Copper-Catalyzed Aerobic Oxidation and Cleavage/Formation of C-S Bond: a Novel Synthesis of Aryl Methyl Sulfones from Aryl Halides and DMSO

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Supporting Information

Contents

A. General Information

All the reagents were analytical grade and used without further purification, unless stated otherwise. $^{18}O_2$ gas (^{18}O, >97%) was purchased from Shanghai Research Institute of Chemical Industry, Shanghai, China). $H_2{}^{18}O$ (98%) was purchased from Alfa Aesar. ^1H and ^{13}C NMR spectra were recorded using a Bruker Avance 400 MHz NMR spectrometer. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively, chloroform is solvent with TMS as the internal standard. Mass spectra were recorded on a Shimadzu GCMS-QP5050A spectrometer at an ionization voltage of 70 eV equipped with a DB-WAX capillary column (internal diameter: 0.25 mm, length: 30 m). HRMS analysis was performed in a MAT95XP high resolution mass spectrometer. TLC was performed by using commercially prepared 100–400 mesh silica gel plates (GF254) and visualization was effected at 254 nm.

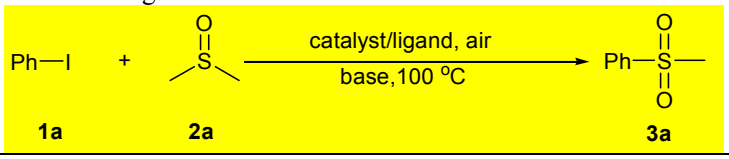
B. General Procedures for the Synthesis of Aryl Methyl Sulfones

In a typical procedure, iodobenzene **1a** (0.25 mmol), DMSO **2a** (2 mL), acetyl acetone (0.25 mmol), Cu_2O (0.025 mmol), and *t*-BuOK (0.75 mmol) were added into the reactor in turn. The reaction was carried out at 100 ^oC under air atmosphere with reflux for 20 h. After the reaction finished, the mixture was diluted with the saturated NaCl aqueous solution and extracted with ethyl acetate (3 × 5 mL). The organic layers were combined, and then dried with anhydrous $MgSO_4$. After the solvent was removed by rotovapor, the product was purified by column chromatograph with a mixture of petroleum ether and ethyl acetate (volume ratio 5:1).

With 2 equiv of $H_2{}^{18}O$ as the isotope-labeling agent, the experimental procedure is the same as mentioned above.

C. Effect of Ligands on the Reaction

Table 1. Effect of Ligands on the Reaction [a]



Entry	Catalyst	Base	Ligand	Yield of **3a** (%)[b]
1	Cu_2O	*t*-BuOK	L1	92
2	Cu_2O	*t*-BuOK	L2	15
3	Cu_2O	*t*-BuOK	L3	53
4	Cu_2O	*t*-BuOK	L4	9
5	Cu_2O	*t*-BuOK	L5	<5
6	Cu_2O	*t*-BuOK	L6	65

L1: R1 = Me R2 = Me

L2: R1 = Ph R2 = Ph

L3: R1 = isopropyl R2 = isopropyl

L4: R1 = Me R2 = Me

L5: R1 = tert-butyl R2 = CF_3

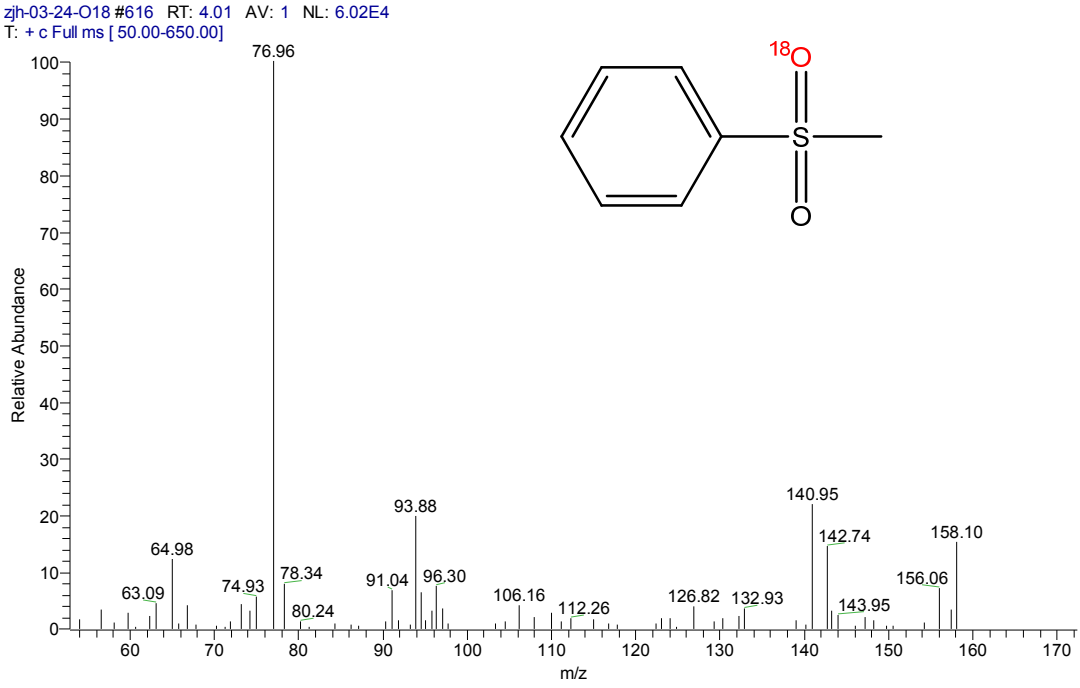
L6: R1 = H R2 = H

[a] Reaction conditions: PhI (0.25 mmol), DMSO (2.0 mL), ligand (1 equiv), *t*-BuOK (3 equiv), Cu_2O (0.025 mmol) at 100 °C for 20 h. [b] Isolated yield.

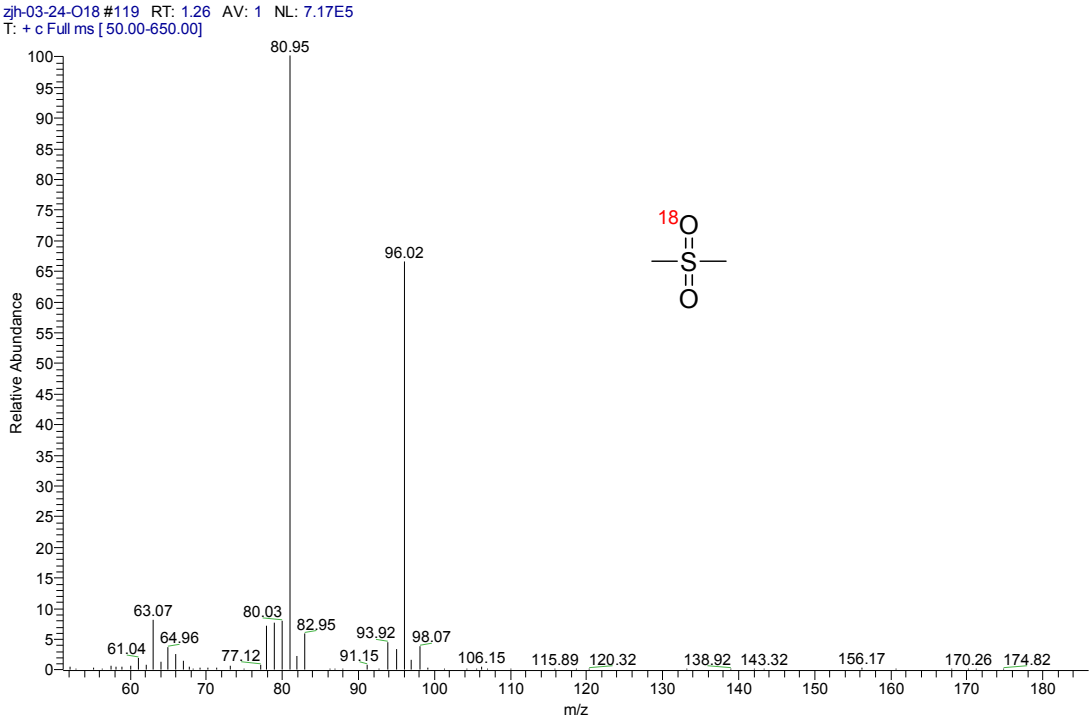
D. ^{18}O-labeling experiment with $^{18}O_2$

Iodobenzene **1a** (0.25 mmol), Cu_2O (3.6 mg, 0.025 mmol), *t*-BuOK (84 mg, 0.75 mmol), acetyl acetonate (20 mg, 0.25 mmol), and DMSO (2 mL) were first added into the dried Schlenk tube in turn. Then, the reaction was carried out at 100 °C with magnetic stirring under $^{18}O_2$ (balloon) for 20 h. After the reaction finished, the reaction mixture was diluted with the saturated NaCl aqueous solution and extracted with ethyl acetate. The organic layers were combined, and then dried with anhydrous $MgSO_4$. After the solvent was removed by rotovapor, the product was purified by column chromatograph with a mixture of petroleum ether and ethyl acetate (volume ratio 5:1).

The mass spectrum pattern of ^{18}O-labeled phenyl methyl sulfone (**3a**):

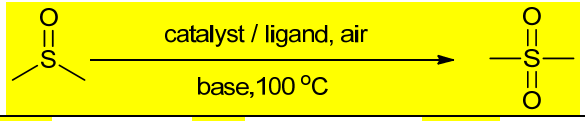


The mass spectrum pattern of ^{18}O-labeled dimethyl sulfone:



E. Extra mechanistic studies

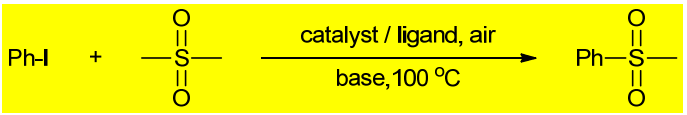
Table 2 Effect of Catalyst, Ligand and Base on the Oxdiation of DMSO to Dimethyl Sulfone [a]



Entry	Catalyst	Base	Ligand	Yield (%)[b]
1	Cu_2O	None	acetyl acetone	30
2	None	*t*-BuOK	acetyl acetone	NR
3	Cu_2O	*t*-BuOK	None	NR

[a] *Reaction conditions*: DMSO (2.0 mL), acetyl acetone (1 equiv), *t*-BuOK (3 equiv), Cu_2O (10 mol %) at 100 °C for 20 h. [b] Determined by GC.

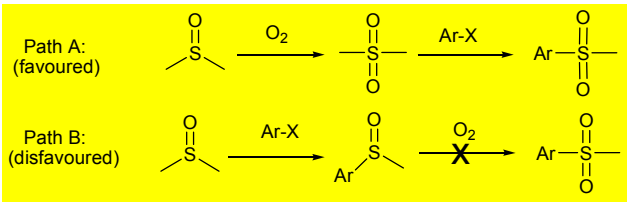
Table 3 Effect of Catalyst, Ligand and Base on the Coupling Reaction of PhI with Dimethyl Sulfone [a]



Entry	Catalyst	Base	Ligand	Yield of 3a (%)[b]
1	None	*t*-BuOK	acetyl acetone	NR
2	Cu_2O	None	acetyl acetone	NR
3	Cu_2O	*t*-BuOK	None	Trace
4	Cu_2O	*t*-BuOK	acetyl acetone	18

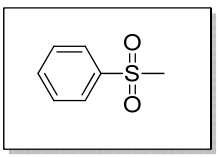
[a] *Reaction conditions*: nitroethane (2 mL) as the solvent, Ph-I (0.25 mmol), dimethyl sulfone (3 equiv), acetyl acetone (1 equiv), *t*-BuOK (3 equiv), Cu_2O (10 mol %) at 100 °C for 20 h. [b] Determined by GC.

Base on our experimental results, a possible reaction pathway was proposed in Scheme 1.



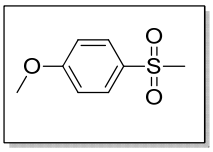
Scheme 1 A Plausible Reaction Pathway

F. Analytical Data for 3a-3p



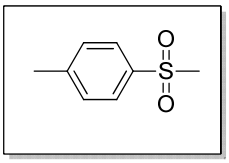
Methylsulfonylbenzene[1] (3a)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J*= 8.0 Hz, 2H), 7.65 (t, *J*= 8.0 Hz, 1H), 7.57 (t, *J*= 7.6 Hz, 2H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 133.7, 129.3, 127.3, 44.4; MS (EI) *m/z*: 77, 94, 141, 156; HRMS (*m/z*) calcd for $C_7H_8SO_2$: 156.0243, found 156.0245.



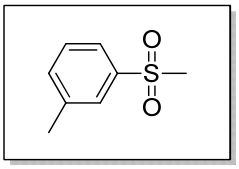
1-Methoxy-4-(methylsulfonyl)benzene[2] (3b)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J*= 8.8 Hz, 2H), 7.02 (d, *J*= 8.8 Hz, 2H), 3.88 (s, 3H), 3.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7, 132.3, 129.6, 114.5, 55.7, 44.9; MS (EI) *m/z*: 77, 91, 107, 123, 171, 186.



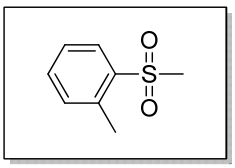
1-Methyl-4-(methylsulfonyl)benzene[3] (3c)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J*= 8.0 Hz, 2H), 7.34 (d, *J*= 8.0 Hz, 2H), 3.01(s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 137.6, 129.9, 127.3, 44.5, 21.5; MS (EI) *m/z*: 77, 91, 107, 155, 170.



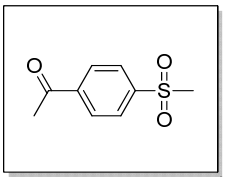
1-Methyl-3-(methylsulfonyl)benzene[4] (3d)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.51 (m, 2H), 7.45 (d, *J*= 5.2 Hz, 2H), 3.04(s, 3H), 2.45(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4, 139.7, 134.4, 129.2, 127.6, 124.4, 44.5, 21.3; MS (EI) *m/z*: 65, 91, 107, 155, 170.



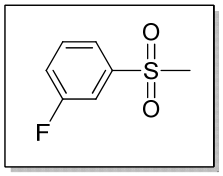
1-Methyl-2-(methylsulfonyl)benzene[5] (3e)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J*= 7.2 Hz, 1H), 7.51 (t, *J*= 6.8 Hz, 1H), 7.36 (q, *J*= 7.6 Hz, 2H), 3.07(s, 3H), 2.70(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 137.5, 133.6, 132.7, 129.2, 126.7, 43.6, 20.2; MS (EI) *m/z*: 39, 65, 91, 107, 155, 170.



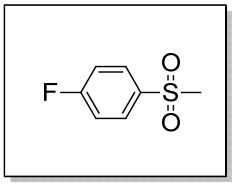
1-(4-(Methylsulfonyl)phenyl)ethanone[6] (3f)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10-8.13 (m, 2H), 8.04-8.06 (m, 2H), 3.08 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6, 144.2, 140.9, 129.1, 127.8, 44.3, 26.9; MS (EI) *m/z*: 43, 77, 91, 121, 152, 183, 198.



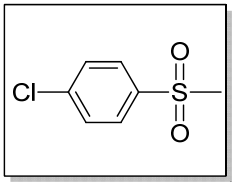
1-Fluoro-3-(methylsulfonyl)benzene[7] (3g)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J*= 8.0 Hz, 1H), 7.64-7.47 (m, 1H), 7.55-7.60 (m, 1H), 7.34-7.38 (m, 1H), 3.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7, 161.2, 142.6, 142.5, 131.3, 131.3, 123.2, 123.2, 121.1, 120.9, 114.9, 114.7, 44.3; MS (EI) *m/z*: 75, 95, 112, 159, 174.



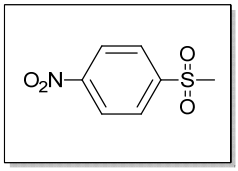
1-Fluoro-2-(methylsulfonyl)benzene[4] (3h)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.98 (m, 2H), 7.23(d, *J*= 8.4 Hz, 2H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 164.4, 136.6, 136.0, 130.3, 130.2, 116.7, 116.5, 44.6; MS (EI) *m/z*: 75, 95, 111, 159, 174.



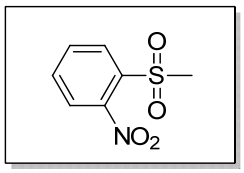
1-Chloro-4-(methylsulfonyl)benzene[6] (3i)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J*= 8.4 Hz, 2H), 7.47 (d, *J*= 8.4 Hz, 2H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 139.0, 129.7, 128.9, 44.5; MS (EI) *m/z*: 50, 76, 111, 127, 175, 190.



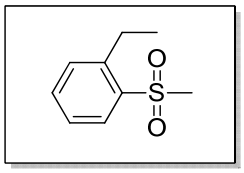
1-(Methylsulfonyl)-4-nitrobenzene[6] (3j)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, J= 8.8 Hz, 2H), 8.16 (d, J= 8.8 Hz, 2H), 3.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9, 145.9, 129.0, 124.6, 44.3; MS (EI) *m/z*: 50, 63, 76, 92, 109, 122, 139, 186, 201.



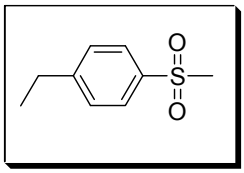
1-(Methylsulfonyl)-2-nitrobenzene[8] (3k)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.82 (d, J= 8.4 Hz, 3H), 3.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 134.9, 134.2, 132.8, 131.4, 124.9, 45.1; MS (EI) *m/z*: 50, 63, 79, 109, 139, 155, 186, 201.



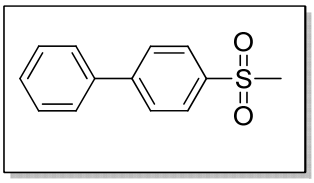
1-Ethyl-2-(methylsulfonyl)benzene (3l)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J= 8.0 Hz, 1H), 7.54 (t, J= 7.2 Hz, 1H), 7.32-7.50 (m, 2H), 3.03-3.08 (m, 5H), 1.31(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 138.2, 133.7, 130.9, 129.2, 126.4, 44.5, 25.9, 15.8; MS (EI) *m/z*: 78, 91, 104, 121, 151, 169, 184.



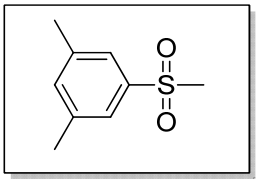
1-Ethyl-4-(methylsulfonyl)benzene[9] (3m)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J= 8.4 Hz, 2H), 7.38 (d, J= 8.4 Hz, 2H), 3.03 (s, 3H), 2.74 (q, J= 7.6 Hz, 2H), 1.27 (t, J= 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 137.9, 128.8, 127.5, 44.6, 28.9, 15.1; MS (EI) *m/z*: 79, 91, 105, 121, 169, 184.



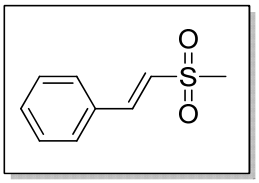
4-(Methylsulfonyl)-1,1'-biphenyl[10] (3n)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J= 8.4 Hz, 2H), 7.77 (d, J= 8.4 Hz, 2H), 7.61 (d, J= 8.0 Hz, 2H), 7.43-7.51 (m, 3H), 3.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7, 139.1, 129.1, 128.6, 127.9, 127.9, 127.3, 44.6; MS (EI) m/z: 63, 77, 115, 141, 152, 169, 217, 232.



1,3-Dimethyl-5-(methylsulfonyl)benzene[6] (3o)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (s, 2H), 7.26 (s, 1H), 3.03 (s, 3H), 2.40 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 139.4, 135.2, 124.7, 44.4, 21.1; MS (EI) *m/z*: 39, 77, 105, 121, 169, 184.



(*E*)-(2-(Methylsulfonyl)vinyl)benzene [11] (3p)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J=15.6 Hz, 1H), 7.51 (d, J= 6.4 Hz, 2H), 7.40-7.43 (m, 3H), 6.92 (d, J=15.6 Hz, 1H), 3.03(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.0, 132.0, 131.4, 129.1, 128.5, 126.1, 43.2; MS (EI) *m/z*: 77, 91, 102, 119, 149, 167, 182.

G. Reference

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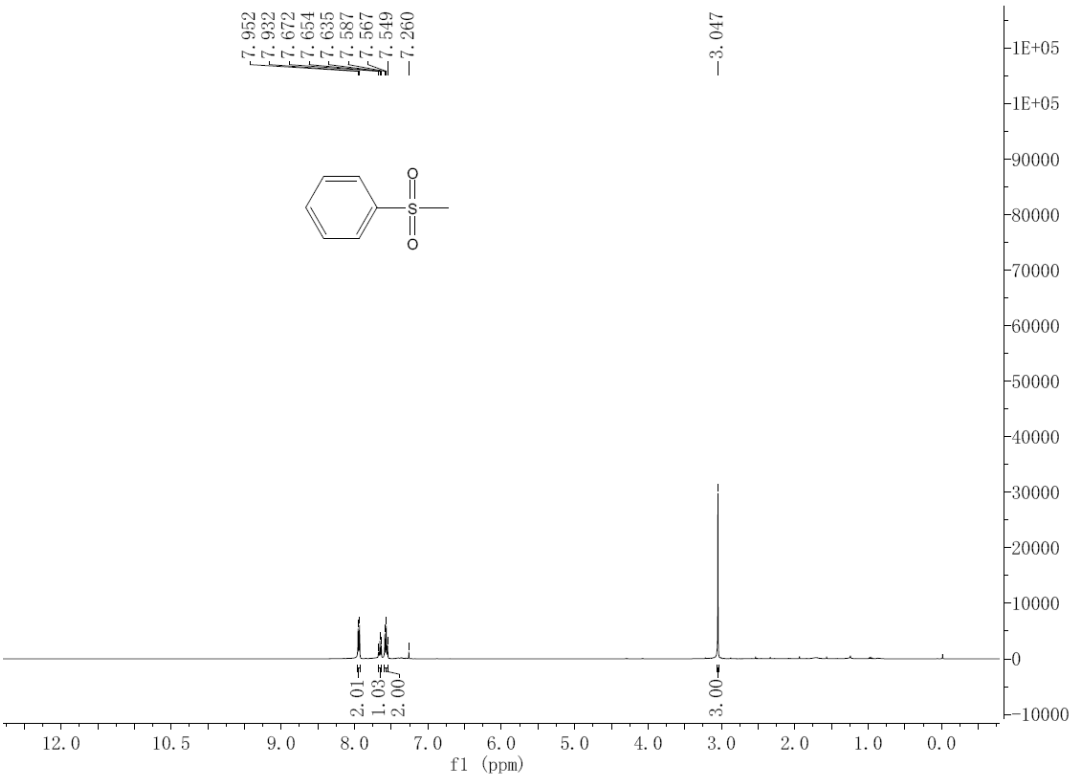
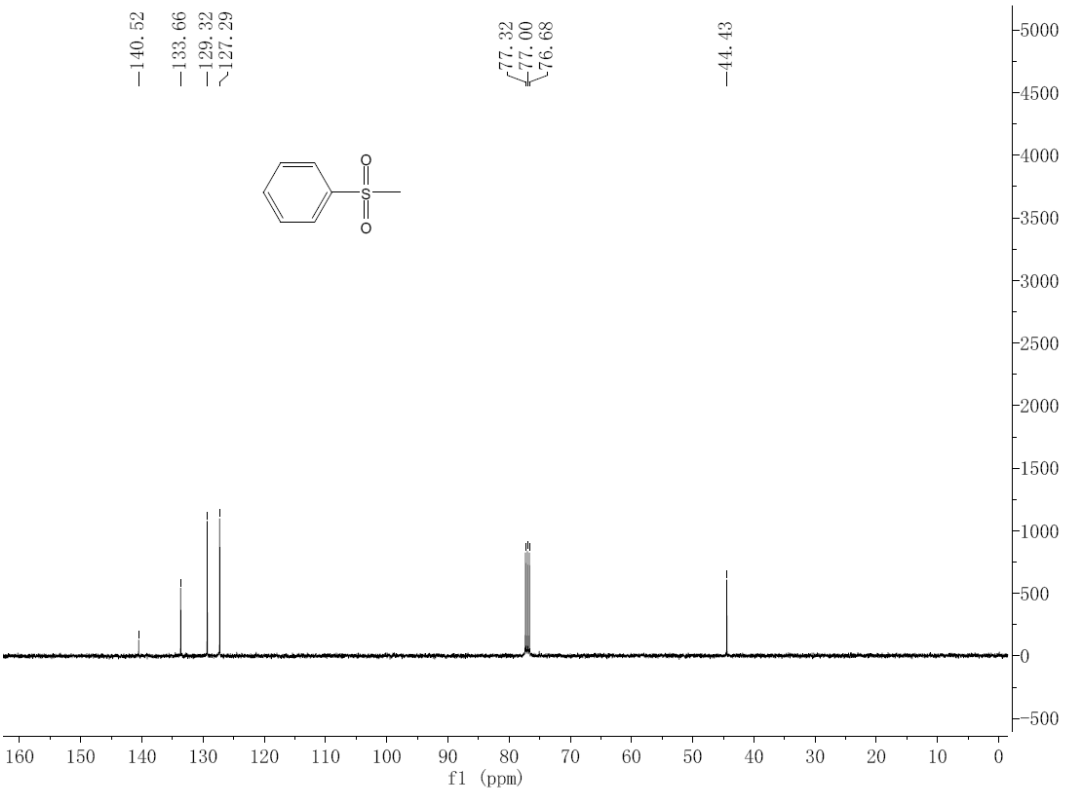
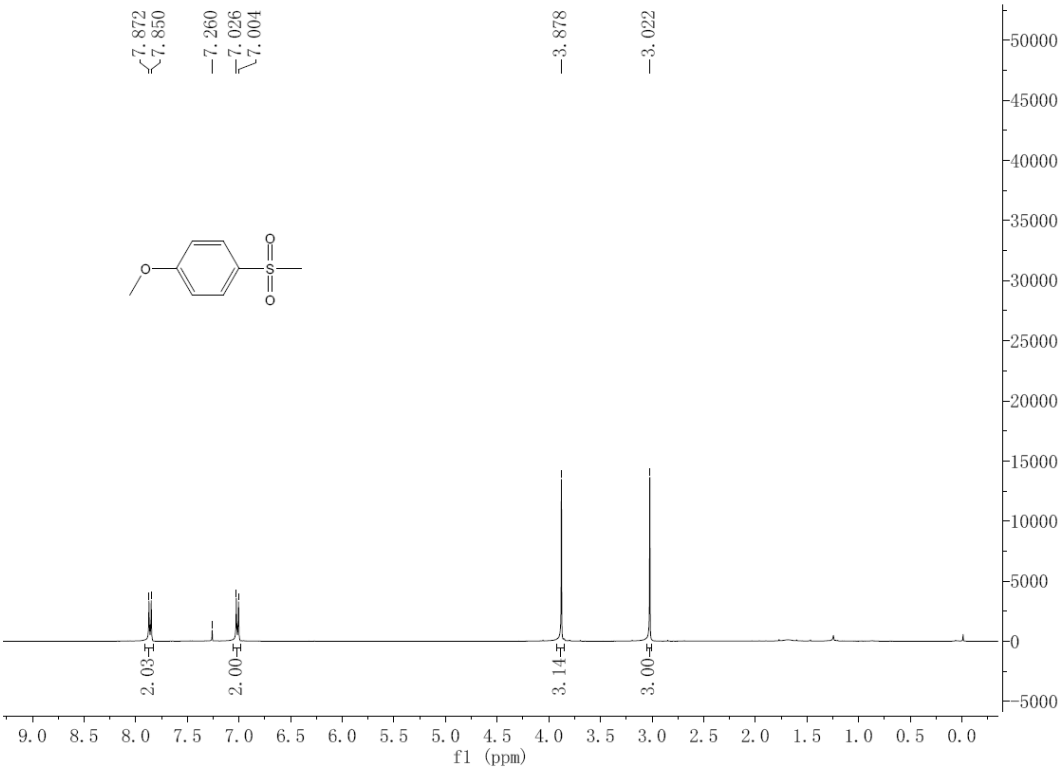
H. NMR Spectra



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7.026
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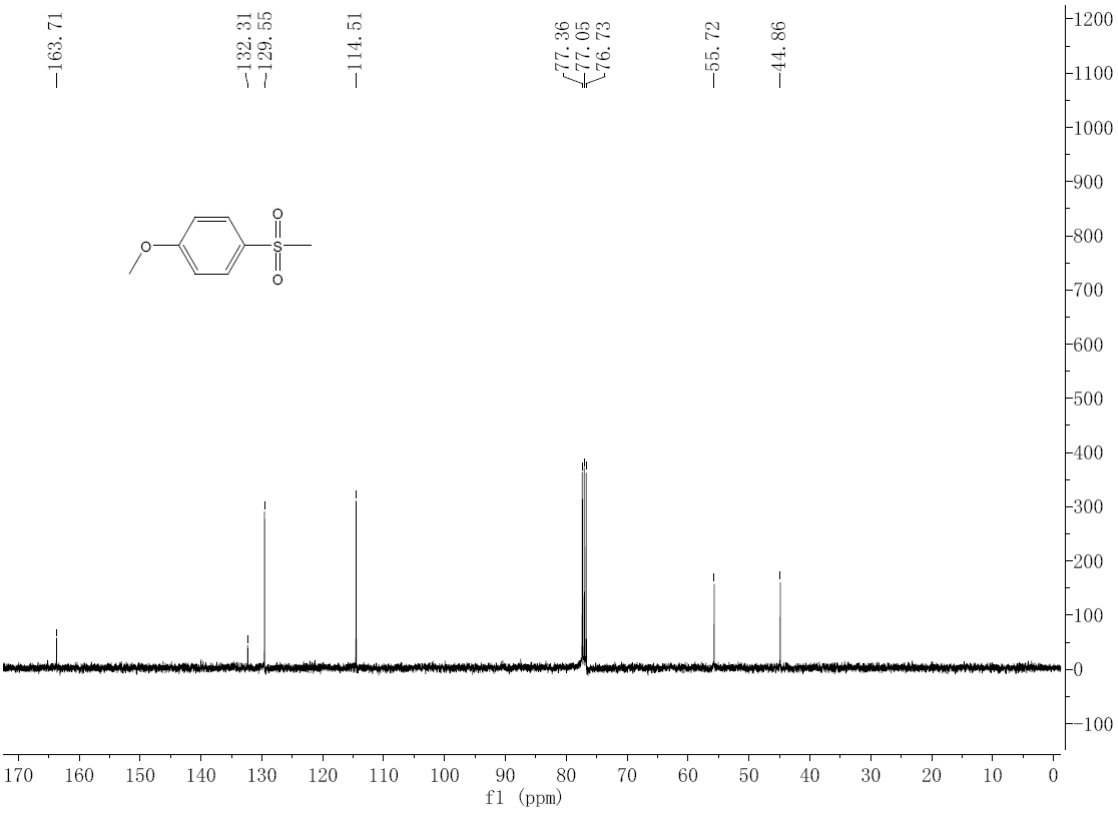
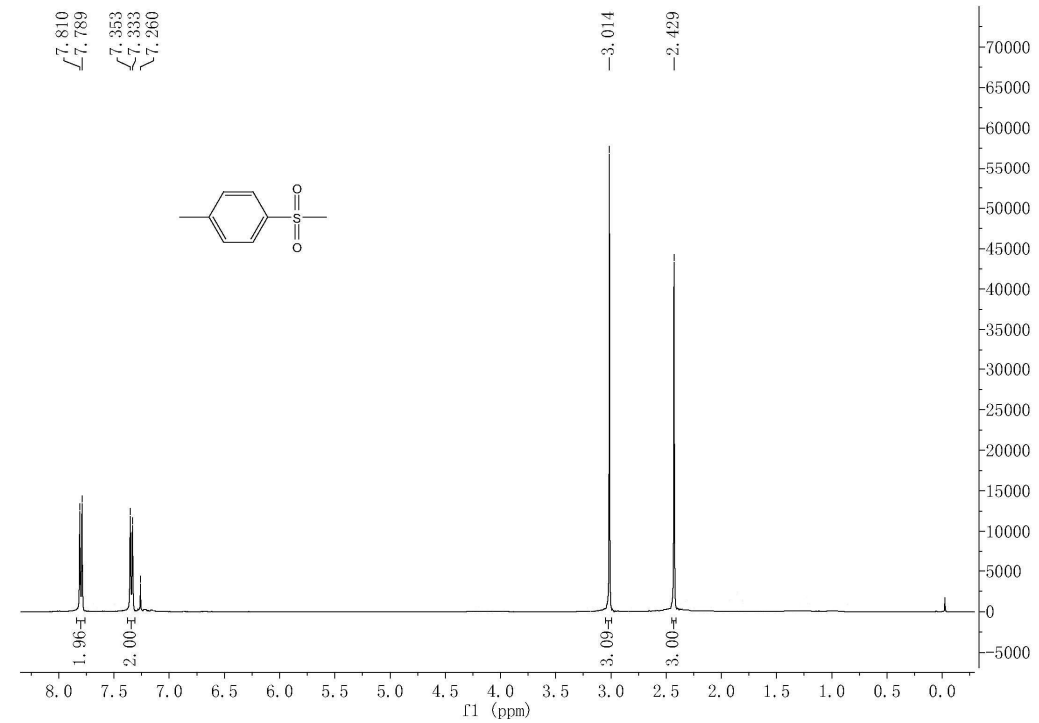
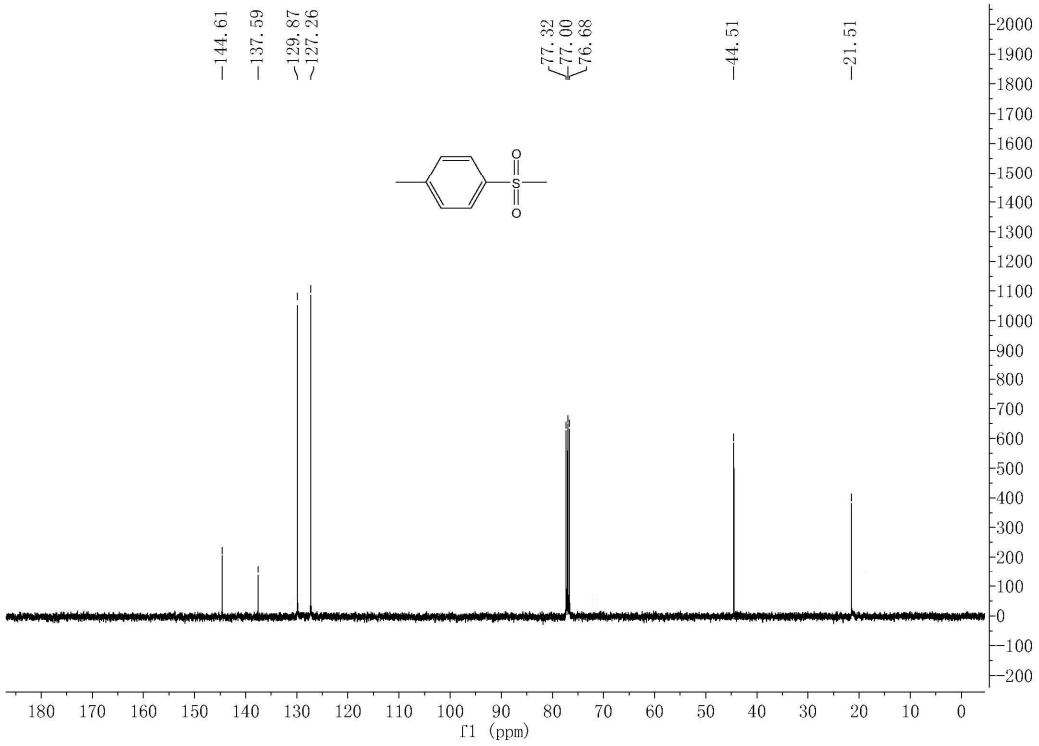
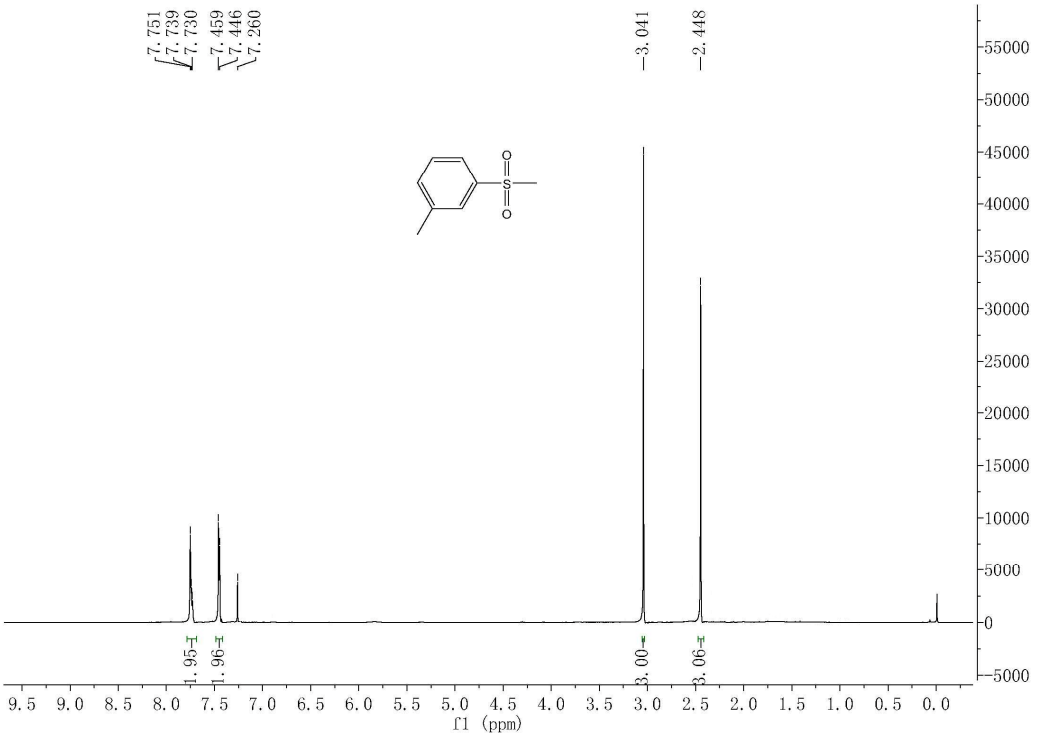
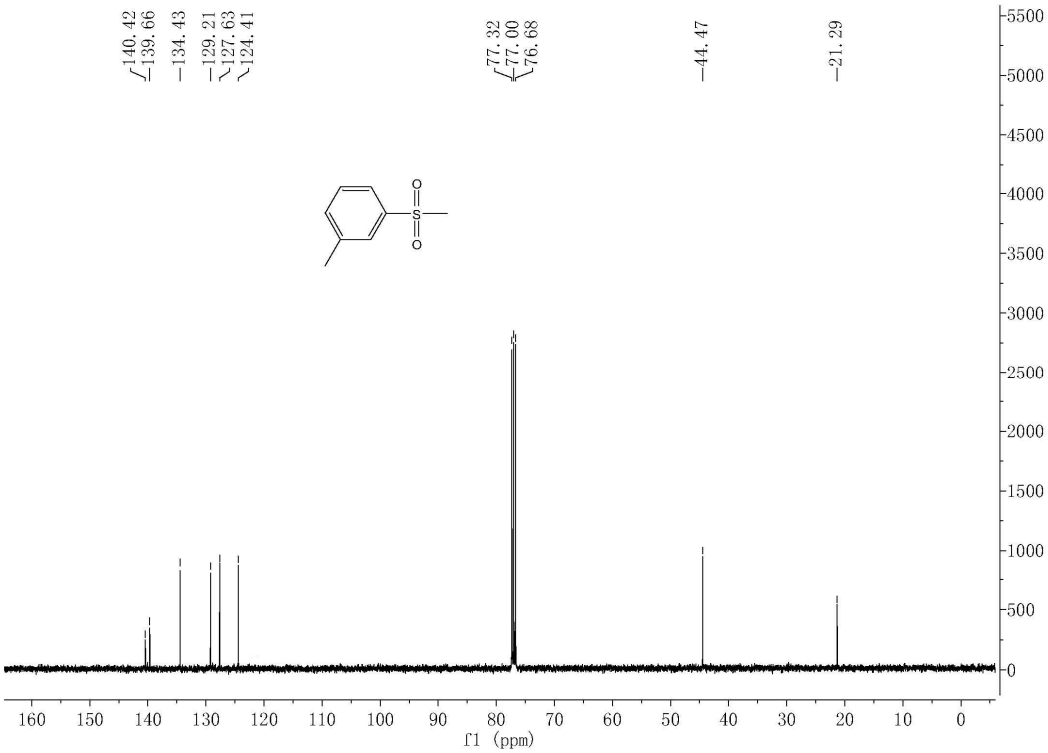
2.03
2.00
3.14
3.00
f1 (ppm)

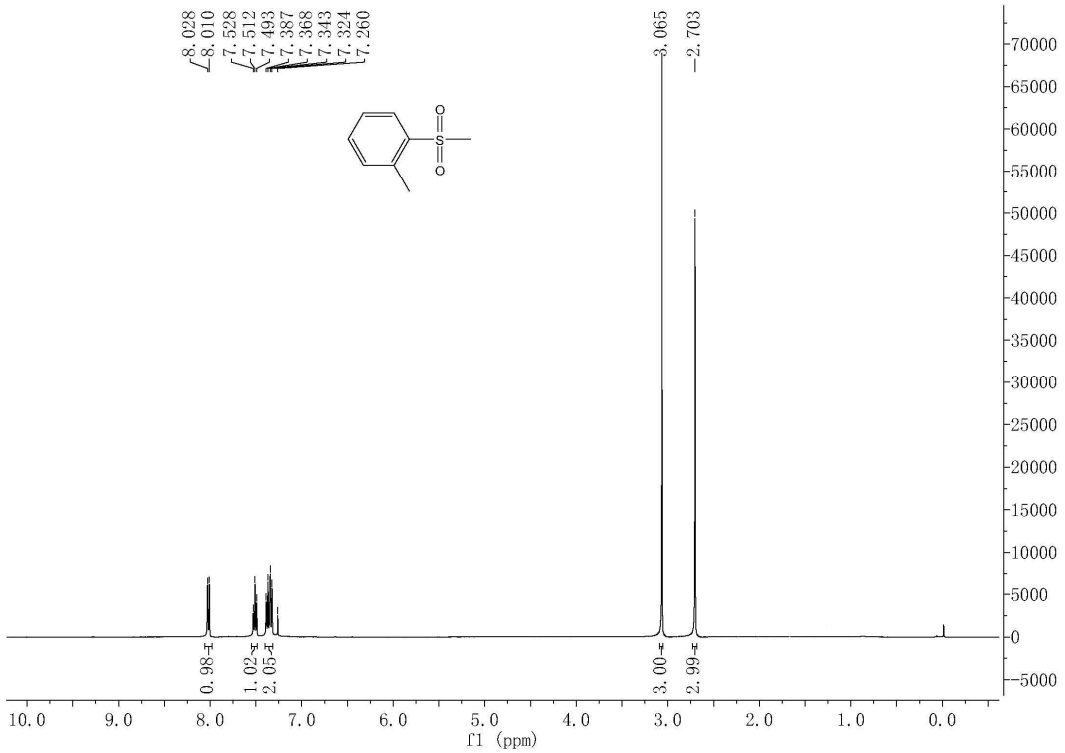

163.71
132.31
129.55
114.51
77.36
77.05
76.73
55.72
44.86
f1 (ppm)

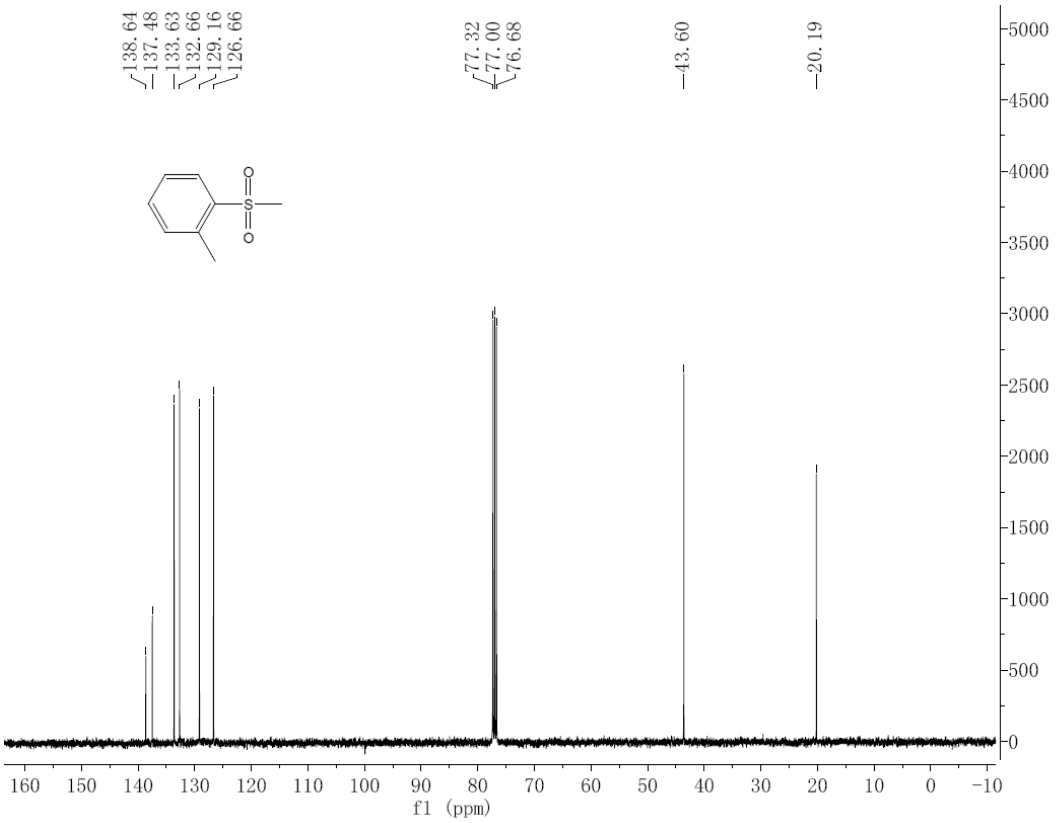

7.810
7.789
7.353
7.333
7.260
3.014
2.429
1.96
2.00
3.09
3.00
f1 (ppm)

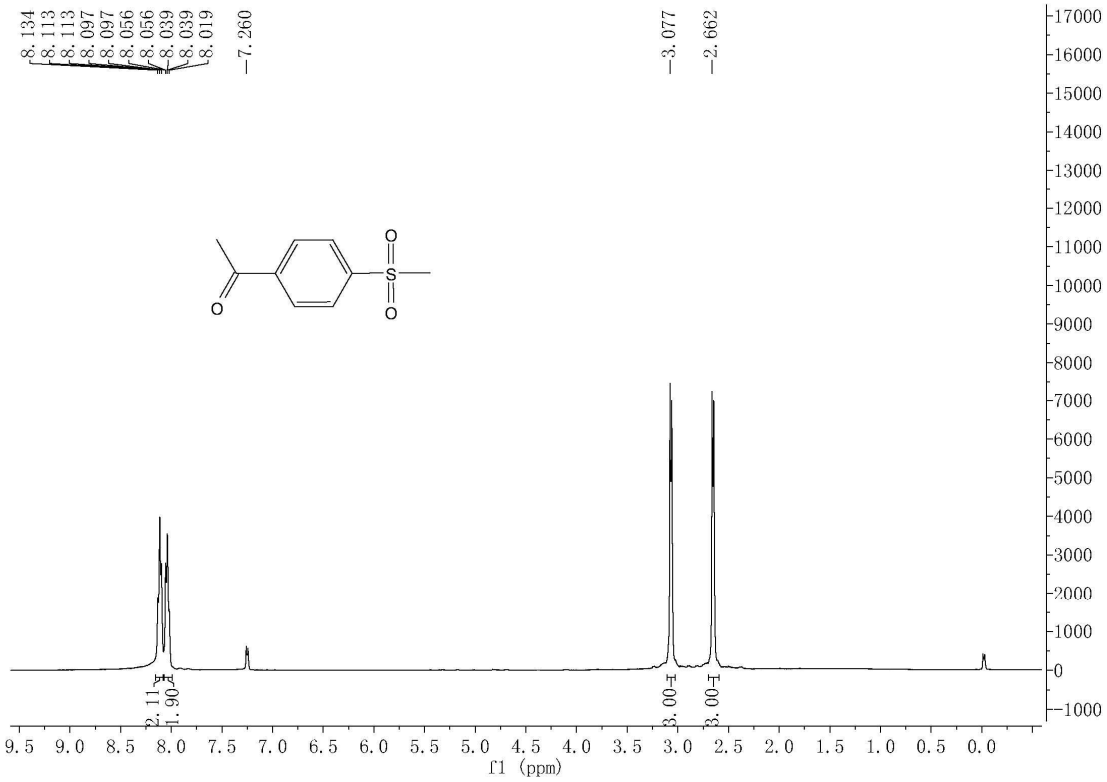

144.61
137.59
129.87
127.26
77.32
77.00
76.68
44.51
21.51
f1 (ppm)

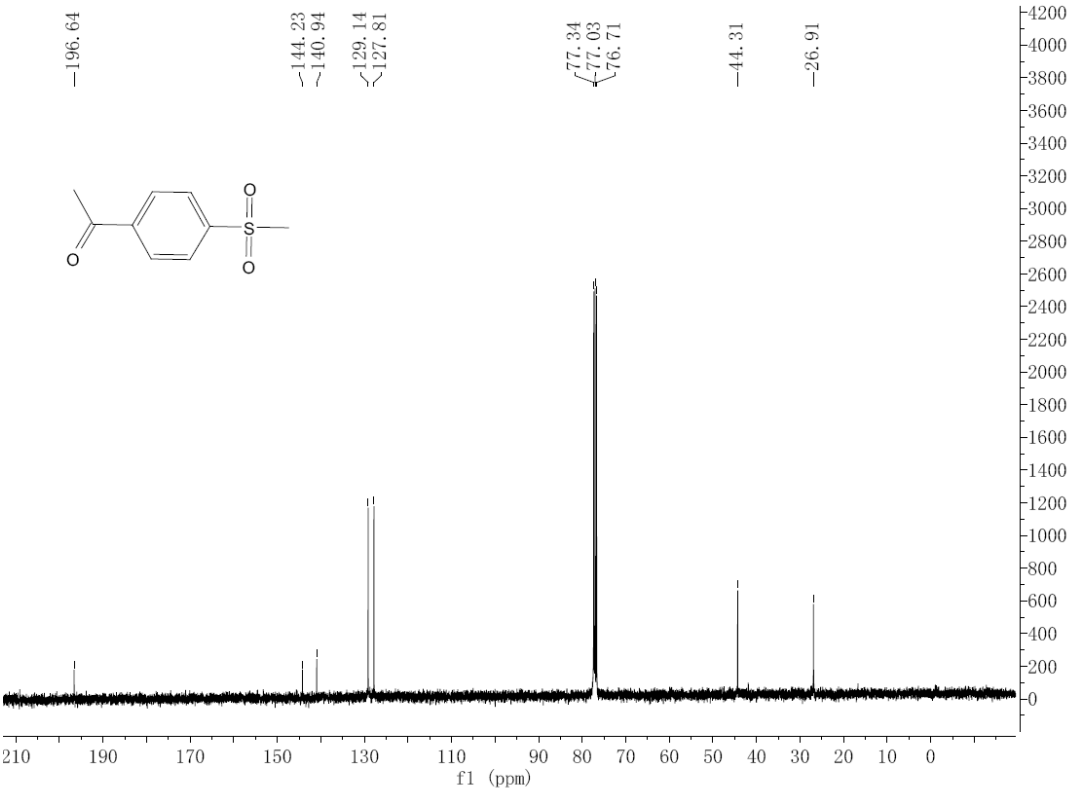

7.751
7.739
7.730
7.459
7.446
7.260
3.041
2.448
1.95
1.96
3.00
3.06
f1 (ppm)

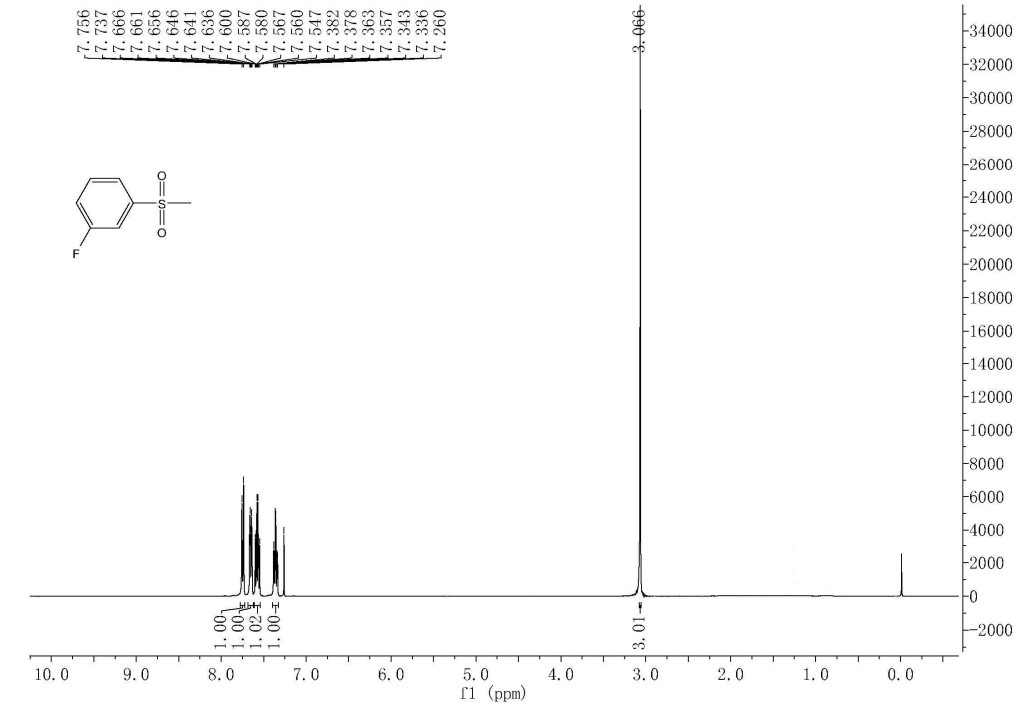

140.42
139.66
134.43
129.21
127.63
124.41
77.32
77.00
76.68
44.47
21.29
f1 (ppm)


8.028
8.010
7.528
7.512
7.493
7.387
7.368
7.343
7.324
7.260
3.065
2.703
0.98
1.02
2.05
3.00
2.99
f1 (ppm)


138.64
137.48
133.63
132.66
129.16
126.66
77.32
77.00
76.68
43.60
20.19
f1 (ppm)


8.134
8.113
8.113
8.097
8.097
8.056
8.056
8.039
8.039
8.019
7.260
3.077
2.662
2.11
1.90
3.00
3.00
f1 (ppm)


196.64
144.23
140.94
129.14
127.81
77.34
77.03
76.71
44.31
26.91
f1 (ppm)


7.756
7.737
7.666
7.661
7.656
7.646
7.641
7.636
7.600
7.587
7.580
7.567
7.560
7.547
7.382
7.378
7.363
7.357
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7.336
7.260
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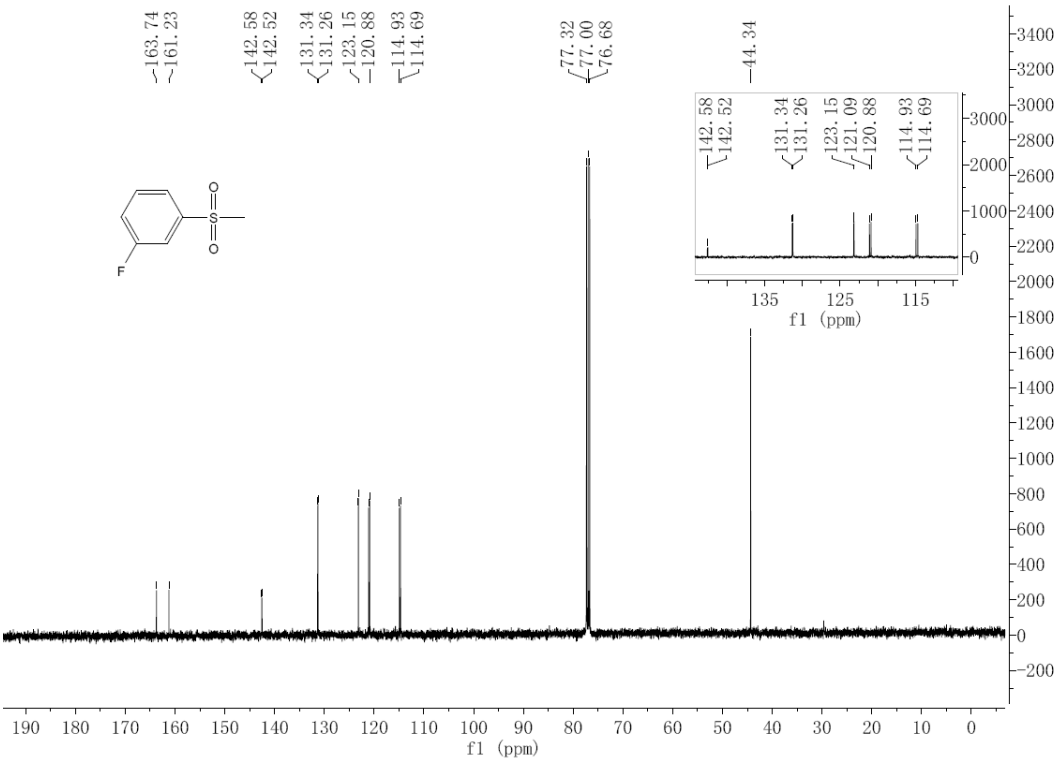
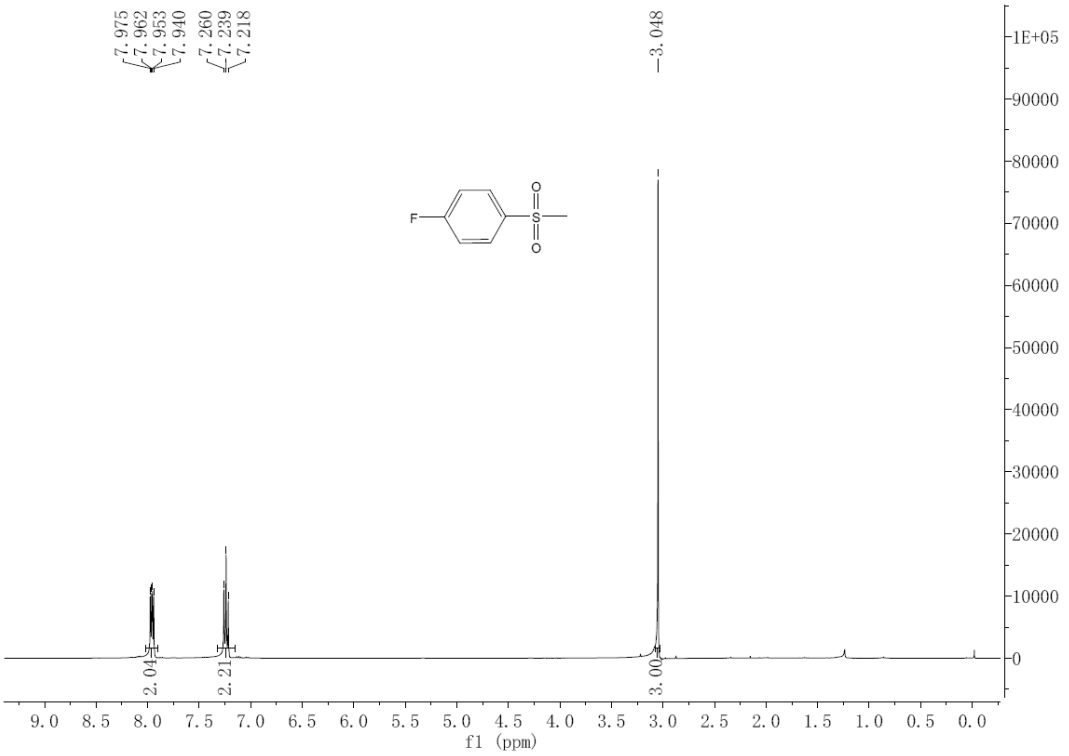
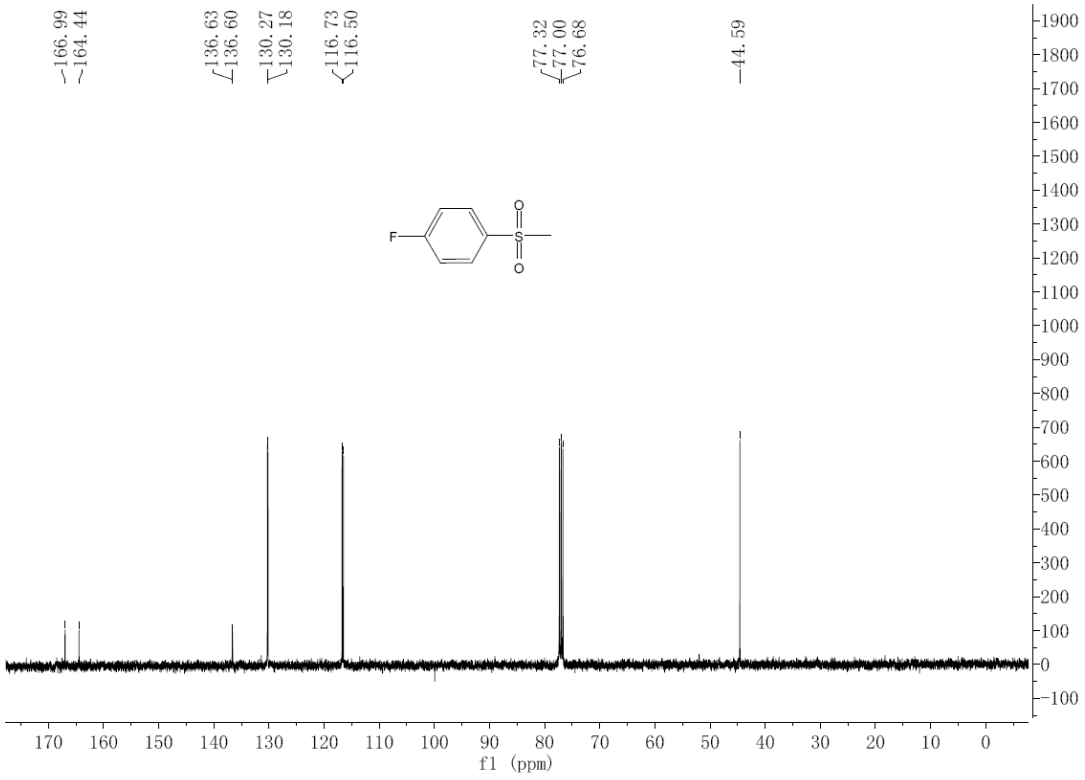
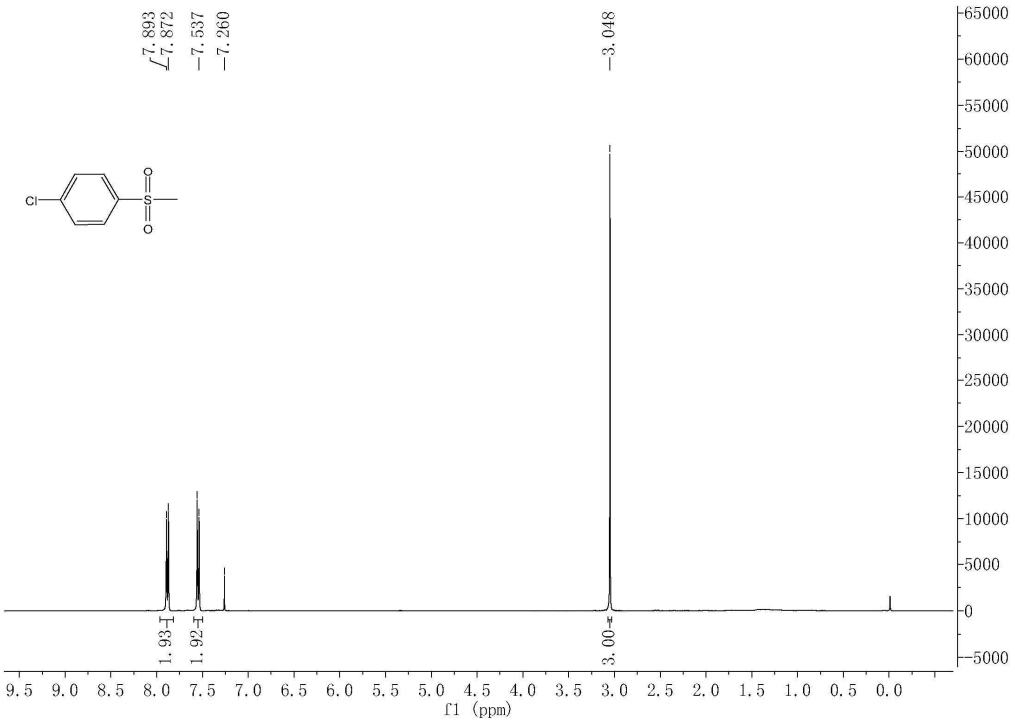
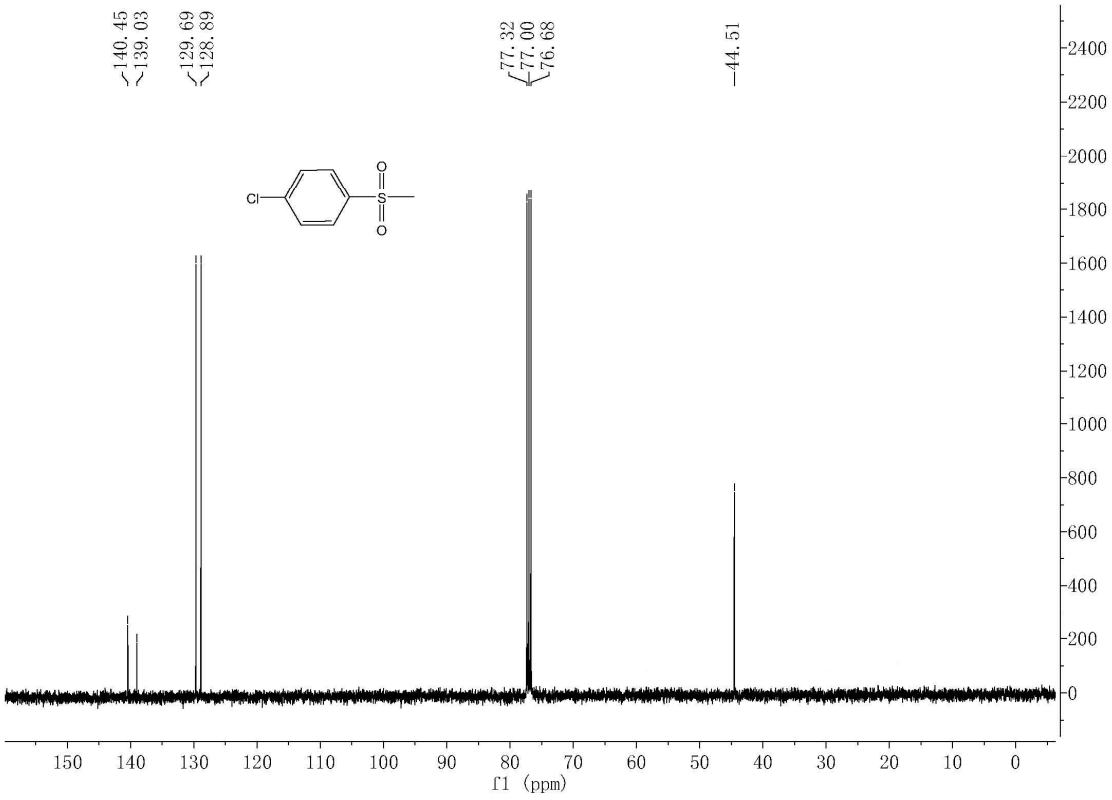
1.00
1.02
1.00
3.01
f1 (ppm)

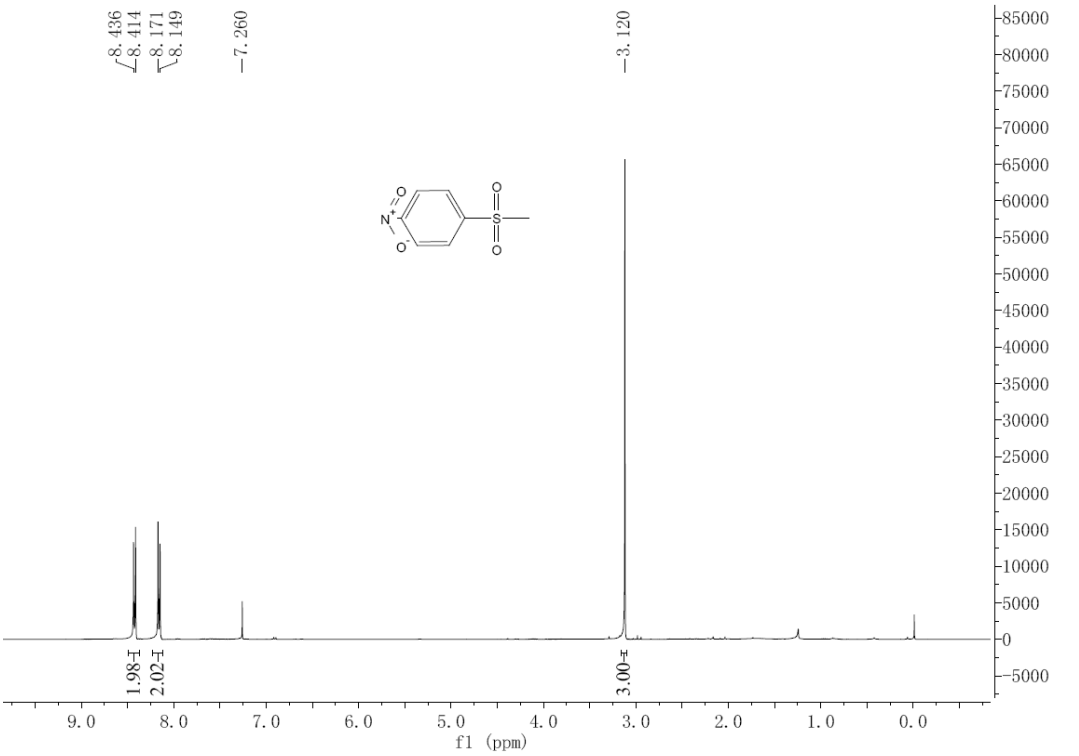

163.74
161.23
142.58
142.52
131.34
131.26
123.15
120.88
114.93
114.69
77.32
77.00
76.68
44.34
f1 (ppm)

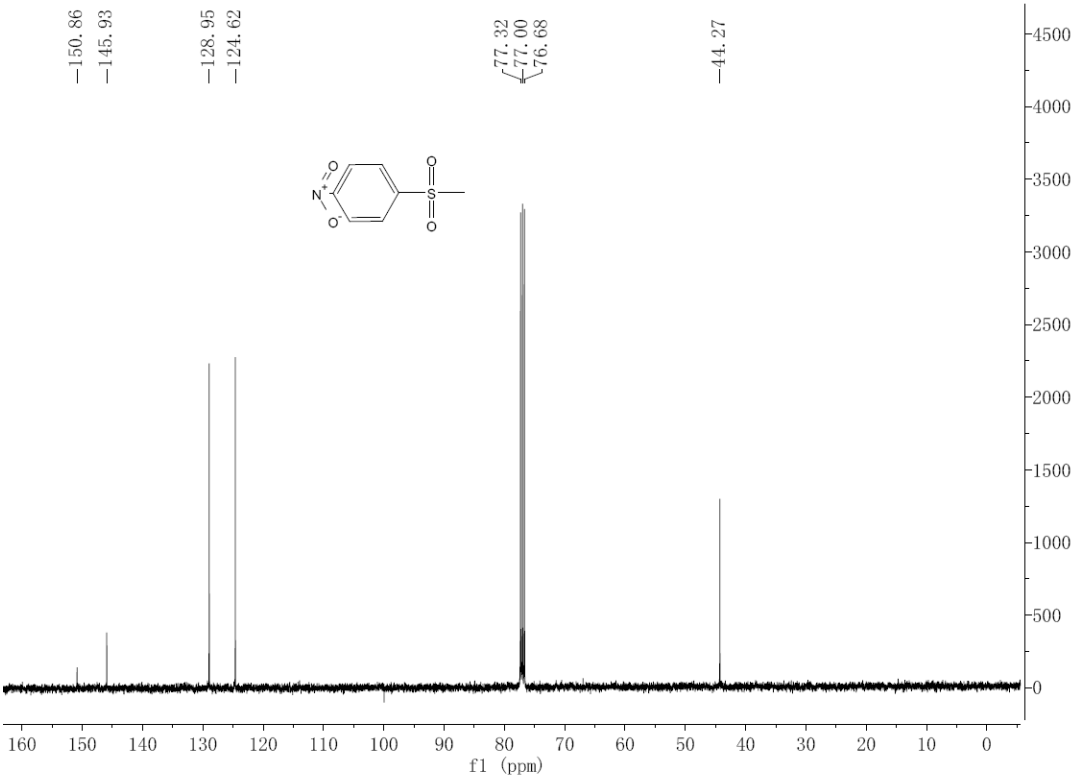

7.975
7.962
7.953
7.940
7.260
7.239
7.218
3.048
F
O
S
O
2.04
2.21
3.00
f1 (ppm)

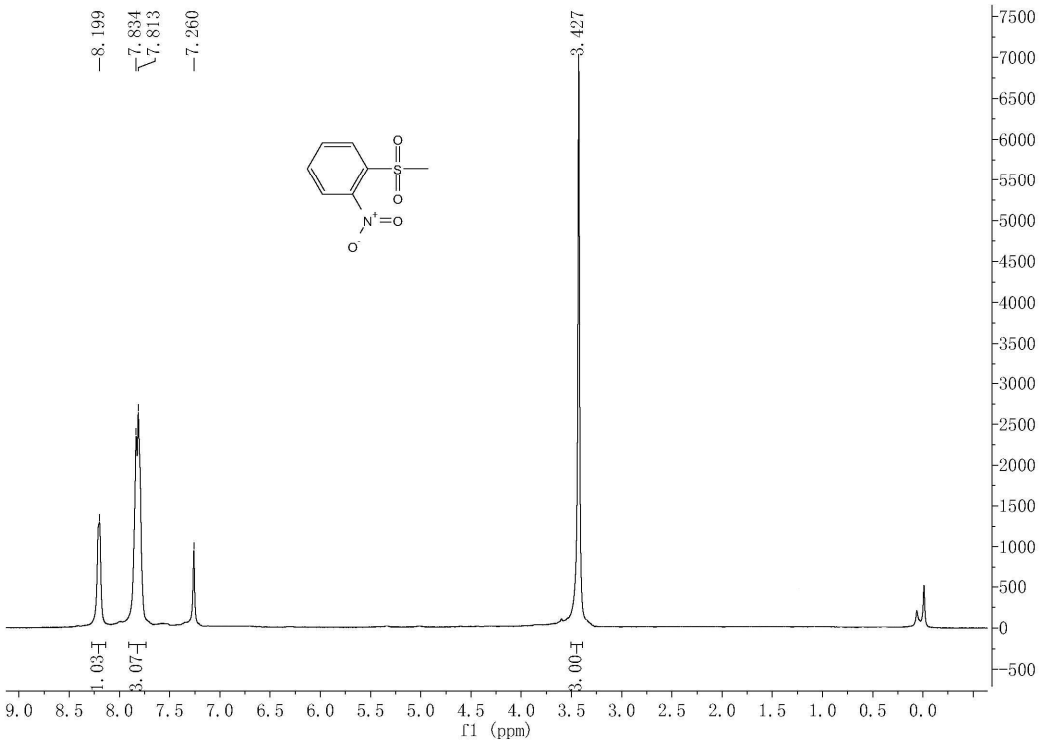

166.99
164.44
136.63
136.60
130.27
130.18
116.73
116.50
77.32
77.00
76.68
44.59
F
O
S
O
f1 (ppm)

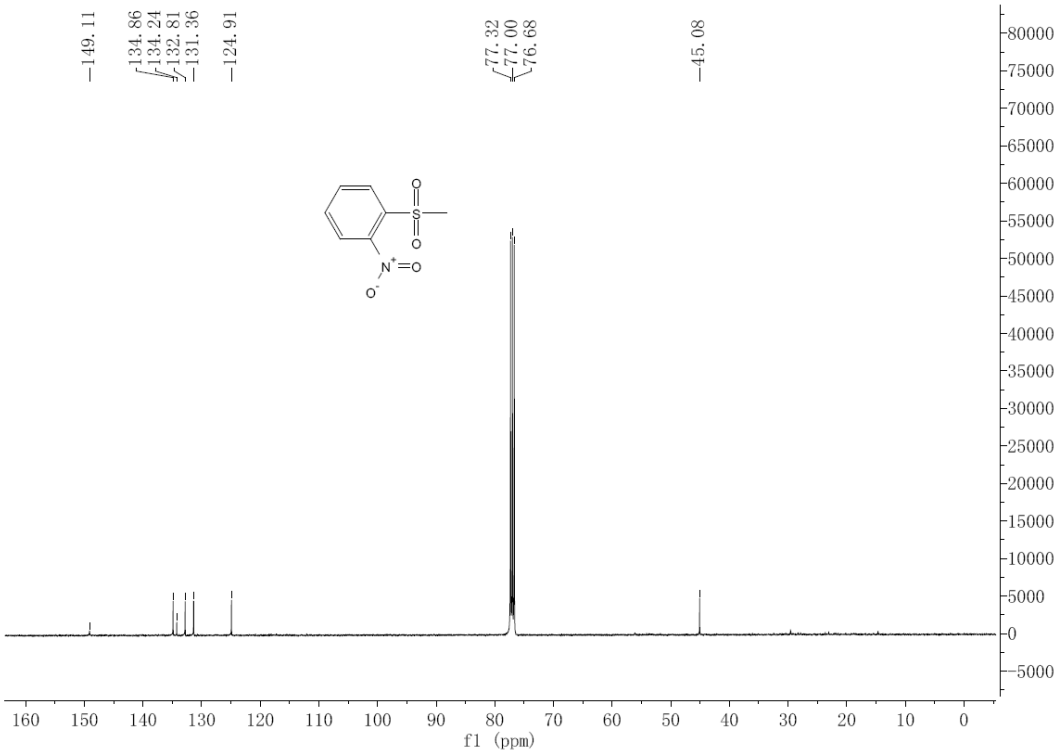

7.893
7.872
7.537
7.260
3.048
Cl
O
S
O
1.93
1.92
3.00
f1 (ppm)

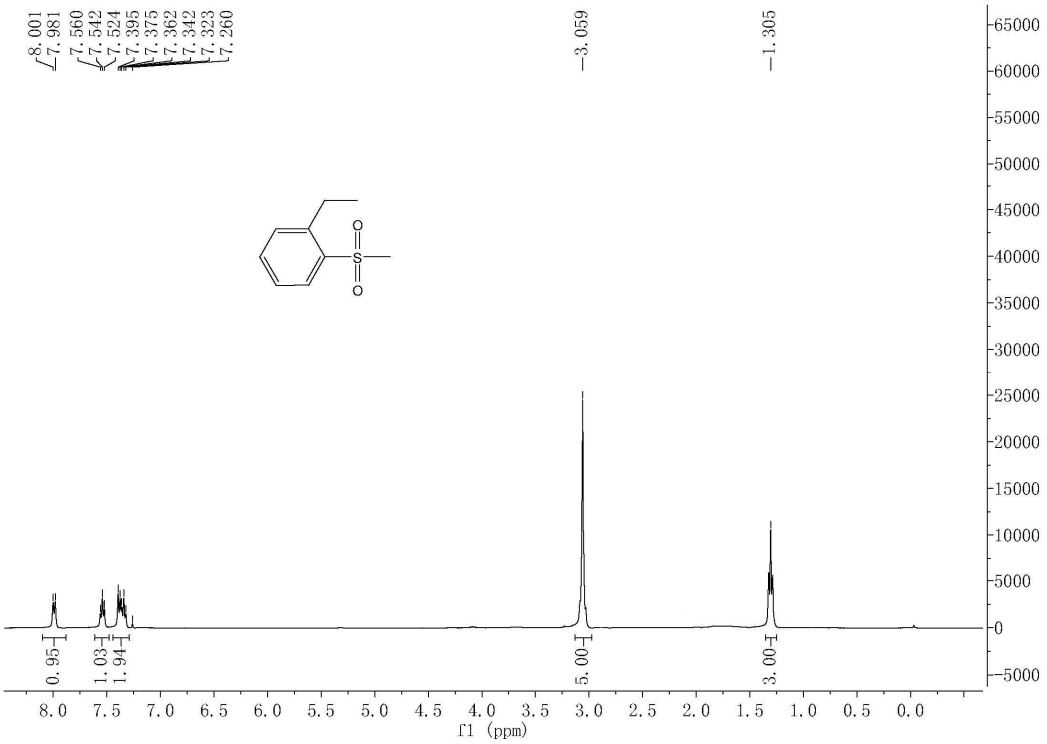

140.45
139.03
129.69
128.89
77.32
77.00
76.68
44.51
Cl
O
S
O
f1 (ppm)

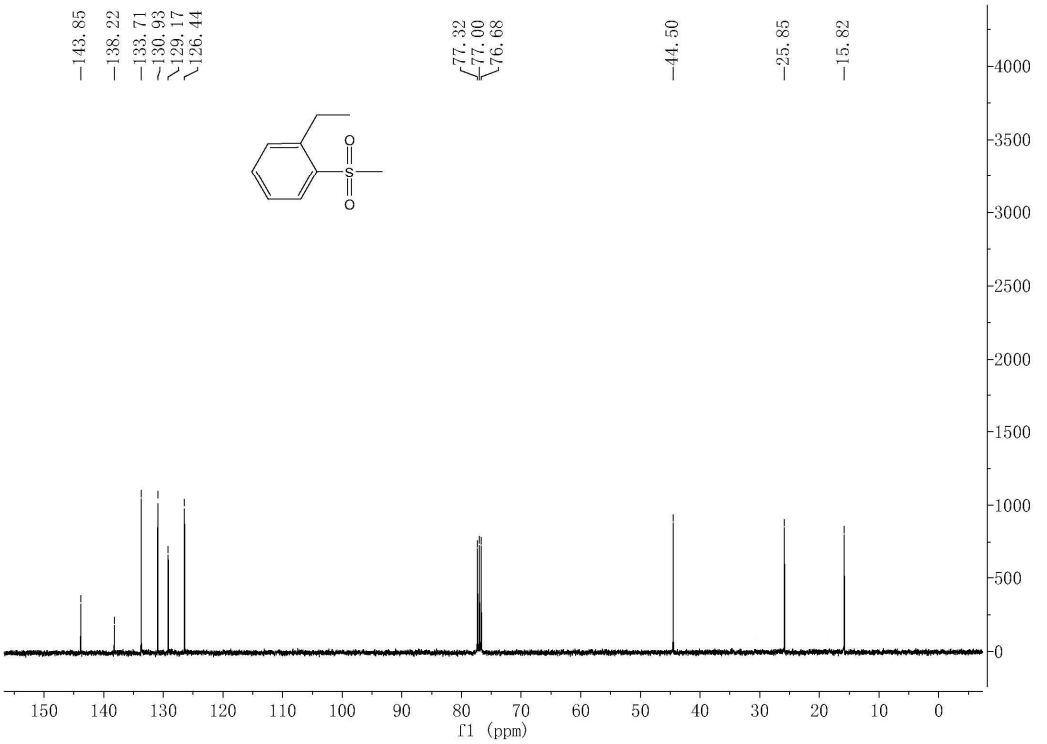

8.436
8.414
8.171
8.149
7.260
3.120
1.98
2.02
3.00
f1 (ppm)

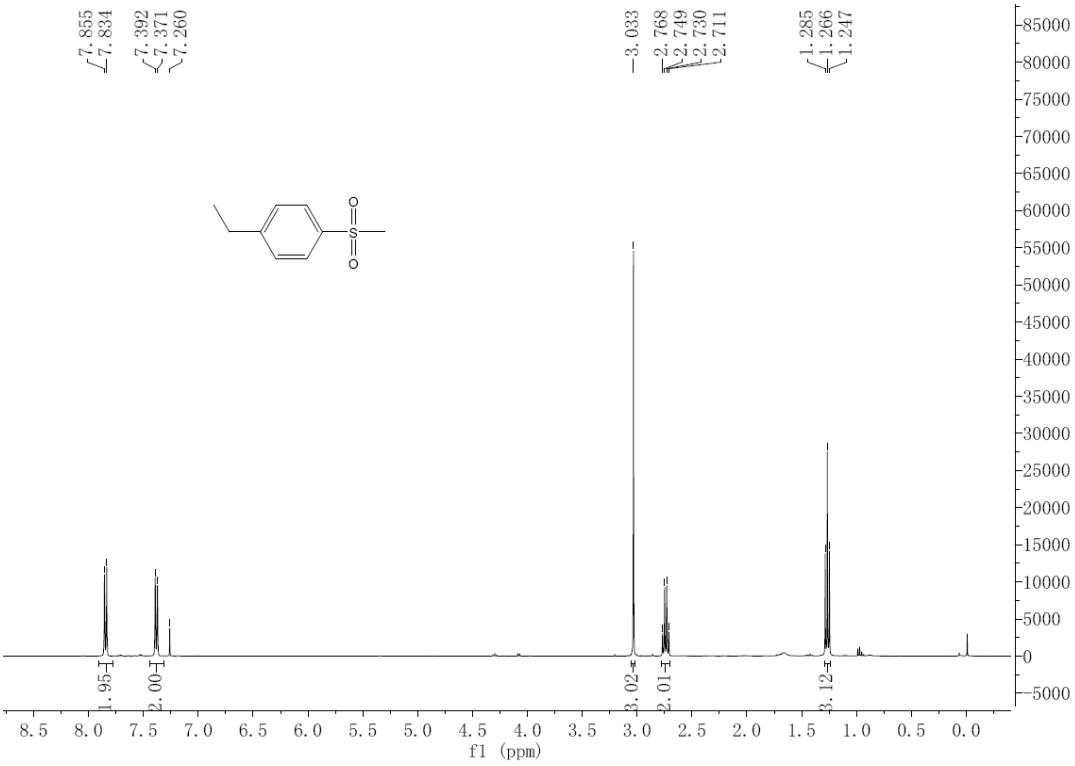

150.86
145.93
128.95
124.62
77.32
77.00
76.68
44.27
f1 (ppm)

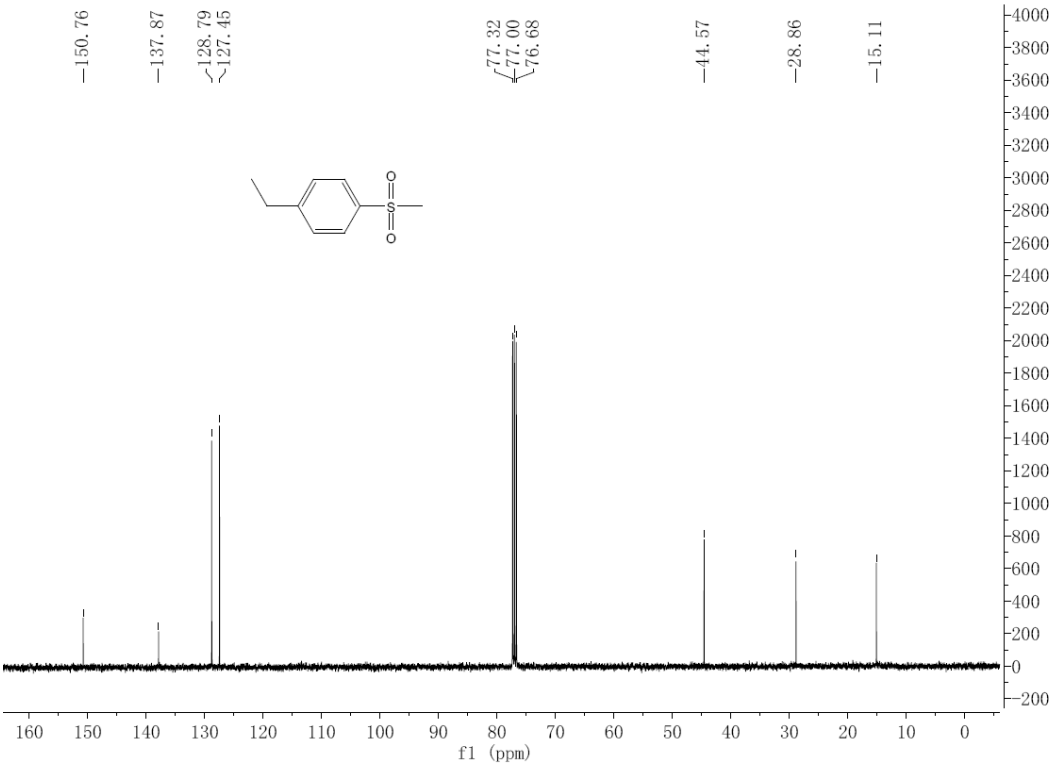

8.199
7.834
7.813
7.260
3.427
1.03
3.07
3.00
f1 (ppm)


149.11
134.86
134.24
132.81
131.36
124.91
77.32
77.00
76.68
45.08
f1 (ppm)


8.001
7.981
7.560
7.542
7.524
7.395
7.375
7.362
7.342
7.323
7.260
3.059
1.305
0.95
1.03
1.94
5.00
3.00
f1 (ppm)


143.85
138.22
133.71
130.93
129.17
126.44
77.32
77.00
76.68
44.50
25.85
15.82
f1 (ppm)


7.855
7.834
7.392
7.371
7.260
3.033
2.768
2.749
2.730
2.711
1.285
1.266
1.247
1.95
2.00
3.02
2.01
3.12
f1 (ppm)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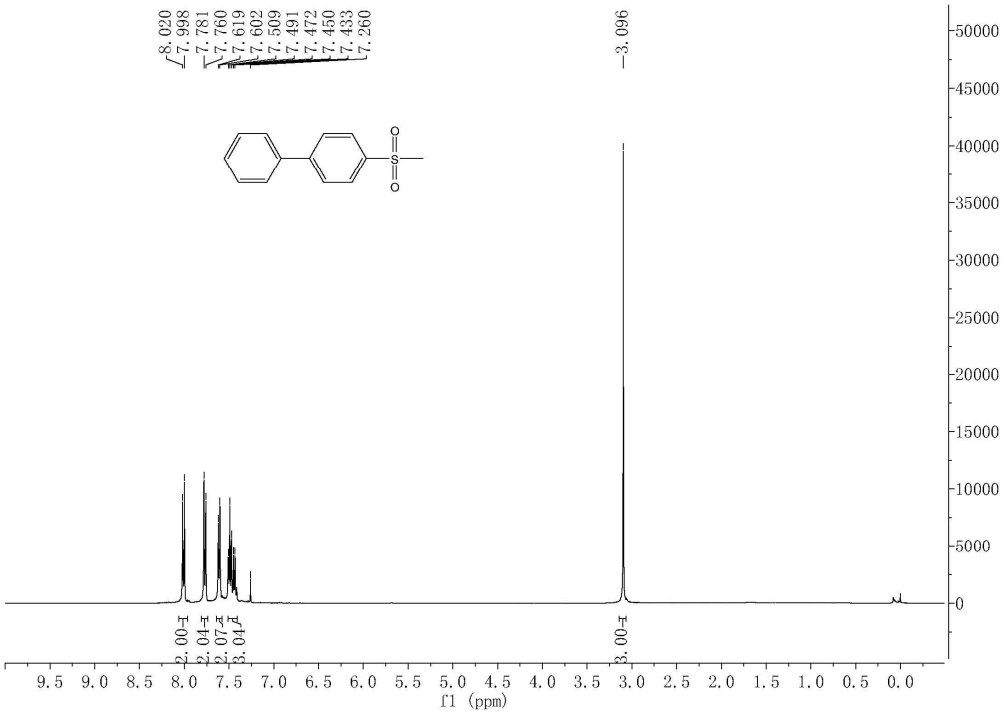
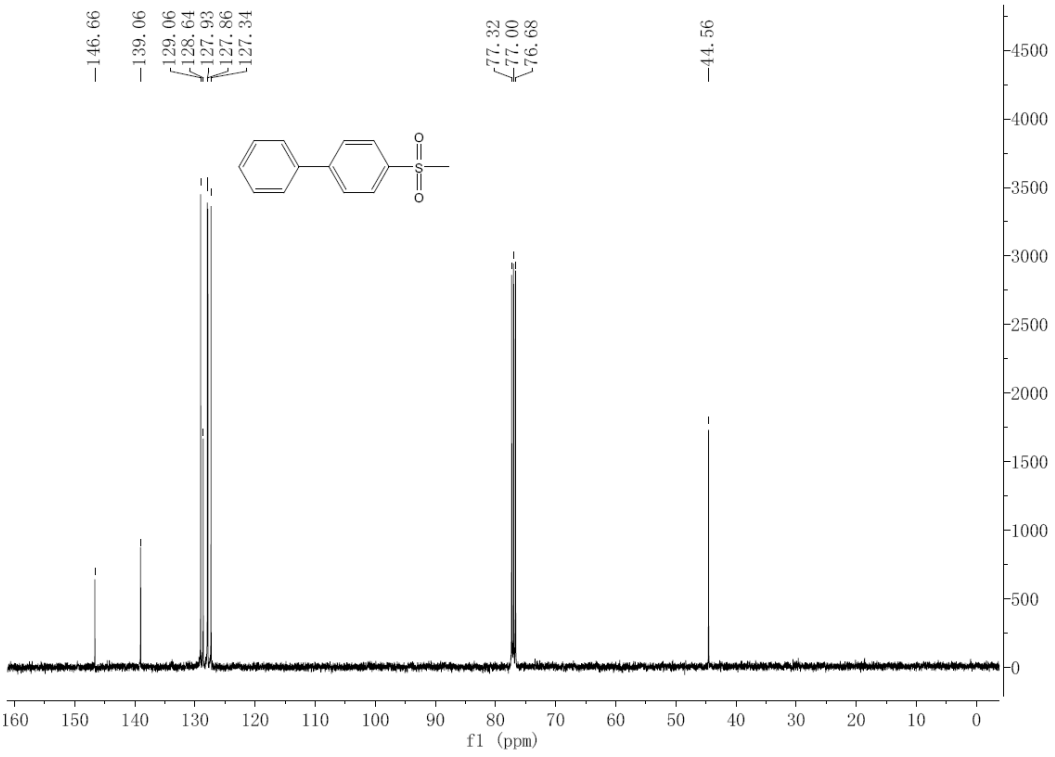
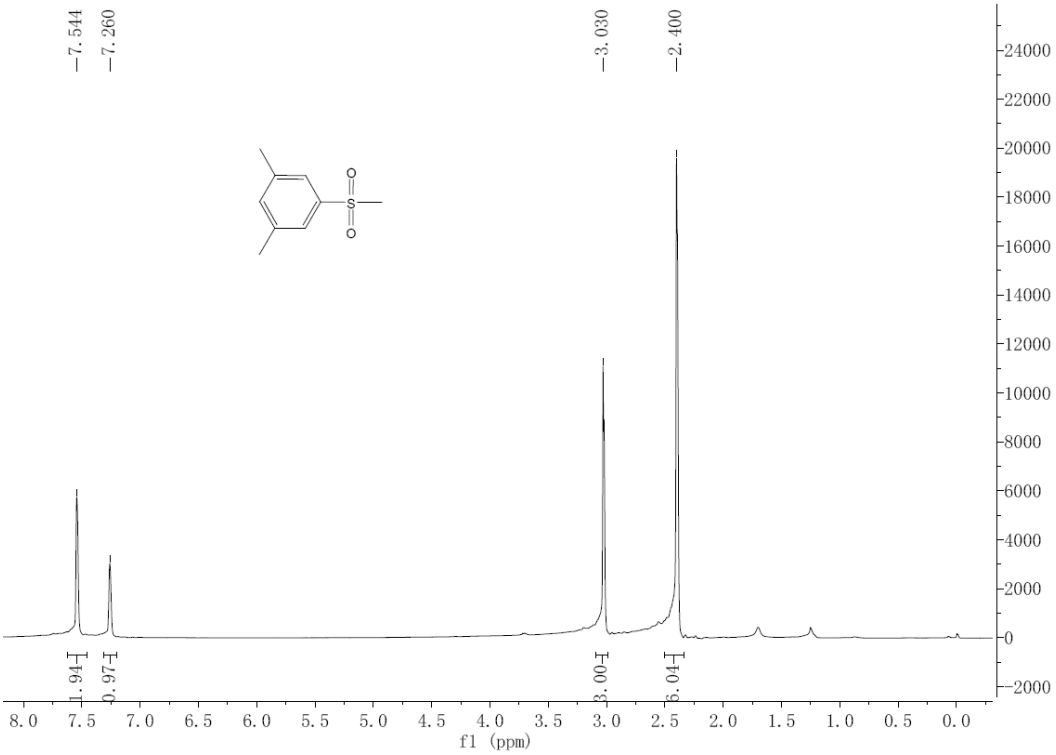
128.79
127.45
77.32
77.00
76.68
44.57
28.86
15.11
f1 (ppm)


8.020
7.998
7.781
7.760
7.619
7.602
7.509
7.491
7.472
7.450
7.433
7.260
3.096
2.00
2.04
2.07
3.04
3.00
f1 (ppm)


146.66
139.06
129.06
128.64
127.93
127.86
127.34
77.32
77.00
76.68
44.56
f1 (ppm)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2.400
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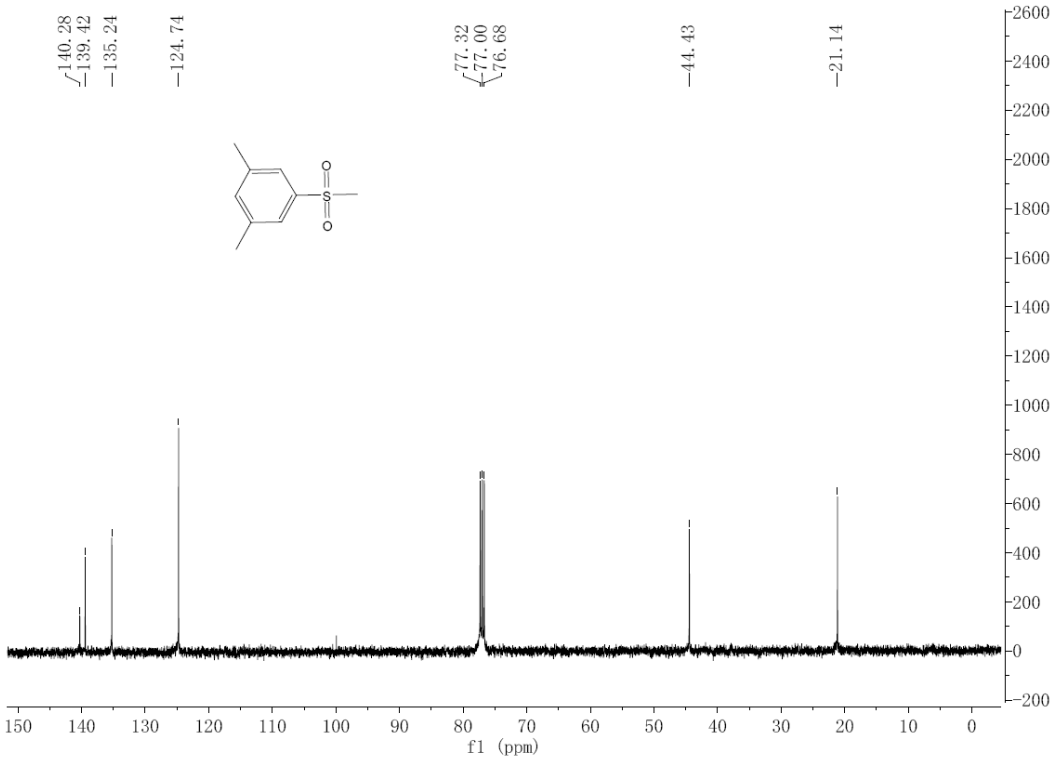
0.97
3.00
6.04
f1 (ppm)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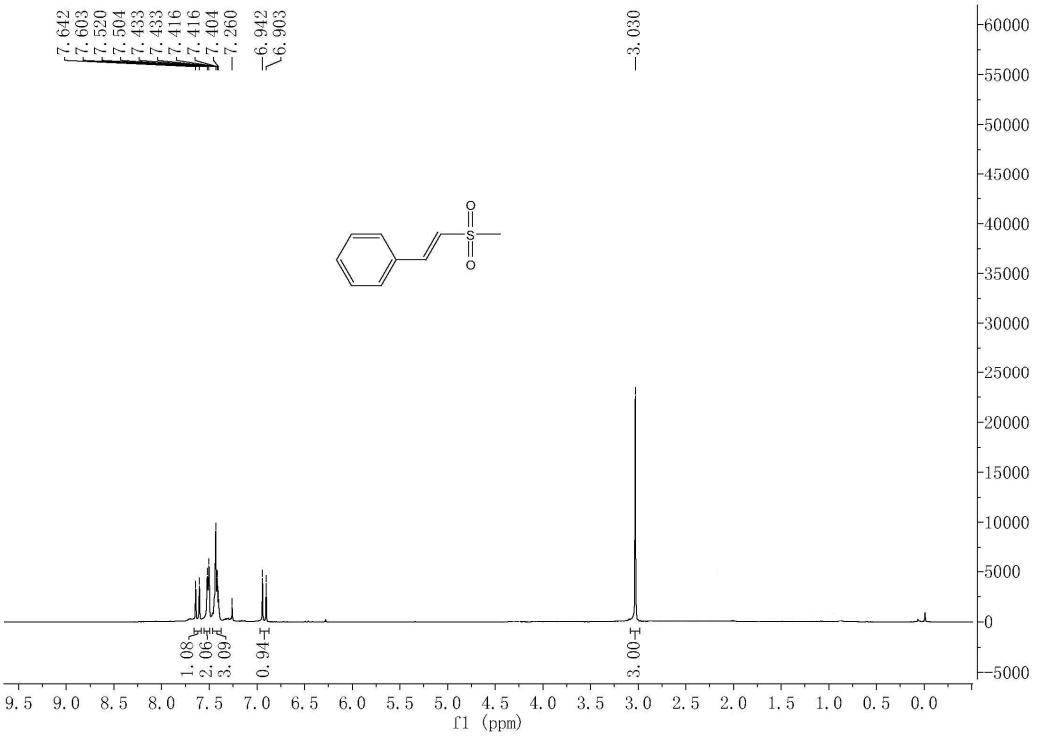
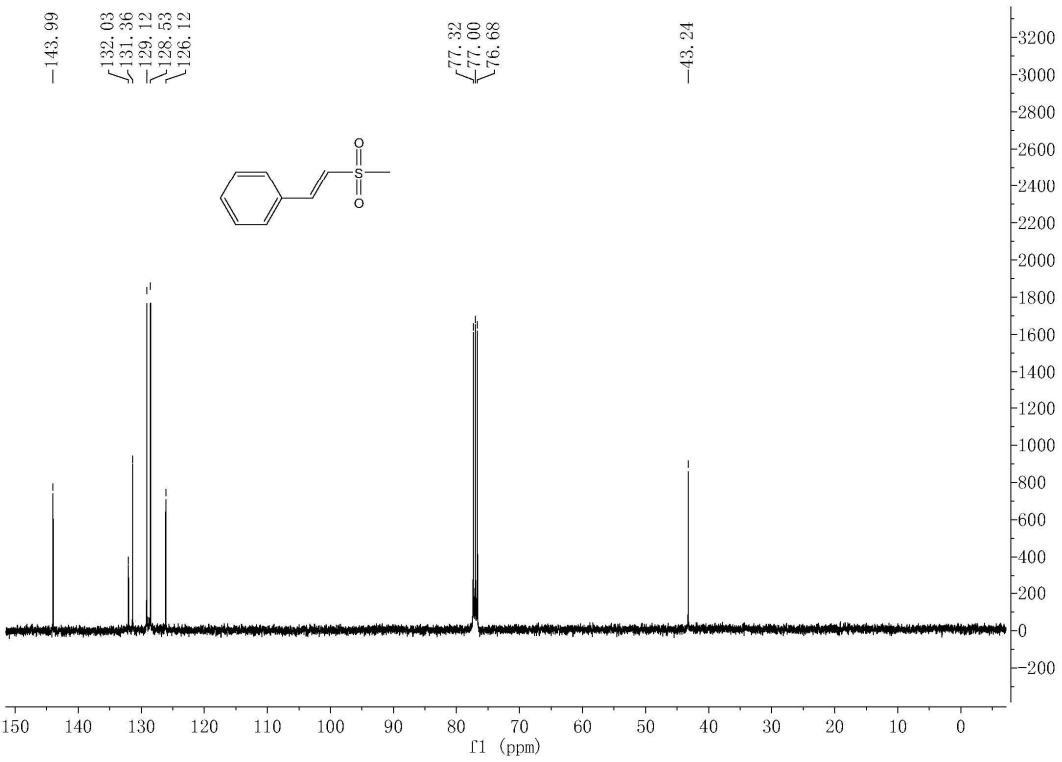
135.24
124.74
77.32
77.00
76.68
44.43
21.14
f1 (ppm)


7.642
7.603
7.520
7.504
7.433
7.433
7.416
7.416
7.404
7.260
6.942
6.903
3.030
1.08
2.06
3.09
0.94
3.00
f1 (ppm)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129.12
128.53
126.12
77.32
77.00
76.68
43.24
f1 (ppm)