Supporting Information

Transition Metal-free Synthesis of 3-Substituted Quinolines through Formal [4+2] Annulation of Anthranils and Enaminones

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Contents

1. Table S1. Optimization studies[a]

Entry	Amout of **1a** (x mmol)	Amout of **2a** (y mmol)	Additive	Solvent	Temp. (°C)	Yield[b] (%)
1	0.4	0.2	TFA	EtOH	110	27
2	0.4	0.2	MSA	EtOH	110	31
3	0.4	0.2	Hexanoic acid	EtOH	110	0
4	0.4	0.2	Acetic anhydride	EtOH	110	0
5	0.4	0.2	HOAc	EtOH	110	0
6	0.4	0.2	MSA	HFIP	110	5
7	0.4	0.2	MSA	DME	110	11
8	0.4	0.2	MSA	*n*-Octanol	110	0
9	0.4	0.2	MSA	IPE	110	26
10	0.4	0.2	MSA	*dioxane*	110	18
11	0.4	0.2	MSA	THF	110	29
12	0.4	0.2	MSA	MOE	110	2
13	0.4	0.2	MSA	DMSO	110	0
14	0.4	0.2	/	DMSO	110	0
15	0.4	0.2	MSA/KBr	EtOH	110	58
16	0.4	0.2	MSA/KBr	EtOH	110	37
17	0.4	0.2	MSA/KI	EtOH	110	89
18	0.4	0.2	MSA/NaI	EtOH	110	90
19	0.4	0.2	MSA/$K_2S_2O_8$	EtOH	110	16
20	0.4	0.2	MSA/NaI	EtOH	70	43
21	0.4	0.2	MSA/NaI	EtOH	80	65
22	0.4	0.2	MSA/NaI	EtOH	90	84
23	0.4	0.2	MSA/NaI	EtOH	120	90

[a] Reaction conditions: **1a** (x mmol), **2a** (y mmol), additive (1 .5 equiv), solvent (2 mL), 110 °C, under air 12 h. [b] Isolated yield.

2.Gram-scale Preparation of 3aa

A mixture of benzo[c]isoxazole (**1a**) (12 mmol, 2.0 equiv), (*E*)-3-(dimethylamino)-1-phenylprop-2-en-1-one (**2a**) (1050.6 mg, 6.0 mmol, 1.0 equiv) and NaI (1350 mg, 1.5 equiv) were added in a 100 mL round bottom flask equipped with a stirring bar. Dry EtOH (20 mL) and methanesulfonic acid (MSA) (9 mmol, 1.5 equiv) were added and the mixture was stirred at 110 °C in a preheated oil bath for 12 h under air atmosphere. Then the mixture was cooled to room temperature and concentrated in vacuo and the resulting residue was purified by flash column chromatography on silica gel with EtOAc/petroleum ether, affording product **3aa** as a yellow solid in 85% yield (1.192 g, 5.1 mmol).

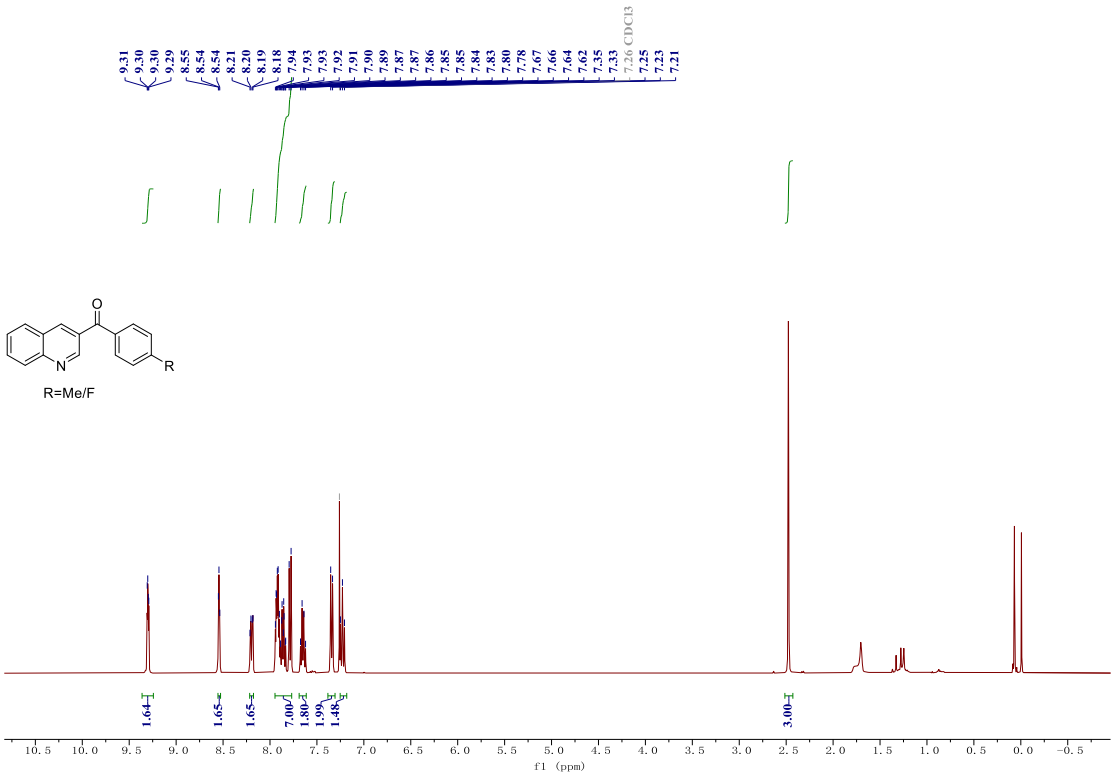
3.Competition Experiments

A mixture of (*E*)-3-(dimethylamino)-1-(*p*-tolyl)prop-2-en-1-one (**2b**) (37.8 mg, 0.2 mmol, 1.0 equiv), (*E*)-3-(dimethylamino)-1-(4-fluorophenyl)prop-2-en-1-one (**2g**) (38.6 mg, 0.2 mmol, 1.0 equiv), benzo[c]isoxazole (**1a**) (23.8 mg, 0.2 mmol, 1.0 equiv) and NaI (45 mg, 0.3 mmol,1.5 equiv) were added in a Schlenk sealed tube equipped with a stirring bar. Dry EtOH (2.0 mL) and MSA (0.3mmol, 1.5 equiv) were added and the mixture was stirred at 110 °C in a pre-heated oil bath for 12 h under air atmosphere. Then, the mixture was cooled to room temperature and concentrated in vacuo and the resulting residue was purified by flash column chromatography on

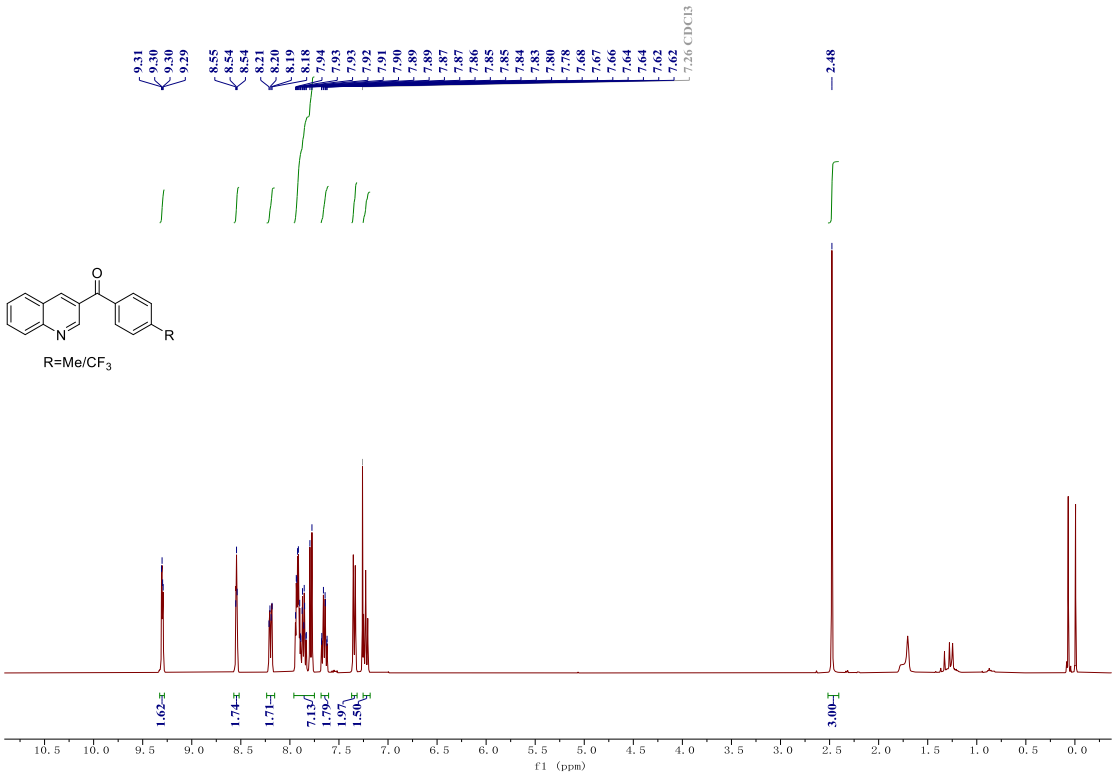
silica gel with EtOAc/petroleum ether to give a mixture of products **3ab** and **3ag** at a ratio of 1:0.64.

A mixture of (*E*)-3-(dimethylamino)-1-(p-tolyl)prop-2-en-1-one (**2b**) (37.8 mg, 0.2 mmol, 1.0 equiv), (*E*)-3-(dimethylamino)-1- (4-(trifluoromethyl)phenyl)prop-2-en-1-one (**2m**) (48.6 mg, 0.2 mmol, 1.0 equiv), benzo[c]isoxazole (**1a**) (23.8 mg, 0.2 mmol, 1.0 equiv) and NaI (45 mg, 0.3 mmol,1.5 equiv) were added in a Schlenk sealed tube equipped with a stirring bar. Dry EtOH (2.0 mL) and MSA (0.3mmol, 1.5 equiv) were added and the mixture was stirred at 110 ºC in a pre-heated oil bath for 12 h under air atmosphere. Then the mixture was cooled to room temperature and concentrated in vacuo and the resulting residue was purified by flash column chromatography on silica gel with EtOAc/petroleum ether to give a mixture of products **3ab** and **3am** at a ratio of 1:0.62.

4.NMR Spectra

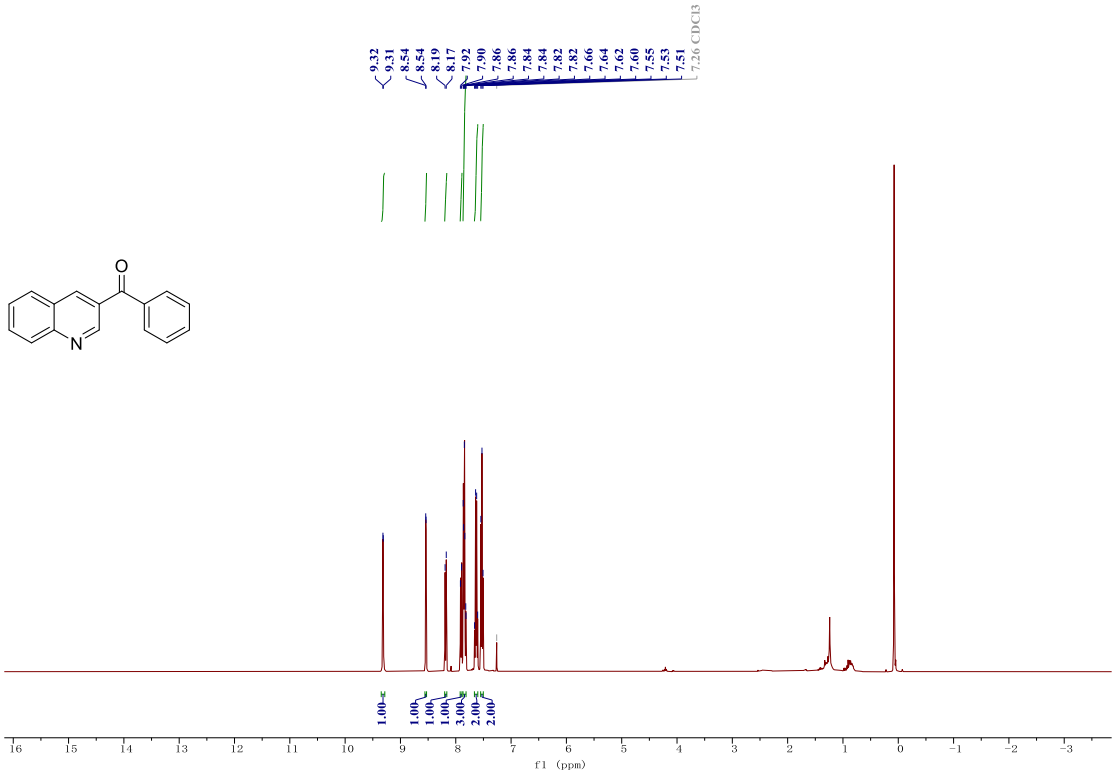


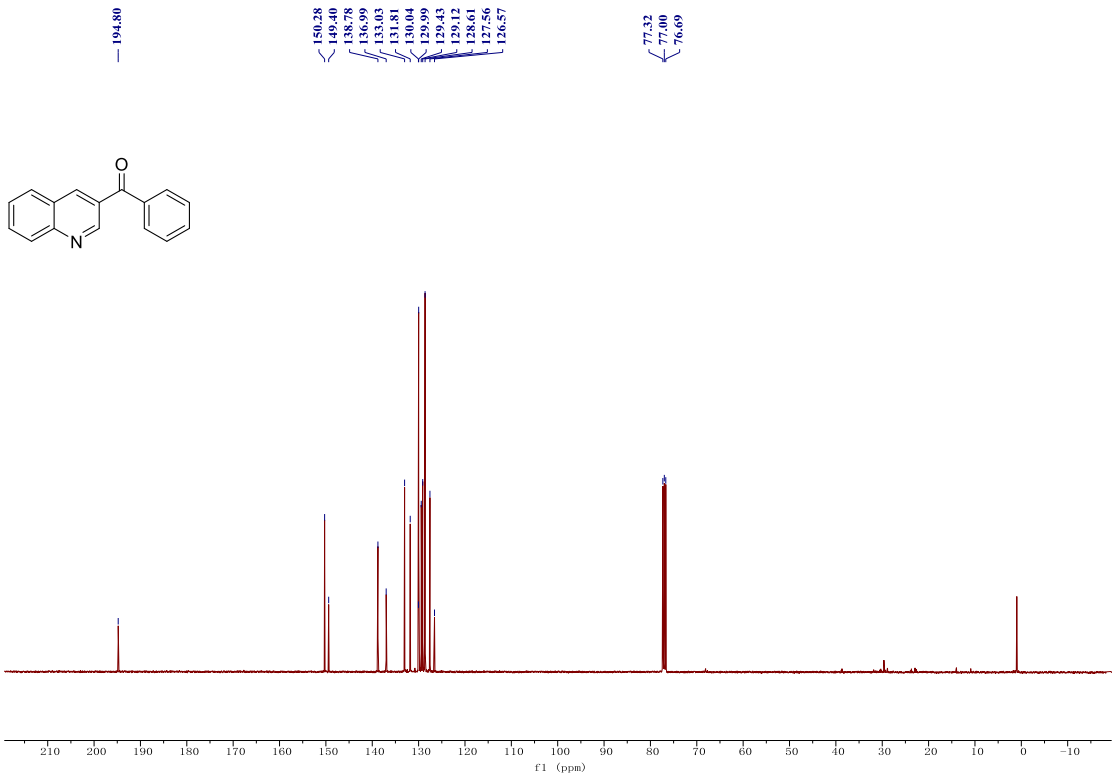
^{1}H NMR of the mixture of **3ab** and **3ag** for the competition experiment



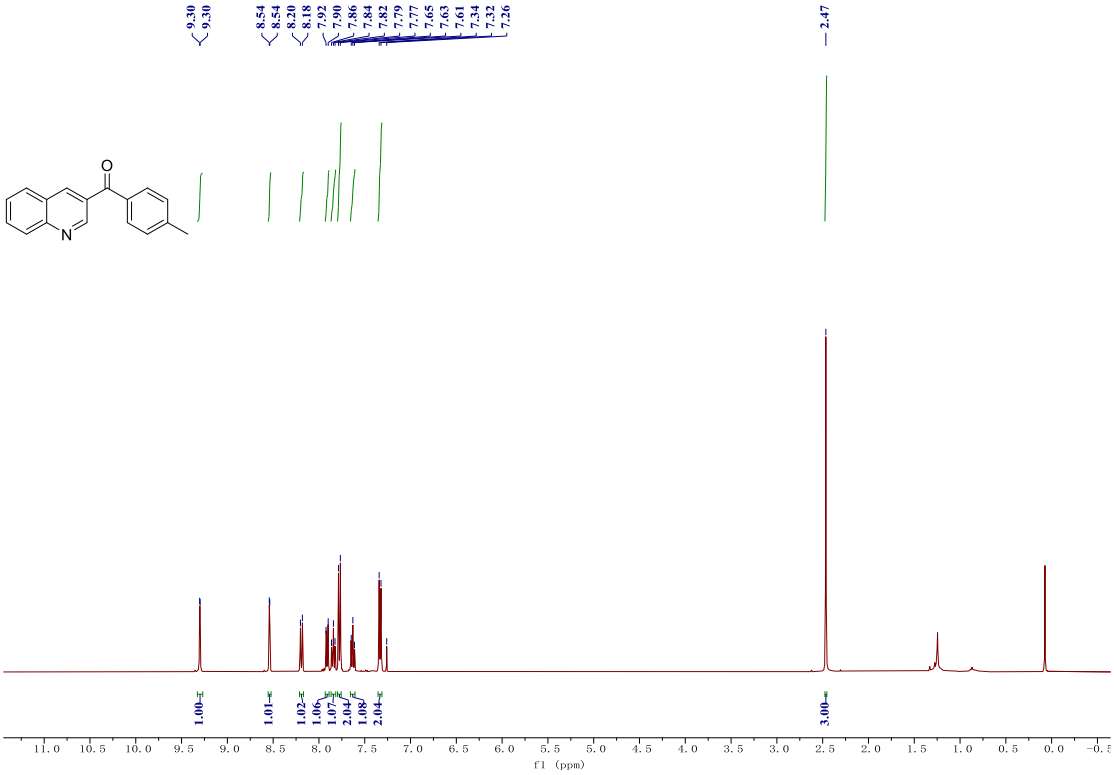
^{1}H NMR of the mixture of **3ab** and **3am** for the competition experiment

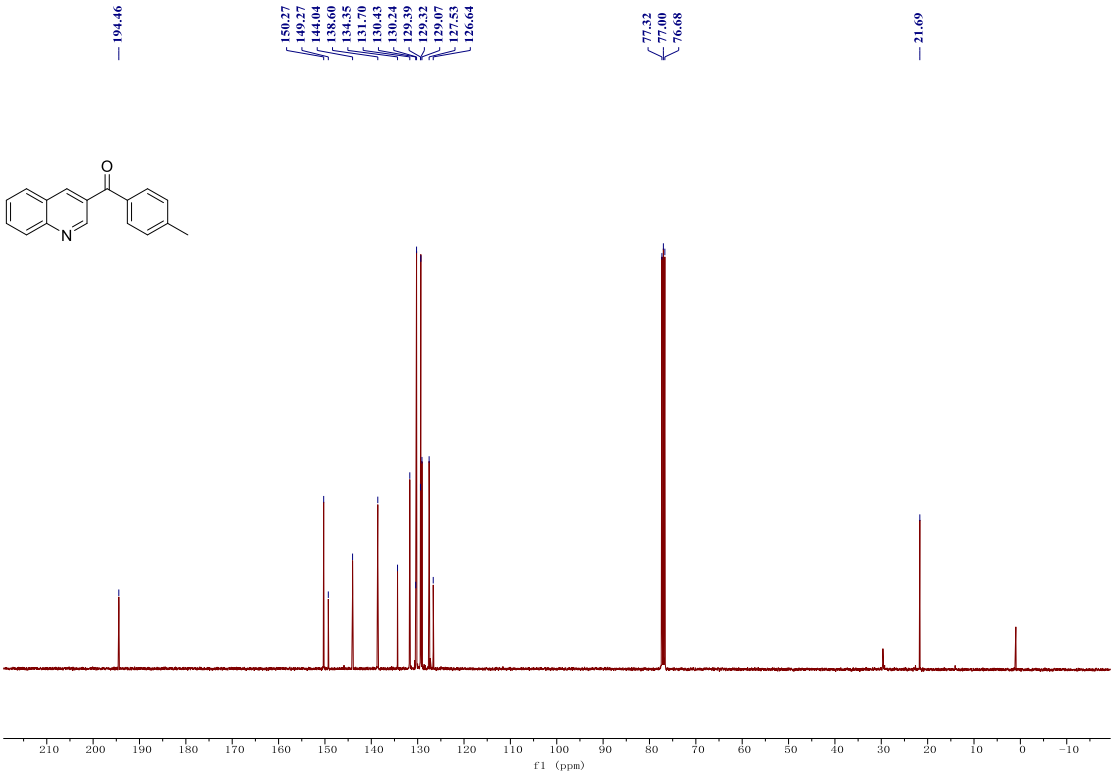
^{1}H NMR and ^{13}C NMR for **3aa**



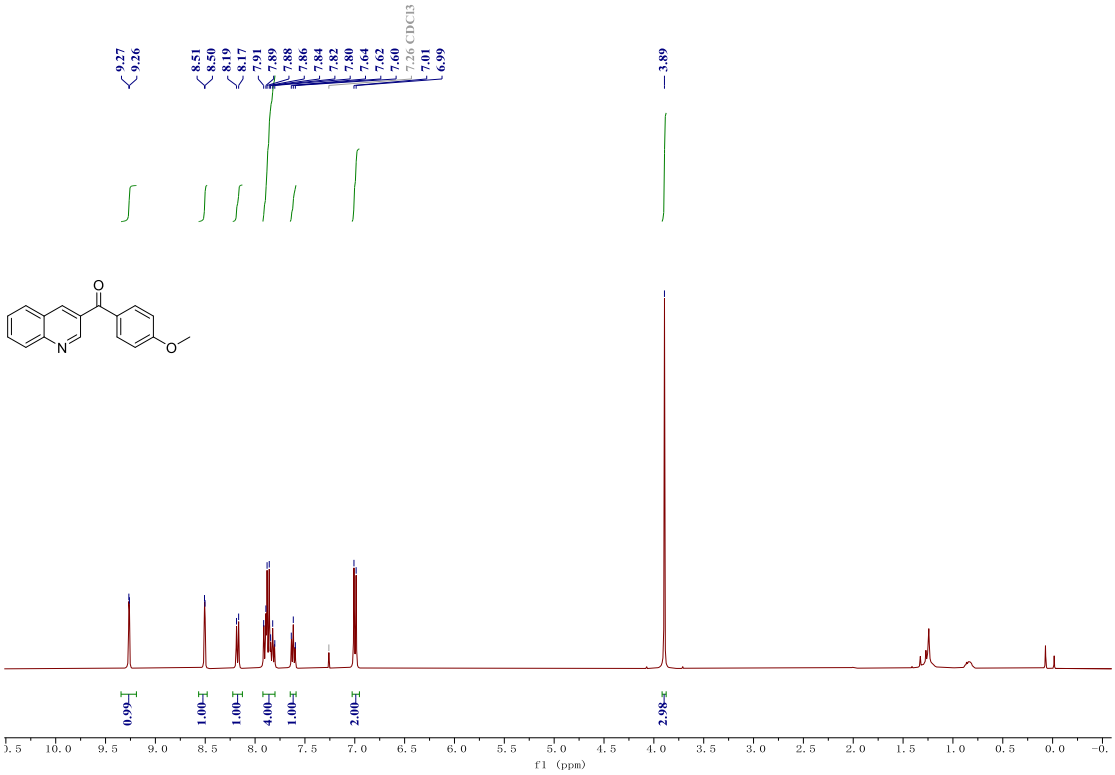


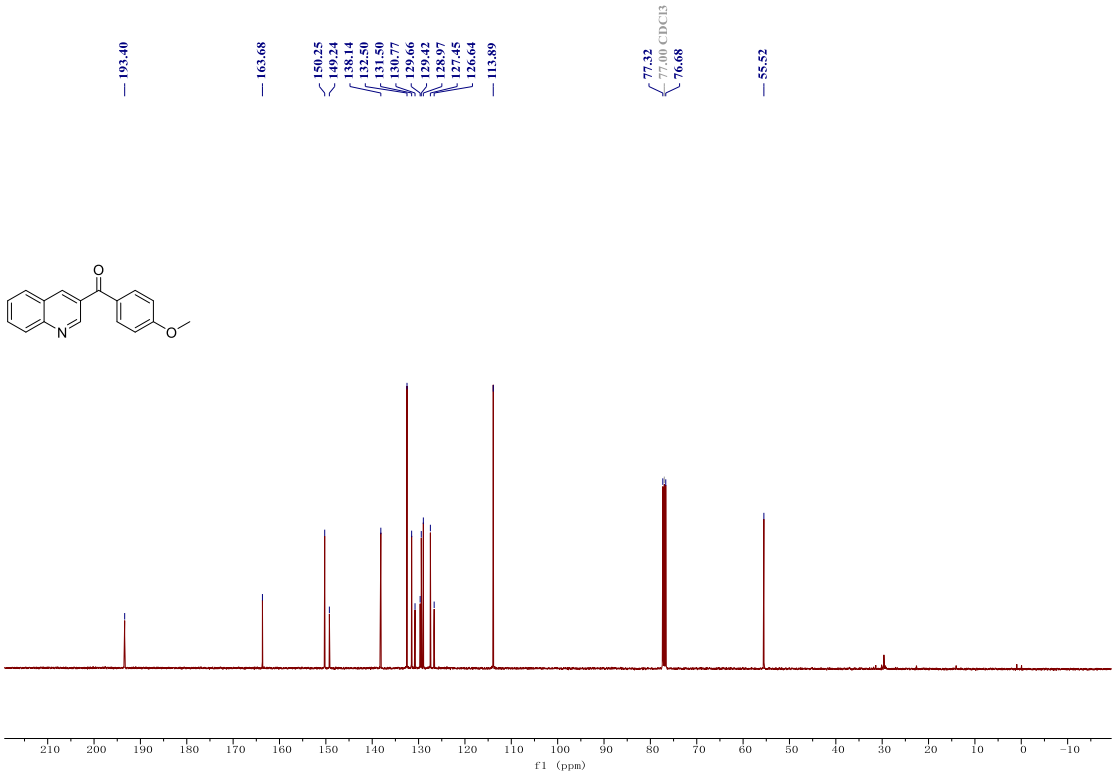
^{1}H NMR and ^{13}C NMR for **3ab**



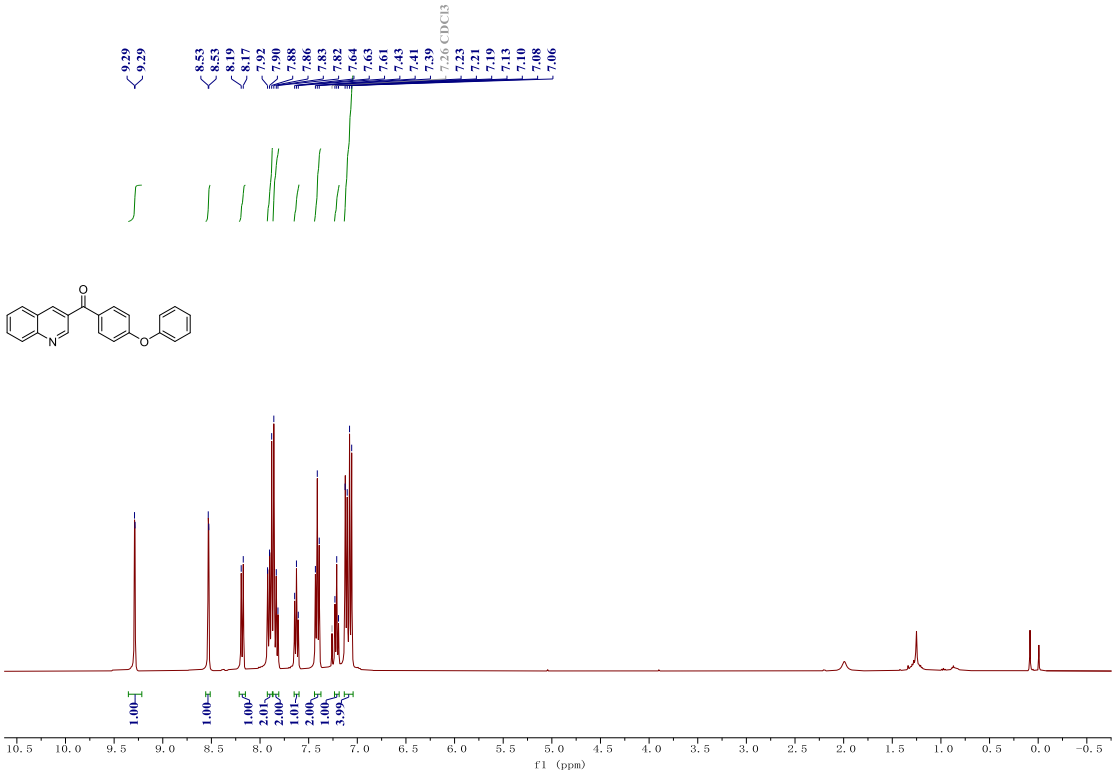


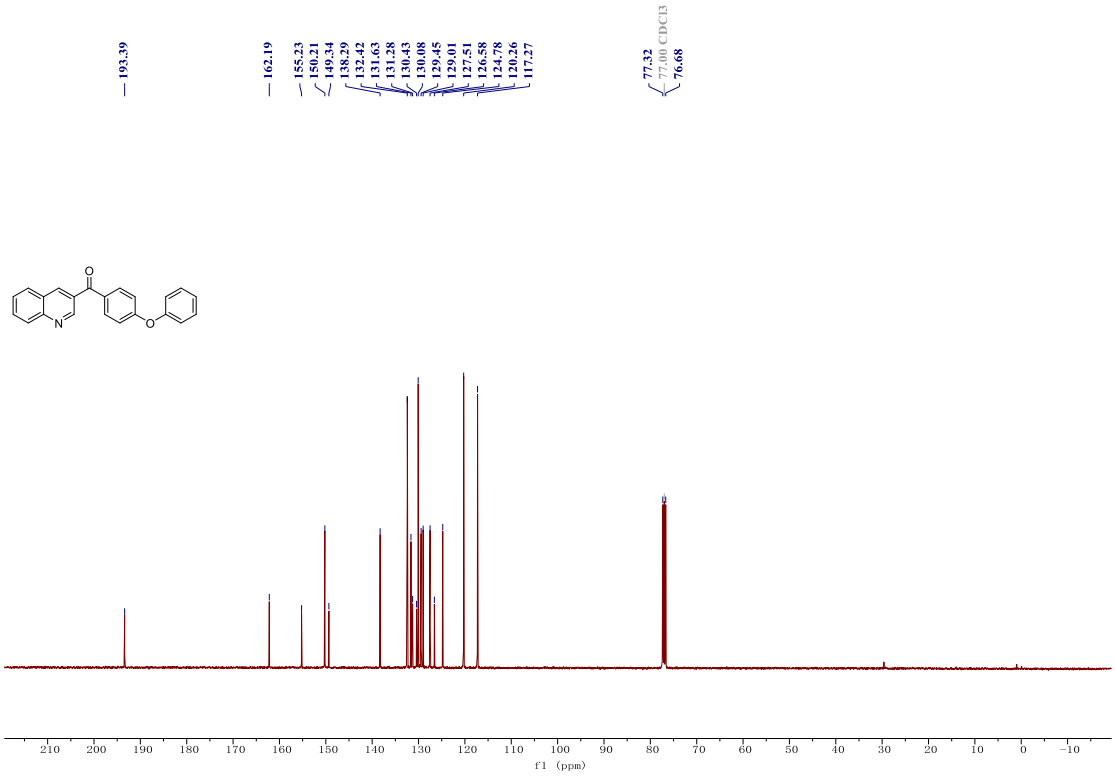
^{1}H NMR and ^{13}C NMR for **3ac**



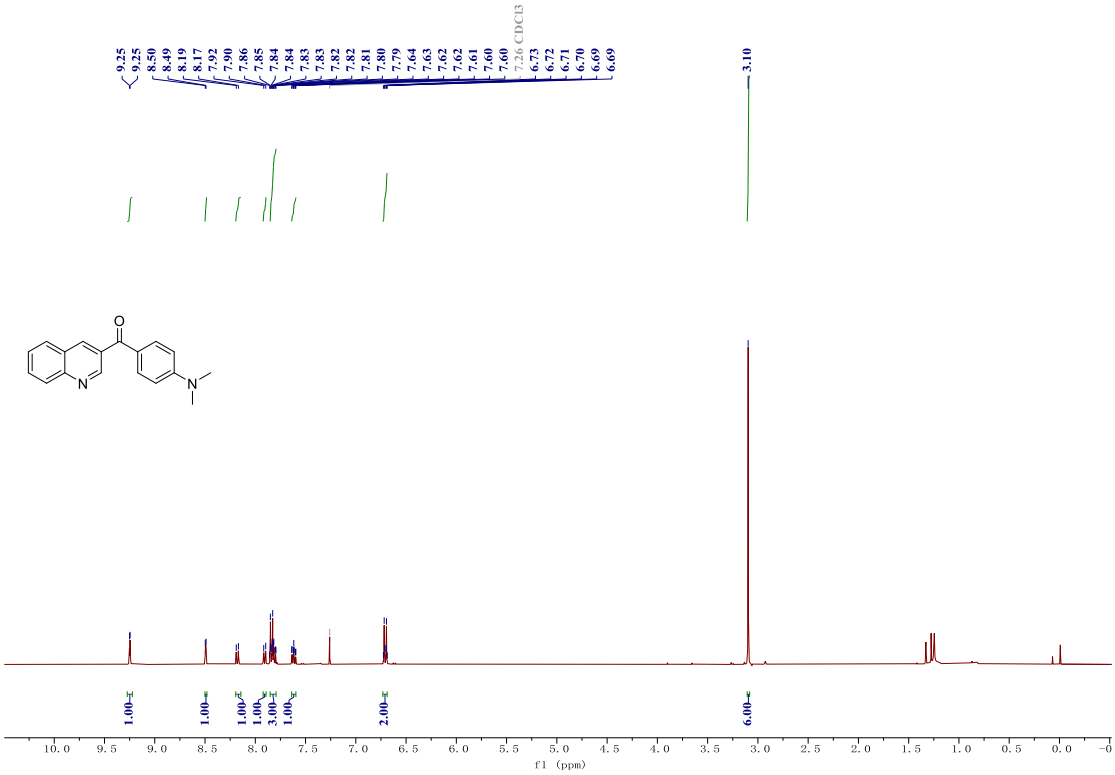


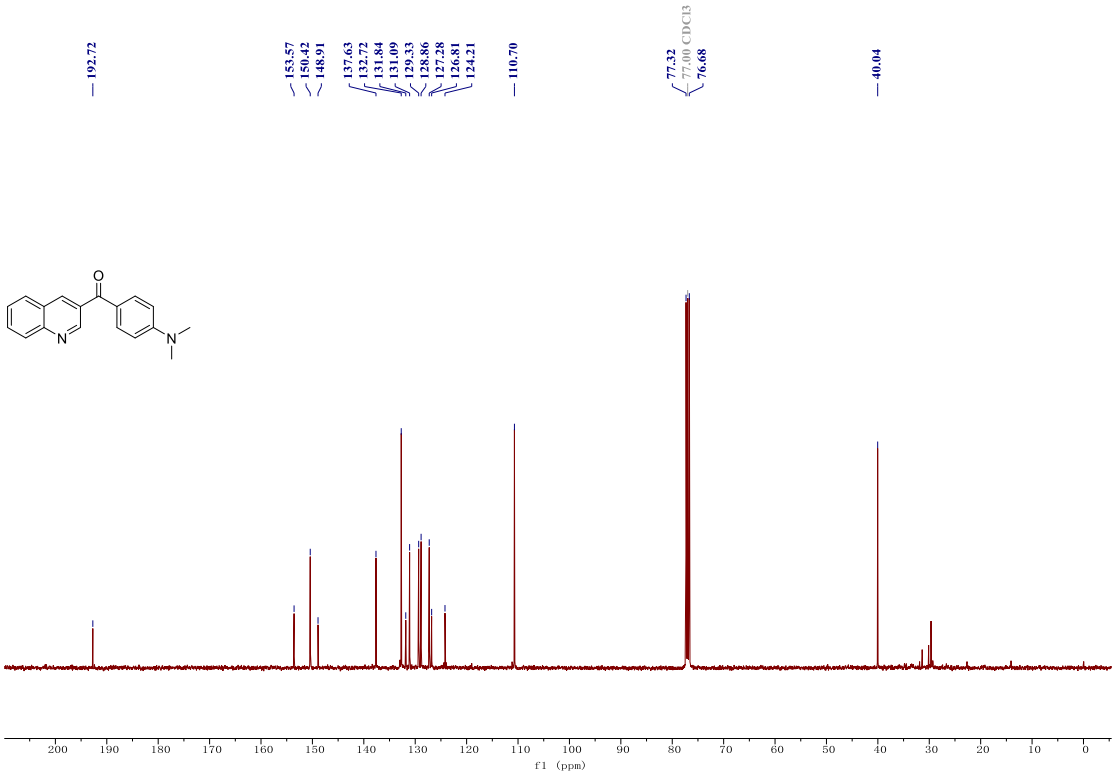
^{1}H NMR and ^{13}C NMR for **3ad**



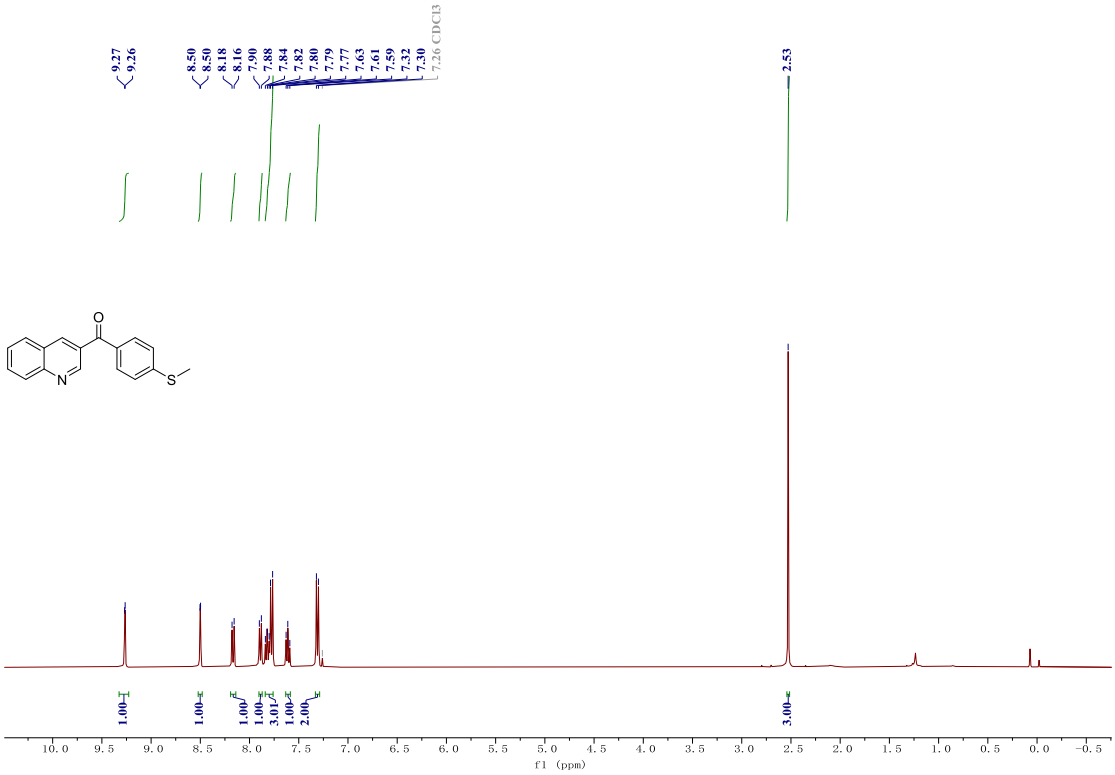


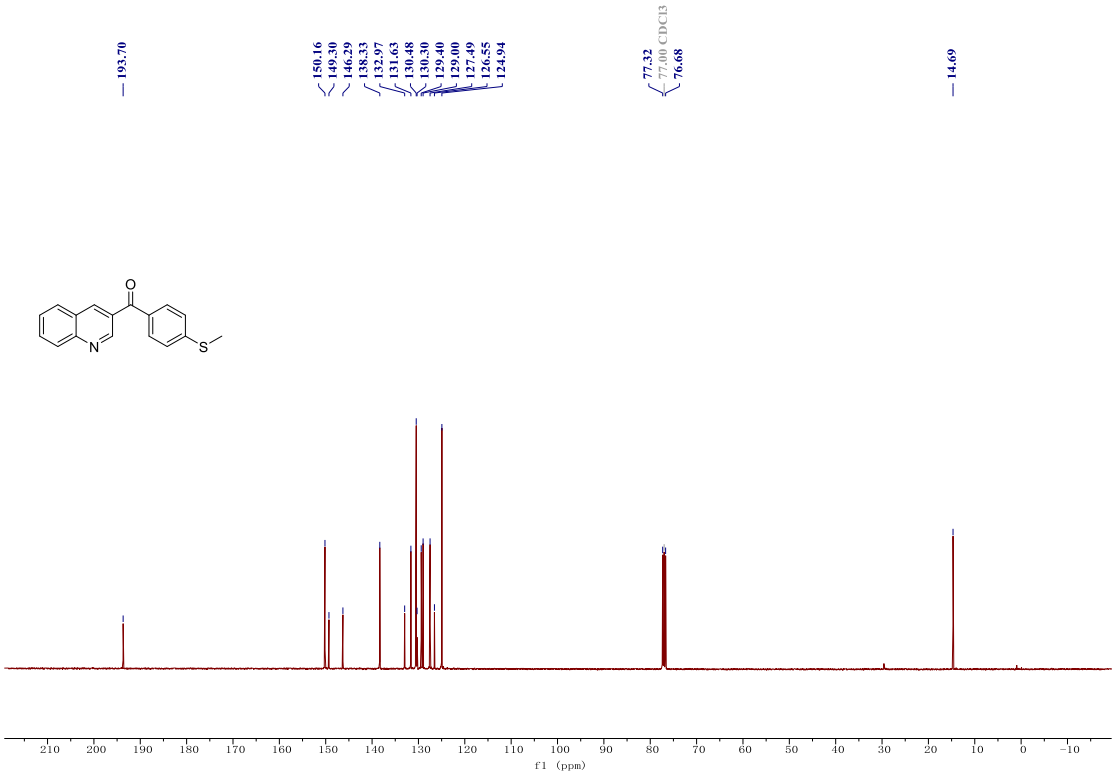
^{1}H NMR and ^{13}C NMR for **3ae**



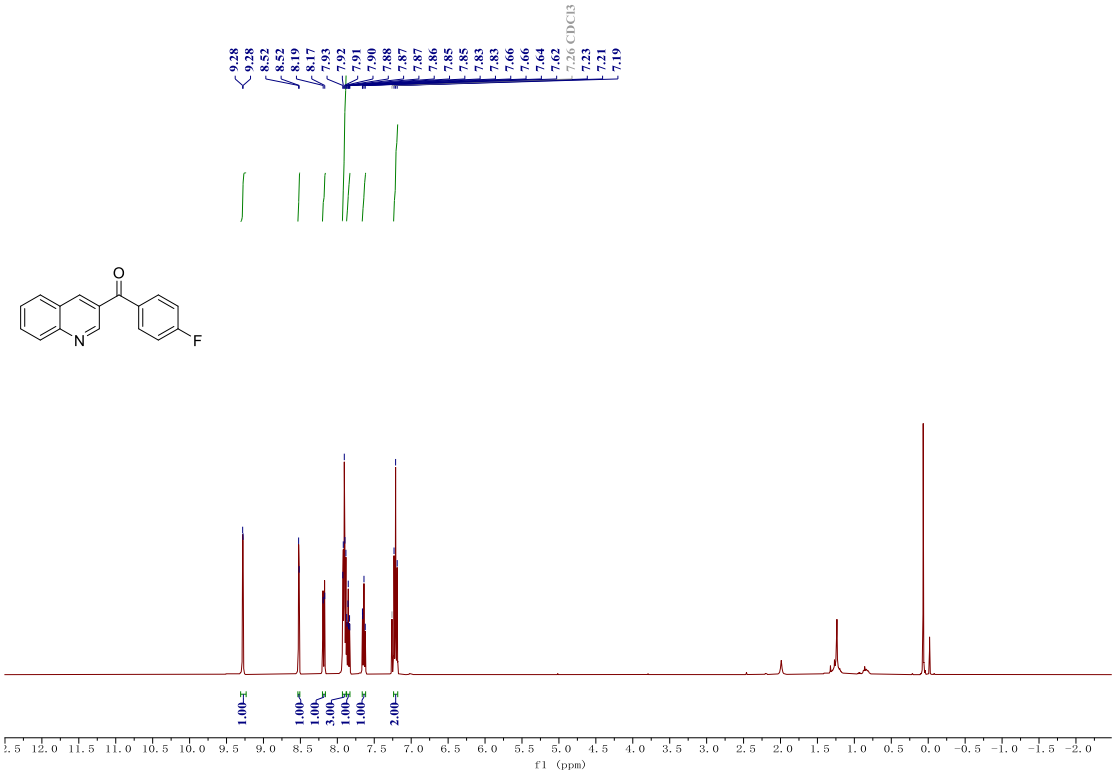


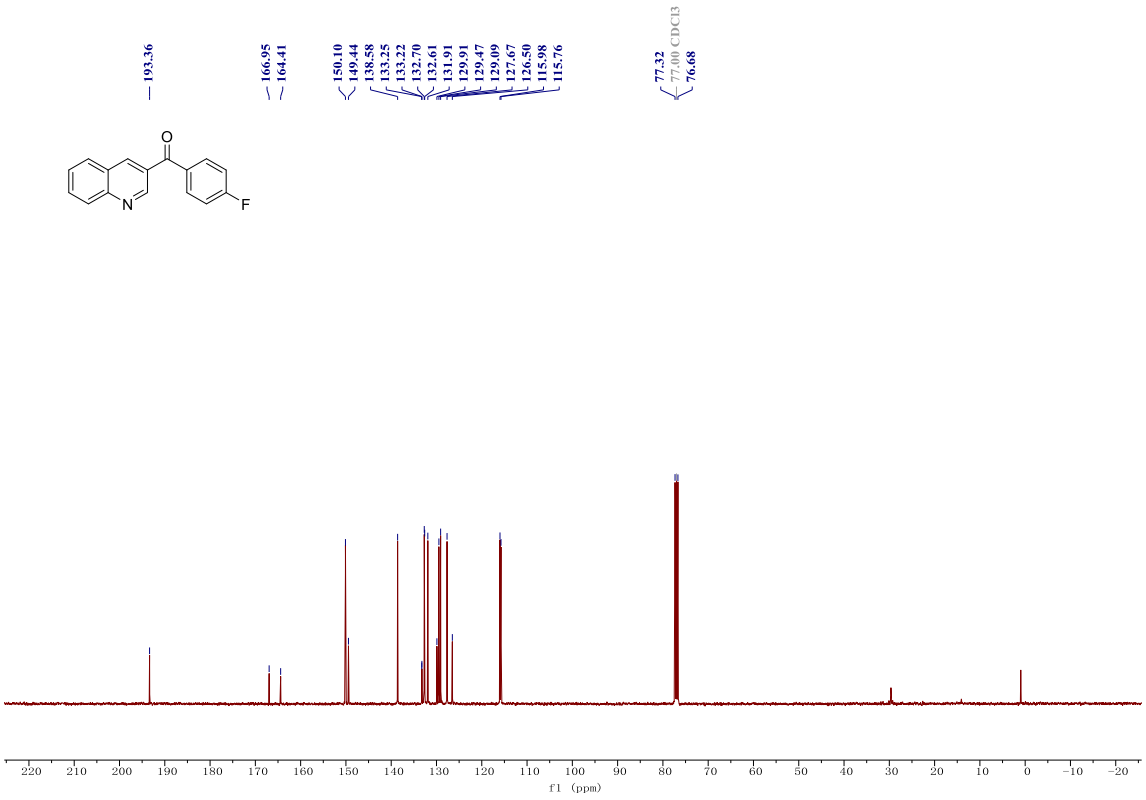
^{1}H NMR and ^{13}C NMR for **3af**

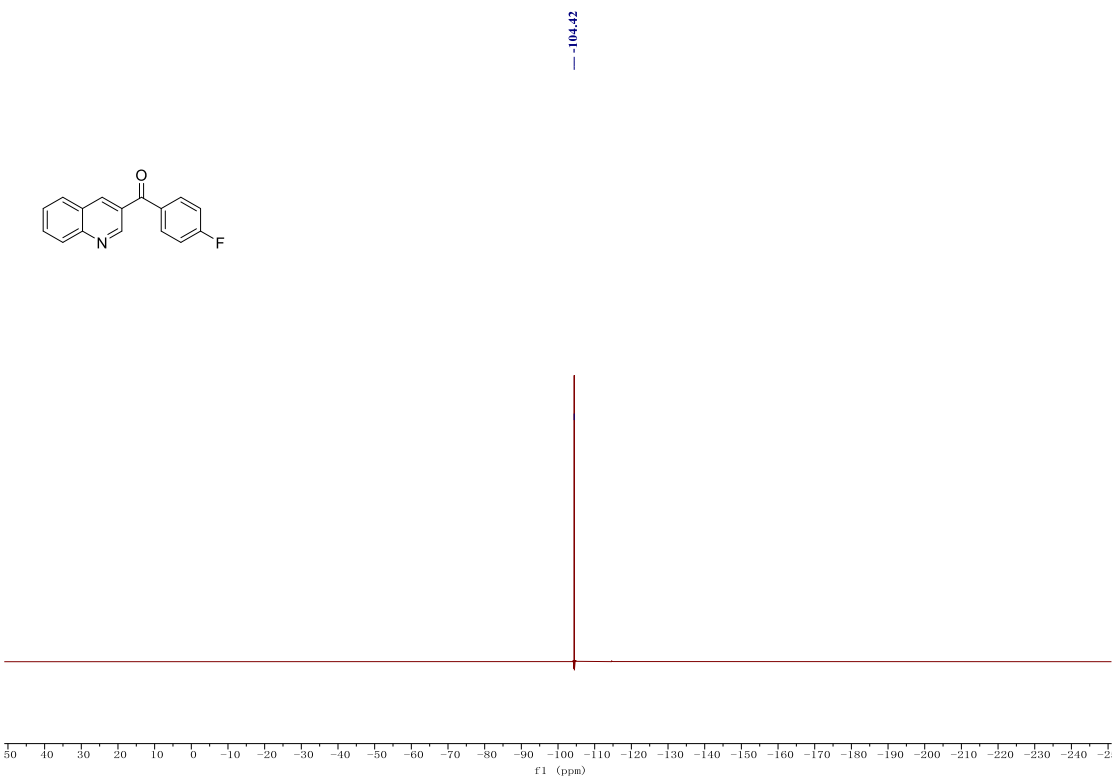




^{1}H NMR, ^{13}C NMR and ^{19}F NMR for **3ag**



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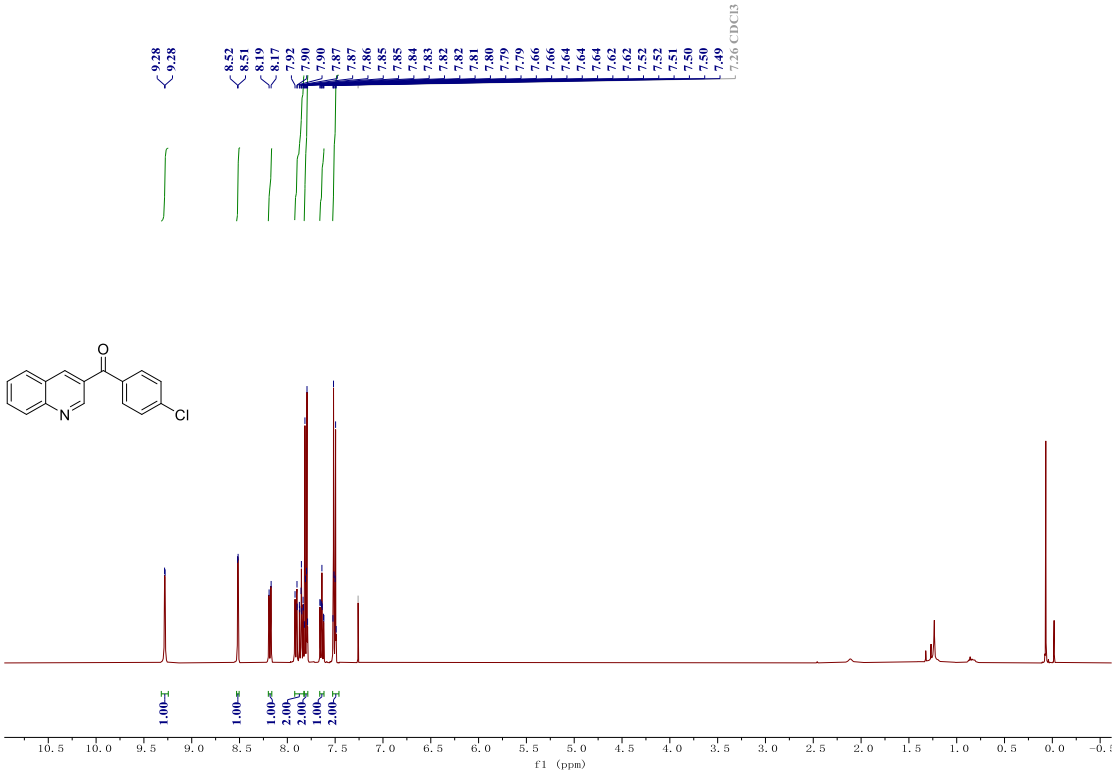
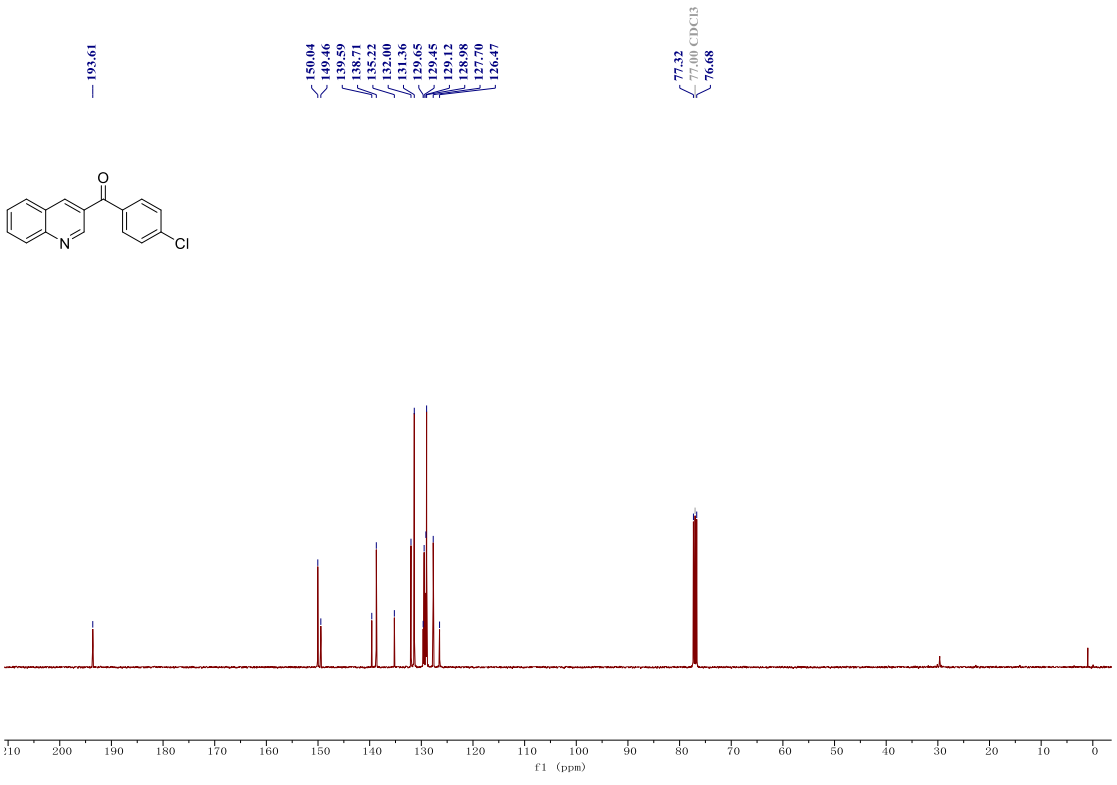
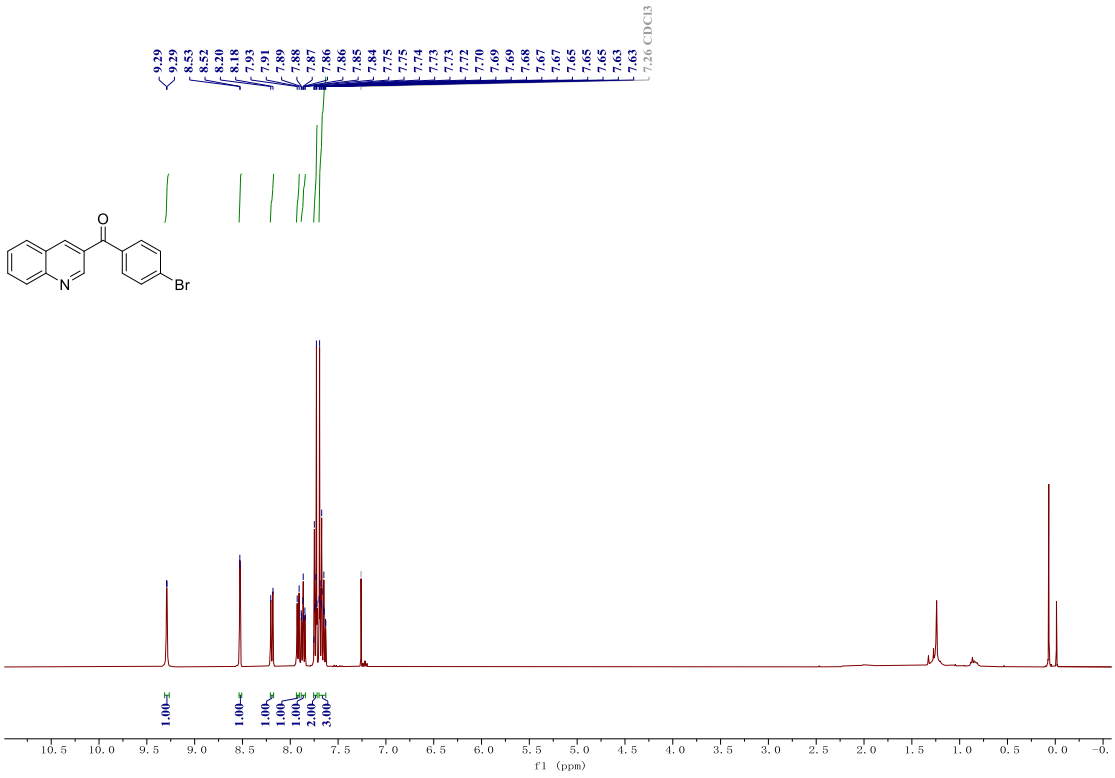
f1 (ppm)

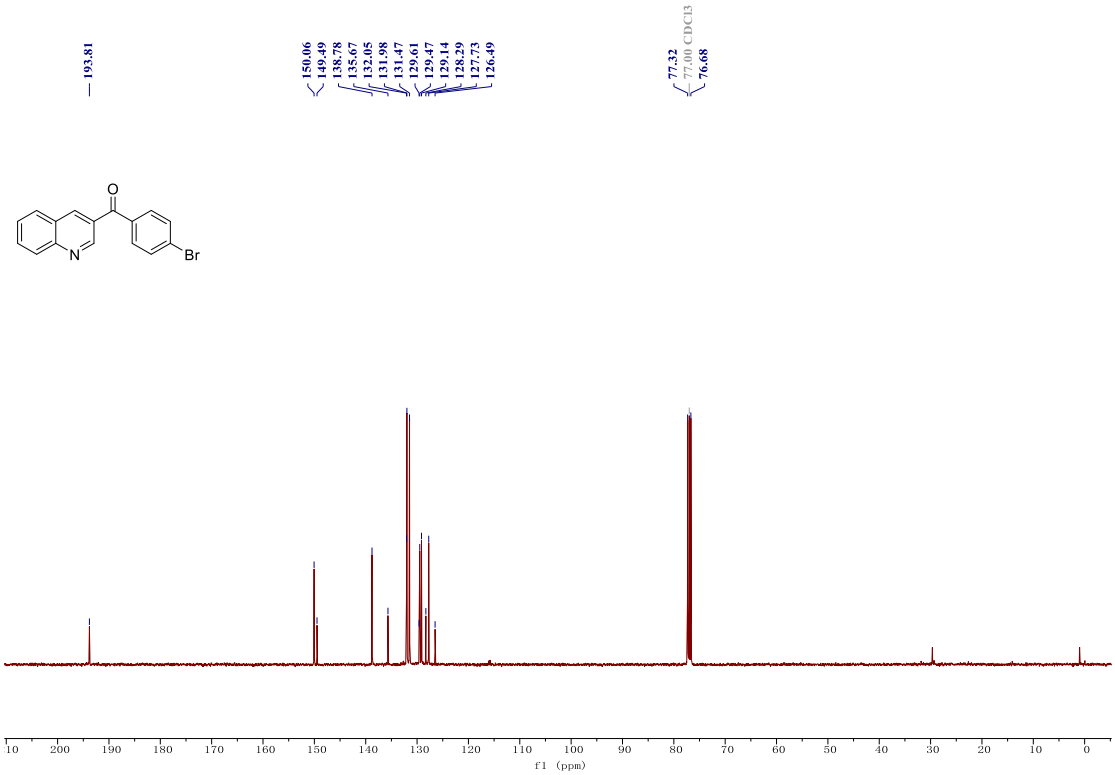
^{1}H NMR and ^{13}C NMR for **3ah**



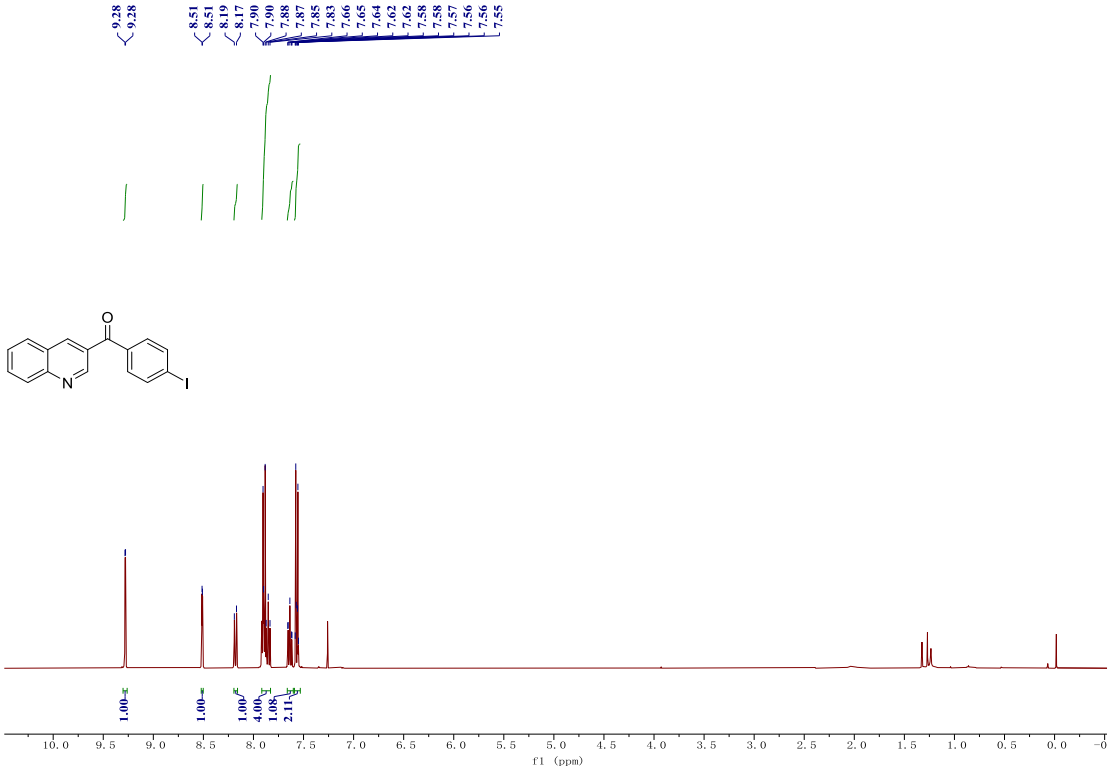


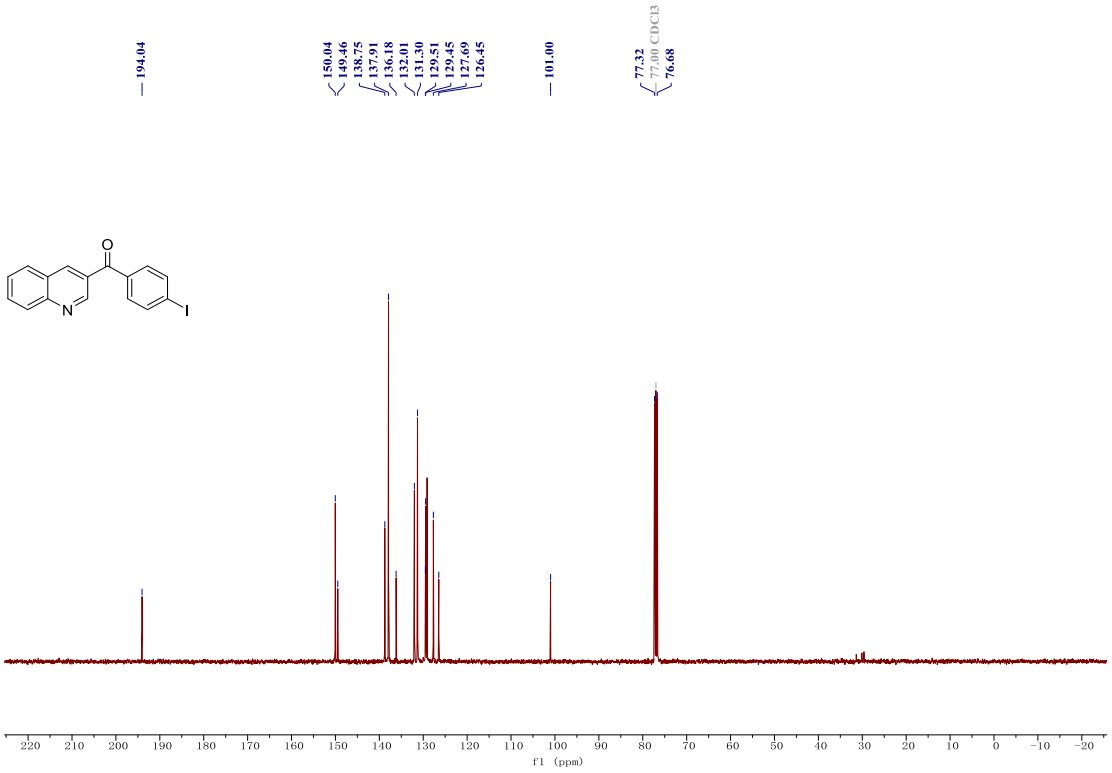
^{1}H NMR and ^{13}C NMR for **3ai**



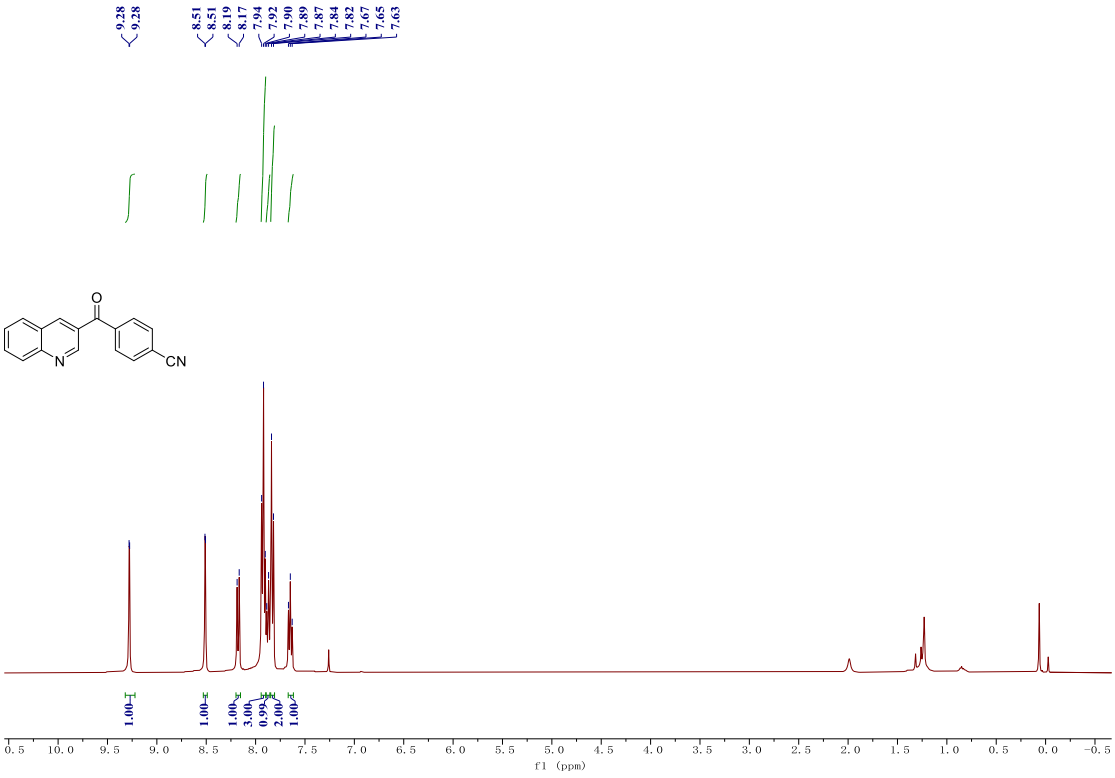


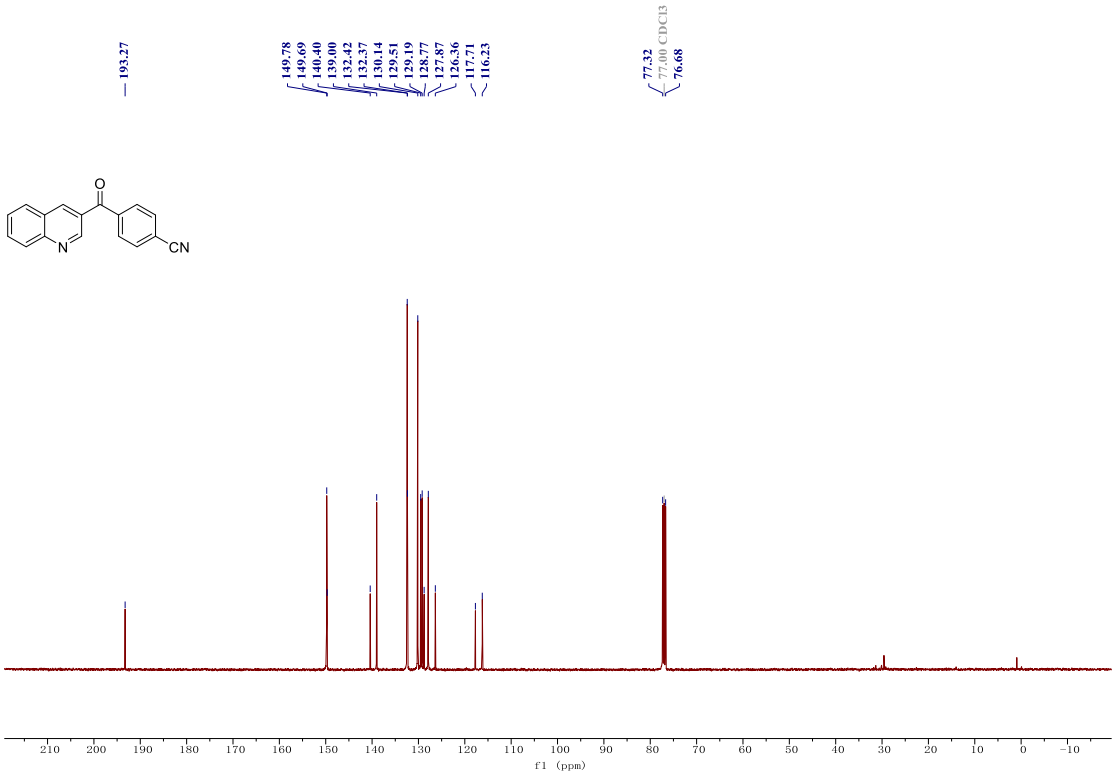
^{1}H NMR and ^{13}C NMR for **3aj**



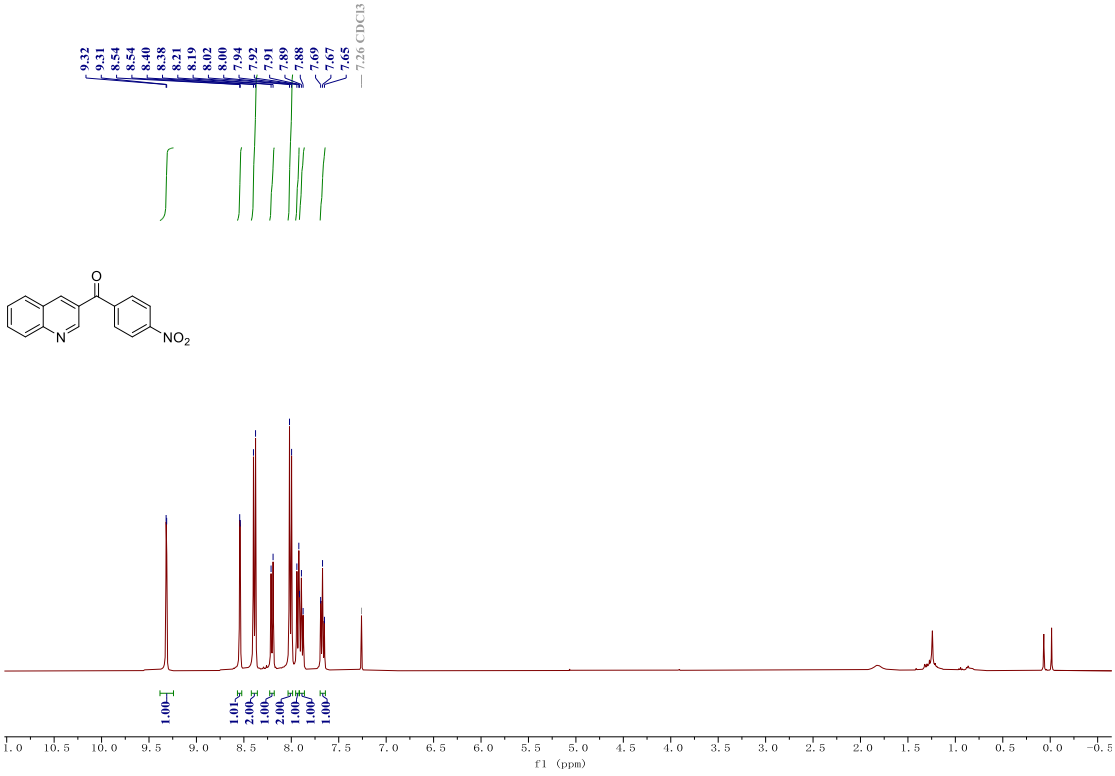


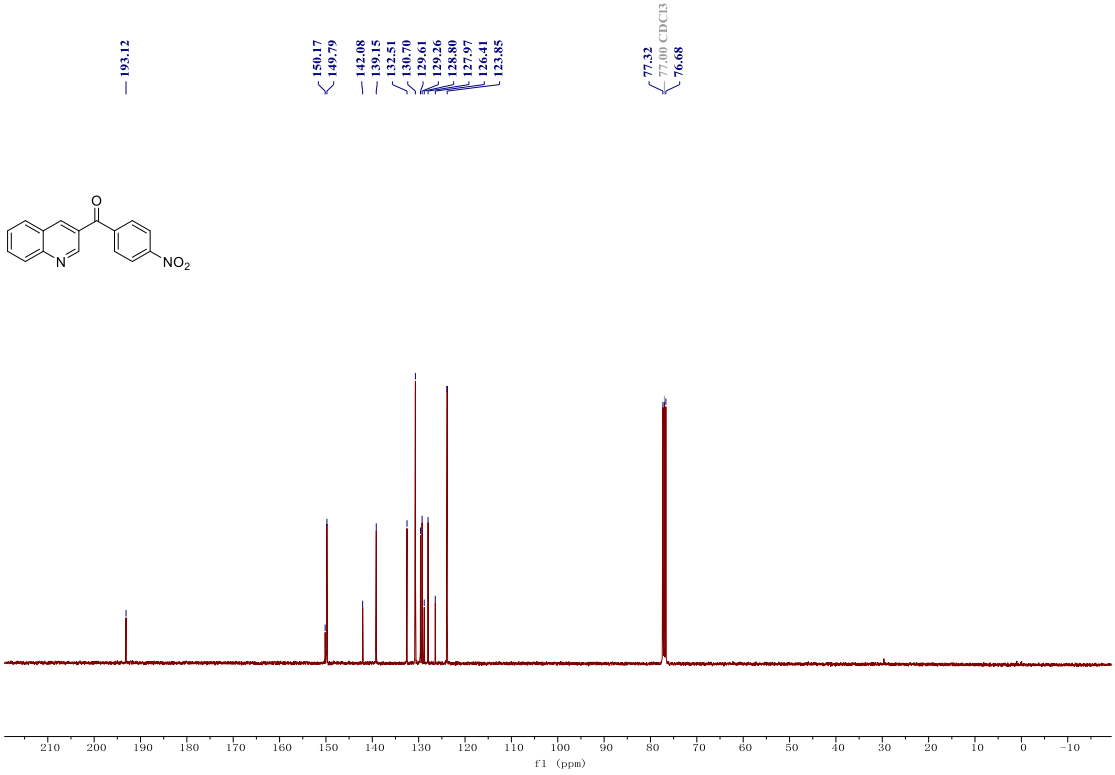
^{1}H NMR and ^{13}C NMR for **3ak**



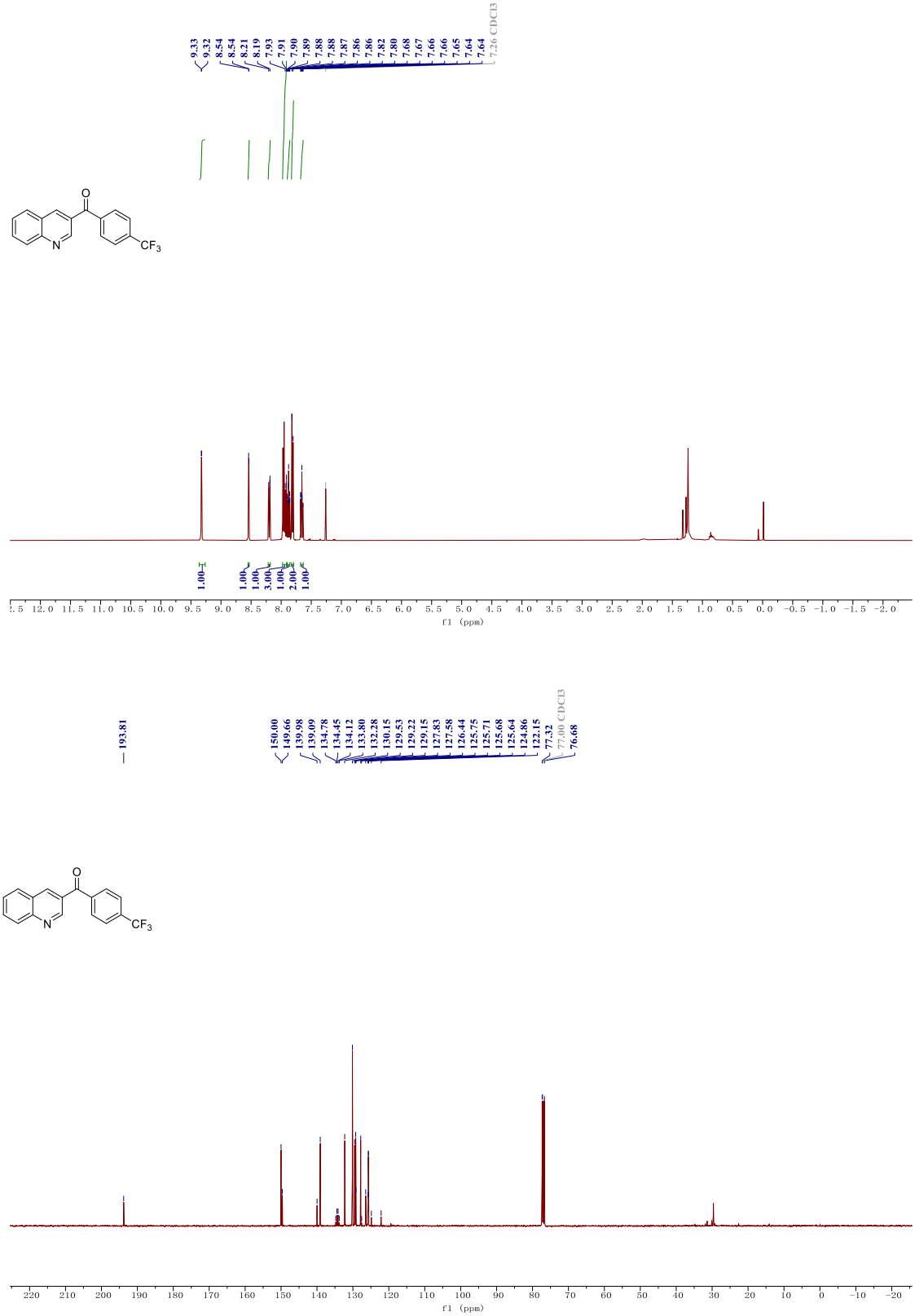


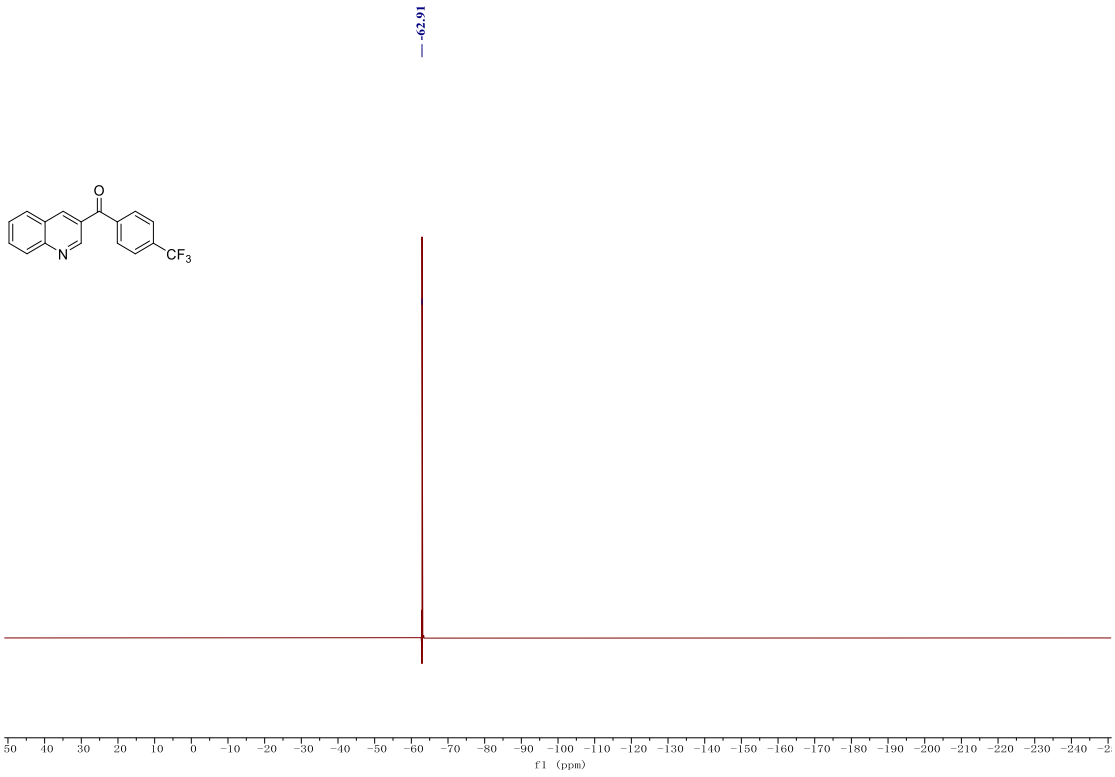
^{1}H NMR and ^{13}C NMR for **3al**





^{1}H NMR, ^{13}C NMR and ^{19}F NMR for **3am**

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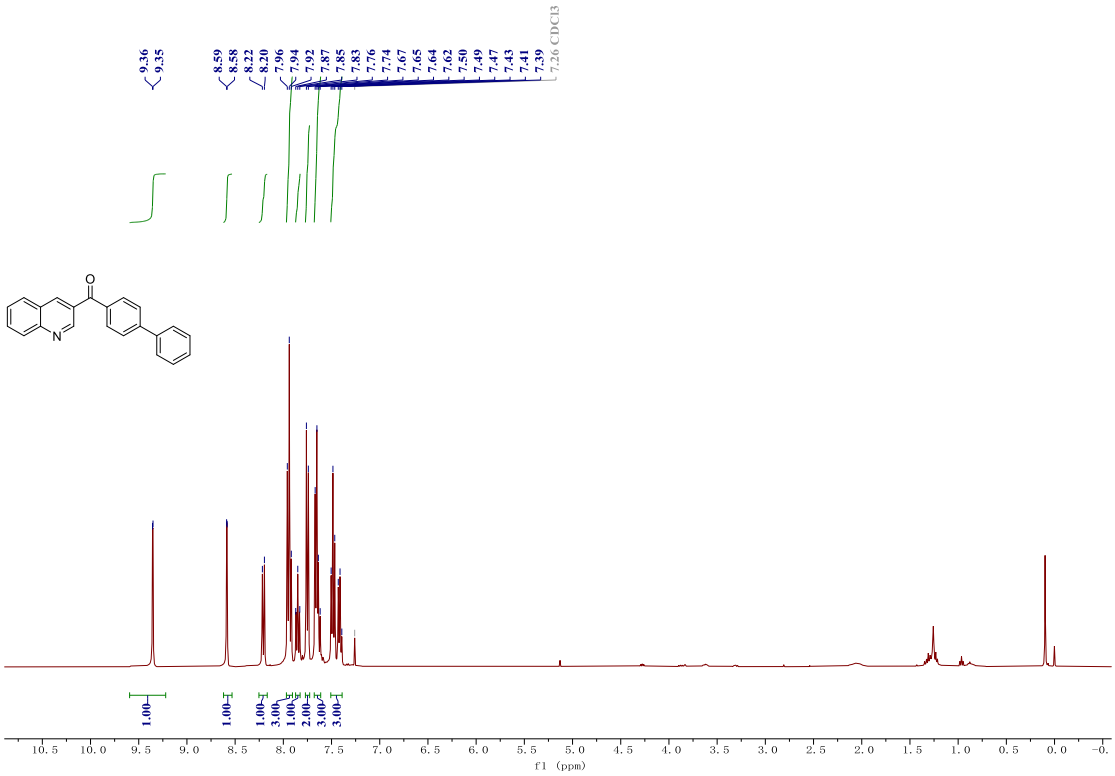
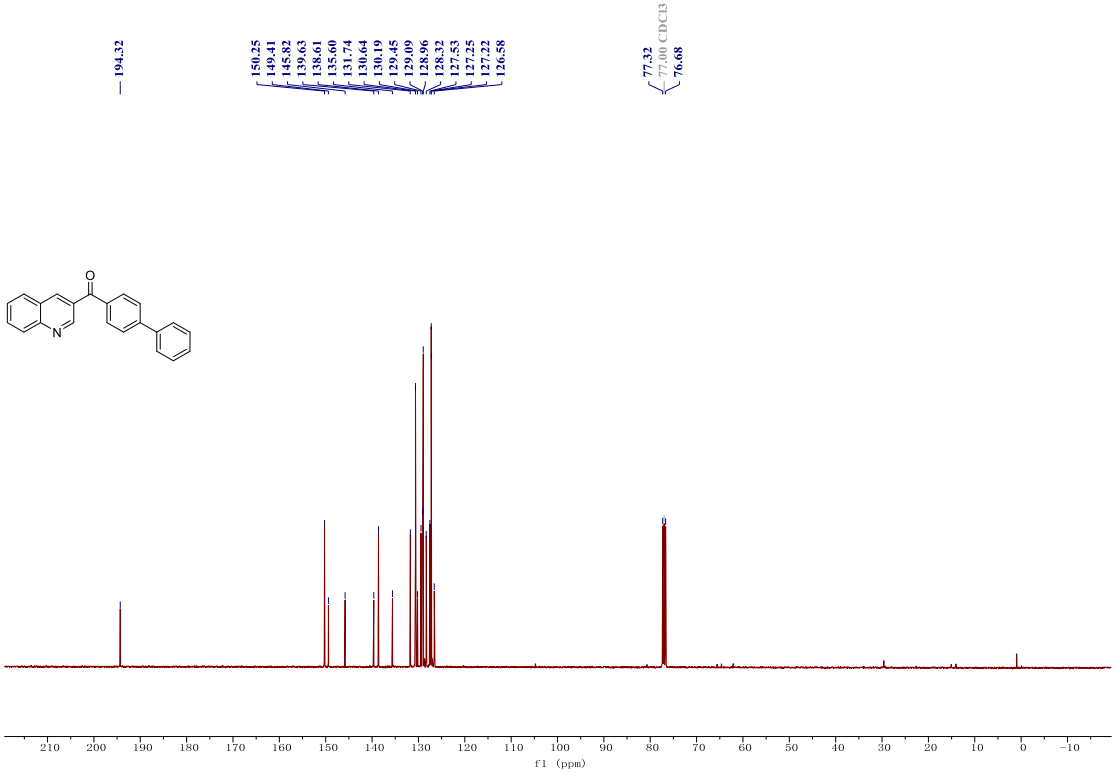
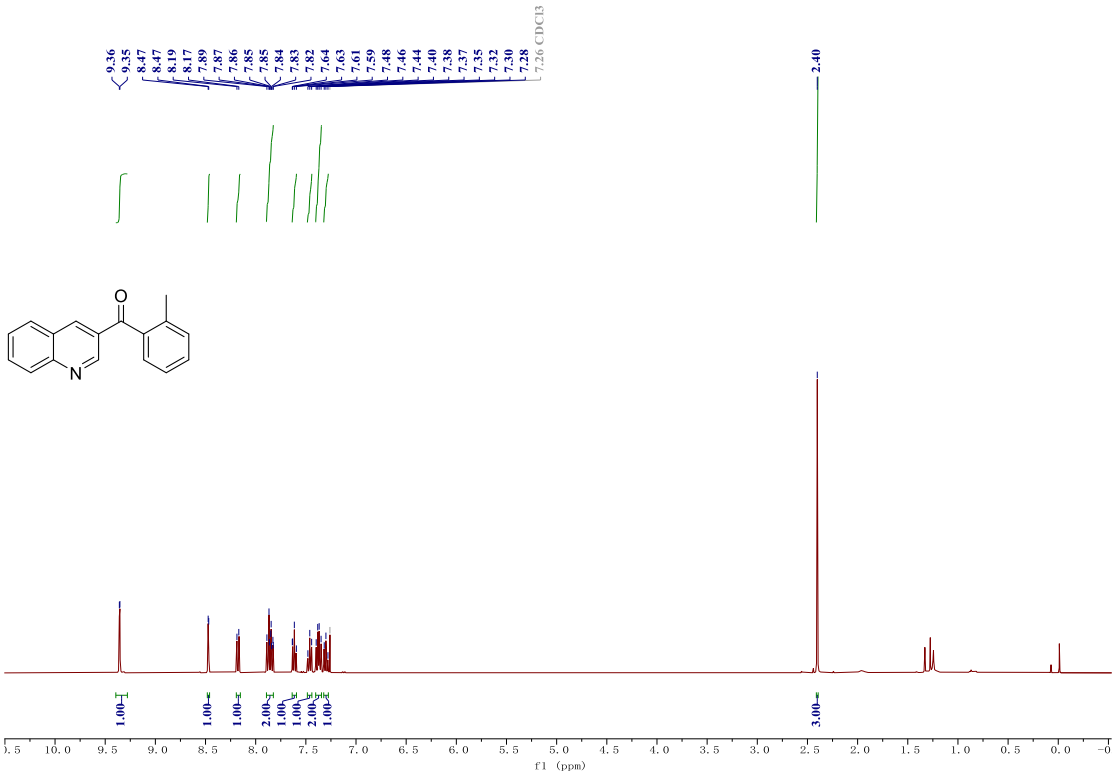
f1 (ppm)

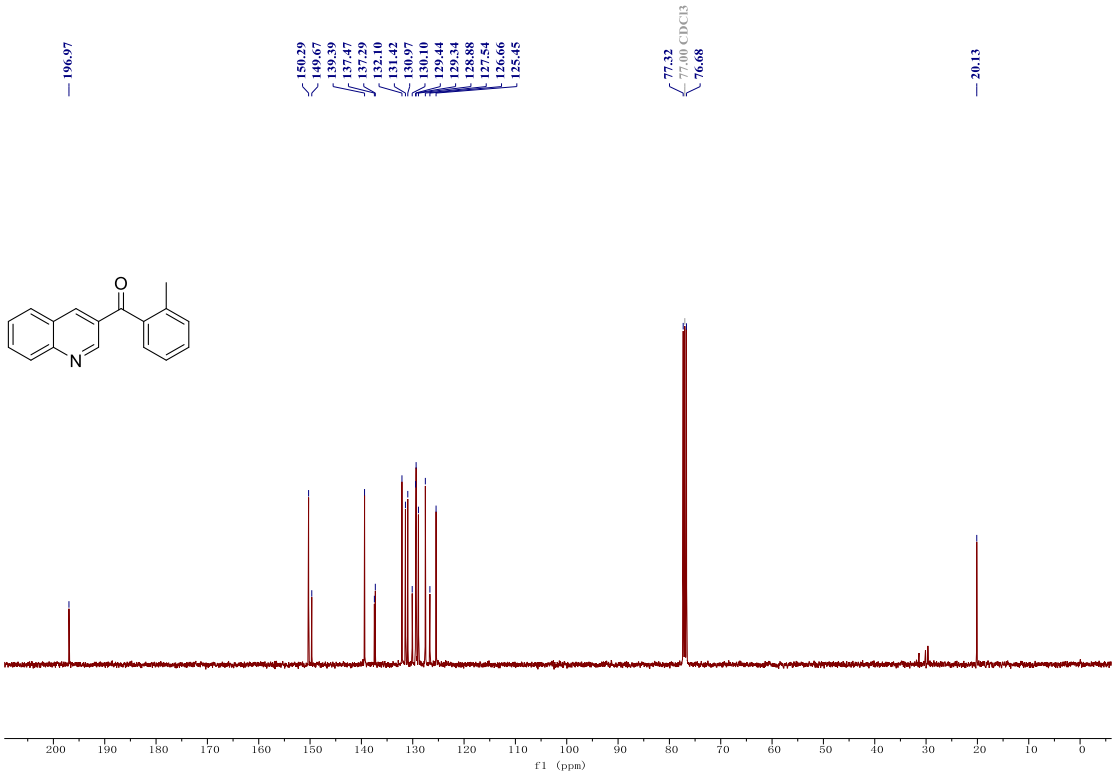
^{1}H NMR and ^{13}C NMR for **3an**



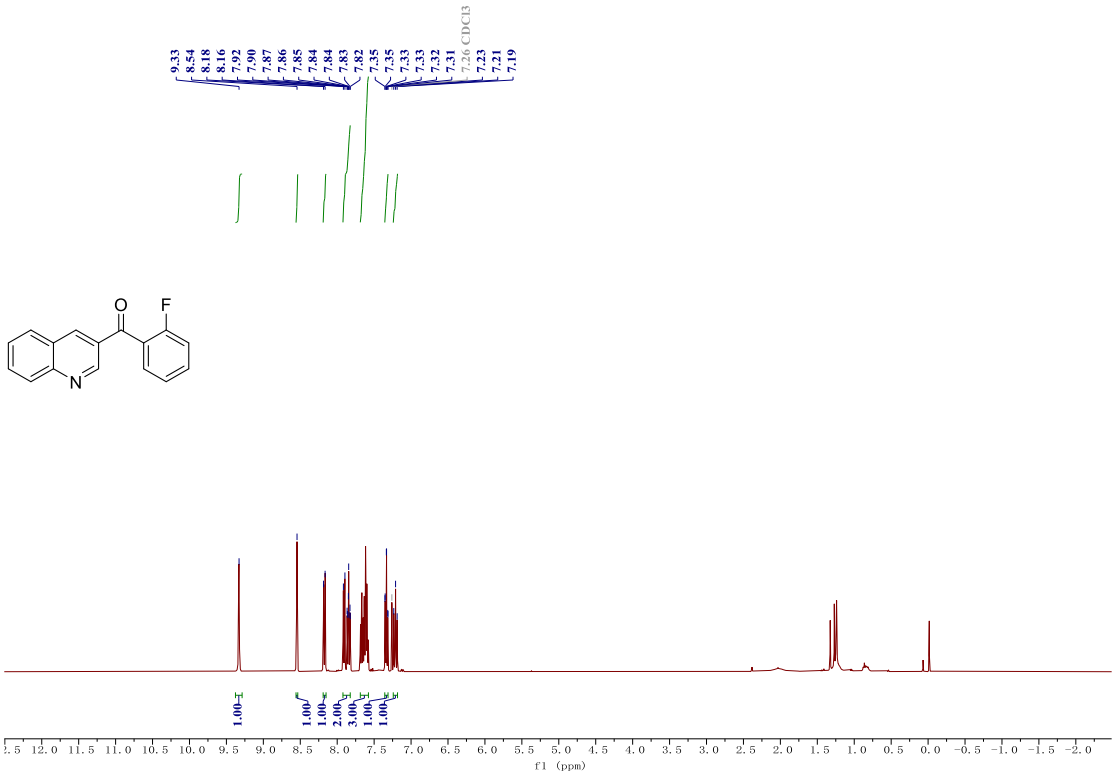


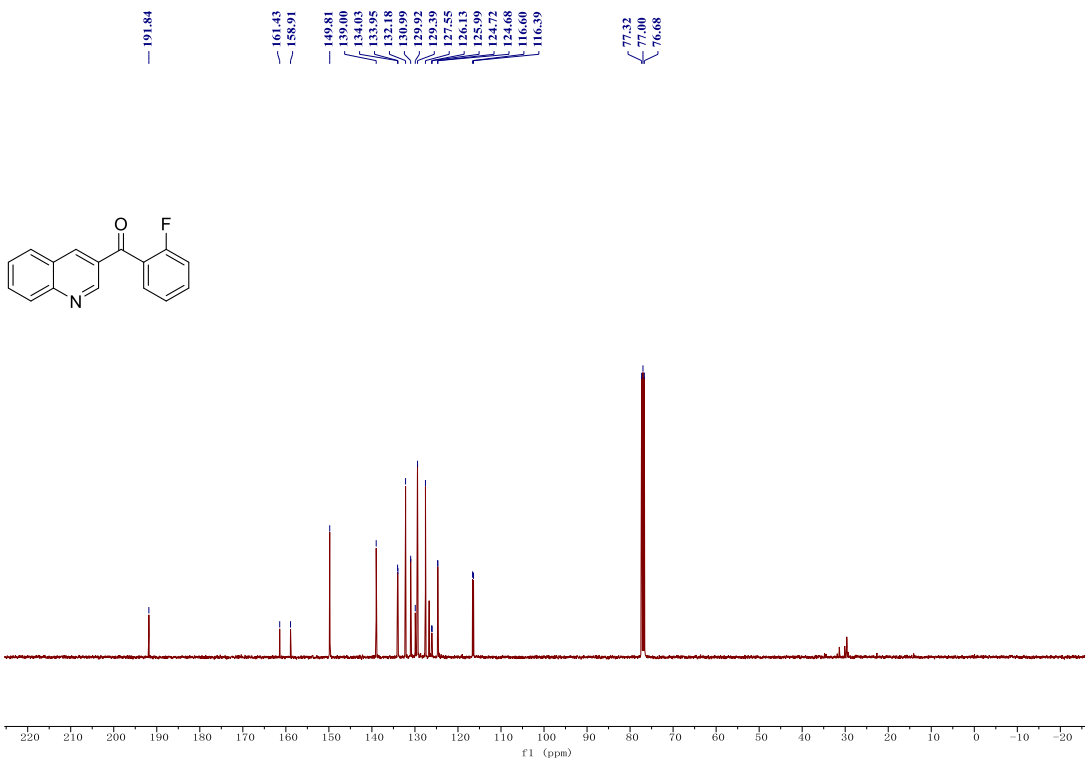
^{1}H NMR and ^{13}C NMR for **3ao**

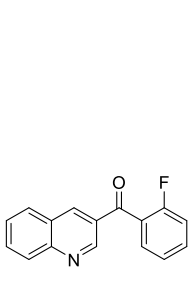




^{1}H NMR, ^{13}C NMR and ^{19}F NMR for **3ap**



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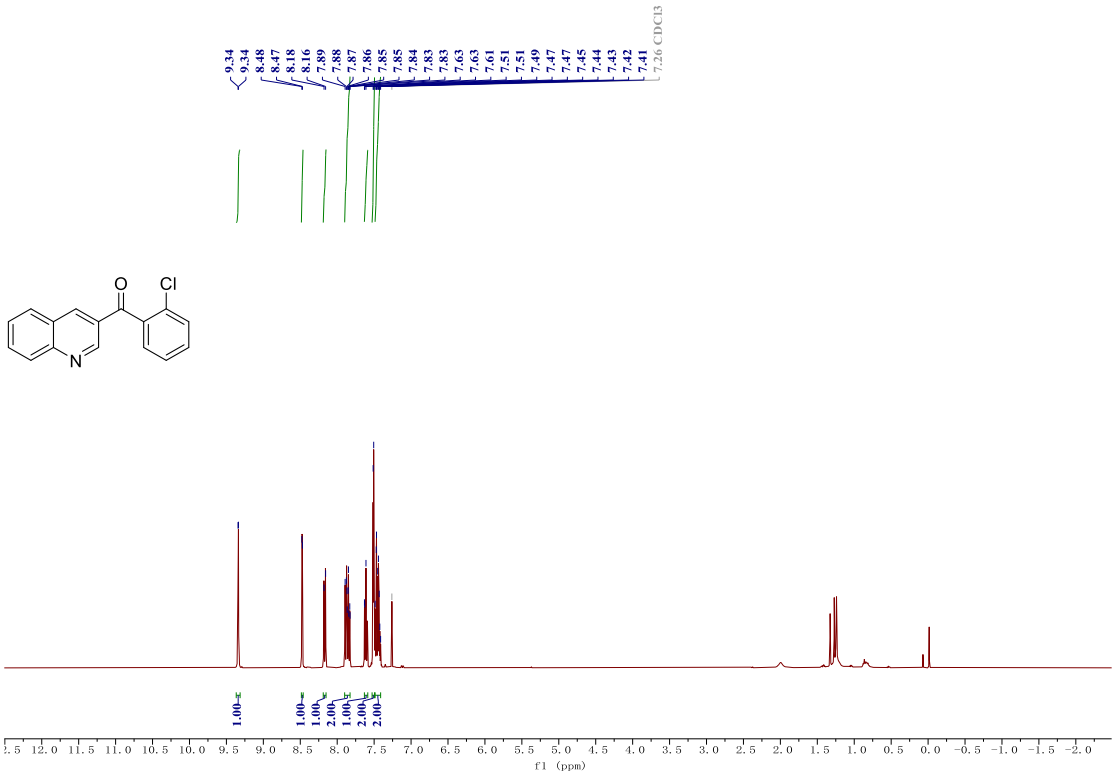
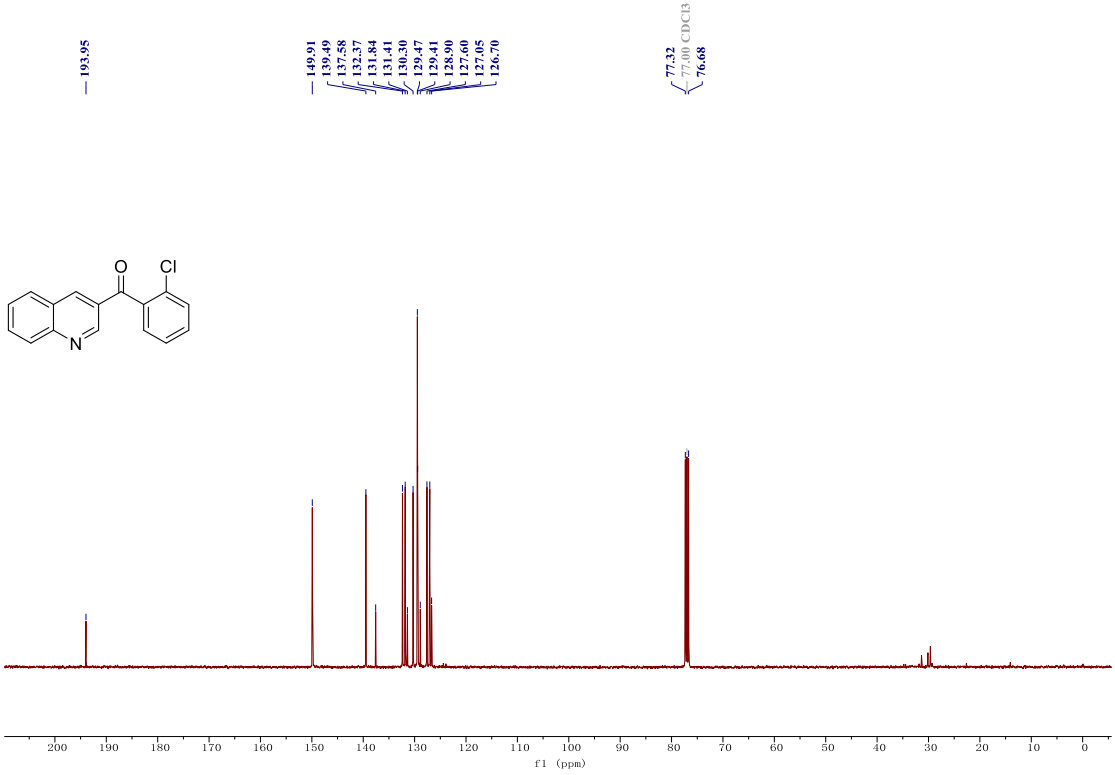
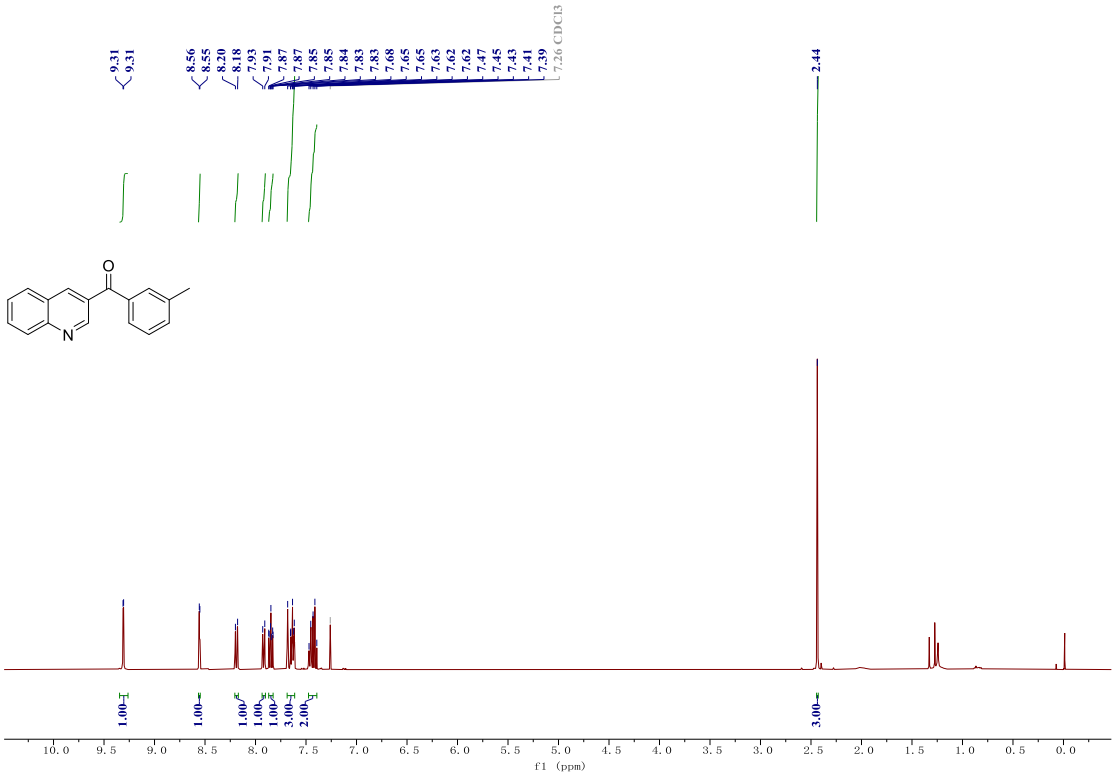
f1 (ppm)

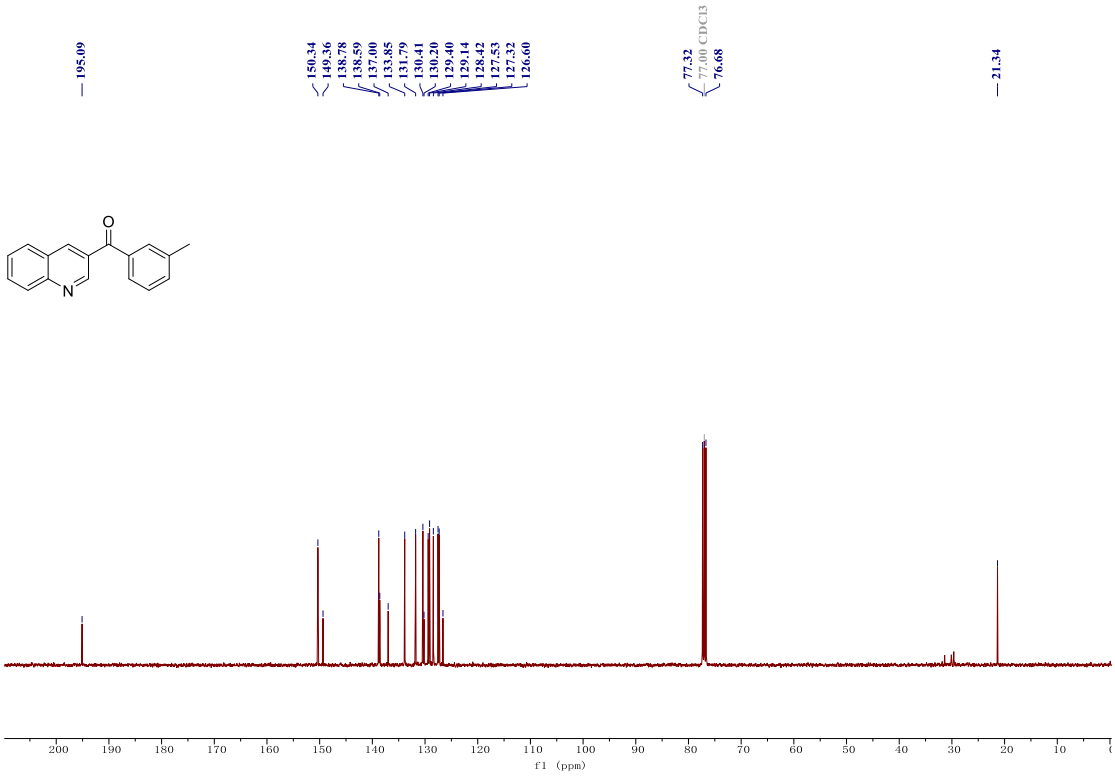
^{1}H NMR and ^{13}C NMR for **3aq**



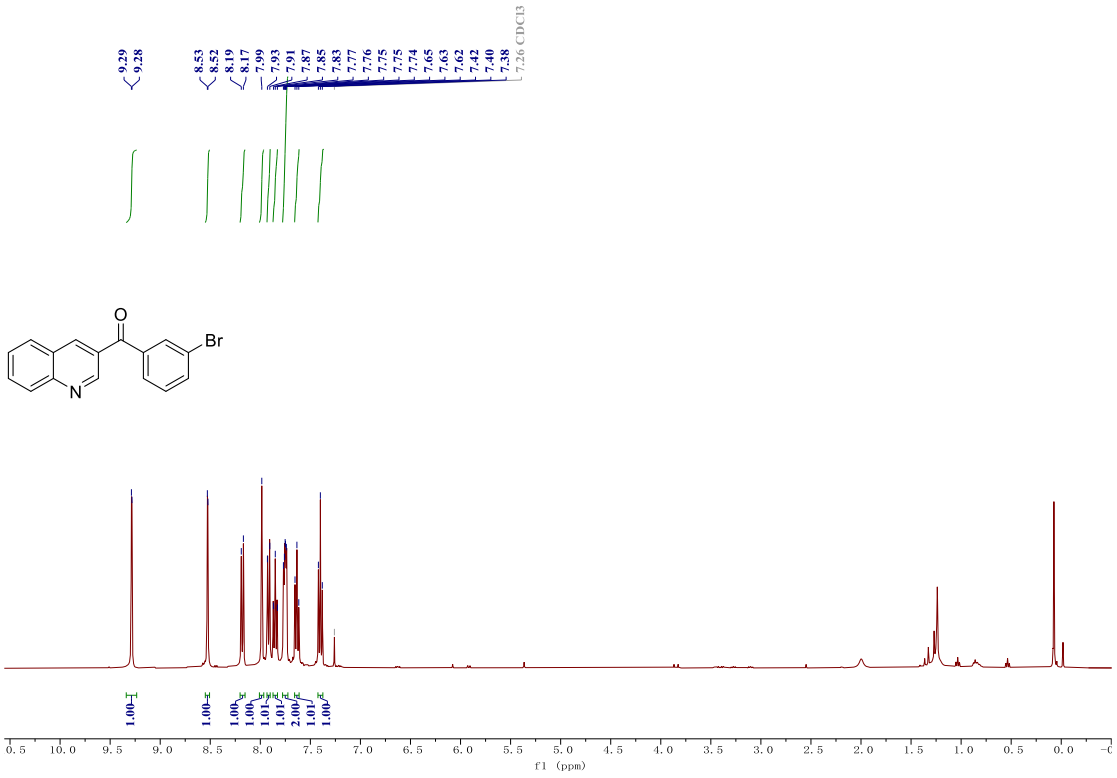


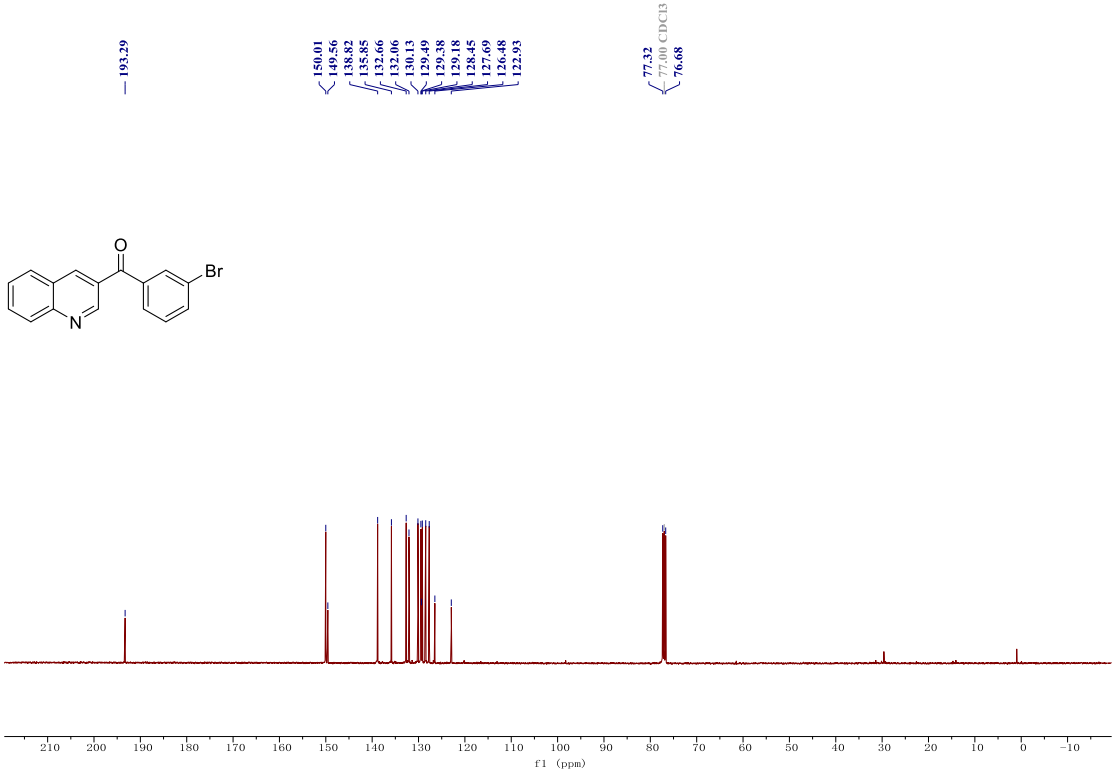
^{1}H NMR and ^{13}C NMR for **3ar**



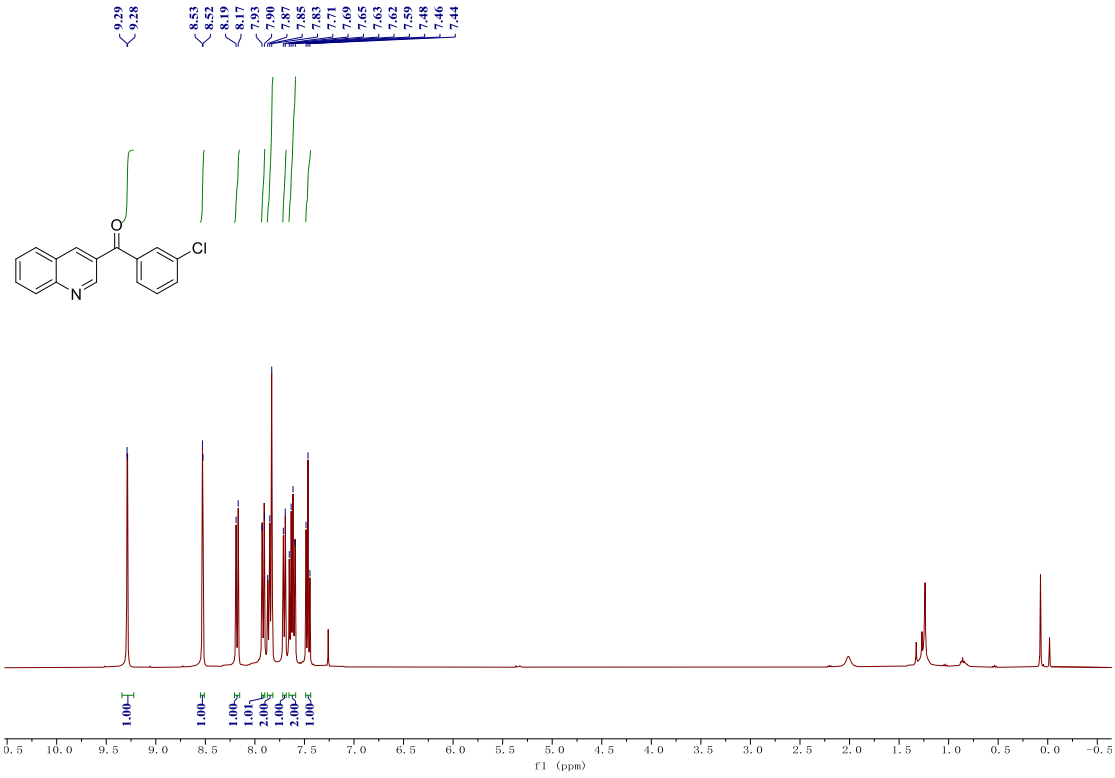


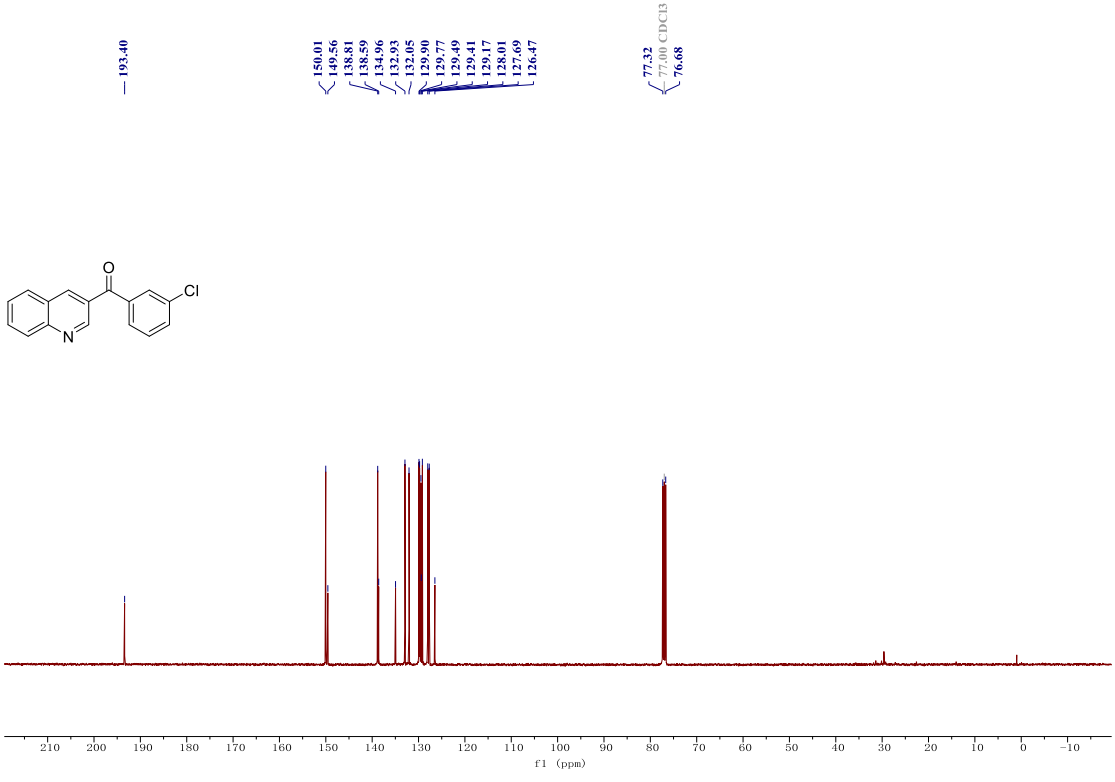
^{1}H NMR and ^{13}C NMR for **3as**



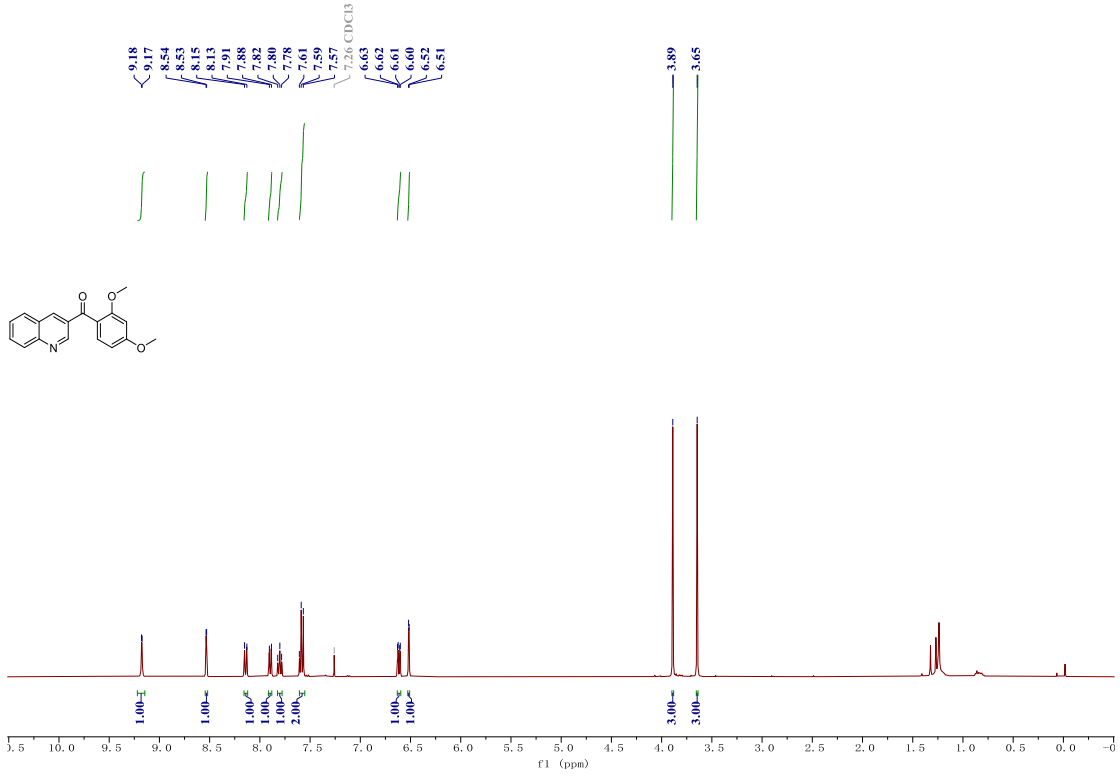


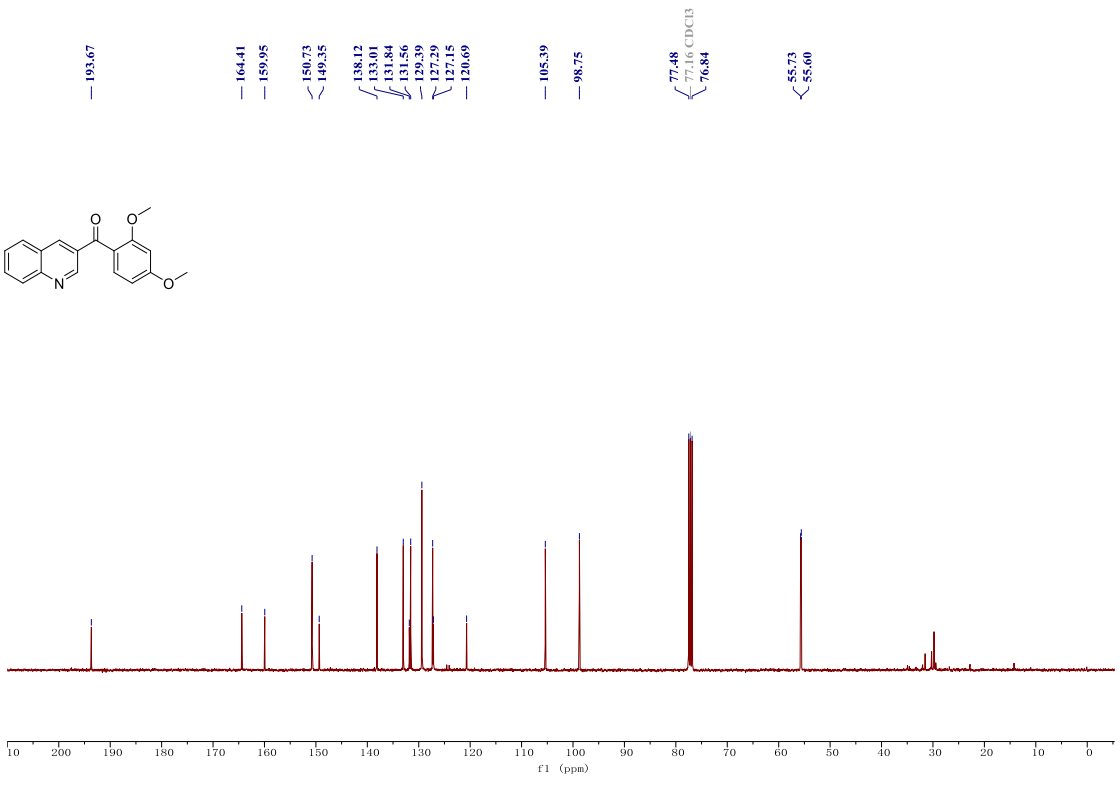
^{1}H NMR and ^{13}C NMR for **3at**



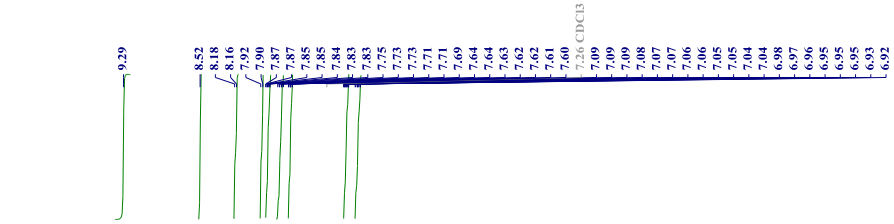


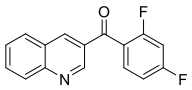
^{1}H NMR and ^{13}C NMR for **3au**

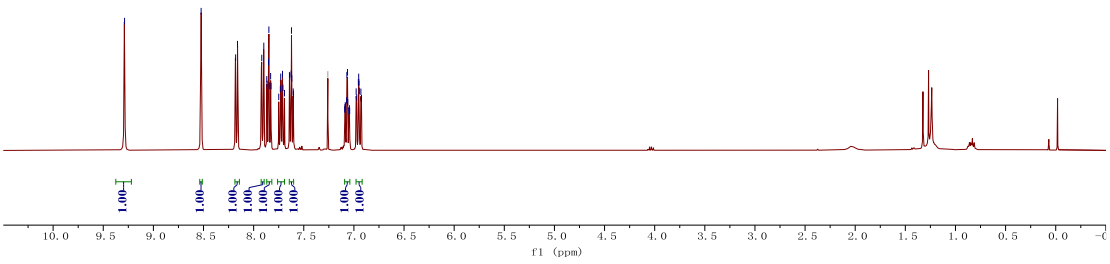


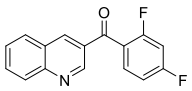


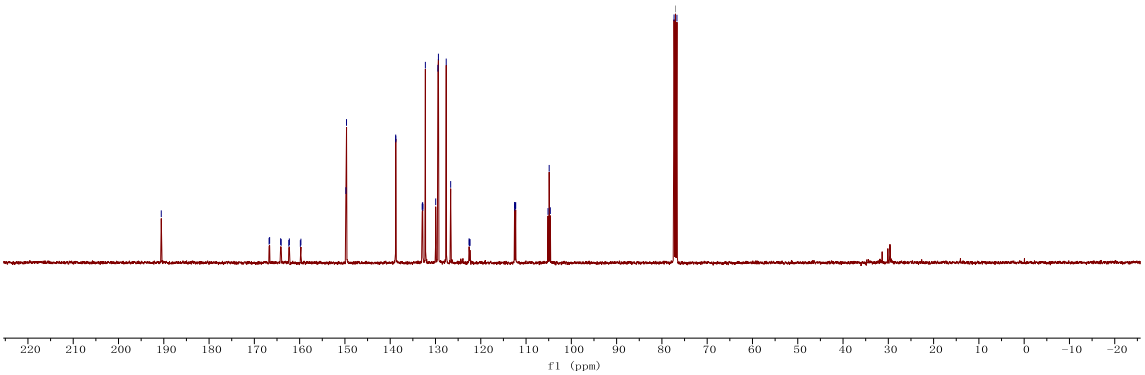
^{1}H NMR, ^{13}C NMR and ^{19}F NMR for **3av**

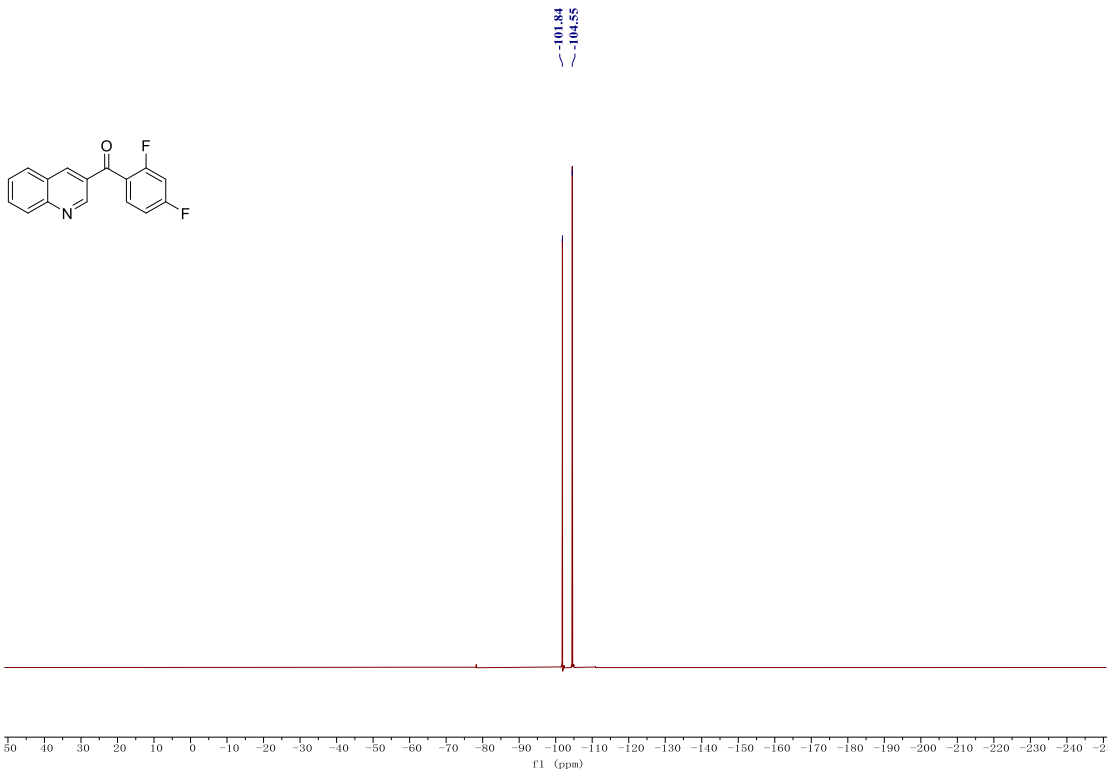




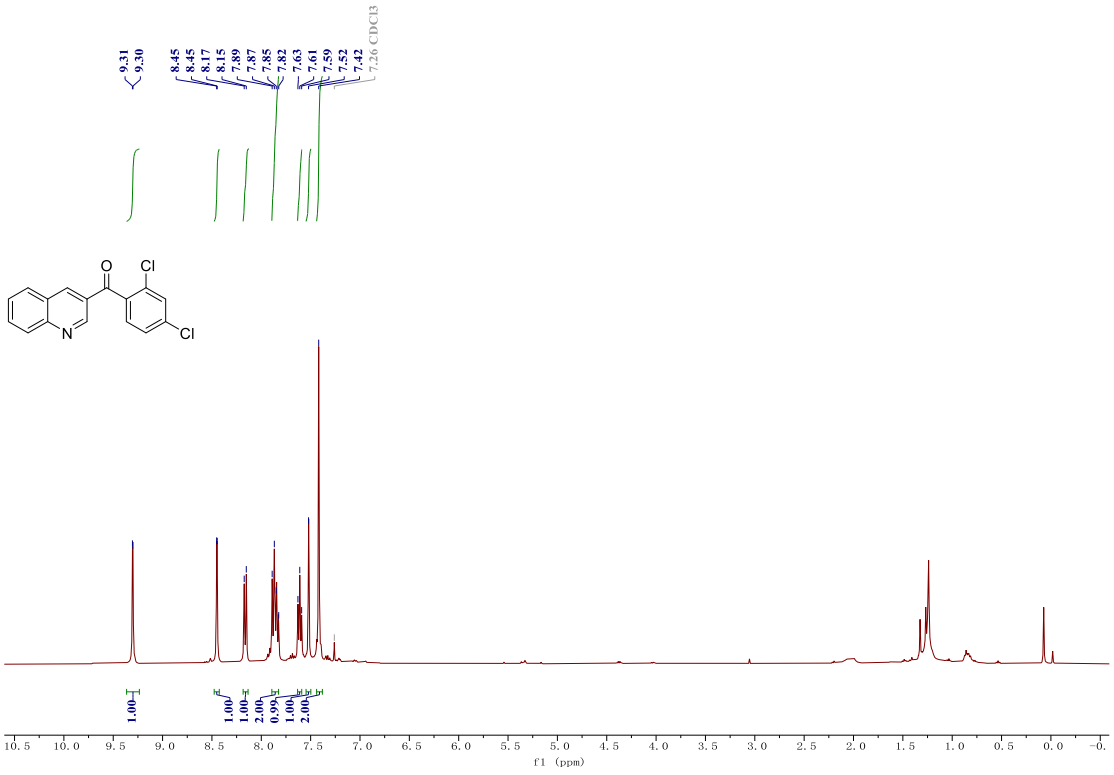


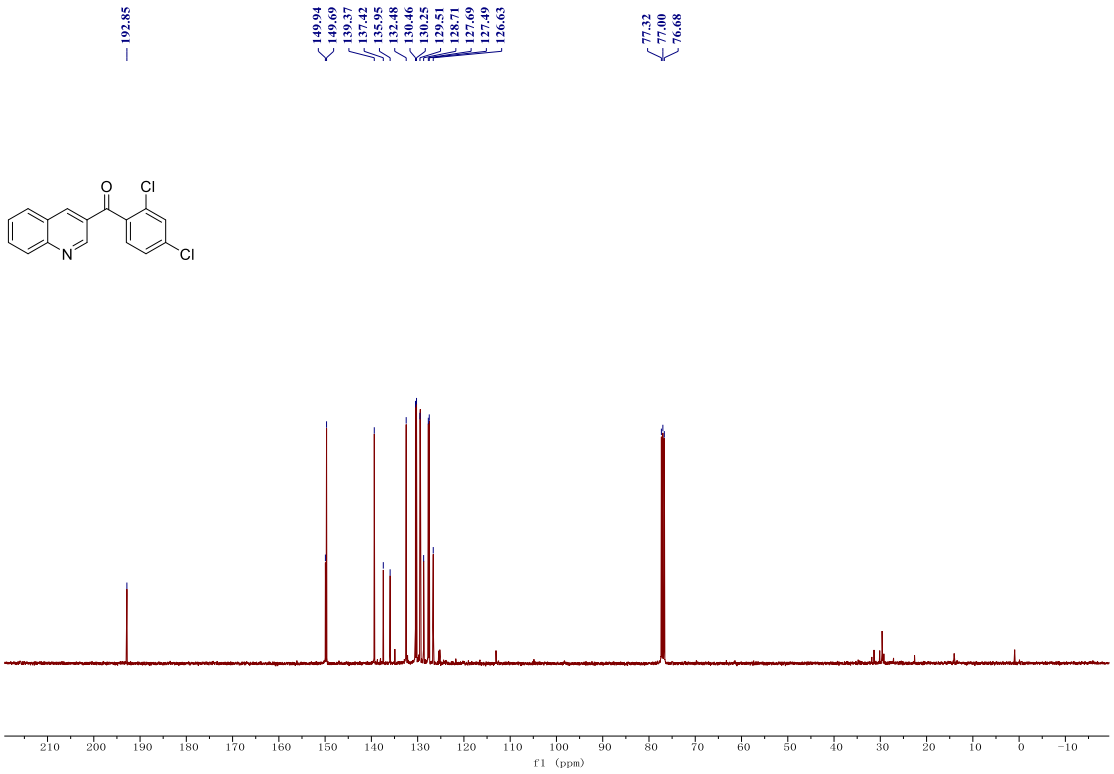




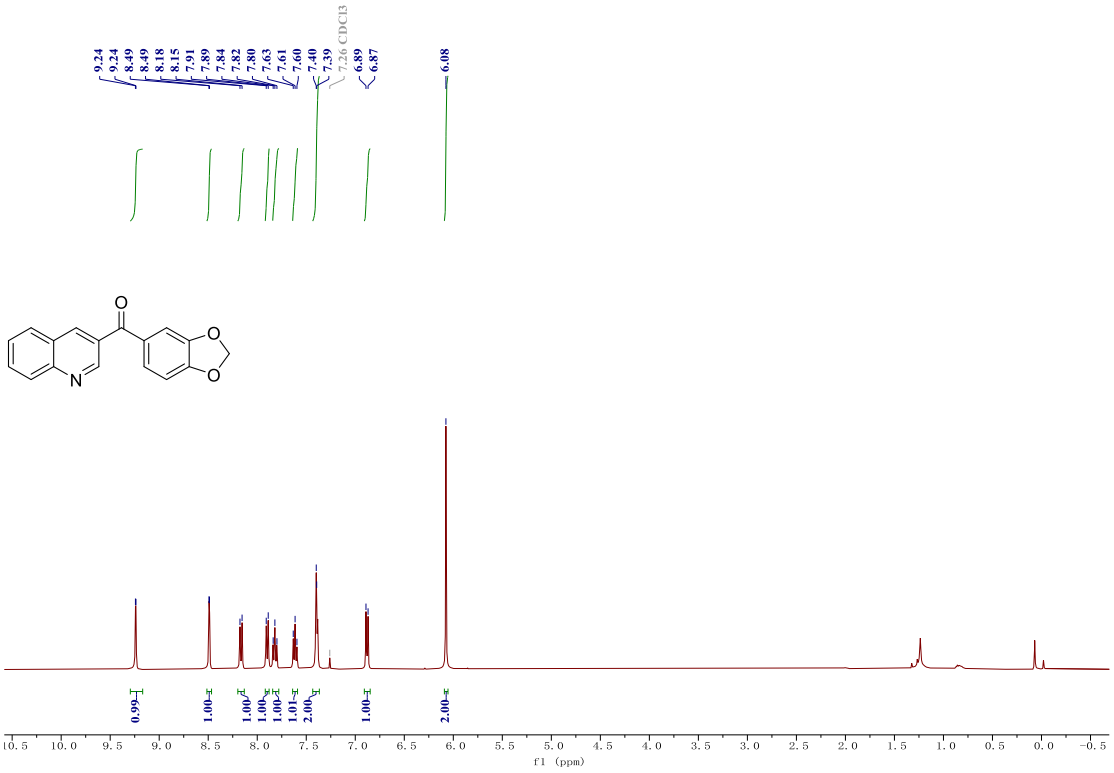

-101.84
-104.55
O
F
N
F
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -2
f1 (ppm)

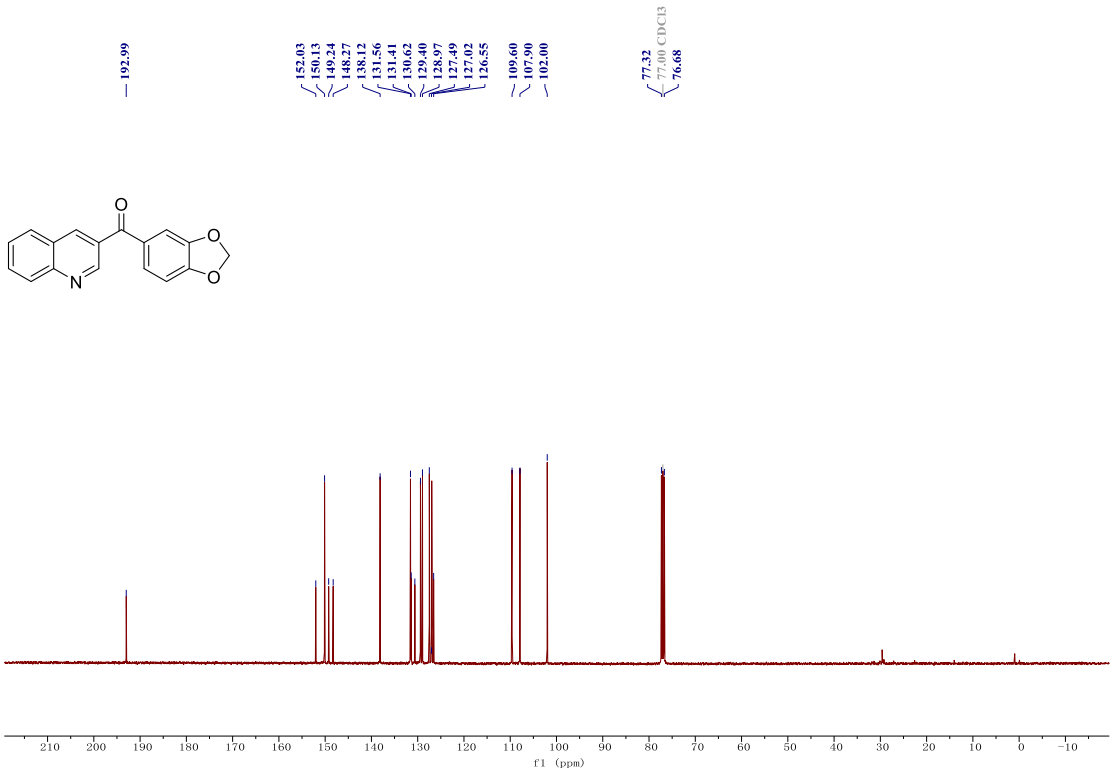
^{1}H NMR and ^{13}C NMR for **3aw**



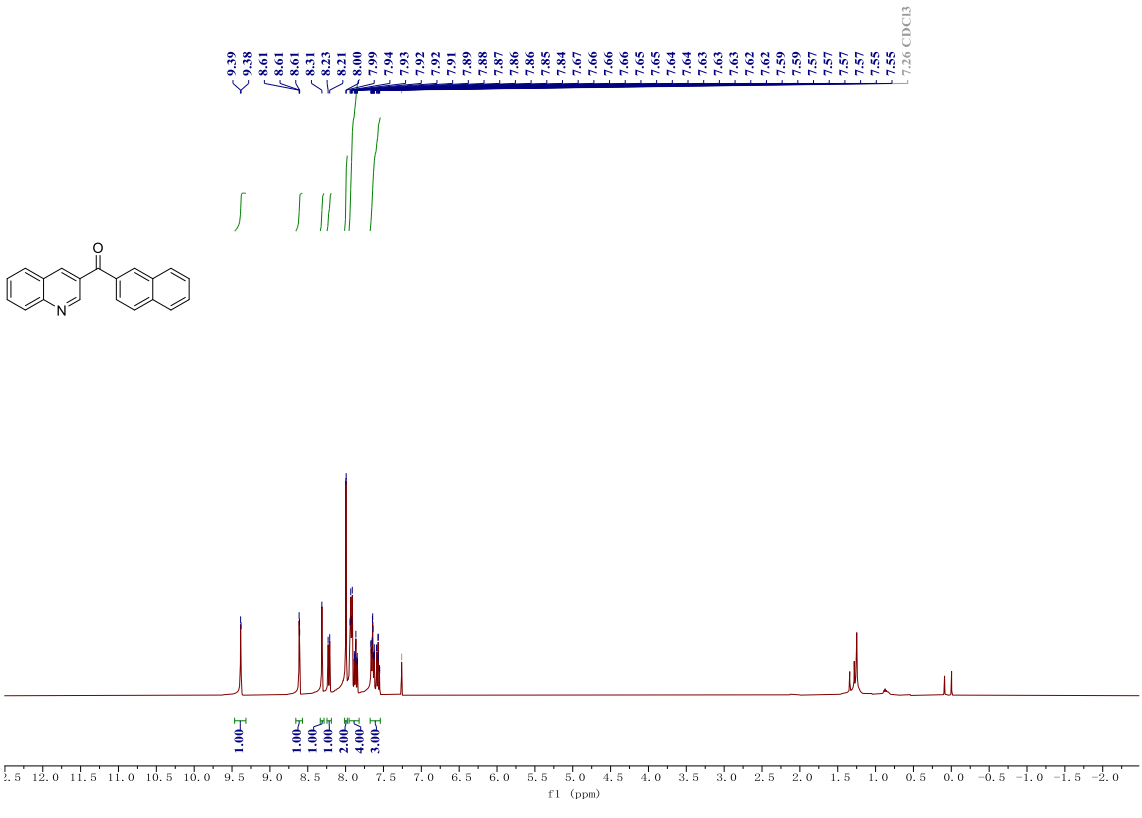


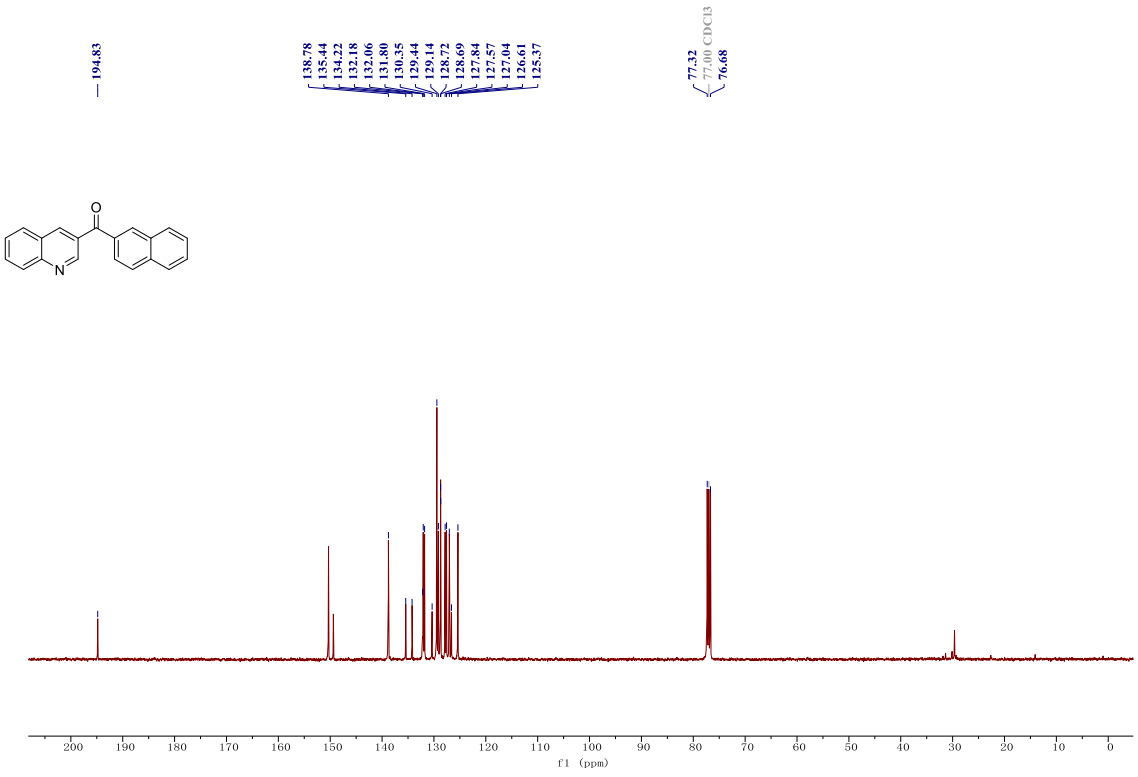
^{1}H NMR and ^{13}C NMR for **3ax**



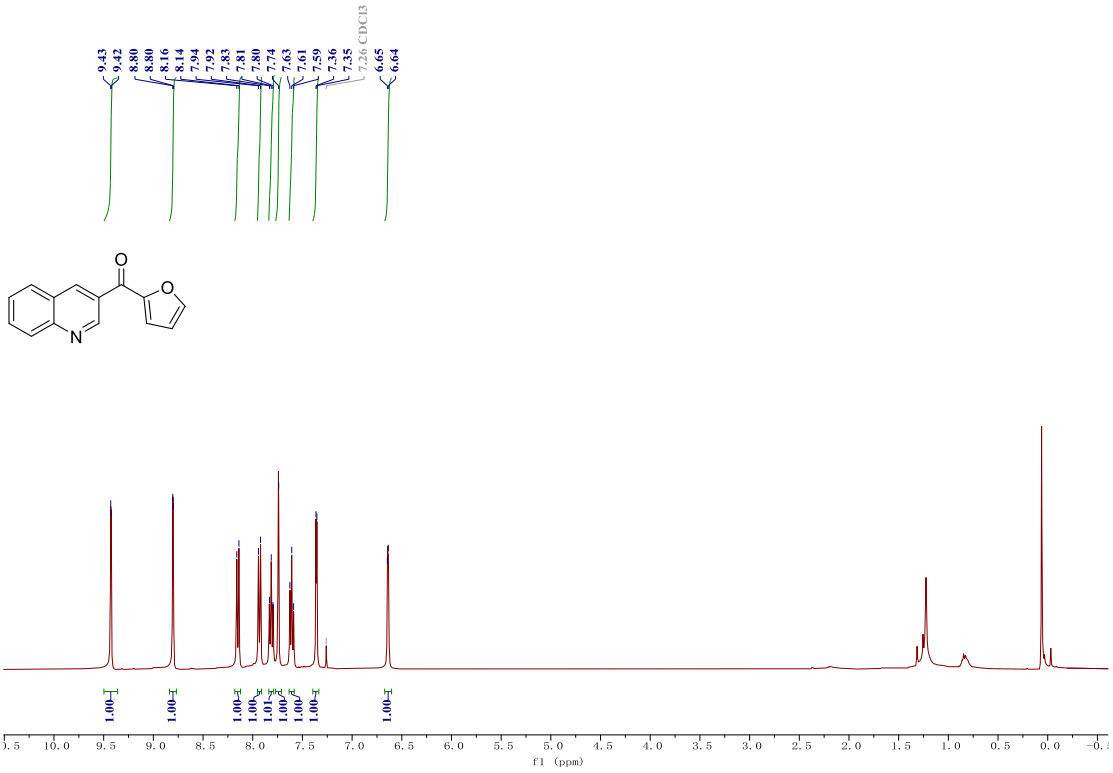


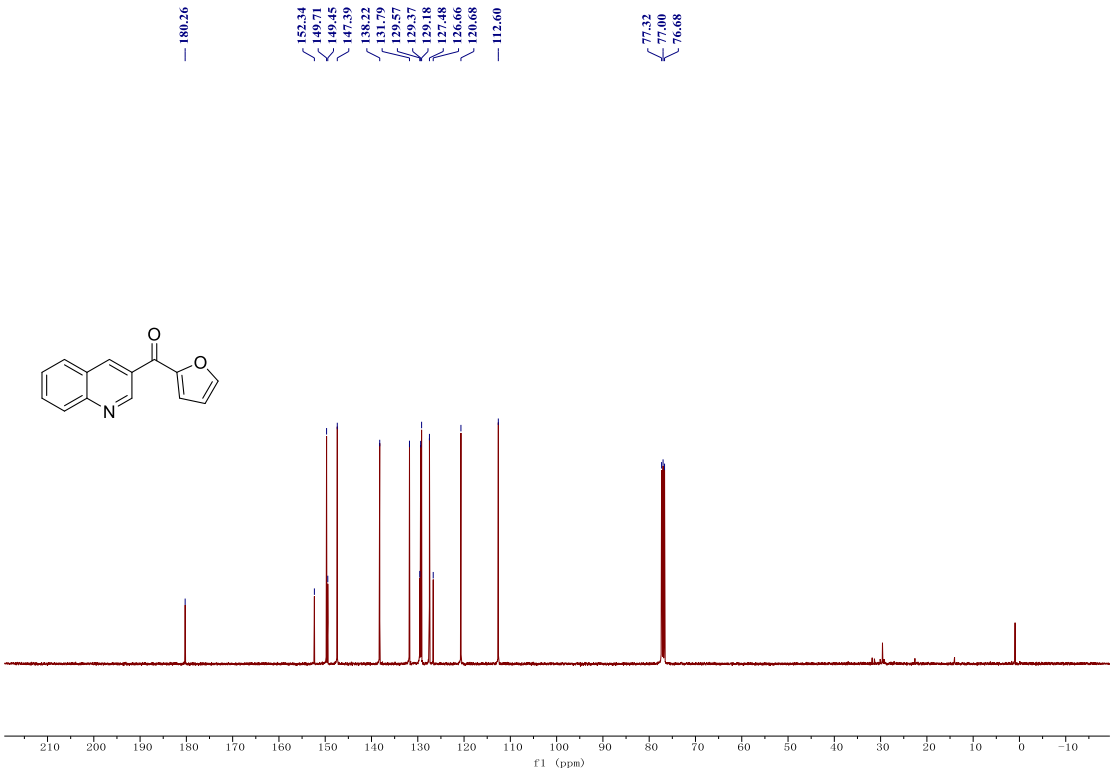
^{1}H NMR and ^{13}C NMR for **3ay**



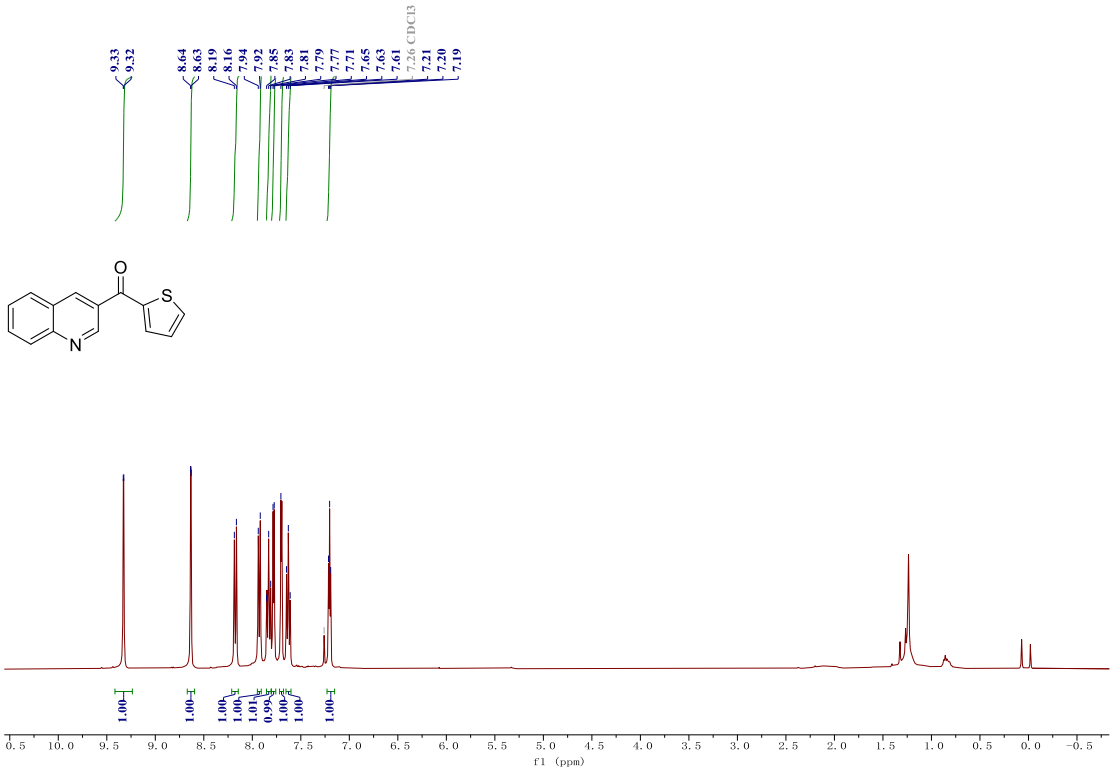


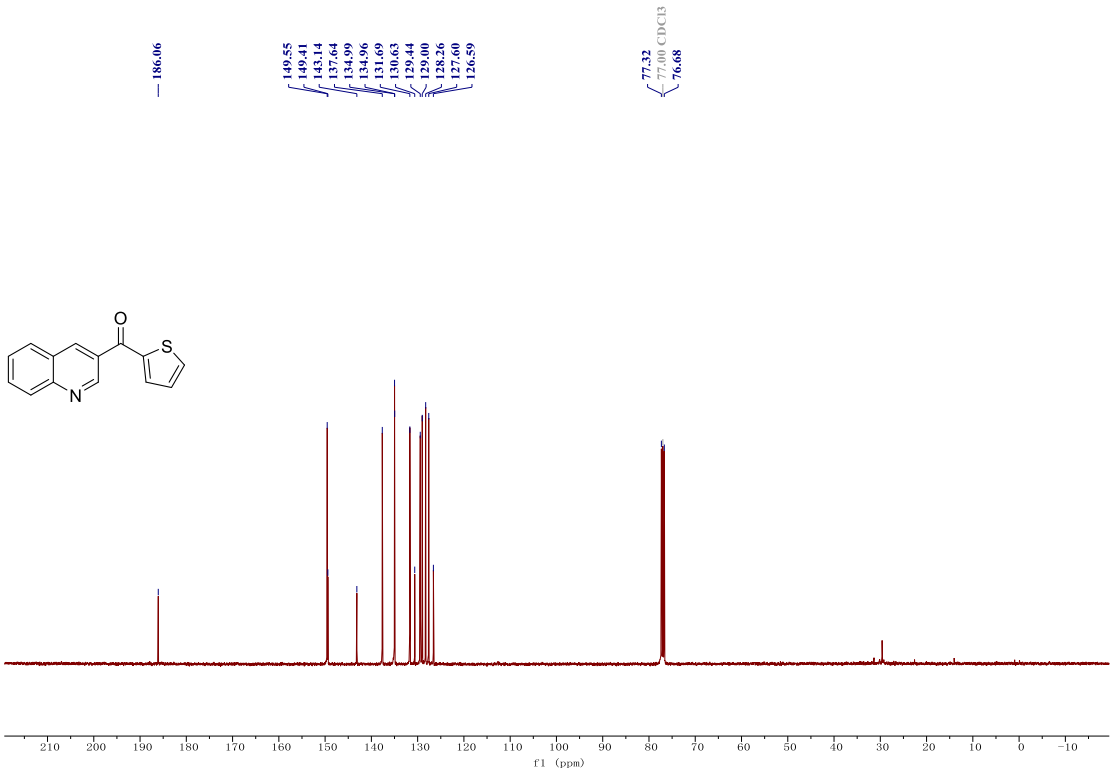
^{1}H NMR and ^{13}C NMR for **3az**



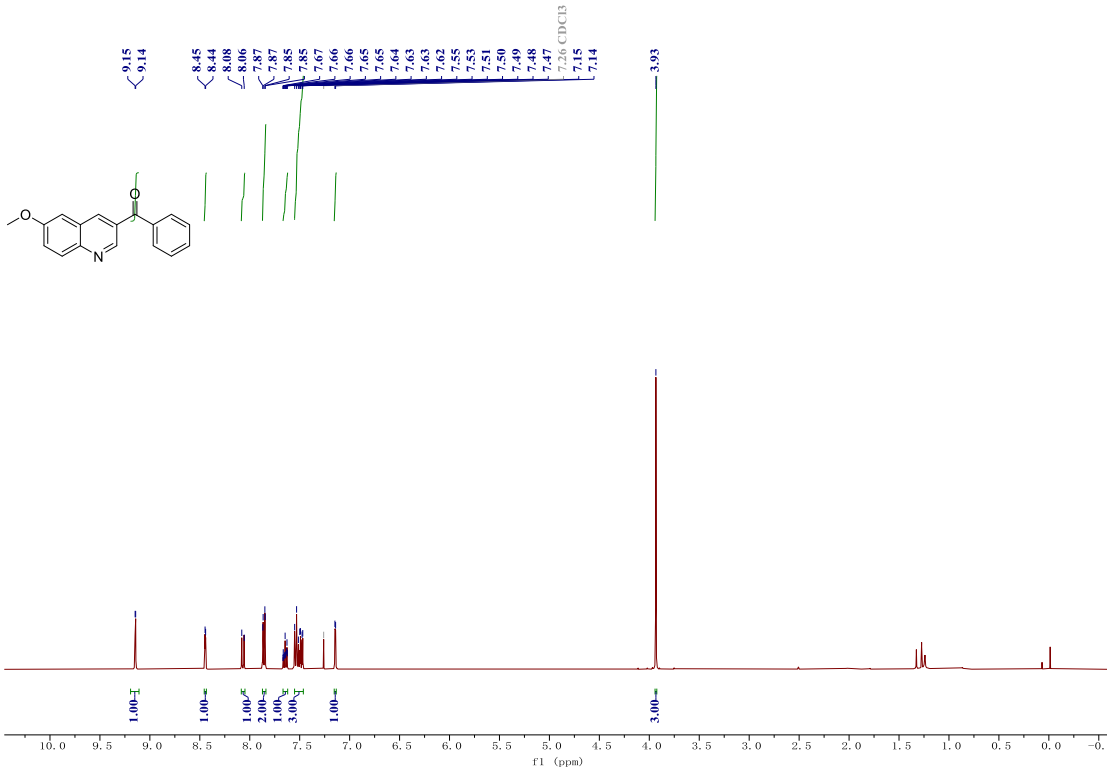


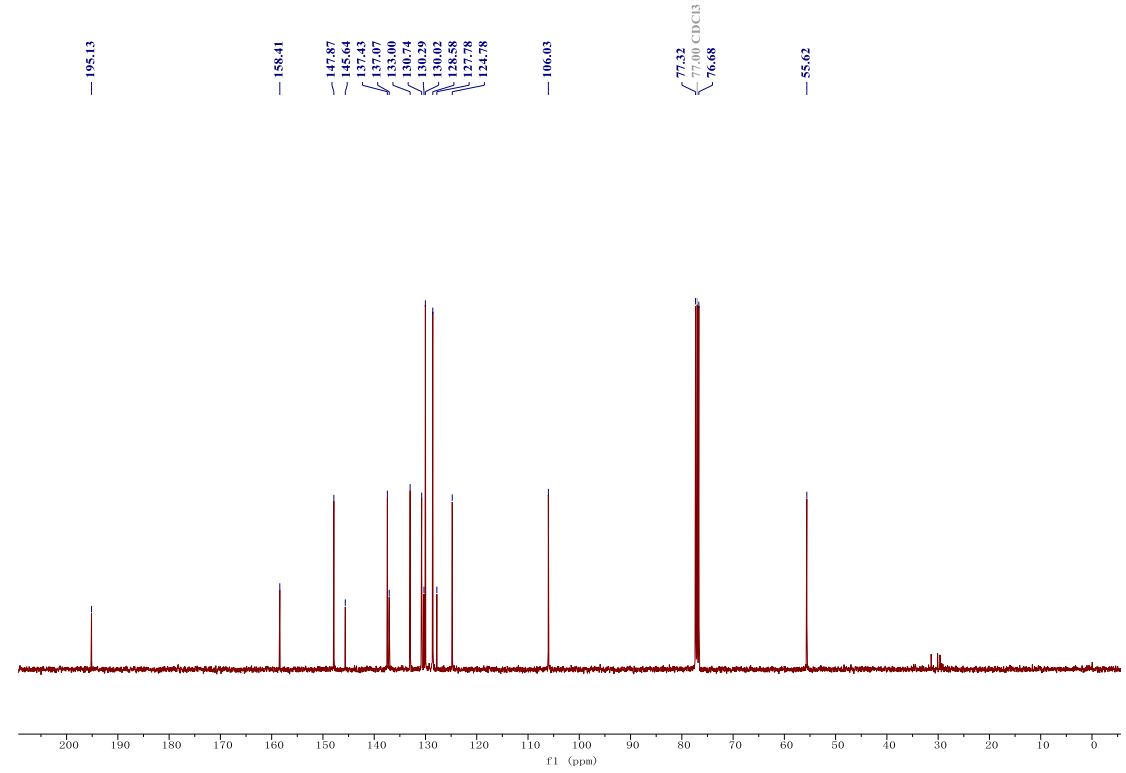
^{1}H NMR and ^{13}C NMR for **3az'**



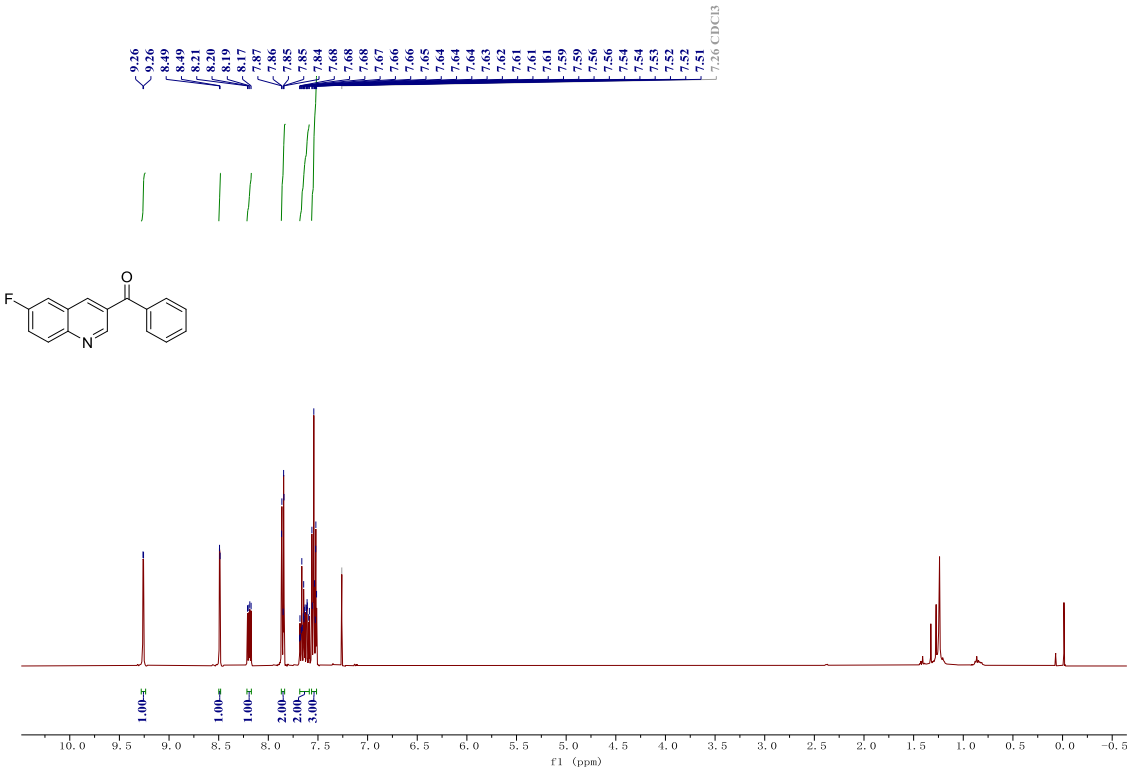


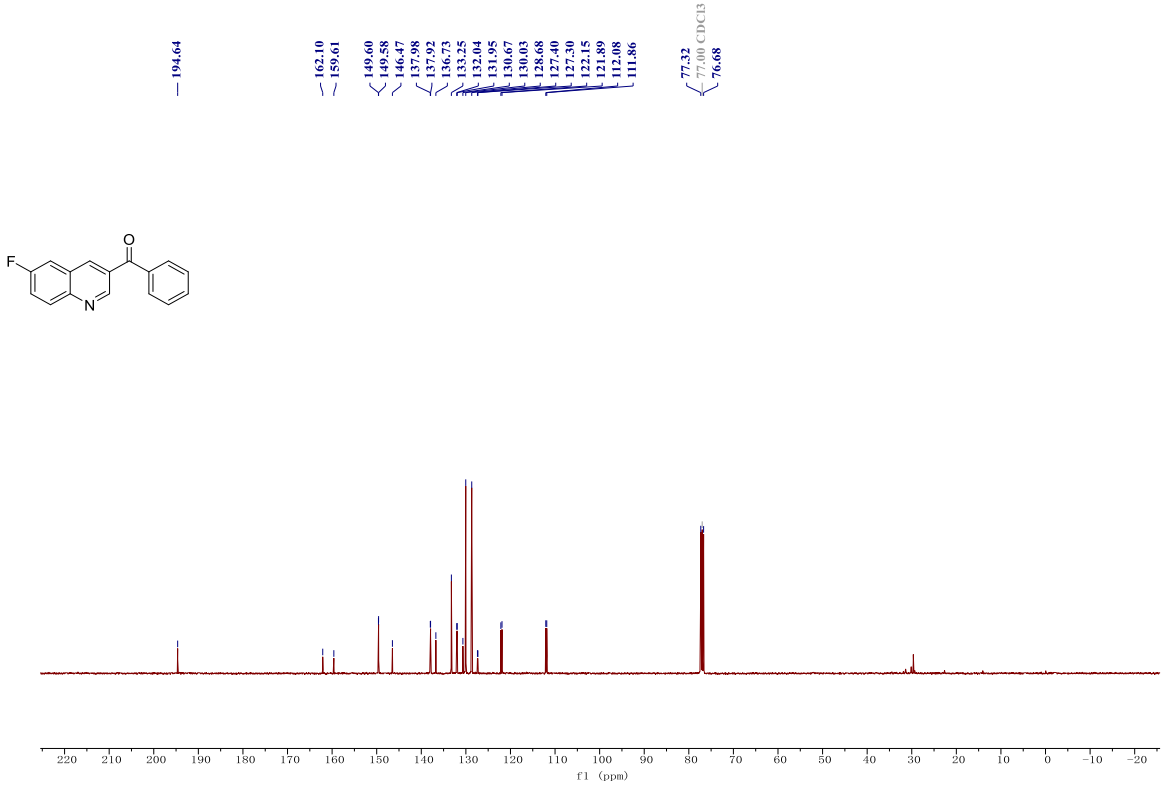
^{1}H NMR and ^{13}C NMR for **3ba**

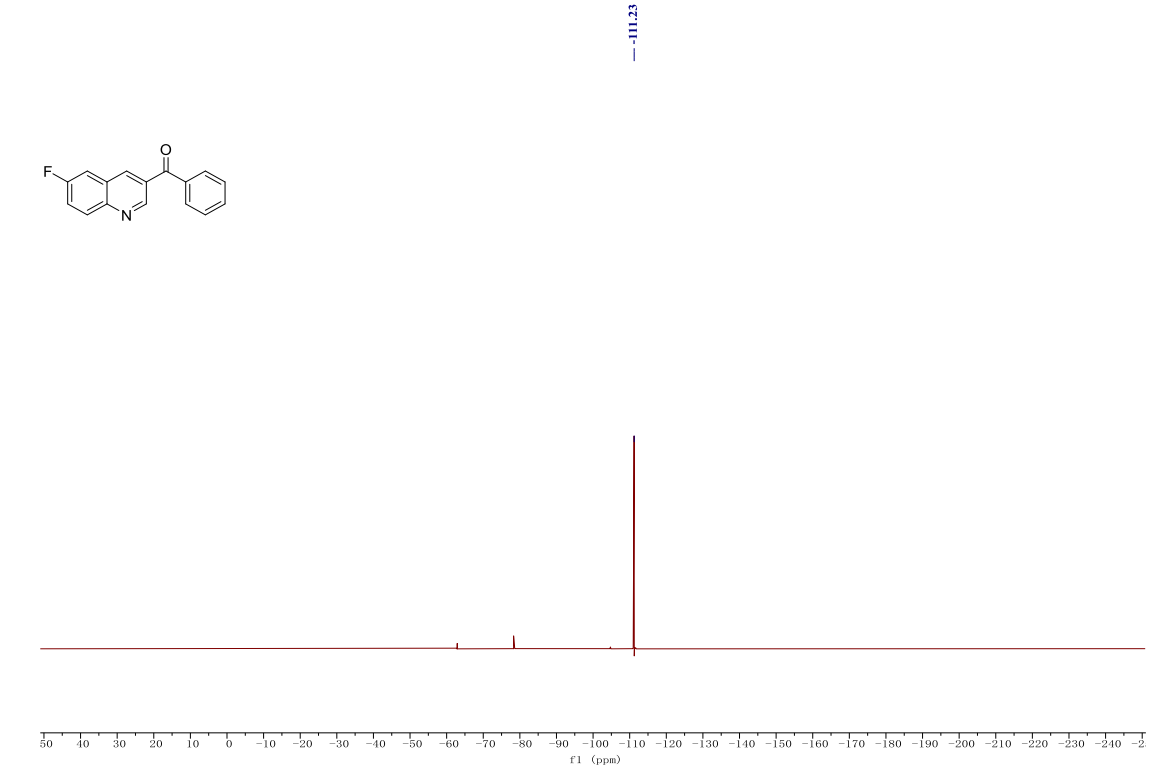




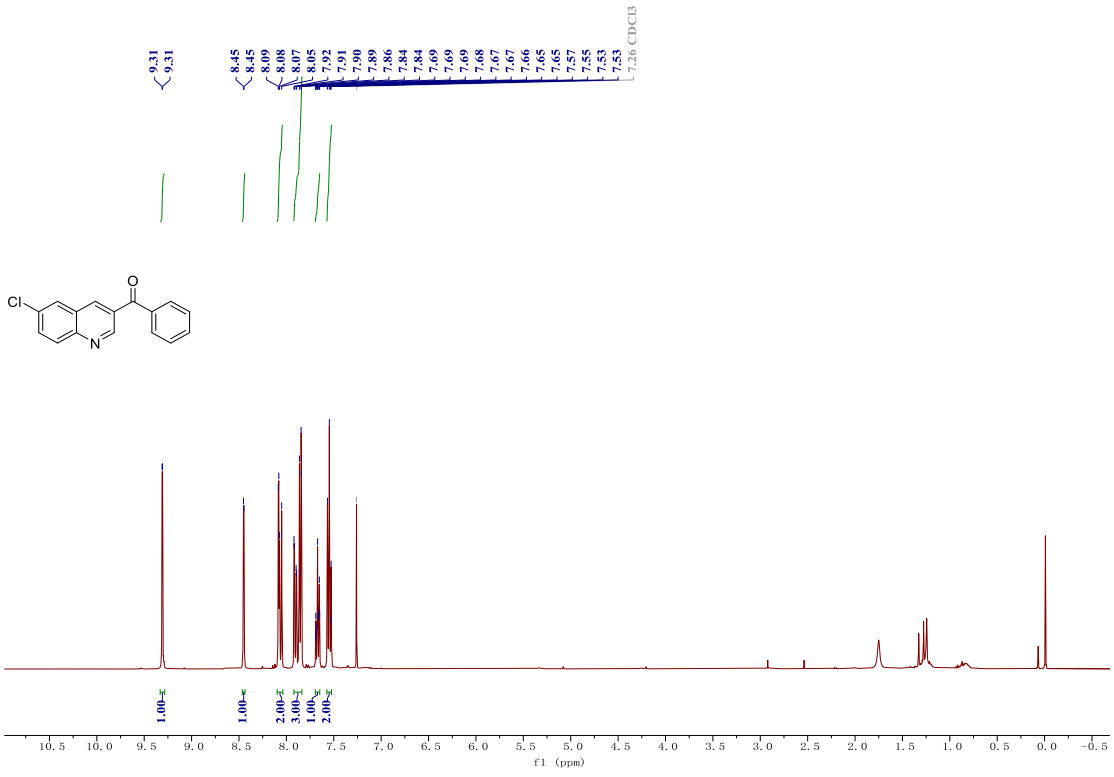
^{1}H NMR, ^{13}C NMR and ^{19}F NMR for **3ca**

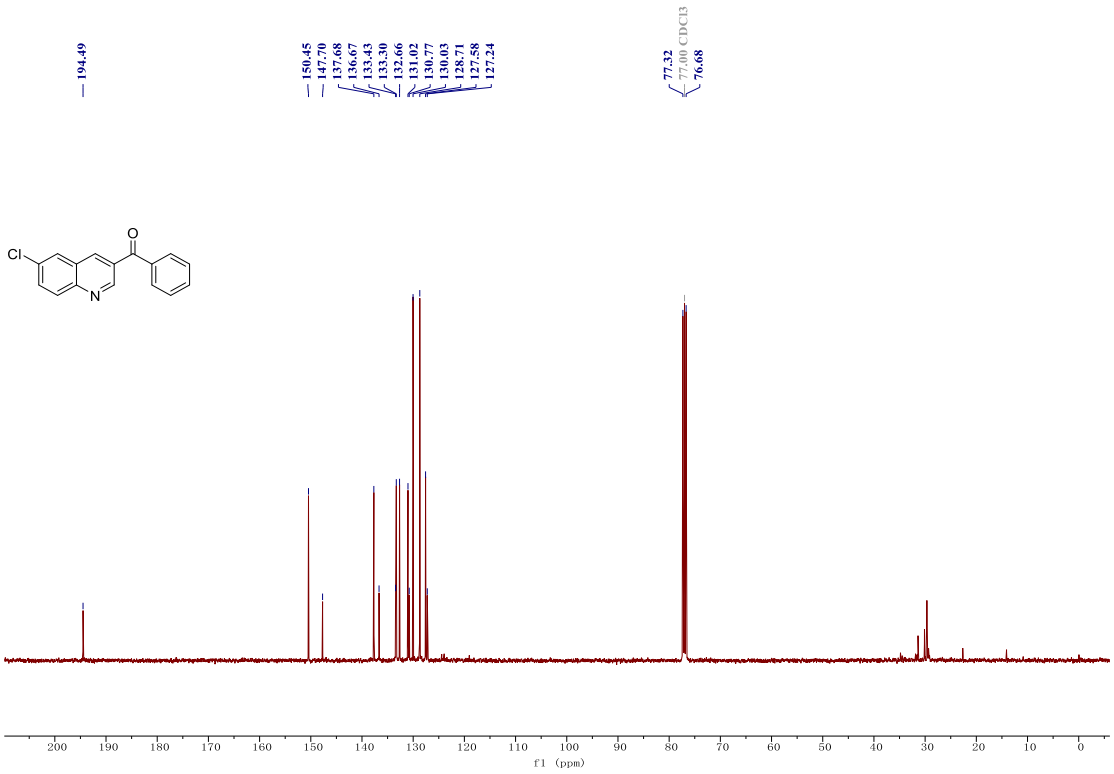



194.64
162.10
159.61
149.60
149.58
146.47
137.98
137.92
136.73
133.25
132.04
131.95
130.67
130.03
128.68
127.40
127.30
122.15
121.89
112.08
111.86
77.32
77.00 CDCl3
76.68
F
O
N
f1 (ppm)

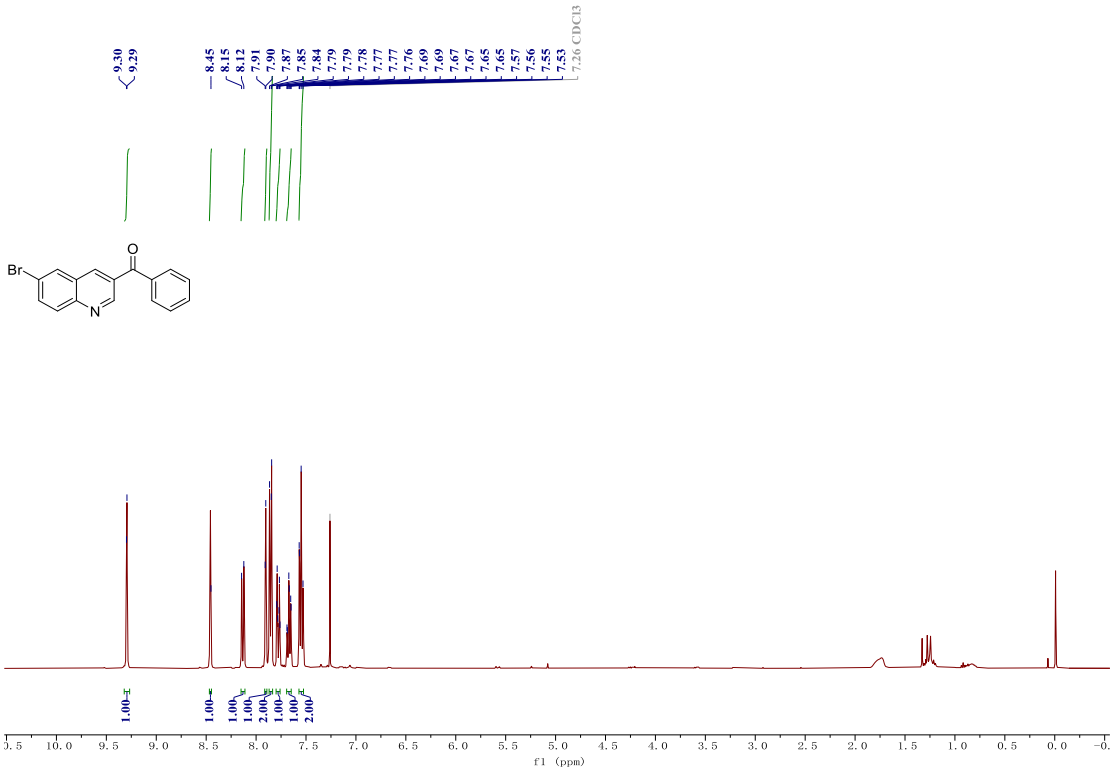

-111.23
F
O
N
f1 (ppm)

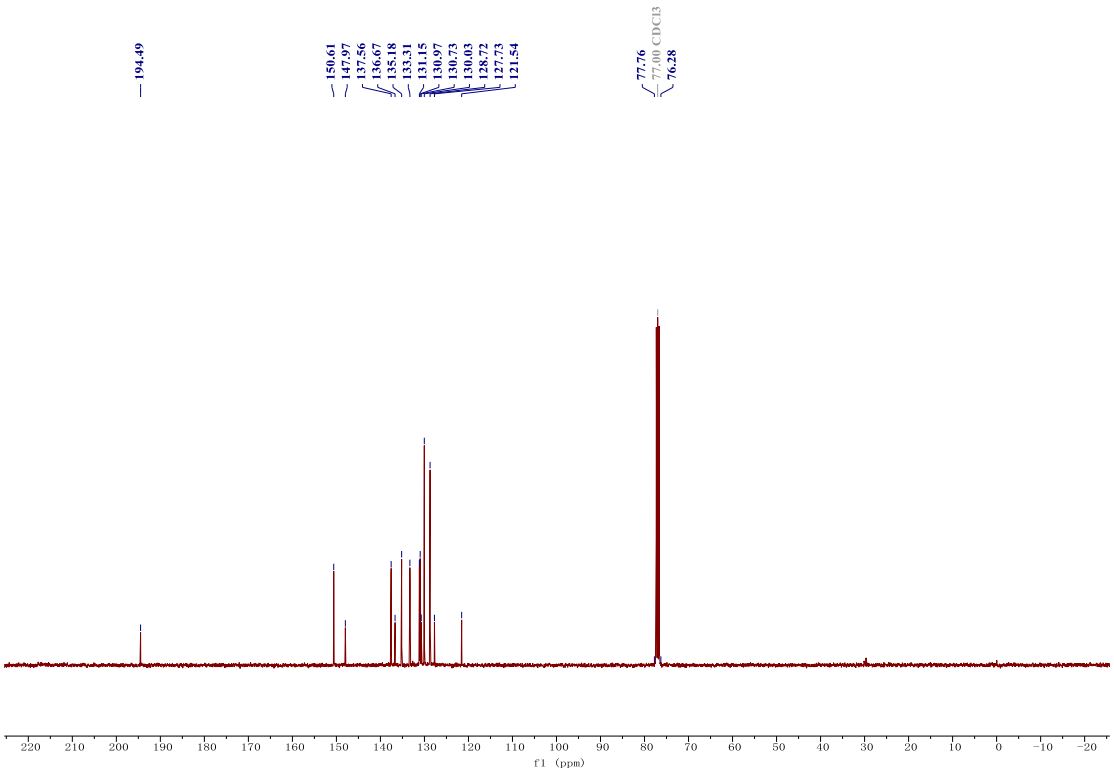
^{1}H NMR and ^{13}C NMR for **3da**



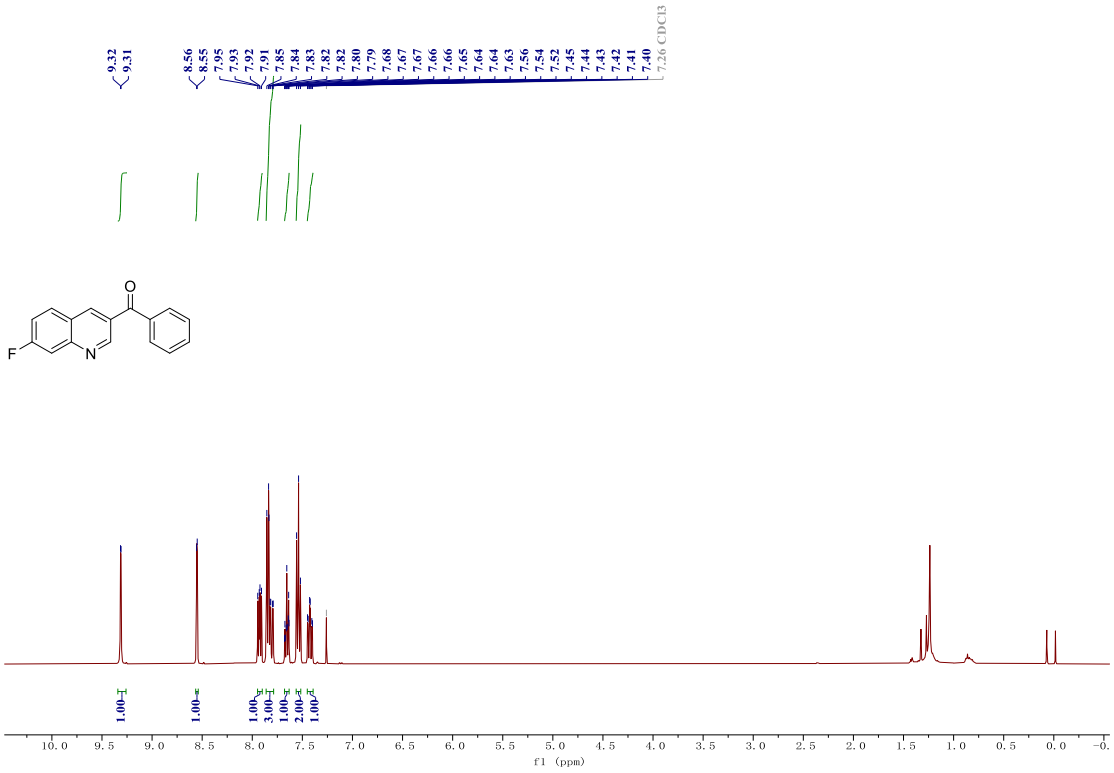


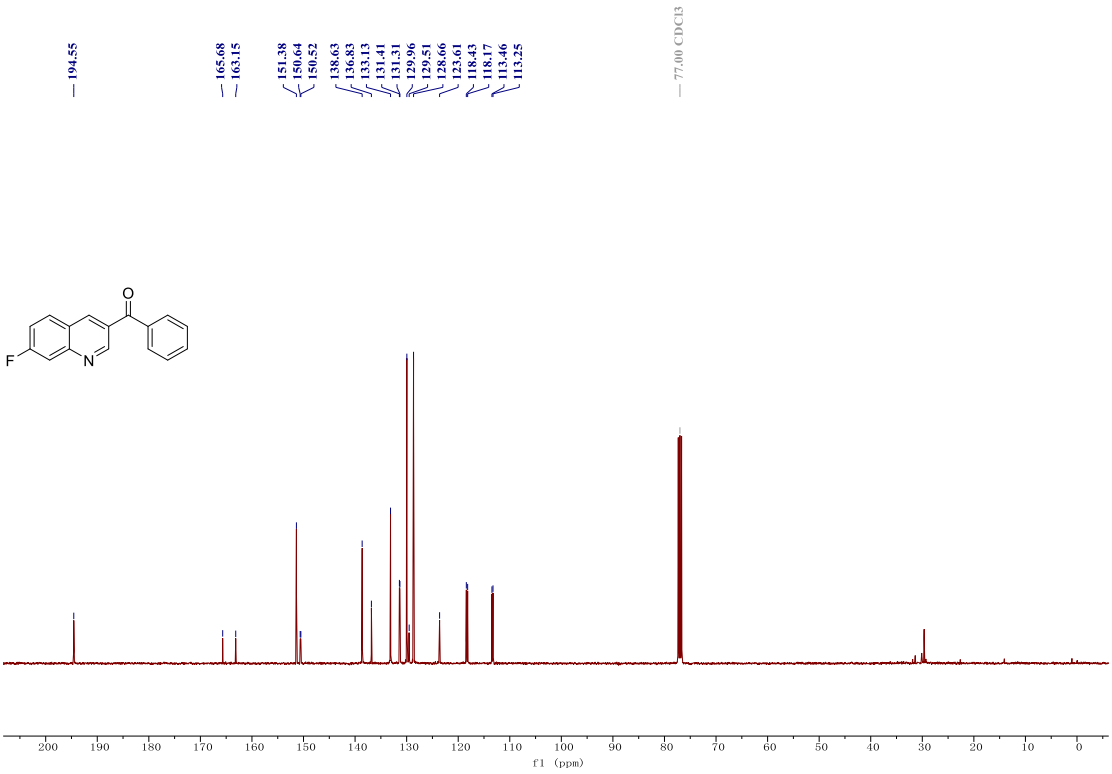
^{1}H NMR and ^{13}C NMR for **3ea**

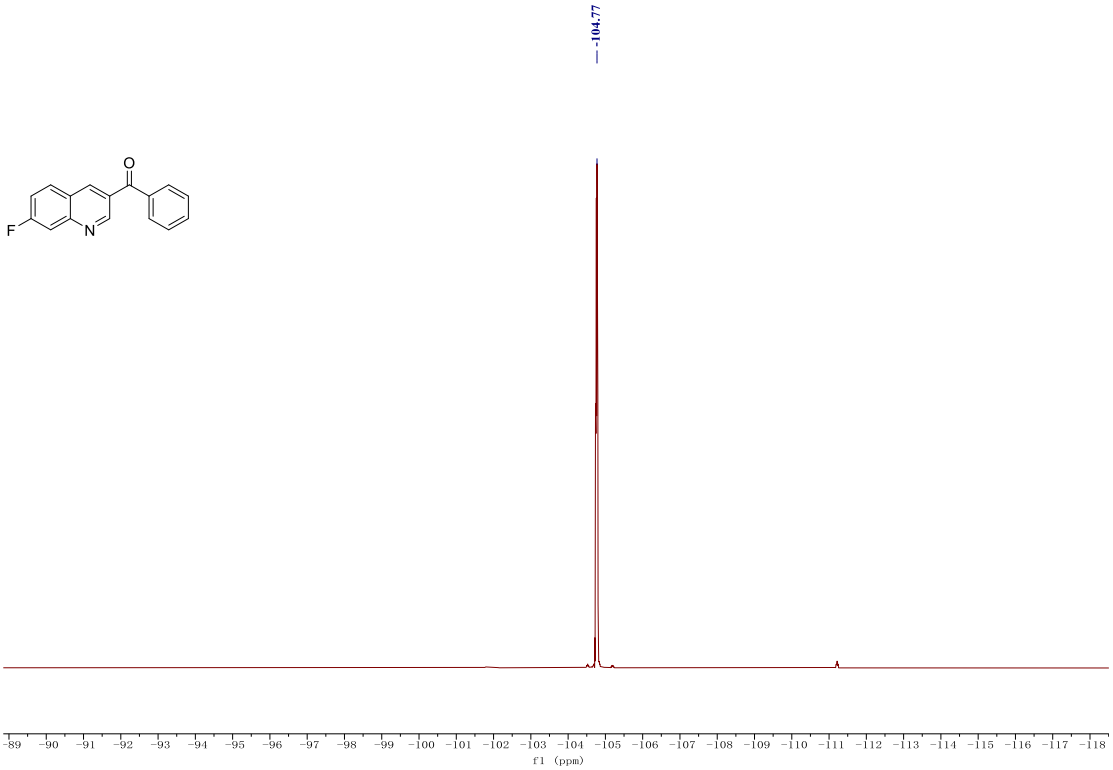




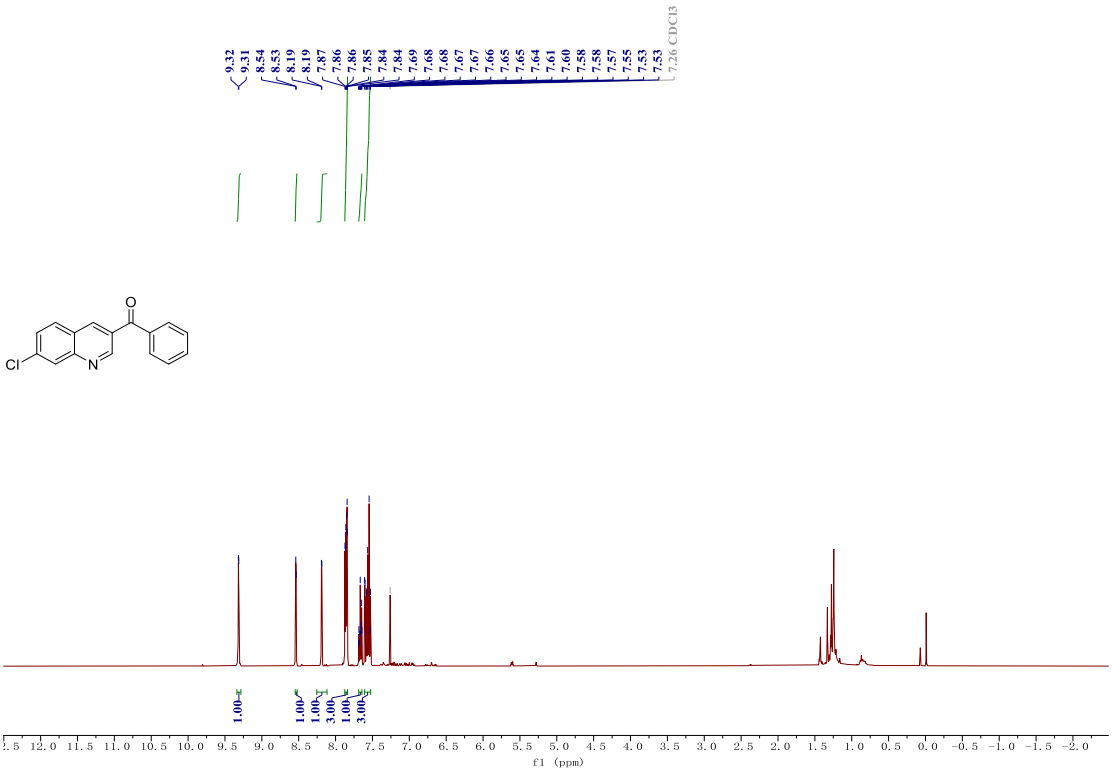
^{1}H NMR, ^{13}C NMR and ^{19}F NMR for **3fa**

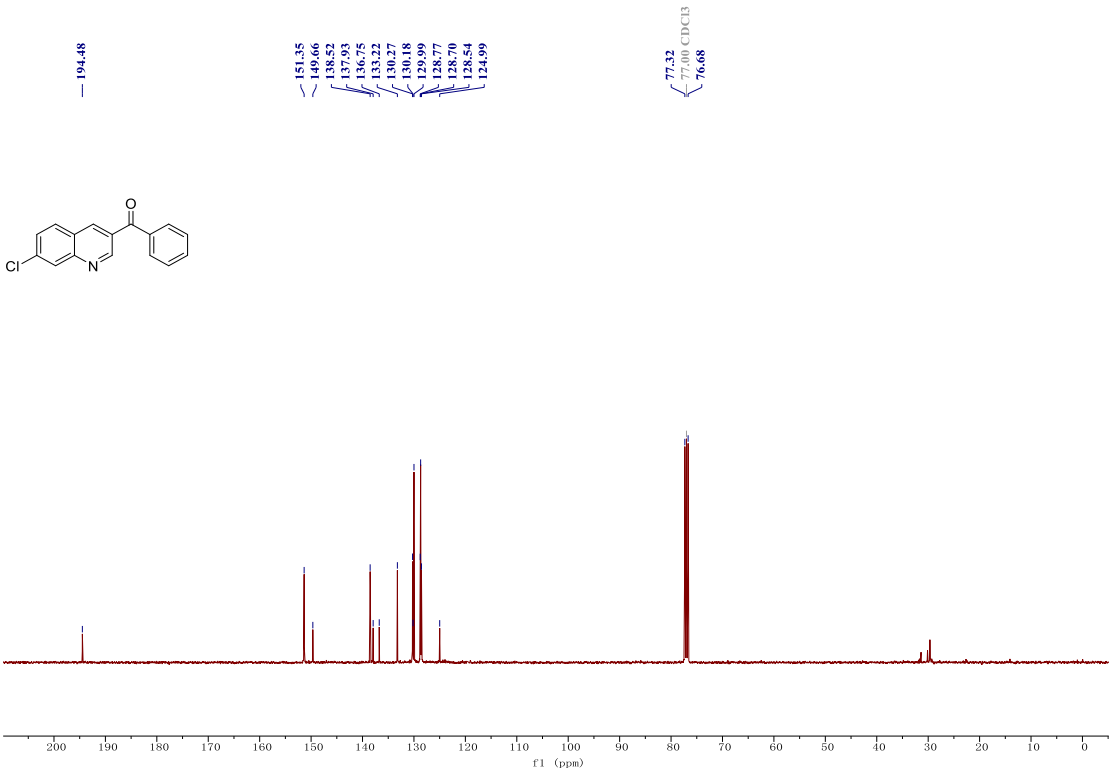



194.55
165.68
163.15
151.38
150.64
150.52
138.63
136.83
133.13
131.41
131.31
129.96
129.51
128.66
123.61
118.43
118.17
113.46
113.25
77.00 CDCl3
O
F
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

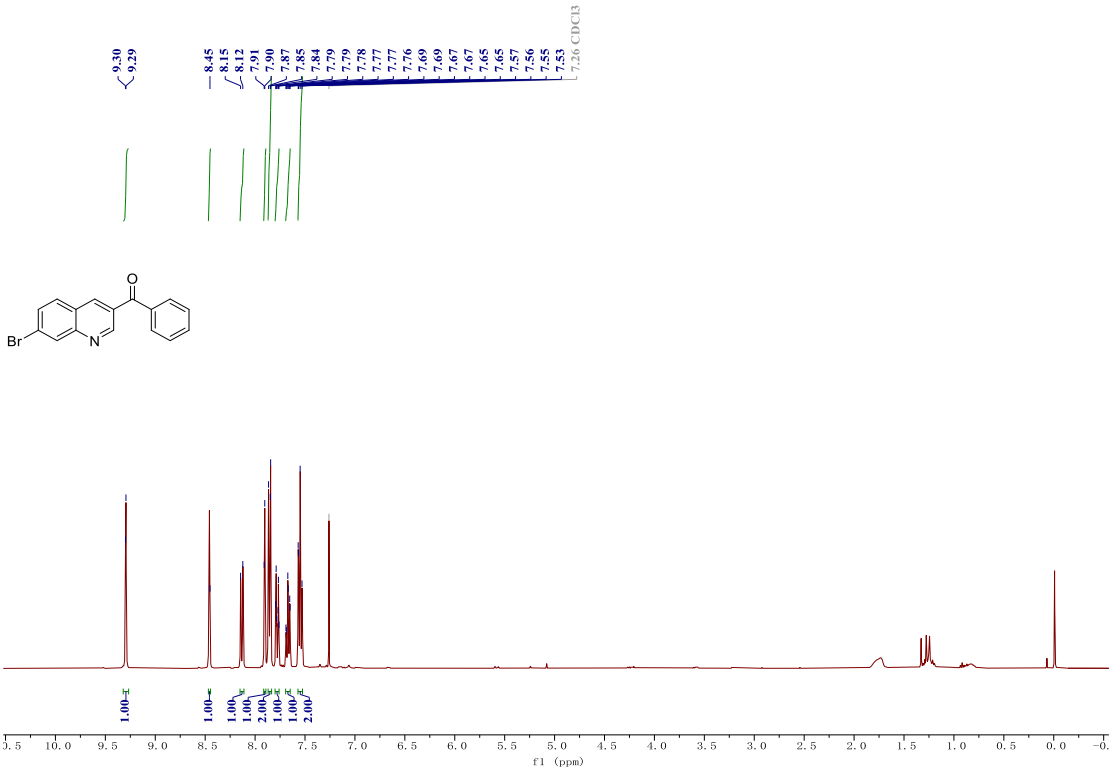

-104.77
O
F
N
-89 -90 -91 -92 -93 -94 -95 -96 -97 -98 -99 -100 -101 -102 -103 -104 -105 -106 -107 -108 -109 -110 -111 -112 -113 -114 -115 -116 -117 -118
f1 (ppm)

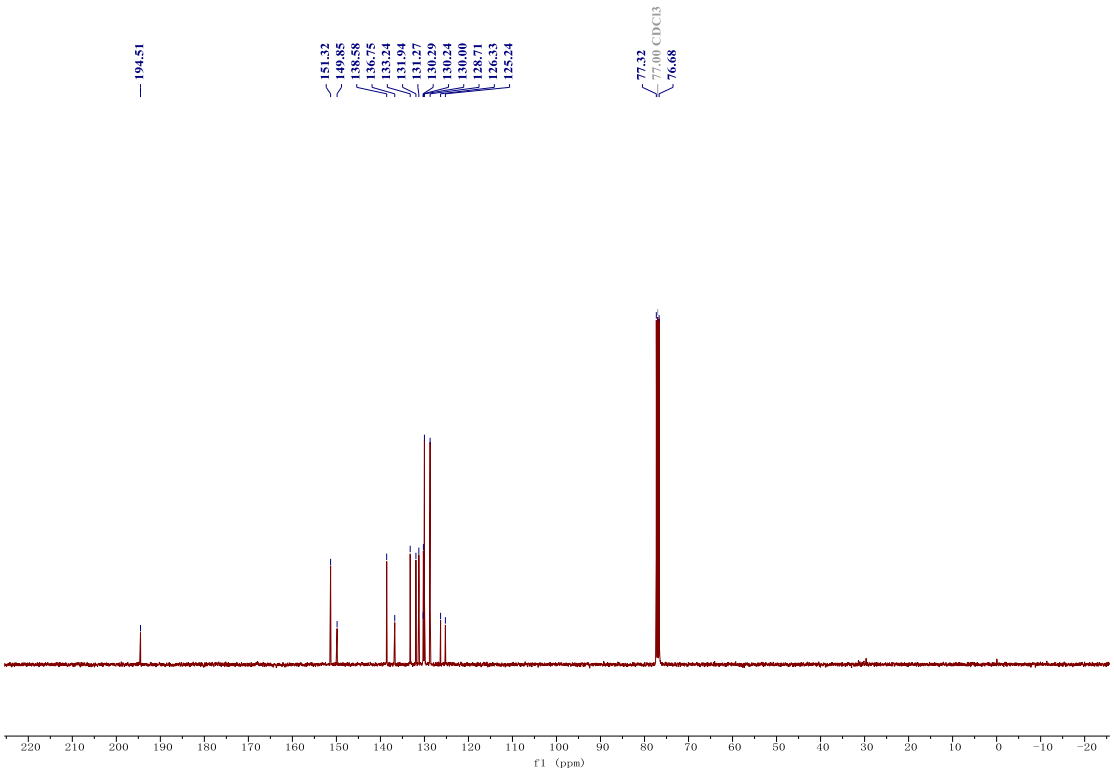
^{1}H NMR and ^{13}C NMR for **3ga**



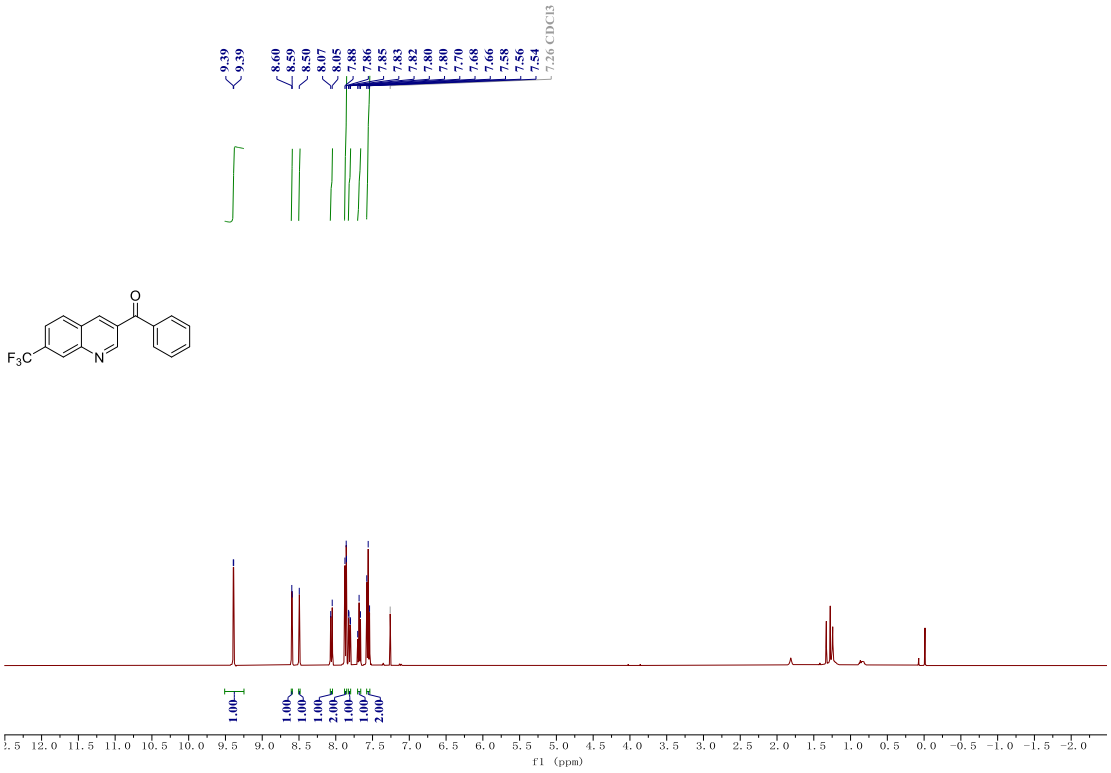


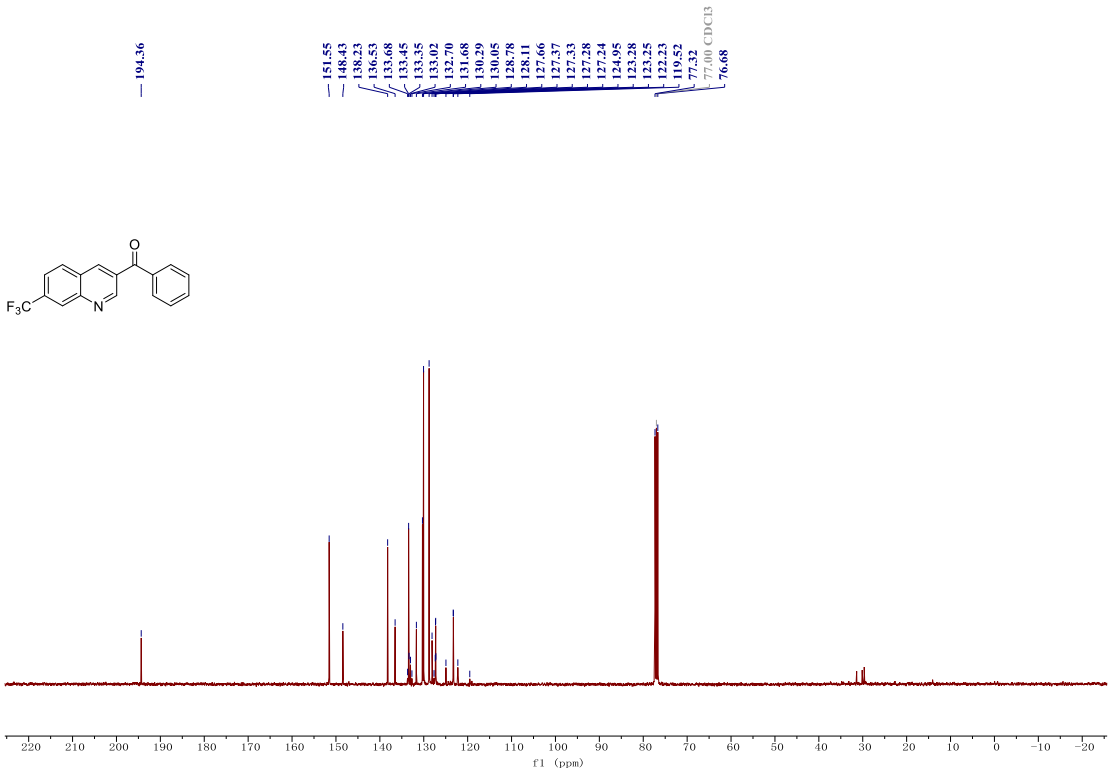
^{1}H NMR and ^{13}C NMR for **3ha**

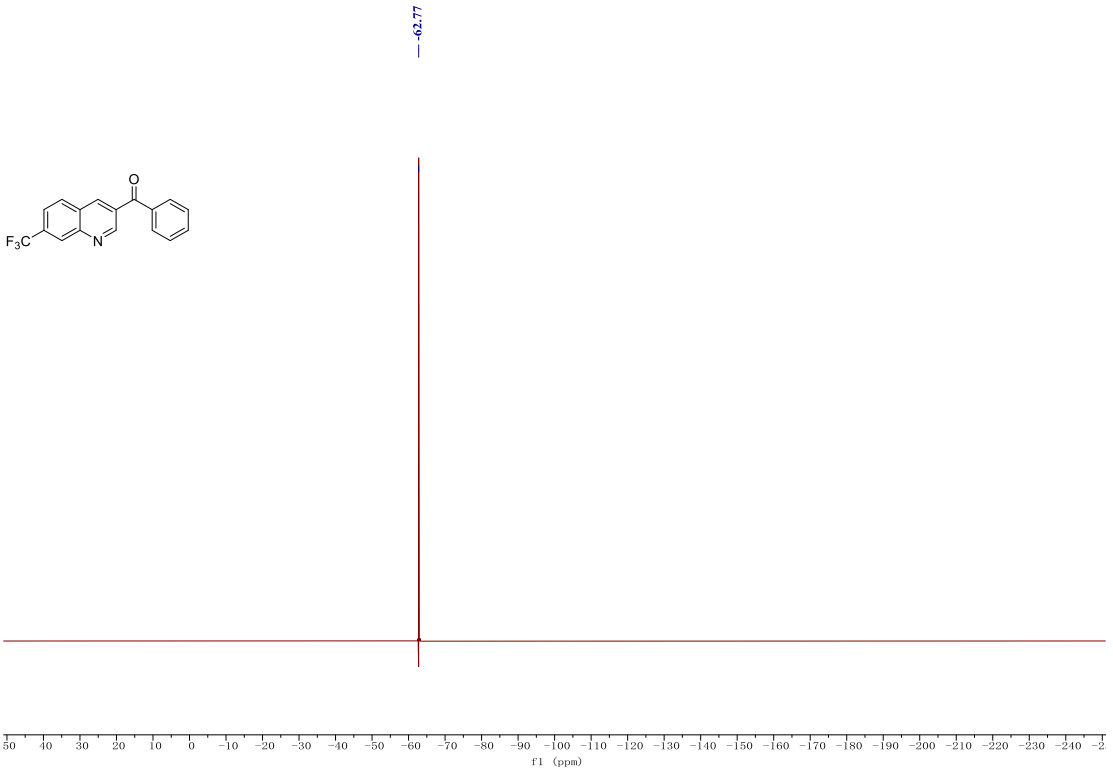




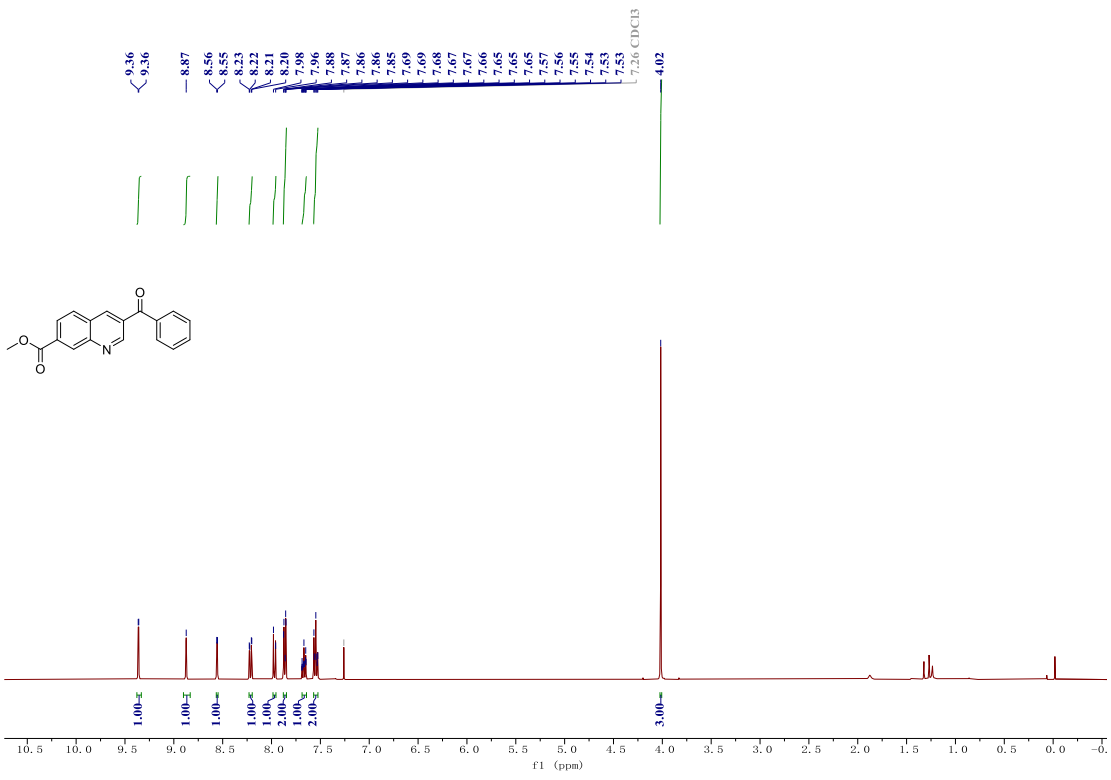
^{1}H NMR and ^{13}C NMR for **3ia**

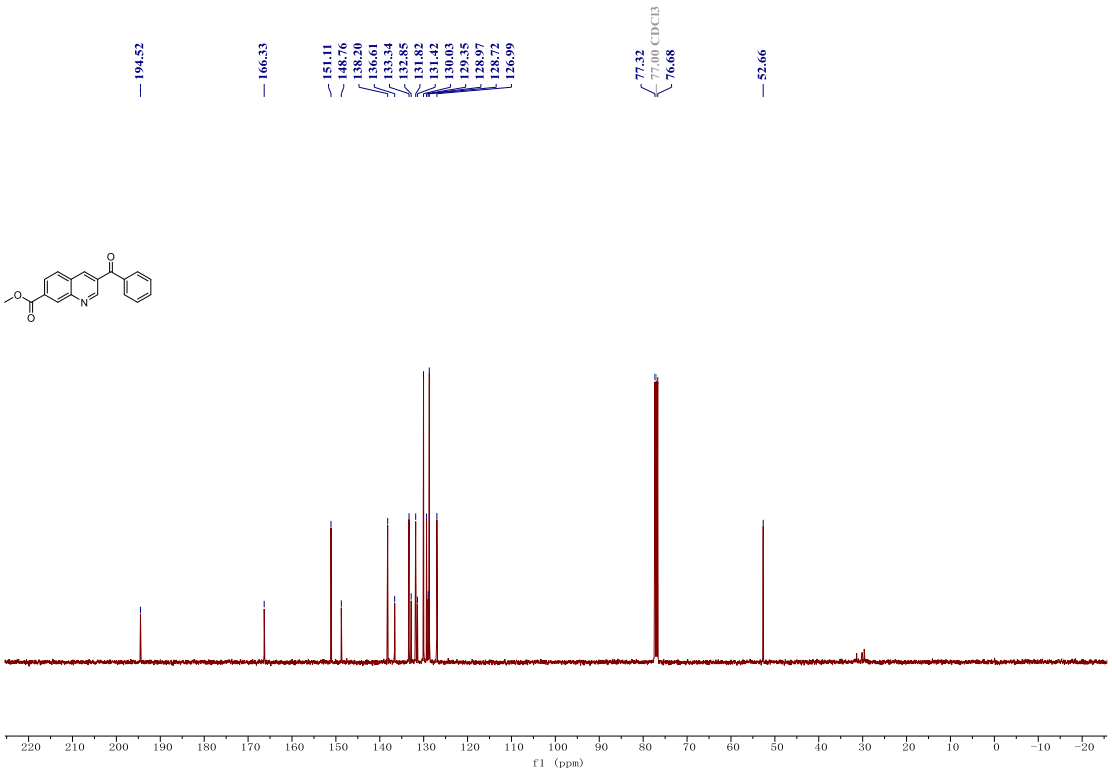



194.36
151.55
148.43
138.23
136.53
133.68
133.45
133.35
133.02
132.70
131.68
130.29
130.05
128.78
128.11
127.66
127.37
127.33
127.28
127.24
124.95
123.28
123.25
122.23
119.52
77.32
77.00 CDCl3
76.68
O
F3C
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
f1 (ppm)

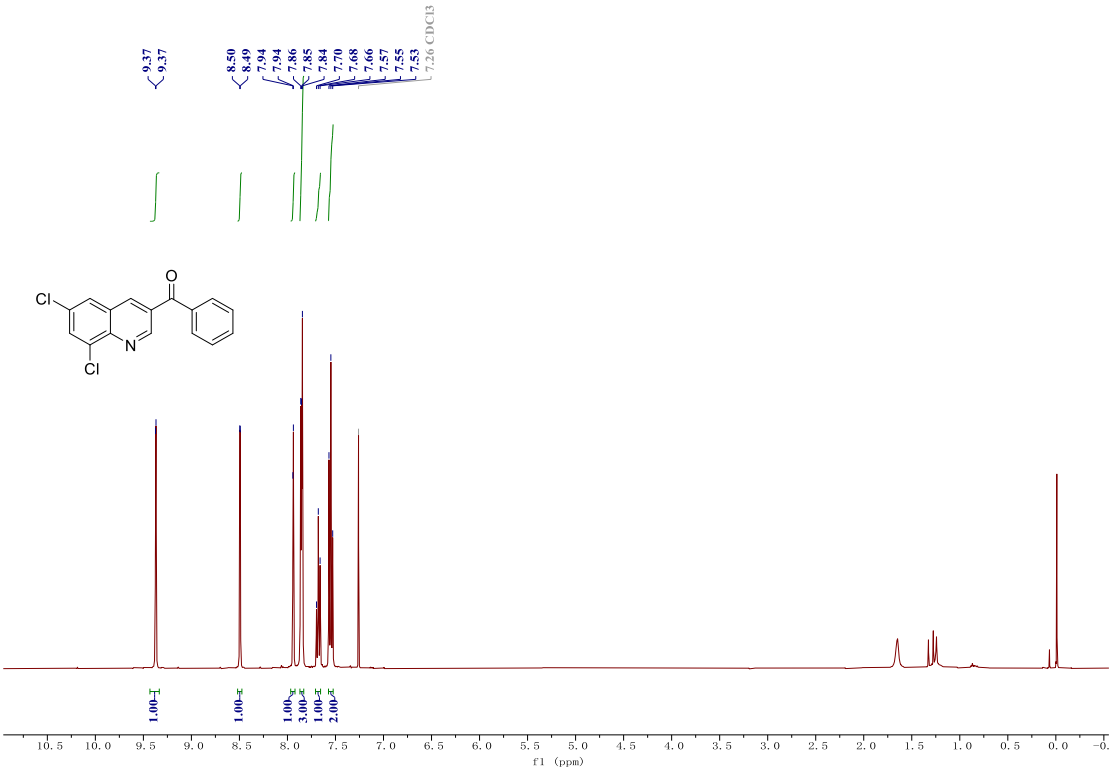

-62.77
O
F3C
N
50 40 30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −220 −230 −240 −2
f1 (ppm)

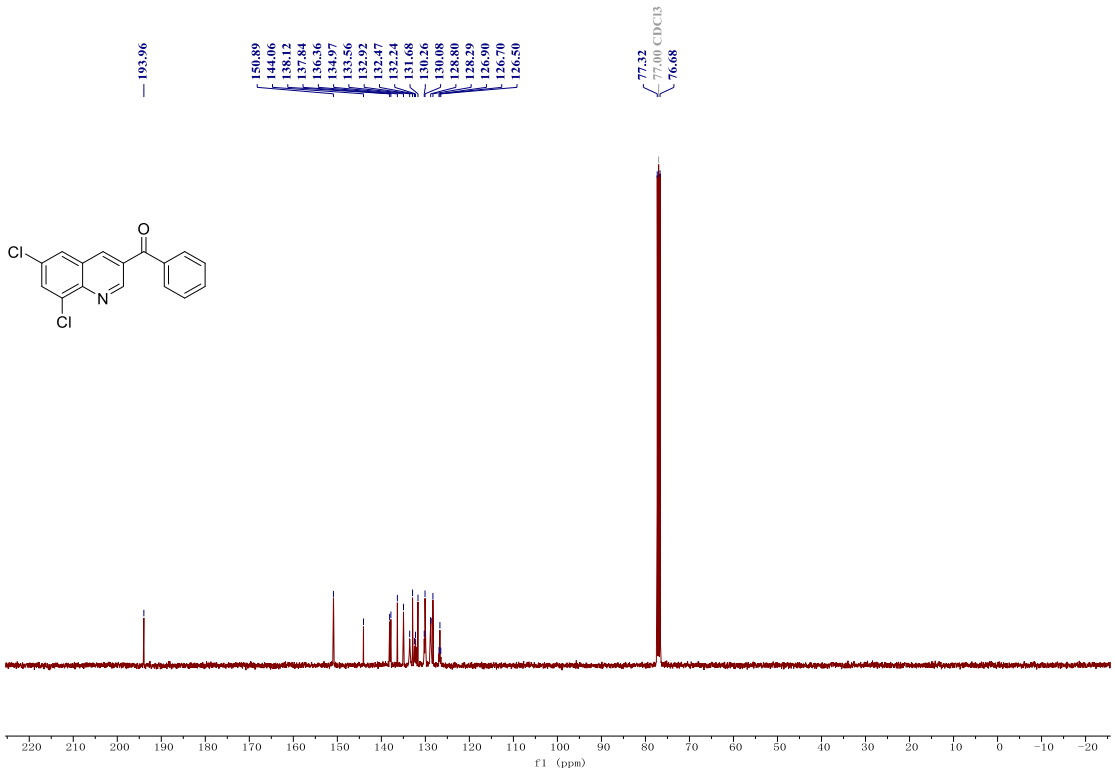
^{1}H NMR and ^{13}C NMR for **3ja**



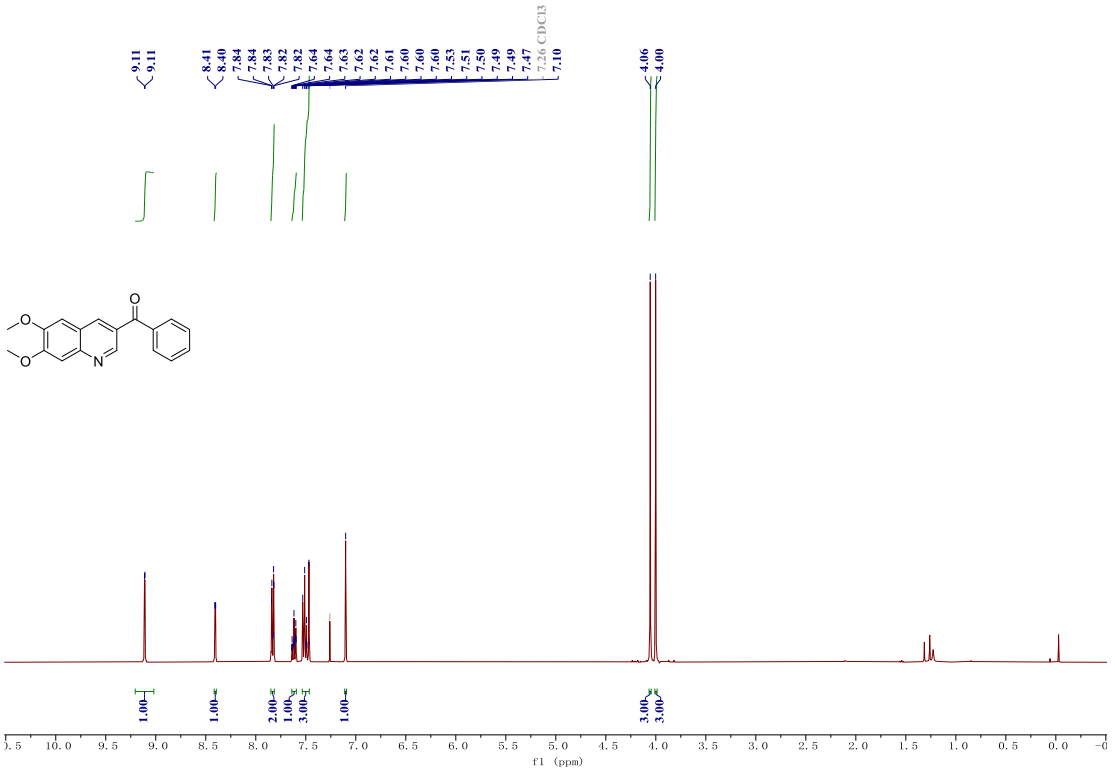


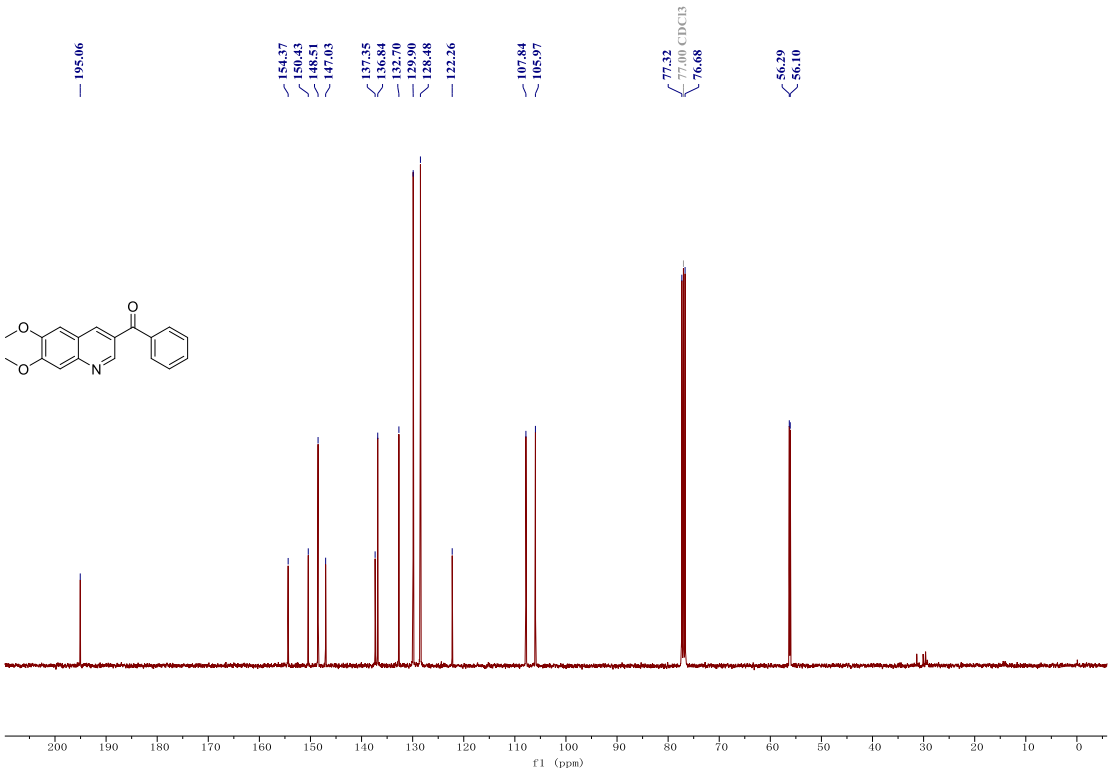
^{1}H NMR and ^{13}C NMR for **3ka**



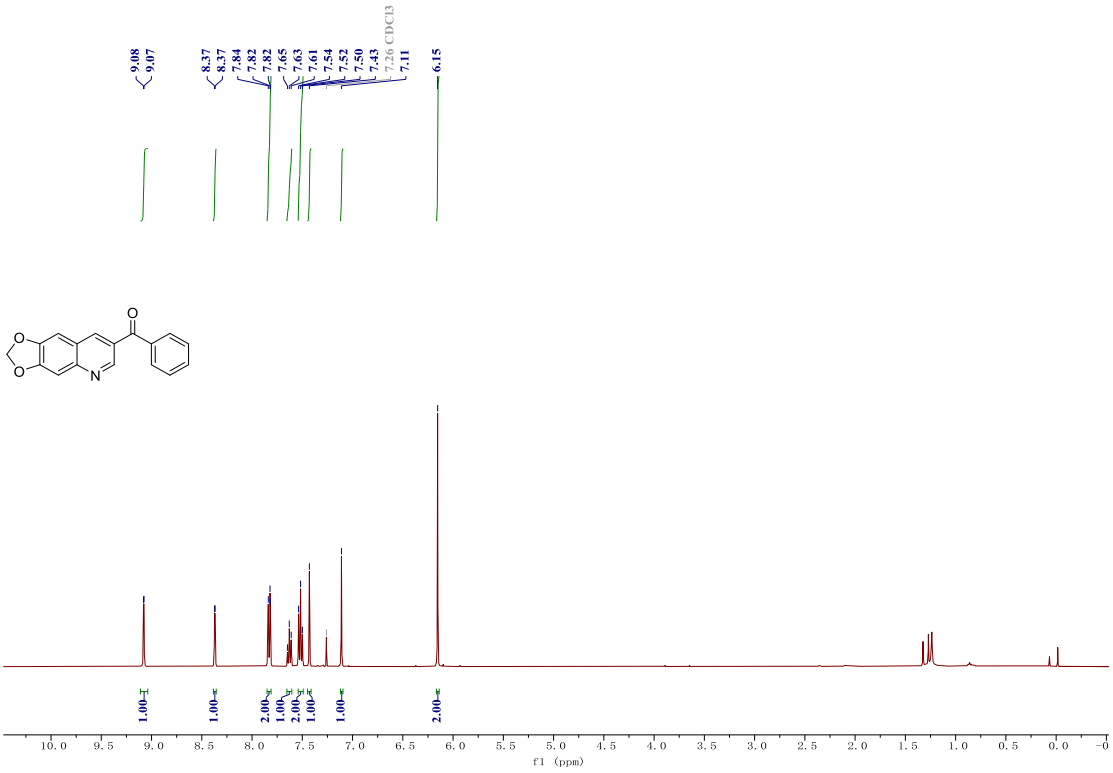


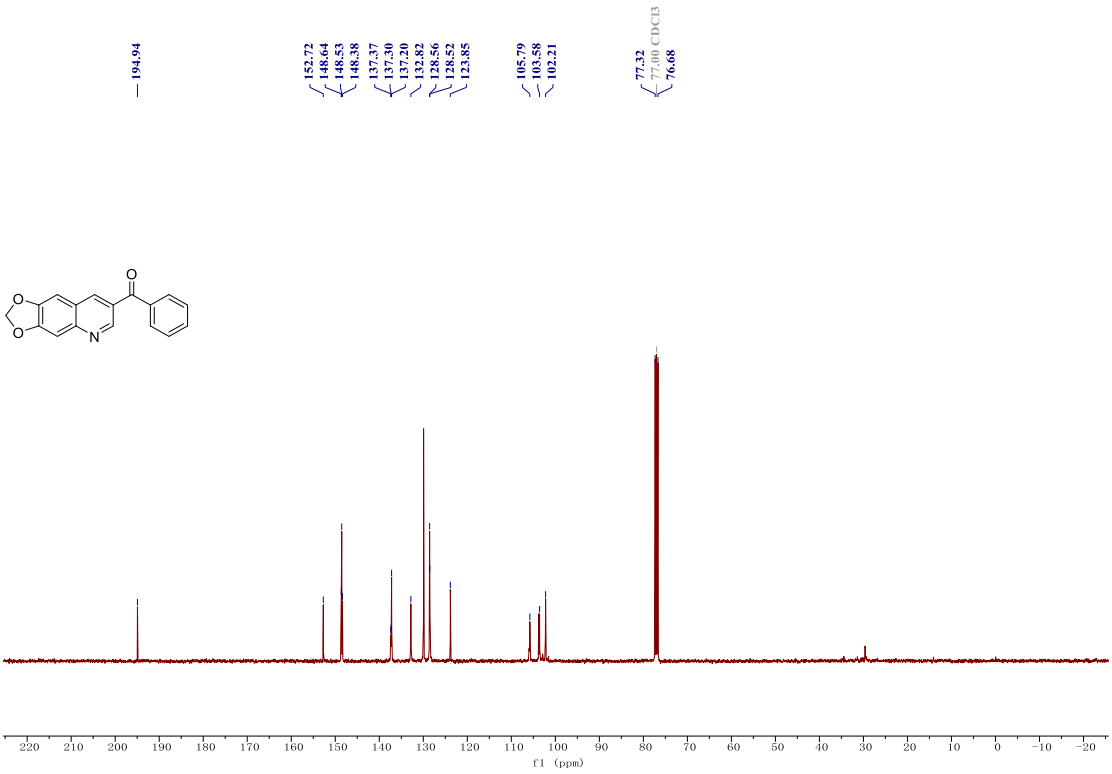
^{1}H NMR and ^{13}C NMR for **3la**



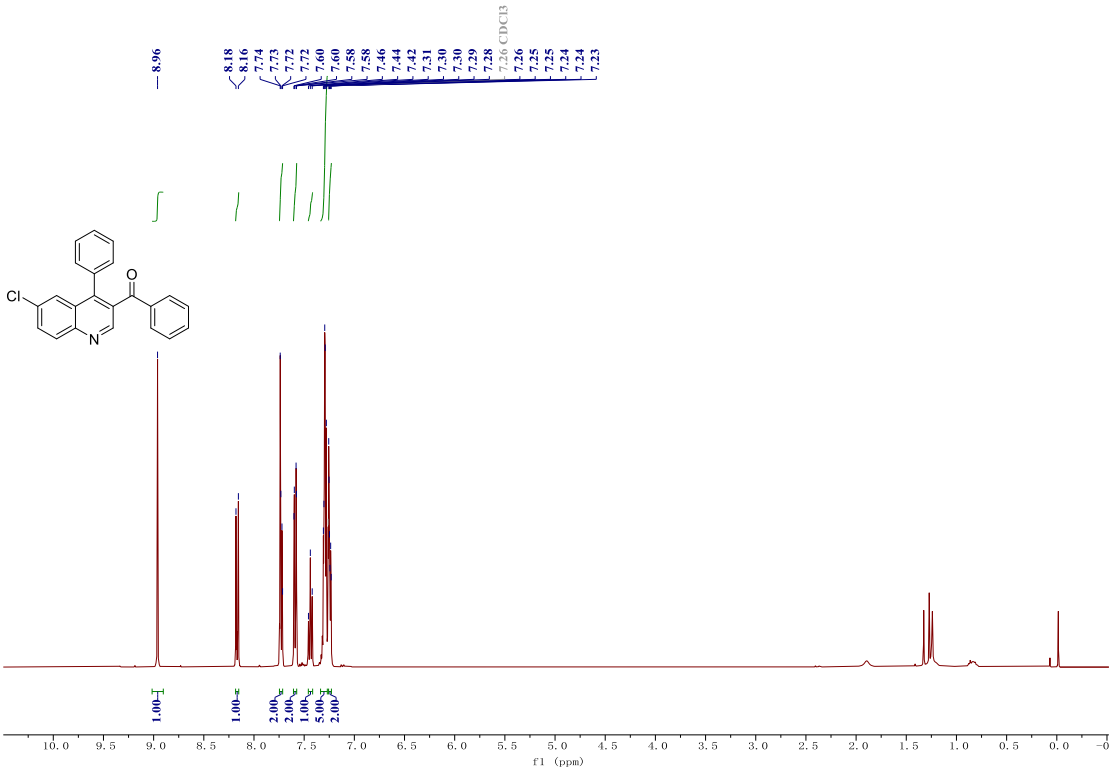


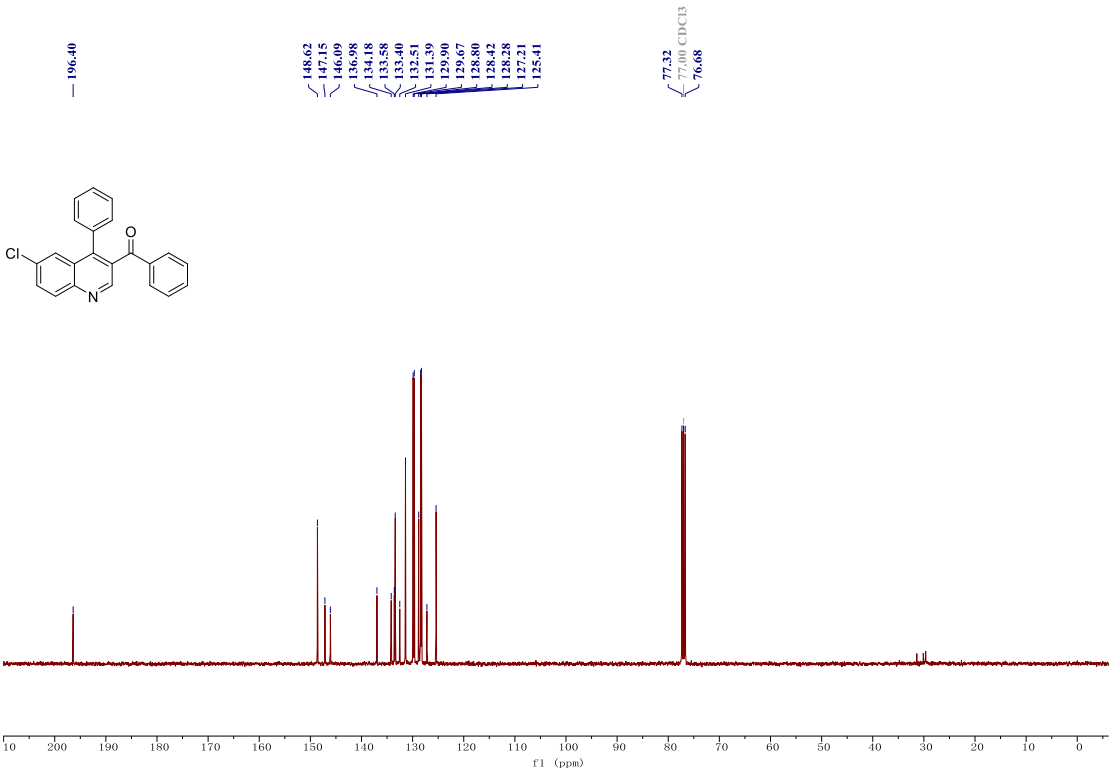
^{1}H NMR and ^{13}C NMR for **3ma**





^{1}H NMR and ^{13}C NMR for **3na**




196.40
148.62
147.15
146.09
136.98
134.18
133.58
133.40
132.51
131.39
129.90
129.67
128.80
128.42
128.28
127.21
125.41
77.32
77.00 CDCl3
76.68
Cl
O
N
f1 (ppm)