Supplementary data

A Cascade Markovnikov Addition / Lewis Acid-Catalyzed Rearrangement of Methylenaziridines with Carboxylic Acids: Continuous-Flow Synthesis of α-Amidoketones

Bin Pan,† Hao-Tian Sun,† Feng Li, Qing-Bao Zhang, Shan-Shan Zhang , Jia-Hao Wang, Meng-Rui Xu, Jing-Tian Ge, Zi-Qing Hu, Shang Lv, Guo-Fu Huang* and Li-Juan Feng*

Corresponding author at: Shandong Engineering Research Center of Green and High-value Marine Fine Chemical, Weifang University of Science and Technology, Shouguang, China.

E-mail address: 280525600@qq.com (G.F. Huang); ljfeng@alum.imr.ac.cn (L. J. Feng)

Table of Contents

1. General information

^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker DRX-400 or Bruker DRX-600 spectrometers (400 MHz or 600 MHz for ^{1}H NMR, 100 MHz or 151 MHz for ^{13}C NMR, see details of each compound) using $CDCl_3$, or dimethyl sulfoxide-d_6 as solvent. Tetramethylsilane (δ=0), $CDCl_3$ (7.27 ppm) or dimethyl sulfoxide-d6 (2.50 ppm) serves as the internal standard for ^{1}H NMR and $CDCl_3$ (77.16 ppm) or dimethyl sulfoxide-d6 (39.52 ppm) for ^{13}C NMR. Coupling constants (*J*) are reported in Hz and refer to apparent peak multiplications. High-resolution mass spectra were measured on the Thermo Scientific Q Exactive MS. Chromatography was performed on silica gel (300-400 mesh). TLC analysis was performed using glass-backed plates coated with 0.2 mm silica.

Commercially available reagents were used throughout without further purification. All solvents were purified and dried according to the standard procedures. All aryl acids, alkyl acids, Indomethacin, Febuxostat, Deferasirox, Fluticasone 17β-carboxylic acid, Naproxen were purchased from Shanghai Aladdin Bio-Chem Technology and used without further purification. All Fmoc-protected amino acids were purchased from GL Bio-chem Technology and used without further purification. Silica gel (300-400 mesh) was purchased from Rushan hongyuan silica gel Co., Ltd.

2. Experiment Procedures and Characterization Data

2.1 General Synthesis Procedure of 3 in batch

Carboxylic acids **1** (0.5 mmol, 1 eq.), 2-Methyleneaziridines **2** (0.5 mmol, 1 eq.), $Sc(OTf)_3$ (10 mol%) and DCE (5 mL) were added into a tube. The reaction mixture was stirred and monitored by TLC. When the reaction was over, the solvent was removed under reduced pressure and the residue was purified by a flash silica gel column chromatography to give the corresponding **3**.

2.2 Continuous Flow System

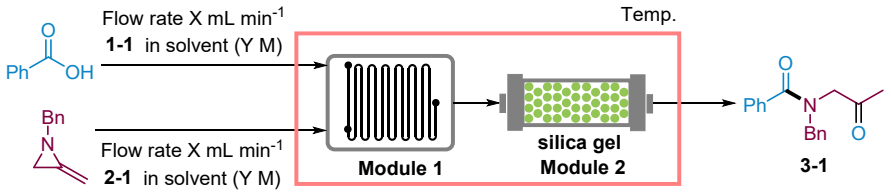
Fig S1 Continuous flow system

General information: In the continuous flow system, reagents were delivered by two HPLC pumps (M1010, Shandong

Huachuang Meixi Instrument Co., Ltd.). The quartz glass plate-type reactor Module 1 (Shanghai Yanzheng Experimental Instrument Co., Ltd.) had a maximum liquid volume of 130 μL (dimensions: length 49.6 mm, width 80.4 mm), and the packed-bed reactor Module 2 (SHIMADZU stainless steel column, length：75 mm, ID：4.6 mm,) connected using stainless steel tube (OD: 1/16, ID: 0.75 mm) and PEEK connectors. A ractangular quartz glass tank served as the heating container, utilizing water or trimethylsilicone oil as the heating medium. The continuous flow system was illustrated in Fig S1.

Optimization of system parameters: The flow rate, concentration of substrates and the reaction temperature were optimized as shown in Table S1.

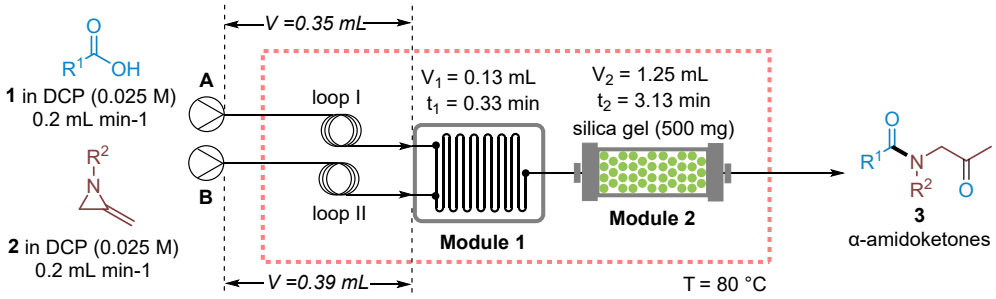
Table S1 Optimization of reaction conditions [a]



Entry	Solvent	Silican gel weight (mg)	Flow rate X (mL· min^{-1})	Concentration Y	Temp. (°C)	Yield [%][b]
1[d]	DCE	500	-	-	60	80
2	DCE	500	0.075	0.2 M	60	64
3	DCE	500	0.075	0.2 M	70	80
4	DCE	500	0.075	0.2 M	80	95
5	DCE	500	0.15	0.2 M	80	81
6	DCP	500	0.15	0.2 M	90	quant.[c]
7	DCP	500	0.2	0.2 M	90	92
8	DCP	500	0.3	0.2 M	90	75
9	DCP	500	0.2	0.1 M	90	quant.
10	DCP	300	0.2	0.1 M	90	88
11	DCP	100	0.2	0.1 M	90	75
12[e]	DCP	500	0.2	0.1 M	90	71

[a] reaction conditions: **1-1** (0.2 mmol), **2-1** (0.2 mmol), extra dry solvent (water≤30 ppm).
[b] HPLC yield.
[c] quant. means quantitative yield.
[d] batch reaction in 5 mL DCE for 10 h.
[e] without Module 1

Continuous flow synthesis:



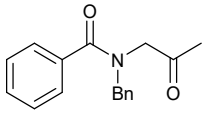
Initially, the whole system was charged with anhydrous DCP. Subsequently, the solutions of compound **1** (0.2 mmol, 0.1 M in DCP) and compound **2** (0.2 mmol, 0.1 M in DCP) were simultaneously delivered into the preheating loop I and II by pumps A and B, respectively. Both pumps operated at a flow rate of 0.2 mL/min, combining to produce a merged stream that flowed through the microchannel reactor (V = 130 μL, t_1 = 15.6 s) at an overall rate of 0.4 mL/min. The reaction stream then passed through the packed-

bed reactor (Module 2). After the reaction solution was collected, the entire system was flushed with 2 mL of anhydrous solvent. The solvent was removed under reduced pressure and the residue was purified by a flash silica gel column chromatography to give the corresponding **3**.

For indomethacin and febuxostat, a pre-mixed solution of MAs and substrate acids was required and delivered into the system using a single pump. The reaction solution collected after the first cycle was subsequently reintroduced into the continuous flow system. The reaction solution obtained after the second cycle was then purified via flash silica gel column chromatography to yield the corresponding product **3**.

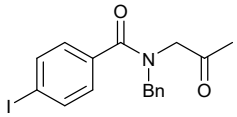
2.3 Experimental data for 3

***N*-benzyl-*N*-(2-oxopropyl)benzamide (3-1)**[1,2]



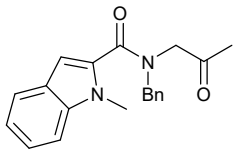
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (132.1 mg, 99% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.16 (m, 10H), 4.79 and 4.58 (2◊s, 2H), 4.21 and 3.91 (2◊s, 2H), 2.17 and 1.90 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.77, 172.59, 136.38, 135.41, 130.11, 129.11, 128.69, 128.00, 127.14, 127.08, 77.16, 54.23, 53.98, 27.66; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{18}NO_2$ 268.1338; Found 268.1333.

***N*-benzyl-4-iodo-*N*-(2-oxopropyl)benzamide (3-2)**



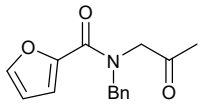
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (174.8 mg, 89% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.29 – 7.02 (m, 7H), 4.65 and 4.46 (2◊s, 2H), 4.12 and 3.82 (2◊s, 2H), 2.07 and 1.83 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.80, 202.32, 171.53, 137.73, 135.96, 134.70, 129.07, 128.87, 128.68, 128.56, 128.18, 128.00, 126.88, 96.33, 96.09, 57.52, 54.28, 53.85, 49.19, 27.53, 27.14. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{17}INO_2$ 394.0304; Found 394.0268.

***N*-benzyl-5-methyl-*N*-(2-oxopropyl)-*1H*-indole-2-carboxamide (3-3)**



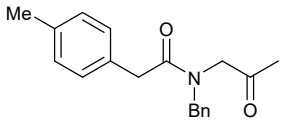
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (155.2 mg, 97% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.51 (m, 1H), 7.41 – 7.24 (m, 6H), 7.12 (t, 1H), 6.68 and 6.52 (2◊s, 1H), 4.82 (s, 2H), 4.26 (s, 2H), 3.90 (s, 3H), 2.20 and 1.94 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.37, 165.63, 138.22, 136.45, 129.18, 128.01, 127.03, 126.52, 123.56, 121.79, 120.40, 110.03, 103.01, 100.12, 77.16, 54.65, 54.26, 31.40, 27.62; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{21}N_2O_2$ 321.1603; Found 321.1606.

***N*-benzyl-*N*-(2-oxopropyl)furan-2-carboxamide (3-4)**



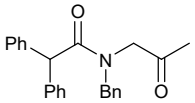
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (124.6 mg, 97% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 and 7.61 (2◊s, 1H), 7.39 – 7.22 (m, 6H), 6.58 and 6.48 (2◊s, 1H), 4.77 and 4.72 (2◊s, 2H), 4.19 and 4.12 (2◊s, 2H), 2.16 and 2.04 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.71, 165.63, 144.16, 143.11, 136.32, 129.16, 128.81, 128.55, 127.88, 126.45, 120.37, 110.28, 77.49, 77.17, 76.85, 57.55, 55.22, 53.55, 49.62, 27.43. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{16}NO_3$ 258.1130; Found 258.1113.

_N_-benzyl-_N_-(2-oxopropyl)-2-(_p_-tolyl)acetamide (3-5)



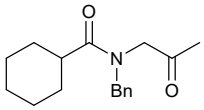
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (146.0 mg, 99% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.03 (m, 9H), 4.65 and 4.59 (2◊s, 2H), 4.11 and 3.99 (2◊s, 2H), 3.81 and 3.60 (2◊s, 2H), 2.35 (s, 3H), 2.11 and 1.99 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.23, 202.96, 172.02, 171.65, 136.84, 136.49, 136.11, 131.52, 131.49, 129.52, 129.44, 128.97, 128.74, 128.68, 128.65, 128.43, 127.91, 127.64, 126.86, 77.16, 56.53, 55.12, 52.53, 49.81, 40.80, 40.13, 27.38, 26.98, 21.08; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{22}NO_2$ 296.1615; Found 296.1612.

_N_-benzyl-_N_-(2-oxopropyl)-2,2-diphenylacetamide (3-6)



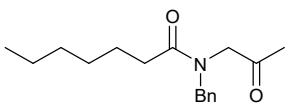
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (157.1 mg, 88% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.17 (m, 15H), 5.32 and 4.96 (2◊s, 2H), 4.74 and 4.64 (2◊s, 2H), 4.19 and 4.04 (2◊s, 2H), 2.18 and 2.05 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.11, 203.07, 172.77, 172.41, 139.28, 138.87, 136.91, 136.40, 129.14, 129.08, 129.04, 128.67, 128.59, 128.44, 127.96, 127.65, 127.26, 127.18, 126.62, 77.16, 56.48, 55.88, 55.08, 54.47, 52.46, 50.23, 27.48, 27.13; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{24}NO_2$ 358.1807; Found 358.1813.

_N_-benzyl-_N_-(2-oxopropyl)cyclohexanecarboxamide (3-7)



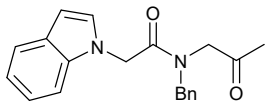
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (133.8 mg, 98% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.18 (m, 3H), 7.08 (m, 2H), 4.53 and 4.50 (2◊s, 2H), 3.95 and 3.93 (2◊s, 2H), 2.63 – 2.38 (m, 1H), 2.00 (s, 3H), 1.60 (m, 7H), 1.21 – 1.10 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.55, 203.37, 177.09, 176.77, 137.22, 136.66, 129.03, 128.73, 128.26, 127.90, 127.58, 126.77, 77.16, 56.40, 55.11, 52.05, 49.57, 41.17, 40.57, 29.58, 29.54, 27.42, 27.17, 25.85, 25.82, 25.78; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{24}NO_2$ 274.1807; Found 274.1815.

_N_-benzyl-_N_-(2-oxopropyl)heptanamide (3-8)



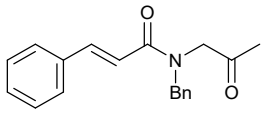
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (134.8 mg, 98% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.17 (m, 3H), 7.14 – 7.03 (m, 2H), 4.52 and 4.51 (2◊s, 2H), 4.01 and 3.91 (2◊s, 2H), 2.38 – 2.06 (m, 2H), 2.02 and 1.99 (2◊s, 2H), 1.62 – 1.55 (m, 2H), 1.20 (m, 6H), 0.78 (t, J = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.55, 203.17, 174.10, 173.63, 137.14, 136.48, 129.08, 128.77, 128.50, 127.94, 127.69, 126.79, 77.16, 56.59, 55.17, 52.29, 49.77, 33.20, 32.96, 31.75, 31.71, 29.81, 29.13, 27.45, 27.18, 25.27, 25.20, 22.62, 14.14; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{16}NO_2$ 276.1964; Found 276.1980.

***N*-benzyl-2-(*1H*-indol-1-yl)-*N*-(2-oxopropyl)acetamide (3-9)**



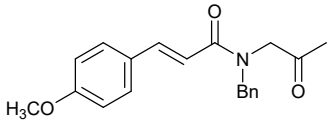
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (142.4 mg, 89% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, 1H), 7.25 (m, 9H), 6.55 (d, 1H), 4.95 and 4.72 (2◊s, 2H), 4.61 and 4.57 (2◊s, 2H), 4.14 and 3.79 (2◊s, 2H), 2.08 and 1.85 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.68, 202.35, 168.37, 136.68, 136.49, 136.26, 135.56, 129.32, 128.81, 128.72, 128.67, 128.42, 128.32, 127.95, 126.72, 122.23, 122.01, 121.25, 121.15, 119.95, 119.80, 109.15, 109.05, 102.65, 102.42, 77.16, 55.83, 55.61, 51.90, 50.80, 48.32, 47.61, 27.38, 26.98; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{21}N_2O_2$ 321.1603; Found 321.1606.

(*E*)-*N*-benzyl-*N*-(2-oxopropyl)-3-(4-(trifluoromethyl)phenyl)acrylamide (3-10)



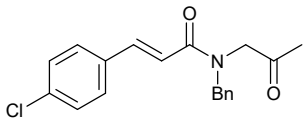
Ethyl acetate/petroleum ether (1:8, v/v) as the eluent; colorless oil (143.6 mg, 98% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 15.3 Hz, 1H), 7.48 – 7.24 (m, 10H), 6.92 and 6.57 (2◊d, *J* = 15.4 Hz, 1H), 4.75 (s, 2H), 4.22 and 4.16 (2◊s, 2H), 2.17 and 2.11 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.43, 203.33, 167.37, 167.25, 144.15, 143.95, 136.74, 136.40, 135.02, 129.89, 129.07, 128.82, 128.77, 128.55, 127.97, 127.77, 126.79, 116.77, 116.48, 77.47, 77.15, 76.83, 56.73, 55.85, 52.36, 50.44, 27.44, 27.18. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{20}NO_2$ 294.1494; Found 294.1505.

(*E*)-*N*-benzyl-3-(4-methoxyphenyl)-*N*-(2-oxopropyl)acrylamide (3-11)



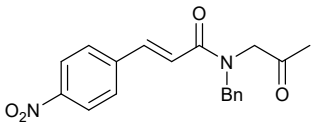
Ethyl acetate/petroleum ether (1:8, v/v) as the eluent; colorless oil (156.7 mg, 97% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 15.3 Hz, 1H), 7.41 – 7.21 (m, 7H), 6.83 (m, 2H), 6.77 (d, *J* = 15.3 Hz, 1H), 4.72 (s, 2H), 4.19 and 4.13 (2◊s, 2H), 3.77 (s, 3H), 2.10 (d, *J* = 23.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.68, 203.47, 167.62, 167.47, 161.03, 143.81, 143.71, 136.87, 136.54, 129.67, 129.55, 128.99, 128.69, 128.47, 127.87, 127.70, 126.76, 114.21, 114.09, 113.88, 77.16, 56.74, 55.88, 55.31, 52.30, 50.40, 27.36, 27.11; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{22}NO_2$ 324.1600; Found 324.1577.

(*E*)-*N*-benzyl-3-(4-chlorophenyl)-*N*-(2-oxopropyl)acrylamide (3-12)



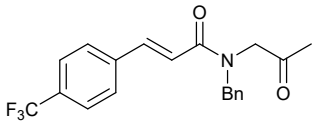
Ethyl acetate/petroleum ether (1:8, v/v) as the eluent; colorless oil (152.1 mg, 93% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 15.4 Hz, 1H), 7.42 – 7.20 (m, 10H), 6.88 and 6.54 (2◊d, 15.4 Hz, 1H), 4.73 (s, 2H), 4.21 and 4.13 (2◊s, 2H), 2.16 and 2.09 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.51, 167.50, 143.14, 142.96, 136.69, 136.07, 133.90, 129.72, 129.53, 129.48, 129.45, 129.17, 128.94, 128.41, 128.20, 127.13, 117.70, 117.43, 77.16, 57.08, 56.24, 52.76, 50.88, 27.82, 27.58; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{19}ClNO_2$ 328.1104; Found 328.1081.

(*E*)-*N*-benzyl-3-(4-nitrophenyl)-*N*-(2-oxopropyl)acrylamide (3-13)



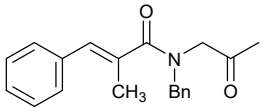
Ethyl acetate/petroleum ether (1:8, v/v) as the eluent; colorless oil (160.6 mg, 95% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 – 7.97 (m, 2H), 7.68 (d, *J* = 15.5 Hz, 1H), 7.54 – 7.46 (m, 2H), 7.24 (m, 5H), 6.97 and 6.64 (2◊d, 15.4 Hz, 1H), 4.67 and 4.64 (2◊s, 2H), 4.17 and 4.12 (2◊s, 2H), 2.09 and 2.03 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.89, 202.78, 166.43, 148.21, 141.32, 141.26, 141.15, 140.85, 136.41, 136.13, 129.18, 128.84, 128.55, 128.51, 128.16, 127.92, 126.73, 124.12, 121.36, 121.01, 77.16, 56.62, 55.97, 52.47, 50.60, 27.45, 27.25; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{19}N_2O_4$ 339.1345; Found 339.1333.

_N_-benzyl-_N_-(2-oxopropyl)cinnamamide (3-14)



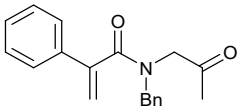
Ethyl acetate/petroleum ether (1:8, v/v) as the eluent; colorless oil (175.1 mg, 97% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 15.4 Hz, 1H), 7.48 (q, *J* = 8.4 Hz, 4H), 7.32 – 7.15 (m, 5H), 6.91 and 6.57 (2◊d, 15.4 Hz, 1H), 4.67 and 4.65 (2◊s, 2H), 4.15 and 4.08 (2◊s, 2H), 2.09 and 2.02 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.00, 166.85, 142.31, 142.05, 138.52, 136.58, 136.29, 131.87, 131.54, 131.22, 130.90, 129.19, 128.87, 128.63, 128.14, 126.80, 125.89, 125.85, 125.81, 125.77, 125.31, 122.61, 119.55, 119.22, 77.16, 56.72, 55.95, 52.49, 50.59, 27.48, 27.23; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{19}F_3NO_2$ 362.1368; Found 362.1353.

(*E*)-*N*-benzyl-2-methyl-*N*-(2-oxopropyl)-3-phenylacrylamide (3-15)



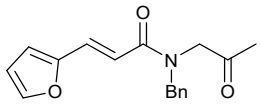
Ethyl acetate/petroleum ether (1:10, v/v) as the eluent; colorless oil (142.8 mg, 93% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.21 (m, 10H), 6.71 (s, 1H), 4.71 (s, 2H), 4.12 (s, 2H), 2.14 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.86, 174.58, 136.48, 135.82, 132.48, 130.10, 129.12, 129.05, 128.42, 127.95, 127.61, 127.17, 77.16, 53.95, 53.56, 29.77, 27.57, 16.32. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{22}NO_2$ 308.1651; Found 308.1628.

_N_-benzyl-_N_-(2-oxopropyl)-2-phenylacrylamide (3-16)



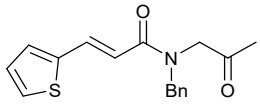
Ethyl acetate/petroleum ether (1:10, v/v) as the eluent; colorless oil (137.7 mg, 94% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.03 (m, 10H), 5.78 and 5.67 (2◊s, 1H), 5.45 and 5.35 (2◊s, 1H), 4.75 and 4.49 (2◊s, 2H), 4.14 and 3.88 (2◊s, 2H), 2.12 and 1.84 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.74, 202.70, 171.87, 171.25, 144.63, 144.30, 136.55, 136.01, 135.26, 135.14, 129.02, 128.95, 128.92, 128.90, 128.56, 128.00, 127.87, 127.41, 126.04, 125.87, 114.85, 114.20, 77.16, 56.65, 53.45, 53.20, 48.55, 27.60, 26.99; HRMS (ESI) *m/z*: $[M-H]^-$ Calcd for $C_{19}H_{18}NO_2$ 292.1338; Found 292.1318.

(*E*)-*N*-benzyl-3-(furan-2-yl)-*N*-(2-oxopropyl)acrylamide (3-17)



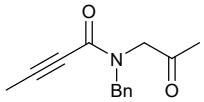
Ethyl acetate/petroleum ether (1:10, v/v) as the eluent; colorless oil (135.8 mg, 96% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 15.0 Hz, 1H), 7.41 – 7.29 (m, 5H), 7.21 (s, 1H), 6.83 (d, *J* = 15.0 Hz, 1H), 6.55 (d, *J* = 2.9 Hz, 1H), 6.43 (s, 1H), 4.72 (s, 2H), 4.18 and 4.13 (2◊s, 2H), 2.14 and 2.10 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.77, 167.62, 151.89, 144.60, 136.76, 131.16, 131.05, 129.40, 129.14, 128.90, 128.34, 128.13, 127.31, 114.95, 114.85, 114.28, 112.65, 77.16, 57.00, 56.07, 52.66, 50.80, 27.80, 27.56; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{18}NO_3$ 284.1287; Found 284.1287.

(*E*)-*N*-benzyl-N-(2-oxopropyl)-3-(thiophen-2-yl)acrylamide (3-18)



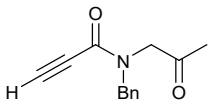
Ethyl acetate/petroleum ether (1:10, v/v) as the eluent; colorless oil (142.0 mg, 95% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 15.0 Hz, 1H), 7.37 – 7.20 (m, 7H), 7.00 (t, *J* = 4.2 Hz, 1H), 6.73 and 6.36 (2◊d, *J* = 15.0 Hz, 1H), 4.70 (s, 2H), 4.19 and 4.11 (2◊s, 2H), 2.14 and 2.09 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.34, 167.06, 166.92, 140.23, 136.77, 136.69, 136.43, 130.64, 129.08, 128.78, 128.53, 128.09, 128.02, 127.74, 127.63, 126.93, 115.37, 115.22, 77.16, 56.64, 55.85, 52.39, 50.45, 27.44, 27.19; HRMS (ESI) *m/z*: $[M-H]^-$ Calcd for $C_{17}H_{16}NO_2S$ 298.0902; Found 298.0883.

***N*-benzyl-*N*-(2-oxopropyl)but-2-ynamide (3-19)**



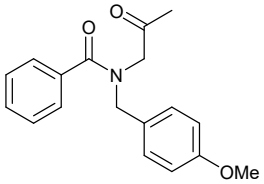
Ethyl acetate/petroleum ether (1:10, v/v) as the eluent; colorless oil (97.3 mg, 85% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.15 (m, 5H), 4.76 and 4.56 (2◊s, 2H), 4.13 and 3.97 (2◊s, 2H), 2.01 and 1.99 (2◊s, 3H), 1.95 and 1.90 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.10, 202.35, 155.34, 155.17, 135.87, 128.98, 128.86, 128.56, 128.19, 127.96, 127.91, 127.81, 90.45, 90.04, 77.16, 73.09, 72.93, 57.32, 53.45, 53.17, 48.66, 27.35, 27.12, 4.19, 4.08; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{16}NO_2$ 230.1180; found 230.1181.

***N*-benzyl-*N*-(2-oxopropyl)-3-(trimethylsilyl)propiolamide (3-20)**



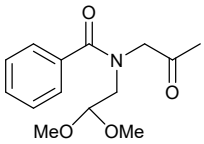
Ethyl acetate/petroleum ether (1:10, v/v) as the eluent; colorless oil (69.8 mg, 65% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.18 (m, 5H), 4.76 and 4.56 (2◊s, 2H), 4.13 and 3.97 (2◊s, 2H), 2.01 and 1.99 (2◊s, 3H), 1.95 and 1.90 (2◊s, 3H). HRMS (ESI) *m/z*: $[M-H]^+$ Calcd for $C_{13}H_{12}NO_2$ 214.0868; found 214.0860.

***N*-(4-methoxybenzyl)-*N*-(2-oxopropyl)benzamide (3-22)**



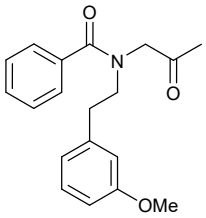
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (139.6 mg, 94% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.36 (m, 5H), 7.23 – 6.87 (m, 4H), 4.71 and 4.50 (2◊s, 2H), 4.19 and 3.89 (2◊s, 2H), 3.80 (s, 3H), 2.16 and 1.89 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.18, 202.74, 172.25, 159.30, 136.12, 135.48, 129.97, 129.90, 129.76, 128.56, 128.43, 127.99, 126.94, 126.36, 114.34, 113.82, 57.38, 55.31, 53.92, 53.30, 48.44, 27.50, 27.05. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{20}NO_3$ 298.1443; Found 298.1445.

_N_-(2,2-dimethoxyethyl)-_N_-(2-oxopropyl)benzamide (3-23) [1]



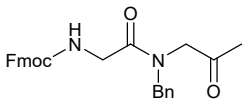
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (117.9 mg, 89% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.26 (m, 5H), 4.56 and 4.29 (2◊m, 1H), 4.42 and 4.19 (2◊s, 2H), 3.60 and 3.36 (2◊d, 2H), 3.42 (s, 3H), 3.22 (s, 3H), 2.21 and 1.94 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.95, 202.64, 172.64, 172.42, 135.95, 135.81, 129.63, 128.53, 128.47, 126.70, 126.39, 104.24, 103.60, 77.16, 60.22, 56.27, 55.03, 54.65, 52.22, 49.13, 27.18, 26.81. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{20}NO_4$ 266.1392; Found 266.1370.

_N_-(3-methoxyphenethyl)-_N_-(2-oxopropyl)benzamide (3-24)



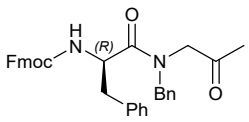
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (146.2 mg, 94% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (m, 6H), 6.70 – 6.34 (m, 3H), 4.16 (s, 1H), 3.73 – 3.62 (m, 4H), 3.39 (t, J = 7.1 Hz, 1H), 2.86 and 2.62 (2◊t, J = 7.1 Hz, 2H), 2.12 and 1.79 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.25, 202.79, 172.24, 171.97, 159.75, 140.73, 139.28, 136.23, 135.76, 129.63, 129.50, 128.55, 128.37, 126.48, 126.19, 121.14, 120.97, 114.45, 114.29, 112.05, 111.92, 77.16, 59.96, 55.09, 55.03, 51.81, 48.82, 35.21, 33.74, 27.41, 26.89. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{22}NO_3$ 312.1600; Found 312.1589.

(9*H*-fluoren-9-yl)methyl (2-(benzyl(2-oxopropyl)amino)-2-oxoethyl)carbamate (3-25)



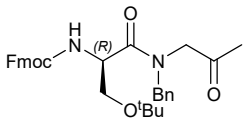
Ethyl acetate/petroleum ether (1:2, v/v) as the eluent; colorless oil (207.8 mg, 94% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.4 Hz, 2H), 7.61 (d, J = 7.3 Hz, 2H), 7.40 – 7.29 (m, 7H), 7.20 – 7.29 (m, 2H), 5.94 and 5.85 (2◊s, 1H), 4.63 and 4.52 (2◊s, 2H), 4.38 and 4.36 (2◊s, 2H), 4.23 (m, 2H), 4.14 (s, 1H), 4.01 – 3.89 (m, 1H), 2.11 and 2.08 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.43, 201.98, 169.04, 168.96, 156.27, 143.96, 141.34, 135.97, 135.00, 129.23, 128.89, 128.50, 128.31, 128.03, 127.76, 127.15, 126.99, 125.25, 120.03, 77.16, 67.24, 55.35, 55.17, 51.25, 50.29, 47.18, 42.67, 42.57, 27.33, 27.20; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{27}N_2O_4$ 443.1971; Found 443.1984.

(9*H*-fluoren-9-yl)methyl (*R*)-(1-(benzyl(2-oxopropyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (3-26)



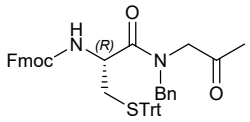
Ethyl acetate/petroleum ether (1:4, v/v) as the eluent; colorless oil (236.7 mg, 89% yield), ^{1}H NMR (400 MHz, DMSO) δ 8.03 (dd, J = 10.8, 9.0 Hz, 1H), 7.88 (d, J = 7.6 Hz, 2H), 7.67 (t, J = 7.7 Hz, 2H), 7.41 (dd, J = 9.2, 5.5 Hz, 2H), 7.32 – 7.14 (m, 12H), 4.76 – 4.57 (m, 2H), 4.56 – 4.23 (m, 2H), 4.19 – 4.11 (m, 3H), 4.05 (d, J = 6.8 Hz, 1H), 3.01 – 2.83 (m, 2H), 2.09 and 2.02 (2◊s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 204.10, 203.54, 172.19, 155.93, 155.90, 143.76, 143.72, 140.70, 137.95, 137.68, 137.32, 137.12, 129.40, 129.32, 128.63, 128.32, 128.13, 128.11, 127.67, 127.53, 127.40, 127.09, 127.00, 126.40, 126.31, 125.42, 125.36, 120.10, 65.86, 56.73, 56.06, 52.44, 52.14, 51.51, 49.61, 46.58, 39.52, 37.33, 37.23, 26.97; HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{34}H_{32}N_2O_4Na$ 555.2260; Found 555.2255.

(9*H*-fluoren-9-yl)methyl (*R*)-(1-(benzyl(2-oxopropyl)amino)-3-(tert-butoxy)-1-oxopropan-2-yl)carbamate (3-27)



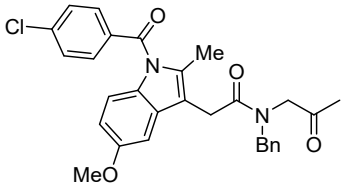
Ethyl acetate/petroleum ether (1:4, v/v) as the eluent; colorless oil (232.3 mg, 88% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.4 Hz, 2H), 7.53 (d, *J* = 7.0 Hz, 2H), 7.33 – 7.13 (m, 9H), 5.65 – 5.59 (m, 1H), 5.13 – 4.87 (m, 1H), 4.60 – 4.40 (m, 1H), 4.29 – 4.01 (m, 4H), 3.89 – 3.71 (m, 1H), 3.53 – 3.39 (m, 2H), 2.02 and 2.00 (2◊s, 3H), 1.11 – 1.02 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.99, 202.86, 172.10, 171.92, 155.77, 144.02, 143.92, 141.40, 136.30, 135.69, 129.01, 128.72, 128.62, 128.13, 127.80, 127.73, 127.54, 127.16, 125.29, 120.07, 77.16, 73.90, 67.20, 63.77, 63.32, 56.48, 55.13, 52.31, 51.23, 51.15, 50.09, 47.24, 27.40, 27.22; HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{32}H_{36}N_2O_5Na$ 551.2522; Found 551.2532.

(9*H*-fluoren-9-yl)methyl (*R*)-(1-(benzyl(2-oxopropyl)amino)-1-oxo-3-(tritylthio)propan-2-yl)carbamate（3-28）



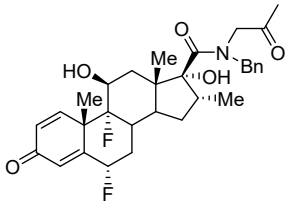
Ethyl acetate/petroleum ether (1:4, v/v) as the eluent; colorless oil (310.3 mg, 85% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.62 (m, 2H), 7.51 (dd, *J* = 8.4, 5.1 Hz, 2H), 7.32 (dd, *J* = 9.5, 4.9 Hz, 7H), 7.24 – 6.99 (m, 17H), 5.39 – 5.19 (m, 1H), 4.78 – 4.56 (m, 1H), 4.26 – 4.11 (m, 4H), 3.99 – 3.61 (m, 2H), 2.62 – 2.49 (m, 2H), 1.94 and 1.90 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.37, 202.27, 171.59, 171.31, 155.72, 144.62, 144.57, 143.99, 143.88, 143.77, 141.41, 141.37, 136.11, 135.26, 129.78, 129.74, 129.05, 128.82, 128.37, 128.22, 128.14, 128.12, 127.84, 127.80, 127.63, 127.22, 126.96, 125.34, 120.05, 77.16, 67.40, 67.32, 67.25, 56.22, 54.73, 51.91, 50.50, 50.08, 47.20, 34.83, 27.41, 27.10; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{47}H_{43}N_2O_4S$ 731.2944; Found 731.2921.

N-benzyl-2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-N-(2-oxopropyl)acetamide（3-29）



Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (205.1 mg, 89% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.40 (m, 4H), 7.31 – 7.26 (m, 3H), 7.19 – 7.06 (m, 2H), 6.99 – 6.87 (m, 2H), 6.68 – 6.64 (m, 1H), 4.69 and 4.63 (2◊s, 2H), 4.14 and 4.06 (2◊s, 2H), 3.80 (s, 3H), 3.81 and 3.62 (2◊s, 2H), 2.33 and 2.25 (2◊s, 3H), 2.11 and 1.88 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.83, 202.42, 171.01, 170.64, 168.33, 168.21, 156.23, 156.12, 139.23, 139.07, 136.78, 136.10, 135.81, 135.23, 134.01, 131.23, 131.15, 130.86, 130.80, 130.56, 129.14, 129.06, 129.01, 128.72, 128.46, 127.88, 127.73, 126.42, 115.12, 114.99, 113.16, 112.84, 112.02, 111.87, 101.17, 101.08, 77.16, 56.49, 55.73, 55.69, 55.63, 52.43, 50.22, 30.09, 29.73, 27.39, 26.80, 13.54. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{28}N_3O_3S$ 462.1851; Found 462.1811.

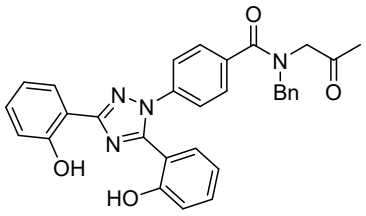
(6S,9R,10S,11S,13S,16R,17R)-N-benzyl-6,9-difluoro-11,17-dihydroxy-10,13,16-trimethyl-3-oxo-N-(2-oxopropyl)-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[a]phenanthrene-17-carboxamide（3-30）



Ethyl acetate/petroleum ether (1:10, v/v) as the eluent; colorless oil (238.1 mg, 88% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 5H), 7.11 (d, *J* = 10.1 Hz, 1H), 6.35 (s, 1H), 6.27 (d, *J* = 10.1 Hz, 1H), 5.40–5.23 (2m, 1H), 5.02 (d, *J* = 14.6 Hz, 0.5H), 4.24 (m, 1H), 4.14 (d, *J* = 14.6 Hz, 1H), 4.06 (dd, *J* = 14.2, 7.1 Hz, 0.5H), 3.97 (br, s, 0.5H), 3.74 (dd, *J* = 31.7, 13.4 Hz, 0.5H).

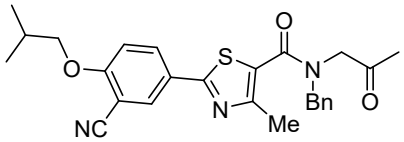
3.30–3.24 (m, 1H), 3.04–3.01 (m, 1H), 2.93–2.89 (s, 1H), 2.74–2.66 (m, 0.5H), 2.37–2.27 (m, 1H), 2.19–2.18 (m, 2H), 2.10–1.96 (m, 2H), 1.69–1.65 (m, 3H), 1.46–1.35 (m, 4H), 1.23–1.11 (m, 4H), 1.05–0.90 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.13, 186.08, 171.42, 168.23, 162.49, 151.66, 139.76, 138.51, 136.66, 129.91, 128.80, 128.59, 128.51, 128.39, 128.18, 127.77, 127.34, 127.24, 120.95, 109.68, 100.35, 98.58, 93.39, 90.84, 90.27, 87.73, 85.89, 77.16, 71.91, 71.71, 71.54, 60.55, 57.99, 54.64, 53.95, 51.76, 50.92, 49.65, 48.55, 48.39, 48.32, 44.67, 42.90, 42.79, 39.36, 39.14, 38.13, 36.37, 36.01, 35.80, 33.89, 32.89, 32.41, 32.27, 29.76, 29.42, 26.61, 24.62, 23.04, 22.99, 21.14, 17.78, 17.14, 16.76, 16.30, 15.91, 14.92, 14.26. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{31}H_{38}F_2NO_5$ 542.2718; Found 542.2689.

N-benzyl-4-(3,5-bis(2-hydroxyphenyl)-1H-1,2,4-triazol-1-yl)-N-(2-oxopropyl)benzamide (3-31)



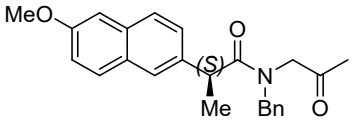
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (194.3 mg, 75% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.34 (bs, 1H), 9.65 and 9.59 (2◊s, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.56 (m, 2H), 7.41 – 7.35 (m, 6H), 7.22 – 6.96 (m, 6H), 6.67 (t, *J* = 7.3 Hz, 1H), 4.80 and 4.63 (2◊s, 2H), 4.29 and 3.99 (2◊s, 2H), 2.21 and 1.99 (2◊s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.23, 171.09, 159.60, 158.14, 156.63, 152.25, 135.84, 133.19, 131.96, 129.31, 128.87, 128.29, 127.79, 127.73, 126.98, 126.48, 120.04, 119.33, 118.53, 117.29, 113.34, 110.03, 77.16, 54.60, 54.11, 27.69. HRMS (ESI) *m/z*: $[M-H]^-$ Calcd for $C_{31}H_{25}N_4O_4$ 517.1876; Found 517.1842.

N-benzyl-2-(3-cyano-4-isobutoxyphenyl)-4-methyl-N-(2-oxopropyl)thiazole-5-carboxamide (3-32)



Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (223.7 mg, 97% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.95 (d, *J* = 8.8 Hz, 1H), 7.33 – 7.24 (m, 3H), 7.12 (s, 2H), 6.94 (d, *J* = 8.8 Hz, 1H), 4.60 (s, 2H), 4.17 (s, 2H), 3.82 (d, *J* = 6.4 Hz, 2H), 2.56 (s, 3H), 2.19 – 1.99 (m, 4H), 1.02 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.94, 164.93, 164.49, 162.15, 154.29, 135.50, 132.43, 131.74, 129.05, 128.42, 128.20, 127.28, 125.90, 123.14, 115.48, 112.69, 102.76, 75.61, 54.29, 53.76, 28.13, 27.46, 19.05, 16.44. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{28}N_3O_3S$ 462.1851; Found 462.1811.

(S)-N-benzyl-2-(6-methoxynaphthalen-2-yl)-N-(2-oxopropyl)propenamide (3-33)

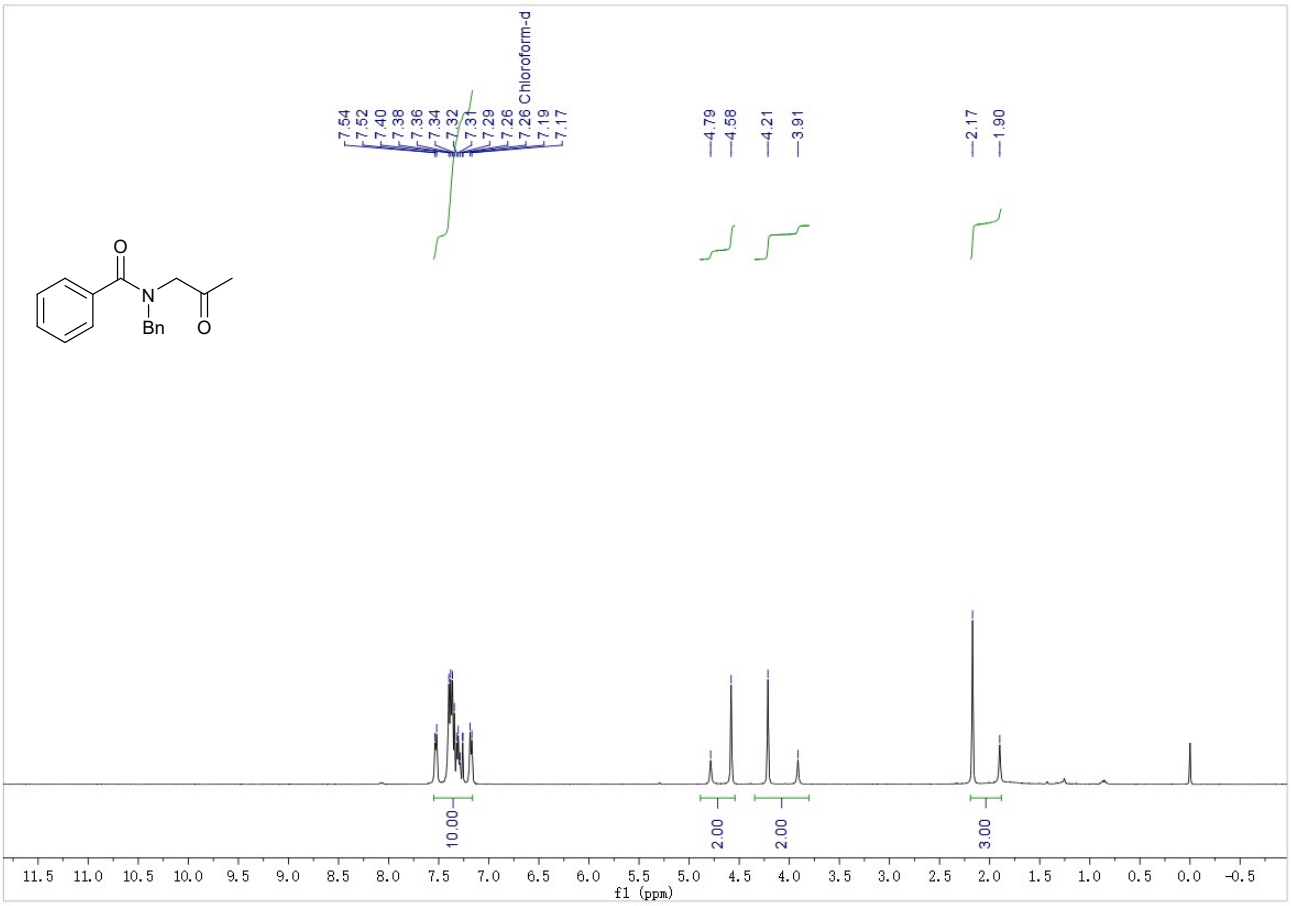


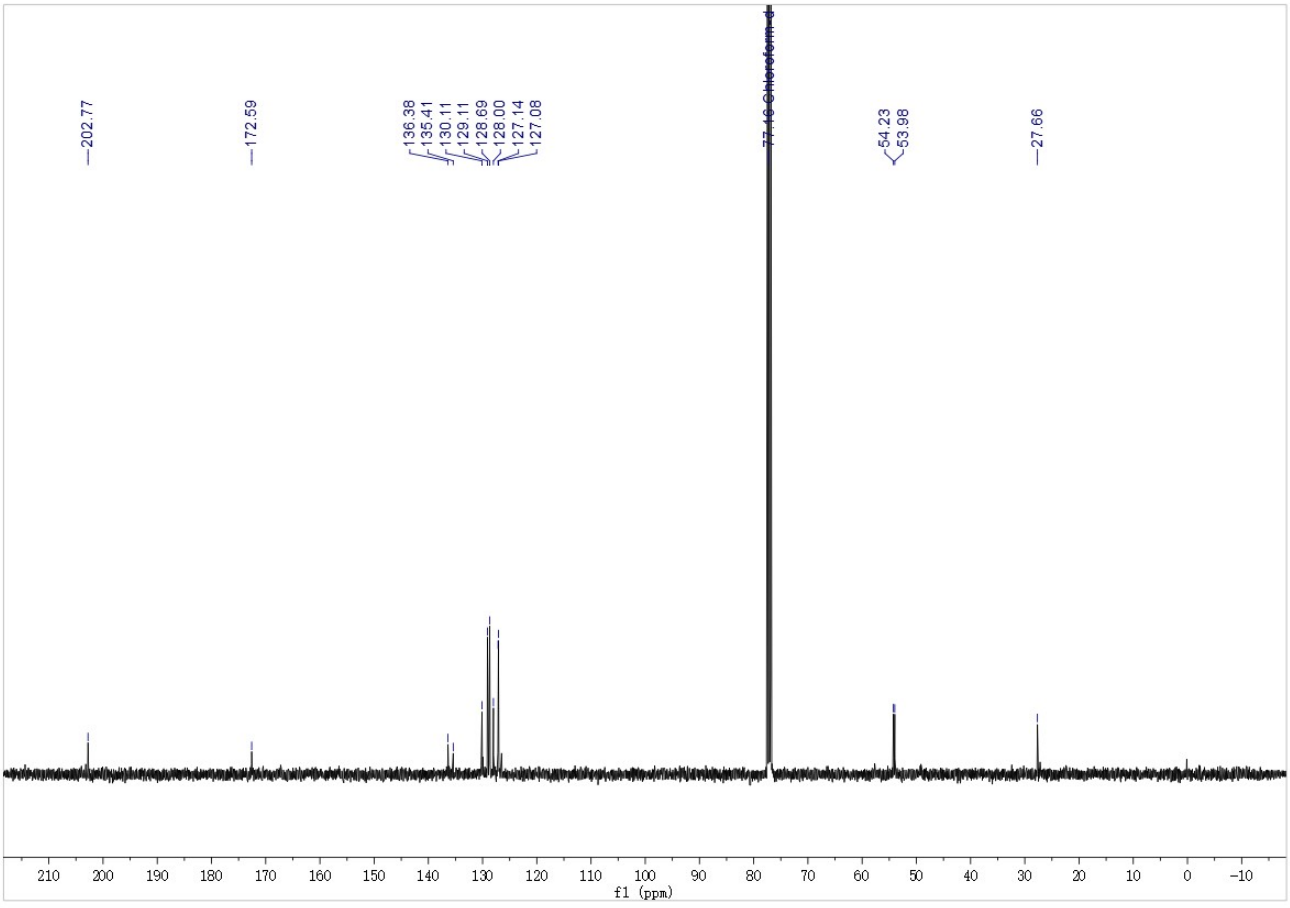
Ethyl acetate/petroleum ether (1:5, v/v) as the eluent; colorless oil (178.2 mg, 95% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 11H), 5.03 and 4.75 (2◊d, *J* = 16.6 Hz, 1H), 4.36 and 3.87 (2◊d, *J* = 17.1 Hz, 2H), 4.14 – 3.68 (m, 2H), 2.56 (s, 3H), 2.13 and 1.93 (2◊s, 3H), 1.57 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.38, 174.79, 157.76, 136.63, 136.34, 133.71, 129.45, 129.27, 129.20, 129.00, 128.74, 128.32, 127.89, 127.66, 126.87, 126.26, 126.04, 125.74, 119.37, 119.12, 105.73, 77.16, 56.34, 55.52, 55.46, 52.15, 50.08, 43.97, 43.14, 27.51, 27.06, 21.13, 20.97. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{26}NO_3$ 376.1913; Found 376.1921.

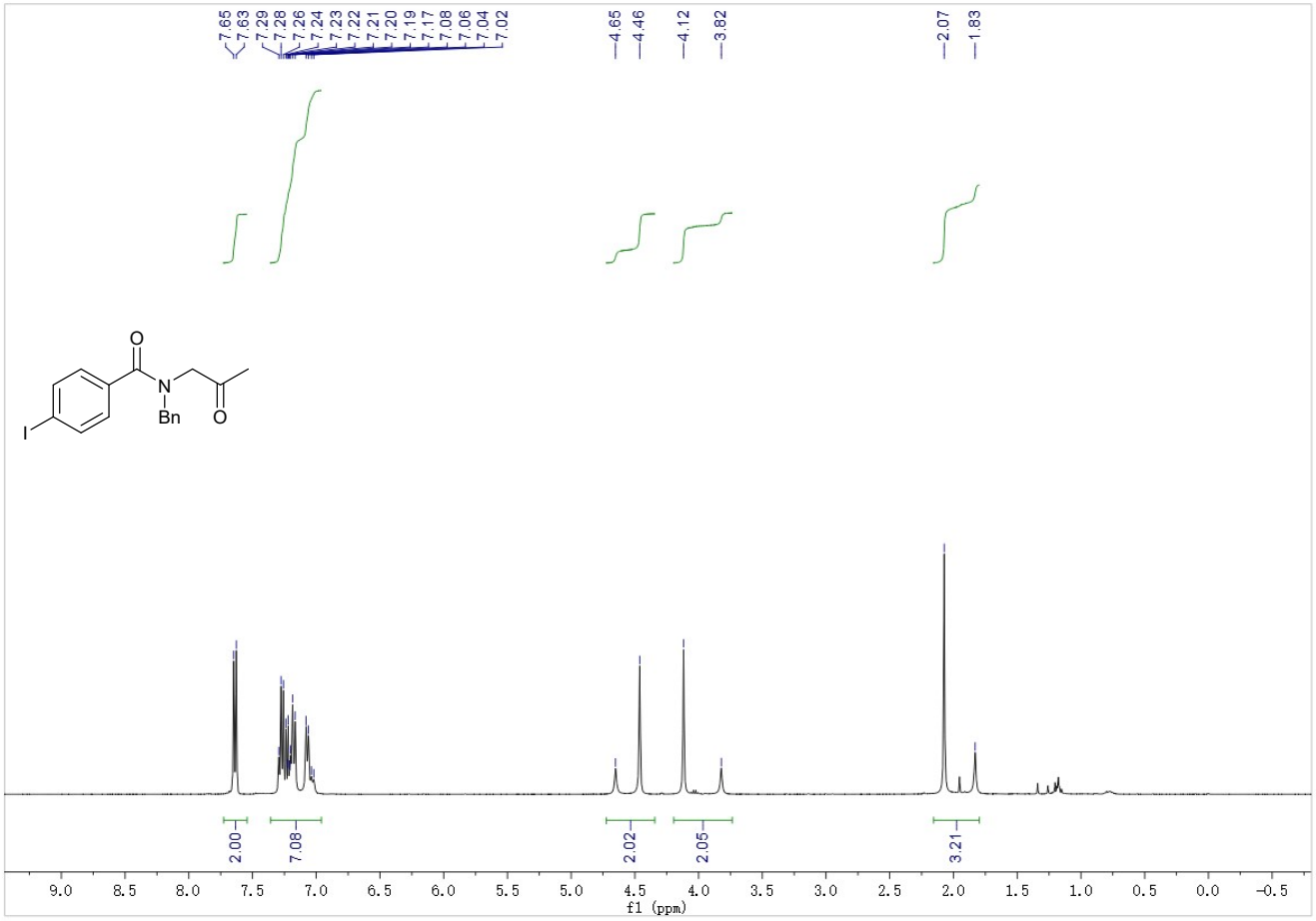
3. References

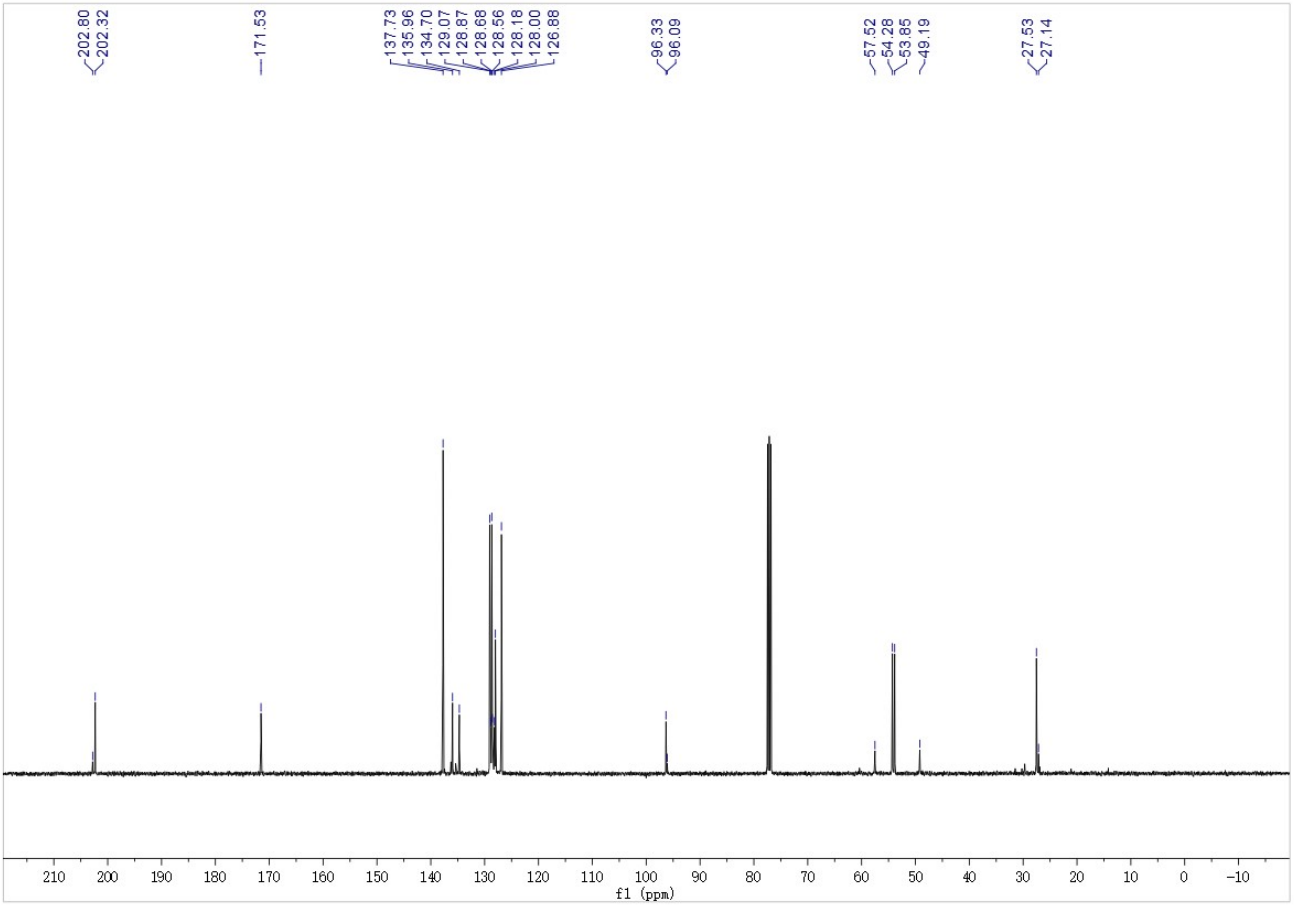
(1) B. H. Oh, I. Nakamura and Y. Yamamoto, *J. Org. Chem.,* 2004, **69**, 2856−2858;
(2) K. Holthusen, W. Leitner and G. Franciò, *J. Org. Chem.,* 2016, **81**, 4823−4828;

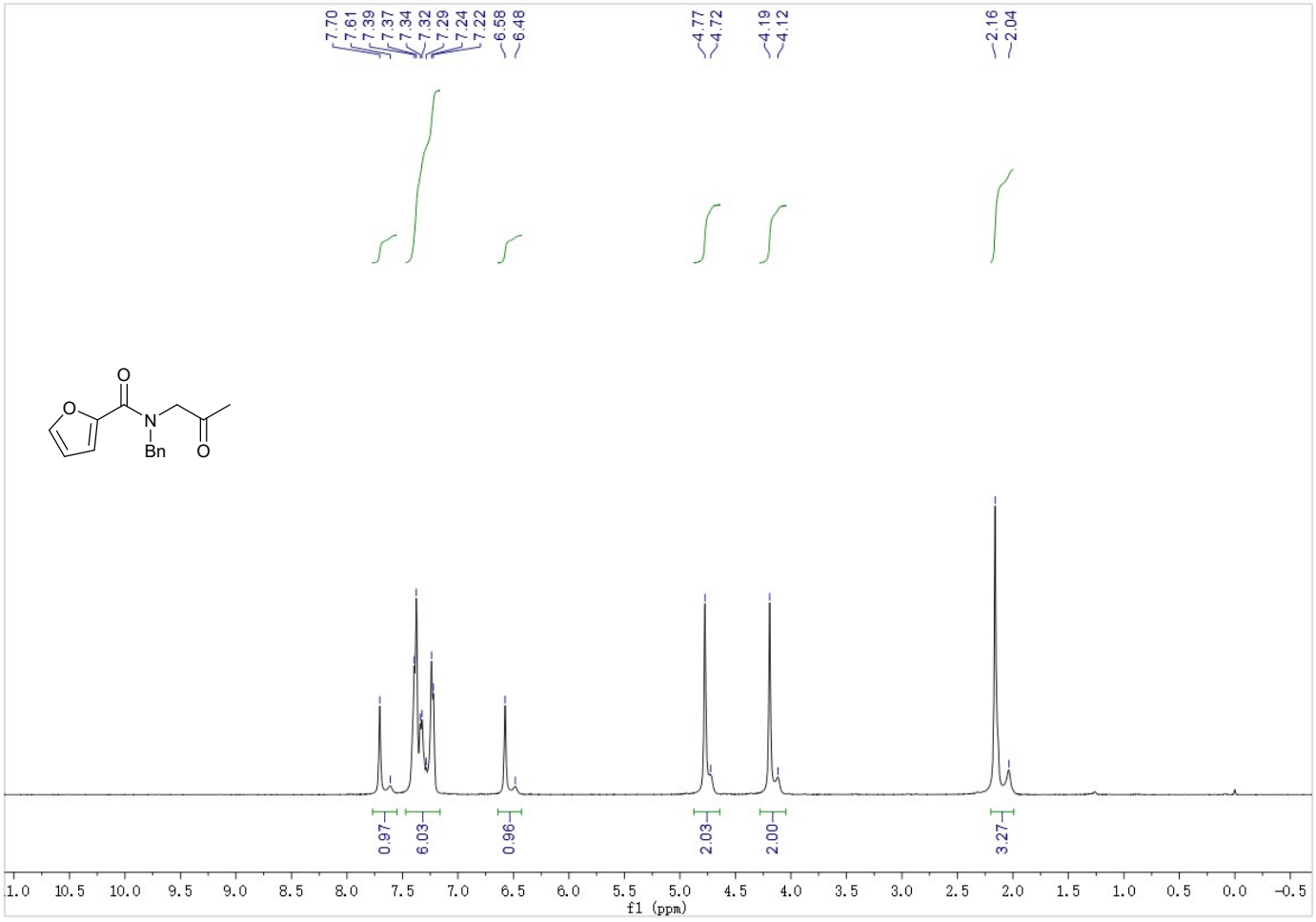
4. Copy of NMR Spectra

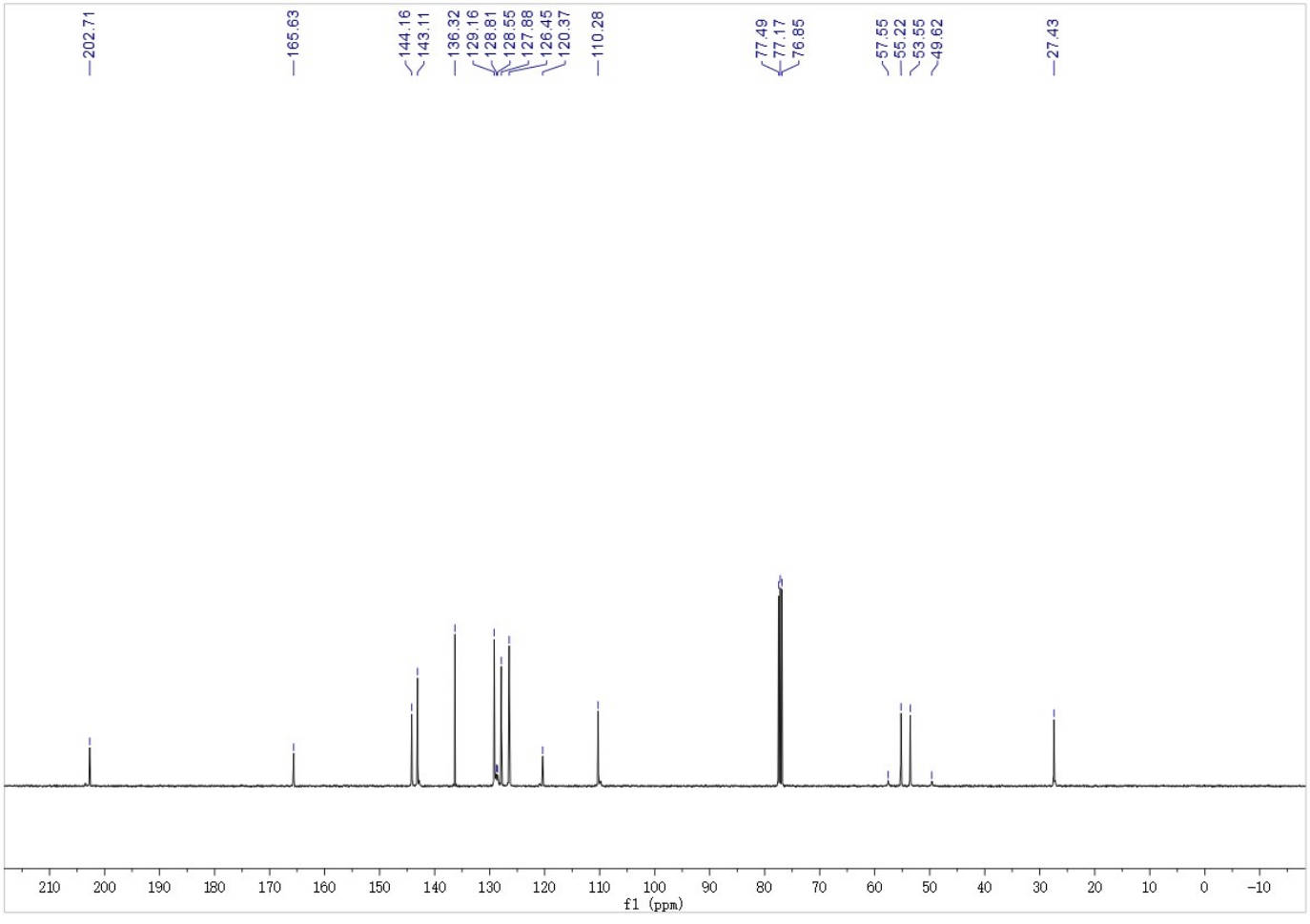


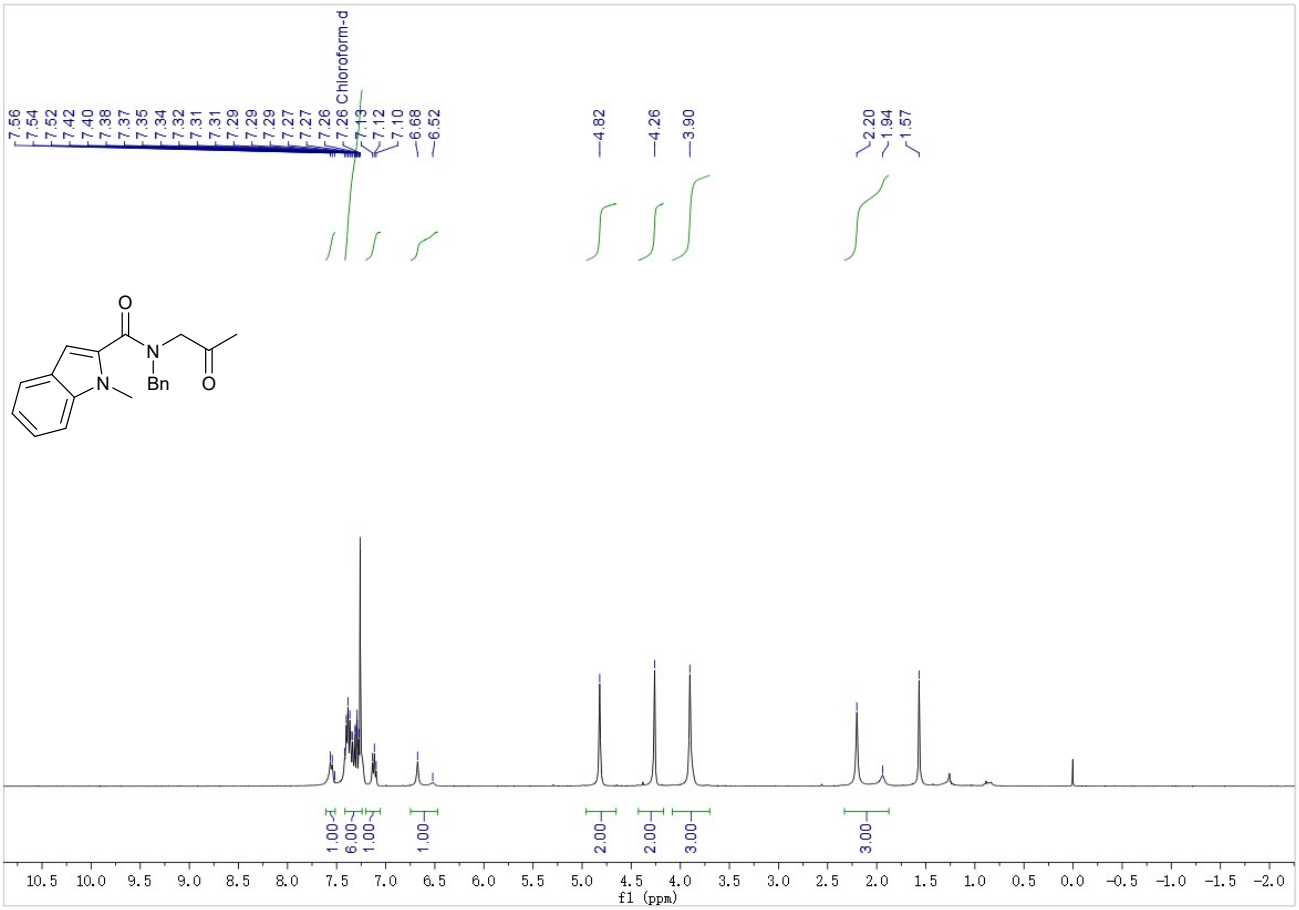


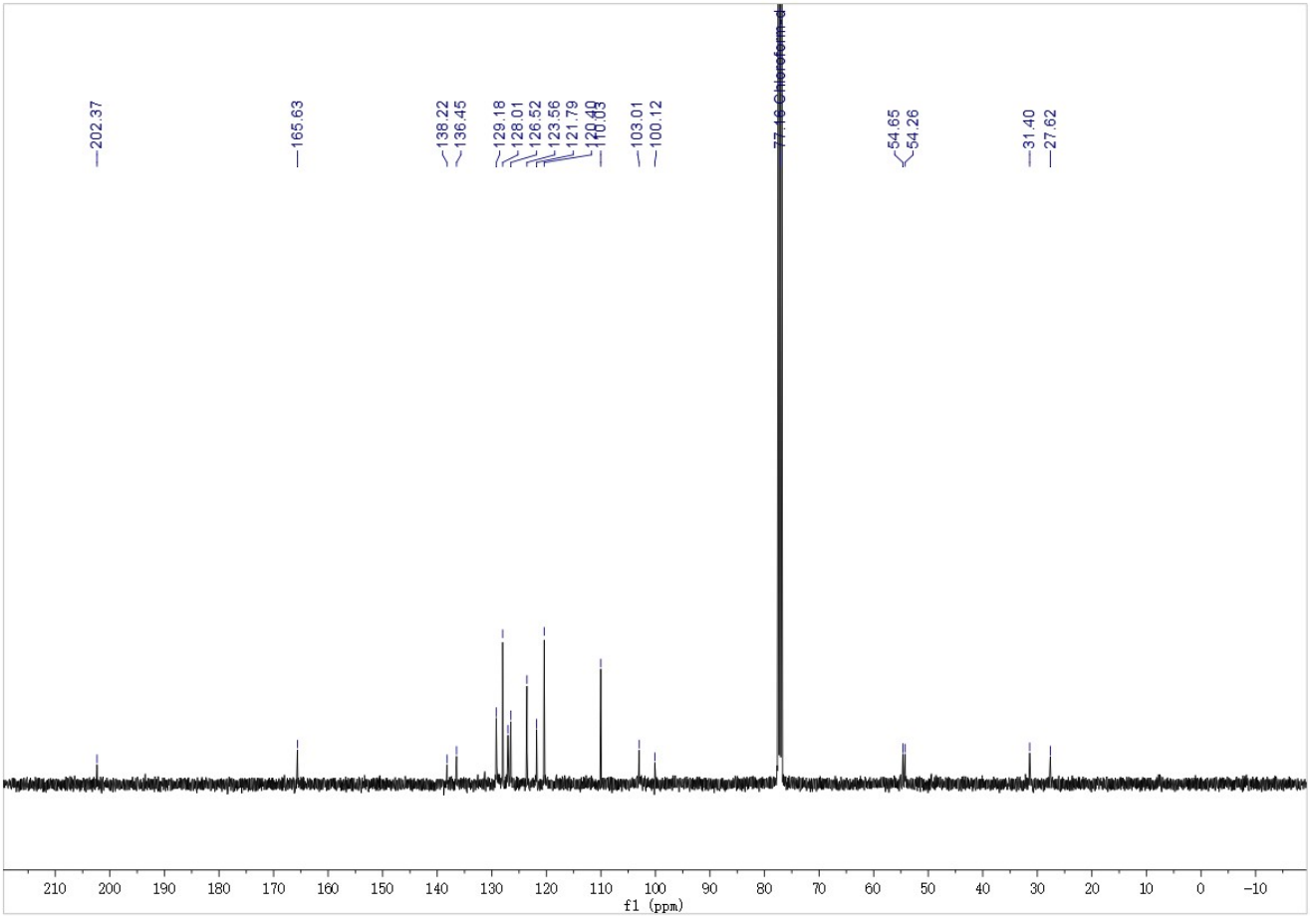

7.65
7.63
7.29
7.28
7.26
7.24
7.23
7.22
7.21
7.20
7.19
7.17
7.08
7.06
7.04
7.02
4.65
4.46
4.12
3.82
2.07
1.83
O
N
Bn
O
I
2.00
7.08
2.02
2.05
3.21
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

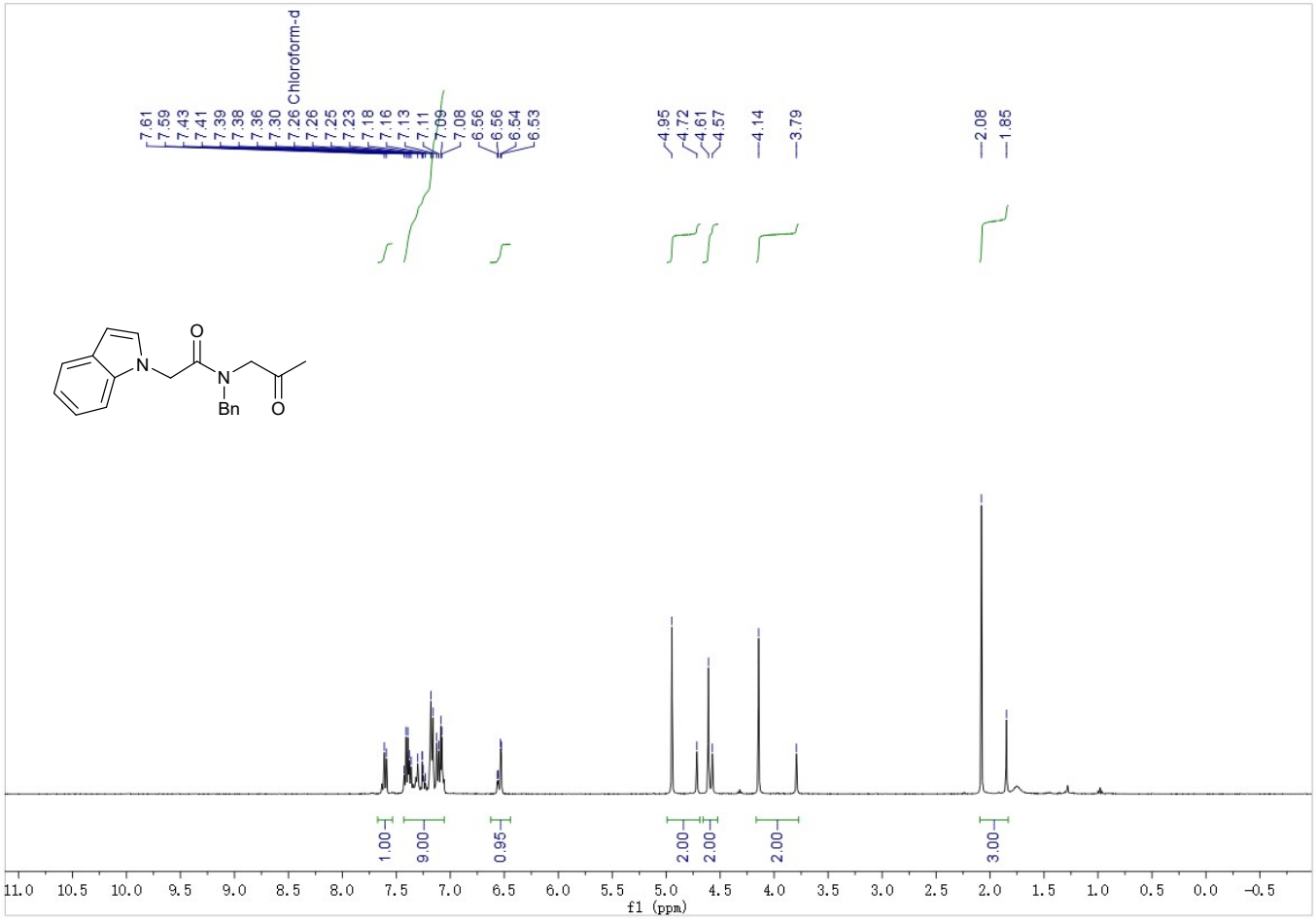

202.80
202.32
171.53
137.73
135.96
134.70
129.07
128.87
128.68
128.56
128.18
128.00
126.88
96.33
96.09
57.52
54.28
53.85
49.19
27.53
27.14
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

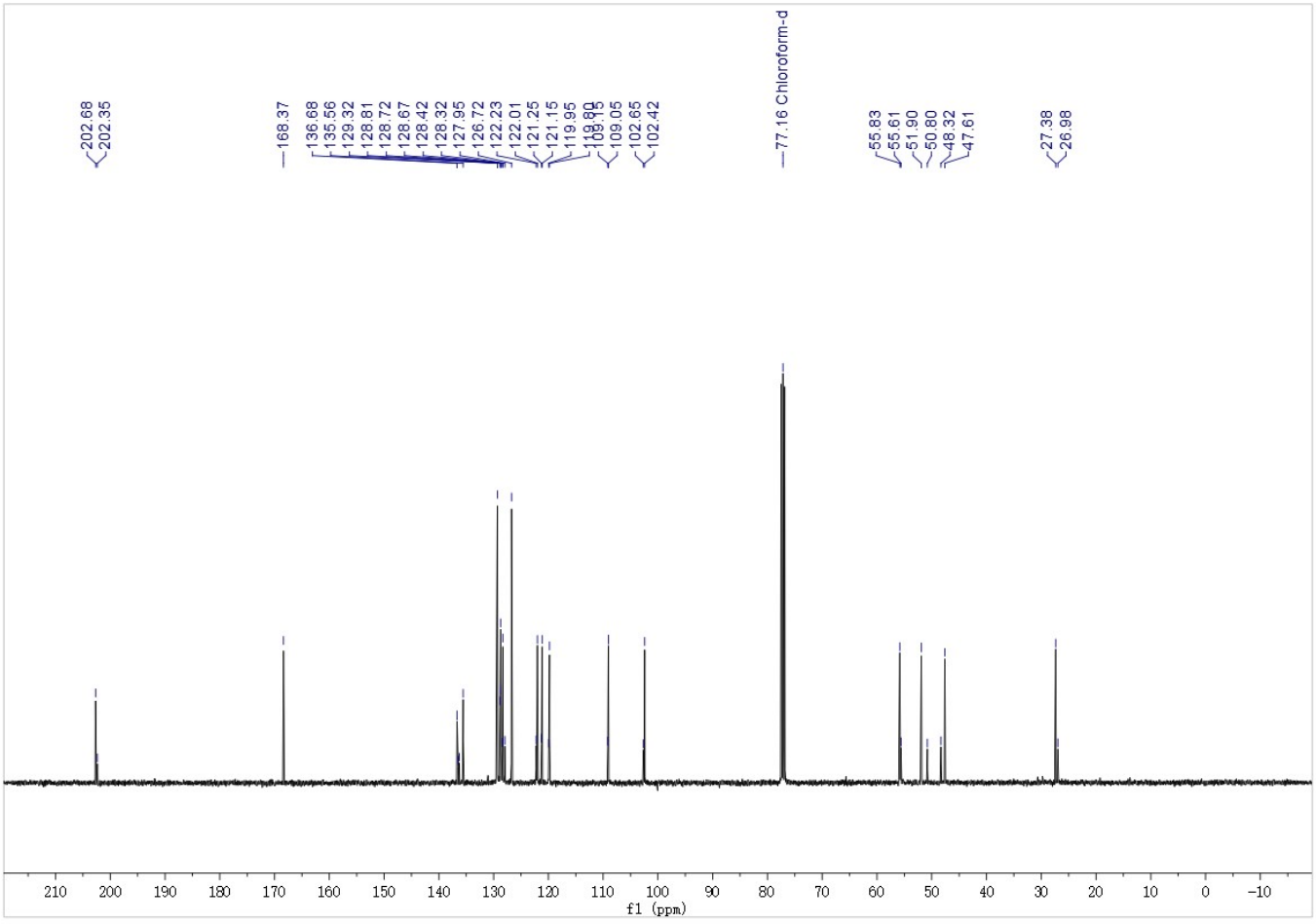

7.70
7.61
7.39
7.37
7.34
7.32
7.29
7.24
7.22
6.58
6.48
4.77
4.72
4.19
4.12
2.16
2.04
O
O
N
Bn
O
0.97
6.03
0.96
2.03
2.00
3.27
f1 (ppm)

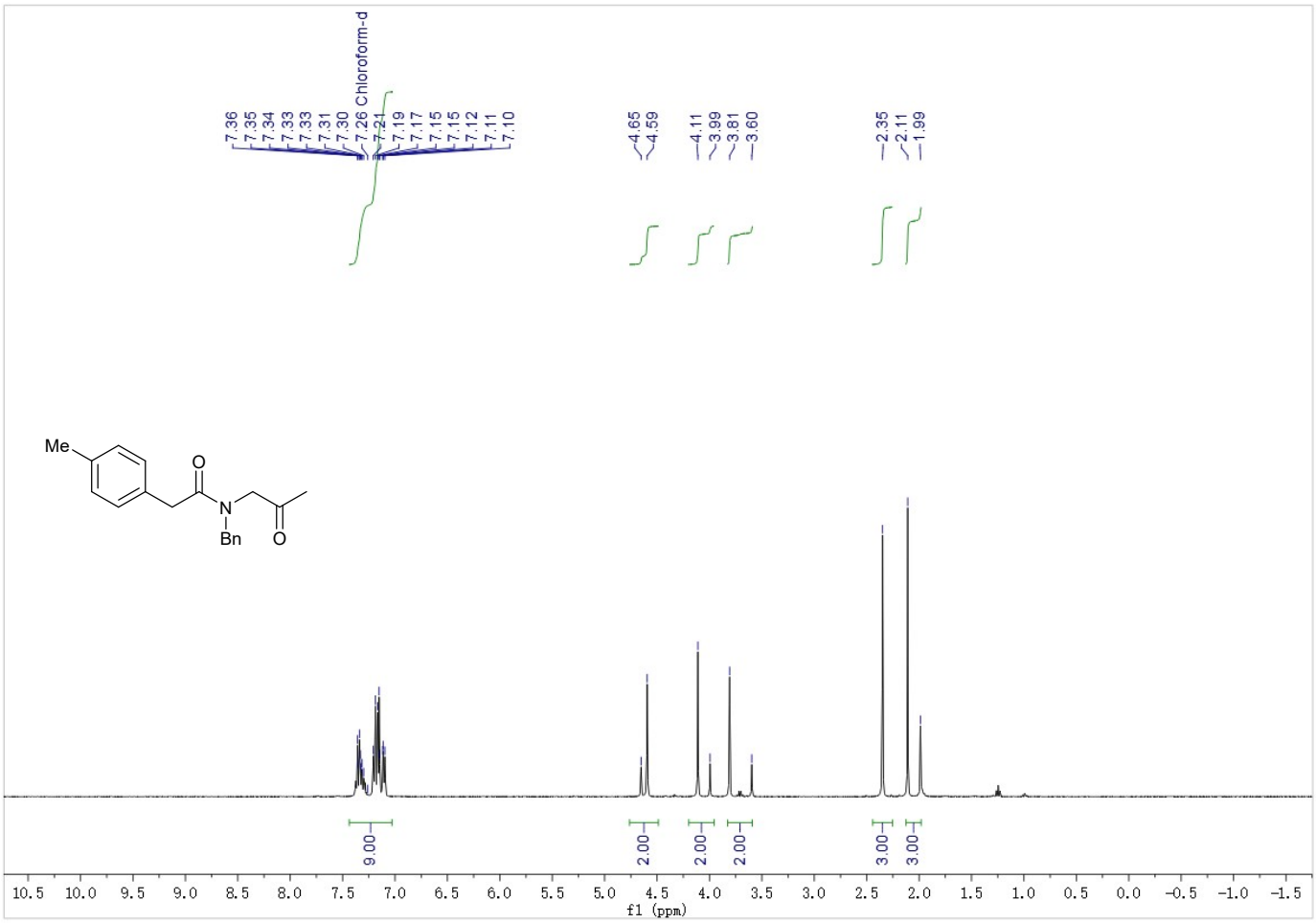

202.71
165.63
144.16
143.11
136.32
129.16
128.81
128.55
127.88
126.45
120.37
110.28
77.49
77.17
76.85
57.55
55.22
53.55
49.62
27.43
f1 (ppm)

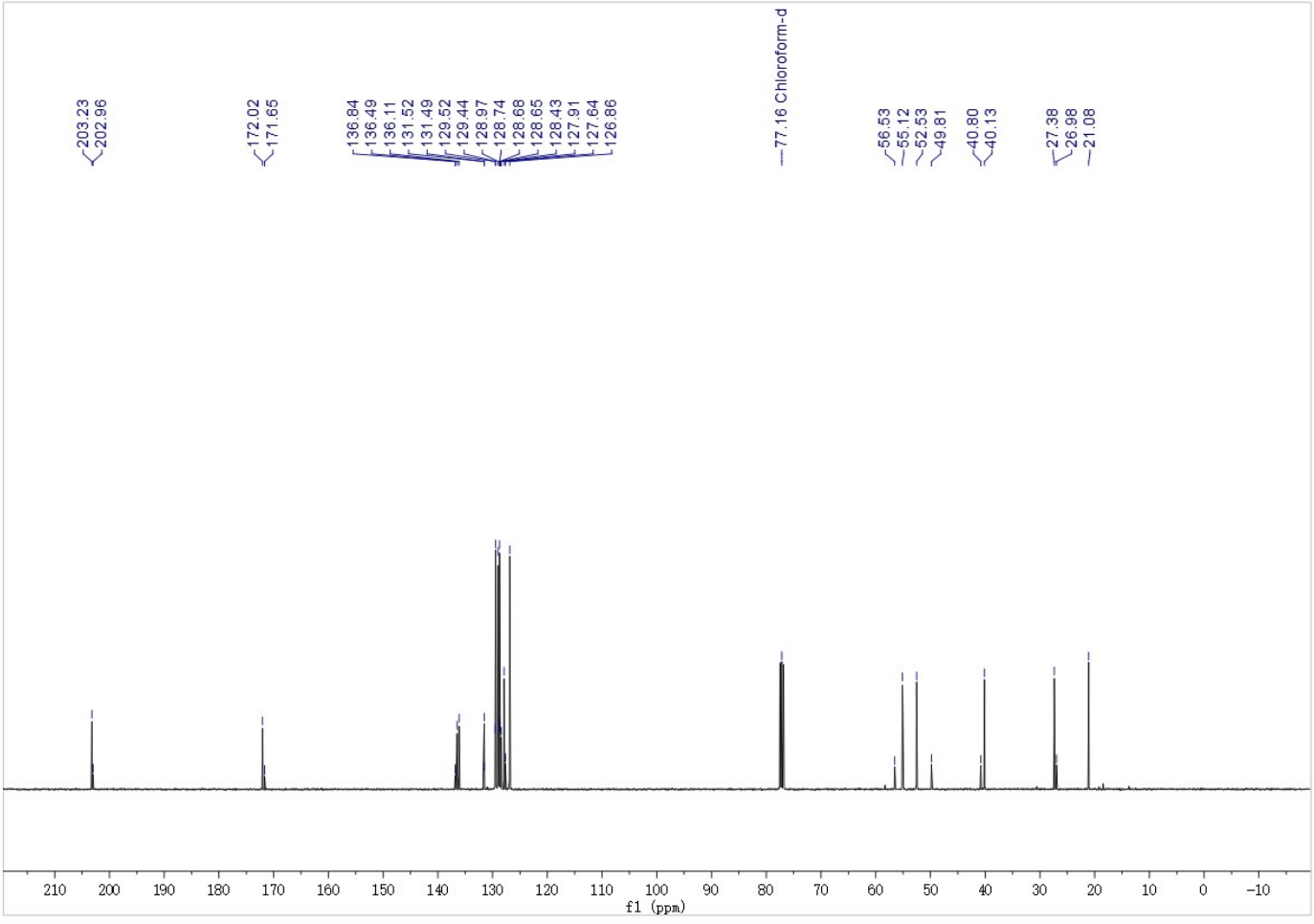

7.56
7.54
7.52
7.42
7.40
7.38
7.37
7.35
7.34
7.32
7.31
7.31
7.29
7.29
7.29
7.27
7.27
7.26
7.26 Chloroform-d
7.13
7.12
7.10
6.68
6.52
4.82
4.26
3.90
2.20
1.94
1.57
O
N
Bn
O
N
1.00
6.00
1.00
1.00
2.00
2.00
3.00
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)

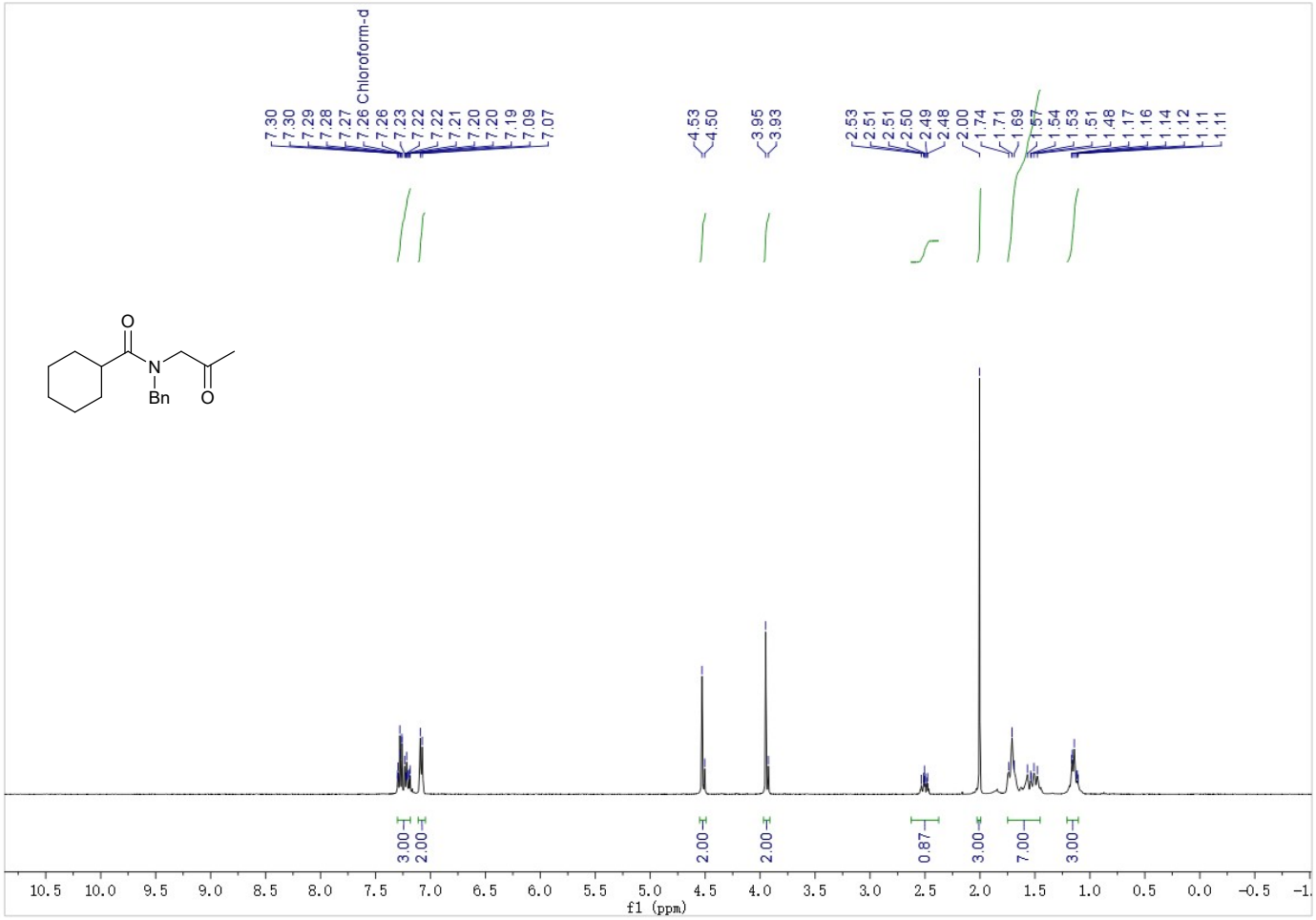

202.37
165.63
138.22
136.45
129.18
128.01
126.52
123.56
121.79
120.49
110.03
103.01
100.12
77.16 Chloroform-d
54.65
54.26
31.40
27.62
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

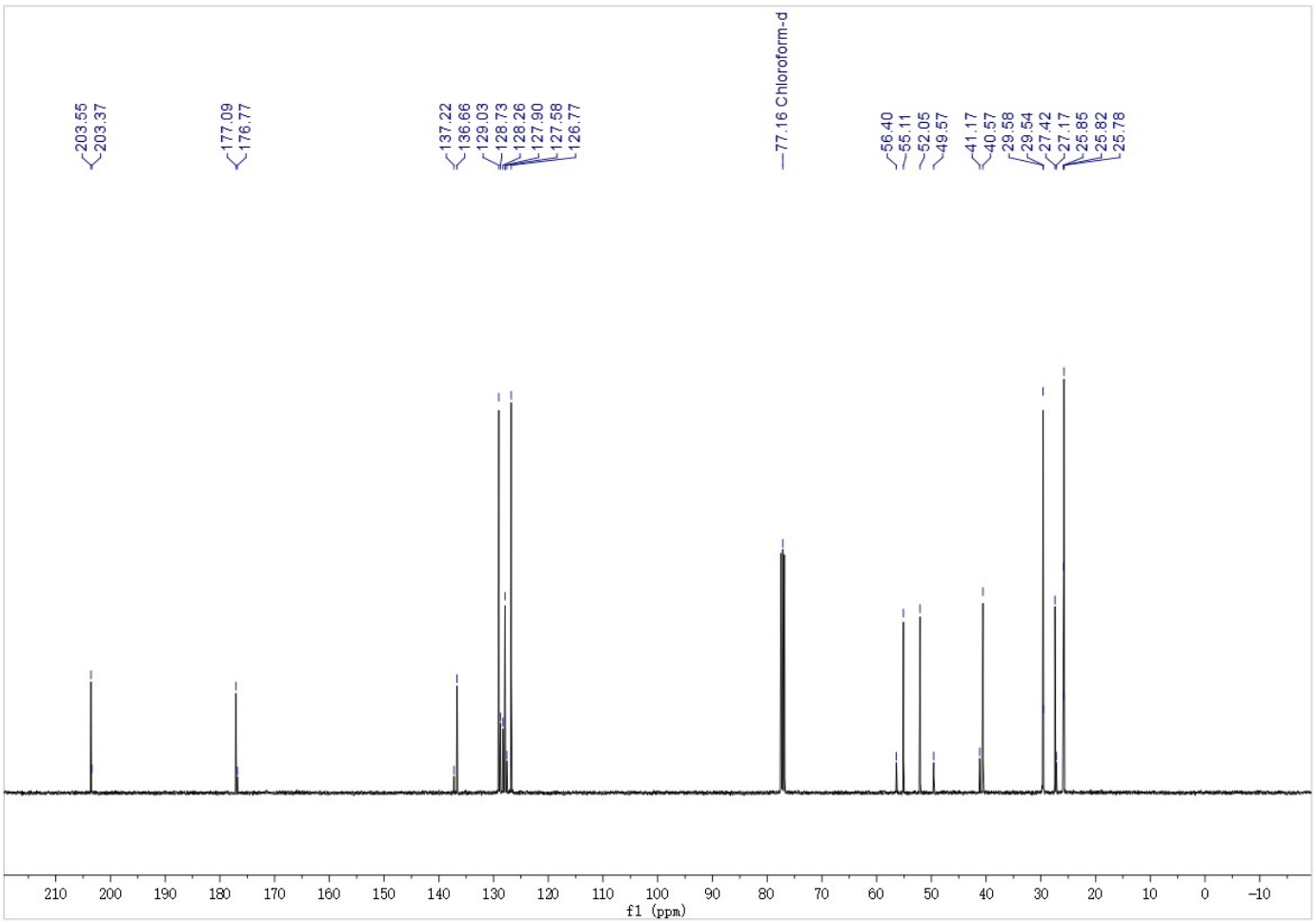

7.61
7.59
7.43
7.41
7.39
7.38
7.36
7.30
7.26 Chloroform-d
7.26
7.25
7.23
7.18
7.16
7.13
7.11
7.09
7.08
6.56
6.56
6.54
6.53
4.95
4.72
4.61
4.57
4.14
3.79
2.08
1.85
O
N
N
Bn
O
1.00
9.00
0.95
2.00
2.00
2.00
3.00
f1 (ppm)

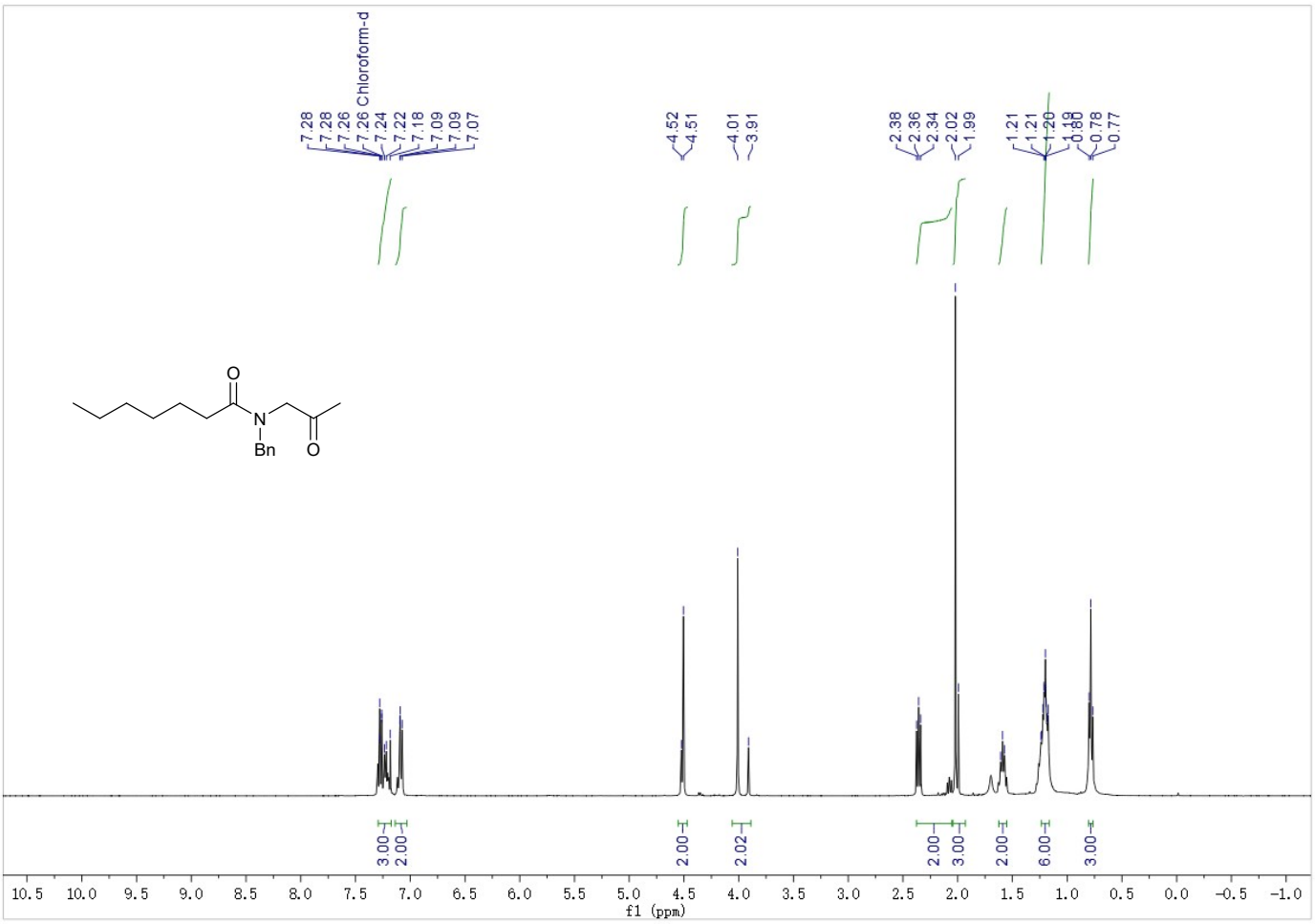

202.68
202.35
168.37
136.68
135.56
129.32
128.81
128.72
128.67
128.42
128.32
127.95
126.72
122.23
122.01
121.25
121.15
119.95
109.80
109.15
109.05
102.65
102.42
77.16 Chloroform-d
55.83
55.61
51.90
50.80
48.32
47.61
27.38
26.98
f1 (ppm)

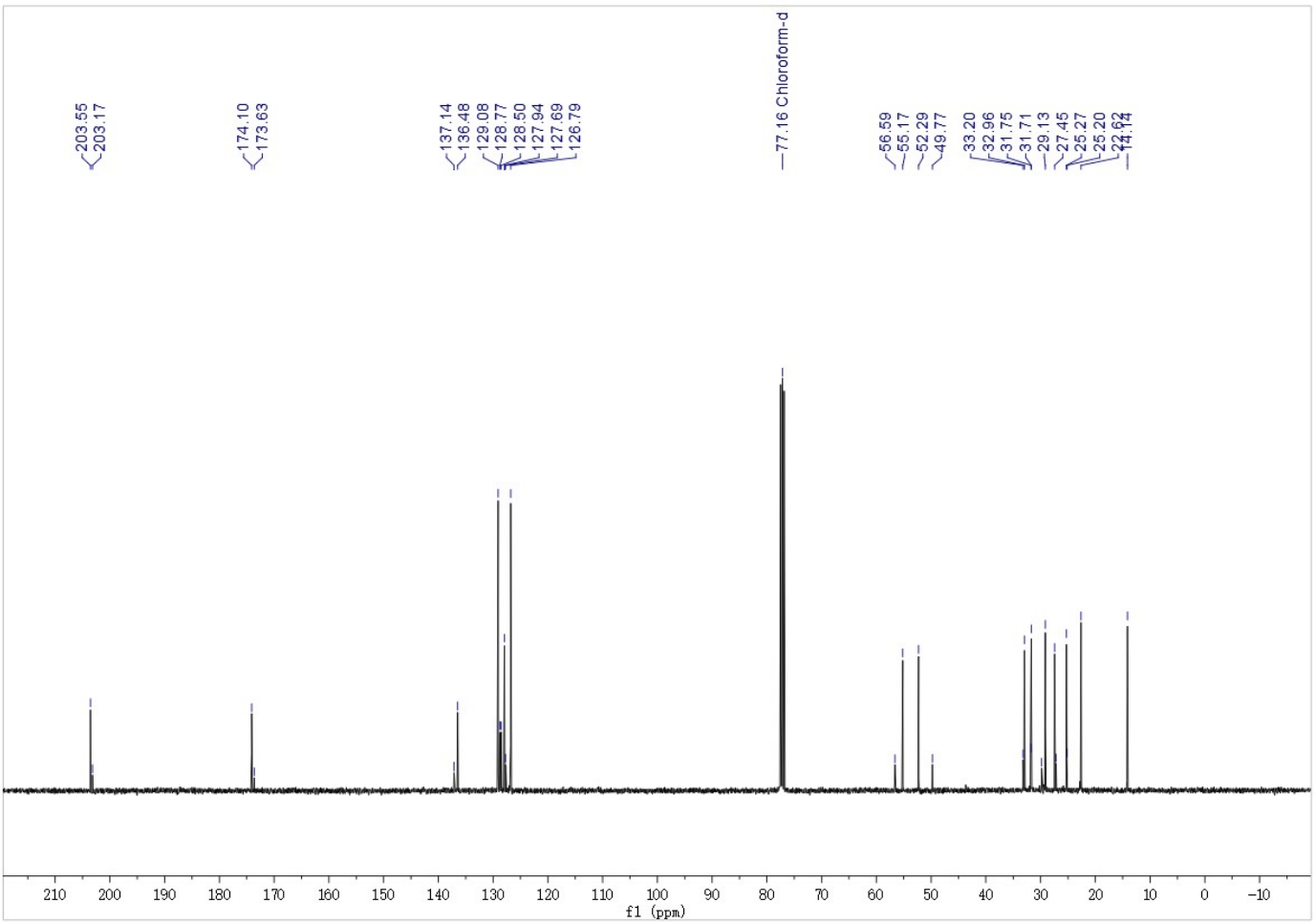

7.36
7.35
7.34
7.33
7.33
7.31
7.30
7.26 Chloroform-d
7.21
7.19
7.17
7.15
7.15
7.12
7.11
7.10
4.65
4.59
4.11
3.99
3.81
3.60
2.35
2.11
1.99
Me
O
N
Bn
O
9.00
2.00
2.00
2.00
3.00
3.00
f1 (ppm)

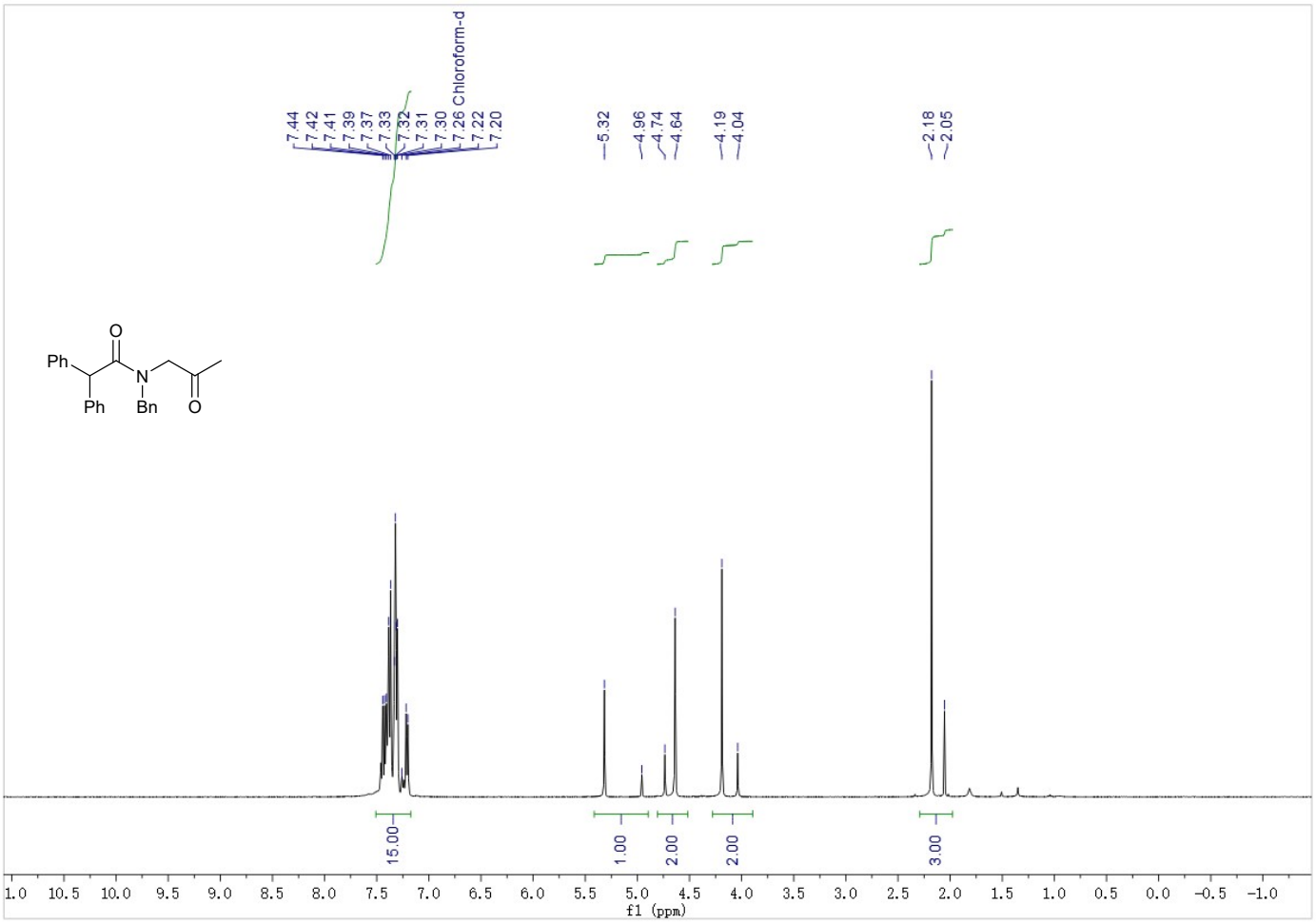

203.23
202.96
172.02
171.65
136.84
136.49
136.11
131.52
131.49
129.52
129.44
128.97
128.74
128.68
128.65
128.43
127.91
127.64
126.86
77.16 Chloroform-d
56.53
55.12
52.53
49.81
40.80
40.13
27.38
26.98
21.08
f1 (ppm)

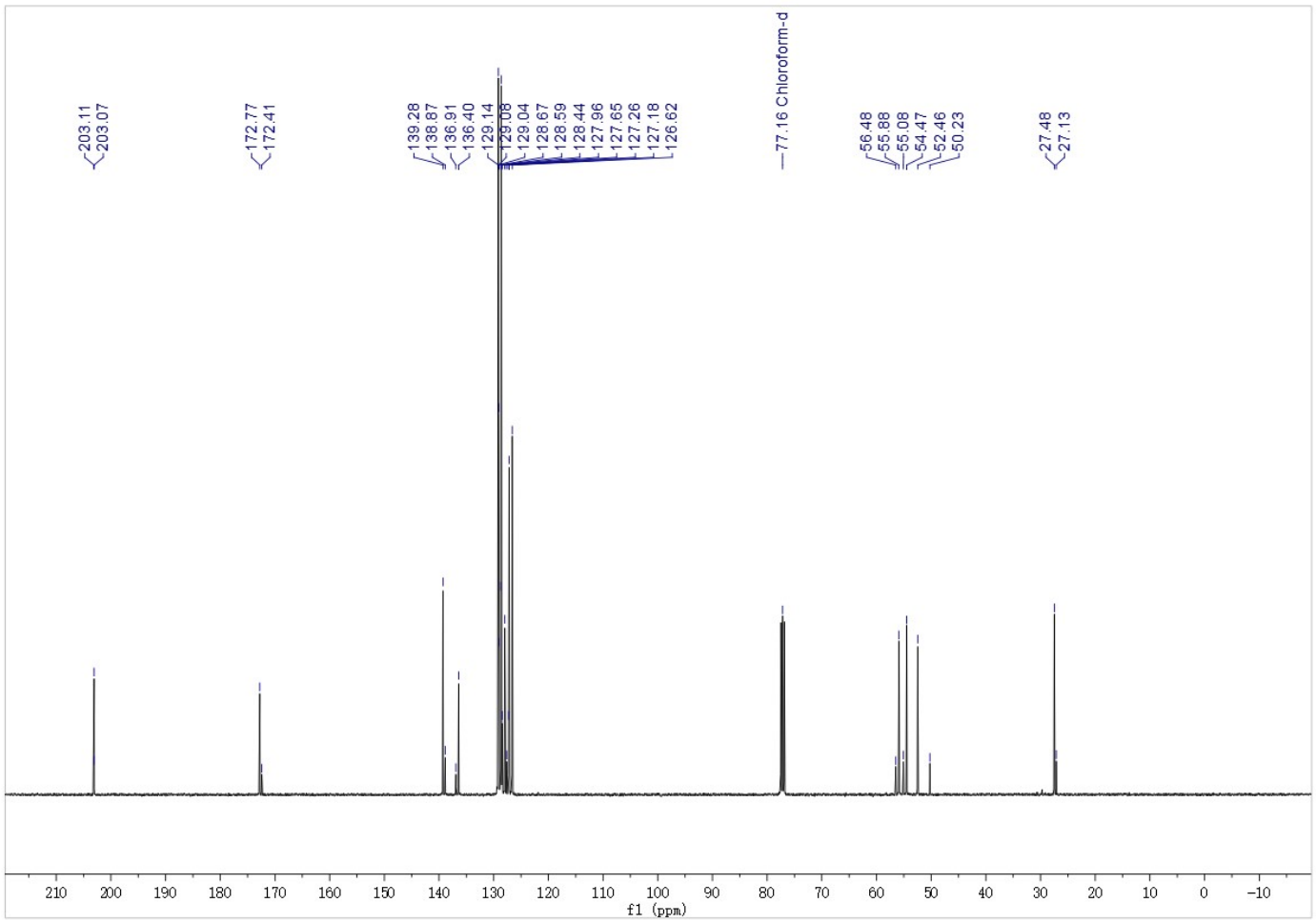

7.30
7.30
7.29
7.28
7.27
7.26 Chloroform-d
7.26
7.23
7.22
7.22
7.21
7.20
7.20
7.19
7.09
7.07
4.53
4.50
3.95
3.93
2.53
2.51
2.51
2.50
2.49
2.48
2.00
1.74
1.71
1.69
1.57
1.54
1.53
1.51
1.48
1.17
1.16
1.14
1.12
1.11
1.11
O
N
Bn
O
3.00
2.00
2.00
2.00
0.87
3.00
7.00
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

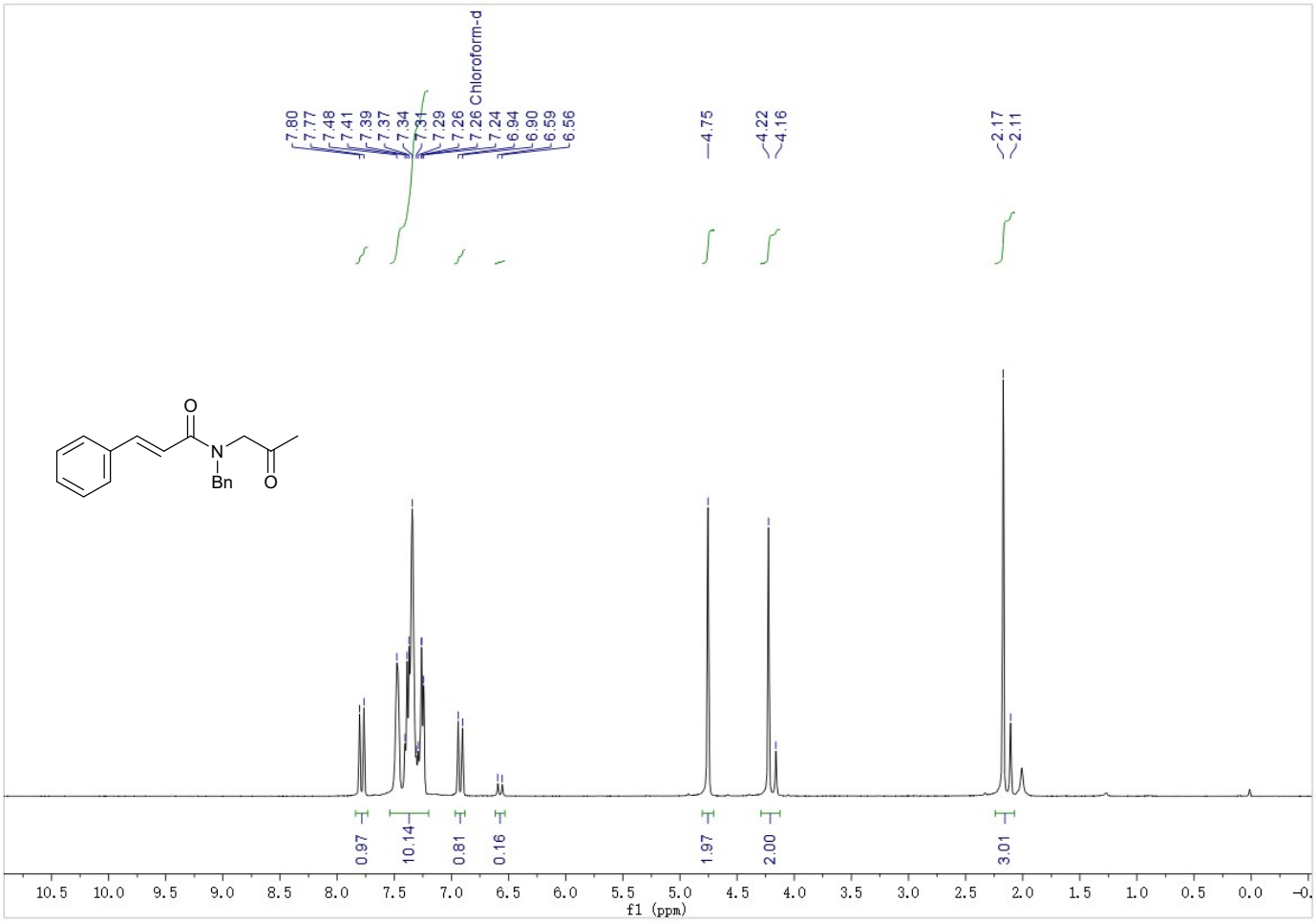

203.55
203.37
177.09
176.77
137.22
136.66
129.03
128.73
128.26
127.90
127.58
126.77
77.16 Chloroform-d
56.40
55.11
52.05
49.57
41.17
40.57
29.58
29.54
27.42
27.17
25.85
25.82
25.78
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

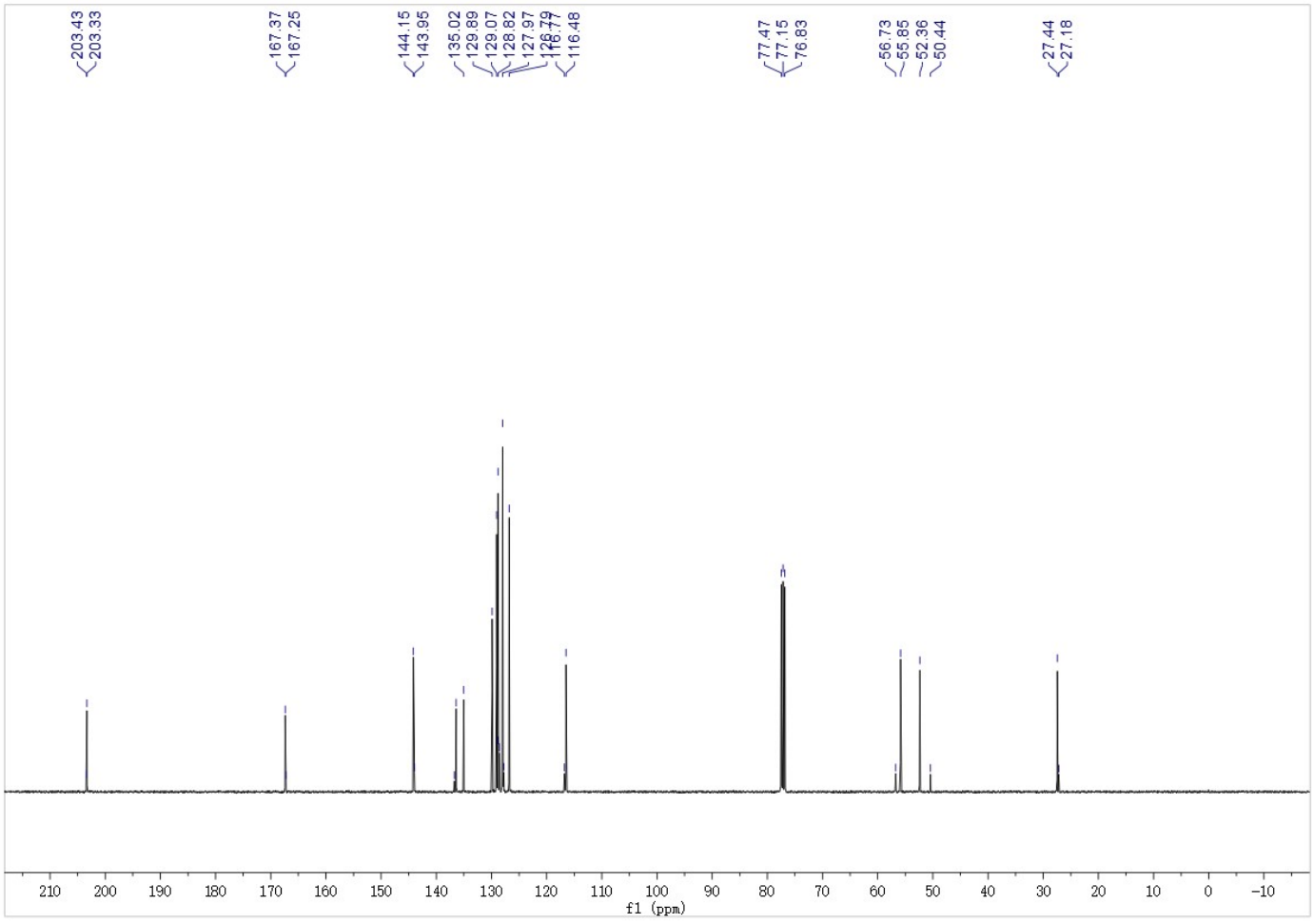

7.28
7.28
7.26
7.26 Chloroform-d
7.24
7.22
7.18
7.09
7.09
7.07
4.52
4.51
4.01
3.91
2.38
2.36
2.34
2.02
1.99
1.21
1.21
1.20
0.80
0.78
0.77
O
N
Bn
O
3.00
2.00
2.00
2.02
2.00
3.00
2.00
6.00
3.00
f1 (ppm)

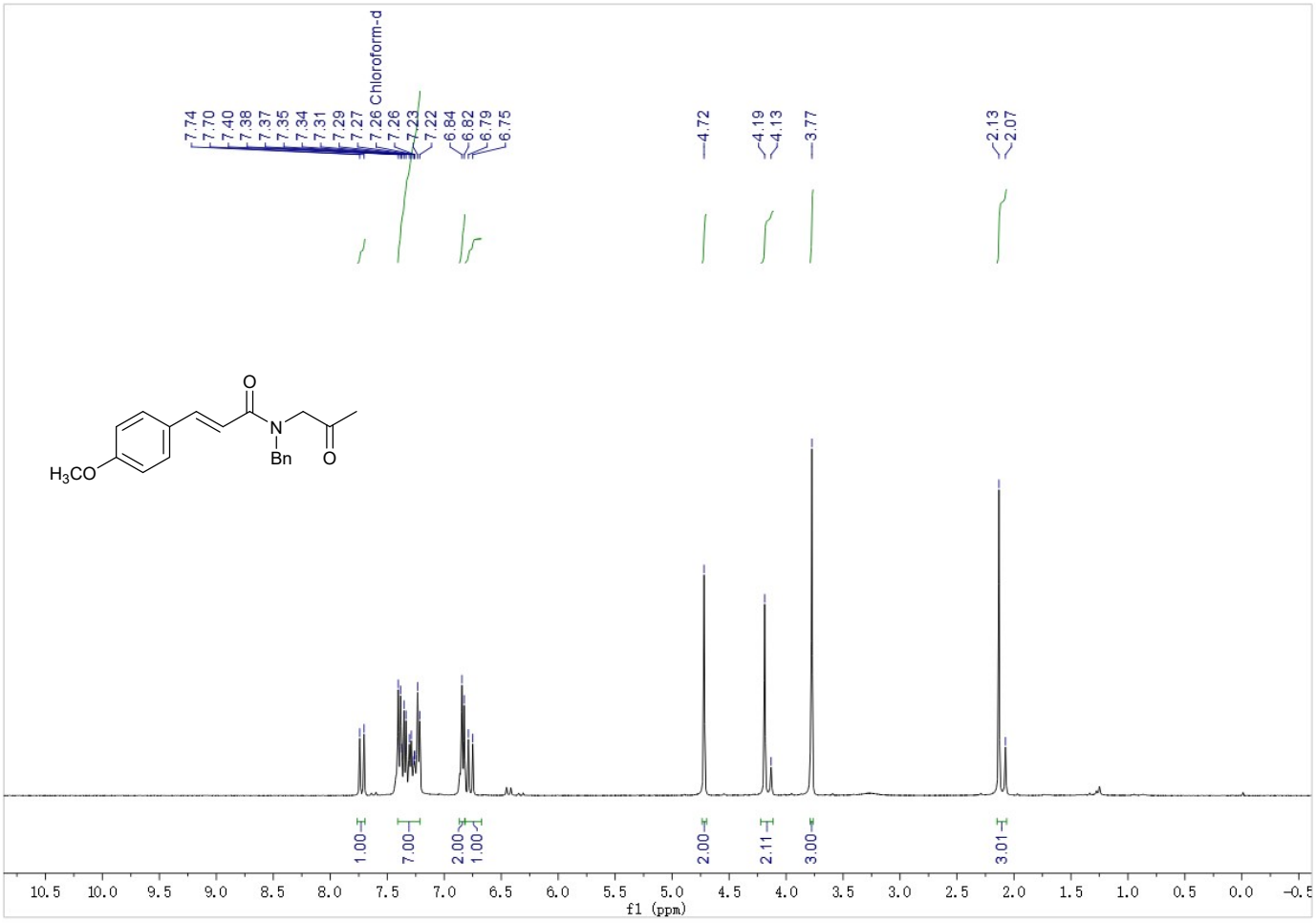

203.55
203.17
174.10
173.63
137.14
136.48
129.08
128.77
128.50
127.94
127.69
126.79
77.16 Chloroform-d
56.59
55.17
52.29
49.77
33.20
32.96
31.75
31.71
29.13
27.45
25.27
25.20
22.62
14.14
f1 (ppm)

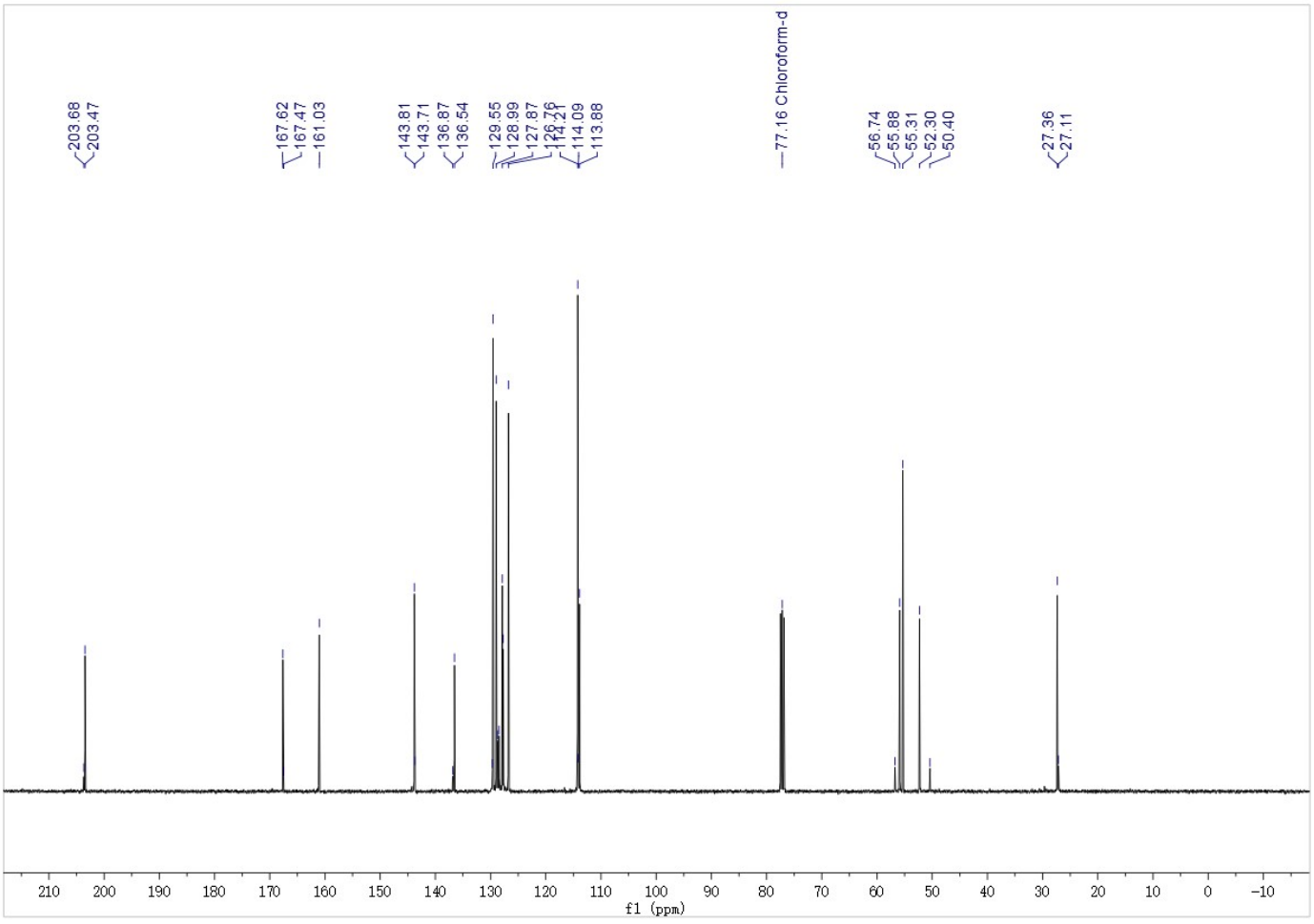

7.44
7.42
7.41
7.39
7.37
7.33
7.32
7.31
7.30
7.26 Chloroform-d
7.22
7.20
5.32
4.96
4.74
4.64
4.19
4.04
2.18
2.05
Ph
O
N
Ph
Bn
O
15.00
1.00
2.00
2.00
3.00
f1 (ppm)

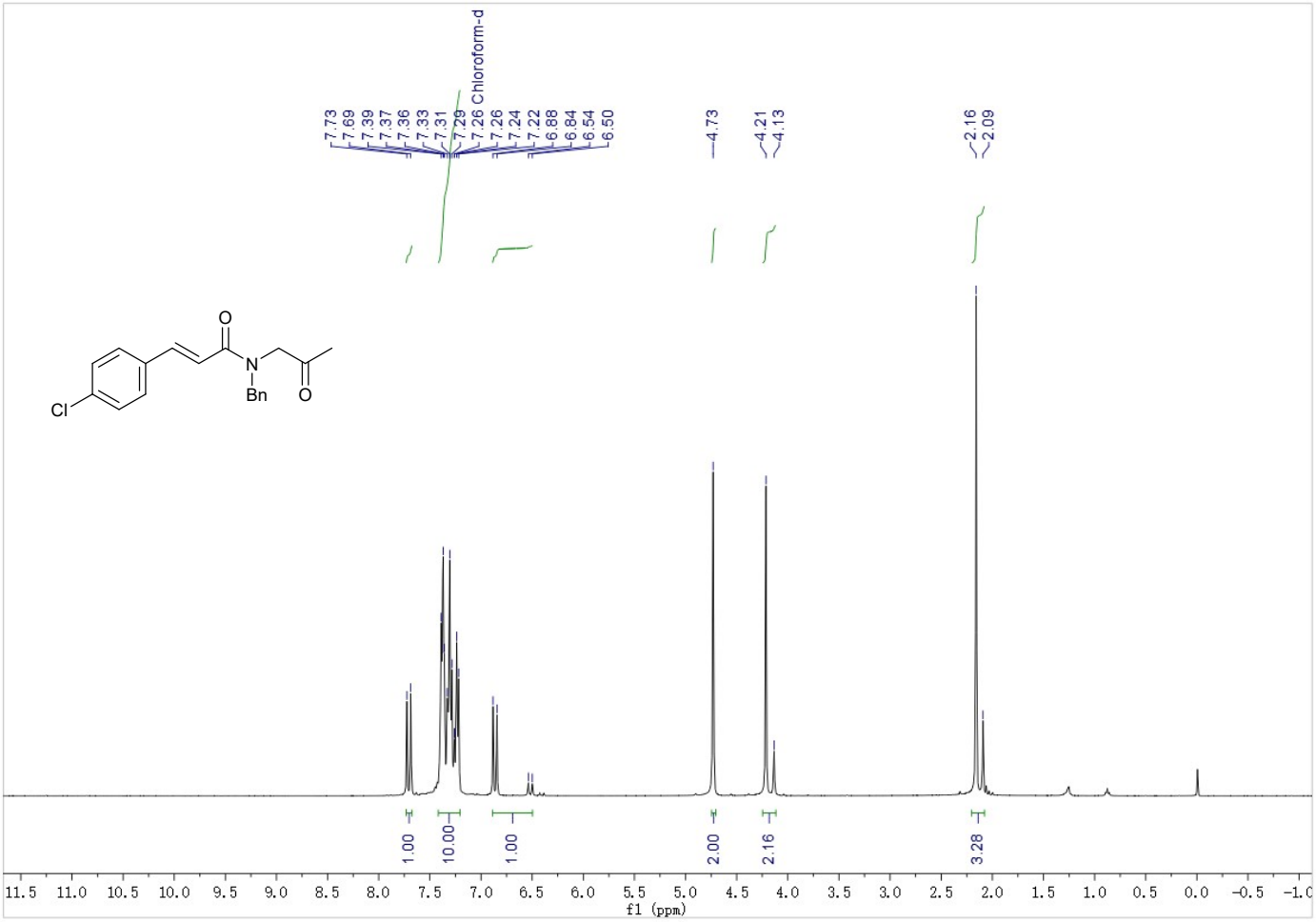

203.11
203.07
172.77
172.41
139.28
138.87
136.91
136.40
129.14
129.08
129.04
128.67
128.59
128.44
127.96
127.65
127.26
127.18
126.62
77.16 Chloroform-d
56.48
55.88
55.08
54.47
52.46
50.23
27.48
27.13
f1 (ppm)

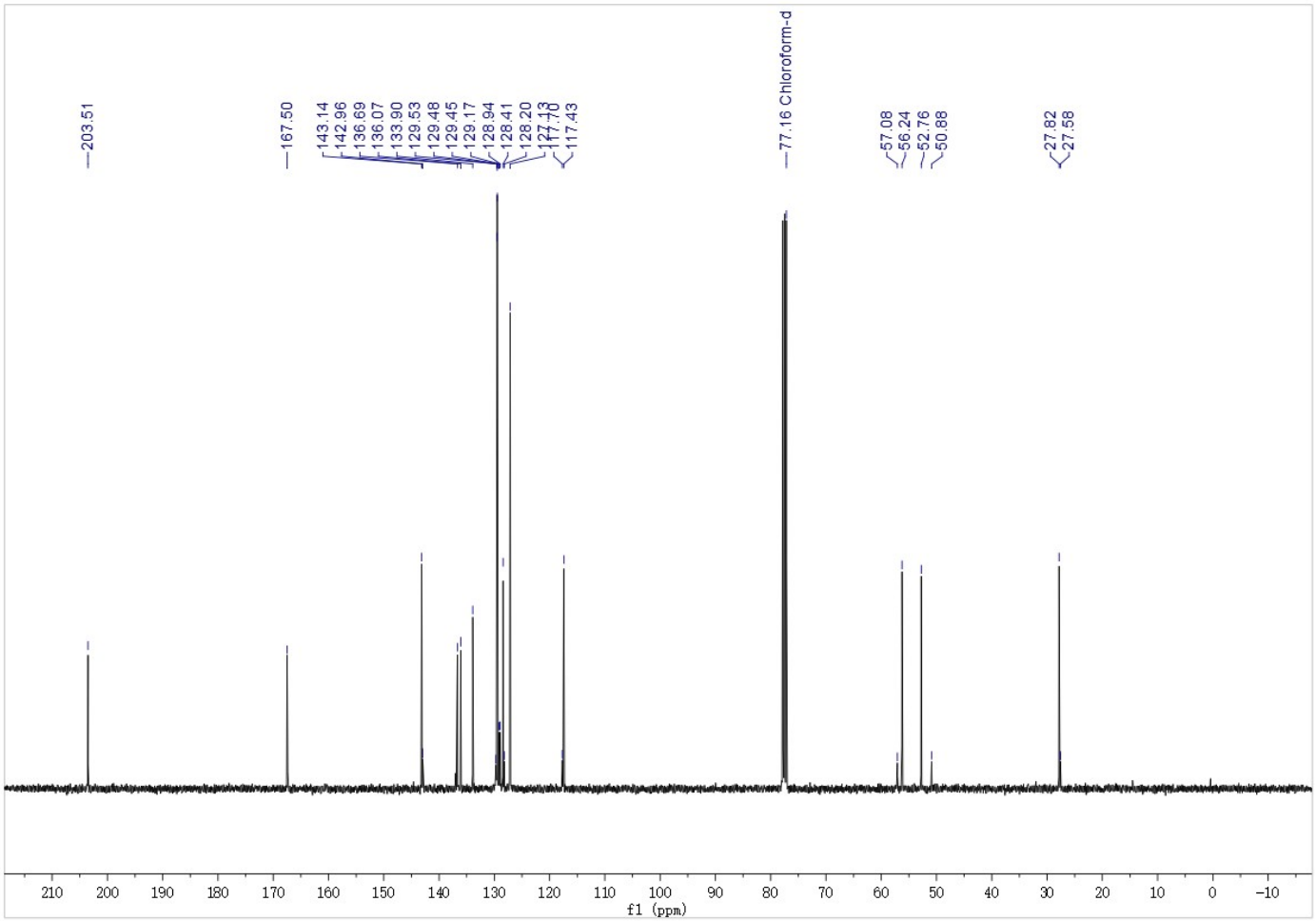

7.80
7.77
7.48
7.41
7.39
7.37
7.34
7.31
7.29
7.26
Chloroform-d
7.26
7.24
6.94
6.90
6.59
6.56
4.75
4.22
4.16
2.17
2.11
O
N
Bn
O
0.97
10.14
0.81
0.16
1.97
2.00
3.01
f1 (ppm)

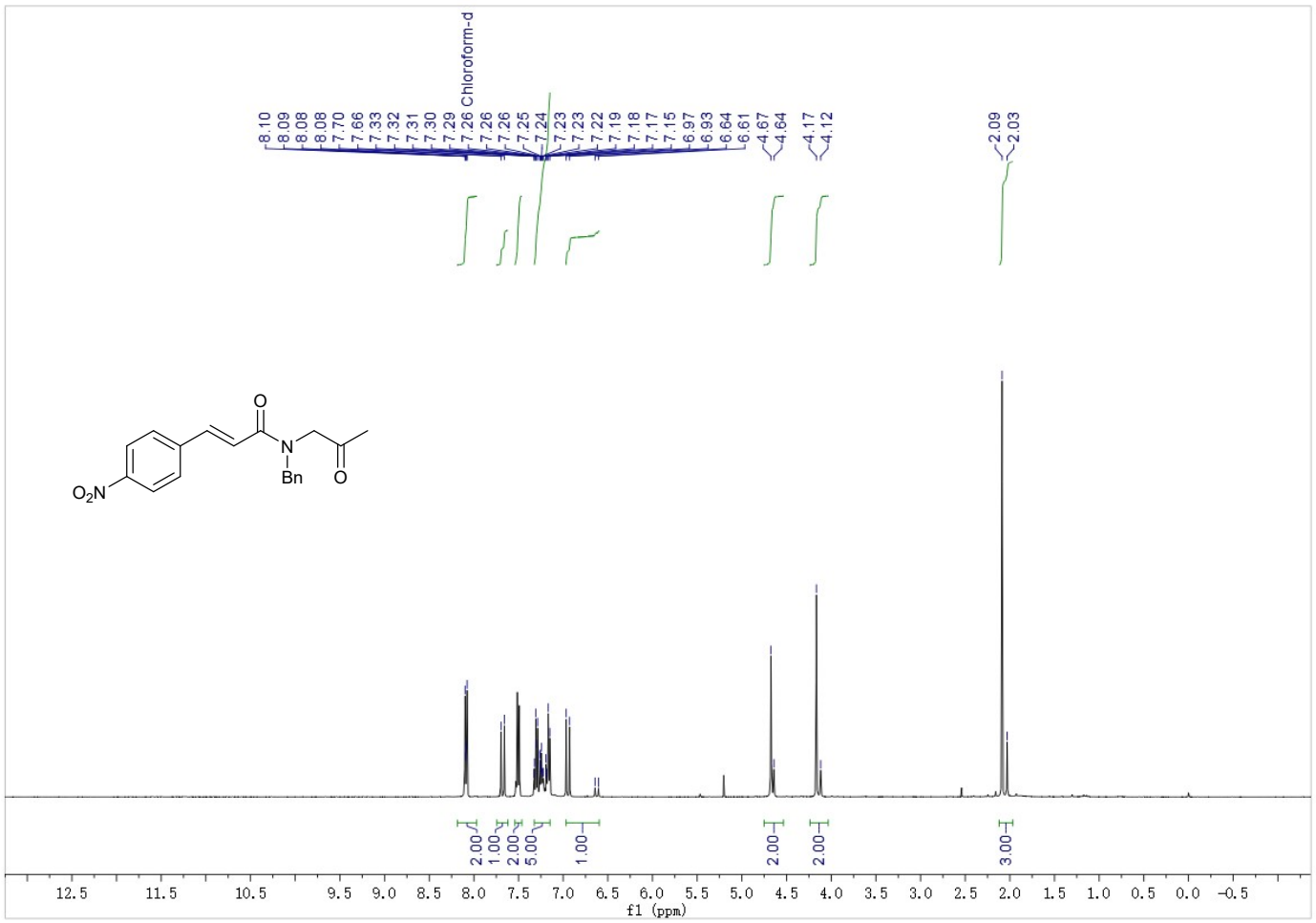

203.43
203.33
167.37
167.25
144.15
143.95
135.02
129.89
129.07
128.82
127.97
116.48
77.47
77.15
76.83
56.73
55.85
52.36
50.44
27.44
27.18
f1 (ppm)

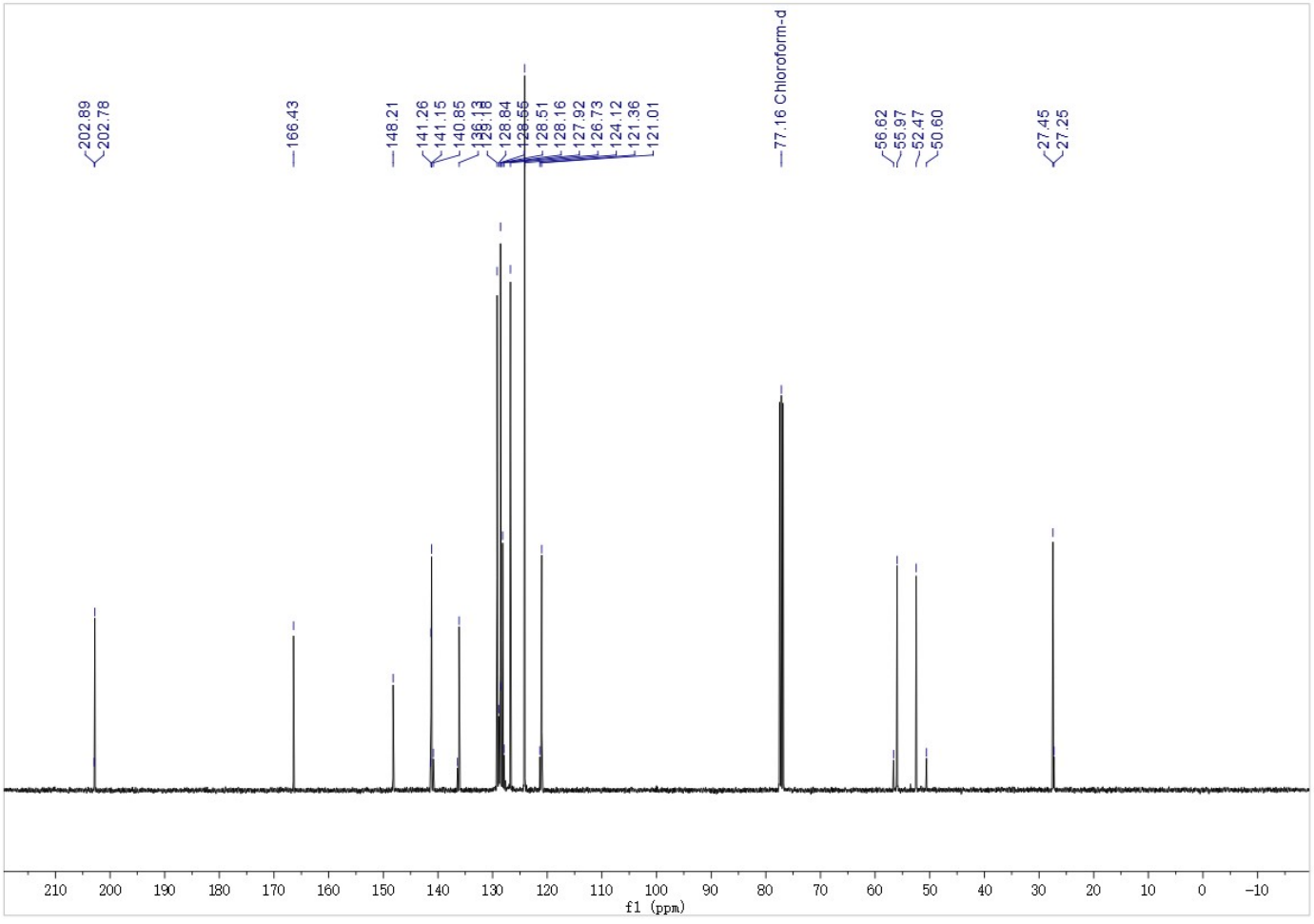

7.74
7.70
7.40
7.38
7.37
7.35
7.34
7.31
7.29
7.27
7.26 Chloroform-d
7.26
7.23
7.22
6.84
6.82
6.79
6.75
4.72
4.19
4.13
3.77
2.13
2.07
O
N
Bn
O
H3CO
1.00
7.00
2.00
1.00
2.00
2.11
3.00
3.01
f1 (ppm)

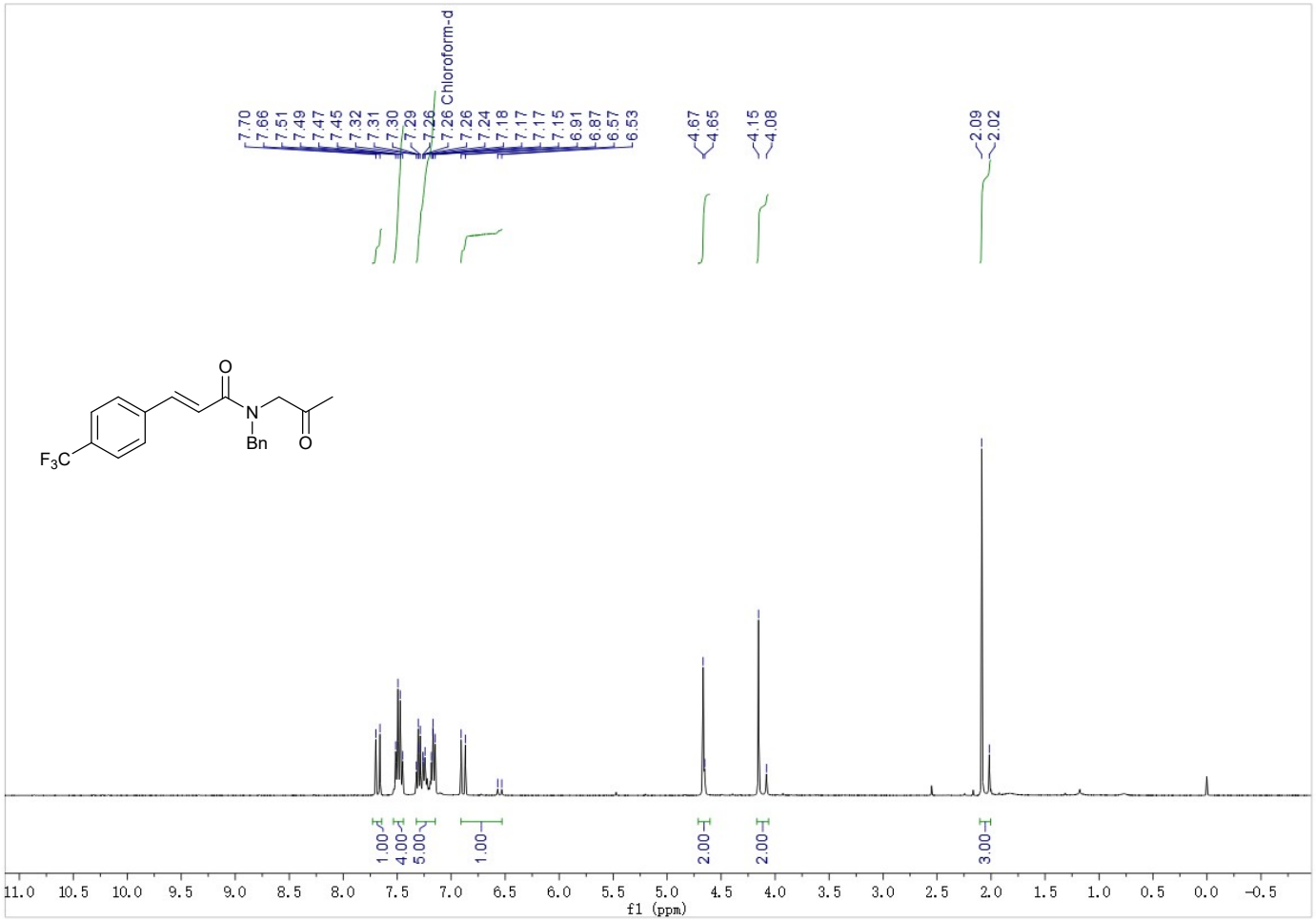

203.68
203.47
167.62
167.47
161.03
143.81
143.71
136.87
136.54
129.55
128.99
127.87
126.76
114.21
114.09
113.88
77.16 Chloroform-d
56.74
55.88
55.31
52.30
50.40
27.36
27.11
f1 (ppm)

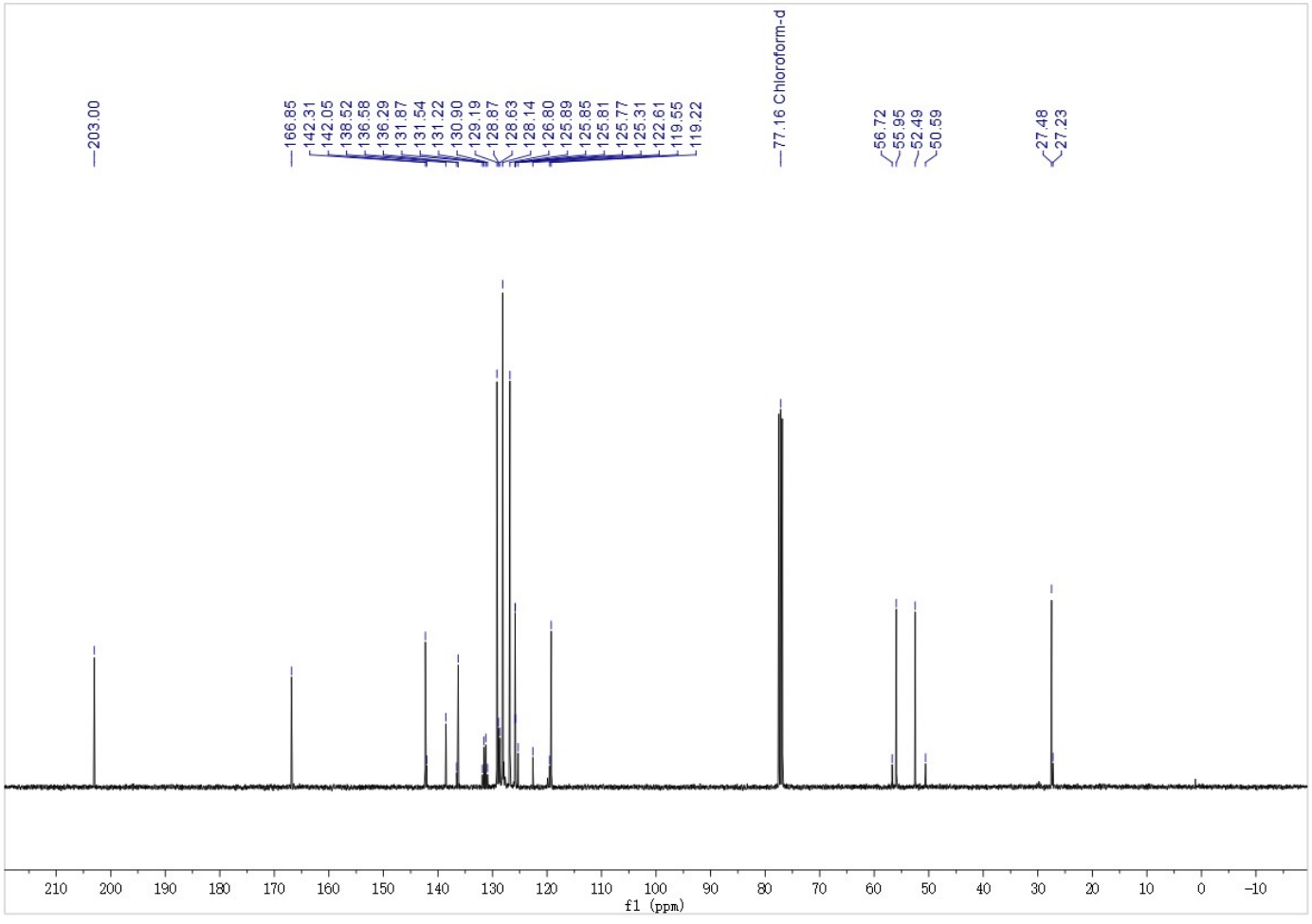

7.73
7.69
7.39
7.37
7.36
7.33
7.31
7.29
7.26 Chloroform-d
7.26
7.24
7.22
6.88
6.84
6.54
6.50
4.73
4.21
4.13
2.16
2.09
O
N
Bn
O
Cl
1.00
10.00
1.00
2.00
2.16
3.28
f1 (ppm)

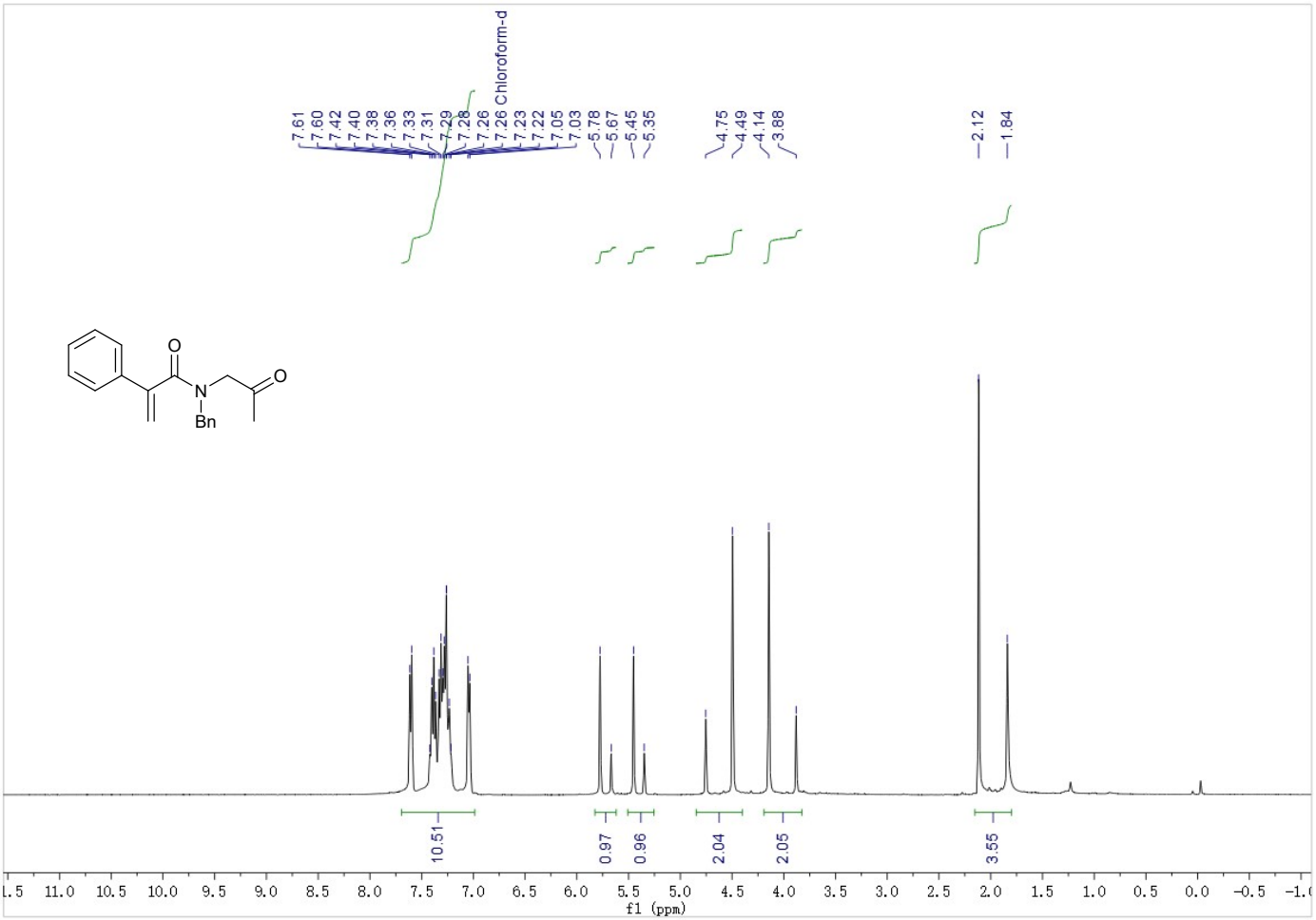

203.51
167.50
143.14
142.96
136.69
136.07
133.90
129.53
129.48
129.45
129.17
128.94
128.41
128.20
127.13
117.70
117.43
77.16 Chloroform-d
57.08
56.24
52.76
50.88
27.82
27.58
f1 (ppm)

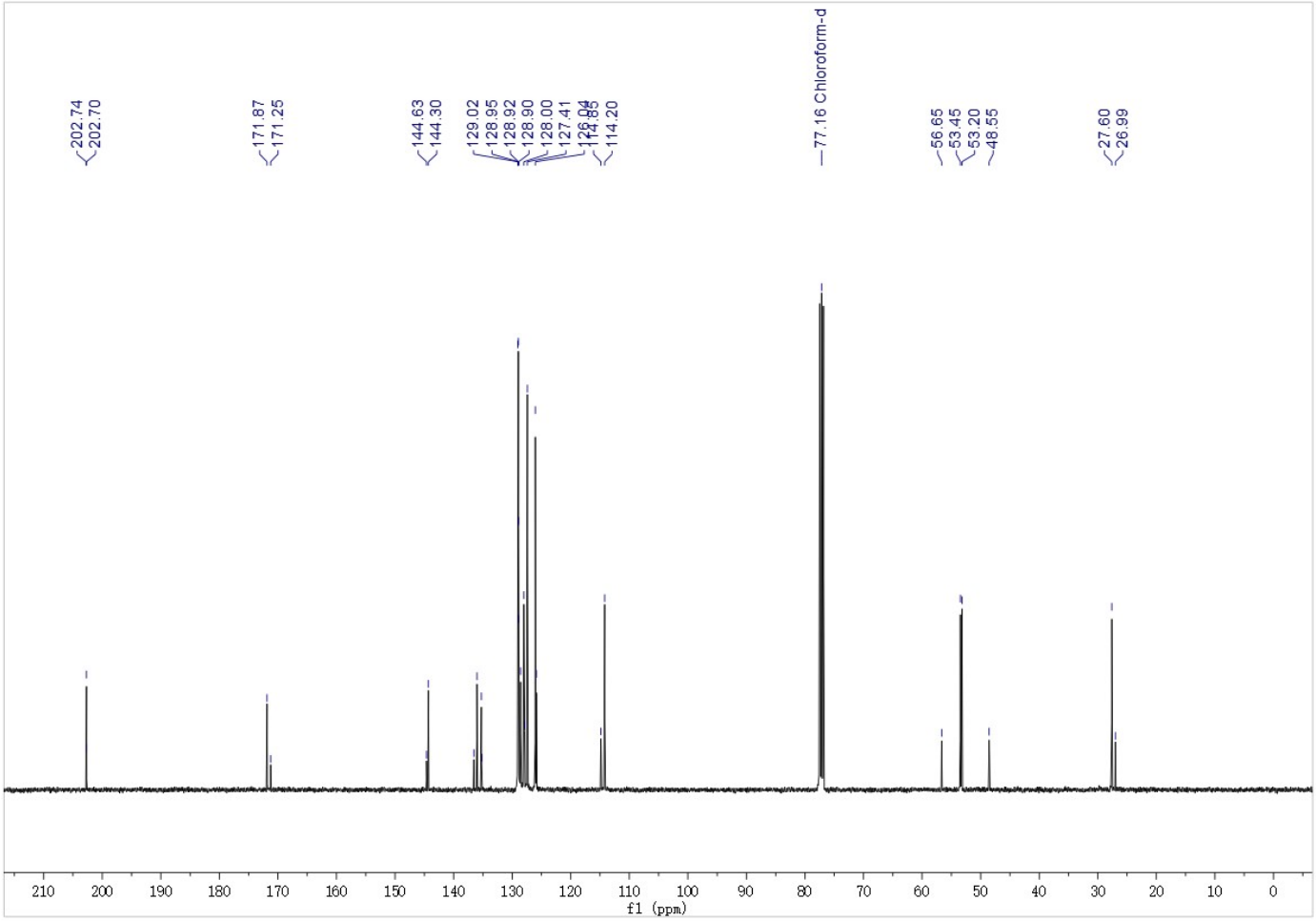

8.10
8.09
8.08
8.08
7.70
7.66
7.33
7.32
7.31
7.30
7.29
7.26 Chloroform-d
7.26
7.26
7.25
7.24
7.23
7.23
7.22
7.19
7.18
7.17
7.15
6.97
6.93
6.64
6.61
4.67
4.64
4.17
4.12
2.09
2.03
O
N
Bn
O
O2N
2.00
1.00
2.00
5.00
1.00
2.00
2.00
3.00
f1 (ppm)

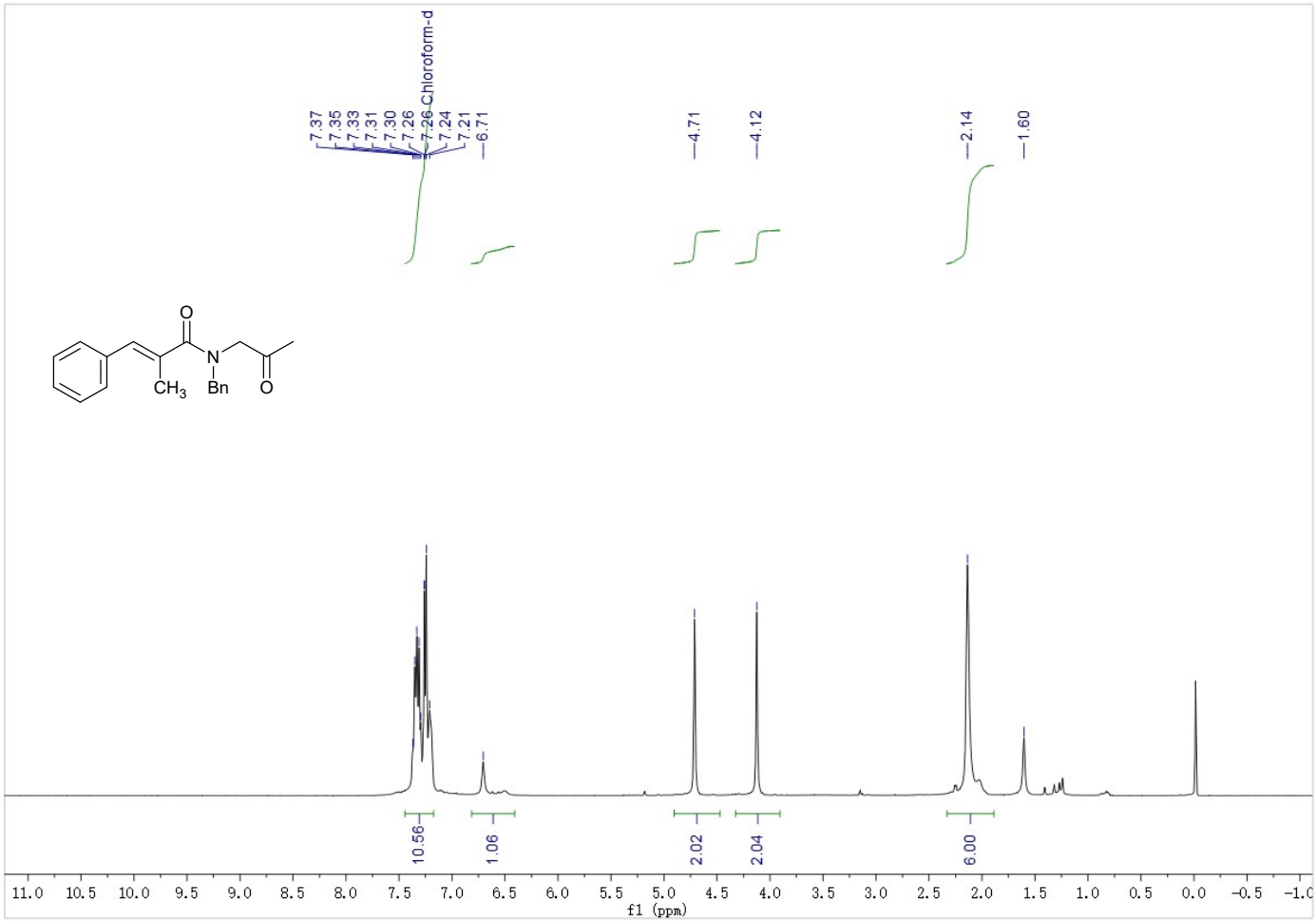

202.89
202.78
166.43
148.21
141.26
141.15
140.85
128.84
128.55
128.51
128.16
127.92
126.73
124.12
121.36
121.01
77.16 Chloroform-d
56.62
55.97
52.47
50.60
27.45
27.25
f1 (ppm)

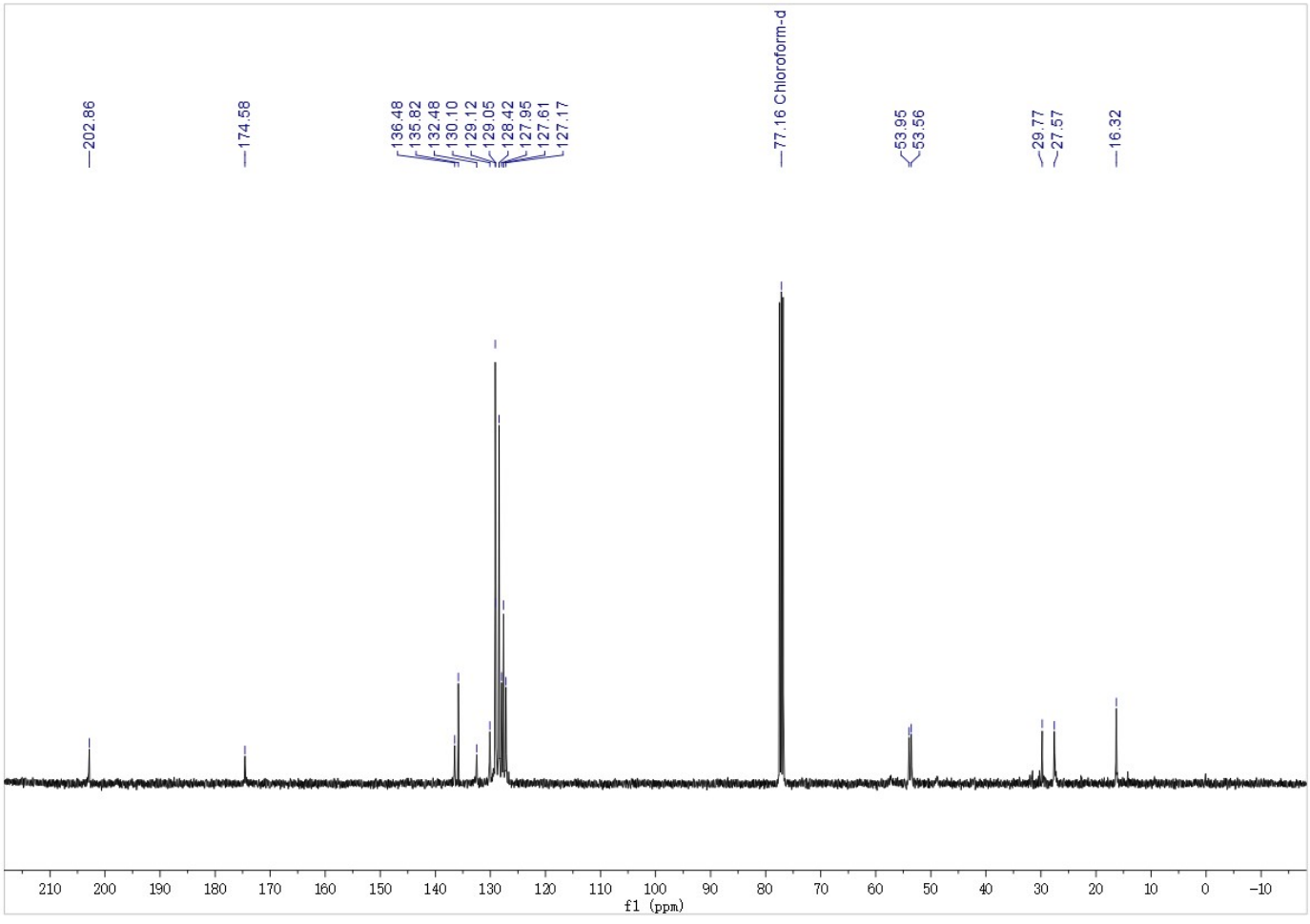

7.70
7.66
7.51
7.49
7.47
7.45
7.32
7.31
7.30
7.29
7.26
7.26 Chloroform-d
7.26
7.24
7.18
7.17
7.17
7.15
6.91
6.87
6.57
6.53
4.67
4.65
4.15
4.08
2.09
2.02
O
N
Bn
O
F3C
1.00
4.00
5.00
1.00
2.00
2.00
3.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

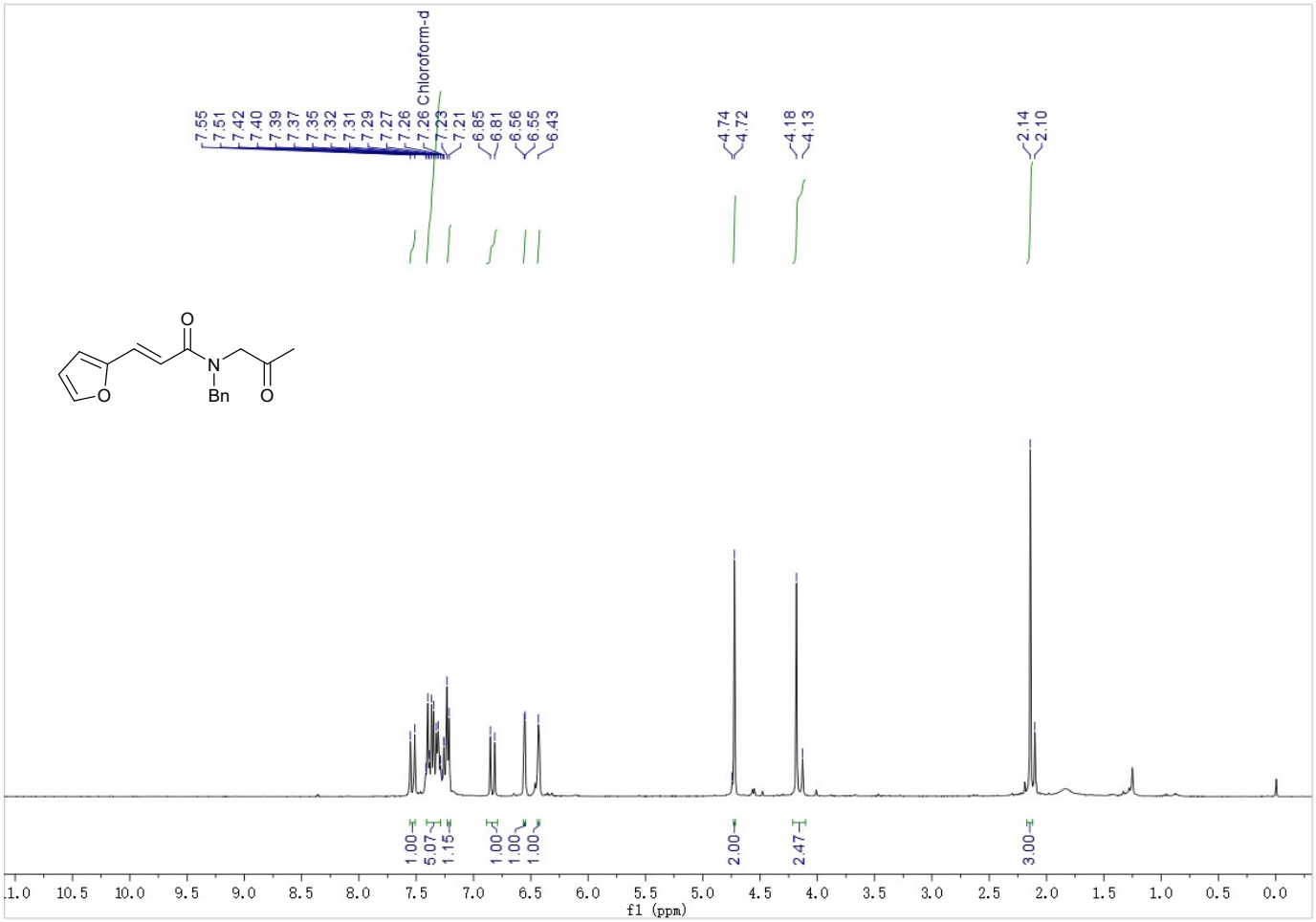

203.00
166.85
142.31
142.05
138.52
136.58
136.29
131.87
131.54
131.22
130.90
129.19
128.87
128.63
128.14
126.80
125.89
125.85
125.81
125.77
125.31
122.61
119.55
119.22
77.16 Chloroform-d
56.72
55.95
52.49
50.59
27.48
27.23
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

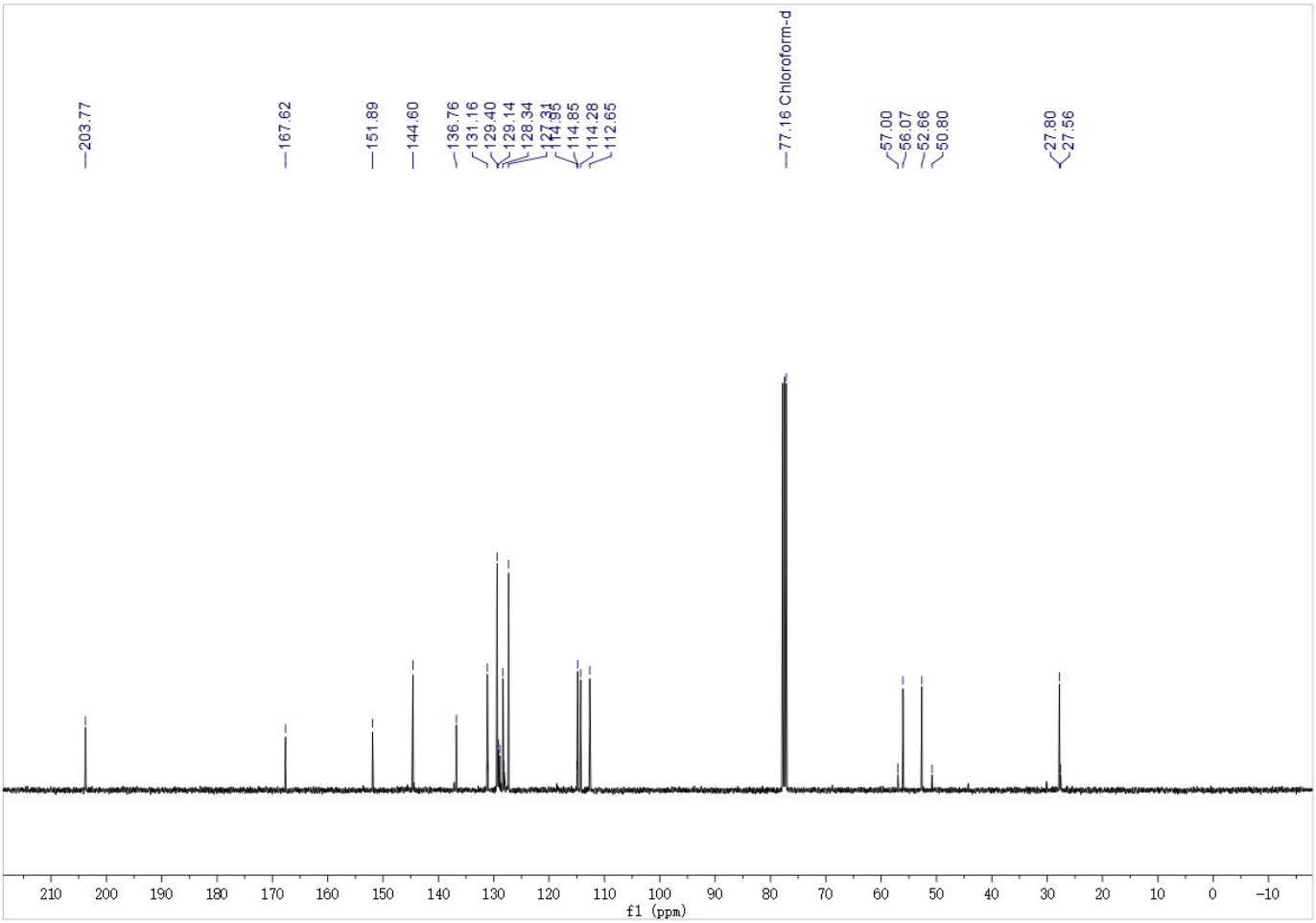

7.61
7.60
7.42
7.40
7.38
7.36
7.33
7.31
7.29
7.28
7.26 Chloroform-d
7.26
7.23
7.22
7.05
7.03
5.78
5.67
5.45
5.35
4.75
4.49
4.14
3.88
2.12
1.84
O
N
Bn
O
10.51
0.97
0.96
2.04
2.05
3.55
f1 (ppm)

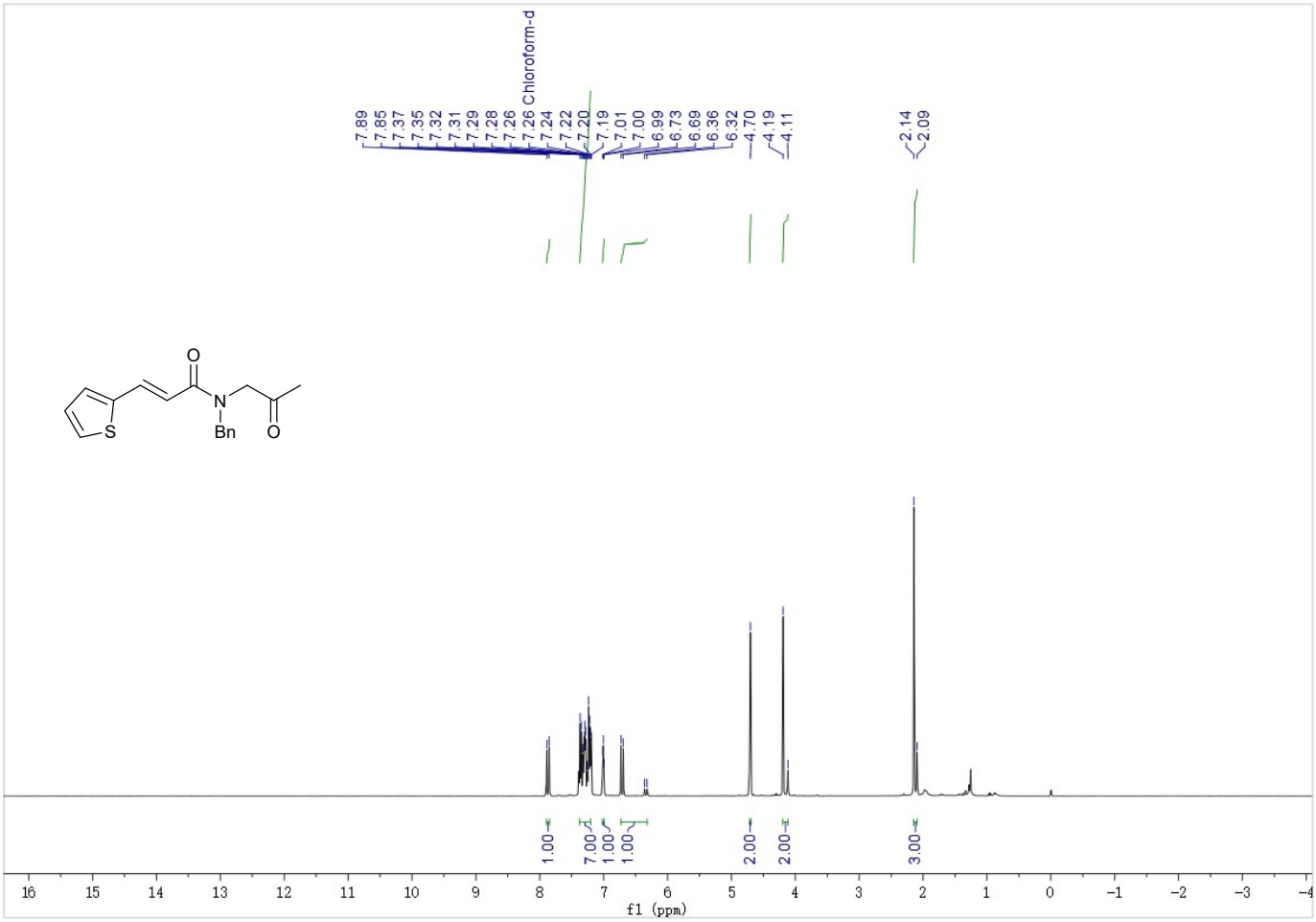

202.74
202.70
171.87
171.25
144.63
144.30
129.02
128.95
128.92
128.90
128.00
127.41
114.20
77.16 Chloroform-d
56.65
53.45
53.20
48.55
27.60
26.99
f1 (ppm)

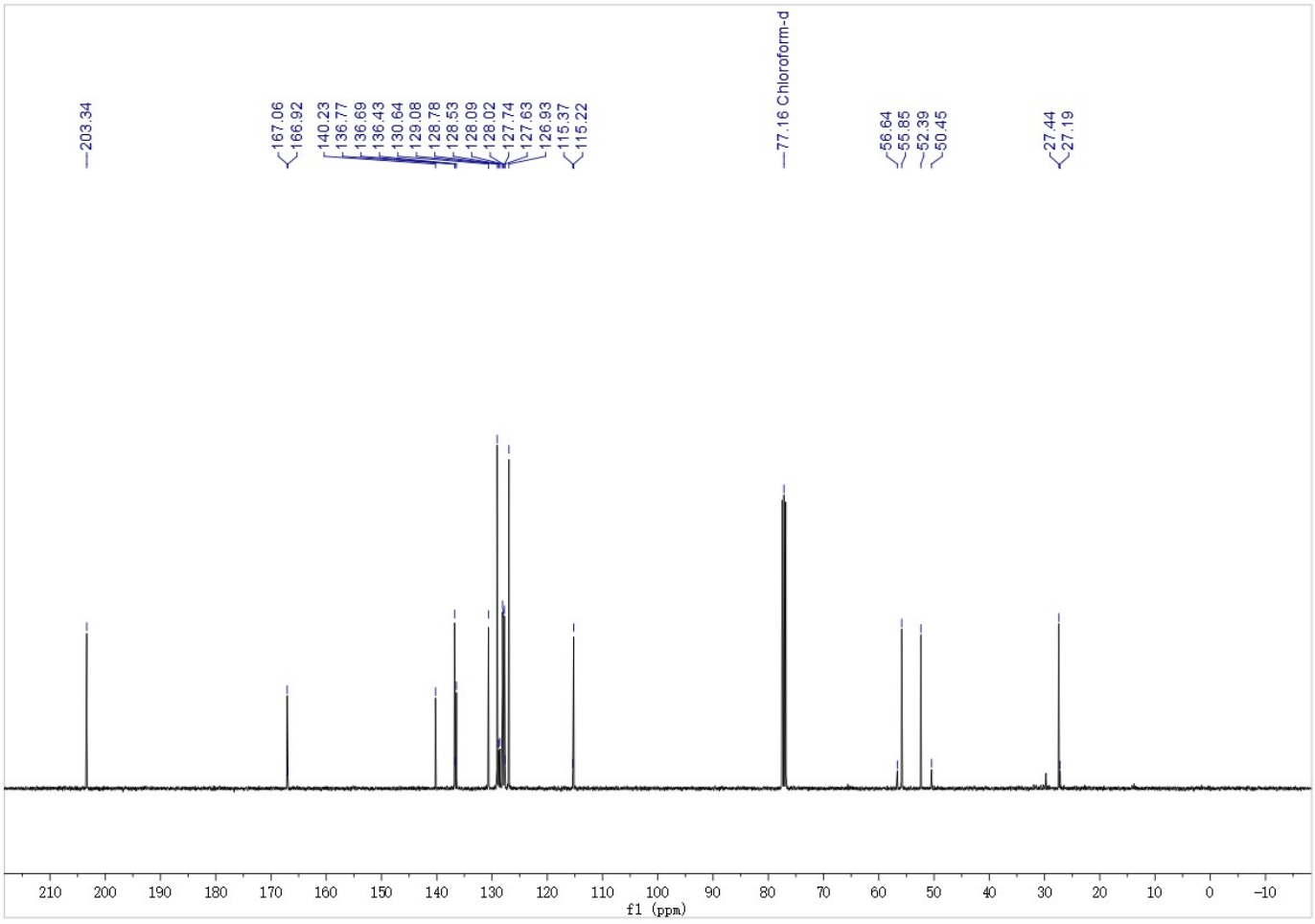

7.37
7.35
7.33
7.31
7.30
7.26
7.26 Chloroform-d
7.24
7.21
6.71
4.71
4.12
2.14
1.60
O
N
CH3
Bn
O
10.56
1.06
2.02
2.04
6.00
f1 (ppm)

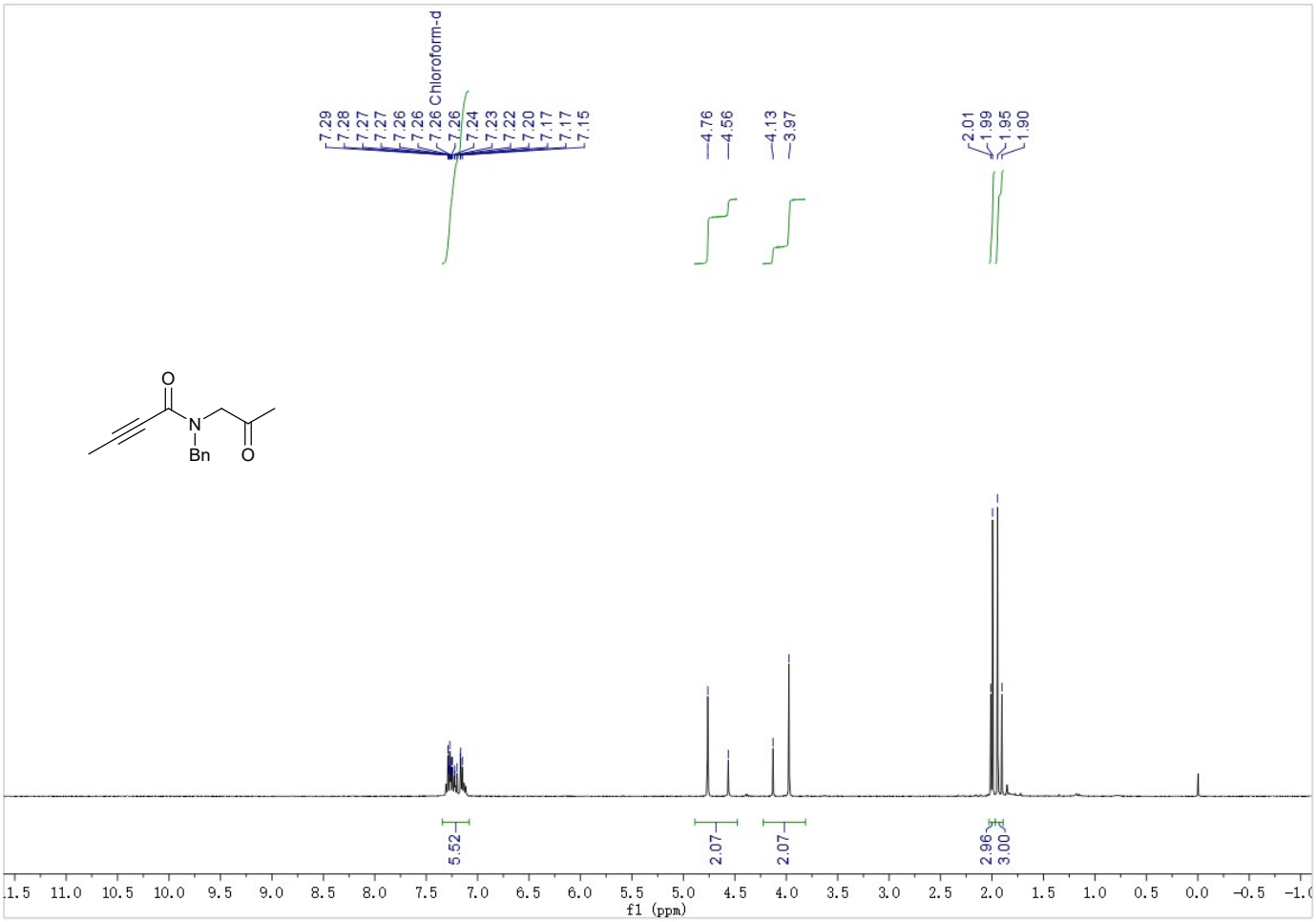

202.86
174.58
136.48
135.82
132.48
130.10
129.12
129.05
128.42
127.95
127.61
127.17
77.16 Chloroform-d
53.95
53.56
29.77
27.57
16.32
f1 (ppm)

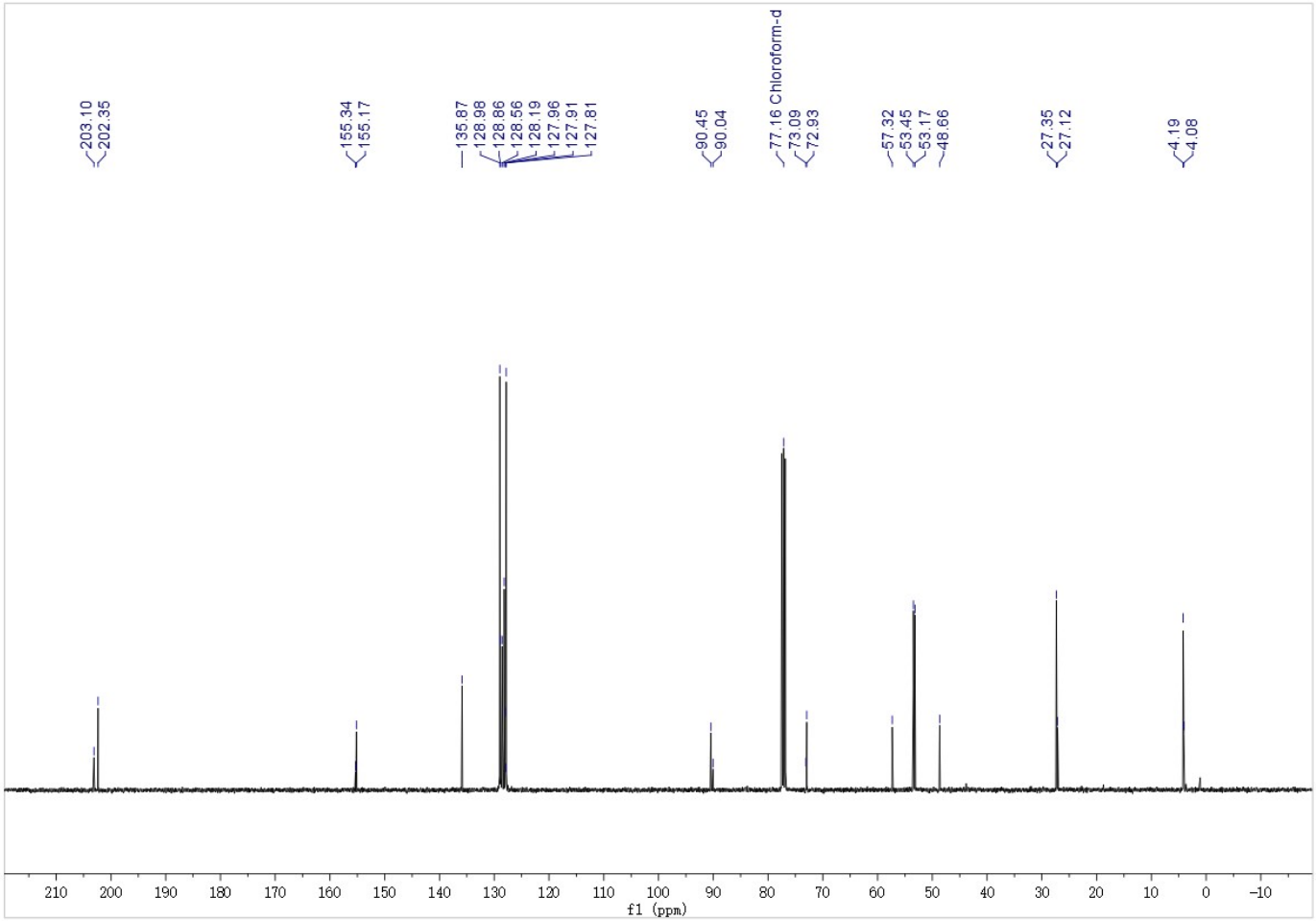

7.55
7.51
7.42
7.40
7.39
7.37
7.35
7.32
7.31
7.29
7.27
7.26
Chloroform-d
7.23
7.21
6.85
6.81
6.56
6.55
6.43
4.74
4.72
4.18
4.13
2.14
2.10
O
N
Bn
O
O
1.00
5.07
1.15
1.00
1.00
1.00
2.00
2.47
3.00
f1 (ppm)

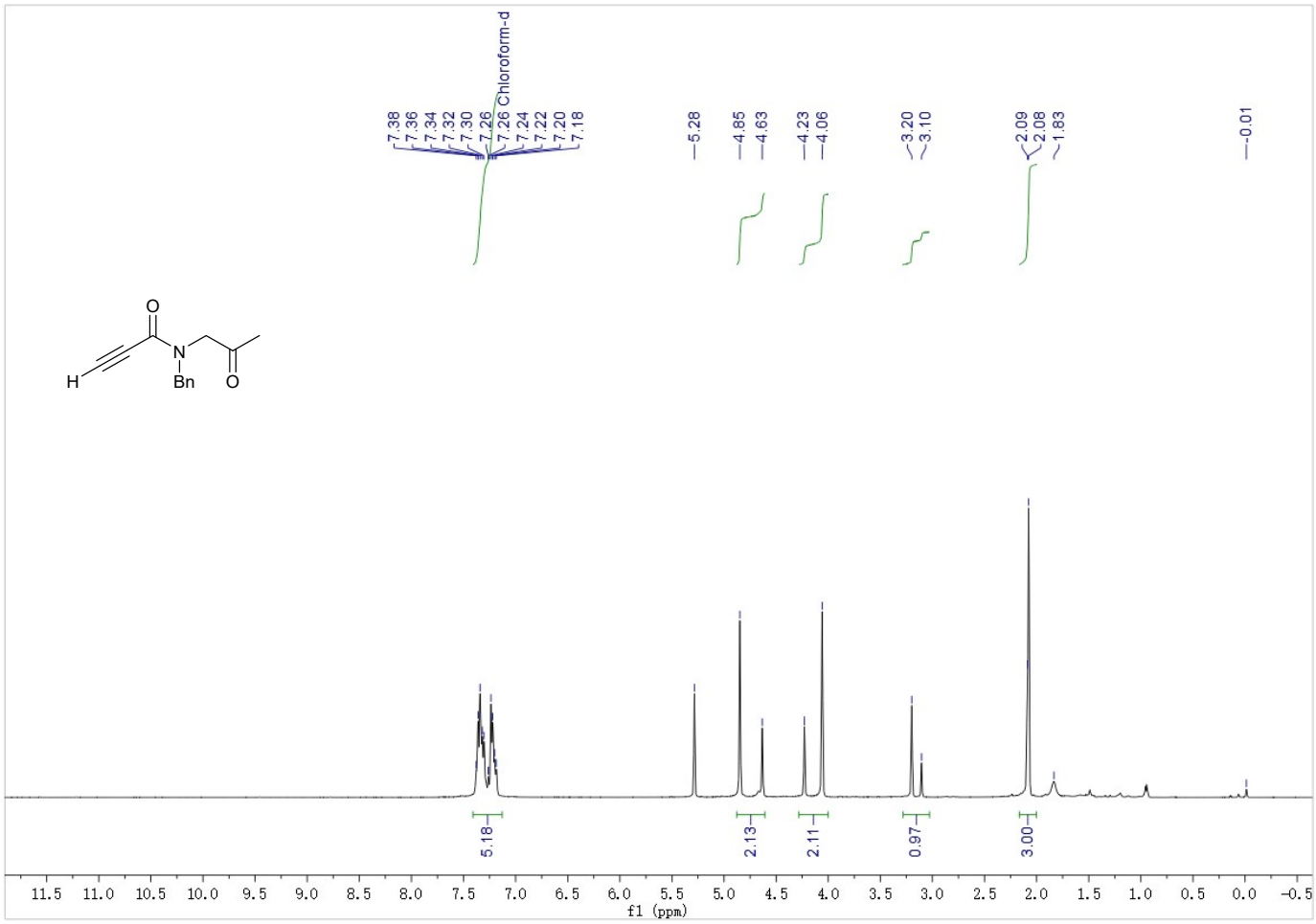

203.77
167.62
151.89
144.60
136.76
131.16
129.40
129.14
128.34
114.85
114.28
112.65
Chloroform-d
57.00
56.07
52.66
50.80
27.80
27.56
f1 (ppm)

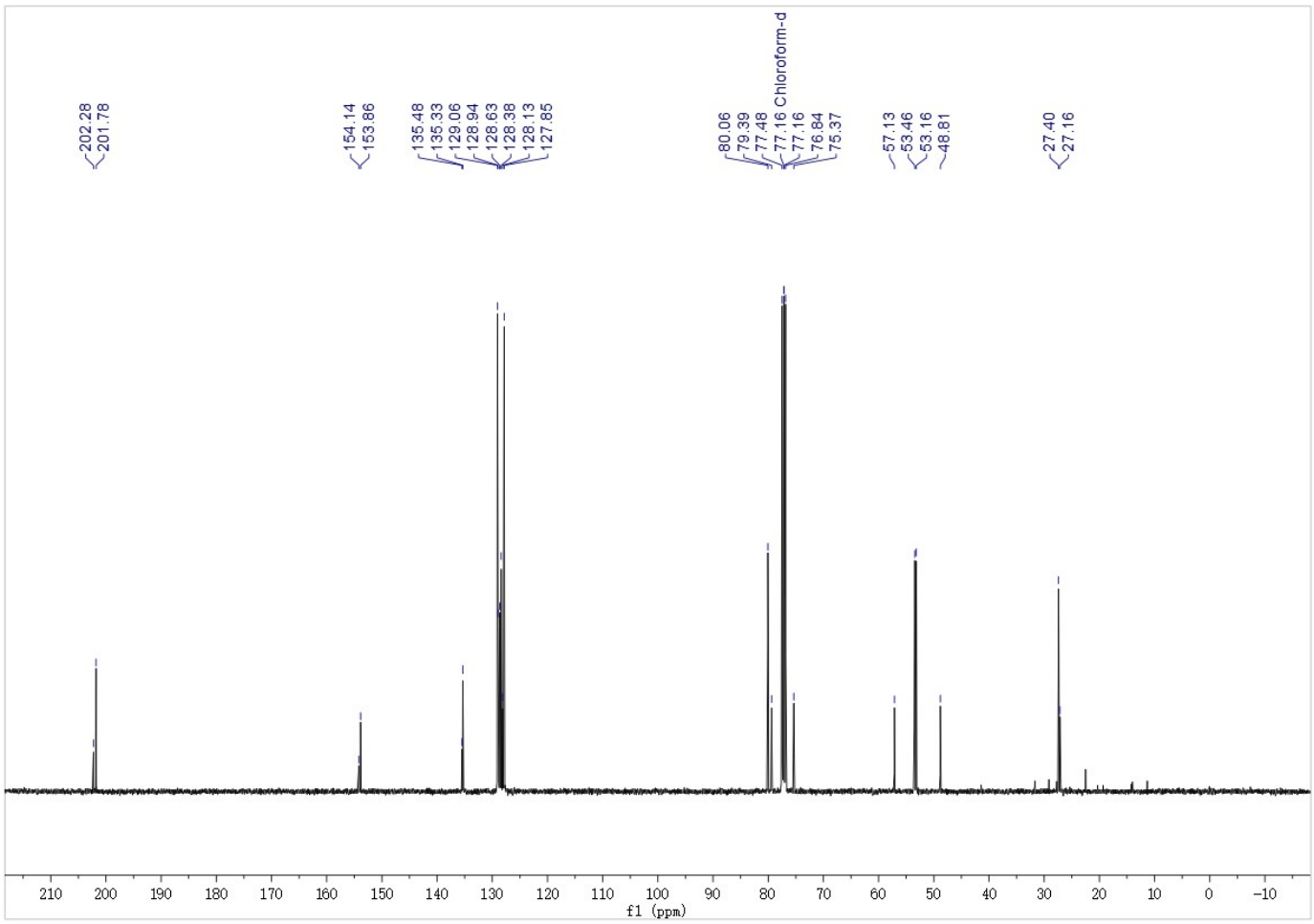

Chloroform-d
7.89
7.85
7.37
7.35
7.32
7.31
7.29
7.28
7.26
7.26
7.24
7.22
7.20
7.19
7.01
7.00
6.99
6.73
6.69
6.36
6.32
4.70
4.19
4.11
2.14
2.09
O
N
Bn
O
S
1.00
7.00
1.00
1.00
2.00
2.00
3.00
f1 (ppm)

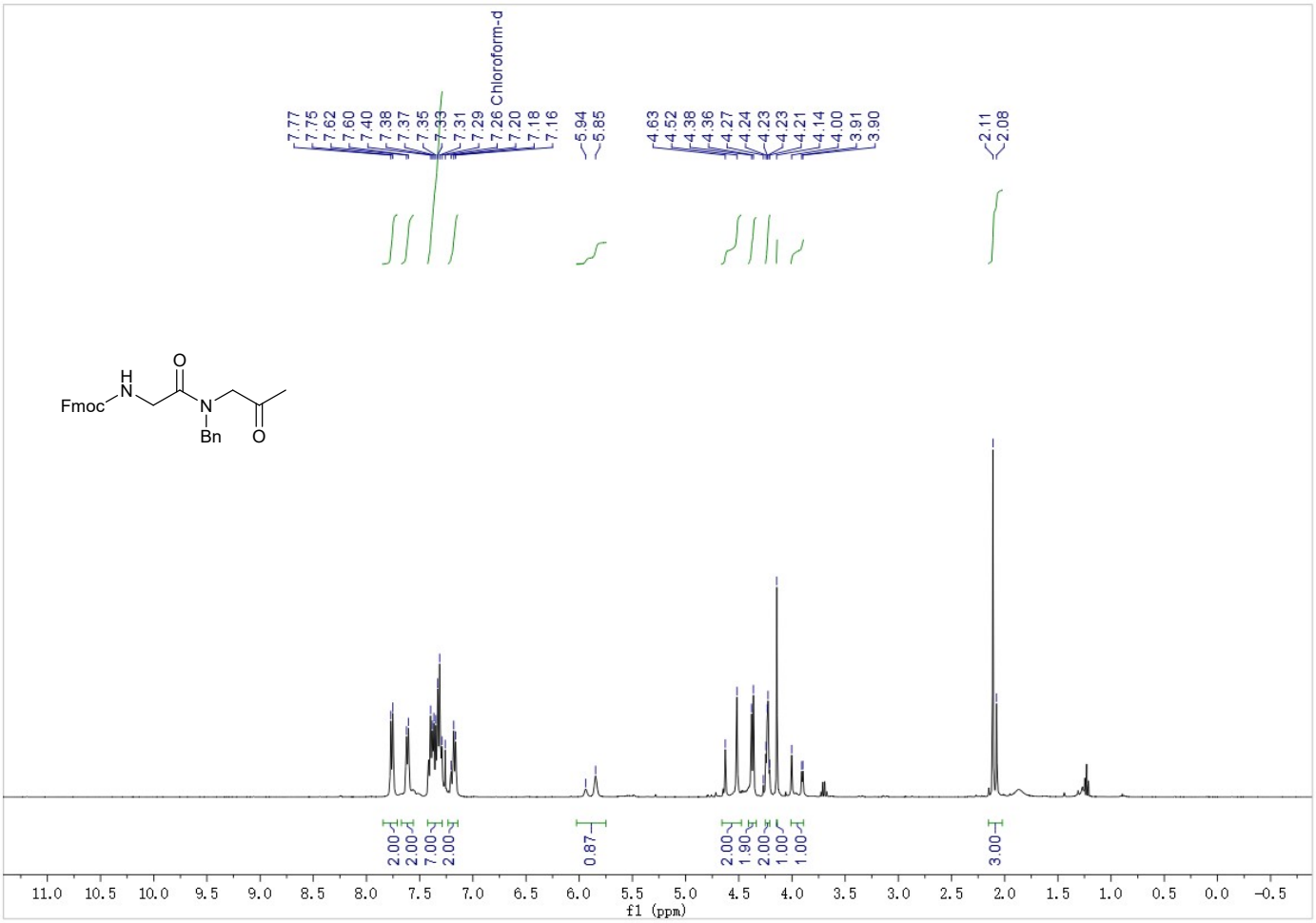

203.34
167.06
166.92
140.23
136.77
136.69
136.43
130.64
129.08
128.78
128.53
128.09
128.02
127.74
127.63
126.93
115.37
115.22
77.16 Chloroform-d
56.64
55.85
52.39
50.45
27.44
27.19
f1 (ppm)

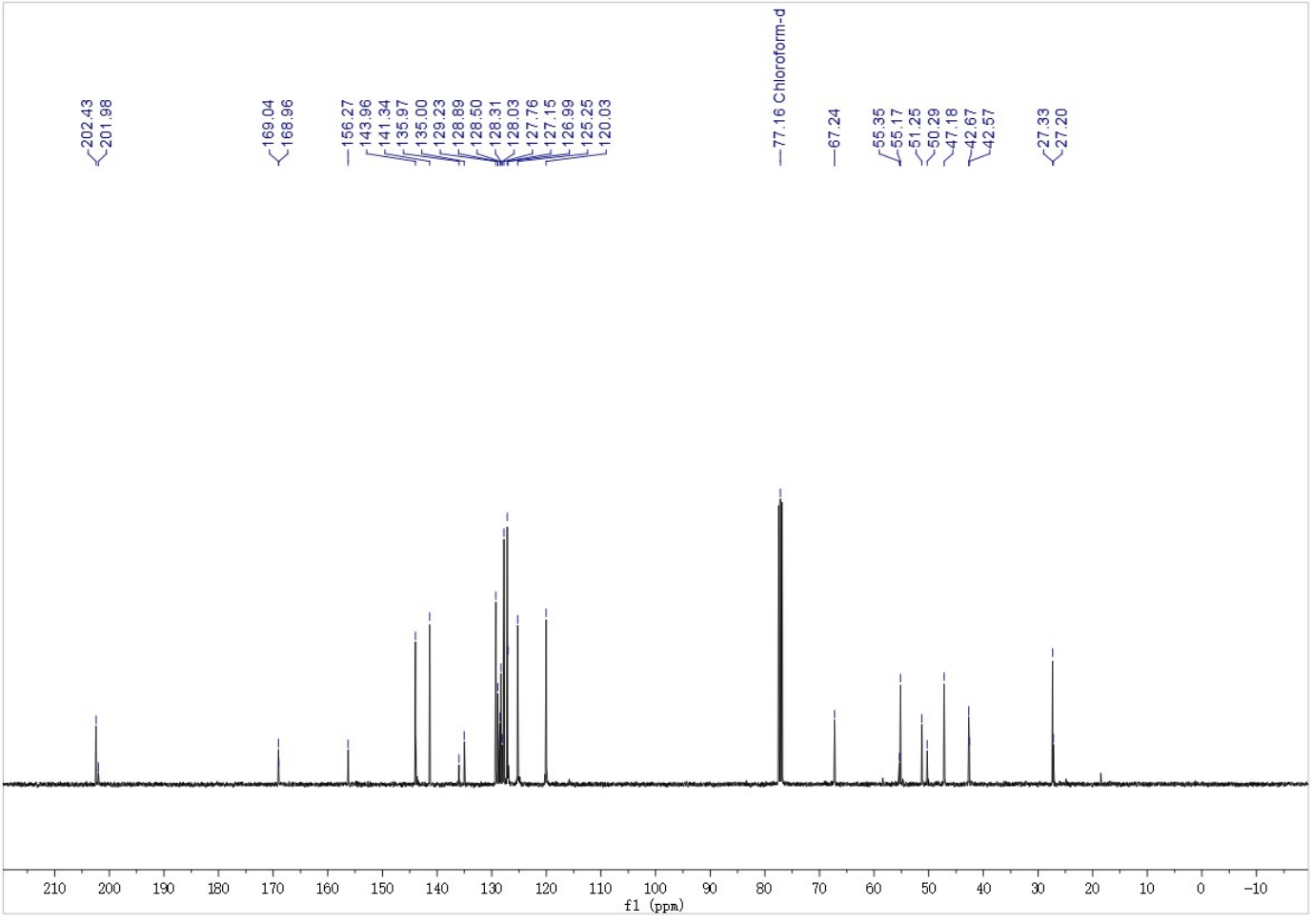

7.29
7.28
7.27
7.27
7.26
7.26
7.26 Chloroform-d
7.26
7.24
7.23
7.22
7.20
7.17
7.17
7.15
4.76
4.56
4.13
3.97
2.01
1.99
1.95
1.90
O
N
Bn
O
5.52
2.07
2.07
2.96
3.00
f1 (ppm)

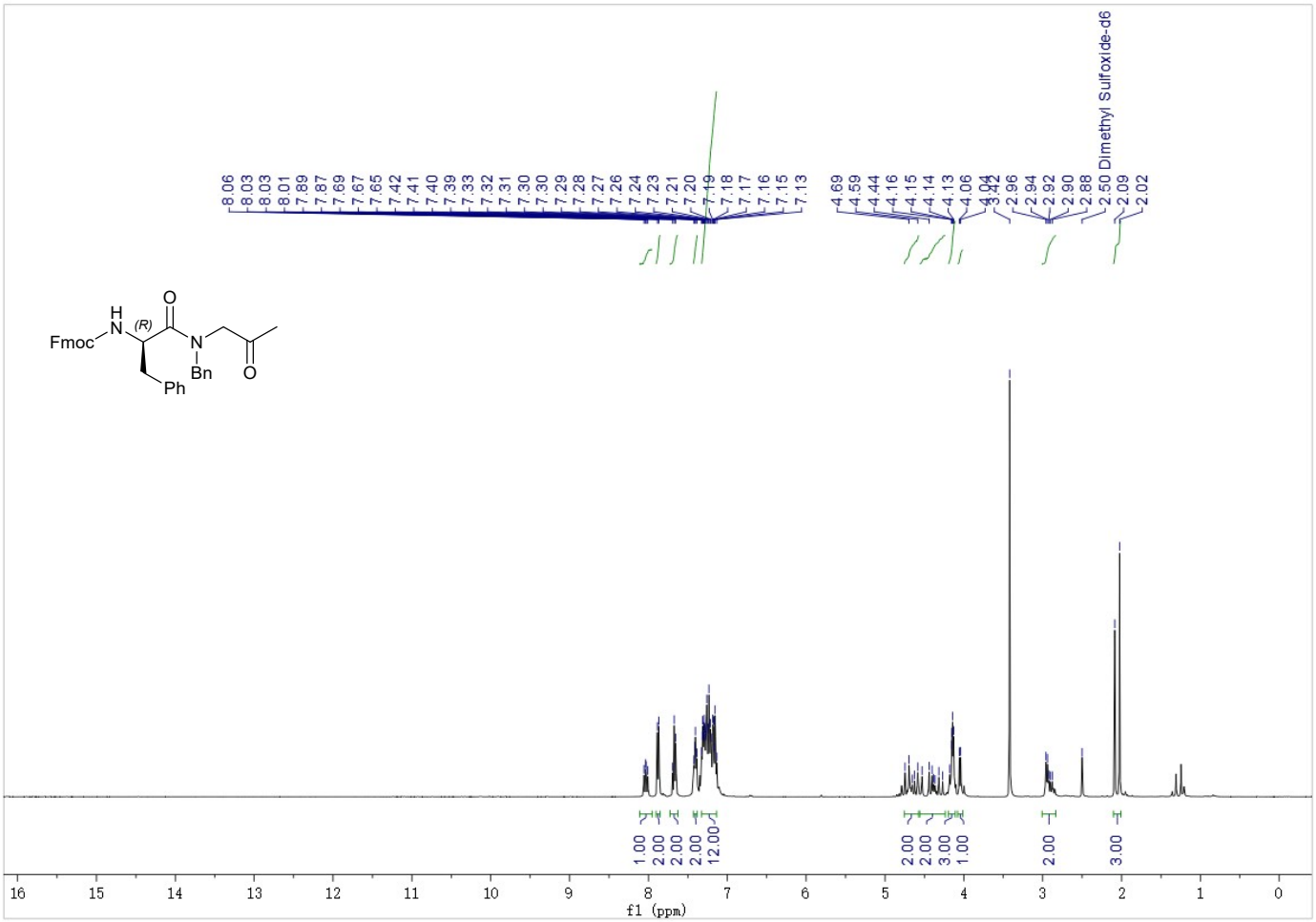

203.10
202.35
155.34
155.17
135.87
128.98
128.86
128.56
128.19
127.96
127.91
127.81
90.45
90.04
77.16 Chloroform-d
73.09
72.93
57.32
53.45
53.17
48.66
27.35
27.12
4.19
4.08
f1 (ppm)

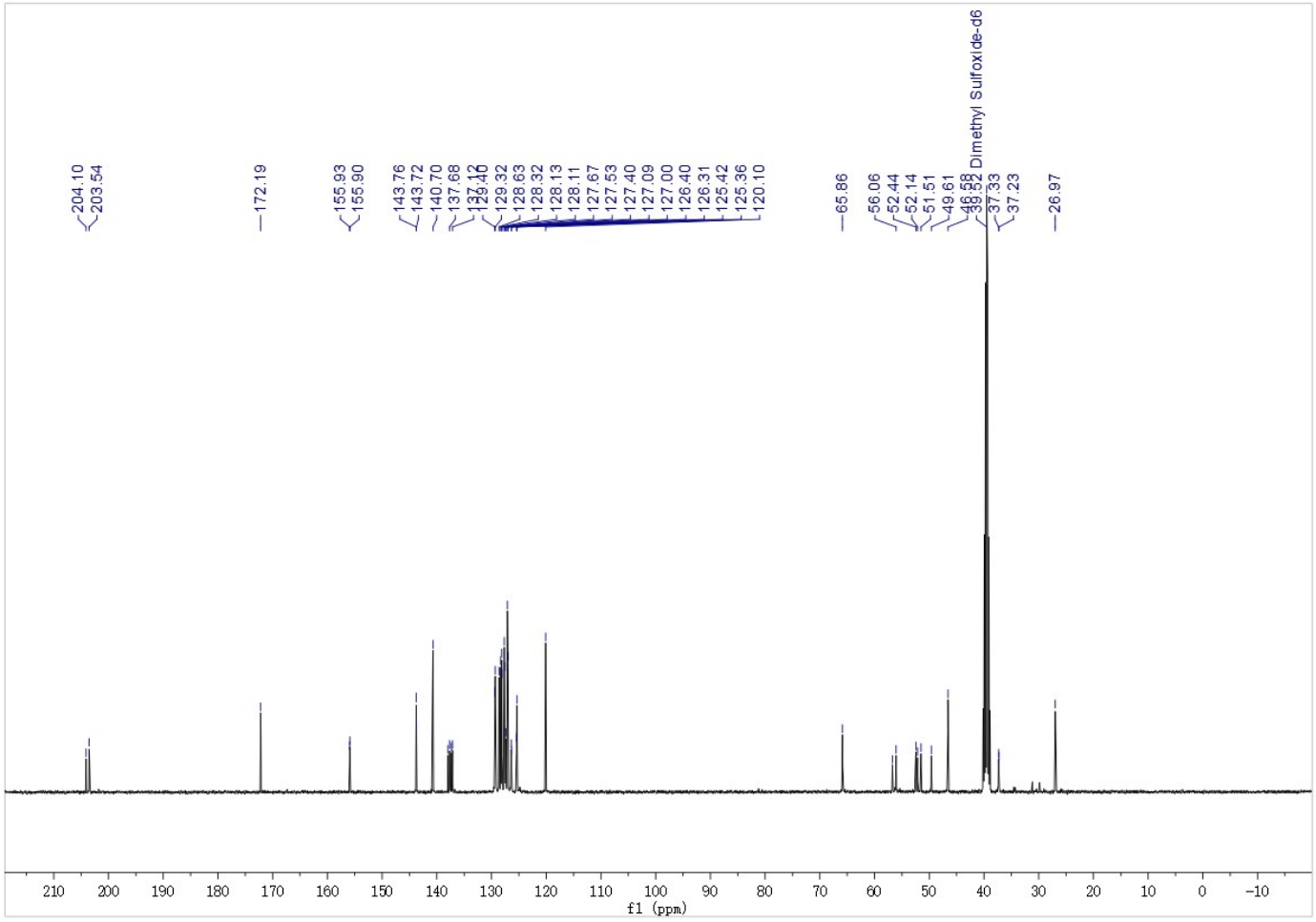

7.38
7.36
7.34
7.32
7.30
7.26
7.26 Chloroform-d
7.24
7.22
7.20
7.18
5.28
4.85
4.63
4.23
4.06
3.20
3.10
2.09
2.08
1.83
0.01
O
N
Bn
H
O
5.18
2.13
2.11
0.97
3.00
f1 (ppm)

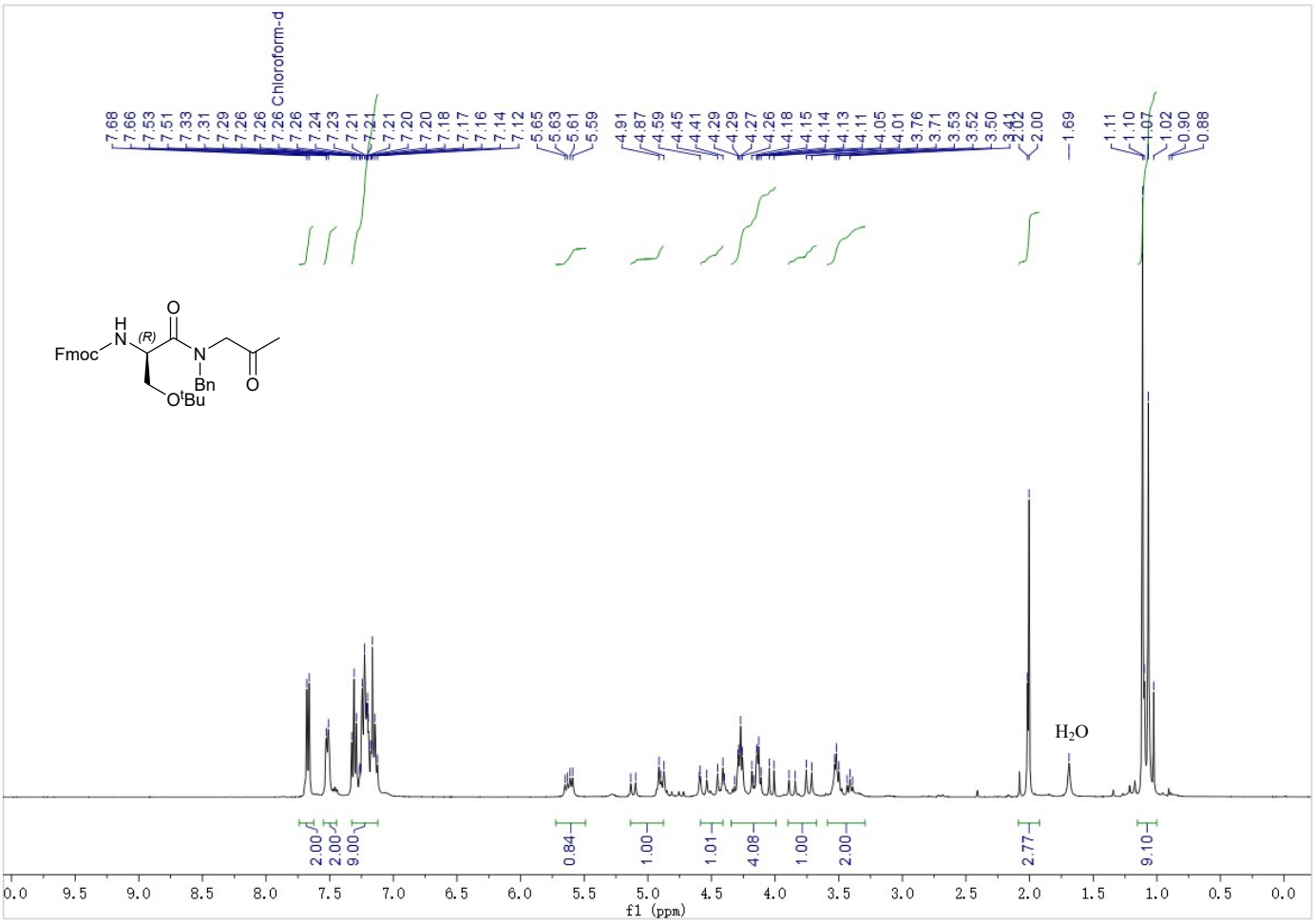

202.28
201.78
154.14
153.86
135.48
135.33
129.06
128.94
128.63
128.38
128.13
127.85
80.06
79.39
77.48
77.16 Chloroform-d
77.16
76.84
75.37
57.13
53.46
53.16
48.81
27.40
27.16
f1 (ppm)

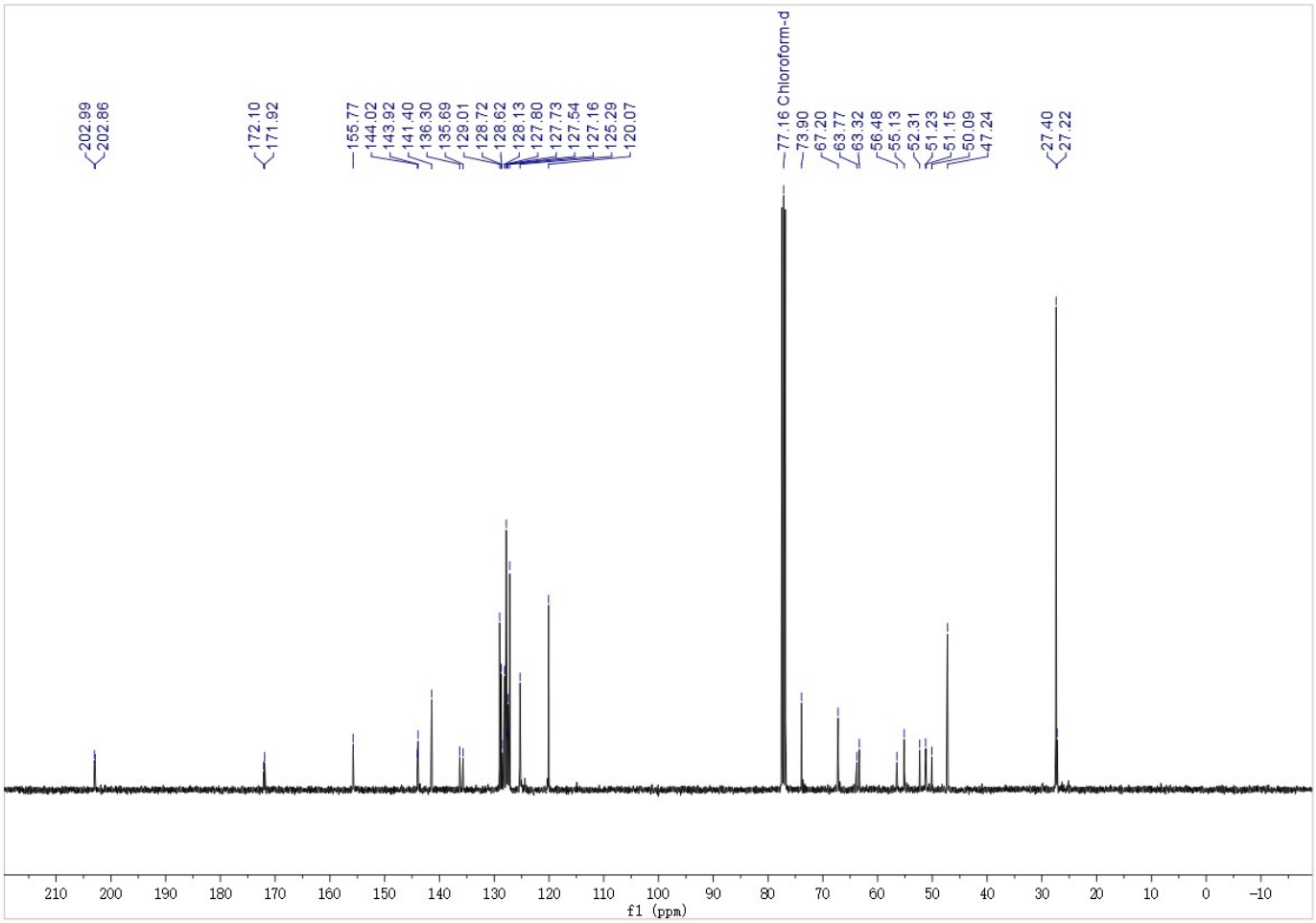

Chloroform-d
7.77
7.75
7.62
7.60
7.40
7.38
7.37
7.35
7.33
7.31
7.29
7.26
7.20
7.18
7.16
5.94
5.85
4.63
4.52
4.38
4.36
4.27
4.24
4.23
4.23
4.21
4.14
4.00
3.91
3.90
2.11
2.08
Fmoc
H
N
O
N
Bn
O
2.00
2.00
7.00
2.00
0.87
2.00
1.90
2.00
1.00
1.00
3.00
f1 (ppm)

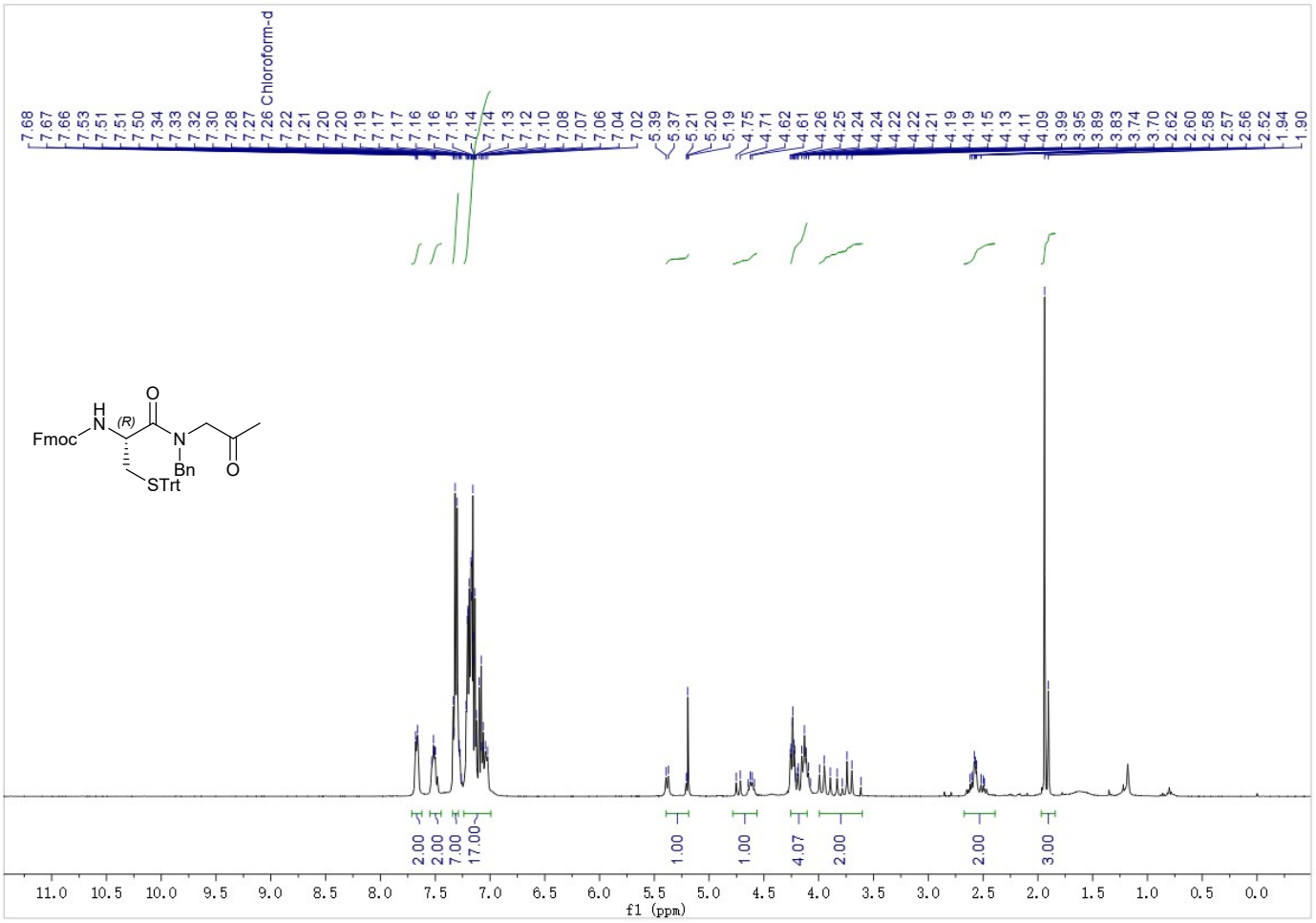

202.43
201.98
169.04
168.96
156.27
143.96
141.34
135.97
135.00
129.23
128.89
128.50
128.31
128.03
127.76
127.15
126.99
125.25
120.03
77.16 Chloroform-d
67.24
55.35
55.17
51.25
50.29
47.18
42.67
42.57
27.33
27.20
f1 (ppm)

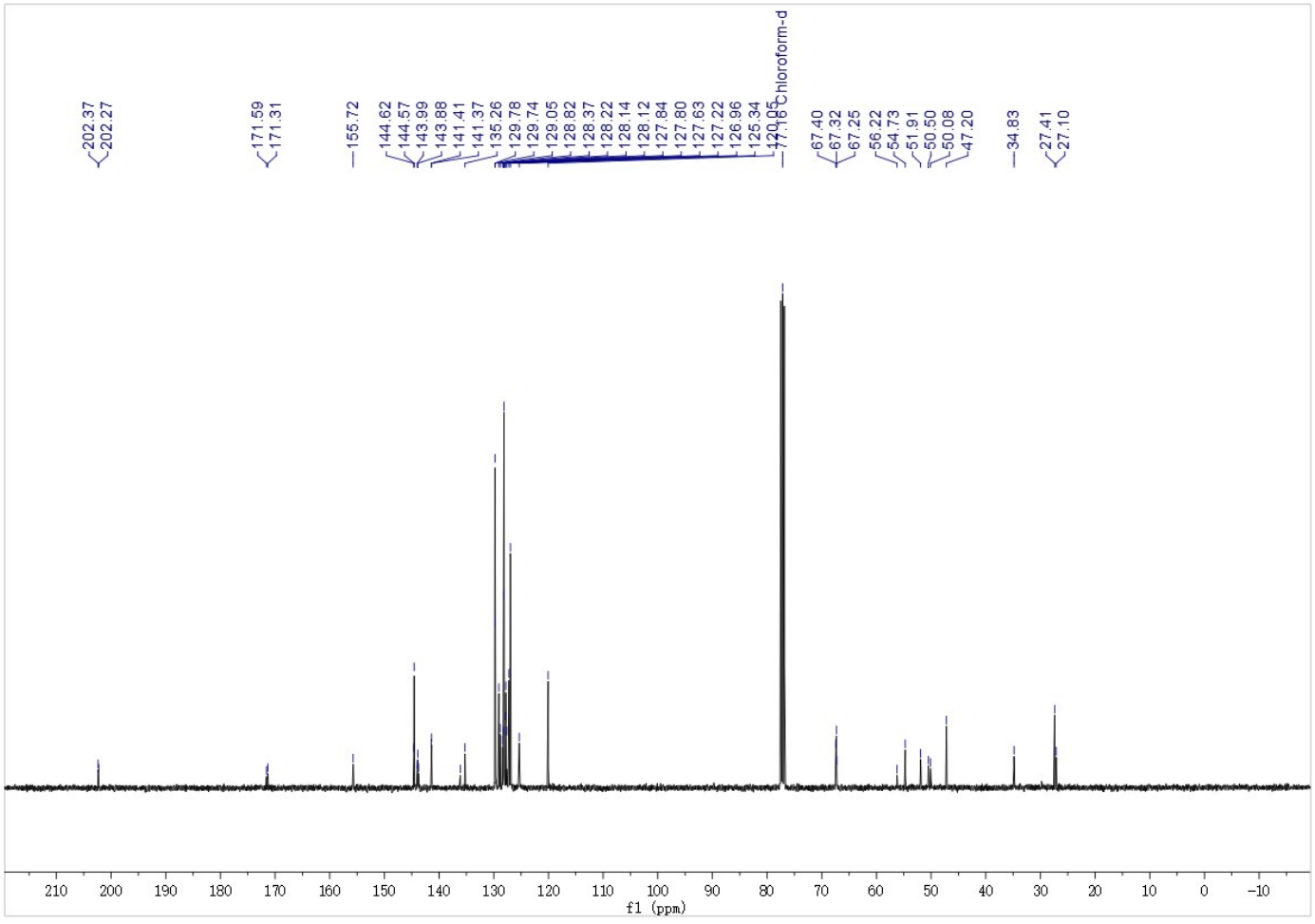

Dimethyl Sulfoxide-d6
Fmoc
(R)
Bn
Ph
f1 (ppm)

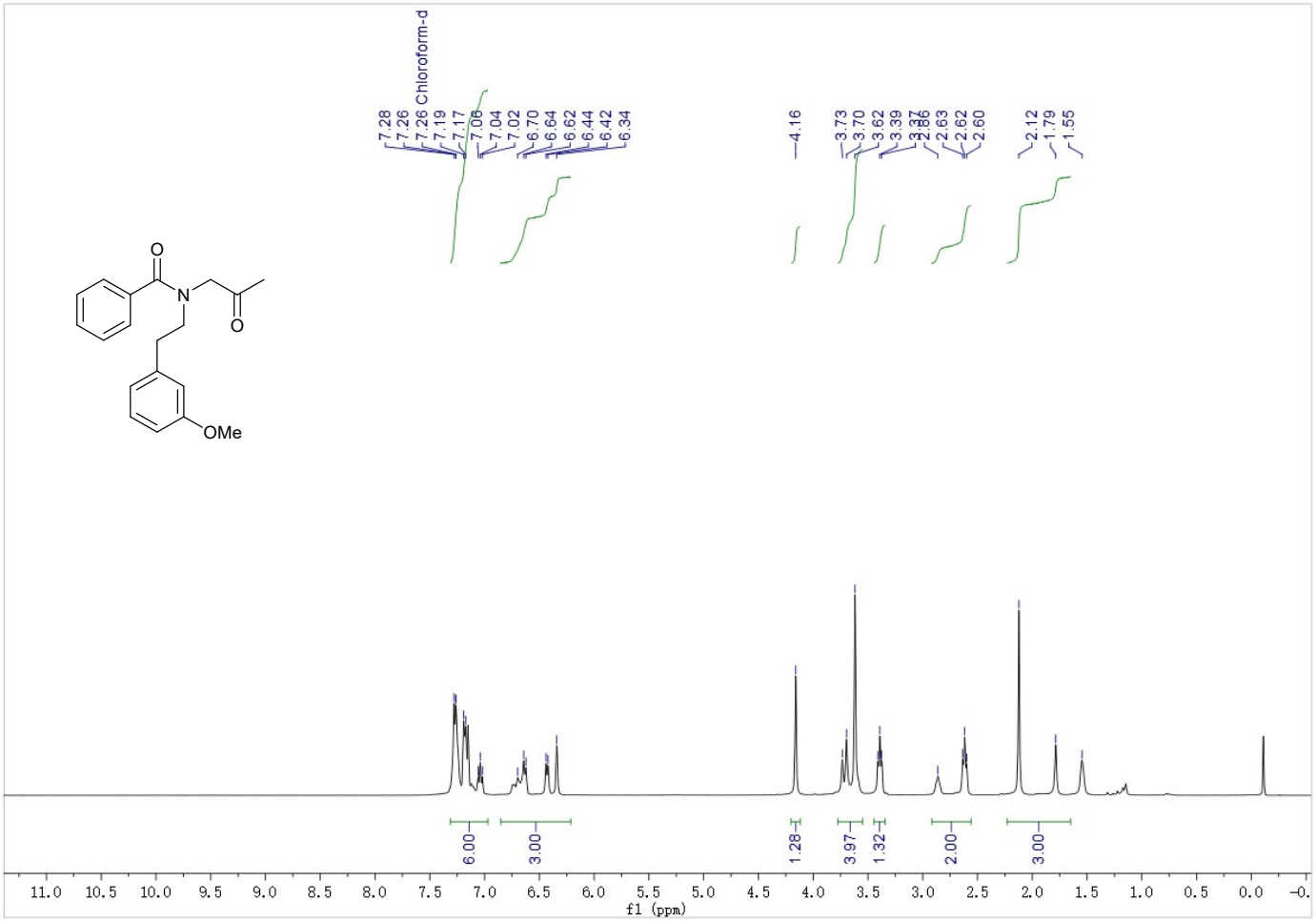

Dimethyl Sulfoxide-d6
f1 (ppm)

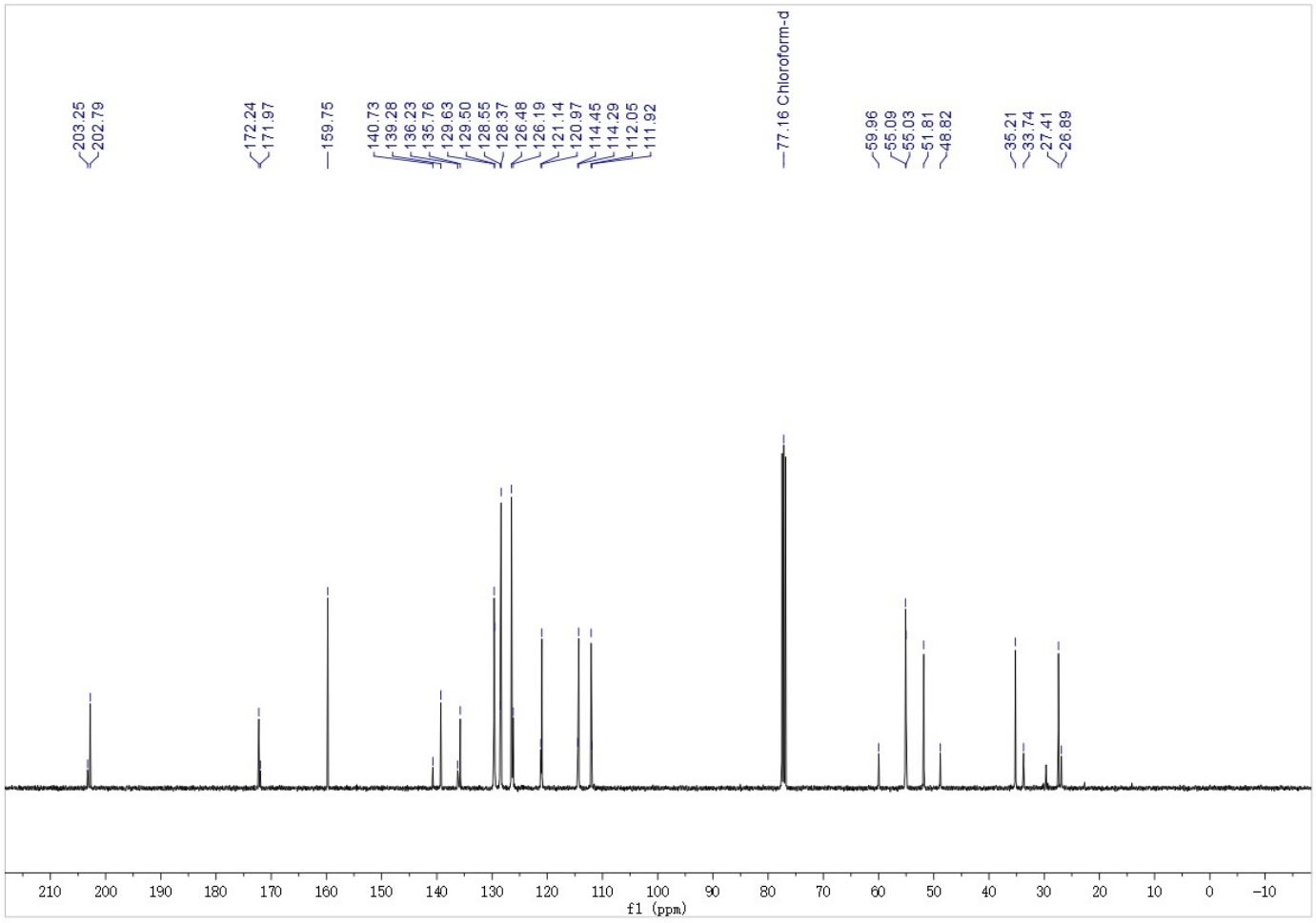

Chloroform-d
7.68 7.66 7.53 7.51 7.33 7.31 7.29 7.26 7.26 7.26 7.24 7.23 7.21 7.21 7.21 7.20 7.20 7.18 7.17 7.16 7.14 7.12
5.65 5.63 5.61 5.59
4.91 4.87 4.59 4.45 4.41 4.29 4.29 4.27 4.26 4.18 4.15 4.14 4.13 4.11 4.05 4.01 3.76 3.71 3.53 3.52 3.50 3.41 3.02
2.00
1.69
1.11 1.10 1.07 1.02 0.90 0.88
Fmoc
(R)
Bn
O^{t}Bu
H_2O
2.00 2.00 9.00 0.84 1.00 1.01 4.08 1.00 2.00 2.77 9.10
f1 (ppm)

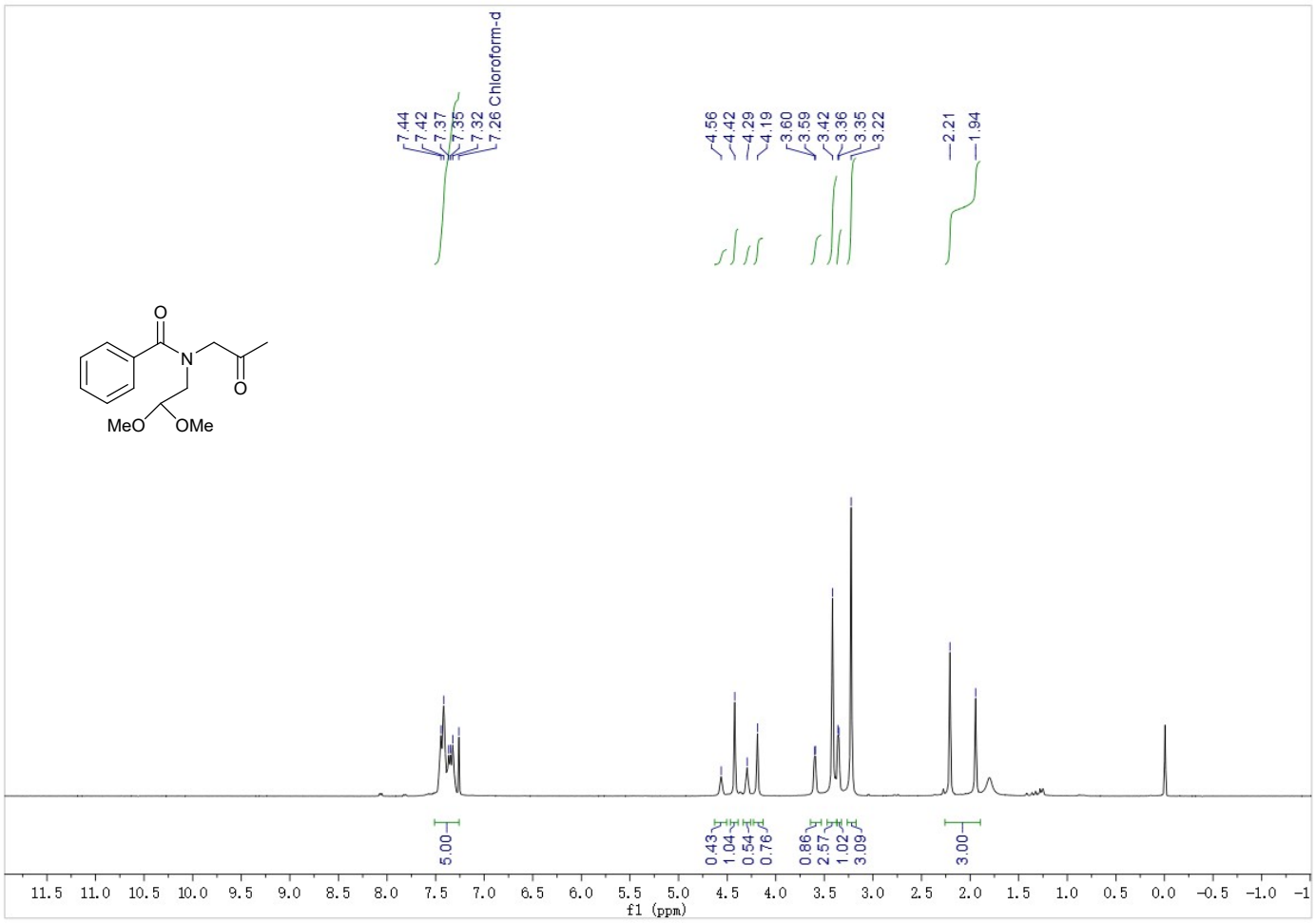

202.99 202.86
172.10 171.92
155.77 144.02 143.92 141.40 136.30 135.69 129.01 128.72 128.62 128.13 127.80 127.73 127.54 127.16 125.29 120.07
77.16 Chloroform-d
73.90 67.20 63.77 63.32 56.48 55.13 52.31 51.23 51.15 50.09 47.24
27.40 27.22
f1 (ppm)

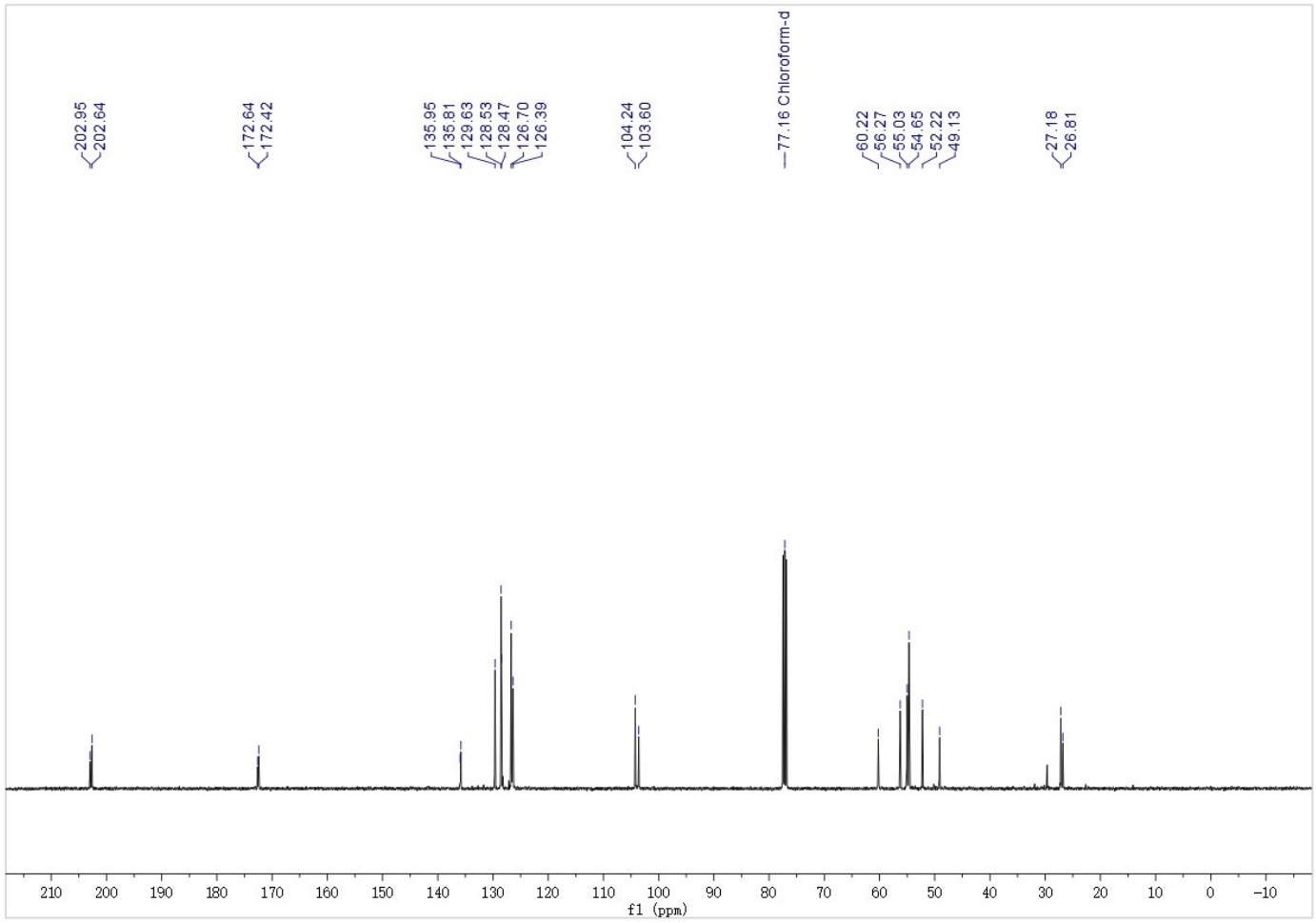

Chloroform-d
7.68 7.67 7.66 7.53 7.51 7.51 7.50 7.34 7.33 7.32 7.30 7.28 7.27 7.26 7.22 7.21 7.20 7.20 7.19 7.17 7.17 7.16 7.16 7.15 7.14 7.14 7.13 7.12 7.10 7.08 7.07 7.06 7.04 7.02 5.39 5.37 5.21 5.20 5.19 4.75 4.71 4.62 4.61 4.26 4.25 4.24 4.24 4.22 4.22 4.21 4.19 4.19 4.15 4.13 4.11 4.09 3.99 3.95 3.89 3.83 3.74 3.70 2.62 2.60 2.58 2.57 2.56 2.52 1.94 1.90
Fmoc
H
N
(R)
O
N
Bn
O
STrt
2.00 2.00 7.00 17.00 1.00 1.00 4.07 2.00 2.00 3.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

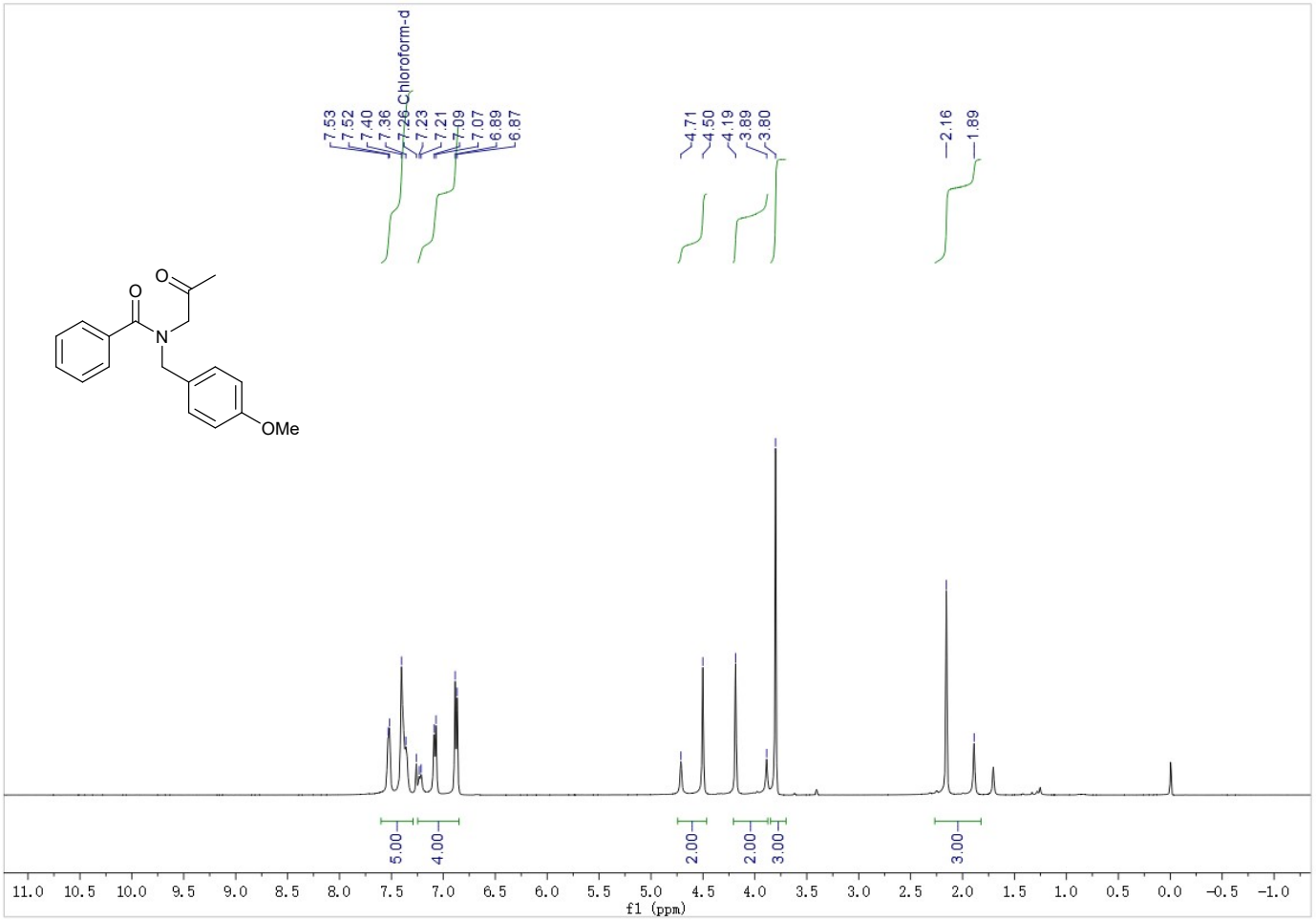

202.37 202.27 171.59 171.31 155.72 144.62 144.57 143.99 143.88 141.41 141.37 135.26 129.78 129.74 129.05 128.82 128.37 128.22 128.14 128.12 127.84 127.80 127.63 127.22 126.96 125.34 120.05 77.16 Chloroform-d 67.40 67.32 67.25 56.22 54.73 51.91 50.50 50.08 47.20 34.83 27.41 27.10
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

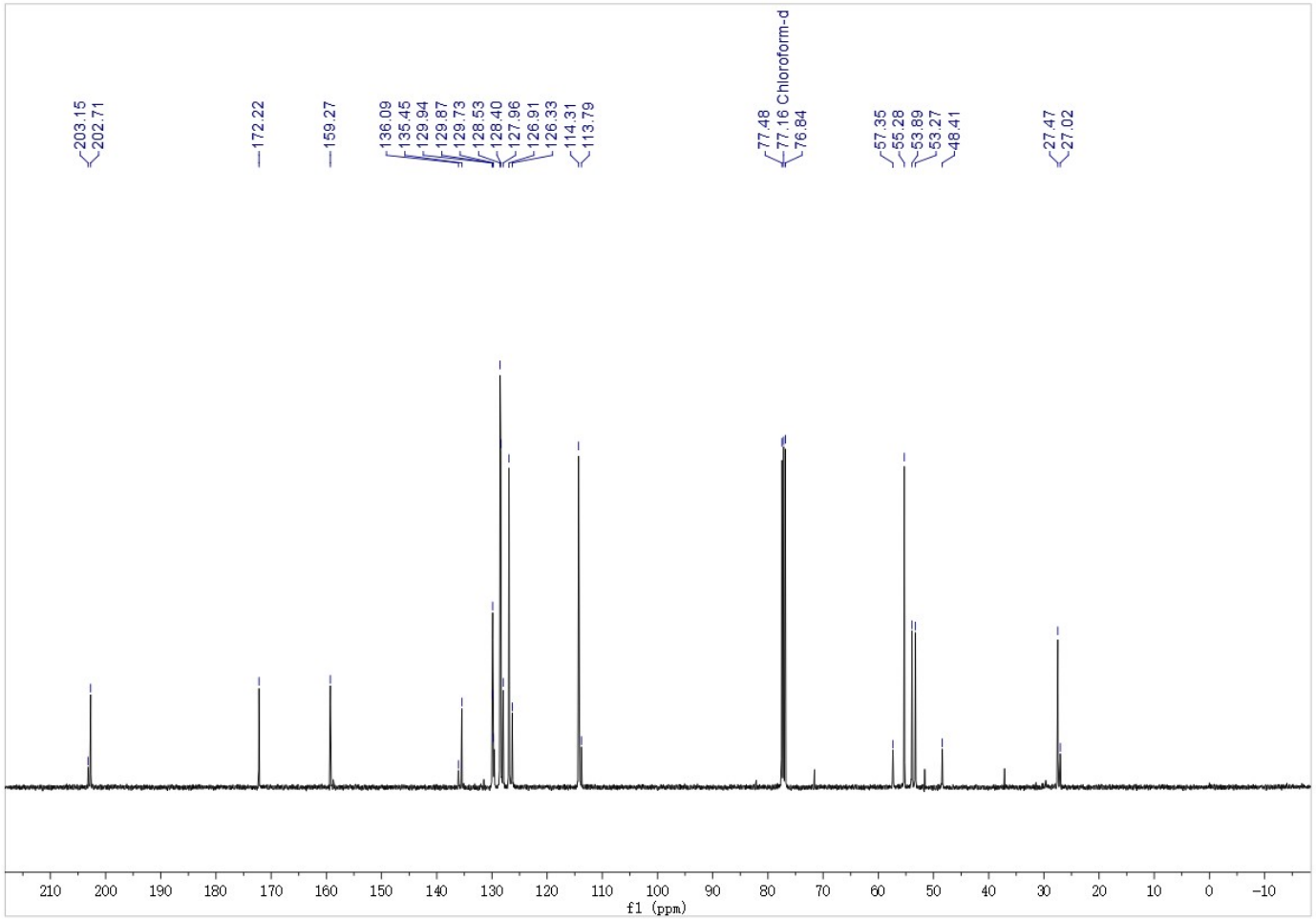

7.28
7.26
7.26 Chloroform-d
7.19
7.17
7.08
7.04
7.02
6.70
6.64
6.62
6.44
6.42
6.34
4.16
3.73
3.70
3.62
3.39
2.63
2.62
2.60
2.12
1.79
1.55
O
N
O
OMe
6.00
3.00
1.28
3.97
1.32
2.00
3.00
f1 (ppm)

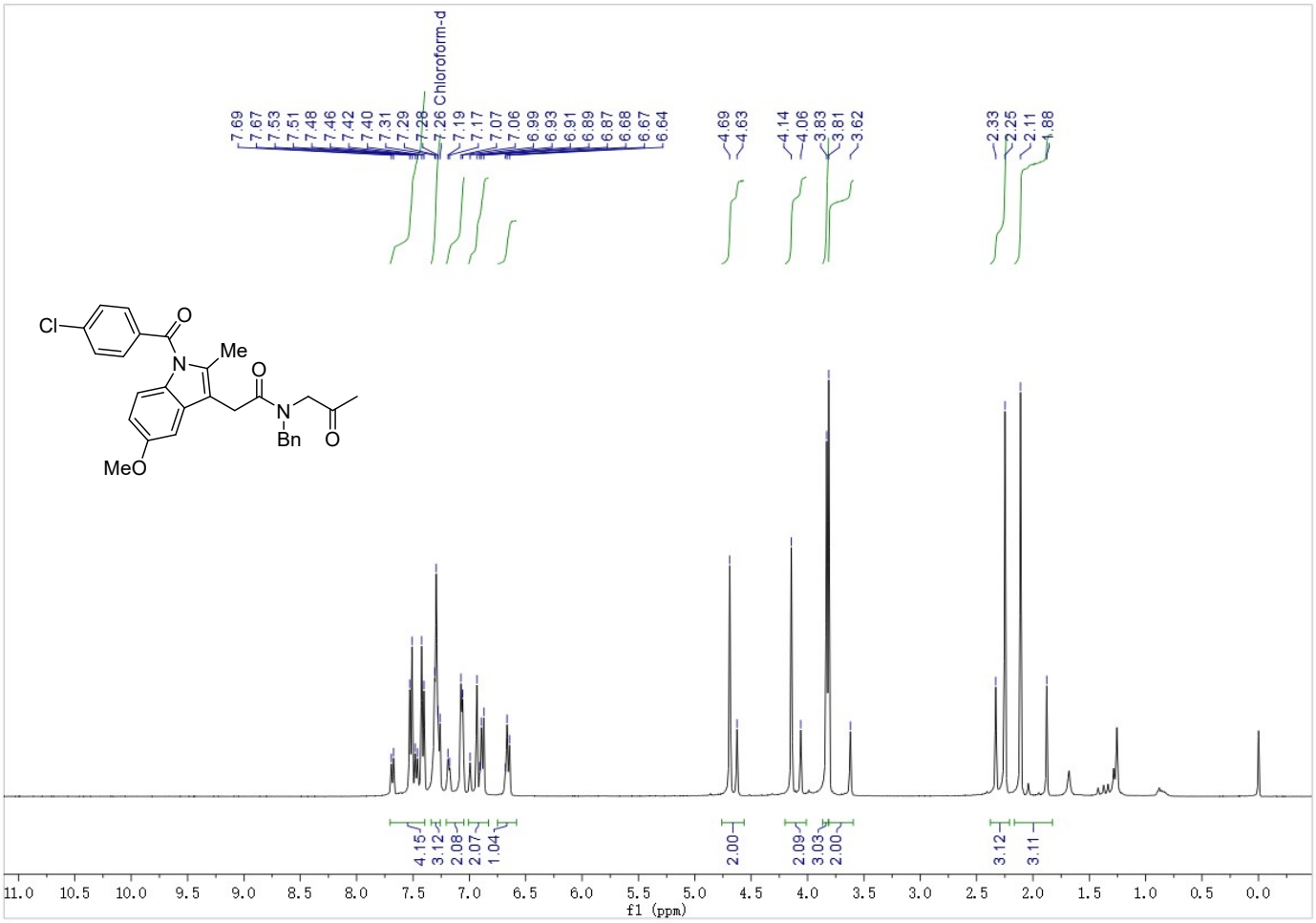

203.25
202.79
172.24
171.97
159.75
140.73
139.28
136.23
135.76
129.63
129.50
128.55
128.37
126.48
126.19
121.14
120.97
114.45
114.29
112.05
111.92
77.16 Chloroform-d
59.96
55.09
55.03
51.81
48.82
35.21
33.74
27.41
26.89
f1 (ppm)

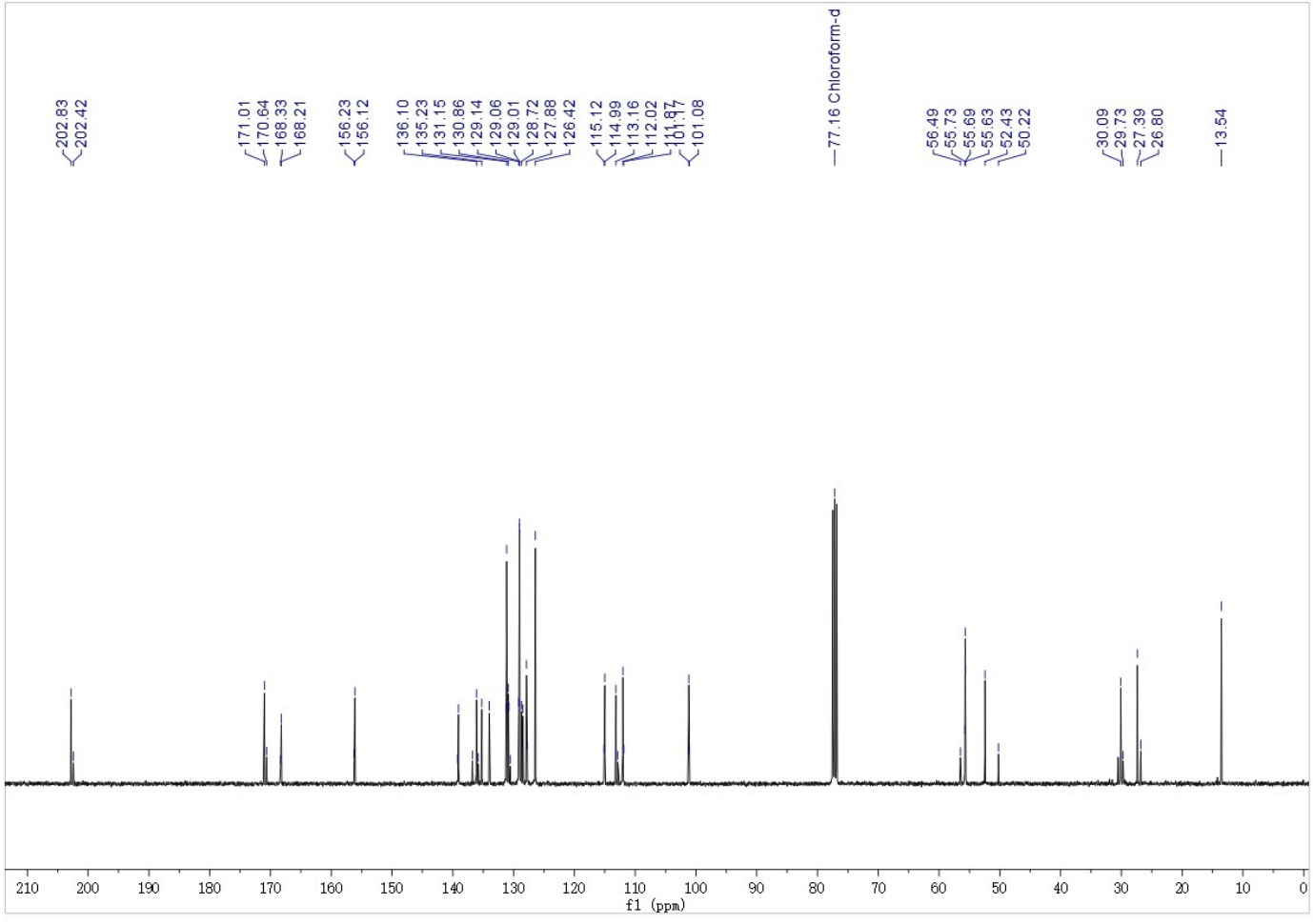

7.44
7.42
7.37
7.35
7.32
7.26 Chloroform-d
4.56
4.42
4.29
4.19
3.60
3.59
3.42
3.36
3.35
3.22
2.21
1.94
O
N
O
MeO
OMe
5.00
0.43
1.04
0.54
0.76
0.86
2.57
1.02
3.09
3.00
f1 (ppm)

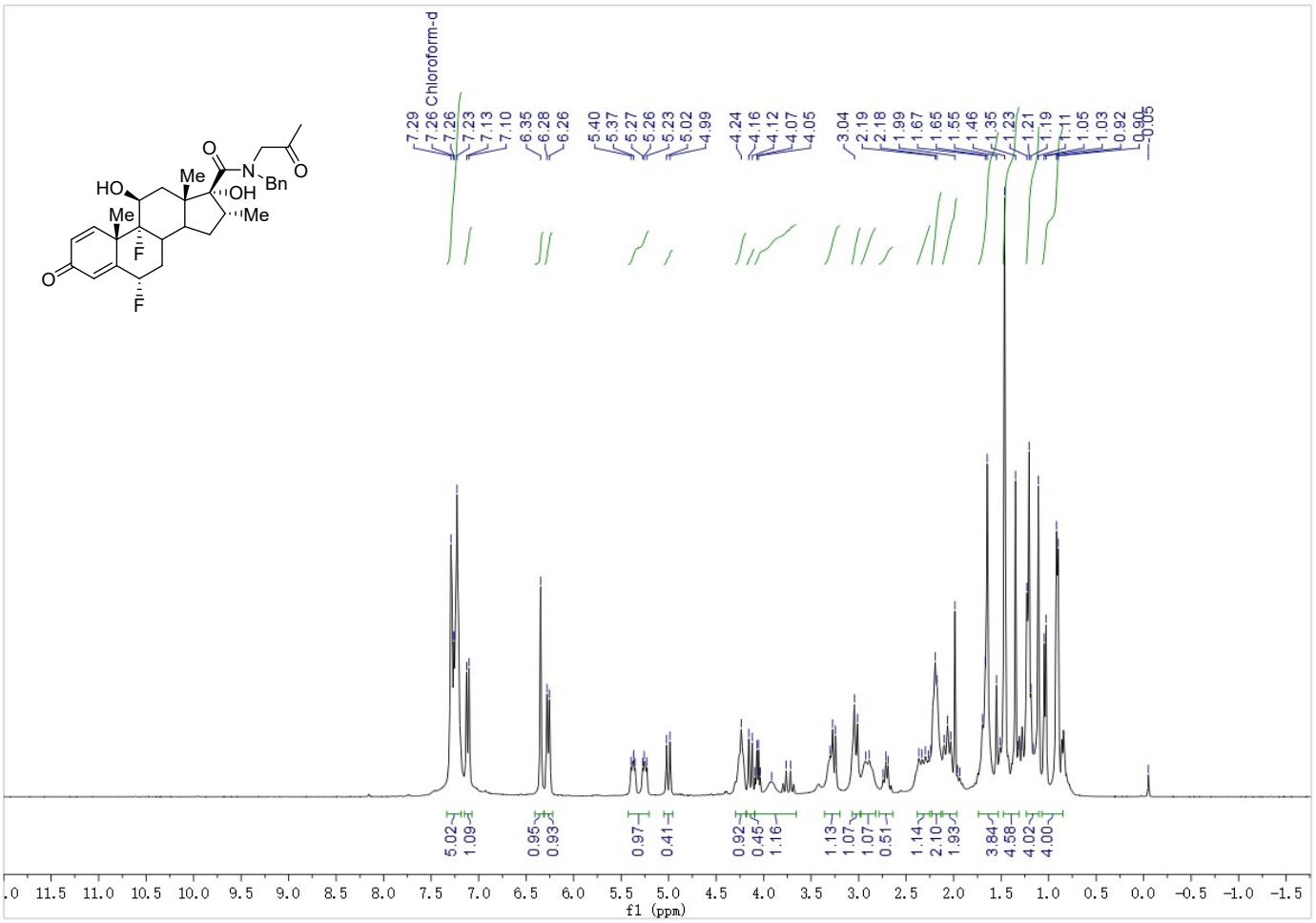

202.95
202.64
172.64
172.42
135.95
135.81
129.63
128.53
128.47
126.70
126.39
104.24
103.60
77.16 Chloroform-d
60.22
56.27
55.03
54.65
52.22
49.13
27.18
26.81
f1 (ppm)

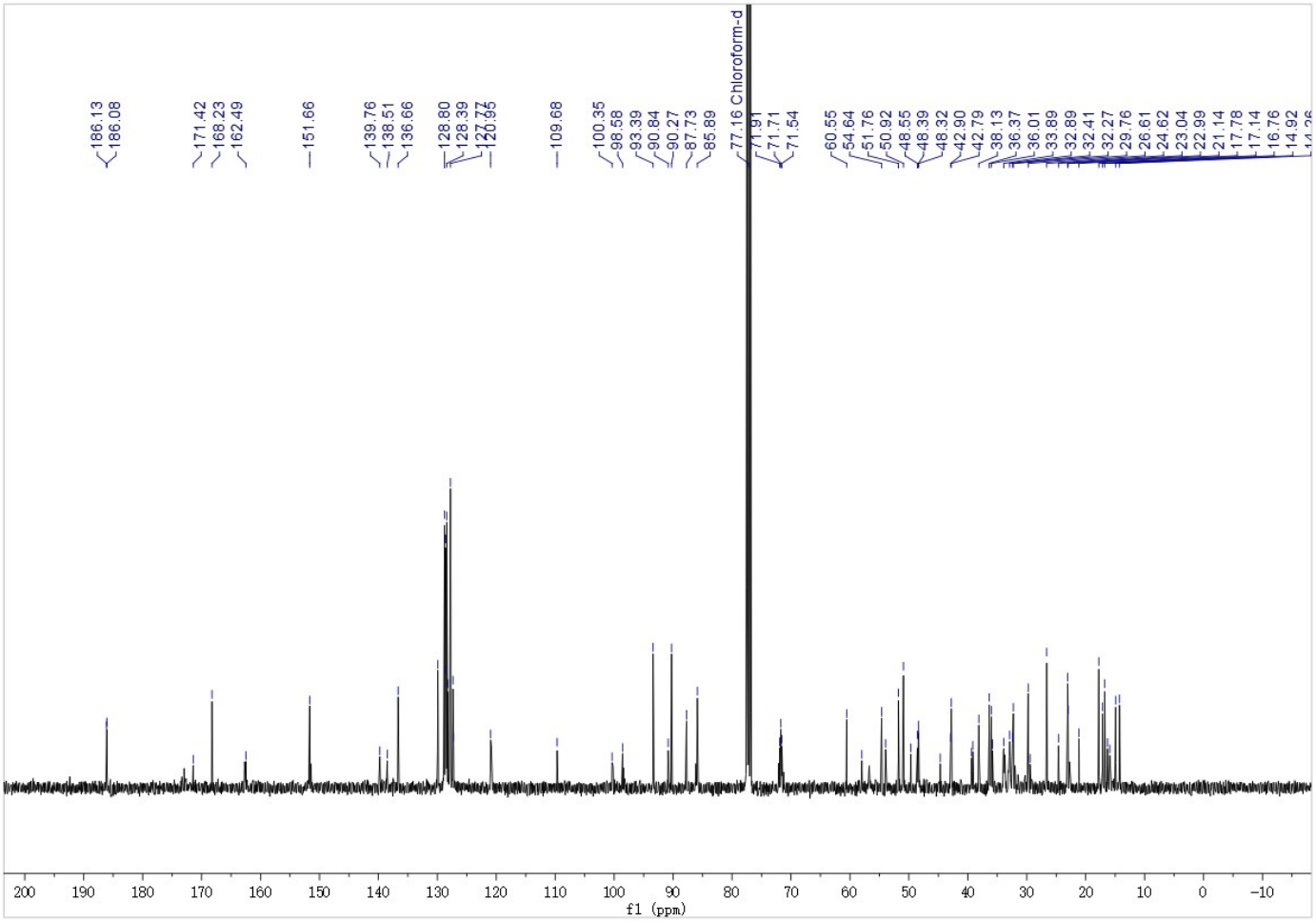

7.53
7.52
7.40
7.36
7.26 Chloroform-d
7.23
7.21
7.09
7.07
6.89
6.87
4.71
4.50
4.19
3.89
3.80
2.16
1.89
O
O
N
OMe
5.00
4.00
2.00
2.00
3.00
3.00
f1 (ppm)

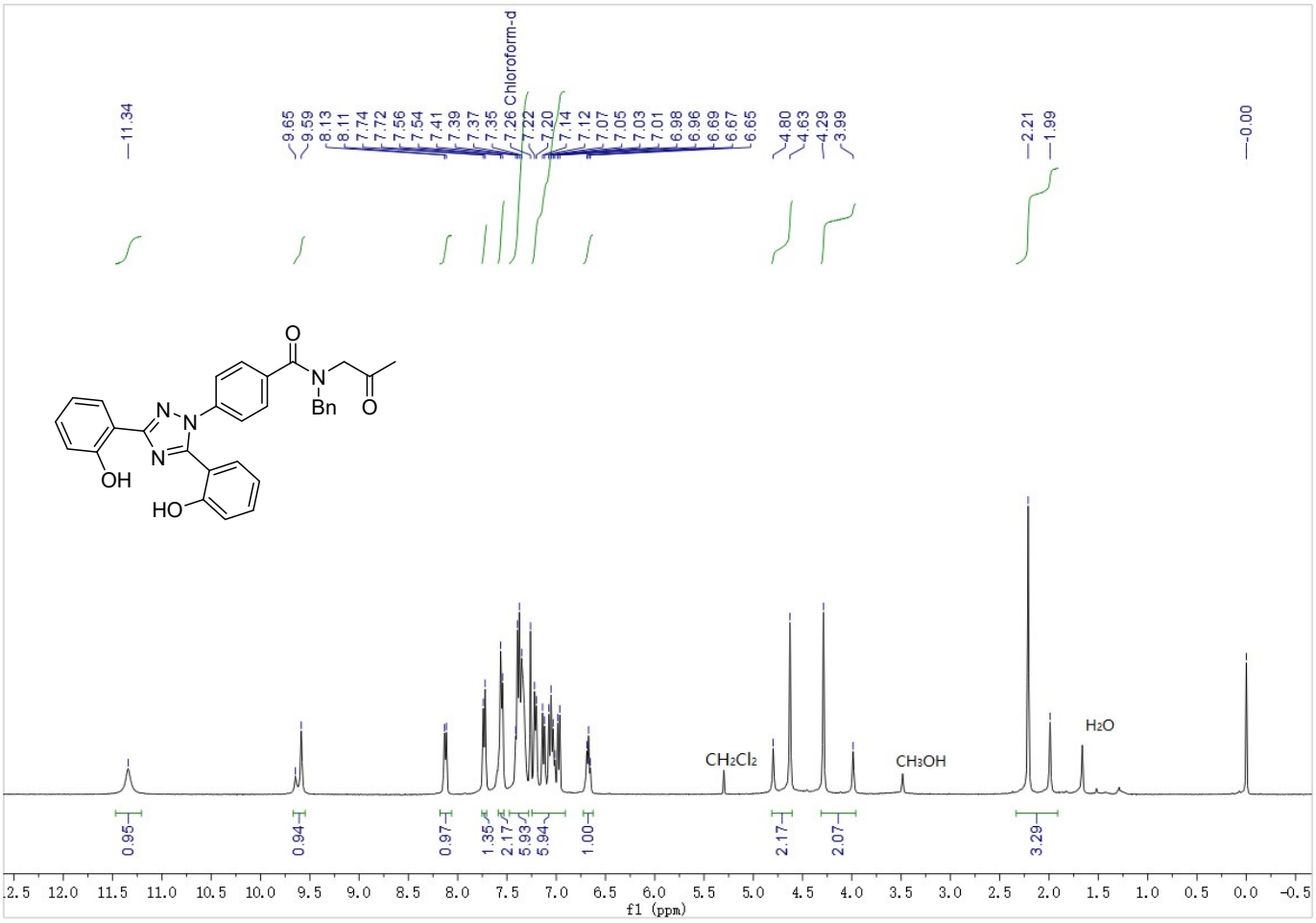

203.15
202.71
172.22
159.27
136.09
135.45
129.94
129.87
129.73
128.53
128.40
127.96
126.91
126.33
114.31
113.79
77.48
77.16 Chloroform-d
76.84
57.35
55.28
53.89
53.27
48.41
27.47
27.02
f1 (ppm)

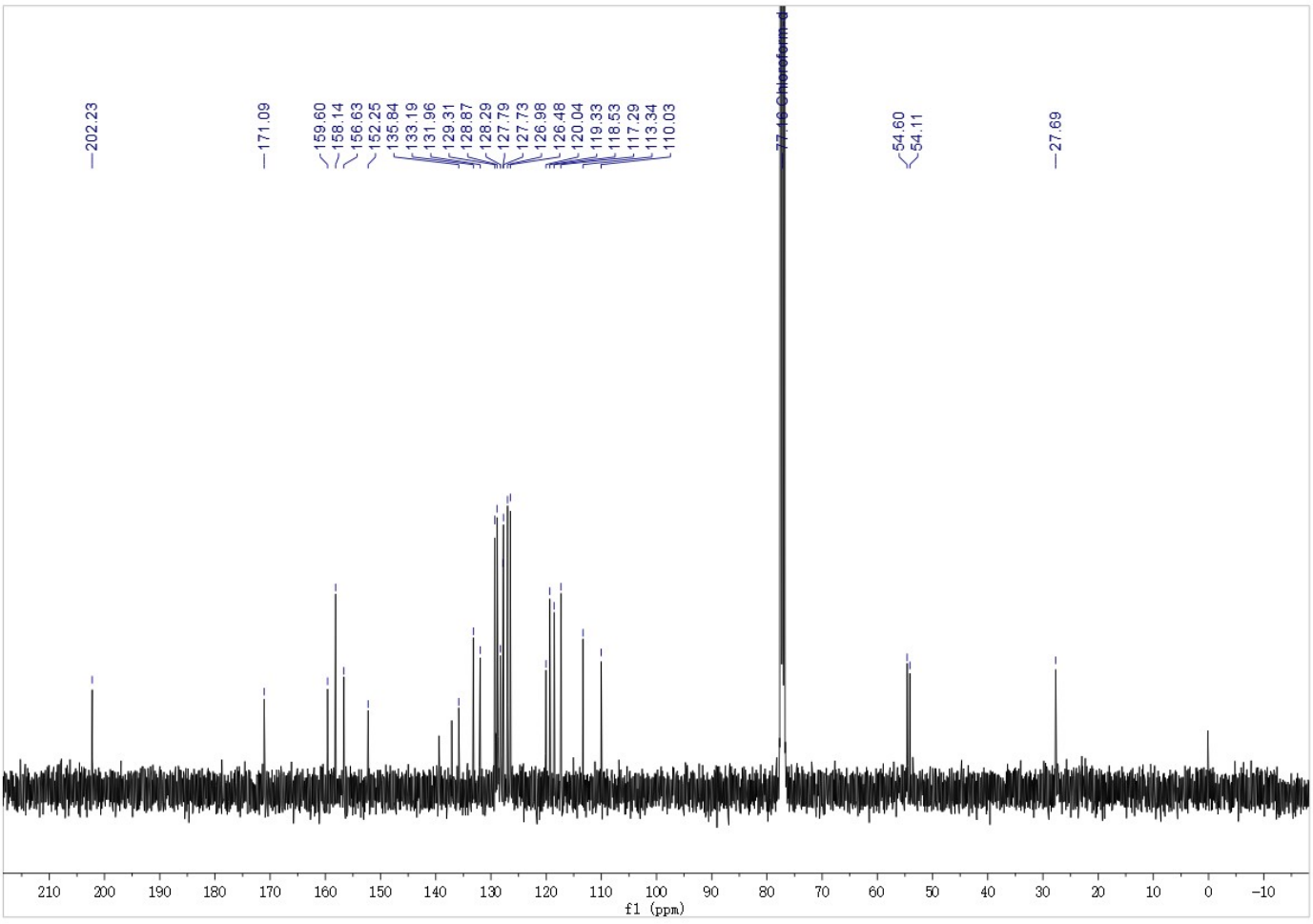

7.69
7.67
7.53
7.51
7.48
7.46
7.42
7.40
7.31
7.29
7.28
7.26 Chloroform-d
7.19
7.17
7.07
7.06
6.99
6.93
6.91
6.89
6.87
6.68
6.67
6.64
4.69
4.63
4.14
4.06
3.83
3.81
3.62
2.33
2.25
2.11
1.88
Cl
O
N
Me
O
N
Bn
O
MeO
4.15
3.12
2.08
2.07
1.04
2.00
2.09
3.03
2.00
3.12
3.11
f1 (ppm)

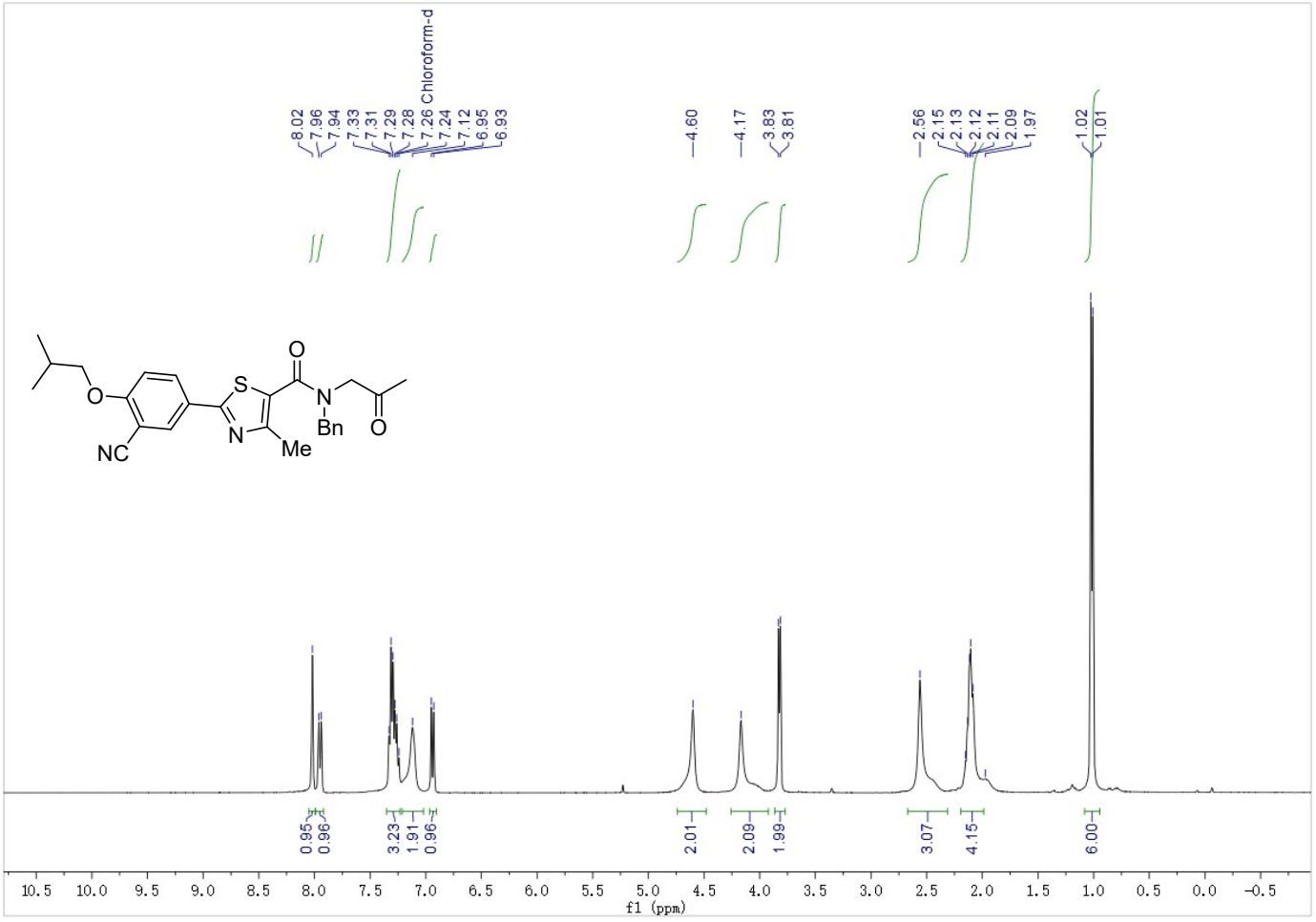

202.83
202.42
171.01
170.64
168.33
168.21
156.23
156.12
136.10
135.23
131.15
130.86
129.14
129.06
129.01
128.72
127.88
126.42
115.12
114.99
113.16
112.02
111.87
111.17
101.08
77.16 Chloroform-d
56.49
55.73
55.69
55.63
52.43
50.22
30.09
29.73
27.39
26.80
13.54
f1 (ppm)

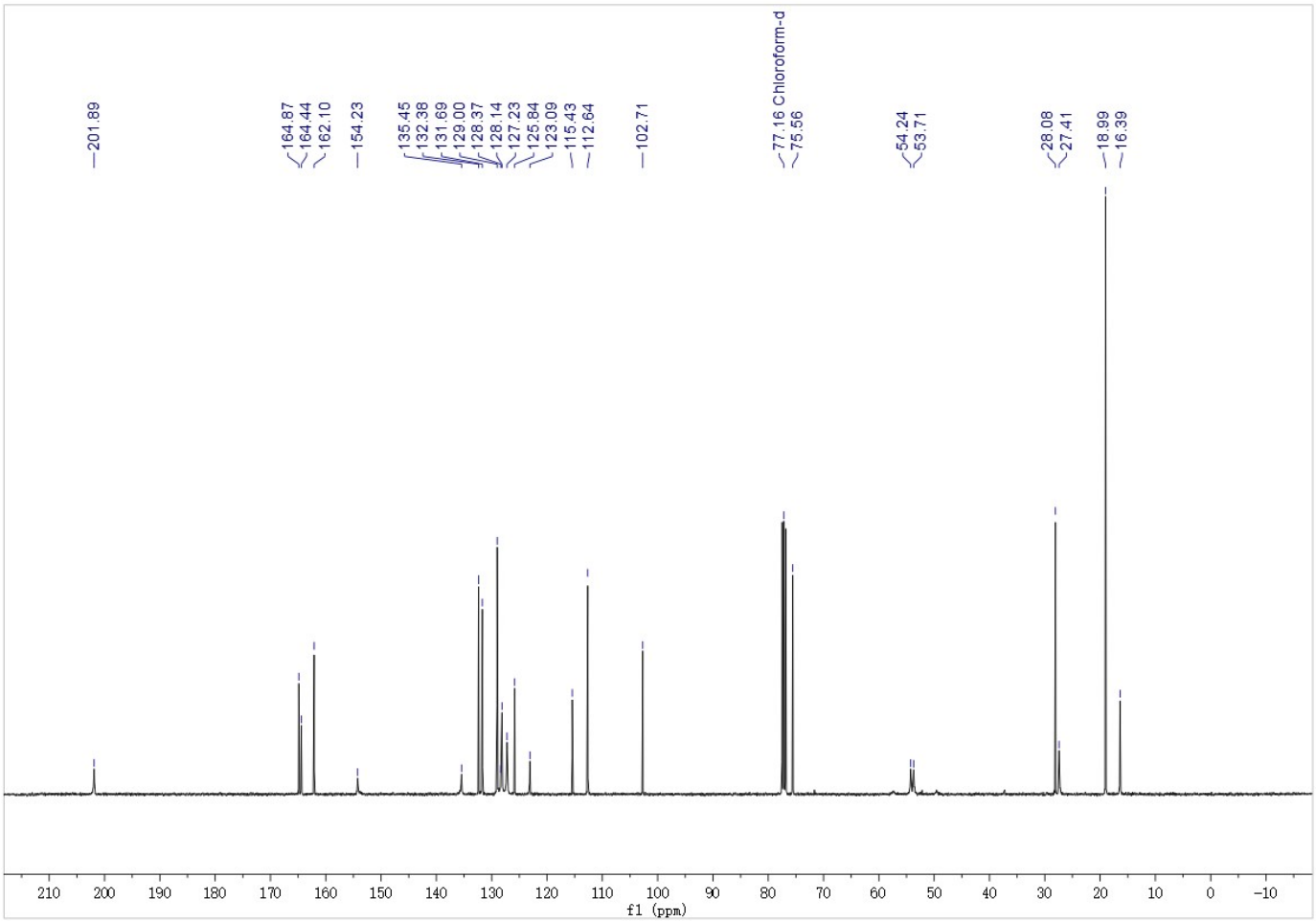

HO
Me
Me
F
O
F
Me
OH
N
Bn
O
O
7.29
7.26 Chloroform-d
7.26
7.23
7.13
7.10
6.35
6.28
6.26
5.40
5.37
5.27
5.26
5.23
5.02
4.99
4.24
4.16
4.12
4.07
4.05
3.04
2.19
2.18
1.99
1.67
1.65
1.55
1.46
1.35
1.23
1.21
1.19
1.11
1.05
1.03
0.92
0.90
0.05
5.02
1.09
0.95
0.93
0.97
0.41
0.92
0.45
1.16
1.13
1.07
1.07
0.51
1.14
2.10
1.93
3.84
4.58
4.02
4.00
f1 (ppm)

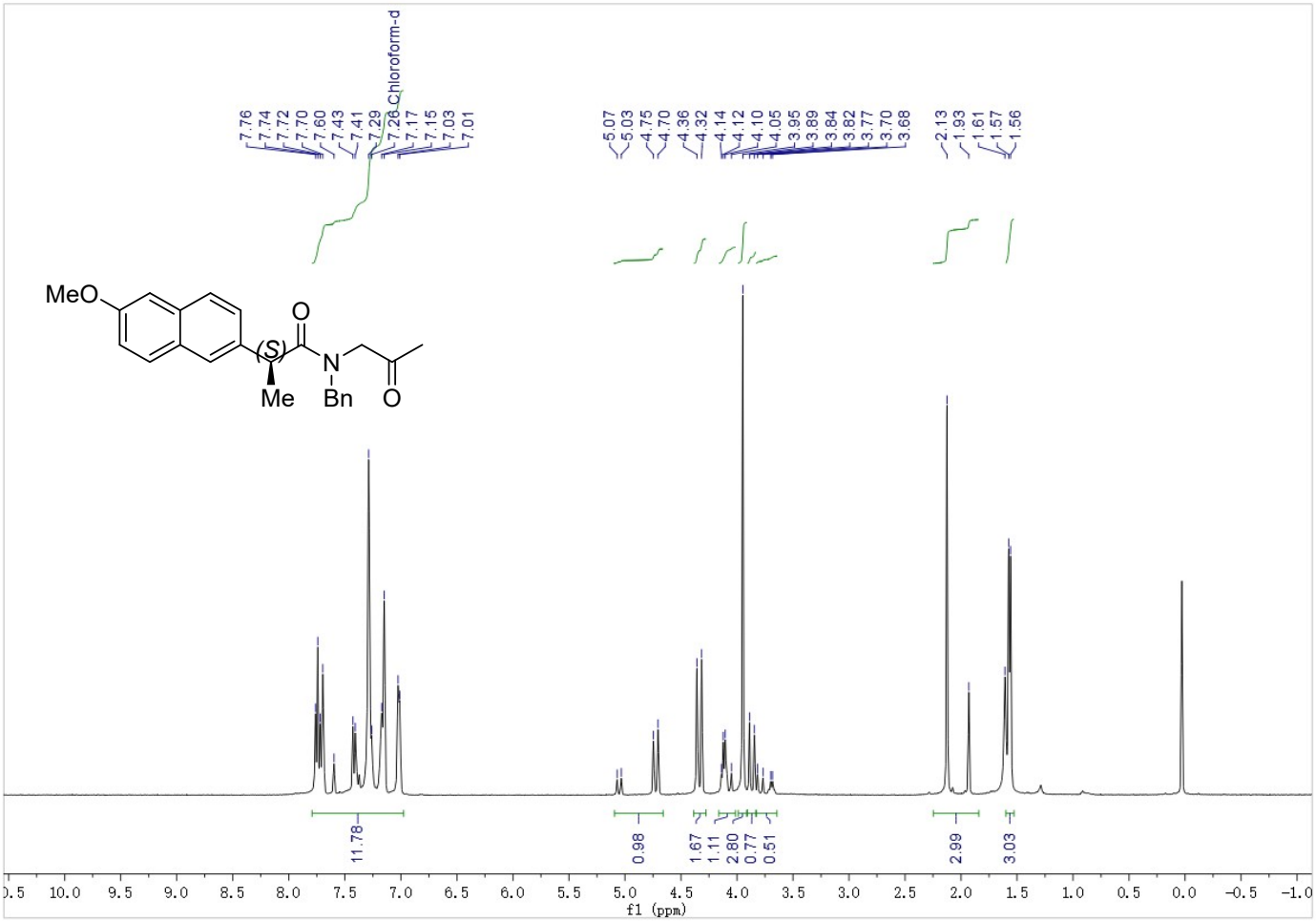

186.13
186.08
171.42
168.23
162.49
151.66
139.76
138.51
136.66
128.80
128.39
109.68
100.35
98.58
93.39
90.84
90.27
87.73
85.89
77.16 Chloroform-d
71.91
71.71
71.54
60.55
54.64
51.76
50.92
48.55
48.39
48.32
42.90
42.79
38.13
36.37
36.01
33.89
32.89
32.41
32.27
29.76
26.61
24.62
23.04
22.99
21.14
17.78
17.14
16.76
14.92
f1 (ppm)

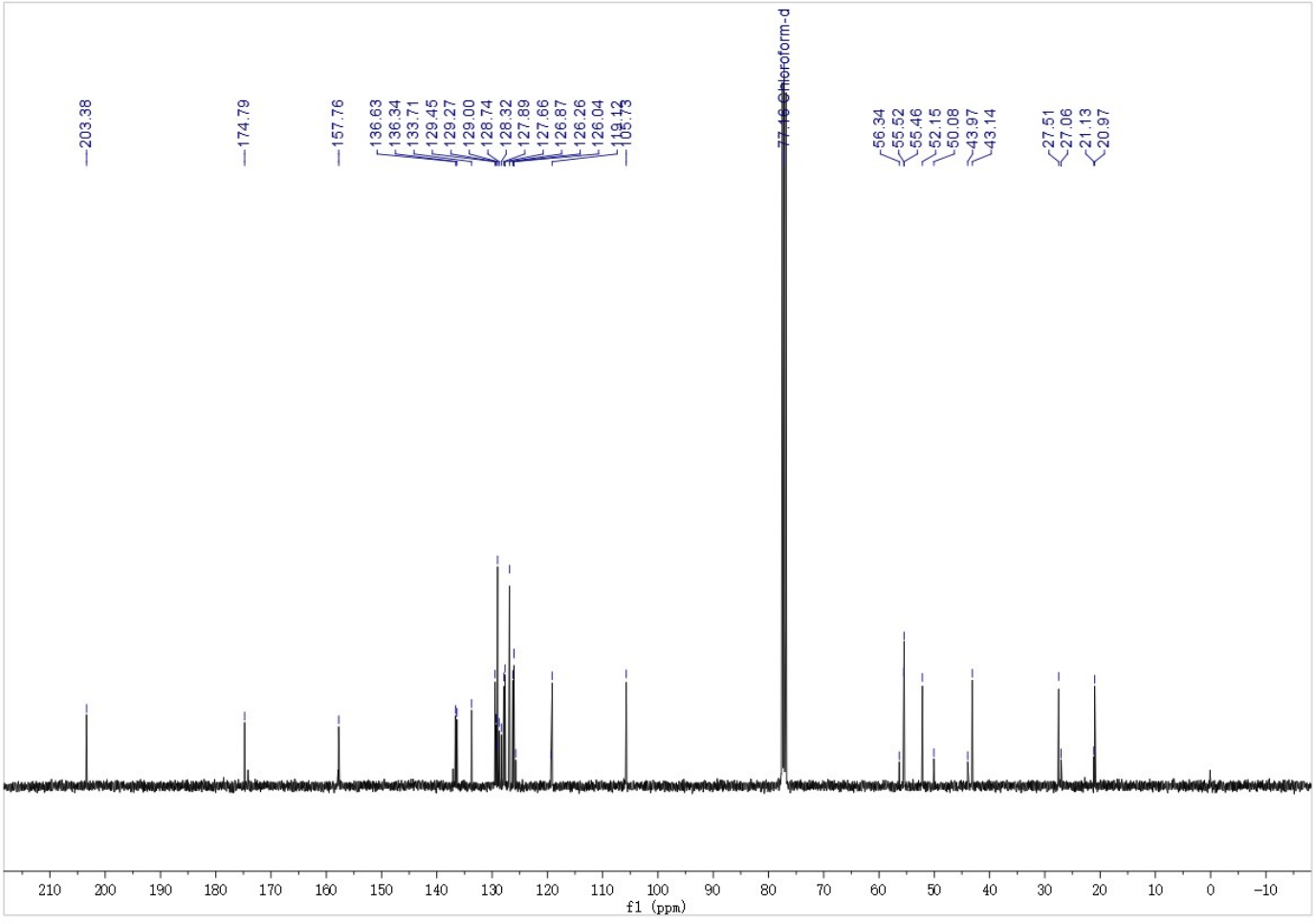

11.34
9.65
9.59
8.13
8.11
7.74
7.72
7.56
7.54
7.41
7.39
7.37
7.35
7.26 Chloroform-d
7.22
7.20
7.14
7.12
7.07
7.05
7.03
7.01
6.98
6.96
6.69
6.67
6.65
4.80
4.63
4.29
3.99
2.21
1.99
0.00
O
N
Bn
O
N
N
N
OH
HO
CH2Cl2
CH3OH
H2O
0.95
0.94
0.97
1.35
2.17
5.93
5.94
1.00
2.17
2.07
3.29
f1 (ppm)


202.23
171.09
159.60
158.14
156.63
152.25
135.84
133.19
131.96
129.31
128.87
128.29
127.79
127.73
126.98
126.48
120.04
119.33
118.53
117.29
113.34
110.03
77.16 Chloroform-d
54.60
54.11
27.69
f1 (ppm)


8.02
7.96
7.94
7.33
7.31
7.29
7.28
7.26 Chloroform-d
7.24
7.12
6.95
6.93
4.60
4.17
3.83
3.81
2.56
2.15
2.13
2.12
2.11
2.09
1.97
1.02
1.01
O
S
N
O
N
Bn
O
O
N
Me
NC
0.95
0.96
3.23
1.91
0.96
2.01
2.09
1.99
3.07
4.15
6.00
f1 (ppm)


201.89
164.87
164.44
162.10
154.23
135.45
132.38
131.69
129.00
128.37
128.14
127.23
125.84
123.09
115.43
112.64
102.71
77.16 Chloroform-d
75.56
54.24
53.71
28.08
27.41
18.99
16.39
f1 (ppm)


7.76
7.74
7.72
7.70
7.60
7.43
7.41
7.29
7.26 Chloroform-d
7.17
7.15
7.03
7.01
5.07
5.03
4.75
4.70
4.36
4.32
4.14
4.12
4.10
4.05
3.95
3.89
3.84
3.82
3.77
3.70
3.68
2.13
1.93
1.61
1.57
1.56
MeO
O
(S)
N
Me
Bn
O
11.78
0.98
1.67
1.11
2.80
0.77
0.51
2.99
3.03
f1 (ppm)


203.38
174.79
157.76
136.63
136.34
133.71
129.45
129.27
129.00
128.74
128.32
127.89
127.66
126.87
126.26
126.04
77.16 Chloroform-d
56.34
55.52
55.46
52.15
50.08
43.97
43.14
27.51
27.06
21.13
20.97
f1 (ppm)