Electronic Supporting Information

Tandem cycloaddition-decarboxylation of *α*-keto acid and isocyanide under oxidant-free condition towards monosubstituted oxazoles

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Contents

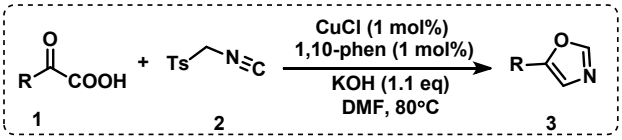
1、General Considerations

All chemicals were received from chemical suppliers commercially without further purification. All ^{1}H NMR and ^{13}C NMR spectra were obtained on a 600 MHz spectrometer in $CDCl_3$ with TMS as internal standard at room temperature. Gas chromatography (GC) analyses were recorded by Agilent 7820A (FID detector from AGILENT 7820). Thin layer chromatography (TLC) was employed with glass 0.25 mm silica gel plates. Column chromatography was performed on silica gel (200−300 mesh). High-resolution mass spectra (HRMS) were obtained using a Bruker microTOFII focus spectrometer(ESI).

2、Experimental procedure for preparation of substituted α-oxocarboxylic acids[1]

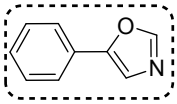
Corresponding methyl ketones were oxidated with excess SeO_2 to obtain all kinds of desired substituted α-oxocarboxylic acids according to previous literatures. In addition, pyruvate(**1n**) was directly provided by the supplier.

3、Experimental procedure for the synthesis of monosubstituted oxazoles (3a-m)



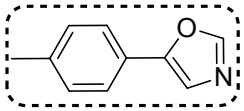
General procedure for the synthesis of 3a: To a 5 mL round bottom flask, the mixture of α-oxo-2-phenylacetic acid **1a** (0.55 mmol, 83.3 mg) and KOH (0.55 mmol, 25.3 mg,) in DMF (1 mL), was stirred at room temperature for 1 h. After **1a** was consumed traced by TLC, TosMIC **2** (0.5 mmol, 97.6 mg) and CuCl (1 mol%, 1.3 mg)/1,10-Phenanthroline (1 mol%, 0.9 mg) was added. The vial was stirring in oil bath at 80°C for another 5 hours in air atmosphere, and monitored by TLC. Followed by TosMIC (**2**) was exhausted completely, the reaction was cooled down to room temperature and quenched in (10 mL) saturated NaCl solution then extracted with EtOAc (3×10 mL). Organic layers was combined and solvent was evaporated, then the residue was purified by flash column chromatography (petroleum ether : ethyl acetate = 9 : 1) to get 5-phenyloxazole **3a** as yellow liquid.

4、Characterizations of Products



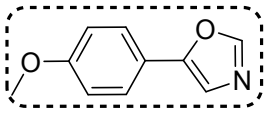
5-phenyloxazole (3a)[2]

Yellow liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.67–7.65 (m, 2H), 7.44–7.42 (m, 2H), 7.35 (s, 1H), 7.34–7.33 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 151.6, 150.5, 128.9, 128.7, 127.7, 124.4, 121.4. HRMS (ESI-TOF) Calcd for C_9H_8NO ($[M+H]^+$) 146.0600. Found 146.0601.



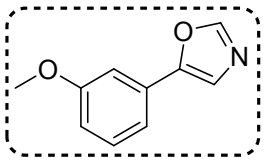
5-(p-tolyl)oxazole (3b)[3, 4]

Yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.31 (s, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.7, 149.1, 137.7, 128.6, 124.0, 123.3, 119.8, 20.3. HRMS (ESI-TOF) Calcd for $C_{10}H_{10}NO$ ($[M+H]^+$) 160.0761. Found 160.0766.



5-(4-methoxyphenyl)oxazole (3c)[3]

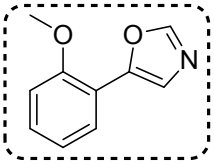
Yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.60–7.58 (m, 2H), 7.23 (s, 1H), 6.97–6.95 (m, 2H), 3.85 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.9, 151.6, 149.9, 125.9, 120.6, 120.0, 114.4, 55.4. HRMS (ESI-TOF) Calcd for $C_{10}H_{10}NO_2$ ($[M+H]^+$) 176.0706. Found 176.0710.



5-(3-methoxyphenyl)oxazole (3d)

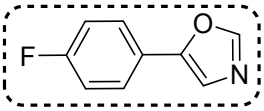
Yellow liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.36-7.35 (m, 1H),7.34-7.33(d, *J* = 7.8 Hz, 1H), 7.26-7.25 (d, *J* = 7.8 Hz, 1H), 7.20–7.18 (m, 1H), 6.90 (m, 1H), 3.86 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.0, 151.4, 150.5, 130.1, 129.0,

121.8, 116.9, 114.4, 109.8, 55.4. HRMS (ESI-TOF) Calcd for $C_{10}H_{10}NO_2$ ($[M+H]^+$) 176.0706. Found 176.0710.



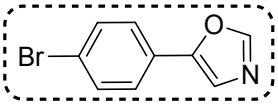
5-(2-methoxyphenyl)oxazole (**3e**)

Yellow liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.57 (s, 1H), 7.32 (t, *J* = 7.8 Hz, *J* = 15.6 Hz, 1H), 7.06 (s, *J* = 7.2 Hz, *J* = 15.0 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 3.98 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.7, 149.5, 129.3, 126.1, 125.5, 120.8, 117.0, 110.9, 55.5. HRMS (ESI-TOF) Calcd for $C_{10}H_{10}NO_2$ ($[M+H]^+$) 176.0706. Found 176.0710.



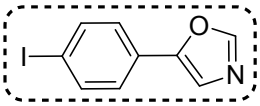
5-(4-fluorophenyl)oxazole (**3f**)[3]

Yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.65-7.62 (m, 2H), 7.30 (s, 1H), 7.14-7.11 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.7, 162.1, 150.5, 126.5, 124.2, 121.2, 116.1. ^{19}F NMR δ 104.1. HRMS (ESI-TOF) Calcd for C_9H_7FNO ($[M+H]^+$) 164.0386. Found 164.0381.



5-(4-bromophenyl)oxazole (**3g**)

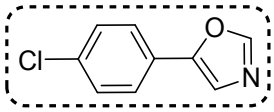
Yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.55-7.50 (m, 4H), 7.36 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.0, 149.7, 131.1, 125.6, 124.8, 121.6 120.9. HRMS (ESI-TOF) Calcd for C_9H_7BrNO ($[M+H]^+$) 223.9567. Found 223.9562.



5-(4-iodophenyl)oxazole (**3h**)

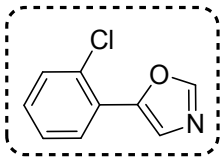
Yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.77-7.76 (m, 2H), 7.40-7.38 (m, 2H), 7.38 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.7, 138.1, 127.2, 126.0,

122.1, 94.2. HRMS (ESI-TOF) Calcd for C_9H_7INO ($[M+H]^+$) 271.9567. Found 271.9561.



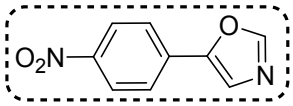
5-(4-chlorophenyl)oxazole (3i)[3]

Yellow solid. ^1H NMR (600 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 9.0 Hz, 2H), 7.35 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.6, 134.5, 129.2, 126.3, 125.7, 121.9. HRMS (ESI-TOF) Calcd for C_9H_7ClNO ($[M]^+$) 179.0138. Found 179.0143.



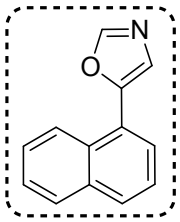
5-(2-chlorophenyl)oxazole (3j)

Yellow liquid. ^1H NMR (600 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.80 (s, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, *J* = 15.0 Hz, 1H), 7.28 (t, *J* = 7.2 Hz, *J* = 15.0 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 151.9, 150.3, 148.1, 130.7, 129.3, 127.9, 127.1, 126.6, 126.4. HRMS (ESI-TOF) Calcd for C_9H_7ClNO ($[M]^+$) 179.0138. Found 179.0143.



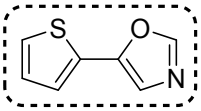
5-(4-nitrophenyl)oxazole (3k)[3]

Yellow solid. ^1H NMR (600 MHz, $CDCl_3$) δ 8.31 (d, *J* = 9.0 Hz, 2H), 8.04 (s, 1H), 7.83 (d, *J* = 9.0 Hz, 2H), 7.58 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.8, 148.5 146.4, 132.4, 123.8, 123.8, 123.5. HRMS (ESI-TOF) Calcd for $C_9H_7N_2O_3$ ($[M+H]^+$) 191.0451. Found 191.0446.



5-(naphthalen-1-yl)oxazole (3l)

Yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 1H), 8.07 (s, 1H), 7.92 – 7.91 (m, 2H), 7.75 (dd, *J* = 7.2 Hz, *J* = 0.6 Hz, 1H), 7.57–7.53 (m, 3H), 7.46 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.8, 149.8, 132.8, 129.2, 128.8, 127.7, 126.1, 125.7, 125.3, 124.3, 124.1, 123.9, 123.8. HRMS (ESI-TOF) Calcd for $C_{13}H_{10}NO$ ($[M+H]^+$) 196.0772. Found196.0777.



5-(thiophen-2-yl)oxazole (**3m**)

Yellow liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.35 (dd, *J* = 4.8 Hz, *J* = 1.2 Hz, 1H), 7.33 (dd, *J* = 3.6 Hz, *J* = 1.2 Hz, 1H), 7.22 (s, 1H), 7.09 (dd, *J* = 3.6 Hz, *J* = 1.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.9, 146.1, 128.5, 126.8, 124.9, 123.7, 120.2. HRMS (ESI-TOF) Calcd for C_7H_4NOS ($[M-H]^+$) 150.0092. Found 150.0088.

5、References

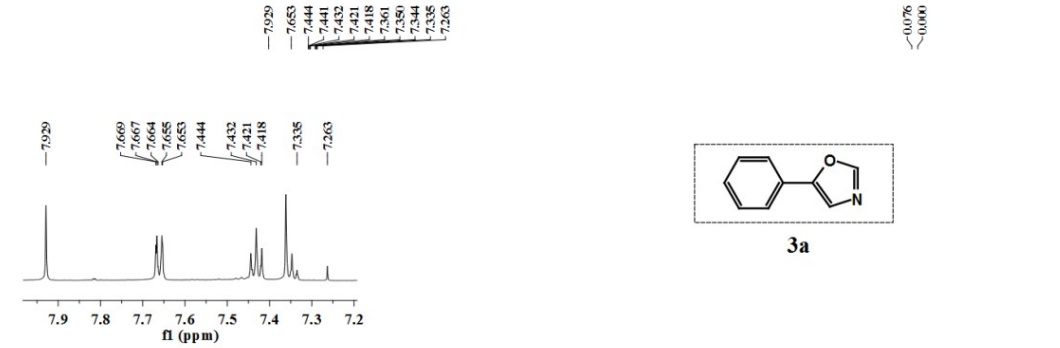
[1]. K. Wadhwa, C. Yang, P. R. West, K.C. Deming, S.R. Chemburkar, R. E. Reddy. *Syn. Commun*. **2008,** *38(24),* 4434-4444.

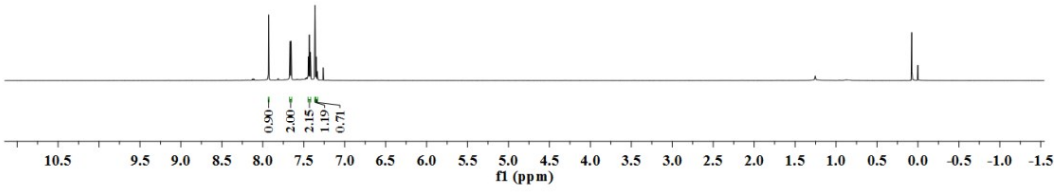
[2]. N. A. Strotman, H. R. Chobanian, Y. Guo, J. He, J. E. Wilson. *Org. Lett*. **2010,** *12(16),* 3578-3581.

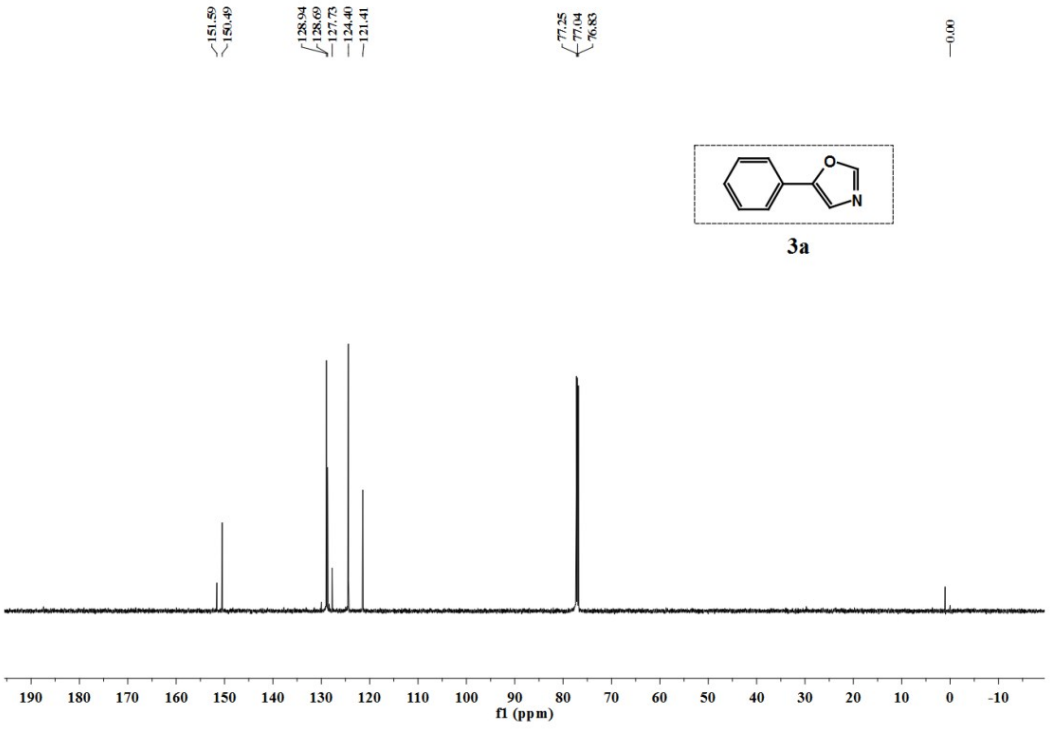
[3]. A. G. M. Barrett, S. M. Cramp, A. J. Hennessy, P. A. Procopiou, R. S. Roberts. *Org. Lett*. **2001,** *3(2),* 271-273.

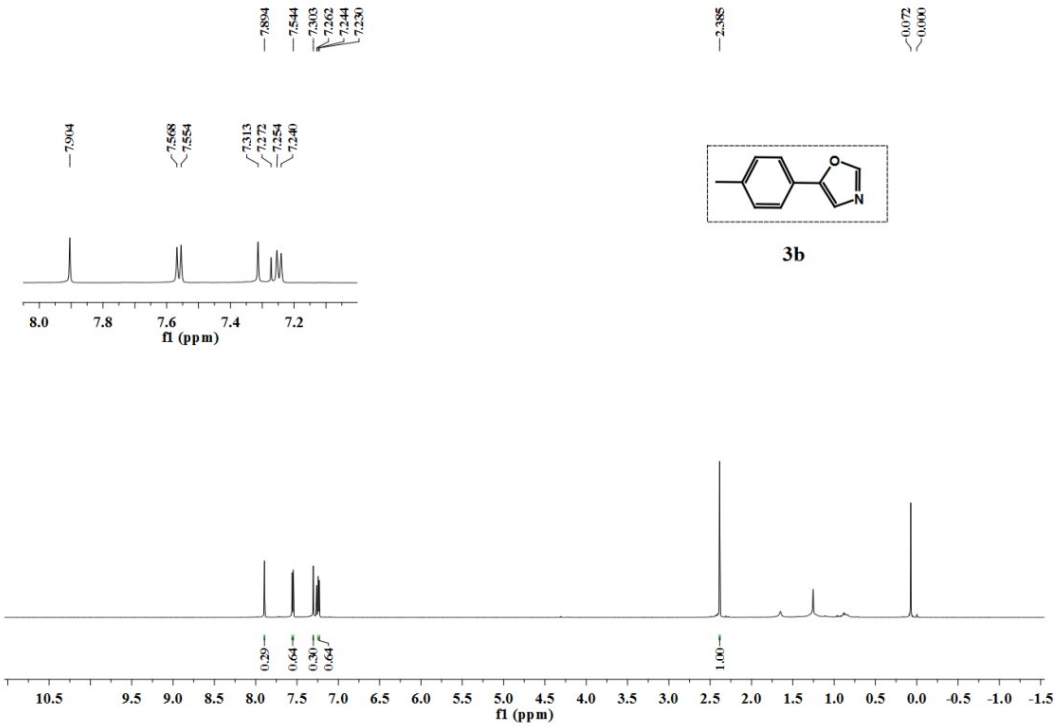
[4]. B. A. Kulkarni, A. Ganesan. *Tetrahedron Lett*. **1999**, *40*, 5637-5638.

6、^{1}HNMR and ^{13}CNMR Spectra of Products





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7.230
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7.313
7.272
7.254
7.240
8.0
7.8
7.6
7.4
7.2
f1 (ppm)
3b
0.29
0.64
0.30
0.64
1.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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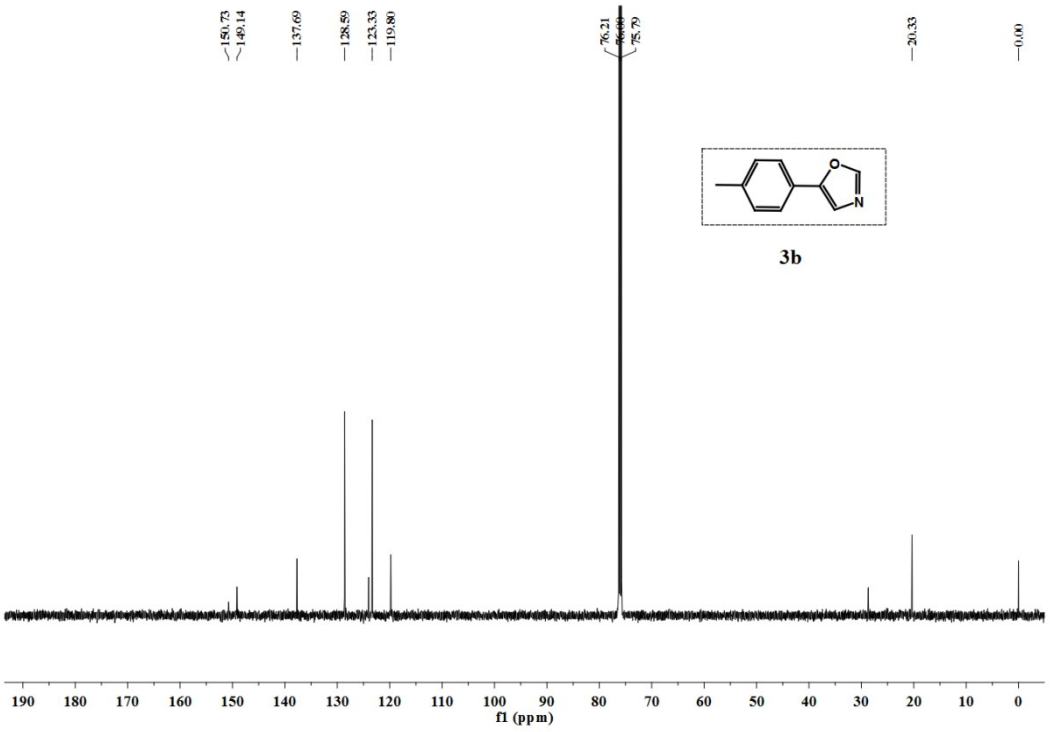
f1 (ppm)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3b
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180
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130
120
110
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90
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70
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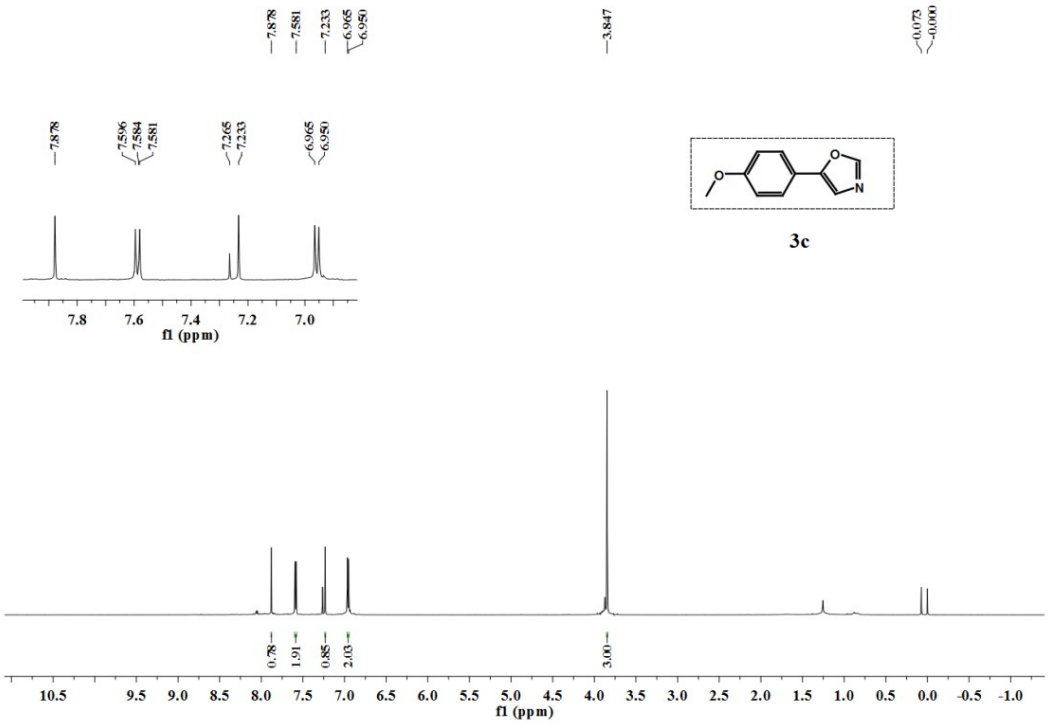
50
40
30
20
10
0
f1 (ppm)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7.233
7.8
7.6
7.4
7.2
7.0
f1 (ppm)
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O
N
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0.85
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3.00
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8.5
8.0
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7.0
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5.0
4.5
4.0
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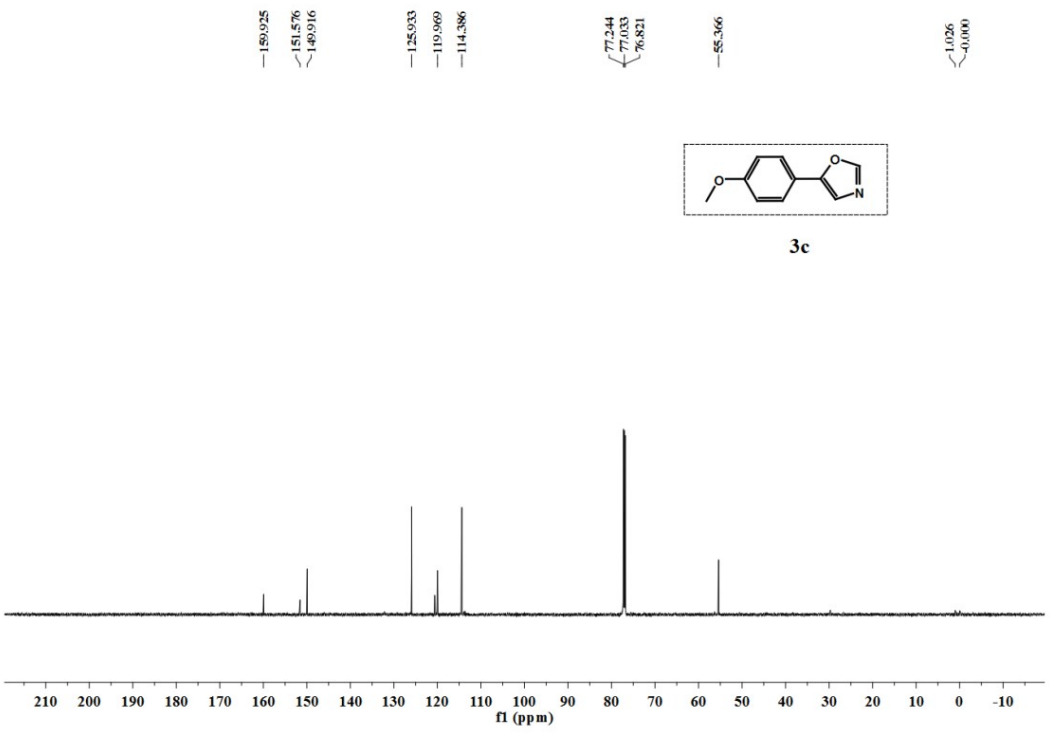
-1.0
f1 (ppm)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O
N
3c
210
200
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180
170
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140
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80
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60
50
40
30
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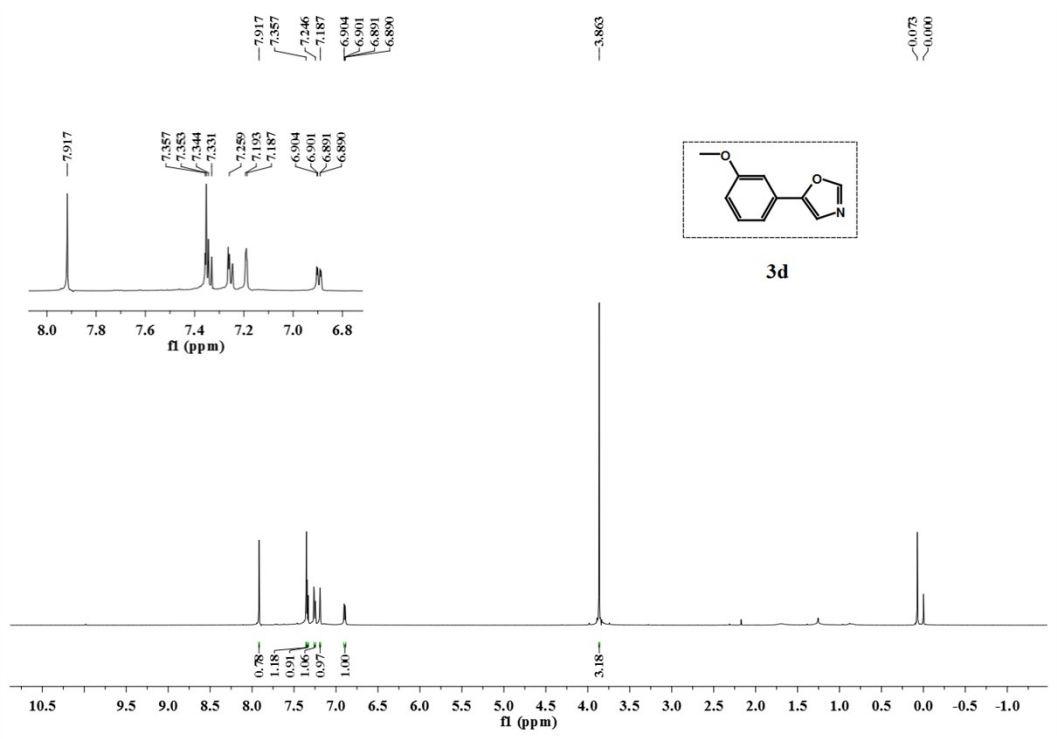
f1 (ppm)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7.357
7.353
7.344
7.331
7.259
7.193
7.187
6.904
6.901
6.891
6.890
8.0 7.8 7.6 7.4 7.2 7.0 6.8
f1 (ppm)
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N
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1.06
0.97
1.00
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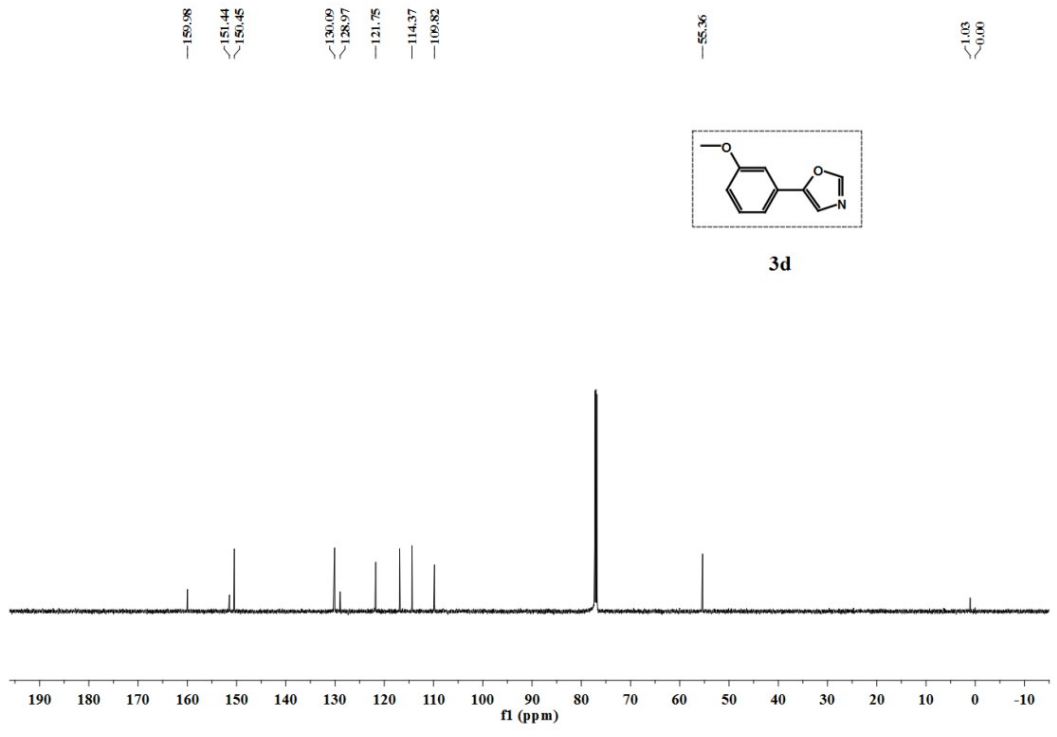
f1 (ppm)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N
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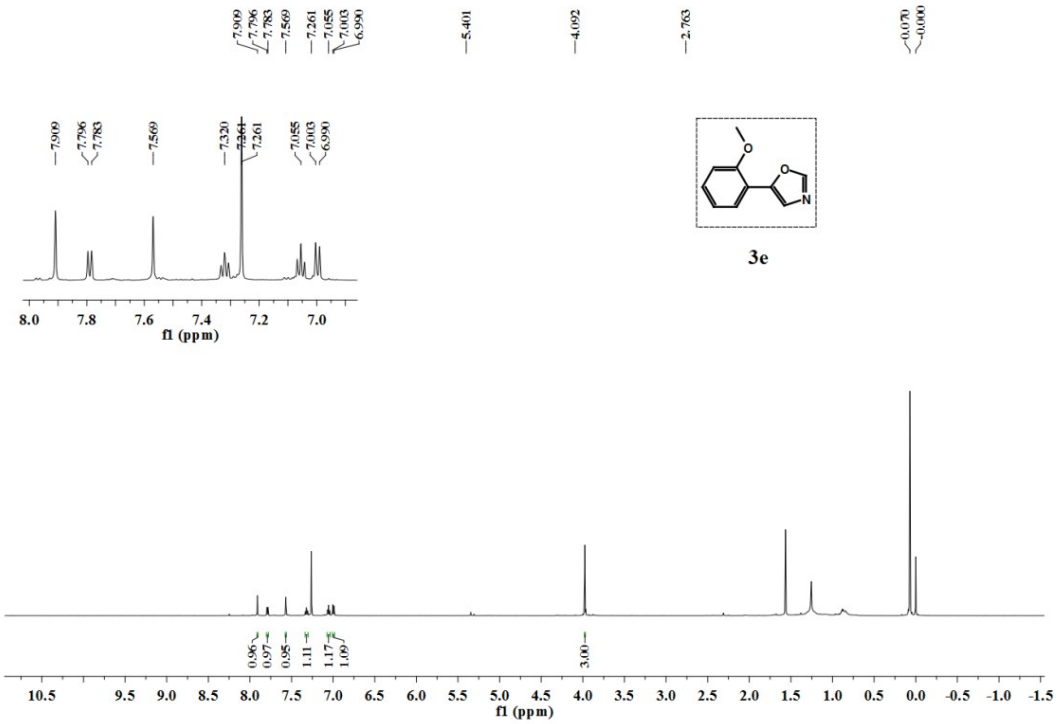
f1 (ppm)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7.320
7.264
8.0
7.8
7.6
7.4
7.2
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f1 (ppm)
O
O
N
3e
0.96
0.97
0.95
1.11
1.17
1.09
3.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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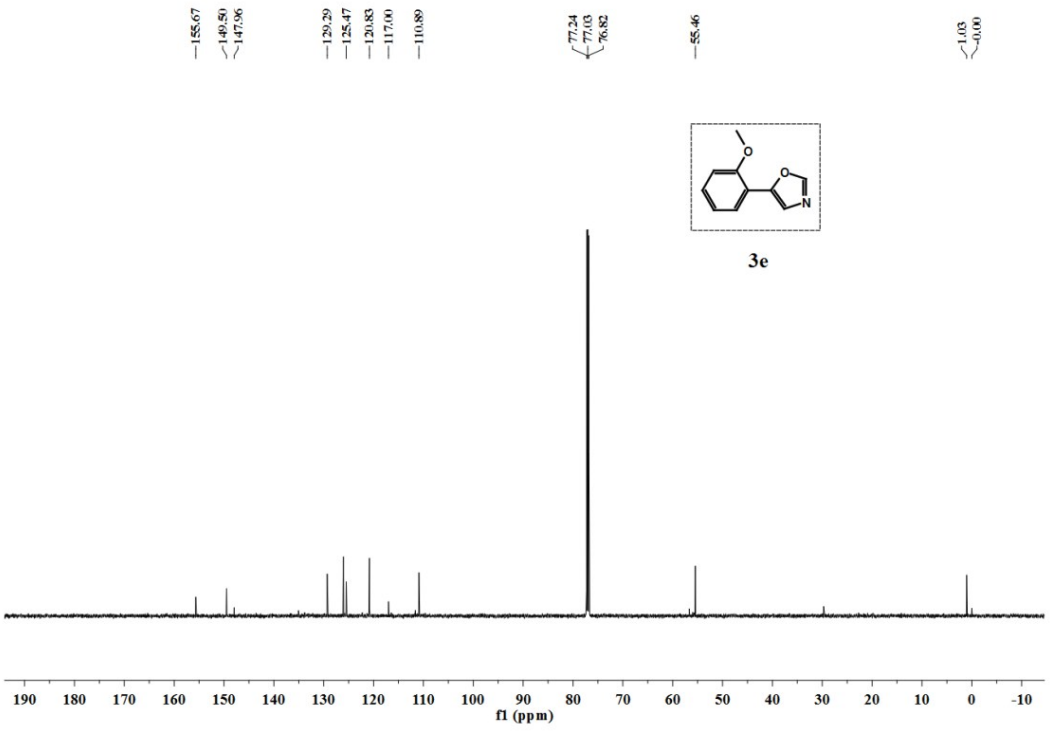
-1.5
f1 (ppm)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125.47
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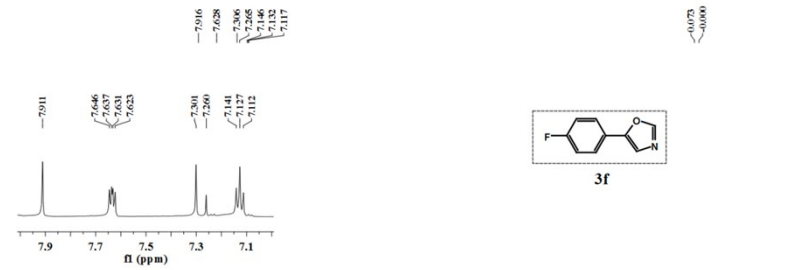
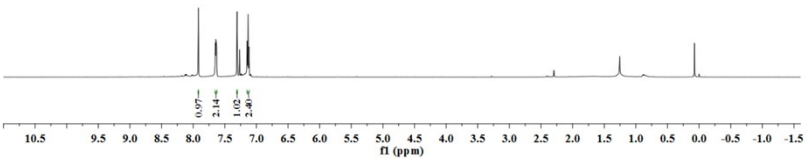
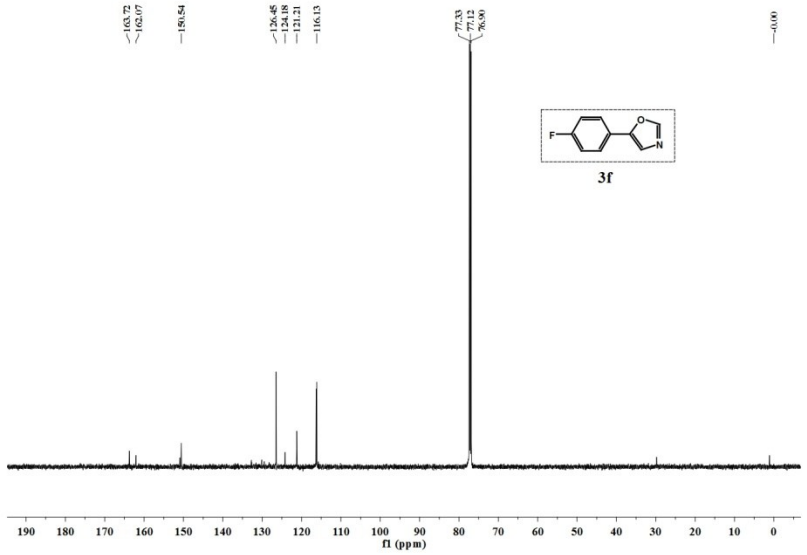
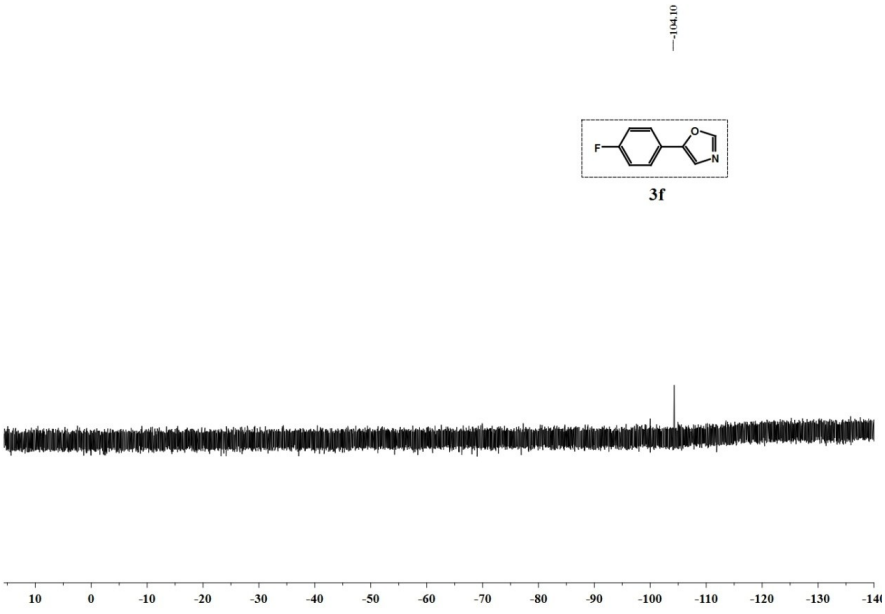
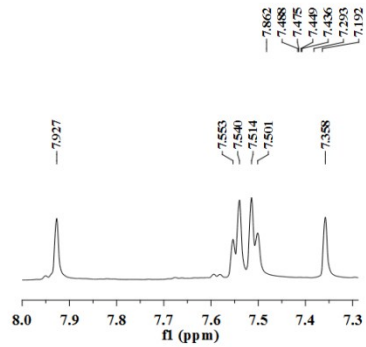
117.00
110.89
77.24
77.03
76.82
55.46
1.03
-0.00
O
O
N
3e
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

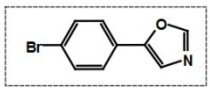

7.916
7.628
7.306
7.268
7.146
7.133
7.117
0.073
0.000
7.911
7.646
7.637
7.631
7.623
7.301
7.260
7.141
7.127
7.112
F
O
N
3f
7.9
7.7
7.5
7.3
7.1
f1 (ppm)


0.97
2.14
1.02
2.40
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)


163.72
162.07
150.54
126.46
124.18
121.21
116.13
77.33
77.12
76.91
0.00
F
O
N
3f
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

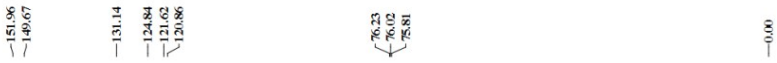

-104.10
F
O
N
3f
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140

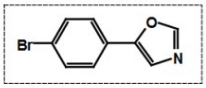

7.862
7.488
7.475
7.449
7.436
7.293
7.192
7.927
7.553
7.540
7.514
7.501
7.388
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3
f1 (ppm)


Br
O
N

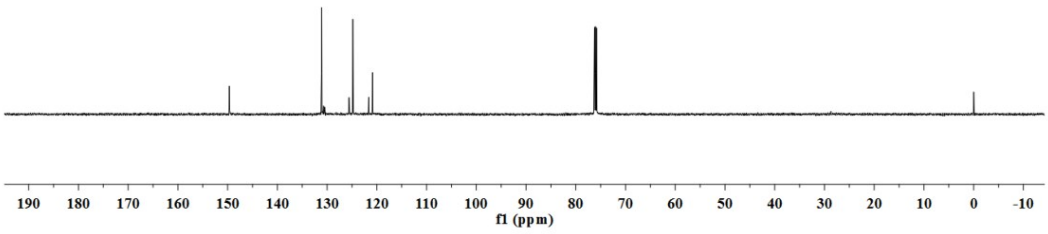
3g

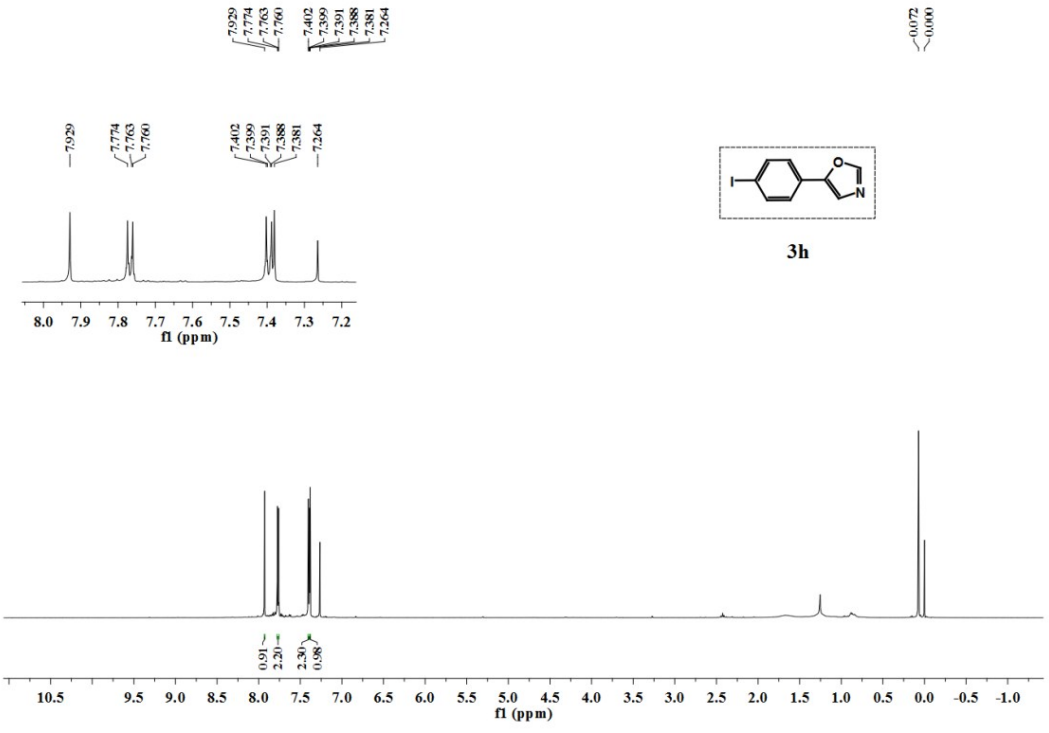
0.00
0.92
4.28
1.00
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

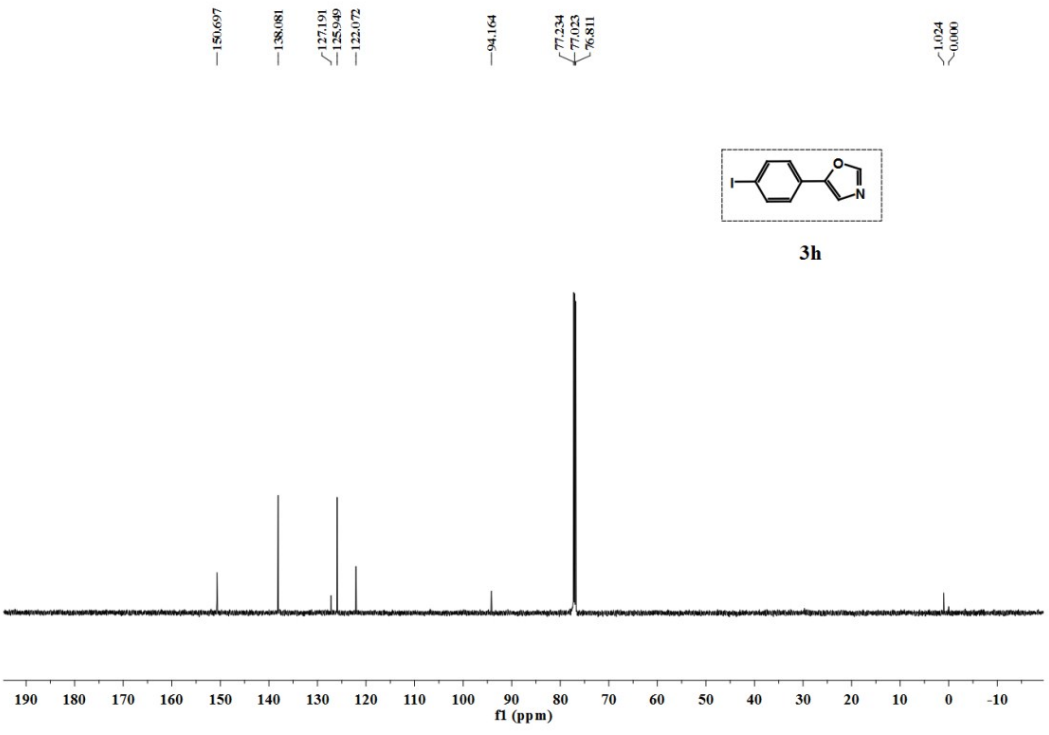

151.96
149.67
131.14
124.84
121.62
120.86
76.23
76.02
75.81
0.00


Br
O
N

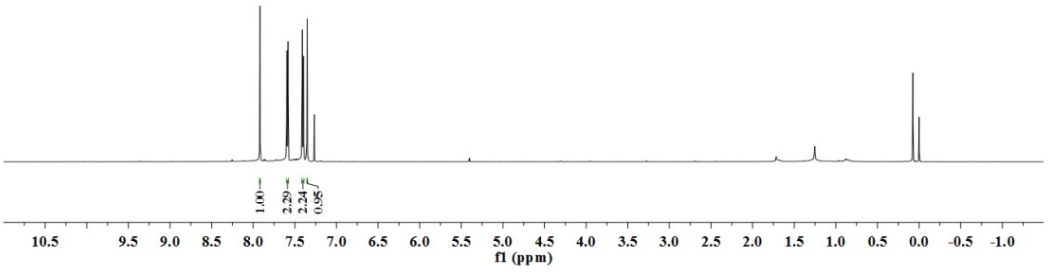
3g

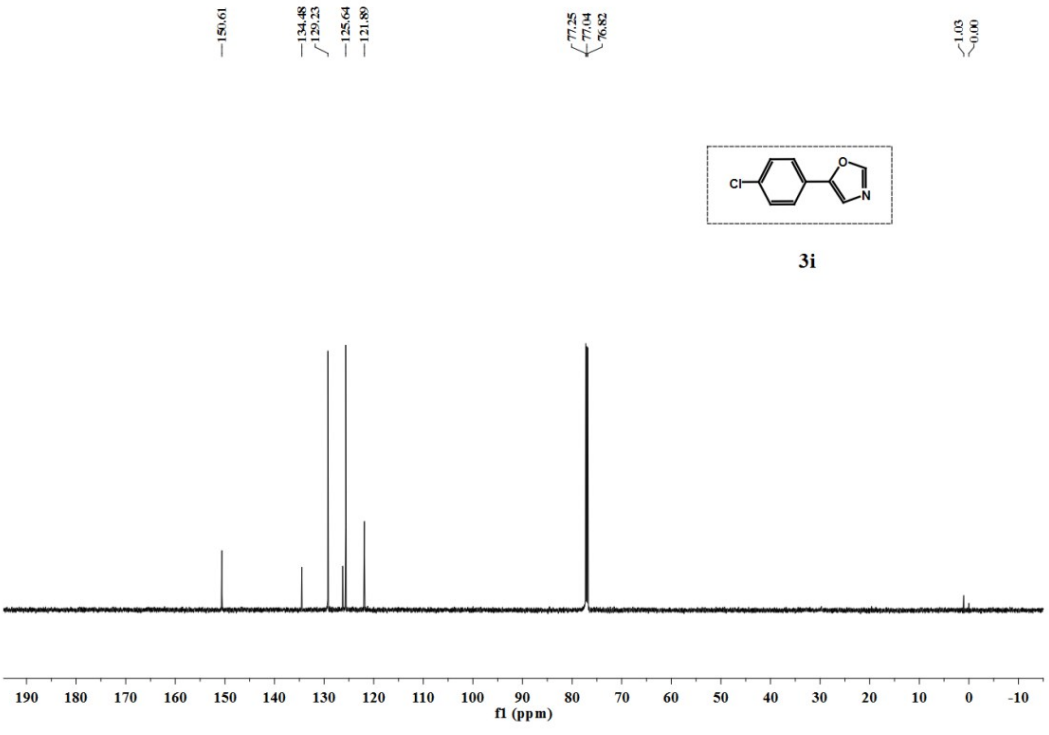

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

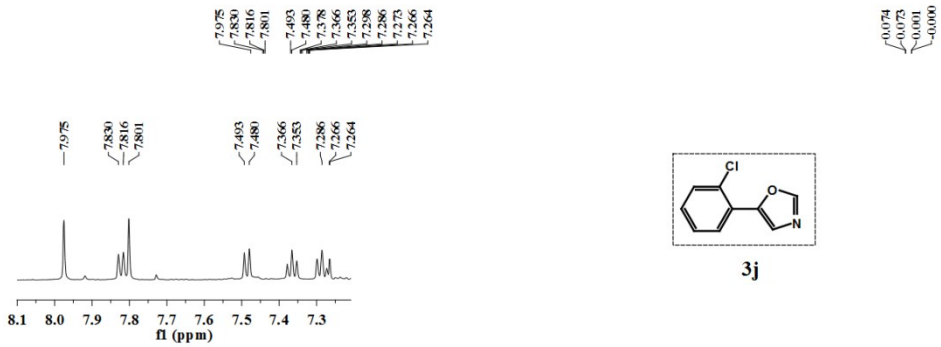

7.929
7.774
7.763
7.760
7.402
7.399
7.391
7.388
7.381
7.264
0.072
0.000
I
O
N
3h
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2
f1 (ppm)
0.91
2.20
2.30
0.98
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

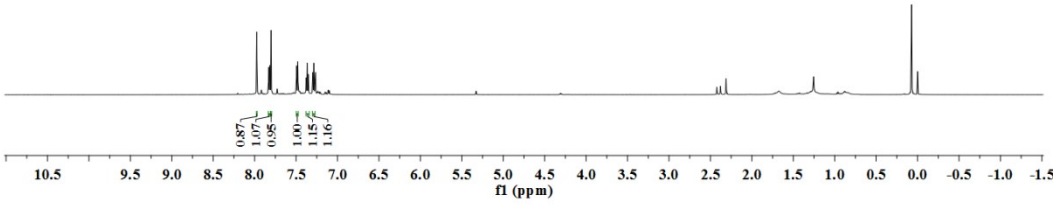

150.697
138.081
127.191
125.949
122.072
94.164
77.234
77.023
76.811
1.024
0.000
I
O
N
3h
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

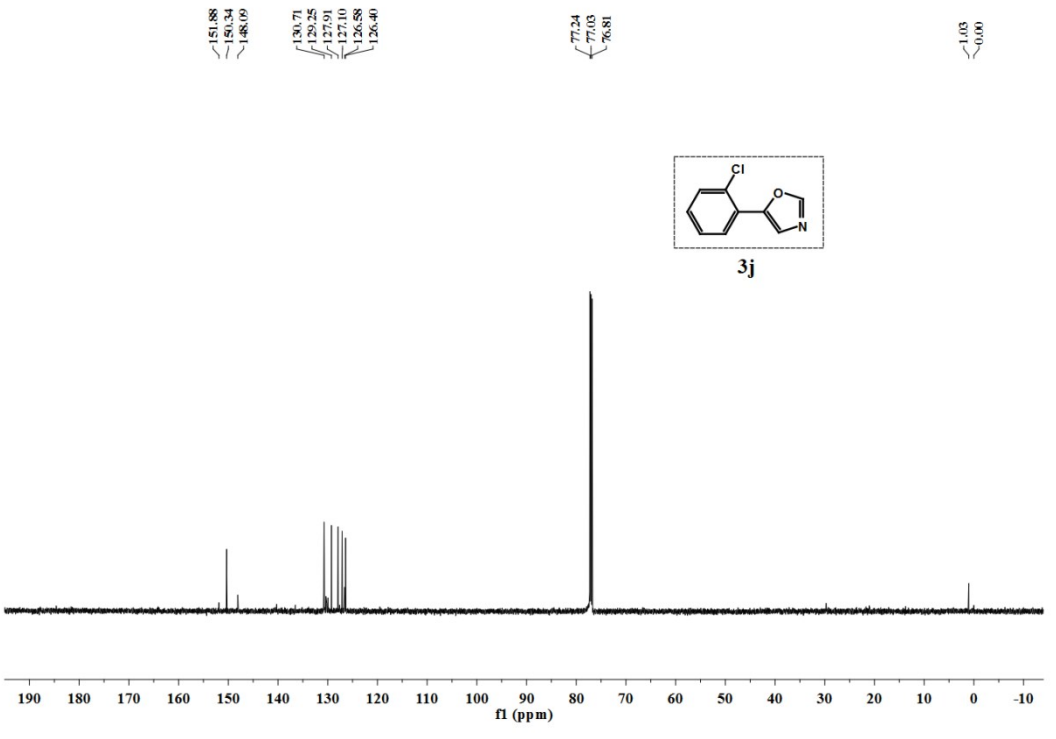

7.920
7.596
7.582
7.411
7.396
7.352
7.266
0.074
0.000
Cl
O
N
3i
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2
f1 (ppm)

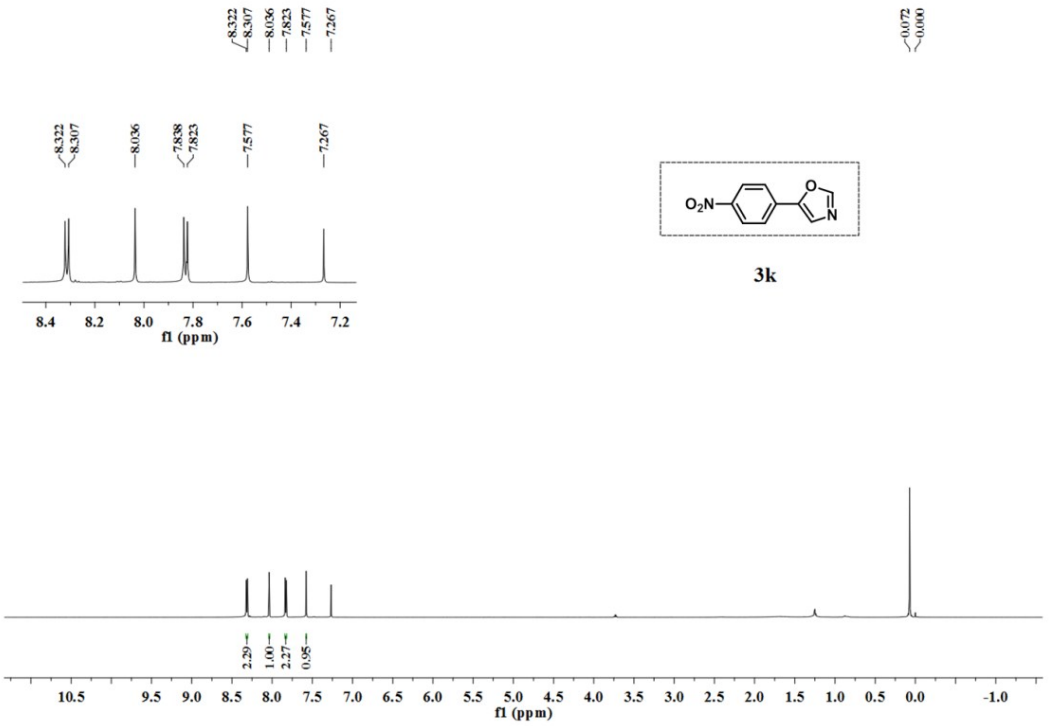

1.00
2.29
2.24
0.95
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

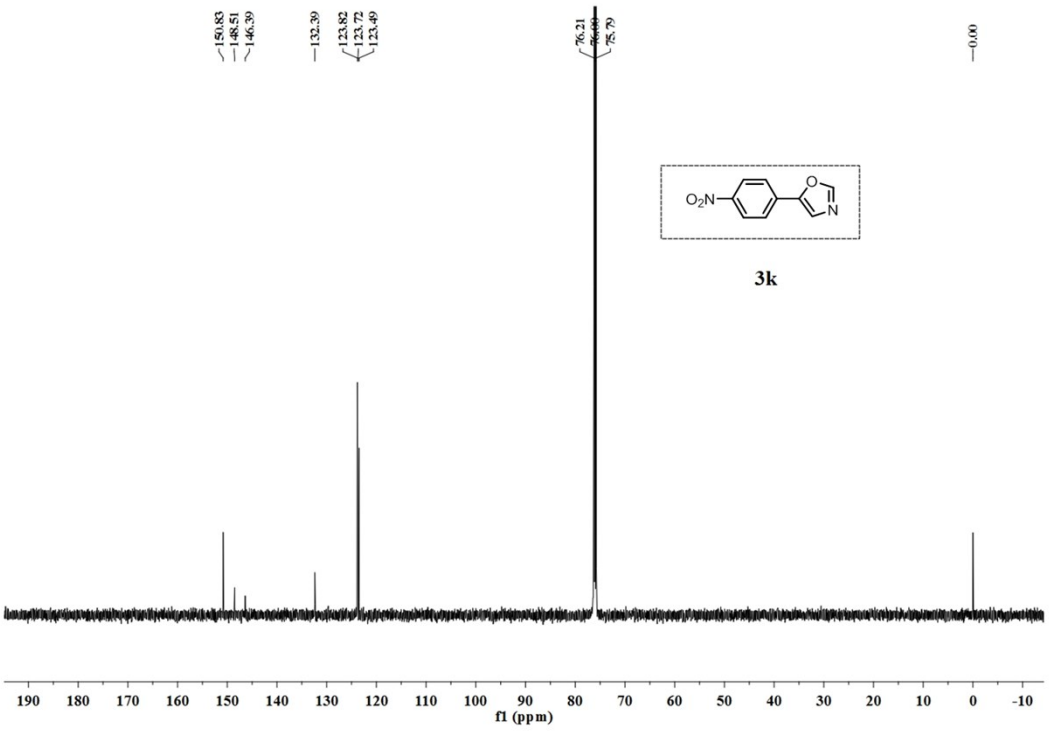

150.61
134.48
129.23
125.64
121.89
77.25
77.04
76.82
1.03
0.00
Cl
O
N
3i
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

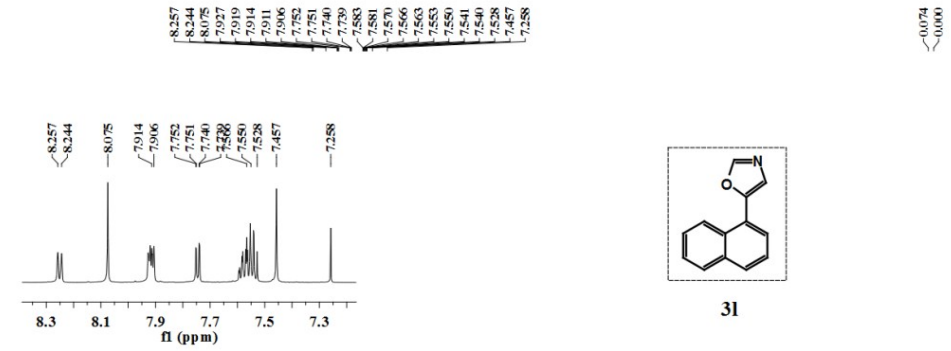

7.975
7.830
7.816
7.801
7.493
7.480
7.378
7.366
7.353
7.298
7.286
7.273
7.266
7.264
0.074
0.073
0.001
-0.000
Cl
O
N
3j
8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3
f1 (ppm)

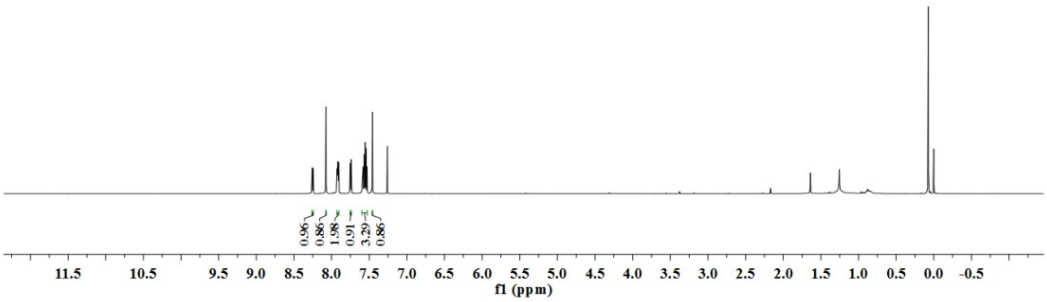

0.87
1.07
0.98
1.00
1.15
1.16
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

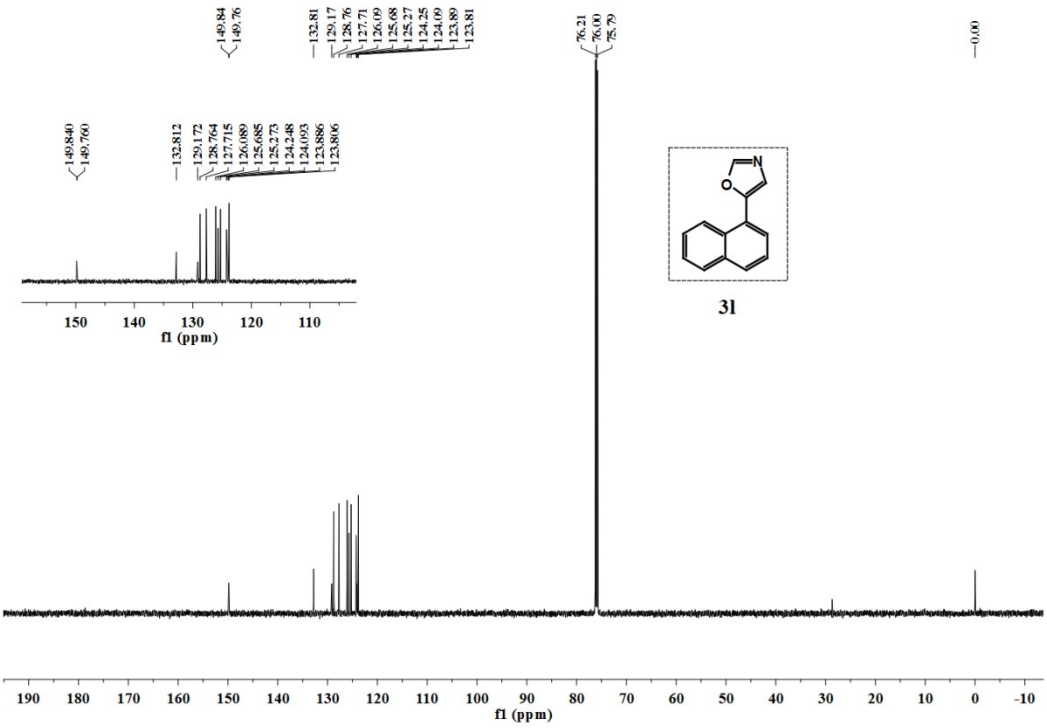

151.88
150.34
148.09
130.71
129.25
127.91
127.10
126.58
126.40
77.24
77.03
76.81
1.03
0.00
Cl
O
N
3j
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

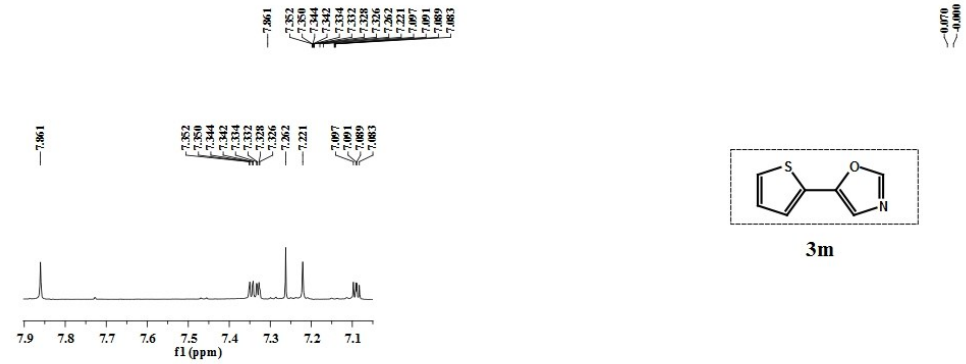

8.322
8.307
8.036
7.838
7.823
7.577
7.267
0.072
0.000
O2N
O
N
3k
2.29
1.00
2.27
0.95
f1 (ppm)

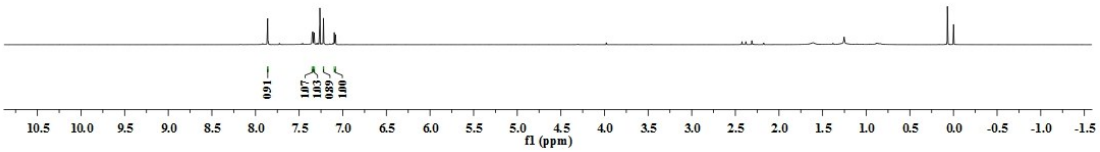

150.83
148.51
146.39
132.39
123.82
123.72
123.49
76.21
77.00
75.79
0.00
O2N
O
N
3k
f1 (ppm)

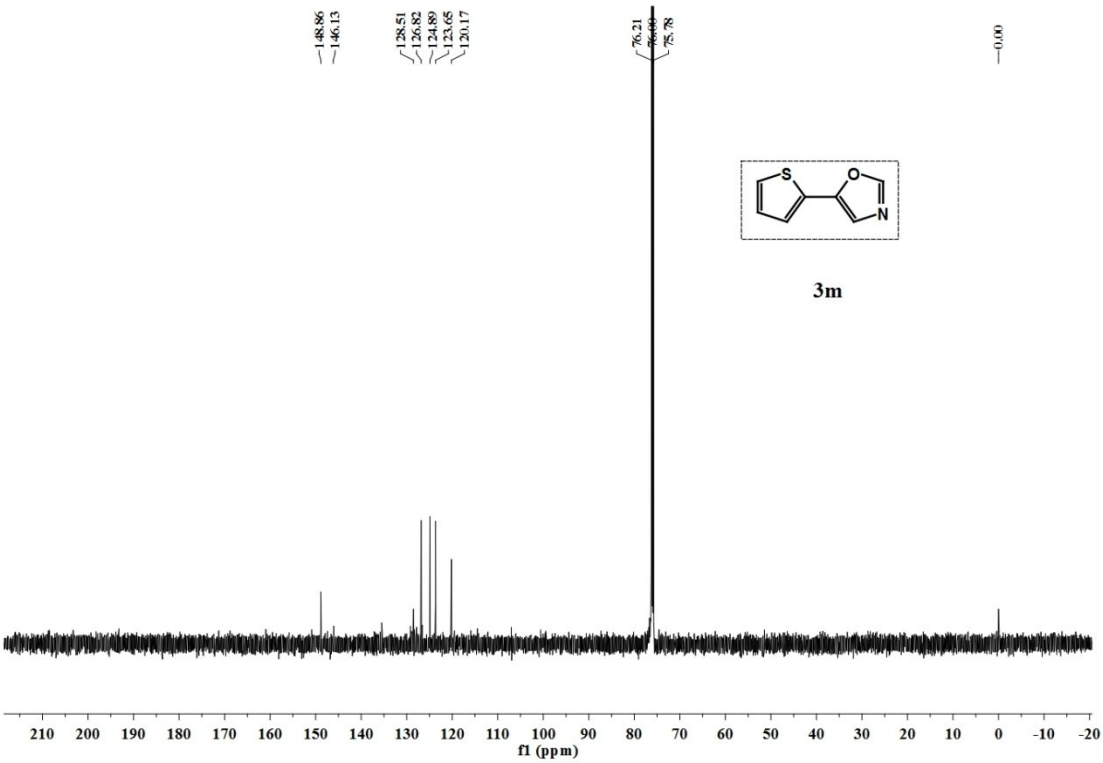

8.257
8.244
8.075
7.927
7.919
7.914
7.911
7.906
7.752
7.751
7.740
7.739
7.583
7.581
7.570
7.566
7.563
7.553
7.550
7.541
7.540
7.528
7.457
7.258
0.074
0.000
8.257
8.244
8.075
7.914
7.906
7.752
7.751
7.740
7.588
7.580
7.528
7.457
7.258
8.3
8.1
7.9
7.7
7.5
7.3
f1 (ppm)
N
O
31


0.96
0.86
1.98
0.91
3.29
0.86
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


149.84
149.76
132.81
129.17
128.76
127.71
126.09
125.68
125.27
124.25
124.09
123.89
123.81
76.21
76.00
75.79
0.00
149.840
149.760
132.812
129.172
128.764
127.715
126.089
125.685
125.273
124.248
124.093
123.886
123.806
150
140
130
120
110
f1 (ppm)
N
O
31
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.861
7.352
7.350
7.344
7.342
7.334
7.332
7.328
7.326
7.262
7.221
7.097
7.091
7.089
7.083
0.070
0.000
S
O
N
3m
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1
f1 (ppm)


0.91
1.07
1.03
0.89
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 -1.0 -1.5
f1 (ppm)


148.86
146.13
128.51
126.82
124.89
123.65
120.17
76.21
76.00
75.78
0.00
S
O
N
3m
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)