Supporting Information

Organocatalytic cascade nucleophilic/aza-Michael addition reactions: Metal-free catalytic strategy for the synthesis of hydantoins

Lei Xie,*[a] Lei Sun,[a] Ping Wu,[a] Zhaoxue Wang,[a] Chenyi Zhao,[a] Lingang Wu*[a], Xiaojing Li,[a] Zhenzhen Gao,[a] Wanxing Liu,*[b] and Shao-zhen Nie*[a]

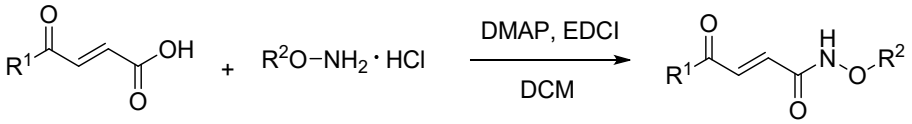
[a]*School of Pharmaceutical Sciences, College of Chemistry and Chemical Engineering, Liaocheng University.*
[b]*The Non-Public Enterprise Service Center of Liaocheng, Liaocheng 252000, Shandong, P. R. China.*

Contents

1. General information

All reactions were carried out under an atmosphere of air in oven dried glassware with magnetic stirring. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Organic solutions were concentrated under reduced pressure on a rotary evaporator or an oil pump. Flash column chromatography was performed using Qingdao Haiyang flash silica gel (100–200 mesh). NMR spectra were recorded with a Bruker Avance DPX400 spectrometer with tetramethylsilane as the internal standard. Mass spectra were acquired with an Agilent 6520 Q-TOF MS system equipped with an Electrospray ionization (ESI) source. Melting points were determined on a Stuard SMP3 melting point apparatus. X-raycrystallographic data were collected using a Bruker APEX-II CCD.

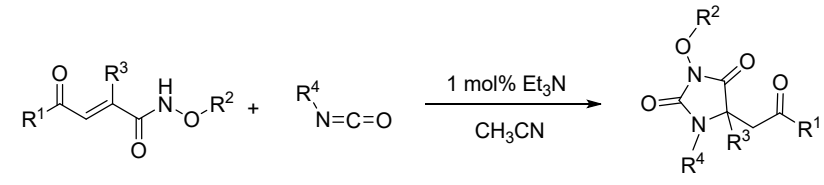
2. General procedure for the synthesis of *β*-oxo-acrylamide 1



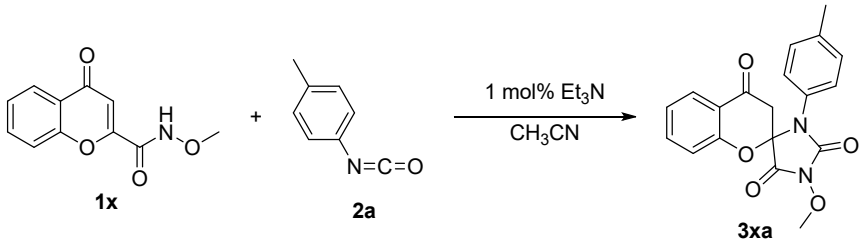
1

A mixture of EDCI (1.34g, 7 mmol, 1.4 equiv), DMAP (0.85g, 7 mmol, 1.4 equiv), aroyl or alkanoyl acrylic acids[1] (5 mmol, 1.0 equiv), and *O*-alkylhydroxylamine HCl (6 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL) was stirred at room temperature for 2 h. After completing reaction, the reaction mixture was diluted with dichloromethane (25 mL) and water (50 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane (20 mL × 3). The combined organic phase was washed with brine (20 mL), and then dried over Na_2SO_4. After filtration, the solvent was concentrated in vacuo. The crude products were purified by column chromatography with petroleum ether and ethyl acetate as an eluent.

3. General procedure for the cascade reactions of *β*-oxo-acrylamides 1 and isocyanates 2



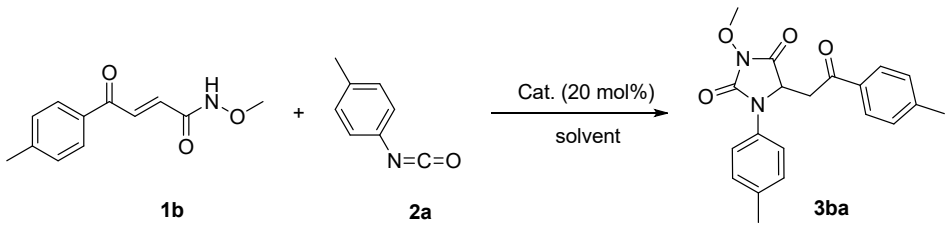
1 **2** **3**

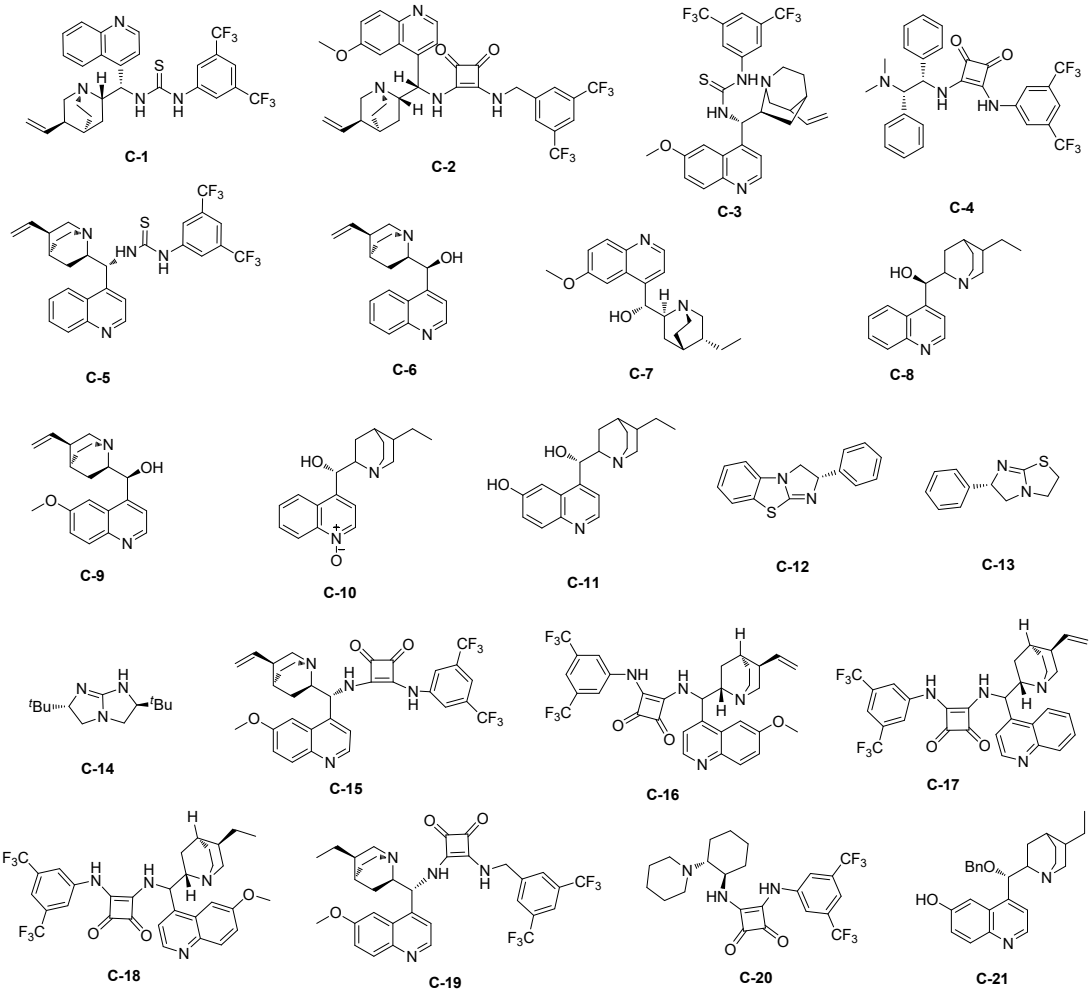


1x **2a** **3xa**

To a stirred solution of *β*-oxo-acrylamide **1** (0.20 mmol) and isocyanates **2** (0.22 mmol) in anhydrous CH_3CN (2.0 mL), Et_3N (0.01 equiv.) was added. Then the reaction mixture was stirred at room temperature and monitored by TLC. After the reaction was complete, solvent was removed under reduced pressure, the mixture was subjected to flash column chromatography (PE/EtOAc =3:1 or 1:1) to furnish the corresponding product **3**.

4. Optimization of reaction conditions for the organocatalytic asymmetric cascade reaction of *β*-oxo-acrylamides 1b and isocyanates 2a[a]





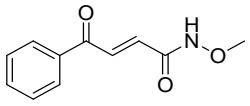
Entry	Cat.	Solvent	Time(h)	Yield(%)[b]	ee(%)[c]
1	**C-1**	DCM	24	75	0
2	**C-2**	DCM	24	73	12
3	**C-3**	DCM	24	70	-4
4	**C-4**	DCM	24	trace	nd[d]
5	**C-5**	DCM	24	76	17
6	**C-6**	DCM	24	80	2
7	**C-7**	DCM	24	77	-2
8	**C-8**	DCM	24	82	0

9	**C-9**	DCM	24	83	2
10	**C-10**	DCM	24	73	-2
11	**C-11**	DCM	24	85	25
12	**C-12**	DCM	24	65	7
13	**C-13**	DCM	24	67	0
14	**C-14**	DCM	24	trace	nd
15	**C-15**	DCM	24	88	0
16	**C-16**	DCM	24	87	31
17	**C-17**	DCM	24	83	28
18	**C-18**	DCM	24	85	20
19	**C-19**	DCM	24	80	-7
20	**C-20**	DCM	24	trace	nd
21	**C-21**	DCM	24	76	13
22	**C-16**	DCE	24	88	15
23	**C-16**	CH_3CN	24	90	5
24	**C-16**	toluene	24	75	40
25	**C-16**	$CHCl_3$	24	80	27

[a]Reactions were carried out with **1b** (0.20 mmol), **2a** (0.22 mmol), and 20 mol% catalyst in 2 mL of solvent at rt. [b]Isolated yields. .[c]Determined by HPLC analysis. [d]Not determined.

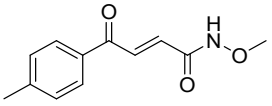
5. Characterization of the *β*-oxo-acrylamides 1

(E)-N-methoxy-4-oxo-4-phenylbut-2-enamide (1a)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1a**. White solid; mp: 106.2 – 108.4 °C; 358.8 mg; 35% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.75 (s, 1H), 8.03 (d, *J* = 6.7 Hz, 2H), 7.84 (d, *J* = 11.9 Hz, 1H), 7.70 (dd, *J* = 9.3, 3.6 Hz, 1H), 7.59 (dd, *J* = 7.3, 5.3 Hz, 2H), 6.80 (dd, *J* = 15.4, 2.8 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 189.76, 160.95, 136.91, 134.32, 133.71, 133.02, 129.50, 129.16, 63.85. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{11}H_{12}NO_3$: 206.0817, Found: 206.0847.

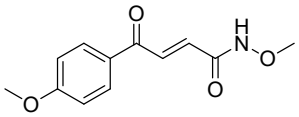
(E)-N-methoxy-4-oxo-4-(p-tolyl)but-2-enamide (1b)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1b**. White solid; mp: 106.2 – 108.6 °C; 470.9 mg; 43% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.76 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.87 (d, *J* = 15.3 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 15.3 Hz, 1H), 3.72 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 189.05, 161.12,

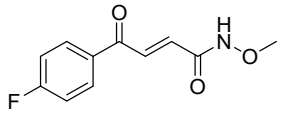
144.99, 134.41, 133.34, 133.07, 130.05, 129.31, 63.93, 21.68. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{12}H_{13}NO_3Na$: 242.0793, Found: 242.0797.

(E)-N-methoxy-4-(4-methoxyphenyl)-4-oxobut-2-enamide (1c)



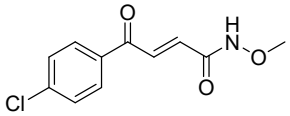
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1c**. White solid; mp: 103.6 – 105.2 °C; 305.5 mg; 26% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.74 (s, 1H), 8.05 (d, *J* = 8.8 Hz, 2H), 7.89 (d, *J* = 13.5 Hz, 1H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 15.3 Hz, 1H), 3.88 (s, 3H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 187.62, 164.24, 161.21, 133.03, 132.93, 131.66, 129.84, 114.77, 63.91, 56.11. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{12}H_{14}NO_4$: 236.0923, Found: 236.0950.

(E)-4-(4-fluorophenyl)-N-methoxy-4-oxobut-2-enamide (1d)



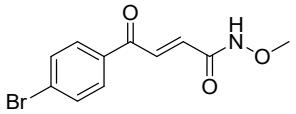
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1d**. White solid; mp: 112.4 – 113.9 °C; 412.6 mg; 37% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.73 (s, 1H), 8.16 – 8.09 (m, 2H), 7.83 (d, *J* = 12.7 Hz, 1H), 7.42 – 7.34 (m, 2H), 6.80 (d, *J* = 15.3 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 188.24, 165.84 (d, *J* = 253.0 Hz), 160.99, 133.78, 133.64, 132.85, 132.27 (d, *J* = 9.6 Hz), 116.53 (d, *J* = 22.0 Hz), 63.81. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{11}H_{11}FNO_3$: 224.0723, Found: 224.0752.

(E)-4-(4-chlorophenyl)-N-methoxy-4-oxobut-2-enamide (1e)



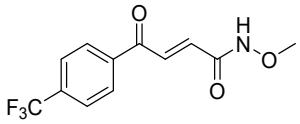
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1e**. White solid; mp: 113.5 – 115.5 °C; 394.4 mg; 33% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.74 (s, 1H), 8.11 – 8.02 (m, 2H), 7.90 – 7.77 (m, 1H), 7.67 – 7.62 (m, 2H), 6.83 (d, *J* = 15.3 Hz, 1H), 3.74 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 188.65, 157.29, 139.27, 135.56, 134.01, 132.51, 131.06, 129.57, 63.79. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{11}H_{11}ClNO_3$: 240.0427, Found: 240.0475.

(E)-4-(4-bromophenyl)-N-methoxy-4-oxobut-2-enamide (1f)



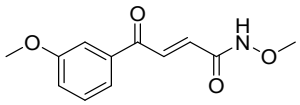
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1f**. White solid; mp: 120.7 – 122.2 °C; 367.9 mg; 26% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.73 (s, 1H), 8.00 – 7.95 (m, 2H), 7.86 – 7.76 (m, 3H), 6.81 (d, *J* = 15.3 Hz, 1H), 3.73 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 188.90, 160.67, 135.90, 134.04, 132.54, 131.14, 128.51, 63.79. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{11}H_{11}BrNO_3$: 283.9922, Found: 283.9948.

(E)-N-methoxy-4-oxo-4-(4-(trifluoromethyl)phenyl)but-2-enamide (1g)



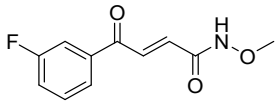
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1g**. White solid; mp: 105.3 – 107.8 °C; 398.3 mg; 27% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.78 (s, 1H), 8.22 (d, *J* = 8.1 Hz, 2H), 7.94 (d, *J* = 8.3 Hz, 2H), 7.84 (d, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 15.4 Hz, 1H), 3.74 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 189.34, 160.78, 140.09, 134.55, 133.35 (q, *J* = 31.6 Hz), 132.78, 129.95, 126.35 (q, *J* = 3.4 Hz), 124.16 (q, *J* = 272.8 Hz), 63.81. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{12}H_{10}NO_3NaF_3$: 296.0516, Found: 296.0510.

(E)-N-methoxy-4-(3-methoxyphenyl)-4-oxobut-2-enamide (1h)



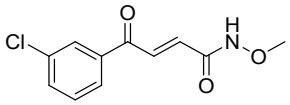
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1h**. White solid; mp: 90.4 – 92.9 °C; 352.5 mg; 30% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.75 (s, 1H), 7.83 (d, *J* = 15.3 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.27 (d, *J* = 8.1 Hz, 1H), 6.80 (d, *J* = 15.4 Hz, 1H), 3.84 (s, 3H), 3.70 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 189.52 (s), 161.05 (s), 160.06 (s), 138.28 (s), 133.74 (s), 133.09 (s), 130.66 (s), 121.81 (s), 120.59 (s), 113.21 (s), 63.94 (s), 55.84 (s). HRMS (ESI) m/z $[M+H]^+$calcd for $C_{12}H_{14}NO_4$: 236.0923, Found: 236.0956.

(E)-4-(3-fluorophenyl)-N-methoxy-4-oxobut-2-enamide (1i)



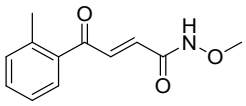
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1i**. White solid; mp: 95.3 – 98.1 °C; 423.7 mg; 38% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.77 (s, 1H), 7.90 (d, *J* = 7.5 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.64 (dt, *J* = 13.8, 3.9 Hz, 1H), 7.57 (t, *J* = 8.1 Hz, 1H), 6.82 (dd, *J* = 15.3, 2.0 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 188.77, 162.75 (d, *J* = 245.8 Hz), 160.89, 139.07, 134.27, 132.79, 131.74 (d, *J* = 7.9 Hz), 125.51, 121.24 (d, *J* = 21.2 Hz), 115.52 (d, *J* = 22.6 Hz), 63.93. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{11}H_{11}FNO_3$: 224.0723, Found: 224.0752.

(E)-4-(3-chlorophenyl)-N-methoxy-4-oxobut-2-enamide (1j)



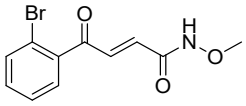
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1j**. White solid; mp: 99.5 – 102.0 °C; 442.2 mg; 37% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.72 (s, 1H), 7.99 (t, *J* = 4.2 Hz, 2H), 7.88 – 7.76 (m, 1H), 7.76 – 7.73 (m, 1H), 7.62 – 7.58 (m, 1H), 6.80 (d, *J* = 15.4 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 188.71, 160.77, 138.71, 134.41, 134.30, 133.91, 132.61, 131.42, 128.63, 127.85, 63.75. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{11}H_{11}ClNO_3$: 240.0427, Found: 240.0437.

(E)-N-methoxy-4-oxo-4-(o-tolyl)but-2-enamide (1k)



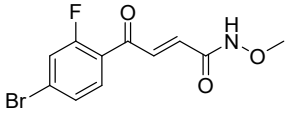
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1k**. White solid; mp: 112.5 – 114.6 °C; 284.7 mg; 26% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.67 (s, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 6.6 Hz, 3H), 6.57 (d, *J* = 15.6 Hz, 1H), 3.70 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 194.69, 160.86, 137.58, 136.33, 134.38, 131.99, 131.96, 129.35, 126.36, 63.79, 20.57. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{12}H_{13}NO_3Na$: 242.0793, Found: 242.0797.

(E)-4-(2-bromophenyl)-N-methoxy-4-oxobut-2-enamide (1l)



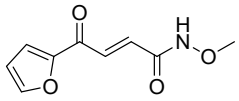
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1l**. White solid; mp: 95.9 – 98.2 °C; 353.8 mg; 25% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.66 (s, 1H), 7.76 (d, *J* = 7.7 Hz, 1H), 7.57 – 7.52 (m, 2H), 7.49 (ddd, *J* = 7.9, 6.4, 2.9 Hz, 1H), 7.18 (d, *J* = 14.5 Hz, 1H), 6.49 (d, *J* = 15.7 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 194.13, 160.27, 139.89, 135.86, 135.50, 133.77, 132.95, 129.90, 128.44, 118.97, 63.72. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{11}H_{11}BrNO_3$: 283.9922, Found: 283.9943.

(E)-4-(4-bromo-2-fluorophenyl)-N-methoxy-4-oxobut-2-enamide (1m)



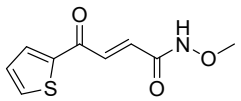
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1m**. White solid; mp: 132.8 – 133.6 °C; 526.8 mg; 35% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.72 (s, 1H), 7.82 – 7.71 (m, 2H), 7.61 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.56 – 7.44 (m, 1H), 6.74 (d, *J* = 15.4 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 187.65, 160.93 (d, *J* = 258.0 Hz), 134.12, 132.68 (d, *J* = 2.4 Hz), 128.83 (d, *J* = 3.3 Hz), 127.98 (d, *J* = 10.5 Hz), 125.12 (d, *J* = 12.2 Hz), 120.84, 120.64, 63.89. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{11}H_{10}BrFNO_3$: 301.9828, Found: 301.9859.

(E)-4-(furan-2-yl)-N-methoxy-4-oxobut-2-enamide (1n)



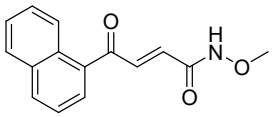
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1n**. Yellow solid; mp: 121.8 – 123.5 °C; 360.8 mg; 37% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.75 (s, 1H), 8.14 (d, *J* = 1.0 Hz, 1H), 7.81 (d, *J* = 2.7 Hz, 1H), 7.70 (d, *J* = 12.1 Hz, 1H), 6.87 (d, *J* = 15.3 Hz, 1H), 6.82 (dd, *J* = 3.6, 1.6 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 176.28, 160.81, 152.67, 149.81, 132.91, 132.66, 121.48, 113.66, 63.86. HRMS (ESI) m/z $[M+H]^+$calcd for $C_9H_{10}NO_4$: 196.0610, Found: 196.0637.

(E)-N-methoxy-4-oxo-4-(thiophen-2-yl)but-2-enamide (1o)



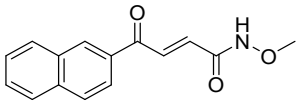
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1o**. White solid; mp: 103.2 – 105.6 °C; 400.9 mg; 38% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.76 (s, 1H), 8.18 (d, *J* = 37.8 Hz, 2H), 7.81 (d, *J* = 14.5 Hz, 1H), 7.31 (d, *J* = 3.7 Hz, 1H), 6.83 (d, *J* = 14.7 Hz, 1H), 3.70 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 181.54, 160.91, 144.47, 137.46, 135.48, 133.13, 132.75, 129.78, 63.96. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_9H_9NO_3SNa$: 234.0201, Found: 234.0208.

(E)-N-methoxy-4-(naphthalen-1-yl)-4-oxobut-2-enamide (1p)



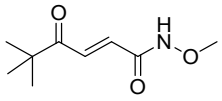
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1p**. White solid; mp: 137.1 – 138.2 °C; 548.3 mg; 43% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.71 (s, 1H), 8.38 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 8.06 (d, *J* = 7.4 Hz, 1H), 8.00 (d, *J* = 6.9 Hz, 1H), 7.64 (dt, *J* = 22.5, 11.6 Hz, 4H), 6.71 (d, *J* = 15.6 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 193.97, 160.87, 136.75, 134.94, 134.46, 133.91, 133.34, 130.18, 129.55, 129.13, 128.46, 127.17, 125.55, 125.37, 63.86. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{15}H_{13}NO_3Na$: 278.0793, Found: 278.0793.

(E)-N-methoxy-4-(naphthalen-2-yl)-4-oxobut-2-enamide (1q)



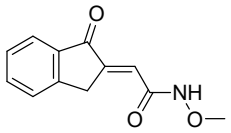
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1q**. White solid; mp: 142.7 – 143.4 °C; 573.8 mg; 45% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.79 (s, 1H), 8.83 (s, 1H), 8.21 (d, *J* = 8.1 Hz, 1H), 8.03 (dt, *J* = 16.3, 8.3 Hz, 4H), 7.67 (dt, *J* = 14.8, 7.1 Hz, 2H), 6.89 (d, *J* = 15.3 Hz, 1H), 3.74 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 189.33, 161.13, 135.76, 134.25, 133.64, 133.07, 132.70, 131.71, 130.38, 129.59, 129.21, 128.17, 127.56, 124.21, 55.49. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{15}H_{13}NO_3Na$: 278.0793, Found: 278.0793.

(E)-N-methoxy-5,5-dimethyl-4-oxohex-2-enamide (1r)



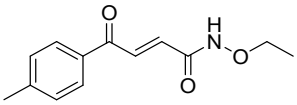
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1r**. White solid; mp: 110.8 – 112.5 °C; 138.8 mg; 15% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.66 (s, 1H), 7.44 (d, *J* = 13.1 Hz, 1H), 6.67 (d, *J* = 15.3 Hz, 1H), 3.69 (s, 3H), 1.13 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 203.64, 160.96, 132.41, 132.04, 63.79, 43.46, 25.82. HRMS (ESI) m/z $[M+H]^+$calcd for $C_9H_{16}NO_3$: 186.1130, Found: 186.1159.

(E)-N-methoxy-2-(1-oxo-1H-inden-2(3H)-ylidene)acetamide (1s)



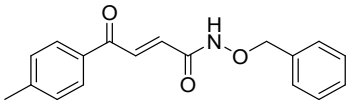
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1s**. White solid; mp: 158.3 – 159.4 °C; 368.9 mg; 34% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.73 (s, 1H), 7.81 – 7.72 (m, 2H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 6.61 (s, 1H), 4.12 (s, 2H), 3.73 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 193.66, 162.20, 151.49, 146.60, 136.98, 136.26, 128.25, 127.42, 124.30, 120.87, 63.92, 32.18. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{12}H_{11}NO_3Na$: 240.0637, Found: 240.0643.

(E)-N-ethoxy-4-oxo-4-(p-tolyl)but-2-enamide (1t)



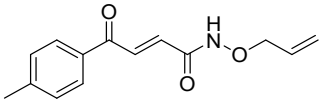
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1t**. White solid; mp: 120.7 – 122.2 °C; 454.4 mg; 39% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.61 (s, 1H), 7.95 (d, *J* = 8.2 Hz, 2H), 7.84 (d, *J* = 14.8 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 15.3 Hz, 1H), 3.92 (t, *J* = 15.9 Hz, 2H), 2.41 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 189.06, 161.19, 144.92, 134.47, 133.57, 132.90, 130.05, 129.28, 71.39, 21.68, 14.00. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{16}NO_3$: 234.1130, Found: 234.1160.

(E)-N-(benzyloxy)-4-oxo-4-(p-tolyl)but-2-enamide (1u)



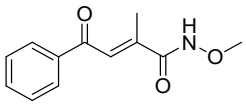
Flash column chromatography on silica gel (eluent: PE/EtOAc = 5/1, v/v) was performed to afford **1u**. White solid; mp: 98.4 – 100.7 °C; 634.3 mg; 43% yield; ^{1}H NMR (500 MHz, DMSO) δ 11.72 (s, 1H), 7.93 (t, *J* = 8.9 Hz, 2H), 7.86 (d, *J* = 12.5 Hz, 1H), 7.47 – 7.36 (m, 7H), 6.82 (d, *J* = 15.3 Hz, 1H), 4.94 (s, 2H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 189.06, 161.39, 144.95, 136.21, 134.47, 133.44, 133.06, 130.07, 129.29, 128.86, 77.51, 21.70. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{18}H_{18}NO_3$: 296.1287, Found: 296.1289.

(E)-N-(allyloxy)-4-oxo-4-(p-tolyl)but-2-enamide (1v)



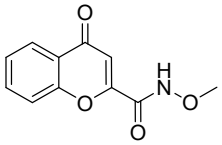
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1v**. White solid; mp: 75.4 – 77.1 °C; 392.0 mg; 32% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.10 (d, *J* = 14.7 Hz, 1H), 7.96 (d, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.17 (dd, *J* = 25.3, 11.2 Hz, 1H), 6.03 (dd, *J* = 16.6, 10.0 Hz, 1H), 5.38 (d, *J* = 17.1 Hz, 1H), 5.31 (d, *J* = 10.0 Hz, 1H), 4.53 (s, 2H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.21, 162.33, 145.27, 134.16, 133.78, 132.27, 131.89, 129.64, 129.14, 121.08, 77.62, 21.79. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{14}H_{16}NO_3$: 246.1130, Found: 246.1176.

(E)-N-methoxy-2-methyl-4-oxo-4-phenylbut-2-enamide (1w)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **1w**. White solid; mp: 74.4 – 75.1 °C; 459.9 mg; 42% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.23 (s, 1H), 7.83 (d, *J* = 7.7 Hz, 2H), 7.46 (t, *J* = 7.3 Hz, 1H), 7.34 (dd, *J* = 15.2, 7.5 Hz, 3H), 3.72 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.32, 166.93, 142.82, 137.44, 133.64, 128.77, 128.59, 128.01, 64.22, 14.97. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{12}H_{13}NO_3Na$: 242.0793, Found: 242.0797.

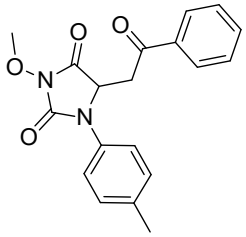
N-methoxy-4-oxo-4H-chromene-2-carboxamide (1x)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 1/1, v/v) was performed to afford **1x**. White solid; mp: 186.4 – 187.1 °C; 503.7 mg; 46% yield; ^{1}H NMR (500 MHz, DMSO) δ 12.59 (s, 1H), 8.05 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.93 – 7.86 (m, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 6.83 (s, 1H), 3.81 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 177.40, 156.68, 155 .50, 155.32, 135.51, 126.52, 125.39, 124.17, 119.15, 111.19, 64.00. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{11}H_{10}NO_4$: 220.0610, Found: 220.0614.

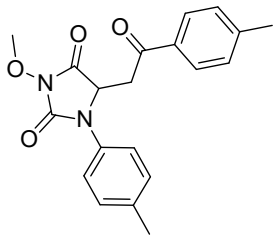
6. Characterization of the hydantoins 3

3-methoxy-5-(2-oxo-2-phenylethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3aa)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3aa**. White solid; mp: 133.8 – 135.2 °C; 66.2 mg; 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.19 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 4.86 (t, *J* = 3.9 Hz, 1H), 4.16 (s, 3H), 3.60 (dd, *J* = 18.3, 4.3 Hz, 1H), 3.53 (dd, *J* = 18.3, 3.6 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.83, 166.75, 151.38, 136.48, 135.69, 133.84, 131.88, 130.15, 128.72, 127.99, 123.18, 64.95, 54.94, 36.28, 20.94. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{19}N_2O_4$: 339.1345, Found: 339.1354.

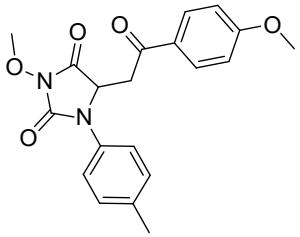
3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3ba)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford

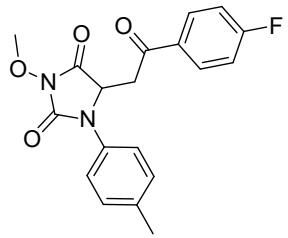
3ba. White solid; mp:137.2 – 139.2 °C; 69.0 mg; 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.12 (dd, *J* = 8.4, 2.1 Hz, 4H), 7.06 (d, *J* = 8.3 Hz, 2H), 4.77 (t, *J* = 3.9 Hz, 1H), 4.09 (s, 3H), 3.51 (dd, *J* = 18.3, 4.3 Hz, 1H), 3.42 (dd, *J* = 18.2, 3.5 Hz, 1H), 2.30 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.36, 166.83, 151.40, 144.84, 136.43, 133.25, 131.91, 130.12, 129.39, 128.11, 123.20, 64.93, 54.98, 36.16, 21.69, 20.94. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{21}N_2O_4$: 353.1501, Found: 353.1517.

3-methoxy-5-(2-(4-methoxyphenyl)-2-oxoethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3ca)



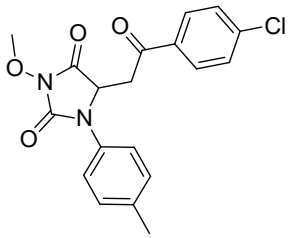
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3ca**. White solid; mp: 122.4 – 123.6 °C; 69.9 mg; 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 – 7.65 (m, 2H), 7.12 (d, *J* = 8.5 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.9 Hz, 2H), 4.77 (t, *J* = 3.9 Hz, 1H), 4.09 (s, 3H), 3.77 (s, 3H), 3.48 (dd, *J* = 18.1, 4.3 Hz, 1H), 3.40 (dd, *J* = 18.1, 3.5 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.08, 166.89, 164.04, 151.41, 136.40, 131.94, 130.35, 130.11, 128.78, 123.20, 113.86, 64.93, 55.54, 55.03, 35.93, 20.94. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{21}N_2O_5$: 369.1450, Found: 369.1461.

5-(2-(4-fluorophenyl)-2-oxoethyl)-3-methoxy-1-(p-tolyl)imidazolidine-2,4-dione (3da)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3da**. White solid; mp: 117.8 – 119.9 °C; 69.1 mg; 97% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.69 (m, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.99 (t, *J* = 8.5 Hz, 2H), 4.78 (t, *J* = 3.9 Hz, 1H), 4.07 (s, 3H), 3.49 (dd, *J* = 18.2, 4.3 Hz, 1H), 3.41 (dd, *J* = 18.2, 3.5 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.31, 166.70, 166.12 (d, *J* = 256.4 Hz),151.35, 136.52, 132.13 (d, *J* = 2.9 Hz), 131.84, 130.73 (d, *J* = 9.5 Hz), 130.15, 123.15, 115.91 (d, *J* = 22.1 Hz), 64.96, 54.91, 36.14, 20.93. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}FN_2O_4$: 357.1251, Found: 357.1260.

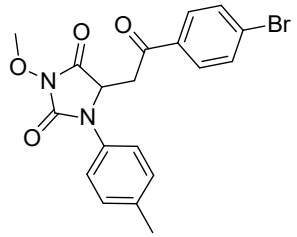
5-(2-(4-chlorophenyl)-2-oxoethyl)-3-methoxy-1-(p-tolyl)imidazolidine-2,4-dione (3ea)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford

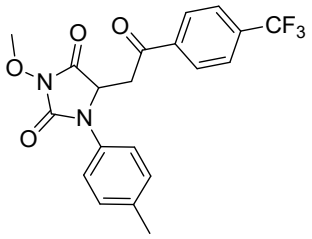
3ea. White solid; mp: 153.2 – 155.1 °C; 71.4 mg; 96% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 – 7.68 (m, 2H), 7.40 – 7.35 (m, 2H), 7.20 – 7.12 (m, 4H), 4.86 (t, *J* = 3.9 Hz, 1H), 4.15 (s, 3H), 3.56 (dd, *J* = 18.2, 4.3 Hz, 1H), 3.48 (dd, *J* = 18.2, 3.6 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.70, 166.61, 151.30, 140.45, 136.59, 133.98, 131.80, 130.18, 129.38, 129.08, 123.16, 64.98, 54.89, 36.22, 20.94.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}ClN_2O_4$: 373.0955, Found: 373.0962.

5-(2-(4-bromophenyl)-2-oxoethyl)-3-methoxy-1-(p-tolyl)imidazolidine-2,4-dione (3fa)



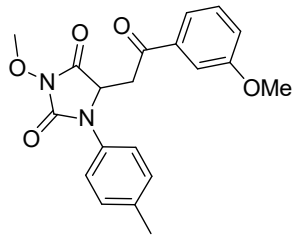
Flash column chromatography on silica gel (eluent: PE/EtOAc = 2/1, v/v) was performed to afford **3fa**. White solid; mp:172.2 – 174.9 °C; 81.5 mg; 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.6 Hz, 2H), 7.55 (d, *J* = 8.6 Hz, 2H), 7.20 – 7.12 (m, 4H), 4.85 (t, *J* = 3.9 Hz, 1H), 4.16 (s, 3H), 3.55 (dd, *J* = 18.2, 4.3 Hz, 1H), 3.48 (dd, *J* = 18.2, 3.6 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.90, 166.59, 151.29, 136.61, 134.37, 132.08, 131.78, 130.19, 129.45, 129.22, 123.17, 64.98, 54.88, 36.21, 20.95.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{19}BrN_2O_4$: 417.0450, Found: 417.0452.

3-methoxy-5-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3ga)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3ga**. White solid; mp: 152.3 – 154.2 °C; 75.5 mg; 93% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.17 (q, *J* = 8.5 Hz, 4H), 4.89 (t, *J* = 3.9 Hz, 1H), 4.16 (s, 3H), 3.61 (dd, *J* = 18.3, 4.3 Hz, 1H), 3.54 (dd, *J* = 18.3, 3.6 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.14, 166.48, 151.25, 138.25, 136.68, 135.09 (q, *J* = 32.8 Hz), 131.73, 130.22, 128.35, 125.82 (q, *J* = 3.6 Hz), 123.36 (q, *J* = 272.9 Hz), 123.15, 65.02, 54.84, 36.53, 20.92.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{18}F_3N_2O_4$: 407.1219, Found: 407.1218.

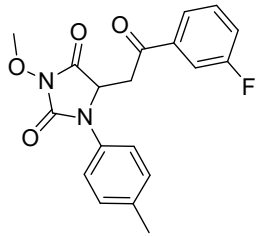
3-methoxy-5-(2-(3-methoxyphenyl)-2-oxoethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3ha)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 2/1, v/v) was performed to afford

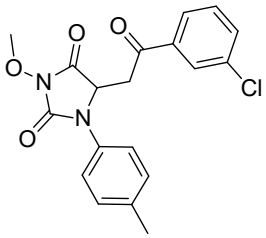
3ha. White solid; mp: 80.3 – 82.4 °C; 69.9 mg; 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 3H), 7.12 (d, *J* = 8.5 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.04 – 6.98 (m, 1H), 4.77 (t, *J* = 3.8 Hz, 1H), 4.09 (s, 3H), 3.73 (s, 3H), 3.52 (dd, *J* = 18.3, 4.2 Hz, 1H), 3.44 (dd, *J* = 18.3, 3.5 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.70, 166.75, 159.85, 151.39, 137.00, 136.48, 131.87, 130.15, 129.69, 123.18, 120.58, 120.40, 112.14, 64.97, 55.46, 54.96, 36.39, 20.94.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{21}N_2O_5$: 369.1450, Found: 369.1458.

5-(2-(3-fluorophenyl)-2-oxoethyl)-3-methoxy-1-(p-tolyl)imidazolidine-2,4-dione (3ia)



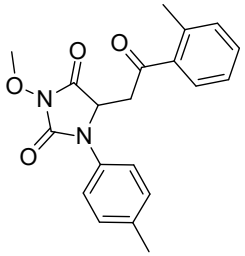
Flash column chromatography on silica gel (eluent: PE/EtOAc = 2/1, v/v) was performed to afford **3ia**. White solid; mp: 108.5 – 110.8 °C; 64.6 mg; 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.45 (d, *J* = 9.2 Hz, 1H), 7.39 (td, *J* = 8.0, 5.5 Hz, 1H), 7.24 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.17 (q, *J* = 8.5 Hz, 4H), 4.86 (t, *J* = 3.9 Hz, 1H), 4.16 (s, 3H), 3.57 (dd, *J* = 18.3, 4.3 Hz, 1H), 3.50 (dd, *J* = 18.3, 3.5 Hz, 1H), 2.30 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 193.76, 166.55, 162.75 (d, *J* = 248.9 Hz), 151.29, 137.64 (d, *J* = 6.2 Hz), 136.61, 131.78, 130.46 (d, *J* = 7.6 Hz), 130.19, 123.76 (d, *J* = 2.8 Hz), 123.16, 120.93 (d, *J* = 21.3 Hz), 114.78 (d, *J* = 22.7 Hz), 64.98, 54.86, 36.40, 20.93.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}FN_2O_4$: 357.1251, Found: 357.1259.

5-(2-(3-chlorophenyl)-2-oxoethyl)-3-methoxy-1-(p-tolyl)imidazolidine-2,4-dione (3ja)



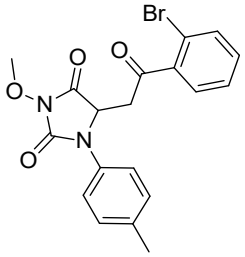
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3ja**. White solid; mp:149.6 – 151.7 °C; 68.5 mg; 92% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (t, *J* = 1.7 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.26 (t, *J* = 7.9 Hz, 1H), 7.08 (dd, *J* = 20.3, 8.5 Hz, 4H), 4.79 (t, *J* = 3.9 Hz, 1H), 4.07 (s, 3H), 3.48 (dd, *J* = 18.4, 4.3 Hz, 1H), 3.42 (dd, *J* = 18.4, 3.6 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.84, 165.54, 150.26, 136.07, 135.55, 134.02, 132.72, 130.72, 129.14, 129.04, 127.04, 125.03, 122.10, 63.93, 53.81, 35.29, 19.89. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}ClN_2O_4$: 373.0955, Found: 373.0966.

3-methoxy-5-(2-oxo-2-(o-tolyl)ethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3ka)



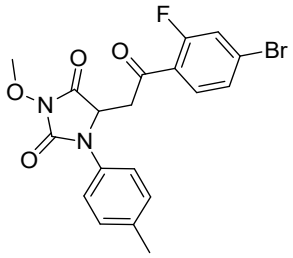
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3ka**. White solid; mp: 52.4 – 53.1 °C; 68.3 mg; 97% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 2H), 7.11 (dt, *J* = 21.5, 8.5 Hz, 6H), 4.78 (t, *J* = 4.0 Hz, 1H), 4.08 (s, 3H), 3.42 (d, *J* = 1.5 Hz, 1H), 3.41 (d, *J* = 1.0 Hz, 1H), 2.30 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.30, 166.82, 151.36, 138.75, 136.51, 136.15, 132.15, 132.07, 131.89, 130.16, 128.43, 125.72, 123.21, 64.91, 55.15, 38.94, 21.16, 20.96.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{21}N_2O_4$: 353.1501, Found: 353.1512.

5-(2-(2-bromophenyl)-2-oxoethyl)-3-methoxy-1-(p-tolyl)imidazolidine-2,4-dione (3la)



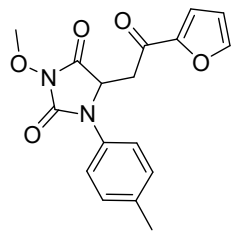
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3la**. White solid; mp: 131.8 – 132.6 °C; 81.5 mg; 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.4 Hz, 1H), 7.25 – 7.16 (m, 4H), 7.11 (dd, *J* = 12.8, 5.5 Hz, 3H), 4.79 (t, *J* = 4.1 Hz, 1H), 4.08 (s, 3H), 3.52 (dd, *J* = 18.5, 4.5 Hz, 1H), 3.46 (dd, *J* = 18.5, 3.7 Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.57, 166.31, 151.14, 139.72, 136.54, 133.87, 132.39, 131.86, 130.16, 128.97, 127.52, 123.22, 118.74, 65.01, 55.00, 40.31, 20.98.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{19}BrN_2O_4$: 417.0450, Found: 417.0453.

5-(2-(4-bromo-2-fluorophenyl)-2-oxoethyl)-3-methoxy-1-(p-tolyl)imidazolidine-2,4-dione (3ma)



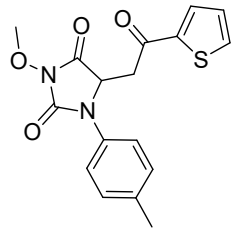
Flash column chromatography on silica gel (eluent: PE/EtOAc = 2/1, v/v) was performed to afford **3ma**. White solid; mp: 122.5 – 123.1 °C; 77.3 mg; 89% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (t, *J* = 8.2 Hz, 1H), 7.28 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.21 (dd, *J* = 10.6, 1.7 Hz, 1H), 7.14 – 7.07 (m, 4H), 4.74 (t, *J* = 3.9 Hz, 1H), 4.08 (s, 3H), 3.52 – 3.39 (m, 2H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.85, 191.81, 166.53, 161.62 (d, *J* = 259.2 Hz), 151.31, 136.54, 131.80, 131.73 (d, *J* = 2.8 Hz), 130.18, 129.38 (d, *J* = 10.1 Hz), 128.38 (d, *J* = 3.1 Hz), 123.07, 122.88 (d, *J* = 12.9 Hz), 120.36 (d, *J* = 26.8 Hz), 64.94, 54.92 (d, *J* = 2.7 Hz), 40.84 (d, *J* = 9.3 Hz), 20.96. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}BrFN_2O_4$: 435.0356, Found: 435.0348.

5-(2-(furan-2-yl)-2-oxoethyl)-3-methoxy-1-(p-tolyl)imidazolidine-2,4-dione (3na)



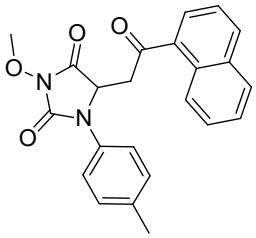
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3na**. White solid; mp: 144.4 – 146.1 °C; 61.0 mg; 93% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 0.9 Hz, 1H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 3.6 Hz, 1H), 6.42 (dd, *J* = 3.6, 1.6 Hz, 1H), 4.76 (t, *J* = 4.1 Hz, 1H), 4.07 (s, 3H), 3.41 (dd, *J* = 18.1, 4.5 Hz, 1H), 3.33 (dd, *J* = 18.1, 3.7 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.60, 166.36, 151.55, 151.14, 146.95, 136.42, 131.85, 130.10, 123.06, 117.93, 112.61, 64.95, 54.66, 36.06, 20.95.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{17}H_{17}N_2O_5$: 329.1137, Found: 329.1151.

3-methoxy-5-(2-oxo-2-(thiophen-2-yl)ethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3oa)



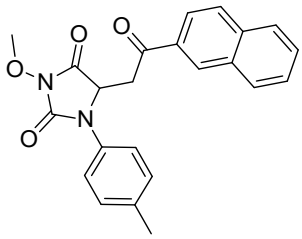
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3oa**. White solid; mp: 143.4 – 145.1 °C; 64.7 mg; 94% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 4.9 Hz, 1H), 7.44 (d, *J* = 3.7 Hz, 1H), 7.12 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 2H), 6.97 (t, *J* = 4.2 Hz, 1H), 4.76 (t, *J* = 3.8 Hz, 1H), 4.05 (s, 3H), 3.46 (dd, *J* = 17.9, 4.3 Hz, 1H), 3.40 (dd, *J* = 17.9, 3.4 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.47, 166.44, 151.23, 142.51, 136.48, 134.75, 132.62, 131.84, 130.12, 128.25, 123.18, 64.98, 54.97, 36.80, 20.94.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{17}H_{17}N_2O_4S$: 345.0909, Found: 345.0922.

3-methoxy-5-(2-(naphthalen-1-yl)-2-oxoethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3pa)



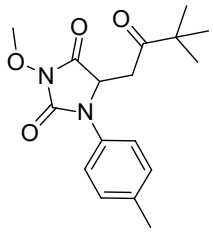
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3pa**. White solid; mp: 135.2 – 137.6 °C; 76.1 mg; 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.78 – 7.73 (m, 1H), 7.50 – 7.42 (m, 3H), 7.33 – 7.27 (m, 1H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 4.84 (t, *J* = 4.0 Hz, 1H), 4.11 (s, 3H), 3.61 (dd, *J* = 18.2, 4.3 Hz, 1H), 3.55 (dd, *J* = 18.2, 3.7 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.65, 166.79, 151.39, 136.63, 134.11, 133.85, 133.58, 131.90, 130.23, 129.89, 128.46, 128.35, 127.96, 126.75, 125.47, 124.16, 123.42, 65.02, 55.40, 39.56, 20.96.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{23}H_{21}N_2O_4$: 389.1501, Found: 389.1512.

3-methoxy-5-(2-(naphthalen-2-yl)-2-oxoethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3qa)



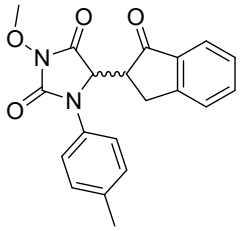
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3qa**. Light yellow solid; mp:140.2 – 142.3 °C; 74.5 mg; 96% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.75 (qd, *J* = 8.4, 5.2 Hz, 4H), 7.53 – 7.48 (m, 1H), 7.47 – 7.42 (m, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 8.3 Hz, 2H), 4.83 (t, *J* = 3.9 Hz, 1H), 4.11 (s, 3H), 3.67 (dd, *J* = 18.1, 4.3 Hz, 1H), 3.57 (dd, *J* = 18.1, 3.5 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.83, 166.83, 151.43, 136.50, 135.80, 133.03, 132.25, 131.91, 130.16, 129.99, 129.56, 128.94, 128.65, 127.82, 127.03, 123.35, 123.25, 64.99, 55.10, 36.37, 20.91.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}N_3O_6$: 389.1501, Found: 389.1512.

5-(3,3-dimethyl-2-oxobutyl)-3-methoxy-1-(p-tolyl)imidazolidine-2,4-dione (3ra)



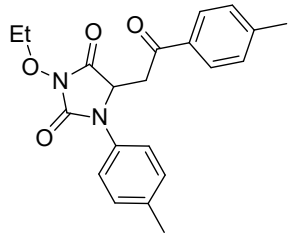
Flash column chromatography on silica gel (eluent: PE/EtOAc = 5/1, v/v) was performed to afford **3ra**. White solid; mp: 139.1 – 141.8 °C; 57.2 mg; 90% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.07 (m, 4H), 4.66 (dd, *J* = 4.3, 3.6 Hz, 1H), 4.05 (s, 3H), 3.11 (dd, *J* = 18.3, 4.5 Hz, 1H), 2.93 (dd, *J* = 18.3, 3.4 Hz, 1H), 2.26 (s, 3H), 0.84 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.76, 166.87, 151.22, 136.26, 131.80, 129.99, 122.92, 64.91, 54.66, 44.00, 34.75, 25.92, 20.95. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{17}H_{23}N_2O_4$: 319.1658, Found: 319.1681.

3-methoxy-5-(1-oxo-2,3-dihydro-1H-inden-2-yl)-1-(p-tolyl)imidazolidine-2,4-dione (3sa)



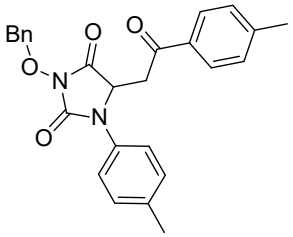
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3sa**. White solid; mp: 145.1 – 146.4 °C; 67.2 mg; 96% yield; 4:1 dr; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.71 (m, 0.25H), 7.52 – 7.44 (m, 1.29H), 7.34 – 7.27 (m, 2.55H), 7.21 – 7.12 (m, 2.56H), 6.88 (q, *J* = 8.5 Hz, 4.09H), 5.17 (d, *J* = 3.2 Hz, 0.25H), 5.11 (d, *J* = 1.5 Hz, 1H), 3.99 (s, 3H), 3.96 (s, 0.75H), 3.24 – 3.14 (m, 2.40H), 3.02 (m, 1.34H), 2.70 – 2.64 (m, 0.26H), 2.27 (s, 0.75H), 2.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.30, 202.61, 165.72, 164.37, 152.38, 151.00, 137.22, 137.02, 136.45, 135.90, 135.31, 135.27, 130.99, 130.26, 129.57, 127.95, 127.47, 126.43, 126.35, 124.88, 124.22, 123.77, 123.39, 65.59, 65.50, 59.76, 59.04, 46.67, 45.96, 28.28, 26.79, 20.99, 20.90. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{20}H_{18}N_2O_4Na$: 373.1164, Found: 373.1163.

3-ethoxy-5-(2-oxo-2-(p-tolyl)ethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3ta)



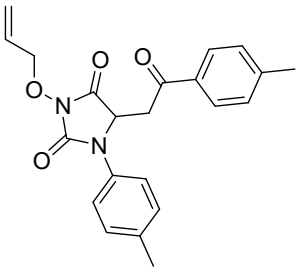
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3ta**. White solid; mp: 88.4 – 89.1 °C; 71.7 mg; 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 4H), 7.14 (d, *J* = 8.2 Hz, 2H), 4.86 (t, *J* = 3.9 Hz, 1H), 4.41 (q, *J* = 7.0 Hz, 2H), 3.55 (d, *J* = 4.4 Hz, 1H), 3.53 – 3.45 (m, 1H), 2.37 (s, 3H), 2.29 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.31, 167.23, 151.78, 144.78, 136.29, 133.32, 132.04, 130.08, 129.36, 128.11, 123.09, 73.55, 54.88, 36.18, 21.68, 20.93, 13.64.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{21}H_{23}N_2O_4$: 367.1458, Found: 367.1479.

3-(benzyloxy)-5-(2-oxo-2-(p-tolyl)ethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3ua)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3ua**. Colorless viscous oil; 81.3 mg; 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.54 (m, 2H), 7.52 (d, *J* = 6.0 Hz, 2H), 7.30 (d, *J* = 3.6 Hz, 3H), 7.10 (t, *J* = 7.3 Hz, 4H), 7.04 (d, *J* = 7.2 Hz, 2H), 5.31 – 5.21 (m, 2H), 4.78 (d, *J* = 1.5 Hz, 1H), 3.44 (dd, *J* = 18.0, 1.8 Hz, 1H), 3.35 (d, *J* = 18.2 Hz, 1H), 2.28 (s, 3H), 2.20 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 194.41, 167.01, 151.63, 144.79, 136.26, 133.90, 133.31, 132.05, 130.08, 129.99, 129.37, 129.18, 128.50, 128.14, 123.04, 79.32, 54.87, 36.34, 21.69, 20.94. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{26}H_{24}N_2O_4Na$: 451.1634, Found: 451.1639.

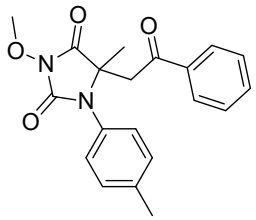
3-(allyloxy)-5-(2-oxo-2-(p-tolyl)ethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3va)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3va**. White solid; mp: 119.6 – 120.3 °C; 68.1 mg; 90% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.11 (dd, *J* = 8.0, 5.9 Hz, 4H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.08 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.41 (dd, *J* = 17.2, 1.1 Hz, 1H), 5.32 (d, *J* = 10.3 Hz, 1H), 4.82 (t, *J* = 4.0 Hz, 1H), 4.72 (d, *J* = 6.6 Hz, 2H), 3.49 (dd, *J* = 18.2, 4.5 Hz, 1H), 3.38 (dd, *J* = 18.2, 3.6 Hz, 1H), 2.29 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.31, 167.24, 151.69, 144.79, 136.27, 133.29, 132.02, 131.28, 130.07, 129.37, 128.13, 123.03, 122.03, 78.41, 54.82, 36.34, 21.69, 20.93.

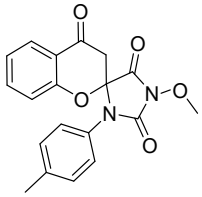
HRMS (ESI) m/z $[M+H]^+$calcd for $C_{22}H_{23}N_2O_4$: 379.1658, Found: 379.1669.

3-methoxy-5-methyl-5-(2-oxo-2-phenylethyl)-1-(p-tolyl)imidazolidine-2,4-dione (3wa)



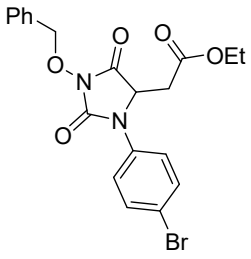
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3wa**. White solid; mp: 139.4 – 140.1 °C; 65.5 mg; 93% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.54 – 7.44 (m, 1H), 7.35 (dd, *J* = 10.9, 4.8 Hz, 2H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.95 – 6.76 (m, 2H), 4.12 (s, 3H), 3.38 (d, *J* = 18.4 Hz, 1H), 3.23 (d, *J* = 18.4 Hz, 1H), 2.22 (s, 3H), 1.53 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.49, 170.29, 152.35, 138.96, 135.68, 133.89, 130.39, 128.80, 128.57, 127.96, 64.66, 62.32, 43.27, 24.50, 21.08. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{21}N_2O_4$: 353.1501, Found: 353.1517.

1'-methoxy-3'-(p-tolyl)spiro[chroman-2,4'-imidazolidine]-2',4,5'-trione (3xa)



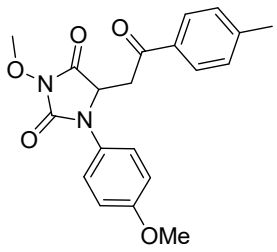
Flash column chromatography on silica gel (eluent: PE/EtOAc = 1/1, v/v) was performed to afford **3xa**. White solid; mp: 138.1 – 139.3 °C; 58.4 mg; 83% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.45 (ddd, *J* = 8.9, 7.4, 1.7 Hz, 1H), 7.17 – 7.09 (m, 4H), 7.01 – 6.96 (m, 2H), 3.99 (s, 3H), 3.07 (d, *J* = 16.9 Hz, 1H), 3.00 (d, *J* = 16.9 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.26, 162.93, 157.90, 150.38, 139.71, 136.66, 130.39, 128.84, 128.55, 126.44, 122.81, 119.82, 117.53, 88.36, 65.88, 40.98, 29.71, 21.17. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{19}H_{16}N_2O_5Na$: 375.0957, Found: 375.0959.

Ethyl 2-(1-(benzyloxy)-3-(4-bromophenyl)-2,5-dioxoimidazolidin-4-yl)acetate (3ye)



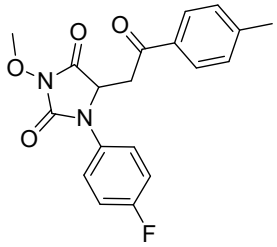
Flash column chromatography on silica gel (eluent: PE/EtOAc = 5/1, v/v) was performed to afford **3ye**. White solid; mp: 131.7 – 132.3 °C; 85.6 mg; 96% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.36 (m, 4H), 7.40 – 7.23 (m, 3H), 7.18 – 7.13 (m, 2H), 5.15 (s, 2H), 4.59 (dd, *J* = 4.7, 3.7 Hz, 1H), 4.04 – 3.92 (m, 2H), 2.87 (dd, *J* = 17.4, 3.6 Hz, 1H), 2.72 (dd, *J* = 17.4, 4.9 Hz, 1H), 1.09 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.34, 164.70, 150.12, 132.68, 132.47, 131.59, 128.89, 128.32, 127.52, 122.98, 118.52, 78.48, 60.51, 53.66, 31.76, 12.97. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{20}H_{19}N_2O_5BrNa$: 469.0375, Found: 469.0383.

3-methoxy-1-(4-methoxyphenyl)-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3bb)



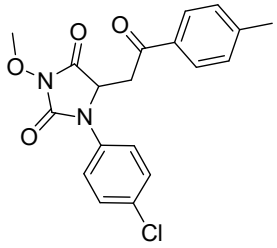
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3bb**. White solid; mp: 119.6 – 121.5 °C; 67.7 mg; 92% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1 Hz, 2H), 7.11 (dd, *J* = 15.5, 6.3 Hz, 4H), 6.78 (d, *J* = 8.9 Hz, 2H), 4.71 (t, *J* = 3.8 Hz, 1H), 4.09 (s, 3H), 3.69 (s, 3H), 3.44 (d, *J* = 4.1 Hz, 1H), 3.42 (d, *J* = 3.7 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.39, 166.94, 158.27, 151.66, 144.87, 133.26, 129.41, 128.10, 127.09, 125.64, 114.83, 64.94, 55.60, 55.49, 36.23, 21.70. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{21}N_2O_5$: 369.1450, Found: 369.1460.

1-(4-fluorophenyl)-3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3bc)



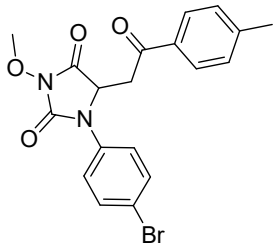
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3bc**. White solid; mp:152.4 – 154.4 °C; 67.6 mg; 96% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.30 – 7.26 (m, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.03 (t, *J* = 8.5 Hz, 2H), 4.85 (t, *J* = 3.8 Hz, 1H), 4.16 (s, 3H), 3.56 (dd, *J* = 18.3, 4.1 Hz, 1H), 3.51 (dd, *J* = 18.3, 3.6 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.33, 166.61, 160.76 (d, *J* = 247.0 Hz), 151.51, 145.06, 133.10, 130.51 (d, *J* = 3.0 Hz), 129.46, 128.09, 125.34 (d, *J* = 8.6 Hz), 116.47 (d, *J* = 22.8 Hz), 64.99, 55.21, 36.13, 21.69.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}FN_2O_4$: 357.1251, Found: 357.1261.

1-(4-chlorophenyl)-3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3bd)



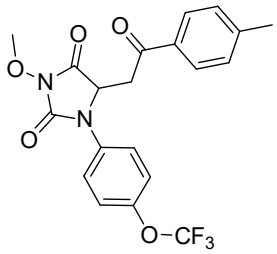
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3bd**. White solid; mp: 152.3 – 153.7 °C; 72.9 mg; 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1 Hz, 2H), 7.23 (q, *J* = 8.9 Hz, 4H), 7.14 (d, *J* = 8.0 Hz, 2H), 4.80 (t, *J* = 3.7 Hz, 1H), 4.09 (s, 3H), 3.53 (dd, *J* = 18.3, 4.2 Hz, 1H), 3.49 – 3.42 (m, 1H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.18, 166.38, 151.24, 145.12, 133.22, 133.04, 131.79, 129.67, 129.48, 128.11, 123.97, 65.01, 54.67, 36.07, 21.71.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}ClN_2O_4$: 373.0955, Found: 373.0962.

1-(4-bromophenyl)-3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3be)



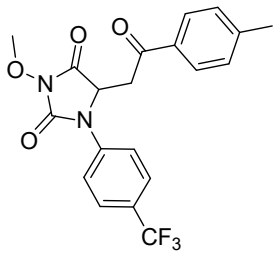
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3be**. White solid; mp: 157.5 – 159.8 °C; 79.1 mg; 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.22 (dd, *J* = 16.1, 8.4 Hz, 4H), 4.87 (t, *J* = 3.8 Hz, 1H), 4.16 (s, 3H), 3.61 (dd, *J* = 18.3, 4.2 Hz, 1H), 3.52 (dd, *J* = 18.3, 3.4 Hz, 1H), 2.38 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 194.20, 166.36, 151.18, 145.12, 133.77, 133.03, 132.61, 129.48, 128.12, 124.16, 119.51, 65.01, 54.57, 36.05, 21.71.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{19}BrN_2O_4$: 417.0450, Found: 417.0457.

3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)-1-(4-(trifluoromethoxy)phenyl)imidazolidine-2,4-dione (3bf)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3bf**. White solid; mp:93.1 – 95.2 °C; 79.3 mg; 94% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 9.0 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 4H), 4.83 (t, *J* = 3.8 Hz, 1H), 4.09 (s, 3H), 3.54 (dd, *J* = 18.2, 4.2 Hz, 1H), 3.46 (dd, *J* = 18.2, 3.4 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.23, 166.31, 151.32, 146.82, 145.15, 133.15 (d, *J* = 23.8 Hz), 129.48, 128.11, 124.02, 122.15,120.35 (d, *J* = 257.7 Hz), 65.04, 54.77, 36.09, 21.69.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{18}F_3N_2O_5$: 423.1168, Found: 423.1176.

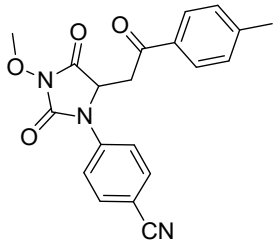
3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)-1-(4-(trifluoromethyl)phenyl)imidazolidine-2,4-dione (3bg)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3bg**. White solid; mp: 143.2 – 145.7 °C; 77.1 mg; 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 4.90 (t, *J* = 3.8 Hz, 1H), 4.09 (s, 3H), 3.60 (dd, *J* = 18.3, 4.3 Hz, 1H), 3.50 (dd, *J* = 18.3, 3.4 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.15, 166.10, 151.15, 145.22, 138.03, 132.95,

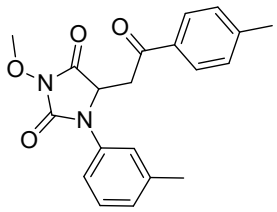
129.48, 128.13, 127.62 (q, J = 33.0 Hz), 126.70 (q, J = 3.6 Hz), 123.73 (q, J = 271.9 Hz),121.62, 65.04, 54.21, 36.00, 21.69. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{18}F_3N_2O_4$: 407.1219, Found: 407.1222.

4-(3-methoxy-2,4-dioxo-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidin-1-yl)benzonitrile (3bh)



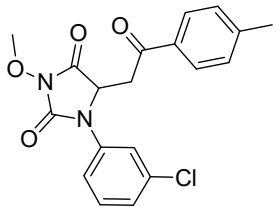
Flash column chromatography on silica gel (eluent: PE/EtOAc = 1/1, v/v) was performed to afford **3bh**. White solid; mp: 133.2 – 134.8 °C; 65.3 mg; 90% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 – 7.63 (m, 4H), 7.58 – 7.53 (m, 2H), 7.22 (d, J = 8.1 Hz, 2H), 4.96 (t, J = 3.8 Hz, 1H), 4.16 (s, 3H), 3.69 (dd, J = 18.3, 4.3 Hz, 1H), 3.59 (dd, J = 18.3, 3.3 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.93, 165.71, 150.96, 145.41, 139.02, 133.54, 132.83, 129.56, 128.14, 121.32, 118.16, 108.90, 65.09, 53.95, 36.02, 21.73.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{18}N_3O_4$: 364.1297, Found: 364.1247.

3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)-1-(m-tolyl)imidazolidine-2,4-dione (3bi)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3bi**. White solid; mp: 136.5 – 138.6 °C; 68.3 mg; 97% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 8.2 Hz, 2H), 7.13 (dt, J = 21.5, 8.2 Hz, 4H), 7.00 (d, J = 8.0 Hz, 1H), 6.93 (d, J = 7.6 Hz, 1H), 4.79 (t, J = 3.9 Hz, 1H), 4.09 (s, 3H), 3.52 (dd, J = 18.2, 4.3 Hz, 1H), 3.43 (dd, J = 18.2, 3.5 Hz, 1H), 2.30 (s, 3H), 2.22 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 194.41, 166.74, 151.33, 144.84, 139.66, 134.49, 133.27, 129.38, 129.29, 128.11, 127.26, 123.89, 119.86, 64.92, 54.87, 36.17, 21.69, 21.42.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{21}N_2O_4$: 353.1501, Found: 353.1516.

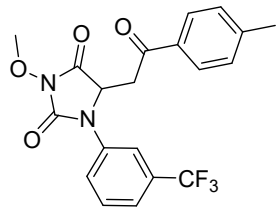
1-(3-chlorophenyl)-3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3bj)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3bj**. White solid; mp: 159.2 – 160.2 °C; 71.4 mg; 96% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, J = 8.2 Hz, 2H), 7.34 (t, J = 1.7 Hz, 1H), 7.22 – 7.12 (m, 4H), 7.08 (d, J = 7.8 Hz, 1H), 4.80 (t, J = 3.7 Hz, 1H), 4.09 (s, 3H), 3.56 (dd, J = 18.3, 4.2 Hz, 1H), 3.48 (dd, J = 18.3, 3.3 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.20, 166.26, 151.15, 145.09, 135.94, 135.22, 133.06,

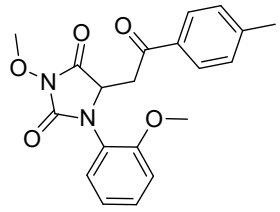
130.48, 129.46, 128.15, 126.26, 122.57, 120.30, 64.99, 54.53, 36.03, 21.71.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}ClN_2O_4$: 373.0955, Found: 373.0966.

3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)-1-(3-(trifluoromethyl)phenyl)imidazolidine-2,4-dione (3bk)



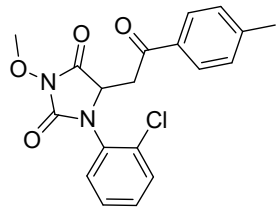
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3bk**. Colorless viscous oil; 75.5 mg; 93% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.62 (m, 3H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.50 – 7.39 (m, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 4.95 (t, *J* = 3.8 Hz, 1H), 4.16 (s, 3H), 3.62 (dd, *J* = 18.3, 4.1 Hz, 1H), 3.57 (dd, *J* = 18.3, 3.6 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.20, 166.18, 151.27, 145.17, 135.47, 132.98, 131.95 (q, *J* = 32.8 Hz), 130.16, 129.47, 128.12, 125.50, 123.47 (q, *J* = 272.8 Hz), 122.67 (q, *J* = 3.6 Hz), 119.00 (q, *J* = 3.8 Hz), 65.03, 54.49, 36.04, 21.68.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{18}F_3N_2O_4$: 407.1219, Found: 407.1224.

3-methoxy-1-(2-methoxyphenyl)-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3bl)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 1/1, v/v) was performed to afford **3bl**. Colorless viscous oil; 67.7 mg; 92% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.19 (dd, *J* = 12.3, 3.5 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 2H), 7.05 (dd, *J* = 7.8, 1.6 Hz, 1H), 6.84 (d, *J* = 7.9 Hz, 1H), 6.78 (td, *J* = 7.7, 0.9 Hz, 1H), 4.78 (t, *J* = 4.0 Hz, 1H), 4.10 (s, 3H), 3.70 (s, 3H), 3.39 (dd, *J* = 18.2, 4.2 Hz, 1H), 3.28 (dd, *J* = 18.2, 3.9 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.51, 167.73, 155.36, 152.29, 144.65, 133.43, 130.02, 129.82, 129.37, 128.03, 122.49, 121.19, 111.91, 64.87, 56.09, 55.69, 36.63, 21.69.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{21}N_2O_5$: 369.1450, Found: 369.1460.

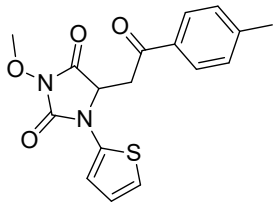
1-(2-chlorophenyl)-3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3bm)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3bm**. Colorless viscous oil; 69.2 mg; 93% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.0 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.21 – 7.17 (m, 1H), 7.12 (dd, *J* = 17.5, 5.7 Hz, 4H), 4.86 (dd, *J*

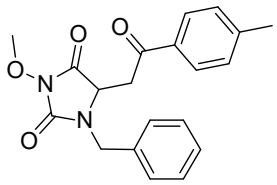
= 3.7, 2.6 Hz, 1H), 4.10 (d, *J* = 1.6 Hz, 3H), 3.51 – 3.43 (m, 1H), 3.27 (dd, *J* = 18.4, 2.4 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.47, 167.16, 152.00, 144.98, 133.14, 132.74, 131.68, 130.93, 130.68, 130.11, 129.47, 128.07, 128.03, 65.01, 55.97, 36.60, 21.72.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}ClN_2O_4$: 373.0955, Found: 373.0966.

3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)-1-(thiophen-2-yl)imidazolidine-2,4-dione (3bn)



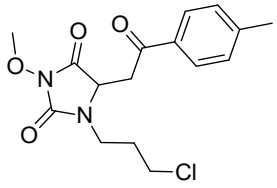
Flash column chromatography on silica gel (eluent: PE/EtOAc = 3/1, v/v) was performed to afford **3bn**. Colorless viscous oil; 64.6 mg; 94% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.05 (dd, *J* = 5.5, 1.0 Hz, 1H), 6.88 (dd, *J* = 5.5, 3.8 Hz, 1H), 6.74 (dd, *J* = 3.7, 1.1 Hz, 1H), 4.72 (t, *J* = 3.8 Hz, 1H), 4.17 (s, 3H), 3.80 (dd, *J* = 18.4, 4.2 Hz, 1H), 3.60 (dd, *J* = 18.4, 3.4 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.30, 166.40, 151.11, 145.05, 136.31, 133.14, 129.49, 128.19, 125.48, 121.89, 119.11, 64.98, 56.85, 36.10, 21.73. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{17}H_{16}N_2O_4S$: 345.0909, Found: 345.0913.

1-benzyl-3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3bo)



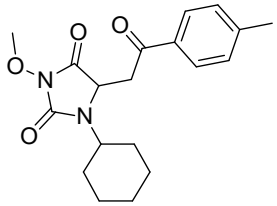
Flash column chromatography on silica gel (eluent: PE/EtOAc = 5/1, v/v) was performed to afford **3bn**. White solid; mp: 121.6 – 123.8 °C; 59.8 mg; 85% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.18 – 7.10 (m, 6H), 7.10 – 7.04 (m, 1H), 4.57 (d, *J* = 15.s4 Hz, 1H), 4.29 (d, *J* = 15.4 Hz, 1H), 4.21 (dd, *J* = 5.2, 3.4 Hz, 1H), 4.03 (s, 3H), 3.40 (dd, *J* = 18.2, 3.4 Hz, 1H), 3.23 (dd, *J* = 18.2, 5.2 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.38, 167.44, 153.41, 144.84, 135.55, 133.10, 129.35, 128.90, 128.11, 128.08, 128.06, 65.02, 53.91, 45.79, 37.43, 21.73. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{21}N_2O_4$: 353.1501, Found: 353.1511.

1-(3-chloropropyl)-3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3bp)



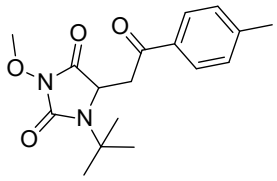
Flash column chromatography on silica gel (eluent: PE/EtOAc = 5/1, v/v) was performed to afford **3bo**. Colorless viscous oil; 55.4 mg; 82% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 4.39 (dd, *J* = 5.9, 3.0 Hz, 1H), 3.98 (d, *J* = 5.3 Hz, 3H), 3.67 (dd, *J* = 18.4, 3.1 Hz, 1H), 3.60 (dt, *J* = 14.6, 7.3 Hz, 1H), 3.50 – 3.43 (m, 2H), 3.40 (dd, *J* = 18.4, 5.9 Hz, 1H), 3.18 – 3.09 (m, 1H), 2.36 (s, 3H), 2.04 – 1.93 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.55, 167.38, 153.17, 145.23, 133.08, 129.62, 128.29, 65.09, 54.20, 42.06, 39.71, 37.93, 30.64, 21.76.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{16}H_{20}ClN_2O_4$: 339.1112, Found: 339.1123.

1-cyclohexyl-3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3bq)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 5/1, v/v) was performed to afford **3bp**. Colorless viscous oil; 57.8 mg; 84% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 4.29 (t, *J* = 4.1 Hz, 1H), 4.01 (s, 3H), 3.66 (dd, *J* = 18.2, 4.1 Hz, 1H), 3.60 – 3.52 (m, 1H), 3.42 (dd, *J* = 18.2, 4.1 Hz, 1H), 2.36 (s, 3H), 1.75 – 1.60 (m, 5H), 1.35 – 1.25 (m, 1H), 1.25 – 1.13 (m, 3H), 1.05 – 0.95 (m, 1H).^{13}C NMR (126 MHz, $CDCl_3$) δ 194.37, 167.66, 152.68, 144.93, 133.47, 129.59, 128.17, 64.79, 53.86, 52.80, 38.65, 31.59, 30.44, 25.80, 25.16, 21.74. HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{25}N_2O_4$: 345.1814, Found: 345.1826.

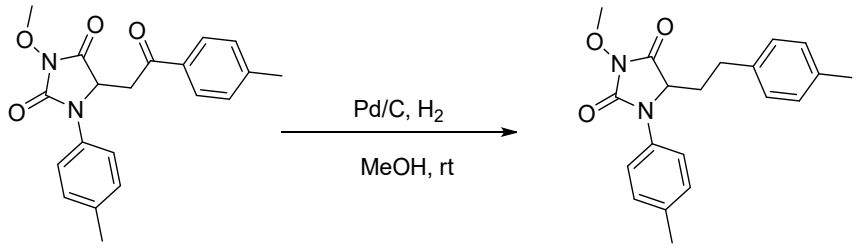
1-(tert-butyl)-3-methoxy-5-(2-oxo-2-(p-tolyl)ethyl)imidazolidine-2,4-dione (3br)



Flash column chromatography on silica gel (eluent: PE/EtOAc = 5/1, v/v) was performed to afford **3bq**. White solid; mp:130.2 – 132.7°C; 50.9 mg; 80% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.21 (s, 2H), 4.30 (dd, *J* = 5.2, 2.6 Hz, 1H), 3.98 (s, 3H), 3.71 (dd, *J* = 18.0, 5.3 Hz, 1H), 3.46 (dd, *J* = 18.0, 2.6 Hz, 1H), 2.35 (s, 3H), 1.35 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.45, 167.34, 153.14, 144.84, 133.73, 129.55, 128.16, 64.52, 56.26, 53.49, 40.05, 28.57, 21.72.HRMS (ESI) m/z $[M+H]^+$calcd for $C_{17}H_{23}N_2O_4$: 319.1658, Found: 319.1665.

7. Transformation of the products 3ba

3-methoxy-5-(4-methylphenethyl)-1-(p-tolyl)imidazolidine-2,4-dione (4)[2]



3ba **4**

To a solution of **3ba** (100 mg, 0.3 mmol) in MeOH (3.0 mL) added 10% Pd/C (9 mg). The reaction mixture was stirred at rt for 24 hours. After filtration through a plug of Celite, the volatiles were removed under reduced pressure and the residue was purified via flash column chromatography (PE/EA = 2/1) to afford compound **4** as a white solid in 70% yield. mp: 131.5 – 132.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, *J* = 15.2 Hz, 4H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.87 (d, *J* = 7.8 Hz, 2H), 4.45 (dd, *J* = 6.7, 3.1 Hz, 1H), 3.93 (s, 3H), 2.59 – 2.47 (m, 2H), 2.28 (s, 3H), 2.22 (d, *J* = 5.6 Hz, 3H), 2.20 – 2.13 (m, 1H), 2.04 – 1.96 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.30, 149.69, 135.45, 134.97, 131.15, 129.00, 128.21, 127.27, 121.10, 64.40, 56.46, 29.10,

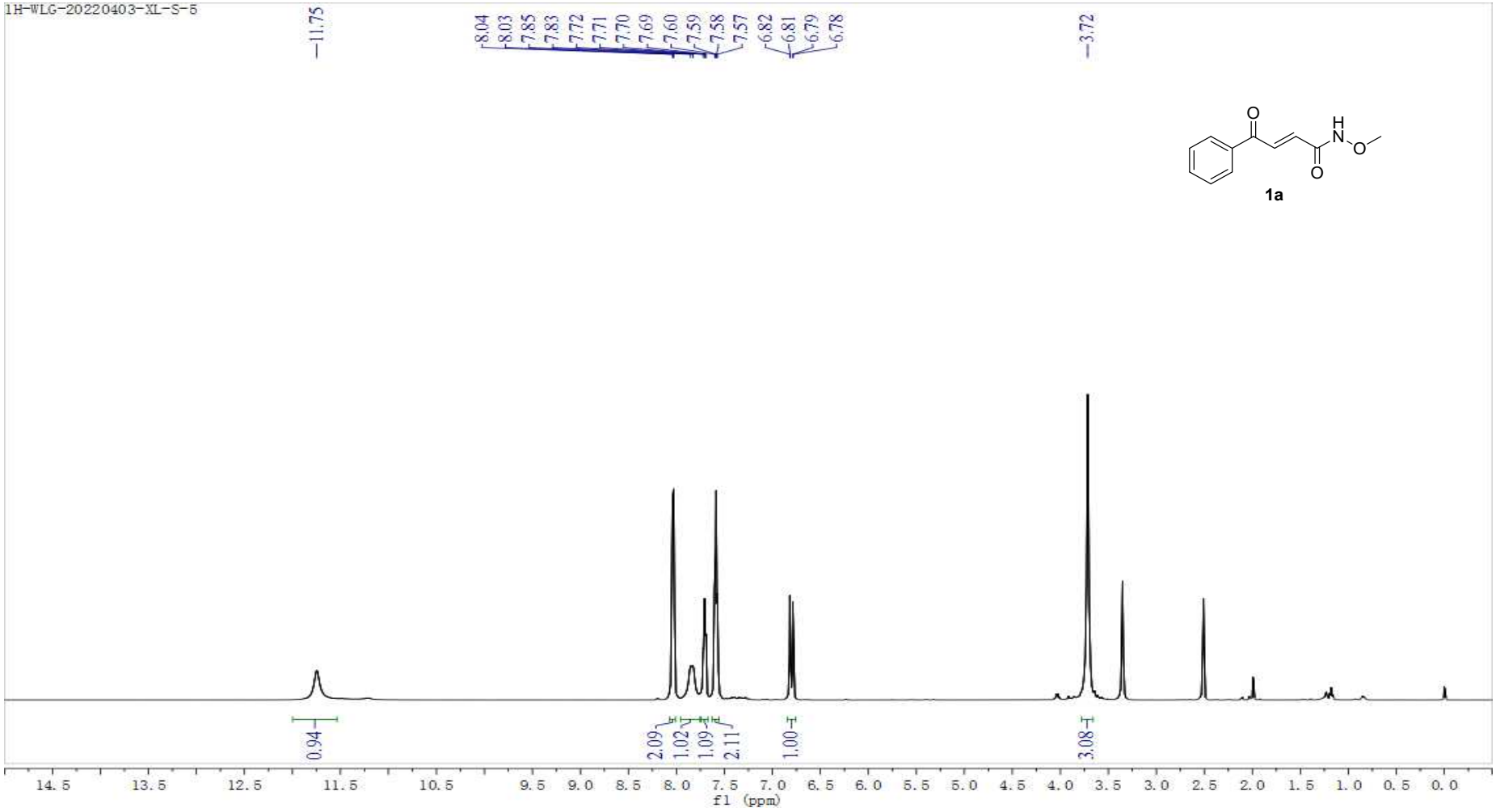
27.94, 19.96, 19.91. HRMS (ESI) m/z $[M+Na]^+$calcd for $C_{20}H_{22}N_2O_3Na$: 361.1528, Found: 361.1533.

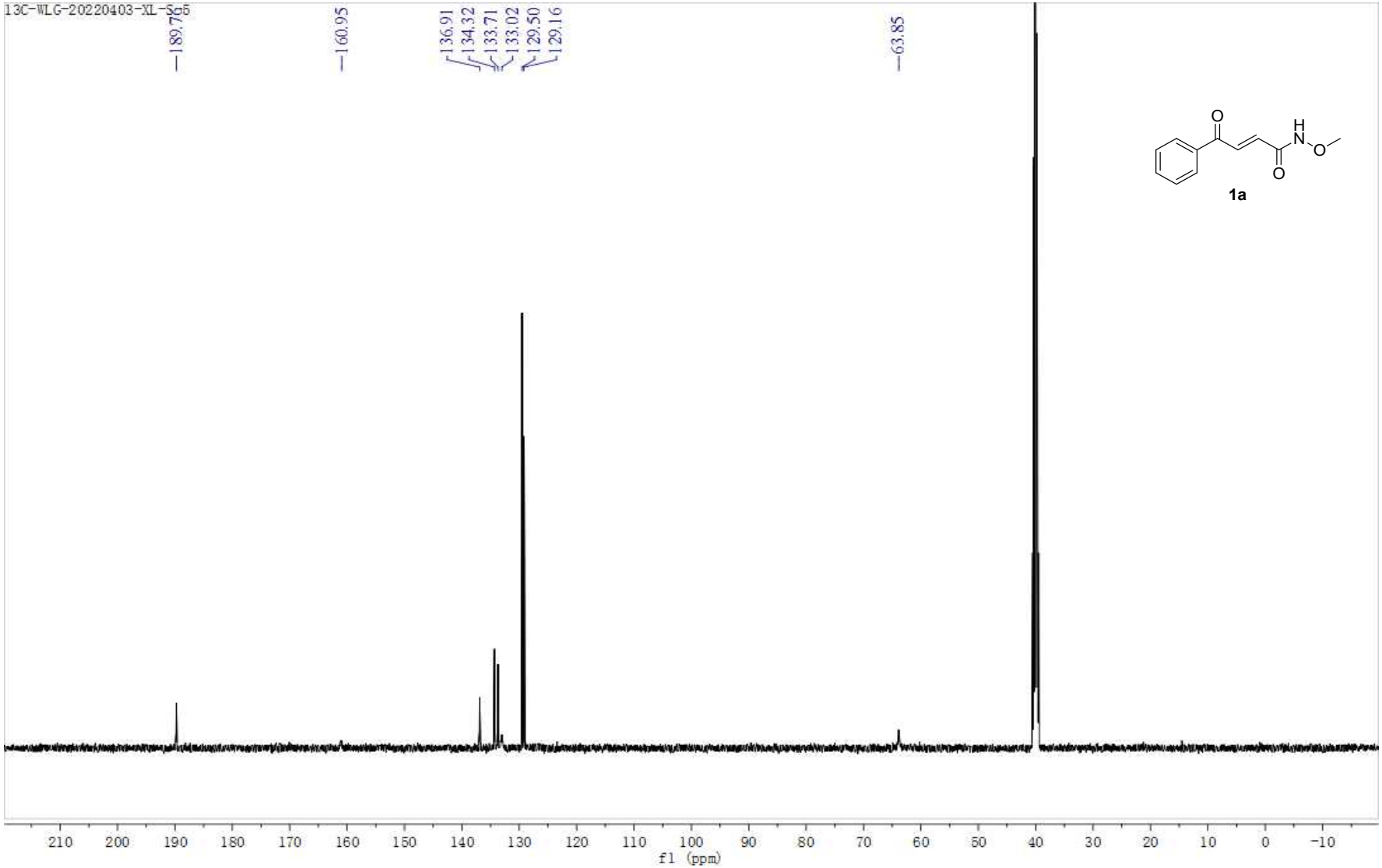
8. Reference

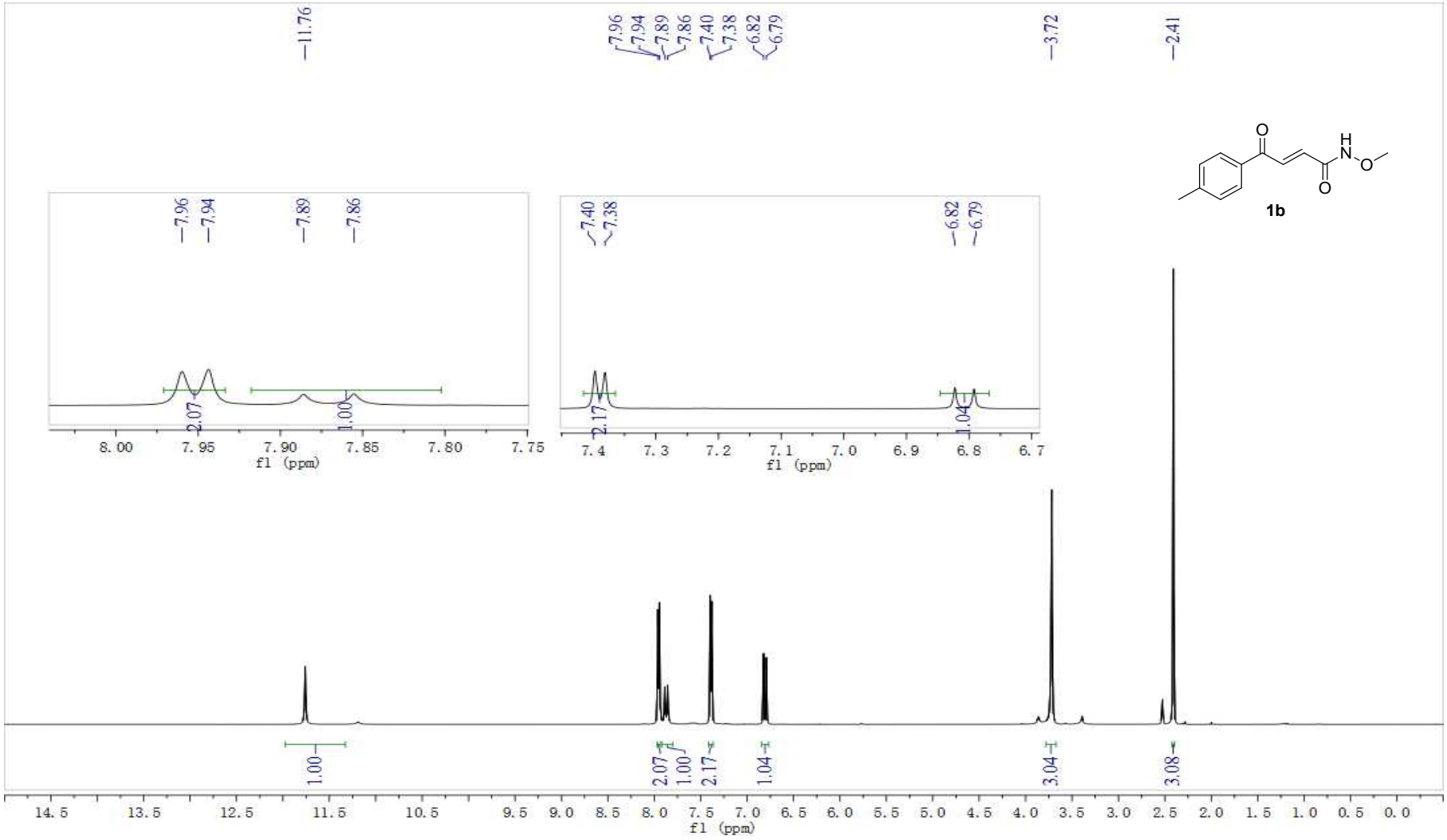
1. (a) Ren, J., Xu, J., Zhang, G., Xu, C., Zhao, L., You, X., Wang, J. *Bioorg. Med. Chem. Lett.,* **2019**, *29*, 539-543; (b) Zhao, W. W., Liu, Y. K. *Org. Chem. Front.*, **2017**, *4*, 2358-2363.

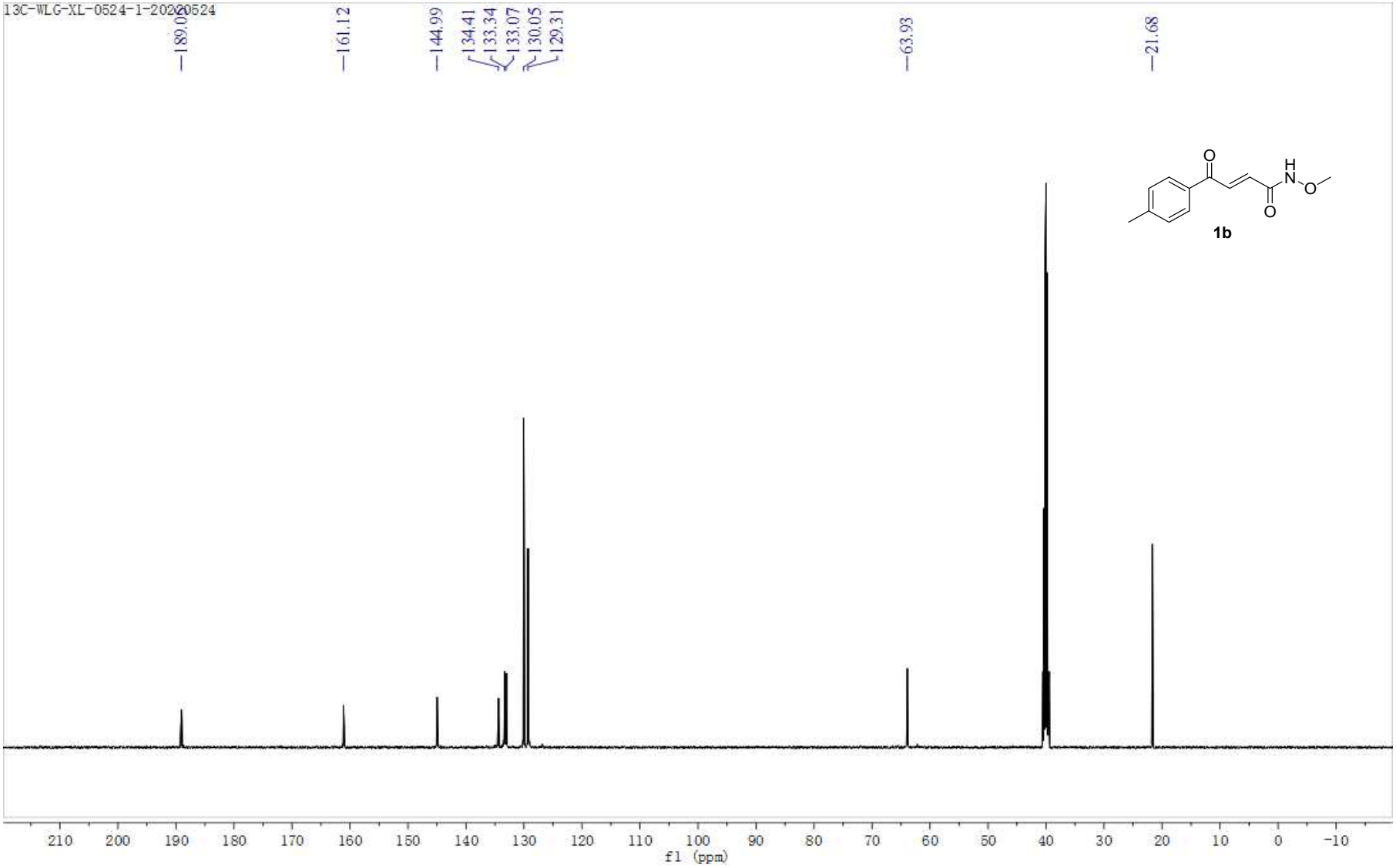
2. Xie, L., Ma, H., Li, J., Yu, Y., Qin, Z., Fu, B. *Org. Chem. Front.*, **2017**, *4*, 1858-1862.

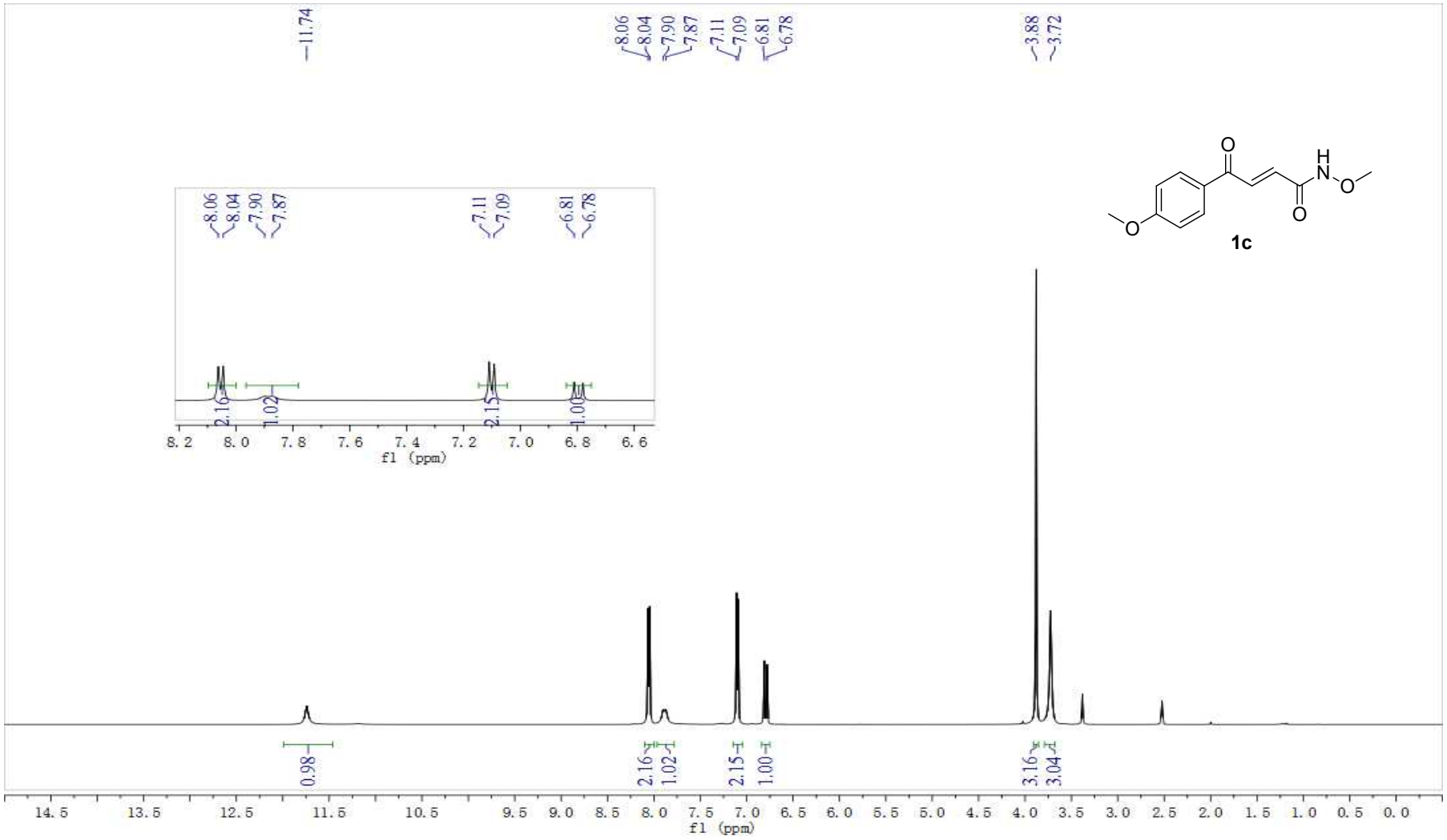
9. ^{1}H and ^{13}C NMR spectra of all products

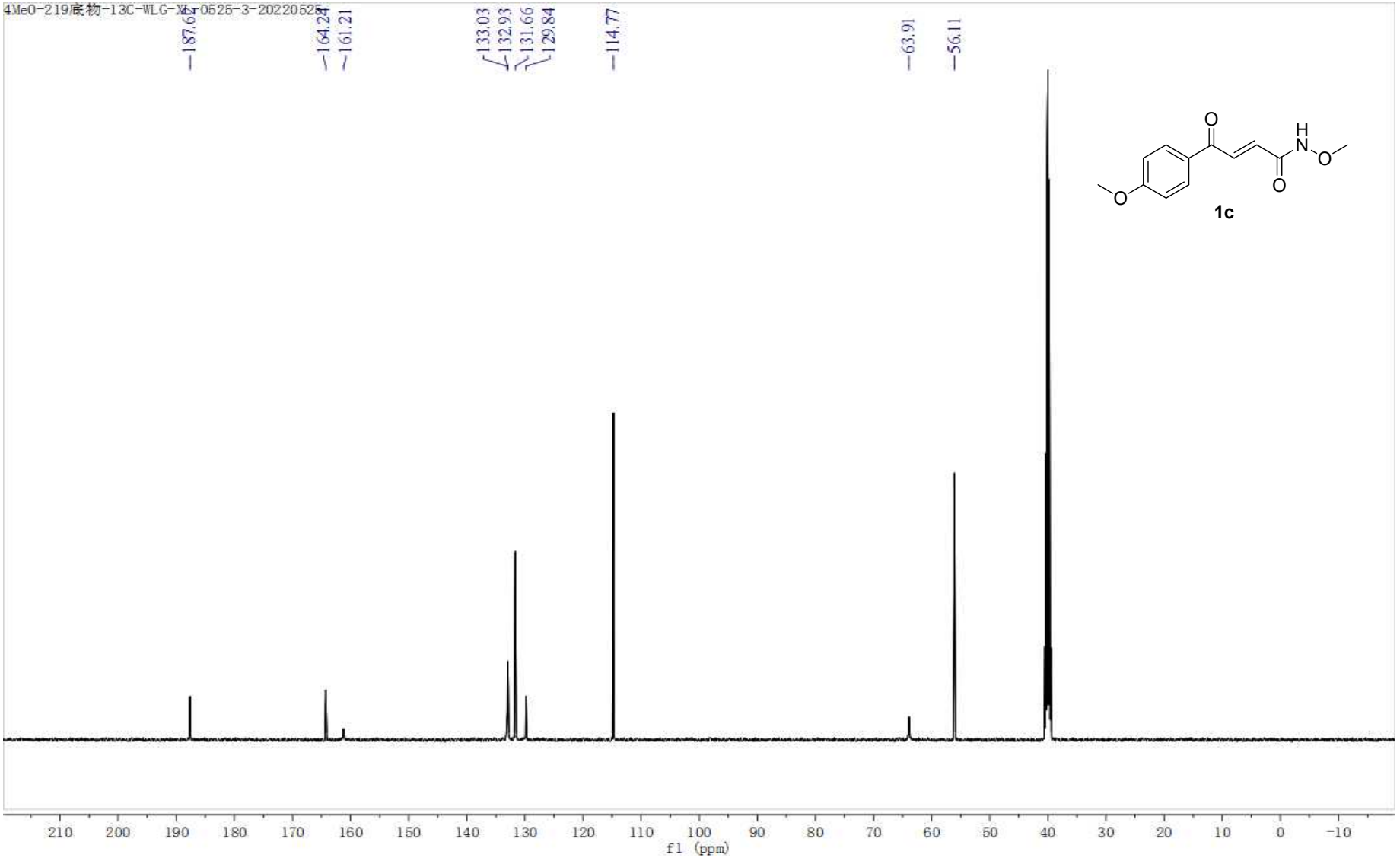


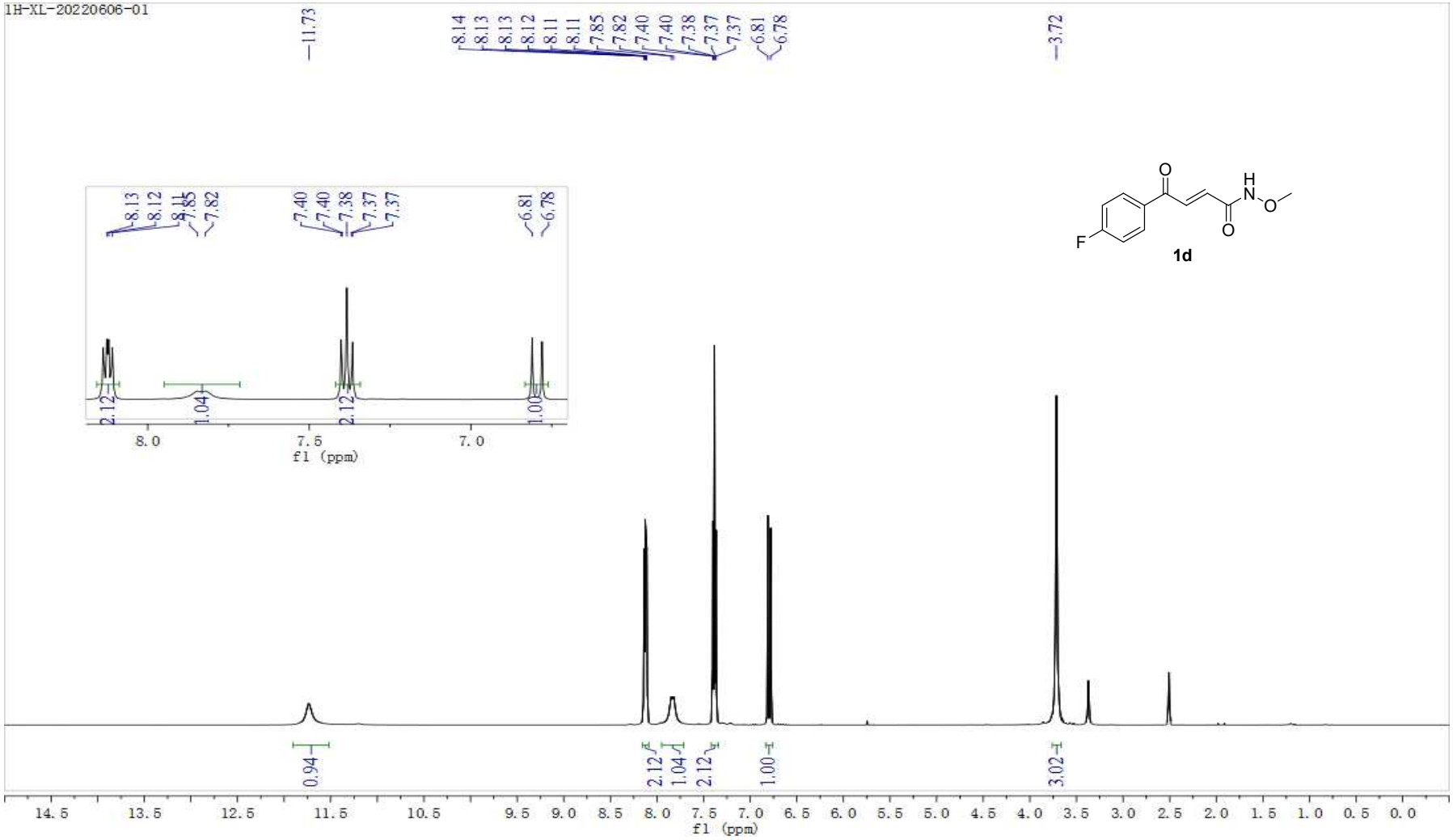

13C-WLG-20220403-XL-S05
189.75
160.95
136.91
134.32
133.71
133.02
129.50
129.16
63.85
O
H
N
O
O
1a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

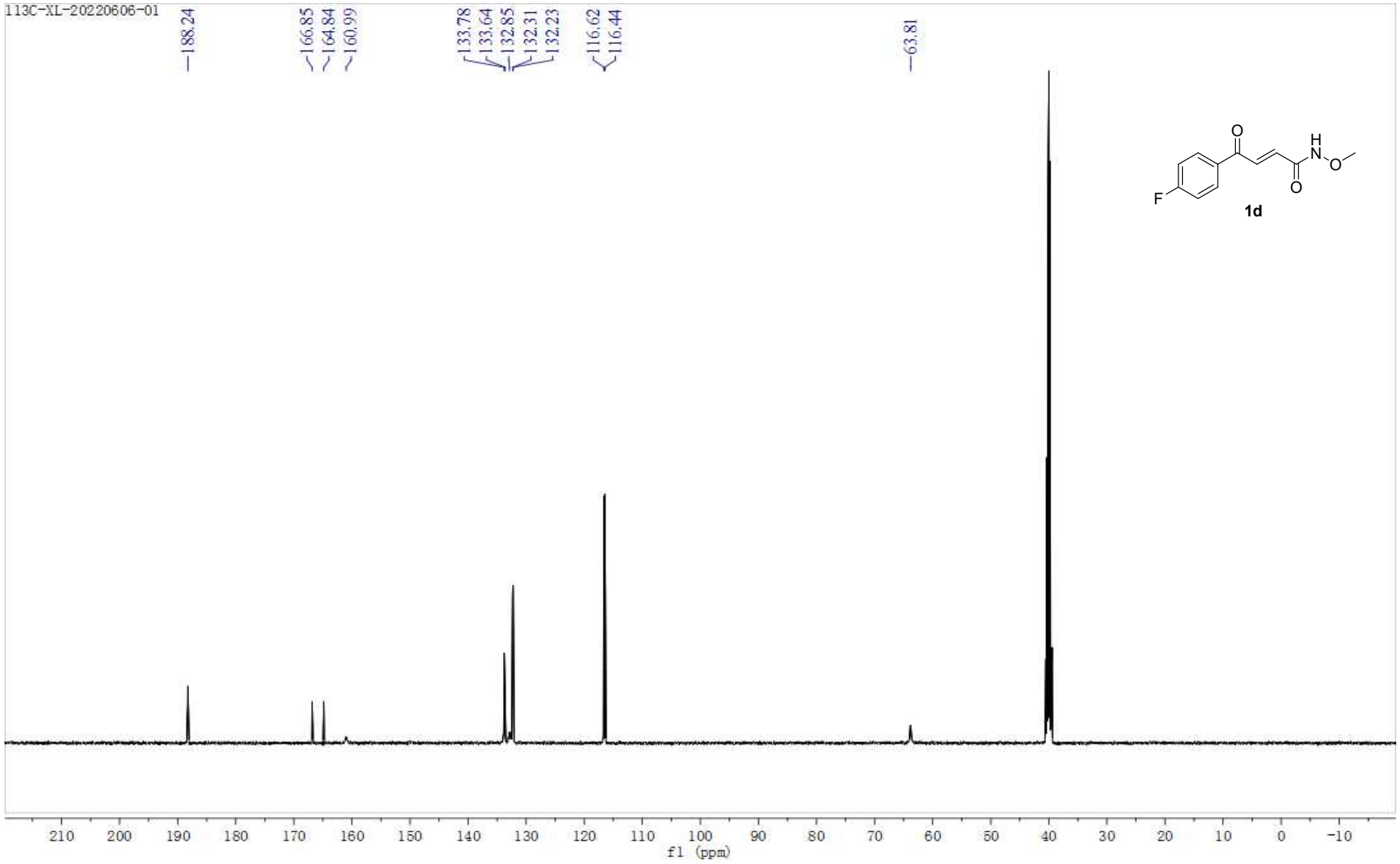

11.76
7.96
7.94
7.89
7.86
7.40
7.38
6.82
6.79
3.72
2.41
1b
f1 (ppm)
1.00
2.07
1.00
2.17
1.04
3.04
3.08

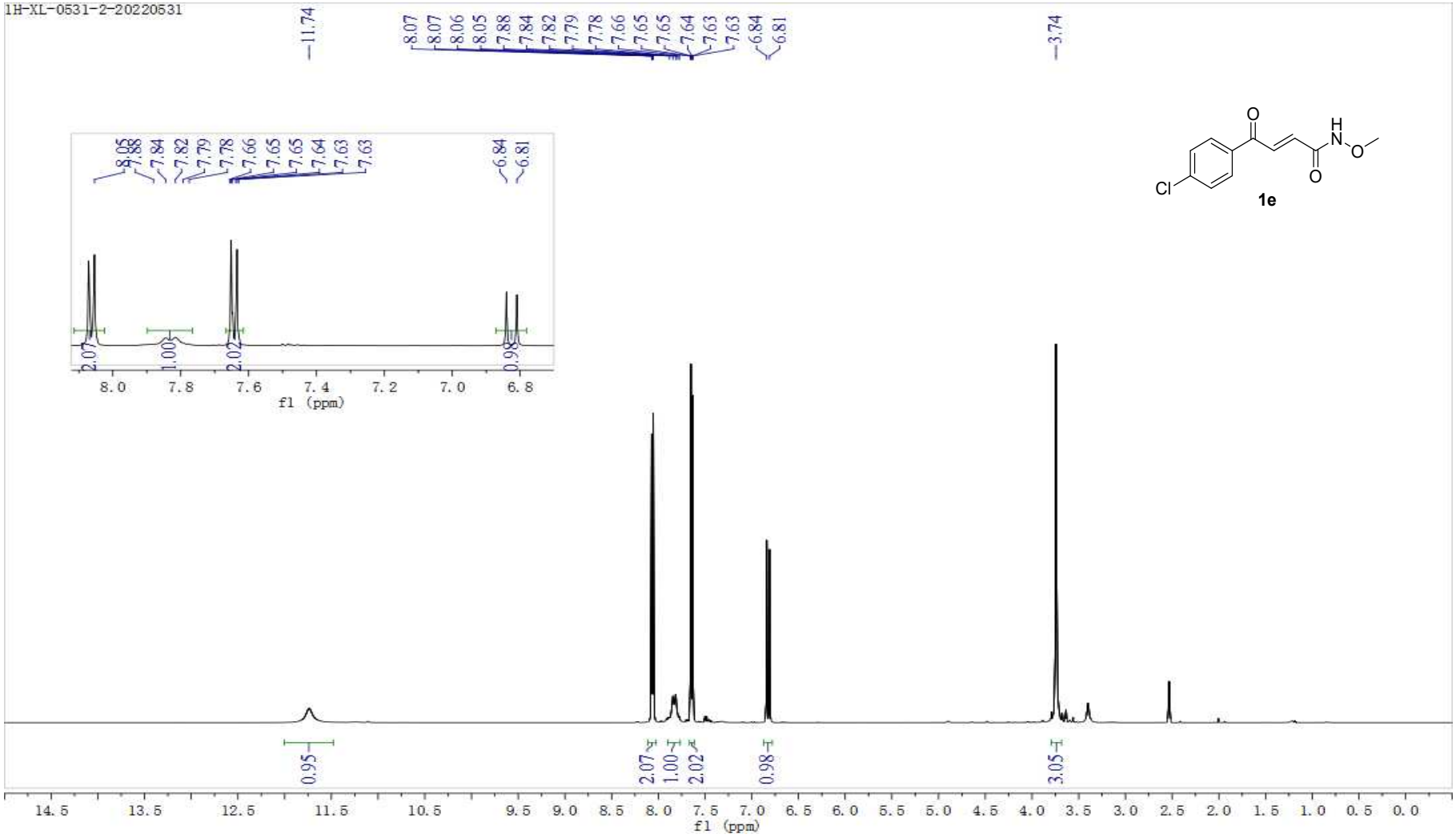

13C-WLG-XL-0524-1-20200524
189.05
161.12
144.99
134.41
133.34
133.07
130.05
129.31
63.93
21.68
O
H
N
O
O
1b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

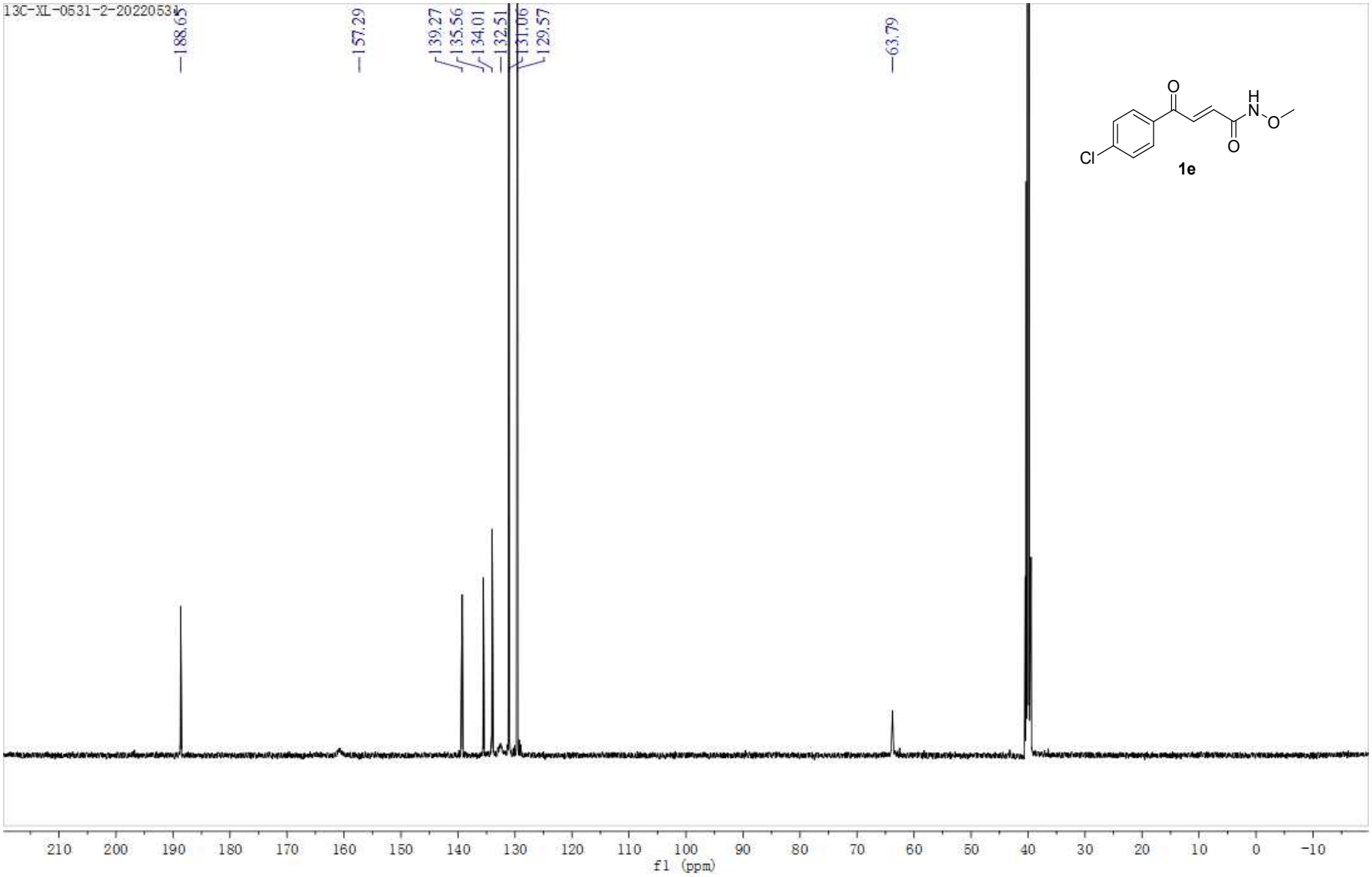

11.74
8.06
8.04
7.90
7.87
7.11
7.09
6.81
6.78
3.88
3.72
1c
f1 (ppm)
0.98
2.16
1.02
2.15
1.00
3.16
3.04

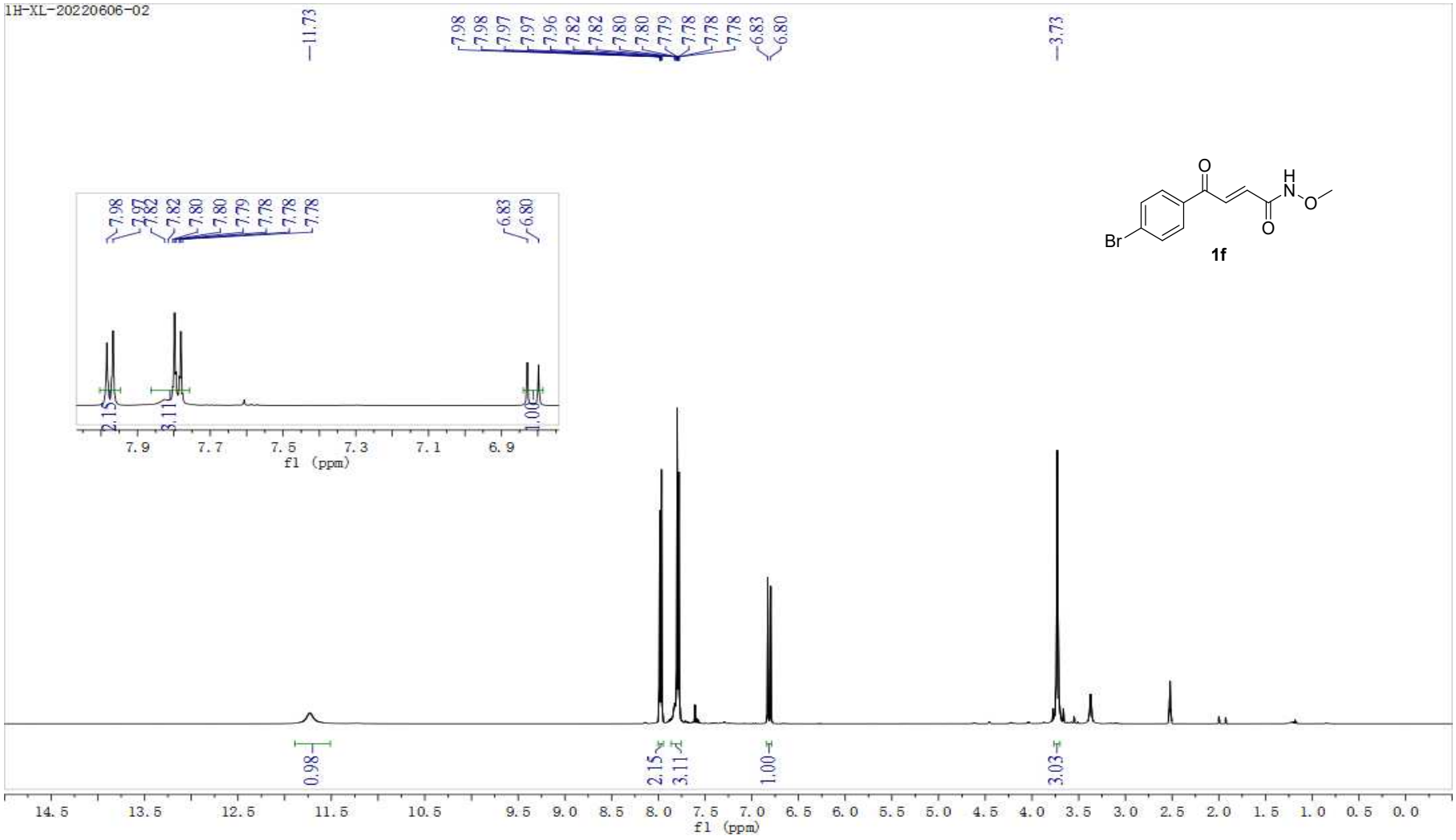

4MeO-219底物-13C-WLG-Xu-0525-3-20220525
187.62
164.24
161.21
133.03
132.93
131.66
129.84
114.77
63.91
56.11
O
H
N
O
O
O
1c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

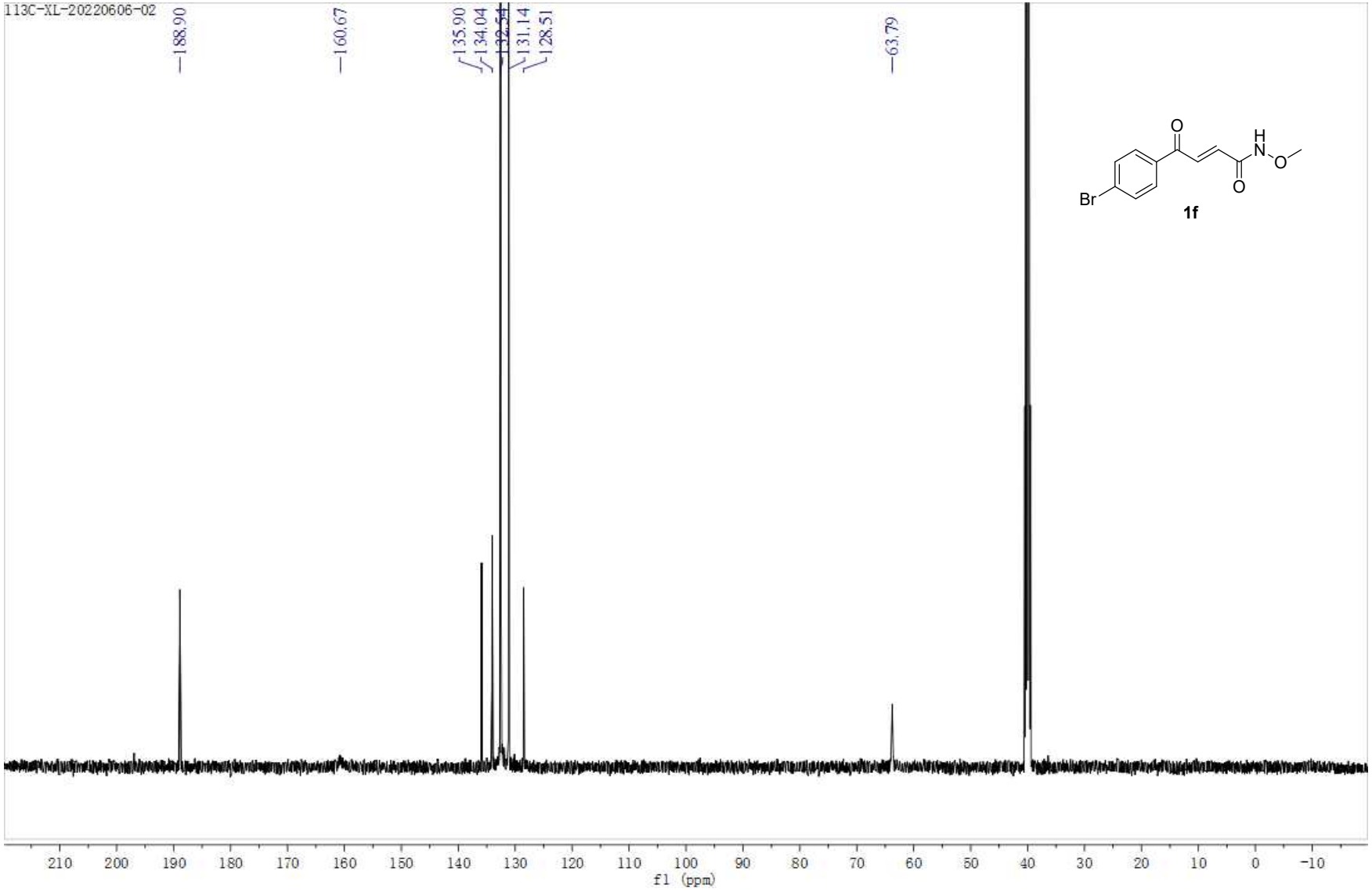

1H-XL-20220606-01
11.73
8.14
8.13
8.13
8.12
8.11
8.11
7.85
7.82
7.40
7.40
7.38
7.37
7.37
6.81
6.78
3.72
F
O
H
N
O
O
1d
f1 (ppm)
0.94
2.12
1.04
2.12
1.00
3.02

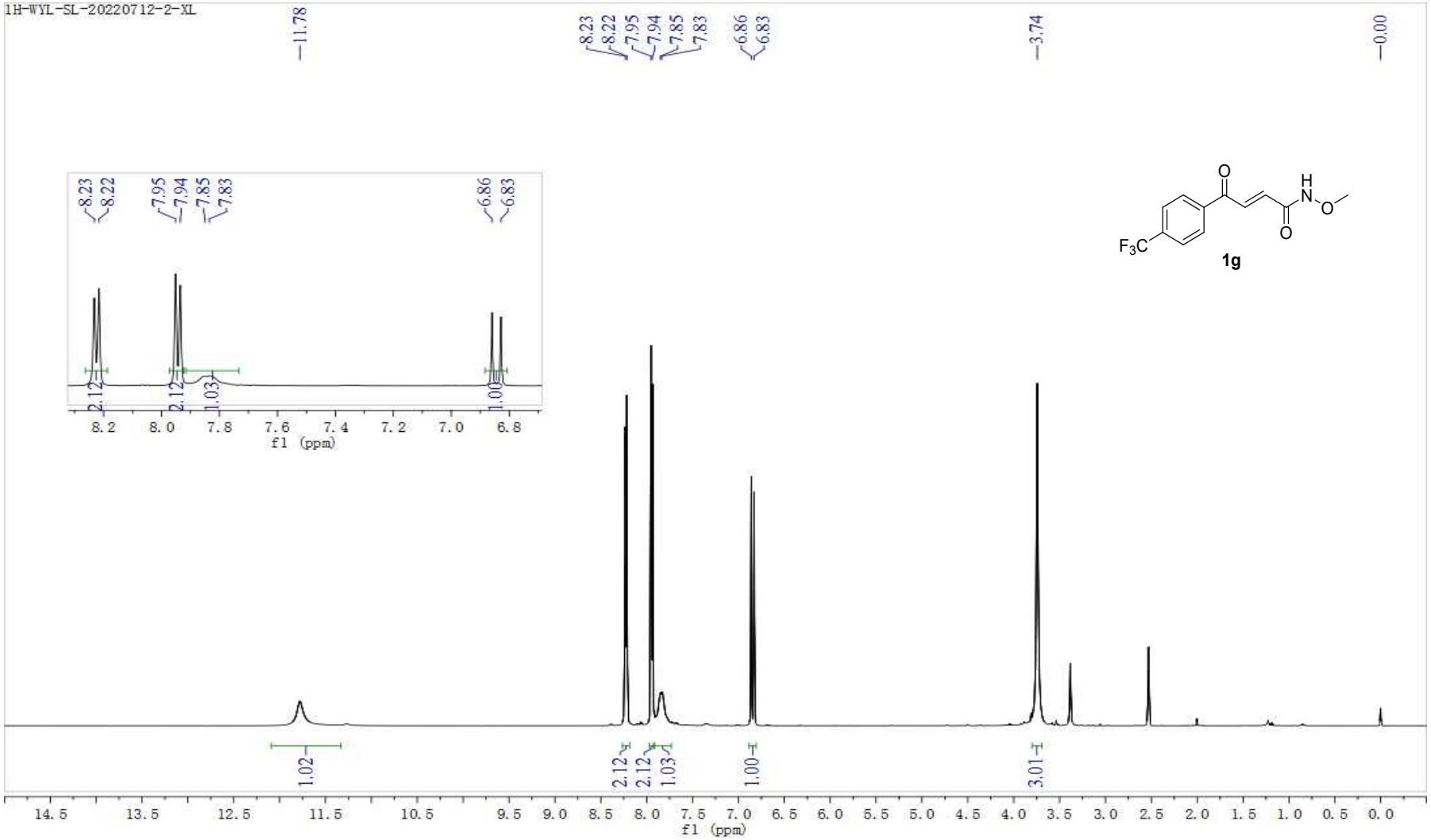

113C-XL-20220606-01
188.24
166.85
164.84
160.99
133.78
133.64
132.85
132.31
132.23
116.62
116.44
63.81
F
O
H
N
O
O
1d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

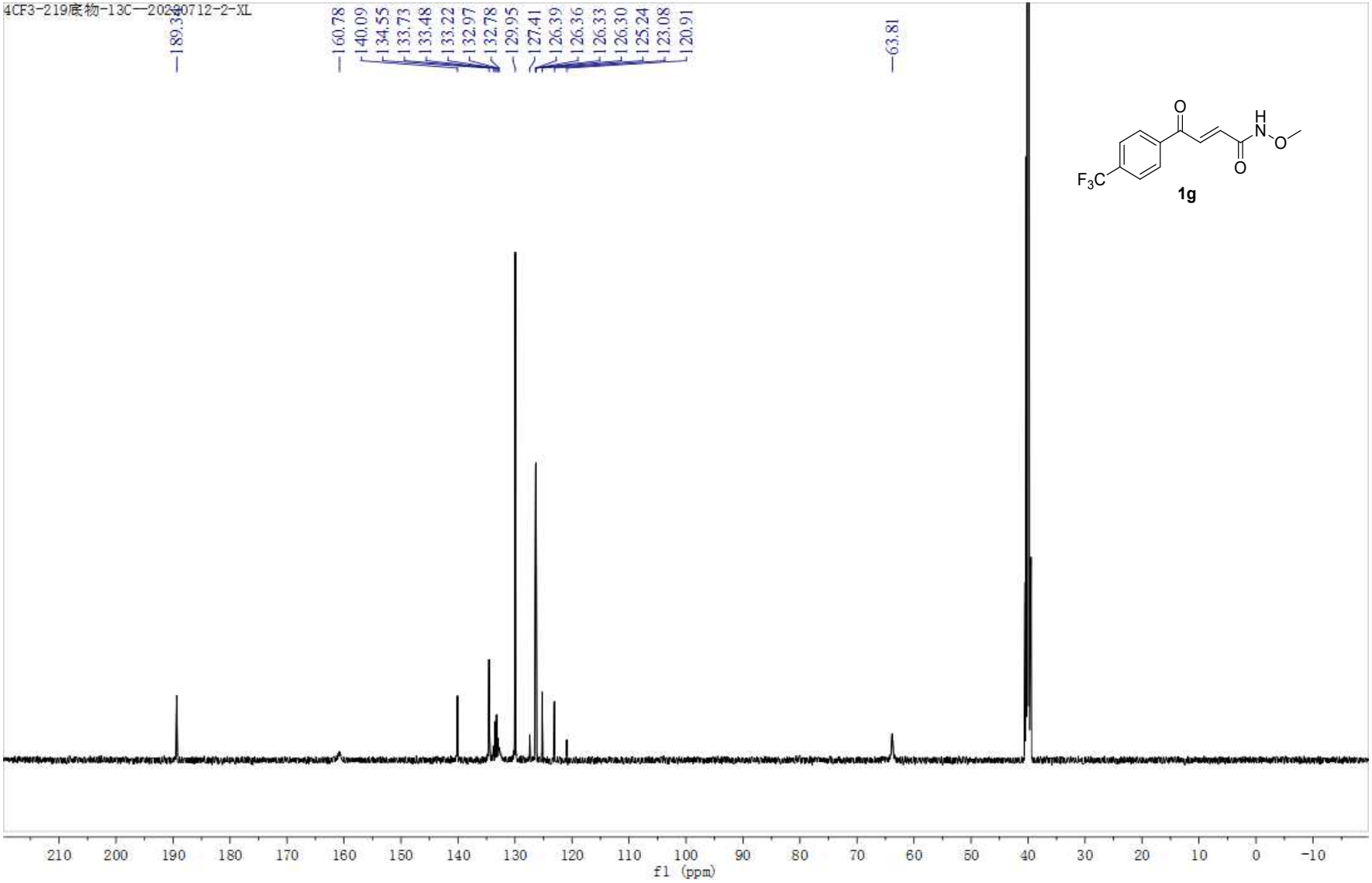

1H-XL-0531-2-20220531
11.74
8.07
8.07
8.06
8.05
7.88
7.84
7.82
7.79
7.78
7.66
7.65
7.65
7.64
7.63
7.63
6.84
6.81
3.74
Cl
1e
f1 (ppm)
0.95
2.07
1.00
2.02
0.98
3.05

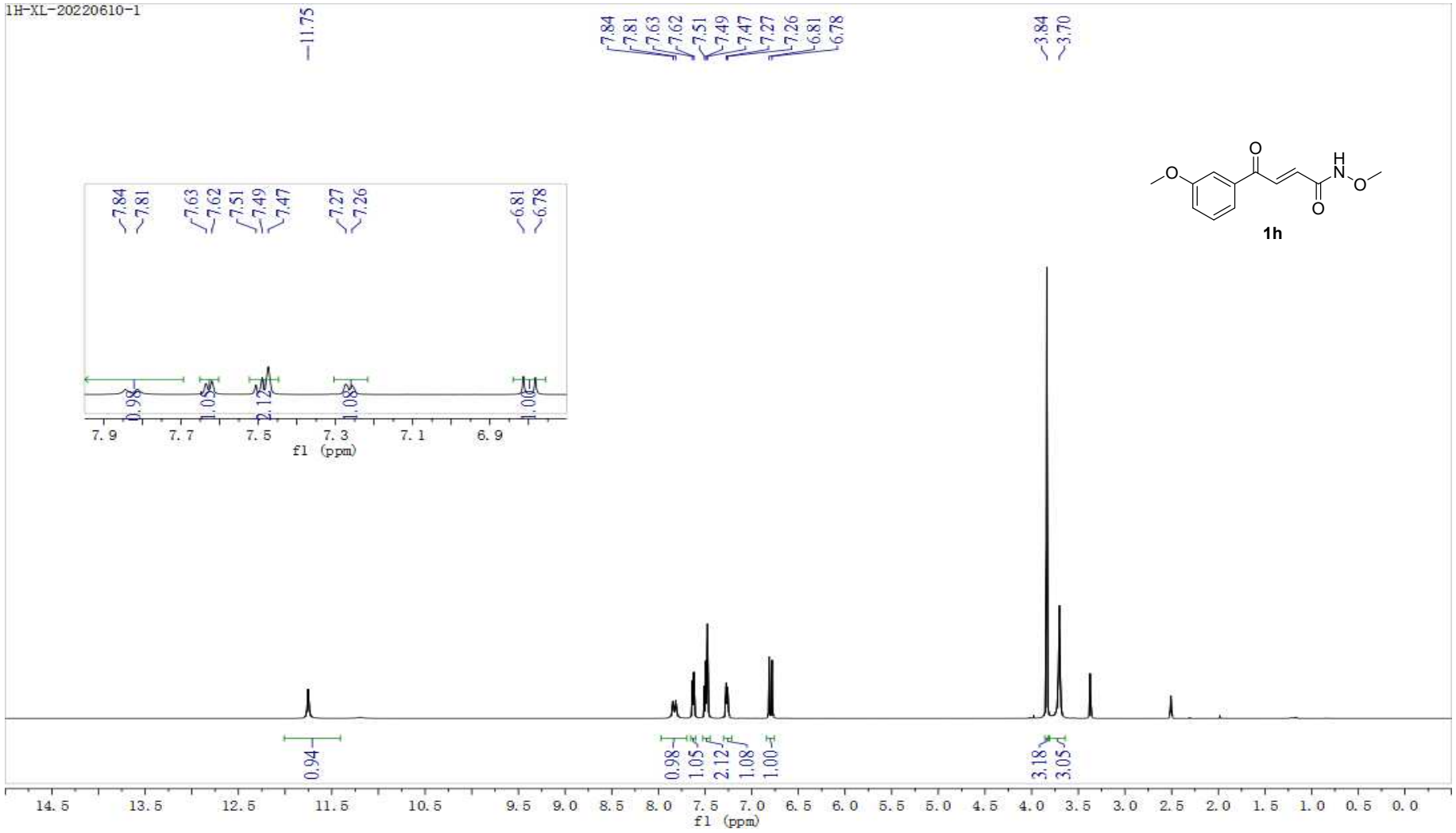

13C-XL-0531-2-20220534
188.65
157.29
139.27
135.56
134.01
132.51
131.06
129.57
63.79
O
H
N
O
O
Cl
1e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

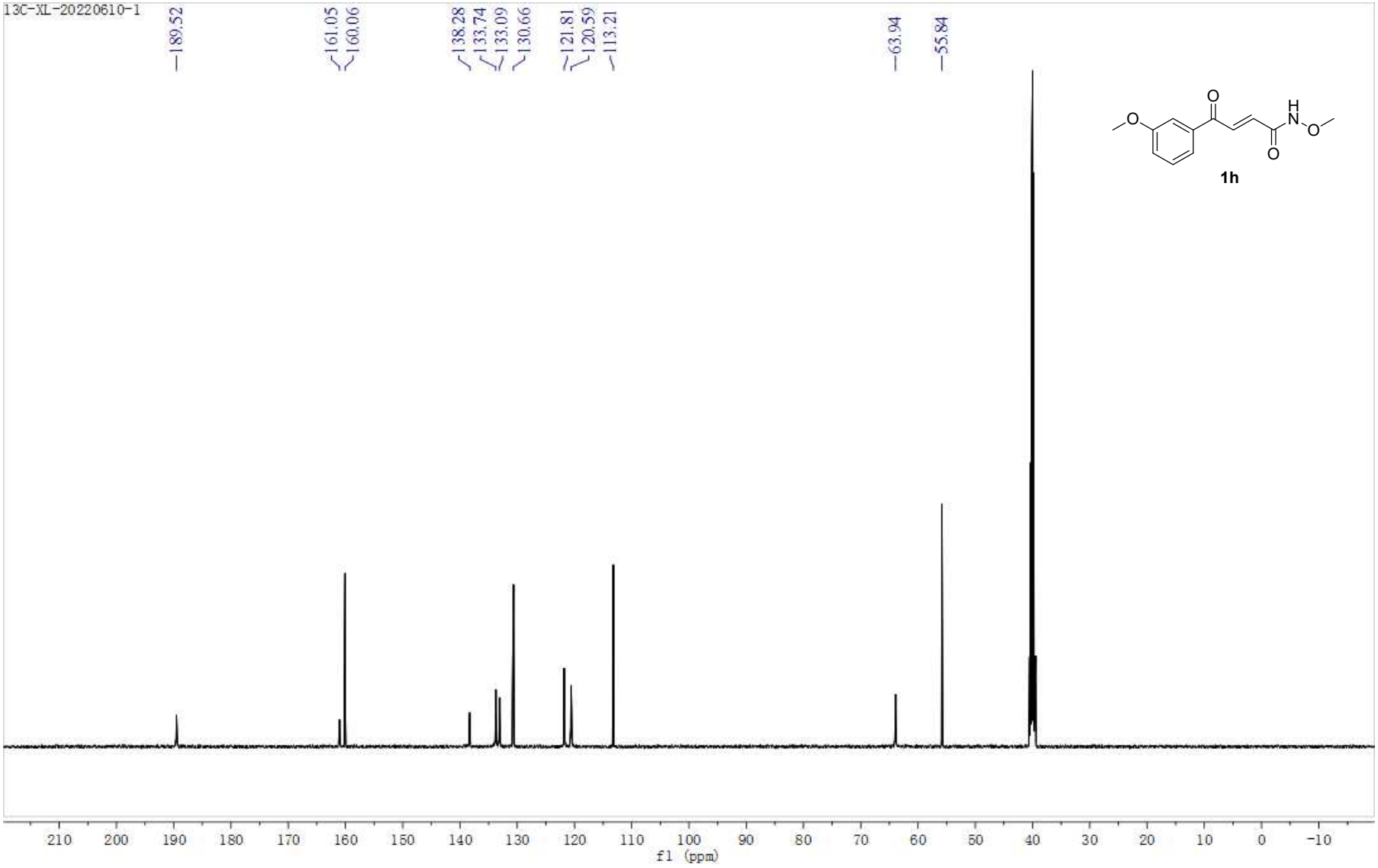

1H-XL-20220606-02
11.73
7.98
7.98
7.97
7.97
7.96
7.82
7.82
7.80
7.80
7.79
7.78
7.78
7.78
6.83
6.80
3.73
Br
1f
2.15
3.11
1.00
f1 (ppm)
0.98
2.15
3.11
1.00
3.03
f1 (ppm)

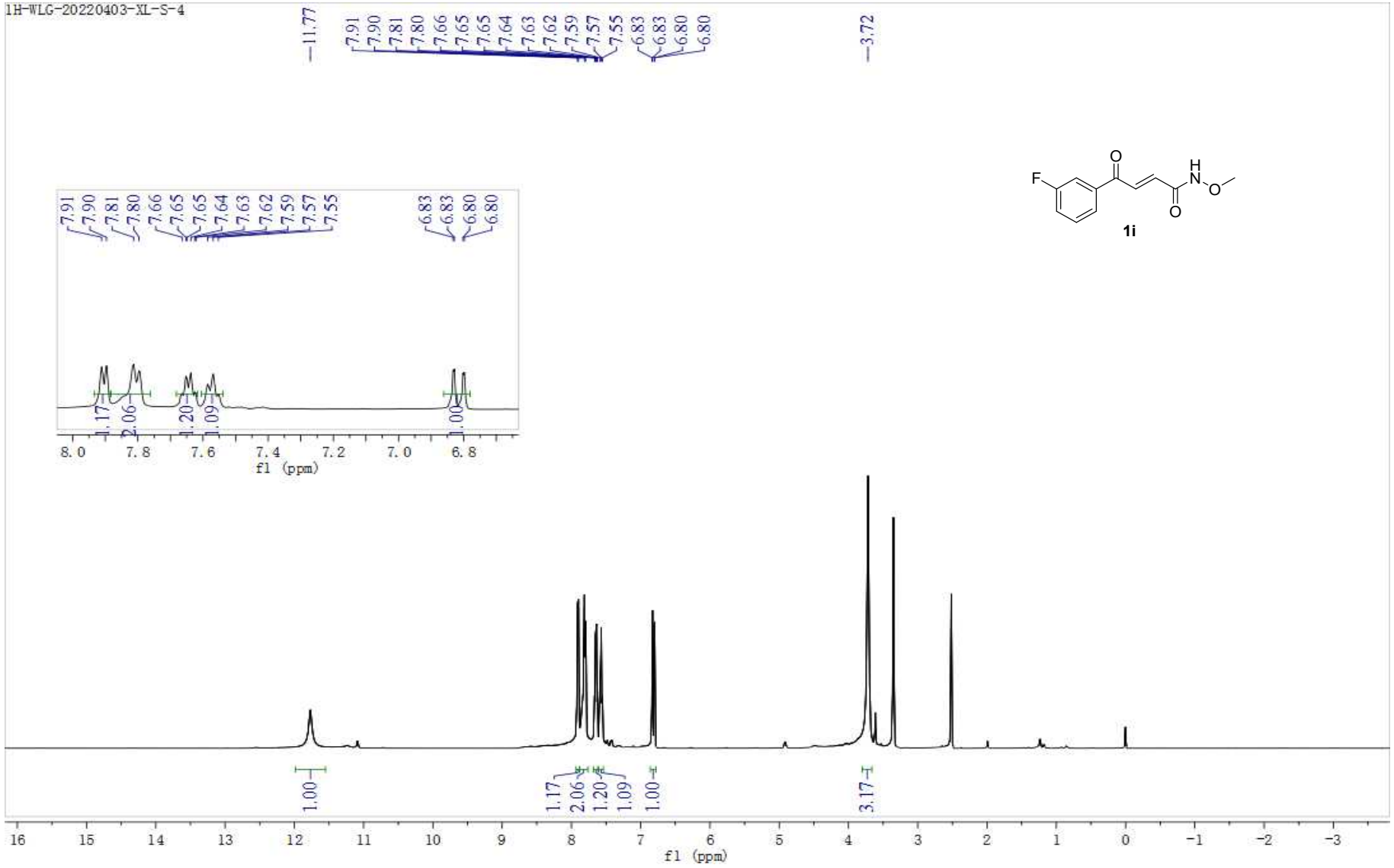

113C-XL-20220606-02
188.90
160.67
135.90
134.04
131.14
128.51
63.79
Br
1f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

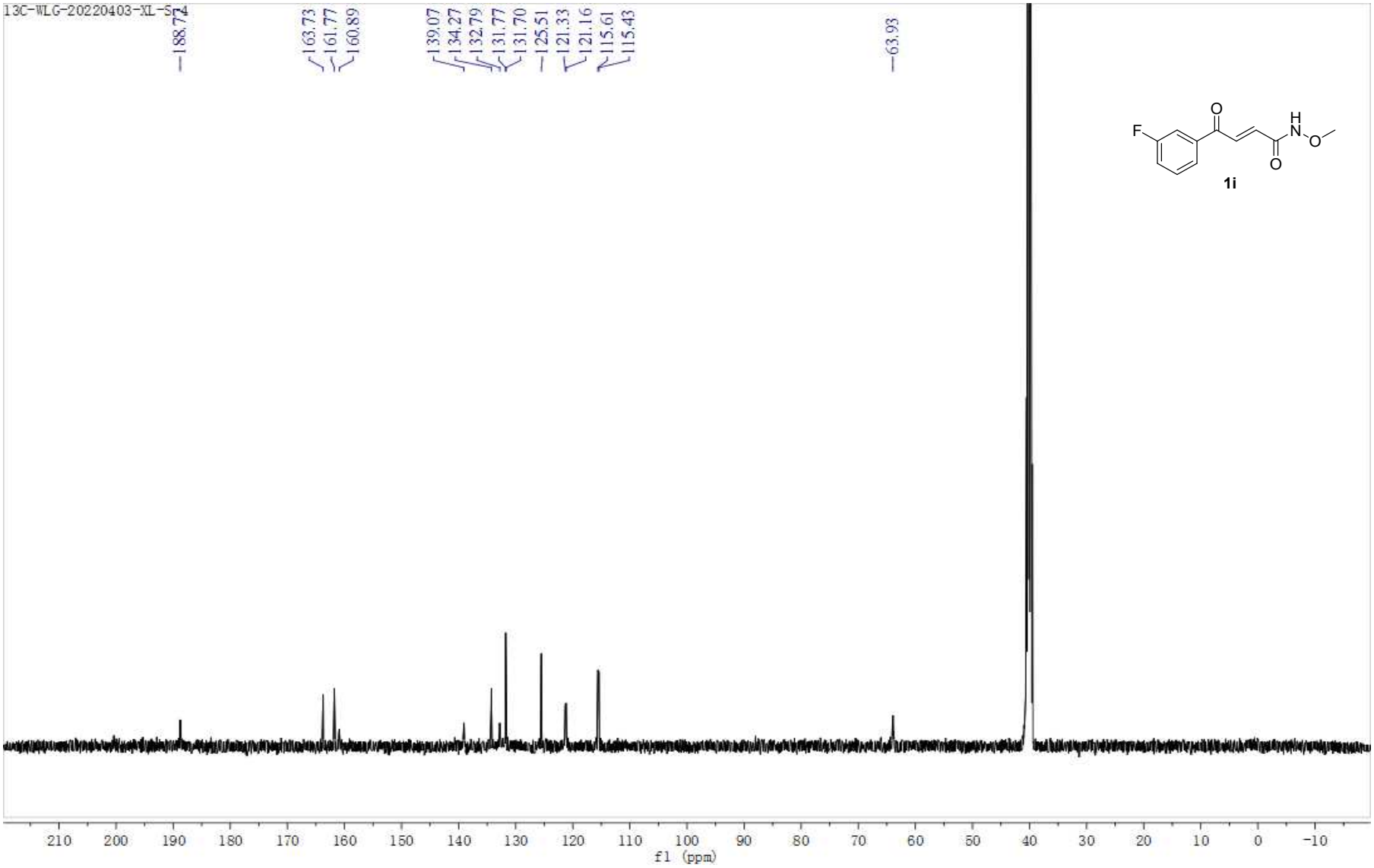

1H-WYL-SL-20220712-2-XL
11.78
8.23
8.22
7.95
7.94
7.85
7.83
6.86
6.83
3.74
0.00
1.02
2.12
2.12
1.03
1.00
3.01
f1 (ppm)
1g

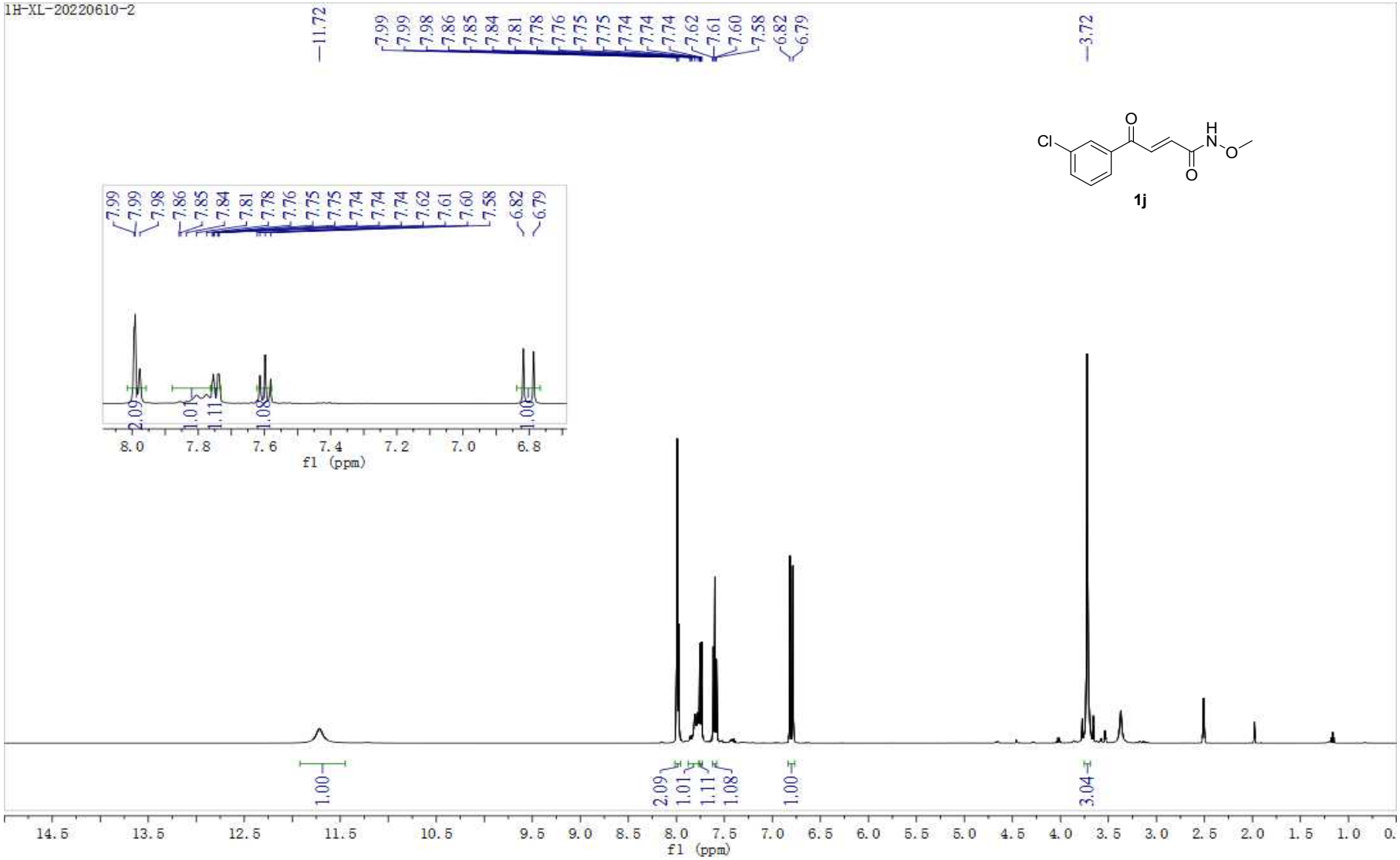

4CF3-219底物-13C—20240712-2-XL
189.36
160.78
140.09
134.55
133.73
133.48
133.22
132.97
132.78
129.95
127.41
126.39
126.36
126.33
126.30
125.24
123.08
120.91
63.81
O
H
N
O
O
F3C
1g
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

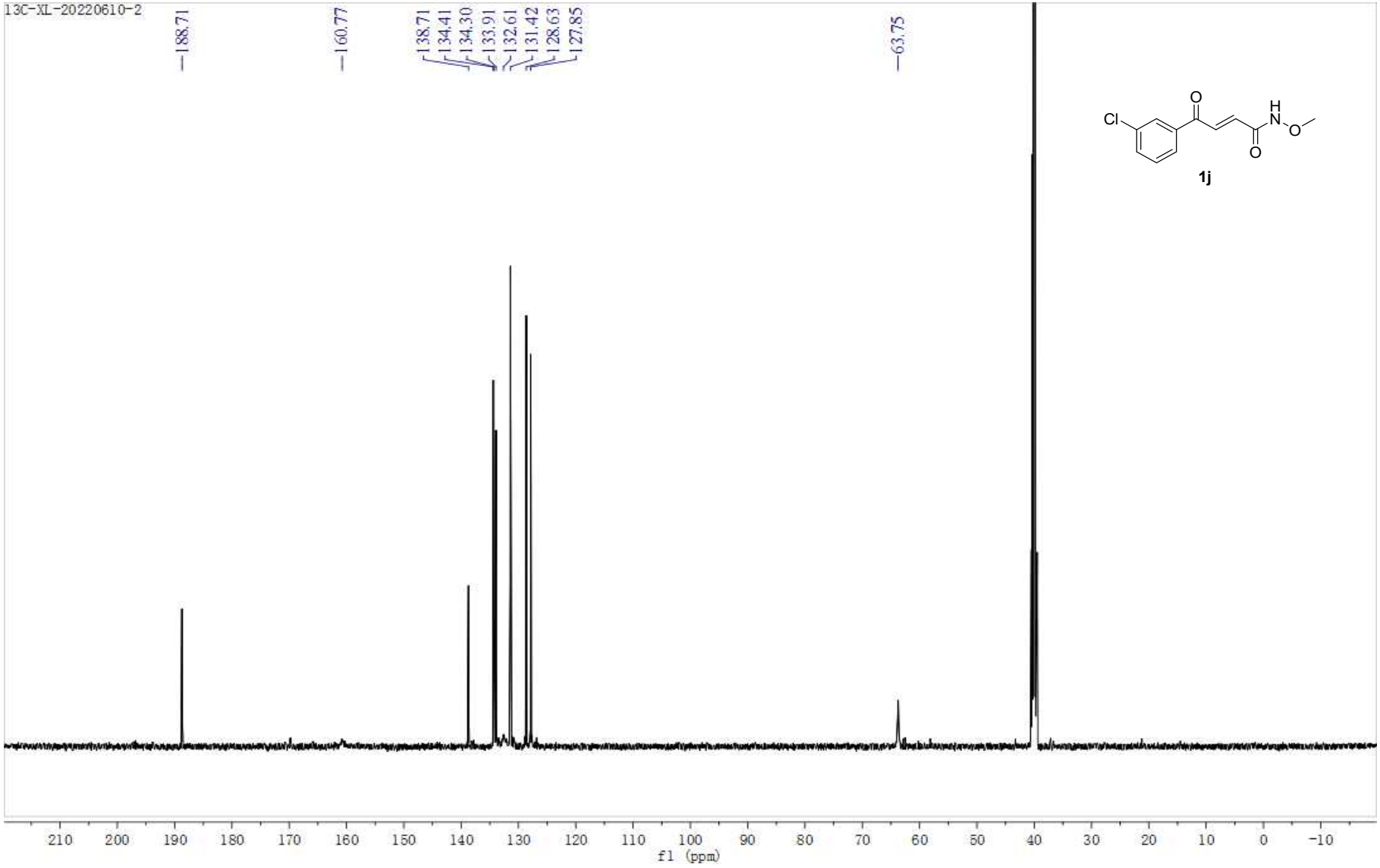

1H-XL-20220610-1
11.75
7.84
7.81
7.63
7.62
7.51
7.49
7.47
7.27
7.26
6.81
6.78
3.84
3.70
1h
f1 (ppm)

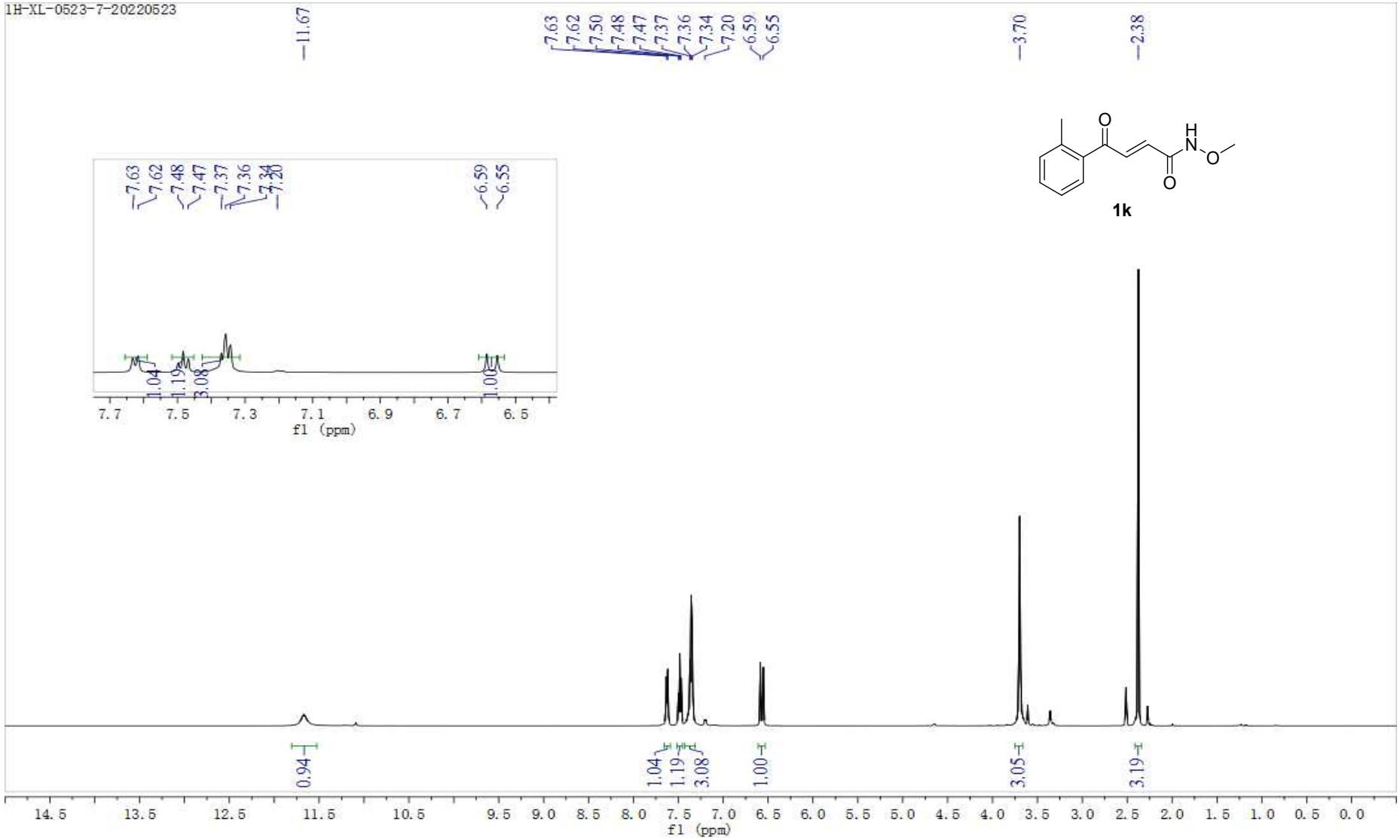

13C-XL-20220610-1
189.52
161.05
160.06
138.28
133.74
133.09
130.66
121.81
120.59
113.21
63.94
55.84
O
H
N
O
O
O
1h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

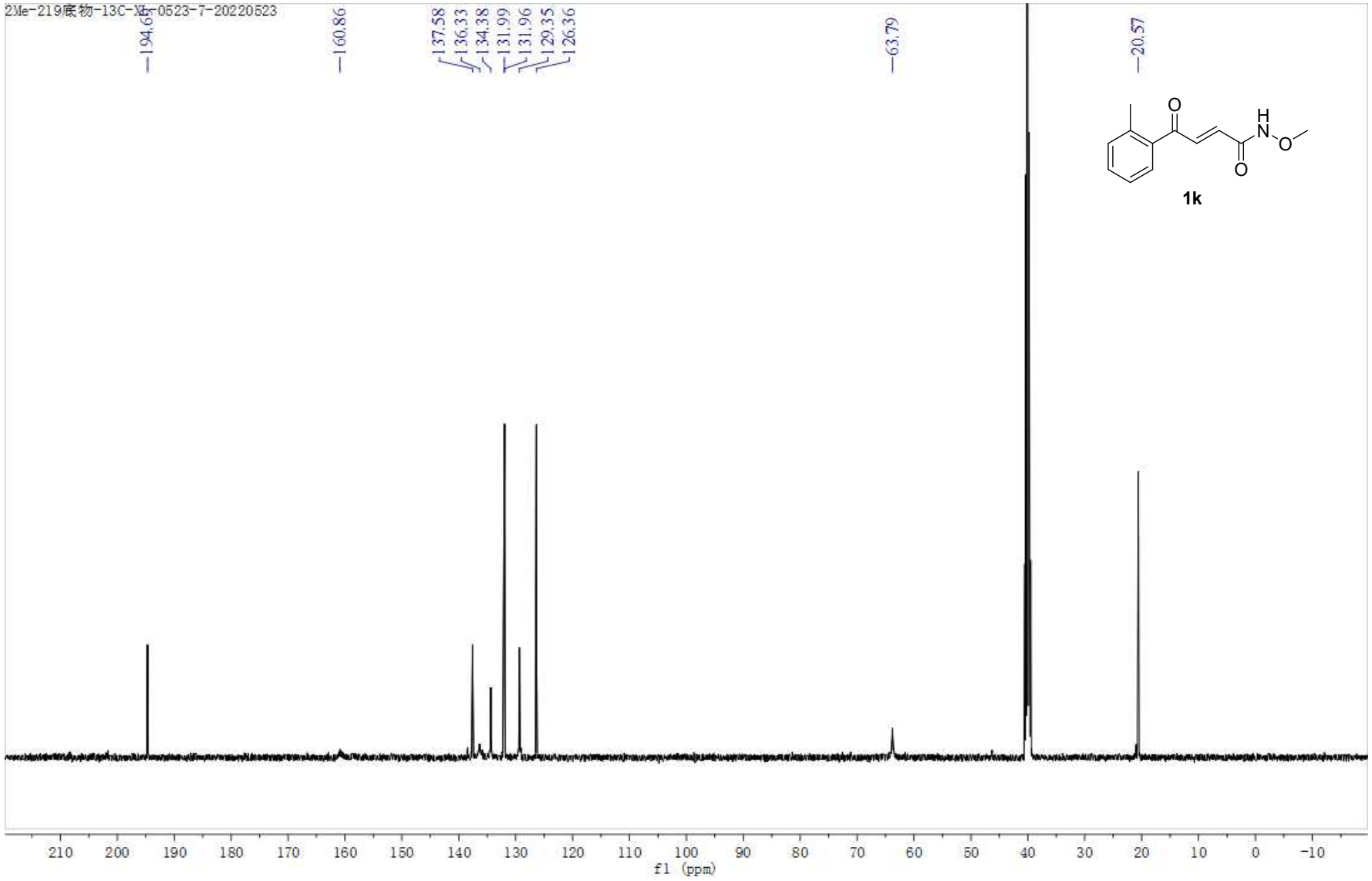

1H-WLG-20220403-XL-S-4
11.77
7.91
7.90
7.81
7.80
7.66
7.65
7.65
7.64
7.63
7.62
7.59
7.57
7.55
6.83
6.83
6.80
6.80
3.72
F
O
H
N
O
O
1i
1.17
2.06
1.20
1.09
1.00
8.0
7.8
7.6
7.4
7.2
7.0
6.8
f1 (ppm)
1.00
1.17
2.06
1.20
1.09
1.00
3.17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
−3
f1 (ppm)

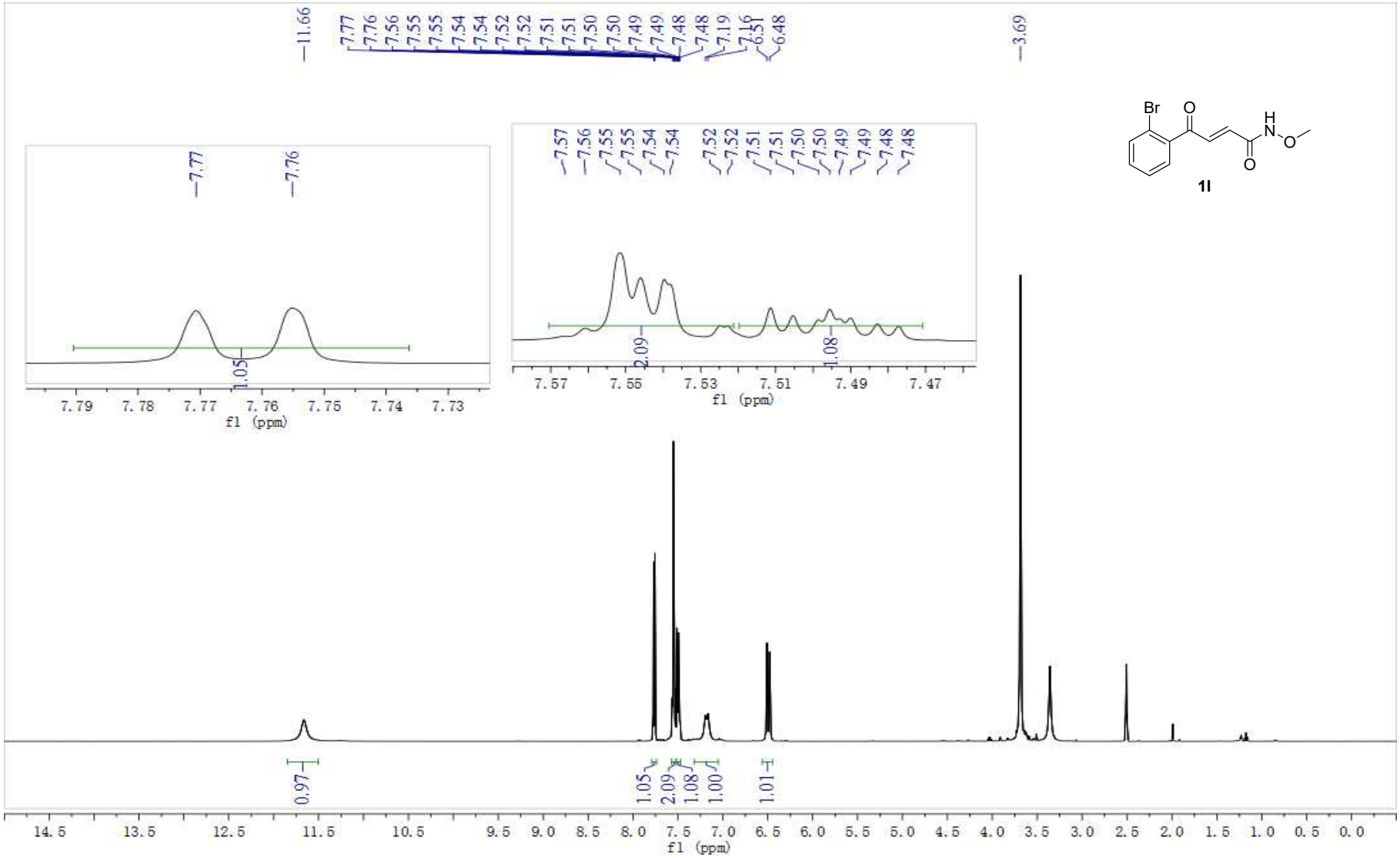

13C-WLG-20220403-XL-S4
188.72
163.73
161.77
160.89
139.07
134.27
132.79
131.77
131.70
125.51
121.33
121.16
115.61
115.43
63.93
F
O
H
N
O
O
1i
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

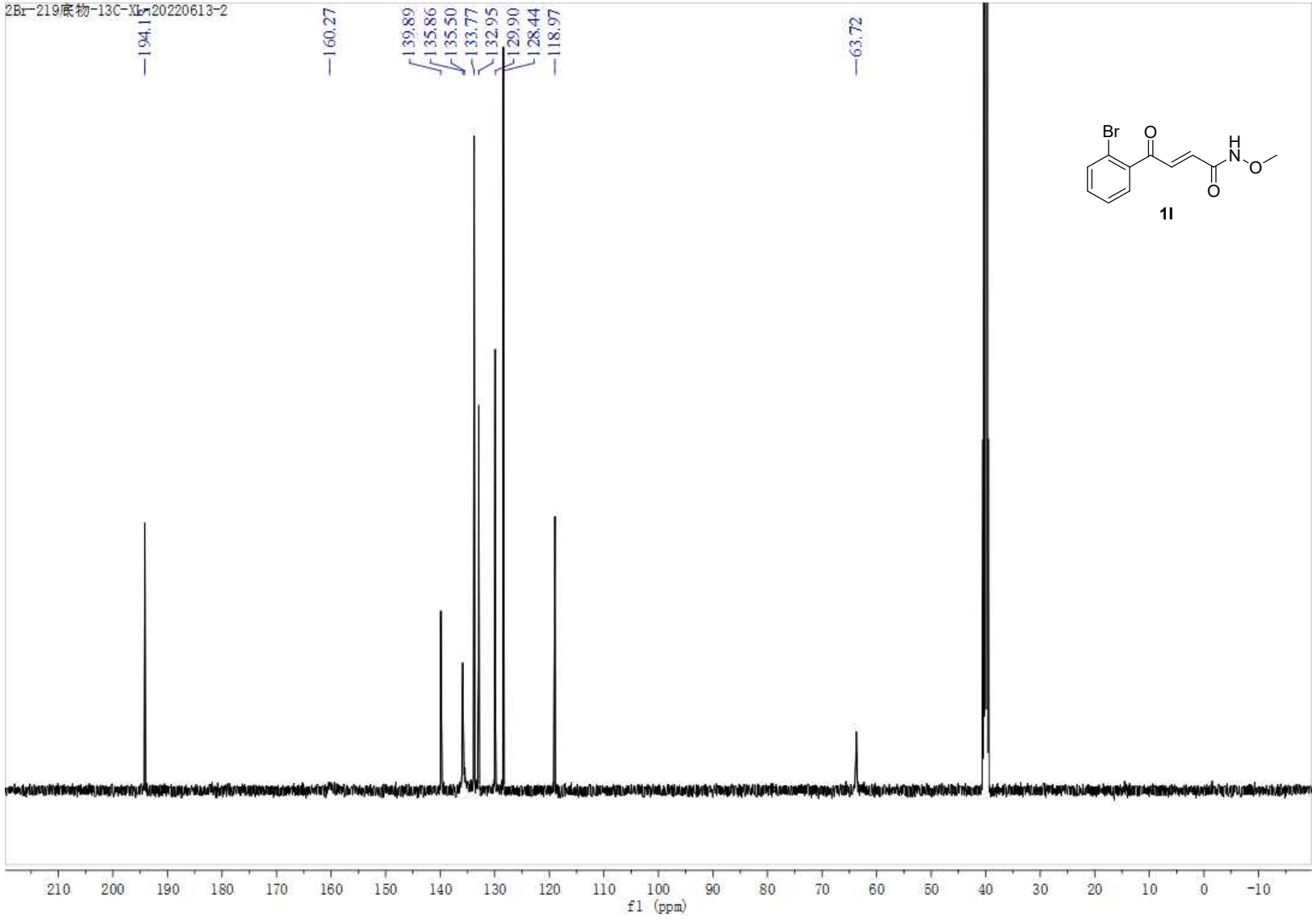

1H-XL-20220610-2
11.72
7.99
7.99
7.98
7.86
7.85
7.84
7.81
7.78
7.76
7.75
7.75
7.74
7.74
7.74
7.62
7.61
7.60
7.58
6.82
6.79
3.72
Cl
O
H
N
O
O
1j
f1 (ppm)
1.00
2.09
1.01
1.11
1.08
1.00
3.04

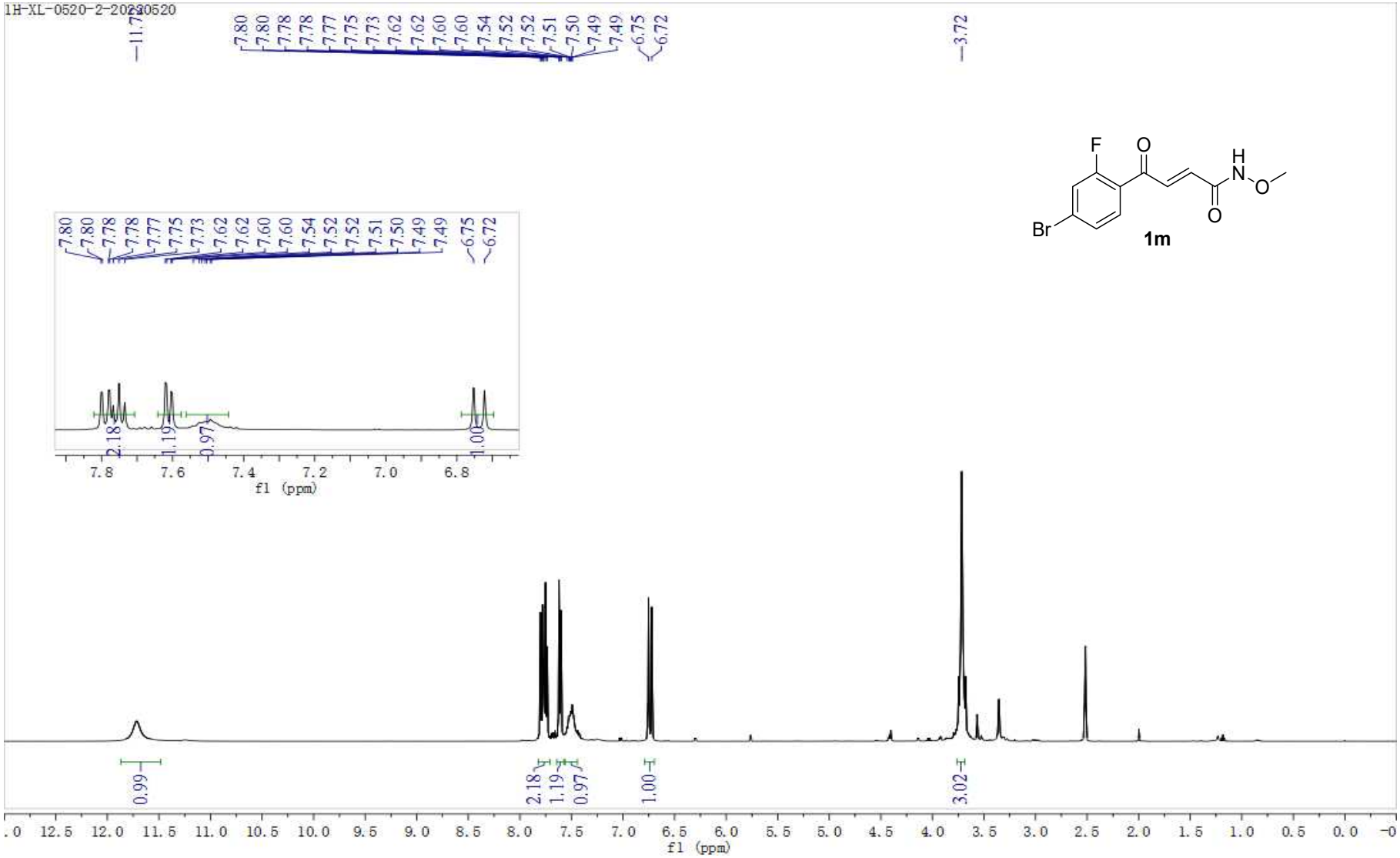

13C-XL-20220610-2
188.71
160.77
138.71
134.41
134.30
133.91
132.61
131.42
128.63
127.85
63.75
Cl
O
H
N
O
O
1j
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

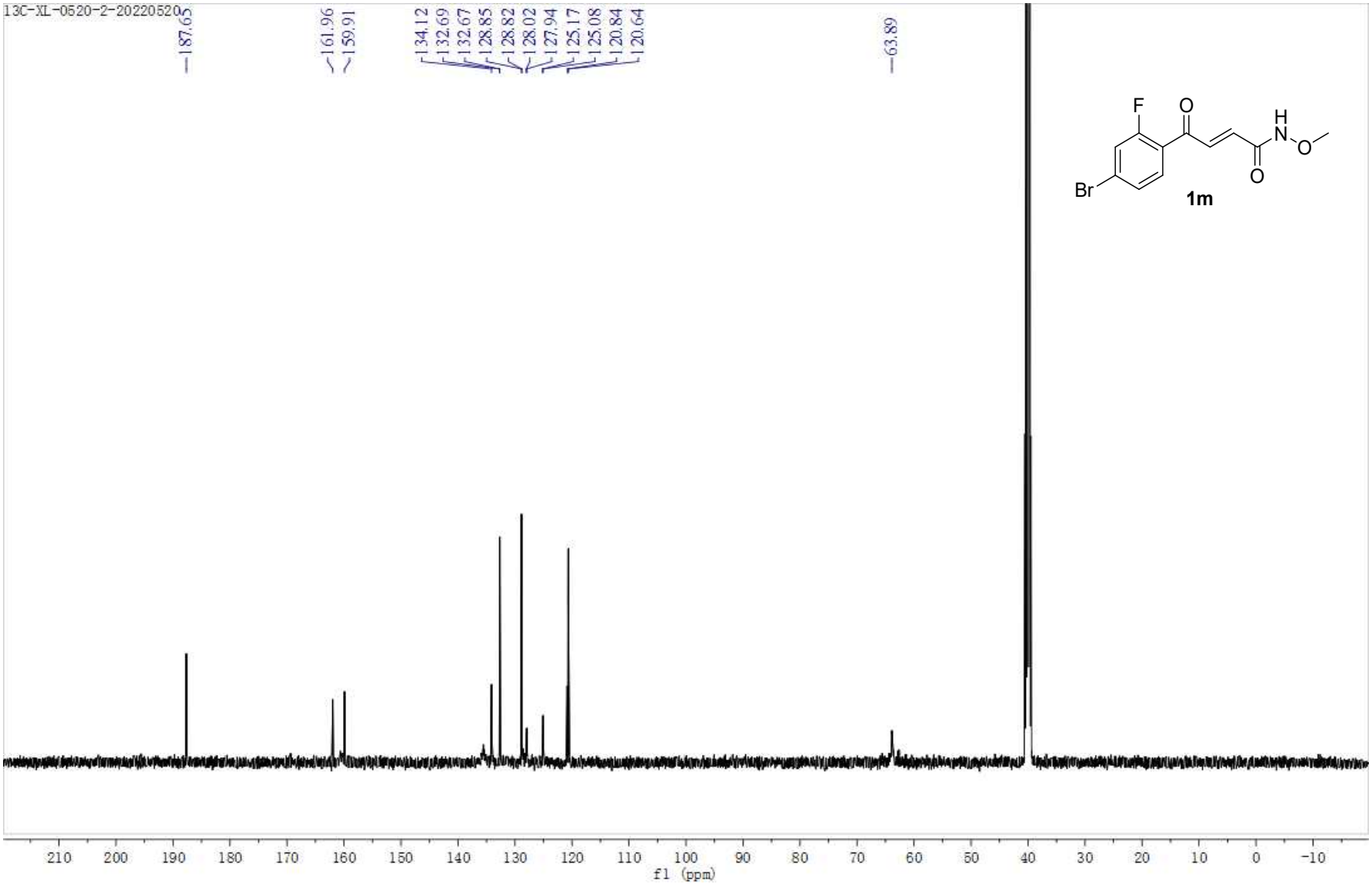

1H-XL-0523-7-20220523
11.67
7.63
7.62
7.50
7.48
7.47
7.37
7.36
7.34
7.20
6.59
6.55
3.70
2.38
1k
f1 (ppm)

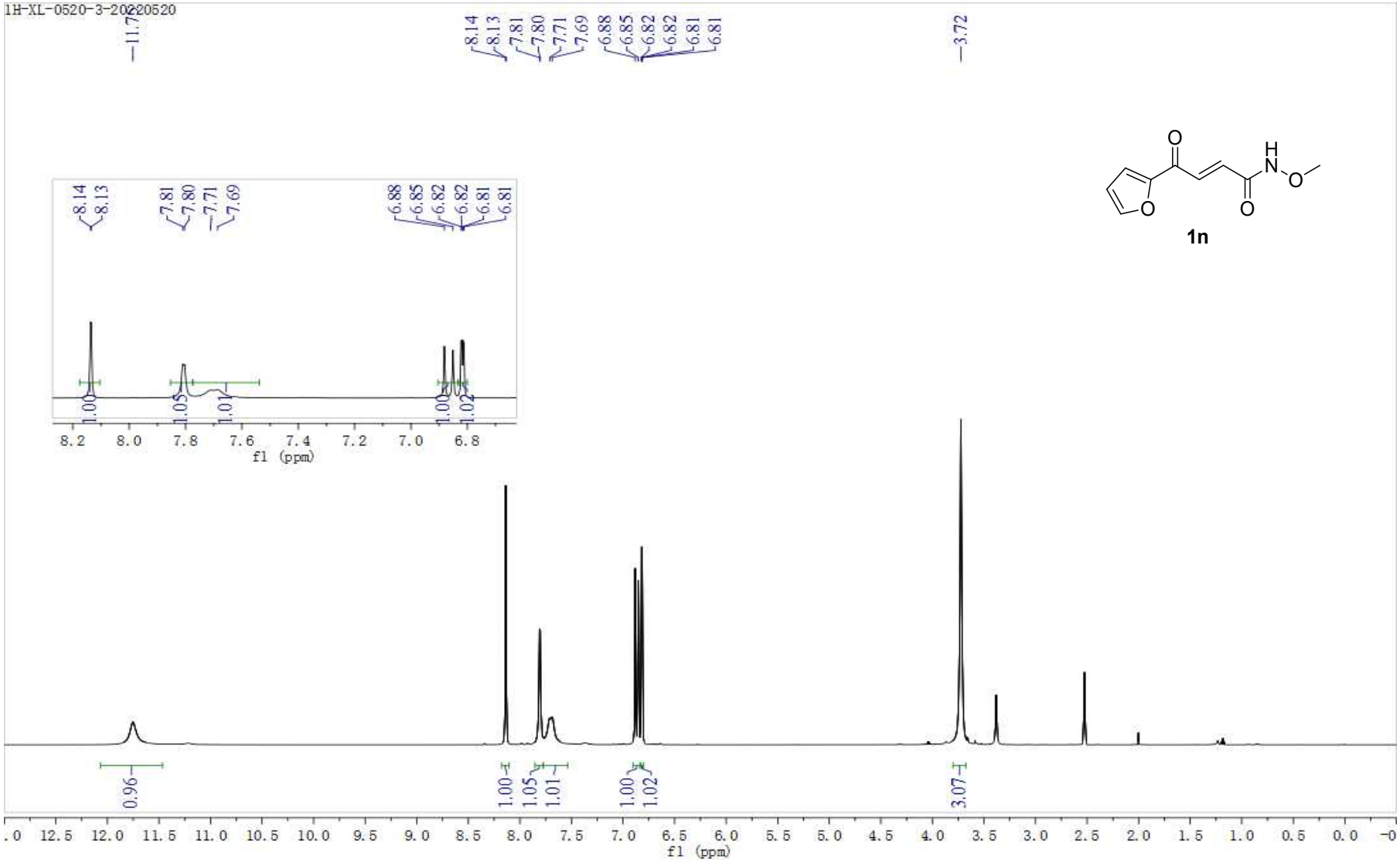

2Me-219底物-13C-XY-0523-7-20220523
194.65
160.86
137.58
136.33
134.38
131.99
131.96
129.35
126.36
63.79
20.57
O
H
N
O
O
1k
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


11.66
7.77
7.76
7.56
7.55
7.55
7.54
7.54
7.52
7.52
7.51
7.51
7.50
7.50
7.49
7.49
7.48
7.48
7.19
7.16
6.51
6.48
3.69
Br
O
H
N
O
O
1l
f1 (ppm)
0.97
1.05
2.09
1.08
1.00
1.01

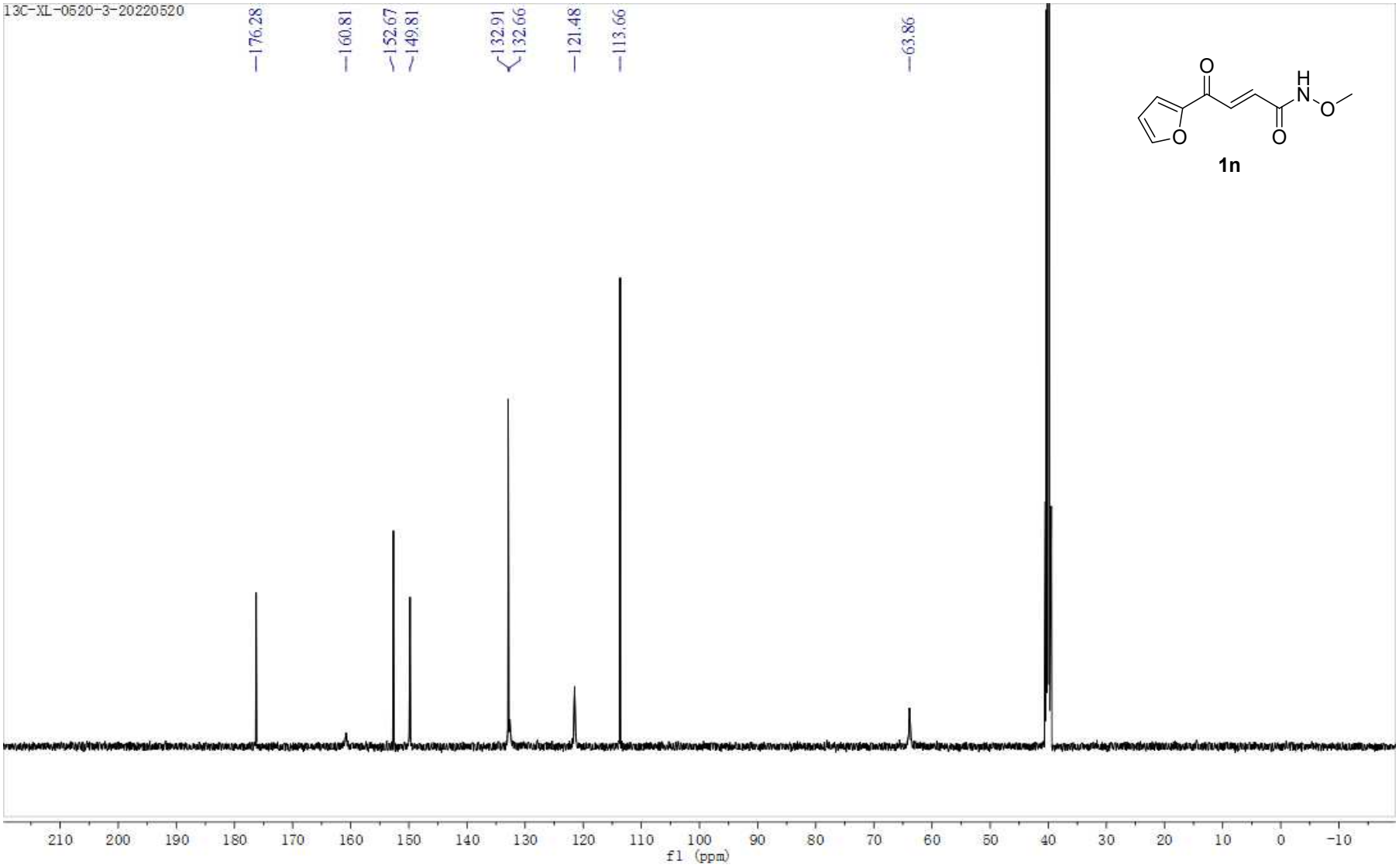

2Br-219底物-13C-XL-20220613-2
194.15
160.27
139.89
135.86
135.50
133.77
132.95
129.90
128.44
118.97
63.72
Br
O
H
N
O
O
1l
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

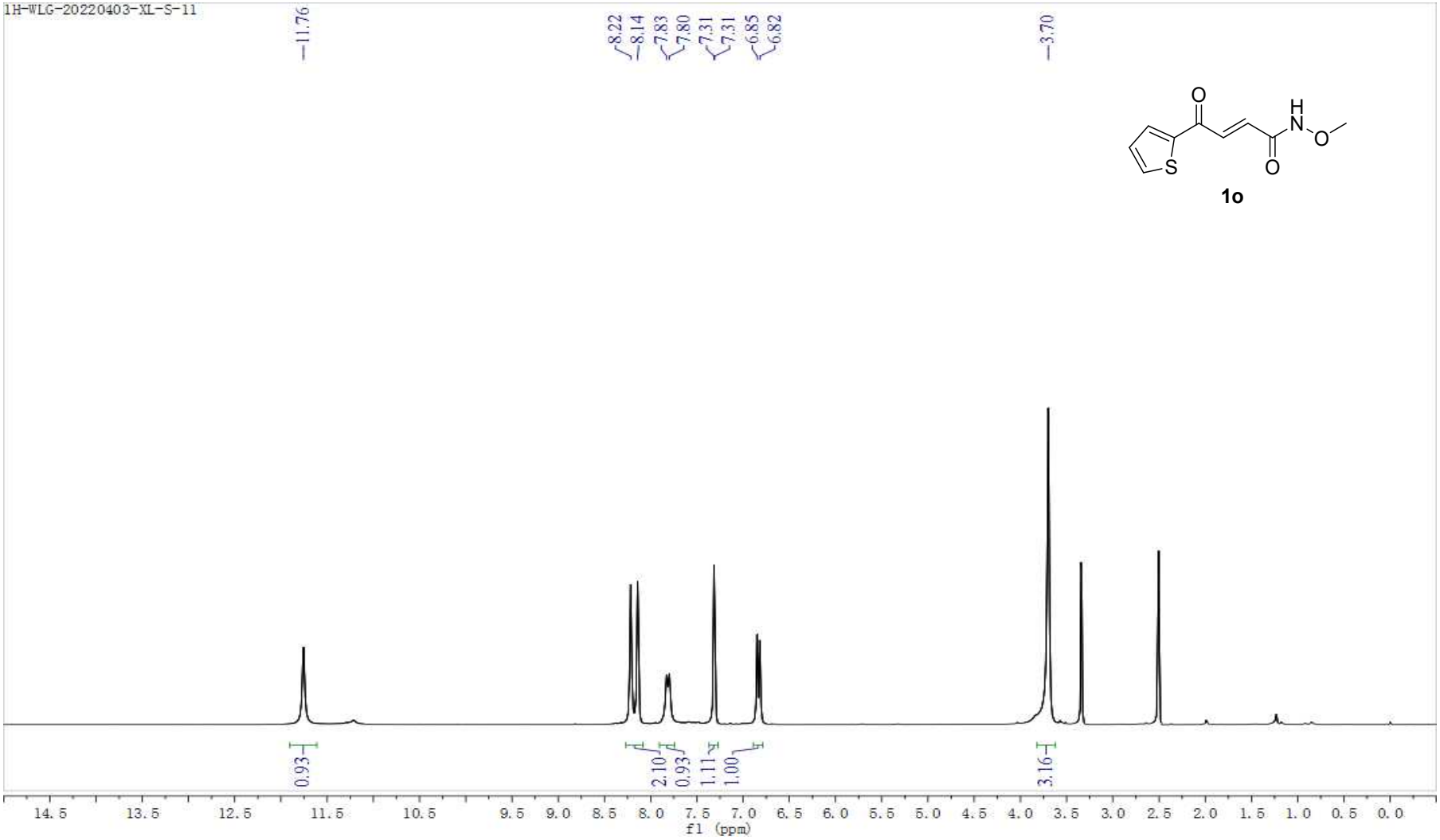

1H-XL-0520-2-20200520
11.72
7.80
7.80
7.78
7.78
7.77
7.75
7.73
7.62
7.62
7.60
7.60
7.54
7.52
7.52
7.51
7.50
7.49
7.49
6.75
6.72
3.72
F
O
H
N
O
Br
O
1m
2.18
1.19
0.97
1.00
7.8
7.6
7.4
7.2
7.0
6.8
f1 (ppm)
0.99
2.18
1.19
0.97
1.00
3.02
f1 (ppm)

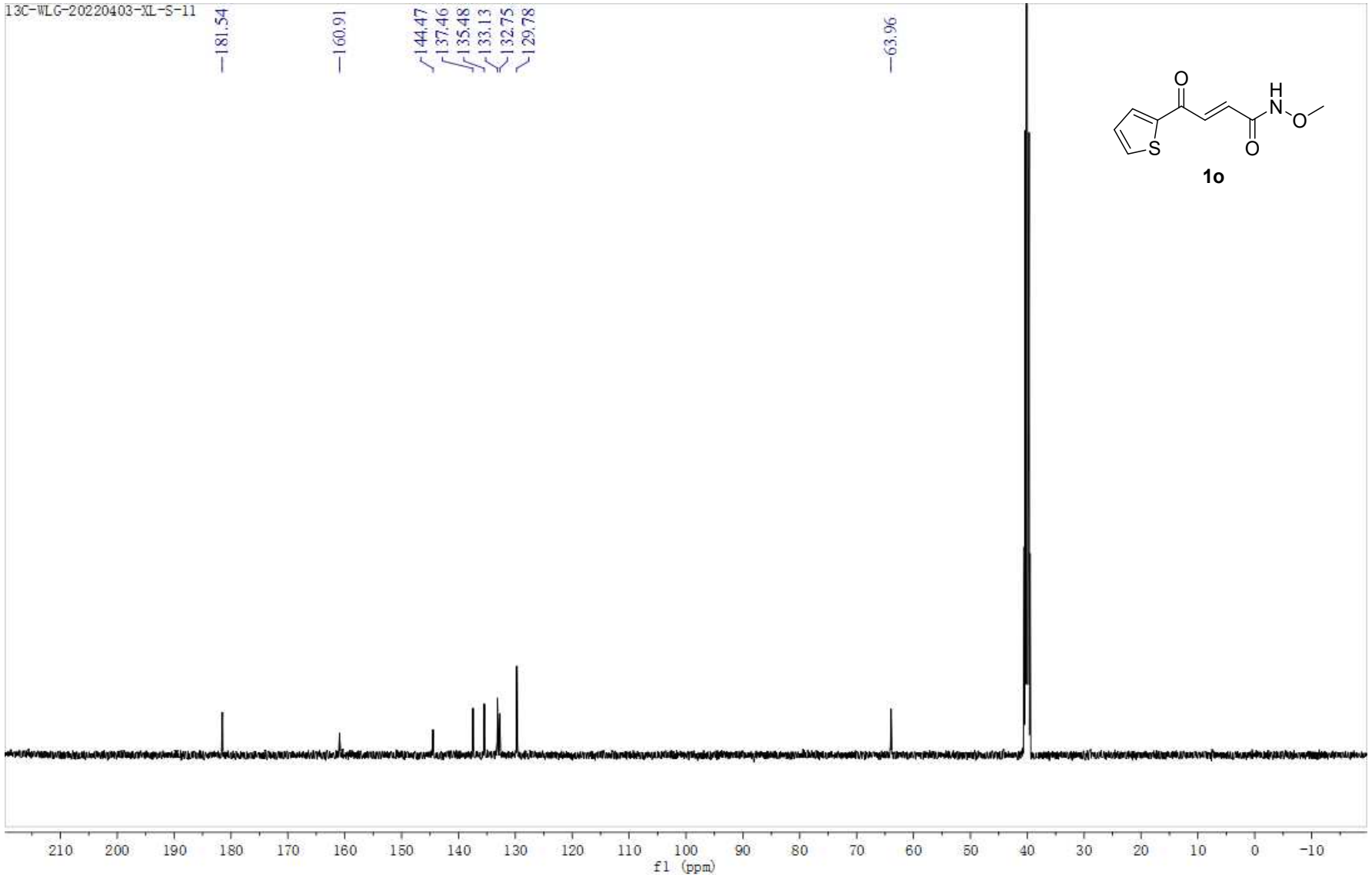

13C-XL-0520-2-20220520
187.65
161.96
159.91
134.12
132.69
132.67
128.85
128.82
128.02
127.94
125.17
125.08
120.84
120.64
63.89
F
O
H
N
O
O
Br
1m
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

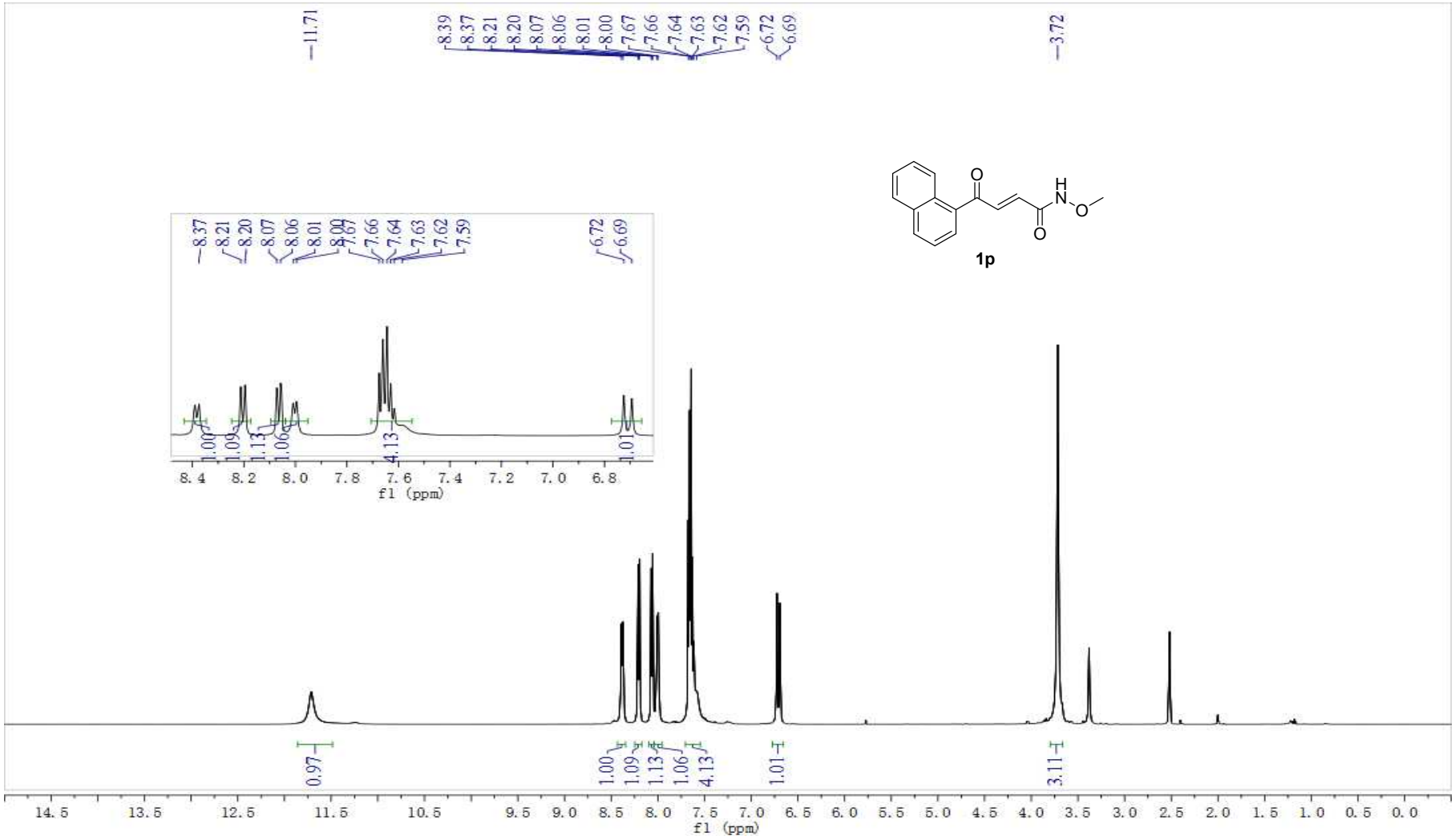

1H-XL-0520-3-20220520
11.72
8.14
8.13
7.81
7.80
7.71
7.69
6.88
6.85
6.82
6.82
6.81
6.81
3.72
1.00
1.05
1.01
1.00
1.02
f1 (ppm)
0.96
1.00
1.05
1.01
1.00
1.02
3.07
f1 (ppm)

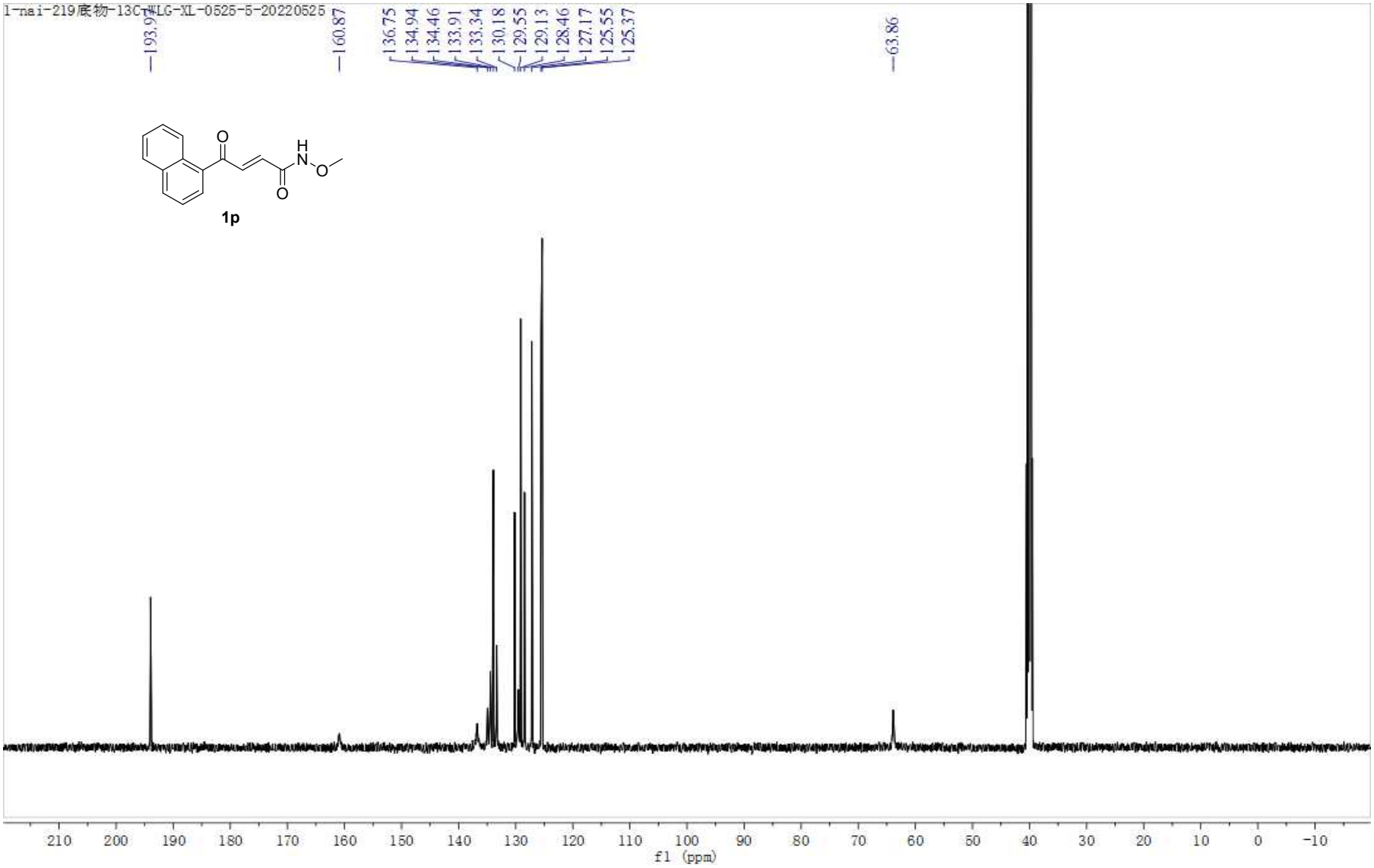
1n

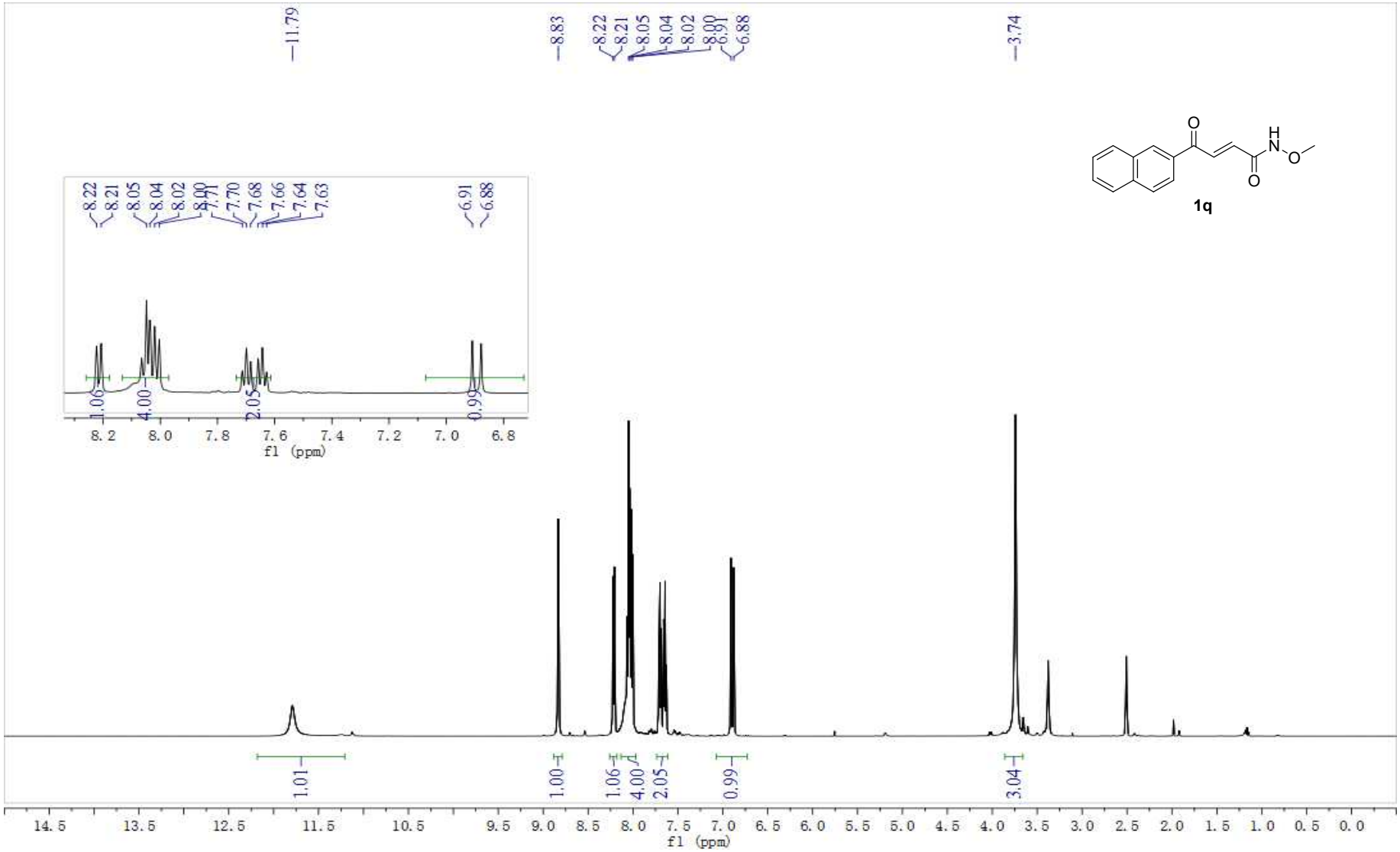

13C-XL-0520-3-20220520
176.28
160.81
152.67
149.81
132.91
132.66
121.48
113.66
63.86
O
H
N
O
O
O
1n
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

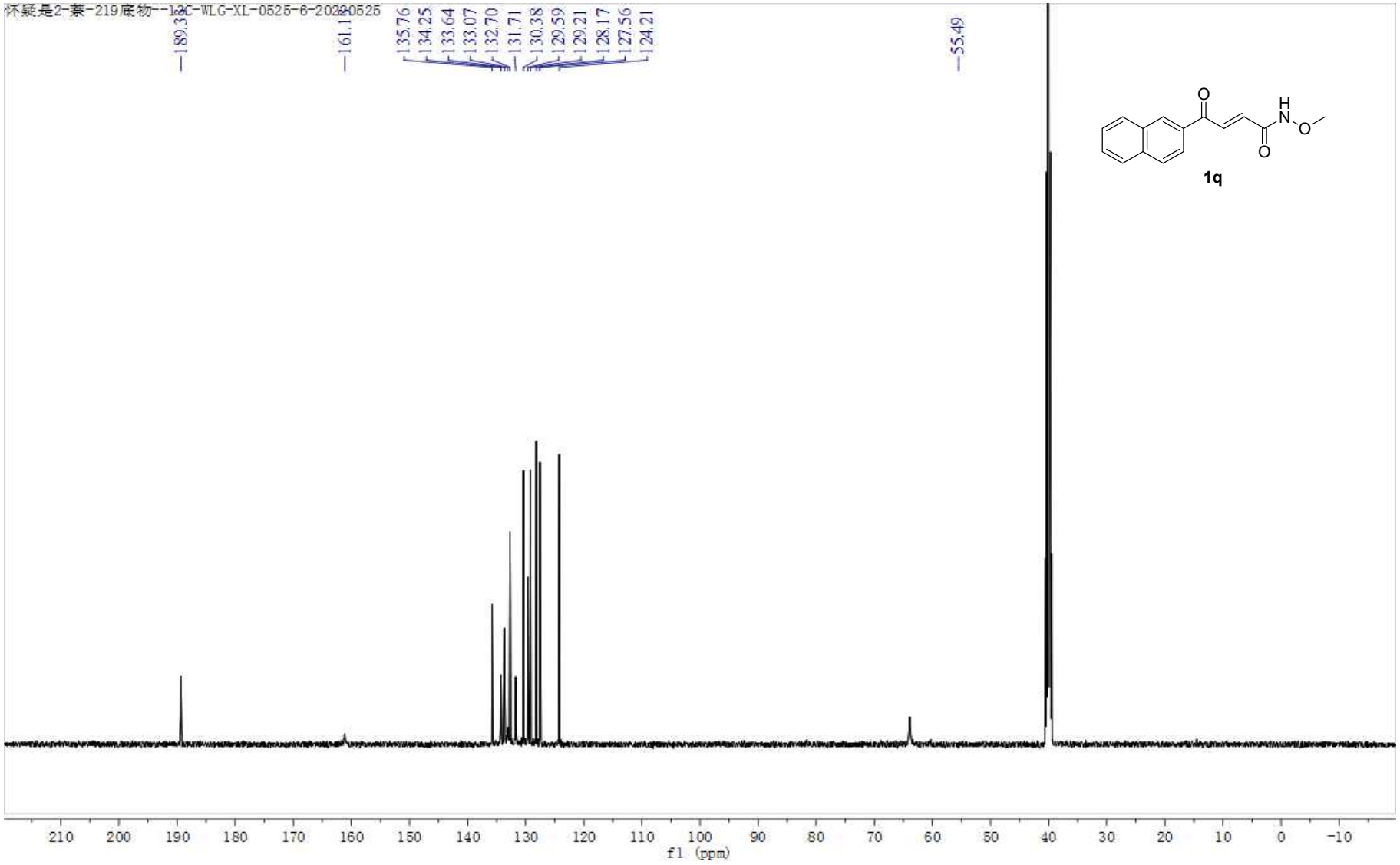

1H-WLG-20220403-XL-S-11
11.76
8.22
8.14
7.83
7.80
7.31
7.31
6.85
6.82
3.70
O
H
N
O
S
O
1o
0.93
2.10
0.93
1.11
1.00
3.16
14.5 13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

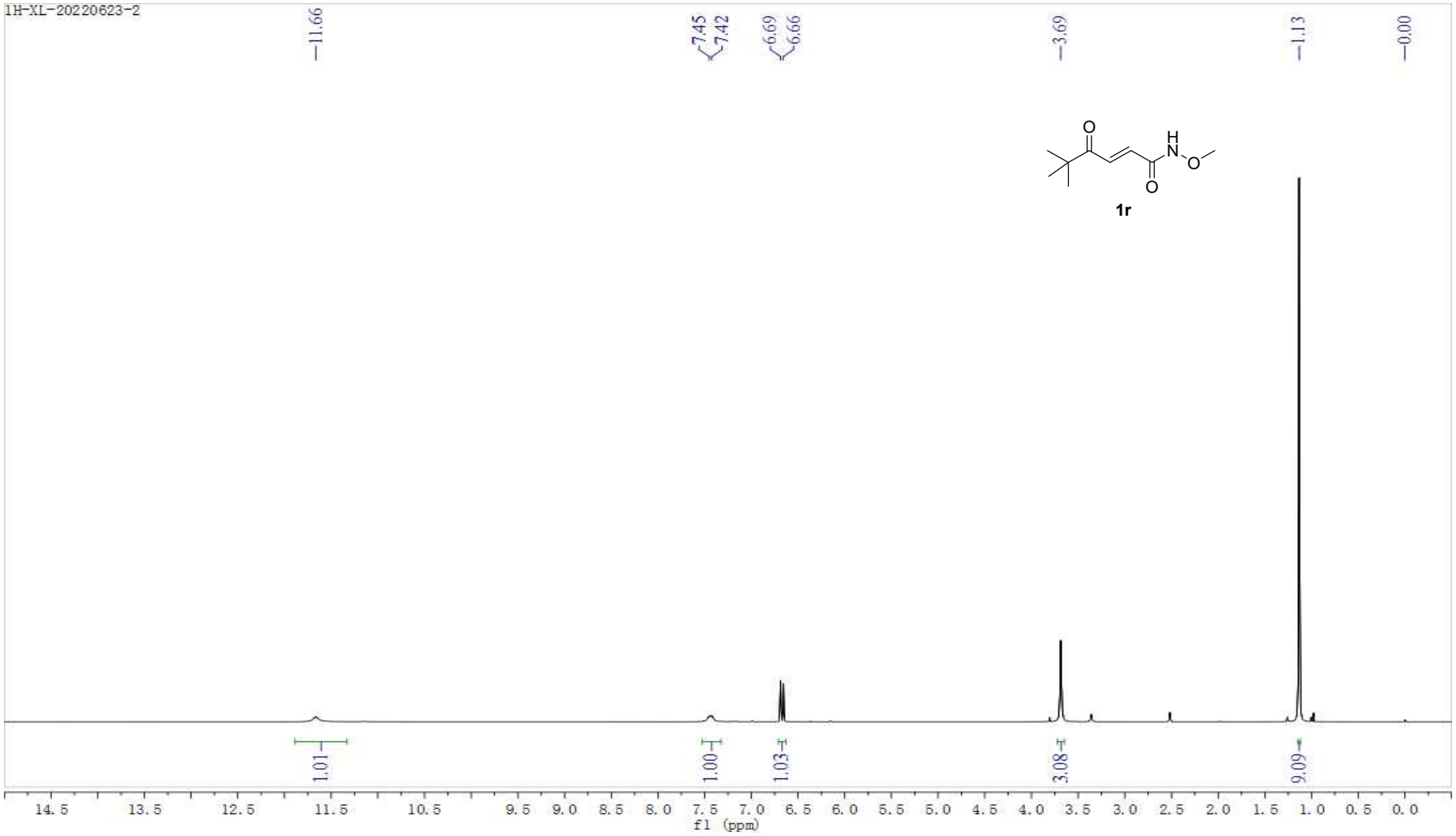

13C-WLG-20220403-XL-S-11
181.54
160.91
144.47
137.46
135.48
133.13
132.75
129.78
63.96
O
H
N
O
S
O
1o
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

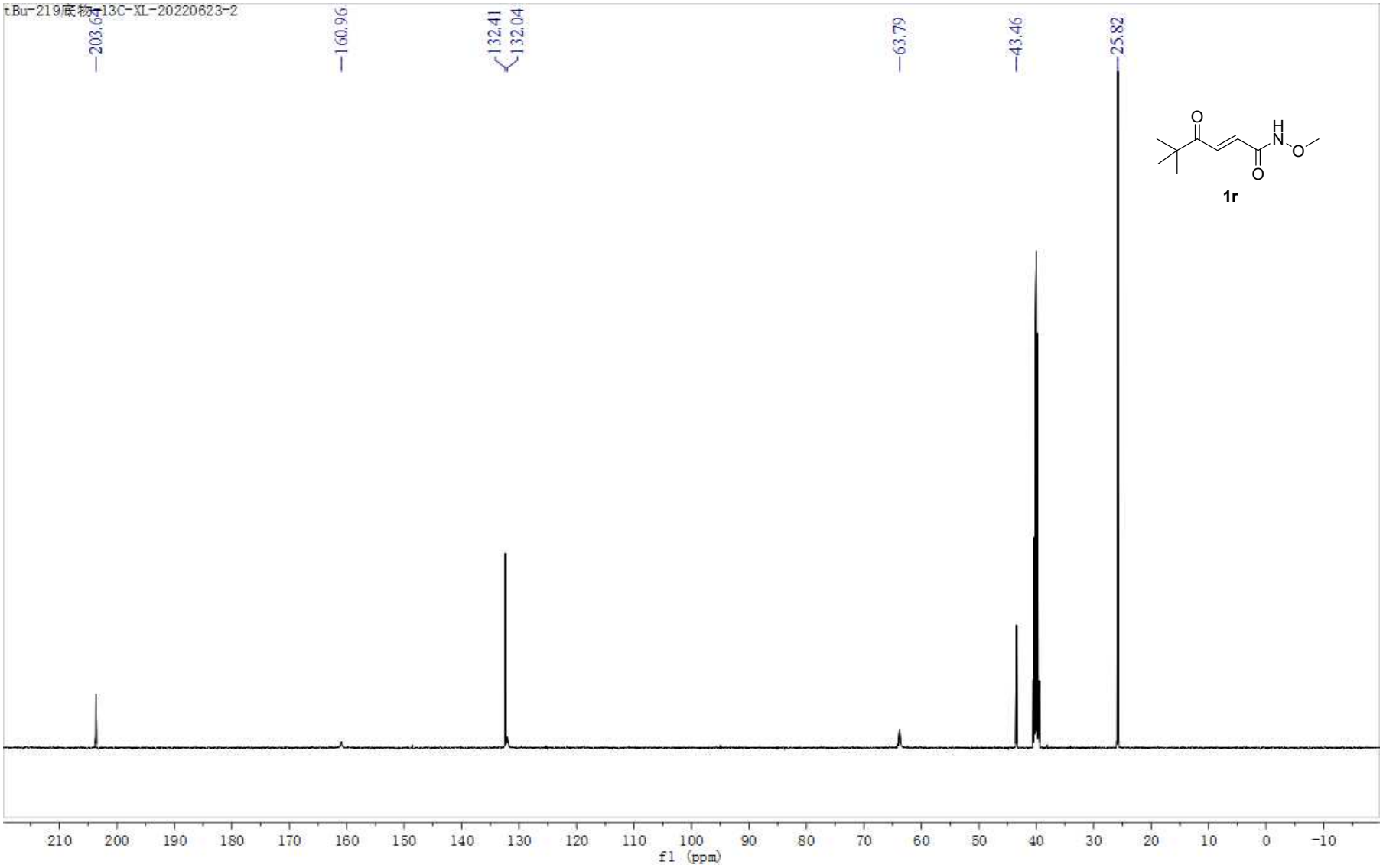

11.71
8.39
8.37
8.21
8.20
8.07
8.06
8.01
8.00
7.67
7.66
7.64
7.63
7.62
7.59
6.72
6.69
3.72
O
H
N
O
O
1p
f1 (ppm)
0.97
1.00
1.09
1.13
1.06
4.13
1.01
3.11

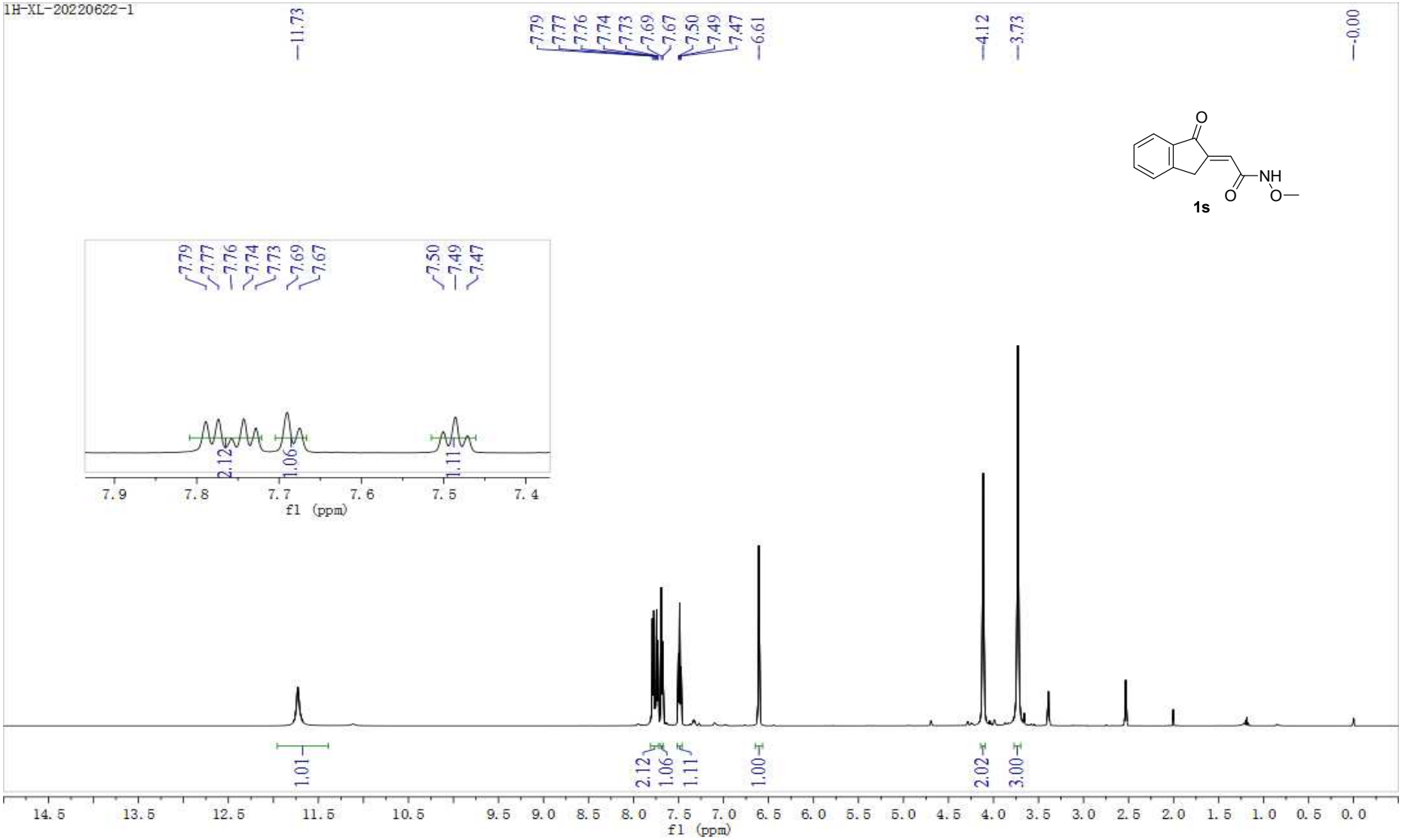

1-nai-219底物-13C-WLG-XL-0525-5-20220525
193.97
160.87
136.75
134.94
134.46
133.91
133.34
130.18
129.55
129.13
128.46
127.17
125.55
125.37
63.86
O
H
N
O
O
1p
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

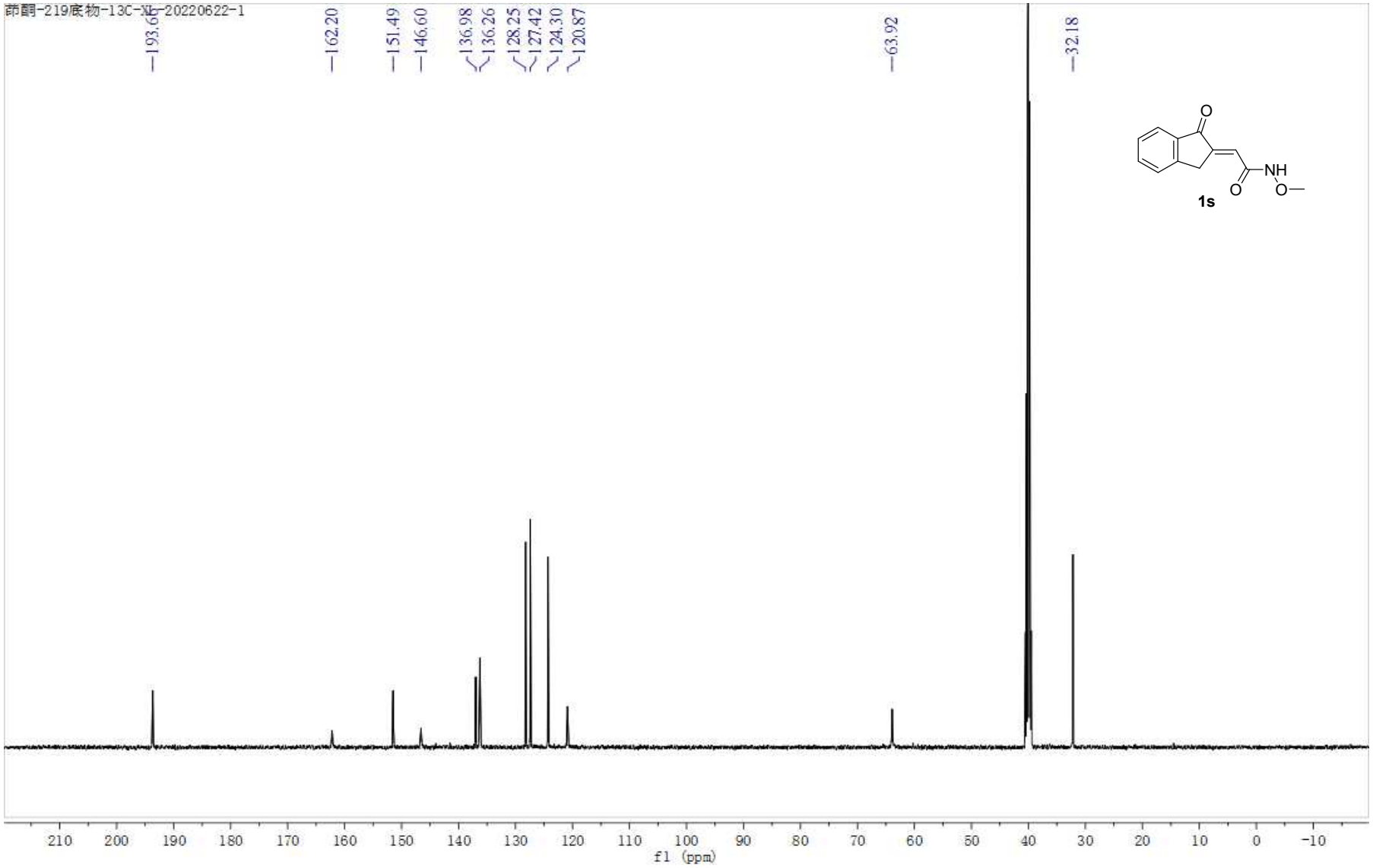

11.79
8.83
8.22
8.21
8.05
8.04
8.02
8.00
7.91
6.88
3.74
8.22
8.21
8.05
8.04
8.02
8.00
7.71
7.70
7.68
7.66
7.64
7.63
6.91
6.88
1.06
4.00
2.05
0.99
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
f1 (ppm)
O
H
N
O
O
1q
1.01
1.00
1.06
4.00
2.05
0.99
3.04
14.5
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

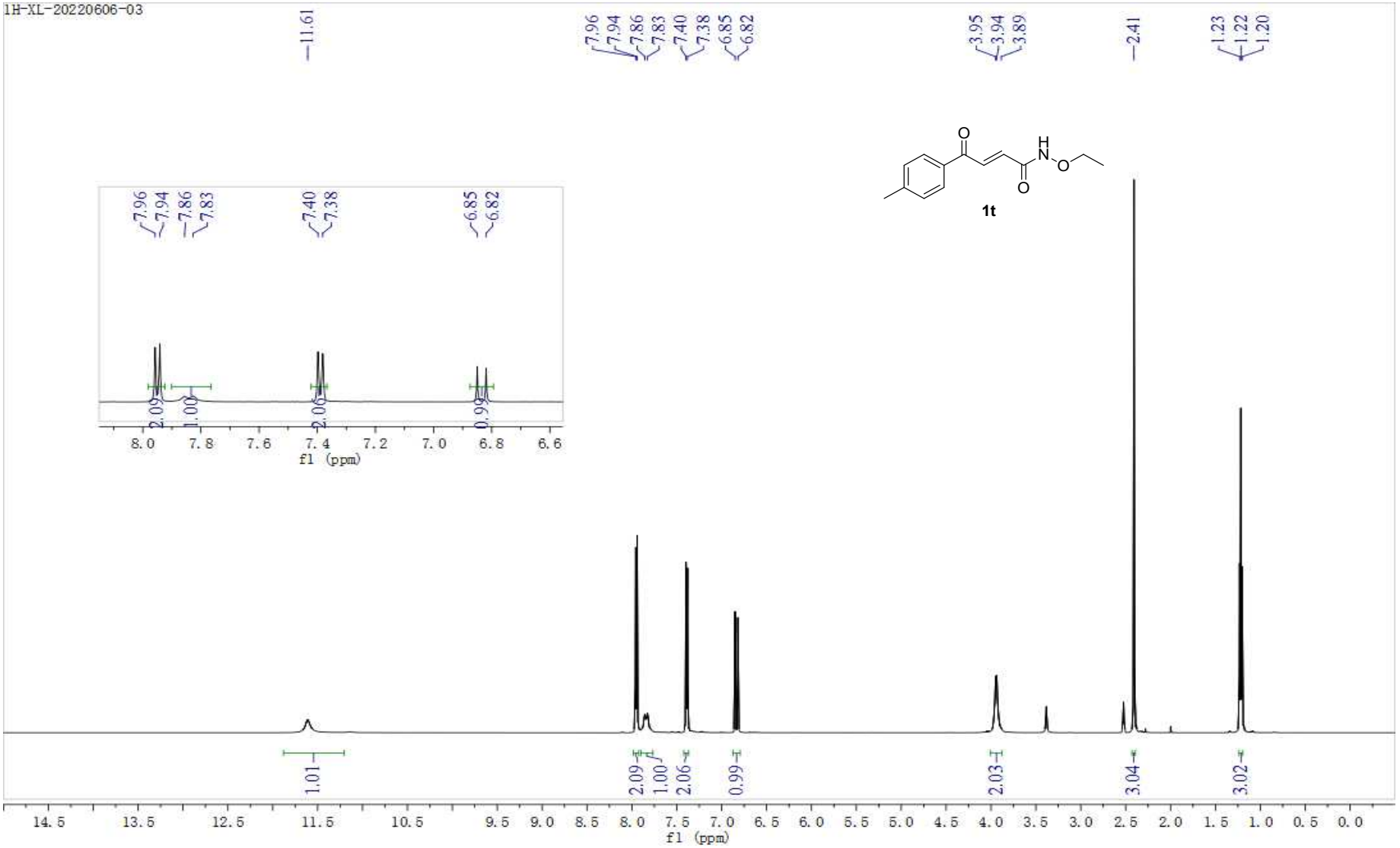

189.38
161.18
135.76
134.25
133.64
133.07
132.70
131.71
130.38
129.59
129.21
128.17
127.56
124.21
55.49
O
H
N
O
O
1q
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

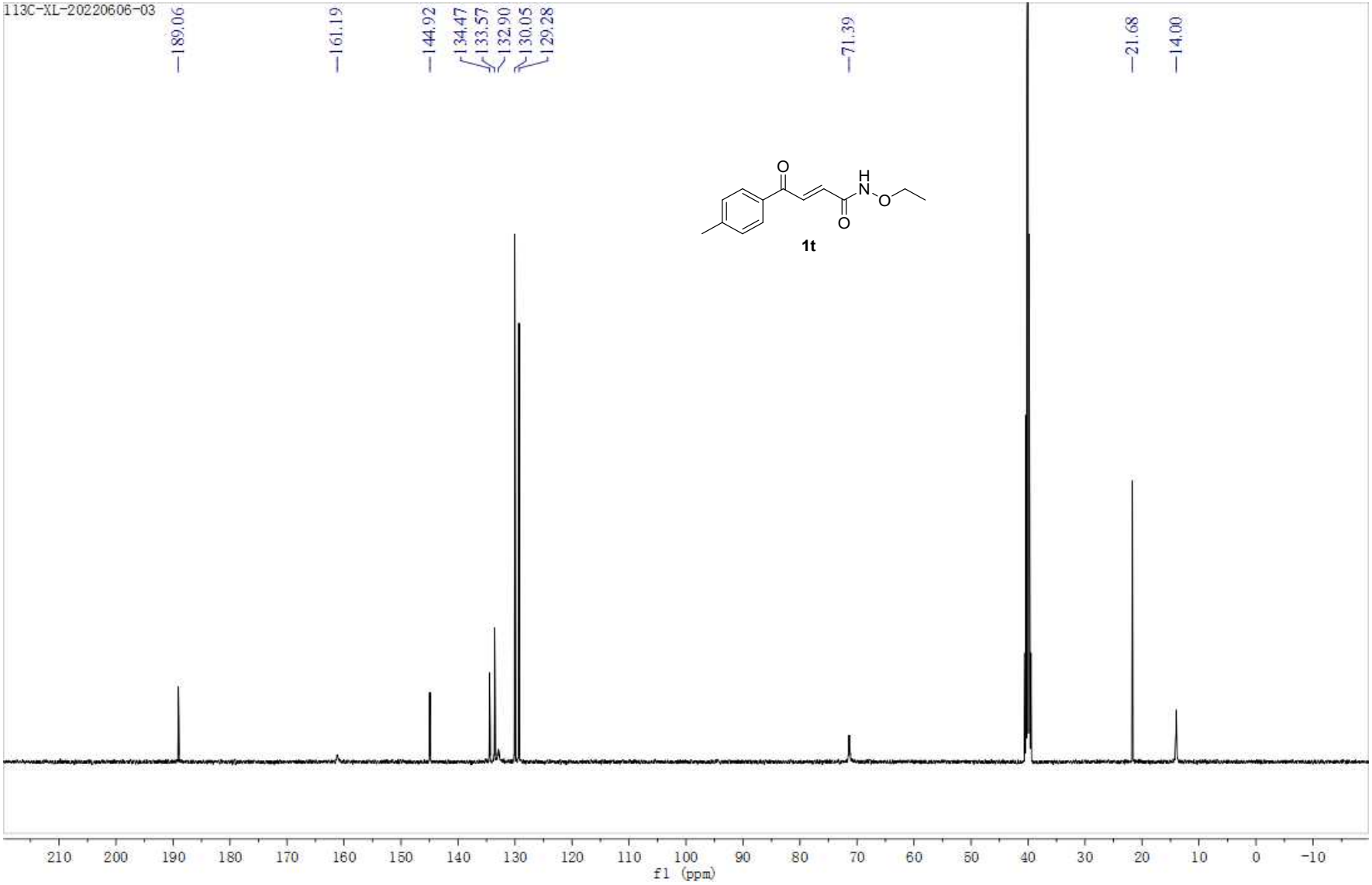

1H-XL-20220623-2
11.66
7.45
7.42
6.69
6.66
3.69
1.13
0.00
1r
1.01
1.00
1.03
3.08
9.09
f1 (ppm)

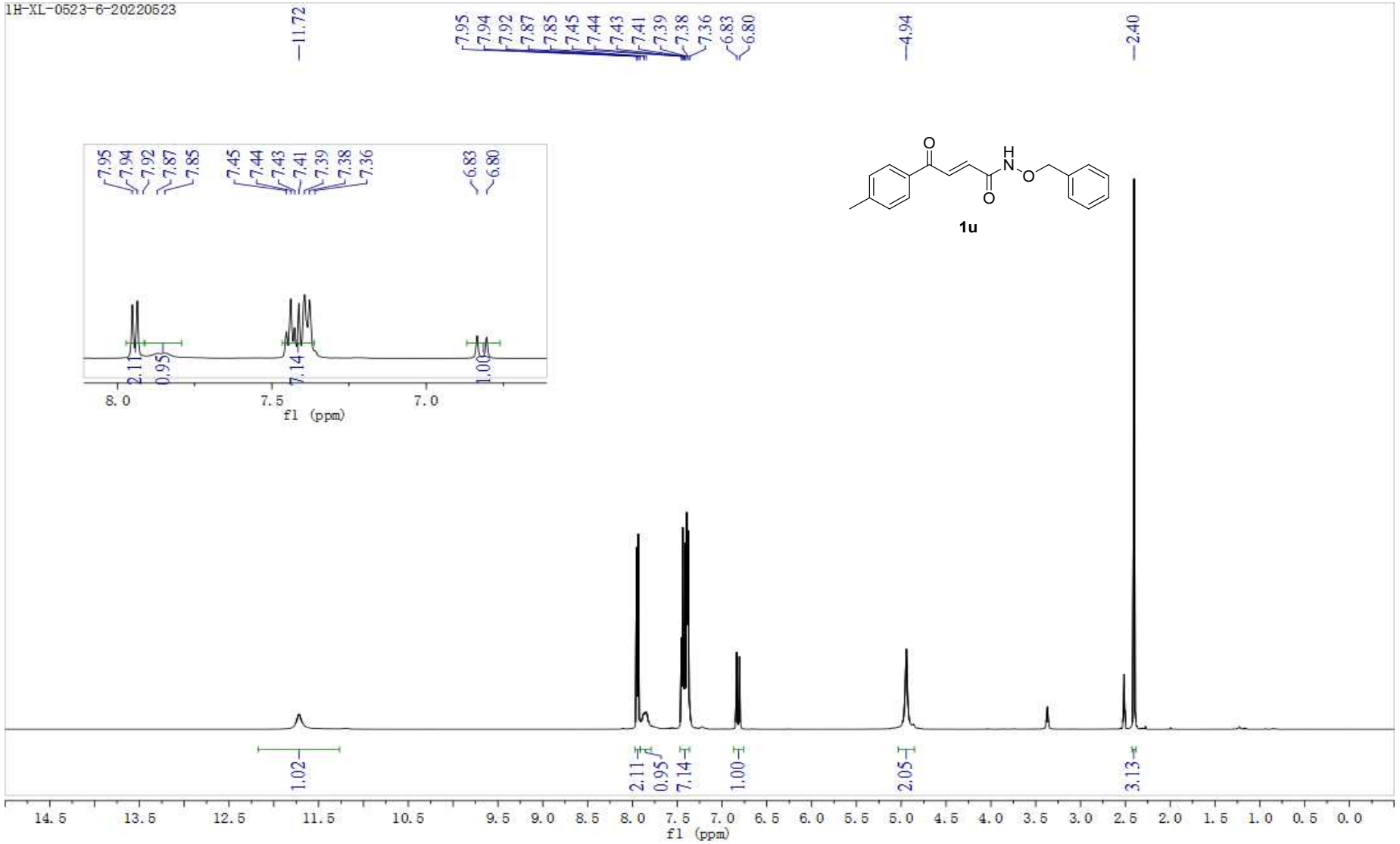

tBu-219底物-13C-XL-20220623-2
203.64
160.96
132.41
132.04
63.79
43.46
25.82
O
H
N
O
O
1r
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

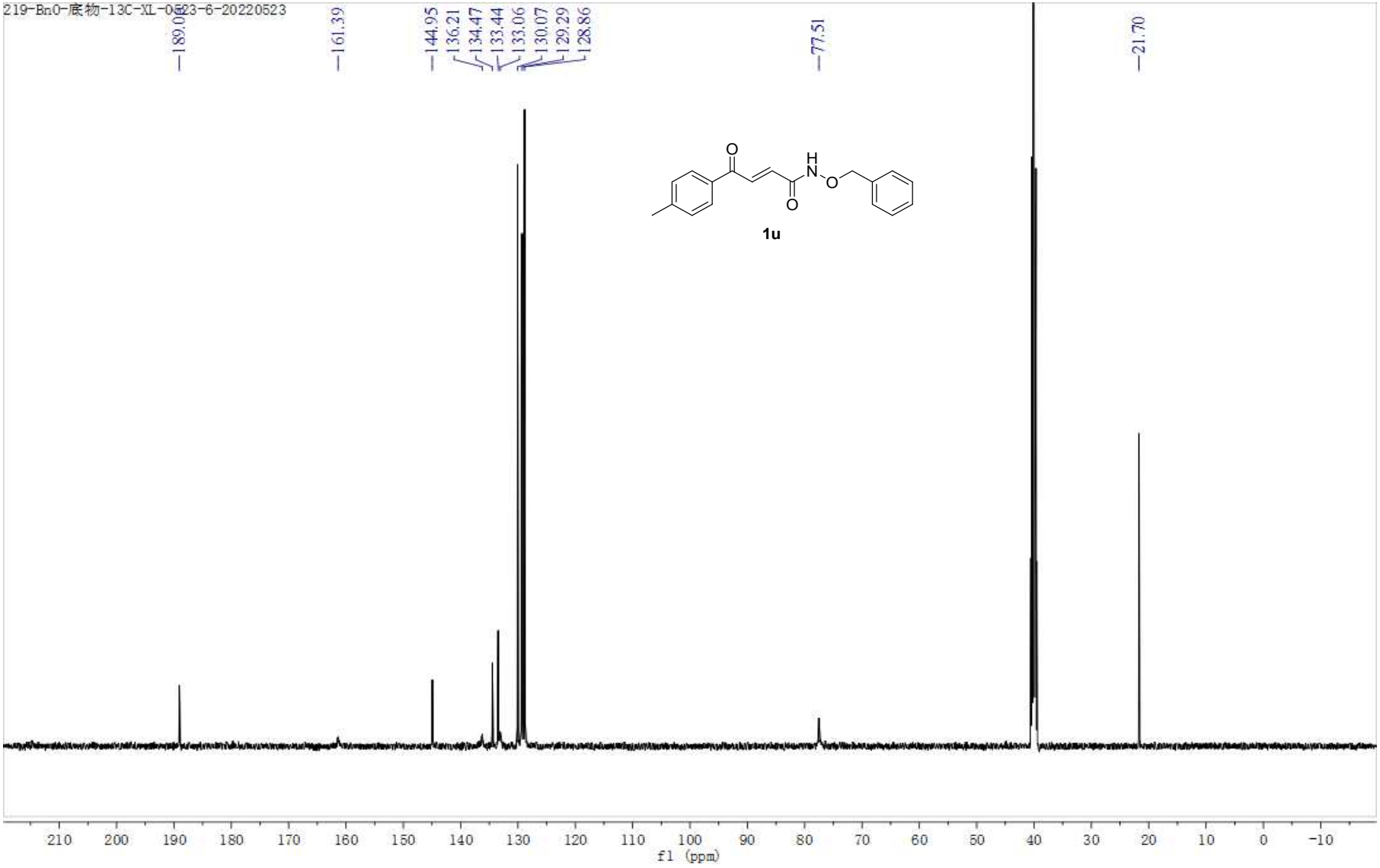

1H-XL-20220622-1
11.73
7.79
7.77
7.76
7.74
7.73
7.69
7.67
7.50
7.49
7.47
6.61
4.12
3.73
0.00
O
NH
O
O
1s
2.12
1.06
1.11
f1 (ppm)
1.01
1.00
2.02
3.00
f1 (ppm)

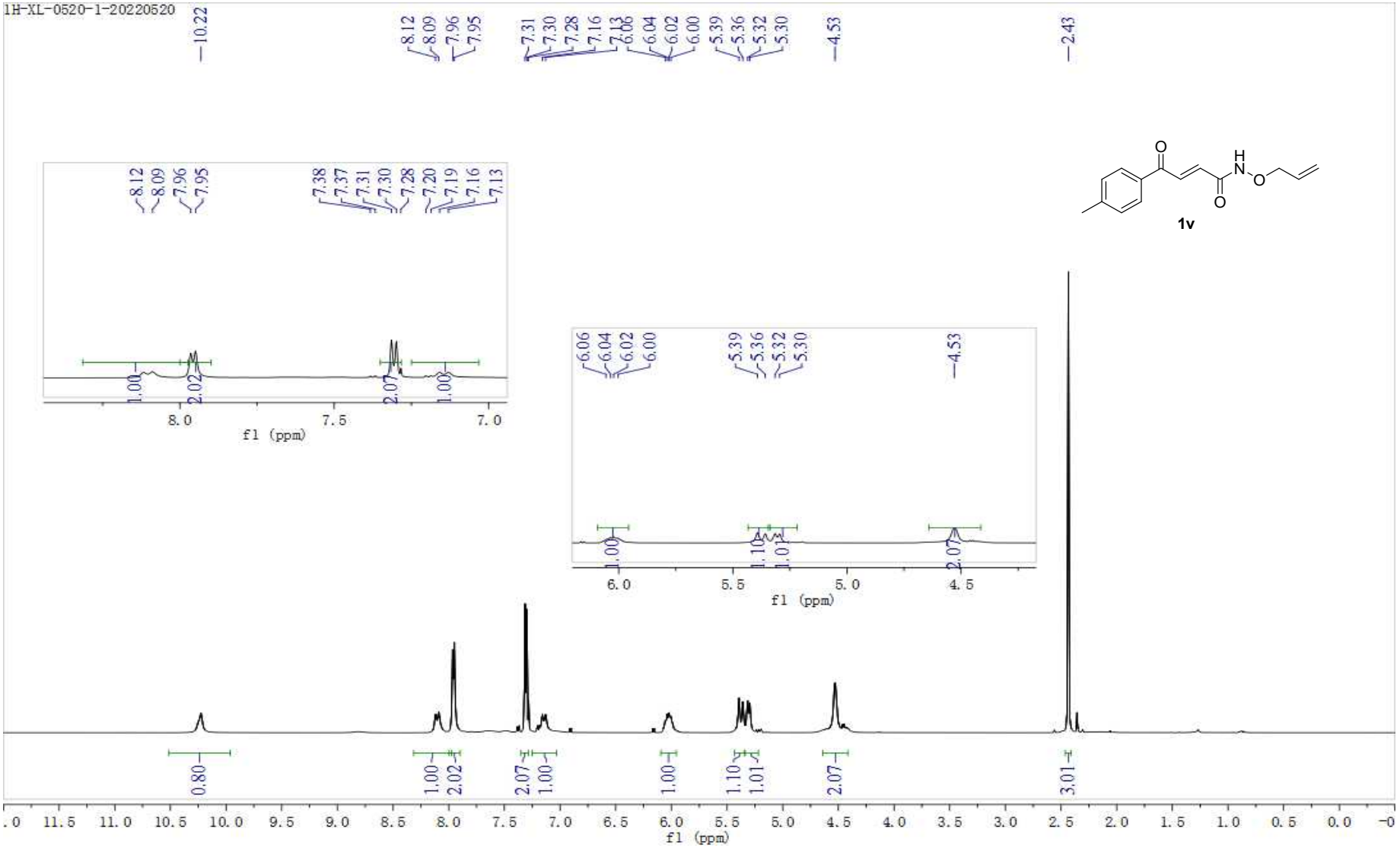

茚酮-219底物-13C-XL-20220622-1
193.66
162.20
151.49
146.60
136.98
136.26
128.25
127.42
124.30
120.87
63.92
32.18
O
NH
O
O
1s
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

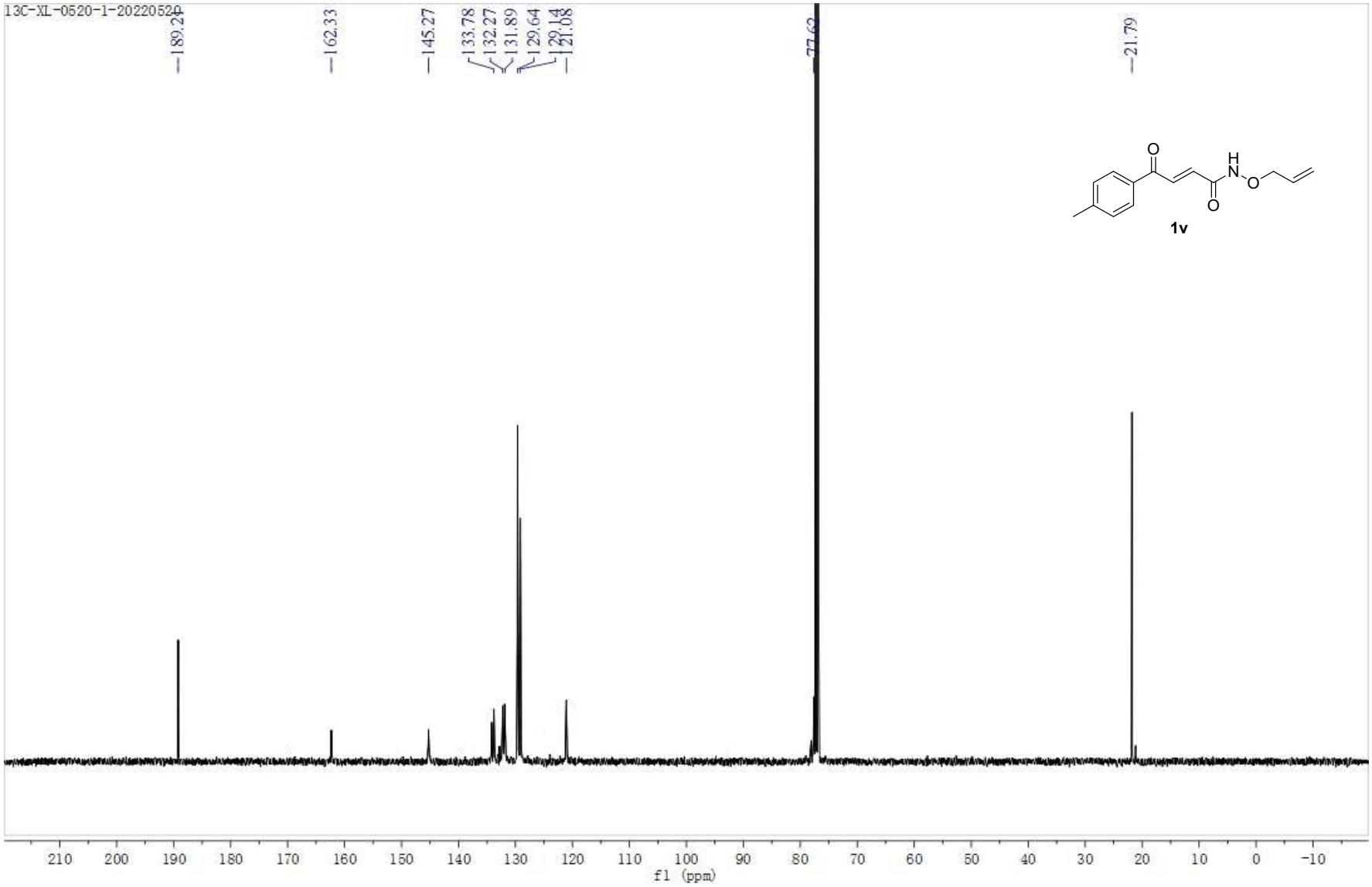

1H-XL-20220606-03
11.61
7.96
7.94
7.86
7.83
7.40
7.38
6.85
6.82
3.95
3.94
3.89
2.41
1.23
1.22
1.20
1t
f1 (ppm)

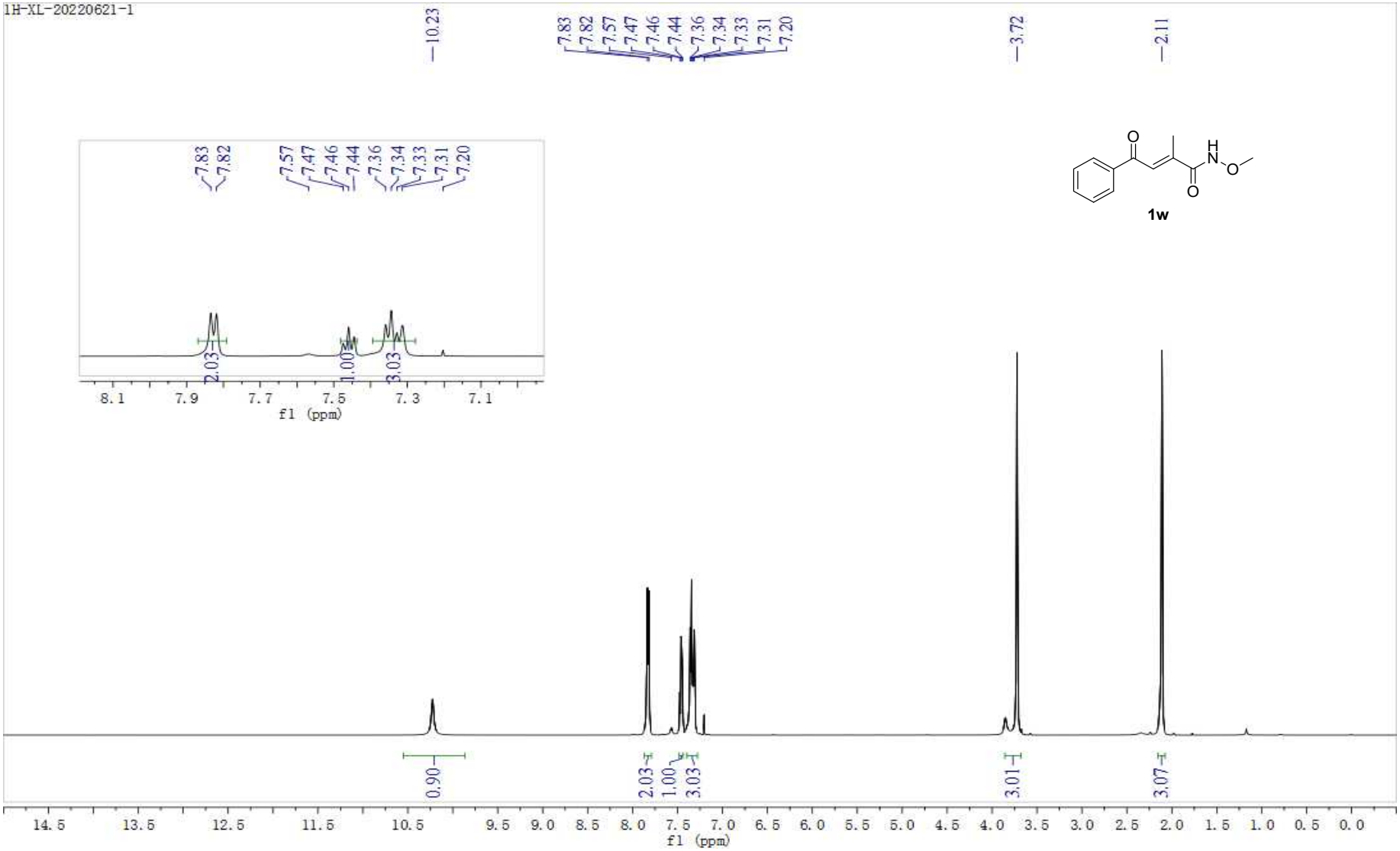

113C-XL-20220606-03
189.06
161.19
144.92
134.47
133.57
132.90
130.05
129.28
71.39
21.68
14.00
O
H
N
O
O
1t
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

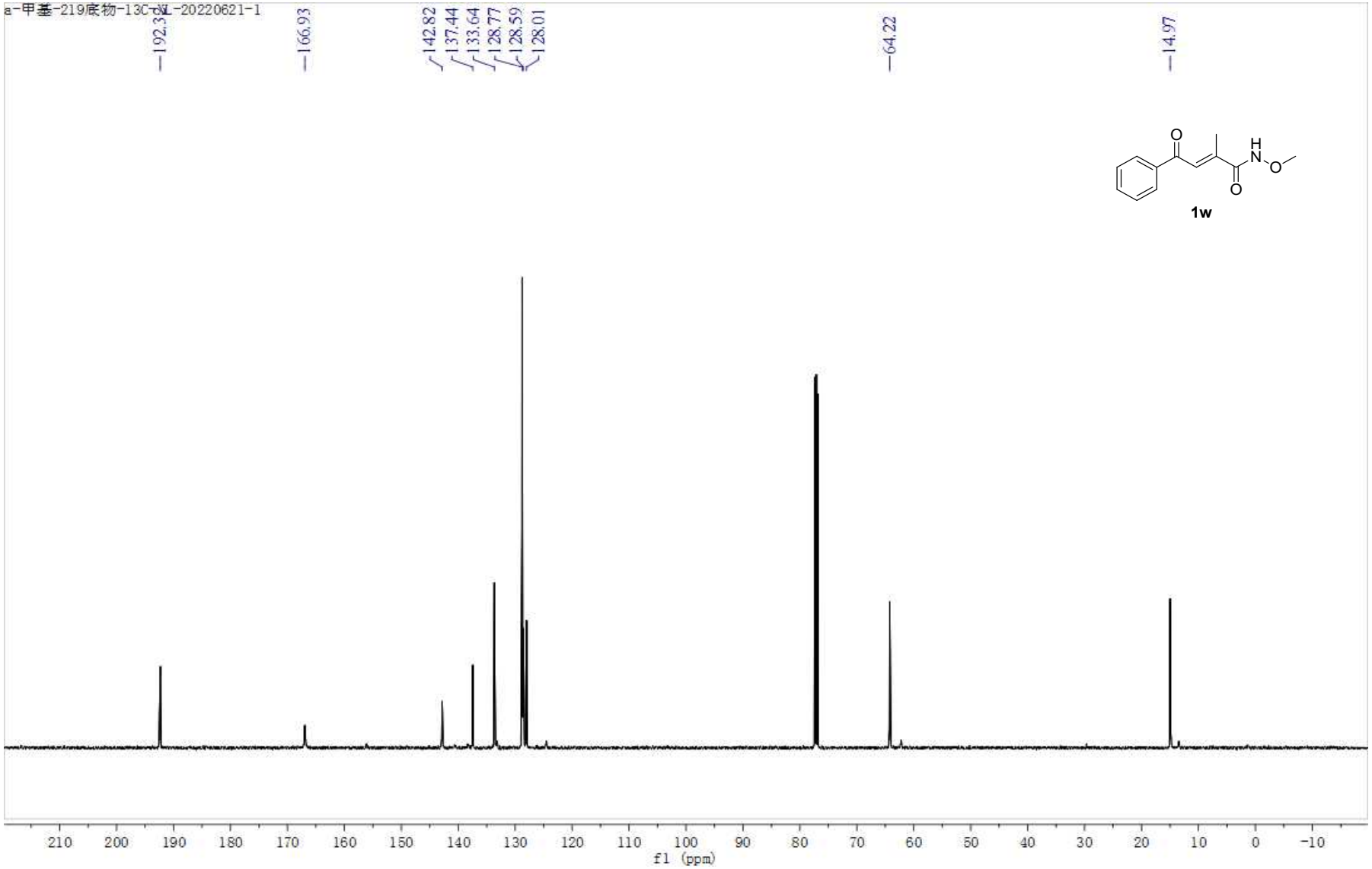

1H-XL-0523-6-20220523
11.72
7.95
7.94
7.92
7.87
7.85
7.45
7.44
7.43
7.41
7.39
7.38
7.36
6.83
6.80
4.94
2.40
1u
f1 (ppm)

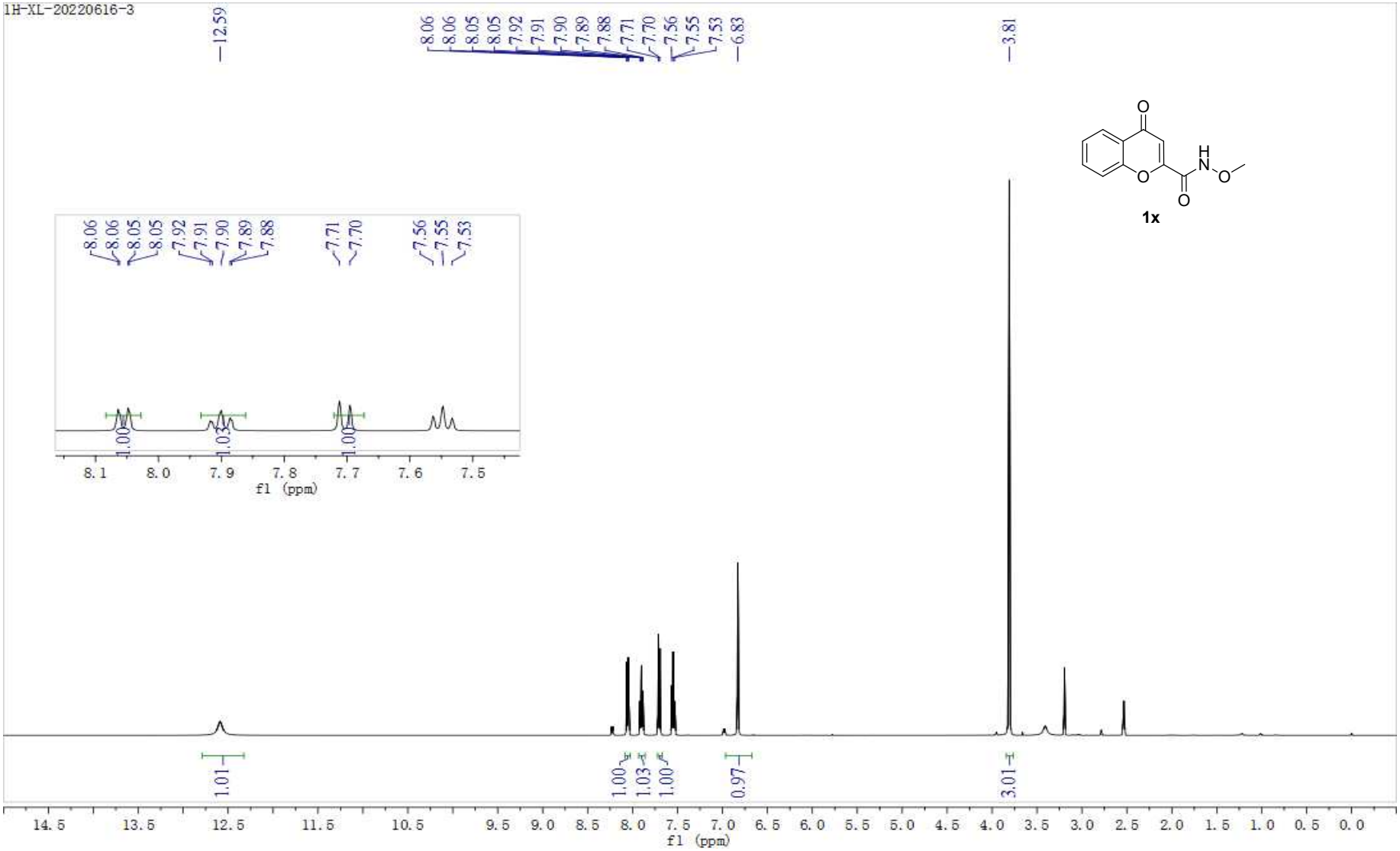

219-Bn0-底物-13C-XL-0523-6-20220523
189.08
161.39
144.95
136.21
134.47
133.44
133.06
130.07
129.29
128.86
77.51
21.70
O
H
N
O
O
1u
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

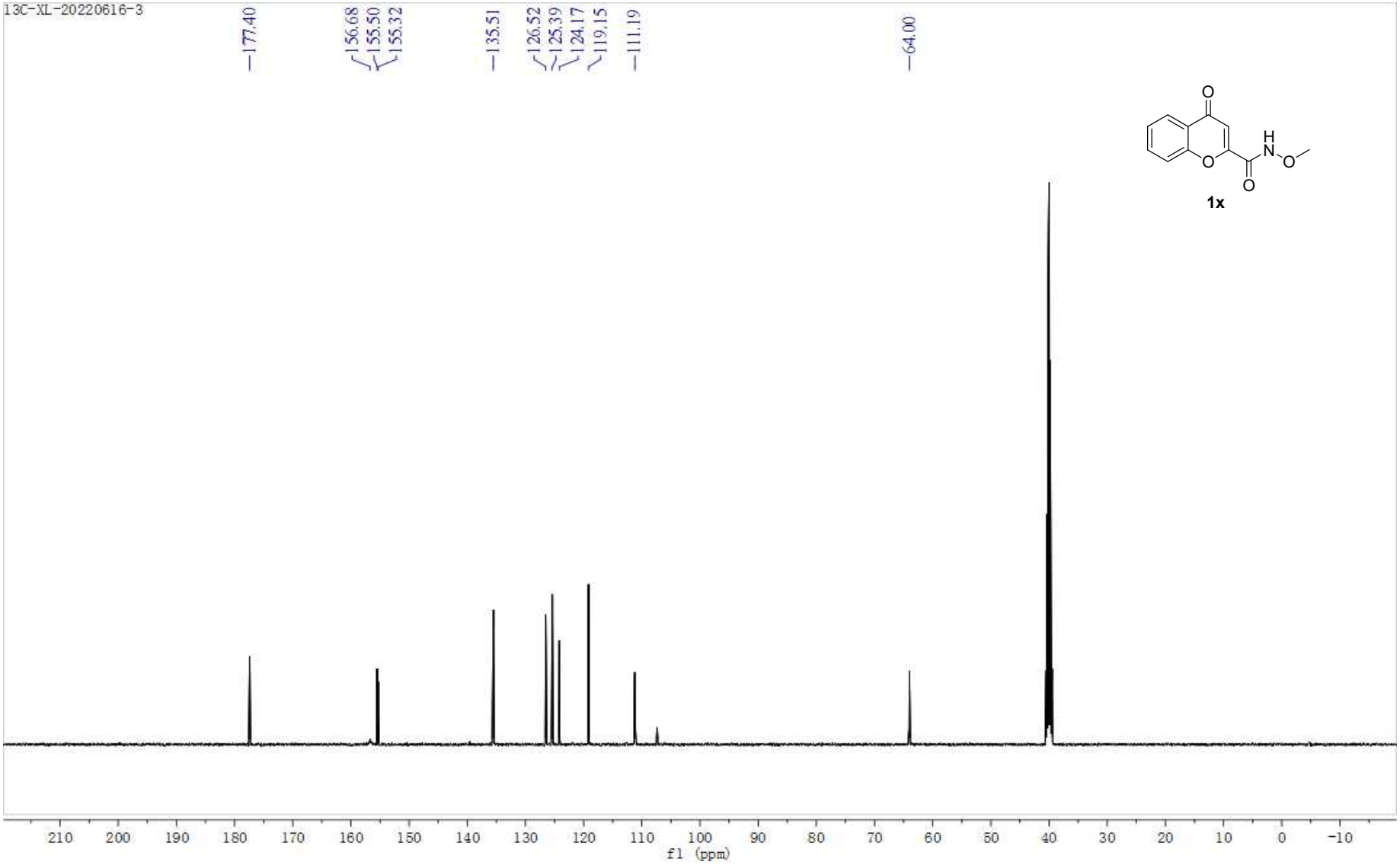

1H-XL-0520-1-20220520
10.22
8.12
8.09
7.96
7.95
7.31
7.30
7.28
7.16
7.13
6.06
6.04
6.02
6.00
5.39
5.36
5.32
5.30
4.53
2.43
1v
f1 (ppm)

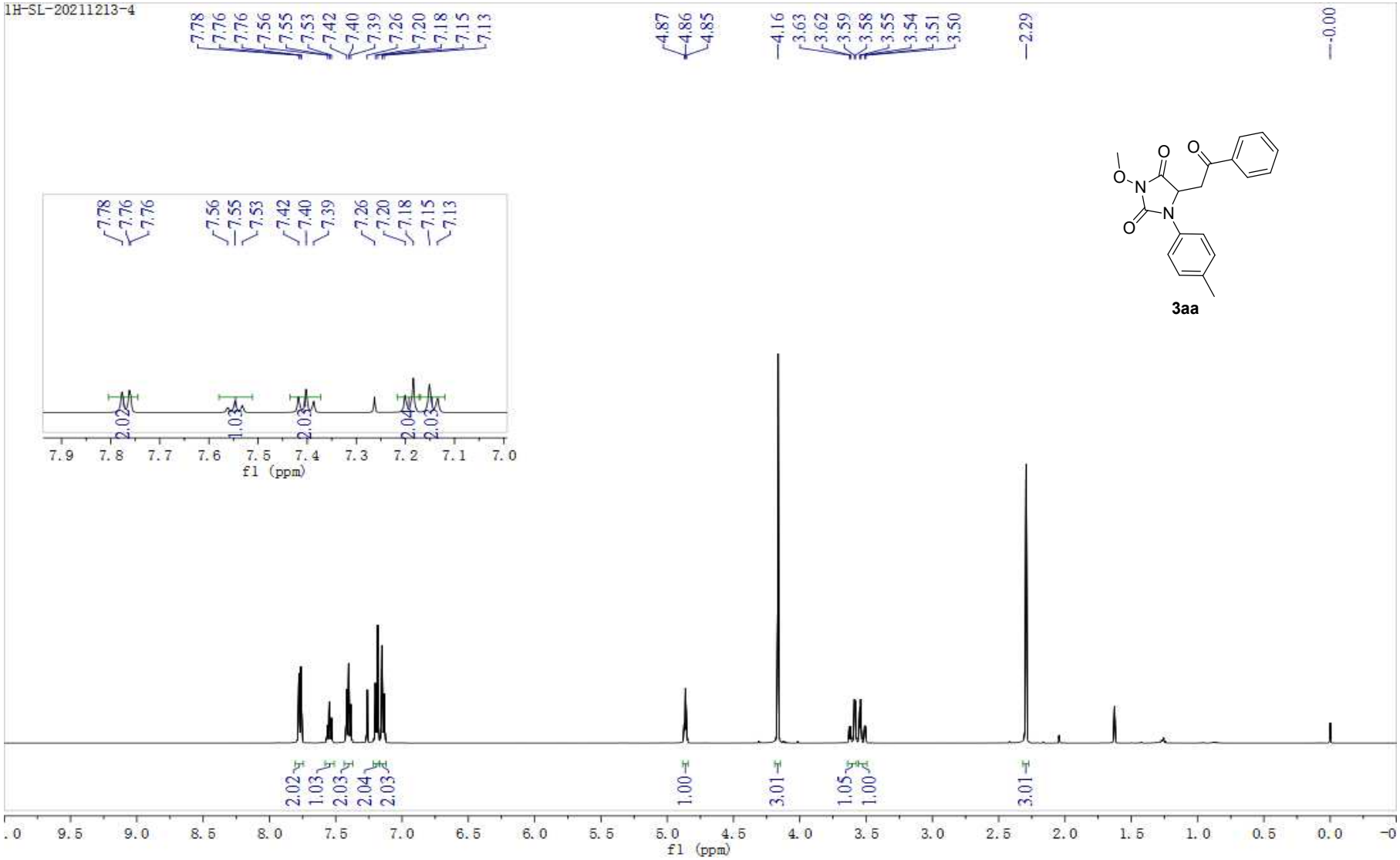

13C-XL-0520-1-20220520
189.29
162.33
145.27
133.78
132.27
131.89
129.64
29.14
27.08
77.62
21.79
O
H
N
O
O
1v
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

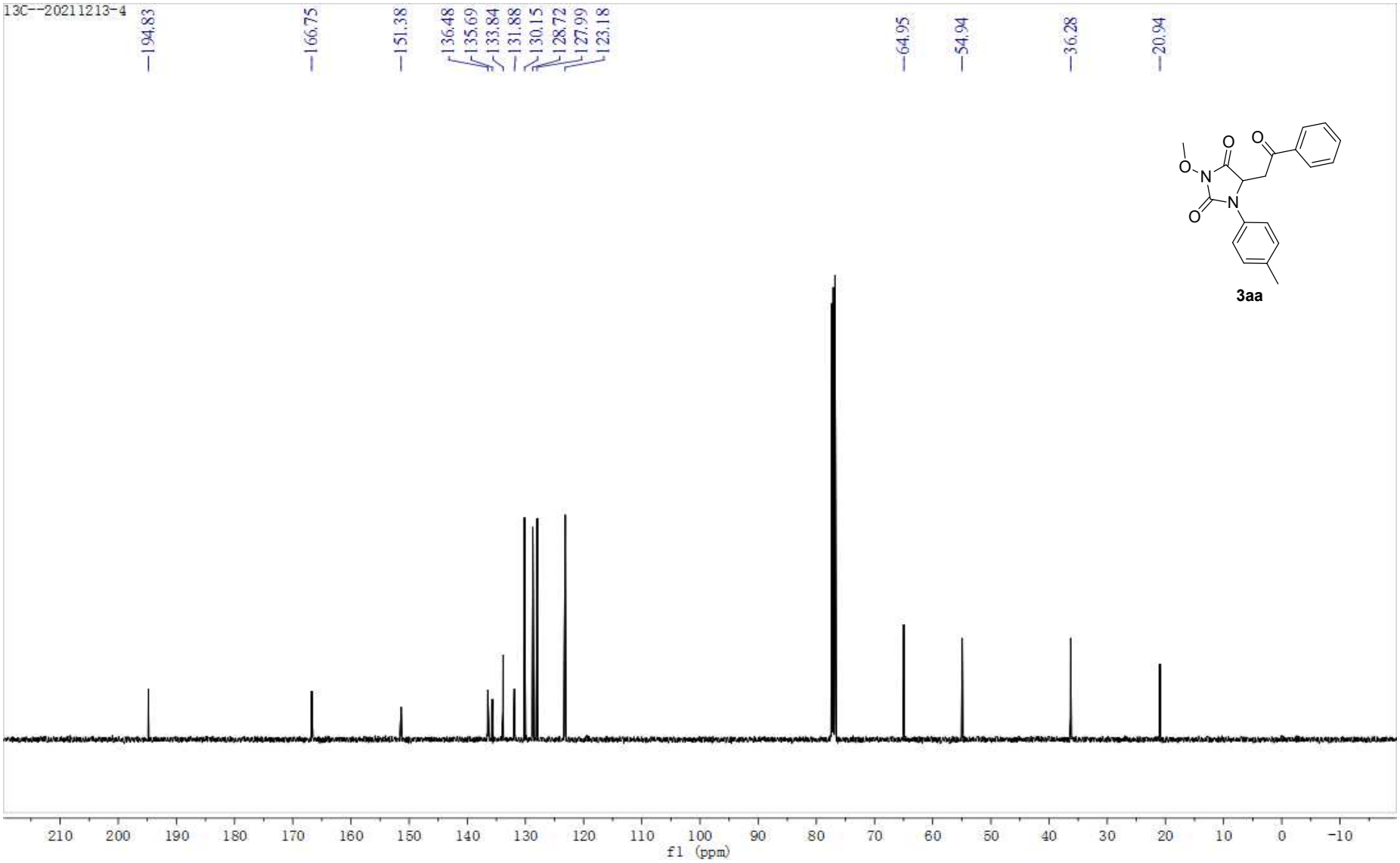

1H-XL-20220621-1
10.23
7.83
7.82
7.57
7.47
7.46
7.44
7.36
7.34
7.33
7.31
7.20
3.72
2.11
1w
f1 (ppm)
0.90
2.03
1.00
3.03
3.01
3.07

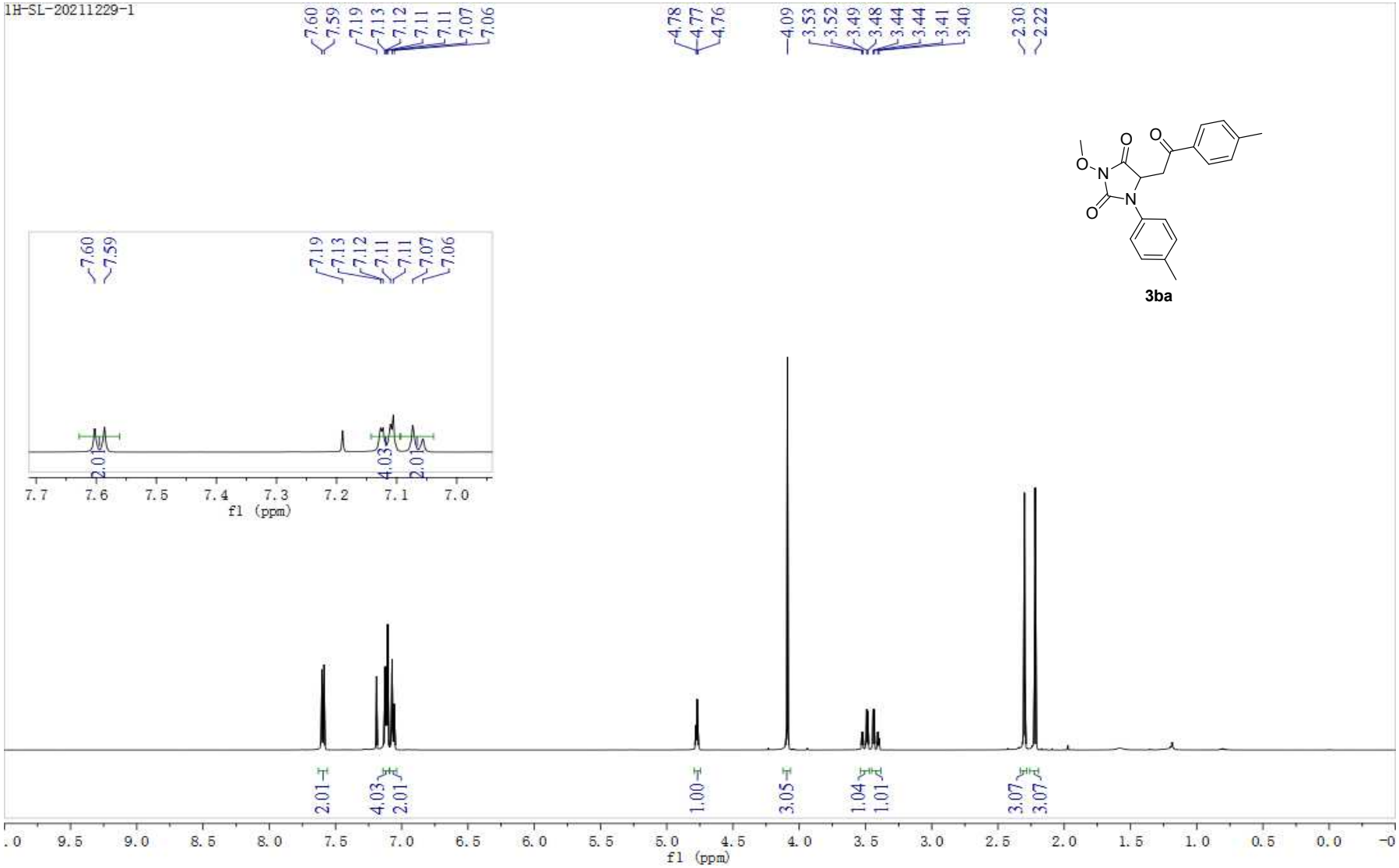

a-甲基-219底物-13C-双-20220621-1
192.32
166.93
142.82
137.44
133.64
128.77
128.59
128.01
64.22
14.97
O
H
N
O
O
1w
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

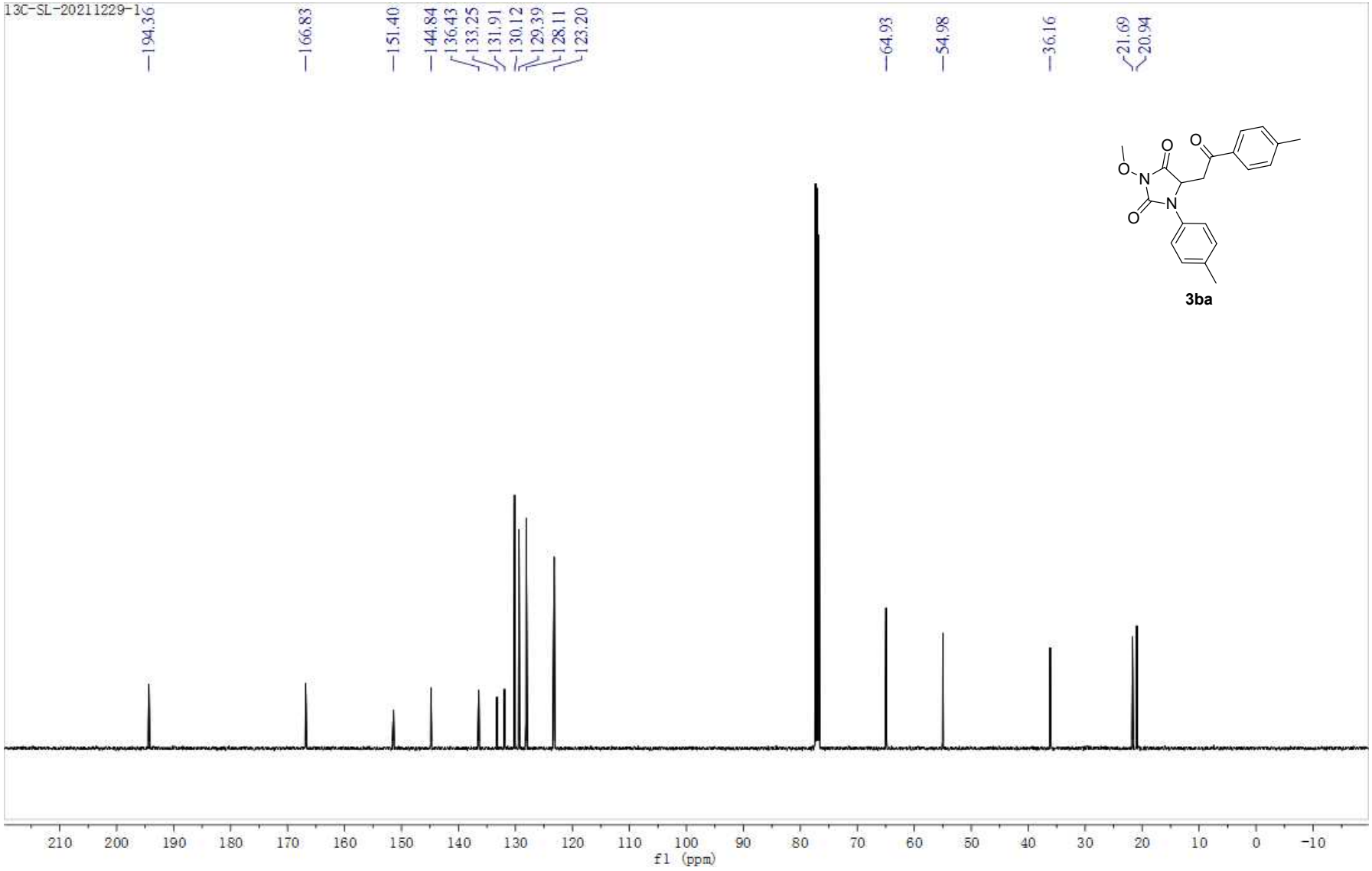

1H-XL-20220616-3
12.59
8.06
8.06
8.05
8.05
7.92
7.91
7.90
7.89
7.88
7.71
7.70
7.56
7.55
7.53
6.83
3.81
1x
fl (ppm)
1.01
1.00
1.03
1.00
0.97
3.01

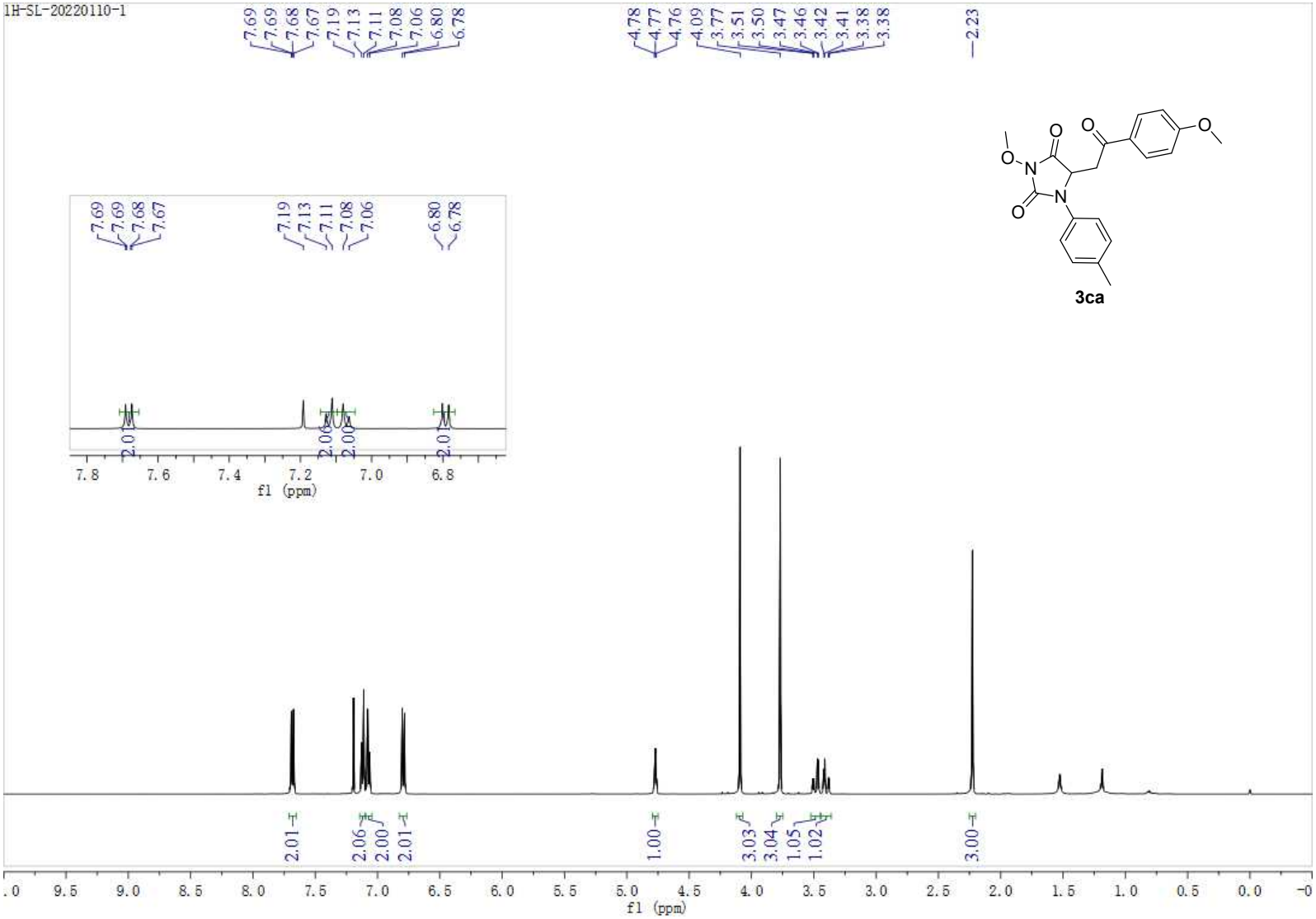

13C-XL-20220616-3
177.40
156.68
155.50
155.32
135.51
126.52
125.39
124.17
119.15
111.19
64.00
1x
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

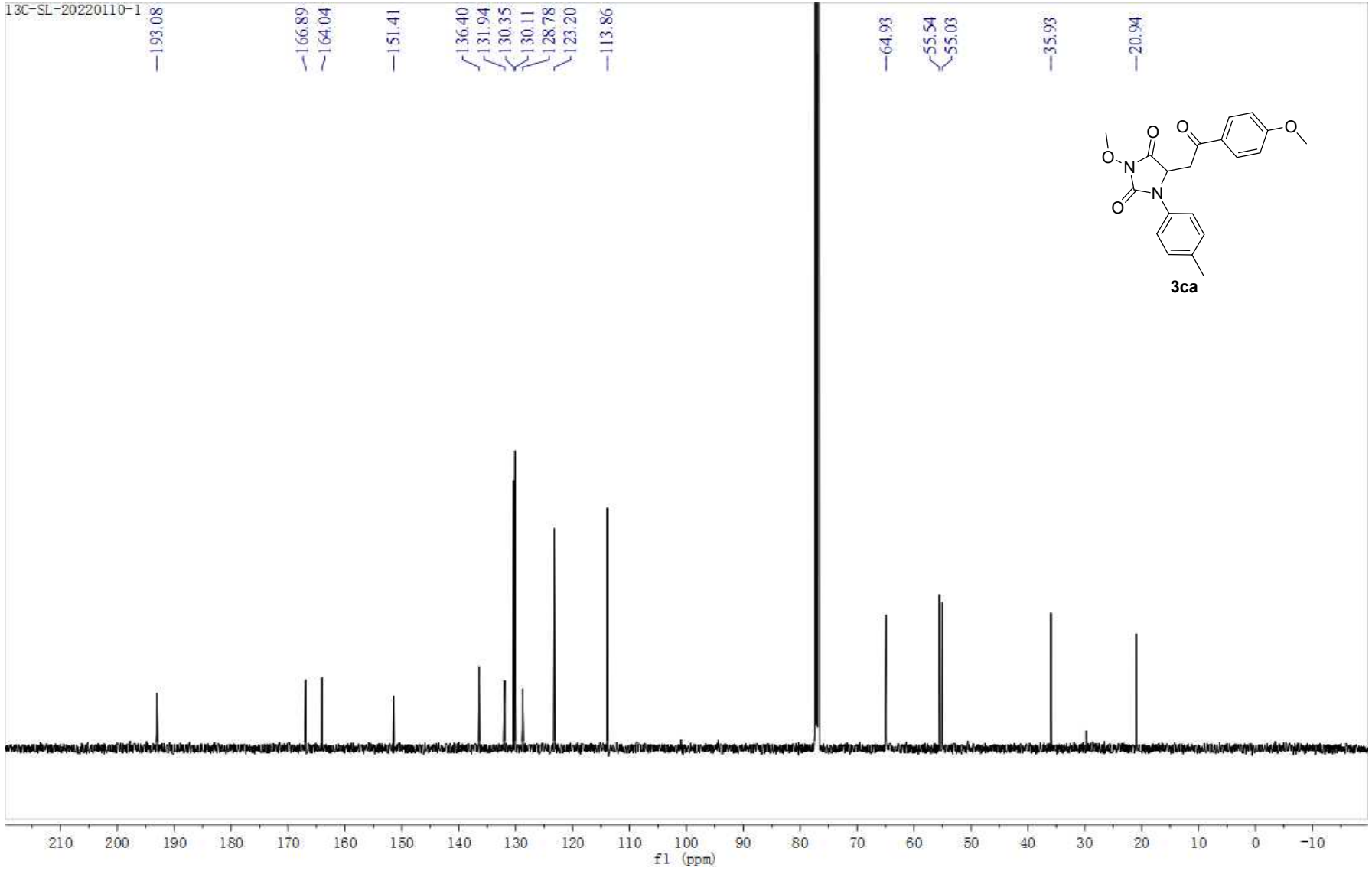

1H-SL-20211213-4
7.78
7.76
7.76
7.56
7.55
7.53
7.42
7.40
7.39
7.26
7.20
7.18
7.15
7.13
4.87
4.86
4.85
4.16
3.63
3.62
3.59
3.58
3.55
3.54
3.51
3.50
2.29
0.00
3aa
f1 (ppm)
2.02
1.03
2.03
2.04
2.03
1.00
3.01
1.05
1.00
3.01

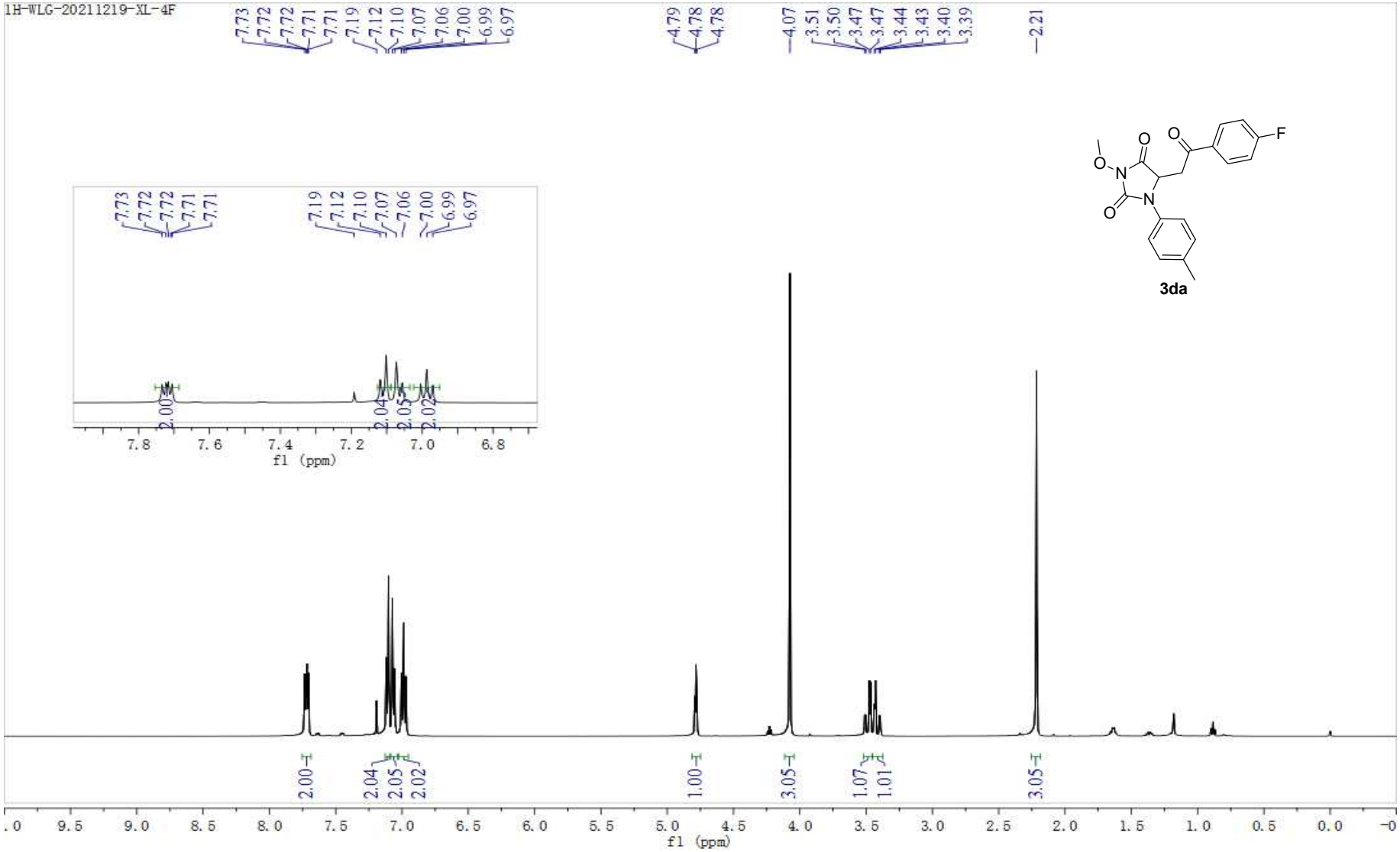

13C--20211213-4
194.83
166.75
151.38
136.48
135.69
133.84
131.88
130.15
128.72
127.99
123.18
64.95
54.94
36.28
20.94
3aa
f1 (ppm)

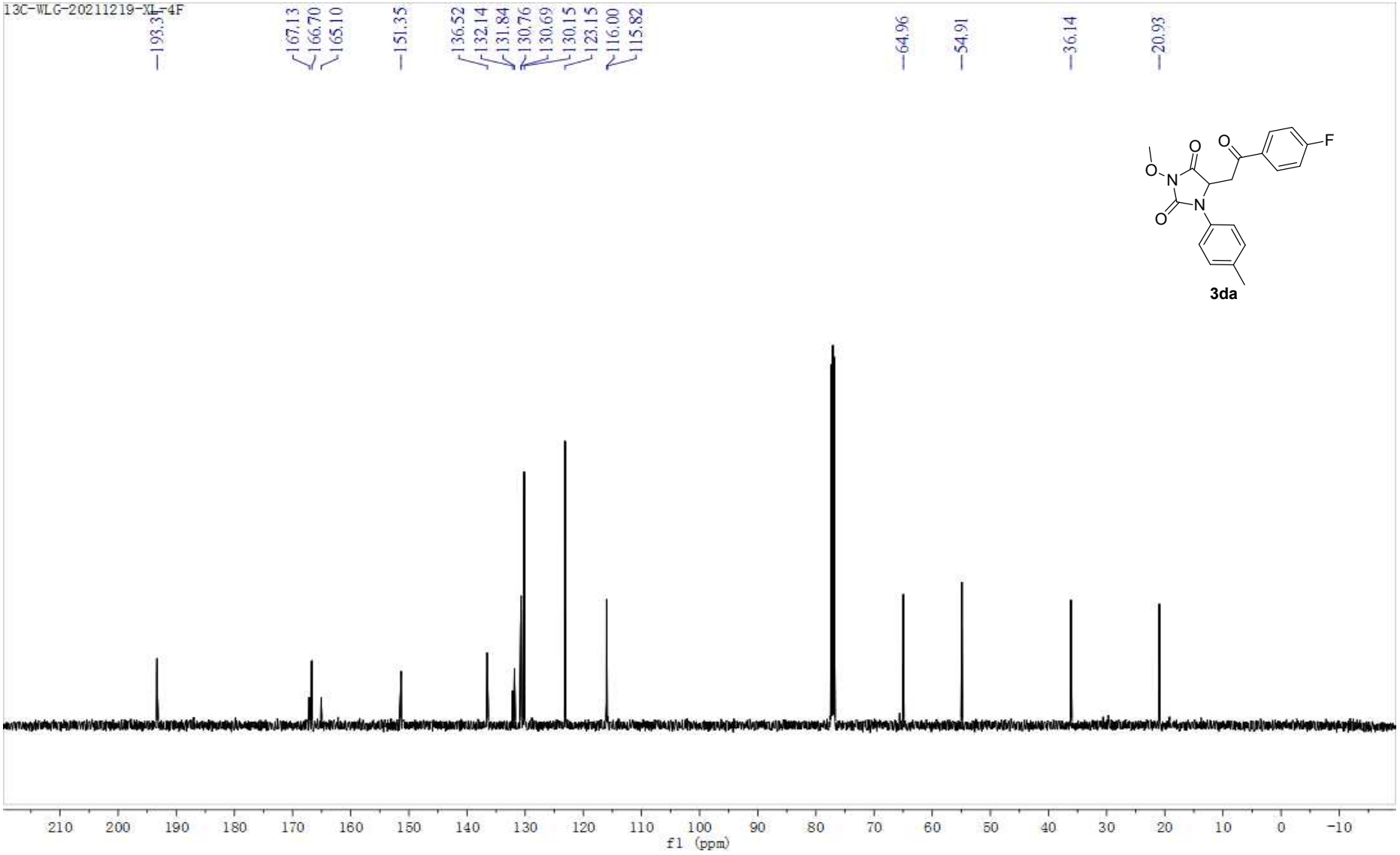

1H-SL-20211229-1
7.60
7.59
7.19
7.13
7.12
7.11
7.11
7.07
7.06
4.78
4.77
4.76
4.09
3.53
3.52
3.49
3.48
3.44
3.44
3.41
3.40
2.30
2.22
3ba
f1 (ppm)
2.01
4.03
2.01
1.00
3.05
1.04
1.01
3.07
3.07

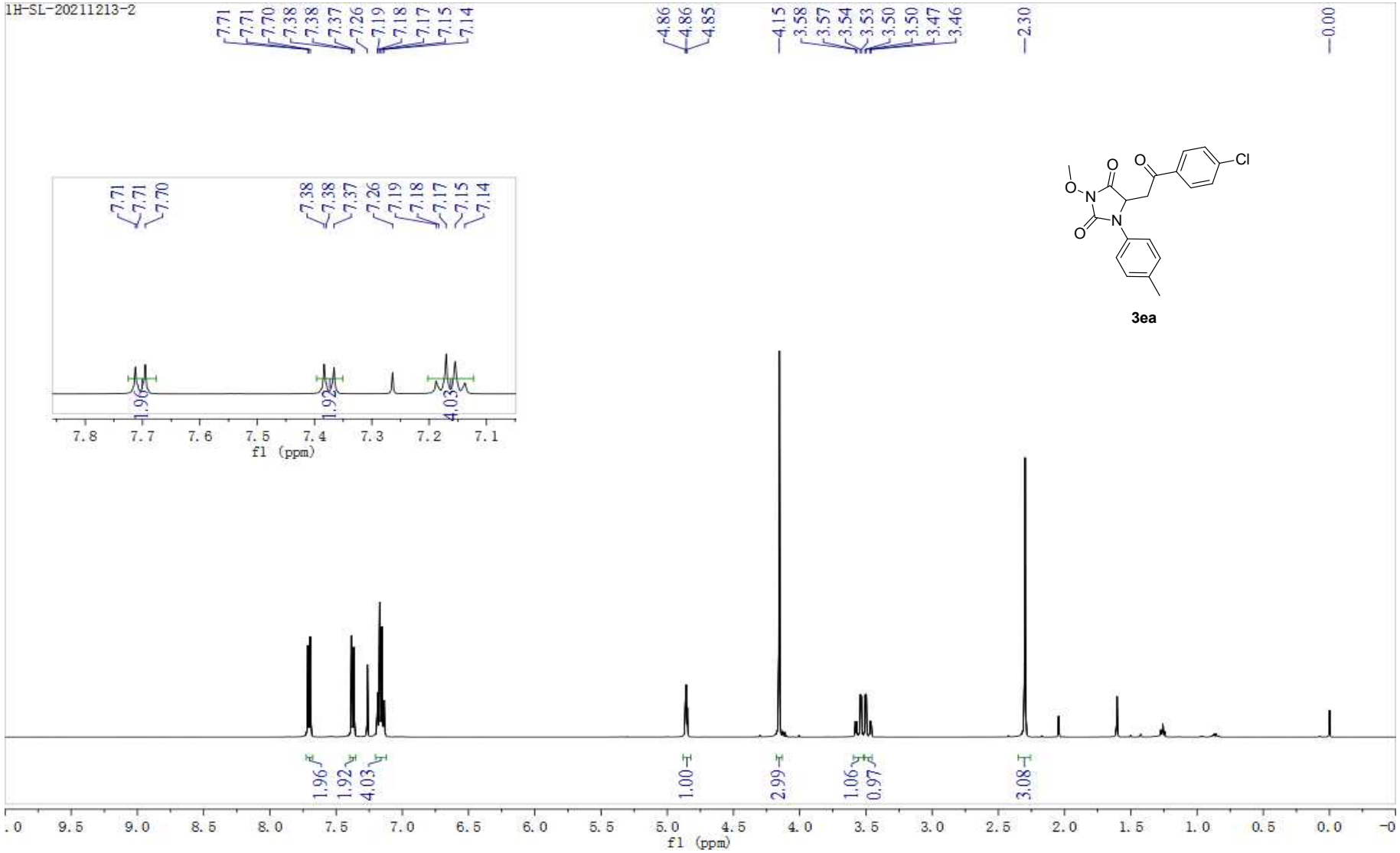

13C-SL-20211229-1
194.36
166.83
151.40
144.84
136.43
133.25
131.91
130.12
129.39
128.11
123.20
64.93
54.98
36.16
21.69
20.94
3ba
f1 (ppm)

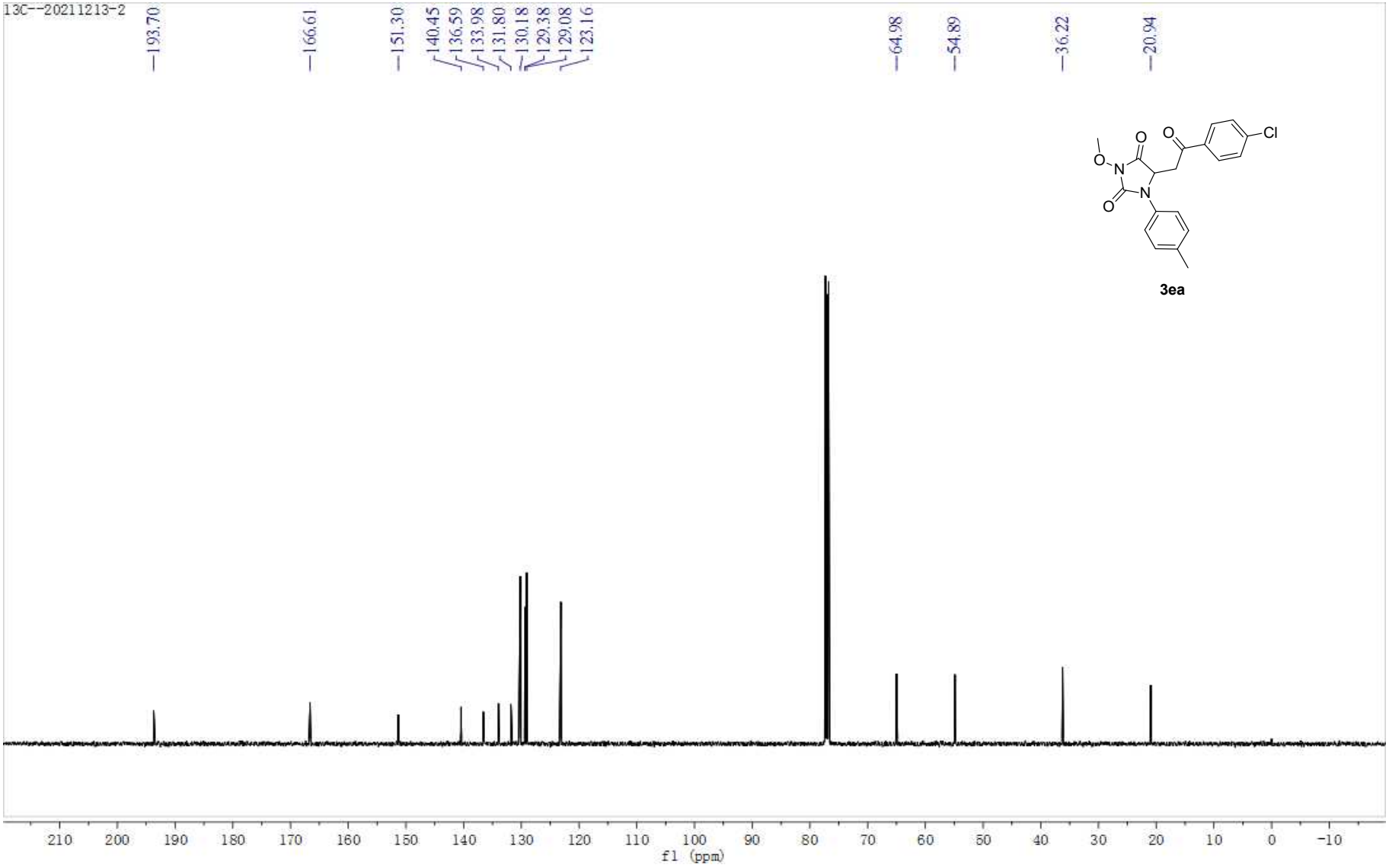

1H-SL-20220110-1
7.69
7.69
7.68
7.67
7.19
7.13
7.11
7.08
7.06
6.80
6.78
4.78
4.77
4.76
4.09
3.77
3.51
3.50
3.47
3.46
3.42
3.41
3.38
3.38
2.23
3ca
f1 (ppm)
2.01
2.06
2.00
2.01
1.00
3.03
3.04
1.05
1.02
3.00

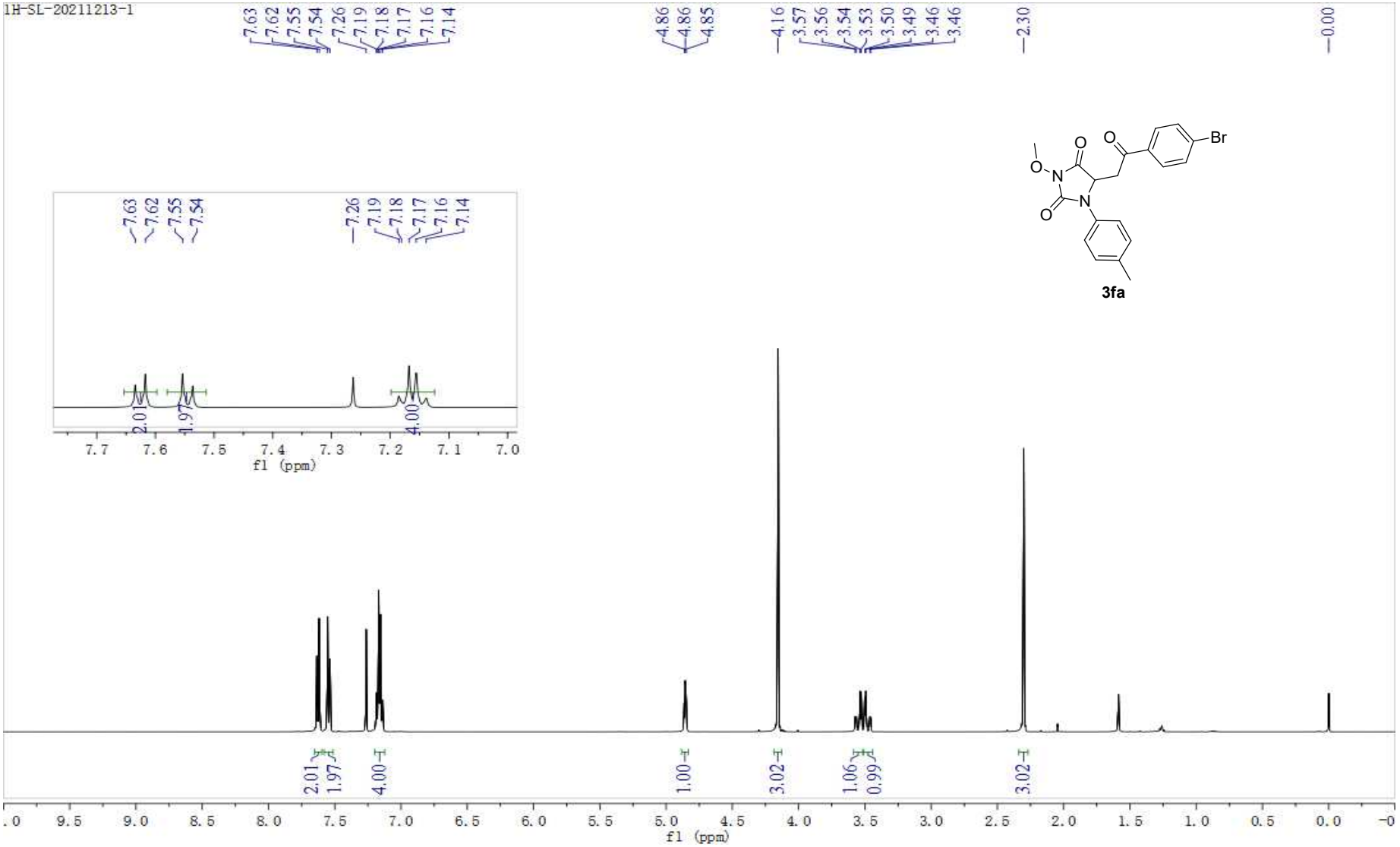

13C-SL-20220110-1
193.08
166.89
164.04
151.41
136.40
131.94
130.35
130.11
128.78
123.20
113.86
64.93
55.54
55.03
35.93
20.94
3ca
f1 (ppm)

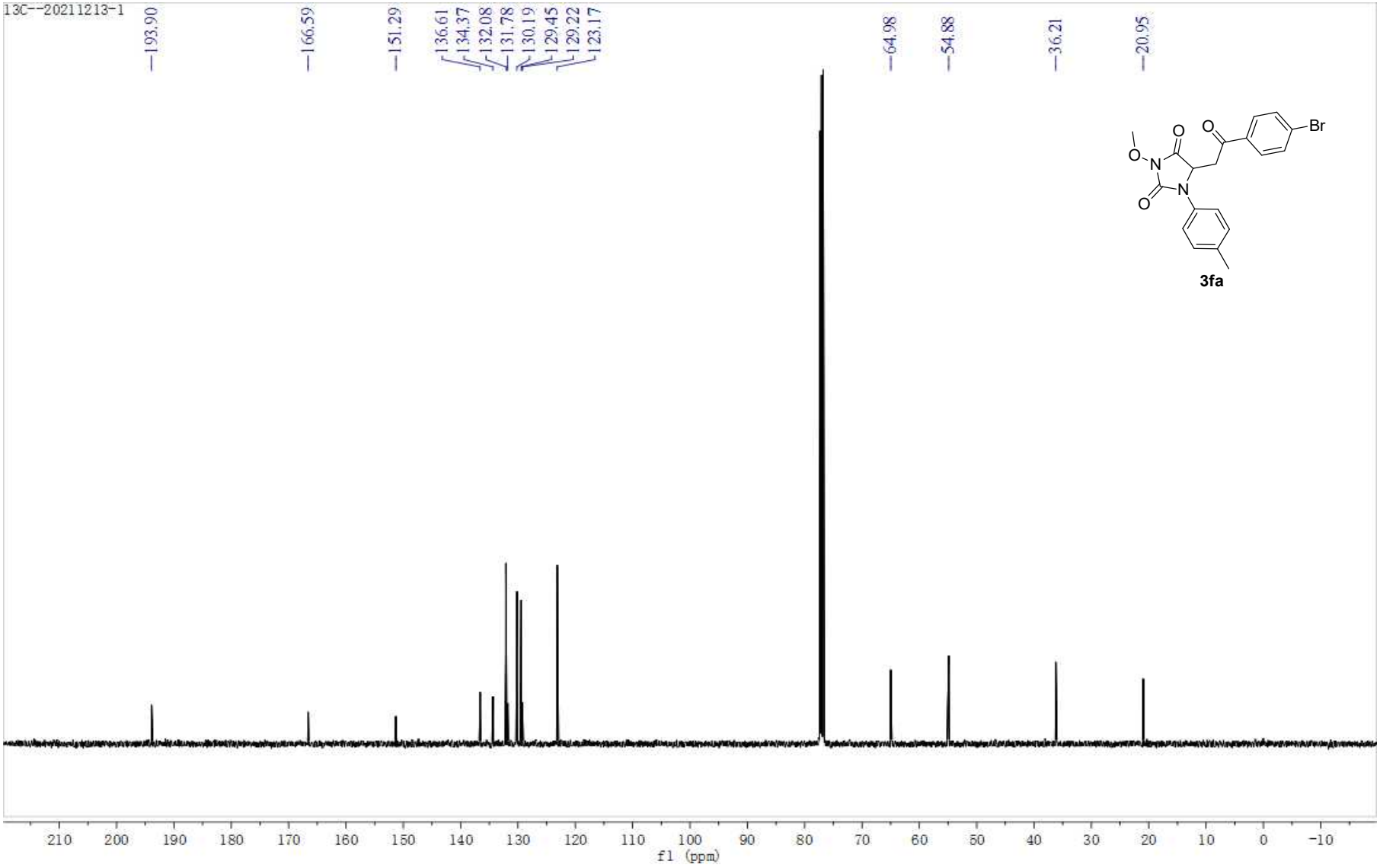

1H-WLG-20211219-XL-4F
7.73
7.72
7.72
7.71
7.71
7.19
7.12
7.10
7.07
7.06
7.00
6.99
6.97
4.79
4.78
4.78
4.07
3.51
3.50
3.47
3.47
3.44
3.43
3.40
3.39
2.21
F
O
O
O
N
O
N
3da
f1 (ppm)
2.00
2.04
2.05
2.02
1.00
3.05
1.07
1.01
3.05

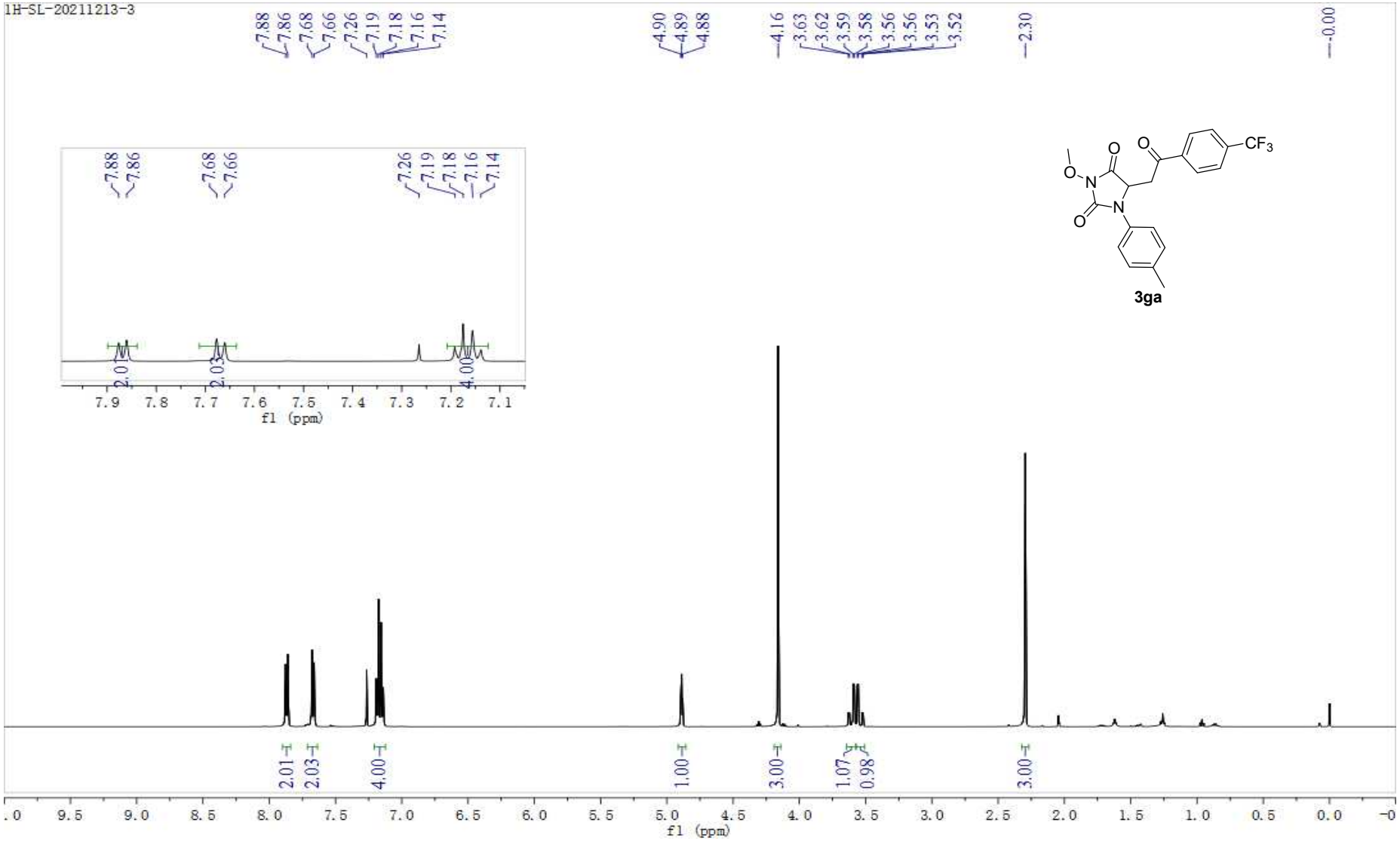

13C-WLG-20211219-XL-4F
193.34
167.13
166.70
165.10
151.35
136.52
132.14
131.84
130.76
130.69
130.15
123.15
116.00
115.82
64.96
54.91
36.14
20.93
O
O
N
O
N
O
F
3da
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

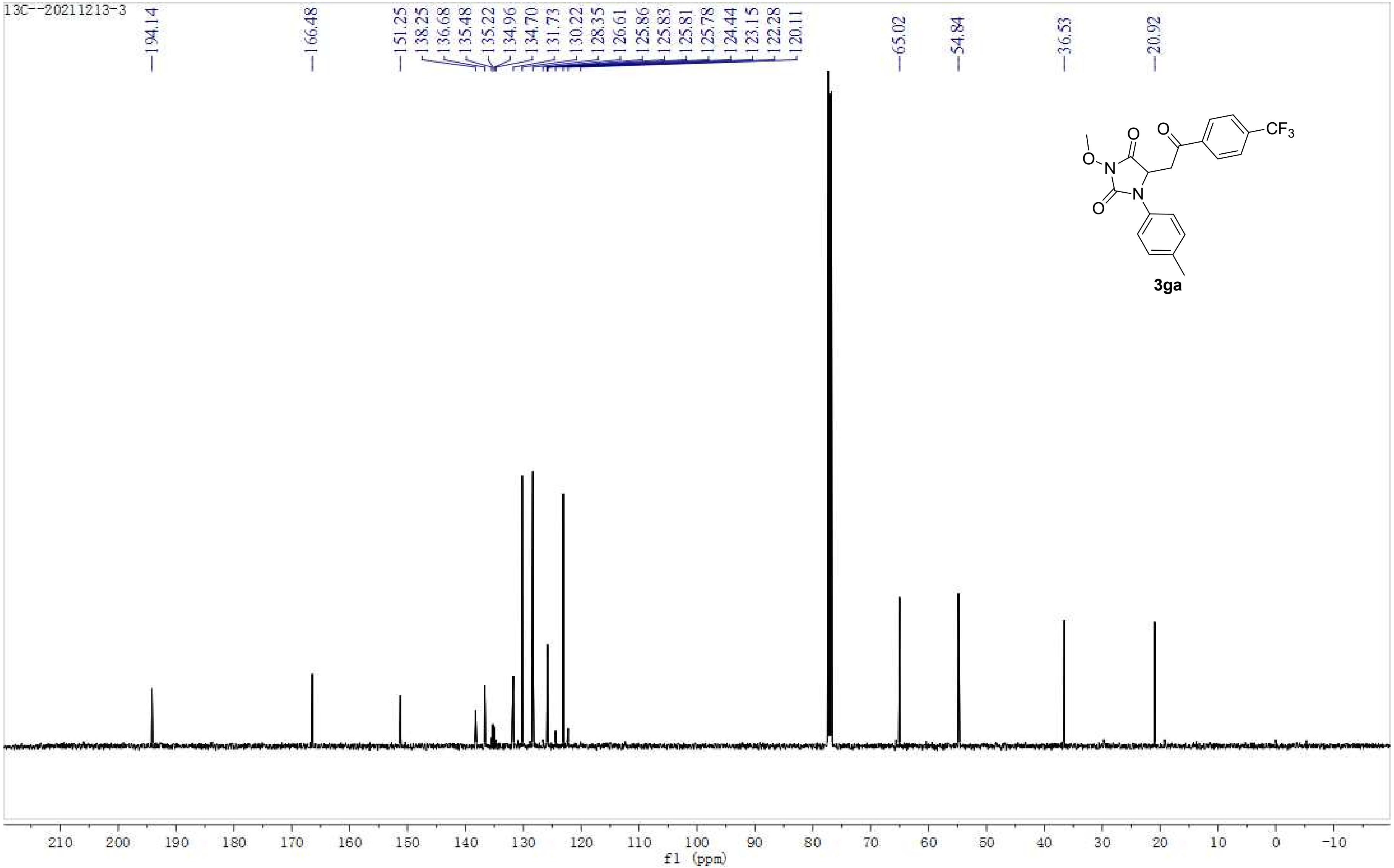

1H-SL-20211213-2
7.71
7.71
7.70
7.38
7.38
7.37
7.26
7.19
7.18
7.17
7.15
7.14
4.86
4.86
4.85
4.15
3.58
3.57
3.54
3.53
3.50
3.50
3.47
3.46
2.30
0.00
Cl
O
O
O
N
N
O
3ea
1.96
1.92
4.03
1.00
2.99
1.06
0.97
3.08
f1 (ppm)

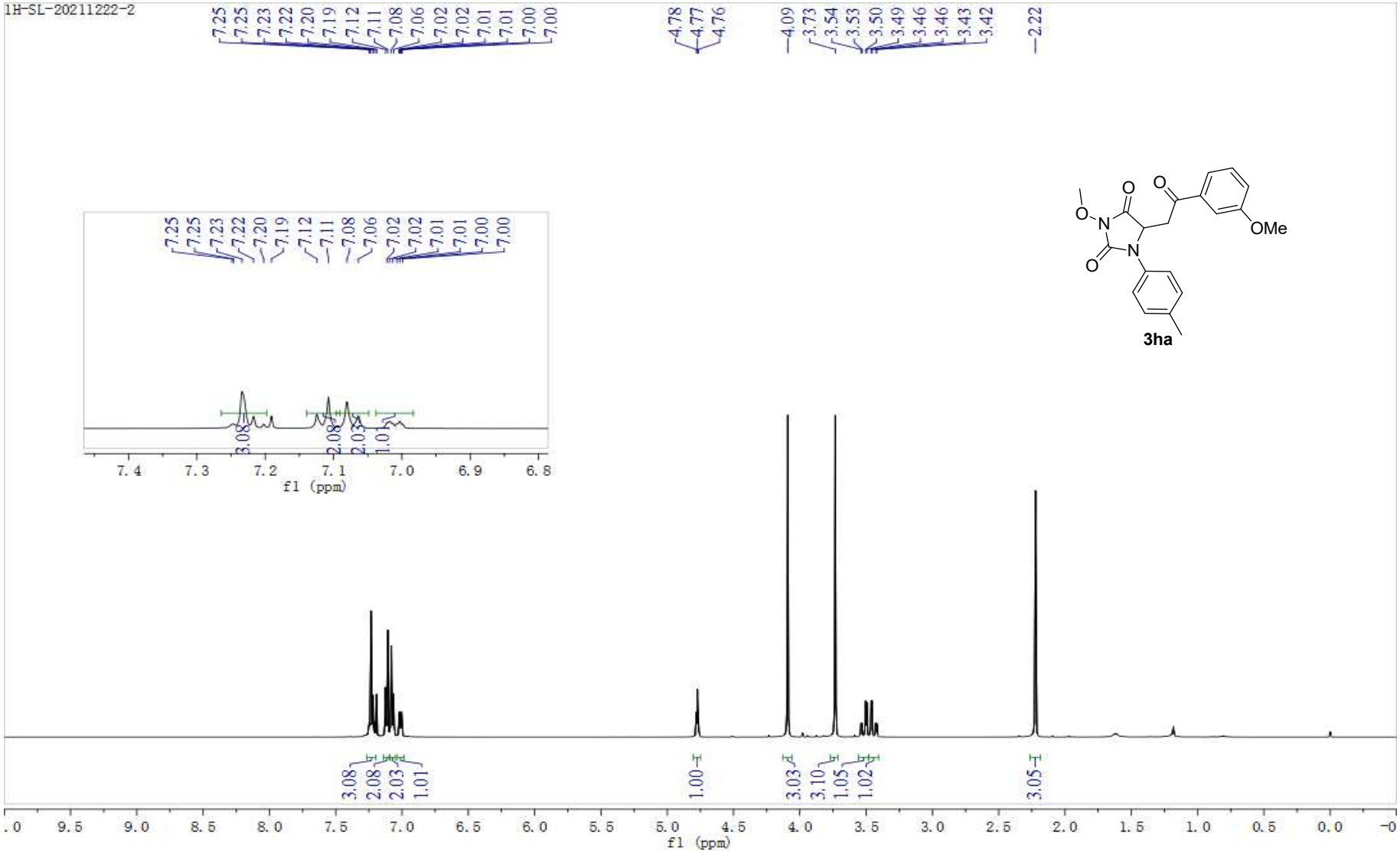

13C--20211213-2
193.70
166.61
151.30
140.45
136.59
133.98
131.80
130.18
129.38
129.08
123.16
64.98
54.89
36.22
20.94
O
O
O
N
N
O
Cl
3ea
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

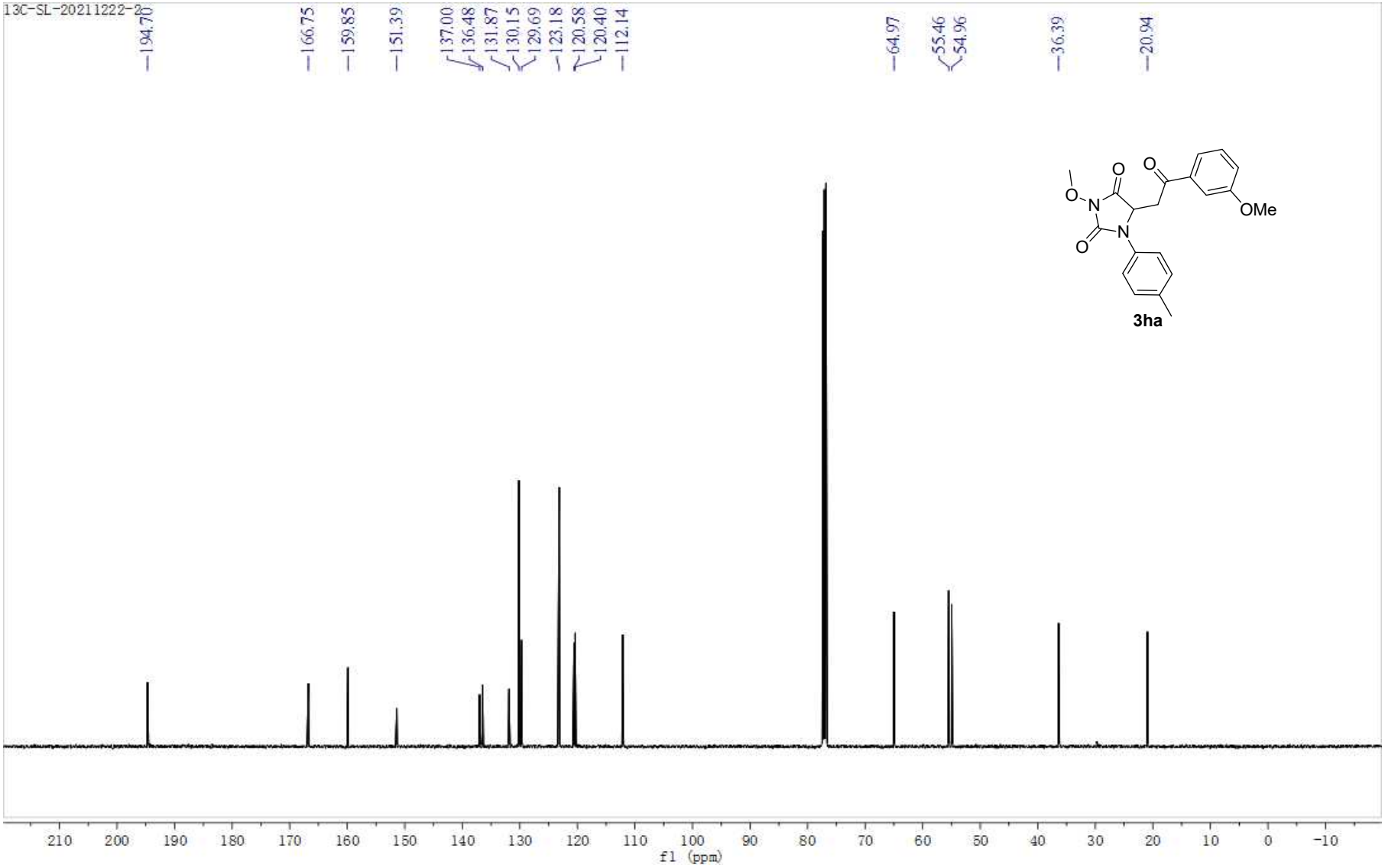

1H-SL-20211213-1
7.63
7.62
7.55
7.54
7.26
7.19
7.18
7.17
7.16
7.14
4.86
4.86
4.85
4.16
3.57
3.56
3.54
3.53
3.50
3.49
3.46
3.46
2.30
0.00
Br
O
O
N
O
N
3fa
2.01
1.97
4.00
1.00
3.02
1.06
0.99
3.02
f1 (ppm)

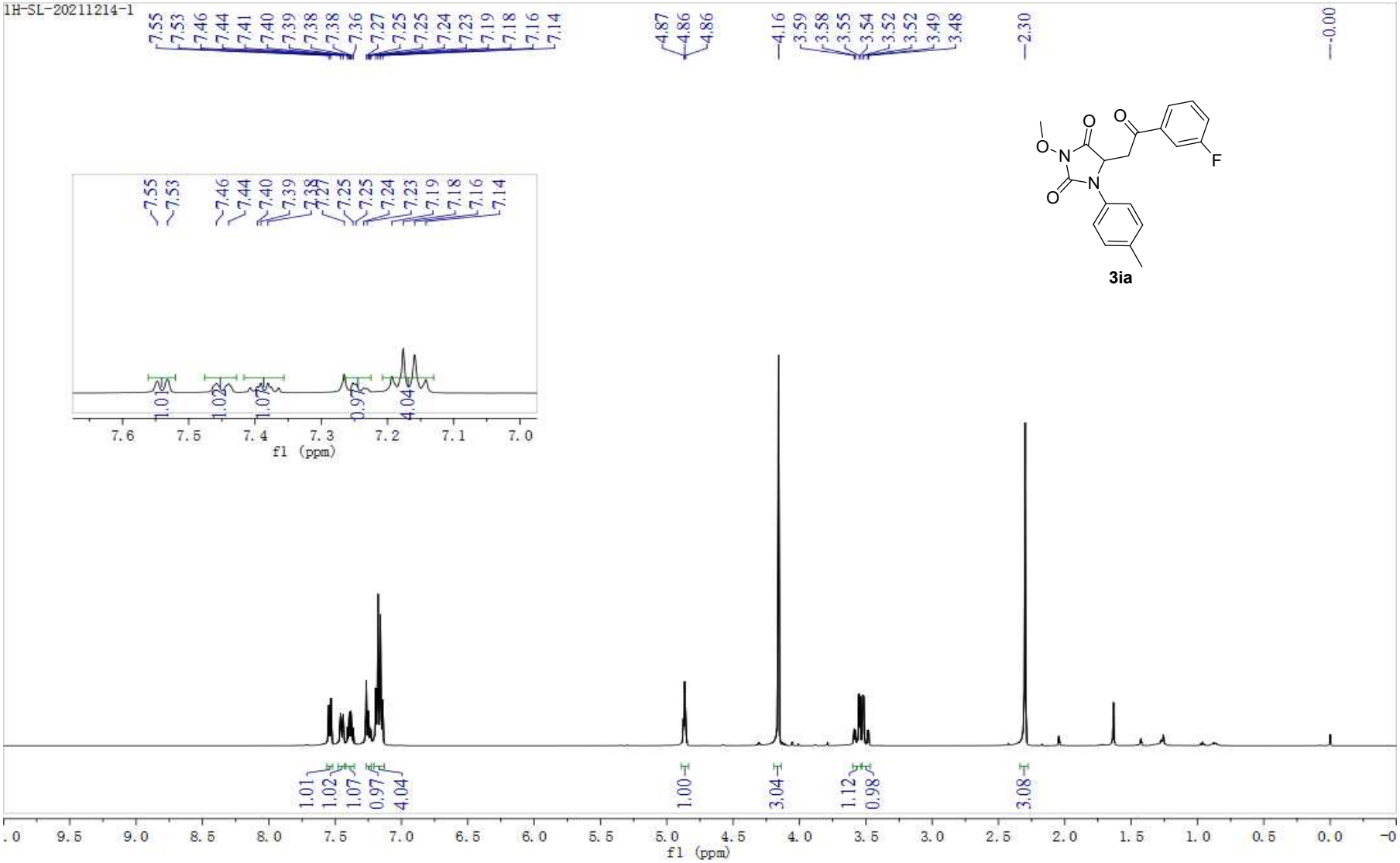

13C--20211213-1
193.90
166.59
151.29
136.61
134.37
132.08
131.78
130.19
129.45
129.22
123.17
64.98
54.88
36.21
20.95
O
O
O
N
N
Br
3fa
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

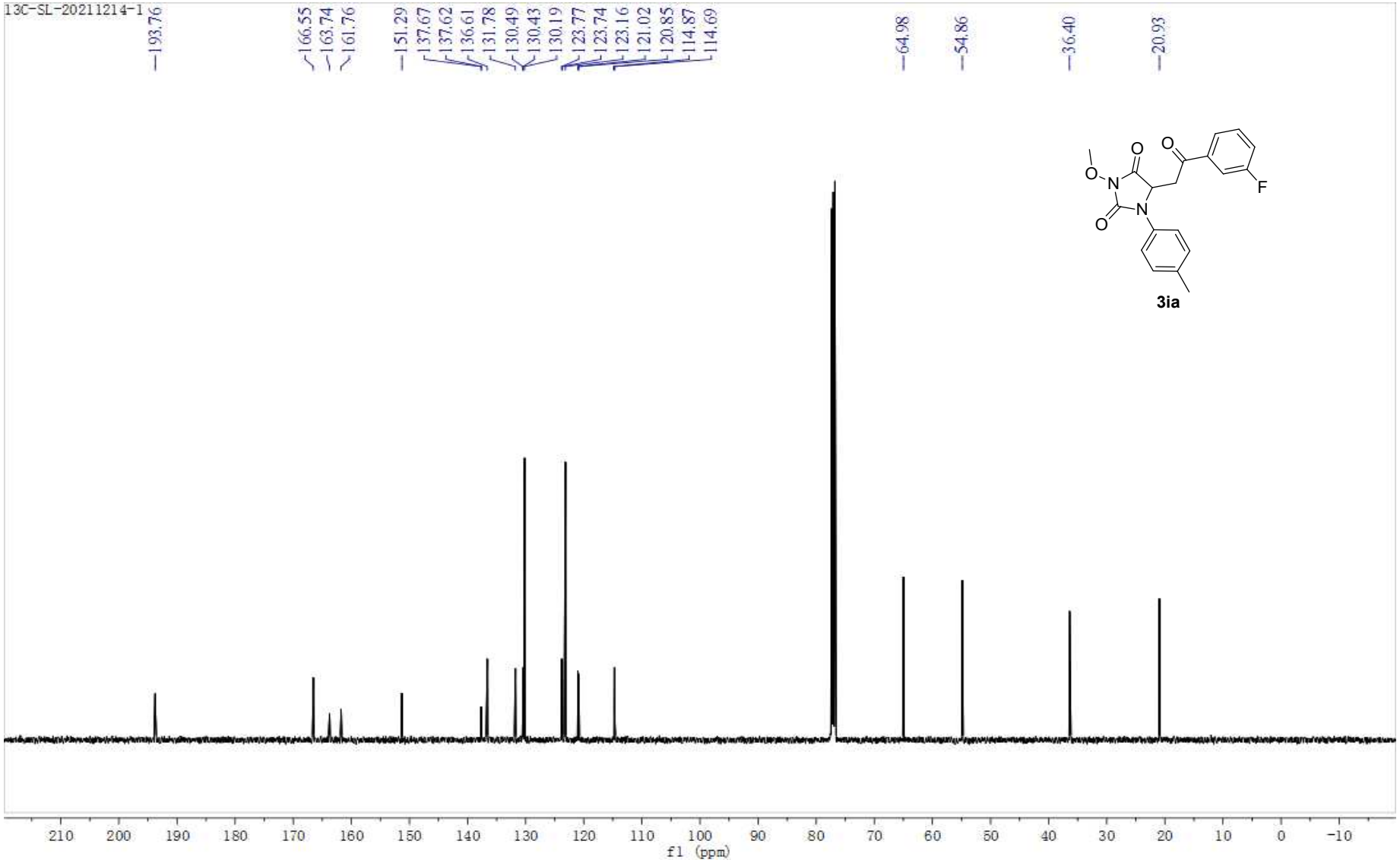

1H-SL-20211213-3
7.88
7.86
7.68
7.66
7.26
7.19
7.18
7.16
7.14
4.90
4.89
4.88
4.16
3.63
3.62
3.59
3.58
3.56
3.56
3.53
3.52
2.30
-0.00
CF3
3ga
2.01
2.03
4.00
1.00
3.00
1.07
0.98
3.00
f1 (ppm)

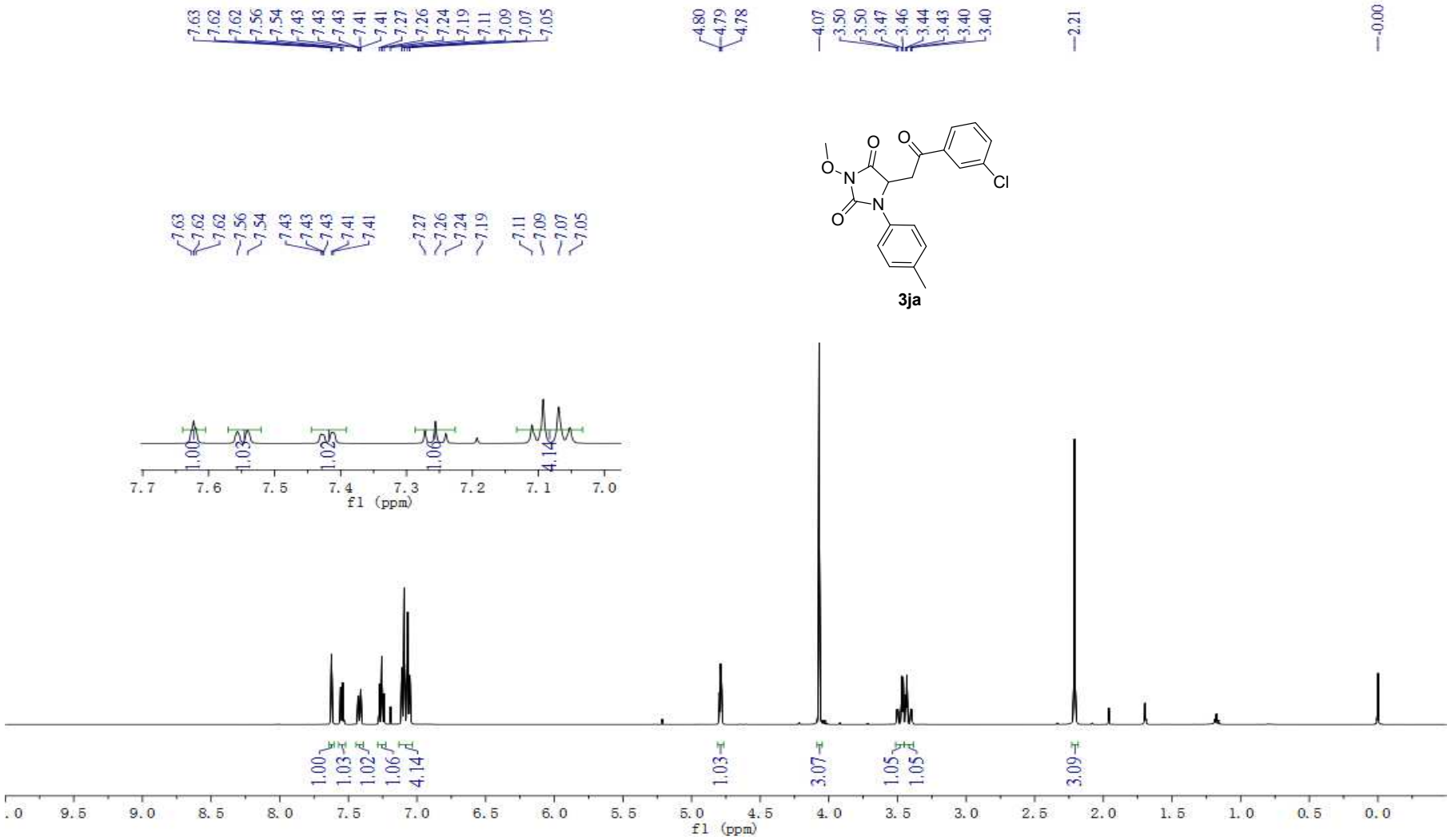

13C--20211213-3
194.14
166.48
151.25
138.25
136.68
135.48
135.22
134.96
134.70
131.73
130.22
128.35
126.61
125.86
125.83
125.81
125.78
124.44
123.15
122.28
120.11
65.02
54.84
36.53
20.92
O
O
CF3
O
N
N
O
3ga
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

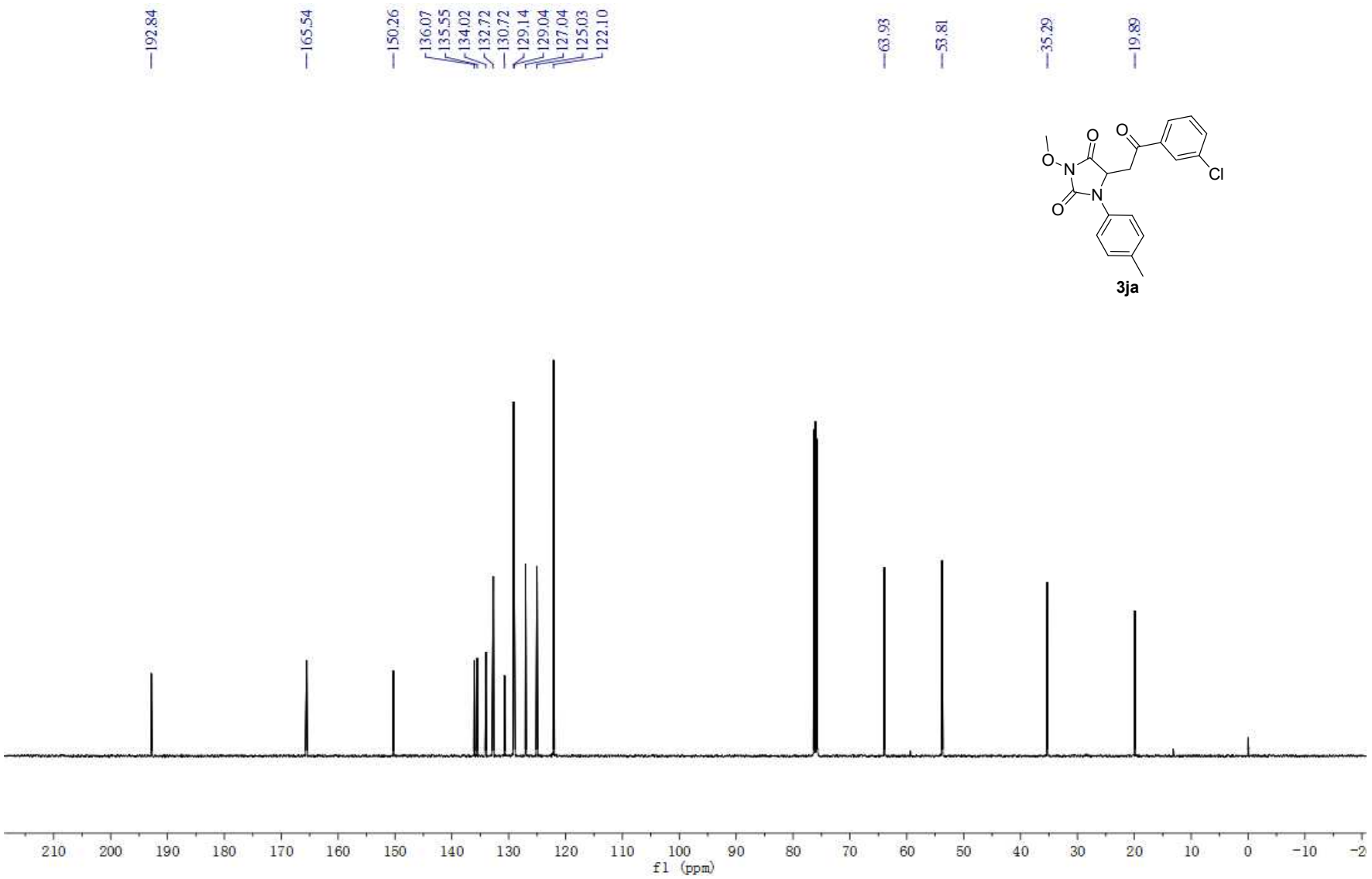

1H-SL-20211222-2
7.25 7.25 7.23 7.22 7.20 7.19 7.12 7.11 7.08 7.06 7.02 7.02 7.01 7.01 7.00 7.00
4.78 4.77 4.76
4.09 3.73 3.54 3.53 3.50 3.49 3.46 3.46 3.43 3.42
2.22
O
O
N
O
N
O
OMe
3ha
3.08 2.08 2.03 1.01
7.4 7.3 7.2 7.1 7.0 6.9 6.8
f1 (ppm)
1.00 3.03 3.10 1.05 1.02 3.05
9.5 9.0 8.5 8.0 7.5 7.0 6.5 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)

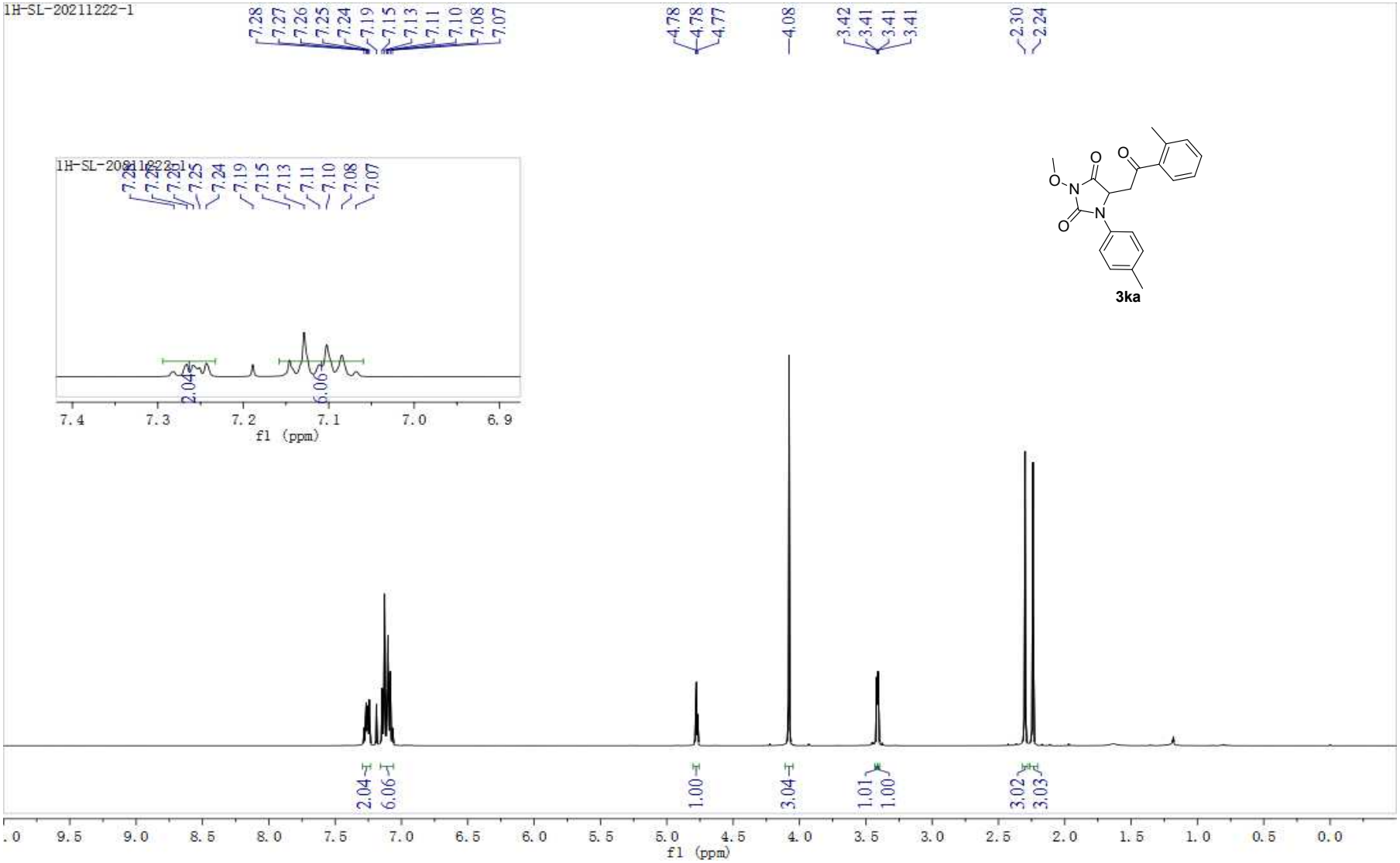

13C-SL-20211222-2
194.70
166.75
159.85
151.39
137.00
136.48
131.87
130.15
129.69
123.18
120.58
120.40
112.14
64.97
55.46
54.96
36.39
20.94
OMe
3ha
f1 (ppm)

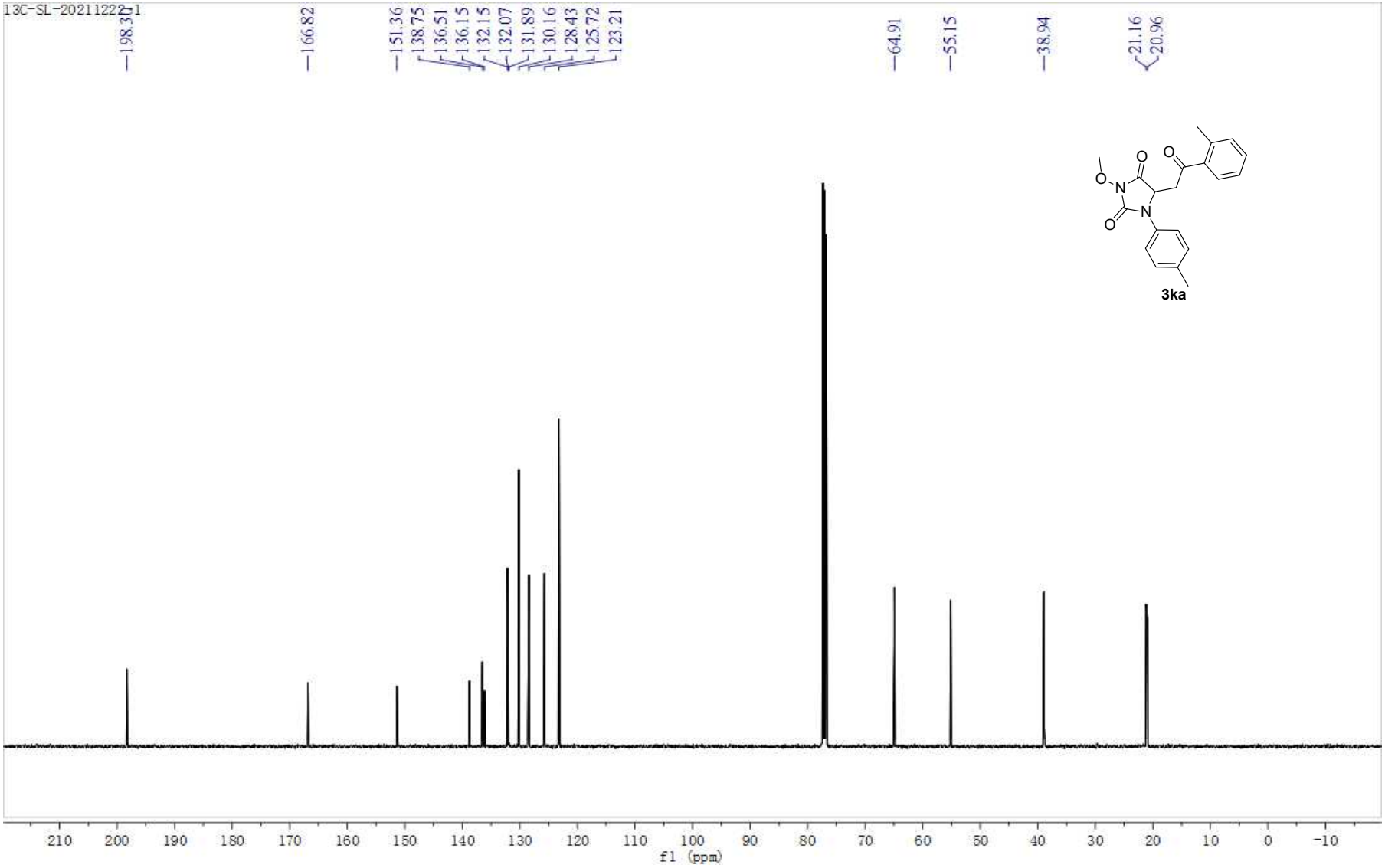

1H-SL-20211214-1
7.55
7.53
7.46
7.44
7.41
7.40
7.39
7.38
7.38
7.36
7.27
7.25
7.25
7.24
7.23
7.19
7.18
7.16
7.14
4.87
4.86
4.86
4.16
3.59
3.58
3.55
3.54
3.52
3.52
3.49
3.48
2.30
0.00
O
O
O
N
N
F
3ia
1.01
1.02
1.07
0.97
4.04
1.00
3.04
1.12
0.98
3.08
f1 (ppm)

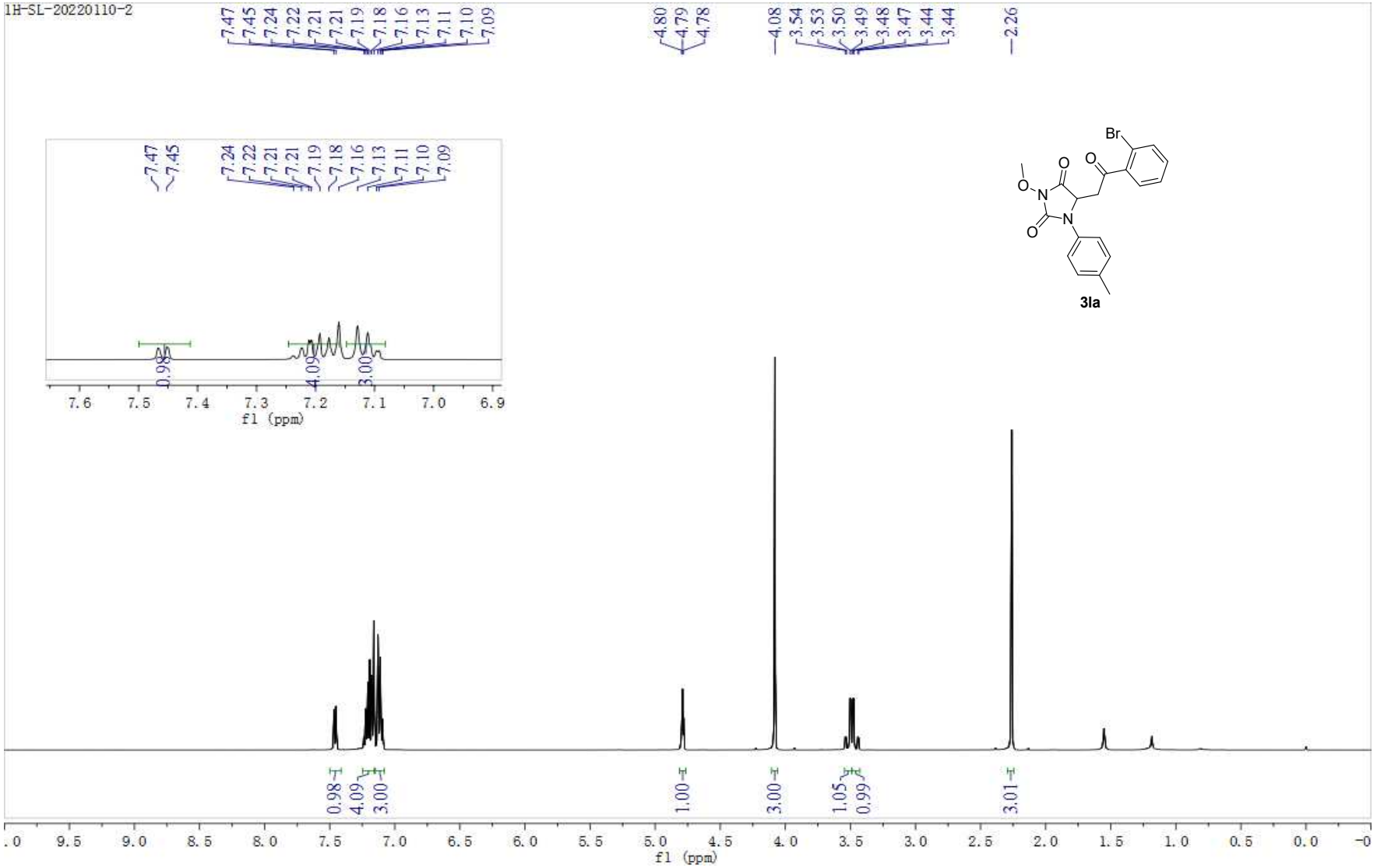

13C-SL-20211214-1
193.76
166.55
163.74
161.76
151.29
137.67
137.62
136.61
131.78
130.49
130.43
130.19
123.77
123.74
123.16
121.02
120.85
114.87
114.69
64.98
54.86
36.40
20.93
O
O
O
N
N
O
F
3ia
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

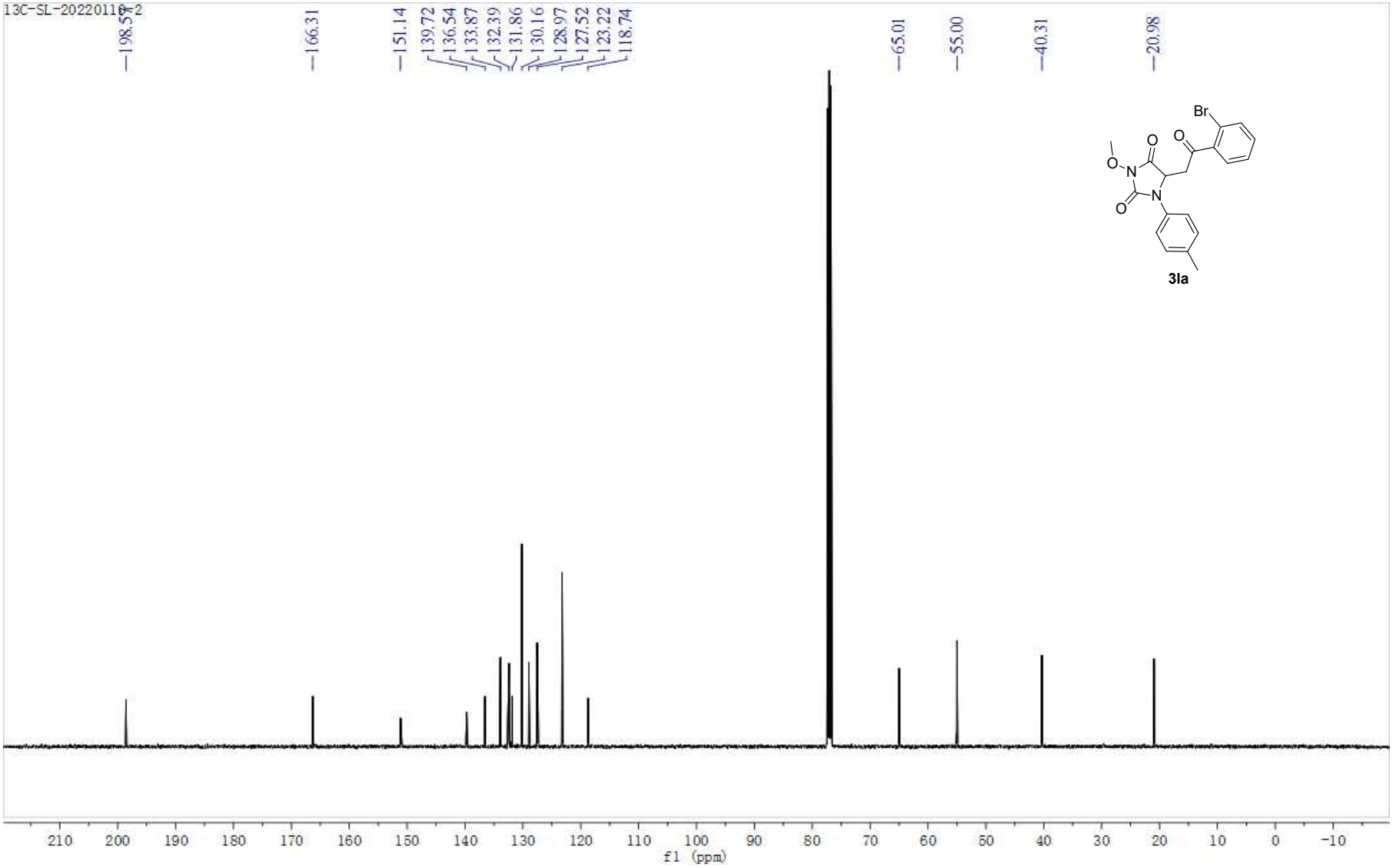

7.63
7.62
7.62
7.56
7.54
7.43
7.43
7.43
7.41
7.41
7.27
7.26
7.24
7.19
7.11
7.09
7.07
7.05
4.80
4.79
4.78
4.07
3.50
3.50
3.47
3.46
3.44
3.43
3.40
3.40
2.21
0.00
O
O
O
N
N
Cl
3ja
1.00
1.03
1.02
1.06
4.14
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)
1.00
1.03
1.02
1.06
4.14
1.03
3.07
1.05
1.05
3.09
9.5
9.0
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)

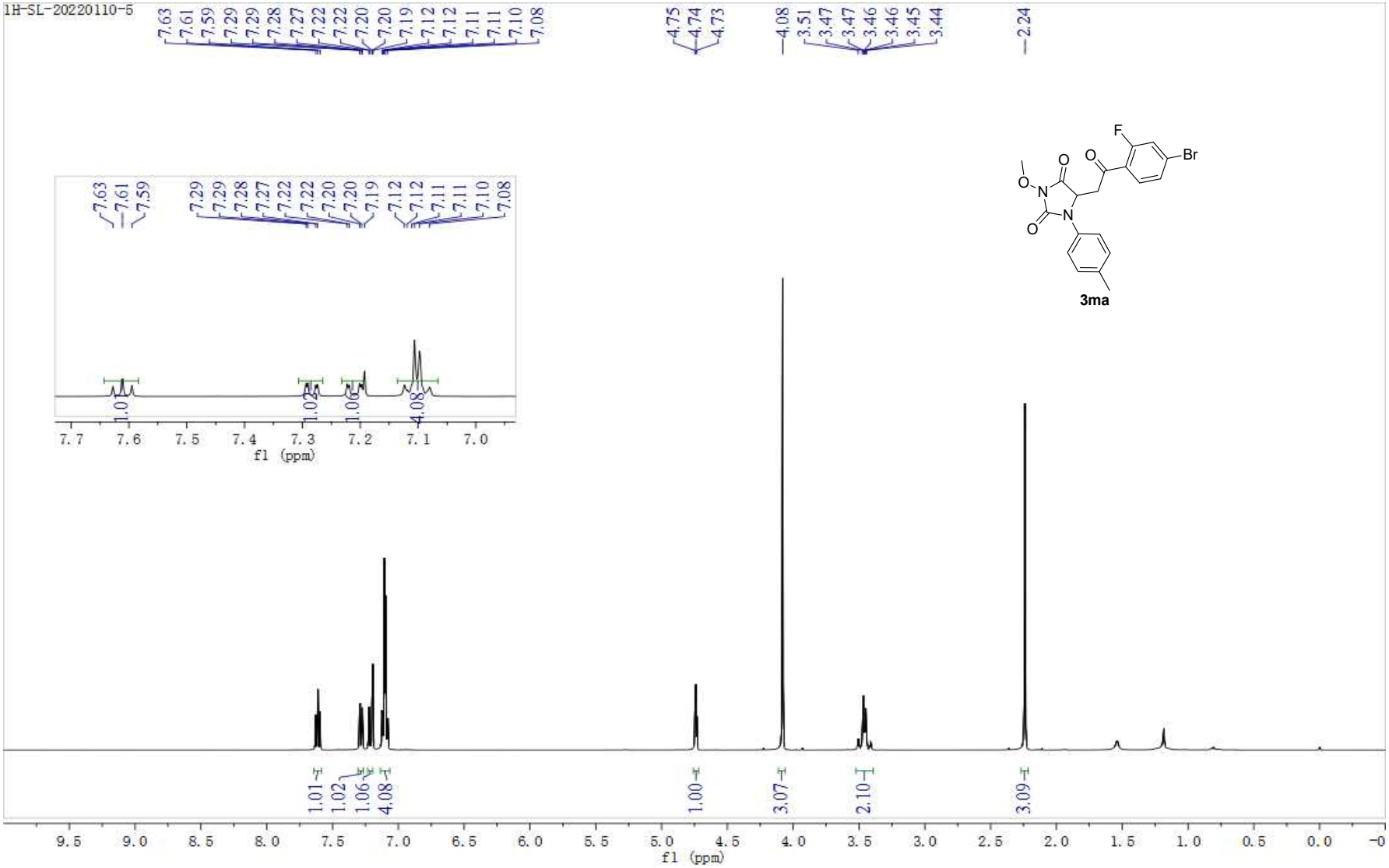

192.84
165.54
150.26
136.07
135.55
134.02
132.72
130.72
129.14
129.04
127.04
125.03
122.10
63.93
53.81
35.29
19.89
O
O
N
O
N
O
Cl
3ja
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−2
f1 (ppm)

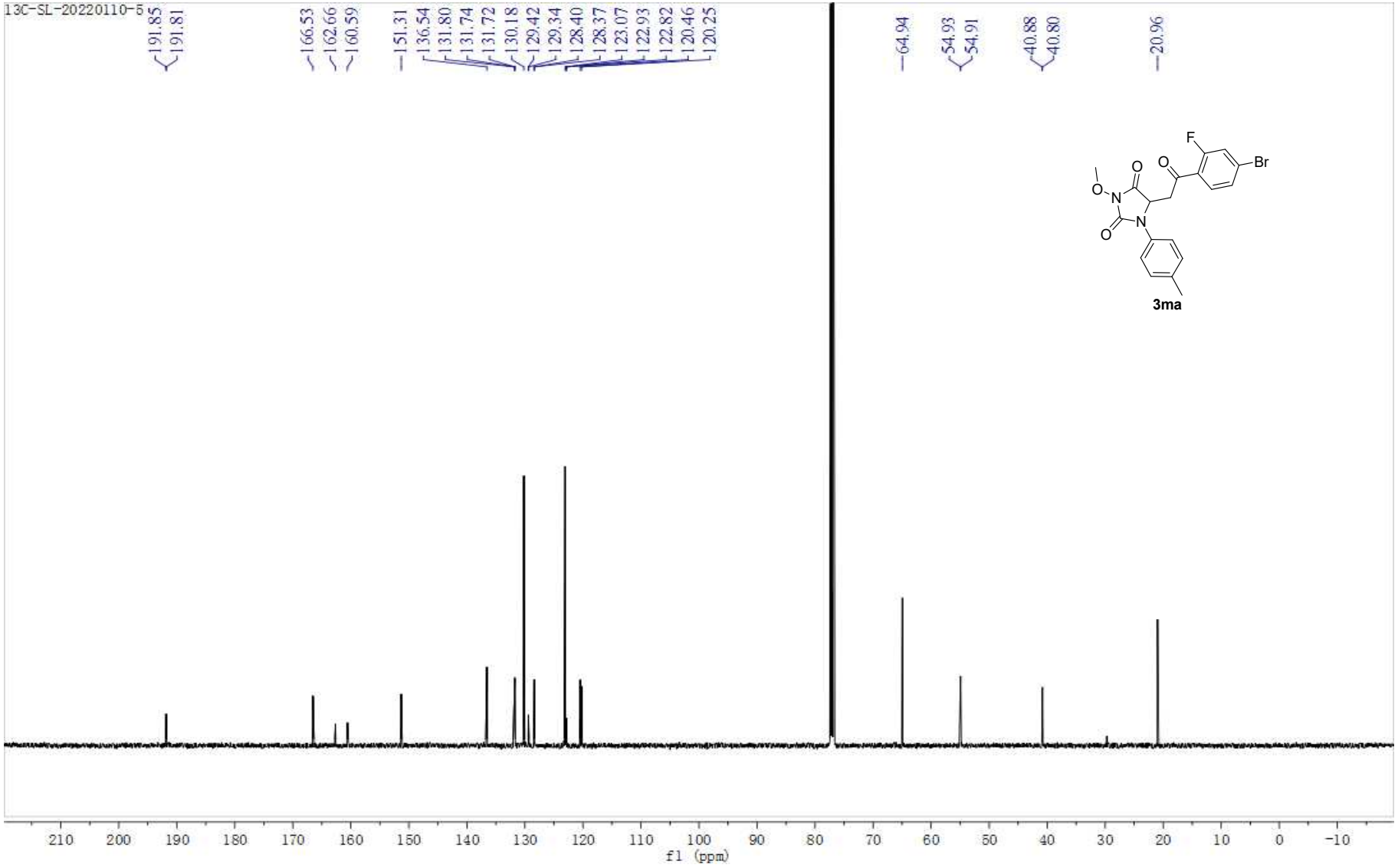

1H-SL-20211222-1
7.28
7.27
7.26
7.25
7.24
7.19
7.15
7.13
7.11
7.10
7.08
7.07
4.78
4.78
4.77
4.08
3.42
3.41
3.41
3.41
2.30
2.24
1H-SL-20211222-1
2.04
6.06
7.4
7.3
7.2
7.1
7.0
6.9
f1 (ppm)
O
O
N
O
N
3ka
2.04
6.06
1.00
3.04
1.01
1.00
3.02
3.03
f1 (ppm)

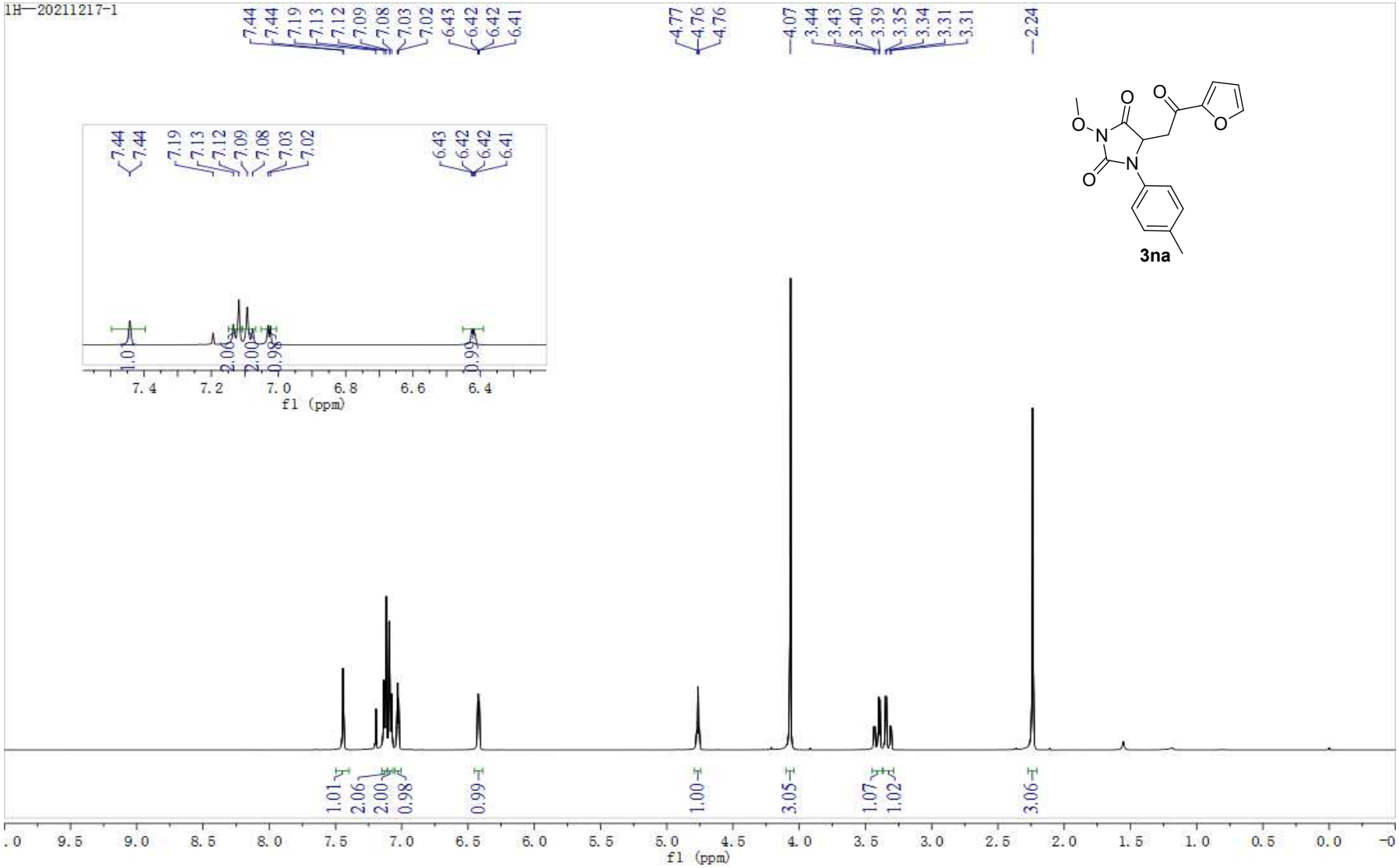

13C-SL-20211222-1
198.30
166.82
151.36
138.75
136.51
136.15
132.15
132.07
131.89
130.16
128.43
125.72
123.21
64.91
55.15
38.94
21.16
20.96
3ka
f1 (ppm)

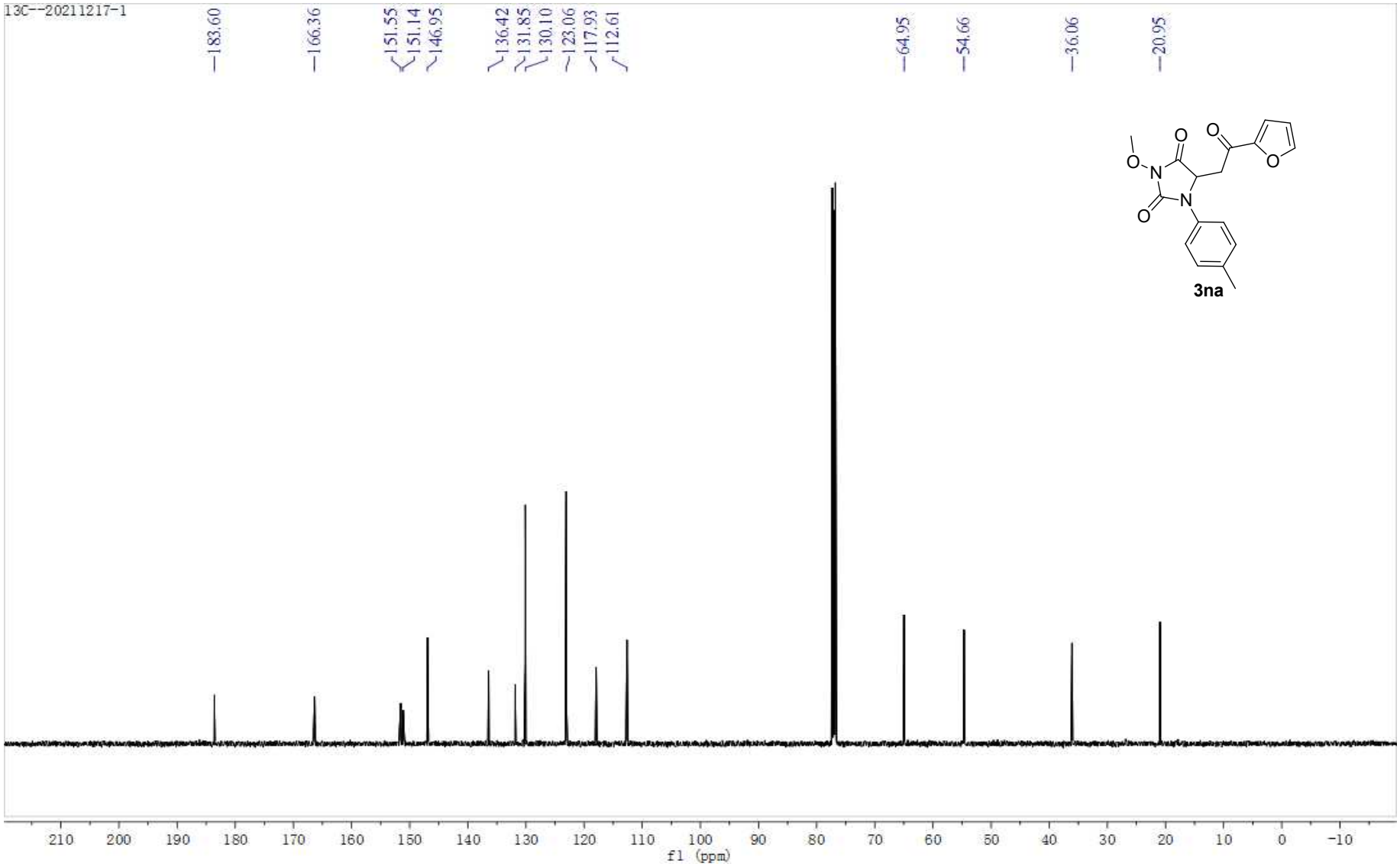

1H-SL-20220110-2
7.47
7.45
7.24
7.22
7.21
7.21
7.19
7.18
7.16
7.13
7.11
7.10
7.09
4.80
4.79
4.78
4.08
3.54
3.53
3.50
3.49
3.48
3.47
3.44
3.44
2.26
0.98
4.09
3.00
f1 (ppm)
Br
O
O
N
O
N
3la
0.98
4.09
3.00
1.00
3.00
1.05
0.99
3.01
f1 (ppm)

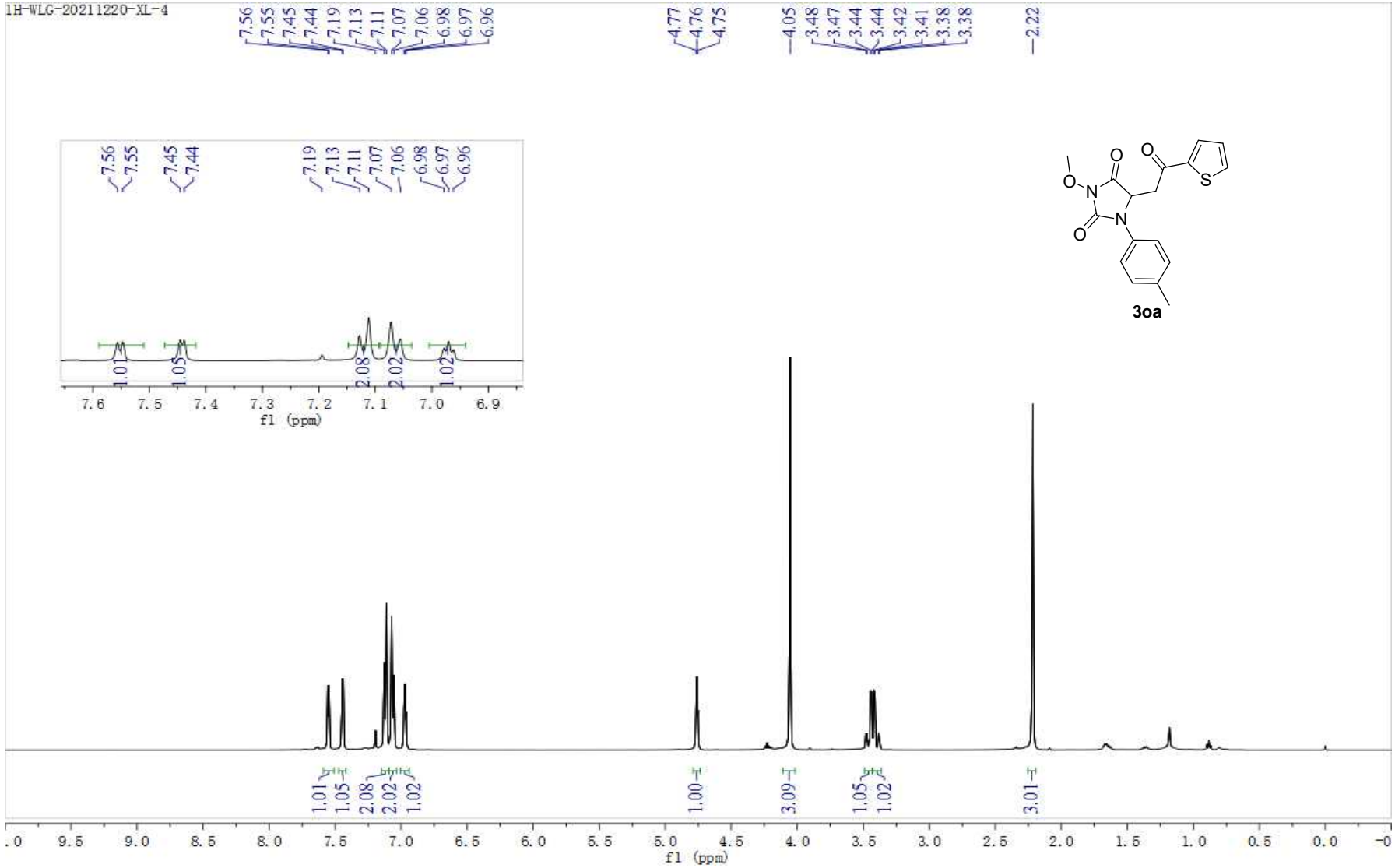

13C-SL-20220118-2
198.57
166.31
151.14
139.72
136.54
133.87
132.39
131.86
130.16
128.97
127.52
123.22
118.74
65.01
55.00
40.31
20.98
Br
O
O
O
N
N
O
3la
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

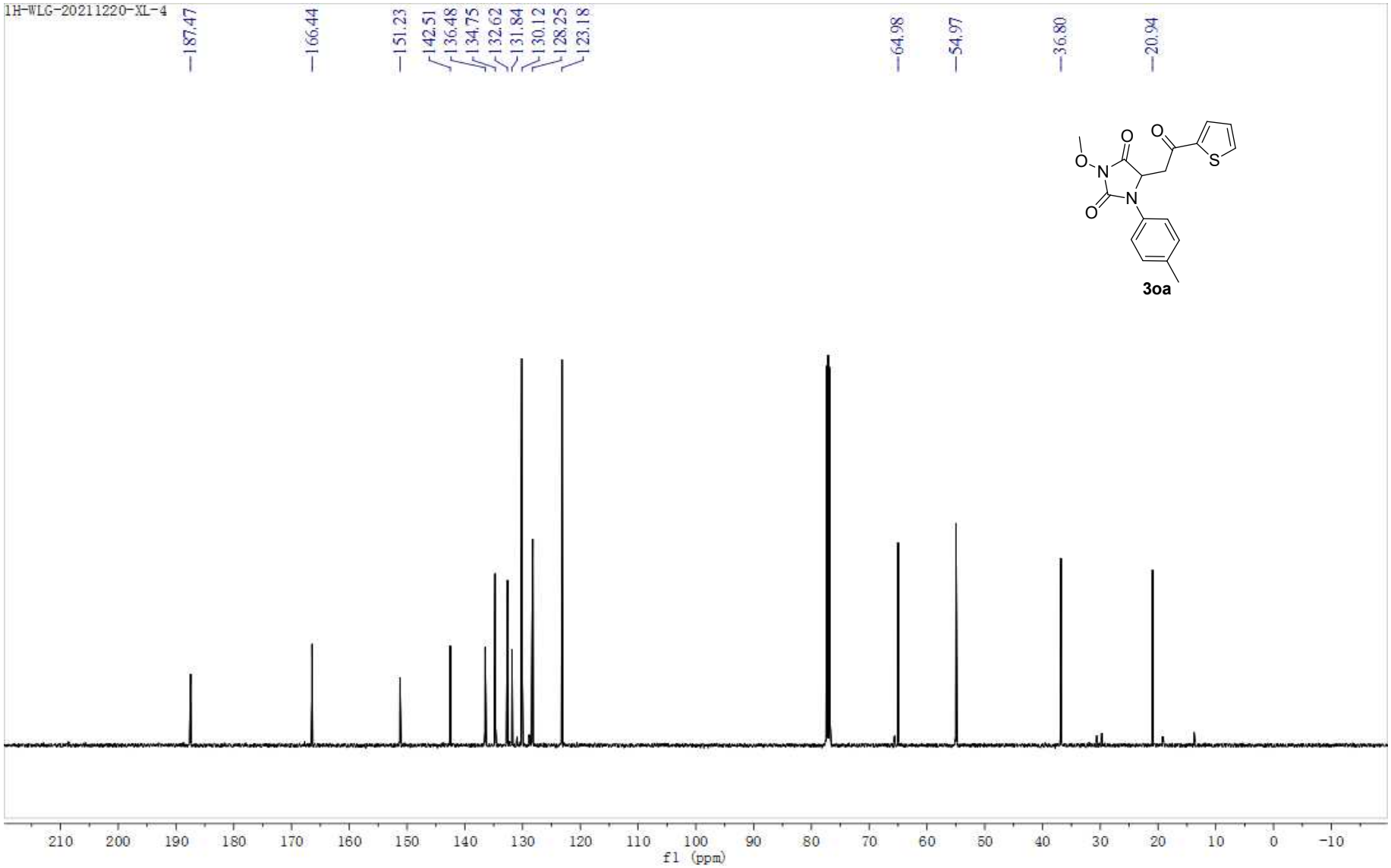

1H-SL-20220110-5
7.63
7.61
7.59
7.29
7.29
7.28
7.27
7.22
7.22
7.20
7.20
7.19
7.12
7.12
7.11
7.11
7.10
7.08
4.75
4.74
4.73
4.08
3.51
3.47
3.47
3.46
3.46
3.45
3.44
2.24
F
Br
O
O
O
N
N
O
3ma
1.01
1.02
1.06
4.08
1.00
3.07
2.10
3.09
f1 (ppm)

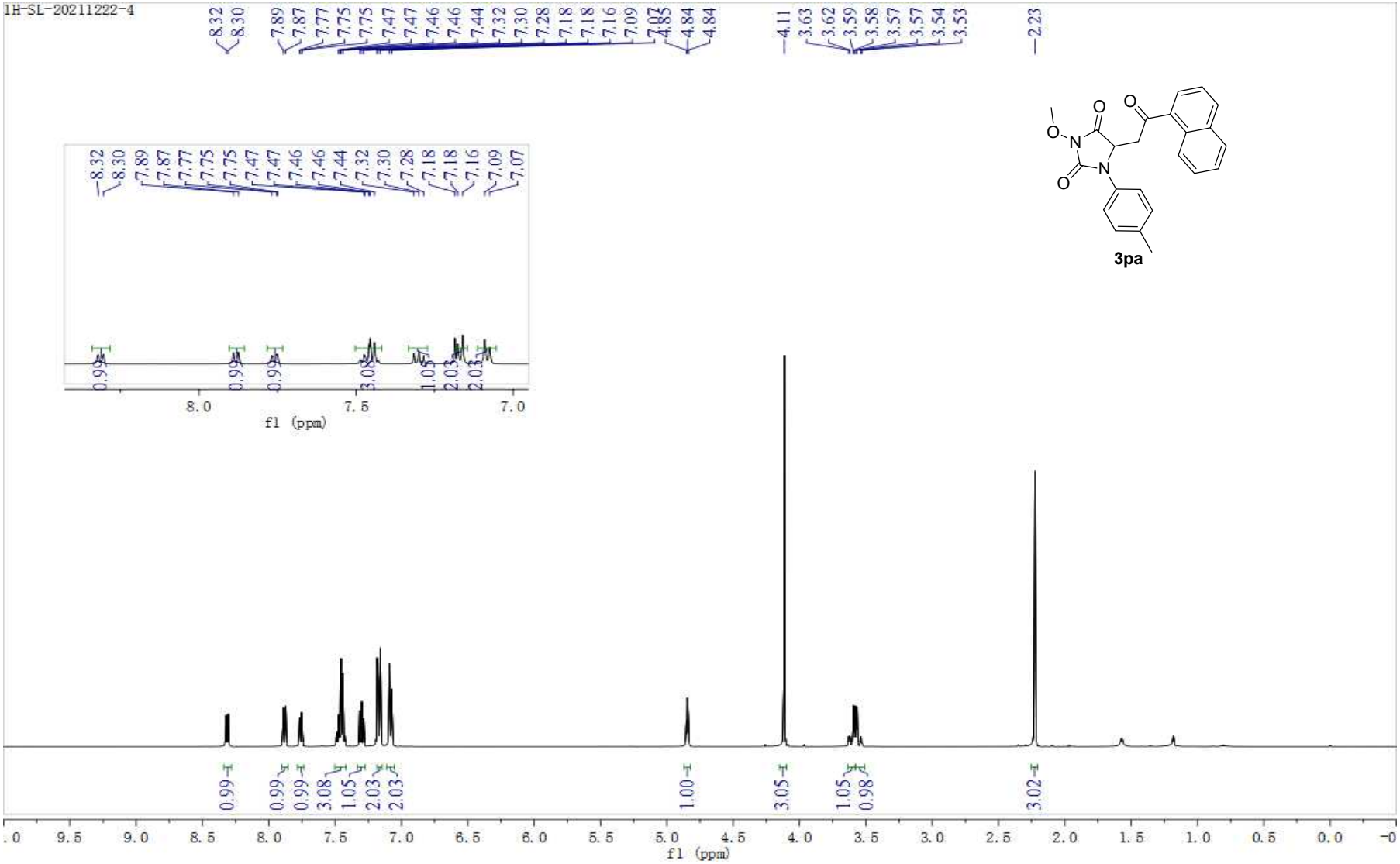

13C-SL-20220110-5
191.85
191.81
166.53
162.66
160.59
151.31
136.54
131.80
131.74
131.72
130.18
129.42
129.34
128.40
128.37
123.07
122.93
122.82
120.46
120.25
64.94
54.93
54.91
40.88
40.80
20.96
F
Br
O
O
O
N
N
O
3ma
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

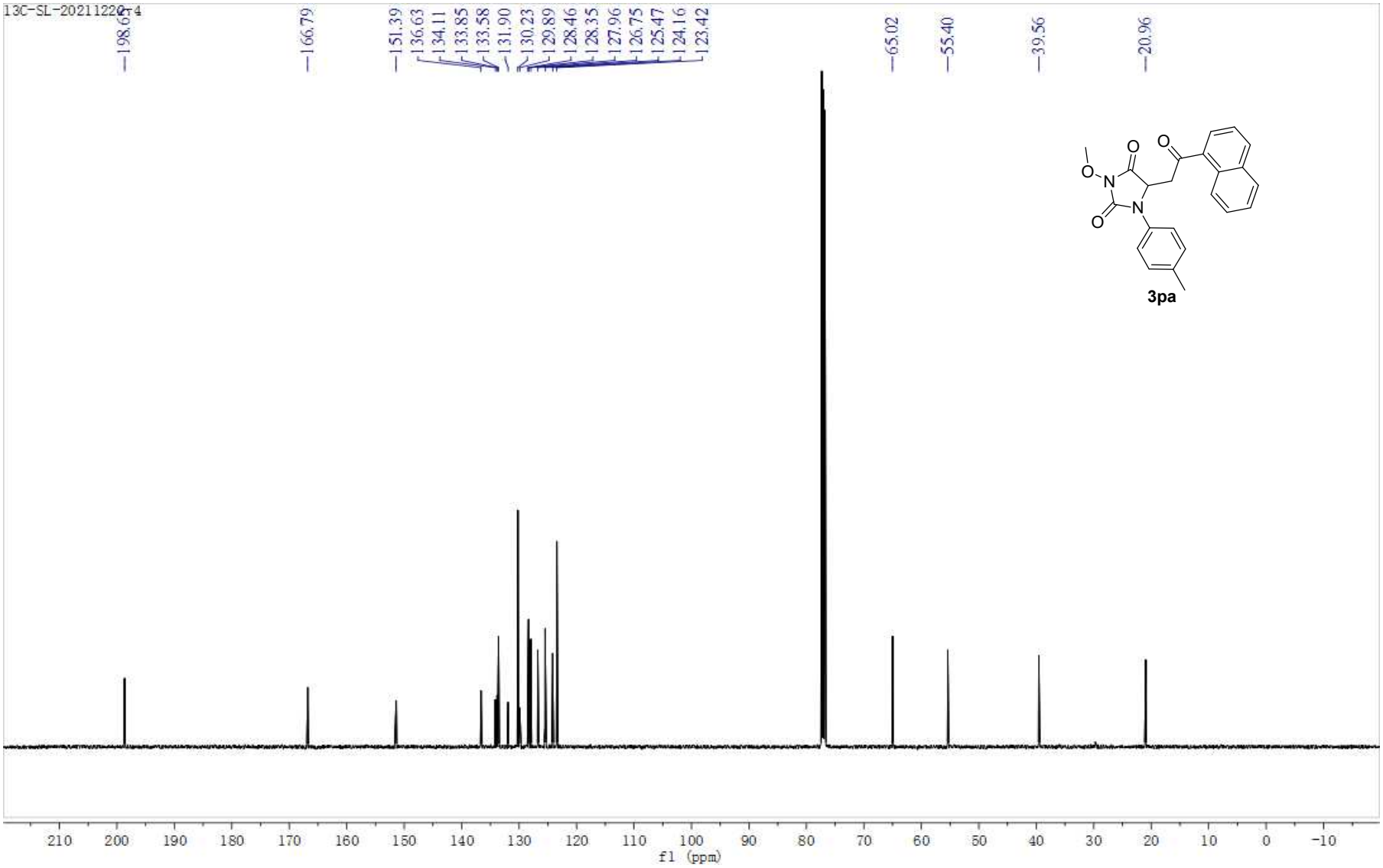

1H—20211217-1
7.44
7.44
7.19
7.13
7.12
7.09
7.08
7.03
7.02
6.43
6.42
6.42
6.41
4.77
4.76
4.76
4.07
3.44
3.43
3.40
3.39
3.35
3.34
3.31
3.31
2.24
3na
f1 (ppm)
1.01
2.06
2.00
0.98
0.99
1.00
3.05
1.07
1.02
3.06

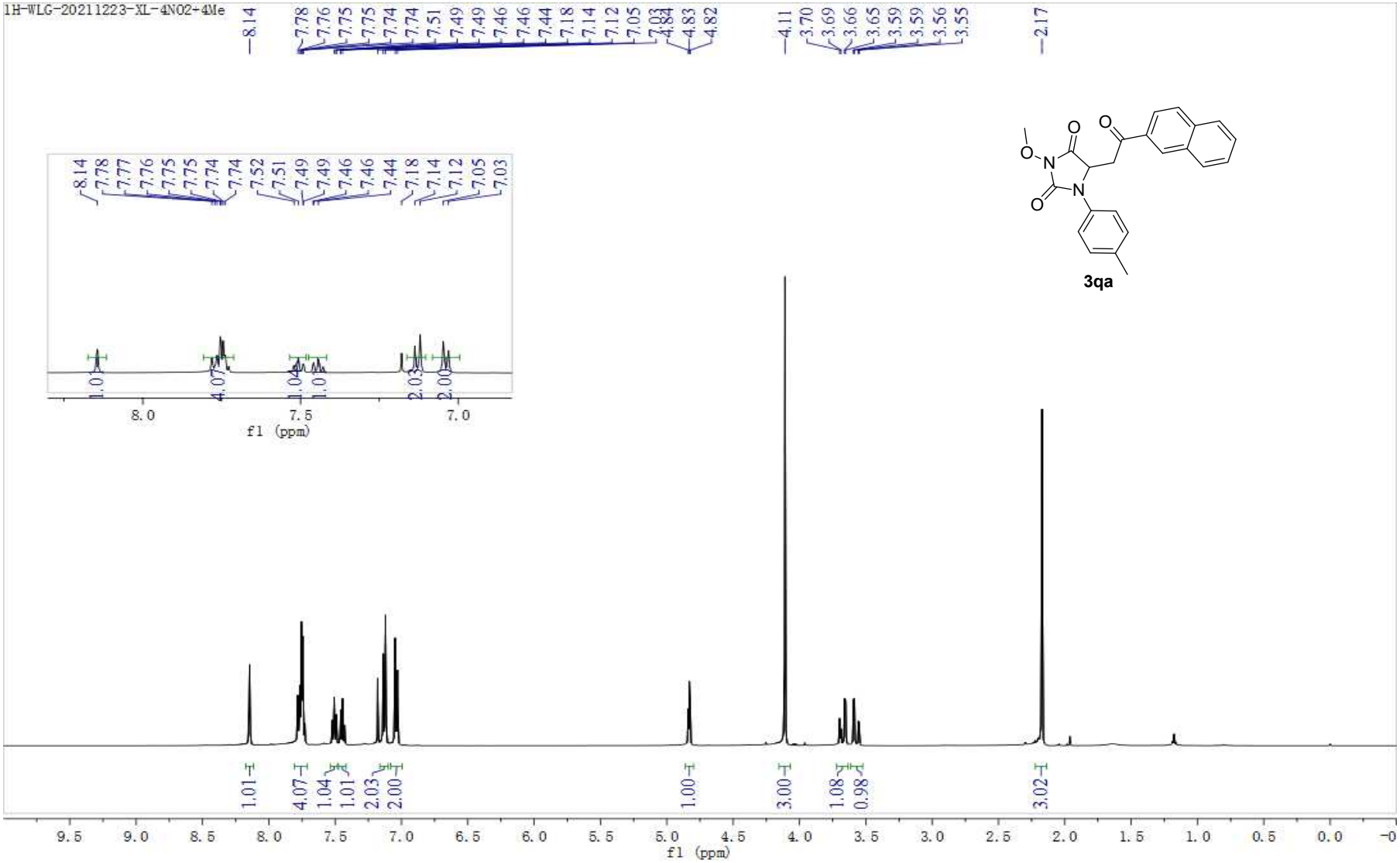

13C--20211217-1
183.60
166.36
151.55
151.14
146.95
136.42
131.85
130.10
123.06
117.93
112.61
64.95
54.66
36.06
20.95
3na
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

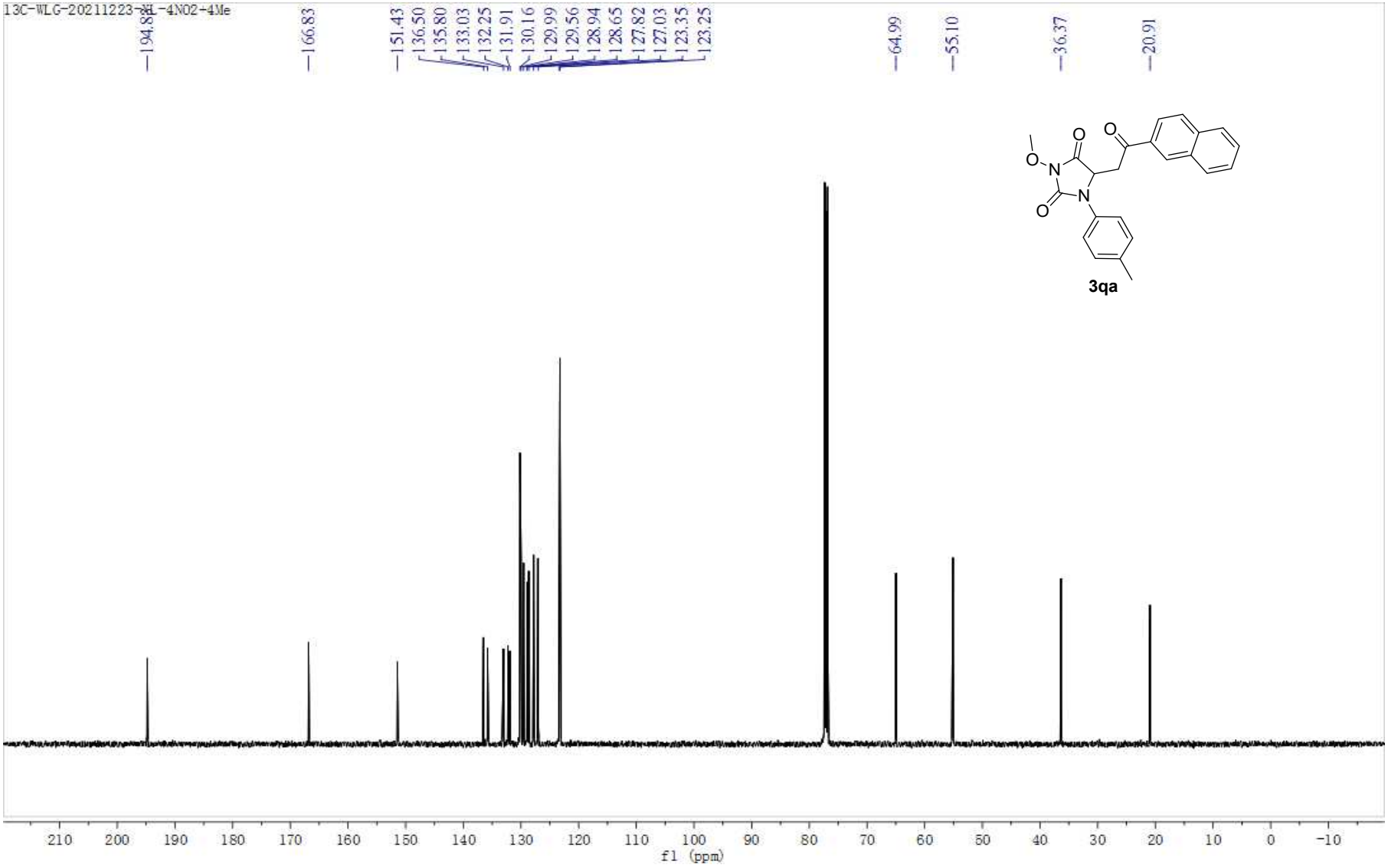

1H-WLG-20211220-XL-4
7.56
7.55
7.45
7.44
7.19
7.13
7.11
7.07
7.06
6.98
6.97
6.96
4.77
4.76
4.75
4.05
3.48
3.47
3.44
3.44
3.42
3.41
3.38
3.38
2.22
1.01
1.05
2.08
2.02
1.02
1.00
3.09
1.05
1.02
3.01
f1 (ppm)
3oa

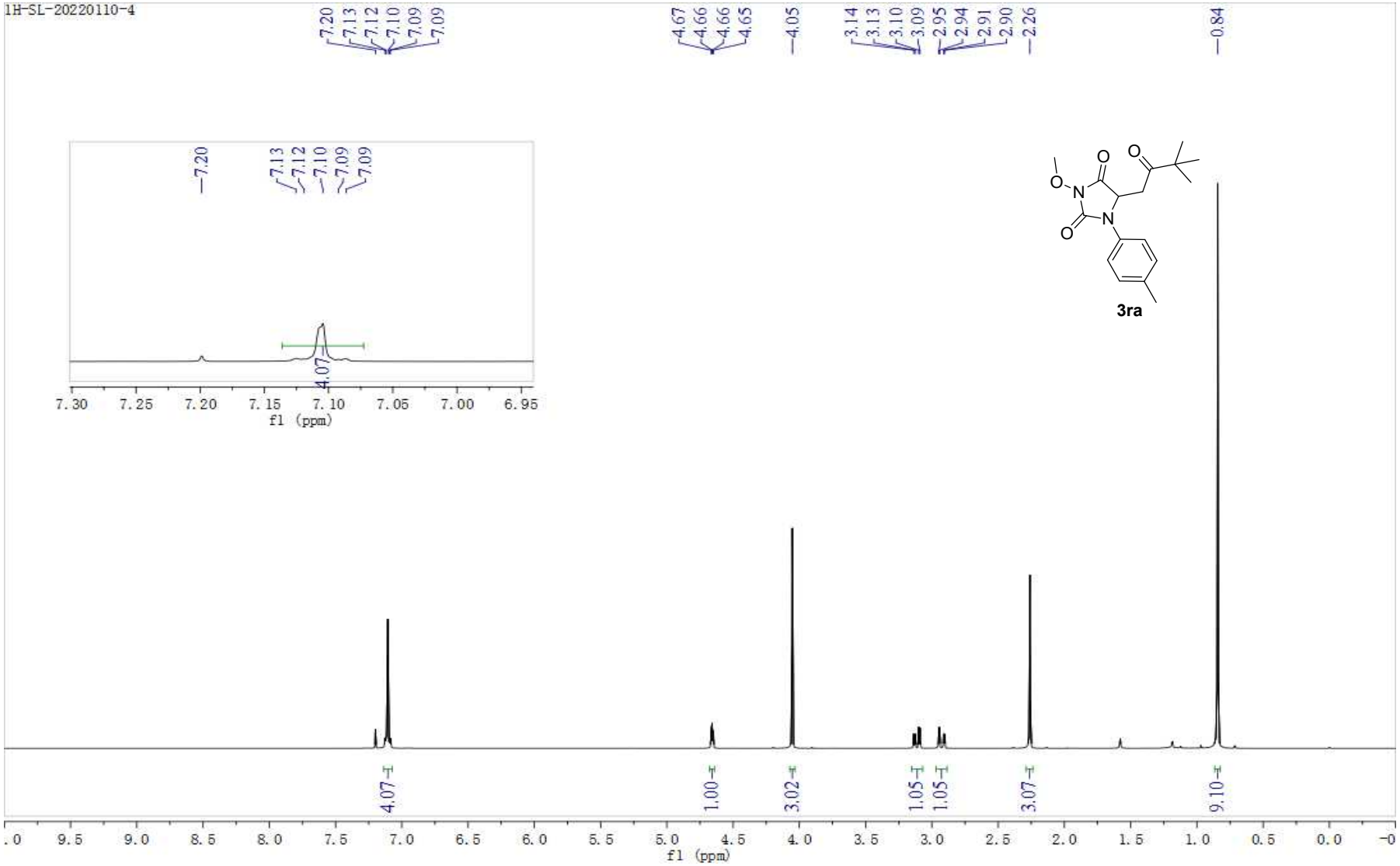

1H-WLG-20211220-XL-4
187.47
166.44
151.23
142.51
136.48
134.75
132.62
131.84
130.12
128.25
123.18
64.98
54.97
36.80
20.94
O
N
O
O
N
O
S
3oa
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

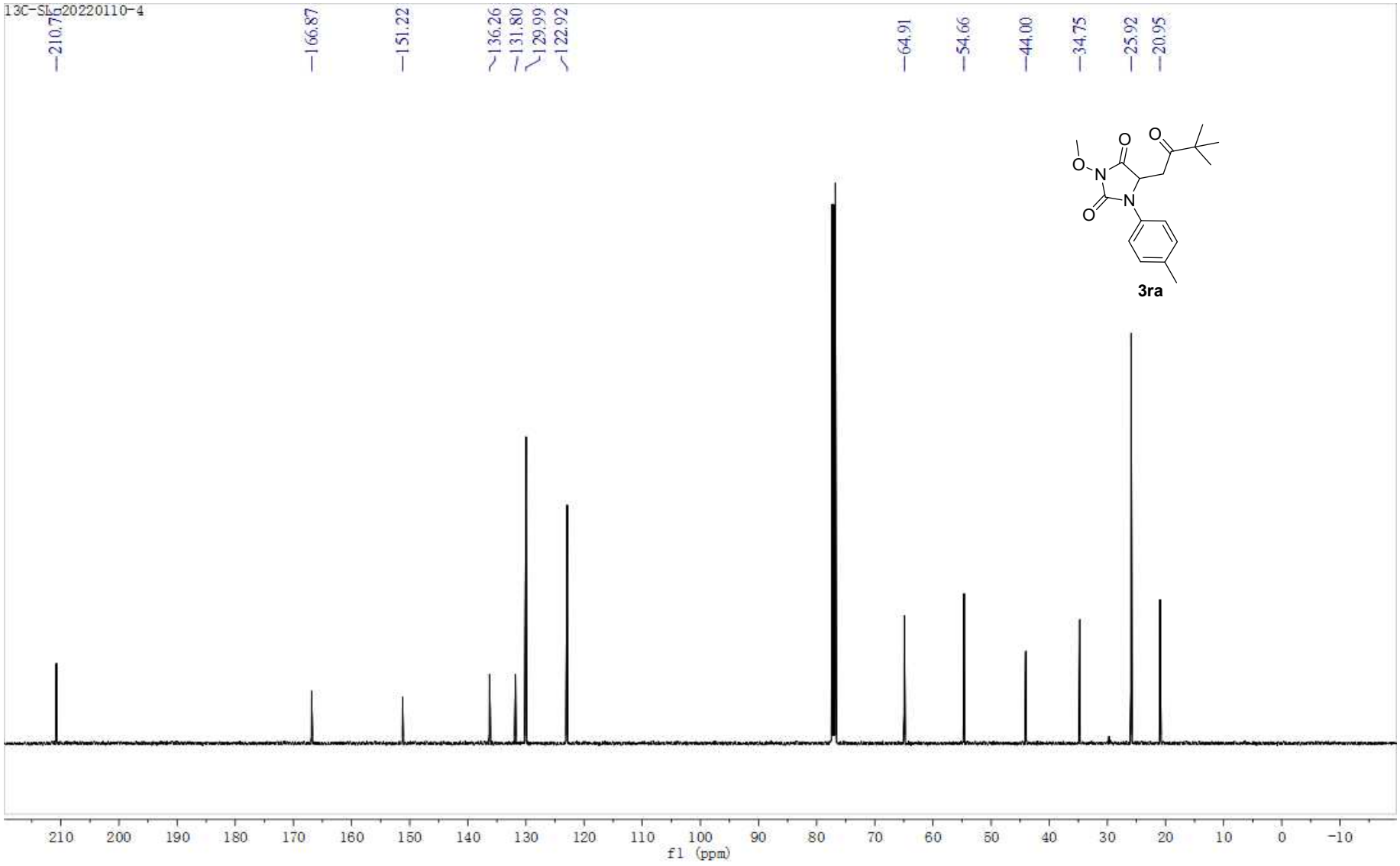

1H-SL-20211222-4
8.32
8.30
7.89
7.87
7.77
7.75
7.75
7.47
7.47
7.46
7.46
7.44
7.32
7.30
7.28
7.18
7.18
7.16
7.09
7.07
4.85
4.84
4.84
4.11
3.63
3.62
3.59
3.58
3.57
3.57
3.54
3.53
2.23
3pa
f1 (ppm)
0.99
0.99
0.99
3.08
1.05
2.03
2.03
1.00
3.05
1.05
0.98
3.02

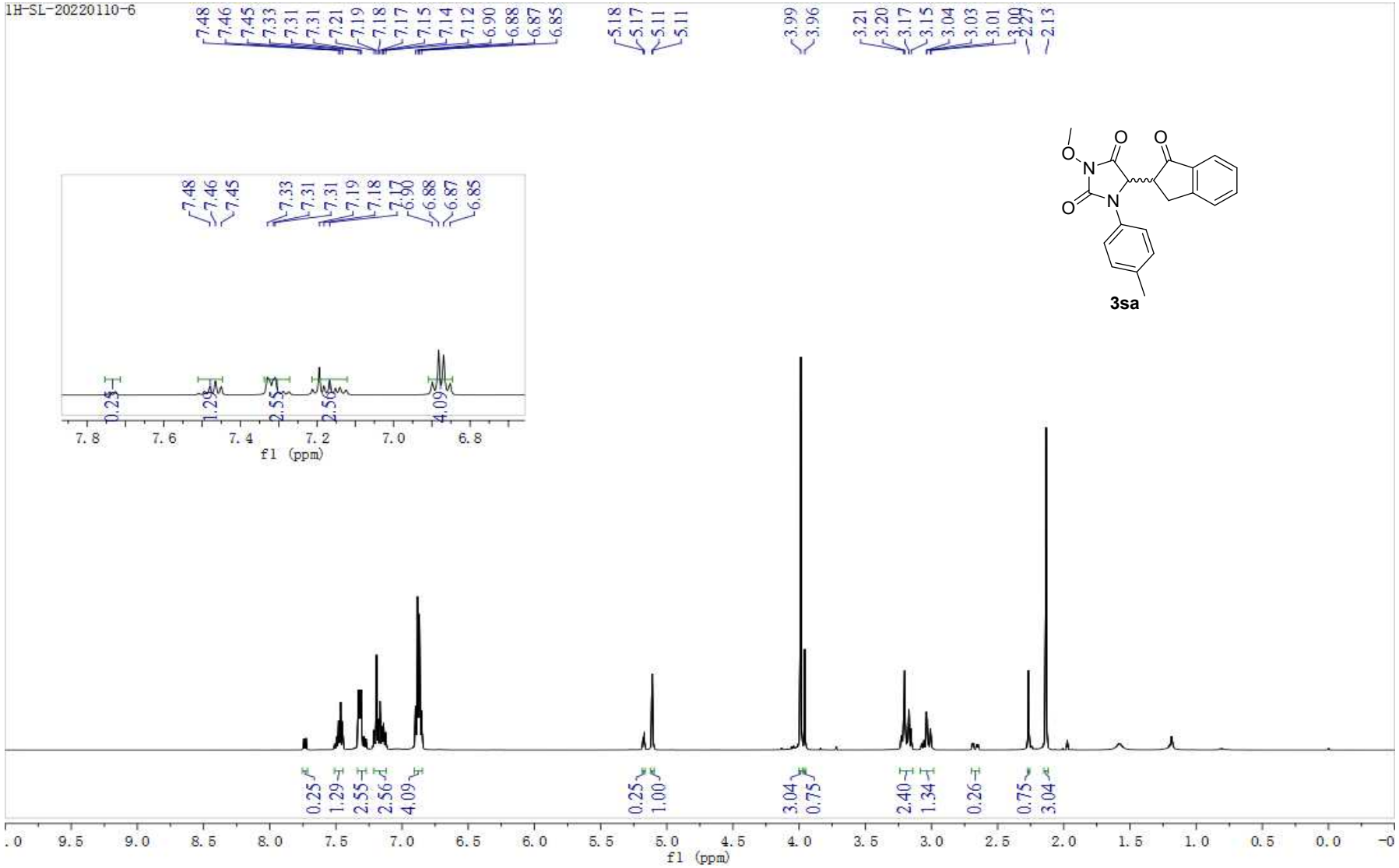

13C-SL-20211220-4
198.67
166.79
151.39
136.63
134.11
133.85
133.58
131.90
130.23
129.89
128.46
128.35
127.96
126.75
125.47
124.16
123.42
65.02
55.40
39.56
20.96
3pa
f1 (ppm)

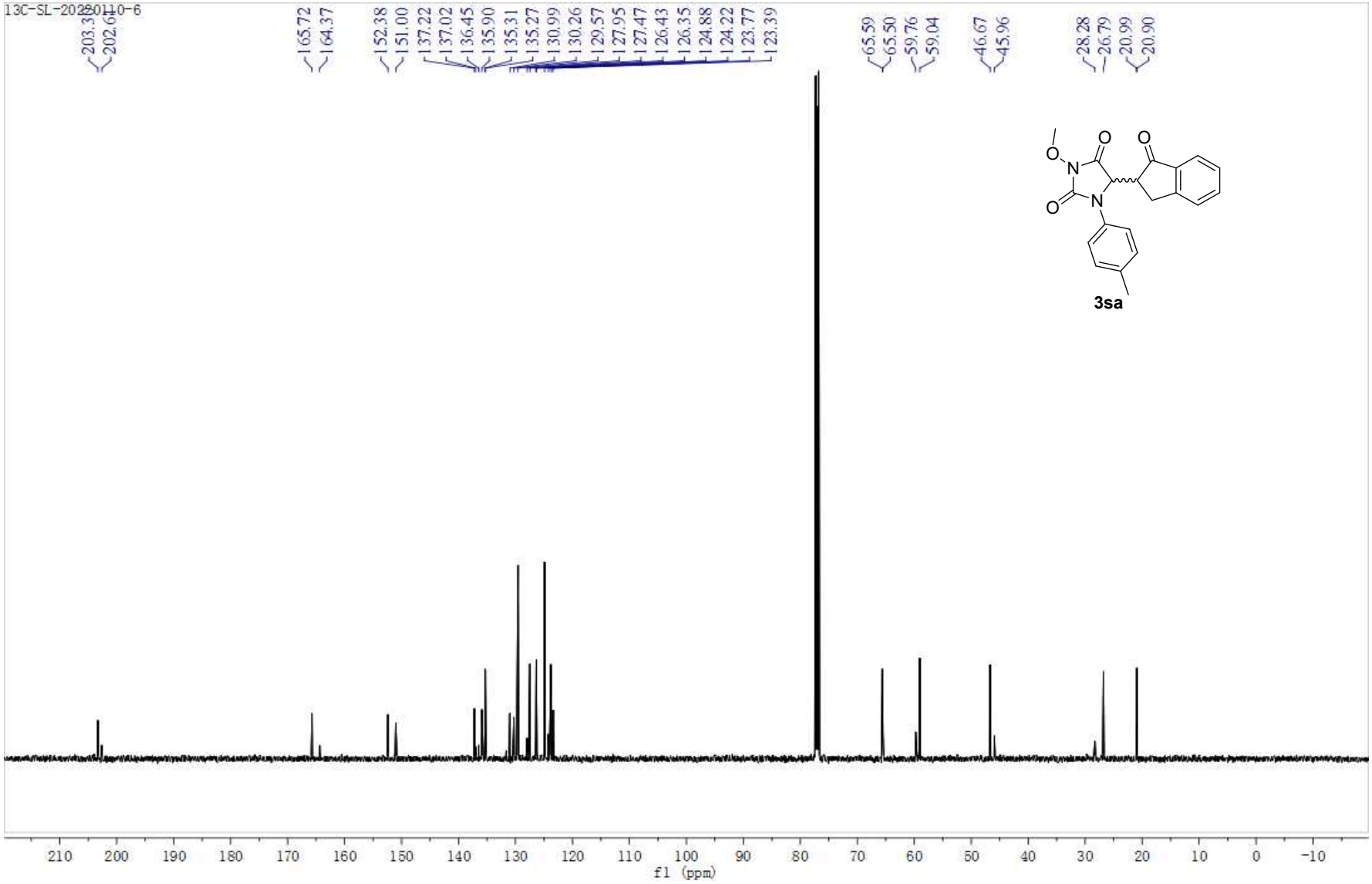

1H-WLG-20211223-XL-4NO2+4Me
8.14
7.78
7.76
7.75
7.75
7.74
7.74
7.51
7.49
7.49
7.46
7.46
7.44
7.18
7.14
7.12
7.05
7.03
4.84
4.83
4.82
4.11
3.70
3.69
3.66
3.65
3.59
3.59
3.56
3.55
2.17
1.01
4.07
1.04
1.01
2.03
2.00
1.00
3.00
1.08
0.98
3.02
f1 (ppm)
3qa

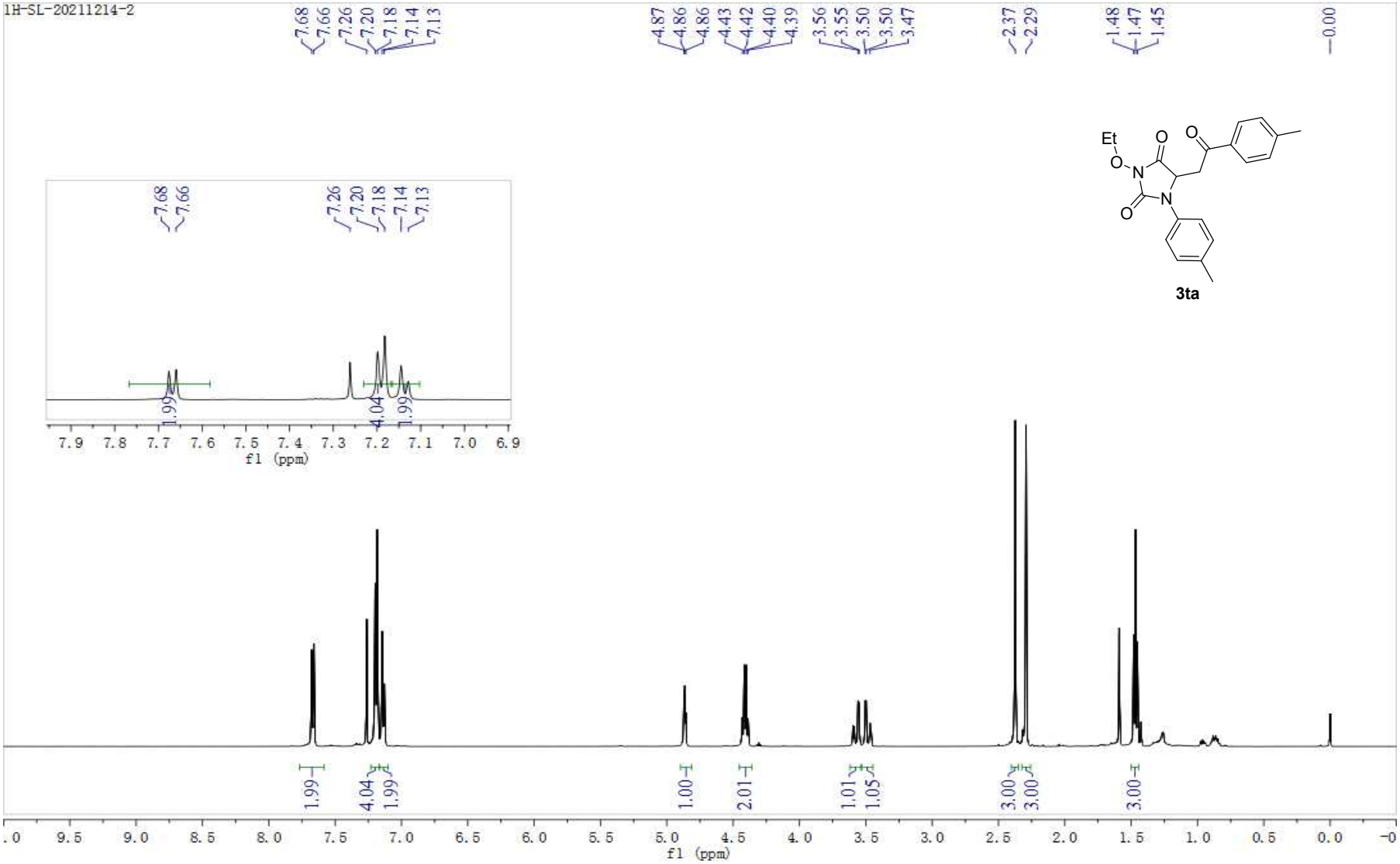

13C-WLG-20211223-3L-4NO2-4Me
194.88
166.83
151.43
136.50
135.80
133.03
132.25
131.91
130.16
129.99
129.56
128.94
128.65
127.82
127.03
123.35
123.25
64.99
55.10
36.37
20.91
O
O
N
O
N
O
3qa
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

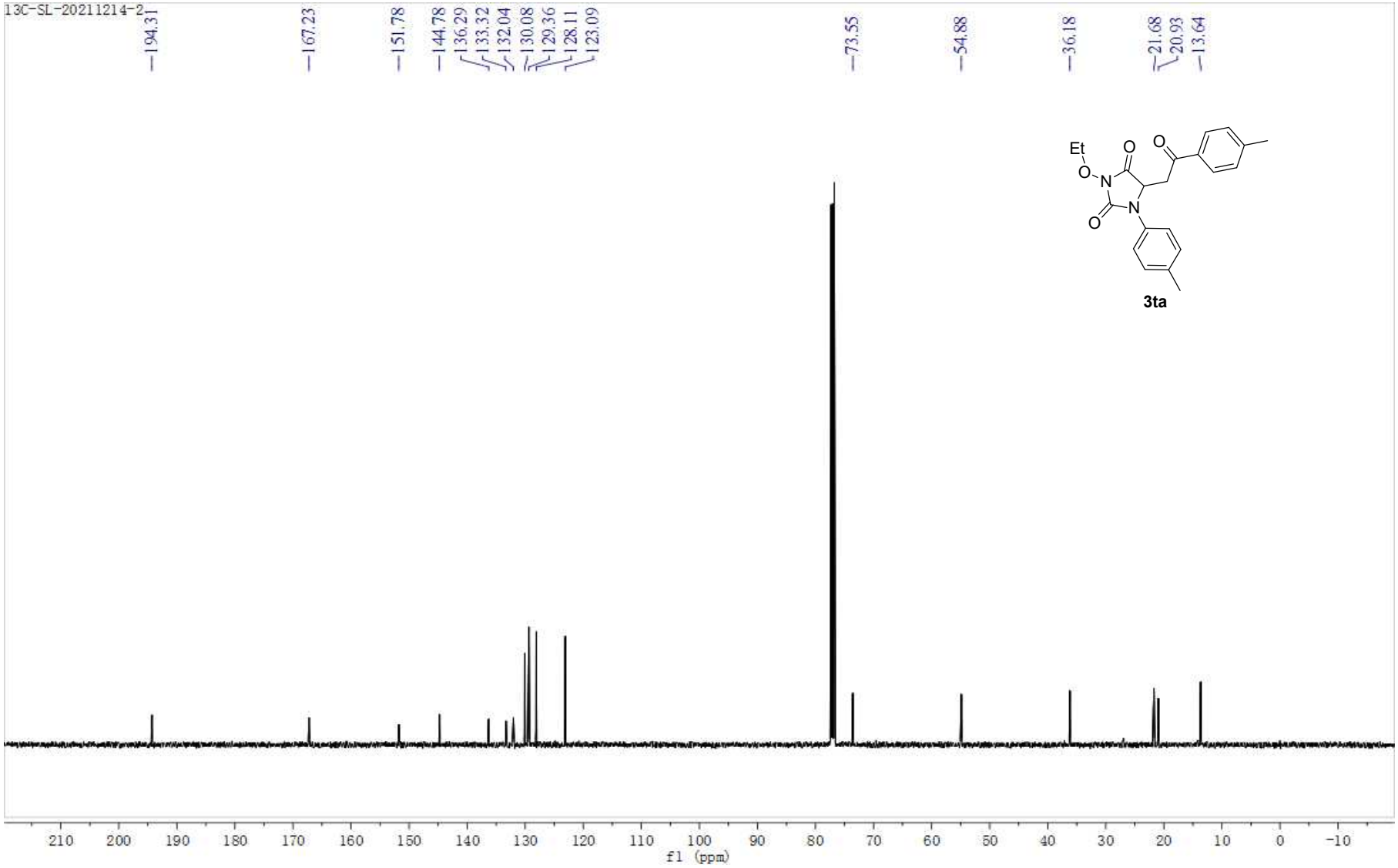

1H-SL-20220110-4
7.20
7.13
7.12
7.10
7.09
7.09
4.67
4.66
4.66
4.65
4.05
3.14
3.13
3.10
3.09
2.95
2.94
2.91
2.90
2.26
0.84
4.07
7.30
7.25
7.20
7.15
7.10
7.05
7.00
6.95
f1 (ppm)
3ra
4.07
1.00
3.02
1.05
1.05
3.07
9.10
f1 (ppm)

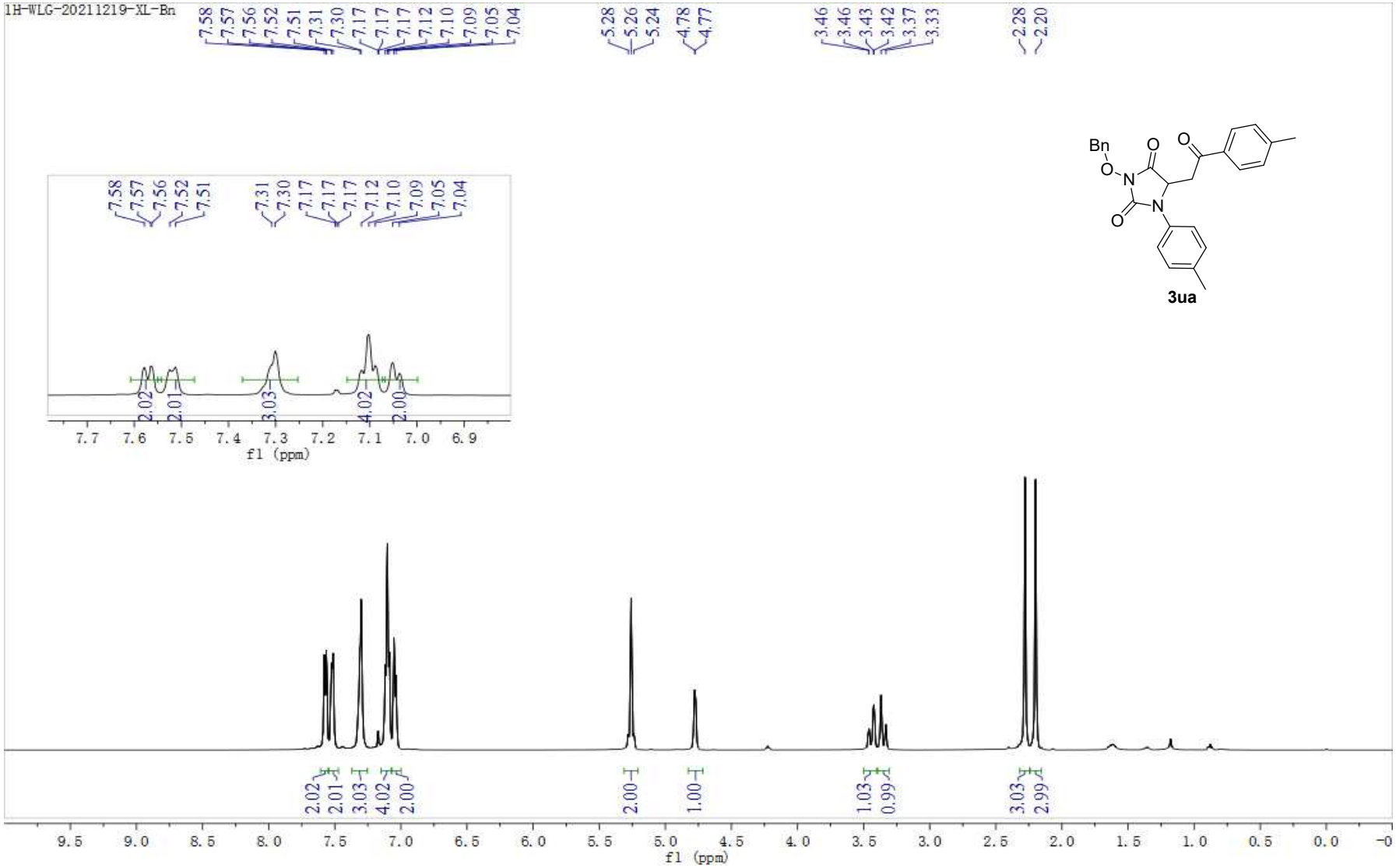

13C-SLq20220110-4
210.75
166.87
151.22
136.26
131.80
129.99
122.92
64.91
54.66
44.00
34.75
25.92
20.95
3ra
f1 (ppm)

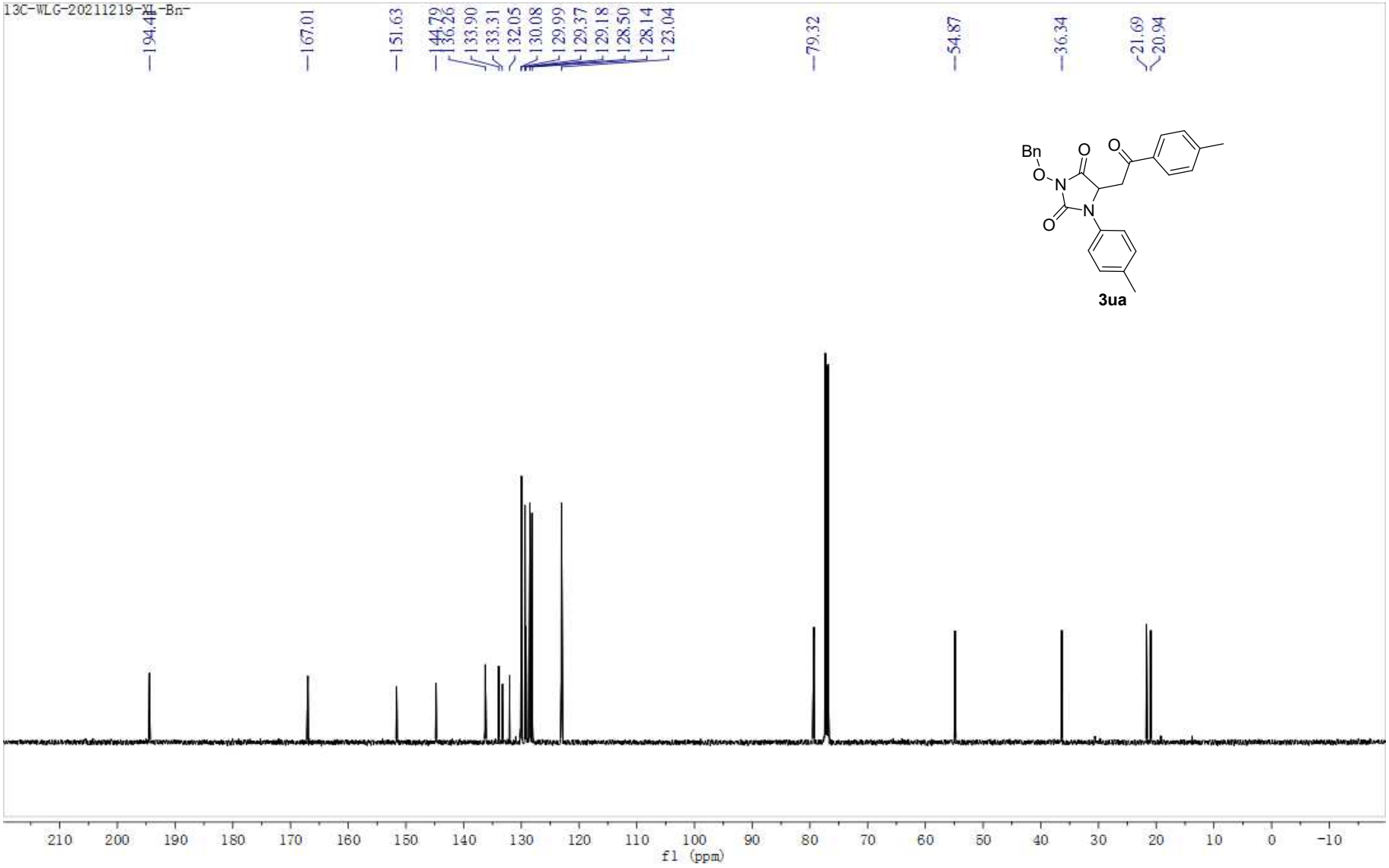

1H-SL-20220110-6
7.48
7.46
7.45
7.33
7.31
7.31
7.21
7.19
7.18
7.17
7.15
7.14
7.12
6.90
6.88
6.87
6.85
5.18
5.17
5.11
5.11
3.99
3.96
3.21
3.20
3.17
3.15
3.04
3.03
3.01
2.27
2.13
0.25
1.29
2.55
2.56
4.09
0.25
1.00
3.04
0.75
2.40
1.34
0.26
0.75
3.04
f1 (ppm)
3sa

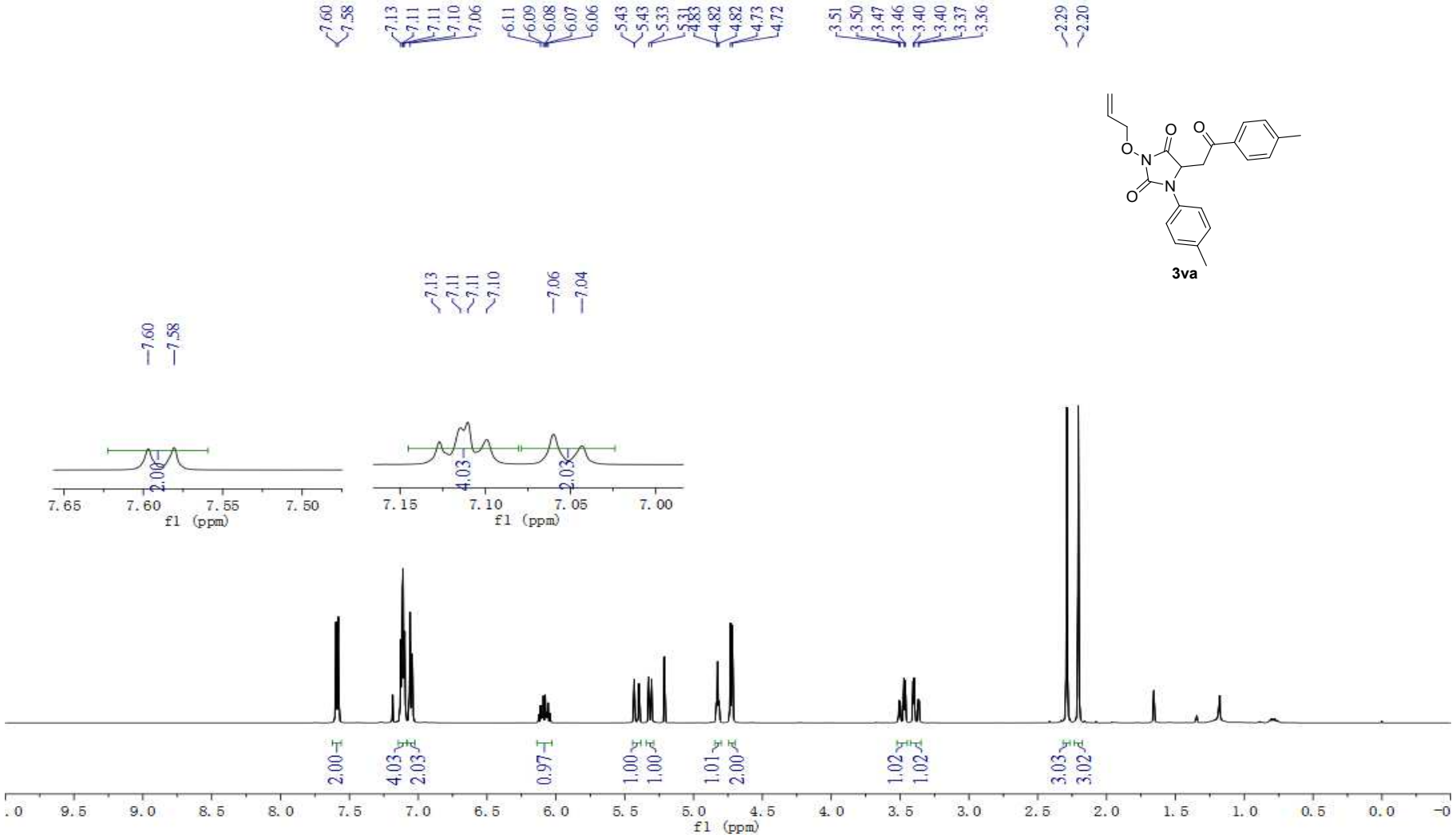

13C-SL-20220110-6
203.38
202.68
165.72
164.37
152.38
151.00
137.22
137.02
136.45
135.90
135.31
135.27
130.99
130.26
129.57
127.95
127.47
126.43
126.35
124.88
124.22
123.77
123.39
65.59
65.50
59.76
59.04
46.67
45.96
28.28
26.79
20.99
20.90
O
N
O
O
N
O
3sa
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

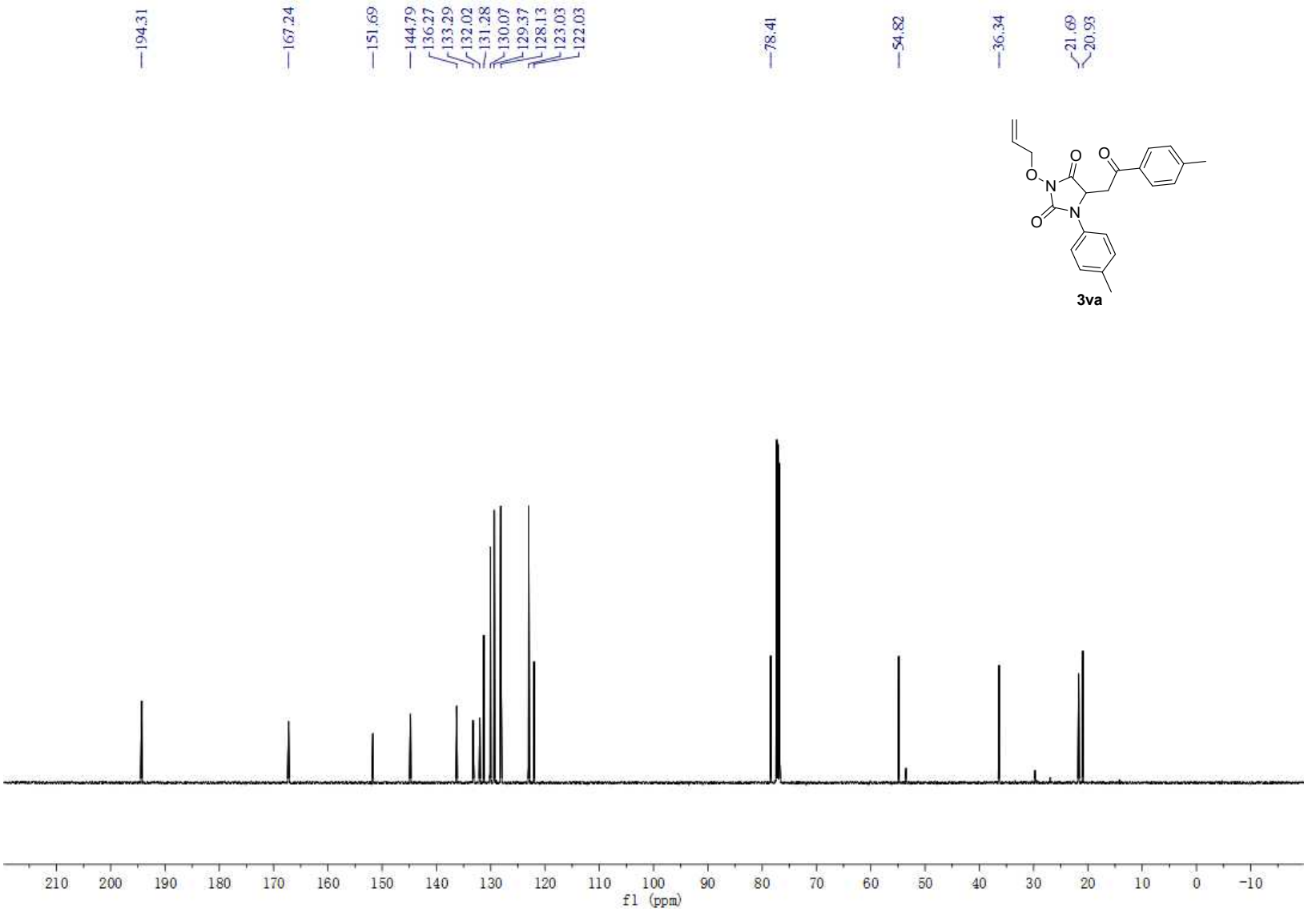

1H-SL-20211214-2
7.68
7.66
7.26
7.20
7.18
7.14
7.13
4.87
4.86
4.86
4.43
4.42
4.40
4.39
3.56
3.55
3.50
3.50
3.47
2.37
2.29
1.48
1.47
1.45
0.00
Et
O
N
O
O
N
O
3ta
1.99
4.04
1.99
f1 (ppm)
1.99
4.04
1.99
1.00
2.01
1.01
1.05
3.00
3.00
3.00
f1 (ppm)

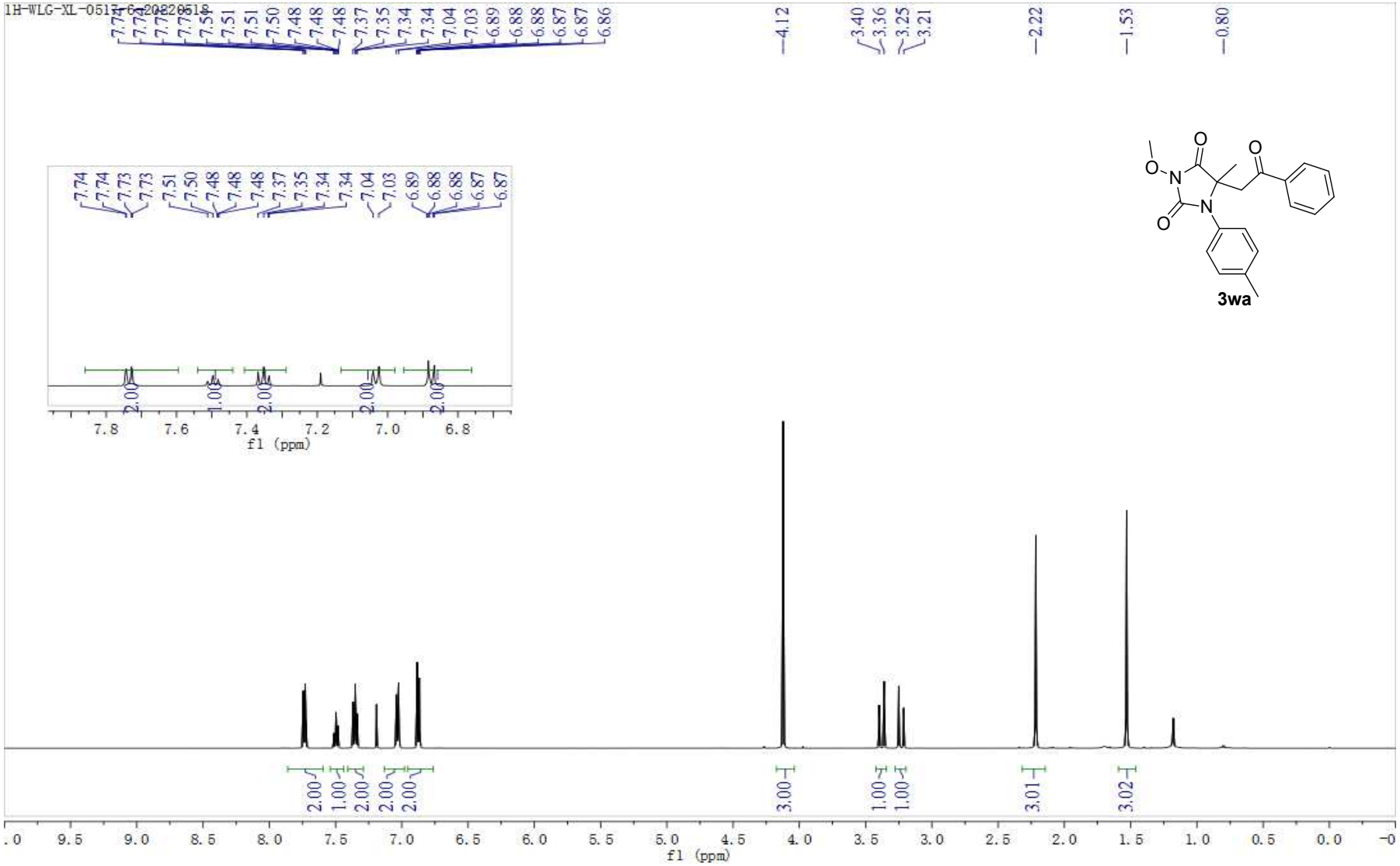

13C-SL-20211214-2
194.31
167.23
151.78
144.78
136.29
133.32
132.04
130.08
129.36
128.11
123.09
73.55
54.88
36.18
21.68
20.93
13.64
Et
O
N
O
O
N
O
3ta
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

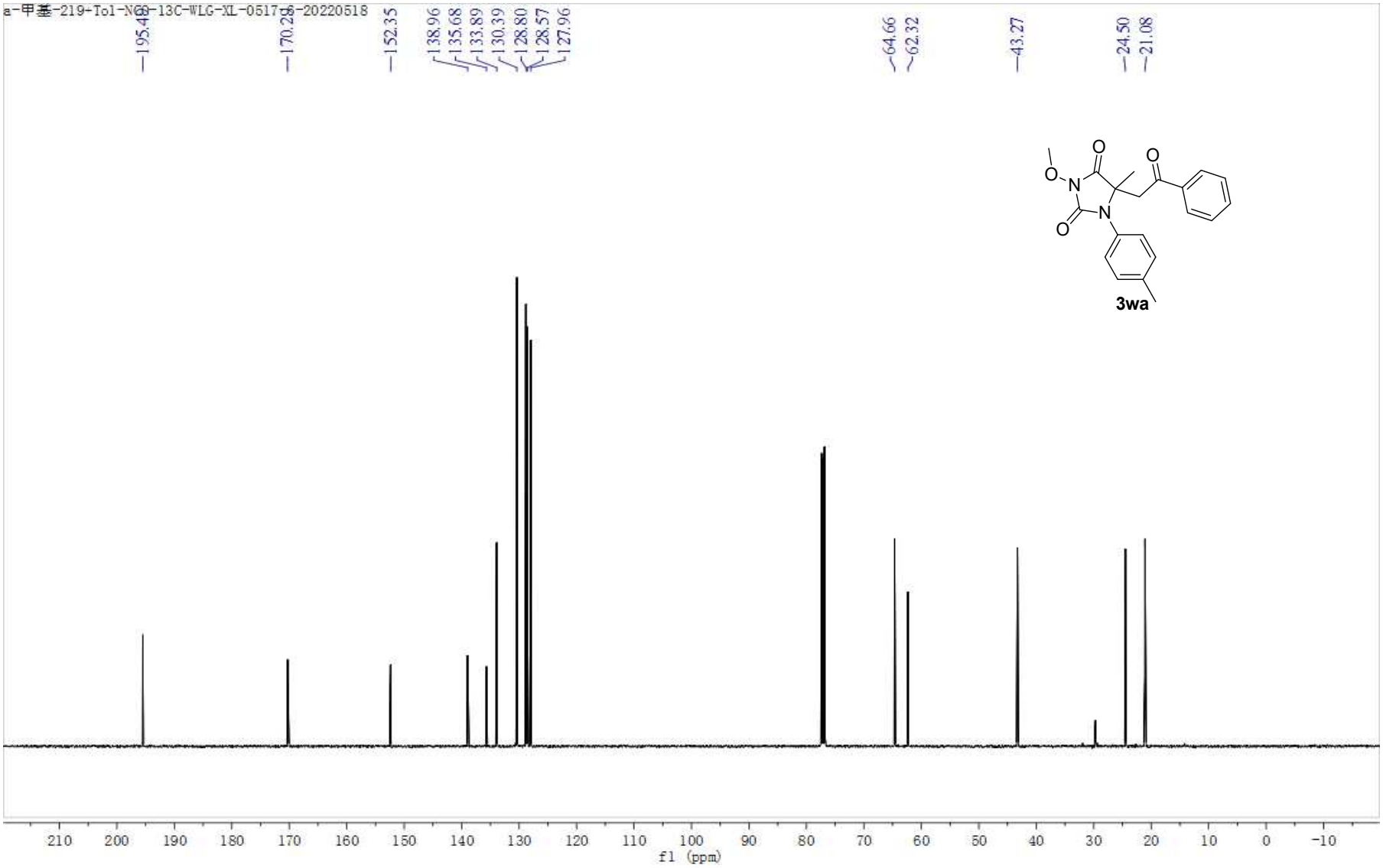

1H-WLG-20211219-XL-Bn
7.58 7.57 7.56 7.52 7.51 7.31 7.30 7.17 7.17 7.17 7.12 7.10 7.09 7.05 7.04
5.28 5.26 5.24
4.78 4.77
3.46 3.46 3.43 3.42 3.37 3.33
2.28 2.20
Bn
O
N
O
O
N
O
3ua
2.02 2.01 3.03 4.02 2.00
f1 (ppm)
2.00 1.00 1.03 0.99 3.03 2.99
f1 (ppm)

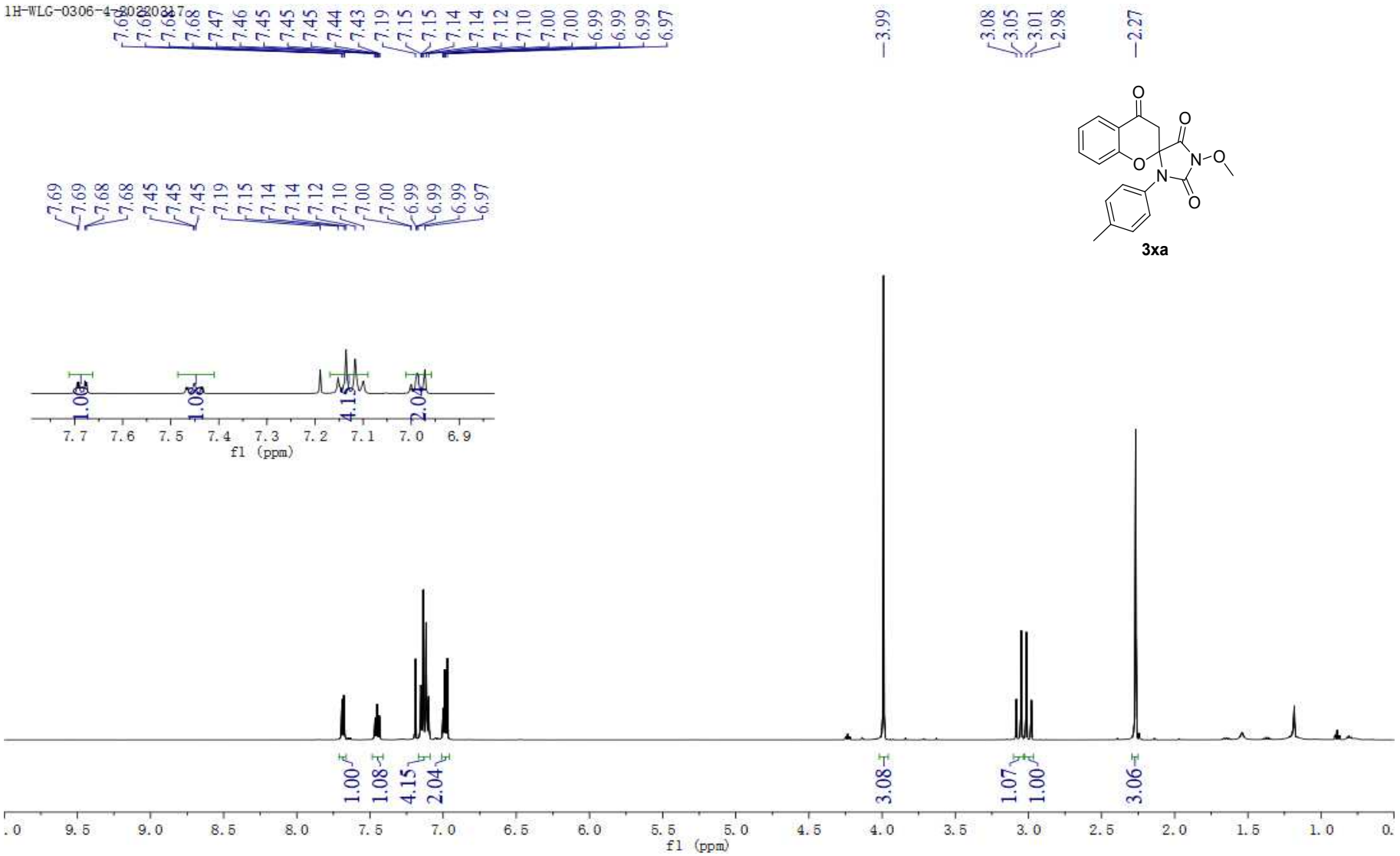

13C-WLG-20211219-XI-Bn-
194.44
167.01
151.63
144.79
136.26
133.90
133.31
132.05
130.08
129.99
129.37
129.18
128.50
128.14
123.04
79.32
54.87
36.34
21.69
20.94
Bn
O
N
O
O
N
O
O
3ua
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

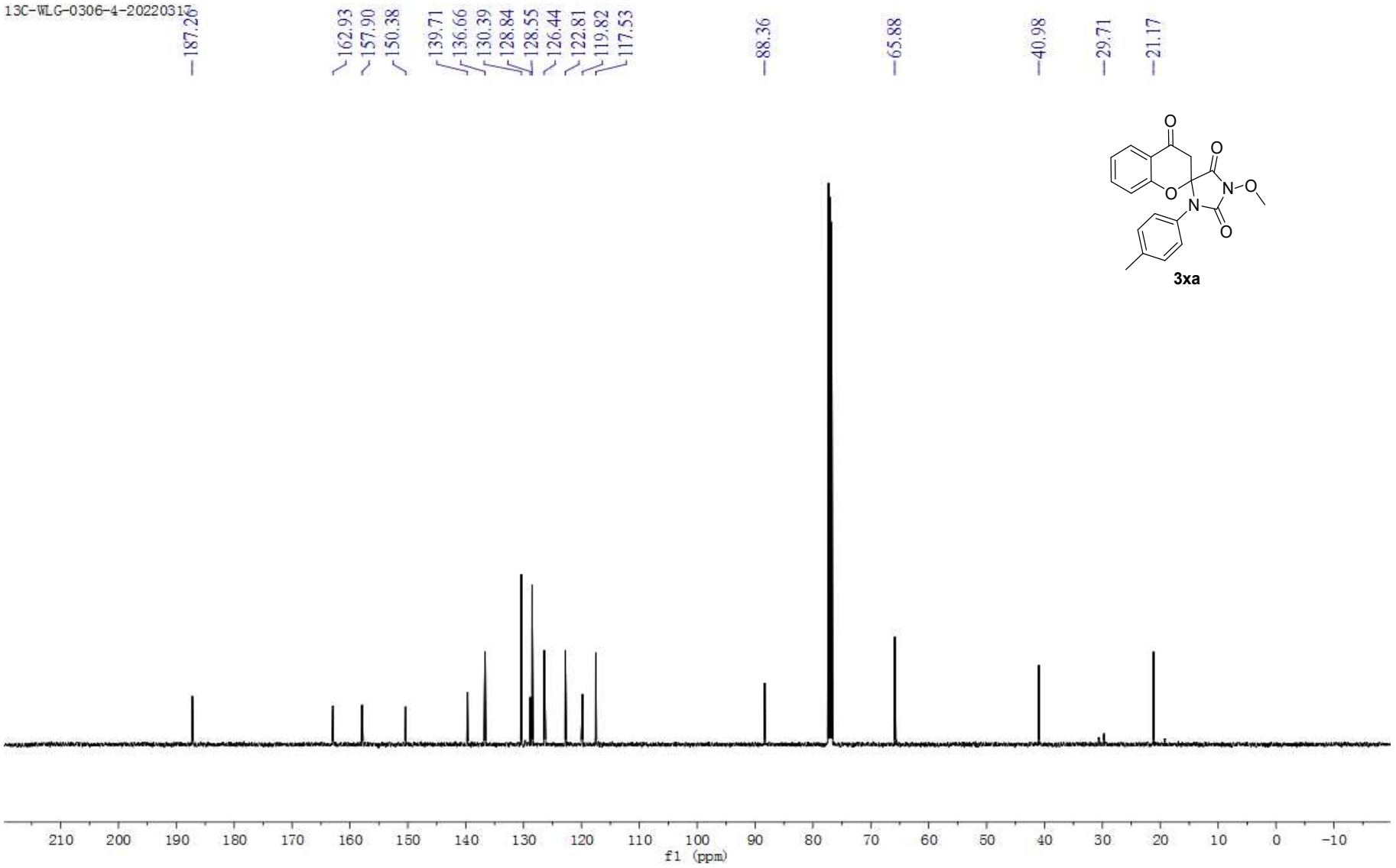

7.60
7.58
7.13
7.11
7.11
7.10
7.06
6.11
6.09
6.08
6.07
6.06
5.43
5.43
5.33
5.31
4.83
4.82
4.82
4.73
4.72
3.51
3.50
3.47
3.46
3.40
3.40
3.37
3.36
2.29
2.20
3va
2.00
4.03
2.03
0.97
1.00
1.00
1.01
2.00
1.02
1.02
3.03
3.02
f1 (ppm)

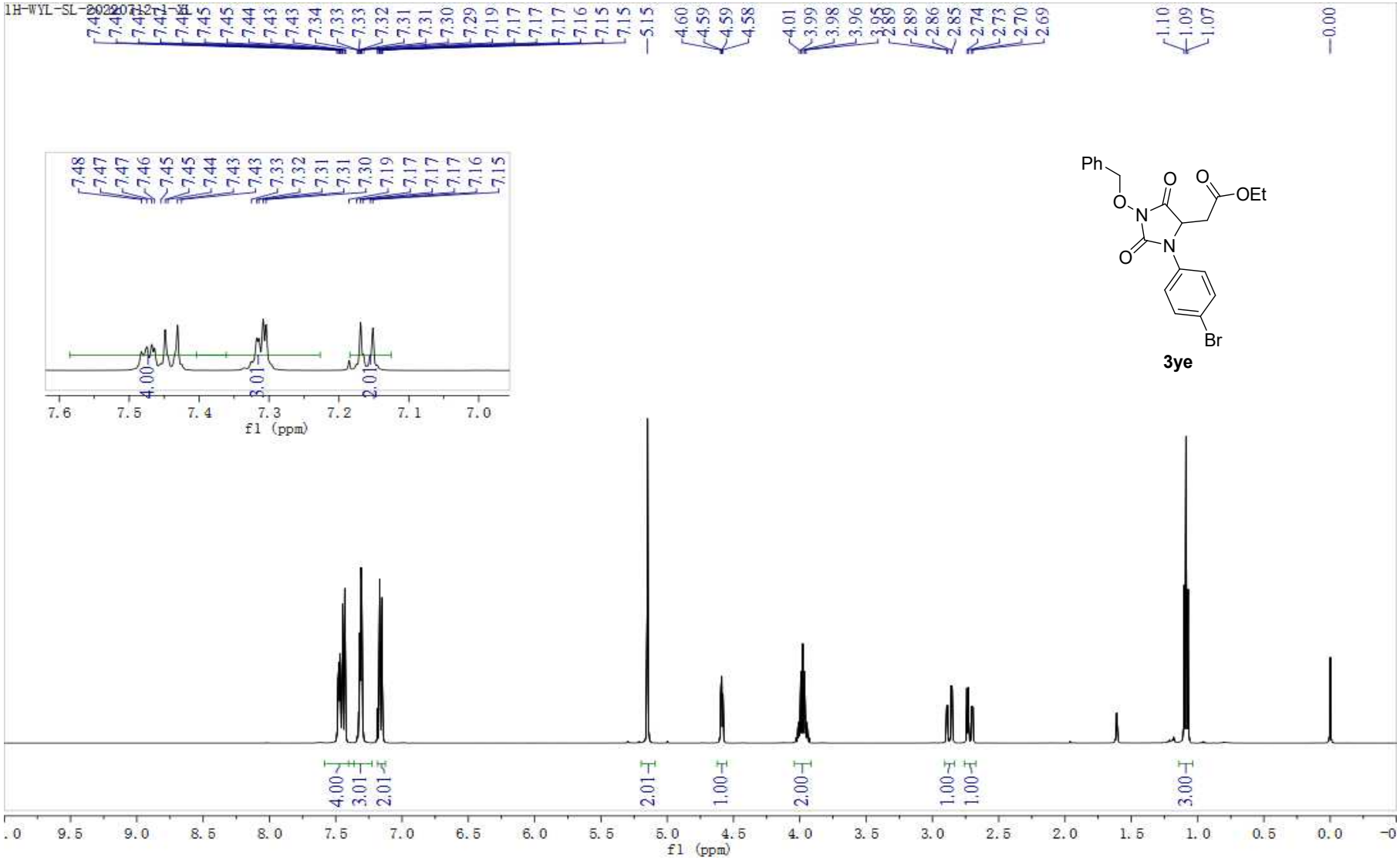

194.31
167.24
151.69
144.79
136.27
133.29
132.02
131.28
130.07
129.37
128.13
123.03
122.03
78.41
54.82
36.34
21.69
20.93
O
O
O
N
N
O
O
3va
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

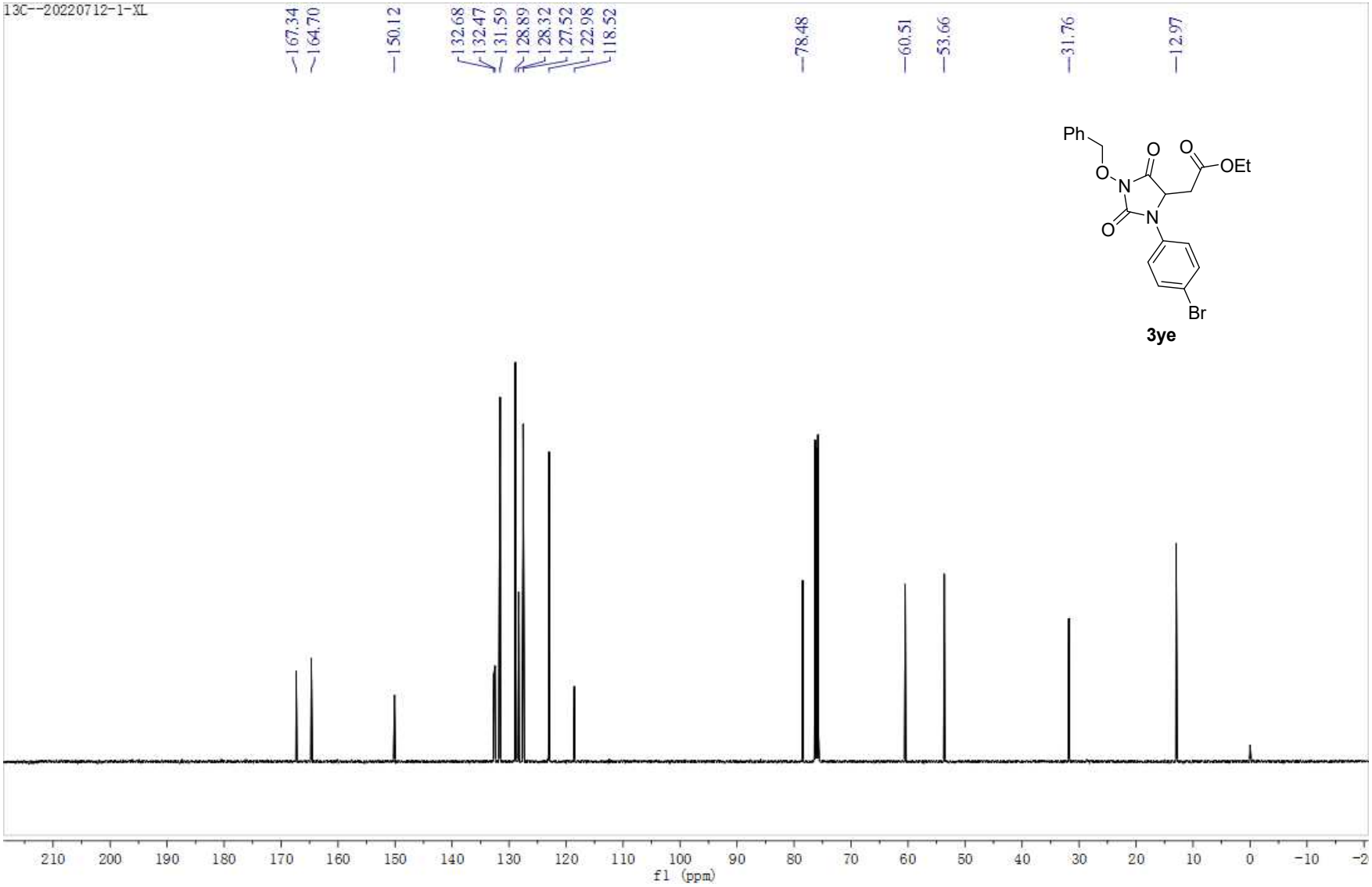

1H-WLG-XL-0517-6-20220518
7.74 7.74 7.73 7.73 7.51 7.50 7.48 7.48 7.48 7.37 7.35 7.34 7.34 7.04 7.03 6.89 6.88 6.88 6.87 6.87 6.86
4.12
3.40 3.36 3.25 3.21
2.22
1.53
0.80
3wa
f1 (ppm)
2.00 1.00 2.00 2.00 2.00 3.00 1.00 1.00 3.01 3.02

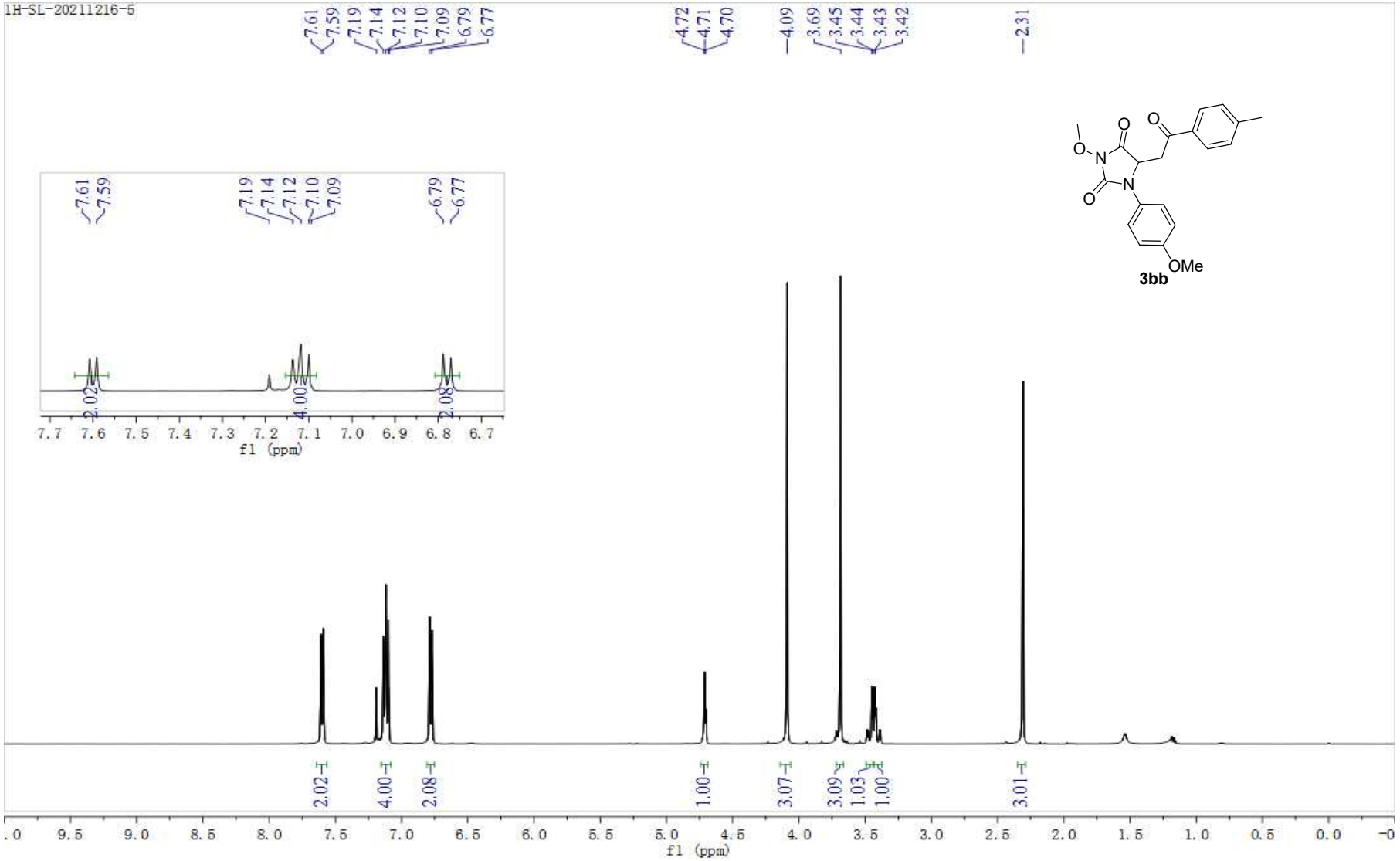

a-甲基-219-Tol-NCG-13C-WLG-XL-0517-8-20220518
195.49
170.28
152.35
138.96
135.68
133.89
130.39
128.80
128.57
127.96
64.66
62.32
43.27
24.50
21.08
3wa
f1 (ppm)

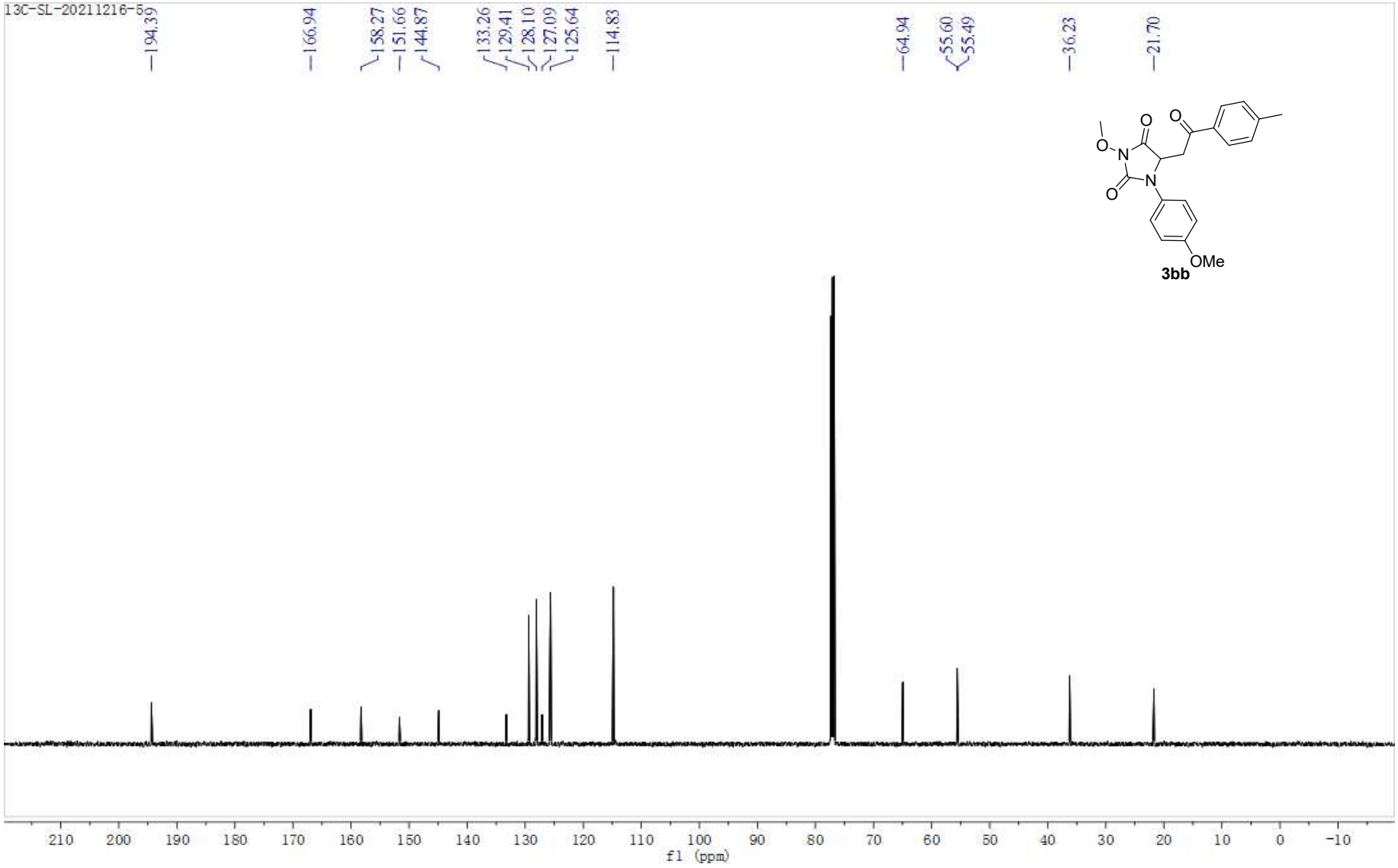

1H-WLG-0306-4-20220317
7.69
7.69
7.68
7.68
7.47
7.46
7.45
7.45
7.45
7.44
7.43
7.19
7.15
7.15
7.14
7.14
7.12
7.10
7.00
7.00
6.99
6.99
6.99
6.97
3.99
3.08
3.05
3.01
2.98
2.27
3xa
1.00
1.08
4.15
2.04
3.08
1.07
1.00
3.06
f1 (ppm)

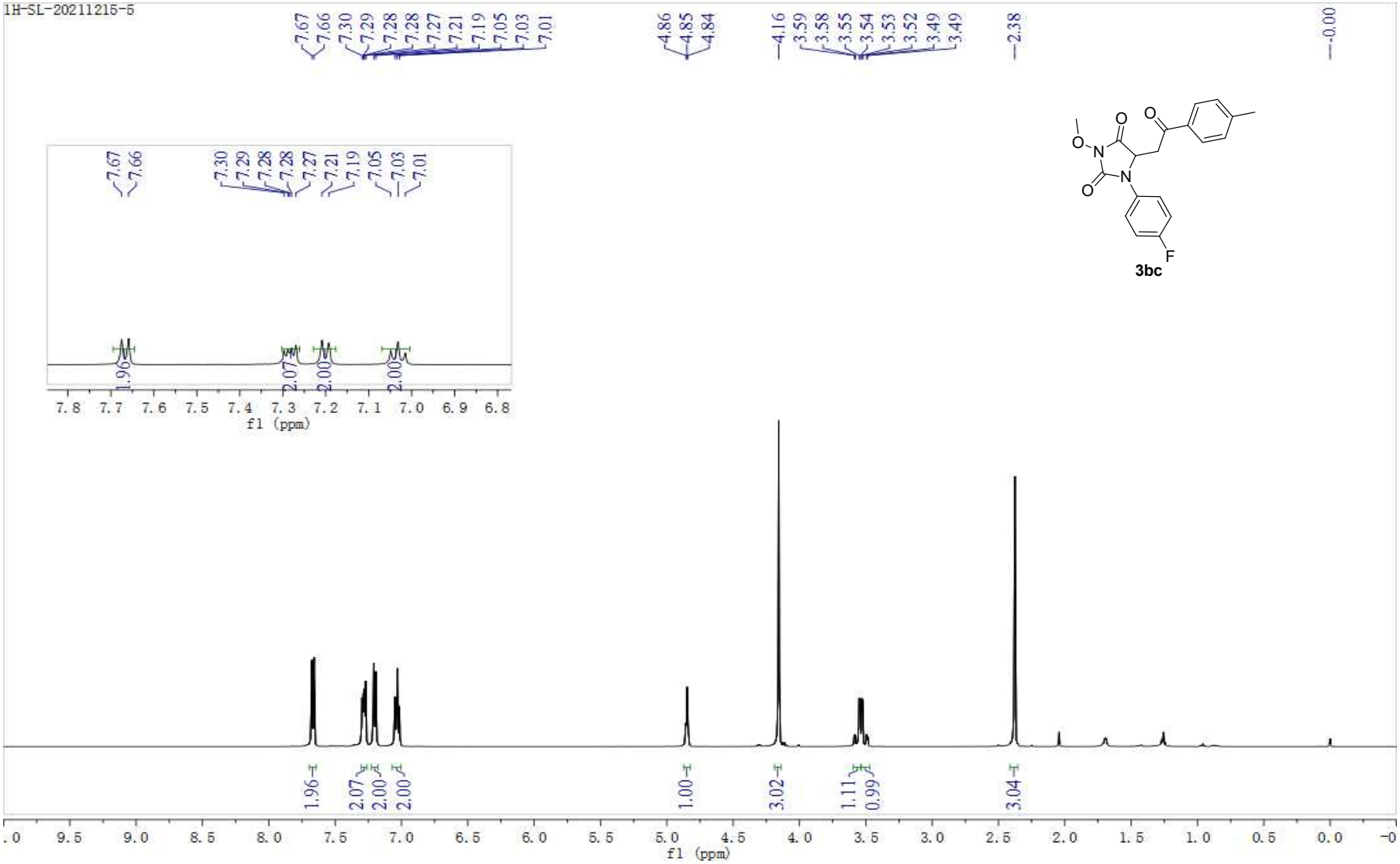

13C-WLG-0306-4-20220317
187.26
162.93
157.90
150.38
139.71
136.66
130.39
128.84
128.55
126.44
122.81
119.82
117.53
88.36
65.88
40.98
29.71
21.17
O
O
O
N
O
N
O
3xa
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

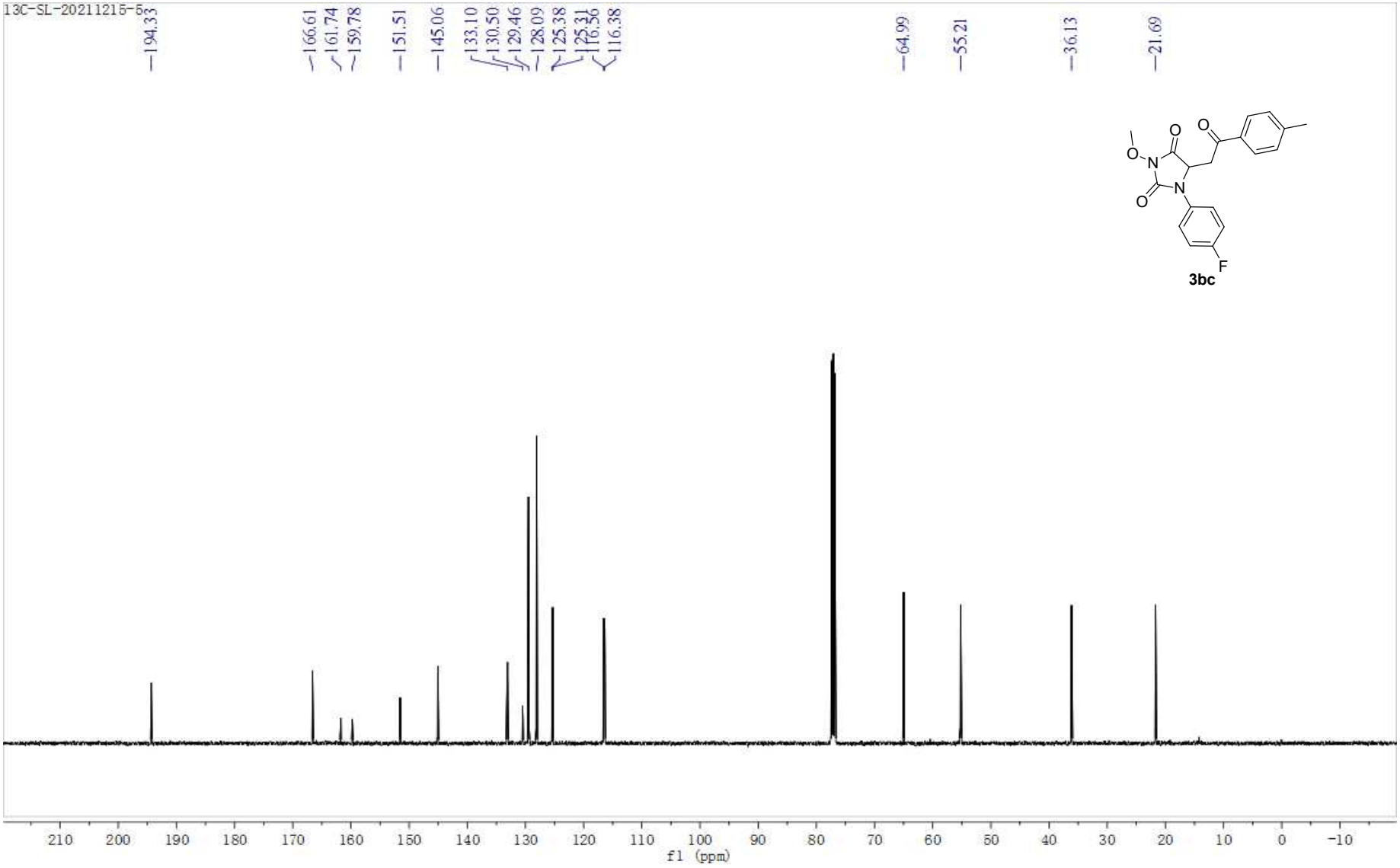

Ph
O
O
OEt
N
N
O
Br
3ye
f1 (ppm)

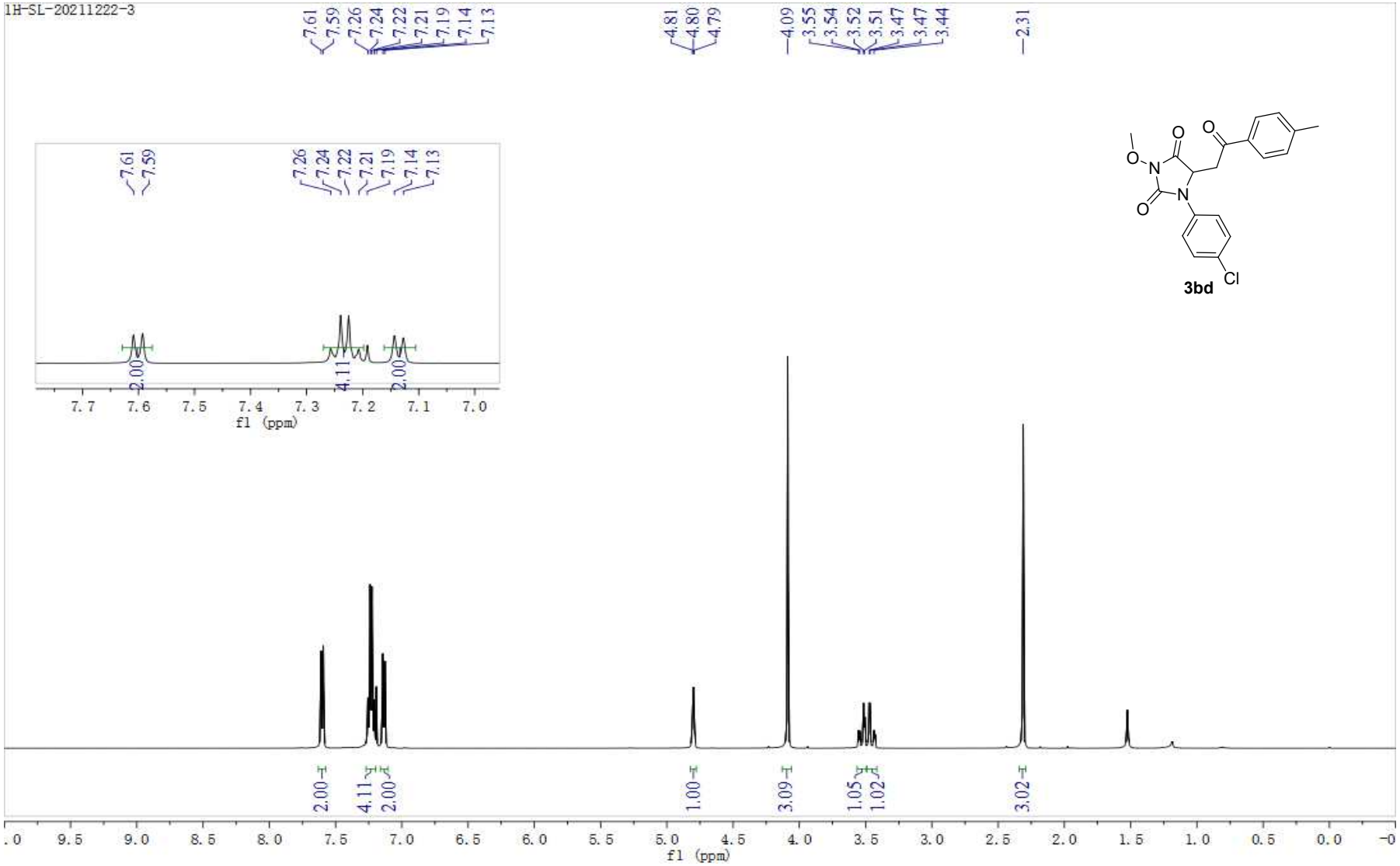

13C--20220712-1-XL
167.34
164.70
150.12
132.68
132.47
131.59
128.89
128.32
127.52
122.98
118.52
78.48
60.51
53.66
31.76
12.97
Ph
O
O
OEt
O
N
O
N
Br
3ye
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-2
f1 (ppm)

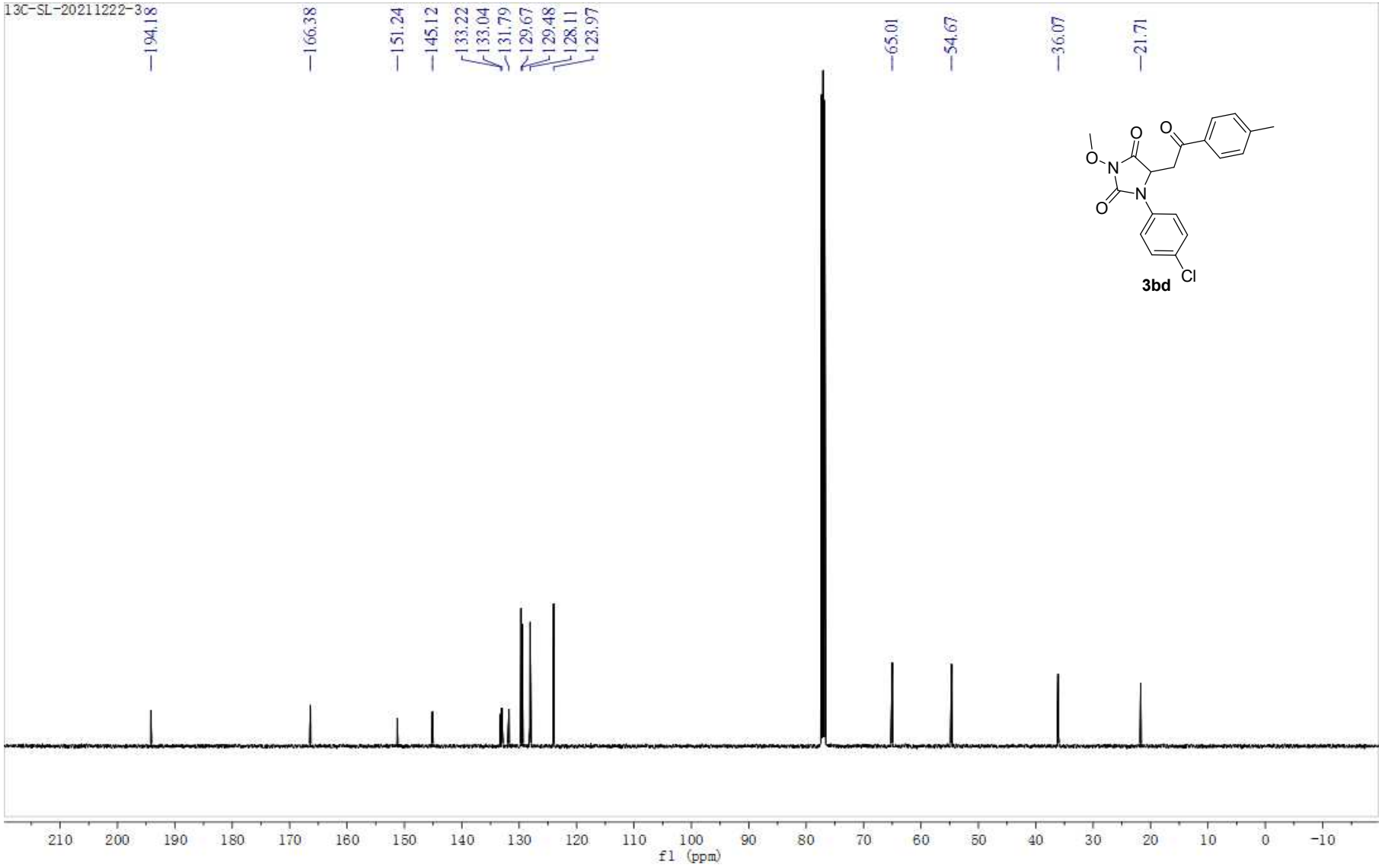

1H-SL-20211216-5
7.61
7.59
7.19
7.14
7.12
7.10
7.09
6.79
6.77
4.72
4.71
4.70
4.09
3.69
3.45
3.44
3.43
3.42
2.31
2.02
4.00
2.08
1.00
3.07
3.09
1.03
1.00
3.01
f1 (ppm)
3bb

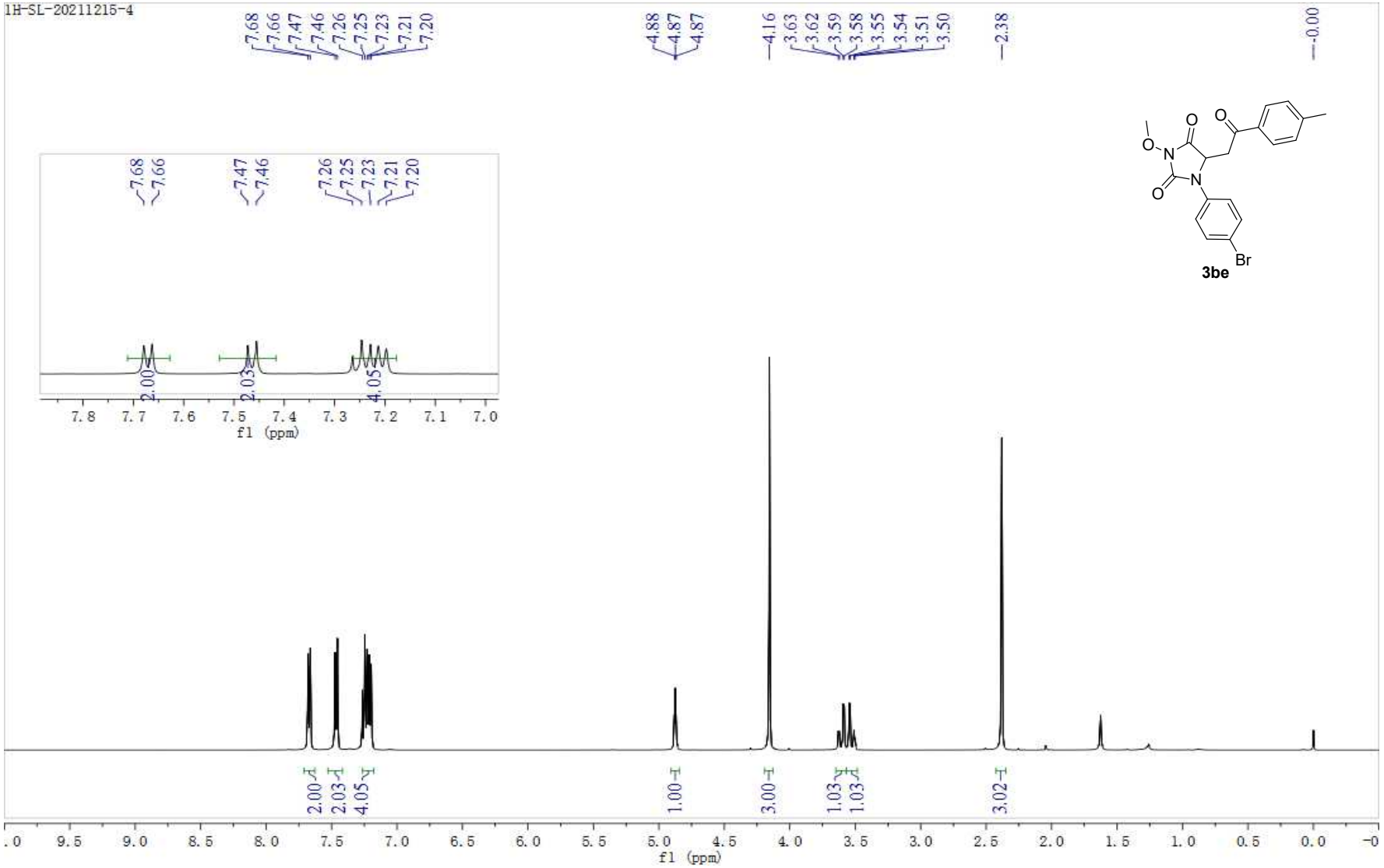

13C-SL-20211216-5
194.39
166.94
158.27
151.66
144.87
133.26
129.41
128.10
127.09
125.64
114.83
64.94
55.60
55.49
36.23
21.70
O
O
N
O
N
O
OMe
3bb
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

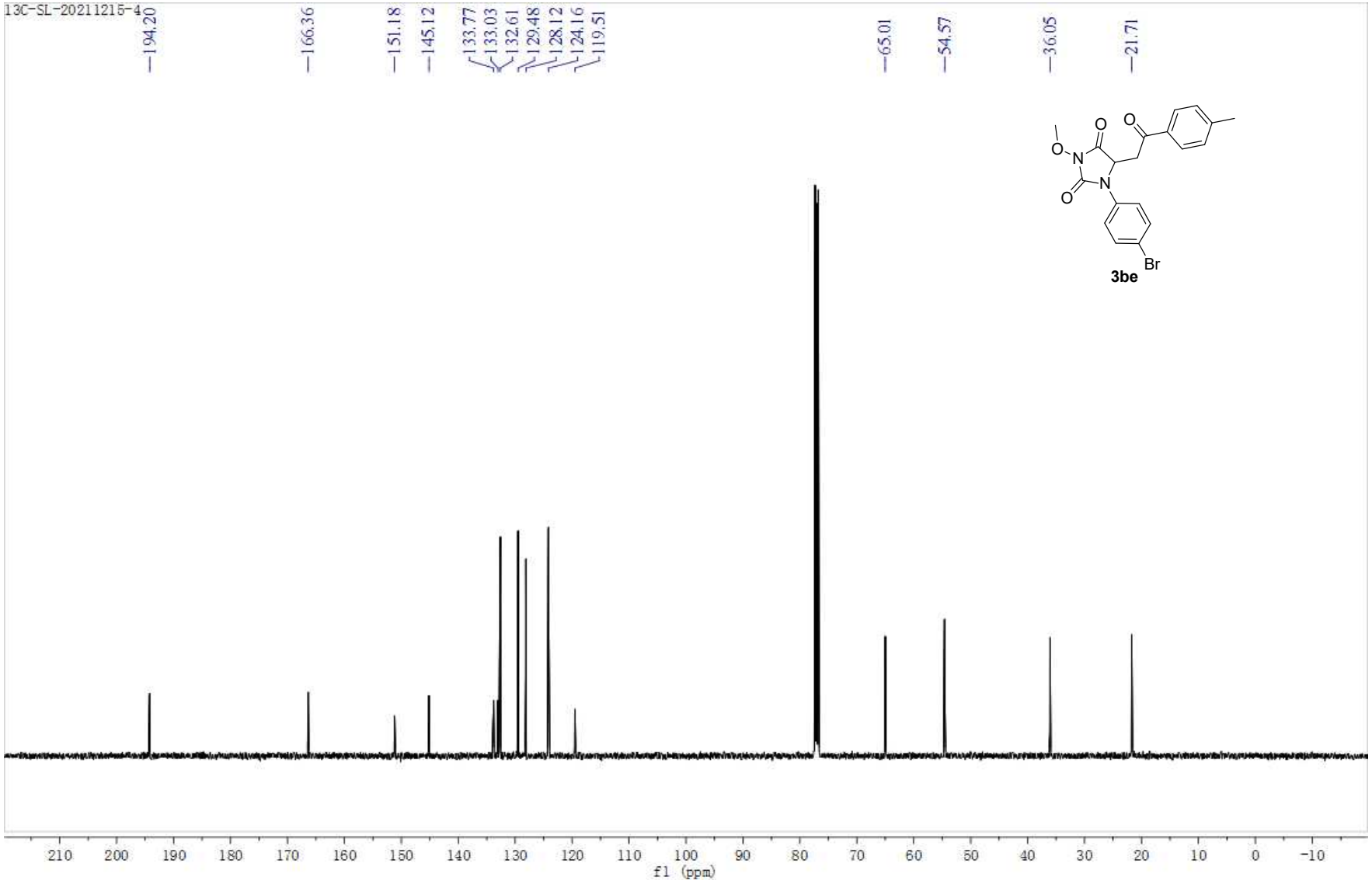

1H-SL-20211215-5
7.67
7.66
7.30
7.29
7.28
7.28
7.27
7.21
7.19
7.05
7.03
7.01
4.86
4.85
4.84
4.16
3.59
3.58
3.55
3.54
3.53
3.52
3.49
3.49
2.38
0.00
1.96
2.07
2.00
2.00
f1 (ppm)
1.00
3.02
1.11
0.99
3.04
3bc

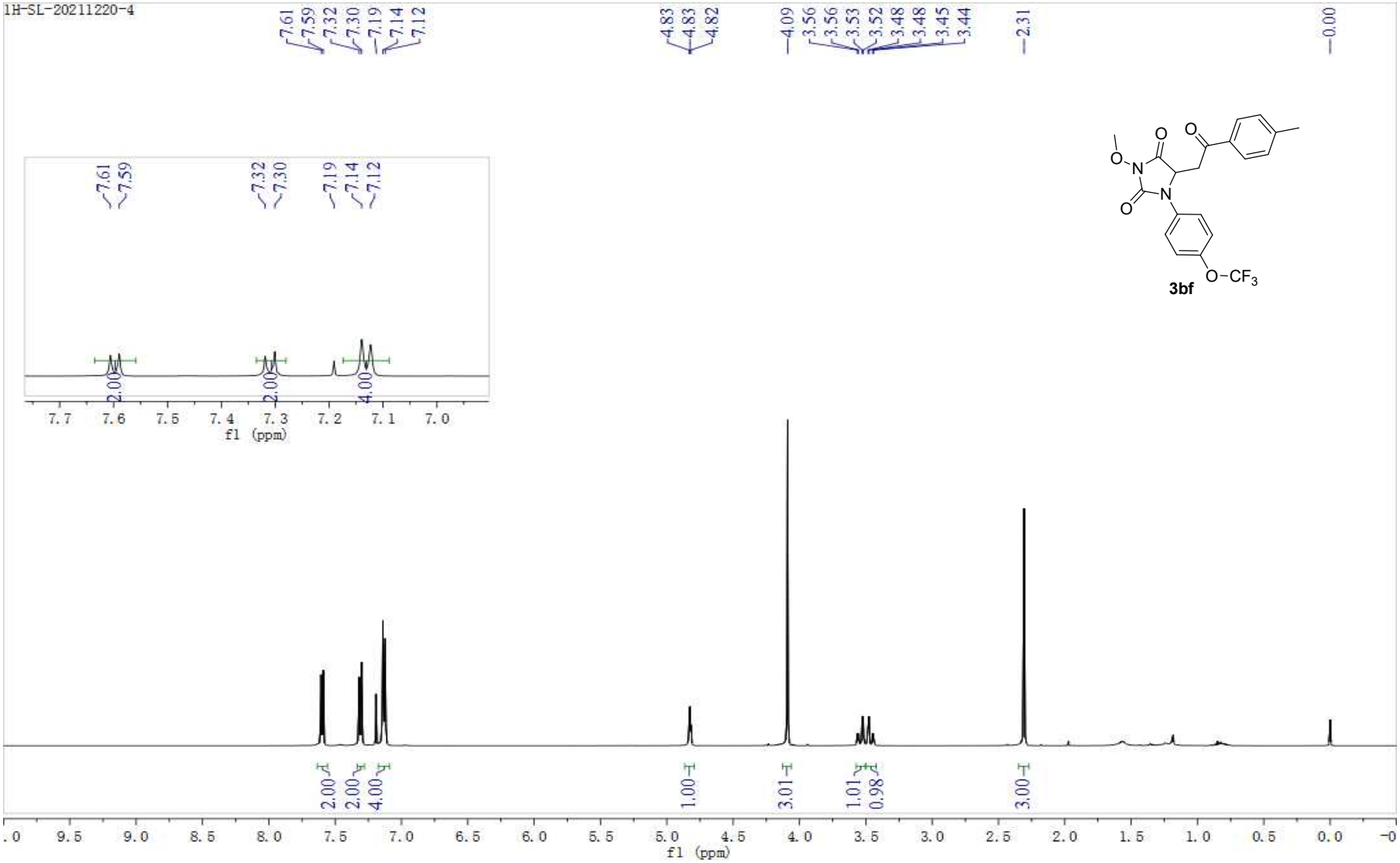

13C-SL-20211215-5
194.33
166.61
161.74
159.78
151.51
145.06
133.10
130.50
129.46
128.09
125.38
125.31
116.56
116.38
64.99
55.21
36.13
21.69
O
O
N
O
N
O
F
3bc
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

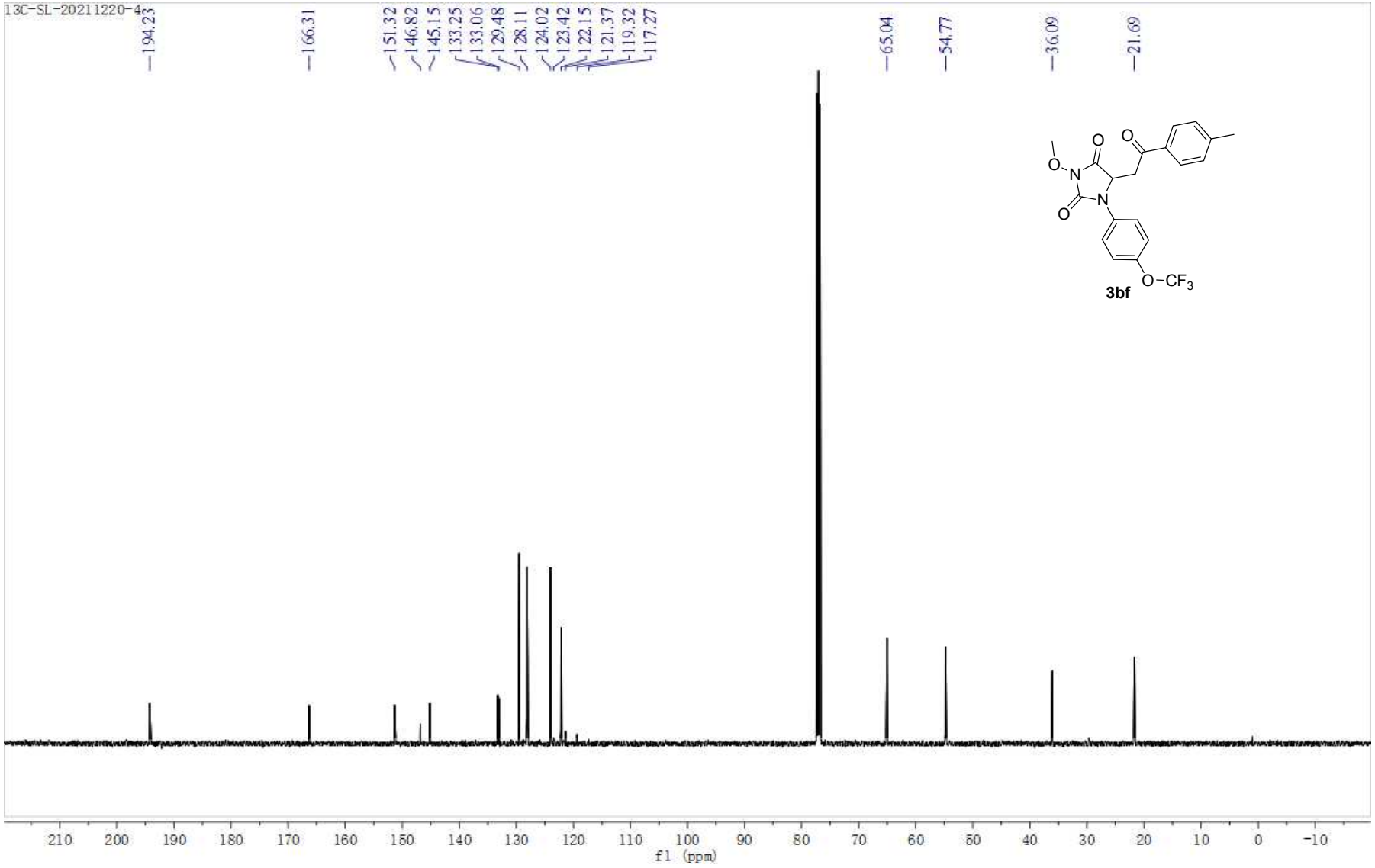

1H-SL-20211222-3
7.61
7.59
7.26
7.24
7.22
7.21
7.19
7.14
7.13
4.81
4.80
4.79
4.09
3.55
3.54
3.52
3.51
3.47
3.47
3.44
2.31
2.00
4.11
2.00
f1 (ppm)
3bd
Cl
2.00
4.11
2.00
1.00
3.09
1.05
1.02
3.02
f1 (ppm)

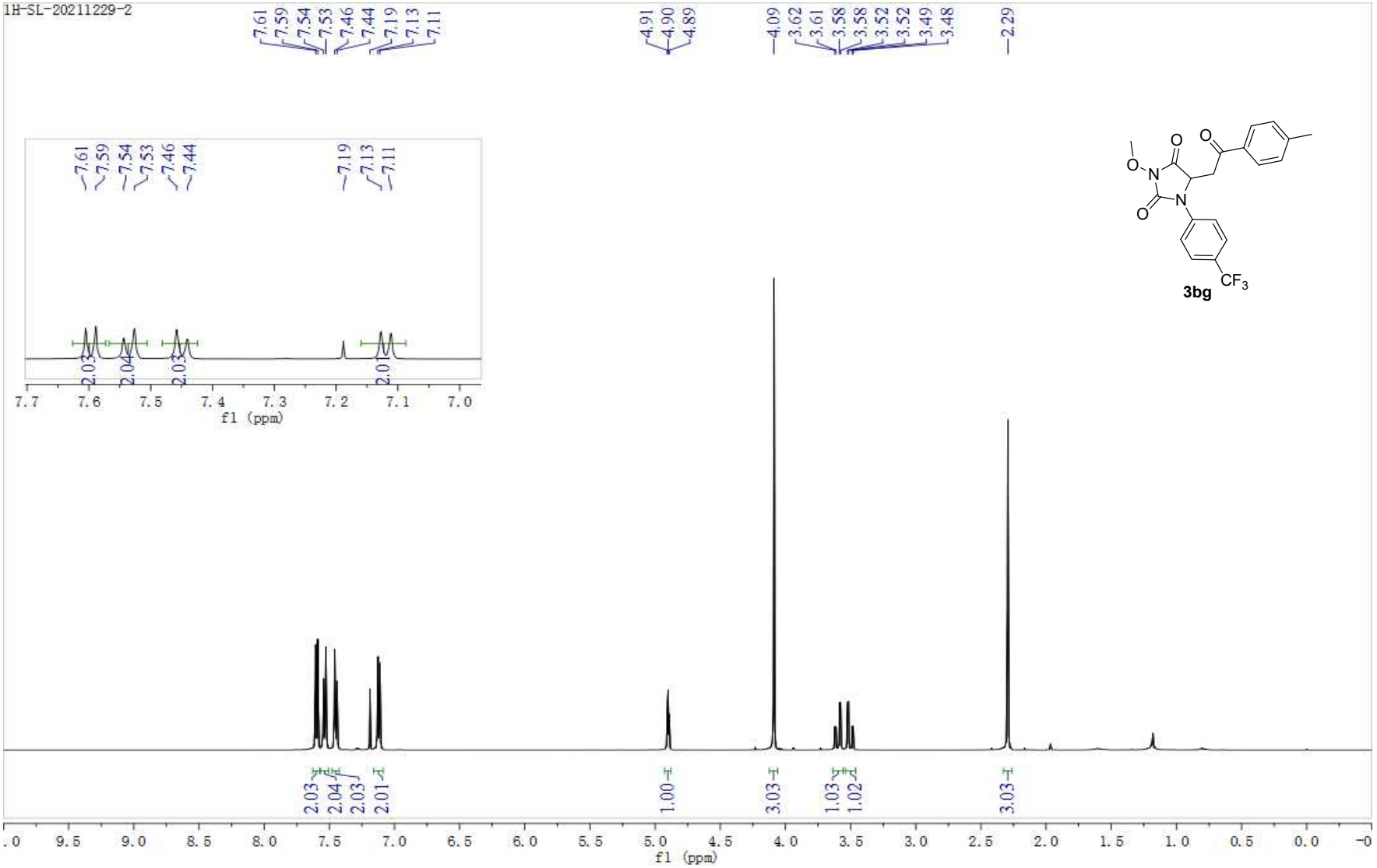

13C-SL-20211222-3
194.18
166.38
151.24
145.12
133.22
133.04
131.79
129.67
129.48
128.11
123.97
65.01
54.67
36.07
21.71
O
O
O
N
N
O
Cl
3bd
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

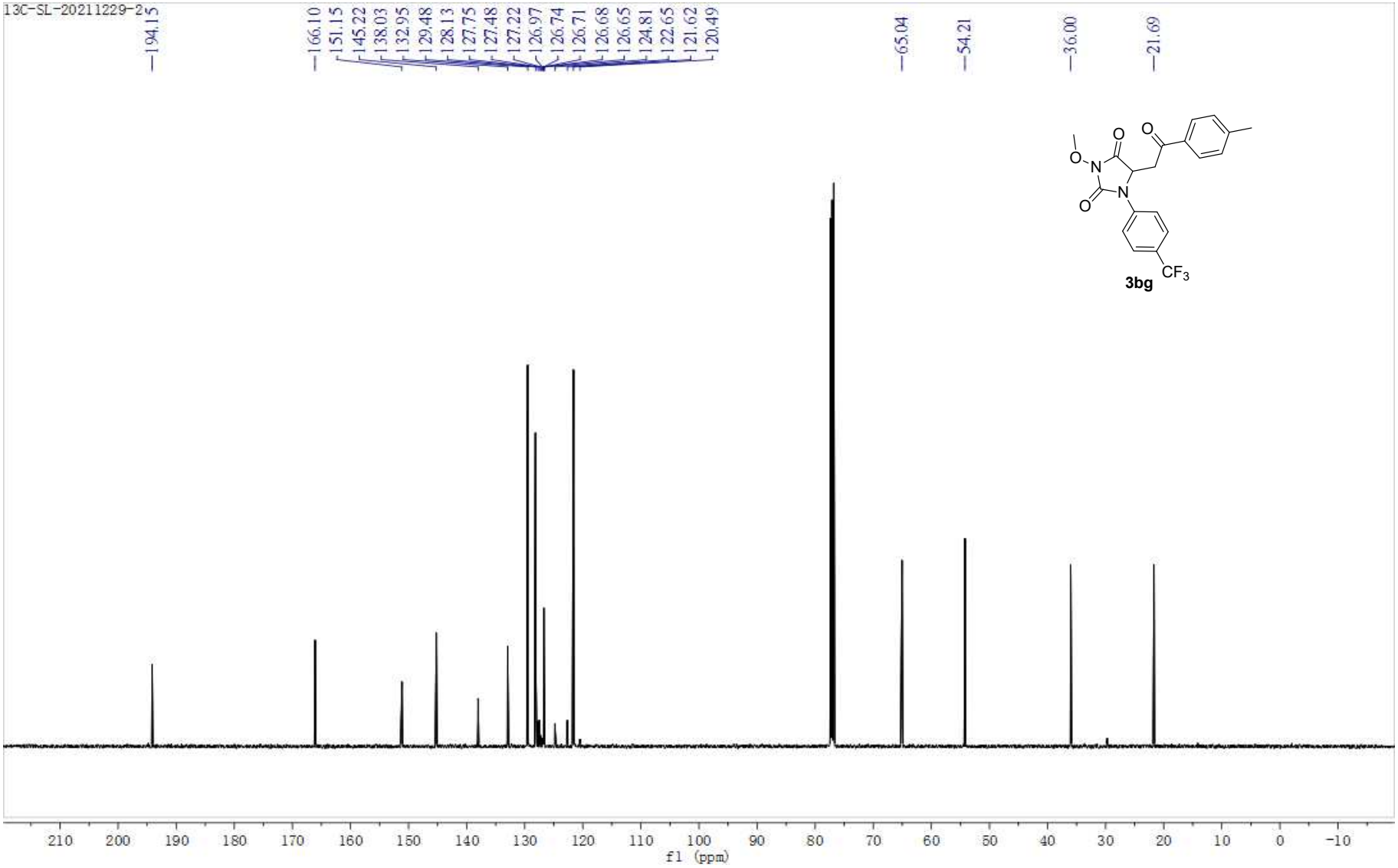

1H-SL-20211215-4
7.68
7.66
7.47
7.46
7.26
7.25
7.23
7.21
7.20
4.88
4.87
4.87
4.16
3.63
3.62
3.59
3.58
3.55
3.54
3.51
3.50
2.38
0.00
2.00
2.03
4.05
f1 (ppm)
1.00
3.00
1.03
1.03
3.02
f1 (ppm)
3be
Br

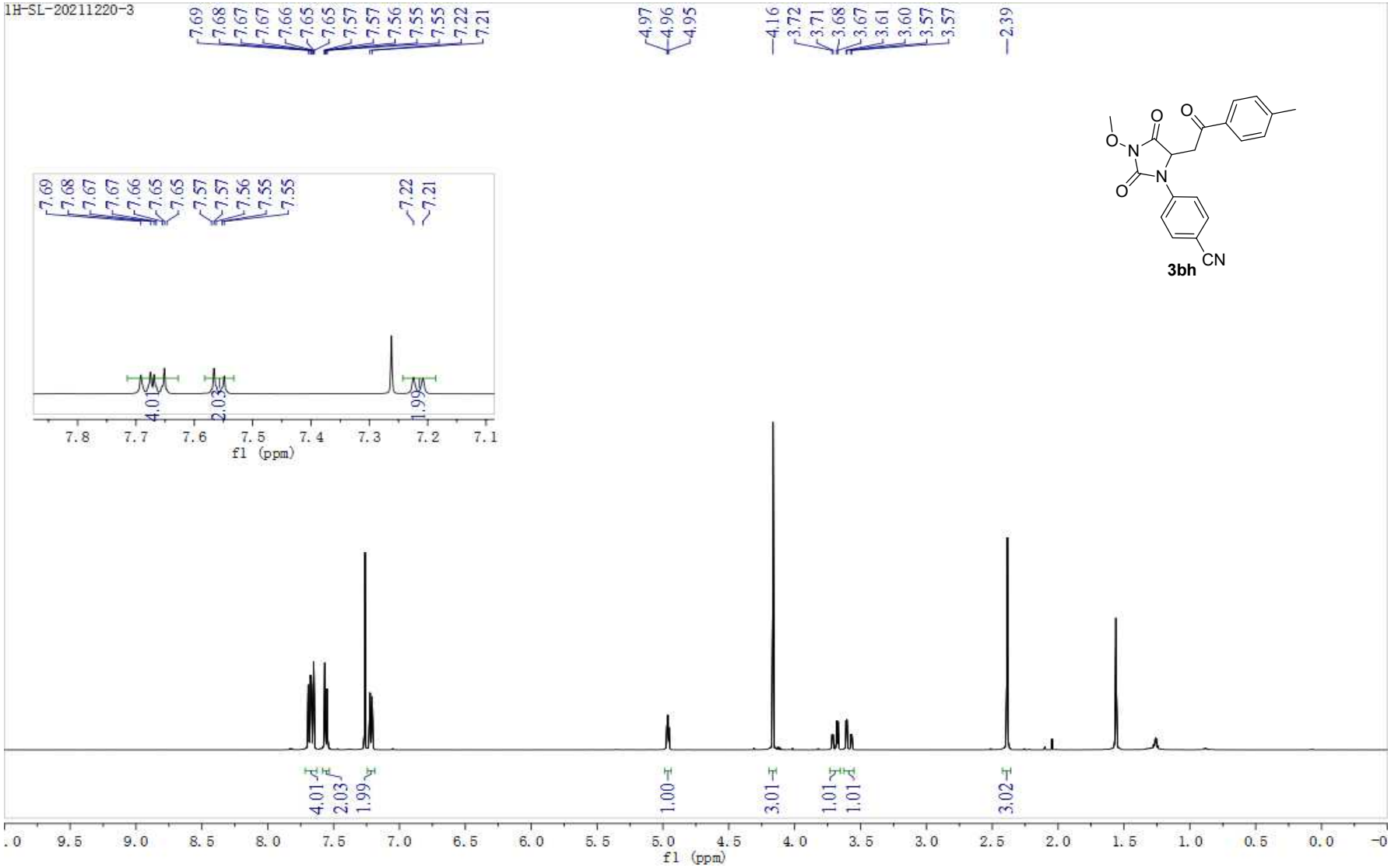

13C-SL-20211215-4
194.20
166.36
151.18
145.12
133.77
133.03
132.61
129.48
128.12
124.16
119.51
65.01
54.57
36.05
21.71
O
O
O
N
N
O
Br
3be
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

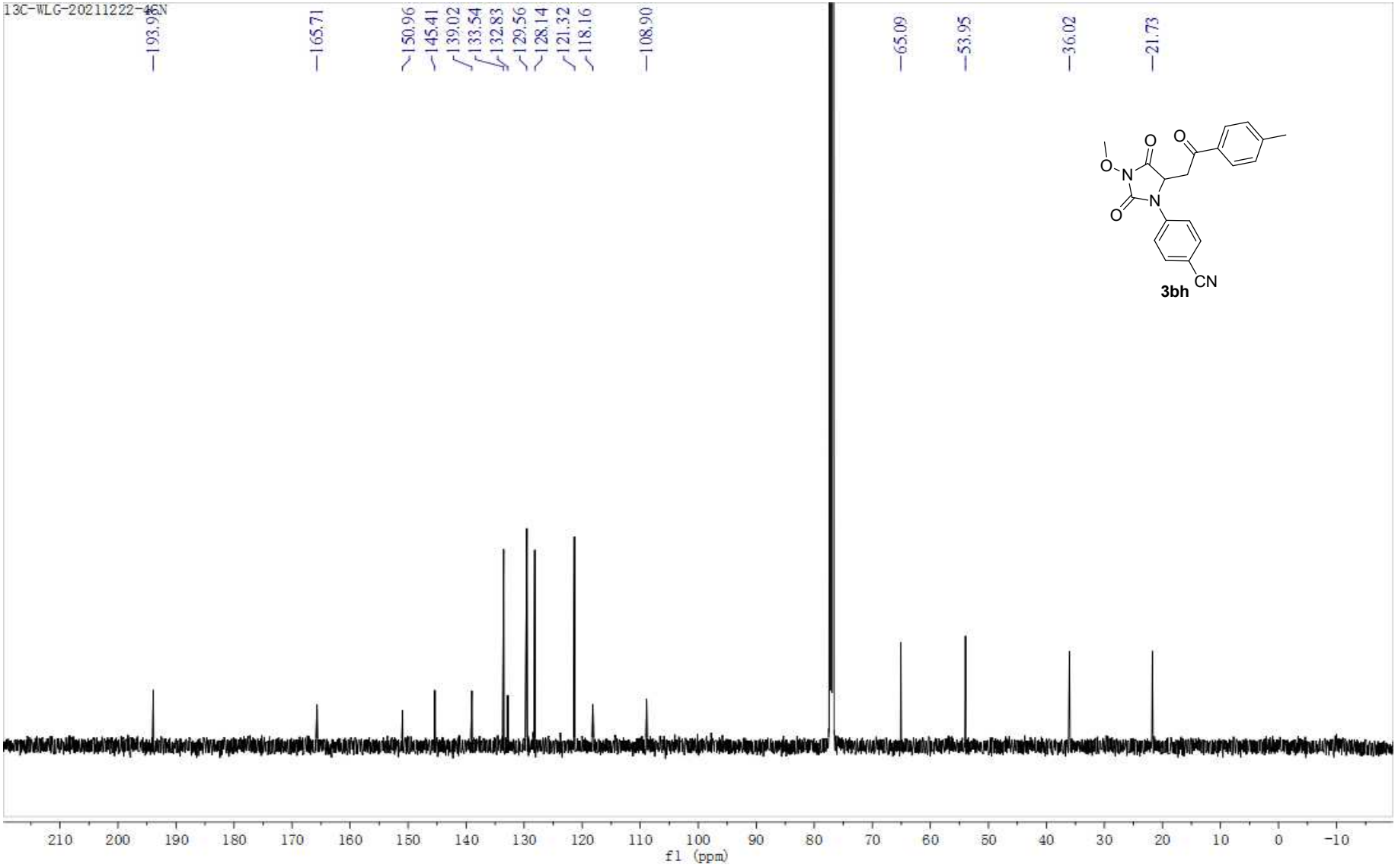

1H-SL-20211220-4
7.61
7.59
7.32
7.30
7.19
7.14
7.12
4.83
4.83
4.82
4.09
3.56
3.56
3.53
3.52
3.48
3.48
3.45
3.44
2.31
0.00
2.00
2.00
4.00
1.00
3.01
1.01
0.98
3.00
f1 (ppm)
3bf

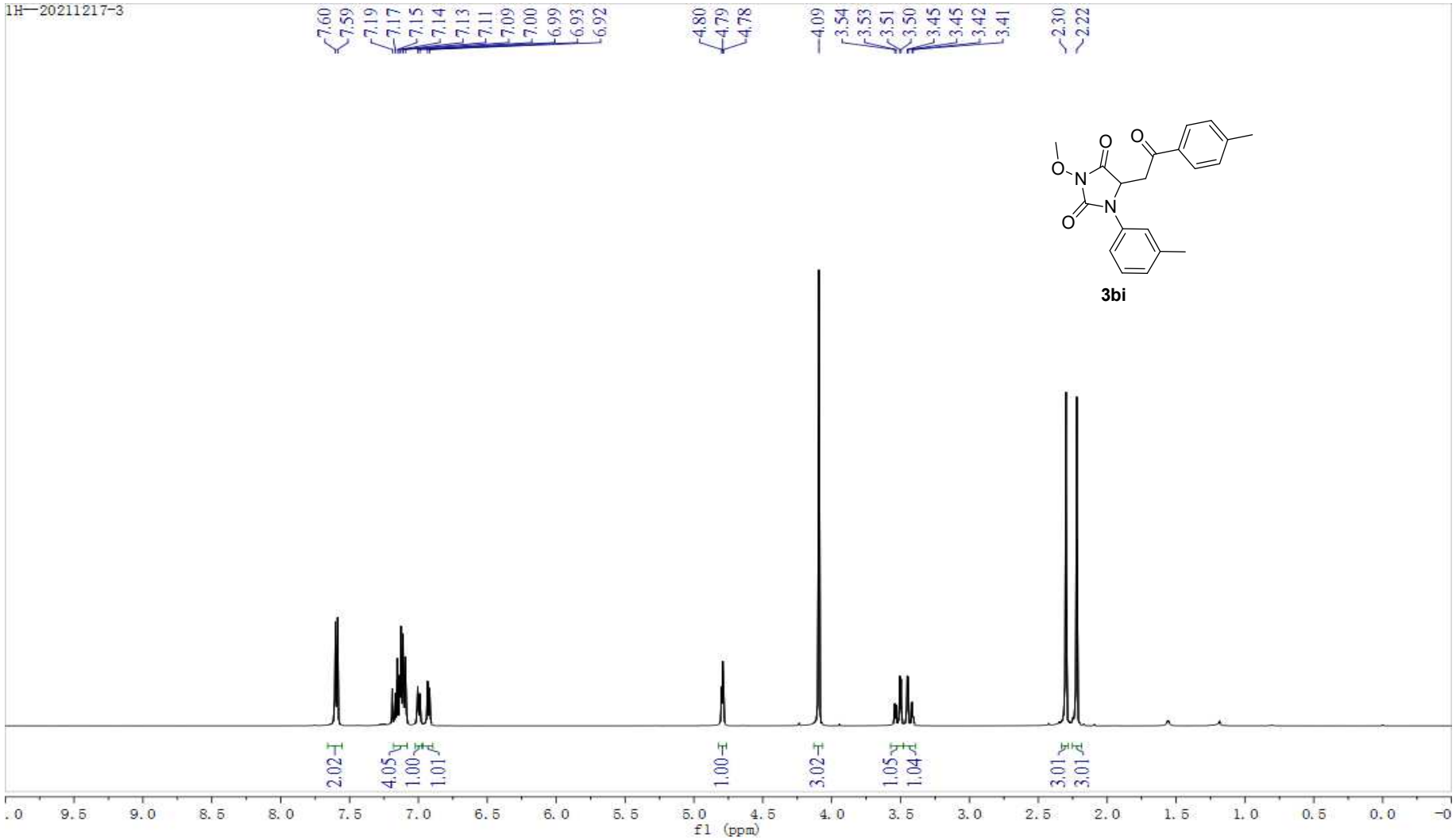

13C-SL-20211220-4
194.23
166.31
151.32
146.82
145.15
133.25
133.06
129.48
128.11
124.02
123.42
122.15
121.37
119.32
117.27
65.04
54.77
36.09
21.69
O
O
N
O
N
O
O−CF3
3bf
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)


1H-SL-20211229-2
7.61
7.59
7.54
7.53
7.46
7.44
7.19
7.13
7.11
4.91
4.90
4.89
4.09
3.62
3.61
3.58
3.58
3.52
3.52
3.49
3.48
2.29
2.03
2.04
2.03
2.01
1.00
3.03
1.03
1.02
3.03
f1 (ppm)
3bg

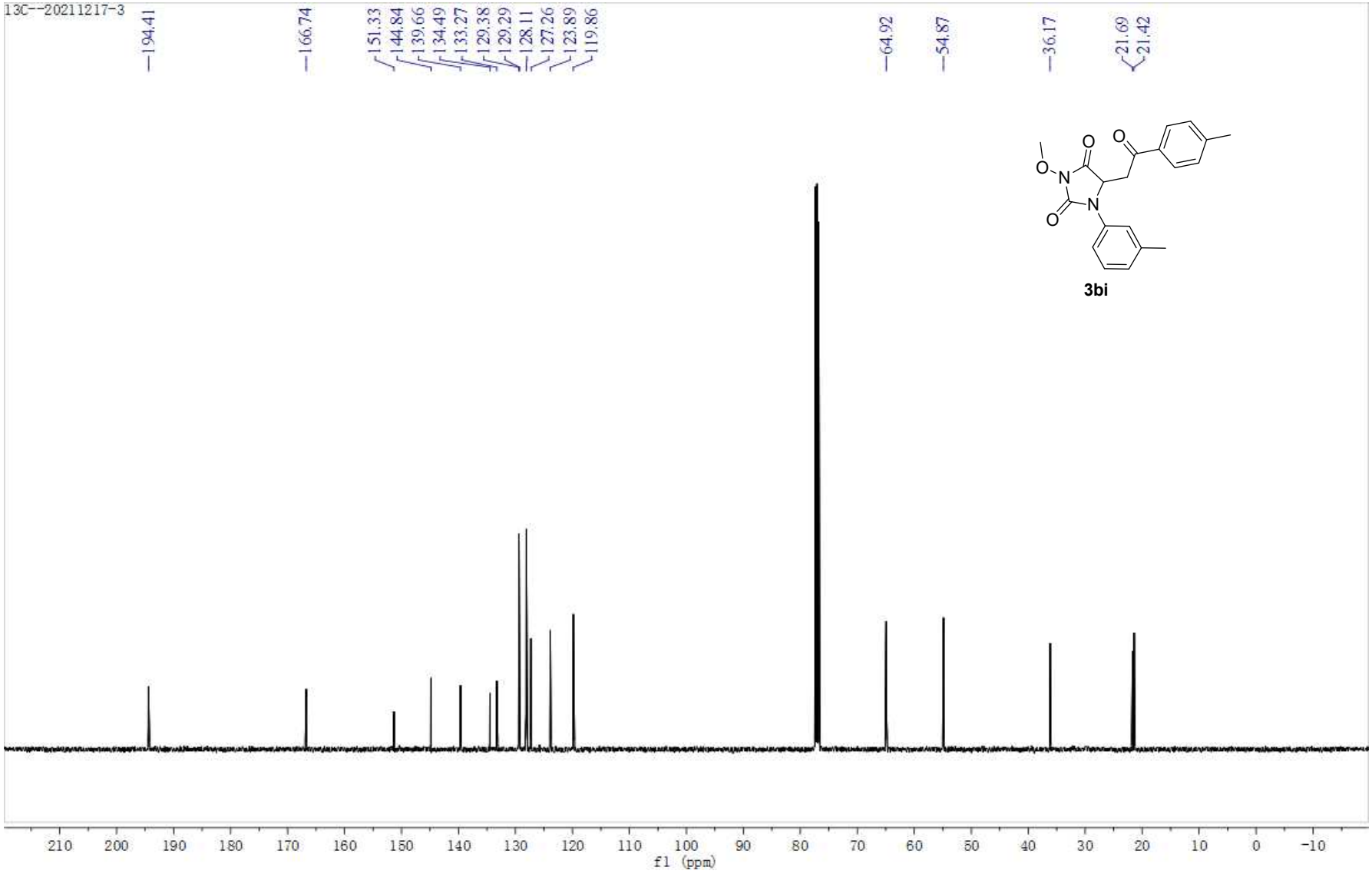

13C-SL-20211229-2
194.15
166.10
151.15
145.22
138.03
132.95
129.48
128.13
127.75
127.48
127.22
126.97
126.74
126.71
126.68
126.65
124.81
122.65
121.62
120.49
65.04
54.21
36.00
21.69
3bg
f1 (ppm)

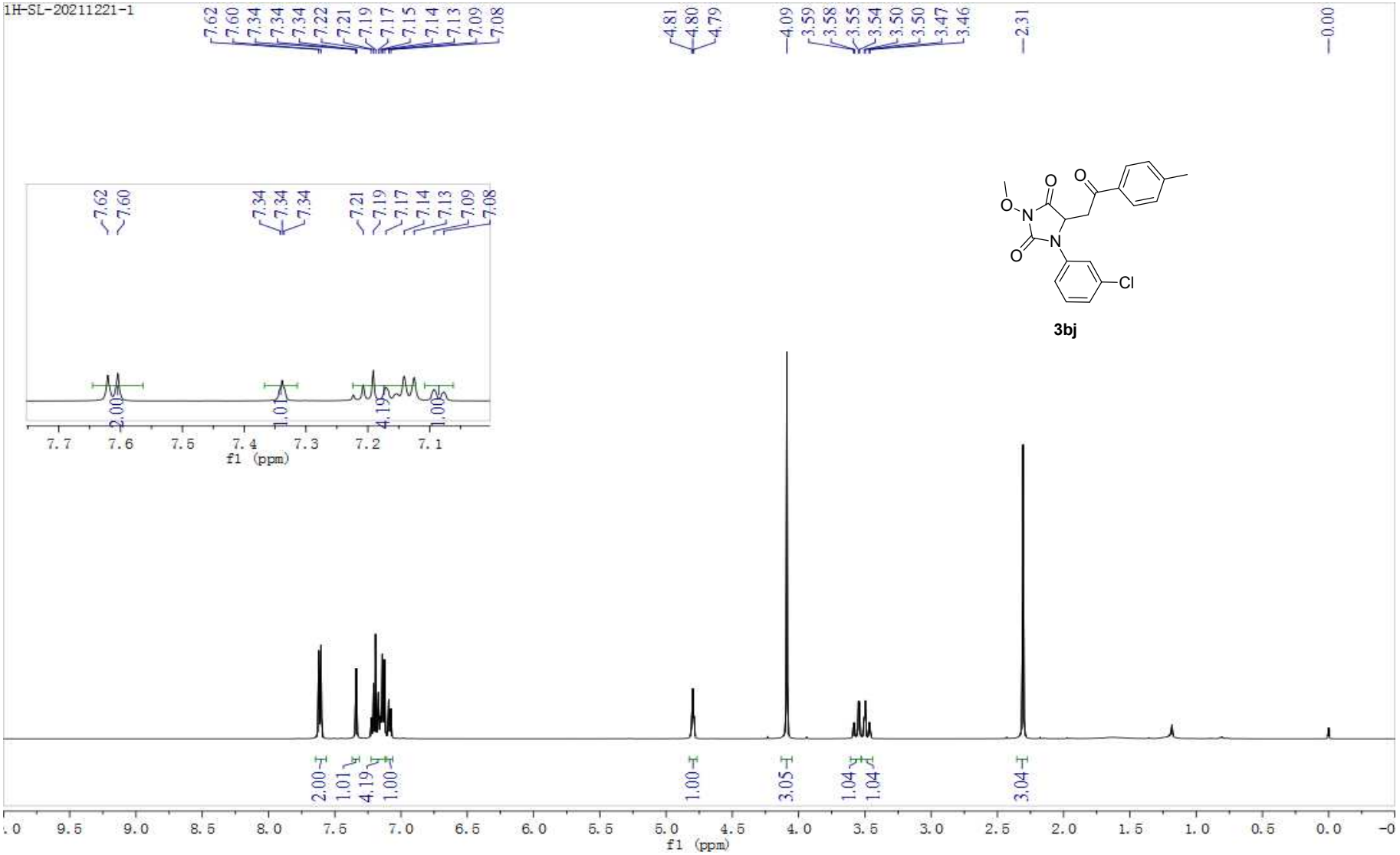

1H-SL-20211220-3
7.69
7.68
7.67
7.67
7.66
7.65
7.65
7.57
7.57
7.56
7.55
7.55
7.22
7.21
4.97
4.96
4.95
4.16
3.72
3.71
3.68
3.67
3.61
3.60
3.57
3.57
2.39
4.01
2.03
1.99
f1 (ppm)
1.00
3.01
1.01
1.01
3.02
f1 (ppm)
3bh
CN

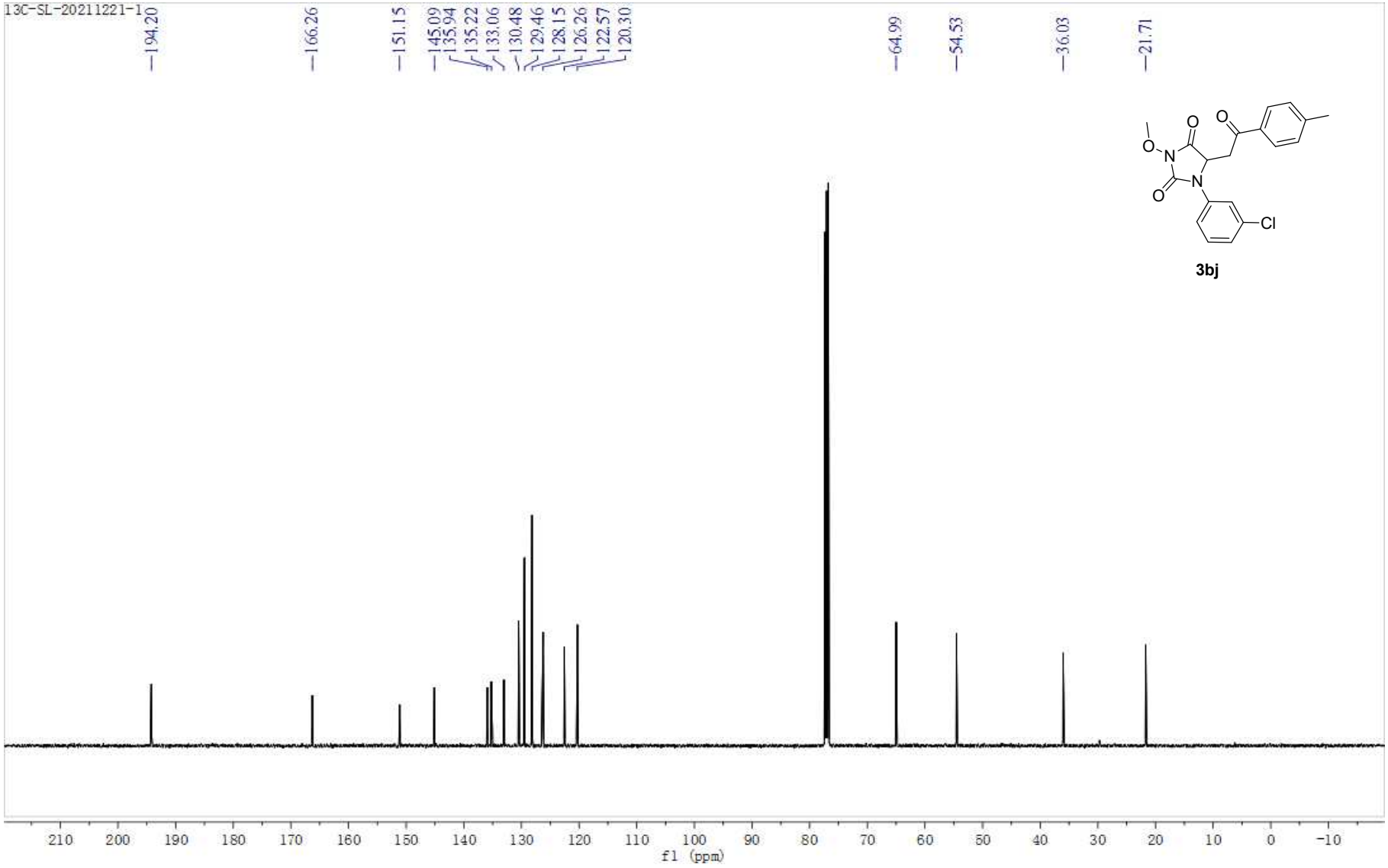

13C-WLG-20211222-46N
193.96
165.71
150.96
145.41
139.02
133.54
132.83
129.56
128.14
121.32
118.16
108.90
65.09
53.95
36.02
21.73
3bh
CN
f1 (ppm)

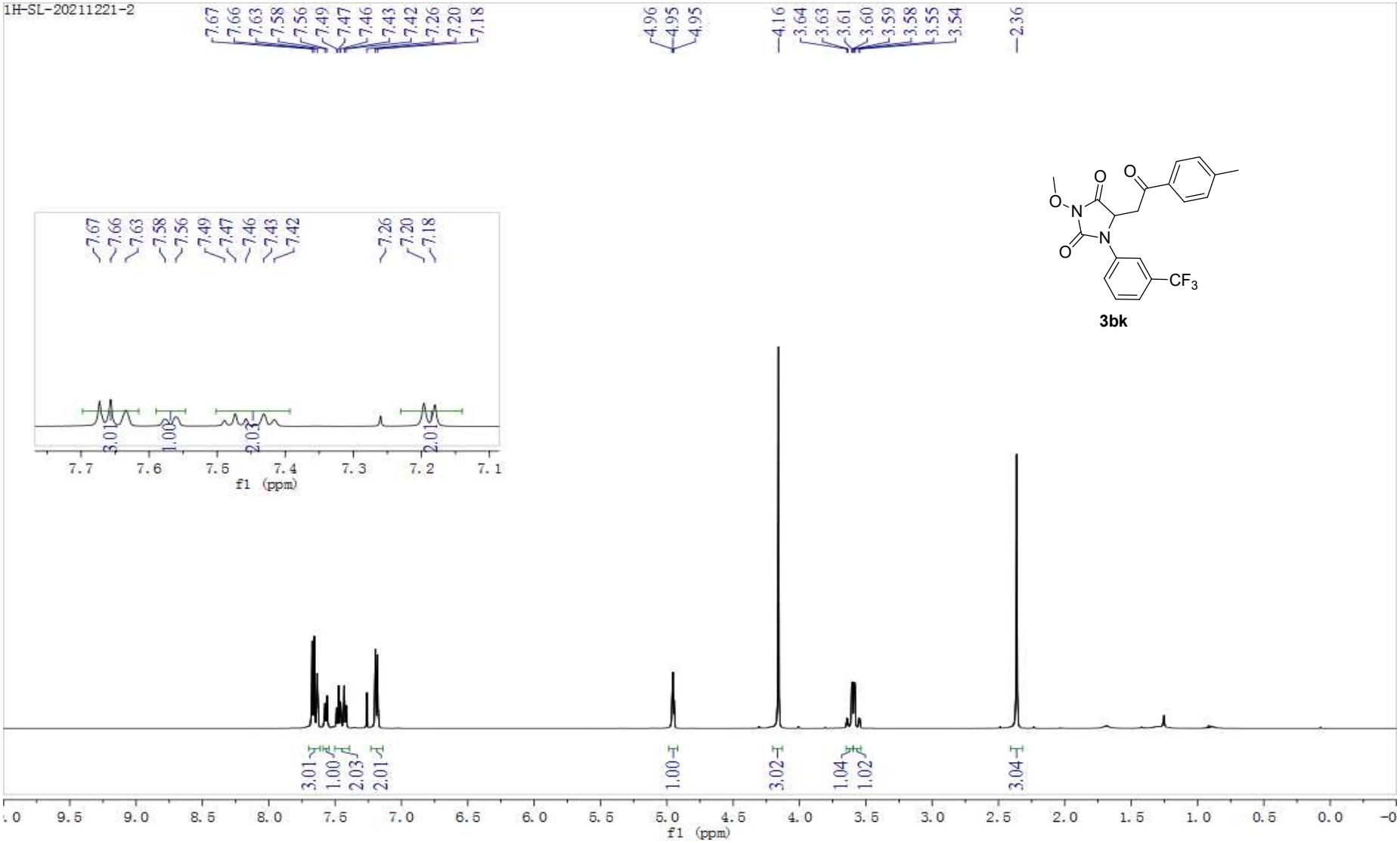

1H—20211217-3
7.60
7.59
7.19
7.17
7.15
7.14
7.13
7.11
7.09
7.00
6.99
6.93
6.92
4.80
4.79
4.78
4.09
3.54
3.53
3.51
3.50
3.45
3.45
3.42
3.41
2.30
2.22
2.02
4.05
1.00
1.01
1.00
3.02
1.05
1.04
3.01
3.01
f1 (ppm)

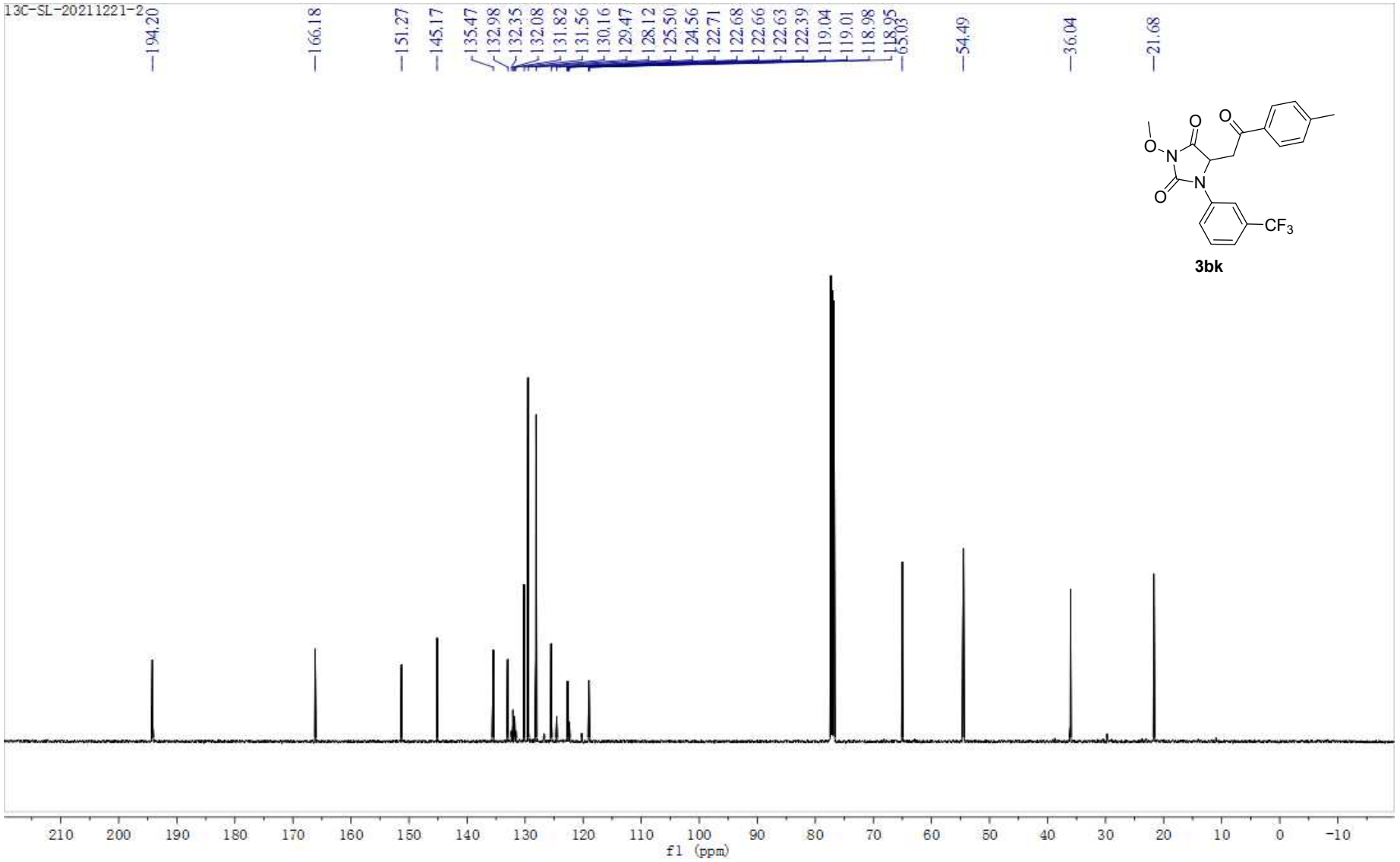
3bi

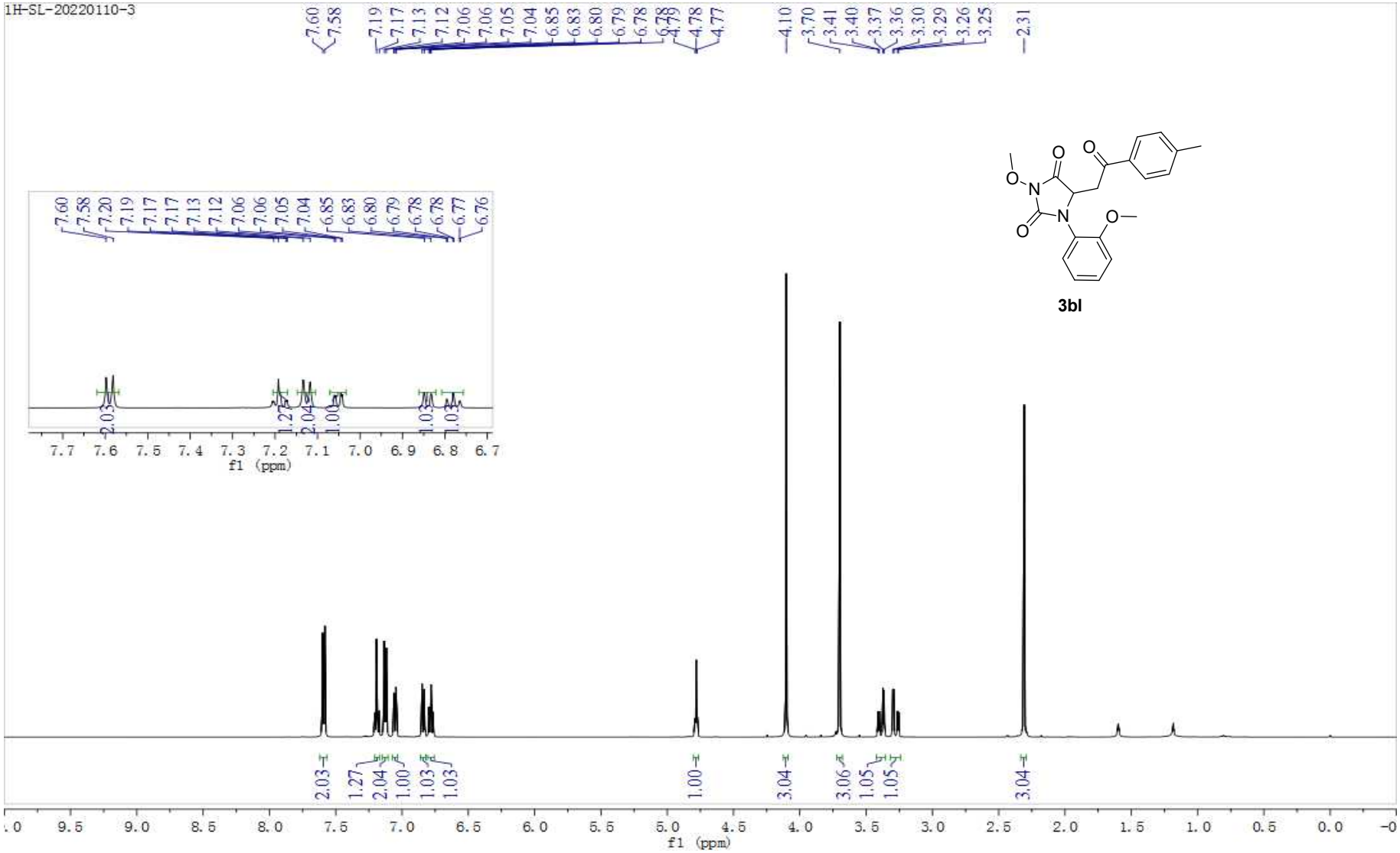

13C--20211217-3
194.41
166.74
151.33
144.84
139.66
134.49
133.27
129.38
129.29
128.11
127.26
123.89
119.86
64.92
54.87
36.17
21.69
21.42
O
O
O
N
N
O
3bi
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

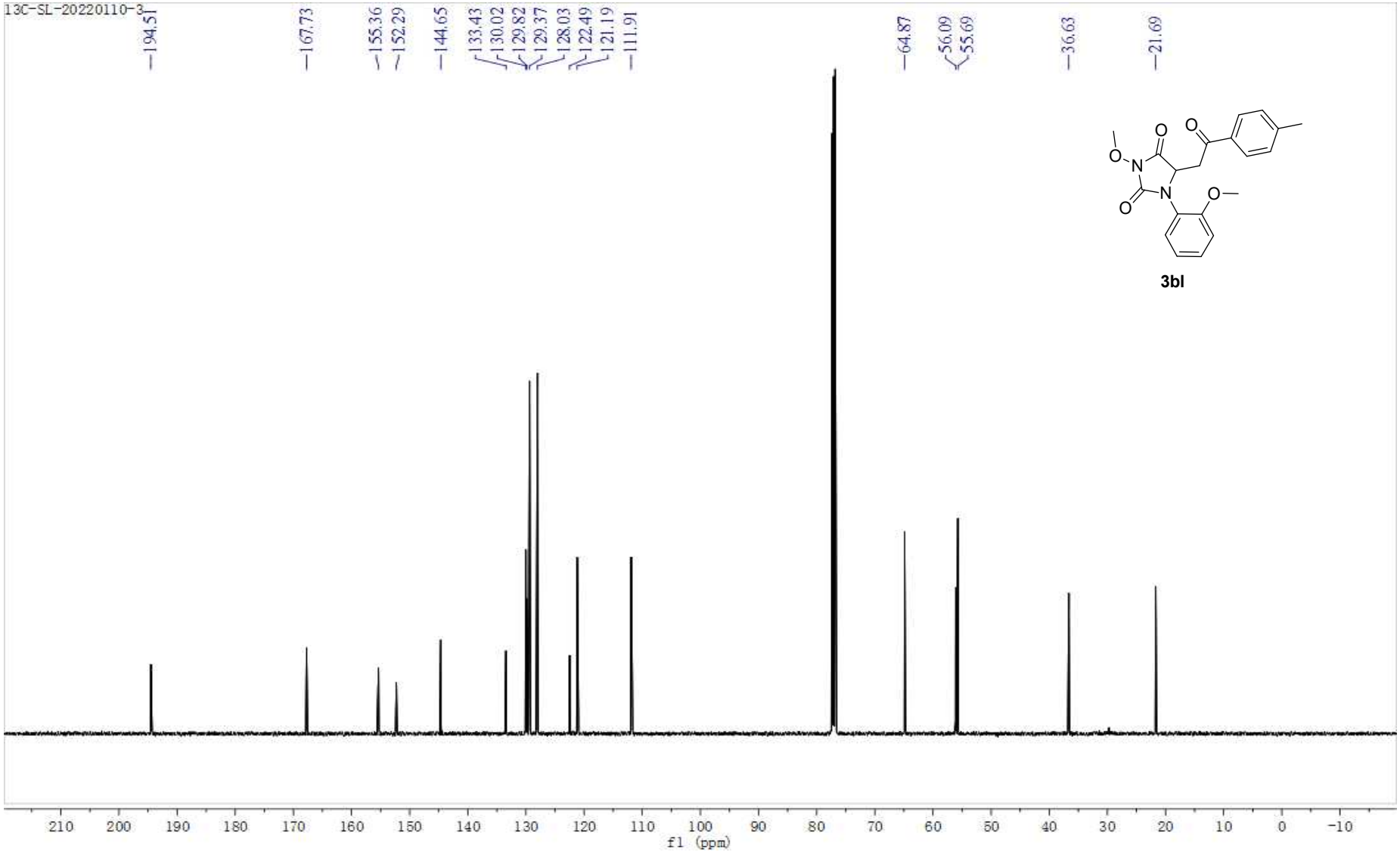

1H-SL-20211221-1
7.62
7.60
7.34
7.34
7.34
7.22
7.21
7.19
7.17
7.15
7.14
7.13
7.09
7.08
4.81
4.80
4.79
4.09
3.59
3.58
3.55
3.54
3.50
3.50
3.47
3.46
2.31
0.00
O
O
O
N
N
Cl
3bj
2.00
1.01
4.19
1.00
1.00
3.05
1.04
1.04
3.04
f1 (ppm)

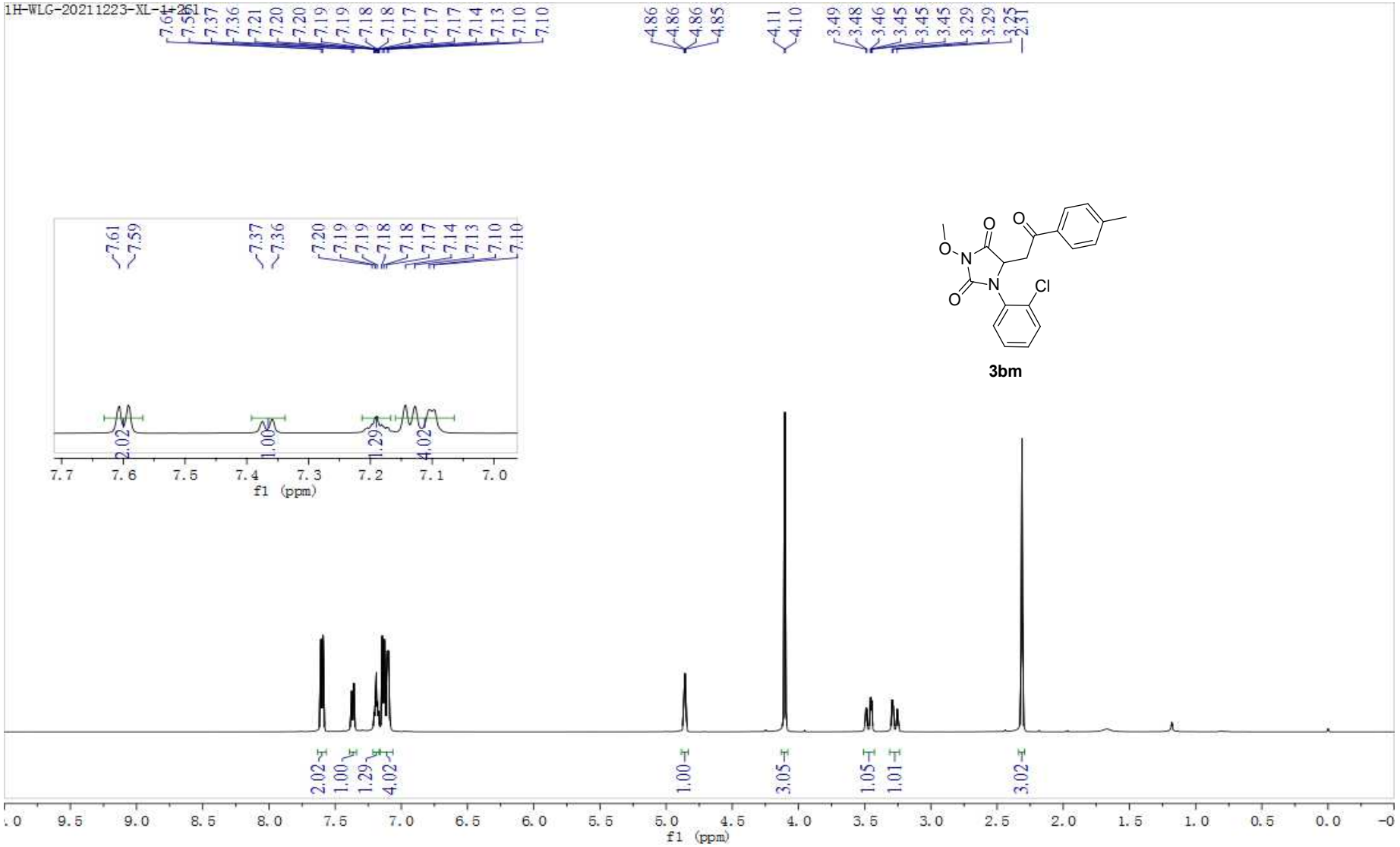

13C-SL-20211221-1
194.20
166.26
151.15
145.09
135.94
135.22
133.06
130.48
129.46
128.15
126.26
122.57
120.30
64.99
54.53
36.03
21.71
O
O
O
N
N
O
Cl
3bj
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

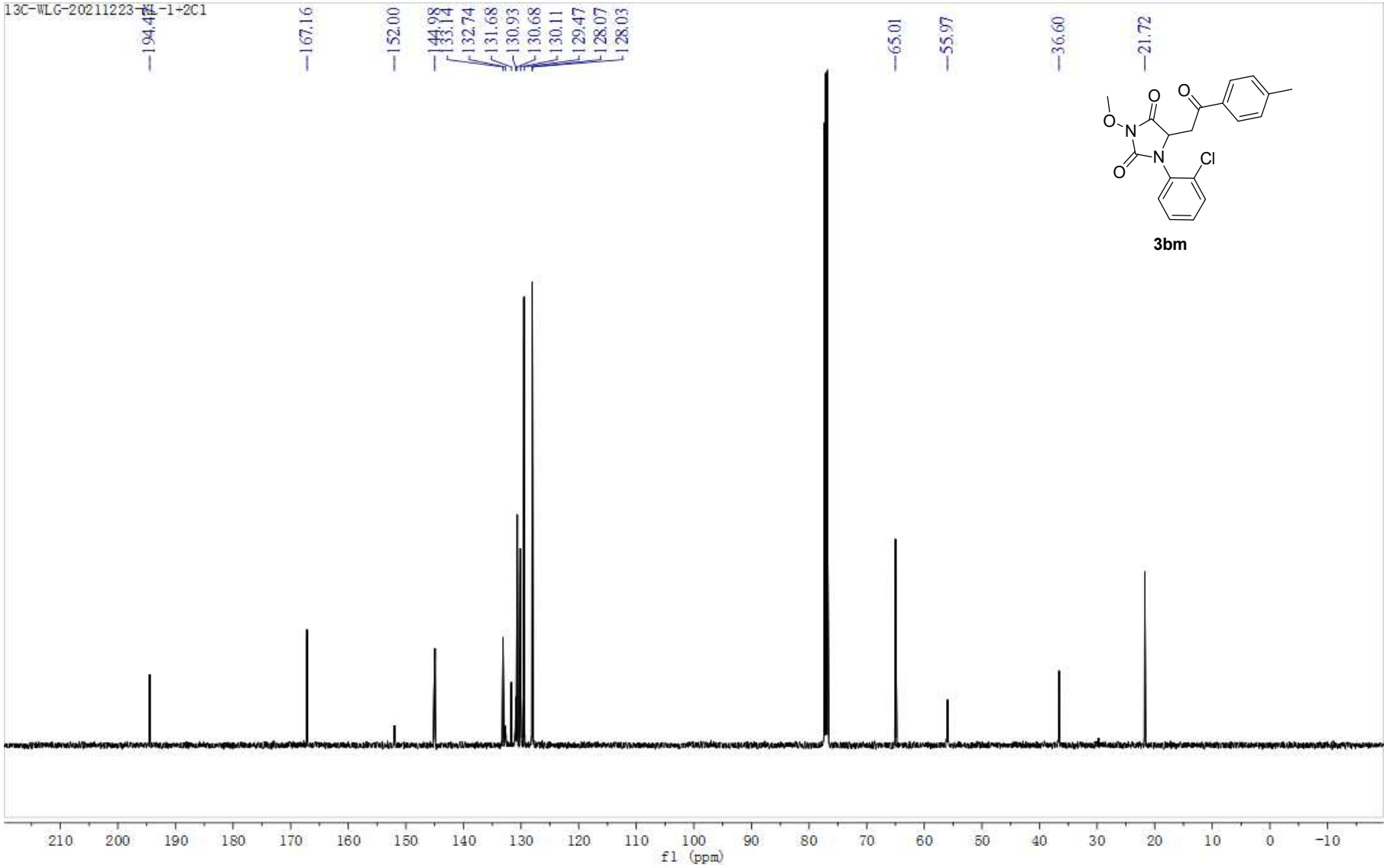

1H-SL-20211221-2
7.67
7.66
7.63
7.58
7.56
7.49
7.47
7.46
7.43
7.42
7.26
7.20
7.18
4.96
4.95
4.95
4.16
3.64
3.63
3.61
3.60
3.59
3.58
3.55
3.54
2.36
O
O
N
O
N
CF3
3bk
3.01
1.00
2.03
2.01
1.00
3.02
1.04
1.02
3.04
f1 (ppm)

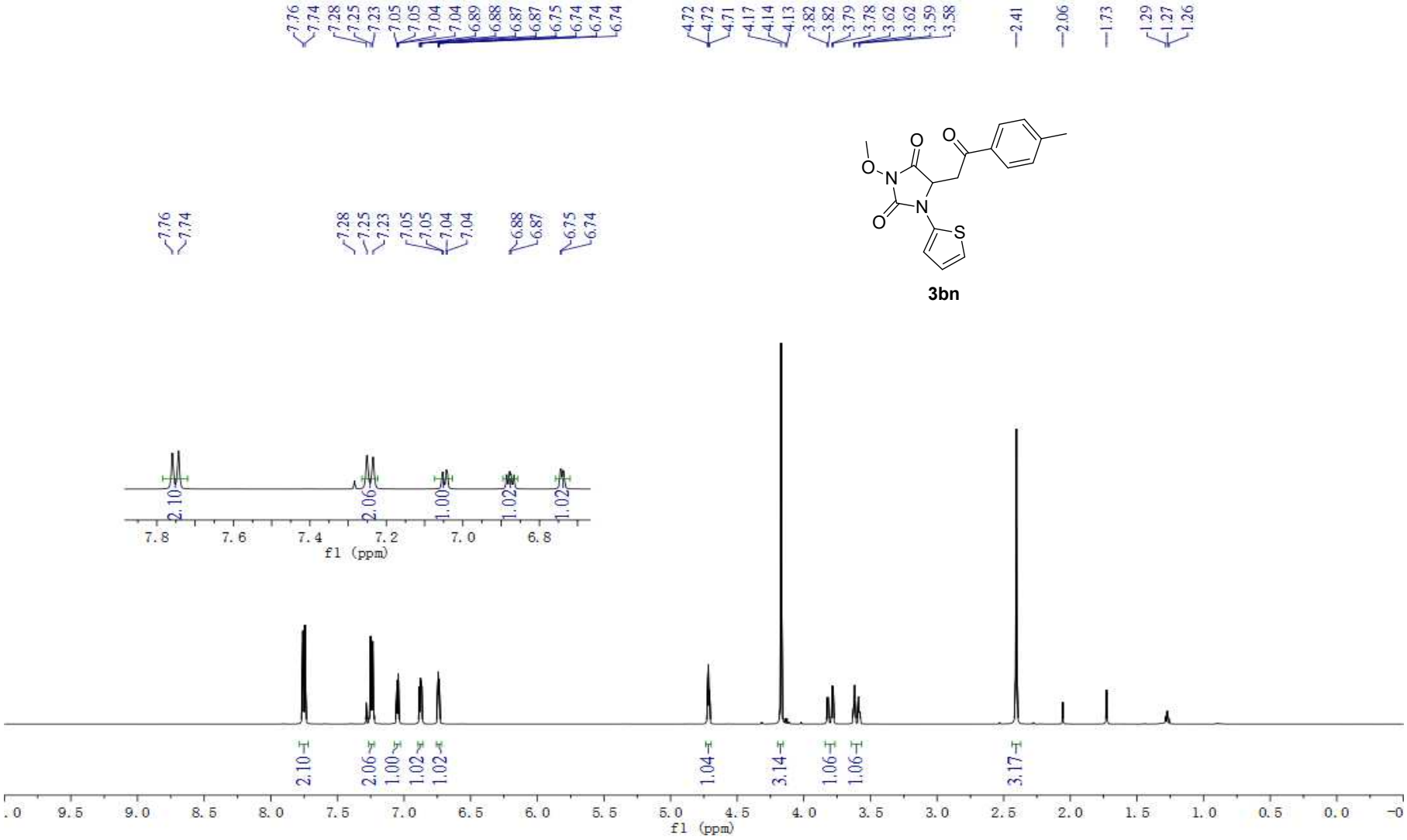

13C-SL-20211221-2
194.20
166.18
151.27
145.17
135.47
132.98
132.35
132.08
131.82
131.56
130.16
129.47
128.12
125.50
124.56
122.71
122.68
122.66
122.63
122.39
119.04
119.01
118.98
118.95
65.03
54.49
36.04
21.68
O
O
O
N
N
O
CF3
3bk
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

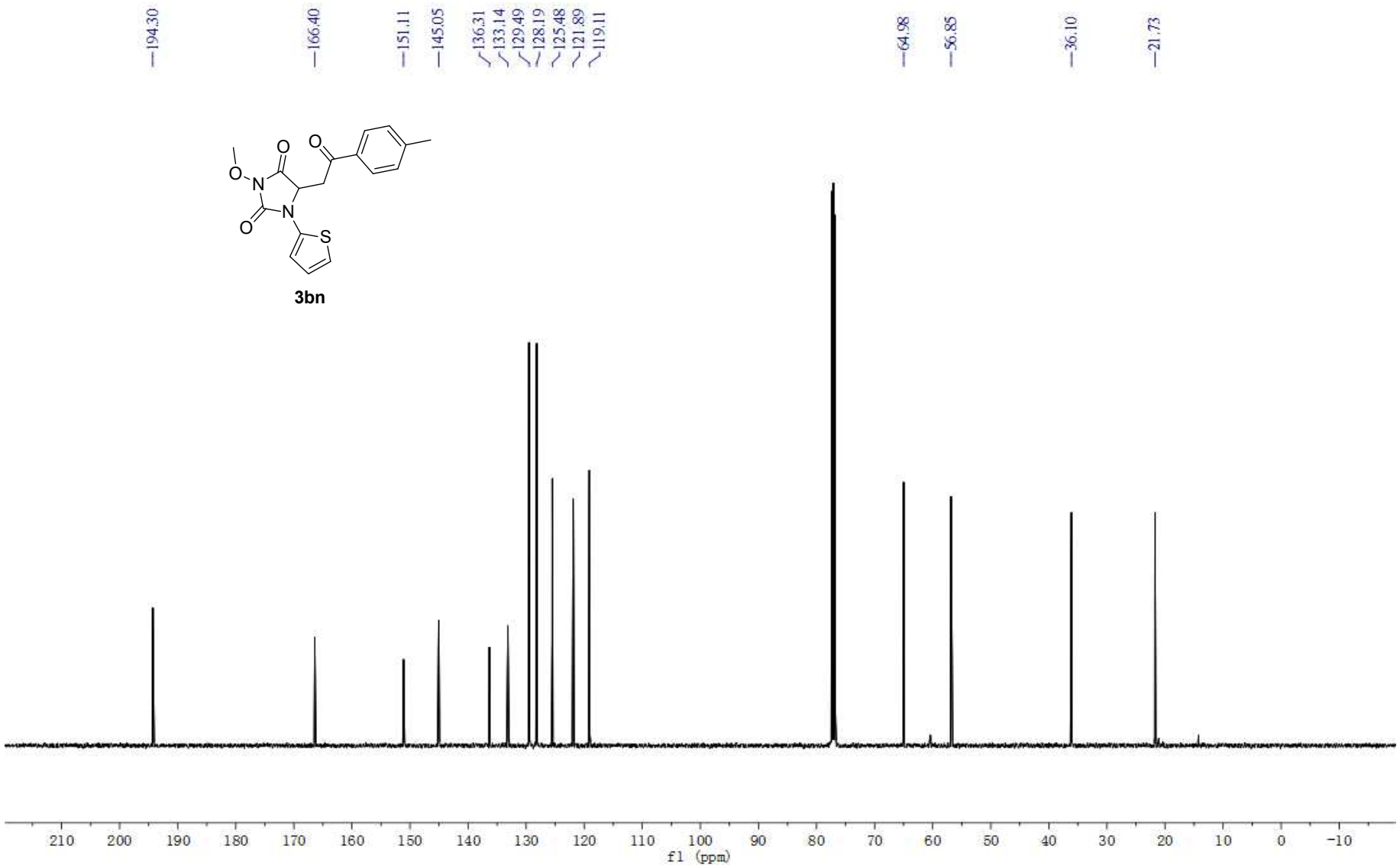

1H-SL-20220110-3
7.60
7.58
7.19
7.17
7.13
7.12
7.06
7.06
7.05
7.04
6.85
6.83
6.80
6.79
6.78
6.78
4.78
4.77
4.10
3.70
3.41
3.40
3.37
3.36
3.30
3.29
3.26
3.25
2.31
7.60
7.58
7.20
7.19
7.17
7.17
7.13
7.12
7.06
7.06
7.05
7.04
6.85
6.83
6.80
6.79
6.78
6.78
6.77
6.76
2.03
1.27
2.04
1.00
1.03
1.03
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)
O
O
O
N
N
O
O
3bl
2.03
1.27
2.04
1.00
1.03
1.03
1.00
3.04
3.06
1.05
1.05
3.04
.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
f1 (ppm)

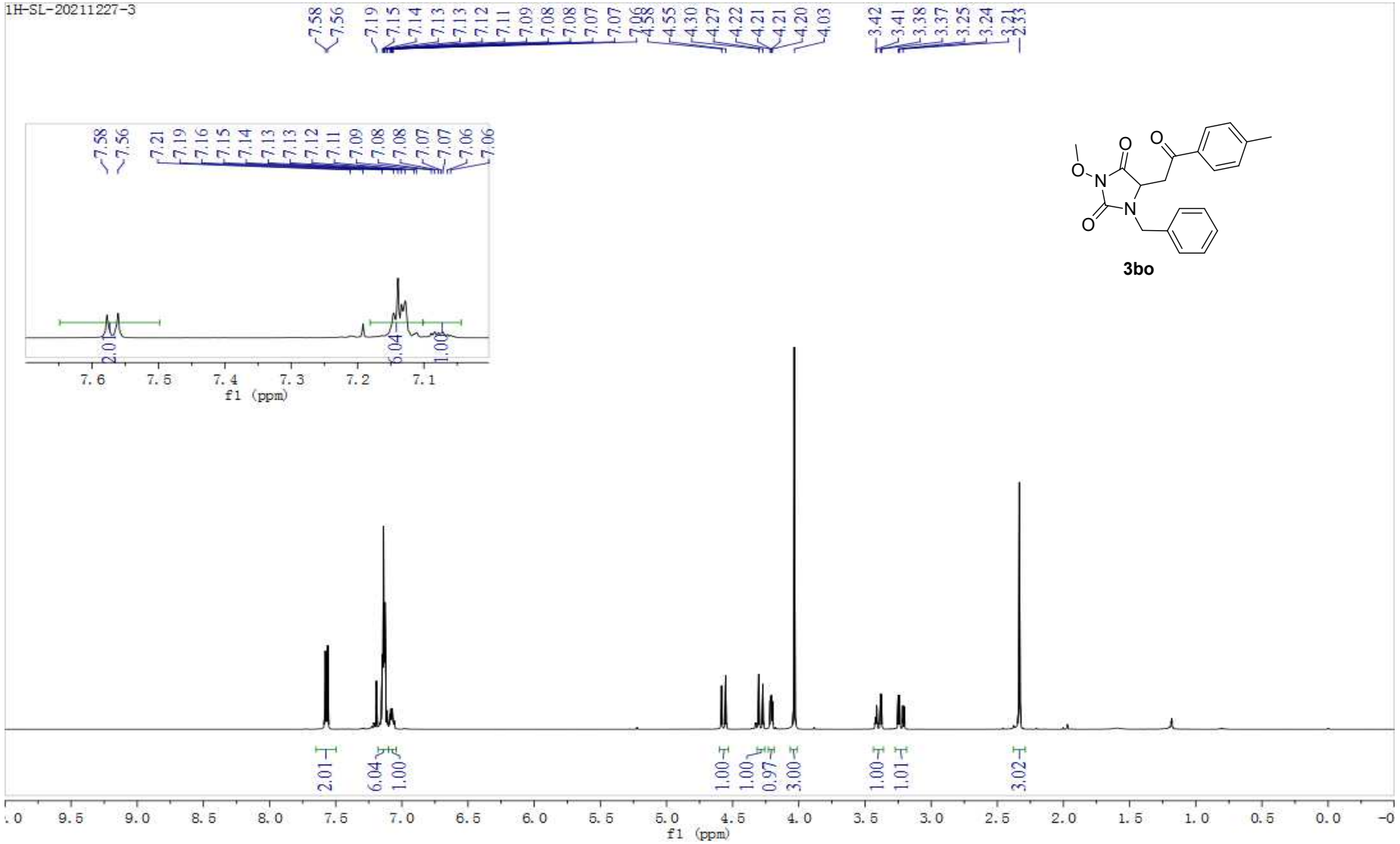

13C-SL-20220110-3
194.51
167.73
155.36
152.29
144.65
133.43
130.02
129.82
129.37
128.03
122.49
121.19
111.91
64.87
56.09
55.69
36.63
21.69
3bl
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

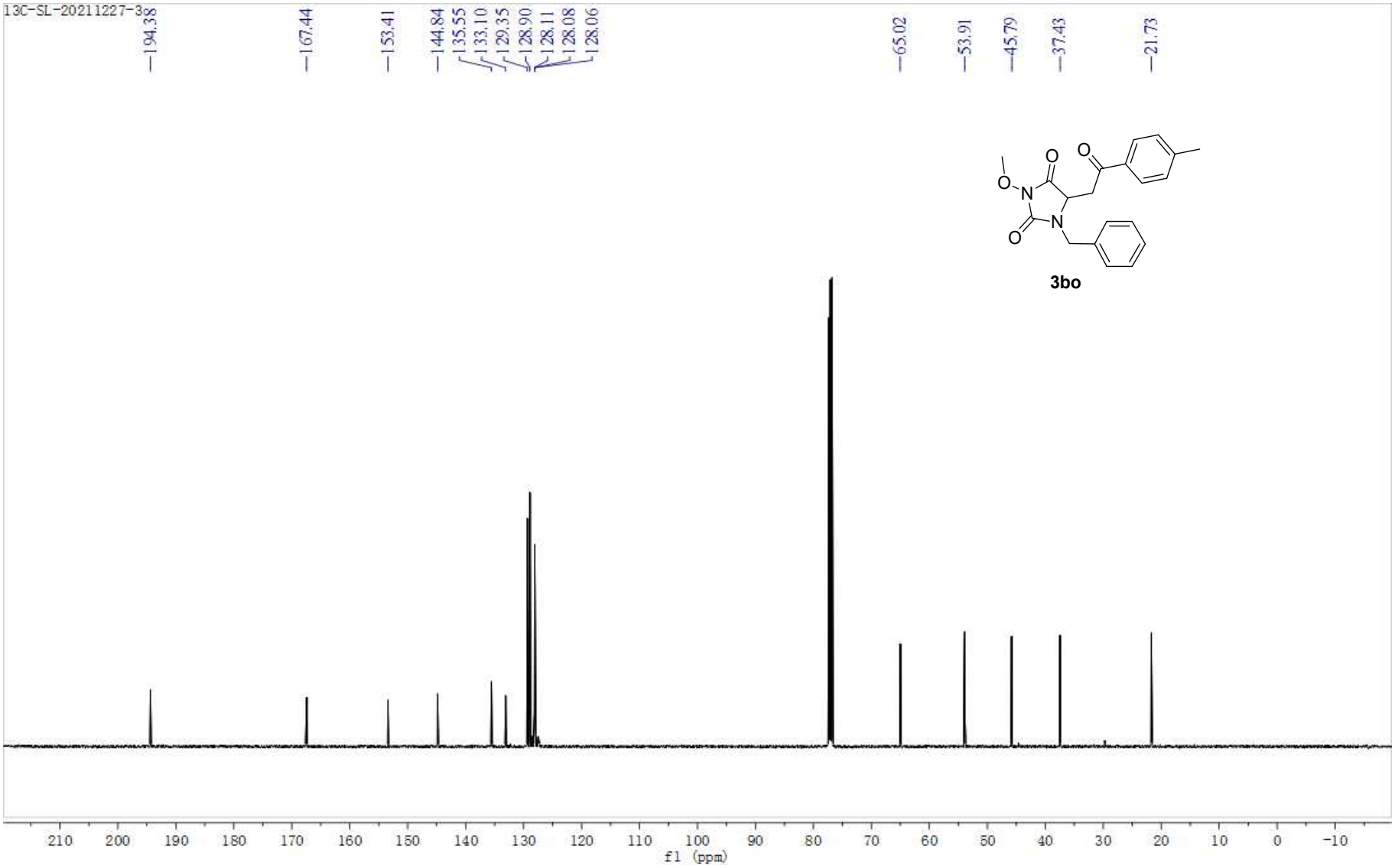

1H-WLG-20211223-XL-1-261
7.61
7.59
7.37
7.36
7.20
7.19
7.19
7.18
7.18
7.17
7.14
7.13
7.10
7.10
4.86
4.86
4.86
4.85
4.11
4.10
3.49
3.48
3.46
3.45
3.45
3.45
3.29
3.29
3.25
2.31
2.02
1.00
1.29
4.02
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)
O
O
O
N
N
Cl
3bm
2.02
1.00
1.29
4.02
1.00
3.05
1.05
1.01
3.02
f1 (ppm)

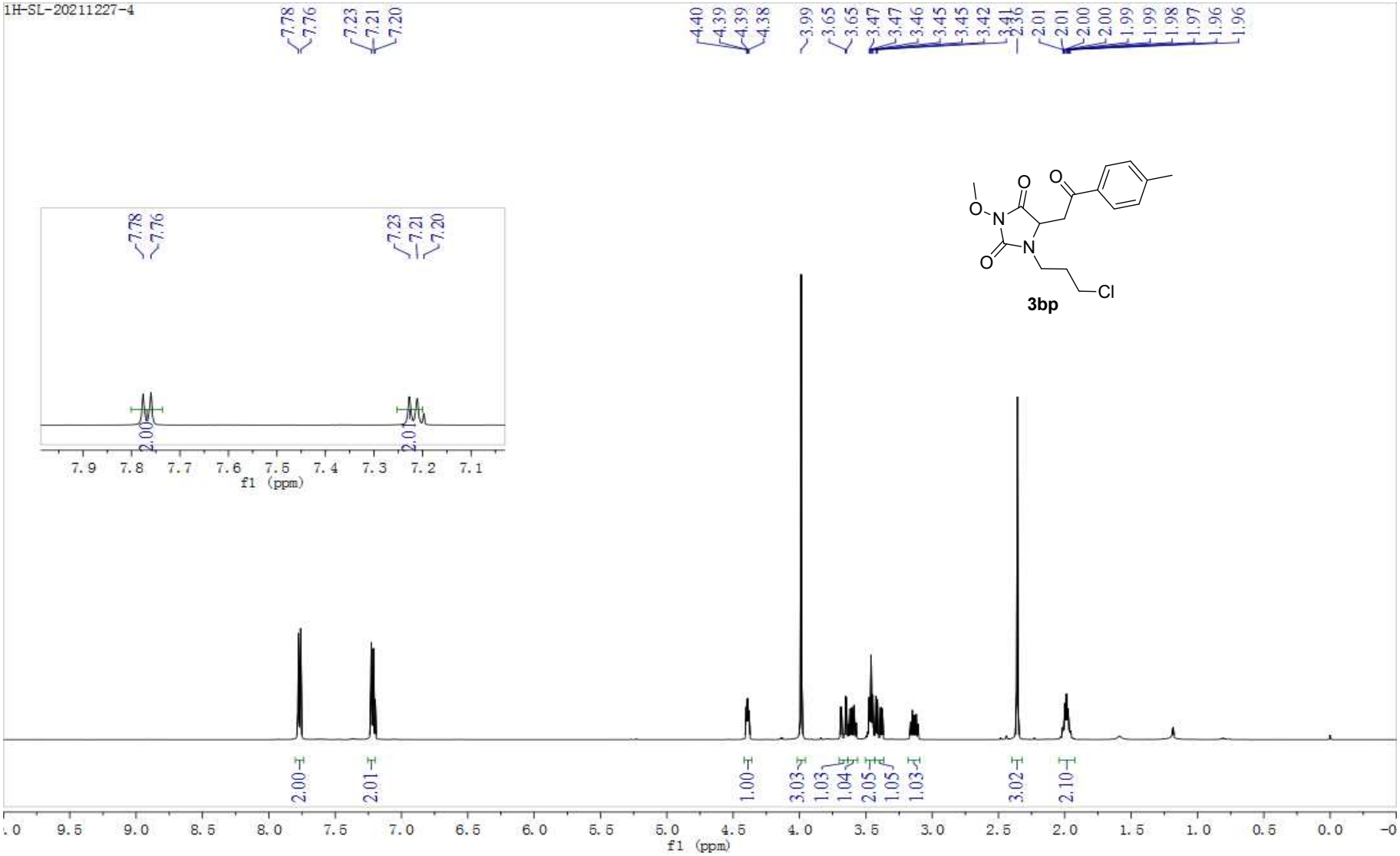

13C-WLG-20211223-WL-1+2C1
194.48
167.16
152.00
144.98
133.14
132.74
131.68
130.93
130.68
130.11
129.47
128.07
128.03
65.01
55.97
36.60
21.72
O
O
N
O
N
Cl
3bm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

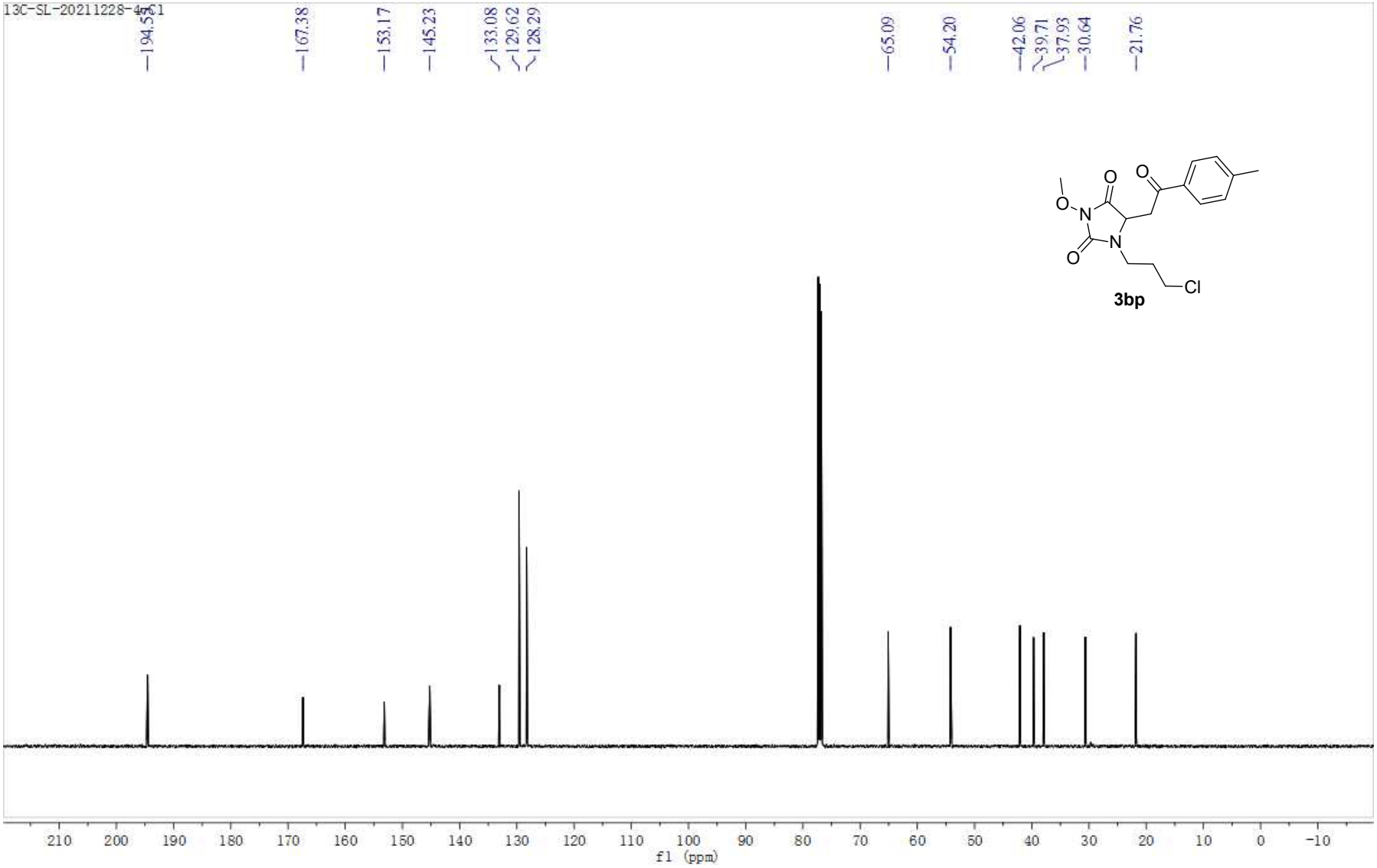

7.76
7.74
7.28
7.25
7.23
7.05
7.05
7.04
7.04
6.89
6.88
6.87
6.87
6.75
6.74
6.74
6.74
4.72
4.72
4.71
4.17
4.14
4.13
3.82
3.82
3.79
3.78
3.62
3.62
3.59
3.58
2.41
2.06
1.73
1.29
1.27
1.26
O
O
O
N
N
S
3bn
2.10
2.06
1.00
1.02
1.02
f1 (ppm)
1.04
3.14
1.06
1.06
3.17
f1 (ppm)

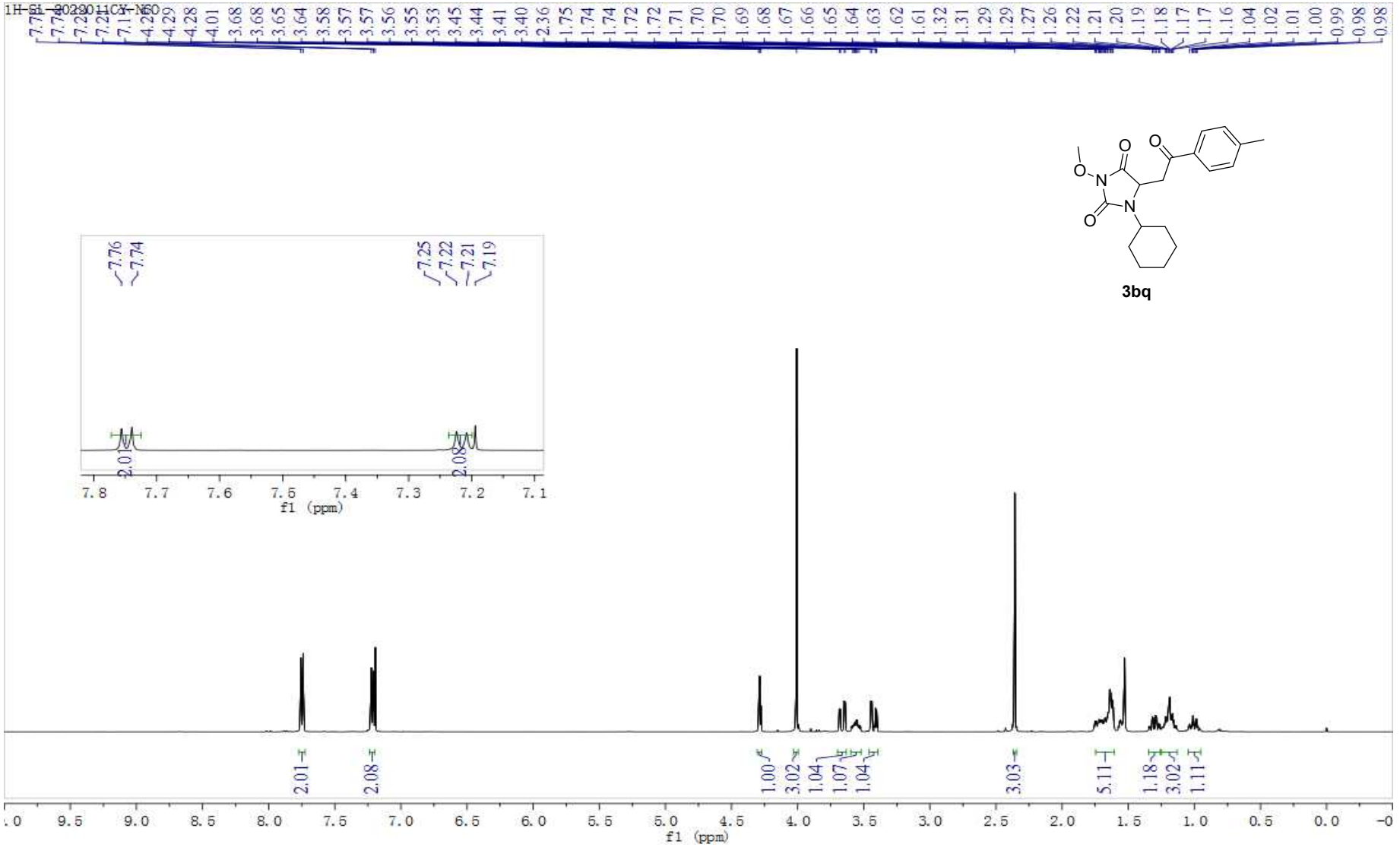

194.30
166.40
151.11
145.05
136.31
133.14
129.49
128.19
125.48
121.89
119.11
64.98
56.85
36.10
21.73
O
O
N
O
N
O
S
3bn
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

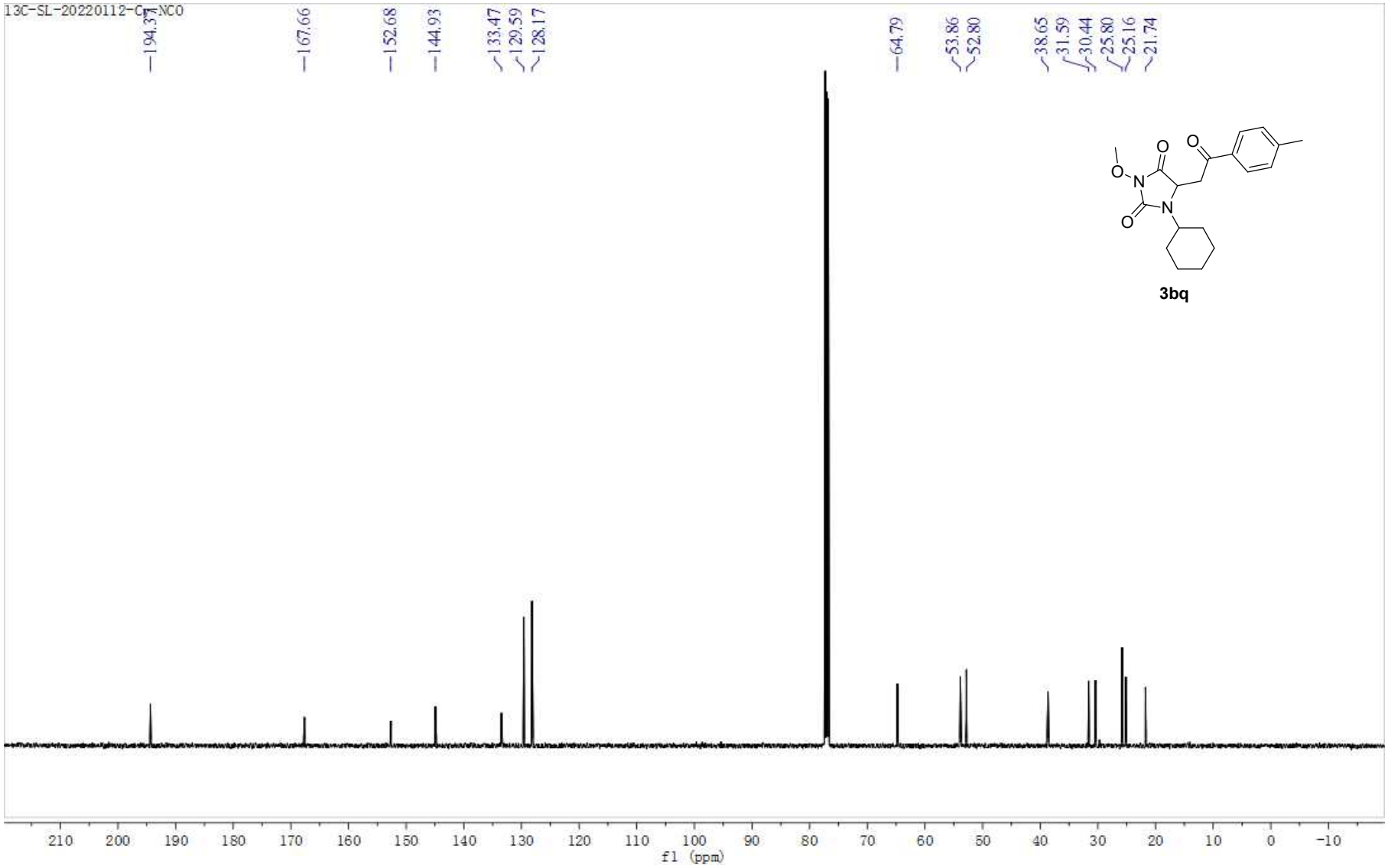

1H-SL-20211227-3
7.58
7.56
7.19
7.15
7.14
7.13
7.13
7.12
7.11
7.09
7.08
7.08
7.07
7.07
7.06
4.58
4.55
4.30
4.27
4.22
4.21
4.21
4.20
4.03
3.42
3.41
3.38
3.37
3.25
3.24
3.21
2.33
7.21
7.16
2.01
6.04
1.00
7.6
7.5
7.4
7.3
7.2
7.1
f1 (ppm)
O
N
O
O
N
O
3bo
2.01
6.04
1.00
1.00
1.00
0.97
3.00
1.00
1.01
3.02
f1 (ppm)

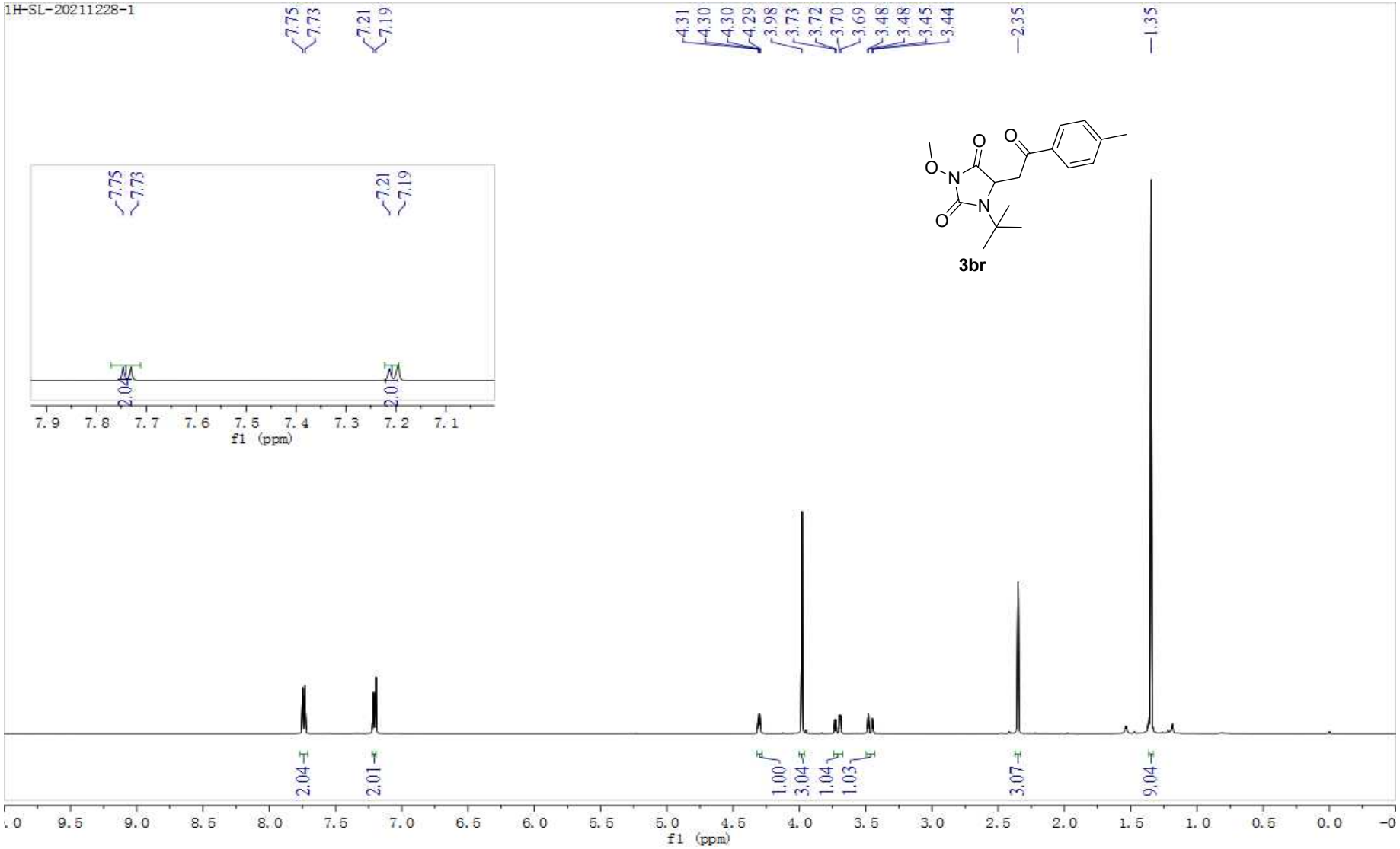

13C-SL-20211227-3
194.38
167.44
153.41
144.84
135.55
133.10
129.35
128.90
128.11
128.08
128.06
65.02
53.91
45.79
37.43
21.73
3bo
f1 (ppm)

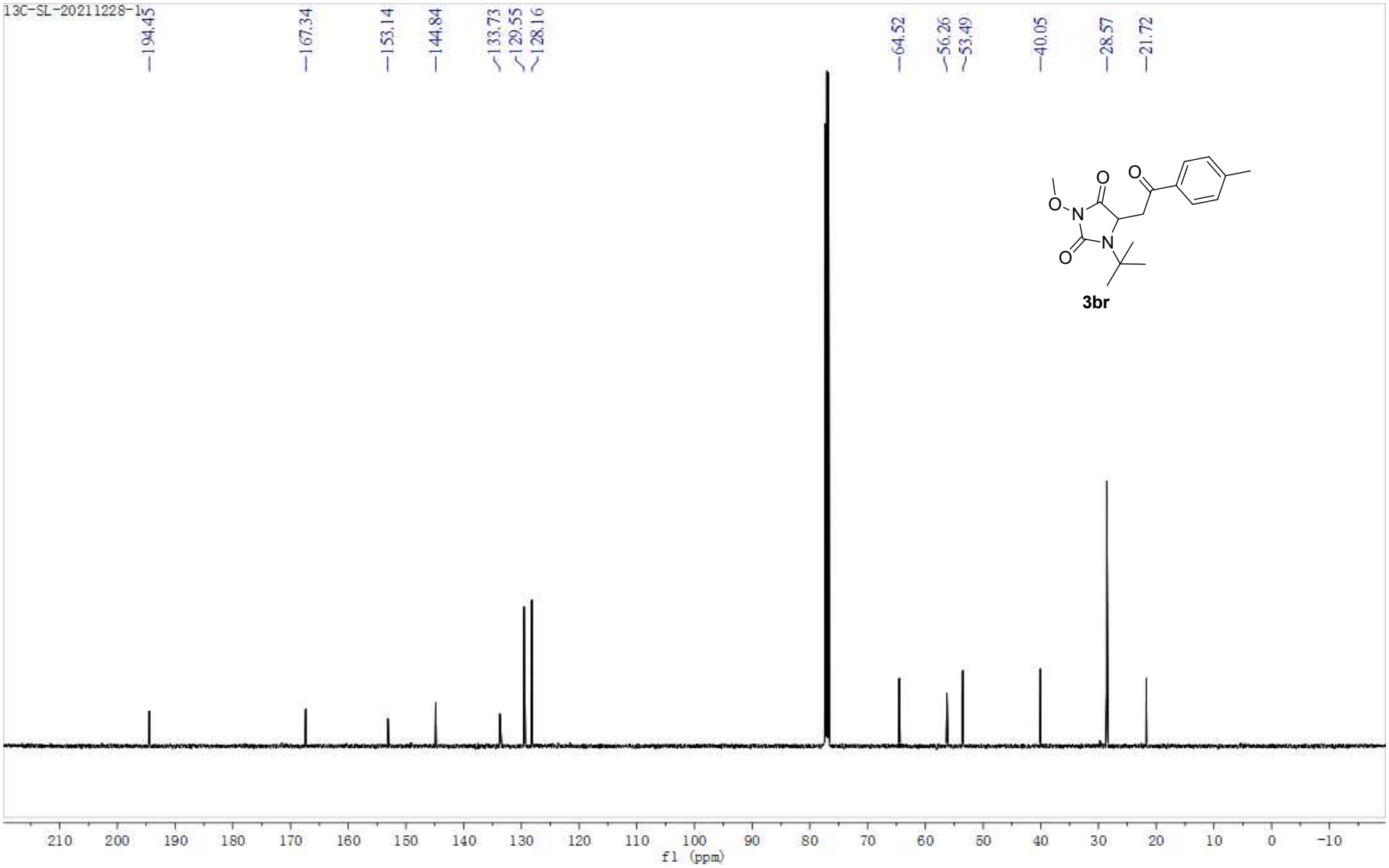

1H-SL-20211227-4
7.78
7.76
7.23
7.21
7.20
4.40
4.39
4.39
4.38
3.99
3.65
3.65
3.47
3.47
3.46
3.45
3.45
3.42
3.41
2.36
2.01
2.01
2.00
2.00
1.99
1.99
1.98
1.97
1.96
1.96
O
O
O
N
N
Cl
3bp
2.00
2.01
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1
f1 (ppm)
2.00
2.01
1.00
3.03
1.03
1.04
2.05
1.05
1.03
3.02
2.10
f1 (ppm)

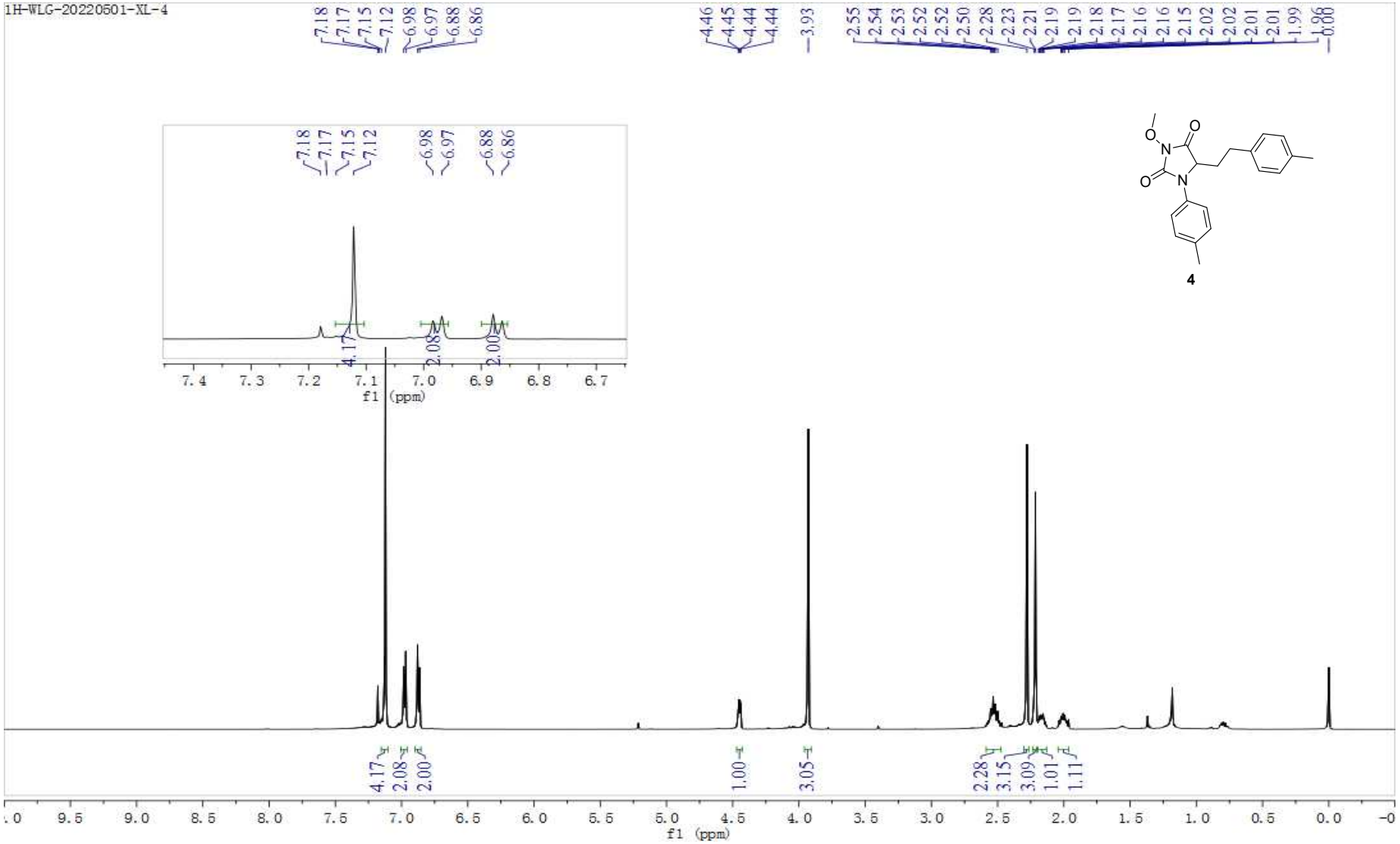

13C-SL-20211228-4-21
194.53
167.38
153.17
145.23
133.08
129.62
128.29
65.09
54.20
42.06
39.71
37.93
30.64
21.76
O
O
O
N
N
Cl
3bp
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

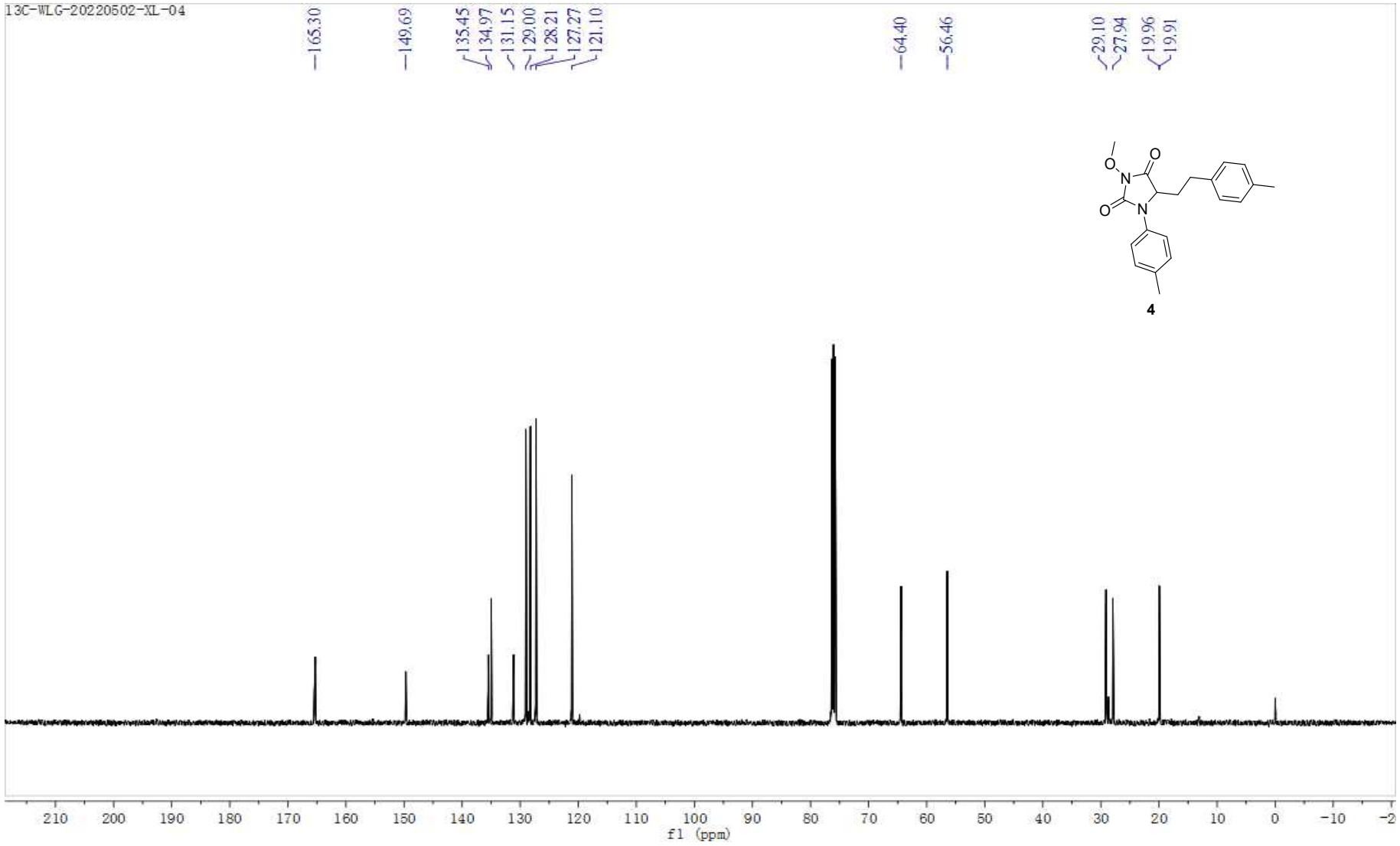

3bq
f1 (ppm)


13C-SL-20220112-C-NCO
194.37
167.66
152.68
144.93
133.47
129.59
128.17
64.79
53.86
52.80
38.65
31.59
30.44
25.80
25.16
21.74
3bq
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)


1H-SL-20211228-1
7.75
7.73
7.21
7.19
4.31
4.30
4.30
4.29
3.98
3.73
3.72
3.70
3.69
3.48
3.48
3.45
3.44
2.35
1.35
3br
2.04
2.01
1.00
3.04
1.04
1.03
3.07
9.04
f1 (ppm)

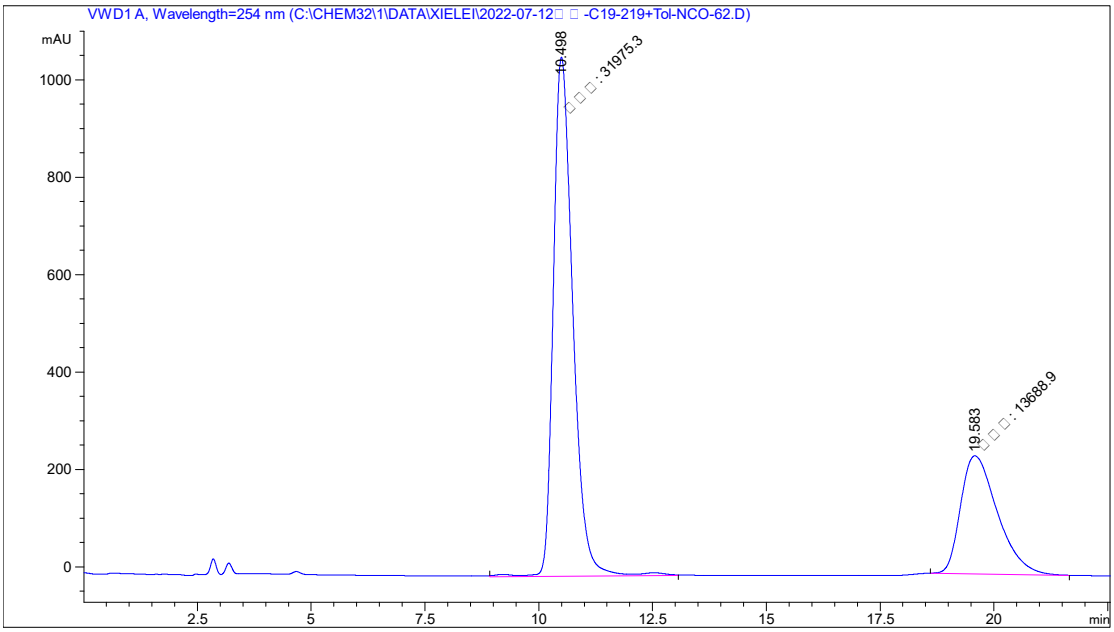

13C-SL-20211228-1
194.45
167.34
153.14
144.84
133.73
129.55
128.16
64.52
56.26
53.49
40.05
28.57
21.72
3br
f1 (ppm)


1H-WLG-20220501-XL-4
7.18
7.17
7.15
7.12
6.98
6.97
6.88
6.86
4.46
4.45
4.44
4.44
3.93
2.55
2.54
2.53
2.52
2.52
2.50
2.28
2.23
2.21
2.19
2.19
2.18
2.17
2.16
2.16
2.15
2.02
2.02
2.01
2.01
1.99
1.86
6.00
4.17
2.08
2.00
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
f1 (ppm)
4
1.00
3.05
2.28
3.15
3.09
1.01
1.11
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)

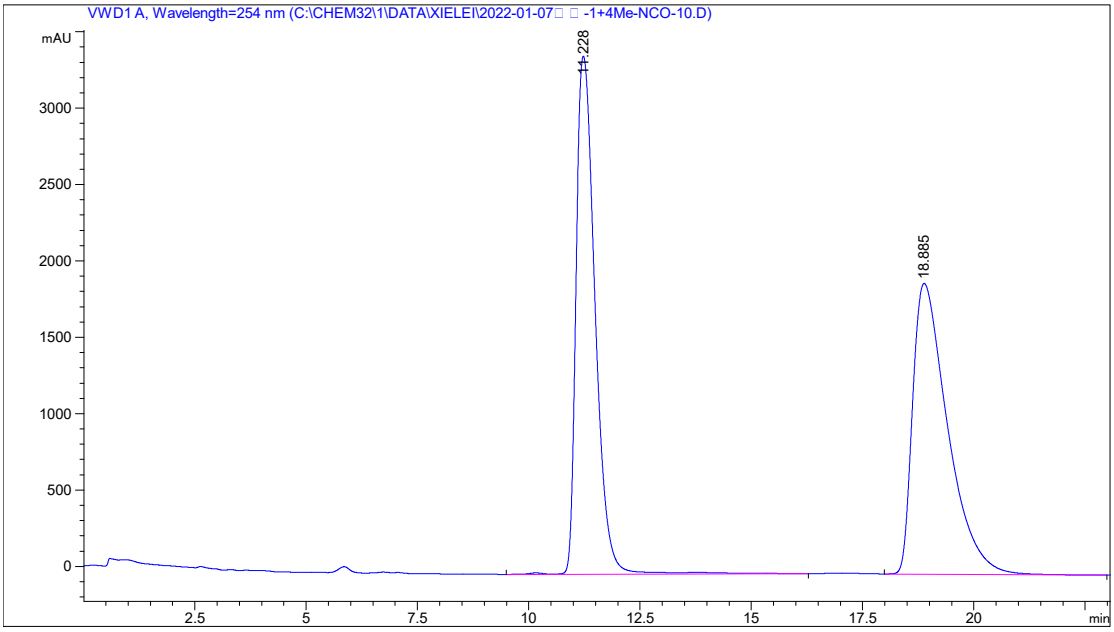

13C-WLG-20220602-XL-04
165.30
149.69
135.45
134.97
131.15
129.00
128.21
127.27
121.10
64.40
56.46
29.10
27.94
19.96
19.91
4
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −2
f1 (ppm)

10. HPLC Chromatograms for the product 3ba

Daicel Chiralcel OD-H, n-hexane/i-PrOH = 70:30, 1.0 mL/min, 254 nm; t_R (major) = 10.498 min, t_R (minor) = 19.583 min; 40% ee.

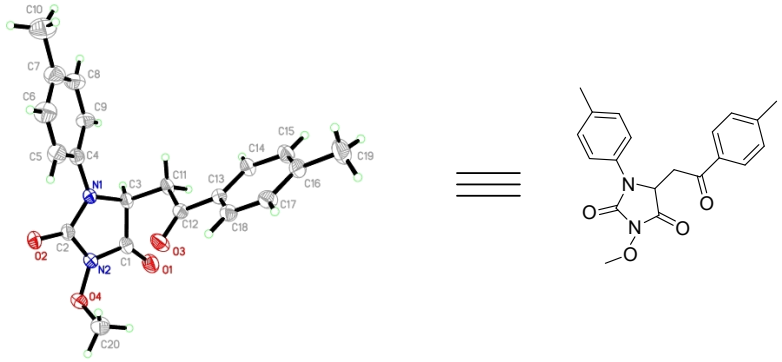


#	Time	Area	Height	Width	Symmetry	Area%
1	10.498	31975.3	1066.8	0.4996	0.68	70.023
2	19.583	13688.9	242.7	0.94	0.606	29.977



#	Time	Area	Height	Width	Symmetry	Area%
1	11.228	100985.1	3392	0.4582	0.583	49.279
2	18.885	103939.3	1903.7	0.825	0.458	50.721

11. X-Ray Crystallographic Data of 3ba



Empirical formula	$C_{20}H_{20}N_2O_4$
Formula weight	352.38
Temperature/K	296.15
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.5244(17)
b/Å	15.008(2)
c/Å	12.4894(18)
α/°	90
β/°	116.449(2)
γ/°	90
Volume/Å^3	2101.8(5)
Z	4
ρ_{calc}g/cm^3	1.114
μ/mm^{-1}	0.078
F(000)	744.0
Crystal size/mm^3	0.2 × 0.15 × 0.1
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.542 to 55.5
Index ranges	-16 ≤ h ≤ 11, -19 ≤ k ≤ 19, -14 ≤ l ≤ 15
Reflections collected	12706
Independent reflections	4864 [R_{int} = 0.0260, R_{sigma} = 0.0345]
Data/restraints/parameters	4864/0/238
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0494, wR_2 = 0.1306
Final R indexes [all data]	R_1 = 0.0836, wR_2 = 0.1497
Largest diff. peak/hole / e Å^{-3}	0.16/-0.21