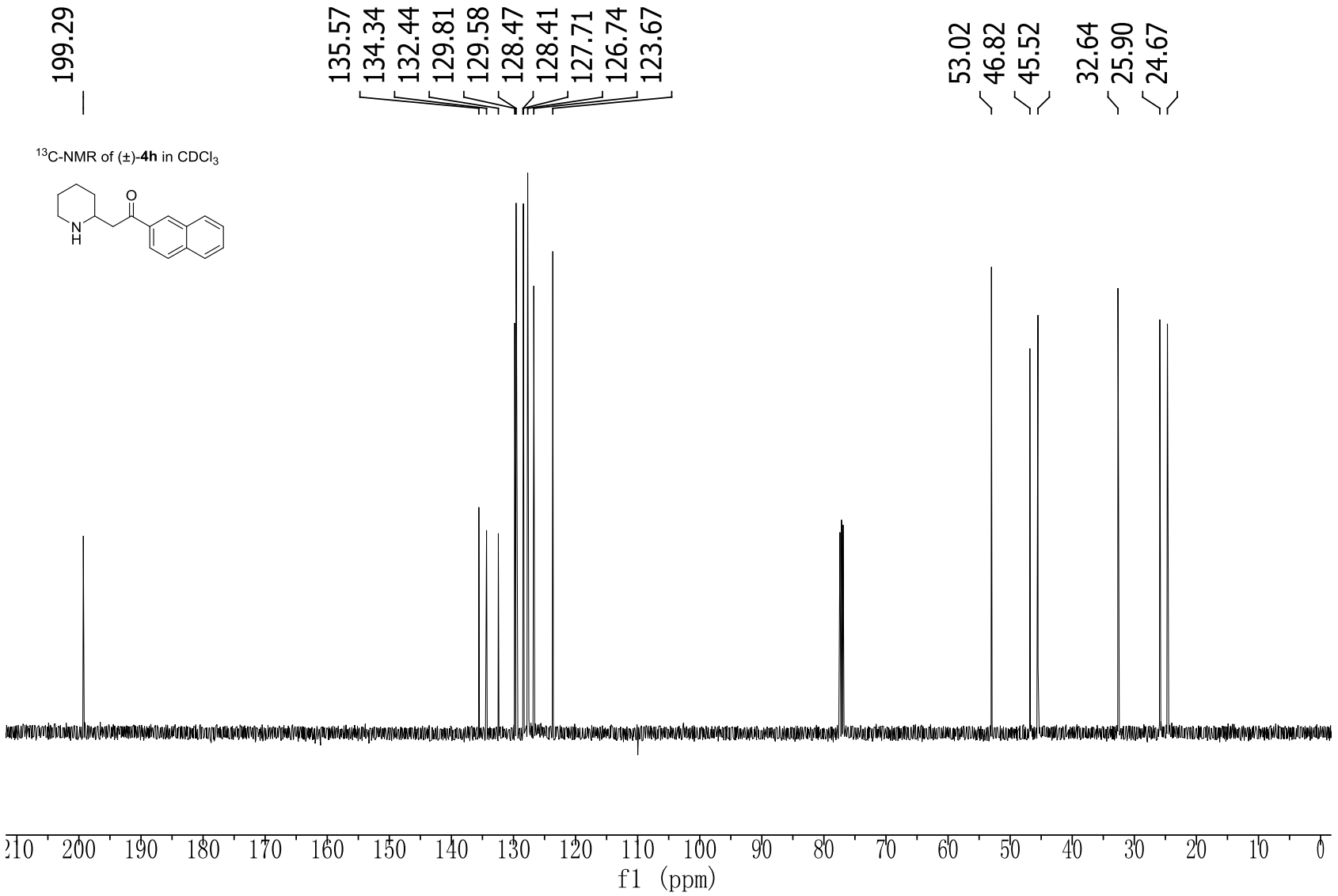
^{13}C-NMR of (±)-**4f** in $CDCl_3$

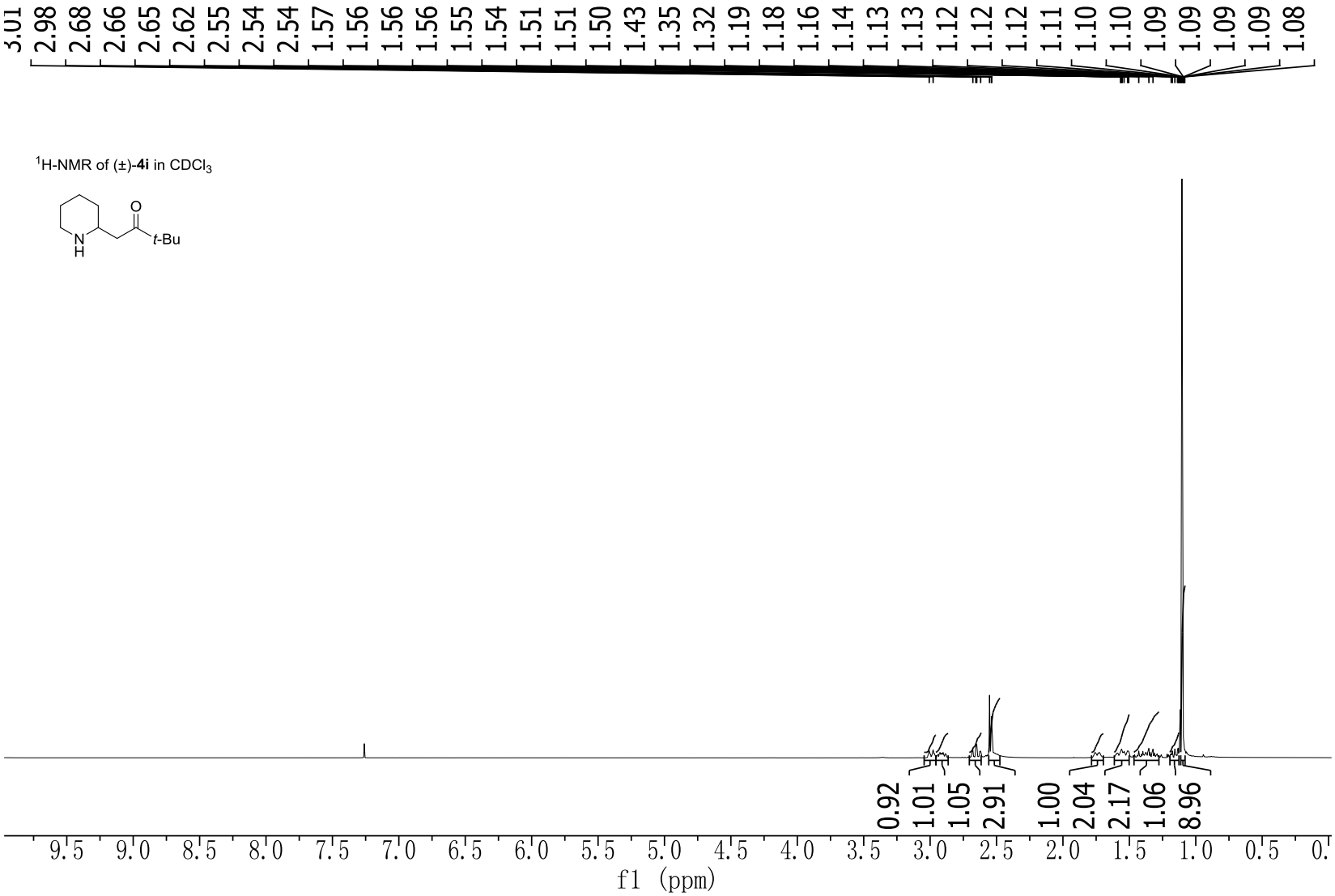


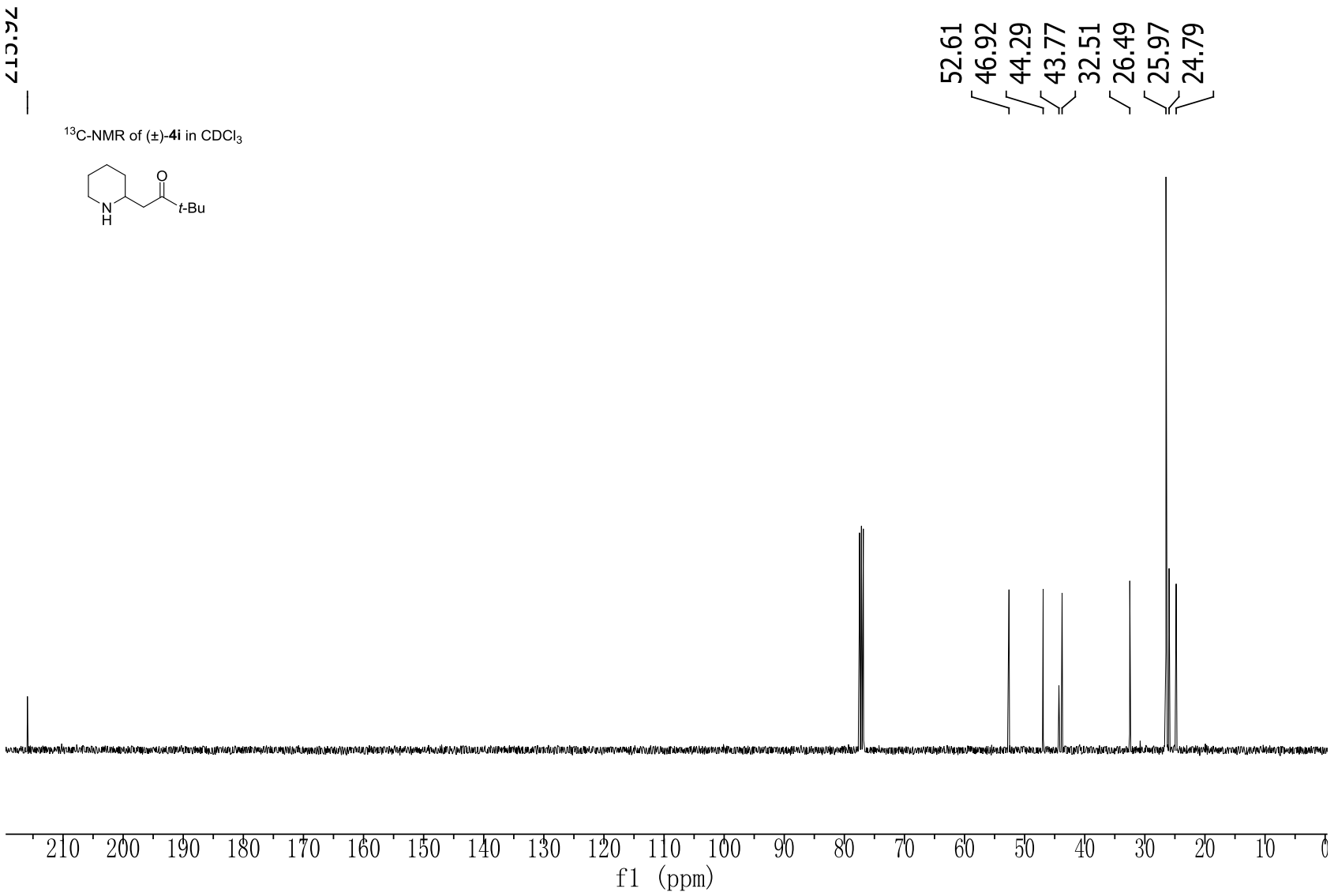
^{1}H-NMR of (±)-**4g** in $CDCl_3$

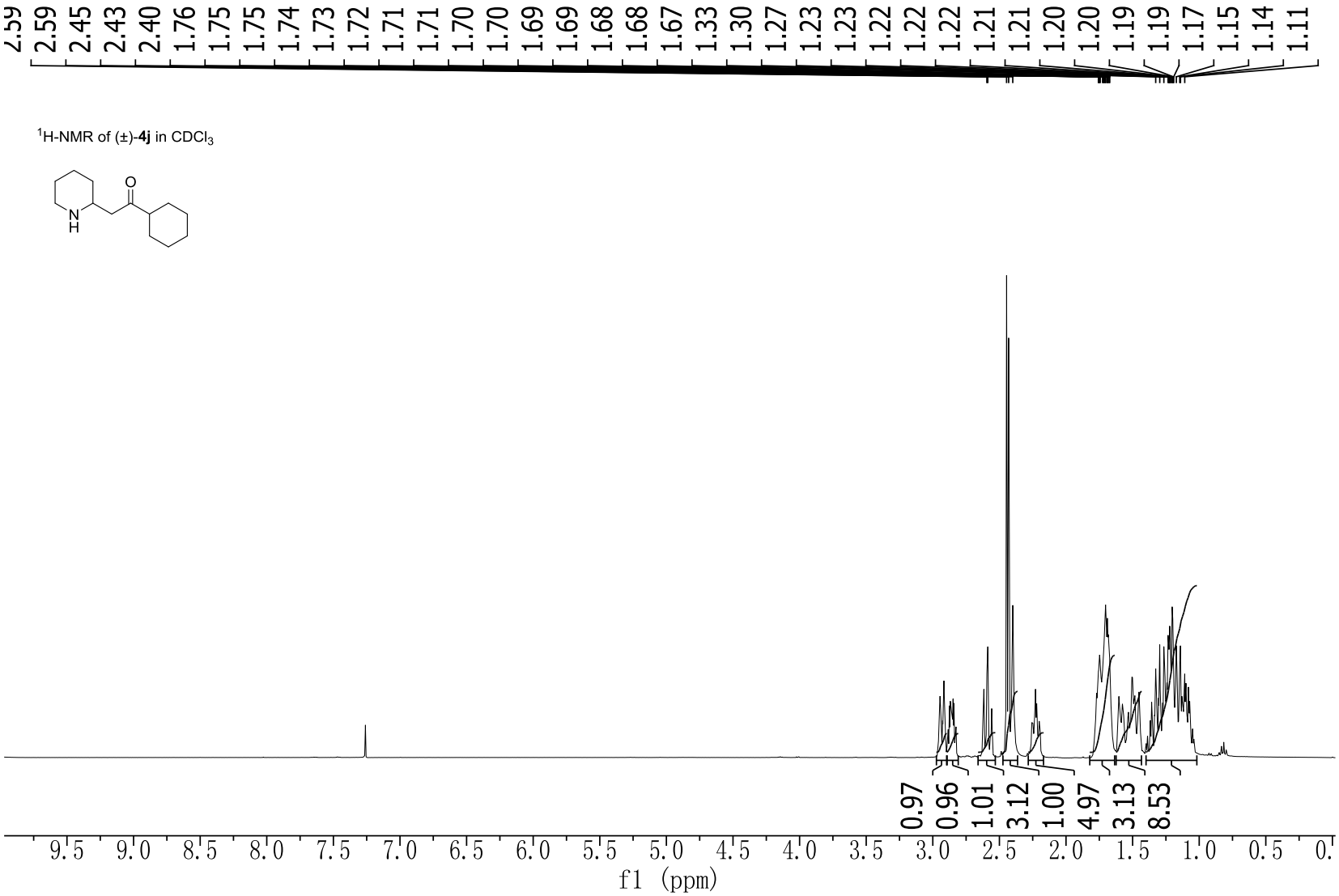

202.27
139.13
131.82
130.78
130.58
128.82
126.96
52.95
49.36
46.58
32.00
25.45
24.35
13C-NMR of (±)-4g in CDCl3
O
Cl
N
H
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

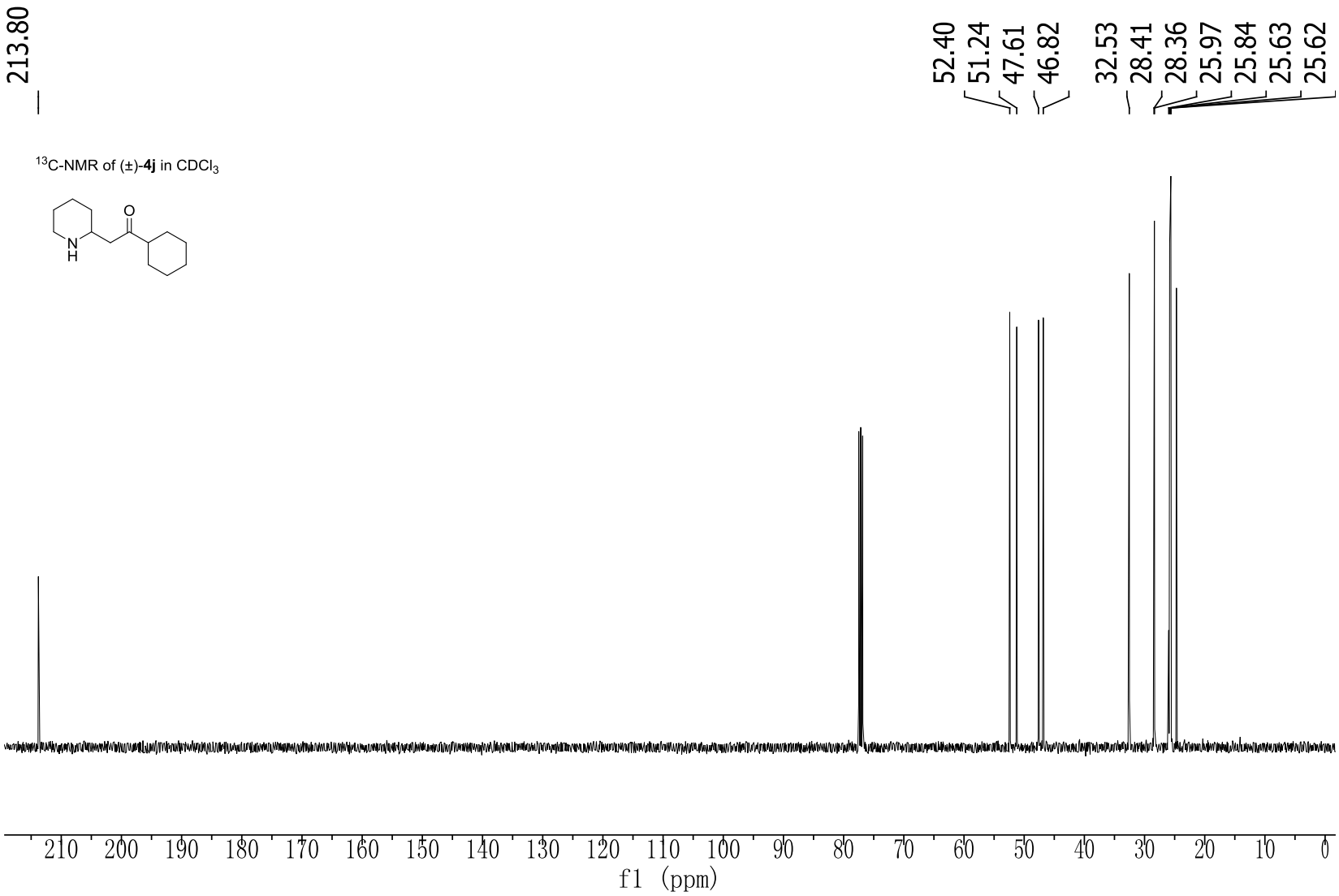

8.44
8.44
8.44
8.00
7.99
7.98
7.98
7.93
7.93
7.91
7.91
7.84
7.83
7.83
7.82
7.81
7.56
7.56
7.54
7.54
7.52
7.52
7.51
7.51
7.51
3.20
3.17
3.17
3.17
3.16
3.15
3.14
3.11
3.06
3.04
2.72
2.71
1.41
^{1}H-NMR of (±)-**4h** in $CDCl_3$
O
N
H
0.92
0.95
0.94
1.82
1.76
2.89
1.81
1.00
0.99
1.06
1.03
3.26
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

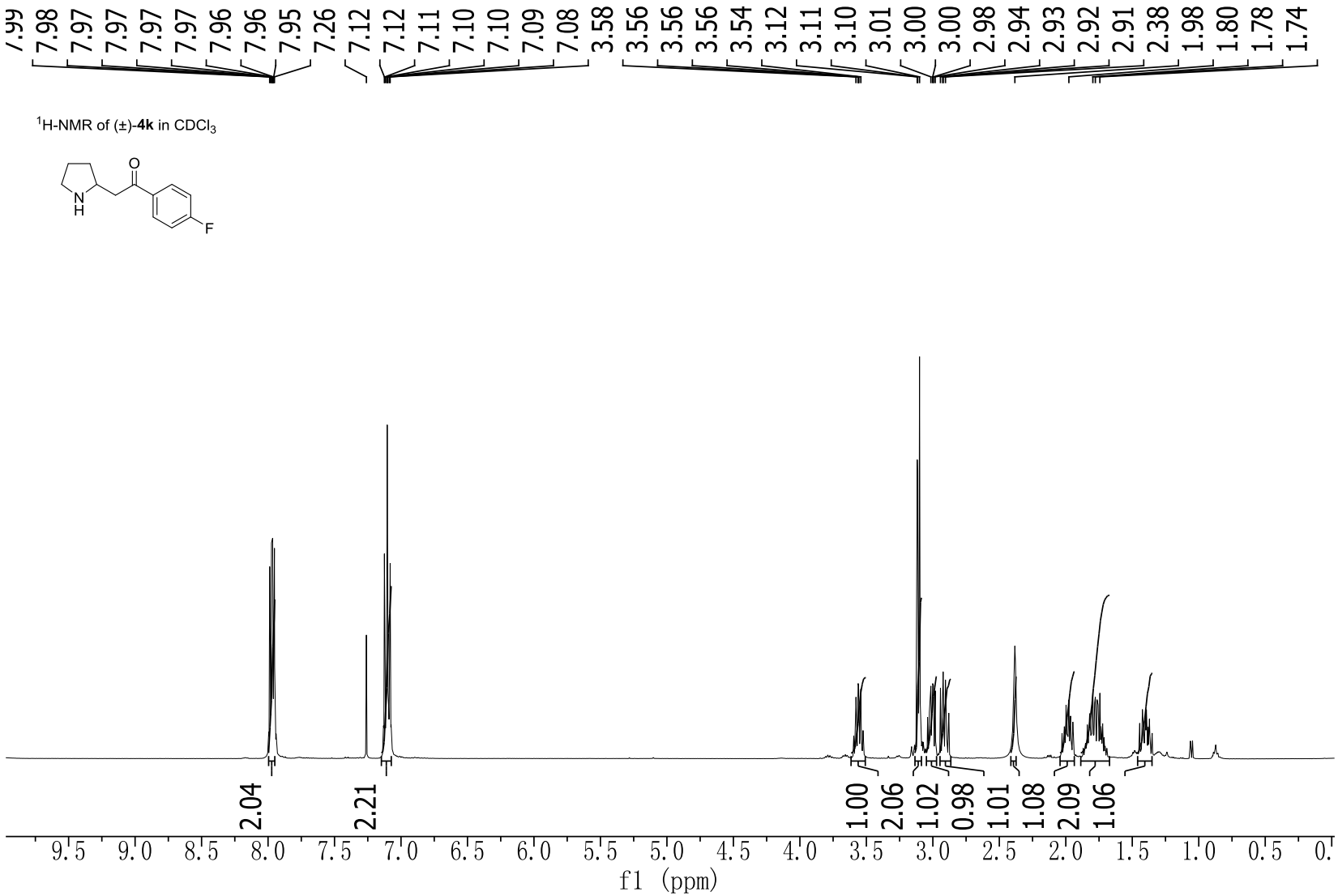

199.29
135.57
134.34
132.44
129.81
129.58
128.47
128.41
127.71
126.74
123.67
53.02
46.82
45.52
32.64
25.90
24.67
13C-NMR of (±)-4h in CDCl3
O
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


3.01
2.98
2.68
2.66
2.65
2.62
2.55
2.54
2.54
1.57
1.56
1.56
1.56
1.55
1.54
1.51
1.51
1.50
1.43
1.35
1.32
1.19
1.18
1.16
1.14
1.13
1.13
1.12
1.12
1.12
1.11
1.10
1.10
1.09
1.09
1.09
1.09
1.08
^{1}H-NMR of (±)-**4i** in $CDCl_3$
O
N
H
t-Bu
0.92
1.01
1.05
2.91
1.00
2.04
2.17
1.06
8.96
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.
f1 (ppm)


77.17
52.61
46.92
44.29
43.77
32.51
26.49
25.97
24.79
^{13}C-NMR of (±)-**4i** in $CDCl_3$
O
N
H
t-Bu
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


2.59
2.59
2.45
2.43
2.40
1.76
1.75
1.75
1.74
1.73
1.72
1.71
1.71
1.70
1.70
1.69
1.69
1.68
1.68
1.67
1.33
1.30
1.27
1.23
1.23
1.22
1.22
1.22
1.21
1.21
1.20
1.20
1.19
1.19
1.17
1.15
1.14
1.11
^{1}H-NMR of (±)-**4j** in $CDCl_3$
O
N
H
0.97
0.96
1.01
3.12
1.00
4.97
3.13
8.53
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.
f1 (ppm)

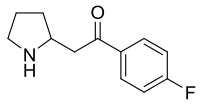

213.80
52.40
51.24
47.61
46.82
32.53
28.41
28.36
25.97
25.84
25.63
25.62
13C-NMR of (±)-4j in CDCl3
O
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

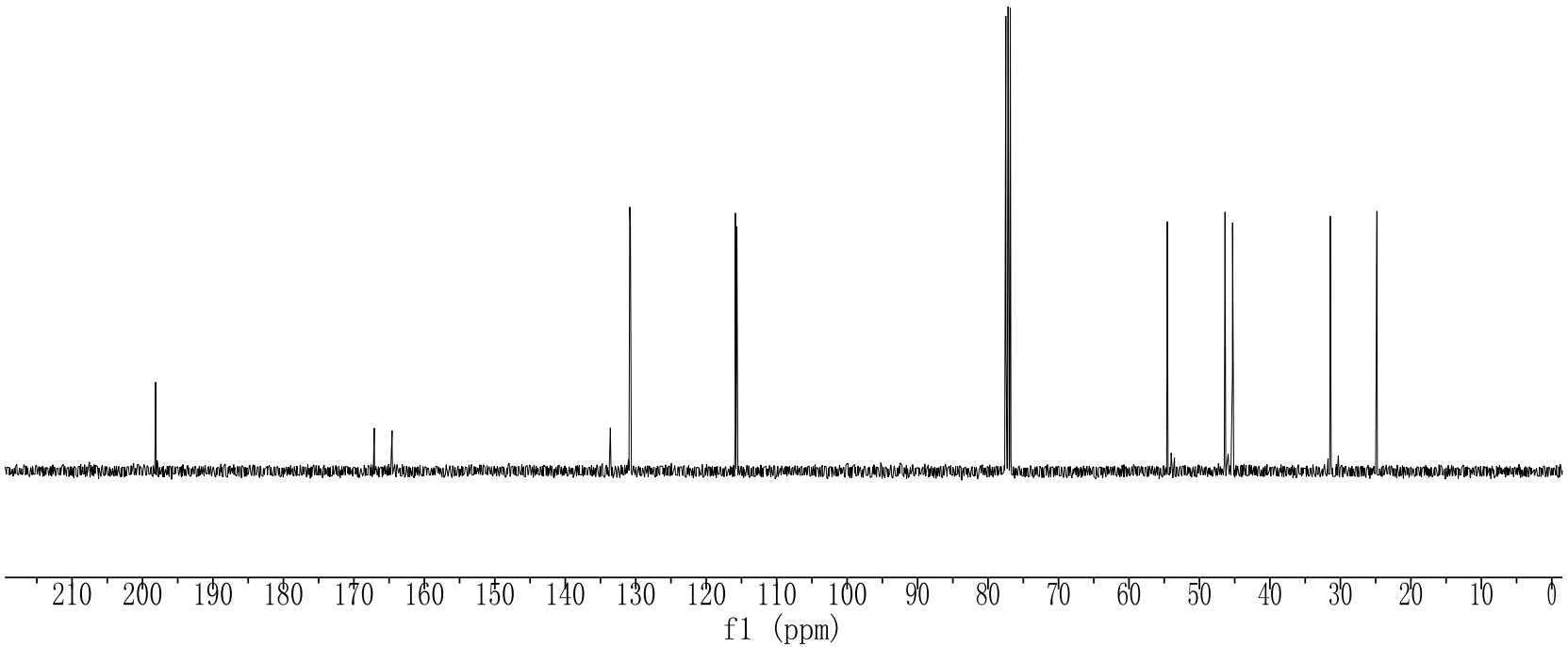


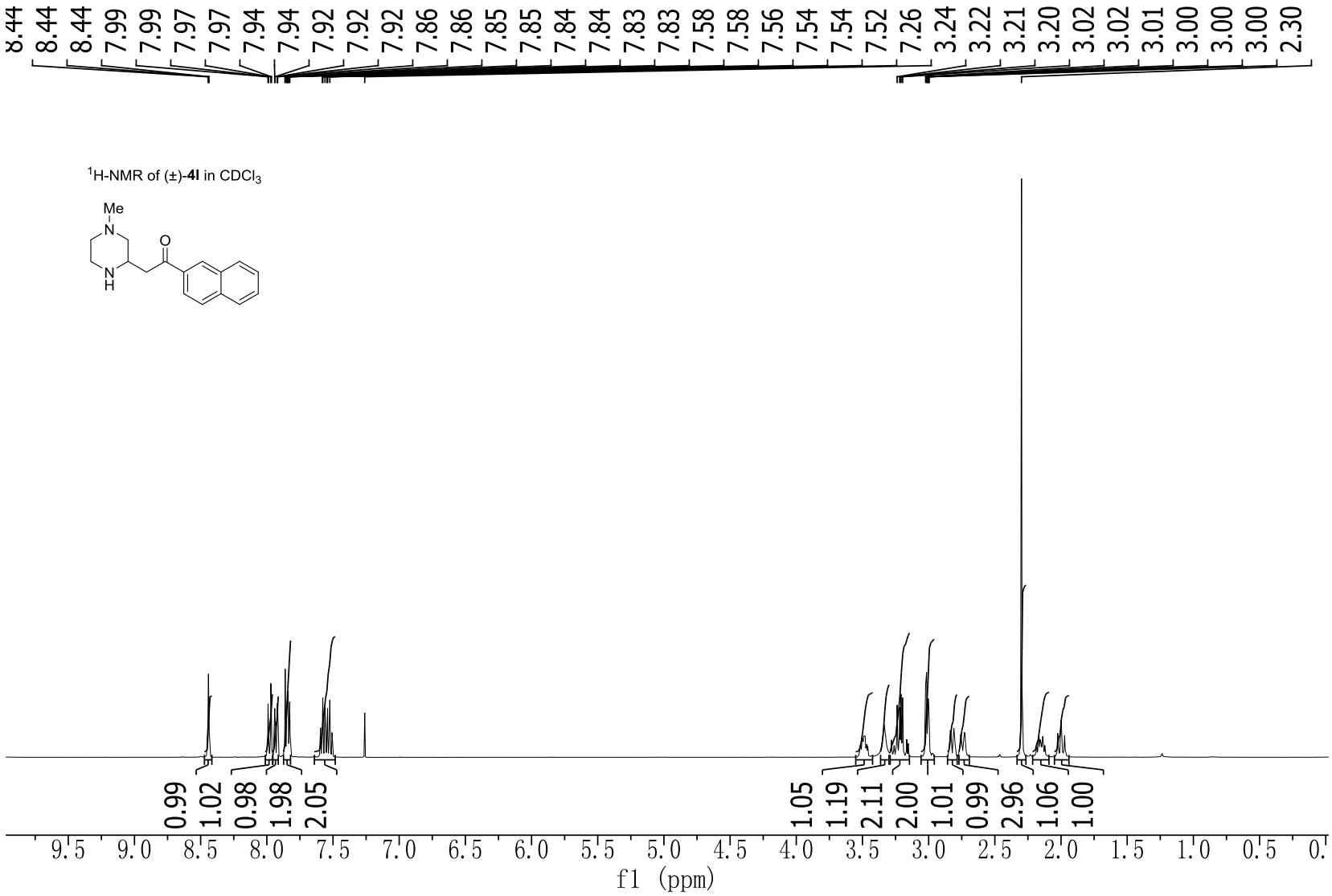
^{1}H-NMR of (±)-**4k** in $CDCl_3$

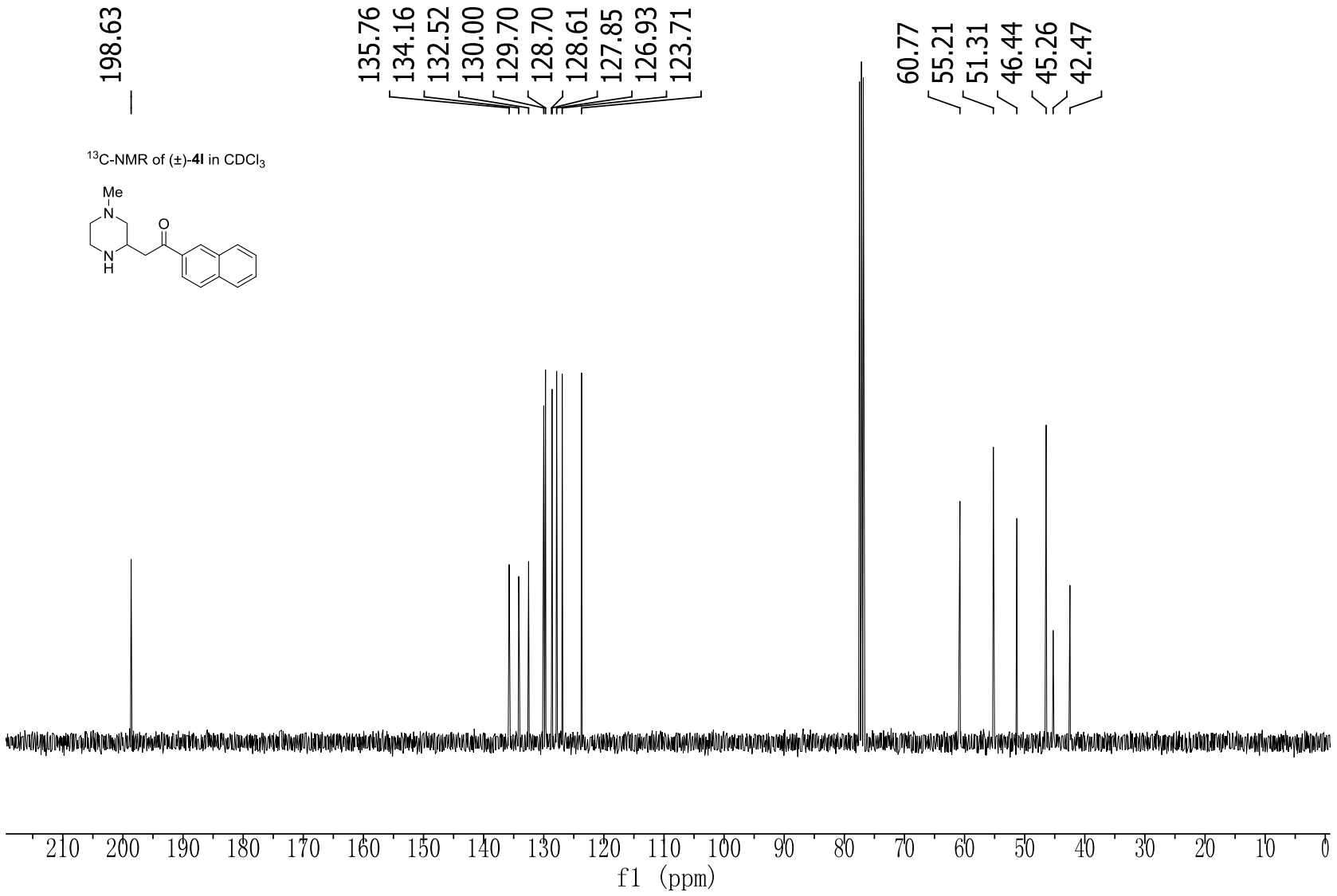
198.14
167.10
164.57
133.63
133.60
130.85
130.76
115.87
115.65
54.56
46.37
45.31
31.43
24.82

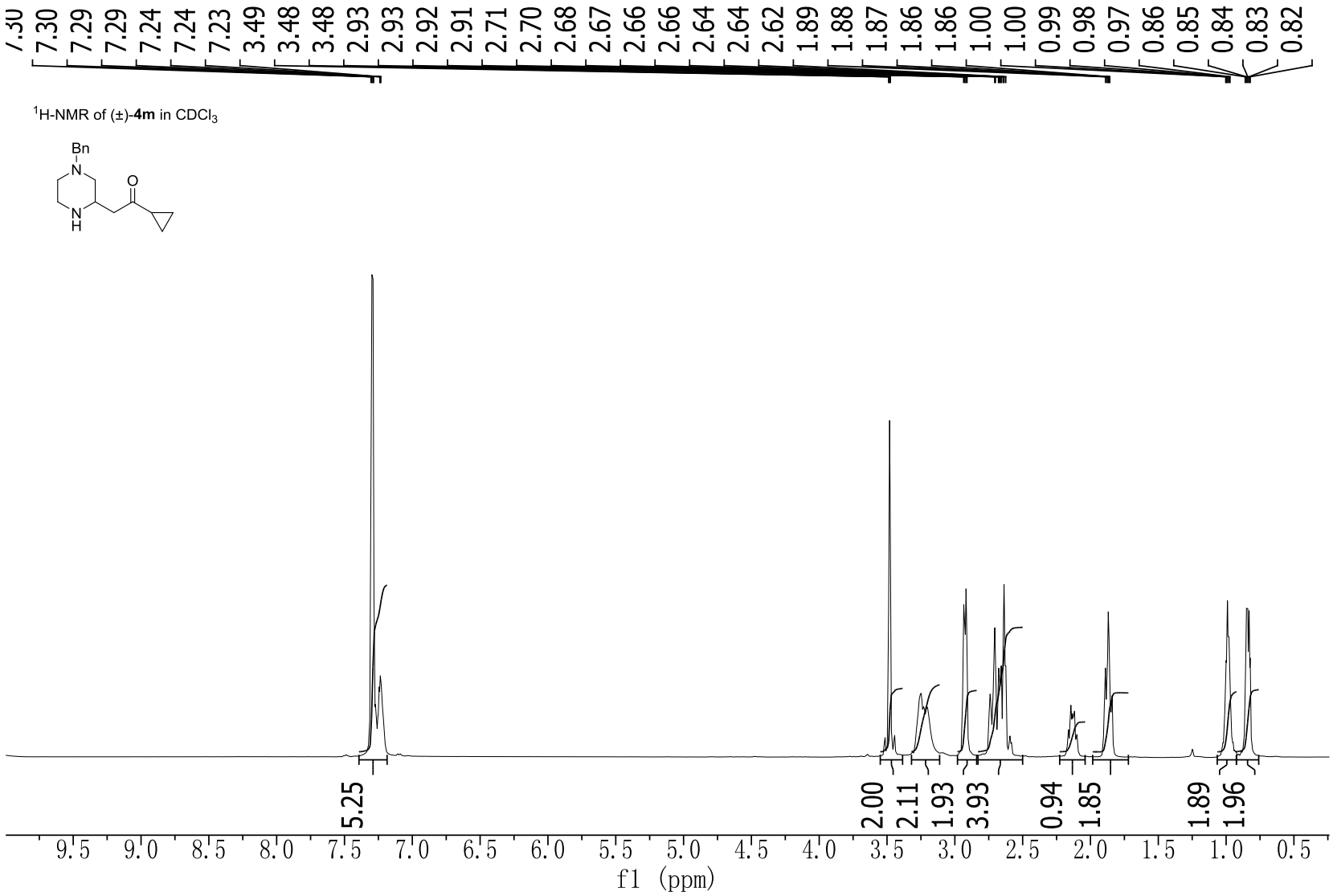
^{13}C-NMR of (±)-**4k** in $CDCl_3$



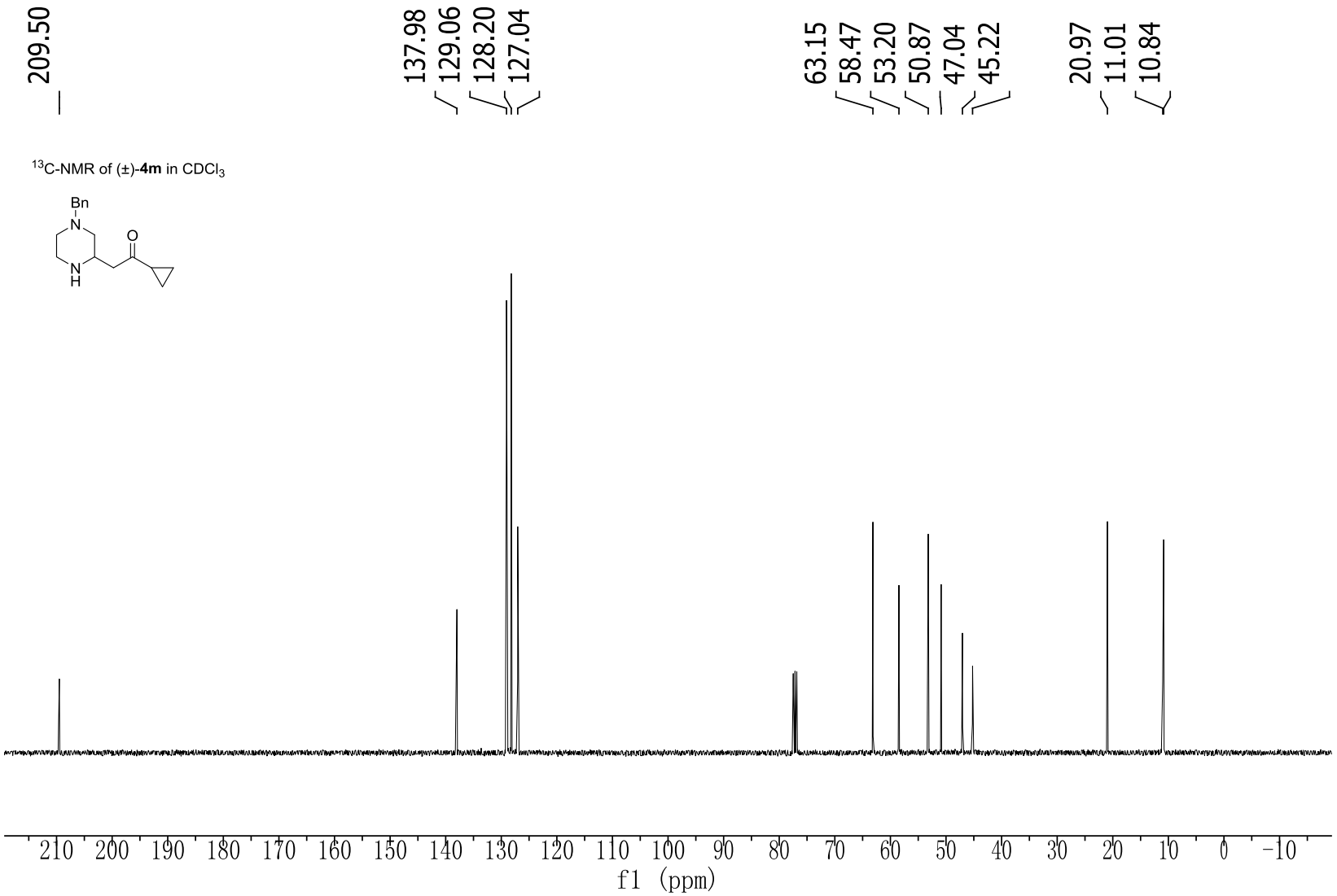


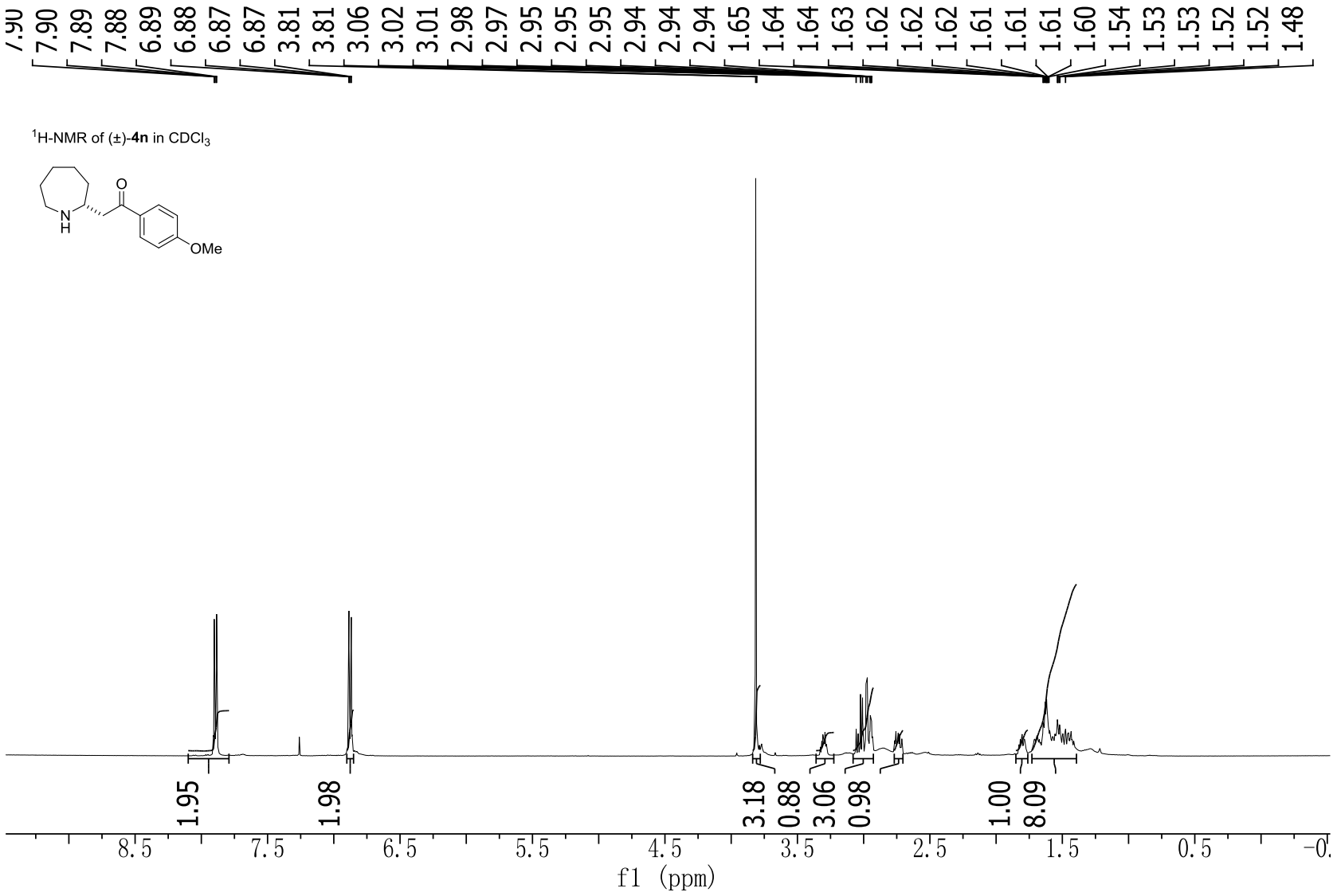

8.44 8.44 8.44 7.99 7.99 7.97 7.97 7.94 7.94 7.92 7.92 7.92 7.86 7.86 7.85 7.85 7.84 7.84 7.83 7.83 7.58 7.58 7.56 7.54 7.54 7.52 7.26 3.24 3.22 3.21 3.20 3.02 3.02 3.01 3.00 3.00 3.00 2.30
1H-NMR of (±)-4l in CDCl3
Me
N
O
N
H
0.99 1.02 0.98 1.98 2.05 1.05 1.19 2.11 2.00 1.01 0.99 2.96 1.06 1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

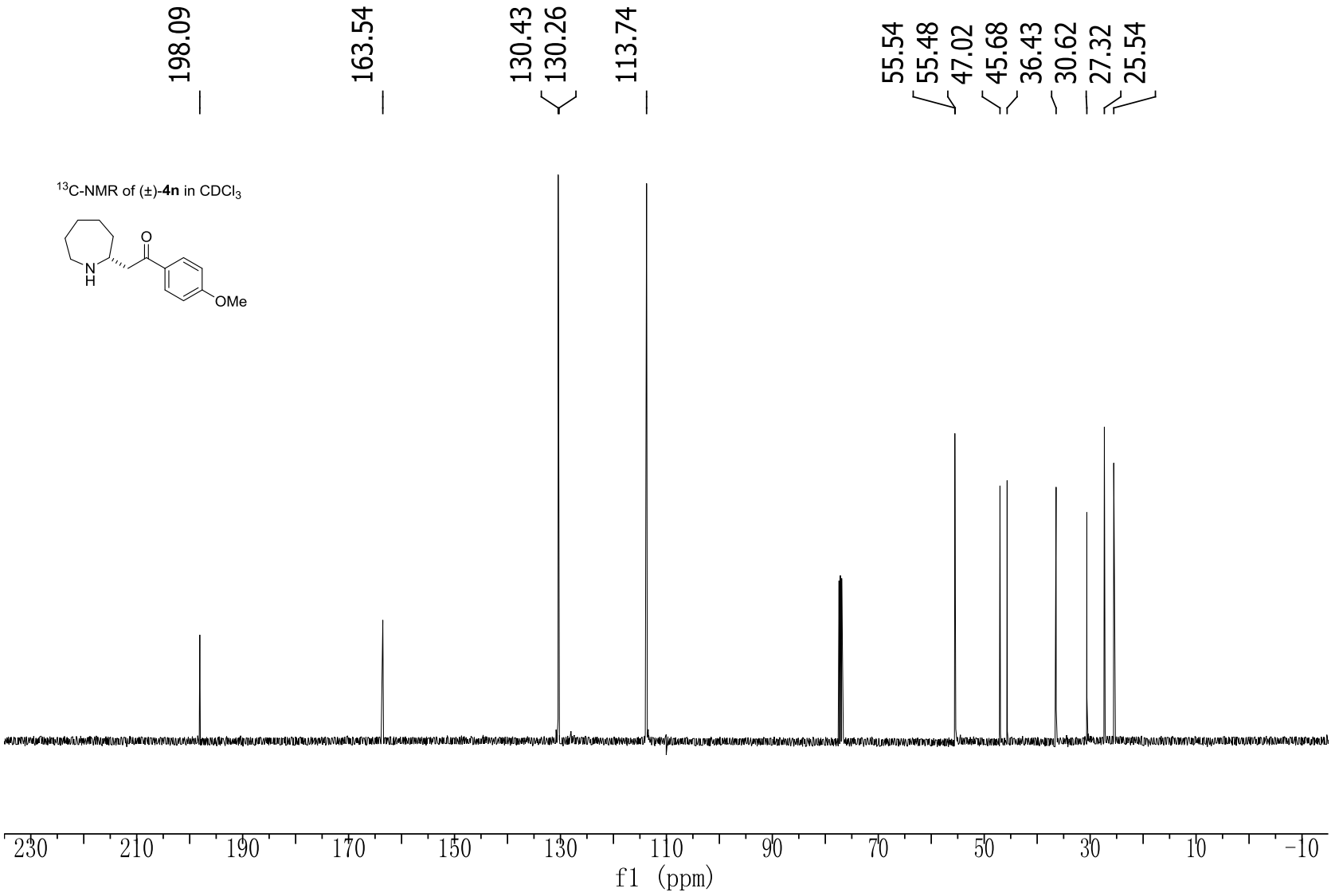

198.63
135.76
134.16
132.52
130.00
129.70
128.70
128.61
127.85
126.93
123.71
60.77
55.21
51.31
46.44
45.26
42.47
13C-NMR of (±)-4l in CDCl3
Me
N
O
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

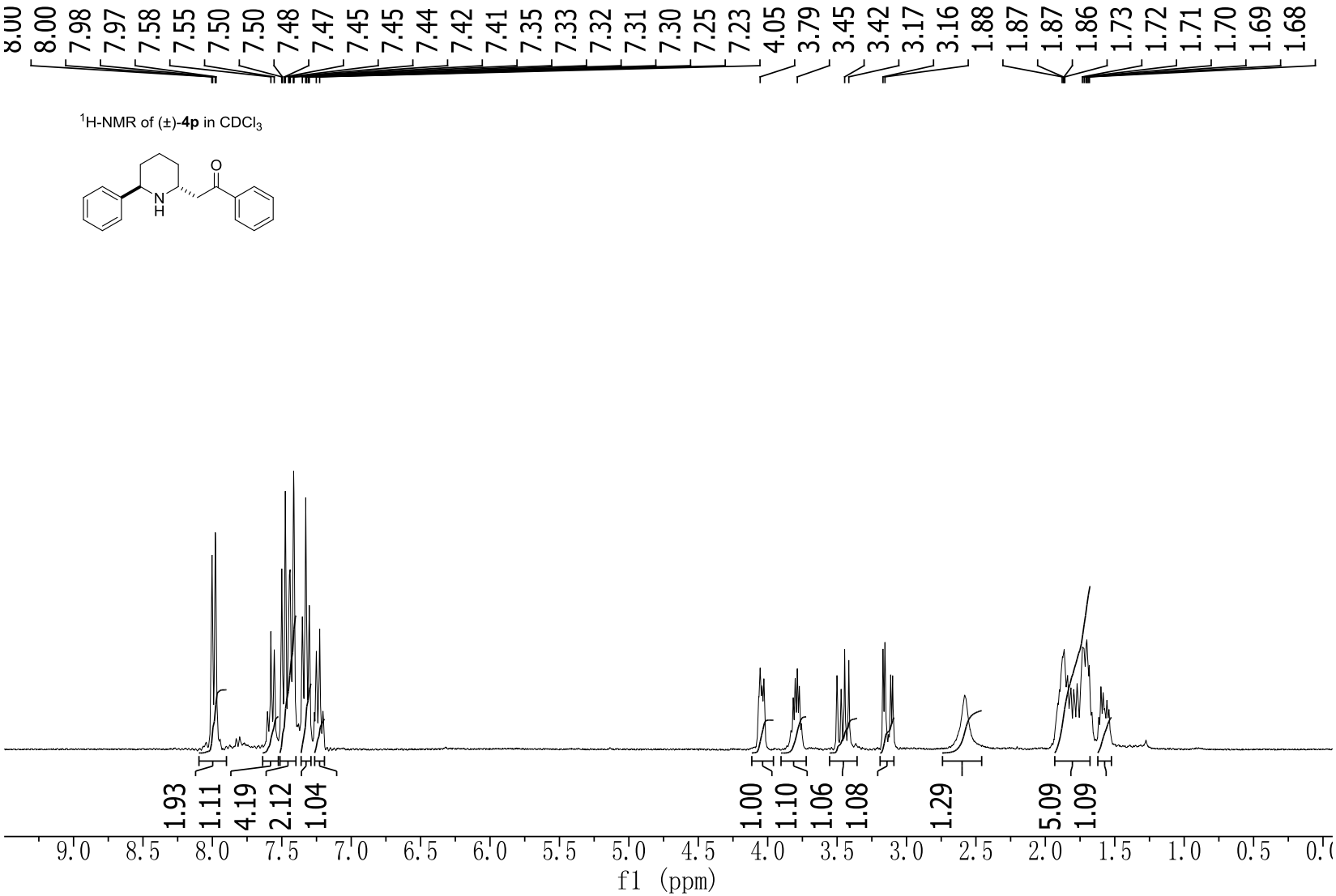


^{1}H-NMR of (±)-**4m** in $CDCl_3$

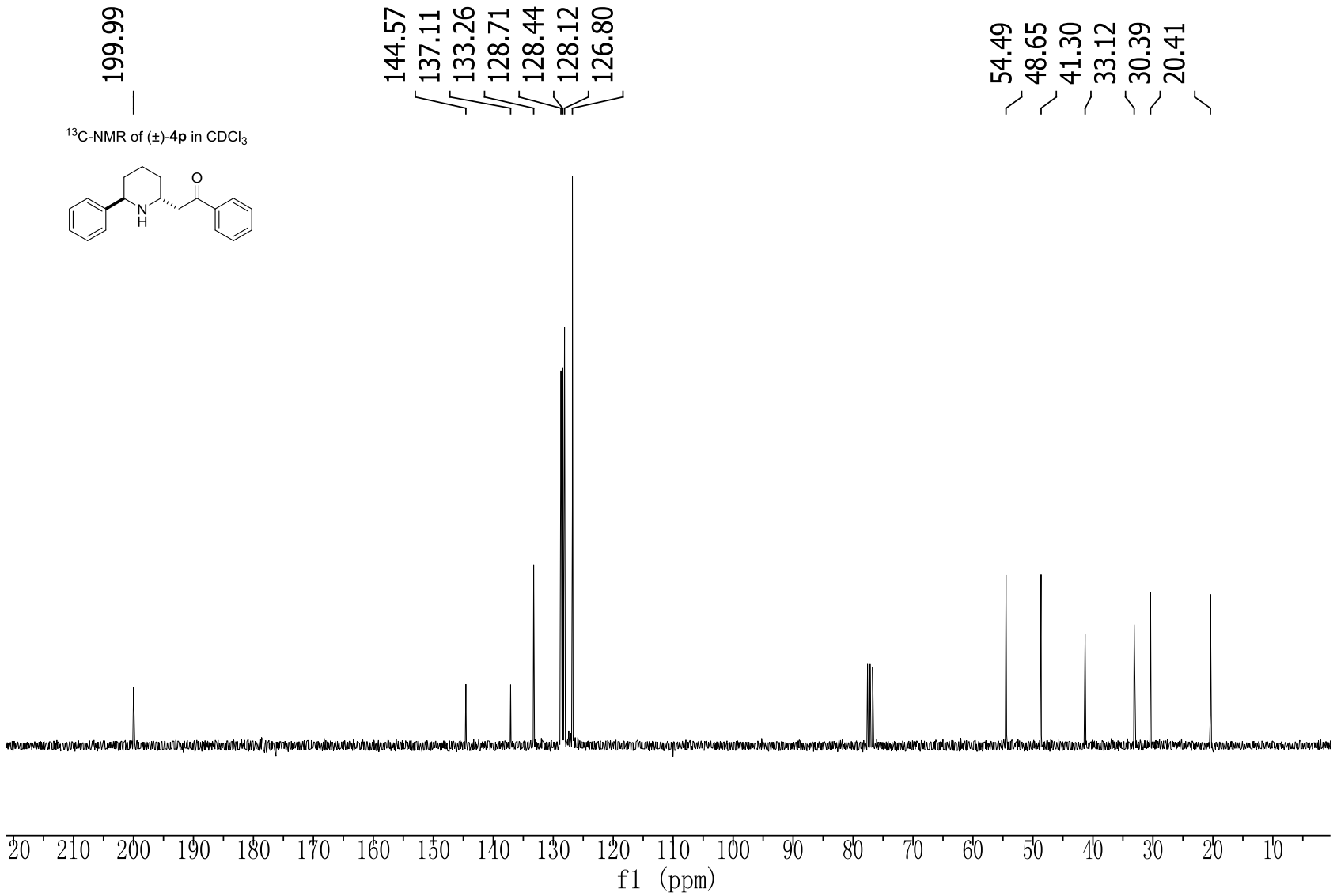

209.50
137.98
129.06
128.20
127.04
63.15
58.47
53.20
50.87
47.04
45.22
20.97
11.01
10.84
^{13}C-NMR of (±)-**4m** in $CDCl_3$
Bn
N
O
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

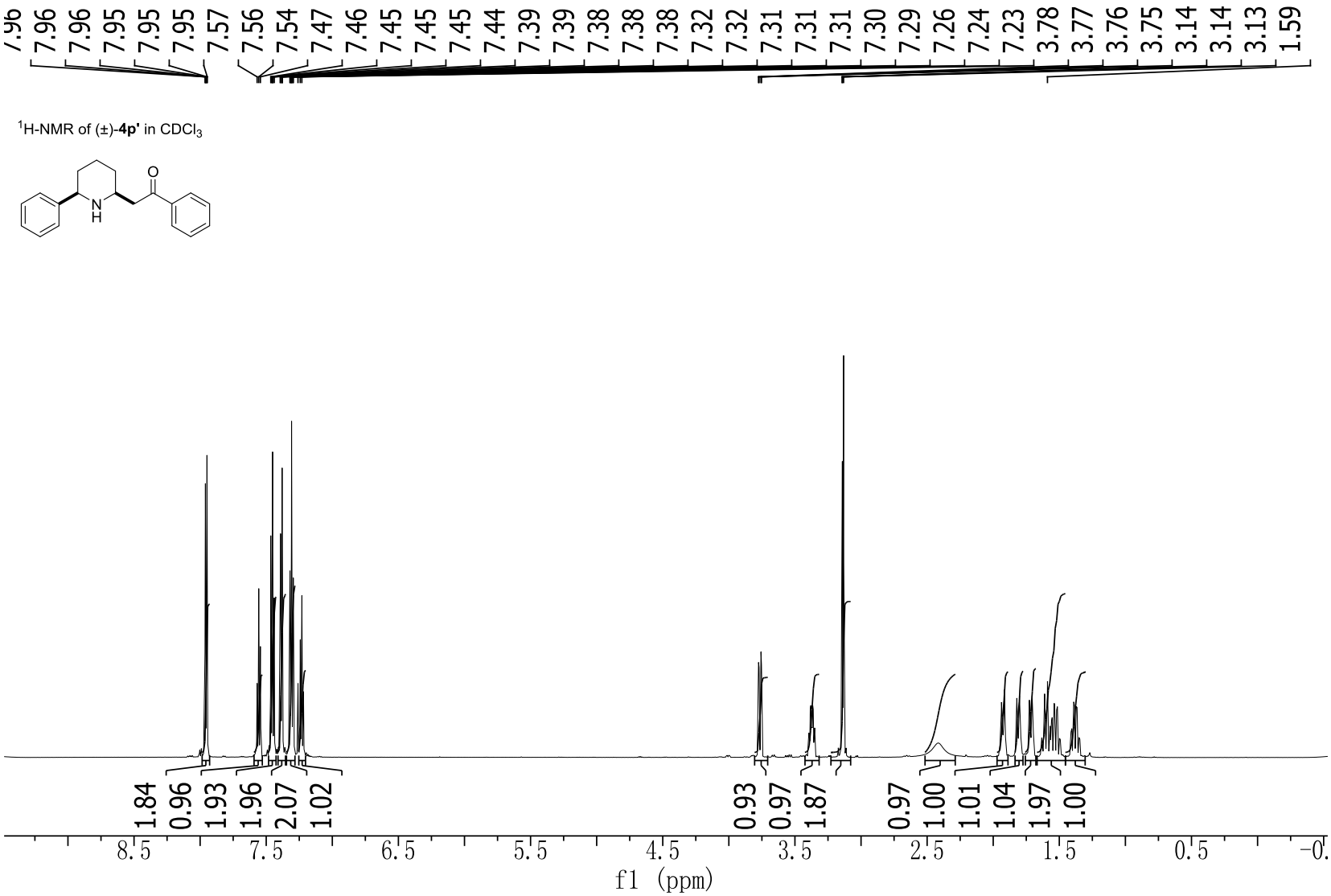

7.90
7.89
7.88
6.89
6.88
6.87
6.87
3.81
3.81
3.06
3.02
3.01
2.98
2.97
2.95
2.95
2.95
2.94
2.94
2.94
1.65
1.64
1.64
1.63
1.62
1.62
1.62
1.61
1.61
1.61
1.60
1.54
1.53
1.53
1.52
1.52
1.48
1H-NMR of (±)-4n in CDCl3
O
N
H
OMe
1.95
1.98
3.18
0.88
3.06
0.98
1.00
8.09
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

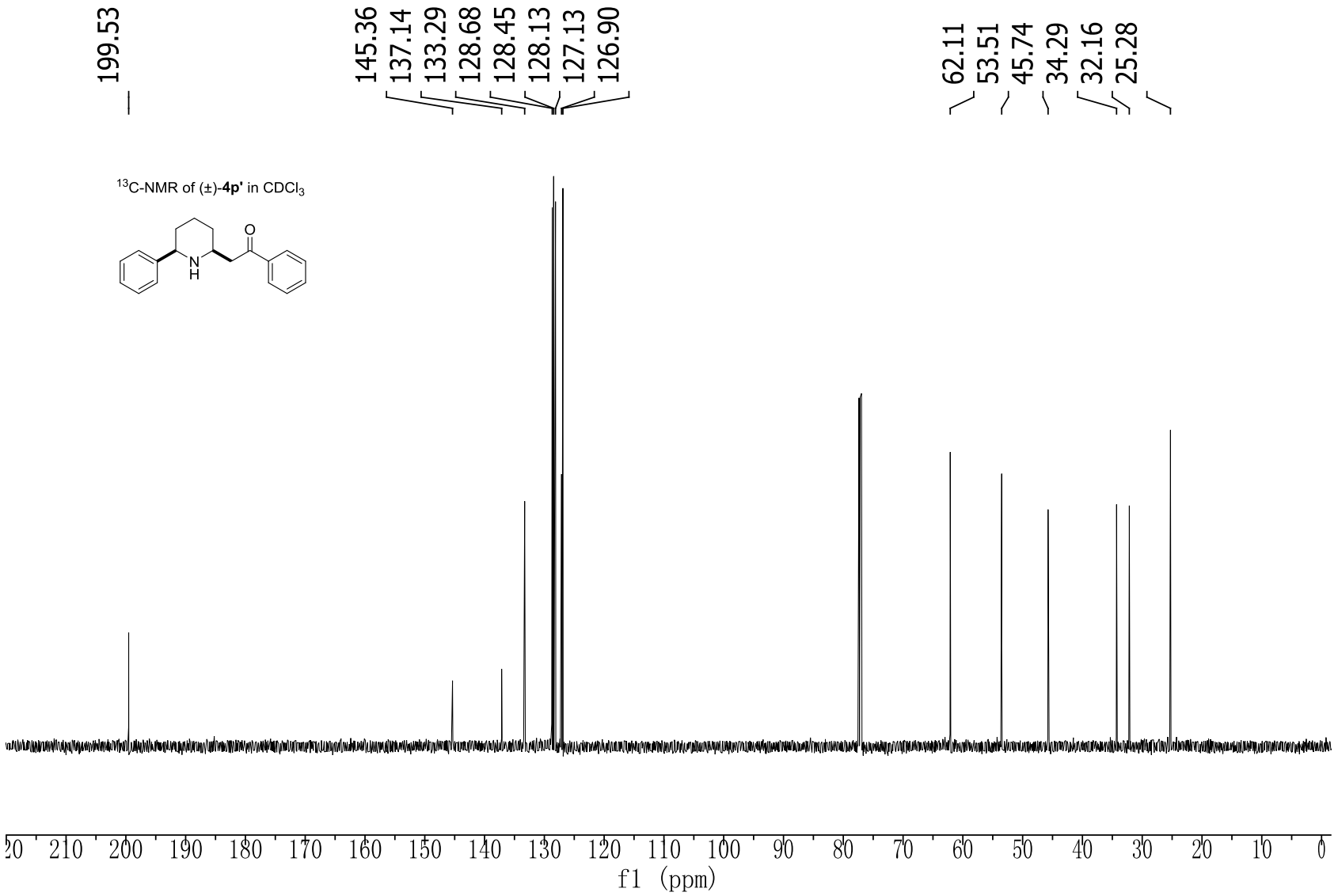

198.09
163.54
130.43
130.26
113.74
55.54
55.48
47.02
45.68
36.43
30.62
27.32
25.54
13C-NMR of (±)-4n in CDCl3
O
N
H
OMe
230
210
190
170
150
130
110
90
70
50
30
10
-10
f1 (ppm)

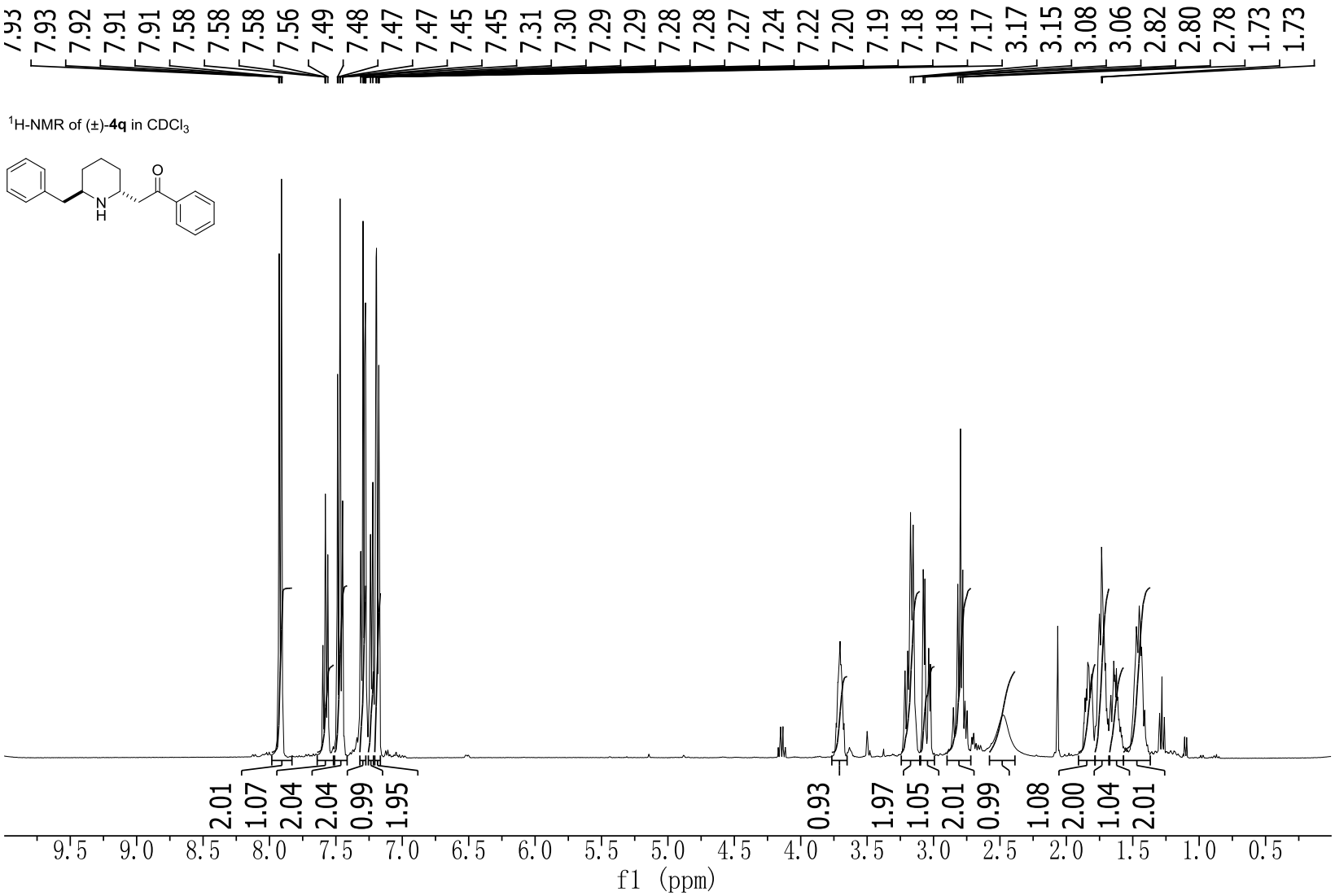


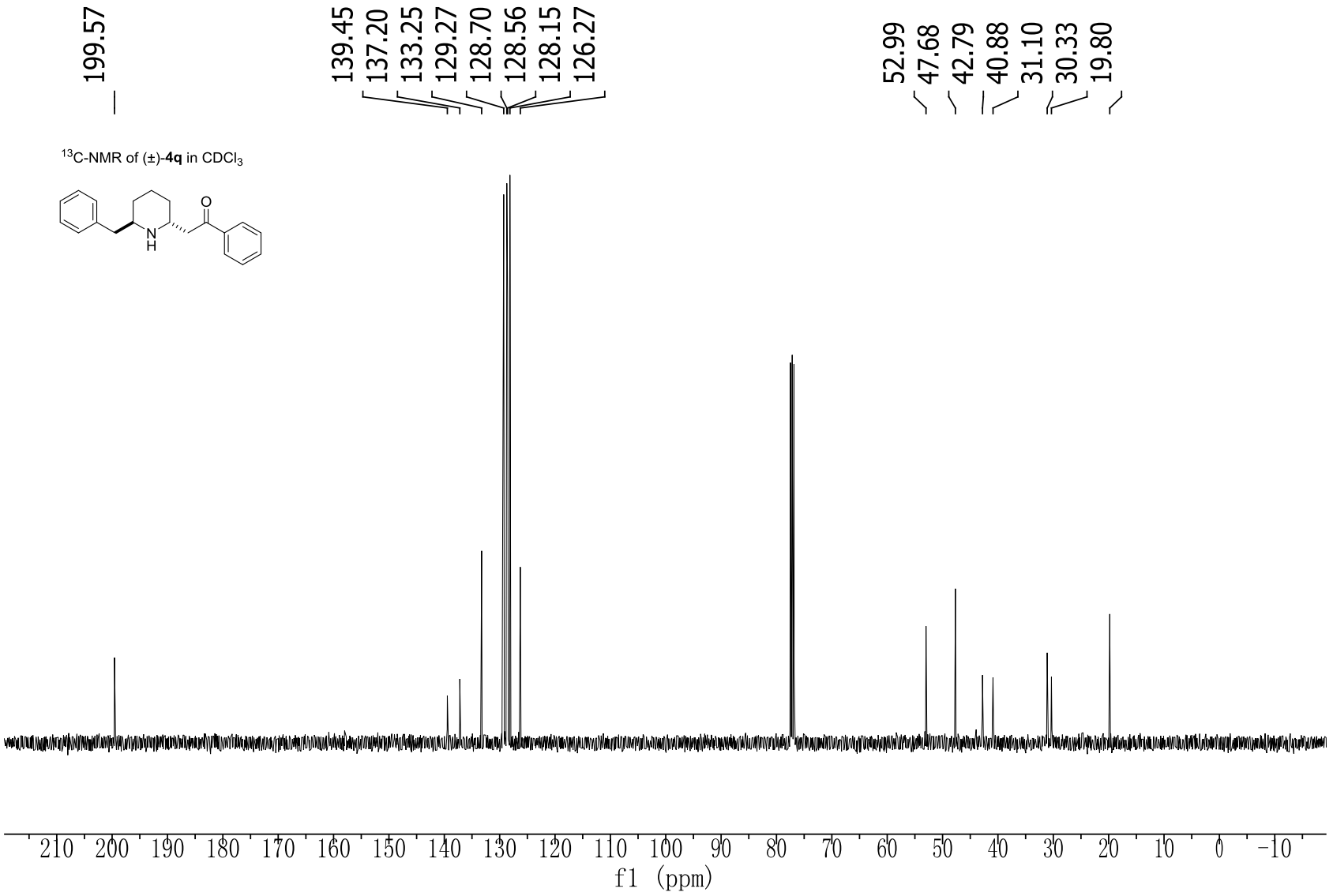
^{1}H-NMR of (±)-**4p** in $CDCl_3$

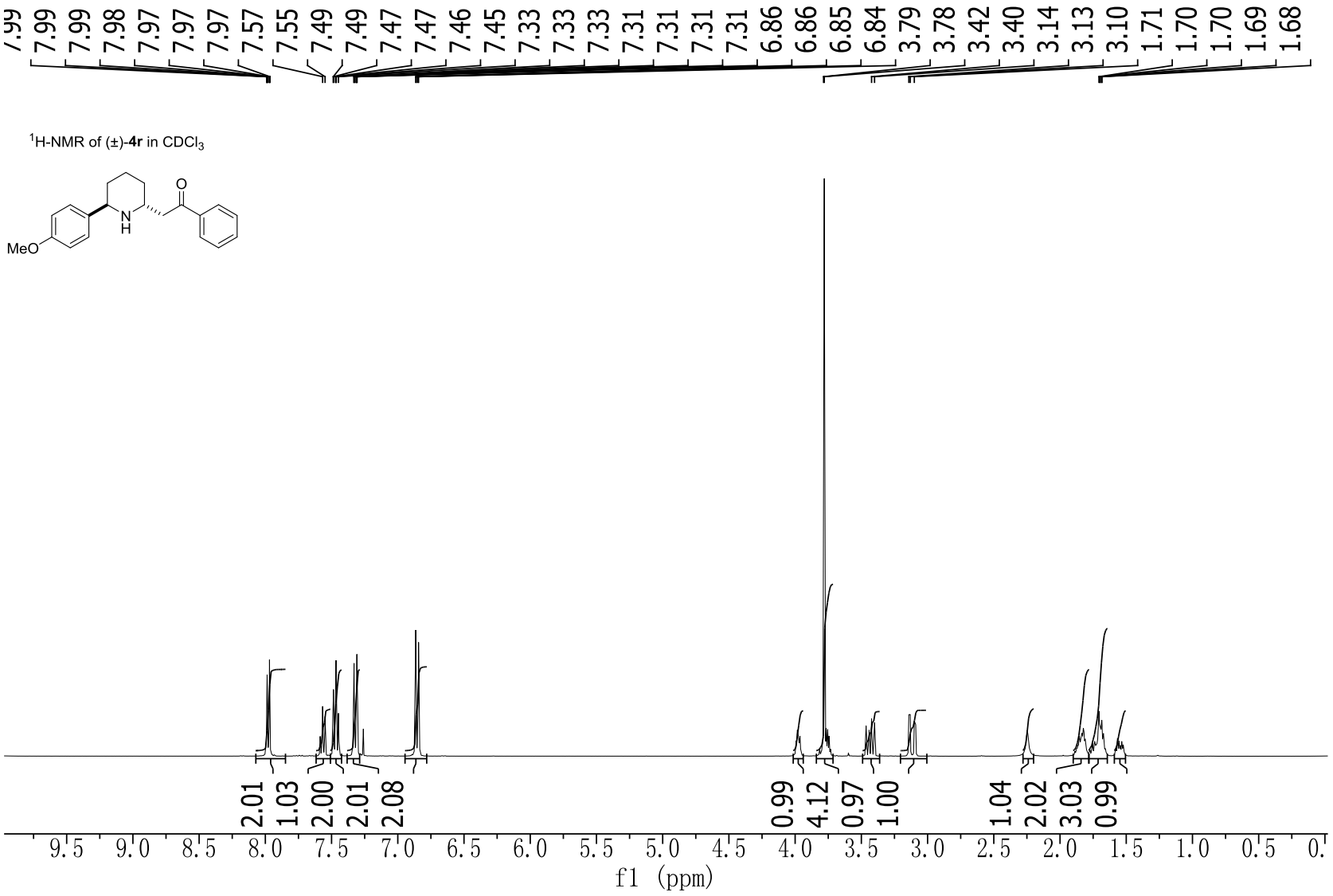

199.99
144.57
137.11
133.26
128.71
128.44
128.12
126.80
54.49
48.65
41.30
33.12
30.39
20.41
13C-NMR of (±)-4p in CDCl3
O
N
H
f1 (ppm)

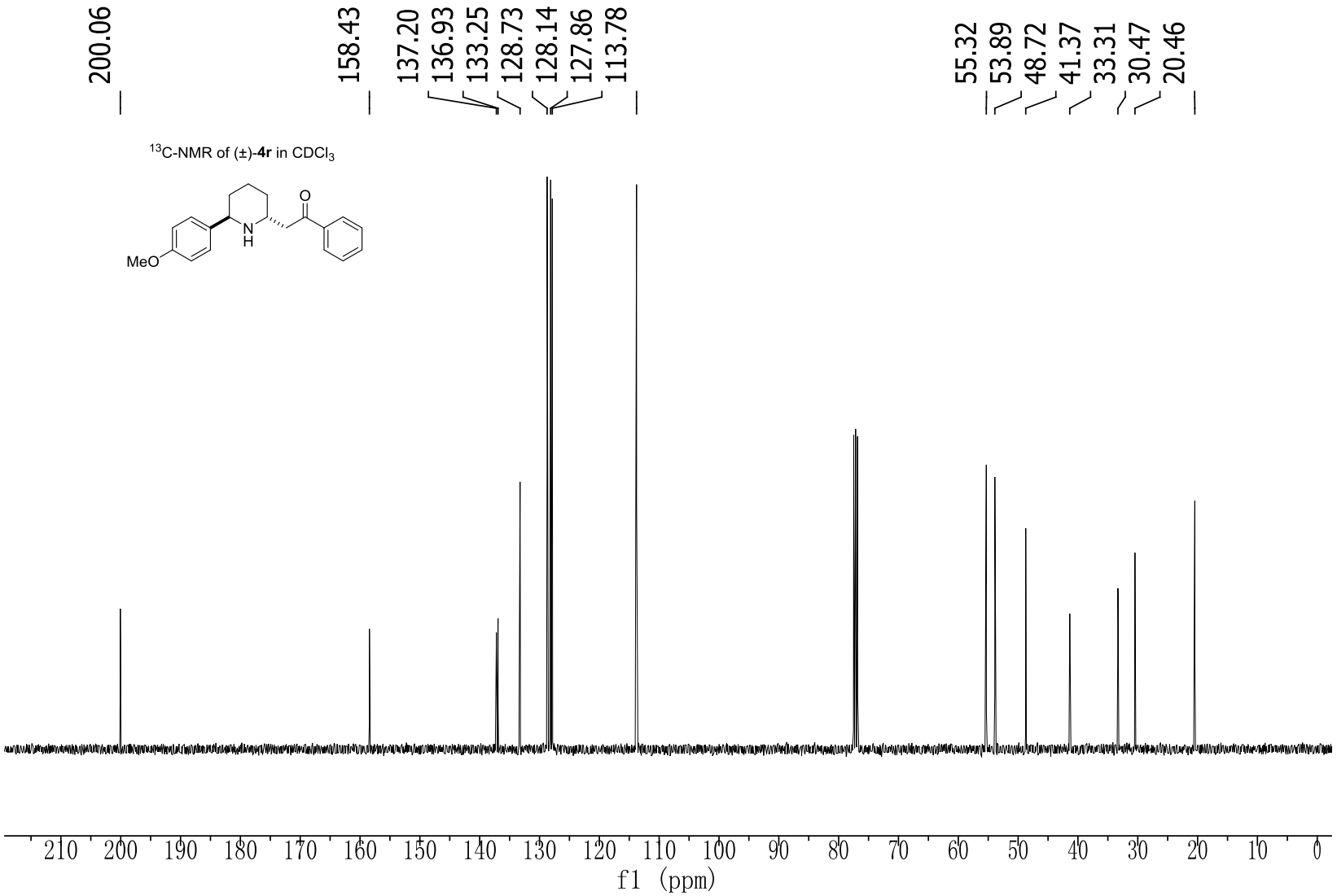

7.96 7.96 7.95 7.95 7.95 7.57 7.56 7.54 7.47 7.46 7.45 7.45 7.45 7.44 7.39 7.39 7.38 7.38 7.38 7.32 7.32 7.31 7.31 7.31 7.30 7.29 7.26 7.24 7.23 3.78 3.77 3.76 3.75 3.14 3.14 3.13 1.59
1H-NMR of (±)-4p' in CDCl3
O
N
H
1.84 0.96 1.93 1.96 2.07 1.02 0.93 0.97 1.87 0.97 1.00 1.01 1.04 1.97 1.00
8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.
f1 (ppm)

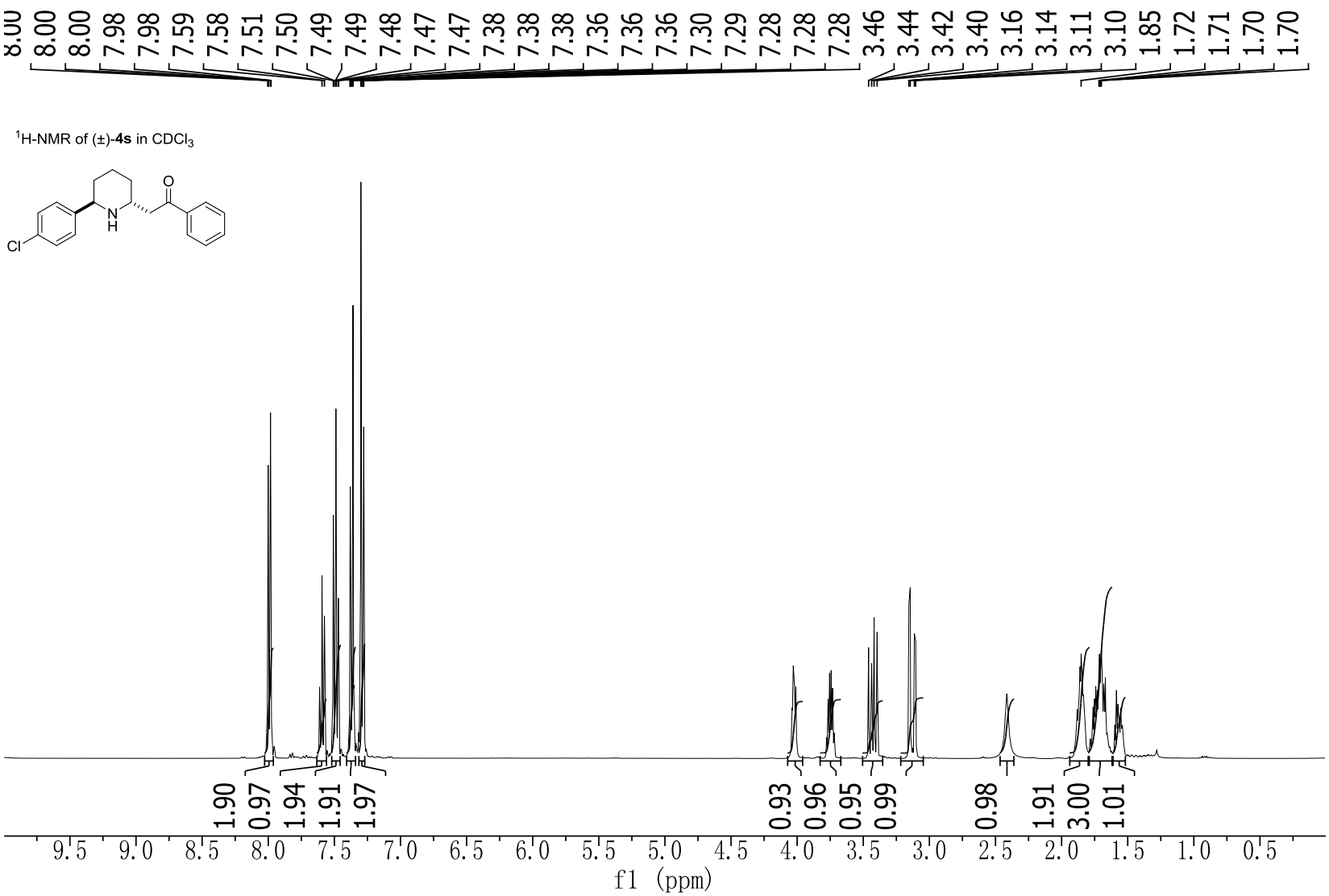

199.53
145.36
137.14
133.29
128.68
128.45
128.13
127.13
126.90
62.11
53.51
45.74
34.29
32.16
25.28
13C-NMR of (±)-4p' in CDCl3
O
N
H
f1 (ppm)

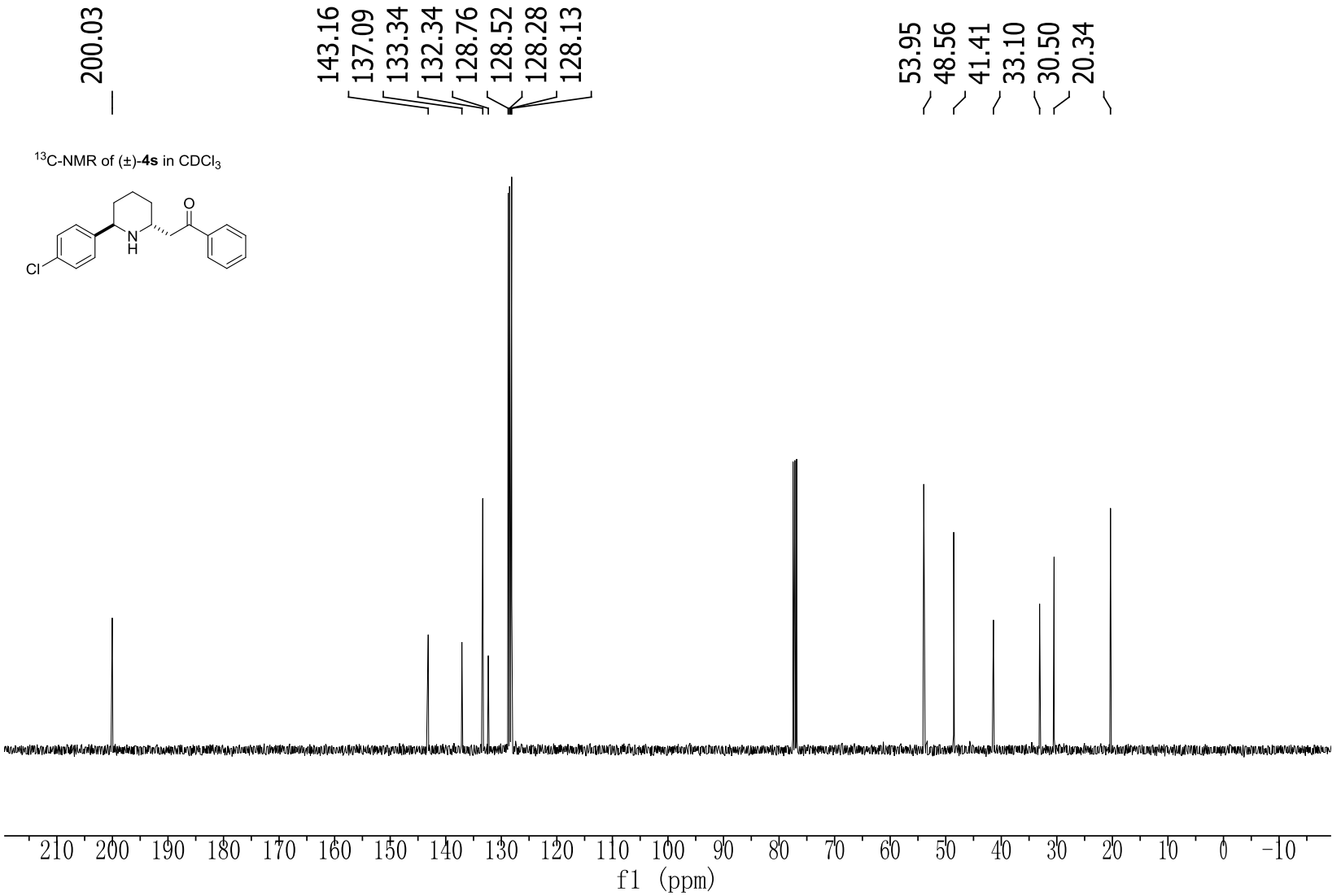

7.93
7.92
7.91
7.91
7.58
7.58
7.58
7.56
7.49
7.48
7.47
7.47
7.45
7.45
7.31
7.30
7.29
7.29
7.28
7.28
7.27
7.24
7.22
7.20
7.19
7.18
7.18
7.17
3.17
3.15
3.08
3.06
2.82
2.80
2.78
1.73
1.73
1H-NMR of (±)-4q in CDCl3
O
N
H
2.01
1.07
2.04
2.04
0.99
1.95
0.93
1.97
1.05
2.01
0.99
1.08
2.00
1.04
2.01
9.5
9.0
8.5
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
f1 (ppm)

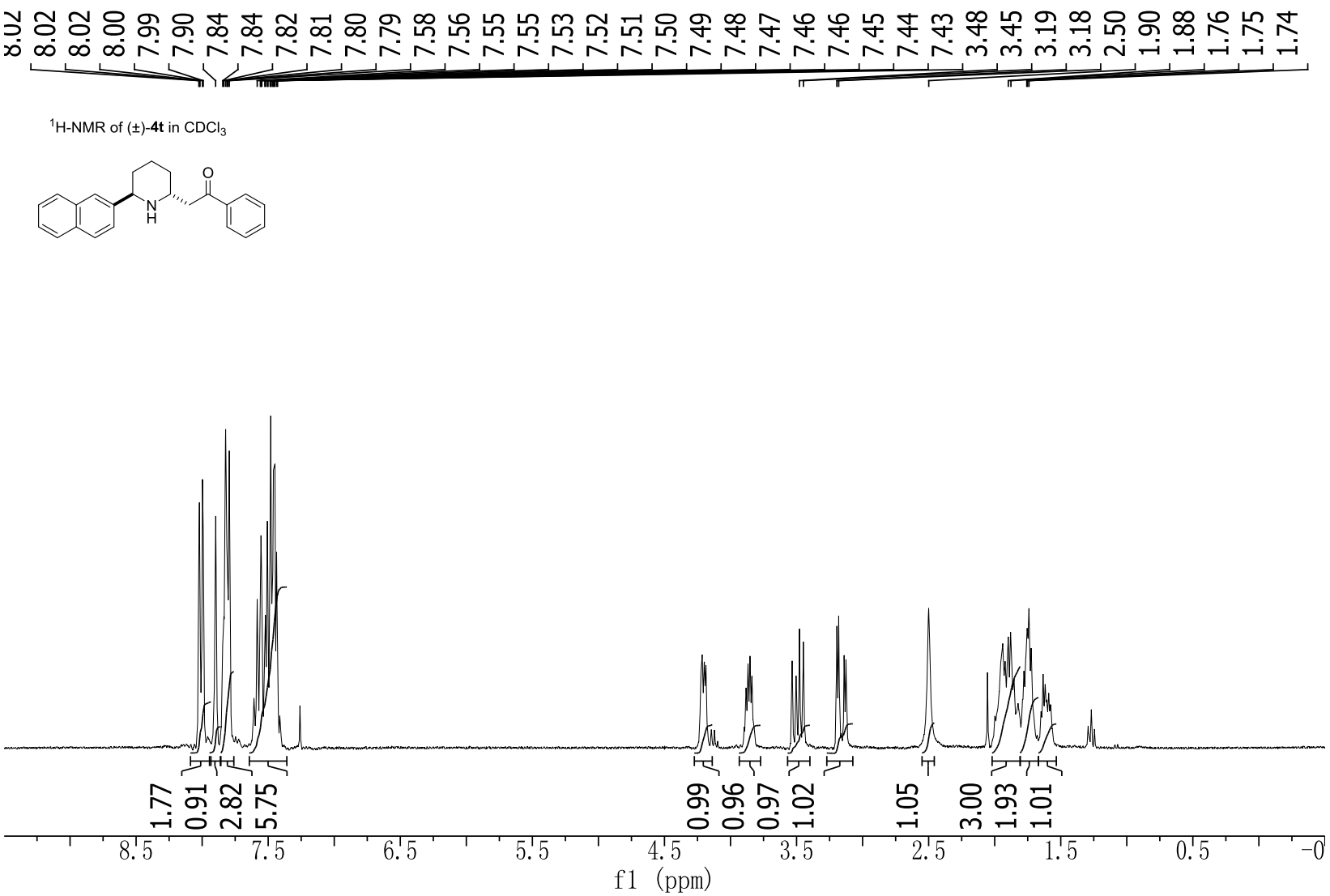

199.57
139.45
137.20
133.25
129.27
128.70
128.56
128.15
126.27
52.99
47.68
42.79
40.88
31.10
30.33
19.80
13C-NMR of (±)-4q in CDCl3
O
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

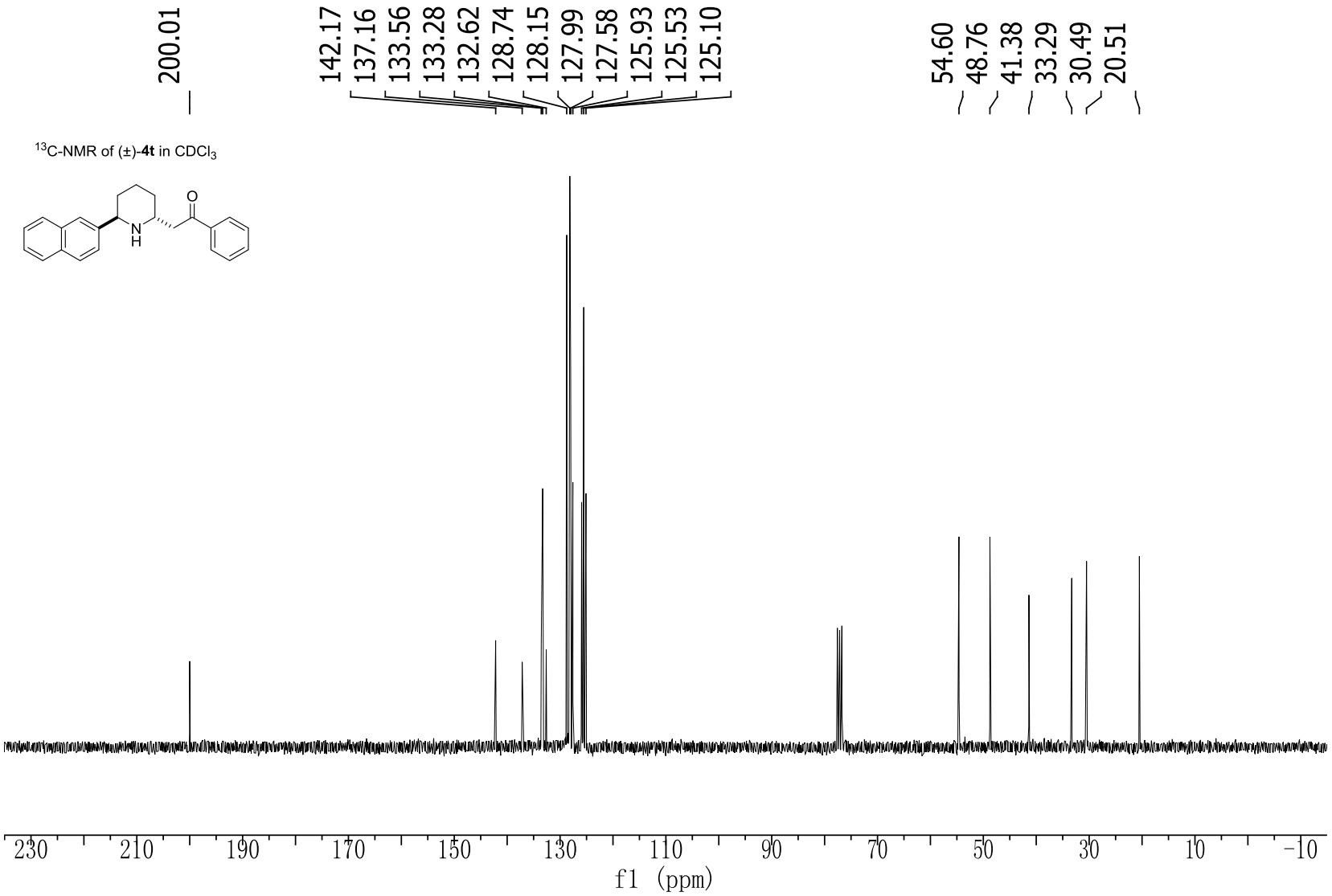

7.99
7.99
7.98
7.97
7.97
7.97
7.57
7.55
7.49
7.49
7.47
7.47
7.46
7.45
7.33
7.33
7.33
7.31
7.31
7.31
7.31
6.86
6.86
6.85
6.84
3.79
3.78
3.42
3.40
3.14
3.13
3.10
1.71
1.70
1.70
1.69
1.68
1H-NMR of (±)-4r in CDCl3
O
N
H
MeO
2.01
1.03
2.00
2.01
2.08
0.99
4.12
0.97
1.00
1.04
2.02
3.03
0.99
9.5
9.0
8.5
8.0
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.
f1 (ppm)

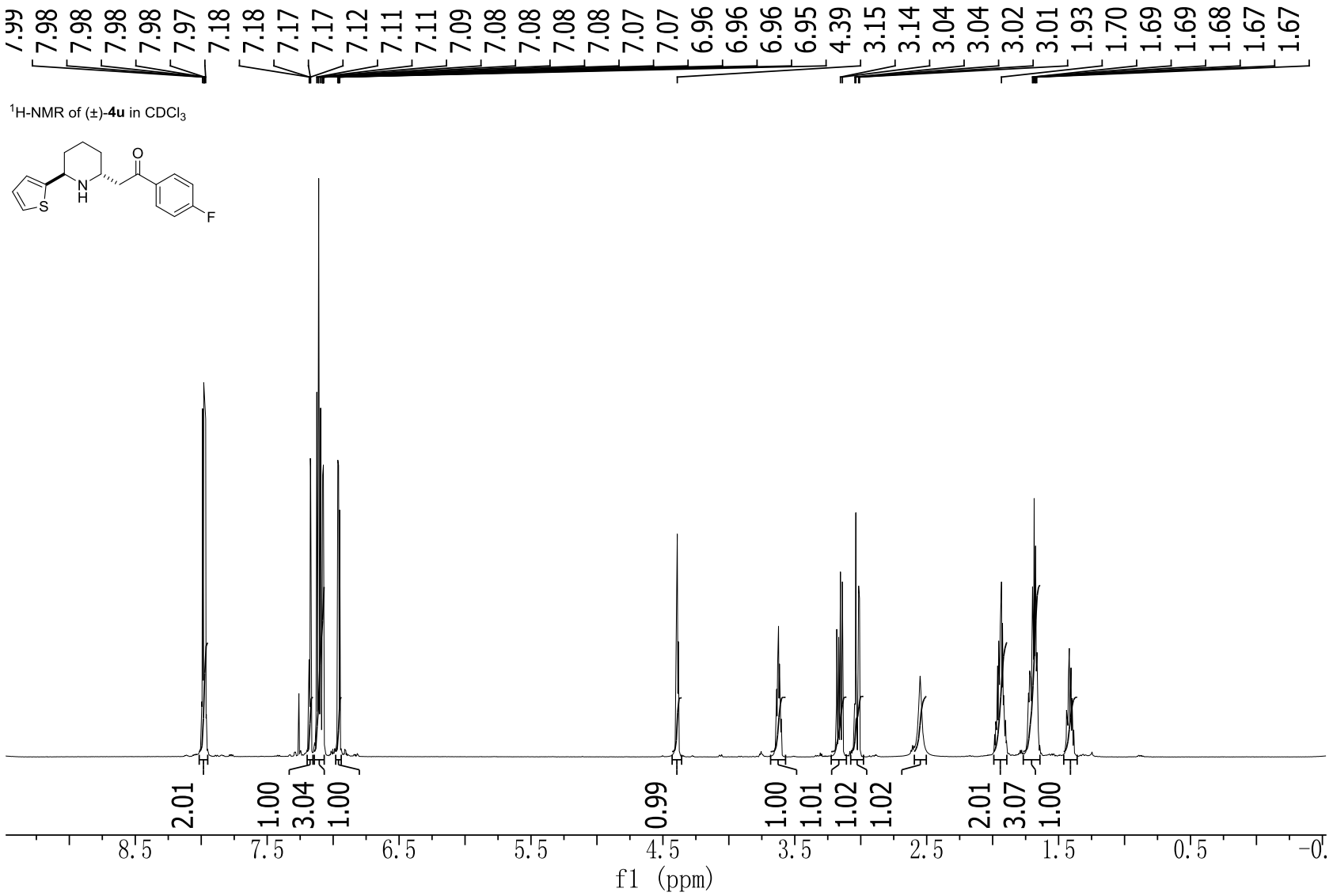

200.06
158.43
137.20
136.93
133.25
128.73
128.14
127.86
113.78
55.32
53.89
48.72
41.37
33.31
30.47
20.46
^{13}C-NMR of (±)-**4r** in $CDCl_3$
MeO
N
H
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.00
8.00
7.98
7.98
7.59
7.58
7.51
7.50
7.49
7.49
7.48
7.47
7.47
7.38
7.38
7.38
7.36
7.36
7.36
7.30
7.29
7.28
7.28
7.28
3.46
3.44
3.42
3.40
3.16
3.14
3.11
3.10
1.85
1.72
1.71
1.70
1.70
1H-NMR of (±)-4s in CDCl3
Cl
N
H
O
1.90
0.97
1.94
1.91
1.97
0.93
0.96
0.95
0.99
0.98
1.91
3.00
1.01
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
f1 (ppm)

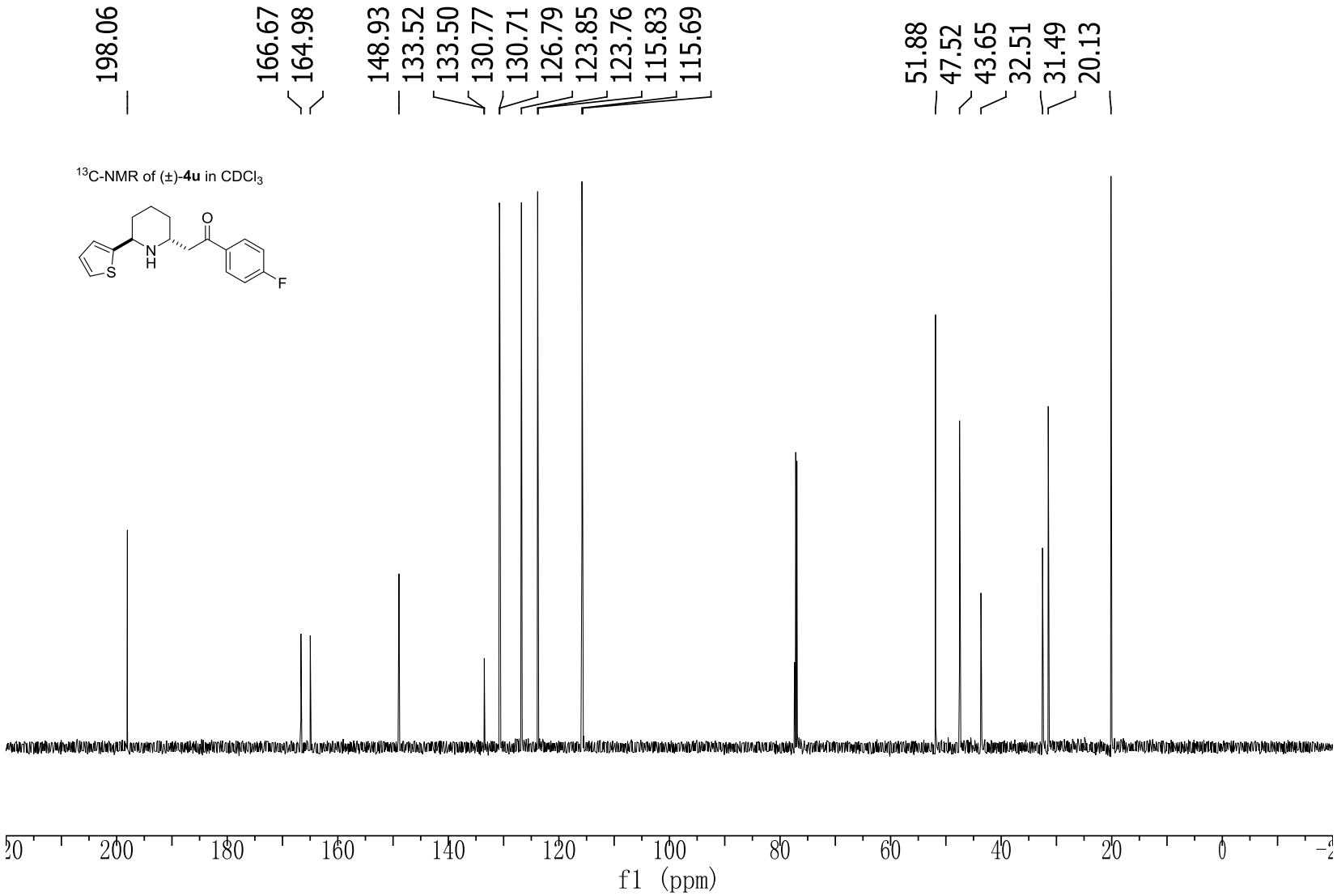

200.03
143.16
137.09
133.34
132.34
128.76
128.52
128.28
128.13
53.95
48.56
41.41
33.10
30.50
20.34
13C-NMR of (±)-4s in CDCl3
O
N
H
Cl
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

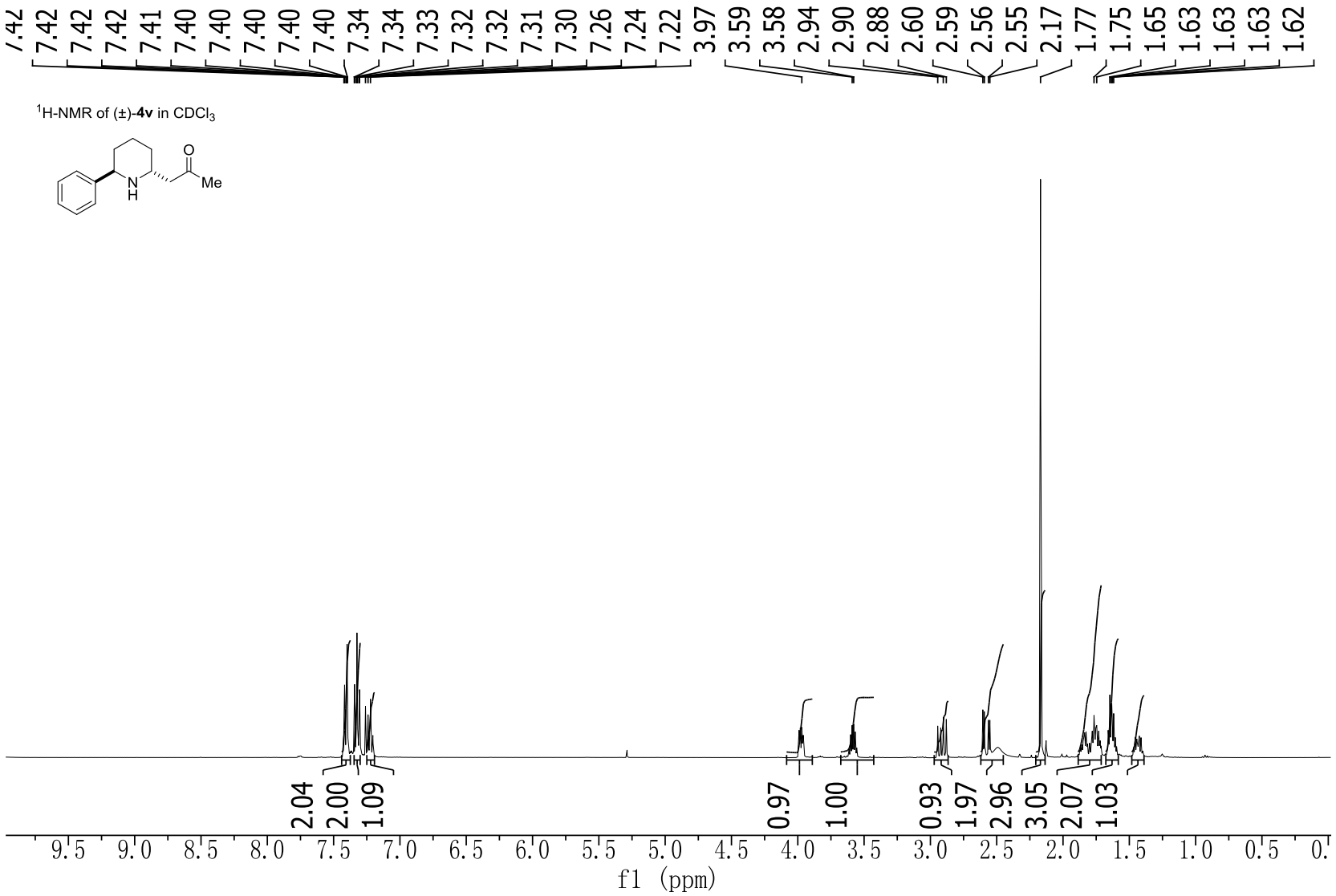

8.02
8.02
8.00
7.99
7.90
7.84
7.84
7.82
7.81
7.80
7.79
7.58
7.56
7.55
7.55
7.53
7.52
7.51
7.50
7.49
7.48
7.47
7.46
7.46
7.45
7.44
7.43
3.48
3.45
3.19
3.18
2.50
1.90
1.88
1.76
1.75
1.74
1H-NMR of (±)-4t in CDCl3
O
N
H
1.77
0.91
2.82
5.75
0.99
0.96
0.97
1.02
1.05
3.00
1.93
1.01
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0
f1 (ppm)

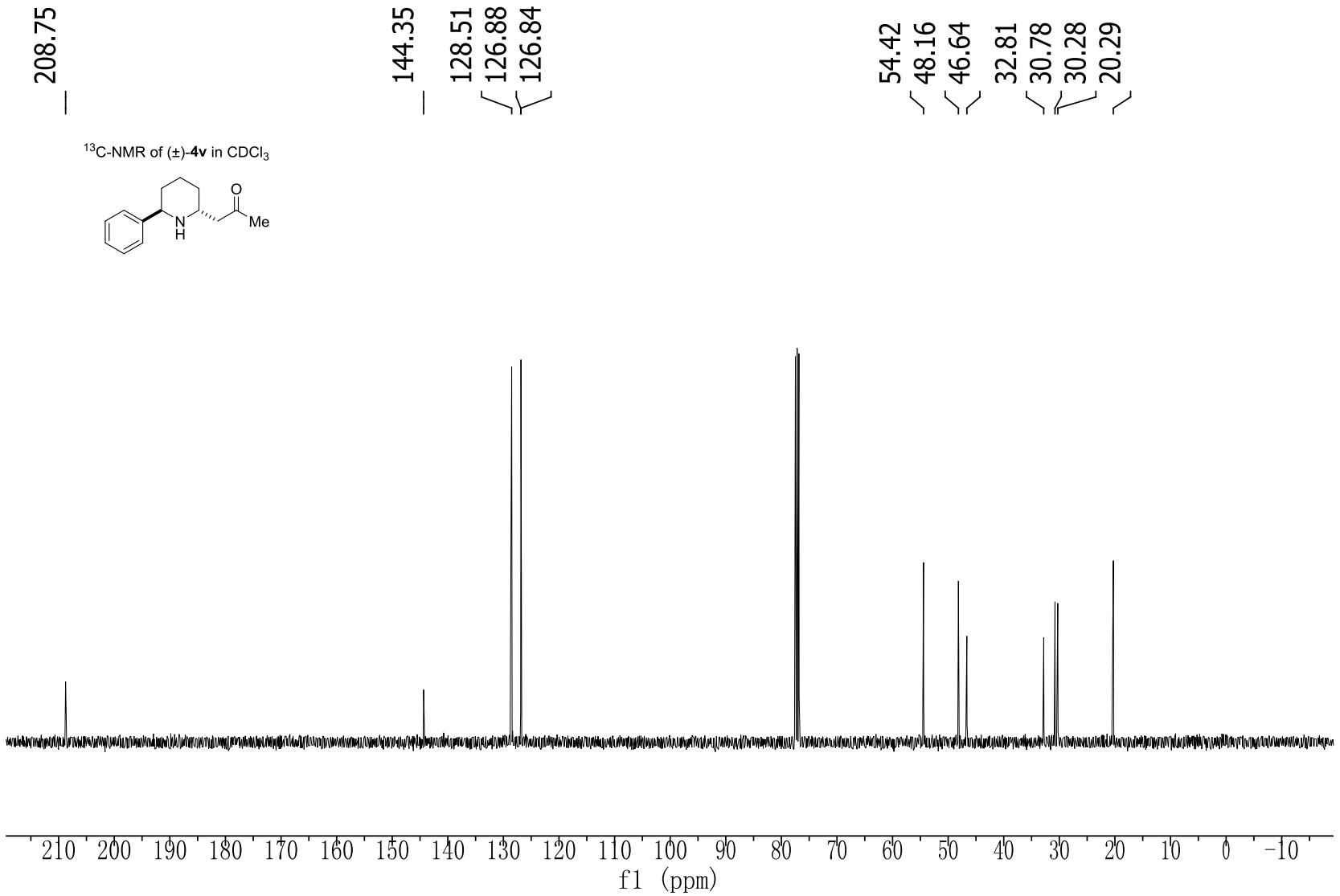

200.01
142.17
137.16
133.56
133.28
132.62
128.74
128.15
127.99
127.58
125.93
125.53
125.10
54.60
48.76
41.38
33.29
30.49
20.51
13C-NMR of (±)-4t in CDCl3
O
N
H
230
210
190
170
150
130
110
90
70
50
30
10
-10
f1 (ppm)

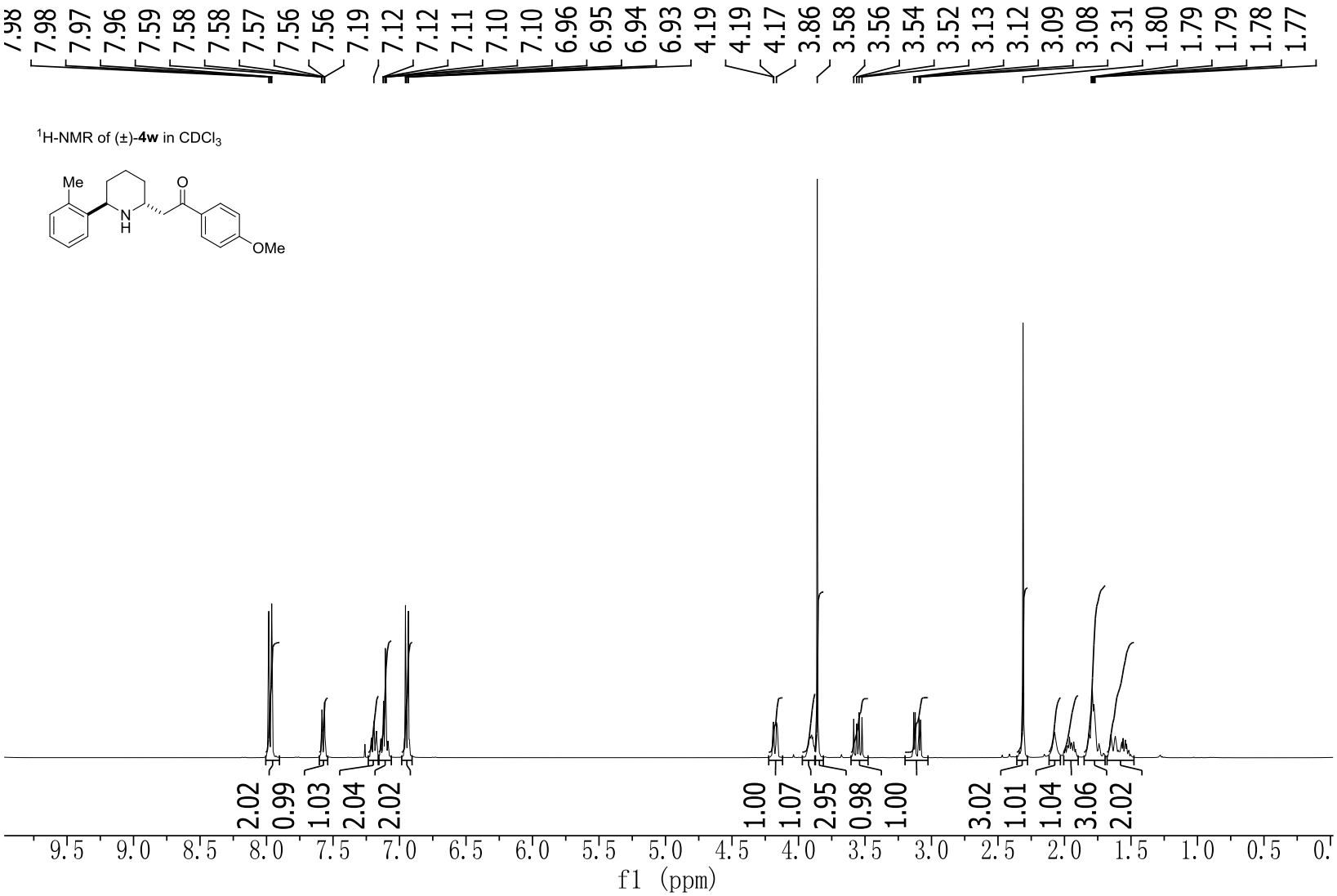


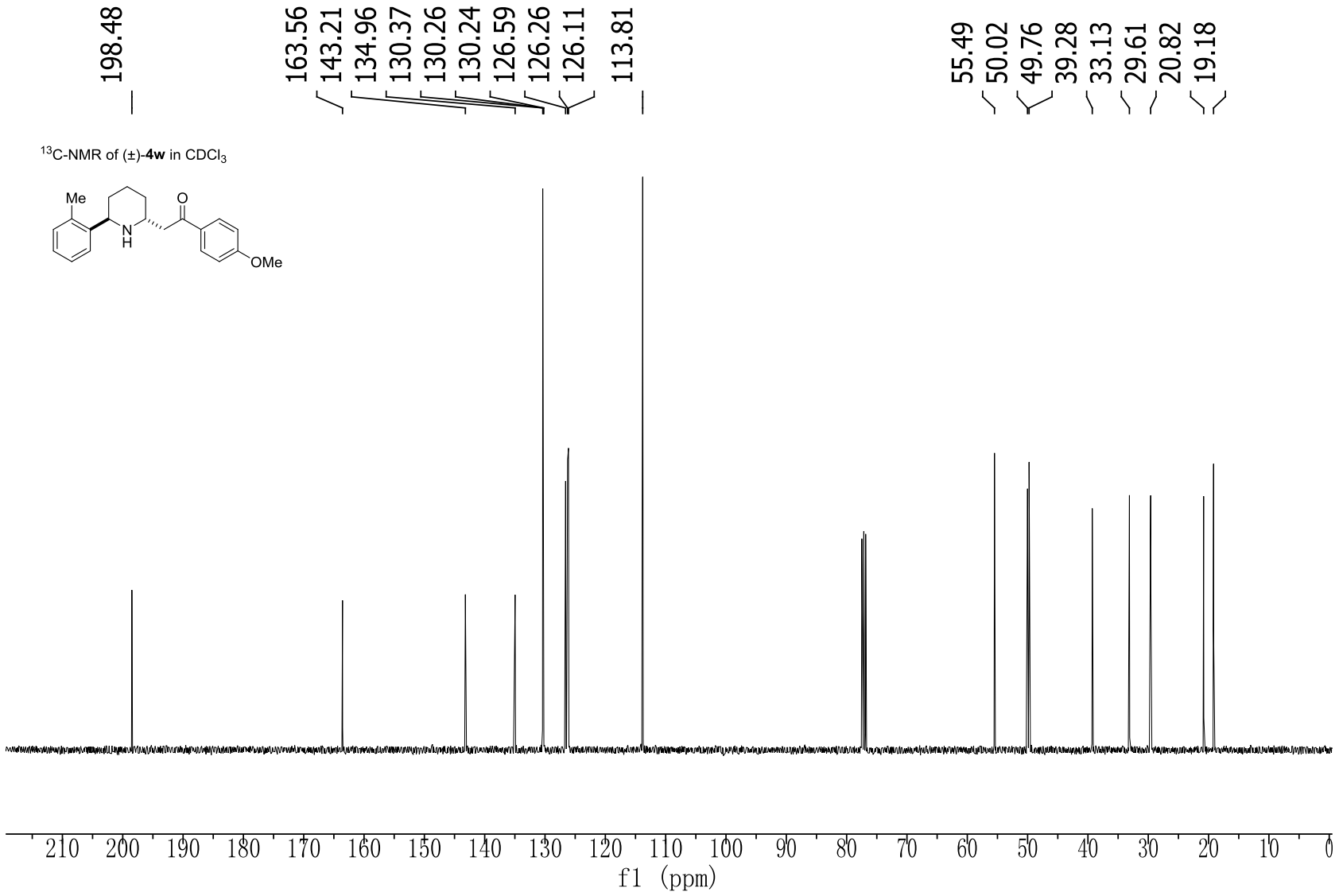
^{1}H-NMR of (±)-**4u** in $CDCl_3$

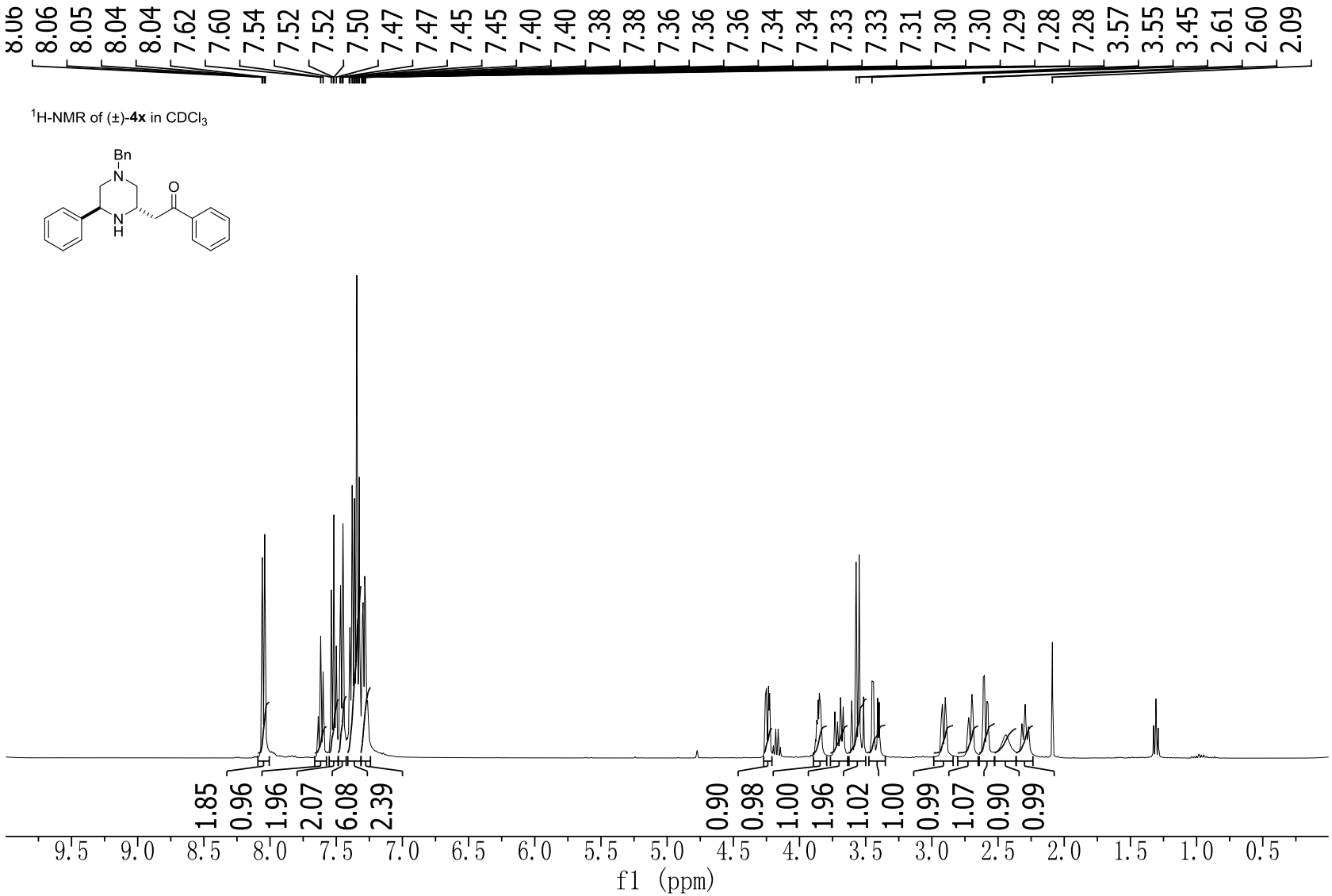

198.06
166.67
164.98
148.93
133.52
133.50
130.77
130.71
126.79
123.85
123.76
115.83
115.69
51.88
47.52
43.65
32.51
31.49
20.13
13C-NMR of (±)-4u in CDCl3
O
N
H
S
F
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


7.42
7.42
7.42
7.41
7.40
7.40
7.40
7.40
7.40
7.34
7.34
7.33
7.32
7.32
7.31
7.30
7.26
7.24
7.22
3.97
3.59
3.58
2.94
2.90
2.88
2.60
2.59
2.56
2.55
2.17
1.77
1.75
1.65
1.63
1.63
1.63
1.62
1H-NMR of (±)-4v in CDCl3
O
Me
N
H
2.04
2.00
1.09
0.97
1.00
0.93
1.97
2.96
3.05
2.07
1.03
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.
f1 (ppm)

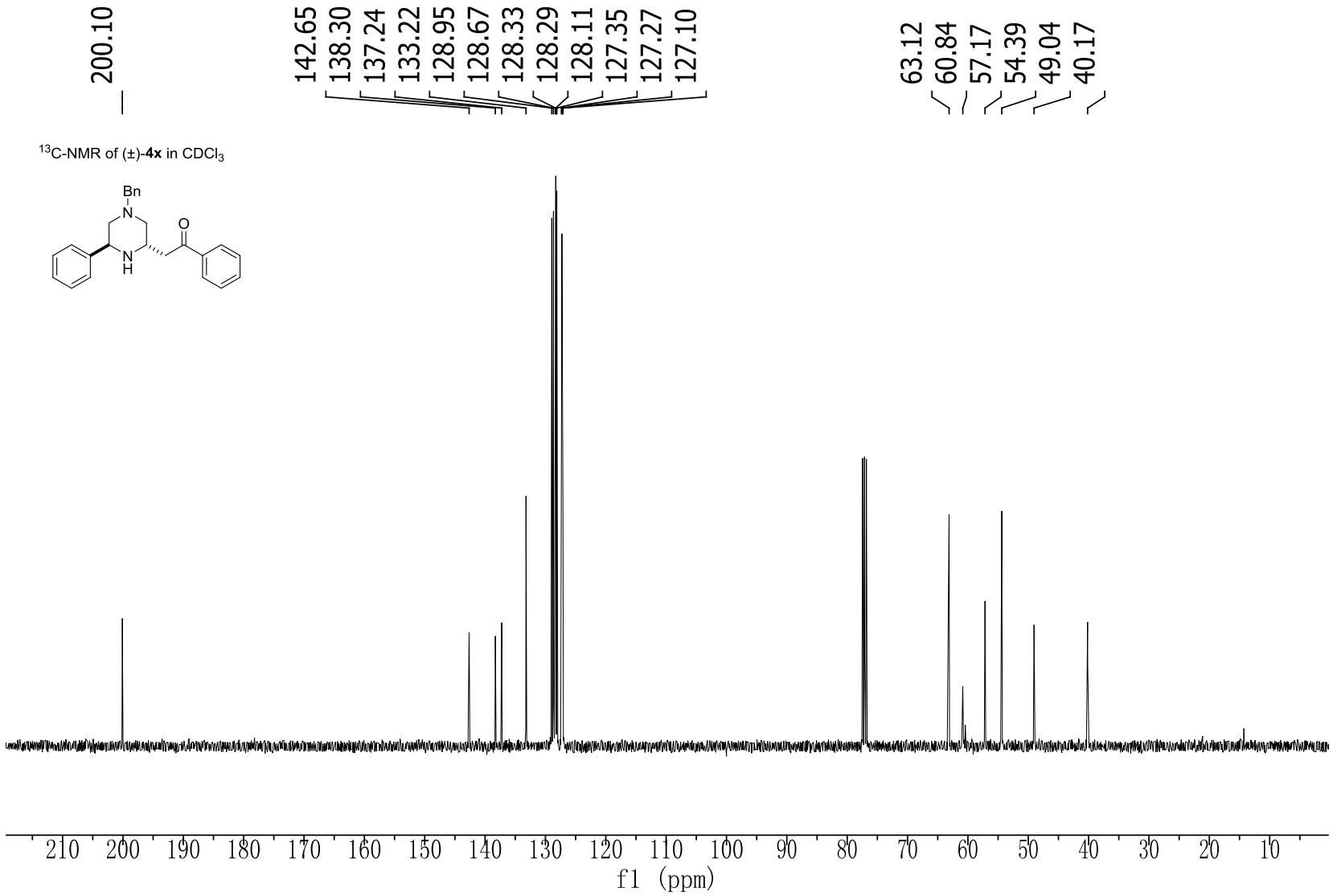

208.75
144.35
128.51
126.88
126.84
54.42
48.16
46.64
32.81
30.78
30.28
20.29
13C-NMR of (±)-4v in CDCl3
O
N
H
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

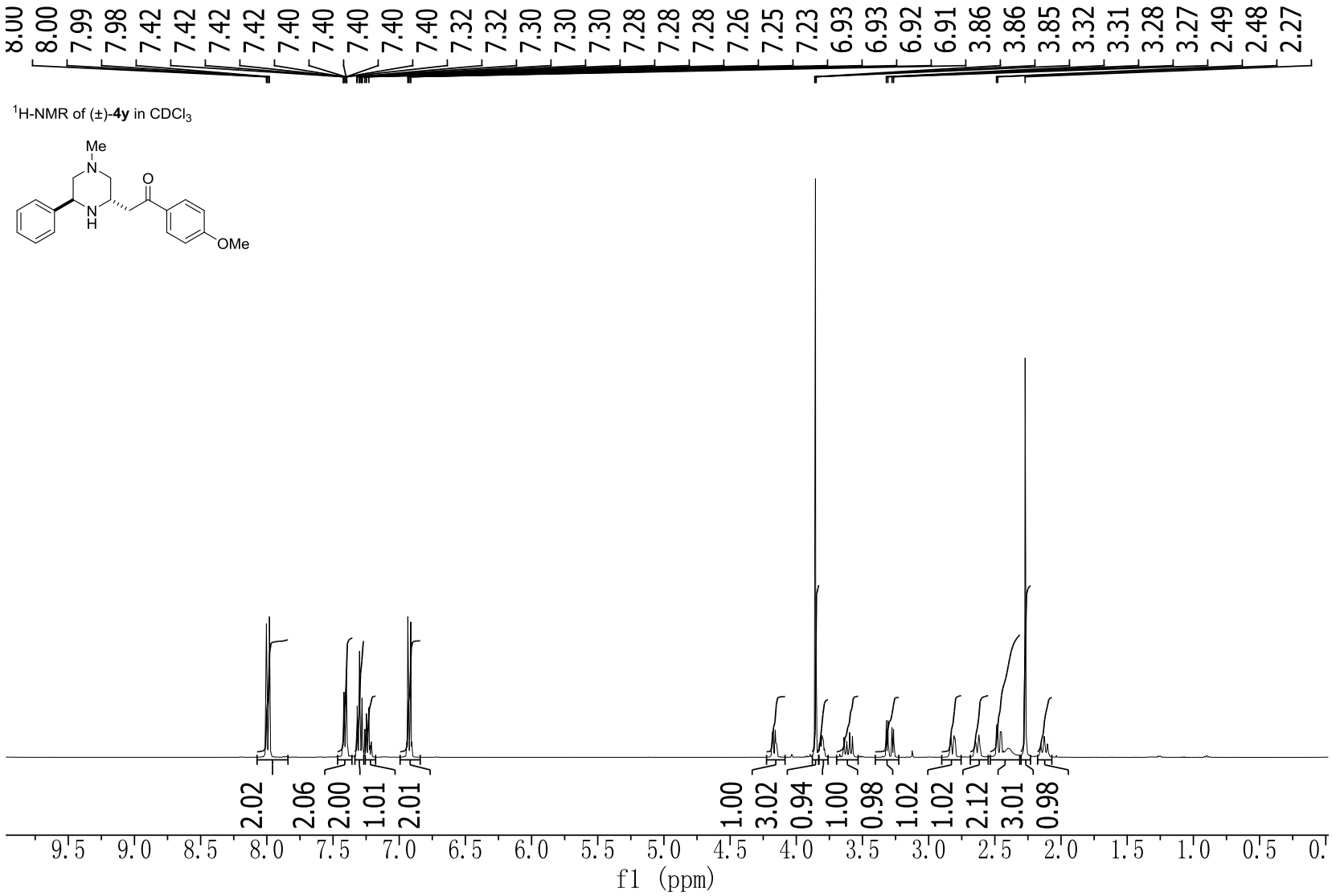

7.98
7.97
7.96
7.59
7.58
7.58
7.57
7.56
7.56
7.19
7.12
7.12
7.11
7.10
7.10
6.96
6.95
6.94
6.93
4.19
4.19
4.17
3.86
3.58
3.56
3.54
3.52
3.13
3.12
3.09
3.08
2.31
1.80
1.79
1.79
1.78
1.77
1H-NMR of (±)-4w in CDCl3
Me
O
N
H
OMe
2.02
0.99
1.03
2.04
2.02
1.00
1.07
2.95
0.98
1.00
3.02
1.01
1.04
3.06
2.02
9.5
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.
f1 (ppm)


198.48
163.56
143.21
134.96
130.37
130.26
130.24
126.59
126.26
126.11
113.81
55.49
50.02
49.76
39.28
33.13
29.61
20.82
19.18
13C-NMR of (±)-4w in CDCl3
Me
O
N
H
OMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

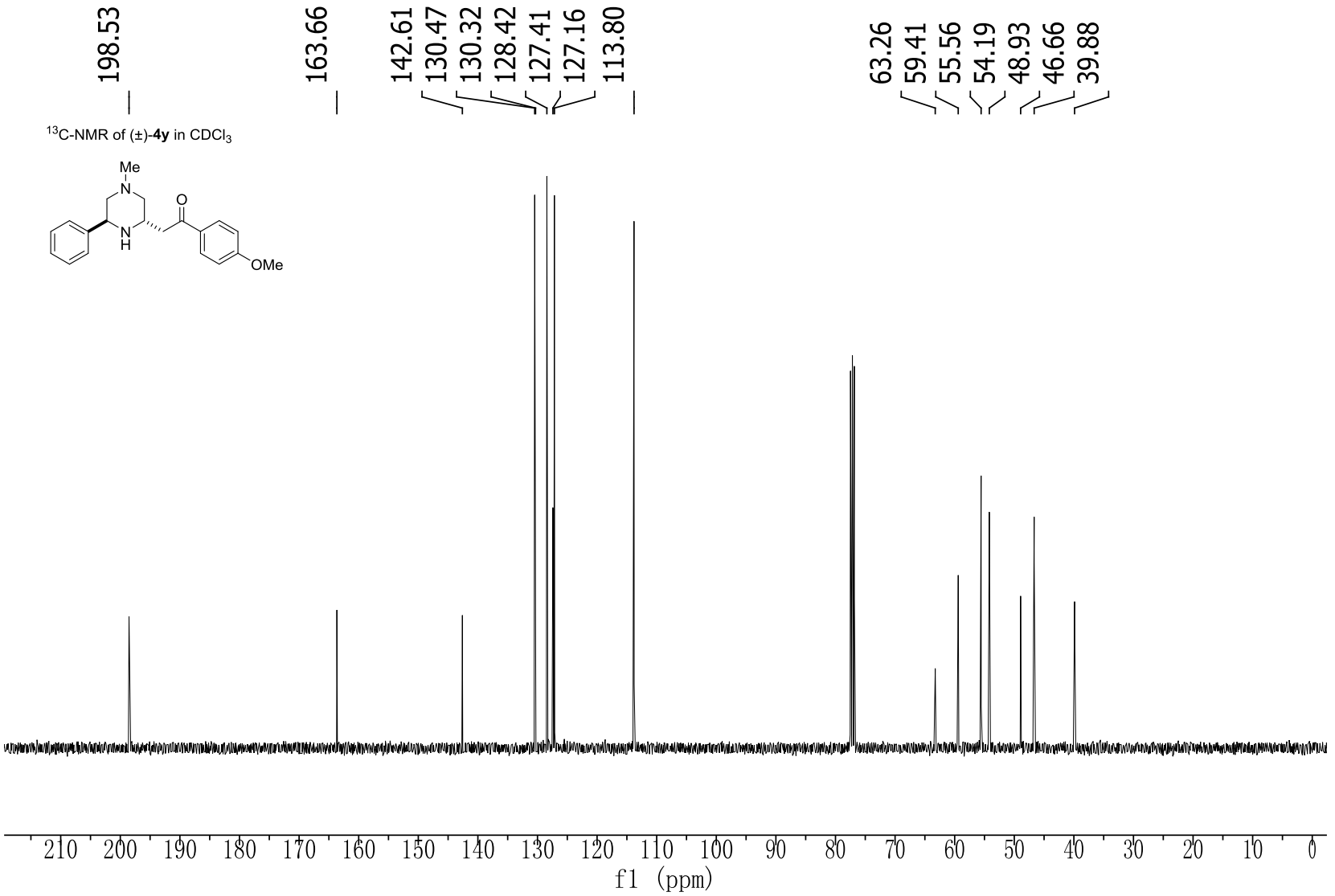


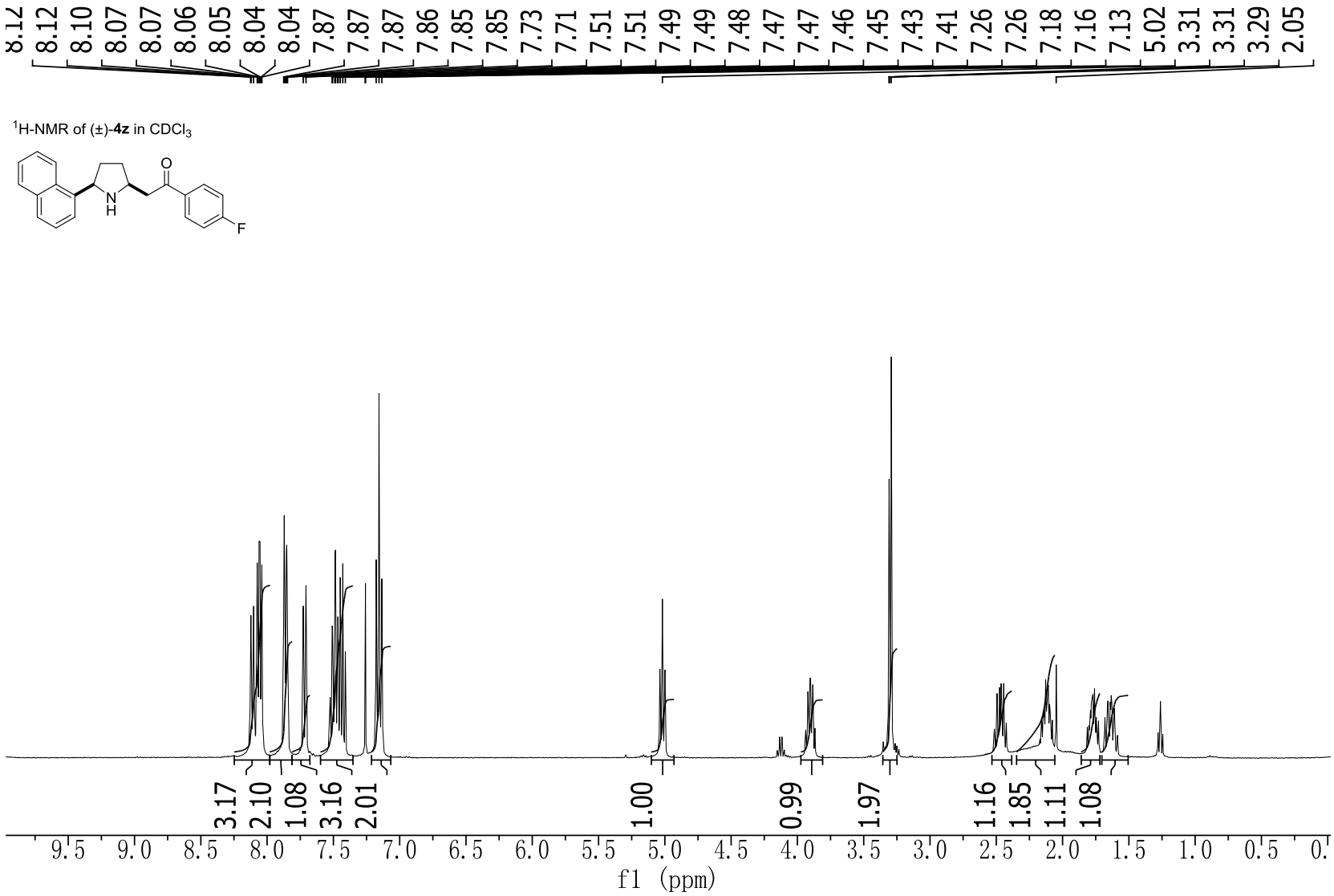
^{1}H-NMR of (±)-**4x** in $CDCl_3$

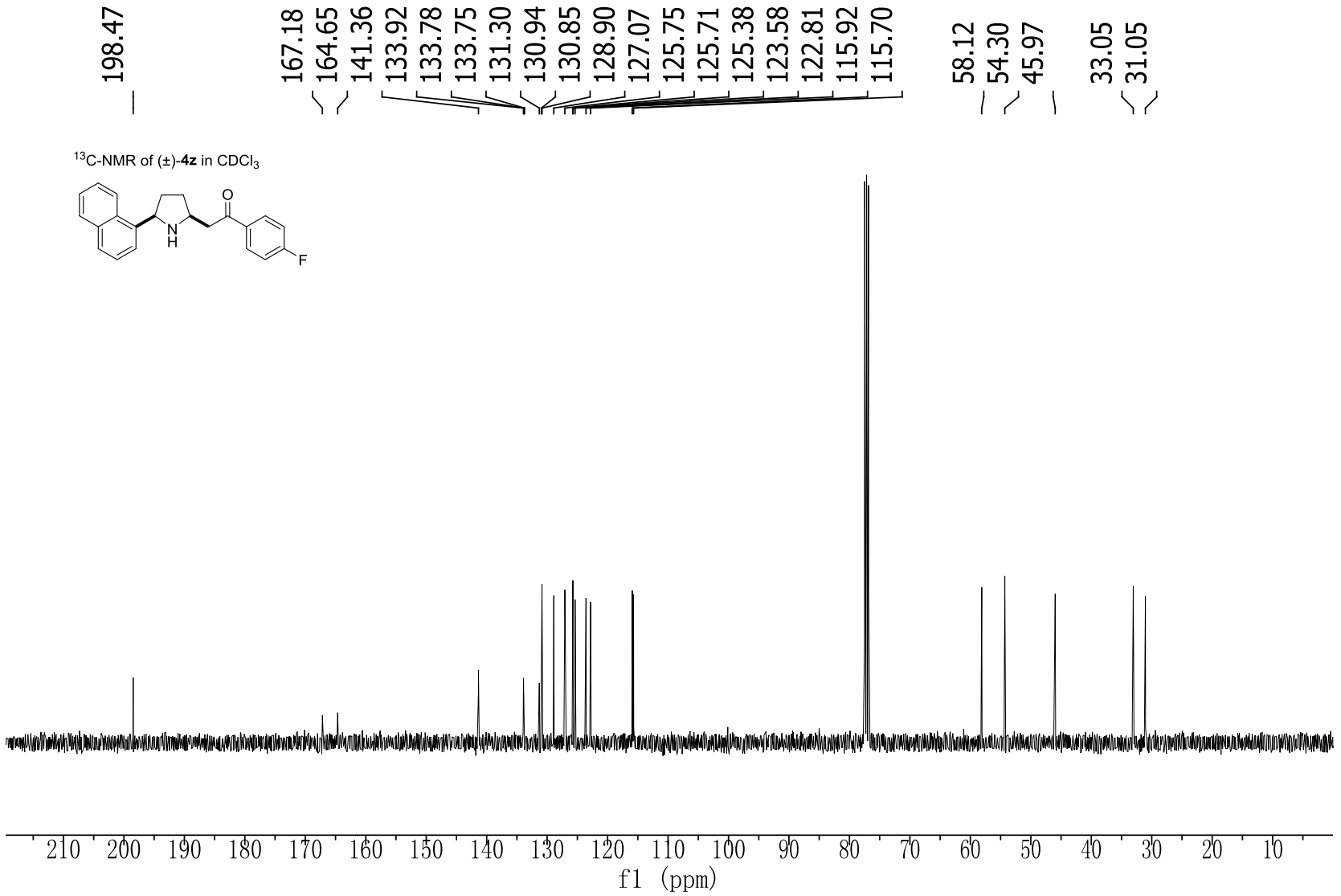

200.10
142.65
138.30
137.24
133.22
128.95
128.67
128.33
128.29
128.11
127.35
127.27
127.10
63.12
60.84
57.17
54.39
49.04
40.17
13C-NMR of (±)-4x in CDCl3
Bn
N
O
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

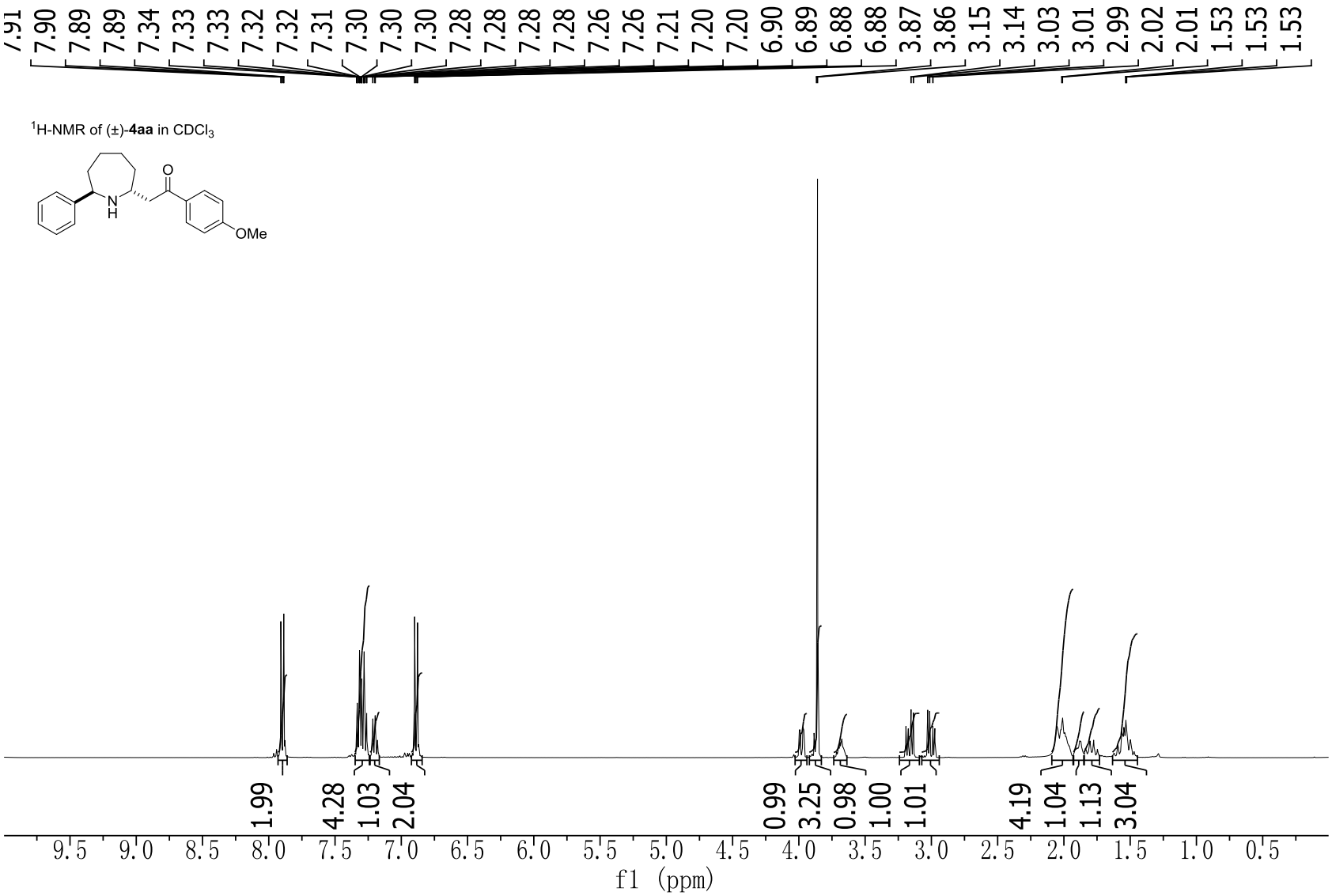


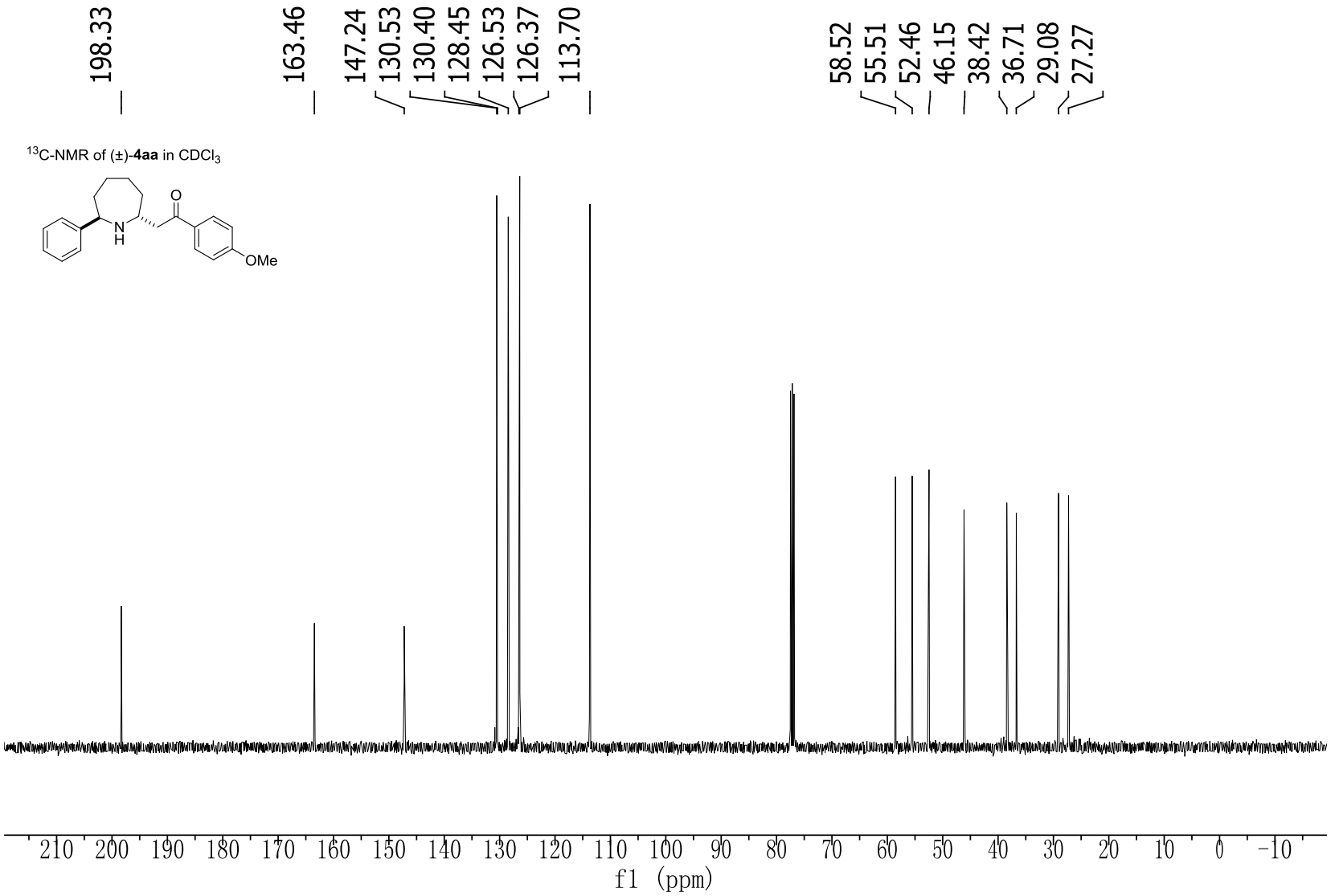
^{1}H-NMR of (±)-**4y** in $CDCl_3$

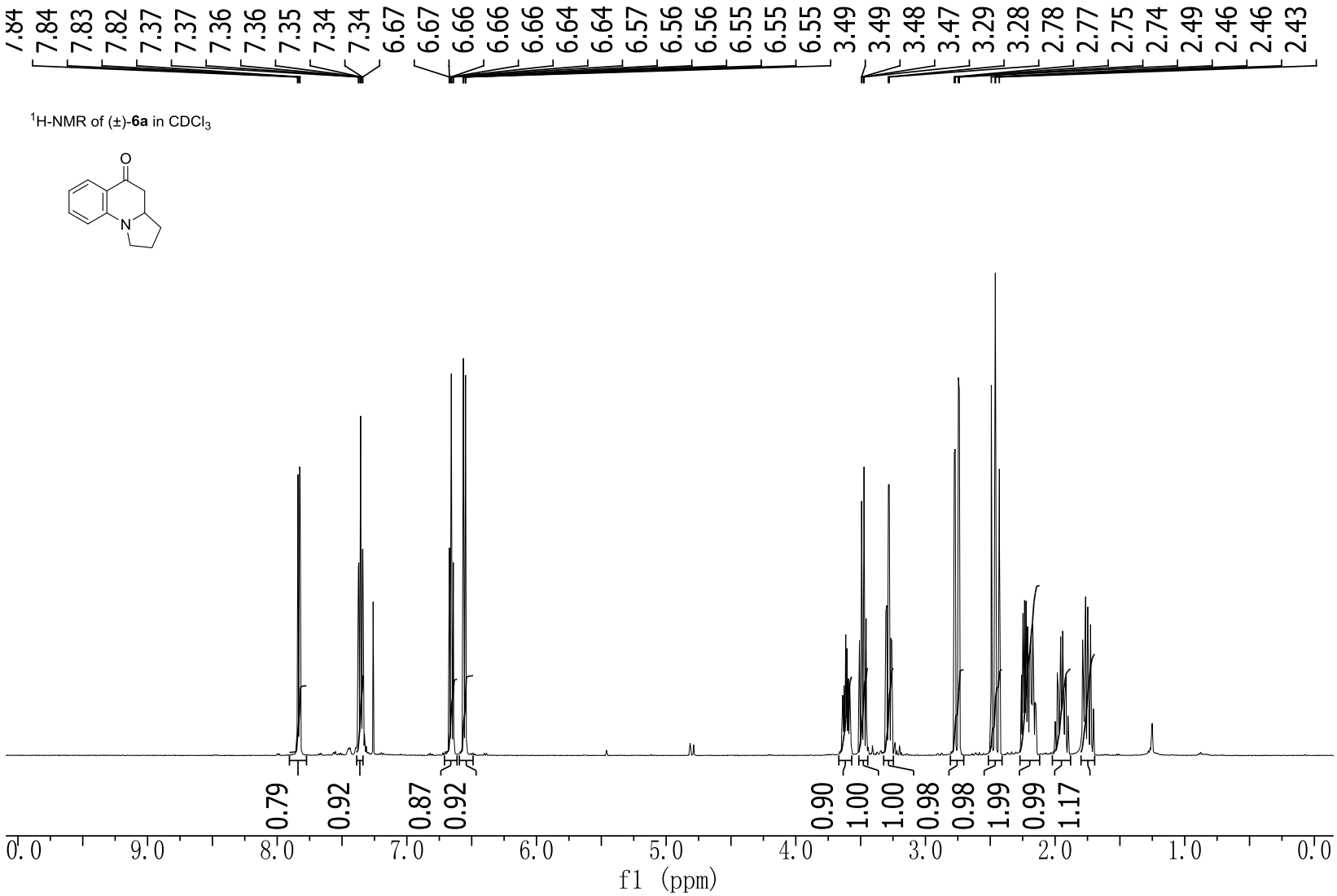

198.53
163.66
142.61
130.47
130.32
128.42
127.41
127.16
113.80
63.26
59.41
55.56
54.19
48.93
46.66
39.88
^{13}C-NMR of (±)-**4y** in $CDCl_3$
Me
N
O
N
H
OMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

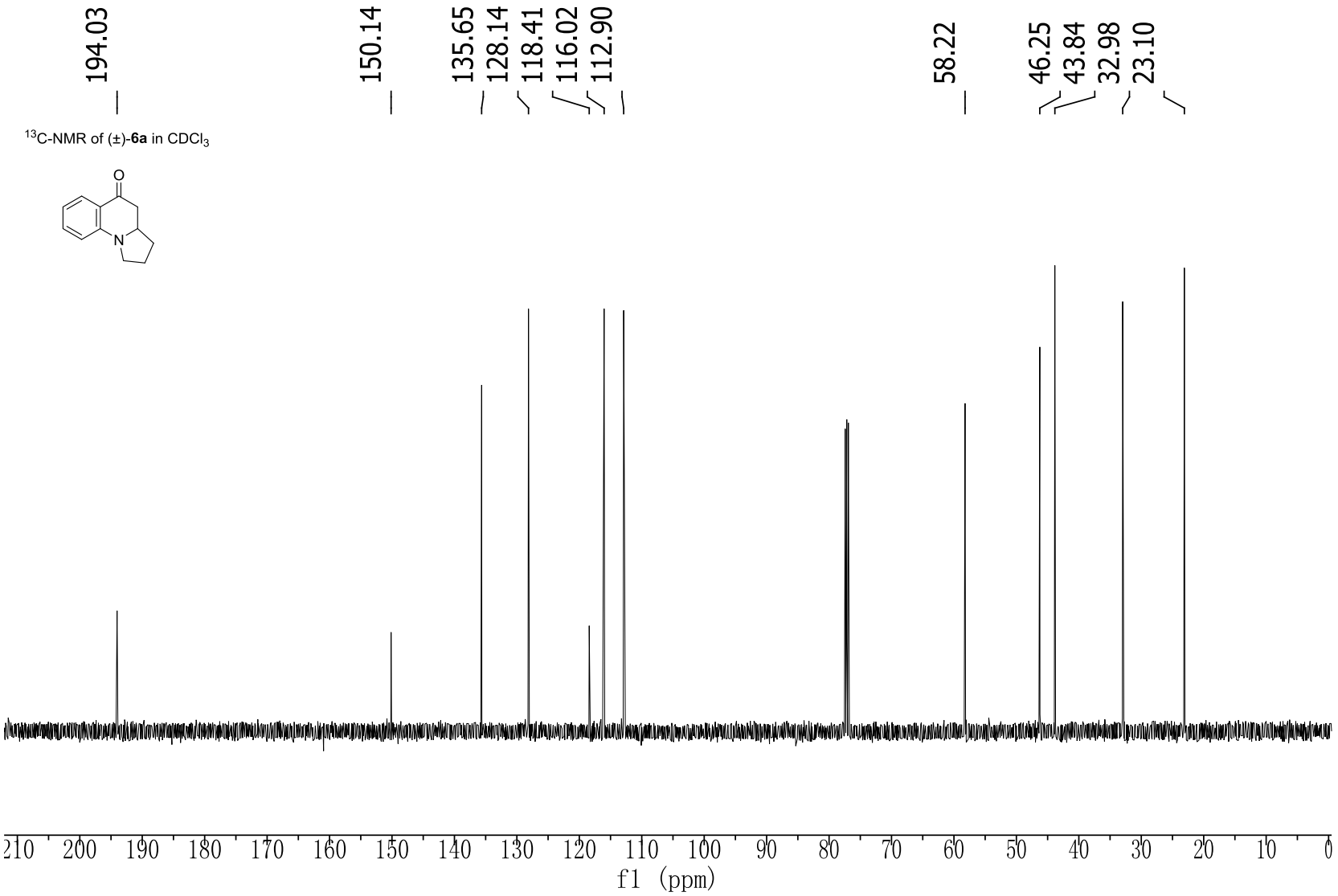

8.12
8.10
8.07
8.07
8.06
8.05
8.04
8.04
7.87
7.87
7.87
7.86
7.85
7.85
7.73
7.71
7.51
7.51
7.49
7.49
7.48
7.47
7.47
7.46
7.45
7.43
7.41
7.26
7.26
7.18
7.16
7.13
5.02
3.31
3.31
3.29
2.05
1H-NMR of (±)-4z in CDCl3
O
N
H
F
3.17
2.10
1.08
3.16
2.01
1.00
0.99
1.97
1.16
1.85
1.11
1.08
9.5
9.0
8.5
8.0
7.5
7.0
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.
f1 (ppm)

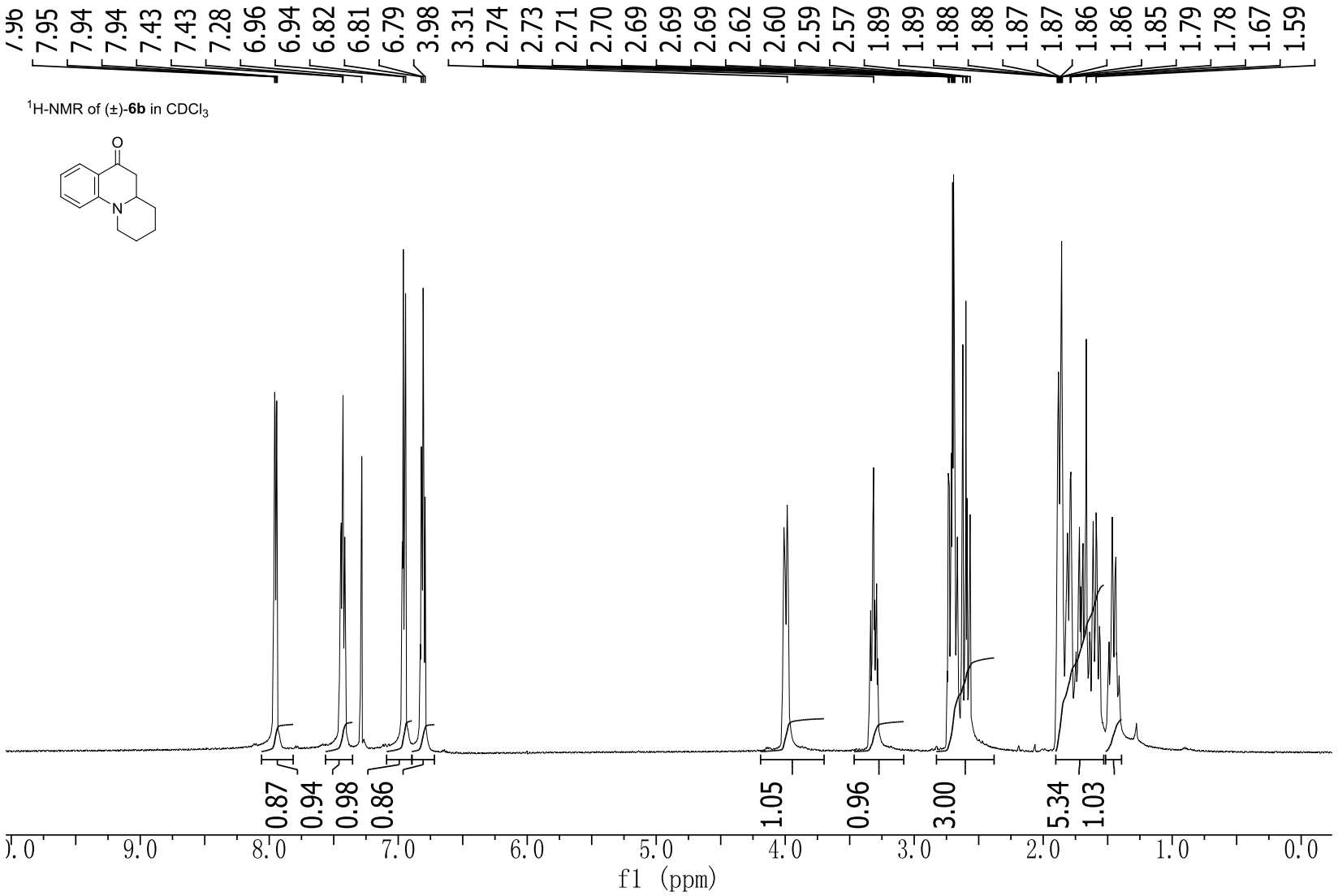

198.47
167.18
164.65
141.36
133.92
133.78
133.75
131.30
130.94
130.85
128.90
127.07
125.75
125.71
125.38
123.58
122.81
115.92
115.70
58.12
54.30
45.97
33.05
31.05
13C-NMR of (±)-4z in CDCl3
O
N
H
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

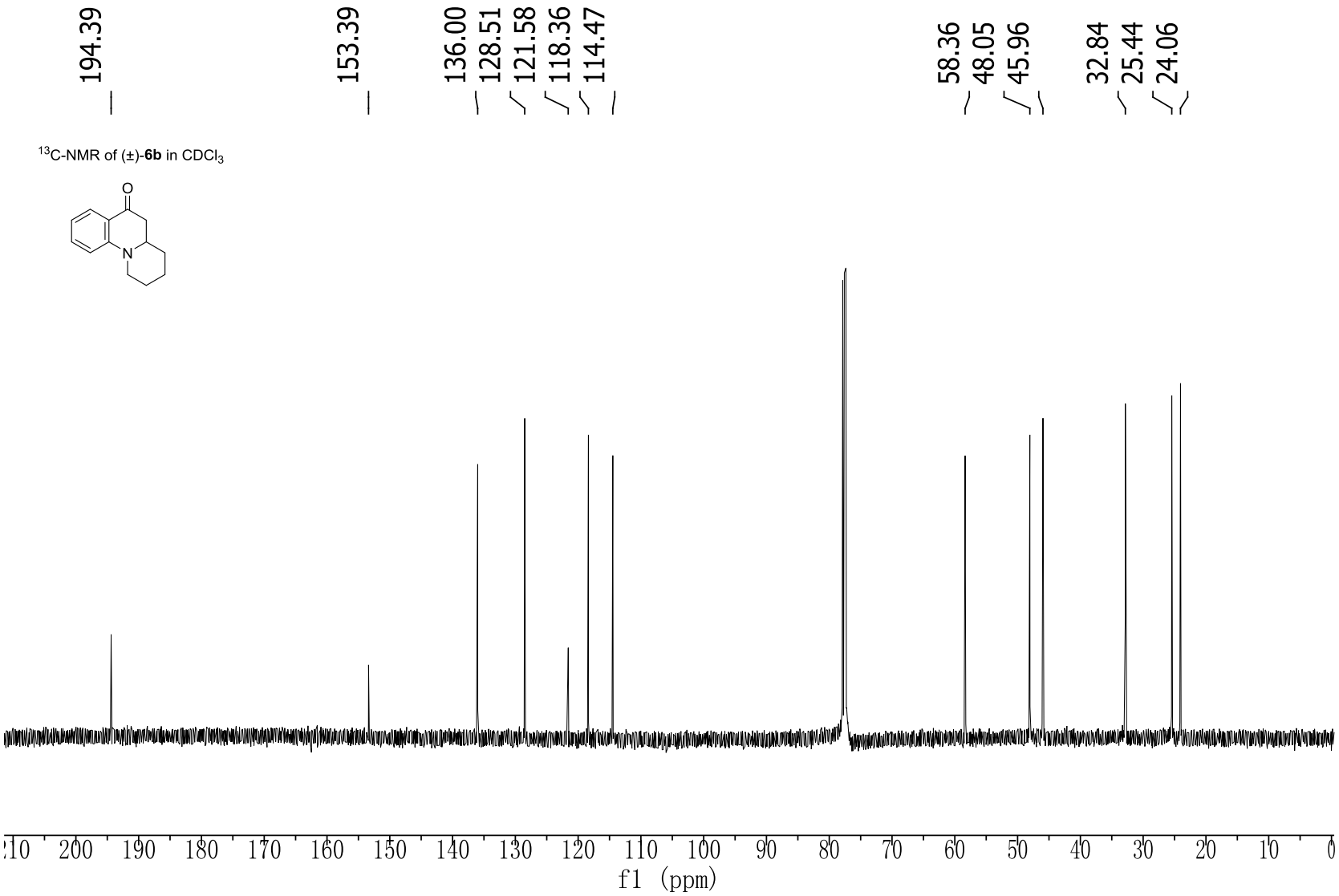

7.91
7.90
7.89
7.89
7.34
7.33
7.33
7.32
7.32
7.31
7.30
7.30
7.30
7.28
7.28
7.28
7.28
7.26
7.26
7.21
7.20
7.20
6.90
6.89
6.88
6.88
3.87
3.86
3.15
3.14
3.03
3.01
2.99
2.02
2.01
1.53
1.53
1.53
1H-NMR of (±)-4aa in CDCl3
O
N
H
OMe
1.99
4.28
1.03
2.04
0.99
3.25
0.98
1.00
1.01
4.19
1.04
1.13
3.04
9.5
9.0
8.5
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
f1 (ppm)

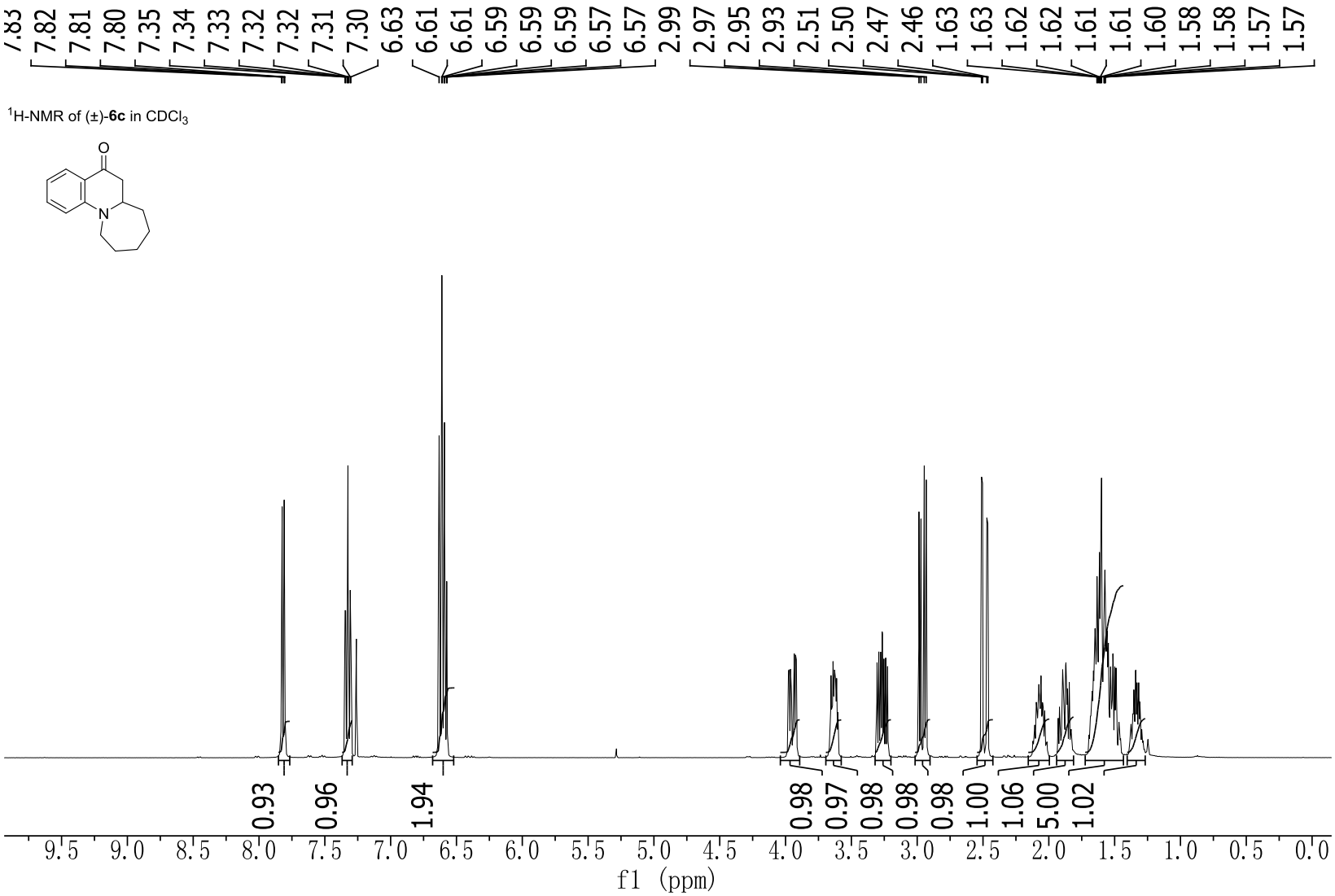

198.33
163.46
147.24
130.53
130.40
128.45
126.53
126.37
113.70
58.52
55.51
52.46
46.15
38.42
36.71
29.08
27.27
13C-NMR of (±)-4aa in CDCl3
O
N
H
OMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.84
7.83
7.82
7.37
7.37
7.36
7.36
7.35
7.34
7.34
6.67
6.67
6.66
6.66
6.66
6.64
6.64
6.57
6.56
6.56
6.55
6.55
6.55
3.49
3.49
3.48
3.47
3.29
3.28
2.78
2.77
2.75
2.74
2.49
2.46
2.46
2.43
1H-NMR of (±)-6a in CDCl3
O
N
0.79
0.92
0.87
0.92
0.90
1.00
1.00
0.98
0.98
1.99
0.99
1.17
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

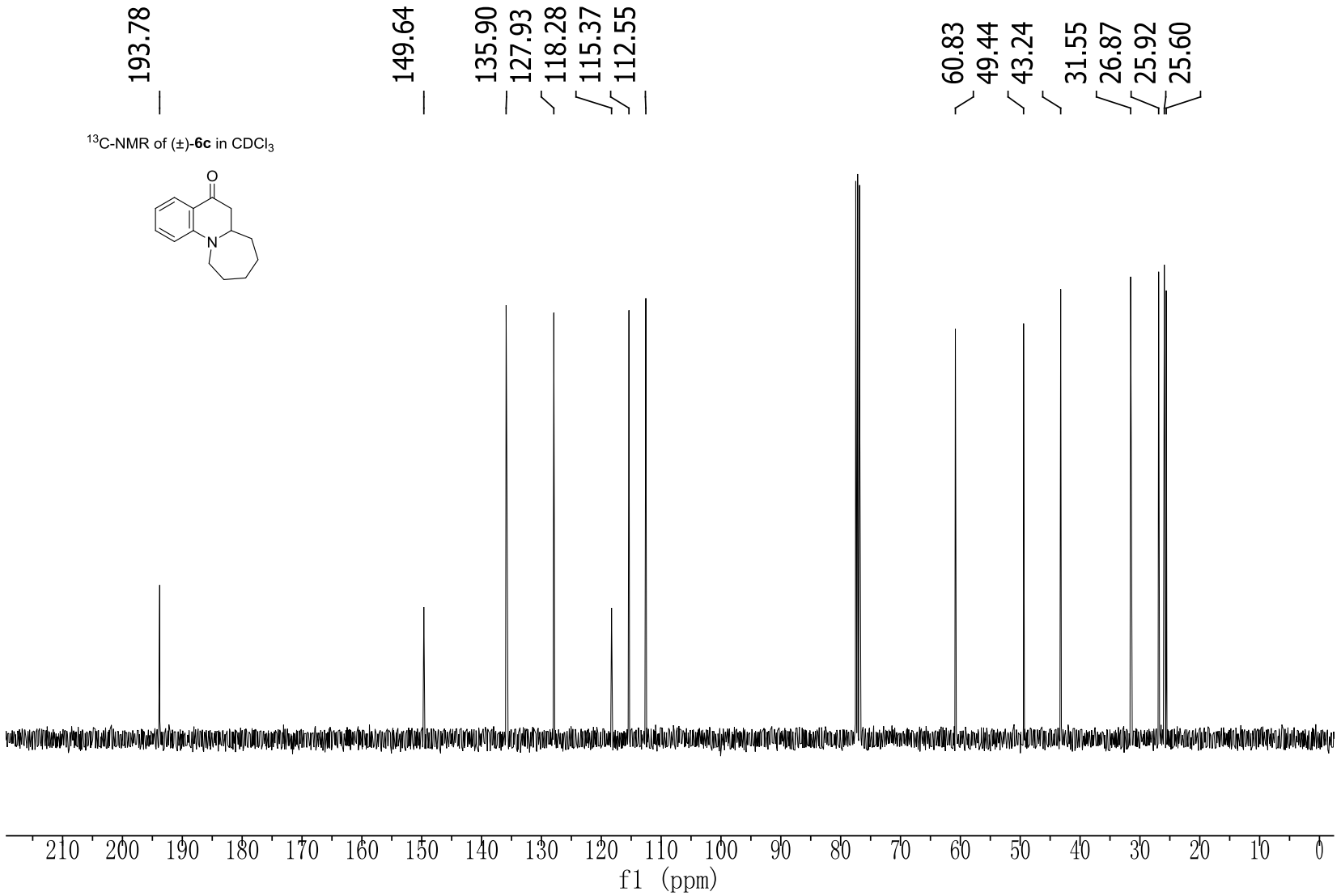

194.03
150.14
135.65
128.14
118.41
116.02
112.90
58.22
46.25
43.84
32.98
23.10
^{13}C-NMR of (±)-**6a** in $CDCl_3$
O
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

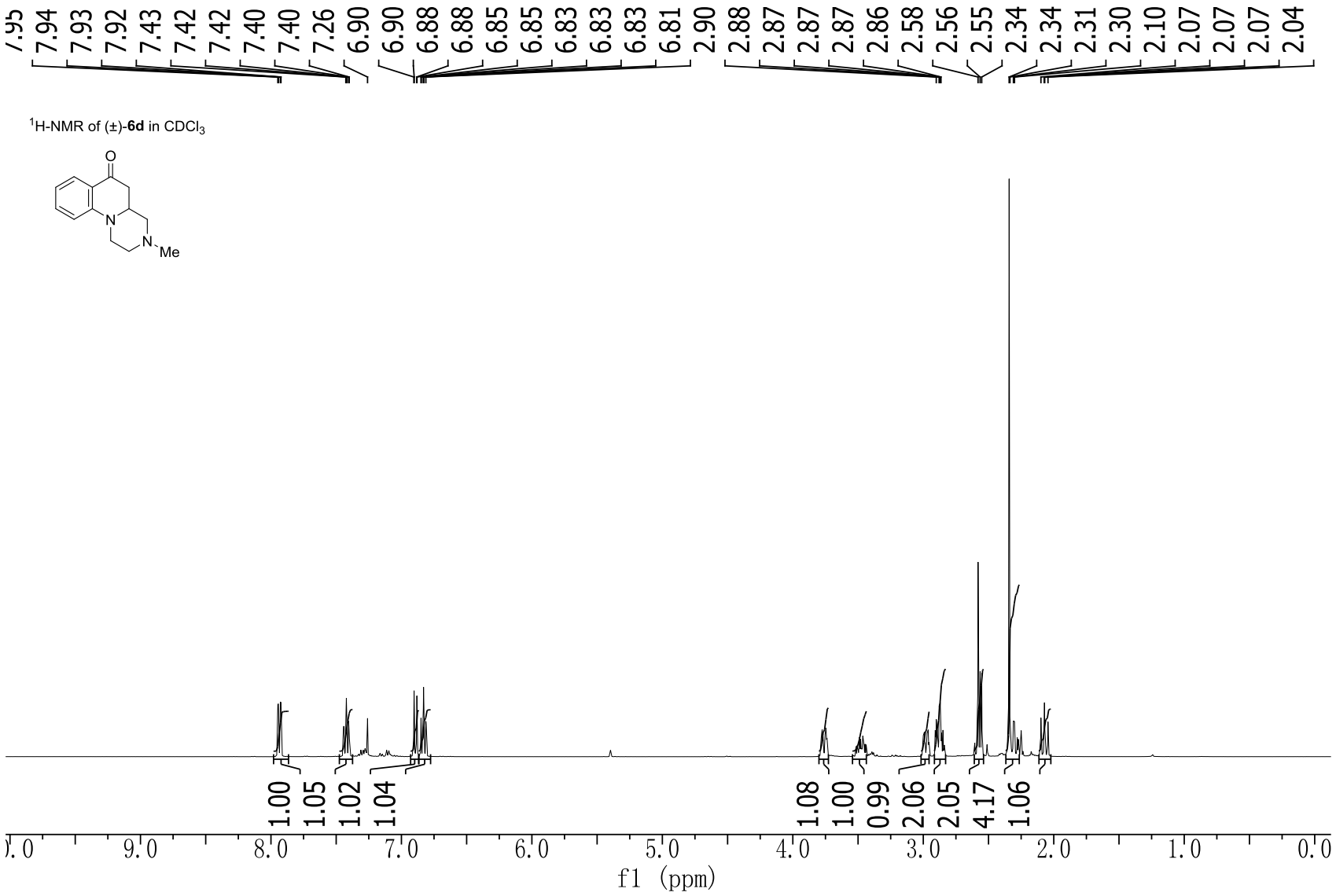

7.96
7.95
7.94
7.94
7.43
7.43
7.28
6.96
6.94
6.82
6.81
6.79
3.98
3.31
2.74
2.73
2.71
2.70
2.69
2.69
2.69
2.62
2.60
2.59
2.57
1.89
1.89
1.88
1.88
1.87
1.87
1.86
1.86
1.85
1.79
1.78
1.67
1.59
1H-NMR of (±)-6b in CDCl3
O
N
0.87
0.94
0.98
0.86
1.05
0.96
3.00
5.34
1.03
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


194.39
153.39
136.00
128.51
121.58
118.36
114.47
58.36
48.05
45.96
32.84
25.44
24.06
^{13}C-NMR of (±)-**6b** in $CDCl_3$
O
N
f1 (ppm)



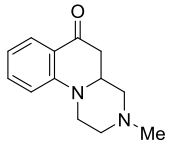
^{1}H-NMR of (±)-**6c** in $CDCl_3$

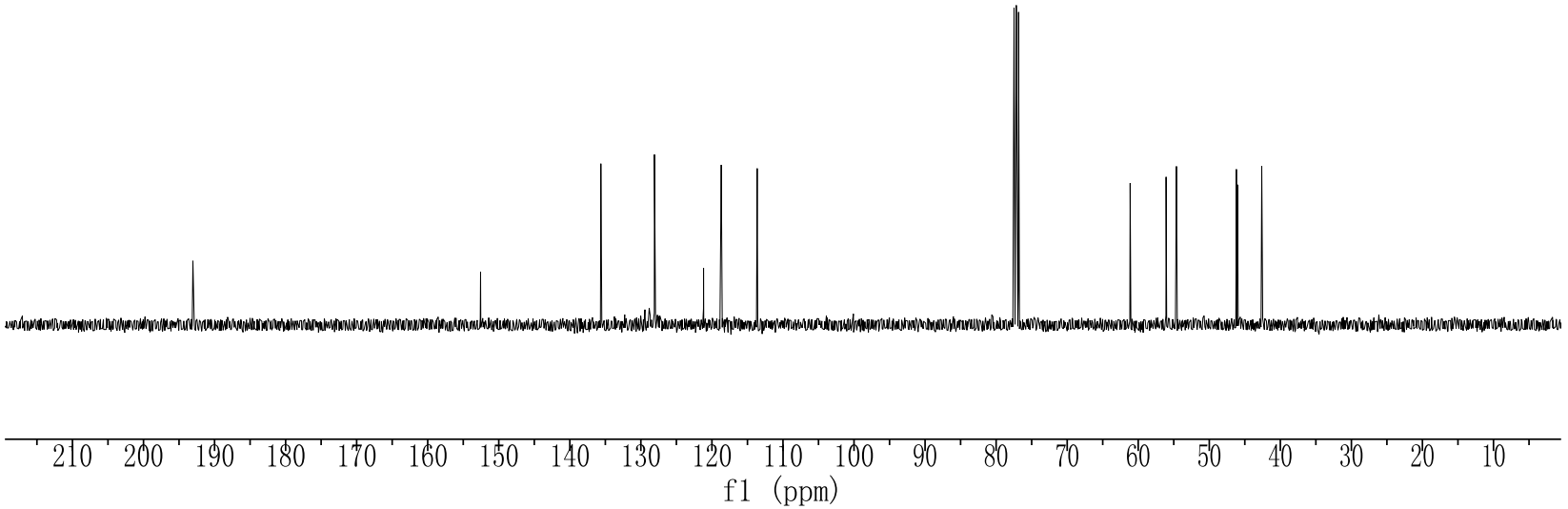

193.78
149.64
135.90
127.93
118.28
115.37
112.55
60.83
49.44
43.24
31.55
26.87
25.92
25.60
^{13}C-NMR of (±)-**6c** in $CDCl_3$
O
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

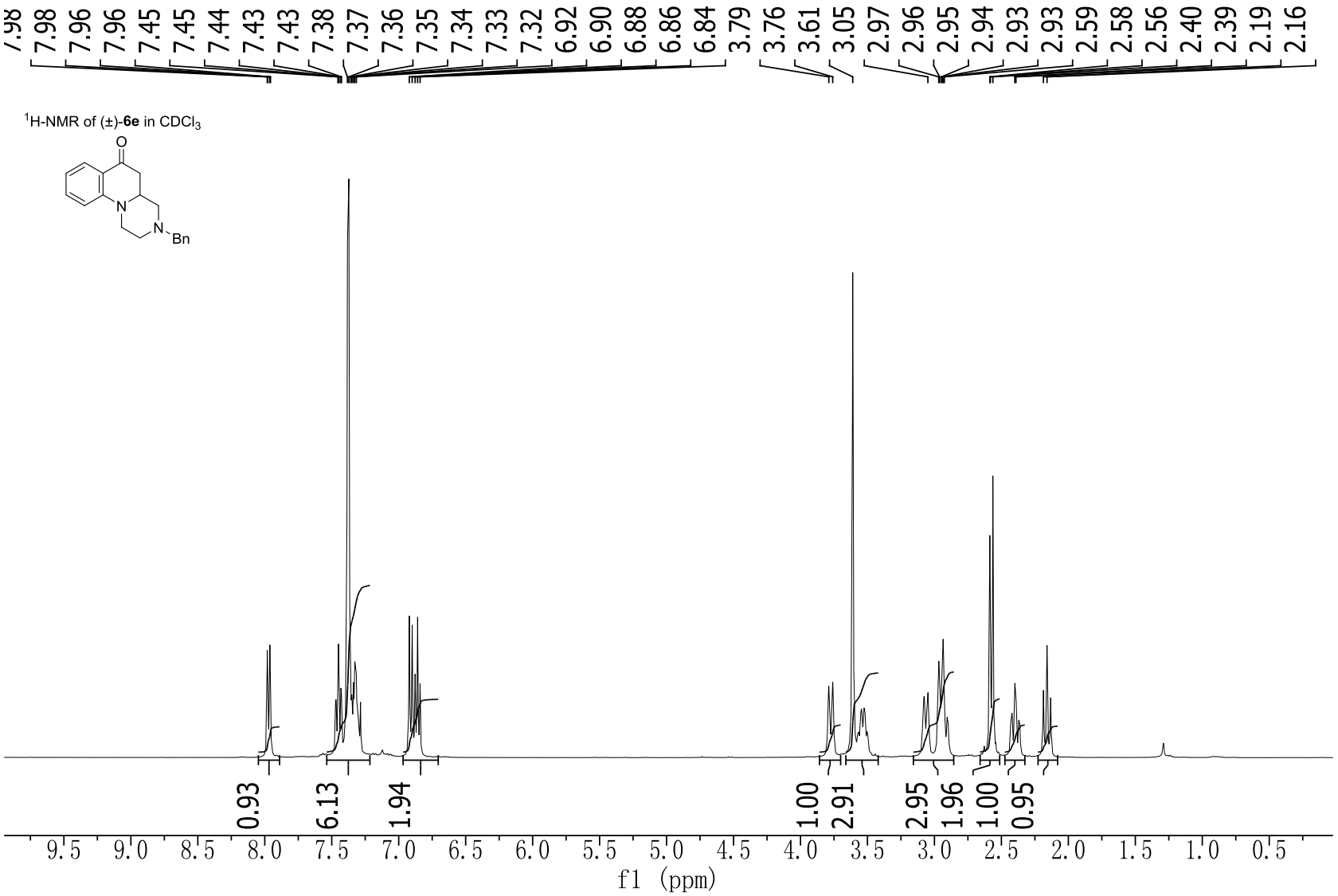

7.95
7.94
7.93
7.92
7.43
7.42
7.42
7.40
7.40
7.26
6.90
6.90
6.88
6.88
6.85
6.85
6.83
6.83
6.83
6.81
2.90
2.88
2.87
2.87
2.87
2.86
2.58
2.56
2.55
2.34
2.34
2.31
2.30
2.10
2.07
2.07
2.07
2.04
1H-NMR of (±)-6d in CDCl3
O
N
N
Me
1.00
1.05
1.02
1.04
1.08
1.00
0.99
2.06
2.05
4.17
1.06
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
f1 (ppm)

193.05
152.56
135.63
128.09
121.18
118.69
113.63
61.14
56.08
54.62
46.19
46.03
42.61

^{13}C-NMR of (±)-**6d** in $CDCl_3$





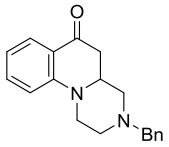

7.98
7.96
7.96
7.45
7.45
7.44
7.43
7.43
7.38
7.37
7.36
7.35
7.34
7.33
7.32
6.92
6.90
6.88
6.86
6.84
3.79
3.76
3.61
3.05
2.97
2.96
2.95
2.94
2.93
2.93
2.59
2.58
2.56
2.40
2.39
2.19
2.16
1H-NMR of (±)-6e in CDCl3
O
N
N
Bn
0.93
6.13
1.94
1.00
2.91
2.95
1.96
1.00
0.95
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

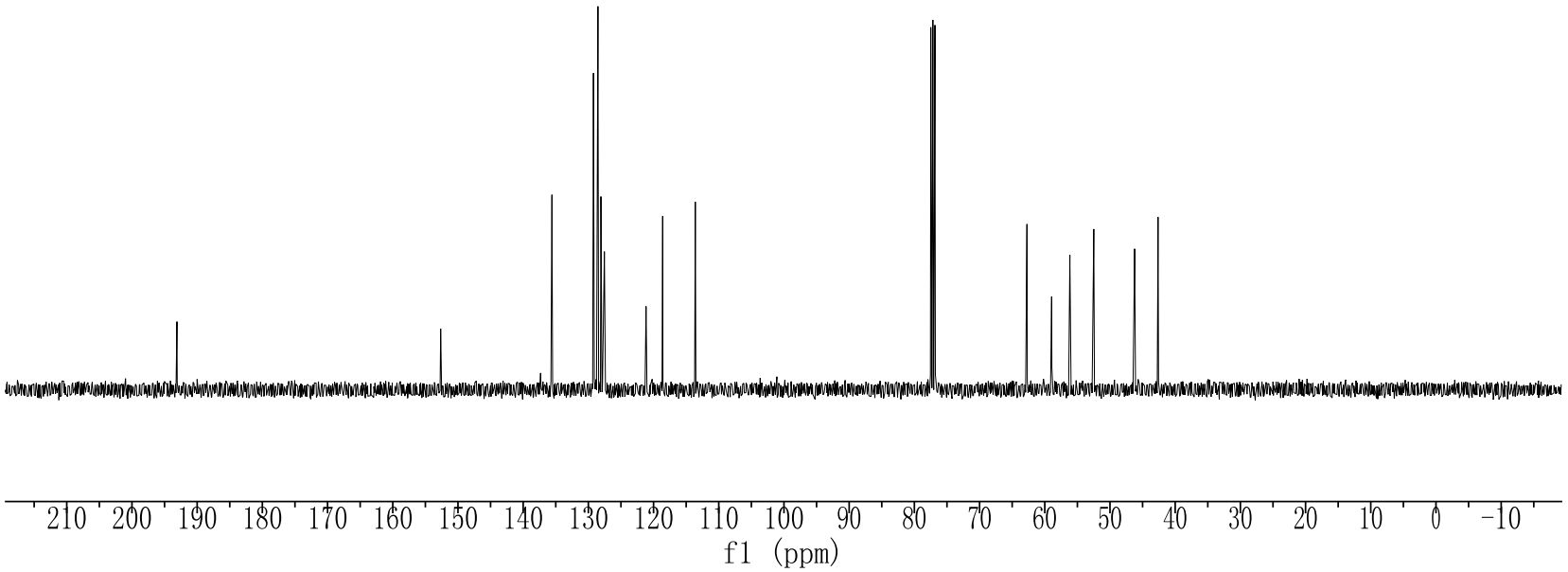
193.10

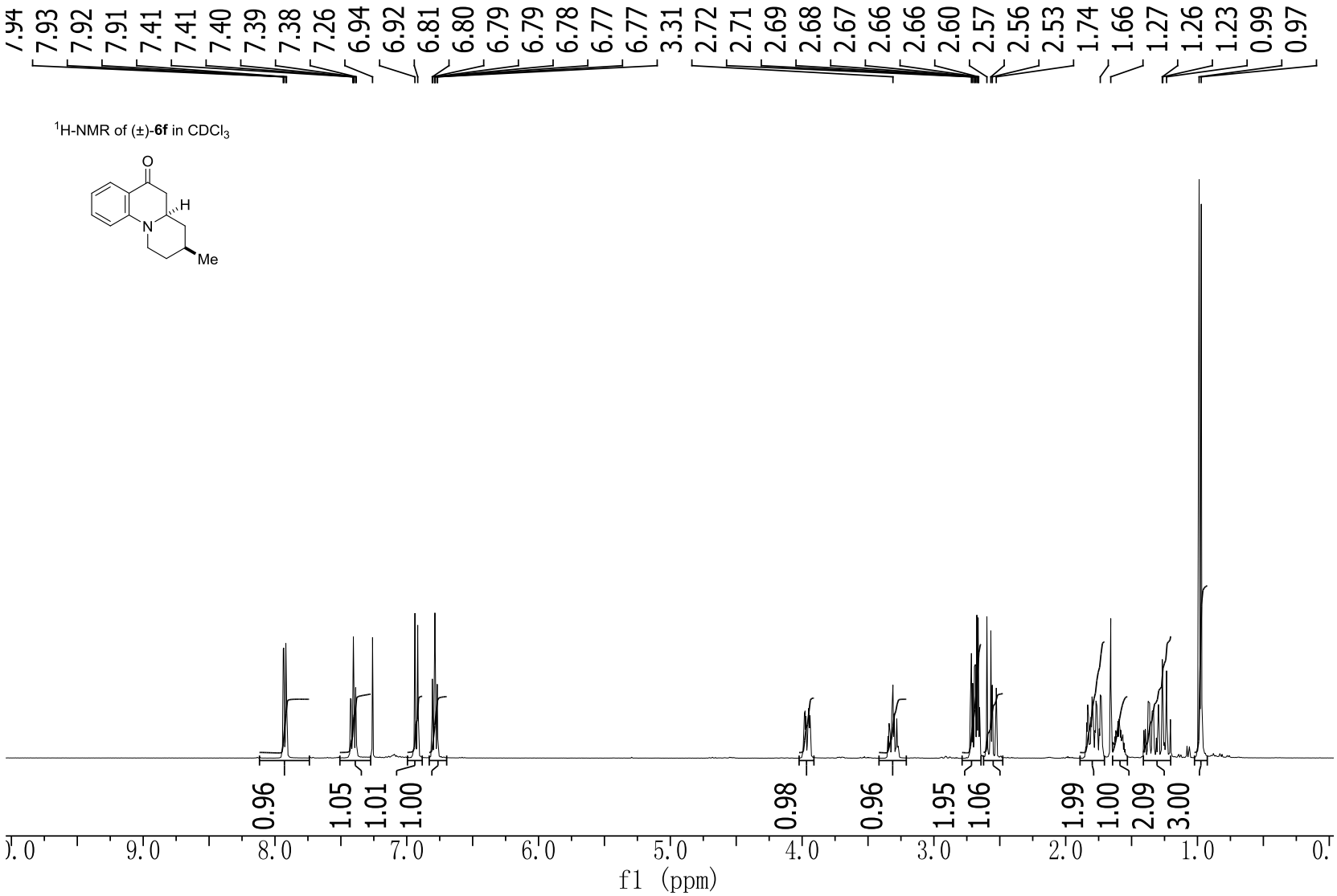
152.65
135.59
129.22
128.53
128.07
127.54
121.15
118.61
113.60

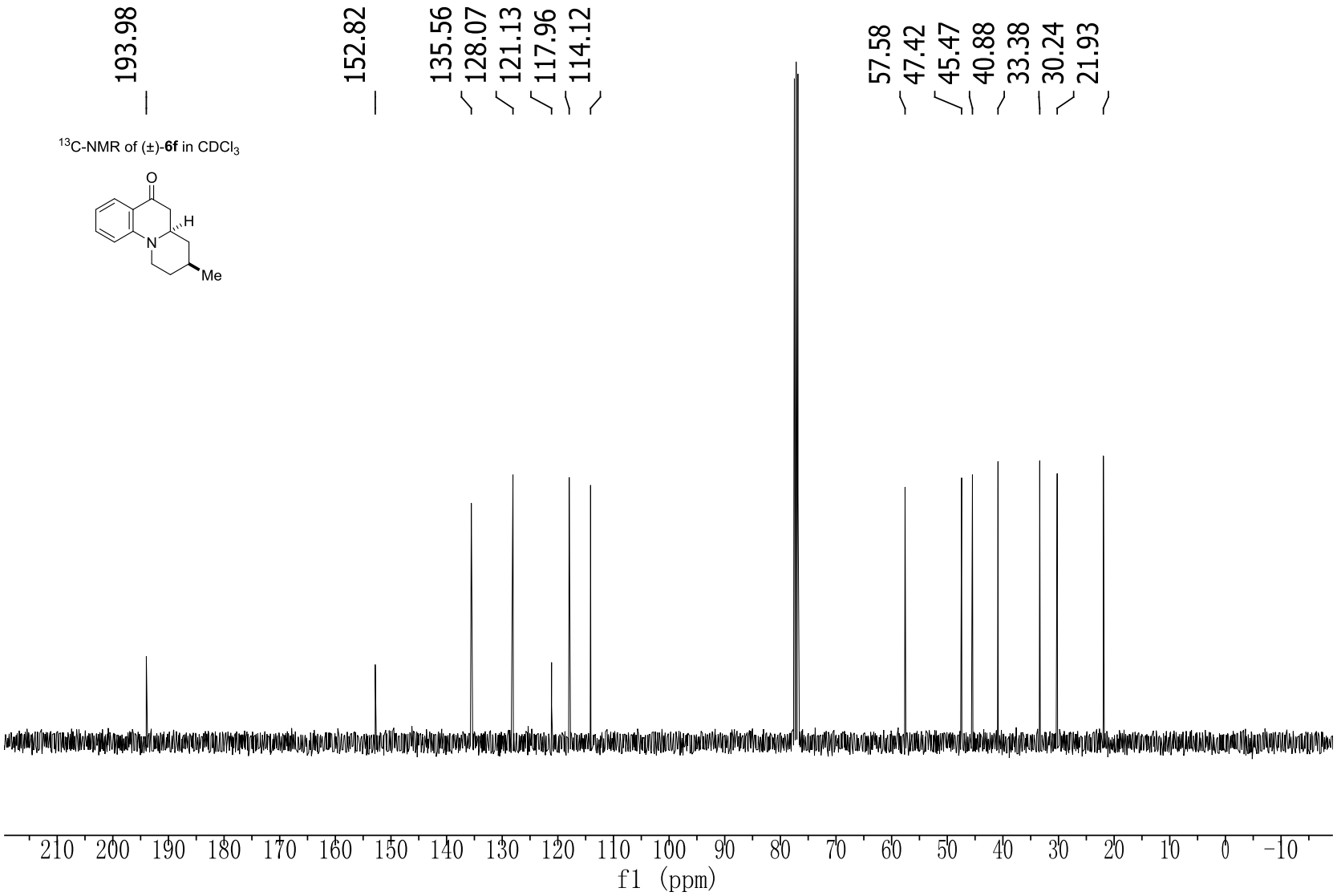
62.73
58.95
56.15
52.48
46.22
42.63

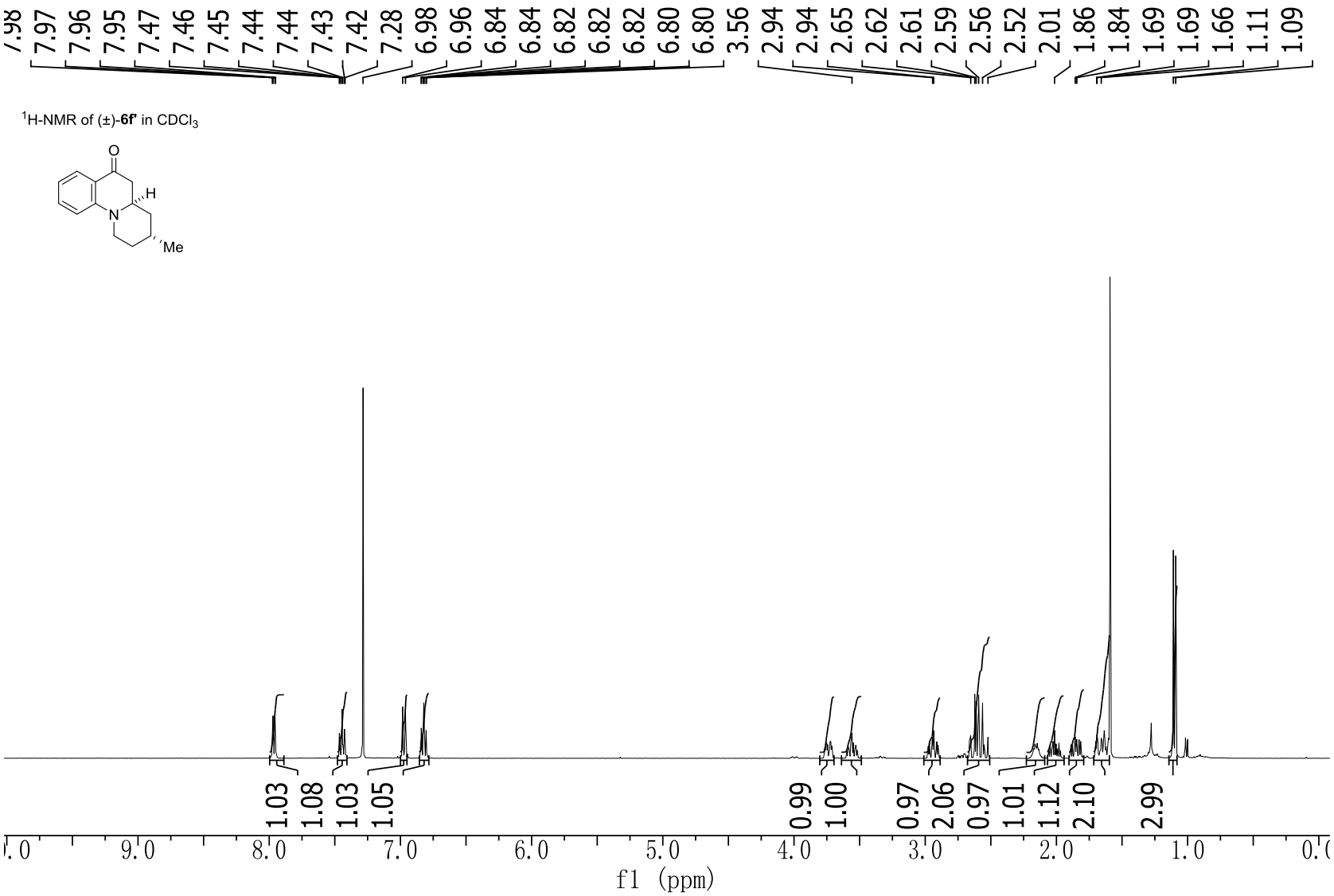
^{13}C-NMR of (±)-**6e** in $CDCl_3$

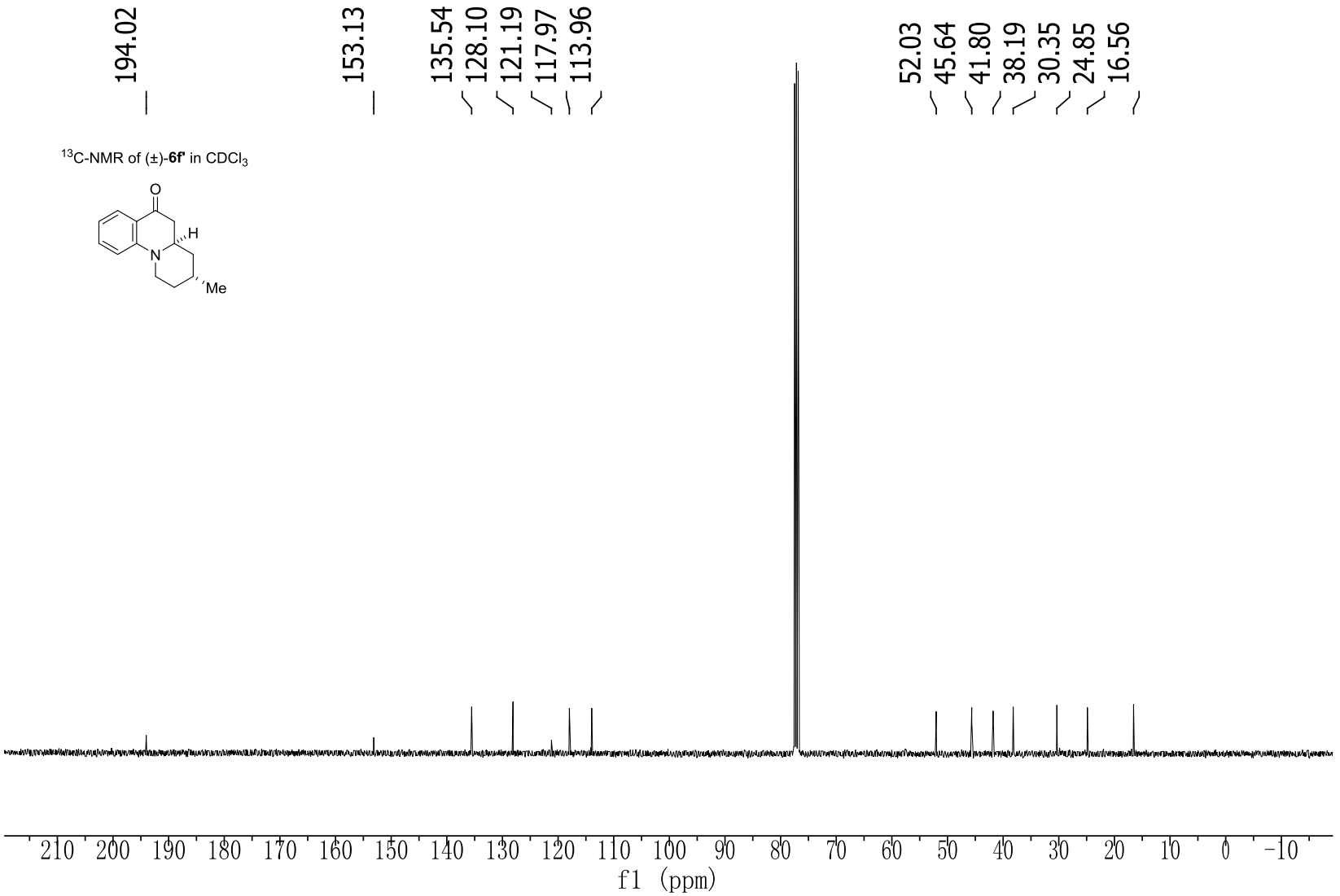


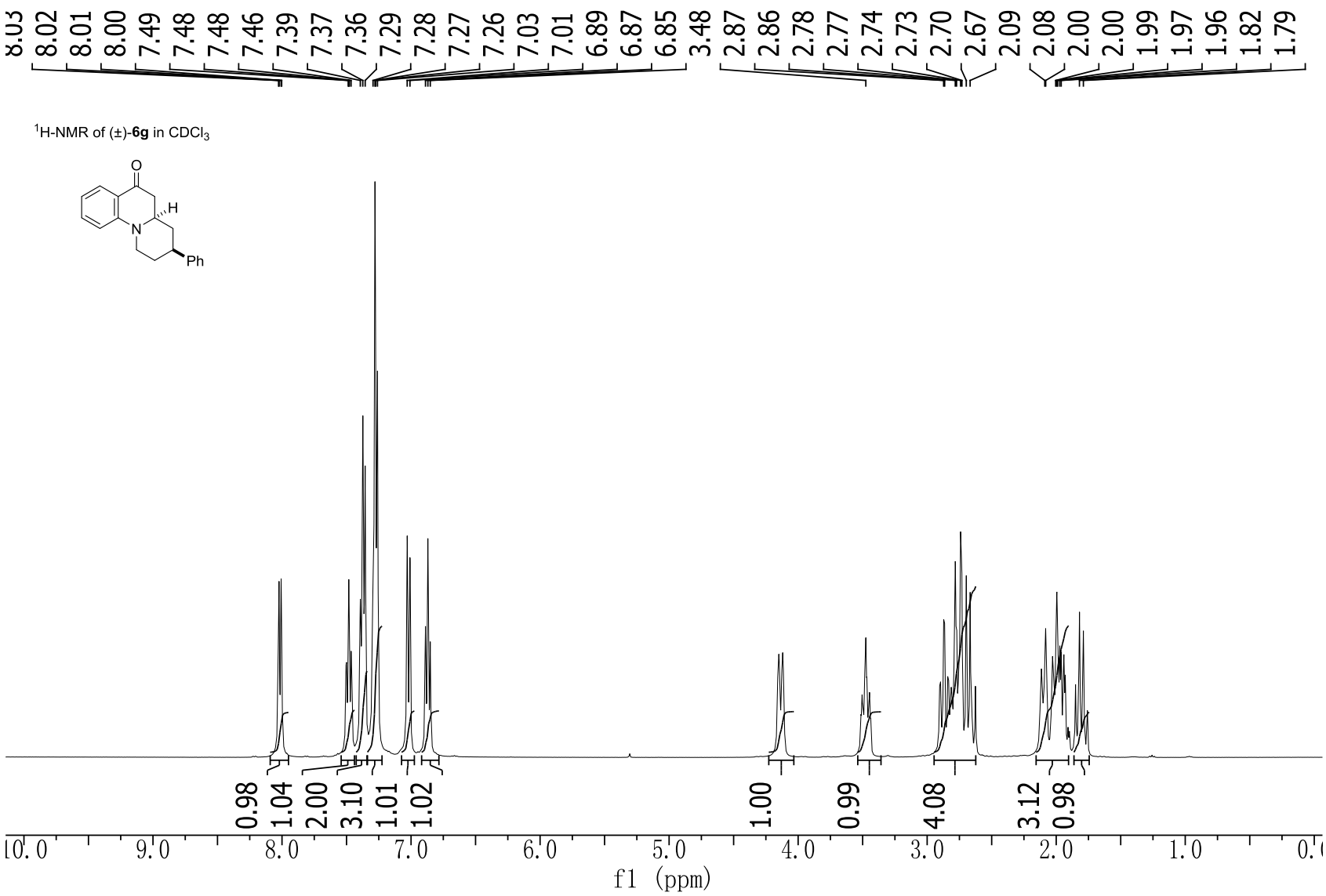


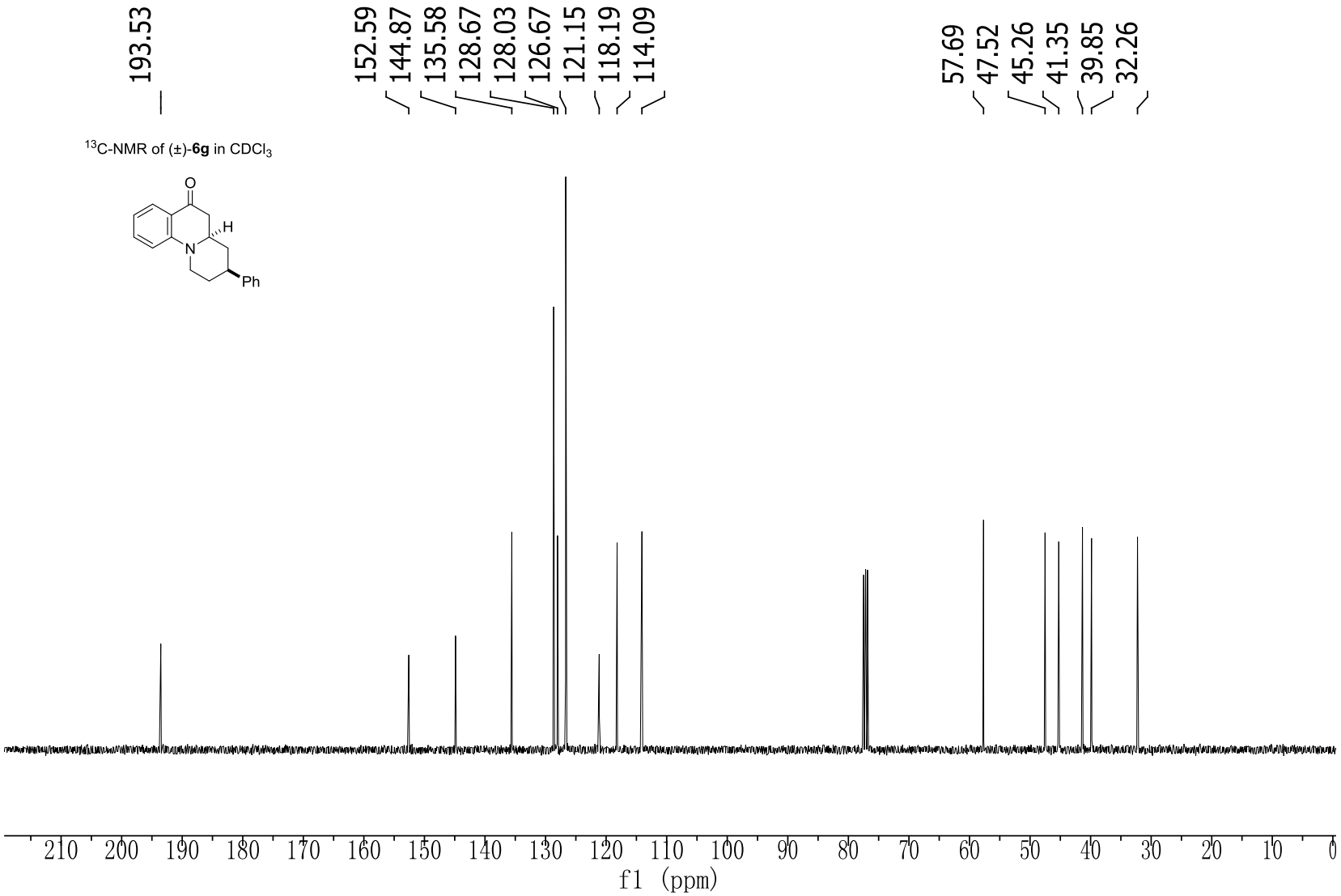

7.94
7.93
7.92
7.91
7.41
7.41
7.40
7.39
7.38
7.26
6.94
6.92
6.81
6.80
6.79
6.79
6.78
6.77
6.77
3.31
2.72
2.71
2.69
2.68
2.67
2.66
2.66
2.60
2.57
2.56
2.53
1.74
1.66
1.27
1.26
1.23
0.99
0.97
1H-NMR of (±)-6f in CDCl3
O
H
N
Me
0.96
1.05
1.01
1.00
0.98
0.96
1.95
1.06
1.99
1.00
2.09
3.00
f1 (ppm)

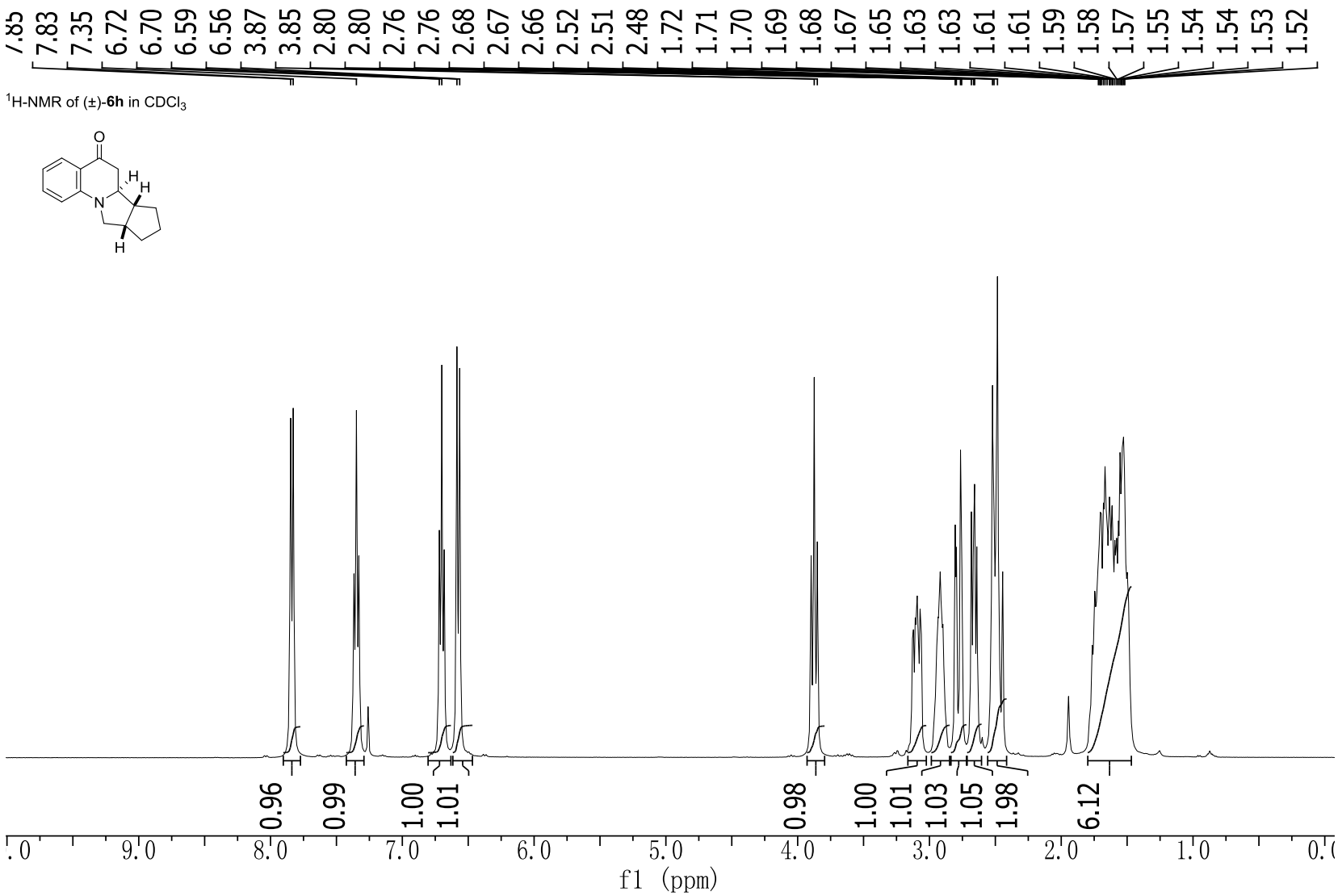

193.98
152.82
135.56
128.07
121.13
117.96
114.12
57.58
47.42
45.47
40.88
33.38
30.24
21.93
^{13}C-NMR of (±)-**6f** in $CDCl_3$
O
H
N
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.98
7.97
7.96
7.95
7.47
7.46
7.45
7.44
7.44
7.43
7.42
7.28
6.98
6.96
6.84
6.84
6.82
6.82
6.82
6.80
6.80
3.56
2.94
2.94
2.65
2.62
2.61
2.59
2.56
2.52
2.01
1.86
1.84
1.69
1.69
1.66
1.11
1.09
1H-NMR of (±)-6f' in CDCl3
O
H
N
Me
1.03
1.08
1.03
1.05
0.99
1.00
0.97
2.06
0.97
1.01
1.12
2.10
2.99
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
f1 (ppm)

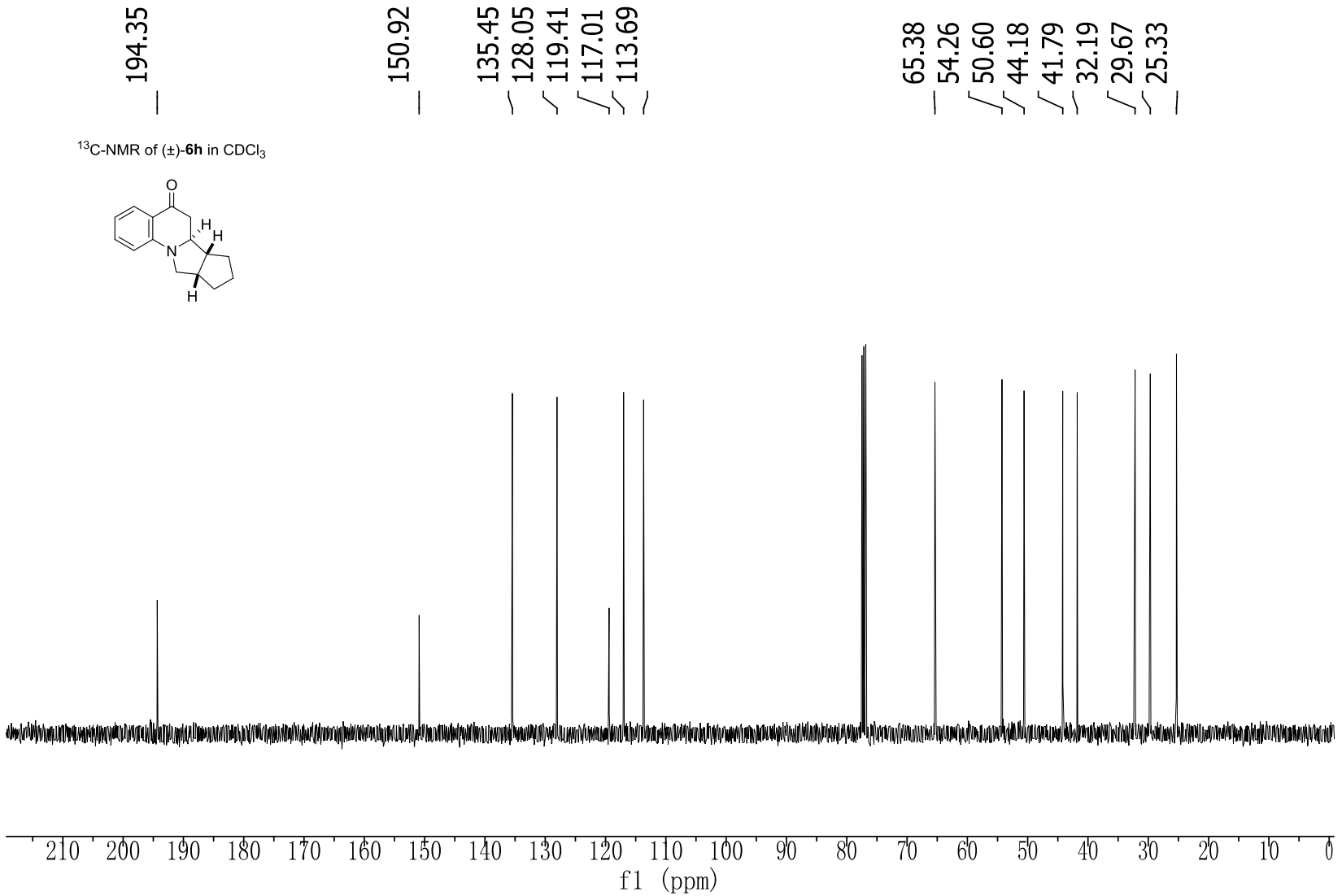

194.02
153.13
135.54
128.10
121.19
117.97
113.96
52.03
45.64
41.80
38.19
30.35
24.85
16.56
^{13}C-NMR of (±)-**6f'** in $CDCl_3$
O
H
N
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

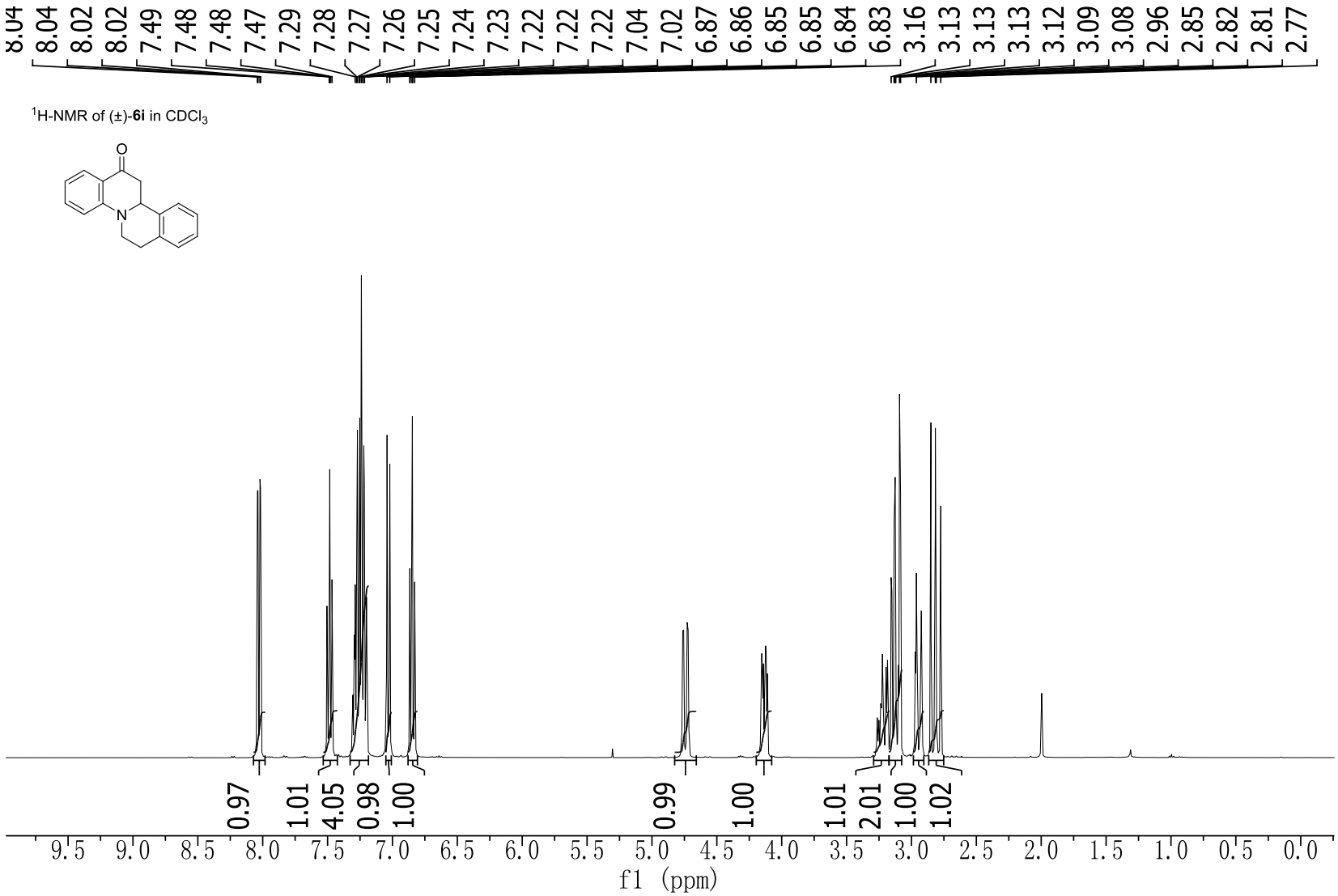

8.03
8.02
8.01
8.00
7.49
7.48
7.48
7.46
7.39
7.37
7.36
7.29
7.28
7.27
7.26
7.03
7.01
6.89
6.87
6.85
3.48
2.87
2.86
2.78
2.77
2.74
2.73
2.70
2.67
2.09
2.08
2.00
2.00
1.99
1.97
1.96
1.82
1.79
1H-NMR of (±)-6g in CDCl3
O
H
N
Ph
0.98
1.04
2.00
3.10
1.01
1.02
1.00
0.99
4.08
3.12
0.98
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
f1 (ppm)

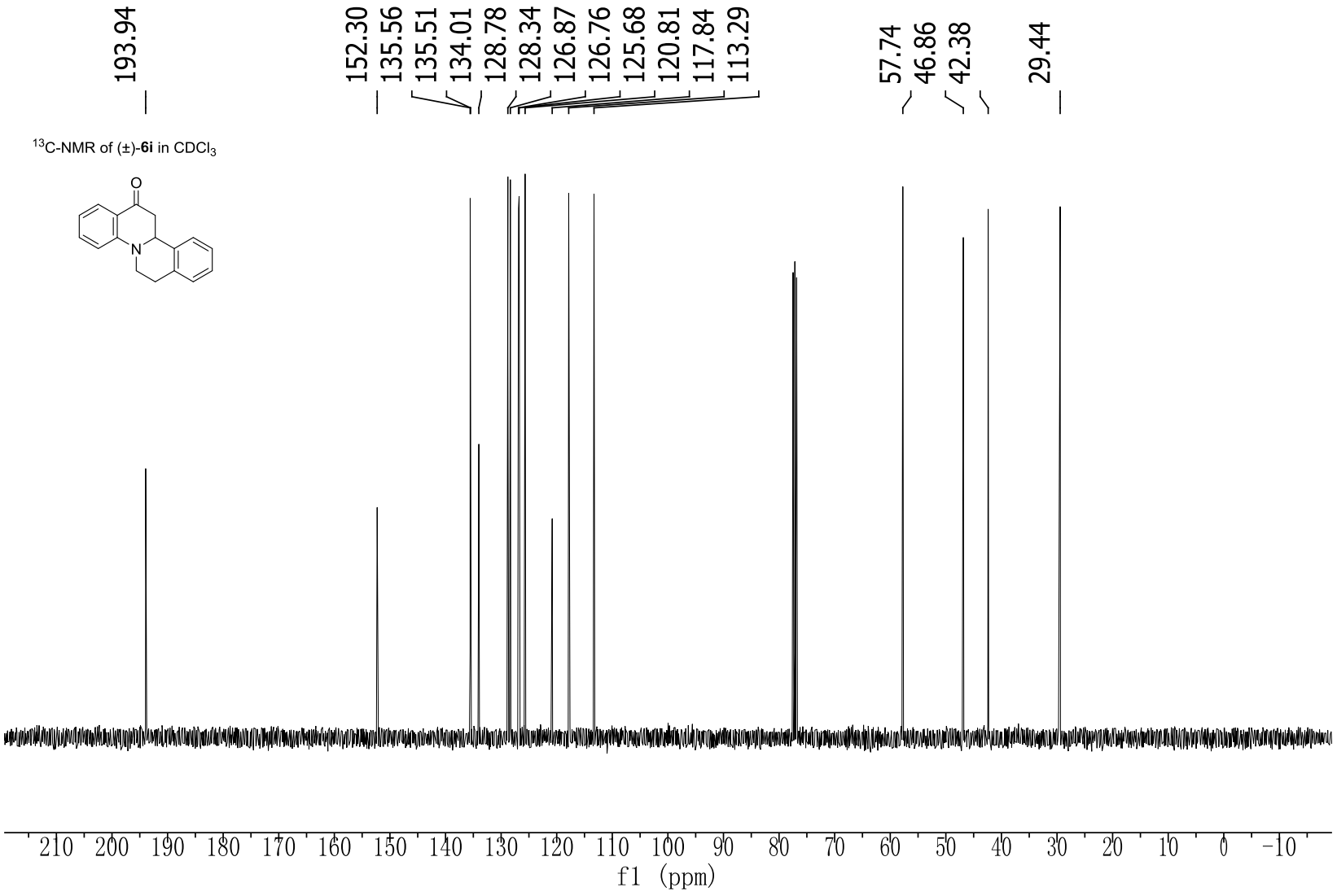

193.53
152.59
144.87
135.58
128.67
128.03
126.67
121.15
118.19
114.09
57.69
47.52
45.26
41.35
39.85
32.26
13C-NMR of (±)-6g in CDCl3
O
H
N
Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

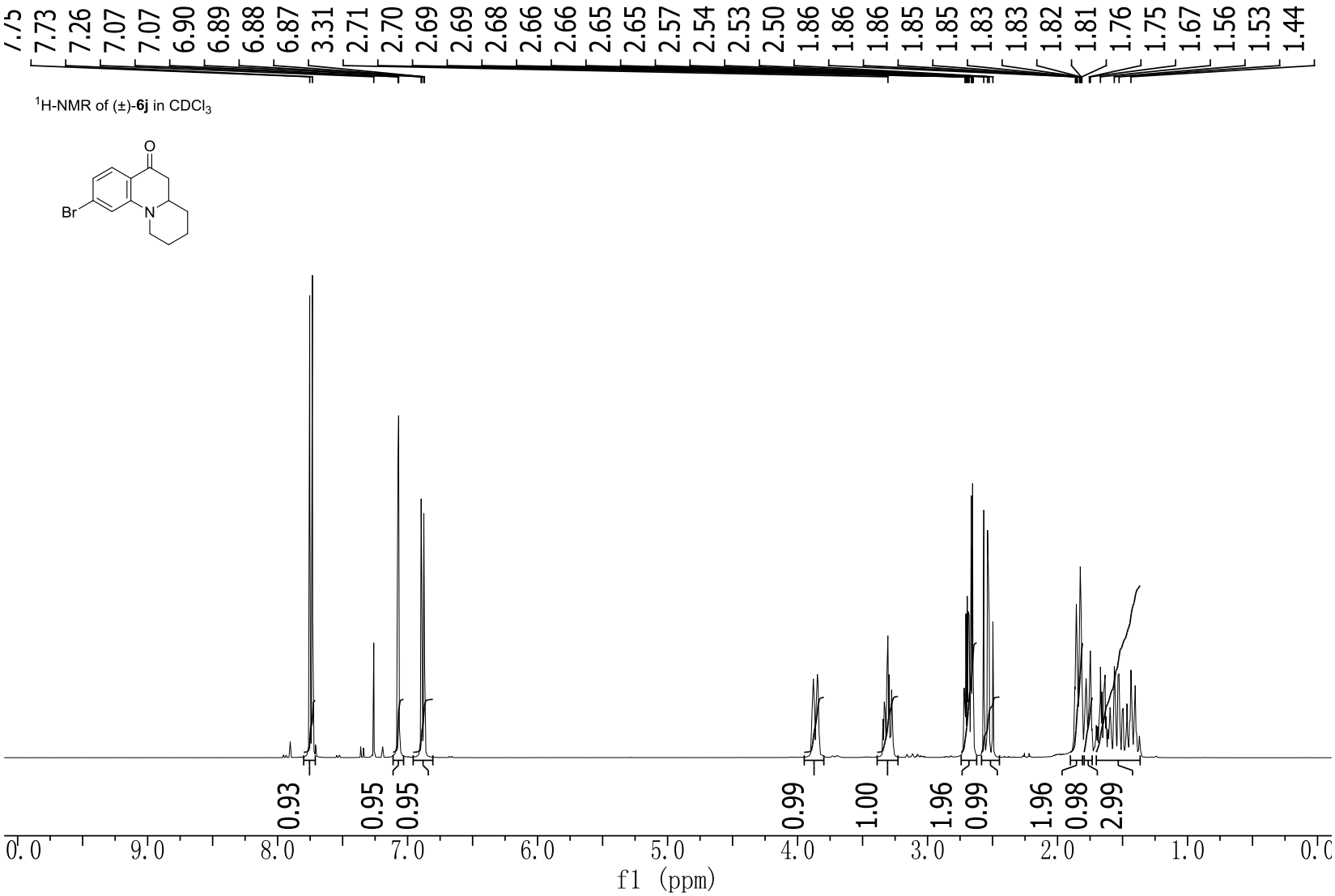


^{1}H-NMR of (±)-**6h** in $CDCl_3$

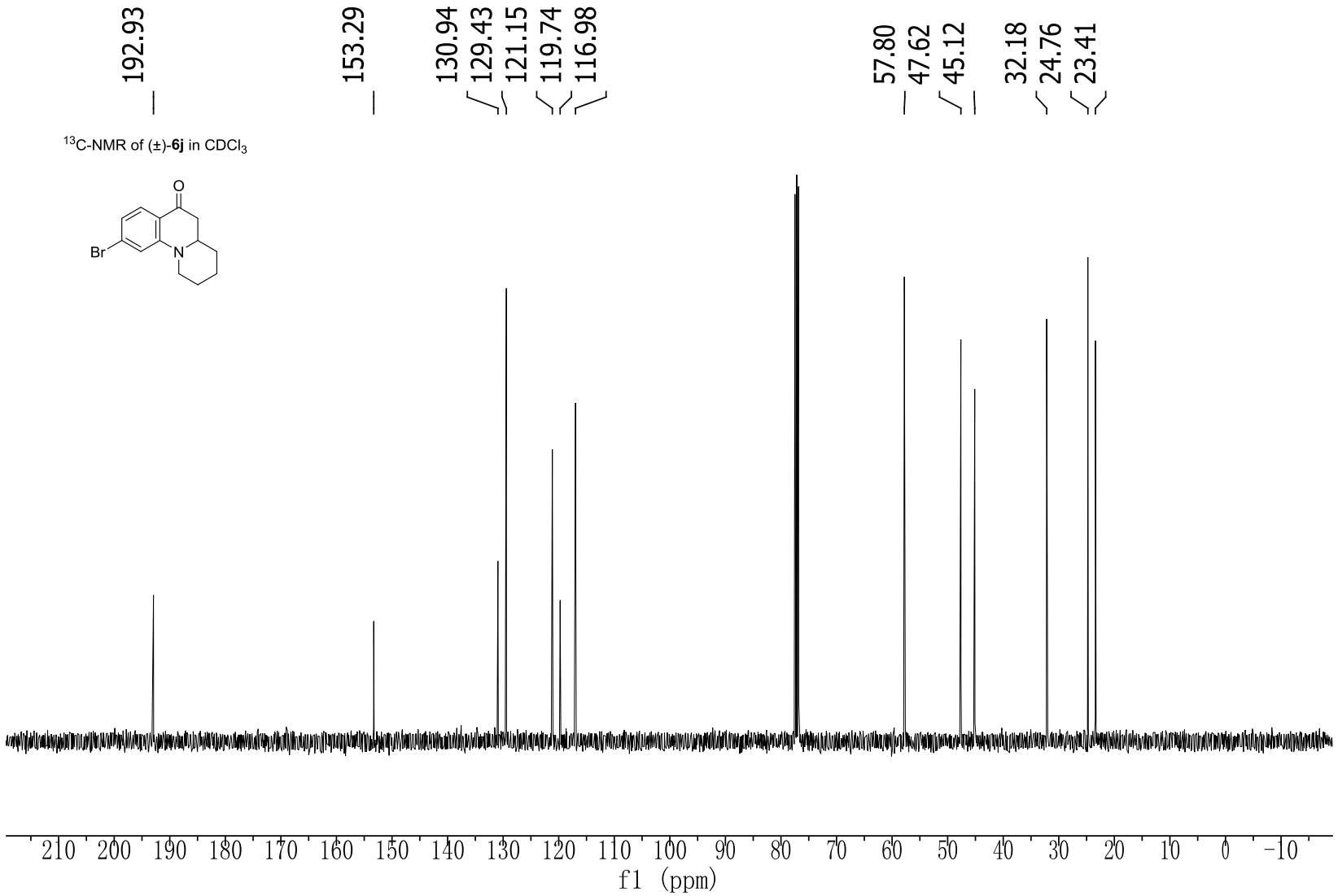

194.35
150.92
135.45
128.05
119.41
117.01
113.69
65.38
54.26
50.60
44.18
41.79
32.19
29.67
25.33
^{13}C-NMR of (±)-**6h** in $CDCl_3$
O
H
H
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

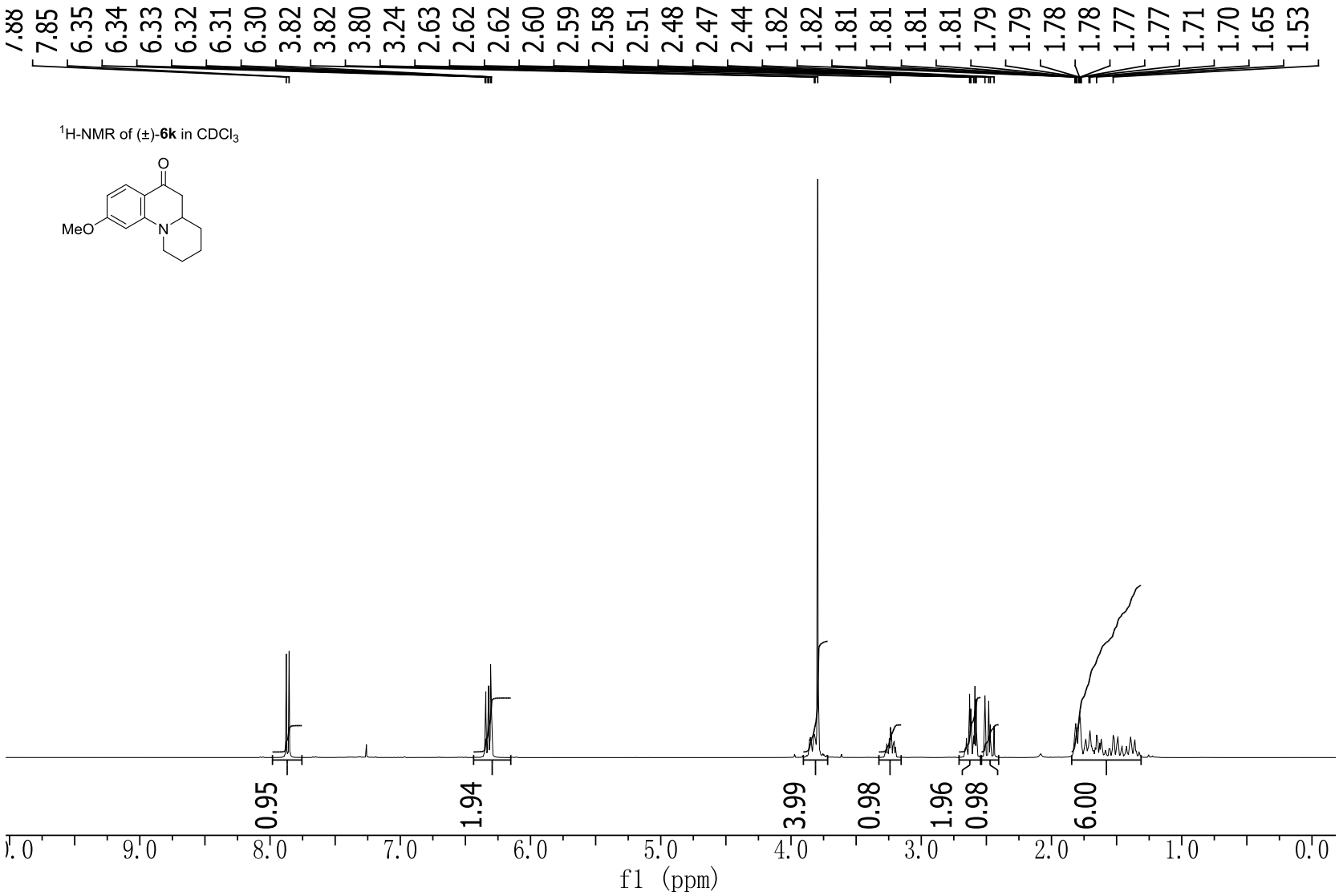

8.04
8.02
8.02
7.49
7.48
7.48
7.47
7.29
7.28
7.27
7.26
7.25
7.24
7.23
7.22
7.22
7.22
7.04
7.02
6.87
6.86
6.85
6.85
6.84
6.83
3.16
3.13
3.13
3.13
3.12
3.09
3.08
2.96
2.85
2.82
2.81
2.77
^{1}H-NMR of (±)-**6i** in $CDCl_3$
O
N
0.97
1.01
4.05
0.98
1.00
0.99
1.00
1.01
2.01
1.00
1.02
9.5 9.0 8.5 8.0 7.5 7.0 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)

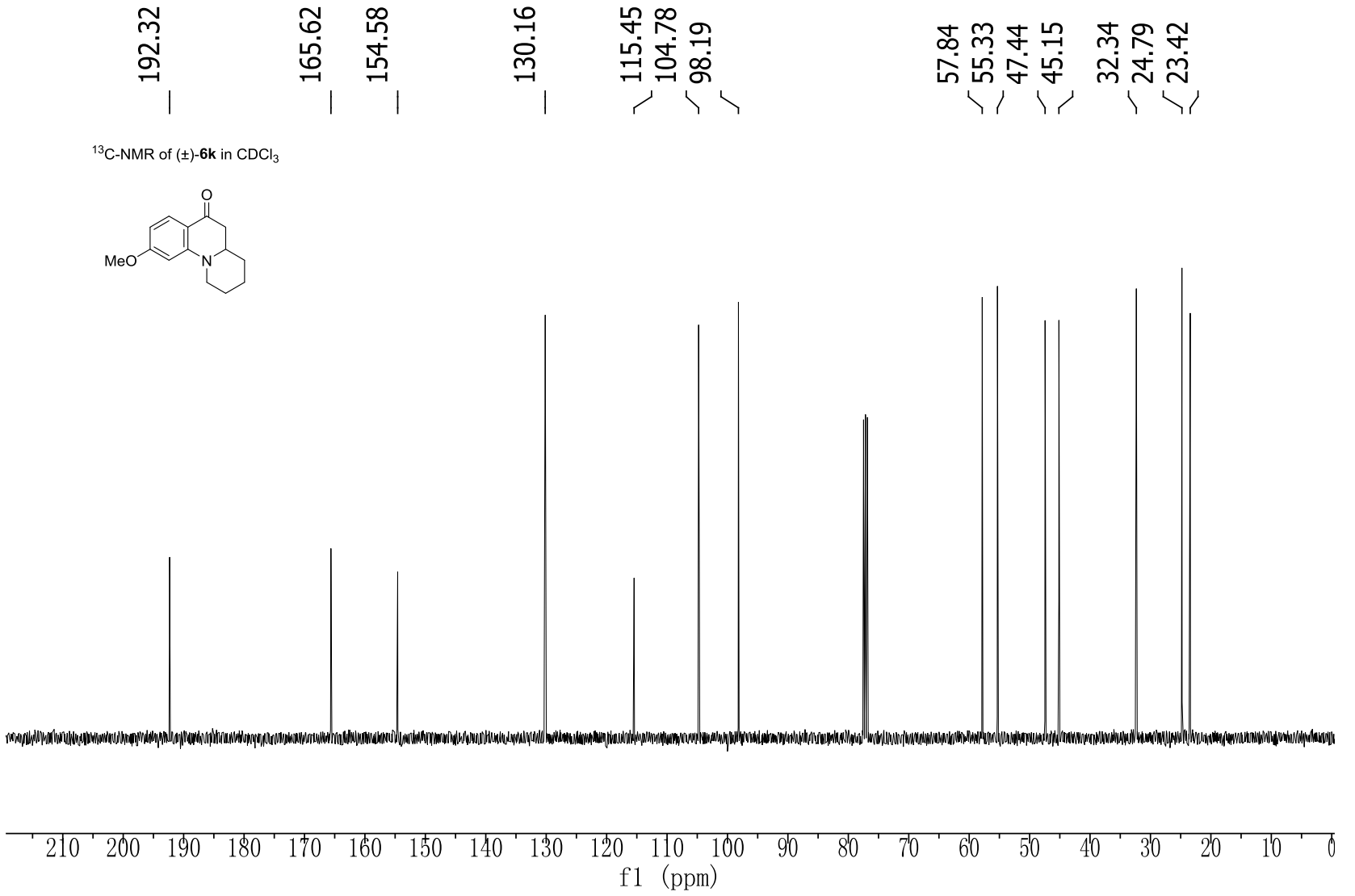

193.94
152.30
135.56
135.51
134.01
128.78
128.34
126.87
126.76
125.68
120.81
117.84
113.29
57.74
46.86
42.38
29.44
^{13}C-NMR of (±)-**6i** in $CDCl_3$
O
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

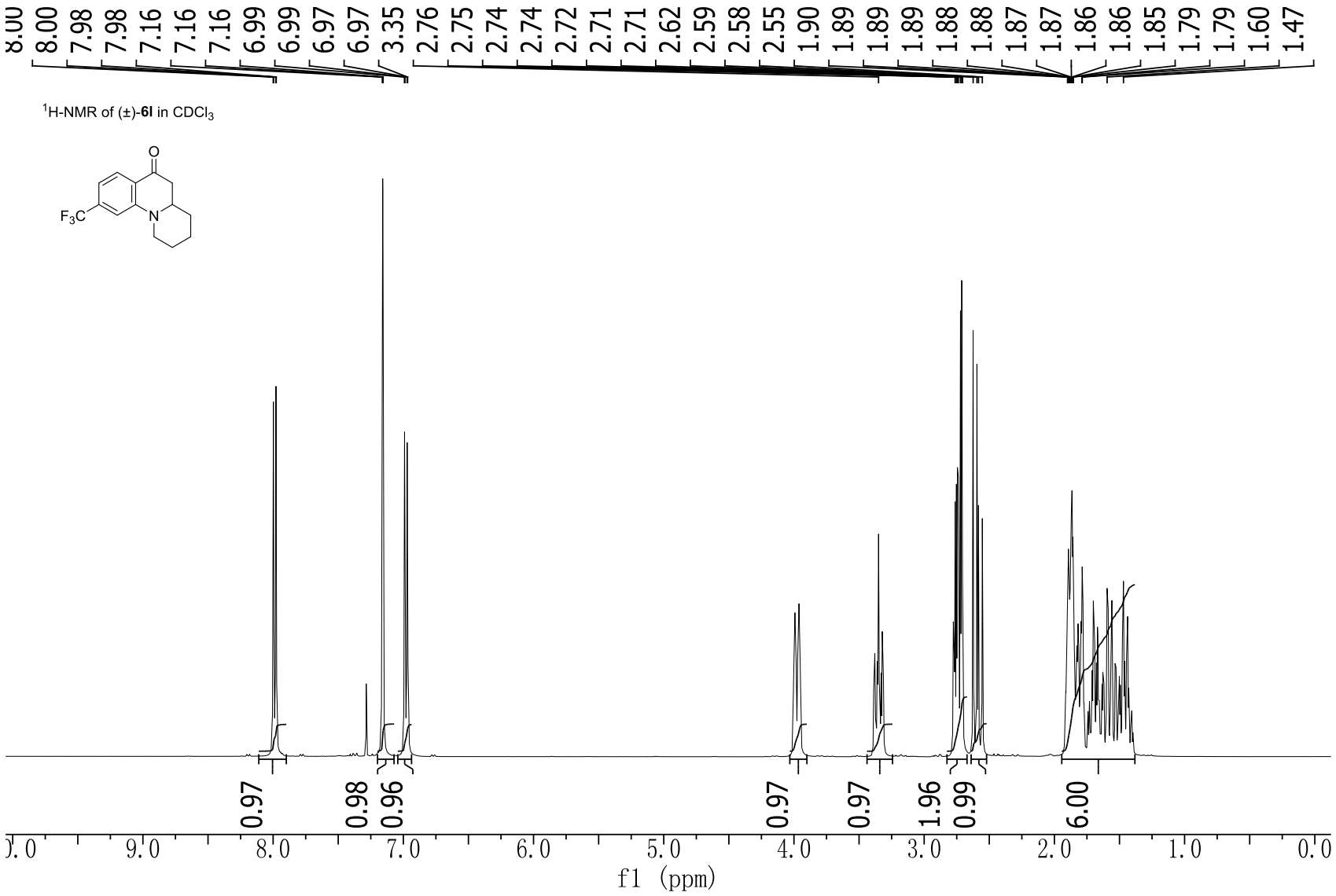


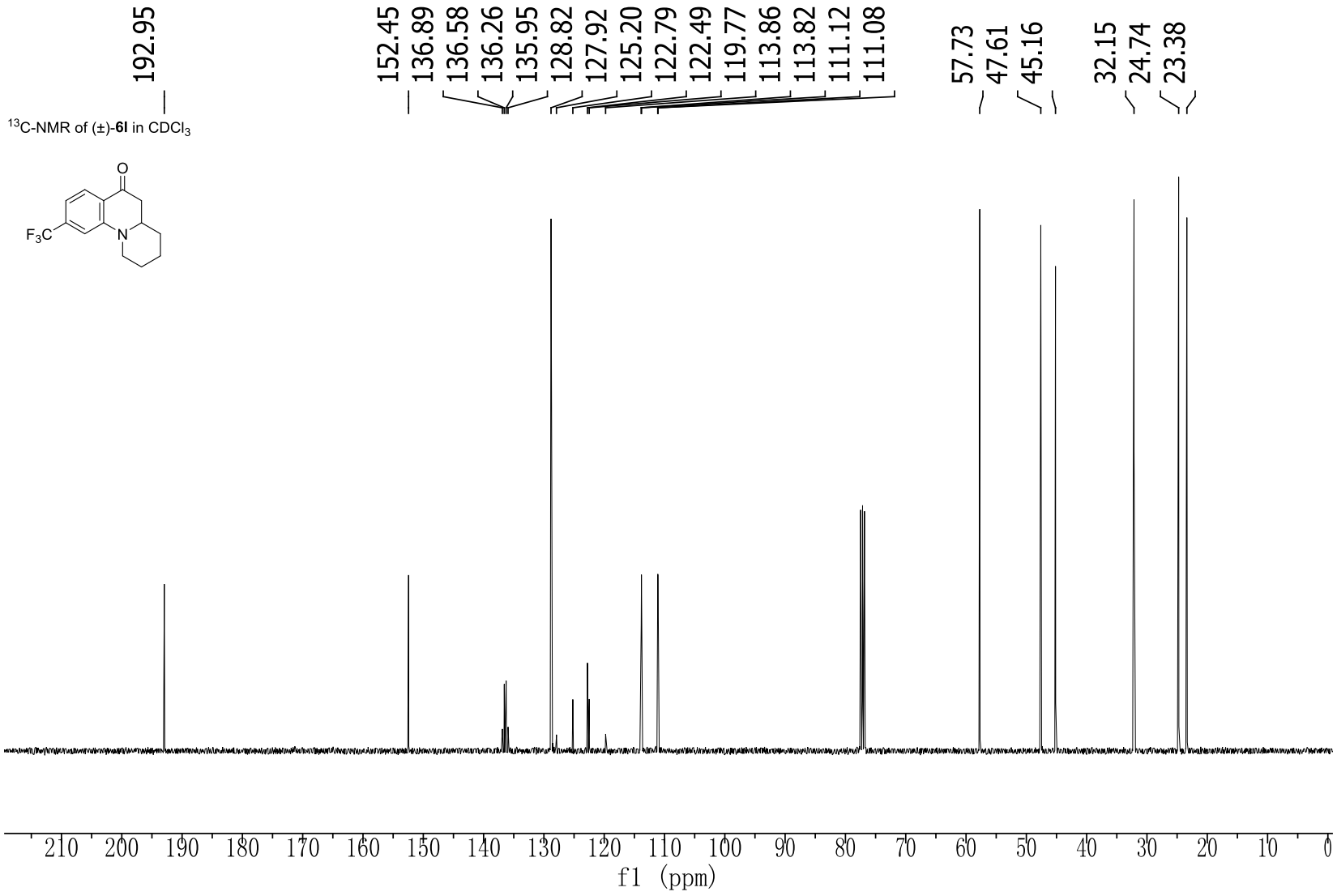
^{1}H-NMR of (±)-**6j** in $CDCl_3$

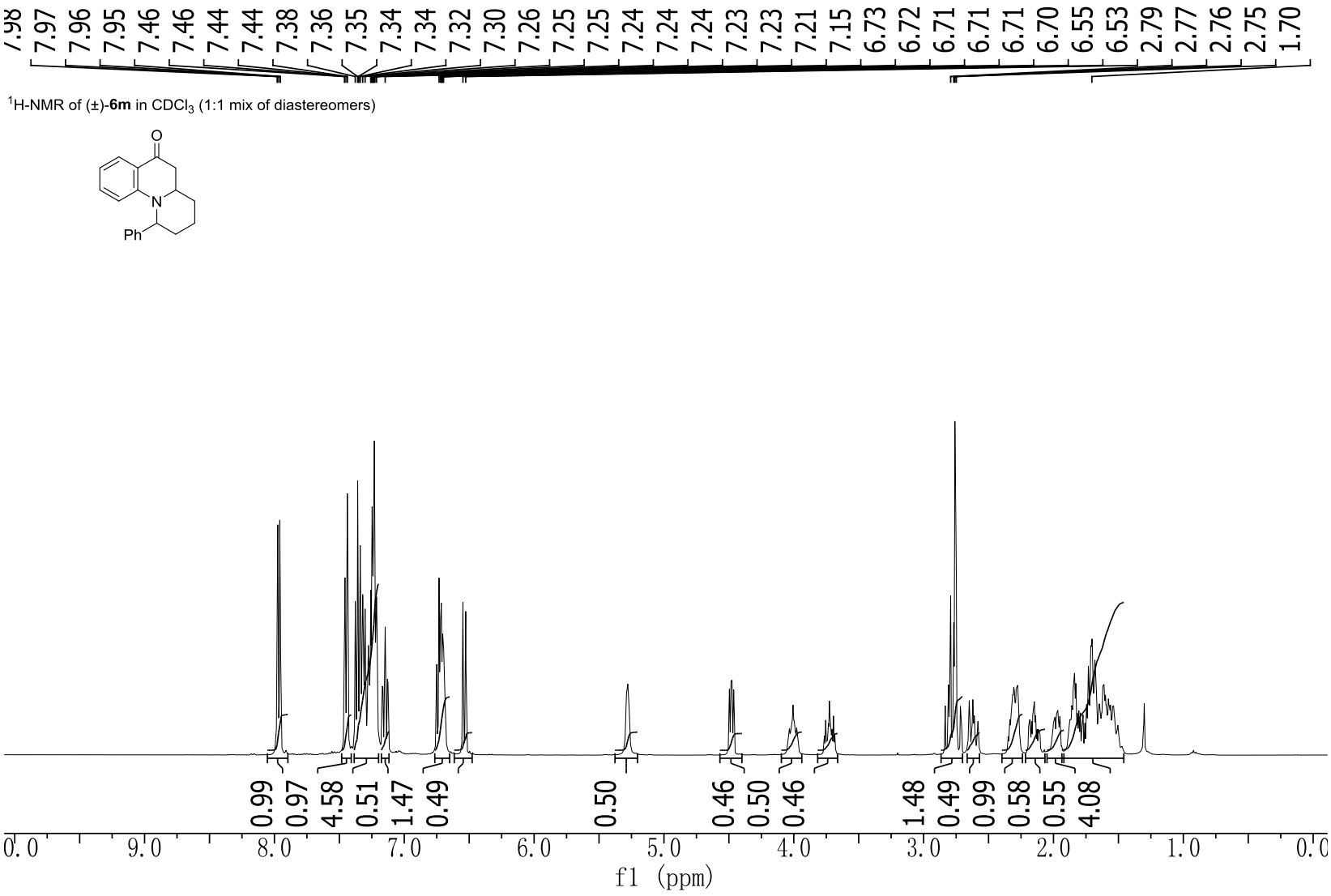

192.93
153.29
130.94
129.43
121.15
119.74
116.98
57.80
47.62
45.12
32.18
24.76
23.41
13C-NMR of (±)-6j in CDCl3
O
Br
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.88
7.85
6.35
6.34
6.33
6.32
6.31
6.30
3.82
3.82
3.80
3.24
2.63
2.62
2.62
2.60
2.59
2.58
2.51
2.48
2.47
2.44
1.82
1.82
1.81
1.81
1.81
1.81
1.79
1.79
1.78
1.78
1.77
1.77
1.71
1.70
1.65
1.53
^{1}H-NMR of (±)-**6k** in $CDCl_3$
O
MeO
N
0.95
1.94
3.99
0.98
1.96
0.98
6.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

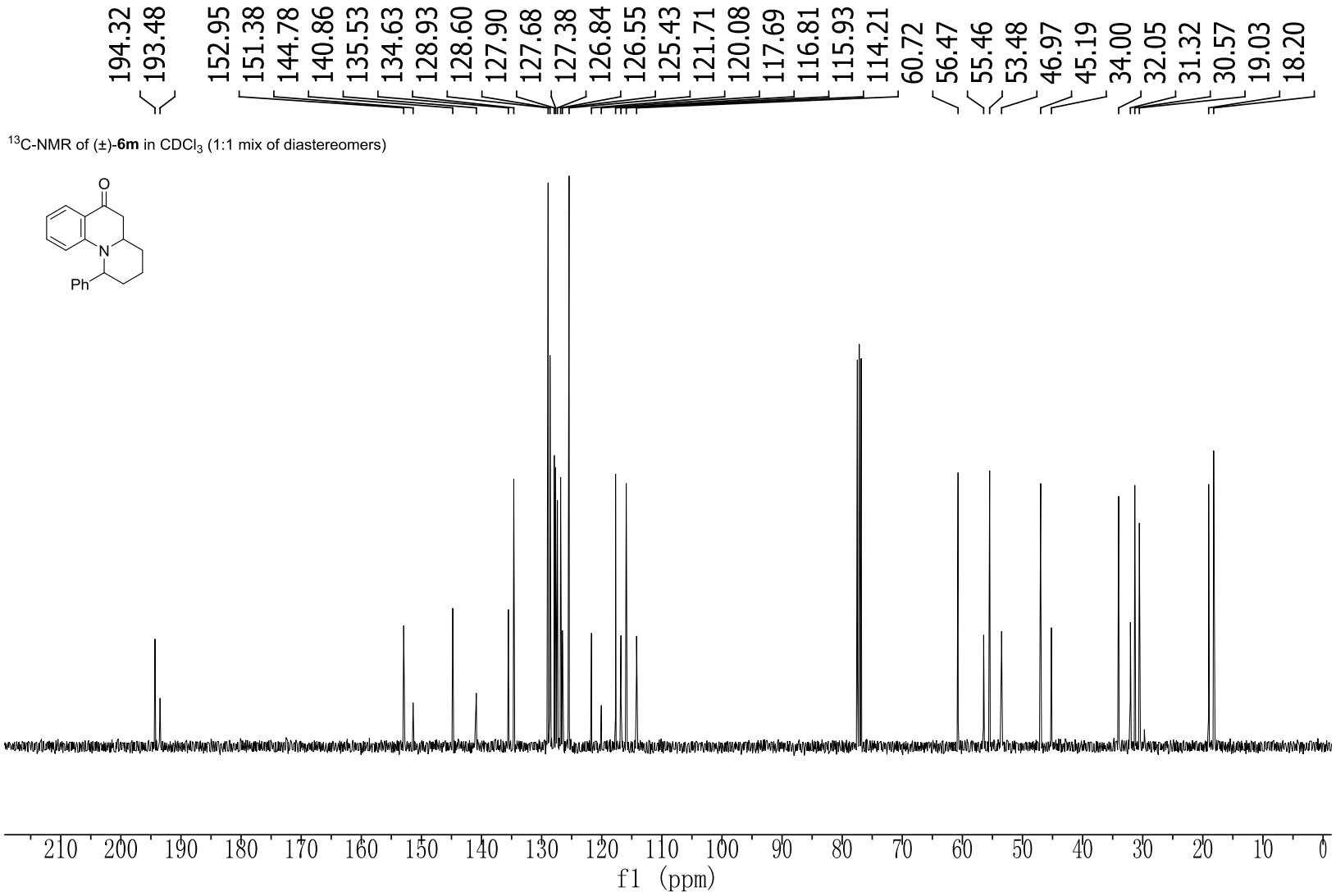

192.32
165.62
154.58
130.16
115.45
104.78
98.19
57.84
55.33
47.44
45.15
32.34
24.79
23.42
^{13}C-NMR of (±)-**6k** in $CDCl_3$
O
MeO
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.00
8.00
7.98
7.98
7.16
7.16
7.16
6.99
6.99
6.97
6.97
3.35
2.76
2.75
2.74
2.74
2.72
2.71
2.71
2.62
2.59
2.58
2.55
1.90
1.89
1.89
1.89
1.88
1.88
1.87
1.87
1.86
1.86
1.85
1.79
1.79
1.60
1.47
1H-NMR of (±)-6l in CDCl3
O
F3C
N
0.97
0.98
0.96
0.97
0.97
1.96
0.99
6.00
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


192.95
152.45
136.89
136.58
136.26
135.95
128.82
127.92
125.20
122.79
122.49
119.77
113.86
113.82
111.12
111.08
57.73
47.61
45.16
32.15
24.74
23.38
^{13}C-NMR of (±)-**6l** in $CDCl_3$
O
F_3C
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



^{1}H-NMR of (±)-**6m** in $CDCl_3$ (1:1 mix of diastereomers)



^{13}C-NMR of (±)-**6m** in $CDCl_3$ (1:1 mix of diastereomers)