Supporting Information

Divergent Copper-mediated Dimerization and Hydroxylation of Benzamides Involving C-H Bond Functionalization

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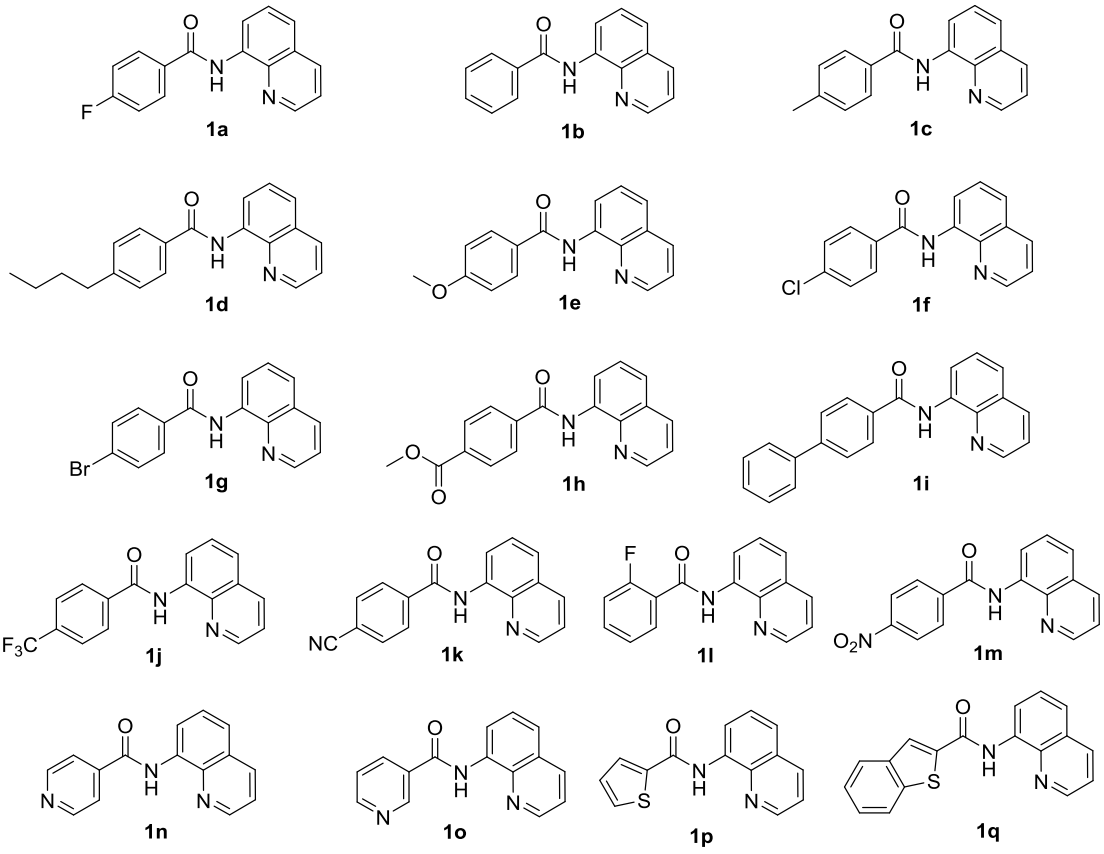
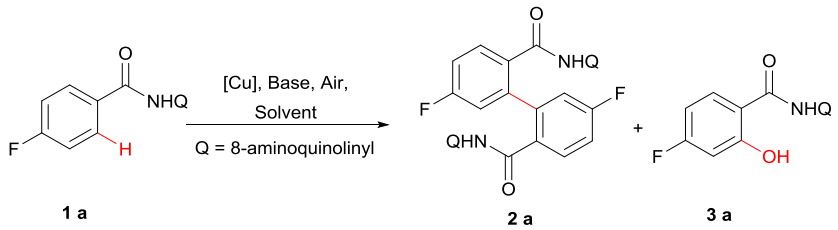
General information

NMR spectra were obtained on a Bruker AV II-400 MHz spectrometer (^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz, and ^{19}F NMR at 375 MHz). The ^{1}H NMR chemical shifts were measured relative to $CDCl_3$ or DMSO-d_6 as the internal reference ($CDCl_3$: δ= 7.26 ppm; DMSO-d_6: δ= 2.50 ppm). The ^{13}C NMR chemical shifts were given using $CDCl_3$ or DMSO-d_6 as the internal standard ($CDCl_3$: δ= 77.16 ppm; DMSO-d_6: δ= 39.52 ppm). Mass spectroscopy data were collected on an HRMS-ESI instrument. Reagents and starting materials were obtained from commercial sources and used without further purification unless otherwise noted. Anhydrous Cu $(OAc)_2$ was purchased from Aldrich. Starting materials 1a-1o were synthesized from the corresponding benzoyl chlorides and 8-aminoquinoline.[1, 2] 1p-1q were synthesized from the corresponding carboxylic acid and 8-aminoquinoline.[3, 4]

Structures of Starting Materials



Optimization of copper-promoted dimerization [a]

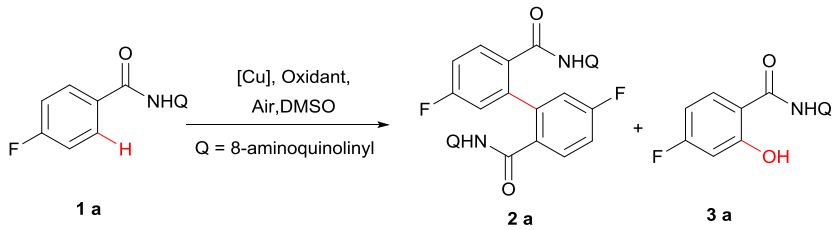


1 a 2 a 3 a

Entry	[Cu] (equiv)	Solvent	Base (equiv)	Temperature (^{o}C)	Yield[b] (**2a** /**3a** %)
1	$Cu(OAc)_2$ (0.5)	EtOH	K_2CO_3 (1.0)	100	9 / <5
2	$Cu(OAc)_2$ (0.5)	CF_3CH_2OH	K_2CO_3 (1.0)	100	18 / <5
3	$Cu(OAc)_2$ (0.5)	Toluene	K_2CO_3 (1.0)	100	9 / <5
4	$Cu(OAc)_2$ (0.5)	DCE	K_2CO_3 (1.0)	100	<5 / <5
5	$Cu(OAc)_2$ (0.5)	Dioxane	K_2CO_3 (1.0)	100	11 / <5
6	$Cu(OAc)_2$ (0.5)	MeCN	K_2CO_3 (1.0)	100	56 / <5
7	$Cu(OAc)_2$ (0.5)	DMF	K_2CO_3 (1.0)	100	72 / 12
8	$Cu(OAc)_2$ (0.5)	DMSO	K_2CO_3 (1.0)	100	78 / <5
9	$Cu(OAc)_2$ (0.5)	NMP	K_2CO_3 (1.0)	100	12 / 18
10	$Cu(OAc)_2$ (0.5)	DMSO	$NaHCO_3$ (1.0)	100	30 / 58
11	$Cu(OAc)_2$ (0.5)	DMSO	KOAc (1.0)	100	25 / 53
12	$Cu(OAc)_2$ (0.5)	DMSO	Na_2CO_3 (1.0)	100	68 / 22
13	$Cu(OAc)_2$ (0.5)	DMSO	Cs_2CO_3 (1.0)	100	71 / 15
14	$Cu(OAc)_2$ (0.5)	DMSO	Na_2HPO_4 (1.0)	100	15 / 53
15	$Cu(OAc)_2$ (0.5)	DMSO	K_2CO_3 (2.0)	100	73 / <5
18	CuI (1.0)	DMSO	K_2CO_3 (1.0)	100	<10 / <10
19	$CuSO_4$(1.0)	DMSO	K_2CO_3 (1.0)	100	<10 / <10
20	$Cu(OAc)_2$.H2O(1.0)	DMSO	K_2CO_3 (1.0)	100	69 / 12
21	$Cu(OAc)_2$ (0.1)	DMSO	K_2CO_3 (1.0)	100	16 / <5
22	$Cu(OAc)_2$ (0.2)	DMSO	K_2CO_3 (1.0)	100	34 / <5
23	$Cu(OAc)_2$ (0.4)	DMSO	K_2CO_3 (1.0)	100	72 / 11
25	$Cu(OAc)_2$ (1.0)	DMSO	K_2CO_3 (1.0)	100	76 / 8
26	$Cu(OAc)_2$ (2.0)	DMSO	K_2CO_3 (1.0)	100	65 / 16
27	$Cu(OAc)_2$ (0.5)	DMSO	K_2CO_3 (1.0)	rt	<5 / <5
28	$Cu(OAc)_2$ (0.5)	DMSO	K_2CO_3 (1.0)	60	12 / 26
29	$Cu(OAc)_2$ (0.5)	DMSO	K_2CO_3 (1.0)	80	61 / 26
30	**$Cu(OAc)_2$ (0.5)**	**DMSO**	**K_2CO_3 (1.0)**	**108**	**84 / <5**
31	$Cu(OAc)_2$ (0.5)	DMSO	K_2CO_3 (1.0)	120	81 / <5
32[c]	$Cu(OAc)_2$ (1.0)	DMSO	K_2CO_3 (1.0)	100	8 / 32
33[c]	$Cu(OAc)_2$ (2.0)	DMSO	K_2CO_3 (1.0)	100	38 / 41
34[d]	$Cu(OAc)_2$ (0.5)	DMSO	K_2CO_3 (1.0)	108	72 / <10

[a] Reaction conditions: **1a** (0.2 mmol), Cu salt, base (0.2 mmol), solvent (2 mL), 100 ^{o}C, air, 1h. [b] Isolated yield. [c] under Ar atmosphere. [d] added 1.0 equiv TEMPO

Optimization of copper-promoted Hydroxylation

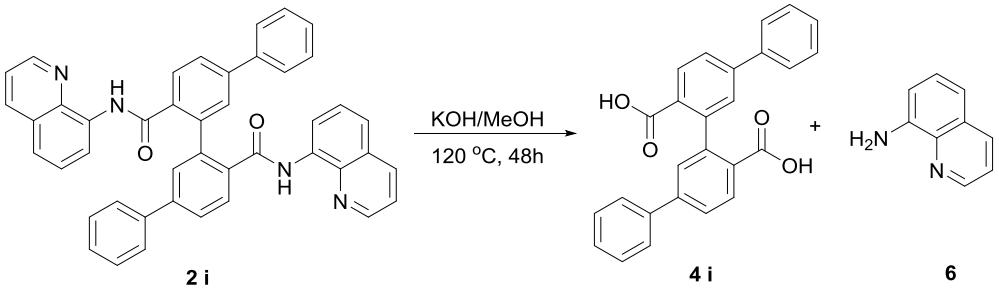


1 a 2 a 3 a

Entry	[Cu] (equiv)	Oxidant (equiv)	Temperature	Yield (**2a** /**3a** %)
1	$Cu(OAc)_2$ (1.0)	AgOAc	100	21 / 65
2	$Cu(OAc)_2$ (1.0)	Ag_2CO_3	100	19 / 56
3	$Cu(OAc)_2$ (1.0)	$K_2S_2O_8$	100	<10 / <5
4	$Cu(OAc)_2$ (1.0)	Oxone	100	34 / 21
5	$Cu(OAc)_2$ (1.0)	NMO	100	<5 / 19
6	$Cu(OAc)_2$ (1.0)	TBAI(0.5)/air	100	53 / 38
7	$Cu(OAc)_2$ (1.0)	TBAI(1.0)/air	100	11 / 68
8	$Cu(OAc)_2$ (1.0)	TBAI(2.0)/air	100	9 / 73
9	$Cu(OAc)_2$ (1.0)	TBAI(3.0)/air	100	<10 / 68
10	$Cu(OAc)_2$ (0.5)	TBAI(2.0)/air	100	<5 / 48
11	$Cu(OAc)_2$ (1.1)	TBAI(2.0)/air	100	<5 / 78
12	$Cu(OAc)_2$ (1.5)	TBAI(2.0)/air	100	<10 / 76
13	$Cu(OAc)_2$ (2.0)	TBAI(2.0)/air	100	9 / 75
14	$Cu(OAc)_2$ (1.1)	TBAI(2.0)/air	rt	<5 / <5
15	$Cu(OAc)_2$ (1.1)	TBAI(2.0)/air	60	<10 / 24
16	**$Cu(OAc)_2$ (1.1)**	**TBAI(2.0)/air**	**90**	**<5 / 78**
17	$Cu(OAc)_2$ (1.1)	TBAI(2.0)/air	110	<10 / 73
18[c]	$Cu(OAc)_2$ (1.1)	TBAI(2.0)/air	100	<5 /42
19[c]	$Cu(OAc)_2$ (2.0)	TBAI(2.0)/air	100	<5 / 63
20[d]	$Cu(OAc)_2$ (1.1)	TBAI(2.0)/air	90	<10 / 65

[a] Reaction conditions: **1a** (0.2 mmol), Cu salt, base (0.2 mmol), solvent (2 mL), 100 ^{o}C, air, 1h. [b] Isolated yield. [c] under Ar atmosphere. [d] added 1.0 equiv TEMPO;

Removal of directing group



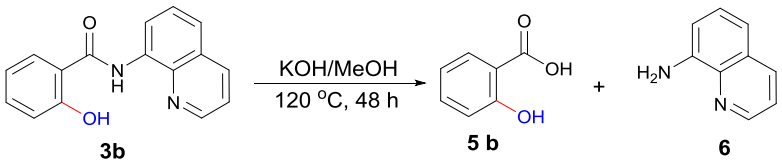
Synthesis of [1, 1':3', 1'':3'', 1'''-quaterphenyl]-4', 6''-dicarboxylic acid (4i)

N4', N6''-di (quinolin-8-yl)-[1, 1':3', 1'':3'', 1'''-quaterphenyl]-4', 6''-dicarboxamide (**2i**) (360 mg, 0.56 mmol, 1.0 equiv) and KOH (1.9 g, 33.6 mmol, 60.0 equiv) were dissolved in MeOH (5 mL). Resulting solution was heated at 120 ºC temperature for 48 h. Mixture was cooled to room temperature, diluted with EtOAc (50 mL), 1M HCl aqueous solution (30 mL) was added. Organic phase was separated, dried over MgSO4, filtered, and evaporated. A purification by flash chromatography (DCM: MeOH= 100: 1 to 10:1) gave **4i** as a white solid in 71% yield, mp 295-297 °C.

^{1}H NMR (400 MHz, DMSO) δ 12.50 (s, 2H), 8.00 (d, *J* = 8.2 Hz, 2H), 7.77 (d, *J* = 7.3 Hz, 6H), 7.53 (d, *J* = 1.8 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 4H), 7.41 (t, *J* = 7.3 Hz, 2H).

^{13}C NMR (100 MHz, DMSO): δ 167.59, 143.70, 142.51, 138.83, 130.41, 129.27, 129.04, 128.60, 128.20, 127.01, 125.13.

HRMS (ESI-TOF) calcd for $C_{26}H_{18}O_4Na$ $[M + Na]^+$: 417.1097, found: 417.1099.



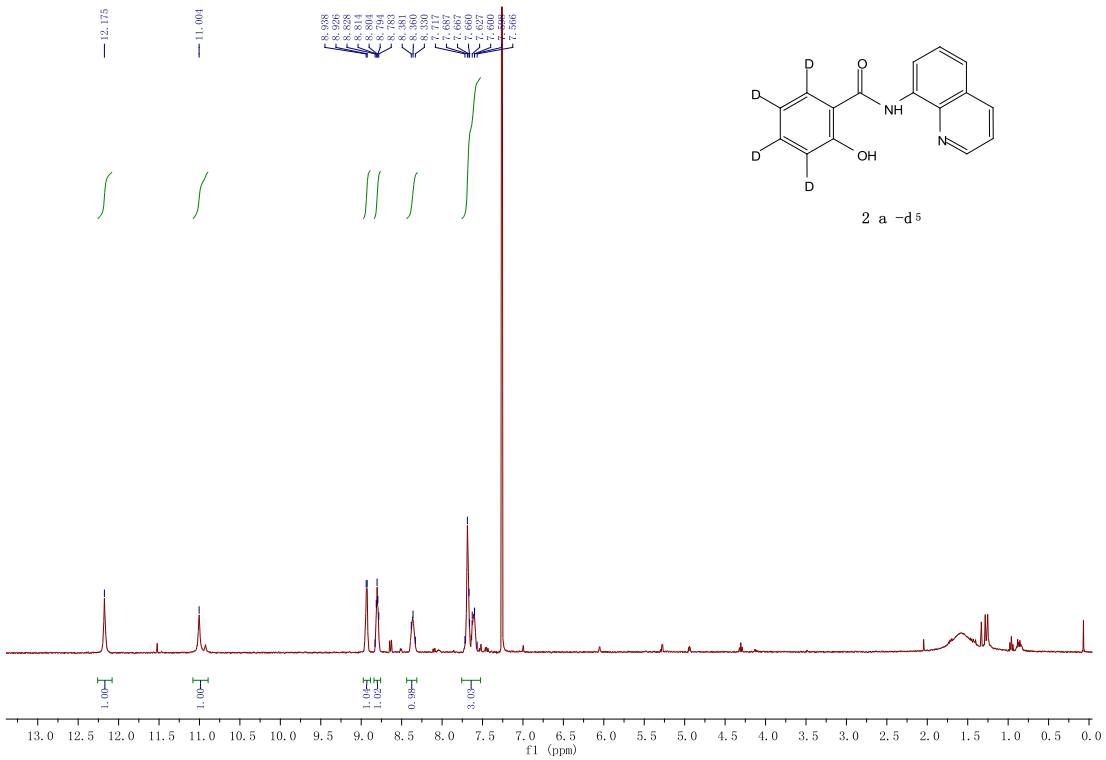
2-hydroxy-N-(quinolin-8-yl)benzamide (**3b**) (160 mg, 0.4 mmol, 1.0 equiv) and KOH (1.35 g, 24.0 mmol, 60.0 equiv) were dissolved in MeOH (10 mL). Resulting solution was heated at 120 °C temperature for 48 h. Mixture was cooled to room temperature, diluted with EtOAc (50 mL),

1M HCl aqueous solution (30 mL) was added. Organic phase was separated, dried over MgSO4, filtered, and evaporated. A purification by flash chromatography (DCM: MeOH= 100: 1 to 10:1) gave **5b** as a white solid in 73% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.37 (s, 1H), 7.94 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.56- 7.52 (m, 1H), 7.02 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.98 – 6.92 (m, 1H).

The Procedure for Kinetic Isotope Effect Experiments

To a 25 mL Schlenk tube were added amide **1b** (50 mg, 0.5 mmol), **1b-d^5** (51 mg, 0.5 mmol) TBAI (738 mg, 2 mmol), Cu (OAc) $_2$(200 mg, 1.1 mmol), DMSO (10 mL). The reaction tube was stirred at room temperature for 5 min and the mixture was then heated at 90 ^{o}C for 20 min under air. the reaction mixture was cooled to room temperature, $Na_2S·xH2O$ (500 mg), CH_2Cl_2 (50 mL) and H_2O (50 mL) were added. Resulting biphasic solution was stirred 10 min at room temperature and filtered through a pad of celite. Organic layer was separated and aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). Combined organic phase was dried with anhydrous $MgSO_4$. After concentration, product was purified by column chromatography on silica gel (PE/EA = 100/1 – 10/1) to give products as a white solid. K_H/K_D = 2.6.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8.926
8.828
8.814
8.804
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7.717
7.687
7.667
7.660
7.627
7.600
7.566
7.546
1.00
1.00
1.04
1.02
0.98
3.03
13.0 12.5 12.0 11.5 11.0 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
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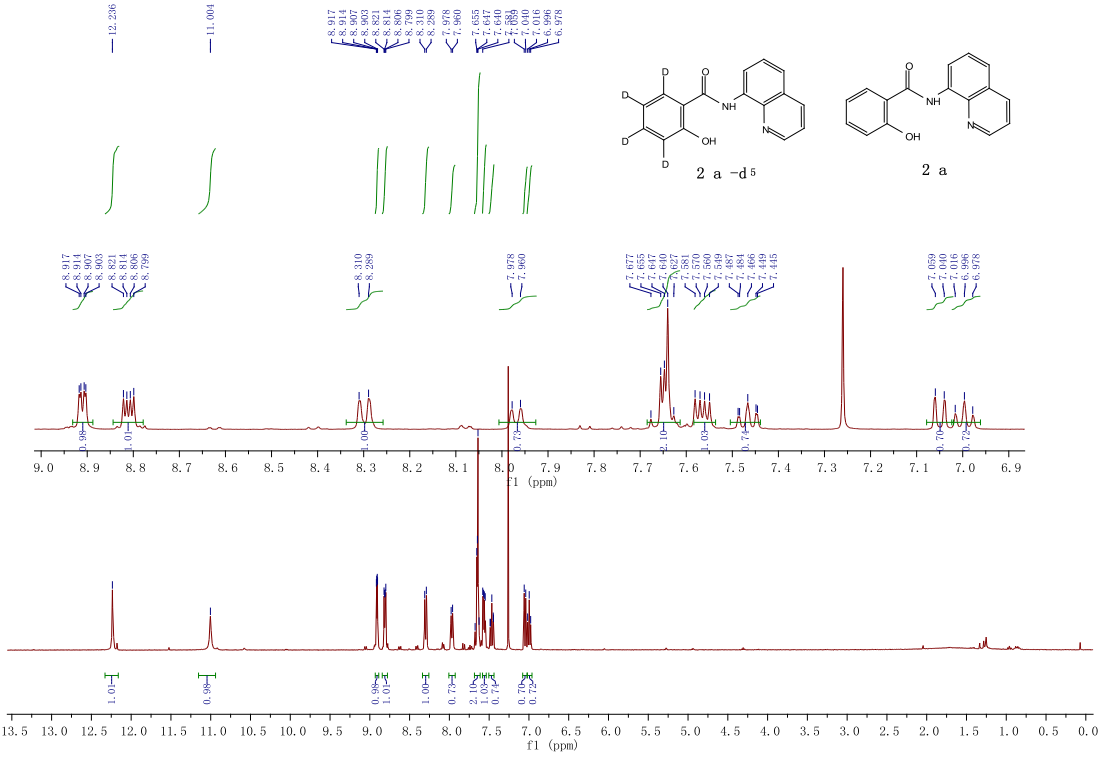
D
O
NH
N
OH
2 a -d5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8.806
8.799
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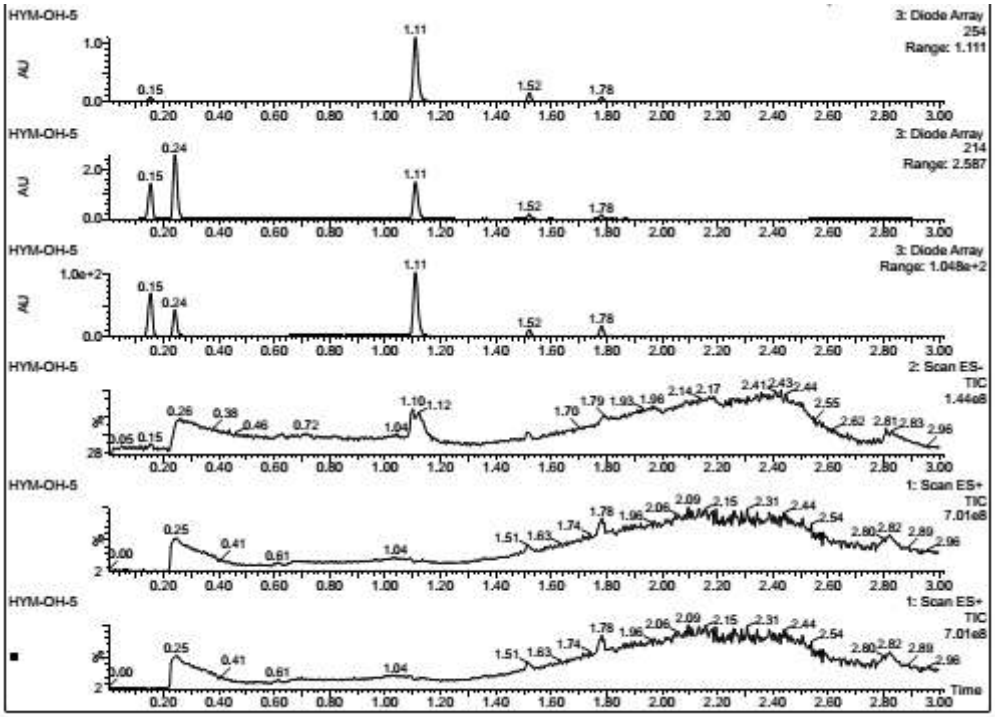
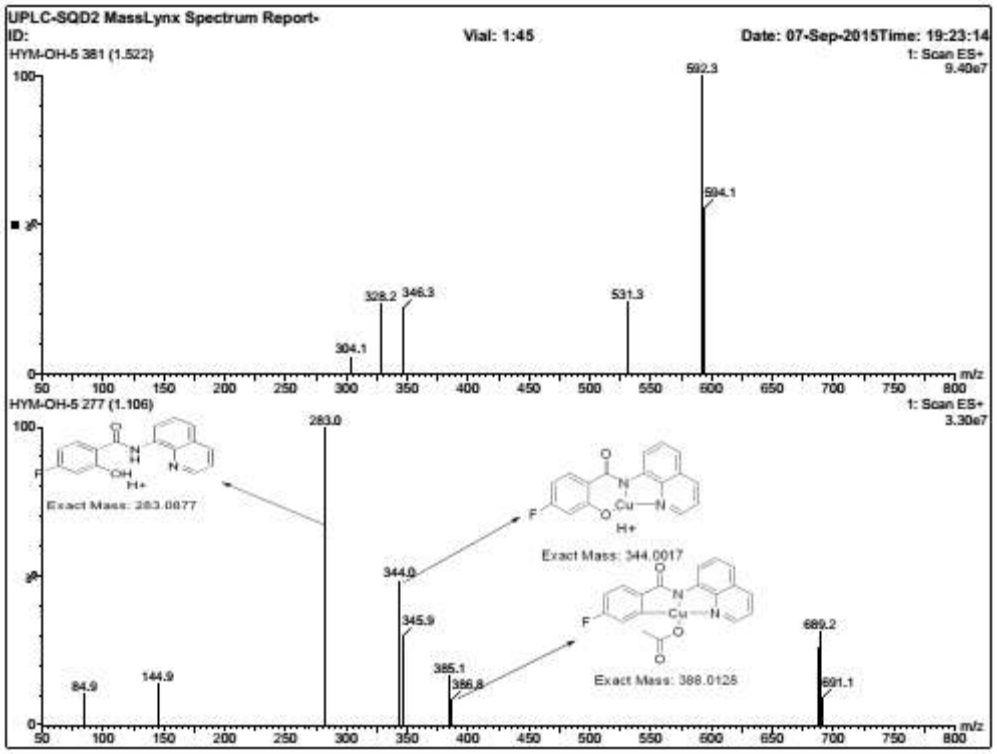
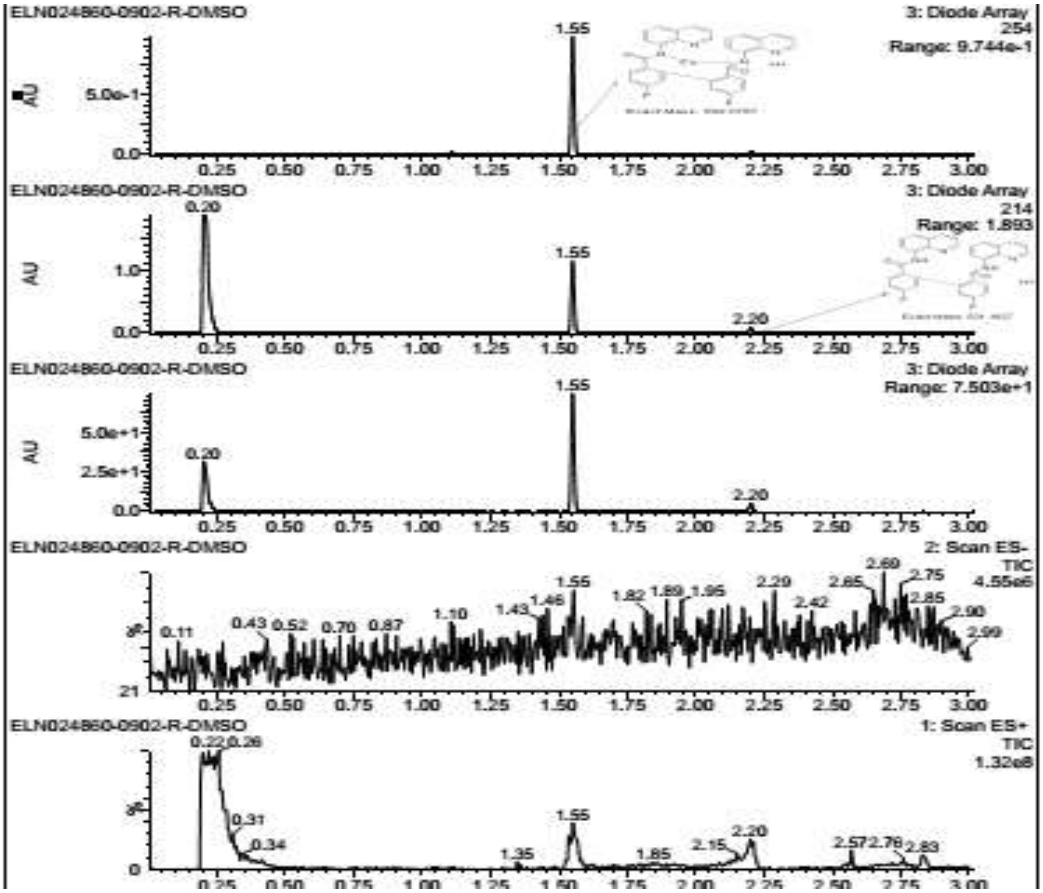
8.289
7.978
7.960
7.655
7.647
7.640
7.627
7.581
7.570
7.560
7.549
7.487
7.484
7.466
7.449
7.445
7.059
7.040
7.016
6.996
6.978
0.98
1.01
1.00
0.73
2.10
1.03
0.74
0.70
0.72
9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9
f1 (ppm)
1.01
0.98
0.98
1.07
1.04
0.73
2.10
1.07
0.74
0.70
0.72
13.5 13.0 12.5 12.0 11.5 11.0 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
f1 (ppm)
D
O
NH
N
OH
2 a -d5
2 a

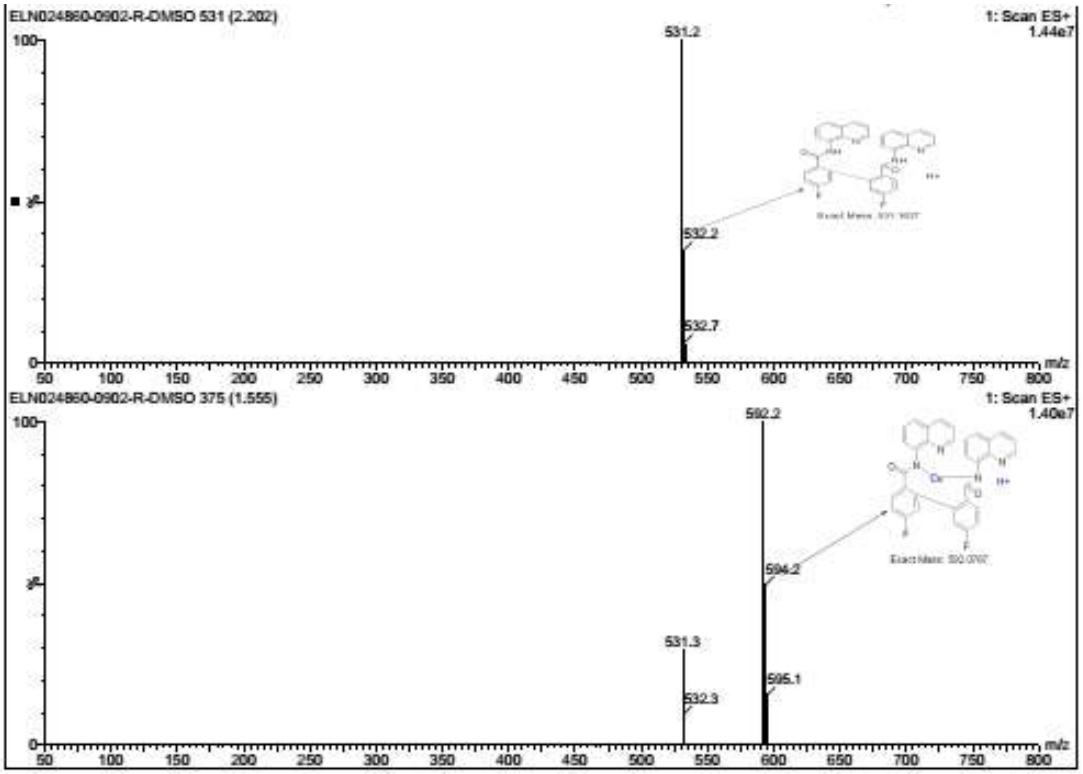
UPLC-MS for Hydroxylation reaction solution before work-up





UPLC-MS for Dimerization reaction solution before work-up





References

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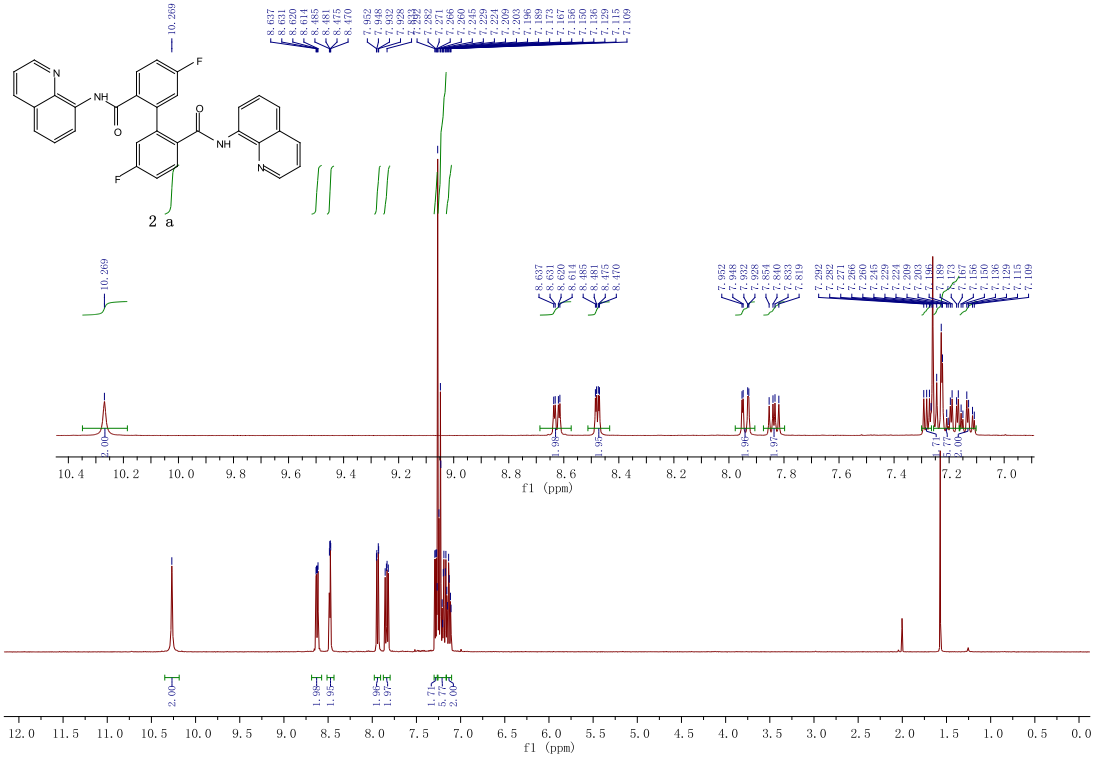
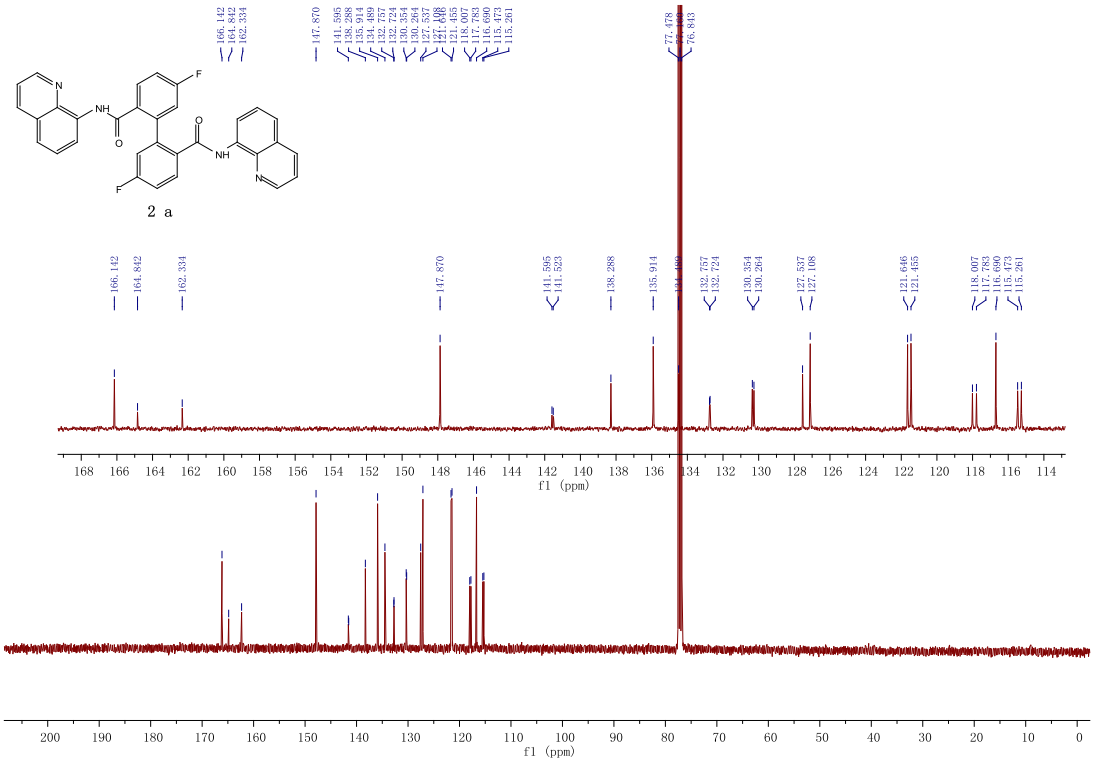
2 L. Grigorjeva and O. Daugulis, Org. Lett., 2014, 16, 4684.

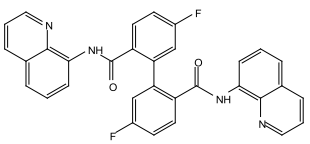
3 L. D. Tran, I. Popov, O. Daugulis, *J. Am. Chem. Soc.,* 2012, 134, 18237

4 K. Takamatsu, K. Hirano and M. Miura, Org. Lett. 2015, 17, 4066

NMR spectra







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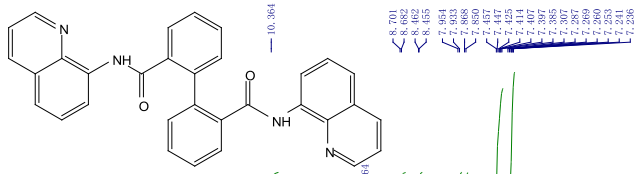

2 b

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7.425
7.414
7.407
7.397
7.385
7.307
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7.253
7.241
7.236
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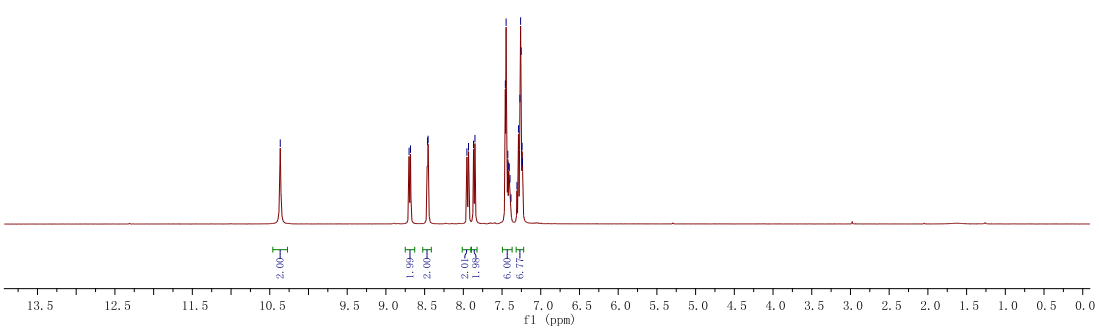
1.99
2.00
2.01
1.98
6.00
6.77
10.8 10.6 10.4 10.2 10.0 9.8 9.6 9.4 9.2 9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2
f1 (ppm)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1.98
6.00
6.77
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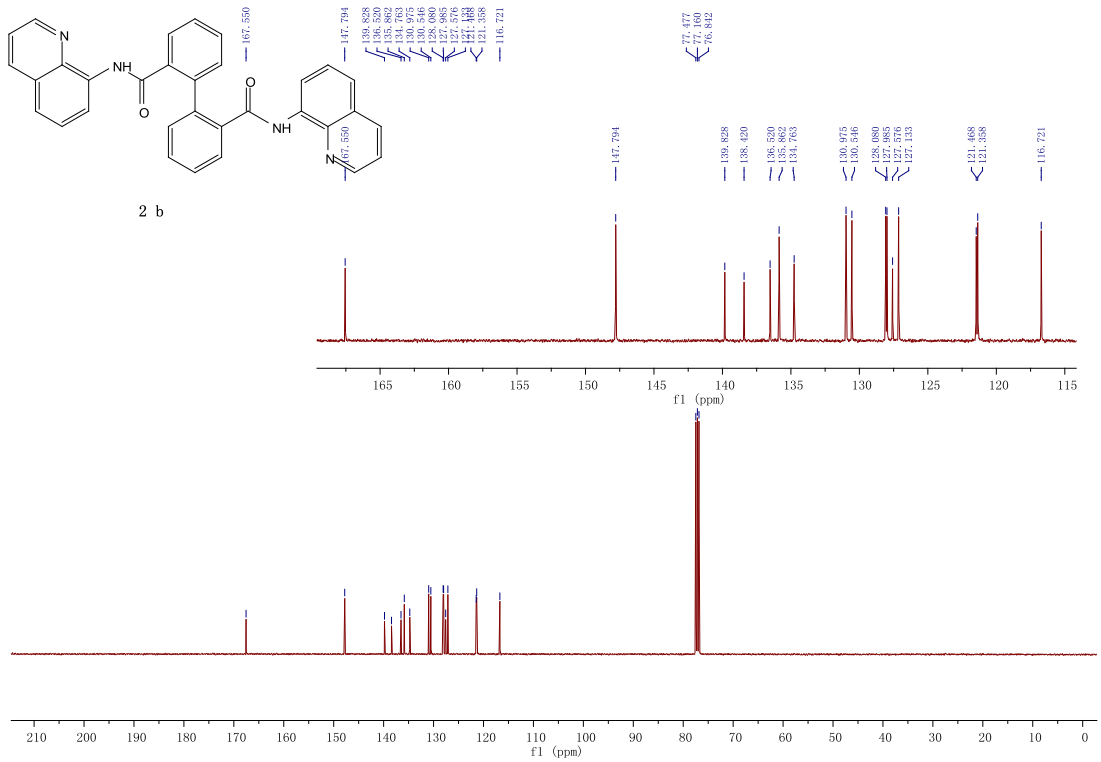
f1 (ppm)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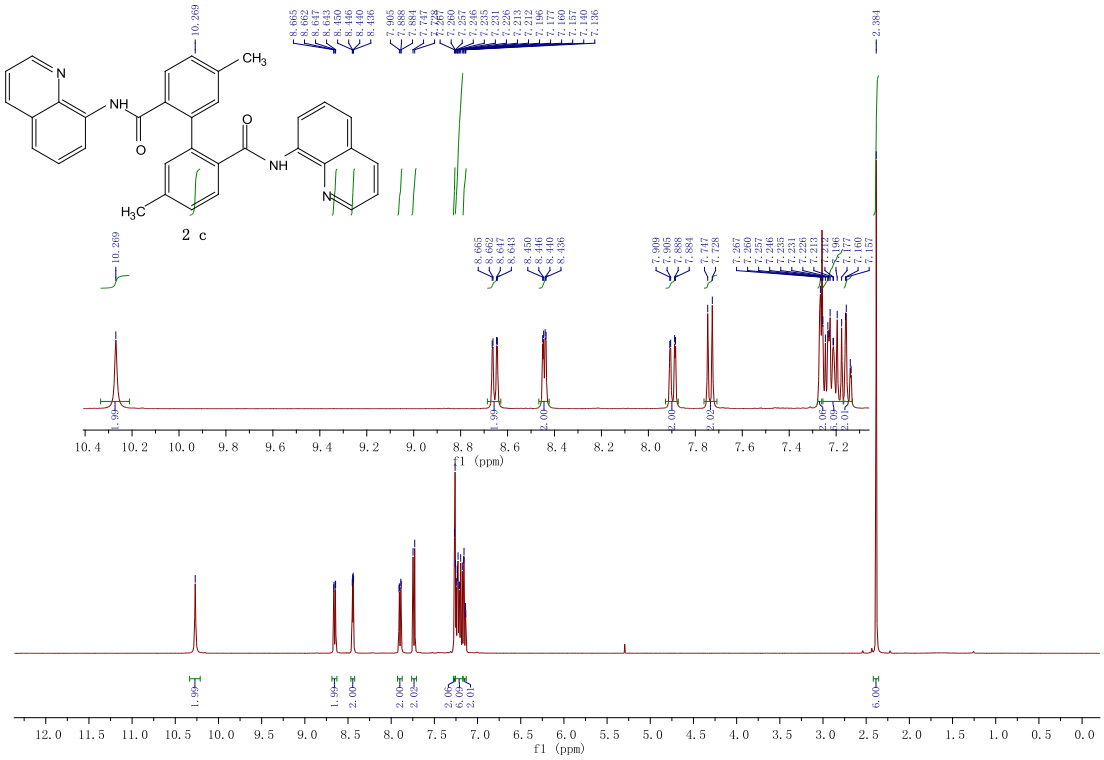
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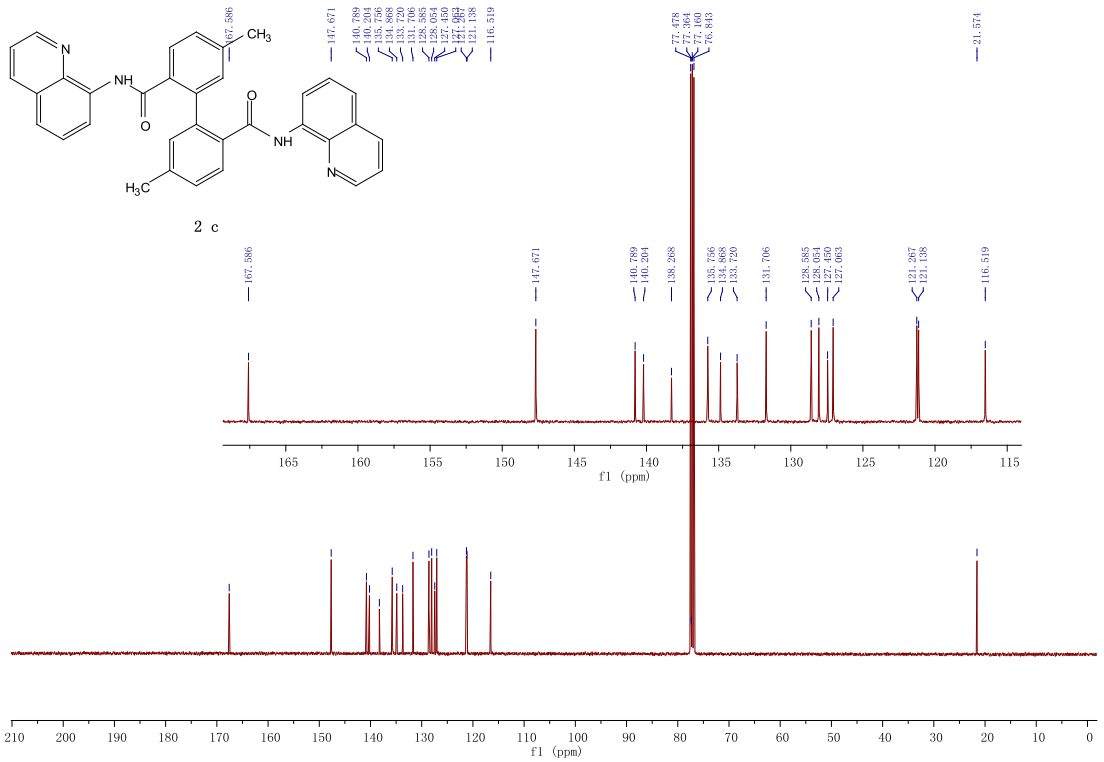
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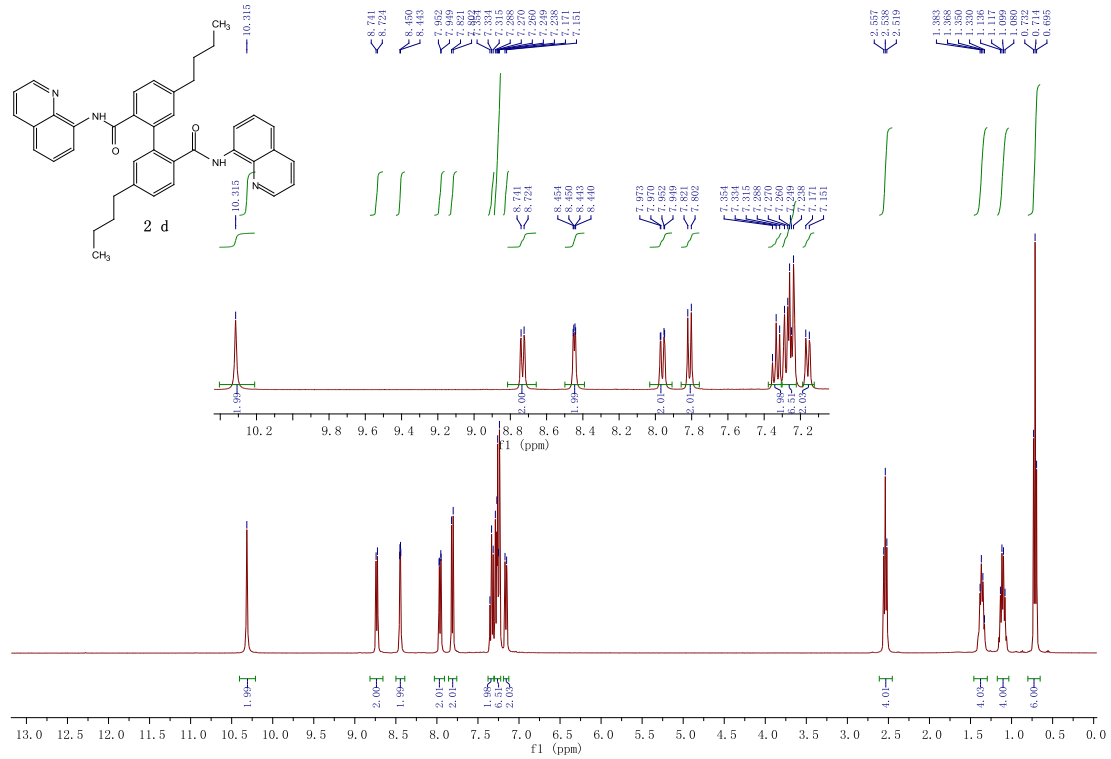
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2.538
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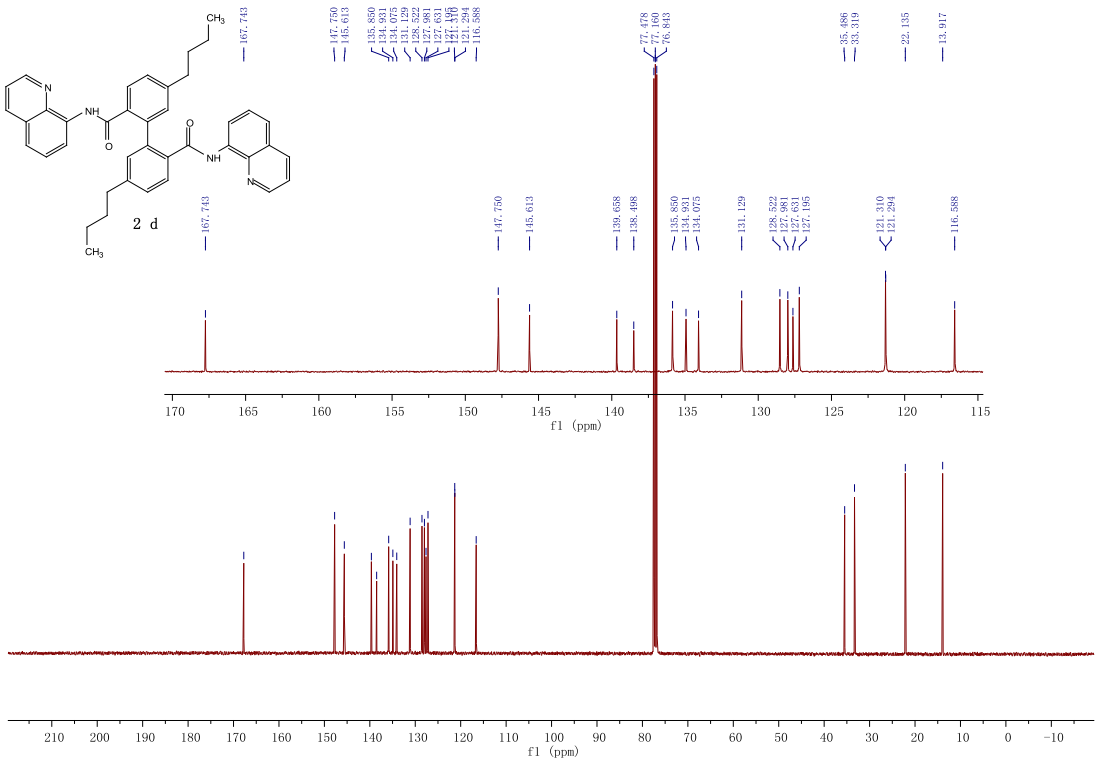
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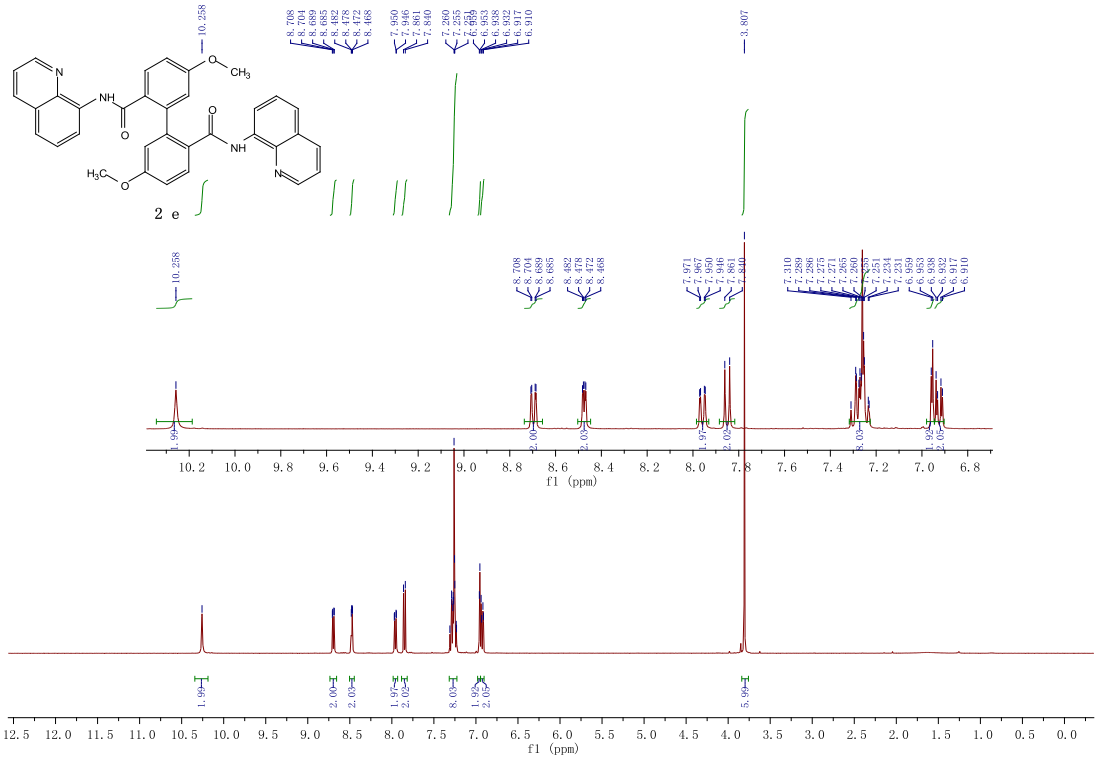
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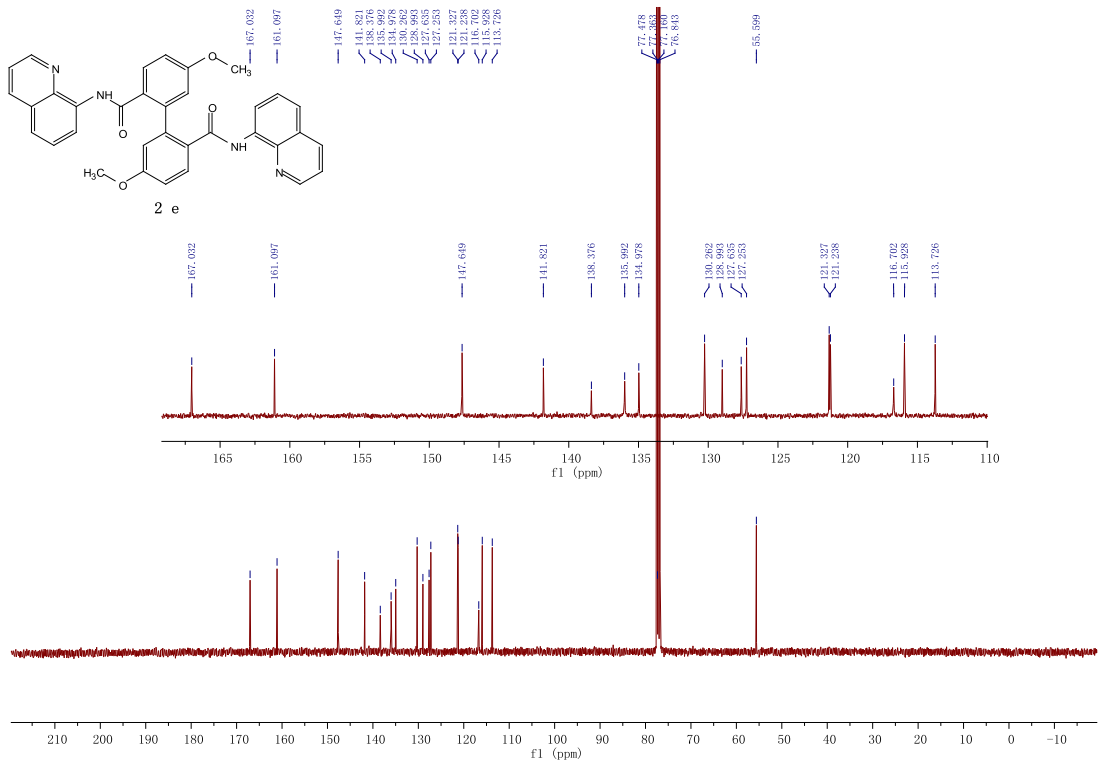
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161.097
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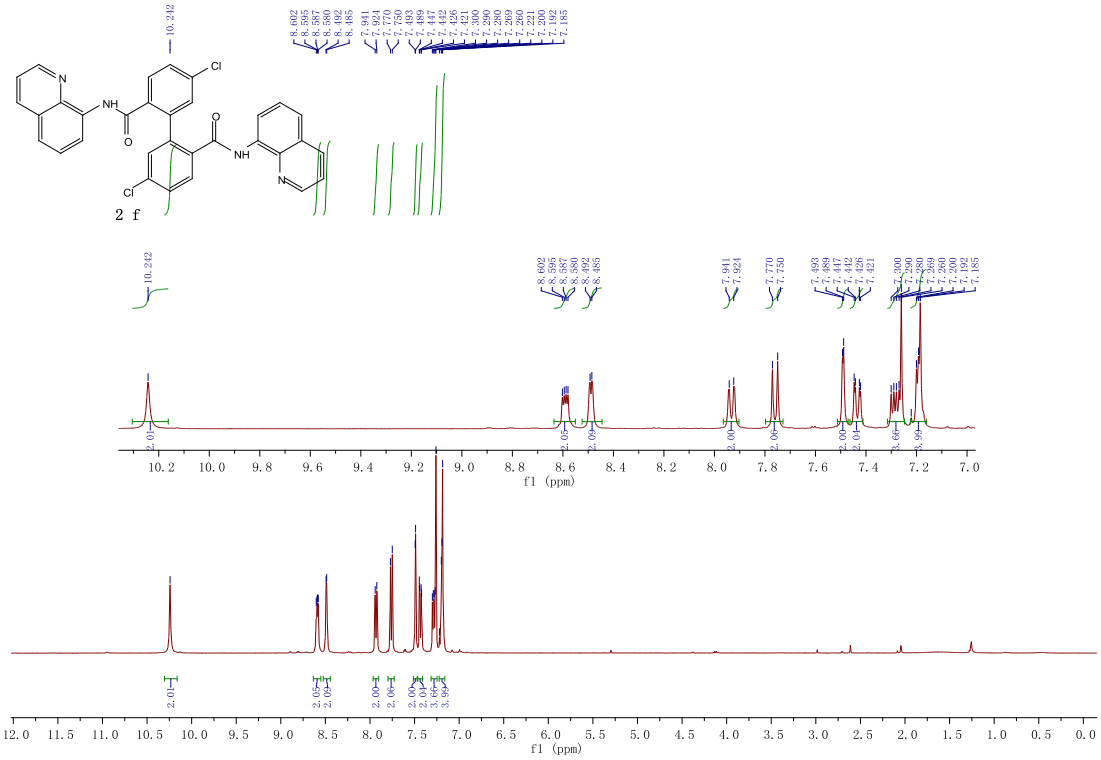
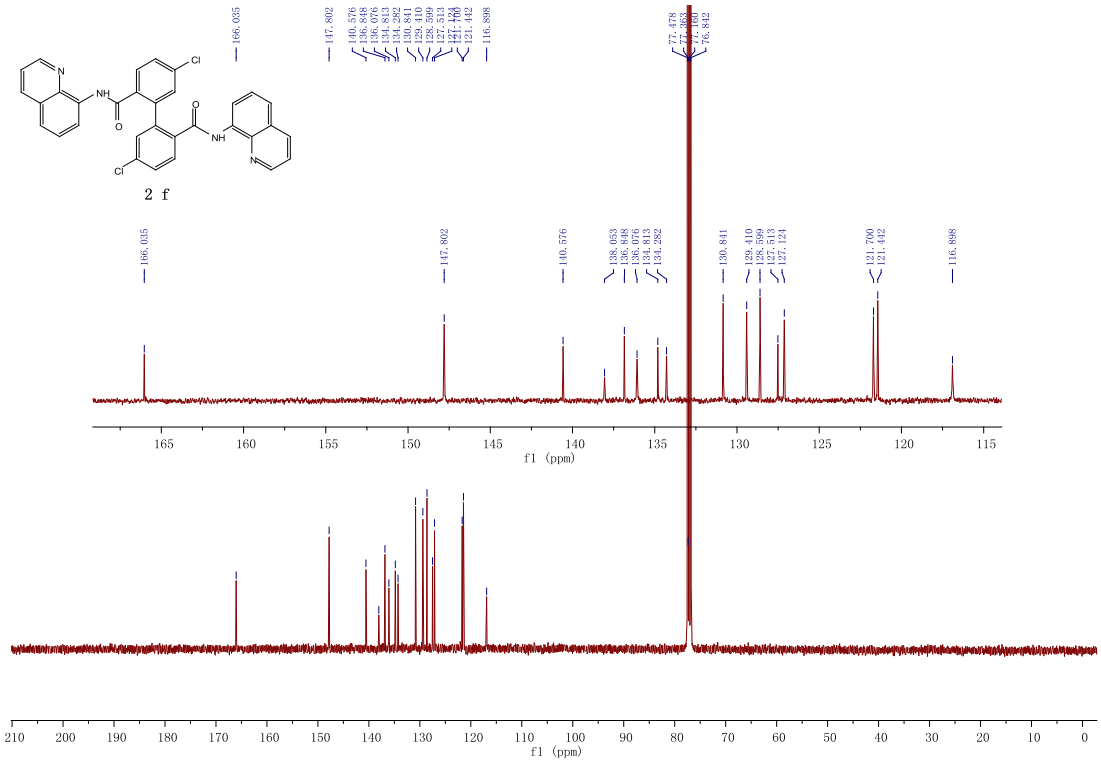
138.376
135.992
134.978
130.262
128.993
127.635
127.253
121.327
121.238
116.702
115.928
113.726
77.478
77.383
77.160
76.843
55.599
f1 (ppm)


2 f
10.242
8.602
8.595
8.587
8.580
8.492
8.485
7.941
7.924
7.770
7.750
7.493
7.489
7.447
7.442
7.426
7.421
7.300
7.290
7.280
7.269
7.260
7.221
7.200
7.192
7.185
2.01
2.05
2.04
2.00
2.06
2.00
2.04
3.66
3.99
f1 (ppm)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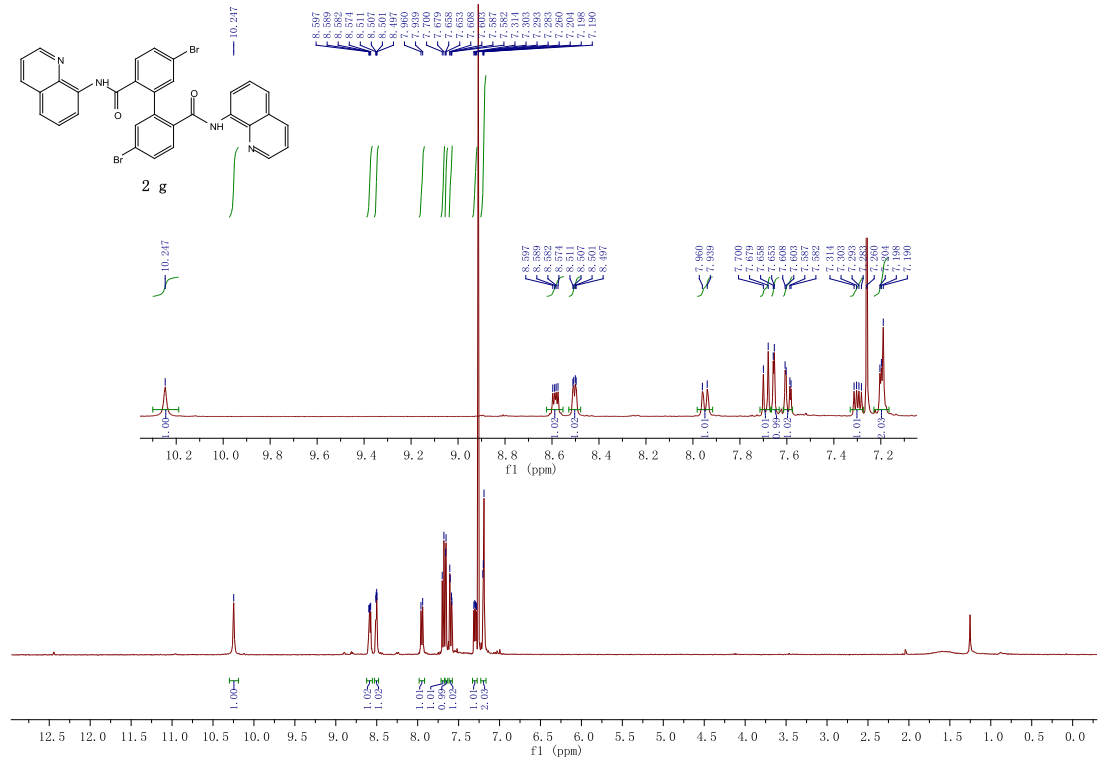
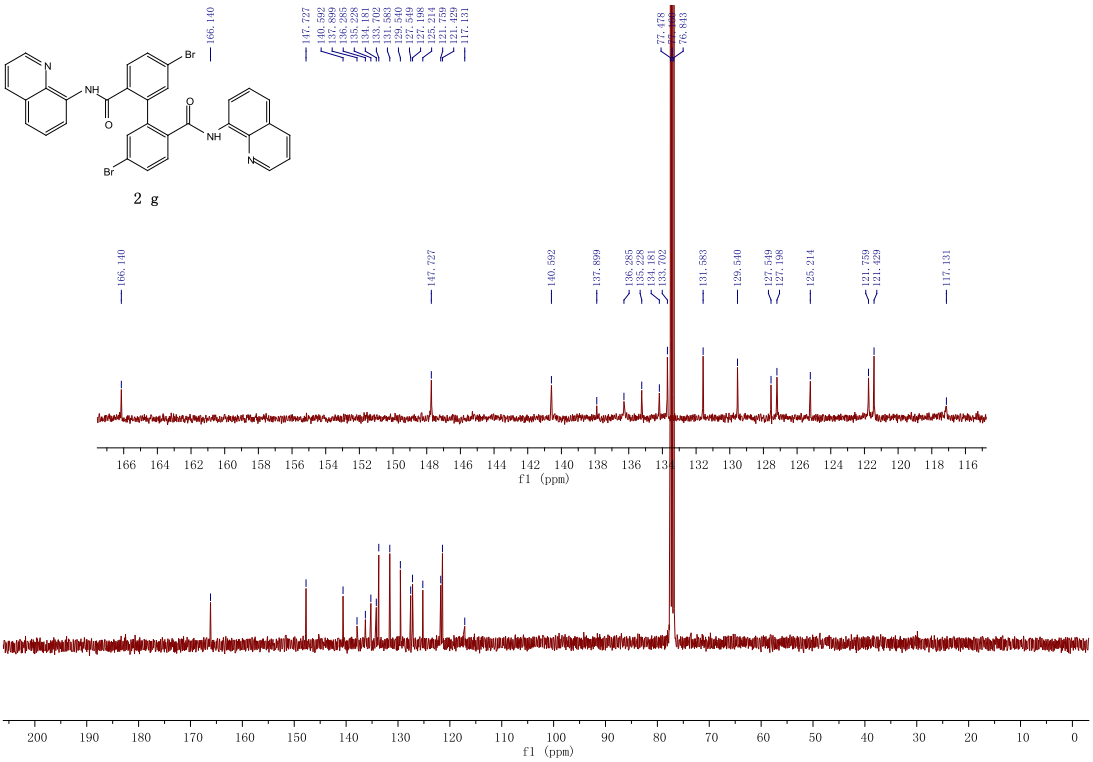
f1 (ppm)


2 g
f1 (ppm)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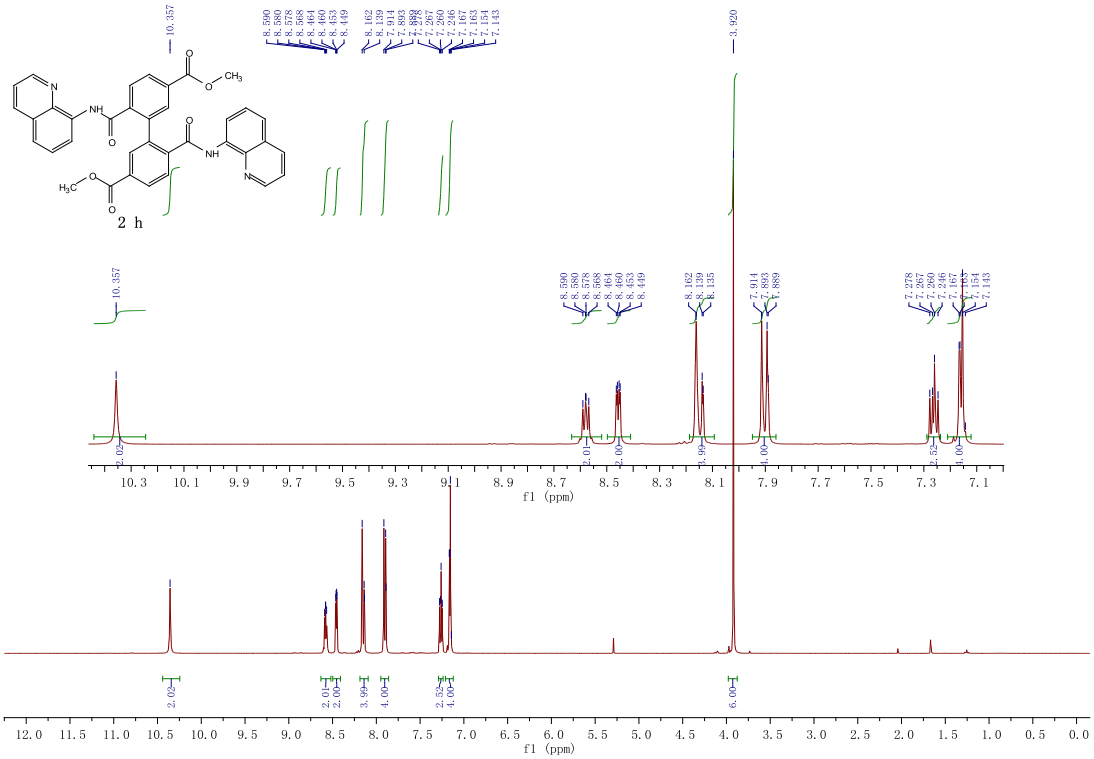
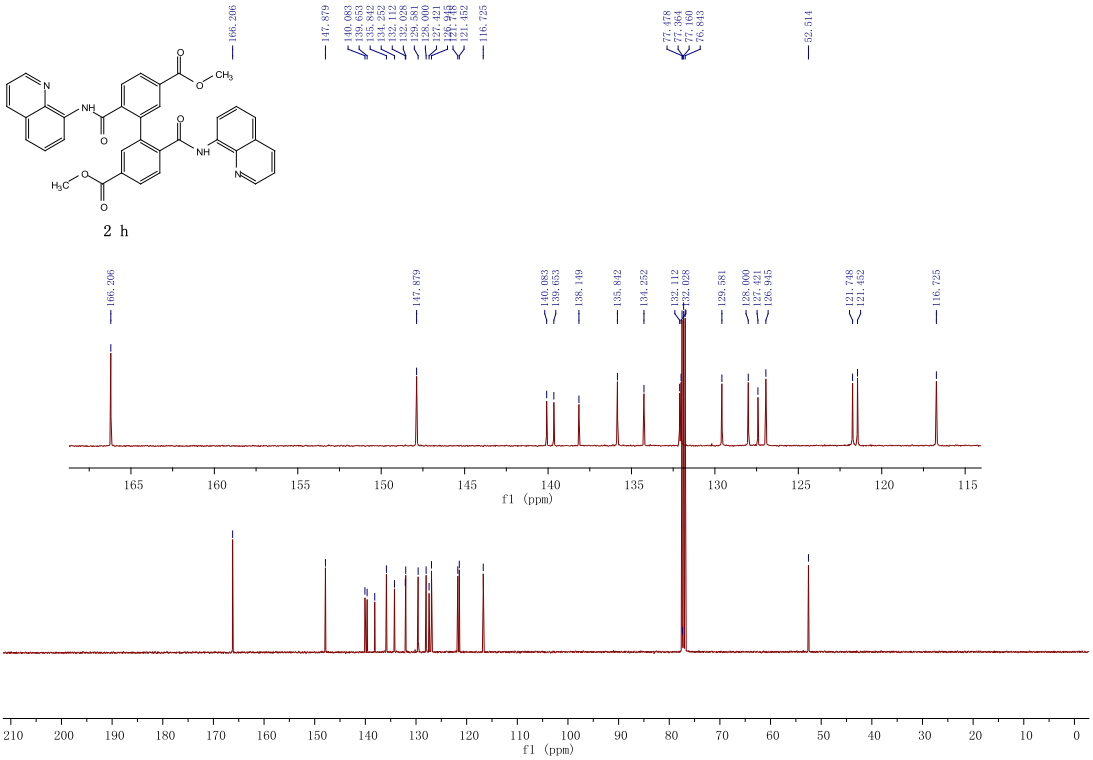
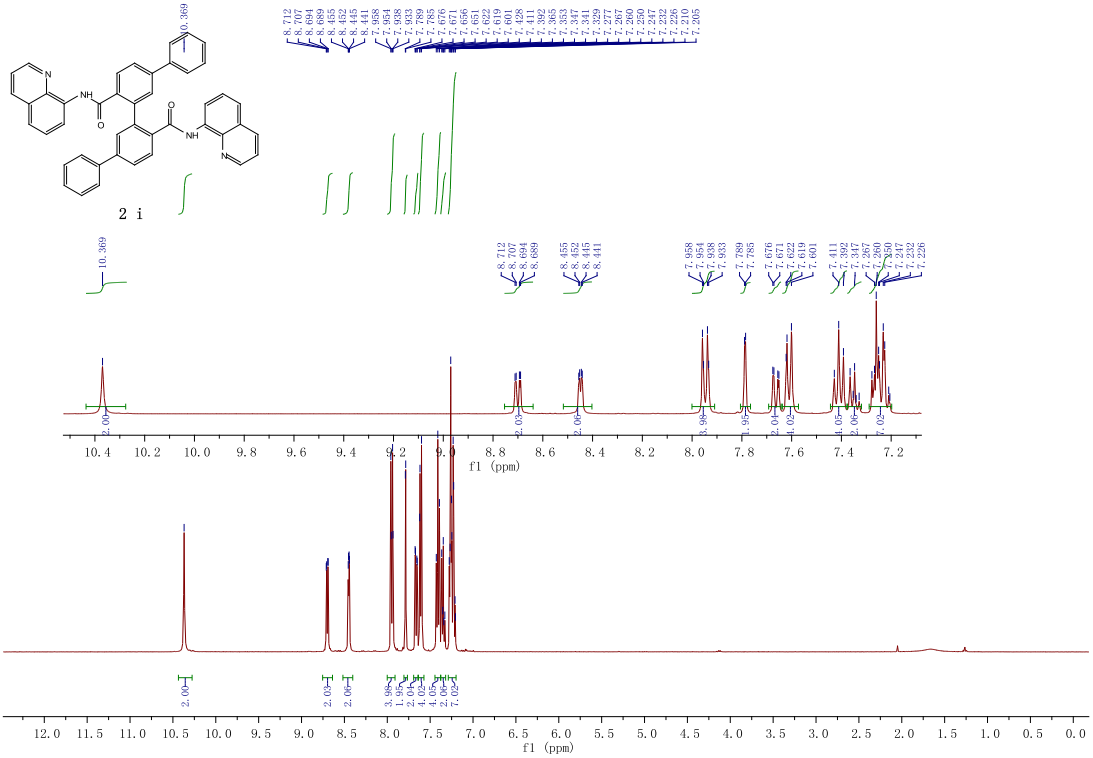
f1 (ppm)

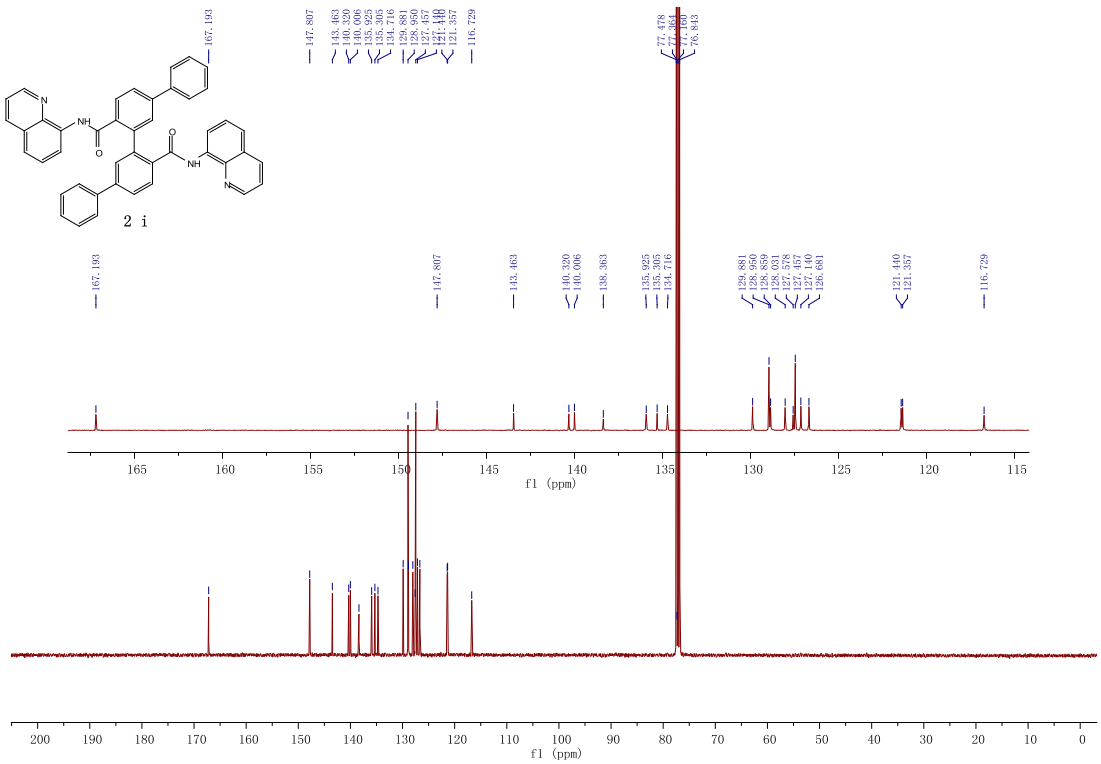

2 h
f1 (ppm)

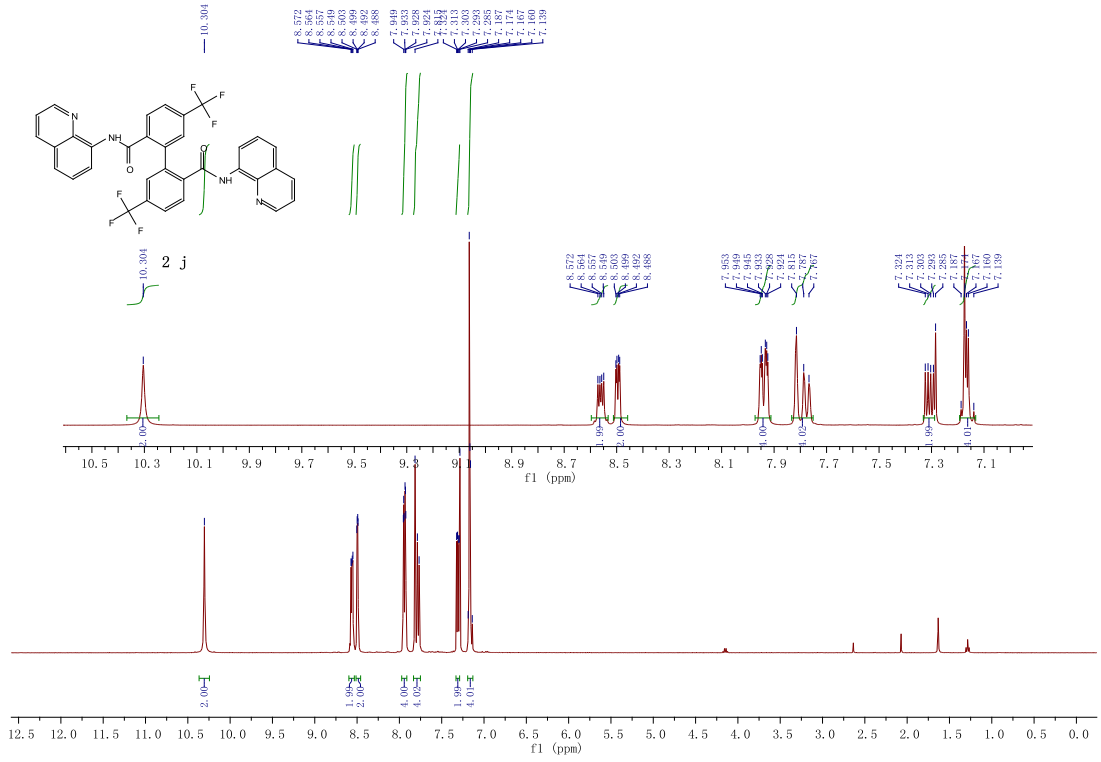


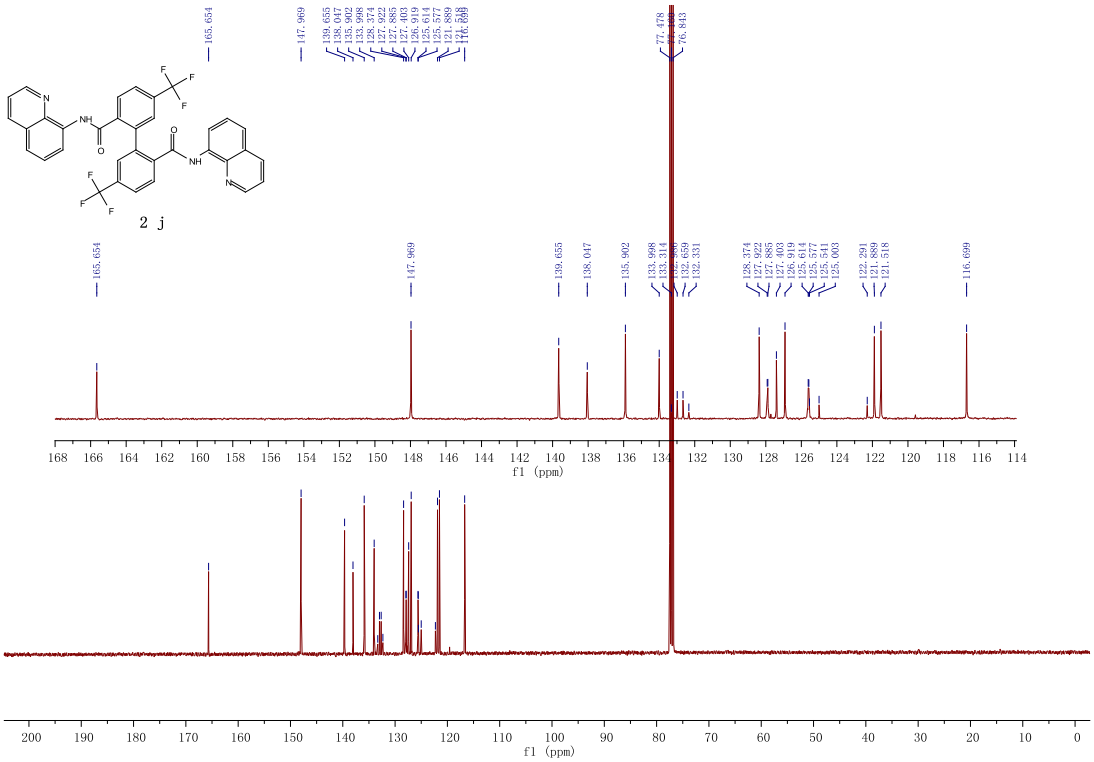
2 h



2 i


2 i
f1 (ppm)


2 j
f1 (ppm)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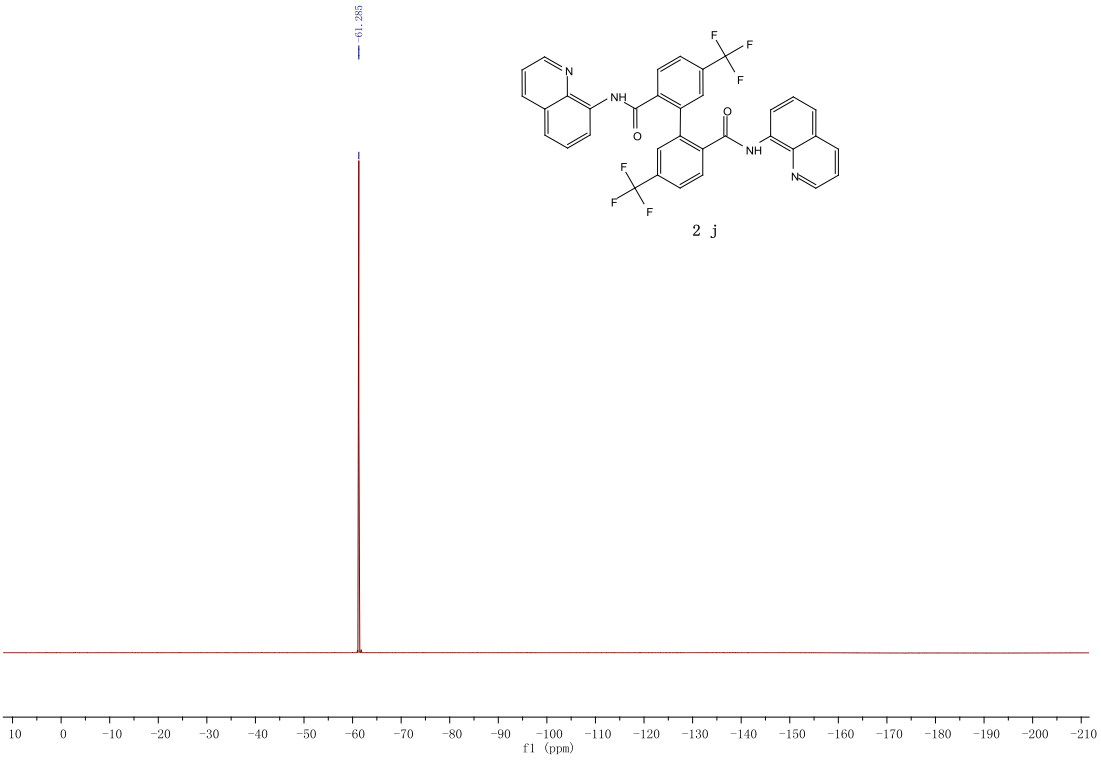
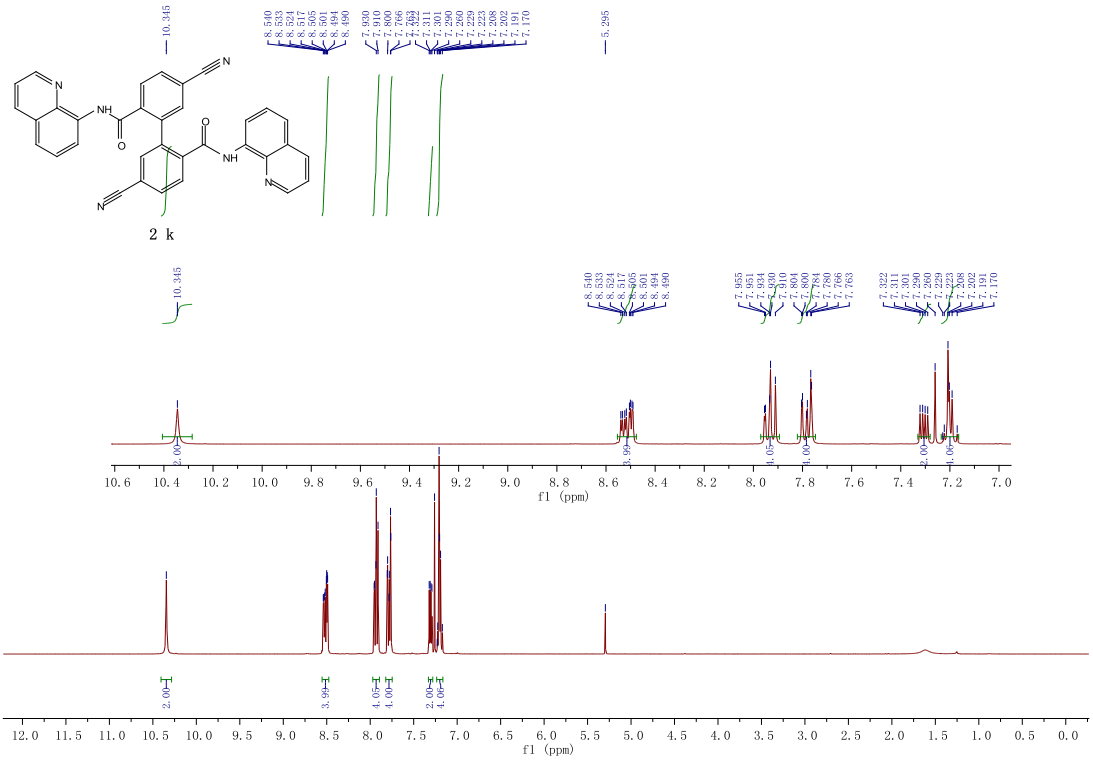
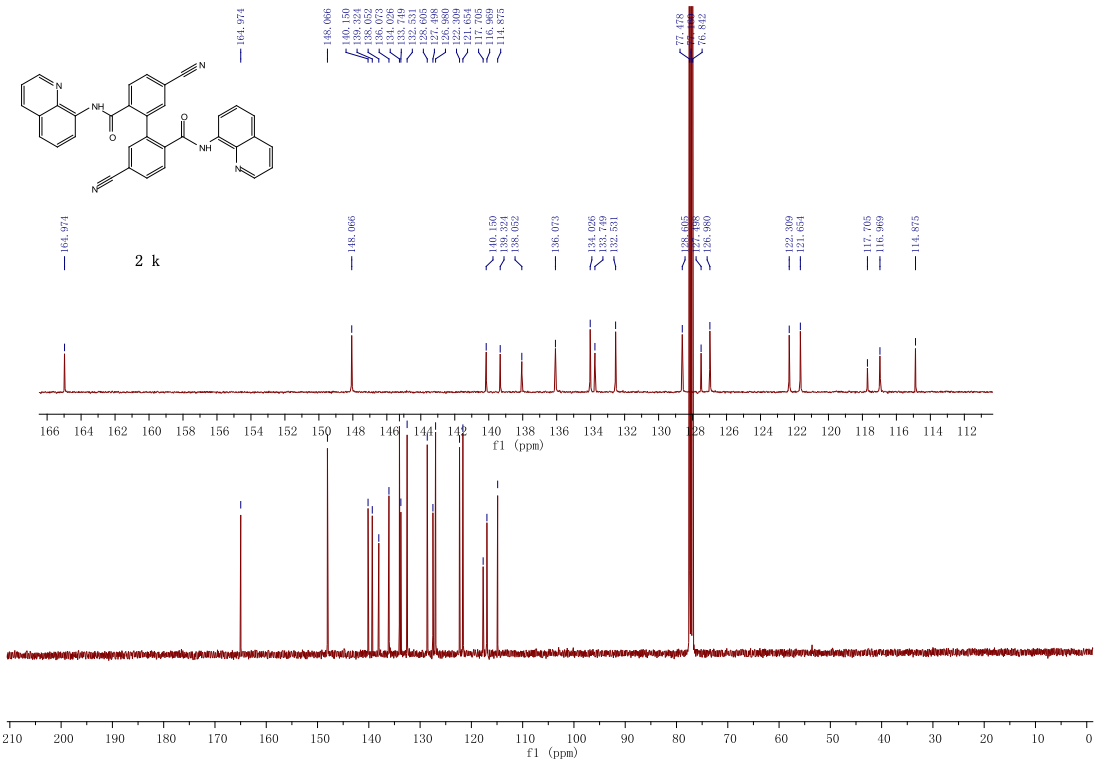
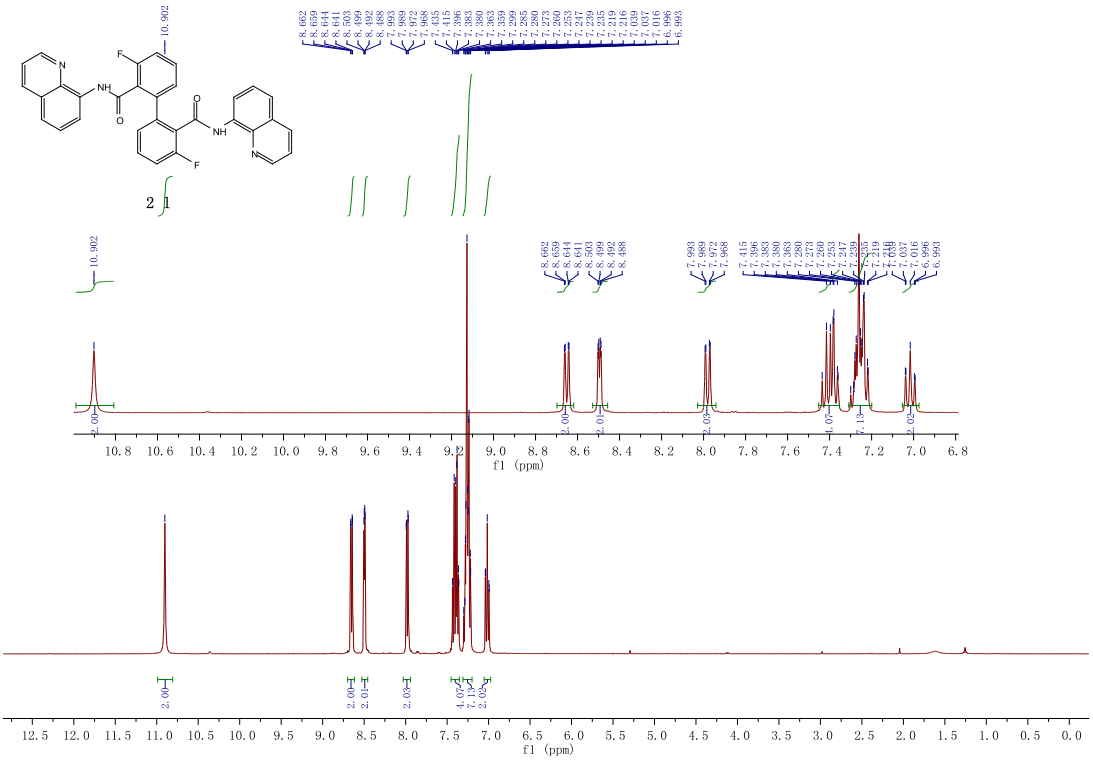
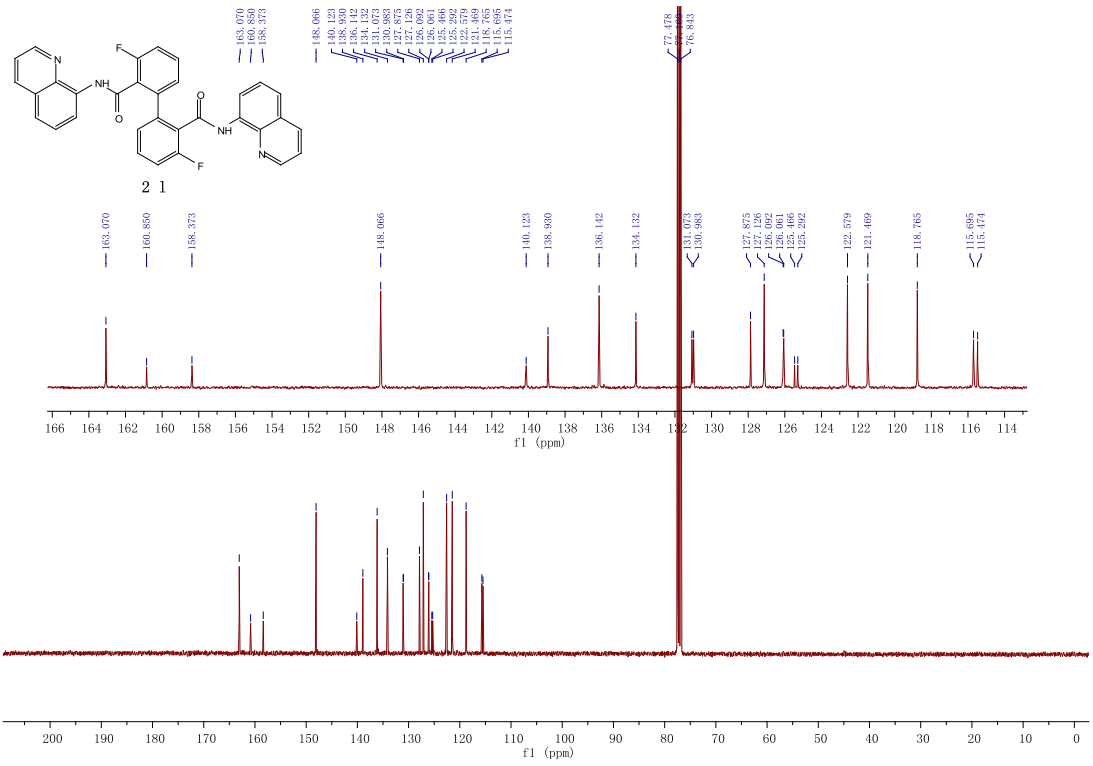
147.969
139.655
138.047
135.902
133.998
128.374
127.922
127.885
127.403
126.819
126.614
125.577
125.541
125.003
122.291
121.889
121.518
116.699
77.478
76.843
2 j
f1 (ppm)

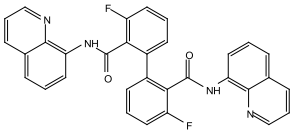

-61.285
2 j
f1 (ppm)


10.345
8.540
8.533
8.524
8.517
8.505
8.501
8.494
8.490
7.930
7.910
7.890
7.785
7.763
7.422
7.311
7.301
7.290
7.260
7.229
7.223
7.208
7.202
7.191
7.170
5.295
2 k
f1 (ppm)


164.974
148.066
140.150
139.324
138.052
136.073
134.026
133.749
132.531
128.605
127.498
126.980
122.309
121.654
117.705
116.969
114.875
77.478
77.162
76.842
2 k
f1 (ppm)

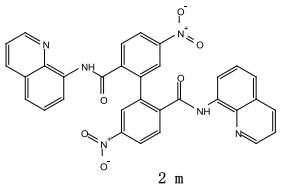

10.902
8.662
8.659
8.644
8.641
8.503
8.499
8.492
8.488
7.993
7.989
7.972
7.968
7.435
7.415
7.396
7.383
7.380
7.363
7.359
7.299
7.295
7.280
7.273
7.260
7.253
7.217
7.239
7.235
7.219
7.216
7.059
7.037
7.016
6.996
6.993
NH
O
F
N
2 1
f1 (ppm)


163.070
160.850
158.373
148.066
140.123
138.930
136.142
134.132
131.073
130.983
127.475
127.125
126.092
126.061
125.466
125.392
122.579
121.469
118.765
115.695
115.474
77.478
76.843
NH
O
F
N
2 1
f1 (ppm)



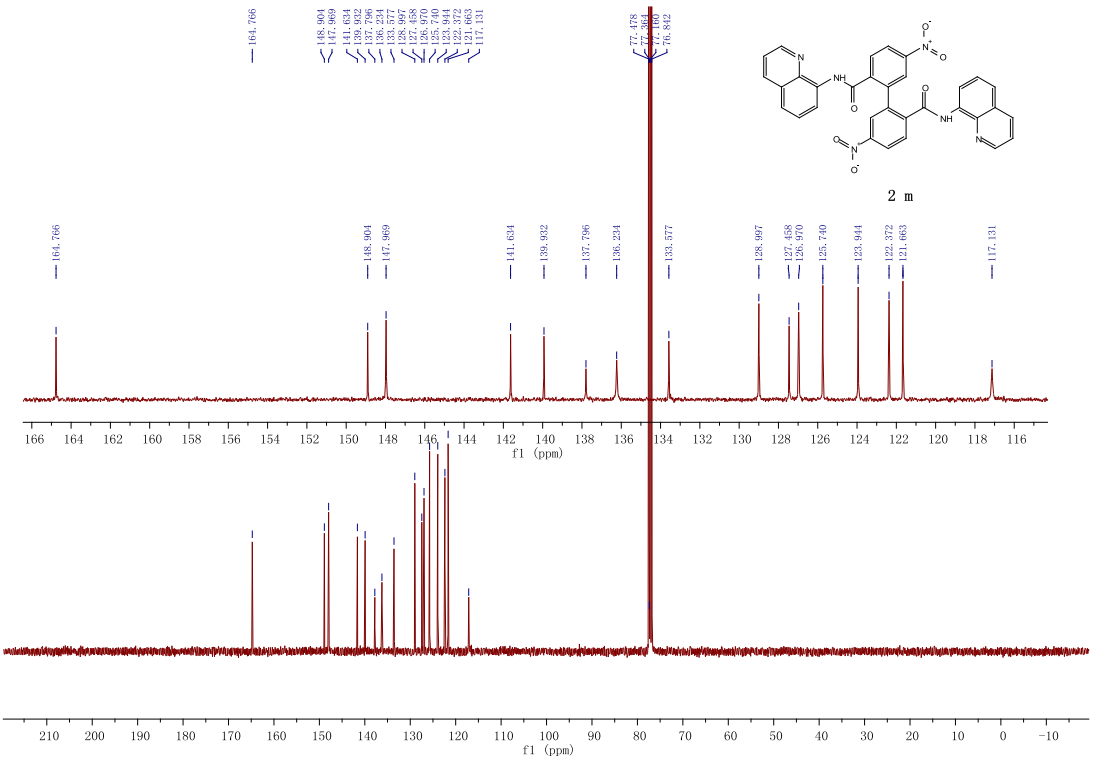
2 l

-115.245
-115.260
-115.271
-115.285
f1 (ppm)



2 m

10.416
8.518
8.513
8.501
8.494
8.489
8.483
8.479
8.395
8.391
8.385
8.380
8.365
8.359
8.015
7.994
7.929
7.327
7.317
7.307
7.286
7.260
7.198
7.193
7.177
7.173
7.156
7.136
f1 (ppm)


164.766
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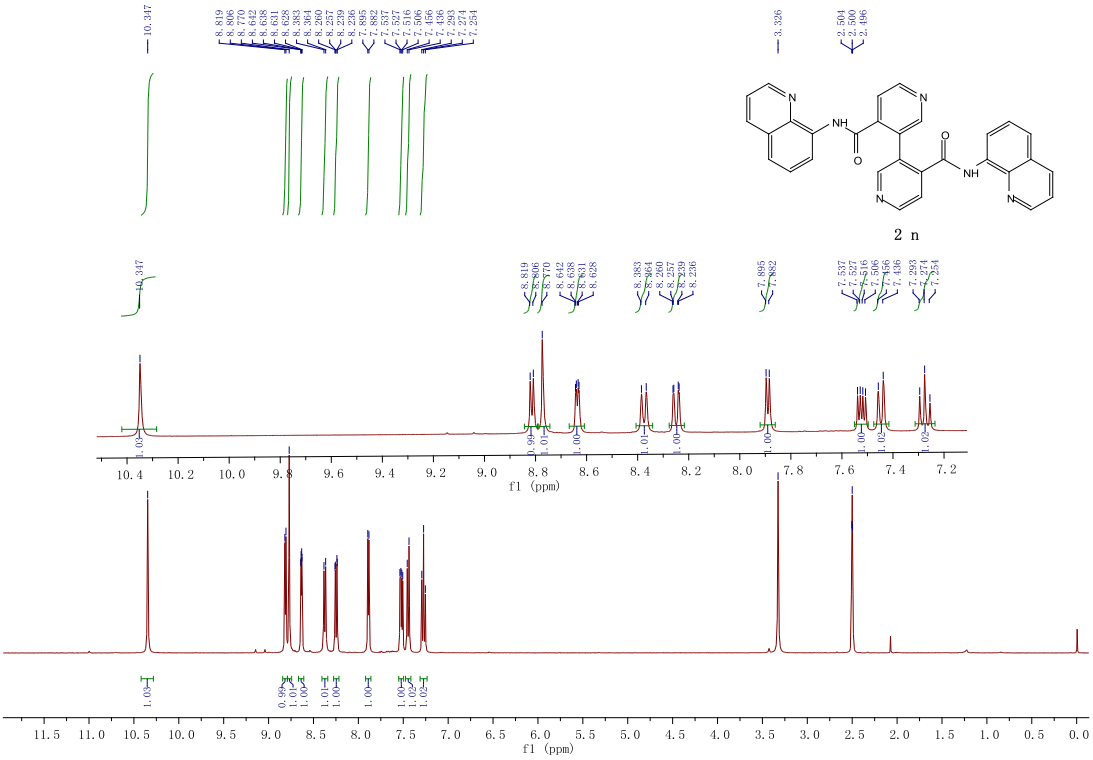
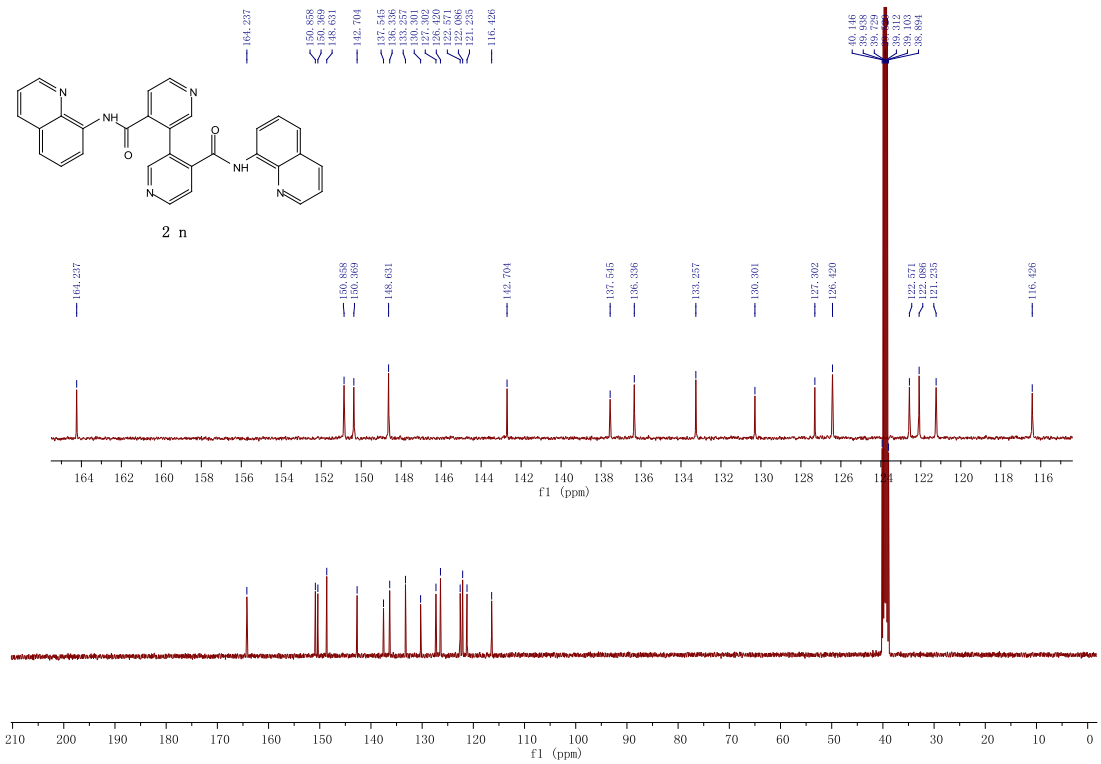
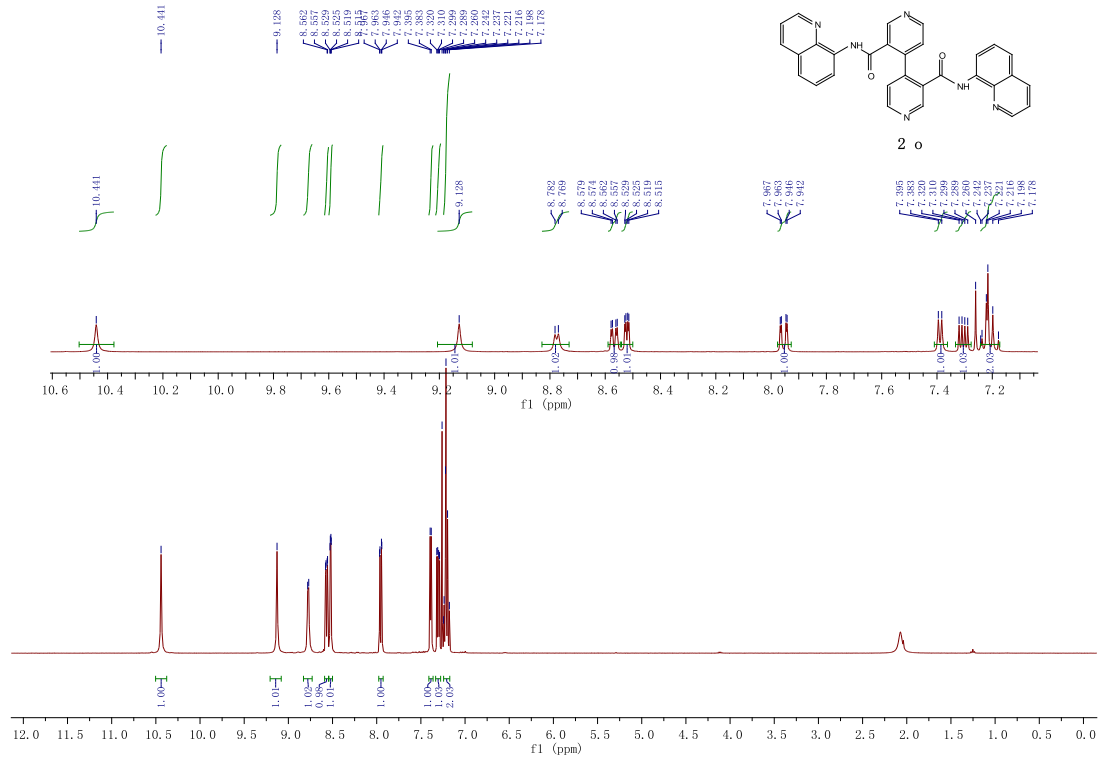
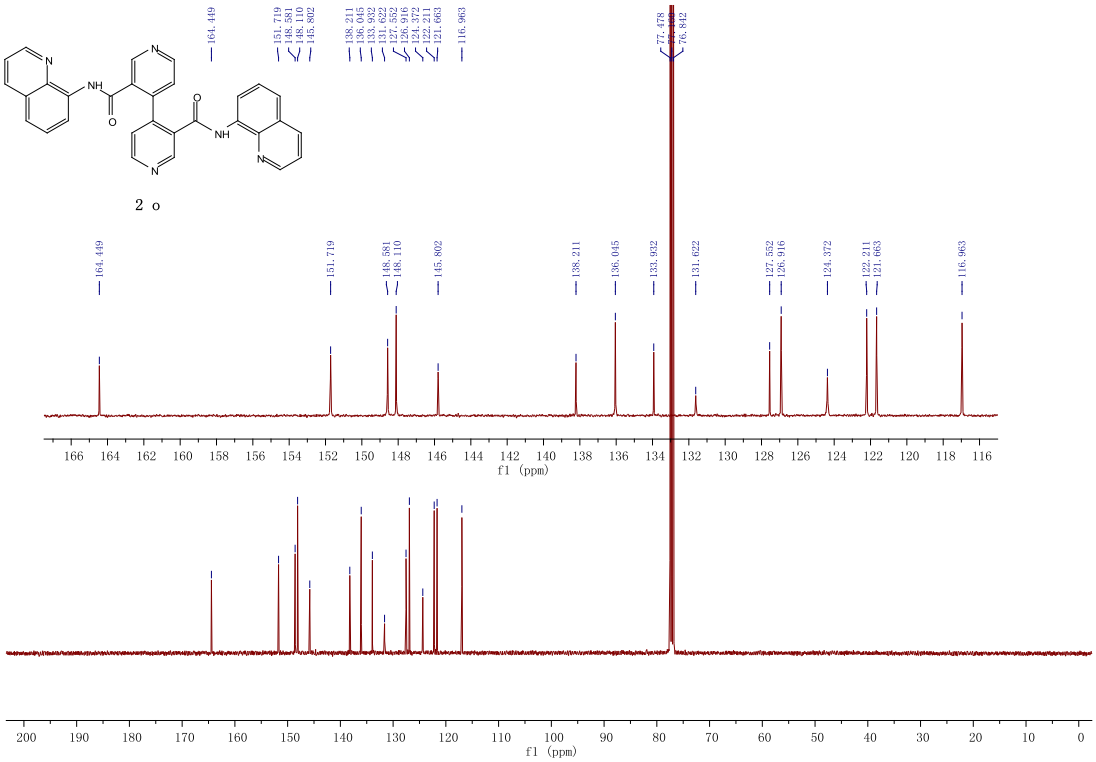
147.969
141.634
139.932
137.796
136.234
133.577
128.997
127.458
126.970
125.740
123.944
122.372
121.663
117.131
77.478
77.364
77.160
76.842
2 m
f1 (ppm)

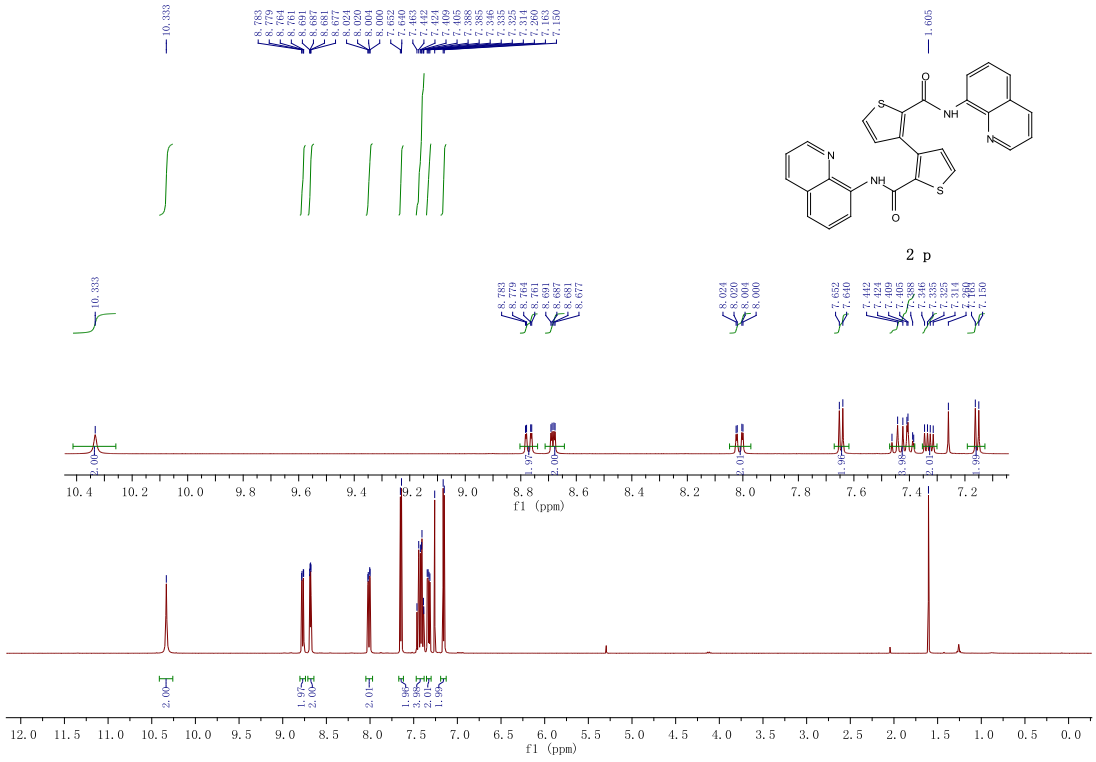

10.347
8.819
8.806
8.770
8.642
8.638
8.631
8.628
8.383
8.364
8.260
8.257
8.239
8.236
7.895
7.882
7.537
7.527
7.516
7.506
7.496
7.436
7.293
7.274
7.254
3.326
2.504
2.500
2.496
2 n
f1 (ppm)


2 n
f1 (ppm)

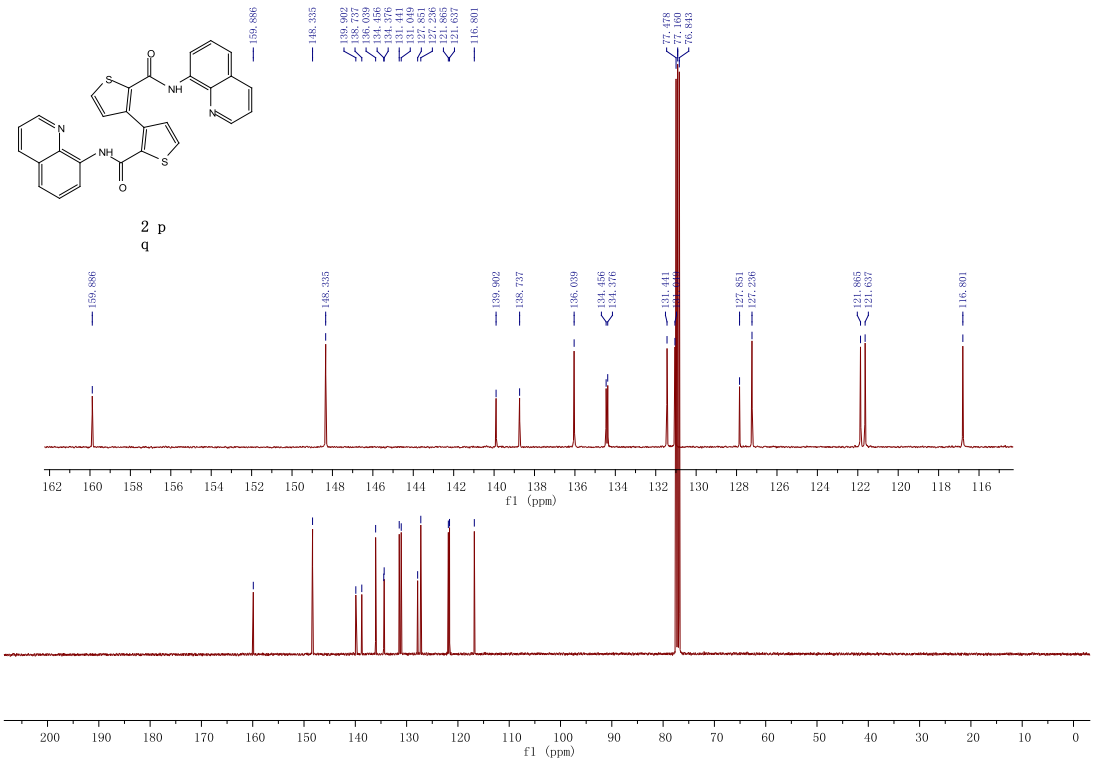

2 o
f1 (ppm)

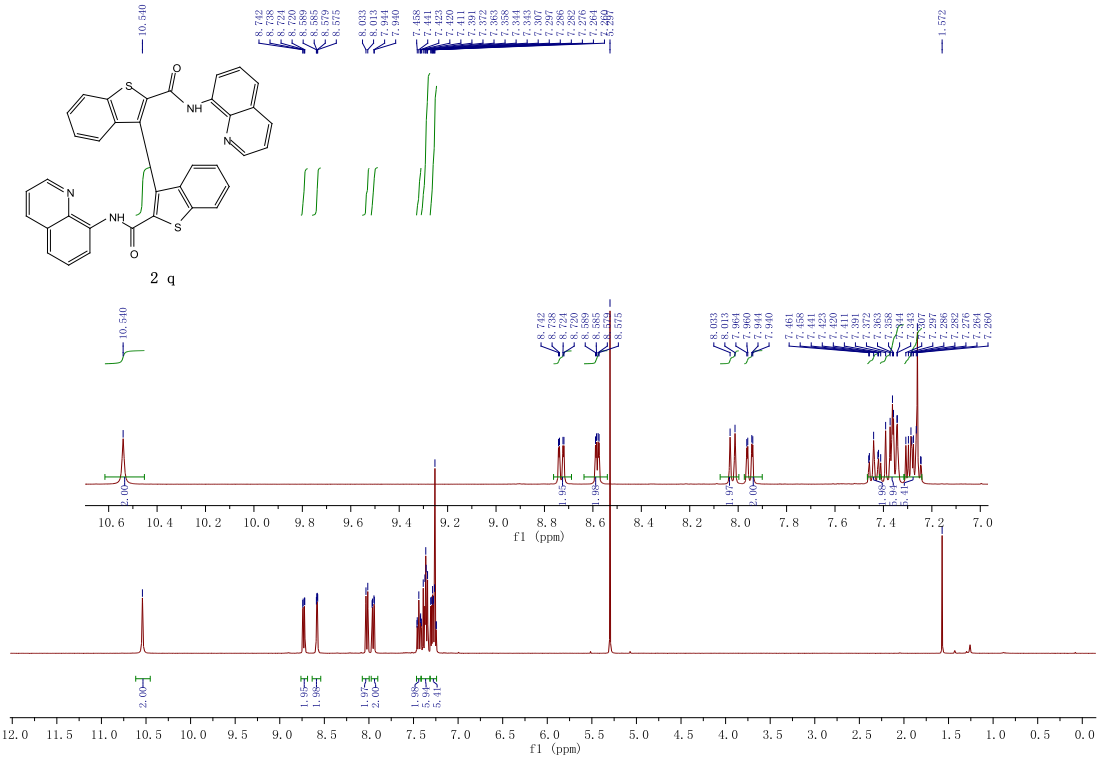


2 o



2 p


159.886
148.335
139.902
138.737
136.039
134.456
134.376
131.441
131.044
127.851
127.236
121.865
121.637
116.801
77.478
77.160
76.843
O
NH
S
N
2 p
q
f1 (ppm)


10.540
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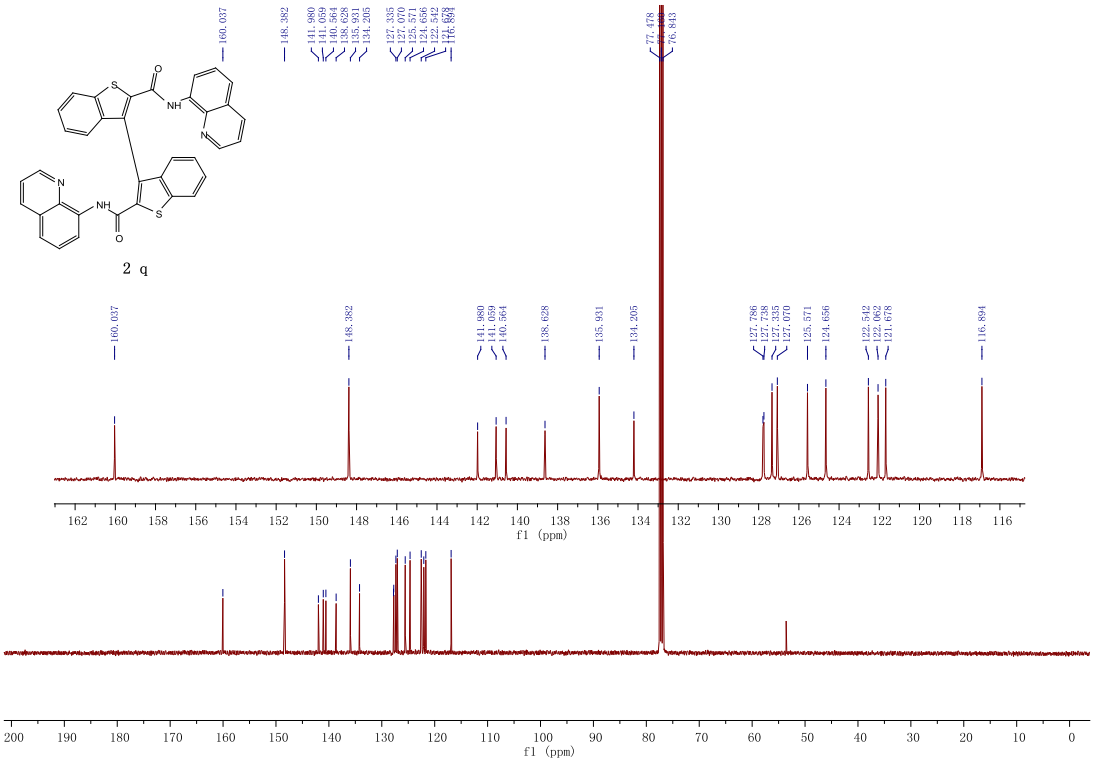
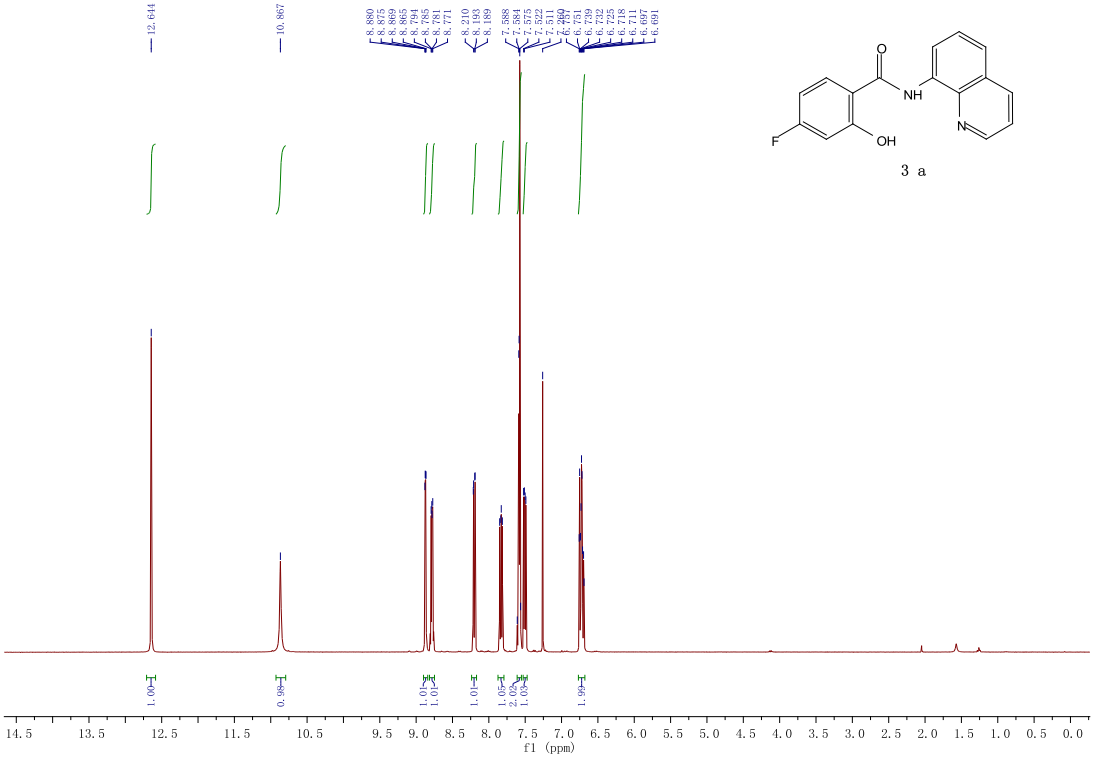
8.738
8.724
8.720
8.589
8.585
8.579
8.575
8.033
8.013
7.944
7.940
7.458
7.441
7.423
7.420
7.411
7.391
7.372
7.363
7.358
7.344
7.343
7.307
7.297
7.286
7.282
7.276
7.264
7.260
1.572
O
NH
S
N
2 q
f1 (ppm)


160.037
148.382
141.980
141.059
140.564
138.628
135.931
134.205
127.335
127.070
125.571
124.656
122.542
122.062
121.678
116.894
77.478
77.160
76.843
O
NH
S
N
f1 (ppm)

2 q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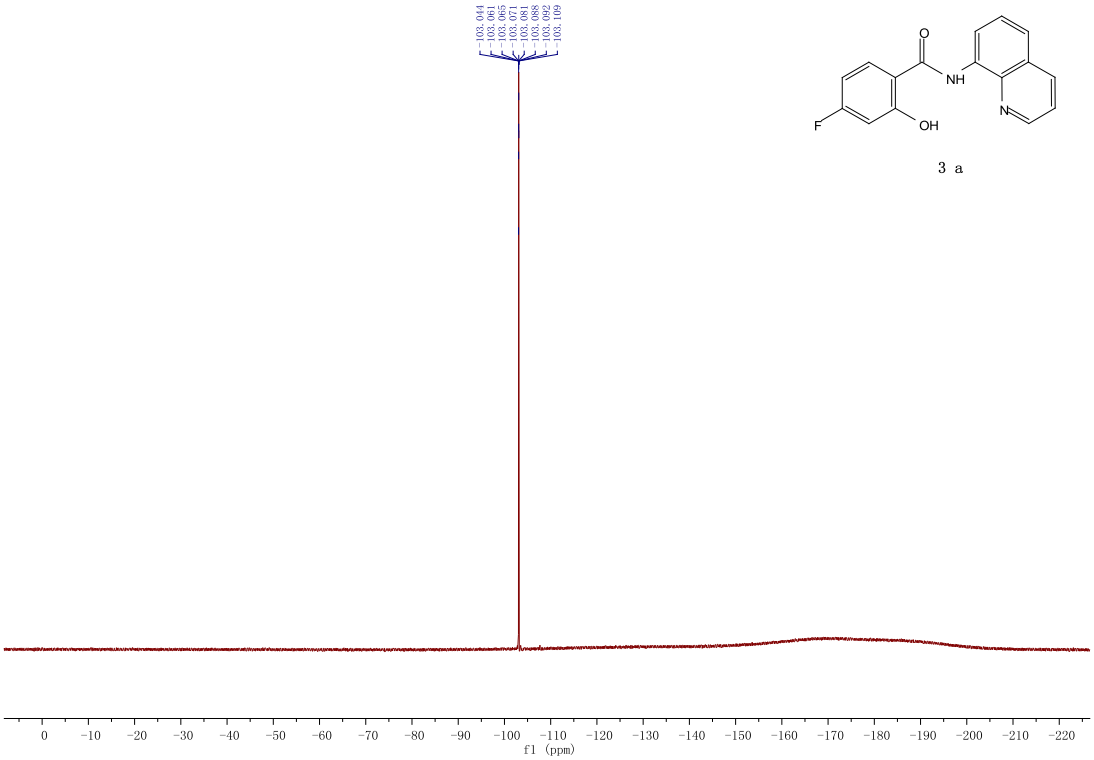
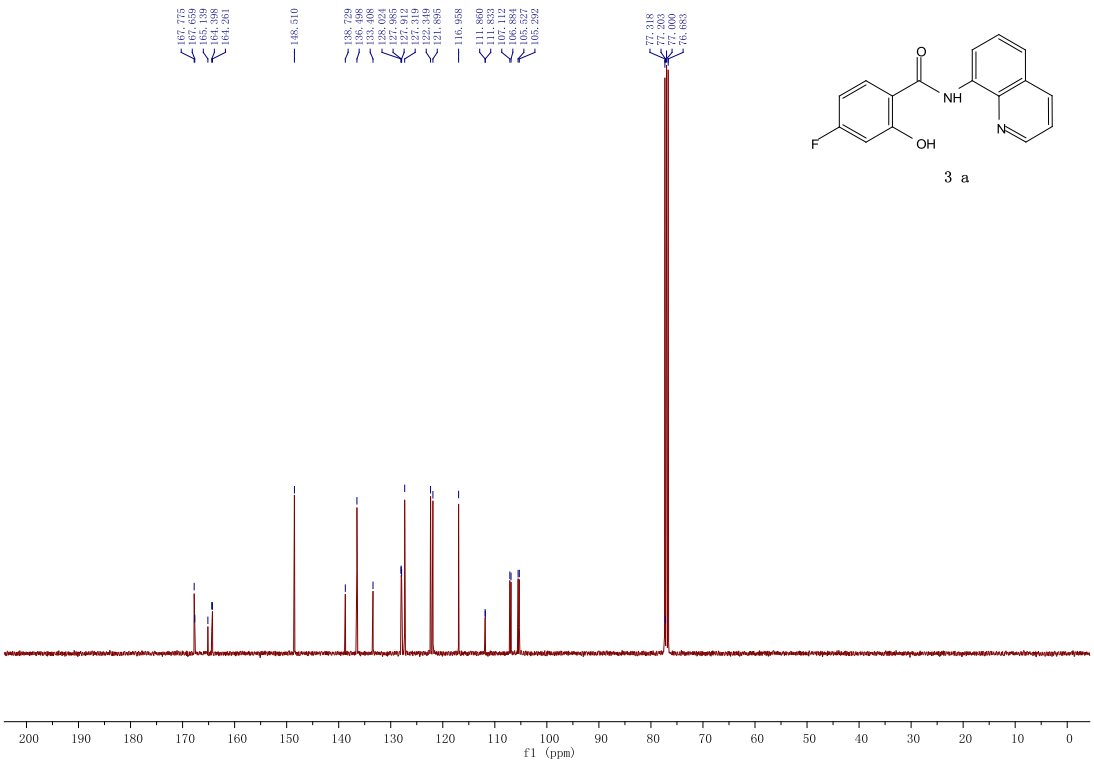
8.890
8.875
8.869
8.865
8.794
8.785
8.781
8.771
8.210
8.193
8.189
7.588
7.584
7.575
7.522
7.511
7.269
6.751
6.739
6.732
6.725
6.718
6.711
6.697
6.691
1.00
0.98
1.01
1.01
1.01
1.05
2.05
1.05
1.99
f1 (ppm)

O
NH
N
F
OH

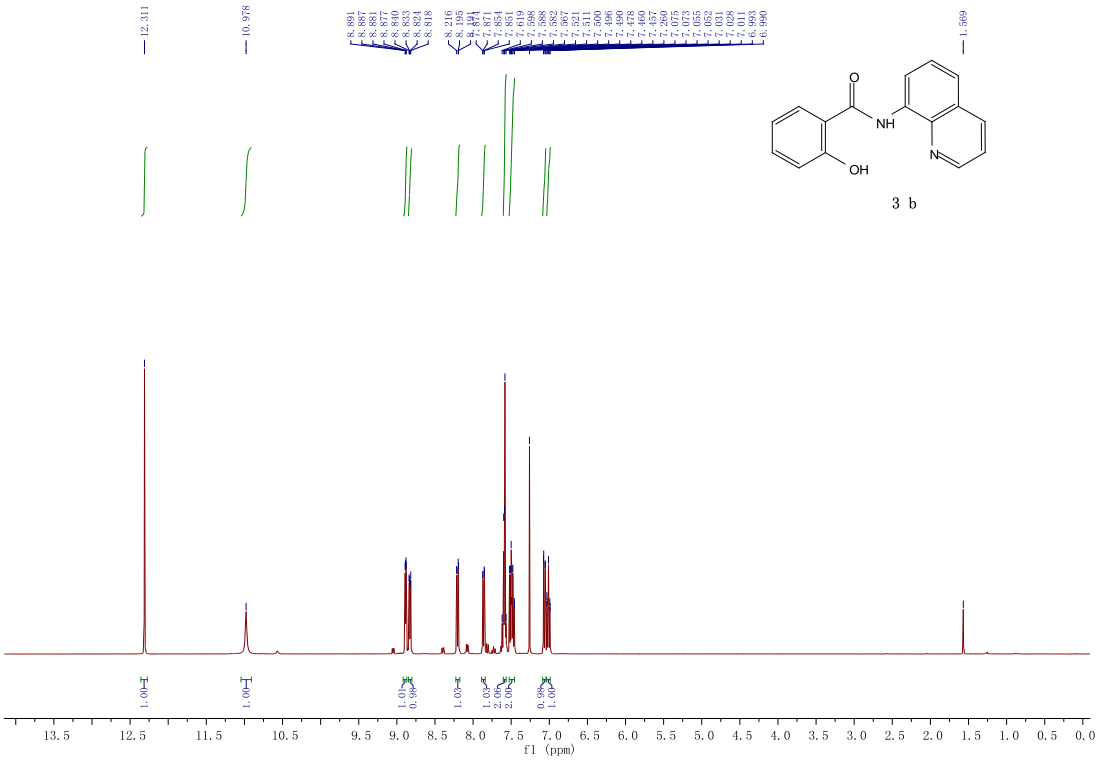
3 a


-103.044
-103.061
-103.065
-103.071
-103.084
-103.088
-103.092
-103.109
O
NH
N
F
OH
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

3 a


167.775
167.659
165.139
164.398
164.261
148.510
138.729
138.498
133.406
132.024
127.985
127.912
127.319
122.349
121.895
116.958
111.860
111.833
107.112
106.884
105.527
105.292
77.318
77.203
77.000
76.683
O
NH
N
F
OH
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3 a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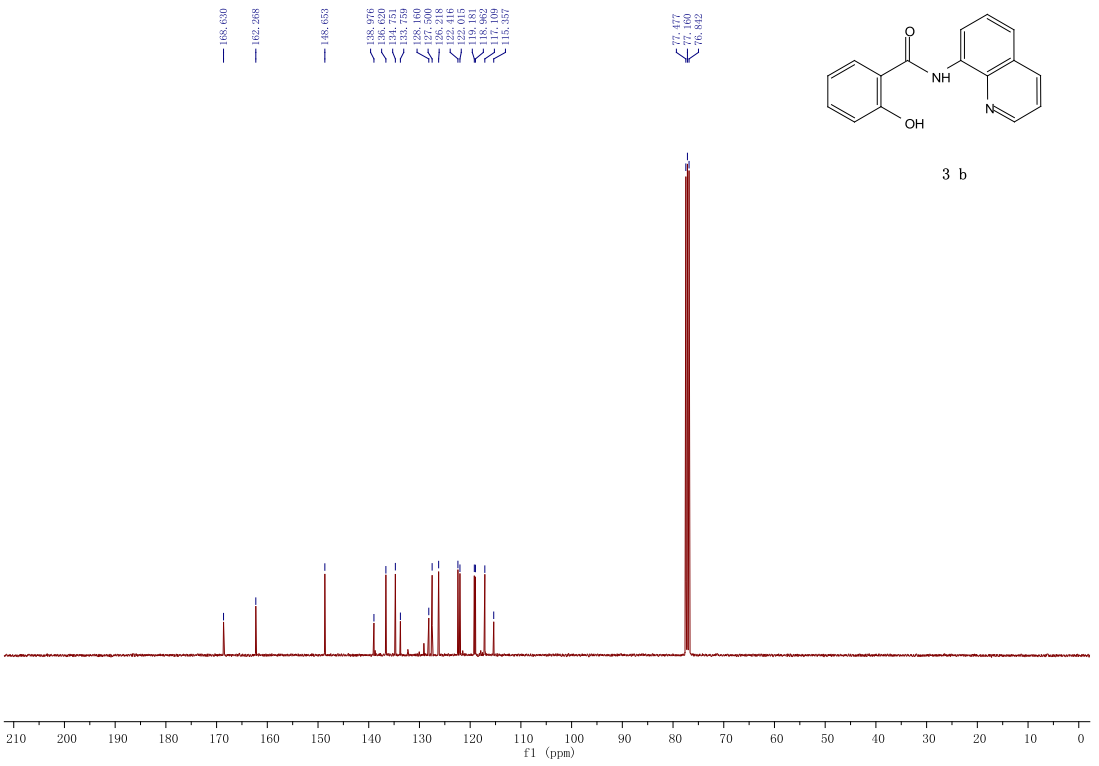
8.881
8.877
8.840
8.833
8.824
8.818
8.216
8.195
8.191
8.187
7.871
7.854
7.851
7.619
7.598
7.588
7.582
7.567
7.521
7.511
7.500
7.496
7.494
7.478
7.460
7.457
7.090
7.075
7.073
7.055
7.052
7.031
7.011
7.028
7.011
6.993
6.990
1.569
O
NH
OH
N
3 b
1.00
1.00
1.01
0.99
1.03
1.02
2.06
2.00
0.98
1.00
13.5
12.5
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)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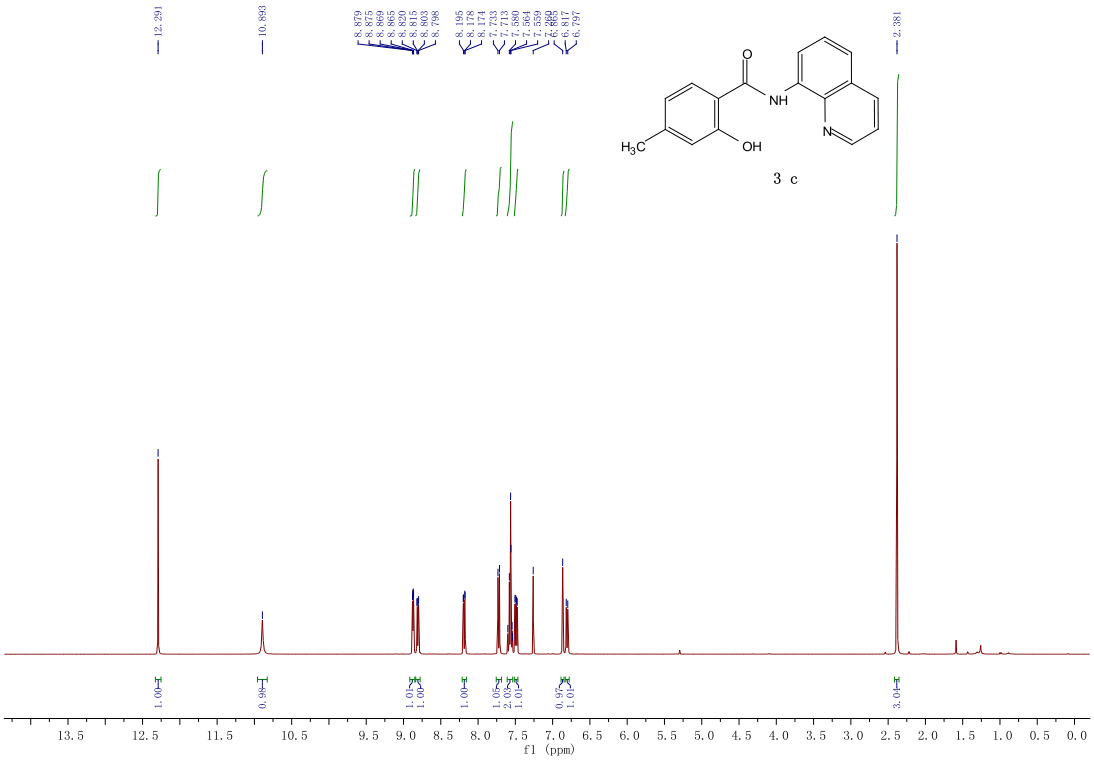
162.268
148.653
138.976
136.620
134.751
133.759
128.160
127.500
126.218
122.416
122.015
119.181
118.962
117.104
115.357
77.477
77.160
76.842
O
NH
OH
N
3 b
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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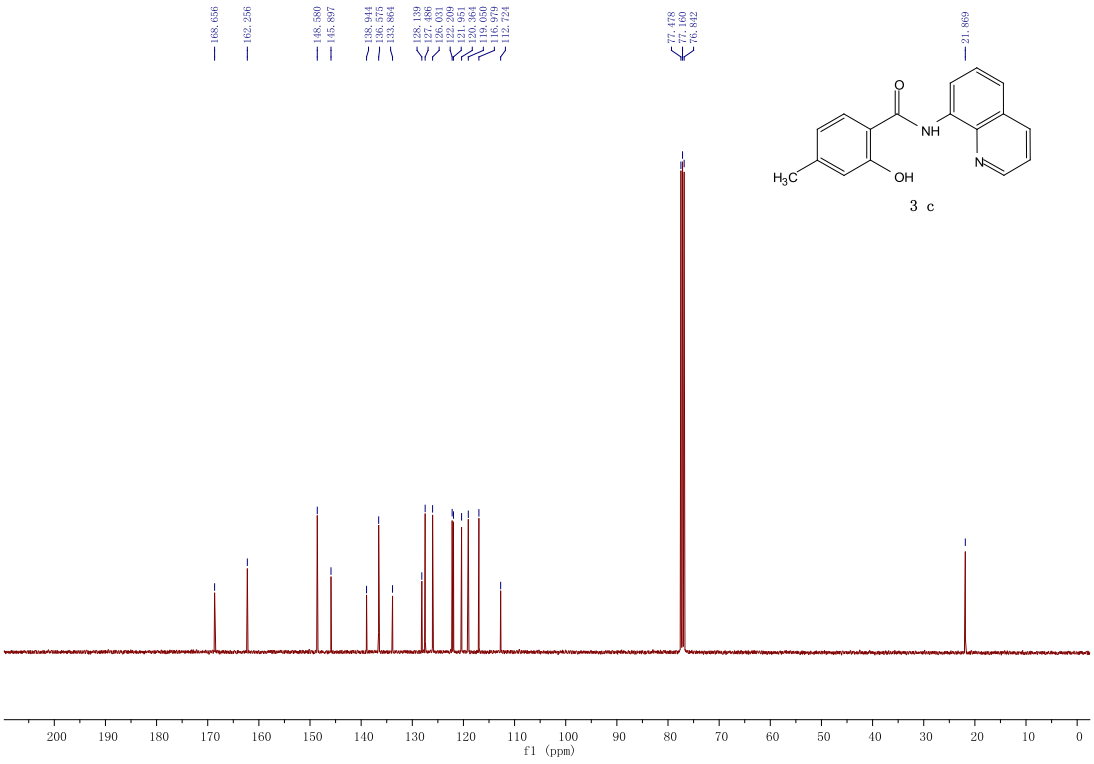
8.875
8.869
8.865
8.820
8.815
8.803
8.798
8.195
8.178
8.174
7.733
7.713
7.680
7.564
7.559
7.269
6.817
6.797
2.381
O
NH
N
H3C
OH
3 c
1.00
0.98
1.01
1.00
1.00
1.05
2.03
1.01
0.97
1.01
3.04
f1 (ppm)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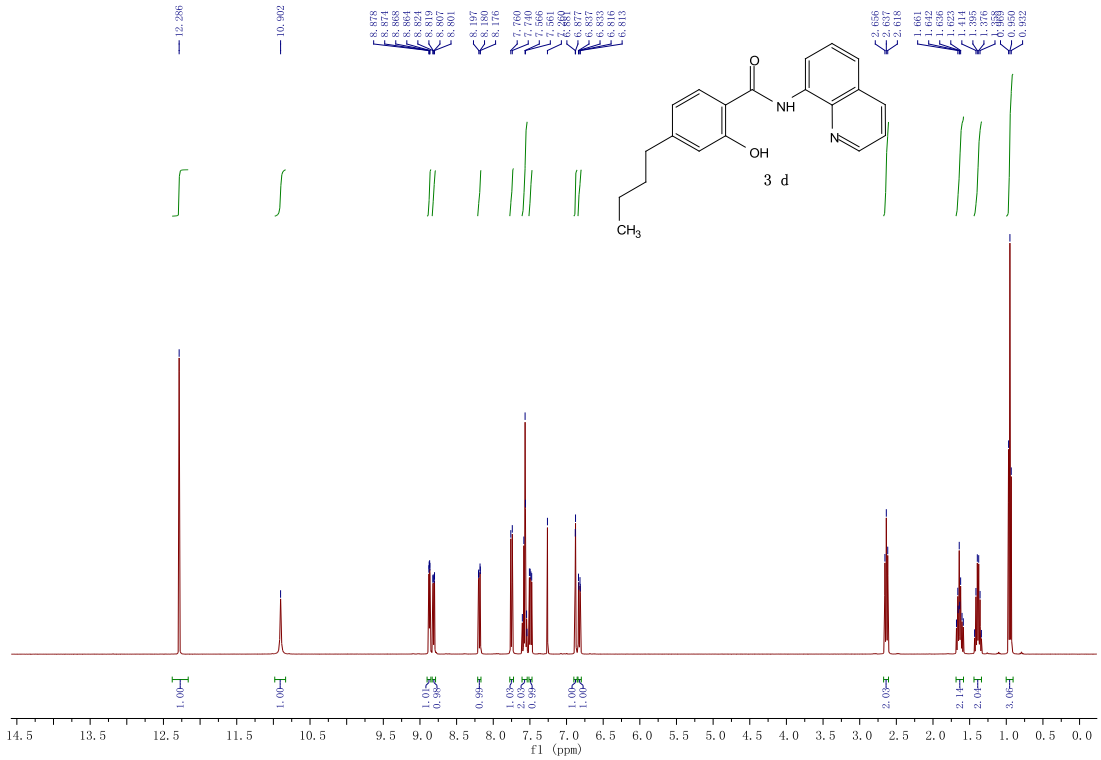
145.897
138.944
136.575
133.864
128.139
127.486
126.071
122.209
121.951
120.364
119.050
116.979
112.724
77.478
77.160
76.842
21.869
O
NH
N
H3C
OH
3 c
f1 (ppm)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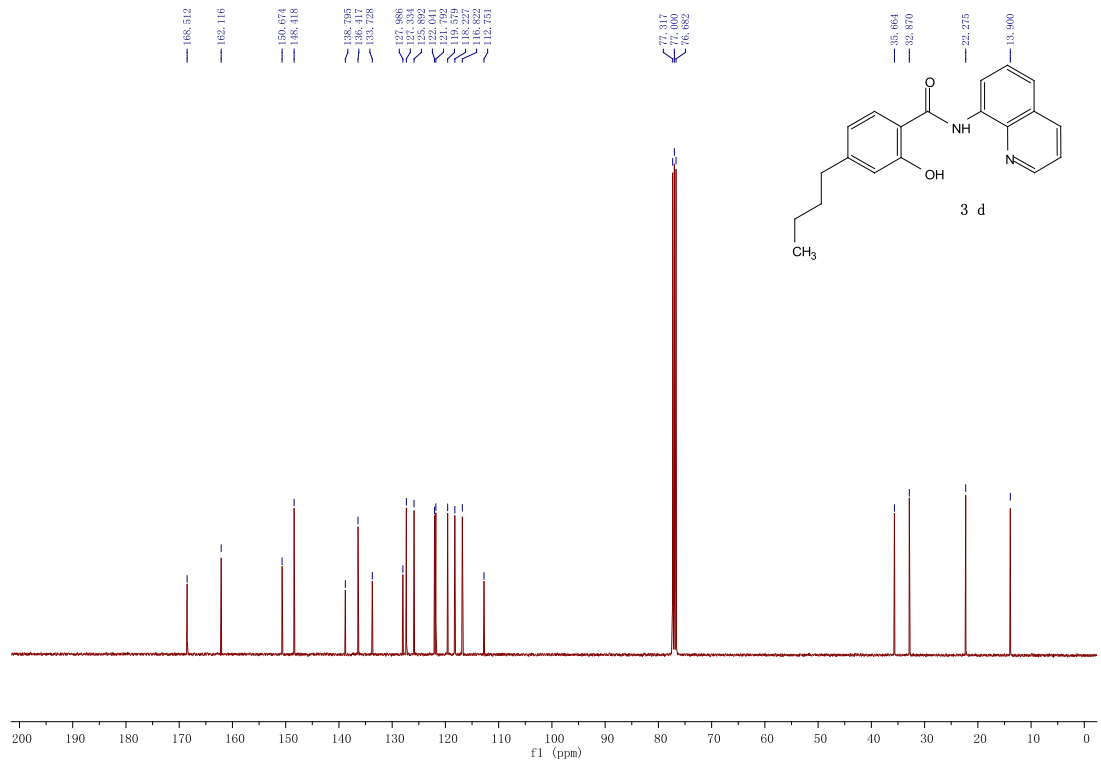
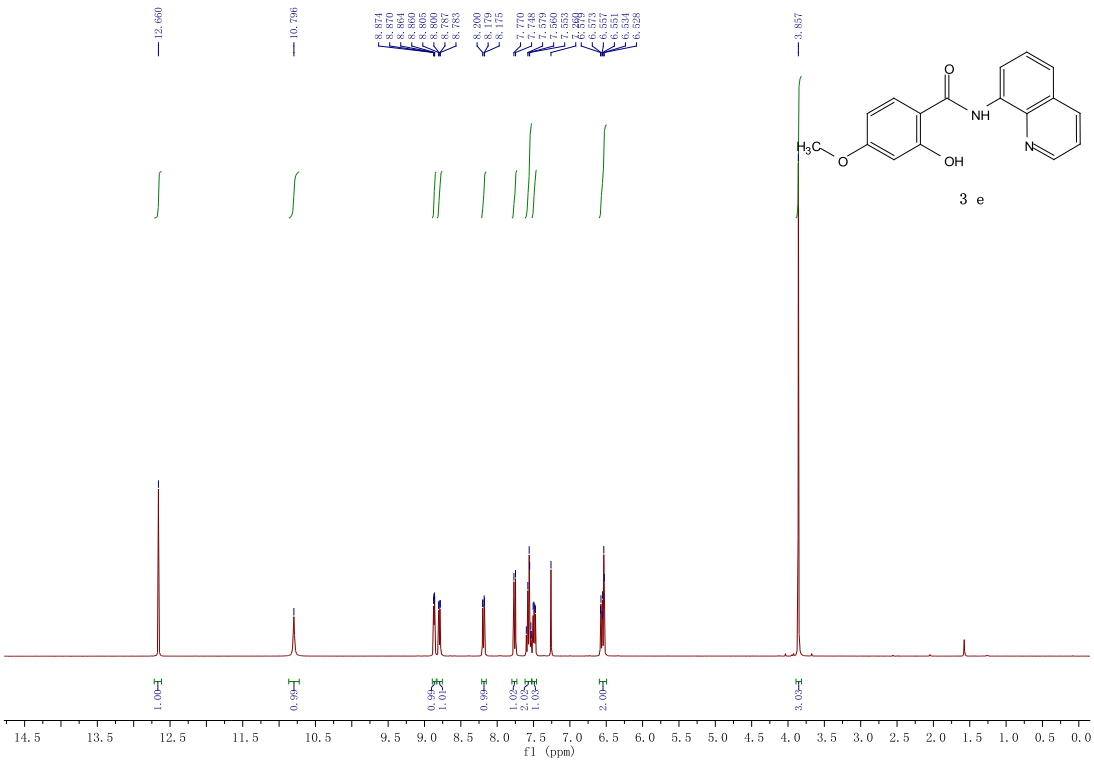
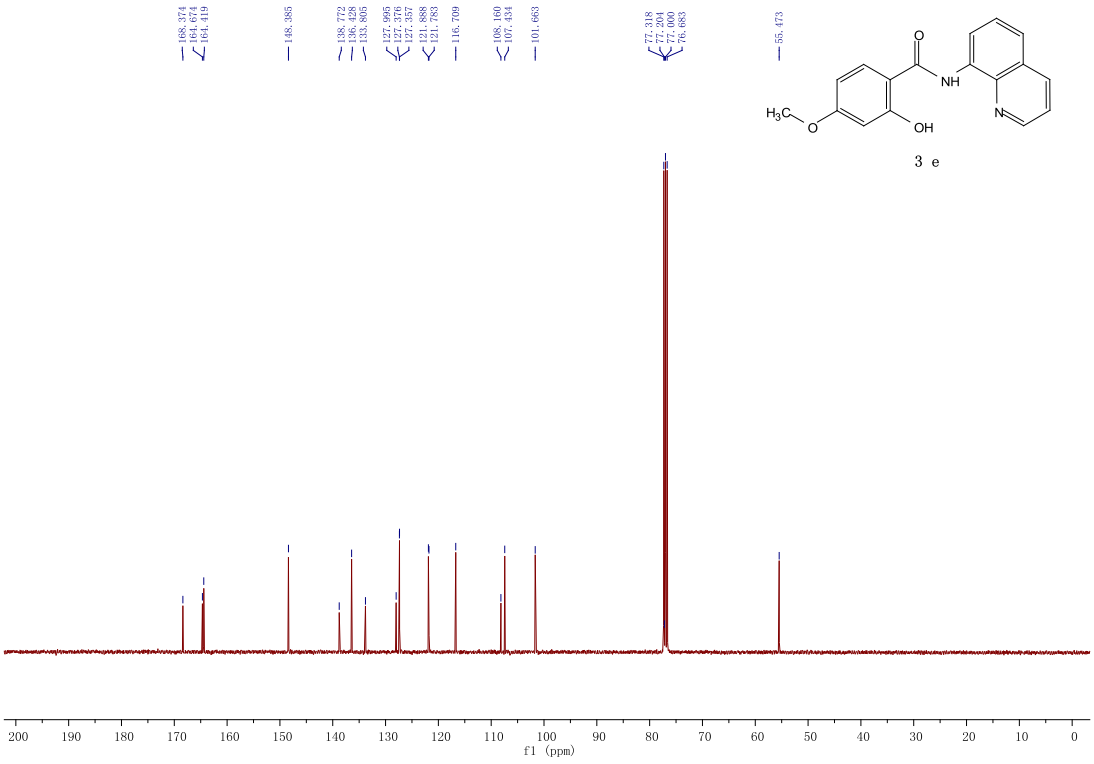
10.962
8.878
8.874
8.868
8.854
8.834
8.819
8.807
8.801
8.197
8.180
8.176
7.760
7.740
7.566
7.561
6.877
6.837
6.833
6.816
6.813
2.656
2.637
2.618
1.661
1.642
1.636
1.623
1.414
1.395
1.376
0.950
0.932
O
NH
N
OH
CH3
3 d
1.00
1.00
1.01
0.98
0.99
1.03
2.03
0.99
1.00
1.00
2.03
2.14
2.04
3.06
f1 (ppm)


168.512
162.116
150.674
148.418
138.795
136.417
133.728
127.986
127.334
125.892
122.041
121.792
119.579
118.227
116.822
112.751
77.317
77.000
76.682
35.664
32.870
22.275
13.900
O
NH
N
OH
CH3
3 d
f1 (ppm)


12.660
10.796
8.874
8.870
8.864
8.860
8.805
8.800
8.787
8.783
8.200
8.179
8.175
7.770
7.748
7.579
7.560
7.553
7.266
6.573
6.557
6.551
6.534
6.528
3.857
1.00
0.99
0.99
1.01
0.99
1.02
2.02
1.08
2.00
3.03
f1 (ppm)

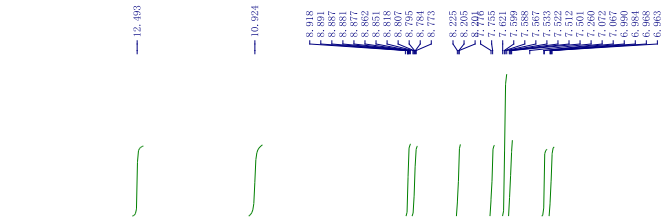
O
NH
H3C
O
OH
N

3 e


168.374
164.674
164.419
148.385
138.772
136.428
133.805
127.995
127.376
127.357
121.888
121.783
116.709
108.160
107.494
101.663
77.318
77.204
77.000
76.683
55.473
f1 (ppm)

O
NH
H3C
O
OH
N

3 e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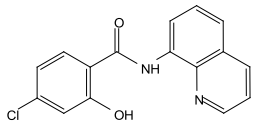
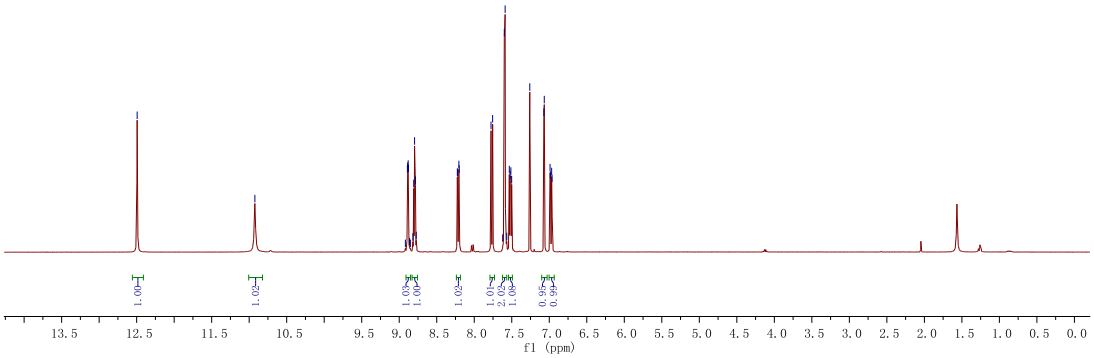
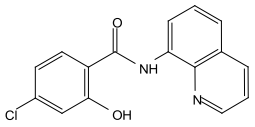
10.924
8.918
8.891
8.887
8.871
8.857
8.862
8.851
8.818
8.807
8.795
8.784
8.773
8.225
8.205
8.174
7.735
7.621
7.599
7.588
7.567
7.533
7.522
7.512
7.501
7.290
7.072
7.067
6.990
6.984
6.968
6.963


O
NH
N
Cl
OH

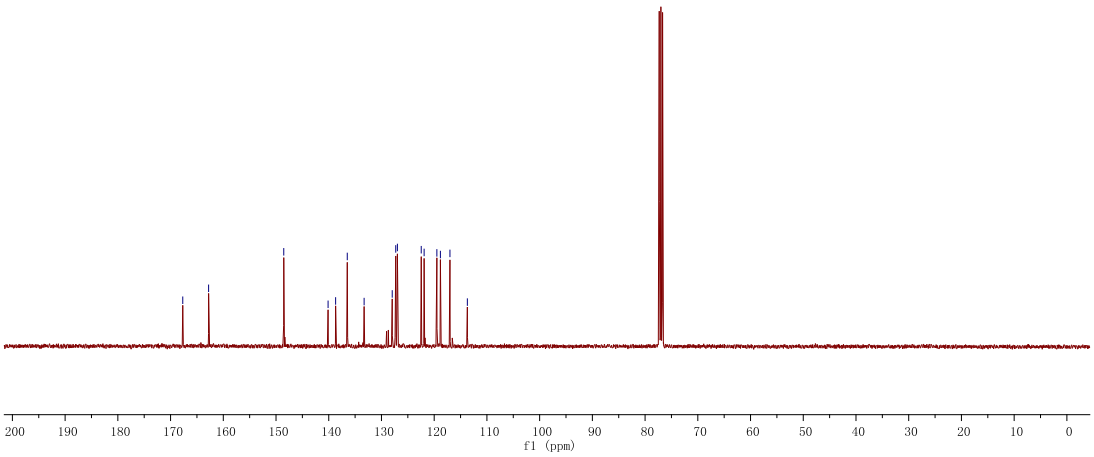
3 f

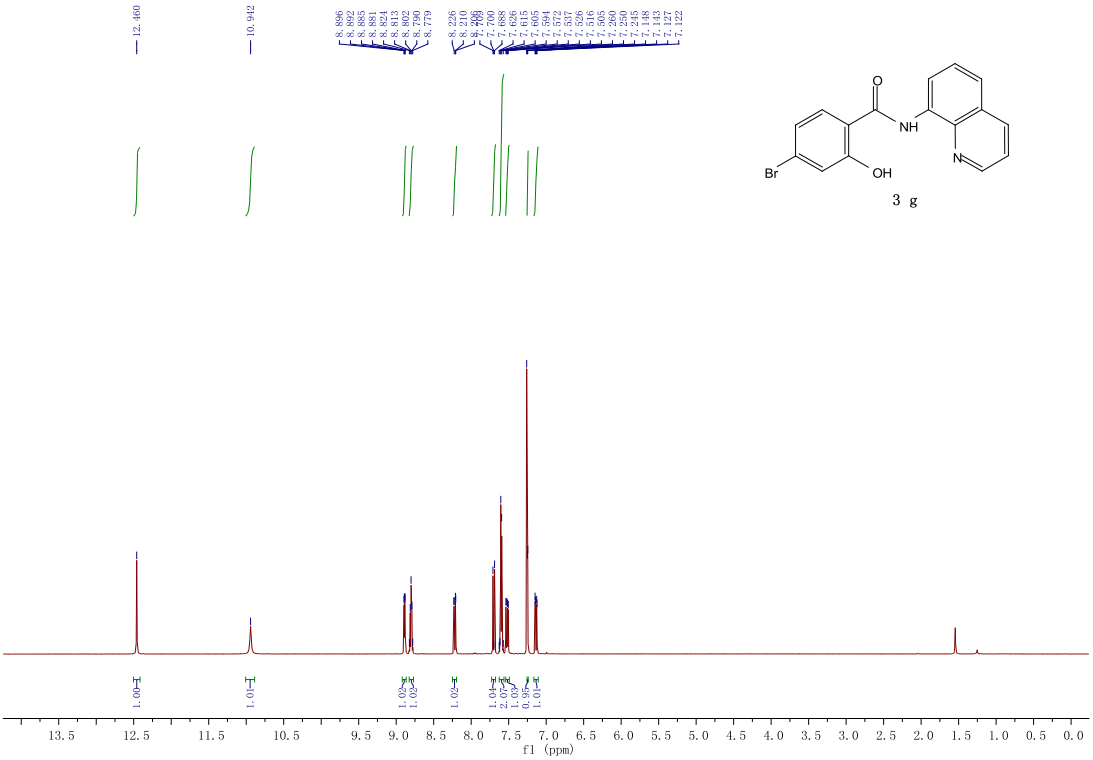

1.06
1.02
1.03
1.06
1.02
1.01
2.02
1.08
0.95
0.99
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

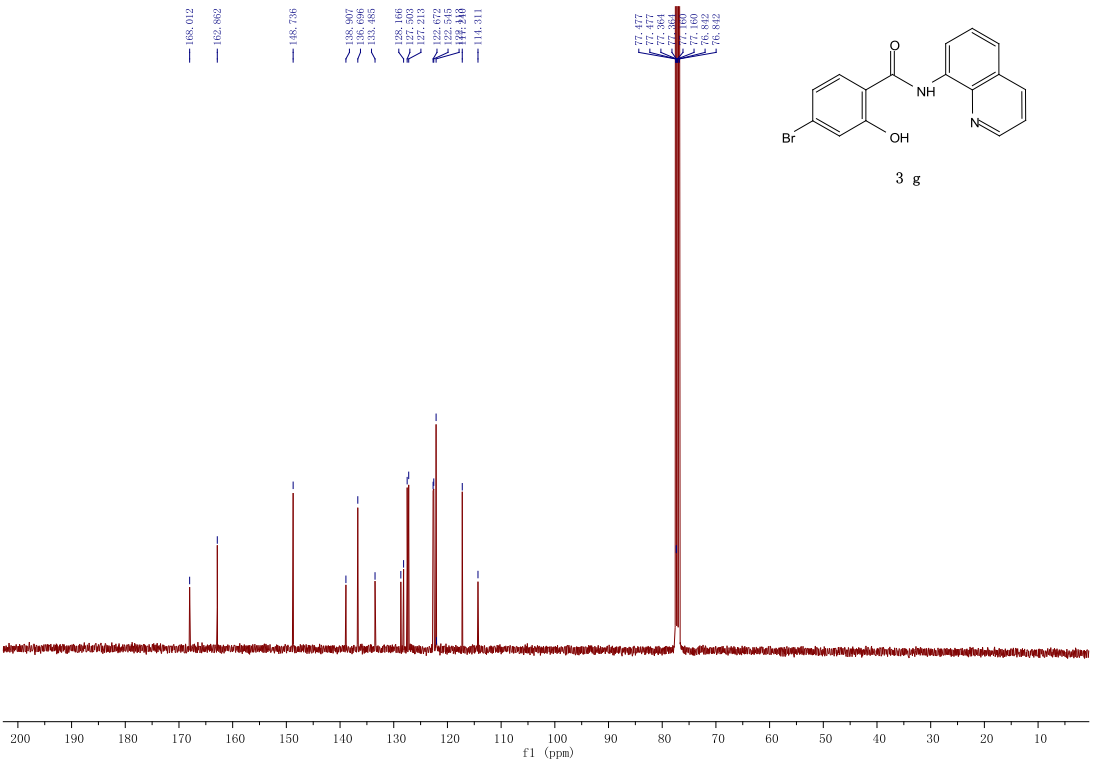

167.687
162.785
148.530
140.125
138.693
136.485
133.291
127.961
127.291
126.978
122.457
121.907
119.401
118.821
117.011
113.709

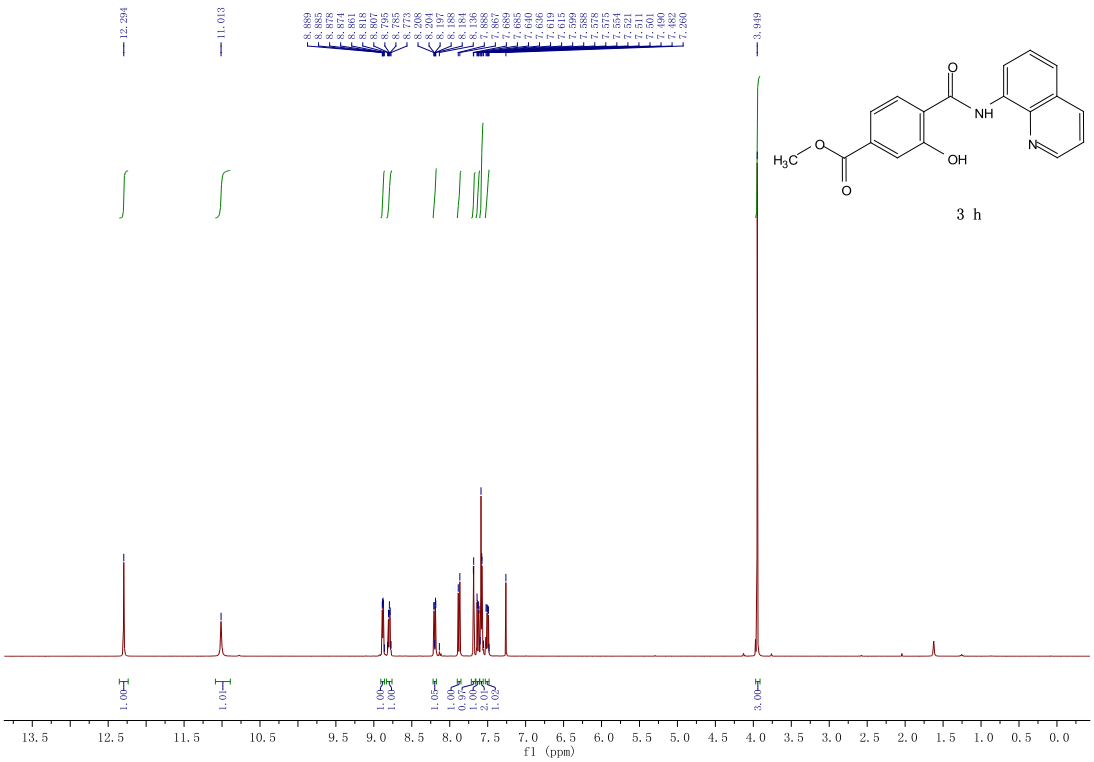

O
NH
N
Cl
OH

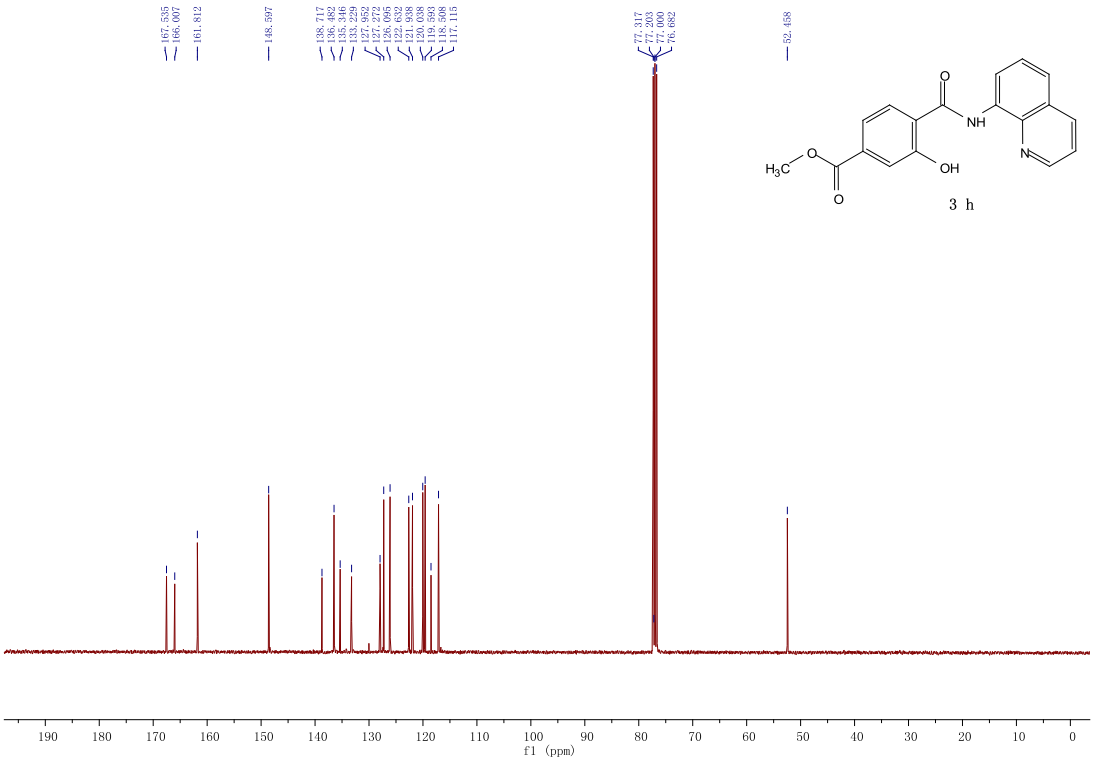
3 f

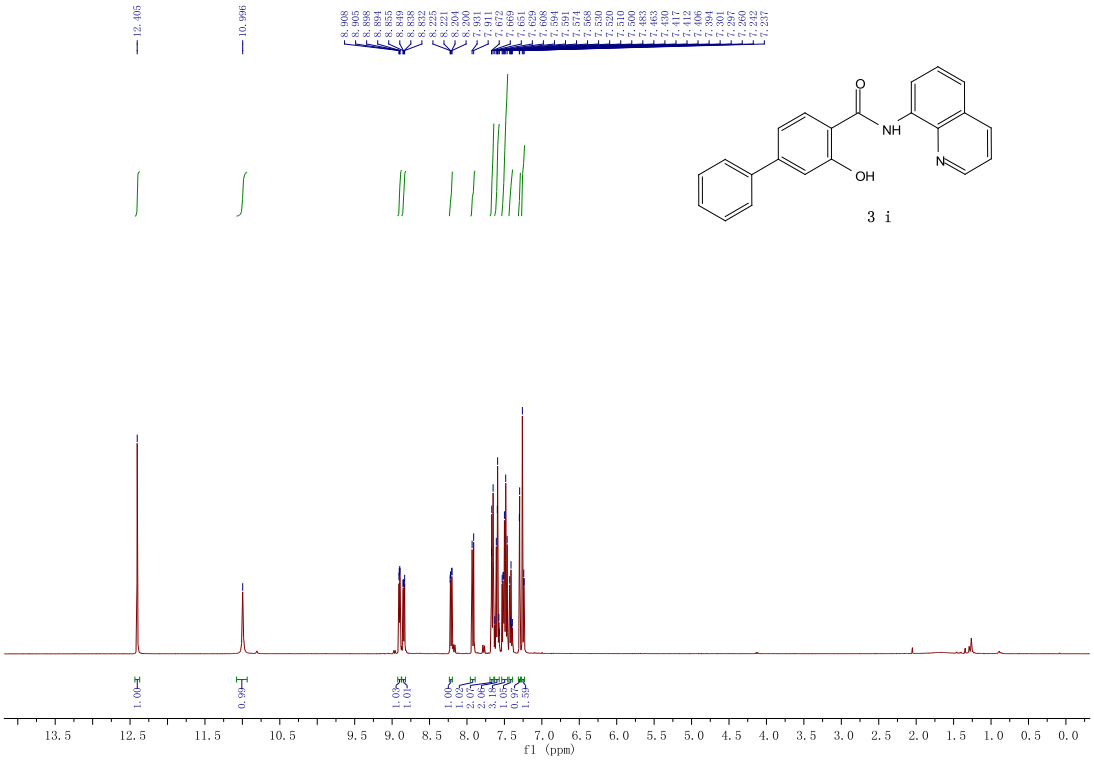

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

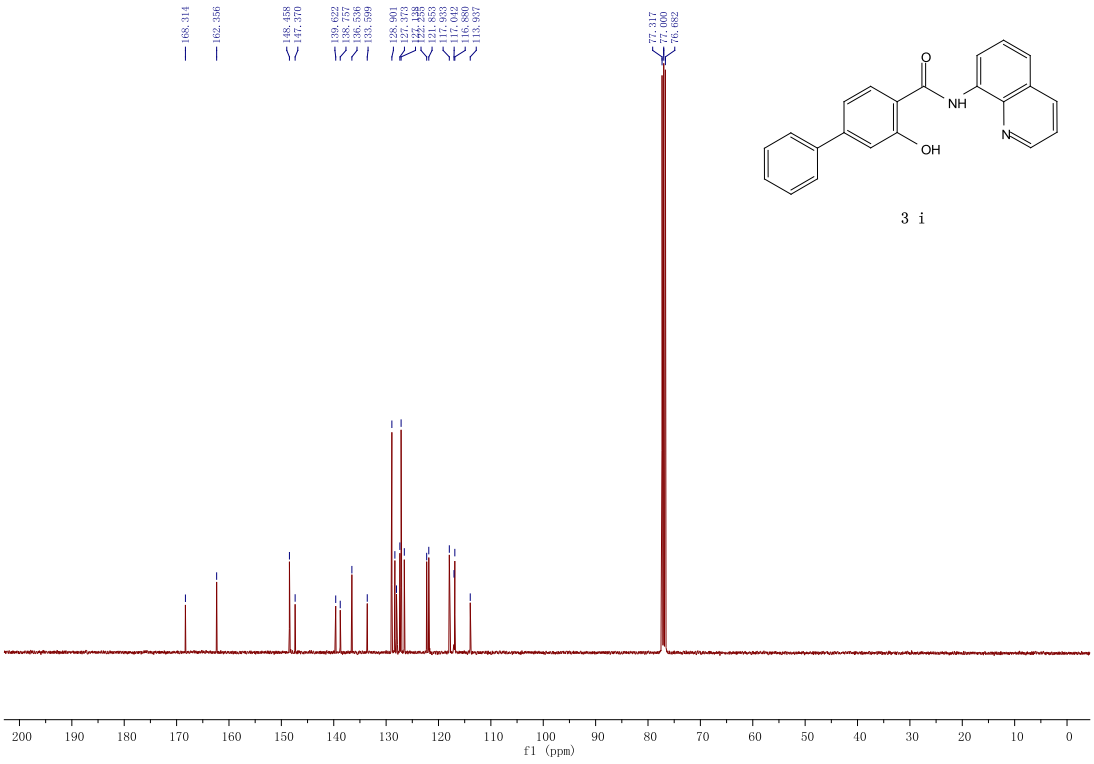

12.460
10.942
8.896
8.892
8.885
8.881
8.824
8.813
8.802
8.790
8.779
8.236
8.210
7.700
7.688
7.626
7.615
7.605
7.594
7.572
7.537
7.526
7.516
7.505
7.260
7.250
7.245
7.148
7.143
7.127
7.122
O
NH
Br
OH
N
3 g
1.00
1.01
1.02
1.02
1.02
1.04
2.07
1.03
0.95
1.04
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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)

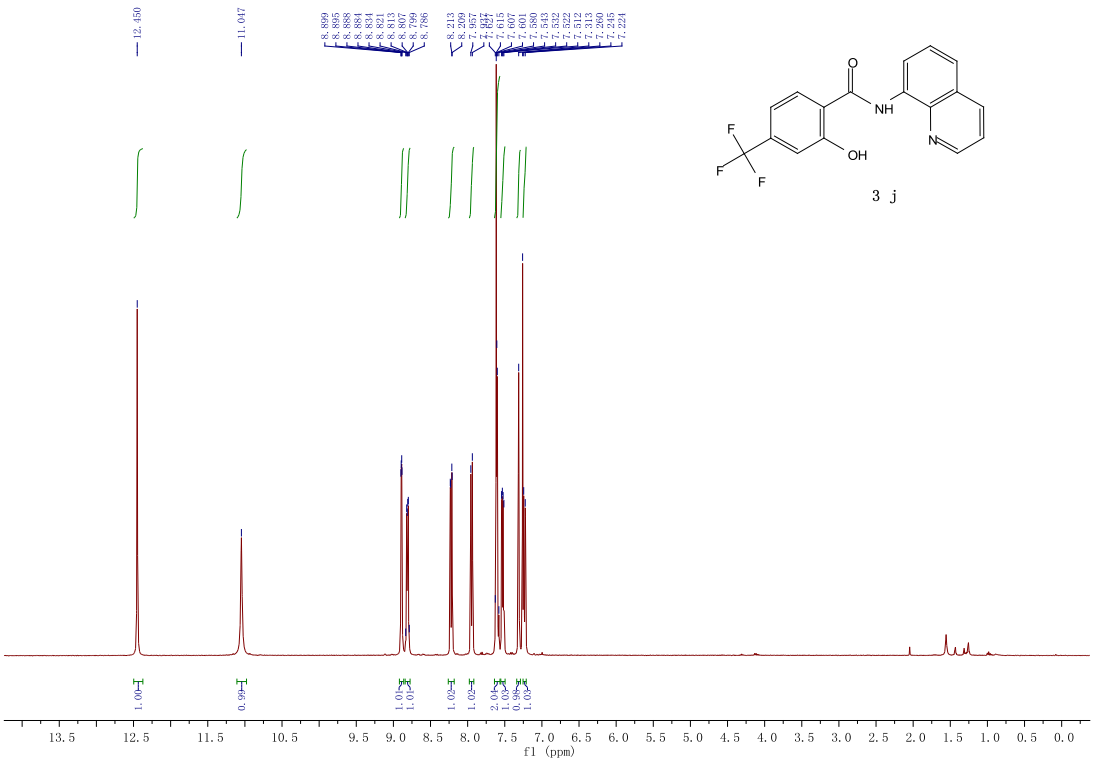

168.012
162.862
148.736
138.907
136.696
133.485
128.166
127.503
127.213
122.672
122.545
114.311
77.477
77.477
77.164
77.000
76.842
76.842
76.842
O
NH
Br
OH
N
3 g
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

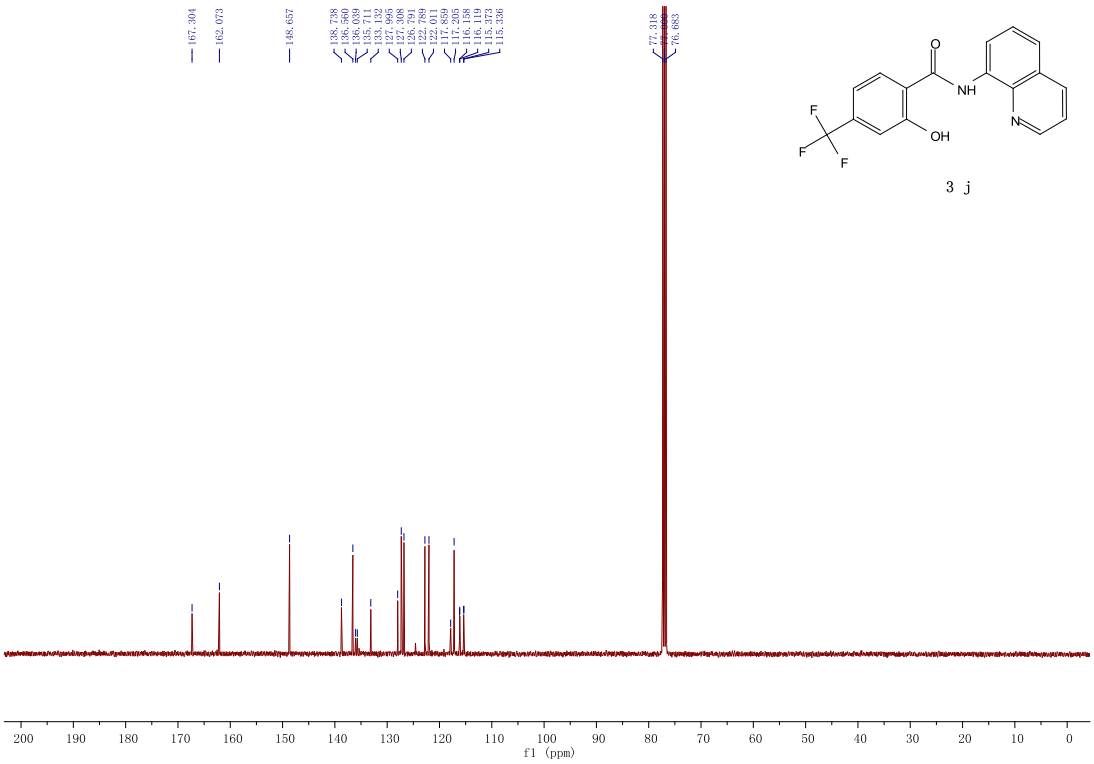

12.294
11.013
8.889
8.885
8.878
8.874
8.861
8.818
8.807
8.795
8.785
8.773
8.208
8.204
8.197
8.188
8.184
8.136
7.888
7.867
7.689
7.685
7.640
7.636
7.619
7.615
7.599
7.588
7.578
7.575
7.554
7.521
7.511
7.501
7.490
7.482
7.260
3.949
1.00
1.01
1.00
1.00
1.05
1.00
0.97
1.00
2.01
1.02
3.00
f1 (ppm)
O
NH
N
OH
O
H3C
O
3 h

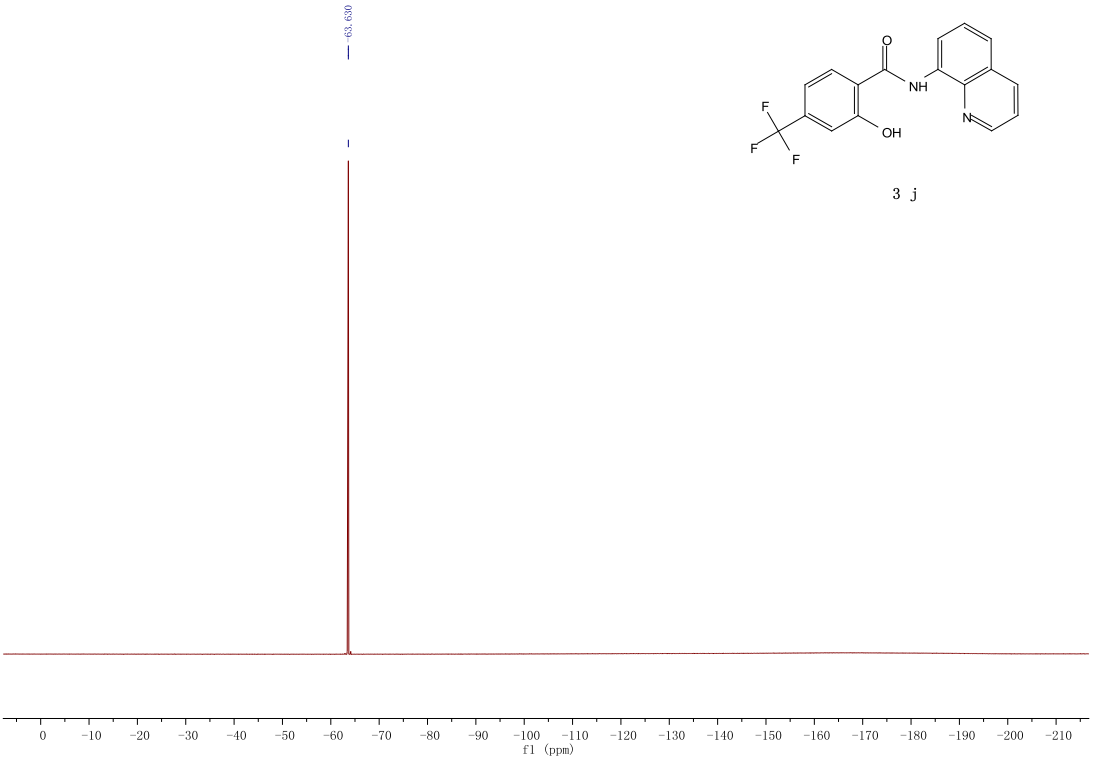

167.535
166.007
161.812
148.597
138.717
136.482
135.346
133.229
127.952
127.272
126.695
122.632
121.958
120.038
119.593
118.508
117.115
77.317
77.000
76.682
52.458
f1 (ppm)
O
NH
N
OH
O
H3C
O
3 h


12.405
10.996
8.908
8.905
8.898
8.894
8.855
8.849
8.838
8.832
8.225
8.221
8.204
8.200
7.931
7.911
7.672
7.669
7.651
7.629
7.608
7.594
7.591
7.574
7.568
7.530
7.520
7.510
7.500
7.483
7.463
7.430
7.417
7.412
7.406
7.394
7.391
7.297
7.260
7.242
7.237
O
NH
N
OH
3 i
1.00
0.99
1.03
1.01
1.00
1.02
2.07
2.06
3.18
1.05
0.97
1.59
13.5
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)

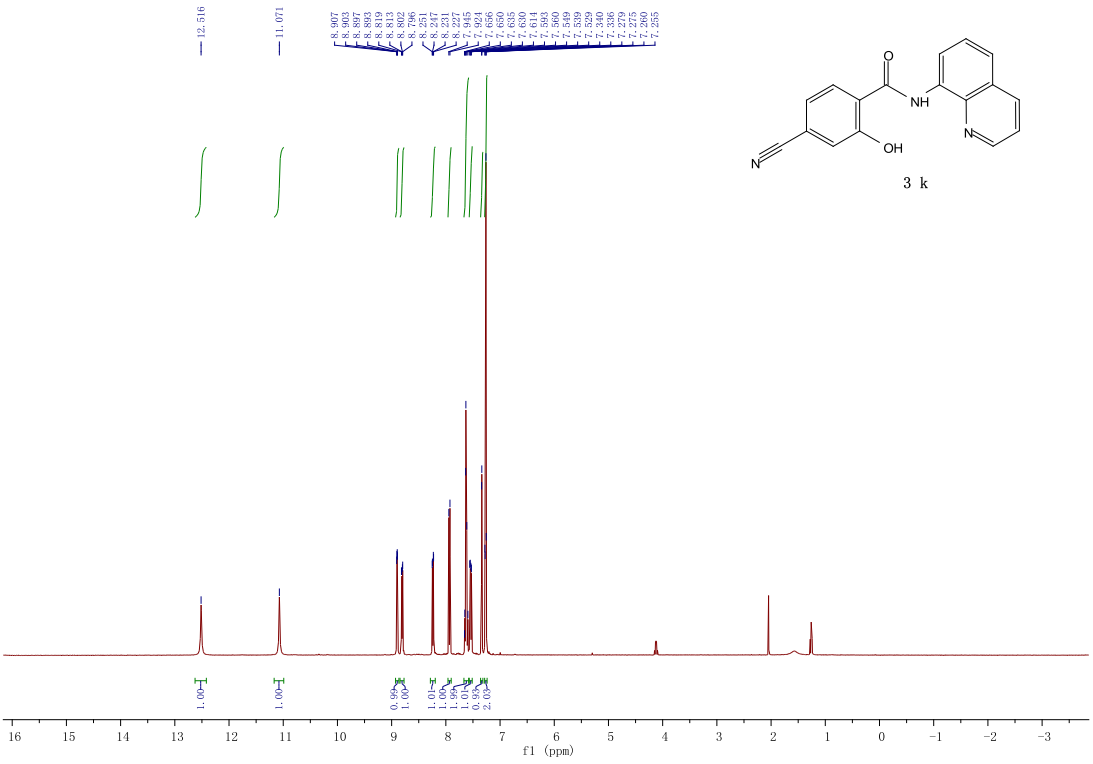

168.314
162.356
148.458
147.370
139.622
138.757
136.536
133.994
128.901
127.373
122.438
121.853
117.933
117.043
116.880
113.937
77.317
77.000
76.682
O
NH
N
OH
3 i
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


12.450
11.047
8.899
8.895
8.888
8.884
8.854
8.821
8.813
8.807
8.799
8.786
8.213
8.209
7.957
7.615
7.607
7.601
7.580
7.543
7.532
7.522
7.512
7.313
7.260
7.245
7.224
O
NH
N
OH
F
F
F
3 j
1.00
0.99
1.01
1.01
1.02
1.02
2.04
1.03
0.98
1.03
f1 (ppm)

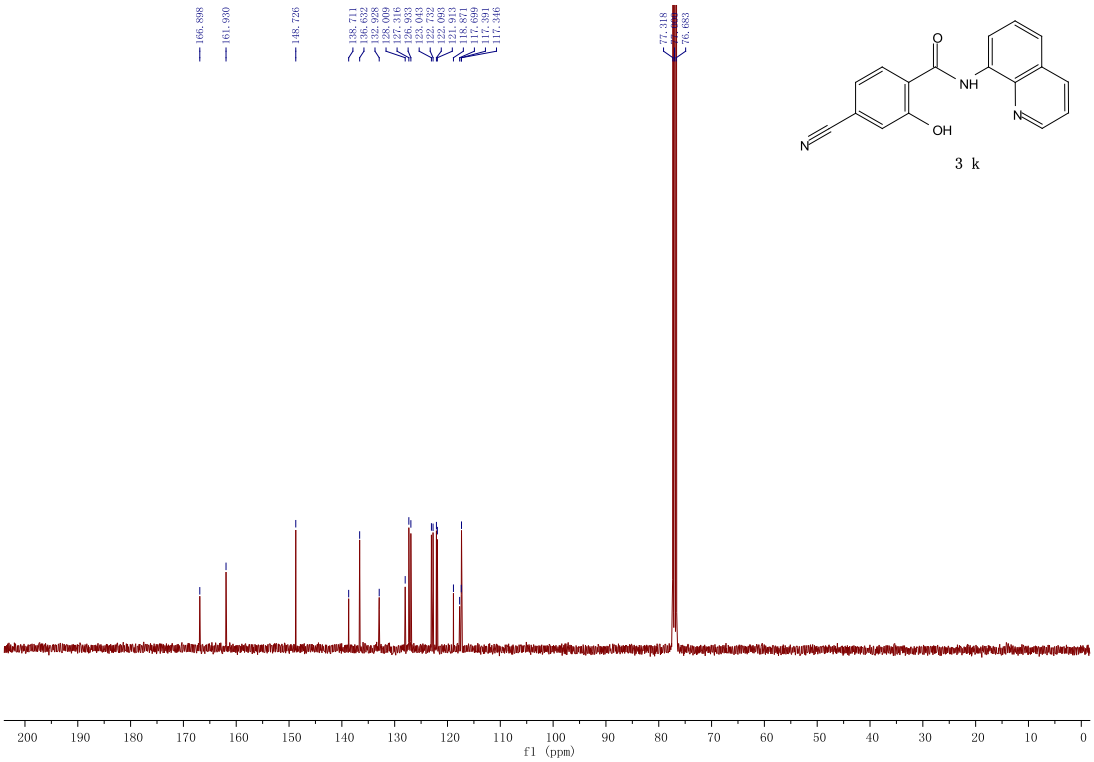

167.304
162.073
148.657
138.738
136.560
135.079
135.711
133.132
127.996
127.308
126.791
122.789
122.011
117.859
117.265
116.198
116.119
115.373
115.336
77.318
77.000
76.683
O
NH
N
OH
F
F
F
3 j
f1 (ppm)


-63.630
O
NH
N
OH
F
F
F
f1 (ppm)

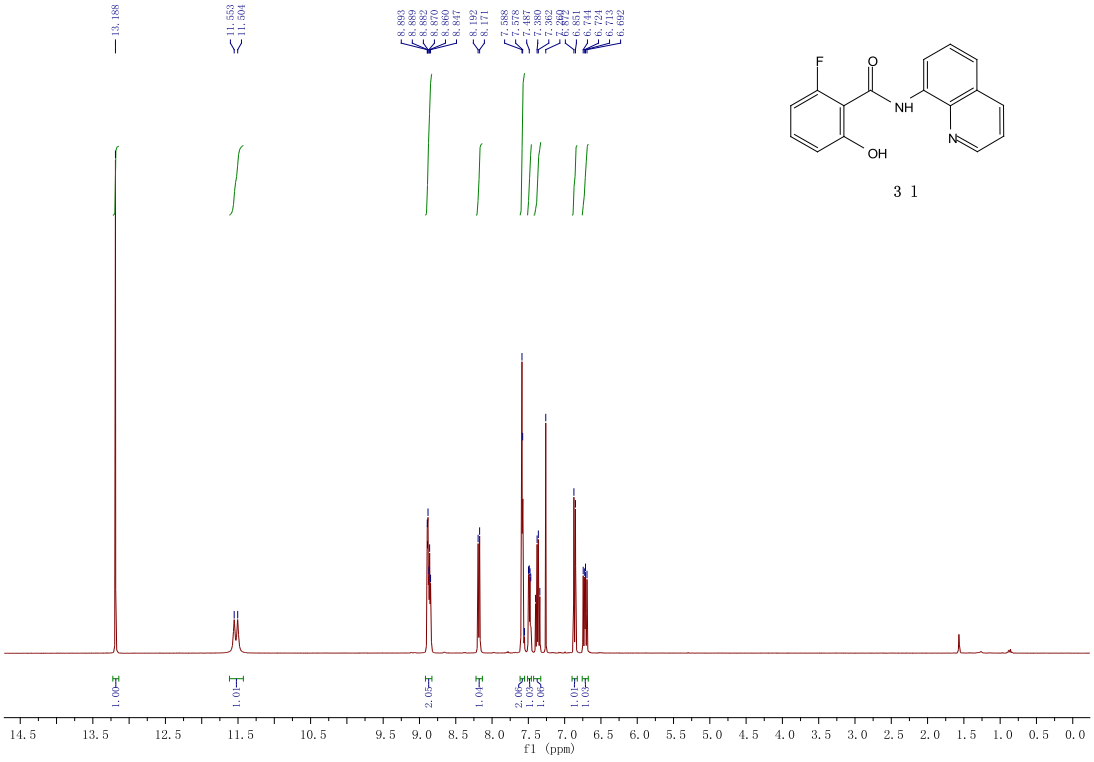
3 j


12.516
11.071
8.907
8.903
8.897
8.893
8.819
8.813
8.802
8.796
8.251
8.247
8.231
8.227
8.145
7.924
7.656
7.650
7.635
7.630
7.614
7.593
7.566
7.549
7.539
7.529
7.340
7.336
7.275
7.270
7.265
7.260
7.255
O
NH
N
OH
N
1.00
1.00
0.99
1.00
1.01
1.00
1.00
1.00
0.93
2.03
f1 (ppm)

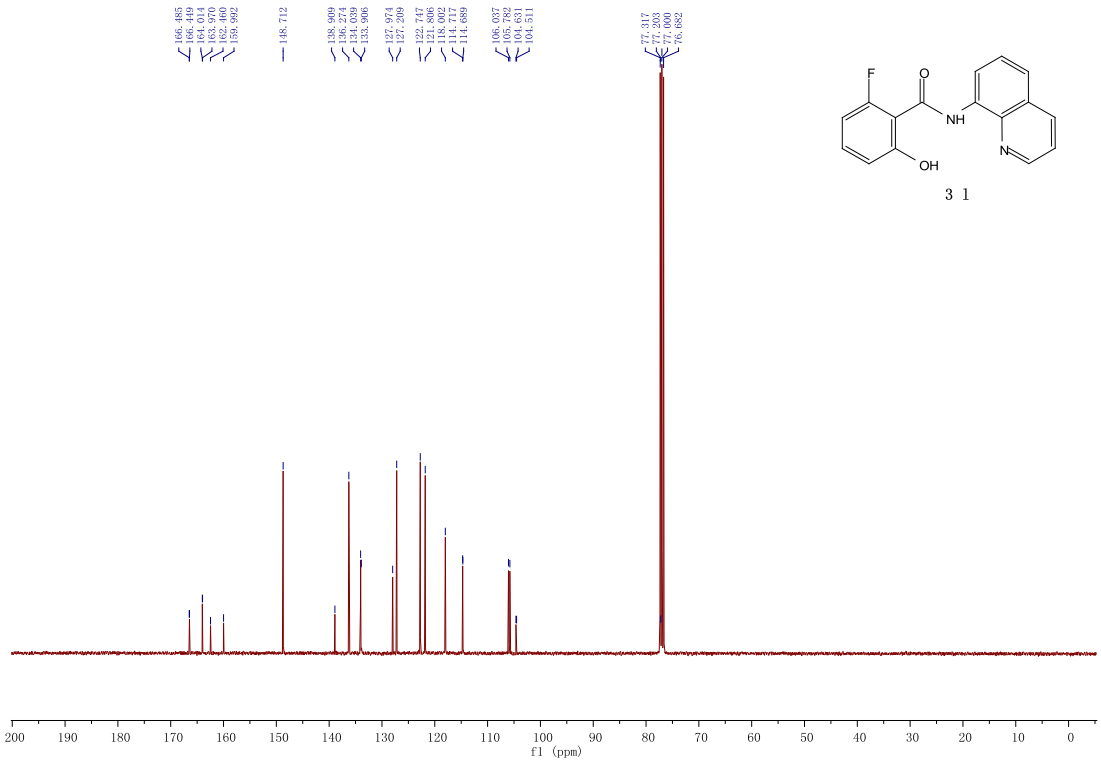
3 k


166.888
161.930
148.726
138.711
136.632
132.928
128.009
127.315
126.933
123.043
122.732
122.093
121.343
118.871
117.699
117.391
117.346
77.318
76.683
O
NH
OH
N
N

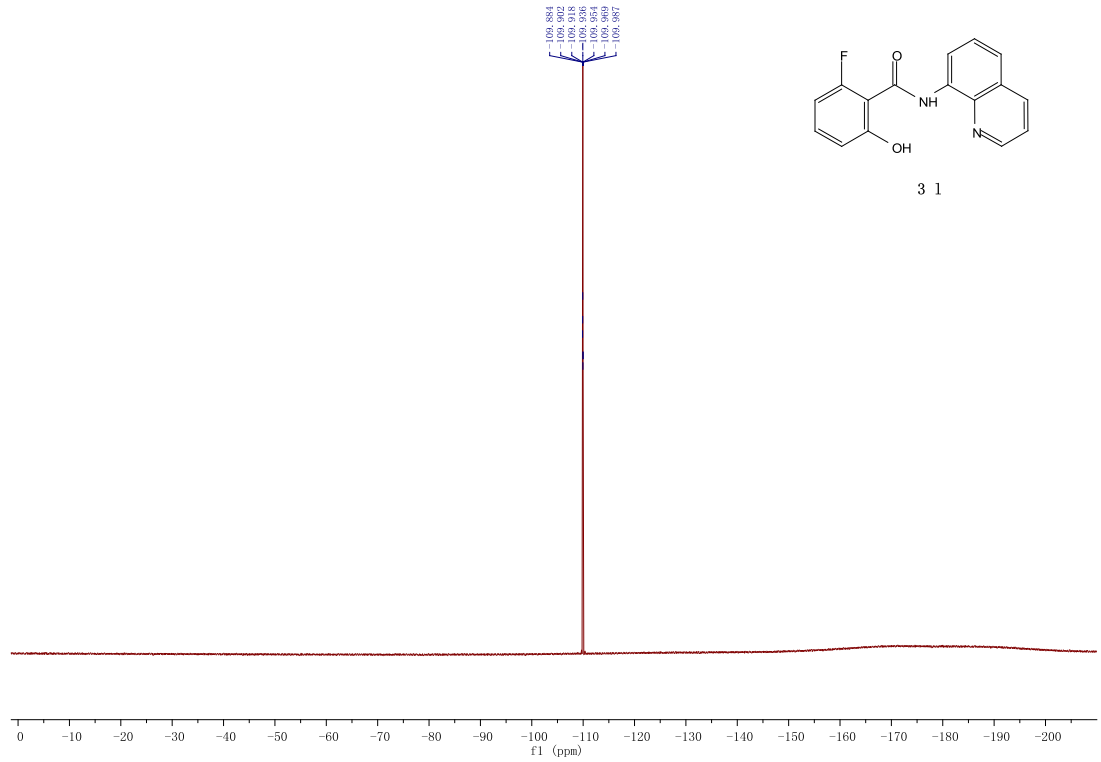
3 k


13.188
11.553
11.504
8.893
8.889
8.882
8.870
8.860
8.847
8.192
8.171
7.588
7.578
7.487
7.380
7.362
6.851
6.744
6.724
6.713
6.692
F
O
NH
OH
N
1.00
1.01
2.05
1.04
2.06
1.05
1.06
1.01
1.05

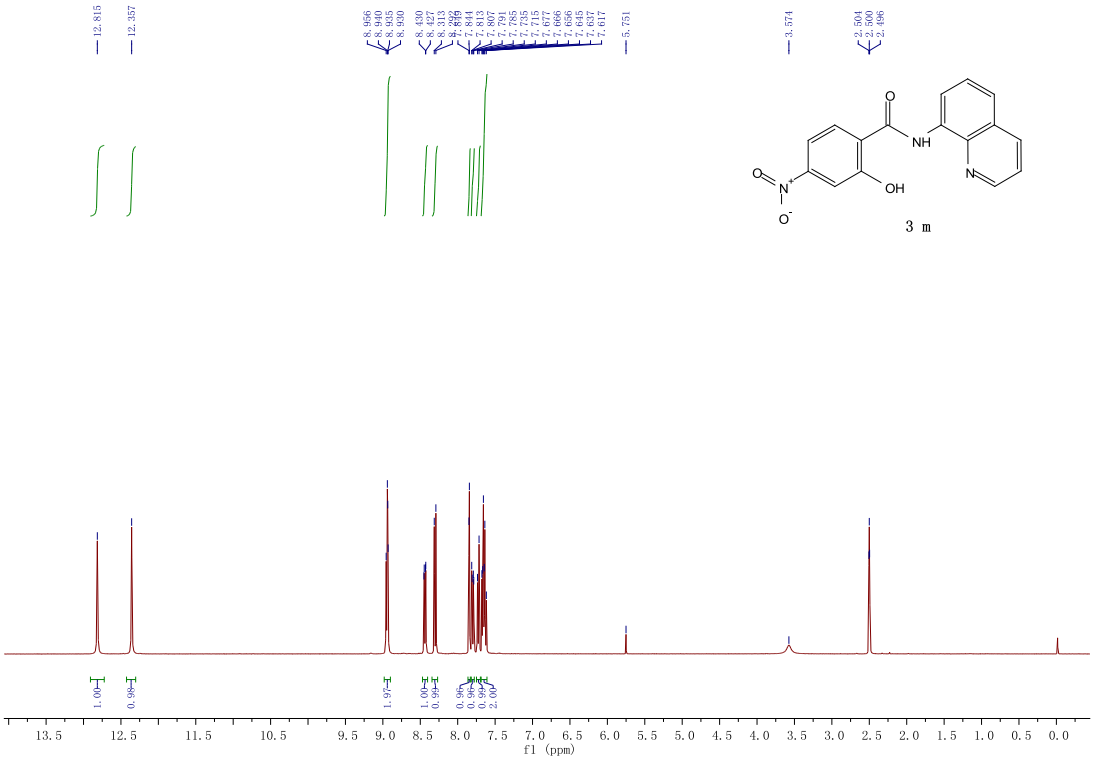
3 l

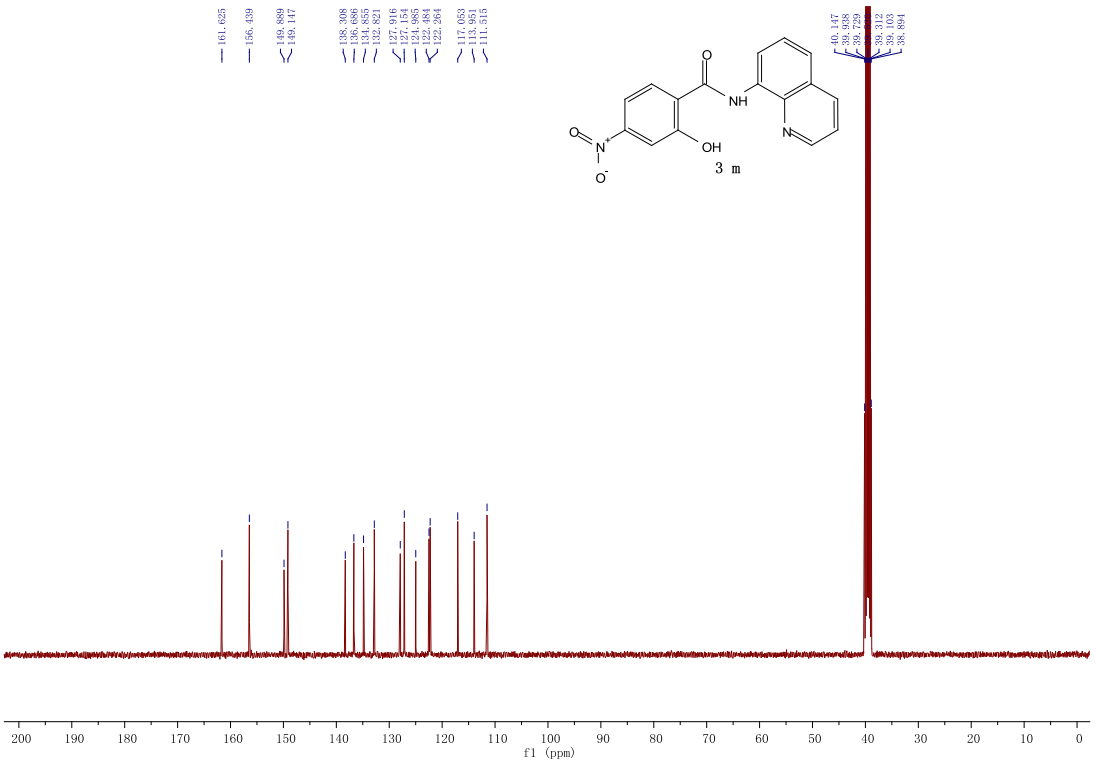

166.485
166.449
164.014
163.970
163.466
159.992
148.712
138.909
136.274
134.039
133.906
127.974
127.209
122.747
121.806
118.002
114.717
114.689
106.037
105.782
104.631
104.511
77.317
77.203
77.000
76.682
F
O
NH
N
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

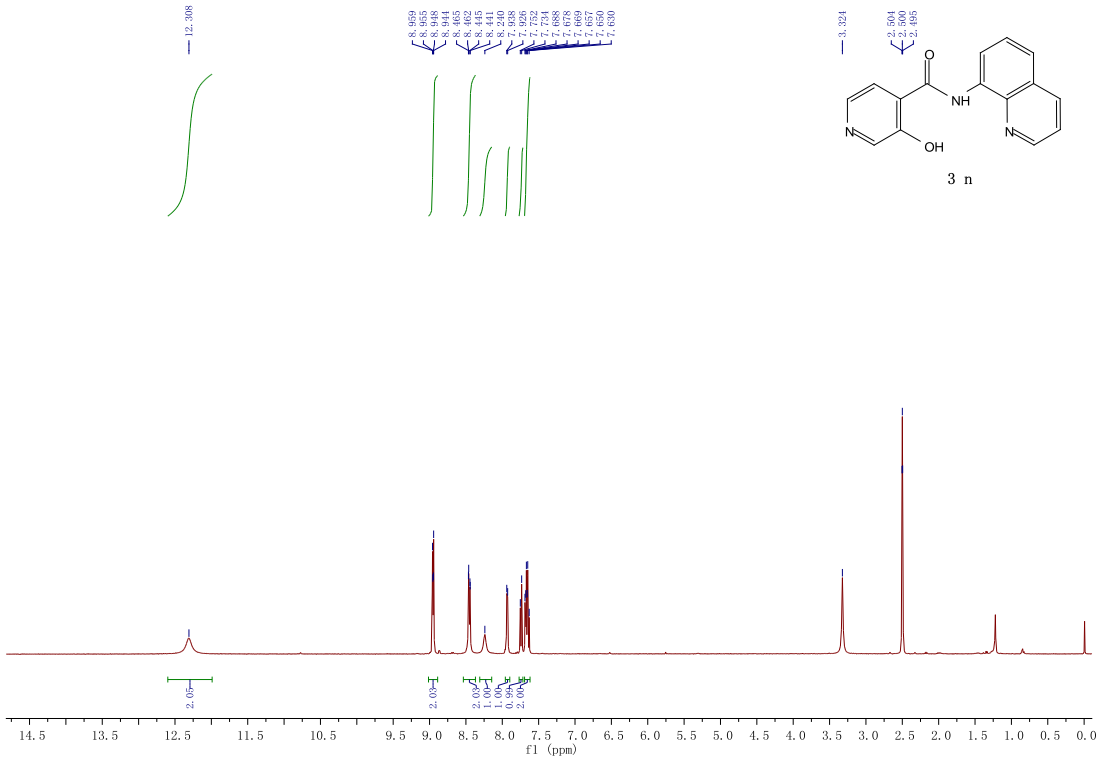
3 1

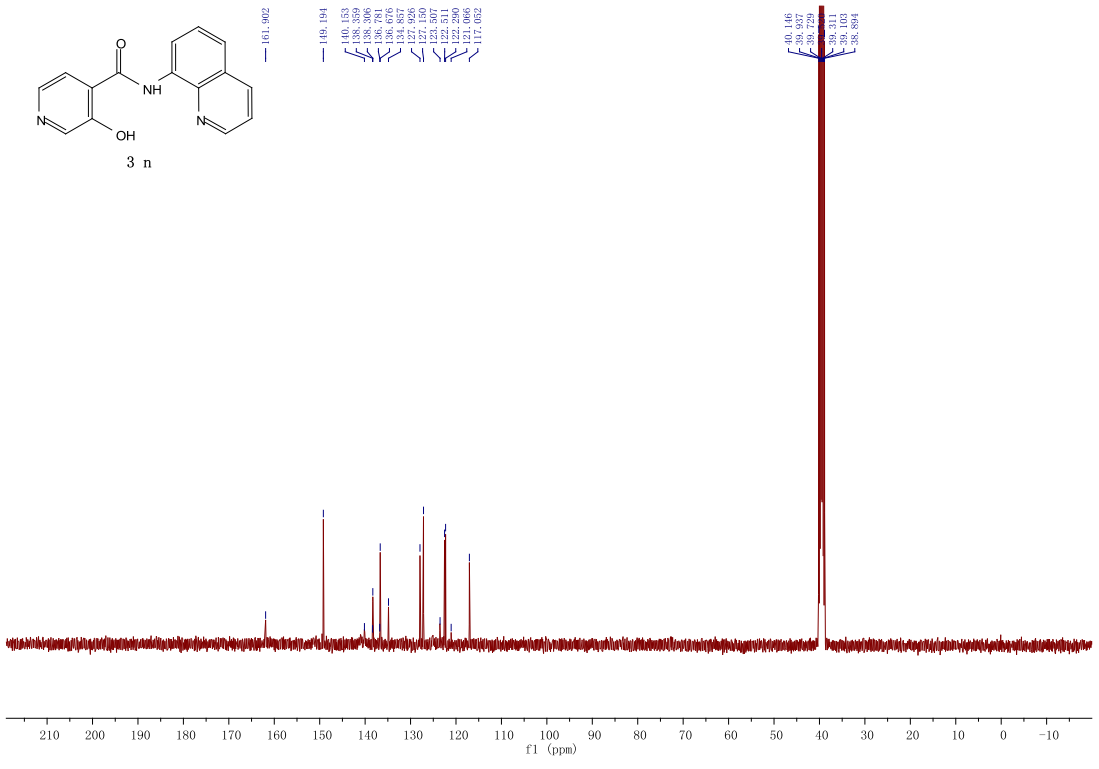

-109.884
-109.902
-109.918
-109.936
-109.954
-109.969
-109.987
F
O
NH
N
OH
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

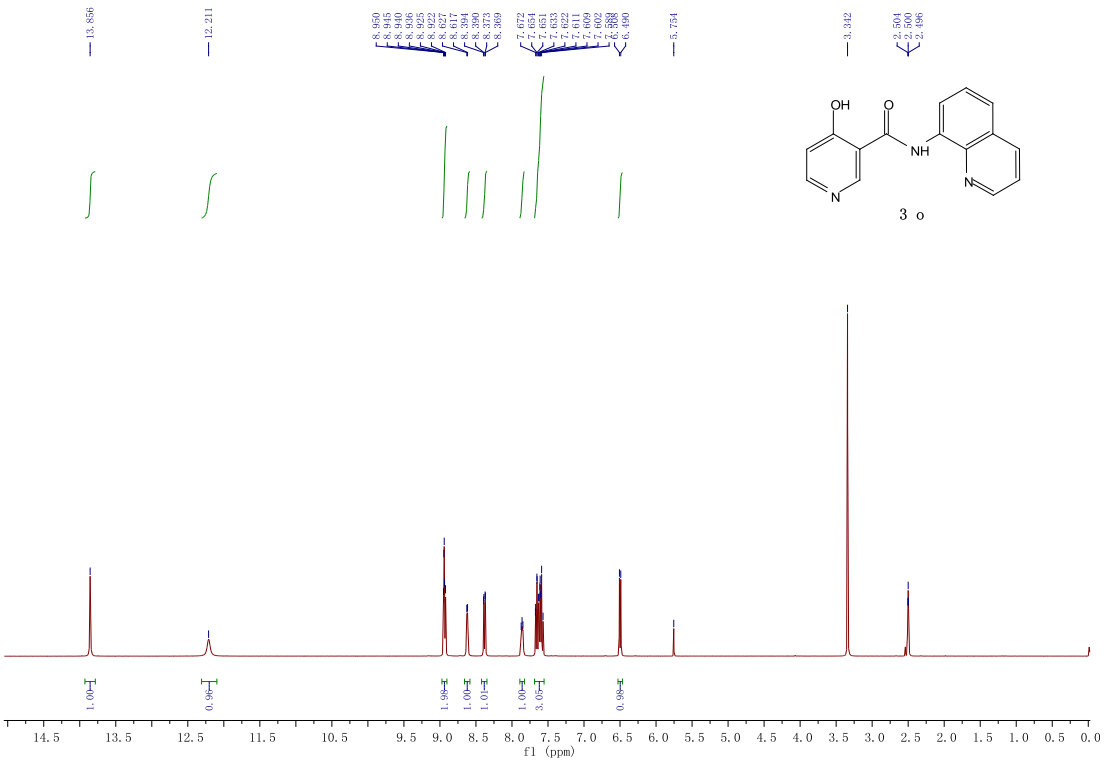
3 1

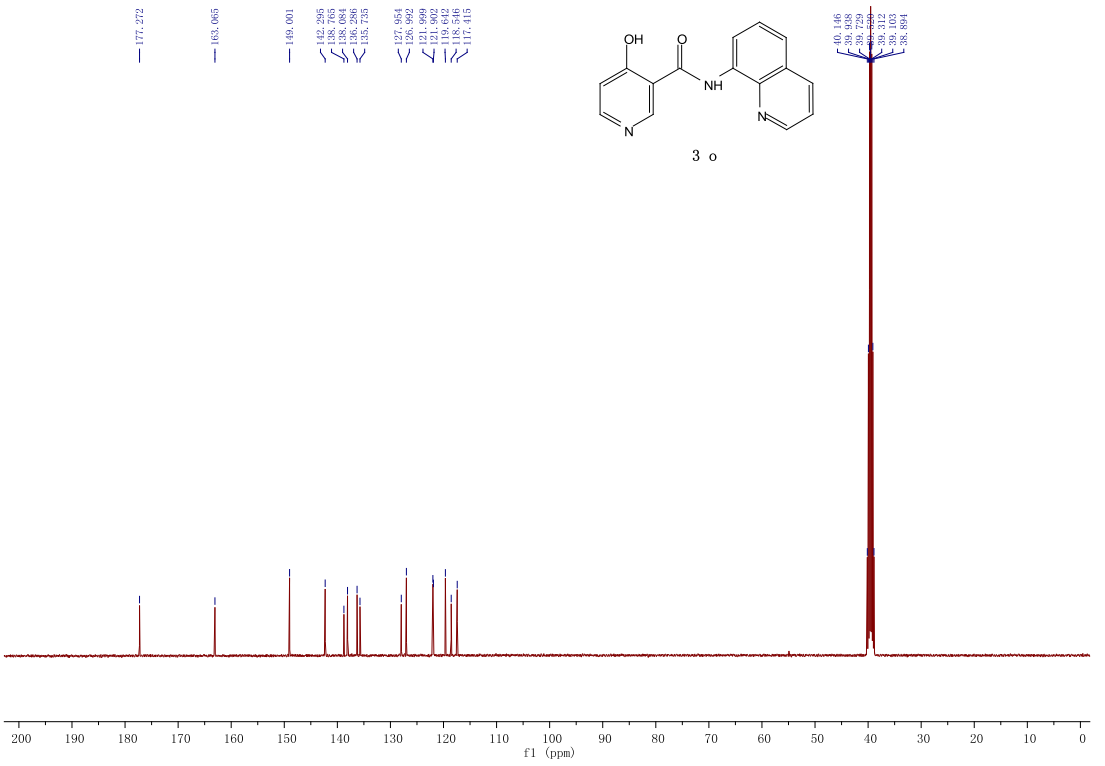

12.815
12.357
8.956
8.940
8.935
8.930
8.430
8.427
8.313
7.814
7.807
7.791
7.785
7.735
7.715
7.677
7.666
7.636
7.615
7.637
7.617
5.751
3.574
2.504
2.500
2.496
O
NH
N
OH
N+
O-
3 m
1.00
0.98
1.97
1.06
0.94
0.96
0.96
0.94
2.06
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

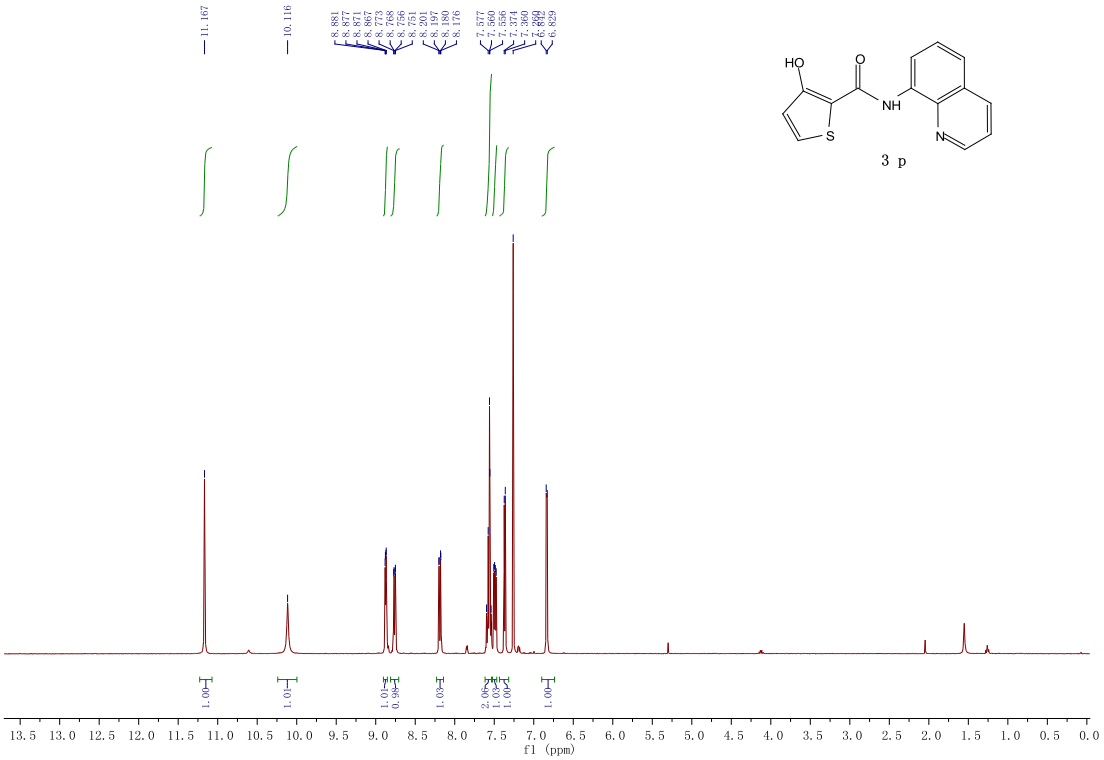

161.625
156.439
149.889
149.147
138.308
136.698
134.855
132.821
127.916
127.154
124.985
122.484
122.264
117.053
113.951
111.515
40.447
39.868
39.729
39.312
39.103
38.894
O
NH
N
OH
N+
O-
3 m
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

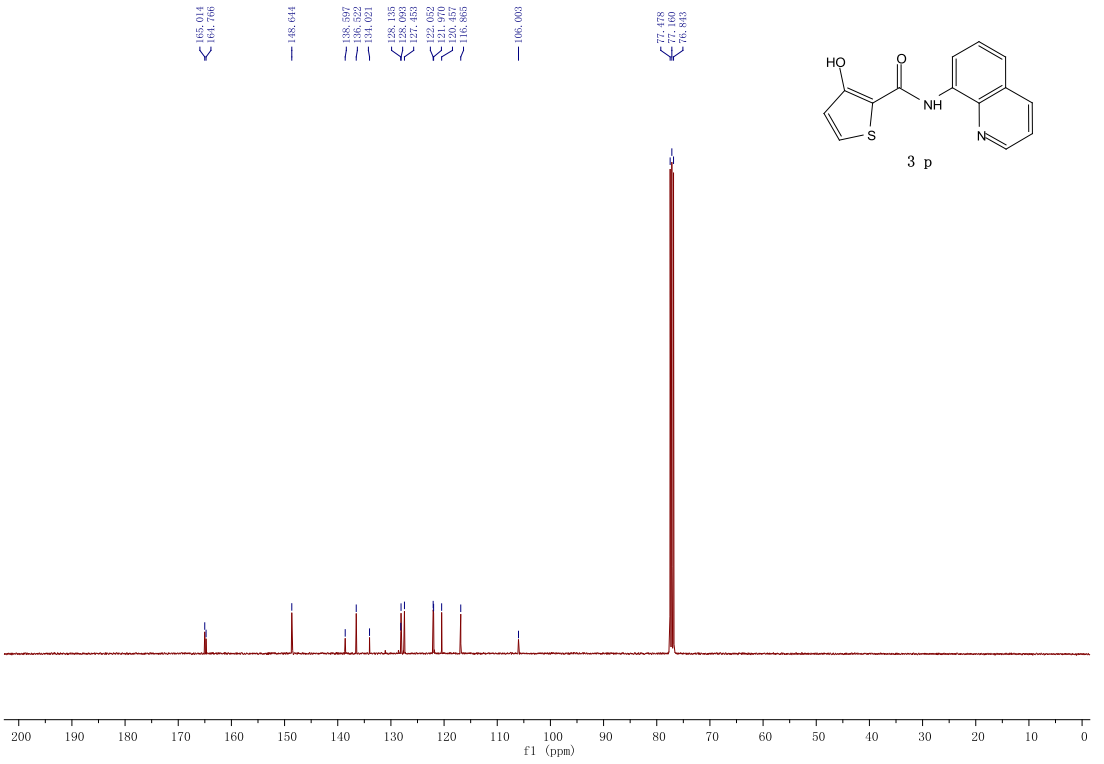

12.308
8.959
8.955
8.948
8.944
8.465
8.462
8.445
8.441
8.240
8.238
7.926
7.752
7.734
7.688
7.678
7.669
7.657
7.650
7.630
3.324
2.504
2.500
2.495
O
NH
N
OH
N
3 n
2.05
2.03
1.00
1.00
0.99
2.00
14.5 13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

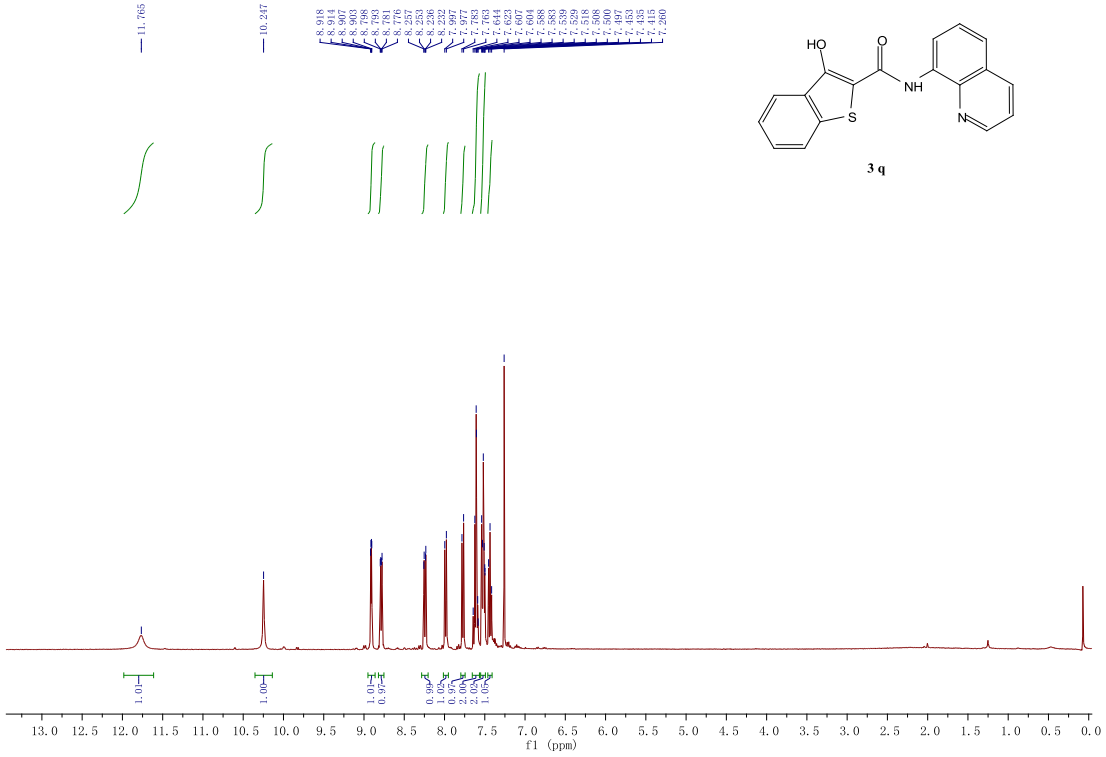

O
NH
N
OH
N
3 n
161.902
149.194
140.153
138.358
138.306
136.781
136.676
134.957
127.926
127.150
123.507
122.511
122.300
121.066
117.052
40.146
39.937
39.729
39.311
39.103
38.894
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

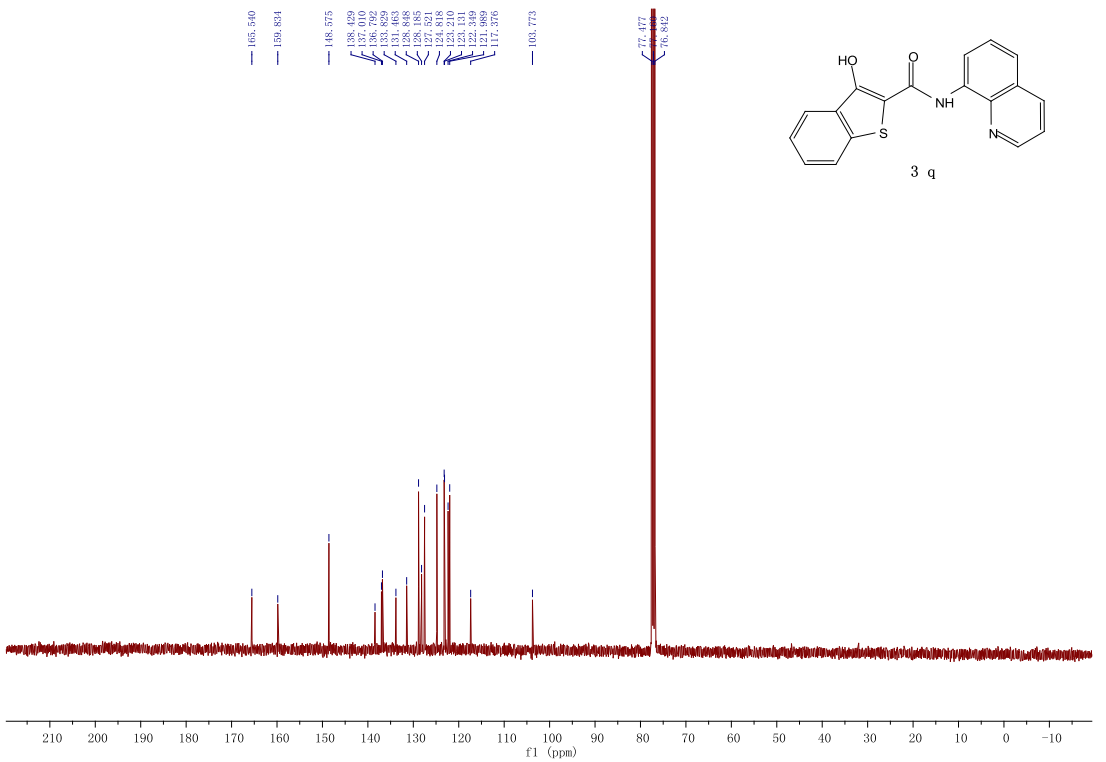

13.856
12.211
8.950
8.945
8.940
8.936
8.925
8.922
8.627
8.617
8.394
8.390
8.373
8.369
7.672
7.654
7.651
7.633
7.622
7.611
7.609
7.602
6.588
6.490
5.754
3.342
2.504
2.500
2.496
OH
O
NH
N
N
3 o
1.00
0.96
1.98
1.04
1.01
1.00
3.05
0.98
f1 (ppm)

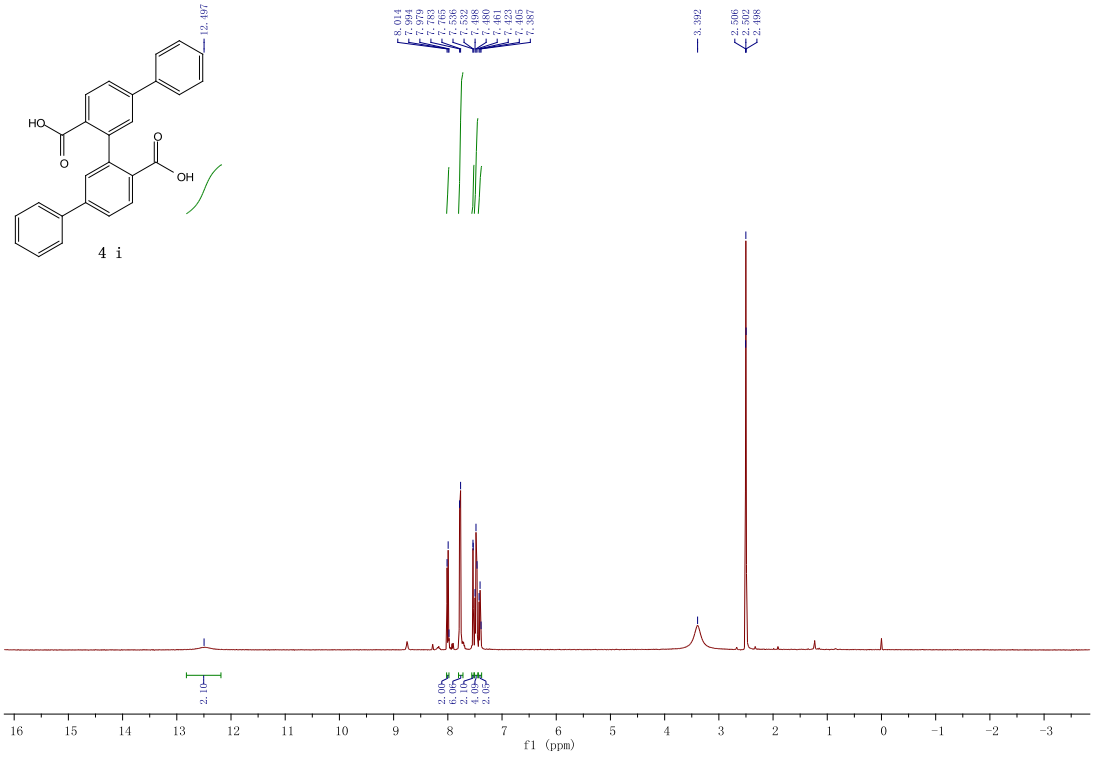

177.272
163.065
149.001
142.295
138.765
138.084
136.298
135.735
127.954
126.992
121.999
121.902
119.642
118.546
117.415
40.146
39.938
39.729
39.520
39.312
39.103
38.894
OH
O
NH
N
N
3 o
f1 (ppm)


11.167
10.116
8.881
8.877
8.871
8.867
8.773
8.768
8.756
8.751
8.201
8.197
8.180
8.176
7.577
7.560
7.556
7.374
7.360
6.844
6.829
HO
O
NH
S
N
3 p
1.00
1.01
1.01
0.98
1.03
2.06
1.06
1.00
1.00
13.5 13.0 12.5 12.0 11.5 11.0 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
f1 (ppm)

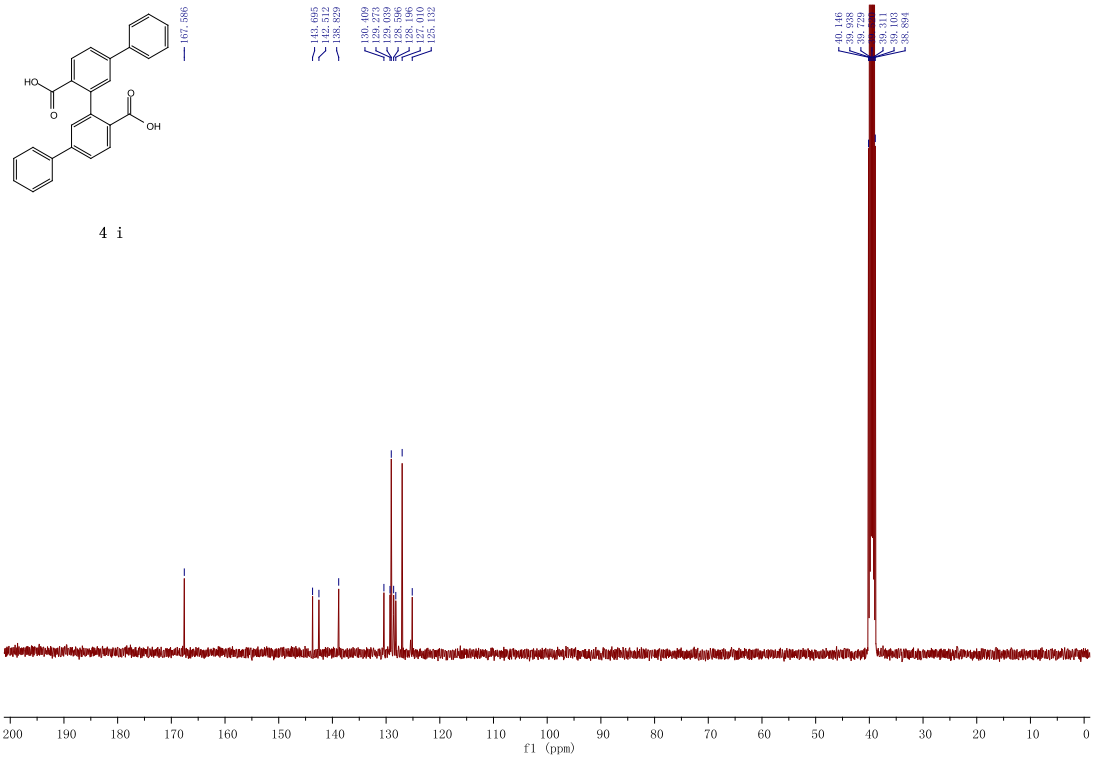

165.014
164.766
148.644
138.597
136.522
131.021
128.135
128.093
127.453
122.052
121.970
120.853
116.865
106.003
77.478
77.160
76.843
HO
O
NH
S
N
3 p
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


11.765
10.247
8.918
8.914
8.907
8.903
8.798
8.793
8.781
8.776
8.257
8.253
8.236
8.232
7.997
7.977
7.783
7.763
7.644
7.623
7.607
7.604
7.583
7.563
7.539
7.529
7.518
7.506
7.500
7.497
7.453
7.435
7.415
7.260
HO
O
NH
S
N
3 q
1.01
1.00
1.01
0.97
0.99
1.00
0.97
2.00
2.02
1.05
13.0 12.5 12.0 11.5 11.0 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
f1 (ppm)


165.540
159.834
148.575
138.429
137.010
135.892
133.839
131.463
128.848
128.185
127.531
124.818
123.210
123.131
122.349
121.998
117.376
103.773
77.477
77.160
76.842
HO
O
NH
S
N
3 q
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)


12.497
8.014
7.994
7.979
7.783
7.765
7.536
7.532
7.498
7.480
7.461
7.423
7.405
7.387
3.392
2.506
2.502
2.498
HO
O
O
OH
2.10
2.06
2.06
2.10
4.09
2.05
f1 (ppm)

4 i


167.586
143.695
142.512
138.829
130.409
129.273
129.059
128.584
128.196
127.010
125.132
40.146
39.958
39.729
39.311
39.103
38.894
HO
O
O
OH
f1 (ppm)

4 i