Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Direct synthesis of 2-methylpyridines via I_2-triggered [3 + 2 + 1] annulation of aryl methyl ketoxime acetates with triethylamine as the carbon source

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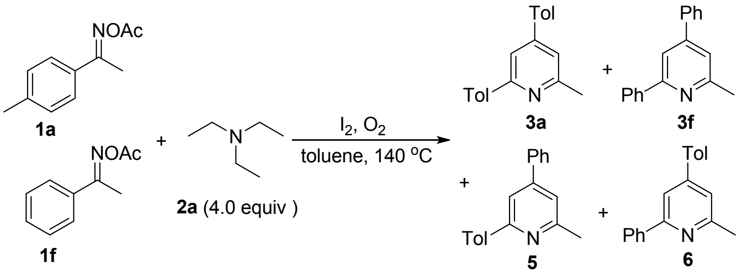
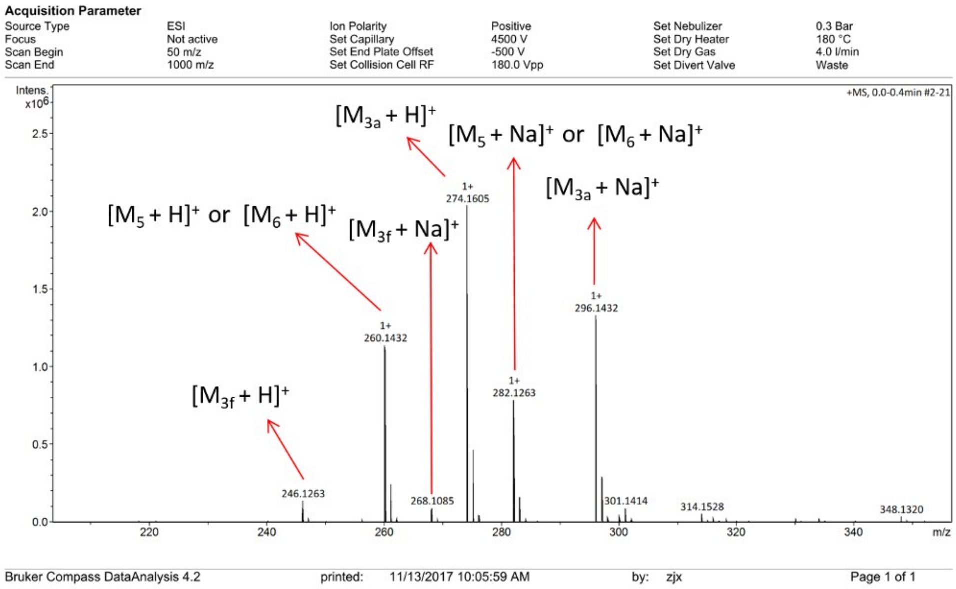
1. The cross-coupling reaction and the spectrogram of HRMS

In order to further confirm our proposed mechanism, we investigated the cross-coupling reaction between two representative substrates 4-methylacetophenone oxime acetate (**1a**) and acetophenone oxime acetate (**1f**) under standard conditions. Fortunately, all the products were successfully identified by HRMS analysis of the crude reaction extract.





Acquisition Parameter

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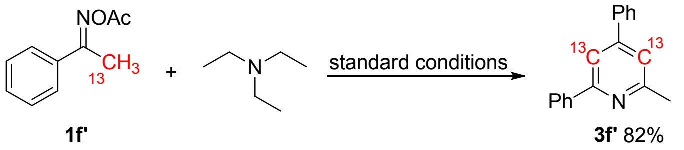
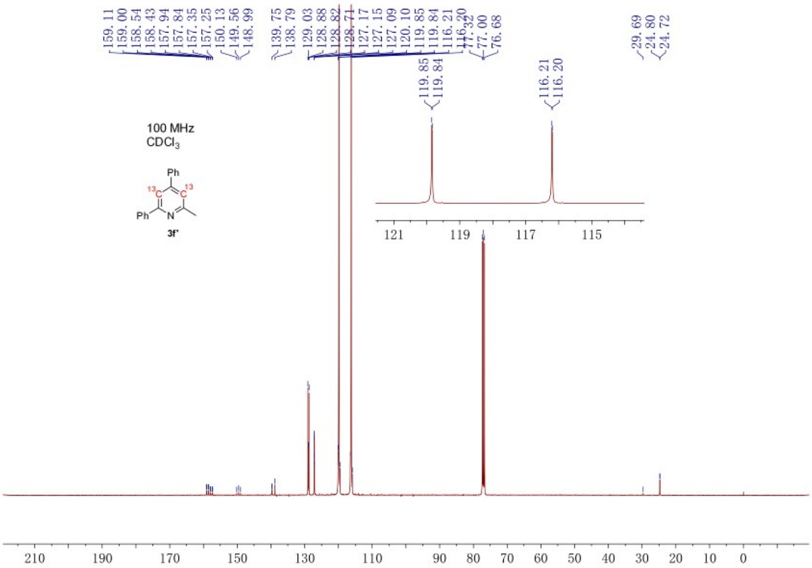
Scan End	1000 m/z	Set Collision Cell RF	180.0 Vpp	Set Divert Valve	Waste

Bruker Compass DataAnalysis 4.2 printed: 11/13/2017 10:05:59 AM by: zjx Page 1 of 1

2. The ^{13}C-labeling and D-labeling experiments and the spectrogram

We further experimented to develop a better understanding of the reaction mechanism by performing ^{13}C-labeling and D-labeling experiments under the optimized conditions using acetophenone-β,β,β-d_3 oxime acetate and acetophenone-β-^{13}C oxime acetate, respectively, as substrates. The corresponding desired products **3f’** and **3f-*d*$_2$** were obtained in 82% and 79% yields, respectively (Scheme 4a and 4b). These experimental results strongly suggested that methyl ketone *O*-acetyloximes provided four carbons to form the pyridine ring. Then, the speculation that the α-C of TEA was integrated into the final pyridines has been demonstrated when TEA-d_{15} was used in this reaction system (Scheme 4c). Both of this deuterated experimental evidences are in agreement with the observation of internal D/H exchange in the 2-methylpyridines.


NOAc
13
CH3
+
standard conditions
Ph
13C
C13
Ph
N
1f'
3f' 82%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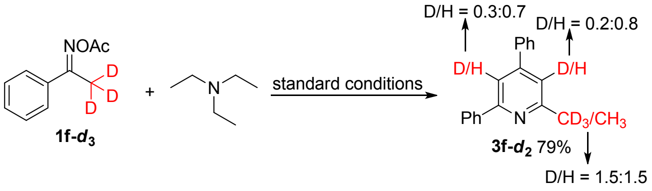
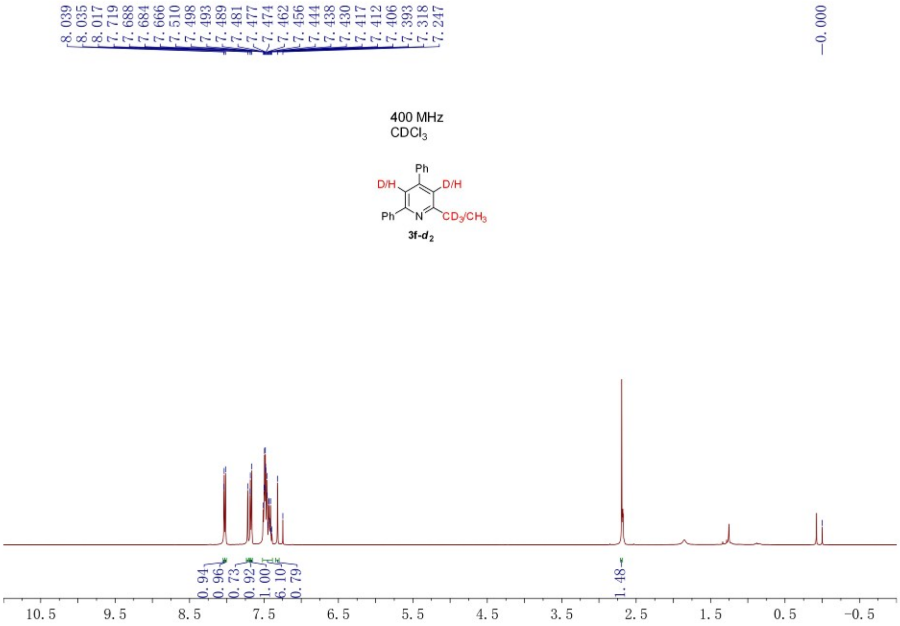
159.00
158.54
158.43
157.94
157.84
157.35
157.25
150.13
149.56
148.99
139.75
138.79
129.03
128.88
128.82
128.71
127.17
127.15
127.09
120.10
119.85
119.84
116.21
116.20
77.32
77.00
76.68
29.69
24.80
24.72
100 MHz
CDCl3
3f'
119.85
119.84
116.21
116.20
121
119
117
115
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0


D/H = 0.3:0.7
D/H = 0.2:0.8
NOAc
D
D
D
+
standard conditions
Ph
D/H
D/H
Ph
N
CD3/CH3
1f-d3
3f-d2 79%
D/H = 1.5:1.5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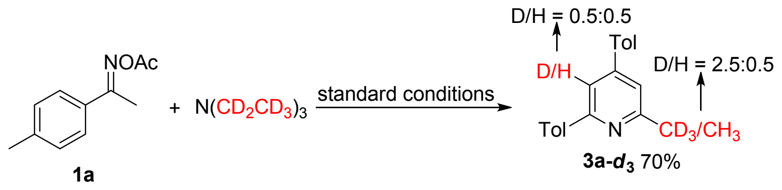
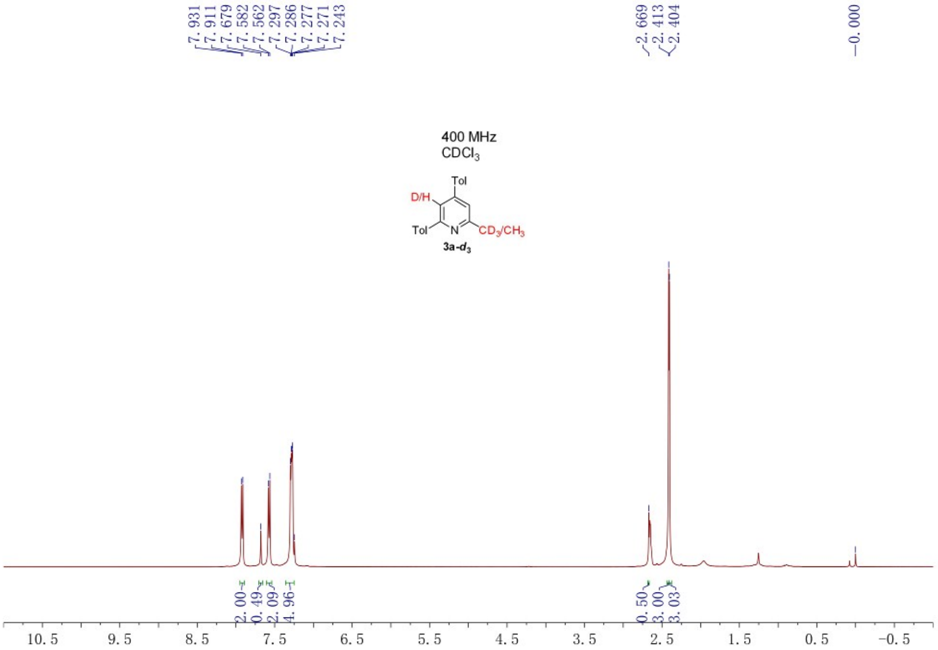
8.035
8.017
7.719
7.688
7.684
7.666
7.510
7.498
7.493
7.489
7.481
7.477
7.474
7.462
7.456
7.444
7.438
7.430
7.417
7.412
7.406
7.393
7.318
7.247
-0.000
400 MHz
CDCl3
3f-d2
0.94
0.96
0.73
0.92
1.00
6.10
0.79
1.48
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5


NOAc
1a
+ N(CD2CD3)3
standard conditions
D/H = 0.5:0.5
Tol
D/H
D/H = 2.5:0.5
Tol
N
CD3/CH3
3a-d3 70%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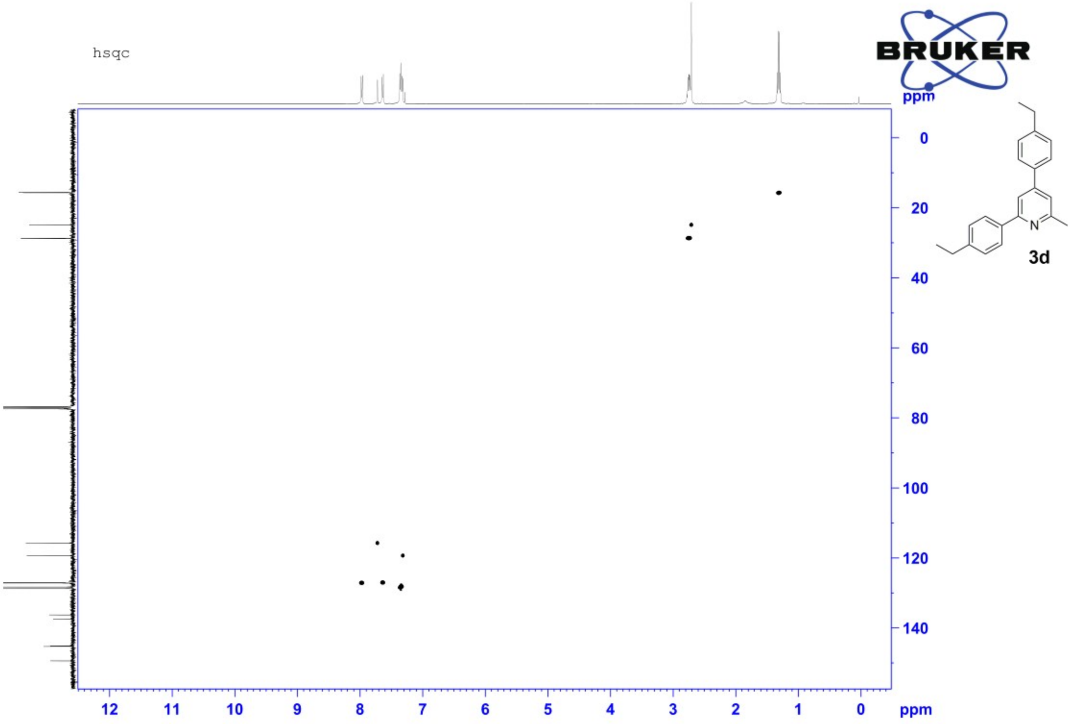
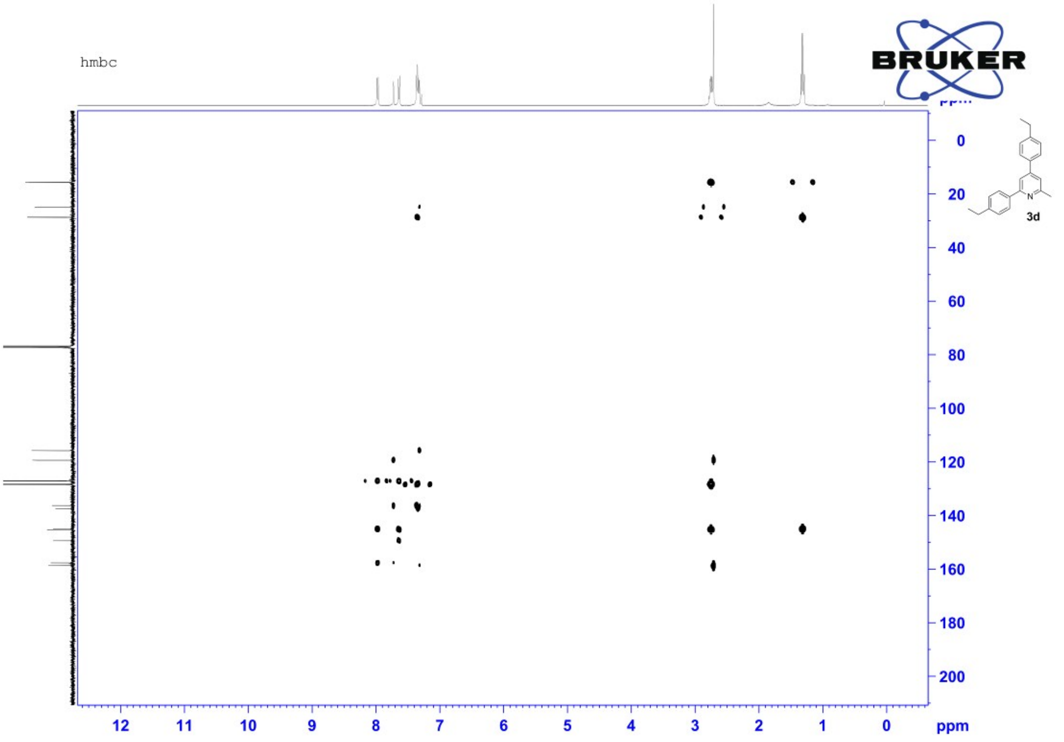
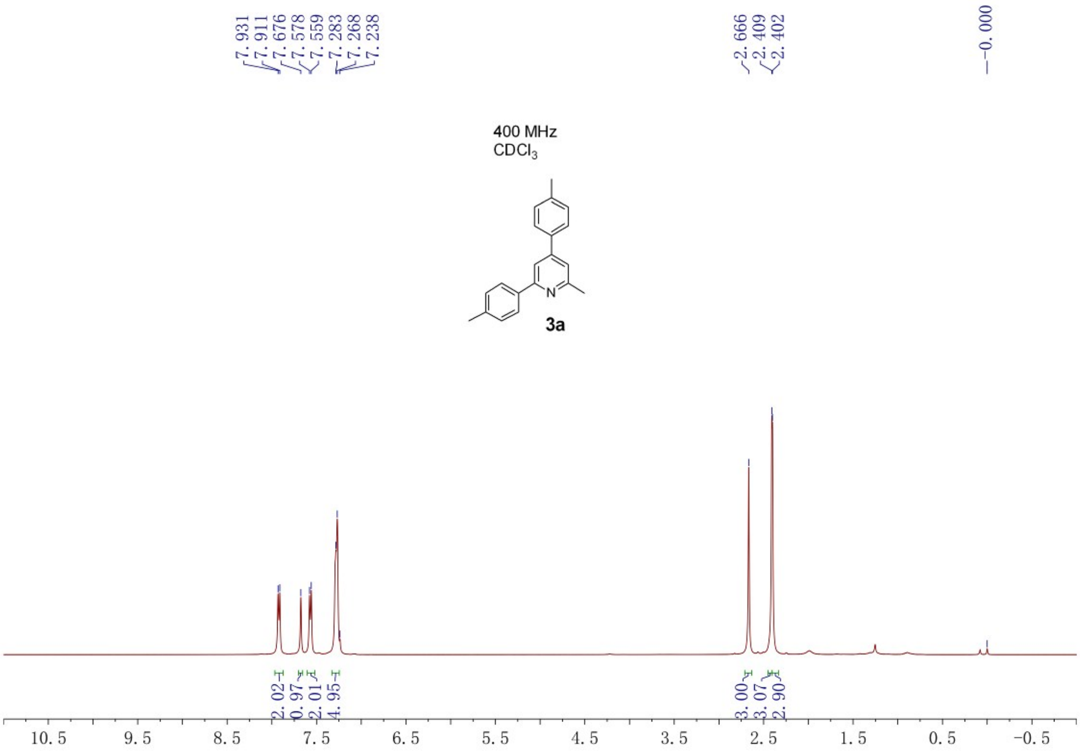
7.911
7.679
7.582
7.562
7.297
7.286
7.277
7.271
7.243
2.669
2.413
2.404
0.000
400 MHz
CDCl3
Tol
D/H
Tol
N
CD3/CH3
3a-d3
2.00
0.49
2.09
4.96
0.50
3.00
3.03
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5

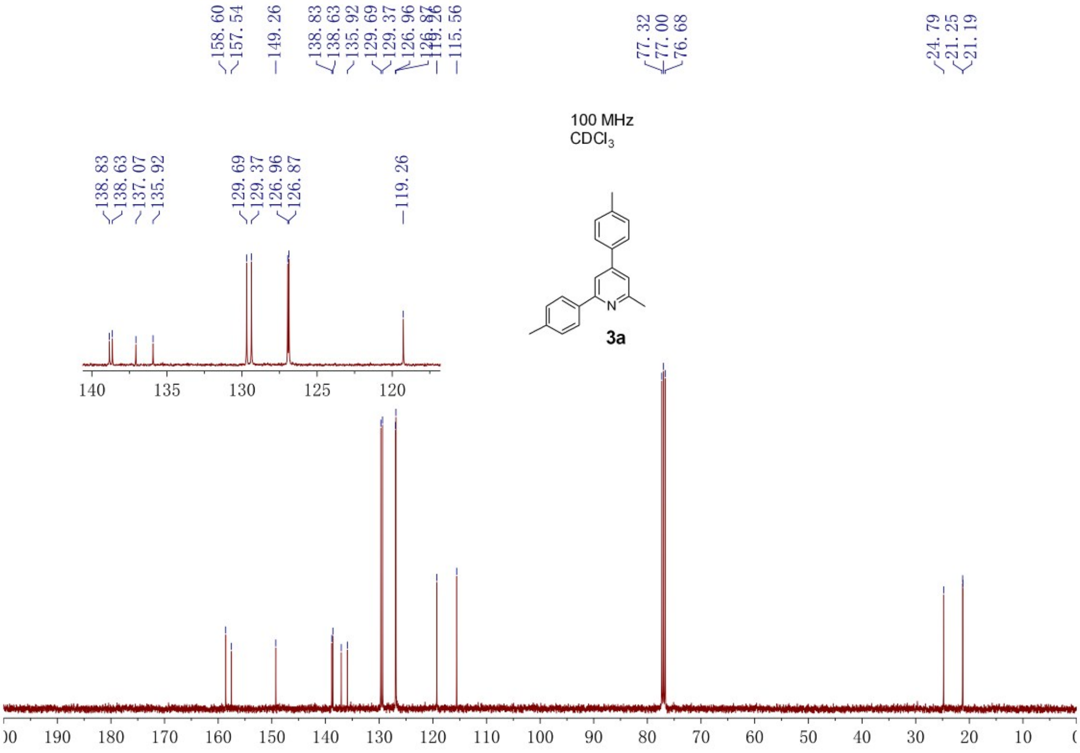
3. The HSQC and HMBC of 3d

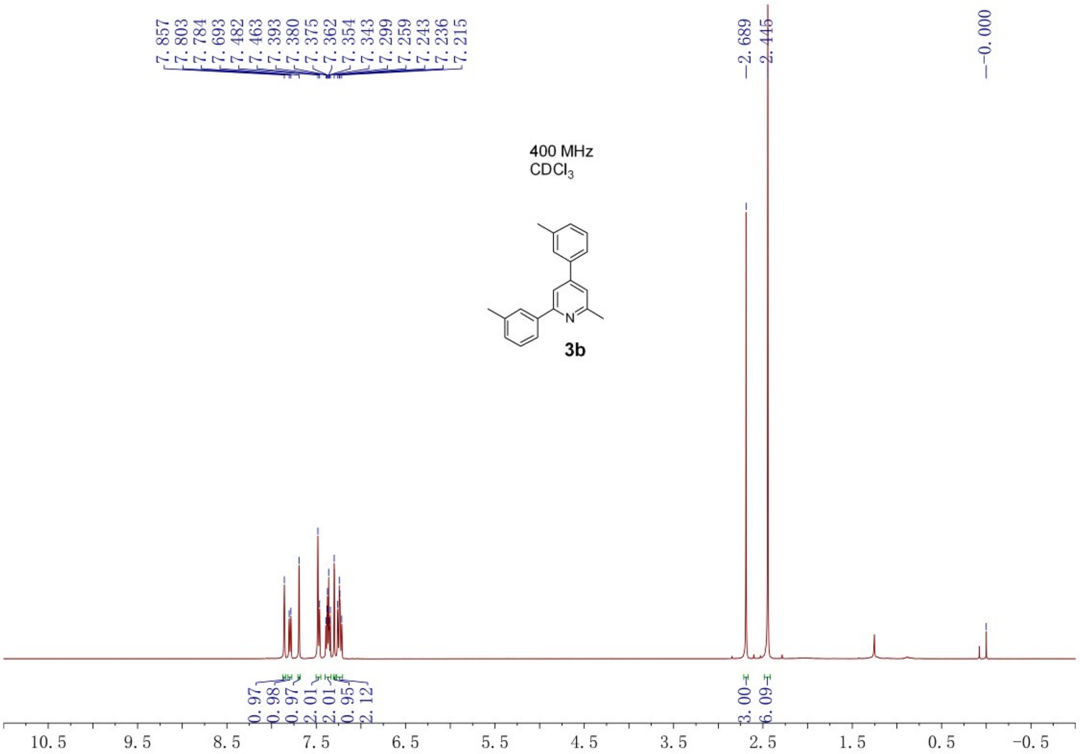




4. ^{1}H and ^{13}C NMR spectra of compounds 3



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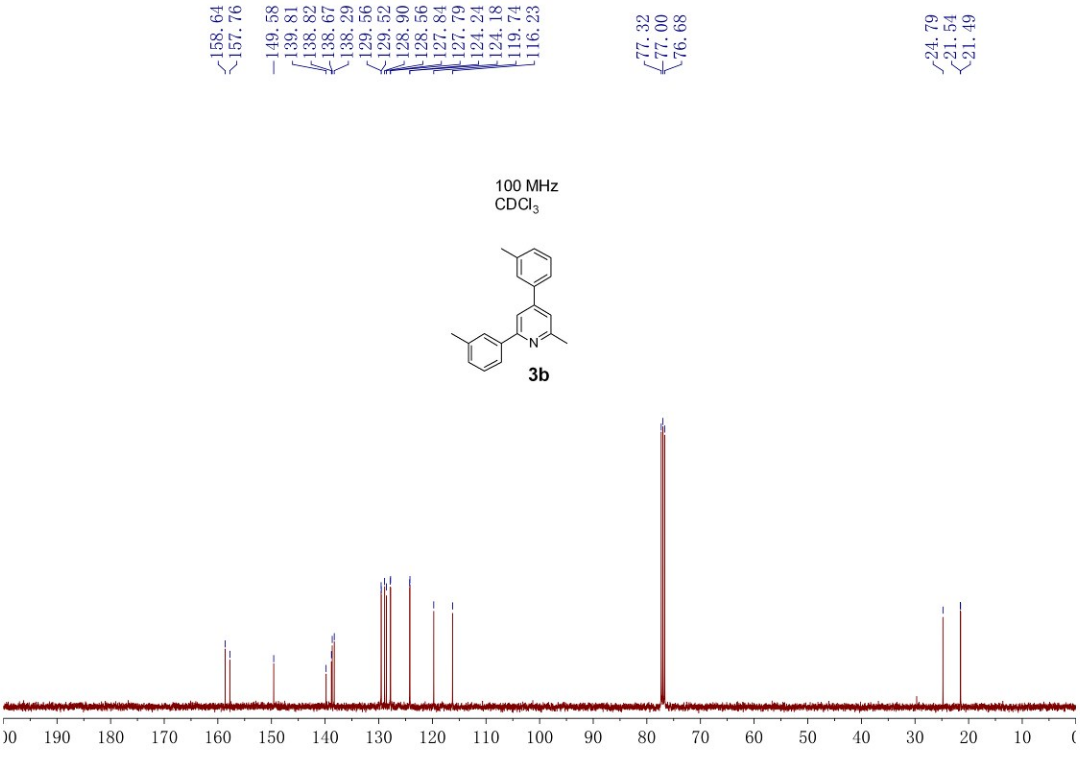
7.803
7.784
7.693
7.482
7.463
7.393
7.380
7.375
7.362
7.354
7.343
7.299
7.259
7.243
7.236
7.215
2.689
2.445
0.000
400 MHz
CDCl$_3$
N
3b
0.97
0.98
0.97
2.01
2.01
0.95
2.12
3.00
6.09
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5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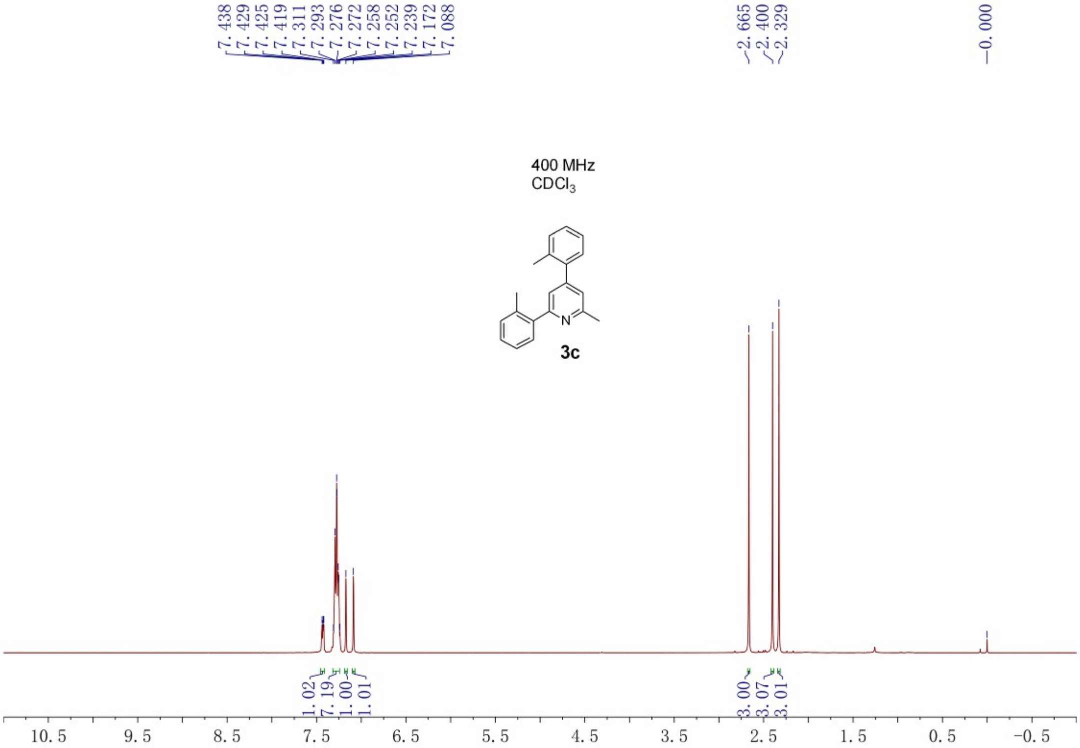
157.76
149.58
139.81
138.82
138.67
138.29
129.56
129.52
128.90
128.56
127.84
127.79
124.24
124.18
119.74
116.23
77.32
77.00
76.68
24.79
21.54
21.49
100 MHz
CDCl$_3$
N
3b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10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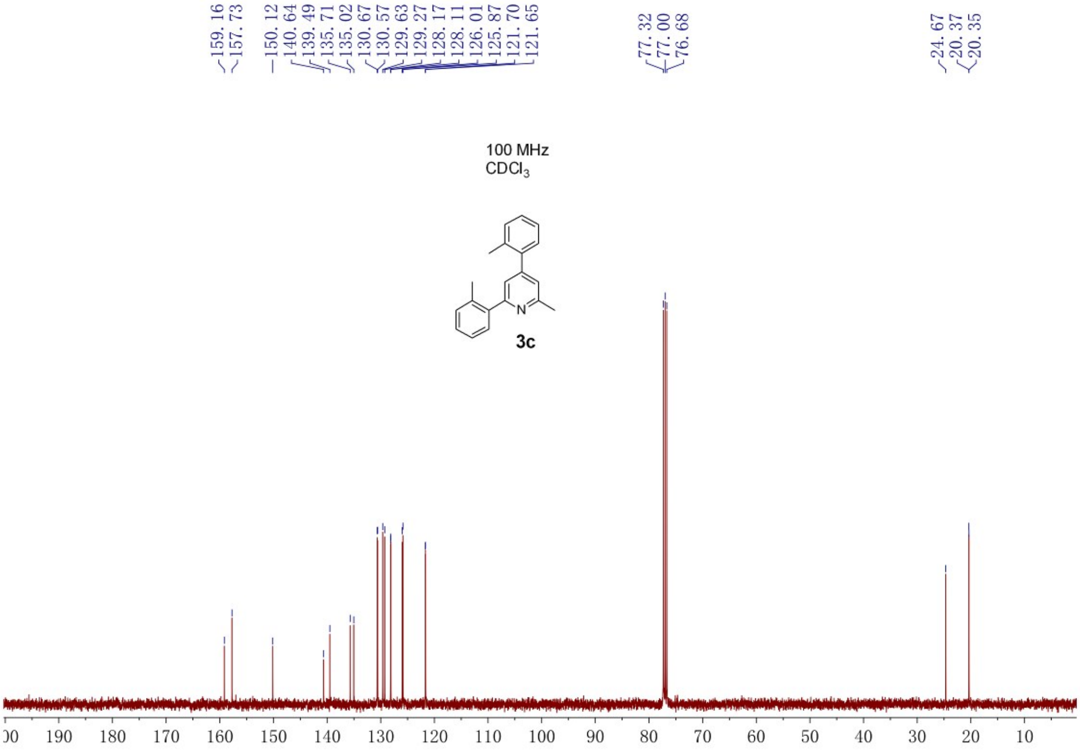
7.425
7.419
7.311
7.293
7.276
7.272
7.258
7.252
7.239
7.172
7.088
2.665
2.400
2.329
0.000
400 MHz
CDCl$_3$
N
3c
1.02
7.19
1.00
1.01
3.00
3.07
3.01
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5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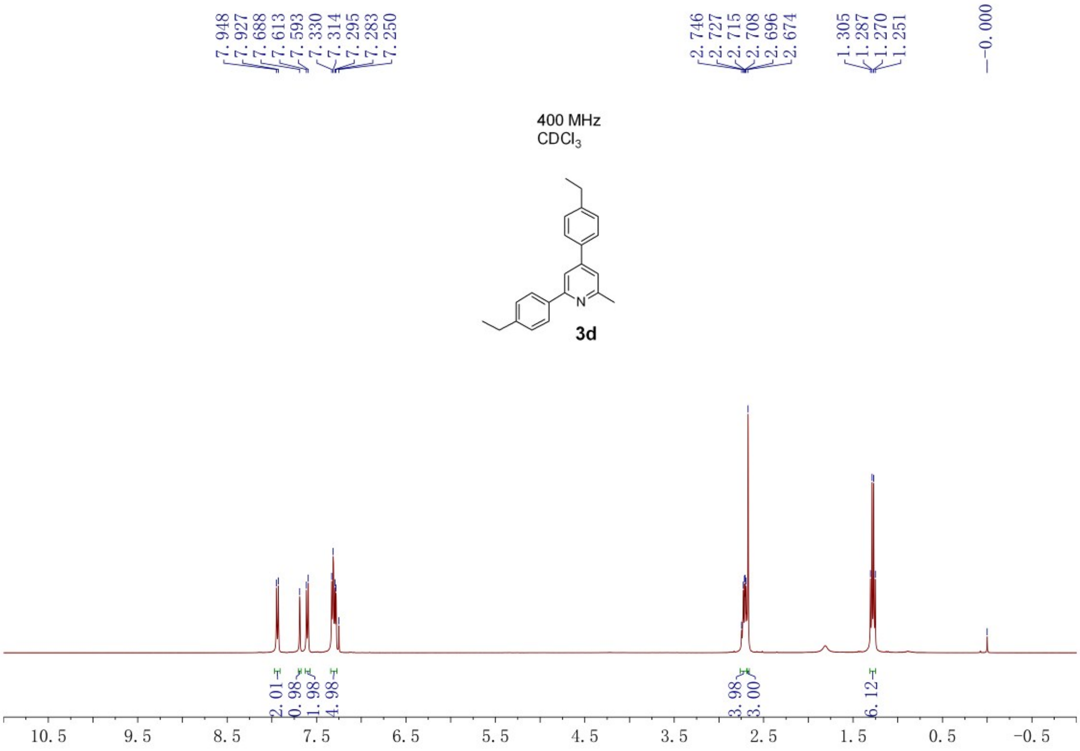
139.49
135.71
135.02
130.67
130.57
129.63
129.27
128.17
128.11
126.01
125.87
121.70
121.65
77.32
77.00
76.68
24.67
20.37
20.35
100 MHz
CDCl$_3$
N
3c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10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7.613
7.593
7.330
7.314
7.295
7.283
7.250
2.746
2.727
2.715
2.708
2.696
2.674
1.305
1.287
1.270
1.251
0.000
400 MHz
CDCl$_3$
N
3d
2.01
0.98
1.98
4.98
3.98
3.00
6.12
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
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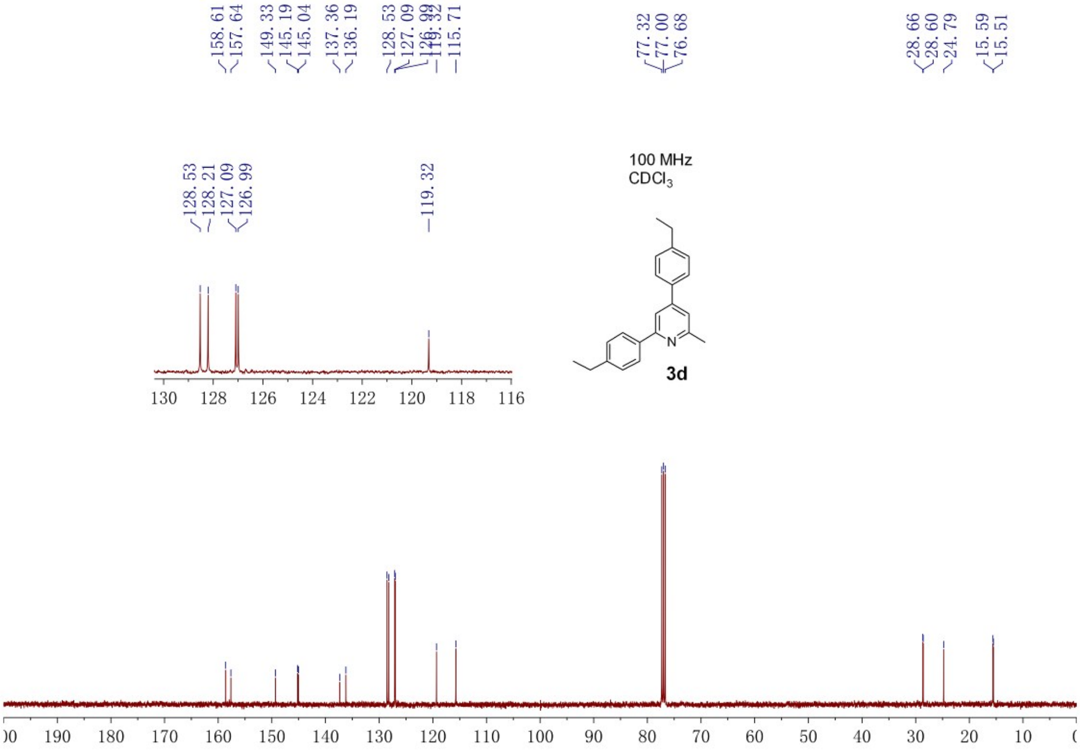
-0.5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149.33
145.19
145.04
137.36
136.19
128.53
127.09
126.99
119.32
115.71
77.32
77.00
76.68
28.66
28.60
24.79
15.59
15.51
128.53
128.21
127.09
126.99
119.32
130
128
126
124
122
120
118
116
100 MHz
CDCl$_3$
N
3d
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180
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160
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120
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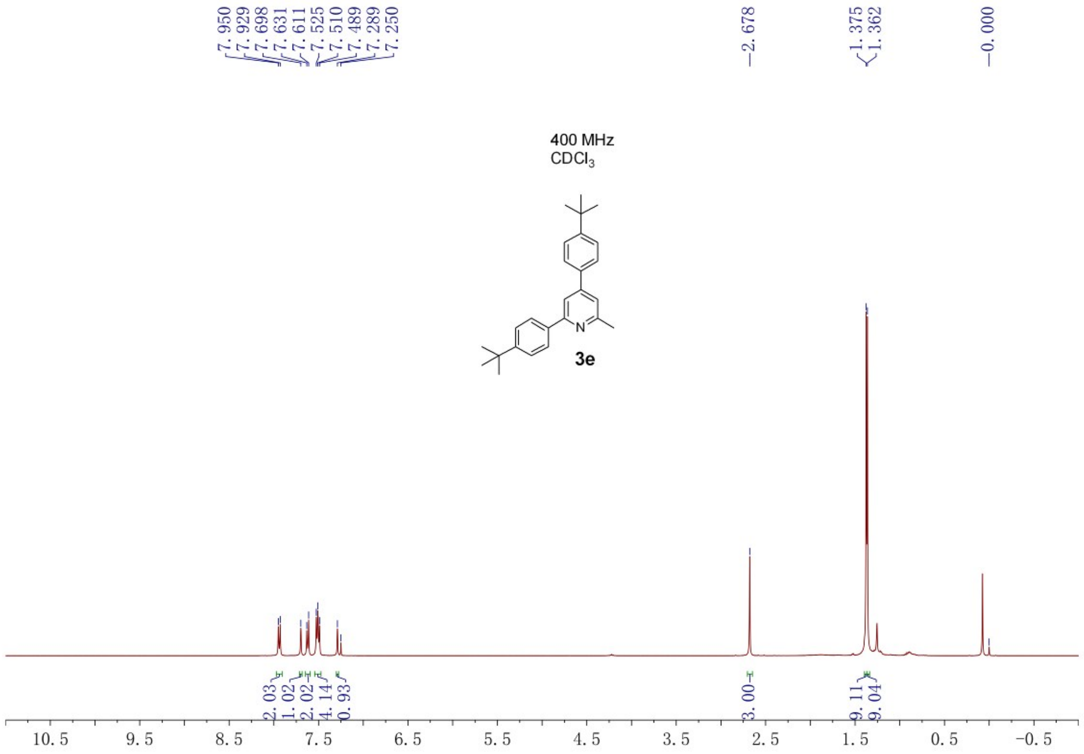
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7.289
7.250
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1.375
1.362
0.000
400 MHz
CDCl$_3$
N
3e
2.03
1.02
2.02
4.14
0.93
3.00
9.11
9.04
10.5
9.5
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7.5
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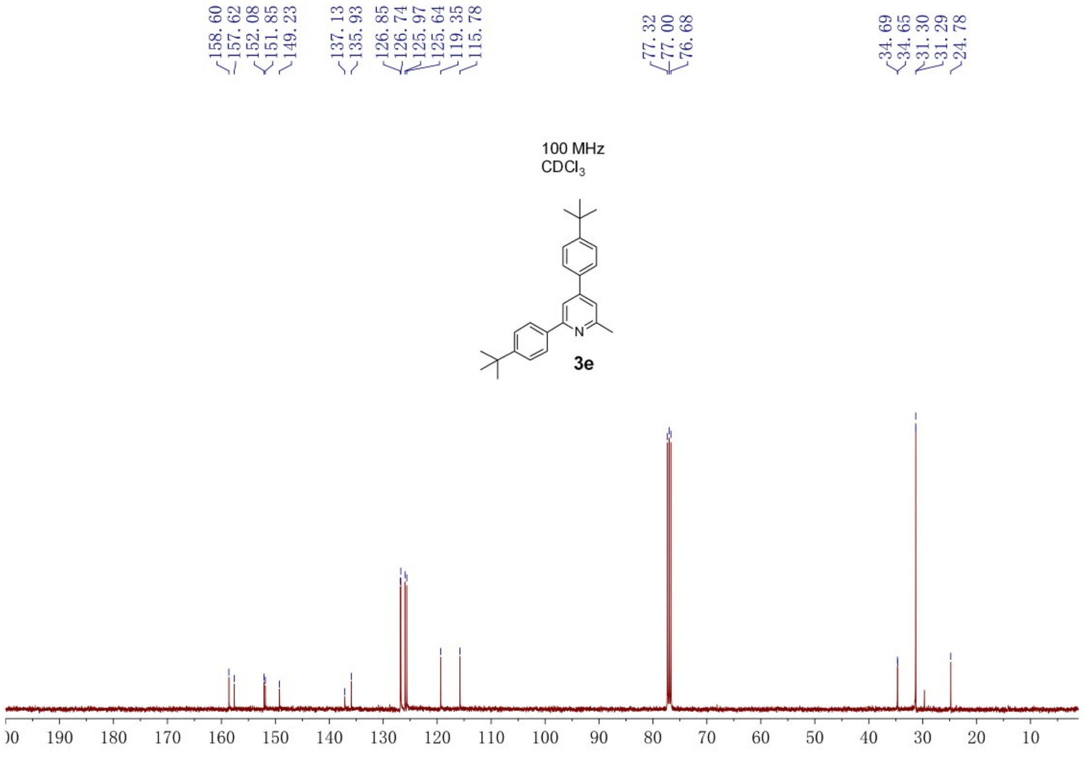
5.5
4.5
3.5
2.5
1.5
0.5
-0.5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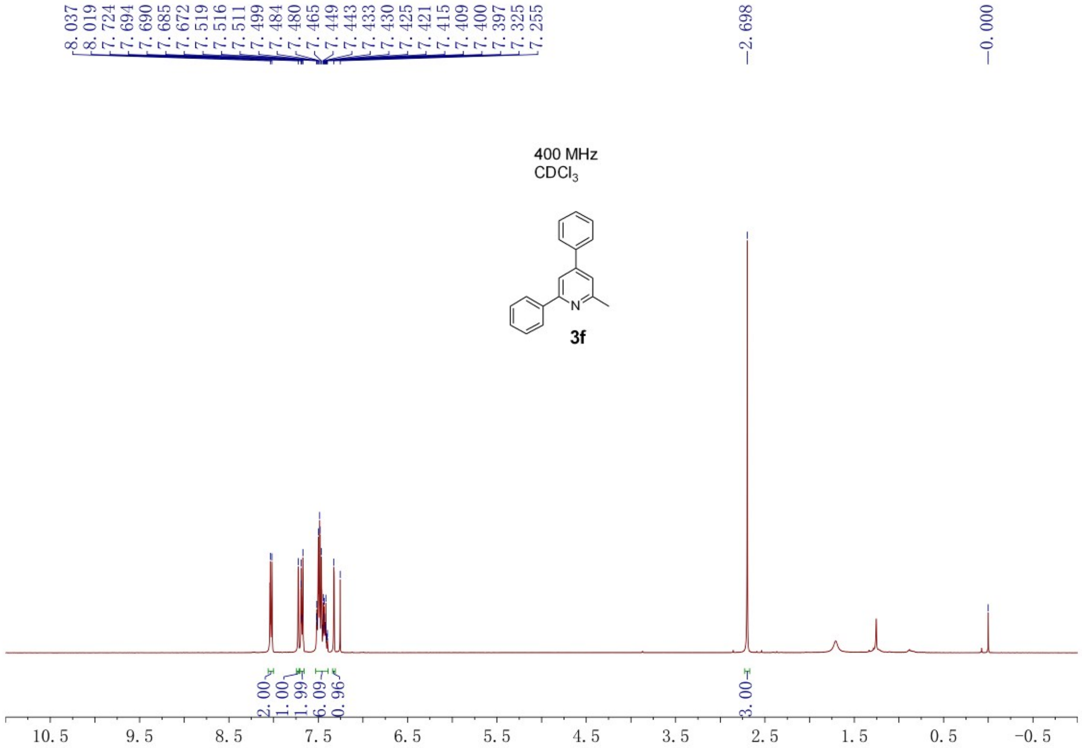
125.97
125.64
119.35
115.78
77.32
77.00
76.68
34.69
34.65
31.30
31.29
24.78
100 MHz
CDCl$_3$
N
3e
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10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7.465
7.449
7.443
7.433
7.430
7.425
7.421
7.415
7.409
7.400
7.397
7.325
7.255
2.698
0.000
400 MHz
CDCl$_3$
N
3f
2.00
1.00
1.99
6.09
0.96
3.00
10.5
9.5
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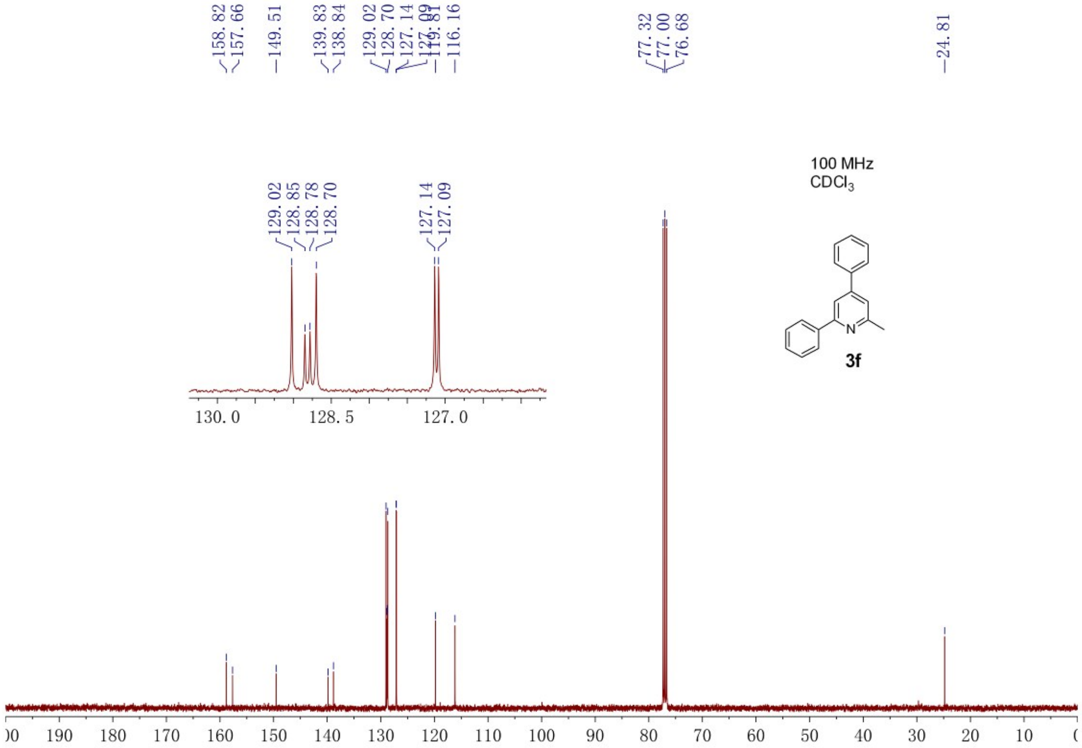
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77.00
76.68
24.81
100 MHz
CDCl$_3$
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128.85
128.78
128.70
127.14
127.09
130.0
128.5
127.0
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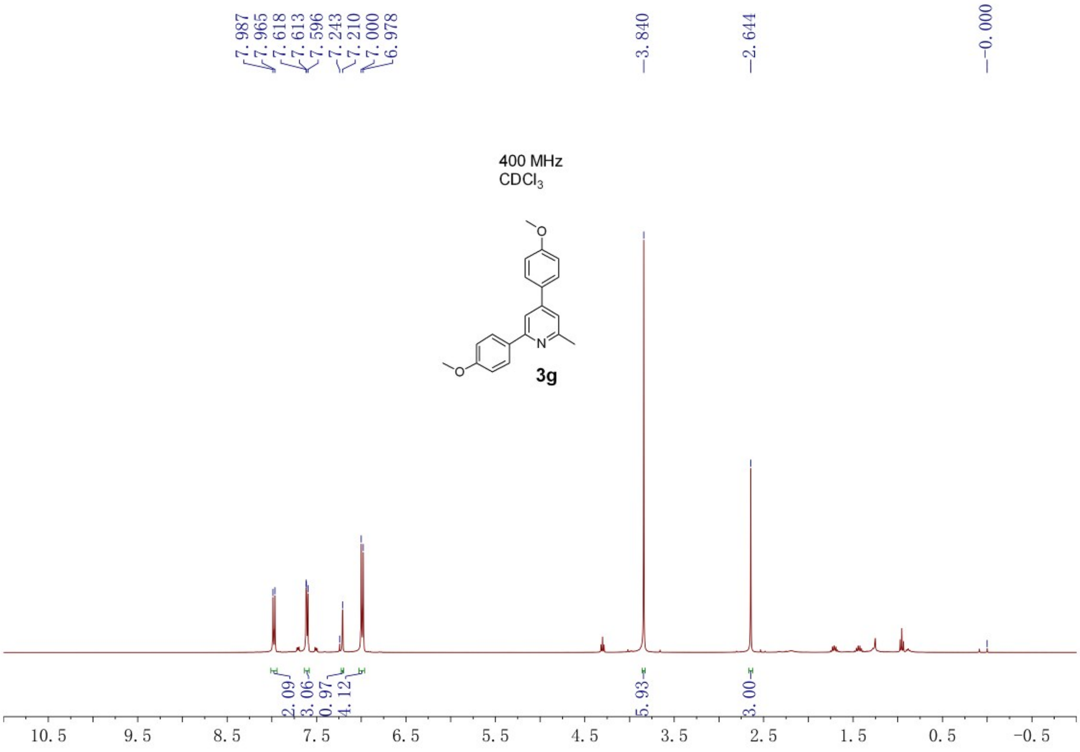
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400 MHz
CDCl3
N
O
O
3g
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5.93
3.00
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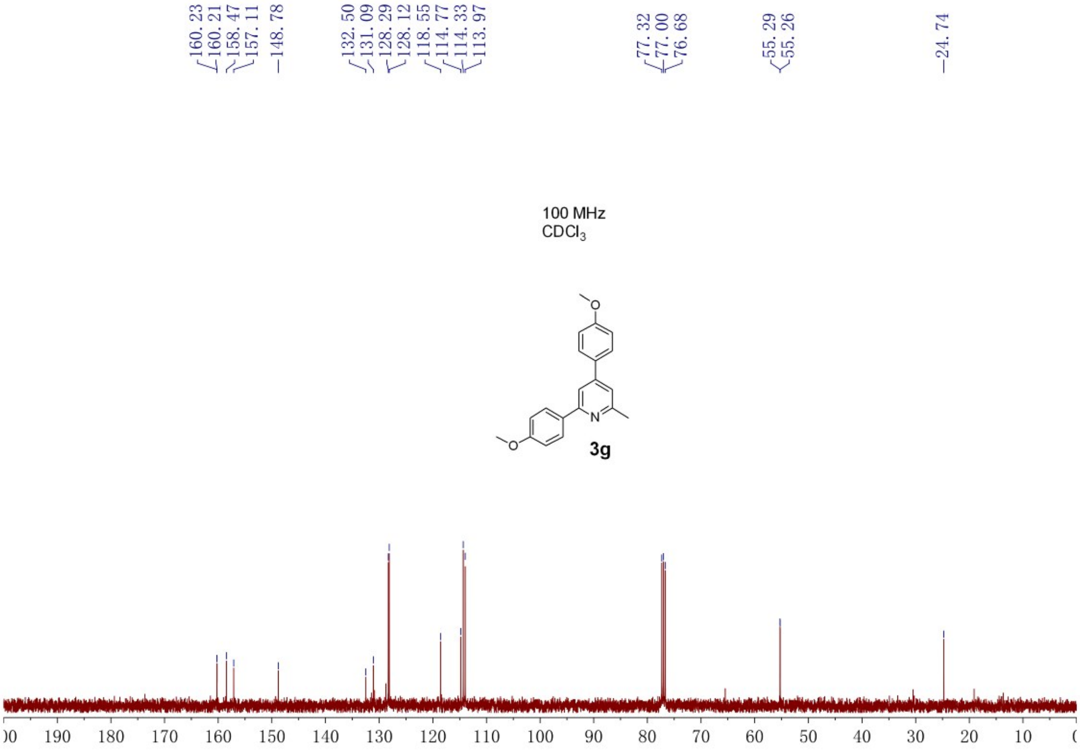
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131.09
128.29
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114.77
114.33
113.97
77.32
77.00
76.68
55.29
55.26
24.74
100 MHz
CDCl3
N
O
O
3g
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40
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20
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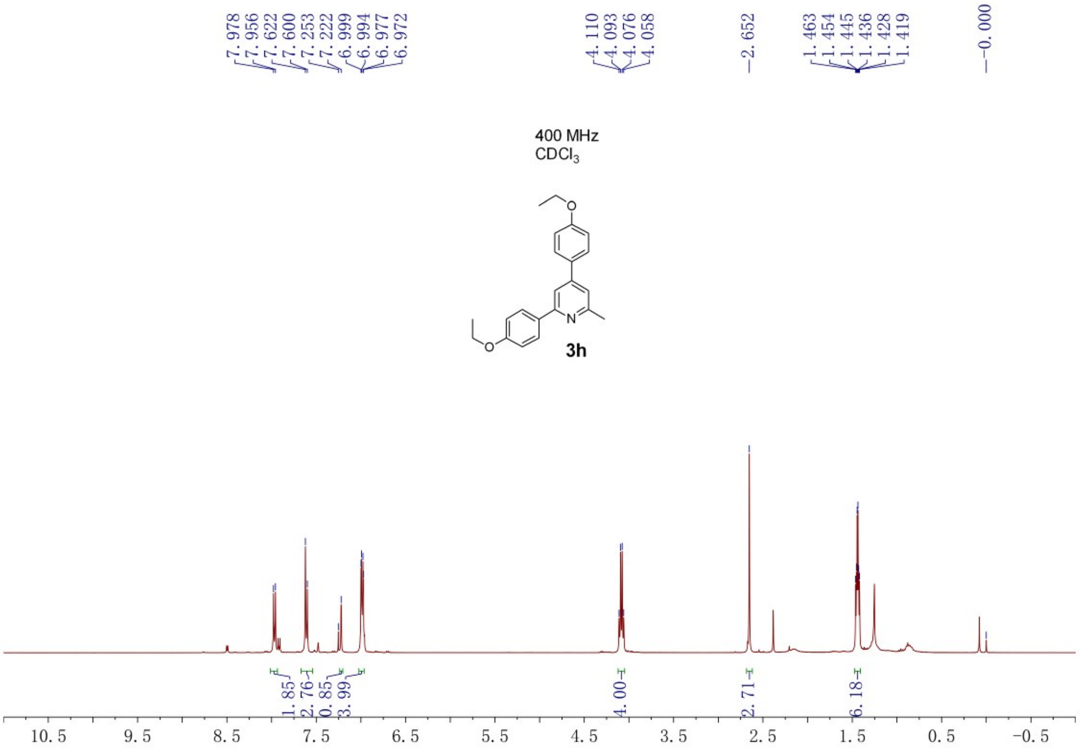
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6.994
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4.110
4.093
4.076
4.058
2.652
1.463
1.454
1.445
1.436
1.428
1.419
0.000
400 MHz
$CDCl_3$
N
O
O
3h
1.85
2.76
0.85
3.99
4.00
2.71
6.18
10.5
9.5
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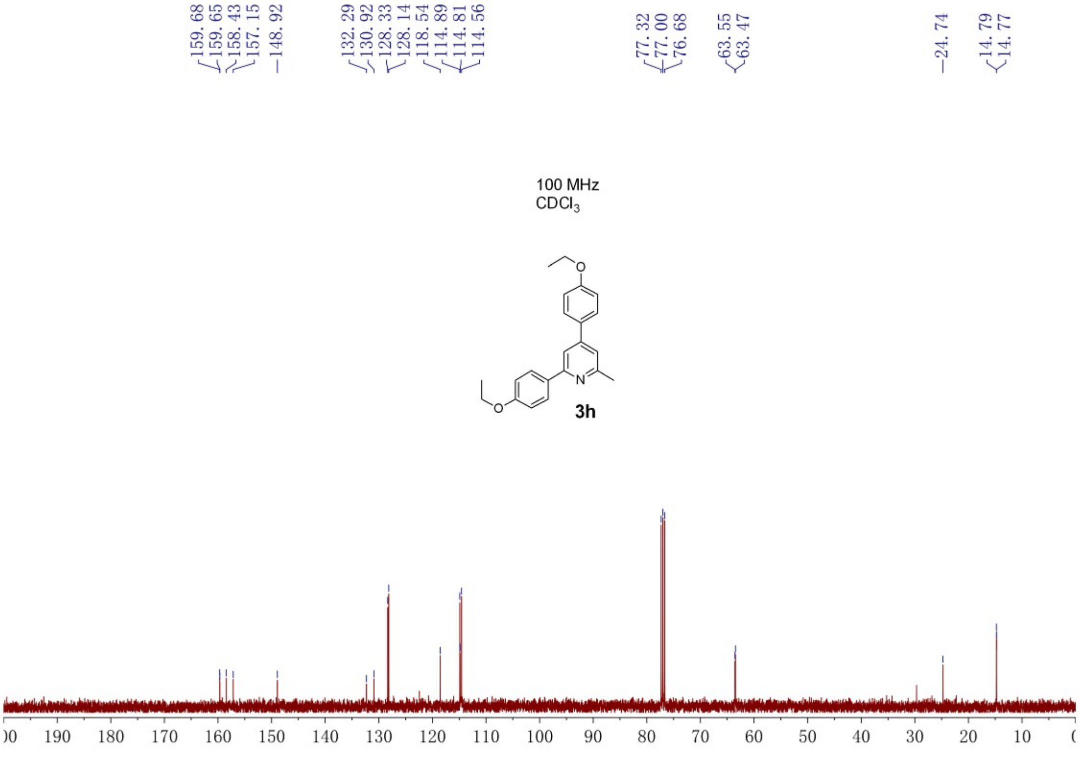
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5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130.92
128.33
128.14
118.54
114.89
114.81
114.56
77.32
77.00
76.68
63.55
63.47
24.74
14.79
14.77
100 MHz
$CDCl_3$
N
O
O
3h
190
180
170
160
150
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130
120
110
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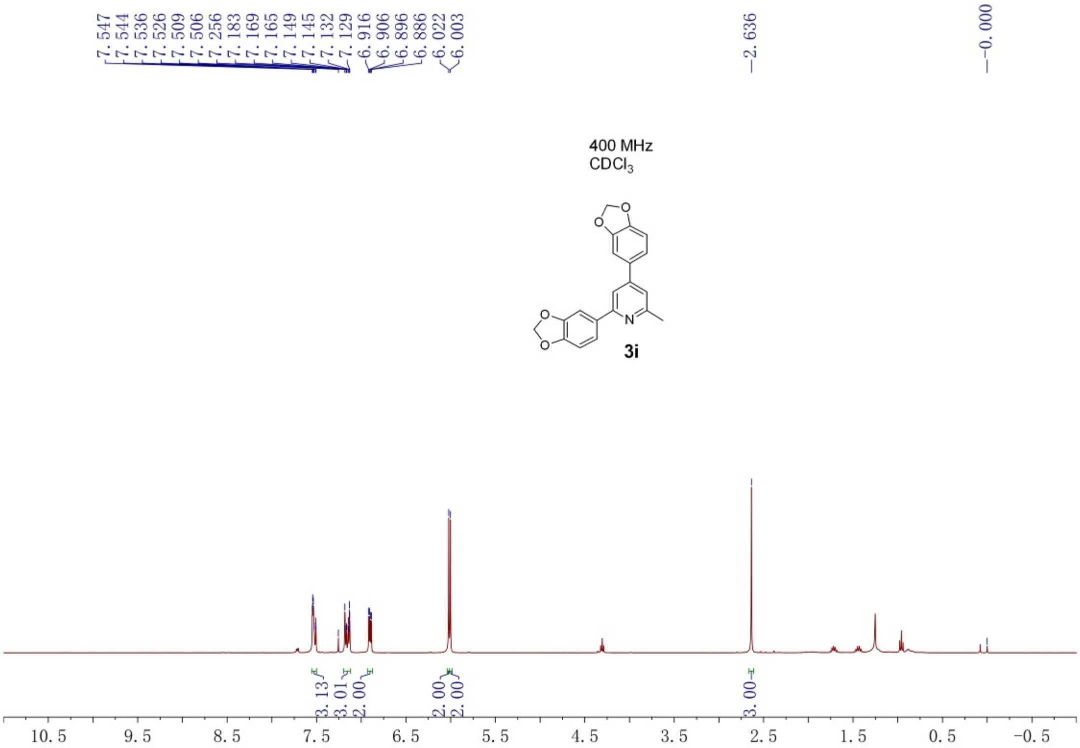
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7.132
7.129
6.916
6.906
6.896
6.886
6.022
6.003
2.636
0.000
400 MHz
CDCl$_3$
O
O
O
O
N
3i
3.13
3.01
2.00
2.00
2.00
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
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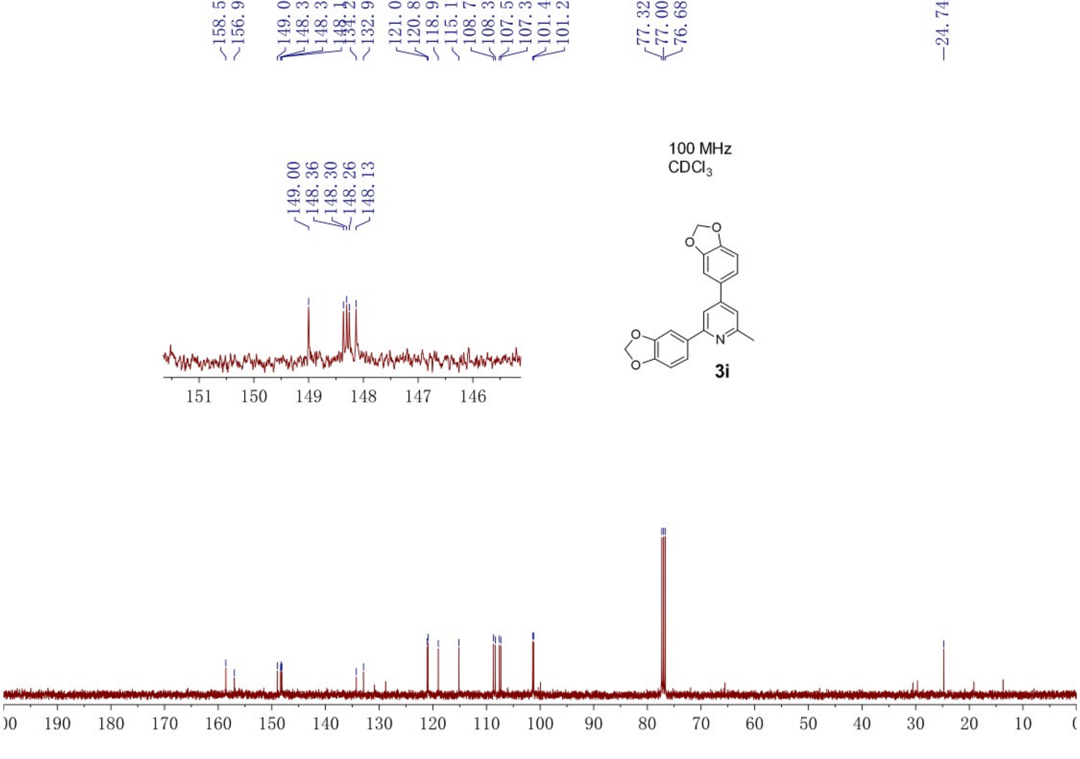
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148.30
148.13
134.25
132.93
121.03
120.89
118.99
115.13
108.73
108.36
107.58
107.32
101.40
101.20
77.32
77.00
76.68
24.74
149.00
148.36
148.30
148.26
148.13
151
150
149
148
147
146
100 MHz
CDCl$_3$
O
O
O
O
N
3i
190
180
170
160
150
140
130
120
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100
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70
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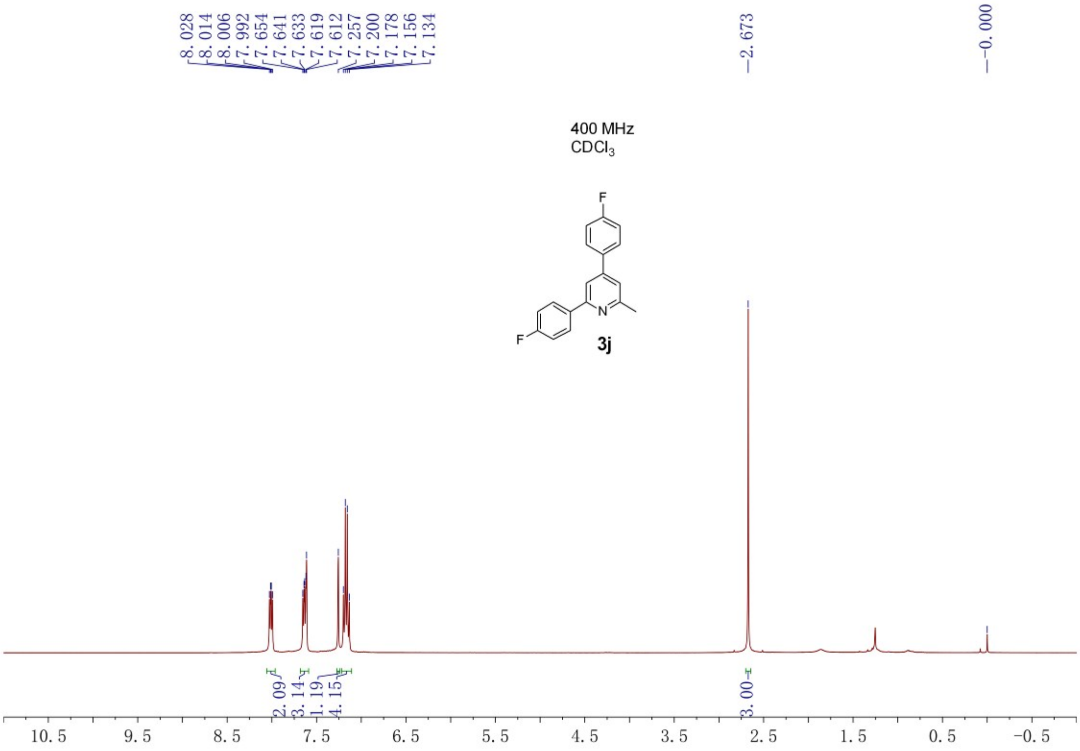
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8.006
7.992
7.654
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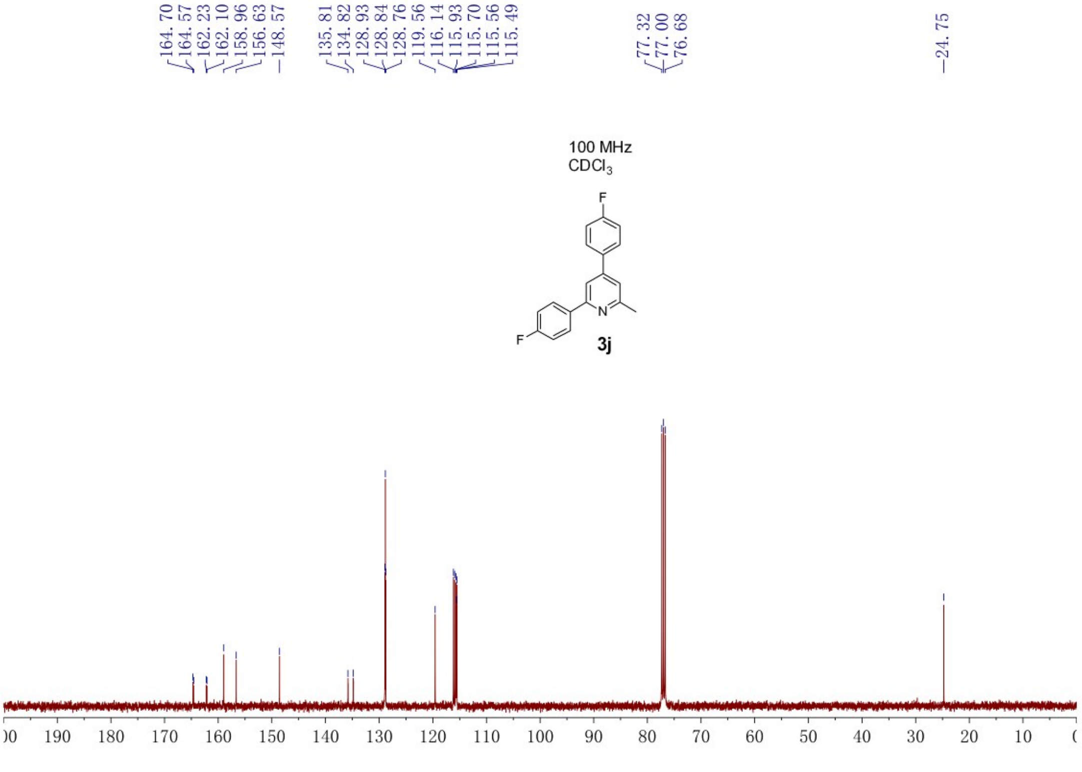
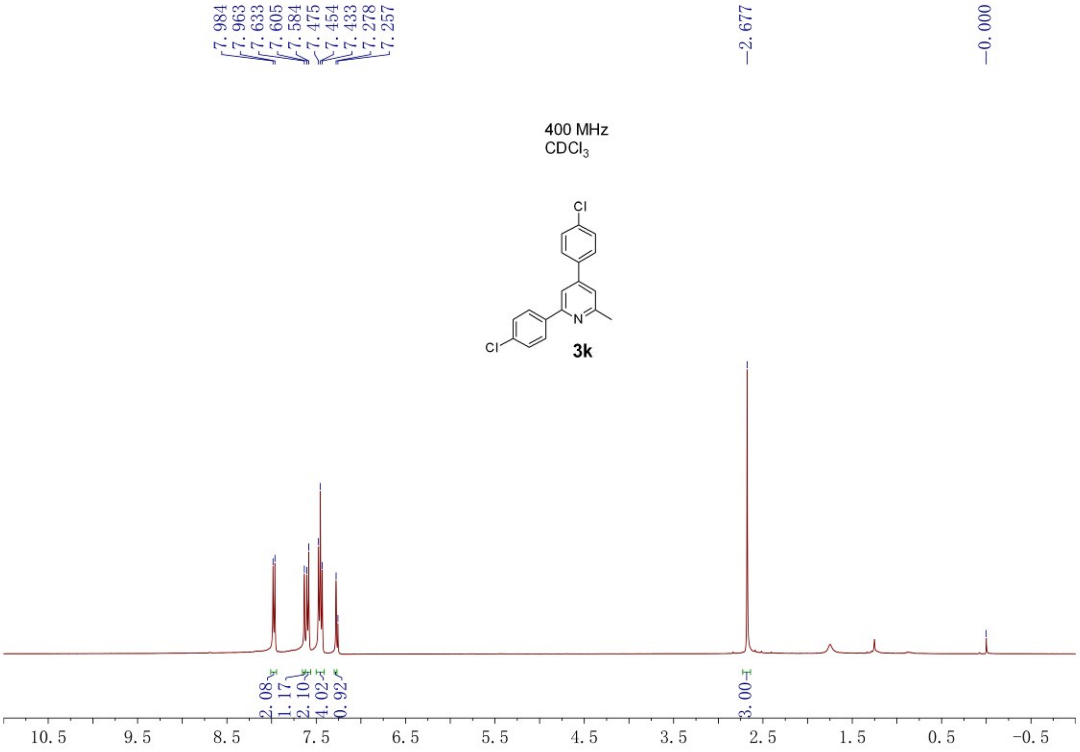
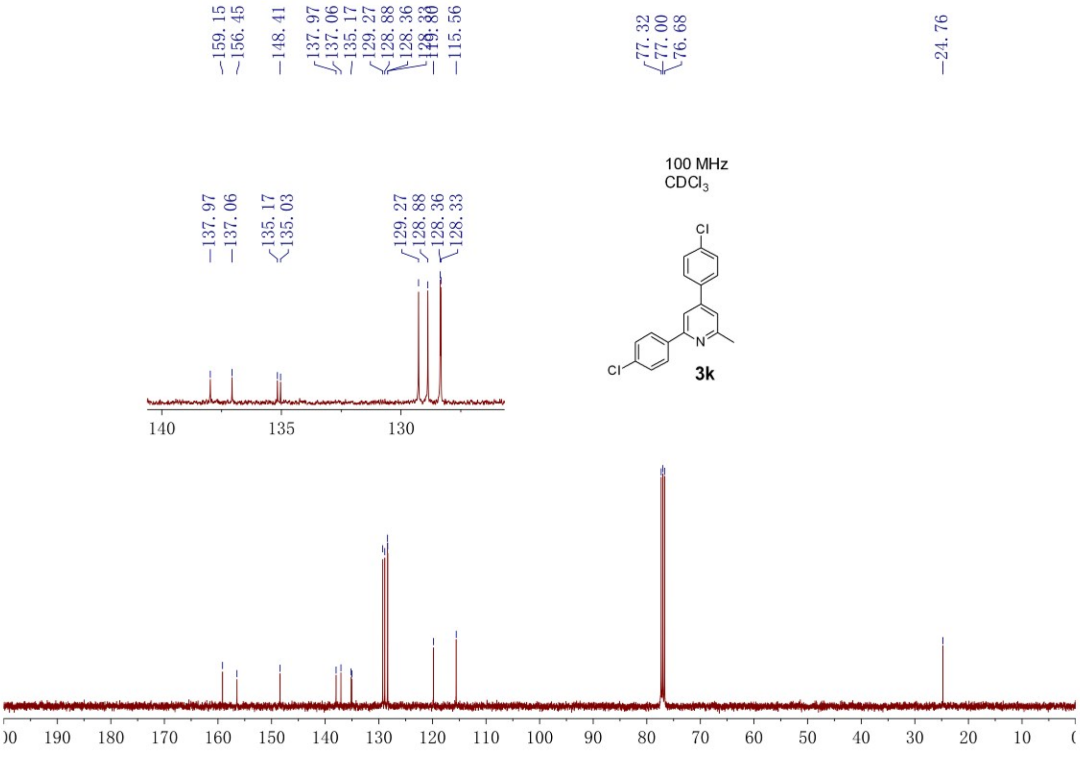
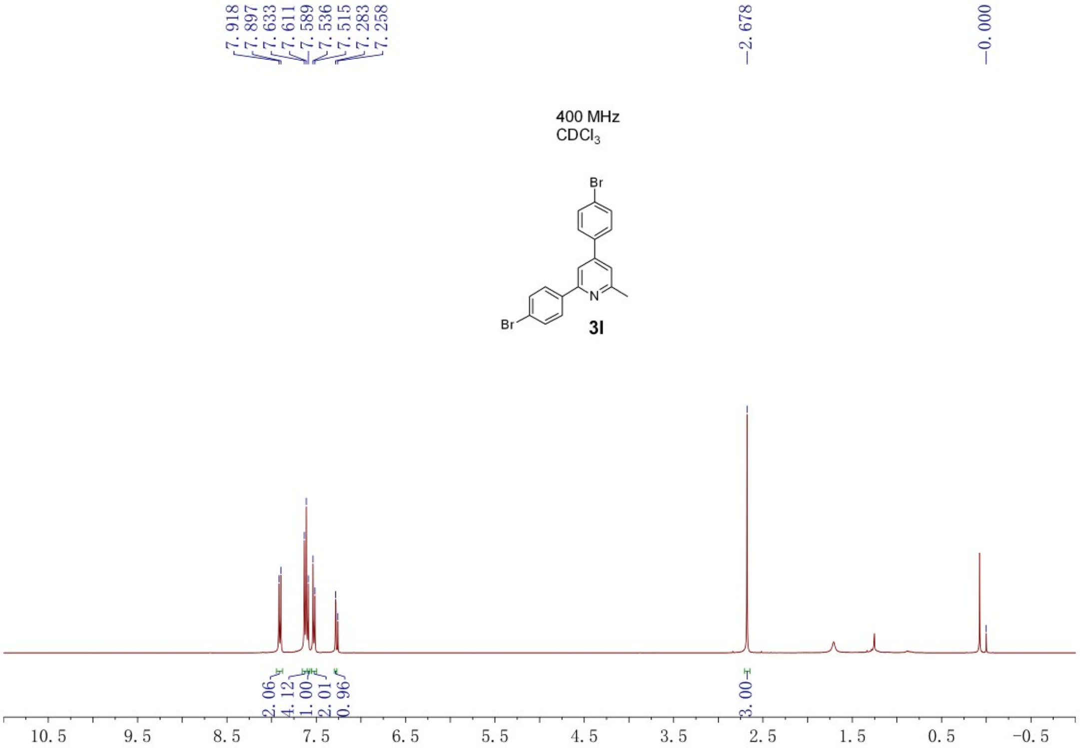
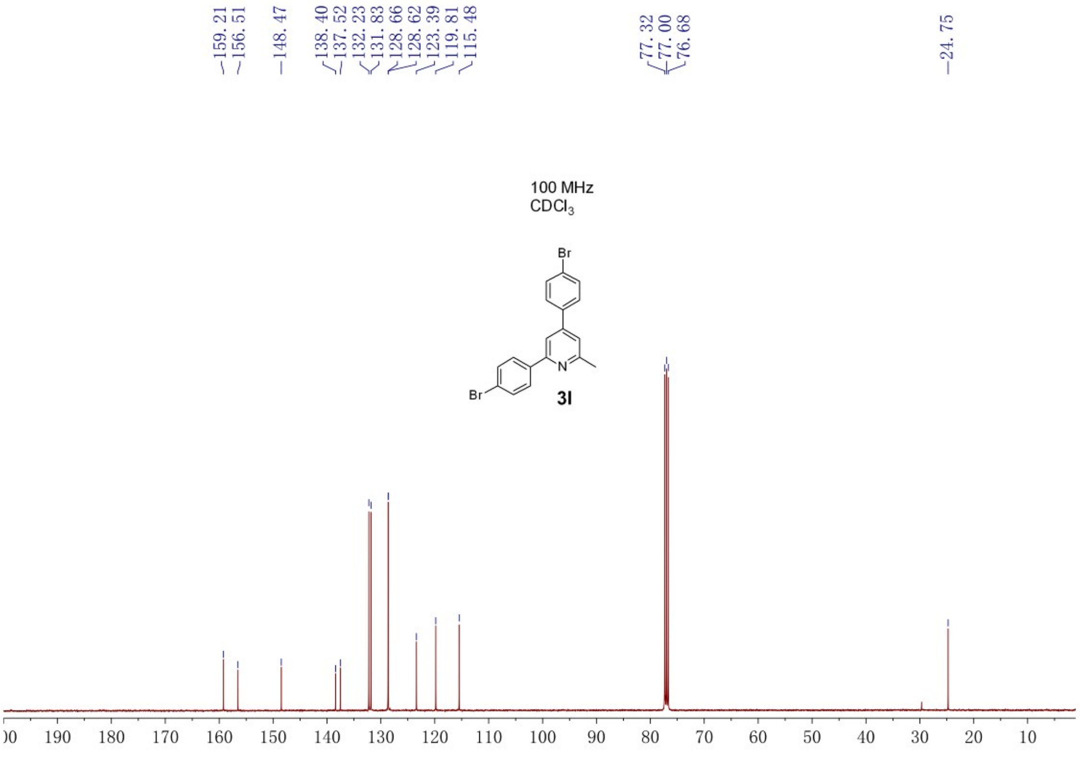
7.633
7.619
7.612
7.257
7.200
7.178
7.156
7.134
2.673
0.000
400 MHz
CDCl3
F
N
F
3j
2.09
3.14
1.19
4.15
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5

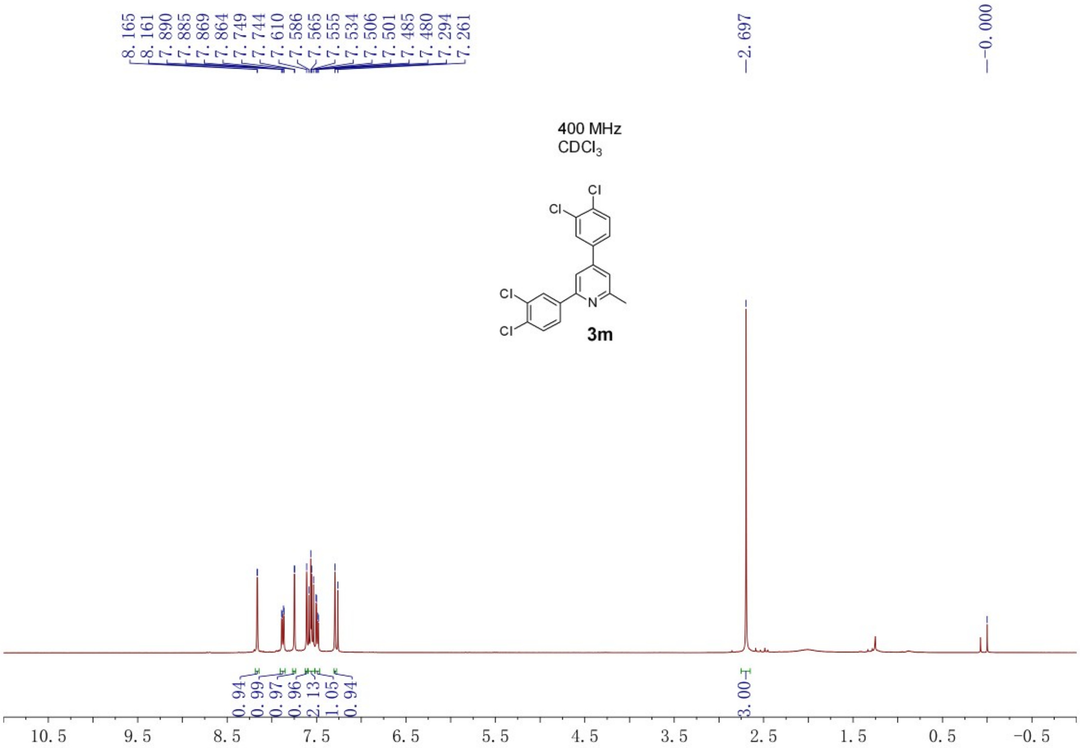

164.70
164.57
162.23
162.10
158.96
156.63
148.57
135.81
134.82
128.93
128.84
128.76
119.56
116.14
115.93
115.70
115.56
115.49
77.32
77.00
76.68
24.75
100 MHz
CDCl3
F
N
F
3j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

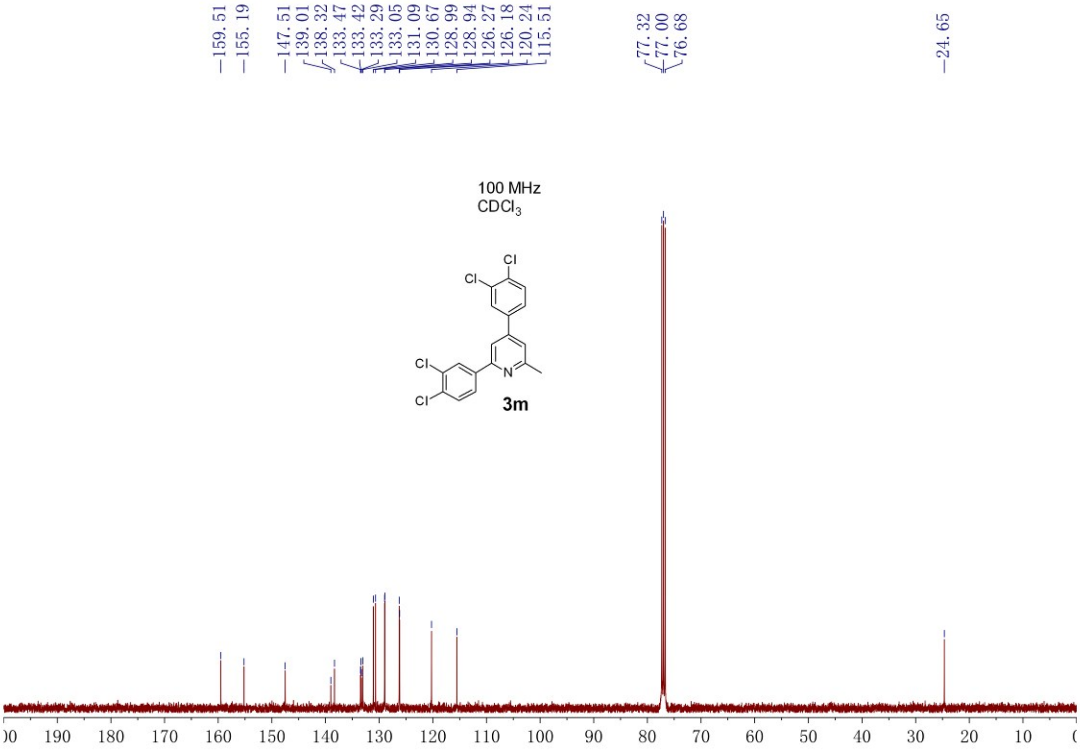

7.984
7.963
7.633
7.605
7.584
7.475
7.454
7.433
7.278
7.257
2.677
0.000
400 MHz
CDCl3
Cl
Cl
N
3k
2.08
1.17
2.10
4.02
0.92
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5

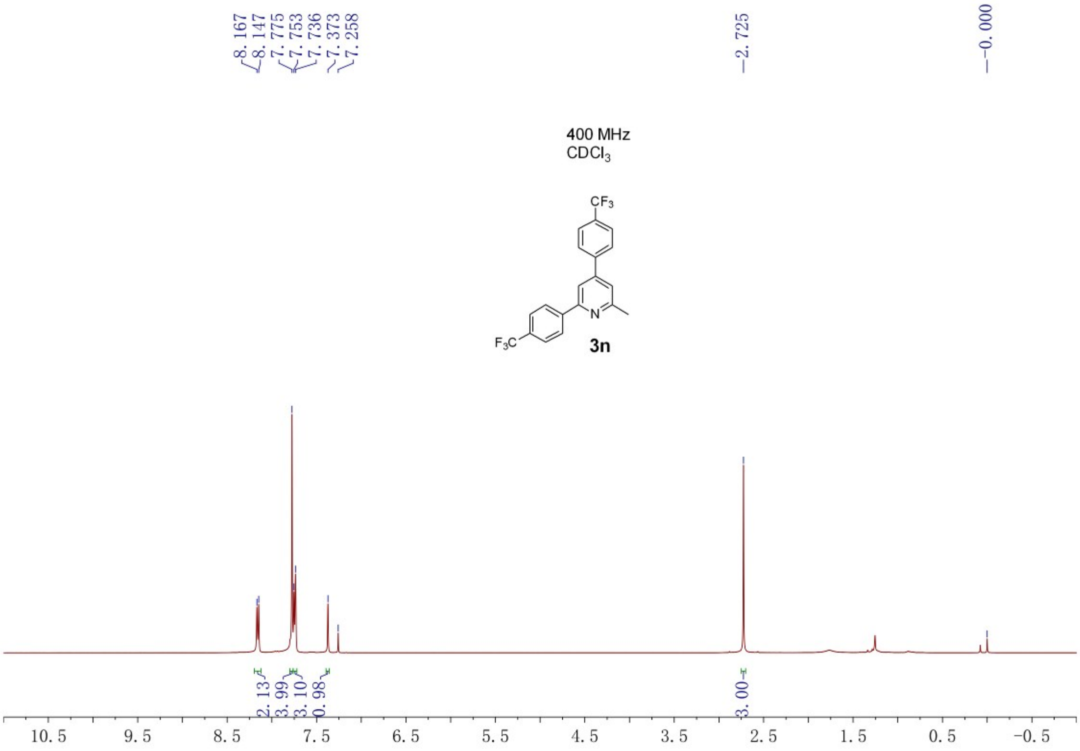

159.15
156.45
148.41
137.97
137.06
135.17
129.27
128.88
128.36
128.33
119.80
115.56
77.32
77.00
76.68
24.76
100 MHz
CDCl3
137.97
137.06
135.17
135.03
129.27
128.88
128.36
128.33
140
135
130
Cl
Cl
N
3k
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

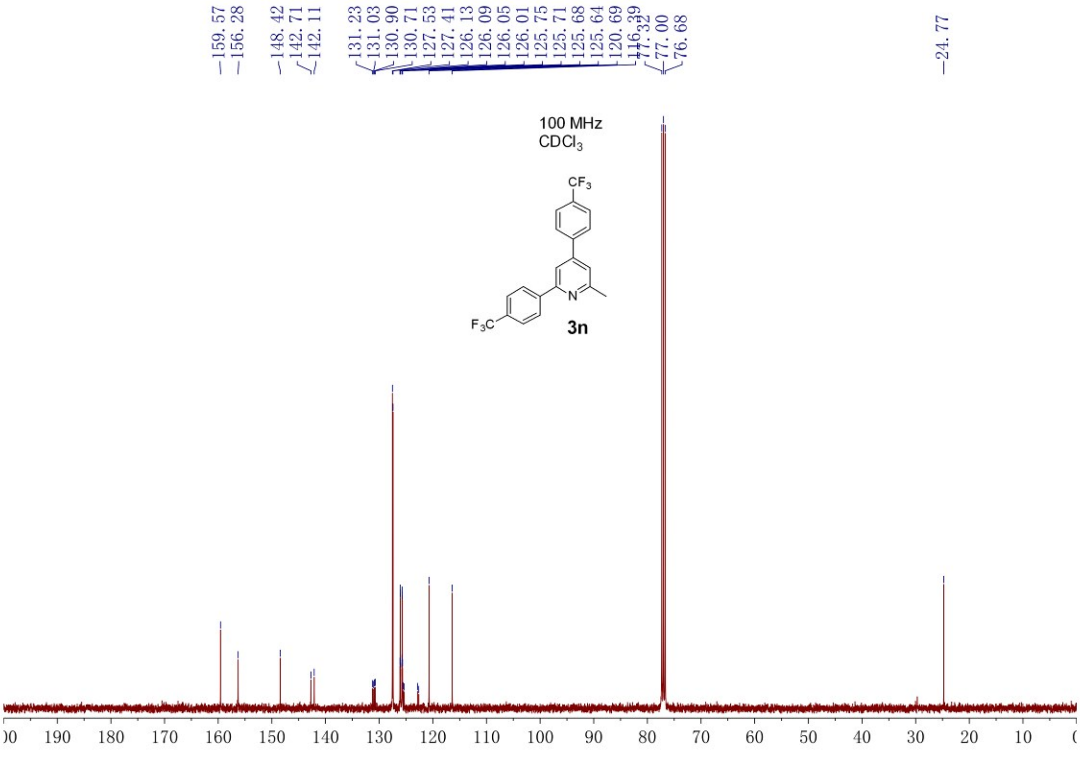

7.918
7.897
7.633
7.611
7.589
7.536
7.515
7.283
7.258
2.678
0.000
400 MHz
CDCl3
Br
Br
N
3l
2.06
4.12
1.00
2.01
0.96
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5

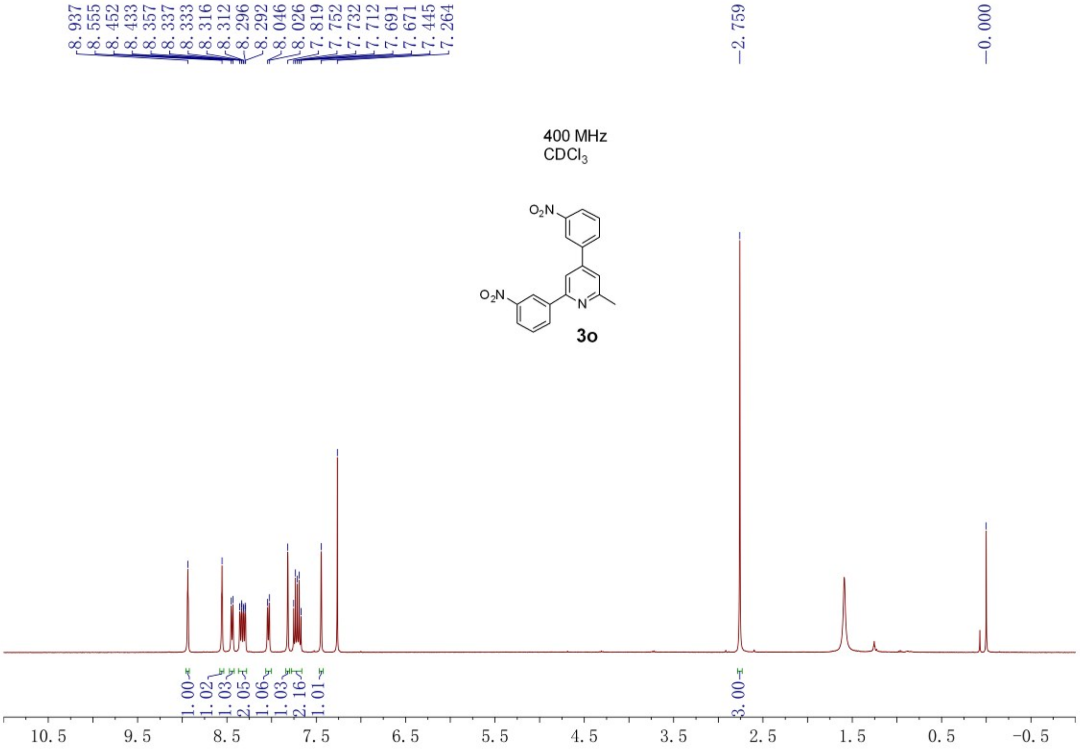

159.21
156.51
148.47
138.40
137.52
132.23
131.83
128.66
128.62
123.39
119.81
115.48
77.32
77.00
76.68
24.75
100 MHz
CDCl3
Br
Br
N
3l
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

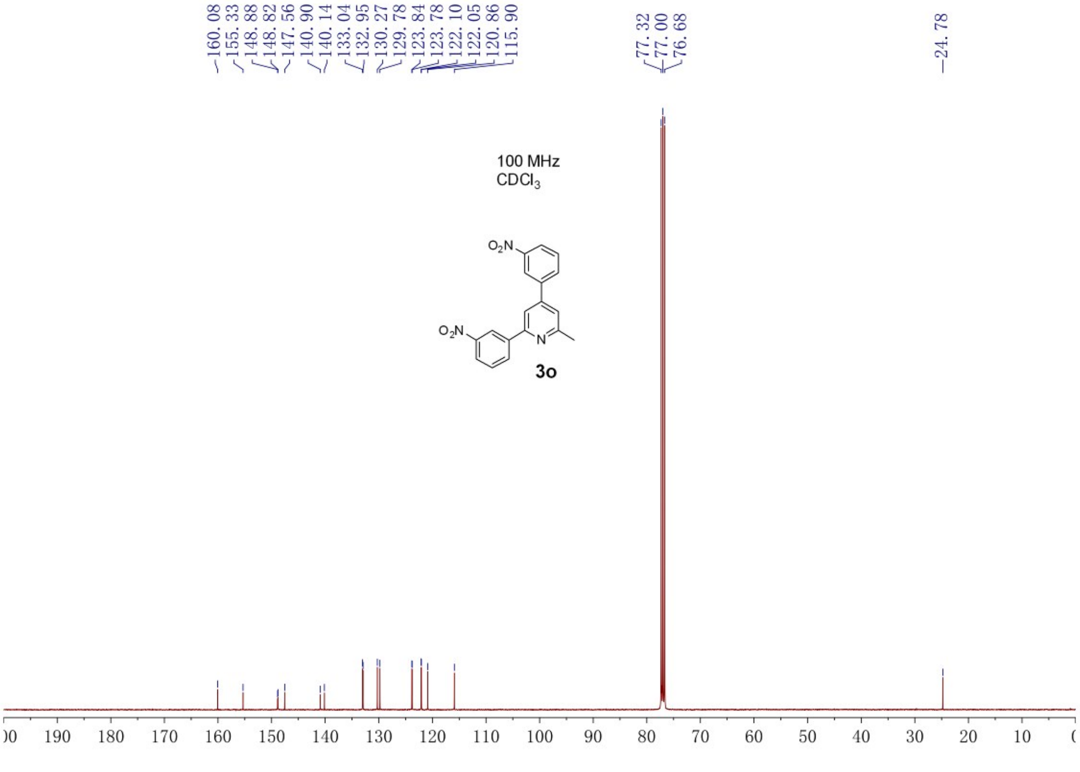

8.165
8.161
7.890
7.885
7.869
7.864
7.749
7.744
7.610
7.586
7.565
7.555
7.534
7.506
7.501
7.485
7.480
7.294
7.261
2.697
0.000
400 MHz
$CDCl_3$
Cl
Cl
Cl
Cl
N
3m
0.94
0.99
0.97
0.96
2.13
1.05
0.94
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5

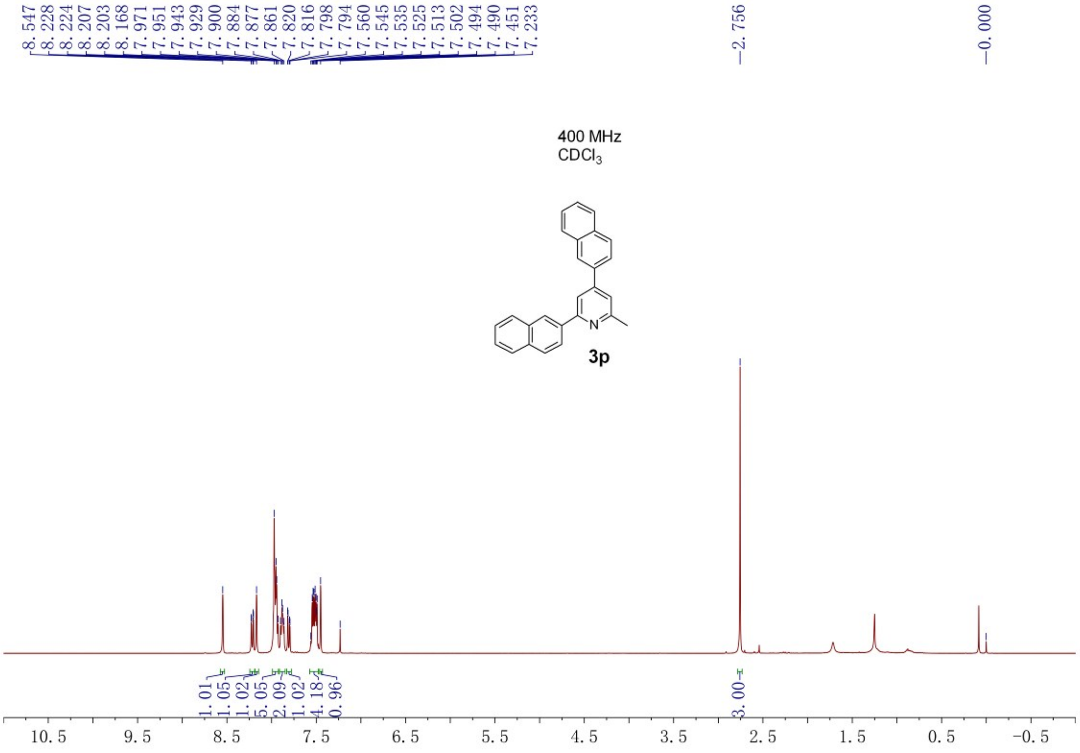

159.51
155.19
147.51
139.01
138.32
133.47
133.42
133.29
133.05
131.09
130.67
128.99
128.94
126.27
126.18
120.24
115.51
77.32
77.00
76.68
24.65
100 MHz
$CDCl_3$
Cl
Cl
Cl
Cl
N
3m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

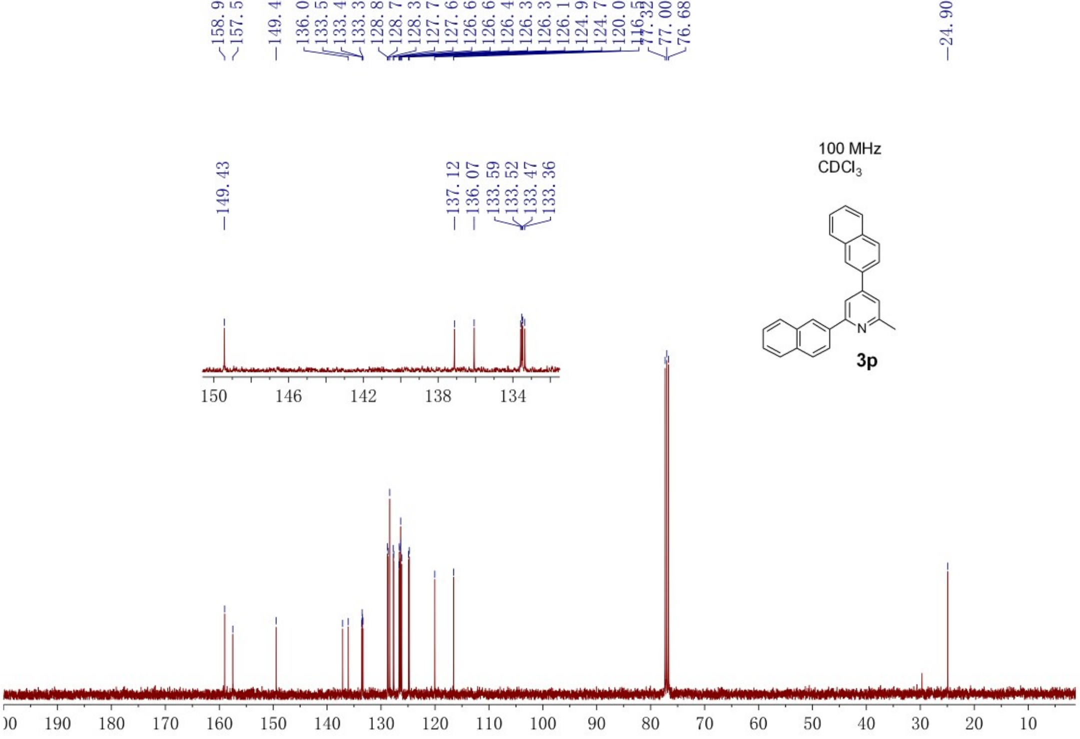

8.167
8.147
7.775
7.753
7.736
7.373
7.258
2.725
0.000
400 MHz
CDCl$_3$
CF$_3$
N
F$_3$C
3n
2.13
3.99
3.10
0.98
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5

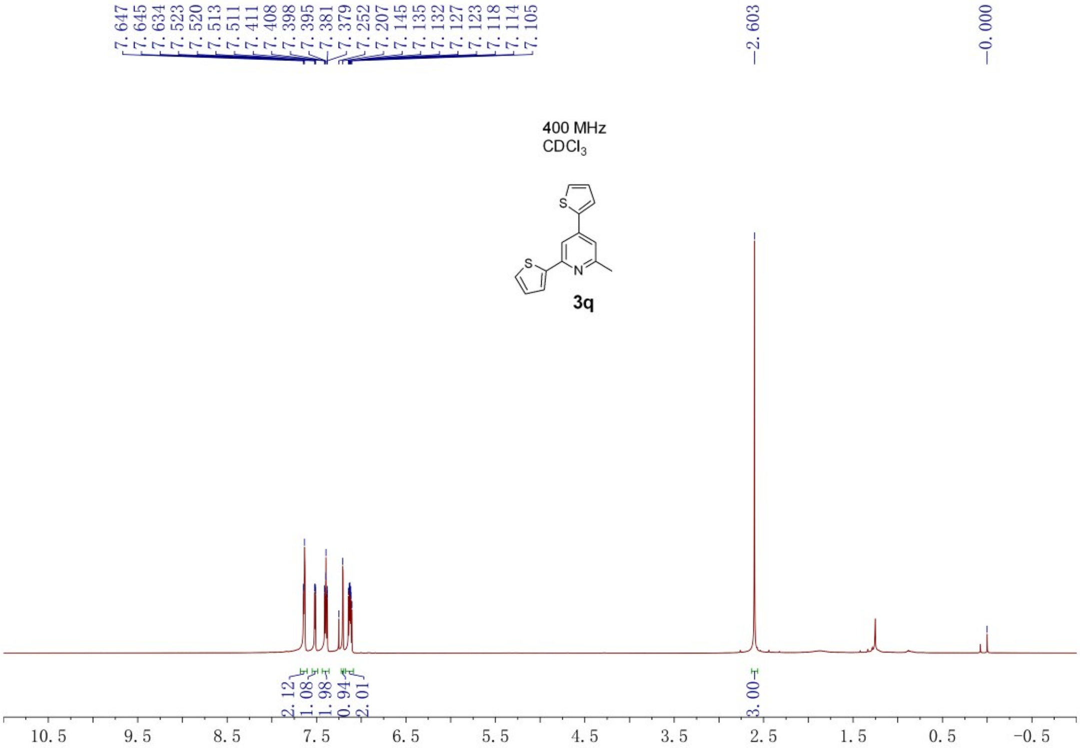

159.57
156.28
148.42
142.71
142.11
131.23
131.03
130.90
130.71
127.53
127.41
126.13
126.09
126.05
126.01
125.75
125.71
125.68
125.64
120.69
116.39
77.32
77.00
76.68
24.77
100 MHz
CDCl$_3$
CF$_3$
N
F$_3$C
3n
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

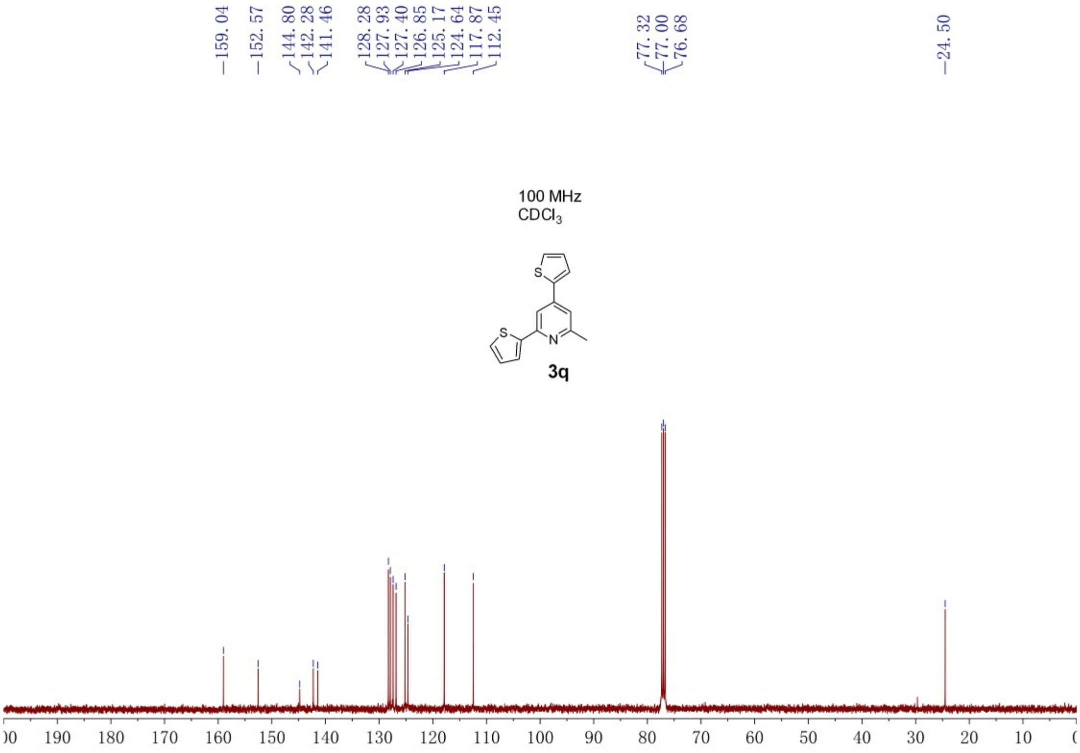

8.937
8.555
8.452
8.433
8.357
8.337
8.333
8.316
8.312
8.296
8.292
8.046
8.026
7.819
7.752
7.732
7.712
7.691
7.671
7.445
7.264
2.759
0.000
400 MHz
CDCl3
O2N
O2N
N
3o
1.00
1.02
1.03
2.05
1.06
1.03
2.16
1.01
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5

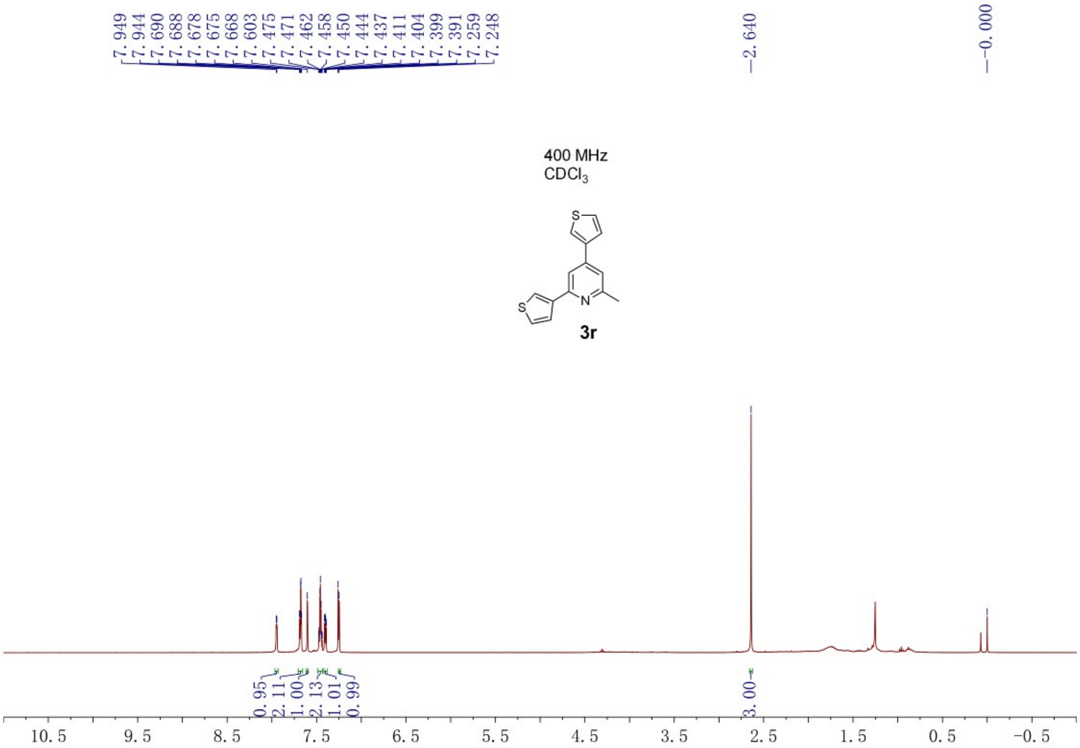

160.08
155.33
148.88
148.82
147.56
140.90
140.14
133.04
132.95
130.27
129.78
123.84
123.78
122.10
122.05
120.86
115.90
77.32
77.00
76.68
24.78
100 MHz
CDCl3
O2N
O2N
N
3o
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

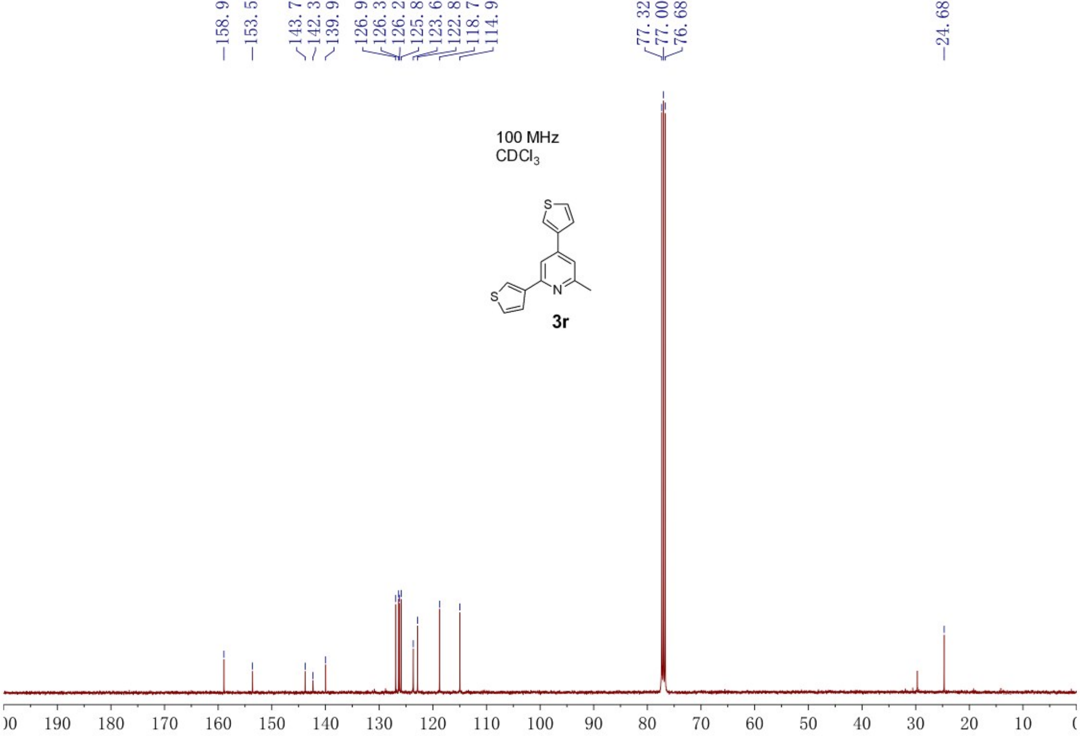

8.547
8.228
8.224
8.207
8.203
8.168
7.971
7.951
7.943
7.929
7.900
7.884
7.877
7.861
7.820
7.816
7.798
7.794
7.560
7.545
7.535
7.525
7.513
7.502
7.494
7.490
7.451
7.233
2.756
0.000
400 MHz
CDCl$_3$
N
3p
1.01
1.05
1.02
5.05
2.09
1.02
4.18
0.96
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5


158.99
157.51
149.43
136.07
133.52
133.47
133.36
128.82
128.71
128.39
127.71
127.65
126.67
126.61
126.44
126.38
126.37
126.18
124.90
124.79
120.04
116.54
77.32
77.00
76.68
24.90
149.43
137.12
136.07
133.59
133.52
133.47
133.36
150
146
142
138
134
100 MHz
CDCl$_3$
N
3p
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


7.647
7.645
7.634
7.523
7.520
7.513
7.511
7.411
7.408
7.398
7.395
7.381
7.379
7.252
7.207
7.145
7.135
7.132
7.127
7.123
7.118
7.114
7.105
2.603
0.000
400 MHz
CDCl3
S
S
N
3q
2.12
1.08
1.98
0.94
2.01
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5


159.04
152.57
144.80
142.28
141.46
128.28
127.93
127.40
126.85
125.17
124.64
117.87
112.45
77.32
77.00
76.68
24.50
100 MHz
CDCl3
S
S
N
3q
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


7.949
7.944
7.690
7.688
7.678
7.675
7.668
7.603
7.475
7.471
7.462
7.458
7.450
7.444
7.437
7.411
7.404
7.399
7.391
7.259
7.248
2.640
0.000
400 MHz
CDCl3
S
S
N
3r
0.95
2.11
1.00
2.13
1.01
0.99
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5


158.93
153.59
143.79
142.32
139.98
126.90
126.37
126.20
125.89
123.65
122.84
118.74
114.95
77.32
77.00
76.68
24.68
100 MHz
CDCl3
S
S
N
3r
190
180
170
160
150
140
130
120
110
100
90
80
70
60
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40
30
20
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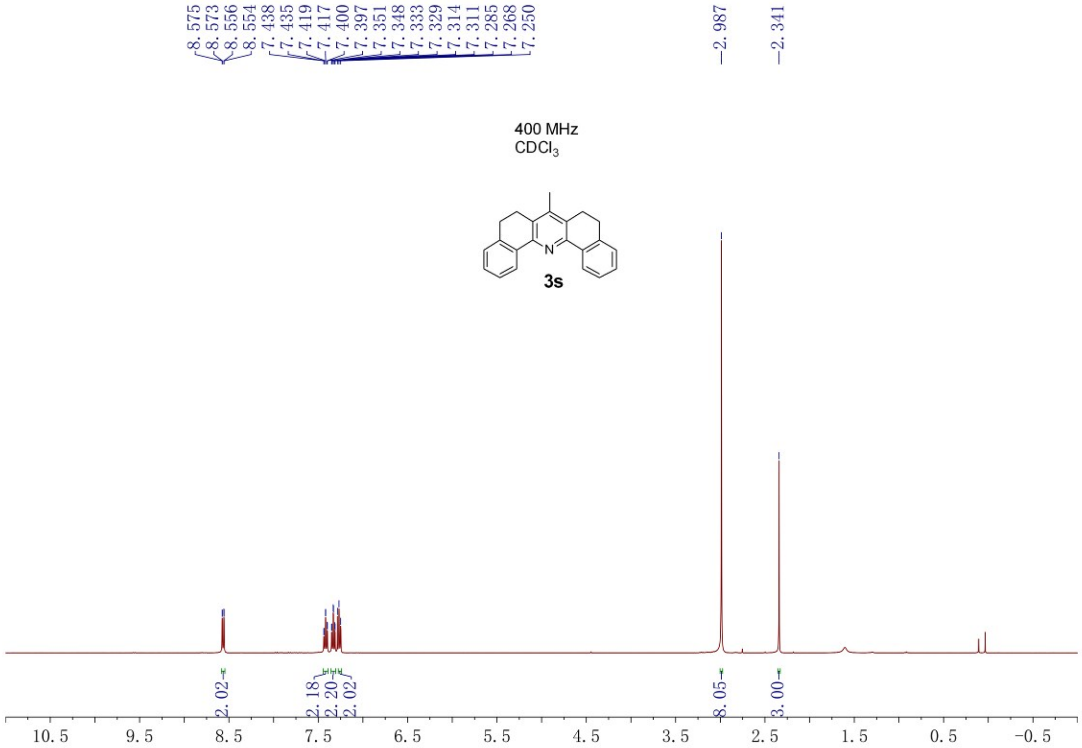
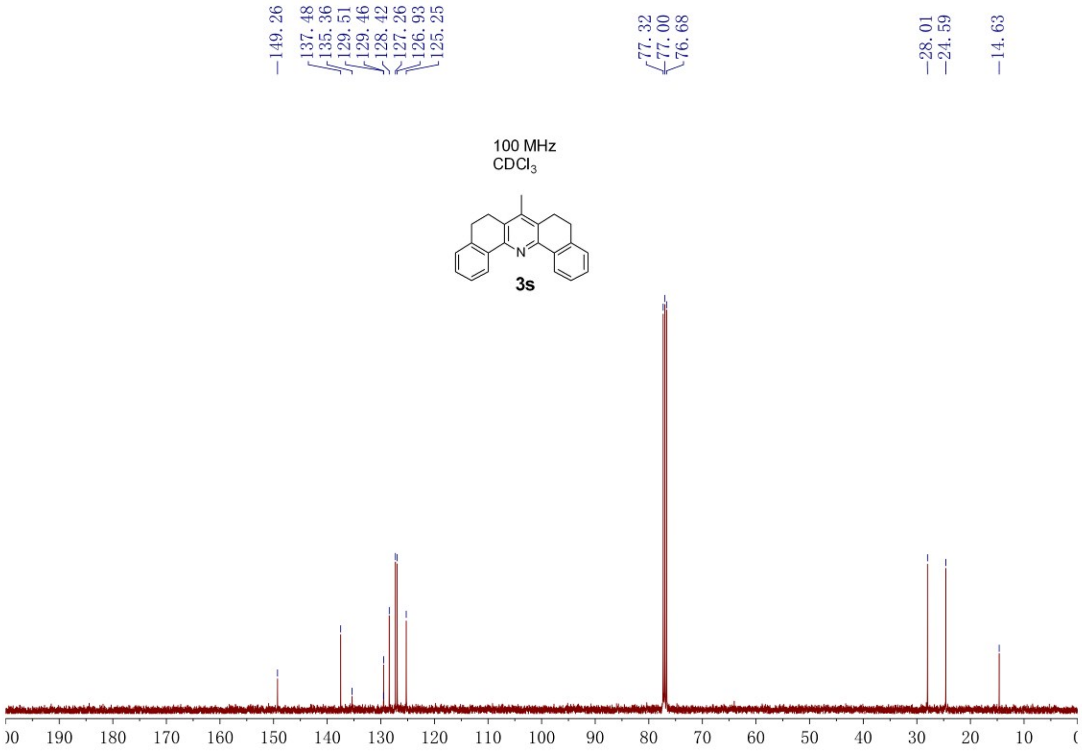
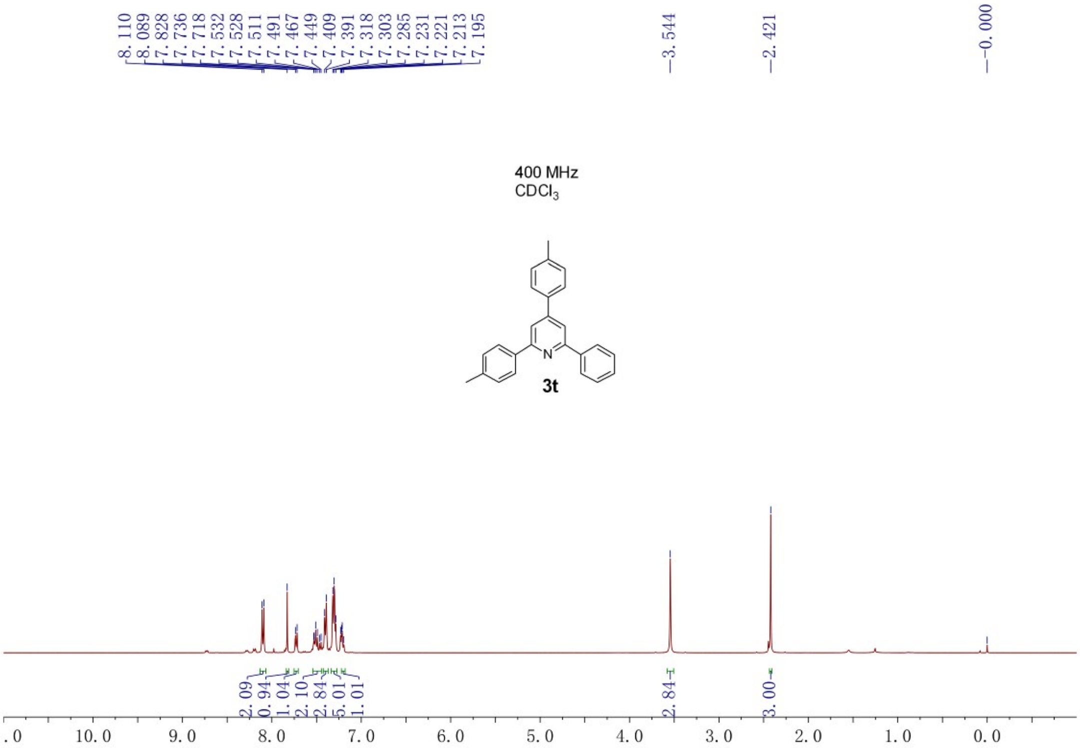

8.575
8.573
8.556
8.554
7.438
7.435
7.419
7.417
7.400
7.397
7.351
7.348
7.333
7.329
7.314
7.311
7.285
7.268
7.250
2.987
2.341
400 MHz
CDCl$_3$
N
3s
2.02
2.18
2.20
2.02
8.05
3.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5


149.26
137.48
135.36
129.51
129.46
128.42
127.26
126.93
125.25
77.32
77.00
76.68
28.01
24.59
14.63
100 MHz
CDCl$_3$
N
3s
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


8.110
8.089
7.828
7.736
7.718
7.532
7.528
7.511
7.491
7.467
7.449
7.409
7.391
7.318
7.303
7.285
7.231
7.221
7.213
7.195
3.544
2.421
0.000
400 MHz
CDCl3
N
3t
2.09
0.94
1.04
2.10
2.84
5.01
1.01
2.84
3.00
.0
10.0
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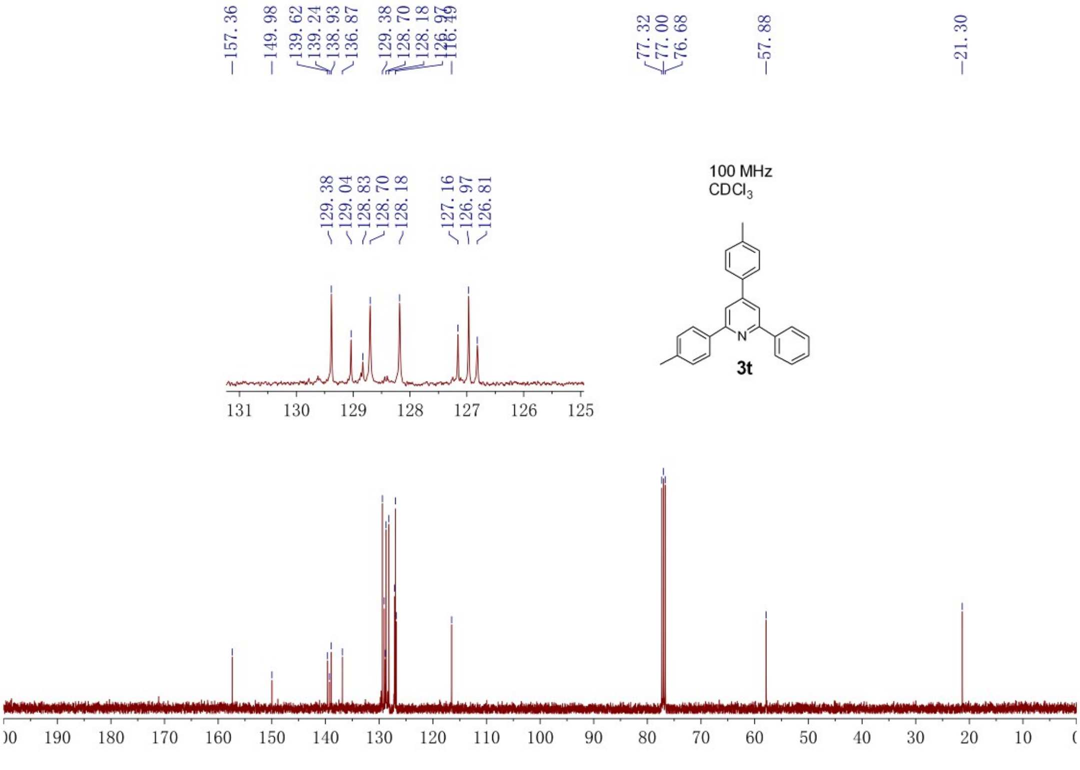
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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149.98
139.62
139.24
138.93
136.87
129.38
128.70
128.18
126.97
116.49
77.32
77.00
76.68
57.88
21.30
129.38
129.04
128.83
128.70
128.18
127.16
126.97
126.81
131
130
129
128
127
126
125
100 MHz
CDCl3
N
3t
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10