

Construction of azaspirocyclic skeletons mediated by the carbonyl of Weinreb amide: formal total synthesis of (±)-cephalotaxine

Jian Zhang,^{*a,b} Jianyin Liu,^a Yuxue Fan,^a Huili Ding,^a Tianfu Liu,^a Shanshan Li,^a
Minghua Jiang^a and Lu Liu^a

^a*School of Pharmacy, Gansu University of Chinese Medicine, Lanzhou 730000, P.R. China.* ^b*Key Laboratory of Chemistry and Quality for TCM of the College of Gansu Province, Lanzhou 730000, P.R. China.*

* Correspondence author: zhangjian@gszy.edu.cn

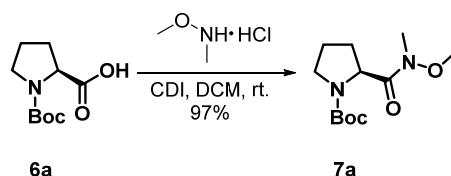
Table of Contents

I. General Information.....	1
II. Experimental Procedures and Spectroscopic Data of Compounds	1-6
III. HPLC Spectra of 9a and 9b.....	7-8
IV. ¹H and ¹³C NMR Spectra of Synthesized Compounds.....	9-30

General procedure

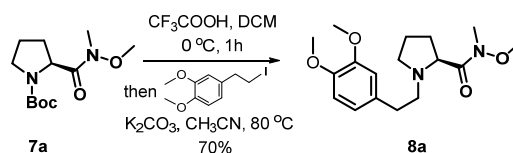
All solvents were redistilled prior to use and anhydrous solvents were treated using standard techniques. All reactions were monitored by thin-layer chromatography using high silica gel GF pre-coated plates (0.25 mm). IR spectra were recorded on a Thermo Nicolet 6700 FT-IR Spectrometer using KBr disks and are reported in frequency of absorption (cm^{-1}). HRMS were acquired by a Waters Micromass Q-ToF MicroTM instrument using the ESI technique. ¹H and ¹³C NMR spectra were recorded on a Bruker AM-400 spectrometer with TMS as an internal standard and CDCl₃ as solvent. Flash column chromatography was conducted on silica gel (200–300 mesh).

Synthesis of compound 7a



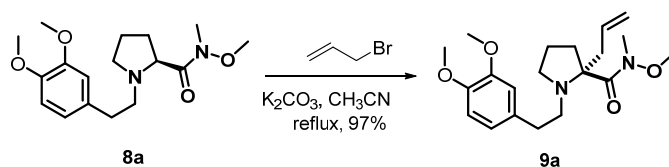
To a solution of N-Boc proline 6a (1.9 g, 8.84 mmol) in DCM (20 mL) was added 1,1'-Carbonyldiimidazole (1.72 g, 10.61 mmol) slowly. The reaction was stirred at room temperature for 1 h. Then N,O-dimethylhydroxylamine hydrochloride (1.035 g, 10.61 mmol) was added and stirred for 3 h. After completion of reaction, water (5 mL) was added and stirred. The organic layer was treated with 1% HCl solution (3 mL) and water (4 mL), dried over Na₂SO₄, filtered and concentrated. The crude product was purified by silica gel column chromatography (PET/EtOAc, 5:1) to give 7a (2.207 g, 97% yield) as a light yellow oil. R_f = 0.25 (petroleum ether : EtOAc = 1:1); IR (film): ν_{max} 2975, 2937, 2879, 1698, 1399, 1164, 1122, 999 cm^{-1} ; ¹H NMR (400 MHz, CDCl₃) δ : 1.36 (s, 5H), 1.40 (s, 4H), 1.76-1.96 (m, 3H), 2.08-2.19 (m, 1H), 3.14 (s, 3H), 3.34-3.45 (m, 1H), 3.47-3.55 (m, 1H), 3.67 (s, 2H), 3.73 (s, 1H), 4.53-4.57 (m, 0.52H), 4.63-4.66 (m, 0.46H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ : 23.3, 23.9, 28.3, 28.4, 29.5, 30.4, 32.2, 32.3, 46.5, 46.8, 56.4, 56.7, 61.1, 61.2, 79.2, 79.4, 153.7, 154.3, 173.2, 173.7 ppm; HRMS (ESI) m/z calcd. for C₁₂H₂₂N₂O₄Na (M+Na)⁺ : 281.1477, found: 281.1467.

Synthesis of compound 8a



To a solution of 7a (472 mg, 1.83 mmol) in dichloromethane (5 mL) was added trifluoroacetic acid (0.5 mL). The reaction mixture was stirred for 1 h at 0 °C. The mixture was concentrated in vacuo. The crude product was then dissolved in acetonitrile (10 mL) and K₂CO₃ (631 mg, 4.58 mmol) was added. Then the iodide (1.07 g, 3.66 mmol) was added to the slurry of K₂CO₃ in acetonitrile. The reaction mixture was refluxed for 10 h at 80 °C, cooled and concentrated in vacuo. The residue was then extracted with EtOAc (5×10 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated. The crude product was purified by silica gel column chromatography (PET/EtOAc, 5:1) to give 8a (410 mg, 70% yield) as a yellow oil. R_f = 0.75 (DCM : MeOH = 10:1); IR (film): ν_{max} 2938, 2834, 1668, 1590, 1516, 1463, 1261, 1156, 1029 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ: 1.77-1.85 (m, 2H), 1.91-1.97 (m, 1H), 2.08-2.13 (m, 1H), 2.36 (q, 1H, J = 8.4 Hz), 2.47-2.54 (m, 1H), 2.74 (t, 2H, J = 8.0 Hz), 2.83-2.90 (m, 1H), 3.15 (s, 3H), 3.30 (td, 1H, J = 8.4, 2.8 Hz), 3.48 (t, 1H, J = 7.6 Hz), 3.63 (s, 3H), 3.80 (s, 3H), 3.82 (s, 3H), 6.69-6.75 (m, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ: 23.1, 29.1, 32.5, 35.0, 53.3, 55.8, 55.8, 56.8, 61.3, 63.6, 111.2, 112.1, 120.4, 133.1, 147.2, 148.7, 175.0 ppm; HRMS (ESI) m/z calcd. for C₁₇H₂₇N₂O₄ (M+H)⁺ : 323.1971, found: 323.1973.

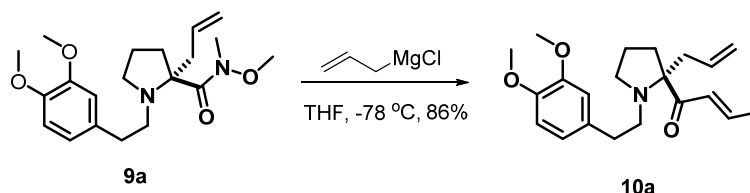
Synthesis of compound 9a



A solution of 8a (853 mg, 2.65 mmol) in acetonitrile (15 mL) was added to a slurry of K₂CO₃ (805 mg, 5.83 mmol) in acetonitrile (5 mL). Then the allyl bromide (0.47 mL, 5.3 mmol) was added to the solution. The reaction mixture was refluxed for 11 h at 80 °C. The reaction mixture was cooled to room temperature, filtered and concentrated by rotary evaporation. The crude product was purified by silica gel column chromatography (DCM/MeOH, 50:1) to give 9a (935 mg, 97% yield) as a light yellow oil. R_f = 0.50 (DCM : MeOH = 10:1); IR (film): ν_{max} 2936, 2833, 1647, 1590, 1515, 1463, 1262, 1156, 1029 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ: 1.75-1.81 (m, 2H), 1.88-1.95 (m, 1H), 2.13 (m, 1H), 2.27 (dd, 1H, J = 13.6, 7.6 Hz), 2.66-2.80 (m, 5H), 3.02-3.11 (m, 2H), 3.13 (s, 3H), 3.59 (s, 3H), 3.83 (s, 3H), 3.85 (s, 3H), 5.00-5.05 (m, 2H), 5.77-5.88 (m, 1H), 6.69-6.71 (m, 2H), 6.75 (d, 1H, J = 8.4 Hz) ppm; ¹³C NMR (100 MHz, CDCl₃) δ: 22.7, 32.9, 34.2, 35.6, 37.5, 50.9, 51.0, 55.8,

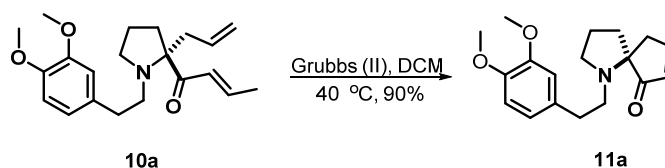
55.9, 60.1, 70.7, 111.1, 112.0, 117.1, 120.5, 133.4, 135.9, 147.2, 148.7, 175.6 ppm; HRMS (ESI) m/z calcd. for $C_{20}H_{31}N_2O_4$ (M+H)⁺ : 363.2284, found: 363.2267.

Synthesis of compound 10a



To a solution of 9a (288 mg, 0.80 mmol) in dry THF (5 mL) was added a 1.0 M solution of allylmagnesium chloride in THF (2.40 mL, 2.40 mmol) maintained under inert atmosphere at -78 °C. The reaction mixture was stirred for 0.5 h. The mixture was quenched with saturated NH_4Cl (1 mL) solution. The aqueous layer was extracted with EtOAc and the combined organic phases were washed with brine (1×10 mL), dried over Na_2SO_4 , filtered and concentrated. The crude oil was purified by silica gel column chromatography (DCM/MeOH, 80:1-10:1) to give 10a (235 mg, 86% yield) as a pale yellow oil. $R_f = 0.55$ (DCM : MeOH = 10:1); IR (film): ν_{max} 3071, 2938, 2831, 1687, 1515, 1463, 1262, 1156, 1030 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 1.77 (d, 2H, $J = 7.2, 2.0$ Hz), 1.84-1.91 (m, 4H), 2.04 (d, 1H, $J = 5.2$ Hz), 2.16 (q, 1H, $J = 8.0$ Hz), 2.52-2.57 (m, 1H), 2.61-2.78 (m, 5H), 3.21-3.25 (m, 1H), 3.83 (s, 3H), 3.84 (s, 3H), 5.01 (t, 2H, $J = 14.0$ Hz), 5.77-5.87 (m, 1H), 6.39 (dd, 1H, $J = 15.2, 1.6$ Hz), 6.66 (t, 2H, $J = 8.0$ Hz), 6.75 (d, 1H, $J = 8.0$ Hz), 6.78-6.88 (dt, 1H, $J = 22.0, 6.8$ Hz) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ : 18.1, 23.2, 33.0, 35.5, 35.5, 50.8, 51.2, 55.8, 55.8, 72.7, 111.0, 112.0, 117.1, 120.6, 126.8, 133.1, 135.9, 141.8, 147.2, 148.7, 202.1 ppm; HRMS (ESI) m/z calcd. for $C_{21}H_{30}NO_3$ (M+H)⁺ : 344.2226, found: 344.2217.

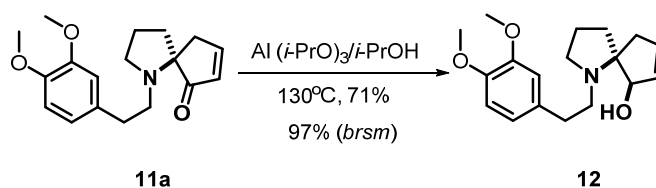
Synthesis of compound 11a



A solution of 10a (154 mg, 0.45 mmol) and Grubbs (II) catalyst (38 mg) in dry DCM (5 mL) was refluxed for 1 h at 40 °C. Then the mixture was concentrated. The crude material was purified by silica gel column chromatography (DCM/MeOH, 80:1-20:1) to give 11a (122 mg, 90% yield) as a brown oil. $R_f = 0.45$ (DCM : MeOH = 15:1); IR (film): ν_{max} 2936, 2832, 1700, 1587, 1515, 1463, 1261, 1156, 1028 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 1.83 (d, 1H, $J = 8.0$ Hz), 1.89-1.96 (m, 1H), 2.01-2.14 (m, 2H), 2.53-2.79 (m, 6H), 3.04 (s, 1H), 3.16-3.20 (m, 1H), 3.83 (s, 3H), 3.85 (s, 3H), 6.10 (d, 1H, $J = 4.0$ Hz), 6.68-6.77 (m, 3H), 7.60-7.63 (m, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ : 21.8, 35.7, 36.8, 39.2, 51.5, 51.8, 55.7, 55.8, 70.9,

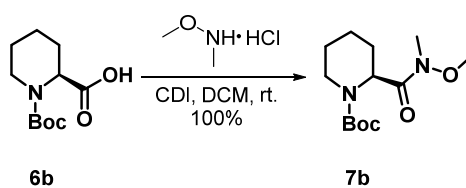
111.1, 112.0, 120.4, 132.9, 133.4, 147.3, 148.7, 162.4, 212.6 ppm; HRMS (ESI) m/z calcd. for $C_{18}H_{24}NO$ ($M+H$)⁺ : 302.1756, found: 302.1760.

Synthesis of compound 12



A solution of 2-propanol (5 mL) was added to aluminium isopropoxide (773 mg, 3.78 mmol) under inert atmosphere. Then a solution of 11a (38 mg, 0.13 mmol) in 2-propanol (5 mL) was added and the mixture was refluxed for 1 h at 130 °C. The solvent was steamed and the residue was stirred for 3 h at 130 °C. The resulting residue was cooled to 0 °C and acidified with a 1N aqueous solution of HCl to pH = 7. The resulting solution was extracted with CH_2Cl_2 . The combined organic layers were dried over Na_2SO_4 , filtered and concentrated. The residue was purified by silica gel chromatography (DCM/MeOH, 50:1-5:1) to give 12 (27 mg, 71% yield) as a colorless oil. R_f = 0.33 (DCM : MeOH = 10:1); IR (film): ν_{max} 3438, 2964, 1647, 1517, 1261, 1159, 1023 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ : 1.77-1.89 (m, 3H), 2.05-2.15 (m, 2H), 2.50-2.60 (m, 2H), 2.69-2.82 (m, 4H), 2.96-3.02 (m, 1H), 3.34-3.39 (m, 1H), 3.84 (s, 3H), 3.86 (s, 3H), 4.23 (s, 1H), 5.76-5.81 (m, 2H), 6.69-6.73 (m, 2H), 6.79 (d, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 22.9, 35.3, 38.1, 39.0, 52.8, 55.8, 72.6, 80.5, 111.8, 112.0, 120.6, 130.9, 132.1, 134.3, 147.5, 148.8 ppm; HRMS (ESI) m/z calcd. for $C_{18}H_{26}NO_3$ ($M+H$)⁺ : 304.1913, found: 304.1899.

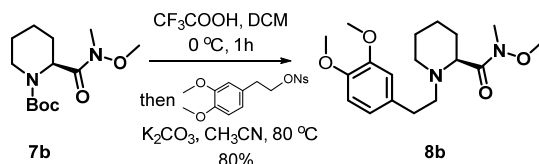
Synthesis of compound 7b



The synthesis method is similar to 7a, a white solid. And the spectroscopic and analytical datas of compound 7b are as follows:

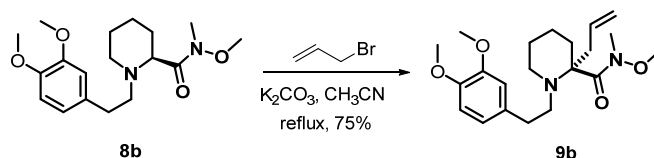
R_f = 0.25 (petroleum ether : EtOAc = 3:1); IR (film): ν_{max} 2973, 2939, 2865, 1693, 1669, 1377, 1161 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ : 1.42 (s, 12H), 1.55-1.71 (m, 3H), 1.97 (d, 1H, J = 12.0 Hz), 3.16 (s, 3H), 3.45 (s, 1H), 3.74 (s, 3H), 3.88 (s, 1H), 4.89 (br s, 0.40H), 5.03 (br s, 0.60H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ : 19.6, 24.9, 26.4, 28.0, 28.4, 32.1, 36.1, 42.3, 50.7, 61.2, 79.6, 155.3, 173.5 ppm; HRMS (ESI) m/z calcd. for $C_{13}H_{24}N_2O_4Na$ ($M+Na$)⁺ : 295.1634, found: 295.1618.

Synthesis of compound 8b



To a solution of 7b (1.341 g, 4.93 mmol) in dichloromethane (5 mL) was added CF_3COOH (0.5 mL). The reaction mixture was stirred at 0 °C for 2 h. The mixture was concentrated in vacuo. The crude product was then dissolved in acetonitrile (15 mL), and K_2CO_3 (1.7 g, 12.33 mmol) was added. Then the 3,4-dimethoxyphenethyl 4-nitrobenzenesulfonate (2.7 g, 7.4 mmol) was added to the slurry of K_2CO_3 in acetonitrile. The reaction mixture was refluxed for 6 h at 80 °C, cooled, and concentrated in vacuo. The residue was then extracted with EtOAc (5×15 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated. The crude product was purified by silica gel column chromatography (DCM/MeOH, 50:1) to give 8b (1.33 g, 80% yield) as a yellow oil. $R_f = 0.45$ (DCM : MeOH = 15:1); IR (film): ν_{max} 2941, 1670, 1517, 1455, 1238, 1026 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 1.29-1.34 (m, 1H), 1.63-1.75 (m, 5H), 2.19 (td, 1H, $J = 10.3, 3.5$ Hz), 2.33-2.39 (m, 1H), 2.70-2.76 (m, 3H), 3.15 (s, 3H), 3.26 (dt, 1H, $J = 11.2, 4.1$ Hz), 3.28 (s, 1H), 3.63 (s, 3H), 3.80 (s, 3H), 3.82 (s, 3H), 6.67-6.75 (m, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ : 19.4, 23.5, 27.0, 31.1, 32.1, 49.4, 55.7, 55.8, 57.0, 58.6, 61.7, 111.3, 112.0, 120.6, 130.1, 147.8, 149.0, 170.1 ppm; HRMS (ESI) m/z calcd. for $\text{C}_{18}\text{H}_{29}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}$) $^+$: 337.2127, found: 337.2122.

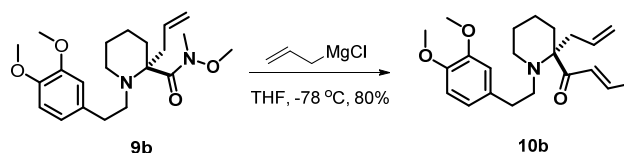
Synthesis of compound 9b



The synthesis method is similar to 9a, a pale yellow oil. And the spectroscopic and analytical datas of compound 9b are as follows:

$R_f = 0.55$ (DCM : MeOH = 10:1); IR (film): ν_{max} 2933, 1652, 1515, 1464, 1261, 1030 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ : 1.49-1.53 (m, 3H), 1.62 (dd, 2H, $J = 12.8, 4.9$ Hz), 1.85-1.90 (m, 1H), 2.45 (q, 1H, $J = 6.8$ Hz), 2.63-2.69 (m, 5H), 2.93-2.99 (m, 1H), 3.41 (s, 3H), 3.66 (s, 3H), 3.83 (s, 3H), 3.84 (s, 3H), 5.02 (td, 2H, $J = 15.6, 2.1$ Hz), 5.90-5.96 (m, 1H), 6.64-6.68 (m, 2H), 6.76 (d, 1H, $J = 8.0$ Hz) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ : 20.3, 24.0, 29.4, 34.9, 36.2, 46.4, 53.1, 55.8, 56.0, 67.4, 111.3, 112.1, 116.6, 120.6, 133.1, 135.9, 147.3, 148.8, 173.3 ppm; HRMS (ESI) m/z calcd. for $\text{C}_{21}\text{H}_{33}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}$) $^+$: 377.2440, found: 377.2424.

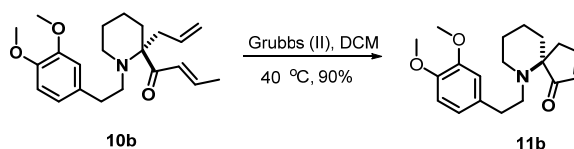
Synthesis of compound 10b



The synthesis method is similar to 10a, a pale yellow oil. And the spectroscopic and analytical datas of compound 10b are as follows:

$R_f = 0.60$ (DCM : MeOH = 10:1); IR (film): ν_{max} 3071, 2936, 2832, 1690, 1626, 1515, 1262, 1030 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 1.40-1.61 (m, 5H), 1.67-1.72 (m, 2H), 1.81 (dd, 3H, $J = 6.8, 1.6$ Hz), 2.33-2.52 (m, 5H), 2.57-2.68 (m, 2H), 2.98 (dt, 1H, $J = 12.0, 3.9$ Hz), 3.84 (s, 3H), 3.85 (s, 3H), 5.01 (dd, 2H, $J = 28.8, 17.2$ Hz), 5.89-5.95 (m, 1H), 6.61-6.64 (m, 2H), 6.74 (t, 1H, $J = 8.0$ Hz), 6.86-6.93 (m, 1 H) ppm; $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 18.1, 19.4, 24.9, 30.0, 31.2, 34.7, 45.5, 54.4, 55.7, 55.8, 69.3, 111.1, 112.2, 116.3, 120.7, 126.8, 133.0, 136.1, 141.7, 147.3, 148.7, 203.5 ppm; HRMS (ESI) m/z calcd. for $\text{C}_{22}\text{H}_{32}\text{NO}_3$ ($\text{M}+\text{H}$) $^+$: 358.2382, found: 358.2369.

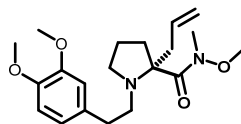
Synthesis of compound 11b



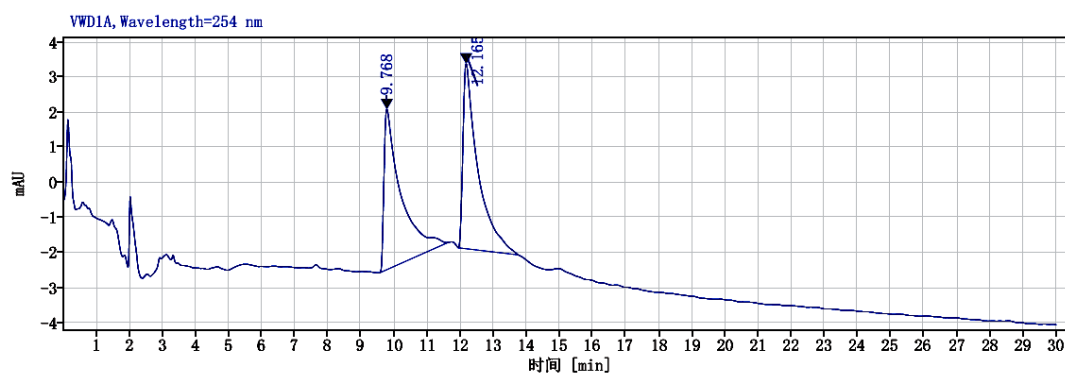
The synthesis method is similar to 11a, a brown oil. And the spectroscopic and analytical datas of compound 11b are as follows:

$R_f = 0.45$ (DCM : MeOH = 10:1); IR (film): ν_{max} 2934, 2833, 1709, 1589, 1515, 1464, 1261, 1142, 1029, 803 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 1.33-1.42 (m, 2H), 1.64-1.79 (m, 5H), 2.17-2.28 (m, 4H), 2.43 (dt, 1H, $J = 19.3, 2.7$ Hz), 2.67-2.77 (m, 3H), 3.07 (q, 1H, $J = 3.5$ Hz), 3.80 (s, 3H), 3.82 (s, 3H), 6.16 (dt, 1H, $J = 6.0, 2.12$ Hz), 6.63-6.65 (m, 2H), 6.73 (d, 1H, $J = 8.6$ Hz), 7.60-7.63 (m, 1H) ppm; $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 21.3, 25.5, 33.5, 34.5, 35.2, 48.9, 55.1, 55.7, 55.8, 67.9, 111.2, 112.2, 120.5, 132.8, 133.2, 147.2, 148.7, 162.5, 211.6 ppm; HRMS (ESI) m/z calcd. for $\text{C}_{19}\text{H}_{26}\text{NO}_3$ ($\text{M}+\text{H}$) $^+$: 316.1913, found: 316.1900.

Figure 1. HPLC Spectrum of 9a



9a

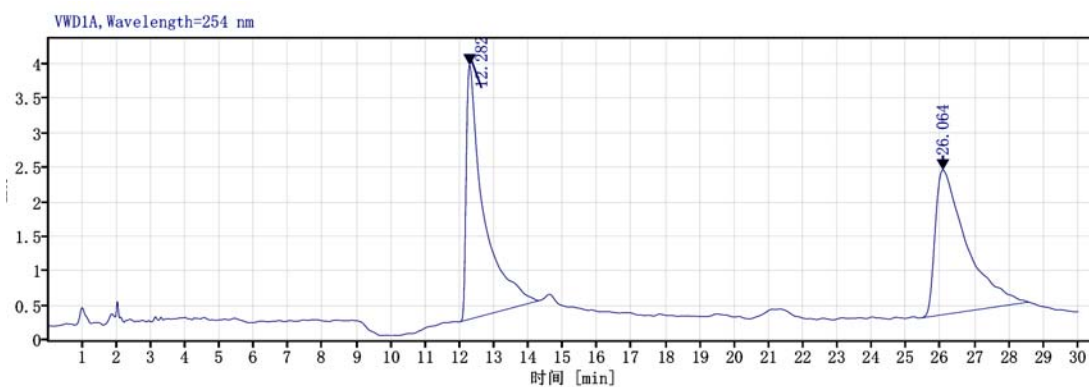
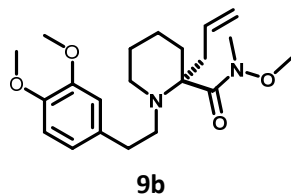


Tested by Agilent 1260 VWD

Signal: VWD1A, Wave length = 254 nm

Retention time[min]	Peak width[min]	Peak area	Peak height	Peak area%
9.768	0.46	162.43	4.57	49.67
12.165	0.42	164.57	5.27	50.33

Figure 2. HPLC Spectrum of 9b



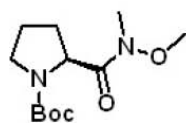
Tested by Agilent 1260 VWD

Signal: VWD1A, Wave length = 254 nm

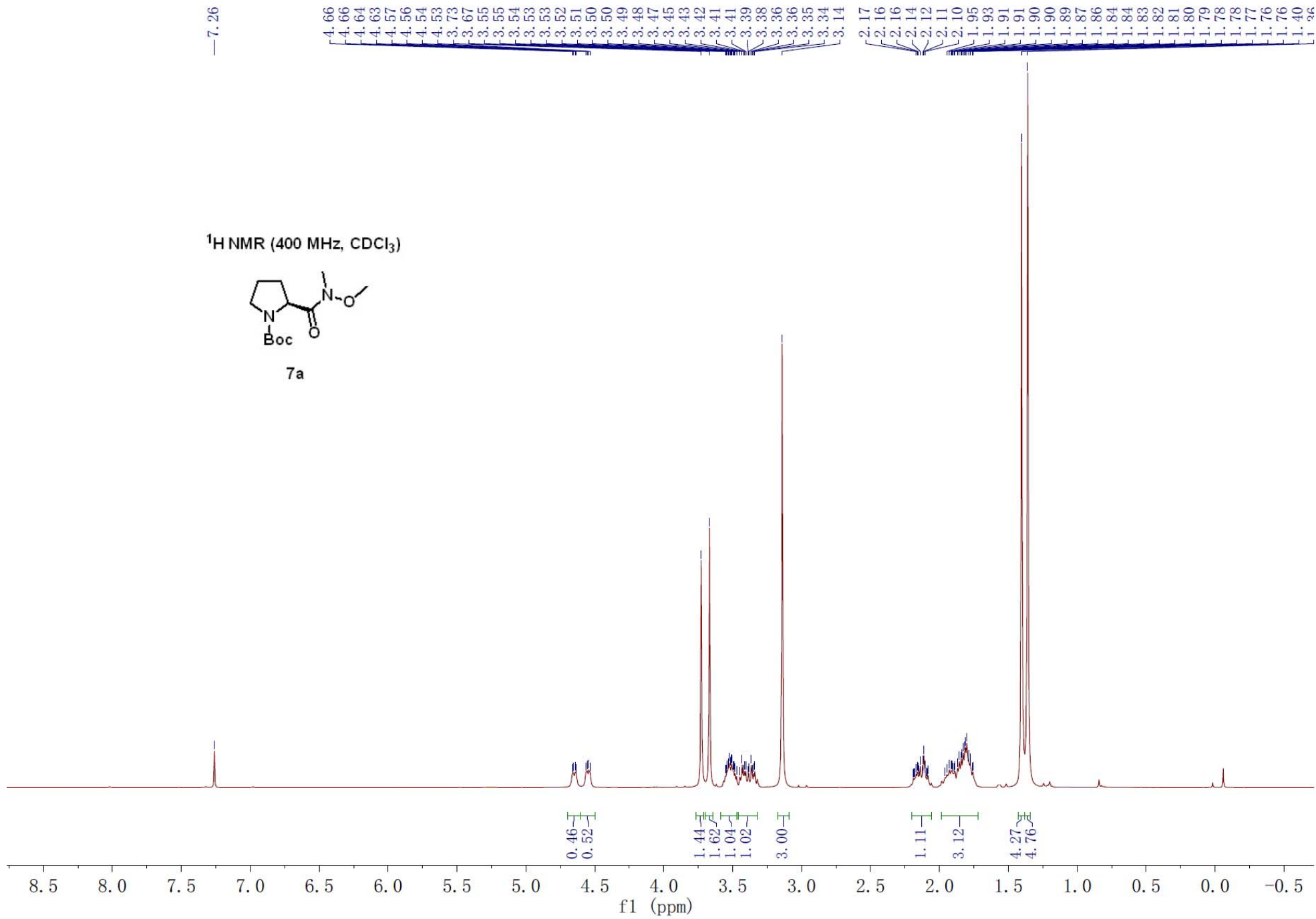
Retention time[min]	Peak width[min]	Peak area	Peak height	Peak area%
12.282	2.32	130.19	3.67	49.52
26.064	0.84	132.74	2.09	50.48

—7.26

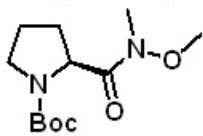
¹H NMR (400 MHz, CDCl₃)



7a



¹³C NMR (100 MHz, CDCl₃)



7a

173.75
173.16

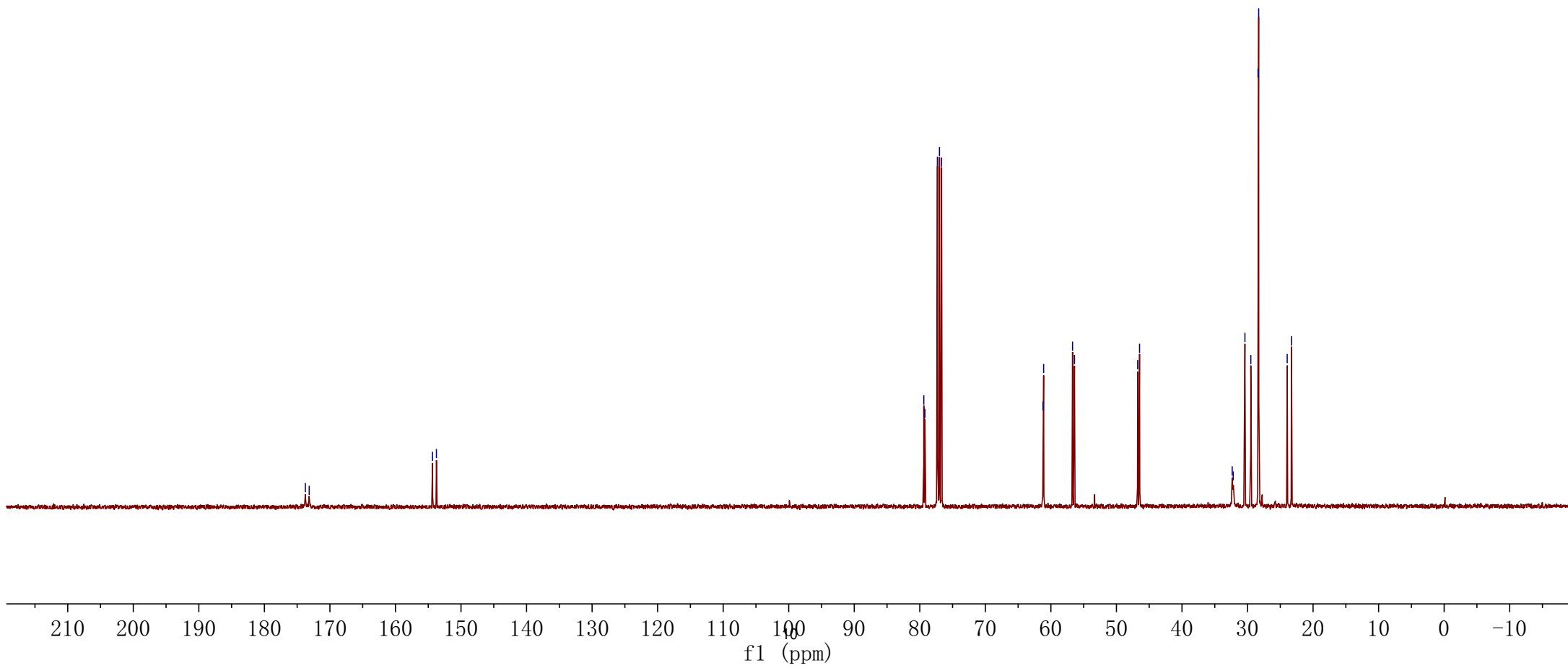
154.35
153.75

79.39
79.22
77.32
77.00
76.68

61.20
61.11
56.70
56.40

46.76
46.47

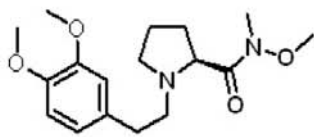
32.34
32.18
30.39
29.50
28.40
28.30
23.95
23.29



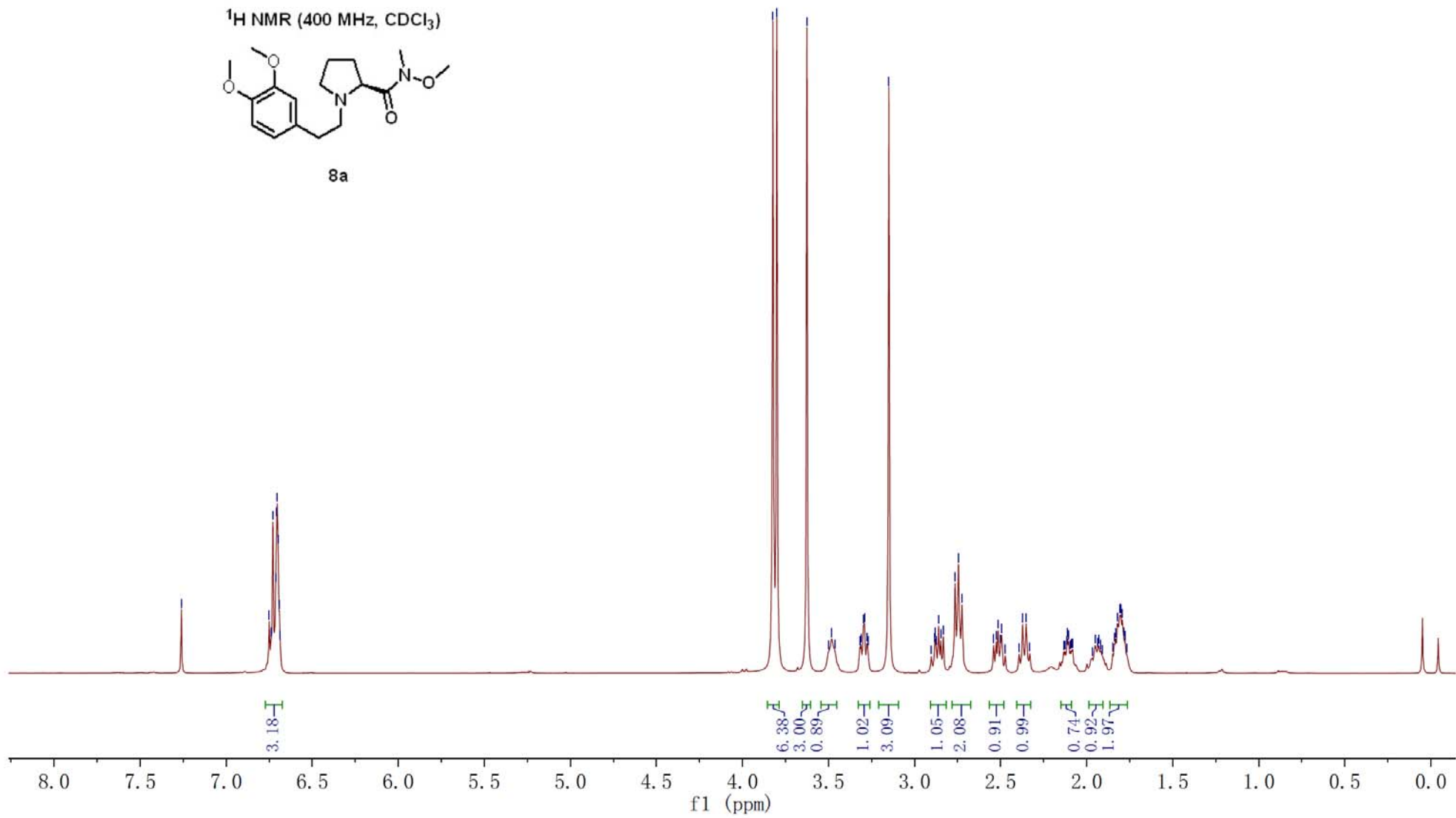
7.26
6.75
6.74
6.73
6.71
6.71
6.70
6.69
6.69

3.82
3.80
3.63
3.50
3.48
3.46
3.32
3.31
3.30
3.29
3.28
3.27
3.15
2.88
2.88
2.87
2.86
2.85
2.83
2.76
2.74
2.72
2.54
2.53
2.51
2.50
2.49
2.37
2.35
2.12
2.11
2.10
1.95
1.94
1.93
1.84
1.83
1.82
1.81
1.80
1.80
1.79
1.78
1.78

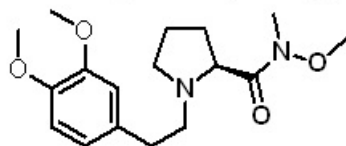
¹H NMR (400 MHz, CDCl₃)



8a



¹³C NMR (100 MHz, CDCl₃)



8a

— 175.00

— 148.71
— 147.20

— 133.07

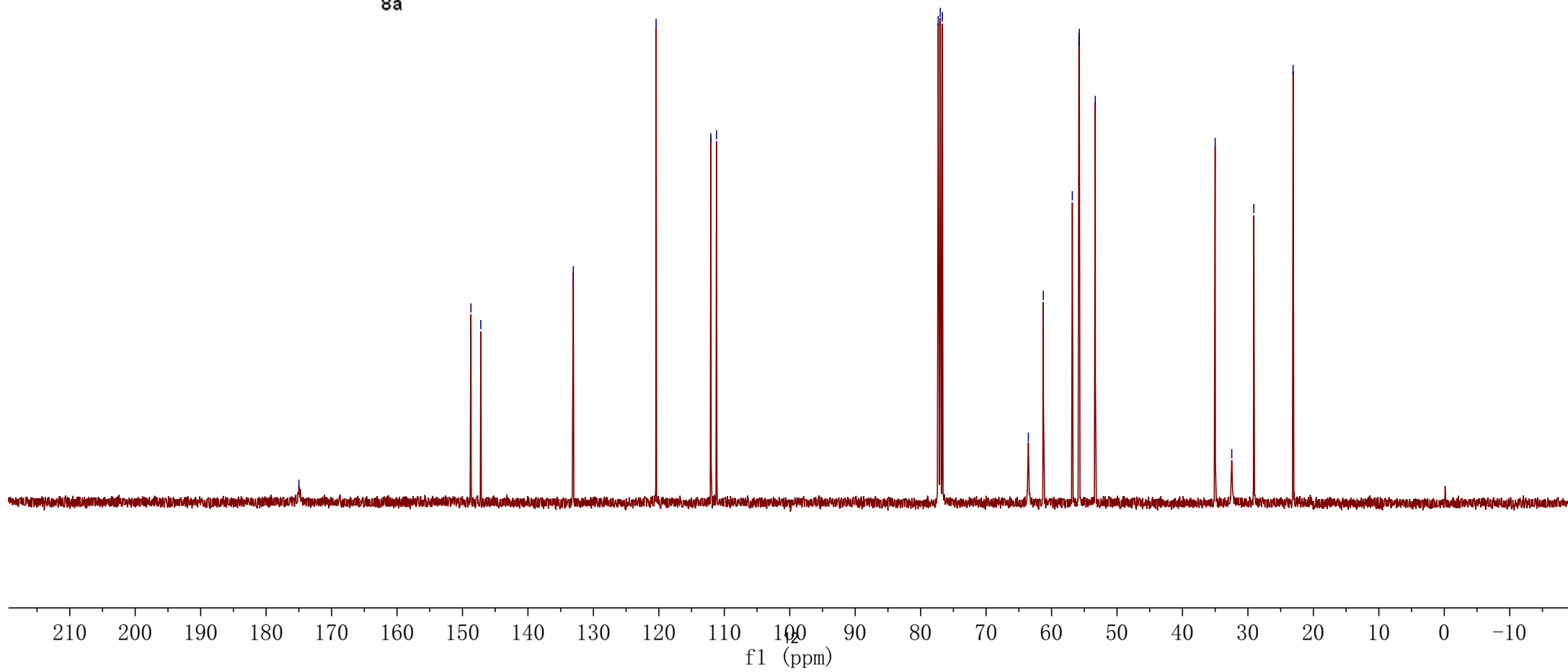
— 120.42

— 112.06
— 111.19

— 77.32
— 77.00
— 76.68

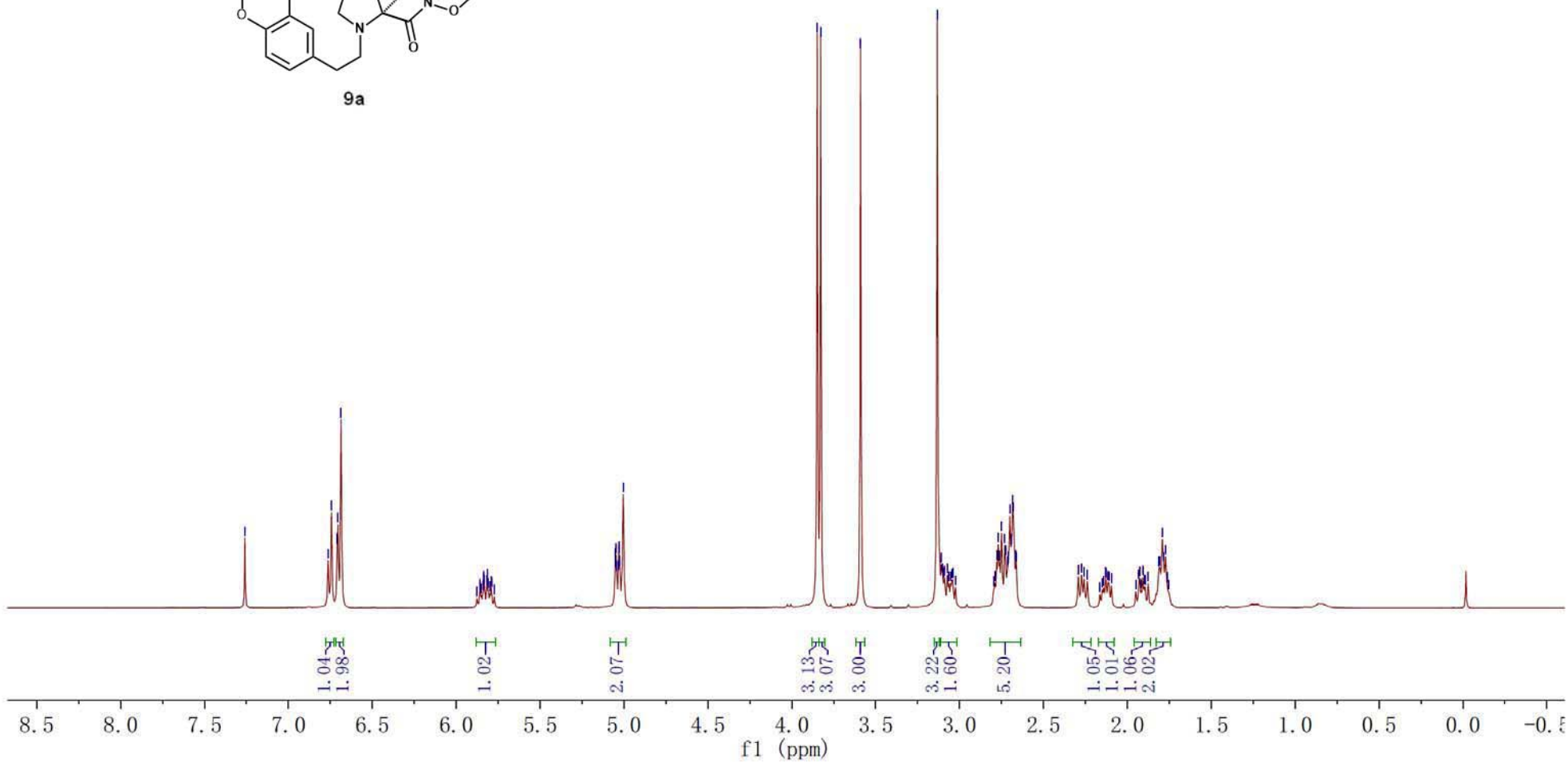
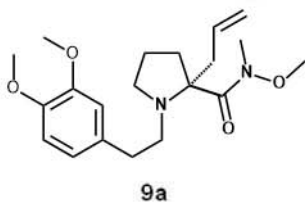
— 63.55
— 61.26
— 56.83
— 55.83
— 55.76
— 53.32

— 35.00
— 32.47
— 29.09
— 23.10

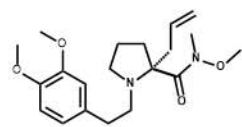


7.26
6.76
6.74
6.71
6.70
6.69
5.86
5.85
5.84
5.83
5.82
5.81
5.80
5.79
5.77
5.05
5.05
5.04
5.03
5.03
5.02
5.00
3.85
3.83
3.59
3.13
3.11
3.10
3.09
3.09
3.07
3.06
3.05
3.05
3.04
3.02
3.02
2.79
2.78
2.77
2.76
2.75
2.73
2.73
2.71
2.71
2.70
2.69
2.68
2.68
2.67
2.66
2.29
2.27
2.26
2.24
2.15
2.14
2.13
2.13
2.12
2.11
2.10
1.95
1.93
1.93
1.92
1.91
1.90
1.89
1.88
1.81
1.81
1.79
1.78
1.77
1.76
1.75

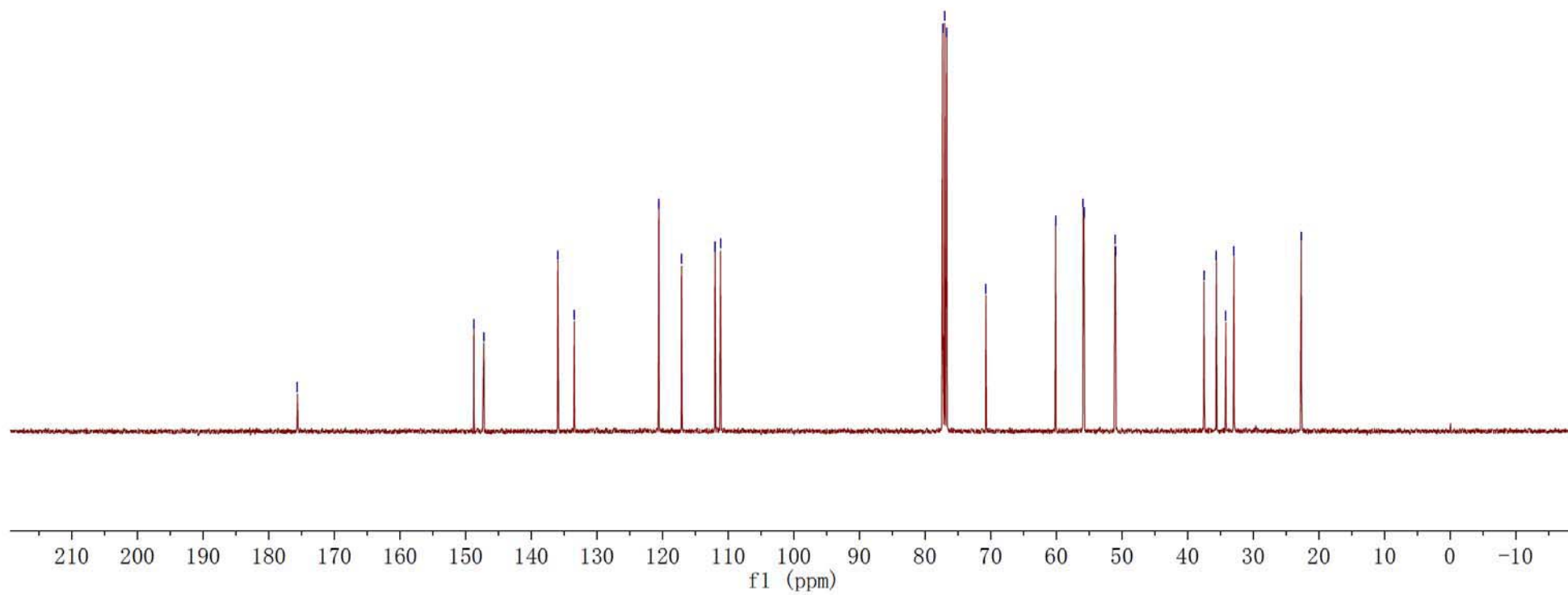
¹H NMR (400 MHz, CDCl₃)

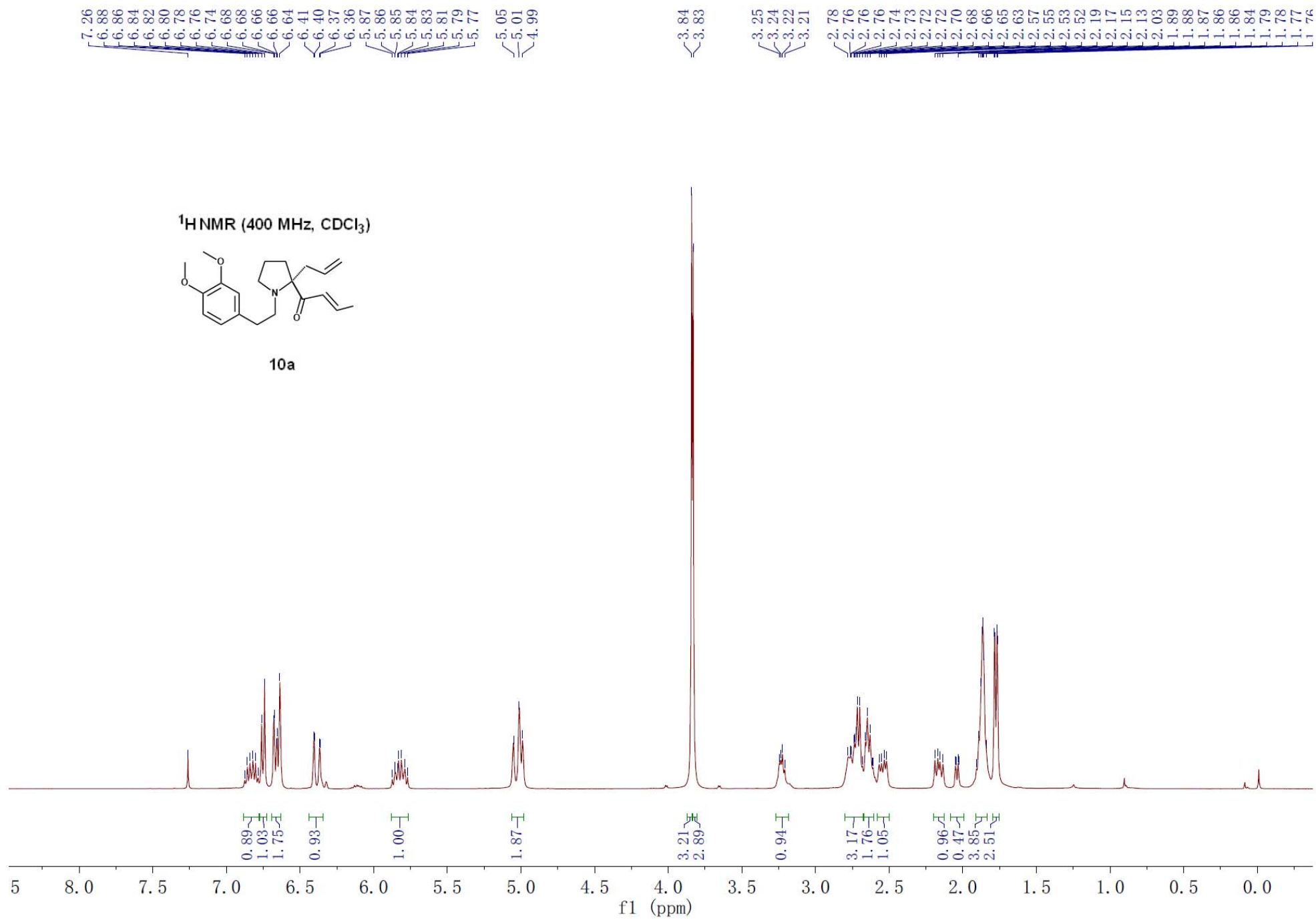


¹³C NMR (100 MHz, CDCl₃)



9a





—202.14

148.67
147.23
141.75
135.88
133.10
126.78
120.61
117.10
112.01
111.04

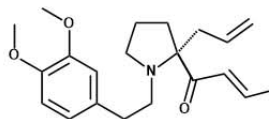
77.32
77.00
76.68
72.66

55.82
55.76
51.21
50.77

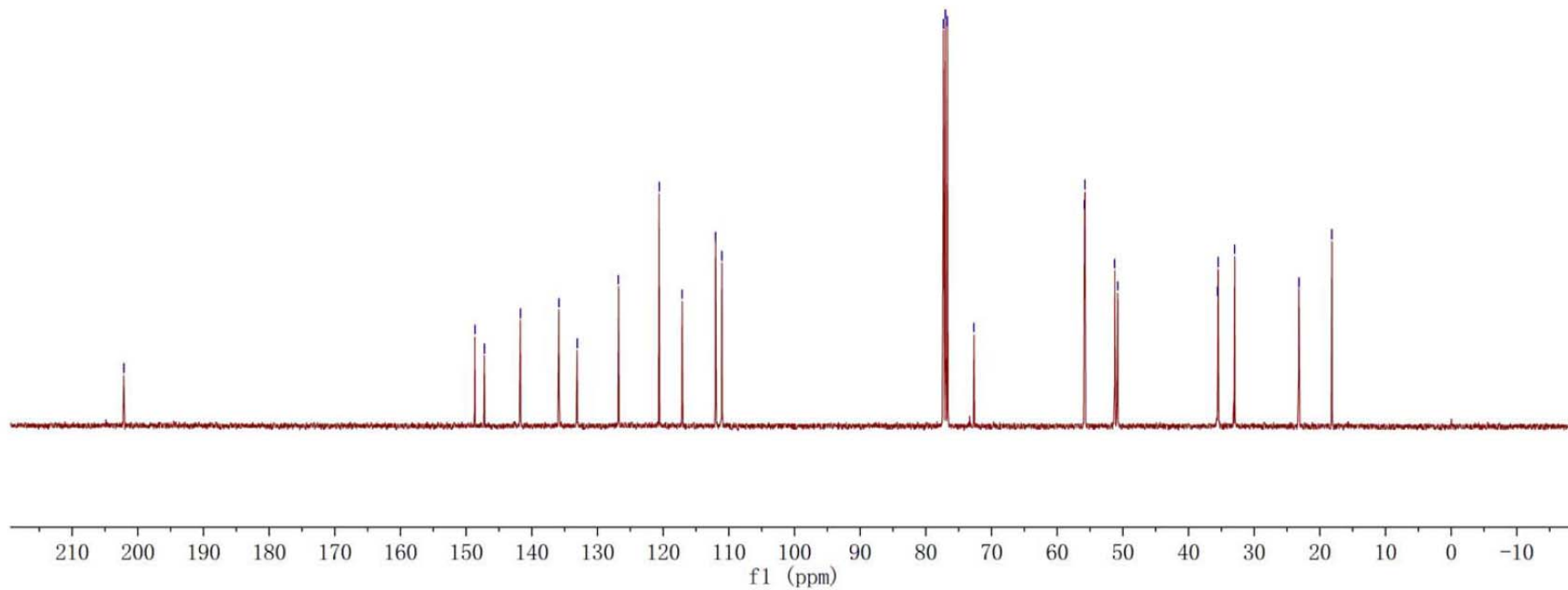
35.53
35.47
32.95

23.19
18.14

¹³C NMR (100 MHz, CDCl₃)



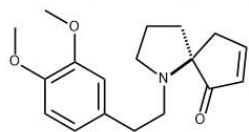
10a



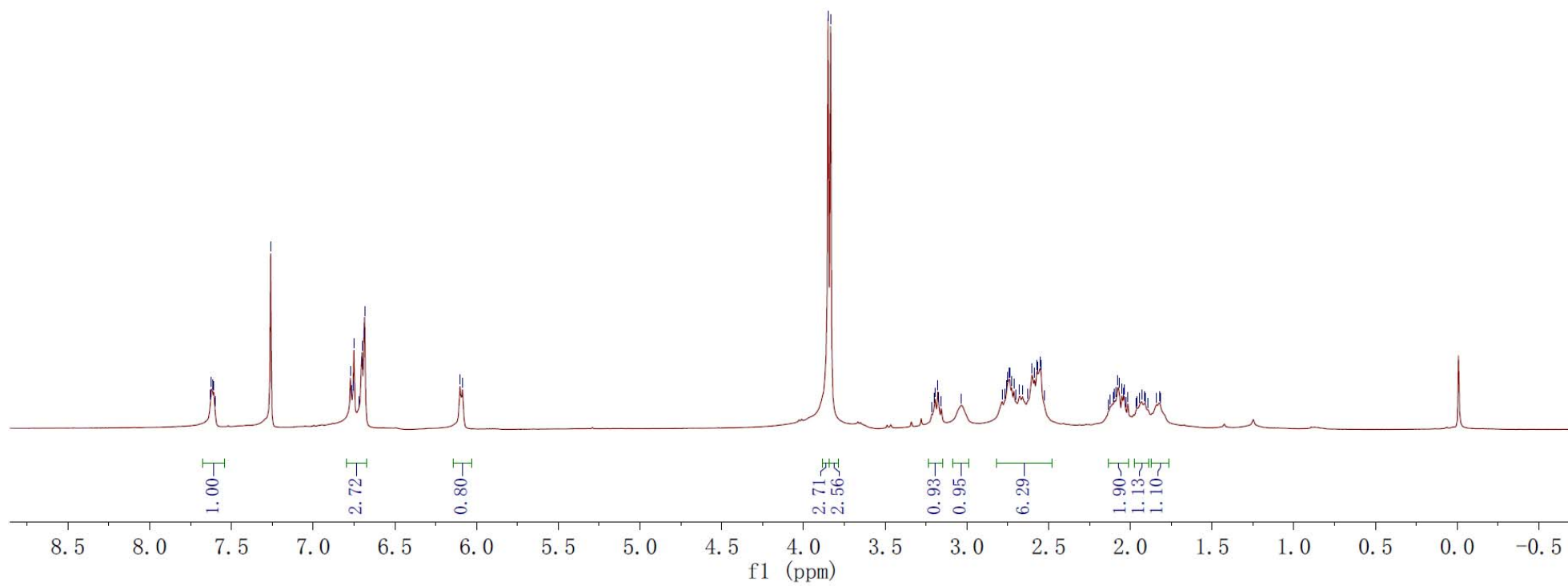
7.63
7.62
7.61
7.61
7.60
7.26
6.77
6.76
6.76
6.75
6.72
6.71
6.70
6.69
6.68
6.10
6.09

3.85
3.83
3.21
3.20
3.19
3.18
3.17
3.16
3.04
2.79
2.77
2.76
2.75
2.74
2.74
2.73
2.71
2.70
2.68
2.66
2.63
2.60
2.59
2.57
2.56
2.55
2.53
2.10
2.10
2.09
2.08
2.07
2.05
2.04
2.04
2.01
1.93
1.91
1.89

¹H NMR (400 MHz, CDCl₃)



11a



—212.61

—162.35

—148.66
—147.25

—133.36
—132.93

—120.42

—112.01
—111.11

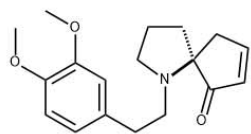
—77.32
—77.00
—76.68
—70.94

—55.82
—55.77
—51.83
—51.47

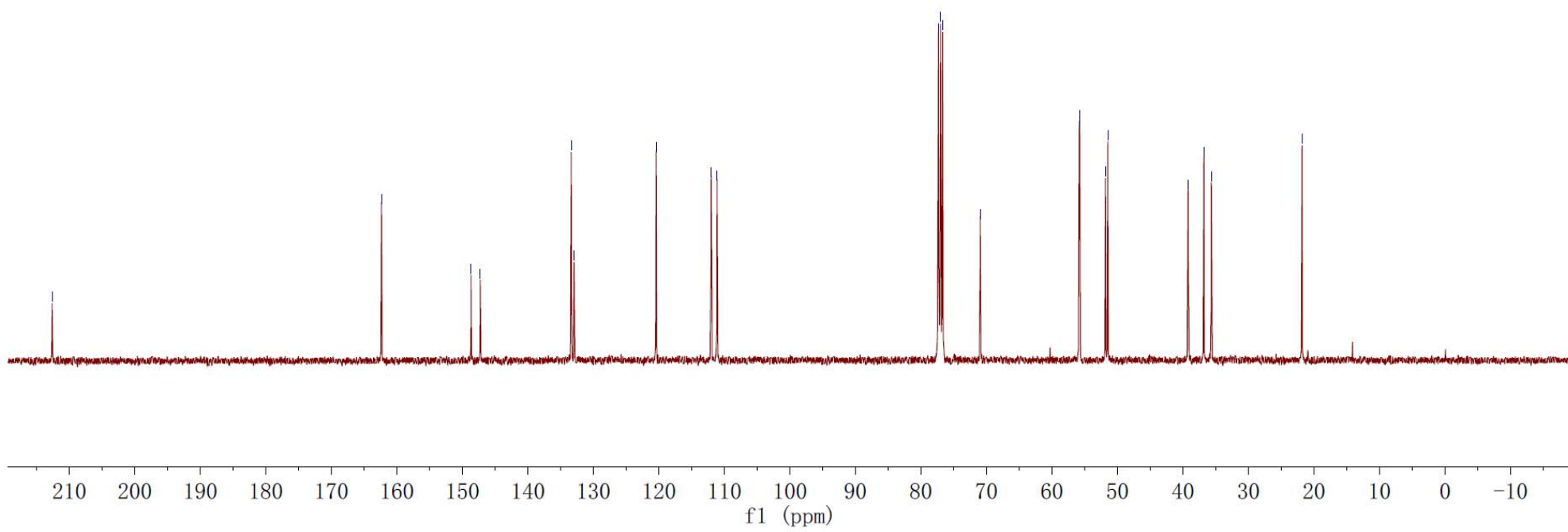
—39.22
—36.82
—35.67

—21.82

¹³C NMR (100 MHz, CDCl₃)



11a



7.26
6.80
6.78
6.73
6.73
6.71
6.71
6.70
6.69

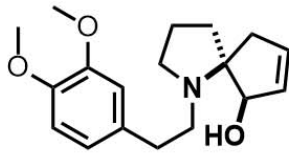
5.81
5.79
5.76

4.23

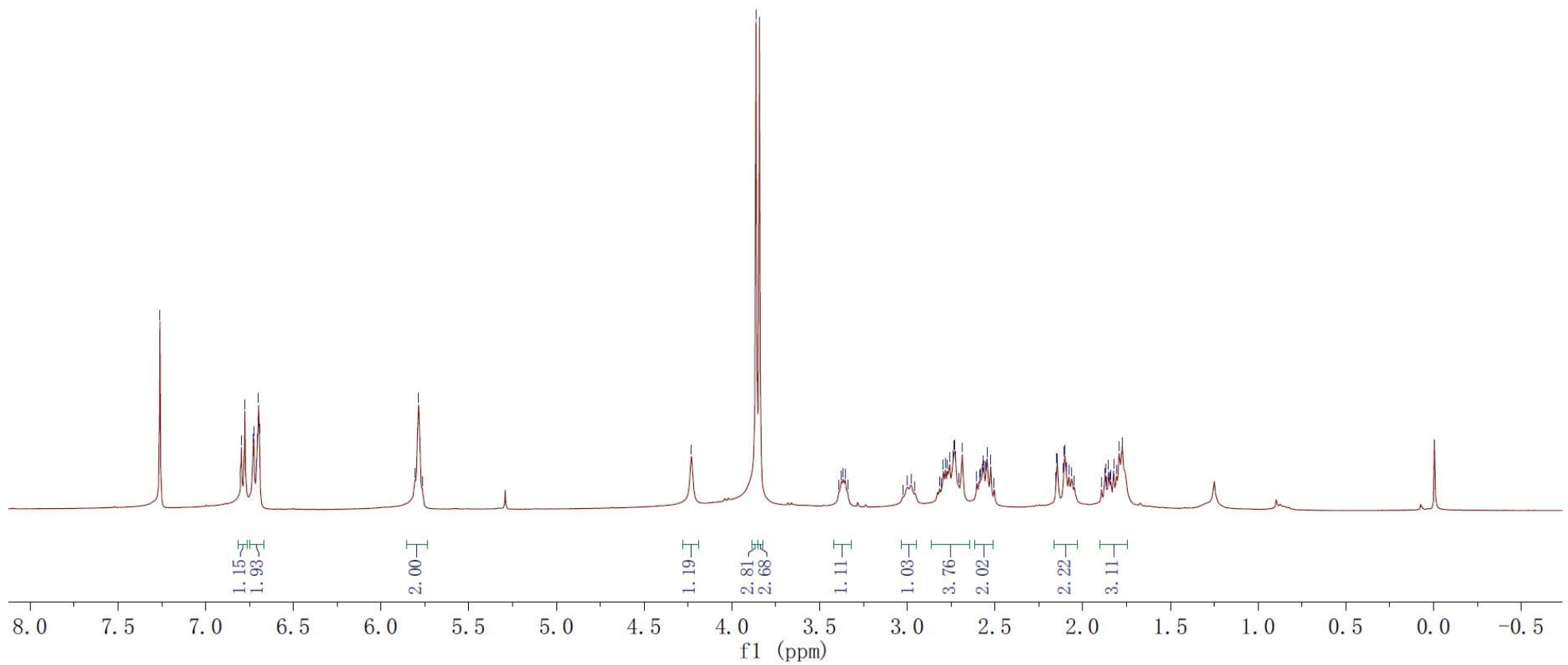
3.86
3.84
3.39
3.38
3.37
3.35
3.34

2.79
2.78
2.77
2.76
2.74
2.73
2.72
2.71
2.69
2.60
2.59
2.58
2.57
2.57
2.56
2.55
2.55
2.52
2.15
2.14
2.11
2.10
2.10
2.09
2.08
2.06
1.88
1.87
1.85
1.85
1.84
1.82
1.81
1.79
1.77

^1H NMR (400 M Hz, CDCl_3)



12



148.81
147.45

134.33
132.06
130.93

120.56

112.04
111.18

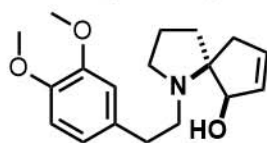
80.45
77.32
77.00
76.68
72.61

55.83
52.83

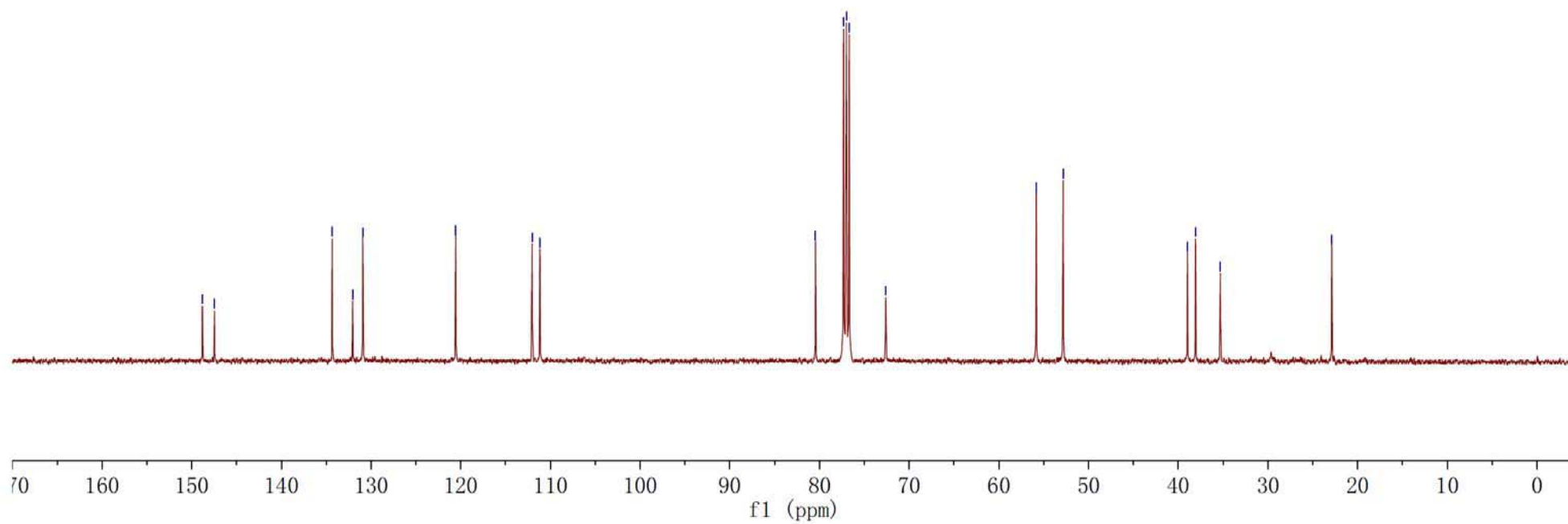
38.96
38.07
35.30

22.88

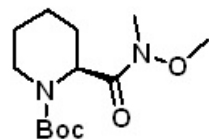
¹³C NMR (100 MHz, CDCl₃)



12



¹H NMR (400 MHz, CDCl₃)



7b

—7.26

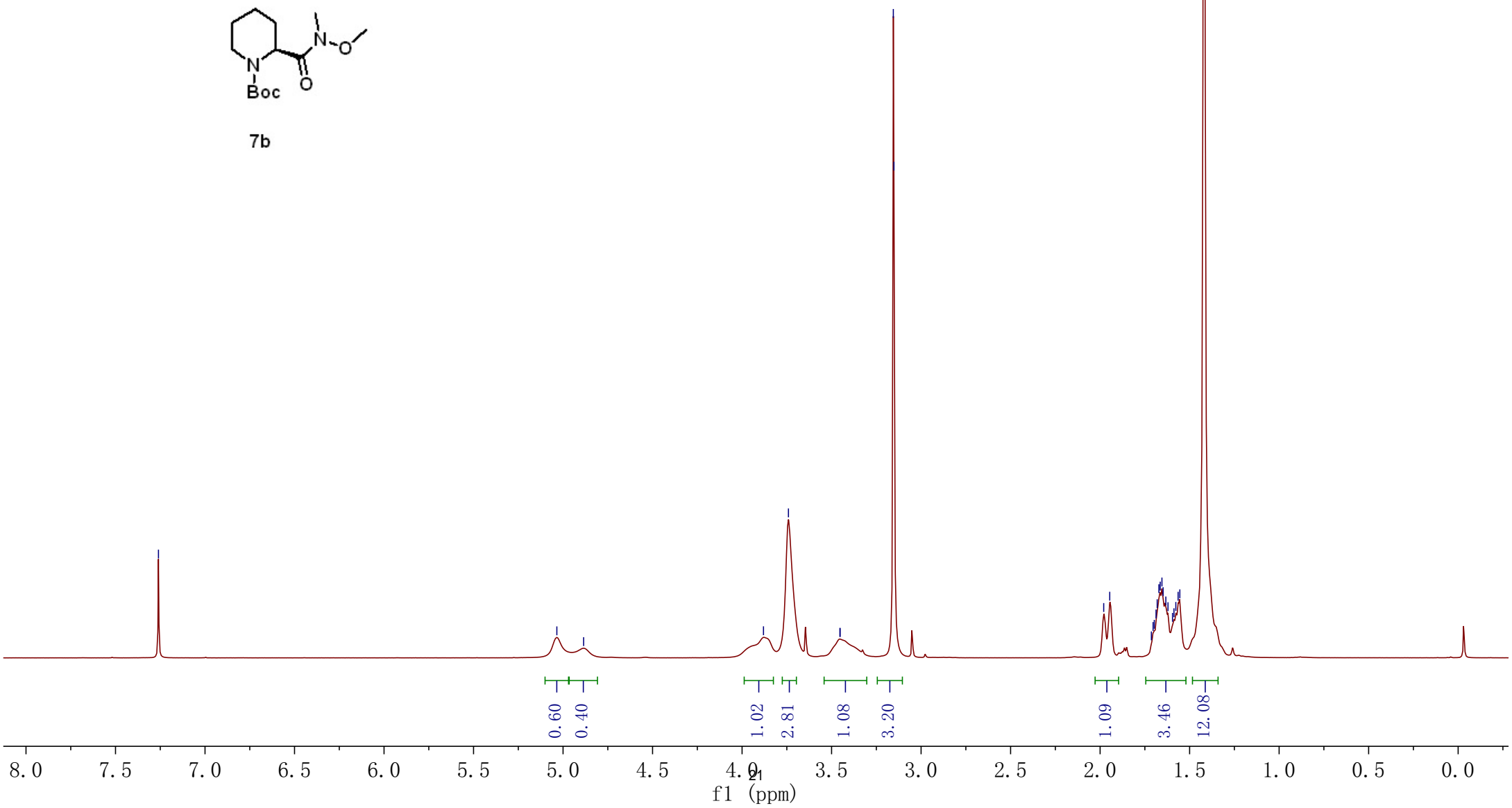
—5.03
—4.89

—3.88
—3.74

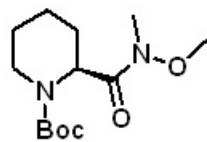
3.45
3.45

3.16
3.15

1.98
1.95
1.71
1.70
1.70
1.69
1.68
1.67
1.66
1.65
1.65
1.63
1.62
1.60
1.59
1.58
1.56
1.55
1.42



¹³C NMR (100 MHz, CDCl₃)



7b

—173.48

—156.31

79.57

77.32

77.00

76.68

—61.22

—50.65

—42.26

36.11

32.12

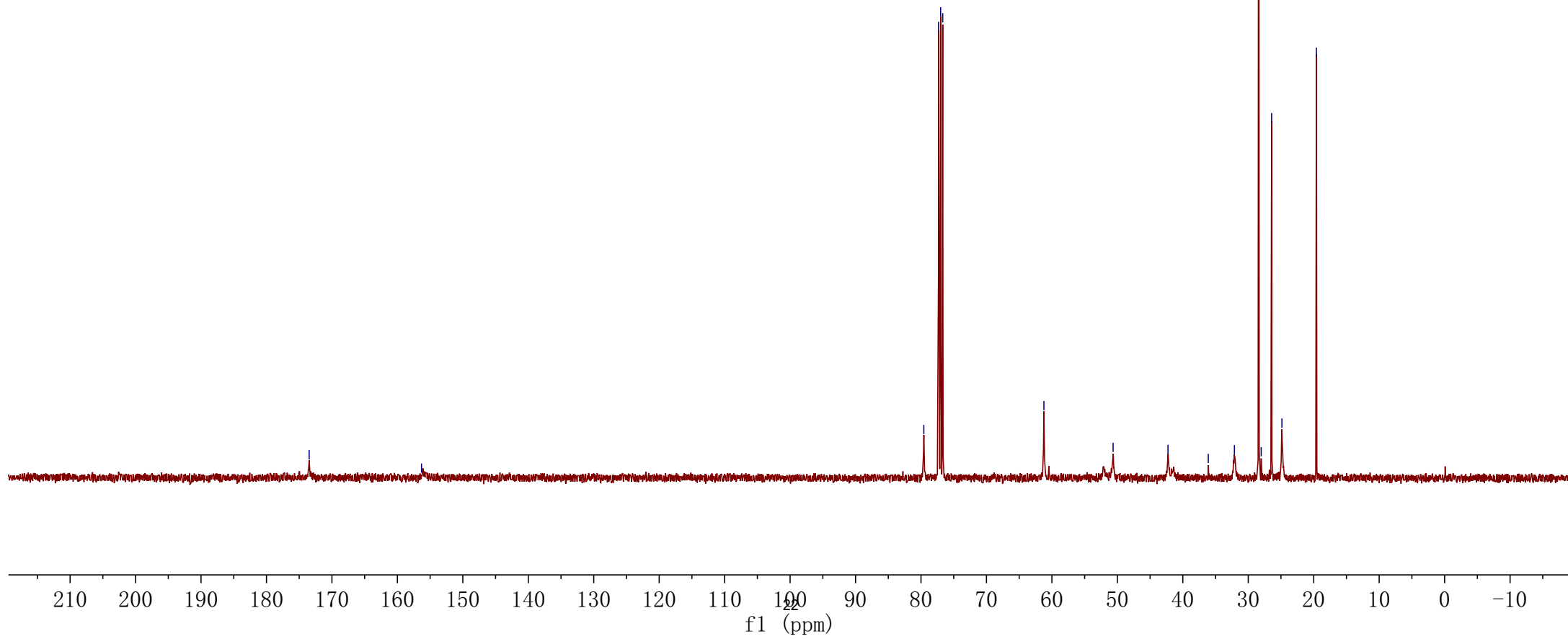
28.41

28.02

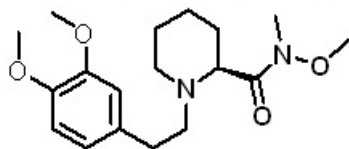
26.43

24.86

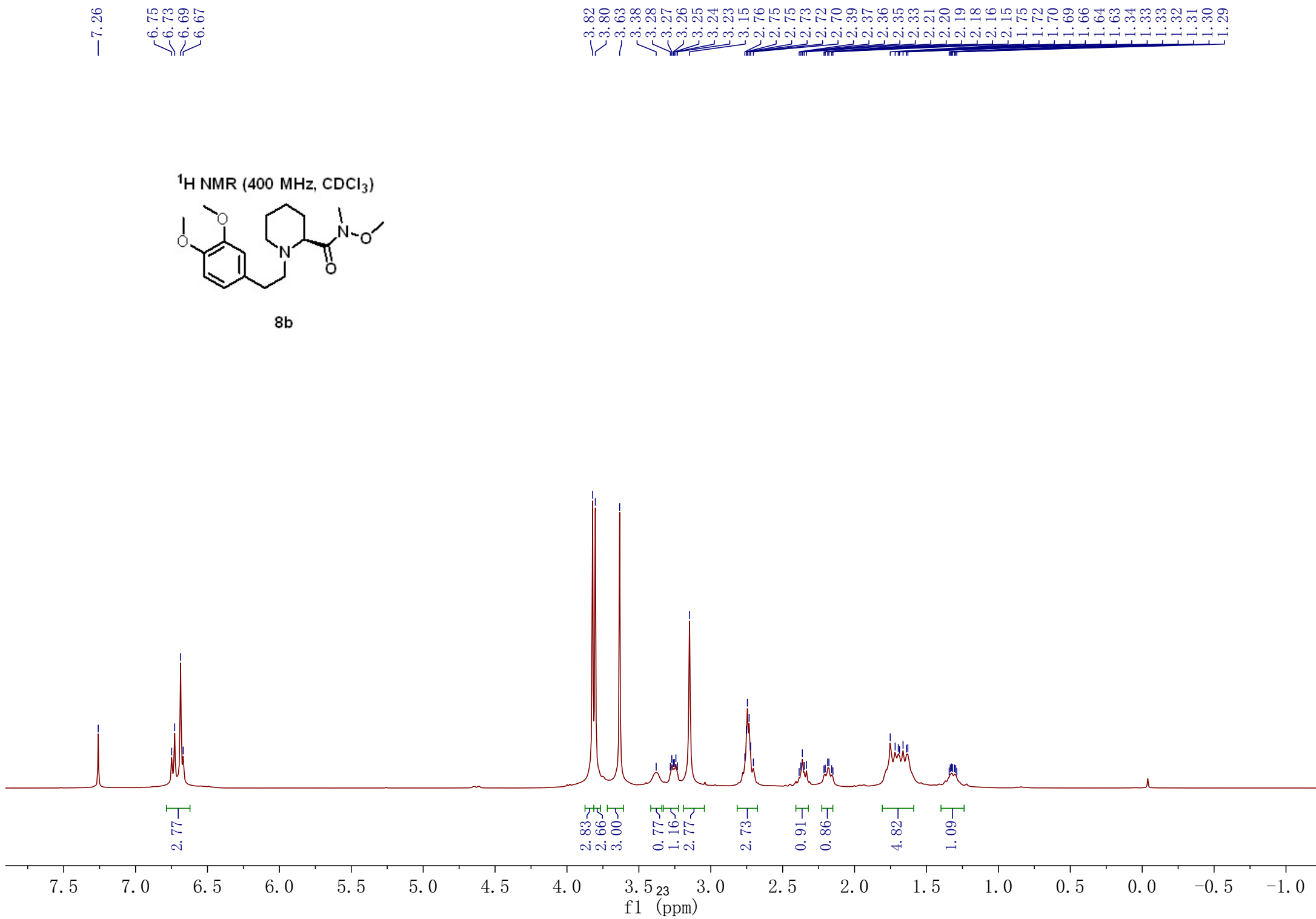
—19.59

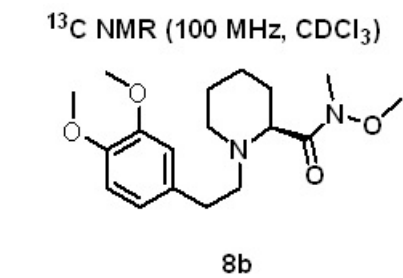


¹H NMR (400 MHz, CDCl₃)

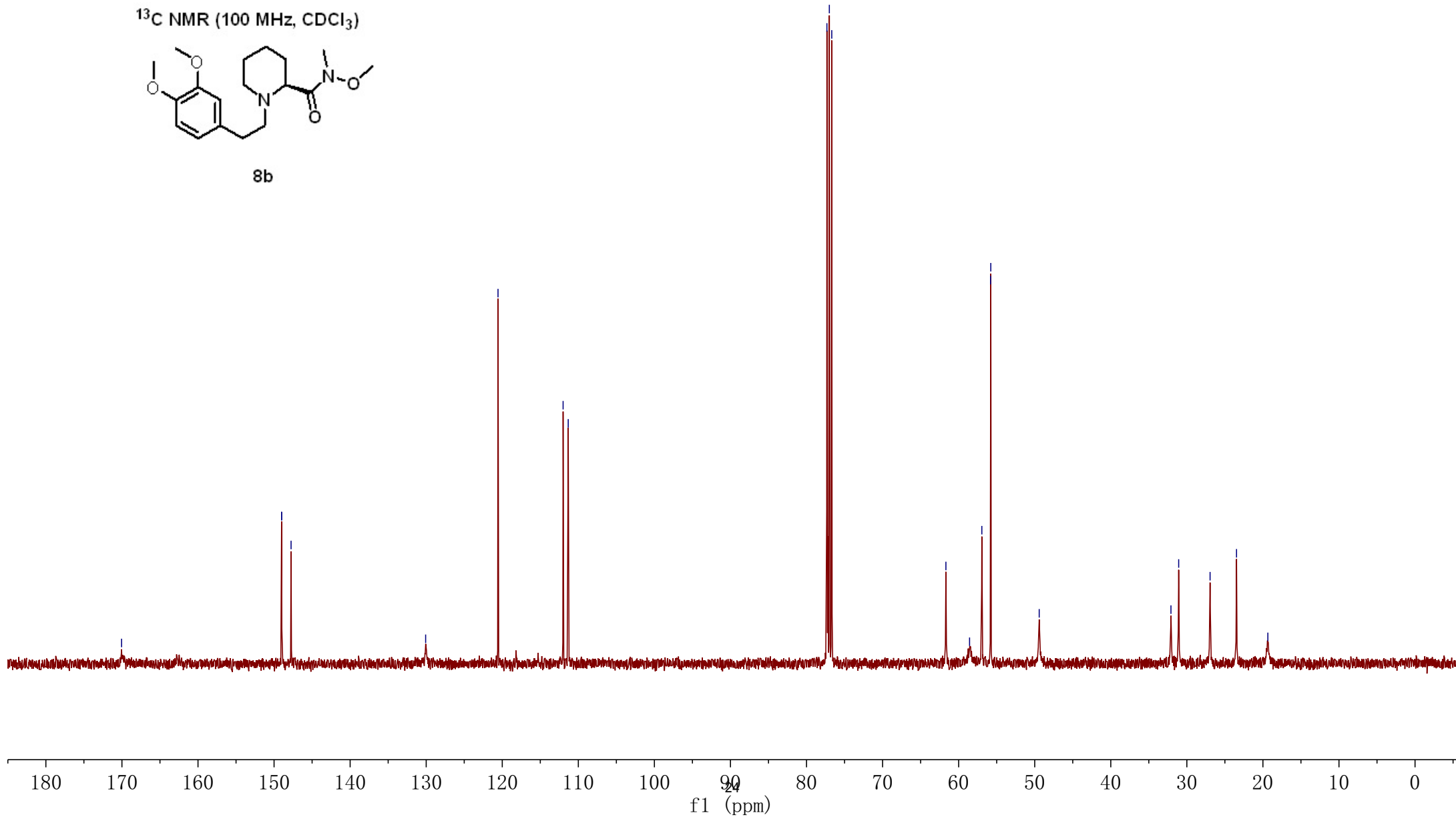


8b

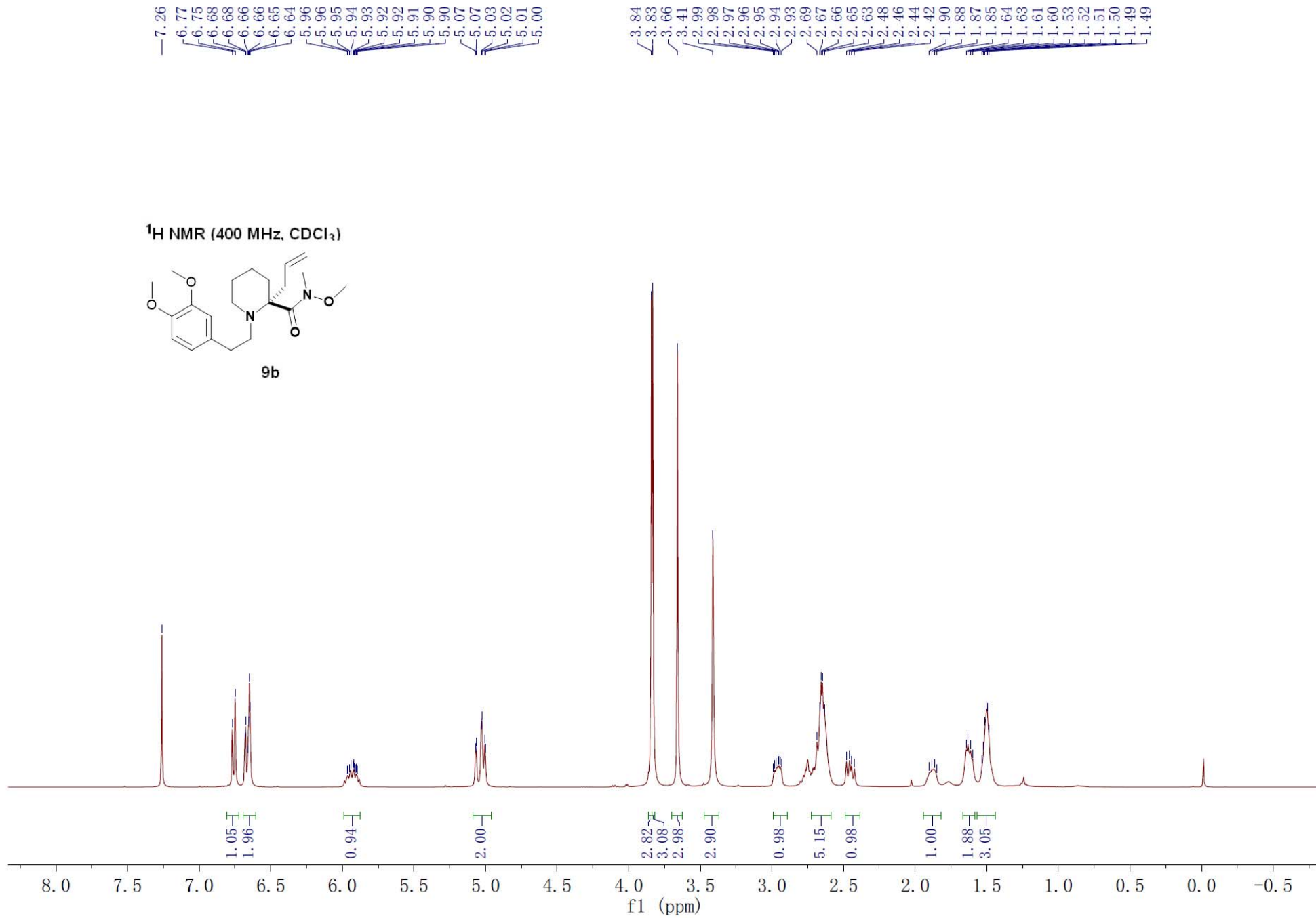
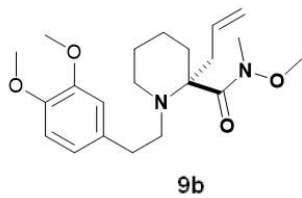




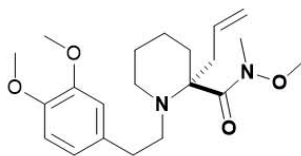
—170.05
149.01
149.01
147.76
—130.07
—120.56
112.00
111.33
77.32
77.00
76.68
61.68
58.56
56.95
55.81
55.77
—49.41
32.09
31.07
26.95
23.47
19.35



¹H NMR (400 MHz, CDCl₃)



¹³C NMR (100 MHz, CDCl₃)



9b

—173.33

—148.81
—147.34

—135.88
—133.09

—120.58
—116.57
—112.10
—111.30

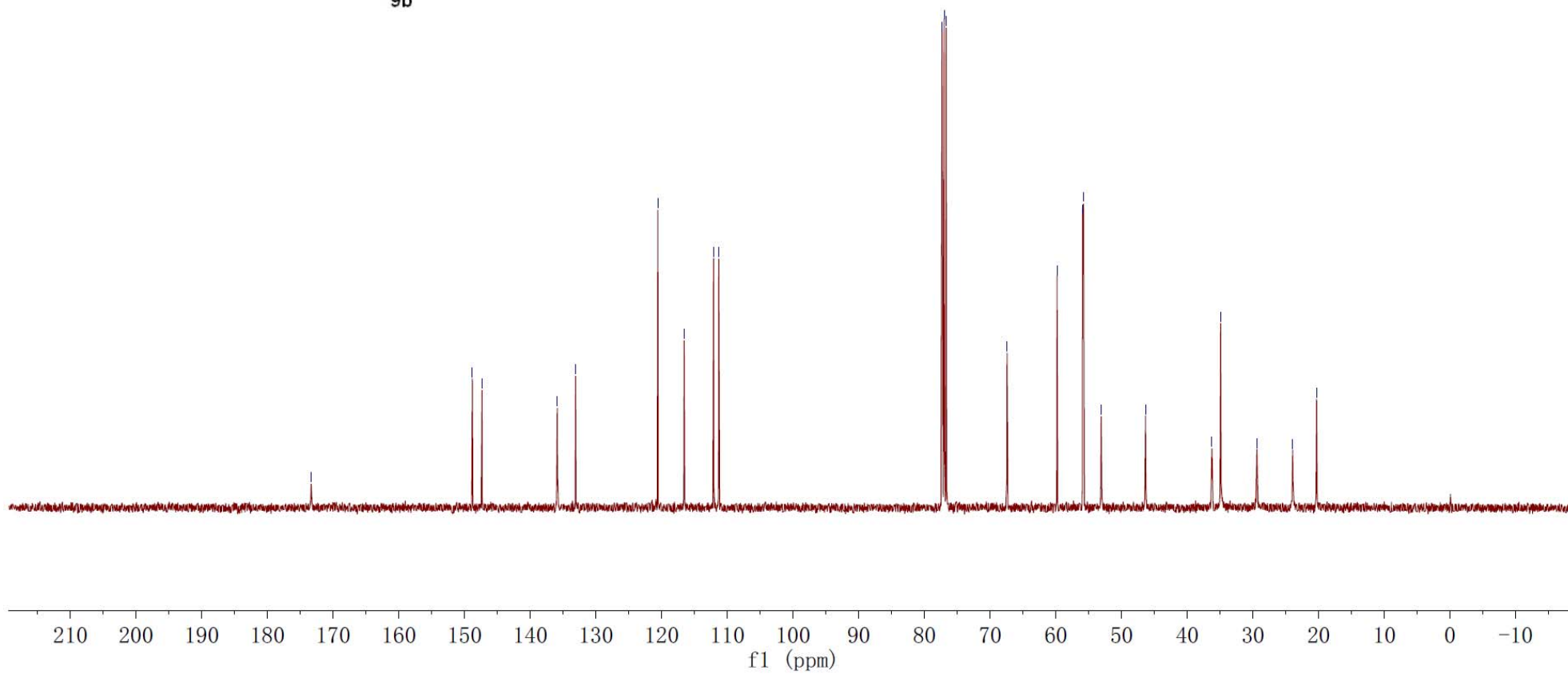
—77.32
—77.00
—76.68

—67.42

—59.81
—55.92
—55.79
—53.09

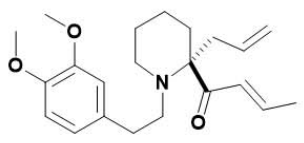
—46.35

—36.24
—34.92
—29.39
—23.95
—20.31

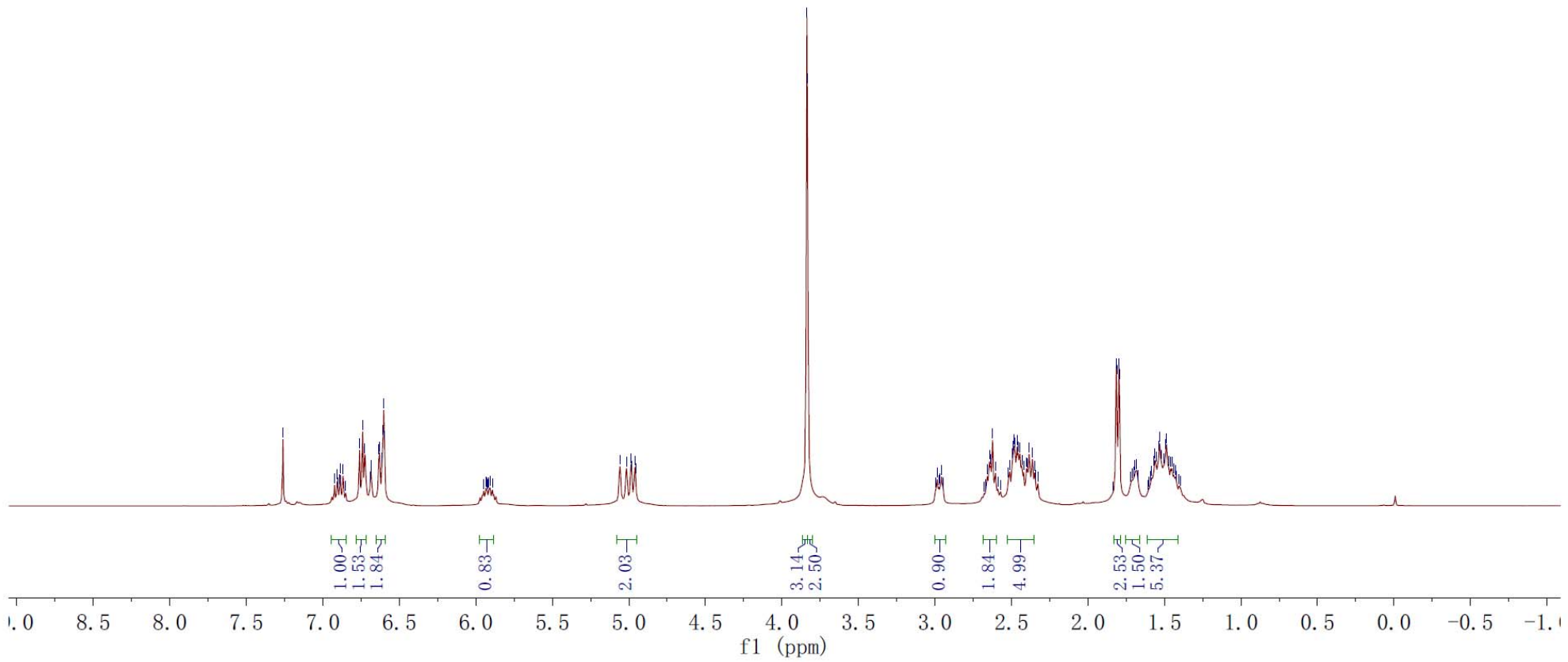


7.26
6.92
6.91
6.89
6.88
6.87
6.76
6.74
6.73
6.69
6.69
6.68
6.63
6.63
6.61
6.61
6.60
6.60
5.93
5.91
5.06
5.02
4.99
4.98
4.96
4.96
3.84
3.83
2.99
2.98
2.97
2.96
2.66
2.64
2.64
2.62
2.60
2.52
2.51
2.49
2.49
2.48
2.48
2.46
2.46
2.44
2.43
2.42
2.40
2.40
2.38
2.36
2.35
2.34
2.33
2.33
1.81
1.80
1.79
1.72
1.71
1.70
1.69
1.68
1.67
1.60
1.59
1.58
1.57
1.56
1.55
1.54
1.53
1.52
1.51
1.49
1.49
1.47
1.46
1.45
1.44
1.43
1.42
1.40
1.40

¹H NMR (400 MHz, CDCl₃)



10b



—203.49

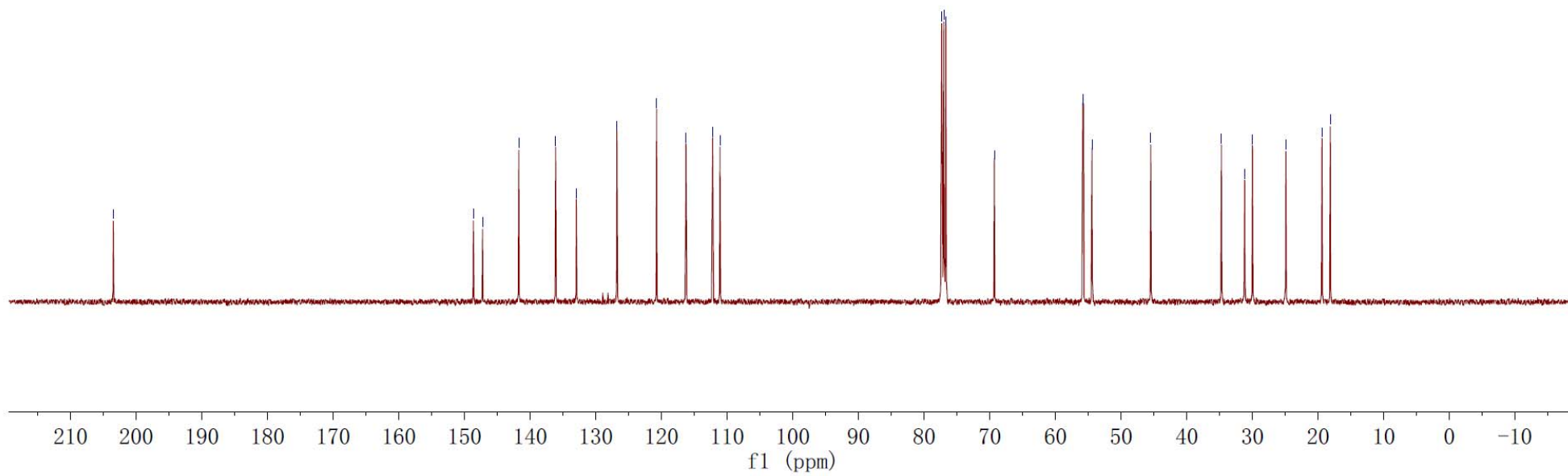
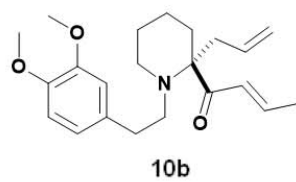
148.66
147.25
141.74
136.12
132.97
—126.79
120.74
116.27
112.21
111.09

77.32
77.00
76.68
—69.31

55.83
55.72
54.43
—45.47

34.71
31.17
29.98
24.91
19.40
18.13

¹³C NMR (100 MHz, CDCl₃)



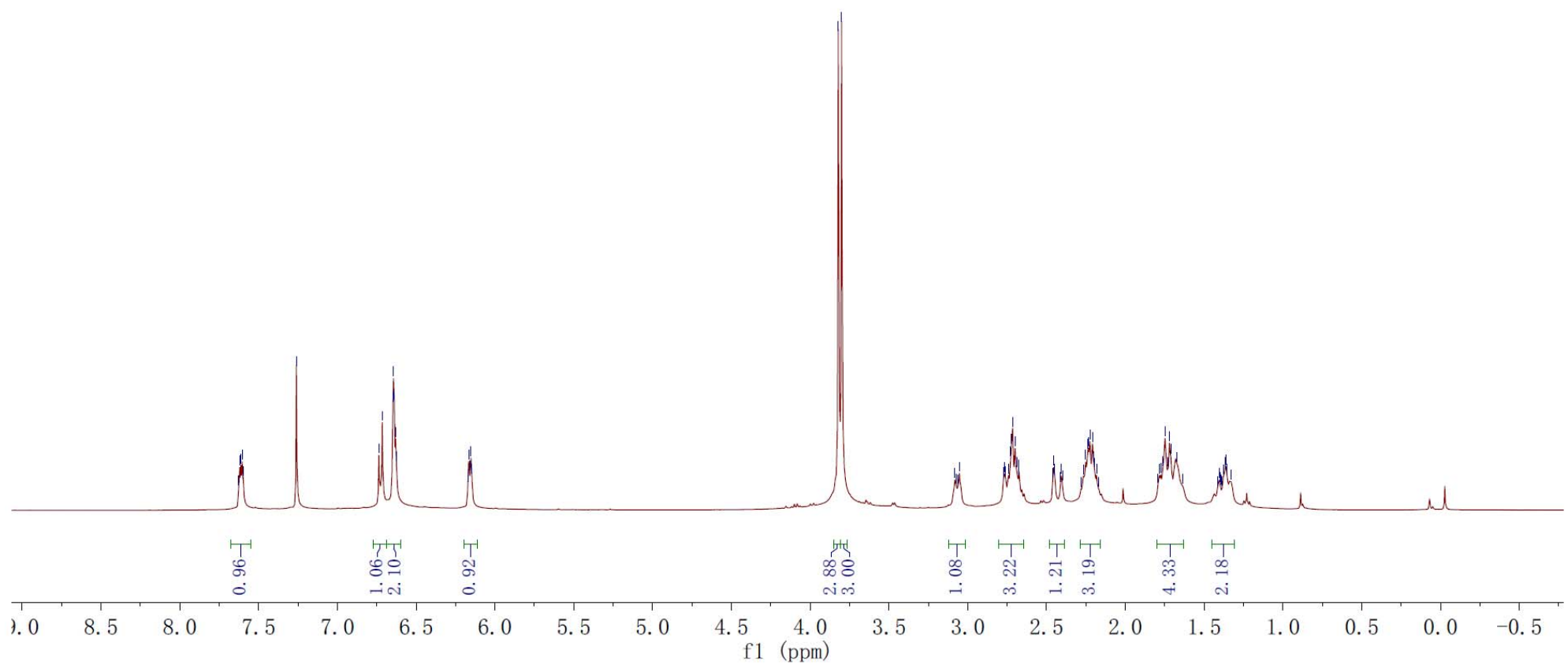
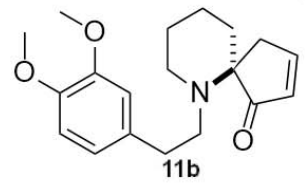
7.63
7.62
7.61
7.60
7.60
7.26
6.74
6.72
6.65
6.64
6.64
6.63
6.63
6.17
6.17
6.16
6.16
6.15
6.15

3.82
3.80

3.08
3.07
3.06
3.05

2.77
2.74
2.73
2.72
2.70
2.69
2.68
2.67
2.45
2.45
2.41
2.25
2.24
2.23
2.22
2.21
2.20
2.19
2.18
1.78
1.76
1.75
1.73
1.72
1.71
1.67
1.37
1.36
1.25

¹H NMR (400 MHz, CDCl₃)



—211.62

—162.54

~148.71
~147.24

~133.17
~132.82

—120.48

~112.16
~112.13
~111.18

~77.32
~77.20
~77.00
~76.91
~76.68
—67.88

~55.83
~55.79
~55.06
—48.89

~35.24
~34.51
~33.50

—25.47
—21.25

¹³C NMR (100 MHz, CDCl₃)

