Supporting Information

Cu-catalyzed aerobic oxidative C-CN bond cleavage of benzyl cyanide for the synthesis of primary amides

Xiuling Chen*, Yanhong Peng,Yan Li, Minghu Wu, Haibing Guo, Jian Wang, Shaofa Sun*

Non-power Nuclear Technology Collaborative Innovation Center, School of Nuclear Technology and Chemistry & Life Science, Hubei University of Science and Technology, Xianning 437100, China
[Fax: (+86)-715-8338072; E-mail: cxl828800@163.com (Dr. X. L. Chen) ; sunshaofa@mail.hbust.com.cn (Prof. S. F. Sun).]

Contents

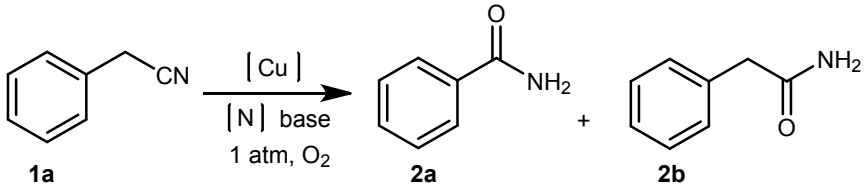
1. General remarks

All non-aqueous reactions and manipulations were performed in air atmosphere. All solvents were dried before use. The reactions were monitored by GC (7820A, Hubei University of Science and Technology) and GC-MS (QP2010, Hunan University). The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Brucker ADVANCE III spectrometer at 400 MHz and 100 MHz, respectively (Hubei University of Science and Technology). Flash column chromatography was performed using silica gel 40-70 μm (200-300 mu). Benzonitriles and substituted-arylacetonitrile were purchased from Energy Chemical, Alfa Aesar, Aladdin or Maya Reagent; were dried before use. The Cu salts and amines were purchased from Energy Chemical, Aladdin.

2. General procedure

5 mol% Cu salts, 0.2 mmol arylacetonitrile, 0.3 mmol N-source, 0.3 mmol base were dissolved in 2 mL CH_3CN under O_2 atmosphere and stirred at 120 ^{o}C in sealed tube (schleck tube which was sealed by a rubber septum). After completion of the reaction, the resulting solution was cooled to room temperature, washed with saturated HCl aqueous solution, and extracted with $CHCl_3$ three times. The organic layer was dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel and eluted with EtOAc/petroleum ether (1/2) to afford the desired product.

3. Optimization of reaction conditions[a]



1a **2a** **2b**

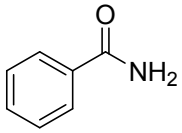
Entry	Cat	[N]	Base	Solvent	**2a**%[c]	**2b**%[b]
1	CuCl	$NH_3.H_2O$	-	CH_3CN	35	20
2	$Cu(OAc)_2$	$NH_3.H_2O$	-	CH_3CN	25	30
3	CuO	$NH_3.H_2O$	-	CH_3CN	40	41
4	$CuCl_2$	$NH_3.H_2O$	-	CH_3CN	50	25
5	Cu_2O	$NH_3.H_2O$		CH_3CN	50	31
6	Cu	$NH_3.H_2O$		CH_3CN	43	35
7	Cu_2O	NH_4Cl	$Ba(OH)_2$	CH_3CN	50	<1
8	Cu_2O	NH_4Cl	KOH	CH_3CN	58	<1
9	Cu_2O	NH_4Cl	$Ca(OH)_2$	CH_3CN	20	<1
10	Cu_2O	NH_4Cl	NaOH	CH_3CN	88	<1
11	CuCl	NH_4Cl	NaOH	CH_3CN	71	<1

12	$CuCl_2$	NH_4Cl	NaOH	CH_3CN	65	<1
13	$Cu(OAc)_2$	NH_4Cl	NaOH	CH_3CN	58	<1
14	CuBr	NH_4Cl	NaOH	CH_3CN	55	<1
15	$CuBr_2$	NH_4Cl	NaOH	CH_3CN	62	<1
16	Cu	NH_4Cl	NaOH	CH_3CN	55	<1
17	Cu_2O	NH_4OAc	NaOH	CH_3CN	63	<1
18	Cu_2O	$(NH_4)_2SO_4$	NaOH	CH_3CN	50	<1
19	Cu_2O	$(NH_4)_2CO_3$	NaOH	CH_3CN	71	<1
20	Cu_2O	Urea	NaOH	CH_3CN	<1	<1
21	Cu_2O	NH_4Cl	-	CH_3CN	--	<1
22	-	NH_4Cl	NaOH	CH_3CN	--	<1
23	Cu_2O	NH_4Cl	NaOH	Toluene	20	<1
24	Cu_2O	NH_4Cl	NaOH	1,4-dioxane	33	<1
25	Cu_2O	NH_4Cl	NaOH	THF	36	<1
26	Cu_2O	NH_4Cl	NaOH	DMF	13	<1
27	Cu_2O	NH_4Cl	NaOH	DMSO	trace	<1
28	Cu_2O	NH_4Cl	NaOH	DCE	21	<1
29	Cu_2O	NH_4Cl	NaOH	C_2H_5OH	trace	<1
30[c]	Cu_2O	NH_4Cl	NaOH	CH_3CN	trace	trace

[a]Reaction conditions: 2-phenylacetonitrile **1a** (0.2 mmol), cat (5 mol%), N source (0.3 mmol), base (0.4 mmol), CH_3CN (2 ml), in 25 mL schlenk tube, 120 °C, O_2 (1 atm), 30 h. [b]Yields were determined by GC using *n*-hexadecane as an internal standard. [c]Air was used as oxidant.

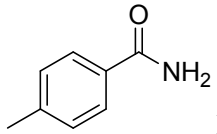
4. ^{1}H NMR and ^{13}C NMR data of products

benzamide (2a)[1]



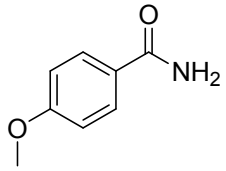
Following the general procedure (EtOAc/petroleum ether 1:2), **2a** was obtained as a white solid, isolated yield: 82%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.04 (s, 1H), 7.88 (d, 1H, *J* = 7.6 Hz), 7.50 (d, 2H, *J* = 7.0 Hz), 7.43 (d, 2H, *J* = 7.6 Hz), 7.40 (s, 1H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 168.7, 134.5, 131.8, 128.7, 127.9; GC-MS: m/z=121.

4-methylbenzamide (2b)[1]



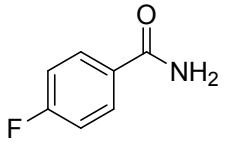
Following the general procedure (EtOAc/petroleum ether 1:2), **2b** was obtained as a white solid, isolated yield: 81%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 7.73 (d, 1H, *J* = 8.0 Hz), 7.26 (d, 2H, *J* = 8.0 Hz), 6.19 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 169.7, 142.6, 129.3, 129.1, 127.4, 21.5; GC-MS: m/z=135.

4-methoxybenzamide (2c)[1]



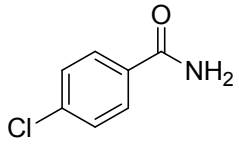
Following the general procedure (EtOAc/petroleum ether 1:2), **2c** was obtained as a white solid, isolated yield: 79%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 7.78 (d, 1H, *J* = 8.4 Hz), 6.93 (d, 2H, *J* = 8.4 Hz), 5.94 (br, 2H), 3.85 (s, 3H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 168.9, 162.6, 129.3, 125.6, 113.8, 55.4; GC-MS: m/z=151.

4-fluorobenzamide (2e)[1]



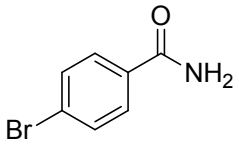
Following the general procedure (EtOAc/petroleum ether 1:2), **2e** was obtained as a white solid, isolated yield: 81%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.02 (s, 1H), 7.93-7.97 (m, 2H), 7.42 (s, 1H), 7.26 (t, 2H, *J* = 8.4 Hz); ^{19}F NMR (376 MHz, DMSO-*d*): δ -109.51 (s, F); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 167.4, 164.4 (d, *J* = 146.9 Hz), 131.1 (d, *J* = 2.9 Hz), 130.4 (d, *J* = 9.0 Hz), 115.5 (d, *J* = 21.6 Hz); GC-MS: m/z=139.

4-chlorobenzamid (2f)[1]



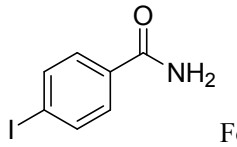
Following the general procedure (EtOAc/petroleum ether 1:2), **2f** was obtained as a white solid, isolated yield: 78%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.05 (s, 1H), 7.82 (d, 1H, *J* = 8.4 Hz), 7.65 (d, 2H, *J* = 8.4 Hz), 7.46 (s, 1H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 167.5, 133.9, 131.7, 130.1, 125.5; GC-MS: m/z=155.

4-bromobenzamide (2g)[1]



Following the general procedure (EtOAc/petroleum ether 1:2), **2g** was obtained as a white solid, isolated yield: 83%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.04 (s, 1H), 7.81 (d, 1H, *J* = 8.0 Hz), 7.65 (d, 2H, *J* = 8.0 Hz), 7.45 (s, 1H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 167.4, 133.9, 131.7, 130.1, 125.5; GC-MS: m/z=198.

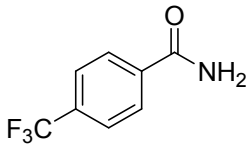
4-iodobenzamide (2h)[2]



Following the general procedure (EtOAc/petroleum ether 1:2), **2h** was obtained as a white solid, isolated yield: 69%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.02 (s, 1H), 7.83

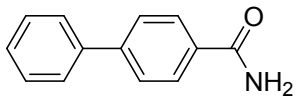
(d, 1H, *J* = 8.4 Hz), 7.65 (d, 2H, *J* = 8.4 Hz), 7.42 (s, 1H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 167.7, 137.6, 134.2, 129.9, 99.3; GC-MS: m/z=246.

4-(trifluoromethyl)benzamide (2i)[1]



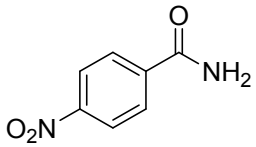
Following the general procedure (EtOAc/petroleum ether 1:2), **2i** was obtained as a white solid, isolated yield: 78%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.20 (s, 1H), 8.06 (d, 1H, *J* = 8.4 Hz), 7.82 (d, 2H, *J* = 8.0 Hz), 7.63 (s, 1H); ^{19}F NMR (376 MHz, DMSO-*d*): δ -61.38 (s, 3F); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 167.2, 138.5, 131.6 (d, *J* = 31.8 Hz), 128.8, 125.6 (q, *J* = 3.7 Hz), 123.1; GC-MS: m/z=189.

[1,1'-biphenyl]-4-carboxamide (2j)[1]



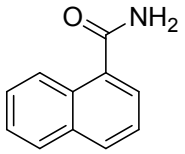
Following the general procedure (EtOAc/petroleum ether 1:2), **2j** was obtained as a white solid, isolated yield: 73%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.04 (s, 1H), 7.96 (d, 1H, *J* = 8.0 Hz), 7.73 (t, 2H, *J* = 9.2 Hz), 7.48 (t, 1H, *J* = 7.2 Hz), 7.41 (d, 1H, *J* = 7.2 Hz),7.38 (s, 1H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 168.1, 143.2, 139.7, 133.5, 129.5, 128.8, 128.6, 128.5, 127.3, 126.9, 125.8; GC-MS: m/z=197.

4-nitrobenzamide (2k)[1]



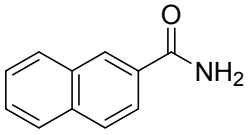
Following the general procedure (EtOAc/petroleum ether 1:2), **2k** was obtained as a white solid, isolated yield: 92%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.27 (t, 3H, *J* = 8.4 Hz), 8.06 (d, 2H, *J* = 8.4 Hz), 7.71 (s, 1H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 166.9, 149.5, 140.4, 1294, 123.9; GC-MS: m/z=166.

1-naphthamide (2l)[1]



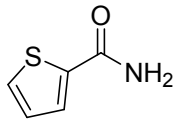
Following the general procedure (EtOAc/petroleum ether 1:2), **2l** was obtained as a white solid, isolated yield: 57%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.49 (s, 1H), 8.14 (s, 1H), 7.97-8.02 (m, 4H), 7.58-7.62 (m, 2H), 7.47 (s, 1H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 168.8, 134.7, 132.6, 131.9, 129.3, 128.3, 128.2, 128.1, 128.0, 127.1, 124.9; GC-MS: m/z=171.

2-naphthamide(2m)[1]



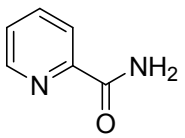
Following the general procedure (EtOAc/petroleum ether 1:2), **2m** was obtained as a white solid, isolated yield: 71%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.46 (d, 1H, *J* = 14.4 Hz), 8.20 (s, 1H), 7.95 (d, 4H, *J* = 14.0 Hz), 7.7 (t, 2H, *J* = 3.2 Hz), 7.49 (s, 1H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 168.4, 134.6, 132.6, 131.9, 129.3, 128.32, 128.29, 128.1, 128.0, 127.2, 124.8; GC-MS: m/z=171.

thiophene-2-carboxamide (2n)[1]



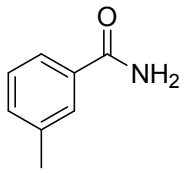
Following the general procedure (EtOAc/petroleum ether 1:2), **2n** was obtained as a white solid, isolated yield: 63%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 7.97 (s, 1H), 7.74 (t, 2H, *J* = 4.2 Hz), 7.38 (s, 1H), 7.13 (t, 1H, *J* = 4.4 Hz); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 163.4, 140.8, 131.5, 129.1, 128.4; GC-MS: m/z=127.

Picolinamide (2o)[1]



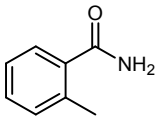
Following the general procedure (EtOAc/petroleum ether 1:2), **2o** was obtained as a white solid, isolated yield: 72%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 8.62 (d, 1H, *J* = 4.4 Hz), 8.13 (s, 1H), 8.04 (d, 1H, *J* = 7.6 Hz), 7.94 (t, 1H, *J* = 7.6 Hz), 7.66 (s, 1H), 7.58 (t, 1H, *J* = 6.0 Hz); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 166.5, 150.7, 148.9, 138.1, 126.9, 122.4; GC-MS: m/z=122.

3-methylbenzamide (2p)[1]



Following the general procedure (EtOAc/petroleum ether 1:2), **2p** was obtained as a white solid, isolated yield: 71%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 7.65 (s, 1H), 7.59 (t, 1H, *J* = 8.4 Hz), 7.29-7.33 (m, 2H), 6.42 (s, 2H); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 170.1, 138.5, 133.4, 132.7, 128.5, 128.1, 124.3, 21.3; GC-MS: m/z=135.

2-methylbenzamide (2q)[3]

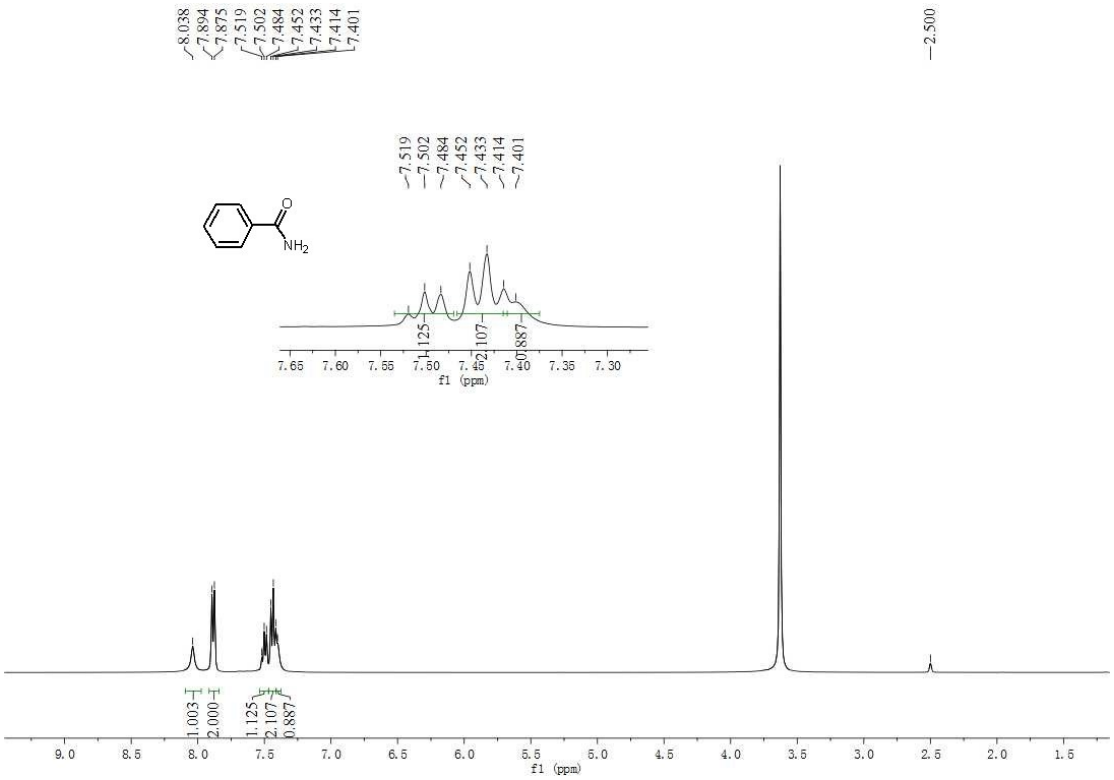


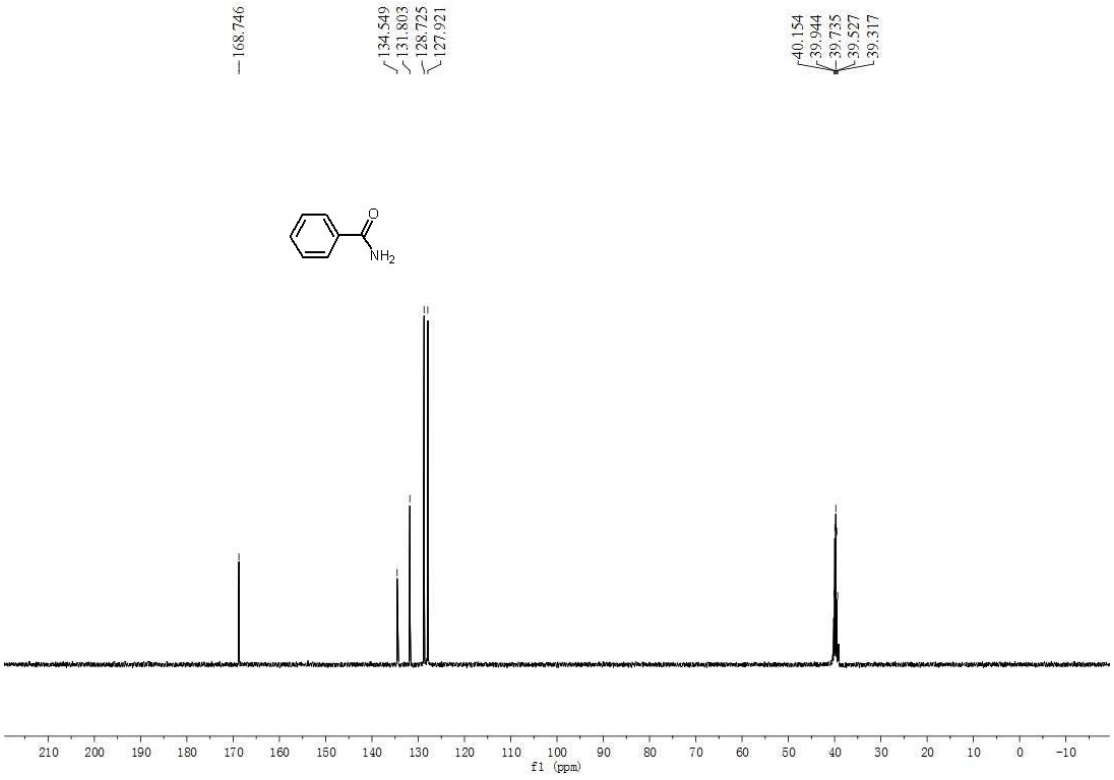
Following the general procedure (EtOAc/petroleum ether 1:2), **2q** was obtained as a white solid, isolated yield: 35%. ^{1}H NMR (DMSO-*d*, 400 MHz): δ 7.74 (s, 1H), 7.29-7.35 (m, 3H), 7.20 (t, 2H, *J* = 8.8 Hz); ^{13}C NMR (DMSO-*d*, 100 MHz): δ 172.0, 137.1, 135.6, 131.0, 129.8, 127.4, 126.0, 20.0; GC-MS: m/z=135.

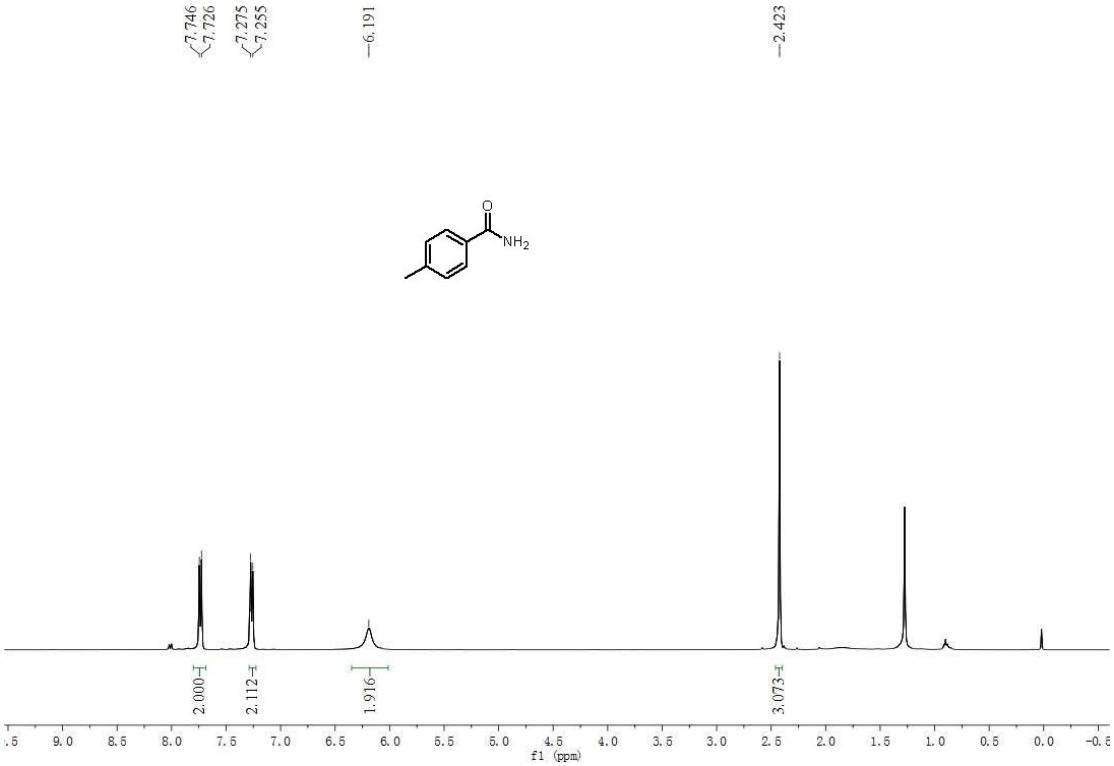
5. References

1. S. U. Dighea and S. Batra, *Adv. Synth. Catal*., 2016, **358**, 500-505.
2. S. Shimokawa, Y. Kawagoe, K. Moriyama and H. Togo, *Org. Lett*., 2016, **18**, 784-787.
3. Y. Wang, K. Yamaguchi and N. Mizuno, *Angew. Chem. Int. Ed*., 2012, **51**, 7250-7253.

6. Copies of ^{1}H, ^{13}C NMR and ^{19}F NMR spectra



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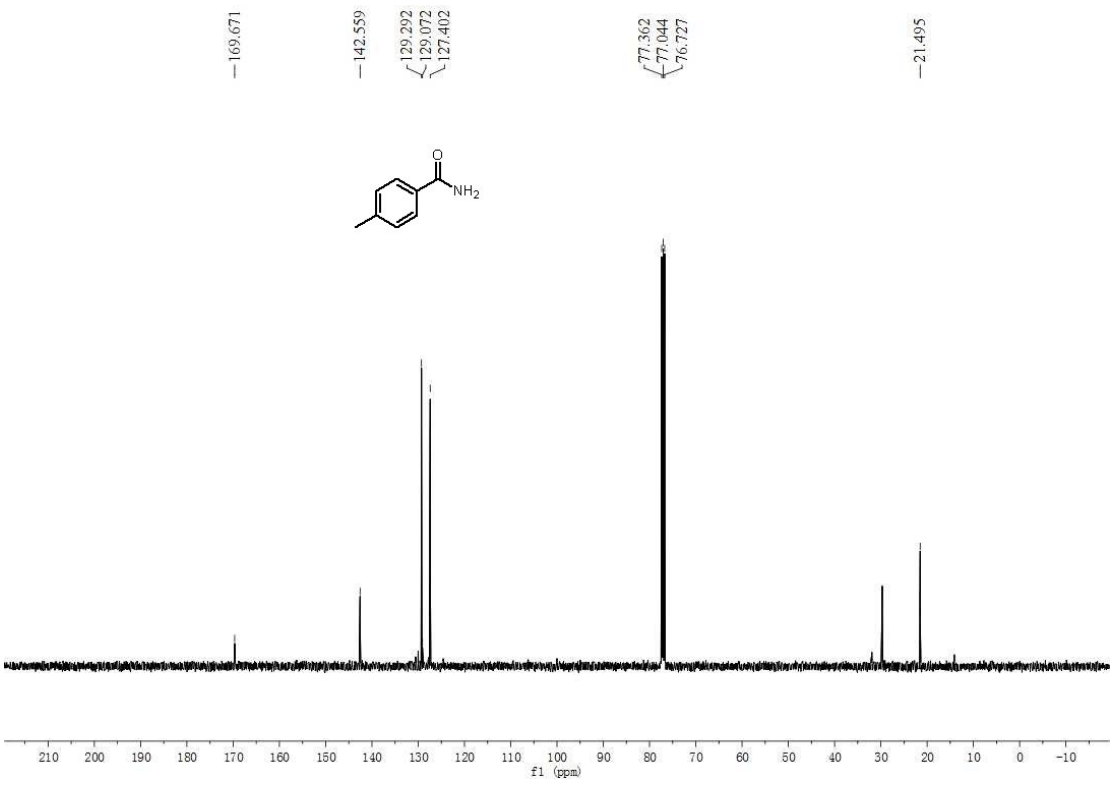
f1 (ppm)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NH2
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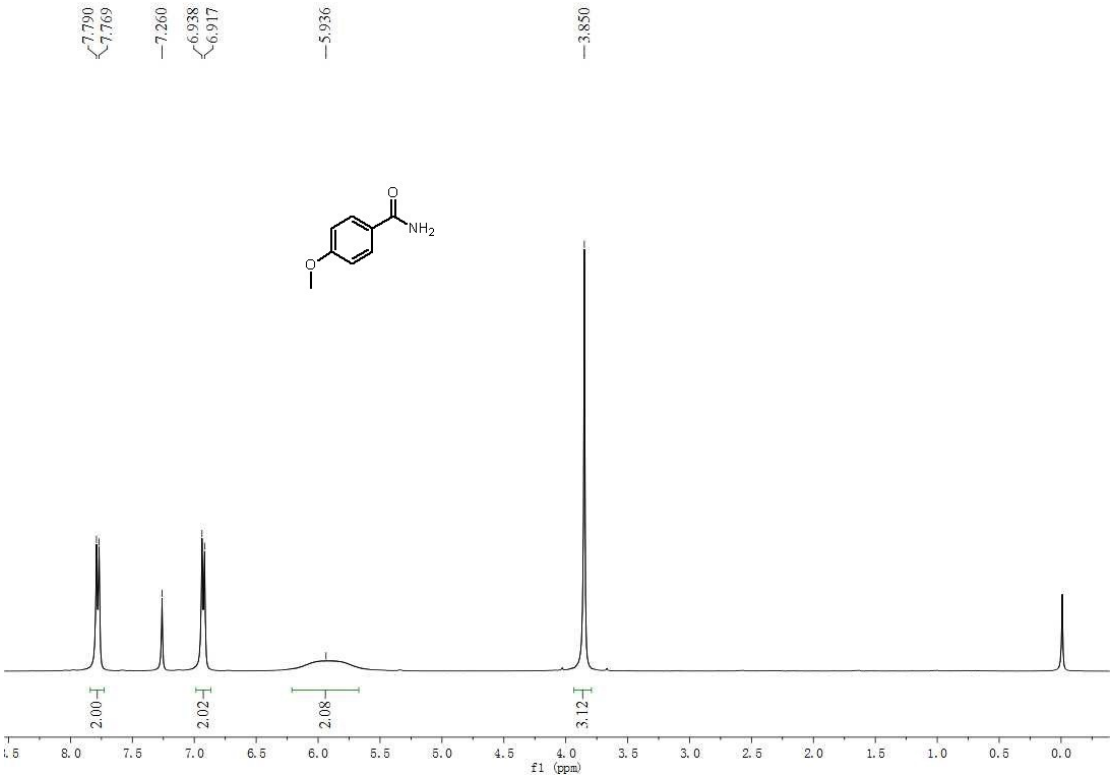
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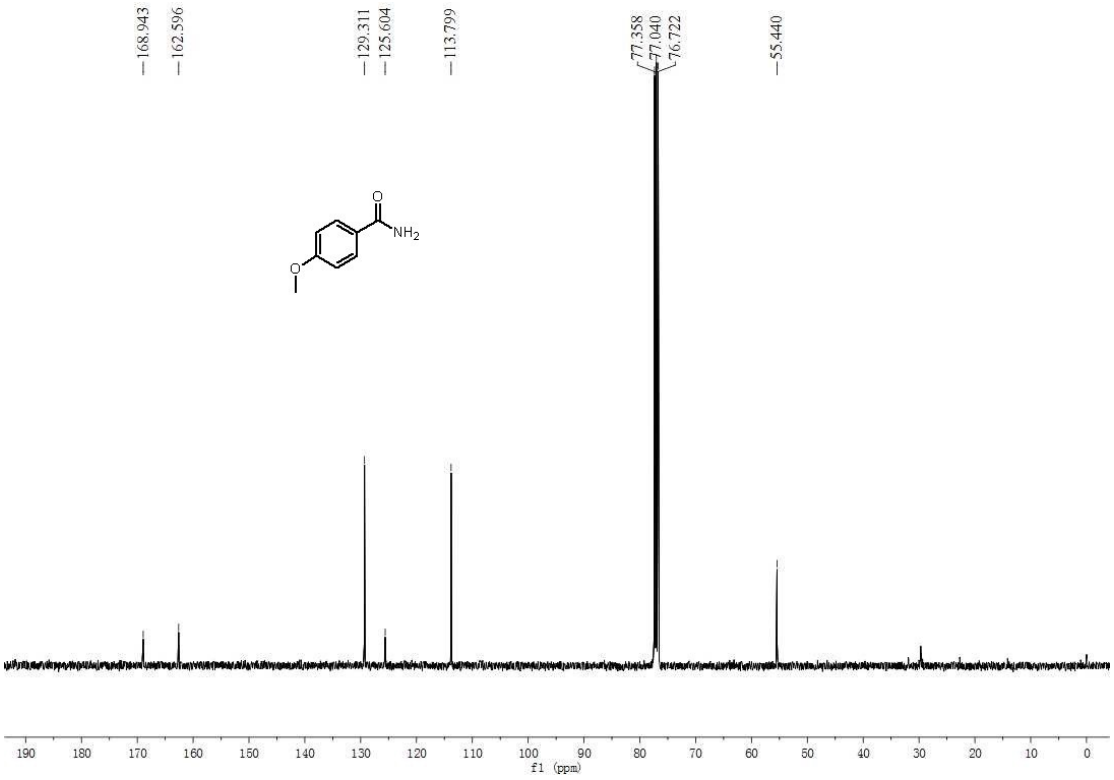
f1 (ppm)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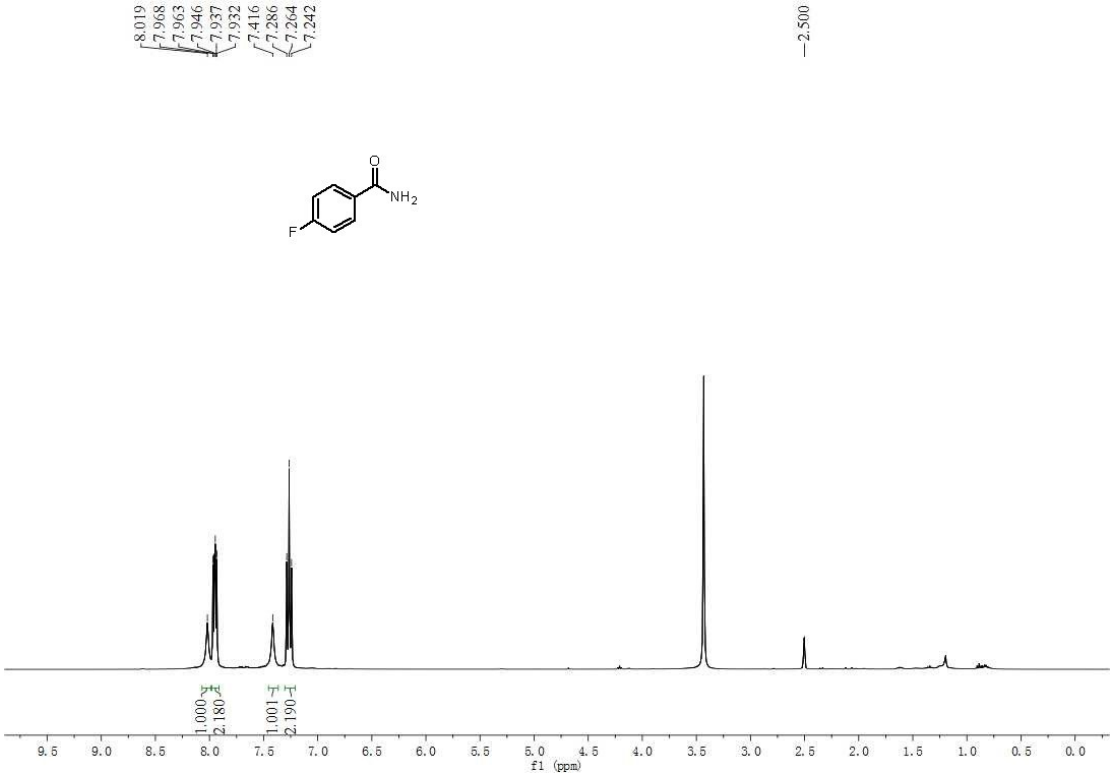
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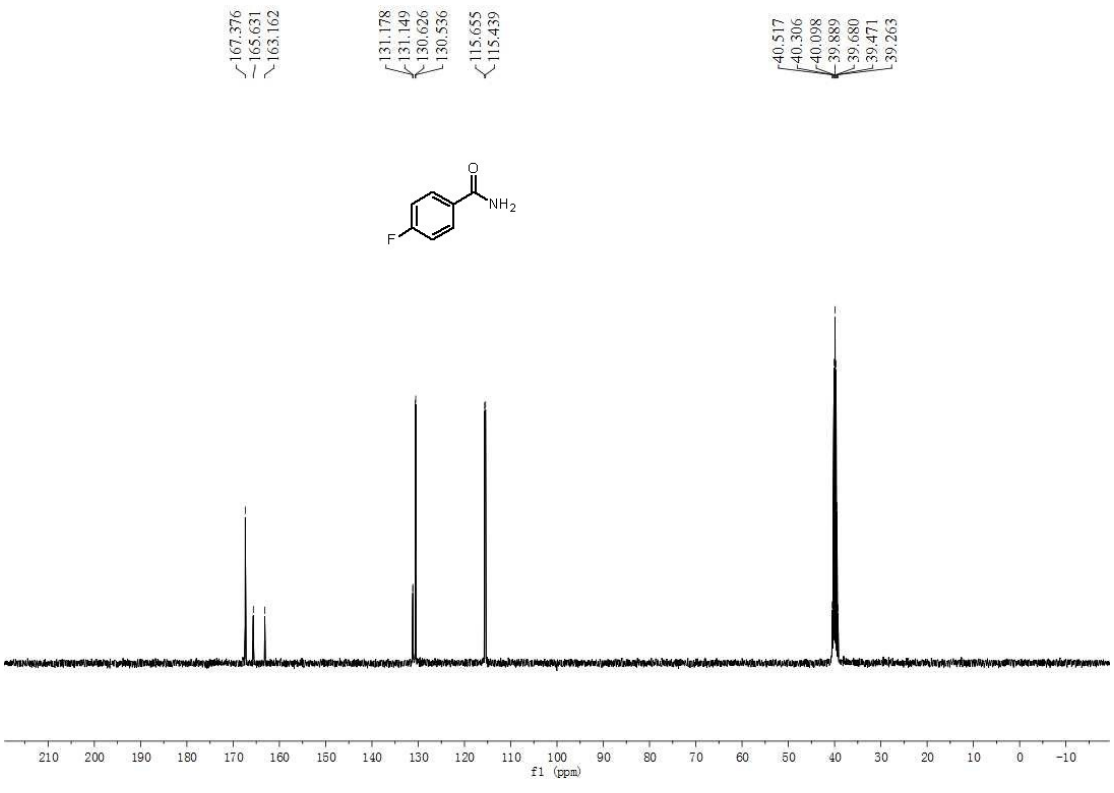
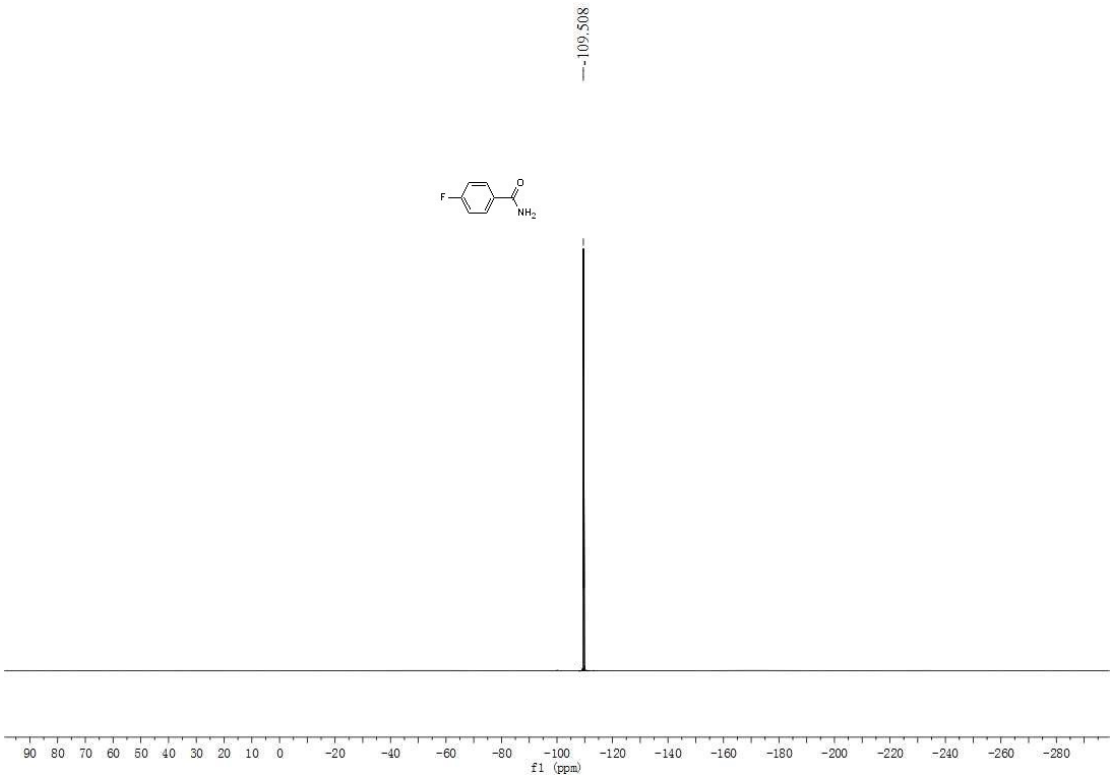
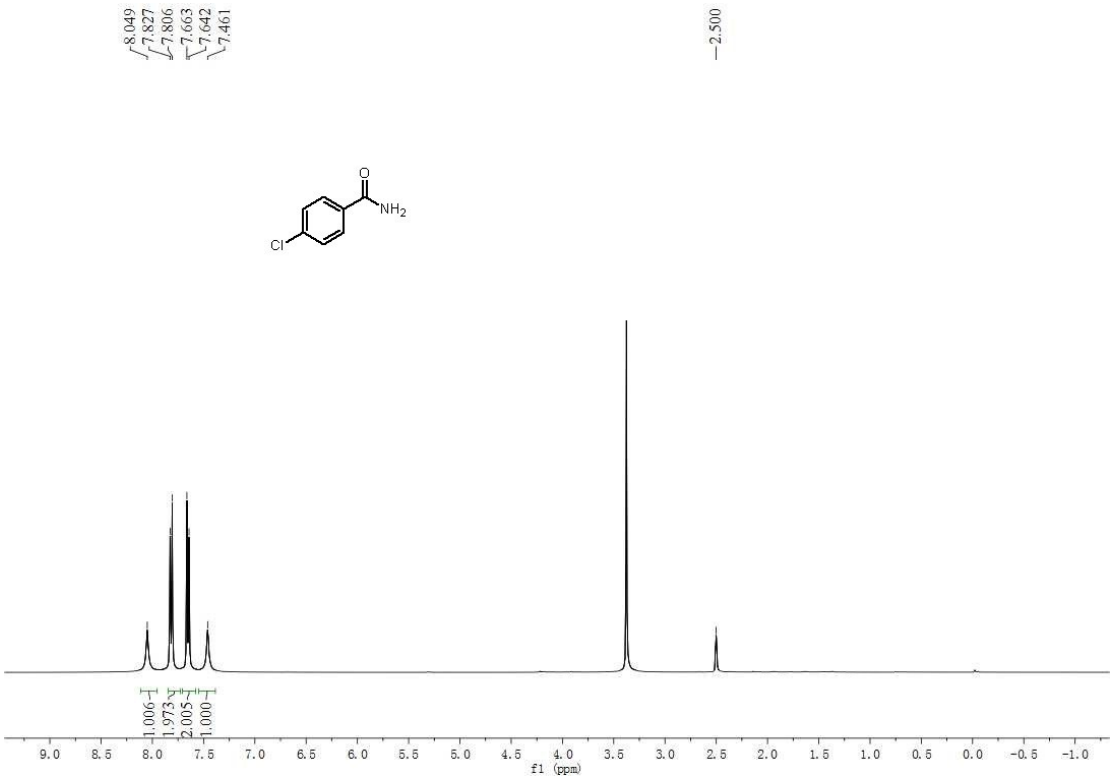
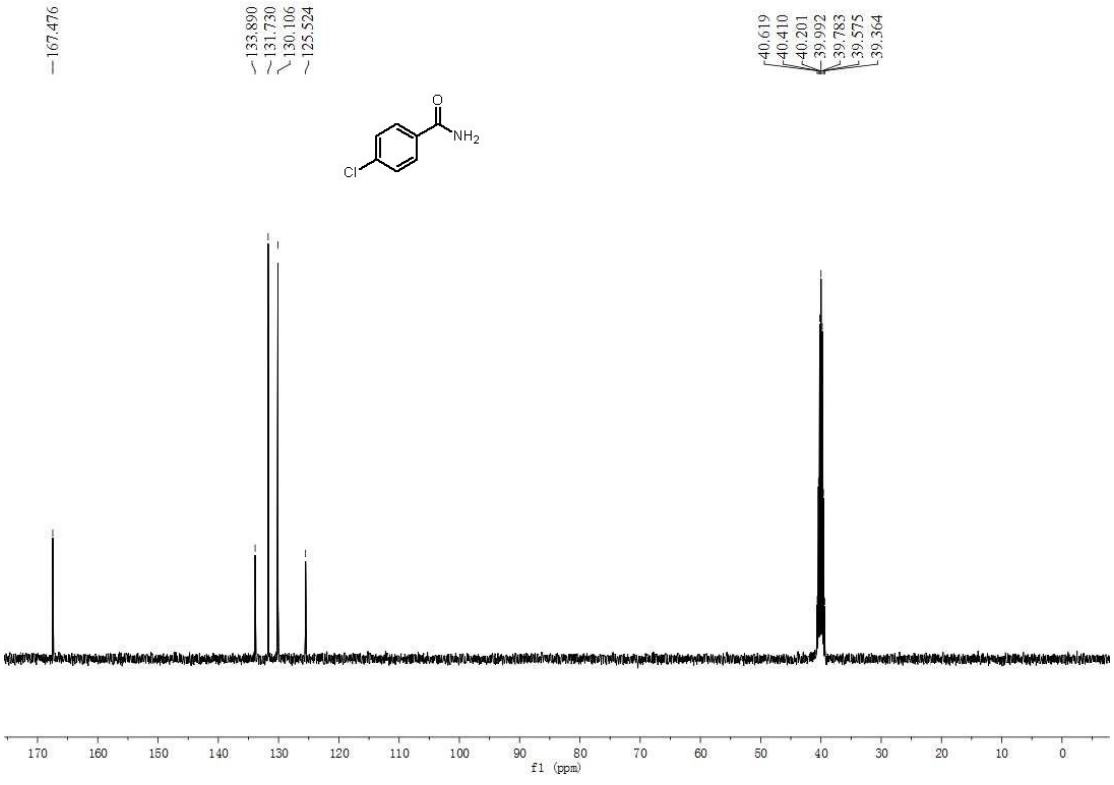
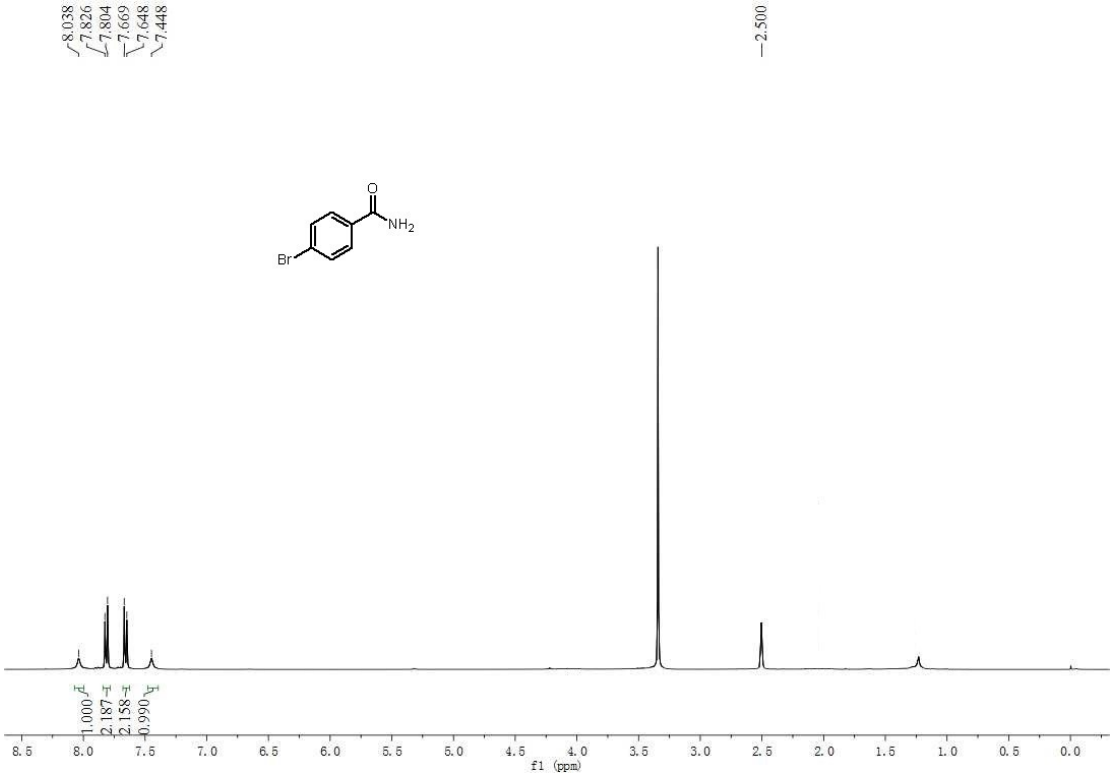
f1 (ppm)

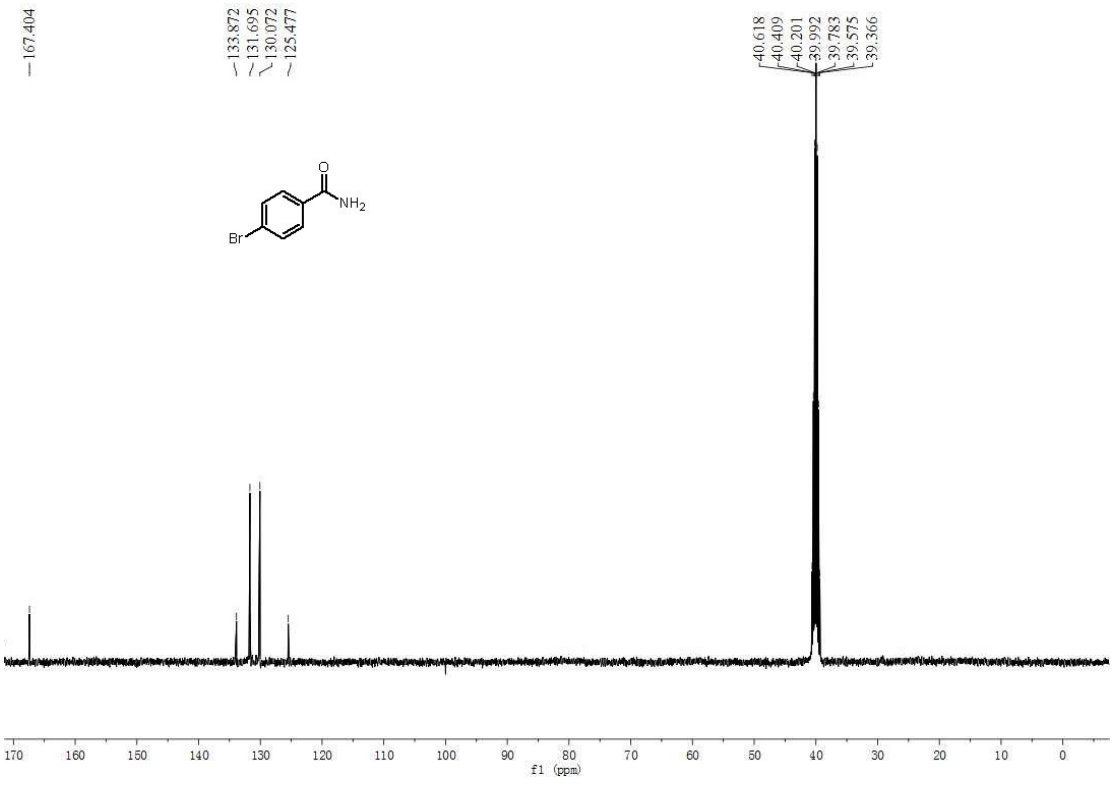

167.376
165.631
163.162
131.178
131.149
130.626
130.536
115.655
115.439
40.517
40.306
40.098
39.889
39.680
39.471
39.263
NH2
F
f1 (ppm)

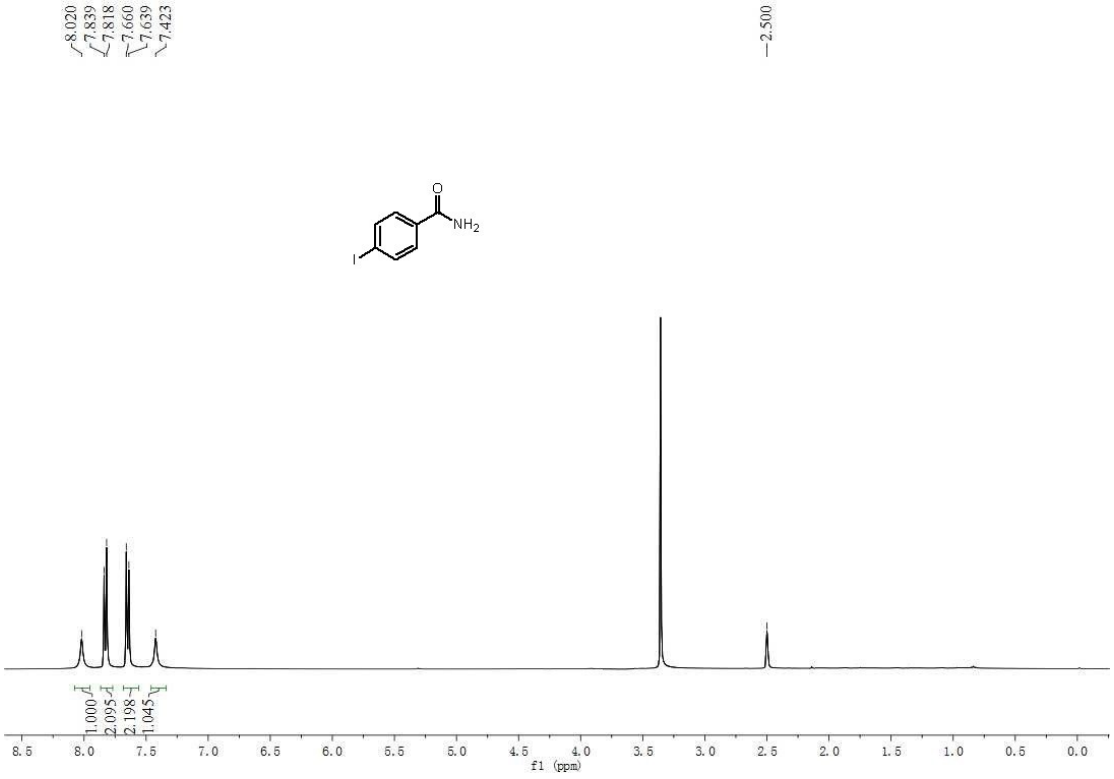

-109.508
F
O
NH2
90 80 70 60 50 40 30 20 10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240 -260 -280
f1 (ppm)

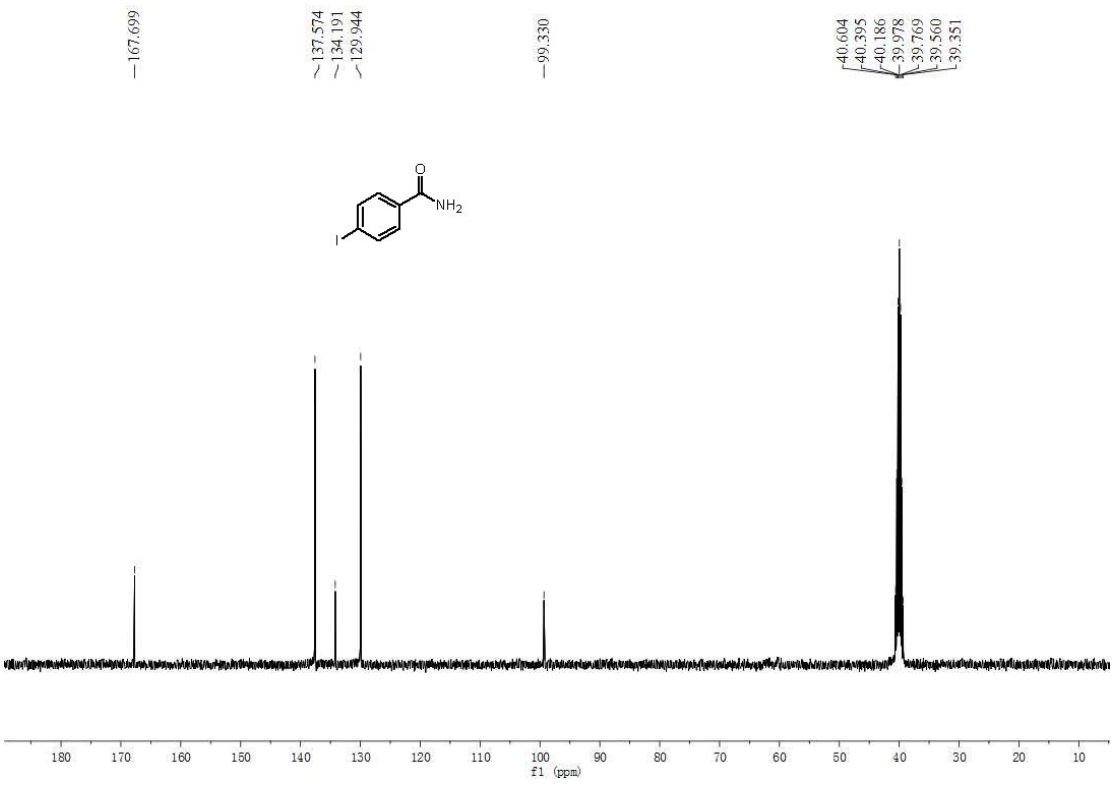

8.049
7.827
7.806
7.663
7.642
7.461
2.500
O
NH2
Cl
1.006
1.973
2.005
1.000
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

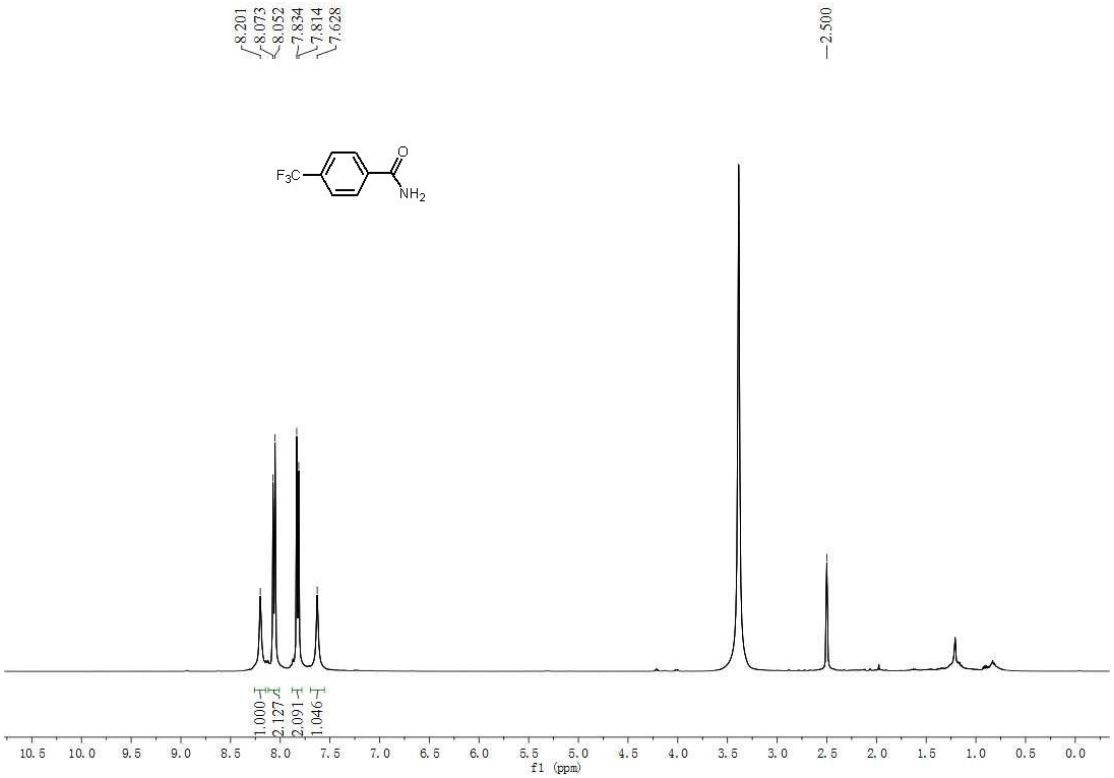

167.476
133.890
131.730
130.106
125.524
40.619
40.410
40.201
39.992
39.783
39.575
39.364
O
NH2
Cl
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

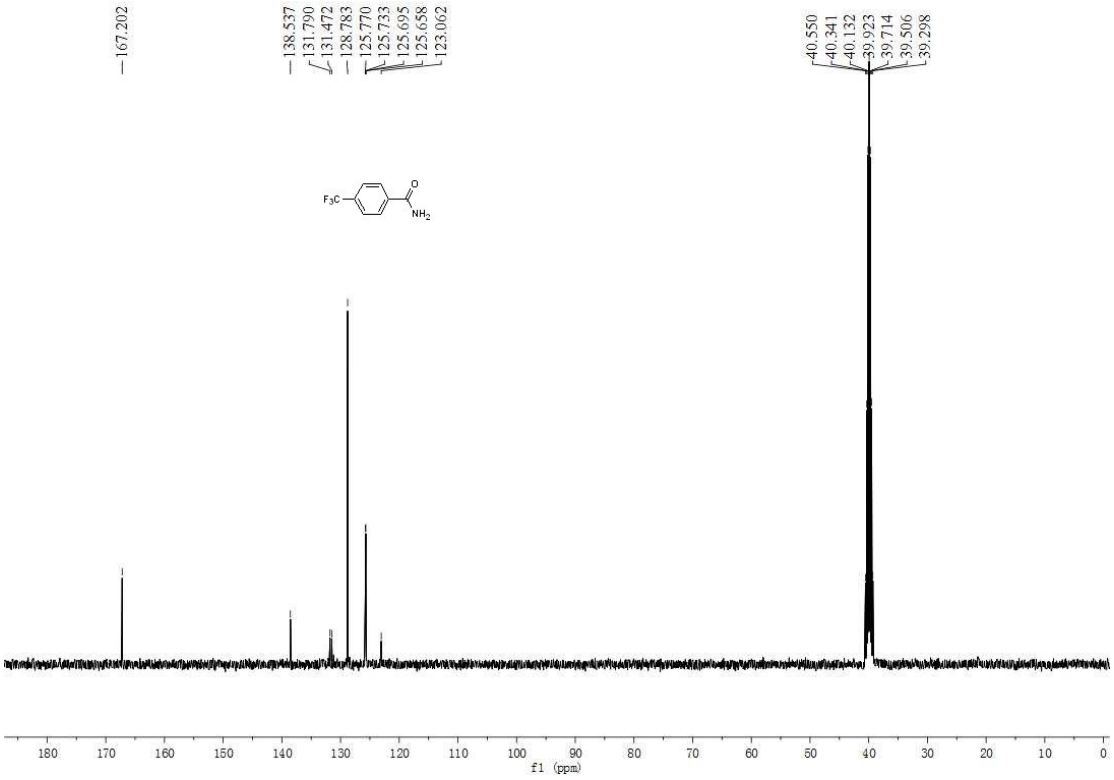

8.038
7.826
7.804
7.669
7.648
7.448
2.500
O
NH2
Br
1.000
2.187
2.158
0.990
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

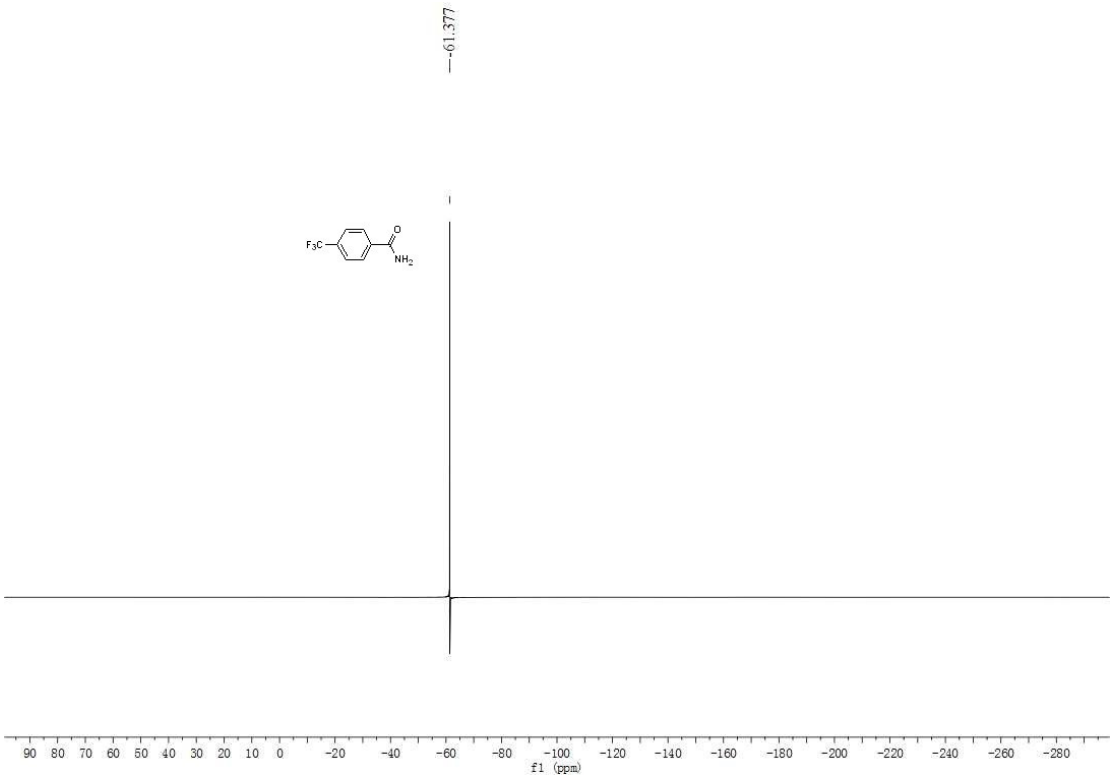

167.404
133.872
131.695
130.072
125.477
40.618
40.409
40.201
39.992
39.783
39.575
39.366
O
NH2
Br
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

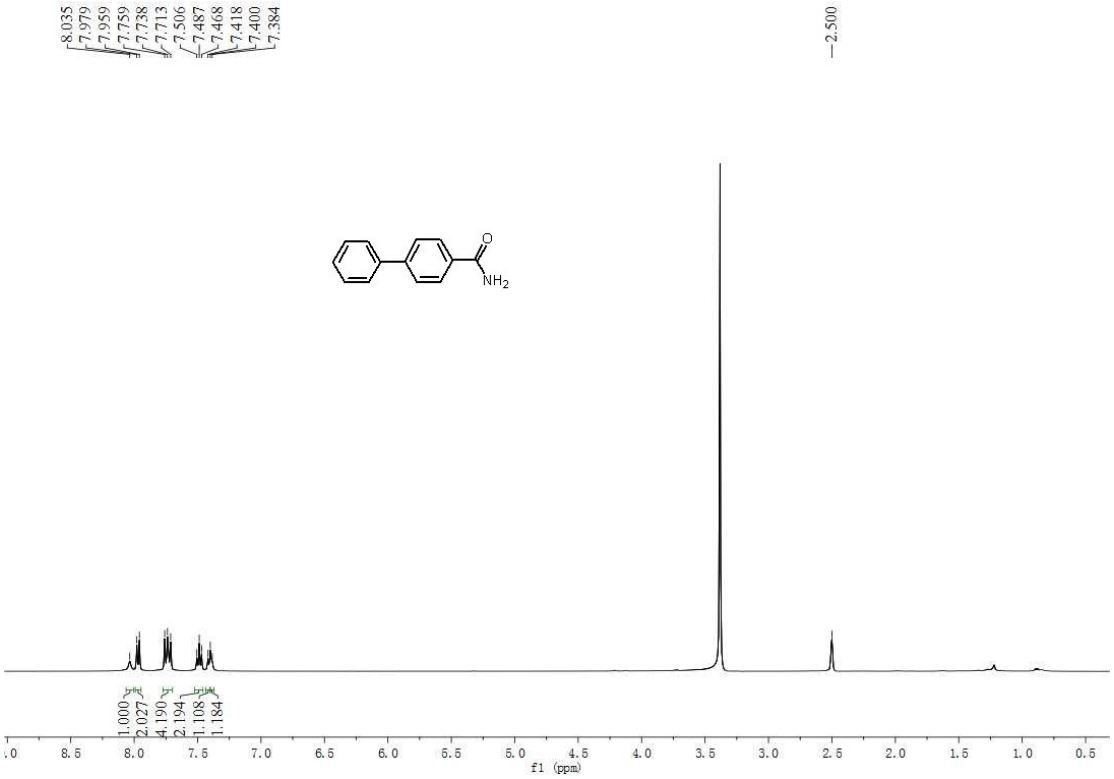

8.020
7.839
7.818
7.660
7.639
7.423
2.500
O
NH2
I
1.000
2.095
2.198
1.045
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

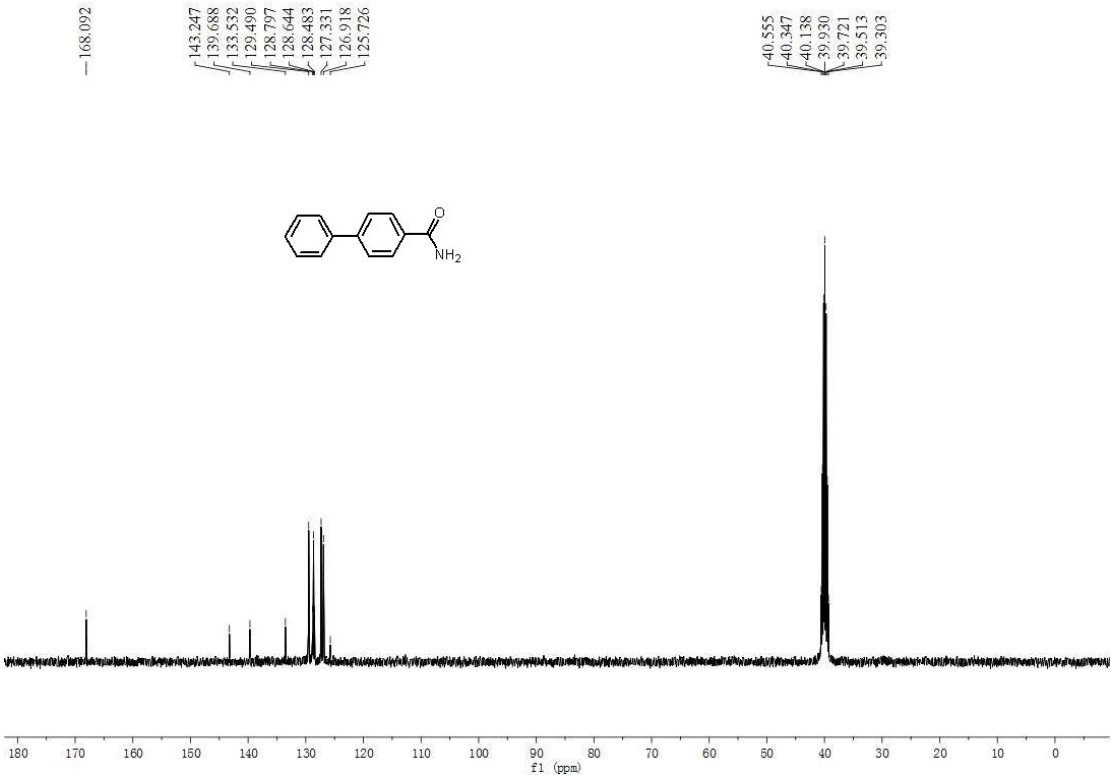

167.699
137.574
134.191
129.944
99.330
40.604
40.395
40.186
39.978
39.769
39.560
39.351
O
NH2
I
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

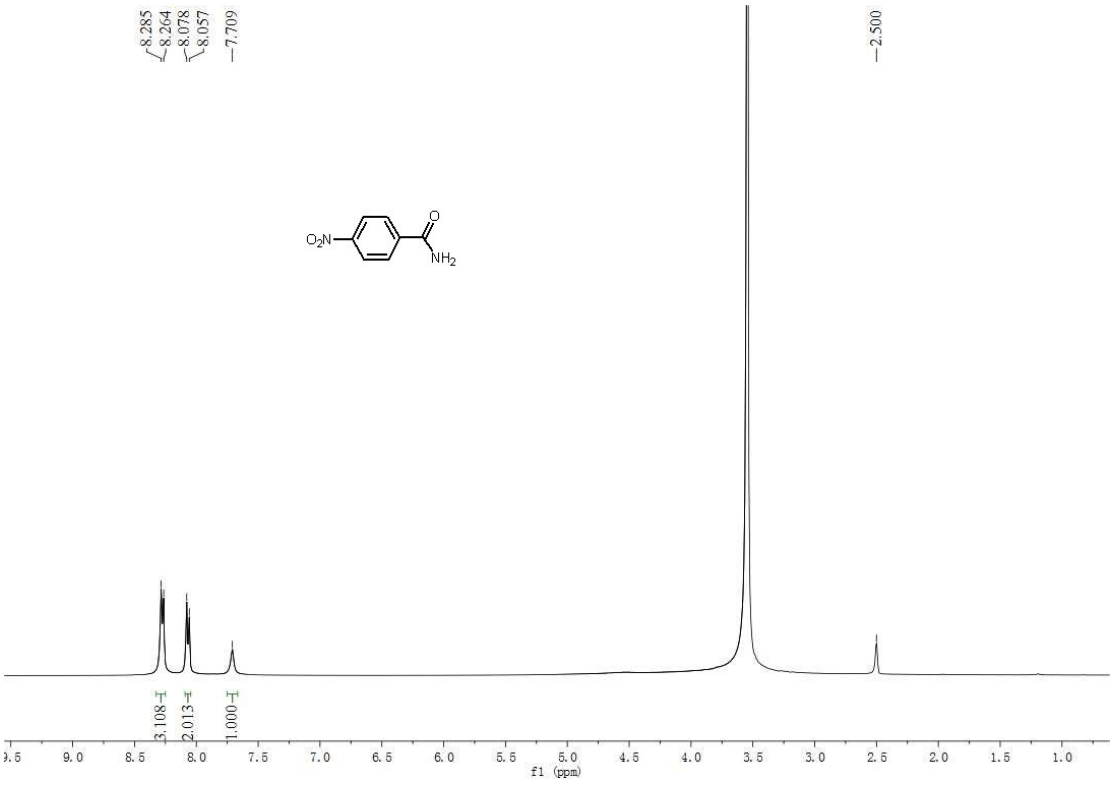

8.201
8.073
8.052
7.834
7.814
7.628
2.500
F3C
O
NH2
1.000
2.127
2.091
1.046
f1 (ppm)

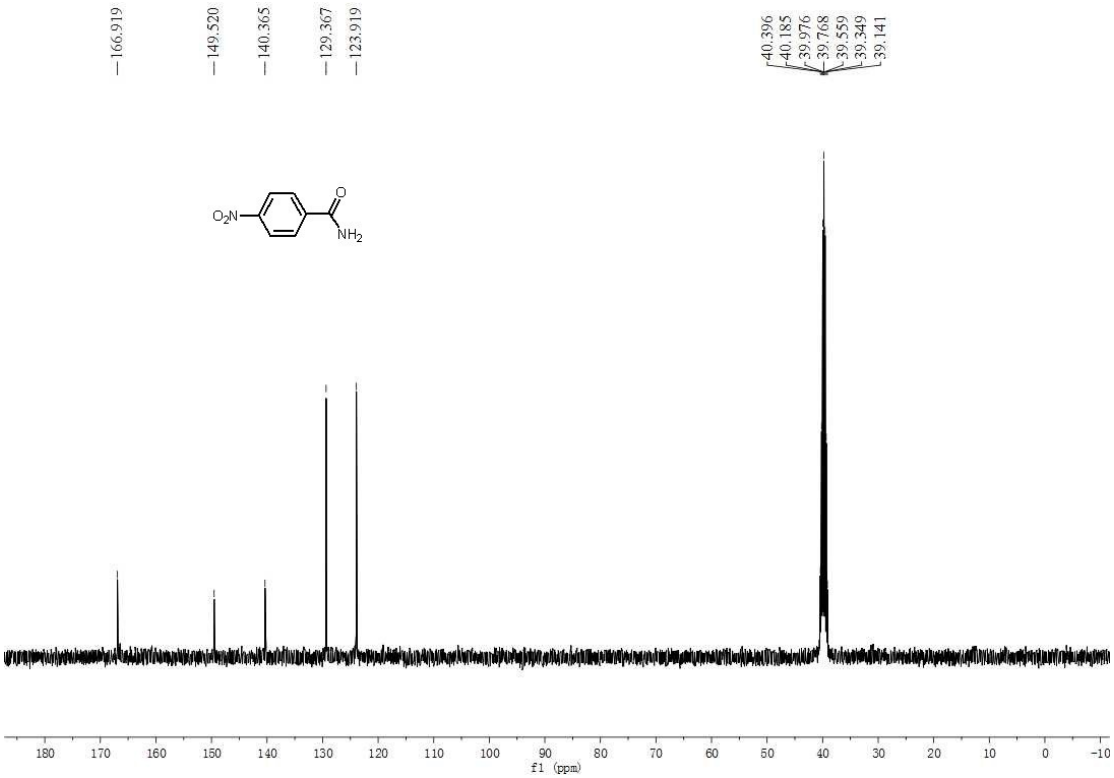

167.202
138.537
131.790
131.472
128.783
125.770
125.733
125.695
125.658
123.062
40.550
40.341
40.132
39.923
39.714
39.506
39.298
F3C
O
NH2
f1 (ppm)

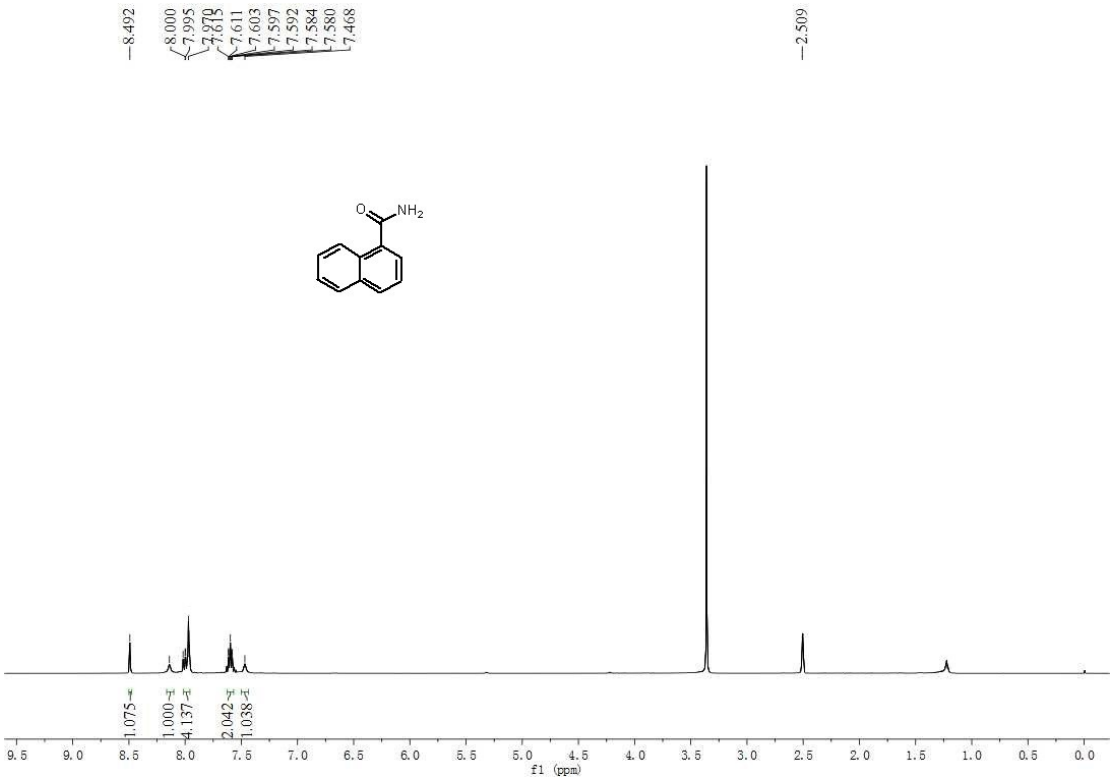

-61.377
F3C
O
NH2
90 80 70 60 50 40 30 20 10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240 -260 -280
f1 (ppm)

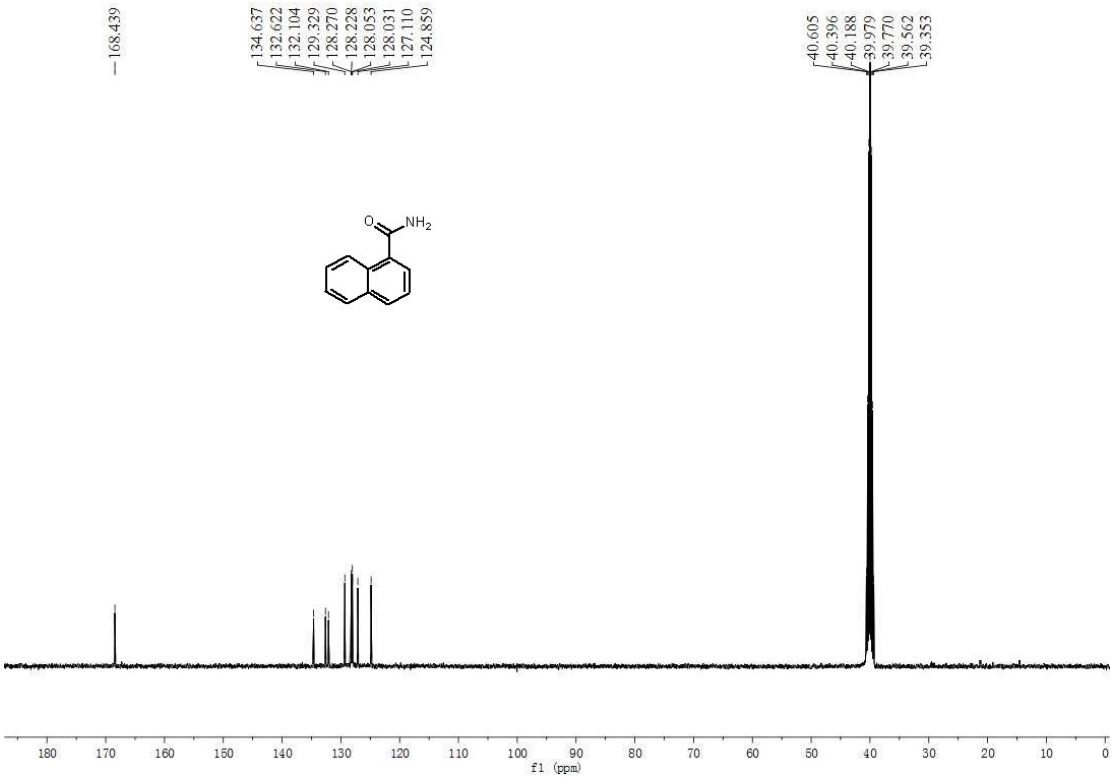

8.035
7.979
7.959
7.759
7.738
7.713
7.506
7.487
7.468
7.418
7.400
7.384
2.500
O
NH2
1.000
2.027
4.190
2.194
1.108
1.184
f1 (ppm)

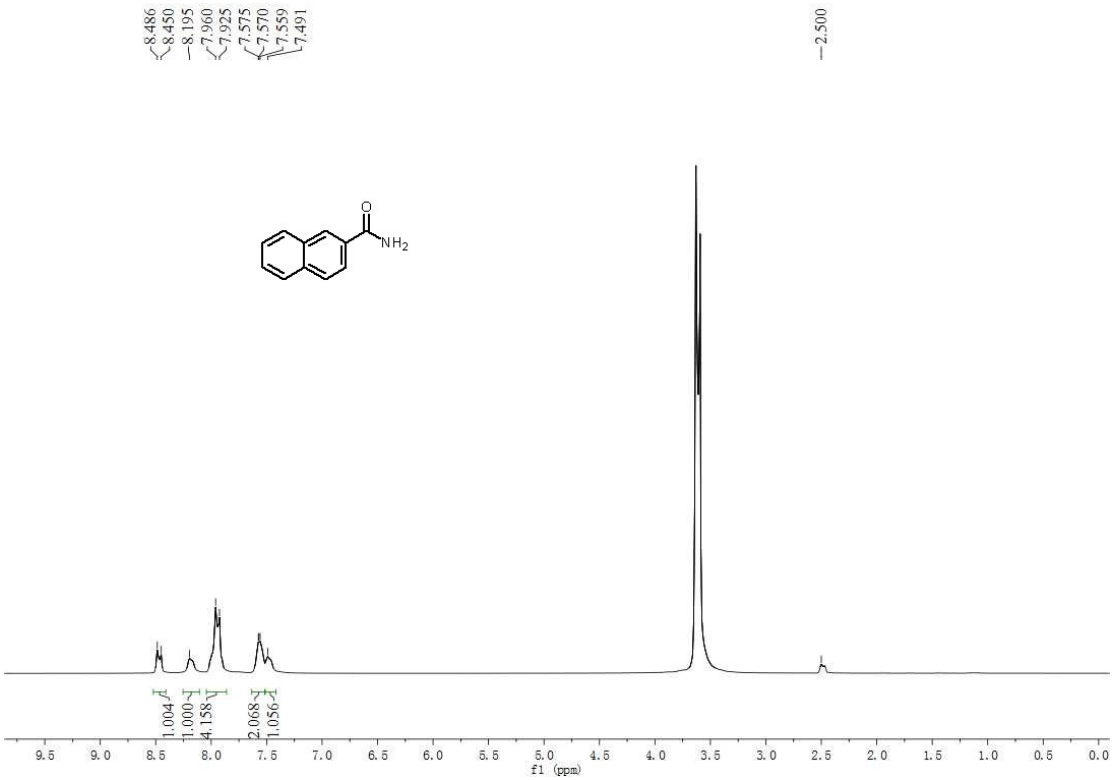

168.092
143.247
139.688
133.532
129.490
128.797
128.644
128.483
127.331
126.918
125.726
40.555
40.347
40.138
39.930
39.721
39.513
39.303
O
NH2
f1 (ppm)

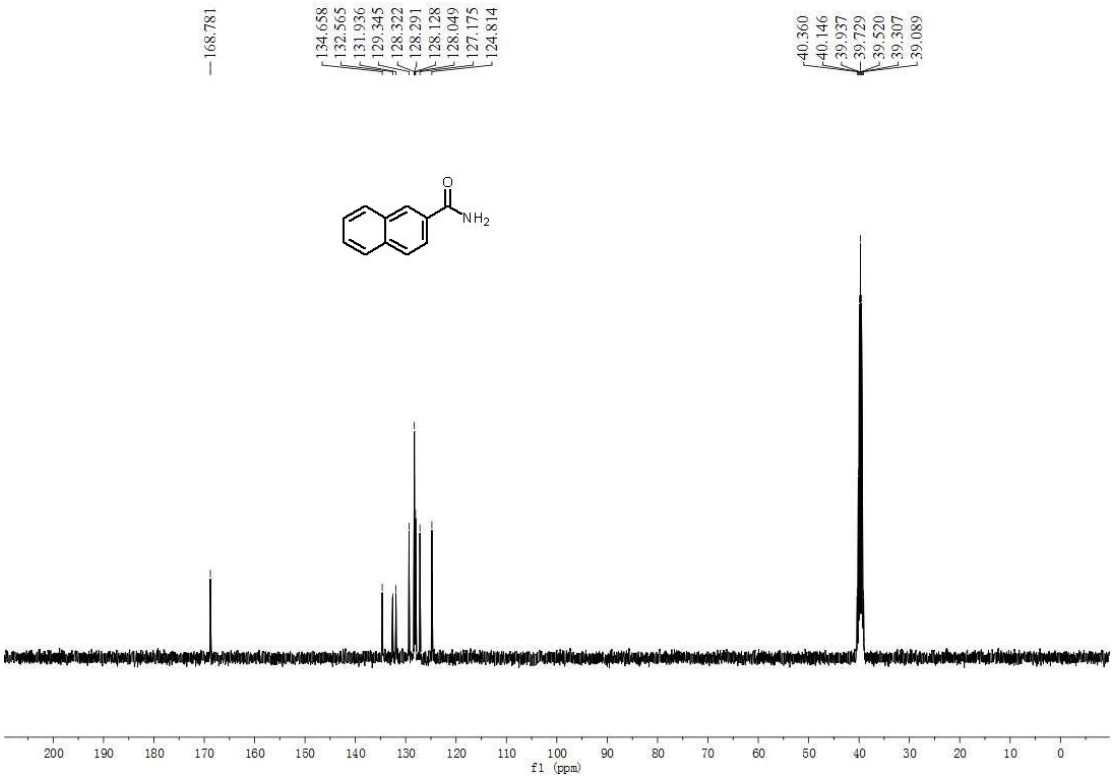

8.285
8.264
8.078
8.057
7.709
2.500
O2N
O
NH2
3.108
2.013
1.000
f1 (ppm)

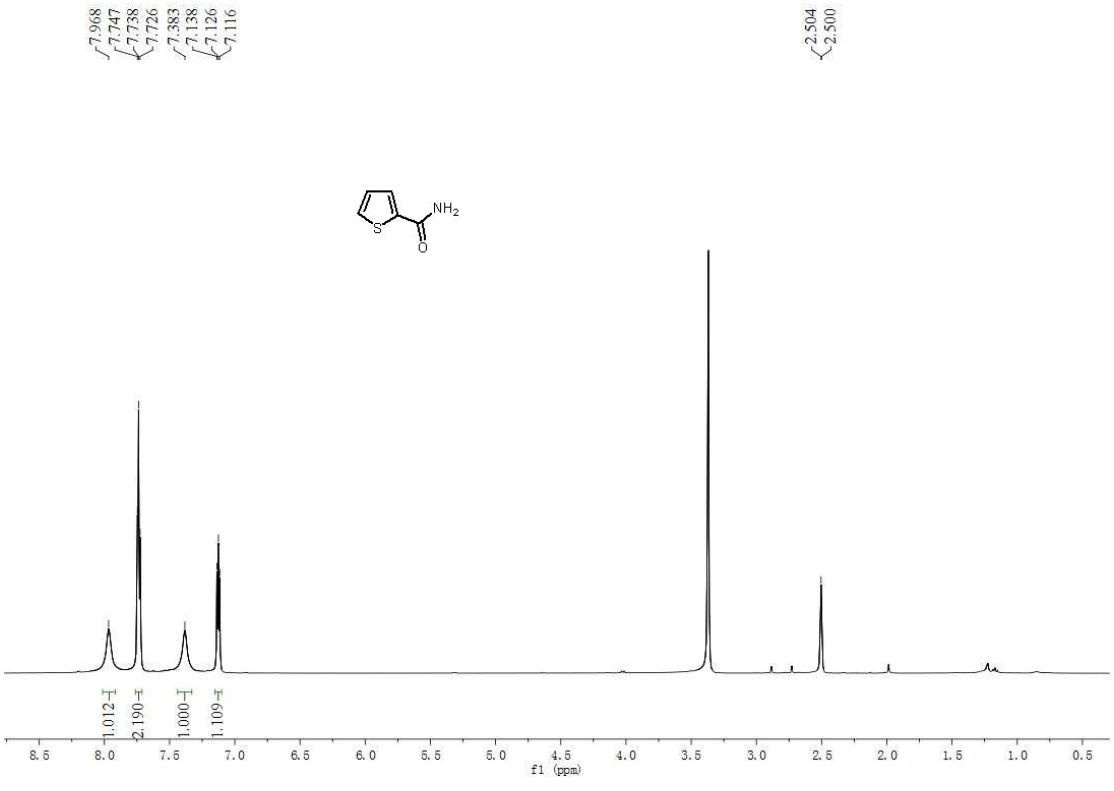

166.919
149.520
140.365
129.367
123.919
40.396
40.185
39.976
39.768
39.559
39.349
39.141
O2N
O
NH2
f1 (ppm)

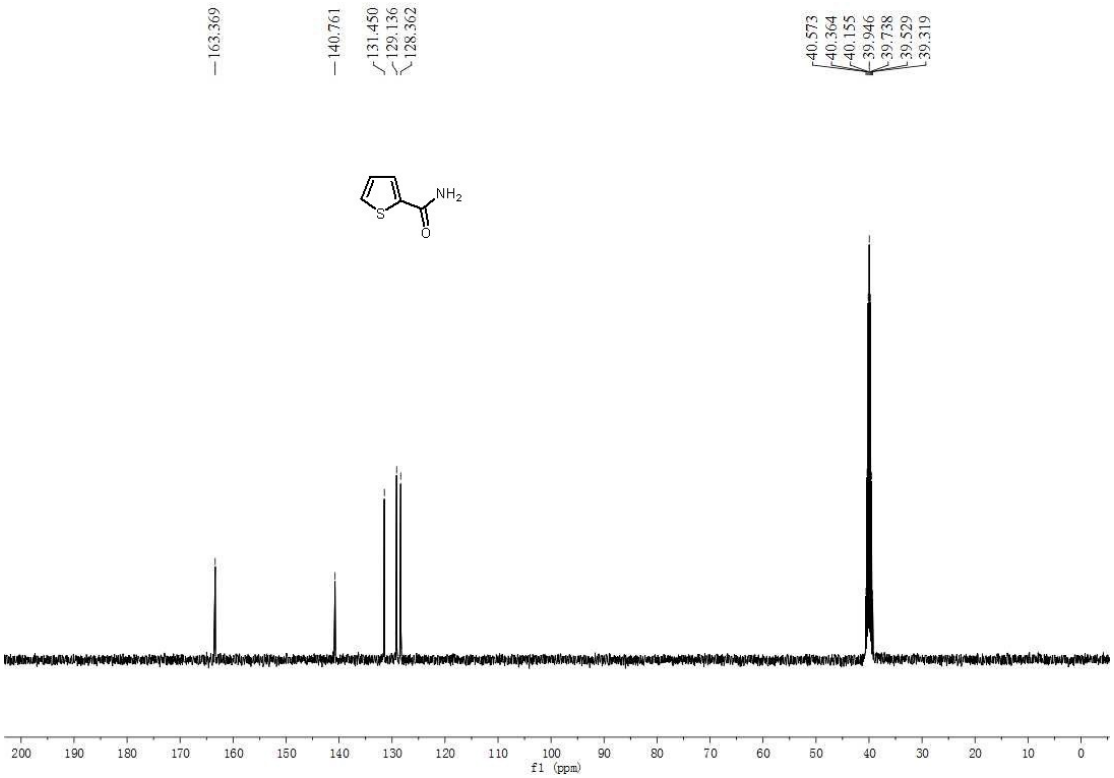

8.492
8.000
7.995
7.970
7.615
7.611
7.603
7.597
7.592
7.584
7.580
7.468
2.509
O
NH2
1.075
1.000
4.137
2.042
1.038
f1 (ppm)

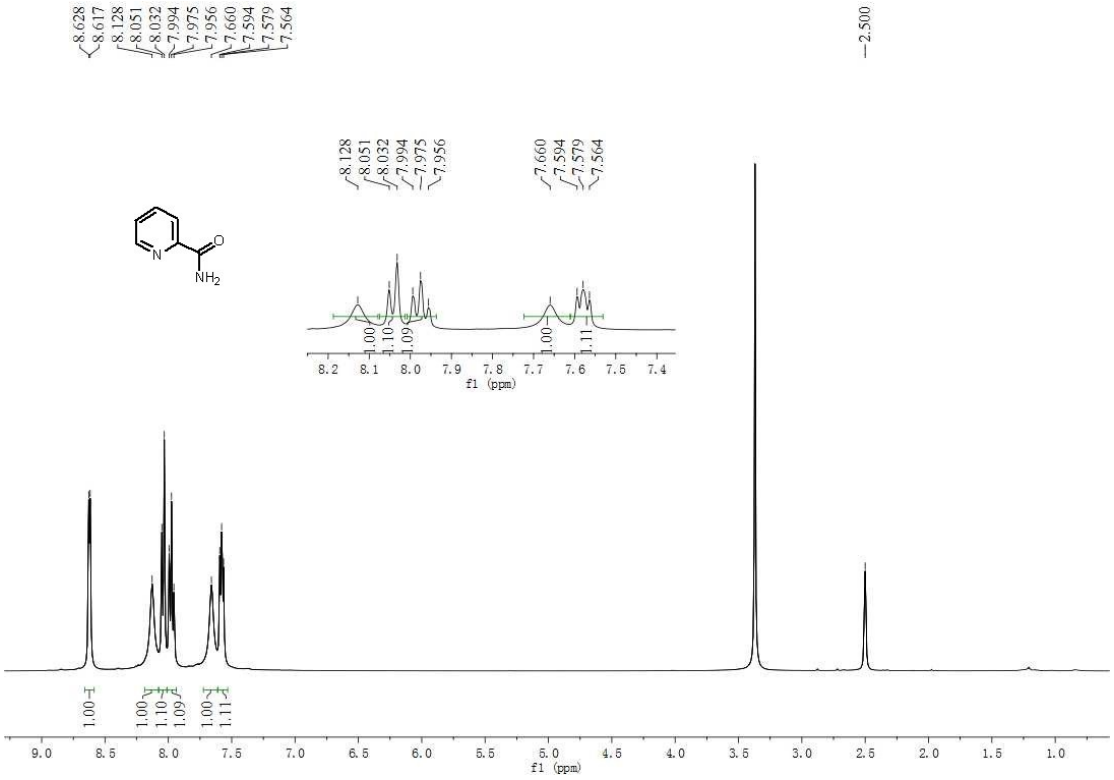

168.439
134.637
132.622
132.104
129.329
128.270
128.228
128.053
128.031
127.110
124.859
40.605
40.396
40.188
39.979
39.770
39.562
39.353
O
NH2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

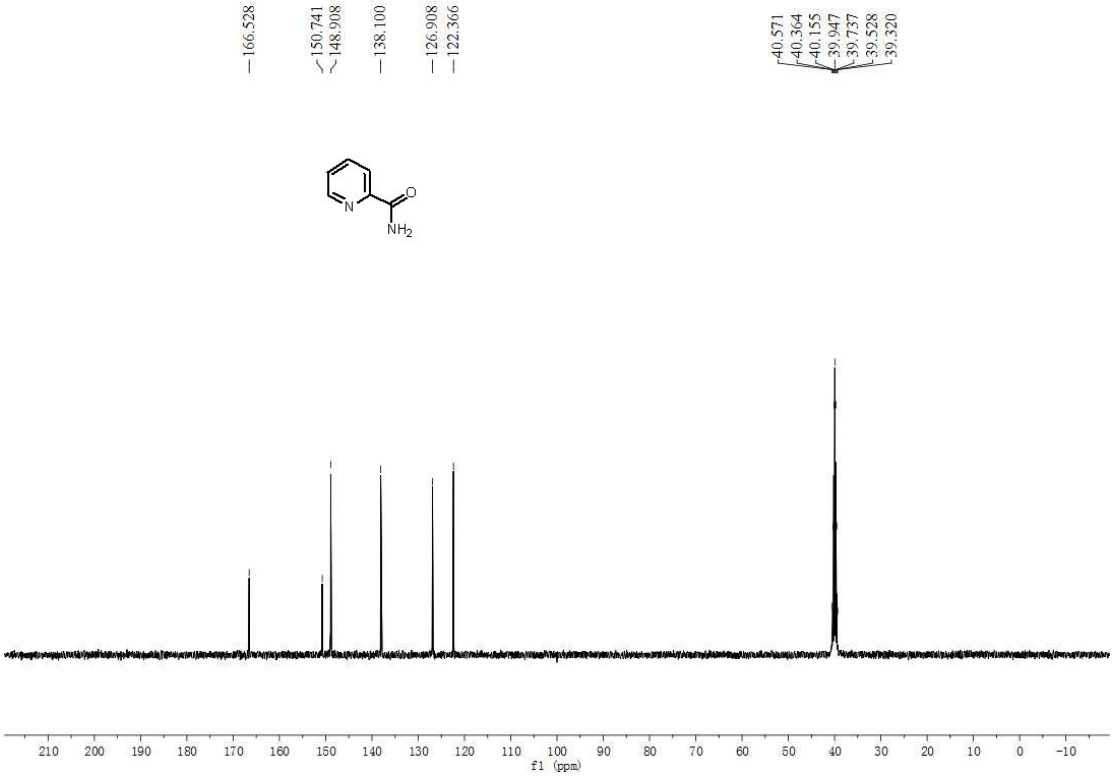

8.486
8.450
8.195
7.960
7.925
7.575
7.570
7.559
7.491
2.500
O
NH2
1.004
1.000
4.158
2.068
1.056
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

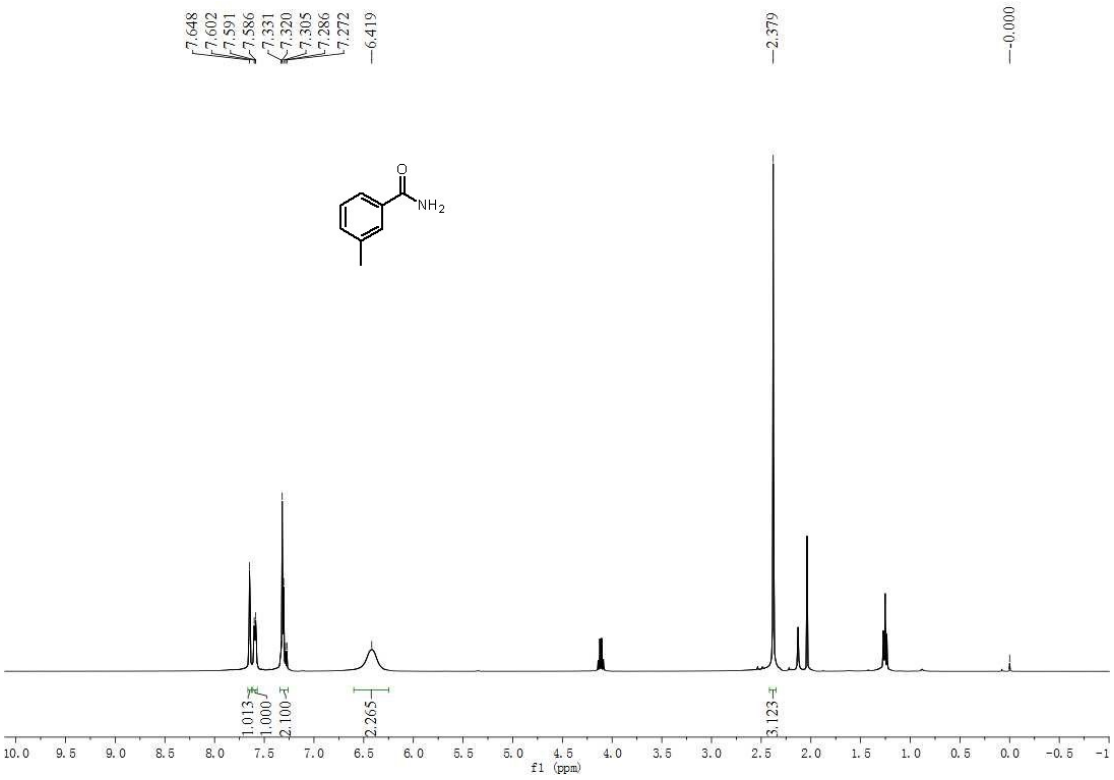

168.781
134.658
132.565
131.936
129.345
128.322
128.291
128.128
128.049
127.175
124.814
40.360
40.146
39.937
39.729
39.520
39.307
39.089
O
NH2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.968
7.747
7.738
7.726
7.383
7.138
7.126
7.116
2.504
2.500
NH2
S
O
1.012
2.190
1.000
1.109
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
f1 (ppm)


163.369
140.761
131.450
129.136
128.362
40.573
40.364
40.155
39.946
39.738
39.529
39.319
NH2
S
O
f1 (ppm)


8.628
8.617
8.128
8.051
8.032
7.994
7.975
7.956
7.660
7.594
7.579
7.564
2.500
N
O
NH2
1.00
1.10
1.09
1.00
1.11
f1 (ppm)


166.528
150.741
148.908
138.100
126.908
122.366
40.571
40.364
40.155
39.947
39.737
39.528
39.320
N
O
NH2
f1 (ppm)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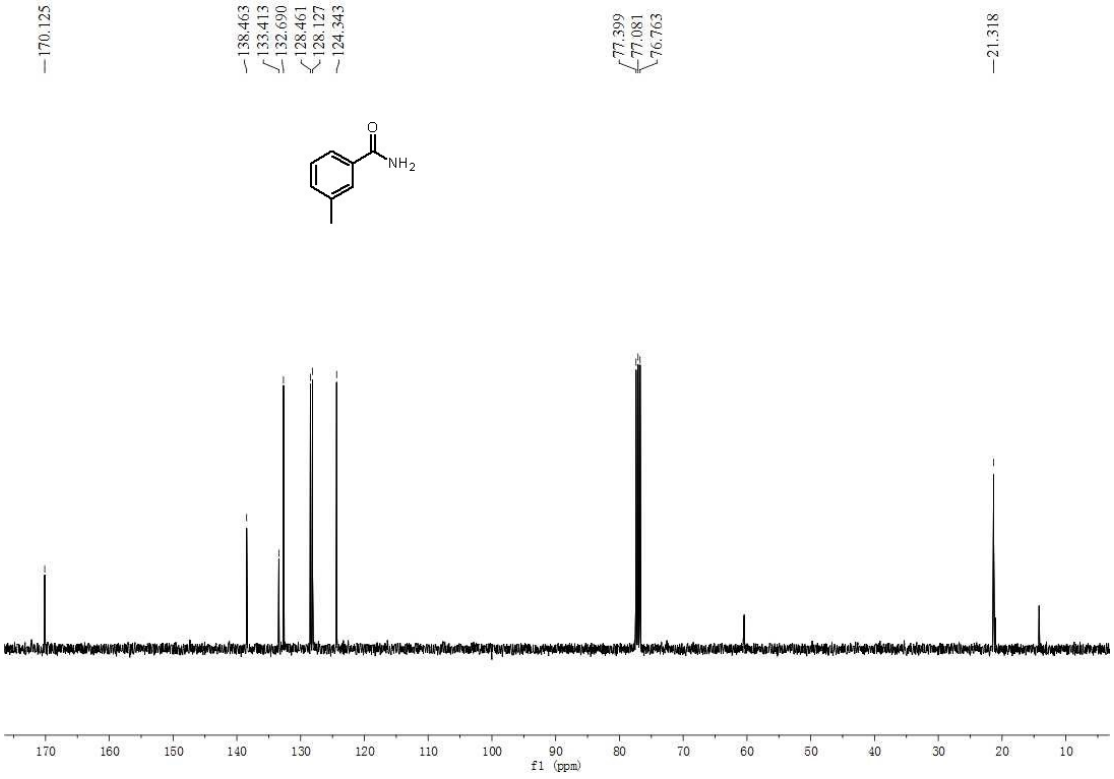
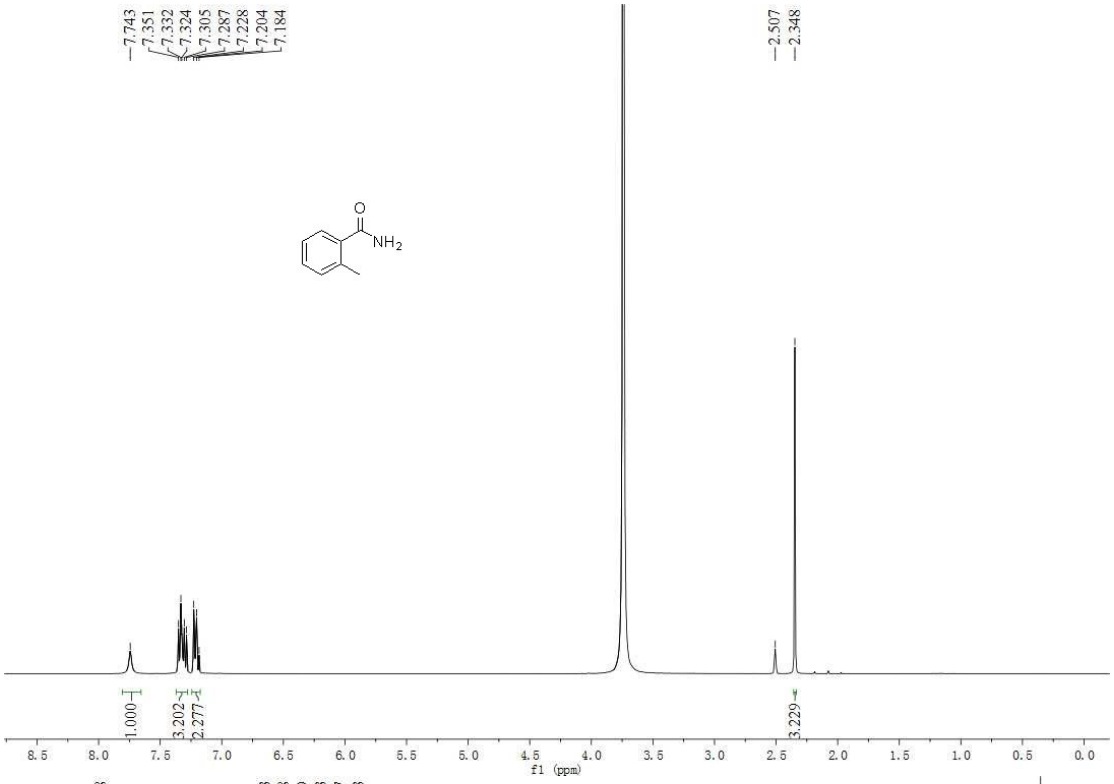
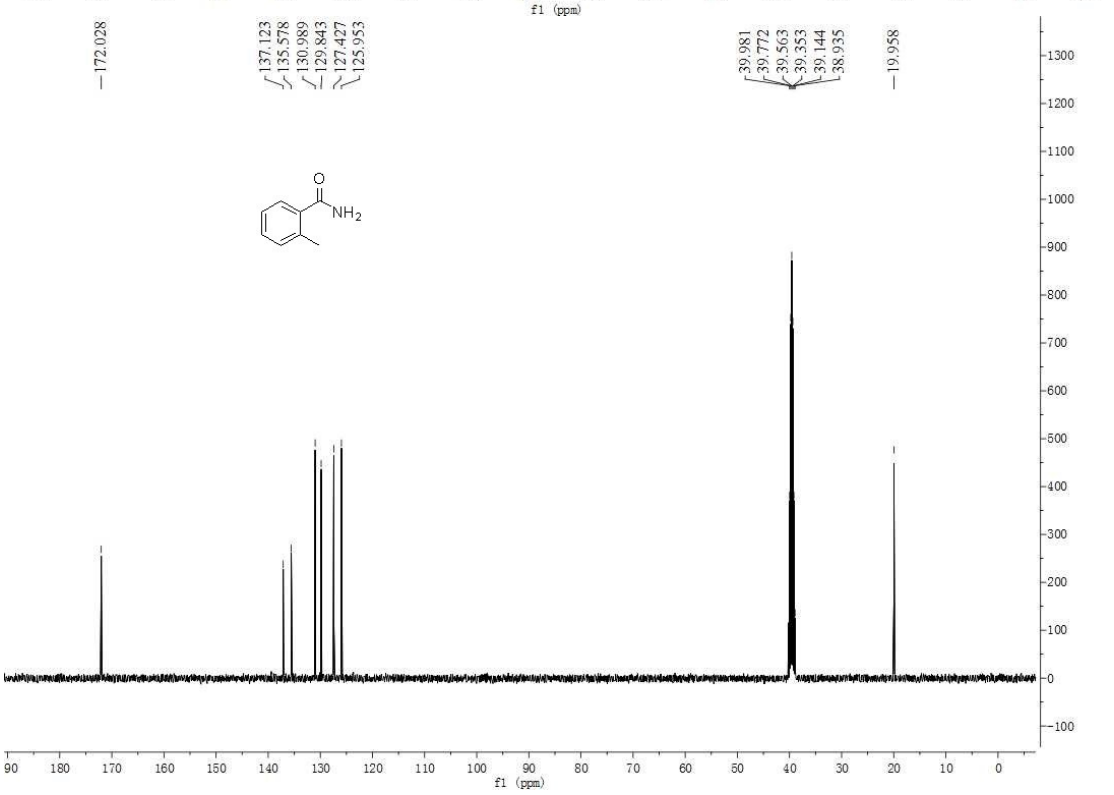
7.602
7.591
7.586
7.331
7.320
7.305
7.286
7.272
6.419
2.379
-0.000
O
NH2
1.013
1.000
2.100
2.265
3.123
f1 (ppm)


170.125
138.463
133.413
132.690
128.461
128.127
124.343
77.399
77.081
76.763
21.318
O
NH2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.743
7.351
7.332
7.324
7.305
7.287
7.228
7.204
7.184
2.507
2.348
O
NH2
1.000
3.202
2.277
3.229
f1 (ppm)


172.028
137.123
135.578
130.989
129.843
127.427
125.953
39.981
39.772
39.563
39.353
39.144
38.935
19.958
O
NH2
f1 (ppm)