Supporting information:

A novel and metal-free approach towards α-ketoamides using TBHP/I_2-promoted tandem reaction of amines with *β*-diketones via C–C bond cleavage

Xiaobin Zhang,[a] Min Wang,[a] Yicheng Zhang,[a] and Lei Wang*[a] [b]

[a] Department of Chemistry, Huaibei Normal University, Huaibei, Anhui 235000, P R China

Tel: + 86-561-3802-069 Fax: + 86-561-3090-518 E-mail: leiwang@chnu.edu.cn

[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P R China

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1. General considerations

All ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz Bruker FT-NMR spectrometers (400 MHz or 100 MHz, respectively). All chemical shifts are given as δ value (ppm) with reference to tetramethylsilane (TMS) as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet. The coupling constants, *J*, are reported in Hertz (Hz). High resolution mass spectroscopy data of the product were collected on a Waters Micromass GCT instrument. Products were purified by flash chromatography on 100–200 mesh silica gels, SiO_2. 1,3-Diaryl diketones were prepared by Claisen condensation of the corresponding ester and ketone (Hu, A.-G.; Lin, W.-B.; *Org. Lett*. **2005**, *7*, 455–58). Unless otherwise noted, the chemicals and solvents were purchased from commercial suppliers either from Aldrich, USA or Shanghai Chemical Company, China and were used without purification prior to use.

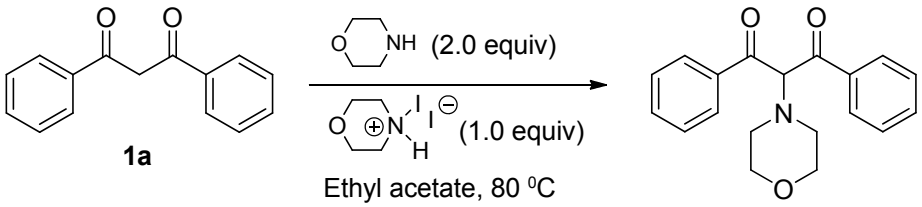
2. General procedure for the synthesis of α-ketoamides

A sealable reaction tube equipped with a magnetic stirrer bar was charged with *β*-diketone (0.5 mmol), secondary amine (1.5 mmol), I_2 (0.20 mmol), *tert*-butyl hydroperoxide (TBHP, 1.5 mmol). The reaction vessel was carried out at 80 °C. After stirring the mixture for 8 h, it was diluted with ethyl acetate, washed with water and brine, dried with Mg_2SO_4. After the solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel (eluant: hexane/ethyl acetate 2:1) to afford the corresponding product.

3. Synthesis of *N*-iodomorpholine-hydrogen iodide[1]

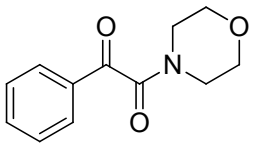
A solution of iodine (2.54 g, 10 mmol) in methanol (40 mL) was treated dropwise with morpholine (0.87 mL, 10 mmol). The solution was stirred for 4 h then solid was isolated by filtration. The solid was transferred to a round bottom flask and dried under vacuum. This procedure gave *N*-iodomorpholine-hydrogen iodide as an orange crystalline powder, which was used without further purification and characterization.

4. Synthesis of 2-morpholino-1,3-diphenylpropane-1,3-dione



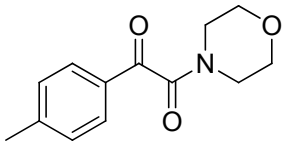
1,3-Diphenylpropane-1,3-dione (**1a**, 5.0 mmol, 1.12 g) and *N*-iodomorpholine-hydrogen iodide (10 mmol, 3.41 g) were added to a solution of morpholine (10 mmol, 0.87 g) in ethyl acetate (20 mL). The reaction was stirred for 8 h at 80 ^{0}C under N_2. After completion of reaction, the mixture was filtered through a thin layer of silica gel. The solvent was evaporated and the residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 7:1) to provide product 2-morpholino-1,3-diphenylpropane-1,3-dione (0.81 g, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 7.6 Hz, 4H), 7.57 (t, *J* = 7.2 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 4H), 5.56 (s, 1H), 3.72 (t, *J* = 4.8 Hz, 4H), 2.82 (t, *J* = 4.8 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.69, 135.82, 133.73, 129.08, 128.65, 78.39, 67.31, 51.09. HRMS (ESI) ([M]+H) Calcd. for $C_{19}H_{20}NO_3$: 310.1443, Found: 310.1438.

5. Characterization data for the products



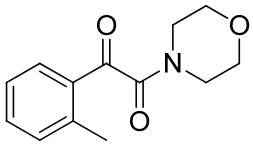
1-Morpholino-2-phenylethane-1,2-dione (3a):[2] Yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 2H), 3.79 (br, s, 4H), 3.65 (t, *J* = 4.8 Hz, 2H), 3.38 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.14, 165.47, 134.94, 133.05, 129.66, 129.10, 66.72, 66.64, 46.26, 41.63.



1-Morpholino-2-(*p*-tolyl)ethane-1,2-dione (3b):[3] Yellow oil.

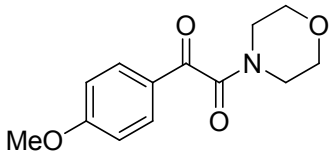
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 3.75 (br, s, 4H), 3.61 (t, *J* = 4.8 Hz, 2H), 3.34 (t, *J* = 4.8 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.88, 165.66, 146.25, 130.64, 129.80, 129.74, 66.69, 66.61, 46.23, 41.55, 21.86.



1-Morpholino-2-(*o*-tolyl)ethane-1,2-dione (3c):[3] Yellow oil.

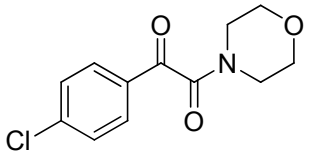
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.35–7.31 (m, 2H), 3.79 (br, s, 4H), 3.68 (t, *J* = 4.4 Hz, 2H), 3.40 (t, *J* = 4.4 Hz, 2H),

2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.08, 166.21, 141.60, 133.85, 132.68, 131.80, 131.55, 126.21, 66.66, 66.63, 46.28, 41.65, 21.76.



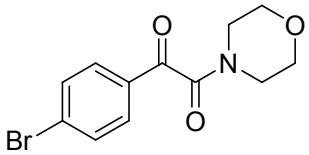
1-(4-Methoxyphenyl)-2-morpholinoethane-1,2-dione (3d):[2] Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 3.90 (s, 3H), 3.79 (br, s, 4H), 3.65 (t, *J* = 4.8 Hz, 2H), 3.38 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.82, 165.83, 165.05, 132.14, 126.12, 114.44, 66.75, 66.66, 55.67, 46.30, 41.57.



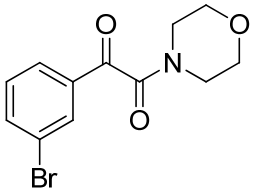
1-(4-Chlorophenyl)-2-morpholinoethane-1,2-dione (3e):[3] Yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 3.78 (br, s, 4H), 3.66 (t, *J* = 4.8 Hz, 2H), 3.38 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.67, 164.90, 141.59, 131.48, 131.02, 129.48, 66.72, 66.62, 46.28, 41.71.



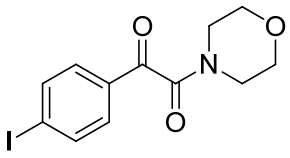
1-(4-Bromophenyl)-2-morpholinoethane-1,2-dione (3f):[3] Yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 3.79 (br, s, 4H), 3.67 (t, *J* = 4.8 Hz, 2H), 3.38 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.88, 164.86, 132.49, 131.90, 131.05, 129.67, 66.73, 66.64, 46.29, 41.72.



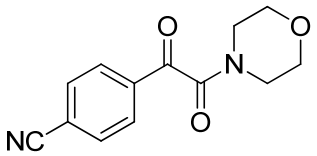
1-(3-Bromophenyl)-2-morpholinoethane-1,2-dione (3g): Yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (s, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 3.77 (br, s, 4H), 3.64 (t, *J* = 4.4 Hz, 2H), 3.36 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.46, 164.59, 137.69, 134.85, 132.33, 130.63, 128.31, 123.32, 66.69, 66.60, 46.27, 41.74. HRMS (EI) ($[M]^+$) Calcd. for $C_{12}H_{12}BrNO_3$: 297.0004, Found: 297.0001.



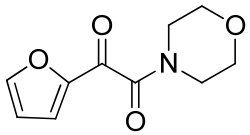
1-(4-Iodophenyl)-2-morpholinoethane-1,2-dione (3h): Yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 5.6 Hz, 2H), 7.64 (d, *J* = 5.2 Hz, 2H), 3.76 (br, s, 4H), 3.63 (br, s, 2H), 3.35 (br, s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.24, 164.83, 138.47, 132.37, 130.78, 103.61, 66.70, 66.61, 46.25, 41.70. HRMS (EI) ($[M]^+$) Calcd. for $C_{12}H_{12}INO_3$: 344.9864, Found: 344.9862.



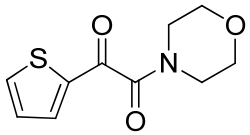
4-(2-Morpholino-2-oxoacetyl)benzonitrile (3i):[4] Yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 3.77 (br, s, 4H), 3.65 (t, *J* = 4.4 Hz, 2H), 3.38 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.05, 164.11, 136.04, 132.78, 130.04, 117.85, 117.54, 66.68, 66.57, 46.29, 41.86.



1-(Furan-2-yl)-2-morpholinoethane-1,2-dione(3j): Yellow oil.

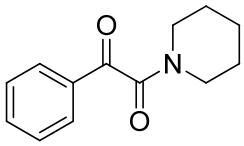
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (s, 1H), 7.40 (d, *J* = 3.6 Hz, 1H), 6.63–6.62 (m, 1H), 3.78 (d, *J* = 4.4 Hz, 2H), 3.75 (d, *J* = 4.0 Hz, 2H), 3.69 (t, *J* = 4.4 Hz, 2H), 3.49 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.77, 163.89, 150.23, 148.91, 122.56, 112.96, 66.77, 66.58, 46.36, 41.97. HRMS (EI) ($[M]^+$) Calcd. for $C_{10}H_{11}NO_4$: 209.0686, Found: 209.0688.



1-Morpholino-2-(thiophen-2-yl)ethane-1,2-dione (3k):[5] Yellow oil.

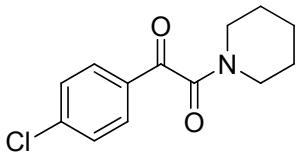
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 3.6 Hz, 1H), 7.81 (d, *J* = 4.8 Hz, 1H), 7.19 (t, *J* = 4.0 Hz, 1H), 3.77 (d, *J* = 4.0 Hz, 4H), 3.68 (t, *J* = 4.4 Hz, 2H), 3.49 (t, *J* =

4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.79, 164.33, 140.30, 136.74, 136.26, 128.71, 66.81, 66.62, 46.45, 41.96.



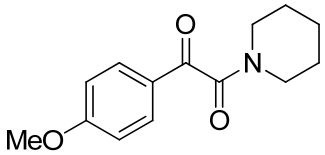
1-Phenyl-2-(piperidin-1-yl)ethane-1,2-dione (3l):[2] Light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 3.70 (br, s, 2H), 3.28 (t, *J* = 5.2 Hz, 2H), 1.69 (br, s, 4H), 1.54 (br, s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.92, 165.46, 134.62, 133.28, 129.54, 128.98, 47.03, 42.16, 26.18, 25.43, 24.35.



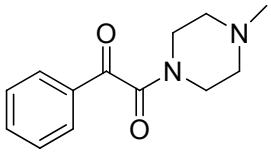
1-(4-Chlorophenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3m):[2] Yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 3.68 (br, s, 2H), 3.27 (t, *J* = 5.6 Hz, 2H), 1.68 (br, s, 4H), 1.54 (br, s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.49, 164.93, 141.22, 131.70, 130.90, 129.38, 47.04, 42.25, 26.23, 25.42, 24.32.



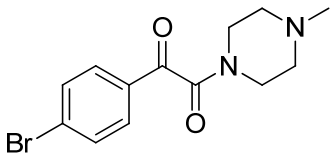
1-(4-Methoxyphenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3n):[2] Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H), 3.62 (br, s, 2H), 3.22 (t, *J* = 5.6 Hz, 2H), 1.62 (br, s, 4H), 1.47 (br, s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.53, 165.68, 164.67, 131.83, 126.21, 114.19, 55.49, 46.91, 41.94, 26.08, 25.32, 24.23.



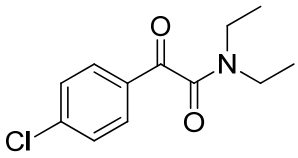
1-(4-Methylpiperazin-1-yl)-2-phenylethane-1,2-dione (3o): Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 7.2 Hz, 2H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 3.79 (t, *J* = 4.8 Hz, 2H), 3.37 (t, *J* = 4.8 Hz, 2H), 2.51 (t, *J* = 4.8 Hz, 2H), 2.38 (t, *J* = 4.8 Hz, 2H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.44, 165.38, 134.79, 133.13, 129.63, 129.03, 54.85, 54.40, 45.92, 45.71, 41.10. HRMS (ESI) ([M]+H) Calcd. for $C_{13}H_{17}N_2O_2$: 233.1290, Found: 233.1285.



1-(4-Bromophenyl)-2-(4-methylpiperazin-1-yl)ethane-1,2-dione (3p): Yellow solid.

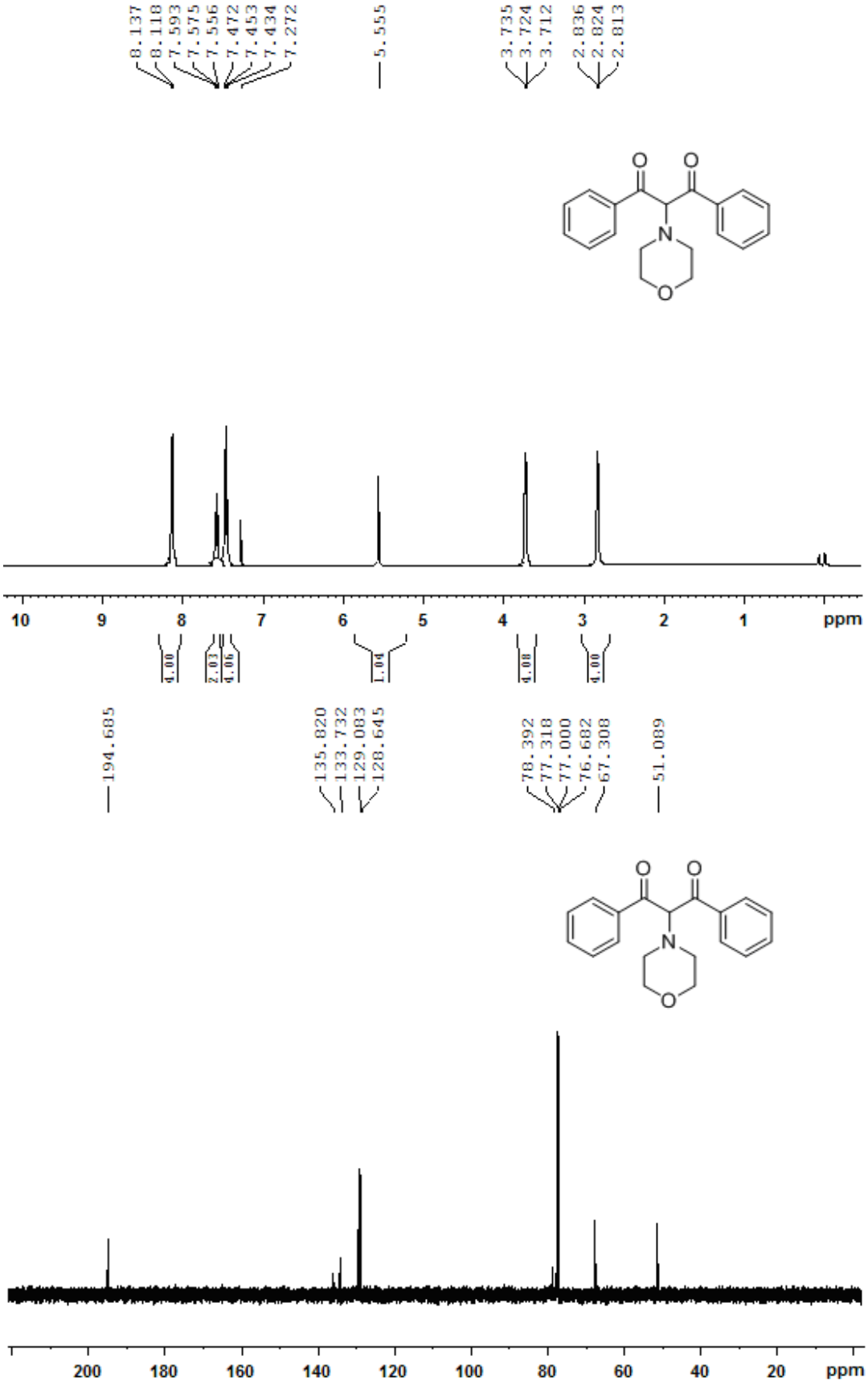
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.8 Hz, 2H), 3.81 (t, *J* = 4.8 Hz, 2H), 3.39 (t, *J* = 4.8 Hz, 2H), 2.55 (t, *J* = 4.8 Hz, 2H), 2.42 (t, *J* = 4.8 Hz, 2H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.18, 164.82, 132.44, 131.03, 54.84, 54.35, 45.84, 45.66, 41.13. HRMS (EI) ($[M]^+$) Calcd. for $C_{12}H_{12}INO_3$: 310.0317, Found: 344.0314.

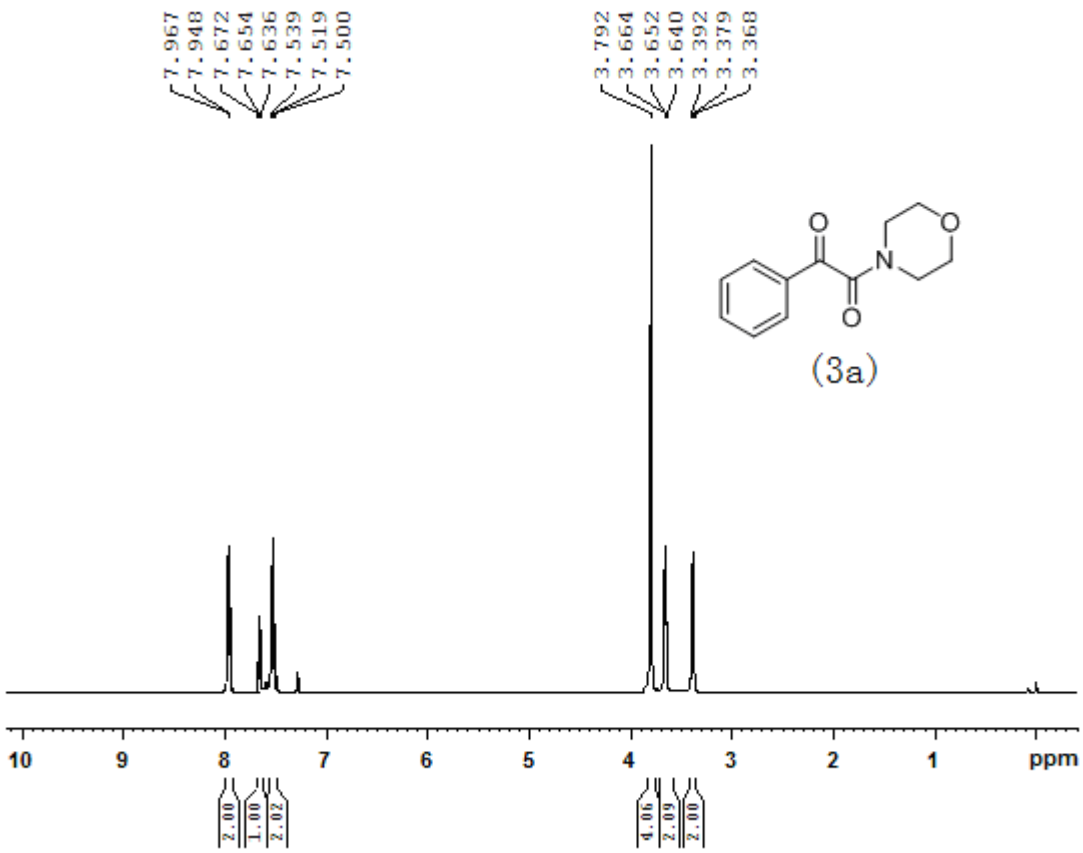


2-(4-Chlorophenyl)-*N*,*N*-diethyl-2-oxoacetamide (3q):[6] Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 3.56 (q, *J* = 7.2 Hz, 2H), 3.24 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.17 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.12, 166.22, 141.14, 131.74, 130.96, 129.34, 42.14, 38.95, 14.16, 12.80.

6. ^{1}H and ^{13}C NMR spectra of the products

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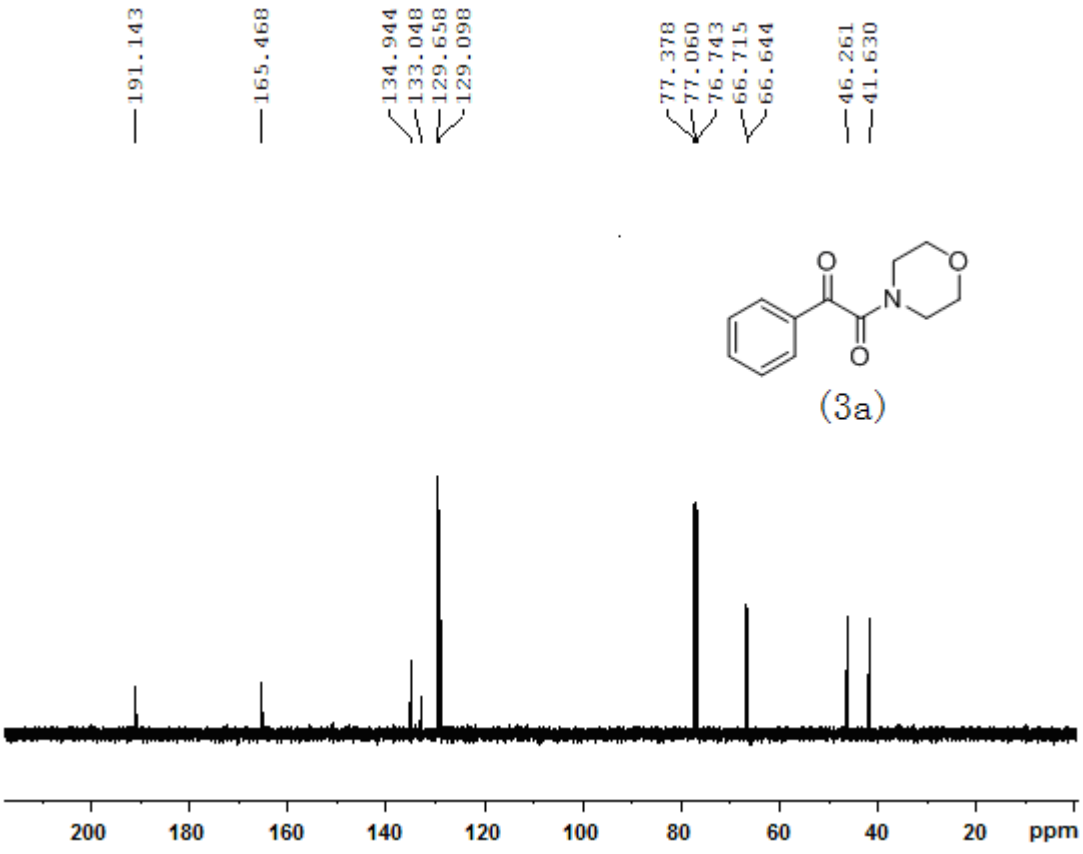
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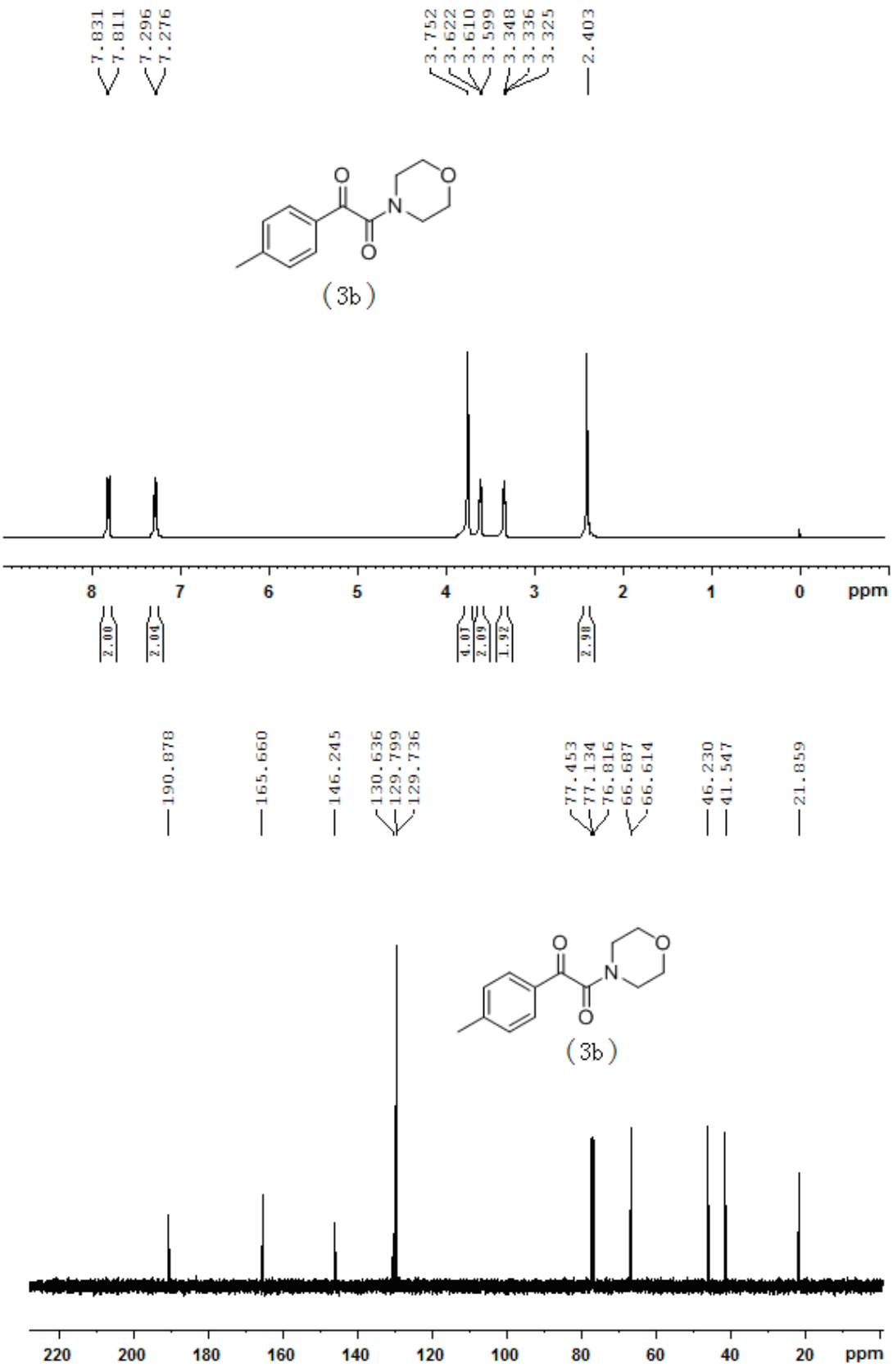

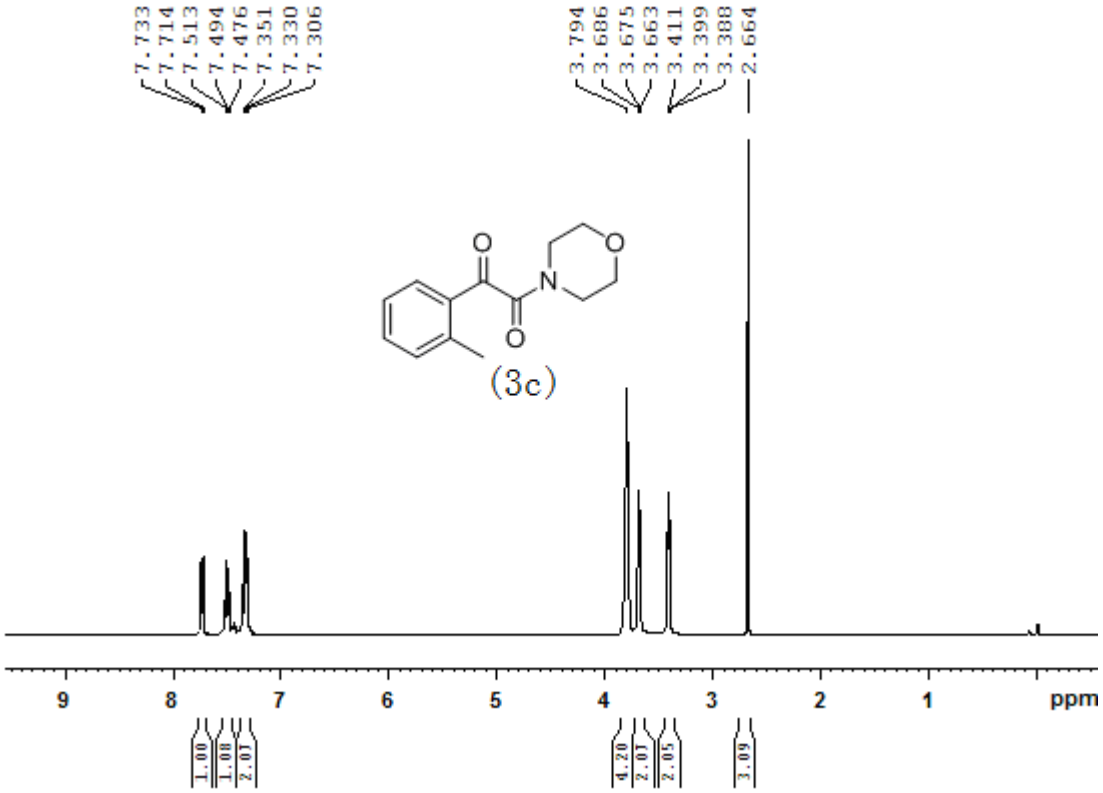
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7.494
7.476
7.351
7.330
7.306
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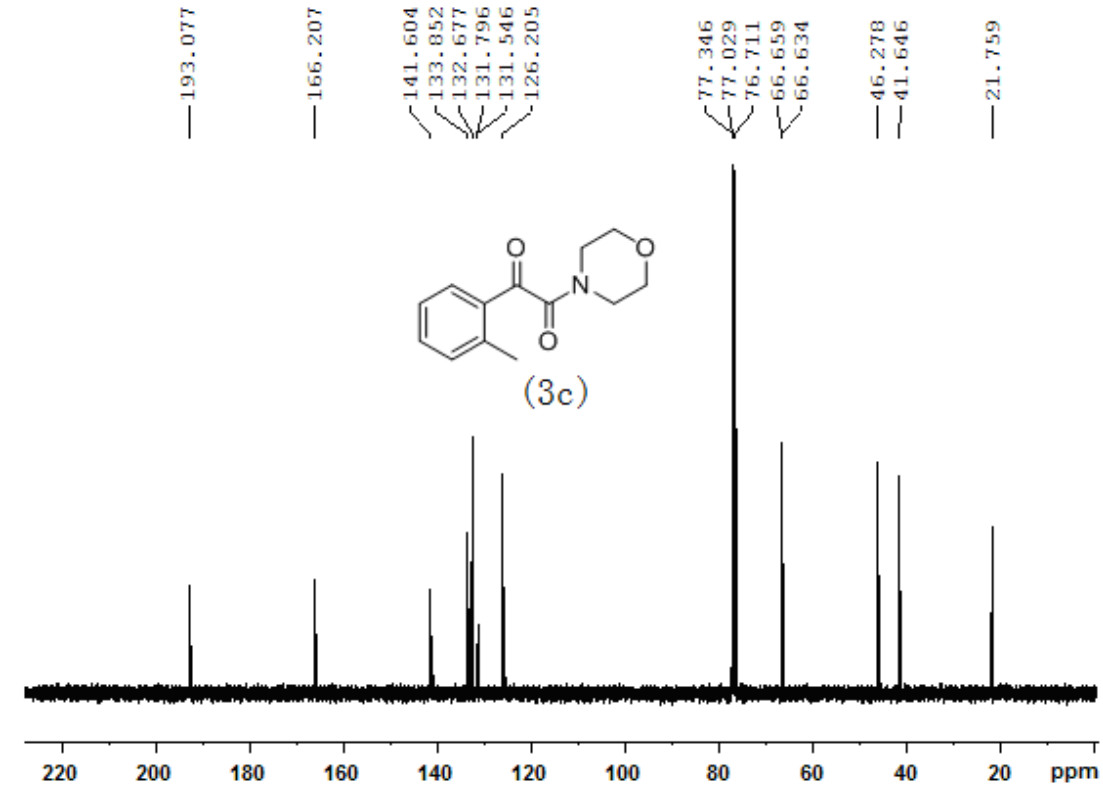
3.686
3.675
3.663
3.411
3.399
3.388
2.664
(3c)
9
8
7
6
5
4
3
2
1
ppm
1.00
1.08
2.07
4.20
2.01
2.05
3.09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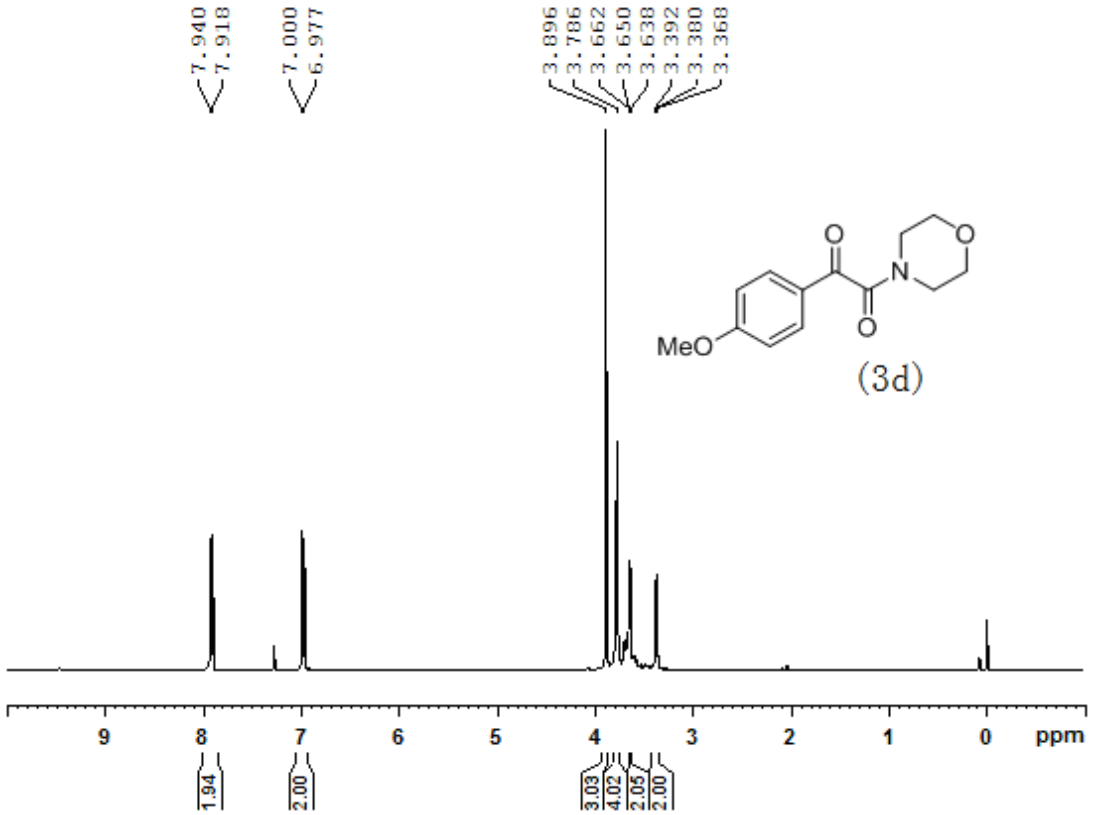
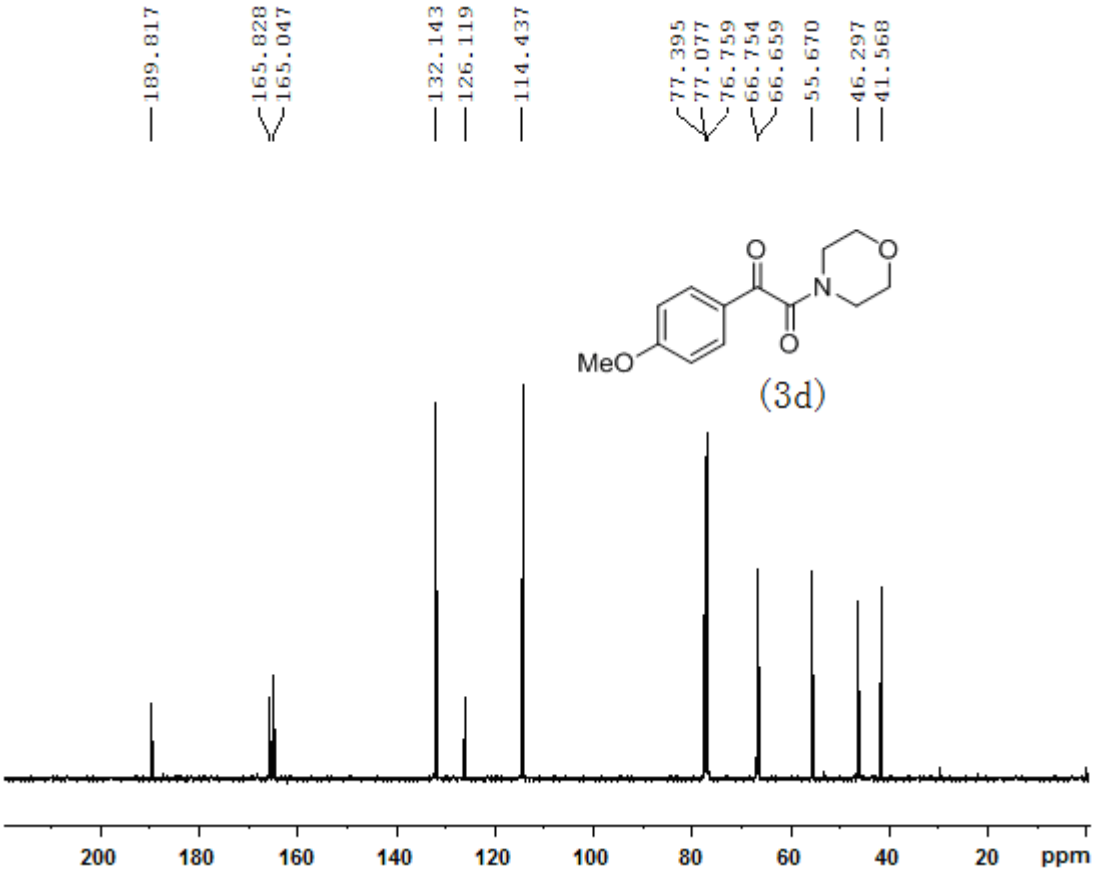
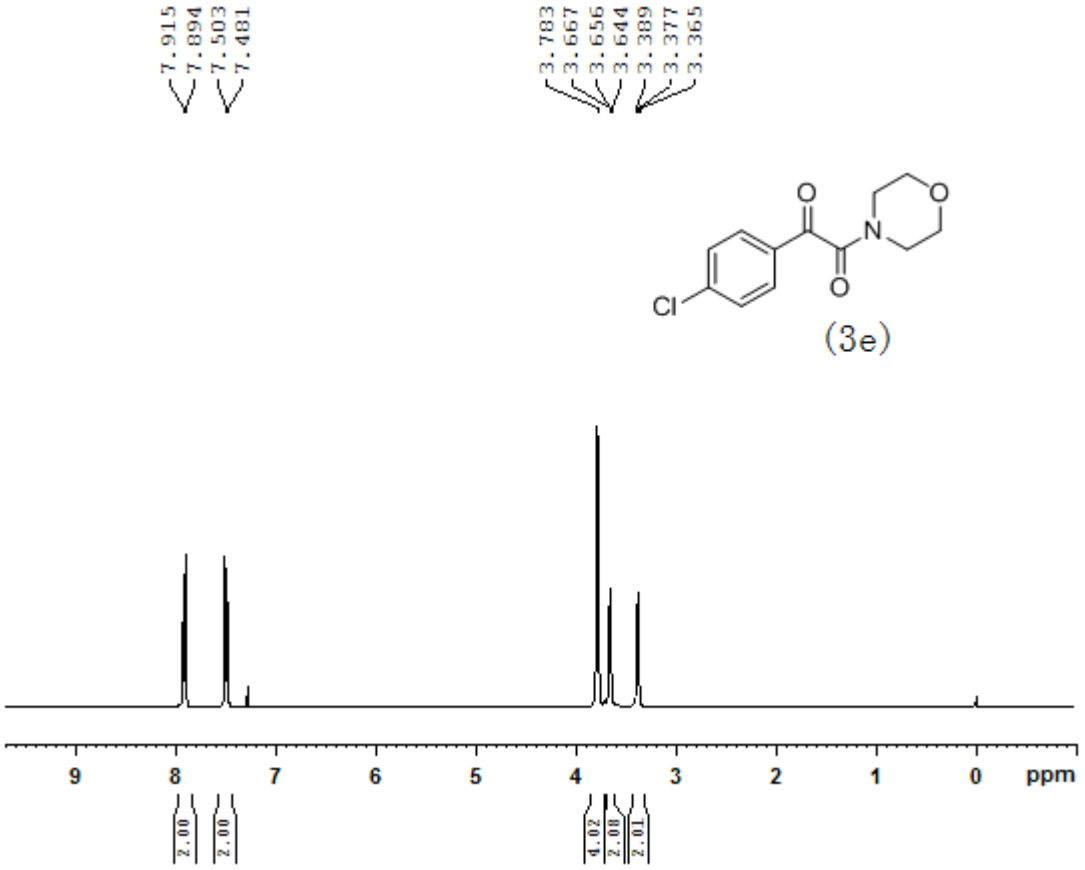
141.604
133.852
132.677
131.796
131.546
126.205
77.346
77.029
76.711
66.659
66.634
46.278
41.646
21.759
(3c)
220
200
180
160
140
120
100
80
60
40
20
ppm



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7.894
7.503
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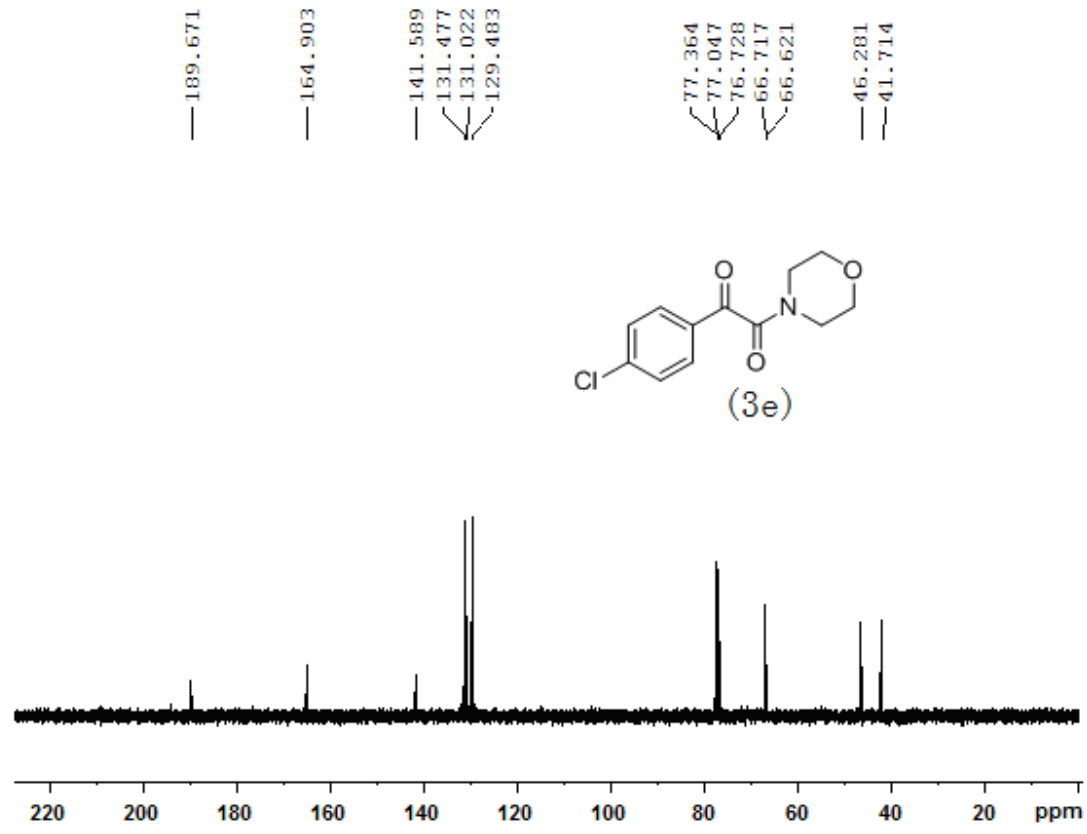
3.783
3.667
3.656
3.644
3.389
3.377
3.365
Cl
(3e)
9
8
7
6
5
4
3
2
1
0
ppm
2.00
2.00
4.02
2.08
2.01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164.903
141.589
131.477
131.022
129.483
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77.047
76.728
66.717
66.621
46.281
41.714
Cl
(3e)
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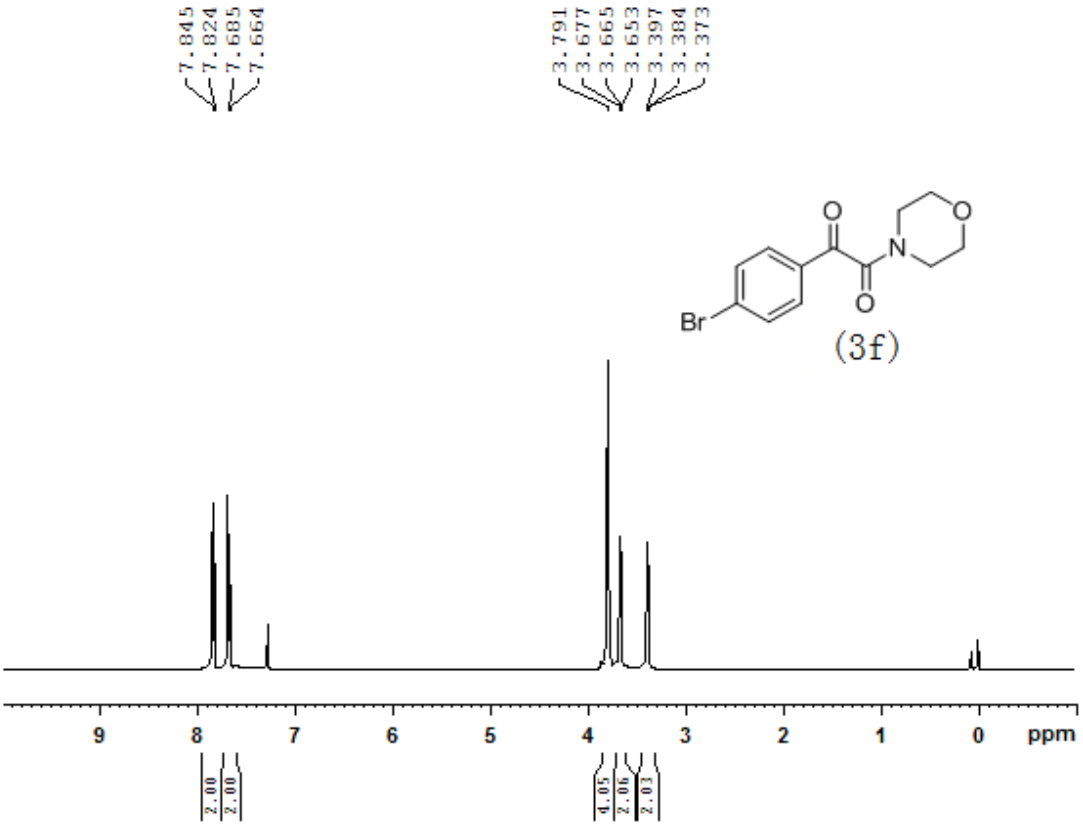
200
180
160
140
120
100
80
60
40
20
ppm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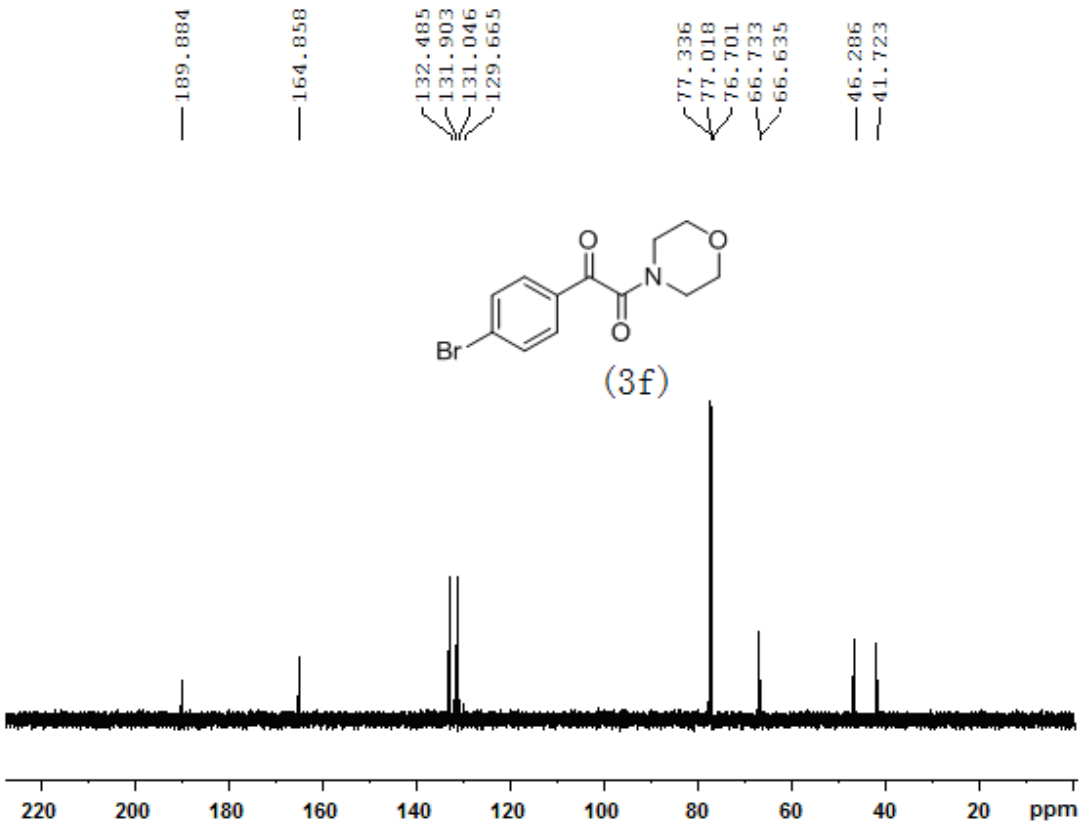
7.824
7.685
7.664
3.791
3.677
3.665
3.653
3.397
3.384
3.373
Br
O
N
O
O
(3f)
9
8
7
6
5
4
3
2
1
0
ppm
2.00
2.00
4.05
2.06
2.03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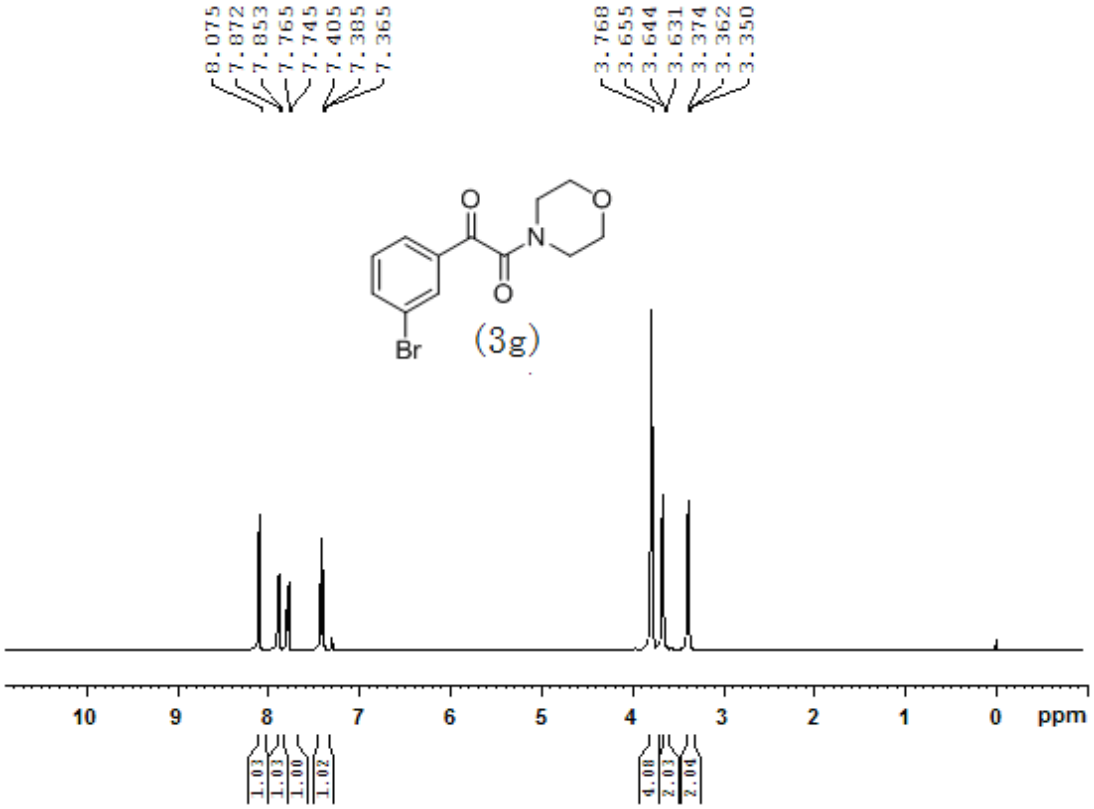
131.903
131.046
129.665
77.336
77.018
76.701
66.733
66.635
46.286
41.723
Br
O
N
O
O
(3f)
220
200
180
160
140
120
100
80
60
40
20
ppm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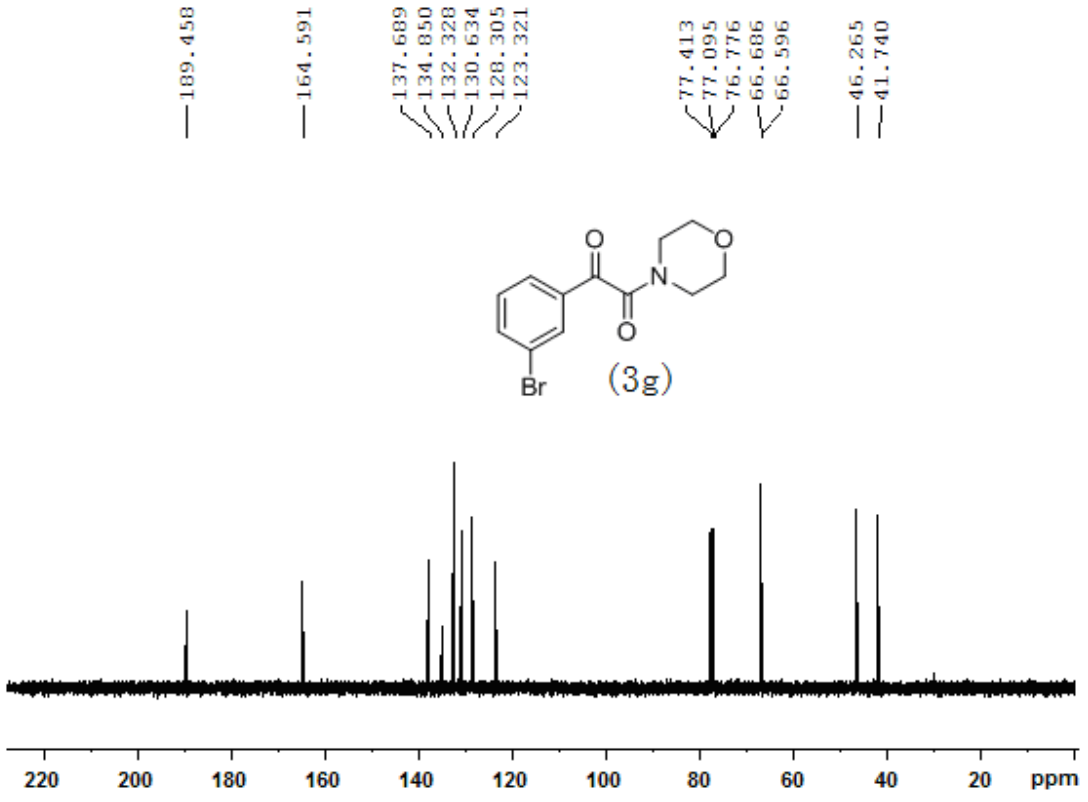
7.872
7.853
7.765
7.745
7.405
7.385
7.365
3.768
3.655
3.644
3.631
3.374
3.362
3.350
O
O
N
O
Br
(3g)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.03
1.03
1.00
1.02
4.08
2.03
2.04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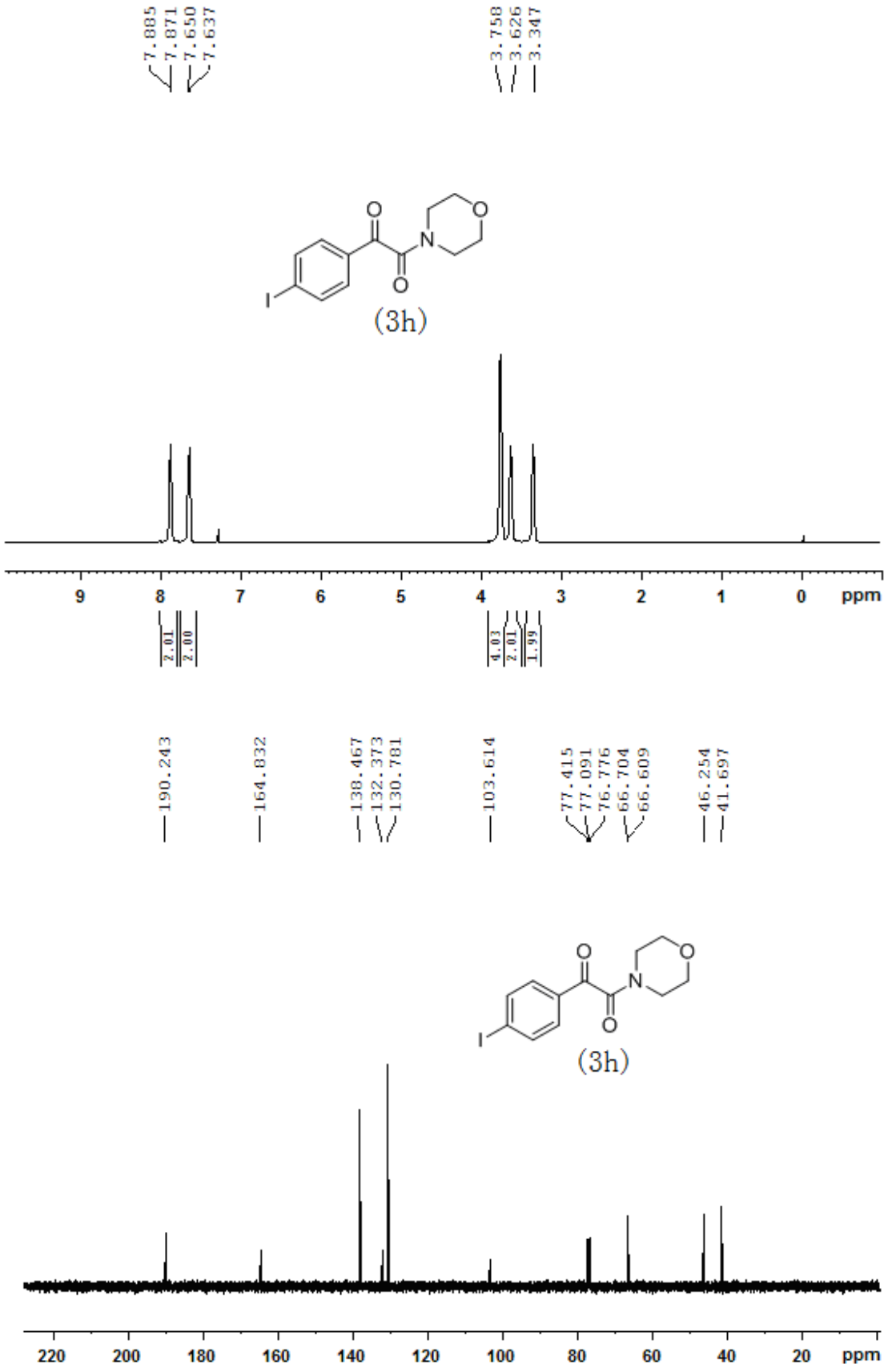
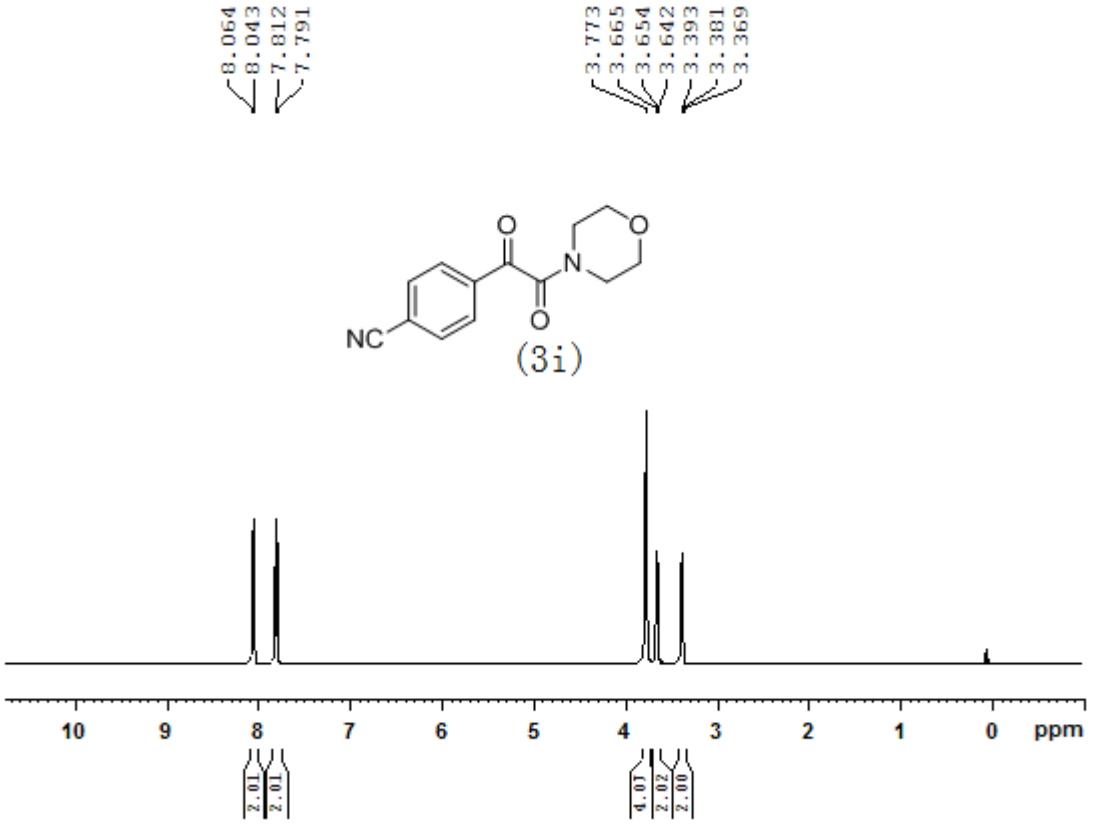
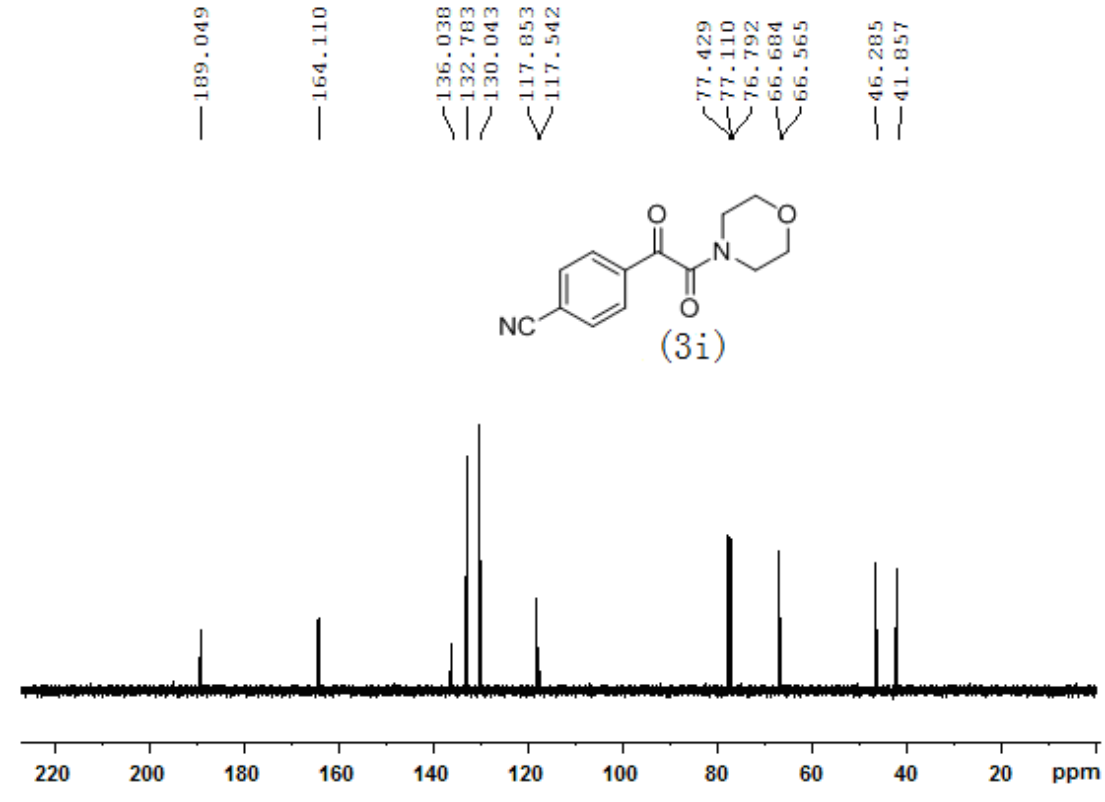
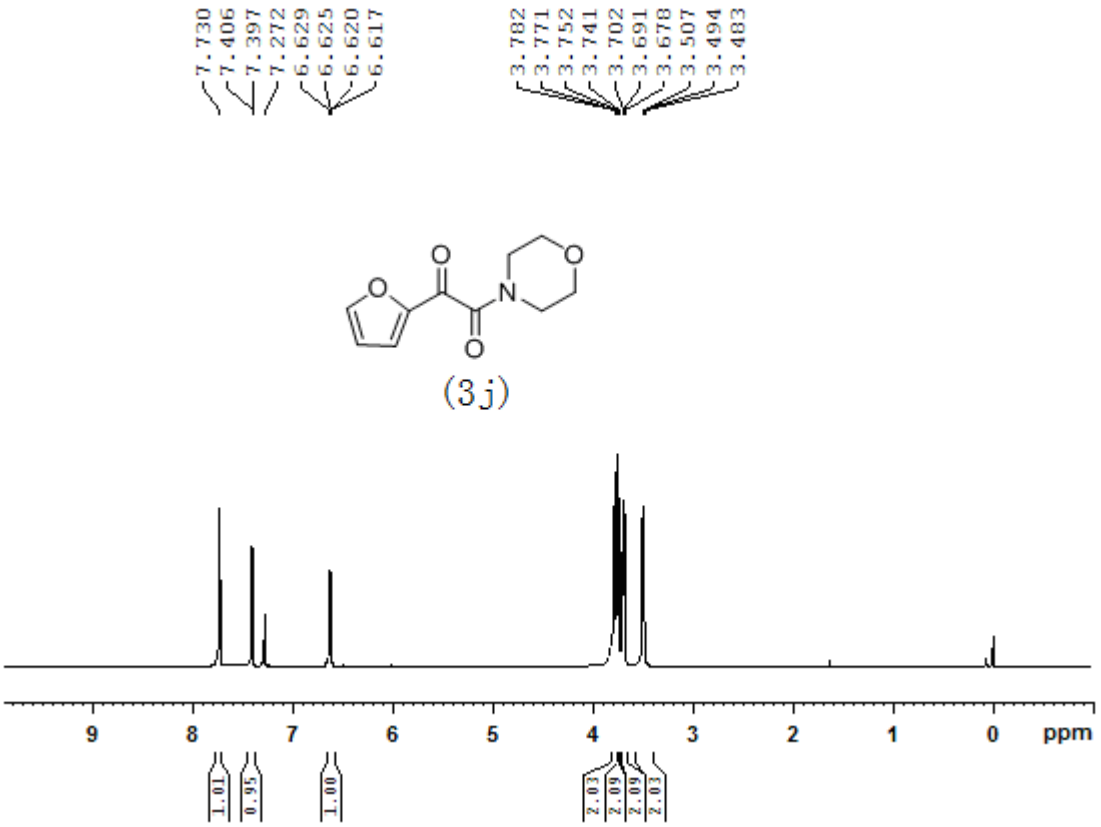
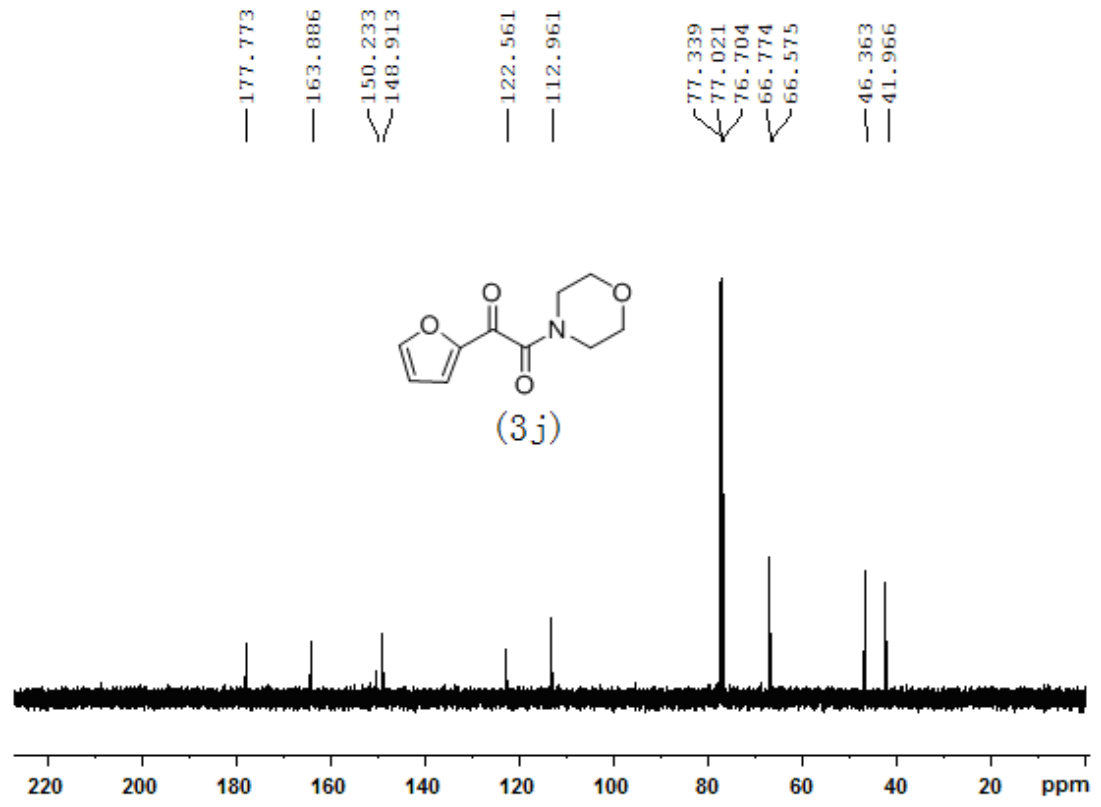
137.689
134.850
132.328
130.634
128.305
123.321
77.413
77.095
76.776
66.686
66.596
46.265
41.740
O
O
N
O
Br
(3g)
220
200
180
160
140
120
100
80
60
40
20
ppm




8.064
8.043
7.812
7.791
3.773
3.665
3.654
3.642
3.393
3.381
3.369
O
O
N
O
NC
(3i)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.01
2.01
4.07
2.02
2.00


189.049
164.110
136.038
132.783
130.043
117.853
117.542
77.429
77.110
76.792
66.684
66.565
46.285
41.857
O
O
N
O
NC
(3i)
220
200
180
160
140
120
100
80
60
40
20
ppm


7.730
7.406
7.397
7.272
6.629
6.625
6.620
6.617
3.782
3.771
3.752
3.741
3.702
3.691
3.678
3.507
3.494
3.483
O
O
N
O
O
(3j)
9
8
7
6
5
4
3
2
1
0
ppm
1.01
0.95
1.00
2.03
2.09
2.09
2.03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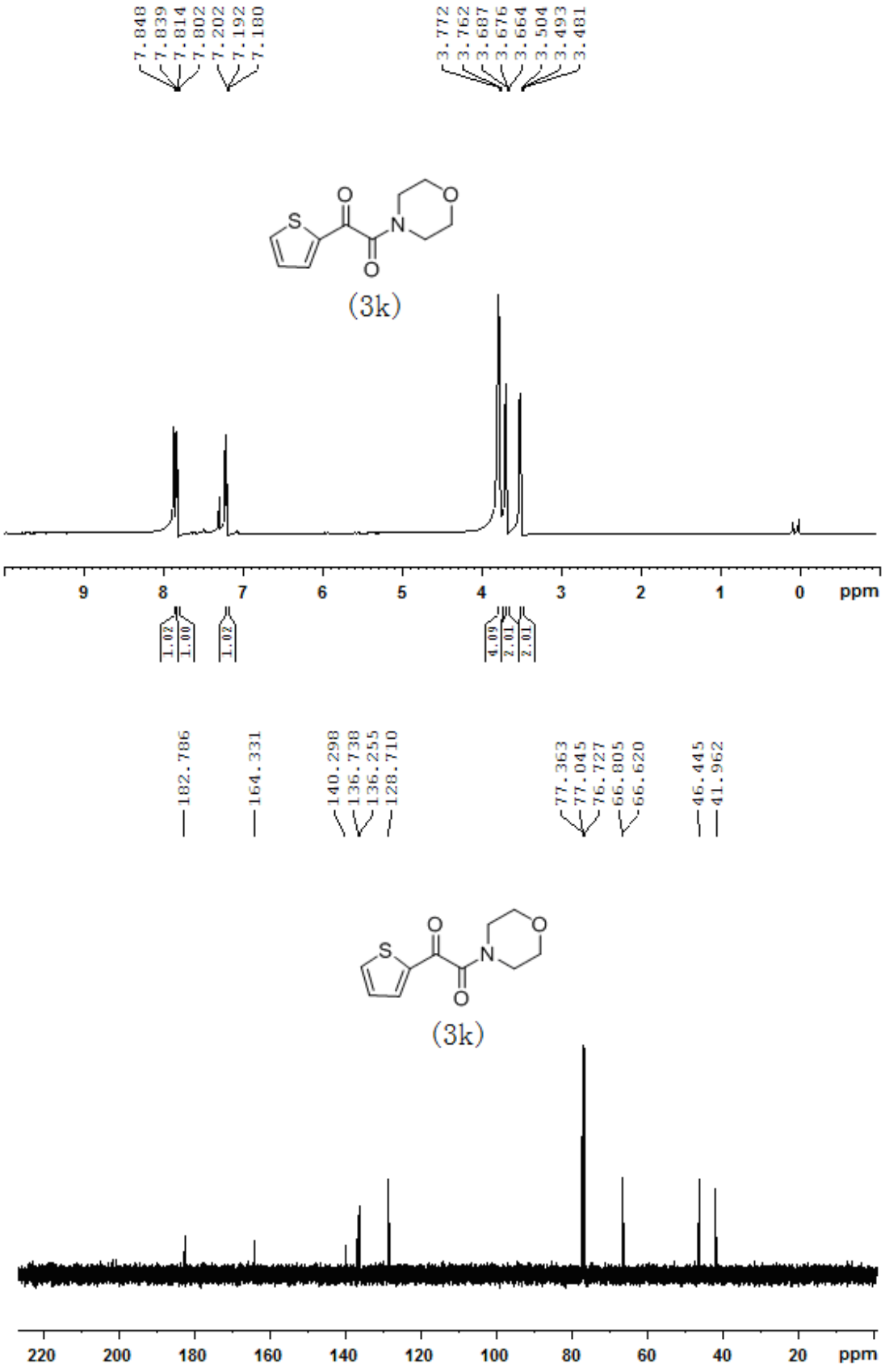
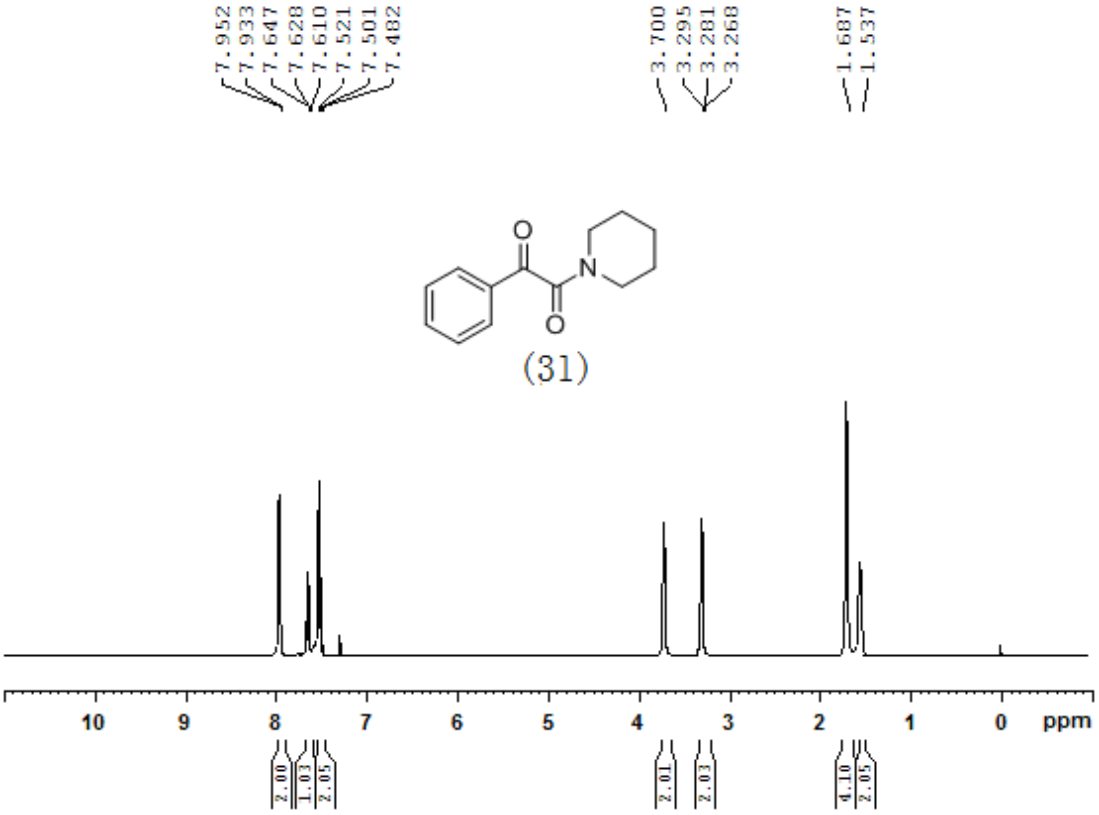
163.886
150.233
148.913
122.561
112.961
77.339
77.021
76.704
66.774
66.575
46.363
41.966
O
O
N
O
O
(3j)
220
200
180
160
140
120
100
80
60
40
20
ppm

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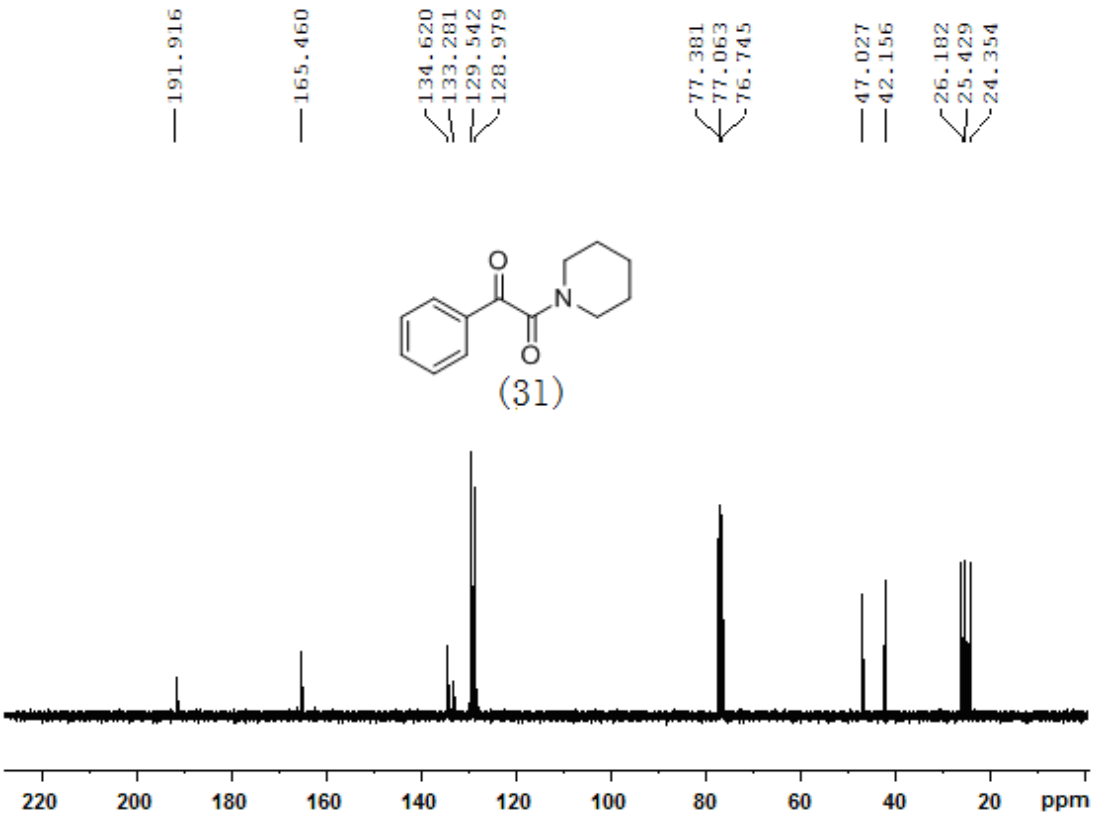
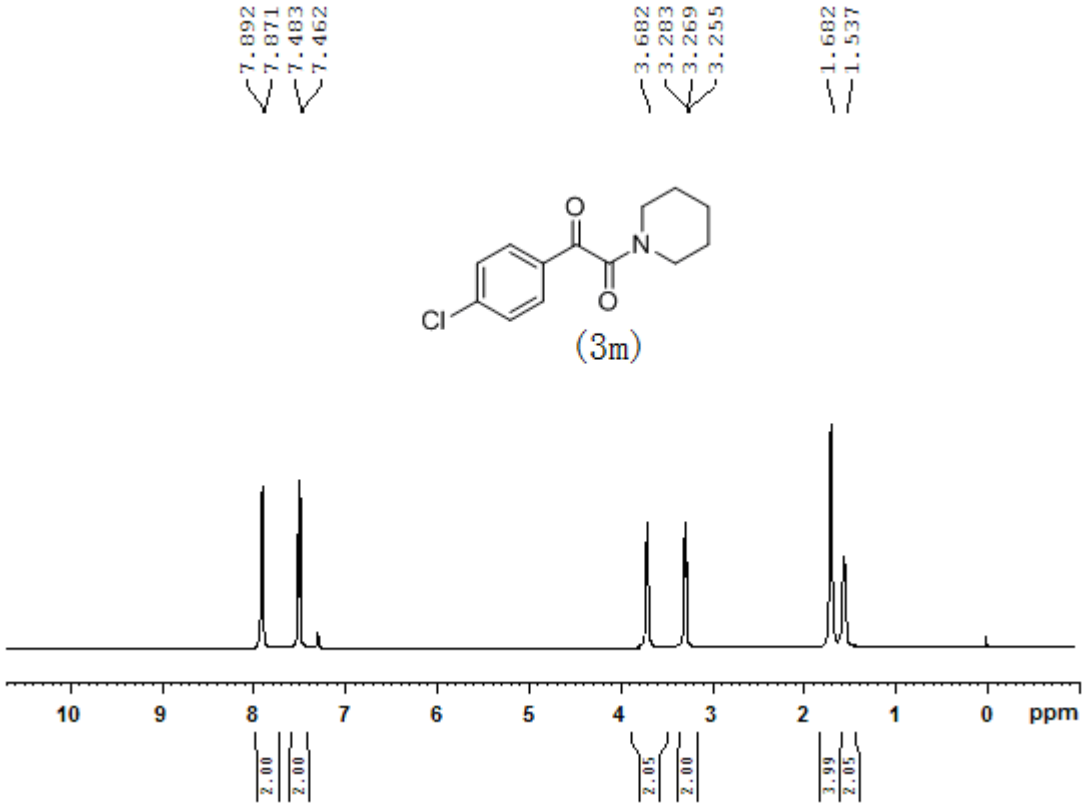
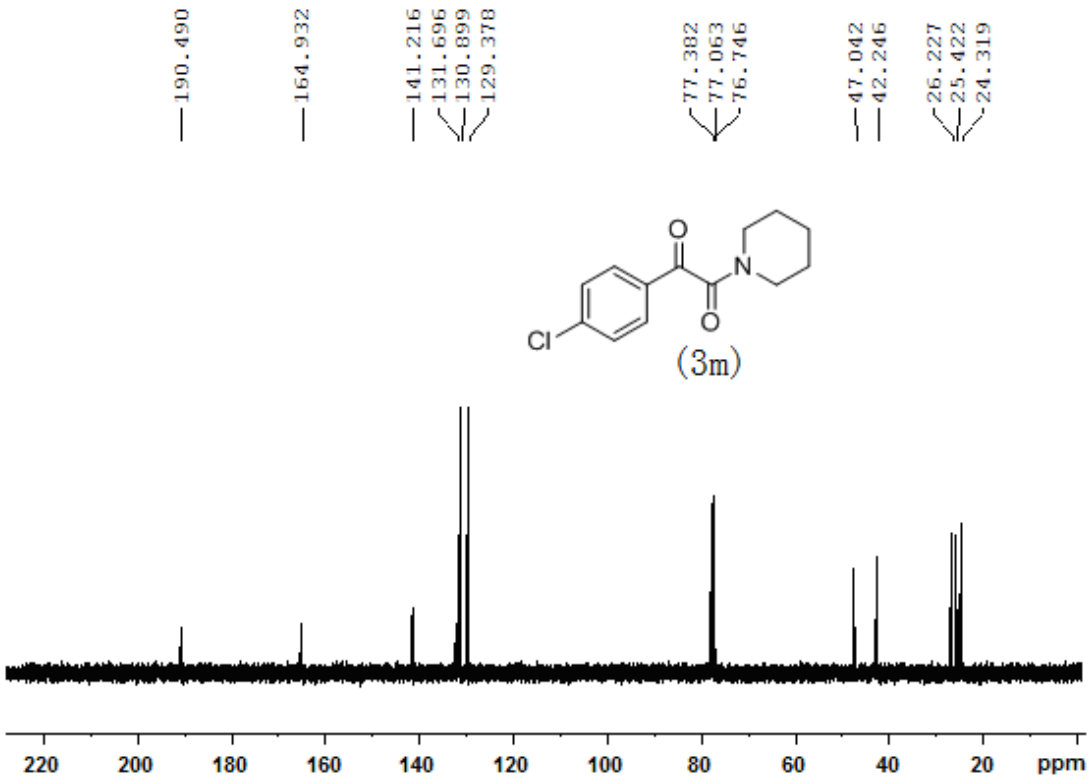
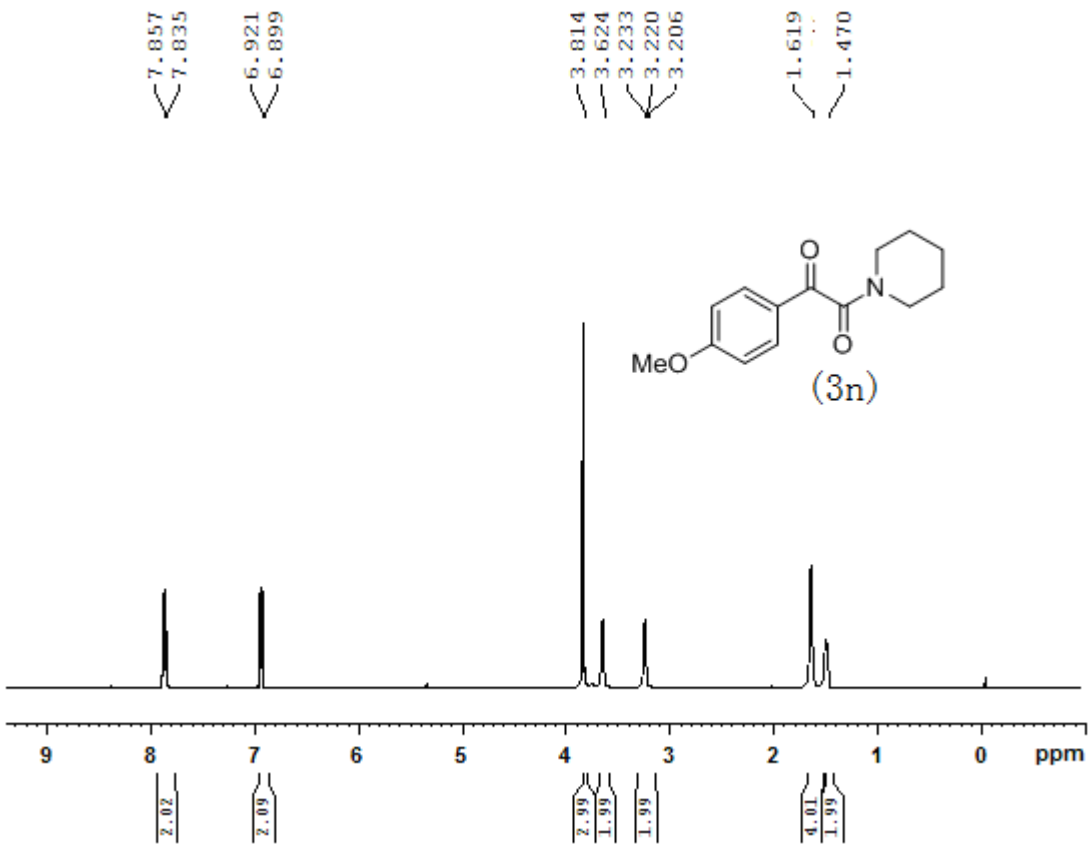
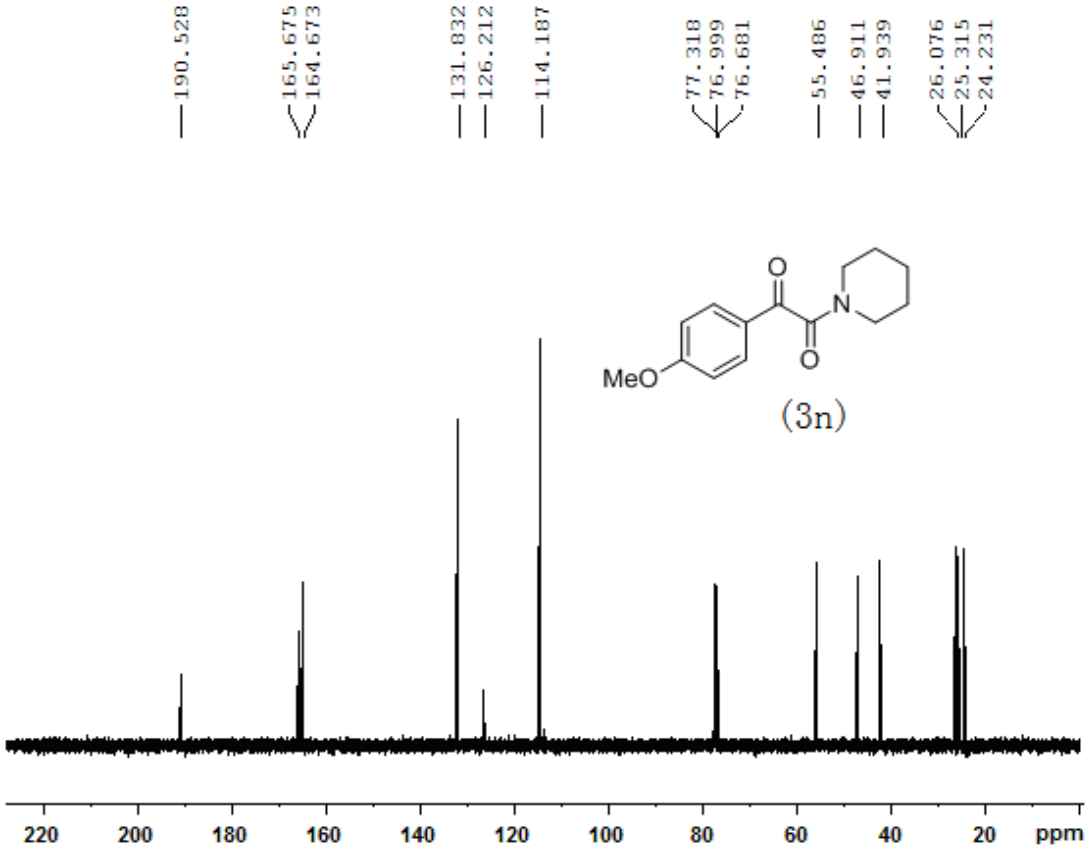
7.933
7.647
7.628
7.610
7.521
7.501
7.482
3.700
3.295
3.281
3.268
1.687
1.537
O
N
O
(31)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.00
1.03
2.05
2.01
2.03
4.10
2.05

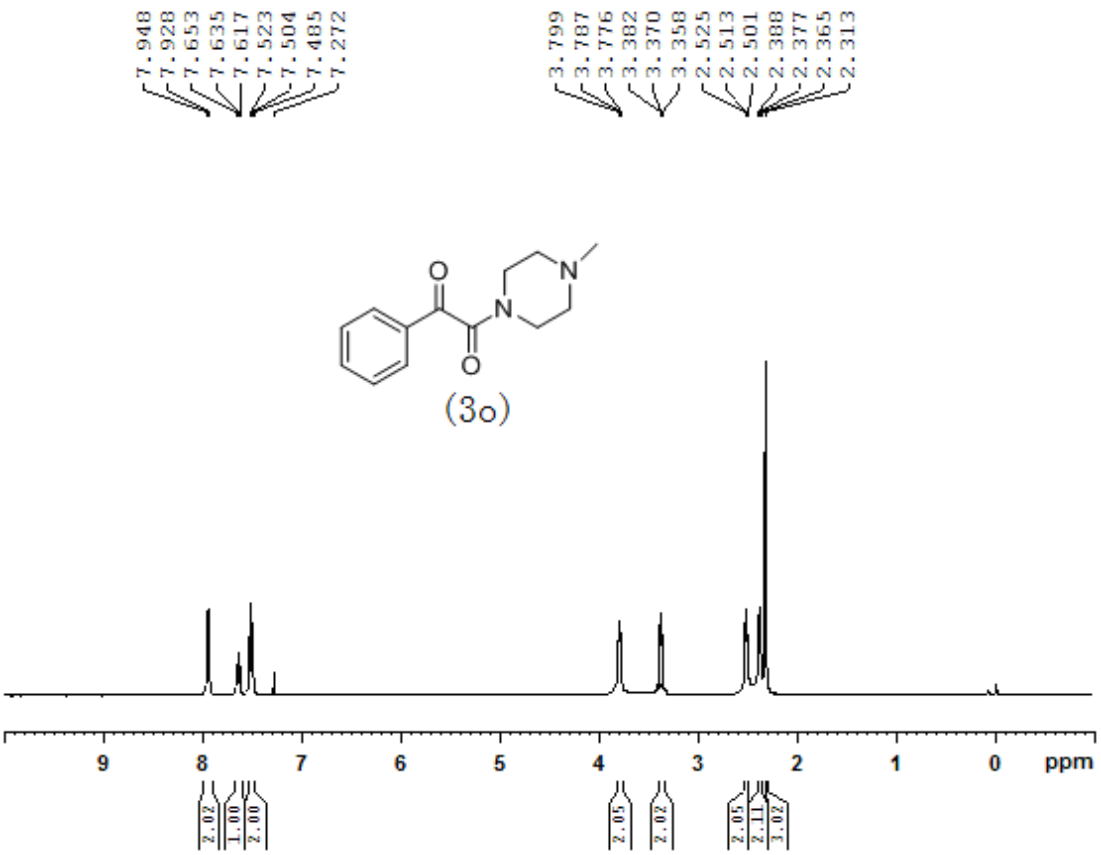

191.916
165.460
134.620
133.281
129.542
128.979
77.381
77.063
76.745
47.027
42.156
26.182
25.429
24.354
O
N
O
(31)
220
200
180
160
140
120
100
80
60
40
20
ppm

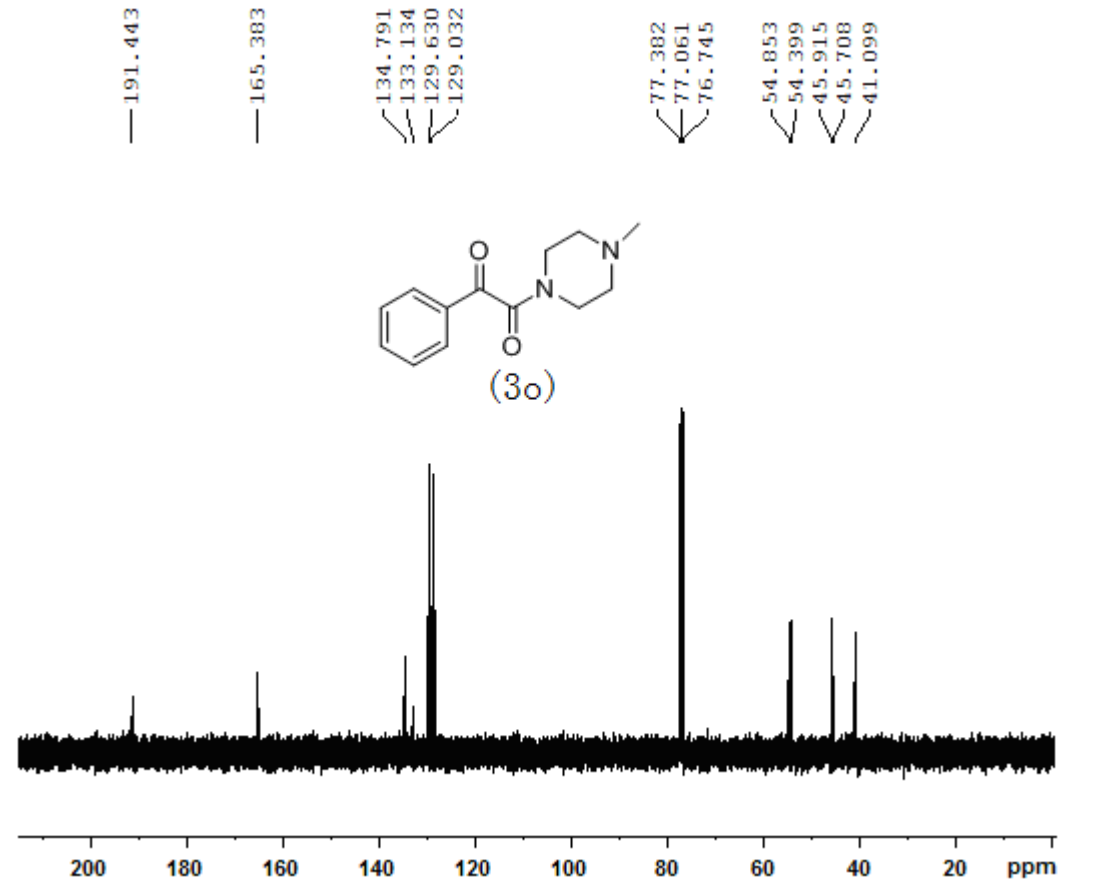


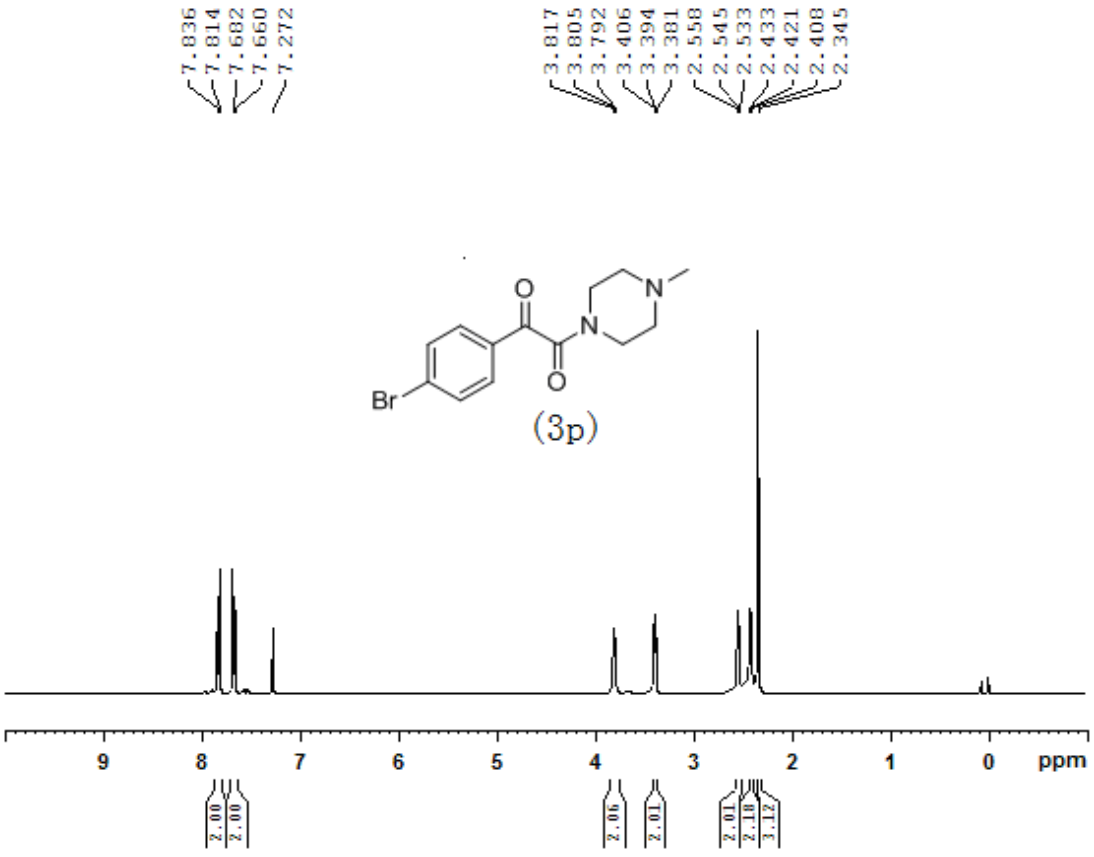


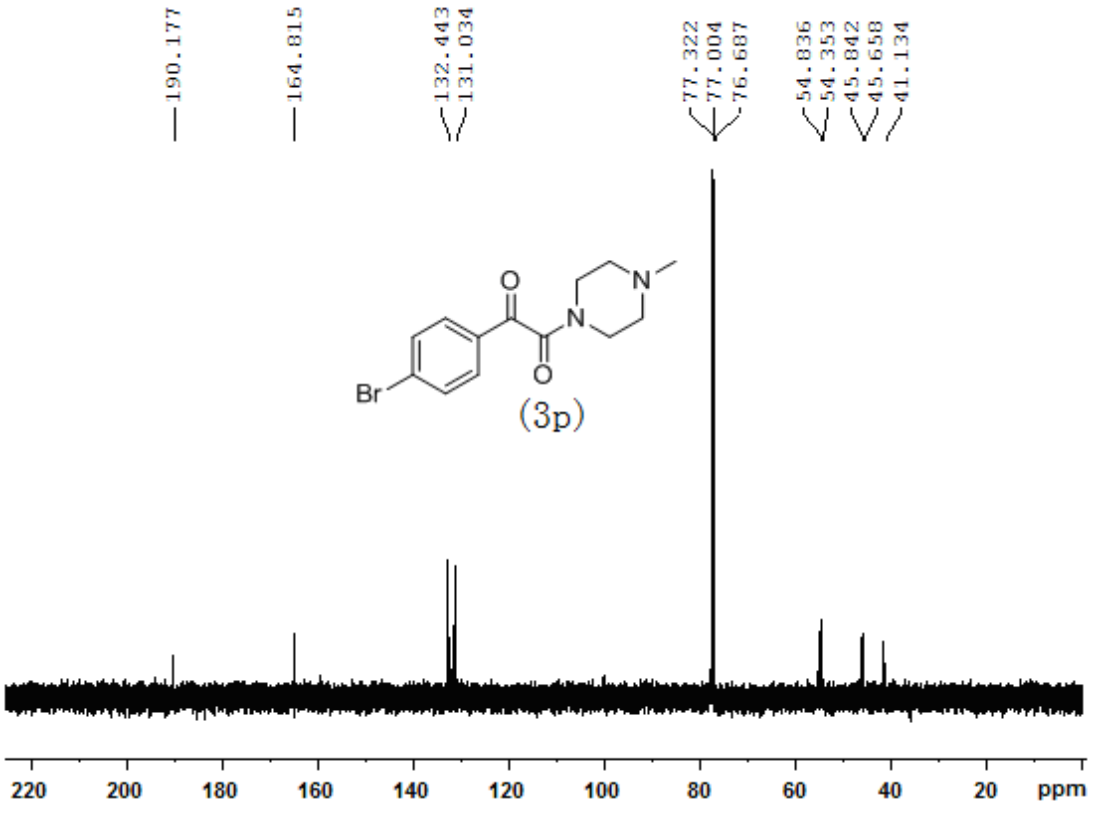


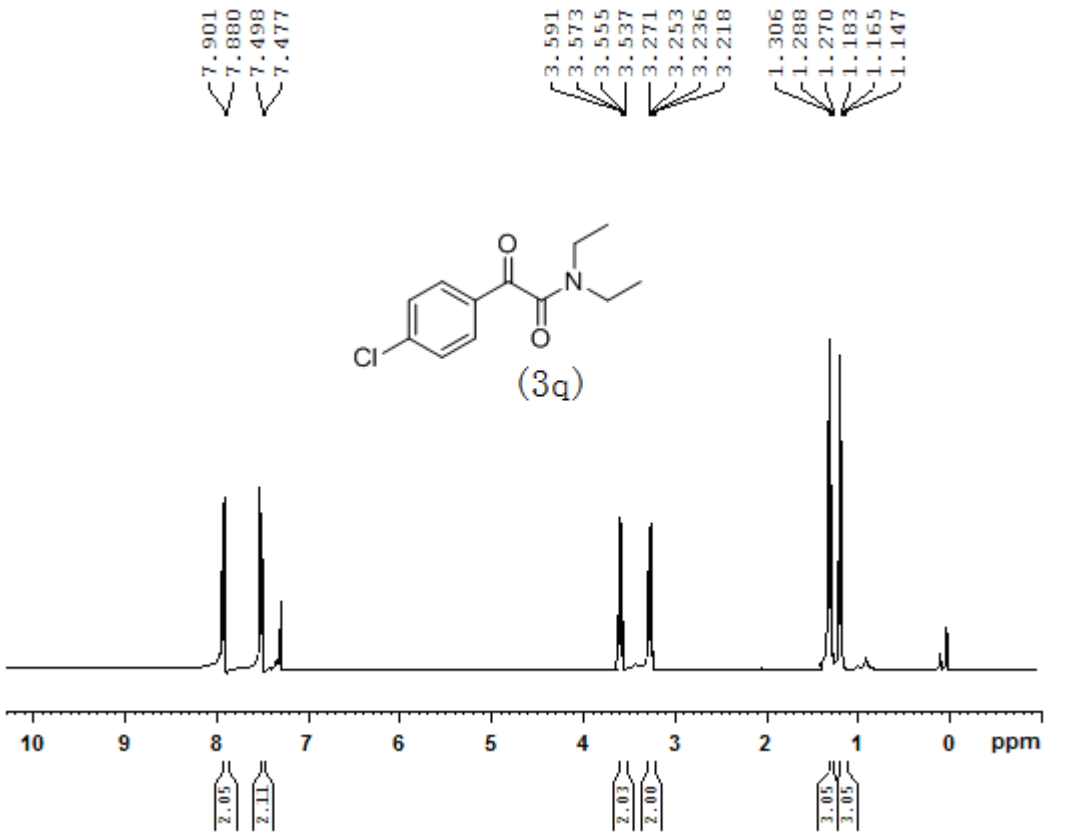








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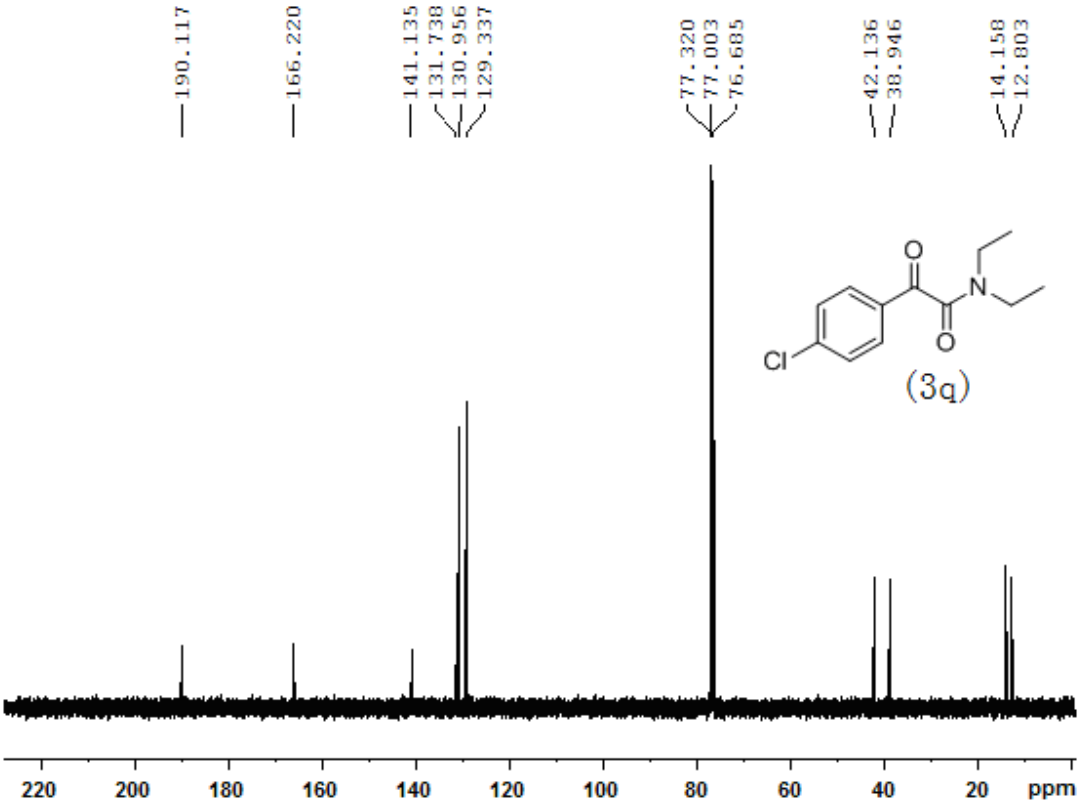
7.880
7.498
7.477
3.591
3.573
3.555
3.537
3.271
3.253
3.236
3.218
1.306
1.288
1.270
1.183
1.165
1.147
Cl
O
N
O
(3q)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.05
2.11
2.03
2.00
3.05
3.05


190.117
166.220
141.135
131.738
130.956
129.337
77.320
77.003
76.685
42.136
38.946
14.158
12.803
Cl
O
N
O
(3q)
220
200
180
160
140
120
100
80
60
40
20
ppm

7. References

1. J. E. Hein, J. C. Tripp, L. B. Krasnova, K. B. Sharpless, V. V. Fokin, *Angew. Chem. Int. Ed.* **2009**, *48*, 8018.

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3. J. Liu, R. Zhang, S. Wang, W. Sun, C. Xia. *Org. Lett.* **2009***, 11*, 1321–1324.

4. E. R. Murphy, J. R. Martinelli, N. Zaborenko, S. L. Buchwald, K. F. Jensen, *Angew. Chem. Int. Ed.* **2007***, 46*, 1734–1737.

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