Supporting Information

Rapid Construction of Indole-fused 8−10 Membered Lactones via a Tandem Reaction

Zhen Li,‡ Shiqiang Ma,‡ Fuhai Liu, Ruize Ma, Jipeng Zhao, Xingang Xie* and Xuegong She

State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, China

*E-mail: xiexg @lzu.edu.cn

Contents

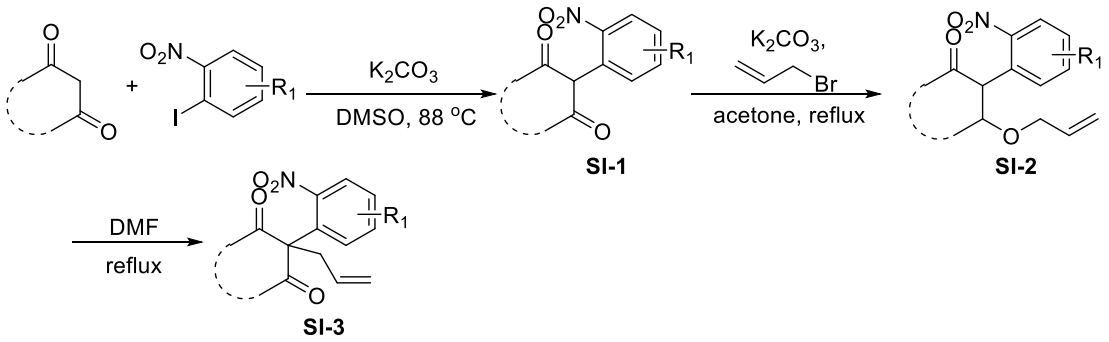
1. General Information

Solvents were purified and dried by standard methods prior to use. All commercially available reagents were used without further purification unless otherwise noted. Oxygen- and moisture-sensitive reactions were carried out under argon atmosphere. Column chromatography was generally performed on silica gel (200-300 mesh) and reactions were monitored by thin layer chromatography (TLC) using silica gel GF254 plates with UV light to visualize the course of reaction.

High-resolution mass spectral analysis (HRMS) data were measured on a Bruker APEXII mass spectrometer by means of the electrospray ionization (ESI) technique. ^{1}H NMR and ^{13}C NMR spectra were recorded on 400 MHz spectrometers. Chemical shifts are reported as δ values relative to internal chloroform (δ 7.26 for 1H NMR and 77.0 for 13C NMR). Melting points were measured on a melting point apparatus and are uncorrected. Oil bath was used as heat source for reactions above room temperature.

2. Preparation and characterization of starting materials

General procedure for the substrates:

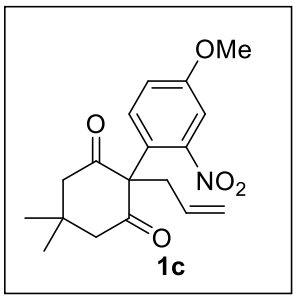


A mixture of 5,5-dimethyl-1,3-cyclohexanedione (5 mmol, 1 equiv), anhydrous K_2CO_3 (15 mmol, 3 equiv), and o-iodonitrobenzene (10 mmol, 2 equiv) in dimethyl sulfoxide (50 ml) was heated to 88 °C for 24 h. After cooling, the mixture was poured into ice water. The resulting solution was acidified with concentrated hydrochloric acid and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated to give the crude compound, which was used in the next reaction without purification.

A mixture of 5,5-dimethyl-2-(2-nitrophenyl)-1,3-cyclohexanedione (5 mmol, 1equiv), K_2CO_3 (1.037 g, 7.5 mmol, 1.5 equiv) and allyl bromide (5 mmol, 1 equiv) in anhydrous acetone (50 ml) was stirred at reflux temperature for 15 h. Then, the mixture was concentrated *in vacuo*, the residue was solubilized with CH_2Cl_2 and washed with water. The aqueous layer was back-extracted with CH_2Cl_2, the combined organic layers

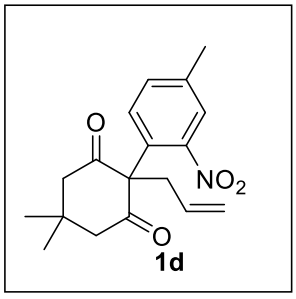
were dried with Na_2SO_4, filtered and concentrated under vacuum.

A solution of 5,5-dimethyl-3-allyloxy-2-(o-nitrophenyl)-2-cyclohexenone (1 mmol) in anhydrous DMF (10 ml) was stirred at reflux temperature for 12 h. Then, the mixture was diluted with ether, the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated to give the compound **1a.**



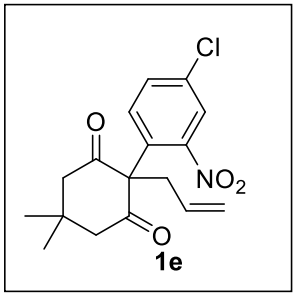
1c

Substrate 1c 2-allyl-2-(4-methoxy-2-nitrophenyl)-5,5-dimethylcyclohexane-1,3-dione was obtained as a white solid. Mp: 85-87 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 0.8 Hz, 1H), 7.12 (d, *J* = 1.6 Hz, 2H), 5.64 – 5.54 (m, 1H), 4.97 – 4.92 (m, 2H), 3.88 (s, 3H), 2.94 (d, *J* = 7.2 Hz, 2H), 2.74 (d, *J* = 14.4 Hz, 2H), 2.58 (d, *J* = 14.4 Hz, 2H), 1.17 (s, 3H), 1.01 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.4, 159.2, 149.8, 132.7, 132.4, 122.2, 119.1, 118.8, 110.4, 73.7, 55.8, 51.8, 38.1, 30.5, 30.3, 29.0; **HRMS ESI** Calcd for $C_{18}H_{21}NO_5$ $[M+Na]^+$: 354.1312, Found: 354.1310.

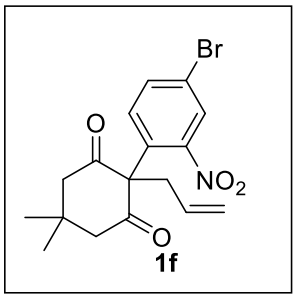


1d

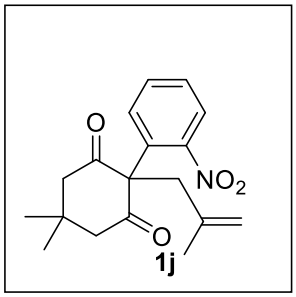
Substrate 1d 2-allyl-2-(4-methyl-2-nitrophenyl)-5,5-dimethylcyclohexane-1,3-dione was obtained as a yellow solid solid. Mp: 105-107 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 1.2 Hz, 1H), 7.41 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 5.59 (ddt, *J* = 17.2, 10.0, 7.2 Hz, 1H), 4.96 – 4.91 (m, 2H), 2.95 (d, *J* = 7.2 Hz, 2H), 2.74 (d, *J* = 14.4 Hz, 2H), 2.58 (d, *J* = 14.4 Hz, 2H), 2.43 (s, 3H), 1.17 (s, 3H), 1.01 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.3, 148.9, 139.5, 133.4, 132.4, 131.6, 127.6, 125.8, 119.1, 74.0, 51.8, 38.1, 30.5, 30.3, 29.0, 20.6; **HRMS ESI** Calcd for $C_{18}H_{21}NO_4$ $[M+H]^+$: 316.1543, Found: 316.1539.



Substrate 1e 2-allyl-2-(4-chloro-2-nitrophenyl)-5,5-dimethylcyclohexane-1,3-dione was obtained as a yellow solid solid. Mp: 139-141 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (t, *J* = 2.4 Hz, 1H), 7.60 – 7.57 (m, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 5.51 (tdd, *J* = 12.8, 6.8, 2.8 Hz, 1H), 5.09 – 4.97 (m, 2H), 3.00 (d, *J* = 6.8 Hz, 2H), 2.69 (s, 4H), 1.22 (d, *J* = 2.0 Hz, 3H), 1.09 (d, *J* = 1.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.1, 149.6, 134.7, 133.1, 132.6, 131.4, 128.8, 125.5, 119.9, 73.5, 51.3, 38.7, 30.4, 30.3, 30.1; **HRMS ESI** Calcd for $C_{17}H_{18}ClNO_4$ $[M+Na]^+$: 358.0817, Found: 358.0813.



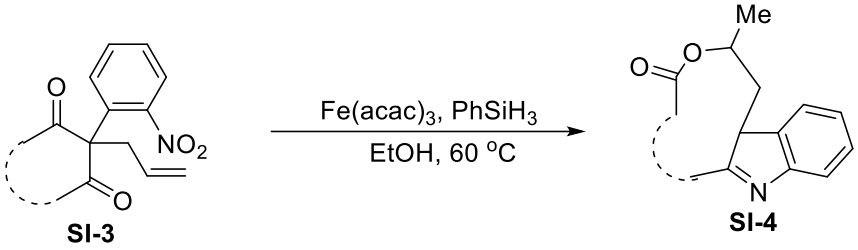
Substrate 1f 2-allyl-2-(4-bromo-2-nitrophenyl)-5,5-dimethylcyclohexane-1,3-dione was obtained as a yellow solid solid. Mp: 138-140 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.73 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 1H), 5.56 – 5.45 (m, 1H), 5.02 (dd, *J* = 12.4, 11.2 Hz, 2H), 3.00 (d, *J* = 6.8 Hz, 2H), 2.69 (s, 4H), 1.21 (s, 3H), 1.09 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.0, 149.6, 135.6, 133.3, 131.3, 129.2, 128.2, 122.1, 119.9, 73.5, 51.2, 38.6, 30.3, 30.3, 30.0; **HRMS ESI** Calcd for $C_{17}H_{18}BrNO_4$ $[M+H]^+$: 380.0492,382.0472, Found: 380.0491,382.0471.



Substrate 1j 5,5-dimethyl-2-(2-methylallyl)-2-(2-nitrophenyl)cyclohexane-1,3-dione was obtained as a white solid. Mp: 113-115 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ

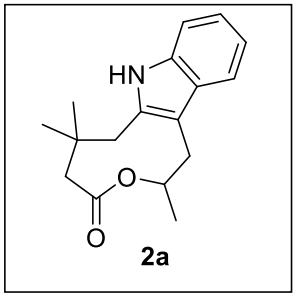
7.92 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 4.72 (s, 1H), 4.45 (s, 1H), 2.99 (s, 2H), 2.74 (d, *J* = 14.4 Hz, 2H), 2.62 (d, *J* = 14.4 Hz, 2H), 1.52 (s, 3H), 1.16 (s, 3H), 1.02 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.7, 149.2, 139.8, 132.5, 132.4, 130.9, 128.9, 125.4, 116.6, 75.2, 51.7, 39.8, 30.4, 30.2, 29.2, 24.6; **HRMS ESI** Calcd for $C_{17}H_{21}NO_4$ $[M+H]^+$: 316.1543, Found: 316.1541.

3. General procedure for the tandem reaction



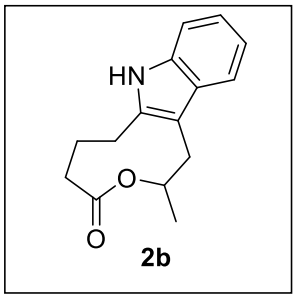
Under an argon atmosphere, a mixture of compound **1a** (0.10 mmol, 1.0 equiv.), $Fe(acac)_3$ (0.10 mmol, 1.0 equiv.), $PhSiH_3$ (0.40 mmol, 4.0 equiv.) in EtOH (1 mL) was stirred at 60 ℃ for 24 h. Then the reaction mixture was cooled to room temperature. EtOH was evaporated to give crude product, which was purified by silica gel column chromatography to afford compound **2a** (20 mg, 74%) as a white solid.

4. Characterization data for the products



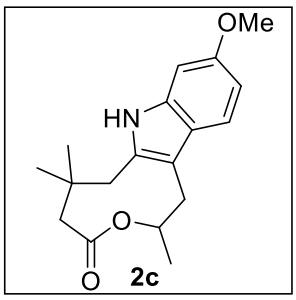
Compound 2a 2,6,6-trimethyl-1,2,5,6,7,8-hexahydro-4H-oxonino[5,4-b]indol-4-one was obtained as a white solid. Mp: 222-224 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.23 – 7.18 (m, 1H), 7.08 (dtd, *J* = 18.8, 7.2, 1.2 Hz, 2H), 4.99 (ddd, *J* = 10.0, 6.4, 2.0 Hz, 1H), 3.10 – 3.01 (m, 2H), 2.68 (dd, *J* = 14.4, 10.0 Hz, 1H), 2.53 (d, *J* = 14.8 Hz, 1H), 2.33 (d, *J* = 11.2 Hz, 1H), 2.02 (d, *J* = 11.2 Hz, 1H), 1.41 (d, *J* = 6.4 Hz, 3H), 1.20 (d, *J* = 2.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.7,

135.2, 133.4, 128.1, 121.5, 119.0, 117.9, 110.1, 109.9, 69.9, 47.7, 37.8, 37.3, 33.8, 32.5, 28.3, 20.2; **HRMS ESI** Calcd for $C_{17}H_{21}NO_2$ $[M+Na]^+$: 294.1465, Found: 294.1460.



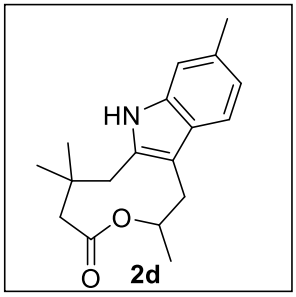
2b

Compound 2b 2-methyl-1,2,5,6,7,8-hexahydro-4H-oxonino[5,4-b]indol-4-one was obtained as a white solid. Mp: 58-60 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.08 (ddd, *J* = 15.6, 14.0, 7.2 Hz, 2H), 5.03 – 4.96 (m, 1H), 3.00 (t, *J* = 12.8 Hz, 2H), 2.85 (dd, *J* = 14.4, 7.6 Hz, 1H), 2.72 (dd, *J* = 14.4, 10.0 Hz, 1H), 2.39 (td, *J* = 11.6, 7.2 Hz, 1H), 2.28 – 2.23 (m, 2H), 2.16 – 2.09 (m, 1H), 1.42 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.2, 136.1, 135.7, 128.2, 121.6, 119.2, 117.8, 110.3, 109.0, 70.2, 34.3, 32.4, 28.0, 24.4, 20.2; **HRMS ESI** Calcd for $C_{15}H_{17}NO_2$ $[M+H]^+$: 244.1332, Found: 244.1327.

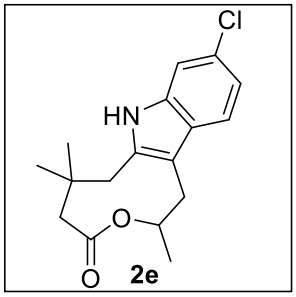


2c

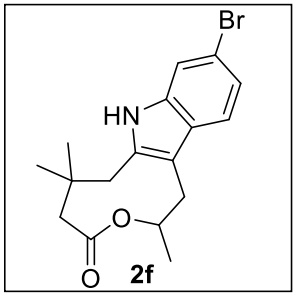
Compound 2c 10-methoxy-2,6,6-trimethyl-1,2,5,6,7,8-hexahydro-4H-oxonino[5,4-b]indol-4-one was obtained as a white solid. Mp: 220-222 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 6.75 – 6.72 (m, 2H), 4.97 (dq, *J* = 12.8, 6.4 Hz, 1H), 3.81 (s, 3H), 3.06 (d, *J* = 14.8 Hz, 1H), 2.97 (d, *J* = 14.0 Hz, 1H), 2.65 (dd, *J* = 14.4, 10.0 Hz, 1H), 2.51 (d, *J* = 14.8 Hz, 1H), 2.32 (d, *J* = 11.2 Hz, 1H), 2.02 (d, *J* = 11.2 Hz, 1H), 1.41 (d, *J* = 6.4 Hz, 3H), 1.23 (s, 3H), 1.20 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.7, 156.2, 135.8, 132.1, 122.5, 118.5, 109.8, 108.7, 94.0, 69.8, 55.7, 47.6, 37.8, 37.4, 33.8, 32.6, 28.4, 20.2; **HRMS ESI** Calcd for $C_{18}H_{23}NO_3$ $[M+H]^+$: 302.1751, Found: 302.1744.



Compound 2d 2,6,6,10-tetramethyl-1,2,5,6,7,8-hexahydro-4H-oxonino[5,4-b]indol-4-one was obtained as a white solid. Mp: 158-160 ^{o}C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.04 (s, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 4.98 (dqd, *J* = 12.8, 6.4, 1.6 Hz, 1H), 3.10 – 2.99 (m, 2H), 2.66 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.54 (d, *J* = 14.8 Hz, 1H), 2.43 (s, 3H), 2.33 (d, *J* = 11.2 Hz, 1H), 2.02 (d, *J* = 11.2 Hz, 1H), 1.41 (d, *J* = 6.4 Hz, 3H), 1.22 (d, *J* = 4.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 135.5, 132.7, 131.2, 126.0, 120.7, 117.5, 110.1, 109.7, 69.9, 47.7, 37.8, 37.4, 33.7, 32.6, 28.3, 21.6, 20.2; **HRMS ESI** Calcd for $C_{18}H_{23}NO_2$ $[M+H]^+$: 286.1802, Found: 286.1799.

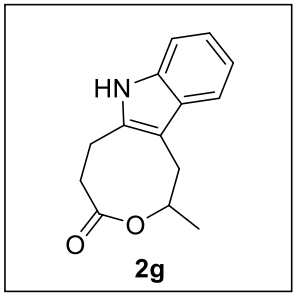


Compound 2e 10-chloro-2,6,6-trimethyl-1,2,5,6,7,8-hexahydro-4H-oxonino[5,4-b]indol-4-one was obtained as a yellow solid solid. Mp: 160-162 ^{o}C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 1.6 Hz, 1H), 7.02 (dd, *J* = 8.4, 1.6 Hz, 1H), 4.97 (dqd, *J* = 12.8, 6.4, 1.6 Hz, 1H), 3.09 (d, *J* = 14.8 Hz, 1H), 2.98 (dd, *J* = 14.8, 1.6 Hz, 1H), 2.66 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.53 (d, *J* = 14.8 Hz, 1H), 2.34 (d, *J* = 11.2 Hz, 1H), 2.03 (d, *J* = 11.2 Hz, 1H), 1.41 (d, *J* = 6.4 Hz, 3H), 1.22 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.7, 135.4, 134.2, 127.5, 126.7, 119.8, 118.8, 110.2, 110.1, 69.7, 47.6, 37.9, 37.4, 33.9, 32.6, 28.4, 20.3; **HRMS ESI** Calcd for $C_{17}H_{20}ClNO_2$ $[M+H]^+$: 306.1255, Found: 306.1253.



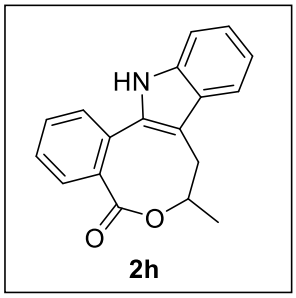
2f

Compound 2f 10-bromo-2,6,6-trimethyl-1,2,5,6,7,8-hexahydro-4H-oxonino[5,4-b]indol-4-one was obtained as a white solid. Mp: 236-238 ^{o}C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.38 (d, *J* = 1.6 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.16 (dd, *J* = 8.4, 1.6 Hz, 1H), 4.97 (dtd, *J* = 12.8, 6.4, 4.8 Hz, 1H), 3.09 (d, *J* = 14.8 Hz, 1H), 2.96 (d, *J* = 1.6 Hz, 1H), 2.67 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.53 (d, *J* = 14.8 Hz, 1H), 2.34 (d, *J* = 11.2 Hz, 1H), 2.03 (d, *J* = 11.2 Hz, 1H), 1.41 (d, *J* = 6.4 Hz, 3H), 1.23 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.6, 135.9, 134.1, 127.0, 122.3, 119.2, 115.1, 113.0, 110.3, 69.7, 47.6, 37.8, 37.3, 33.8, 32.5, 28.4, 20.2; **HRMS ESI** Calcd for $C_{17}H_{20}BrNO_2$ $[M+H]^+$: 350.0750, 352.0730, Found: 350.0749, 352.0746.



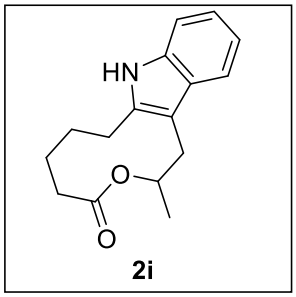
2g

Compound 2g 2-methyl-1,5,6,7-tetrahydrooxocino[5,4-b]indol-4(2H)-one was obtained as a colorless oil liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.28 (s, 1H), 7.15 – 7.07 (m, 2H), 4.99 – 4.95 (m, 1H), 3.45 (ddd, *J* = 14.0, 11.6, 6.4 Hz, 1H), 3.07 – 3.03 (m, 1H), 2.93 – 2.87 (m, 1H), 2.81 (ddd, *J* = 10.0, 9.2, 6.4 Hz, 2H), 2.53 (ddd, *J* = 13.2, 11.6, 5.2 Hz, 1H), 1.47 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.5, 134.8, 134.5, 128.8, 121.6, 119.5, 117.8, 110.6, 109.3, 76.8, 38.0, 32.8, 24.8, 20.4. **HRMS ESI** Calcd for $C_{14}H_{15}NO_2$ $[M+H]^+$: 230.1176, Found: 230.1174.



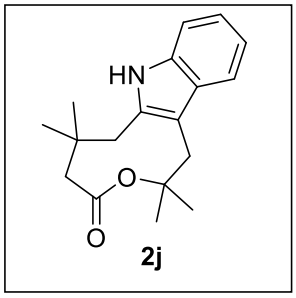
2h

Compound 2h 7-methyl-8,13-dihydrobenzo[6,7]oxocino[5,4-b]indol-5(7H)-one was obtained as a white solid. Mp: 252-254 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.57 (dd, *J* = 7.6, 3.2 Hz, 2H), 7.54 – 7.49 (m, 2H), 7.45 (td, *J* = 7.2, 1.6 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.25 – 7.22 (m, 1H), 7.17 – 7.14 (m, 1H), 5.18 (ddd, *J* = 11.6, 6.0, 2.4 Hz, 1H), 3.43 – 3.36 (m, 1H), 3.03 (dd, *J* = 16.8, 2.4 Hz, 1H), 1.51 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 136.6, 132.3, 131.3, 131.1, 130.6, 129.3, 129.0, 128.8, 128.7, 123.3, 120.1, 118.8, 110.9, 109.1, 74.7, 34.2, 21.7; **HRMS ESI** Calcd for $C_{18}H_{15}NO_2$ $[M+H]^+$: 278.1176, Found: 278.1173.



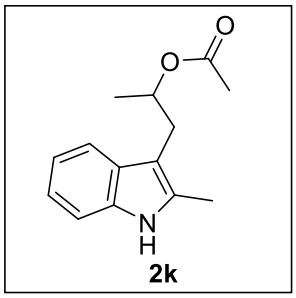
2i

Compound 2i 2-methyl-1,5,6,7,8,9-hexahydrooxecino[5,4-b]indol-4(2H)-one was obtained as a white solid. Mp: 110-112 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.48 – 7.46 (m, 1H), 7.26 (dd, *J* = 6.8, 1.6 Hz, 1H), 7.14 – 7.06 (m, 2H), 5.32 – 5.13 (m, 1H), 3.29 (dd, *J* = 15.2, 4.8 Hz, 1H), 2.81 – 2.69 (m, 3H), 2.49 – 2.43 (m, 1H), 2.18 – 2.08 (m, 1H), 2.07 – 1.97 (m, 1H), 1.91 – 1.76 (m, 2H), 1.60 – 1.53 (m, 1H), 1.29 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 136.5, 135.5, 129.4, 121.0, 119.2, 118.5, 110.1, 107.4, 69.8, 35.5, 28.9, 27.4, 23.0, 22.4, 19.5. **HRMS ESI** Calcd for $C_{16}H_{19}NO_2$ $[M+H]^+$: 258.1489, Found: 258.1486.



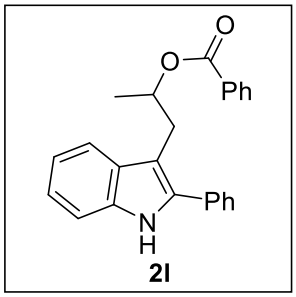
2j

Compound 2j 2,2,6,6-tetramethyl-1,2,5,6,7,8-hexahydro-4H-oxonino[5,4-b]indol-4-one was obtained as a colorless oil liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.47 (d, *J* = 7.2 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.14 – 7.06 (m, 2H), 3.09 (s, 2H), 2.76 (s, 2H), 2.13 (s, 2H), 1.54 (s, 6H), 1.27 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.8, 135.2, 134.8, 129.4, 121.4, 119.3, 119.0, 110.2, 109.7, 83.2, 47.9, 37.2, 37.2, 34.7, 28.2; **HRMS ESI** Calcd for $C_{18}H_{23}NO_2$ $[M+H]^+$: 286.1802, Found: 286.1797.



2k

Compound 2k 1-(2-methyl-1H-indol-3-yl)propan-2-yl acetate was obtained as a colorless oil liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.57 – 7.55 (m, 1H), 7.24 (dd, *J* = 6.4, 2.4 Hz, 1H), 7.12 – 7.06 (m, 2H), 5.12 (dd, *J* = 13.2, 6.4 Hz, 1H), 3.03 (dd, *J* = 14.4, 5.6 Hz, 1H), 2.81 (dd, *J* = 14.4, 7.6 Hz, 1H), 2.38 (s, 3H), 2.00 (s, 3H), 1.21 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7, 135.1, 132.1, 129.0, 121.0, 119.3, 118.3, 110.1, 107.6, 71.7, 30.6, 21.5, 19.5, 11.8; **HRMS ESI** Calcd for $C_{14}H_{17}NO_2$ $[M+Na]^+$: 254.1152, Found: 254.1147.



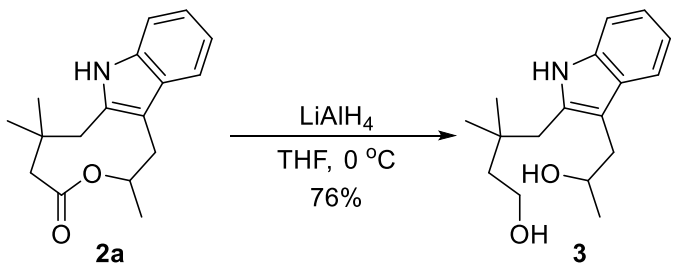
2l

Compound 2l 1-(2-phenyl-1H-indol-3-yl)propan-2-yl benzoate was obtained as a colorless oil liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.92 – 7.90 (m, 2H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.63 – 7.61 (m, 2H), 7.49 (dt, *J* = 14.8, 7.2 Hz, 5H), 7.37 (ddd, *J* = 7.2, 3.6, 1.2 Hz, 4H), 7.17 (ddd, *J* = 14.8, 8.0, 3.6 Hz, 3H), 5.50 (dd, *J* = 13.2, 6.4 Hz, 1H), 3.43 (dd, *J* = 14.4, 6.4 Hz, 1H), 3.20 (dd, *J* = 14.4, 7.2 Hz, 1H), 1.29 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.2, 135.8, 135.7, 133.2, 132.6, 130.8, 129.6, 129.4, 128.9, 128.3, 128.2, 127.8, 122.4, 119.9, 119.6, 110.8, 108.9, 72.2, 31.1, 19.9; **HRMS ESI** Calcd for $C_{24}H_{21}NO_2$ $[M+Na]^+$: 378.1465, Found: 378.1464.

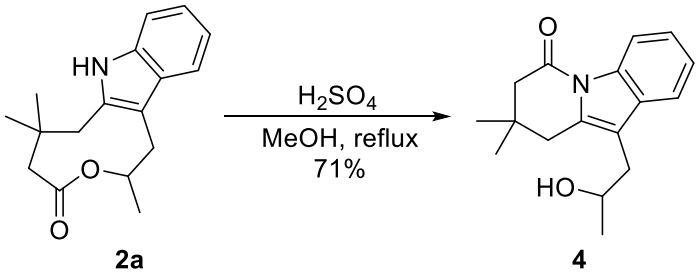
5. X-ray crystallography data for 2a

CCDC	2170036
Empirical formula	$C_{17}H_{21}NO_2$
Formula weight	271.35
Temperature/K	295.99(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	9.8106(2)
b/Å	17.8042(2)
c/Å	9.8334(2)
α/°	90
β/°	119.489(3)
γ/°	90
Volume/Å^3	1495.08(6)
Z	4
ρ_{calc}g/cm^3	1.206
μ/mm^{-1}	0.622
F(000)	584.0
Crystal size/mm^3	0.28 × 0.15 × 0.14
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.936 to 154.97
Index ranges	$-12 \le h \le 11$, $-21 \le k \le 22$, $-9 \le l \le 1$
Reflections collected	14667
Independent reflections	2988 [R_{int} = 0.0364, R_{sigma} =0.0255]
Data/restraints/parameters	2988/0/185
Goodness-of-fit on F^2	1.039
Final R indexes [I>=2σ (I)]	R_1 = 0.0376, wR_2 = 0.1023
Final R indexes [all data]	R_1 = 0.0408, wR_2 = 0.1049
Largest diff. peak/hole / e Å^{-3}	0.21/-0.16

6. Derivatization of 2,3-disubstituted indoles.

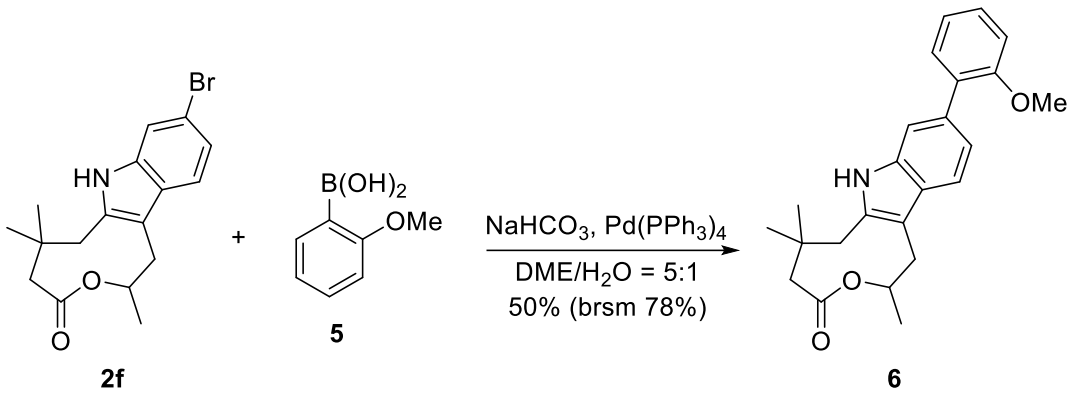


0°C, to the solution of compound **2a** (60 mg, 0.22 mmol) in THF was added $LiAlH_4$ (17 mg, 0.44 mmol) and stirred at 0°C for 2 h. The reaction was quenched by water (17 μL), 10% NaOH (34 μL), water (51 μL). The reaction mixture was filtered through a pad of celite. The filtrare was collected and concentrated in vacuo to give crude product, which was purified by silica gel column chromatography to afford compound **3** (46 mg, 76%) as a colorless oil liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.14 – 7.04 (m, 2H), 4.14 (ddd, *J* = 8.8, 6.4, 4.4 Hz, 1H), 3.91 – 3.82 (m, 2H), 2.92 (dd, *J* = 14.4, 4.4 Hz, 1H), 2.82 – 2.78 (m, 1H), 2.76 (s, 2H), 2.05 (m, 2H), 1.59 (m, 1H), 1.51 – 1.41 (m, 1H), 1.29 (d, *J* = 6.0 Hz, 3H), 0.99 (s, 3H), 0.95 (s, 3H)；**^{13}C NMR** (101 MHz, $CDCl_3$) δ 135.3, 135.2, 128.3, 121.0, 118.8, 118.3, 110.5, 108.9, 68.0, 59.7, 41.9, 37.4, 34.7, 34.7, 28.6, 28.3, 22.7; **HRMS ESI** Calcd for $C_{17}H_{25}NO_2$ $[M+H]^+$: 276.1958, Found: 276.1956.

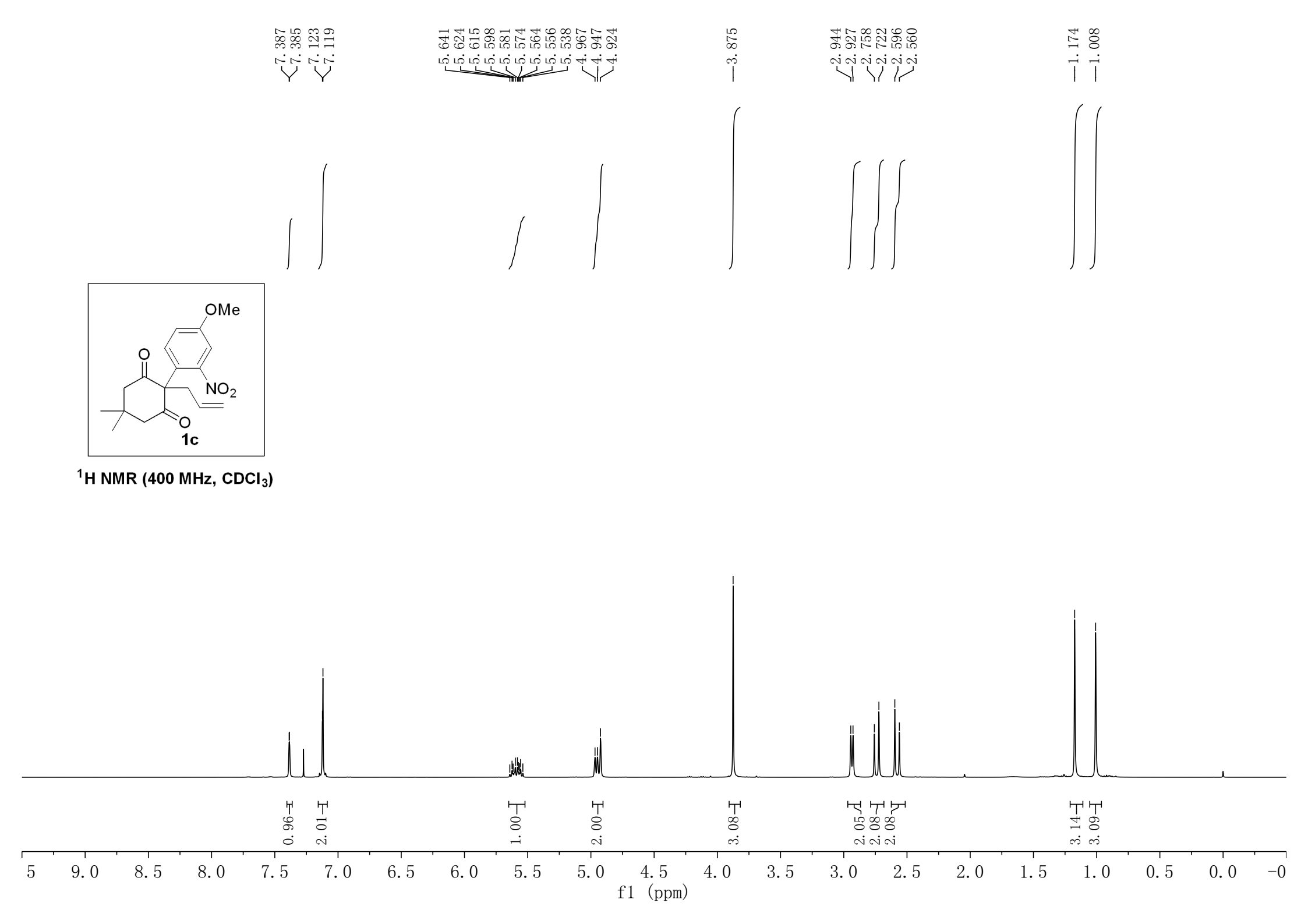


2a **4**

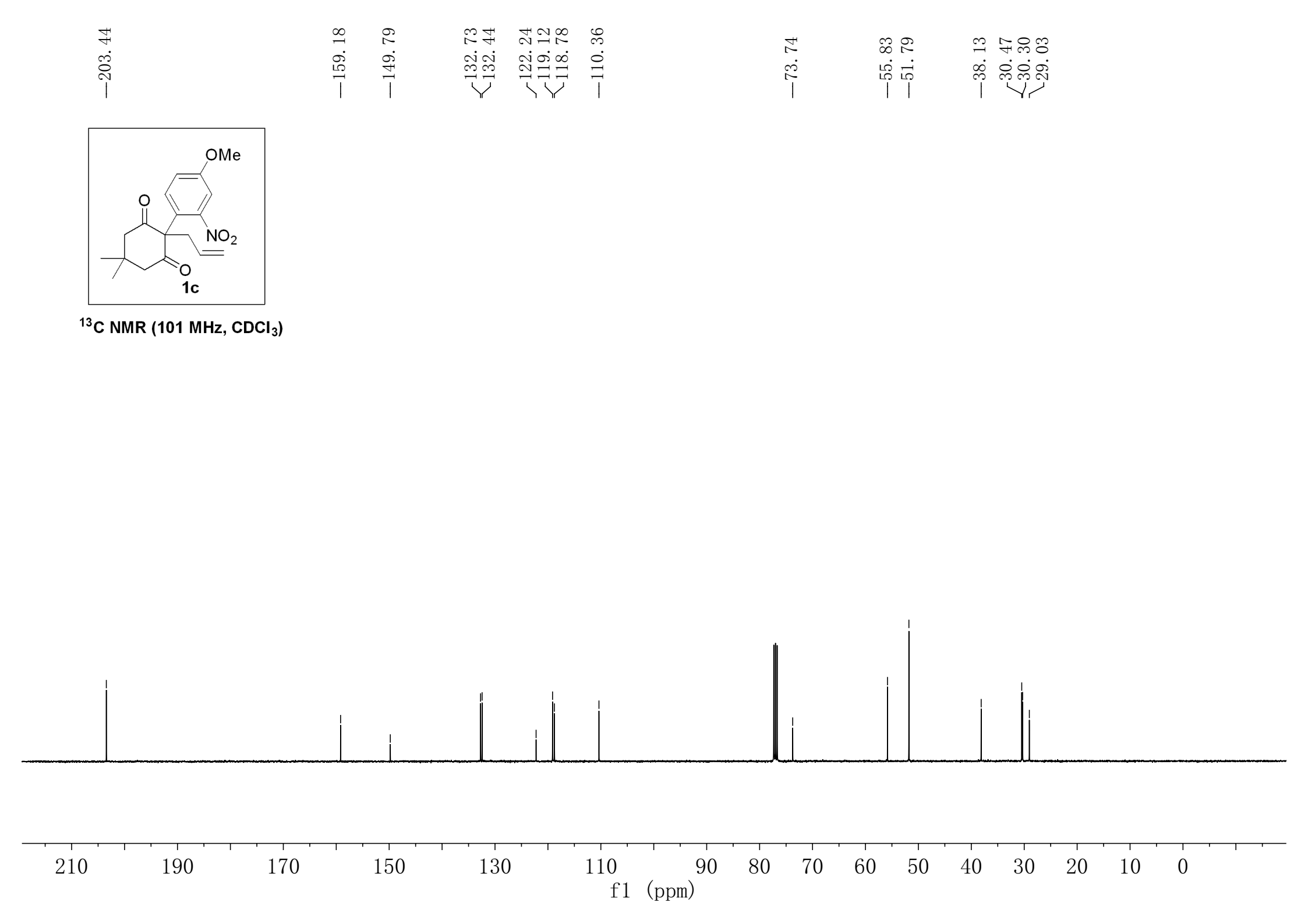
To the solution of compound **2a** (50 mg, 0.18 mmol) in MeOH was added H_2SO_4 (3.8 μL, 0.07 mmol) and stirred at reflux temperature until the **2a** disappears. The reaction mixture was cooled to room temperature and quenched with saturated aqueous solution $NaHCO_3$. Then, MeOH was evaporated. Residue extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with saturated brine and dried over anhydrous Na_2SO_4, the solution was evaporated in vacuo, then purified by silica gel flash column chromatography to afford compound **4** (35 mg, 71%) as a colorless oil liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.43 (dd, *J* = 6.8, 2.0 Hz, 1H), 7.48 (dd, *J* = 6.4, 2.4 Hz, 1H), 7.33 – 7.24 (m, 2H), 4.16 – 4.09 (m, 1H), 2.82 – 2.71 (m, 4H), 2.47 – 2.38 (m, 2H), 2.05 (d, *J* = 13.7 Hz, 1H), 1.29 (d, *J* = 6.4 Hz, 3H), 1.06 (d, *J* = 2.4 Hz, 6H)； **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.8, 134.4, 134.3, 130.7, 124.3, 123.8, 118.2, 116.3, 114.4, 67.5, 47.5, 35.6, 33.9, 32.5, 27.7, 27.7, 23.1; **HRMS ESI** Calcd for $C_{17}H_{21}NO_2$ $[M+H]^+$: 272.1645, Found: 272.1644.

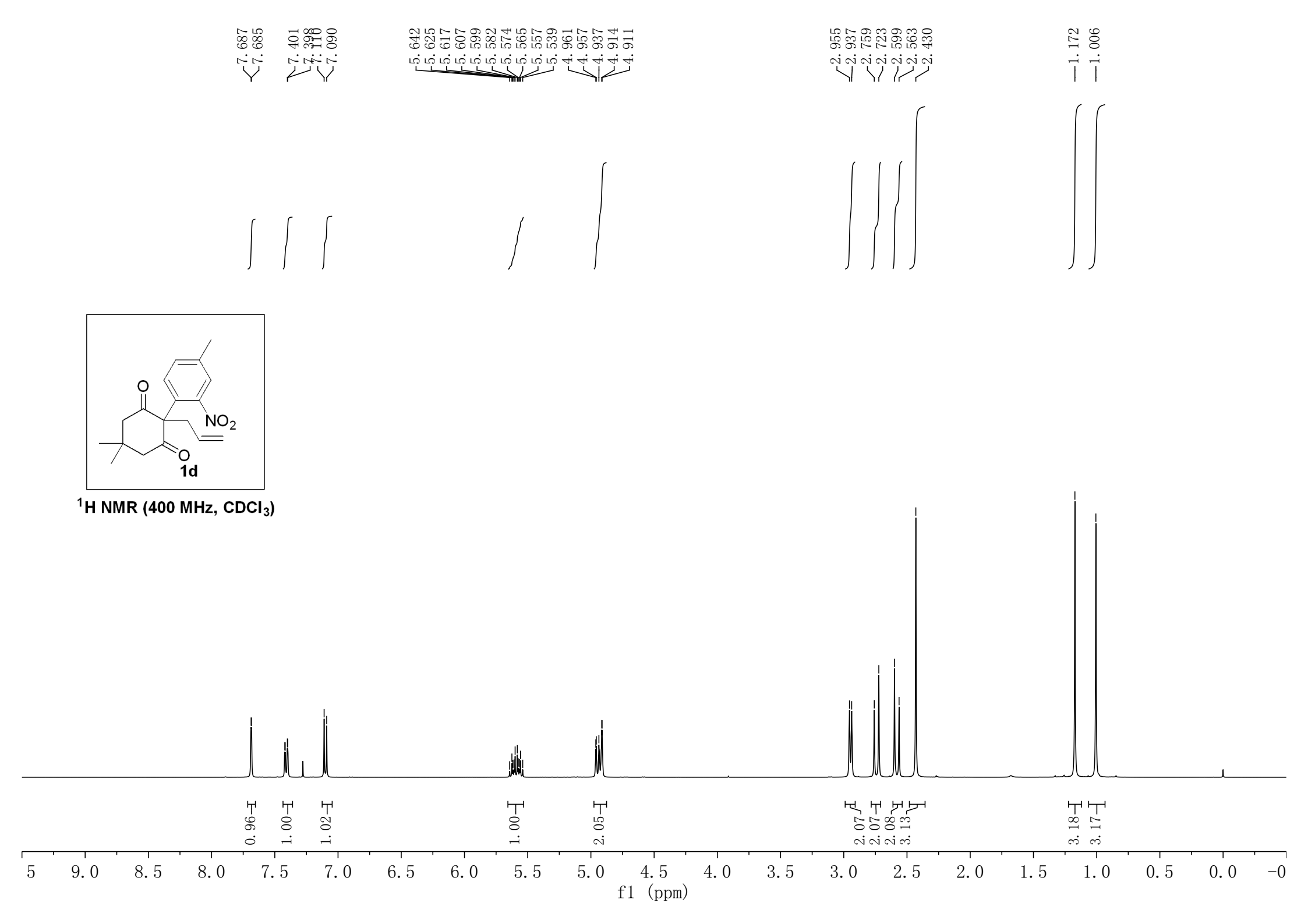


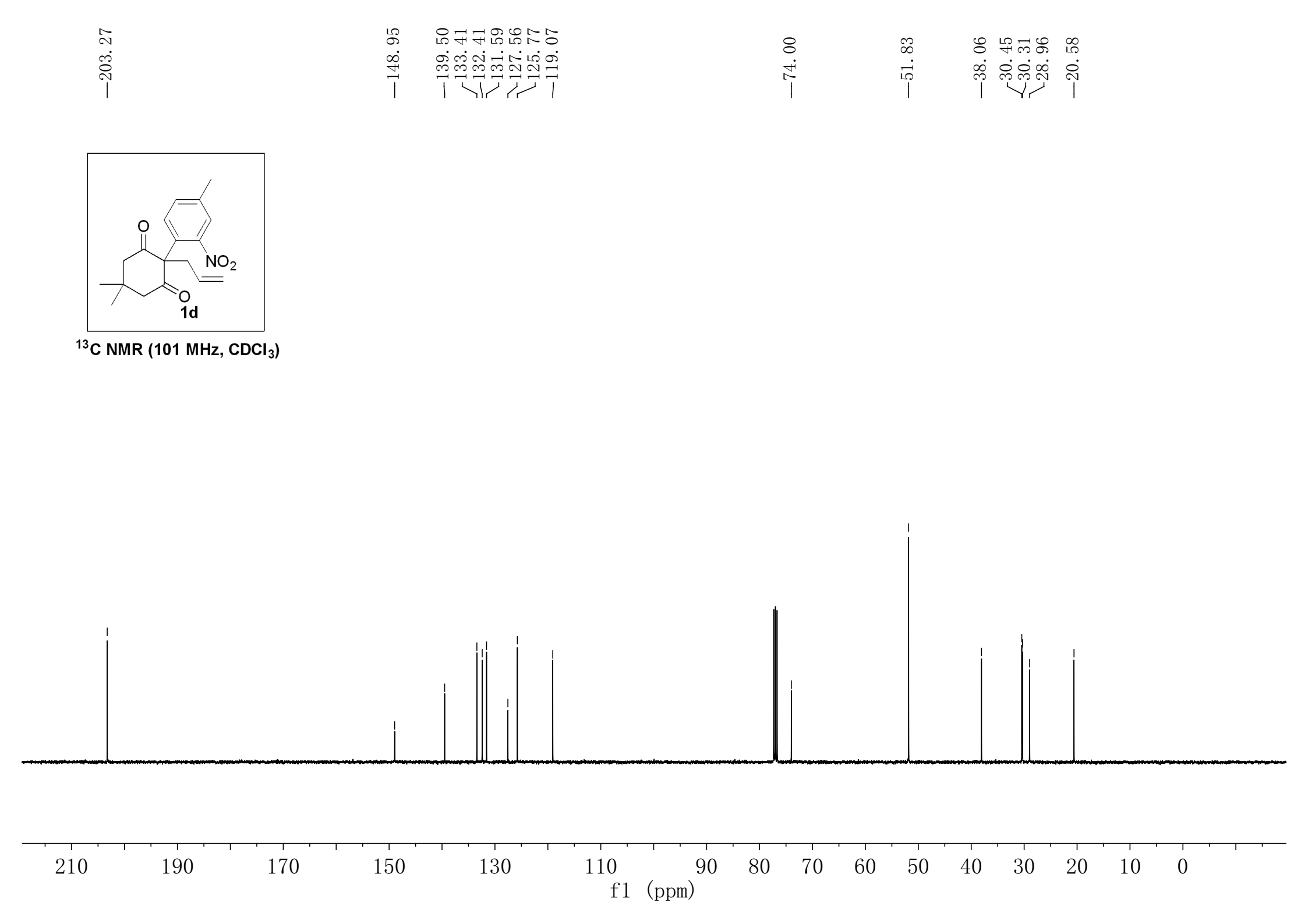
Under argon atmosphere, a mixture of **2f** (20 mg, 0.06 mmol), $NaHCO_3$ (20 mg, 0.24 mmol) and (2-methoxyphenyl)boronic acid **5** (18 mg, 0.12 mmol) in DME (1 mL) and H_2O (0.2 mL) was allowed to stir for 5 min at room temperature.Then $Pd(PPh_3)_4$ (7 mg, 0.006 mmol) was added. The reaction was allowed to stir for 10 min at room temperature and was heated at 95 °C with vigorous stirring for 12 h. Cooled to room temperature, the mixture was diluted with Et_2O followed by filtration through a thin pad of silica gel with Et_2O rinse. Solvent evaporation followed by flash chromatography to afford the product **6** (11 mg, 50%) as a colorless oil liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 0.8 Hz, 1H), 7.36 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.33 – 7.27 (m, 1H), 7.25 – 7.22 (m, 1H), 7.02 (ddd, *J* = 11.2, 8.8, 4.8 Hz, 2H), 5.02 (ddd, *J* = 10.0, 6.4, 1.6 Hz, 1H), 3.81 (s, 3H), 3.14 – 3.04 (m, 2H), 2.70 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.58 (d, *J* = 14.8 Hz, 1H), 2.37 – 2.33 (m, 1H), 2.05 (d, *J* = 11.2 Hz, 1H), 1.43 (d, *J* = 6.4 Hz, 3H), 1.27 (s, 3H), 1.24 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.7, 156.6, 135.2, 133.9, 132.1, 131.9, 131.3, 127.9, 127.3, 121.3, 120.8, 117.3, 111.3, 111.1, 110.1, 70.0, 55.6, 47.7, 37.9, 37.6, 29.7, 22.7, 20.3, 14.1; **HRMS ESI** Calcd for $C_{24}H_{27}NO_3$ $[M+H]^+$: 378.2064, Found: 378.2061.

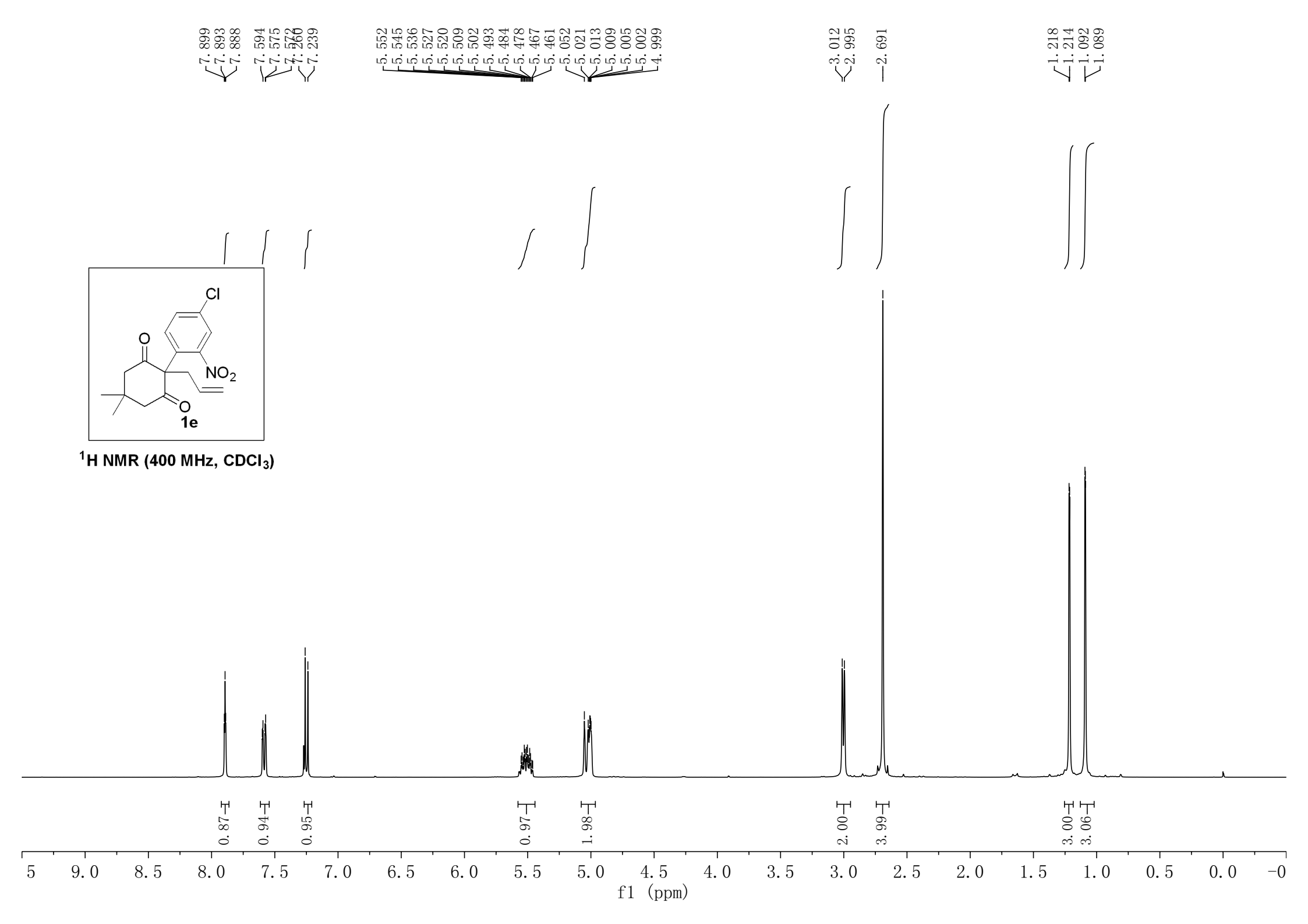


^{1}H NMR (400 MHz, $CDCl_3$)

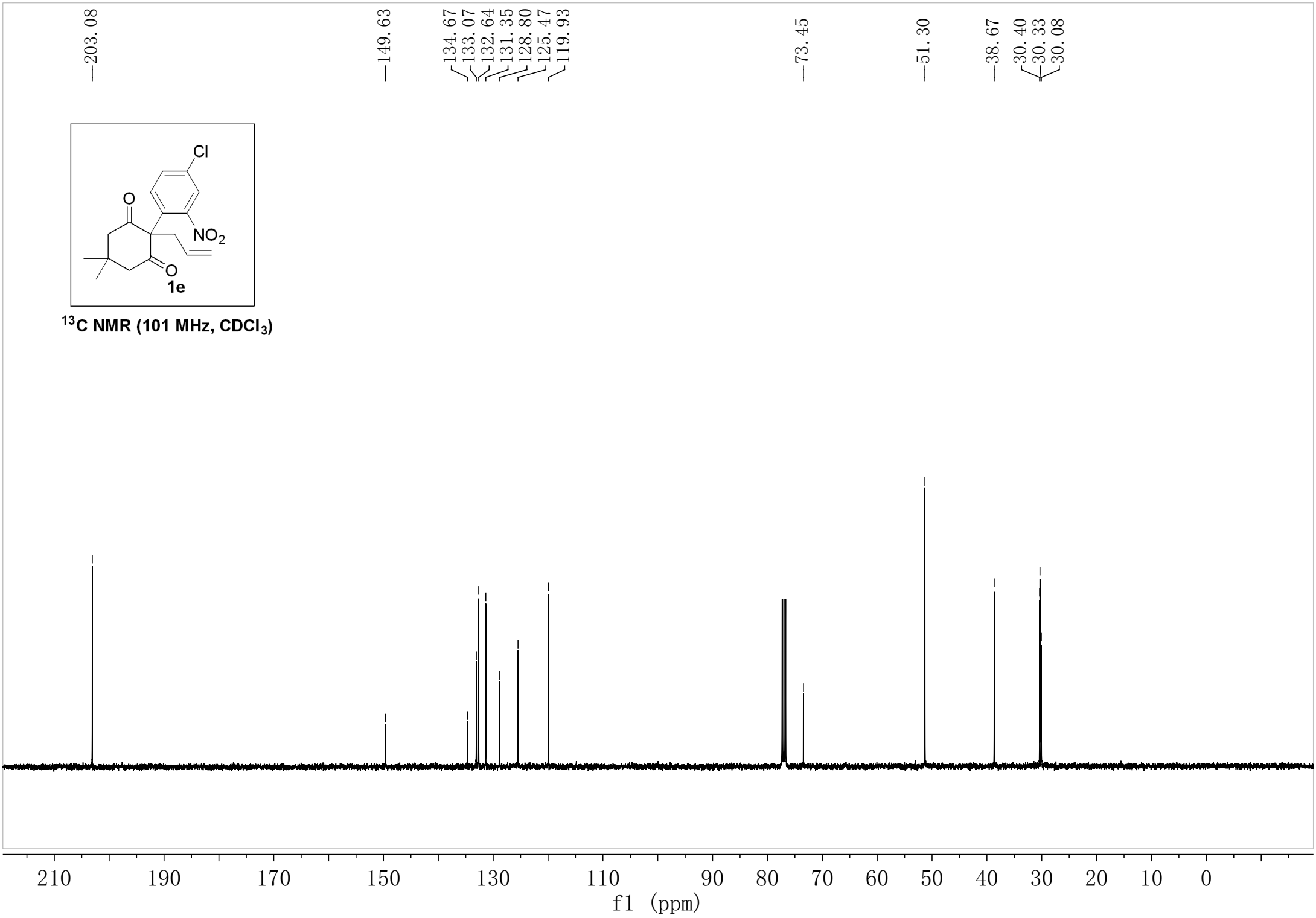

203.44
159.18
149.79
132.73
132.44
122.24
119.12
118.78
110.36
73.74
55.83
51.79
38.13
30.47
30.30
29.03
OMe
O
NO2
O
1c
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

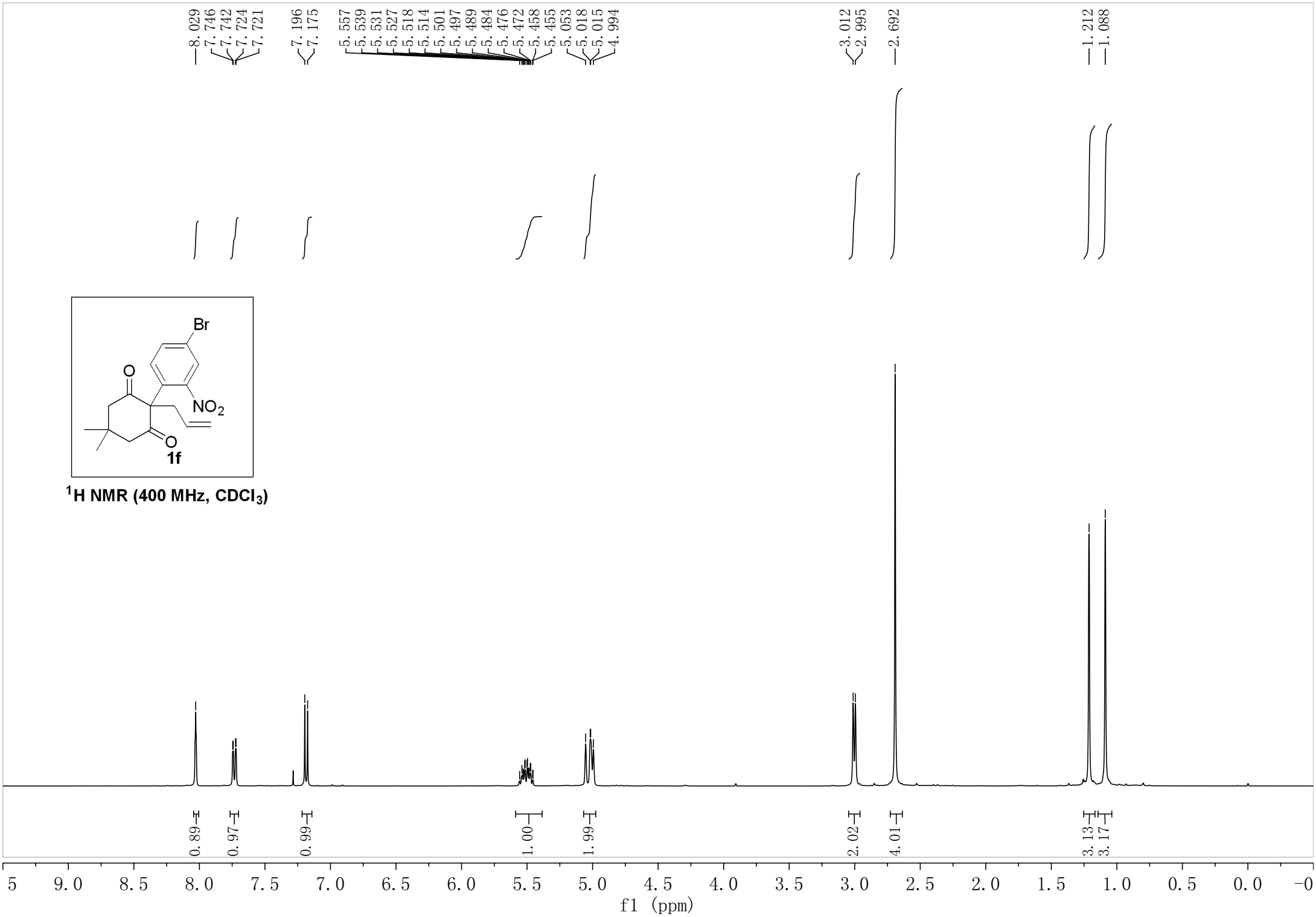

7.687
7.685
7.401
7.398
7.110
7.090
5.642
5.625
5.617
5.607
5.599
5.582
5.574
5.565
5.557
5.539
4.961
4.957
4.937
4.914
4.911
2.955
2.937
2.759
2.723
2.599
2.563
2.430
1.172
1.006
O
NO2
O
1d
1H NMR (400 MHz, CDCl3)
0.96
1.00
1.02
1.00
2.05
2.07
2.07
2.08
3.13
3.18
3.17
f1 (ppm)


203.27
148.95
139.50
133.41
132.41
131.59
127.56
125.77
119.07
74.00
51.83
38.06
30.45
30.31
28.96
20.58
O
NO2
O
1d
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

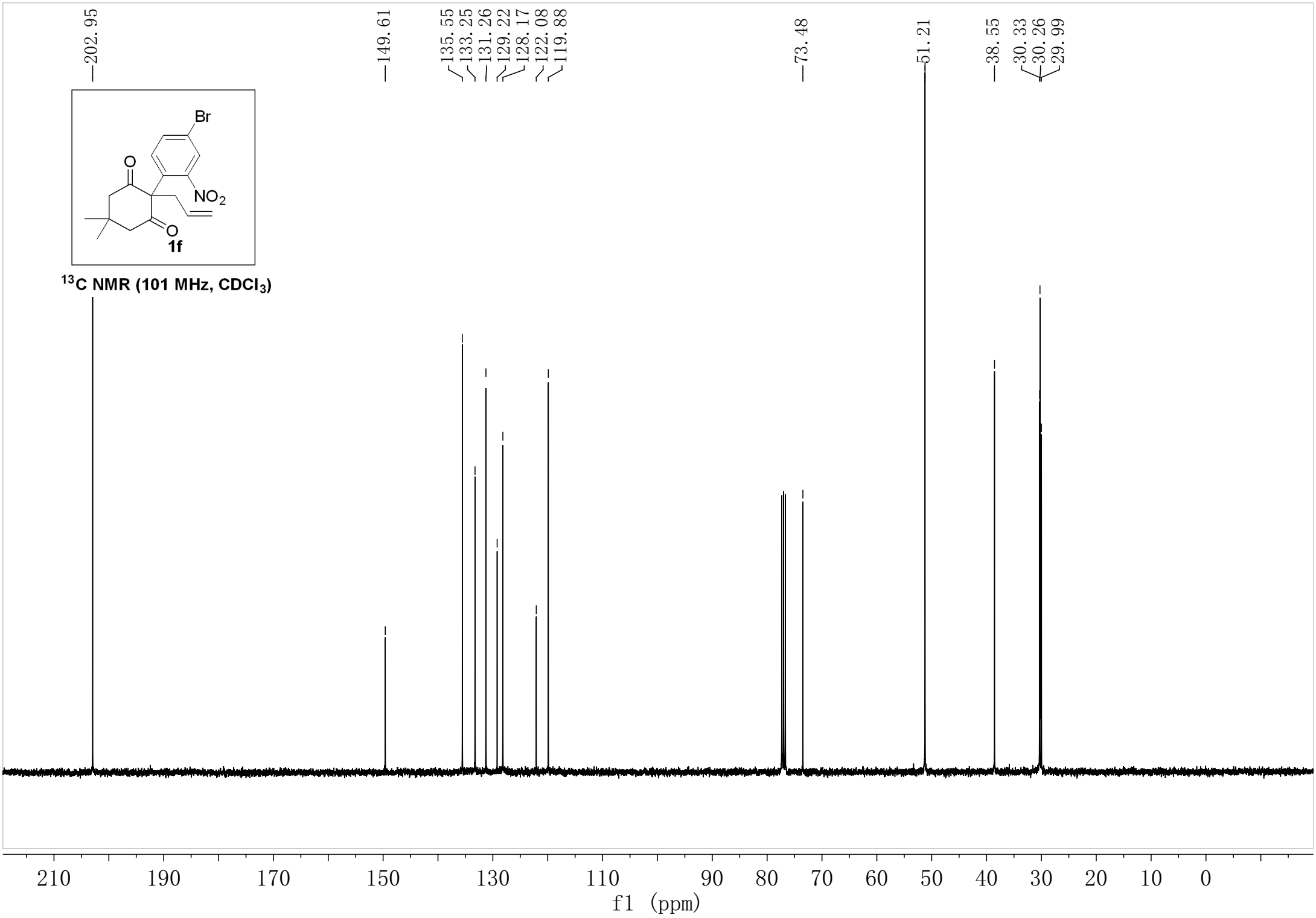


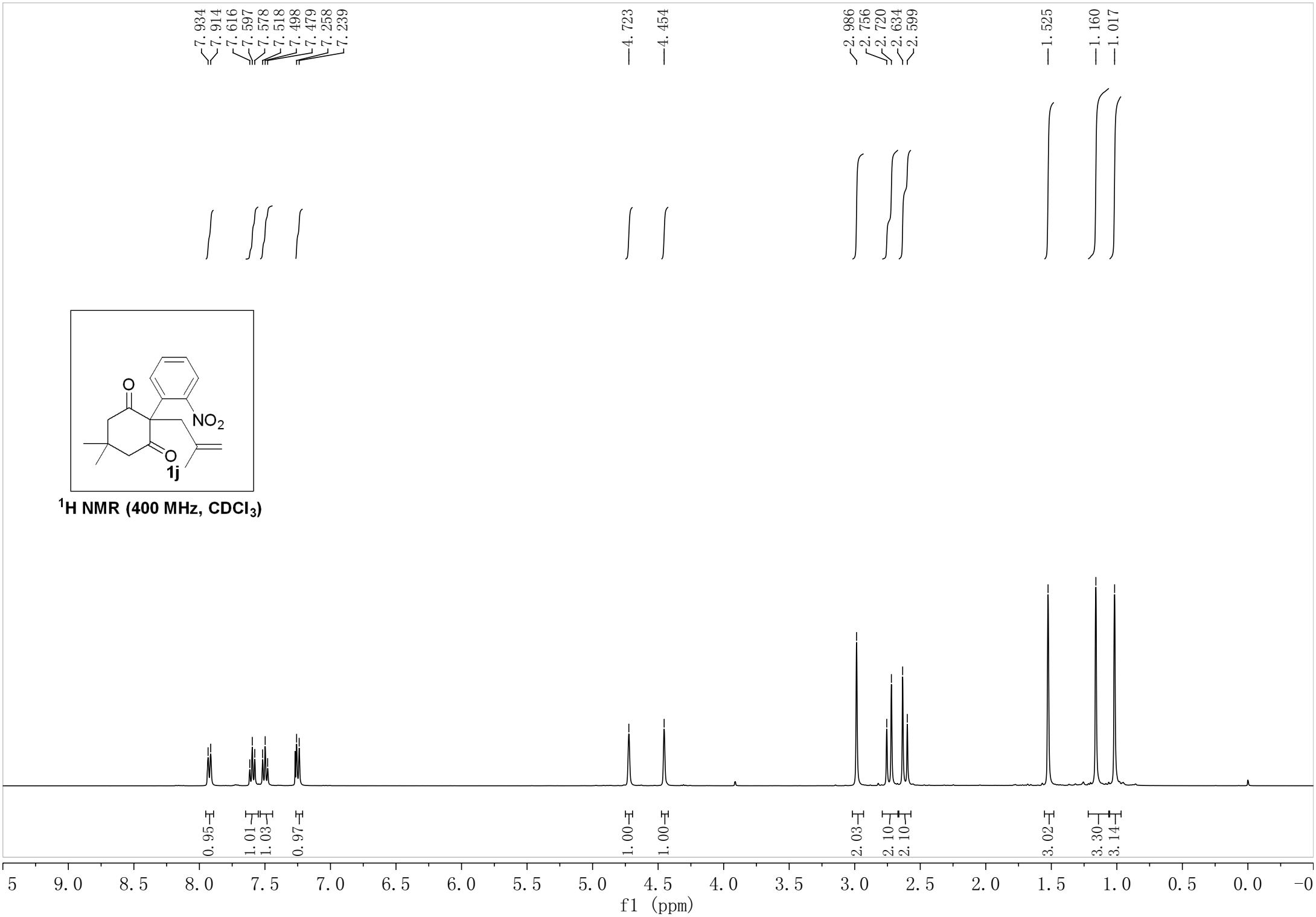
^{1}H NMR (400 MHz, $CDCl_3$)


203.08
149.63
134.67
133.07
132.64
131.35
128.80
125.47
119.93
73.45
51.30
38.67
30.40
30.33
30.08
Cl
O
NO2
O
1e
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

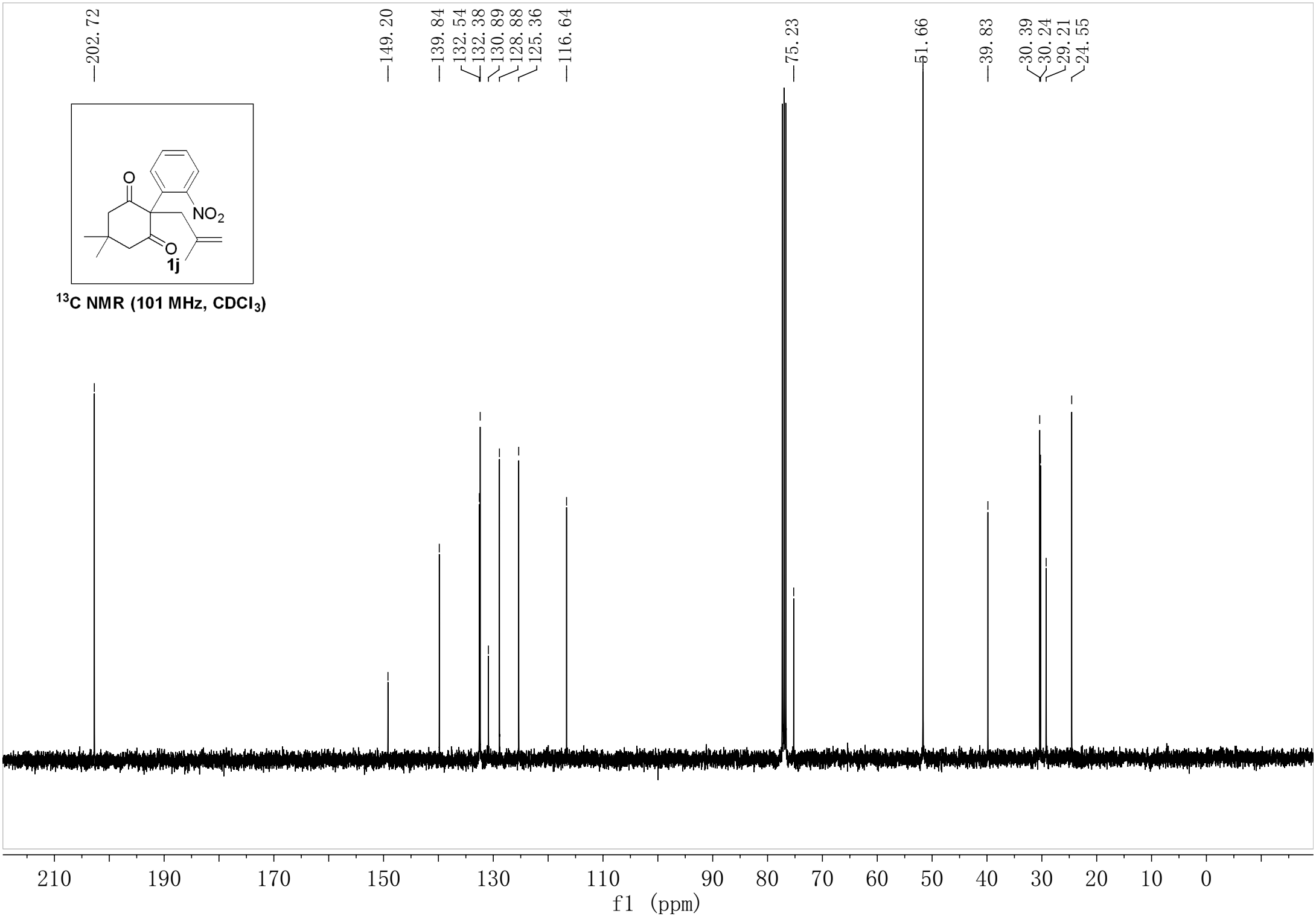


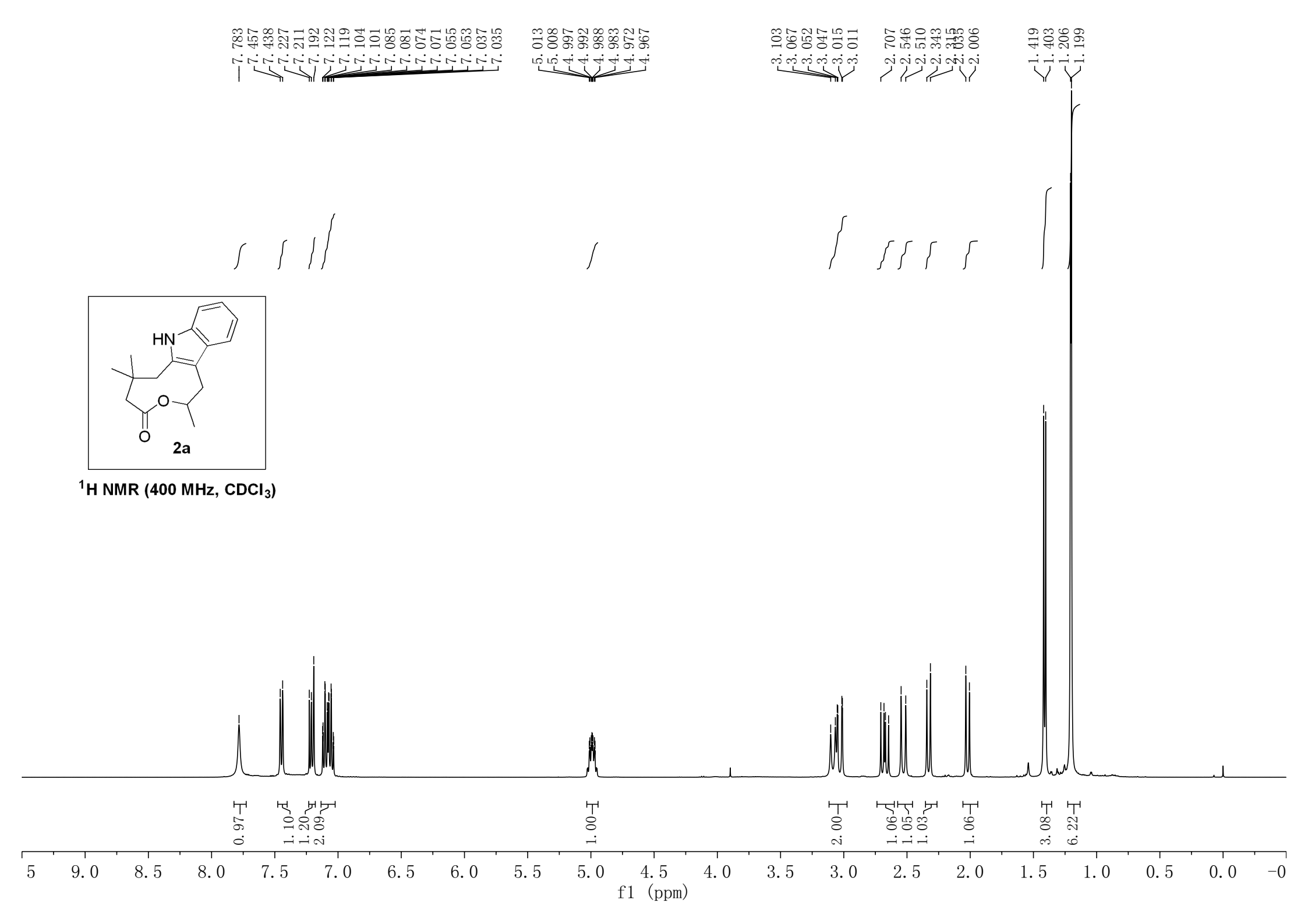
^{1}H NMR (400 MHz, $CDCl_3$)


202.95
149.61
135.55
133.25
131.26
129.22
128.17
122.08
119.88
73.48
51.21
38.55
30.33
30.26
29.99
Br
O
NO2
O
1f
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

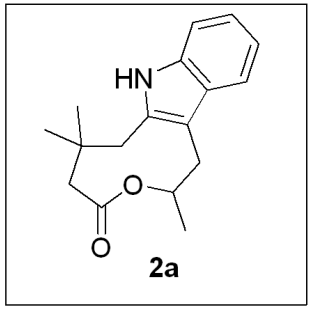


^{1}H NMR (400 MHz, $CDCl_3$)


202.72
149.20
139.84
132.54
132.38
130.89
128.88
125.36
116.64
75.23
51.66
39.83
30.39
30.24
29.21
24.55
O
NO2
O
1j
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



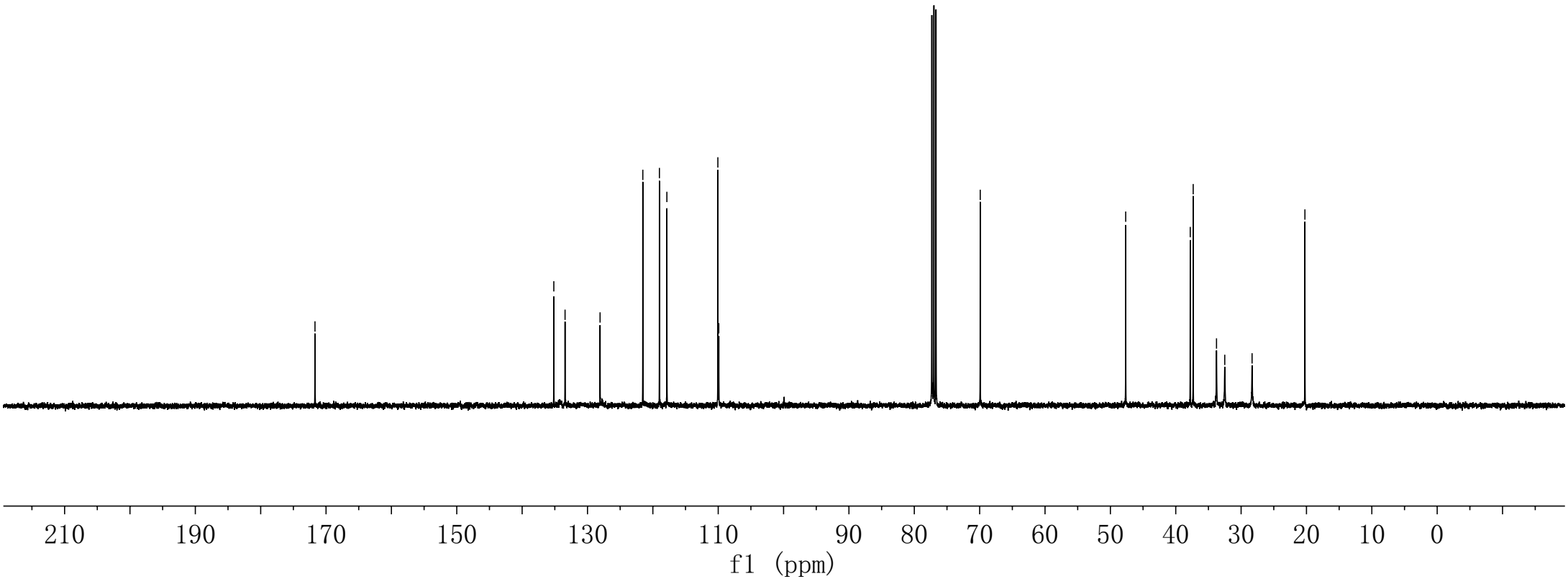
^{1}H NMR (400 MHz, $CDCl_3$)

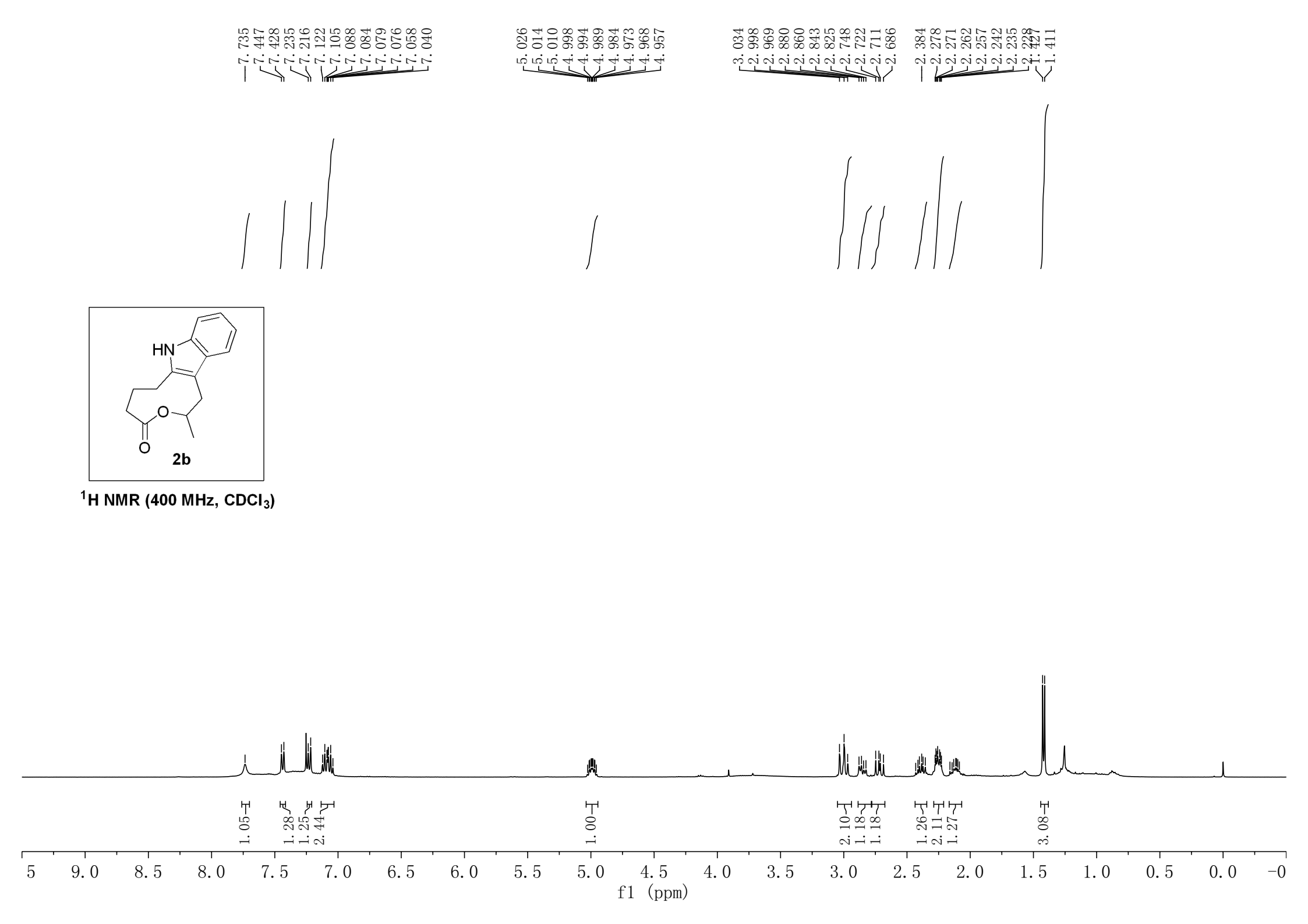


2a

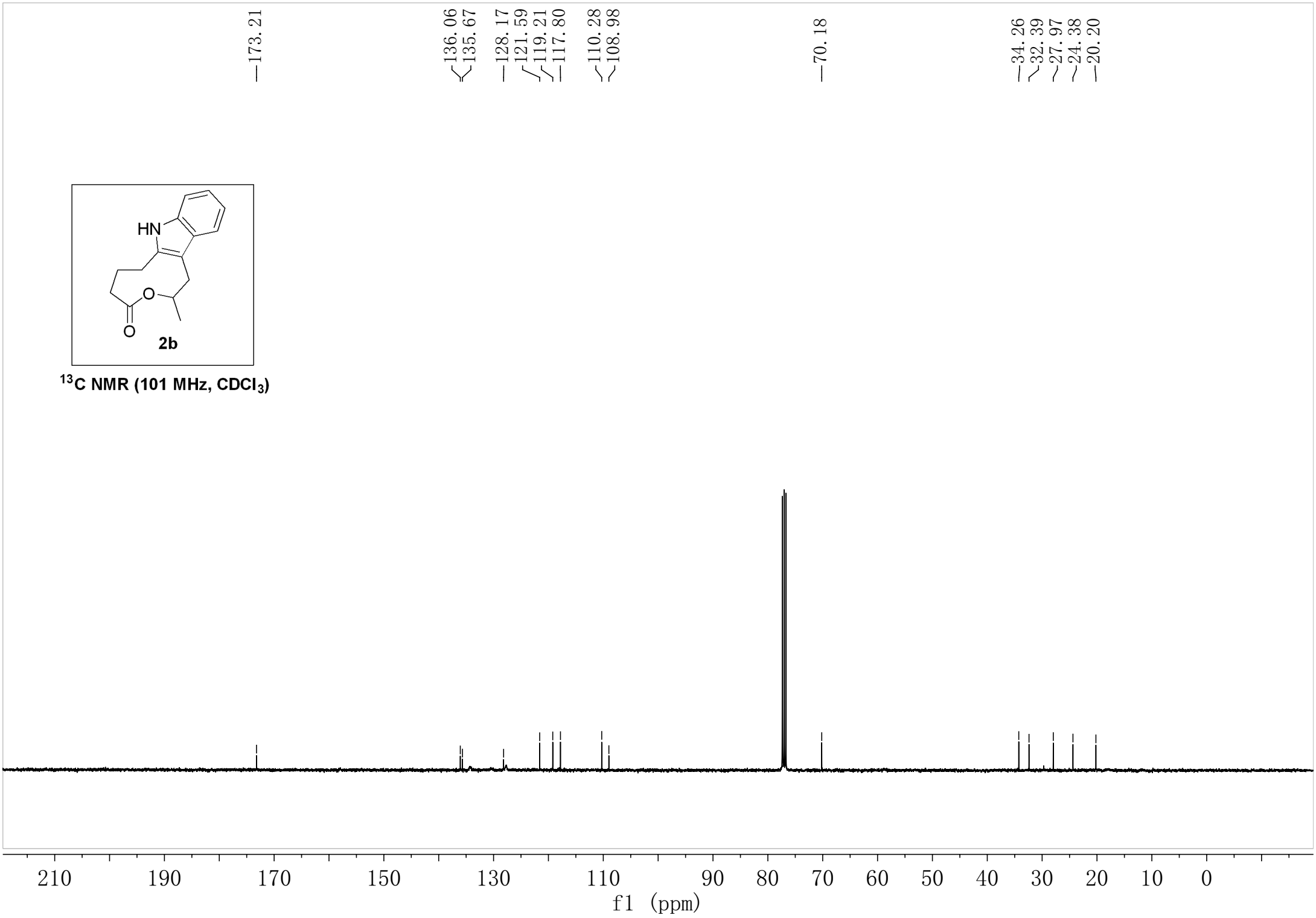
^{13}C NMR (101 MHz, $CDCl_3$)

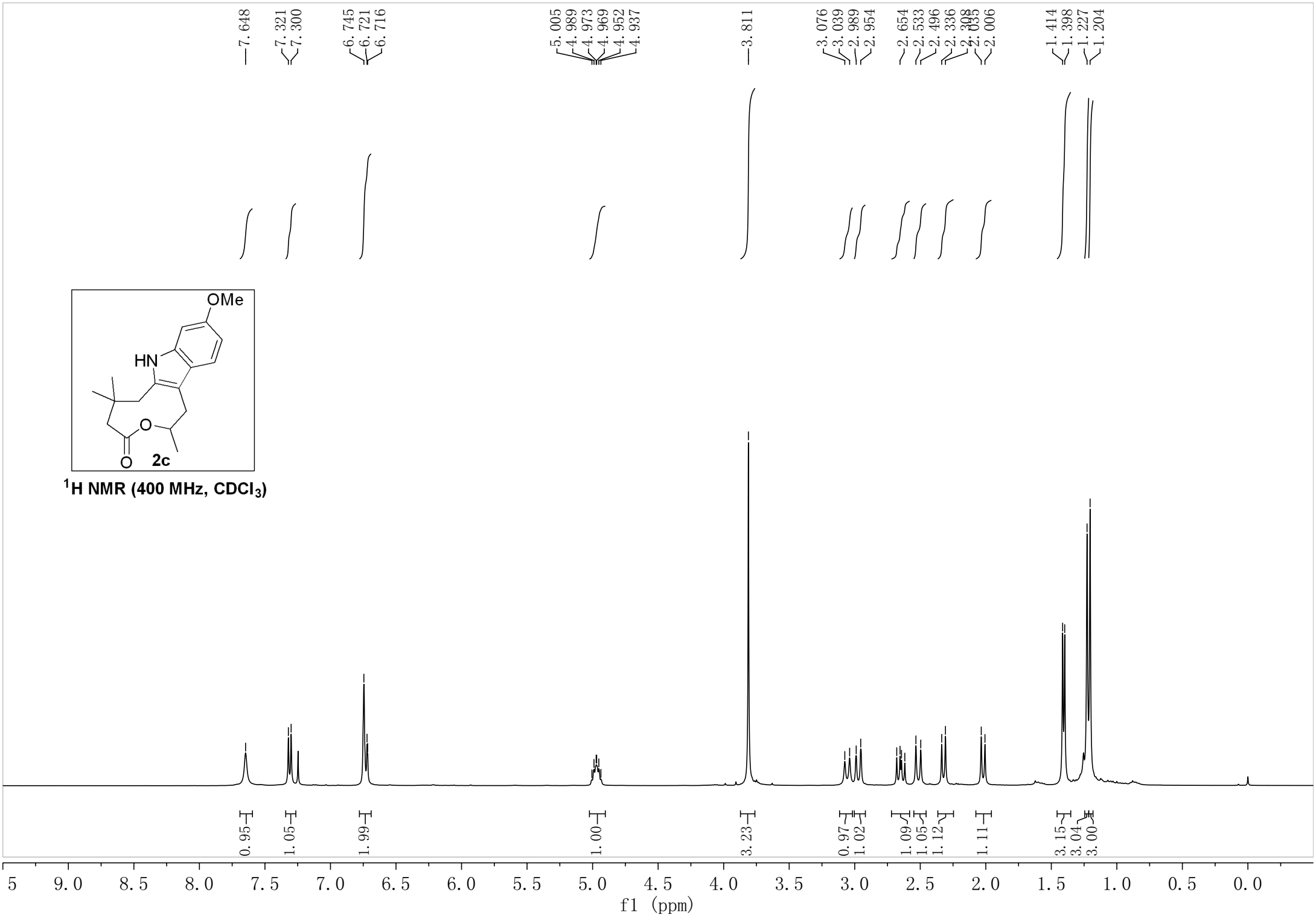
171.69
135.15
133.43
128.07
121.54
119.00
117.85
110.05
109.91
69.91
47.66
37.78
37.33
33.76
32.50
28.32
20.24



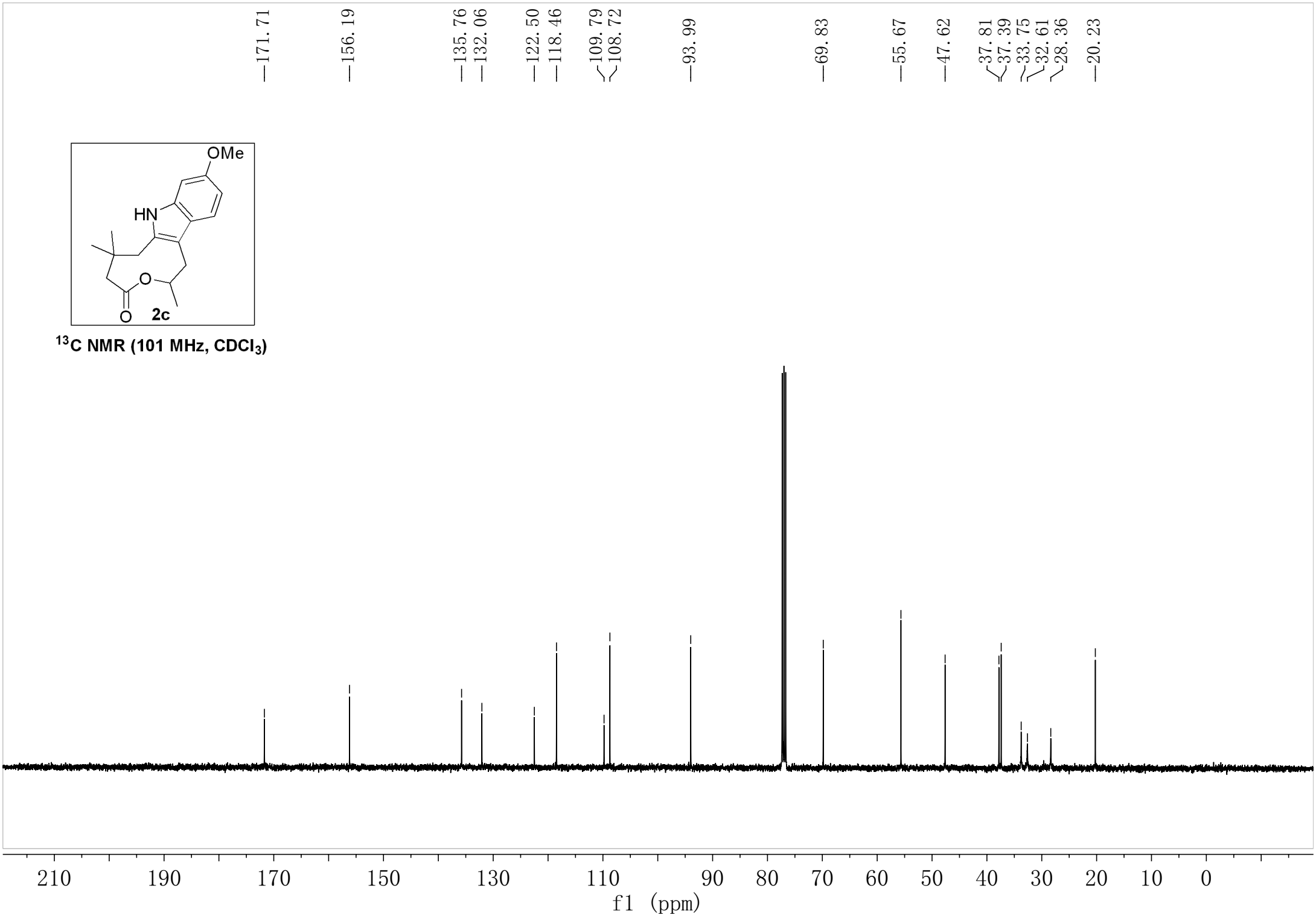


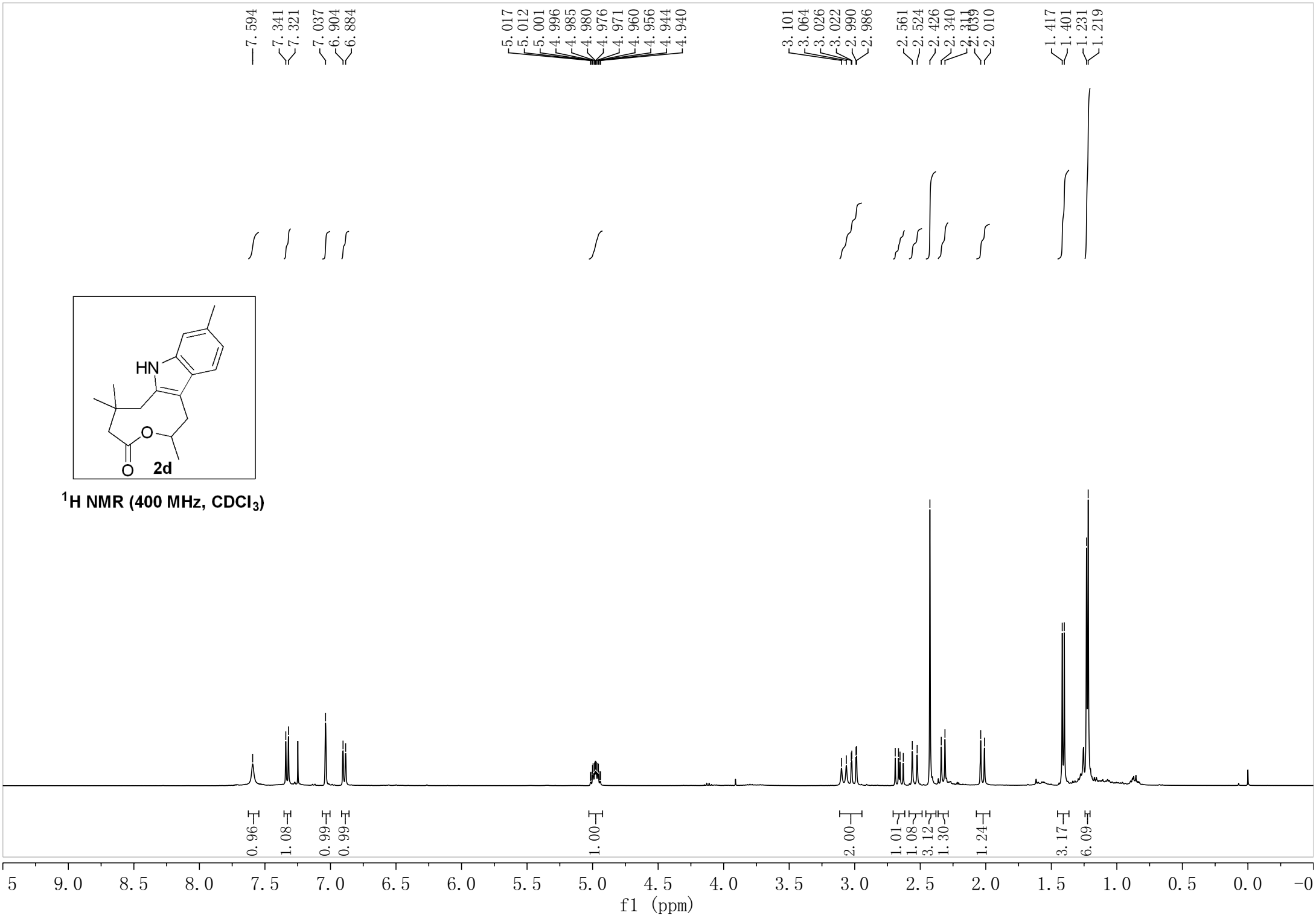
^{1}H NMR (400 MHz, $CDCl_3$)


173.21
136.06
135.67
128.17
121.59
119.21
117.80
110.28
108.98
70.18
34.26
32.39
27.97
24.38
20.20
HN
O
O
2b
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

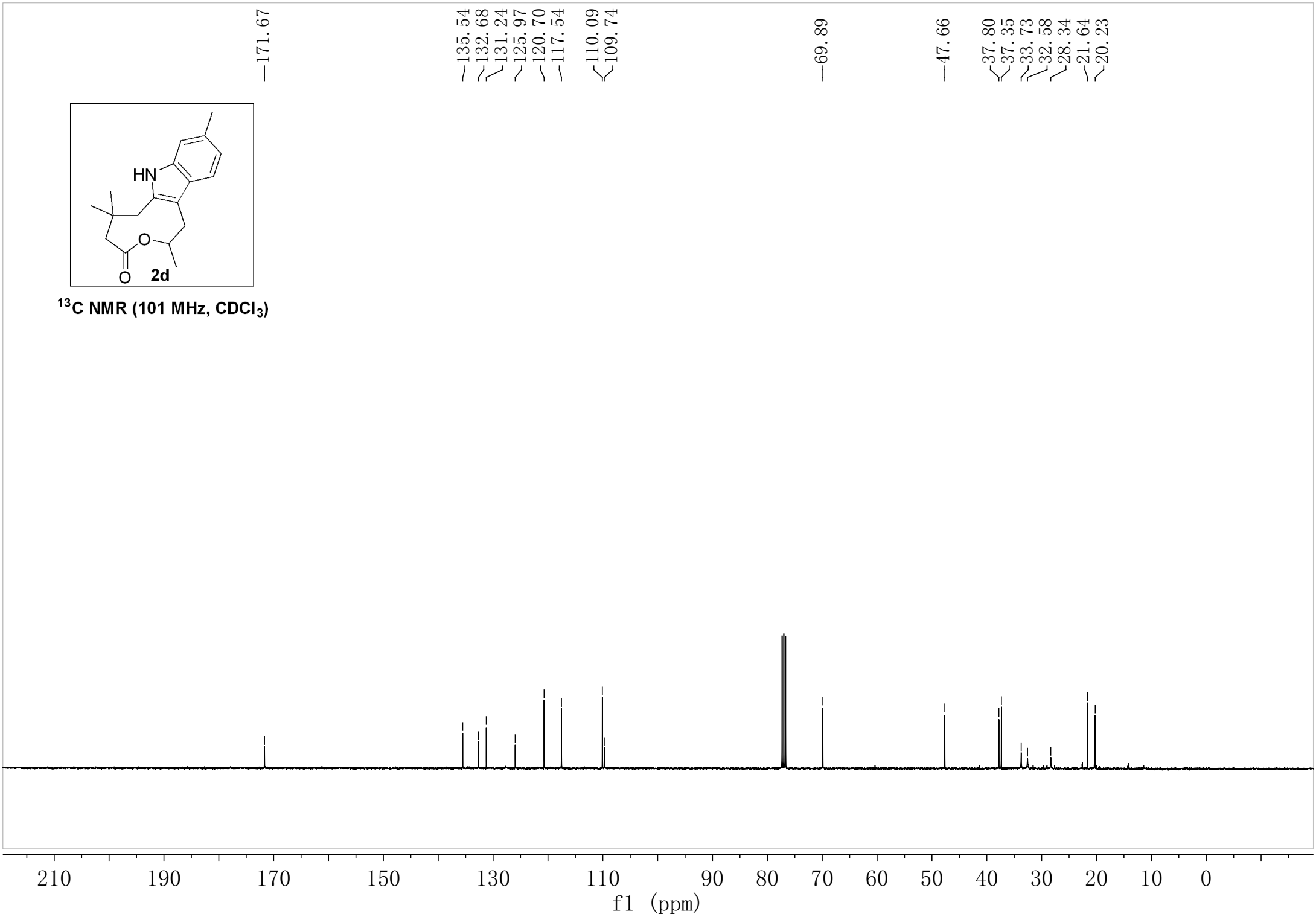


^{1}H NMR (400 MHz, $CDCl_3$)

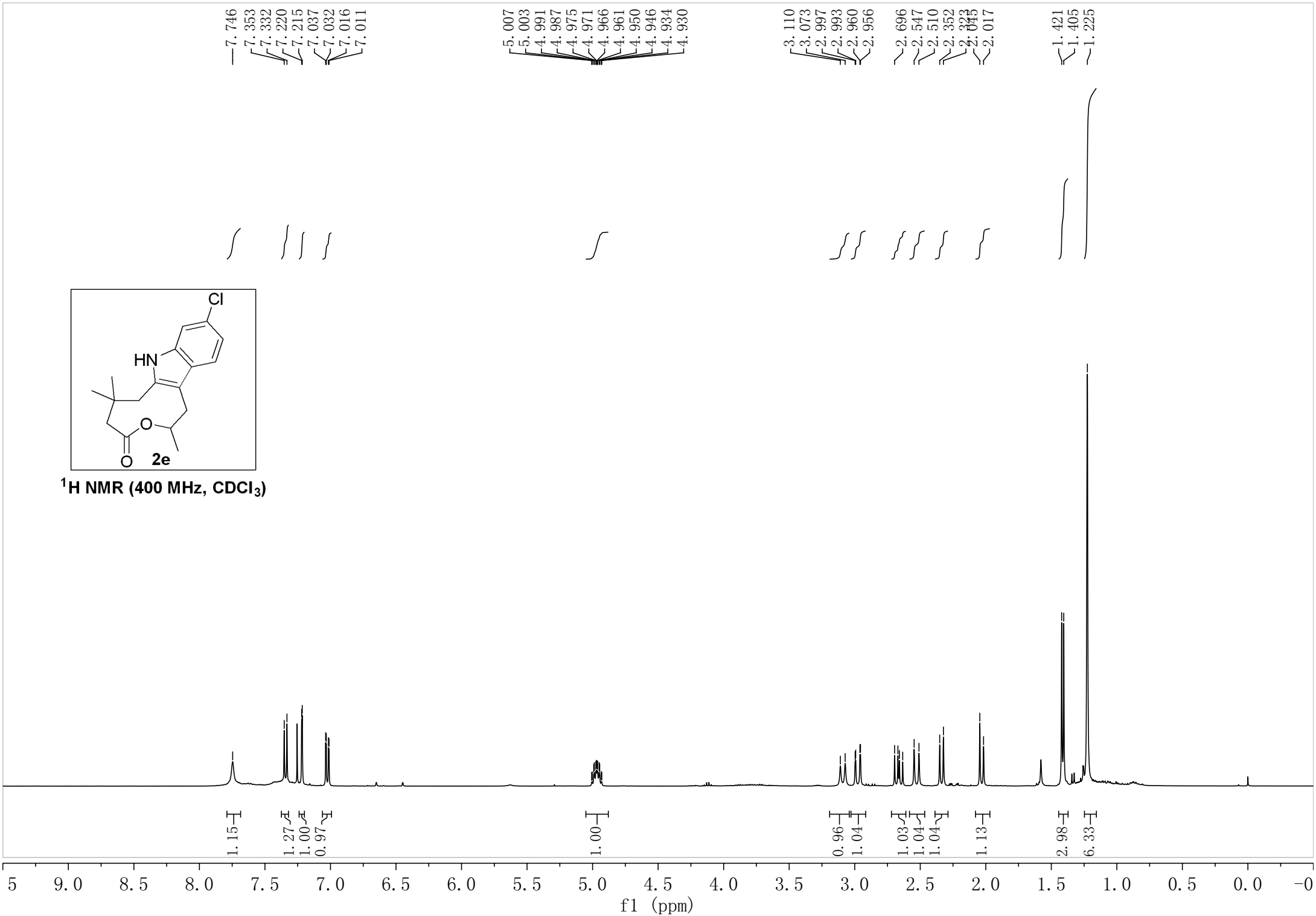

171.71
156.19
135.76
132.06
122.50
118.46
109.79
108.72
93.99
69.83
55.67
47.62
37.81
37.39
33.75
32.61
28.36
20.23
OMe
HN
O
O
2c
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



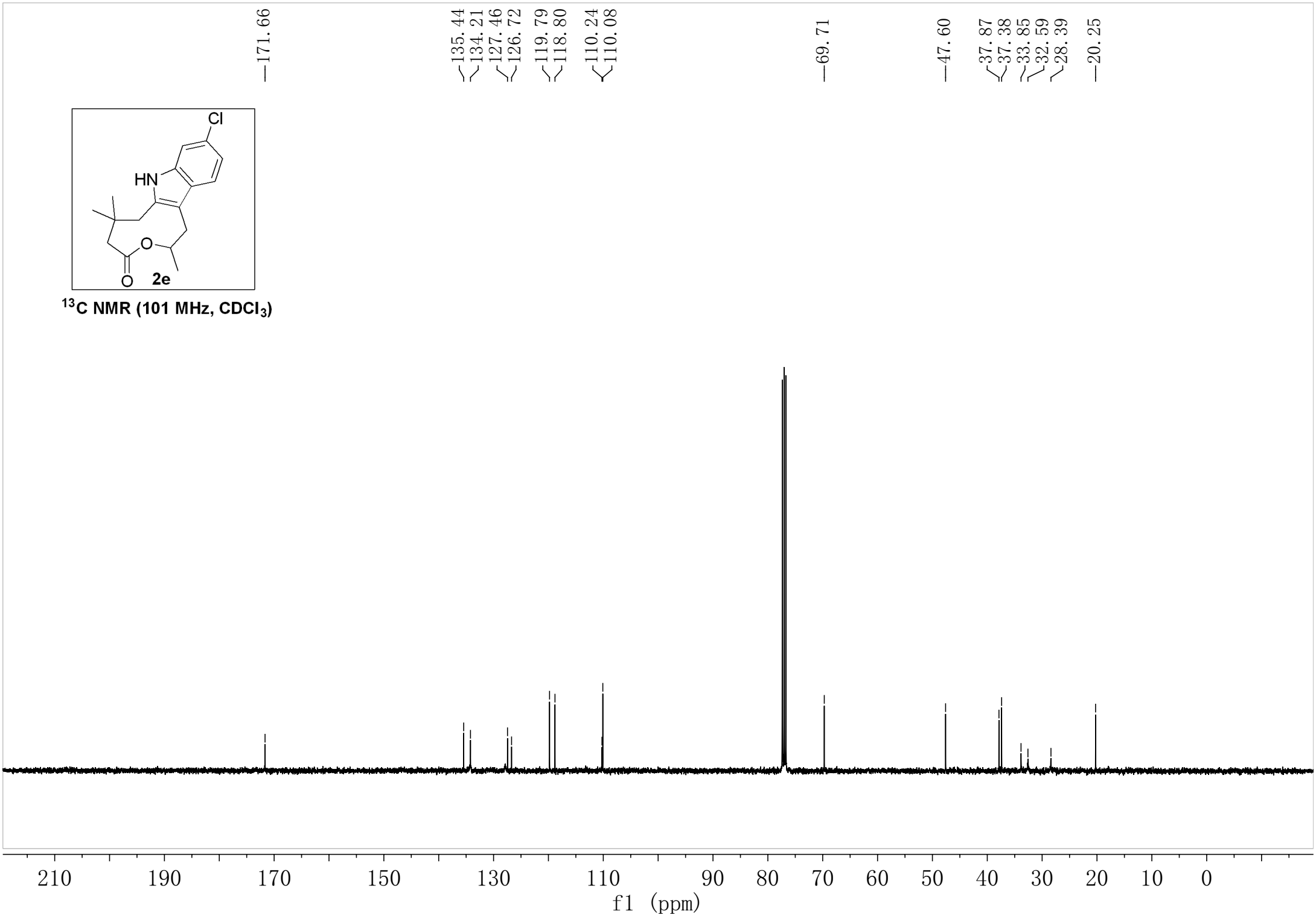
^{1}H NMR (400 MHz, $CDCl_3$)

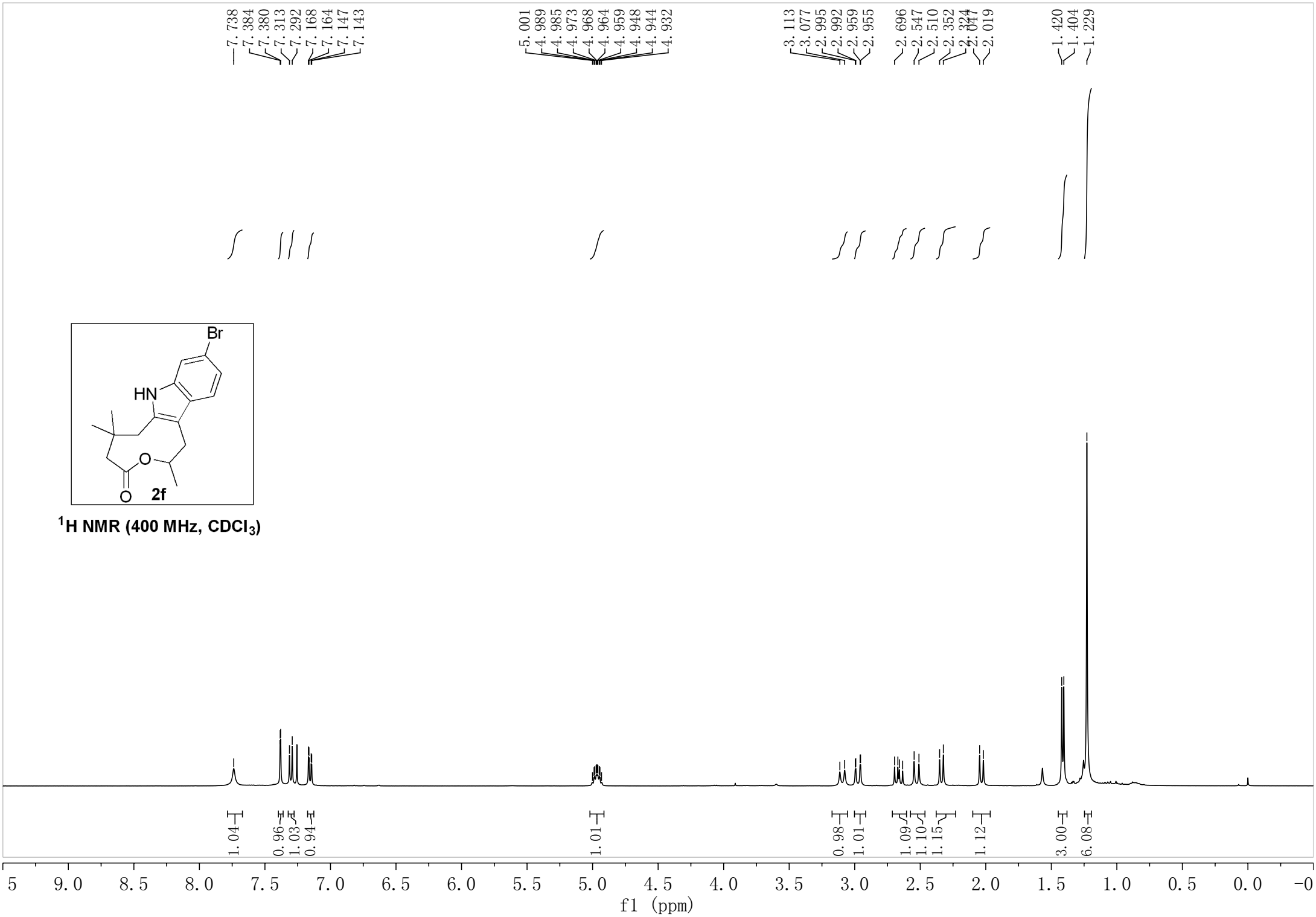


^{13}C NMR (101 MHz, $CDCl_3$)

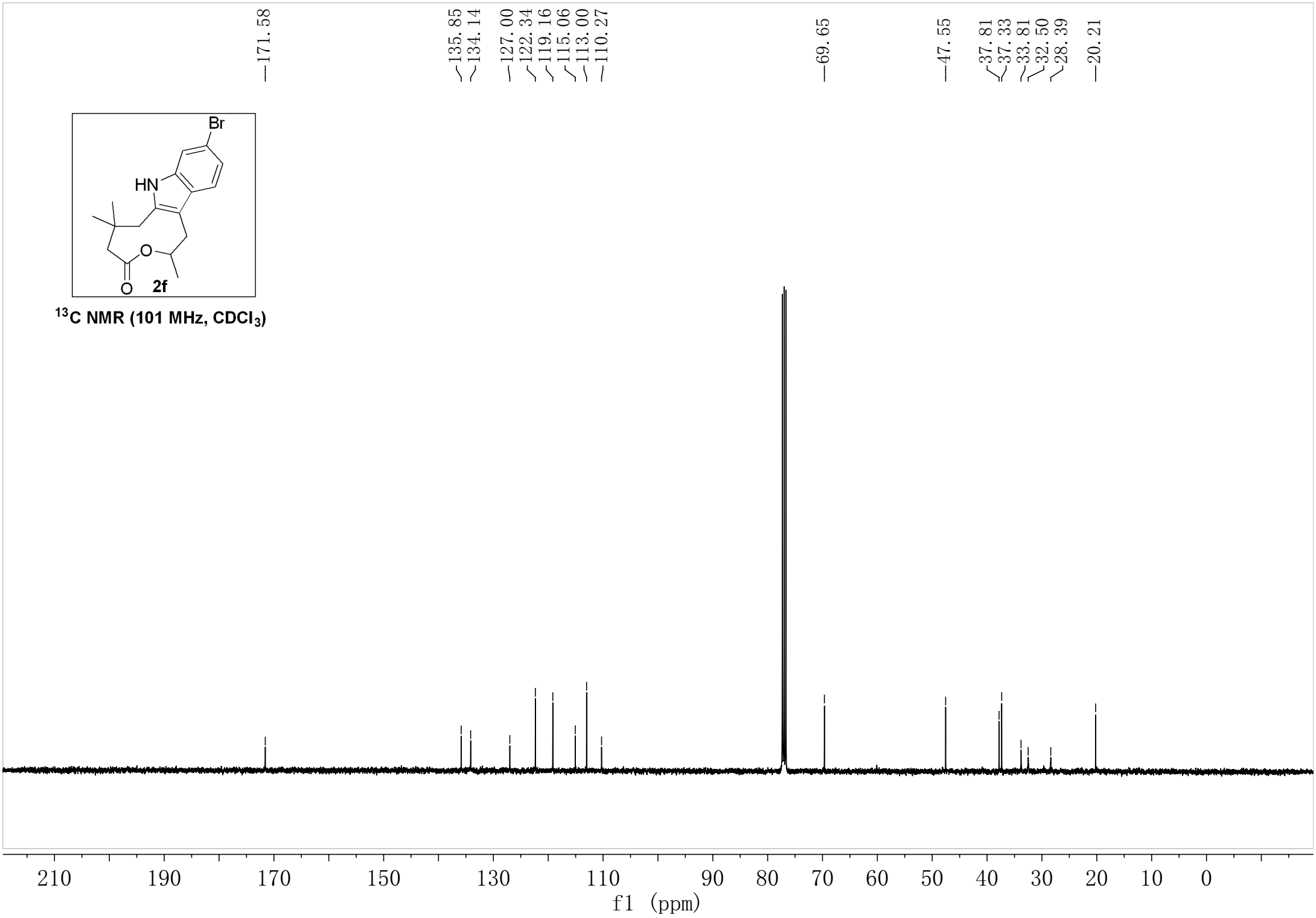


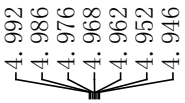
^{1}H NMR (400 MHz, $CDCl_3$)

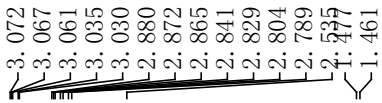

171.66
135.44
134.21
127.46
126.72
119.79
118.80
110.24
110.08
69.71
47.60
37.87
37.38
33.85
32.59
28.39
20.25
Cl
HN
O
O
2e
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

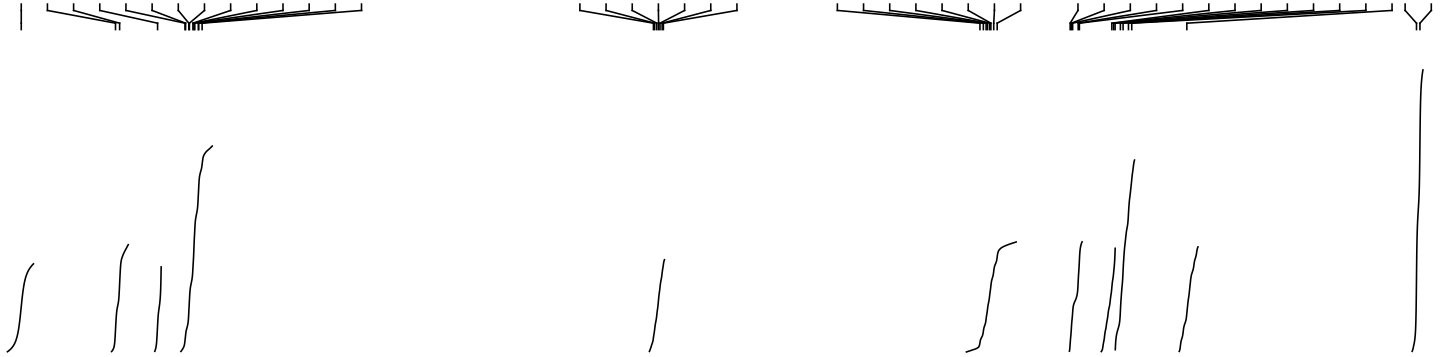


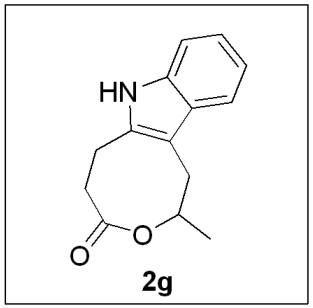
^{1}H NMR (400 MHz, $CDCl_3$)


171.58
135.85
134.14
127.00
122.34
119.16
115.06
113.00
110.27
69.65
47.55
37.81
37.33
33.81
32.50
28.39
20.21
Br
HN
O
O
2f
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



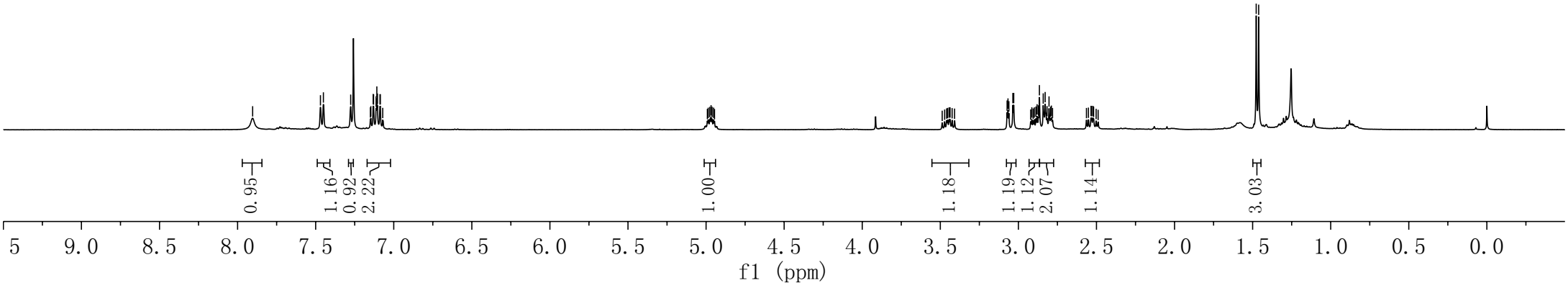


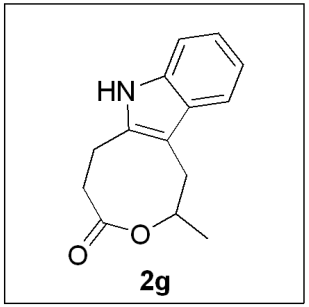




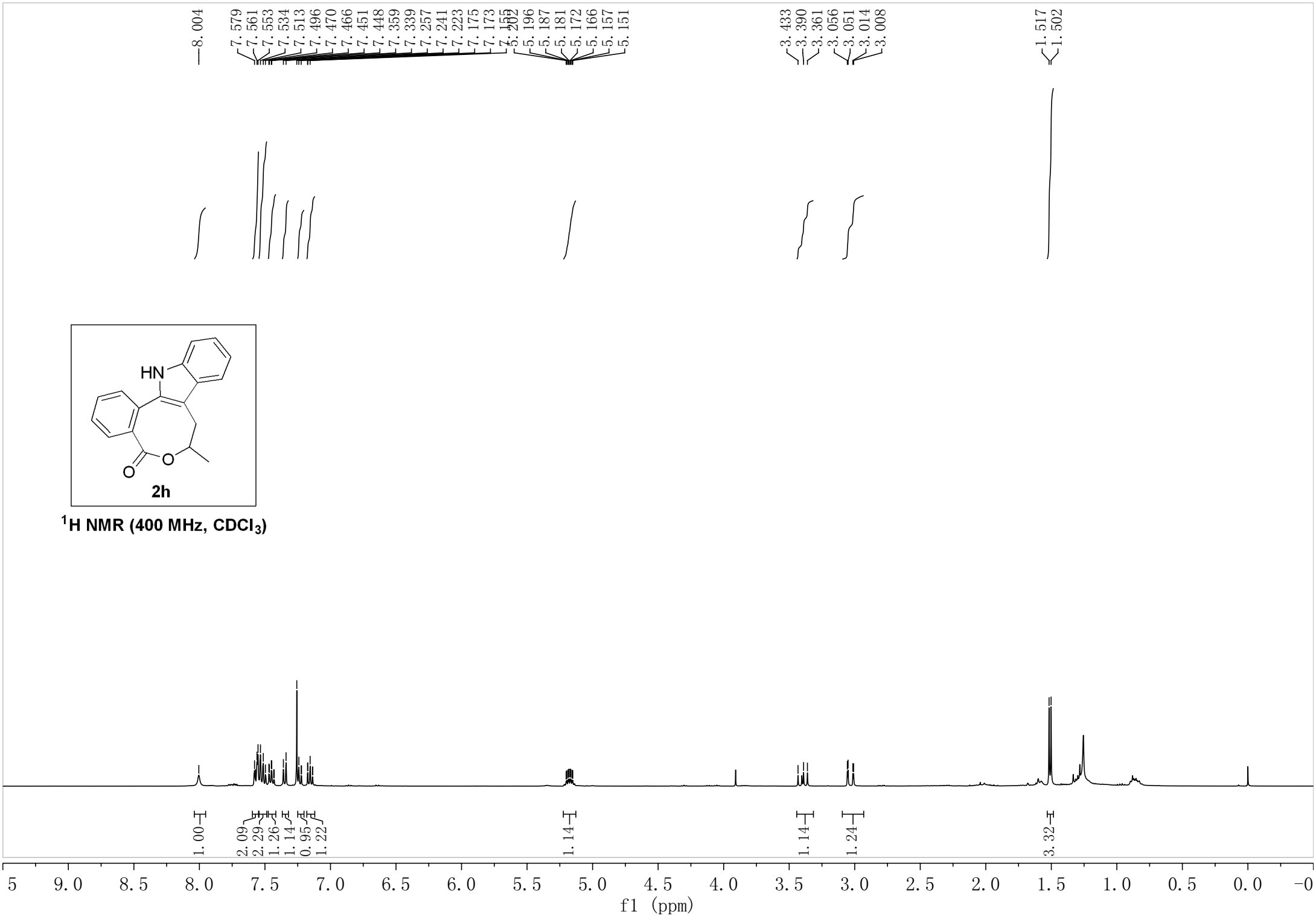
2g

^{1}H NMR (400 MHz, $CDCl_3$)

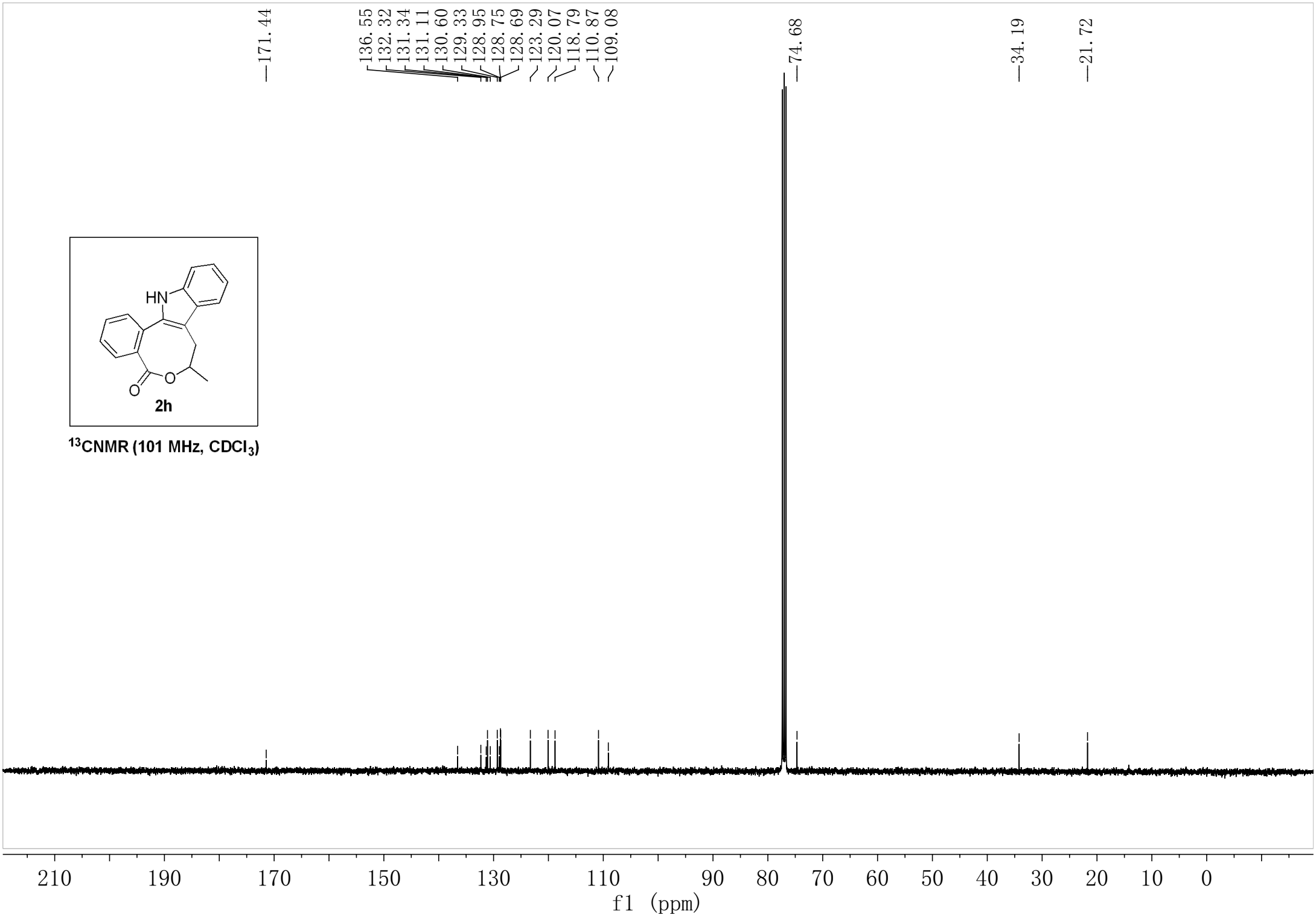


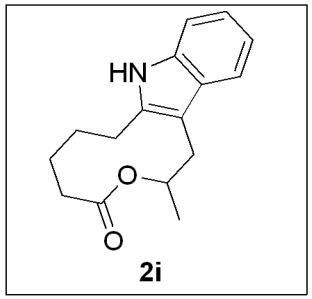


^{13}C NMR (101 MHz, $CDCl_3$)



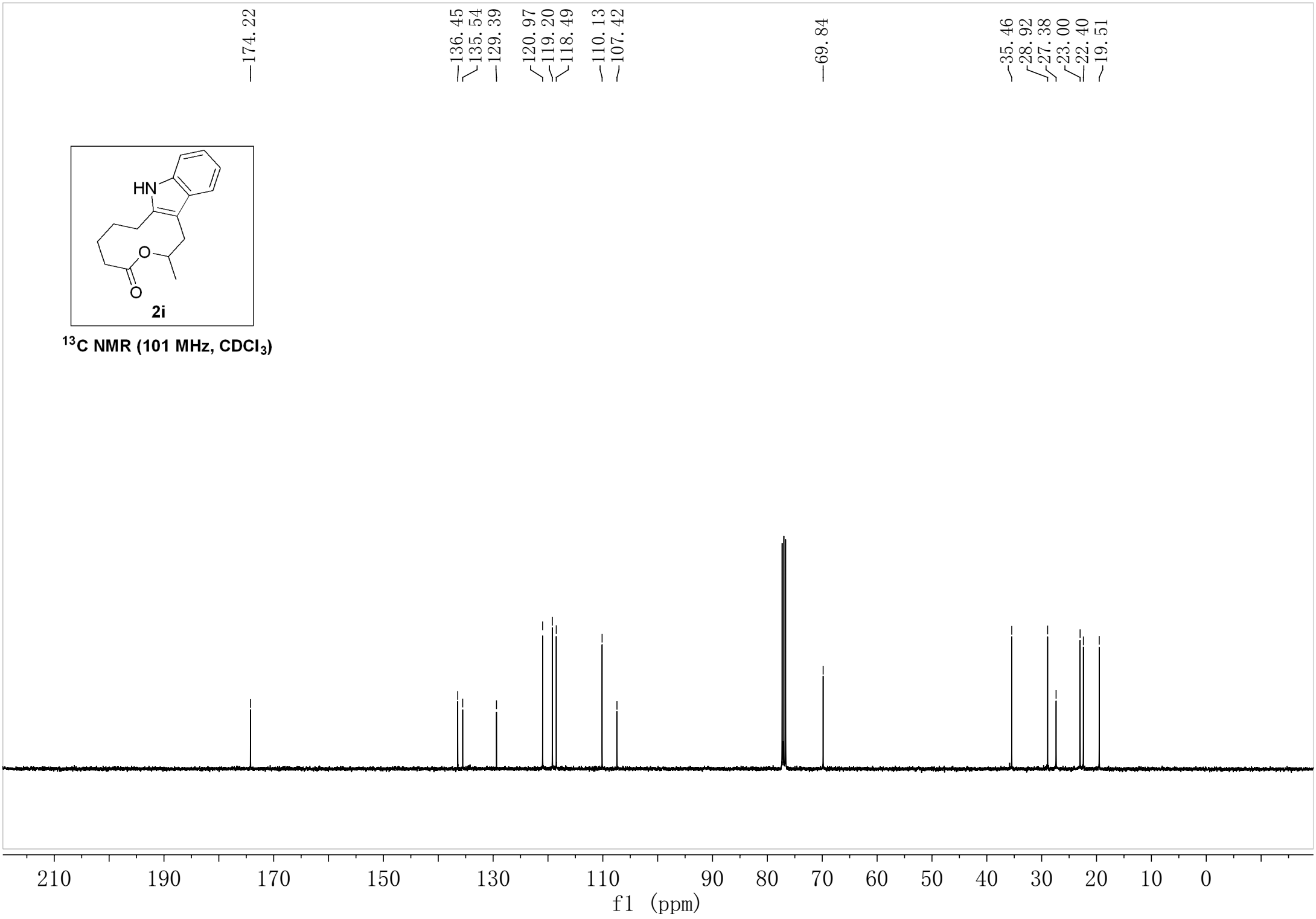
^{1}H NMR (400 MHz, $CDCl_3$)

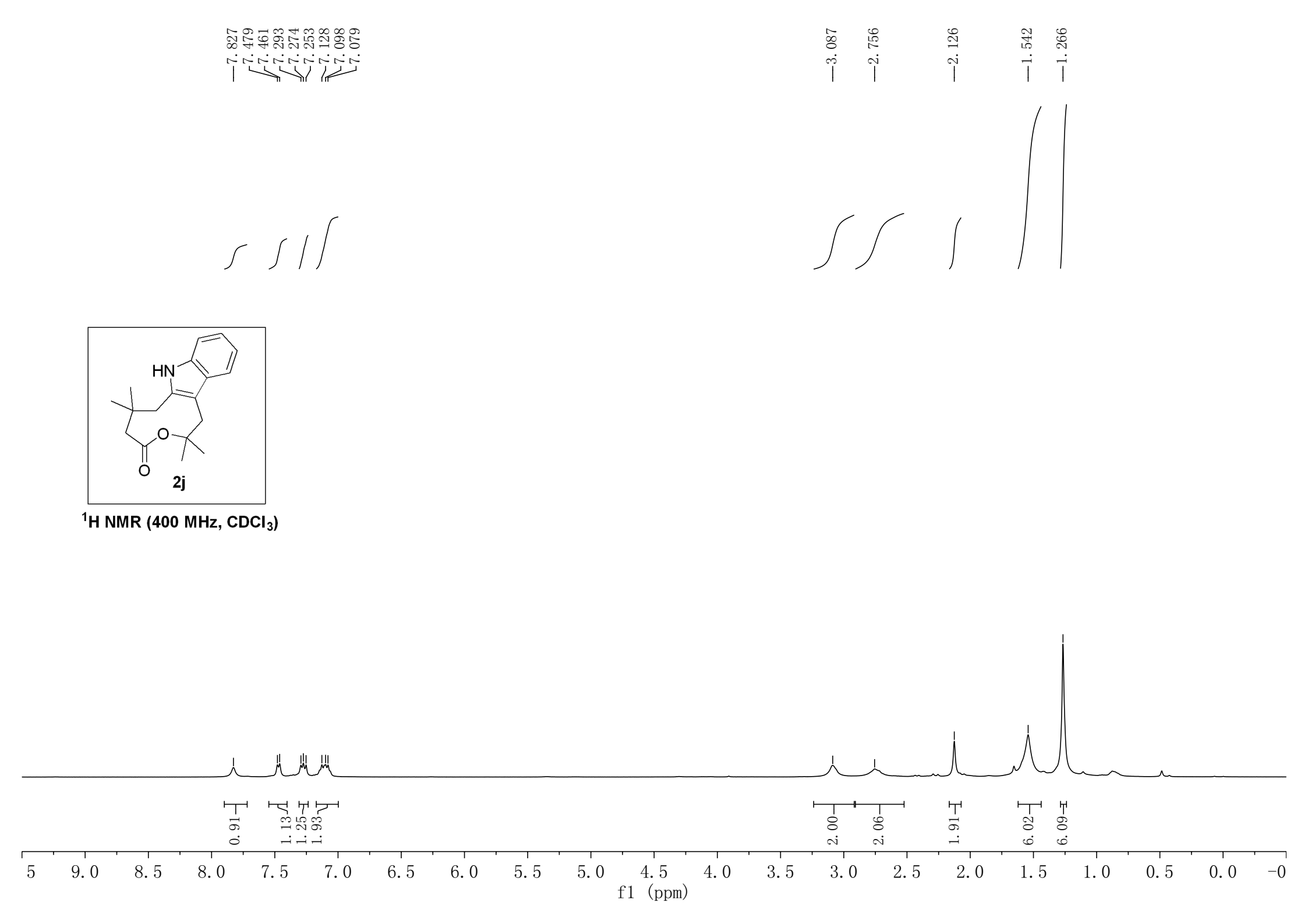

171.44
136.55
132.32
131.34
131.11
130.60
129.33
128.95
128.75
128.69
123.29
120.07
118.79
110.87
109.08
74.68
34.19
21.72
HN
O
O
2h
13CNMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



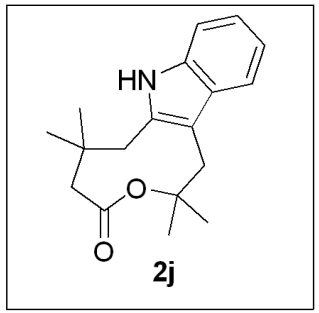
2i

^{1}H NMR (400 MHz, $CDCl_3$)


174.22
136.45
135.54
129.39
120.97
119.20
118.49
110.13
107.42
69.84
35.46
28.92
27.38
23.00
22.40
19.51
HN
O
O
2i
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

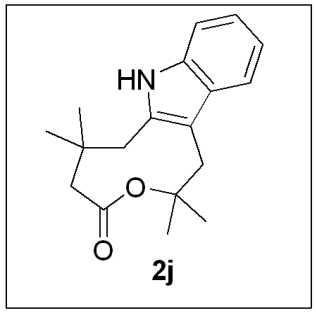


^{1}H NMR (400 MHz, $CDCl_3$)



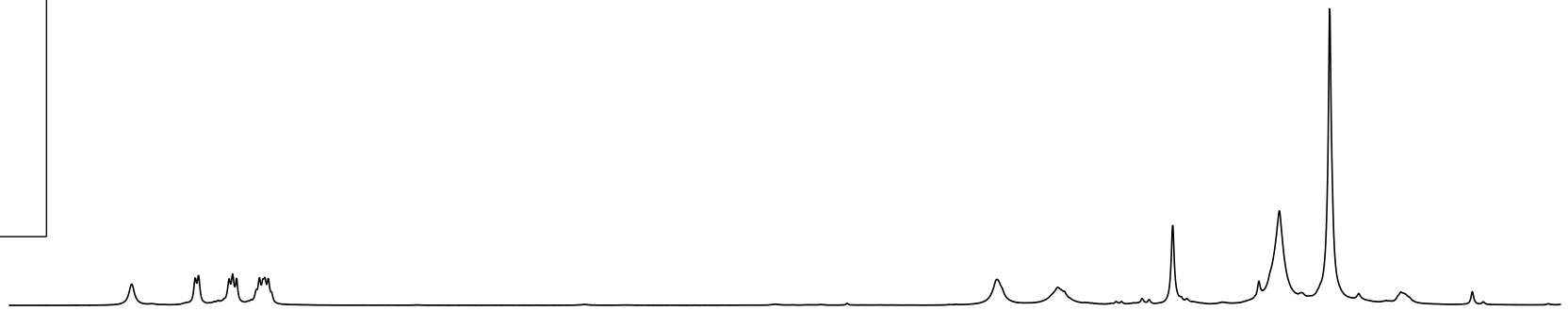
2j

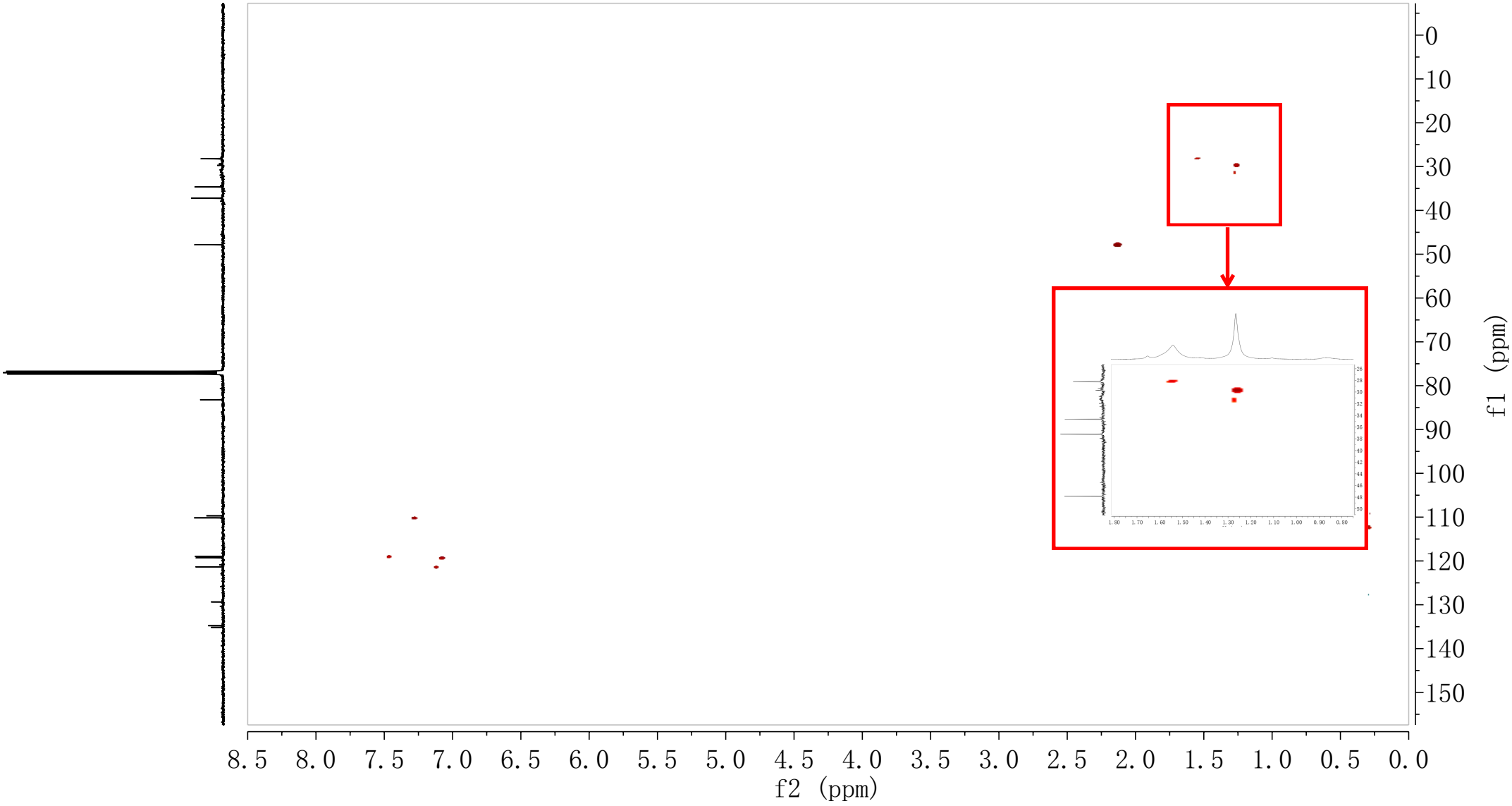
^{13}C NMR (101 MHz, $CDCl_3$)

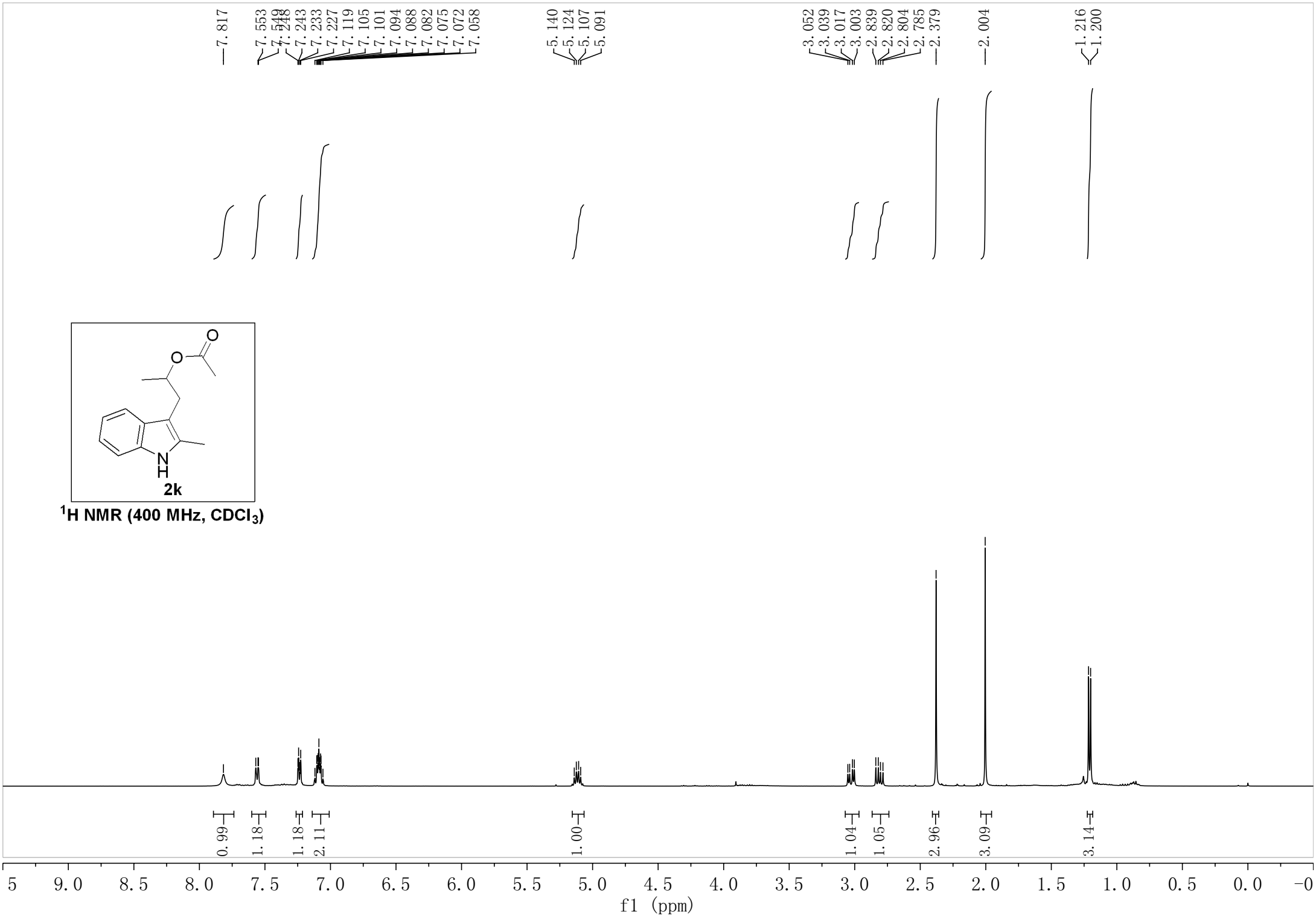

HN
O
O

2j

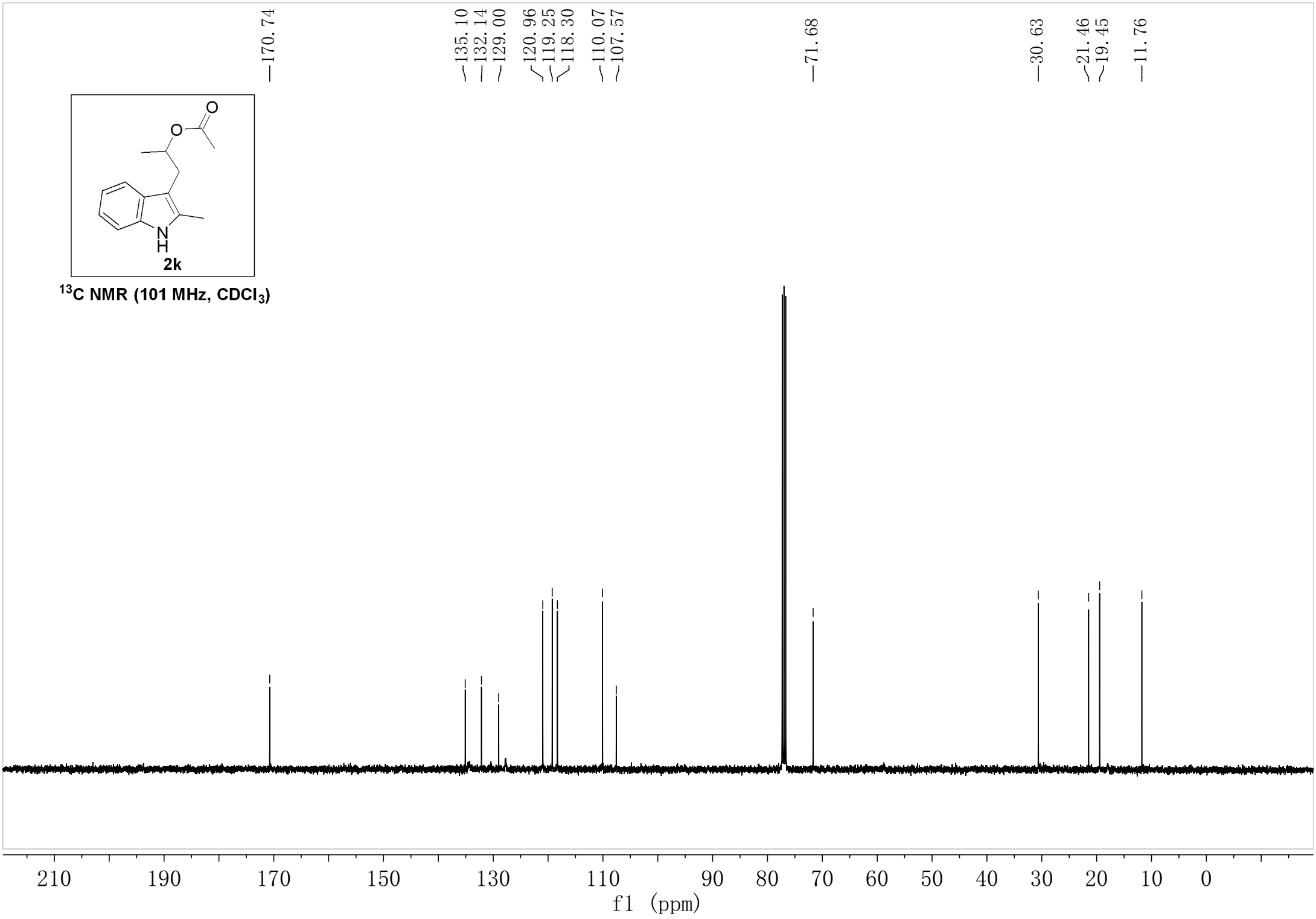
HSQC

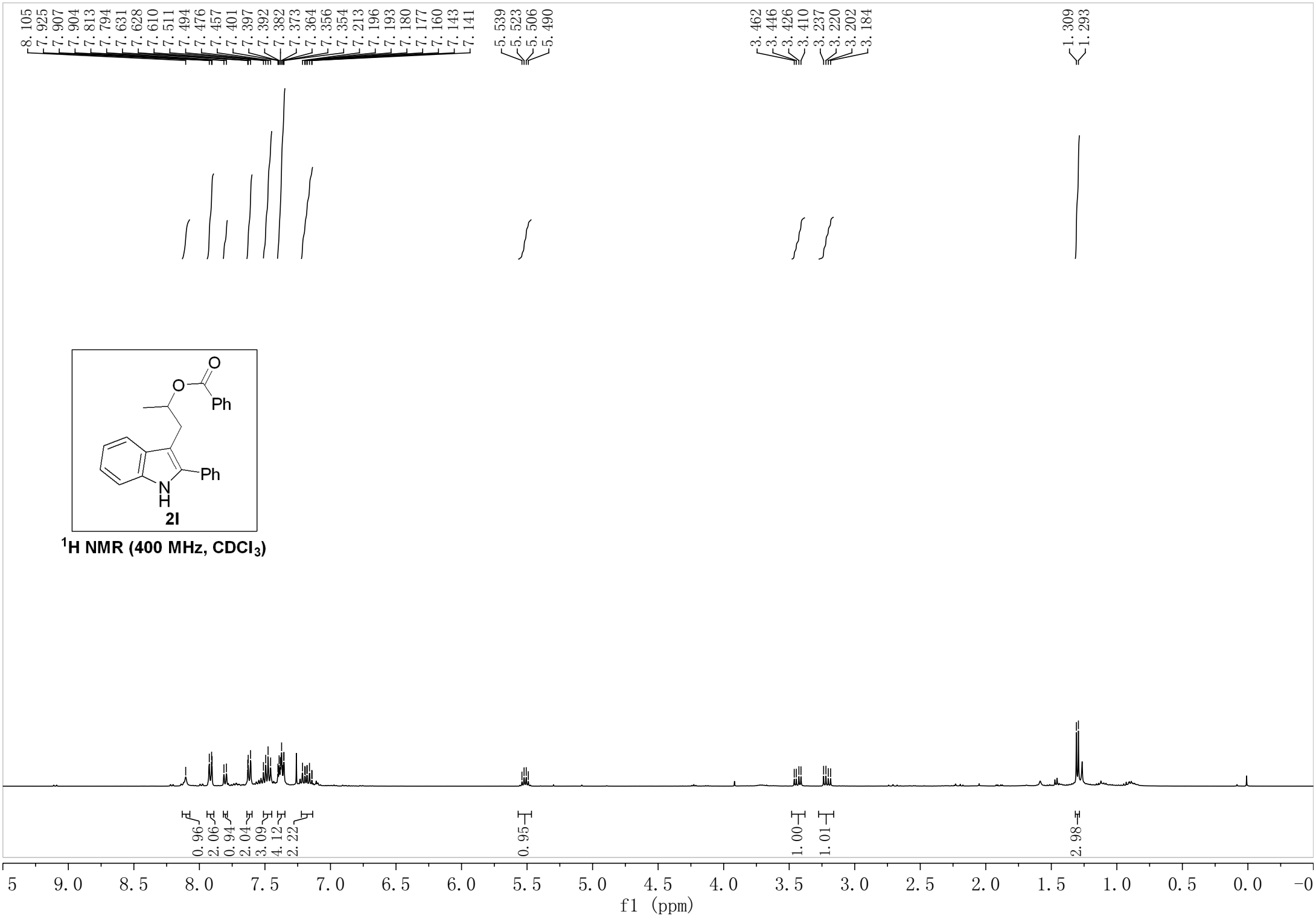



0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)

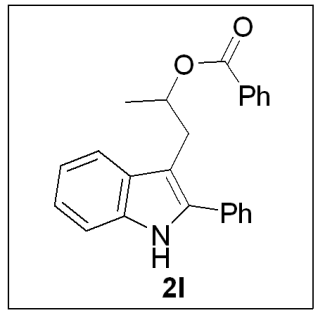


^{1}H NMR (400 MHz, $CDCl_3$)


170.74
135.10
132.14
129.00
120.96
119.25
118.30
110.07
107.57
71.68
30.63
21.46
19.45
11.76
O
O
N
H
2k
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



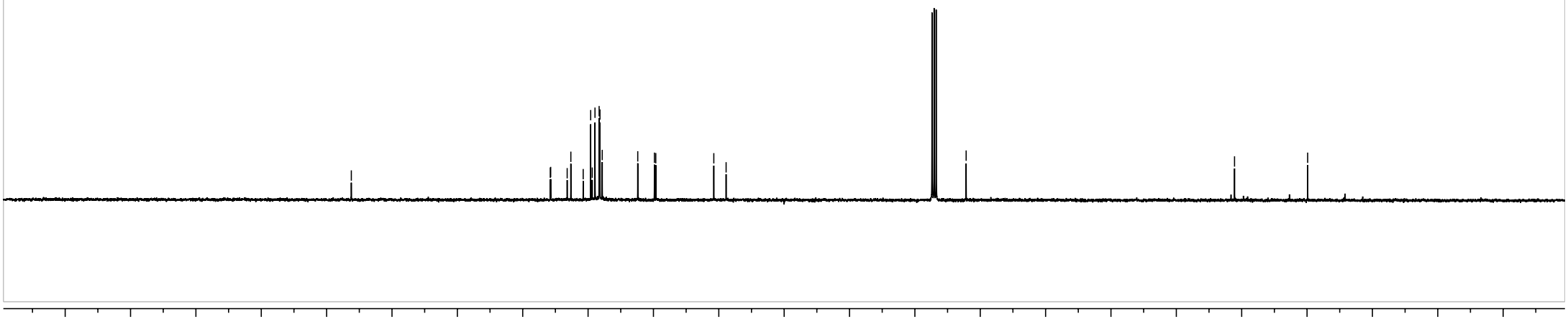
^{1}H NMR (400 MHz, $CDCl_3$)



2l

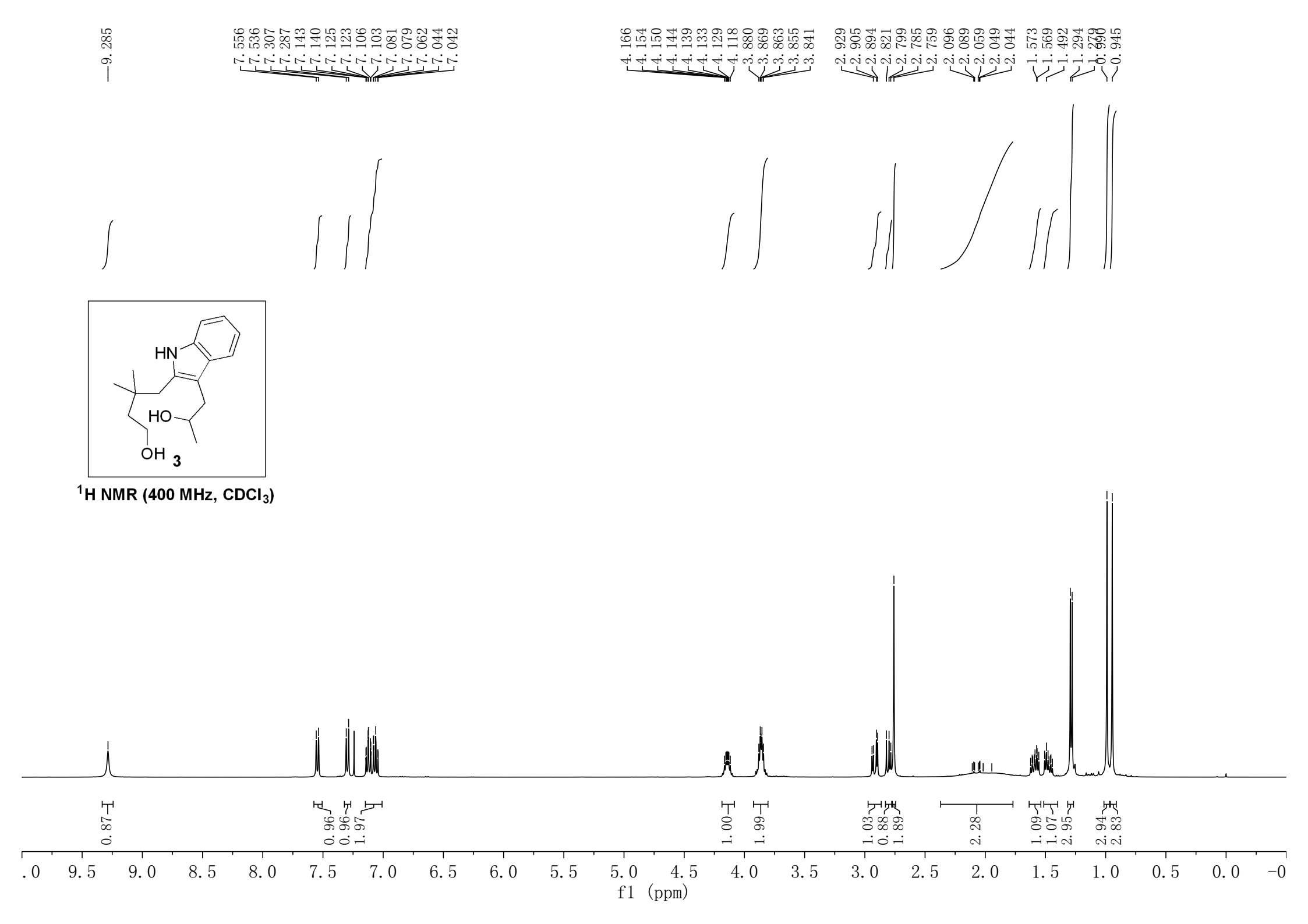
^{13}C NMR (101 MHz, $CDCl_3$)

166.22
135.78
135.72
133.20
132.64
130.75
129.60
129.36
128.94
128.31
128.18
127.84
122.40
119.85
119.64
110.76
108.88
72.16
31.09
19.91

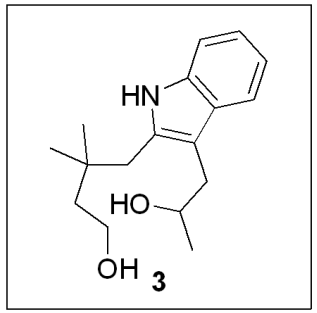


210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

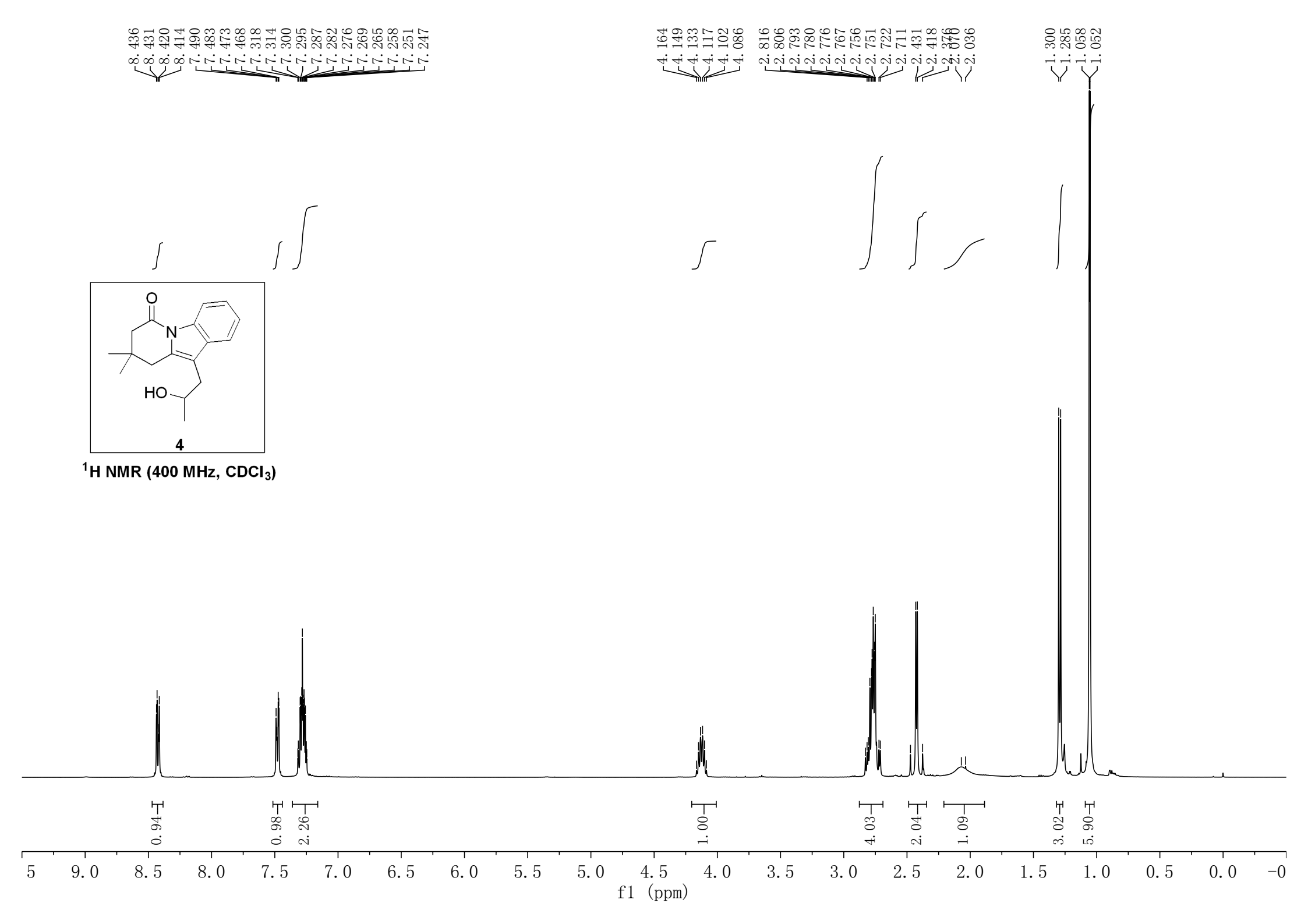


^{1}H NMR (400 MHz, $CDCl_3$)

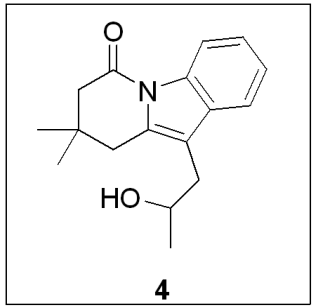


3

^{13}C NMR (101 MHz, $CDCl_3$)

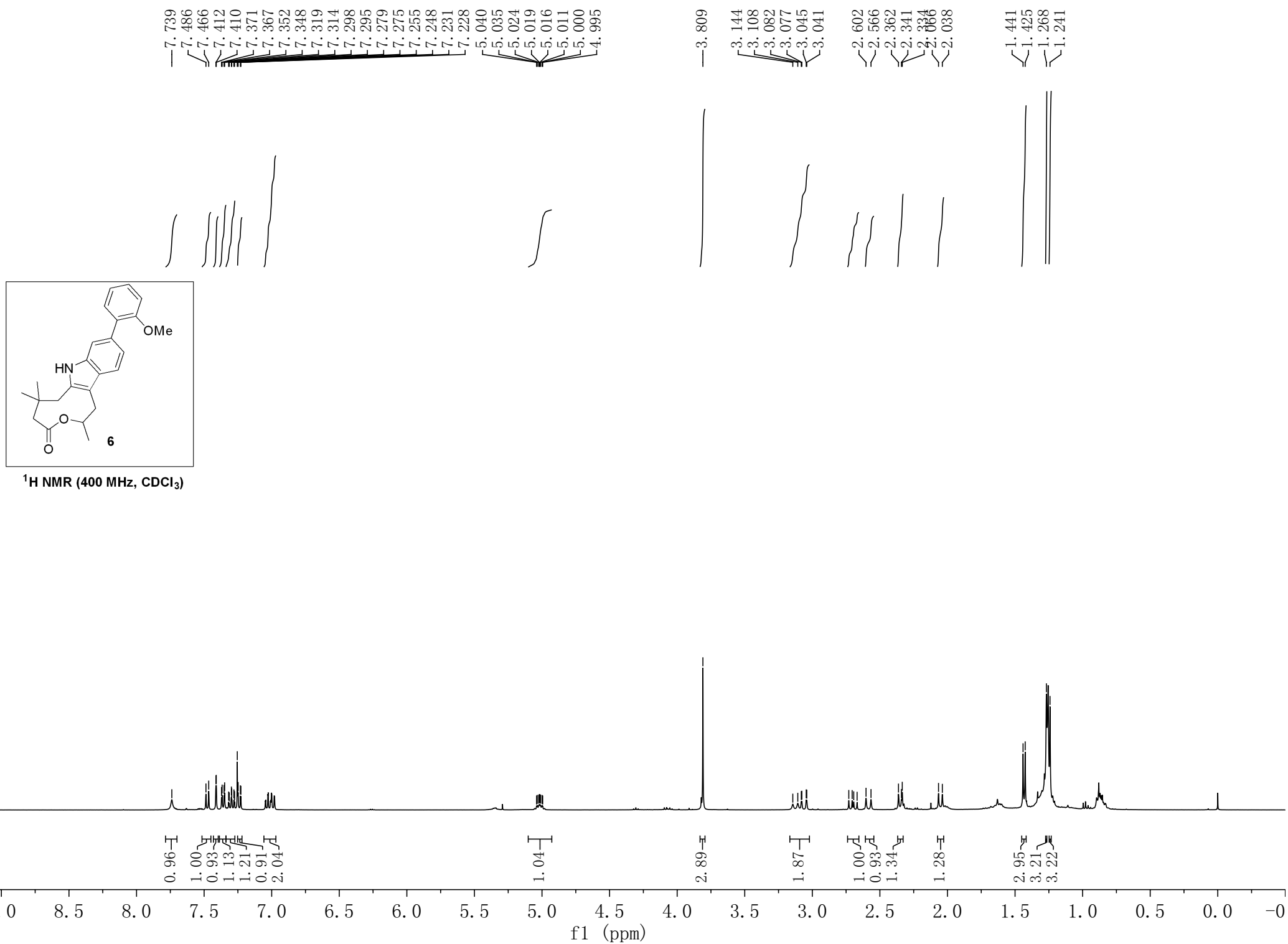


^{1}H NMR (400 MHz, $CDCl_3$)

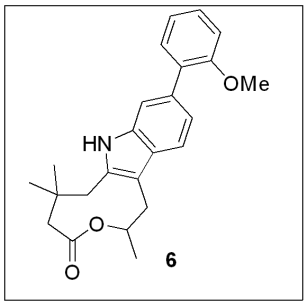


4

^{13}C NMR (101 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (400 MHz, $CDCl_3$)

171.70
156.62
135.22
133.88
132.07
131.94
131.29
127.91
127.27
121.26
120.79
117.33
111.26
111.12
110.06
69.95
55.63
47.70
37.91
37.56
29.72
22.71
20.32
14.14