Supporting Information

Ruthenium (II)-Catalyzed Synthesis of Indazolone-Fused Cinnolines via C-H Coupling with Diazo Compounds

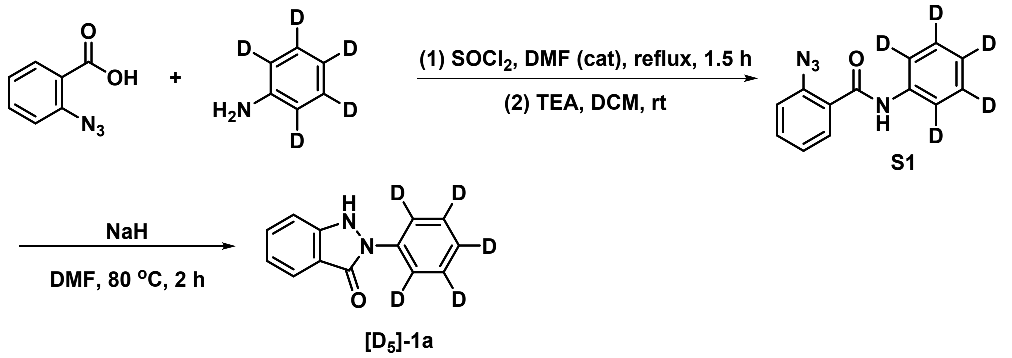
Lin Su,[a] Yu zheng, [b] Peiling Ren,[b] Zhi Luo,[c] Wei Hou,*[a] and Hongtao Xu*[b]

[a]*College of Pharmaceutical Science, and Institute of Drug Development & Chemical Biology (IDD&CB), Zhejiang University of Technology, Hangzhou, 310014, China.*
[b]*Shanghai Institute for Advanced Immunochemical Studies, ShanghaiTech University, Shanghai 201210, China.*
[c]*Shanghai Evergene Biotech Co., Ltd.,Shanghai 201203, China*
Email: xuht@shanghaitech.edu.cn, htxu2010@hotmail.com (Xu, H.T.)
houwei@zjut.edu.cn (Hou, W)

Contents

I. Mechanistic Studies

1. Synthesis of [D_5]-1a



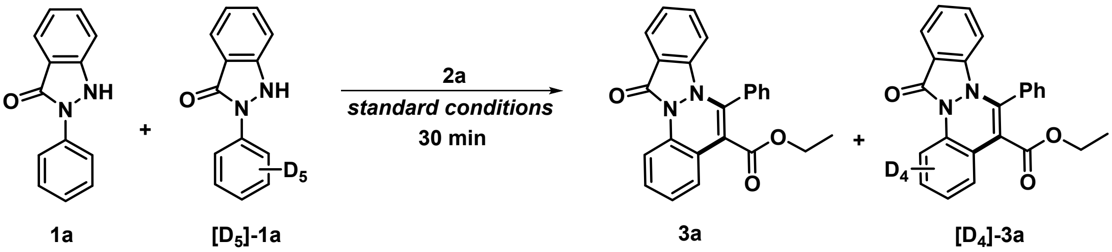
By using commercial available 2-azidobenzoic acid and aniline-D_5, the intermediate **S1** was prepared following a literature method.[23b] A mixture of 2-azidobenzoic acid (490 mg, 3.0 mmol), thionyl chloride (0.87 mL, 12.0 mmol), and DMF (0.1 mL) in DCM (10 mL) was stirred under reflux for 1.5 h. The reaction mixture was cooled to room temperature, evaporated in vacuo, and dried with a high vacuum pump to obtain crude 2-azidobenzoyl chloride. Without purification, 2-azidobenzoyl chloride and aniline-D_5 (284 mg, 2.9 mmol) were dissolved in DCM (15 mL) with an ice-bath. Triethylamine (0.84 mL, 6.0 mmol) was added slowly to the solution, and the resulting mixture was stirred overnight. The reaction mixture was washed with saturated $NaHCO_3$ (20 mL), 1 N HCl (10 ml), and brine (10 ml). The organic phase was dried over Na_2SO_4 and evaporated in vacuo to get the crude product, followed by the purification with silica-gel chromatography (PE : EA = 5 : 1) to afford **S1** (599 mg, 85% yield) as a solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.32 (s, 1H), 8.25 (dd, J = 7.8, 1.2 Hz, 1H), 7.55 (td, J = 7.8, 1.2 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.25 (d, J = 7.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.5, 137.8, 136.8, 132.8, 132.6, 128.5 (t, J = 24 Hz), 125.4, 125.2, 124.0 (t, J = 24.4 Hz), 120.1 (t, J = 24.5 Hz), 118.4. HRMS (ESI) calcd for $[M+H]^+$ $[C_{13}H_6D_5N_4O]^+$ 244.1247, found 244.1258.

To a stirred solution of **S1** (729.9 mg, 3 mmol) in dry DMF (10 mL) was added NaH (87 mg, 3.6 mmol) at room temperature. The resulting reaction mixture was then heated under 80 ℃ with stirring for 2 hours and monitored by TLC. After completion, it was quenched by sat. NH_4Cl aq., extracted with EtOAc, washed with water and brine, and dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the residue was purified by flash column chromatography on silica gel using petroleum ether/EtOAc as the eluent to afford **[D_5]-1a** (581 mg, 90% yield). ^{1}H NMR (500

MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 1H), 7.61 – 7.55 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.27 (t, *J* = 7.5 Hz, 1H), 7.17 (s, 1H). ^{13}C NMR (150 MHz, DMSO-*d6*) δ 160.2, 146.6, 137.4, 132.5, 128.6 (t, *J* = 24.2 Hz), 124.35 (t, *J* = 22.4 Hz), 123.4, 121.8, 118.4 (t, *J* = 24.9 Hz), 118.1, 112.6. HRMS (ESI) calcd for $[M+H]^+$ $[C_{13}H_6D_5N_2O]^+$ 216.1185, found 216.1179.

2. KIE Measurements

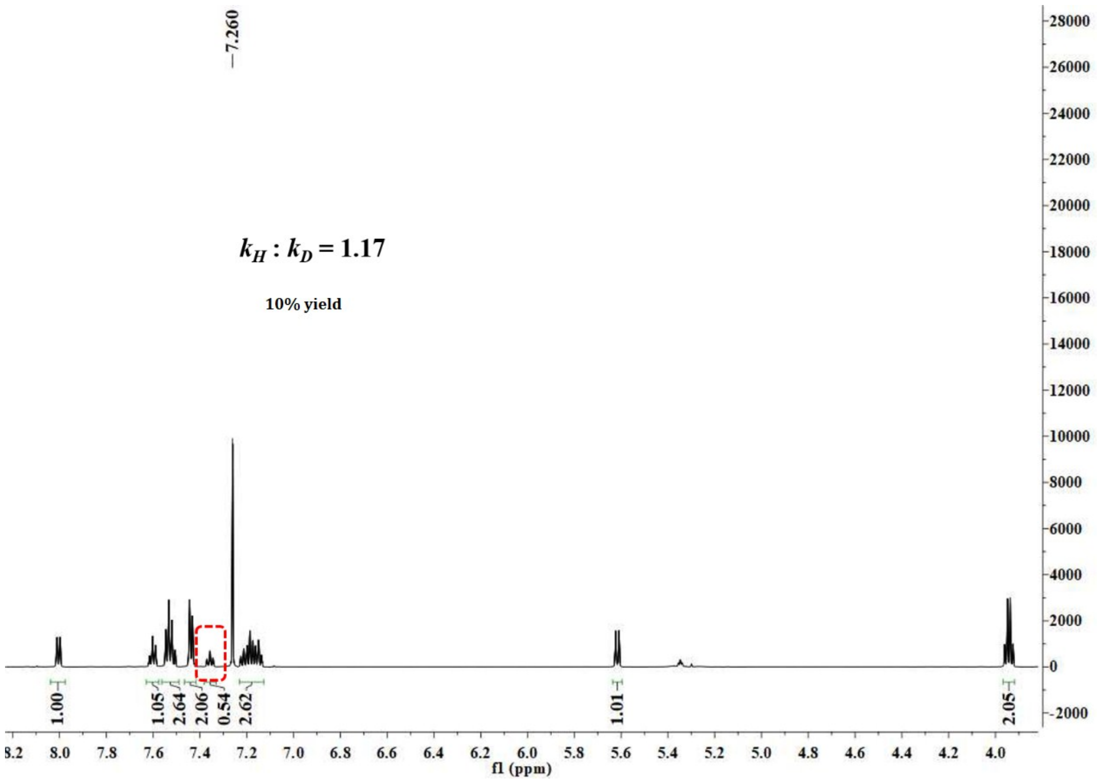
Intermolecular Competition Experiments



1a **[D$_5$]-1a** **3a** **[D$_4$]-3a**

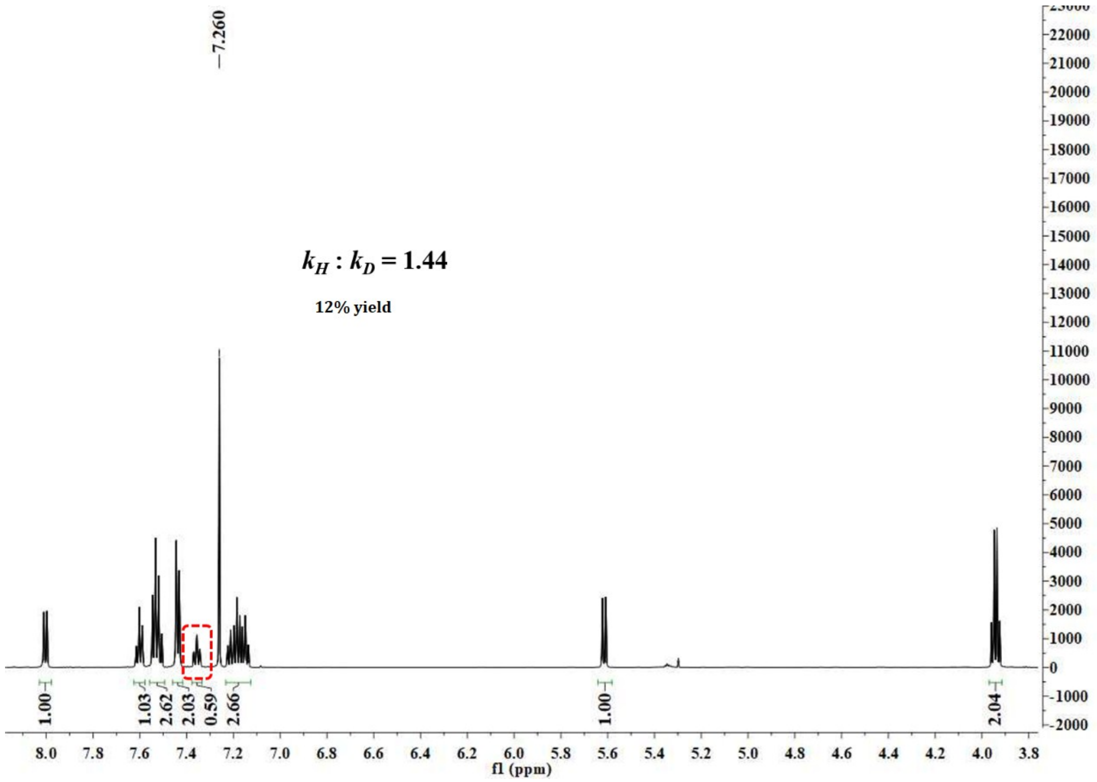
KIE = 1.3
average result
(repeating the experiment twice)

A mixture of **1a** (0.1 mmol) and [D$_5$]-**1a** (0.1 mmol), **2a** (0.1 mmol), [Ru(*p*-cymene)(MeCN)$_3$(SbF$_6$)$_2$] (3 mol %), HOAc (0.1 mmol) and DCE (1 mL) were added to a test tube. The reaction mixture was stirred at 60 ºC for 30 min. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the mixed products **3a** and [D$_4$]-**3a** (10% and 12% yield, respectively). An average KIE value (k_H/k_D = 1.3) was determined on the basis of ^{1}H NMR analysis.



$k_H : k_D = 1.17$

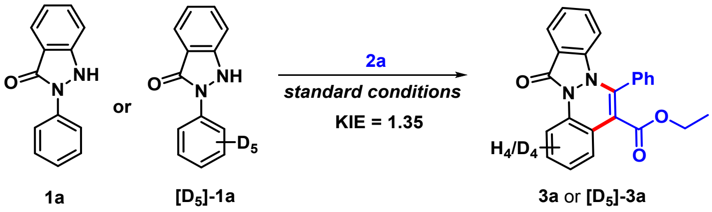
10% yield



$k_H : k_D = 1.44$

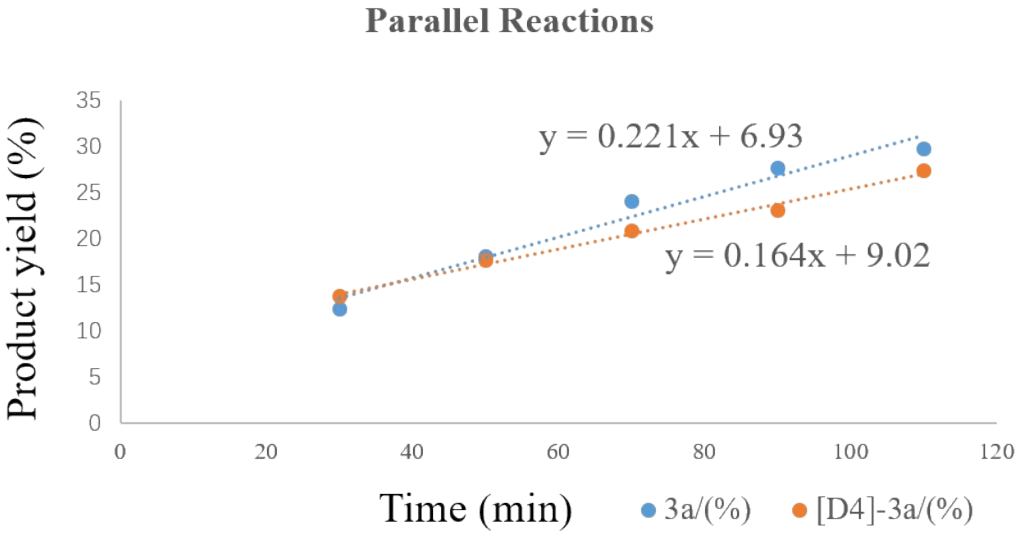
12% yield

Parallel Kinetic Isotope Effect

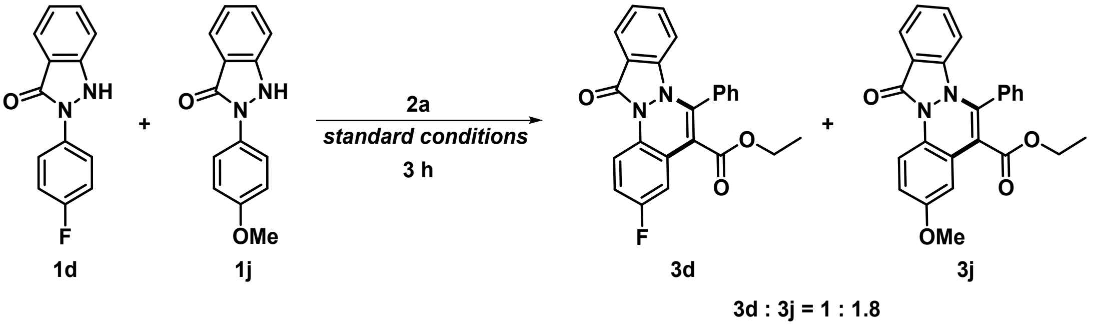


Two parallel reactions of **2a** with **1a** and **[D5]-1a** respectively were performed to determine the KIE value by comparison of the initial rates. Diazo compound **2a** (52 mg, 0.24 mmol), [Ru(*p*-cymene)(MeCN)$_3$(SbF$_6$)$_2$] (5 mg, 3 mol %), and HOAc (12 mg, 0.2 mmol) were added to a solution of **1a** (42 mg, 0.2 mmol) or **[D5]-1a** (43 mg, 0.2 mmol) in DCE (2 mL). The mixture was stirred at 60 °C. A periodic aliquot (100 µL) was abstracted by a pipette and analyzed by ^{1}H NMR with dibromomethane as an internal standard to provide the following conversions:

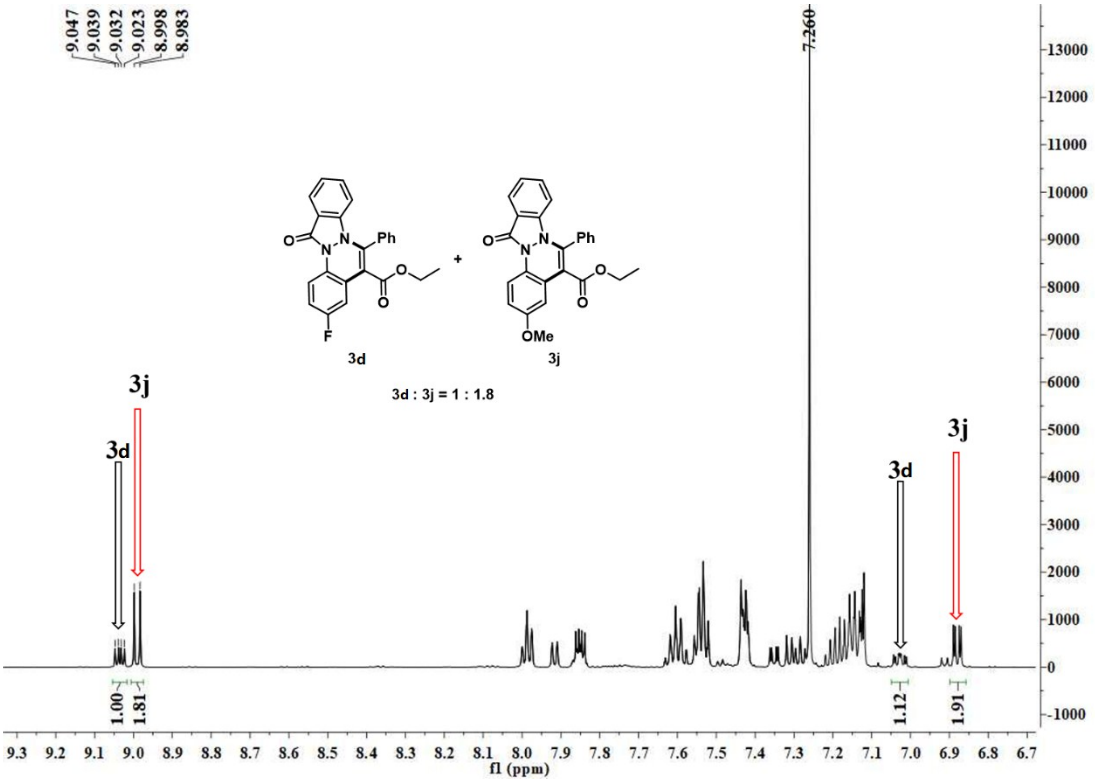
Time/min	30	50	70	90	110
3a/(%)	12.4	18.1	24.1	27.7	29.7
[D$_4$]-**3a**/(%)	13.7	17.6	20.8	23.0	27.4



3. Competitive Reaction

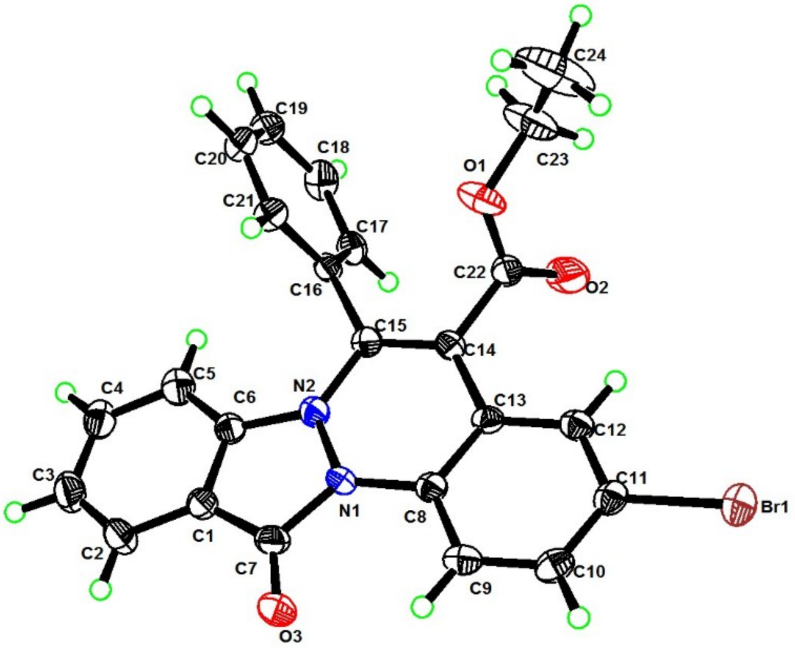


A mixture of **1d** (0.1 mmol), **1j** (0.1 mmol), [Ru(*p*-cymene) $(MeCN)_3(SbF_6)_2$] (3 mol %), HOAc (0.1 mmol), diazo compound **2a** (0.1 mmol) and DCE (1 mL) were added to a test tube. The reaction mixture was stirred at 60 ℃ for 3 h. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford compounds **3d** and **3j** as a mixture, which was characterized by ^1H NMR spectroscopy.



II. Crystal Structure and Data of Product 3f

1. Crystal Structure for 3f

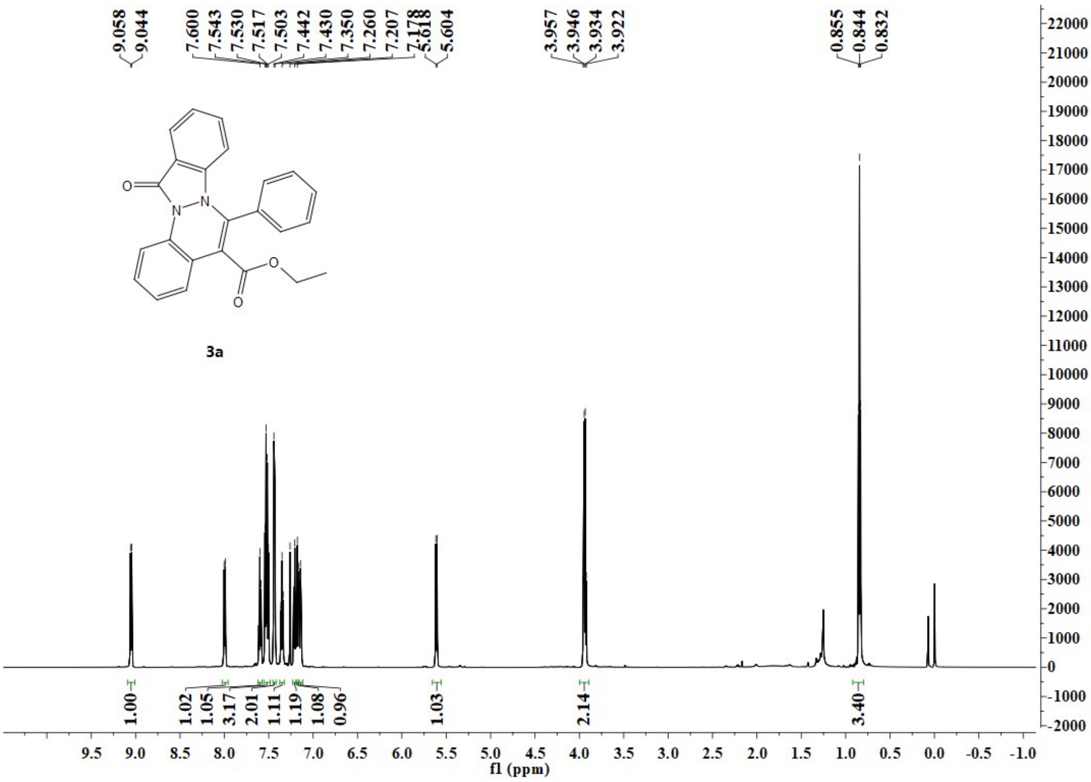


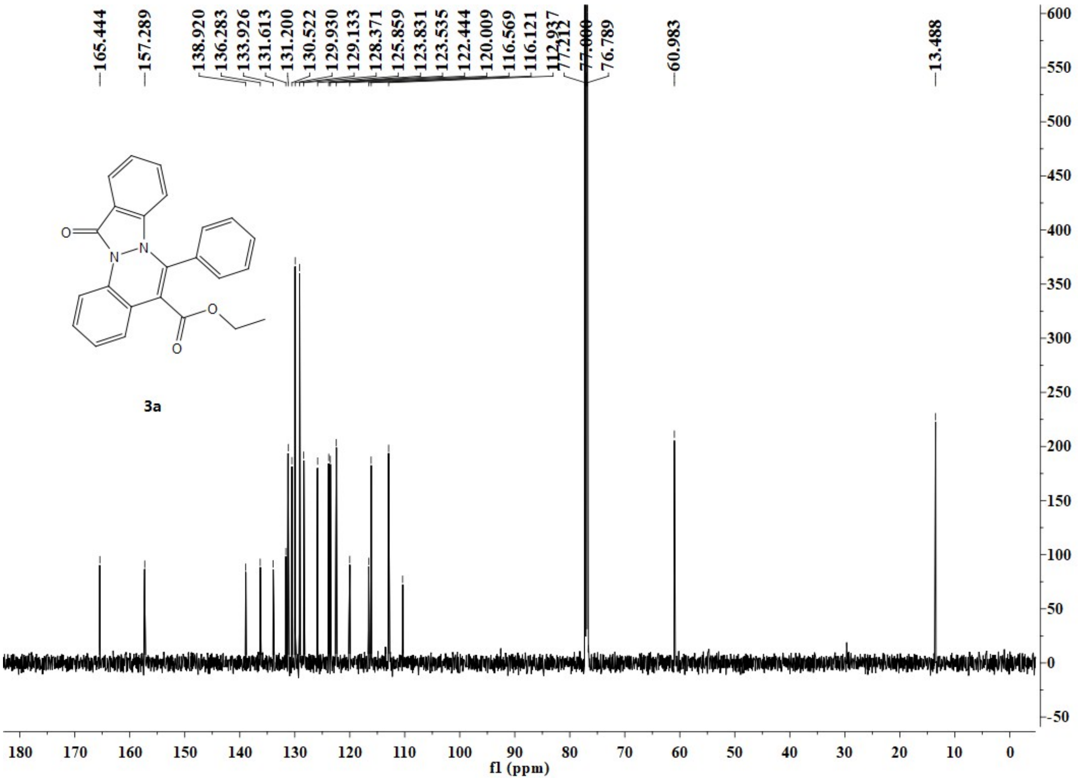
2. Crystal data and structure refinement for 3f

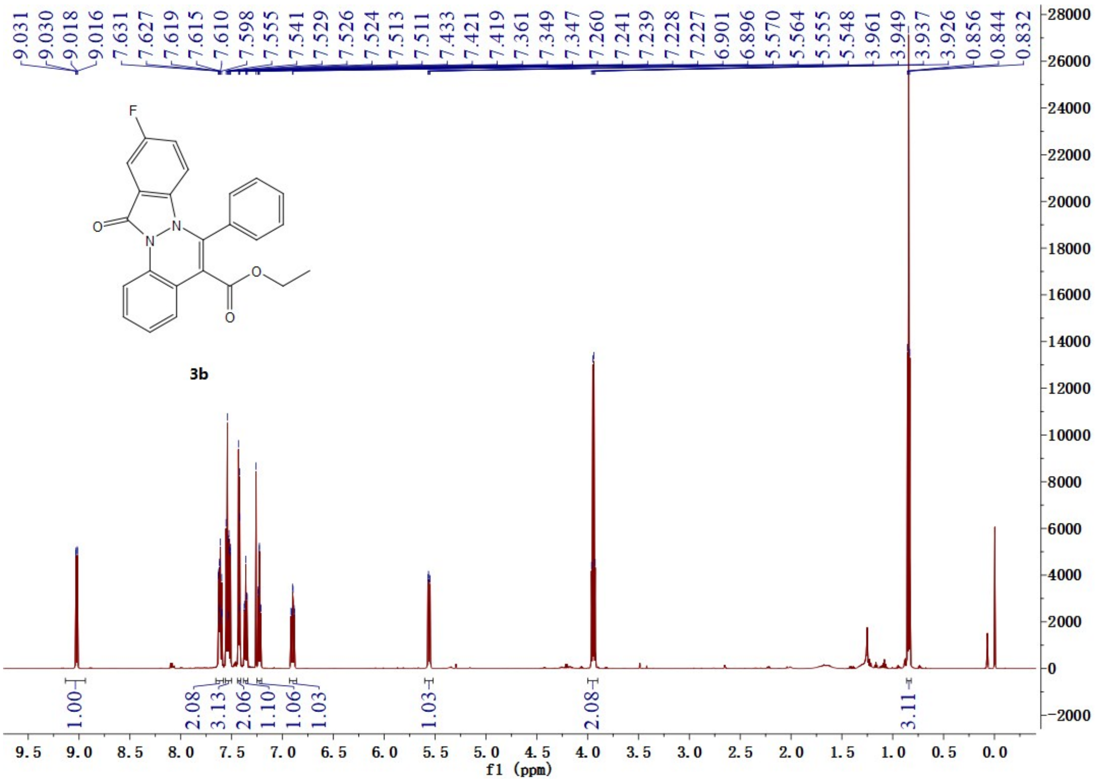
Empirical formula	$C_{24}H_{17}BrN_2O_3$
Formula weight	461.30
Temperature/K	173
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	8.811(3)
b/Å	20.892(8)
c/Å	10.950(4)
α/°	90
β/°	105.717(12)
γ/°	90
Volume/Å^3	1940.3(12)
Z	4
ρ_{calc}g/cm^3	1.579
μ/mm^{-1}	2.149
F(000)	936.0
Crystal size/mm^3	0.28 × 0.15 × 0.12

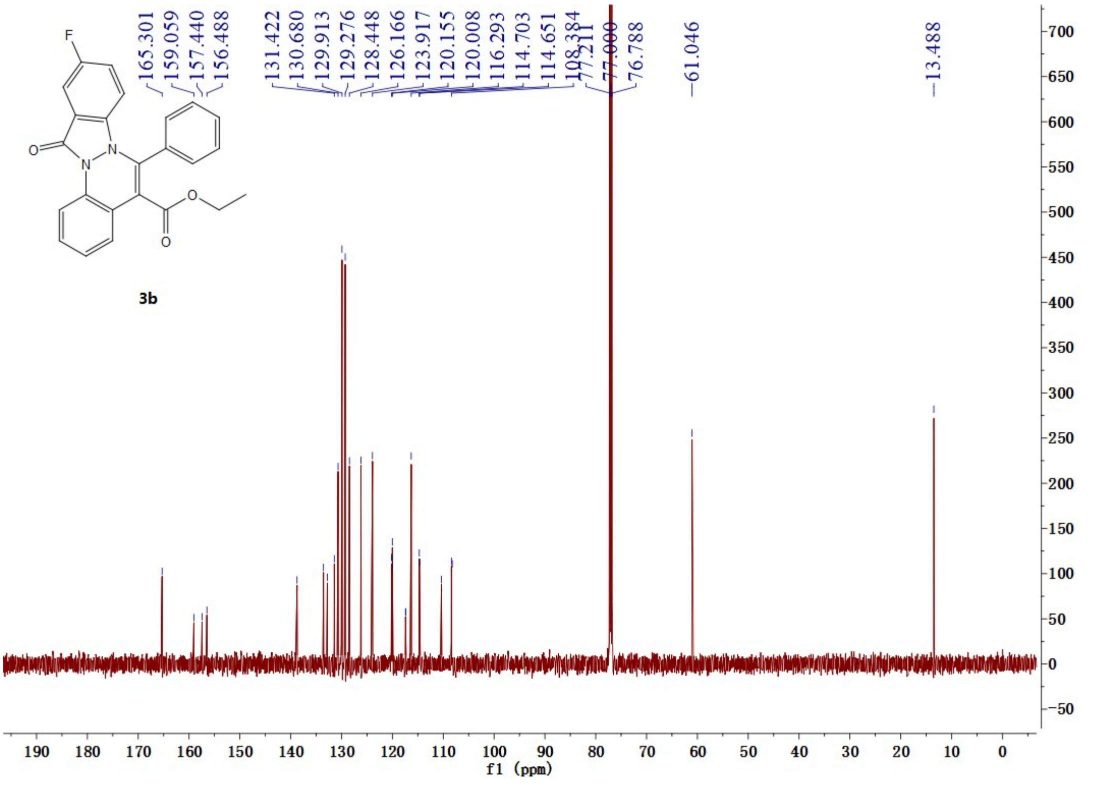
Radiation	MoKα ($\lambda = 0.71073$)
2Θ range for data collection/°	4.328 to 52.992
Index ranges	$-11 \leq h \leq 10$, $-21 \leq k \leq 26$, $-13 \leq l \leq 13$
Reflections collected	12115
Independent reflections	3940 [$R_{int} = 0.0623$, $R_{sigma} = 0.0806$]
Data/restraints/parameters	3940/18/273
Goodness-of-fit on F^2	1.042
Final R indexes [$I>=2\sigma (I)$]	$R_1 = 0.0458$, $wR_2 = 0.1138$
Final R indexes [all data]	$R_1 = 0.0661$, $wR_2 = 0.1245$
Largest diff. peak/hole / e Å^{-3}	0.54/-0.71

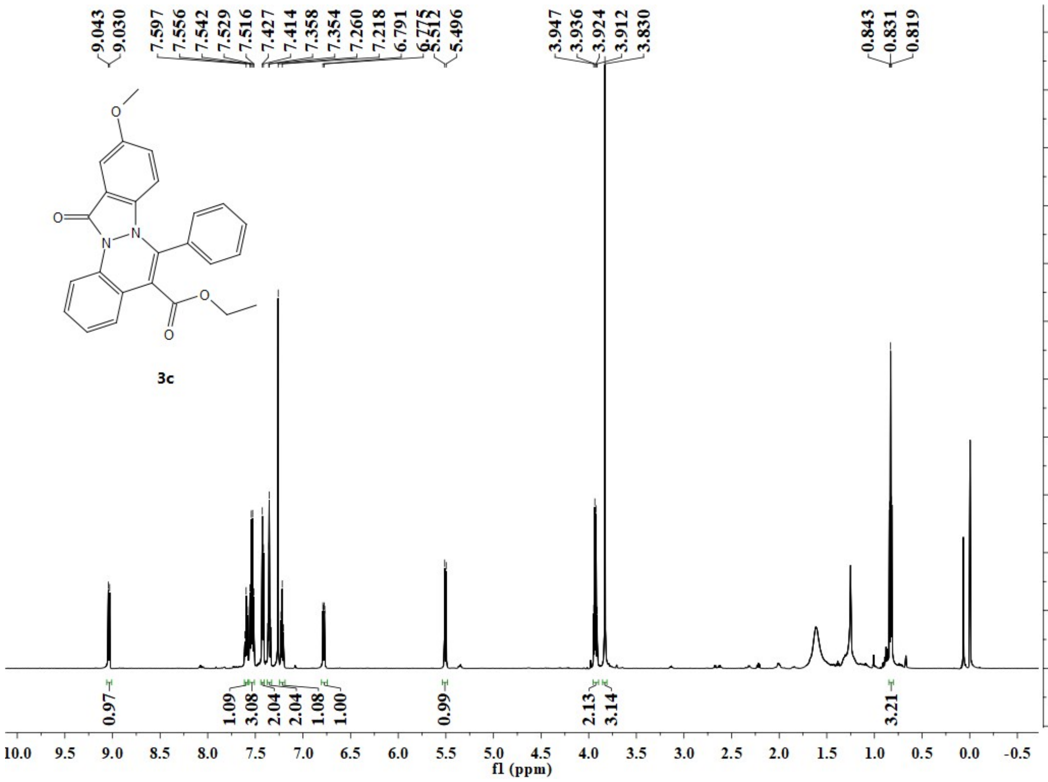
III. Copies of ^{1}H and ^{13}C NMR Spectra

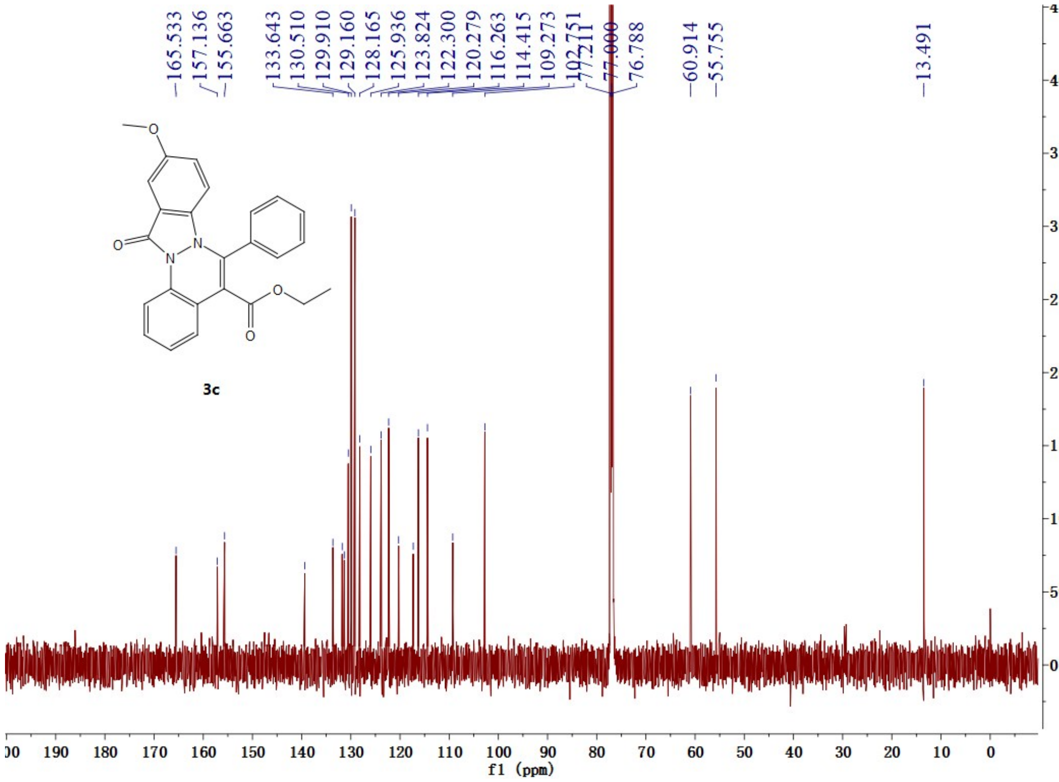


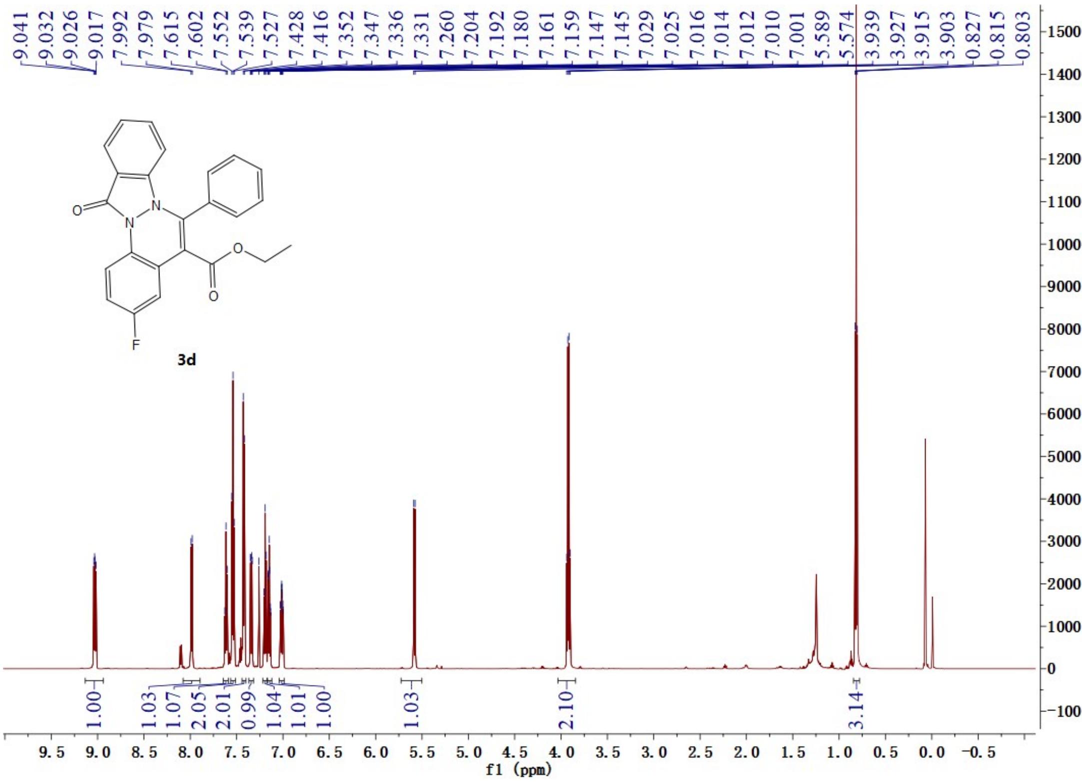


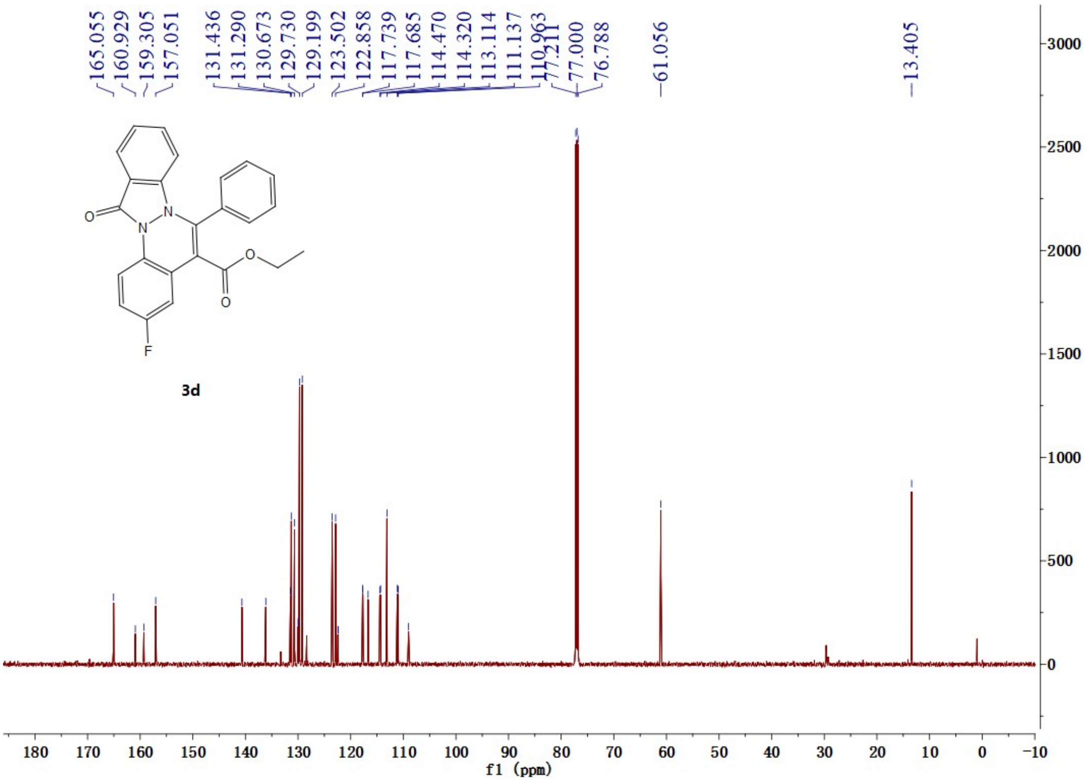

9.031
9.030
9.018
9.016
7.631
7.627
7.619
7.615
7.610
7.598
7.555
7.541
7.529
7.526
7.524
7.513
7.511
7.433
7.421
7.419
7.361
7.349
7.347
7.260
7.241
7.239
7.228
7.227
6.901
6.896
5.570
5.564
5.555
5.548
3.961
3.949
3.937
3.926
0.856
0.844
0.832
F
O
N
N
O
O
3b
1.00
2.08
3.13
2.06
1.10
1.06
1.03
1.03
2.08
3.11
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)
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000

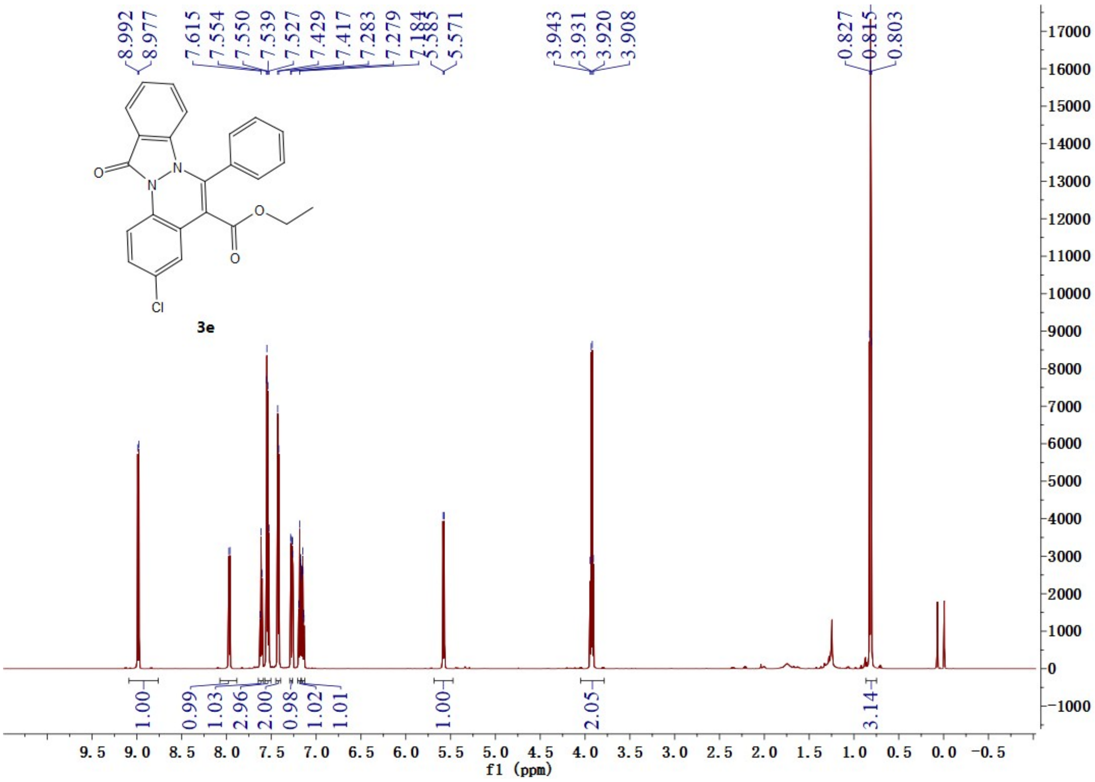

165.301
159.059
157.440
156.488
131.422
130.680
129.913
129.276
128.448
126.166
123.917
120.155
120.008
116.293
114.703
114.651
108.384
77.211
77.000
76.788
61.046
13.488
F
O
N
N
O
O
3b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50

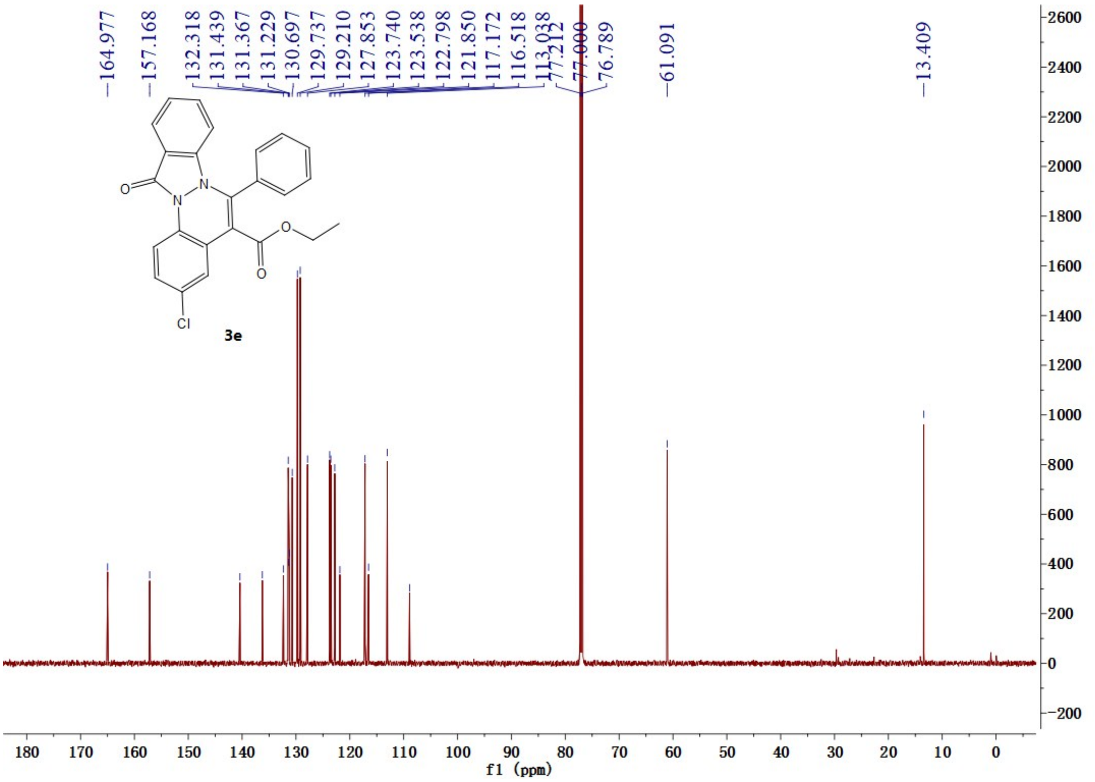

9.043
9.030
7.597
7.556
7.542
7.529
7.516
7.427
7.414
7.358
7.354
7.260
7.218
6.791
6.775
5.512
5.496
3.947
3.936
3.924
3.912
3.830
0.843
0.831
0.819
O
O
N
N
O
3c
0.97
1.09
3.08
2.04
2.04
1.08
1.00
0.99
2.13
3.14
3.21
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

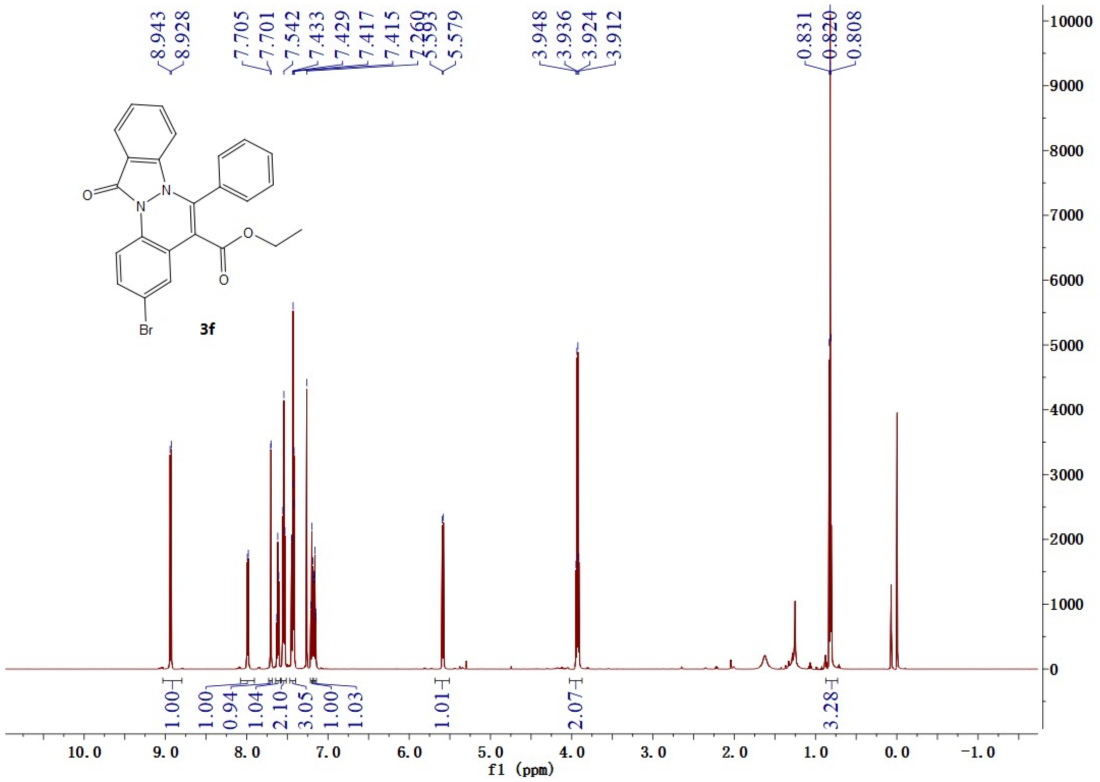

165.533
157.136
155.663
133.643
130.510
129.910
129.160
128.165
125.936
123.824
122.300
120.279
116.263
114.415
109.273
102.751
77.211
77.000
76.788
60.914
55.755
13.491
O
O
N
N
O
3c
450
400
350
300
250
200
150
100
50
0
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

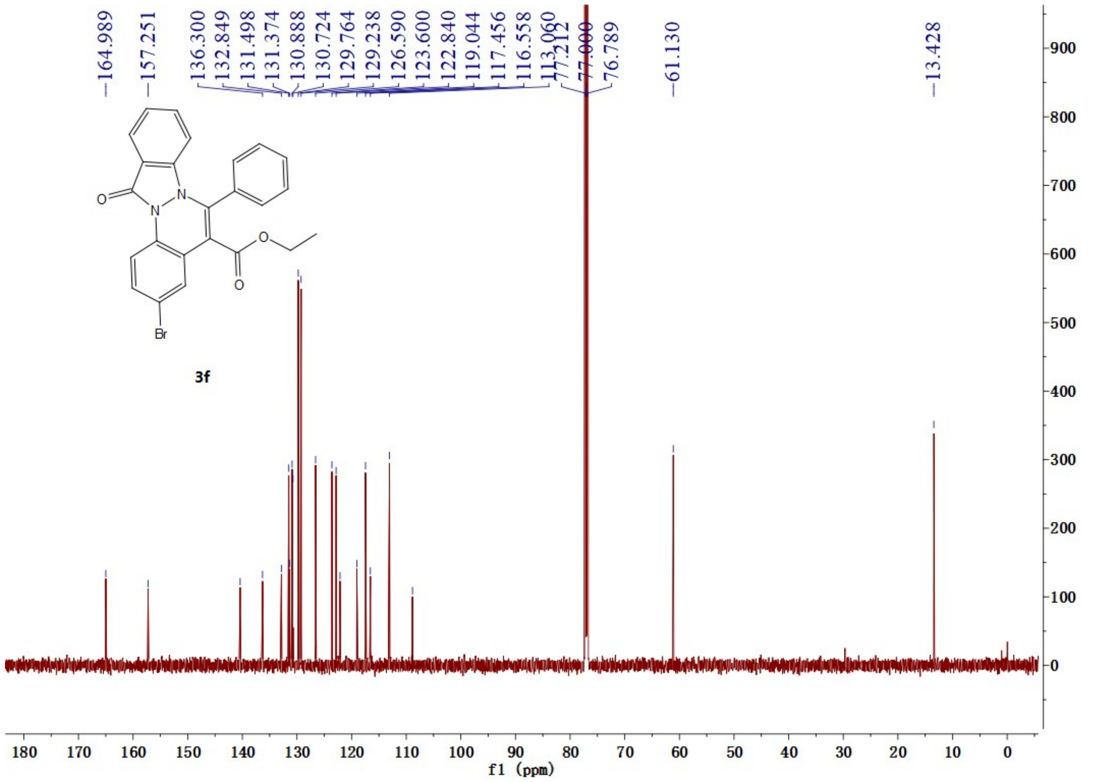

9.041
9.032
9.026
9.017
7.992
7.979
7.615
7.602
7.552
7.539
7.527
7.428
7.416
7.352
7.347
7.336
7.331
7.260
7.204
7.192
7.180
7.161
7.159
7.147
7.145
7.029
7.025
7.016
7.014
7.012
7.010
7.001
5.589
5.574
3.939
3.927
3.915
3.903
0.827
0.815
0.803
O
N
N
O
O
F
3d
1.00
1.03
1.07
2.05
2.01
0.99
1.04
1.01
1.00
1.03
2.10
3.14
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
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)

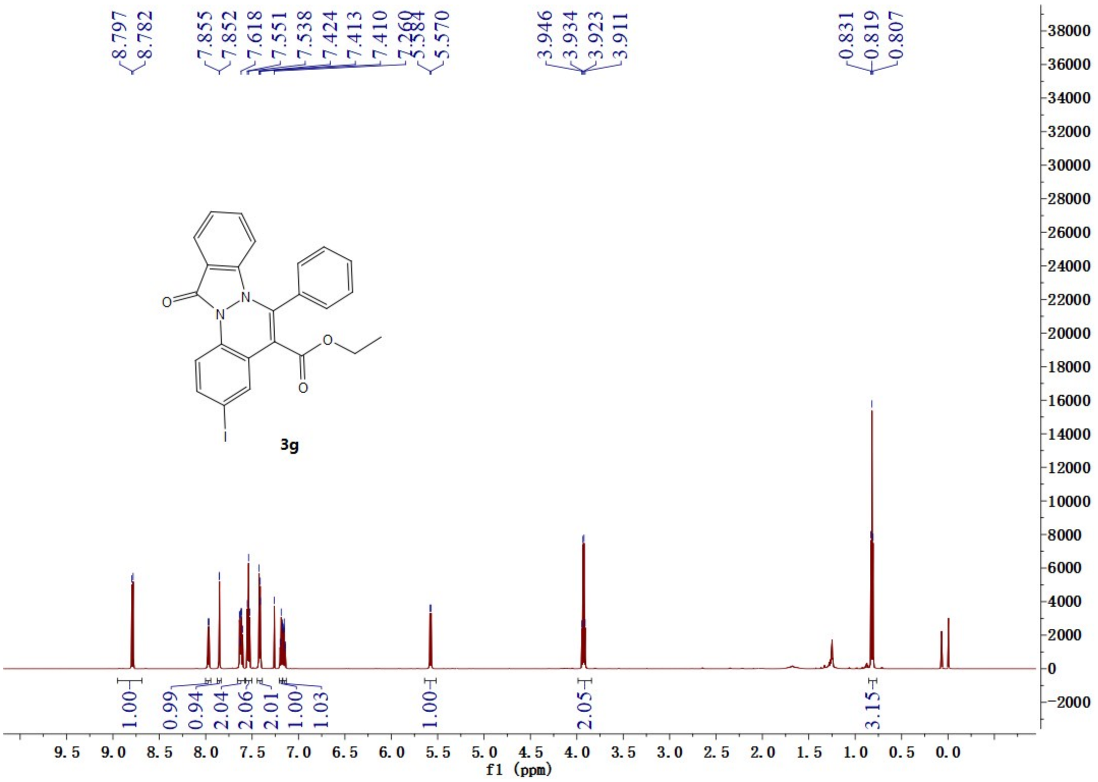

165.055
160.929
159.305
157.051
131.436
131.290
130.673
129.730
129.199
123.502
122.858
117.739
117.685
114.470
114.320
113.114
111.137
110.963
77.211
77.000
76.788
61.056
13.405
O
N
N
O
O
F
3d
3000
2500
2000
1500
1000
500
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.992
8.977
7.615
7.554
7.550
7.539
7.527
7.429
7.417
7.283
7.279
7.184
5.585
5.571
3.943
3.931
3.920
3.908
0.827
0.815
0.803
O
N
N
O
O
Cl
3e
1.00
0.99
1.03
2.96
2.00
0.98
1.02
1.01
1.00
2.05
3.14
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000
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)

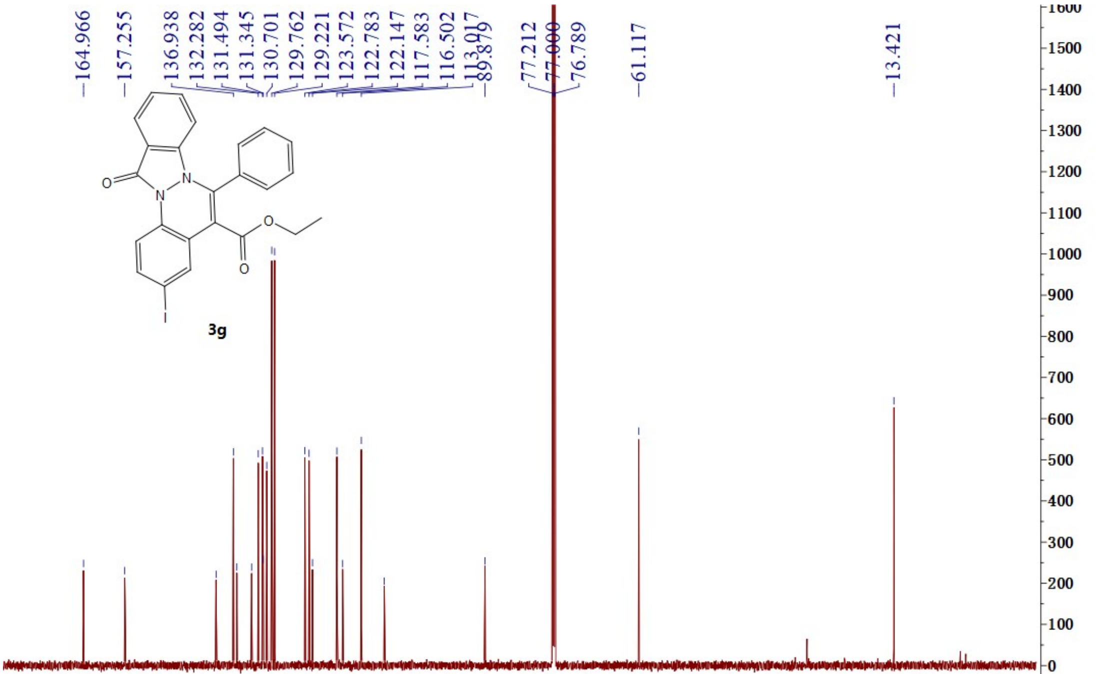

164.977
157.168
132.318
131.439
131.367
131.229
130.697
129.737
129.210
127.853
123.740
123.538
122.798
121.850
117.172
116.518
113.038
77.212
77.000
76.789
61.091
13.409
O
N
N
O
O
Cl
3e
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
−200
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.943
8.928
7.705
7.701
7.542
7.433
7.429
7.417
7.415
7.260
5.593
5.579
3.948
3.936
3.924
3.912
0.831
0.820
0.808
O
N
N
O
O
Br
3f
1.00
1.00
0.94
1.04
2.10
3.05
1.00
1.03
1.01
2.07
3.28
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)

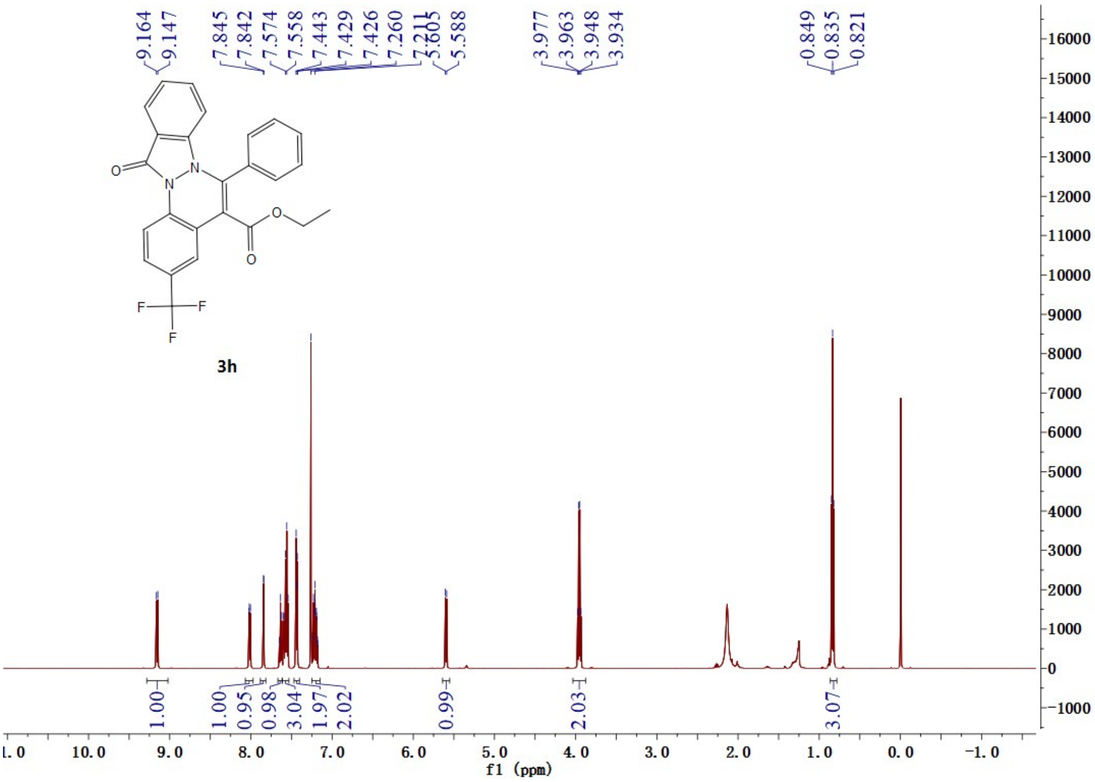

164.989
157.251
136.300
132.849
131.498
131.374
130.888
130.724
129.764
129.238
126.590
123.600
122.840
119.044
117.456
116.558
113.060
77.212
77.000
76.789
61.130
13.428
O
N
N
O
O
Br
3f
900
800
700
600
500
400
300
200
100
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


3g

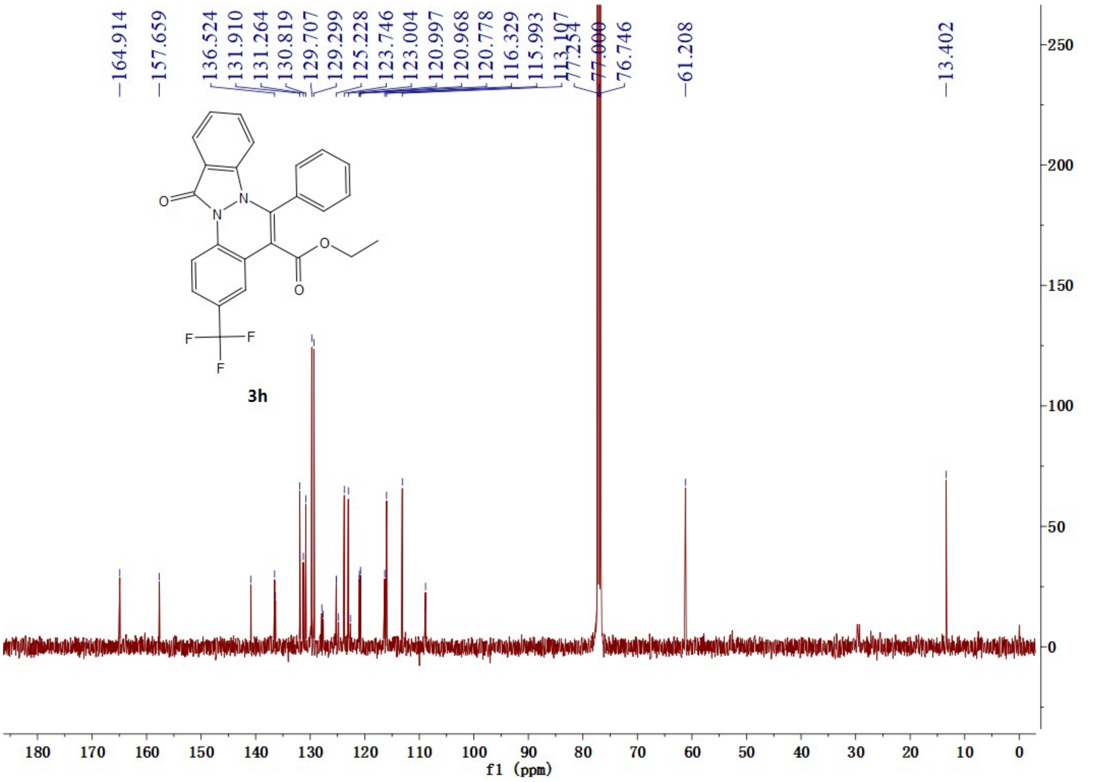
8.797
8.782
7.855
7.852
7.618
7.551
7.538
7.424
7.413
7.410
7.260
5.584
5.570
3.946
3.934
3.923
3.911
0.831
0.819
0.807
1.00
0.99
0.94
2.04
2.06
2.01
1.00
1.03
1.00
2.05
3.15
O
N
N
O
O
I
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
38000 36000 34000 32000 30000 28000 26000 24000 22000 20000 18000 16000 14000 12000 10000 8000 6000 4000 2000 0 −2000


3g

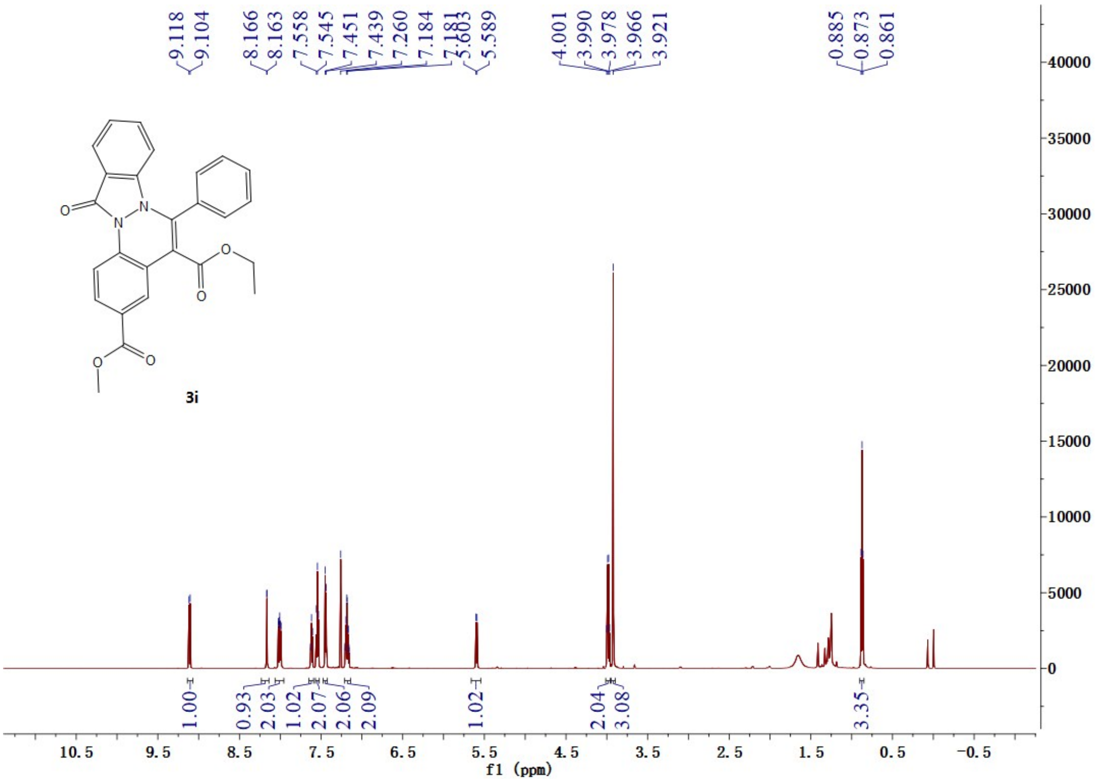
164.966
157.255
136.938
132.282
131.494
131.345
130.701
129.762
129.221
123.572
122.783
122.147
117.583
116.502
113.017
89.879
77.212
77.000
76.789
61.117
13.421
O
N
N
O
O
I
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)
1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 −100

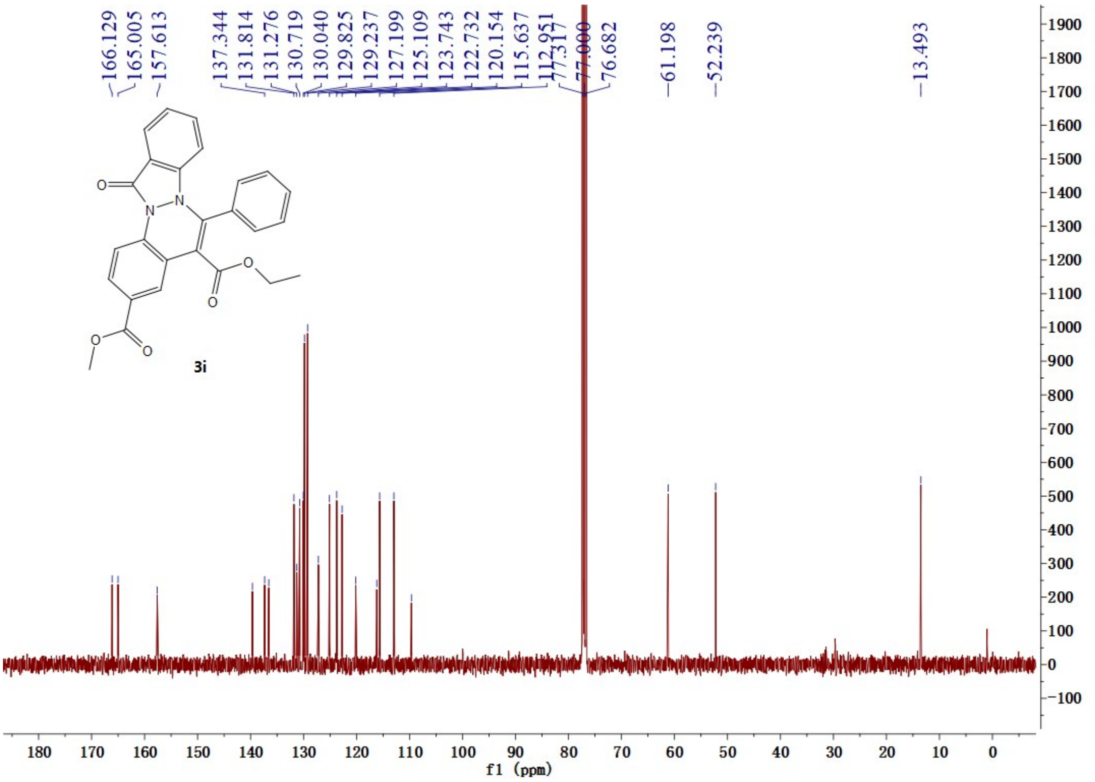

9.164
9.147
7.845
7.842
7.574
7.558
7.443
7.429
7.426
7.260
7.211
5.605
5.588
3.977
3.963
3.948
3.934
0.849
0.835
0.821
O
N
N
O
O
F
F
F
1.00
1.00
0.95
0.98
3.04
1.97
2.02
0.99
2.03
3.07
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000
1.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
−1.0
f1 (ppm)

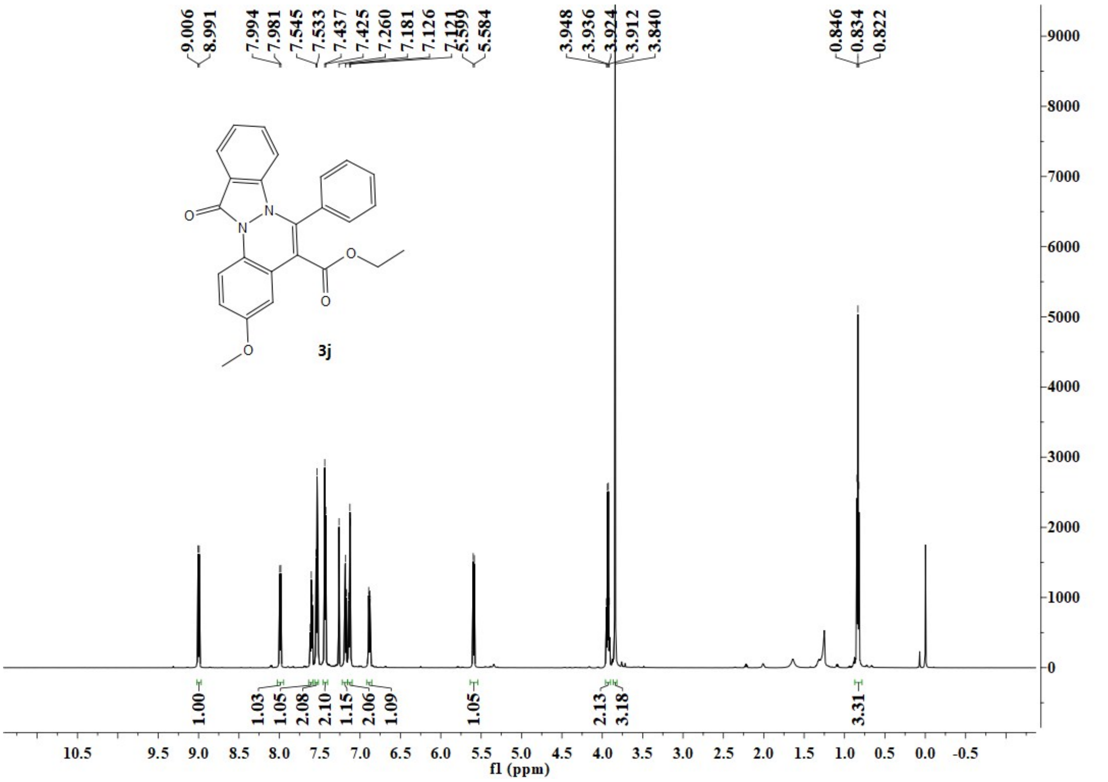
3h

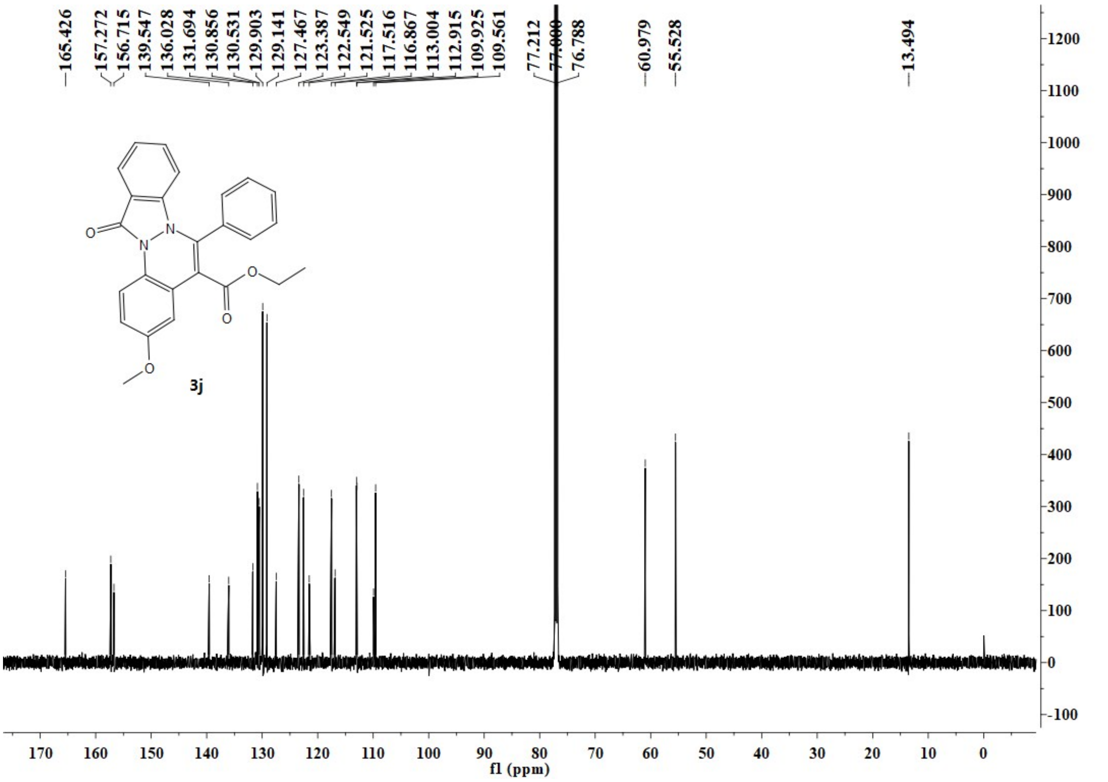

164.914
157.659
136.524
131.910
131.264
130.819
129.707
129.299
125.228
123.746
123.004
120.997
120.968
120.778
116.329
115.993
113.107
77.254
77.000
76.746
61.208
13.402
O
N
N
O
O
F
F
F
250
200
150
100
50
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

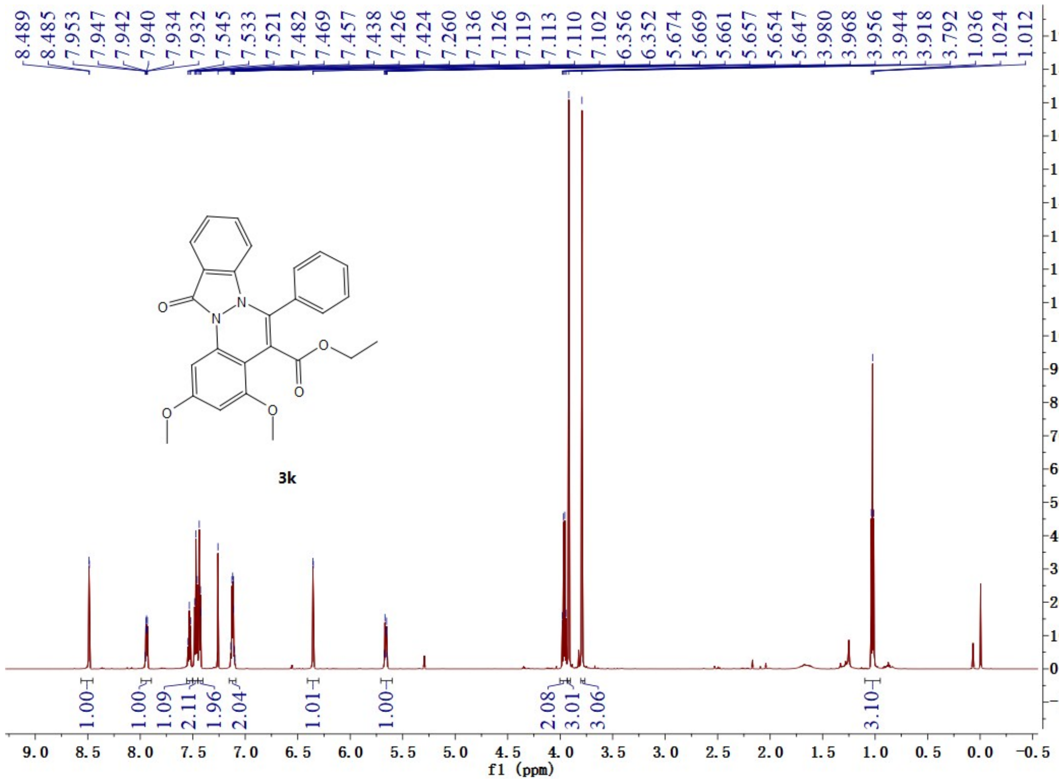
3h

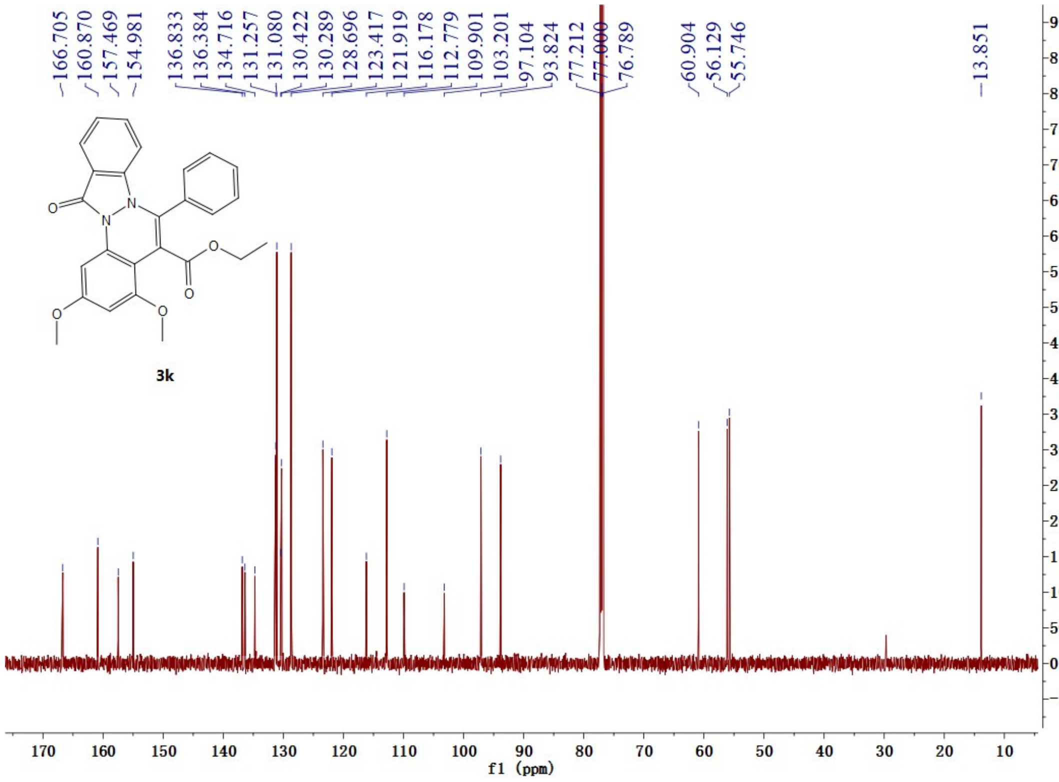

9.118
9.104
8.166
8.163
7.558
7.545
7.451
7.439
7.260
7.184
7.181
5.603
5.589
4.001
3.990
3.978
3.966
3.921
0.885
0.873
0.861
O
N
N
O
O
O
O
3i
1.00
0.93
2.03
1.02
2.07
2.06
2.09
1.02
2.04
3.08
3.35
40000
35000
30000
25000
20000
15000
10000
5000
0
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

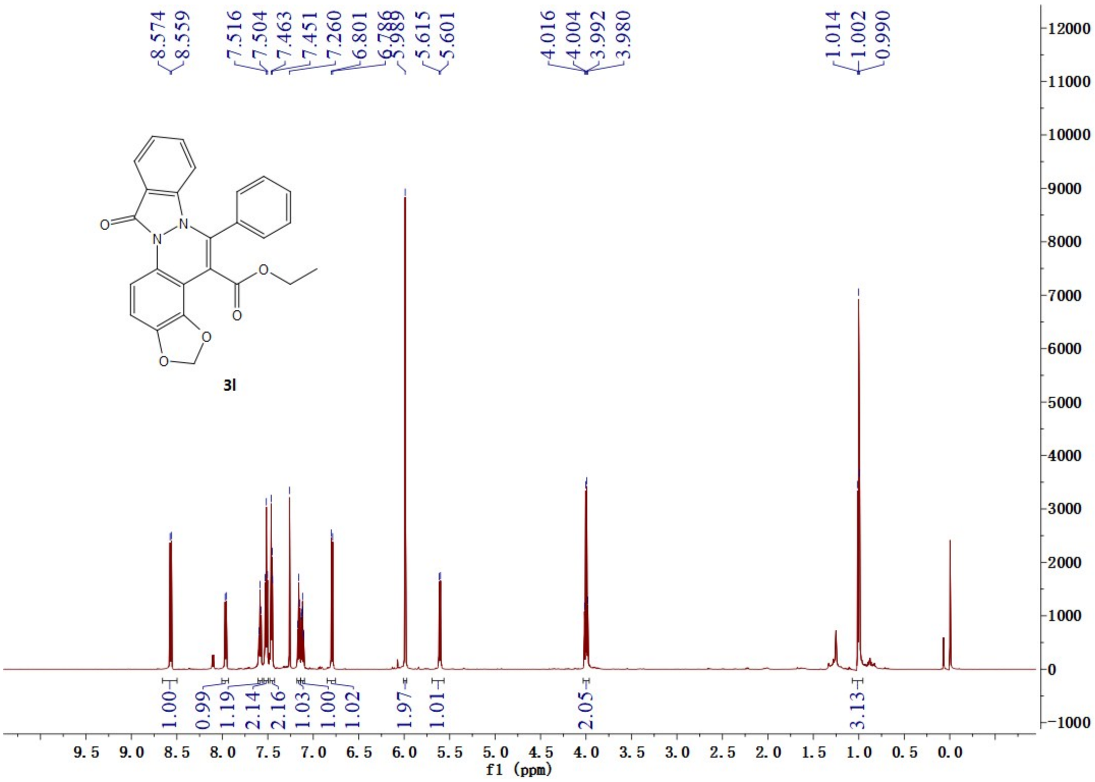

166.129
165.005
157.613
137.344
131.814
131.276
130.719
130.040
129.825
129.237
127.199
125.109
123.743
122.732
120.154
115.637
112.951
77.317
77.000
76.682
61.198
52.239
13.493
O
N
N
O
O
O
O
3i
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

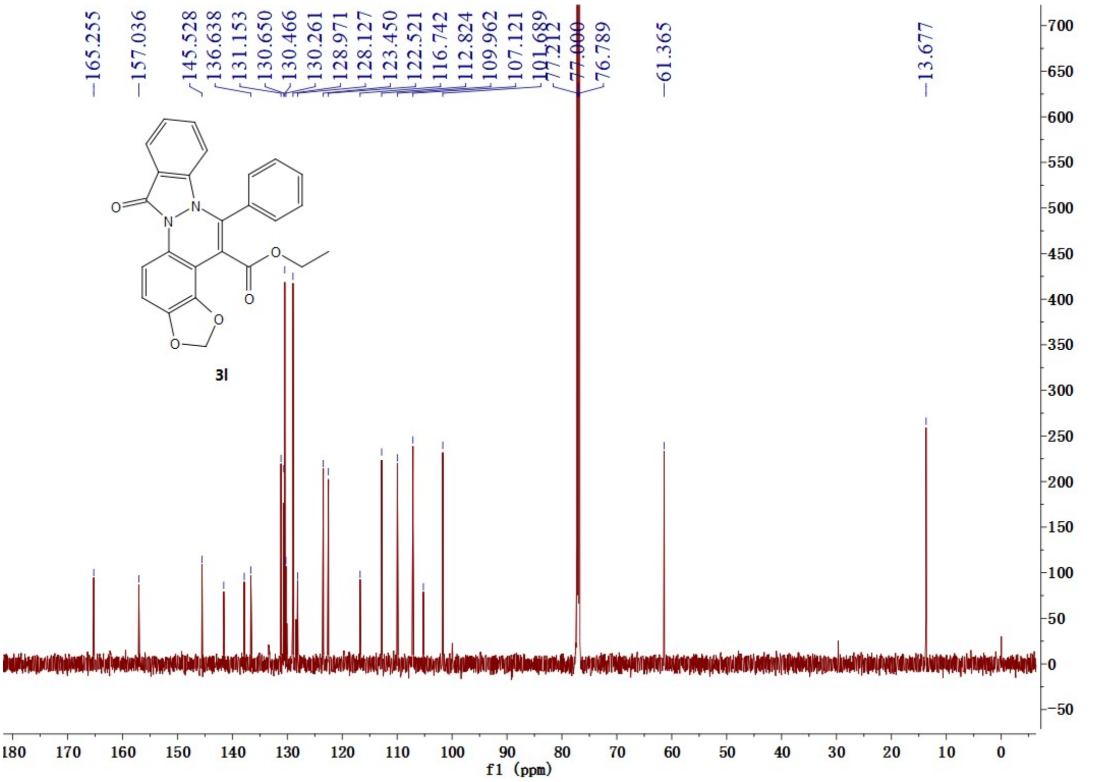

9.006
8.991
7.994
7.981
7.545
7.533
7.437
7.425
7.260
7.181
7.126
7.121
5.599
5.584
3.948
3.936
3.924
3.912
3.840
0.846
0.834
0.822
O
N
N
O
O
O
3j
1.00
1.03
1.05
2.08
2.10
1.15
2.06
1.09
1.05
2.13
3.18
3.31
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
9000
8000
7000
6000
5000
4000
3000
2000
1000
0

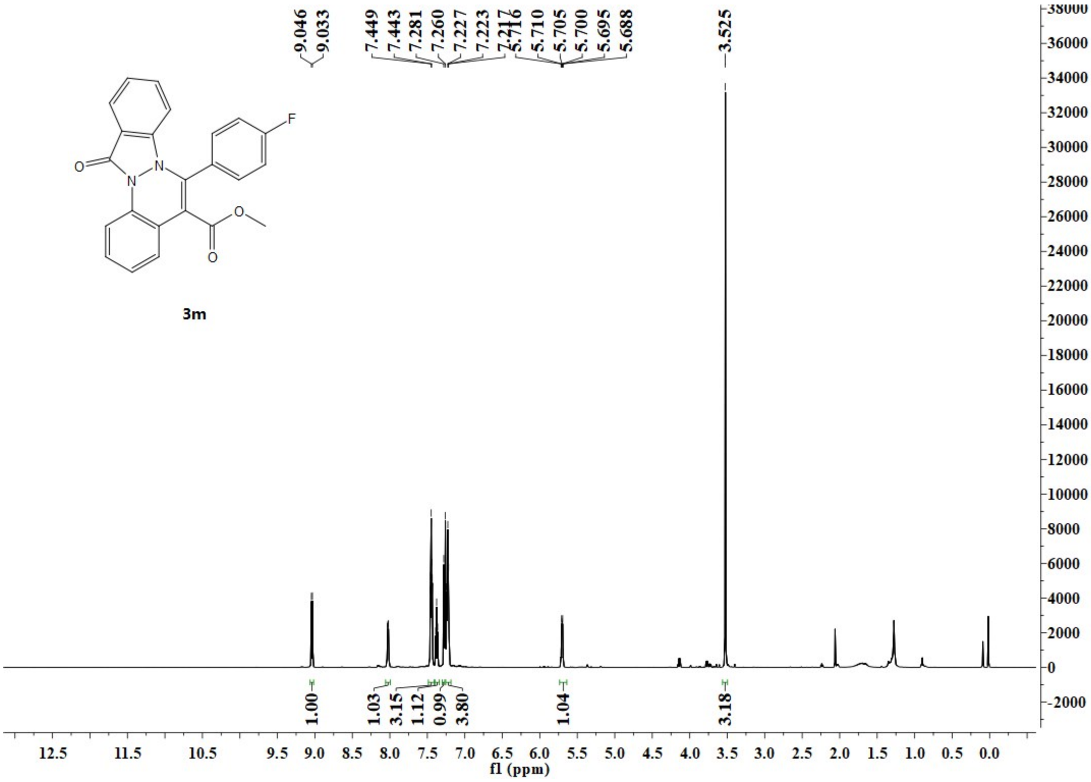

165.426
157.272
156.715
139.547
136.028
131.694
130.856
130.531
129.903
129.141
127.467
123.387
122.549
121.525
117.516
116.867
113.004
112.915
109.925
109.561
77.212
77.000
76.788
60.979
55.528
13.494
O
N
N
O
O
O
3j
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

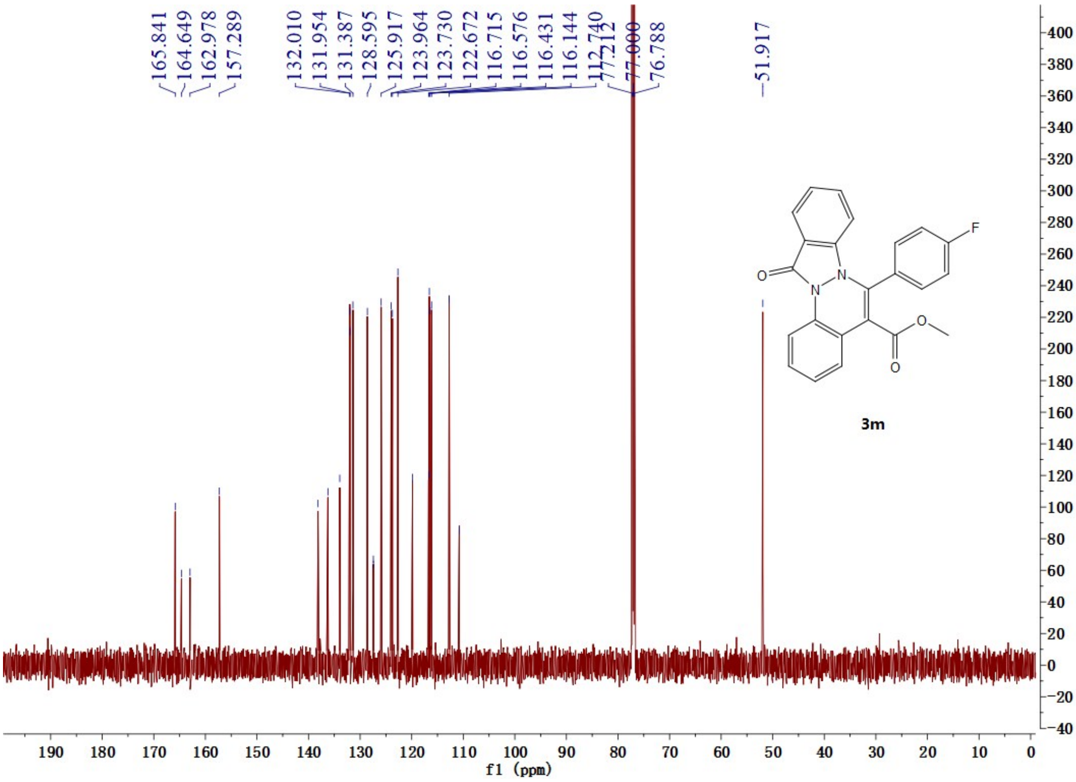

8.489
8.485
7.953
7.947
7.942
7.940
7.934
7.932
7.545
7.533
7.521
7.482
7.469
7.457
7.438
7.426
7.424
7.260
7.136
7.126
7.119
7.113
7.110
7.102
6.356
6.352
5.674
5.669
5.661
5.657
5.654
5.647
3.980
3.968
3.956
3.944
3.918
3.792
1.036
1.024
1.012
3k
1.00
1.00
1.09
2.11
1.96
2.04
1.01
1.00
2.08
3.01
3.06
3.10
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)
19000 18000 17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 −1000

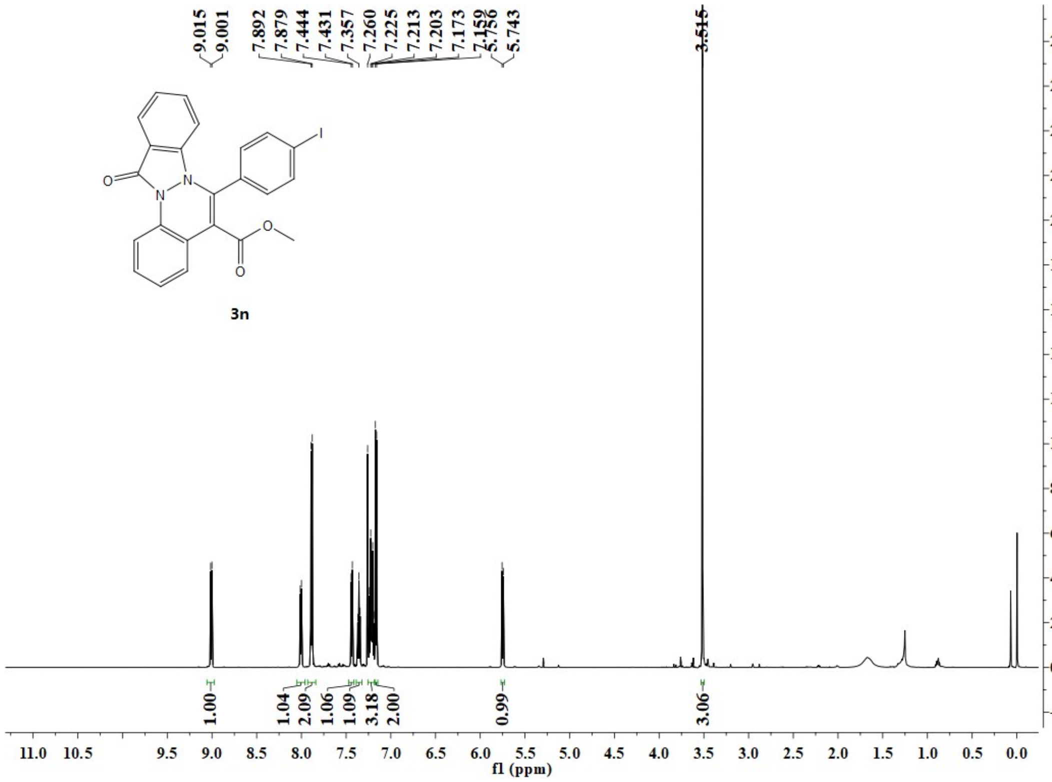

166.705
160.870
157.469
154.981
136.833
136.384
134.716
131.257
131.080
130.422
130.289
128.696
123.417
121.919
116.178
112.779
109.901
103.201
97.104
93.824
77.212
77.000
76.789
60.904
56.129
55.746
13.851
3k
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)
900 850 800 750 700 650 600 550 500 450 400 350 300 250 200 150 100 50 0 −50

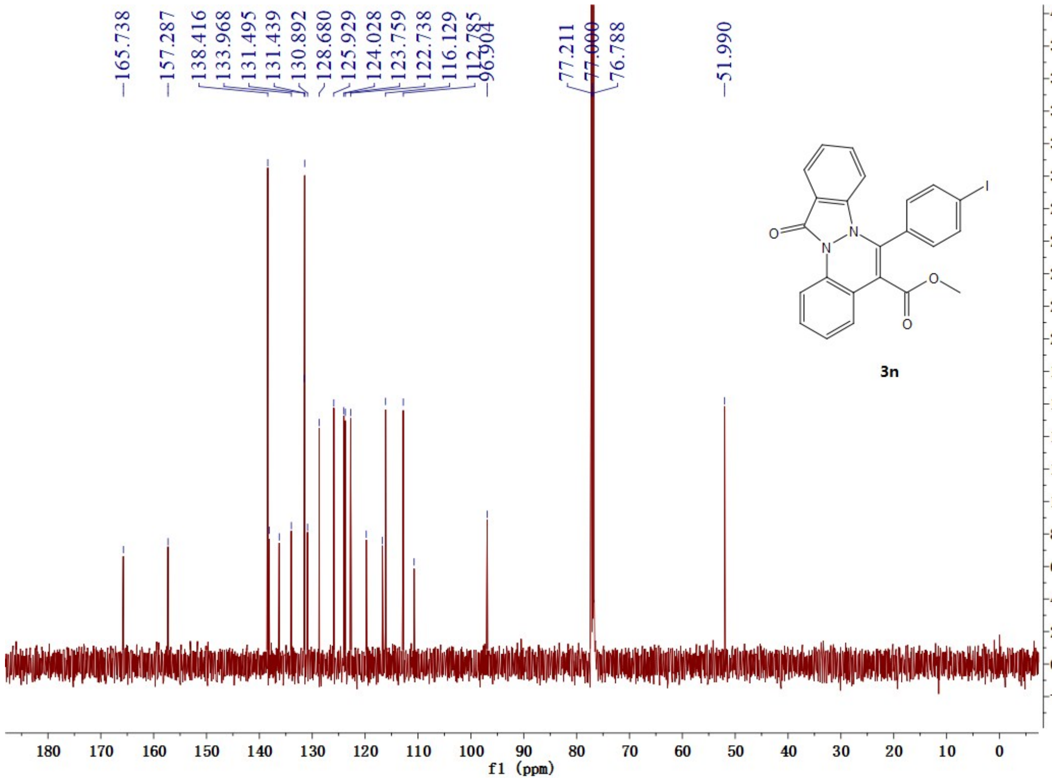

8.574
8.559
7.516
7.504
7.463
7.451
7.260
6.801
6.786
5.989
5.615
5.601
4.016
4.004
3.992
3.980
1.014
1.002
0.990
3l
1.00
0.99
1.19
2.14
2.16
1.03
1.00
1.02
1.97
1.01
2.05
3.13
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000

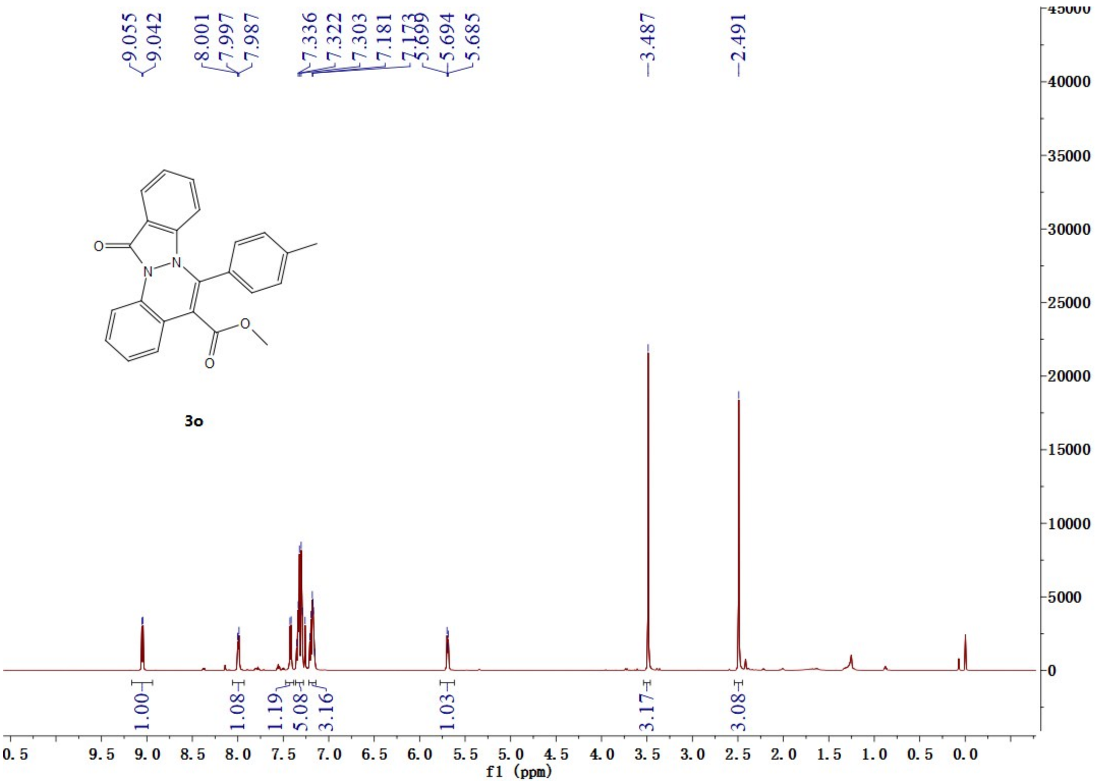

165.255
157.036
145.528
136.638
131.153
130.650
130.466
130.261
128.971
128.127
123.450
122.521
116.742
112.824
109.962
107.121
101.689
77.212
77.000
76.789
61.365
13.677
3l
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
−50

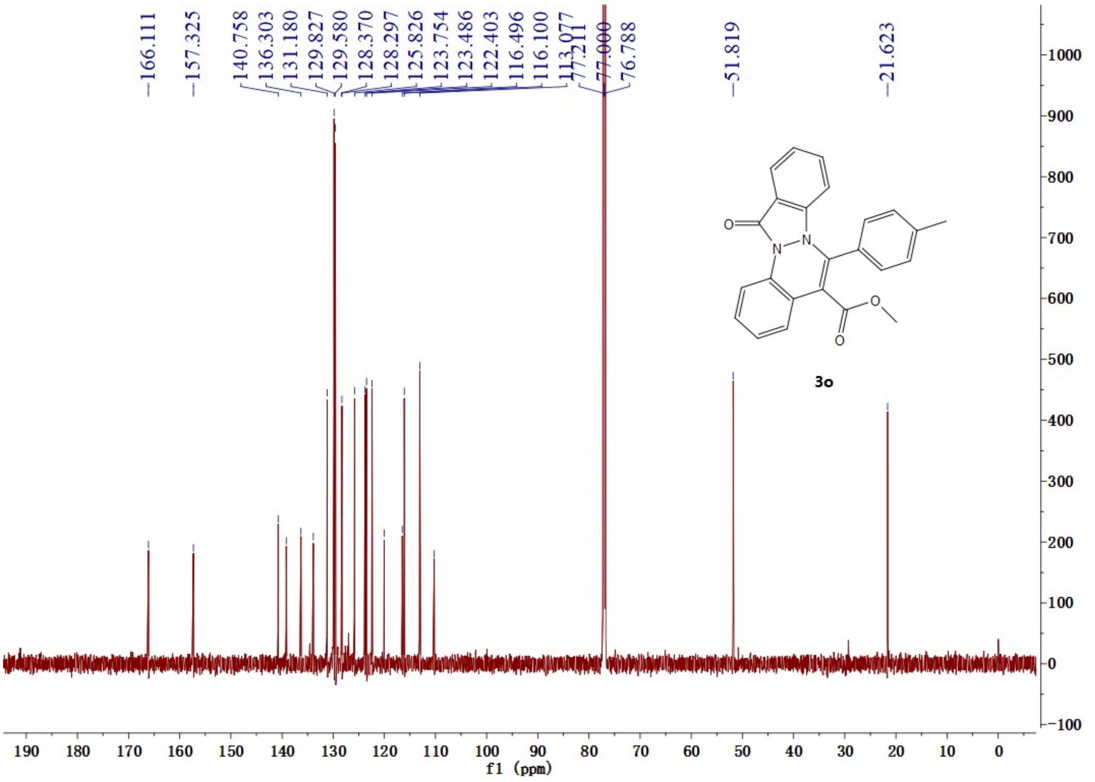

9.046
9.033
7.449
7.443
7.281
7.260
7.227
7.223
7.217
5.716
5.710
5.705
5.700
5.695
5.688
3.525
F
O
N
N
O
O
3m
1.00
1.03
3.15
1.12
0.99
3.80
1.04
3.18
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
38000
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000

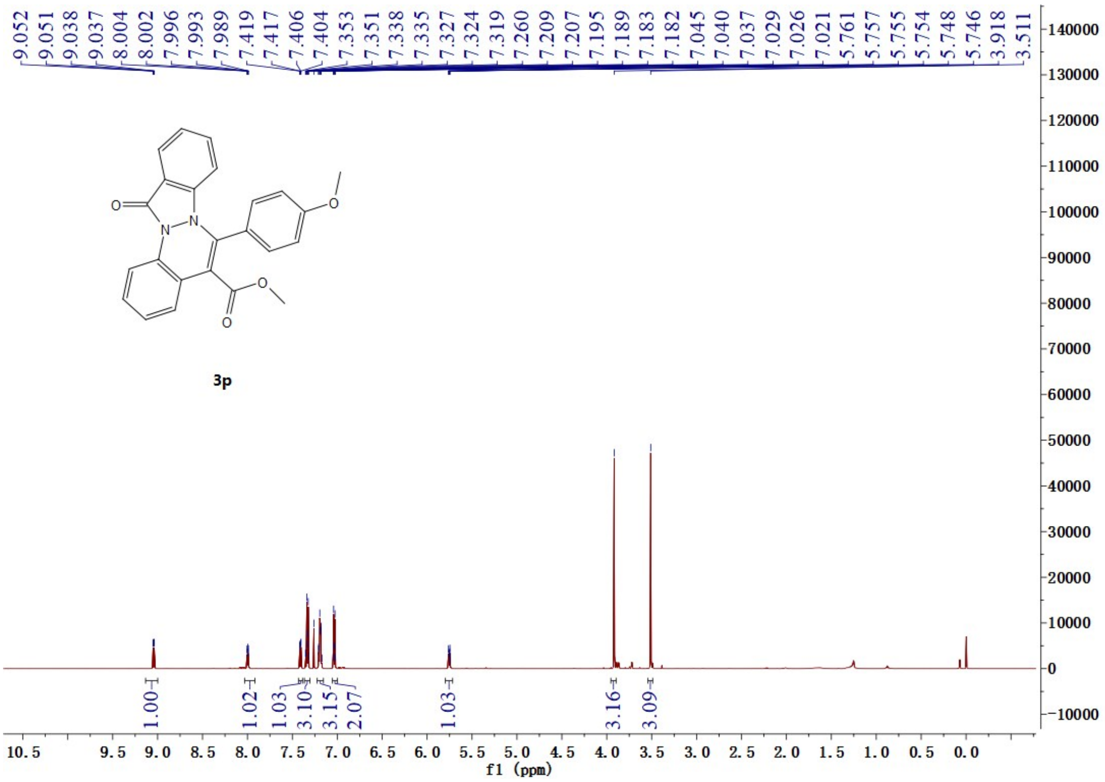

165.841
164.649
162.978
157.289
132.010
131.954
131.387
128.595
125.917
123.964
123.730
122.672
116.715
116.576
116.431
116.144
112.740
77.212
77.000
76.788
51.917
F
O
N
N
O
O
3m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
400
380
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
−20
−40

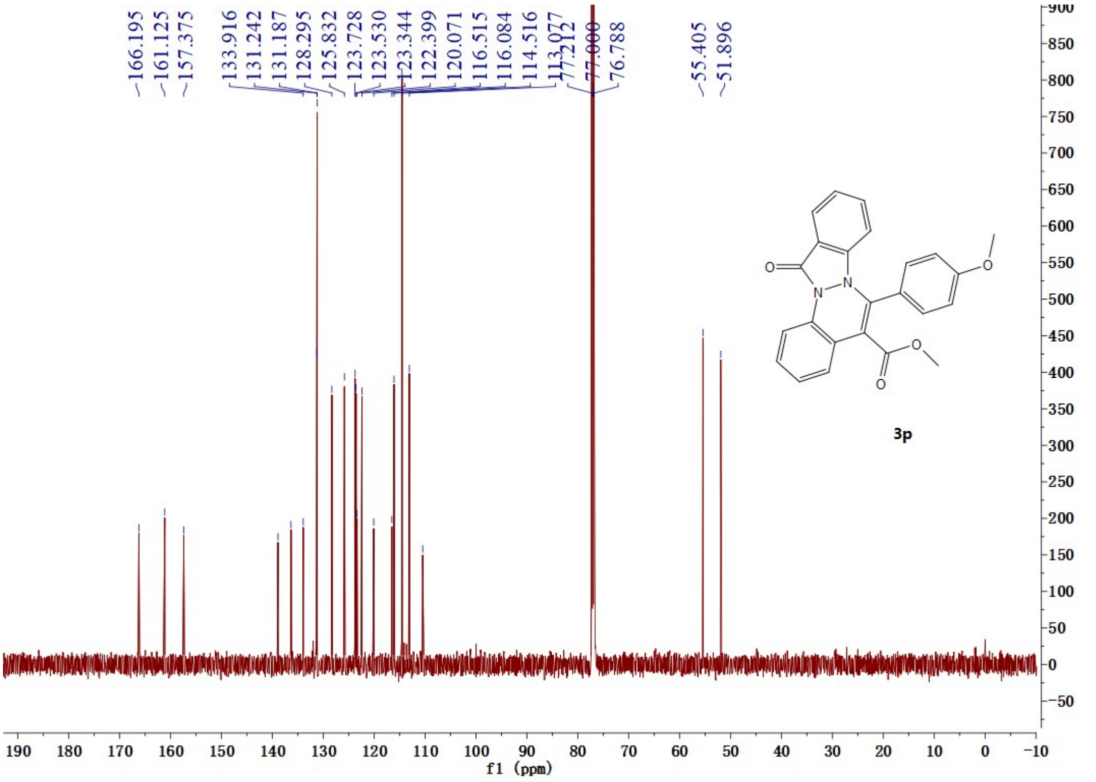

9.015
9.001
7.892
7.879
7.444
7.431
7.357
7.260
7.225
7.213
7.203
7.173
7.159
5.756
5.743
3.515
3n
1.00
1.04
2.09
1.06
1.09
3.18
2.00
0.99
3.06
11.0 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
28000 26000 24000 22000 20000 18000 16000 14000 12000 10000 8000 6000 4000 2000 0 -2000

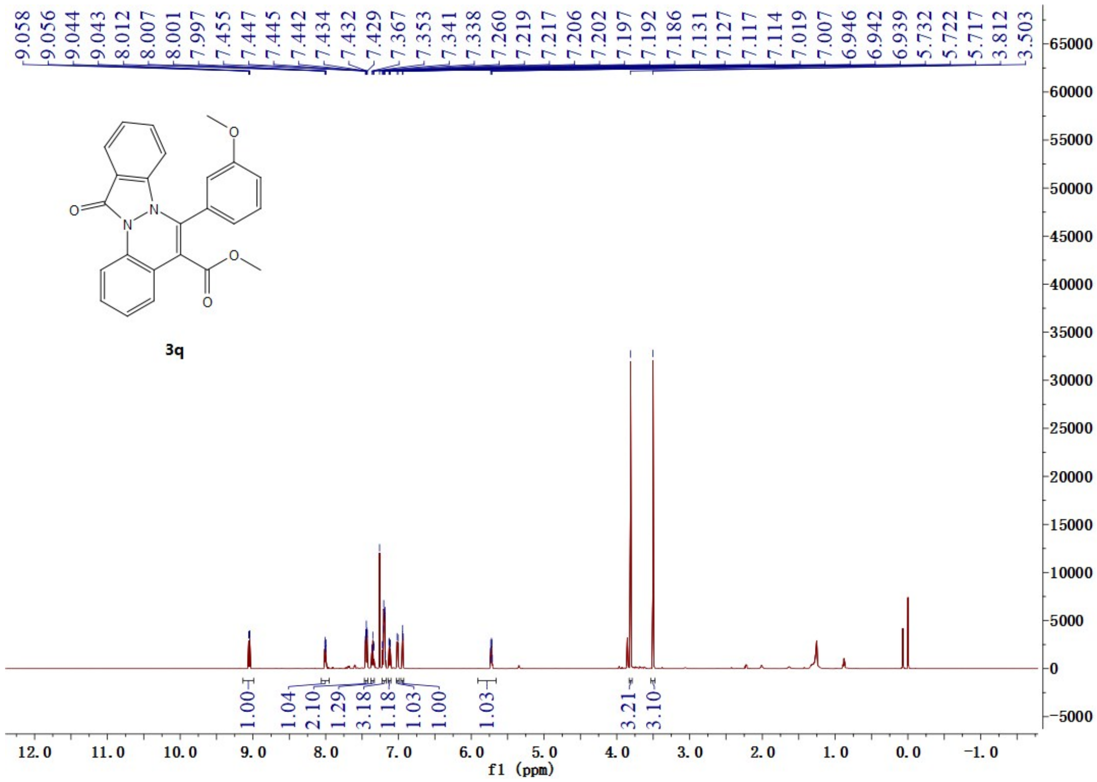

165.738
157.287
138.416
133.968
131.495
131.439
130.892
128.680
125.929
124.028
123.759
122.738
116.129
112.785
96.904
77.211
77.000
76.788
51.990
3n
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20 0 -20

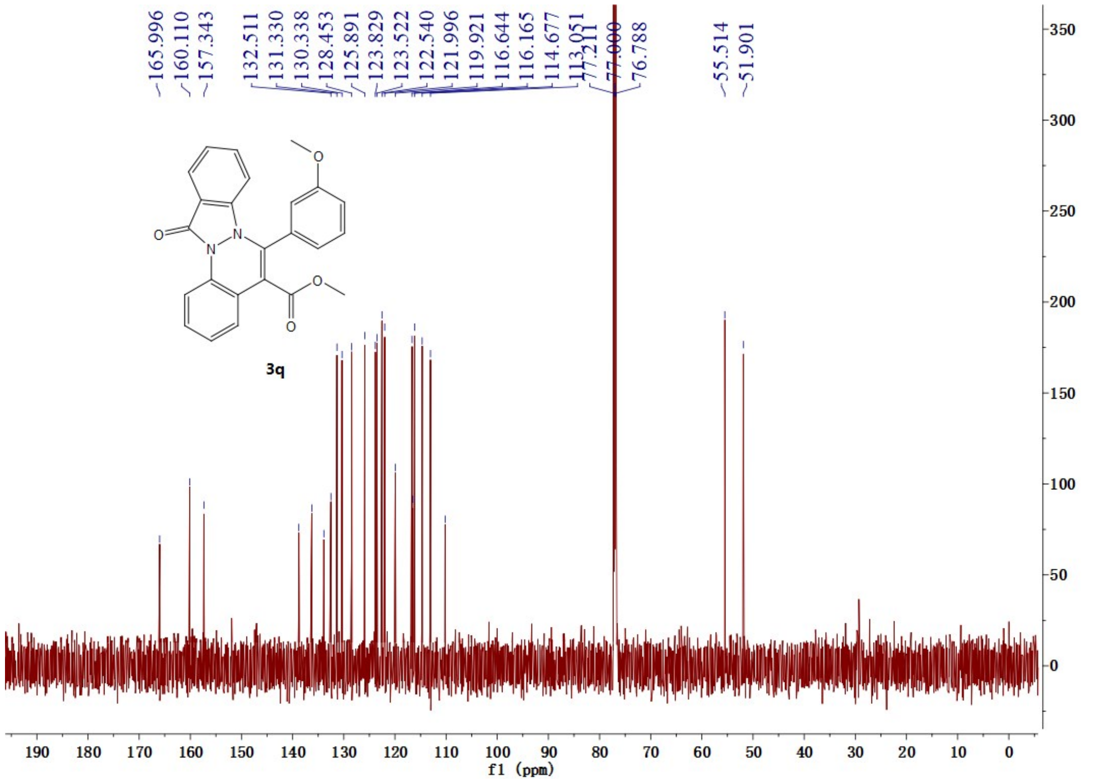

9.055
9.042
8.001
7.997
7.987
7.336
7.322
7.303
7.181
7.173
5.699
5.694
5.685
3.487
2.491
3o
1.00
1.08
1.19
5.08
3.16
1.03
3.17
3.08
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
0.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

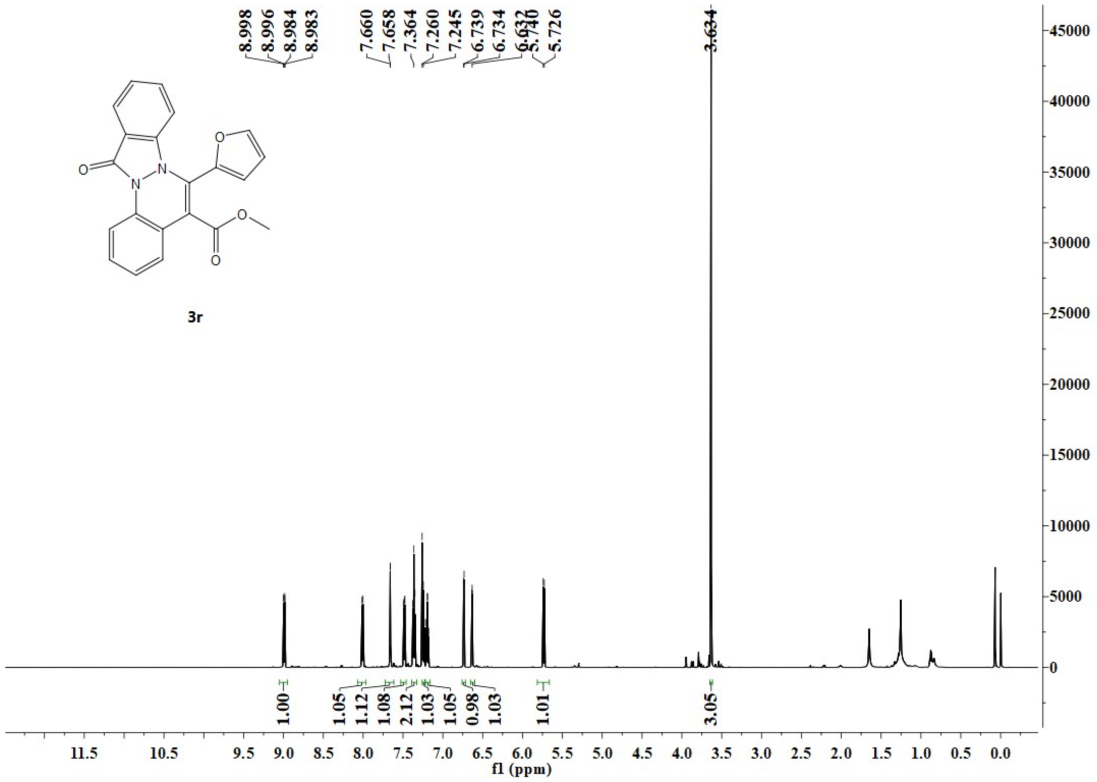

166.111
157.325
140.758
136.303
131.180
129.827
129.580
128.370
128.297
125.826
123.754
123.486
122.403
116.496
116.100
113.077
77.211
77.000
76.788
51.819
21.623
3o
1000
900
800
700
600
500
400
300
200
100
0
−100
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

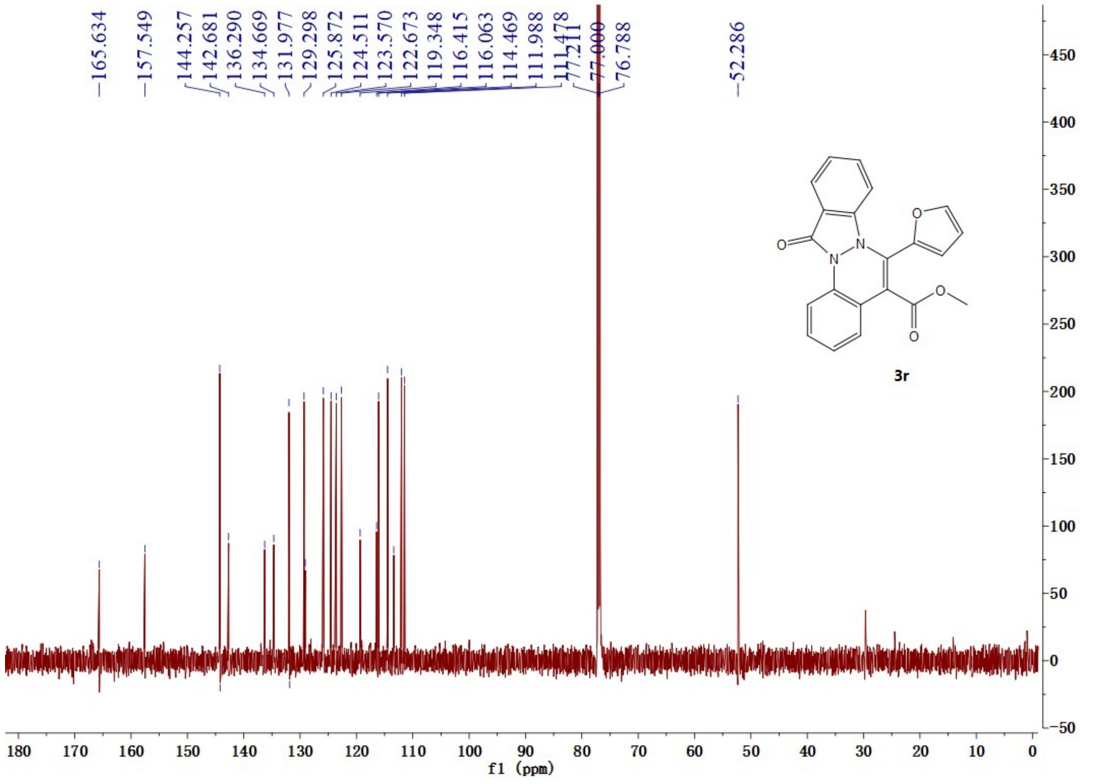

9.052
9.051
9.038
9.037
8.004
8.002
7.996
7.993
7.989
7.419
7.417
7.406
7.404
7.353
7.351
7.338
7.335
7.327
7.324
7.319
7.260
7.209
7.207
7.195
7.189
7.183
7.182
7.045
7.040
7.037
7.029
7.026
7.021
5.761
5.757
5.755
5.754
5.748
5.746
3.918
3.511
O
N
N
O
O
O
3p
1.00
1.02
1.03
3.10
3.15
2.07
1.03
3.16
3.09
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
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
f1 (ppm)

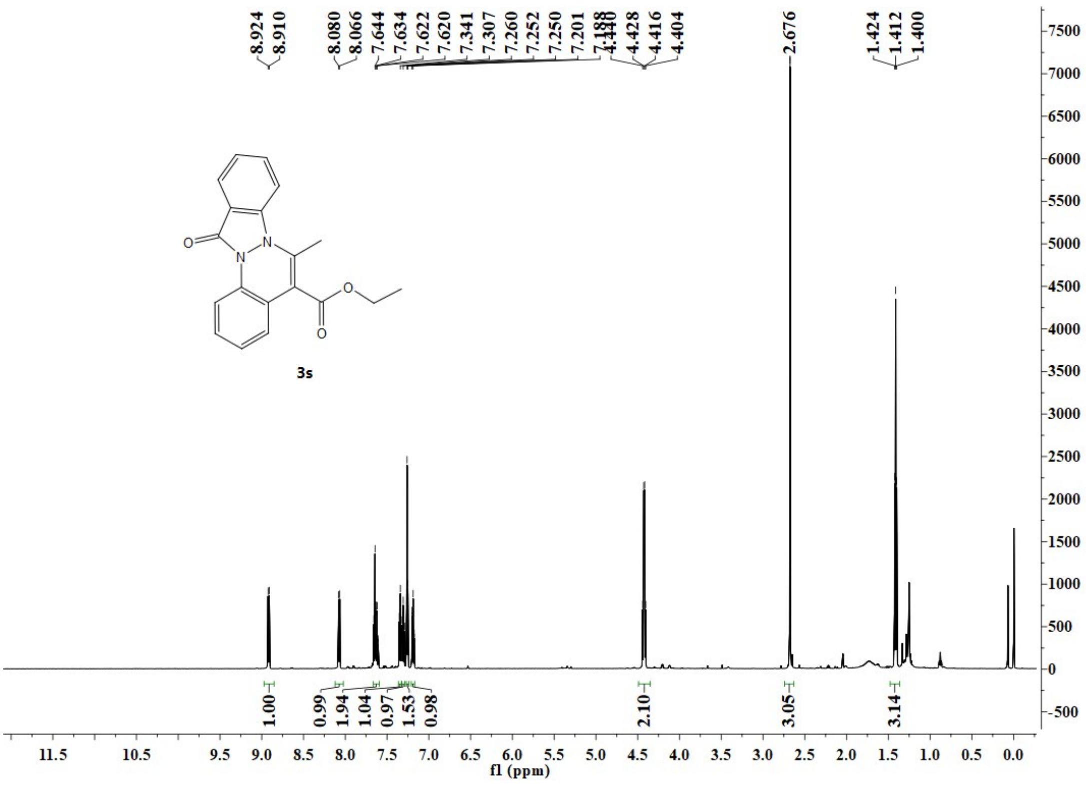

166.195
161.125
157.375
133.916
131.242
131.187
128.295
125.832
123.728
123.530
123.344
122.399
120.071
116.515
116.084
114.516
113.077
77.212
77.000
76.788
55.405
51.896
O
N
N
O
O
O
3p
900
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

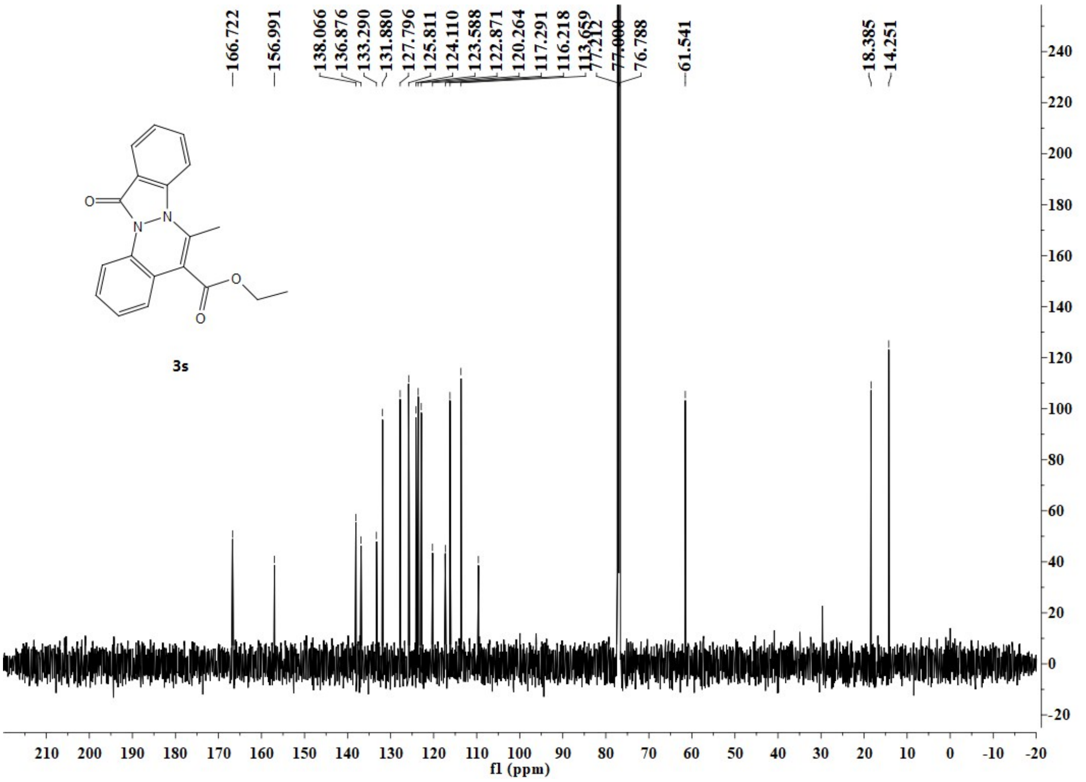

9.058
9.056
9.044
9.043
8.012
8.007
8.001
7.997
7.455
7.447
7.445
7.442
7.434
7.432
7.429
7.367
7.353
7.341
7.338
7.260
7.219
7.217
7.206
7.202
7.197
7.192
7.186
7.131
7.127
7.117
7.114
7.019
7.007
6.946
6.942
6.939
5.732
5.722
5.717
3.812
3.503
3q
1.00
1.04
2.10
1.29
3.18
1.18
1.03
1.00
1.03
3.21
3.10
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f1 (ppm)
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000

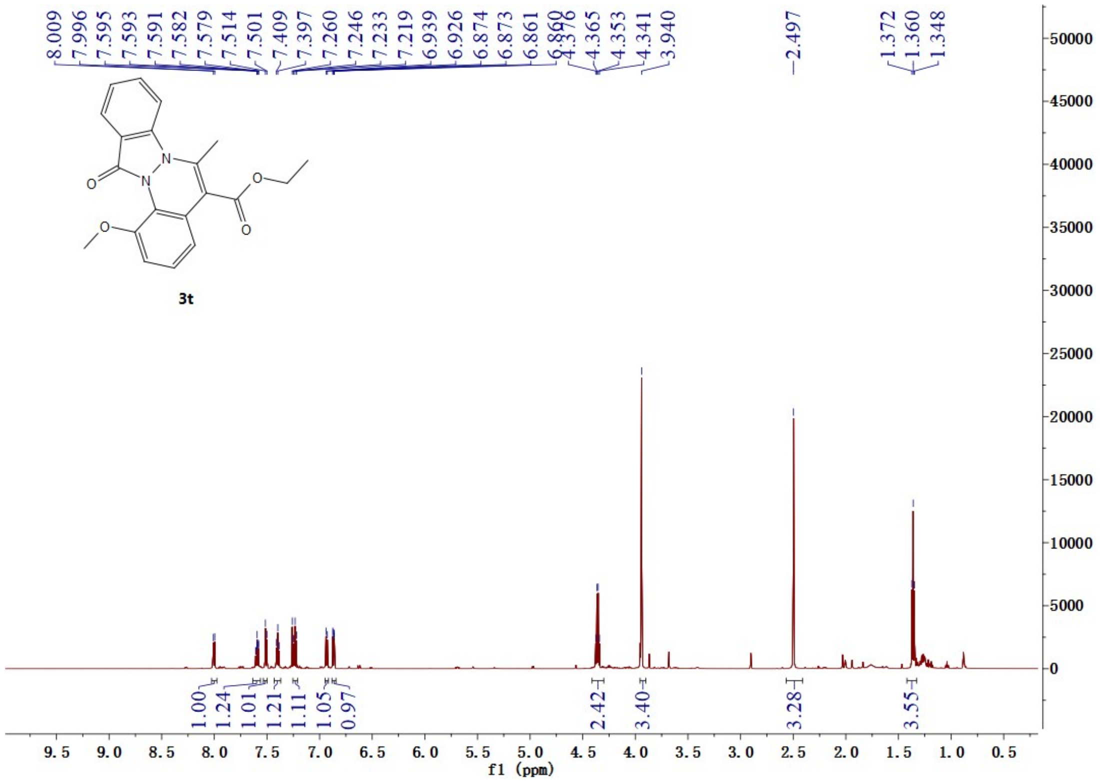

165.996
160.110
157.343
132.511
131.330
130.338
128.453
125.891
123.829
123.522
122.540
121.996
119.921
116.644
116.165
114.677
113.051
77.211
77.000
76.788
55.514
51.901
3q
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
350
300
250
200
150
100
50
0

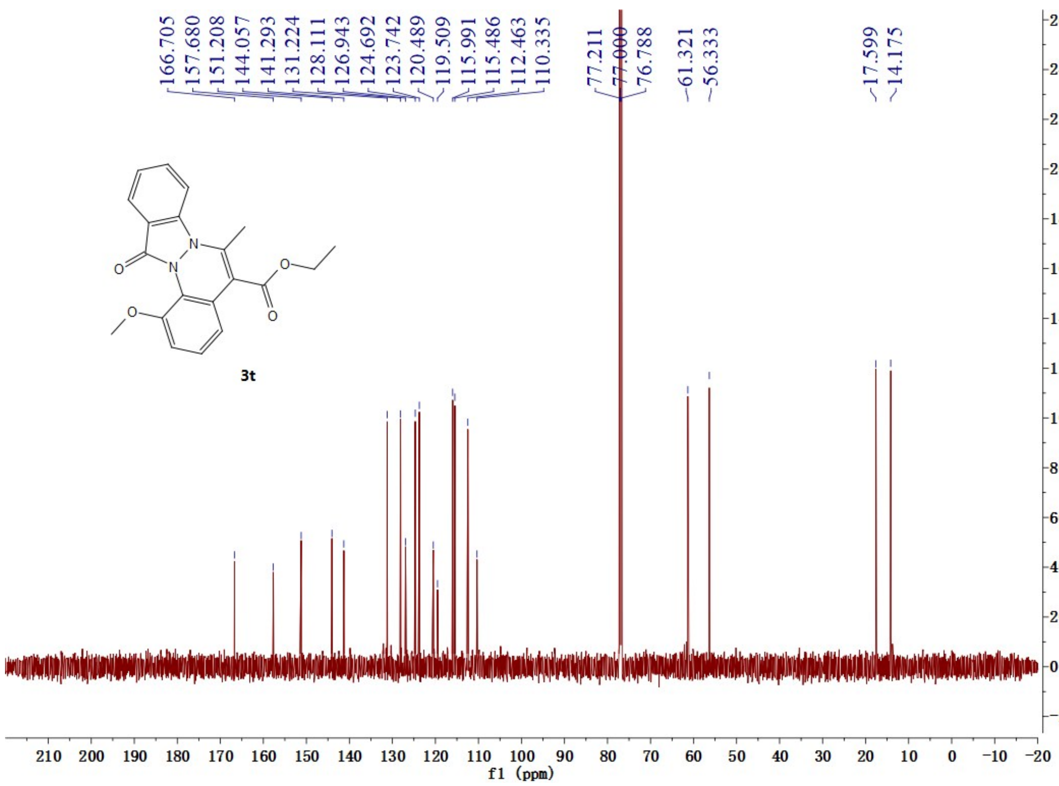

8.998
8.996
8.984
8.983
7.660
7.658
7.364
7.260
7.245
6.739
6.734
6.632
5.740
5.726
3.634
O
N
N
O
O
O
3r
1.00
1.05
1.12
1.08
2.12
1.03
1.05
0.98
1.03
1.01
3.05
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

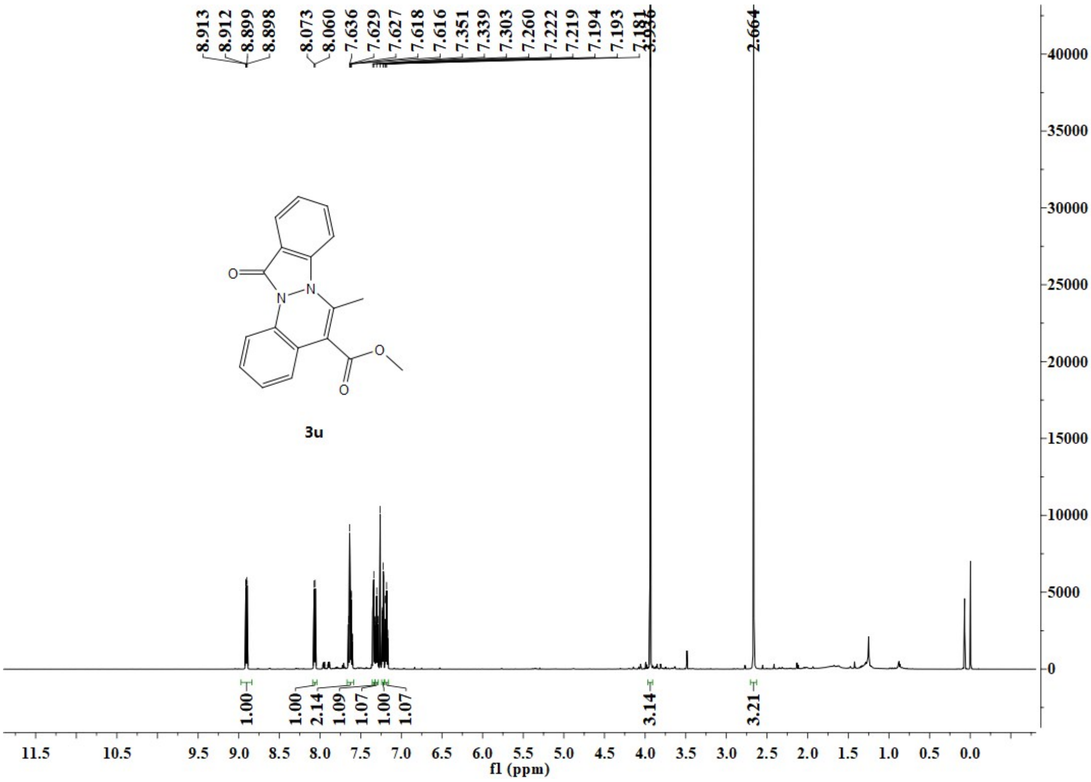

165.634
157.549
144.257
142.681
136.290
134.669
131.977
129.298
125.872
124.511
123.570
122.673
119.348
116.415
116.063
114.469
111.988
111.478
77.211
77.000
76.788
52.286
O
N
N
O
O
O
3r
450
400
350
300
250
200
150
100
50
0
-50
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

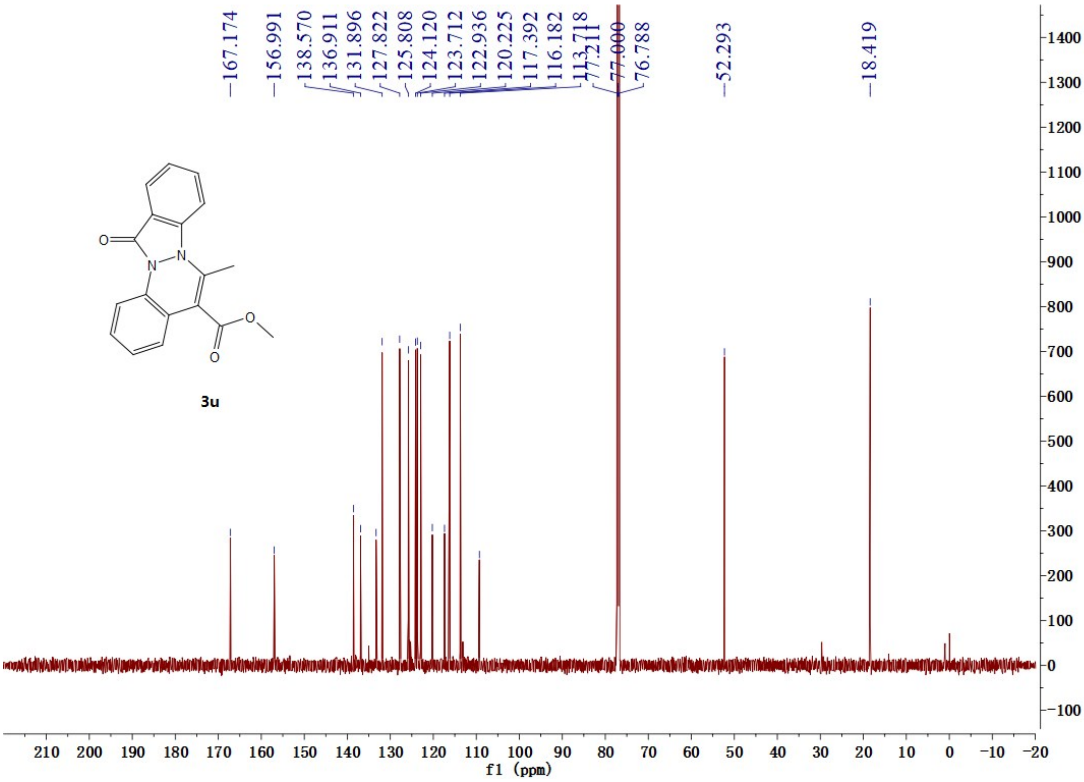

8.924
8.910
8.080
8.066
7.644
7.634
7.622
7.620
7.341
7.307
7.260
7.252
7.250
7.201
7.188
4.440
4.428
4.416
4.404
2.676
1.424
1.412
1.400
3s
1.00
0.99
1.94
1.04
0.97
1.53
0.98
2.10
3.05
3.14
fl (ppm)

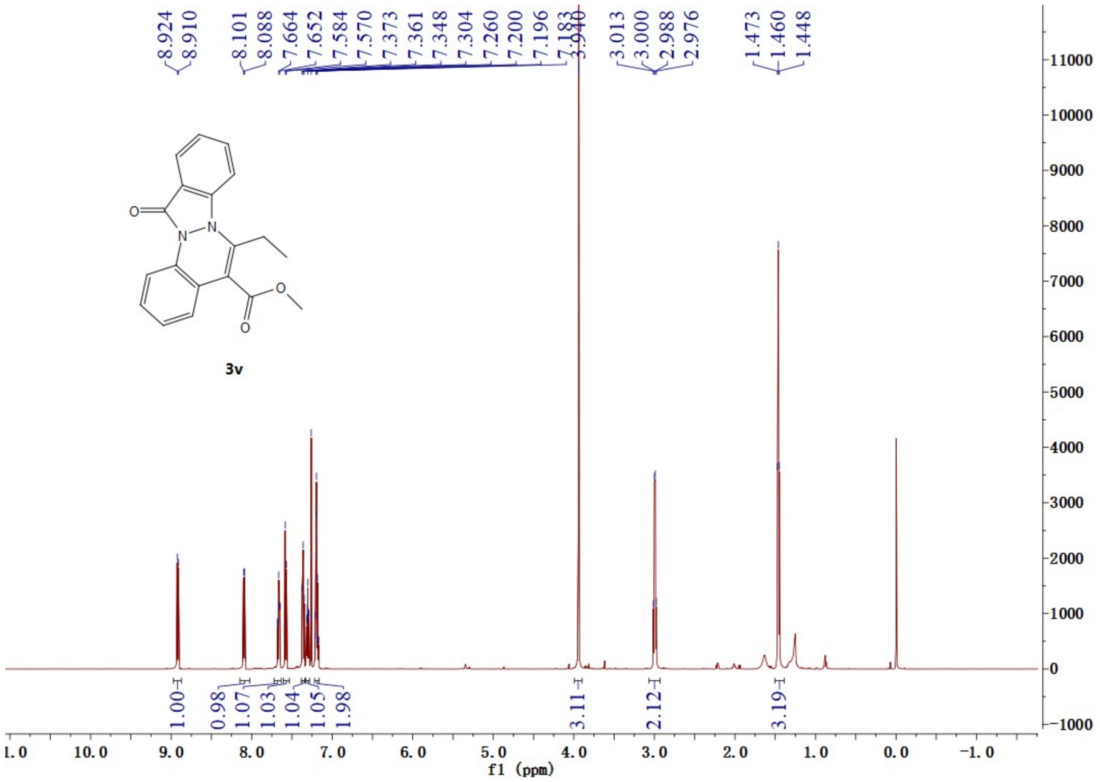

166.722
156.991
138.066
136.876
133.290
131.880
127.796
125.811
124.110
123.588
122.871
120.264
117.291
116.218
113.659
77.212
77.000
76.788
61.541
18.385
14.251
3s
fl (ppm)

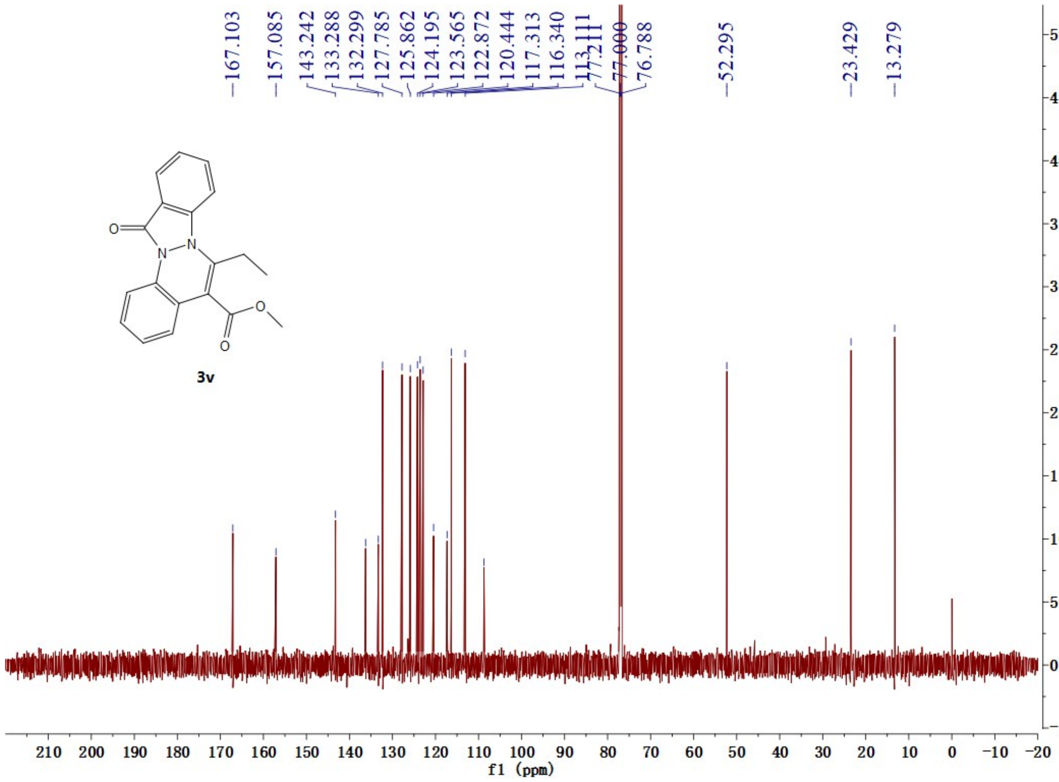

8.009
7.996
7.595
7.593
7.591
7.582
7.579
7.514
7.501
7.409
7.397
7.260
7.246
7.233
7.219
6.939
6.926
6.874
6.873
6.861
6.860
4.376
4.365
4.353
4.341
3.940
2.497
1.372
1.360
1.348
3t
O
N
N
O
O
O
1.00
1.24
1.01
1.21
1.11
1.05
0.97
2.42
3.40
3.28
3.55
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
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
f1 (ppm)

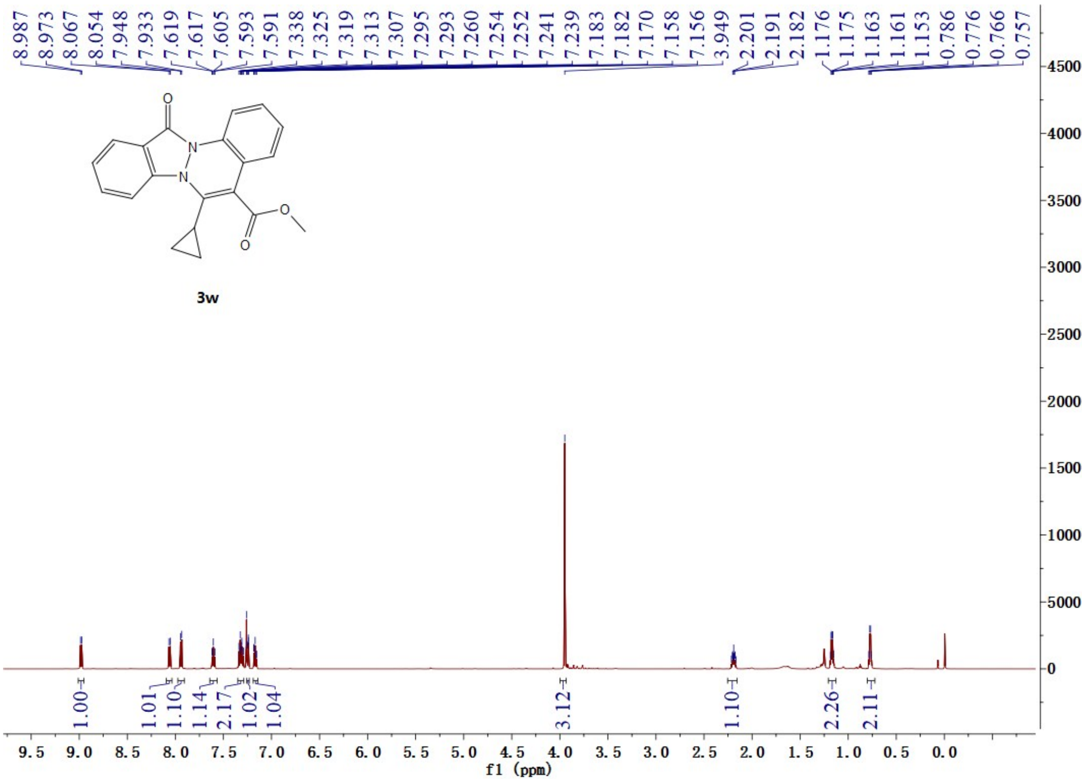

166.705
157.680
151.208
144.057
141.293
131.224
128.111
126.943
124.692
123.742
120.489
119.509
115.991
115.486
112.463
110.335
77.211
77.000
76.788
61.321
56.333
17.599
14.175
3t
O
N
N
O
O
O
260
240
220
200
180
160
140
120
100
80
60
40
20
0
−20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
f1 (ppm)

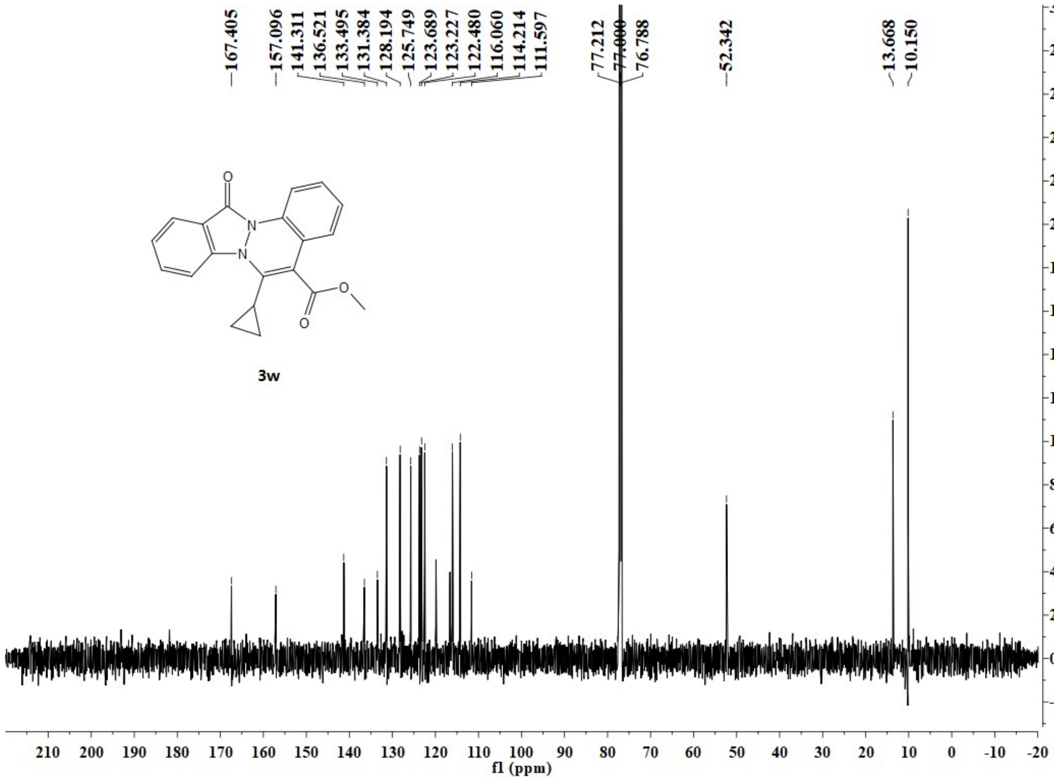

8.913
8.912
8.899
8.898
8.073
8.060
7.636
7.629
7.627
7.618
7.616
7.351
7.339
7.303
7.260
7.222
7.219
7.194
7.193
7.181
3.936
2.664
O
N
N
O
O
3u
1.00
1.00
2.14
1.09
1.07
1.00
1.07
3.14
3.21
40000
35000
30000
25000
20000
15000
10000
5000
0
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

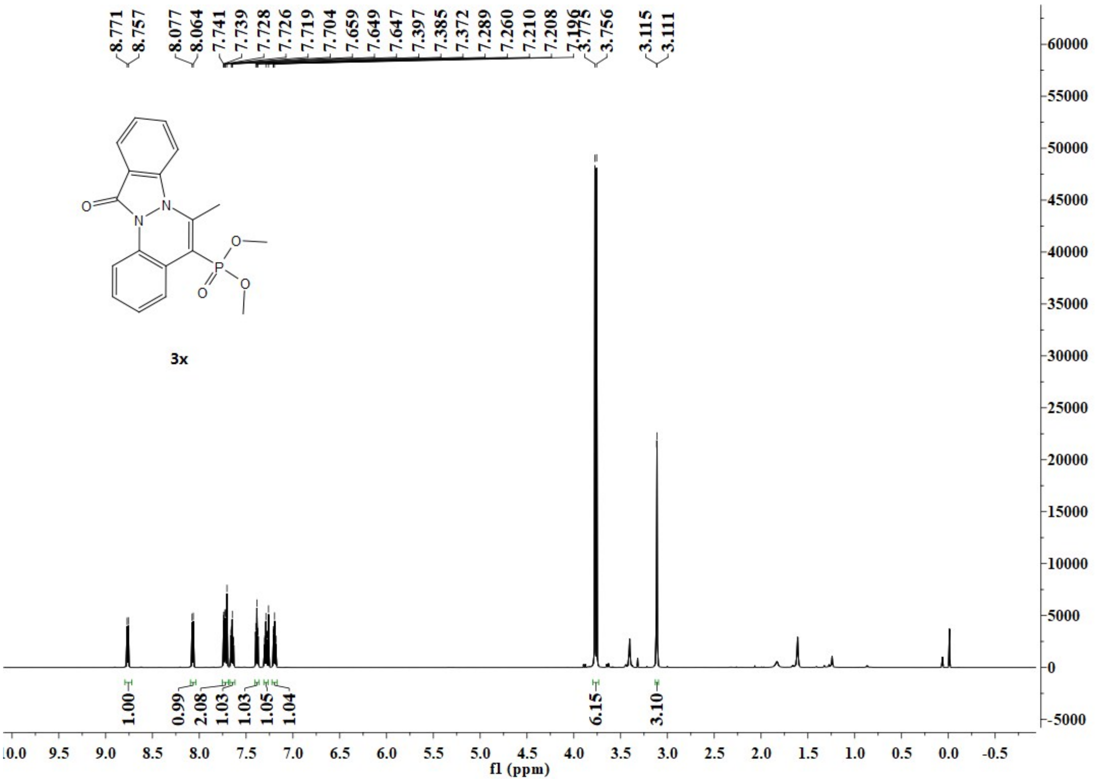

167.174
156.991
138.570
136.911
131.896
127.822
125.808
124.120
123.712
122.936
120.225
117.392
116.182
113.718
77.211
77.000
76.788
52.293
18.419
O
N
N
O
O
3u
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
−100
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
f1 (ppm)

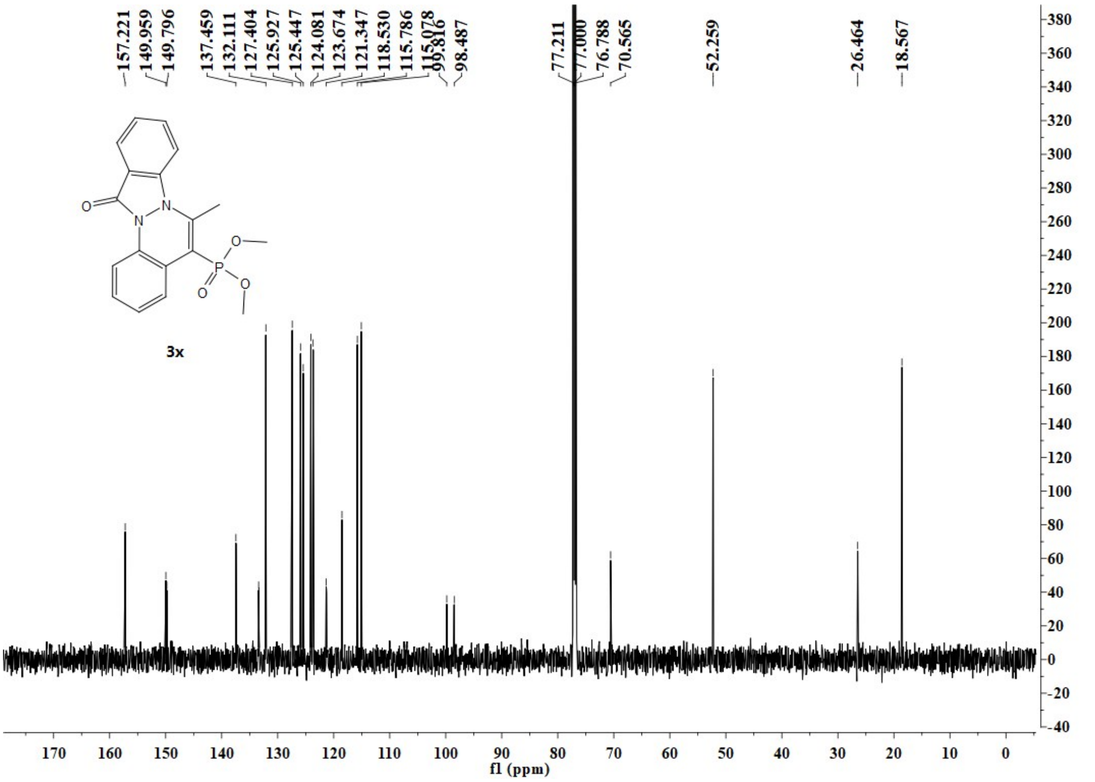

8.924
8.910
8.101
8.088
7.664
7.652
7.584
7.570
7.373
7.361
7.348
7.304
7.260
7.200
7.196
7.183
3.940
3.013
3.000
2.988
2.976
1.473
1.460
1.448
3v
1.00
0.98
1.07
1.03
1.04
1.05
1.98
3.11
2.12
3.19
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000
1.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
−1.0
f1 (ppm)

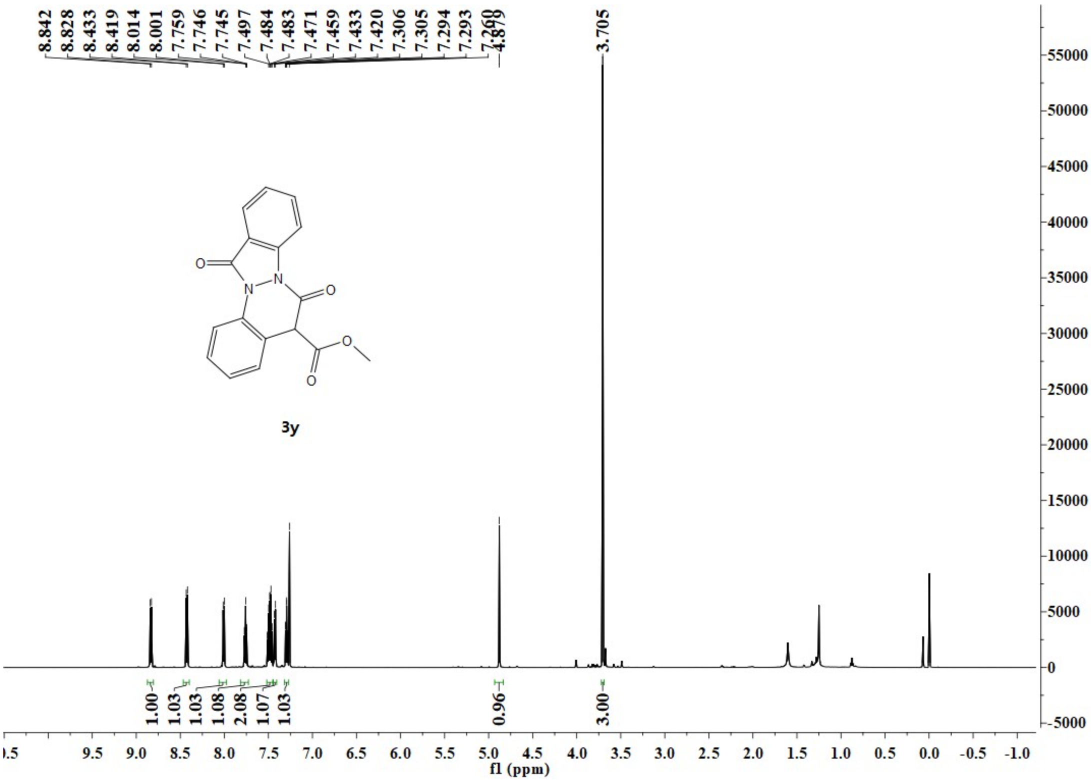

167.103
157.085
143.242
133.288
132.299
127.785
125.862
124.195
123.565
122.872
120.444
117.313
116.340
113.111
77.211
77.000
76.788
52.295
23.429
13.279
3v
500
450
400
350
300
250
200
150
100
50
0
−50
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
f1 (ppm)


3w
8.987
8.973
8.067
8.054
7.948
7.933
7.619
7.617
7.605
7.593
7.591
7.338
7.325
7.319
7.313
7.307
7.295
7.293
7.260
7.254
7.252
7.241
7.239
7.183
7.182
7.170
7.158
7.156
3.949
2.201
2.191
2.182
1.176
1.175
1.163
1.161
1.153
0.786
0.776
0.766
0.757
O
N
N
O
O
1.00
1.01
1.10
1.14
2.17
1.02
1.04
3.12
1.10
2.26
2.11
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

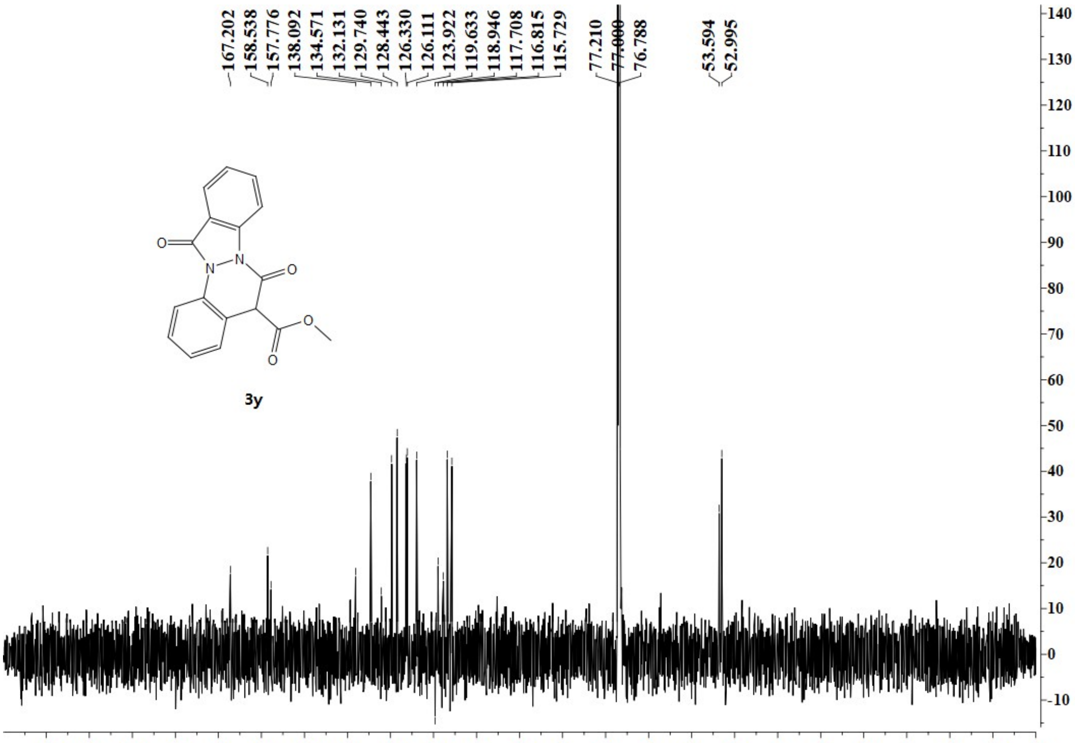

3w
167.405
157.096
141.311
136.521
133.495
131.384
128.194
125.749
123.689
123.227
122.480
116.060
114.214
111.597
77.212
77.000
76.788
52.342
13.668
10.150
O
N
N
O
O
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


8.771
8.757
8.077
8.064
7.741
7.739
7.728
7.726
7.719
7.704
7.659
7.649
7.647
7.397
7.385
7.372
7.289
7.260
7.210
7.208
7.196
3.775
3.756
3.115
3.111
O
N
N
O
P
O
O
3x
1.00
0.99
2.08
1.03
1.03
1.05
1.04
6.15
3.10
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

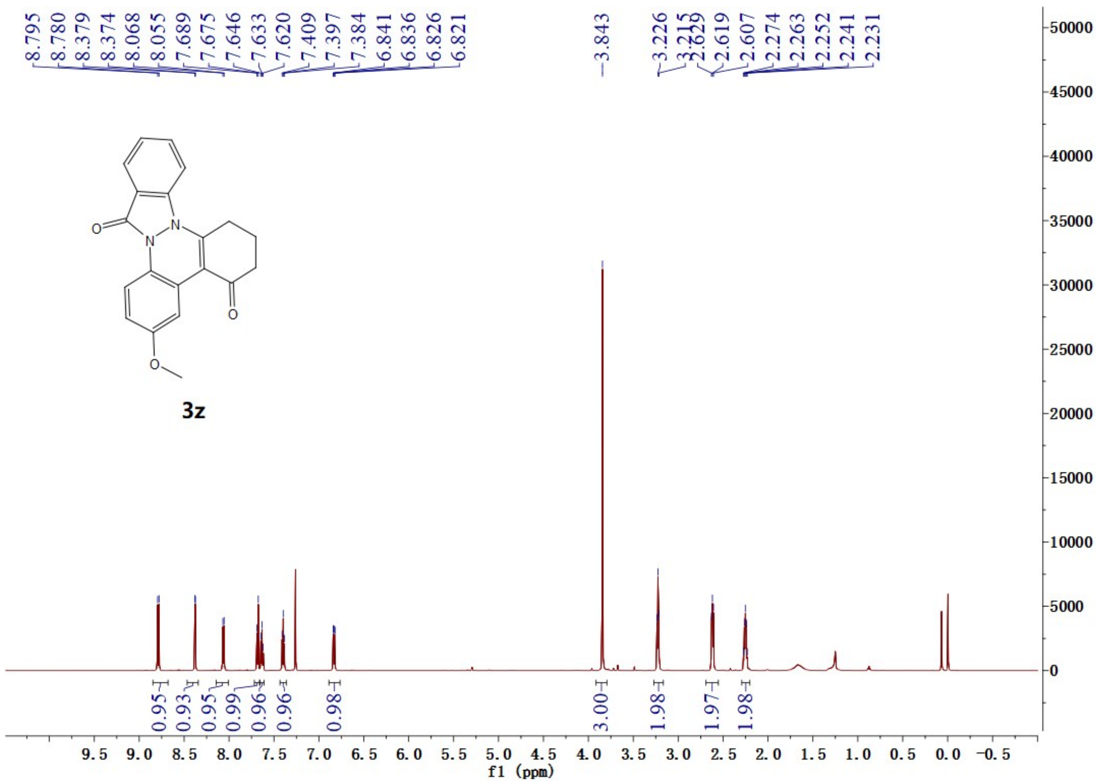

157.221
149.959
149.796
137.459
132.111
127.404
125.927
125.447
124.081
123.674
121.347
118.530
115.786
115.078
99.816
98.487
77.211
77.000
76.788
70.565
52.259
26.464
18.567
O
N
N
O
P
O
O
3x
380
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.842
8.828
8.433
8.419
8.014
8.001
7.759
7.746
7.745
7.497
7.484
7.483
7.471
7.459
7.433
7.420
7.306
7.305
7.294
7.293
7.260
4.879
3.705
O
N
N
O
O
O
1.00
1.03
1.03
1.08
2.08
1.07
1.03
0.96
3.00
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
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)

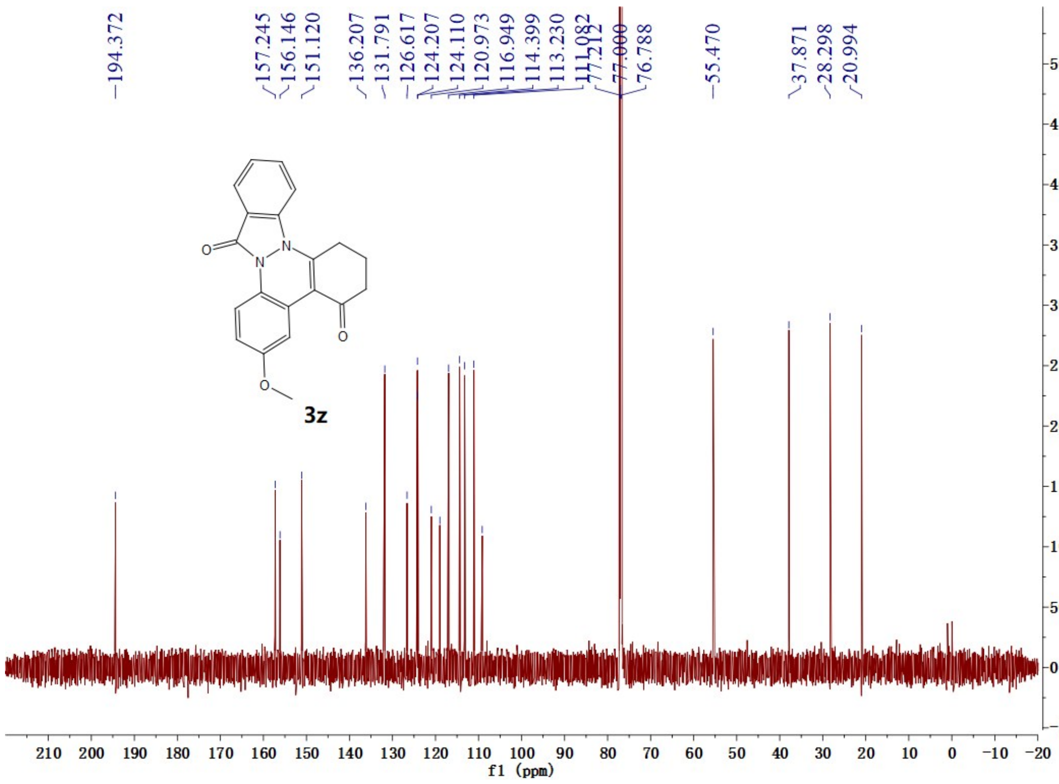
3y


167.202
158.538
157.776
138.092
134.571
132.131
129.740
128.443
126.330
126.111
123.922
119.633
118.946
117.708
116.815
115.729
77.210
77.000
76.788
53.594
52.995
O
N
N
O
O
O
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
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)

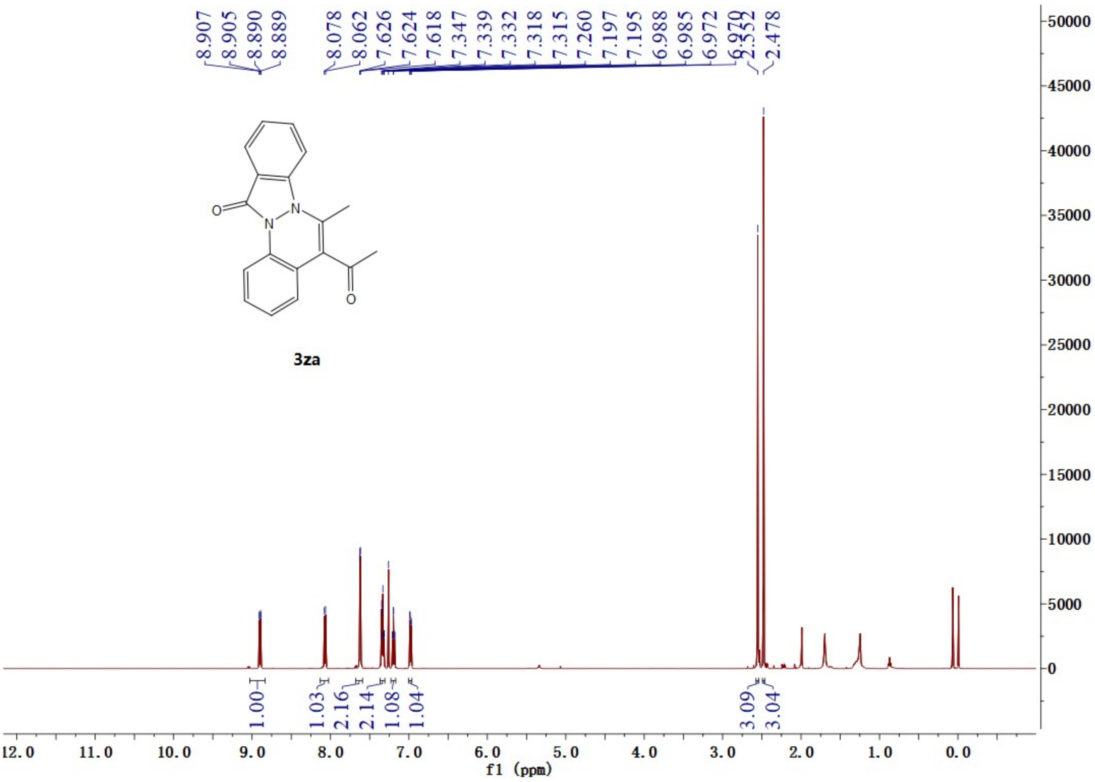
3y

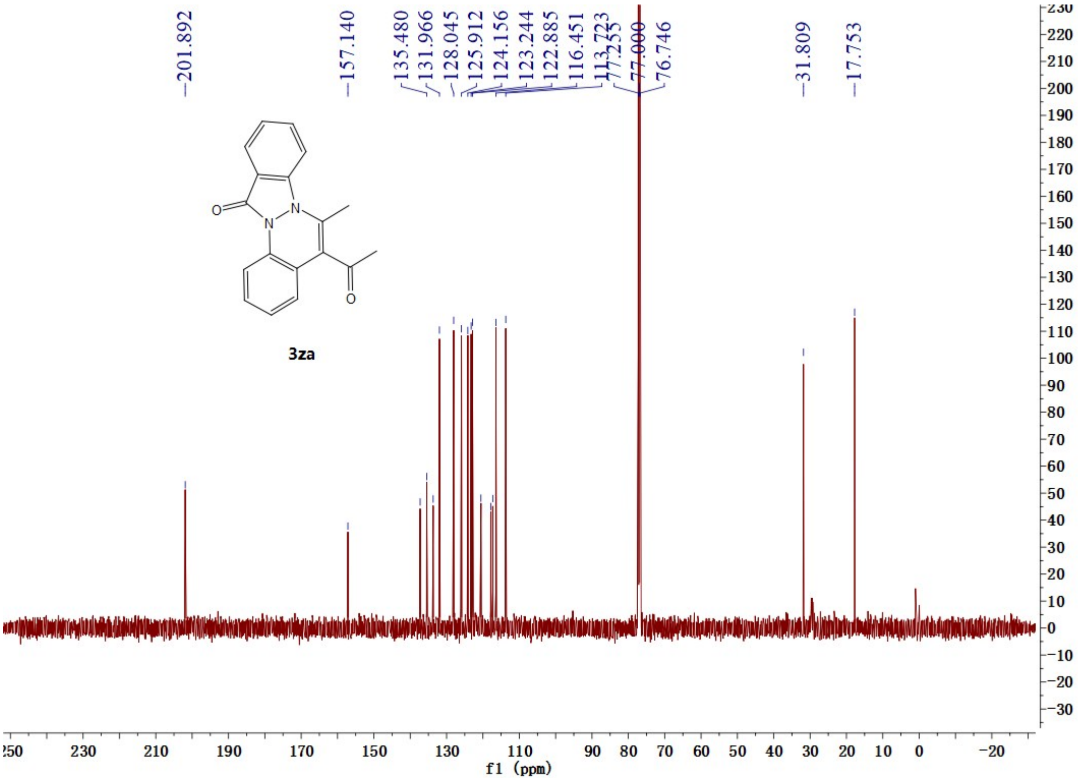


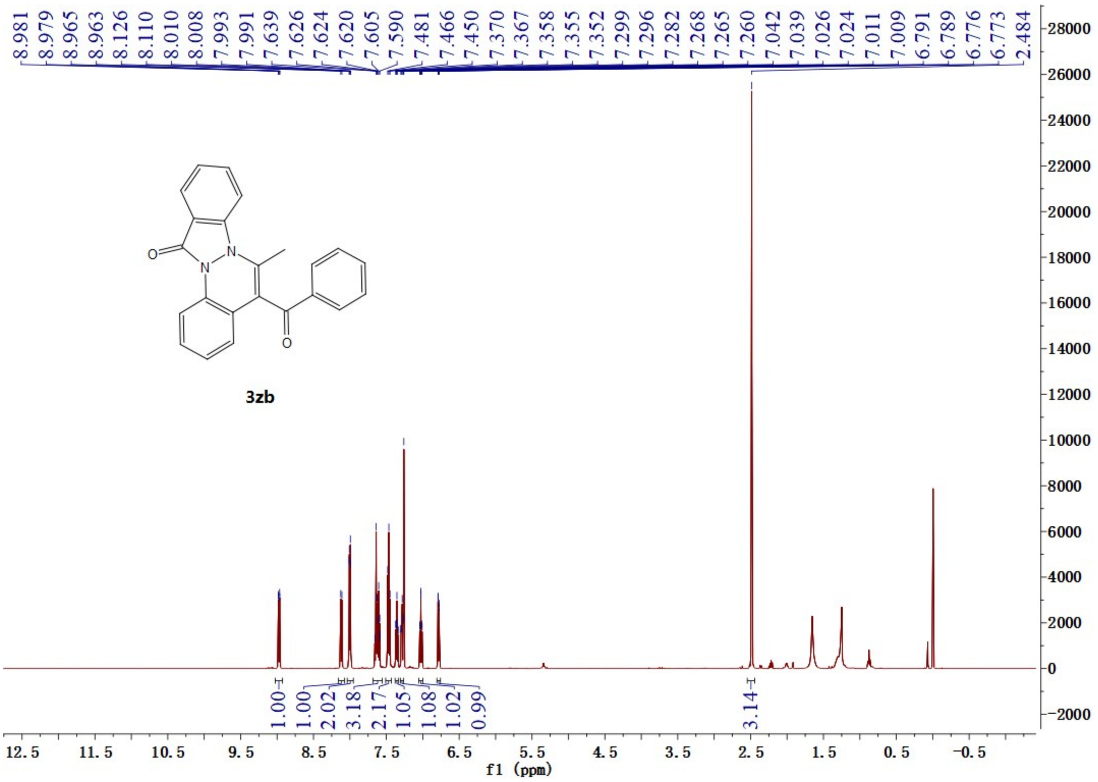
8.795
8.780
8.379
8.374
8.068
8.055
7.689
7.675
7.646
7.633
7.620
7.409
7.397
7.384
6.841
6.836
6.826
6.821
3.843
3.226
3.215
3.204
2.629
2.619
2.607
2.274
2.263
2.252
2.241
2.231
3z
0.95
0.93
0.95
0.99
0.96
0.96
0.98
3.00
1.98
1.97
1.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0

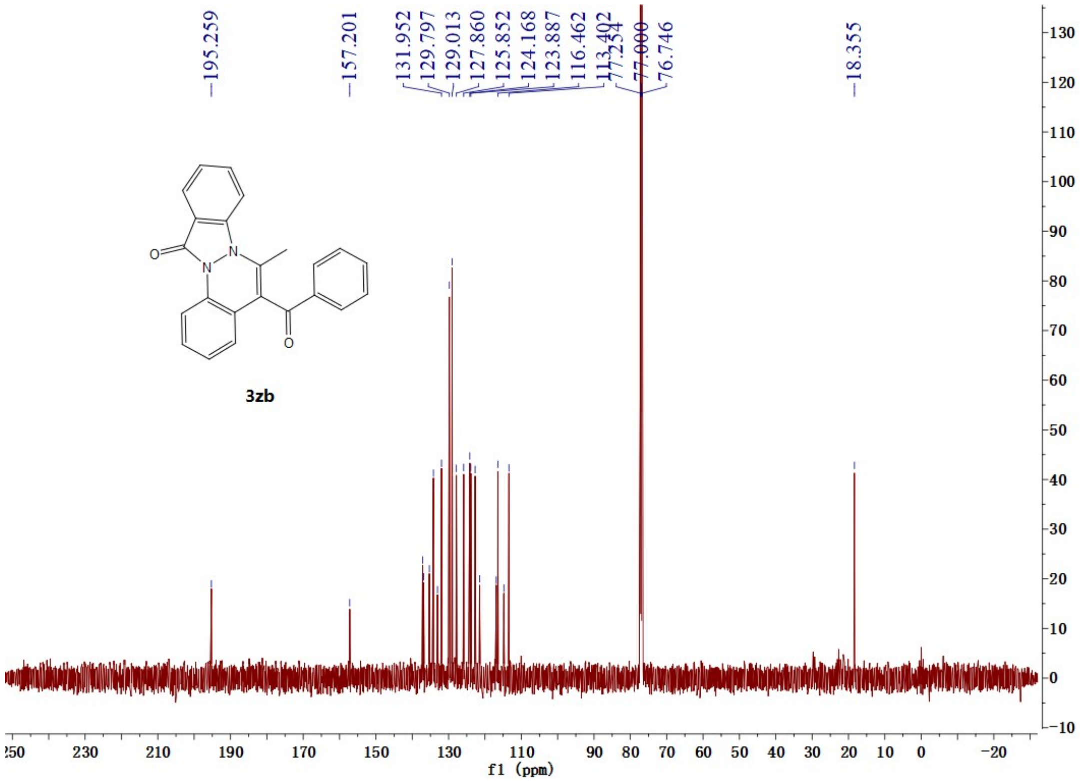


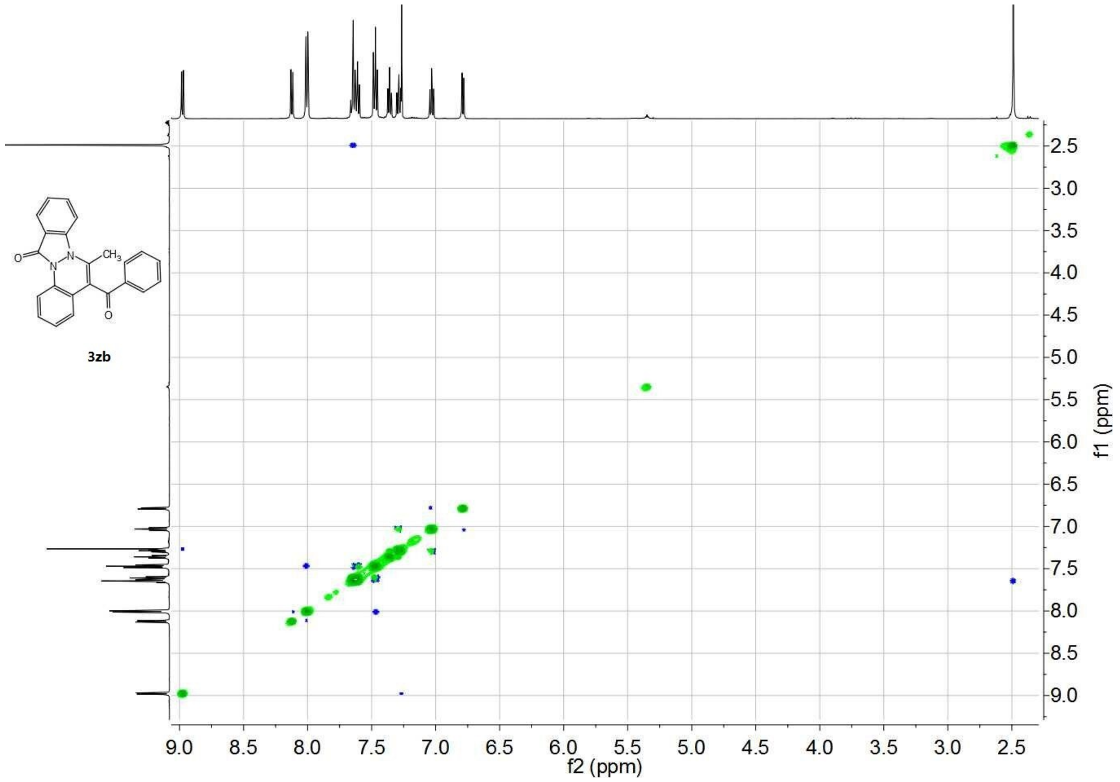
194.372
157.245
156.146
151.120
136.207
131.791
126.617
124.207
124.110
120.973
116.949
114.399
113.230
111.082
77.212
77.000
76.788
55.470
37.871
28.298
20.994
3z
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)
500
450
400
350
300
250
200
150
100
50
0
-50

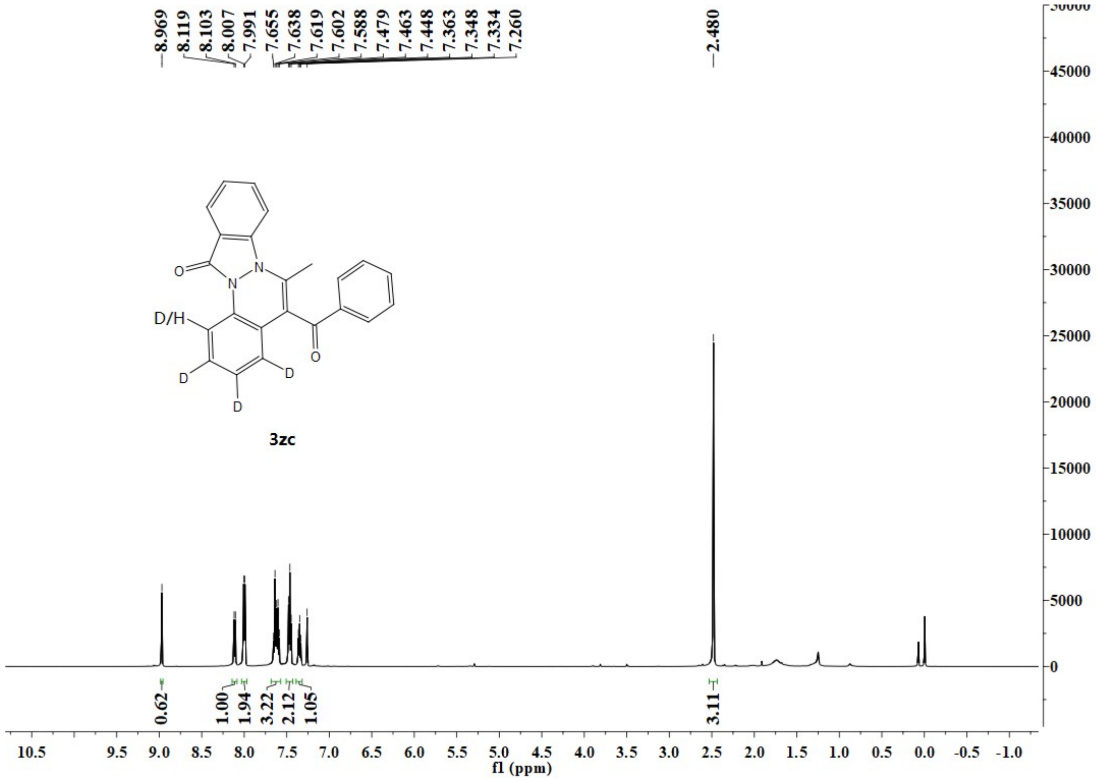

8.907
8.905
8.890
8.889
8.078
8.062
7.626
7.624
7.618
7.347
7.339
7.332
7.318
7.315
7.260
7.197
7.195
6.988
6.985
6.972
6.970
2.552
2.478
O
N
N
O
3za
1.00
1.03
2.16
2.14
1.08
1.04
3.09
3.04
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

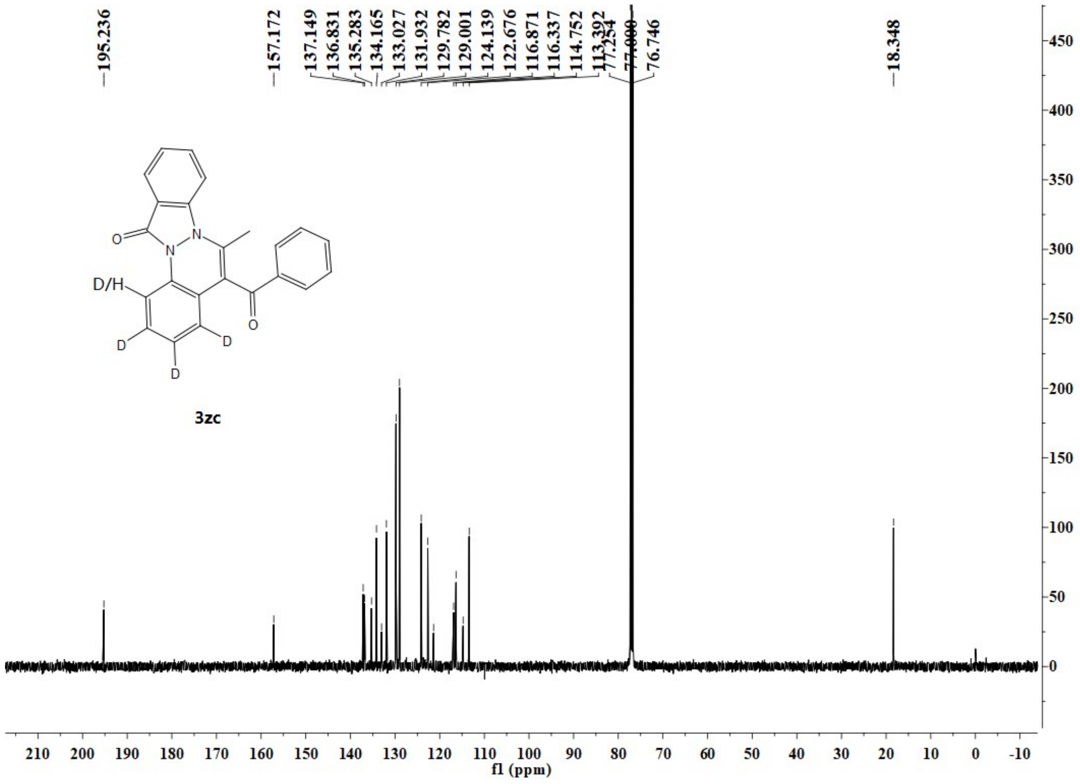

201.892
157.140
135.480
131.966
128.045
125.912
124.156
123.244
122.885
116.451
113.723
77.255
77.000
76.746
31.809
17.753
O
N
N
O
3za
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
250
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-20
f1 (ppm)

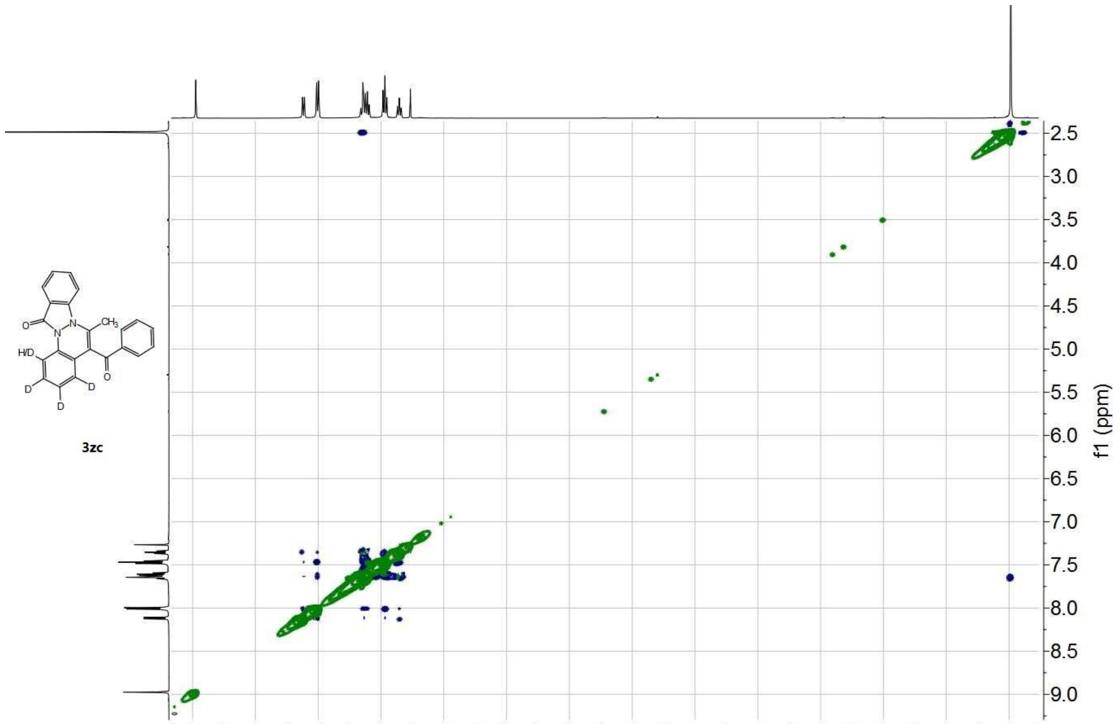

8.981
8.979
8.965
8.963
8.126
8.110
8.010
8.008
7.993
7.991
7.639
7.626
7.624
7.620
7.605
7.590
7.481
7.466
7.450
7.370
7.367
7.358
7.355
7.352
7.299
7.296
7.282
7.268
7.265
7.260
7.042
7.039
7.026
7.024
7.011
7.009
6.791
6.789
6.776
6.773
2.484
3zb
1.00
1.00
2.02
3.18
2.17
1.05
1.08
1.02
0.99
3.14
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
−2000
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0.5
f1 (ppm)

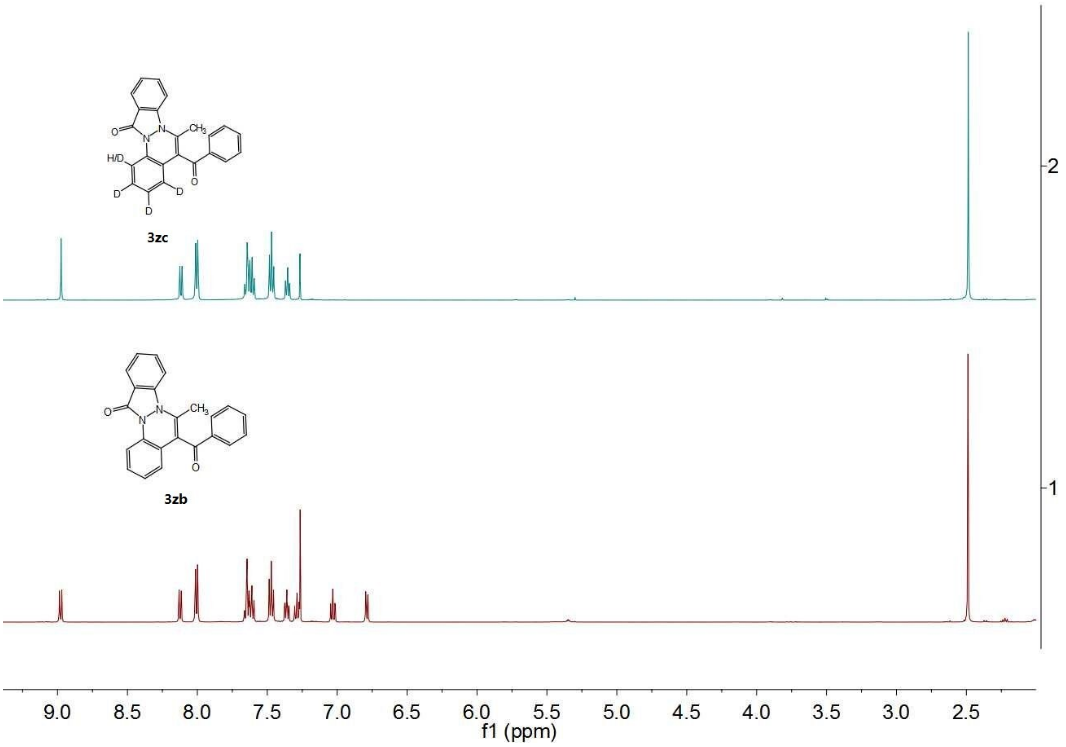

195.259
157.201
131.952
129.797
129.013
127.860
125.852
124.168
123.887
116.462
113.402
77.254
77.000
76.746
18.355
3zb
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
250
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
−20
f1 (ppm)

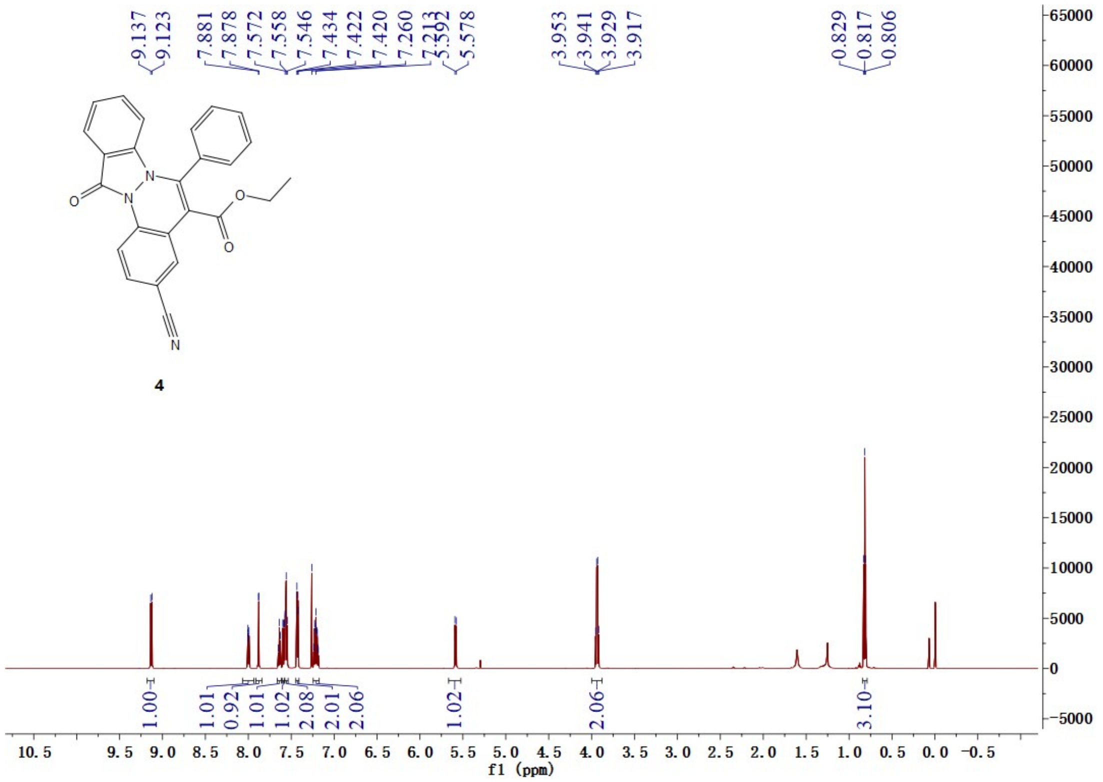

CH3
3zb
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
f2 (ppm)


8.969
8.119
8.103
8.007
7.991
7.655
7.638
7.619
7.602
7.588
7.479
7.463
7.448
7.363
7.348
7.334
7.260
2.480
D/H
D
D
D
3zc
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
0.62
1.00
1.94
3.22
2.12
1.05
3.11
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)

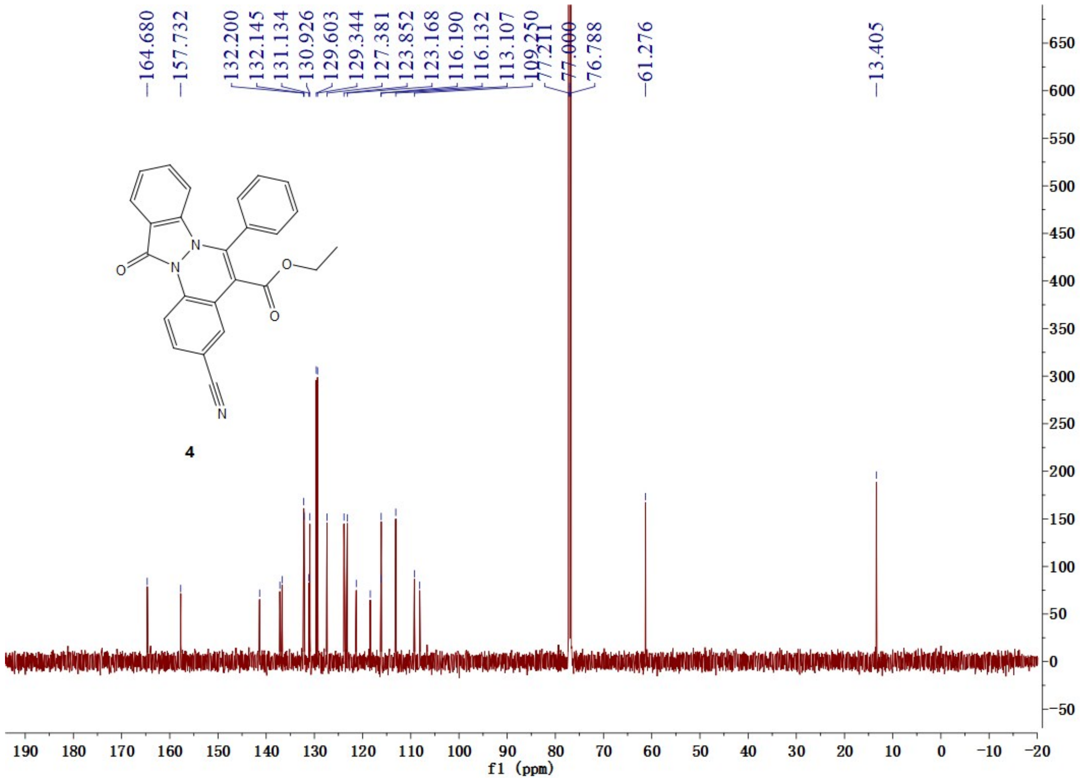

195.236
157.172
137.149
136.831
135.283
134.165
133.027
131.932
129.782
129.001
124.139
122.676
116.871
116.337
114.752
113.392
77.254
77.000
76.746
18.348
O
N
N
D/H
D
D
D
O
3zc
450
400
350
300
250
200
150
100
50
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
N
CH3
H/D
D
D
D
O
3zc
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
f1 (ppm)
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
f2 (ppm)

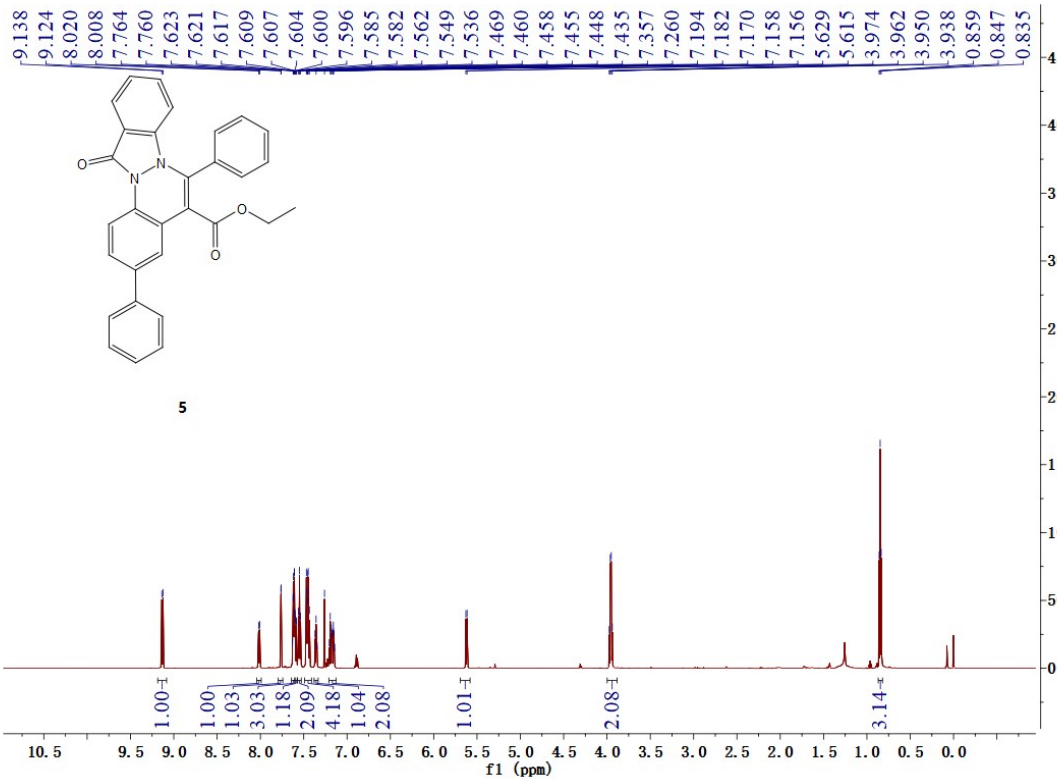

O
N
N
CH3
H/D
D
D
D
O
3zc
O
N
N
CH3
O
3zb
2
1
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
f1 (ppm)

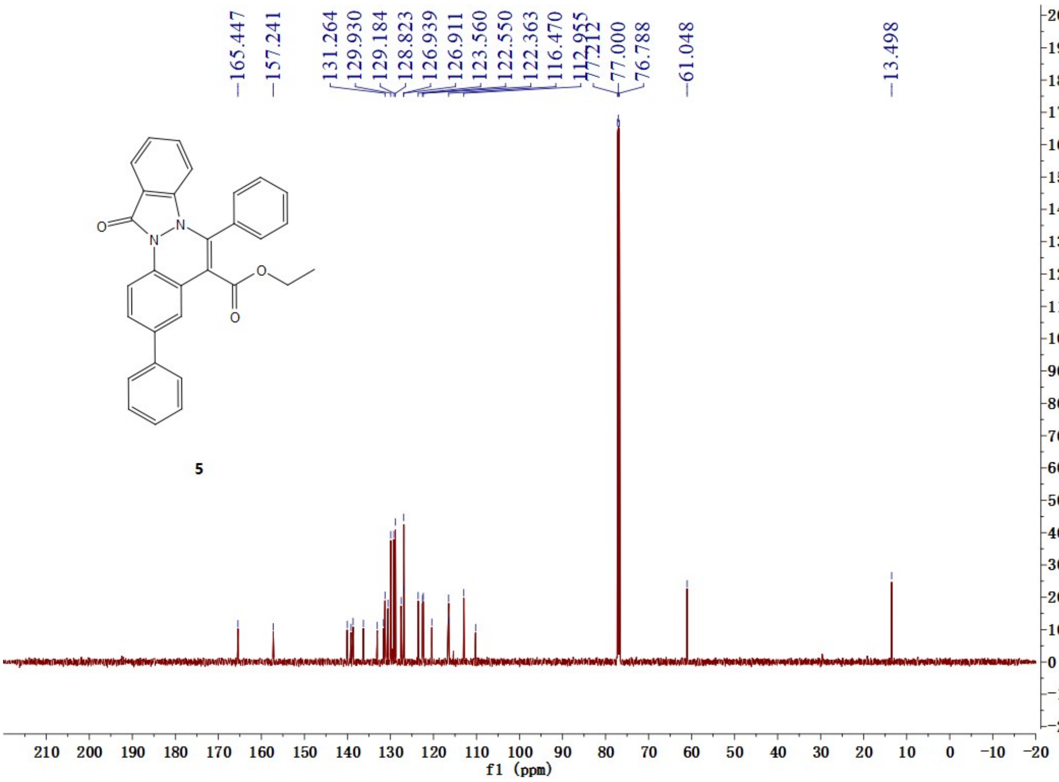

9.137
9.123
7.881
7.878
7.572
7.558
7.546
7.434
7.422
7.420
7.260
7.213
5.592
5.578
3.953
3.941
3.929
3.917
0.829
0.817
0.806
O
N
N
O
O
N
1.00
1.01
0.92
1.01
1.02
2.08
2.01
2.06
1.02
2.06
3.10
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000

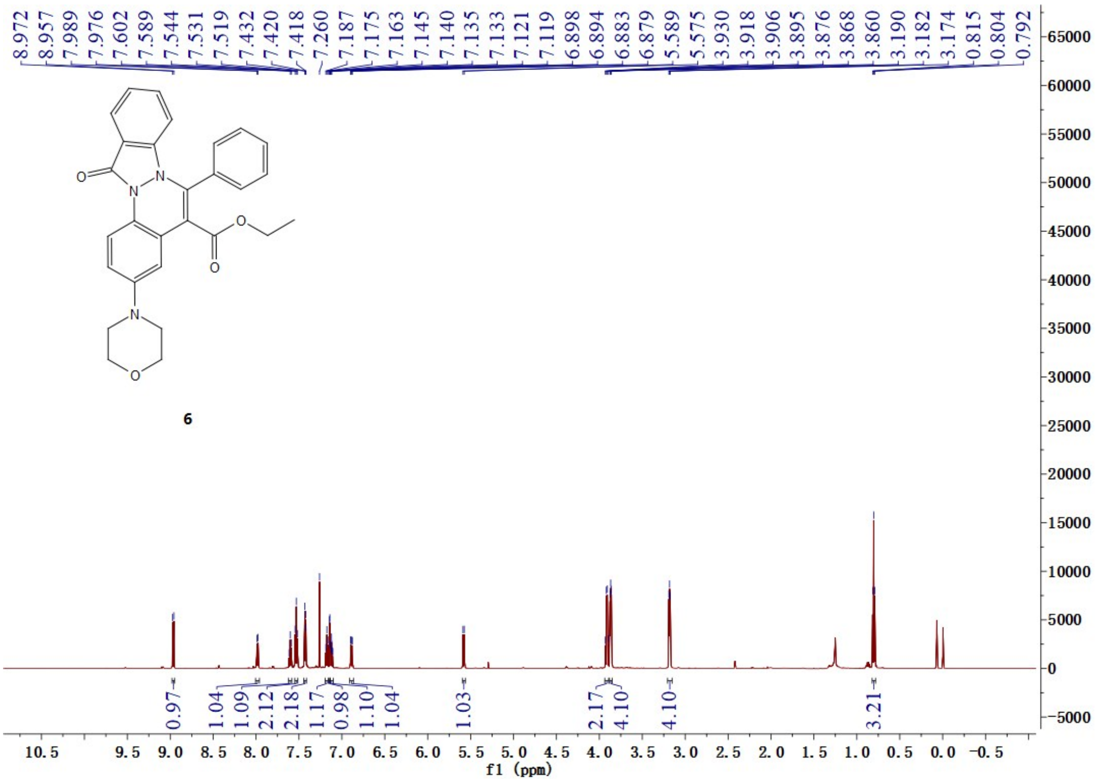
4

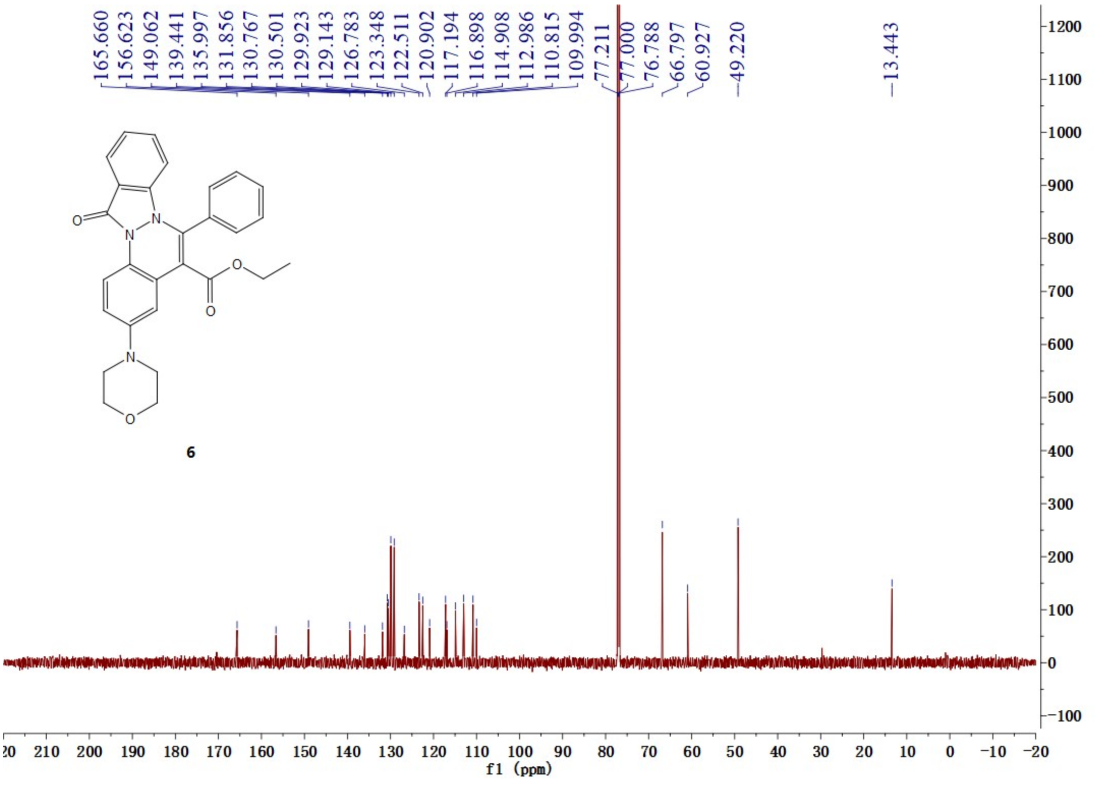

164.680
157.732
132.200
132.145
131.134
130.926
129.603
129.344
127.381
123.852
123.168
116.190
116.132
113.107
109.250
77.211
77.000
76.788
61.276
13.405
O
N
N
O
O
N
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50

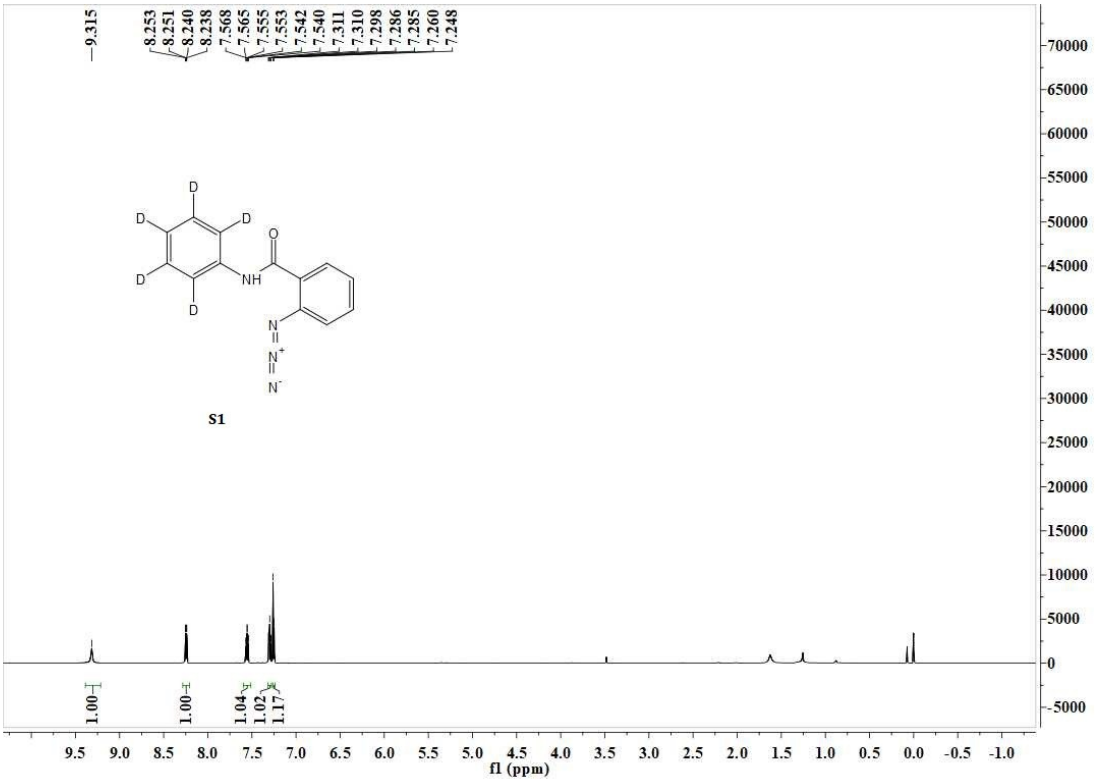
4

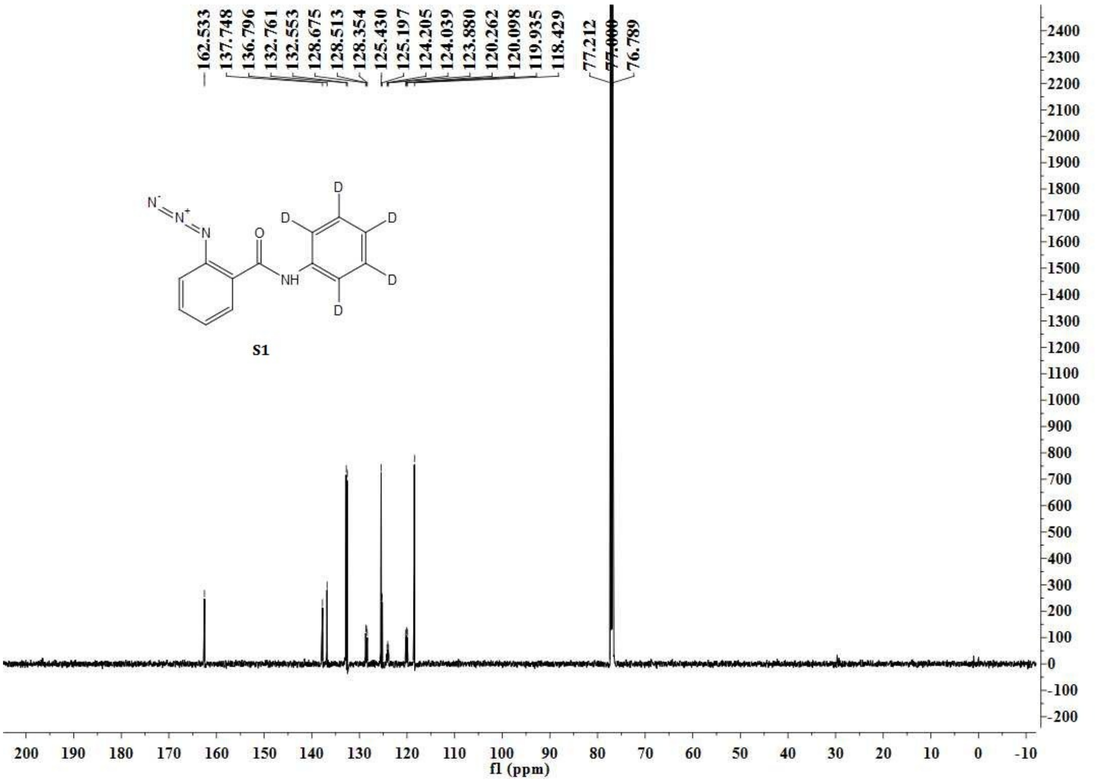

9.138
9.124
8.020
8.008
7.764
7.760
7.623
7.621
7.617
7.609
7.607
7.604
7.600
7.596
7.585
7.582
7.562
7.549
7.536
7.469
7.460
7.458
7.455
7.448
7.435
7.357
7.260
7.194
7.182
7.170
7.158
7.156
5.629
5.615
3.974
3.962
3.950
3.938
0.859
0.847
0.835
O
N
N
O
O
5
1.00
1.00
1.03
3.03
1.18
2.09
4.18
1.04
2.08
1.01
2.08
3.14
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
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
f1 (ppm)

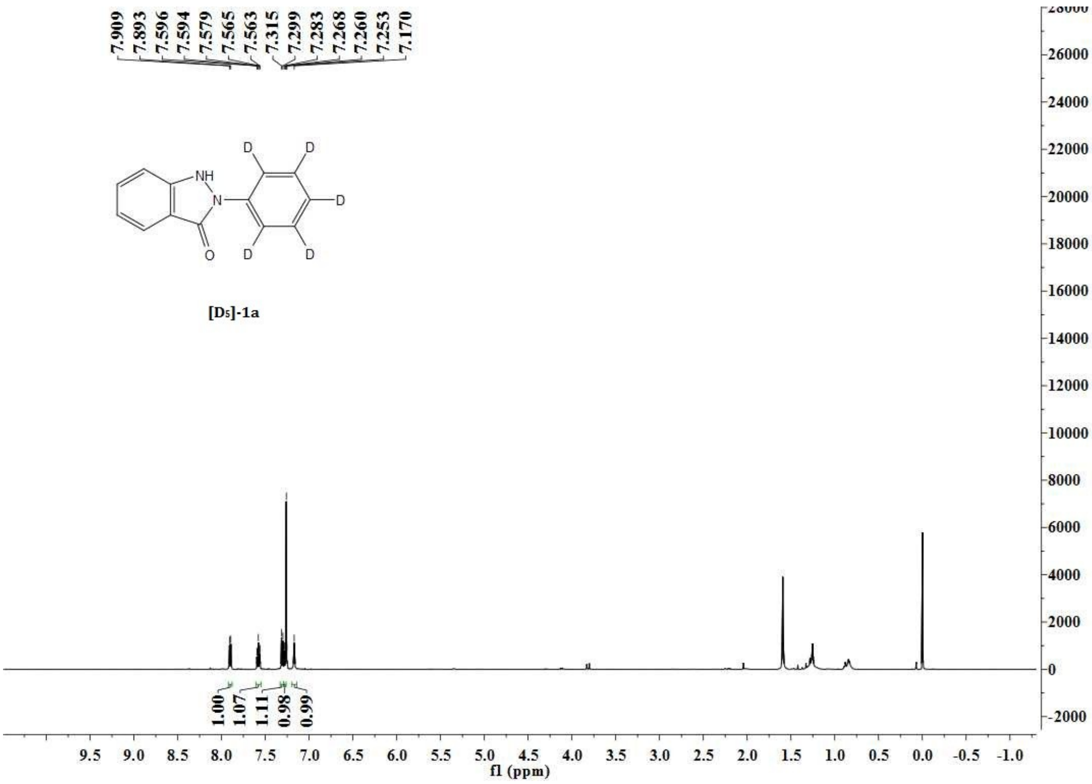

165.447
157.241
131.264
129.930
129.184
128.823
126.939
126.911
123.560
122.550
122.363
116.470
112.955
77.212
77.000
76.788
61.048
13.498
O
N
N
O
O
5
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
−100
−200
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
f1 (ppm)

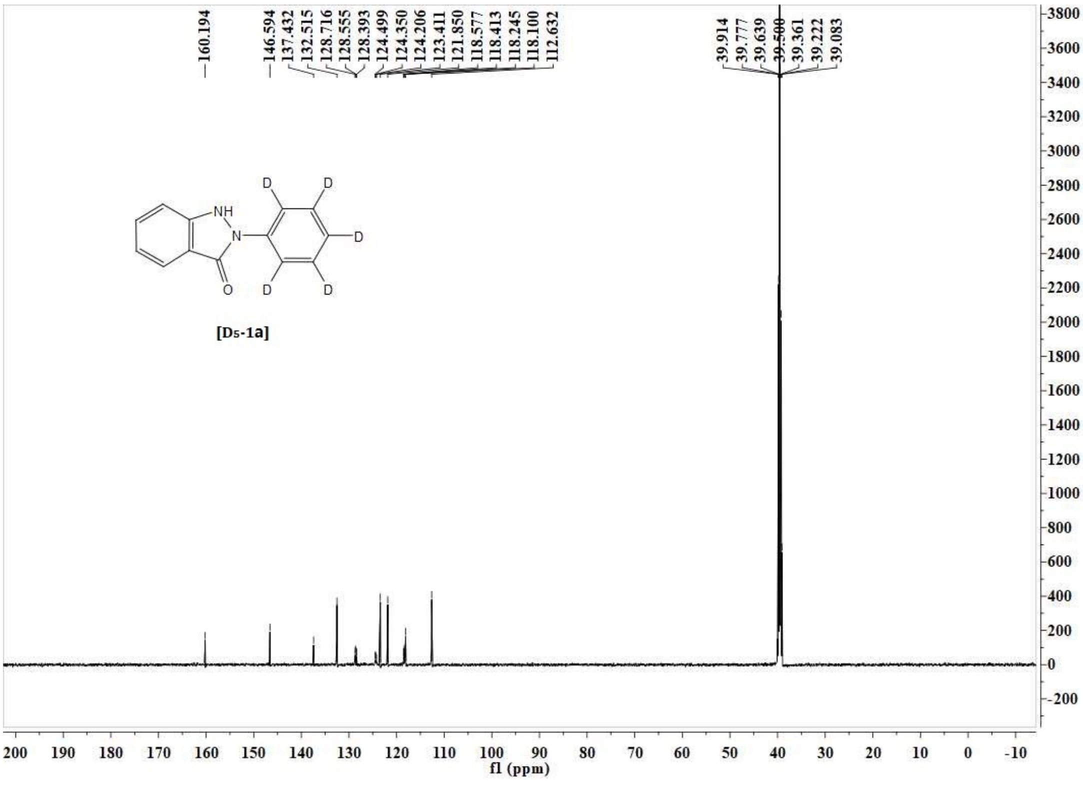

8.972
8.957
7.989
7.976
7.602
7.589
7.544
7.531
7.519
7.432
7.420
7.418
7.260
7.187
7.175
7.163
7.145
7.140
7.135
7.133
7.121
7.119
6.898
6.894
6.883
6.879
5.589
5.575
3.930
3.918
3.906
3.895
3.876
3.868
3.860
3.190
3.182
3.174
0.815
0.804
0.792
O
N
N
O
O
N
O
6
0.97
1.04
1.09
2.12
2.18
1.17
0.98
1.10
1.04
1.03
2.17
4.10
4.10
3.21
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)
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000


165.660
156.623
149.062
139.441
135.997
131.856
130.767
130.501
129.923
129.143
126.783
123.348
122.511
120.902
117.194
116.898
114.908
112.986
110.815
109.994
77.211
77.000
76.788
66.797
60.927
49.220
13.443
O
N
N
O
O
N
O
6
20
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)
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100


9.315
8.253
8.251
8.240
8.238
7.568
7.565
7.555
7.553
7.542
7.540
7.311
7.310
7.298
7.286
7.285
7.260
7.248
D
NH
O
N
N+
N-
S1
1.00
1.00
1.04
1.02
1.17
f1 (ppm)


162.533
137.748
136.796
132.761
132.553
128.675
128.513
128.354
125.430
125.197
124.205
124.039
123.880
120.262
120.098
119.935
118.429
77.212
77.000
76.789
N-
N+
N
O
NH
D
S1
f1 (ppm)


7.909
7.893
7.596
7.594
7.579
7.565
7.563
7.315
7.299
7.283
7.268
7.260
7.253
7.170
NH
N
O
D
D
D
D
D
[D5]-1a
1.00
1.07
1.11
0.98
0.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000


160.194
146.594
137.432
132.515
128.716
128.555
128.393
124.499
124.350
124.206
123.411
121.850
118.577
118.413
118.245
118.100
112.632
39.914
39.777
39.639
39.500
39.361
39.222
39.083
NH
N
O
D
D
D
D
D
[D5-1a]
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200