Supporting Information

Metal-Free Oxidative *para*-Acylation of Unprotected Anilines with Methyl Groups *via* Dual C-H Activation

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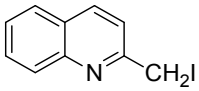
Contents:

General information

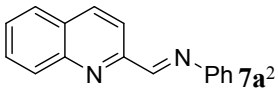
All reactions were carried out under O_2 atmosphere (1 atm) using standard Schlenk technique in the parallel synthesizer. All reagent/reactant were commercially available unless other noted (I_2 and salicylic acid were purchased from Energy Chemical). DMSO used was purchased from Aladdin Chemical. Column chromatography was performed using Silica Gel 60 (particle size 37-54 μm). The pure products were obtained by column chromatography using ethyl acetate/petroleum ether/NEt_3 as the eluent and characterized by NMR spectroscopy using d_6-DMSO as the deuterium reagent. GC analysis was performed on GC 7820A (Shimadzu). GC-MS results were recorded on GC-MS QP2010 (Shimadzu). The ^{1}H NMR and ^{13}C NMR data were acquired on a Brucker ADVANCE III spectrometer (400 MHz for ^{1}H NMR spectroscopy and 100 MHz for ^{13}C NMR spectroscopy). HRMS analysis was conducted at the College of Chemistry and Materials Engineering, Wenzhou University, Wenzhou, 325000, China

***Synthetic procedures for* 5a, 7a, 1a-CD$_3$**



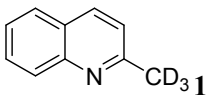
5a[1]

A 25 mL schlenk tube was charged with PPh_3 (0.03 mmol), $NaHCO_3$ (0.45 mmol), I_2 (0.45 mmol) and a stir bar, then degassed and refilled with N_2 for 3 times. After addition of 2 mL anhydrous THF and **1a** (0.3 mmol) under N_2 atmosphere with stirring, the mixture was further stirred overnight at 120°C and then cooled to room temperature. The mixture was quenched with 5-10 mL saturated $Na_2S_2O_3$ solution. Afterwards, the solution was extracted with CH_2Cl_2 (3×3 mL) and washed with brine (3×5 mL). The organic layer was dried over Na_2SO_4 (10-30 min) and concentrated, the residues were passed through a short silica chromatography column (particle size 37–54 μm, petroleum ether/ethyl acetate as eluent) to afford analytically pure product **5a** (yellow solid).



7a[2]

To a 100 mL round bottom flask charged with **6a** (0.383g, 2.44 mmol) and a stir bar, 10 mL anhydrous CH_2Cl_2 was added under N_2 atmosphere. Then aniline (0.227 g, 2.44 mmol) was added dropwise with stirring. The solution was further stirred for 10 h at room temperature. After reaction, the mixture was washed with deionized water and extracted with DCM (2×10 mL), the organic layer was dried over Na_2SO_4 and concentrated to afford analytically pure product **7a** (yellow solid, 0.52g, 92% yield).



1a-CD$_3$[3]

A 10 mL schlenk tube was charged with **1a** (0.135 mL, 1mmol), D_2O (1 mL), PhCOOH (9.15 mg, 0.075 mmol) and a stir bar. The mixture was heated at 80 ^{o}C for 6 h and cooled to room temperature. The mixture was neutralized with 5 mL saturated $NaHCO_3$ aqueous solution and extracted with EA (3×5 mL). The organic layer was dried over Na_2SO_4 and concentrated to afford analytically pure product **1a-CD$_3$** (yellow liquid, D-96%).

KIE experiment procedure

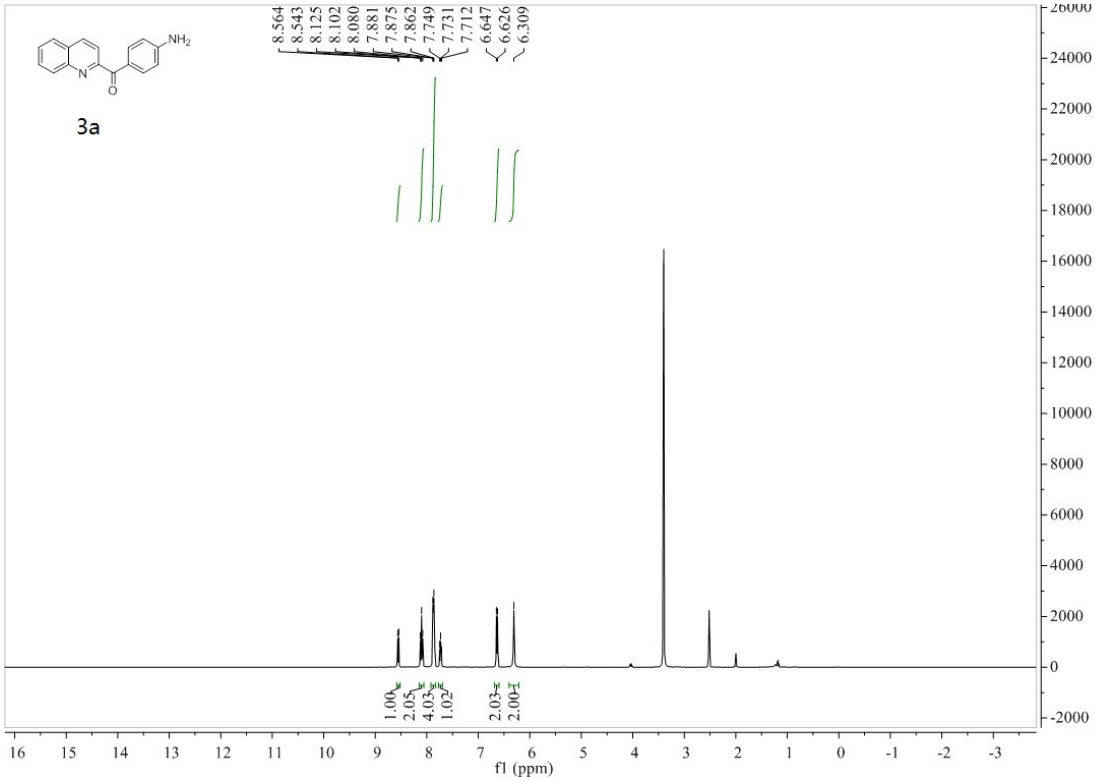
1a-CD$_3$: An oven-dried Schlenk tube containing a stir bar was charged with I_2 (0.04 mmol, 10.2 mg) and salicylic acid (0.04 mmol, 5.6 mg), the tube was degassed and refilled with O_2 for 3 times. Then 0.2 mL DMSO, **1a-CD$_3$** d_3-2-methylquinoline (0.2 mmol, 29.2 mg), **2a** aniline (0.6 mmol, 54 uL) was charged into the tube under O_2 successively. Then the mixture was stirred at 60 ^oC for 3 h. After reaction, the mixture was diluted with 3-5 mL DCE and then neutralized by saturated $NaHCO_3$ aqueous solution. The mixture was analyzed by GC using tridecane as the internal standard and the yield of **3a** was 3.4%. The reaction of **1a** with **2a** gave **3a** in 11% yield at 3 h. Thus, the k_H/k_D = 3.3.

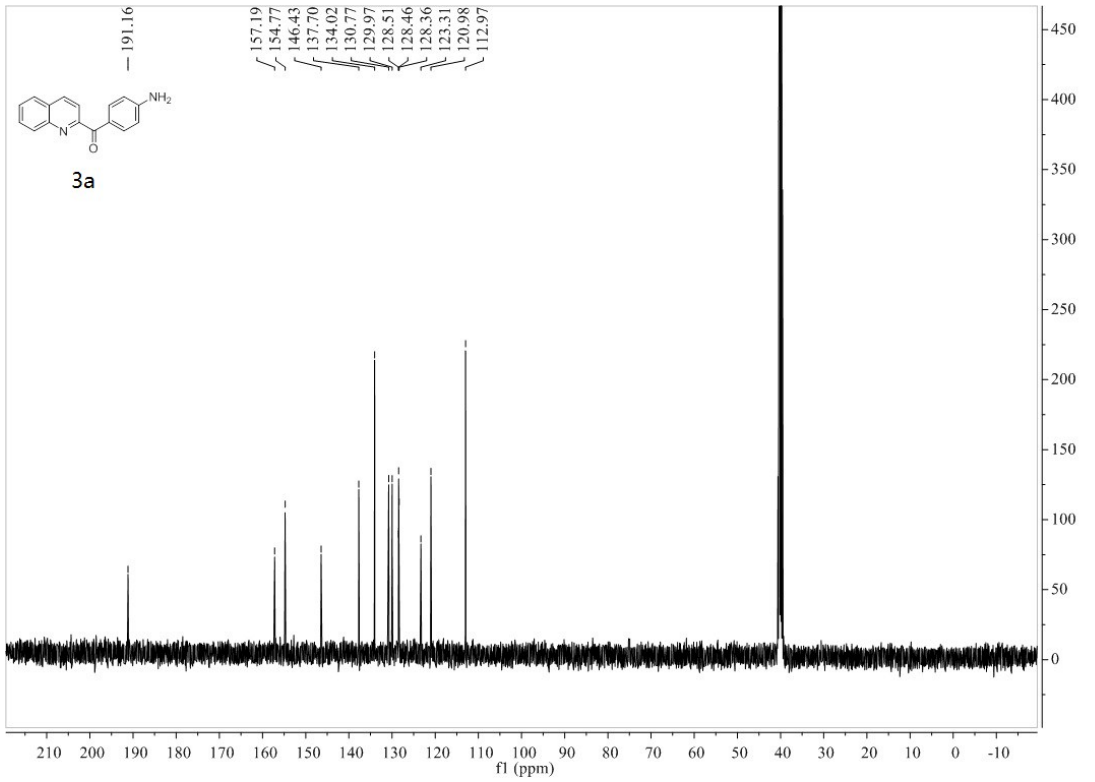
***d*$_5$-PhNH$_2$**: An oven-dried Schlenk tube containing a stir bar was charged with I_2 (0.04 mmol, 10.2 mg) and salicylic acid (0.04 mmol, 5.6 mg), the tube was degassed and refilled with O_2 for 3 times. Then 0.2 mL DMSO, 2-methylquinoline (0.2 mmol, 29.2 mg), **2a** d_5-aniline (0.6 mmol, 54 uL) was charged into the tube under O_2 successively. Then the mixture was stirred at 60 ^oC for 3 h. After reaction, the mixture was diluted with 3-5 mL DCE and then neutralized by saturated $NaHCO_3$ aqueous solution. The mixture was analyzed by GC using tridecane as the internal standard and the yield of **3a**-D_4 was 5.5%. The reaction of **1a** with **2a** gave **3a** in 11% yield at 3 h. the k_H/k_D = 2.0.

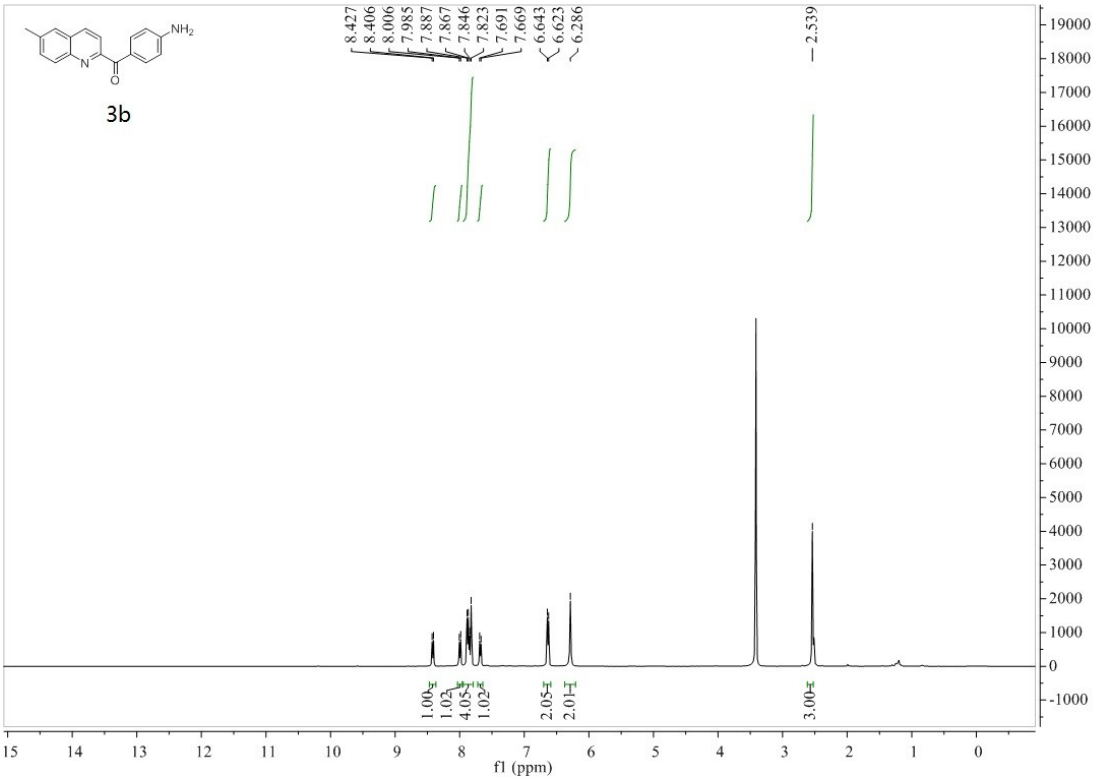
Reference

1. X. Pang, L. Xiang, J. Ma, X. Yang and R. Yan, *RSC Advances,* **2016***, 6,*111713-111717.
2. W. M. Motswainyana, M. O. Onani, A. M. Madiehe, M. Saibu, J. Jacobs, L. van Meervelt, *Inorg. Chimi. Acta*, 2013, **400**, 197-202.
3. M. Liu, X. Chen, T. Chen and S.-F. Yin, *Org. Biomol. Chem.*, 2017, **15**, 2507.

Copies of ^{1}H NMR and ^{13}C NMR spectroscopies



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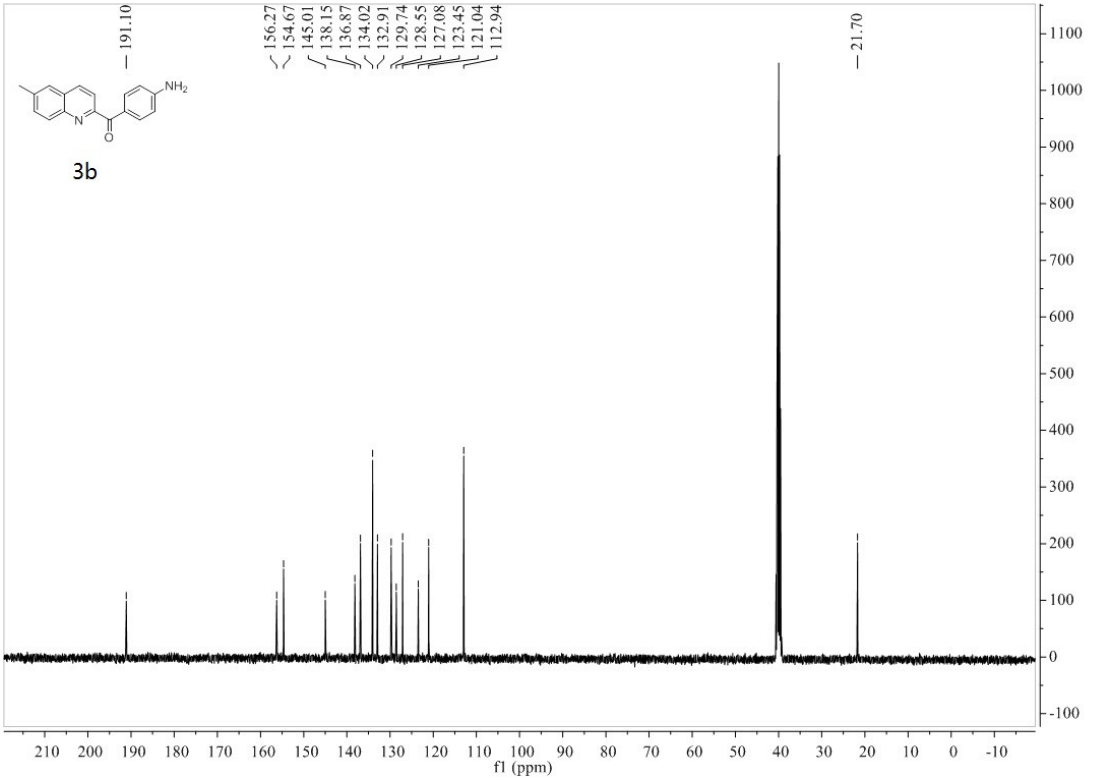
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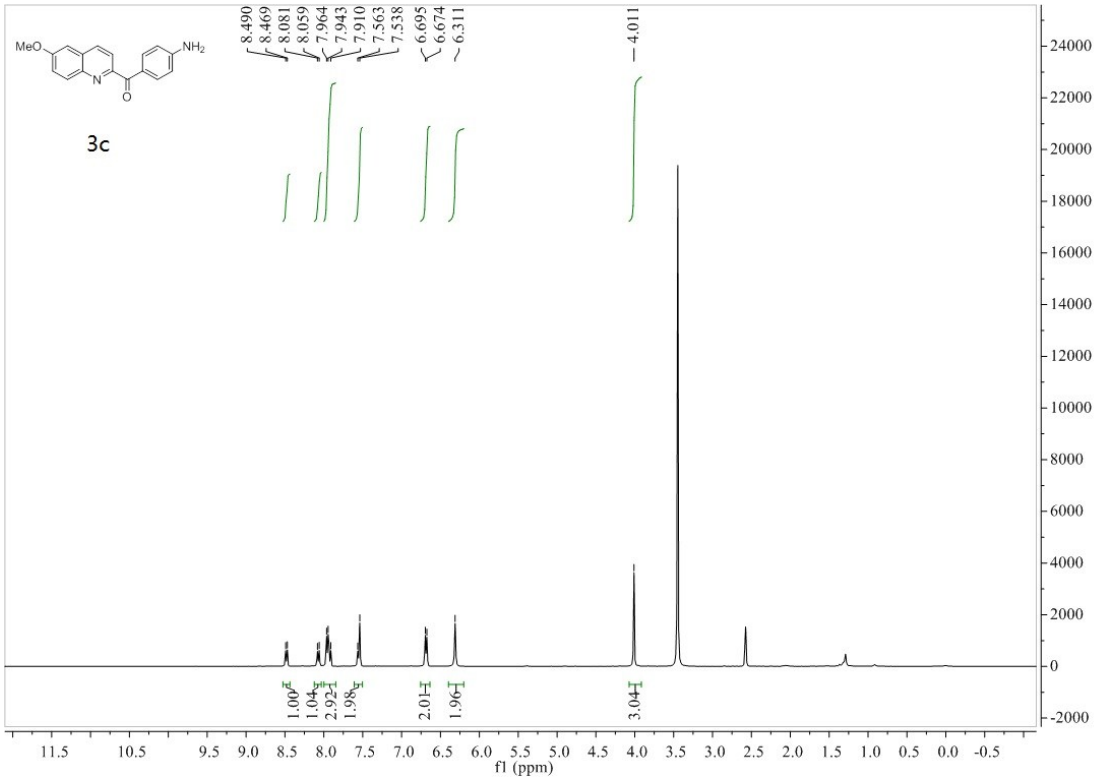
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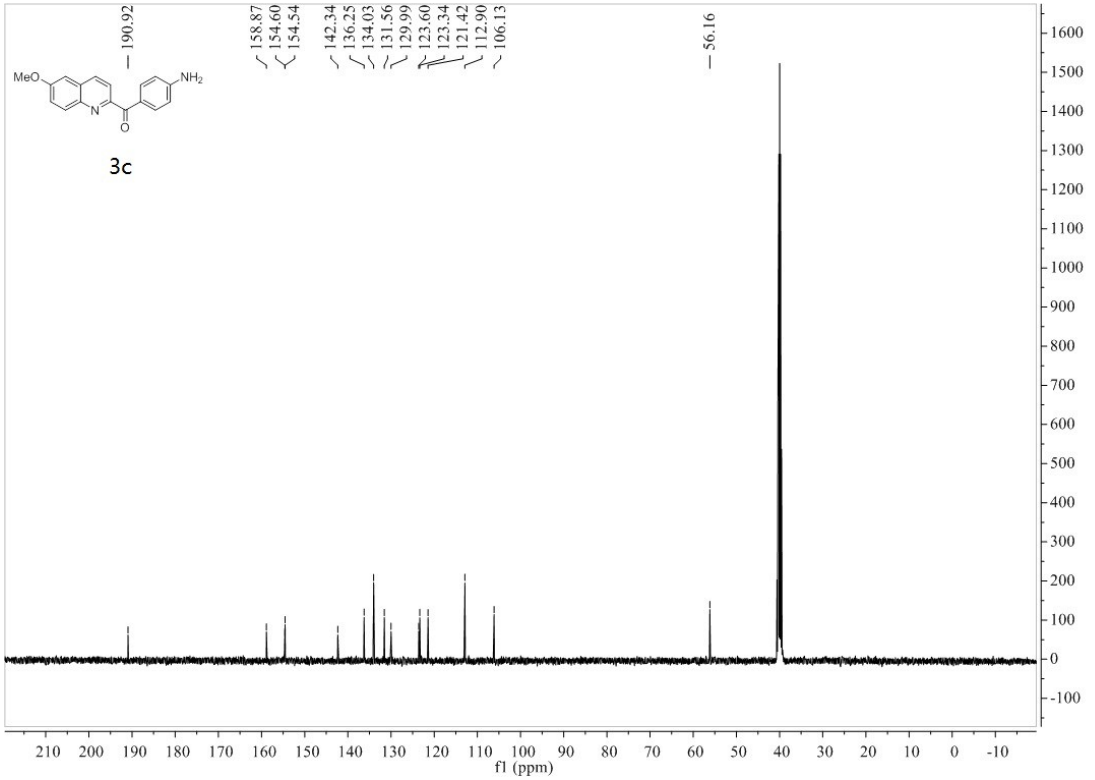
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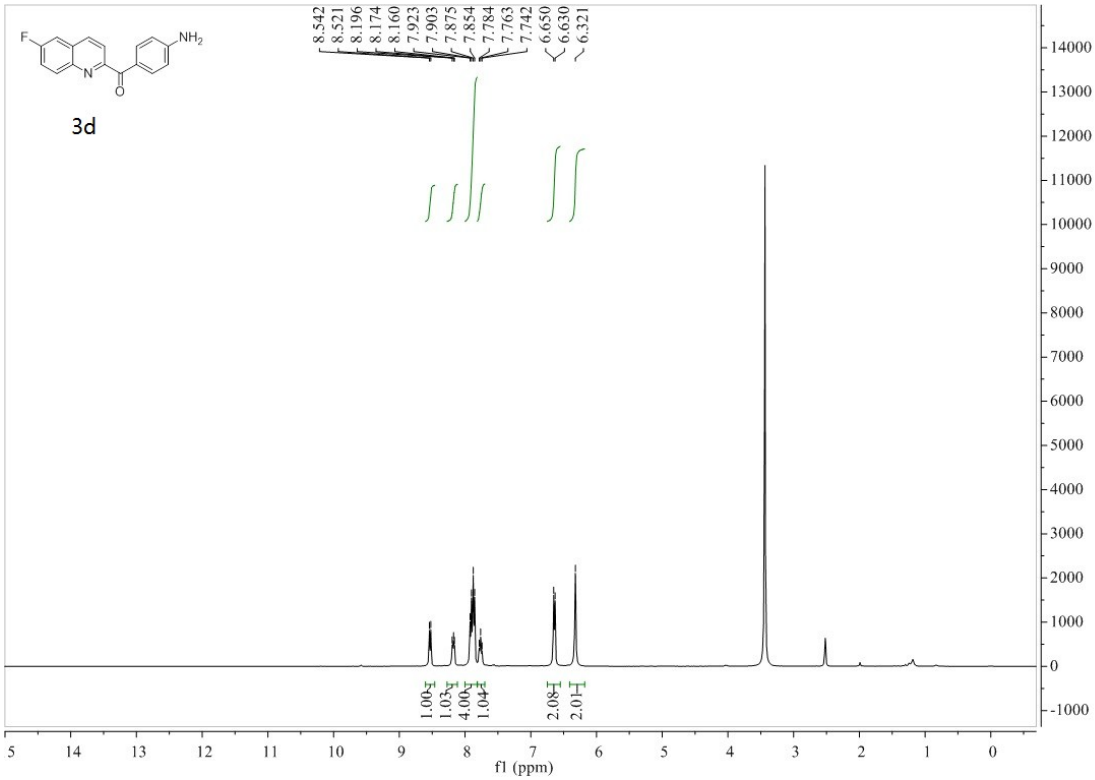
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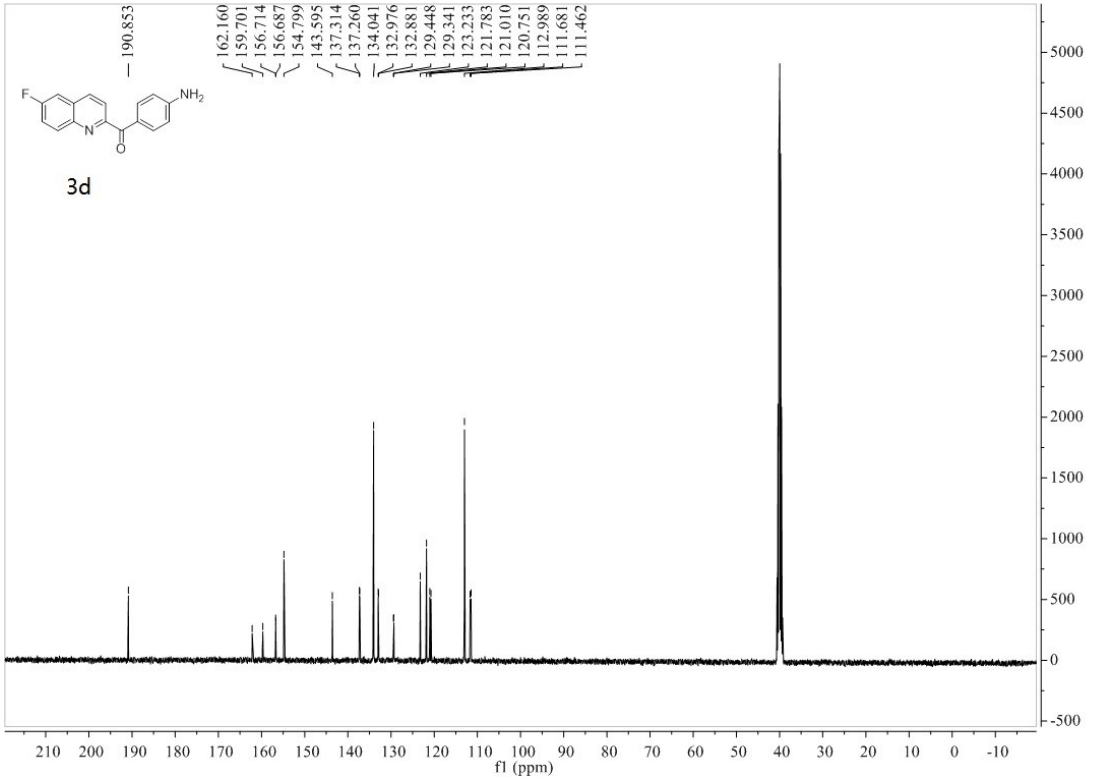
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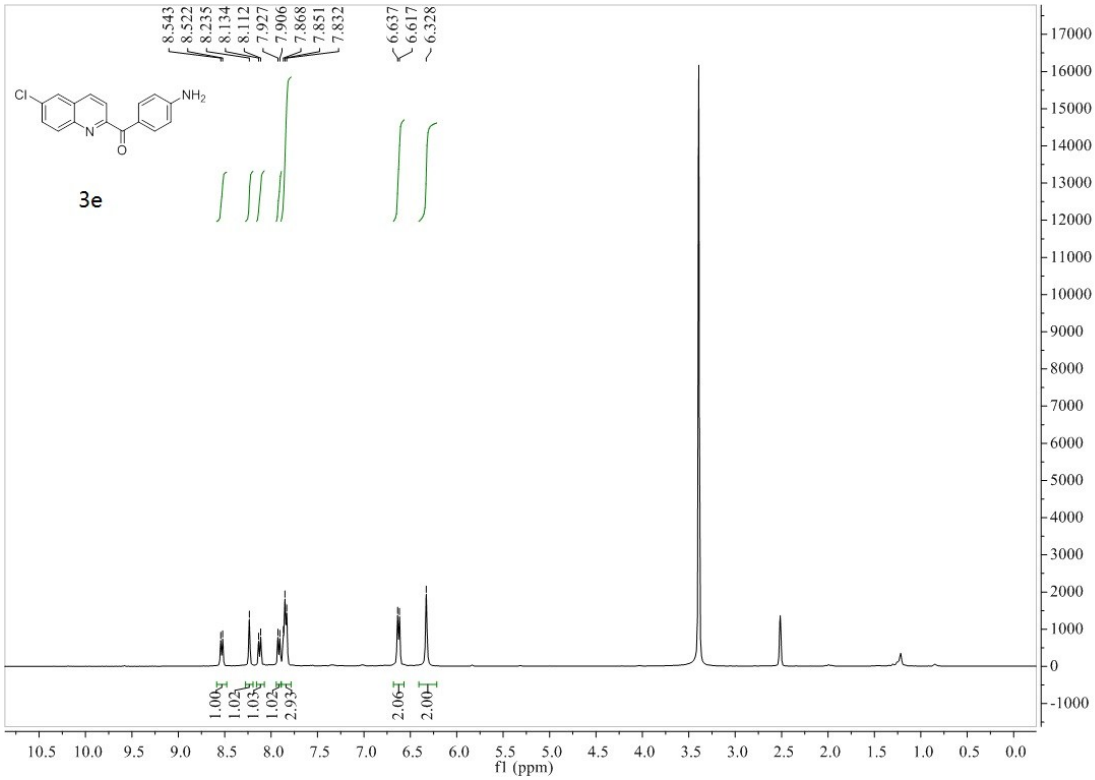
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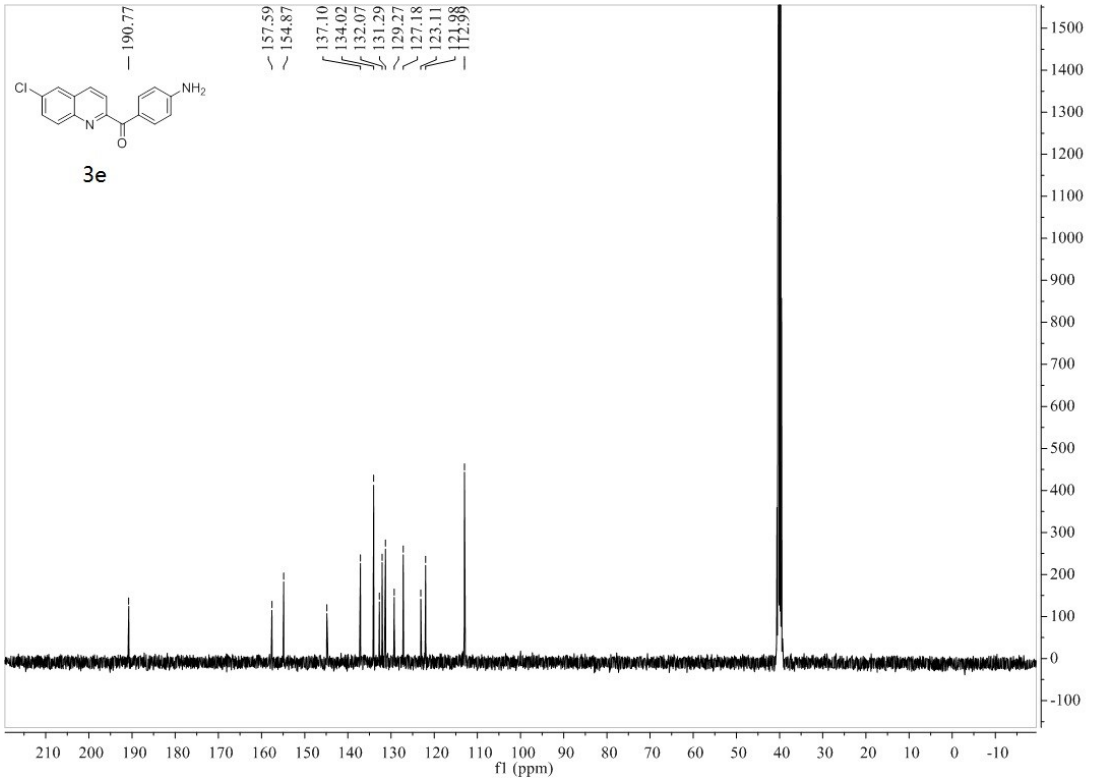
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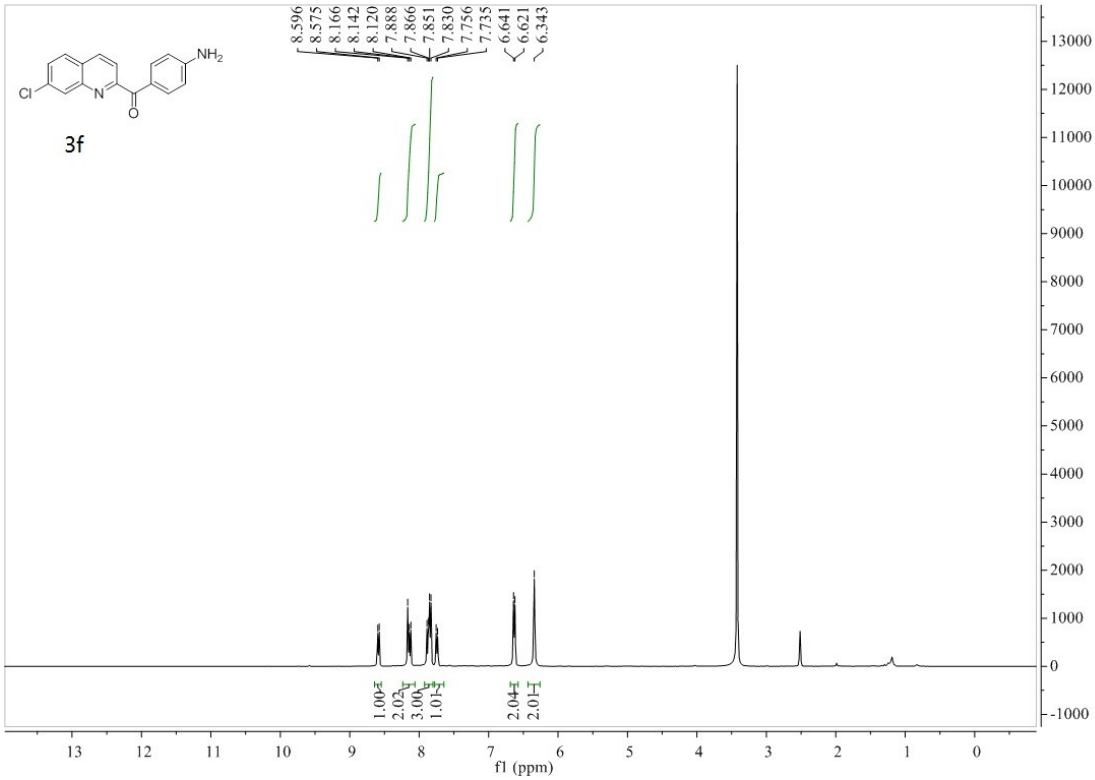
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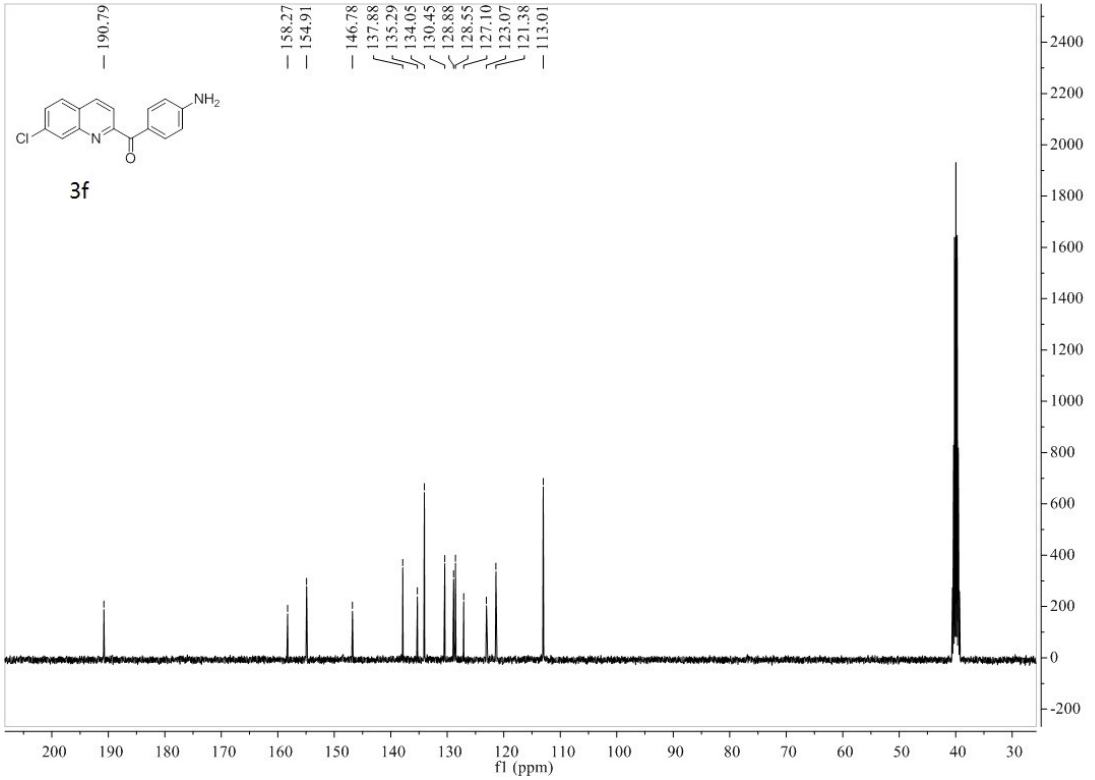
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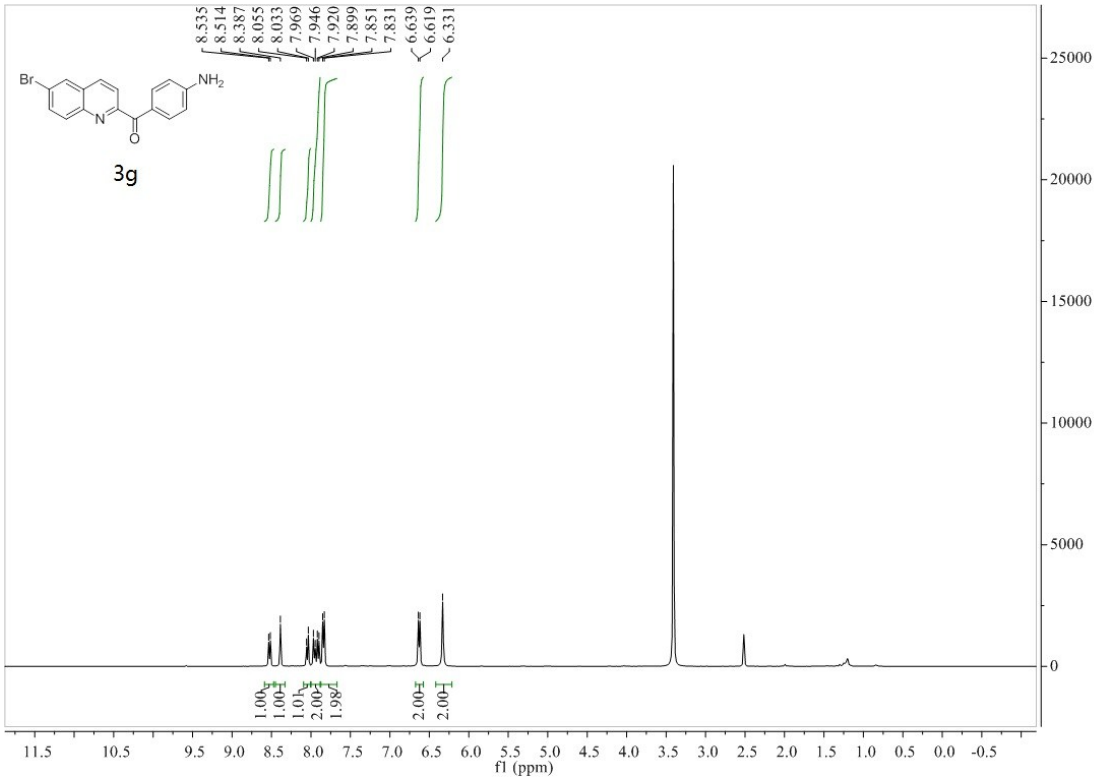
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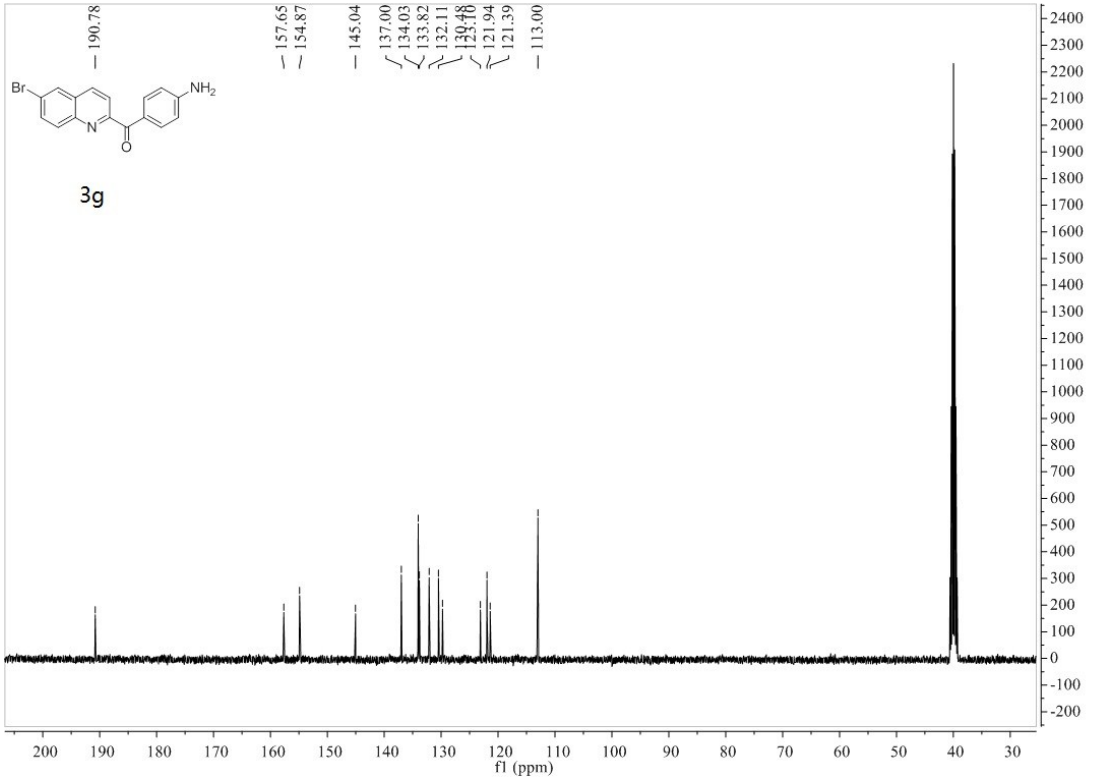
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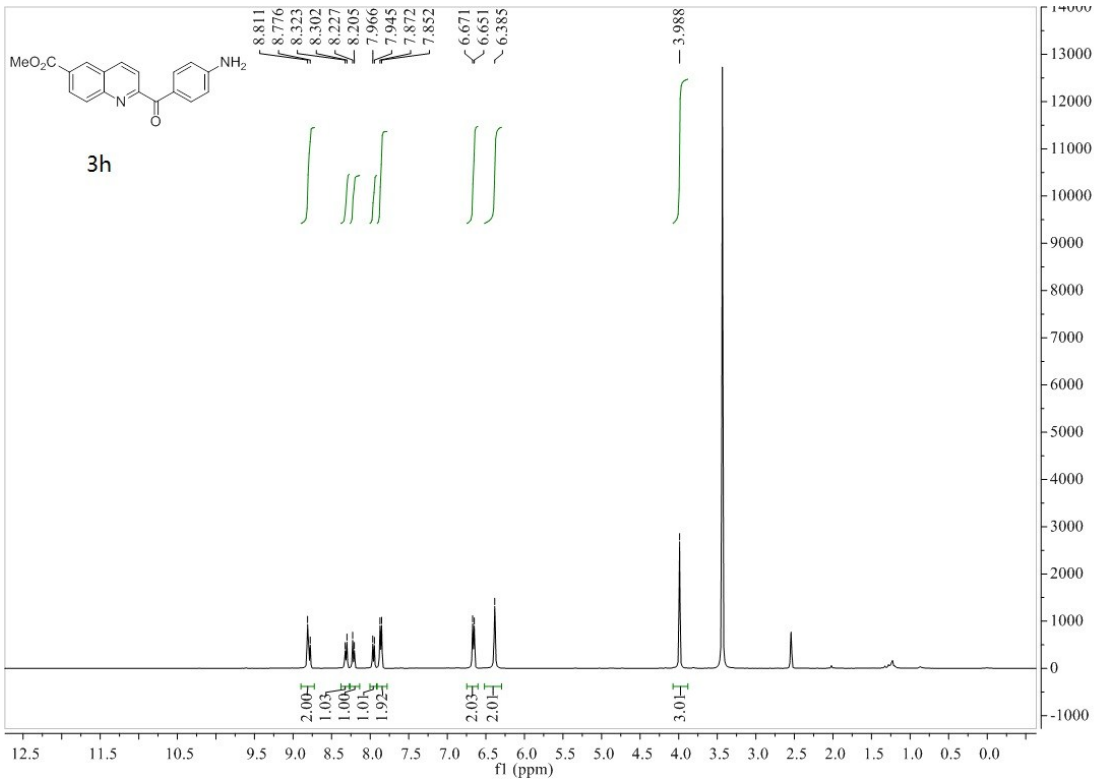
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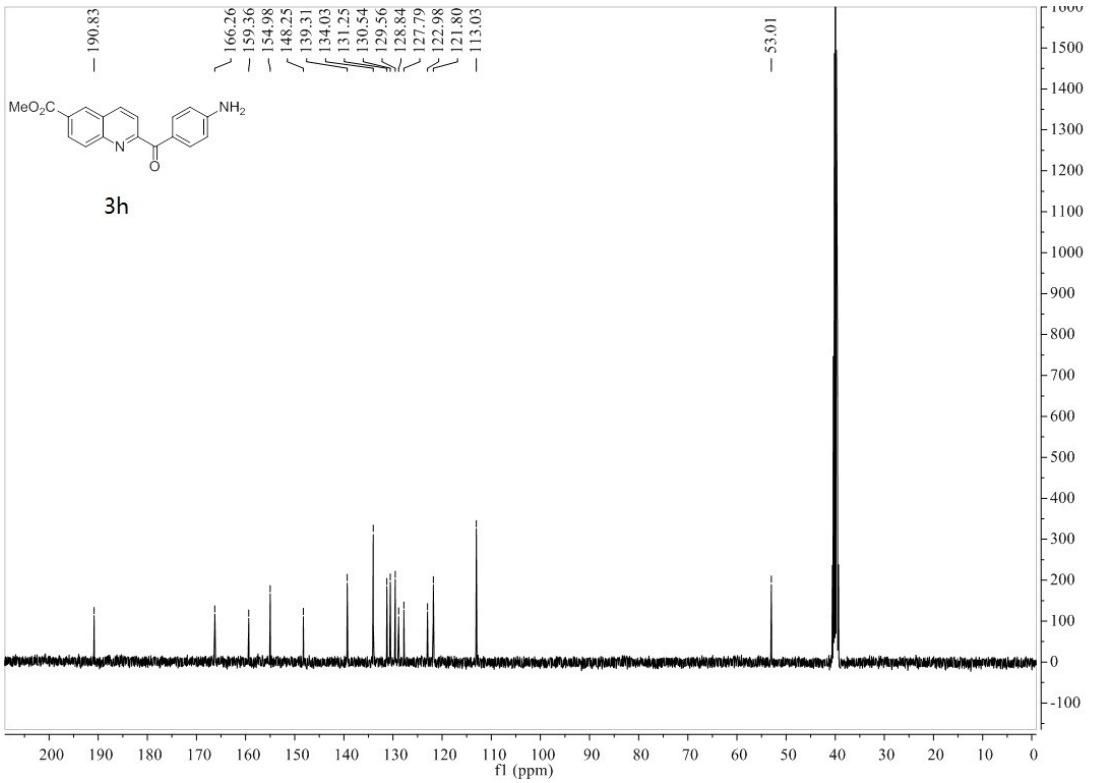
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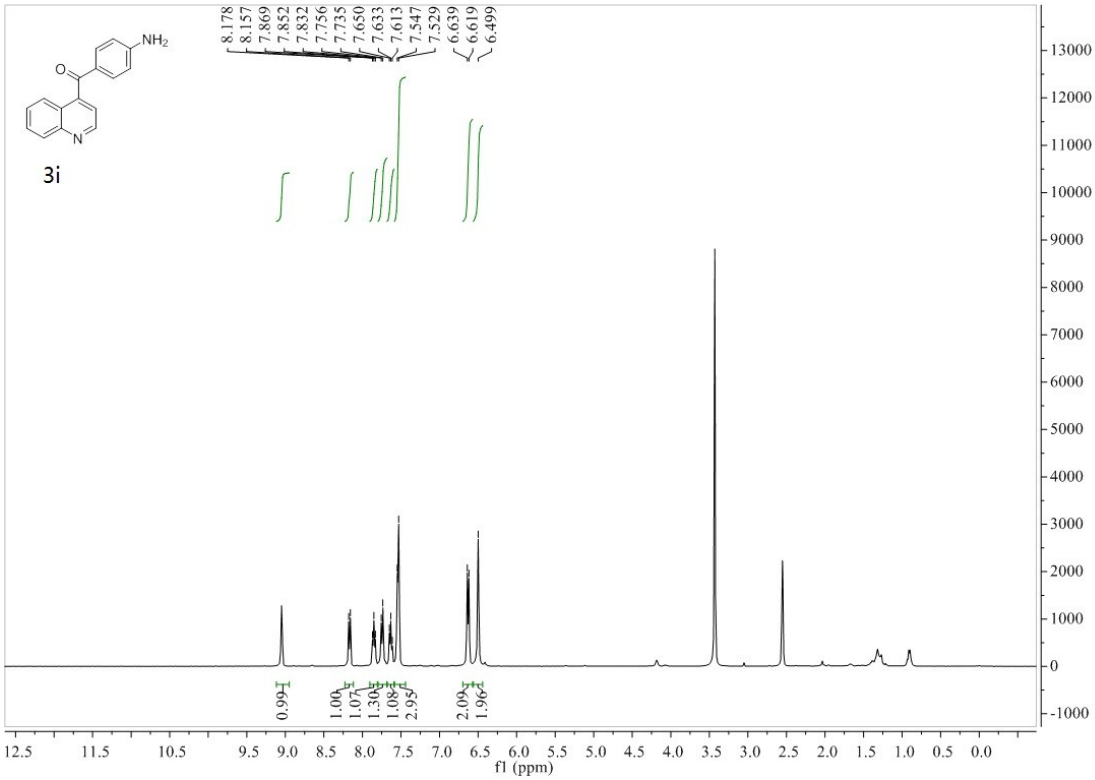
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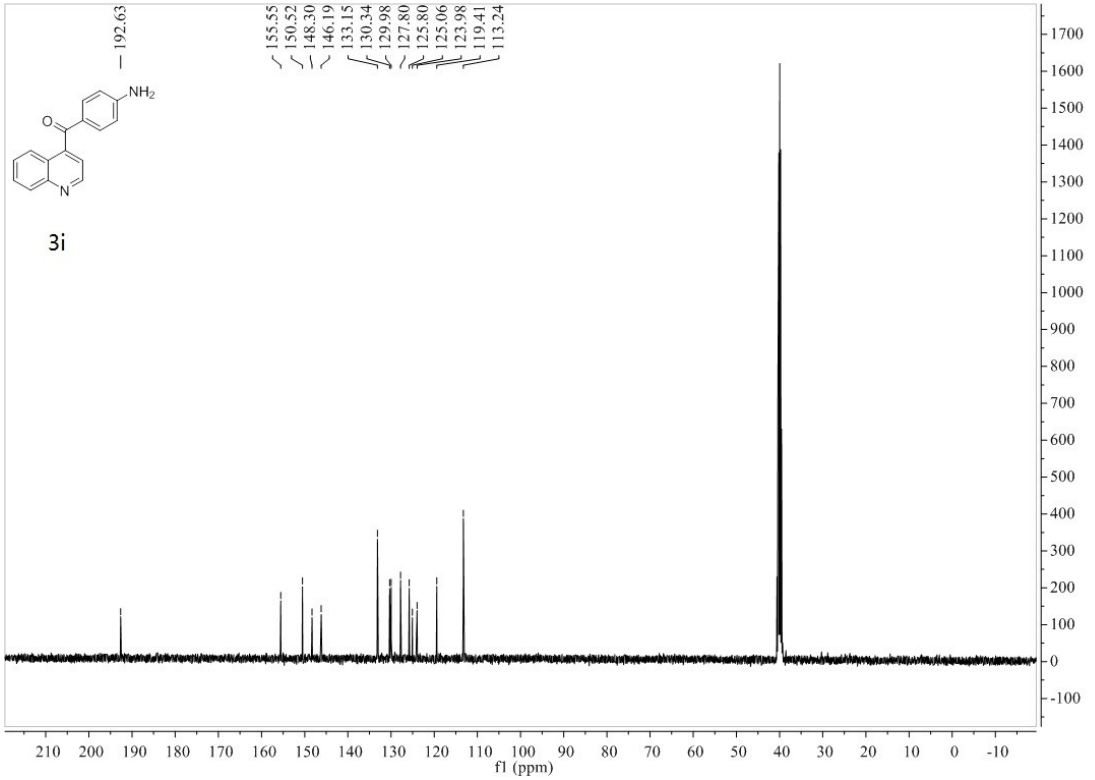
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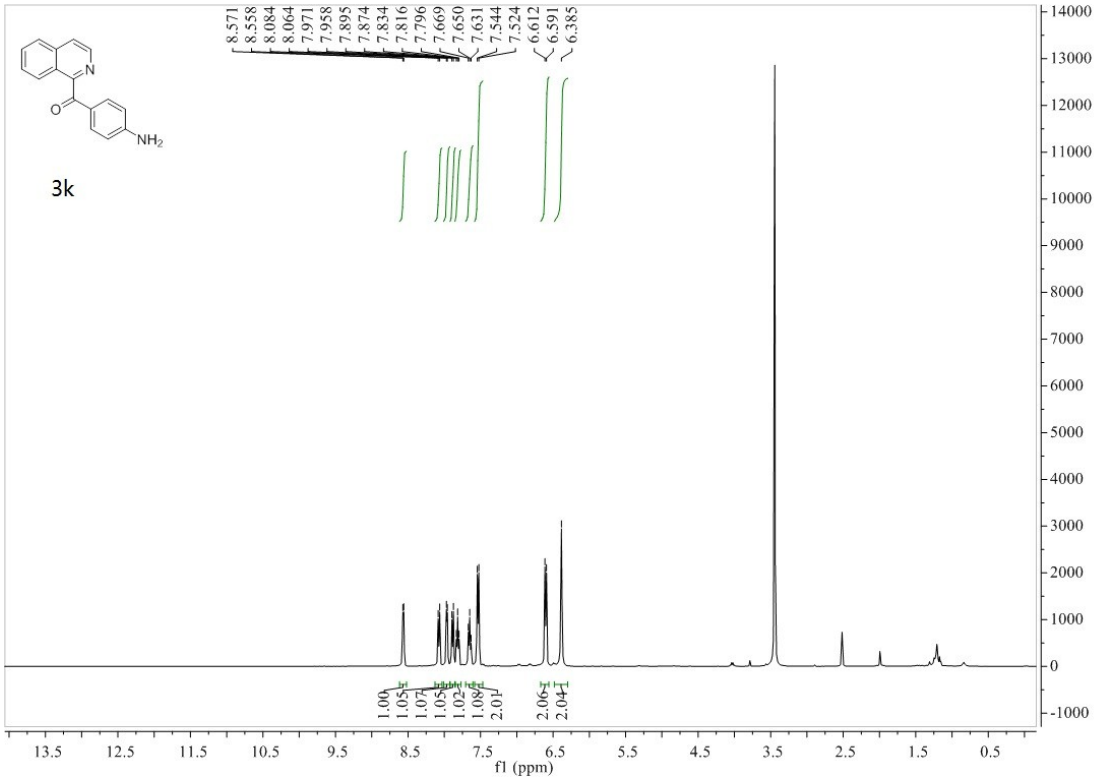
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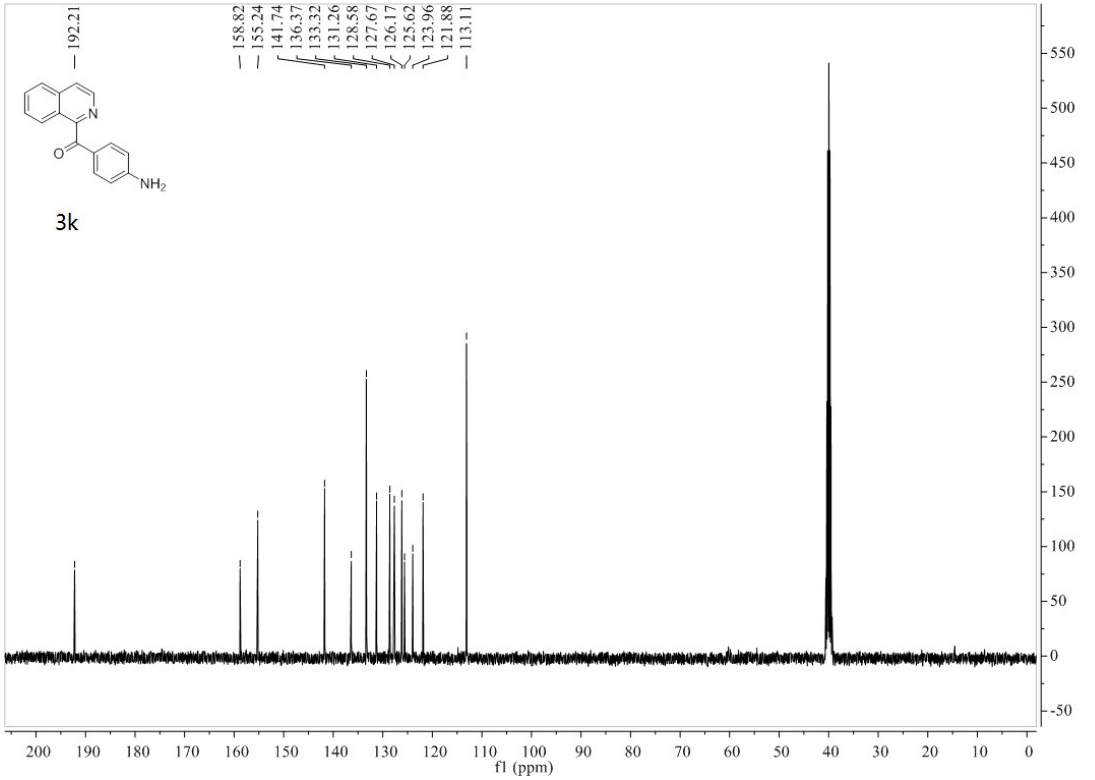
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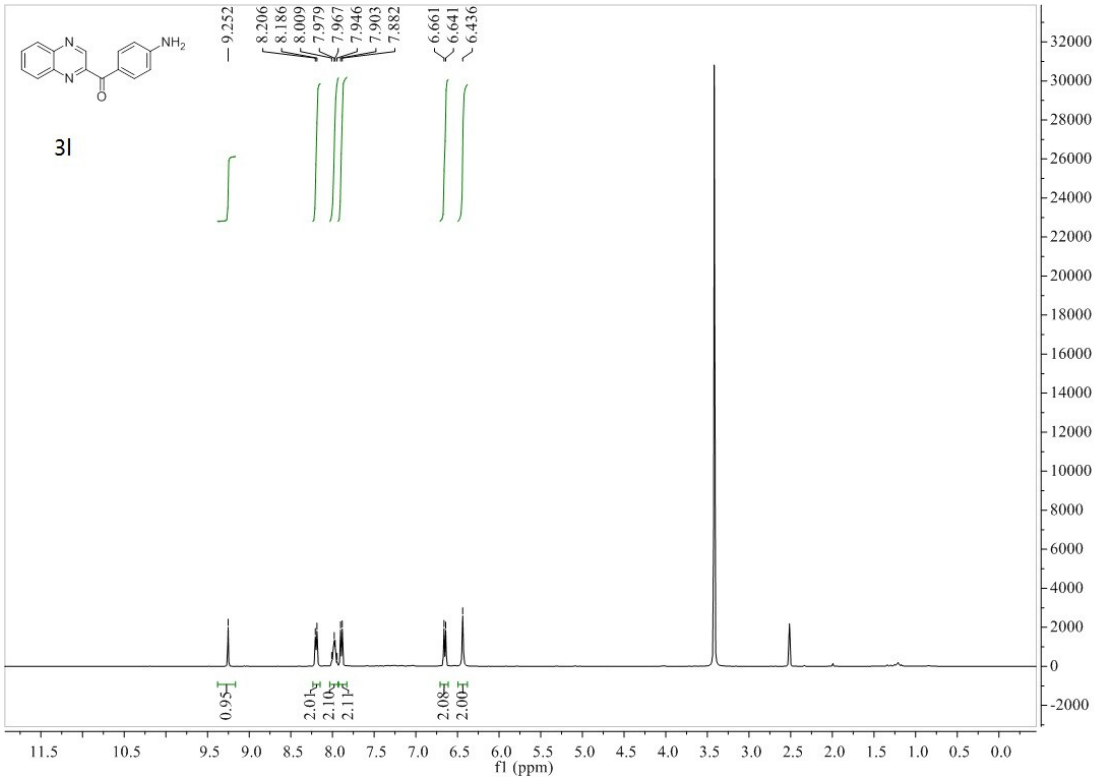
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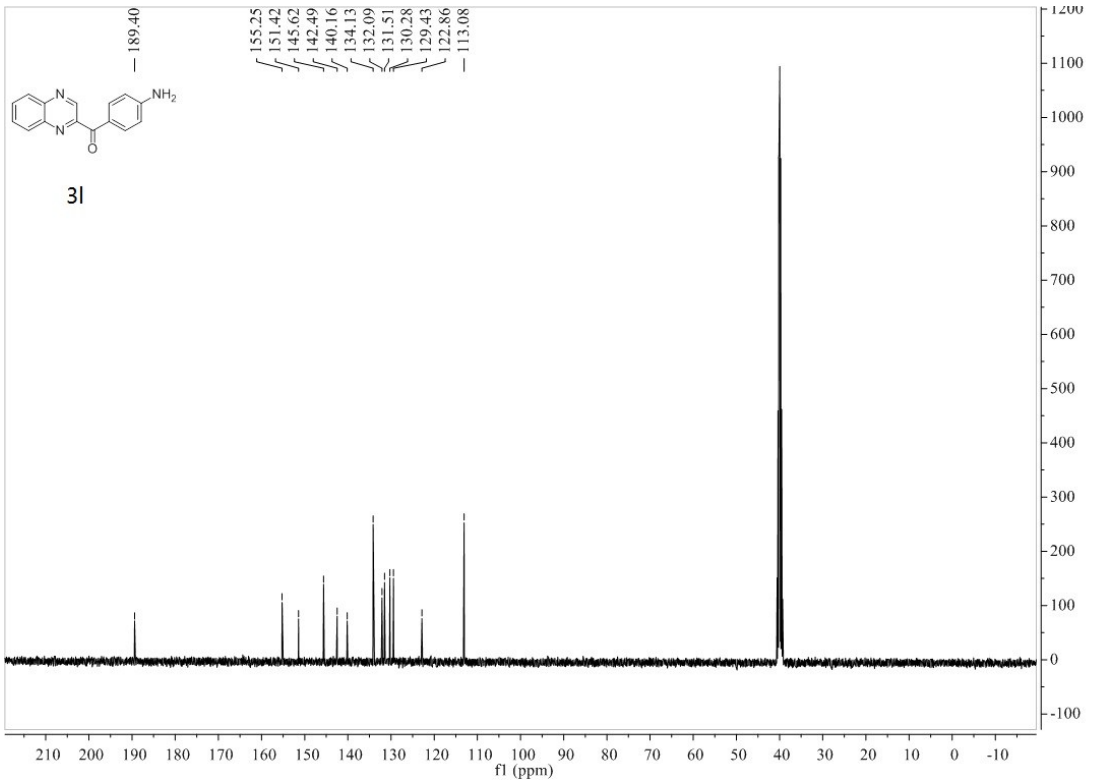
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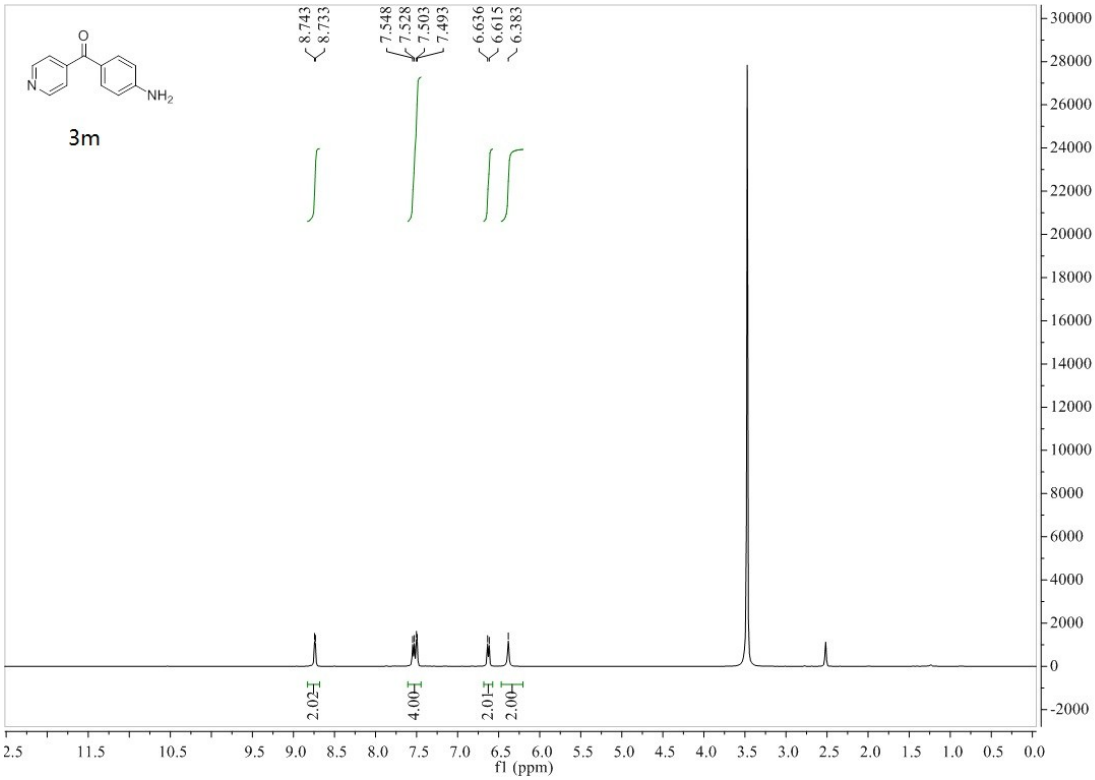
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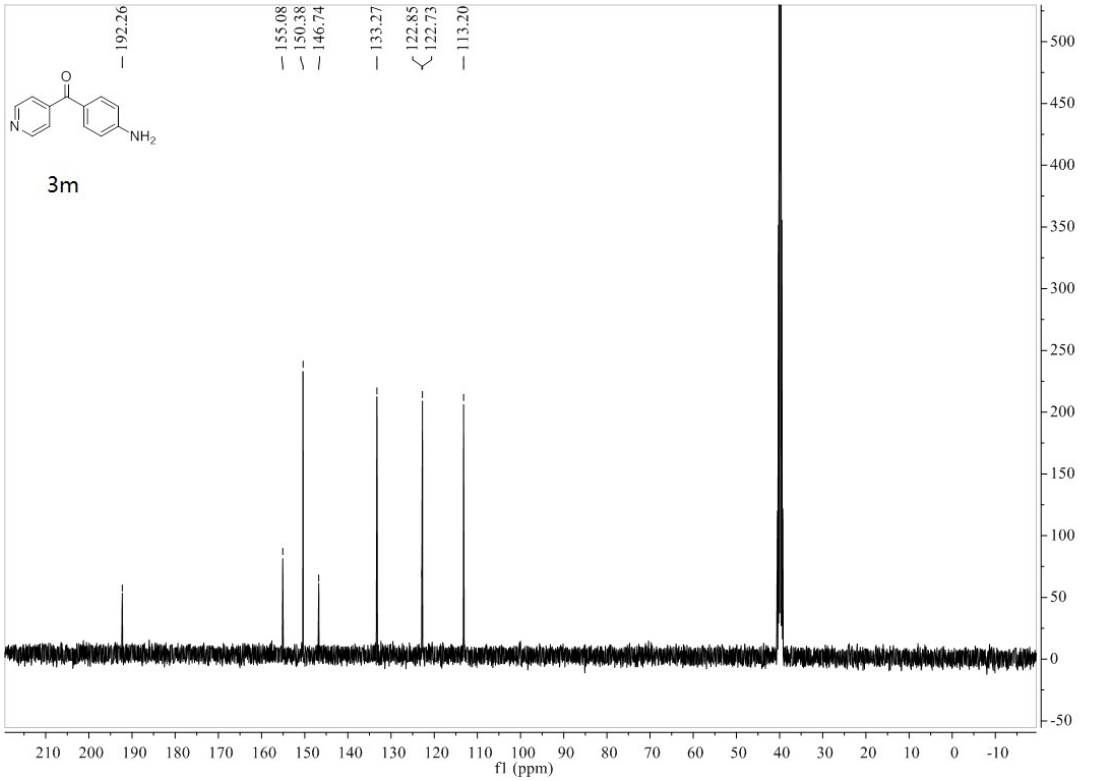
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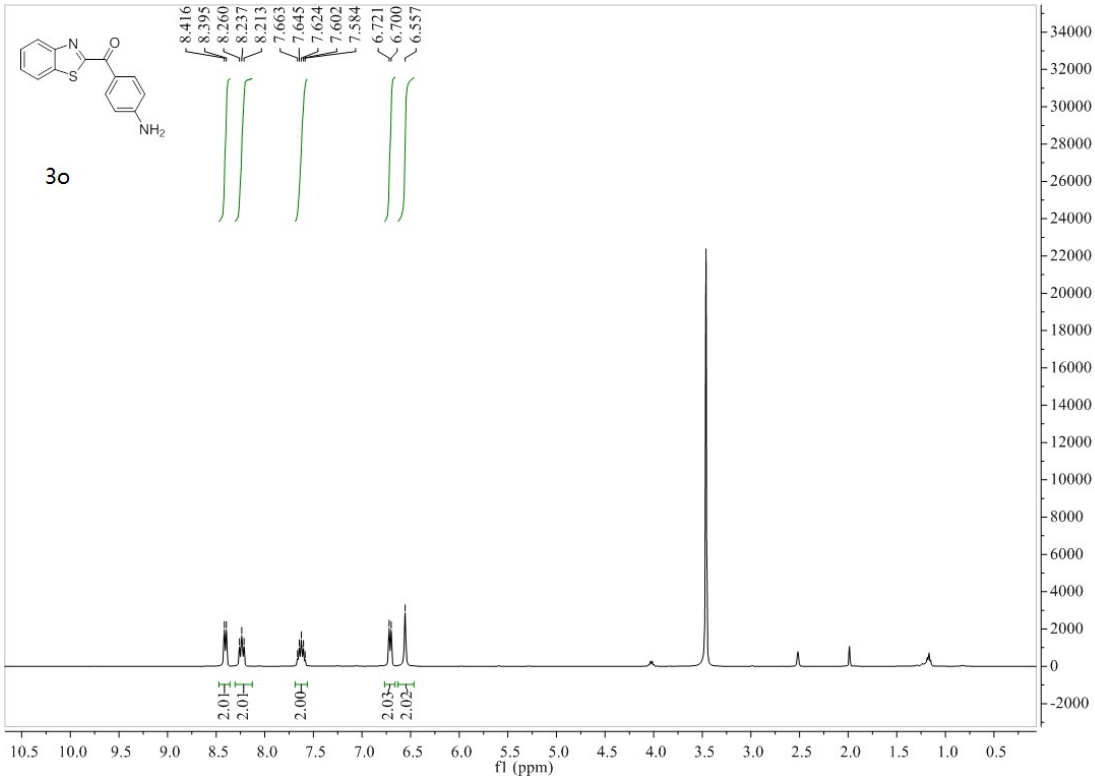
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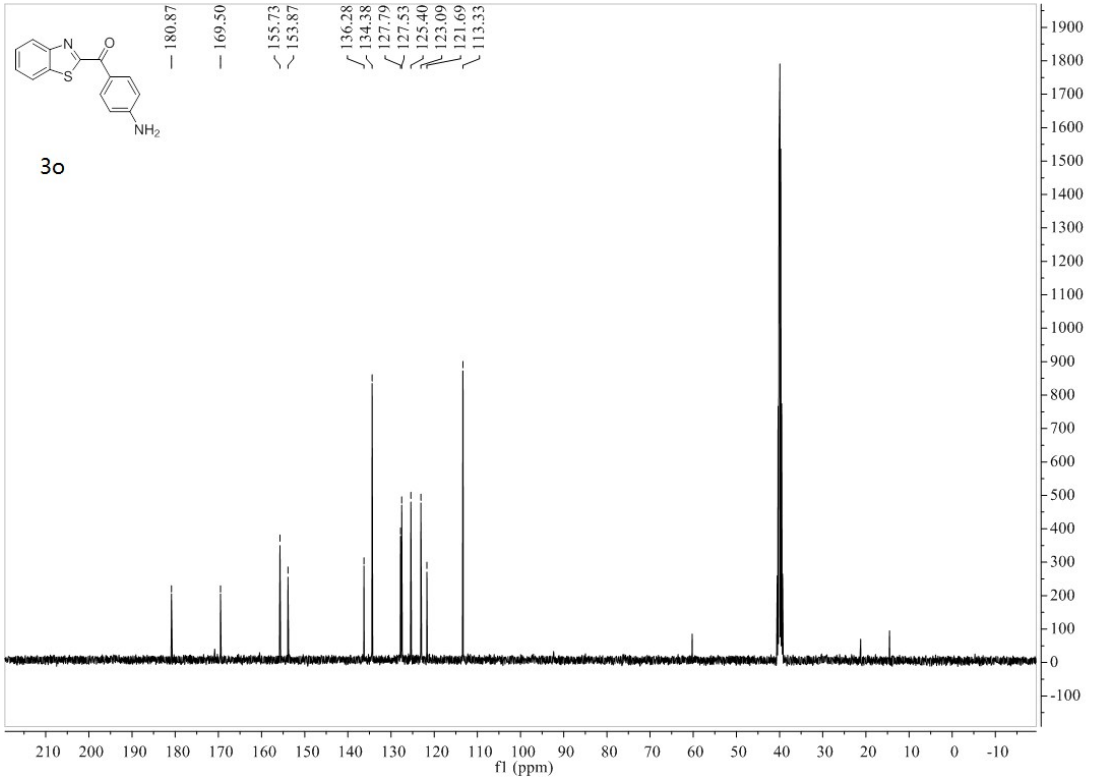
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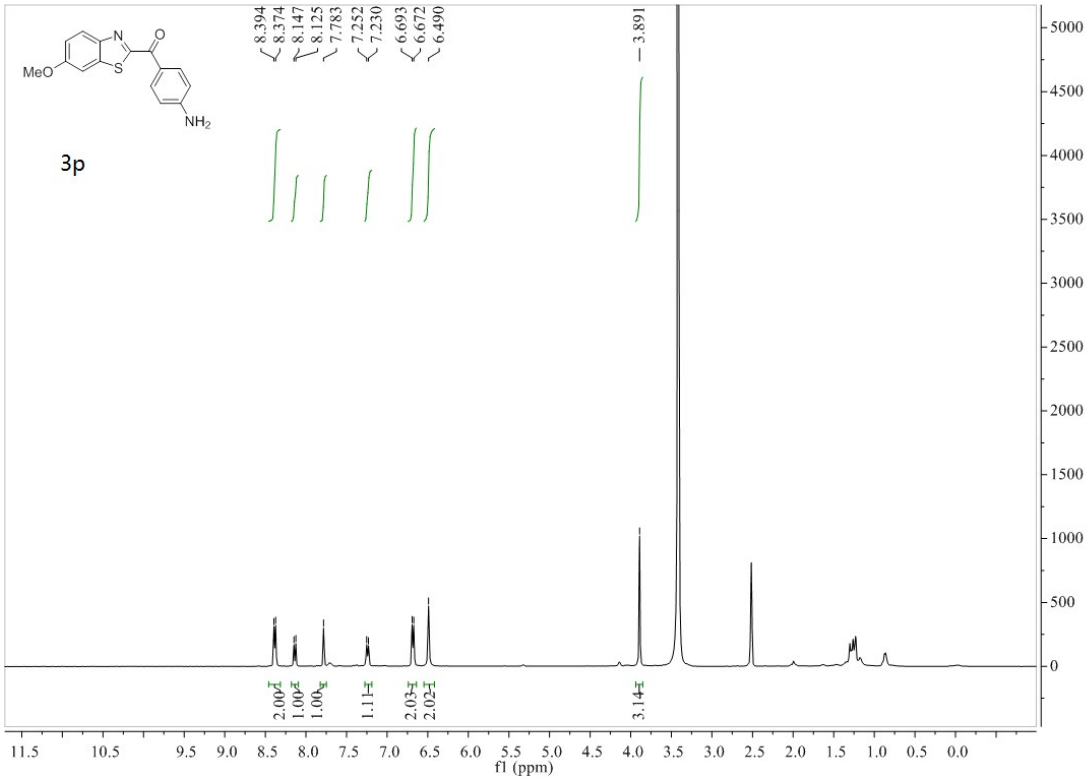
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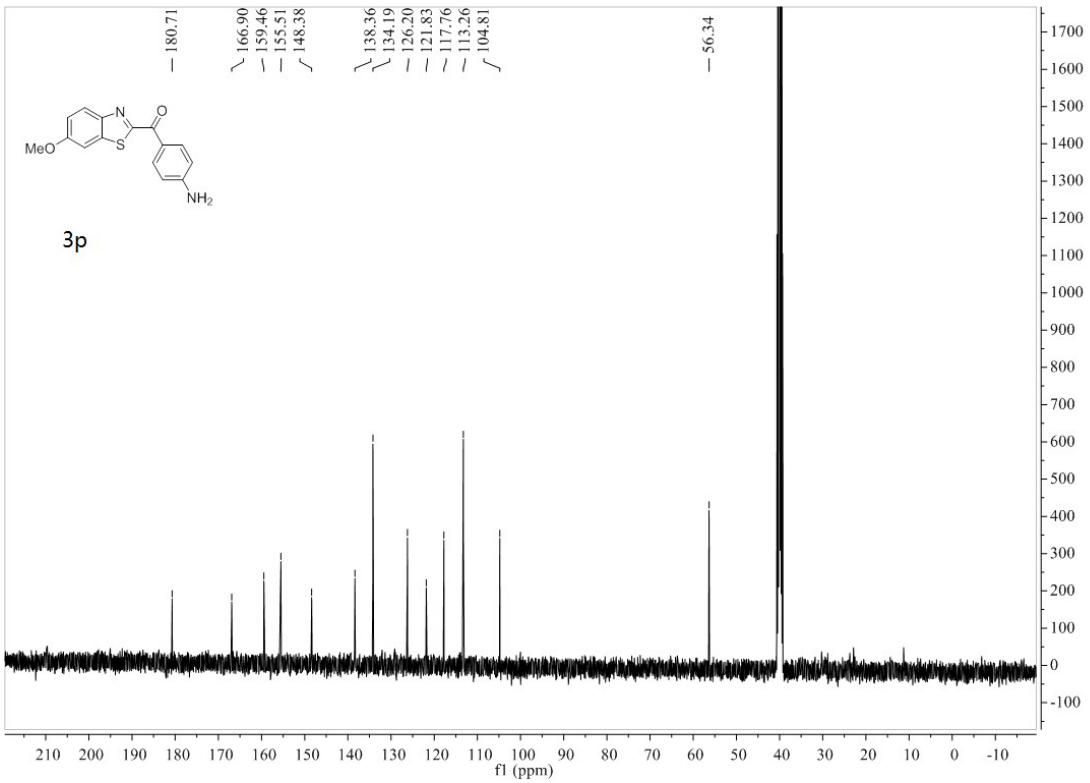
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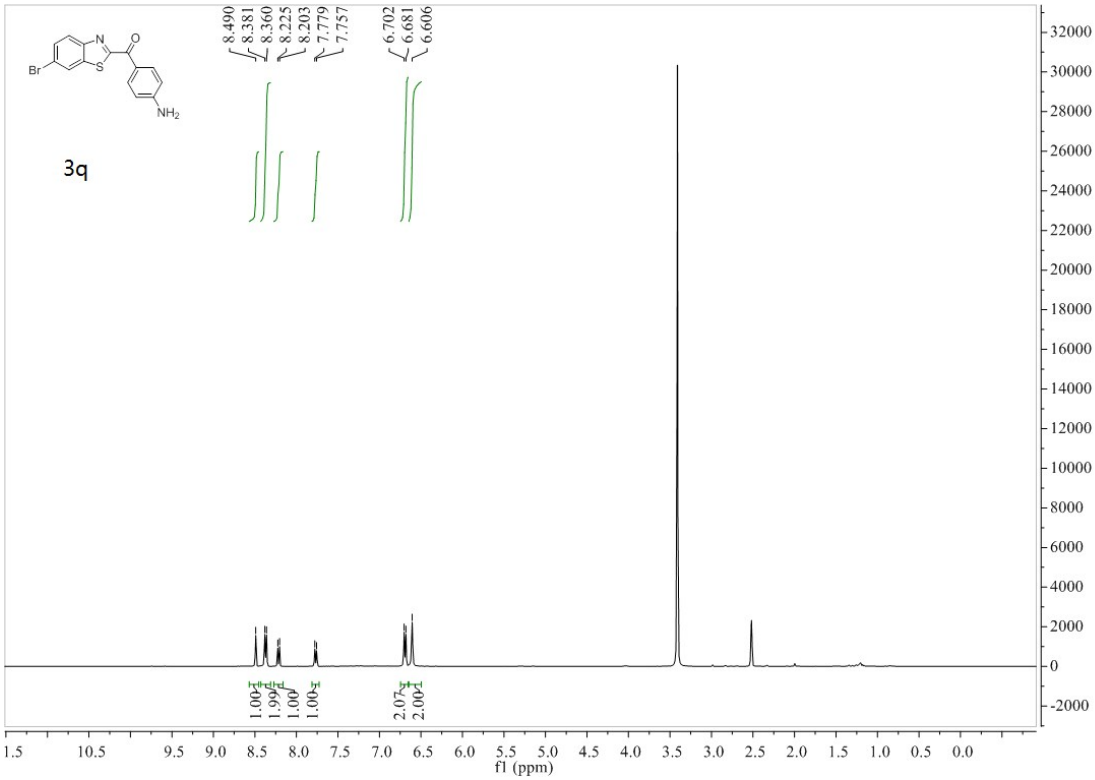
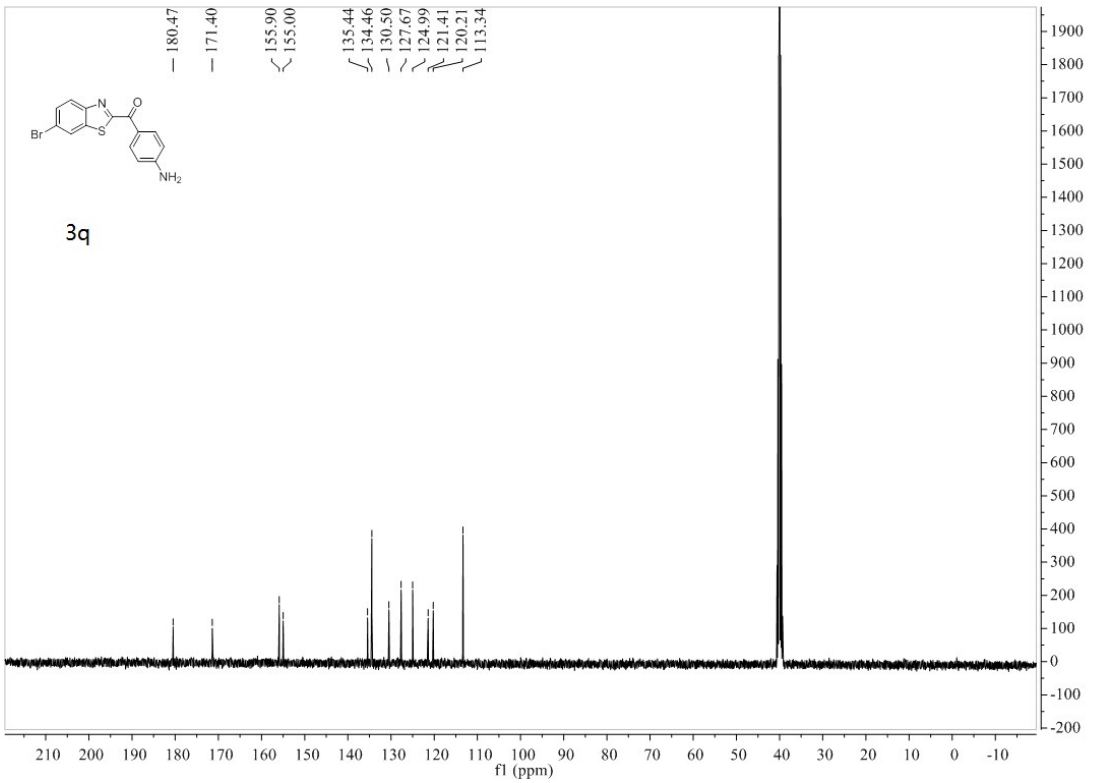
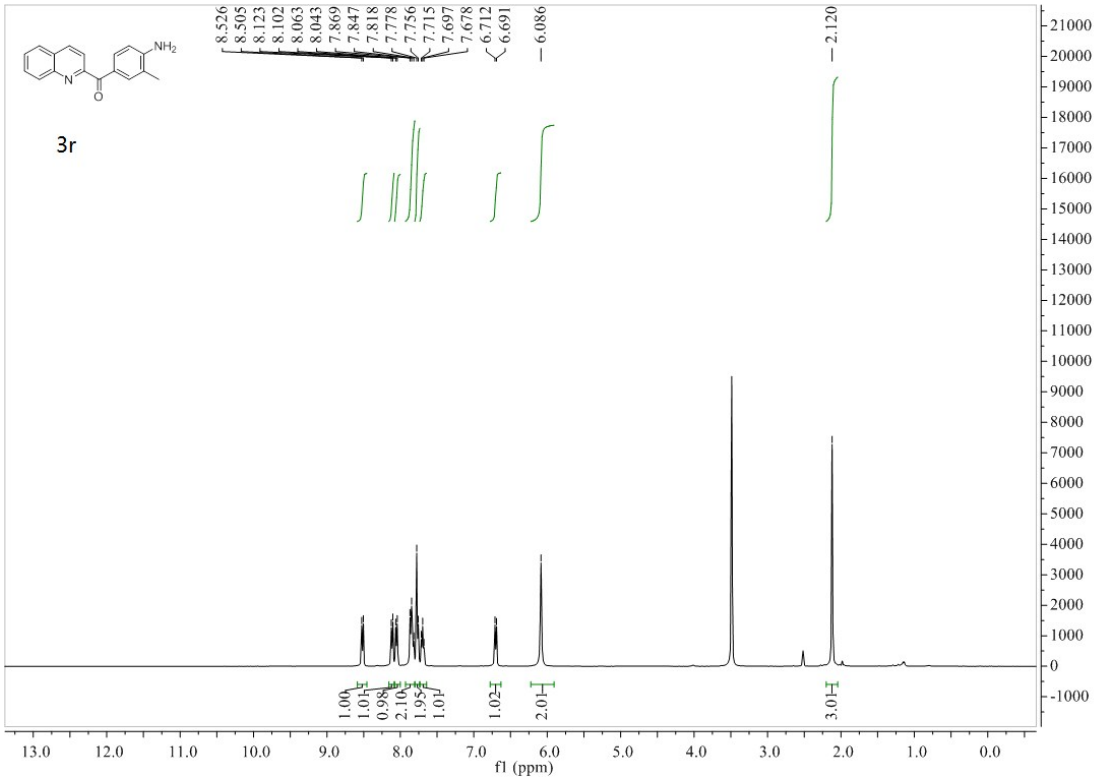
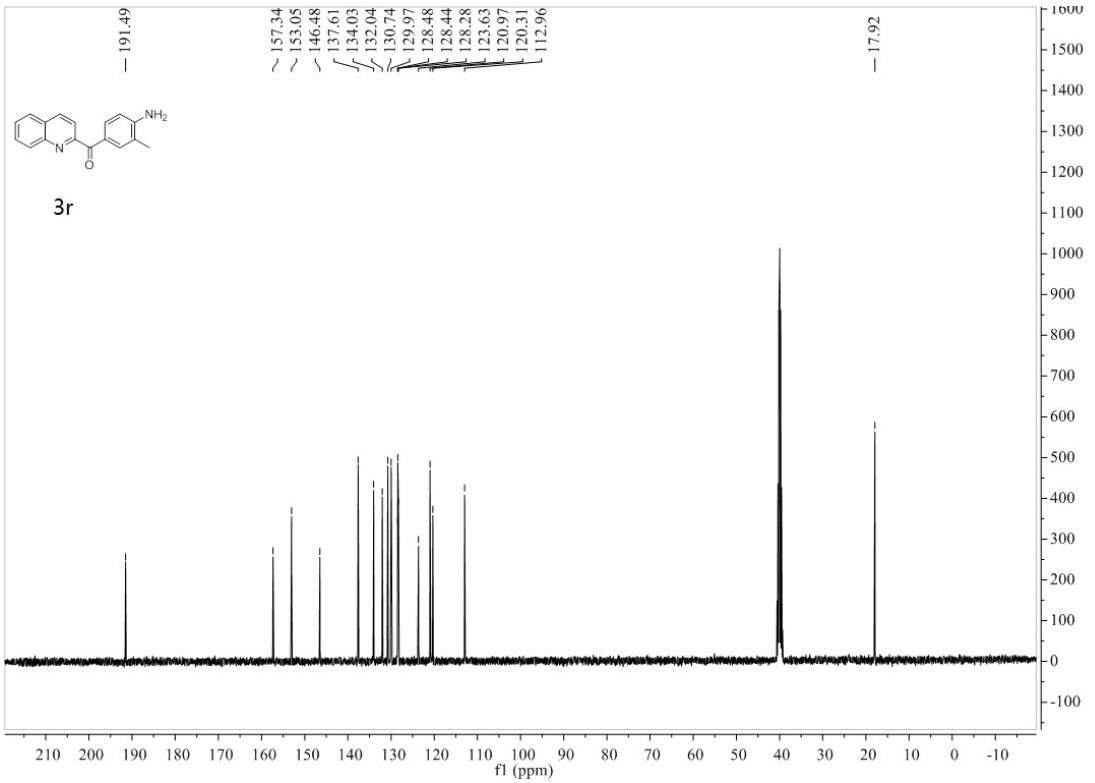
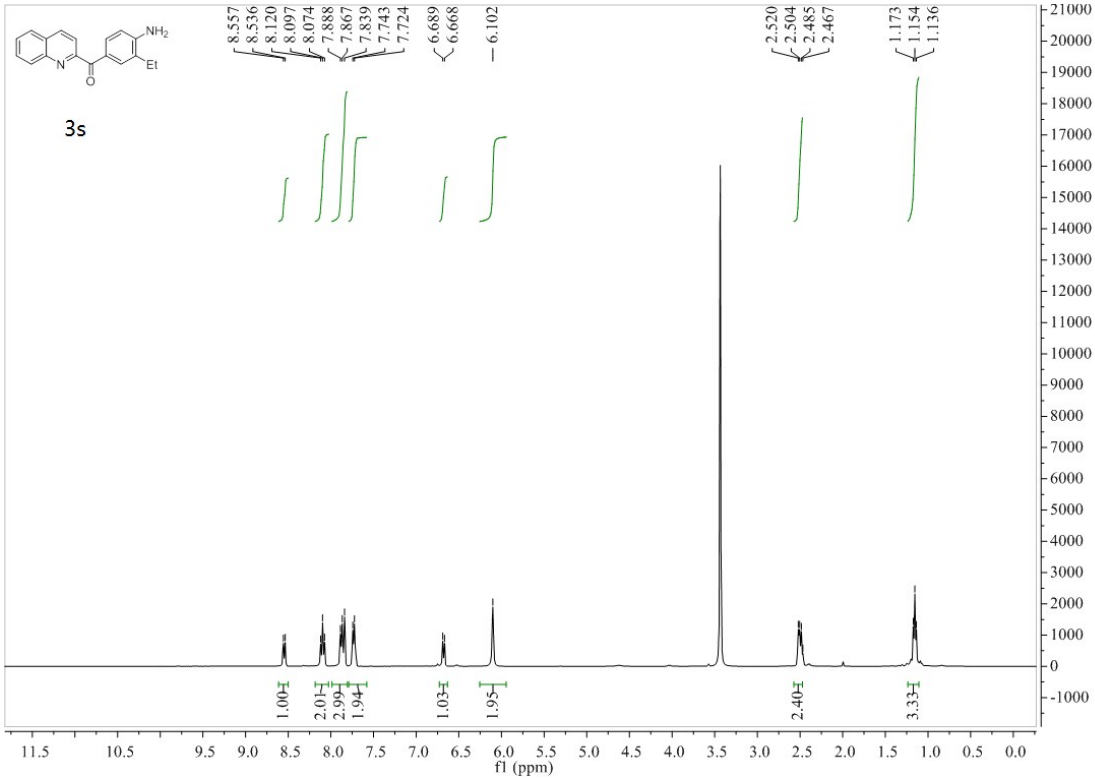
56.34
f1 (ppm)

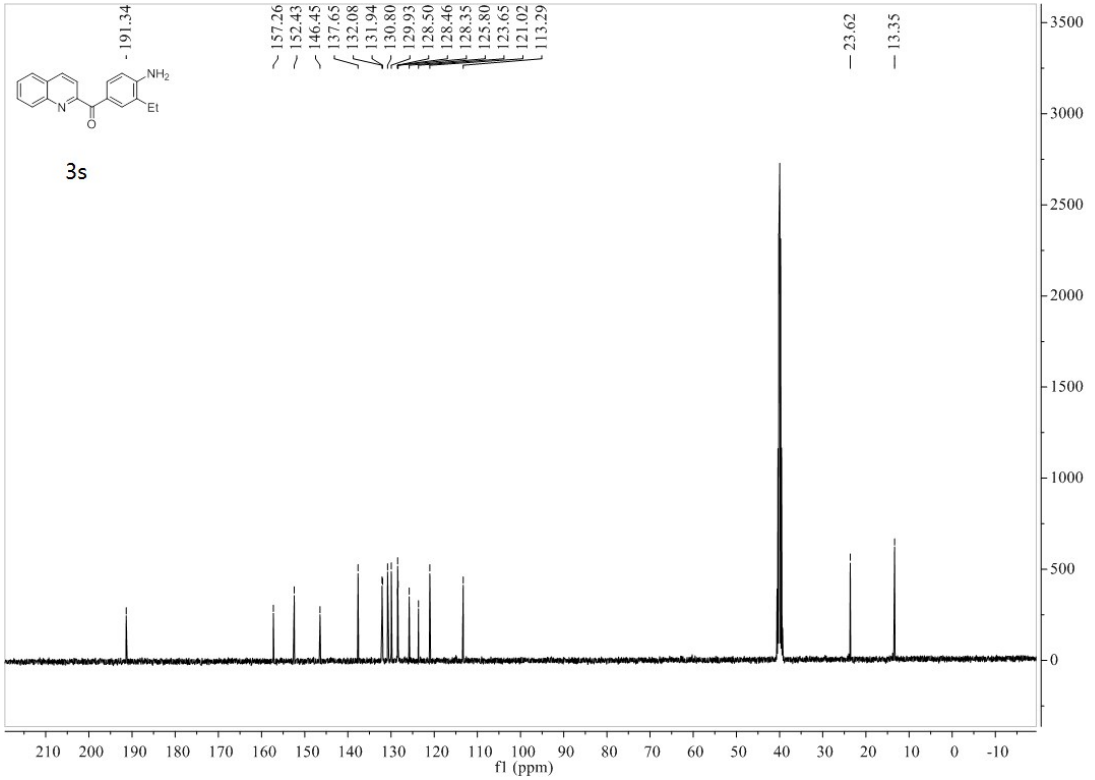

3q
8.490
8.381
8.360
8.225
8.203
7.779
7.757
6.702
6.681
6.606
1.00
1.99
1.00
1.00
2.07
2.00
f1 (ppm)

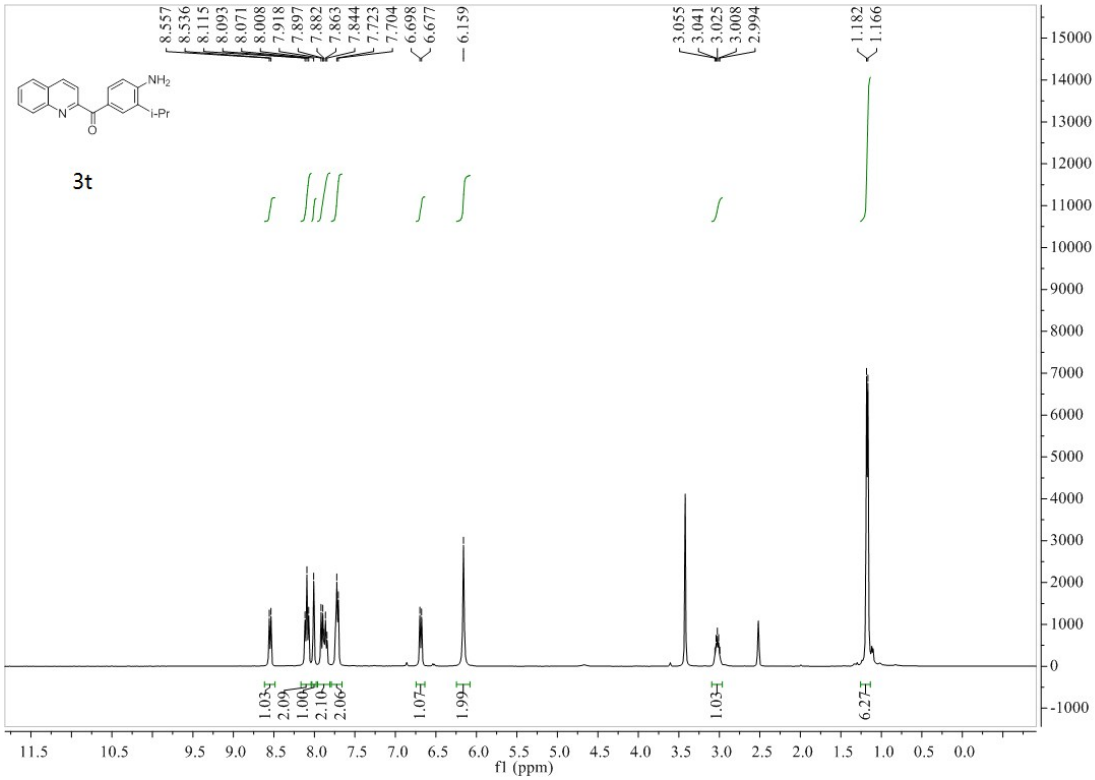

3q
180.47
171.40
155.90
155.00
135.44
134.46
130.50
127.67
124.99
121.41
120.21
113.34
f1 (ppm)

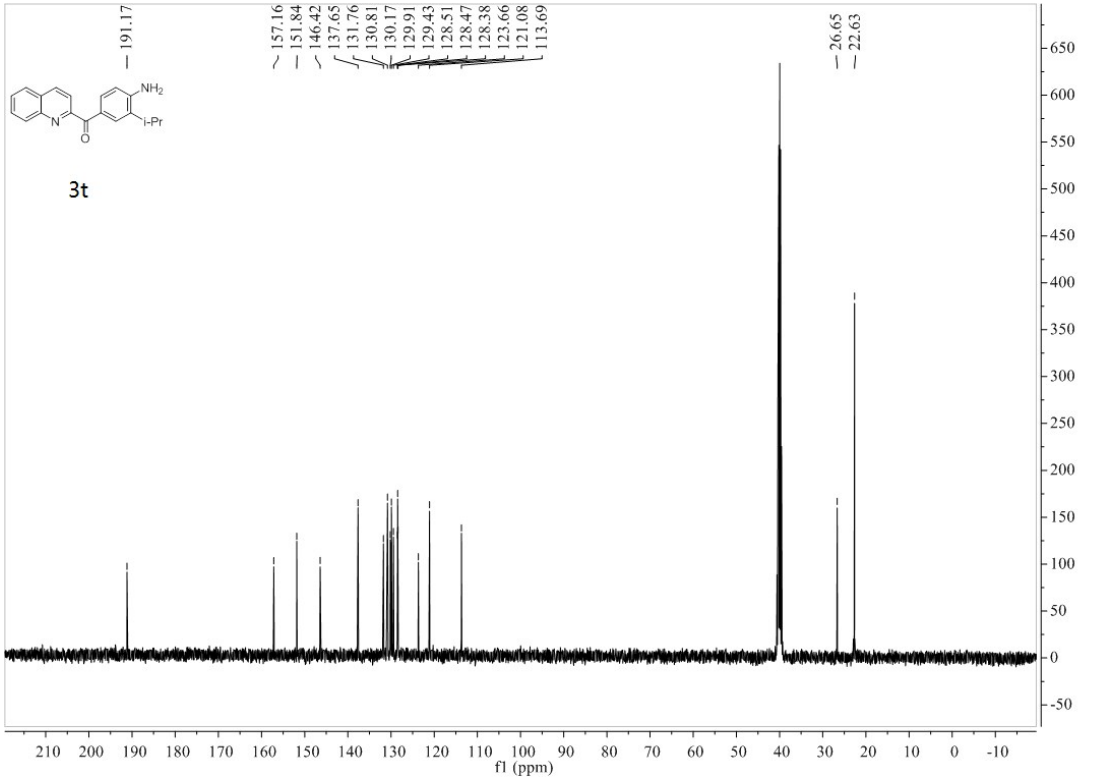

3r
8.526
8.505
8.123
8.102
8.063
8.043
7.869
7.847
7.818
7.778
7.756
7.715
7.697
7.678
6.712
6.691
6.086
2.120
1.00
1.01
0.98
2.10
1.95
1.01
1.02
2.01
3.01
f1 (ppm)

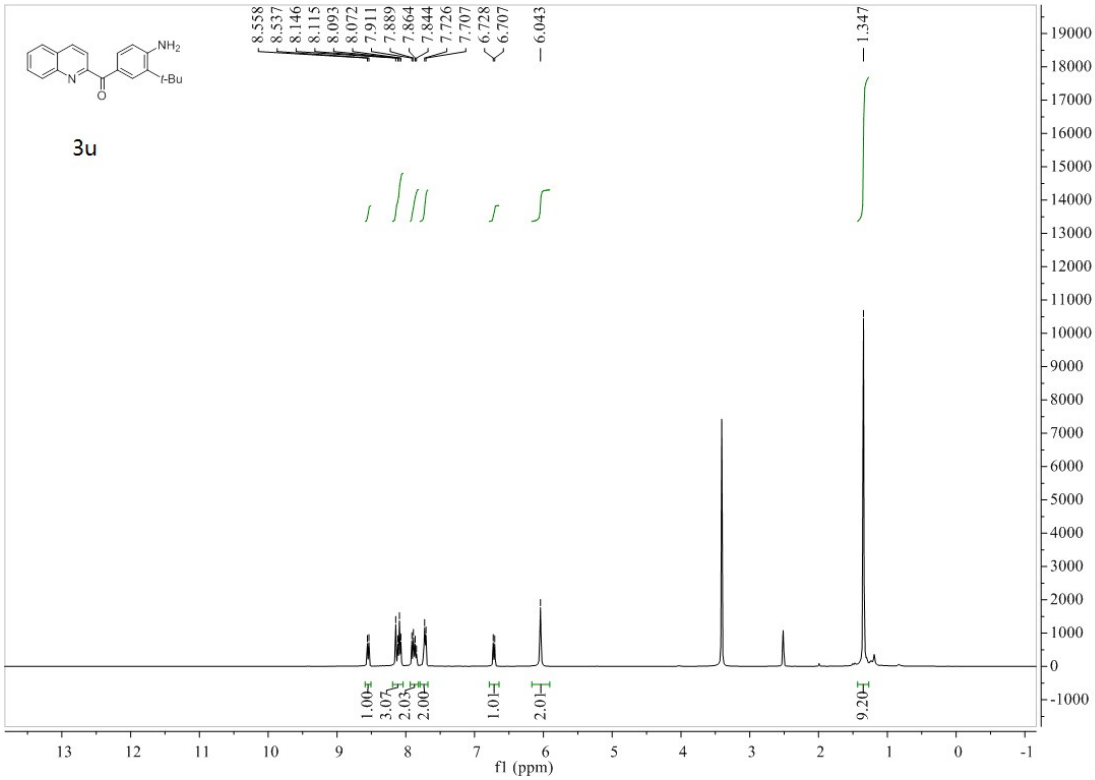

3r
191.49
157.34
153.05
146.48
137.61
134.03
132.04
130.74
129.97
128.48
128.44
128.28
123.63
120.97
120.31
112.96
17.92
f1 (ppm)

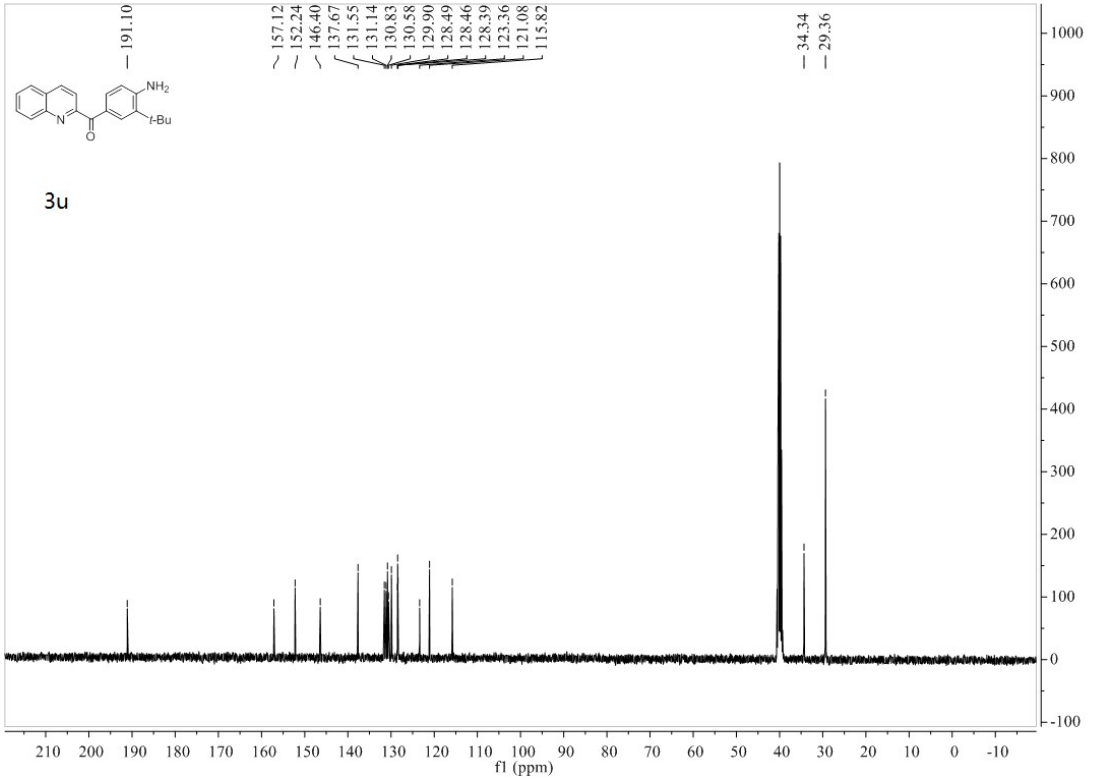

3s
8.557
8.536
8.120
8.097
8.074
7.888
7.867
7.839
7.743
7.724
6.689
6.668
6.102
2.520
2.504
2.485
2.467
1.173
1.154
1.136
1.00
2.01
2.99
1.94
1.03
1.95
2.40
3.33
f1 (ppm)

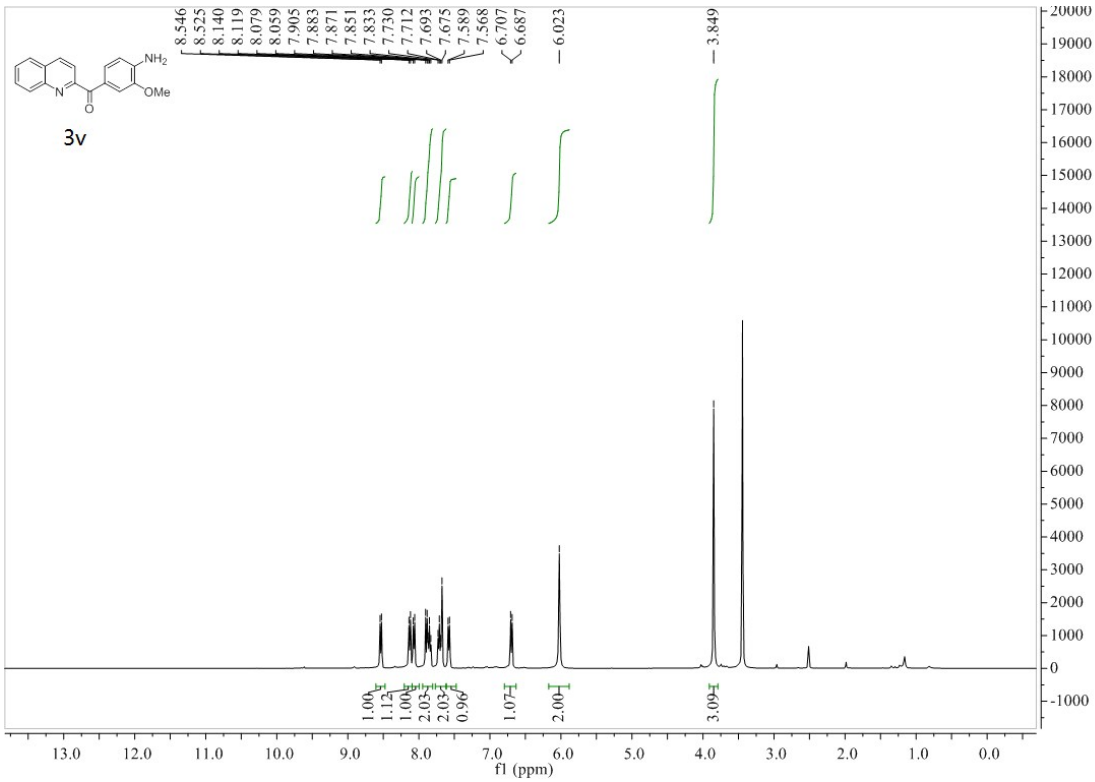

3s
191.34
157.26
152.43
146.45
137.65
132.08
131.94
130.80
129.93
128.50
128.46
128.35
125.80
123.65
121.02
113.29
23.62
13.35
f1 (ppm)

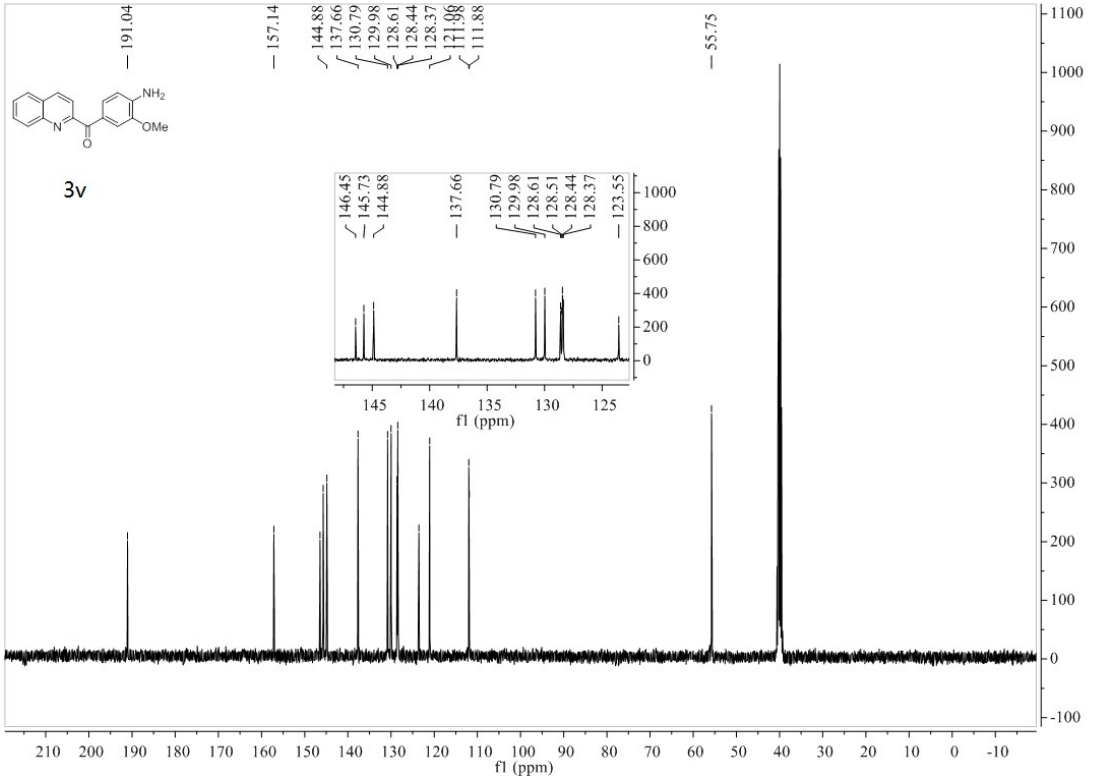

3t
f1 (ppm)

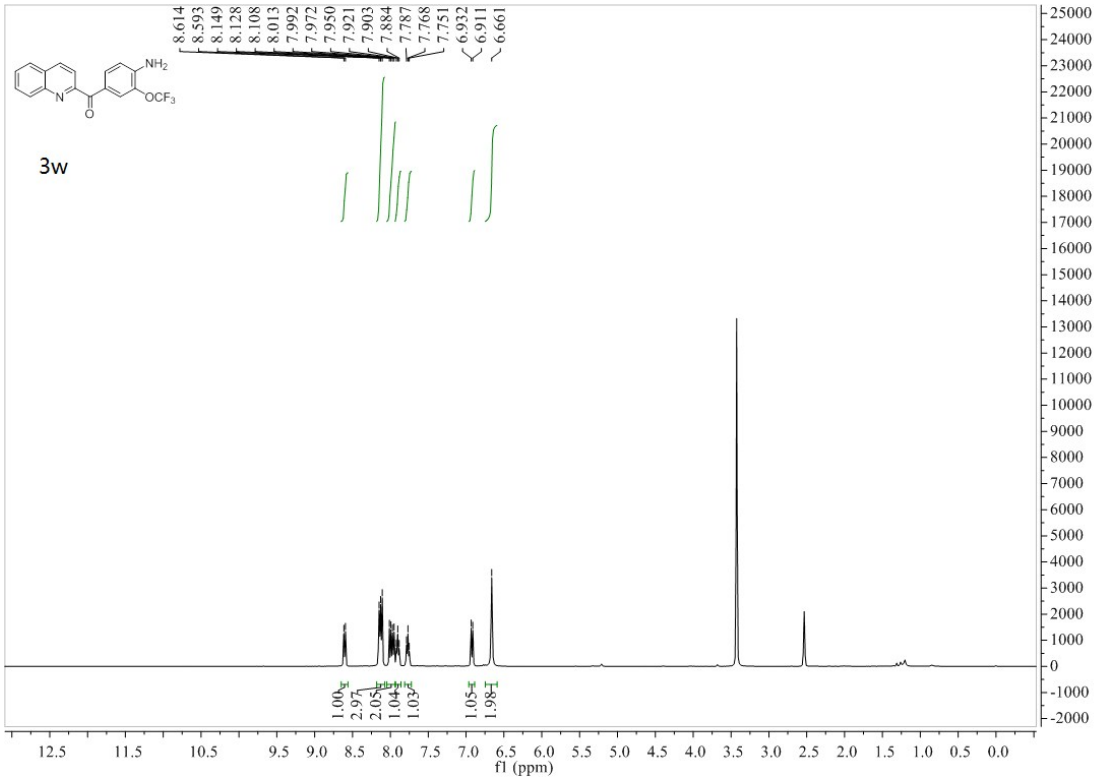

3t
f1 (ppm)

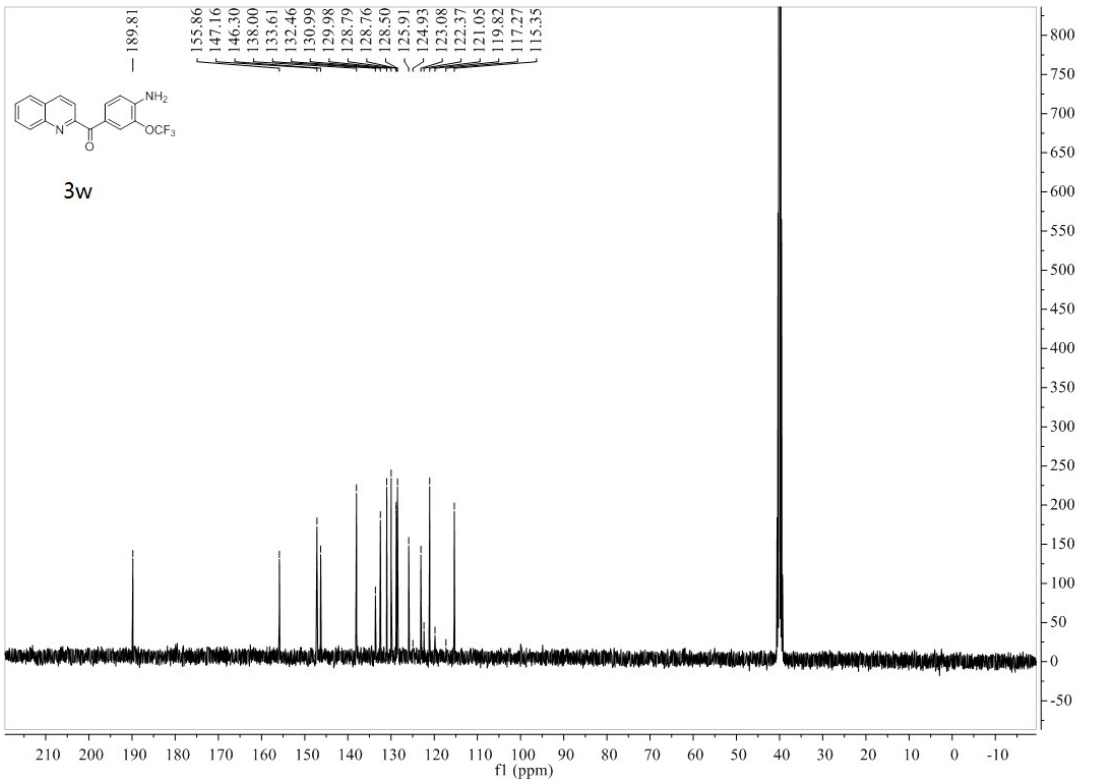

3u
8.558
8.537
8.146
8.115
8.093
8.072
7.911
7.889
7.864
7.844
7.726
7.707
6.728
6.707
6.043
1.347
1.00
3.07
2.03
2.00
1.01
2.01
9.20
f1 (ppm)

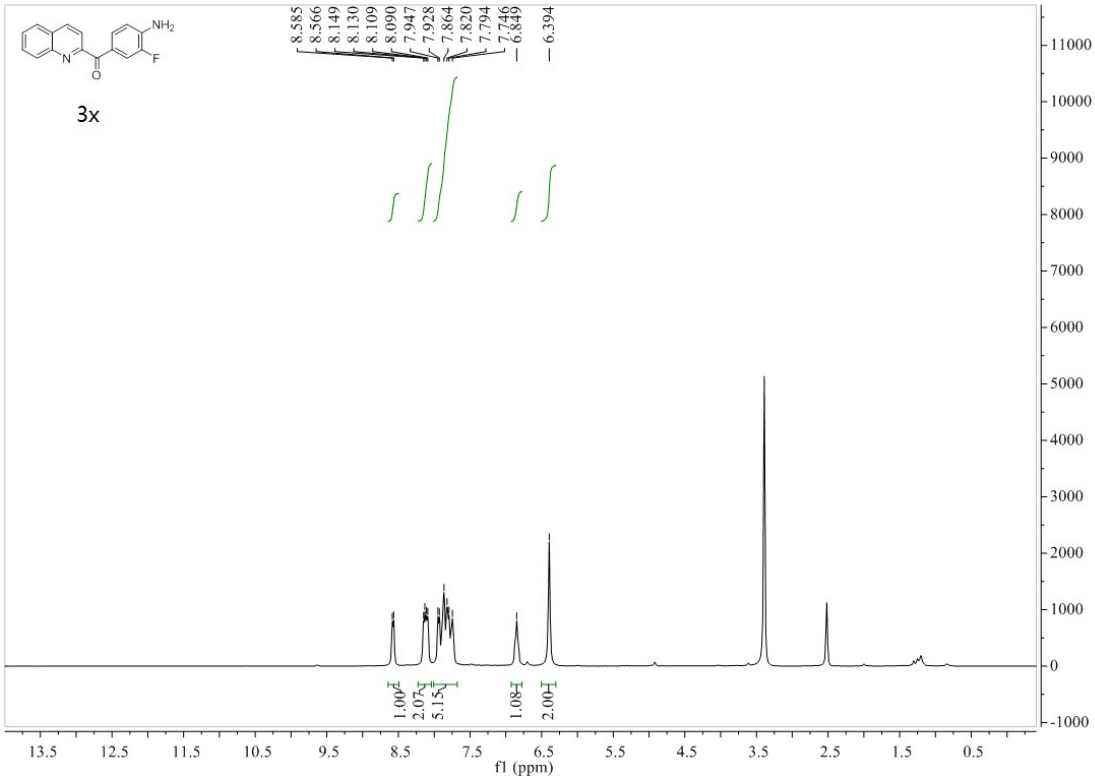

3u
191.10
157.12
152.24
146.40
137.67
131.55
131.14
130.83
130.58
129.90
128.49
128.46
128.39
123.36
121.08
115.82
34.34
29.36
f1 (ppm)

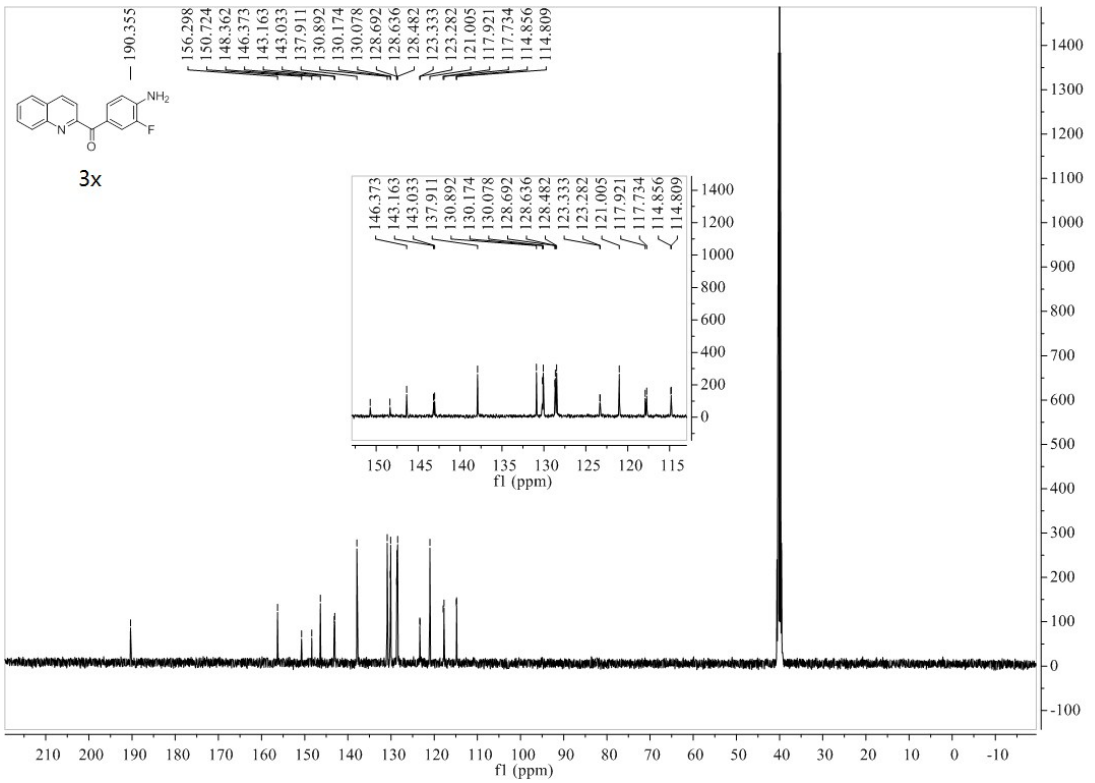

3v
NH2
OMe
8.546
8.525
8.140
8.119
8.079
8.059
7.905
7.883
7.871
7.851
7.833
7.730
7.712
7.693
7.675
7.589
7.568
6.707
6.687
6.023
3.849
1.00
1.12
1.00
2.03
2.03
0.96
1.07
2.00
3.09
f1 (ppm)

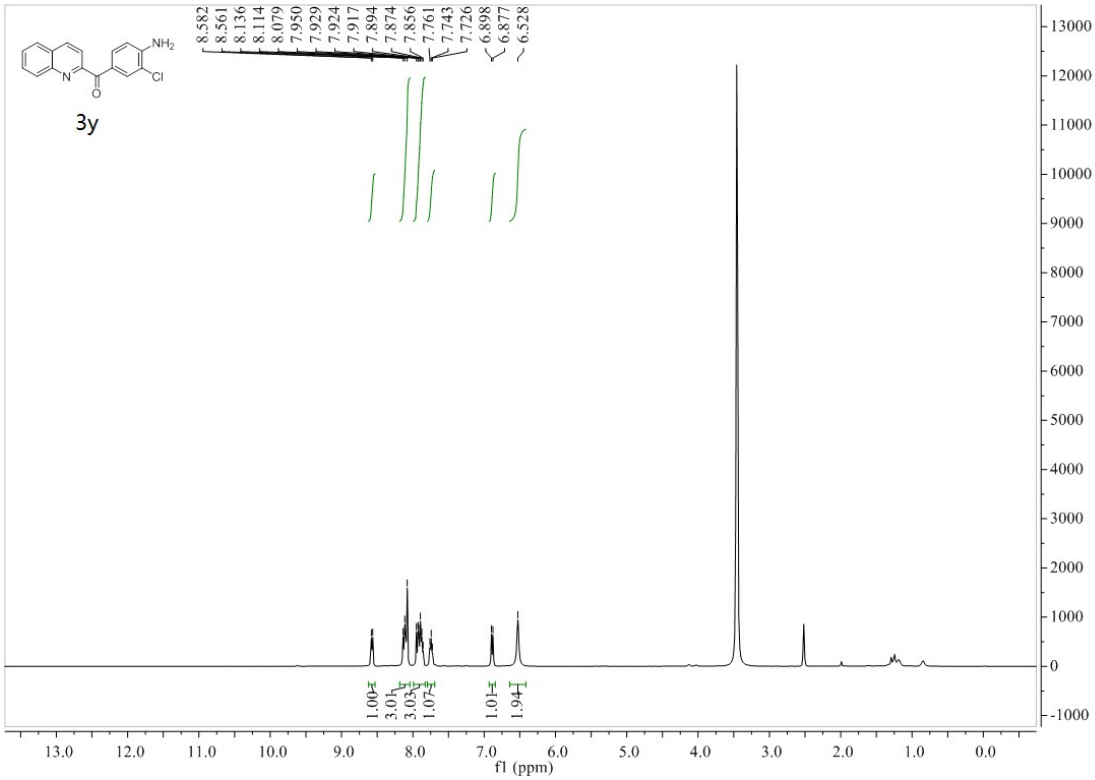

3v
NH2
OMe
191.04
157.14
144.88
137.66
130.79
129.98
128.61
128.44
128.37
121.06
111.88
55.75
146.45
145.73
144.88
137.66
130.79
129.98
128.61
128.51
128.44
128.37
123.55
f1 (ppm)

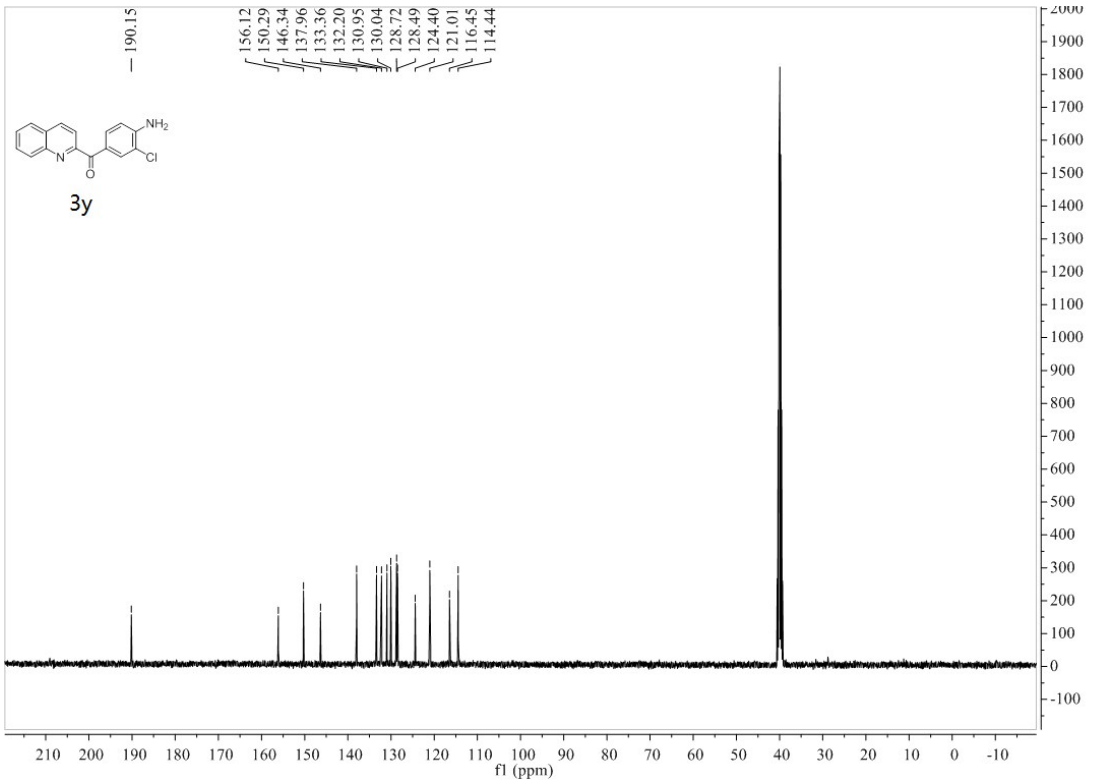

3w
8.614
8.593
8.149
8.128
8.108
8.013
7.992
7.972
7.950
7.921
7.903
7.884
7.787
7.768
7.751
6.932
6.911
6.661
1.00
2.97
2.05
1.04
1.03
1.05
1.98
f1 (ppm)

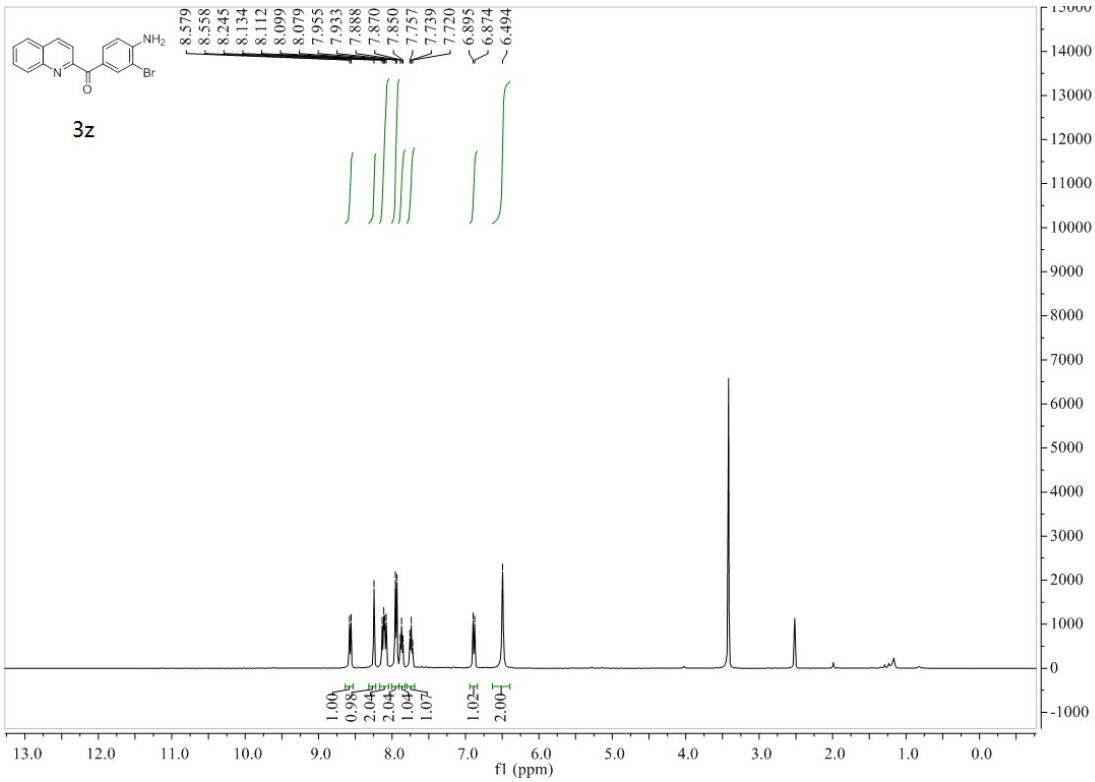

3w
189.81
155.86
147.16
146.30
138.00
133.61
132.46
130.99
129.98
128.79
128.76
128.50
125.91
124.93
123.08
122.37
121.05
119.82
117.27
115.35
f1 (ppm)

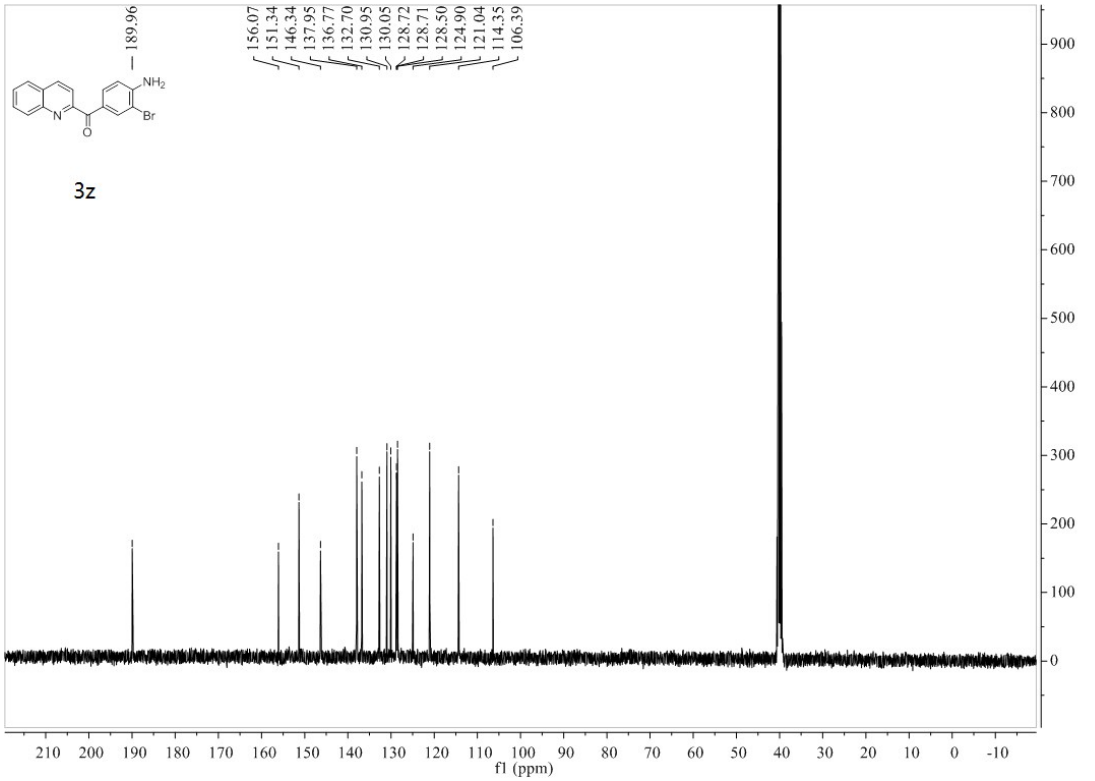

3x
8.585
8.566
8.149
8.130
8.109
8.090
7.947
7.928
7.864
7.820
7.794
7.746
6.849
6.394
1.00
2.07
5.15
1.08
2.00
f1 (ppm)

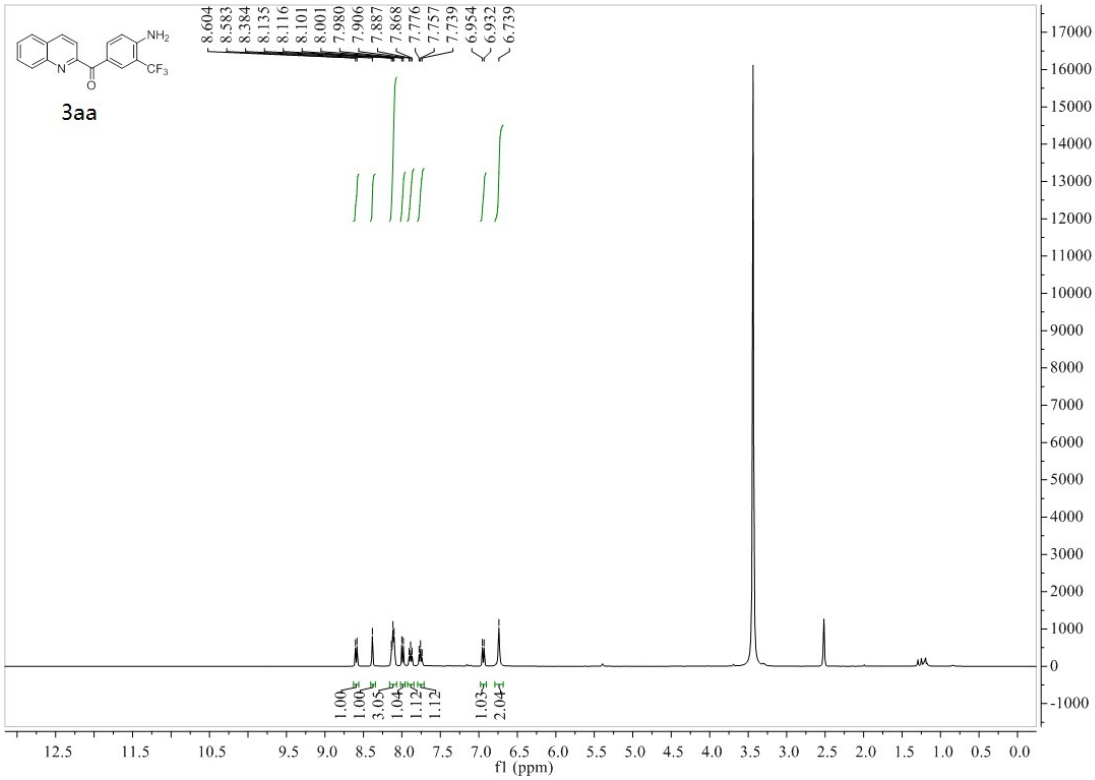

3x
190.355
156.298
150.724
148.362
146.373
143.163
143.033
137.911
130.892
130.174
130.078
128.692
128.636
128.482
123.333
123.282
121.005
117.921
117.734
114.856
114.809
f1 (ppm)

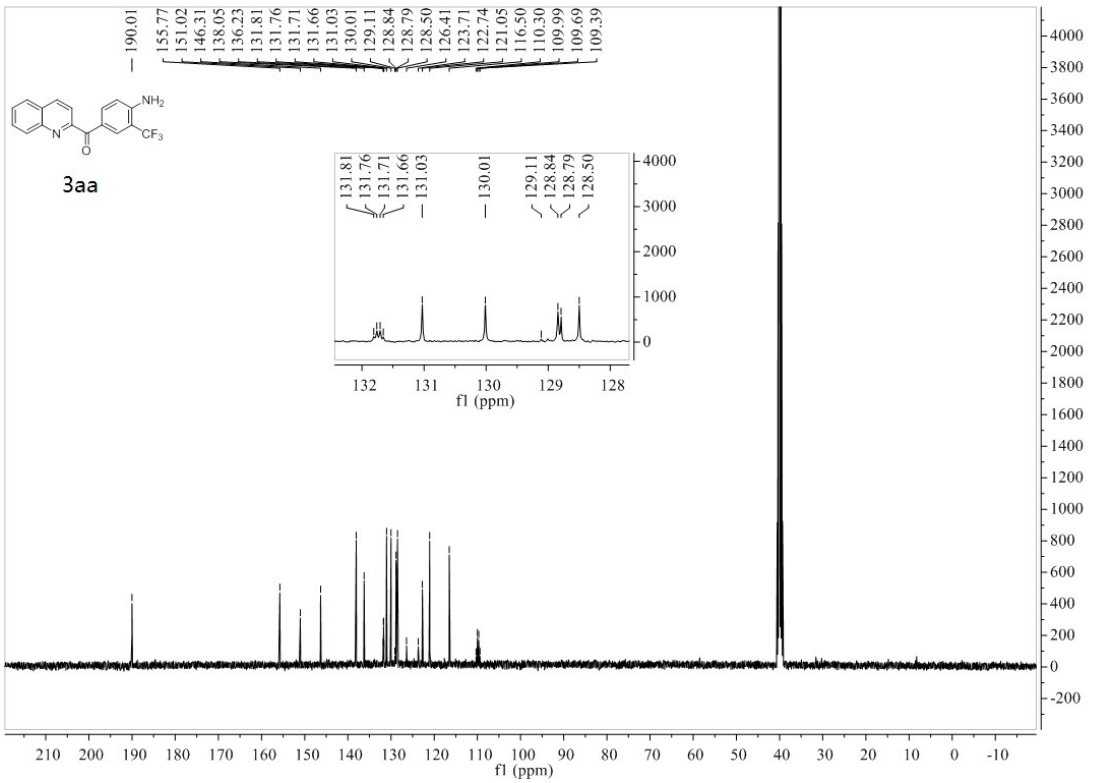

3y
8.582
8.561
8.136
8.114
8.079
7.950
7.929
7.924
7.917
7.894
7.874
7.856
7.761
7.743
7.726
6.898
6.877
6.528
1.00
3.01
3.03
1.07
1.01
1.94
f1 (ppm)

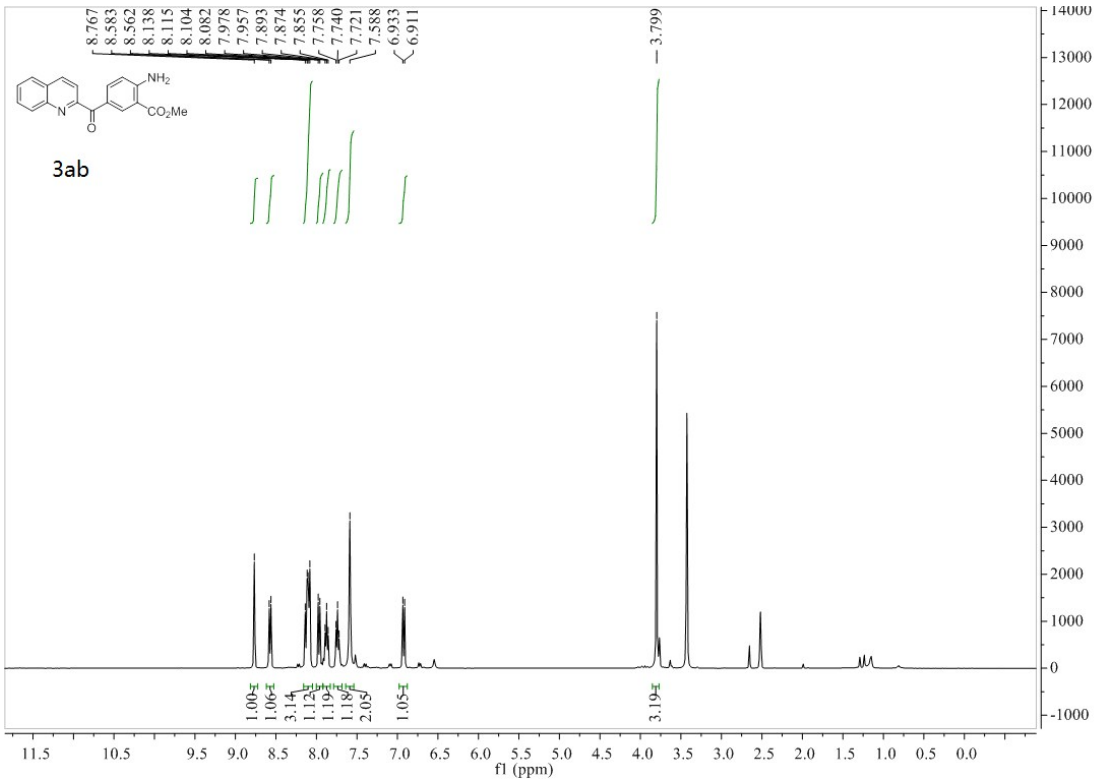

3y
190.15
156.12
150.29
146.34
137.96
133.36
132.20
130.95
130.04
128.72
128.49
124.40
121.01
116.45
114.44
f1 (ppm)


3z
8.579
8.558
8.245
8.134
8.112
8.099
8.079
7.955
7.933
7.888
7.870
7.850
7.757
7.739
7.720
6.895
6.874
6.494
1.00
0.98
2.04
2.04
1.04
1.07
1.02
2.00
f1 (ppm)


3z
189.96
156.07
151.34
146.34
137.95
136.77
132.70
130.95
130.05
128.72
128.71
128.50
124.90
121.04
114.35
106.39
f1 (ppm)


3aa
8.604
8.583
8.384
8.135
8.116
8.101
8.001
7.980
7.906
7.887
7.868
7.776
7.757
7.739
6.954
6.932
6.739
1.00
1.00
3.05
1.04
1.12
1.12
1.03
2.04
f1 (ppm)


3aa
190.01
155.77
151.02
146.31
138.05
136.23
131.81
131.76
131.71
131.66
131.03
130.01
129.11
128.84
128.79
128.50
126.41
123.71
122.74
121.05
116.50
110.30
109.99
109.69
109.39
f1 (ppm)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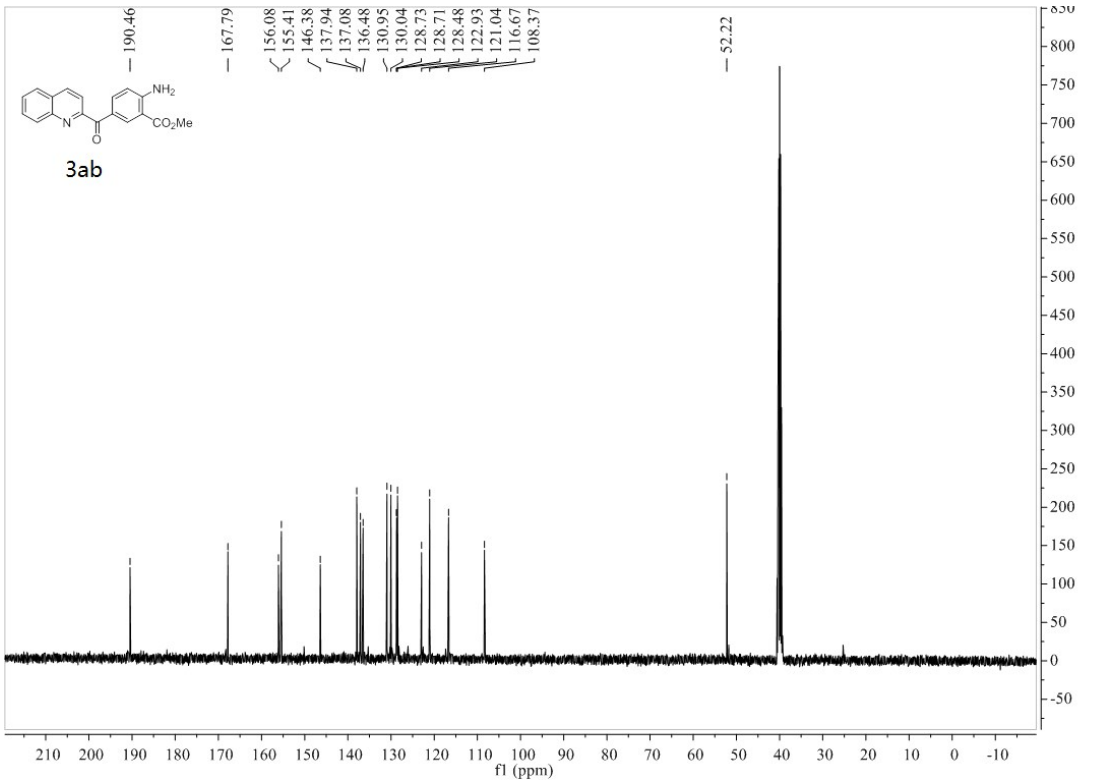
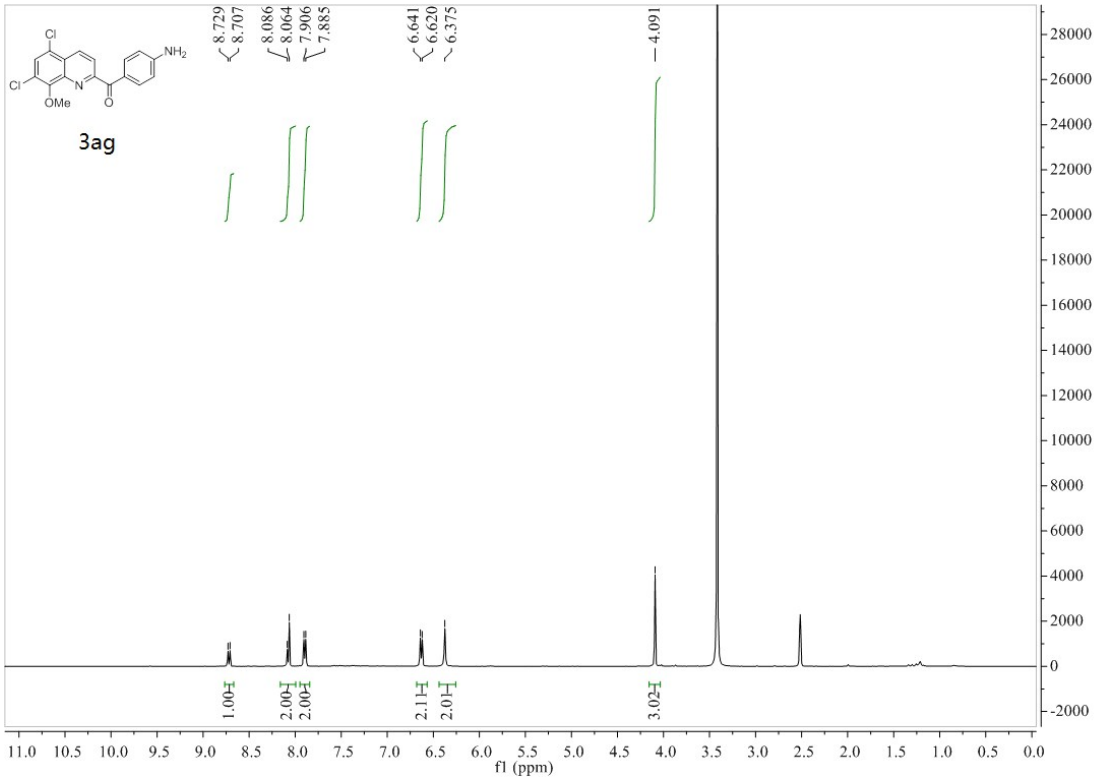
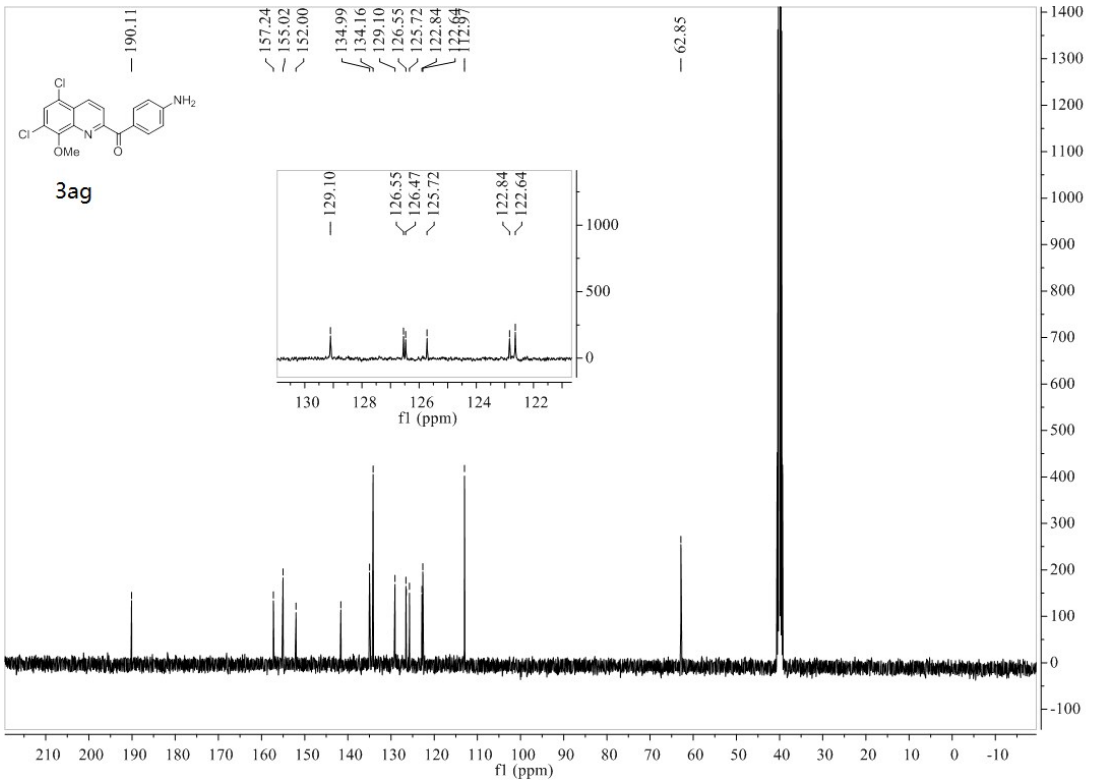
8.583
8.562
8.138
8.115
8.104
8.082
7.978
7.957
7.893
7.874
7.855
7.758
7.740
7.721
7.588
6.933
6.911
3.799
NH2
CO2Me
3ab
1.00
1.06
3.14
1.12
1.19
1.18
2.05
1.05
3.19
f1 (ppm)


190.46
167.79
156.08
155.41
146.38
137.94
137.08
136.48
130.95
130.04
128.73
128.71
128.48
122.93
121.04
116.67
108.37
52.22
NH2
CO2Me
3ab
f1 (ppm)


3ag
8.729
8.707
8.086
8.064
7.906
7.885
6.641
6.620
6.375
4.091
1.00
2.00
2.00
2.1
2.01
3.02
f1 (ppm)


3ag
190.11
157.24
155.02
152.00
134.99
134.16
129.10
126.55
125.72
122.84
122.97
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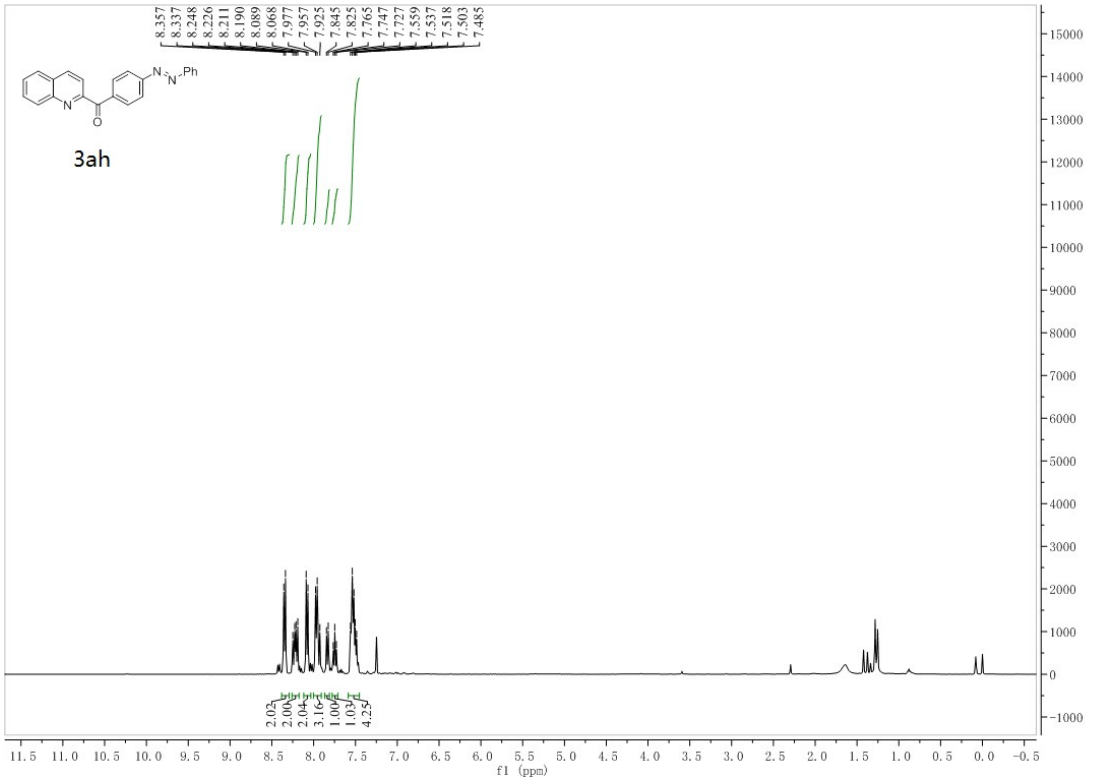
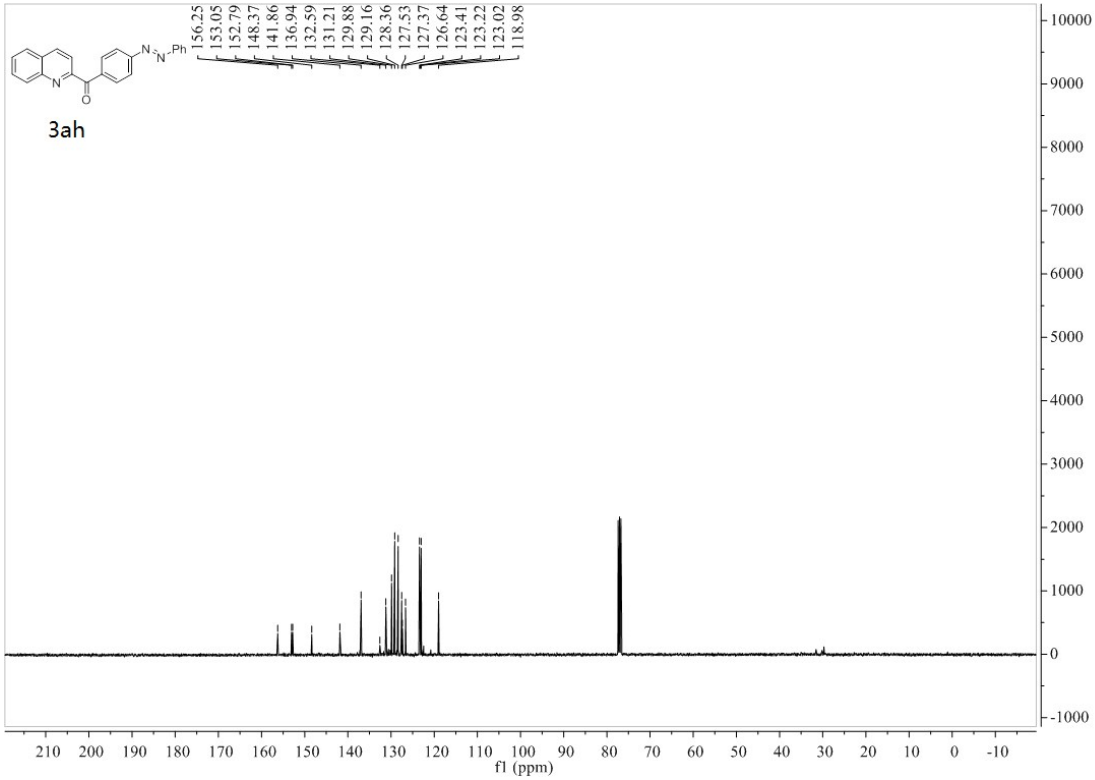
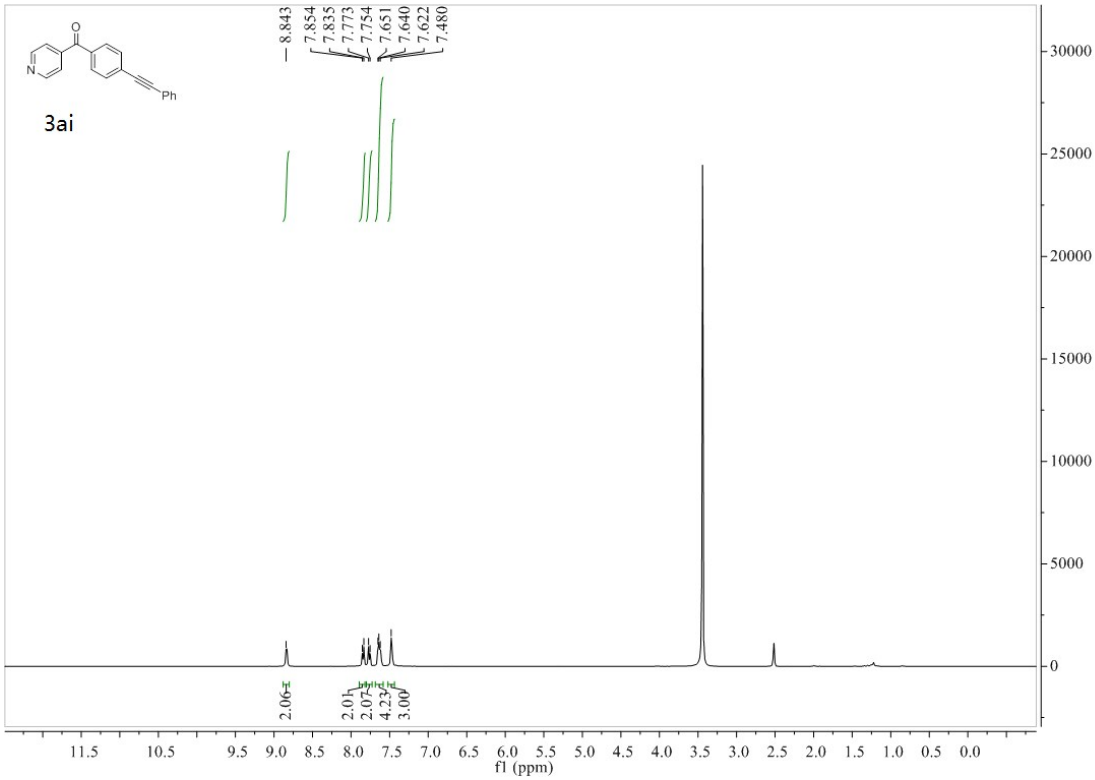
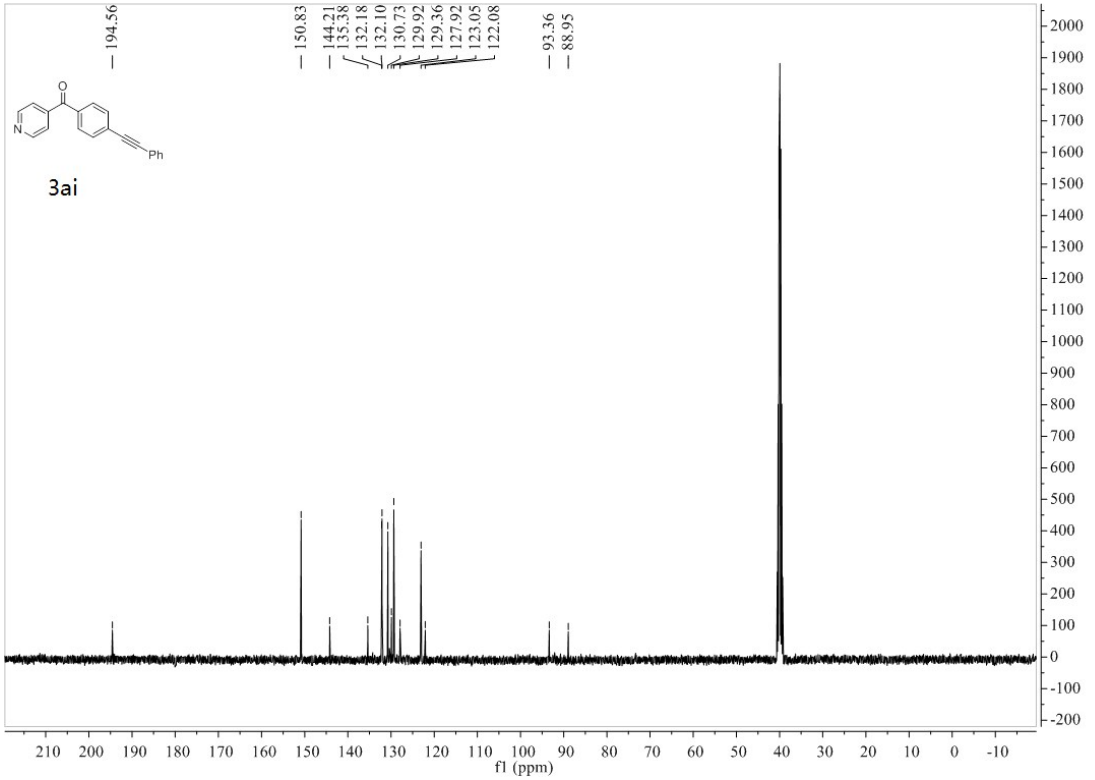
126.47
125.72
122.84
122.64
f1 (ppm)


8.357
8.337
8.248
8.226
8.211
8.190
8.089
8.068
7.977
7.957
7.925
7.845
7.825
7.765
7.747
7.727
7.559
7.537
7.518
7.503
7.485
N
N
Ph
O
3ah
2.02
2.00
2.04
3.16
1.00
1.03
4.25
f1 (ppm)


156.25
153.05
152.79
148.37
141.86
136.94
132.59
131.21
129.88
129.16
128.36
127.53
127.37
126.64
123.41
123.22
123.02
118.98
N
N
Ph
O
3ah
f1 (ppm)


3ai
8.843
7.854
7.835
7.773
7.754
7.651
7.640
7.622
7.480
2.06
2.01
2.07
4.23
3.00
f1 (ppm)


3ai
194.56
150.83
144.21
135.38
132.18
132.10
130.73
129.92
129.36
127.92
123.05
122.08
93.36
88.95
f1 (ppm)