Lactonization with Concomitant 1,2-Aryl Migration and Alkoxylation Mediated by Dialkoxyphenyl Iodides Generated *in situ*

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Supporting Information

Contents

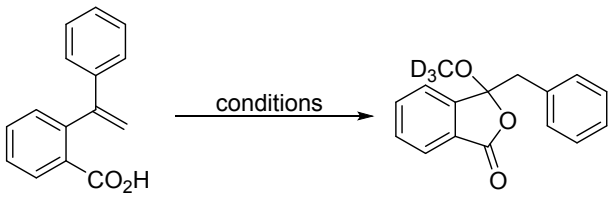
I. General Information

^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz or 600 MHz spectrometer at 25 ^{o}C. Chemical shifts values are given in ppm and referred as the internal standard to TMS: 0.00 ppm. Chemical shifts were expressed in parts per million (δ) downfield from the internal standard tetramethylsilane, and were reported as s (singlet), d (doublet), t (triplet), q (quadruple), dd (doublet of doublet), m (multiplet), etc. The coupling constants *J*, are reported in Hertz (Hz). High resolution mass spectrometry (HRMS) was obtained on a Q-TOF micro spectrometer. HPLC analysis was conducted using Ultimate 3000 and chiral column of Daicel CHIRALCEL AD-H (4.6 mm × 25 cm). Melting points were determined with a Micromelting point apparatus. TLC plates were visualized by exposure to ultraviolet light.

Reagents and solvents were purchased as reagent grade and were used without further purification. All reactions were performed in standard glassware, heated at 70 ^{o}C for 3 h before used. Flash column chromatography was performed over silica gel (200-300 m) using a mixture of ethyl acetate (EtOAc) and petroleum ether (PE).

II. Optimization of Reaction Conditions

Table S1. Optimization of reaction conditions of 3a[a]



1a **3a**

Entry	Oxidant (equiv)	Solvent	CD_3OD (equiv)	T(℃)	Time (h)	Yield (%)[b]
1	PhIO (3.0)	CD_3OD	-	reflux	0.5	40
2	PhIO (3.0)	DCE	8.0	reflux	12	45
3	PhIO (3.0)	DCM	8.0	reflux	2.0	65
4	PhIO (3.0)	DMF	8.0	80	24	NR
5	PhIO (3.0)	toluene	8.0	80	24	NR
6	PhIO (3.0)	EtOAc	8.0	reflux	24	trace
7	PhIO (3.0)	DCM	10.0	reflux	1.0	74
8	PhIO (3.0)	DCM	12.0	reflux	0.5	73
9[c]	PhIO (3.0)	DCM	10.0	reflux	0.2	76
10[d]	**PhIO (3.0)**	**DCM**	**10.0**	**reflux**	**0.2**	**80**
11[e]	PhIO (3.0)	DCM	10.0	reflux	0.2	60

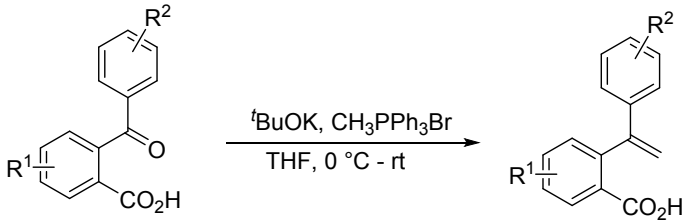
[a] Reaction conditions: **1a** (0.5 mmol) in solvent (5 mL), unless otherwise stated. [b] Isolated yield. [c] BF_3•Et_2O (10% mmol) was added. [d] BF_3•Et_2O (20% mmol) was added. [e] $FeCl_3$ (20% mmol) was added.

Considering the fact that it is not economical to use the costly CD_3OD as solvent as well as reactant for this transformation (Table S1, entry 1), we came to further optimize the reaction conditions by screening other solvents including DCE, DMF, toluene, EtOAc, and DCM. Specifically, when DCE was used as solvent, the reaction afforded the corresponding deuterated product **3a** in 45% yield after refluxing the reaction mixture for 12 h (Table S1, entry 2). Pleasingly, switching DCE to DCM, which possesses a lower boiling point, the desired product **3a** was obtained in an acceptable yield (Table S1, entry 3). Unfortunately, no reaction occurred in each case when DMF or toluene was used as solvent (Table S1, entries 4 -5). EtOAc was also not an appropriate solvent for the reaction as only trace of target product was

observered (Table S1, entry 6). To our pleasant, when 10 equiv of CD_3OD in DCM was applied, the yield of the target product could be improved to 74% yield (Table S1, entry 7). Further improving the dosage of CD_3OD to 12 equiv did not bring about a better outcome (Table S1, entry 8). Much to our delight, the adding of Lewis acids including $BF_3•Et_2O$ or $FeCl_3$ as additive could greatly shorten the reaction time (Table S1, entries 9-11). Finally, the most optimal conditions were concluded to be: 1 equiv of substrate, 3 equiv of PhIO, 10.0 equiv of CD_3OD, 20% mmol of $BF_3•Et_2O$ in DCM at reflux temperature (Table S1, entry 10).

III. Experimental Procedures and Spectroscopic Data

1. General procedure for the synthesis of substrates 1 (1a-m):[1]

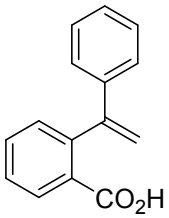


A 1

To a suspension of methyltriphenylphosphonium bromide (7.14 g, 20.0 mmol) in THF (100 mL) was added potassium *tert*-butoxide (3.36 g, 30.0 mmol) at 0 °C. The mixture was stirred for 30 min and then acid **A** (10.0 mmol) was added. The mixture was allowed to warm to room temperature, and stirred for 16 h. After evaporation of THF, the mixture was treated with aq NaOH (10%, 100 mL). The aqueous layer was washed with CH_2Cl_2 (50 mL) and acidified with aq HCl (3 N) to pH = 1. The aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with a saturated aq solution of NaCl (100 mL), dried over $MgSO_4$, and evaporated *in vacuo*. The residue was purified by recystallization from EtOAc/petroleum ether to give the product as a white solid.

2. Spectroscopic Data of Substrates 1 (1a-m):

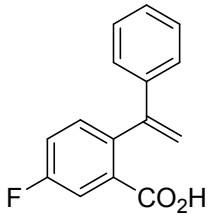
2-(1-Phenylvinyl)benzoic acid (1a)



Following the general procedure, **1a** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (1.4 g, 90% yield); mp: 130-132 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.33 (br s, 1H), 7.93 (d, J = 9.1 Hz, 1H), 7.56 (td, J = 7.5, 1.0 Hz, 1H), 7.43 (td, J = 7.7, 1.0 Hz, 1H), 7.38 (d, J = 7.5 Hz, 1H), 7.27 – 7.19 (m, 5H), 5.67 (s, 1H), 5.23 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3, 149.6, 143.7,

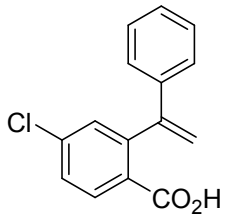
140.9, 132.4, 131.5, 130.7, 129.5, 128.1, 127.6, 127.5, 126.8, 114.4. HRMS (ESI) calcd for $C_{15}H_{12}NaO_2^+$ [M + Na^+] 247.0735, found 247.0738.

5-Fluoro-2-(1-phenylvinyl)benzoic acid (1b)



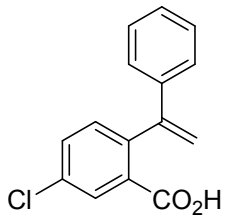
Following the general procedure, **1b** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (1.1 g, 74% yield); mp: 132-134 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (br s, 1H), 7.62 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.35 (dd, *J* = 8.5, 5.5 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.26 – 7.16 (m, 5H), 5.66 (d, *J* = 0.8 Hz, 1H), 5.20 (d, *J* = 0.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0 (d, $^4J_{C\text{-}F}$ = 2.5 Hz), 161.7 (d, $^1J_{C\text{-}F}$ = 249.1 Hz), 148.51, 140.69, 139.7 (d, $^4J_{C\text{-}F}$ = 3.6 Hz), 133.3 (d, $^3J_{C\text{-}F}$ = 7.5 Hz), 131.0 (d, $^3J_{C\text{-}F}$ = 7.4 Hz), 128.16, 127.65, 126.70, 119.5 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 117.5 (d, $^2J_{C\text{-}F}$ = 23.6 Hz), 114.81. HRMS (ESI) calcd for $C_{15}H_{11}FNaO_2^+$ [M + Na^+] 265.0641, found 265.0643.

4-Chloro-2-(1-phenylvinyl)benzoic acid (1c)



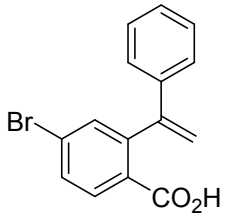
Following the general procedure, **1c** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A pale yellow solid (1.2 g, 68% yield); mp: 143-145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.38 (br s, 1H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.24 (t, *J* = 6.2 Hz, 3H), 7.19 (dd, *J* = 7.5, 2.0 Hz, 2H), 5.68 (s, 1H), 5.22 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 148.4, 145.5, 140.2, 138.8, 132.2, 131.6, 128.2, 127.9, 127.7, 126.7, 115.0. HRMS (ESI) calcd for $C_{15}H_{11}{}^{35}ClNaO_2^+$ [M + Na^+] 281.0340, found 281.0342.

5-Chloro-2-(1-phenylvinyl)benzoic acid (1d)



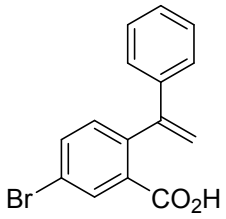
Following the general procedure, **1d** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (1.1 g, 66% yield); mp: 163-165 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (br s, 1H), 7.90 (d, J = 2.3 Hz, 1H), 7.53 (dd, J = 8.2, 2.3 Hz, 1H), 7.32 (d, J = 8.2 Hz, 1H), 7.26 – 7.21 (m, 3H), 7.21 – 7.17 (m, 2H), 5.67 (s, 1H), 5.21 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 148.4, 142.1, 140.5, 133.6, 132.9, 132.5, 130.9, 130.6, 128.2, 127.7, 126.7, 114.9. HRMS (ESI) calcd for $C_{15}H_{11}{}^{35}ClNaO_2^+$ [M + Na^+] 281.0340, found 281.0342.

4-Bromo-2-(1-phenylvinyl)benzoic acid (1e)



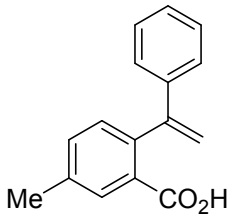
Following the general procedure, **1e** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (1.3 g, 65% yield); mp: 149-151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 1H), 7.60 – 7.52 (m, 2H), 7.24 (dd, J = 7.1, 5.4 Hz, 3H), 7.21 – 7.16 (m, 2H), 5.68 (s, 1H), 5.22 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 148.3, 145.5, 140.2, 134.4, 132.2, 130.9, 128.2, 128.2, 127.7, 127.4, 126.7, 115.0. HRMS (ESI) calcd for $C_{15}H_{11}{}^{79}BrNaO_2^+$ [M + Na^+] 324.9835, found 324.9836.

5-Bromo-2-(1-phenylvinyl)benzoic acid (1f)



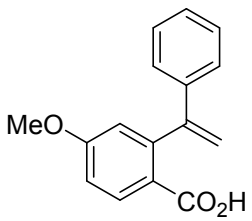
Following the general procedure, **1f** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (0.8 g, 78% yield); mp: 176-178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 2.1 Hz, 1H), 7.68 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.26 – 7.22 (m, 4H), 7.21 – 7.16 (m, 2H), 5.67 (s, 1H), 5.21 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 148.5, 142.5, 140.3, 135.4, 133.5, 133.1, 131.0, 128.2, 127.8, 126.7, 121.4, 114.9. HRMS (ESI) calcd for $C_{15}H_{11}{}^{79}BrNaO_2^+$ [M + Na^+] 324.9835, found 324.9836.

5-Methyl-2-(1-phenylvinyl)benzoic acid (1g)



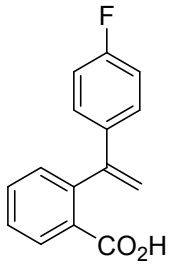
Following the general procedure, **1g** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (0.6 g, 72% yield); mp: 143-145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (br s, 1H), 7.73 (s, 1H), 7.37 (d, *J* = 7.7 Hz, 1H), 7.26 – 7.17 (m, 6H), 5.63 (s, 1H), 5.20 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.5, 141.1, 140.8, 137.6, 133.1, 131.5, 131.1, 129.3, 128.7, 128.1, 127.4, 126.8, 114.2, 21.0. HRMS (ESI) calcd for $C_{16}H_{14}NaO_2^+$ [M + Na^+] 261.0891, found 261.0892.

4-Methoxy-2-(1-phenylvinyl)benzoic acid (1h)



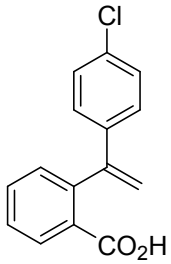
Following the general procedure, **1h** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (0.5 g, 78% yield); mp: 166-168 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 2.8 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.25 – 7.17 (m, 4H), 7.09 (dd, *J* = 8.4, 2.8 Hz, 1H), 5.63 (d, *J* = 1.0 Hz, 1H), 5.19 (d, *J* = 1.0 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 158.8, 149.1, 141.2, 135.9, 132.8, 130.3, 128.1, 127.5, 126.8, 118.5, 115.1, 114.2, 55.6. HRMS (ESI) calcd for $C_{16}H_{14}NaO_3^+$ [M + Na^+] 277.0835, found 277.0839.

2-(1-(4-Fluorophenyl)vinyl)benzoic acid (1i)



Following the general procedure, **1i** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (1.8 g, 89% yield); mp: 143-145 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.44 (br s, 1H), 7.93 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.57 (td, *J* = 7.5, 1.3 Hz, 1H), 7.44 (td, *J* = 7.6, 1.1 Hz, 1H), 7.36 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.21 – 7.14 (m, 2H), 6.96 – 6.89 (m, 2H), 5.60 (s, 1H), 5.20 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.0, 162.3 (d, $^{1}J_{C\text{-}F}$ = 245.2 Hz), 148.6, 143.4, 137.1, 132.6, 131.5, 130.7, 129.3, 128.4 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 127.8, 114.9 (d, $^{2}J_{C\text{-}F}$ = 21.4 Hz), 114.20. HRMS (ESI) calcd for $C_{15}H_{11}FNaO_2^+$ [M + Na^+] 265.0641, found 265.0644.

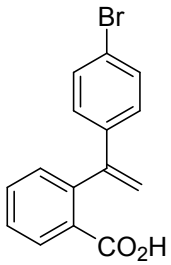
2-(1-(4-Chlorophenyl)vinyl)benzoic acid (1j)



Following the general procedure, **1j** was purified by silica gel chromatography

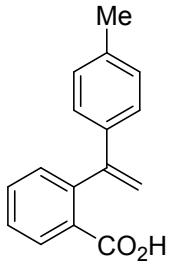
(EtOAc/petroleum ether, 1:1). A white solid (1.7 g, 90% yield); mp: 162-164 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.48 (br s, 1H), 7.95 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.58 (td, *J* = 7.5, 1.4 Hz, 1H), 7.45 (td, *J* = 7.6, 1.3 Hz, 1H), 7.35 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.24 – 7.19 (m, 2H), 7.17 – 7.11 (m, 2H), 5.65 (d, *J* = 0.5 Hz, 1H), 5.23 (d, *J* = 0.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 148.5, 143.2, 139.4, 133.3, 132.7, 131.6, 130.9, 129.1, 128.3, 128.0, 127.9, 114.8. HRMS (ESI) calcd for $C_{15}H_{11}{}^{35}ClNaO_2^+$ [M + Na^+] 281.0345, found 281.0348.

2-(1-(4-Bromophenyl)vinyl)benzoic acid (1k)



Following the general procedure, **1k** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (1.9 g, 89% yield); mp: 143-144 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.58 (td, *J* = 7.5, 1.4 Hz, 1H), 7.45 (td, *J* = 7.6, 1.3 Hz, 1H), 7.36 (td, *J* = 6.6, 1.5 Hz, 3H), 7.12 – 7.05 (m, 2H), 5.66 (s, 1H), 5.23 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 148.6, 143.1, 139.9, 132.7, 131.6, 131.2, 130.9, 129.2, 128.3, 127.9, 121.5, 114.9. HRMS (ESI) calcd for $C_{15}H_{11}{}^{79}BrNaO_2^+$ [M + Na^+] 324.9840, found 324.9842.

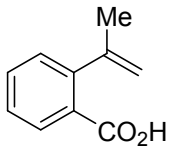
2-(1-(*p*-Tolyl)vinyl)benzoic acid (1l)



Following the general procedure, **1l** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (2.0 g, 88% yield); mp: 133-134 °C. ^{1}H

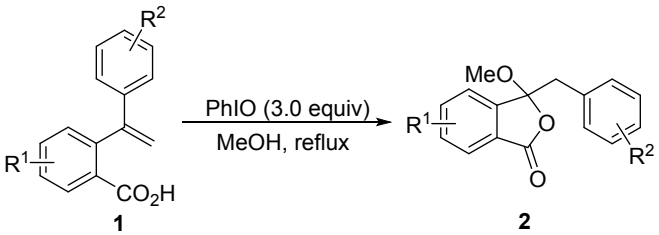
NMR (600 MHz, $CDCl_3$) δ 10.75 (s, 1H), 7.95 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.58 (td, *J* = 7.5, 1.3 Hz, 1H), 7.45 (td, *J* = 7.7, 1.1 Hz, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 5.66 (s, 1H), 5.19 (s, 1H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.6, 149.4, 143.8, 138.1, 137.3, 132.3, 131.5, 130.6, 128.8, 127.5, 126.7, 125.1, 113.5, 21.1. HRMS (ESI) calcd for $C_{16}H_{14}NaO_2^+$ [M + Na^+] 261.0891, found 261.0892.

2-(Prop-1-en-2-yl)benzoic acid (1m)



Following the general procedure, **1m** was purified by silica gel chromatography (EtOAc/petroleum ether, 1:1). A white solid (2.4 g, 85% yield); mp: 70-72 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 11.94 (br s, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.51 (td, *J* = 7.5, 1.1 Hz, 1H), 7.36 (td, *J* = 7.7, 1.0 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 5.14 (s, 1H), 4.91 (s, 1H), 2.14 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.3, 146.6, 146.3, 132.5, 130.7, 129.7, 128.1, 127.0, 113.9, 24.3. HRMS (ESI) calcd for $C_{10}H_{10}NaO_2^+$ [M + Na^+] 185.0573, found 185.0576.

3. General Procedure for the Synthesis of 3-Methoxyisobenzofuran-1(3*H*)-ones 2 (2a-j):

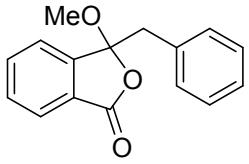


1 2

To a solution of substrate **1** (0.5 mmol) in MeOH (5 mL) was slowly added PhIO (1.5 mmol, 330 mg) at room temperature. The mixture was kept stirring at refluxing until TLC indicated that total consumption of substrate **1**. Then the solvent was removed and the residue was purified by flash column chromatography (5% EtOAc/petroleum ether) to afford the desired compound **2**.

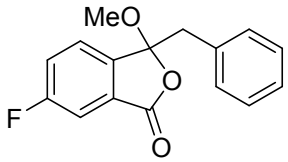
4. Spectroscopic Data of 3-Methoxyisobenzofuran-1(3*H*)-ones 2 (2a-j):

3-Benzyl-3-methoxyisobenzofuran-1(3*H*)-one (2a)



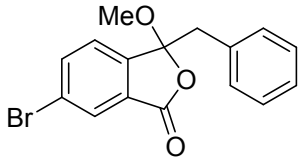
Following the general procedure, **2a** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (112 mg, 88% yield); mp: 93-94 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 7.19 – 7.11 (m, 3H), 7.07 (dd, *J* = 6.4, 3.1 Hz, 2H), 3.44 (d, *J* = 13.8 Hz, 1H), 3.37 (d, *J* = 13.8 Hz, 1H), 3.07 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 145.6, 134.1, 133.5, 130.8, 130.6, 128.2, 128.0, 127.1, 125.4, 123.2, 110.2, 51.4, 44.8. HRMS (ESI) calcd for $C_{16}H_{14}NaO_3^+$ [M + Na^+] 277.0835, found 277.0832.

3-Benzyl-6-fluoro-3-methoxyisobenzofuran-1(3*H*)-one (2b)



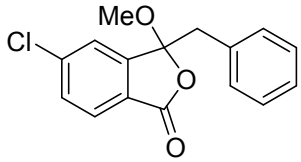
Following the general procedure, **2b** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (103 mg, 76% yield); mp: 101-102 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.0, 2.3 Hz, 1H), 7.32 (td, *J* = 8.5, 2.4 Hz, 1H), 7.20 – 7.14 (m, 4H), 7.06 (dt, *J* = 7.3, 3.6 Hz, 2H), 3.44 (d, *J* = 13.9 Hz, 1H), 3.35 (d, *J* = 13.9 Hz, 1H), 3.10 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.4 (d, $^{4}J_{C\text{-}F}$ = 3.5 Hz), 164.0 (d, $^{1}J_{C\text{-}F}$ = 250.0 Hz), 141.2 (d, $^{4}J_{C\text{-}F}$ = 2.3 Hz), 133.4, 130.7, 130.5 (d, $^{3}J_{C\text{-}F}$ = 8.9 Hz), 128.1, 127.2, 125.0 (d, $^{3}J_{C\text{-}F}$ = 8.6 Hz), 121.8 (d, $^{2}J_{C\text{-}F}$ = 23.7 Hz), 111.9 (d, $^{2}J_{C\text{-}F}$ = 23.6 Hz), 110.1, 51.4, 44.9. HRMS (ESI) calcd for $C_{16}H_{13}FNaO_3^+$ [M + Na^+] 295.0741, found 295.0746.

3-Benzyl-6-bromo-3-methoxyisobenzofuran-1(3*H*)-one (2c)



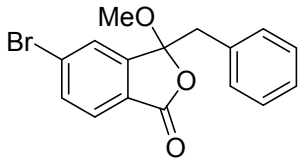
Following the general procedure, **2c** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (117 mg, 70% yield); mp: 105-107 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 1.4 Hz, 1H), 7.73 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.23 – 7.15 (m, 3H), 7.12 – 7.02 (m, 3H), 3.44 (d, *J* = 13.9 Hz, 1H), 3.33 (d, *J* = 13.9 Hz, 1H), 3.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 144.2, 137.1, 133.2, 130.7, 130.2, 128.4, 128.1, 127.3, 124.8, 124.7, 110.2, 51.5, 44.7. HRMS (ESI) calcd for $C_{16}H_{13}{}^{79}BrNaO_3^+$ [M + Na^+] 354.9940, found 354.9943.

3-Benzyl-5-chloro-3-methoxyisobenzofuran-1(3*H*)-one (2d)



Following the general procedure, **2d** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (113 mg, 78% yield); mp: 80-82 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.1 Hz, 1H), 7.48 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.21 (d, *J* = 1.4 Hz, 1H), 7.20 – 7.16 (m, 3H), 7.07 (dt, *J* = 4.2, 3.3 Hz, 2H), 3.41 (d, *J* = 13.9 Hz, 1H), 3.36 (d, *J* = 13.9 Hz, 1H), 3.11 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 147.4, 140.9, 133.1, 131.3, 130.8, 128.2, 127.3, 126.7, 126.5, 123.5, 109.6, 51.6, 44.7. HRMS (ESI) calcd for $C_{16}H_{13}{}^{35}ClNaO_3^+$ [M + Na^+] 311.0445, found 311.0448.

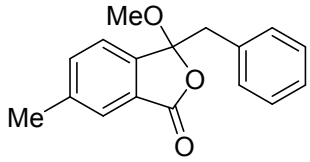
3-Benzyl-5-bromo-3-methoxyisobenzofuran-1(3*H*)-one (2e)



Following the general procedure, **2e** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (153 mg, 92% yield); mp: 110-112 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.38 (d, *J* = 1.2 Hz, 1H), 7.21 – 7.17 (m, 3H), 7.07 (dt, *J* = 4.5, 3.2 Hz, 2H), 3.41 (d, *J*

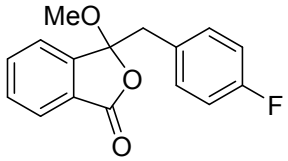
= 14.0 Hz, 1H), 3.36 (d, *J* = 14.0 Hz, 1H), 3.11 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.7, 147.5, 134.1, 133.1, 130.7, 129.3, 128.1, 127.3, 127.2, 126.6, 126.5, 109.5, 51.5, 44.8. HRMS (ESI) calcd for $C_{16}H_{13}{}^{79}BrNaO_3^+$ [M + Na^+] 354.9940, found 354.9945.

3-Benzyl-3-methoxy-6-methylisobenzofuran-1(3*H*)-one (2f)



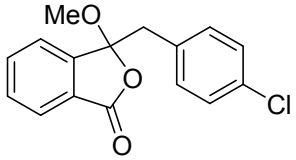
Following the general procedure, **2f** was purified by silica gel chromatography (5% EtOAc/petroleum ether). Colorless oil (120 mg, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.43 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.19 – 7.14 (m, 3H), 7.12 – 7.05 (m, 3H), 3.43 (d, *J* = 13.8 Hz, 1H), 3.33 (d, *J* = 13.8 Hz, 1H), 3.06 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 142.9, 141.0, 135.1, 133.7, 130.8, 128.5, 128.0, 127.0, 125.4, 122.9, 110.1, 51.3, 44.9, 21.3. HRMS (ESI) calcd for $C_{17}H_{16}ClNaO_3^+$ [M + Na^+] 291.0992, found 291.0993.

3-(4-Fluorobenzyl)-3-methoxyisobenzofuran-1(3*H*)-one (2g)



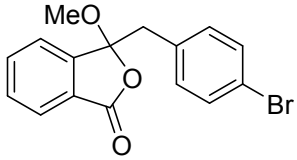
Following the general procedure, **2g** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (125 mg, 92% yield); mp: 111-113 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.04 (dd, *J* = 8.5, 5.5 Hz, 2H), 6.85 (t, *J* = 8.7 Hz, 2H), 3.40 (d, *J* = 14.0 Hz, 1H), 3.35 (d, *J* = 14.0 Hz, 1H), 3.07 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 162.0 (d, $^1J_{C\text{-}F}$ = 244.1 Hz), 145.4, 134.2, 132.3 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 130.7, 129.3 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 128.3, 125.5, 123.0, 114.8 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 110.0, 51.4, 44.1. HRMS (ESI) calcd for $C_{16}H_{13}FNaO_3^+$ [M + Na^+] 295.0741, found 295.0743.

3-(4-Chlorobenzyl)-3-methoxyisobenzofuran-1(3*H*)-one (2h)



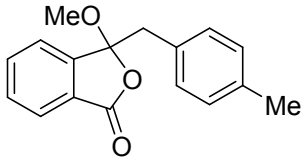
Following the general procedure, **2h** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (118 mg, 82% yield); mp: 102-104 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.66 (td, *J* = 7.5, 1.1 Hz, 1H), 7.53 (td, *J* = 7.5, 0.9 Hz, 1H), 7.26 (dt, *J* = 7.6, 0.8 Hz, 1H), 7.16 – 7.10 (m, 2H), 7.06 – 6.98 (m, 2H), 3.38 (d, *J* = 13.9 Hz, 1H), 3.33 (d, *J* = 13.9 Hz, 1H), 3.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 145.4, 134.2, 133.1, 132.1, 130.8, 128.2, 125.6, 123.0, 109.8, 51.4, 44.2. HRMS (ESI) calcd for $C_{16}H_{13}{}^{35}ClNaO_3^+$ [M + Na^+] 311.0445, found 311.0448.

3-(4-Bromobenzyl)-3-methoxyisobenzofuran-1(3*H*)-one (2i)



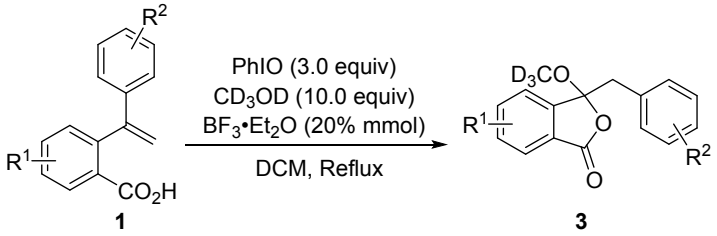
Following the general procedure, **2i** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (148 mg, 89% yield); mp: 67-68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.6 Hz, 1H), 7.66 (td, *J* = 7.5, 1.0 Hz, 1H), 7.54 (td, *J* = 7.5, 0.9 Hz, 1H), 7.32 – 7.28 (m, 2H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.00 – 6.93 (m, 2H), 3.37 (d, *J* = 13.9 Hz, 1H), 3.32 (d, *J* = 13.9 Hz, 1H), 3.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 145.4, 134.2, 132.6, 132.4, 131.2, 130.8, 128.2, 125.6, 123.0, 121.3, 109.7, 51.4, 44.3. HRMS (ESI) calcd for $C_{16}H_{13}{}^{79}BrNaO_3^+$ [M + Na^+] 354.9940, found 354.9942.

3-Methoxy-3-(4-methylbenzyl)isobenzofuran-1(3*H*)-one (2j)



Following the general procedure, **2j** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (125 mg, 93% yield); mp: 51-53 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dt, *J* = 7.6, 0.8 Hz, 1H), 7.64 (td, *J* = 7.5, 1.1 Hz, 1H), 7.51 (td, *J* = 7.5, 0.9 Hz, 1H), 7.26 (t, *J* = 3.8 Hz, 1H), 6.98 – 6.92 (m, 4H), 3.40 (d, *J* = 13.9 Hz, 1H), 3.33 (d, *J* = 13.9 Hz, 1H), 3.07 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 145.7, 136.6, 134.0, 130.6, 130.5, 130.4, 128.7, 128.3, 125.4, 123.1, 110.3, 51.4, 44.4, 21.1. HRMS (ESI) calcd for $C_{17}H_{16}NaO_3^+$ [M + Na^+] 291.0992, found 291.0995.

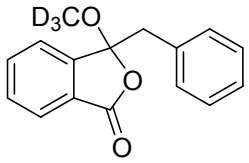
5. General Procedure for the Synthesis of 3-(Methoxy-*d*$_3$)isobenzofuran-1(3*H*)-ones 3 (3a-l):



To a solution of substrate **1** (0.5 mmol) and CD_3OD (5.0 mmol, 160 mg) in DCM (5 mL) was slowly added PhIO (1.5 mmol, 330 mg) and BF_3•Et_2O (20% mmol) at room temperature. The mixture was kept stirring at refluxing until TLC indicated that total consumption of substrate **1**. Then the solvent was removed and the residue was purified by flash column chromatography (5% EtOAc/petroleum ether) to afford the desired compound **3**.

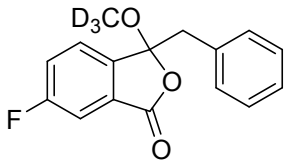
6. Spectroscopic Data of 3-(Methoxy-*d*$_3$)isobenzofuran-1(3*H*)-ones 3 (3a-l):

3-Benzyl-3-(methoxy-*d*$_3$)isobenzofuran-1(3*H*)-one (3a)



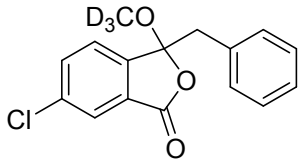
Following the general procedure, **3a** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (104 mg, 80% yield); mp: 94-95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.5, 0.9 Hz, 1H), 7.50 (td, *J* = 7.5, 0.7 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.19 – 7.12 (m, 3H), 7.07 (dt, *J* = 5.3, 3.8 Hz, 2H), 3.44 (d, *J* = 13.8 Hz, 1H), 3.36 (d, *J* = 13.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 145.6, 134.1, 133.5, 130.8, 130.6, 128.3, 128.0, 127.1, 125.4, 123.1, 110.2, 50.6 (t), 44.9. HRMS (ESI) calcd for $C_{16}H_{11}D_3NaO_3^+$ [M + Na^+] 280.1023, found 280.1025.

3-Benzyl-6-fluoro-3-(methoxy-*d*$_3$)isobenzofuran-1(3*H*)-one (3b)



Following the general procedure, **3b** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (111 mg, 80% yield); mp: 102-103 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.1, 2.3 Hz, 1H), 7.32 (td, *J* = 8.5, 2.3 Hz, 1H), 7.20 – 7.14 (m, 4H), 7.06 (dd, *J* = 6.6, 2.9 Hz, 2H), 3.44 (d, *J* = 13.9 Hz, 1H), 3.35 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.4 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 164.0 (d, $^1J_{C\text{-}F}$ = 250.2 Hz), 141.2 (d, $^4J_{C\text{-}F}$ = 2.4 Hz), 133.4, 130.7, 130.5(d, $^3J_{C\text{-}F}$ = 9.1 Hz), 128.1, 127.2, 124.9 (d, $^3J_{C\text{-}F}$ = 8.5 Hz), 121.8 (d, $^2J_{C\text{-}F}$ = 23.7 Hz), 111.9 (d, $^2J_{C\text{-}F}$ = 23.6 Hz), 110.1, 44.9. HRMS (ESI) calcd for $C_{16}H_{10}D_3FNaO_3^+$ [M + Na^+] 298.0929, found 298.0926.

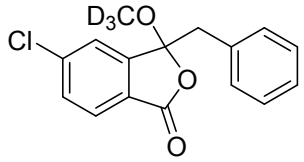
3-Benzyl-6-chloro-3-(methoxy-*d*$_3$)isobenzofuran-1(3*H*)-one (3c)



Following the general procedure, **3c** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (78 mg, 53% yield); mp: 90-92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 1.5 Hz, 1H), 7.58 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.19 (dd,

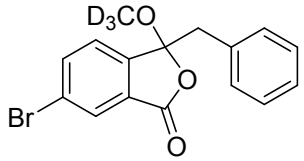
J = 4.2, 2.4 Hz, 3H), 7.11 (d, *J* = 8.1 Hz, 1H), 7.07 (dd, *J* = 6.6, 2.9 Hz, 2H), 3.45 (d, *J* = 13.9 Hz, 1H), 3.33 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 143.8, 137.0, 134.3, 133.2, 130.8, 130.0, 128.2, 127.3, 125.4, 124.4, 110.1, 44.8. HRMS (ESI) calcd for $C_{16}H_{10}D_3{}^{35}ClNaO_3^+$ [M + Na^+] 314.0634, found 314.0636.

3-Benzyl-5-chloro-3-(methoxy-*d*$_3$)isobenzofuran-1(3*H*)-one (3d)



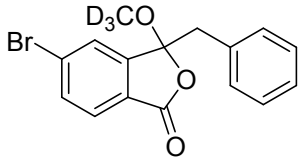
Following the general procedure, **3d** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (108 mg, 73% yield); mp: 79-81 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.1 Hz, 1H), 7.48 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.21 (d, *J* = 1.6 Hz, 1H), 7.19 (dd, *J* = 6.6, 3.6 Hz, 3H), 7.10 – 7.05 (m, 2H), 3.41 (d, *J* = 13.9 Hz, 1H), 3.36 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 147.4, 140.9, 133.1, 131.3, 130.7, 128.2, 127.3, 126.7, 126.5, 123.5, 109.6, 44.7. HRMS (ESI) calcd for $C_{16}H_{10}D_3{}^{35}ClNaO_3^+$ [M + Na^+] 314.0634, found 314.0638.

3-Benzyl-6-bromo-3-(methoxy-*d*$_3$)isobenzofuran-1(3*H*)-one (3e)



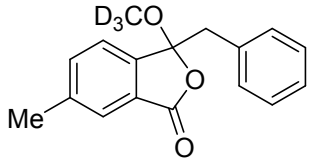
Following the general procedure, **3e** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (122 mg, 72% yield); mp: 106-108 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (d, *J* = 1.5 Hz, 1H), 7.73 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.22 – 7.16 (m, 3H), 7.07 (dt, *J* = 7.4, 3.8 Hz, 2H), 7.05 (d, *J* = 8.1 Hz, 1H), 3.44 (d, *J* = 14.0 Hz, 1H), 3.33 (d, *J* = 14.0 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.1, 144.3, 137.0, 133.2, 130.7, 130.3, 128.4, 128.1, 127.3, 124.8, 124.7, 110.2, 44.7. HRMS (ESI) calcd for $C_{16}H_{10}D_3{}^{79}BrNaO_3^+$ [M + Na^+] 358.0129, found 358.0128.

3-Benzyl-5-bromo-3-(methoxy-*d*$_3$)isobenzofuran-1(3*H*)-one (3f)



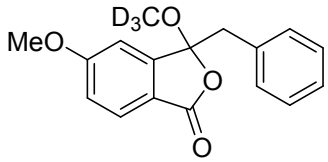
Following the general procedure, **3f** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (129 mg, 76% yield); mp: 111-112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 1.2 Hz, 1H), 7.22 – 7.16 (m, 3H), 7.07 (dt, *J* = 4.2, 3.3 Hz, 2H), 3.41 (d, *J* = 13.9 Hz, 1H), 3.35 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 147.5, 134.2, 133.1, 130.8, 129.4, 128.1, 127.3, 127.1, 126.6, 126.5, 109.5, 44.8. HRMS (ESI) calcd for $C_{16}H_{10}D_3{}^{79}BrNaO_3^+$ [M + Na^+] 358.0129, found 358.0126.

3-Benzyl-3-(methoxy-*d*$_3$)-6-methylisobenzofuran-1(3*H*)-one (3g)



Following the general procedure, **3g** was purified by silica gel chromatography (5% EtOAc/petroleum ether). Colorless oil (96 mg, 70% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.42 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.16 (dd, *J* = 6.7, 3.5 Hz, 3H), 7.08 (dd, *J* = 8.6, 4.2 Hz, 3H), 3.42 (d, *J* = 13.9 Hz, 1H), 3.33 (d, *J* = 13.9 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.0, 142.9, 141.0, 135.1, 133.7, 130.8, 128.5, 128.0, 127.0, 125.4, 122.9, 110.1, 44.9, 21.3. HRMS (ESI) calcd for $C_{17}H_{13}D_3NaO_3^+$ [M + Na^+] 294.1180, found 294.1185.

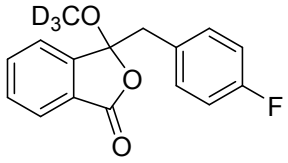
3-Benzyl-5-methoxy-3-(methoxy-*d*$_3$)isobenzofuran-1(3*H*)-one (3h)



Following the general procedure, **3h** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (89 mg, 61% yield); mp: 90-91 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 2.5 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.51 – 7.35 (m, 3H), 7.21 – 7.06 (m, 2H), 3.87 (s, 3H), 3.33 (d, *J* = 16.5 Hz, 1H), 3.27 (d, *J* = 16.6 Hz,

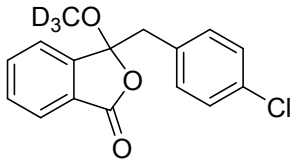
1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 158.9, 139.0, 129.5, 129.0, 128.9, 128.7, 126.0, 125.2, 122.0, 112.9, 106.0, 55.6, 40.4. HRMS (ESI) calcd for $C_{17}H_{13}D_3NaO_4^+$ [M + Na^+] 310.1129, found 310.1126.

3-(4-Fluorobenzyl)-3-(methoxy-*d*$_3$)isobenzofuran-1(3*H*)-one (3i)



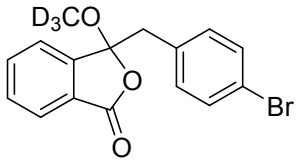
Following the general procedure, **3i** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (77 mg, 55% yield); mp: 112-113 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.66 (td, *J* = 7.5, 1.0 Hz, 1H), 7.53 (td, *J* = 7.5, 0.8 Hz, 1H), 7.26 (d, *J* = 7.7 Hz, 1H), 7.09 – 6.99 (m, 2H), 6.89 – 6.80 (m, 2H), 3.39 (d, *J* = 14.1 Hz, 1H), 3.35 (d, *J* = 14.1 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.6, 162.0 (d, $^1J_{C\text{-}F}$ = 244.3 Hz), 145.5, 134.1, 132.2 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 130.7, 129.3 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 128.3, 125.5, 122.9, 114.9 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 109.9, 44.1. HRMS (ESI) calcd for $C_{16}H_{10}D_3FNaO_3^+$ [M + Na^+] 298.0929, found 298.0928.

3-(4-Chlorobenzyl)-3-(methoxy-*d*$_3$)isobenzofuran-1(3*H*)-one (3j)



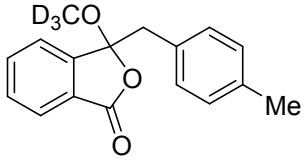
Following the general procedure, **3j** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (105 mg, 71% yield); mp: 102-104 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.66 (td, *J* = 7.5, 0.9 Hz, 1H), 7.53 (td, *J* = 7.5, 0.6 Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.17 – 7.09 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 3.38 (d, *J* = 13.9 Hz, 1H), 3.33 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 145.4, 134.2, 133.1, 132.1, 130.8, 128.2, 125.6, 123.0, 109.8, 50.6 (t), 44.2. HRMS (ESI) calcd for $C_{16}H_{10}D_3{}^{35}ClNaO_2^+$ [M + Na^+] 314.0634, found 314.0636.

3-(4-Bromobenzyl)-3-(methoxy-d_3)isobenzofuran-1(3*H*)-one (3k)



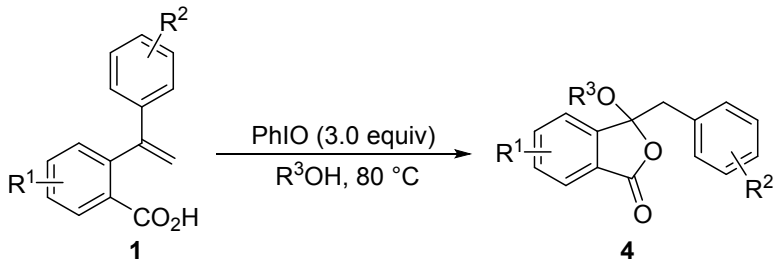
Following the general procedure, **3k** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (115 mg, 68% yield); mp: 66-68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.6 Hz, 1H), 7.66 (td, *J* = 7.5, 1.0 Hz, 1H), 7.59 – 7.49 (m, 1H), 7.34 – 7.28 (m, 2H), 7.24 (s, 1H), 6.99 – 6.92 (m, 2H), 3.37 (d, *J* = 13.9 Hz, 1H), 3.32 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 145.4, 134.2, 132.6, 132.4, 131.2, 130.8, 128.2, 125.6, 122.9, 121.3, 109.7, 44.3. HRMS (ESI) calcd for $C_{16}H_{10}D_3{}^{79}BrNaO_3^+$ [M + Na^+] 358.0129, found 358.0126.

3-(Methoxy-d_3)-3-(4-methylbenzyl)isobenzofuran-1(3*H*)-one (3l)



Following the general procedure, **3l** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (86 mg, 63% yield); mp: 52-54 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.5, 1.0 Hz, 1H), 7.51 (td, *J* = 7.5, 0.8 Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.00 – 6.90 (m, 4H), 3.40 (d, *J* = 13.9 Hz, 1H), 3.33 (d, *J* = 13.9 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 145.7, 136.6, 134.0, 130.6, 130.5, 130.4, 128.7, 128.3, 125.4, 123.1, 110.3, 44.4, 21.1. HRMS (ESI) calcd for $C_{17}H_{13}D_3NaO_3^+$ [M + Na^+] 294.1180, found 294.1186.

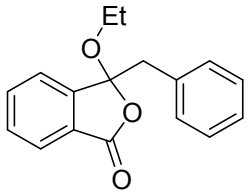
7. General Procedure for the Synthesis of 3-Alkoxyisobenzofuran -1(3*H*)-ones 4 (4a-h):



To a solution of substrate **1** (0.5 mmol) in alcohols (5 mL) was slowly added PhIO (1.5 mmol, 330 mg) at room temperature. The mixture was kept stirring at 80 °C until TLC indicated that total consumption of substrate **1**. Then the solvent was removed and the residue was purified by flash column chromatography (5% EtOAc/petroleum ether) to afford the desired compound **4**.

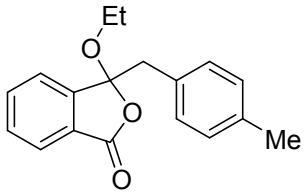
8. Spectroscopic Data of 3-Alkoxyisobenzofuran-1(3*H*)-ones 4 (4a-h):

3-Benzyl-3-ethoxyisobenzofuran-1(3*H*)-one (4a)



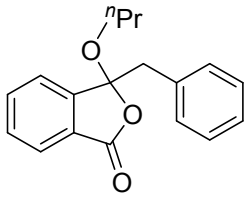
Following the general procedure, **4a** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (97 mg, 72% yield); mp: 76-78 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.61 (td, *J* = 7.5, 1.1 Hz, 1H), 7.48 (td, *J* = 7.5, 0.9 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.18 – 7.11 (m, 3H), 7.09 – 7.00 (m, 2H), 3.50 – 3.34 (m, 3H), 3.06 (dq, *J* = 9.0, 7.0 Hz, 1H), 1.17 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 146.1, 133.9, 133.6, 130.8, 130.4, 128.2, 127.9, 127.0, 125.3, 123.0, 110.1, 59.8, 45.1, 15.1. HRMS (ESI) calcd for $C_{17}H_{16}NaO_3^+$ [M + Na^+] 291.0992, found 291.0996.

3-Ethoxy-3-(4-methylbenzyl)isobenzofuran-1(3*H*)-one (4b)



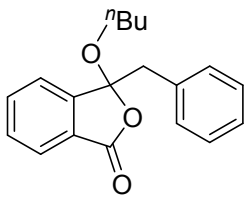
Following the general procedure, **4b** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (92 mg, 65% yield); mp: 67-69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.62 (td, *J* = 7.5, 1.1 Hz, 1H), 7.48 (td, *J* = 7.5, 0.9 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.00 – 6.88 (m, 4H), 3.48 – 3.37 (m, 2H), 3.33 (d, *J* = 13.8 Hz, 1H), 3.05 (dq, *J* = 9.0, 7.0 Hz, 1H), 2.24 (s, 3H), 1.16 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 146.2, 136.5, 133.9, 130.6, 130.4, 130.4, 128.7, 128.3, 125.3, 123.1, 110.2, 59.8, 44.6, 21.1, 15.1. HRMS (ESI) calcd for $C_{19}H_{18}NaO_3^+$ [M + Na^+] 317.1148, found 317.1145.

3-Benzyl-3-propoxyisobenzofuran-1(3*H*)-one (4c)



Following the general procedure, **4c** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (78 mg, 55% yield); mp: 90-91 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.6 Hz, 1H), 7.60 (td, *J* = 7.5, 0.8 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.7 Hz, 1H), 7.17 – 7.13 (m, 3H), 7.07 (dd, *J* = 6.6, 2.9 Hz, 2H), 3.46 (d, *J* = 13.9 Hz, 1H), 3.35 (d, *J* = 13.8 Hz, 1H), 3.33 – 3.28 (m, 1H), 2.92 (dt, *J* = 8.9, 6.6 Hz, 1H), 1.67 – 1.44 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.8, 146.2, 133.8, 133.7, 130.8, 130.4, 128.3, 127.9, 127.0, 125.3, 123.1, 110.0, 65.7, 45.2, 22.8, 10.5. HRMS (ESI) calcd for $C_{18}H_{18}NaO_3^+$ [M + Na^+] 305.1148, found 305.1146.

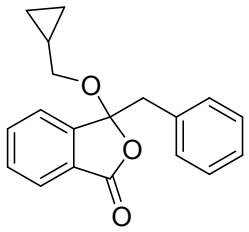
3-Benzyl-3-butoxyisobenzofuran-1(3*H*)-one (4d)



Following the general procedure, **4d** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (107 mg, 72% yield); mp: 91-93 °C. ^{1}H NMR

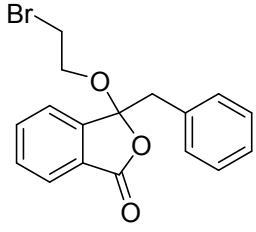
(400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.6 Hz, 1H), 7.60 (td, *J* = 7.5, 1.0 Hz, 1H), 7.49 (td, *J* = 7.5, 0.8 Hz, 1H), 7.15 (dd, *J* = 6.5, 2.6 Hz, 4H), 7.10 – 7.03 (m, 2H), 3.46 (d, *J* = 13.8 Hz, 1H), 3.40 – 3.30 (m, 2H), 2.96 (dt, *J* = 8.9, 6.5 Hz, 1H), 1.56 – 1.47 (m, 2H), 1.39 – 1.25 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 146.2, 133.9, 133.7, 130.8, 130.4, 128.2, 127.9, 127.0, 125.3, 123.1, 110.0, 63.8, 45.2, 31.5, 19.1, 13.7. HRMS (ESI) calcd for $C_{19}H_{20}NaO_3^+$ [M + Na^+] 319.1305, found 319.1306.

3-Benzyl-3-(cyclopropylmethoxy)isobenzofuran-1(3*H*)-one (4e)



Following the general procedure, **4e** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (91 mg, 62% yield); mp: 102-104 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.6 Hz, 1H), 7.61 (td, *J* = 7.5, 0.8 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.17 – 7.10 (m, 3H), 7.09 – 7.00 (m, 2H), 3.48 (d, *J* = 13.9 Hz, 1H), 3.41 (d, *J* = 13.9 Hz, 1H), 3.20 (dd, *J* = 9.9, 6.9 Hz, 1H), 2.86 (dd, *J* = 9.9, 6.9 Hz, 1H), 1.09 – 0.95 (m, 1H), 0.60 – 0.41 (m, 2H), 0.22 – 0.05 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.8, 146.1, 133.9, 133.6, 130.8, 130.4, 128.3, 127.9, 127.0, 125.3, 123.0, 109.9, 68.9, 45.1, 10.4, 3.09, 3.05. HRMS (ESI) calcd for $C_{19}H_{18}NaO_3^+$ [M + Na^+] 317.1148, found 317.1144.

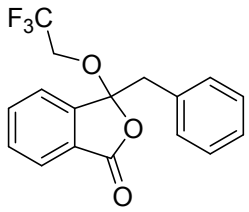
3-Benzyl-3-(2-bromoethoxy)isobenzofuran-1(3*H*)-one (4f)



Following the general procedure, **4f** was purified by silica gel chromatography (5% EtOAc/petroleum ether). Colorless oil (116 mg, 67% yield). ^1H NMR (600 MHz,

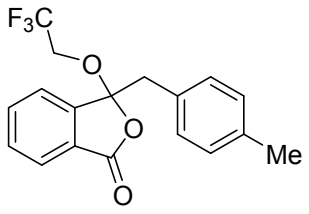
$CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.5, 0.7 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 8.7 Hz, 1H), 7.19 – 7.15 (m, 3H), 7.08 (dd, *J* = 6.4, 3.0 Hz, 2H), 3.71 (dt, *J* = 10.7, 5.4 Hz, 1H), 3.49 (d, *J* = 13.9 Hz, 1H), 3.47 – 3.39 (m, 2H), 3.39 – 3.35 (d, 1H), 3.28 (ddd, *J* = 10.4, 7.6, 5.7 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.4, 145.5, 134.2, 133.3, 130.84, 130.79, 128.04, 128.00, 127.2, 125.4, 123.3, 109.5, 64.0, 45.0, 29.7. HRMS (ESI) calcd for $C_{17}H_{15}{}^{79}BrNaO_3^+$ [M + Na^+] 369.0097, found 369.0095.

3-Benzyl-3-(2,2,2-trifluoroethoxy)isobenzofuran-1(3*H*)-one (4g)



Following the general procedure, **4g** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (134 mg, 83% yield); mp: 59-60 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.68 (td, *J* = 7.5, 1.0 Hz, 1H), 7.56 (td, *J* = 7.5, 0.8 Hz, 1H), 7.28 (s, 1H), 7.21 – 7.13 (m, 3H), 7.06 (dt, *J* = 7.6, 3.8 Hz, 2H), 3.78 (dq, *J* = 11.3, 8.3 Hz, 1H), 3.53 (d, *J* = 13.9 Hz, 1H), 3.43 (d, *J* = 13.9 Hz, 1H), 3.32 (dq, *J* = 11.3, 8.2 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.96 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 144.4, 134.6, 132.7, 131.3, 129.4 (q, $^1J_{C\text{-}F}$ = 261.4 Hz), 127.9, 127.4, 125.7, 124.5, 123.3, 121.8, 109.0, 61.6 (q, $^2J_{C\text{-}F}$ = 35.5 Hz), 44.5. HRMS (ESI) calcd for $C_{17}H_{13}F_3NaO_3^+$ [M + Na^+] 345.0709, found 345.0706.

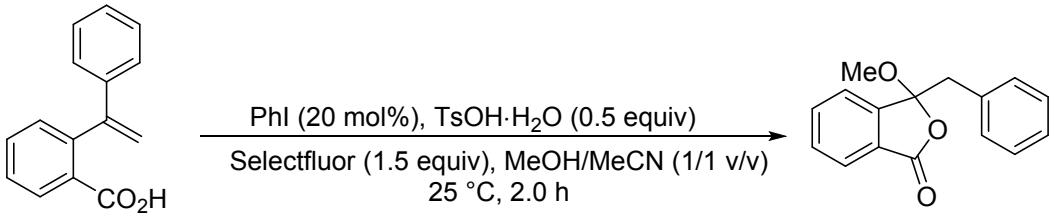
3-(4-Methylbenzyl)-3-(2,2,2-trifluoroethoxy)isobenzofuran-1(3*H*)-one (4h)



Following the general procedure, **4h** was purified by silica gel chromatography (5% EtOAc/petroleum ether). A white solid (108 mg, 64% yield); mp: 98-99 °C. ^{1}H NMR

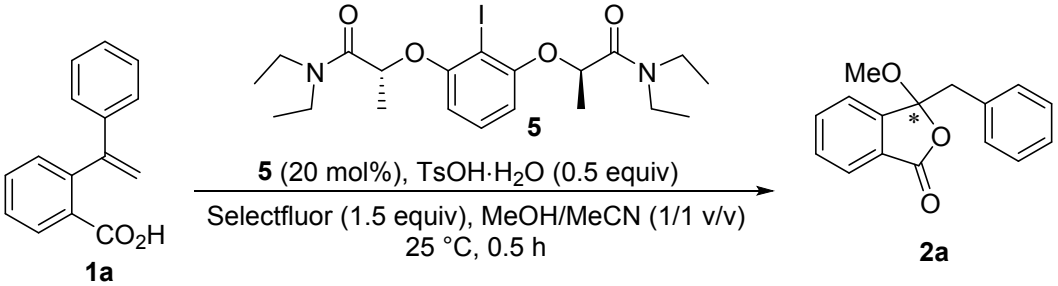
(400 MHz, $CDCl_3$) δ 7.76 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.68 (td, *J* = 7.5, 1.1 Hz, 1H), 7.56 (td, *J* = 7.5, 0.9 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 6.94 (dt, *J* = 6.1, 4.9 Hz, 4H), 3.78 (dq, *J* = 11.3, 8.3 Hz, 1H), 3.49 (d, *J* = 14.0 Hz, 1H), 3.39 (d, *J* = 14.0 Hz, 1H), 3.32 (dq, *J* = 11.3, 8.3 Hz, 1H), 2.25 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.95 (s). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.87, 144.5, 137.0, 134.6, 131.2, 130.6, 129.6, 128.9, 127.9, 125.6, 123.4, 123.2 (q, $^1J_{C\text{-}F}$ = 275.5 Hz), 109.1, 61.6 (q, $^2J_{C\text{-}F}$ = 35.5 Hz), 44.1, 21.0. HRMS (ESI) calcd for $C_{18}H_{15}F_3NaO_3^+$ [M + Na^+] 359.0866, found 359.0863.

9. Procedure for the Synthesis of 3-Methoxyisobenzofuran-1(3*H*)-ones 2a



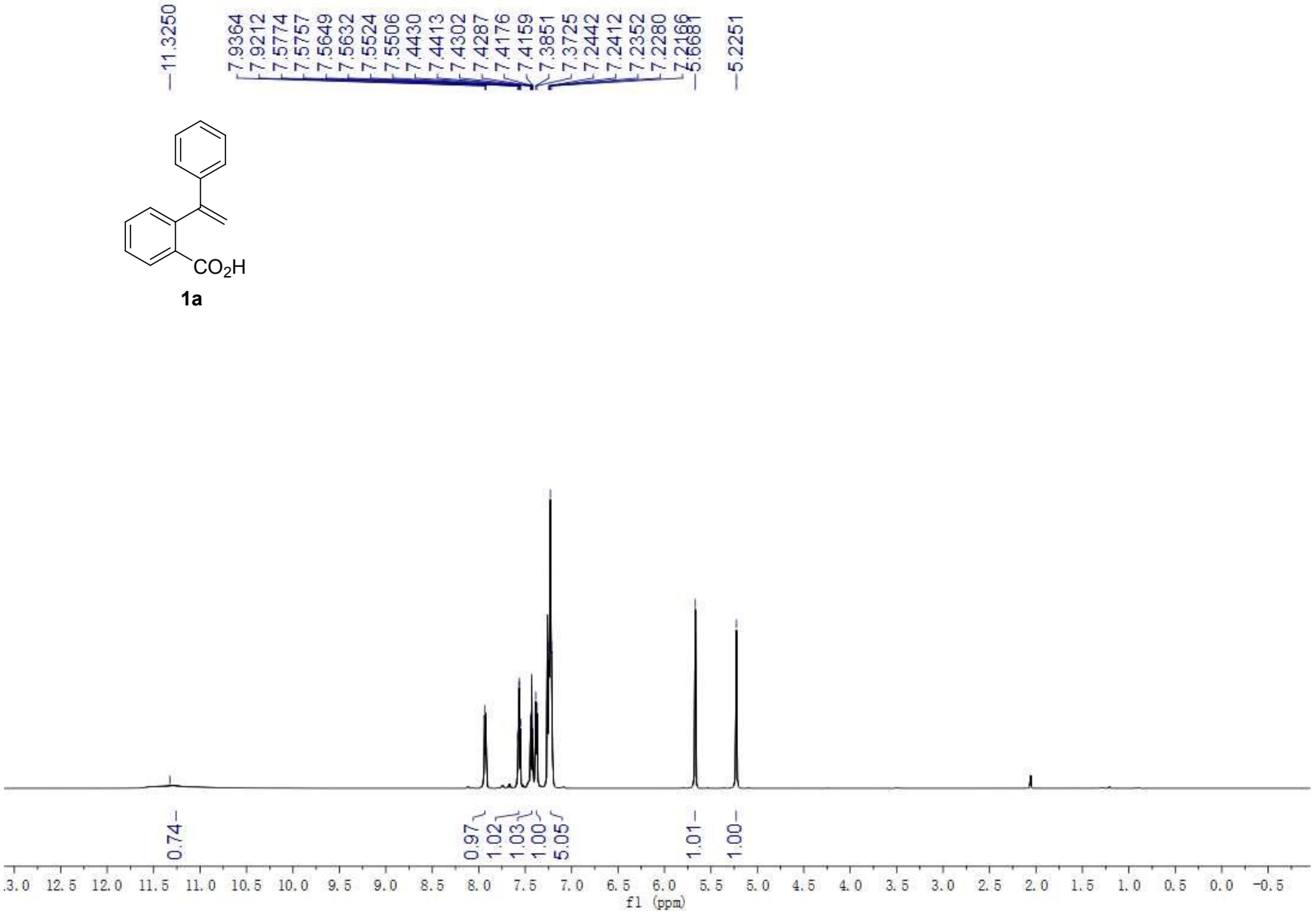
To a Schlenk tube was charged with Selectfluor (265.5 mg, 0.75 mmol), $TsOH{\cdot}H_2O$ (47.5 mg, 0.25 mmol), iodobenzene (20.4 mg, 0.1 mmol) and methanol (1.0 mL). Then a solution of substrate **1a** (112.1 mg, 0.5 mmol) in MeCN (1.0 mL) was added dropwise to the above reaction mixture at room temperature. After the addition was complete, the resulting mixture was stirred at room temperature for another 2.0 hours. Then the solvent was evaoporated and the residue was purified by flash column chromatography (5% EtOAc/petroleum ether) to afford the desired compound **2a** as a white solid (74 mg, 58% yield).

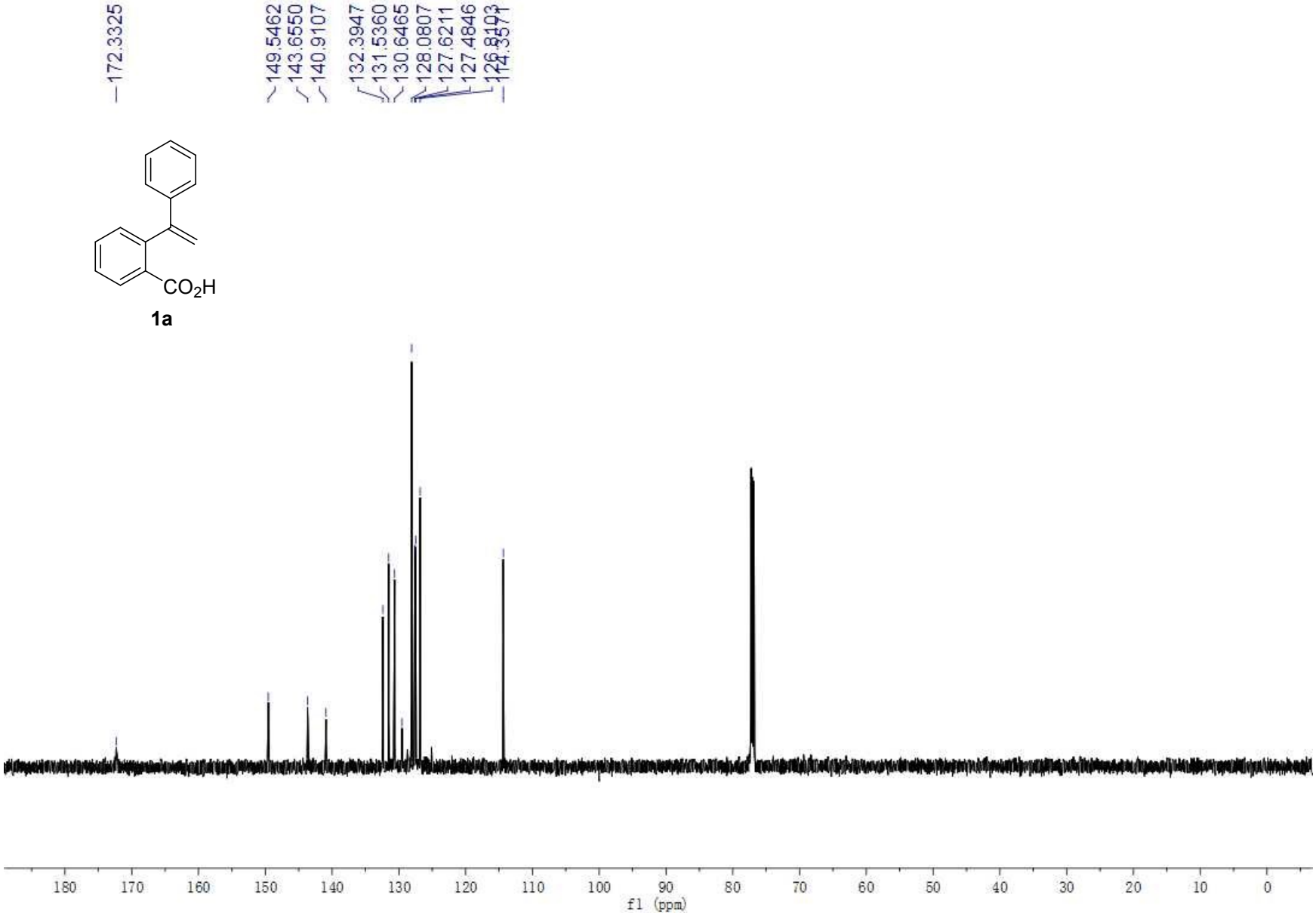
10. Procedure for the Asymmetric Synthesis of 3-Methoxyisobenzofuran-1(3*H*)-ones 2a

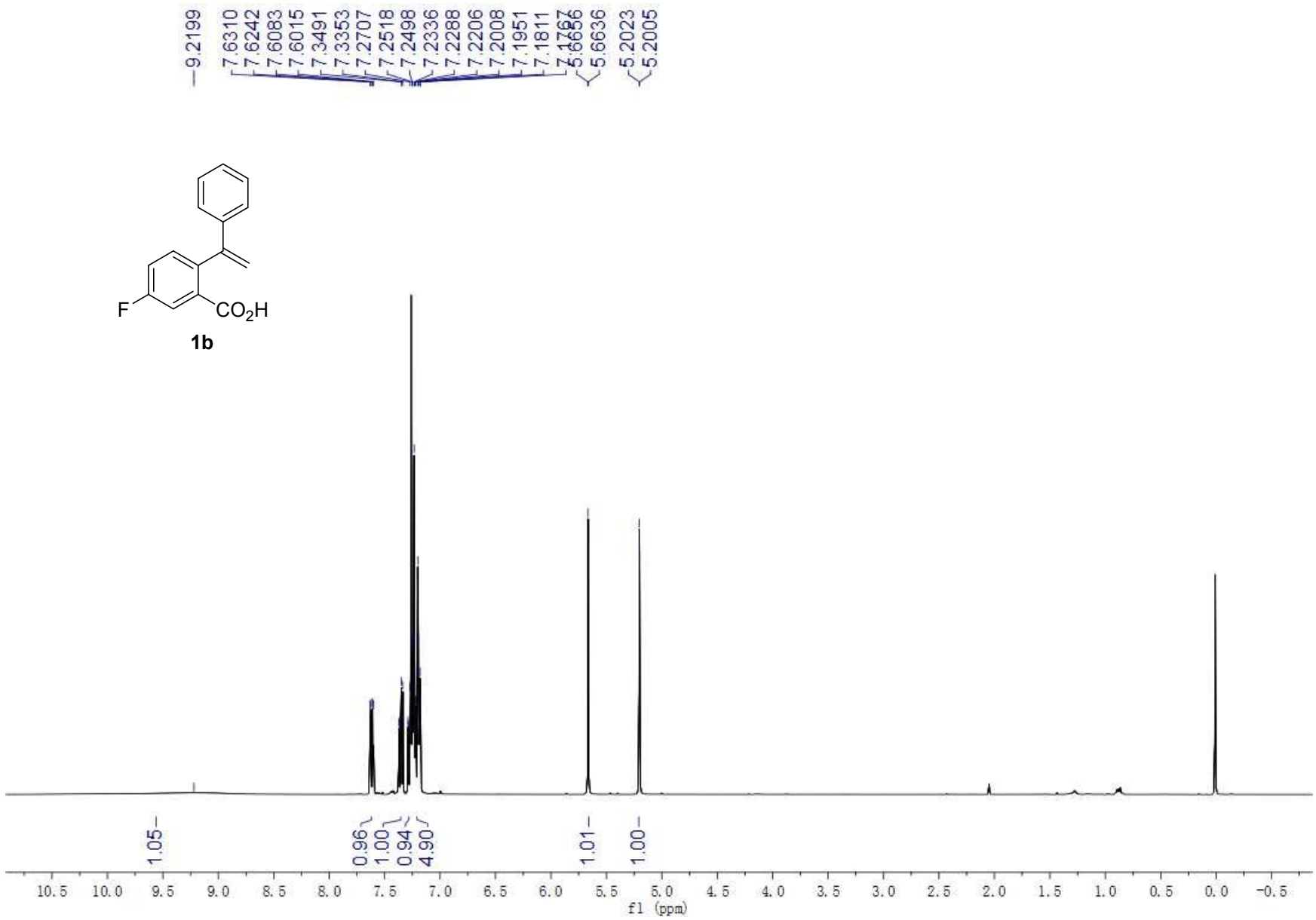


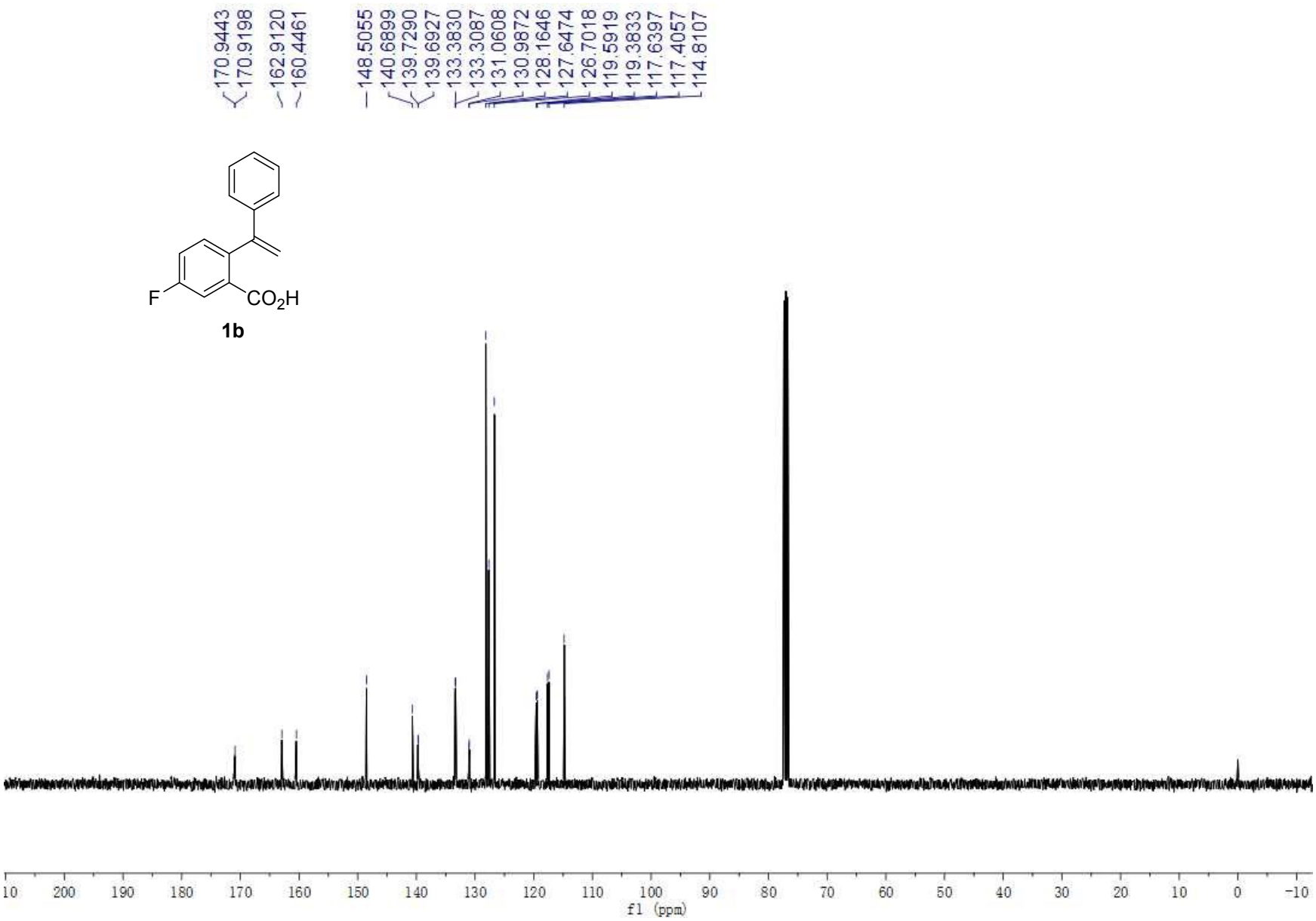
To a Schlenk tube was charged with Selectfluor (265,5 mg, 0.75 mmol), $TsOH{\cdot}H_2O$ (47.5 mg, 0.25 mmol) and chiral organoiodine **5** (49.1 mg, 0.1 mmol) and methanol (1.0 mL). Then a solution of substrate **1a** (112.1 mg, 0.5 mmol) in MeCN (1.0 mL) was added dropwise to the above reaction mixture at room temperature. After the addition was complete, the resulting mixture was stirred at room temperature for another 0.5 hours. Then the solvent was evaporated and the residue was purified by flash column chromatography (5% EtOAc/petroleum ether) to afford the desired compound **2a** as a white solid (92 mg, 72% yield). The *ee* value was determined to be 29% by HPLC analysis on Chiralpak AD-H column (15% isopropanol/hexane, 1 mL/min), UV 254 nm t_1 (minor) = 5.976 min, t_2 (major) = 6.343 min.

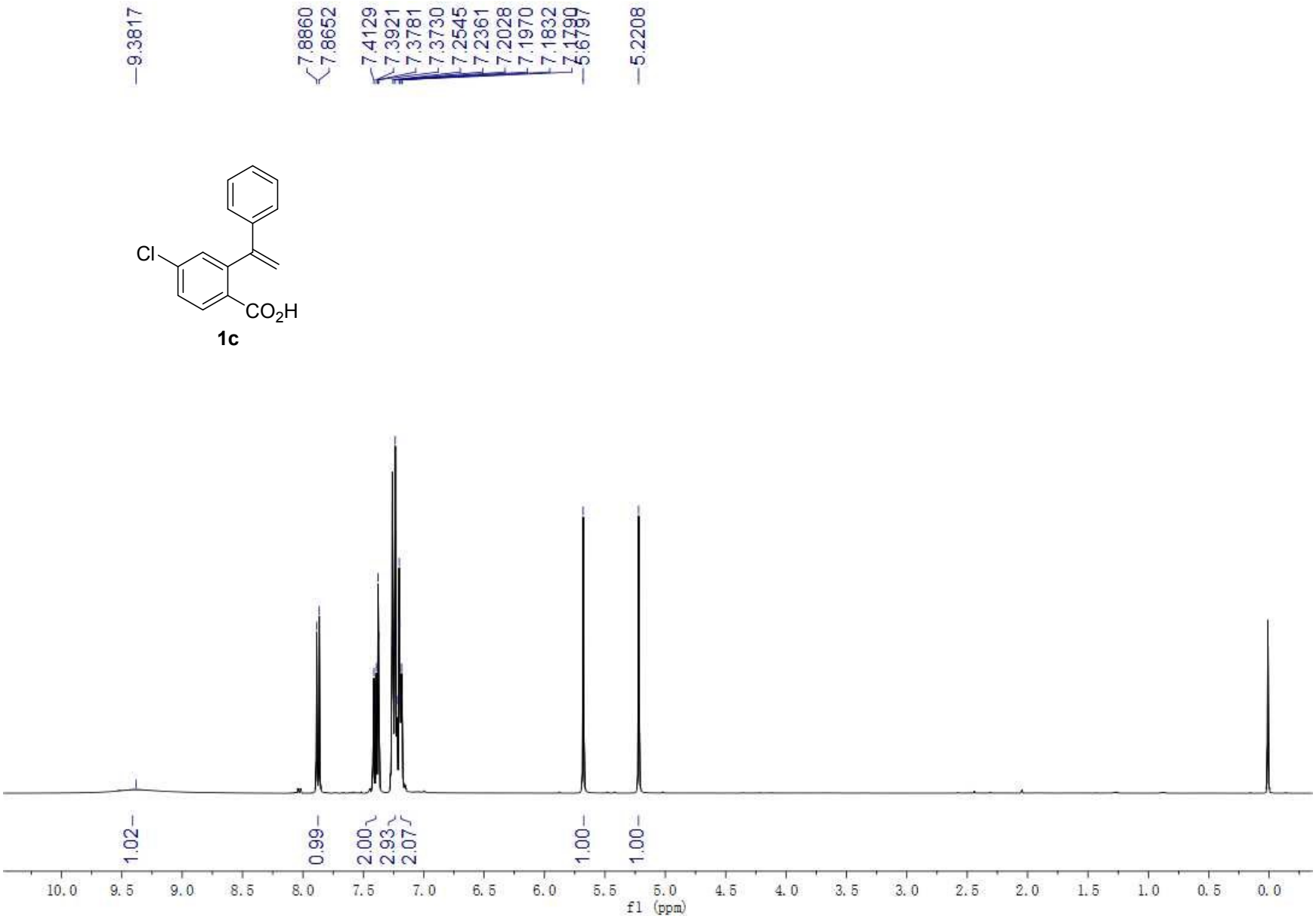
V. ^{1}H and ^{13}C NMR Spectra of Compounds 1a-m, 2a-j, 3a-l and 4a-h:

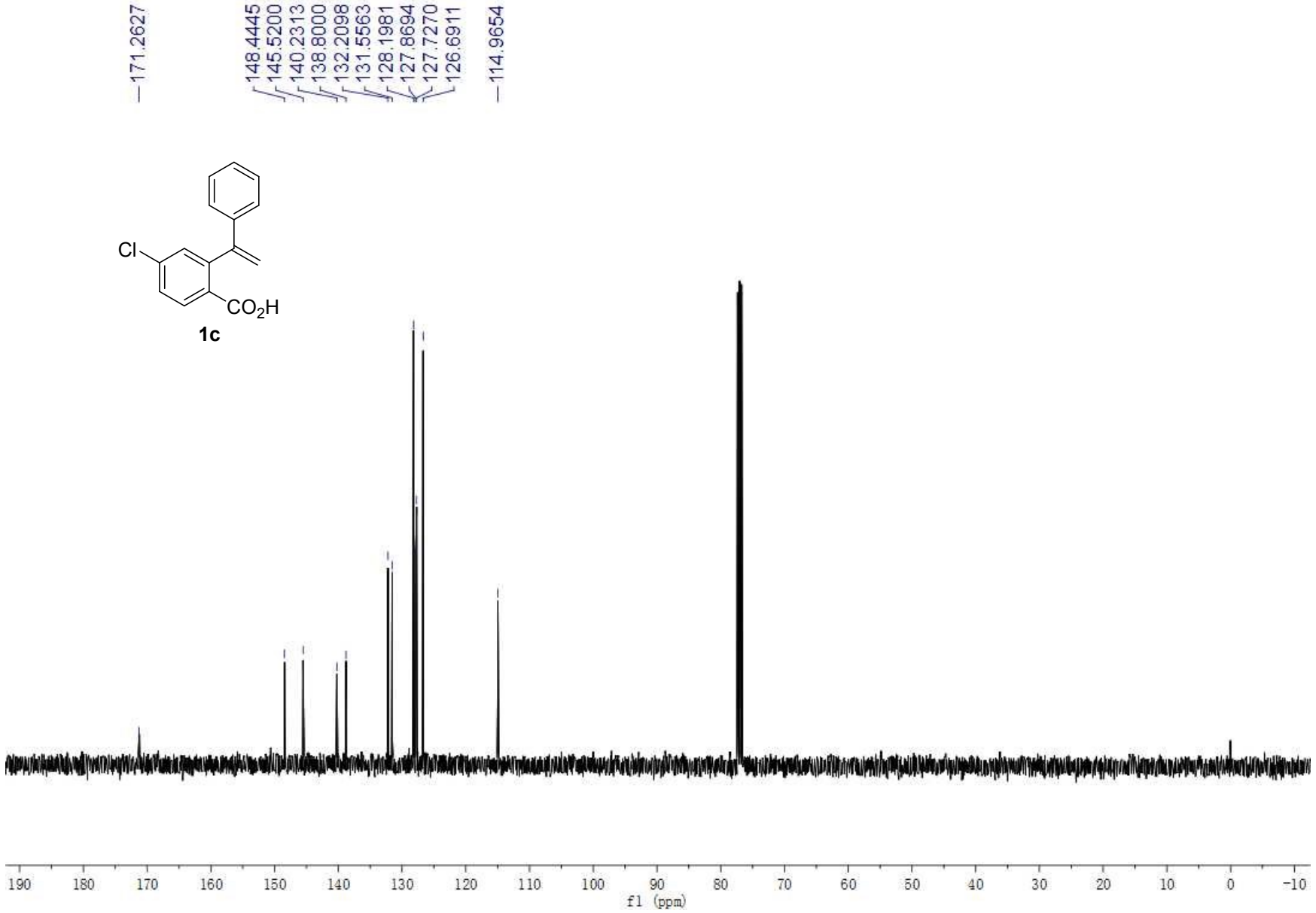


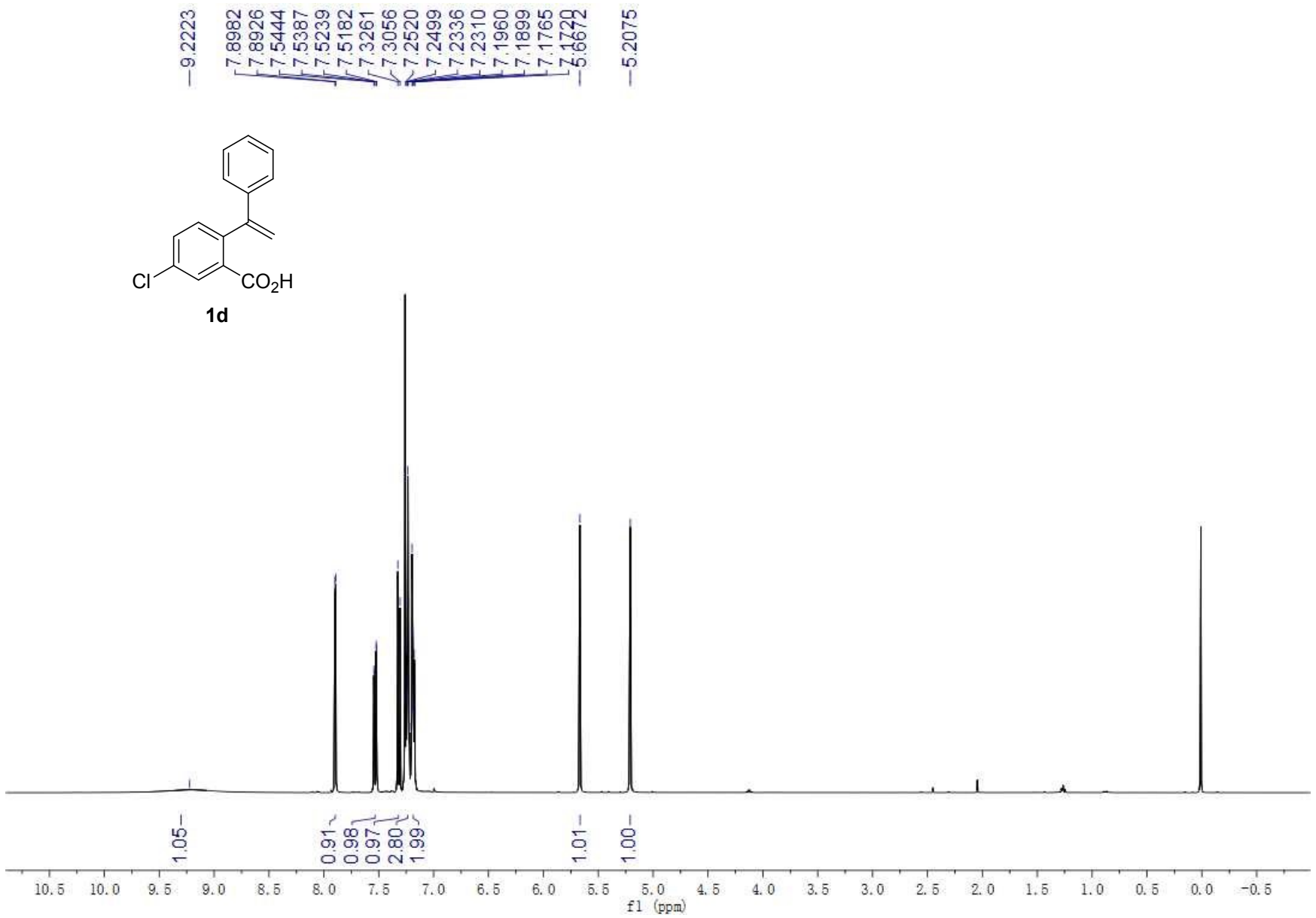

172.3325
149.5462
143.6550
140.9107
132.3947
131.5360
130.6465
128.0807
127.6211
127.4846
126.8193
124.3571
CO2H
1a
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

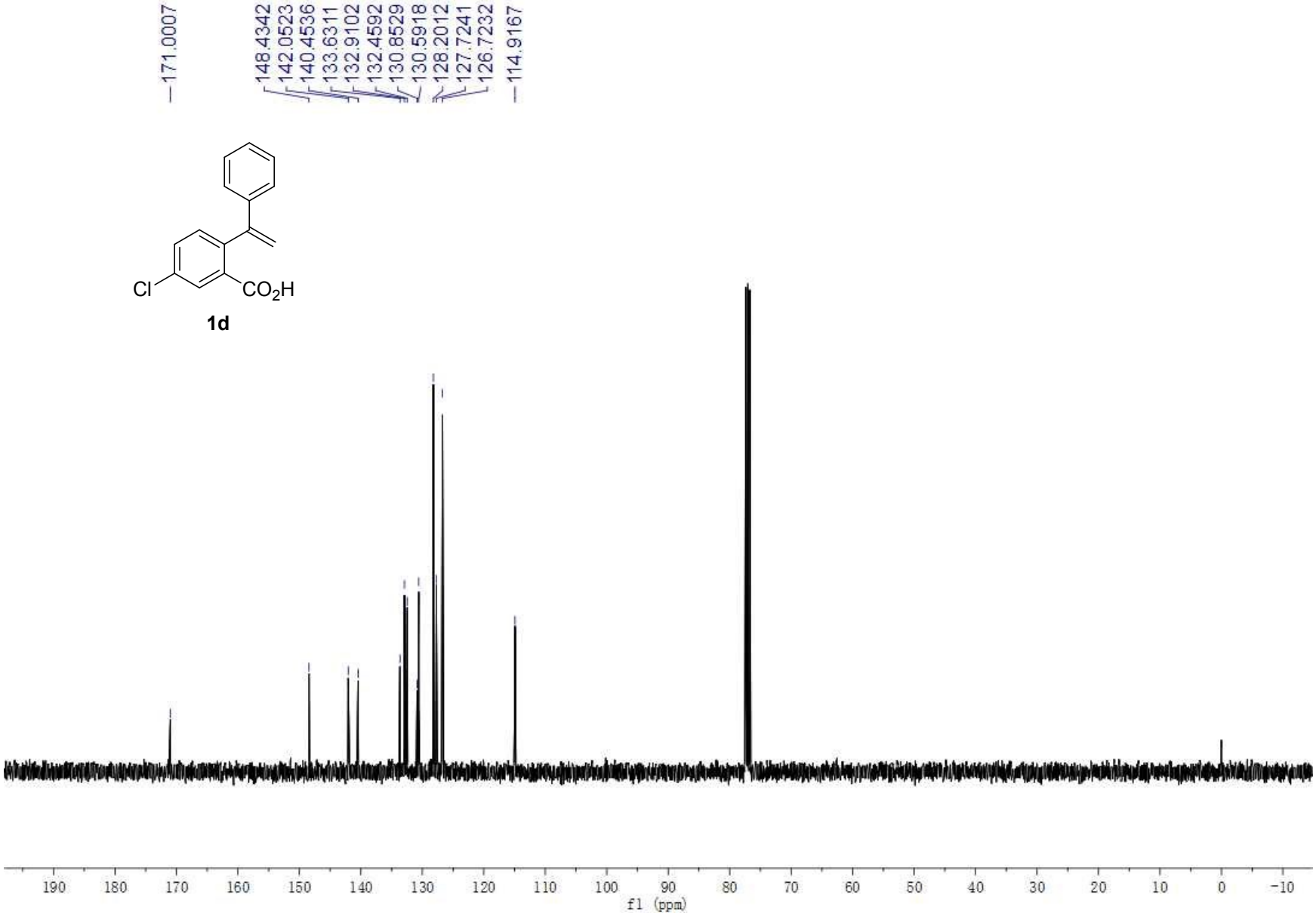

9.2199
7.6310
7.6242
7.6083
7.6015
7.3491
7.3353
7.2707
7.2518
7.2498
7.2336
7.2288
7.2206
7.2008
7.1951
7.1811
5.6856
5.6636
5.2023
5.2005
F
CO2H
1b
1.05
0.96
1.00
0.94
4.90
1.01
1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

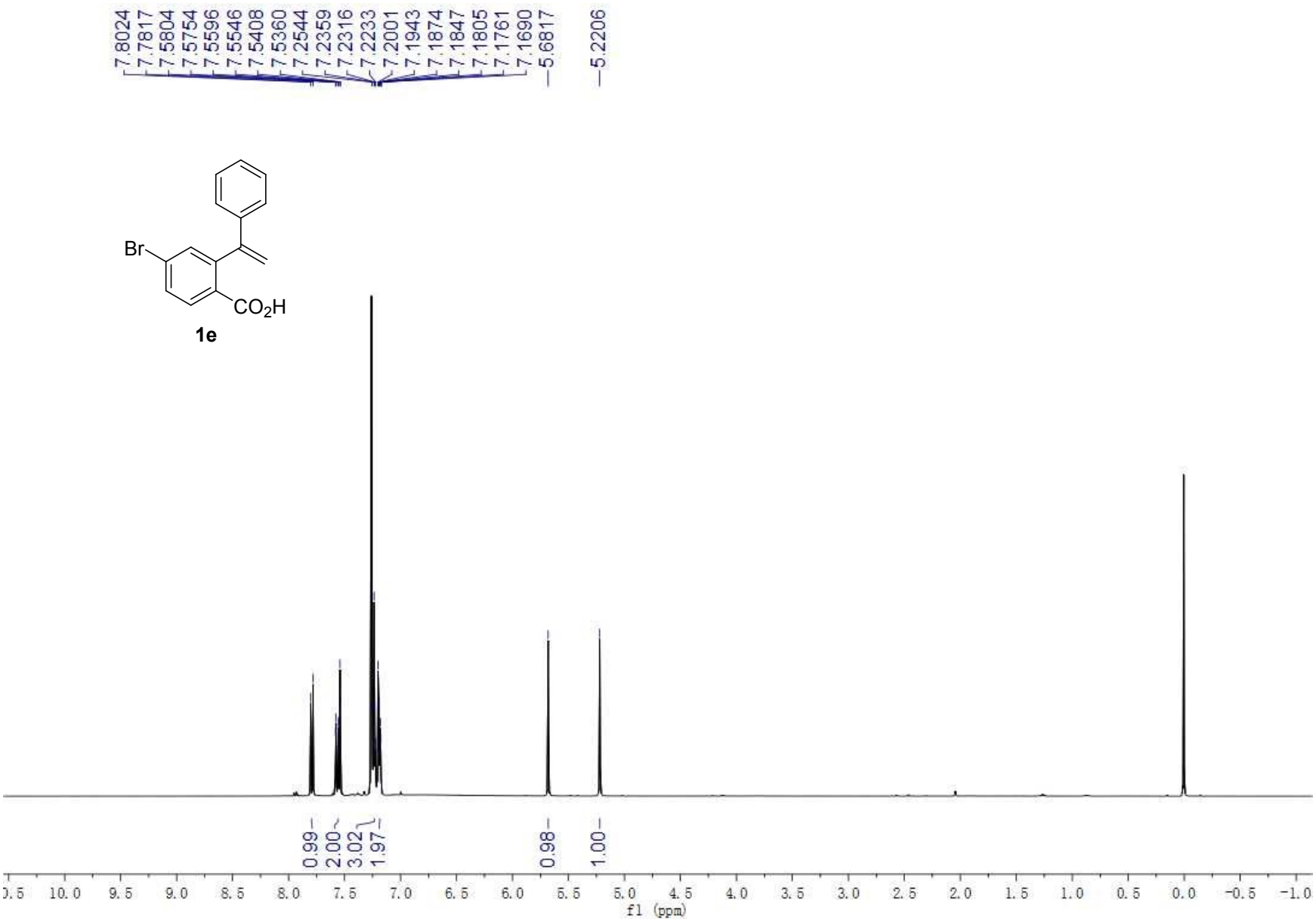

170.9443
170.9198
162.9120
160.4461
148.5055
140.6899
139.7290
139.6927
133.3830
133.3087
131.0608
130.9872
128.1646
127.6474
126.7018
119.5919
119.3833
117.6397
117.4057
114.8107
F
CO2H
1b
f1 (ppm)

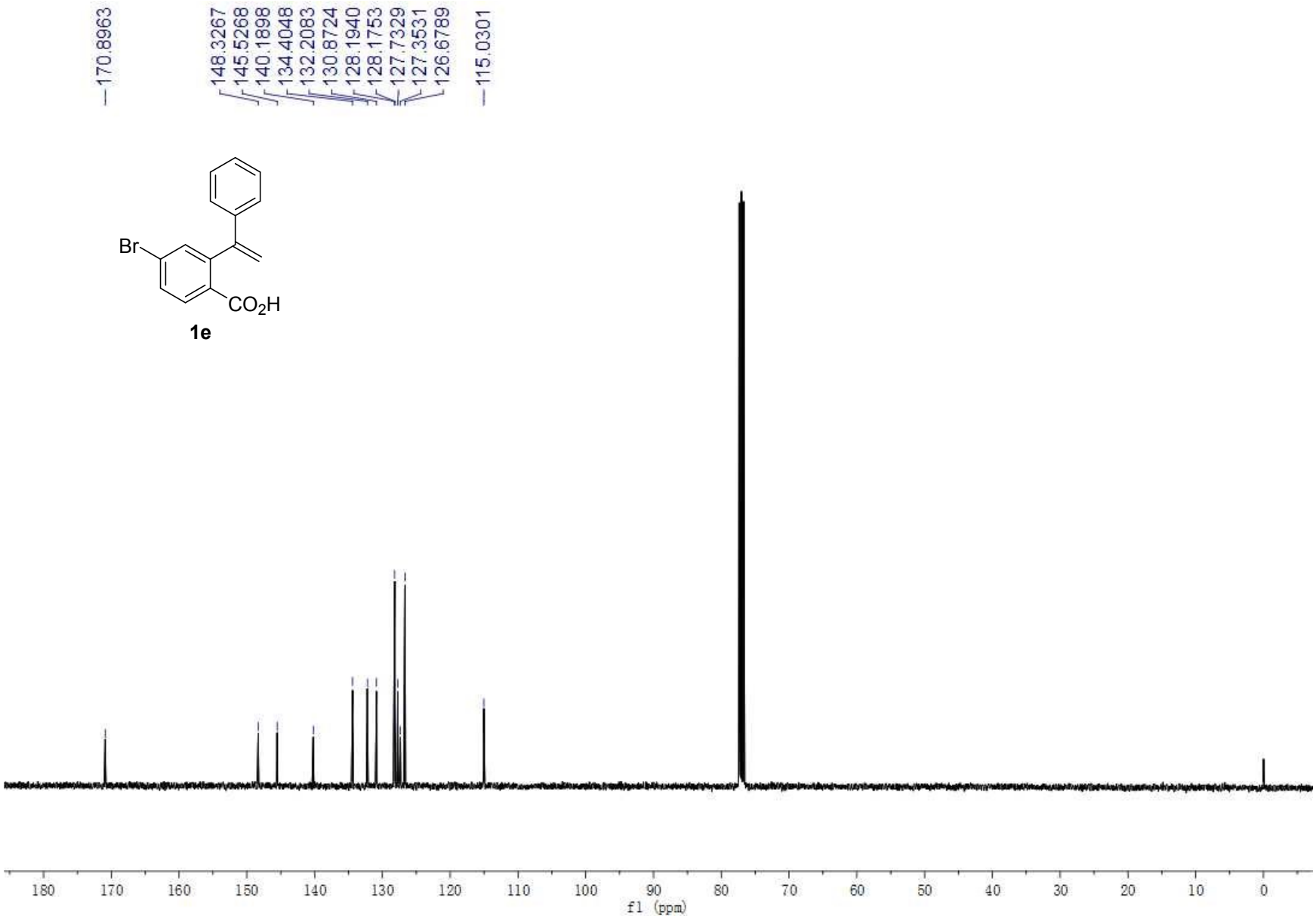

9.3817
7.8860
7.8652
7.4129
7.3921
7.3781
7.3730
7.2545
7.2361
7.2028
7.1970
7.1832
7.1790
5.6797
5.2208
Cl
CO2H
1c
1.02
0.99
2.00
2.93
2.07
1.00
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


171.2627
148.4445
145.5200
140.2313
138.8000
132.2098
131.5563
128.1981
127.8694
127.7270
126.6911
114.9654
Cl
CO2H
1c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


9.2223
7.8982
7.8926
7.5444
7.5387
7.5239
7.5182
7.3261
7.3056
7.2520
7.2499
7.2336
7.2310
7.1960
7.1899
7.1765
7.1720
5.6672
5.2075
Cl
CO2H
1d
1.05
0.91
0.98
0.97
2.80
1.99
1.01
1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


171.0007
148.4342
142.0523
140.4536
133.6311
132.9102
132.4592
130.8529
130.5918
128.2012
127.7241
126.7232
114.9167
Cl
CO2H
1d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.8024
7.7817
7.5804
7.5754
7.5596
7.5546
7.5408
7.5360
7.2544
7.2359
7.2316
7.2233
7.2001
7.1943
7.1874
7.1847
7.1805
7.1761
7.1690
5.6817
5.2206
Br
CO2H
1e
0.99
2.00
3.02
1.97
0.98
1.00
f1 (ppm)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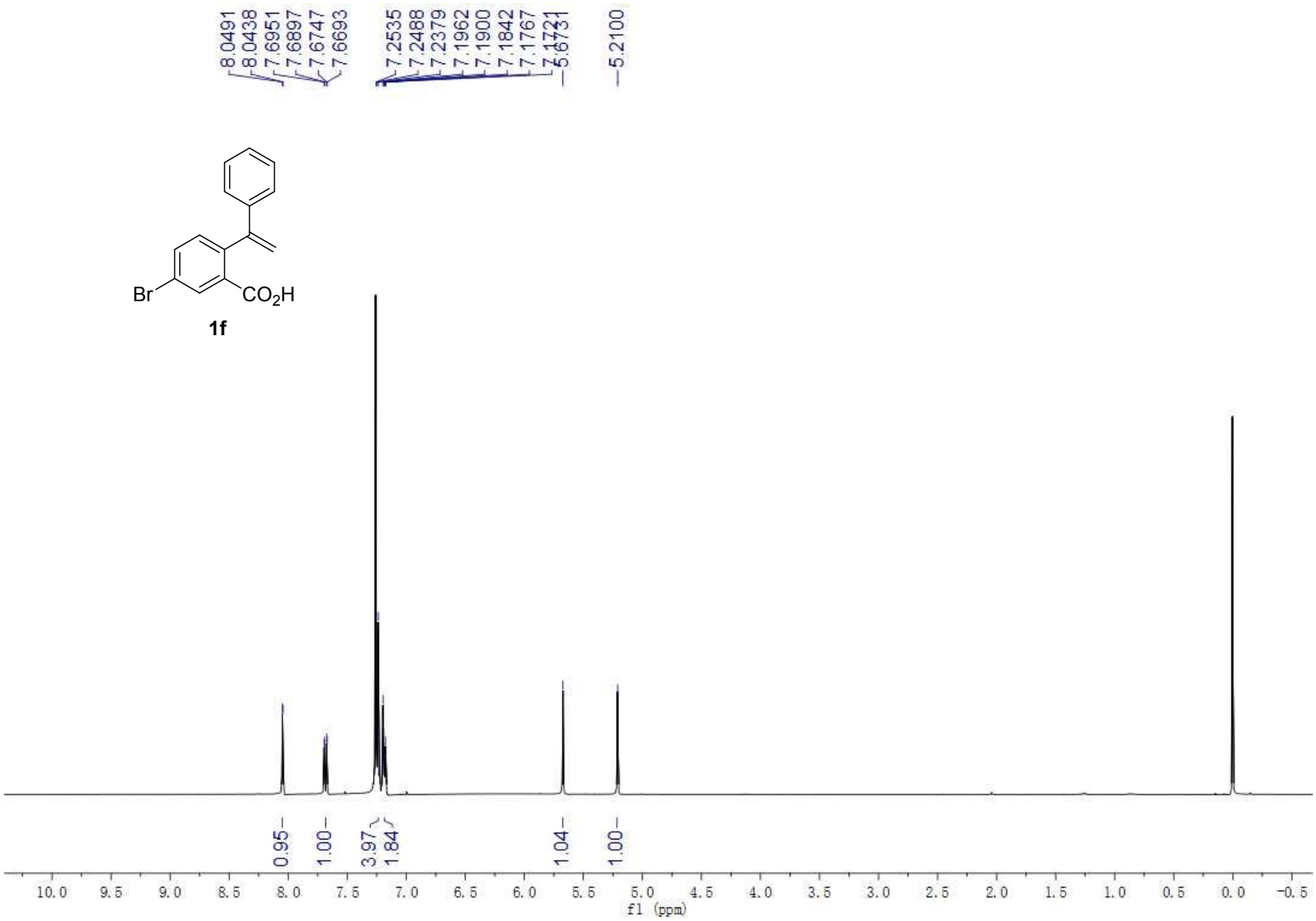
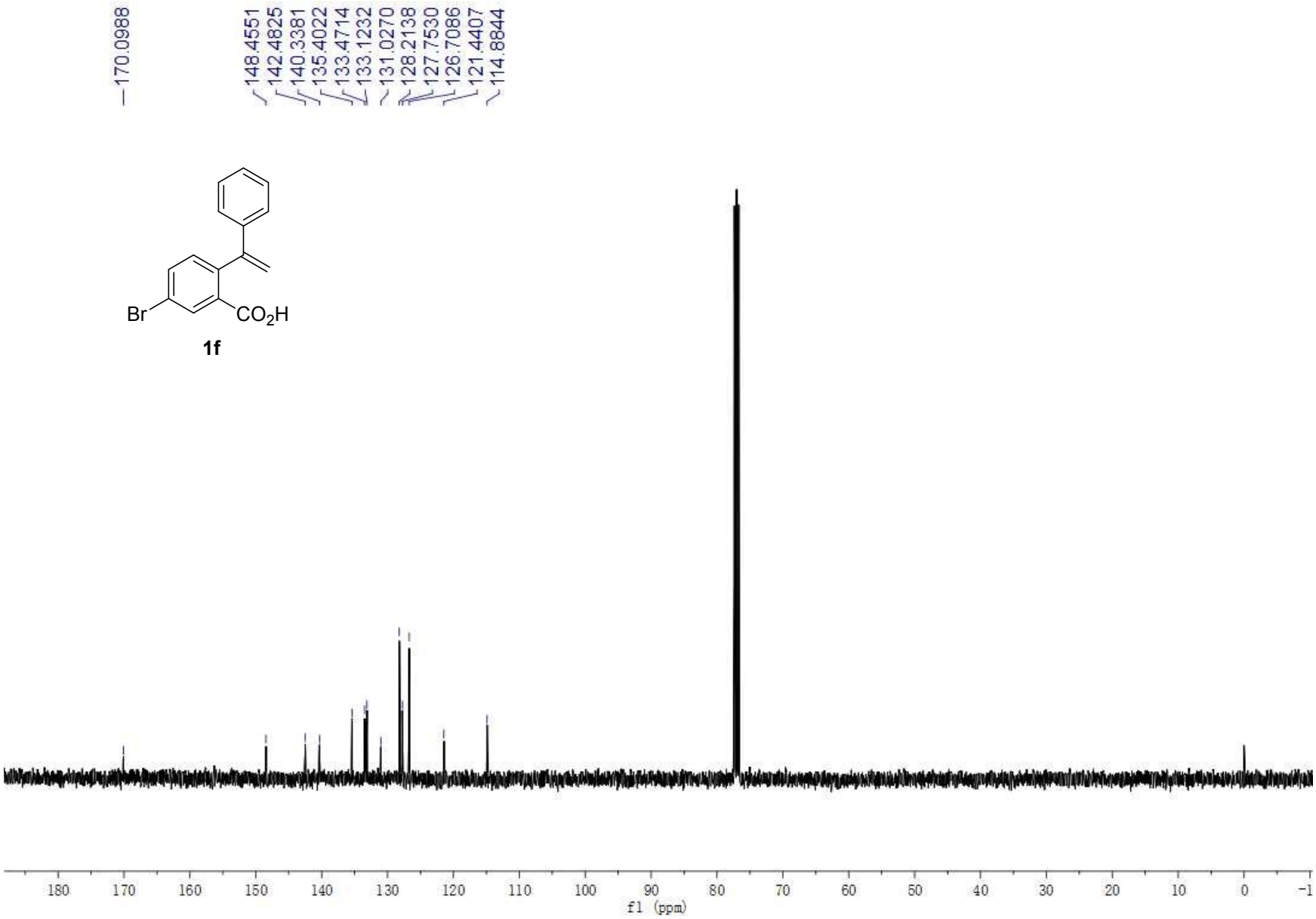
145.5268
140.1898
134.4048
132.2083
130.8724
128.1940
128.1753
127.7329
127.3531
126.6789
115.0301
Br
CO2H
1e
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.0491
8.0438
7.6951
7.6897
7.6747
7.6693
7.2535
7.2488
7.2379
7.1962
7.1900
7.1842
7.1767
7.1721
5.6731
5.2100
Br
CO2H
1f
0.95
1.00
3.97
1.84
1.04
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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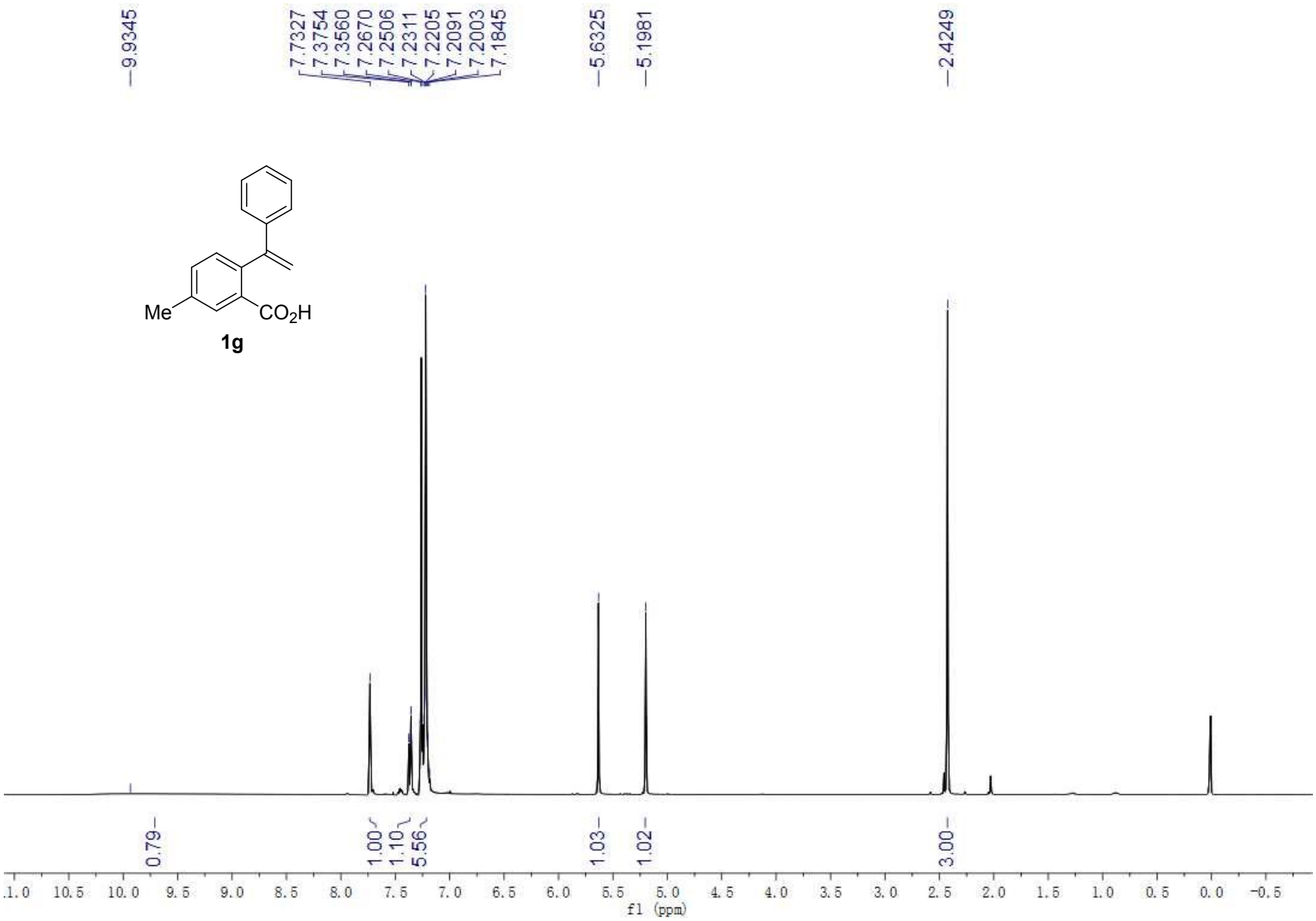
142.4825
140.3381
135.4022
133.4714
133.1232
131.0270
128.2138
127.7530
126.7086
121.4407
114.8844
Br
CO2H
1f
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


9.9345
7.7327
7.3754
7.3560
7.2670
7.2506
7.2311
7.2205
7.2091
7.2003
7.1845
5.6325
5.1981
2.4249
Me
CO2H
1g
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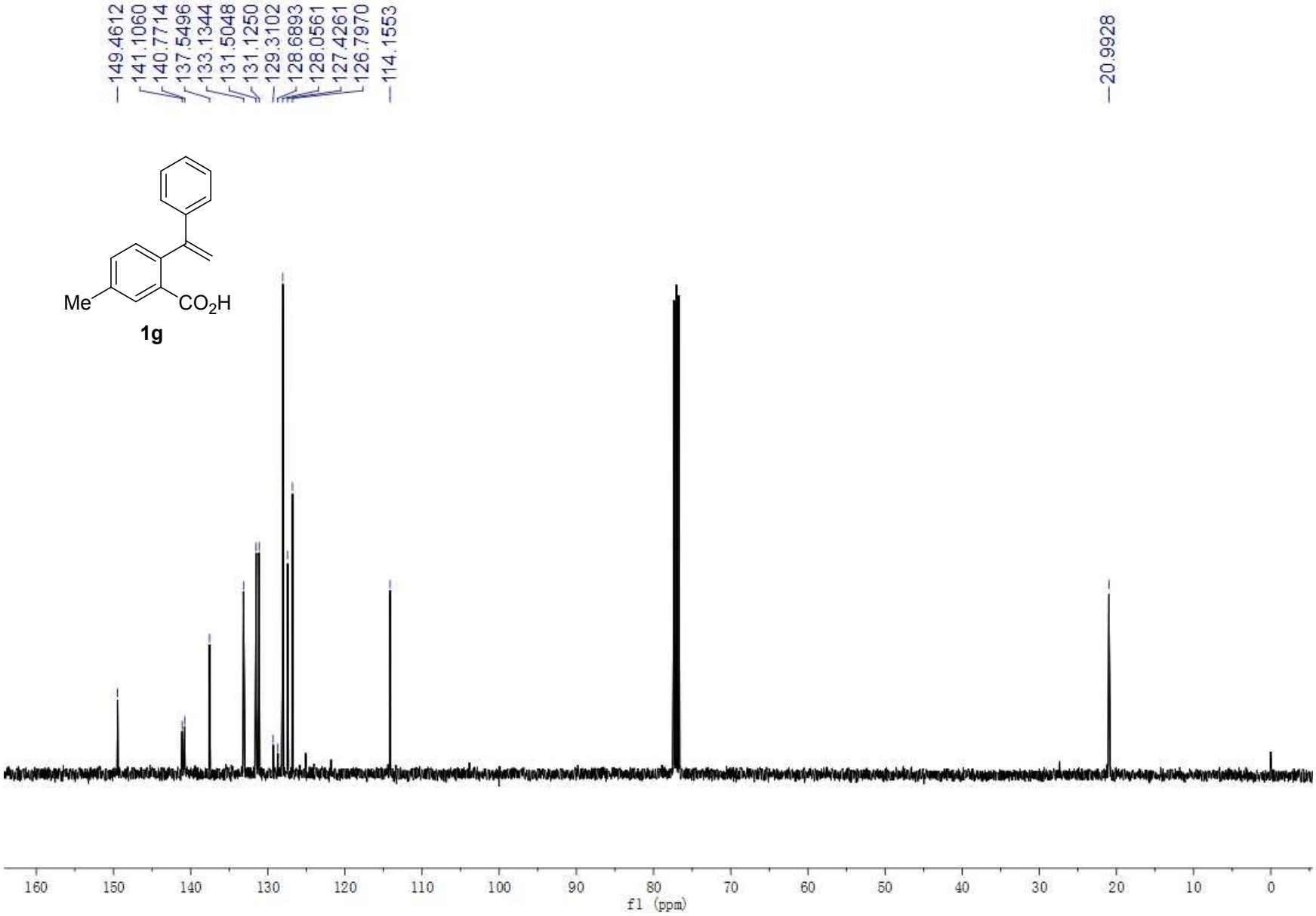
1.00
1.10
5.56
1.03
1.02
3.00
f1 (ppm)


149.4612
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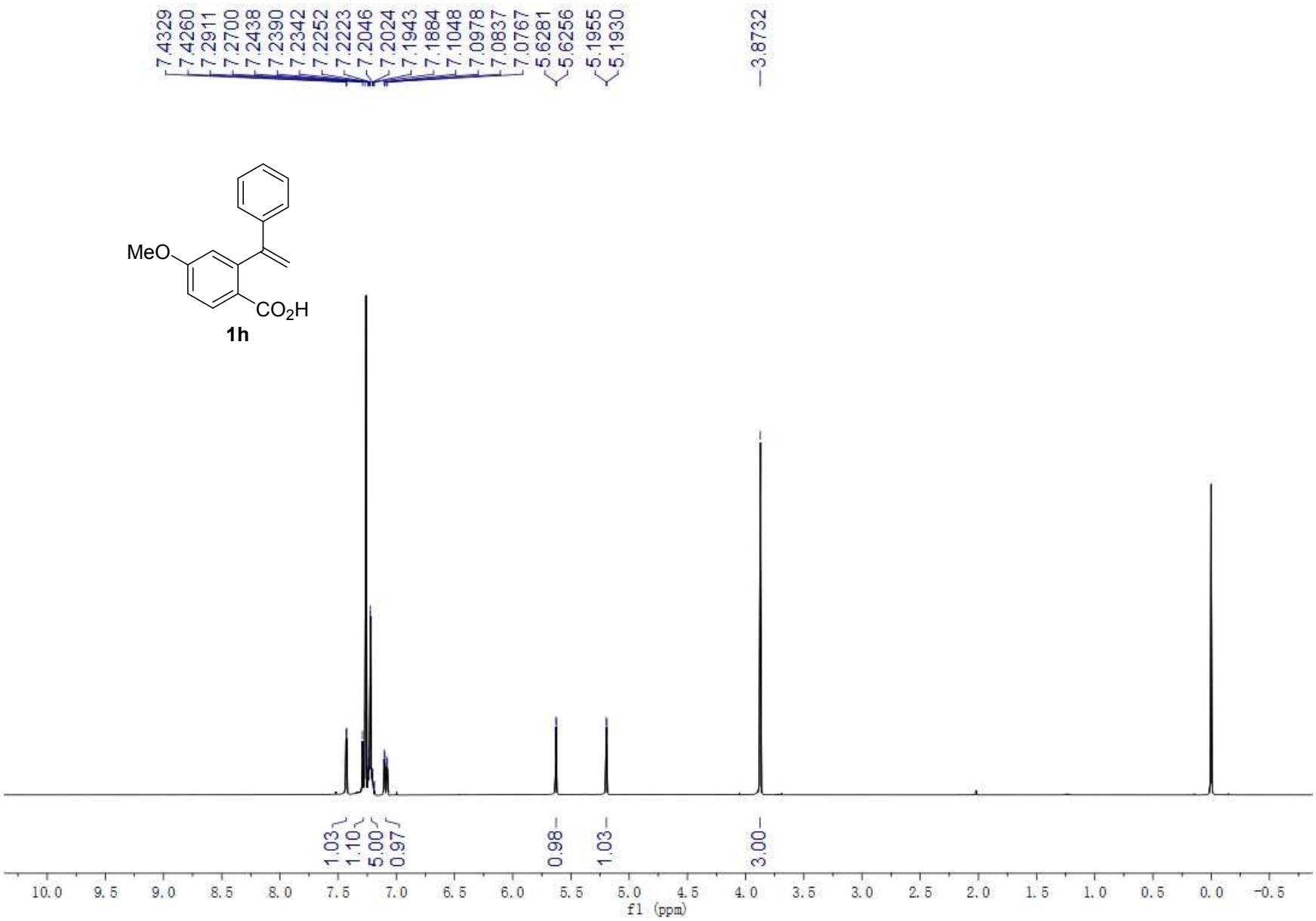
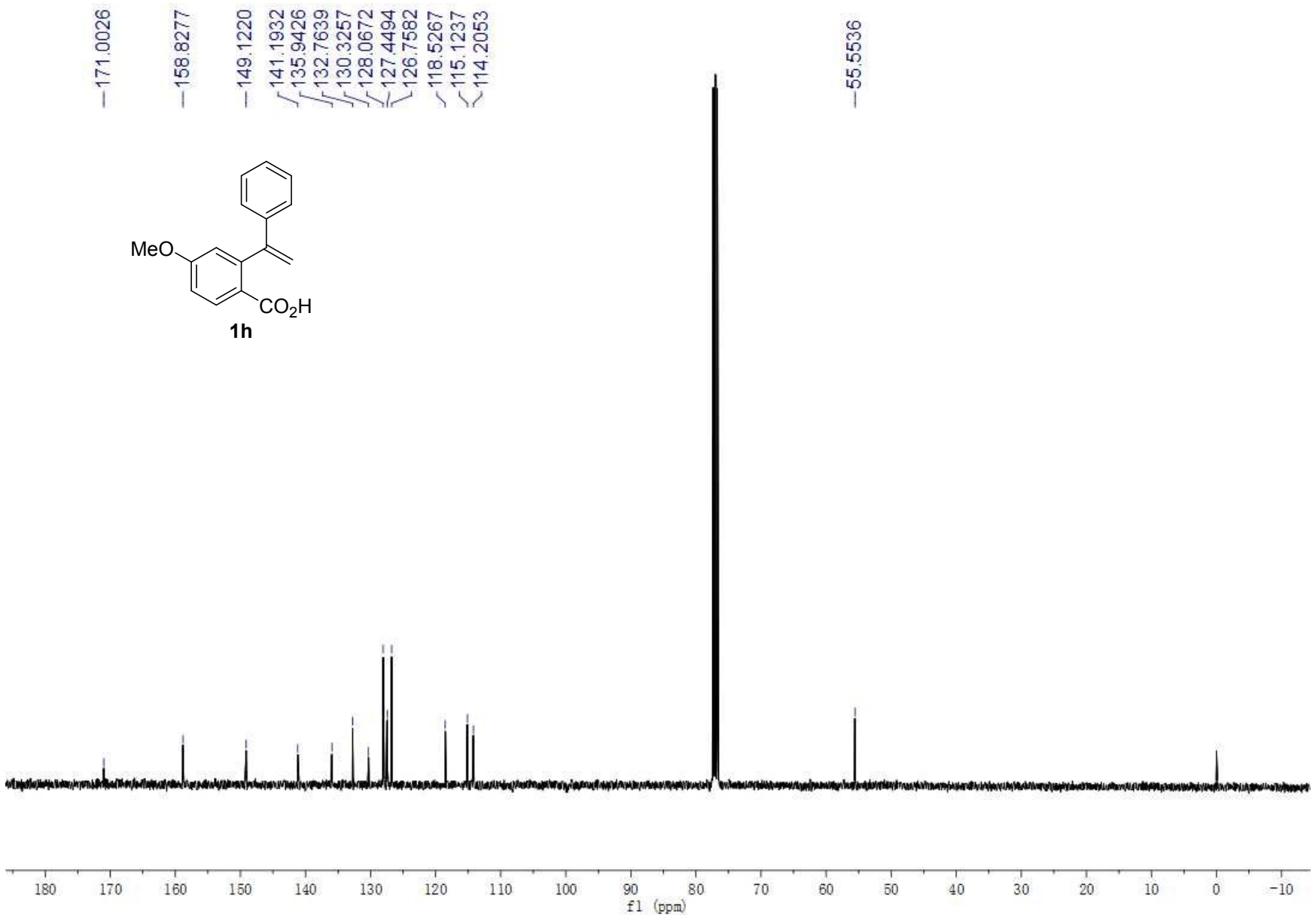
137.5496
133.1344
131.5048
131.1250
129.3102
128.6893
128.0561
127.4261
126.7970
114.1553
20.9928
Me
CO2H
1g
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.4329
7.4260
7.2911
7.2700
7.2438
7.2390
7.2342
7.2252
7.2223
7.2046
7.2024
7.1943
7.1884
7.1048
7.0978
7.0837
7.0767
5.6281
5.6256
5.1955
5.1930
3.8732
MeO
CO2H
1h
1.03
1.10
5.00
0.97
0.98
1.03
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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141.1932
135.9426
132.7639
130.3257
128.0672
127.4494
126.7582
118.5267
115.1237
114.2053
55.5536
MeO
CO2H
1h
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


10.4376
7.9377
7.9358
7.9247
7.9228
7.5713
7.5692
7.5588
7.5566
7.4488
7.4379
7.4361
7.3700
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7.3559
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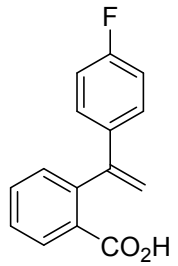
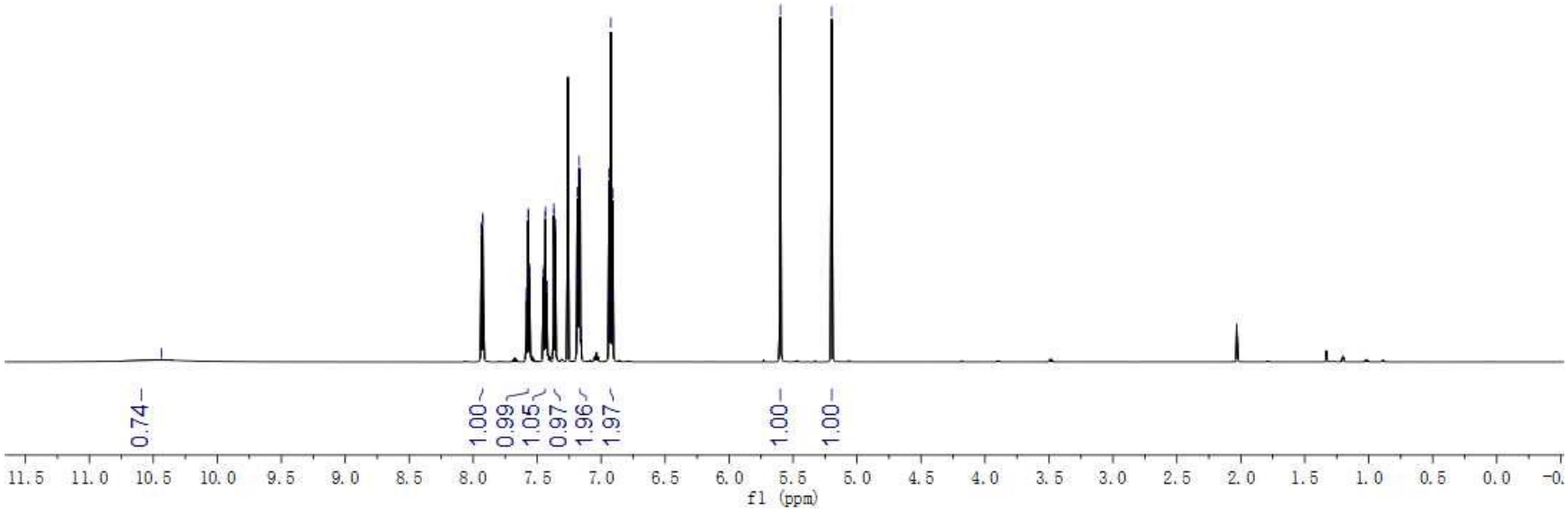
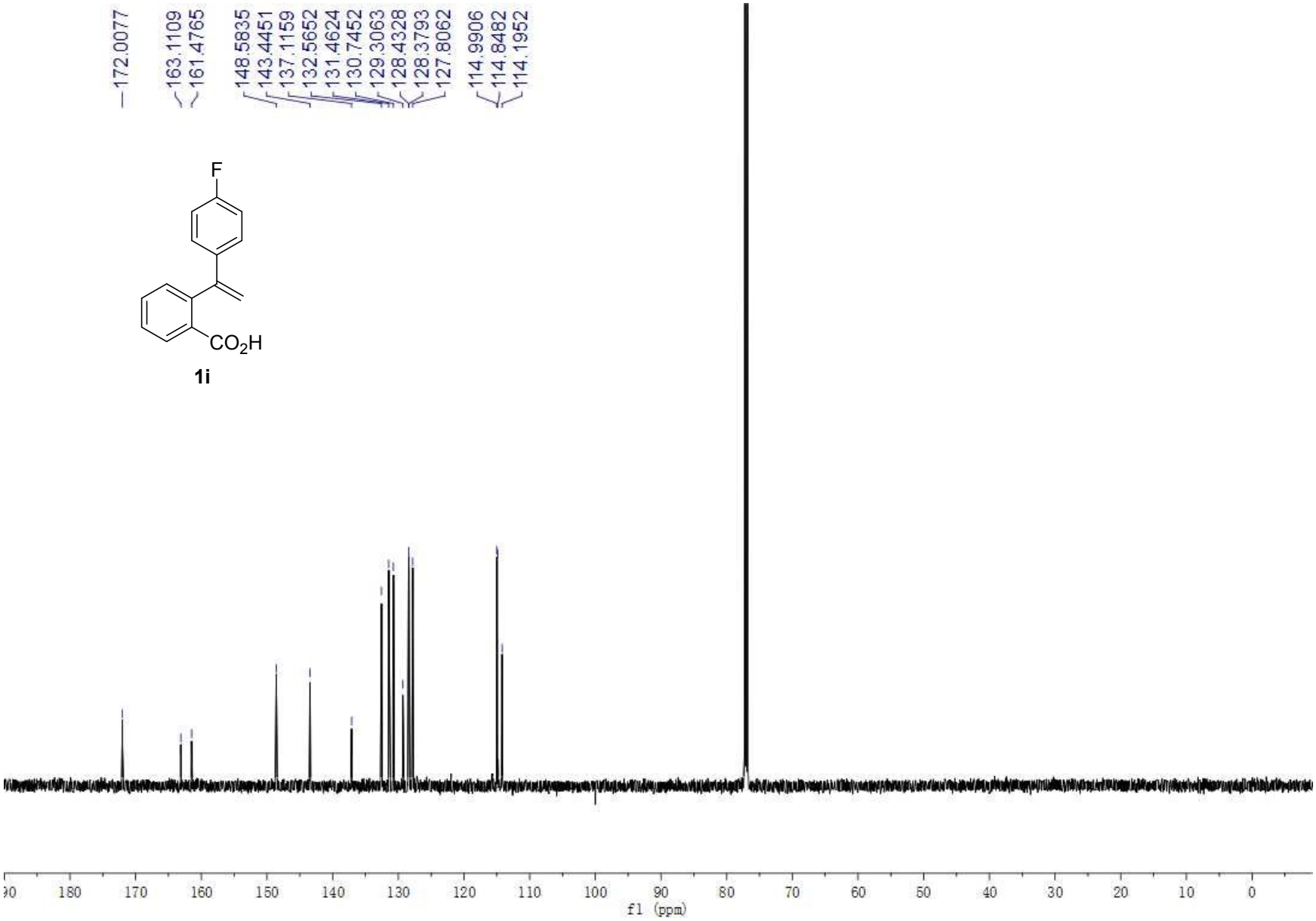
7.1776
7.1719
7.1629
6.9385
6.9240
5.1980


F
CO2H

1i


0.74
1.00
0.99
1.05
0.97
1.96
1.97
1.00
1.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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161.4765
148.5835
143.4451
137.1159
132.5652
131.4624
130.7452
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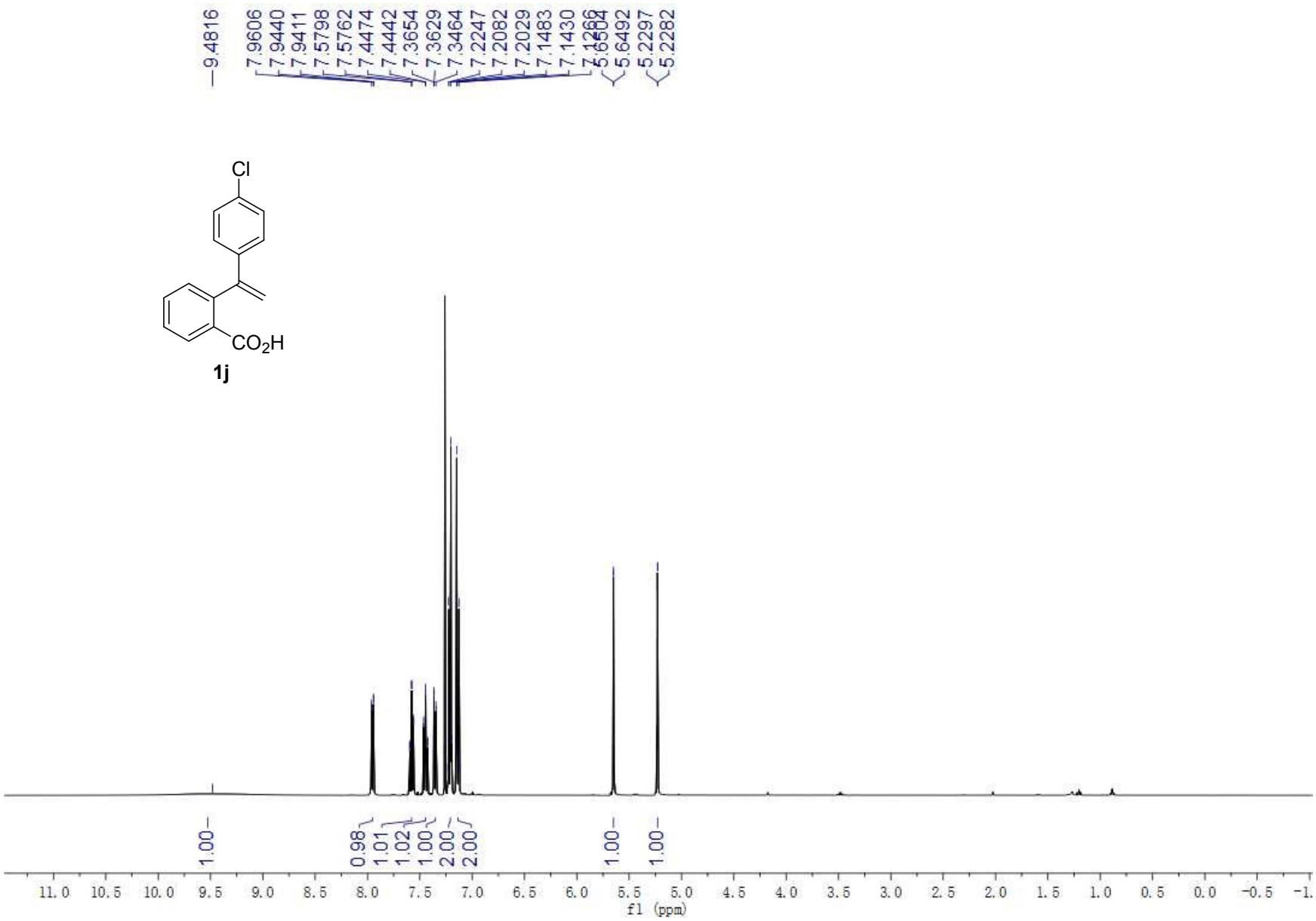
128.3793
127.8062
114.9906
114.8482
114.1952
F
CO2H
1i
f1 (ppm)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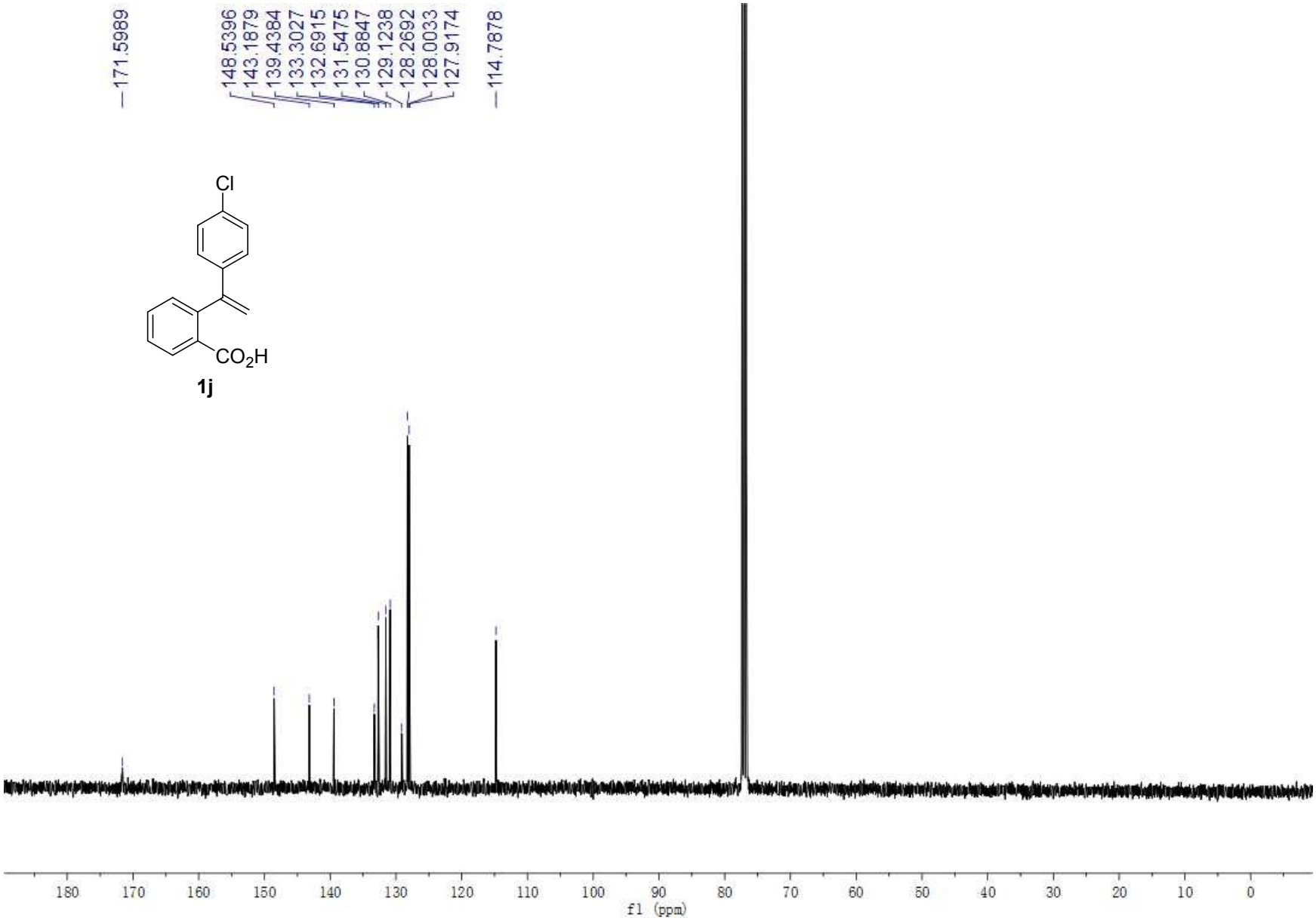
7.9606
7.9440
7.9411
7.5798
7.5762
7.4474
7.4442
7.3654
7.3629
7.3464
7.2247
7.2082
7.2029
7.1483
7.1430
5.6504
5.6492
5.2297
5.2282
Cl
CO2H
1j
1.00
0.98
1.01
1.02
1.00
2.00
2.00
1.00
1.00
f1 (ppm)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133.3027
132.6915
131.5475
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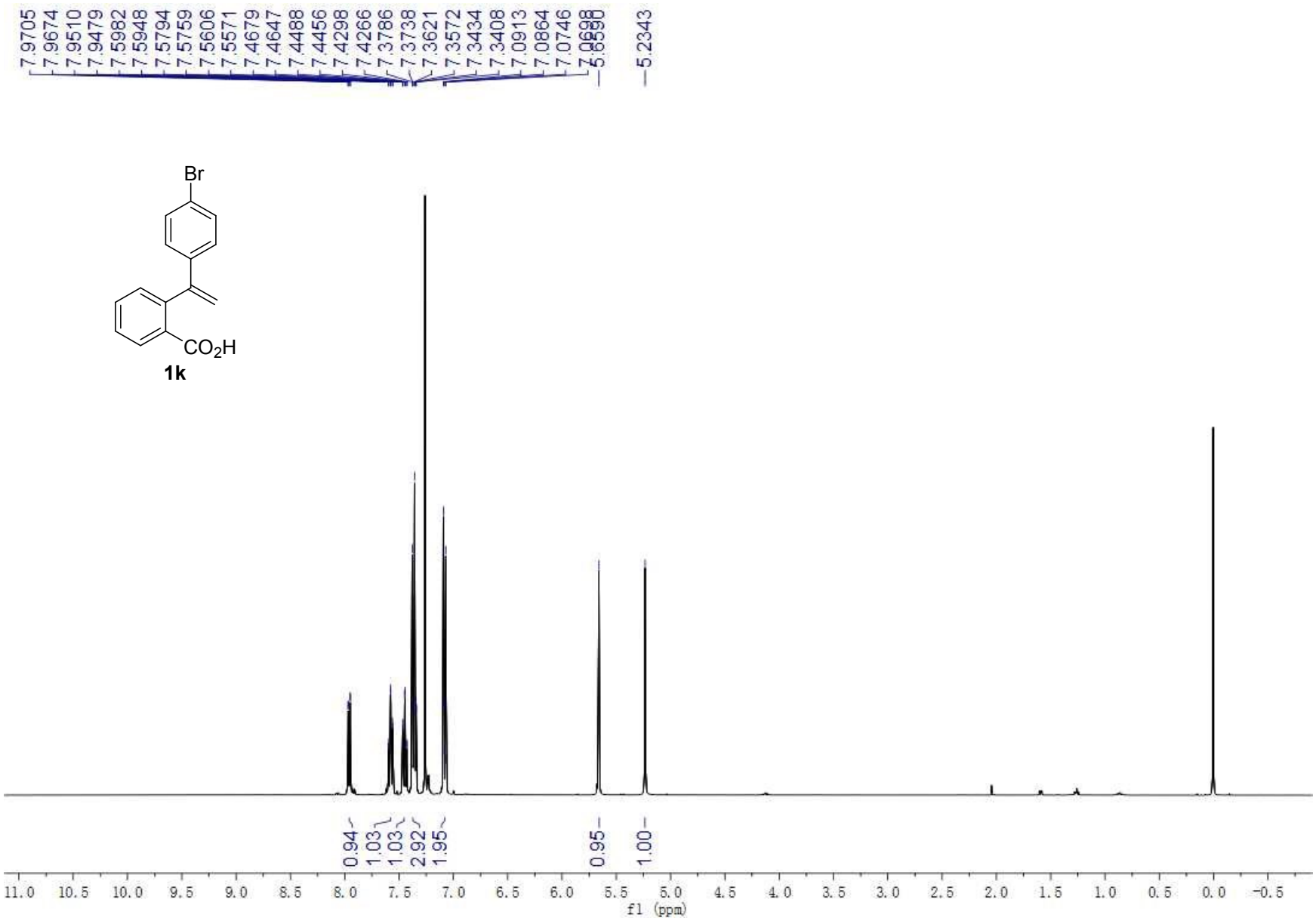
129.1238
128.2692
128.0033
127.9174
114.7878
Cl
CO2H
1j
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.9674
7.9510
7.9479
7.5982
7.5948
7.5794
7.5759
7.5606
7.5571
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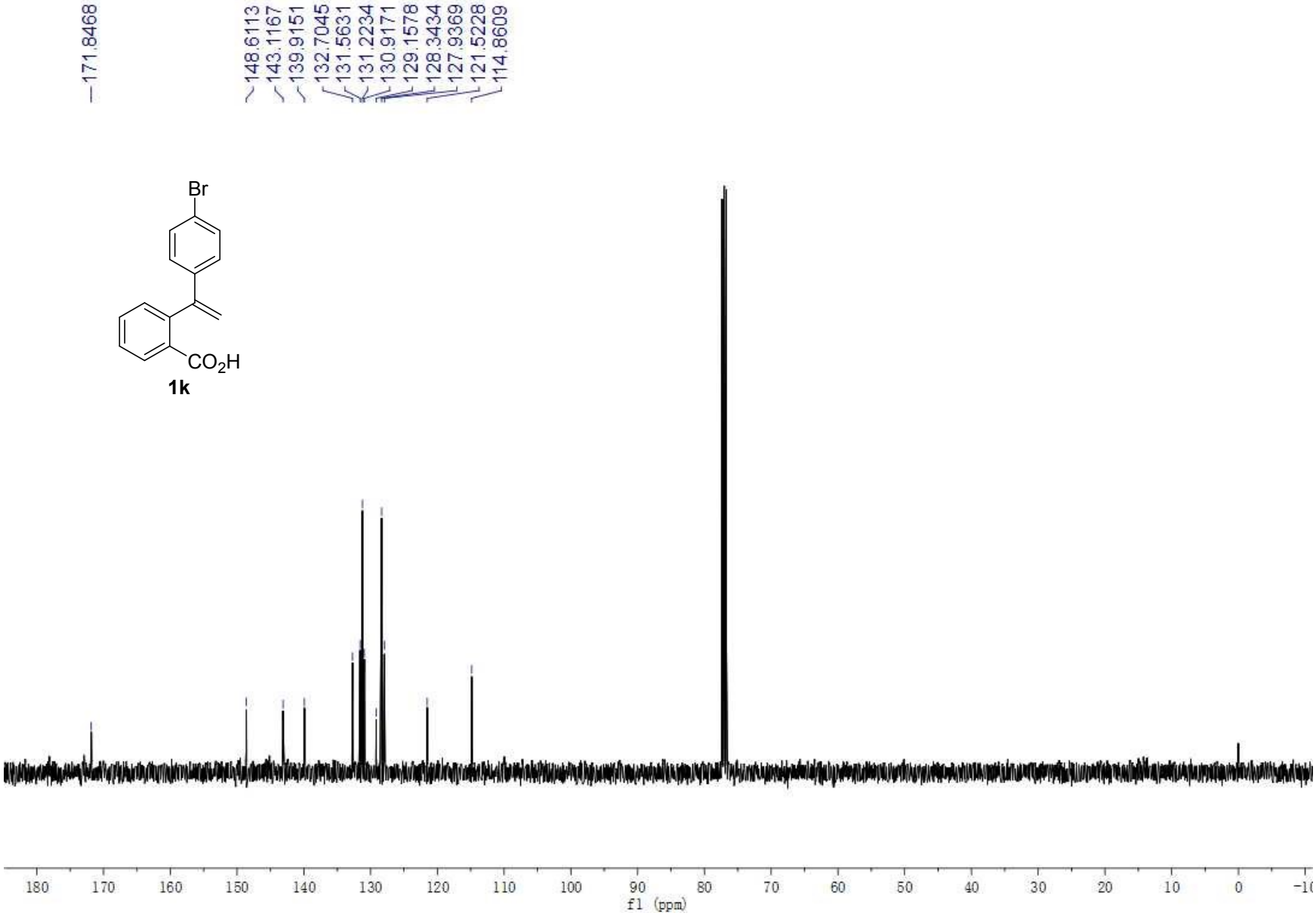
7.4647
7.4488
7.4456
7.4298
7.4266
7.3786
7.3738
7.3621
7.3572
7.3434
7.3408
7.0913
7.0864
7.0746
5.2343
Br
CO2H
1k
0.94
1.03
1.03
2.92
1.95
0.95
1.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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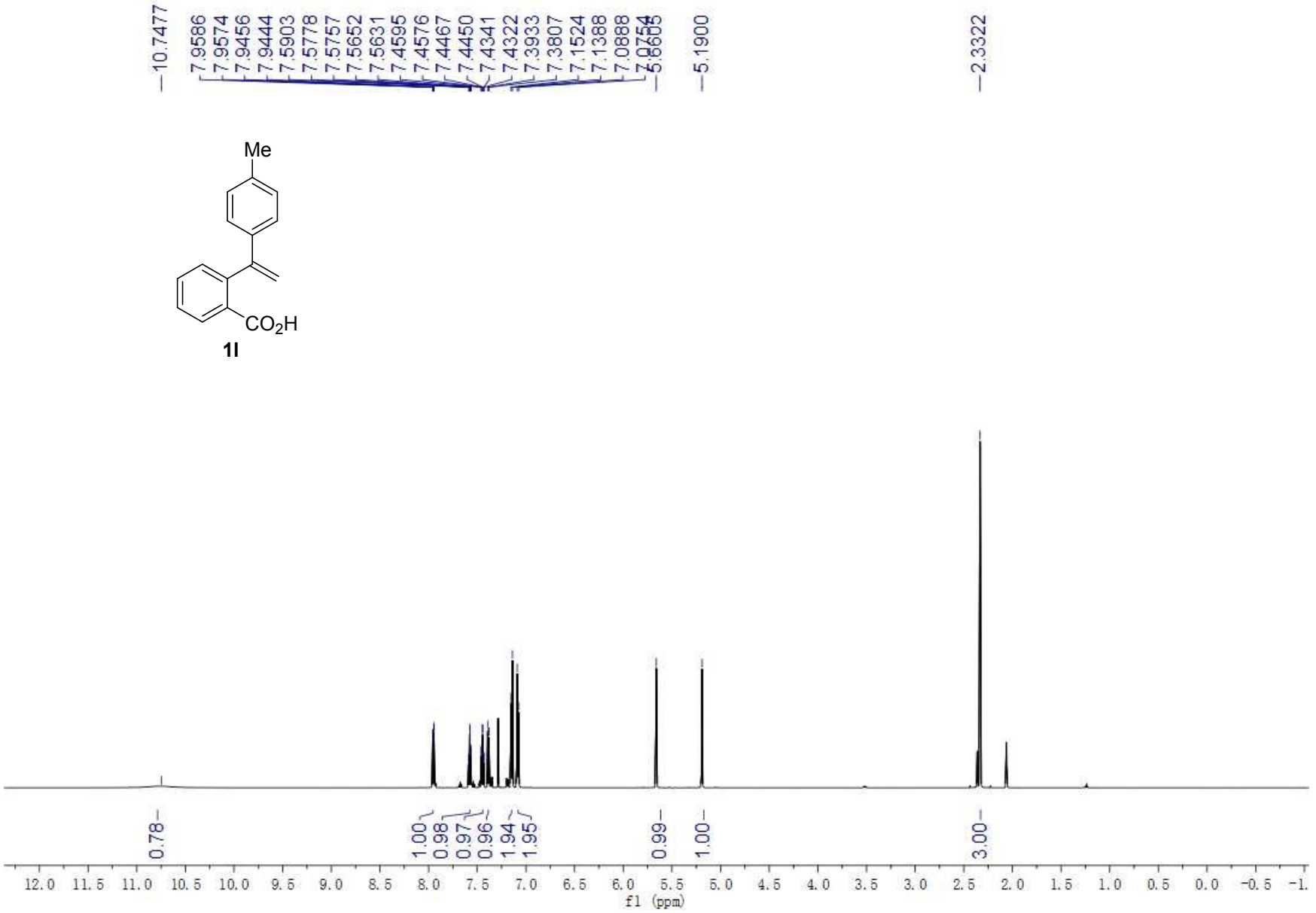
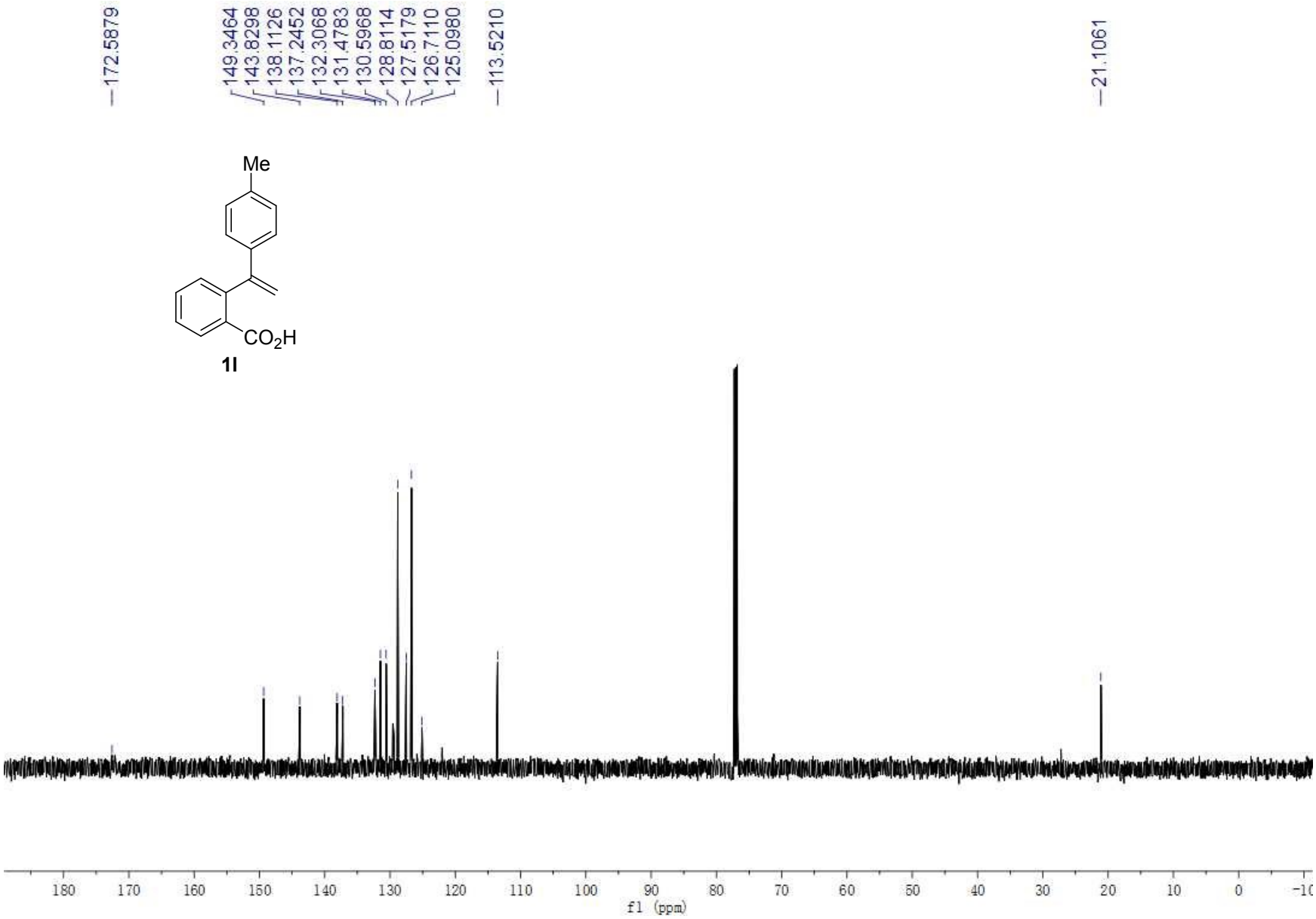
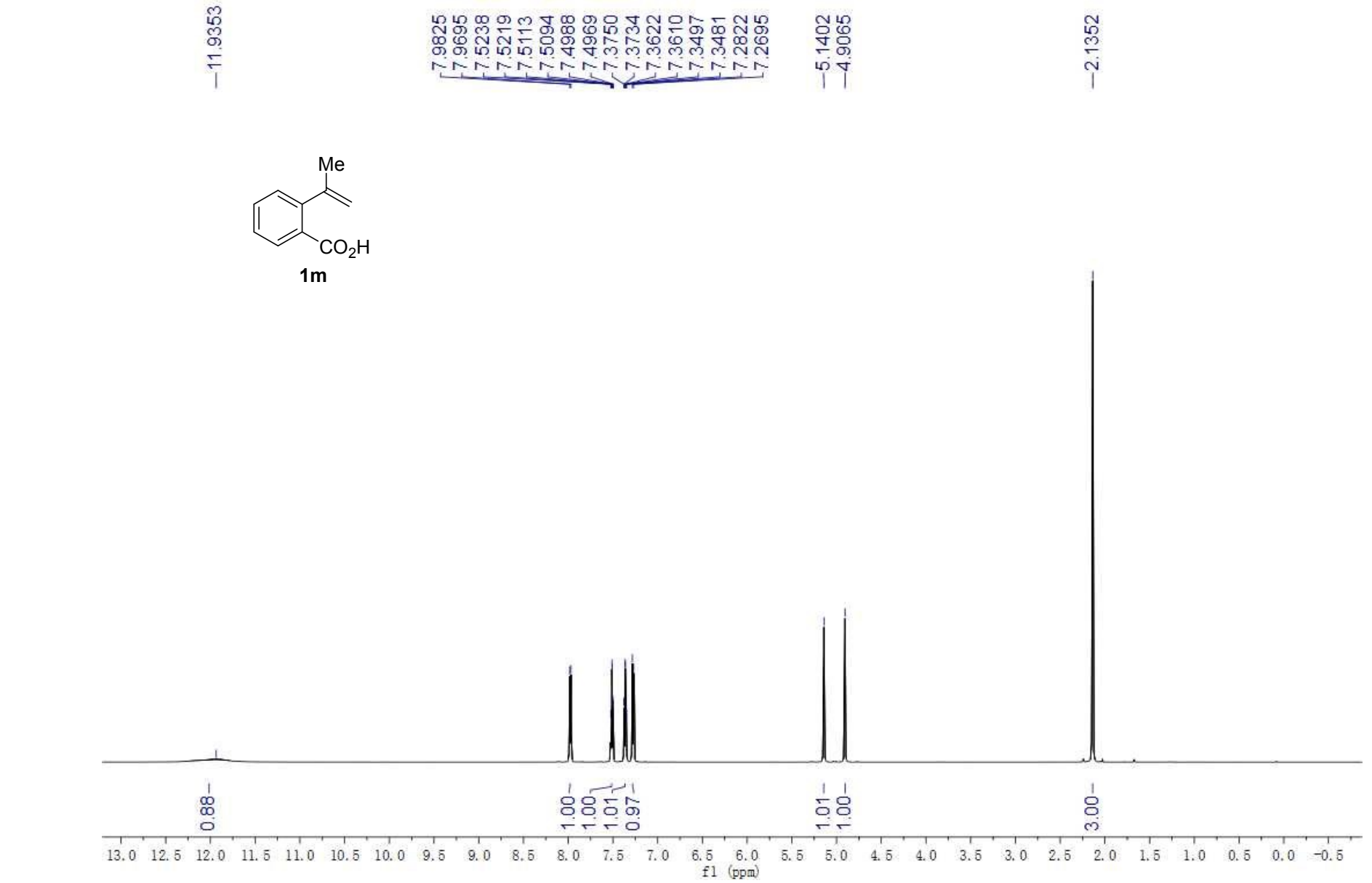
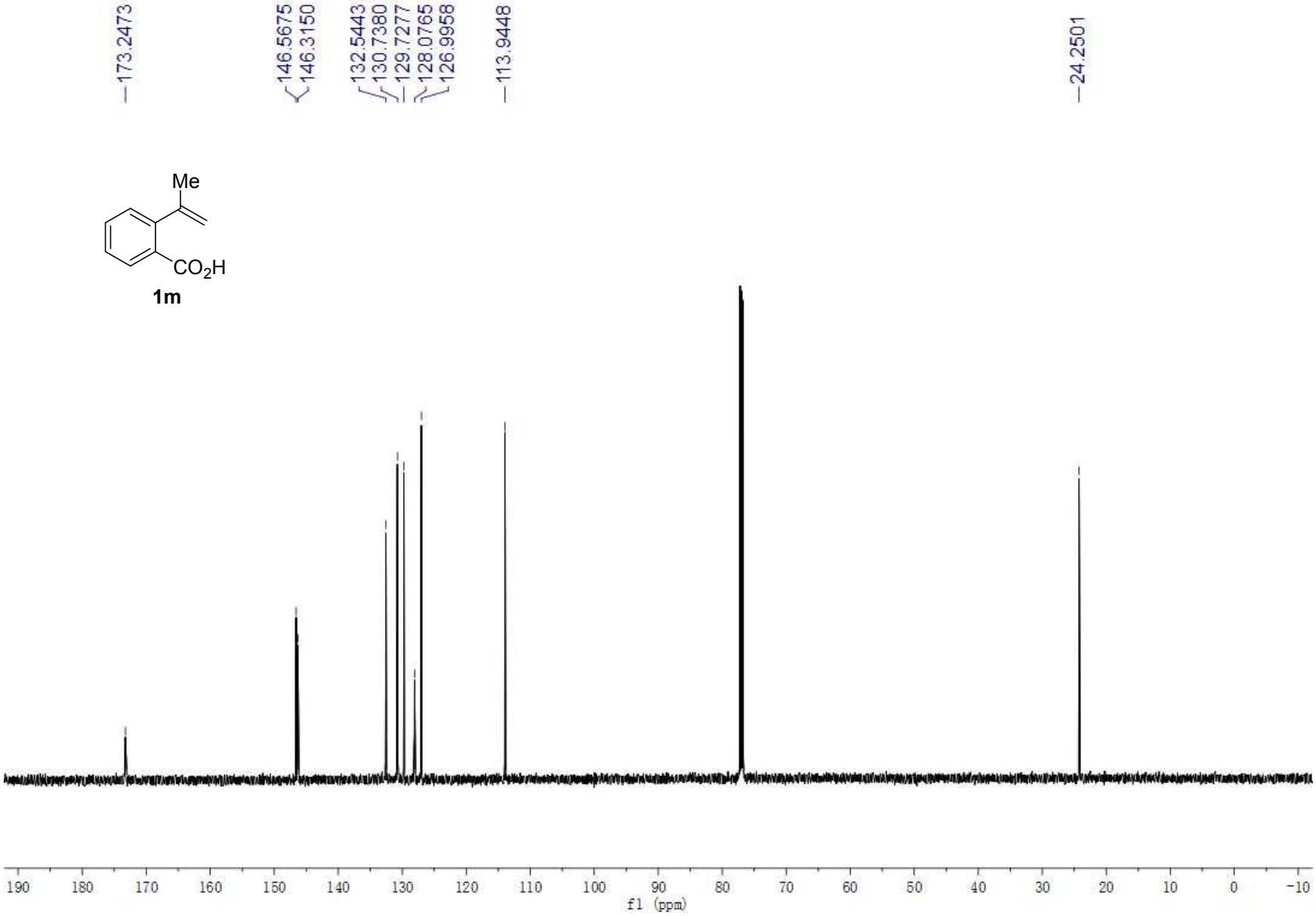
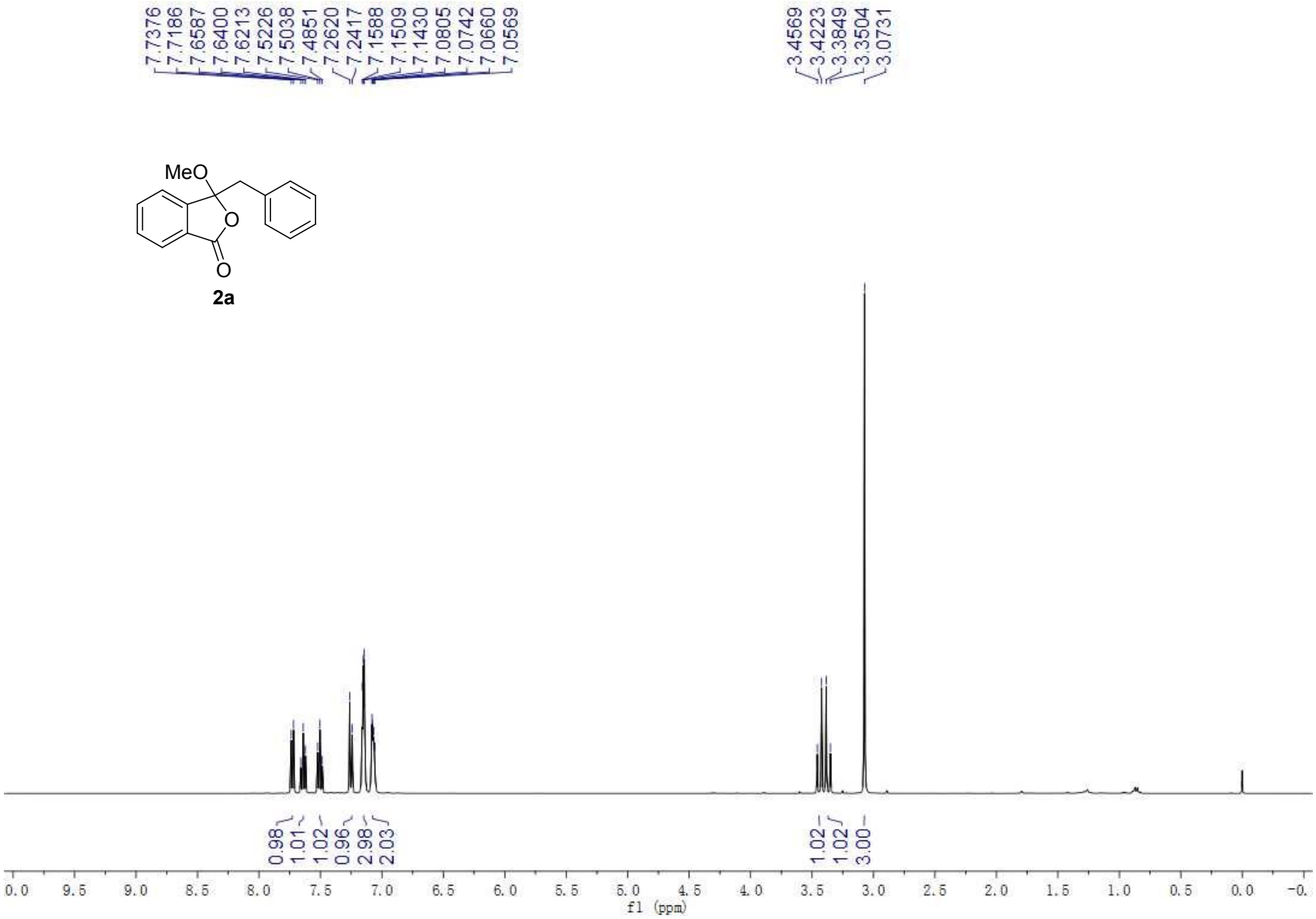
143.1167
139.9151
132.7045
131.5631
131.2234
130.9171
129.1578
128.3434
127.9369
121.5228
114.8609
Br
CO2H
1k
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


10.7477
7.9586
7.9574
7.9456
7.9444
7.5903
7.5778
7.5757
7.5652
7.5631
7.4595
7.4576
7.4467
7.4450
7.4341
7.4322
7.3933
7.3807
7.1524
7.1388
7.0888
5.1900
2.3322
Me
CO2H
1l
0.78
1.00
0.98
0.97
0.96
1.94
1.95
0.99
1.00
3.00
f1 (ppm)

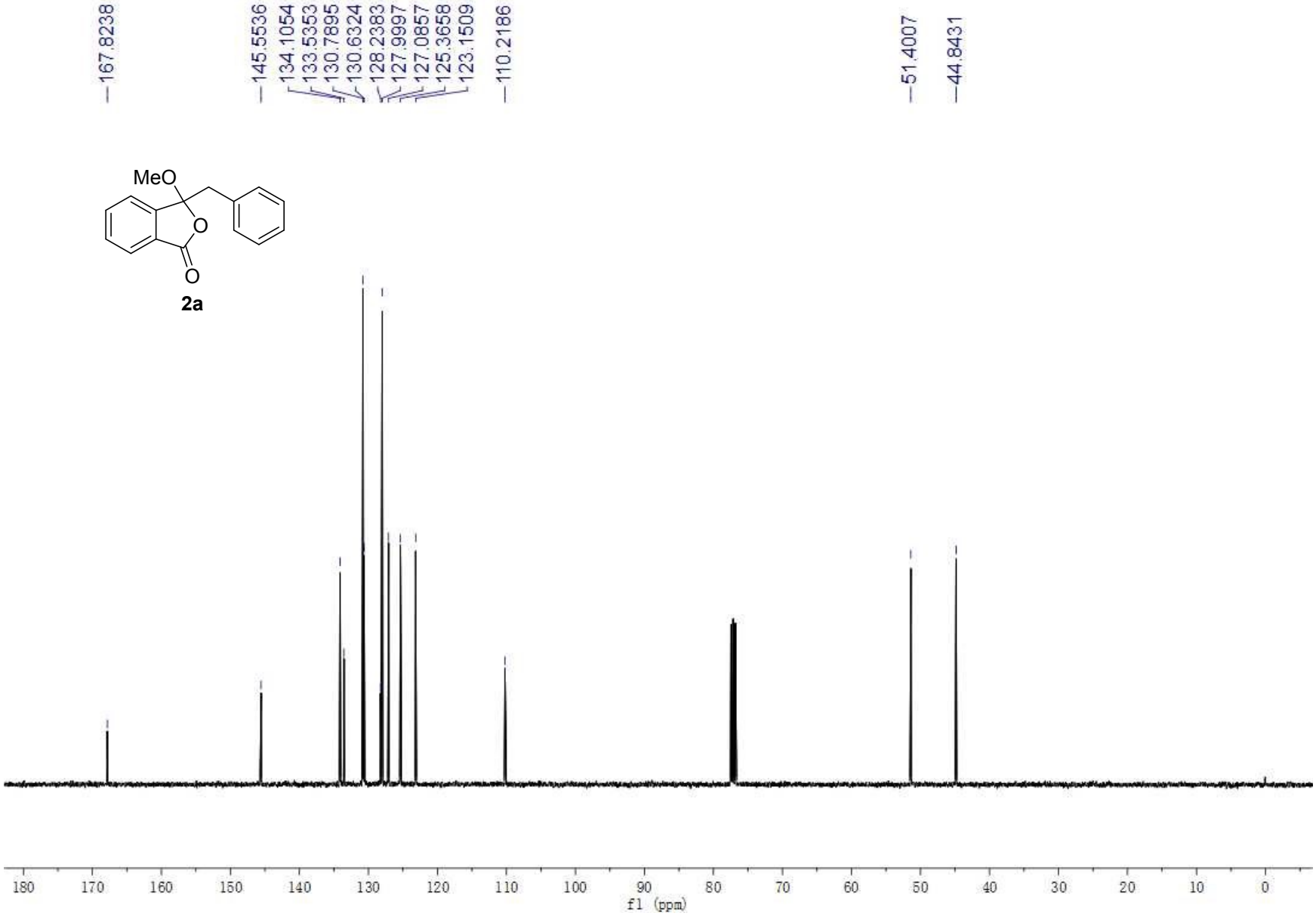

172.5879
149.3464
143.8298
138.1126
137.2452
132.3068
131.4783
130.5968
128.8114
127.5179
126.7110
125.0980
113.5210
21.1061
Me
CO2H
1l
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


11.9353
7.9825
7.9695
7.5238
7.5219
7.5113
7.5094
7.4988
7.4969
7.3750
7.3734
7.3622
7.3610
7.3497
7.3481
7.2822
7.2695
5.1402
4.9065
2.1352
Me
CO2H
1m
0.88
1.00
1.00
1.01
0.97
1.01
1.00
3.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

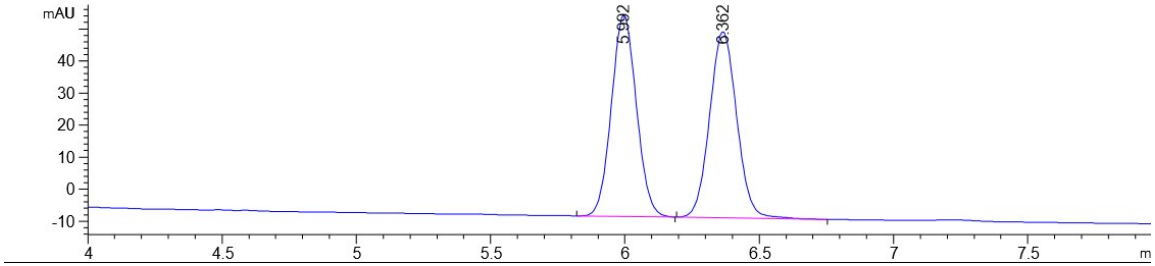

173.2473
146.5675
146.3150
132.5443
130.7380
129.7277
128.0765
126.9958
113.9448
24.2501
Me
CO2H
1m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.7376
7.7186
7.6587
7.6400
7.6213
7.5226
7.5038
7.4851
7.2620
7.2417
7.1588
7.1509
7.1430
7.0805
7.0742
7.0660
7.0569
3.4569
3.4223
3.3849
3.3504
3.0731
MeO
O
O
0.98
1.01
1.02
0.96
2.98
2.03
1.02
1.02
3.00
f1 (ppm)

2a


167.8238
145.5536
134.1054
133.5353
130.7895
130.6324
128.2383
127.9997
127.0857
125.3658
123.1509
110.2186
51.4007
44.8431
MeO
O
O
2a
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

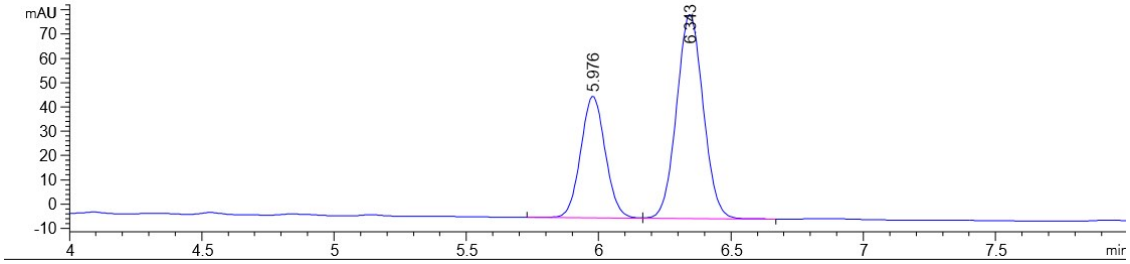
The racemic HPLC spectrum of **2a**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

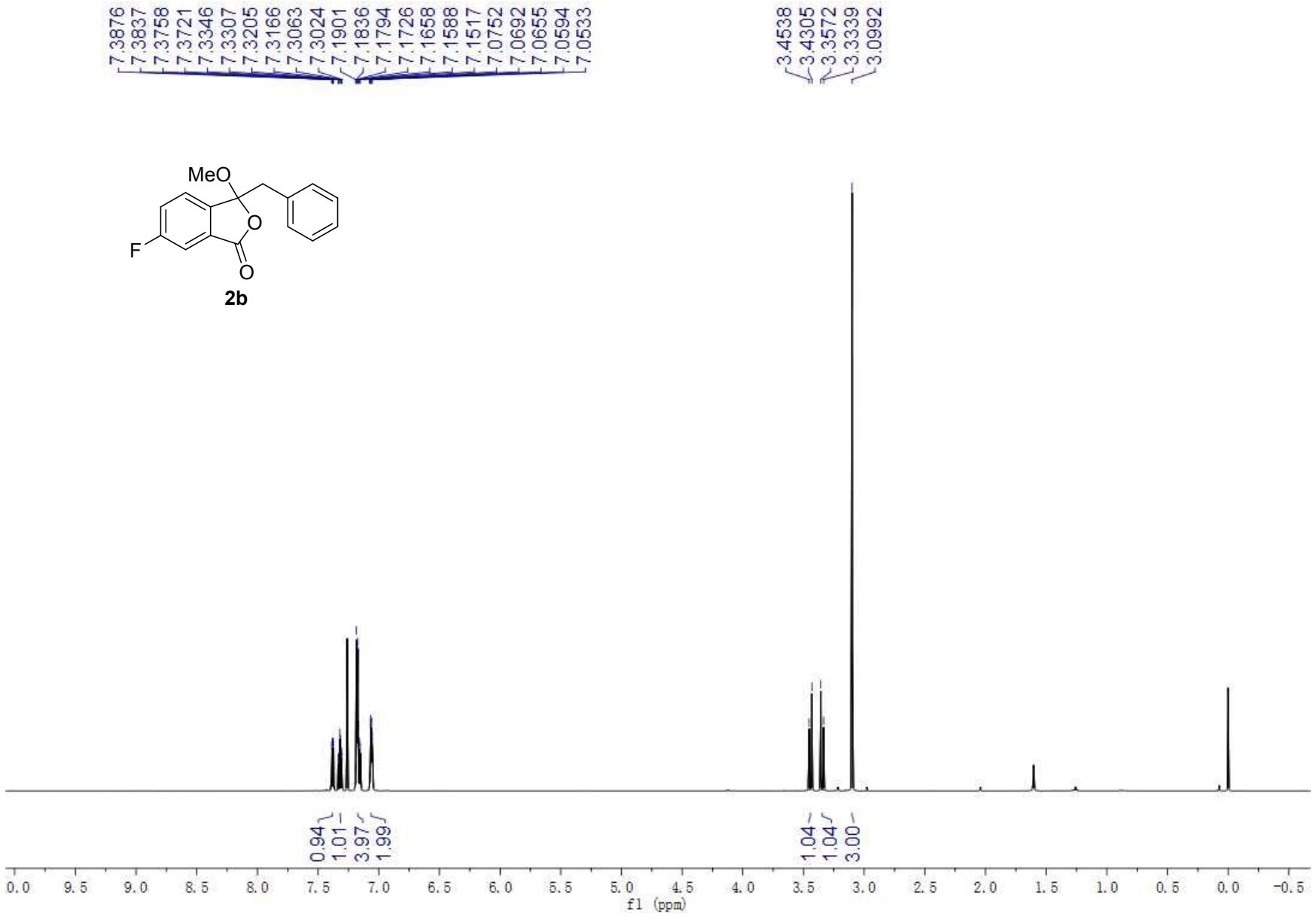
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.992	BB	0.1018	408.62946	62.86820	50.1315
2	6.362	BB	0.1097	406.48639	58.07808	49.8685
Totals :				815.11584	120.94628	

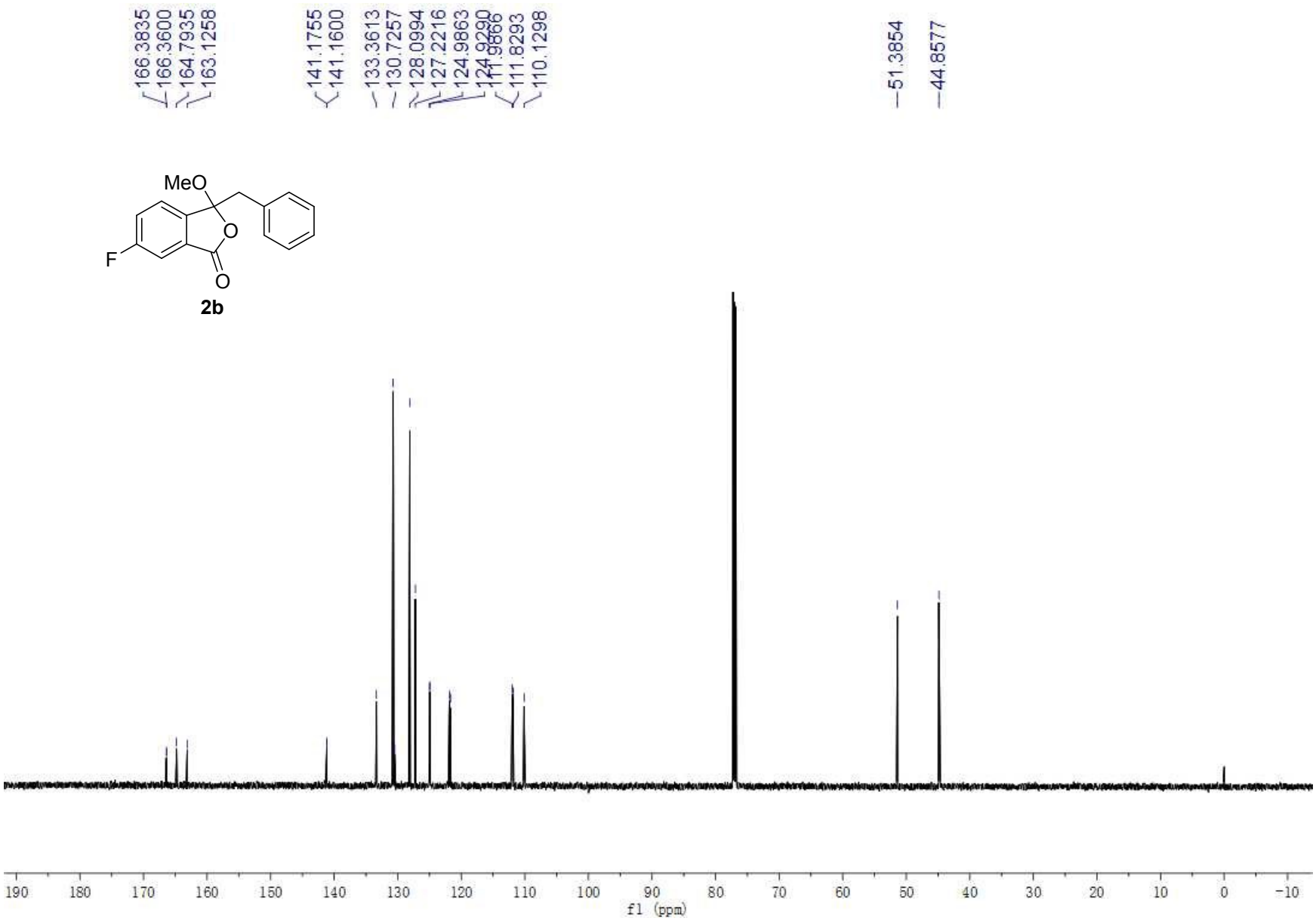
The racemic HPLC spectrum of **2a**

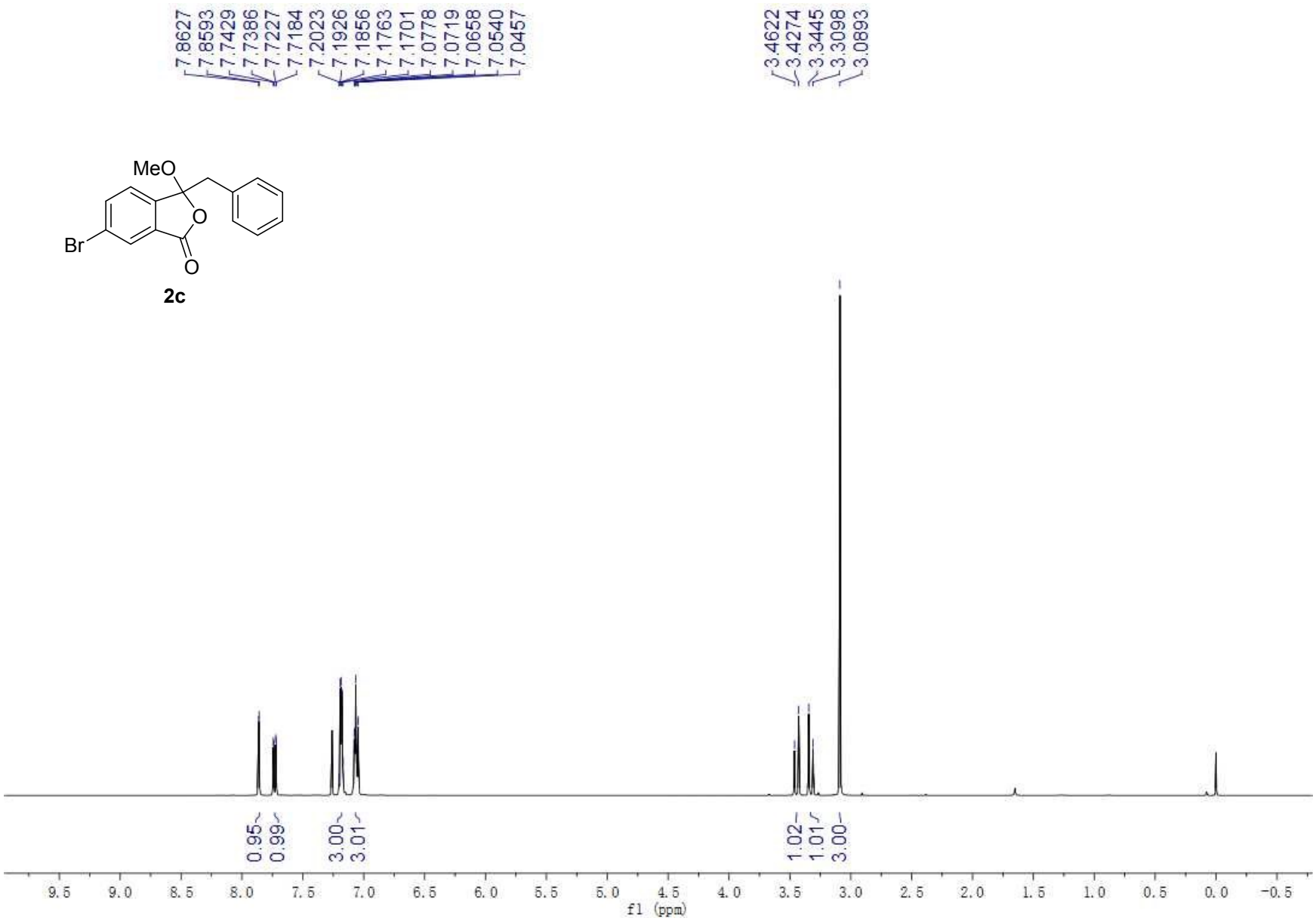


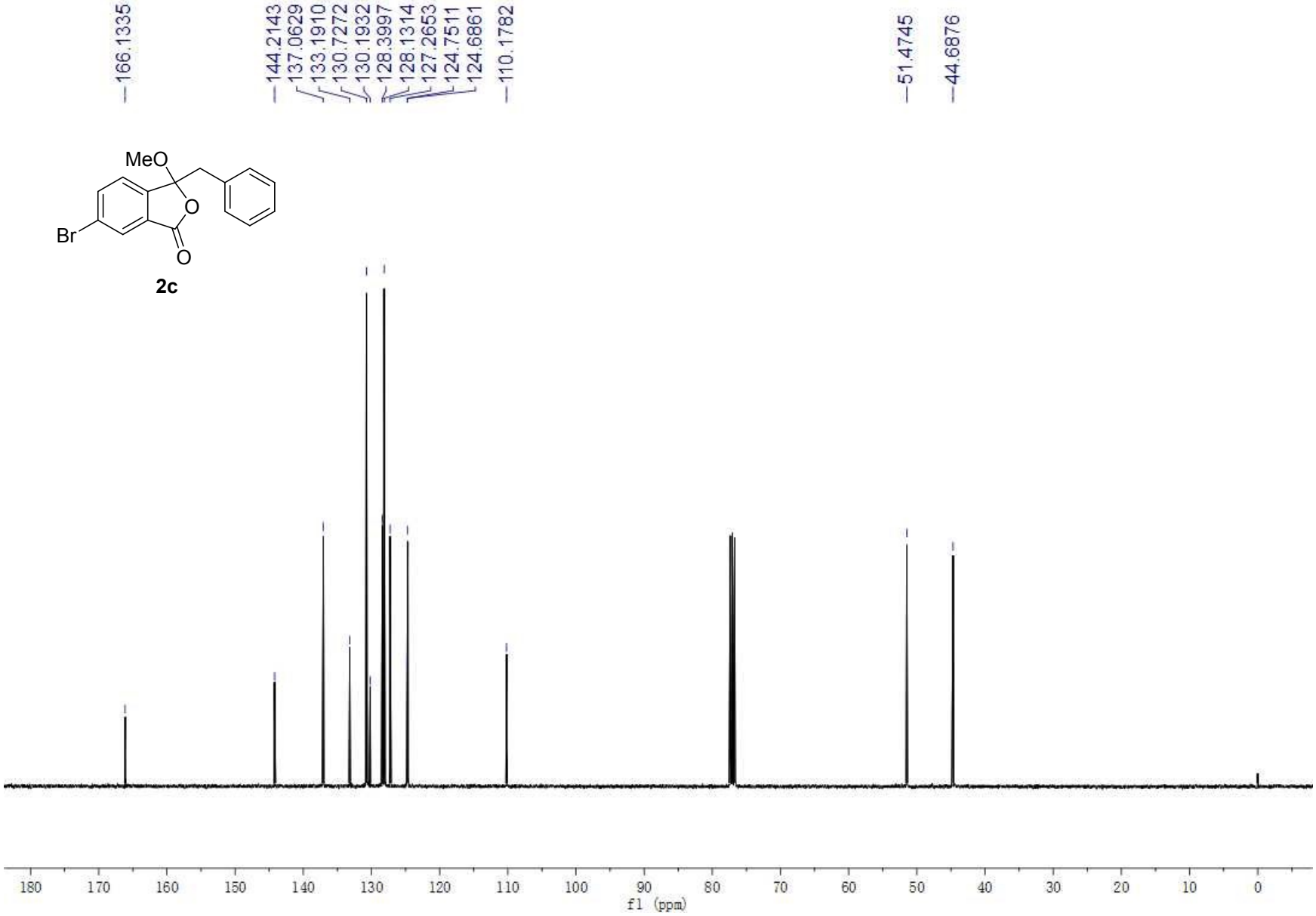
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

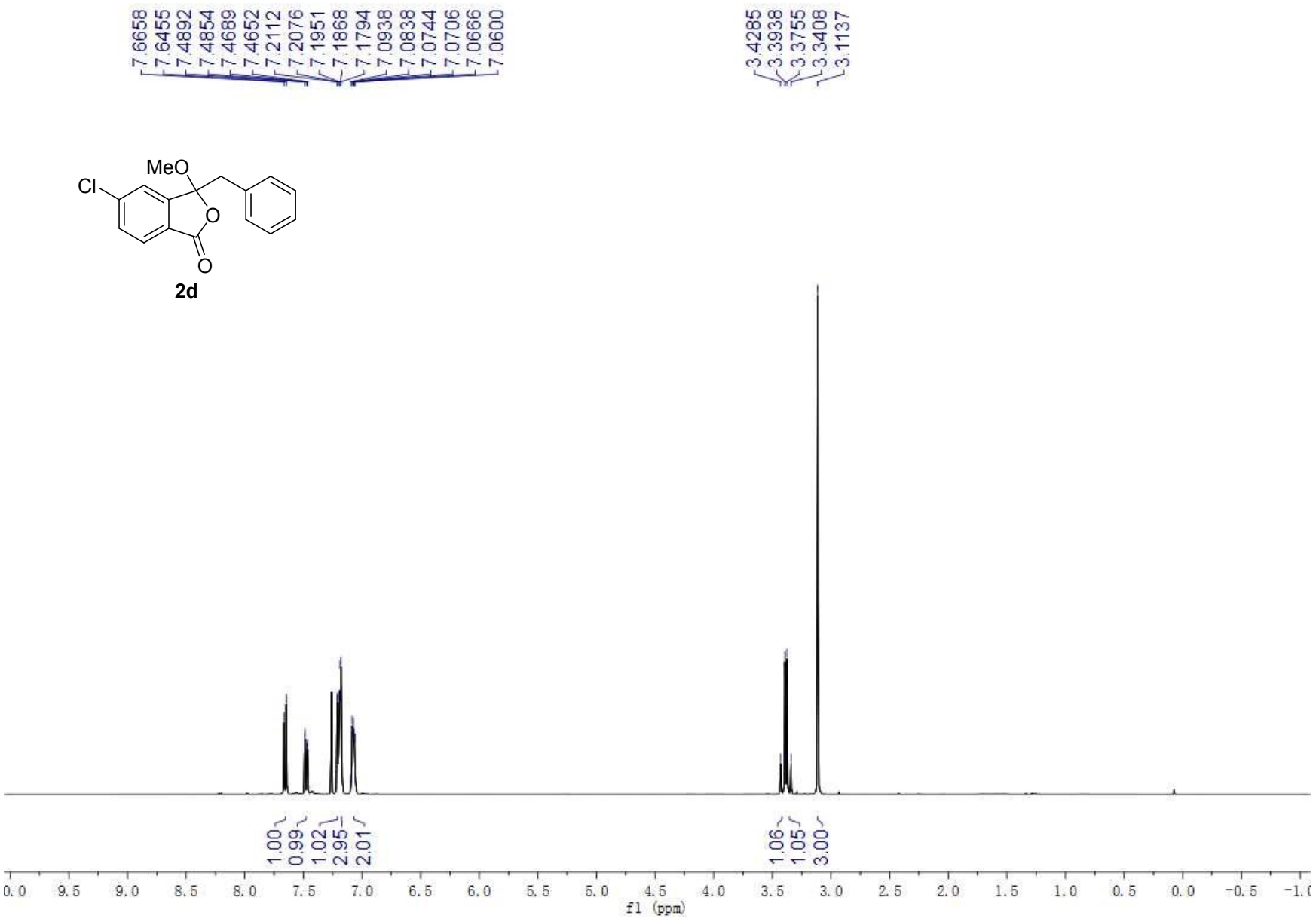
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.976	BV	0.0996	323.97964	50.02637	35.6145
2	6.343	VB	0.1093	585.70581	84.08176	64.3855
Totals :				909.68546	134.10813	


7.3876
7.3837
7.3758
7.3721
7.3346
7.3307
7.3205
7.3166
7.3063
7.3024
7.1901
7.1836
7.1794
7.1726
7.1658
7.1588
7.1517
7.0752
7.0692
7.0655
7.0594
7.0533
3.4538
3.4305
3.3572
3.3339
3.0992
MeO
O
F
O
2b
0.94
1.01
3.97
1.99
1.04
1.04
3.00
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


166.3835
166.3600
164.7935
163.1258
141.1755
141.1600
133.3613
130.7257
128.0994
127.2216
124.9863
124.9290
111.9866
111.8293
110.1298
51.3854
44.8577
MeO
O
F
O
2b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.8627
7.8593
7.7429
7.7386
7.7227
7.7184
7.2023
7.1926
7.1856
7.1763
7.1701
7.0778
7.0719
7.0658
7.0540
7.0457
3.4622
3.4274
3.3445
3.3098
3.0893
MeO
O
Br
O
2c
0.95
0.99
3.00
3.01
1.02
1.01
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


166.1335
144.2143
137.0629
133.1910
130.7272
130.1932
128.3997
128.1314
127.2653
124.7511
124.6861
110.1782
51.4745
44.6876
MeO
O
Br
O
2c
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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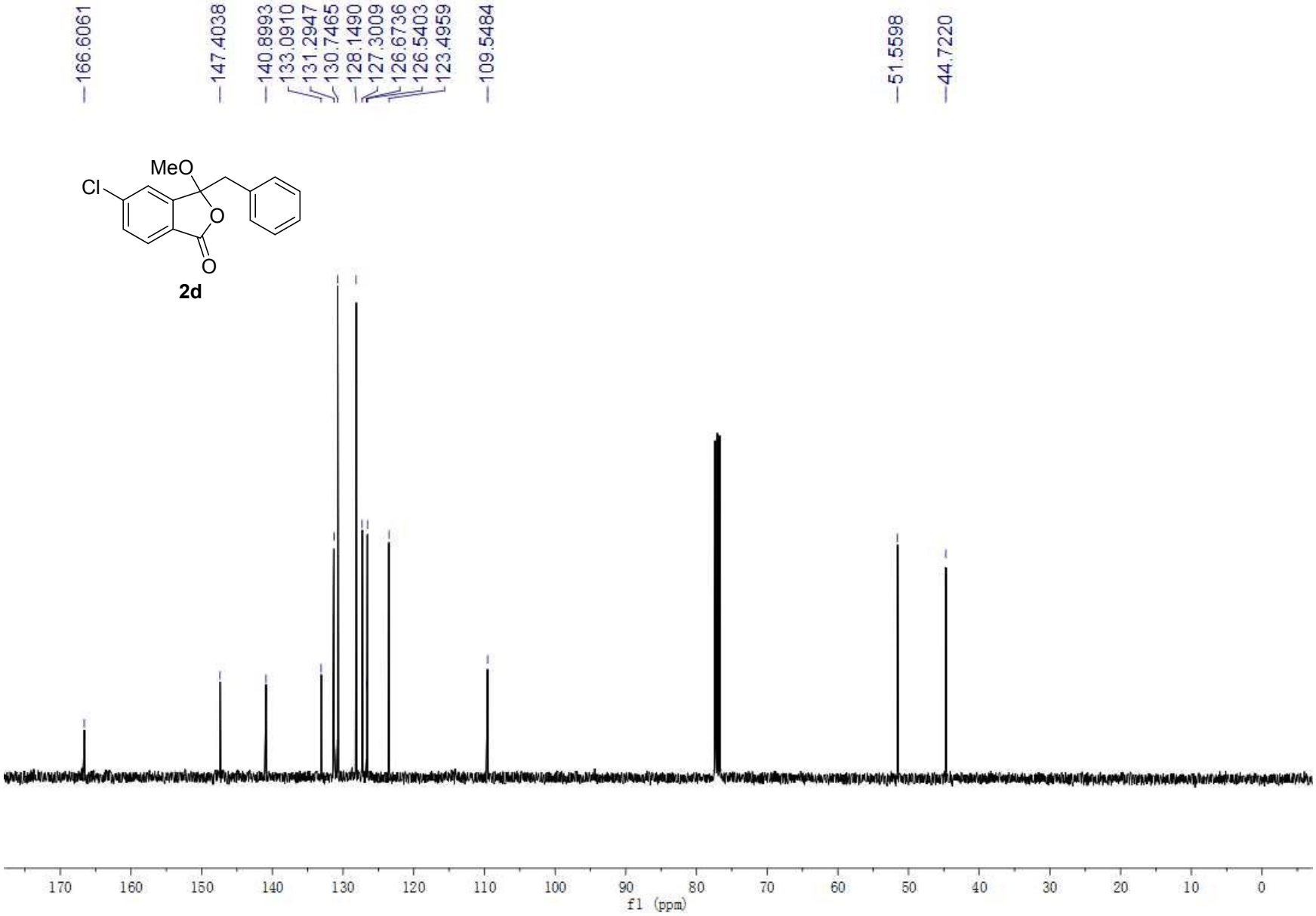
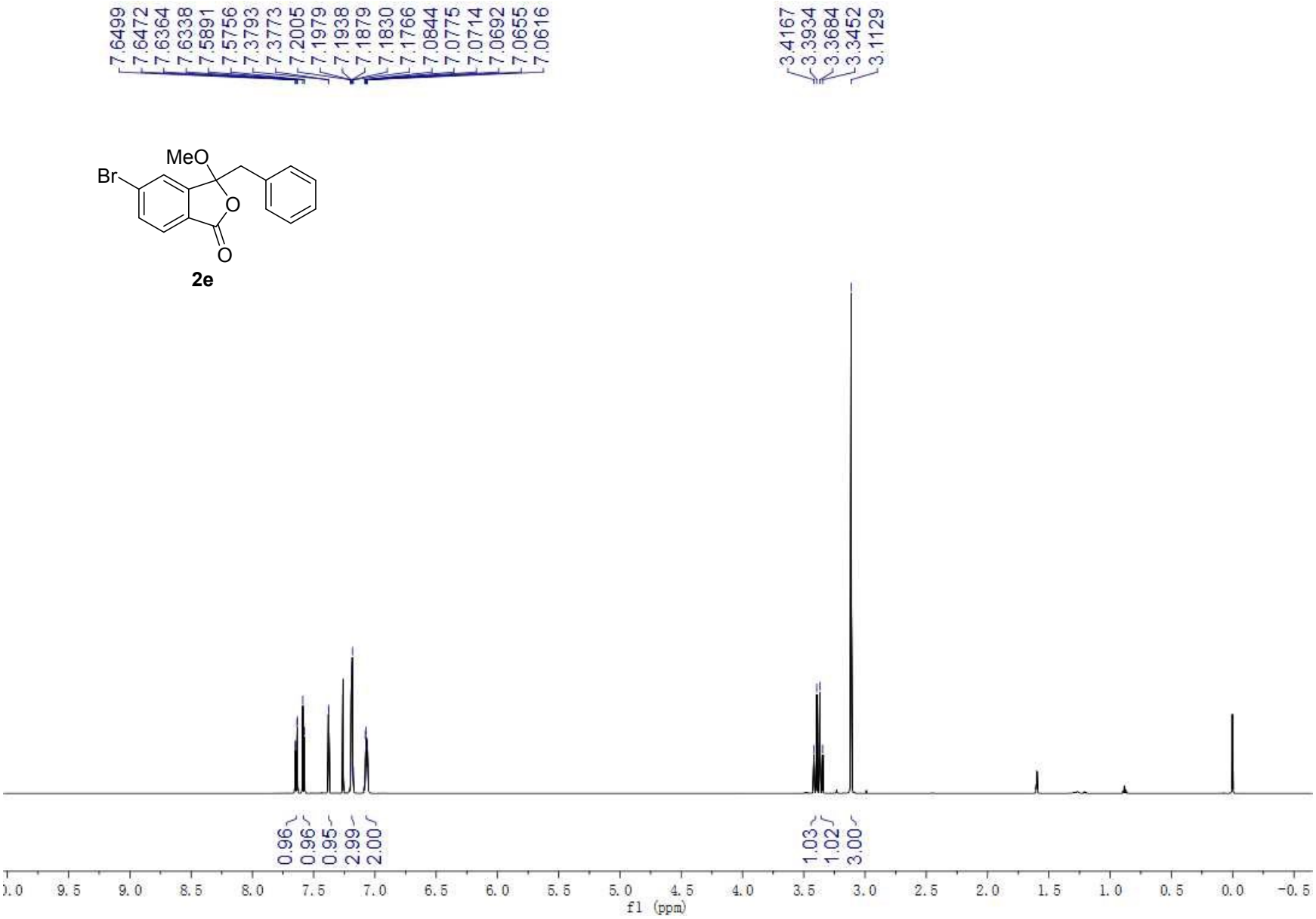
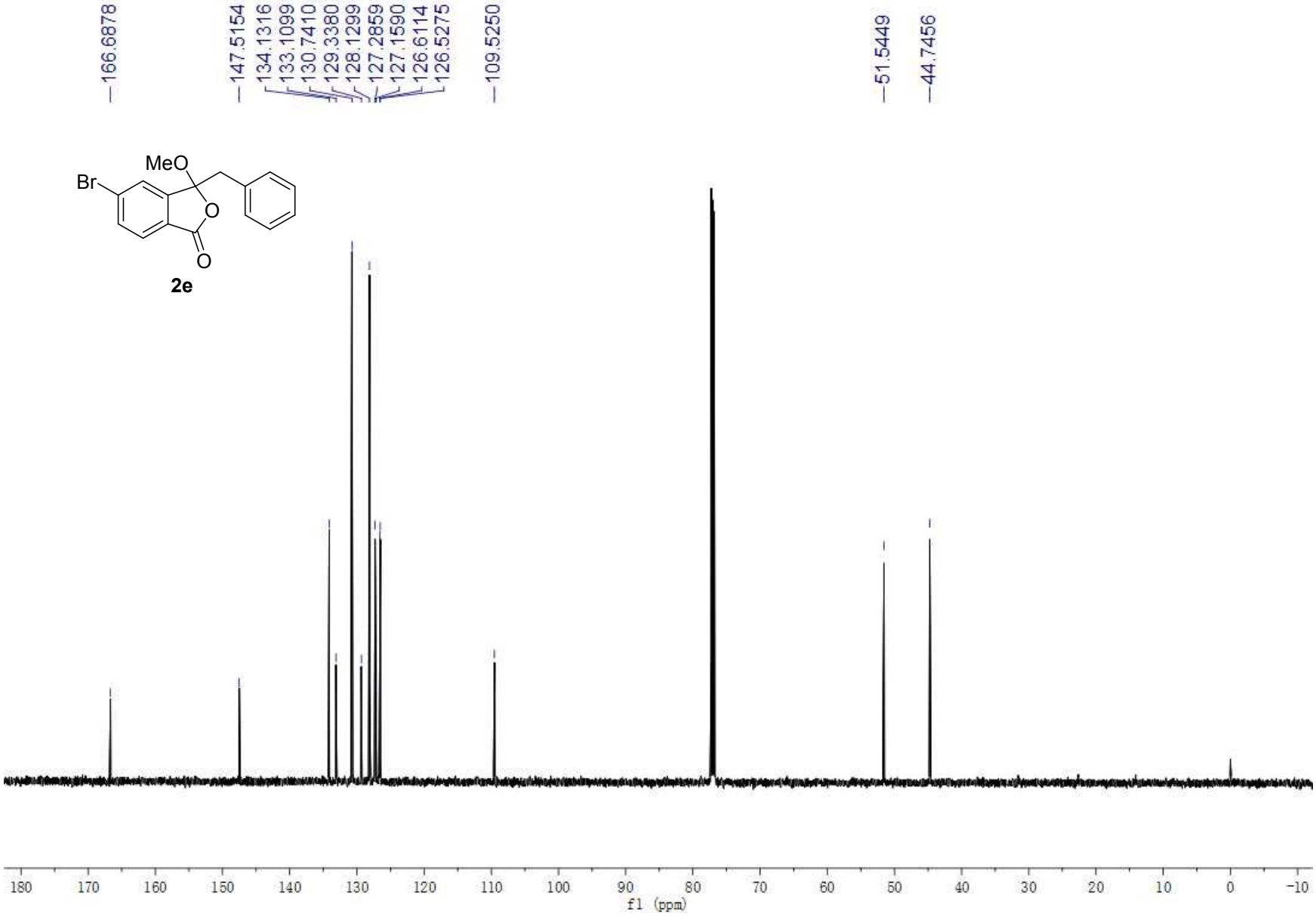
7.6455
7.4892
7.4854
7.4689
7.4652
7.2112
7.2076
7.1951
7.1868
7.1794
7.0938
7.0838
7.0744
7.0706
7.0666
7.0600
3.4285
3.3938
3.3755
3.3408
3.1137
MeO
Cl
O
O
2d
1.00
0.99
1.02
2.95
2.01
1.06
1.05
3.00
f1 (ppm)


166.6061
147.4038
140.8993
133.0910
131.2947
130.7465
128.1490
127.3009
126.6736
126.5403
123.4959
109.5484
51.5598
44.7220
MeO
Cl
O
O
2d
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.6499
7.6472
7.6364
7.6338
7.5891
7.5756
7.3793
7.3773
7.2005
7.1979
7.1938
7.1879
7.1830
7.1766
7.0844
7.0775
7.0714
7.0692
7.0655
7.0616
3.4167
3.3934
3.3684
3.3452
3.1129
MeO
Br
O
O
2e
0.96
0.96
0.95
2.99
2.00
1.03
1.02
3.00
f1 (ppm)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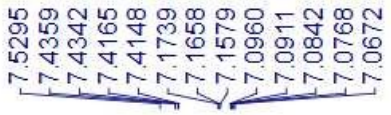
147.5154
134.1316
133.1099
130.7410
129.3380
128.1299
127.2859
127.1590
126.6114
126.5275
109.5250
51.5449
44.7456
MeO
Br
O
O
2e
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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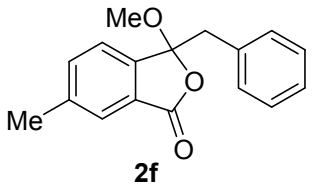
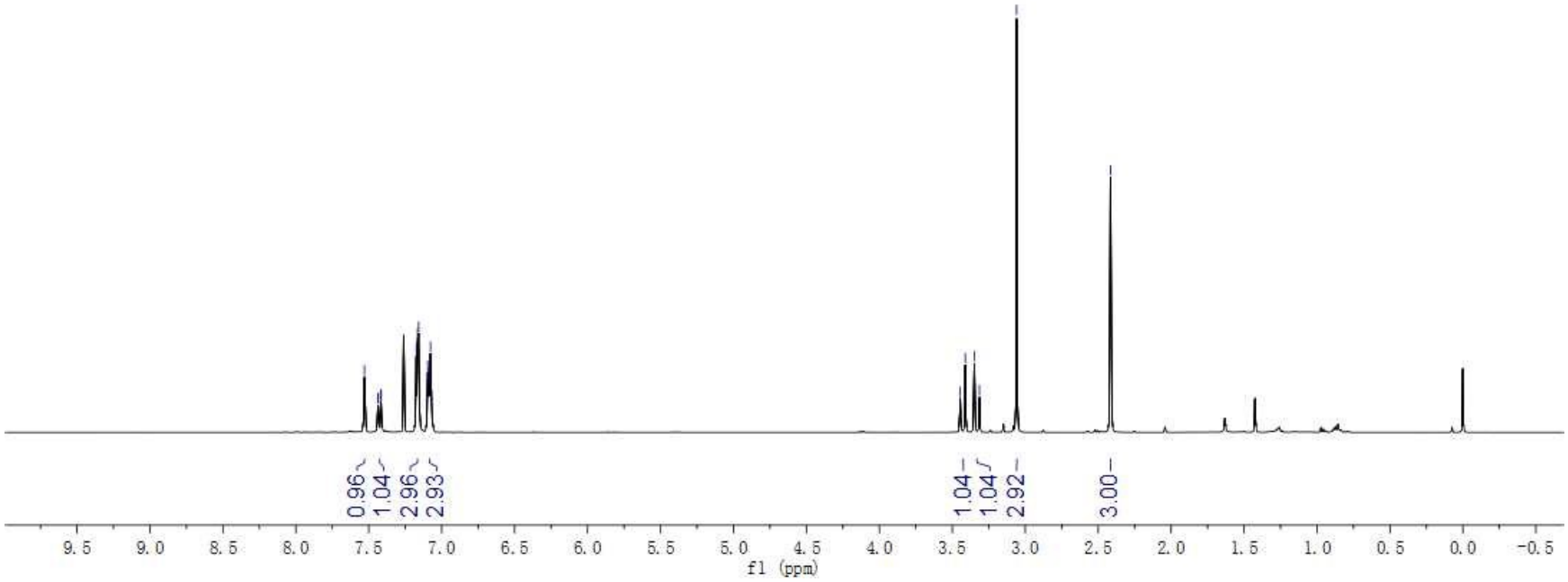
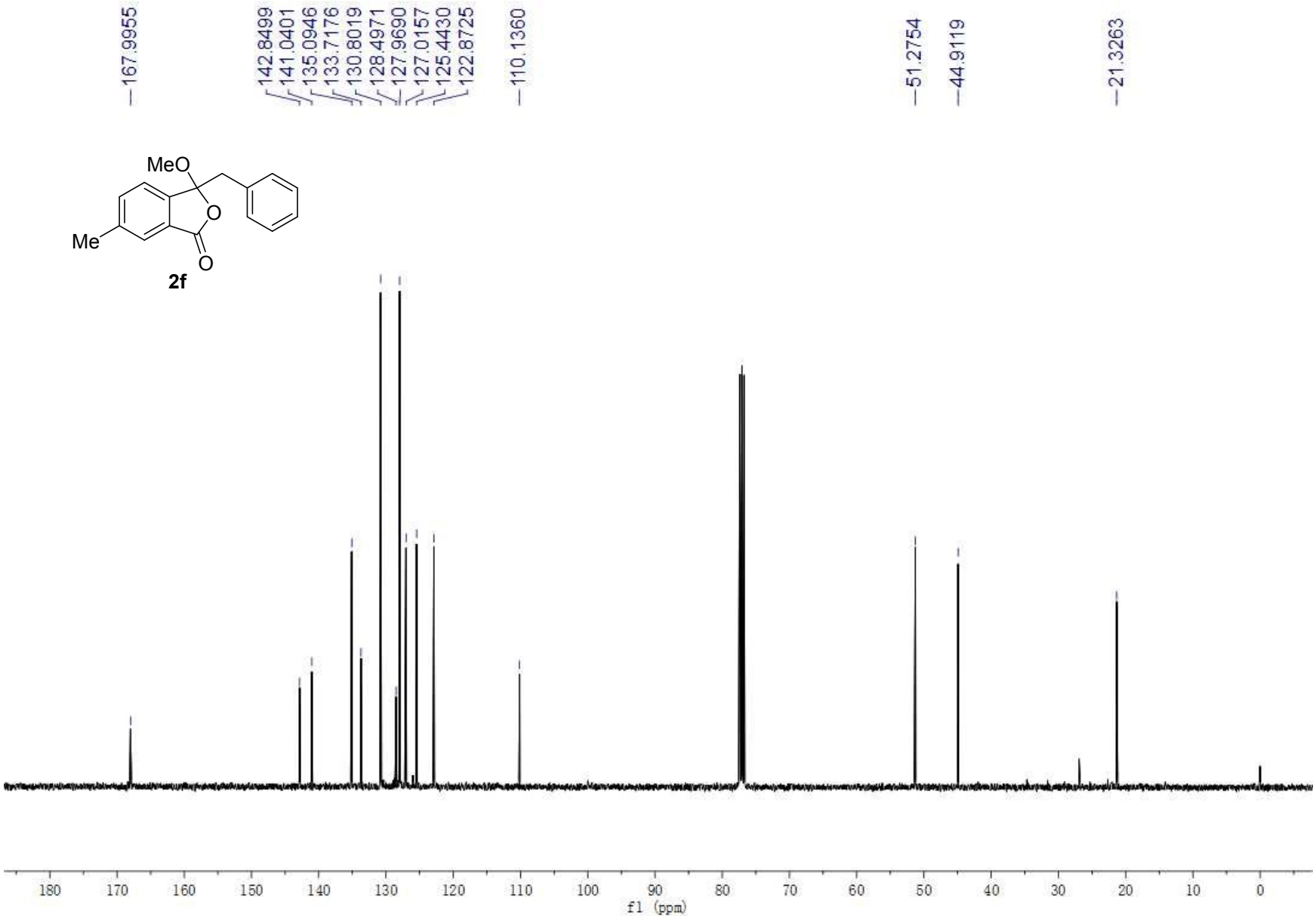
7.4359
7.4342
7.4165
7.4148
7.1739
7.1658
7.1579
7.0960
7.0911
7.0842
7.0768
7.0672


3.4455
3.4110
3.3486
3.3140
3.0590
2.4155


MeO
O
Me
O

2f


0.96
1.04
2.96
2.93
1.04
1.04
2.92
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


167.9955
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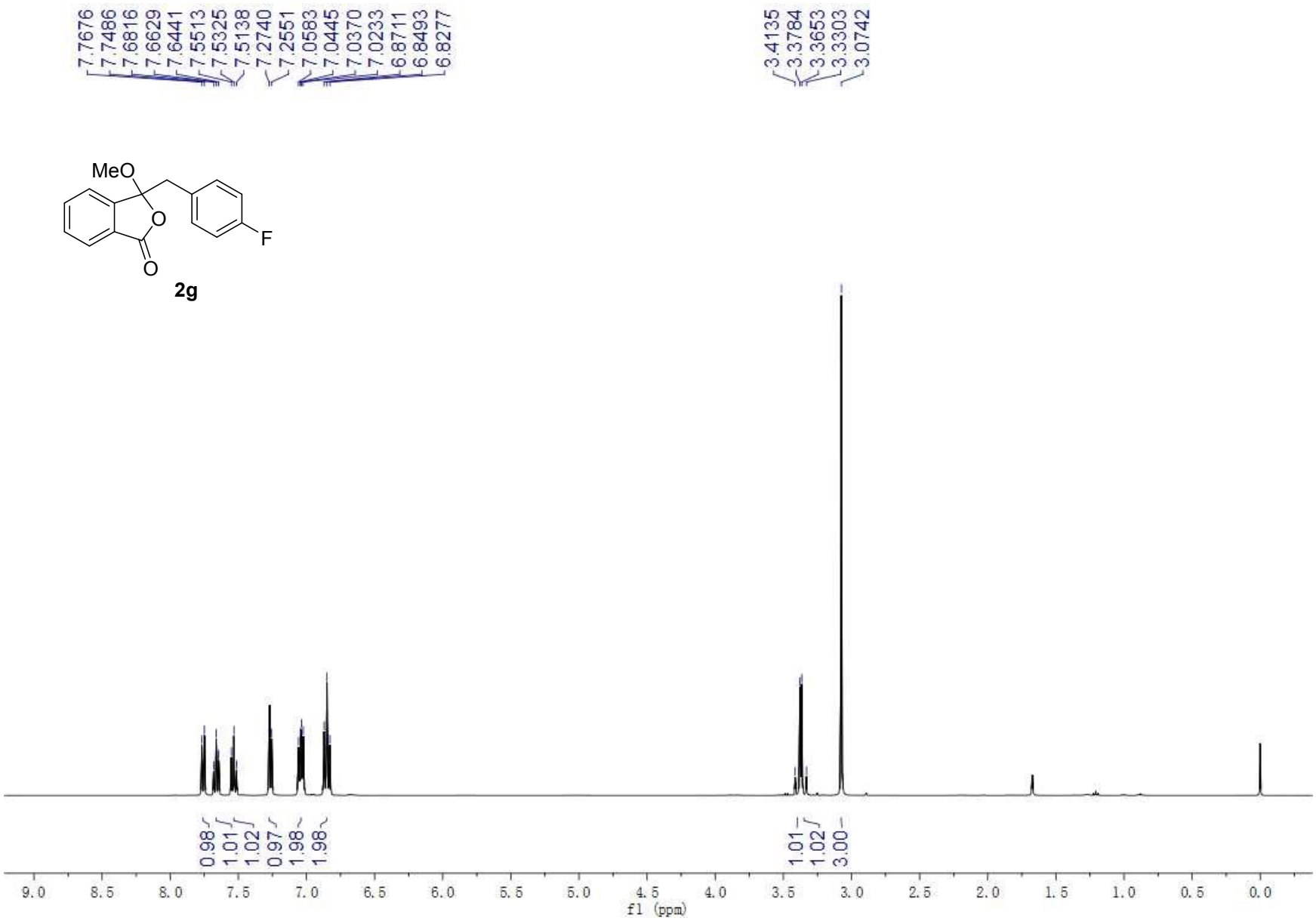
141.0401
135.0946
133.7176
130.8019
128.4971
127.9690
127.0157
125.4430
122.8725
110.1360
51.2754
44.9119
21.3263
MeO
Me
O
O
2f
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.6816
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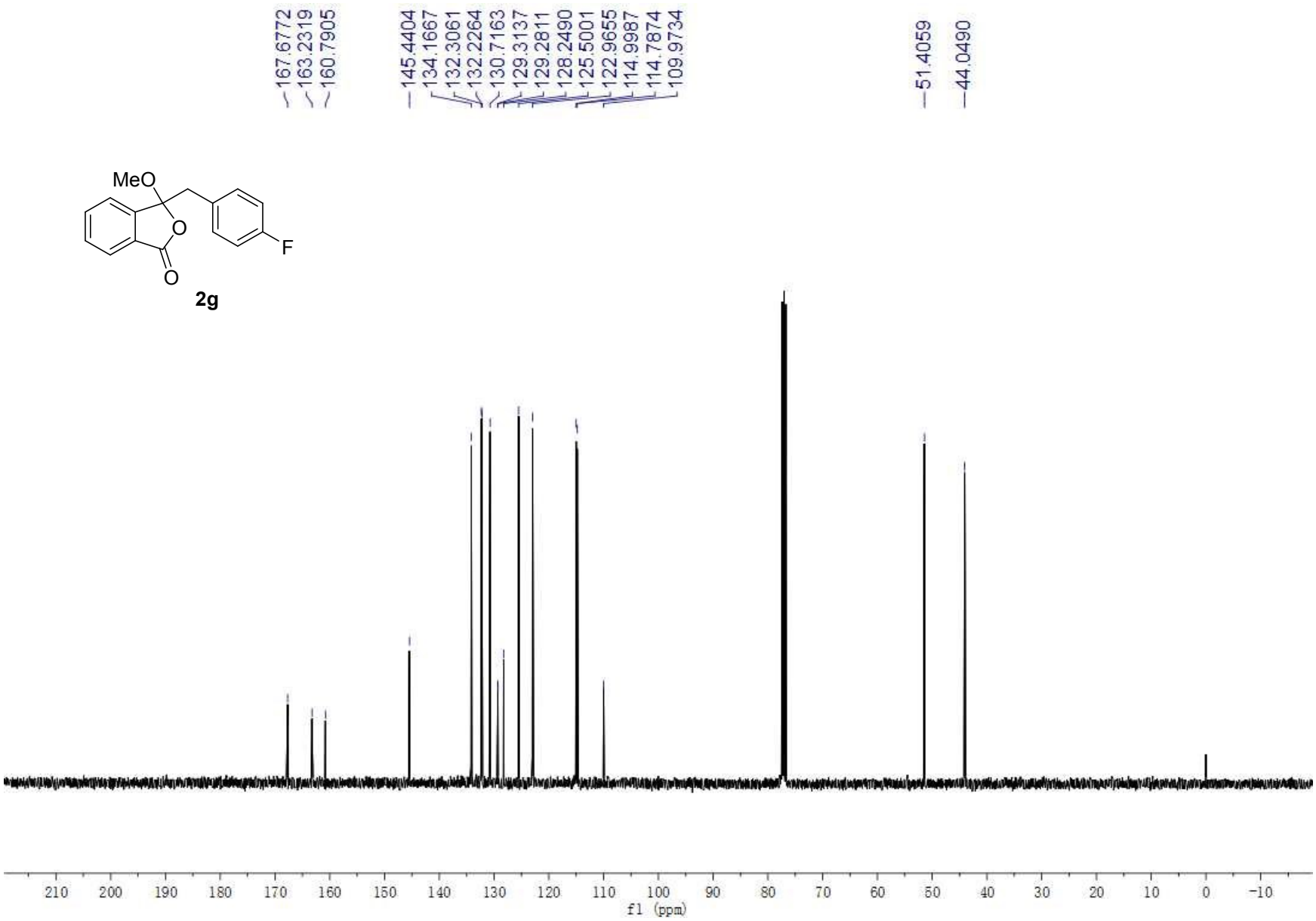
7.6441
7.5513
7.5325
7.5138
7.2740
7.2551
7.0583
7.0445
7.0370
7.0233
6.8711
6.8493
6.8277
3.4135
3.3784
3.3653
3.3303
3.0742
MeO
O
O
F
2g
0.98
1.01
1.02
0.97
1.98
1.98
1.01
1.02
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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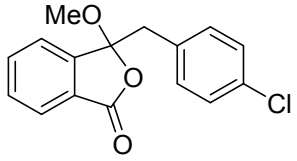
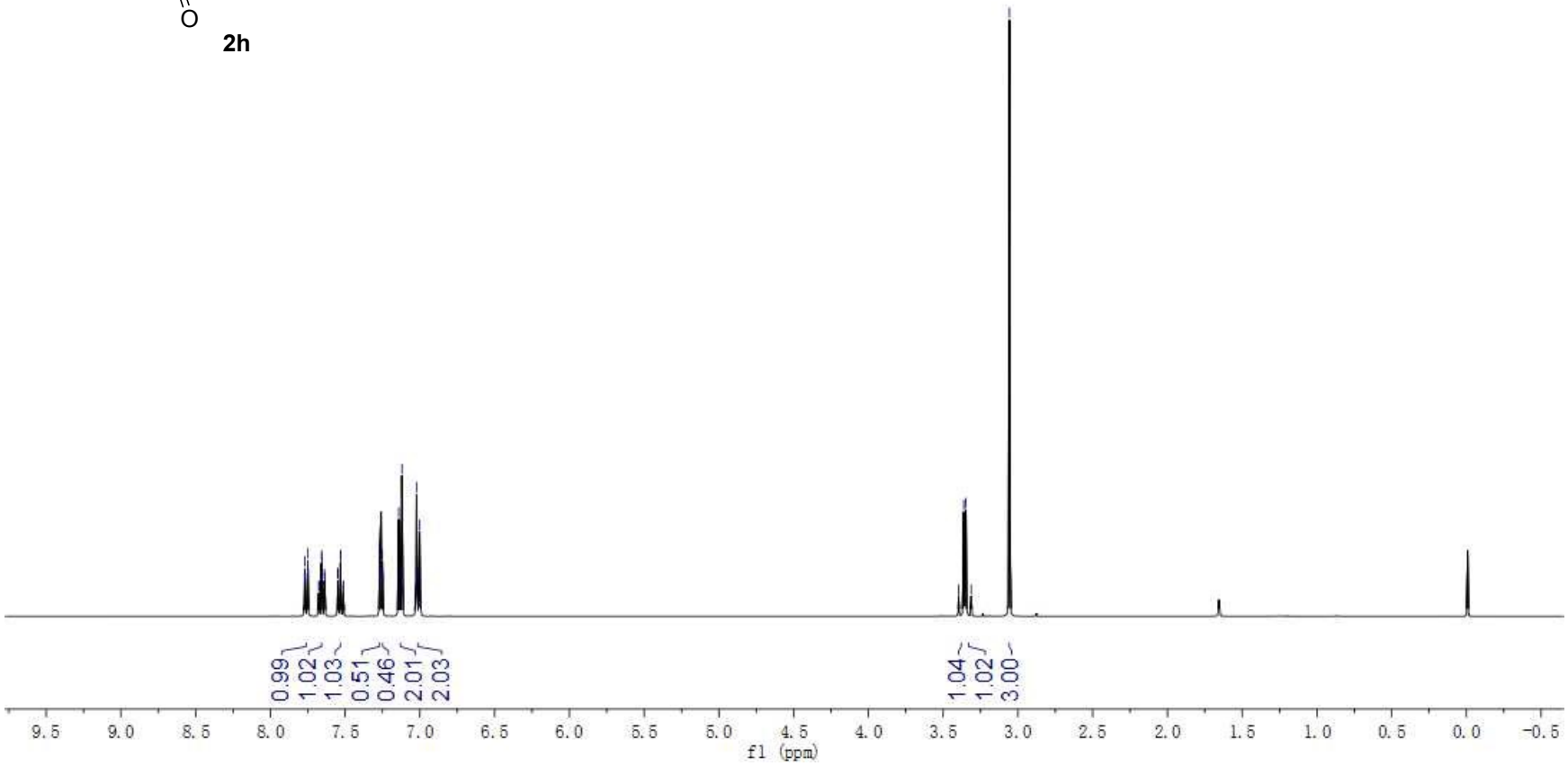
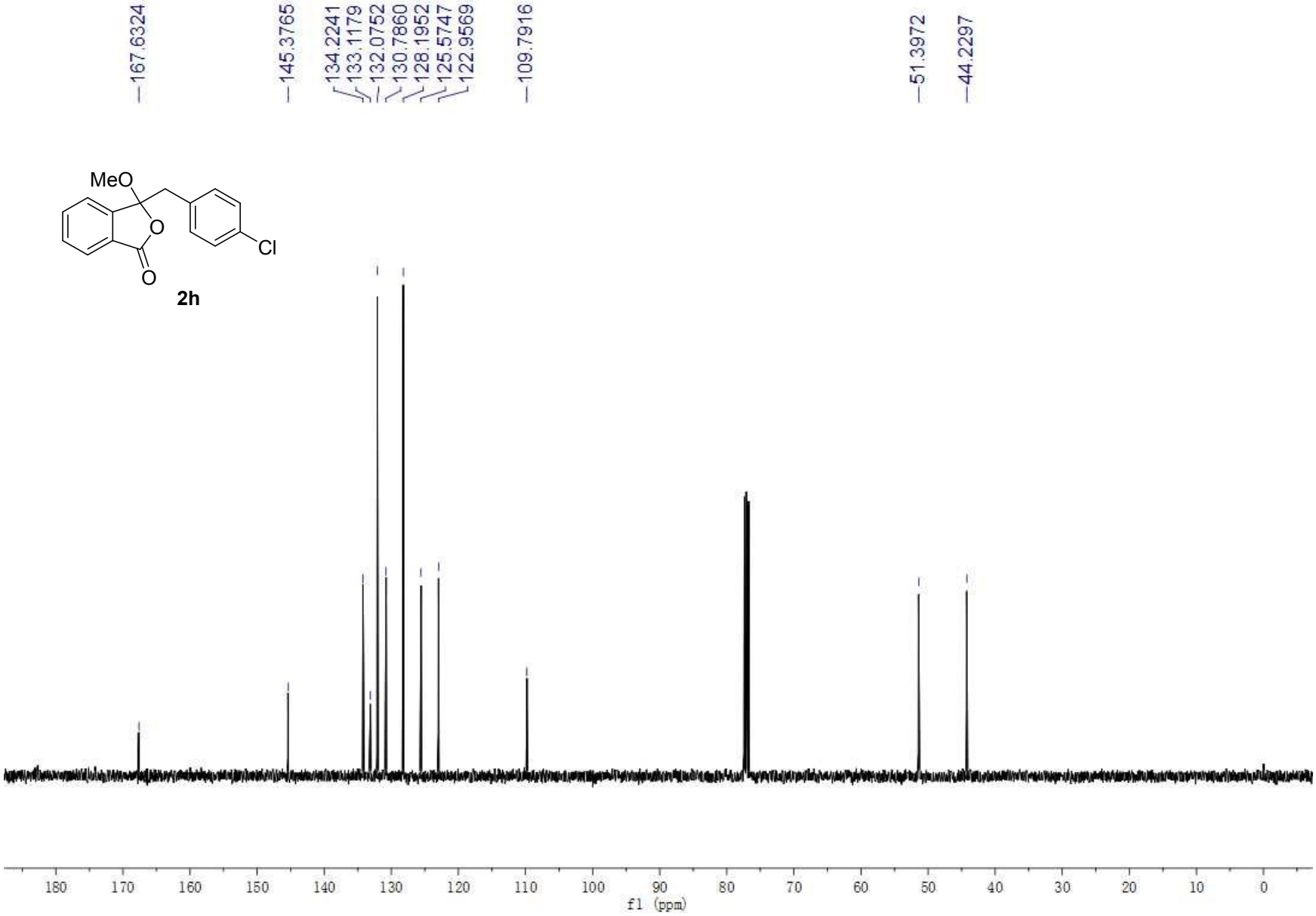
160.7905
145.4404
134.1667
132.3061
132.2264
130.7163
129.3137
129.2811
128.2490
125.5001
122.9655
114.9987
114.7874
109.9734
51.4059
44.0490
MeO
O
O
F
2g
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

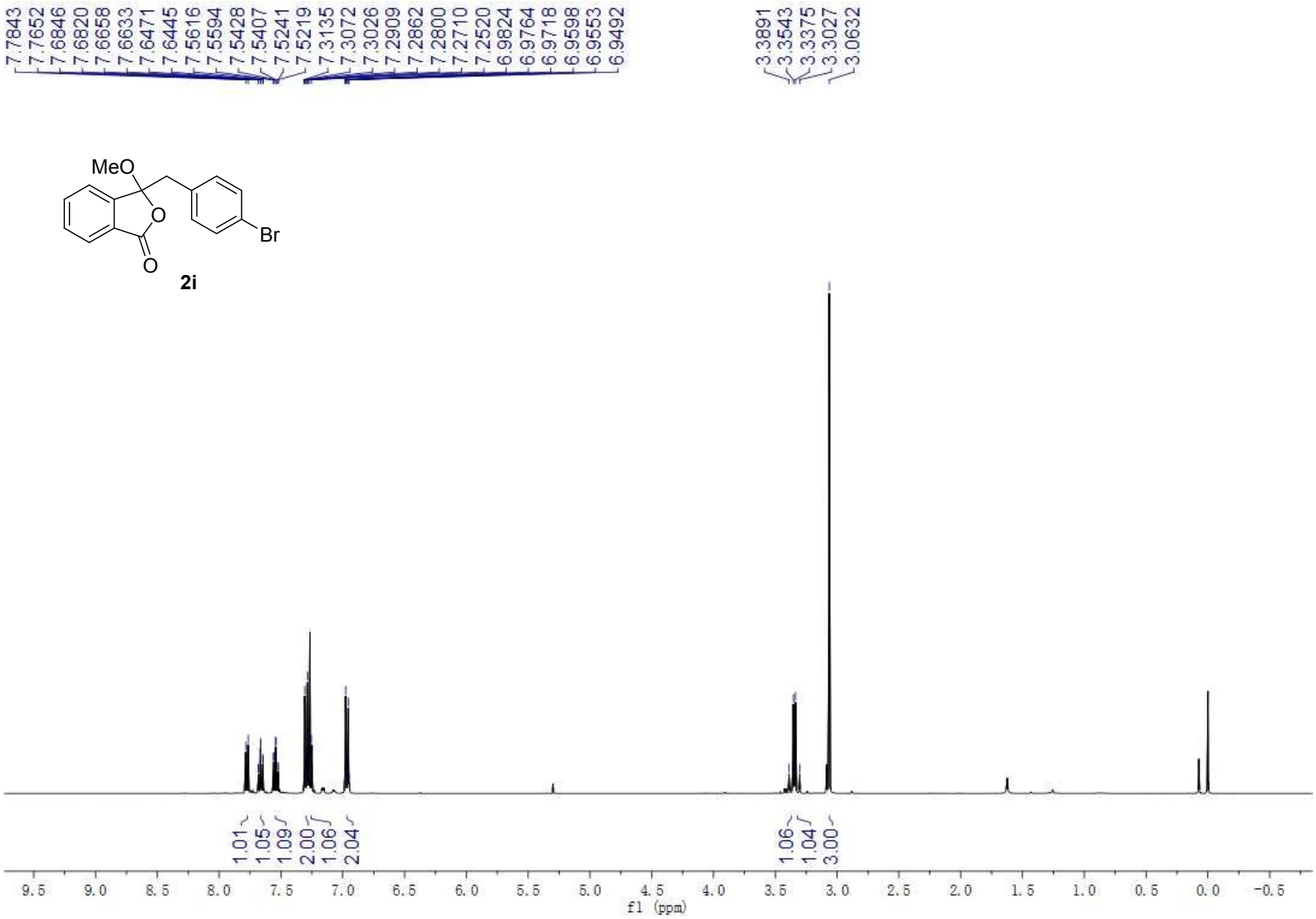

7.7715
7.7693
7.7670
7.7525
7.7503
7.7481
7.6768
7.6741
7.6580
7.6554
7.6392
7.6365
7.5500
7.5477
7.5312
7.5290
7.5125
7.5102
7.2710
7.2691
7.2672
7.2521
7.2501
7.2482
7.1412
7.1363
7.1250
7.1200
7.1139
7.0285
7.0225
7.0175
7.0061
7.0013
3.3868
3.3620
3.3475
3.3127
3.0566


MeO
O
O
Cl

2h


0.99
1.02
1.03
0.51
0.46
2.01
2.03
1.04
1.02
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


167.6324
145.3765
134.2241
133.1179
132.0752
130.7860
128.1952
125.5747
122.9569
109.7916
51.3972
44.2297
MeO
O
O
Cl
2h
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.7843
7.7652
7.6846
7.6820
7.6658
7.6633
7.6471
7.6445
7.5616
7.5594
7.5428
7.5407
7.5241
7.5219
7.3135
7.3072
7.3026
7.2909
7.2862
7.2800
7.2710
7.2520
6.9824
6.9764
6.9718
6.9598
6.9553
6.9492
3.3891
3.3543
3.3375
3.3027
3.0632
MeO
O
O
Br
2i
1.01
1.05
1.09
2.00
1.06
2.04
1.06
1.04
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
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3.0
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2.0
1.5
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0.5
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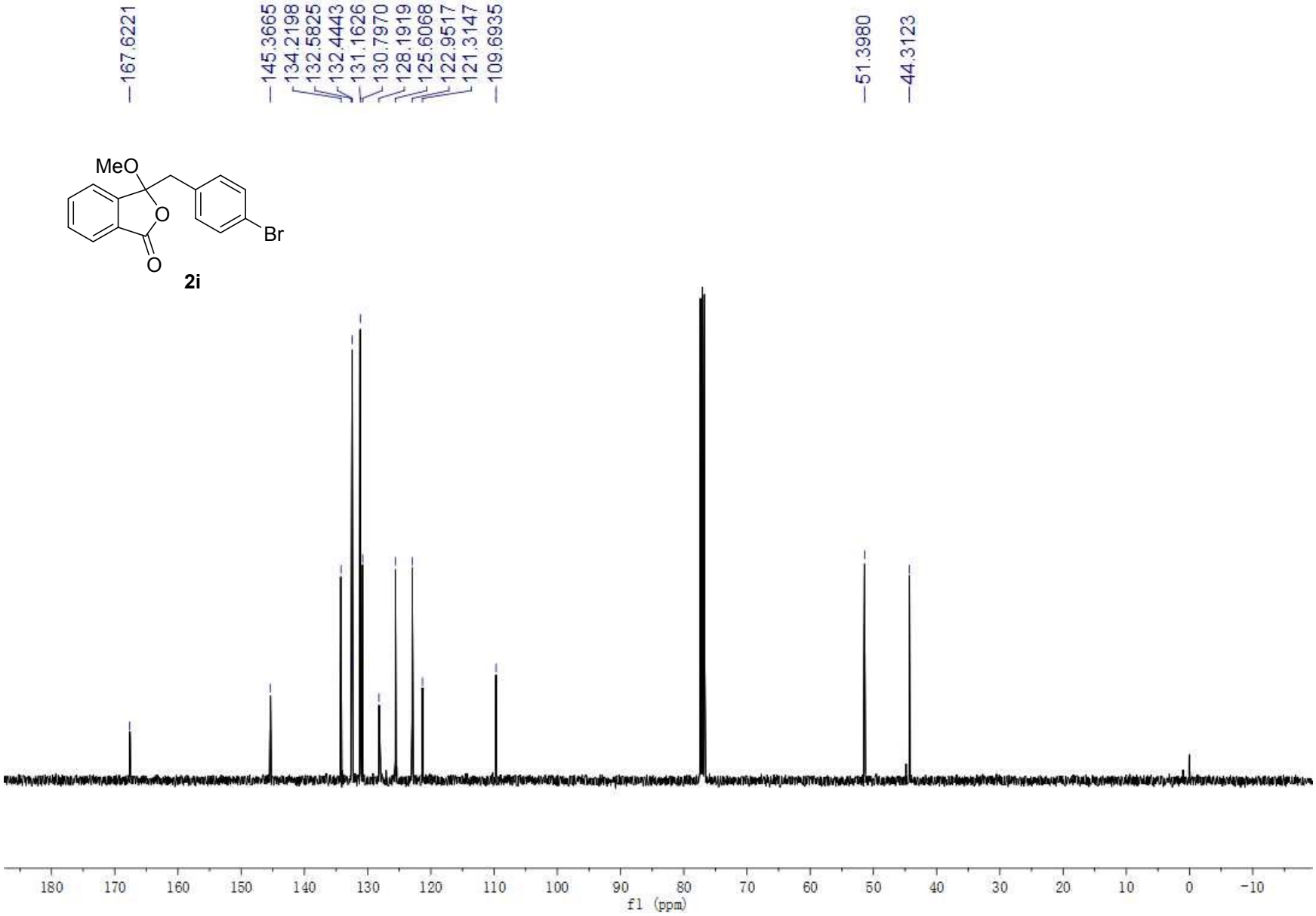
-0.5
f1 (ppm)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132.4443
131.1626
130.7970
128.1919
125.6068
122.9517
121.3147
109.6935
51.3980
44.3123
MeO
O
O
Br
2i
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.7502
7.7481
7.7459
7.7312
7.7291
7.7269
7.6576
7.6549
7.6389
7.6362
7.6201
7.6174
7.5272
7.5250
7.5084
7.5062
7.4897
7.4874
7.2637
7.2595
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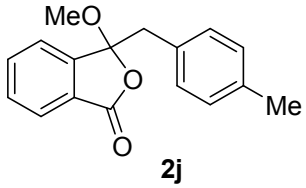
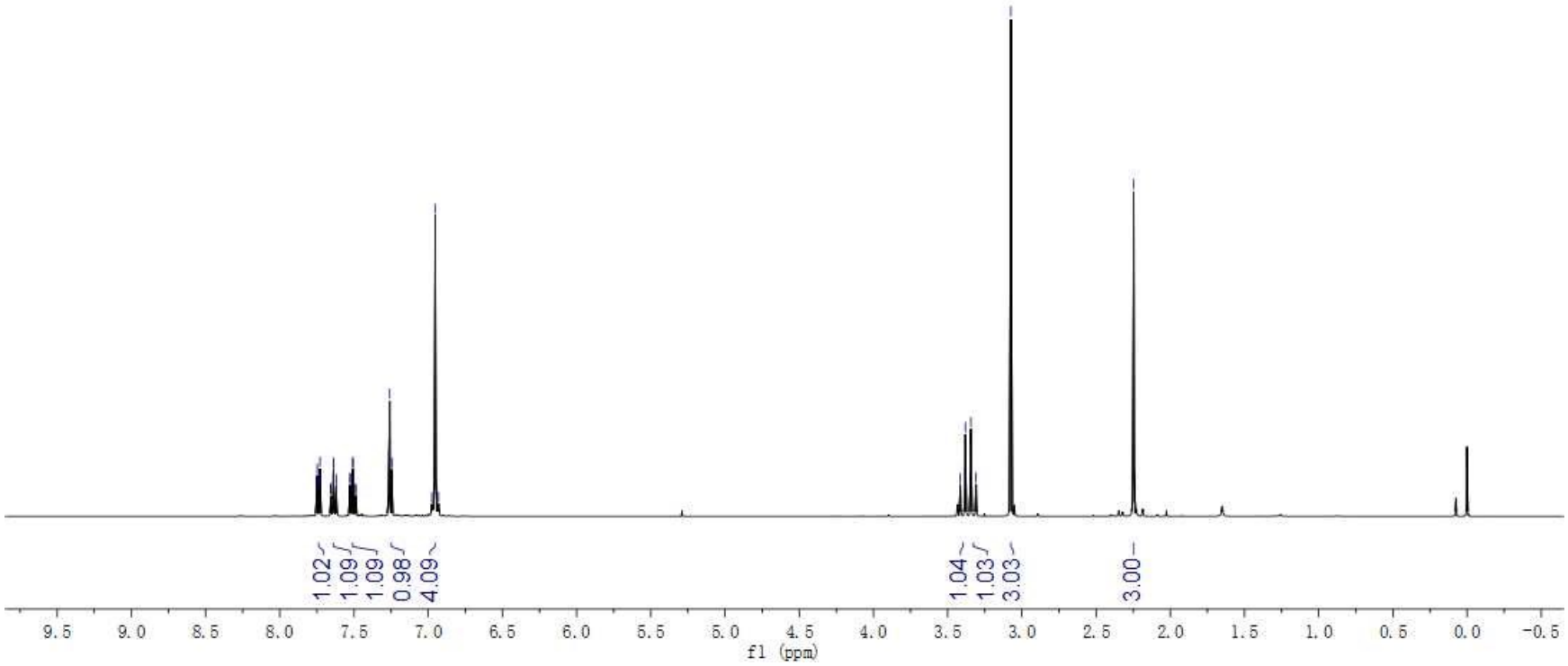
6.9521
6.9298
3.4151
3.3804
3.3432
3.3085
3.0741
2.2466


MeO
O
Me
O

2j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1.09
0.98
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1.04
1.03
3.03
3.00
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9.0
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8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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3.0
2.5
2.0
1.5
1.0
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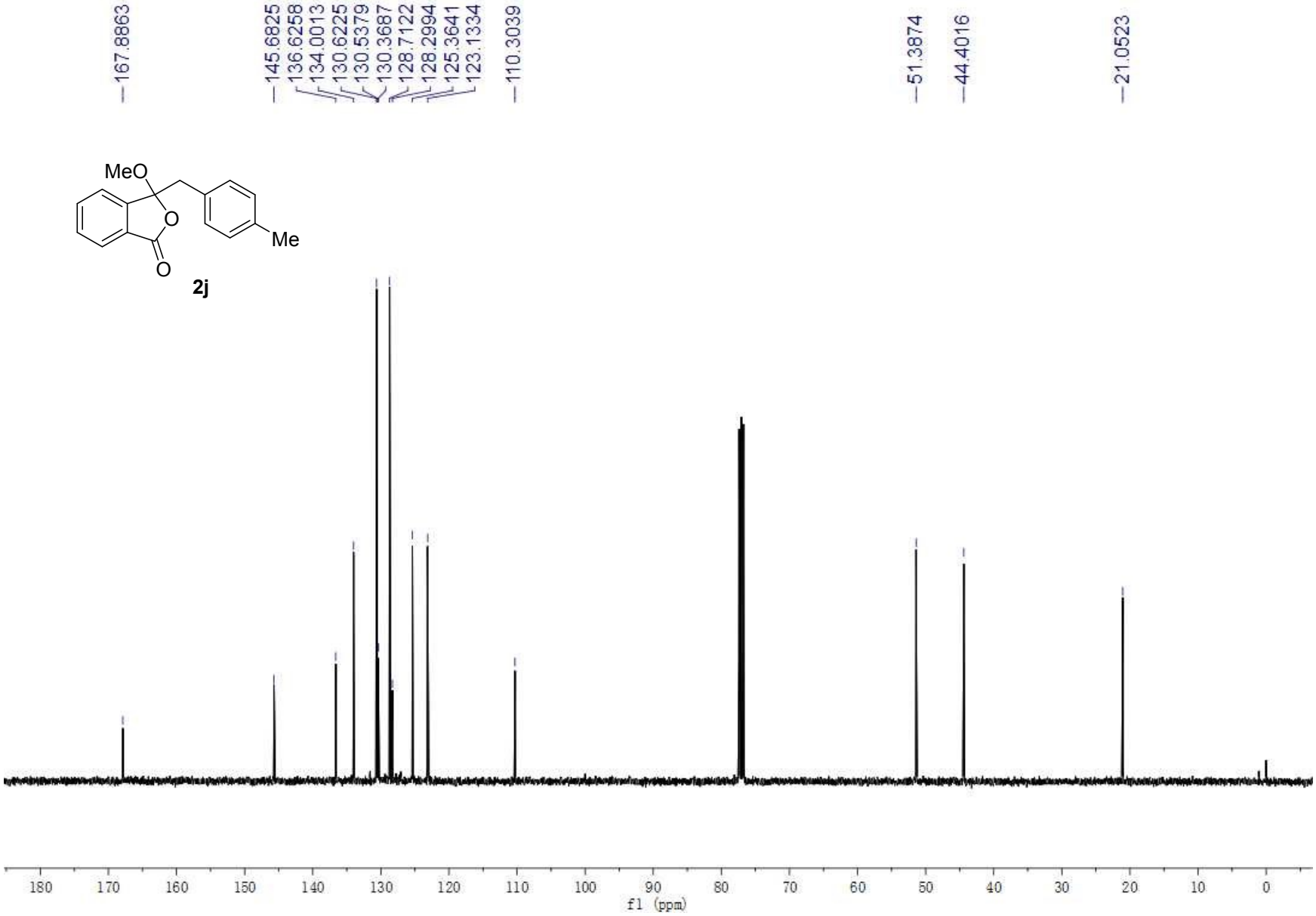
f1 (ppm)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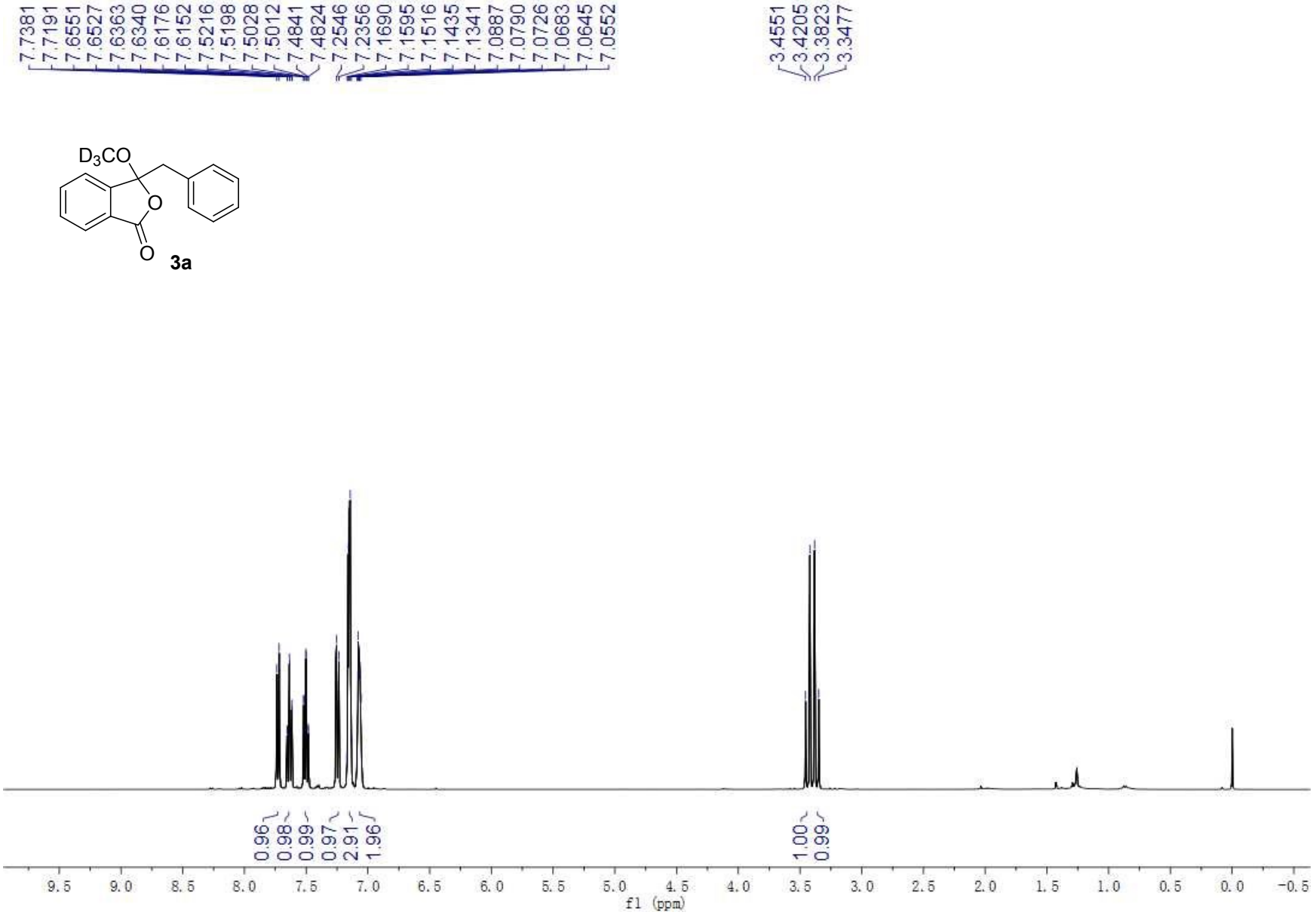
130.5379
130.3687
128.7122
128.2994
125.3641
123.1334
110.3039
51.3874
44.4016
21.0523
MeO
O
O
Me
2j
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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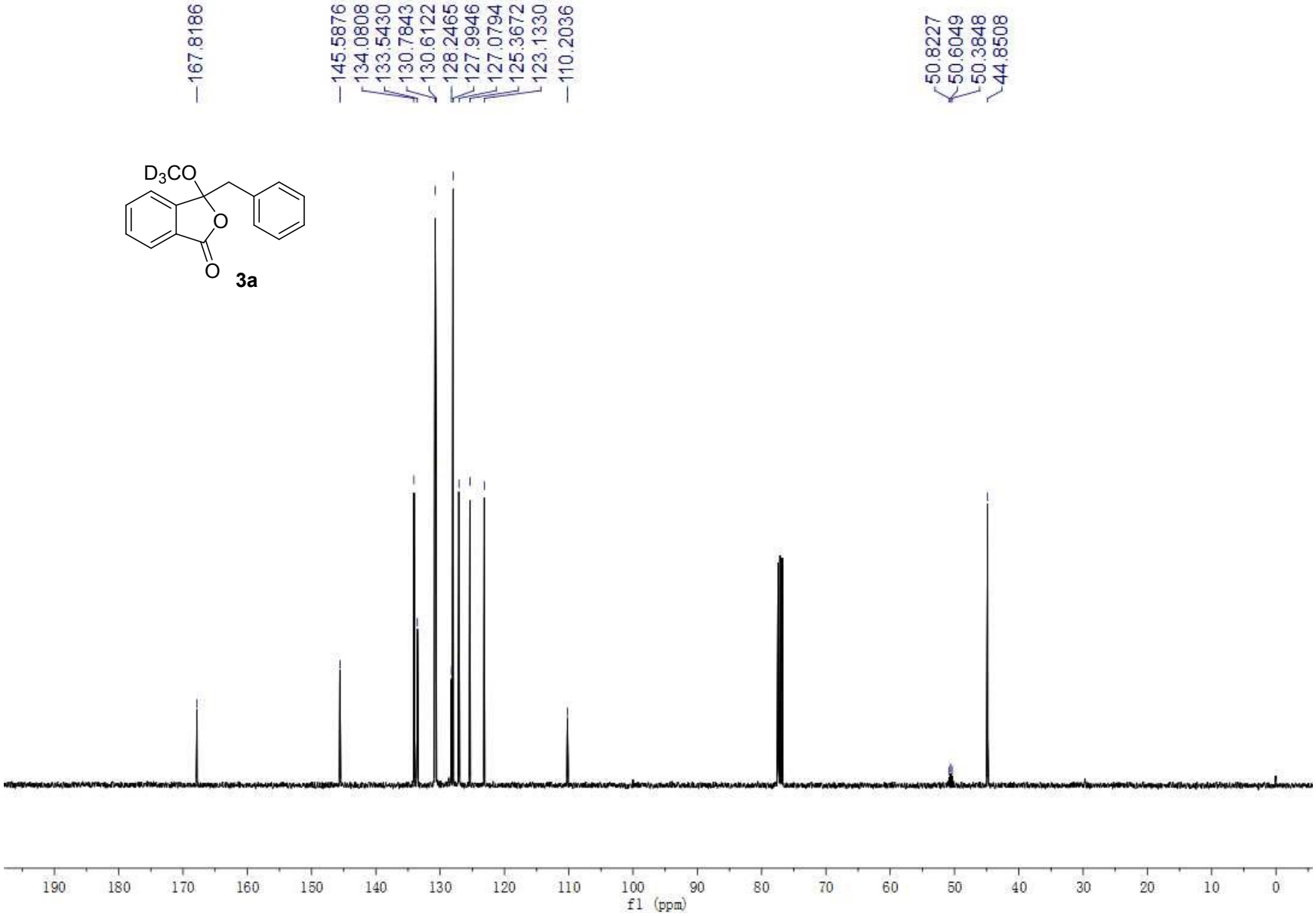
7.6340
7.6176
7.6152
7.5216
7.5198
7.5028
7.5012
7.4841
7.4824
7.2546
7.2356
7.1690
7.1595
7.1516
7.1435
7.1341
7.0887
7.0790
7.0726
7.0683
7.0645
7.0552
3.4551
3.4205
3.3823
3.3477
D3CO
O
O
3a
0.96
0.98
0.99
0.97
2.91
1.96
1.00
0.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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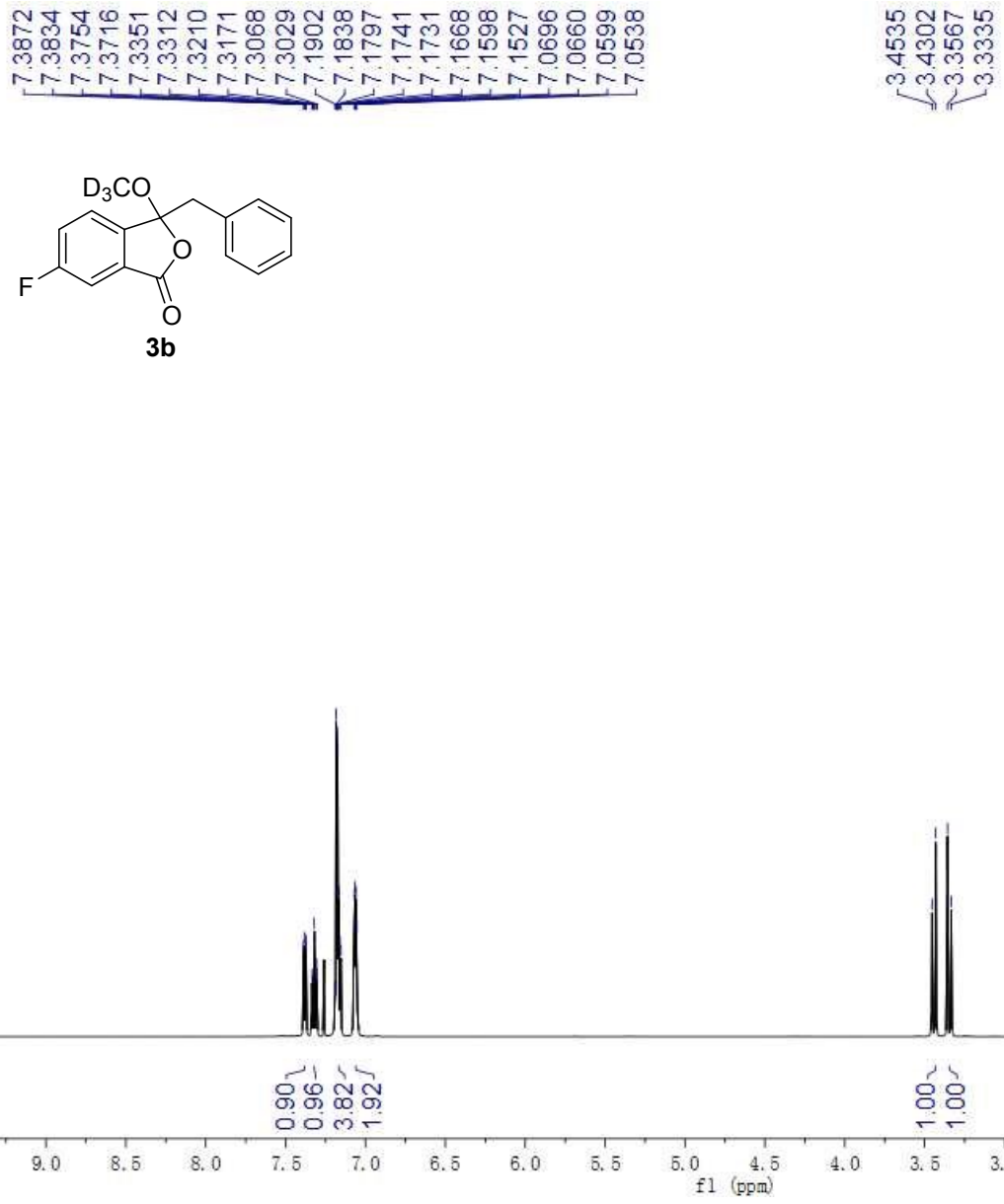
133.5430
130.7843
130.6122
128.2465
127.9946
127.0794
125.3672
123.1330
110.2036
50.8227
50.6049
50.3848
44.8508
D3CO
O
O
3a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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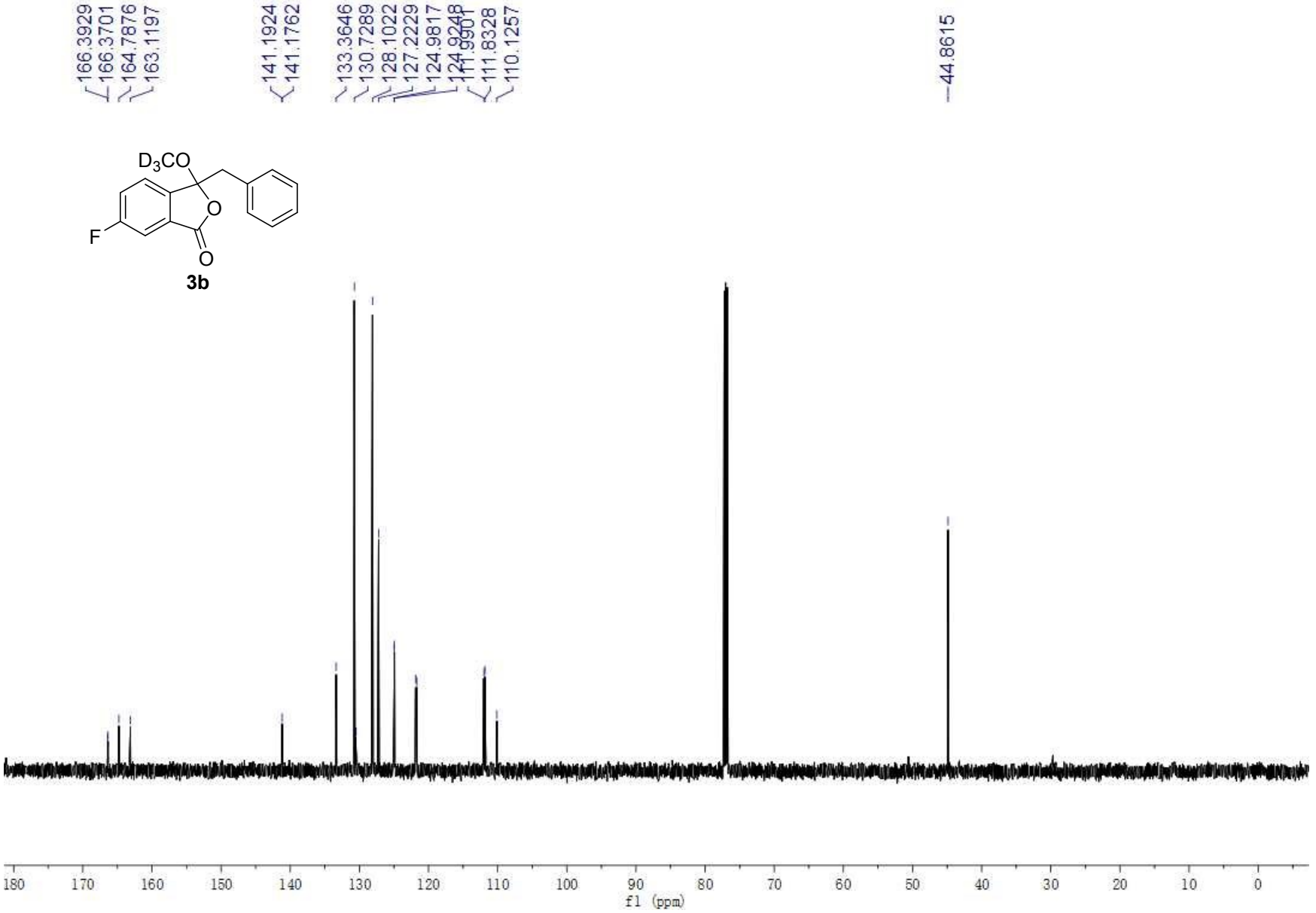
7.3754
7.3716
7.3351
7.3312
7.3210
7.3171
7.3068
7.3029
7.1902
7.1838
7.1797
7.1741
7.1731
7.1668
7.1598
7.1527
7.0696
7.0660
7.0599
7.0538
3.4535
3.4302
3.3567
3.3335
D3CO
O
F
O
3b
0.90
0.96
3.82
1.92
1.00
1.00
f1 (ppm)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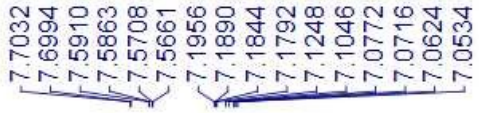
166.3701
164.7876
163.1197
141.1924
141.1762
133.3646
130.7289
128.1022
127.2229
124.9817
124.9248
111.9901
111.8328
110.1257
44.8615
D3CO
O
F
O
3b
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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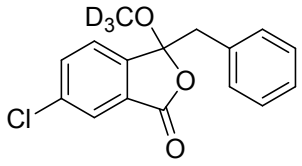
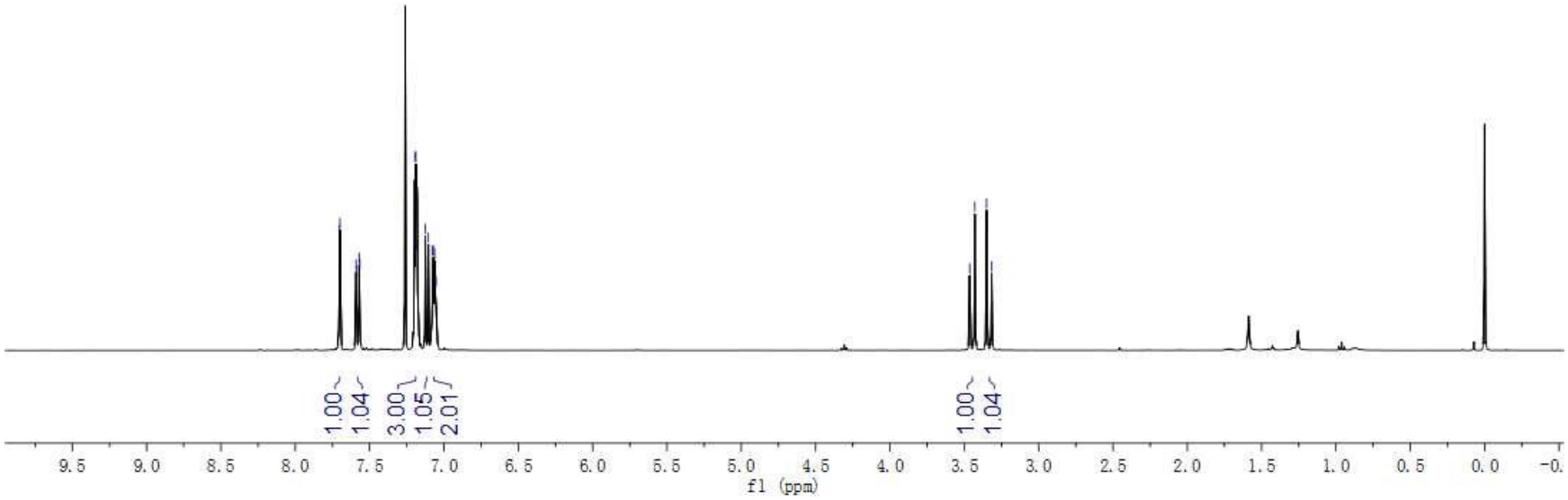
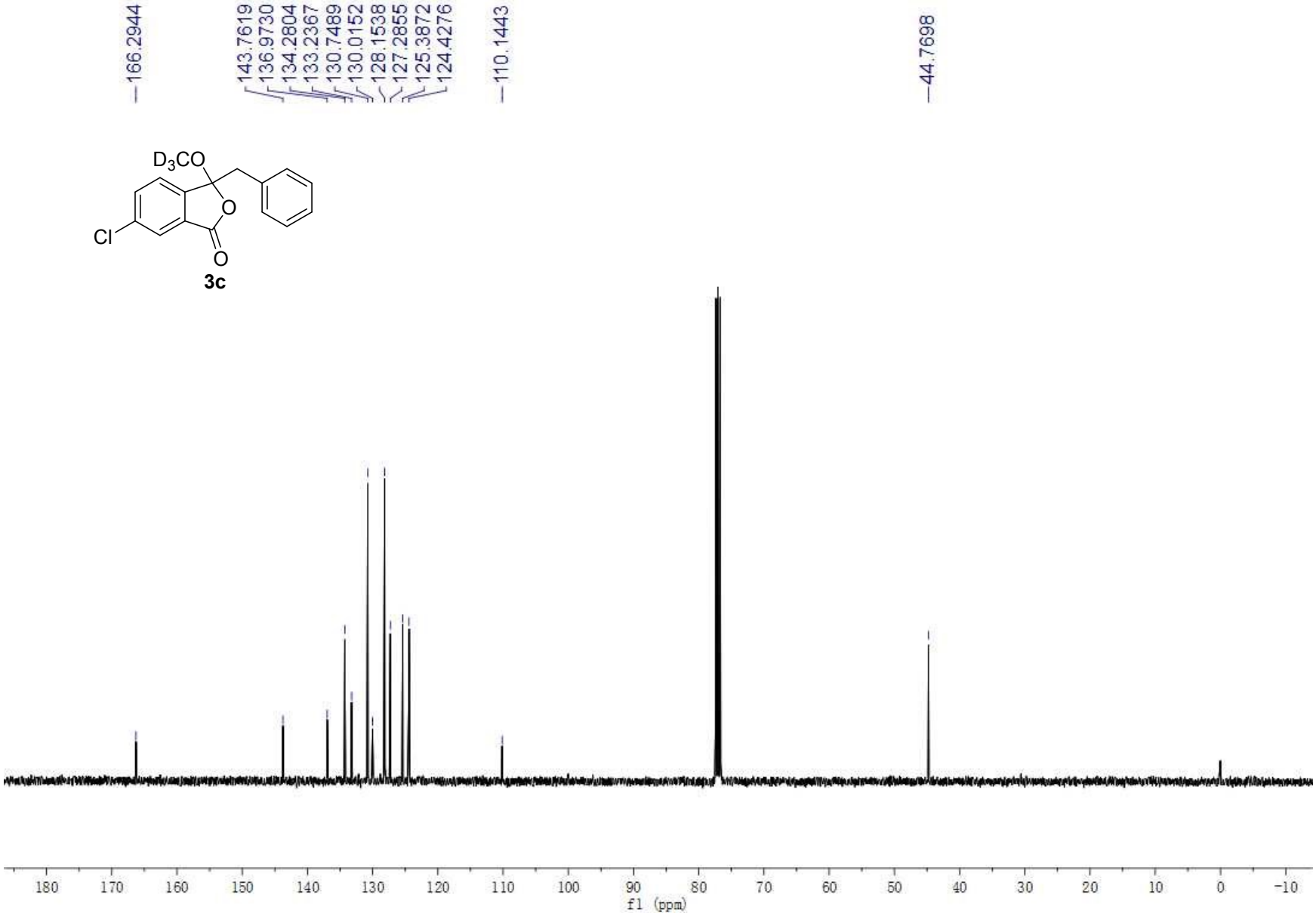
7.5910
7.5863
7.5708
7.5661
7.1956
7.1890
7.1844
7.1792
7.1248
7.1046
7.0772
7.0716
7.0624
7.0534
3.4640
3.4292
3.3505
3.3158


D3CO
O
Cl
O

3c


1.00
1.04
3.00
1.05
2.01
1.00
1.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)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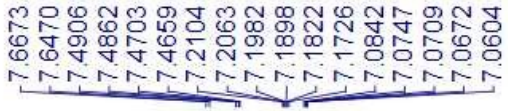
134.2804
133.2367
130.7489
130.0152
128.1538
127.2855
125.3872
124.4276
110.1443
44.7698
D3CO
O
Cl
O
3c
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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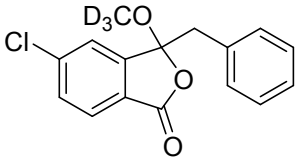
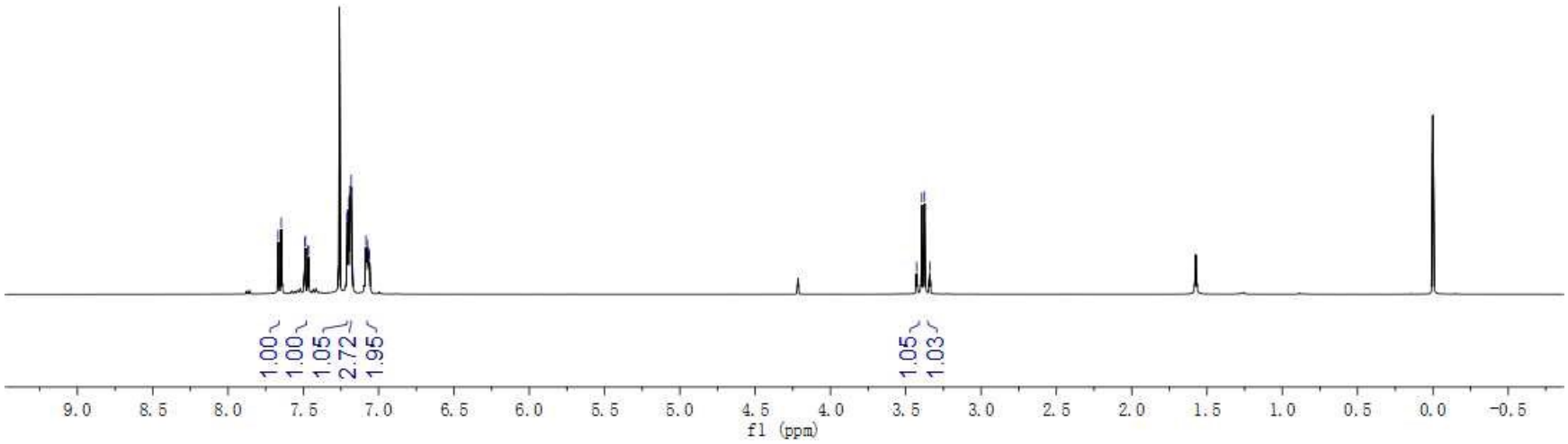
7.4862
7.4703
7.4659
7.2104
7.2063
7.1982
7.1898
7.1822
7.1726
7.0842
7.0747
7.0709
7.0672
7.0604


3.4284
3.3936
3.3753
3.3406


D3CO
Cl
O
O

3d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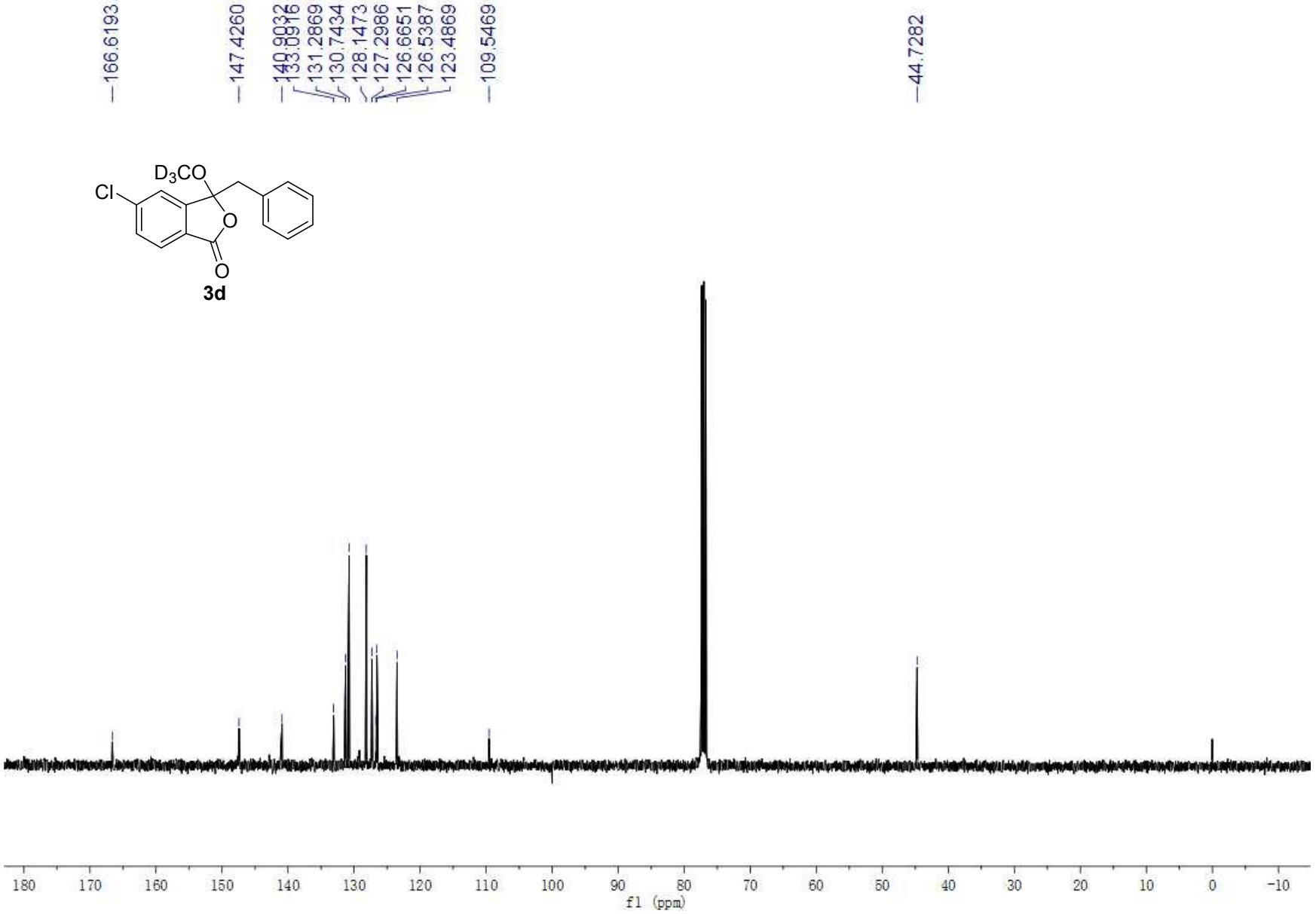
1.00
1.05
2.72
1.95
1.05
1.03
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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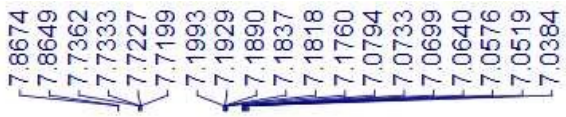
130.7434
128.1473
127.2986
126.6651
126.5387
123.4869
109.5469
44.7282
D3CO
Cl
O
O
3d
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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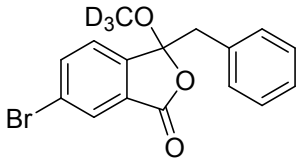
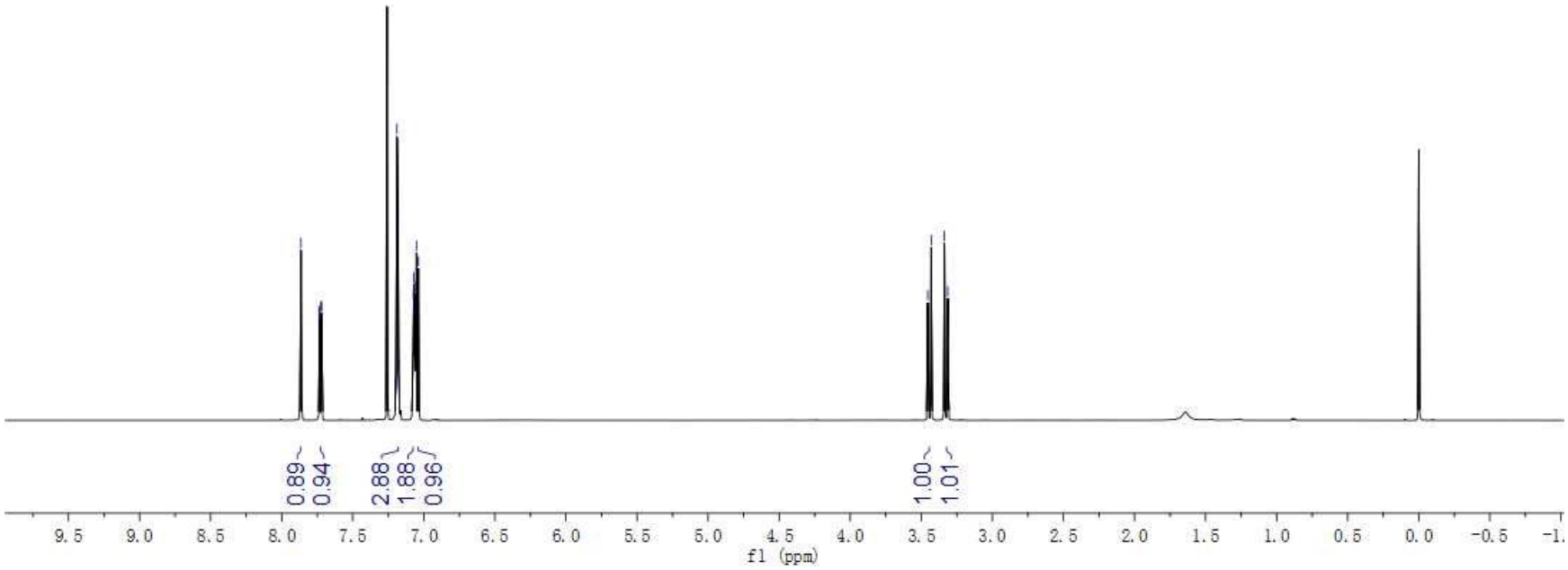
7.8649
7.7362
7.7333
7.7227
7.7199
7.1993
7.1929
7.1890
7.1837
7.1818
7.1760
7.0794
7.0733
7.0699
7.0640
7.0576
7.0519
7.0384
3.4538
3.4305
3.3371
3.3138


D3CO
O
Br
O

3e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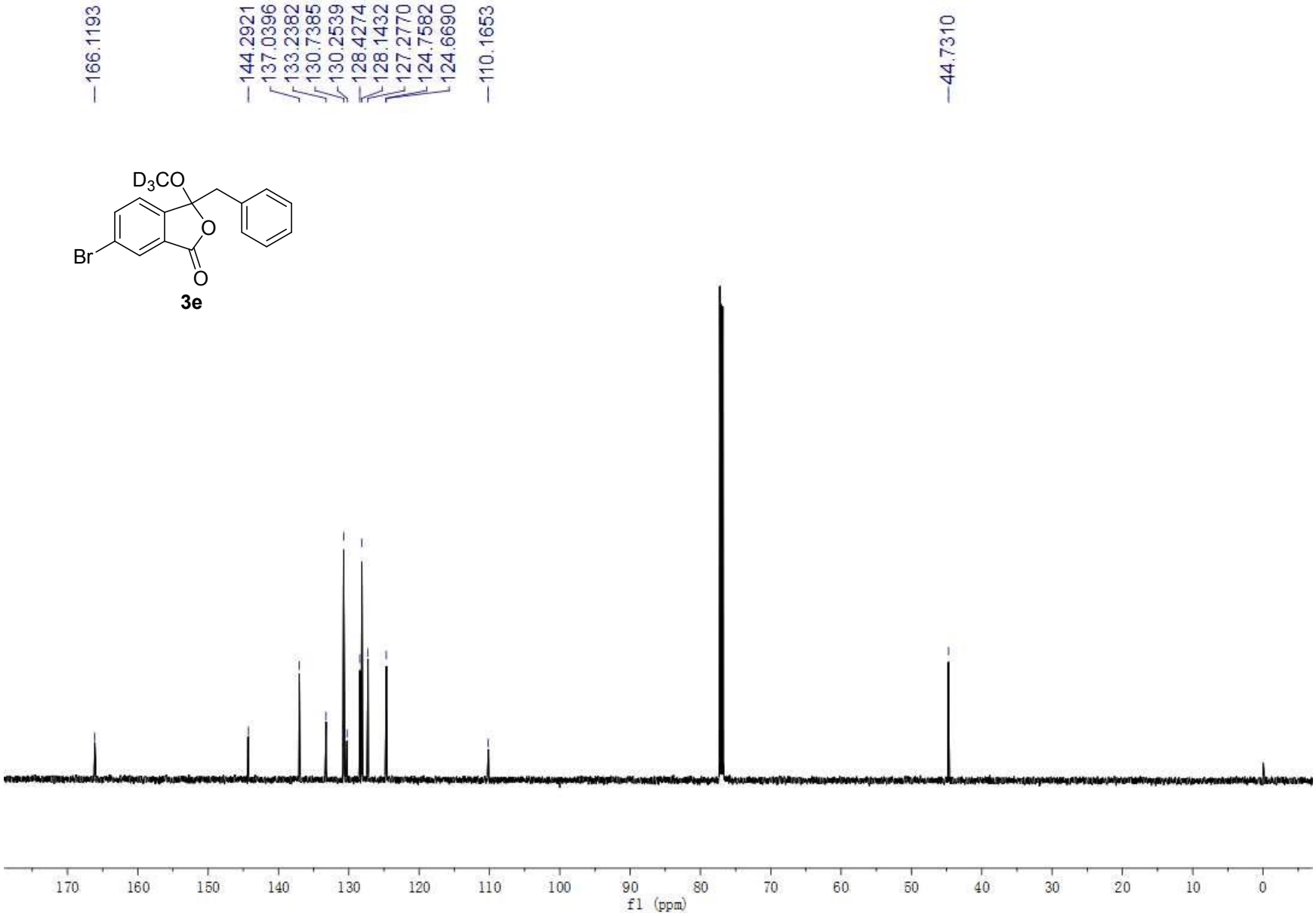
1.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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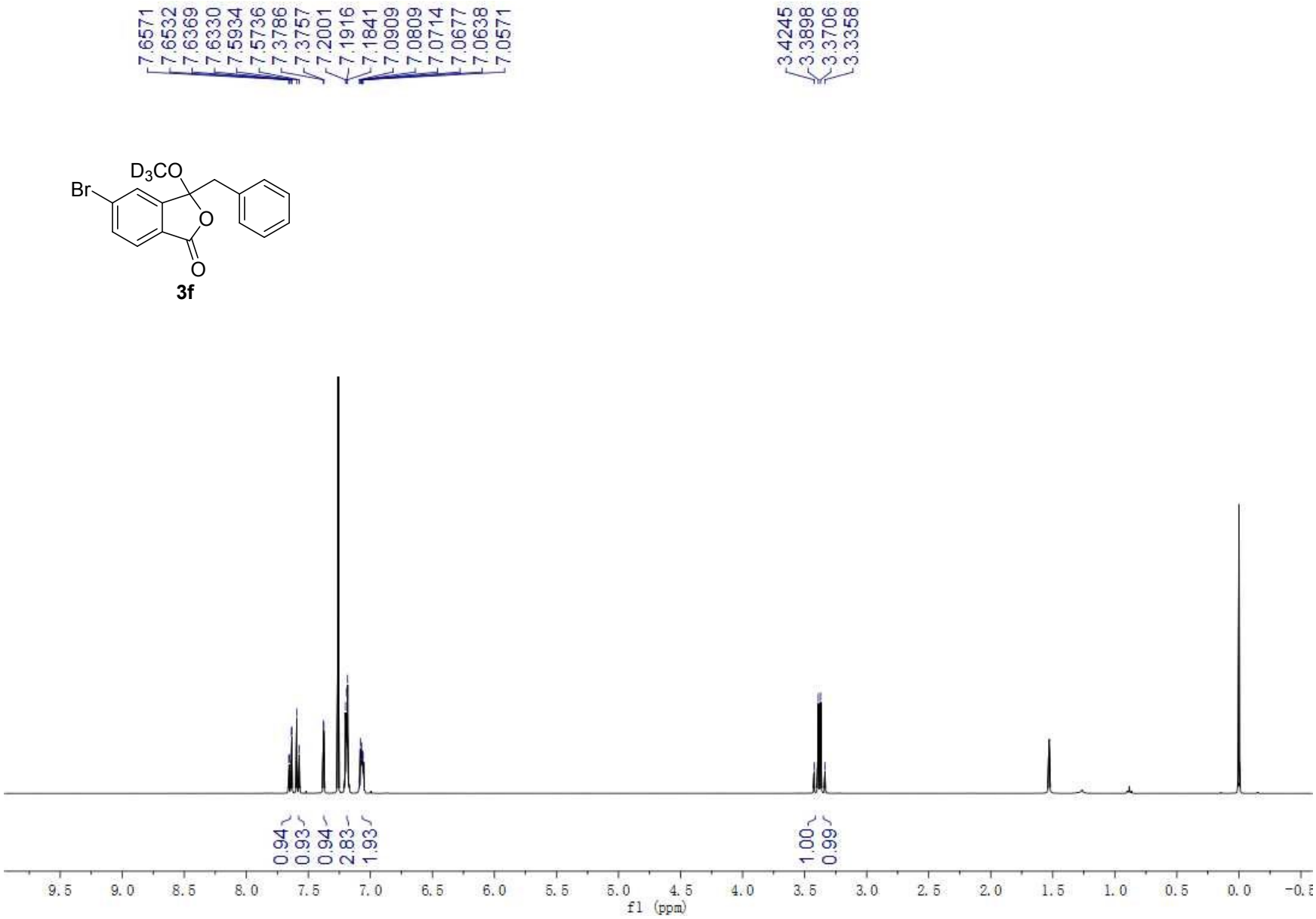
130.2539
128.4274
128.1432
127.2770
124.7582
124.6690
110.1653
44.7310
D3CO
O
Br
O
3e
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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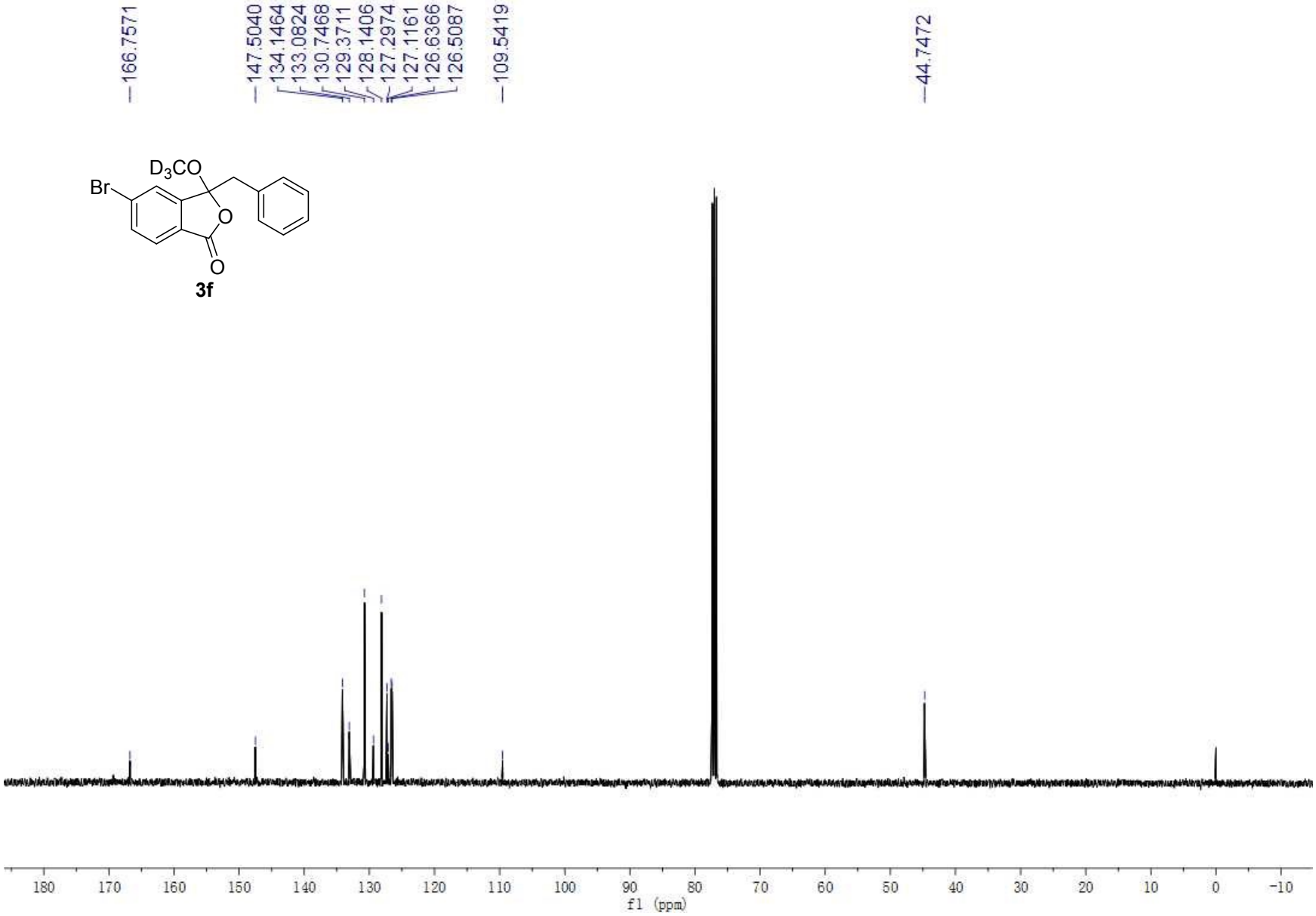
7.1841
7.0909
7.0809
7.0714
7.0677
7.0638
7.0571
3.4245
3.3898
3.3706
3.3358
D3CO
Br
O
O
3f
0.94
0.93
0.94
2.83
1.93
1.00
0.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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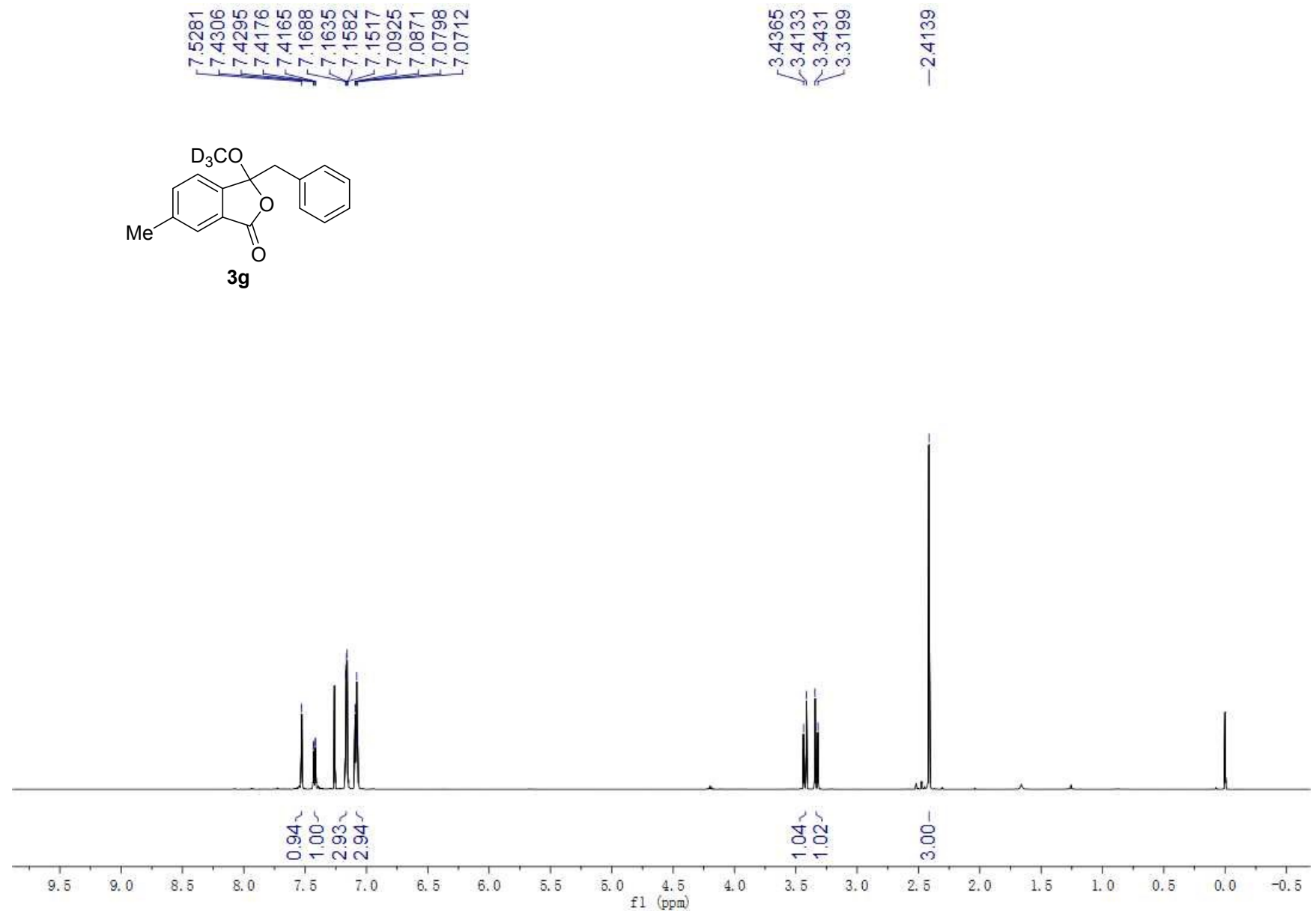
128.1406
127.2974
127.1161
126.6366
126.5087
109.5419
44.7472
D3CO
Br
O
O
3f
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.1635
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7.0925
7.0871
7.0798
7.0712
3.4365
3.4133
3.3431
3.3199
2.4139
D3CO
O
Me
O
3g
0.94
1.00
2.93
2.94
1.04
1.02
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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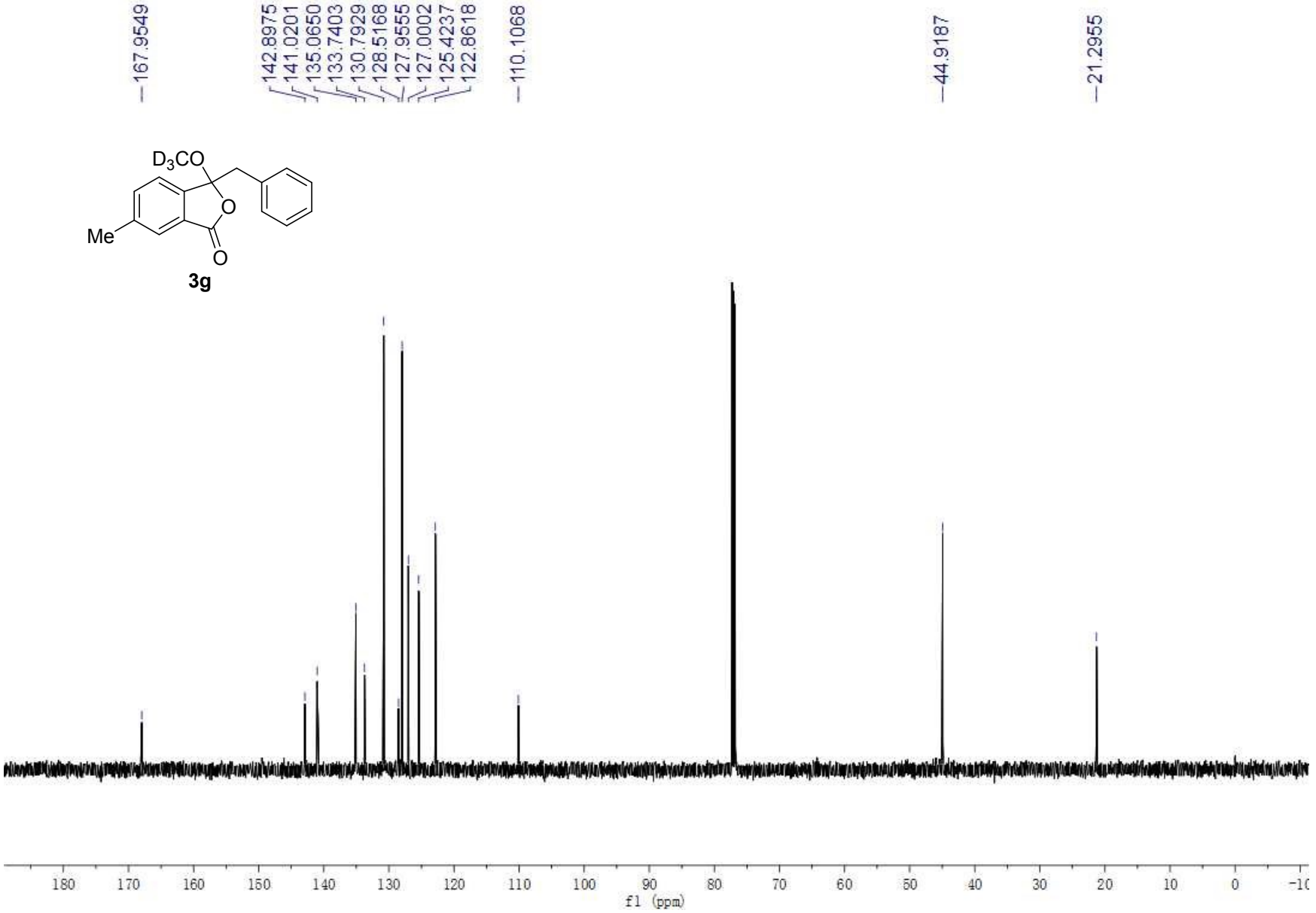
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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133.7403
130.7929
128.5168
127.9555
127.0002
125.4237
122.8618
110.1068
44.9187
21.2955
D3CO
O
Me
O
3g
180
170
160
150
140
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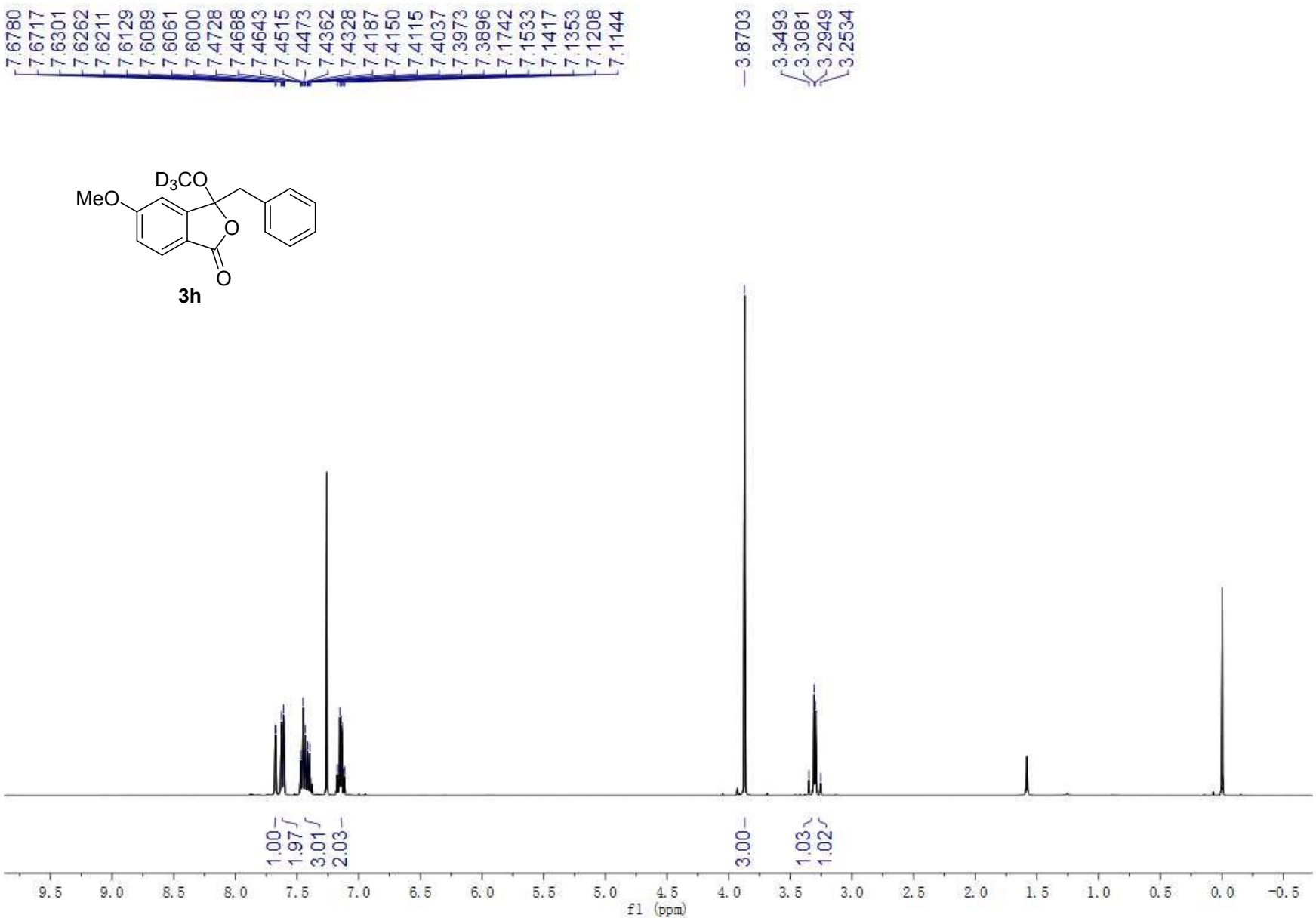
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.6211
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7.4643
7.4515
7.4473
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7.4328
7.4187
7.4150
7.4115
7.4037
7.3973
7.3896
7.1742
7.1533
7.1417
7.1353
7.1208
7.1144
3.8703
3.3493
3.3081
3.2949
3.2534
D3CO
MeO
O
O
3h
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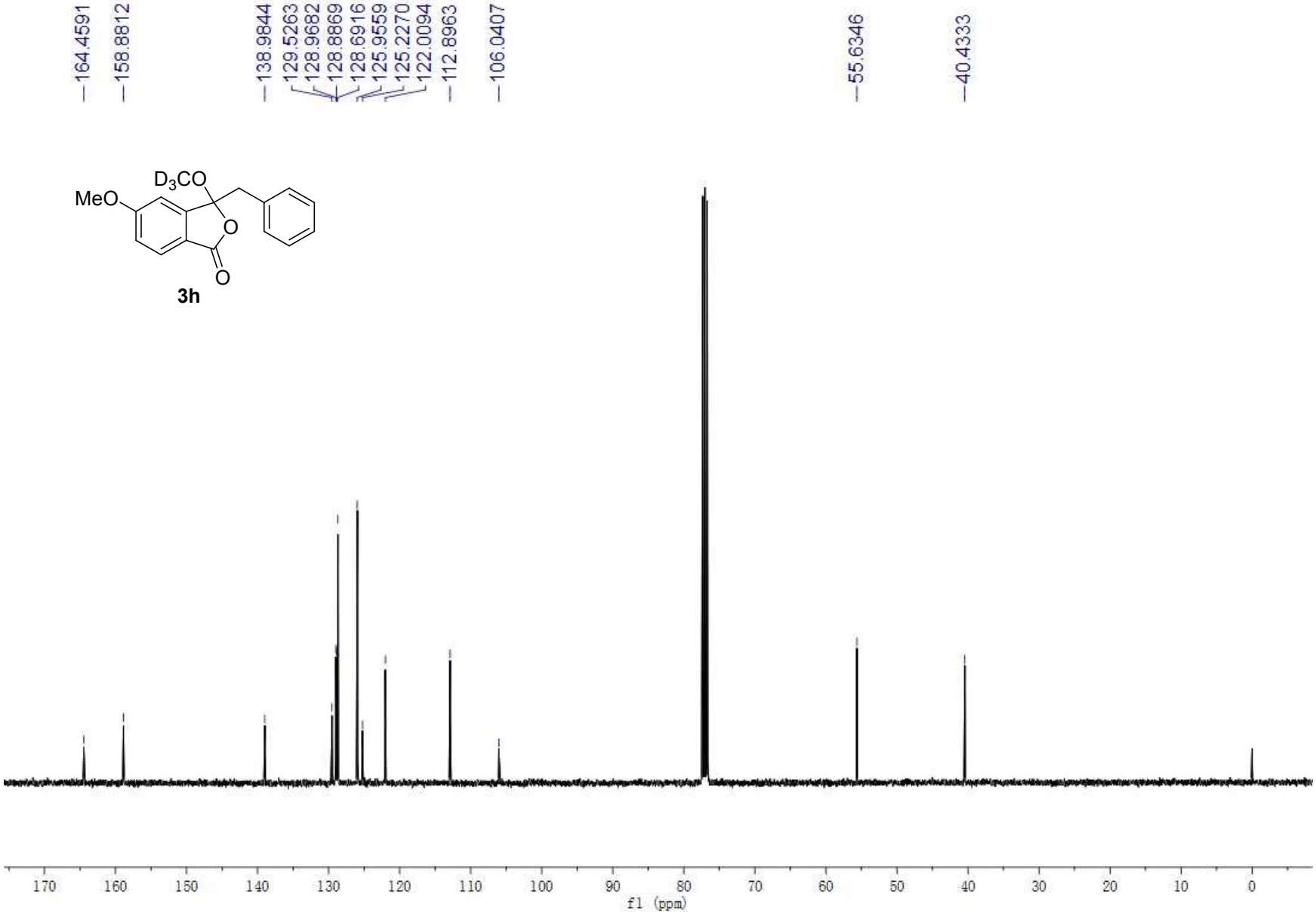
1.97
3.01
2.03
3.00
1.03
1.02
f1 (ppm)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128.9682
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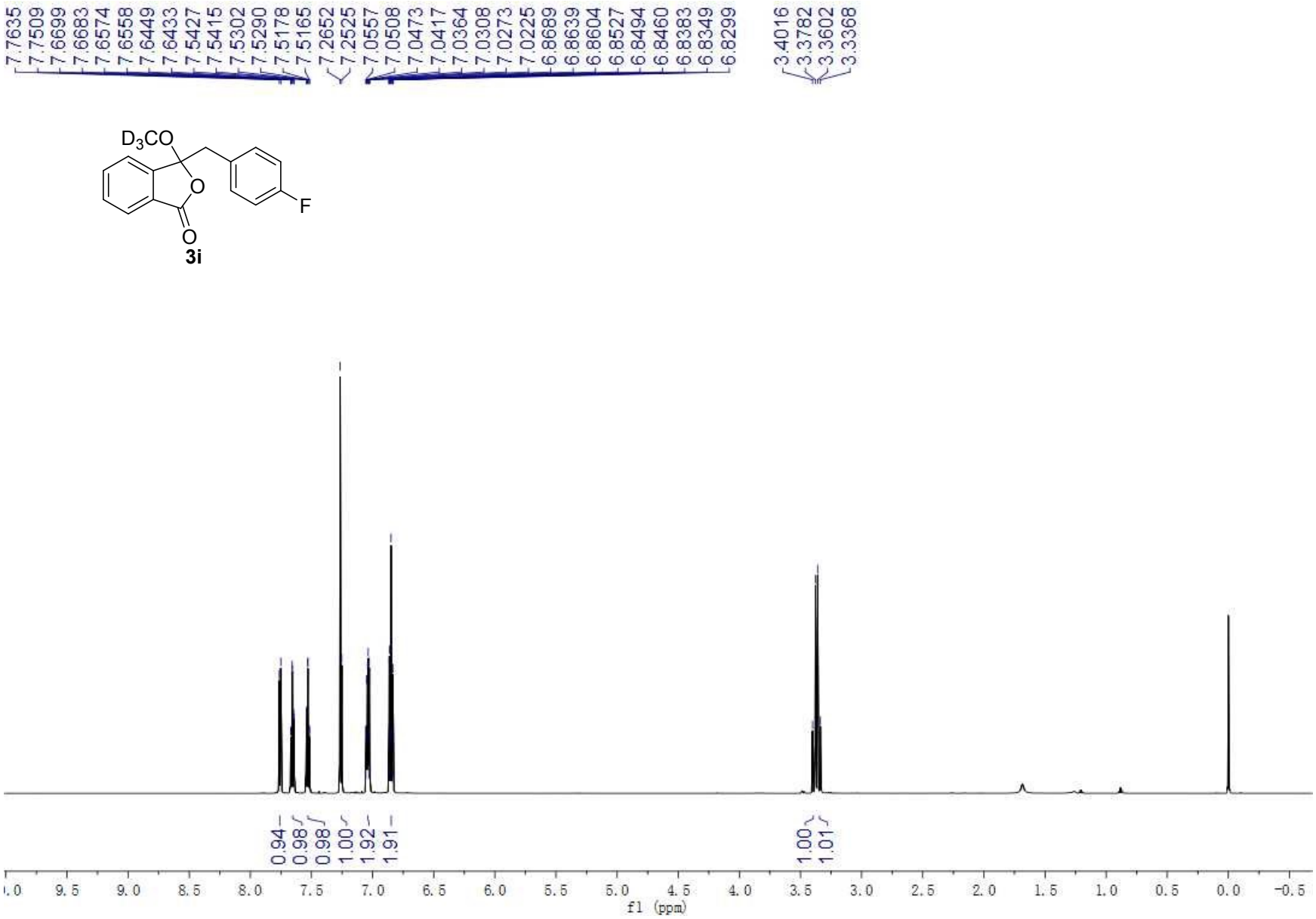
128.6916
125.9559
125.2270
122.0094
112.8963
106.0407
55.6346
40.4333
D3CO
MeO
O
O
3h
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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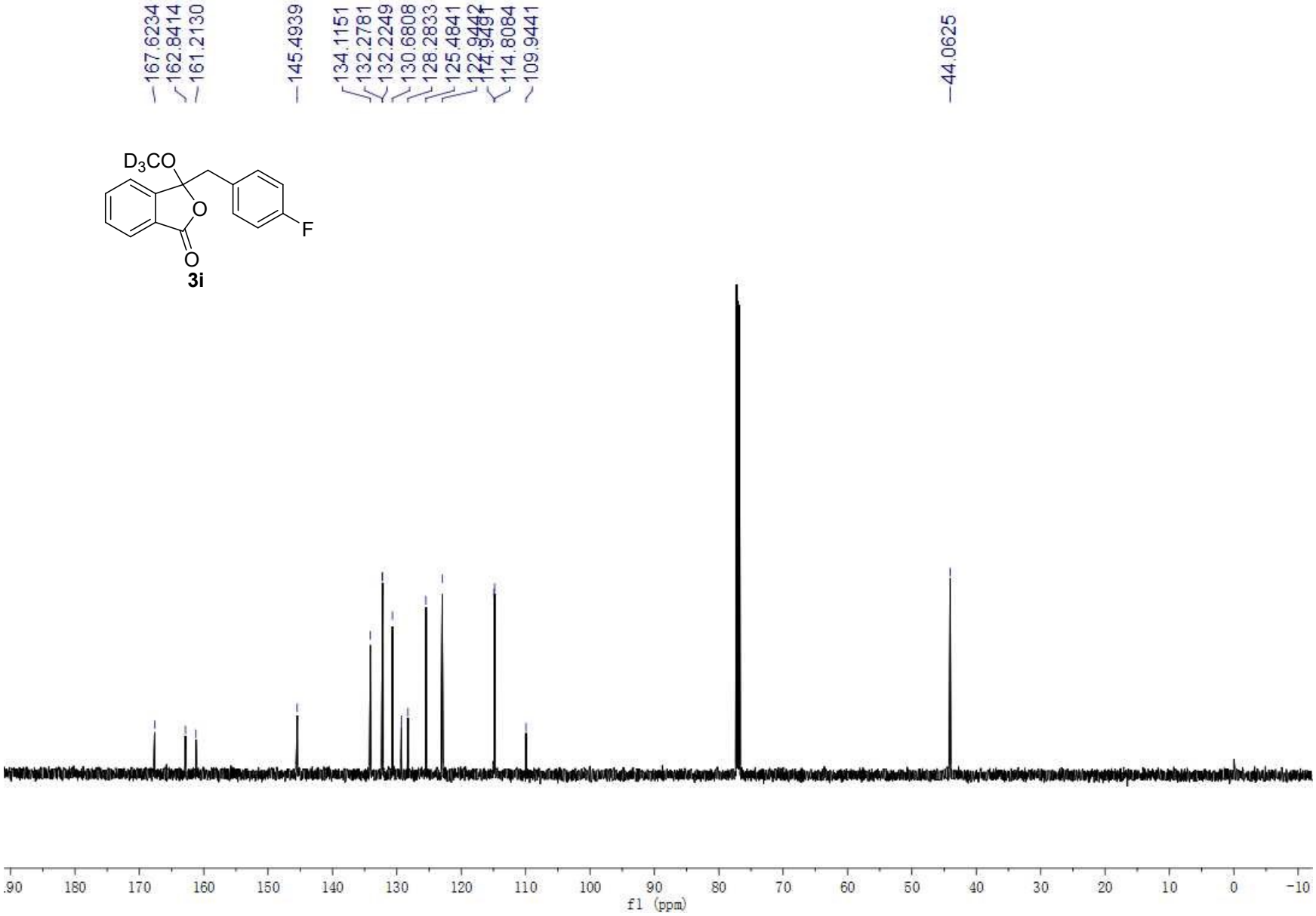
7.7509
7.6699
7.6683
7.6574
7.6558
7.6449
7.6433
7.5427
7.5415
7.5302
7.5290
7.5178
7.5165
7.2652
7.2525
7.0557
7.0508
7.0473
7.0417
7.0364
7.0308
7.0273
7.0225
6.8689
6.8639
6.8604
6.8527
6.8494
6.8460
6.8383
6.8349
6.8299
3.4016
3.3782
3.3602
3.3368
D3CO
O
F
O
3i
0.94
0.98
0.98
1.00
1.92
1.91
1.00
1.01
f1 (ppm)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161.2130
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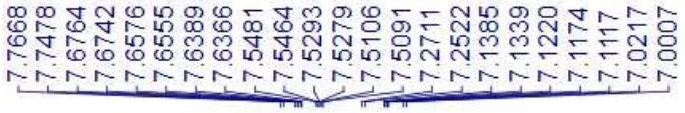
134.1151
132.2781
132.2249
130.6808
128.2833
125.4841
122.9442
114.8084
109.9441
44.0625
D3CO
O
O
F
3i
f1 (ppm)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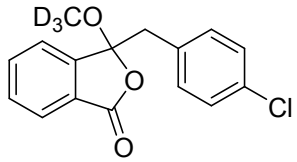
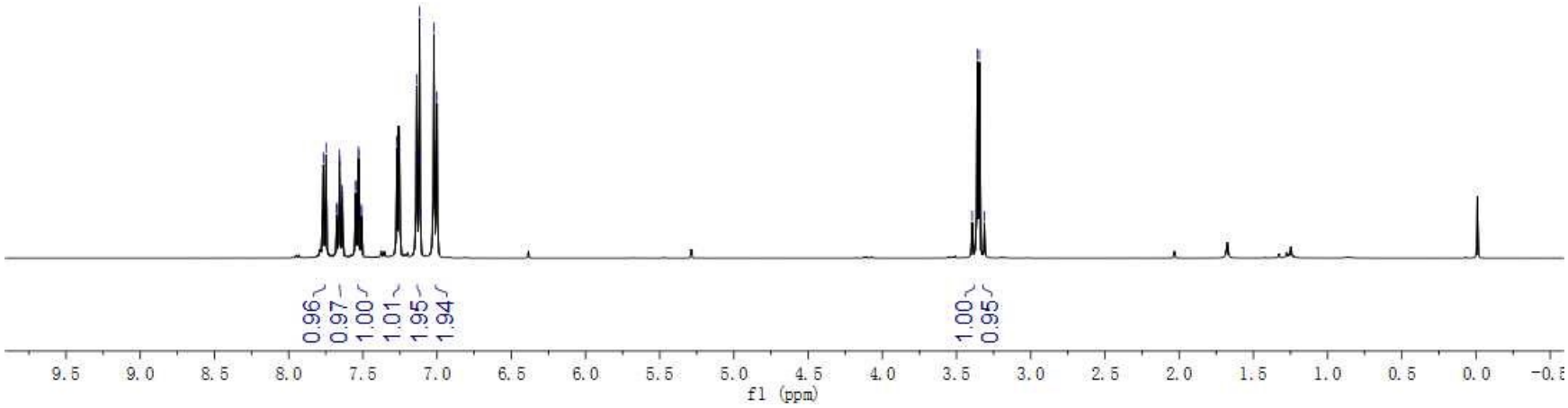
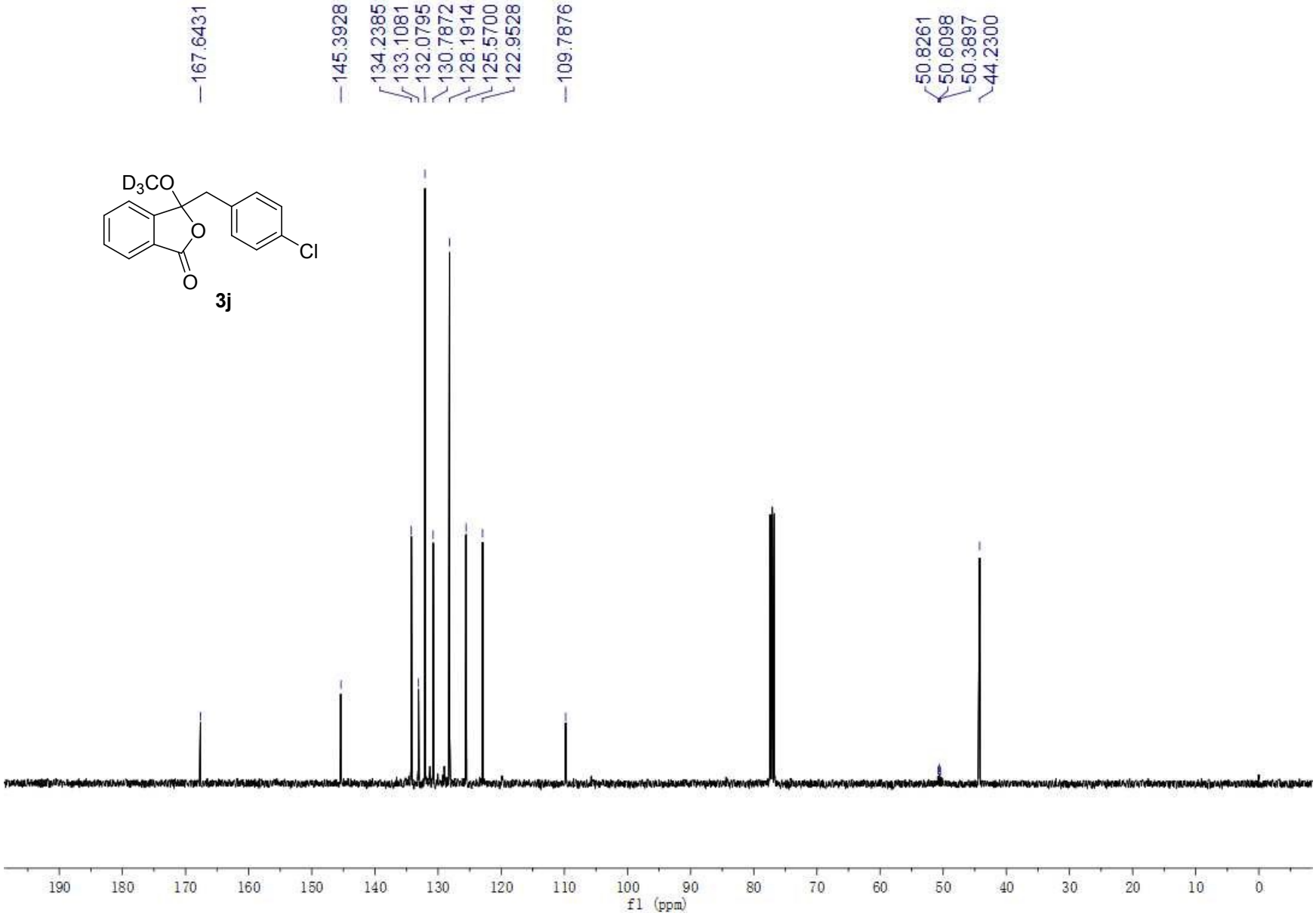
7.6389
7.6366
7.5481
7.5464
7.5293
7.5279
7.5106
7.5091
7.2711
7.2522
7.1385
7.1339
7.1220
7.1174
7.1117
7.0217
7.0007


3.3948
3.3600
3.3463
3.3115


D3CO
O
O
Cl

3j


0.96
0.97
1.00
1.01
1.95
1.94
1.00
0.95
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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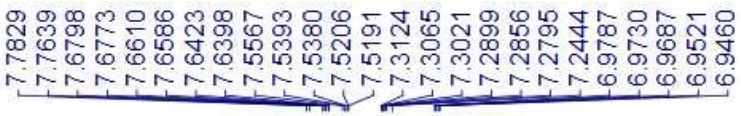
134.2385
133.1081
132.0795
130.7872
128.1914
125.5700
122.9528
109.7876
50.8261
50.6098
50.3897
44.2300
D3CO
O
O
Cl
3j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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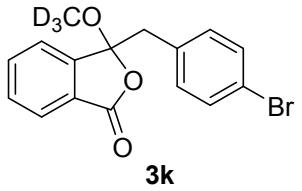
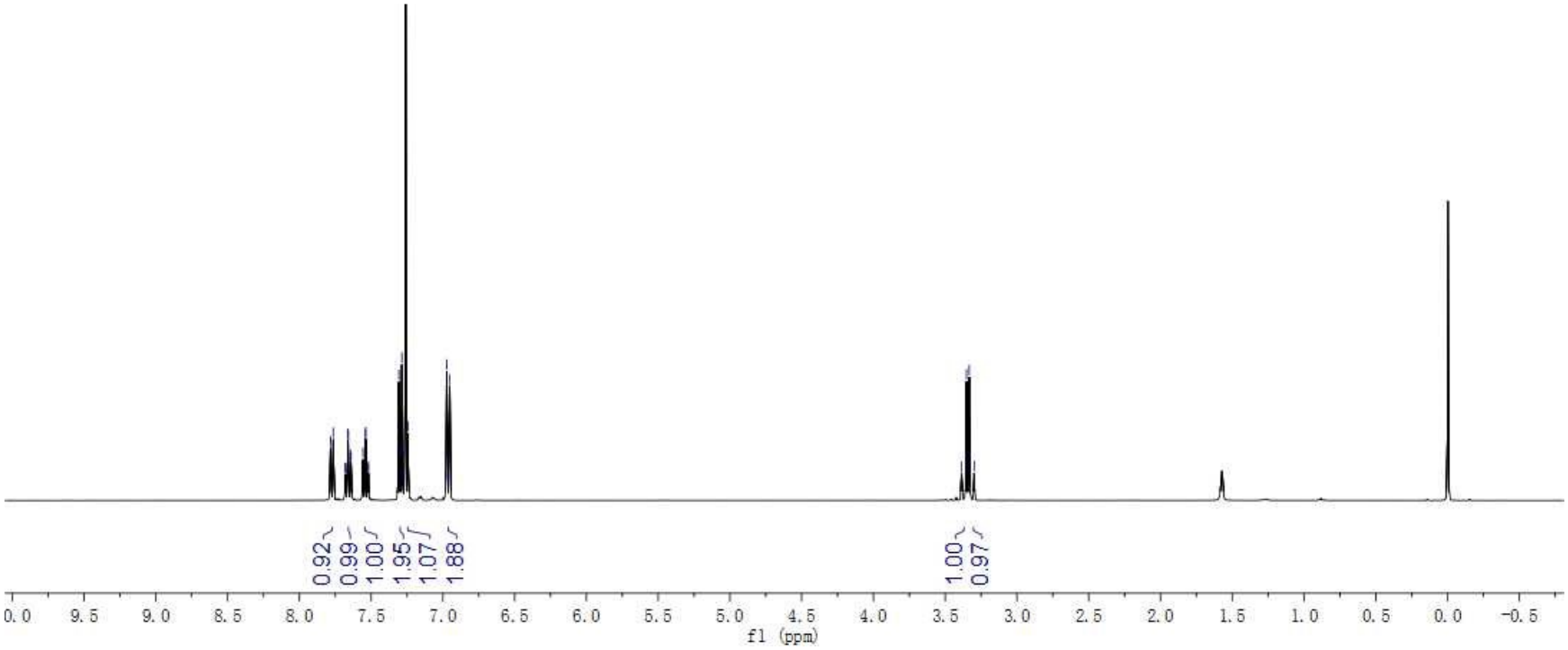
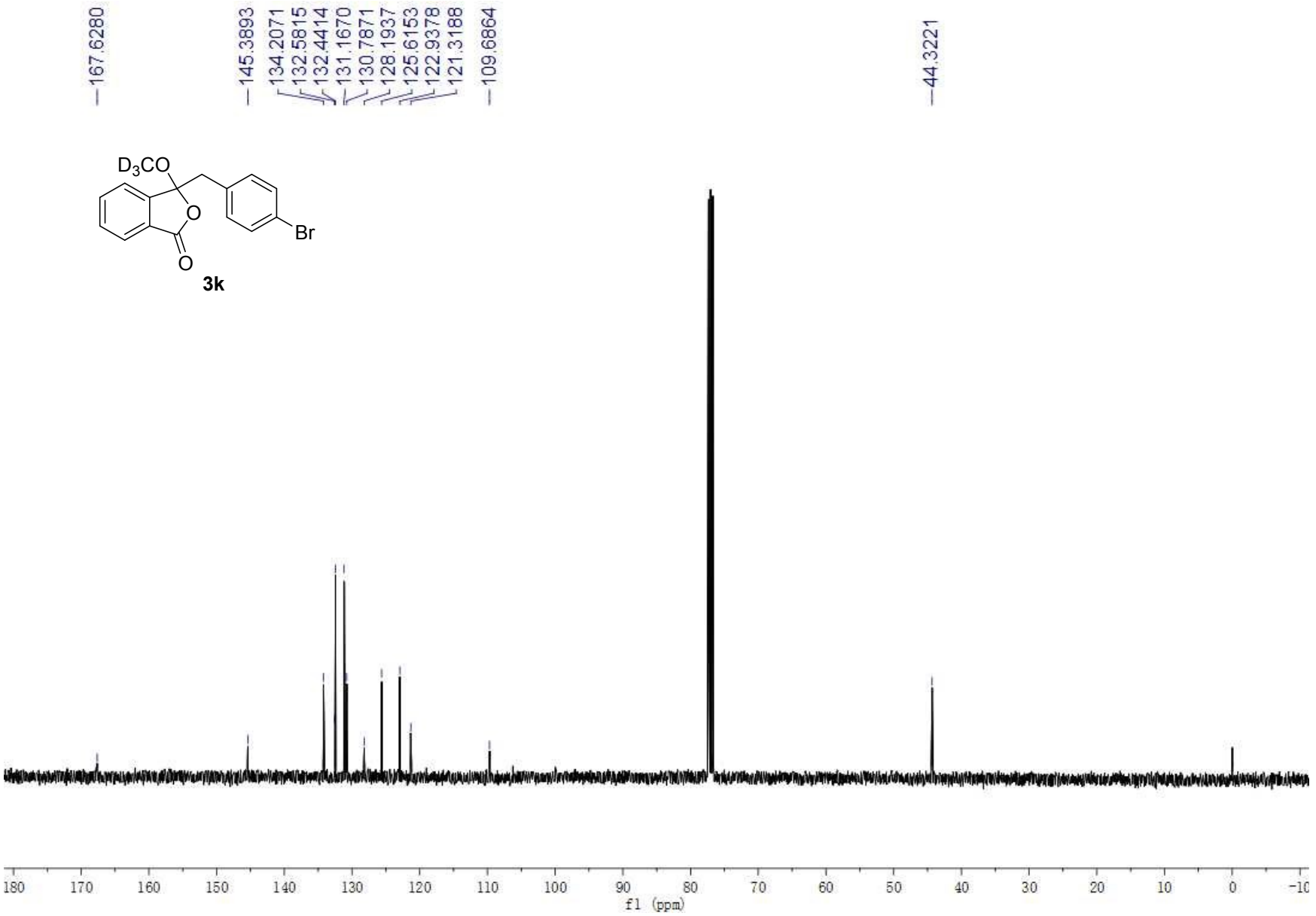
7.7639
7.6798
7.6773
7.6610
7.6586
7.6423
7.6398
7.5567
7.5393
7.5380
7.5206
7.5191
7.3124
7.3065
7.3021
7.2899
7.2856
7.2795
7.2444
6.9787
6.9730
6.9687
6.9521
6.9460


3.3857
3.3510
3.3327
3.2979


D3CO
O
Br
O

3k


0.92
0.99
1.00
1.95
1.07
1.88
1.00
0.97
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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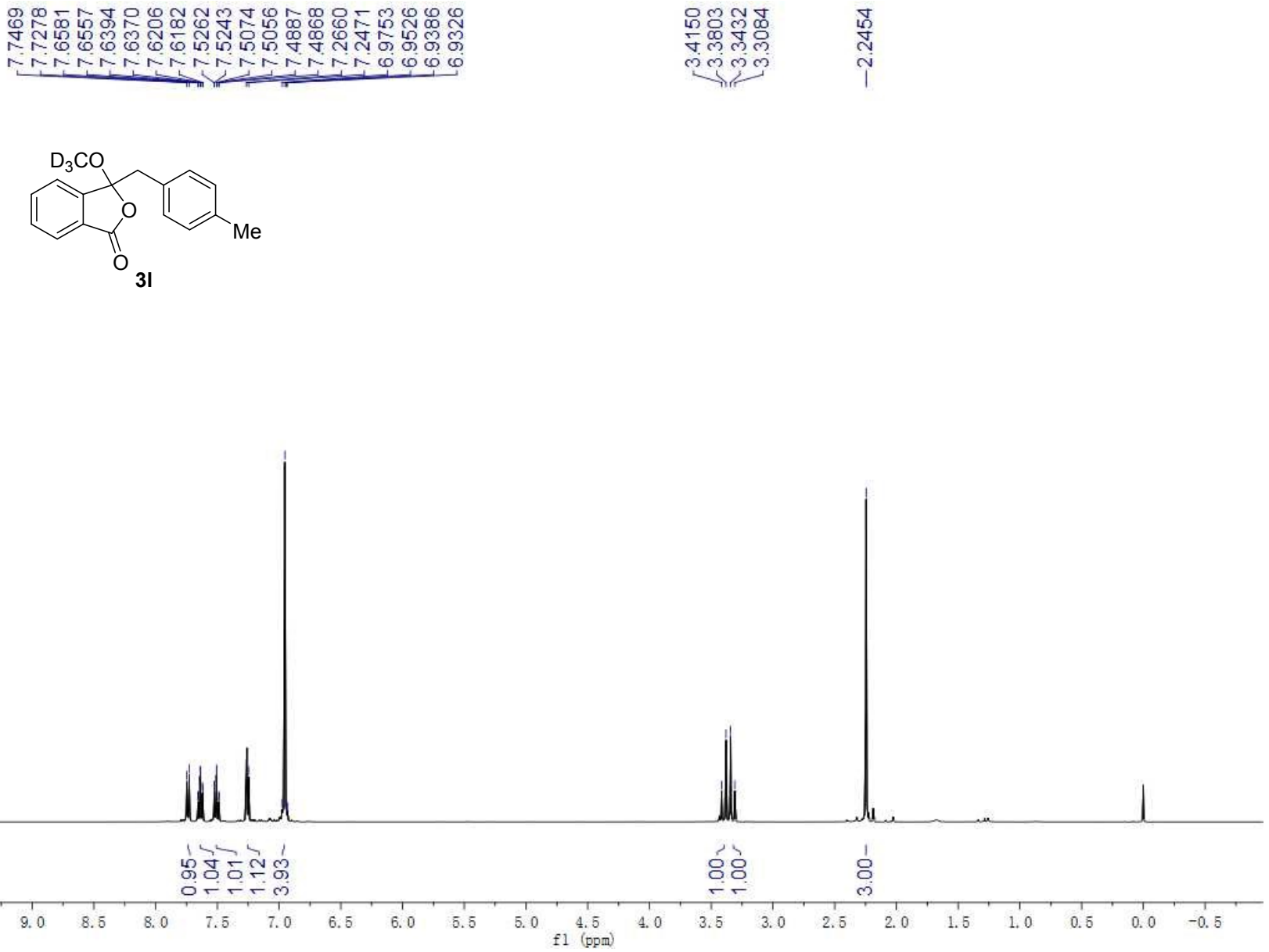
145.3893
134.2071
132.5815
132.4414
131.1670
130.7871
128.1937
125.6153
122.9378
121.3188
109.6864
44.3221
D3CO
O
O
Br
3k
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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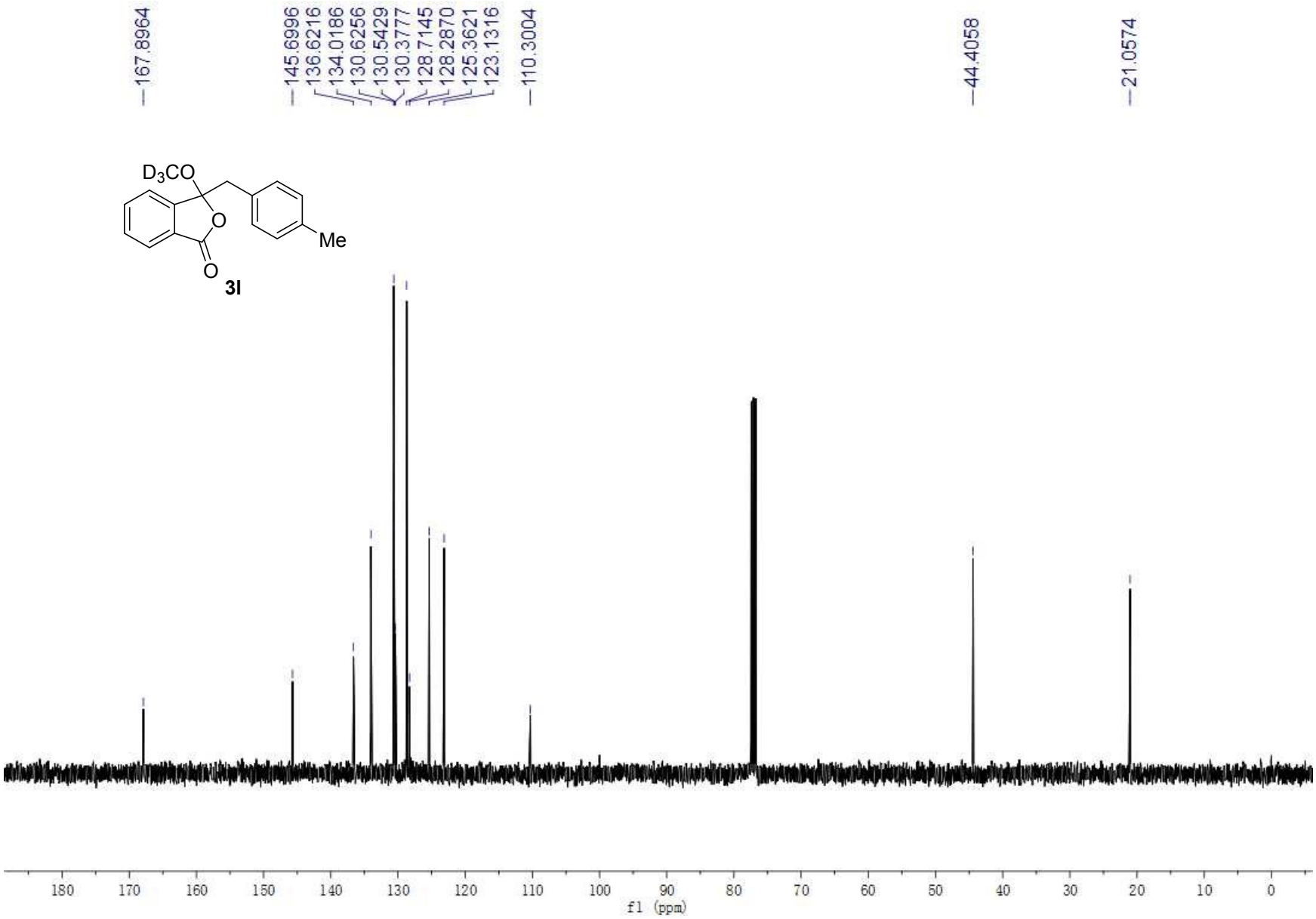
7.6581
7.6557
7.6394
7.6370
7.6206
7.6182
7.5262
7.5243
7.5074
7.5056
7.4887
7.4868
7.2660
7.2471
6.9753
6.9526
6.9386
6.9326
3.4150
3.3803
3.3432
3.3084
2.2454
D3CO
O
O
Me
0.95
1.04
1.01
1.12
3.93
1.00
1.00
3.00
f1 (ppm)

3l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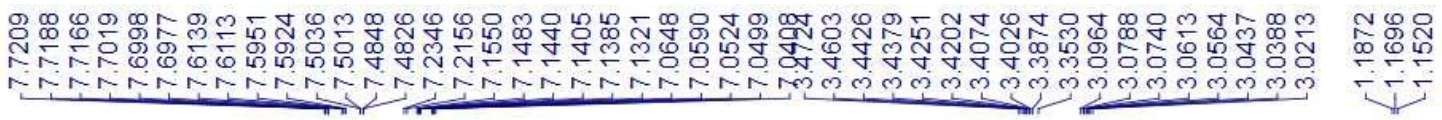
136.6216
134.0186
130.6256
130.5429
130.3777
128.7145
128.2870
125.3621
123.1316
110.3004
44.4058
21.0574
D3CO
O
O
Me
3l
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.7188
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7.7019
7.6998
7.6977
7.6139
7.6113
7.5951
7.5924
7.5036
7.5013
7.4848
7.4826
7.2346
7.2156
7.1550
7.1483
7.1440
7.1405
7.1385
7.1321
7.0648
7.0590
7.0524
7.0499
3.4603
3.4426
3.4379
3.4251
3.4202
3.4074
3.4026
3.3874
3.3530
3.0964
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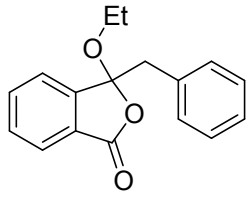
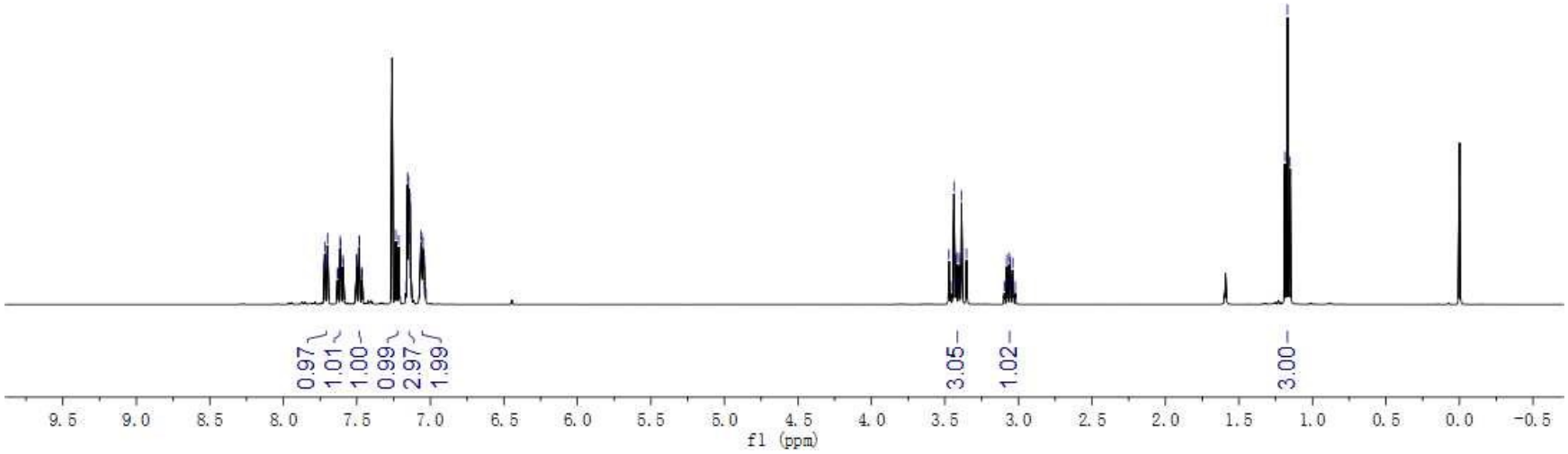
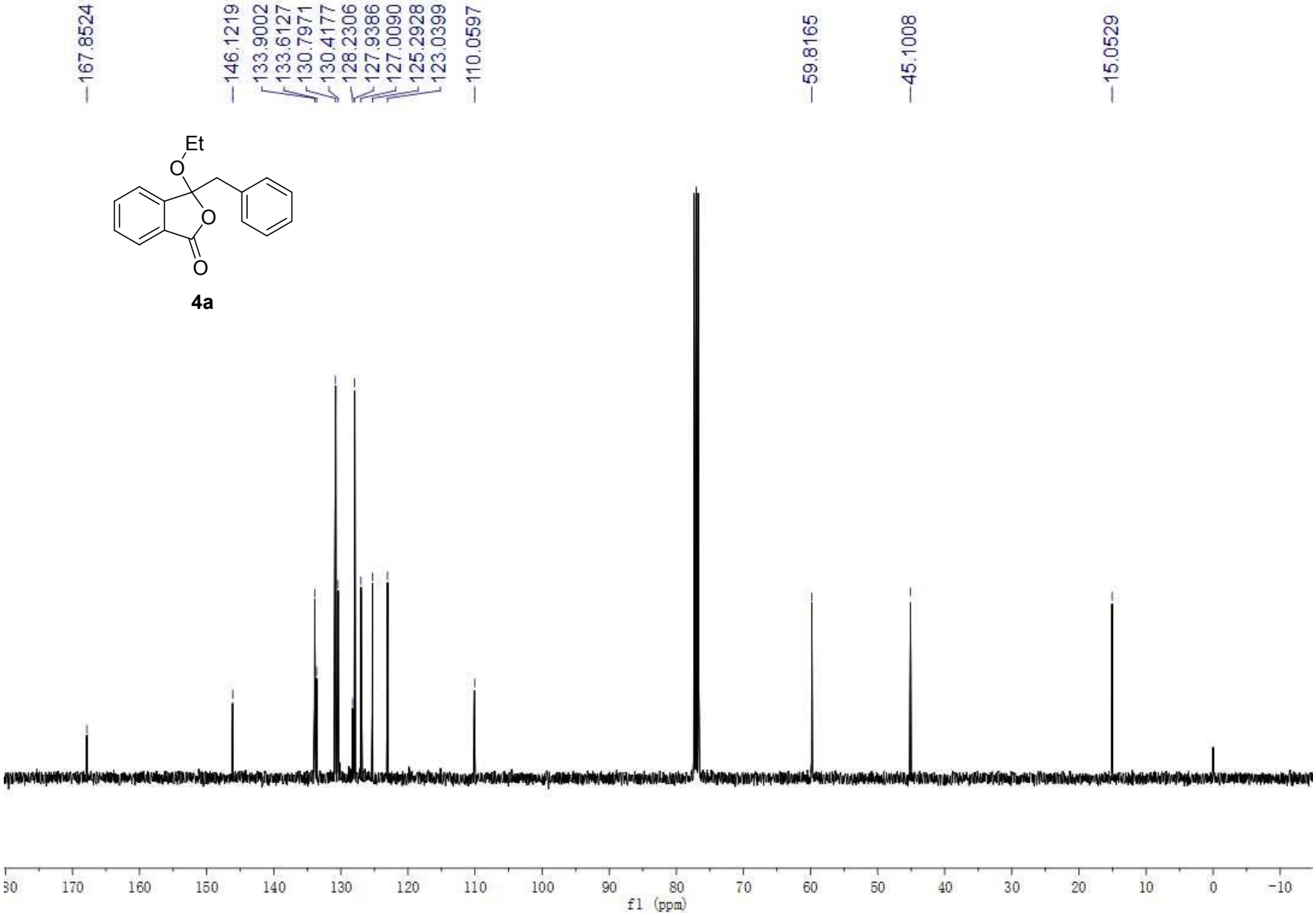
3.0613
3.0564
3.0437
3.0388
3.0213
1.1872
1.1696
1.1520


Et
O
O
O

4a


0.97
1.01
1.00
0.99
2.97
1.99
3.05
1.02
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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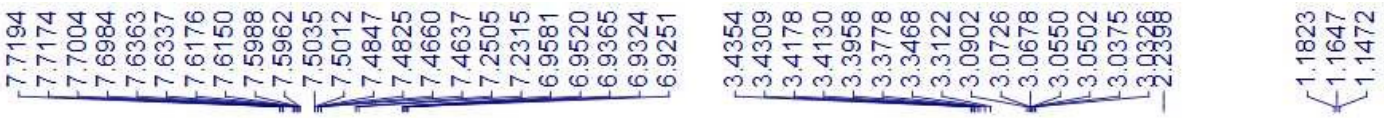
133.9002
133.6127
130.7971
130.4177
128.2306
127.9386
127.0090
125.2928
123.0399
110.0597
59.8165
45.1008
15.0529
Et
O
O
O
4a
f1 (ppm)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7.7174
7.7004
7.6984
7.6363
7.6337
7.6176
7.6150
7.5988
7.5962
7.5035
7.5012
7.4847
7.4825
7.4660
7.4637
7.2505
7.2315
6.9581
6.9520
6.9365
6.9324
6.9251
3.4354
3.4309
3.4178
3.4130
3.3958
3.3778
3.3468
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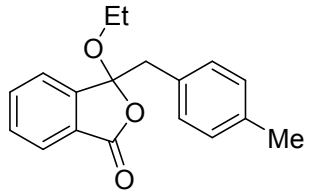
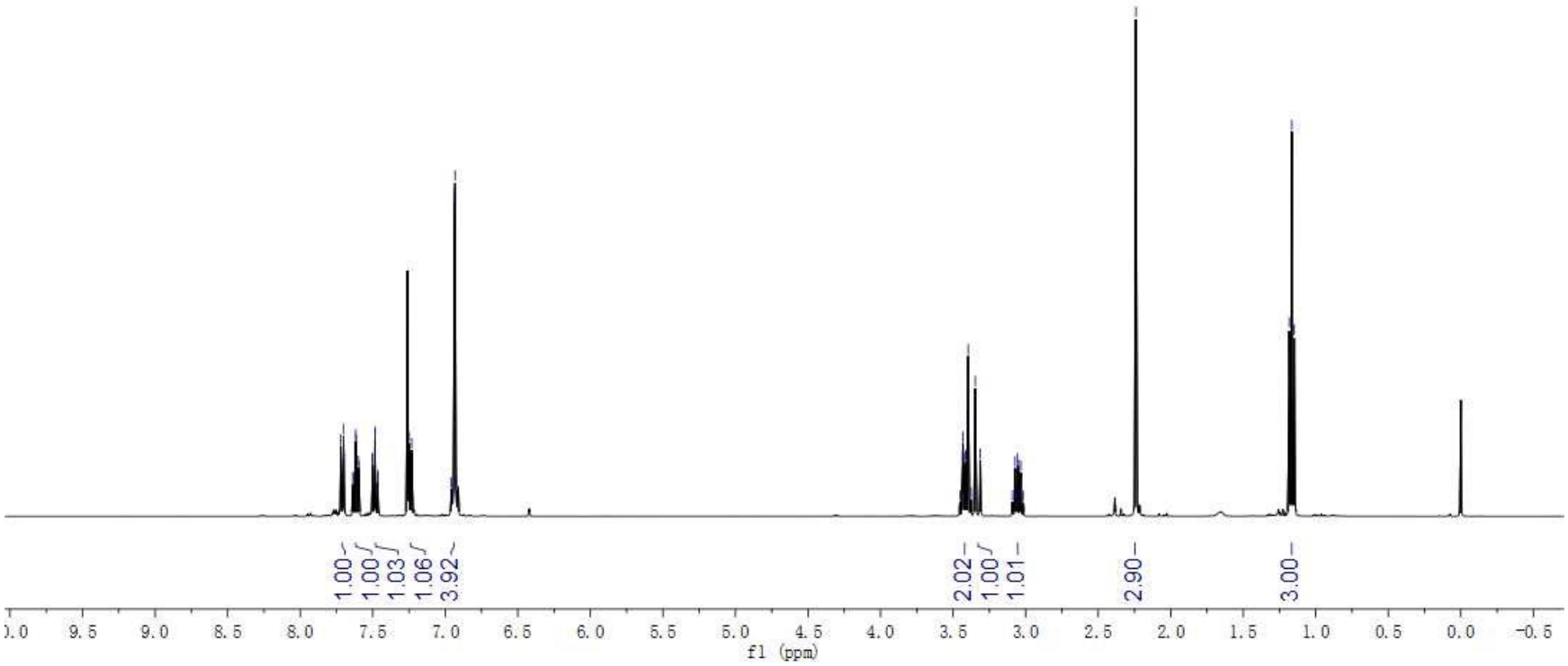
3.0726
3.0678
3.0550
3.0502
3.0375
1.1823
1.1647
1.1472


Et
O
O
O
Me

4b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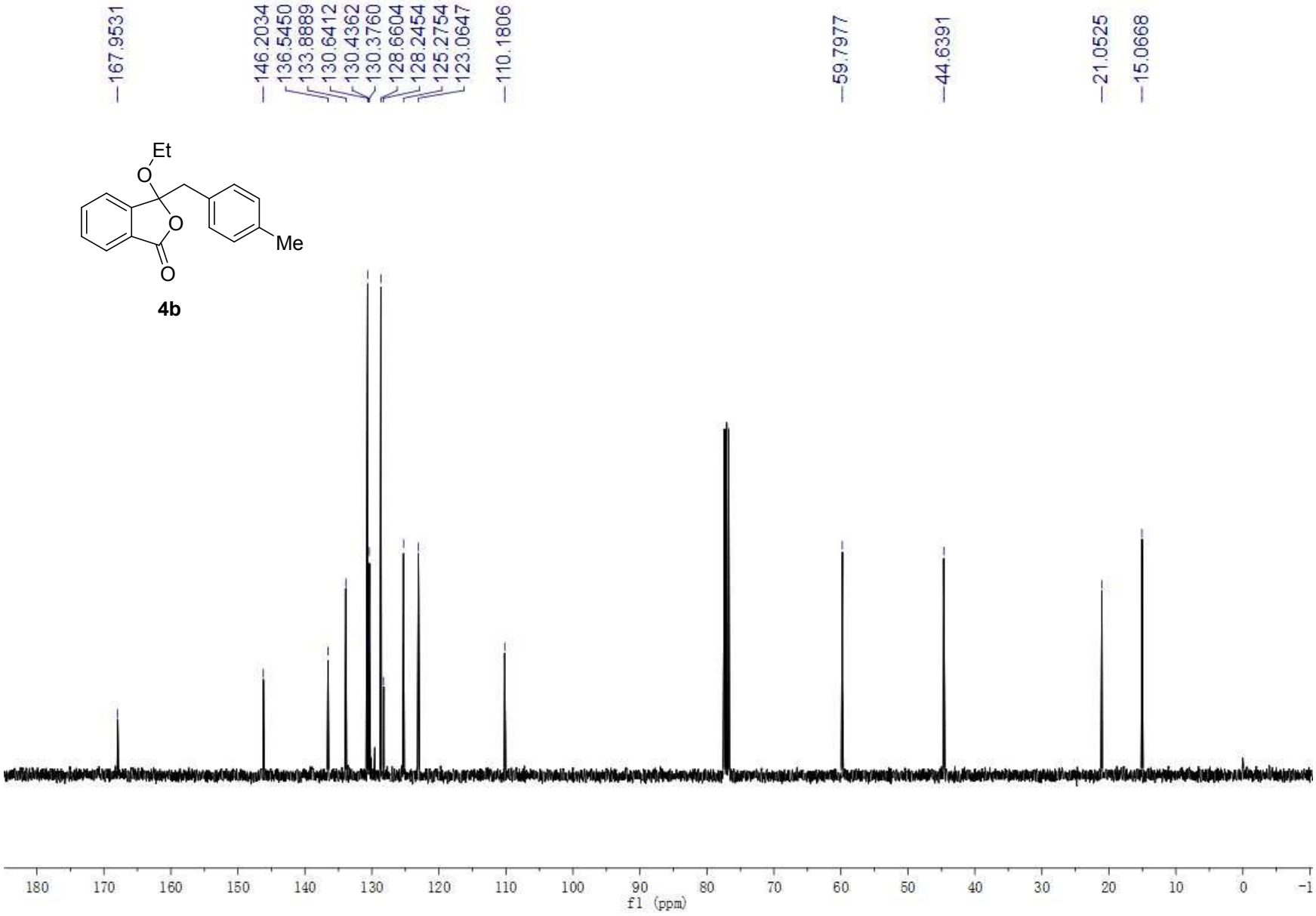
1.00
1.03
1.06
3.92
2.02
1.00
1.01
2.90
3.00
f1 (ppm)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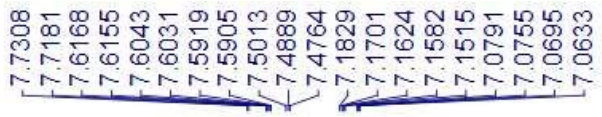
130.6412
130.4362
130.3760
128.6604
128.2454
125.2754
123.0647
110.1806
59.7977
44.6391
21.0525
15.0668
Et
O
O
O
Me
4b
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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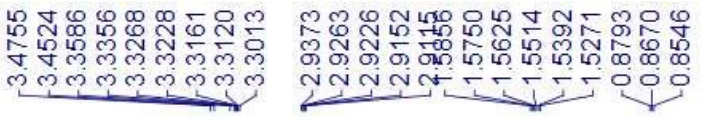
7.6031
7.5919
7.5905
7.5013
7.4889
7.4764
7.1829
7.1701
7.1624
7.1582
7.1515
7.0791
7.0755
7.0695
7.0633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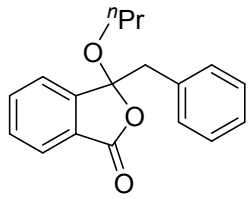
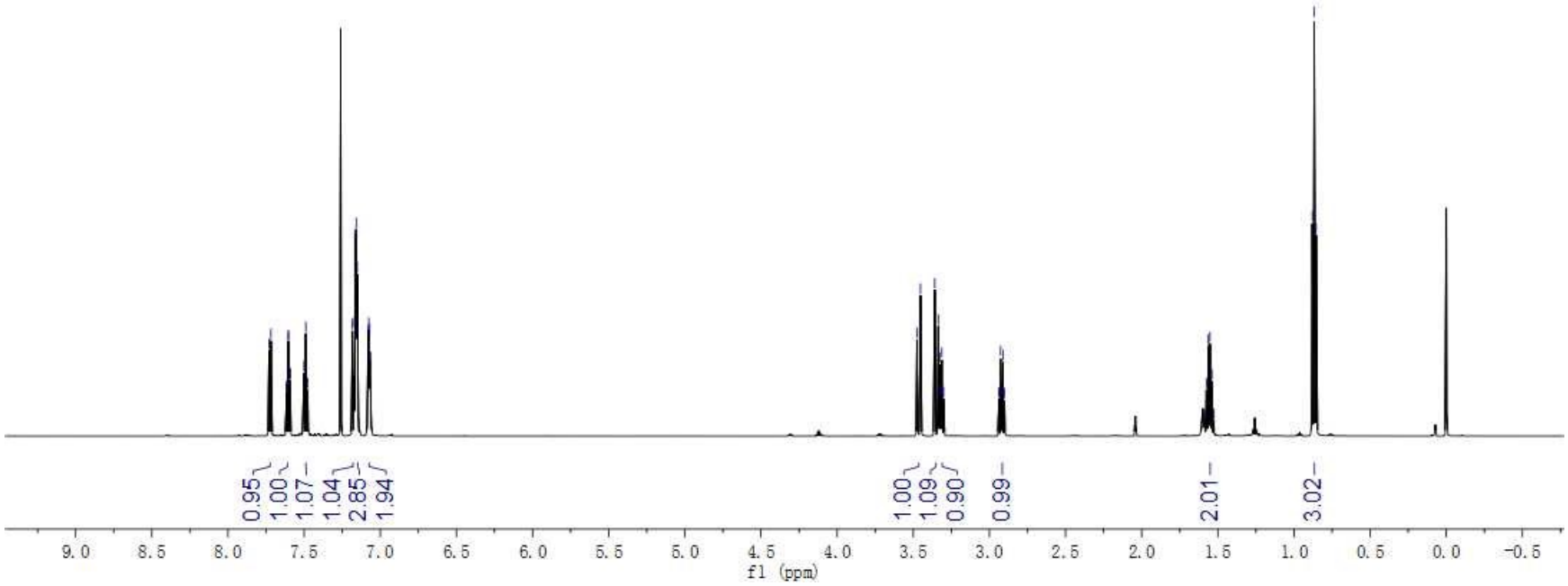
3.3586
3.3356
3.3268
3.3228
3.3161
3.3120
3.3013
2.9373
2.9263
2.9226
2.9152
1.5750
1.5625
1.5514
1.5392
1.5271
0.8793
0.8670
0.8546


nPr
O
O
O

4c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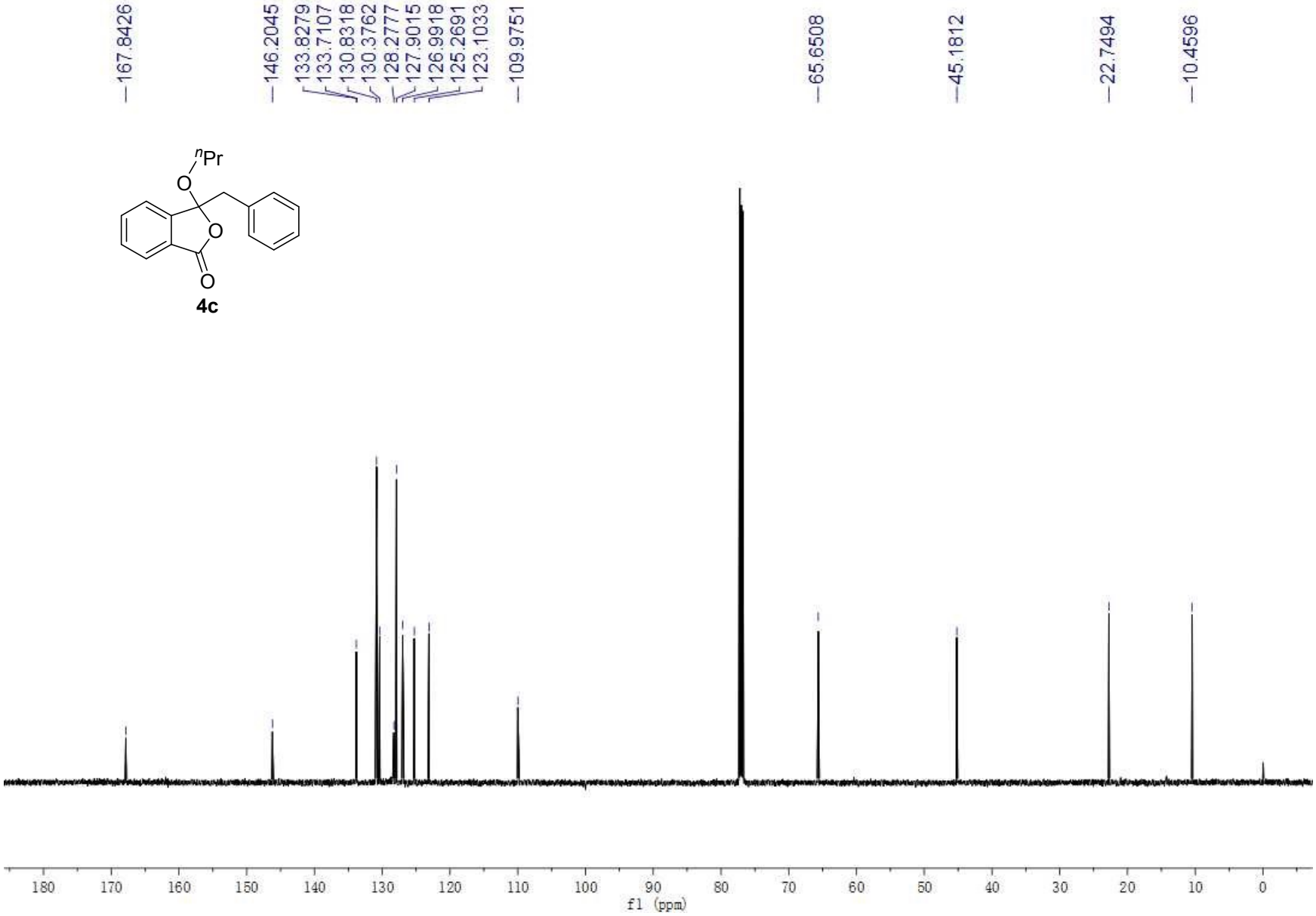
1.07
1.04
2.85
1.94
1.00
1.09
0.90
0.99
2.01
3.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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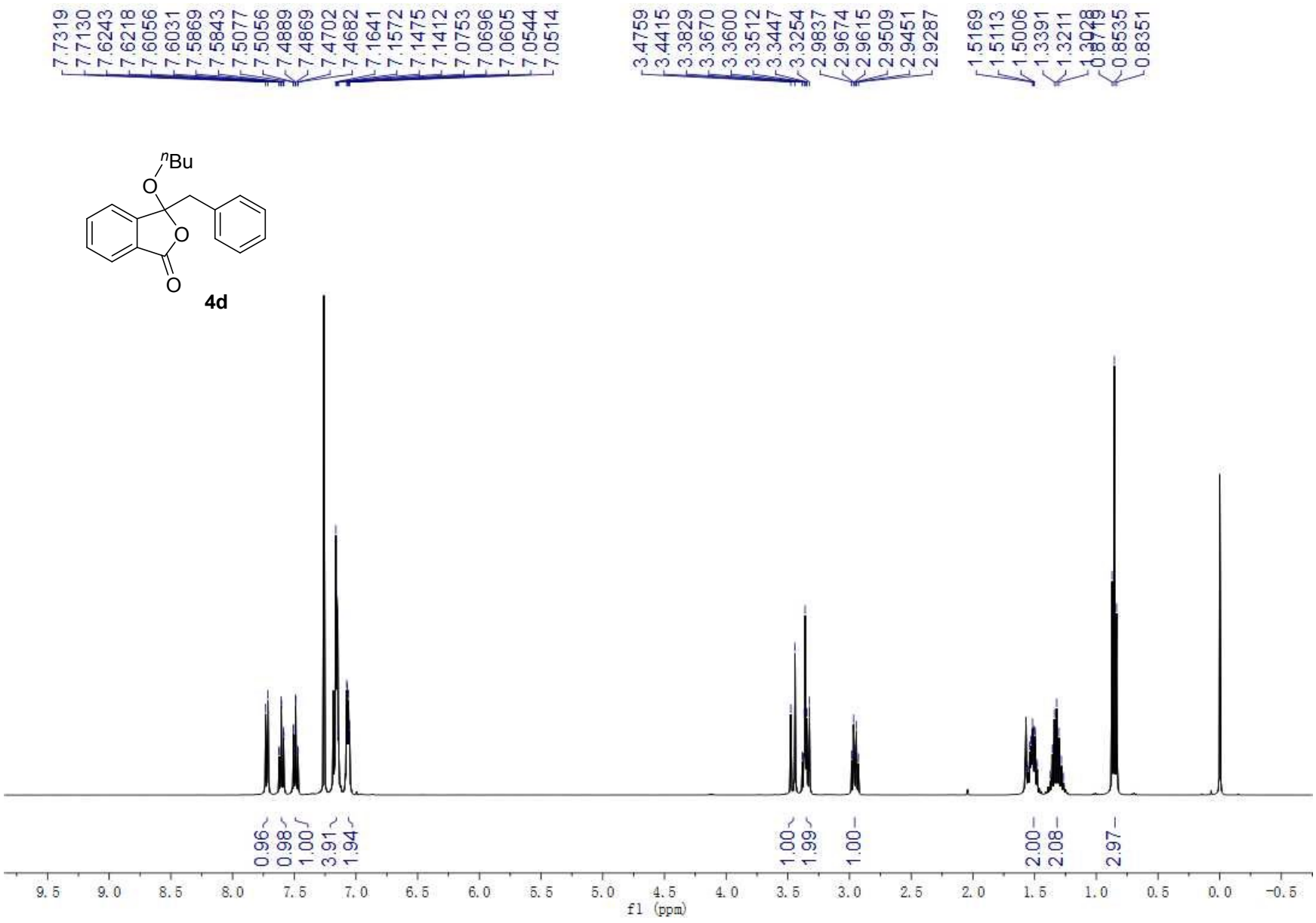
130.3762
128.2777
127.9015
126.9918
125.2691
123.1033
109.9751
65.6508
45.1812
22.7494
10.4596
nPr
O
O
O
4c
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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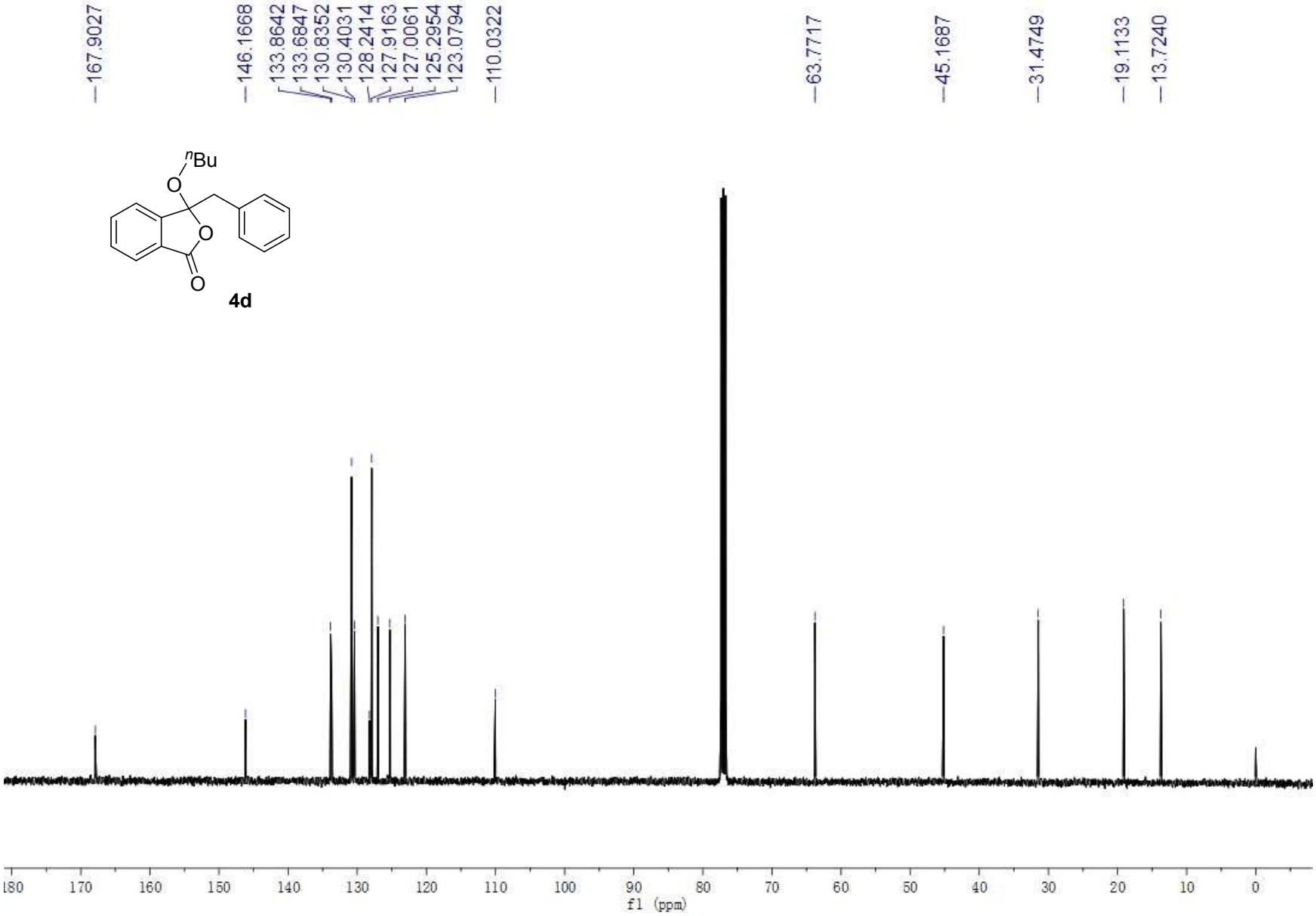
7.6243
7.6218
7.6056
7.6031
7.5869
7.5843
7.5077
7.5056
7.4889
7.4869
7.4702
7.4682
7.1641
7.1572
7.1475
7.1412
7.0753
7.0696
7.0605
7.0544
7.0514
3.4759
3.4415
3.3829
3.3670
3.3600
3.3512
3.3447
3.3254
2.9837
2.9674
2.9615
2.9509
2.9451
2.9287
1.5169
1.5113
1.5006
1.3391
1.3211
0.8719
0.8535
0.8351
nBu
O
O
O
4d
0.96
0.98
1.00
3.91
1.94
1.00
1.99
1.00
2.00
2.08
2.97
f1 (ppm)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133.6847
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130.4031
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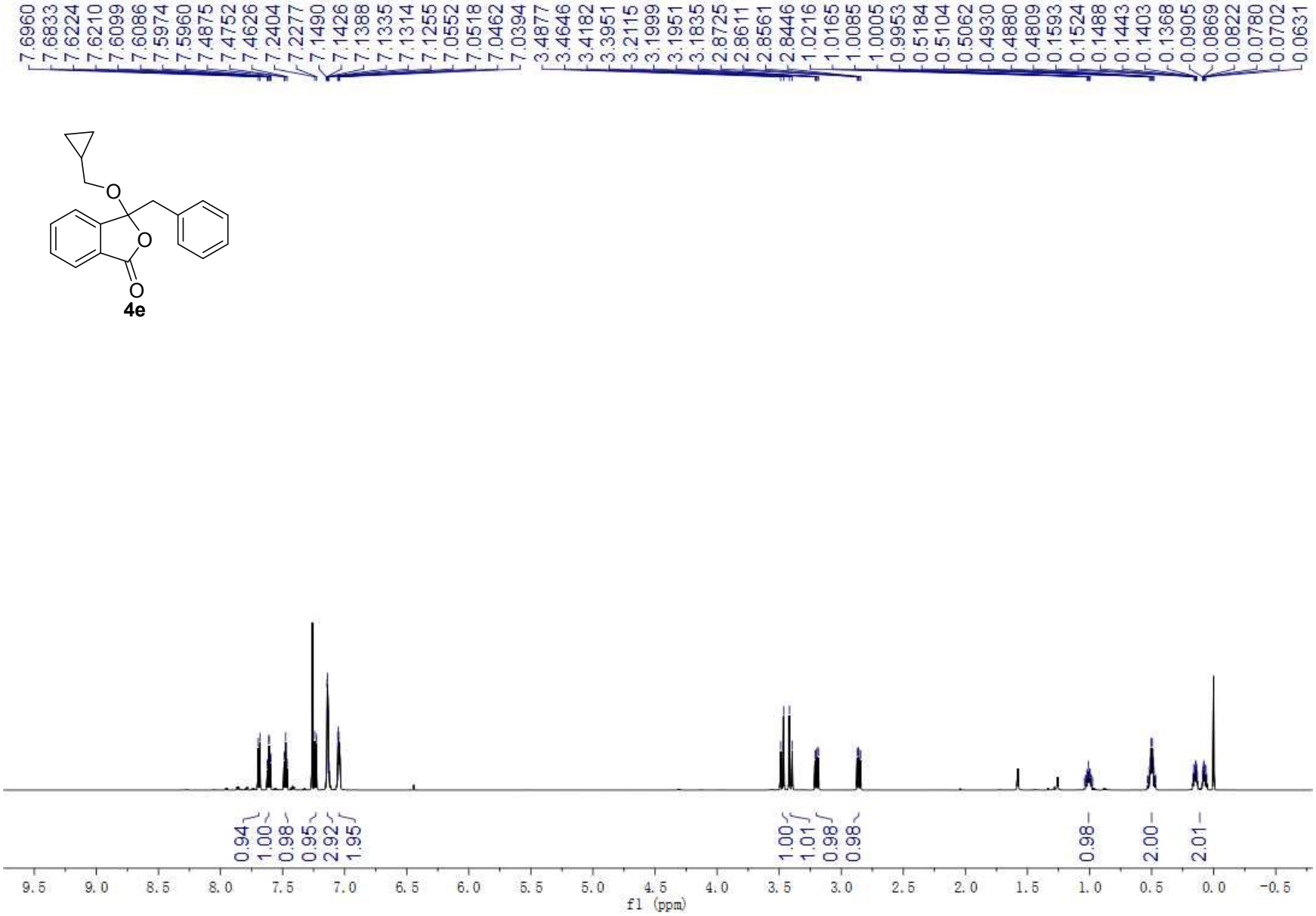
127.9163
127.0061
125.2954
123.0794
110.0322
63.7717
45.1687
31.4749
19.1133
13.7240
nBu
O
O
O
4d
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.6224
7.6210
7.6099
7.6086
7.5974
7.5960
7.4875
7.4752
7.4626
7.2404
7.2277
7.1490
7.1426
7.1388
7.1335
7.1314
7.1255
7.0552
7.0518
7.0462
7.0394
3.4877
3.4646
3.4182
3.3951
3.2115
3.1999
3.1951
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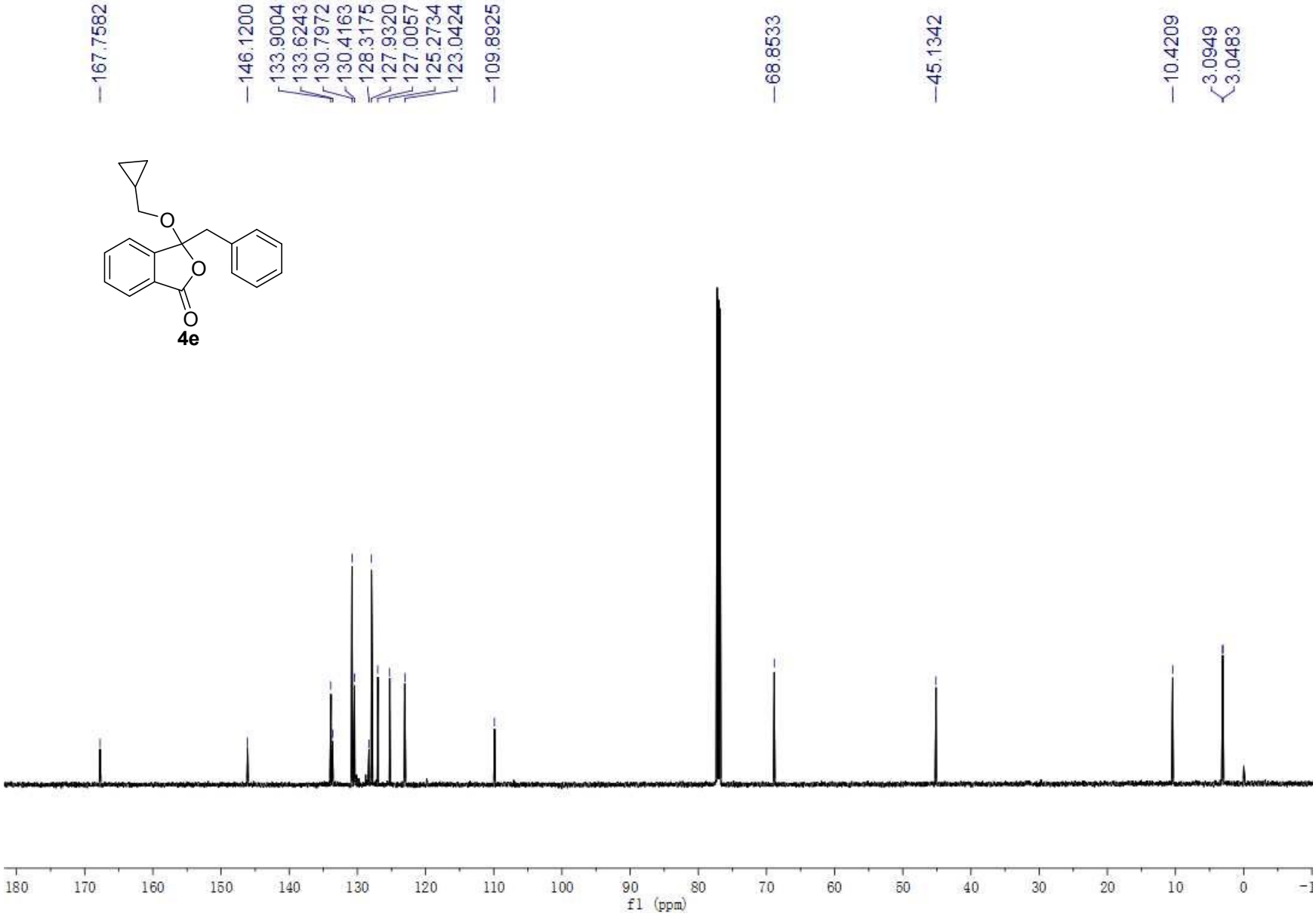
2.8611
2.8561
2.8446
1.0216
1.0165
1.0085
1.0005
0.9953
0.5184
0.5104
0.5062
0.4930
0.4880
0.4809
0.1593
0.1524
0.1488
0.1443
0.1403
0.1368
0.0905
0.0869
0.0822
0.0780
0.0702
0.0631
O
O
O
4e
0.94
1.00
0.98
0.95
2.92
1.95
1.00
1.01
0.98
0.98
0.98
2.00
2.01
f1 (ppm)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O
O
4e
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150
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130
120
110
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70
60
50
40
30
20
10
0
f1 (ppm)


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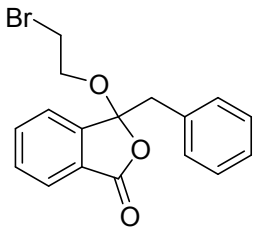
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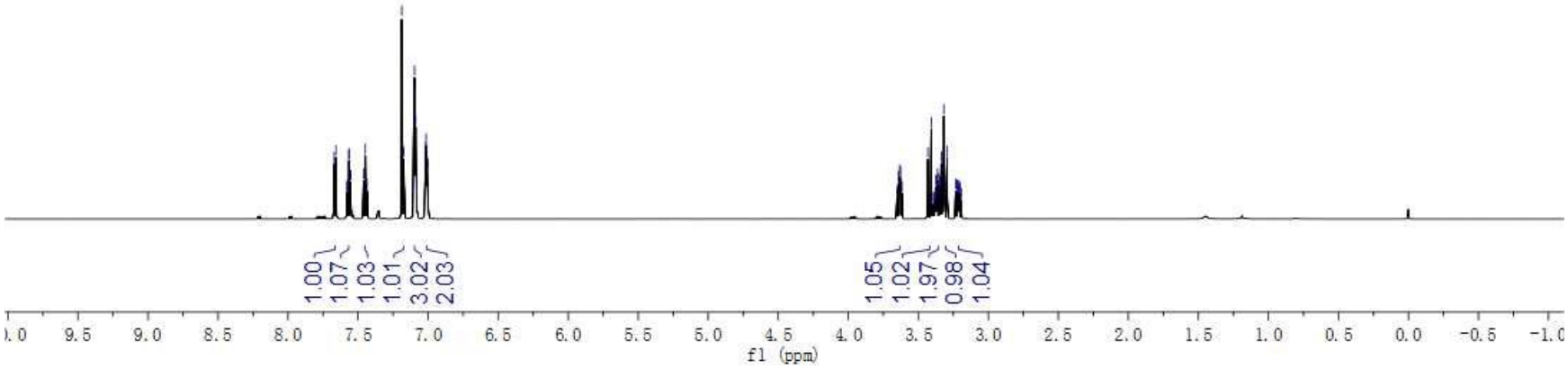
O

4f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8.0
7.5
7.0
6.5
6.0
5.5
5.0
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2.5
2.0
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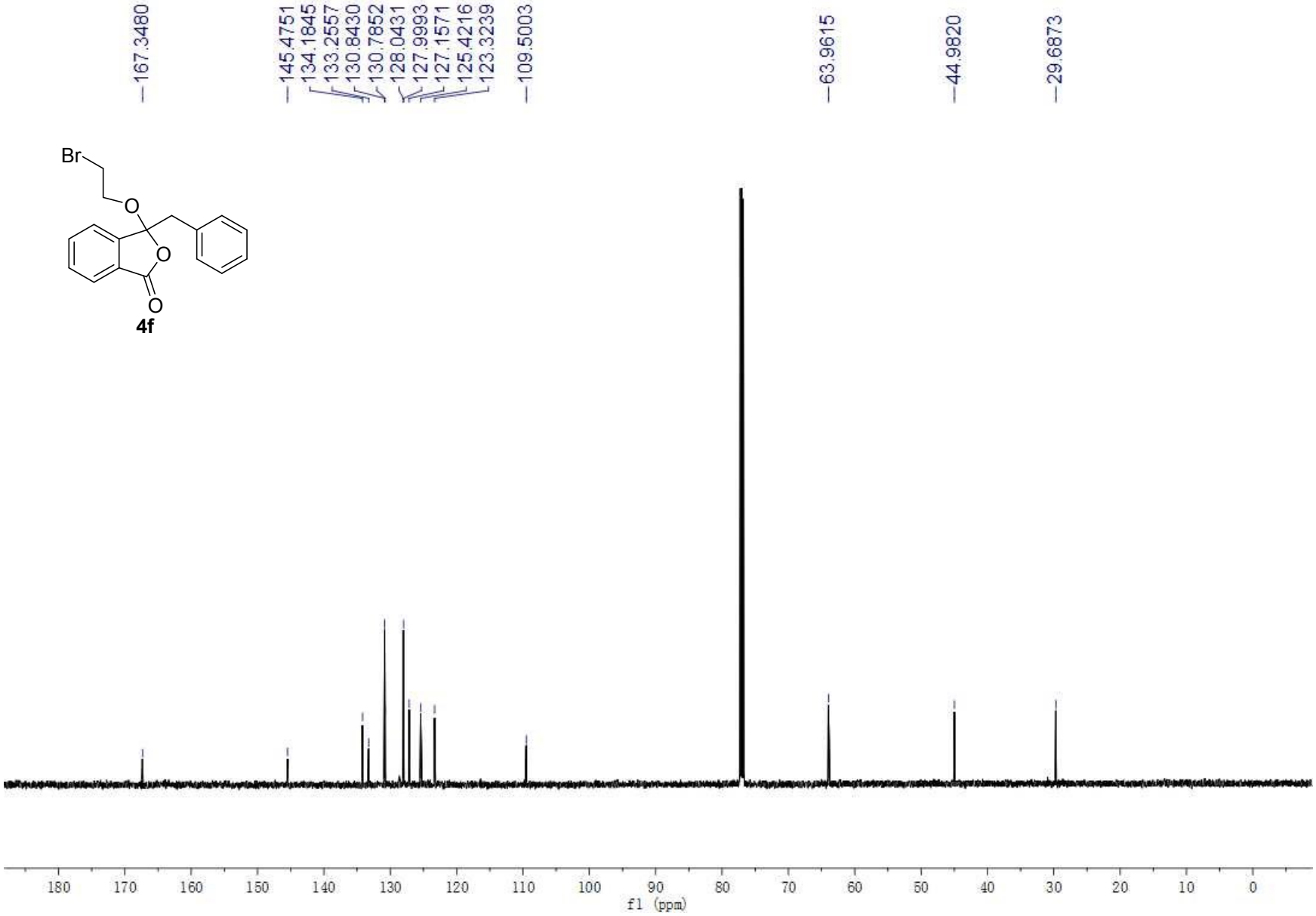
f1 (ppm)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4f
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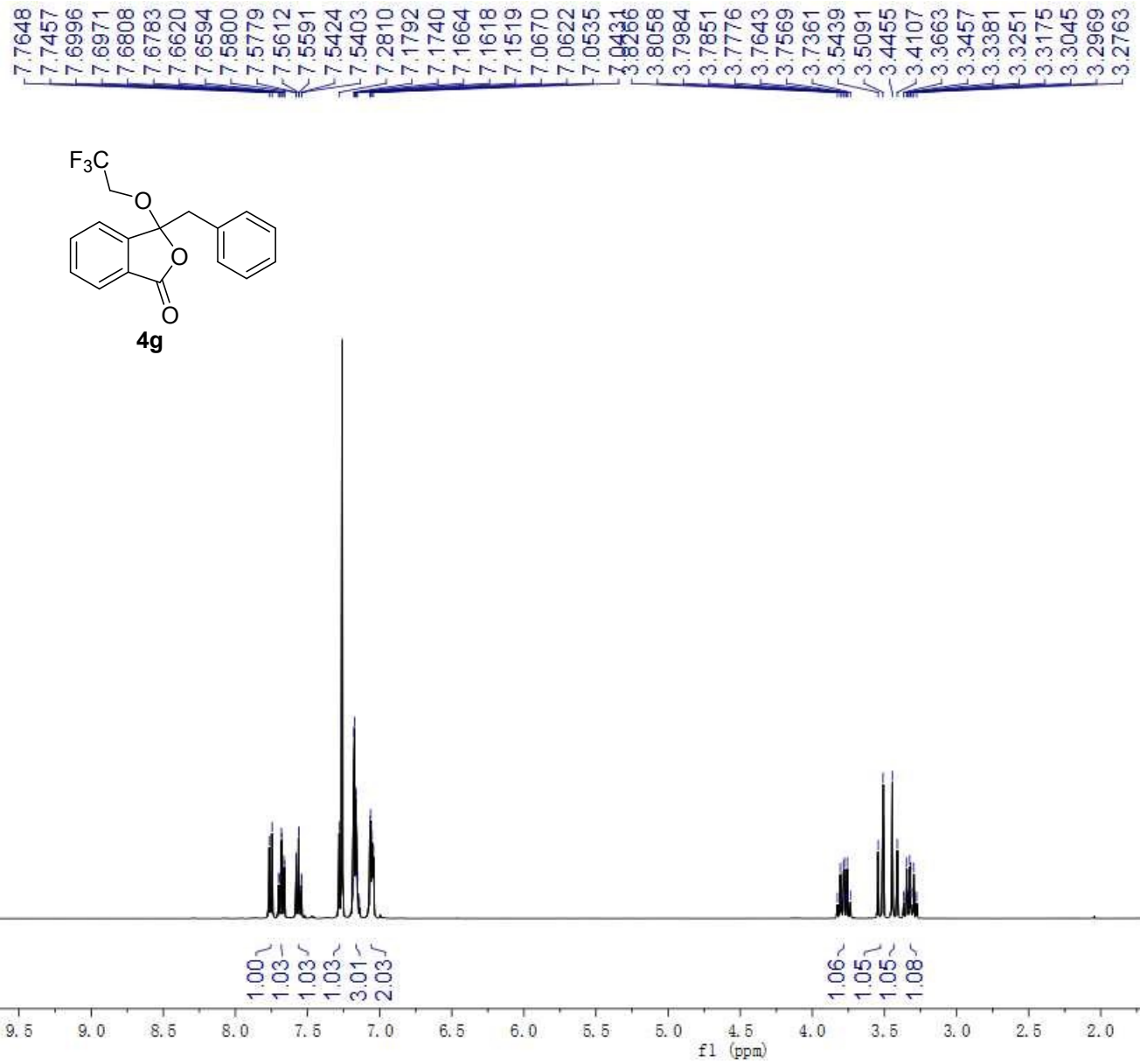
f1 (ppm)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7.5424
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7.1740
7.1664
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7.1519
7.0670
7.0622
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3.3251
3.3175
3.3045
3.2969
3.2763
F3C
O
O
O
4g
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1.03
1.03
1.03
3.01
2.03
1.06
1.05
1.05
1.08
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8.0
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7.0
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6.0
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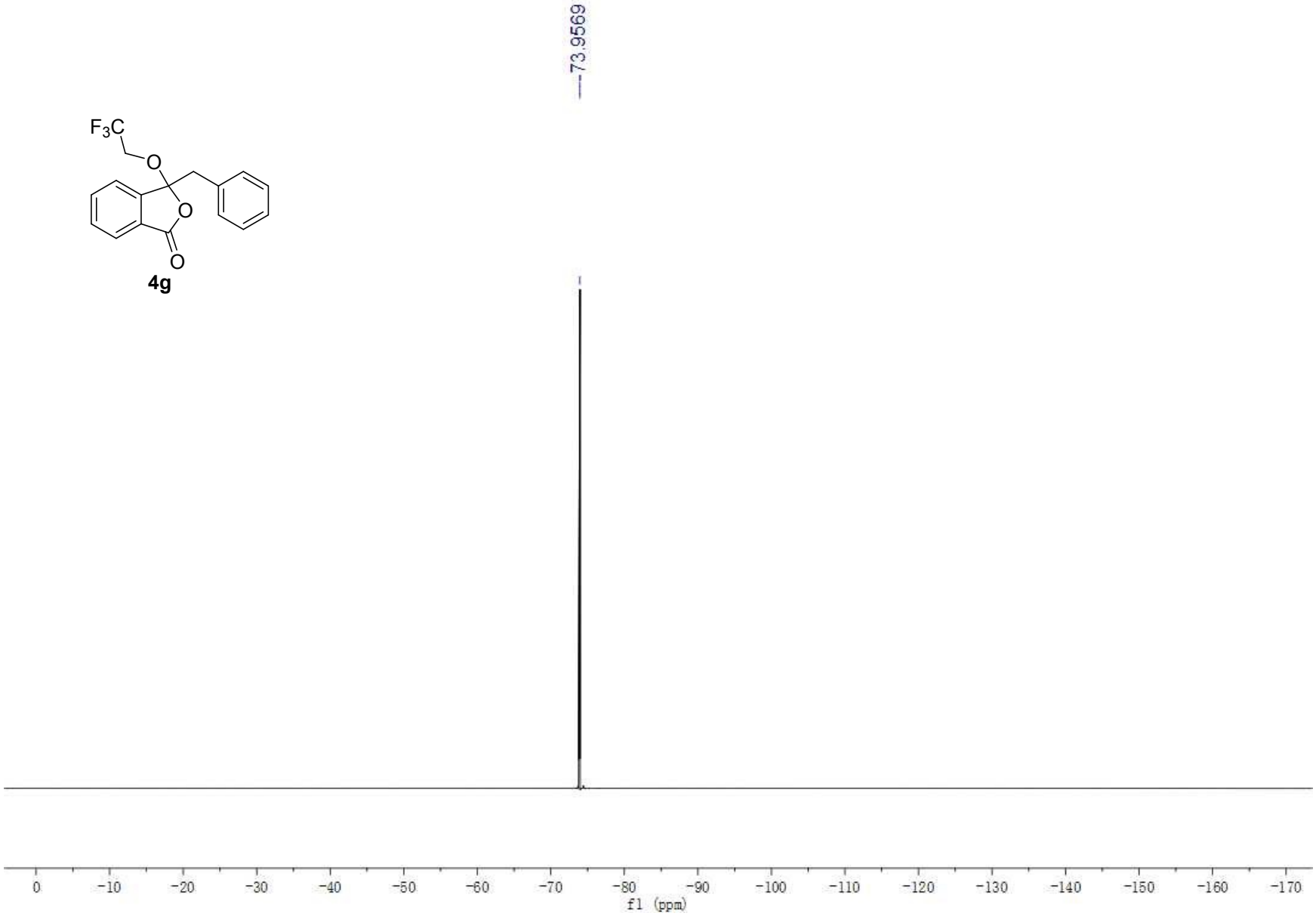
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

F3C
O
O
O

4g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-30
-40
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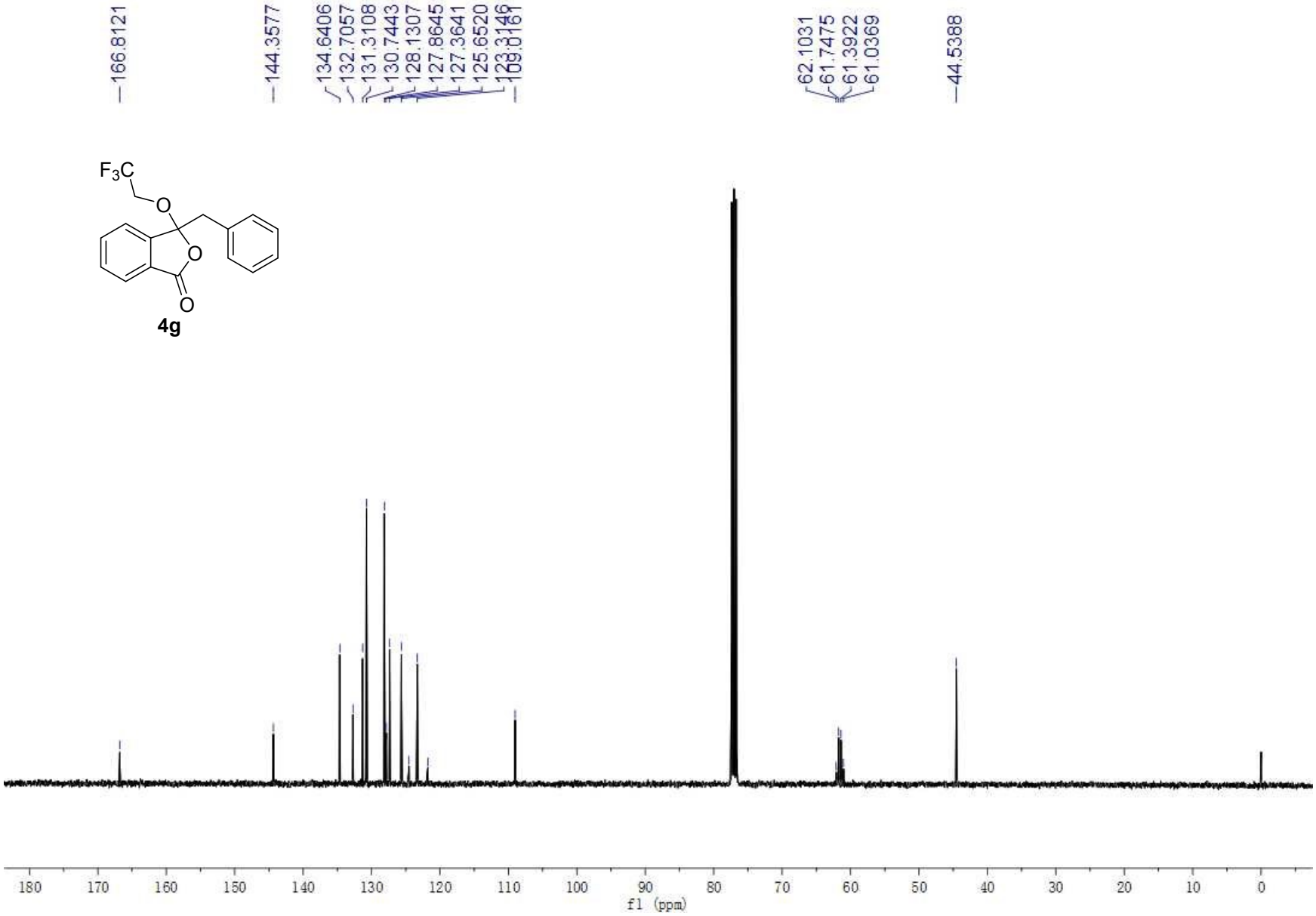
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
f1 (ppm)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61.7475
61.3922
61.0369
44.5388
F3C
O
O
O
4g
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50
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30
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10
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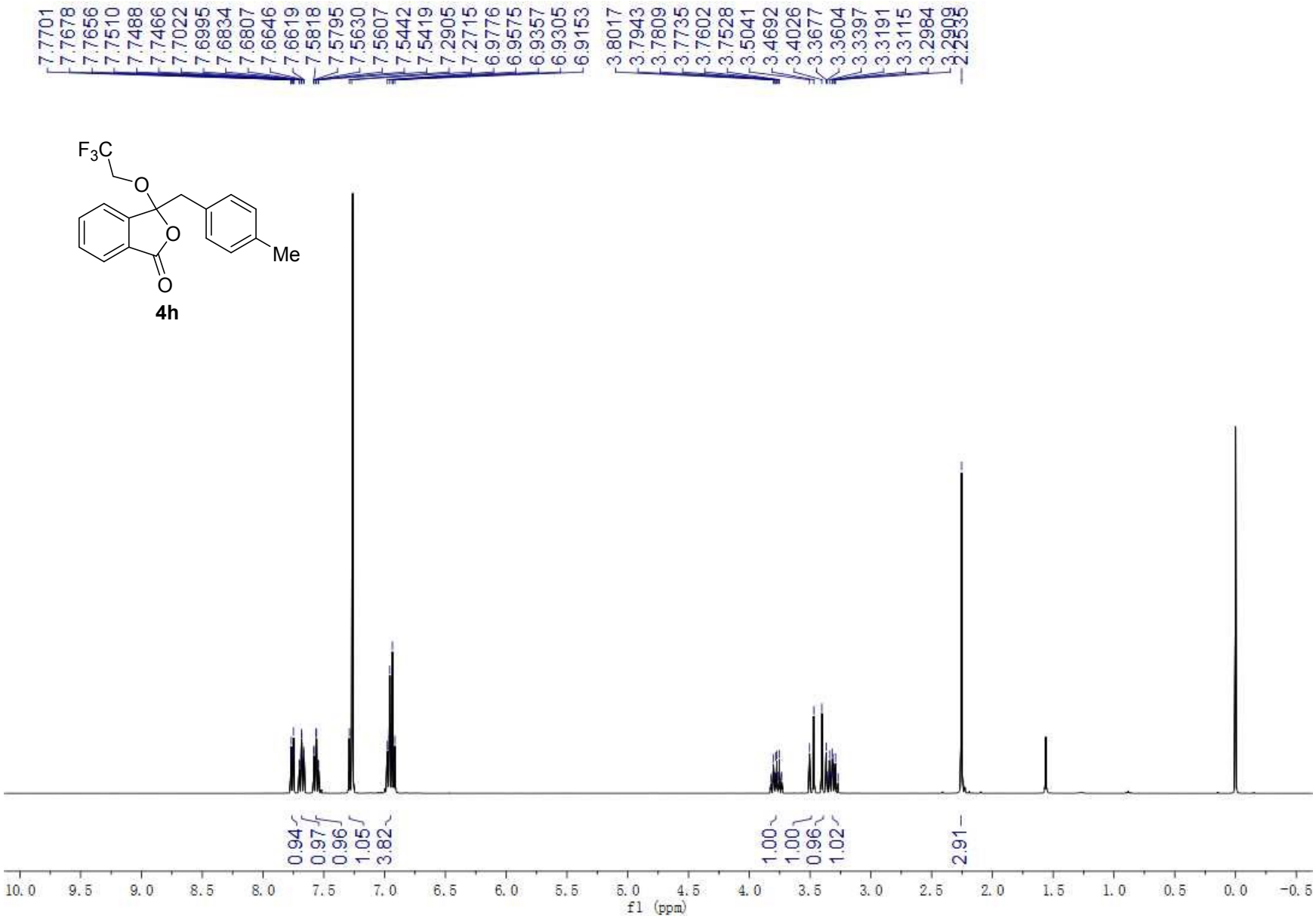
f1 (ppm)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O
O
Me
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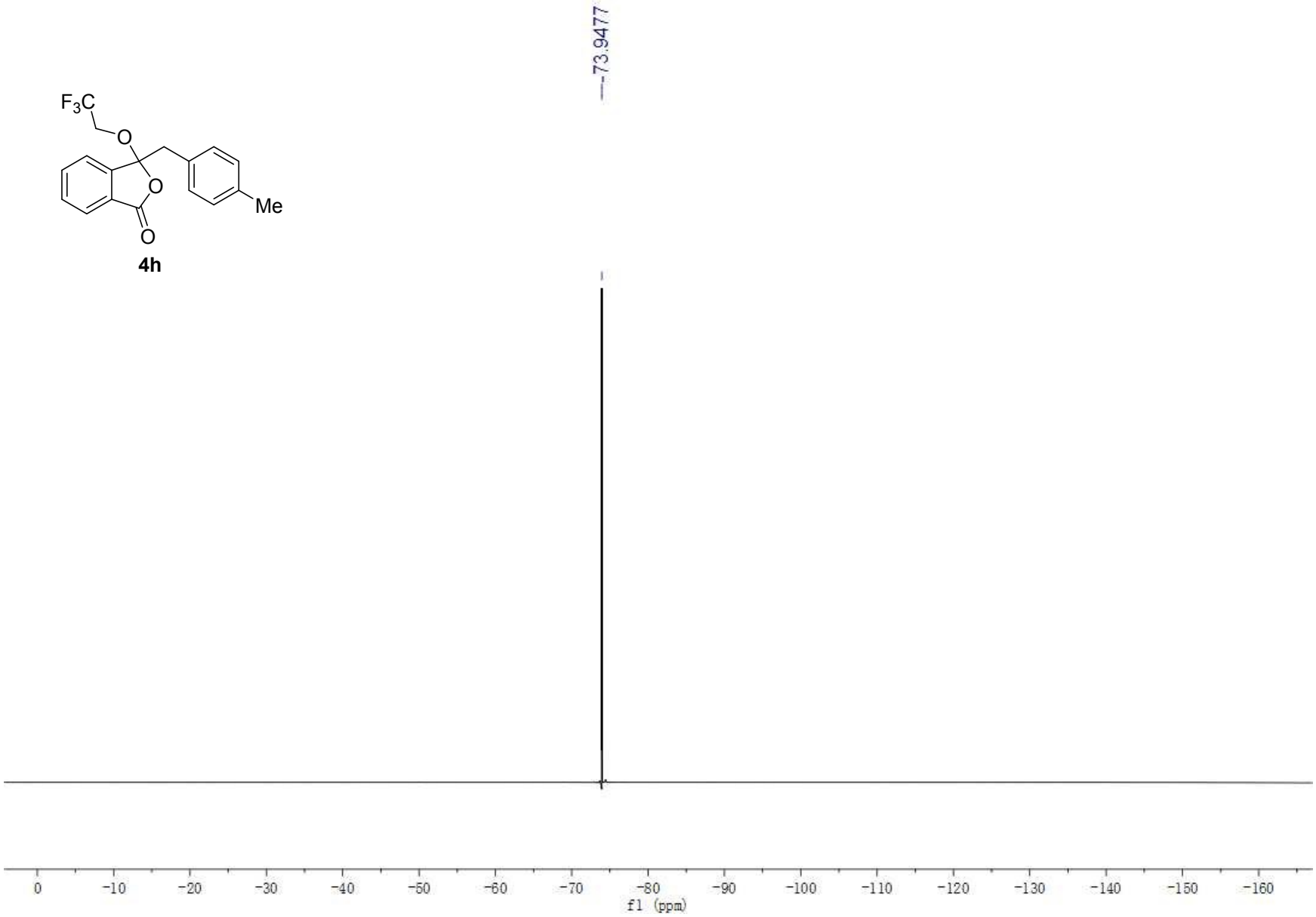
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

F3C
O
O
O
Me

4h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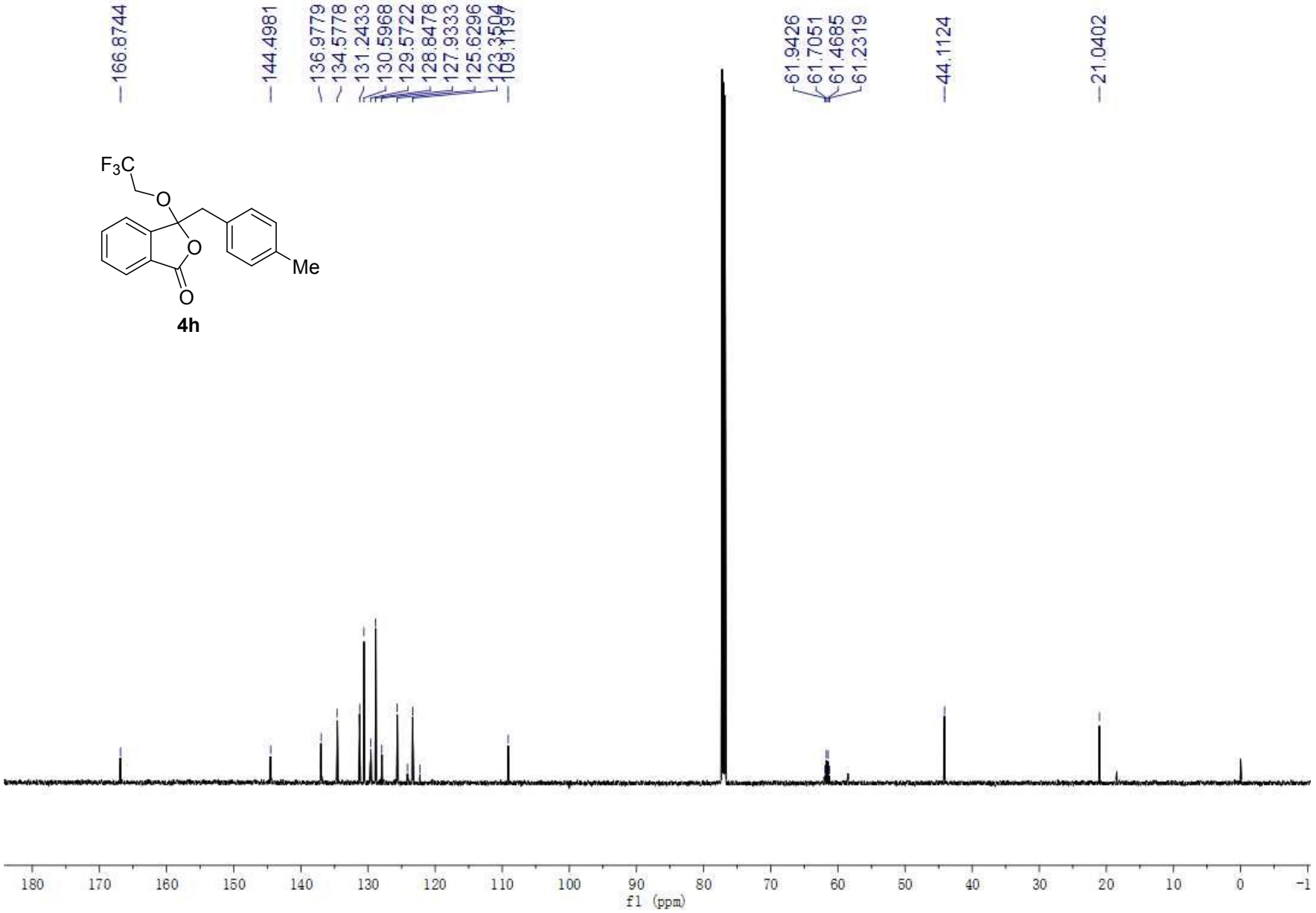
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)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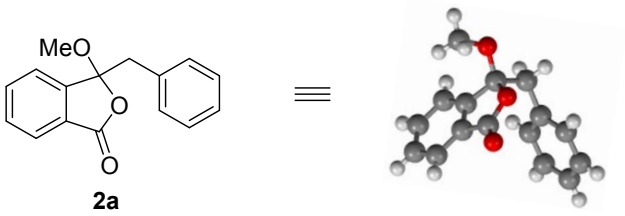
109.1197
61.9426
61.7051
61.4685
61.2319
44.1124
21.0402
F3C
O
O
O
Me
4h
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

V. X-Ray of Compound 2a:



2a

Table 1 Crystal data and structure refinement for 2a.

Identification code	2a
Empirical formula	$C_{16}H_{14}O_3$
Formula weight	254.27
Temperature/K	99.97(11)
Crystal system	monoclinic
Space group	C2/c
a/Å	16.74290(10)
b/Å	10.55120(10)
c/Å	14.69710(10)
α/°	90
β/°	93.2470(10)
γ/°	90
Volume/Å^3	2592.19(3)
Z	8
ρ_{calc}g/cm^3	1.303
μ/mm^{-1}	0.728
F(000)	1072.0
Crystal size/mm^3	0.15 × 0.1 × 0.06
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.914 to 145.806
Index ranges	$-20 \le h \le 20$, $-12 \le k \le 12$, $-16 \le l \le 18$
Reflections collected	45394
Independent reflections	2550 [R_{int} = 0.0393, R_{sigma} = 0.0105]
Data/restraints/parameters	2550/0/173
Goodness-of-fit on F^2	1.088
Final R indexes [I>=2σ (I)]	R_1 = 0.0341, wR_2 = 0.0848
Final R indexes [all data]	R_1 = 0.0350, wR_2 = 0.0855
Largest diff. peak/hole / e Å^{-3}	0.21/-0.29

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 2a. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O2	3354.4(4)	3904.9(7)	5328.9(5)	19.06(18)
O1	4253.2(4)	3534.8(7)	6569.0(5)	21.04(18)
O3	3121.9(5)	4933.5(8)	4004.3(5)	28.3(2)
C1	2093.6(6)	4307.9(9)	6654.0(7)	16.1(2)
C2	1851.7(6)	5345.2(10)	7158.8(7)	16.9(2)
C3	1089.5(6)	5852.6(10)	7013.7(7)	19.1(2)
C4	558.7(6)	5326.9(11)	6358.5(7)	21.2(2)
C5	797.1(7)	4303.3(11)	5843.8(7)	22.9(2)
C6	1560.6(6)	3799.7(10)	5986.8(7)	20.5(2)
C7	2900.9(6)	3706.1(10)	6860.1(7)	17.9(2)
C8	3564.5(6)	4203.5(10)	6286.1(7)	16.1(2)
C9	4956.1(6)	3848.3(11)	6105.4(8)	25.5(3)
C10	3289.1(6)	4977.8(10)	4810.9(7)	18.7(2)
C11	3658.4(6)	5626.8(9)	6276.4(7)	15.1(2)
C12	3473.4(6)	6072.6(10)	5408.4(7)	16.3(2)
C13	3496.7(6)	7359.5(10)	5199.5(7)	20.5(2)
C14	3730.8(6)	8178.8(10)	5900.0(8)	23.2(2)
C15	3935.7(6)	7728.5(10)	6774.1(8)	22.5(2)
C16	3894.2(6)	6443.9(10)	6979.5(7)	18.9(2)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 2a. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\cdots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O2	24.0(4)	17.6(4)	15.9(4)	-3.4(3)	3.5(3)	-1.1(3)
O1	18.3(4)	20.0(4)	25.3(4)	6.3(3)	5.6(3)	5.6(3)
O3	31.1(4)	39.2(5)	14.5(4)	-1.5(3)	-0.7(3)	-2.9(4)
C1	17.6(5)	15.4(5)	15.6(5)	3.3(4)	4.1(4)	-2.5(4)
C2	19.0(5)	15.7(5)	16.0(5)	0.6(4)	1.0(4)	-2.9(4)
C3	22.2(5)	15.9(5)	19.6(5)	0.9(4)	4.2(4)	0.3(4)
C4	17.3(5)	25.5(5)	20.9(5)	4.0(4)	1.2(4)	-0.1(4)
C5	21.8(5)	28.8(6)	17.9(5)	-1.7(4)	-0.8(4)	-6.6(4)
C6	24.2(5)	19.7(5)	18.0(5)	-3.6(4)	5.0(4)	-3.9(4)
C7	20.2(5)	15.3(5)	18.6(5)	3.0(4)	4.1(4)	1.0(4)

C8	18.1(5)	15.6(5)	14.6(5)	-0.6(4)	1.5(4)	2.3(4)
C9	18.7(5)	26.8(6)	31.7(6)	6.6(5)	7.3(4)	5.6(4)
C10	14.9(5)	24.4(6)	17.1(5)	0.2(4)	3.3(4)	0.5(4)
C11	13.1(4)	15.4(5)	17.1(5)	0.4(4)	3.9(4)	1.3(4)
C12	12.4(4)	19.7(5)	16.9(5)	1.4(4)	3.1(4)	1.1(4)
C13	15.9(5)	21.7(5)	24.2(5)	7.8(4)	5.3(4)	3.0(4)
C14	19.0(5)	14.7(5)	36.8(6)	2.6(4)	10.0(4)	0.5(4)
C15	18.9(5)	20.0(5)	29.2(6)	-7.9(4)	7.6(4)	-2.9(4)
C16	18.3(5)	21.9(5)	16.8(5)	-1.9(4)	2.7(4)	-0.3(4)

Table 4 Bond Lengths for 2a.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O2	C8	1.4651(12)	C5	C6	1.3894(16)
O2	C10	1.3651(13)	C7	C8	1.5256(14)
O1	C8	1.3949(12)	C8	C11	1.5101(14)
O1	C9	1.4317(13)	C10	C12	1.4731(15)
O3	C10	1.2034(14)	C11	C12	1.3784(14)
C1	C2	1.3951(14)	C11	C16	1.3858(15)
C1	C6	1.3950(15)	C12	C13	1.3932(15)
C1	C7	1.5086(14)	C13	C14	1.3839(16)
C2	C3	1.3892(15)	C14	C15	1.3943(17)
C3	C4	1.3884(15)	C15	C16	1.3912(16)
C4	C5	1.3899(16)			

Table 5 Bond Angles for 2a.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C10	O2	C8	111.38(8)	O1	C8	C11	114.90(8)
C8	O1	C9	115.42(8)	C11	C8	C7	115.27(8)
C2	C1	C7	120.47(9)	O2	C10	C12	108.08(9)
C6	C1	C2	118.82(10)	O3	C10	O2	121.60(10)
C6	C1	C7	120.64(9)	O3	C10	C12	130.30(10)
C3	C2	C1	120.82(9)	C12	C11	C8	109.27(9)
C4	C3	C2	119.93(10)	C12	C11	C16	121.16(10)
C3	C4	C5	119.71(10)	C16	C11	C8	129.57(9)
C6	C5	C4	120.33(10)	C11	C12	C10	108.22(9)
C5	C6	C1	120.38(10)	C11	C12	C13	121.93(10)
C1	C7	C8	114.61(8)	C13	C12	C10	129.83(10)
O2	C8	C7	108.32(8)	C14	C13	C12	117.07(10)
O2	C8	C11	102.96(8)	C13	C14	C15	121.14(10)
O1	C8	O2	109.08(8)	C16	C15	C14	121.28(10)

O1	C8	C7	106.07(8)		C11	C16	C15	117.39(10)

Table 6 Torsion Angles for 2a.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O2	C8	C11	C12	3.09(10)	C7	C8	C11	C12	-114.63(10)
O2	C8	C11	C16	-176.37(9)	C7	C8	C11	C16	65.91(14)
O2	C10	C12	C11	0.89(11)	C8	O2	C10	O3	179.85(9)
O2	C10	C12	C13	179.15(10)	C8	O2	C10	C12	1.18(11)
O1	C8	C11	C12	121.55(9)	C8	C11	C12	C10	-2.52(11)
O1	C8	C11	C16	-57.91(14)	C8	C11	C12	C13	179.05(9)
O3	C10	C12	C11	-177.62(11)	C8	C11	C16	C15	179.46(10)
O3	C10	C12	C13	0.65(19)	C9	O1	C8	O2	62.92(11)
C1	C2	C3	C4	-0.07(15)	C9	O1	C8	C7	179.39(9)
C1	C7	C8	O2	-62.63(11)	C9	O1	C8	C11	-52.05(12)
C1	C7	C8	O1	-179.60(8)	C10	O2	C8	O1	-125.03(9)
C1	C7	C8	C11	52.05(12)	C10	O2	C8	C7	119.94(9)
C2	C1	C6	C5	-1.39(15)	C10	O2	C8	C11	-2.57(10)
C2	C1	C7	C8	-94.05(11)	C10	C12	C13	C14	-176.76(10)
C2	C3	C4	C5	-0.74(16)	C11	C12	C13	C14	1.30(15)
C3	C4	C5	C6	0.48(16)	C12	C11	C16	C15	0.06(15)
C4	C5	C6	C1	0.60(16)	C12	C13	C14	C15	0.18(15)
C6	C1	C2	C3	1.13(15)	C13	C14	C15	C16	-1.55(16)
C6	C1	C7	C8	89.14(12)	C14	C15	C16	C11	1.40(15)
C7	C1	C2	C3	-175.74(9)	C16	C11	C12	C10	176.99(9)
C7	C1	C6	C5	175.48(9)	C16	C11	C12	C13	-1.44(15)

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 2a.

Atom	*x*	*y*	*z*	U(eq)
H2	2205.2	5701.39	7598.02	20
H3	934.99	6543.63	7354.94	23
H4	45.96	5658.11	6264.46	25
H5	443.76	3953.9	5401.55	28
H6	1717.33	3119.86	5635.74	25
H7A	2851.92	2798.8	6766.09	21
H7B	3056.32	3844.15	7498.26	21
H9A	4880.63	3615.24	5474.98	38
H9B	5406.12	3396.41	6378.28	38
H9C	5052.96	4743.32	6152.02	38

H13	3360.81	7655.06	4614.94	25
H14	3751.76	9044.74	5785.73	28
H15	4103.33	8297.86	7228.75	27
H16	4019.7	6145.2	7565.52	23

VI. References:

1 (a) D. Felipe-Blanco and J. C. Gonzalez-Gomez. *Eur. J. Org. Chem.*, 2019, **2019**, 7735-7744; (b) S. Song, S.-F. Zhu, Y.-B. Yu and Q.-L. Zhou. *Angew. Chem. Int. Ed.*, 2013, **52**, 1556-1559.