Electronic Supplementary Material (ESI) for ChemComm.

Efficient synthesis of 3-hydroxyimino-1-isoindolinones and 3-methyle -ne-1-isoindolinones via Cu-promoted C-H activation-nitroalkylatio -n-intramolecular cyclization tandem processes

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Supporting Information

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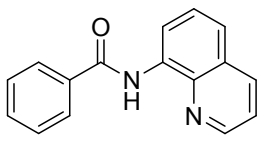
1. General information

^{1}H NMR and ^{13}C NMR were recorded in $CDCl_3$ or DMSO-d_6 at room temperature on the Varian INOVA-400 spectrometer (400 MHz ^{1}H) or Bruker spectrometer (400 MHz ^{1}H). The chemical-shifts scale is based on internal TMS. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; qui, quin tet; sxt, sextet. The coupling constants, *J* are reported in Hertz (Hz). Mass spectros - copy data were collected on an HRMS-ESI instrument.

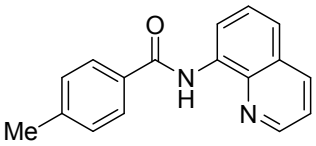
Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Anhydrous $Cu(OAc)_2$ was purchased from Alfa Aesar. All solvents were purified and dried according to standard methods prior to use. Products were purified by flash column chromatography on 200-300 mesh silica gel, SiO_2.

2. Typical procedure for the preparation of benzamides

All benzamides 1 were synthesized from the corresponding benzoic acids or benzoyl chlorides and 8-aminoquinoline. The deuterated amides were synthesized according to a literature method, spectral properties are consistent with literature values.[1] The *n*-nitropropane, *n*-nitrobutane, nitro-isopentane as well as a nitro-phenethane derivative were synthesized according to literature procedures.[2] The following amides were synthesized according to literature procedures.[3]



1a



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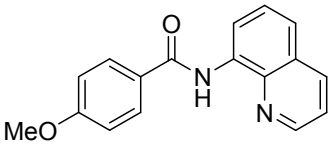

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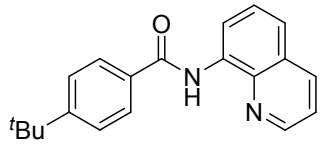

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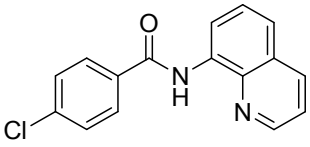

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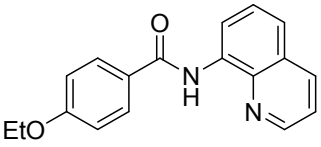

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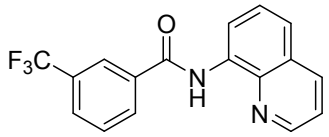

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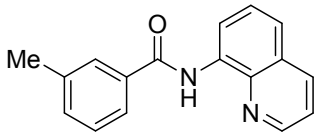

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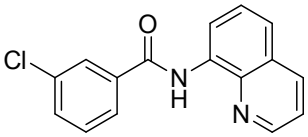

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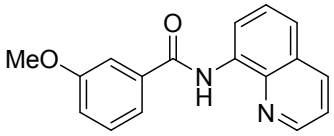

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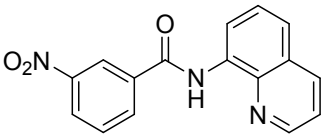

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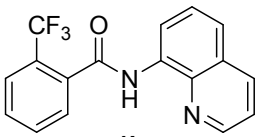

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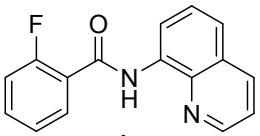

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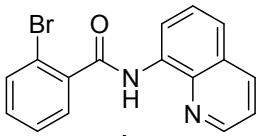

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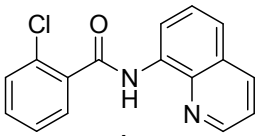

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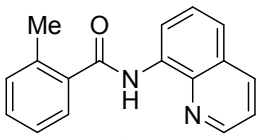

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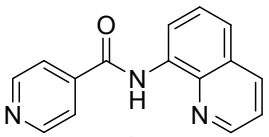

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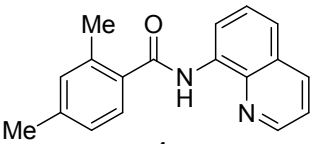

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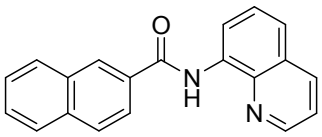
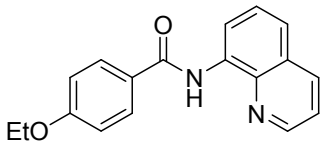


1s

General procedure for the synthesis of benzamide derivatives **1f**, **1r**.

Synthesis of **1f** is representative. 8-Aminoquinoline (1.44 g, 10 mmol) and triethyl - amine (1.7 mL, 12 mmol) were dissolved in anhydrous CH_2Cl_2 (20 mL) in a 100 ml round-bottom flask followed by dropwise addition of 4-ethylbenzoyl chloride (2.18 g, 13 mmol) through syringe. The reaction mixture was stirred overnight. After comple - tion, the reaction was diluted with CH_2Cl_2 (20 mL), washed by aqueous HCl (15 mL, 1N), $NaHCO_3$ (15 mL of saturated aqueous solution), brine (25 mL), and dried over Na_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in petroleum ether/ethyl acetate (8:1) afforded 2.35 g of pure amide (85%) as a white solid.

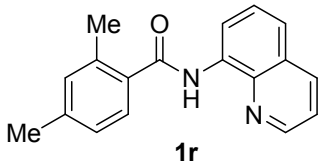
4-Ethyoxyl-N-(quinolin-8-yl)benzamide (1f)



1f

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.67 (s, 1H), 8.93 (d, J = 7.2 Hz, 1H), 8.84 (d, J = 4.0 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 8.4 Hz, 2H), 7.58 (t, J = 8.0, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.47 - 7.44(m, 1H), 7.02 (d, J = 8.4, 2H), 4.11 (q, J = 6.8, 13.6 Hz, 2H), 1.46 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 161.9, 148.2, 138.7, 136.3, 134.8, 129.1, 128.0, 127.5, 127.2, 121.6, 121.3, 116.3, 114.4, 63.7, 14.7.

2,4-dimethyl-N-(8-quinolinyl)benzamide (1r)



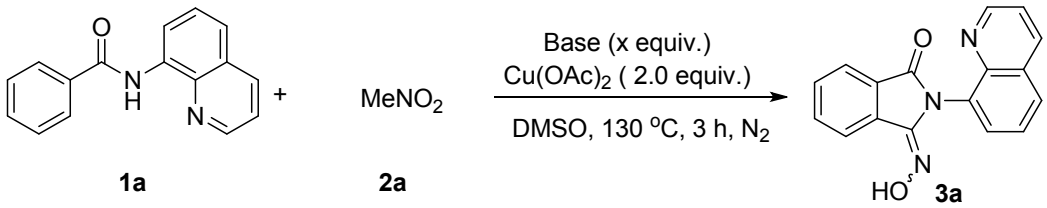
1r

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.95 (d, J = 7.6 Hz, 1H), 8.77 (d, J = 4.0 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.63 - 7.52 (m, 3H), 7.44 (m, 1H), 7.13 (br, 2H), 2.60(s, 3H), 2.39(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 148.2, 140.4, 138.6, 136.8, 136.3, 134.8, 133.7, 132.1, 127.9, 127.4, 126.6, 121.6, 116.3, 21.2, 20.2.

3. Cu(II)-mediated C-H Functionalization to Form Isoindolinones

3.1 Optimization of reaction conditions

Table S1. Screening of different Bases



1a 0.1 mmol

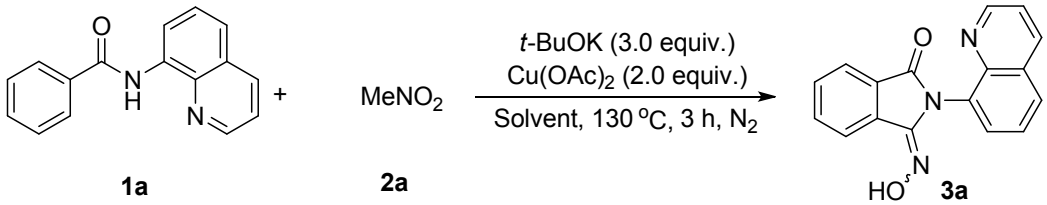
2a 0.5 mmol

Entry	Base (equiv.)	Yield of 3a(%)[a]
1	K_3PO_4 (2.0)	22
2	TMEDA (2.0)	trace
3	KOAc (2.0)	18
4	$NaHCO_3$ (2.0)	15
5	K_2CO_3(2.0)	38

6	KOH (2.0)	32
7	*t*-BuOK (2.0)	46
8	-	0
9	*t*-BuOK (1.0)	39
10	***t*-BuOK (3.0)**	**59**
11	*t*-BuOK (4.0)	46

[a] Isolated yield;

Table S2. Screening of Different Solvents



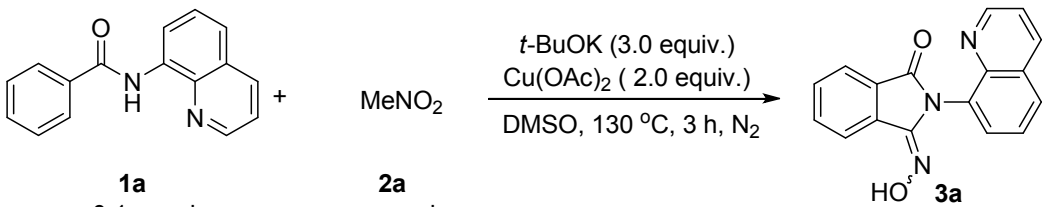
1a 0.1 mmol

2a 0.5 mmol

Entry	**Solvent (2mL)**	**Yield of 3a(%)[a]**
1	**DMSO**	**59**
2	DMF	48
3	DMAC	42
4	MeOH	0
5	DME	0
6	DCE	32
7	O-xylene	31
8	CH_3CN	18
9	dioxane	24
10	toluene	15

[a] Isolated yield;

Table S3. Screening of amount of nitromethane



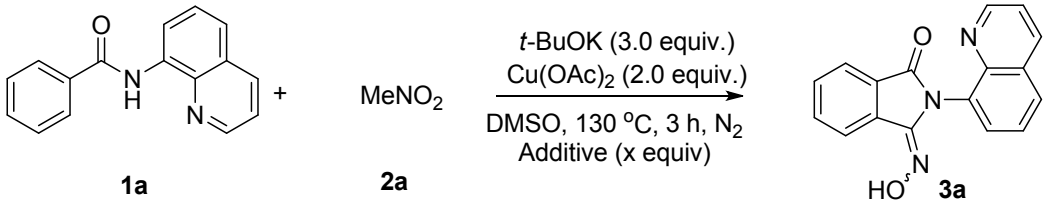
1a 0.1 mmol

2a x mmol

Entry	Nitromethane	Yield of 3a(%)[a]
1	—	0
2	2 equiv.	39
3	4 equiv.	48
4	**5 equiv.**	**59**
5	6 equiv.	58
6	8 equiv.	52
7	10 equiv.	59

[a] Isolated yield;

Table S4. Screening of Additive

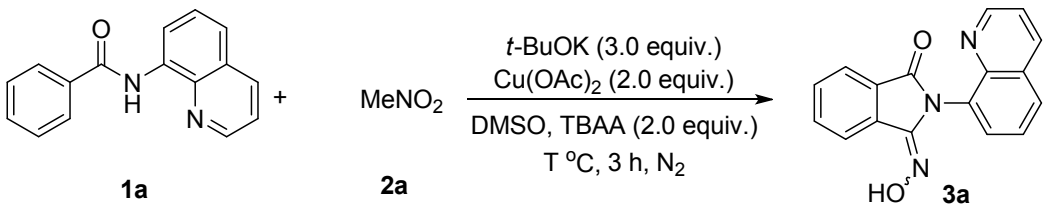


1a 0.1 mmol | **2a** 0.5 mmol | **3a**

Entry	Additive (equiv.)	Yield of 3a(%)[a]
1	0	59
2	TBAI (2.0)	69
3	TBAB (2.0)	61
4	**TBAA (2.0)**	**78**
5	$TBAPF_6$ (2.0)	trace
6	THAB (2.0)	56
7	TBAA (3.0)	76

[a] Isolated yield; TBAI = tetrabutylammonium iodide. TBAB = tetrabutylammonium bromide. TBAA = tetrabutylammonium acetate. $TBAPF_6$ = tetrabutylammonium hexafluorophosphate. THAB = tetraheptylammonium bromide.

Table S5. Screening of Temperation

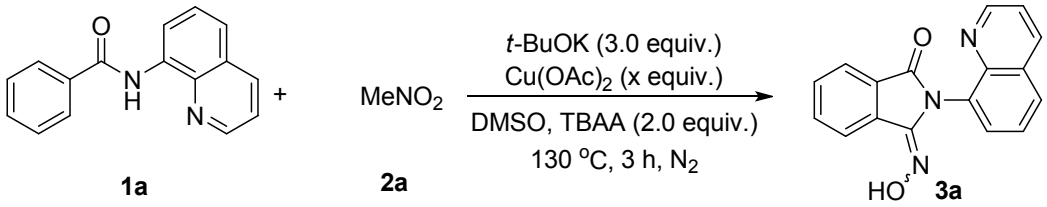


1a 0.1 mmol | **2a** 0.5 mmol | **3a**

Entry	Temp.(°C)	Yield of 3a(%)[a]
1	r.t.	0
2	60	22
3	90	62
4	120	72
5	**130**	**78**
6	140	69

[a] Isolated yield;

Table S6. Screening of Copper salts



1a 0.1 mmol

2a 0.5 mmol

Entry	Copper salts (equiv.)	Yield of 3a(%)[a]
1	**$Cu(OAc)_2$ (2.0)**	**78**
2	$CuBr_2$ (2.0)	61
3	$CuCl_2$ (2.0)	59
4	$Cu(OAc)_2 \cdot H_2O$ (2.0)	64
5	-	0
6	$Cu(OAc)_2$ (1.0)	49
7	$Cu(OAc)_2$ (3.0)	76

[a] Isolated yield;

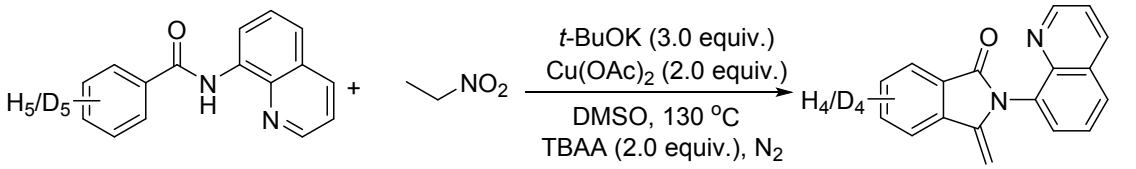
3.2 General procedure for copper-mediated C-H Functionalization to Form Isoindolinones

Benzamide **1** (0.1 mmol), anhydrous $Cu(OAc)_2$ (36 mg, 0.2 mmol), *t*-BuOK (34 mg, 0.3 mmol), nitromethane (31 mg, 0.5 mmol), tetrabutylammonium acetate (60 mg, 0.2 mmol) and anhydrous DMSO (2 mL) were added to a 25-mL Schlenk flask equipped with a high-vacuum PTFE valve-to-glass seal. Then the flask was sealed under N_2 and stirred at 130 °C for 3 h. After the reaction was quenched by addition of water, the mixture was extracted with ethyl acetate, and the combined organic layer was dried

over sodium sulfate. Concentration in vacuo followed by silica gel column purification with petroleum ether/ethyl acetate elutent gave the desired product **3**.

Benzamide **1** (0.1 mmol), anhydrous $Cu(OAc)_2$ (36 mg, 0.2 mmol), *t*-BuOK (34 mg, 0.3 mmol), niroethan (23 mg, 0.3 mmol), tetrabutylammonium acetate (60 mg, 0.2 mmol) and anhydrous DMSO (2 mL) were added to a 25-mL Schlenk flask equipped with a high-vacuum PTFE valve-to-glass seal. Then the flask was sealed under N_2 and stirred at 130 °C for 3 h. After the reaction was quenched by addition of water, the mixture was extracted with ethyl acetate, and the combined organic layer was dried over sodium sulfate. Concentration in vacuo followed by silica gel column purification with petroleum ether/ethyl acetate elutent gave the desired product **4**.

3.3 Deuterium-labeling experiments.



1a/1a-*d*$_5$ **2b** **4a/4a-*d*$_4$**

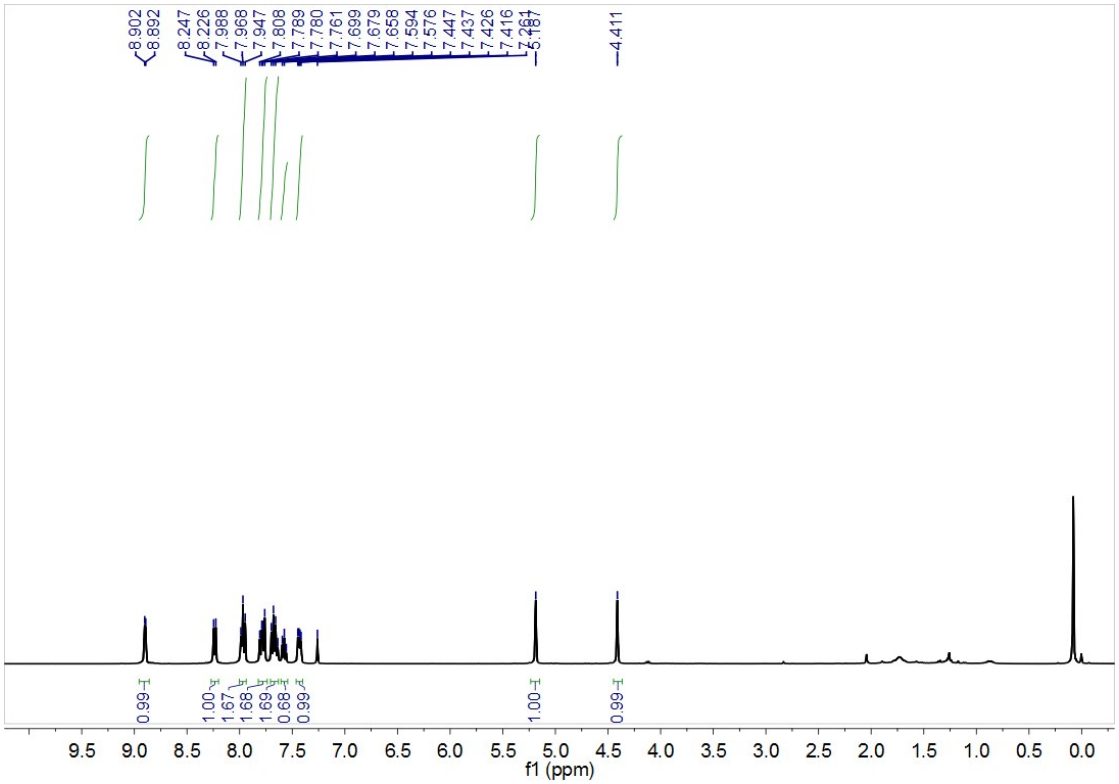
competitive K_H/K_D = 2.1
parallel K_H/K_D = 2.6

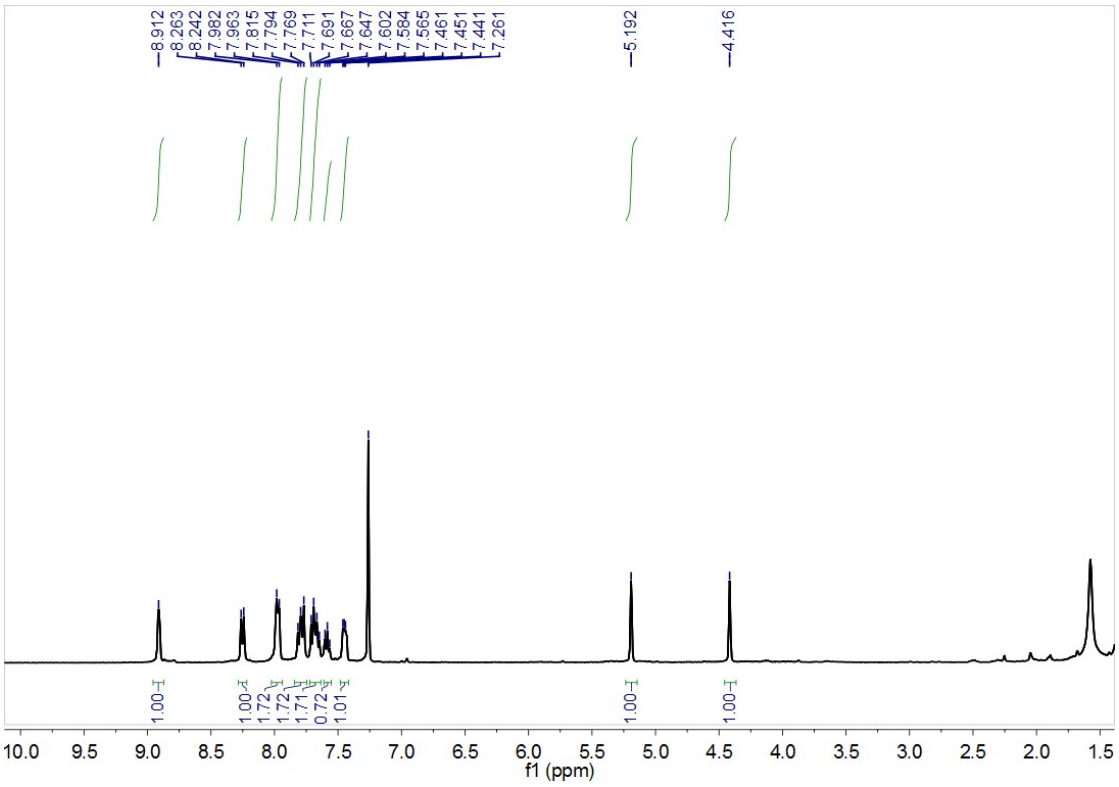
Intermolecular competition KIE Following general procedure: **1a** (50 mg, 0.2 mmol), **1a-*d*$_5$** (50 mg, 0.2 mmol), $Cu(OAc)_2$ (145 mg, 0.8 mmol), *t*-BuOK (135 mg, 1.2 mmol), nitroethane **4a** (150 mg, 2 mmol), tetrabutylammonium acetate (241 mg, 0.8 mmol) and anhydrous DMSO (4 mL) were added to a 75 mL Schlenk flask equipped with a high-vacuum PTFE valve-to-glass seal. Then the flask was sealed under N_2 and stirred at 130 °C for 10 min. The product was separated by column chromatography to give the desired product less than 8 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (d, J = 3.8 Hz, 1H), 8.24 (d, J = 8.2 Hz, 1H), 7.97 (t, J = 8.1 Hz, 1.67H), 7.81-7.76 (m, 1.68H), 7.70-7.63 (m, 1.69H), 7.58 (t, J = 7.4 Hz, 0.68H), 7.43 (dd, J = 8.2, 4.1 Hz, 1H), 5.19 (s, 1H), 4.41 (s, 1H). The KIE value was calculated as k_H/k_D = 2.13.

Intermolecular parallel KIE Following general procedure: **1a** (50 mg, 0.2 mmol) or **1a-*d*$_5$** (50 mg, 0.2 mmol), $Cu(OAc)_2$ (145 mg, 0.8 mmol), *t*-BuOK (135 mg, 1.2 mmol), nitroethane **4a** (150 mg, 2 mmol), tetrabutylammonium acetate (241 mg, 0.8 mmol) and anhydrous DMSO (4 mL) were added to a 75 mL Schlenk flask equipped with a high-vacuum PTFE valve-to-glass seal. Then the flask was sealed under N_2 and stirred at 130 °C for 8 min. The product was separated by column chromatography to give the desired product less than 4 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.91 (d, J = 1.9 Hz, 1H), 8.25 (d, J = 8.2 Hz, 1H), 7.97 (t, J = 7.9 Hz, 1.72H), 7.83-7.75 (m, 1.72H), 7.71-7.65 (m, 1.71H), 7.59 (t, J = 7.3 Hz, 0.72H), 7.45 (dd, J = 7.6, 3.6 Hz, 1H), 5.19 (s, 1H), 4.42 (s, 1H). The KIE value was calculated as k_H/k_D = 2.57.

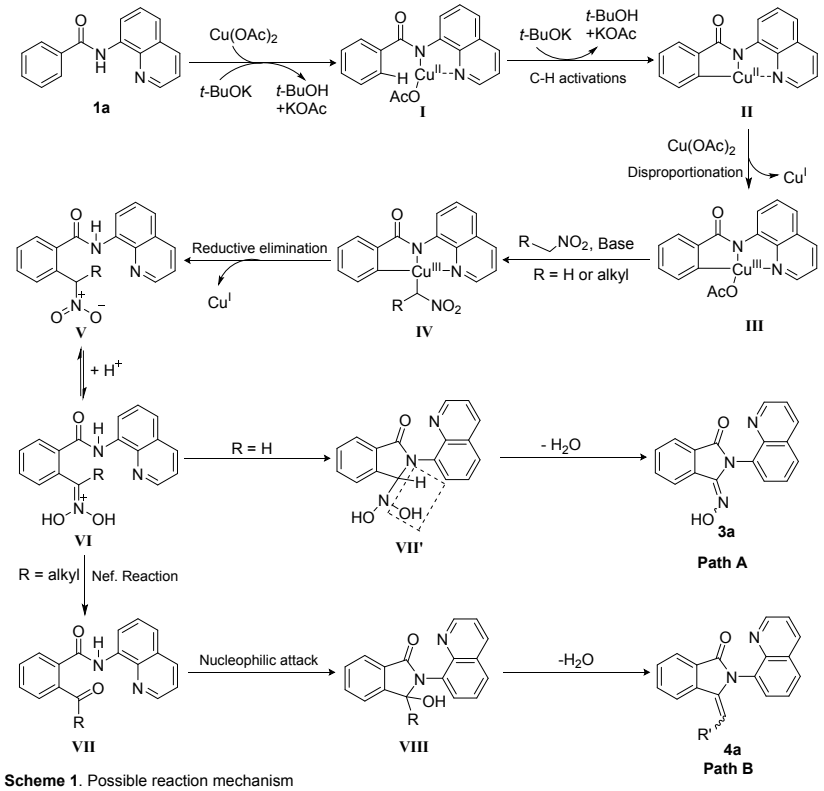




3.4 Possible reaction mechanism.

Though the exact mechanism is still not clear at present, based on the experimental evidences and literature precedents,[4] a plausible mechanism is proposed and depicted

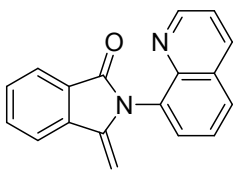
in Scheme 1. As reported before, **1a** first reacts with Cu(II) salt to generate intermediate **I** which subsequently undergoes C-H activation to form intermediate **II**. Intermediate **II** next reacts with Cu(II) salt through disproportion to form Cu(III) intermediate **III**. After reacting with a carboanion generated in situ from nitroalkane and base, **III** will be converted into **IV** which will provide intermediate **V** through reductive elimination. Next **V** is transformed into **VI** via proton shuffling. For the reaction with nitromethane, an intramolecular cyclization takes place to give intermediate **VII'** and the final product **3a** is obtained through dehydration (Path A). As for the reaction with nitroethane and other higher alkyl substituted nitroalkanes, **VI** undergoes a Nef type reaction to give the ketone intermediate **VII** which subsequently cyclizes intramolecularly to give **4a** (Path B).



Scheme 1. Possible reaction mechanism

4. Characterization data of products.

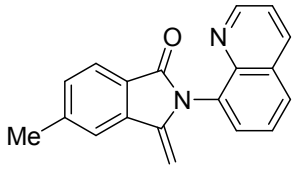
3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4a):



4a

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a white solid in 82 % yield, mp 183-184 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.89 (d, J = 3.6 Hz, 1H), 8.23 (d, J = 8.4 Hz, 1H), 7.97 (t, J = 8.6 Hz, 2H), 7.81-7.76 (m, 2H), 7.69-7.63 (m, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.43 (dd, J = 8.4, 4.0 Hz, 1H), 5.19 (s, 1H), 4.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 167.4, 151.1, 144.7, 144.0, 136.7, 136.2, 132.5, 132.1, 130.9, 129.5, 129.5, 129.4, 129.3, 126.2, 123.6, 121.8, 120.2, 90.2; IR (neat, cm^{-1}) ν 2922, 1717, 1645, 1469, 1396, 887, 824, 696, 623, 467; HRMS (ESI, m/z): calcd for $C_{18}H_{12}N_2O$ $[M+H]^+$: 273.1028; Found: 273.1021.

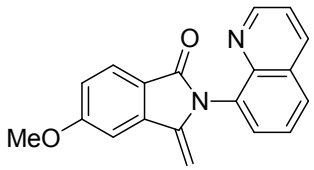
5-methyl-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4b):



4b

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 77 % yield, mp 185-186 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.89 (d, J = 3.6 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 7.6 Hz, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.67 (t, J = 7.8 Hz, 1H), 7.59 (s, 1H), 7.43-7.37 (m, 2H), 5.14 (s, 1H), 4.36 (s, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 151.1, 144.8, 144.1, 142.8, 137.1, 136.2, 132.7, 130.9, 130.6, 129.5, 129.2, 127.0, 126.2, 123.5, 121.7, 120.6, 89.7, 22.0; IR (neat, cm^{-1}) ν 2929, 1703, 1487, 1193, 1081, 892, 671; HRMS (ESI, m/z): calcd for $C_{19}H_{14}N_2O$ $[M+H]^+$: 287.1184; Found: 287.1180.

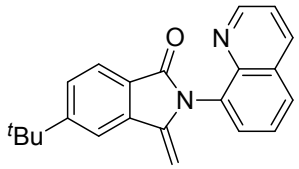
5-methoxy-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4c):



4c

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =2/3) as a yellow solid in 83 % yield, mp 179-180 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (s, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 6.8 Hz, 1H), 7.66 (t, J = 7.8 Hz, 1H), 7.42 (dd, J = 8.4, 4.0 Hz, 1H), 7.24 (d, J = 1.2 Hz, 1H), 7.09 (dd, J = 8.4, 1.2 Hz, 1H), 5.13 (s, 1H), 4.37 (s, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 163.4, 151.0, 144.8, 144.0, 138.9, 136.2, 132.7, 130.9, 129.5, 129.2, 126.2, 125.1, 122.3, 121.7, 116.6, 104.5, 89.8, 55.7; IR (neat, cm^{-1}) ν 3010, 1705, 1490, 1287, 1237, 1174, 1024, 906; HRMS (ESI, m/z): calcd for $C_{19}H_{14}N_2O_2$ $[M+H]^+$: 303.1134; Found: 303.1127.

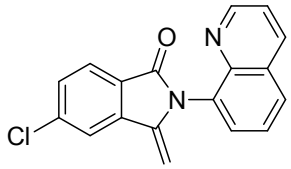
5-(tert-butyl)-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4d):



4d

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a white solid in 75 % yield, mp 215-216 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.89 (d, J = 3.6 Hz, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.92 (t, J = 9.2 Hz, 2H), 7.81 (s, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.68–7.62 (m, 2H), 7.41 (dd, J = 8.0, 4.0 Hz, 1H), 5.20 (s, 1H), 4.38 (s, 1H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 156.0, 150.8, 144.8, 144.4, 136.7, 136.1, 132.7, 130.9, 129.4, 129.2, 127.1, 127.0, 126.2, 123.3, 121.7, 117.0, 89.5, 35.4, 31.3; IR (neat, cm^{-1}) ν 2958, 2309, 1780, 1484, 1197, 1066, 911, 679; HRMS (ESI, m/z): calcd for $C_{22}H_{20}N_2O$ $[M+H]^+$: 329.1654; Found: 329.1647.

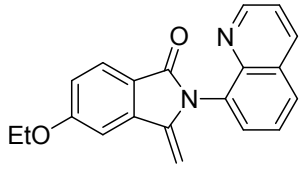
5-chloro-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4e):



4e

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 71 % yield, mp 248-249 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.89 (d, J = 2.8 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 6.4 Hz, 2H), 7.68 (t, J = 7.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.45 (dd, J = 8.2, 4.2 Hz, 1H), 5.18 (s, 1H), 4.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 151.2, 144.6, 143.0, 138.6, 138.2, 136.3, 132.2, 130.8, 130.0, 129.5, 127.8, 126.2, 125.0, 121.9, 120.7, 91.4; IR (neat, cm^{-1}) ν 3012, 1717, 1485, 1182, 1137, 1078, 882, 634, 580; HRMS (ESI, m/z): calcd for $C_{18}H_{11}ClN_2O$ $[M+H]^+$: 307.0638; Found: 307.0633.

5-ethyoxyl-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4f):

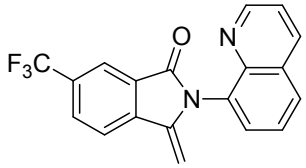


4f

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =2/3) as a white solid in 81 % yield,

mp 203-204 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, J = 3.2 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 7.2 Hz, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.40 (dd, J = 8.0, 4.0 Hz, 1H), 7.23 (s, 1H), 7.07 (d, J = 8.4 Hz, 1H), 5.11 (s, 1H), 4.35 (s, 1H), 4.14 (q, J = 13.6, 6.8 Hz, 2H), 1.47 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 162.7, 151.0, 144.8, 144.0, 138.8, 136.2, 132.7, 130.9, 129.4, 129.1, 126.2, 125.1, 122.0, 121.7, 116.9, 105.0, 89.7, 64.0, 14.6; IR (neat, cm^{-1}) ν 2922, 1715, 1649, 1482, 1294, 1183, 884, 629; HRMS (ESI, m/z): calcd for $C_{20}H_{16}N_2O_2$ $[M+H]^+$: 317.1290; Found: 317.1287.

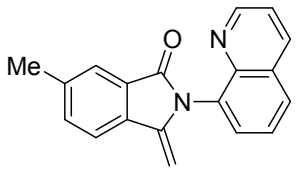
6-trifluoromethyl-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4g):



4g

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/3) as a white solid in 59 % yield, mp 210-211 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.88 (d, J = 2.0 Hz, 1H), 8.24-8.25 (m, 2H), 7.98 (d, J = 8.0 Hz, 1H), 7.90 (s, 2H), 7.78 (d, J =7.2, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.45 (dd, J = 8.4, 4.0 Hz, 1H), 5.30 (s, 1H), 4.53 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 151.2, 144.4, 143.0, 139.5, 136.4, 131.9, 131.9 (q, $J_{C\text{-}F}$ = 32.8 Hz), 131.9, 130.8, 129.9, 129.6, 129.5, 129.0 (q, $J_{C\text{-}F}$ = 3.5 Hz), 126.3, 123.7 (q, $J_{C\text{-}F}$ = 271 Hz),122.0, 121.1 (q, $J_{C\text{-}F}$ = 3.9 Hz), 120.9, 92.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.3; IR (neat, cm^{-1}) ν 2932, 1717, 1645, 1500, 1400, 1326, 1270, 1174, 1128, 841, 797; HRMS (ESI, m/z): calcd for $C_{19}H_{11}F_3N_2O$ $[M+H]^+$: 341.0902; Found: 341.0893.

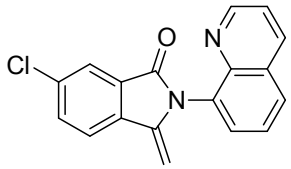
6-methyl-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4h):



4h

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a white solid in 72 % yield, mp 145-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (d, J = 2.0 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.69–7.67 (m, 2H), 7.47 - 7.42 (m, 2H), 5.12 (s, 1H), 4.36 (s, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 151.1, 144.8, 144.1, 140.0, 136.3, 134.3, 133.1, 132.7, 130.9, 129.7, 129.5, 129.2, 126.3, 123.9 121.8, 120.1, 89.5, 21.6; IR (neat, cm^{-1}) ν 2973, 1714, 1644, 1487, 1260, 1182, 1136, 1076, 916, 631; HRMS (ESI, m/z): calcd for $C_{19}H_{14}N_2O$ $[M+H]^+$: 287.1184; Found: 287.1179.

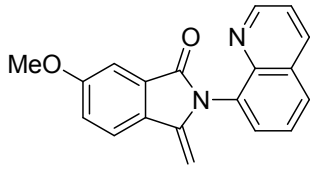
6-chloro-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4i)



4i

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 70 % yield, mp 173-174 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (d, J = 3.6 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.99 – 7.95 (m, 2H), 7.78 -7.69 (m, 3H), 7.62 (d, J = 8.0 Hz, 1H), 7.45 (dd, J = 8.2, 4.0 Hz, 1H), 5.18 (s, 1H), 4.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 151.2, 144.6, 143.2, 136.4, 135.8, 134.9, 132.3, 132.2, 131.0, 130.8, 129.5, 126.3, 123.8, 121.9, 121.6, 91.2; IR (neat, cm^{-1}) ν 3075, 1715, 1640, 1572, 1475, 1397, 1336, 1181, 1137; HRMS (ESI, m/z): calcd for $C_{18}H_{11}ClN_2O$ $[M+H]^+$: 307.0638; Found: 307.0631.

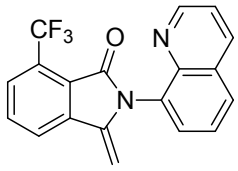
6-methoxy-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4j):



4j

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a white solid in 68 % yield, mp 210-211 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.91 (d, J = 4.0 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 7.2 Hz, 1H), 7.70 – 7.66 (m, 2H), 7.45 - 7.42 (m, 2H), 7.21 (d, J = 8.4, 1H), 5.06 (s, 1H), 4.33 (s, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 161.3, 151.2, 144.8, 143.9, 136.3, 132.7, 131.1, 130.9, 129.6, 129.5, 129.3, 126.2, 121.8, 121.6, 120.7, 106.1, 89.1, 55.8; IR (neat, cm^{-1}) ν 3089, 1713, 1492, 1285, 1186, 1130, 1072, 923, 736; HRMS (ESI, m/z): calcd for $C_{19}H_{14}N_2O_2$ $[M+H]^+$: 303.1134; Found: 303.1125.

3-methylene-2-(quinolin-8-yl)-7-(trifluoromethyl)isoindolin-1-one (4k):

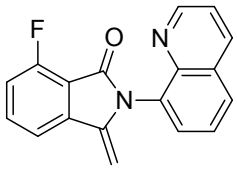


4k

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a white solid in 53 % yield, mp 185-186 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.89 (d, J = 3.9 Hz, 1H), 8.24 (d, J =

8.3 Hz, 1H), 7.99 (dd, J = 14.1, 8.0 Hz, 2H), 7.86 (d, J = 7.6 Hz, 1H), 7.77 (dd, J = 11.3, 7.7 Hz, 2H), 7.68 (t, J = 7.8 Hz, 1H), 7.44 (dd, J = 8.1, 4.0 Hz, 1H), 5.25 (s, 1H), 4.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 151.2, 149.6, 144.6, 142.7, 138.6, 136.3, 132.1, 131.8, 131.0, 129.5, 129.5, 127.0 (q, $J_{C\text{-}F}$ = 24.9 Hz), 126.9, 123.9, 121.9, 91.4; ^{19}F NMR (377 MHz, $CDCl_3$) δ -60.3; IR (neat, cm^{-1}) ν 3075, 1719, 1494, 1388, 1325, 1185, 1136, 1069, 921, 689; HRMS (ESI, m/z): calcd for $C_{19}H_{11}F_3N_2O$ $[M+H]^+$: 341.0902; Found: 341.0899.

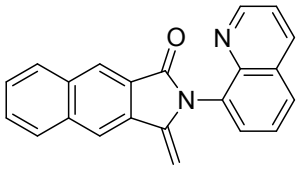
7-fluoro-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4l):



4l

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a white solid in 59 % yield, mp 193-194 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.89 (s, 1H), 8.24 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.69 - 7.57 (m, 3H), 7.44 (dd, J = 7.6, 3.6 Hz, 1H), 7.20 (t, J = 8.2 Hz, 1H), 5.21 (s, 1H), 4.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2 (d, $J_{C\text{-}F}$ = 1.9 Hz), 158.8 (d, $J_{C\text{-}F}$ = 259 Hz), 151.2, 144.6, 143.2 (d, $J_{C\text{-}F}$ = 1.8 Hz), 139.2 (d, $J_{C\text{-}F}$ = 3.2 Hz), 136.3, 134.1, 134.0, 132.1, 130.9, 129.5, 126.2, 121.8, 116.8 (d, $J_{C\text{-}F}$ = 19.3 Hz), 116.5 (d, $J_{C\text{-}F}$ = 13.4 Hz), 116.30 (d, $J_{C\text{-}F}$ = 4.1 Hz), 91.4; ^{19}F NMR (377 MHz, $CDCl_3$) δ -116.8; IR (neat, cm^{-1}) ν 3075, 1718, 1487, 1256, 1186, 1137, 1081, 928, 807, 722, 632; HRMS (ESI, m/z): calcd for $C_{18}H_{11}FN_2O$ $[M+H]^+$: 291.0934; Found: 291.0931.

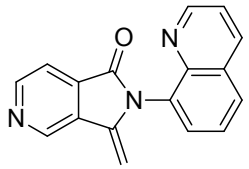
3-methylene-2-(quinolin-8-yl)-2,3-dihydro-1H-benzo[f]isoindol-1-one (4m):



4m

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a white solid in 82 % yield, mp 201-202 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (br, 1H), 8.51 (s, 1H), 8.23 (d, J = 7.2 Hz, 2H), 8.06 (d, J = 8.0 Hz, 1H), 8.00 – 7.95 (m, 2H), 7.82 (d, J = 7.2 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.64 – 7.56 (m, 2H), 7.43 (dd, J = 8.0, 4.0 Hz, 1H), 5.27 (s, 1H), 4.38 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 151.1, 144.6, 144.0, 136.2, 135.4, 133.7, 132.8, 132.5, 130.8, 129.8, 129.5, 129.4, 128.7, 127.9, 127.3, 126.8, 126.2, 124.3, 121.8, 119.5, 88.5; IR (neat, cm^{-1}) ν 3108, 1715, 1485, 1192, 1134, 1072, 912, 839, 684; HRMS (ESI, m/z): calcd for $C_{22}H_{14}N_2O$ $[M+H]^+$: 323.1184; Found: 323.1181.

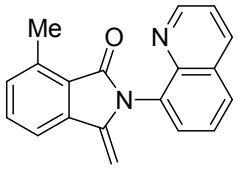
3-methylene-2-(quinolin-8-yl)-2,3-dihydro-1H-pyrrolo[3,4-c]pyridin-1-one (4n):



4n

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 48 % yield, mp 198-199 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 8.89 (s, 2H), 8.26 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 3.6 Hz, 1H), 7.78-7.68 (m, 2H), 7.46 (dd, J = 8.4, 4.0 Hz, 1H), 5.34 (s, 1H), 4.57 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 151.3, 151.0, 150.3, 143.0, 142.0, 136.3, 136.2, 131.8, 130.7, 130.1, 130.0, 129.8, 126.3, 122.1, 122.0, 92.9; IR (neat, cm^{-1}) ν 3065, 1718, 1526, 1487, 1186, 1132, 1072, 933, 836, 685; HRMS (ESI, m/z): calcd for $C_{17}H_{11}N_3O$ $[M+H]^+$: 274.0980; Found: 274.0977.

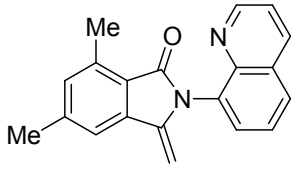
7-methyl-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4p):



4p

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 45 % yield, mp 191-192 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.92 (d, J = 1.2 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 7.96(d, J = 8.0 Hz, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.68 (t, J = 7.7 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.44 (dd, J = 8.0, 4.0 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 5.14 (s 1H), 4.35 (s, 1H), 2.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 151.2, 144.9, 143.9, 137.8, 137.2, 136.2, 132.7, 131.7, 131.6, 131.0, 129.5, 129.2, 126.6, 126.2, 121.7, 117.7, 89.3, 17.5; IR (neat, cm^{-1}) ν 3009, 1713, 1652, 1490, 1399, 1331, 1282, 1181, 1133, 1070; HRMS (ESI, m/z): calcd for $C_{19}H_{14}N_2O$ $[M+H]^+$: 287.1184; Found: 287.1179.

5,7-dimethyl-3-methylene-2-(quinolin-8-yl)isoindolin-1-one (4q):

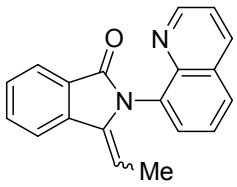


4q

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a white solid in 42 % yield,

mp 174-175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, J = 3.6 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 7.2 Hz, 1H), 7.66 (t, J = 7.8 Hz, 1H), 7.43 - 7.40 (m, 2H), 7.13 (s, 1H), 5.09 (s, 1H), 4.30 (s, 1H), 2.72 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 151.1, 145.0, 144.0, 142.3, 137.6, 137.5, 136.2, 132.9, 132.6, 131.0, 129.4, 129.1, 126.2, 124.3, 121.7, 118.2, 88.8, 21.8, 17.3; IR (neat, cm^{-1}) ν 2953, 1713, 1487, 1186, 1130, 1069, 911, 753; HRMS (ESI, m/z): calcd for $C_{20}H_{16}N_2O$ $[M+H]^+$: 301.1341; Found: 301.1342.

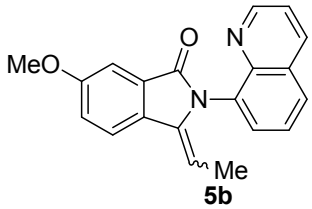
3-ethylidene-2-(quinolin-8-yl)isoindolin-1-one (5a)



5a

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 72 % yield; Approx. 1.2:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, $CDCl_3$): *Z* isomer: δ 8.92 (d, J = 4.1 Hz, 1H), 8.23 (d, J = 8.3 Hz, 1H), 7.94 (t, J = 7.2 Hz, 2H), 7.81 (d, J = 7.2 Hz, 1H), 7.71 (d, J = 7.7 Hz, 1H), 7.66 (t, J = 7.8 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.4 Hz, 1H), 7.44 (dd, J = 8.3, 4.1 Hz, 1H), 5.73 (q, J = 7.7 Hz, 1H), 1.04 (d, J = 7.7 Hz, 3H); *E* isomer: δ 8.90 (d, J = 3.7 Hz, 1H), 8.23 (d, J = 8.3 Hz, 1H), 8.02 (d, J = 7.5 Hz, 1H), 7.97-7.94 (m, 2H), 7.73 (d, J = 7.0 Hz, 1H), 7.66 (t, J = 7.8 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.42 (dd, J = 8.2, 4.1 Hz, 1H), 5.05 (q, J = 7.6 Hz, 1H), 2.11 (d, J = 7.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *Z* isomer: δ 168.3, 151.2, 145.5, 138.3, 136.2, 136.2, 135.2, 131.9, 130.7, 129.1, 128.3, 128.1, 126.2, 126.0, 123.6, 121.7, 119.1, 103.3, 11.4; *E* isomer: δ 166.7, 151.2, 145.0, 138.4, 136.3, 136.0, 132.9, 131.9, 131.4, 130.5, 129.5, 129.2, 128.6, 126.3, 123.9, 123.5, 121.7, 107.6, 12.9; IR (neat, cm^{-1}) *E* isomer: ν 3075, 1717, 1490, 1127, 1064, 928, 672. *Z* isomer: ν 3071, 1713, 1490, 1126, 1133, 1072, 932, 678; HRMS (ESI, m/z): calcd for $C_{19}H_{14}N_2O$ $[M+H]^+$: 287.1184; Found: 287.1181.

3-ethylidene-6-methoxy-2-(quinolin-8-yl)isoindolin-1-one (5b)

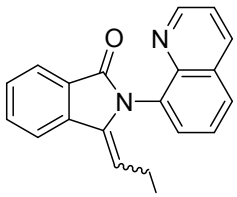


5b

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 75 % yield; Approx. 1:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, $CDCl_3$): *Z* isomer: δ 8.92 (d, J = 3.8 Hz, 1H), 8.23 (d, J = 8.2 Hz, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.80 (d, J = 7.2 Hz, 1H), 7.66 (t, J = 7.7 Hz, 1H), 7.59 (d, J = 8.5 Hz, 1H), 7.43 (dd, J = 8.2, 4.0

Hz, 1H), 7.39 (s, 1H), 7.17 (d, *J* = 8.5 Hz, 1H), 5.59 (q, *J* = 7.6 Hz, 1H), 3.89 (s, 3H), 1.01 (d, *J* = 7.7 Hz, 3H); *E* isomer: *δ* 8.90 (d, *J* = 4.0 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.6 Hz, 1H), 7.72 (d, *J* = 7.2 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.50 (s, 1H), 7.42 (dd, *J* = 8.1, 4.1 Hz, 1H), 7.21 (d, *J* = 8.5 Hz, 1H), 4.94 (q, *J* = 7.6 Hz, 1H), 3.92 (s, 3H), 2.07 (d, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *Z* isomer: *δ* 168.3, 160.4, 151.2, 145.5, 136.2, 136.0, 135.3, 131.4, 130.7, 129.5, 129.1, 129.1, 126.2, 121.7, 120.8, 120.4, 105.6, 102.0, 55.8, 11.4; *E* isomer: *δ* 166.7, 160.3, 151.2, 145.0, 138.1, 136.3, 133.0, 132.1, 131.3, 129.5, 129.2, 129.0, 126.2, 124.6, 121.7, 120.2, 106.5, 105.9, 55.7, 12.8; IR (neat, cm^{-1}) *E* isomer: ν 3007, 1715, 1487, 1280, 1186, 1133, 1072, 911, 678. *Z* isomer: ν 3104, 1708, 1487, 1356, 1278, 1183, 1130, 1074, 921, 678; HRMS (ESI, m/z): calcd for $C_{20}H_{16}N_2O_2$ $[M+H]^+$: 317.1290; Found: 317.1285.

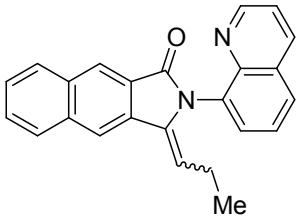
3-propylidene-2-(quinolin-8-yl)isoindolin-1-one (5c)



5c

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 61 % yield; Approx. 1.1:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, $CDCl_3$): *Z* isomer: *δ* 8.91 (d, *J* = 4.0 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 7.94 (t, *J* = 7.4 Hz, 2H), 7.80 (d, *J* = 7.3 Hz, 1H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.68 – 7.59 (m, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.43 (dd, *J* = 8.2, 4.1 Hz, 1H), 5.60 (t, *J* = 7.6 Hz, 1H), 1.45 (m, 1H), 1.21 (m, 7.7 Hz, 1H), 0.63 (t, *J* = 7.5 Hz, 3H); *E* isomer: *δ* 8.90 (d, *J* = 3.2 Hz, 1H), 8.24 (d, *J* = 8.3 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.94 (dd, *J* = 13.4, 7.9 Hz, 2H), 7.74-7.64 (m, 3H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.43 (dd, *J* = 8.2, 4.1 Hz, 1H), 4.96 (t, *J* = 7.6 Hz, 1H), 2.69-2.54 (m, 7.7 Hz, 2H), 1.05 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *Z* isomer: *δ* 168.3, 151.2, 145.4, 138.5, 136.2, 135.3, 134.9, 131.9, 130.6, 129.1, 128.3, 128.2, 126.2, 123.6, 121.8, 119.2, 111.0, 19.1, 14.2; *E* isomer: *δ* 166.8, 151.2, 145.0, 137.2, 136.3, 135.9, 132.9, 131.9, 131.4, 130.5, 129.5, 129.2, 128.6, 126.3, 123.9, 123.5, 121.7, 115.4, 20.7, 14.3; IR (neat, cm^{-1}) *E* isomer: ν 3057, 1719, 1483, 1188, 1130, 1070, 918, 676. *Z* isomer: ν 3002, 1718, 1485, 1186, 1130, 1069, 921, 678; HRMS (ESI, m/z): calcd for $C_{20}H_{16}N_2O$ $[M+ H]^+$: 301.1341; Found: 301.1337.

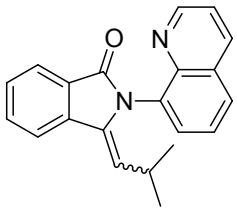
3-propylidene-2-(quinolin-8-yl)-2,3-dihydro-1H-benzo[f]isoindol-1-one (5d)



5d

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 53 % yield; Approx. 1.5:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, $CDCl_3$): *Z* isomer: δ 8.90 (s, 1H), 8.48 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 8.18 (s, 1H), 8.05-8.97 (m, 3H), 7.85 (d, *J* = 7.0 Hz, 1H), 7.68 (t, *J*=7.8 Hz 1H), 7.62-7.53 (m, 2H), 7.44 (dd, *J* = 7.5, 3.3 Hz, 1H), 5.71 (t, *J* = 7.5 Hz, 1H), 1.52 – 1.43 (m, 1H), 1.21-1.09 (m, 1H), 0.65 (t, *J* = 7.4 Hz, 3H); *E* isomer: δ 8.90 (s, 1H), 8.54 (s, 1H), 8.34 (s, 1H), 8.25 (d, *J* = 8.1 Hz, 1H), 8.07 – 7.97 (m, 3H), 7.79 (d, *J* = 7.2 Hz, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.45 – 7.43 (m, 1H), 4.94 (t, *J* = 7.3 Hz, 1H), 2.82 – 2.67 (m, 2H), 1.11 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *Z* isomer: δ 168.3, 151.2, 136.2, 135.6, 134.7, 133.2, 130.5, 129.8, 129.2, 128.5, 127.7, 126.3, 126.2, 124.2, 121.8, 118.0, 109.2,19.1, 14.3; *E* isomer: δ 166.8, 151.2, 137.1, 136.3, 135.5, 133.0, 132.0, 131.3, 129.6, 129.3, 129.0, 127.8, 126.8, 126.3, 124.3, 123.1, 121.8, 113.8, 20.9, 14.4; IR (neat, cm^{-1}) *E* isomer: ν 3090, 1752, 1487, 1186, 1130, 1069, 919, 673. *Z* isomer: ν 3002, 1718, 1490, 1189, 1130, 1074, 914, 676; HRMS (ESI, m/z): calcd for $C_{24}H_{18}N_2O$ $[M+H]^+$: 351.1497; Found: 351.1495.

3-(2-methylpropylidene)-2-(quinolin-8-yl)isoindolin-1-one (5e)

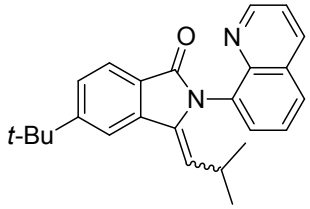


5e

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 46 % yield; Approx. 1.3:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, $CDCl_3$): *Z* isomer: δ 8.90 (d, *J* = 3.6 Hz, 1H), 8.23 (d, *J* = 8.3 Hz, 1H), 7.95 (t, *J* = 9.0 Hz, 2H), 7.81 (d, *J* = 7.2 Hz, 1H), 7.74 (d, *J*= 7.6 Hz, 1H) 7.68 – 7.60 (m, 2H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.43 (d, *J* = 10.7 Hz, 1H), 1.63 – 1.57 (m, 1H), 0.74 (d, *J* = 6.5 Hz, 3H), 0.38 (d, *J* = 6.5 Hz, 3H); *E* isomer: δ 8.89 (d, *J* = 3.4 Hz, 1H), 8.24 (d, *J* = 8.2 Hz, 1H), 8.02 (d, *J* = 7.5 Hz, 1H), 7.97-7.94 (m, 2H), 7.69 (dt, *J* = 17.5, 7.4 Hz, 3H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.43 (dd, *J* = 8.2, 4.1 Hz, 1H), 4.82 (d, *J* = 9.6 Hz, 1H), 3.37-3.29 (m, 1H), 1.09 (d, *J* = 6.6 Hz, 3H), 1.00 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *Z* isomer: δ 168.4, 151.2, 145.4, 138.7, 136.2, 135.5, 134.2, 133.6, 131.8, 130.5, 129.2, 128.3, 126.2, 123.6, 121.8, 119.2, 116.6, 25.1, 23.2, 22.8; *E*

isomer: δ 166.7, 151.0, 145.0, 136.2, 136.0, 135.8, 132.0, 131.3, 130.6, 129.5, 129.2, 128.6, 126.3, 124.0, 123.4, 121.7, 121.3, 26.6, 23.3, 23.2; IR (neat, cm^{-1}) *E* isomer: ν 3084, 1708, 1482, 1186, 1133, 1069, 916, 676. *Z* isomer: ν 3060, 1710, 1482, 1186, 1135, 1069, 916, 678; HRMS (ESI, m/z): calcd for $C_{21}H_{18}N_2O$ $[M+H]^+$: 315.1497; Found: 315.1495.

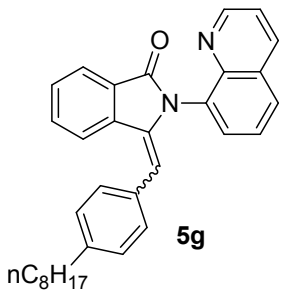
5-(tert-butyl)-3-(2-methylpropylidene)-2-(quinolin-8-yl)isoindolin-1-one (5f)



5f

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 49 % yield; Approx. 1.3:1 mixture of E and Z isomers; ^1H NMR (400 MHz, $CDCl_3$): *Z* isomer: δ 8.90 (d, J = 4.0 Hz, 1H), 8.23 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.86 (d, J = 8.1 Hz, 1H), 7.79 (d, J = 7.2 Hz, 1H), 7.74 (s, 1H), 7.66 (t, J = 7.7 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.42 (dd, J = 8.2, 4.1 Hz, 1H), 5.44 (d, J = 10.6 Hz, 1H), 1.62 – 1.55 (m, 1H), 1.43 (s, 9H), 0.75 (d, J = 6.5 Hz, 3H), 0.39 (d, J = 6.5 Hz, 3H); *E* isomer: δ 8.89 (d, J = 3.6 Hz, 1H), 8.23 (d, J = 8.3 Hz, 1H), 8.00 – 7.93 (m, 3H), 7.72 – 7.66 (m, 2H), 7.60 (d, J = 8.0 Hz, 1H), 7.42 (dd, J = 8.2, 4.1 Hz, 1H), 4.78 (d, J = 9.4 Hz, 1H), 3.37-3.28 (m, 1H), 1.43 (s, 9H), 1.11 (d, J = 6.6 Hz, 3H), 1.02 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *Z* isomer: δ 168.4, 155.7, 151.2, 145.5, 138.6, 136.2, 135.6, 133.9, 130.5, 129.2, 129.2, 126.3, 126.1, 125.8, 123.3, 121.8, 115.8, 115.8, 35.5, 31.4, 25.1, 23.2, 22.8; *E* isomer: δ 166.8, 155.7, 151.0, 145.1, 136.5, 136.2, 135.9, 133.1, 131.4, 129.5, 129.1, 128.2, 126.3, 126.2, 123.6, 121.7, 120.7, 120.3, 35.4, 31.4, 26.8, 23.2, 23.2; IR (neat, cm^{-1}) *E* isomer: ν 3067, 1707, 1483, 1188, 1135, 1068, 918, 674. *Z* isomer: ν 3065, 1709, 1485, 1185, 1134, 1064, 921, 677; HRMS (ESI, m/z): calcd for $C_{25}H_{26}N_2O$ $[M+H]^+$: 371.2123; Found: 371.2119.

3-(4-octylbenzylidene)-2-(quinolin-8-yl)isoindolin-1-one (5g)

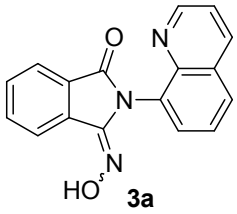


5g

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 42 % yield; Approx. 1:1 mixture of E and Z isomers; ^1H NMR (400 MHz, $CDCl_3$): *Z* isomer: δ 8.84 (d, J = 4.0 Hz, 1H), 7.97 (dd, J = 14.1, 7.9 Hz, 2H), 7.88 (d, J = 7.7 Hz, 1H),

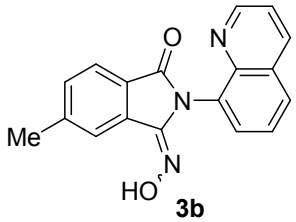
7.70-7.67 (m, 1H), 7.56 (d, J = 7.9 Hz, 2H), 7.48 (d, J = 7.3 Hz, 1H), 7.31 (dd, J = 7.9, 3.6 Hz, 2H), 6.80 (s, 1H), 6.45 (d, J = 7.6 Hz, 2H), 6.33 (d, J = 7.6 Hz, 2H), 2.25 (t, J = 7.5 Hz, 2H), 1.36-1.26 (m, 12H), 0.93-0.90 (m, 3H); *E* isomer: δ 8.93 (d, J = 3.5 Hz, 1H), 8.25 (d, J = 8.1 Hz, 1H), 8.00 – 7.97 (m, 2H), 7.85 (d, J = 7.2 Hz, 1H), 7.71 (t, J = 7.7 Hz, 1H), 7.59 (d, J = 7.8 Hz, 1H), 7.50 (t, J = 7.4 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.29 (d, J = 7.7 Hz, 2H), 7.16 (d, J = 7.7 Hz, 2H), 6.00 (s, 1H), 2.62 (t, J = 7.7 Hz, 2H), 1.31-1.27 (m, 12H), 0.89-0.86 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *Z* isomer: δ 168.1, 150.3, 144.5, 140.8, 138.7, 135.8, 135.7, 132.1, 130.1, 128.9, 128.1, 128.0, 126.3, 125.6, 123.9, 121.1, 119.6, 107.6, 35.3, 31.9, 31.3, 29.5, 29.3, 29.1, 22.7, 14.1; *E* isomer: δ 167.0, 151.2, 145.0, 142.6, 138.5, 136.2, 135.6, 133.0, 132.4, 131.7, 131.4, 130.4, 129.6, 129.4, 129.3, 129.2, 128.5, 126.3, 123.7, 123.3, 121.8, 112.4, 35.7, 31.8, 31.3, 29.4, 29.3, 29.2, 22.6, 14.1; IR (neat, cm^{-1}) *E* isomer: ν 3072, 1715, 1483, 1186, 1133, 1070, 920, 758, 676. *Z* isomer: ν 3060, 1709, 1484, 1187, 1134, 1069, 919, 759, 675; HRMS (ESI, m/z): calcd for $C_{32}H_{32}N_2O$ $[M+H]^+$: 461.2593; Found: 461.2591.

3-(hydroxyimino)-2-(quinolin-8-yl)isoindolin-1-one (3a)



Following the general procedure the title compound was isolated by flash chromatog - raphy (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 78 % yield; Approx. 4:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, DMSO-d_6): major product: δ 11.42 (d, J = 0.7 Hz, 1H), 8.88 – 8.83 (m, 1H), 8.51 – 8.45 (m, 2H), 8.14 (d, J = 8.2 Hz, 1H), 7.97 (d, J = 7.2 Hz, 1H), 7.93-7.86 (m, 3H), 7.81 (d, J = 7.3 Hz, 1H), 7.59 (dd, J = 7.9, 3.8 Hz, 1H); minor product: δ 10.70 (s, 1H), 8.81 (d, J = 3.9 Hz, 1H), 8.45 - 8.43 (m, 1H), 8.05 (d, J = 8.2 Hz, 1H), 7.79 – 7.67 (m, 6H), 7.57-7.54 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): major product: δ 165.9, 151.1, 149.5, 144.0, 136.6, 134.0, 132.0, 131.9, 131.2, 130.6, 129.4, 128.9, 128.4, 127.3, 126.3, 123.3, 122.2; minor product: δ 167.0, 150.7, 144.5, 141.5, 136.3, 135.3, 135.0, 133.7, 130.7, 129.3, 128.8, 128.4, 128.2, 126.1, 123.5, 121.9, 120.6; HRMS (ESI, m/z): calcd for $C_{17}H_{11}N_3O_2$ $[M+H]^+$: 290.0930; Found: 290.0927.

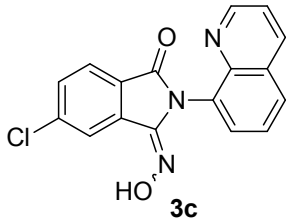
3-(hydroxyimino)-5-methyl-2-(quinolin-8-yl)isoindolin-1-one (3b)



Following the general procedure the title compound was isolated by flash chromatog - raphy (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 71 % yield; Approx.

3.3:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, DMSO-d_6): major product: δ 11.36 (s, 1H), 8.83 (d, J = 3.7 Hz, 1H), 8.46 (d, J = 8.2 Hz, 1H), 8.28 (s, 1H), 8.11 (d, J = 8.2 Hz, 1H), 7.88 (d, J = 7.1 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.62 – 7.54 (m, 2H), 2.52 (s, 3H); minor product: δ 10.61 (s, 1H), 8.79 (d, J = 3.7 Hz, 1H), 8.41 (d, J = 8.2 Hz, 1H), 8.02 (d, J = 8.2 Hz, 1H), 7.85 (s, 1H), 7.71-7.65 (m, 3H), 7.53-7.48 (m, 2H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): major product: δ 165.9, 151.1, 149.6, 144.4, 144.1, 136.5, 132.5, 132.1, 131.2, 129.3, 128.9, 128.9, 128.2, 127.6, 126.3, 123.2, 122.1, 21.7; minor product: δ 167.1, 150.7, 144.5, 144.3, 141.7, 136.3, 135.5, 135.4, 131.5, 129.3, 128.3, 128.2, 126.4, 126.1, 123.3, 121.9, 120.8, 21.6; HRMS (ESI, m/z): calcd for $C_{18}H_{13}N_3O_2$ $[M+H]^+$: 304.1086; Found: 304.1083.

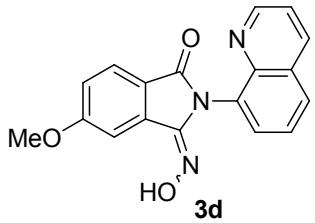
5-chloro-3-(hydroxyimino)-2-(quinolin-8-yl)isoindolin-1-one (3c)



3c

Following the general procedure the title compound was isolated by flash chromatog - raphy (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 61 % yield; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.67 (s, 1H), 8.85 (d, J = 4.1 Hz, 1H), 8.50 (d, J = 8.3 Hz, 1H), 8.43 (s, 1H), 8.15 (d, J = 8.3 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.93-7.87 (m, 2H), 7.75 (t, J = 7.7 Hz, 1H), 7.60 (dd, J = 8.3, 4.3 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 164.9, 151.2, 148.4, 143.9, 138.5, 136.6, 132.0, 131.6, 131.1, 129.7, 129.6, 129.2, 128.9, 126.8, 126.3, 125.2, 122.2; HRMS (ESI, m/z): calcd for $C_{17}H_{10}ClN_3O_2$ $[M+H]^+$: 324.0540; Found: 324.0532.

3-(hydroxyimino)-5-methoxy-2-(quinolin-8-yl)isoindolin-1-one (3d)

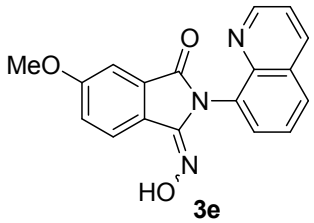


3d

Following the general procedure the title compound was isolated by flash chromatog - raphy (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 81 % yield; Approx. 1.4:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, DMSO-d_6): major product: δ 11.40 (s, 1H), 8.84 (d, J = 4.0 Hz, 1H), 8.48 (d, J = 8.3 Hz, 1H), 8.13 (d, J = 8.2 Hz, 1H), 7.94 (s, 1H), 7.88 (d, J = 7.9 Hz, 2H), 7.74 (t, J = 7.8 Hz, 1H), 7.58 (dd, J = 8.5, 4.3 Hz, 1H), 7.33 (d, J = 8.4 Hz,1H), 3.94 (s, 3H); minor product: δ 10.59 (s, 1H), 8.80 (d, J = 4.1 Hz, 1H), 8.44 (d, J = 8.2 Hz, 1H), 8.04 (d, J = 8.2 Hz, 1H), 7.84-7.79 (m, 2H), 7.68 (t, J = 7.7 Hz, 1H), 7.55 (dd, J = 8.4 Hz, J =4.8Hz, 1H),7.32 (s, 1H) 7.24 (d, J = 8.4 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 166.7,

165.7, 163.8, 163.8, 151.1, 150.6, 149.3, 144.6, 144.1, 141.6, 137.5, 136.5, 136.3, 135.5, 132.1, 131.2, 130.5, 129.3, 128.9, 128.3, 128.2, 126.3, 126.0, 125.2, 125.0, 123.0, 122.1, 121.9, 121.3, 118.0, 117.9, 112.0, 104.5, 56.1; HRMS (ESI, m/z): calcd for $C_{18}H_{13}N_3O_3$ $[M+H]^+$: 320.1035; Found: 320.1032.

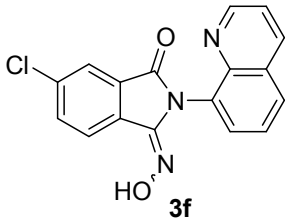
3-(hydroxyimino)-6-methoxy-2-(quinolin-8-yl)isoindolin-1-one (3e)



3e

Following the general procedure the title compound was isolated by flash chromatog - raphy (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 62 % yield; Approx. 5.3:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, DMSO-d_6): major product: δ 11.20 (s, 1H), 8.85 (d, J = 3.9 Hz, 1H), 8.48 (d, J = 8.2 Hz, 1H), 8.34 (d, J = 8.4 Hz, 1H), 8.13 (d, J = 8.2 Hz, 1H),7.90 (d, J = 7.1 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.59 (dd, J = 8.3, 4.2 Hz, 1H), 7.46 (d, J = 1.5 Hz, 1H), 7.41-7.38 (m, 1H), 3.95 (s, 3H). minor product: δ 10.50 (s, 1H), 8.81 (d, J = 3.9 Hz, 1H), 8.44 (d, J = 8.3 Hz, 1H), 8.04 (d, J = 8.1 Hz, 1H), 7.86 (d, J = 7.4 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.55 (dd, J = 8.6 Hz, J = 4.2 Hz, 1H), 7.39-7.37 (m, 1H)7.37-7.34 (m, 1H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): major product: δ 165.8, 162.1, 151.1, 149.4, 144.1, 136.5, 132.8, 132.0, 131.2, 129.4, 128.9, 128.7, 126.3,122.2, 121.3, 120.4, 107.3, 56.1; minor product: δ 166.9, 161.6, 150.7, 144.5, 141.3, 136.3, 135.5, 130.6, 129.3, 128.4, 128.2, 127.4, 126.1, 122.0, 121.9, 121.3, 106.7, 56.0; HRMS (ESI, m/z): calcd for $C_{18}H_{13}N_3O_3$ $[M+H]^+$: 320.1035; Found: 320.1033.

6-chloro-3-(hydroxyimino)-2-(quinolin-8-yl)isoindolin-1-one (3f)

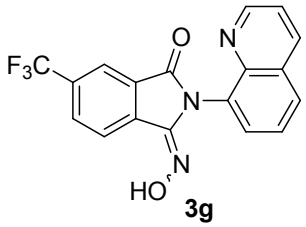


3f

Following the general procedure the title compound was isolated by flash chromatog - raphy (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 65 % yield; Approx. 5.3:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, DMSO-d_6): major product: δ 11.61 (s, 1H), 8.85 (d, J = 4.0 Hz, 1H), 8.49 (d, J = 8.3 Hz, 1H), 8.44 (d, J = 8.1 Hz, 1H), 8.15 (d, J = 8.2 Hz, 1H), 8.02 (s, 1H), 7.95-7.90 (m, 2H), 7.75 (t, J = 7.7 Hz, 1H), 7.59 (dd, J = 8.3, 4.2 Hz, 1H); minor product: δ 10.89 (s, 1H), 8.81 (d, J = 3.9 Hz, 1H), 8.06 (d, J = 8.3 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.90-7.85 (m, 3H), 7.70 (t, J =7.8 Hz, 1H), 7.56 (dd, J = 8.6, J = 3.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6): major product: δ 164.7, 151.3, 148.8, 143.9, 136.7, 134.0, 132.4, 131.6, 131.2, 129.7, 128.9, 128.9, 126.9, 126.4, 123.4, 122.3; minor product: δ 165.7, 150.9, 144.4, 136.4,

135.5, 135.0, 133.8, 133.5, 132.1, 130.5, 129.3, 128.6, 128.3, 126.1, 122.6, 122.0; HRMS (ESI, m/z): calcd for $C_{17}H_{10}ClN_3O_2$ $[M+H]^+$: 324.0540; Found: 324.0537.

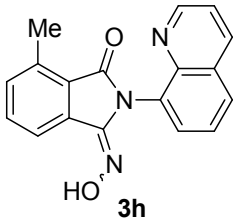
3-(hydroxyimino)-2-(quinolin-8-yl)-6-(trifluoromethyl)isoindolin-1-one (3g)



3g

Following the general procedure the title compound was isolated by flash chromatog - raphy (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 53 % yield; Approx. 5.3:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, DMSO-d_6): major product: δ 11.82 (s, 1H), 8.85 (d, J = 3.7 Hz, 1H) 8.70 – 8.62 (m, 1H), 8.51 (d, J = 8.3 Hz, 1H), 8.28-8.15 (m, 3H), 7.95 (d, J = 7.2 Hz, 1H), 7.77 (t, J = 7.8 Hz, 1H), 7.60 (dd, J = 8.3, 4.0 Hz, 1H). minor product: δ 11.11 (s, 1H), 8.80 (d, J = 3.9 Hz, 1H), 8.46 (d, J = 8.3 Hz, 1H), 8.37 (d, J = 8.0 Hz, 1H), 8.13 – 7.99 (m, 3H), 7.91 (d, J = 7.3 Hz, 1H), 7.71 (t, J = 7.8Hz, 1H), 7.54 (dd, J = 8.9, 4.1 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 164.6, 151.3, 148.6, 143.8, 136.7, 131.9 (q, $J_{C\text{-}F}$ = 32.3 Hz), 131.5, 131.3, 131.2, 131.1 (q, $J_{C\text{-}F}$ = 3.5 Hz), 129.7, 128.9, 128.3, 126.4, 123.7 (q, $J_{C\text{-}F}$ = 271 Hz), 122.3, 120.3 (q, $J_{C\text{-}F}$ = 3.6 Hz); HRMS (ESI, m/z): calcd for $C_{18}H_{10}F_3N_3O_2$ $[M+H]^+$: 358.0803; Found: 358.0800.

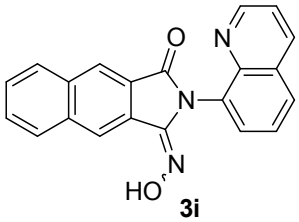
3-(hydroxyimino)-7-methyl-2-(quinolin-8-yl)isoindolin-1-one (3h)



3h

Following the general procedure the title compound was isolated by flash chromatog - raphy (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 75 % yield; Approx. 2.4:1 mixture of E and Z isomers; ^{1}H NMR (400 MHz, DMSO-d_6): major product: δ 11.32 (s, 1H), 8.86 (d, J = 4.0 Hz, 1H), 8.48 (d, J = 8.3 Hz, 1H), 8.31 (d, J = 7.6 Hz, 1H), 8.13 (d, J = 8.2 Hz, 1H), 7.89 (d, J = 7.2 Hz, 1H), 7.77-7.71 (m, 2H), 7.61 – 7.53 (m, 2H), 2.69 (s, 3H); minor product: δ 10.59 (s, 1H), 8.81 (d, J = 4.0 Hz, 1H), 8.44 (d, J = 8.3 Hz, 1H), 8.04 (d, J = 8.2 Hz, 1H), 7.86 (d, J = 7.2 Hz, 1H), 7.77-7.66 (m, 3H), 7.61 – 7.53 (m, 1H), 7.47 (d, J = 7.3 Hz, 1H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, DMSO- d_6): major product: δ 166.6, 151.1, 149.3, 144.1, 137.2, 136.6, 133.9, 133.4, 132.1, 131.3, 129.4, 128.9, 128.9, 127.4, 126.3, 125.0, 122.1, 17.2; minor product: δ 167.7, 150.7, 144.6, 141.5, 137.2, 136.3, 135.5, 135.4, 133.2, 132.4, 129.4, 128.3, 128.2, 126.1, 125.9, 121.9, 118.1, 17.1; HRMS (ESI, m/z): calcd for $C_{18}H_{13}N_3O_2$ $[M+H]^+$: 304.1086; Found: 304.1078.

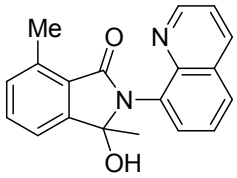
3-(hydroxyimino)-2-(quinolin-8-yl)-2,3-dihydro-1H-benzo[f]isoindol-1-one (3i)



3i

Following the general procedure the title compound was isolated by flash chromatog - raphy (eluent: ethyl acetate/petrol ether =1/1) as a white solid in 61 % yield; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.41 (s, 1H), 9.05 (s, 1H), 8.86 (d, J = 4.0 Hz, 1H), 8.62 (s, 1H), 8.50 (d, J = 8.3 Hz, 1H), 8.29 (d, J = 5.9 Hz, 2H), 8.16 (d, J = 8.3 Hz, 1H), 7.97 (d, J = 7.2 Hz, 1H), 7.80-7.75 (m, 3H), 7.60 (dd, J = 8.3, 4.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 165.8, 162.6, 151.2, 149.5, 143.9, 136.6, 135.5, 133.8, 132.2, 131.1, 130.0, 129.9, 129.5, 128.9, 128.8, 128.4, 127.9, 127.7, 126.4, 124.3, 122.2; HRMS (ESI, m/z): calcd for $C_{21}H_{13}N_3O_2$ [M+H]$^+$: 340.1086; Found: 340.1081.

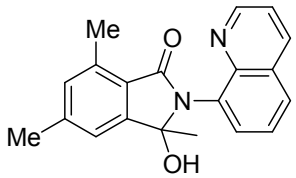
3-hydroxy-3,7-dimethyl-2-(quinolin-8-yl)isoindolin-1-one (4p')



4p'

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a white solid in 21 % yield, mp 201-202 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (d, J = 2.8 Hz, 1H), 8.39 (br, 1H), 8.29 (d, J = 8.3 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 7.82 (d, J = 7.3 Hz, 1H), 7.69 (t, J = 7.7 Hz, 1H), 7.59 – 7.50 (m, 2H), 7.46 (dd, J = 7.8, 4.0 Hz, 1H), 7.29 (d, J = 6.6 Hz, 1H), 2.74 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 150.2, 149.6, 145.0, 138.0, 137.6, 133.7, 132.4, 132.0, 131.1, 129.8, 128.1, 127.0, 126.6, 121.5, 119.0, 89.5, 25.3, 17.5; IR (neat, cm^{-1}) ν 3668, 3080, 1708, 1579, 1480, 1193, 1067, 928, 676; HRMS (ESI, m/z): calcd for $C_{19}H_{16}N_2O_2$ [M+H]$^+$: 305.1290; Found: 305.1296.

3-hydroxy-3,5,7-trimethyl-2-(quinolin-8-yl)isoindolin-1-one (4q')



4q'

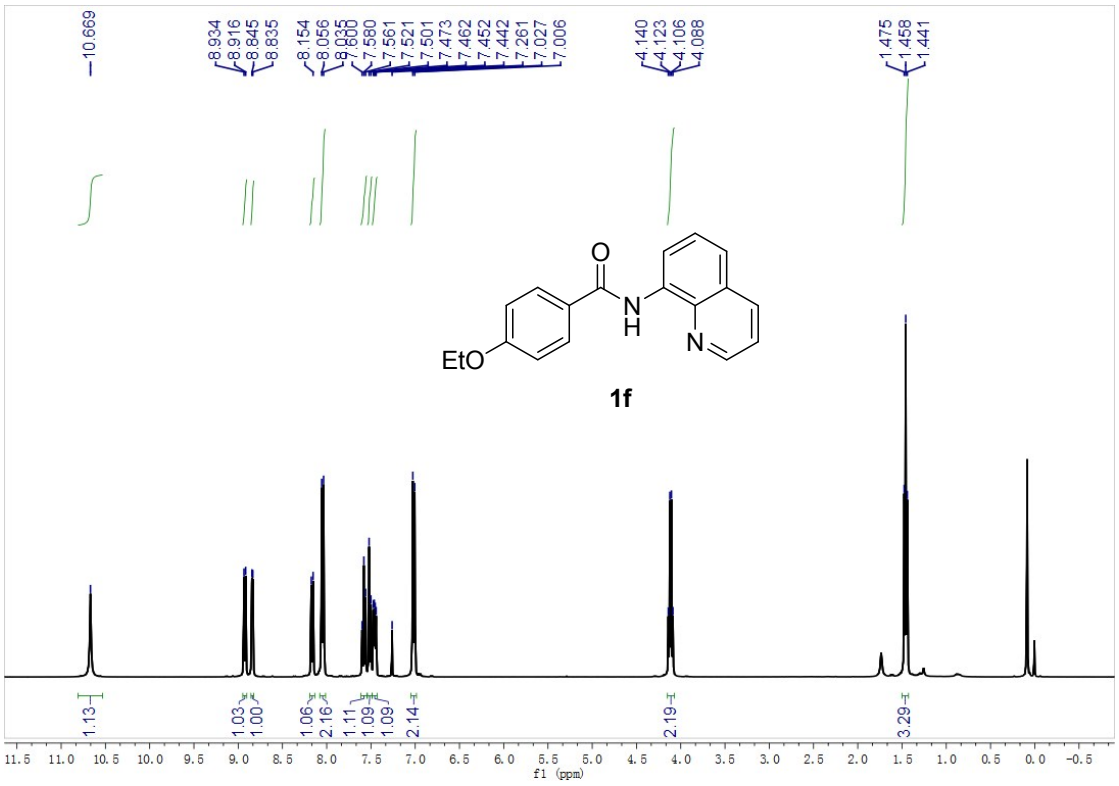
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a white solid in 18 % yield, mp 201-202 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.79 (d, J = 4.2 Hz, 1H), 8.30 (d, J = 8.3 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 7.4 Hz, 1H), 7.69 (t, J = 7.8 Hz,

1H), 7.48 (dd, J = 8.3, 4.3 Hz, 1H), 7.32 (s, 1H), 7.10 (s, 1H), 2.69 (s, 3H), 2.47 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 150.6, 149.6, 145.0, 143.3, 137.8, 137.7, 133.9, 132.1, 129.8, 128.1, 127.0, 124.1, 121.5, 119.6, 89.4, 25.3, 21.8, 17.4; IR (neat, cm^{-1}) ν 3673, 2997, 1718, 1485, 1189, 1064, 914, 676; HRMS (ESI, m/z): calcd for $C_{20}H_{18}N_2O_2$ $[M+H]^+$: 319.1447; Found: 319.1443.

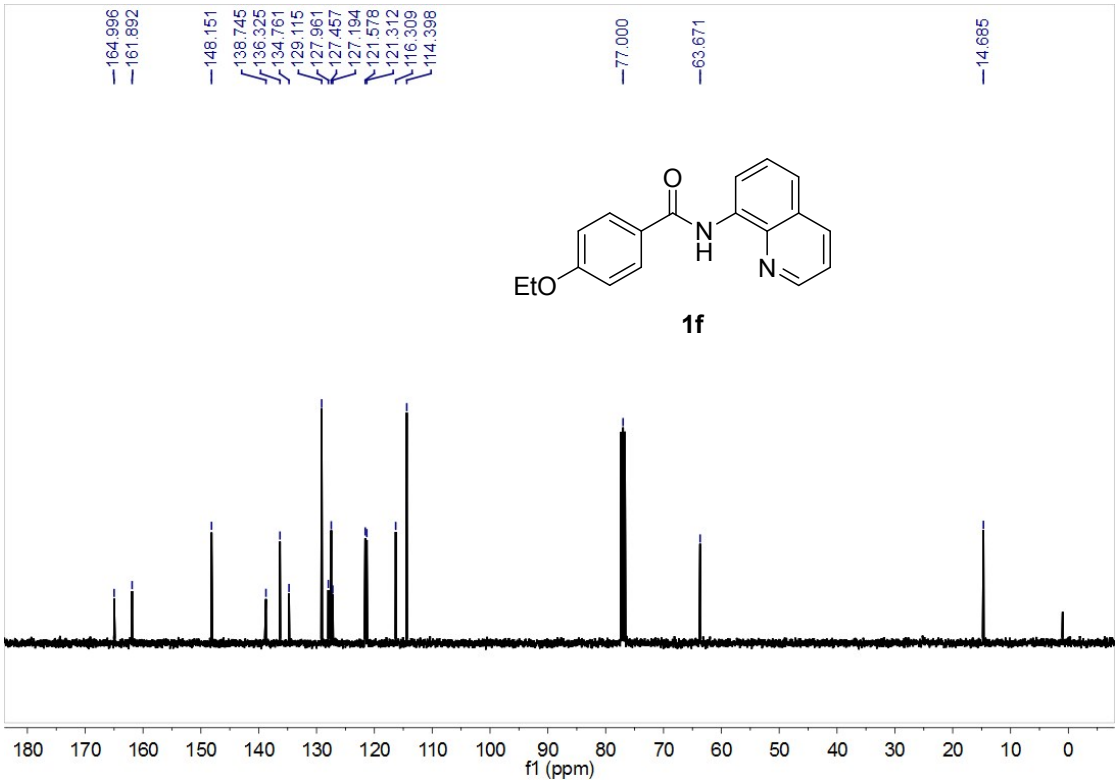
References

1. A. M. Suess, M. Z. Ertem, C. J. Cramer and S. S. Stahl, *J. Am. Chem. Soc.,* 2013, **135**, 9797.
2. N. Kornblum and H. E. Ungnade, *Org. Synth.,1963,* **4**, 724.
3. (a) L. D. Tran, I. Popov, O. Daugulis, *J. Am. Chem. Soc.*, 2012, **134**, 18237; (b) T. Truong, K. Klimovica, O. Daugulis, *J. Am. Chem. Soc.*, 2013, **135**, 9342; (c) L. D. Tran, J. Roane, O. Daugulis, *Angew. Chem., Int. Ed.,* 2013, **52**, 6043; (d) J. Roane, O. Daugulis, *Org. Lett.,* 2013, **15**, 5842; (e) M. Nishino, K. Hirano, T. Satoh, M. Miura, *Angew. Chem. Int. Ed.,* 2013, **52**, 4457.
4. X. Wu, J. Miao, Y. Li, G. Li and H. Ge, *Chem. Sci.*, 2016, **7**, 5260.

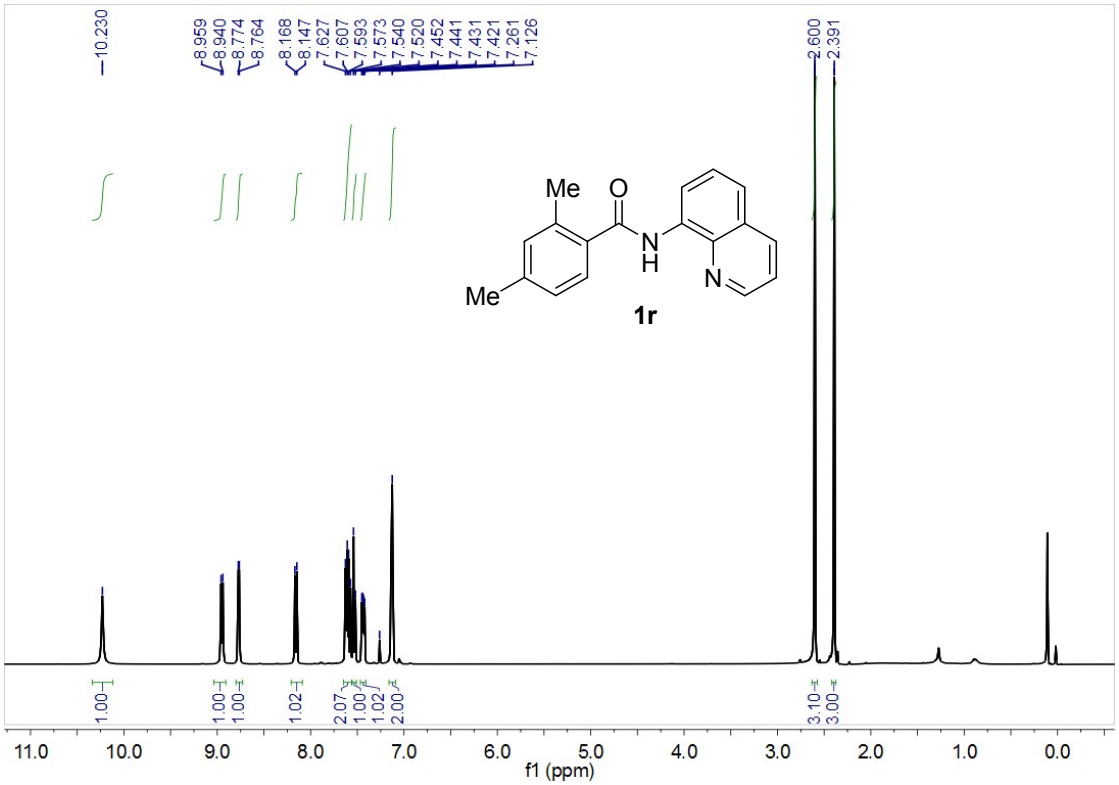
^{1}H NMR Spectrum of **1f**



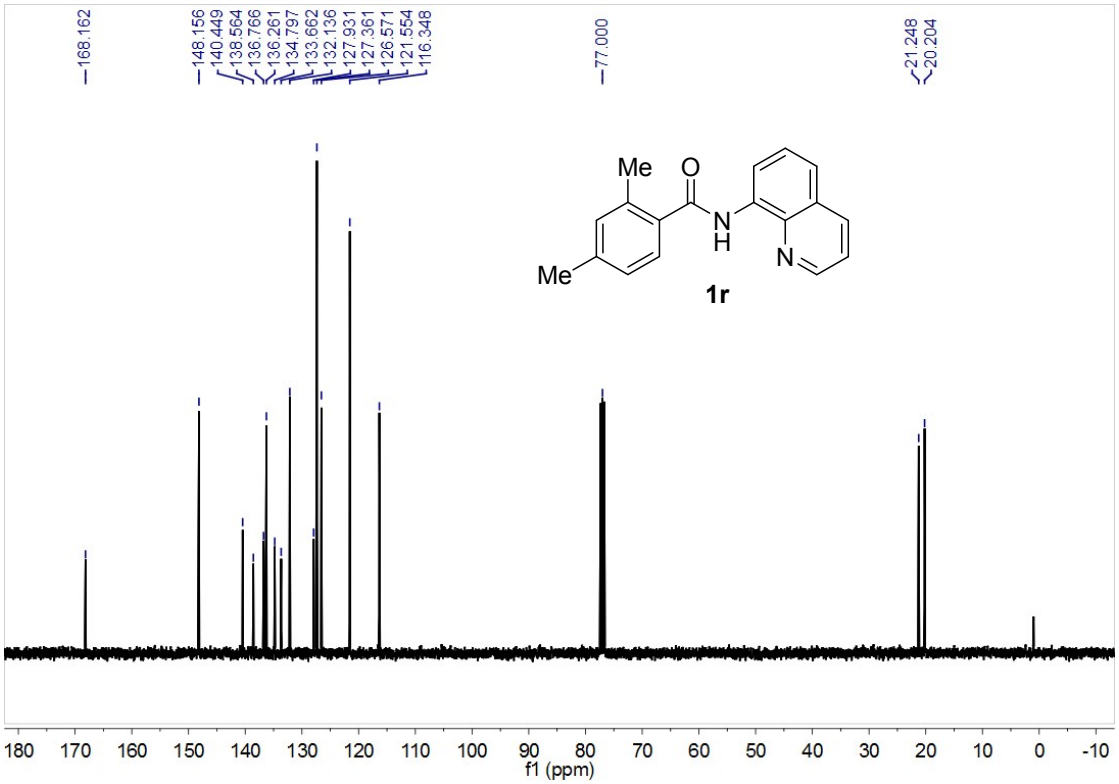
^{13}C NMR Spectrum of **1f**



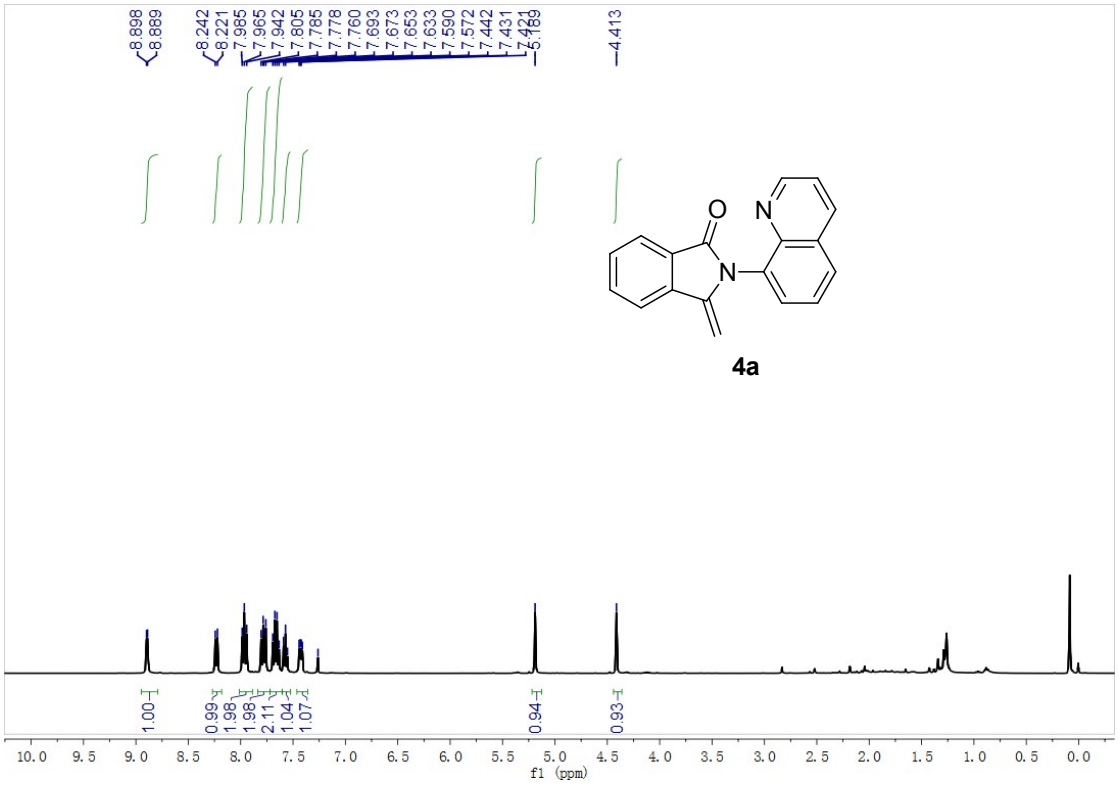
^{1}H NMR Spectrum of **1r**



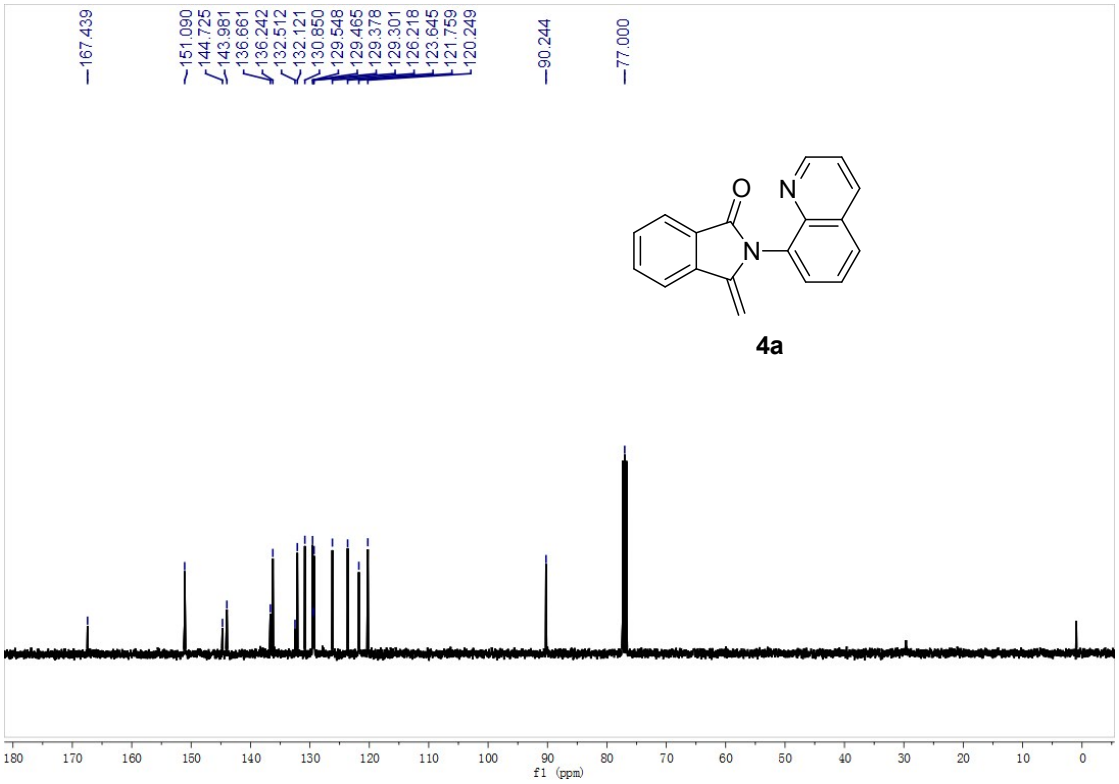
^{13}C NMR Spectrum of **1t**



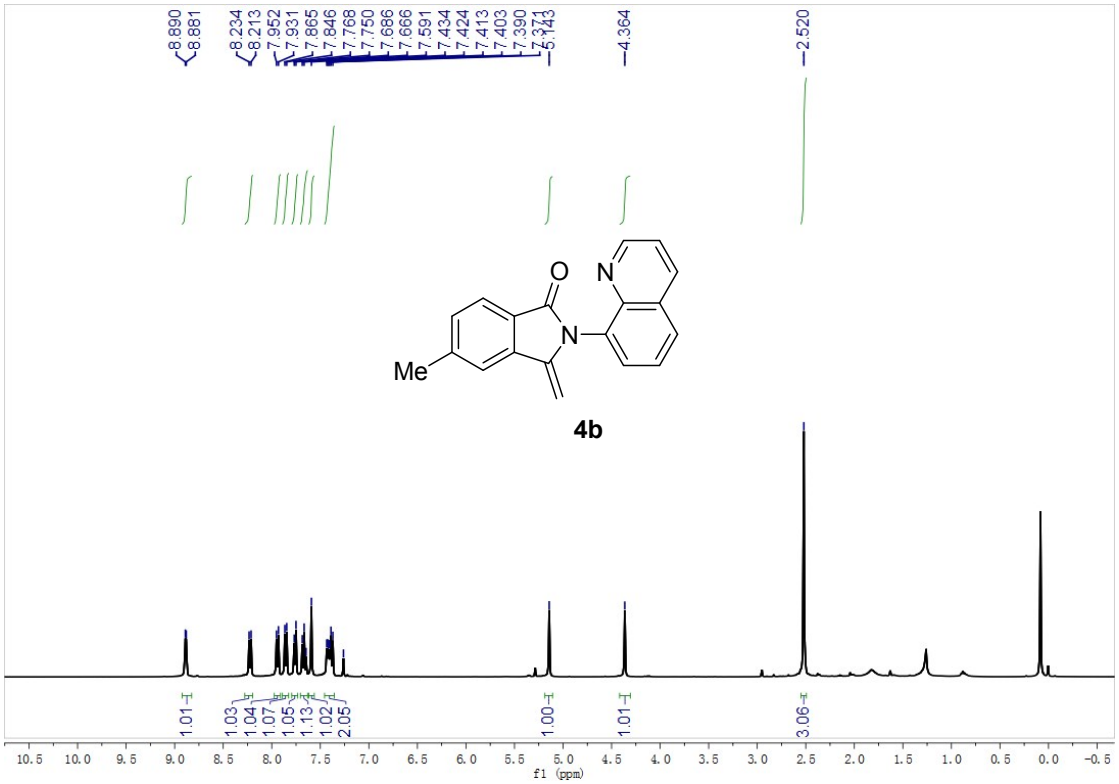
^{1}H NMR Spectrum of **4a**



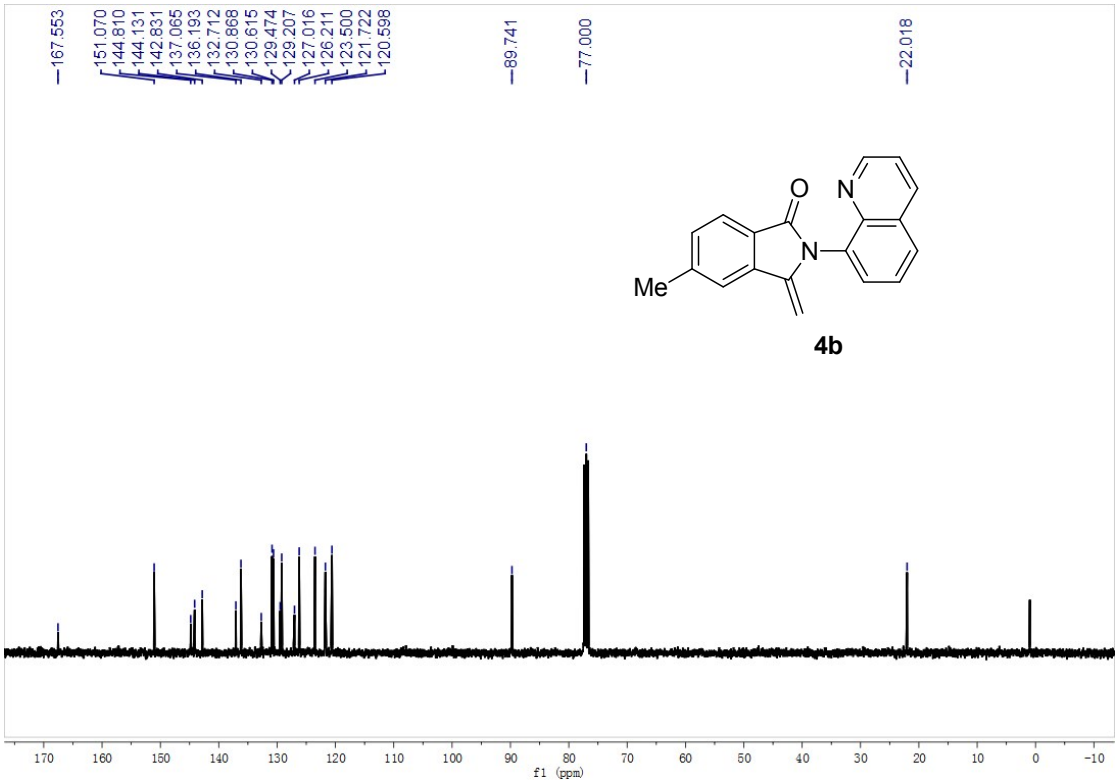
^{13}C NMR Spectrum of **4a**



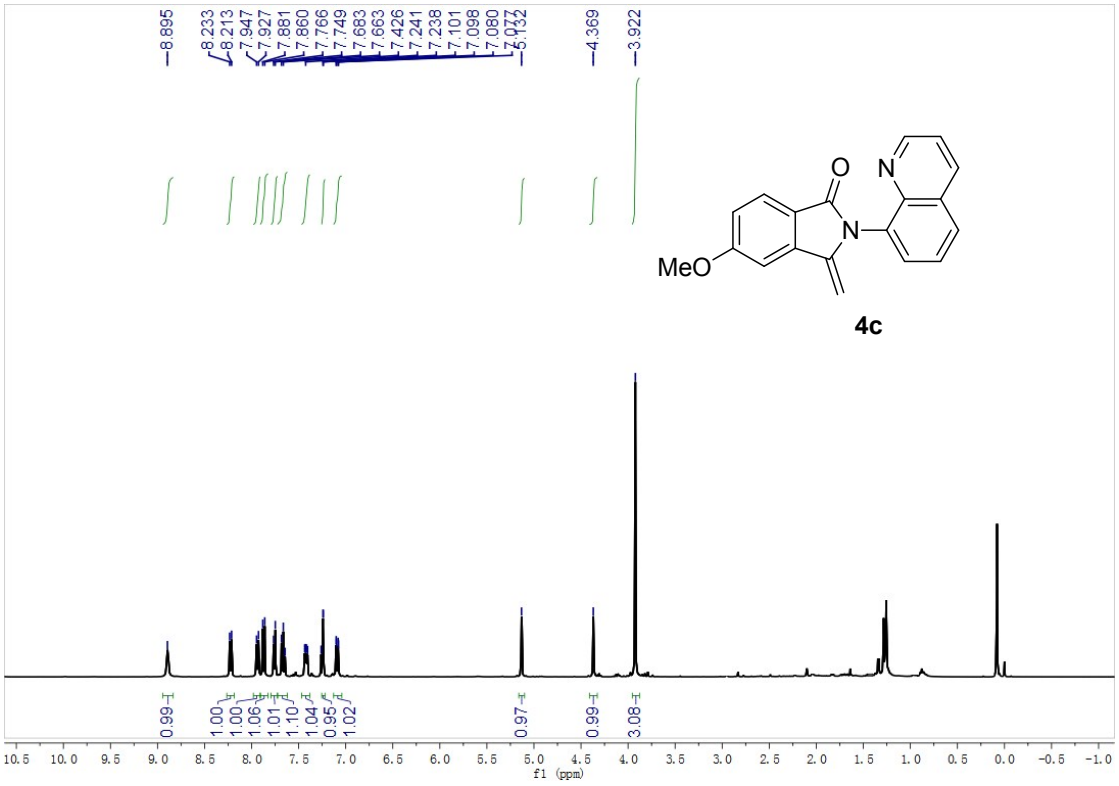
^{1}H NMR Spectrum of **4b**



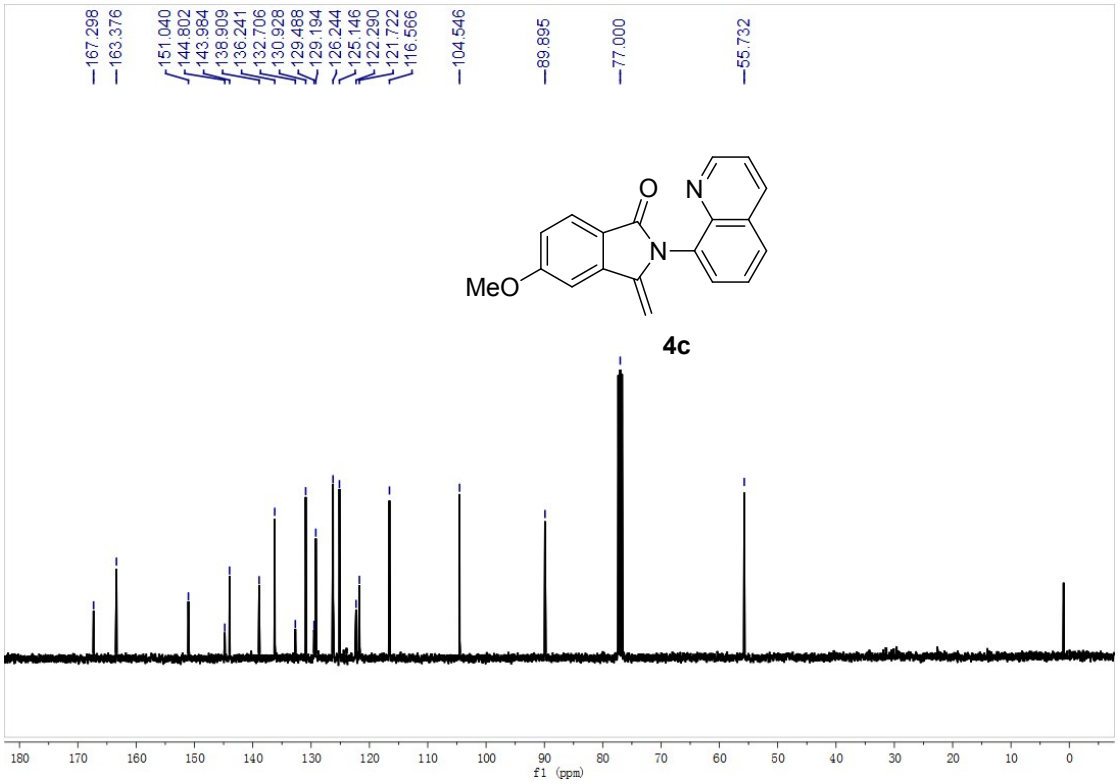
^{13}C NMR Spectrum of **4b**



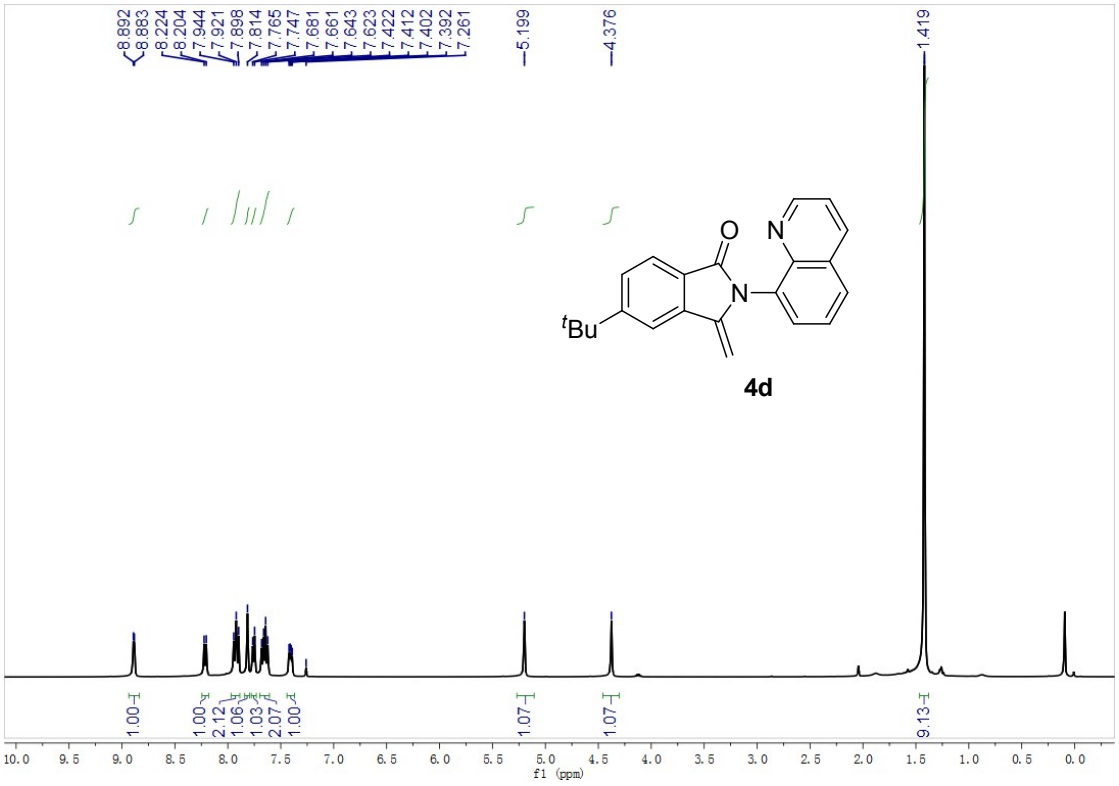
^{1}H NMR Spectrum of **4c**



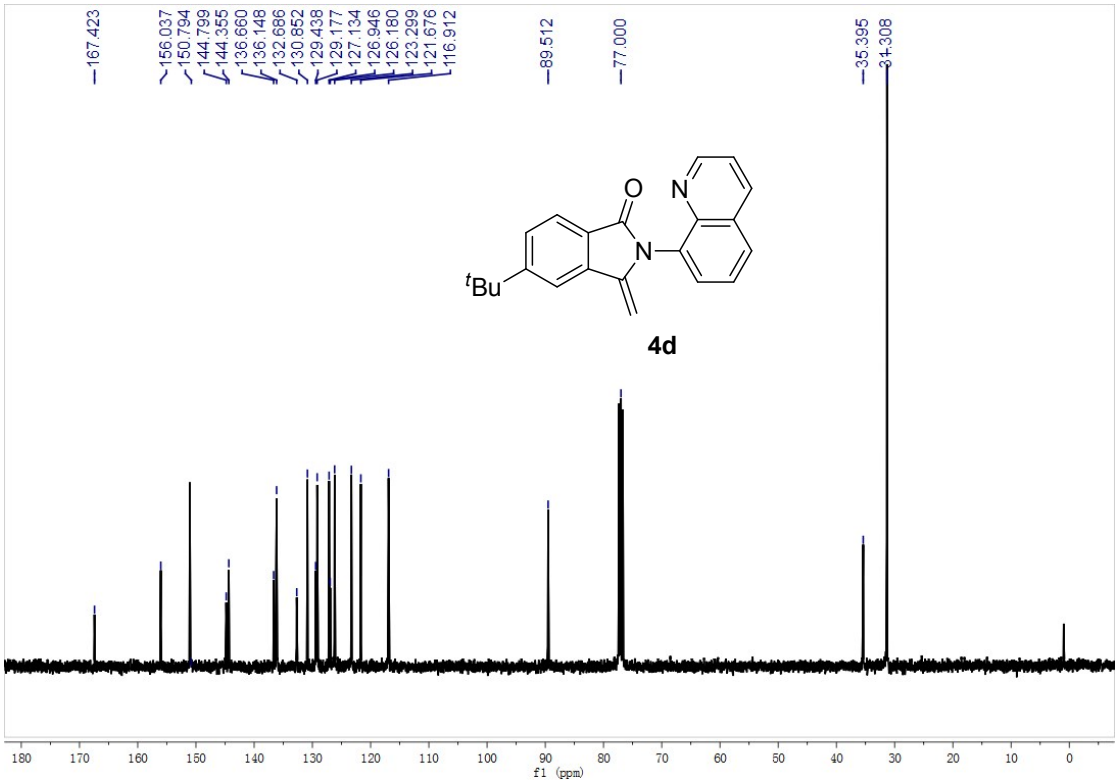
^{13}C NMR Spectrum of **4c**



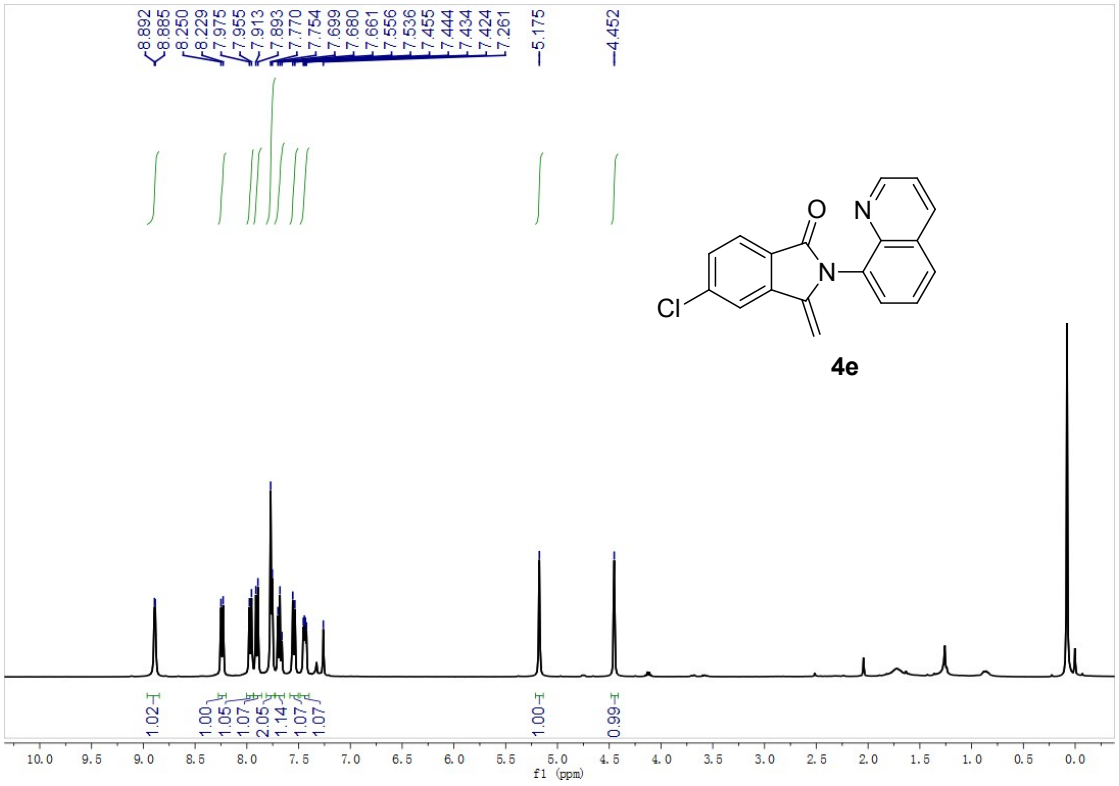
^{1}H NMR Spectrum of **4d**



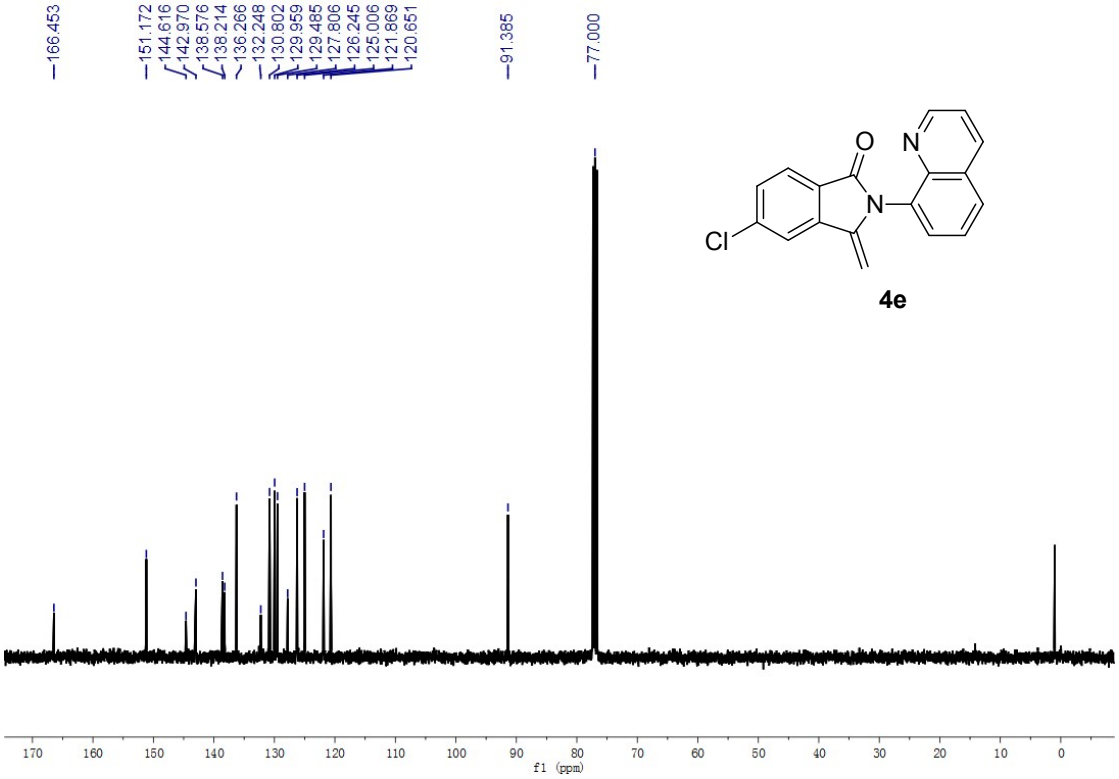
^{13}C NMR Spectrum of **4d**



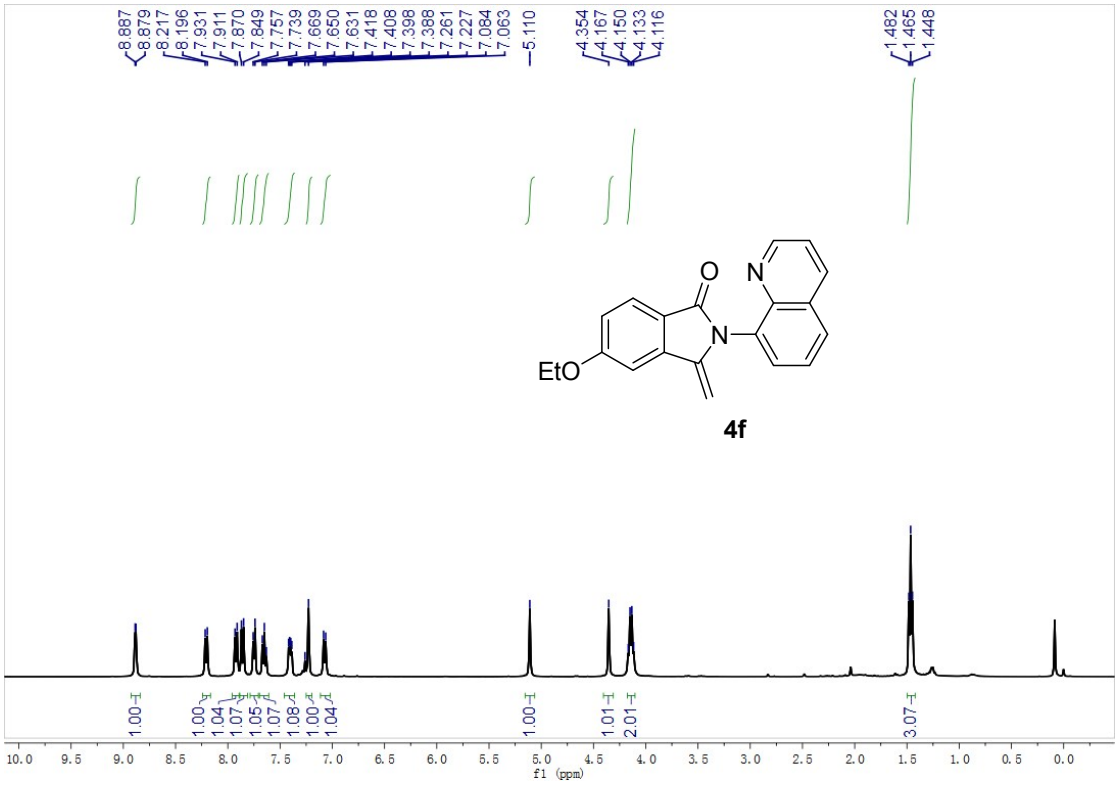
^{1}H NMR Spectrum of **4e**



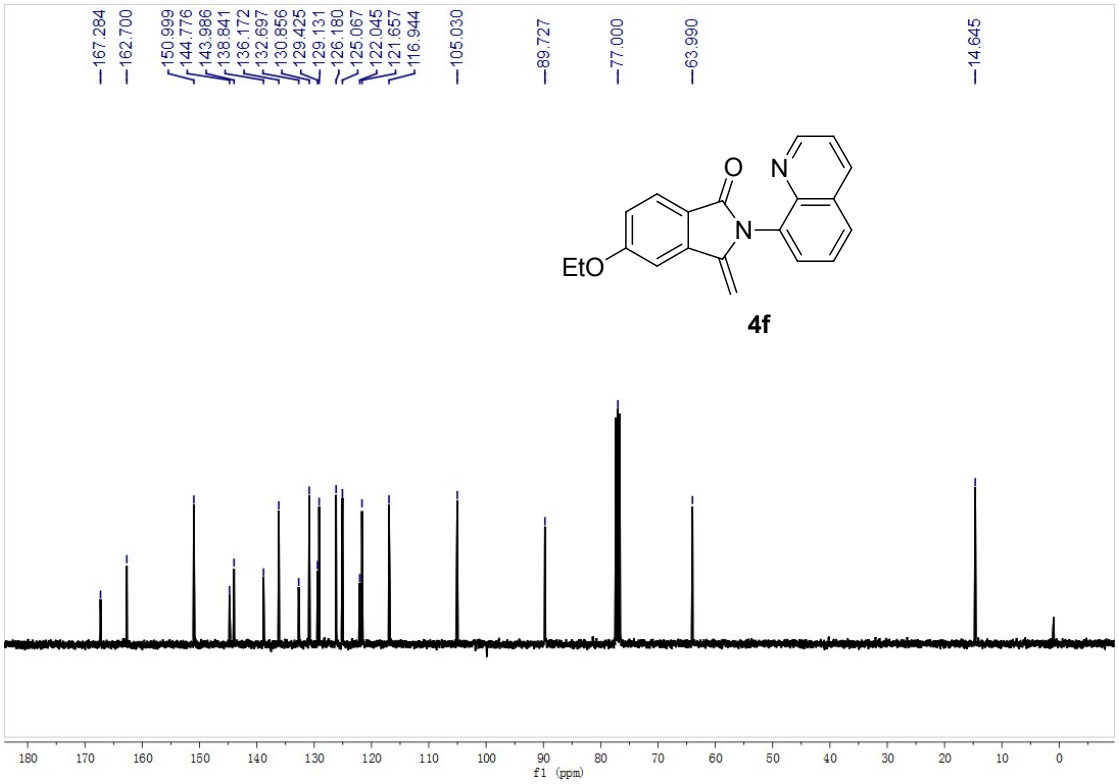
^{13}C NMR Spectrum of **4e**



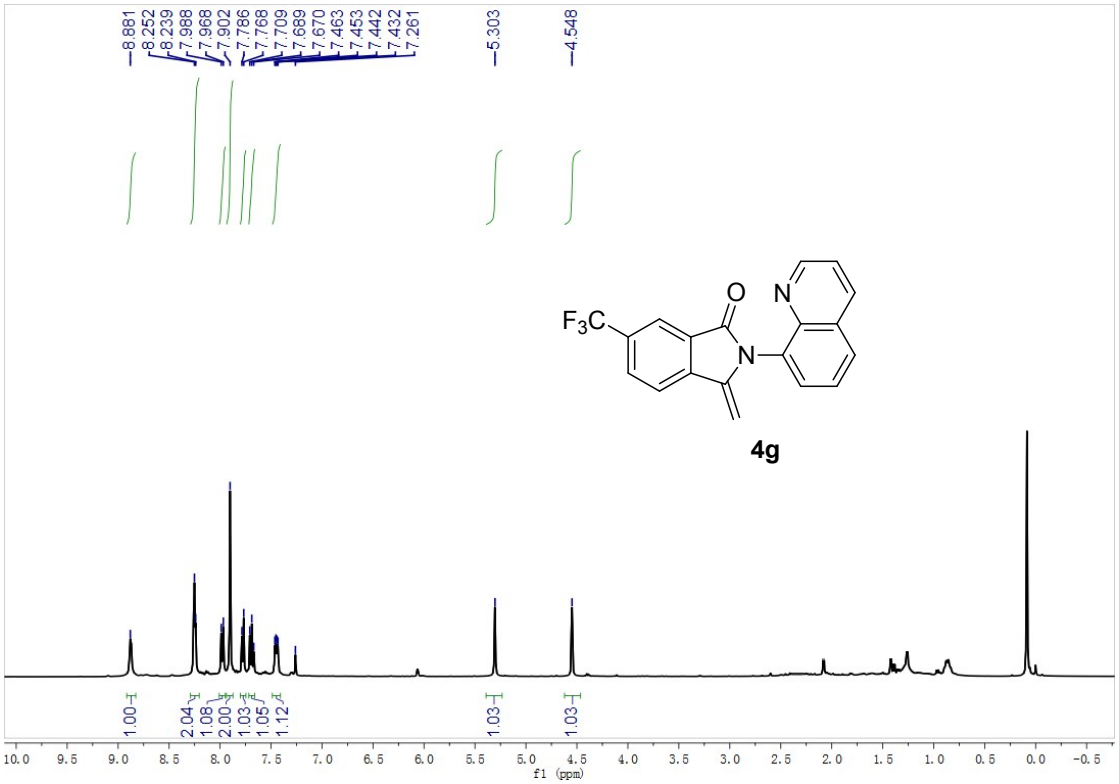
^{1}H NMR Spectrum of **4f**



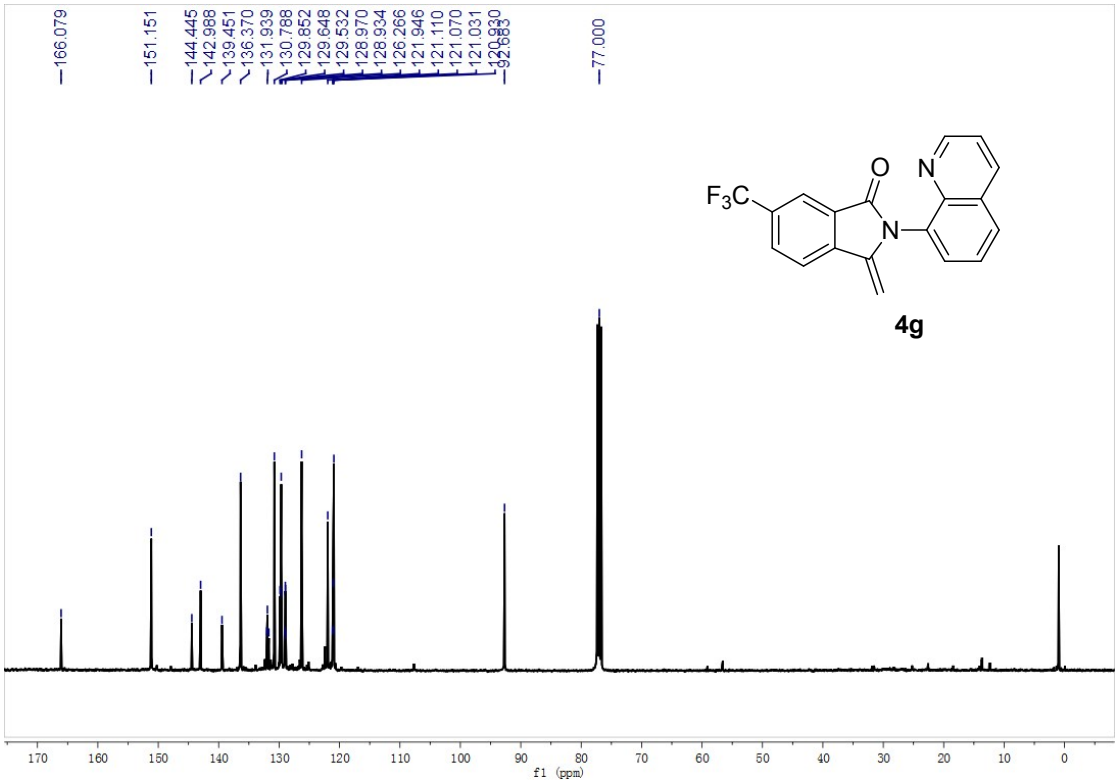
^{13}C NMR Spectrum of **4f**



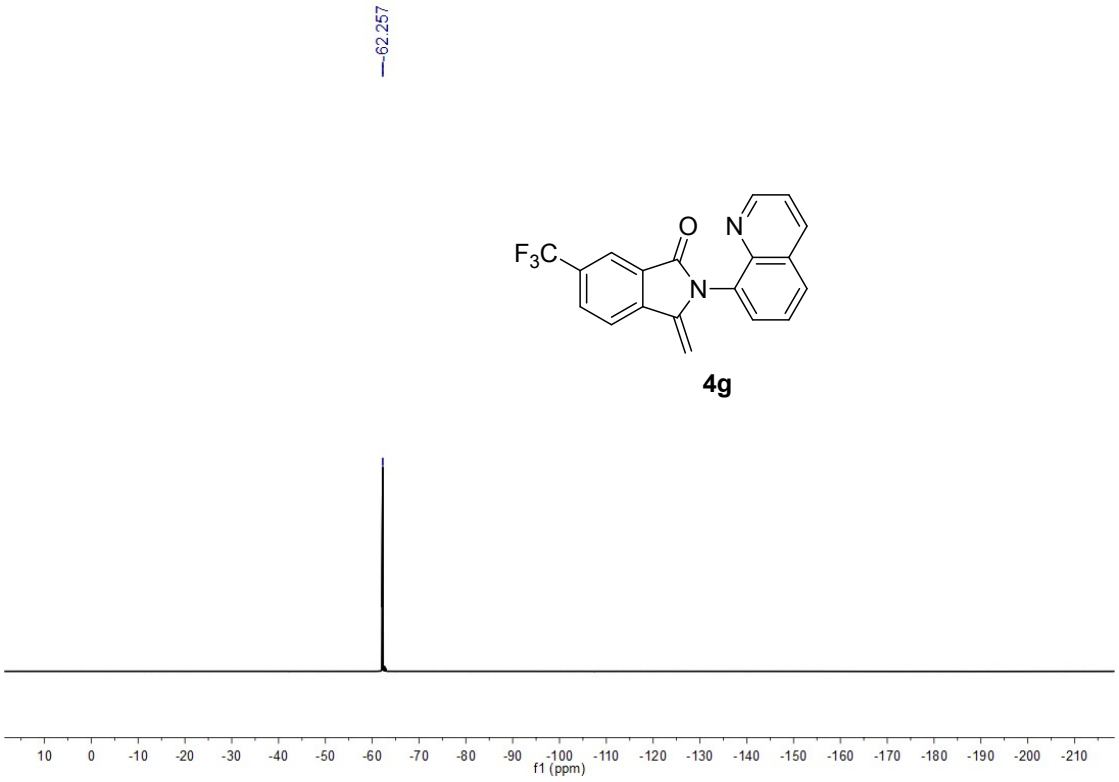
^{1}H NMR Spectrum of **4g**



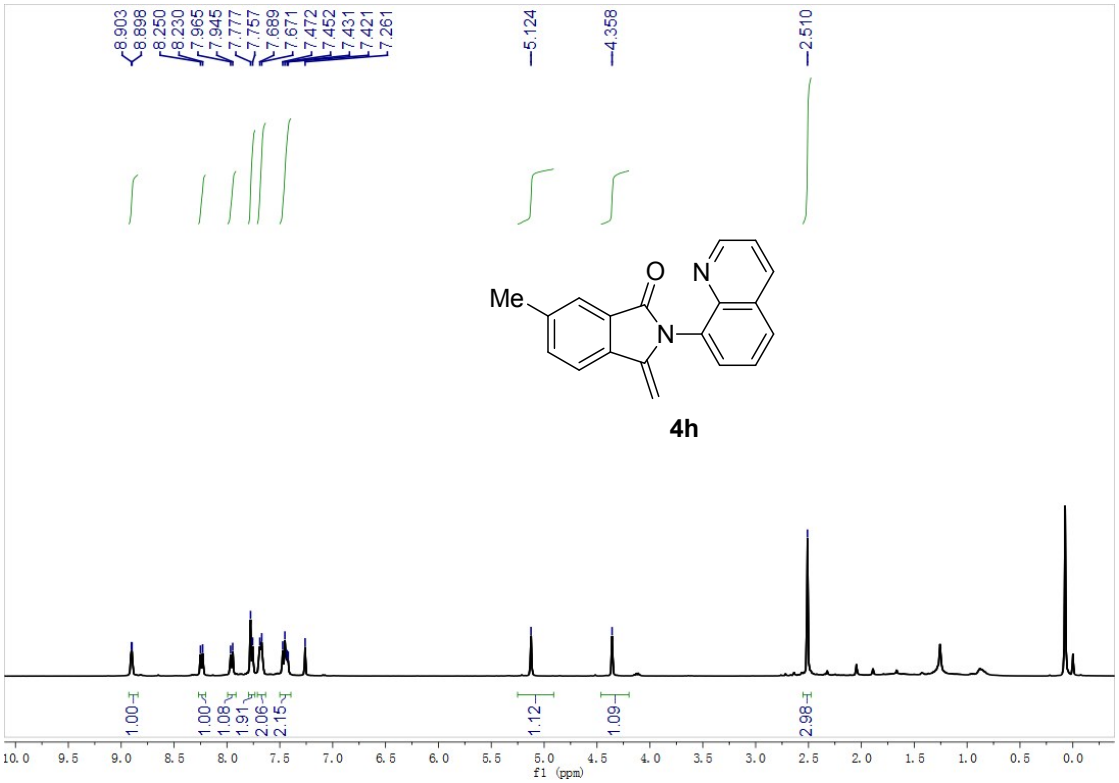
^{13}C NMR Spectrum of **4g**



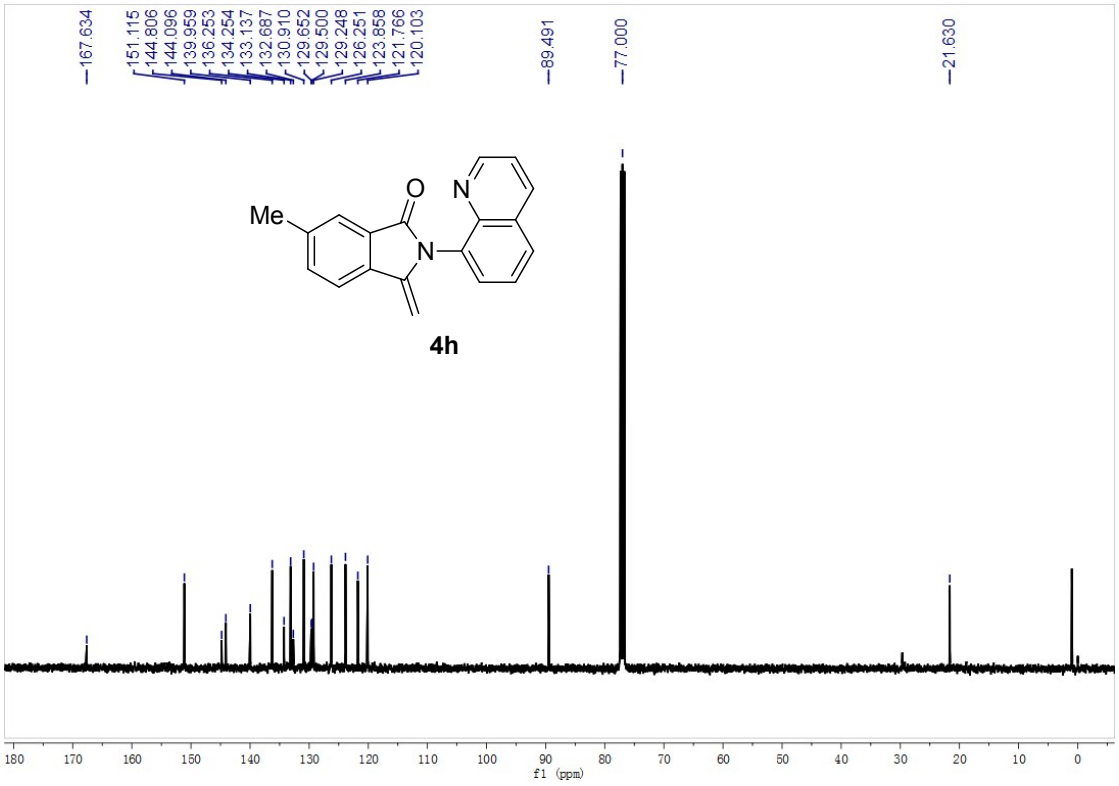
^{19}F NMR Spectrum of **4g**



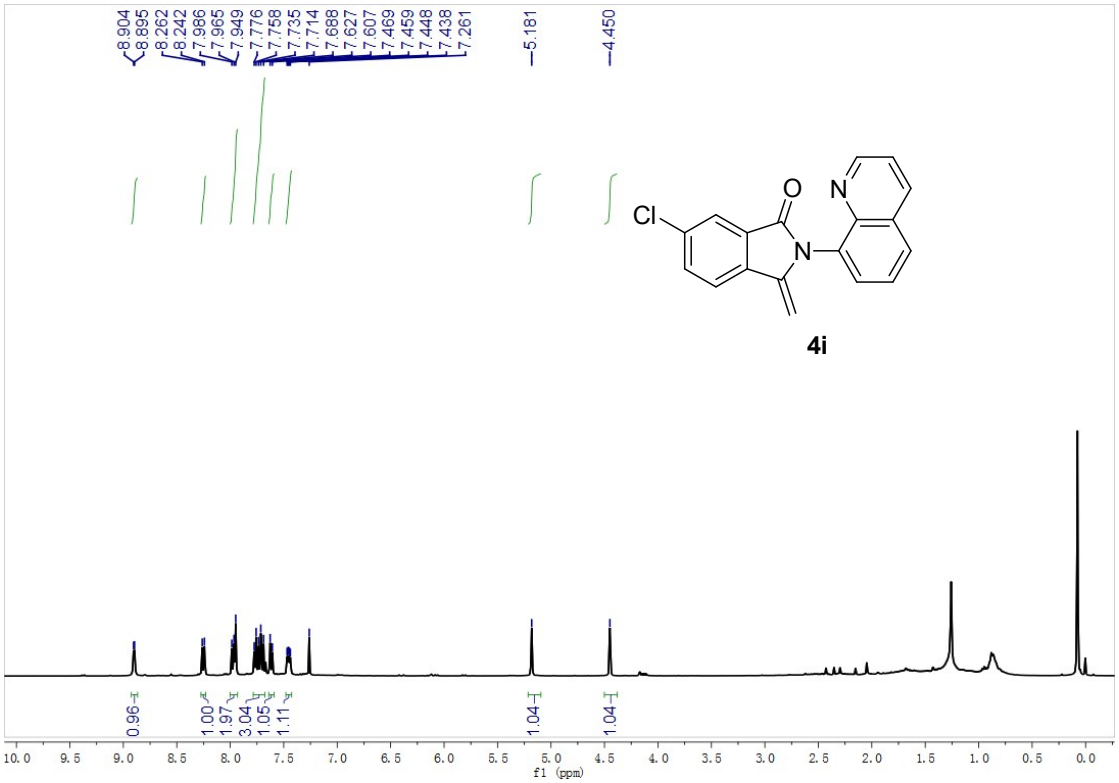
^{1}H NMR Spectrum of **4h**



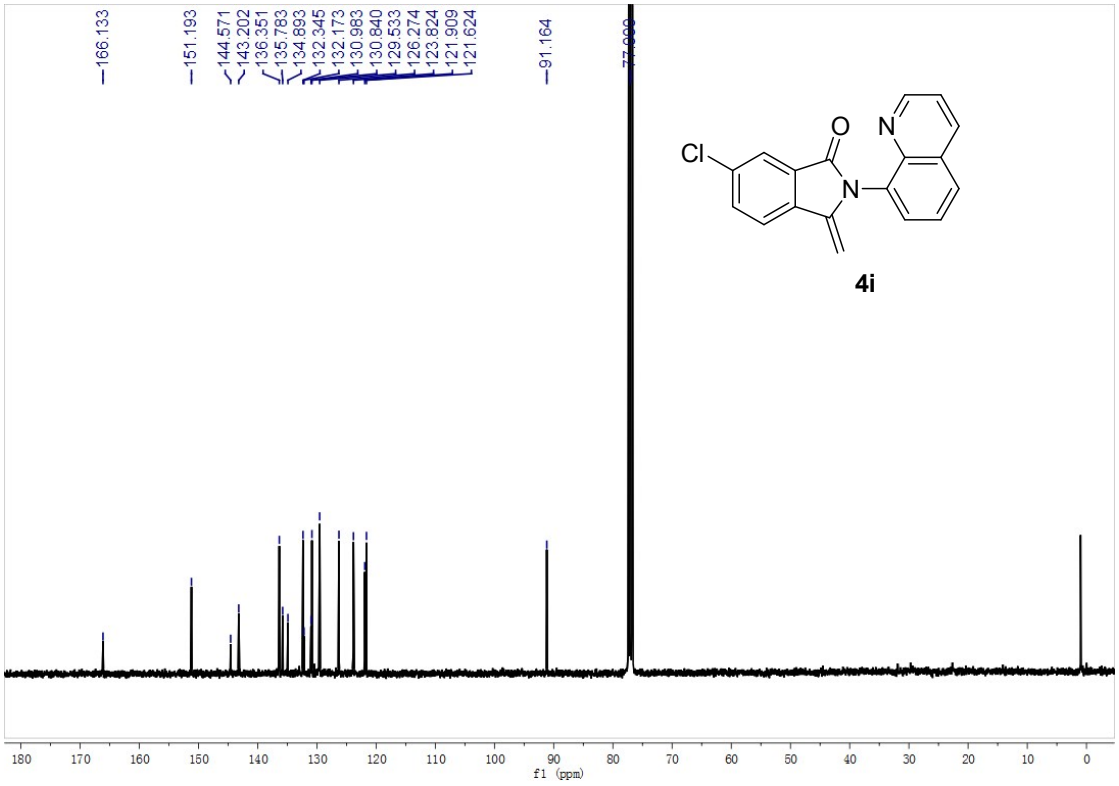
^{13}C NMR Spectrum of **4h**



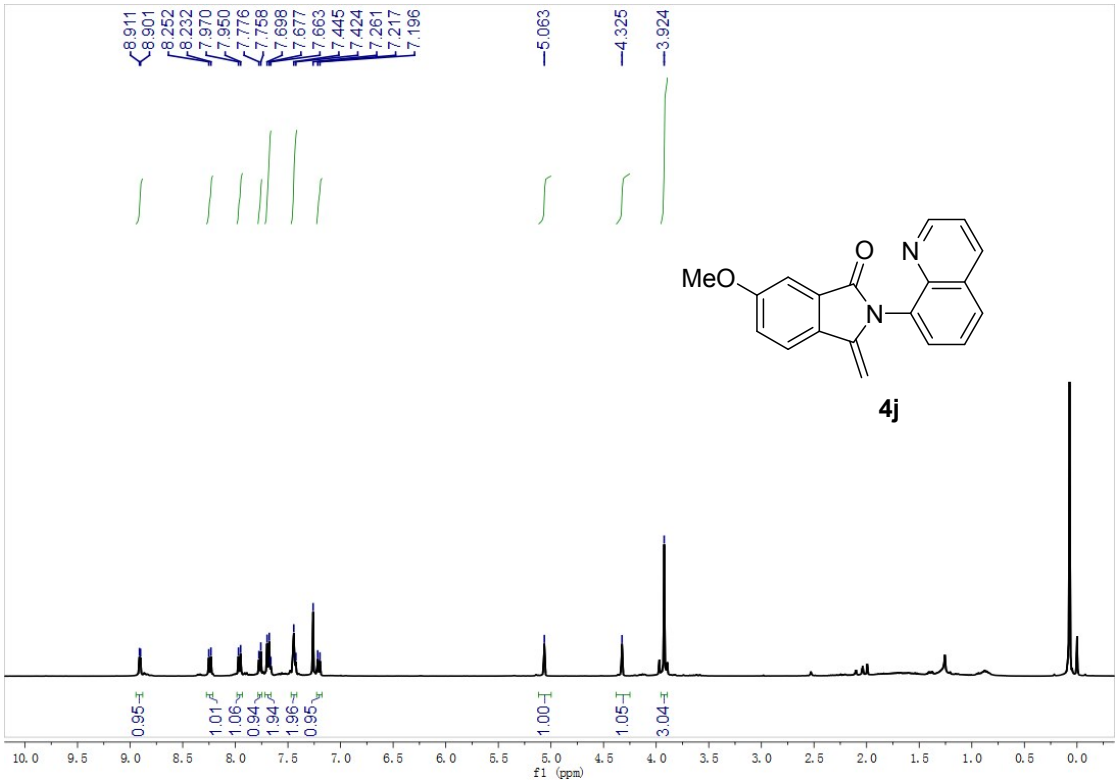
^{1}H NMR Spectrum of **4i**



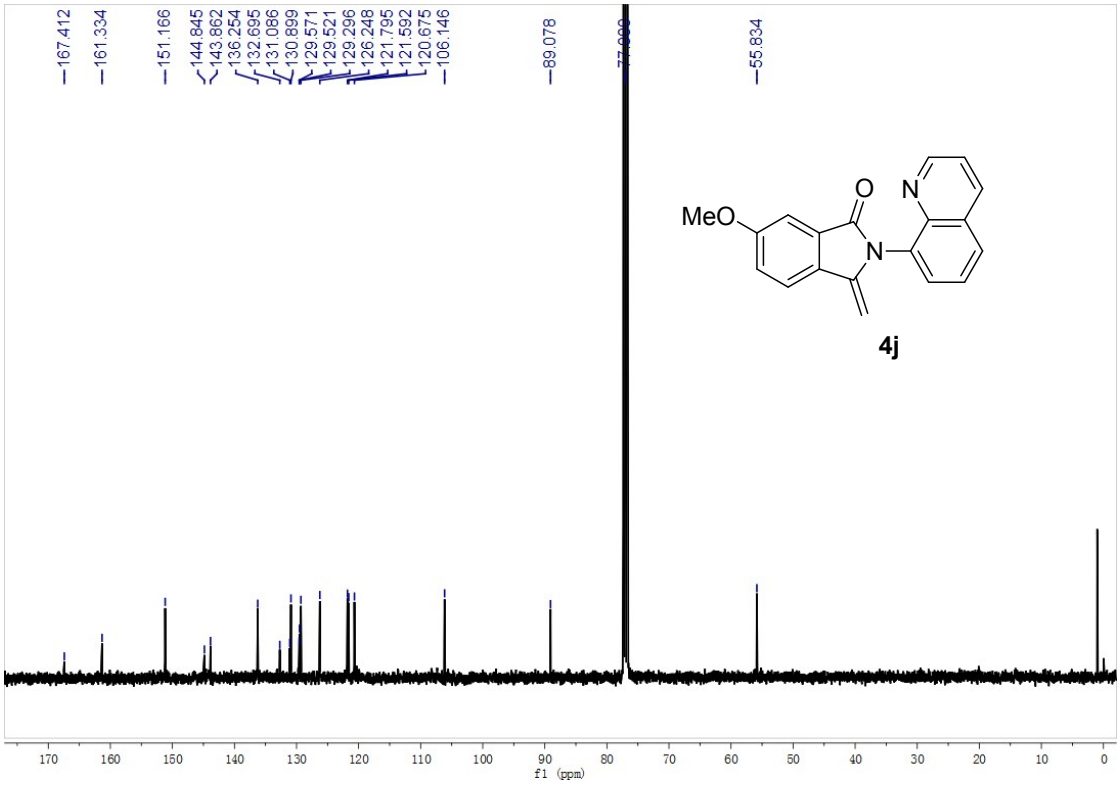
^{13}C NMR Spectrum of **4i**



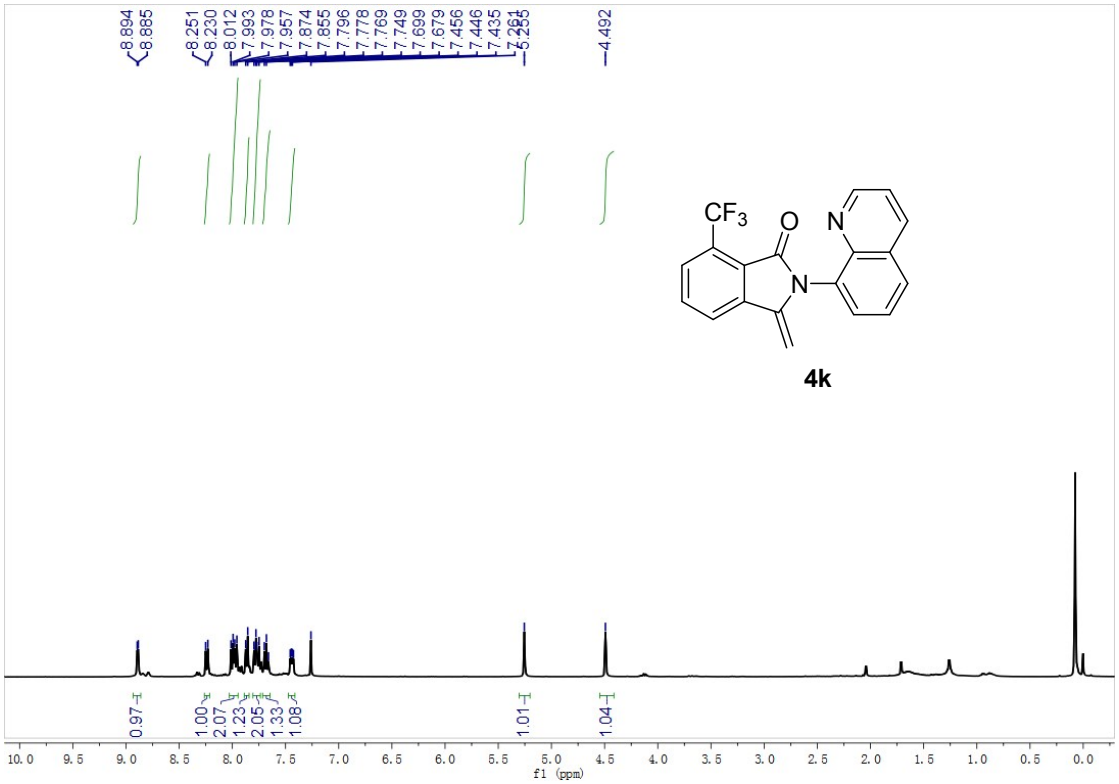
^{1}H NMR Spectrum of **4j**



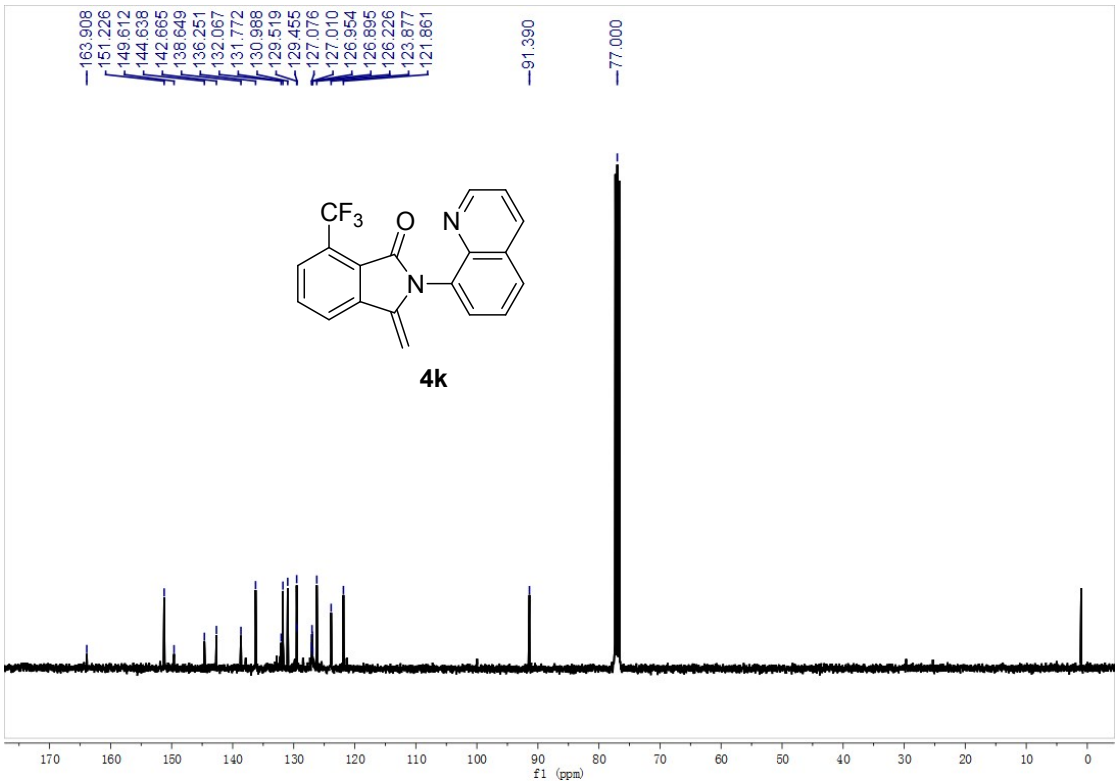
^{13}C NMR Spectrum of **4j**



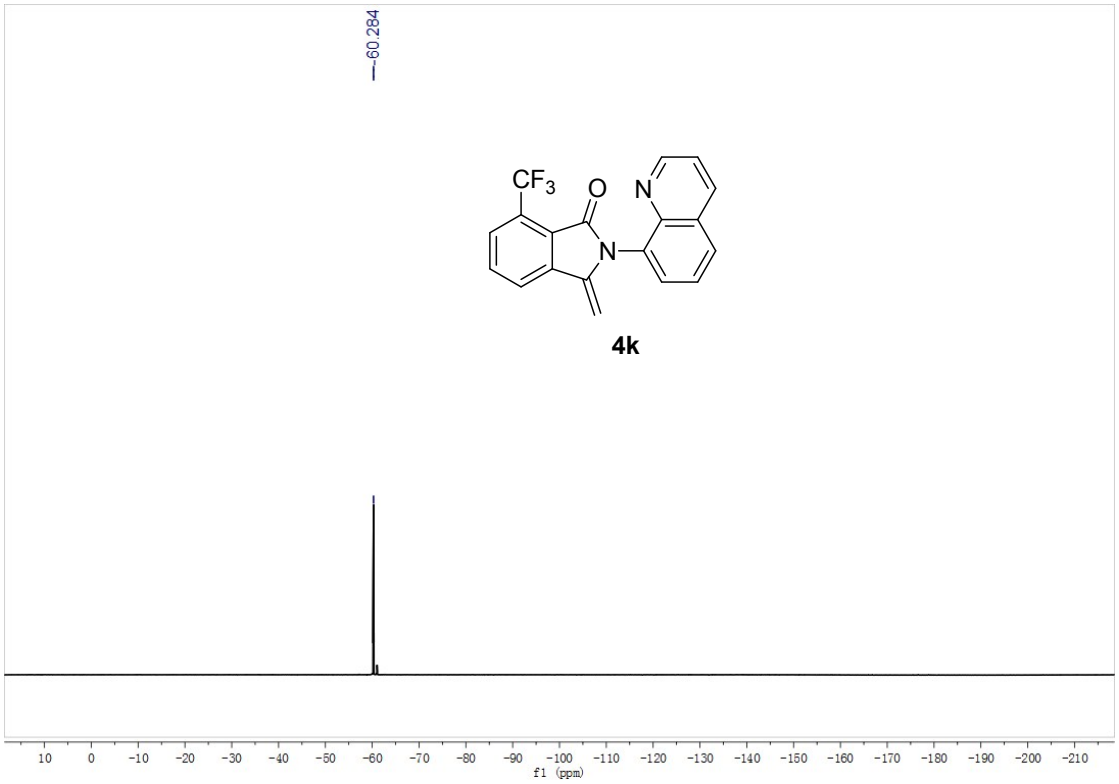
^{1}H NMR Spectrum of **4k**



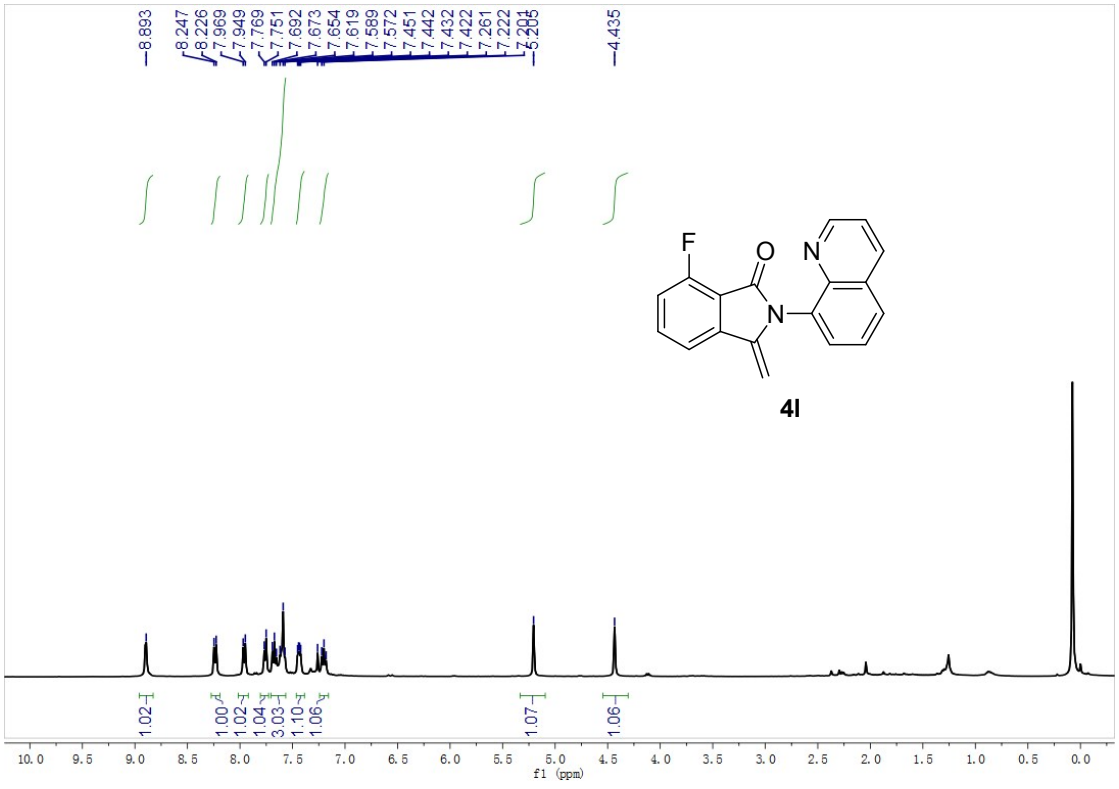
^{13}C NMR Spectrum of **4k**



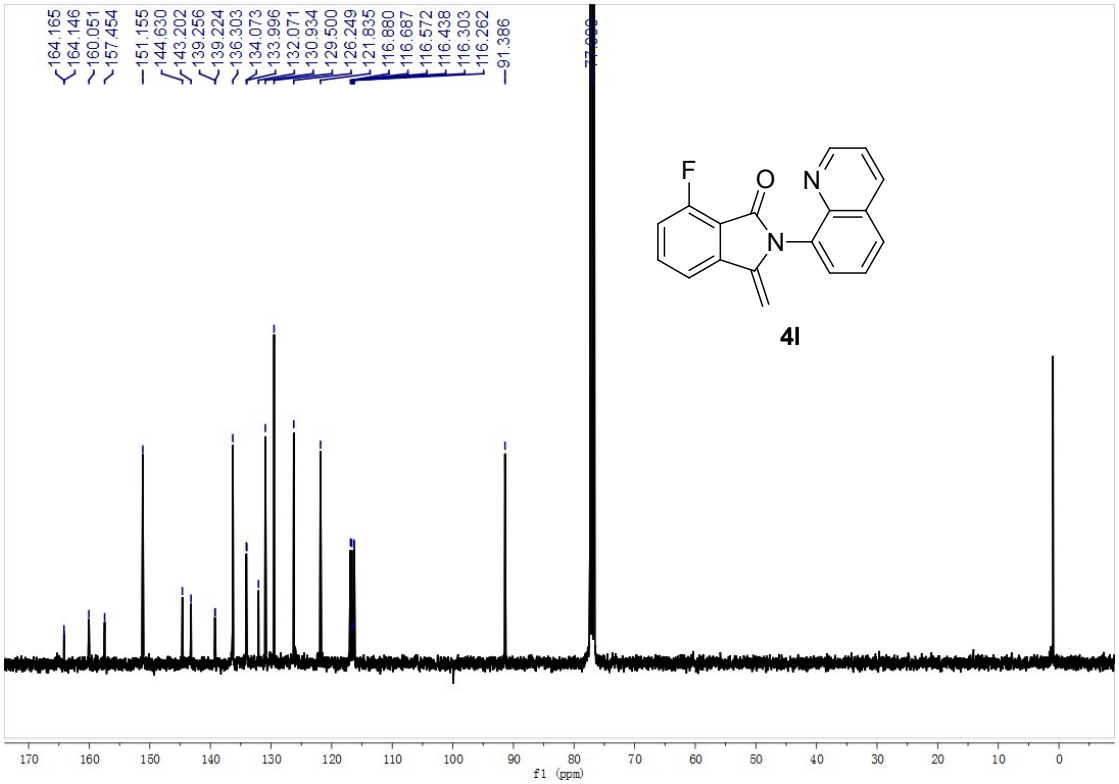
^{19}F NMR Spectrum of **4k**



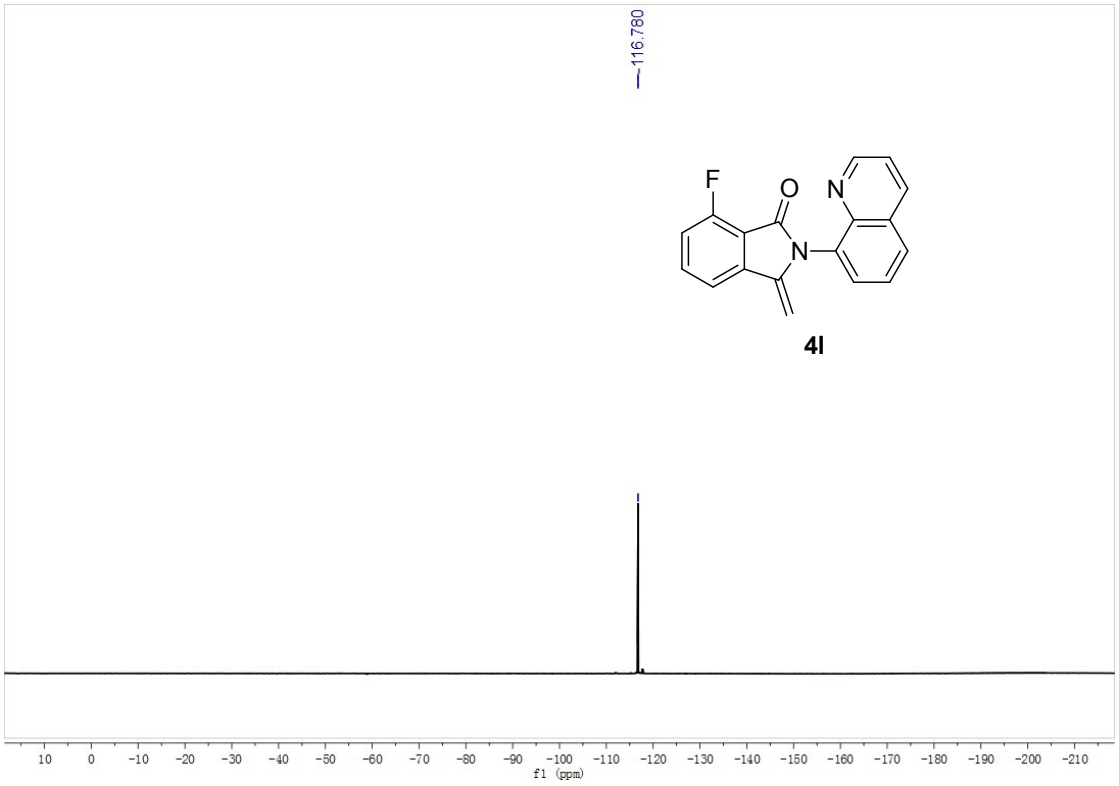
^{1}H NMR Spectrum of **4l**



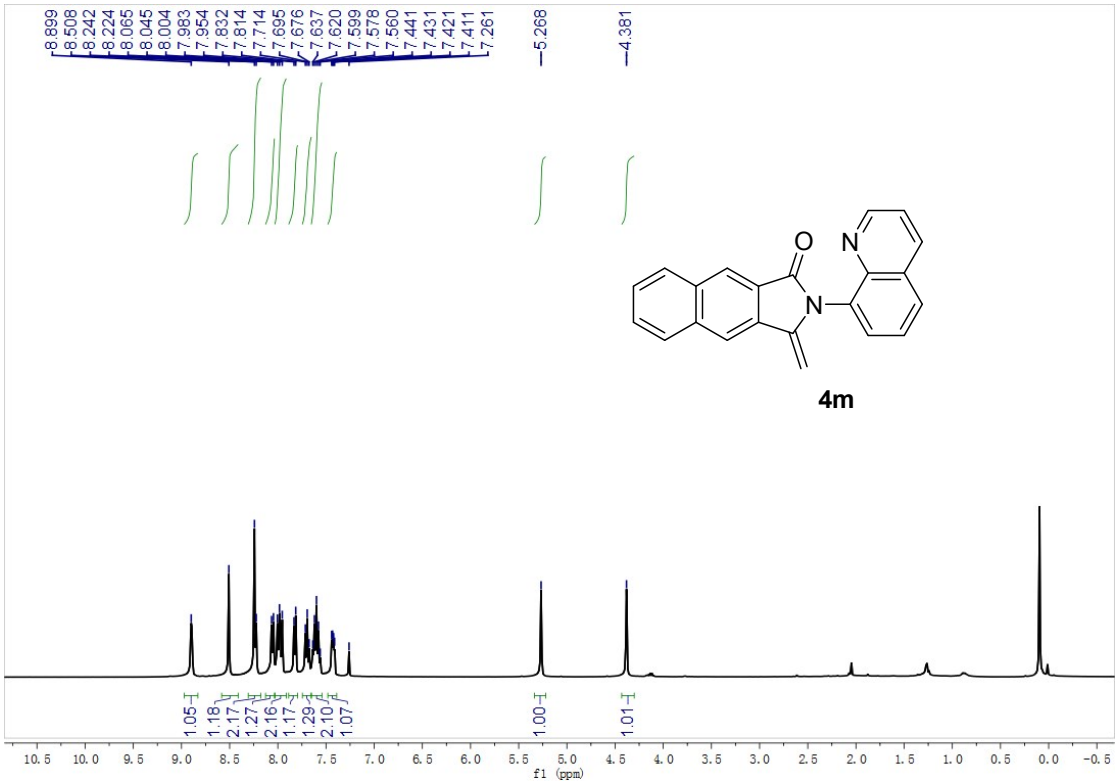
^{13}C NMR Spectrum of **4l**



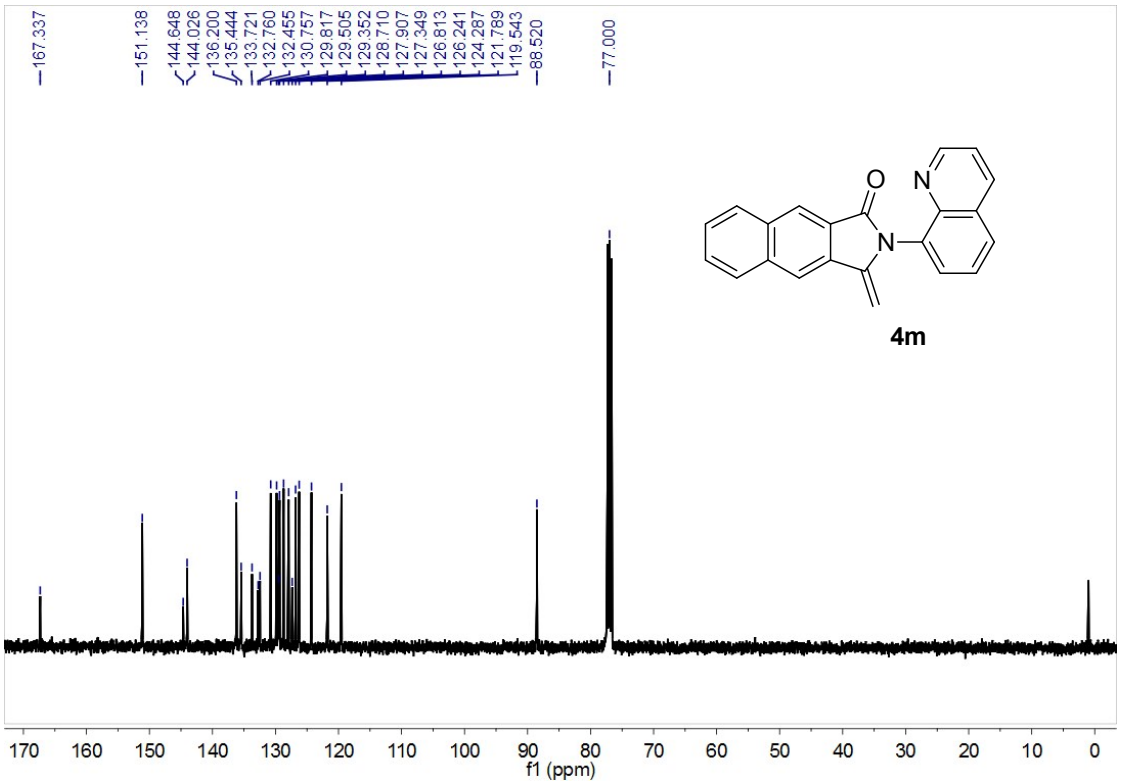
^{19}F NMR Spectrum of **4l**



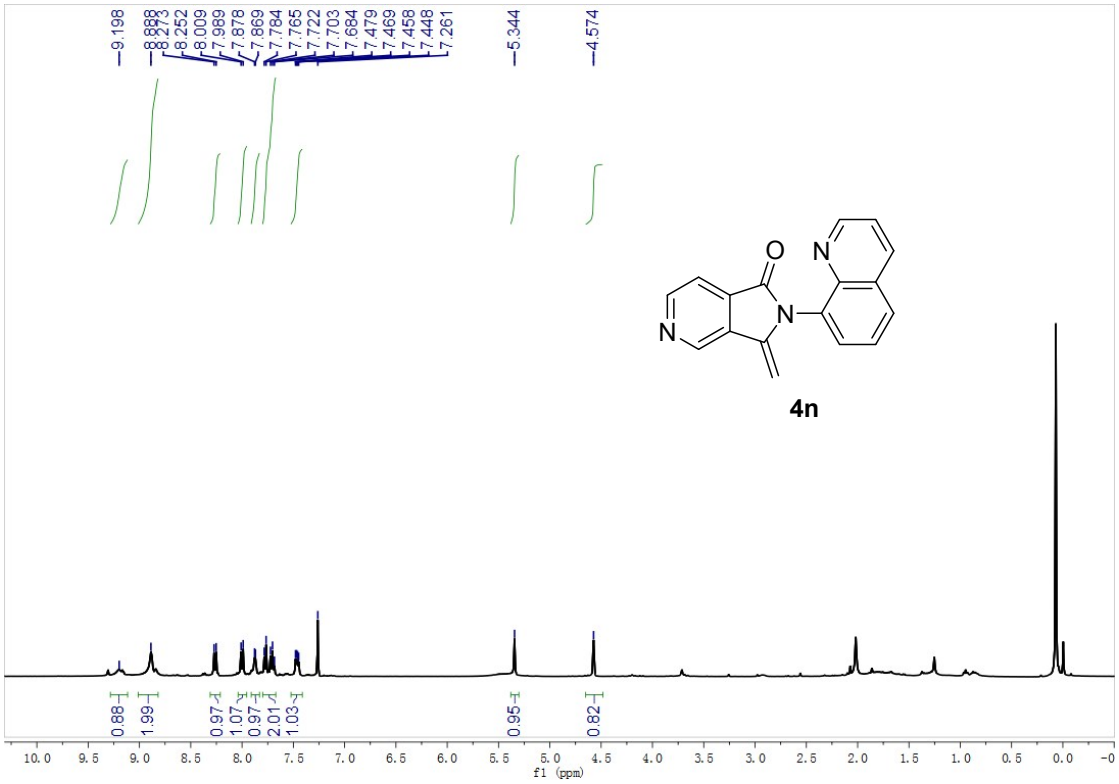
^{1}H NMR Spectrum of **4m**



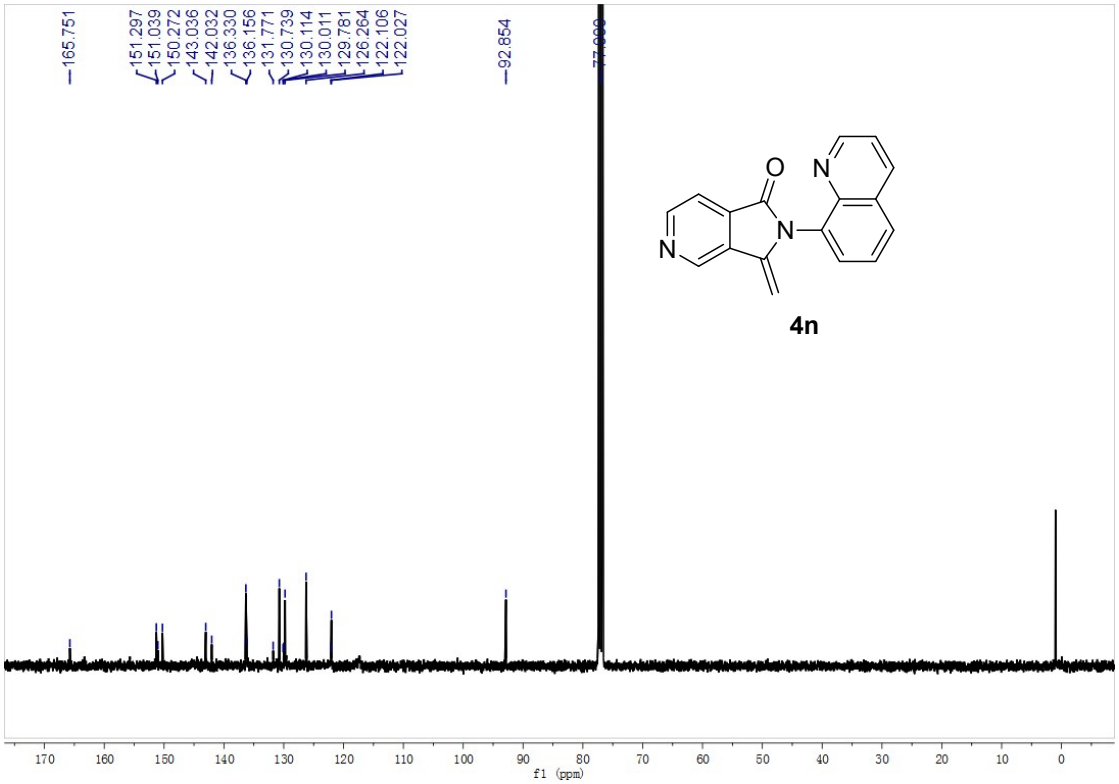
^{13}C NMR Spectrum of **4m**



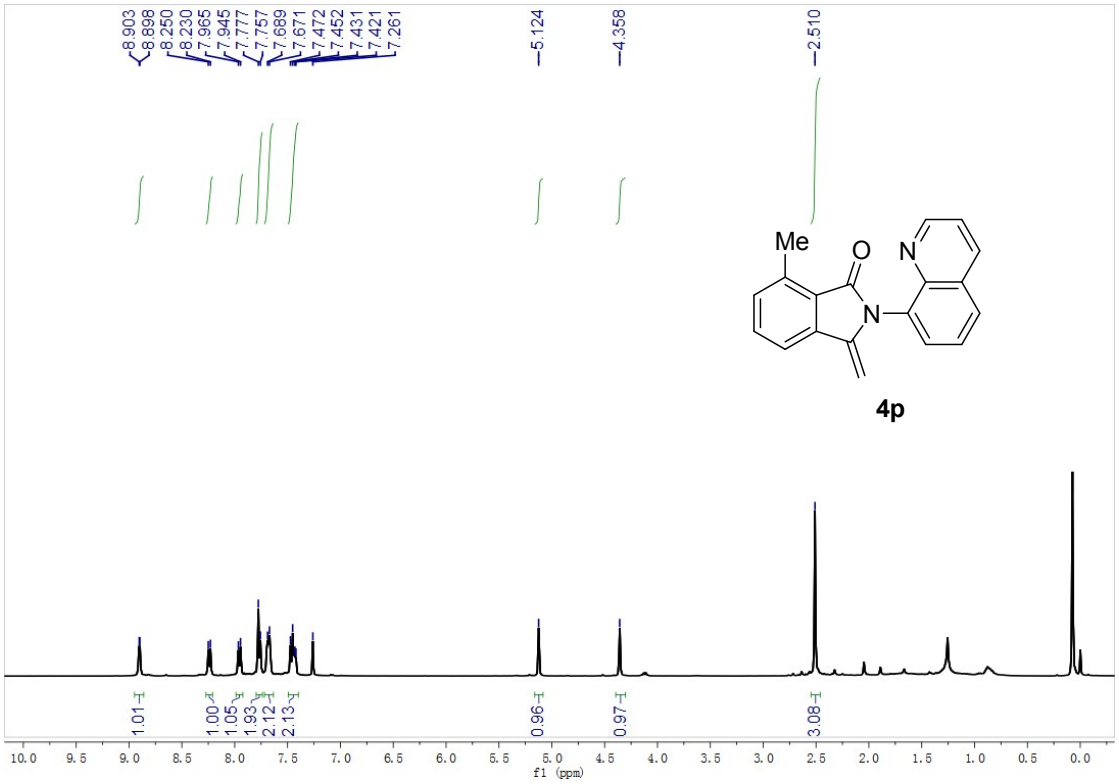
^{1}H NMR Spectrum of **4n**



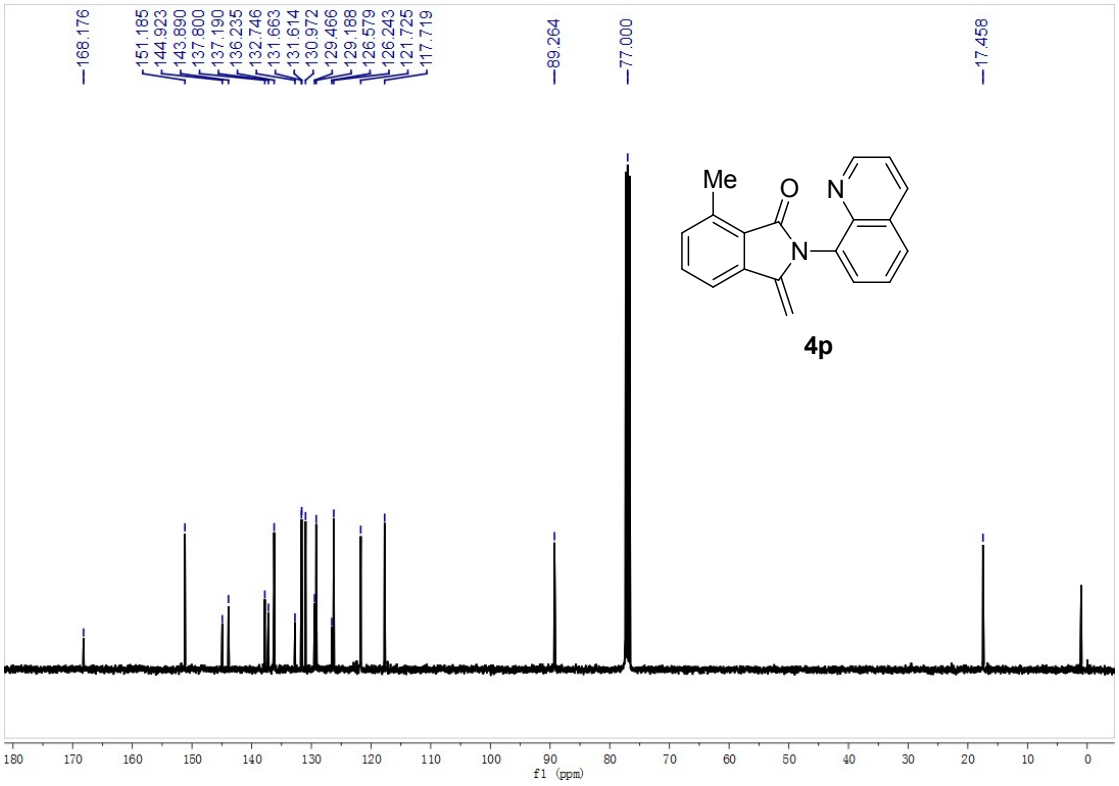
^{13}C NMR Spectrum of **4n**



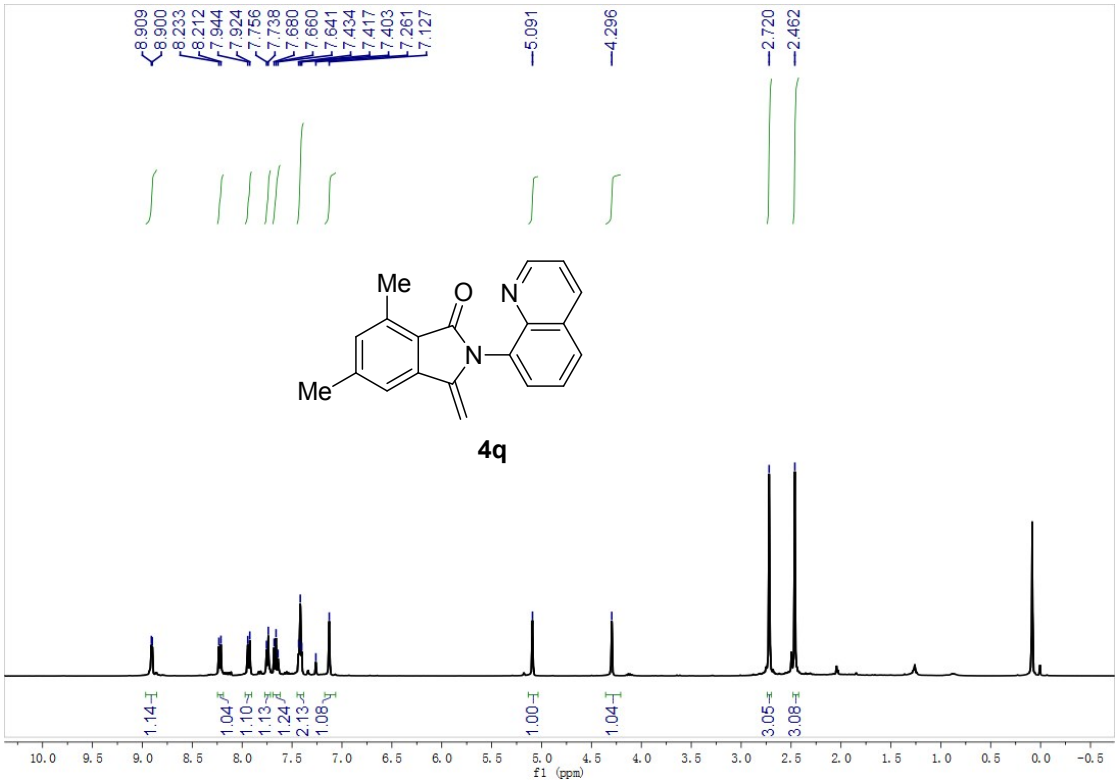
^{1}H NMR Spectrum of **4p**



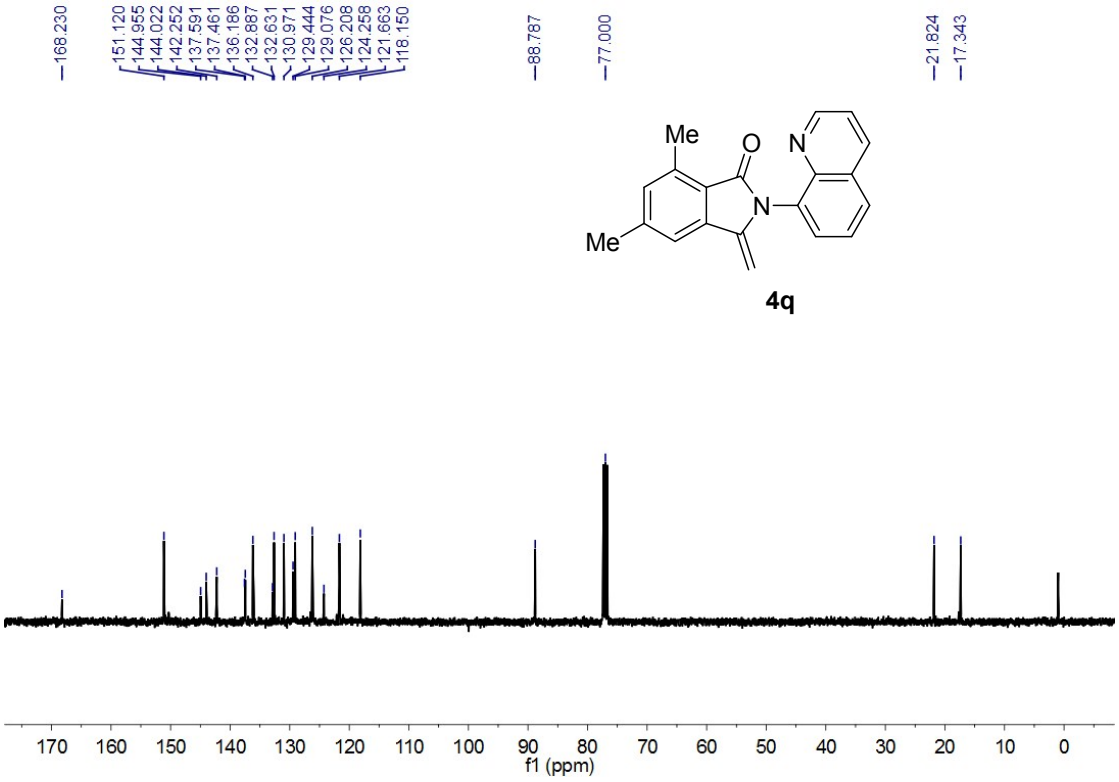
^{13}C NMR Spectrum of **4p**



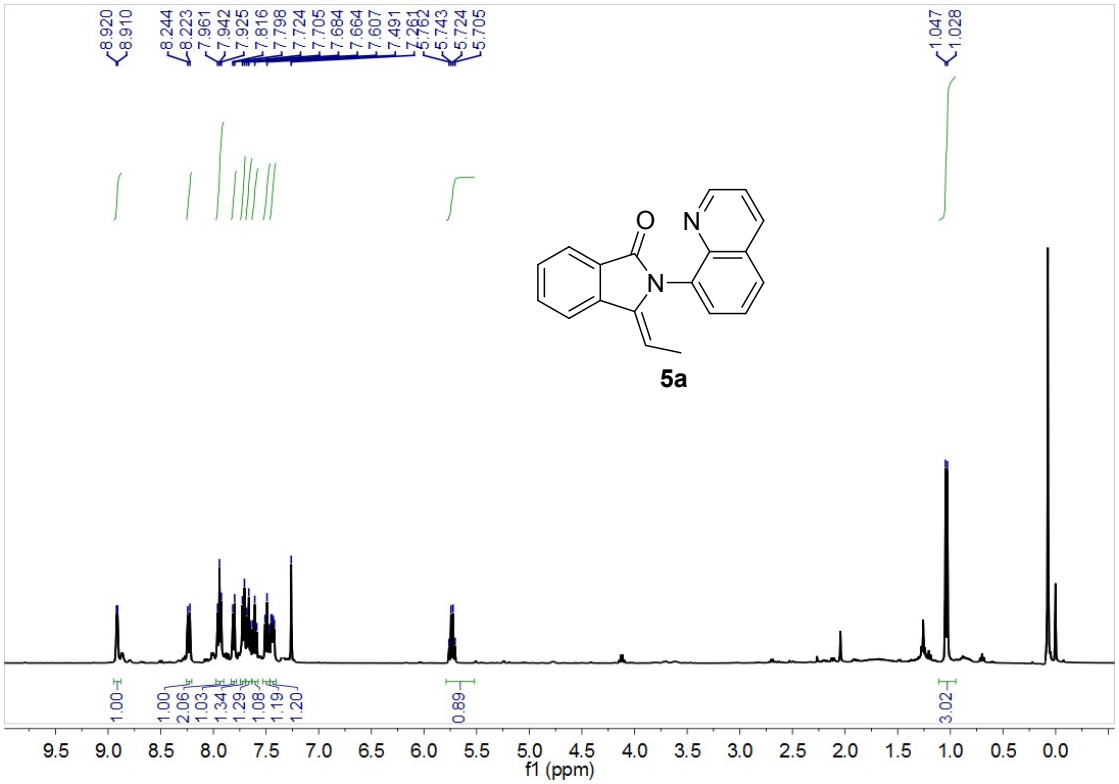
^{1}H NMR Spectrum of **4q**



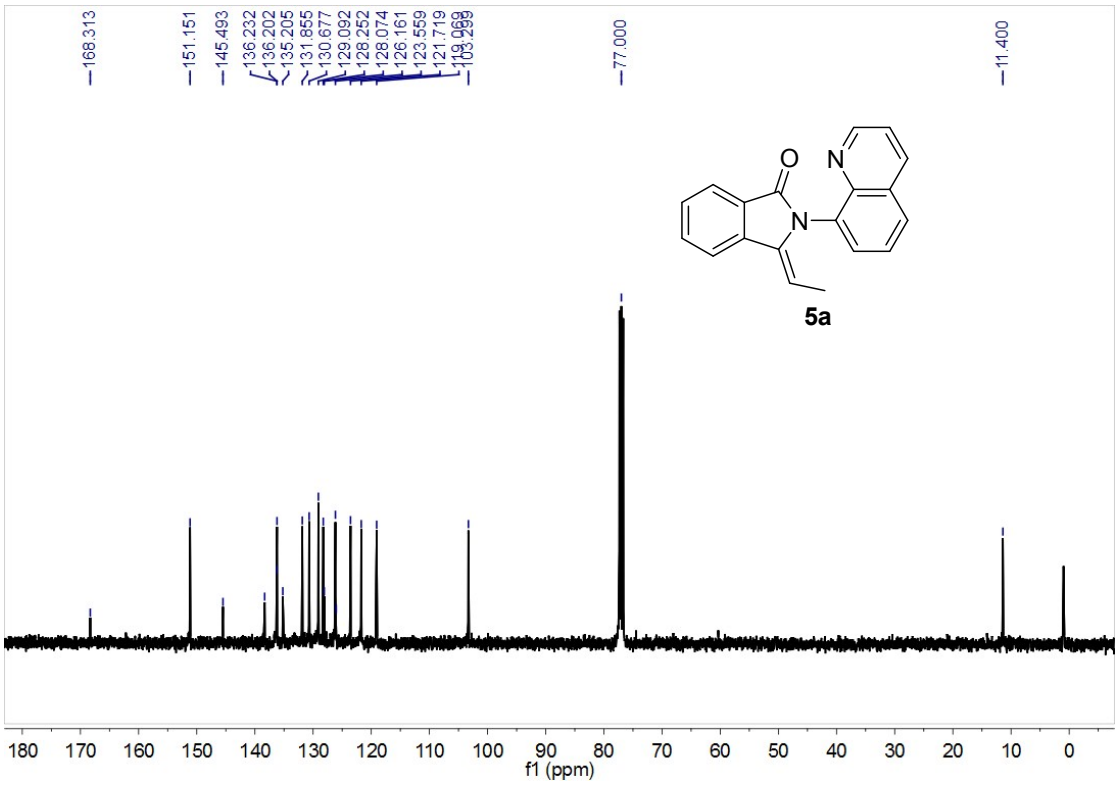
^{13}C NMR Spectrum of **4q**



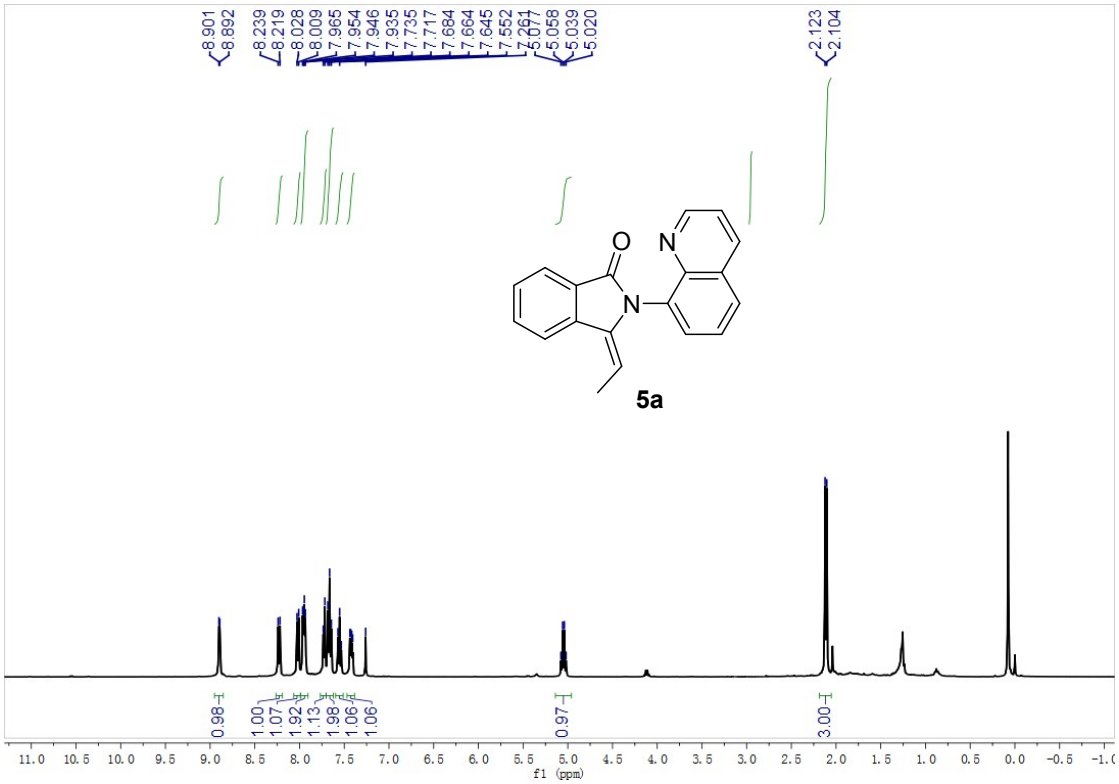
^{1}H NMR Spectrum of **5a (Z isomer)**



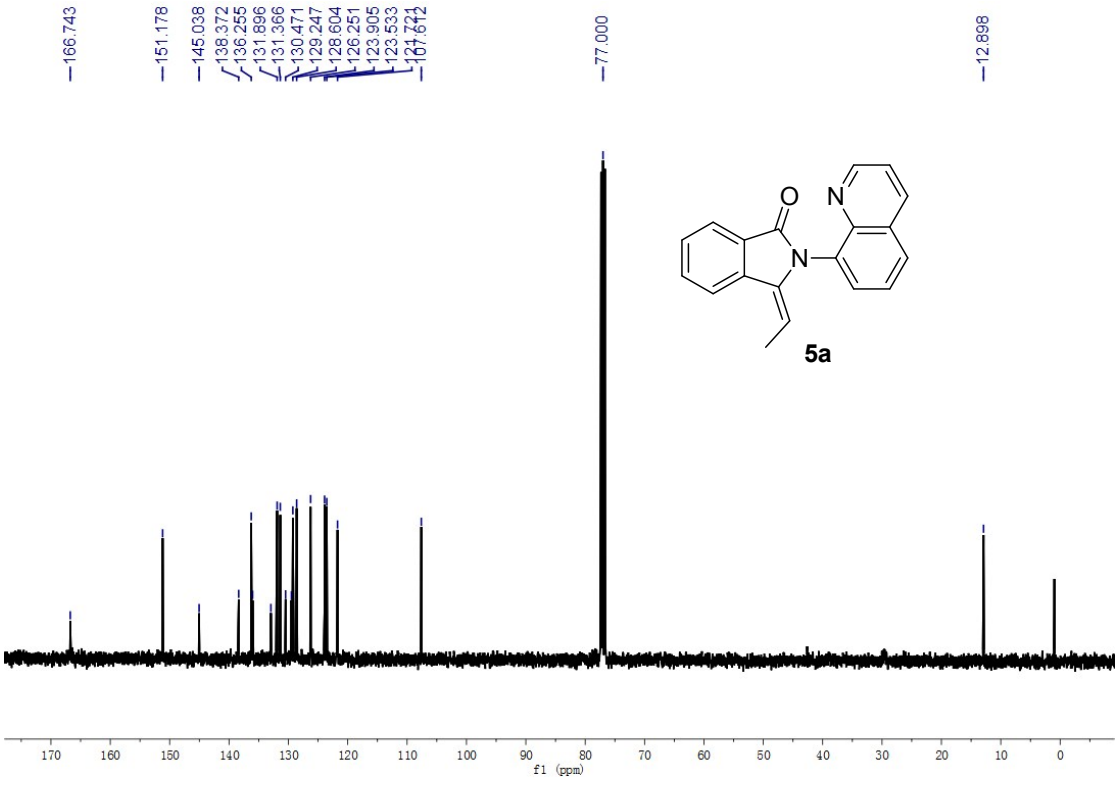
^{13}C NMR Spectrum of **5a (Z isomer)**



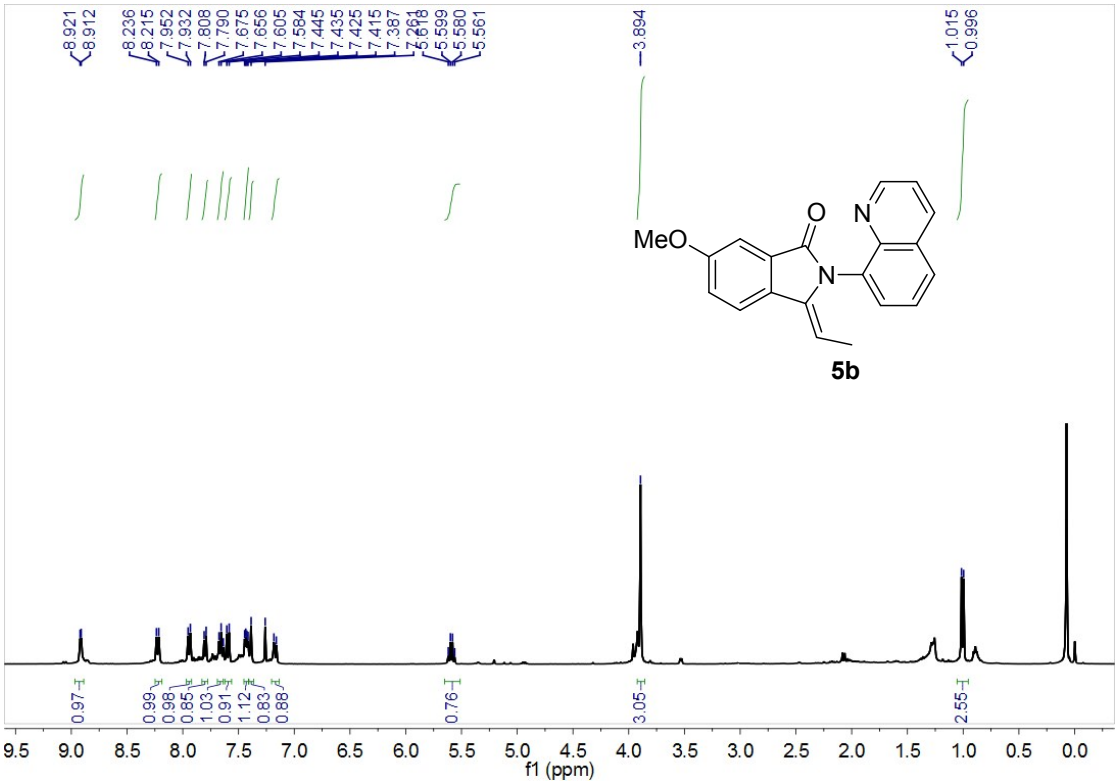
^{1}H NMR Spectrum of **5a (E isomer)**



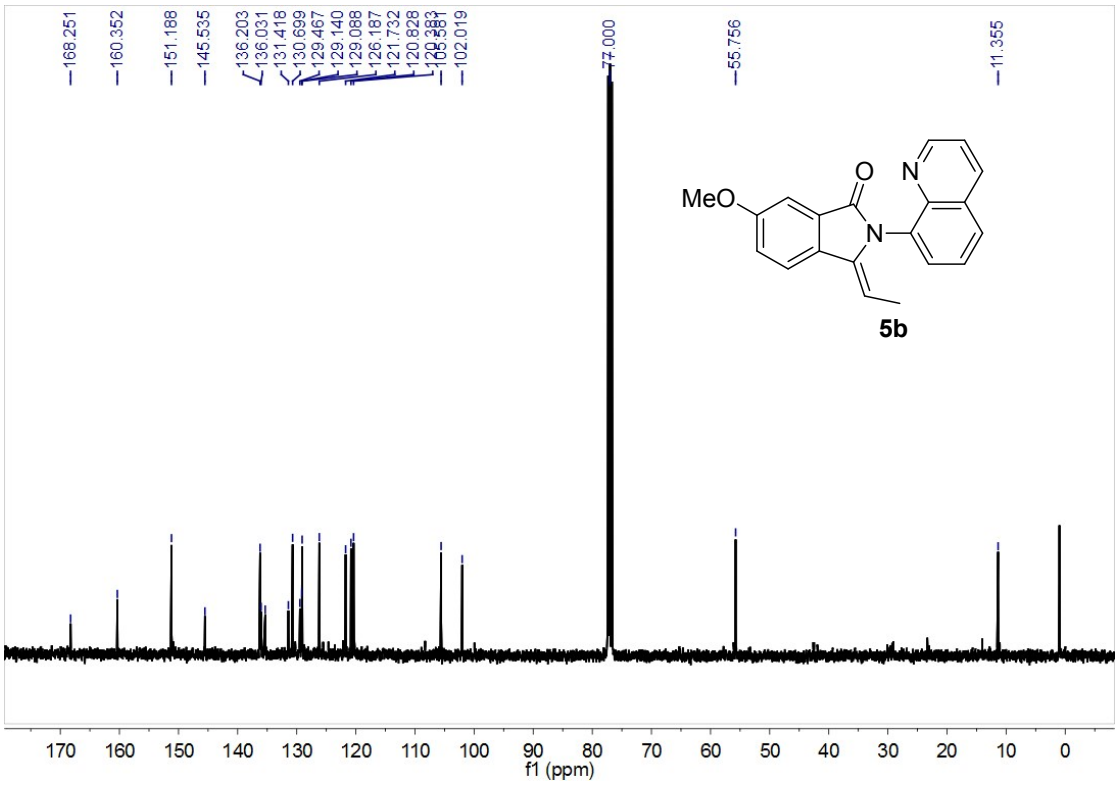
^{13}C NMR Spectrum of **5a (E isomer)**



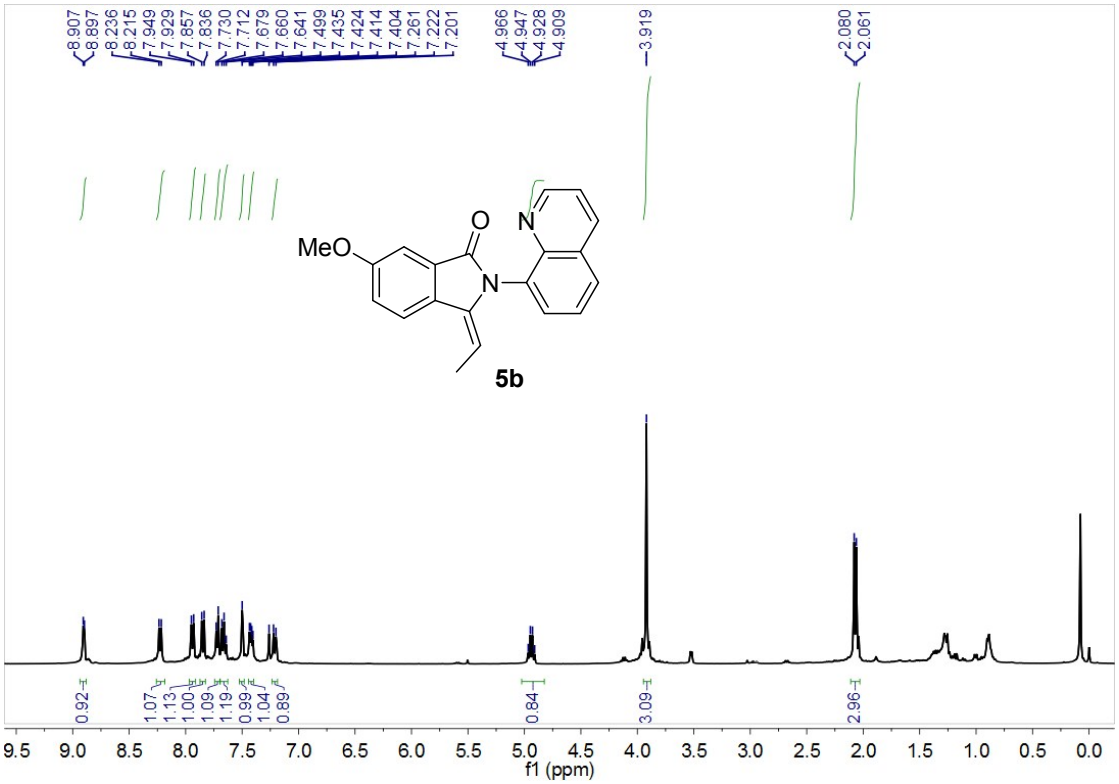
^{1}H NMR Spectrum of **5b (Z isomer)**



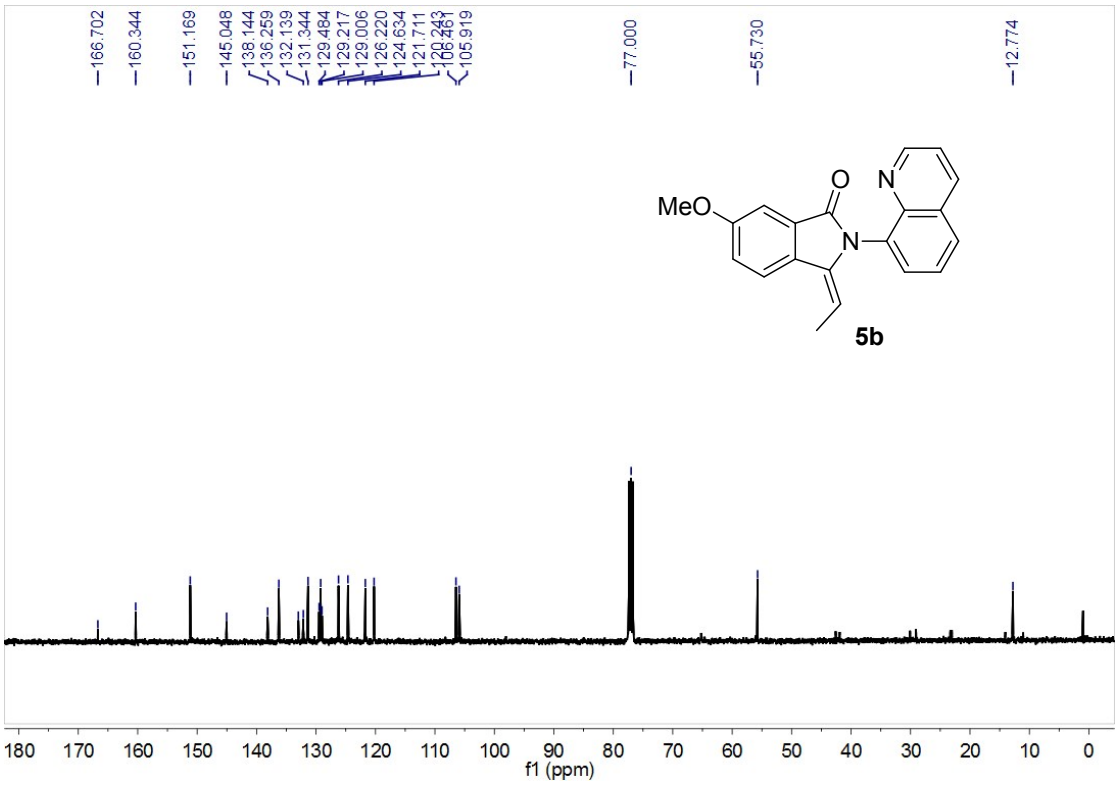
^{13}C NMR Spectrum of **5b (Z isomer)**



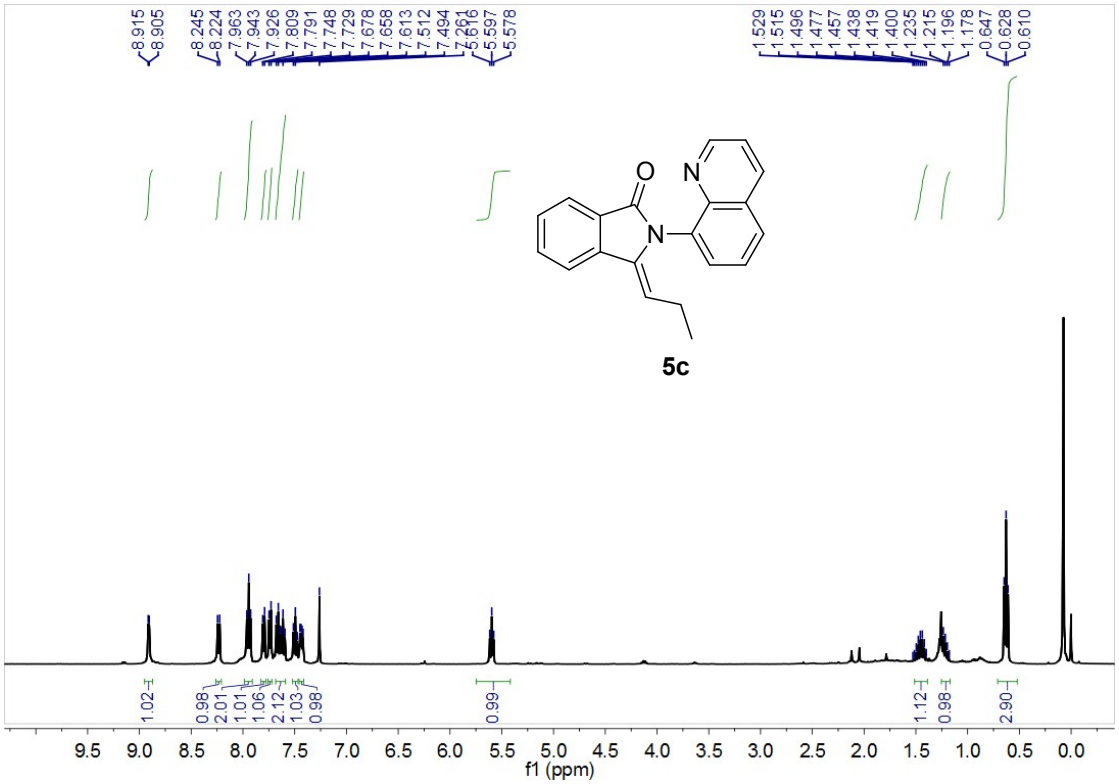
^{1}H NMR Spectrum of **5b (E isomer)**



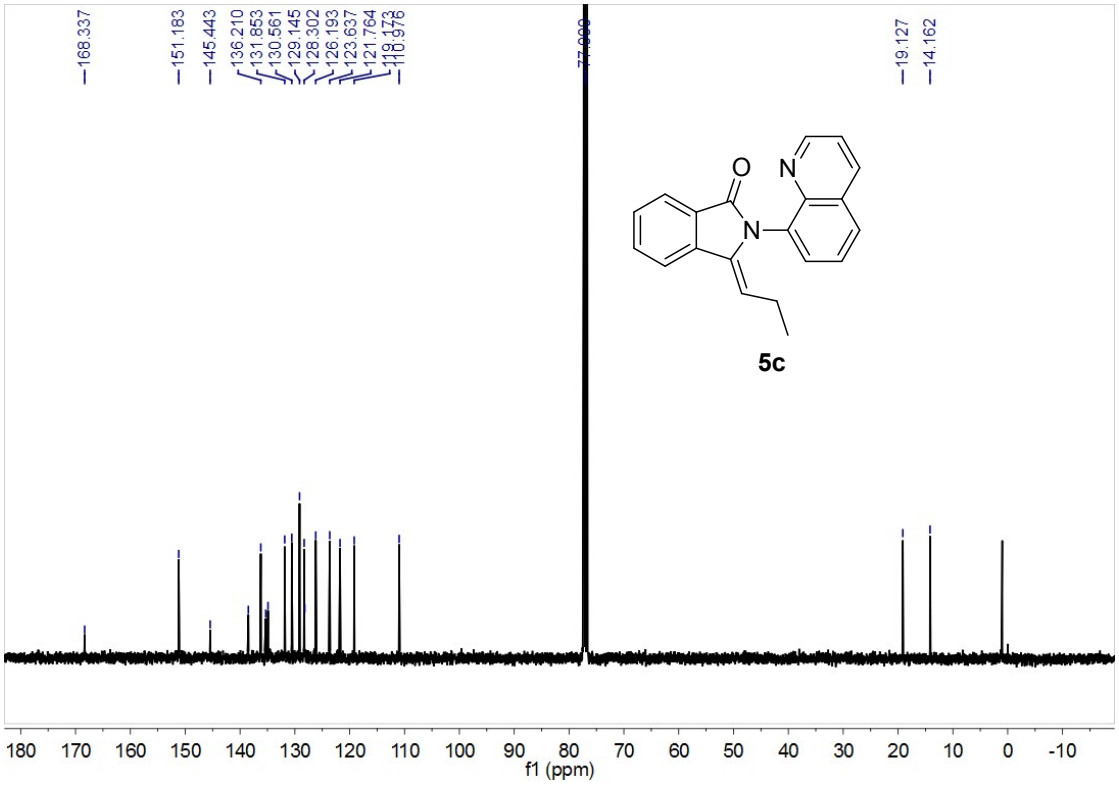
^{13}C NMR Spectrum of **5b (E isomer)**



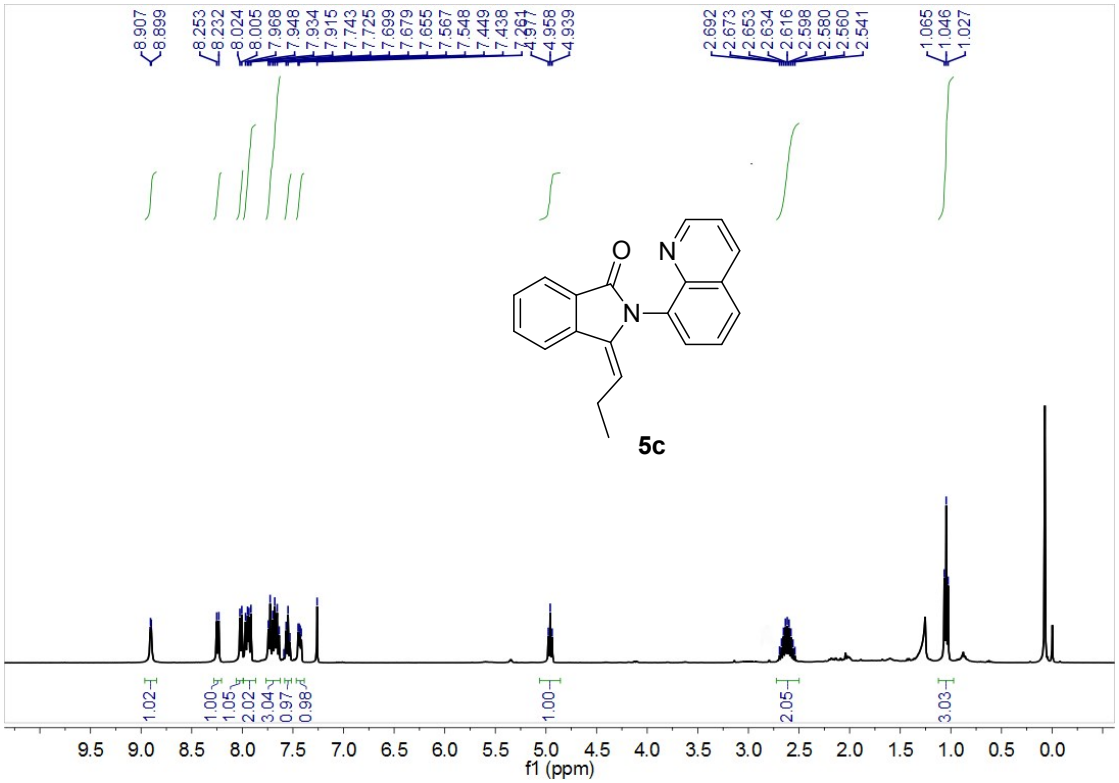
^{1}H NMR Spectrum of **5c (Z isomer)**



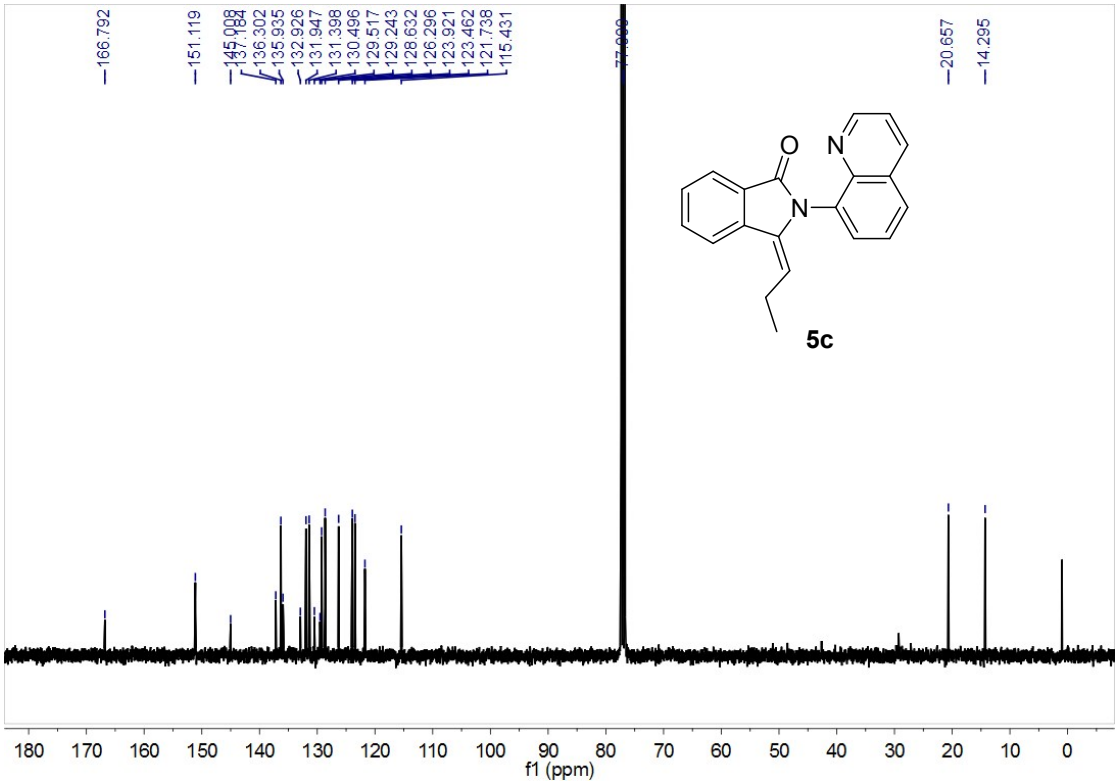
^{13}C NMR Spectrum of **5c (Z isomer)**



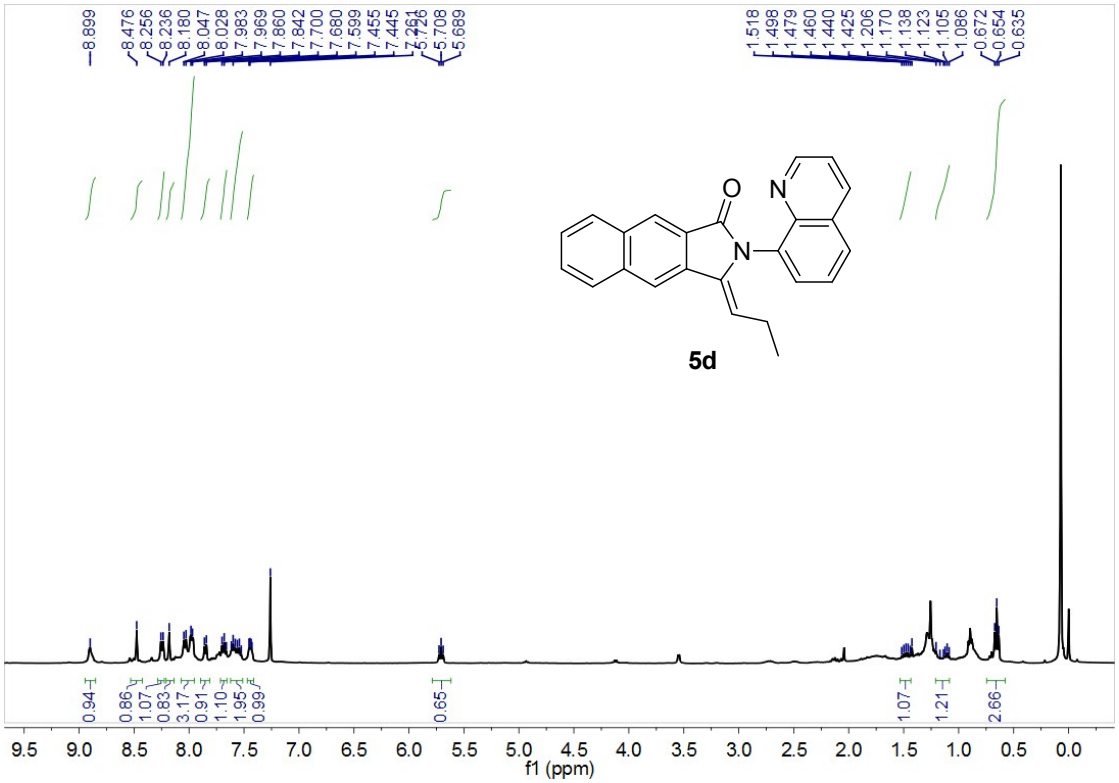
^{1}H NMR Spectrum of **5c (E isomer)**



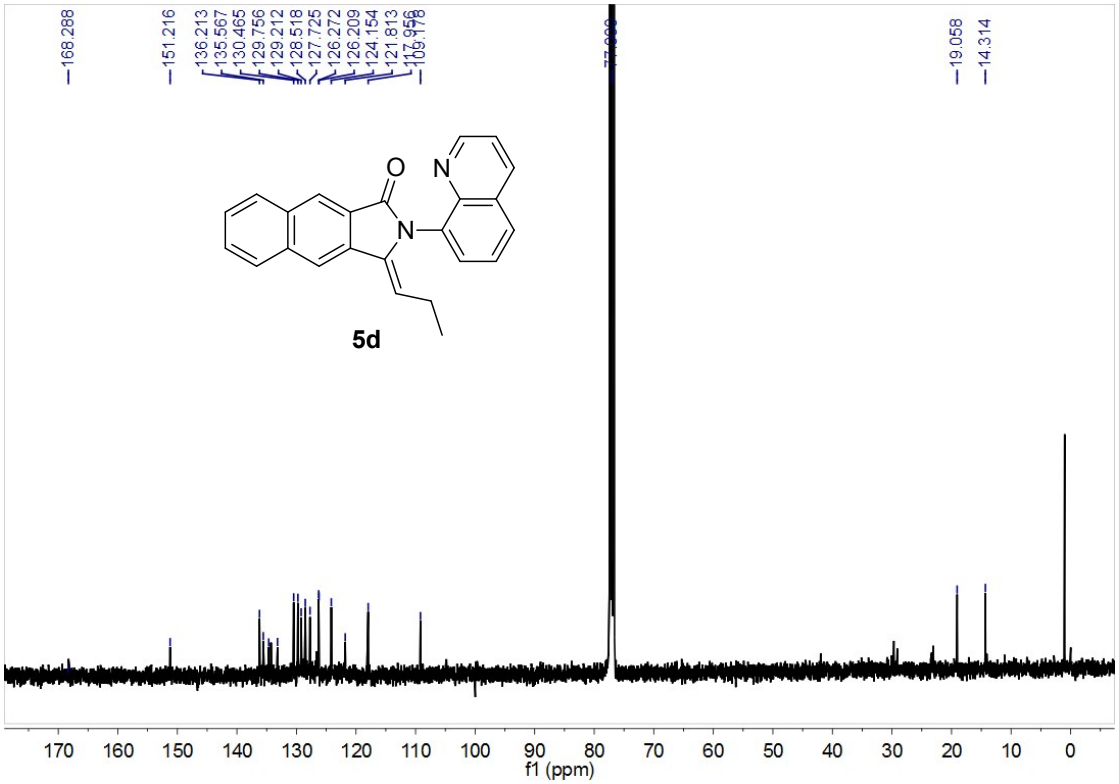
^{13}C NMR Spectrum of **5c (E isomer)**



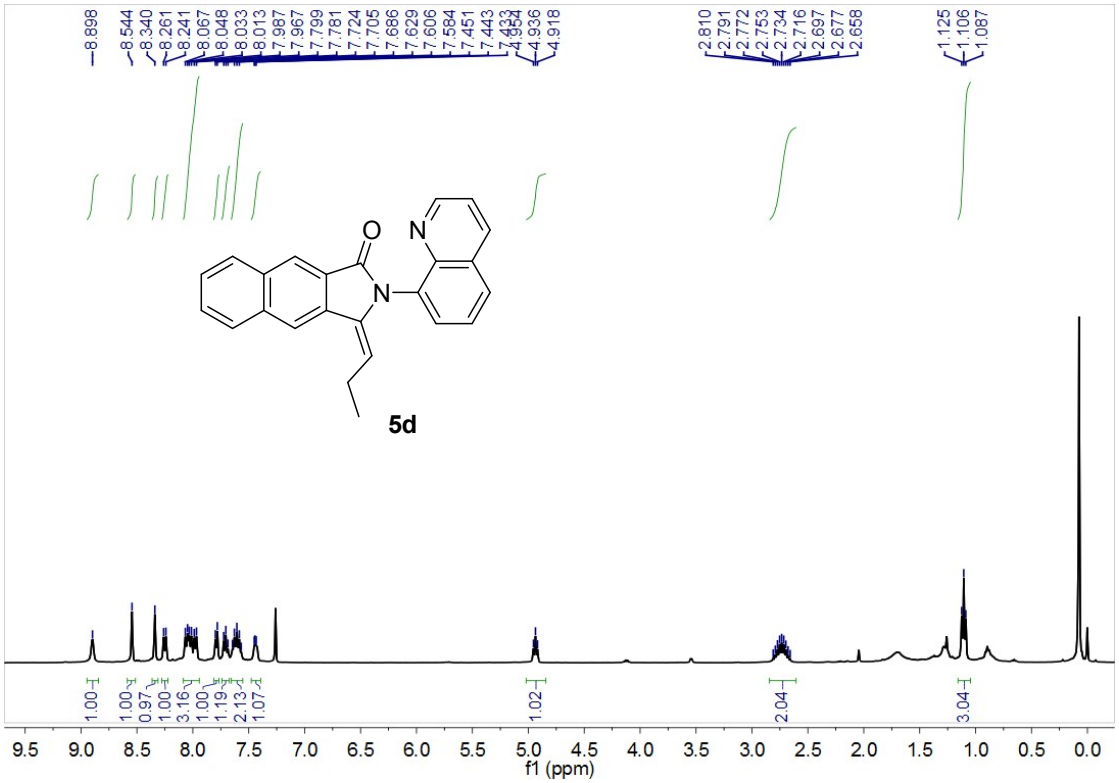
^{1}H NMR Spectrum of **5d (Z isomer)**



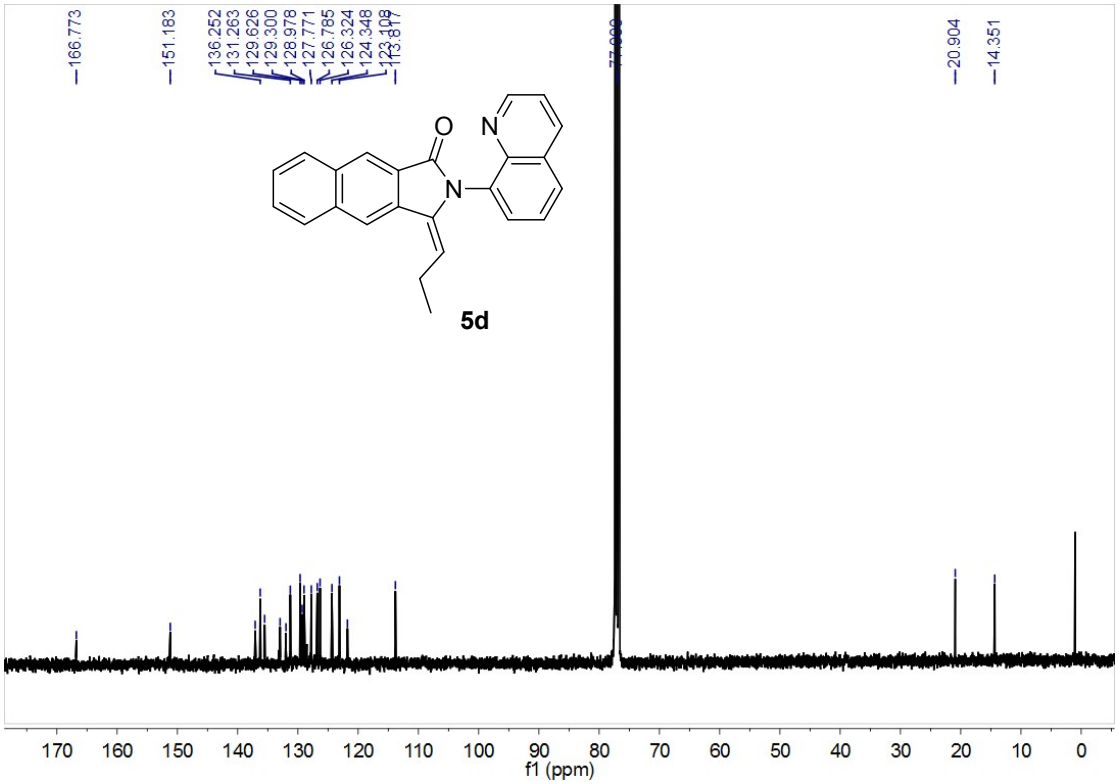
^{13}C NMR Spectrum of **5d (Z isomer)**



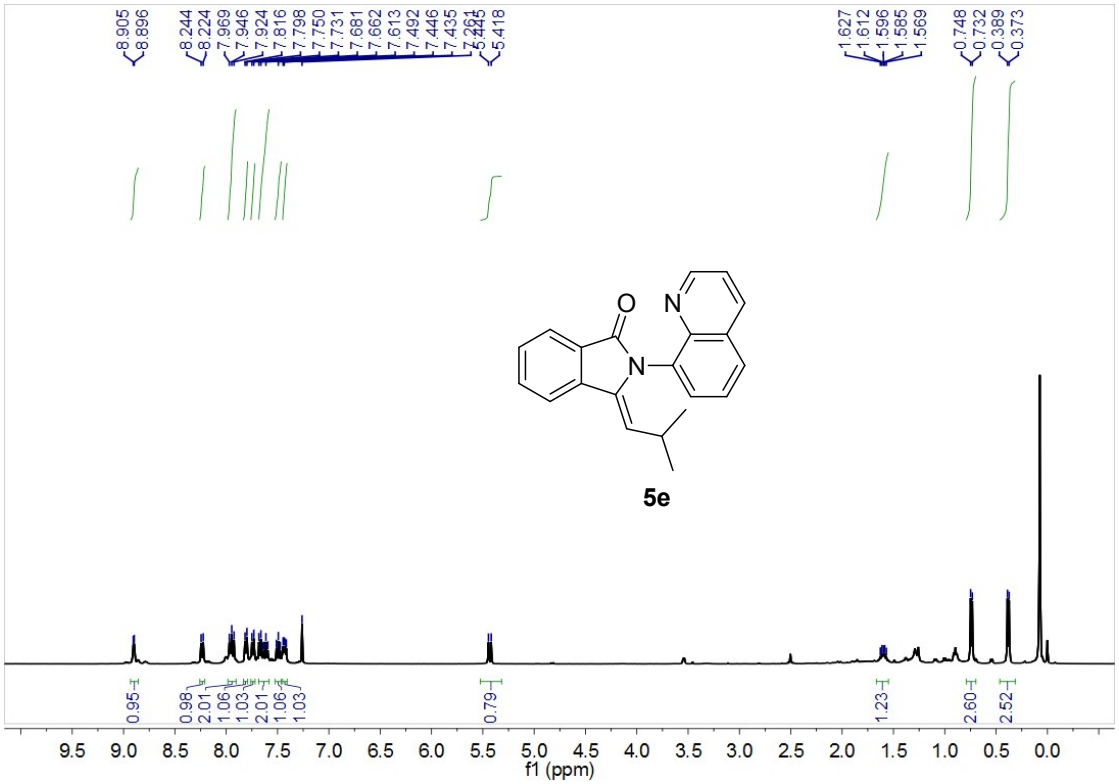
^{1}H NMR Spectrum of **5d (E isomer)**



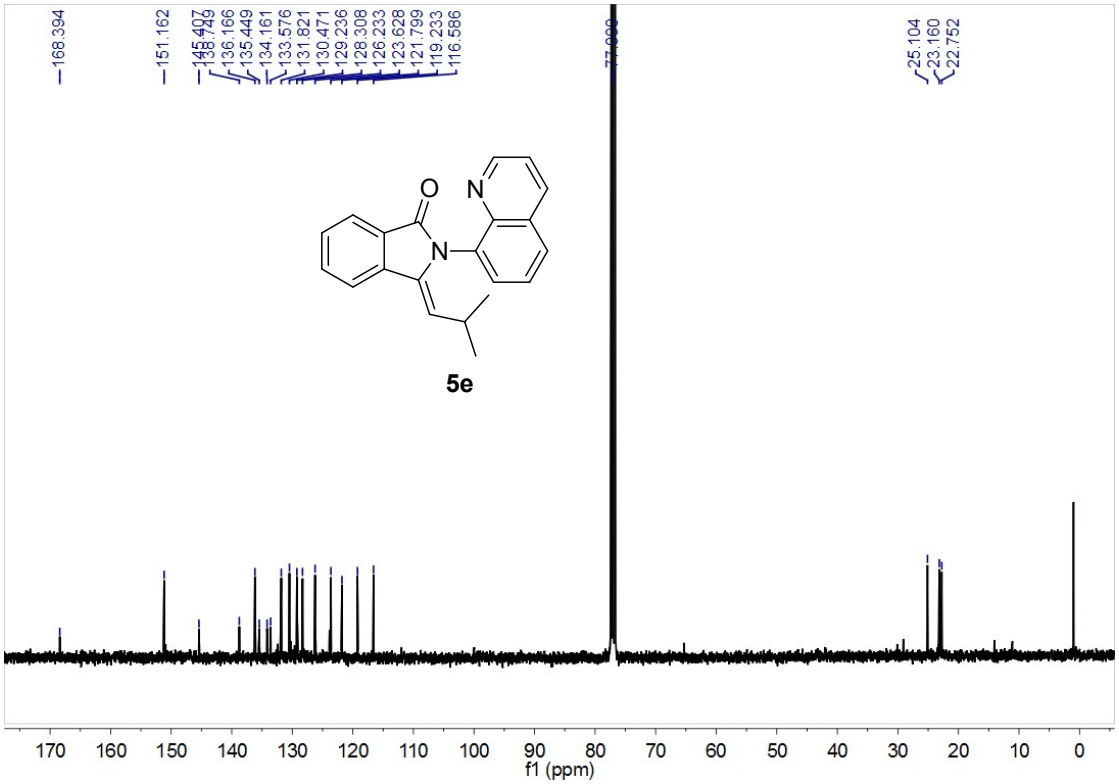
^{13}C NMR Spectrum of **5d (E isomer)**



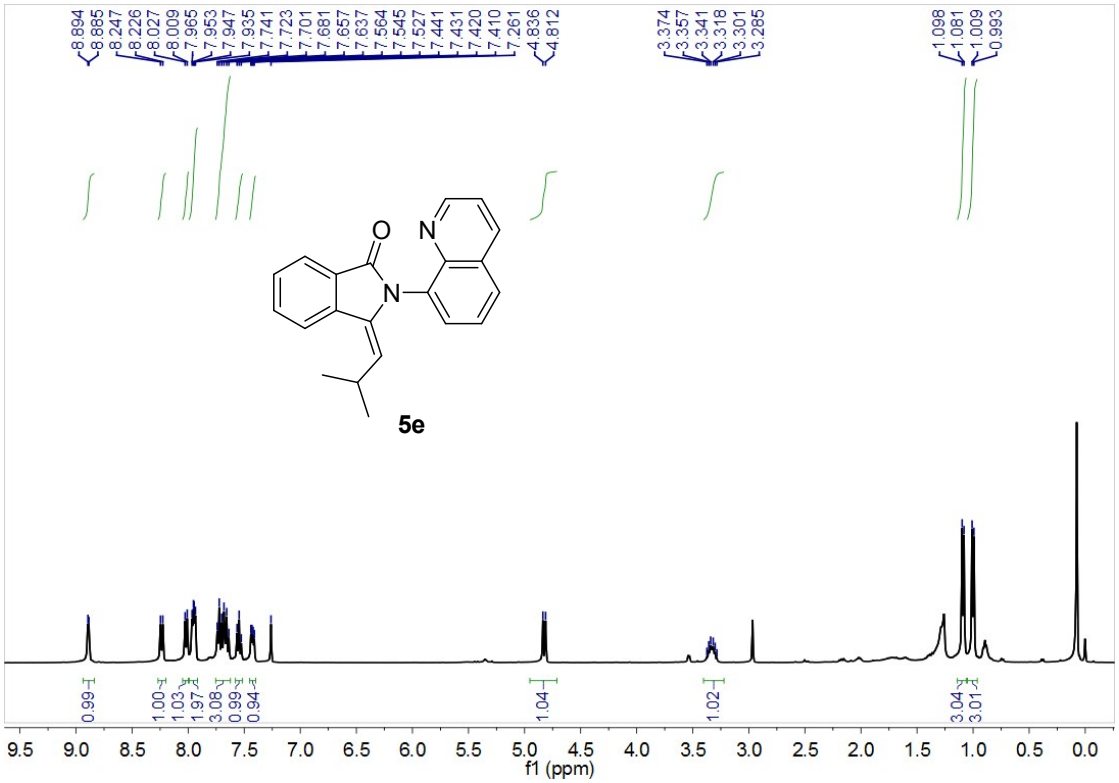
^{1}H NMR Spectrum of **5e (Z isomer)**



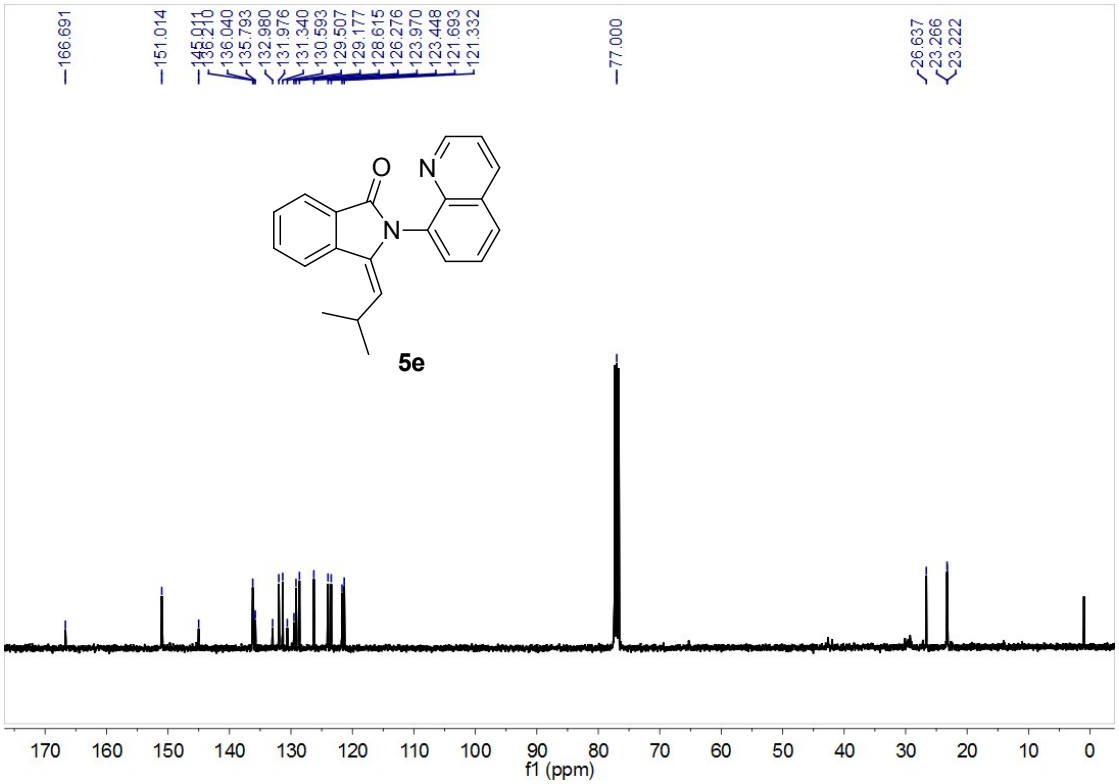
^{13}C NMR Spectrum of **5e (Z isomer)**



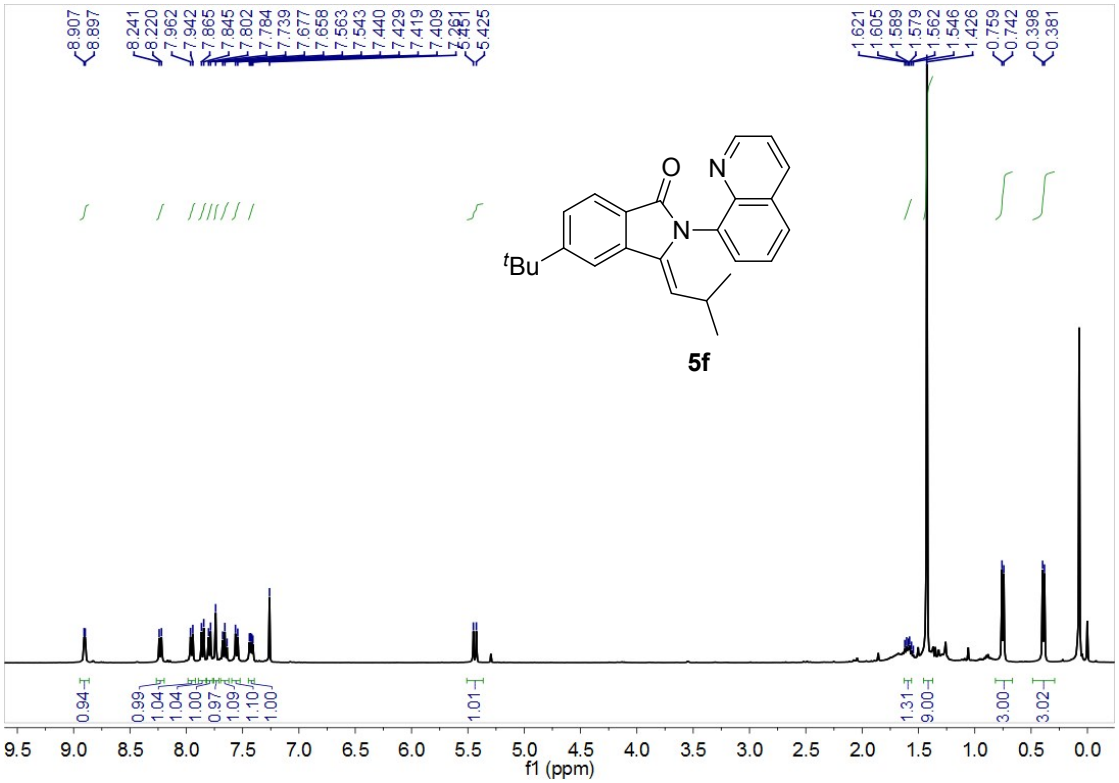
^{1}H NMR Spectrum of **5e (E isomer)**



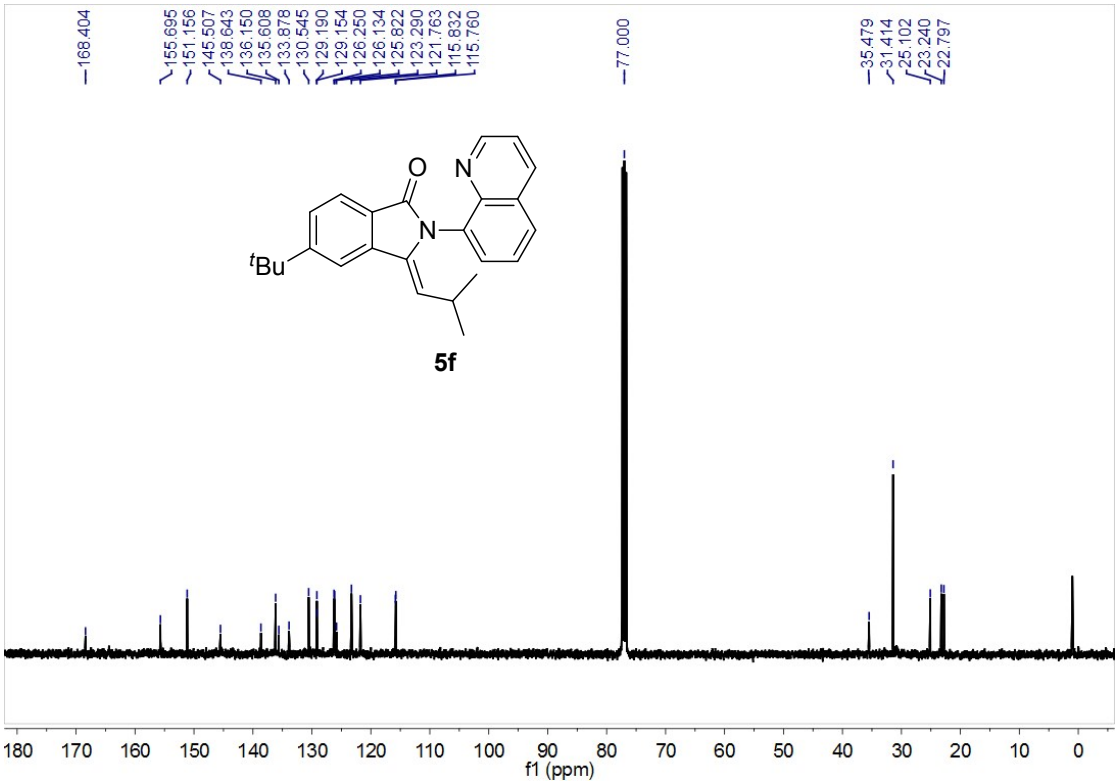
^{13}C NMR Spectrum of **5e (E isomer)**



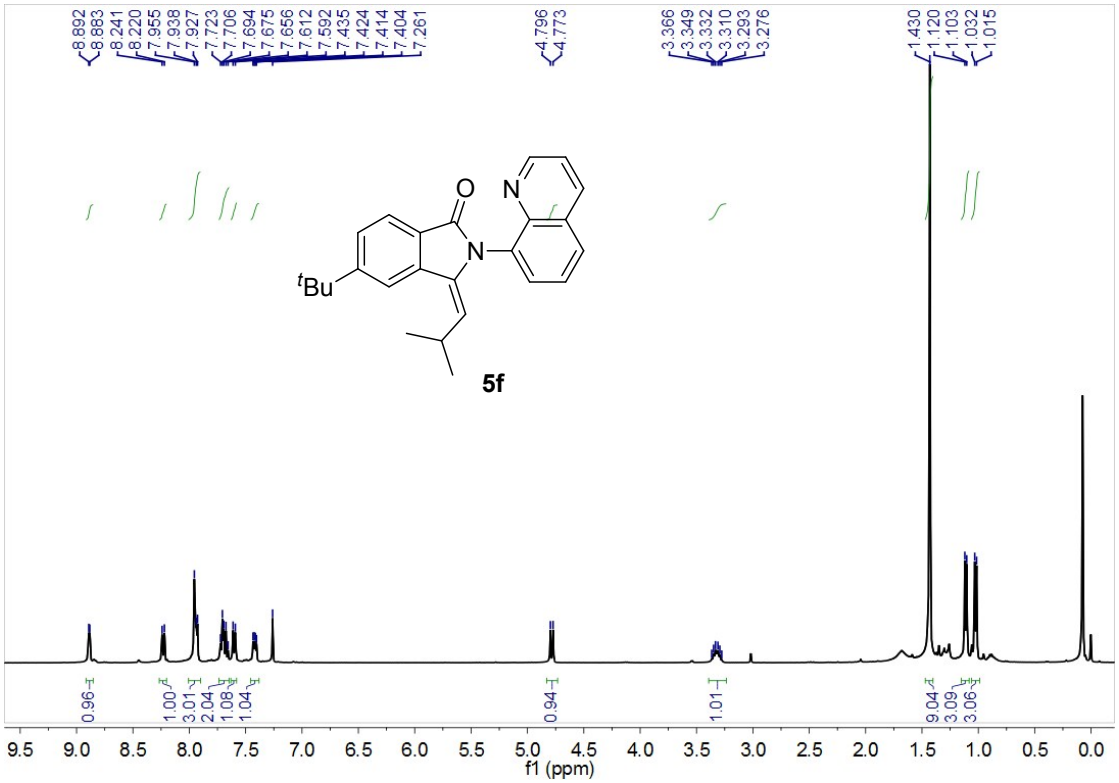
^{1}H NMR Spectrum of **5f (Z isomer)**



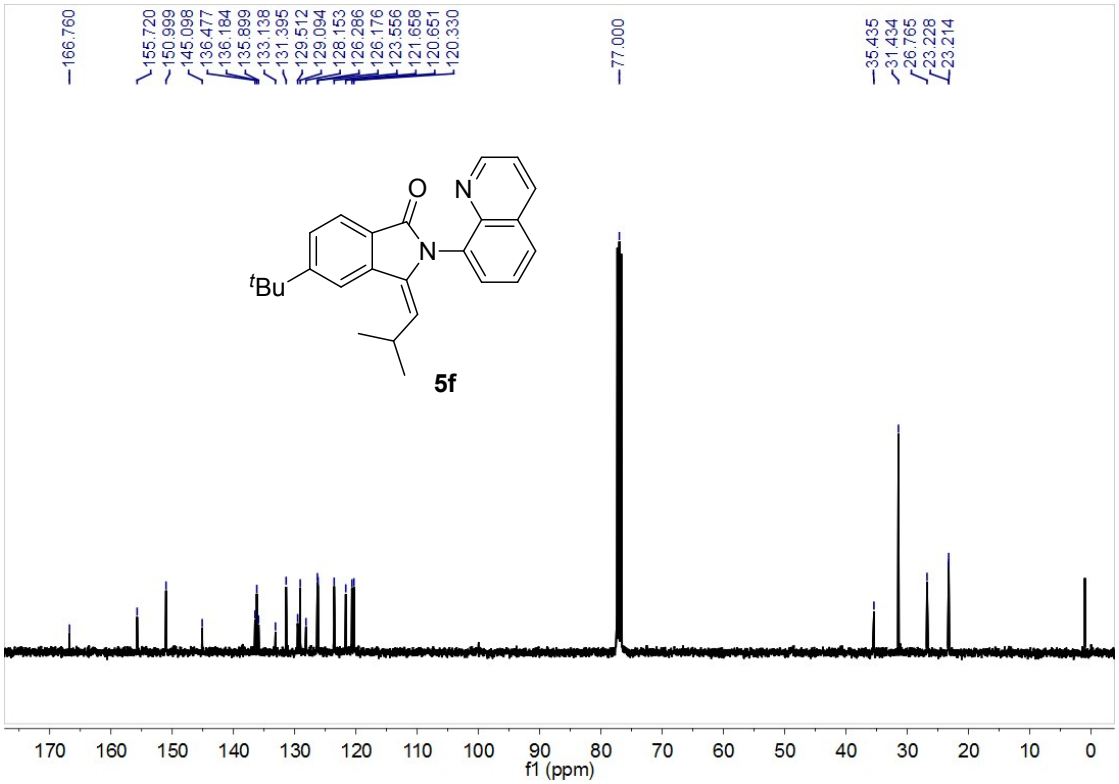
^{13}C NMR Spectrum of **5f (Z isomer)**



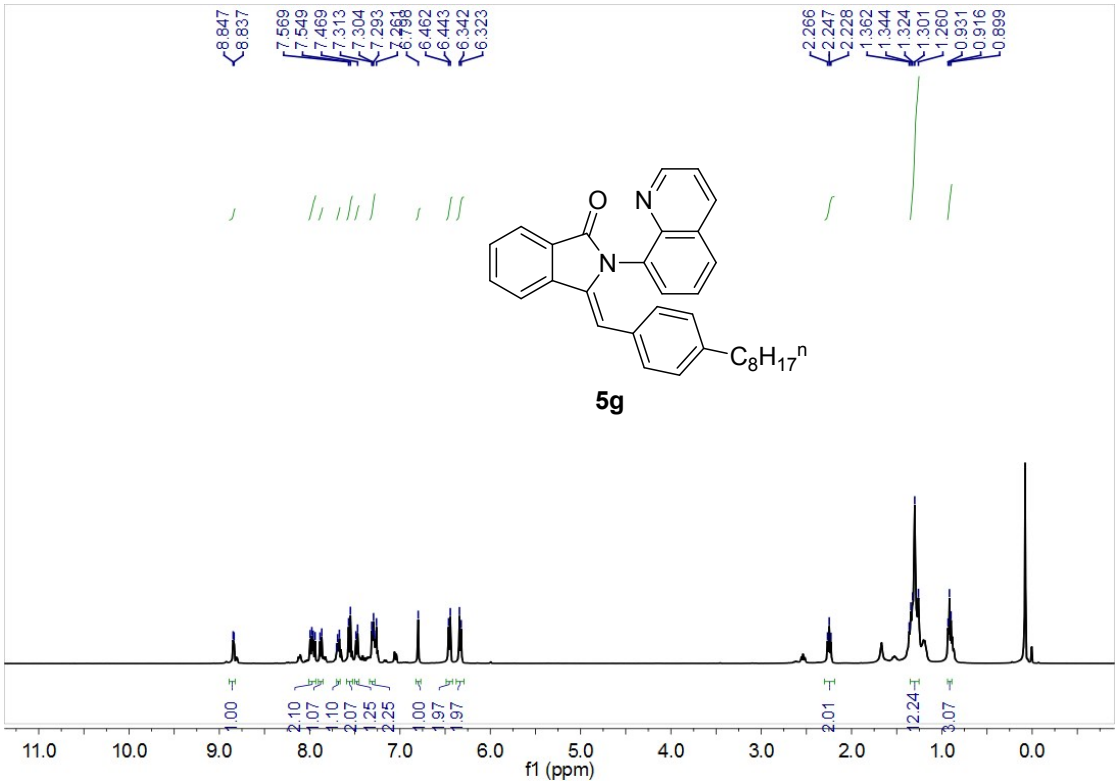
^{1}H NMR Spectrum of **5f (E isomer)**



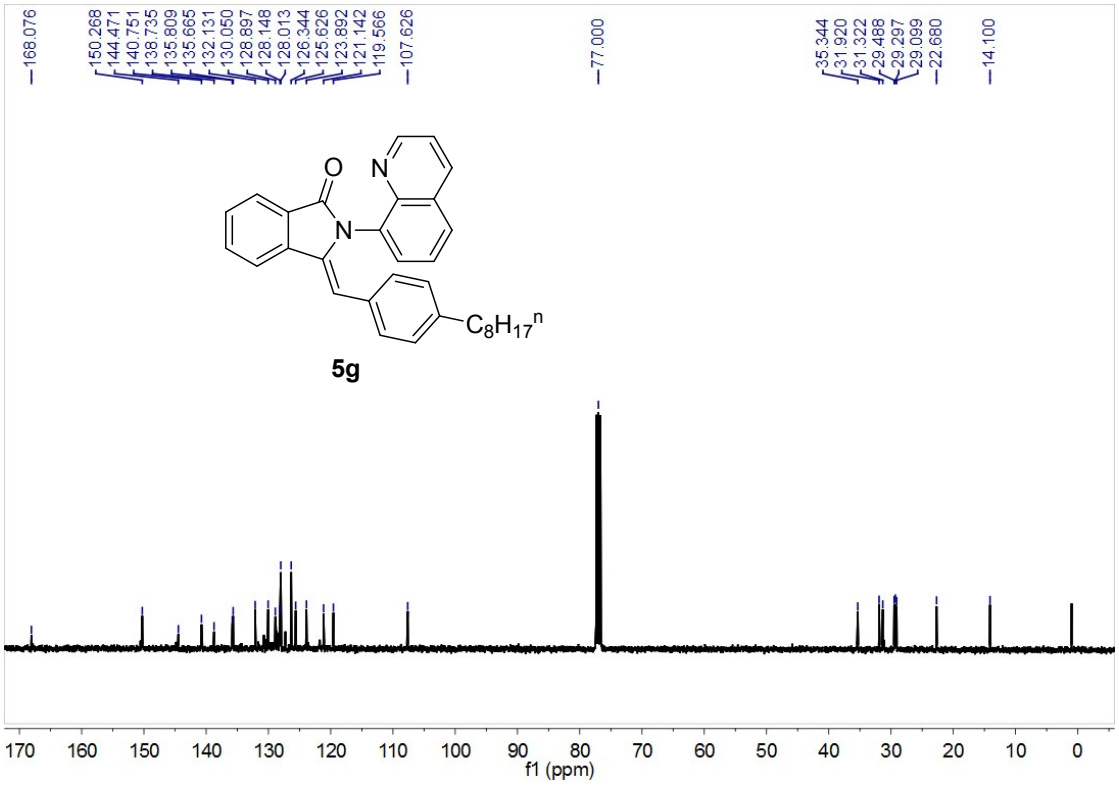
^{13}C NMR Spectrum of **5f (E isomer)**



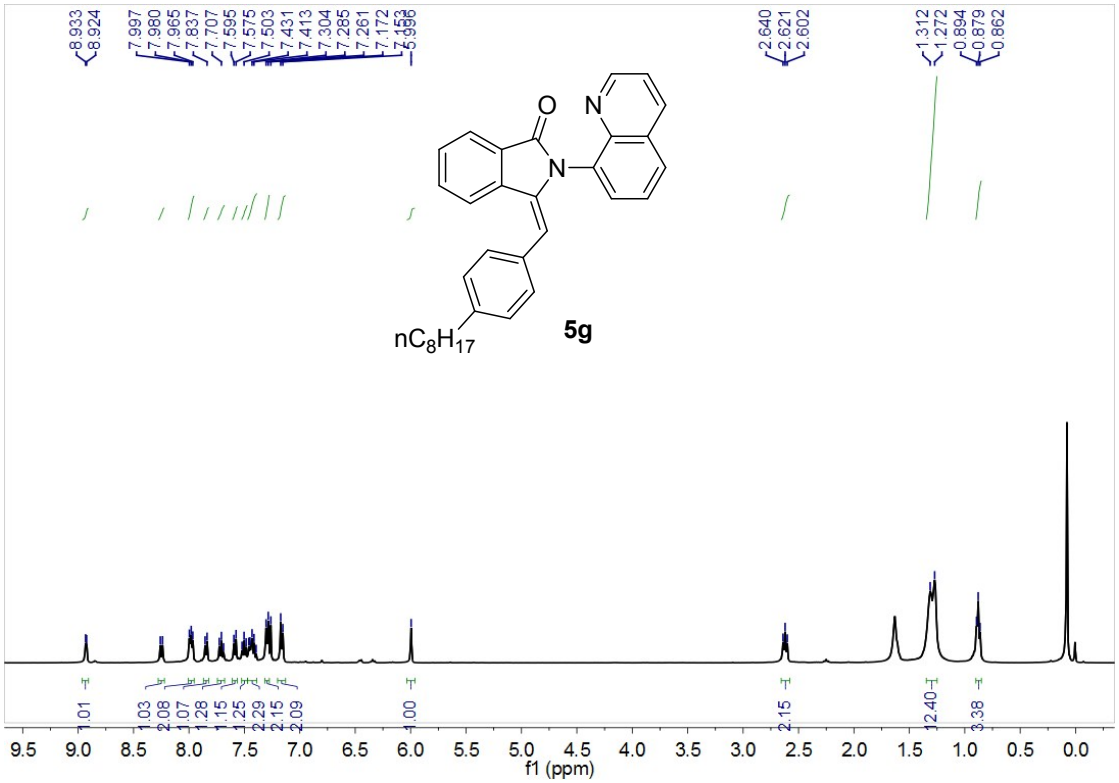
^{1}H NMR Spectrum of **5g (Z isomer)**



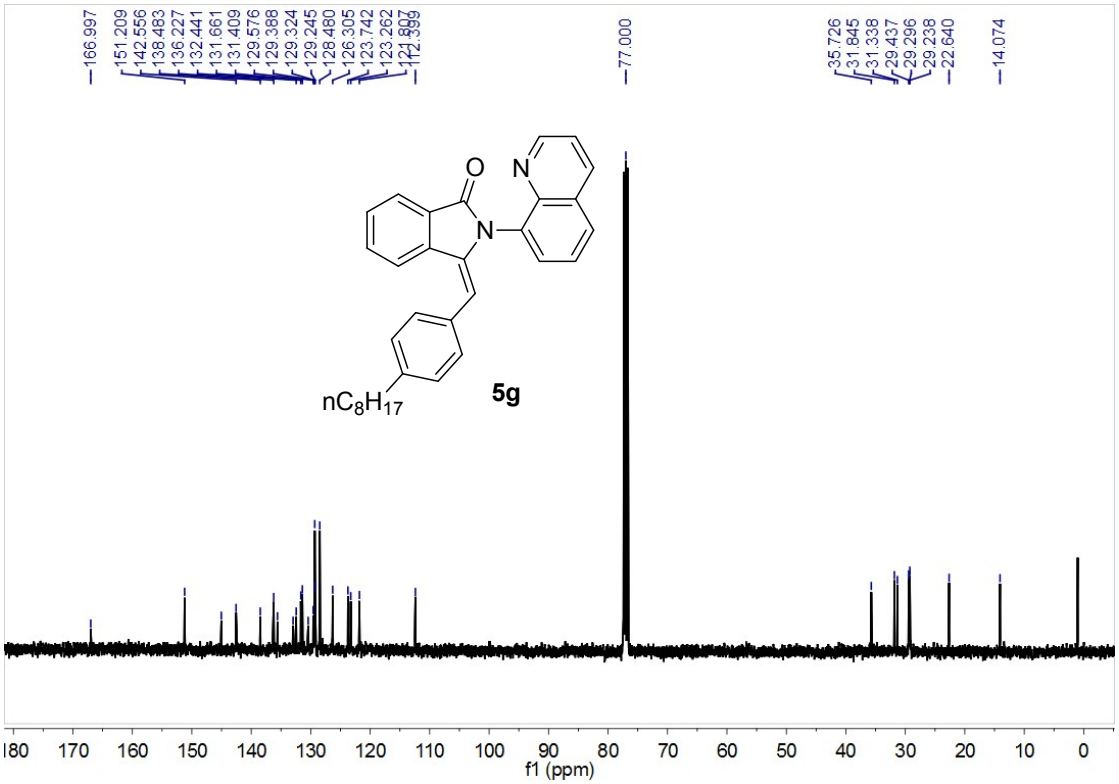
^{13}C NMR Spectrum of **5g (Z isomer)**



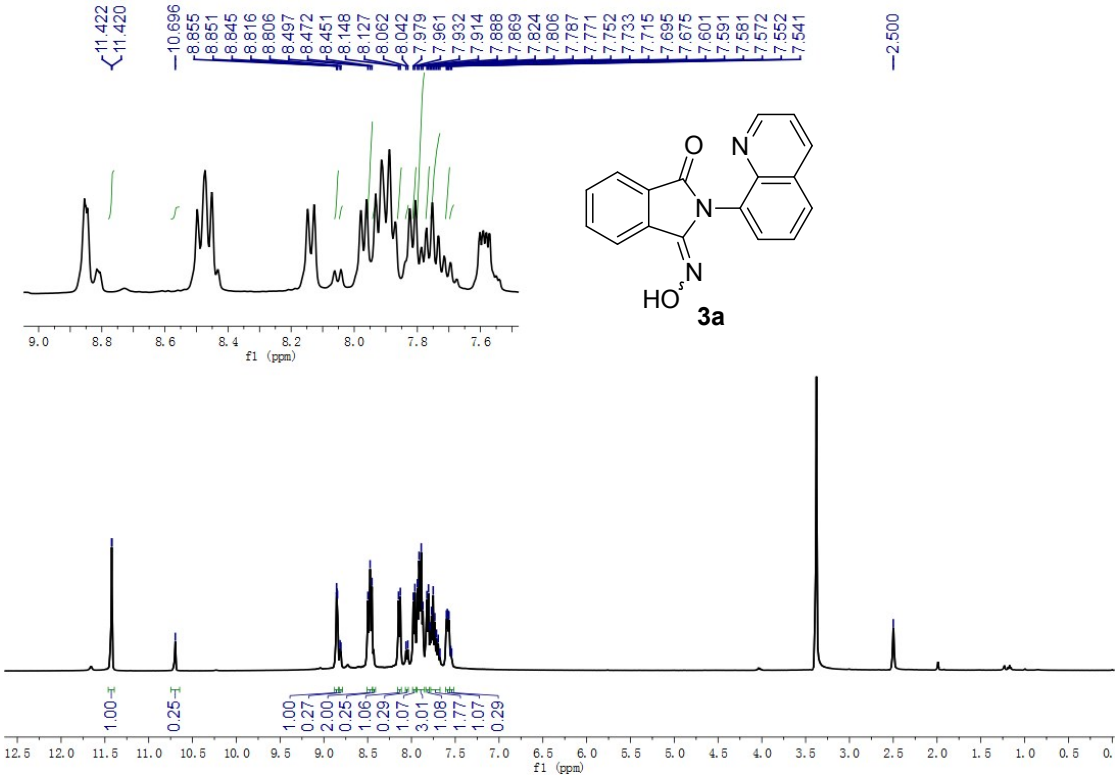
^{1}H NMR Spectrum of **5g (E isomer)**



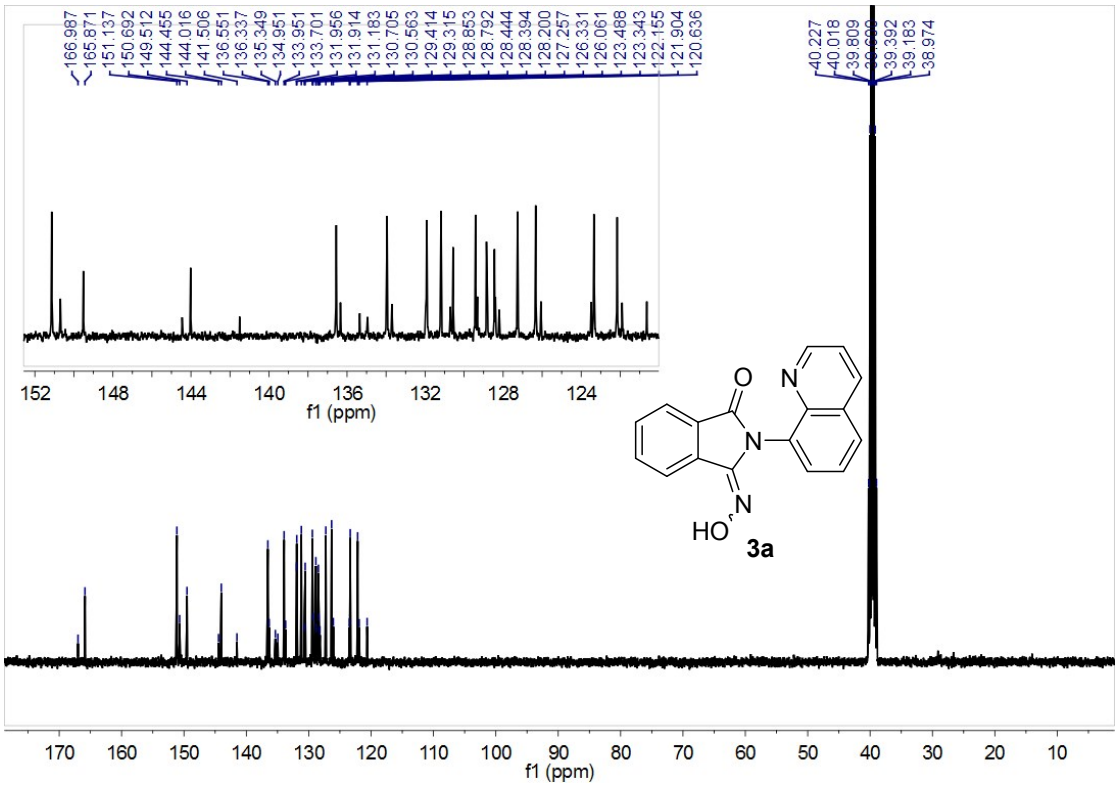
^{13}C NMR Spectrum of **5g (Z isomer)**



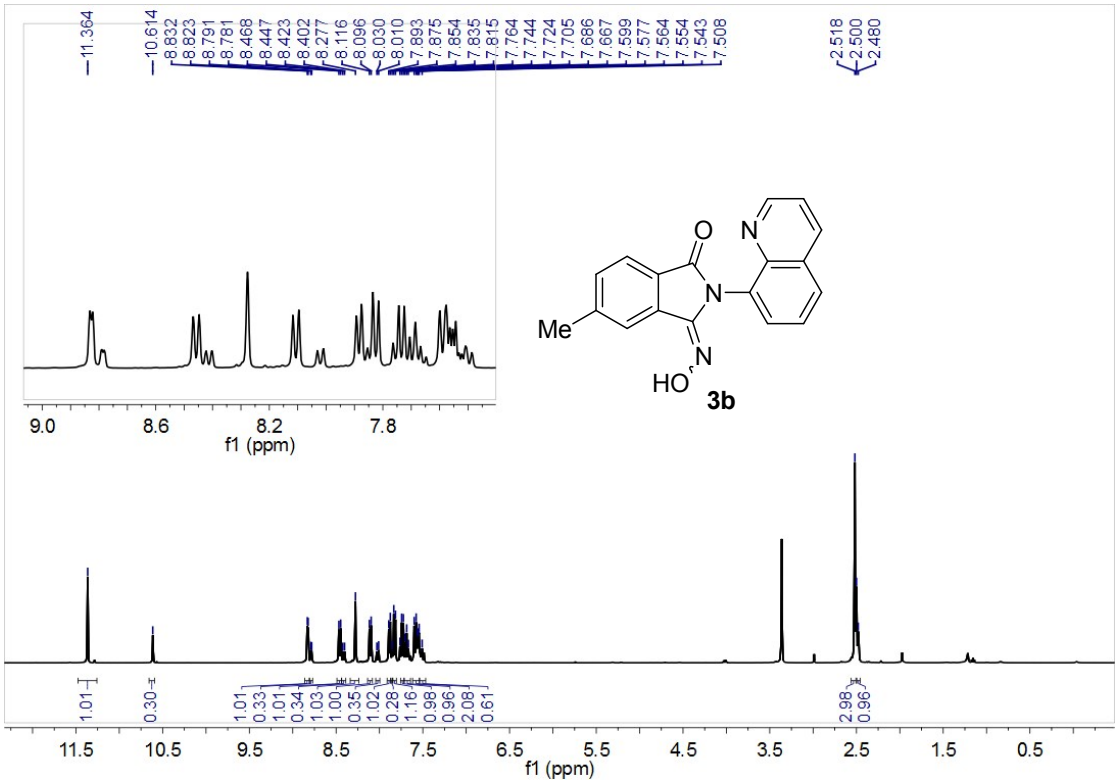
^{1}H NMR Spectrum of **3a**



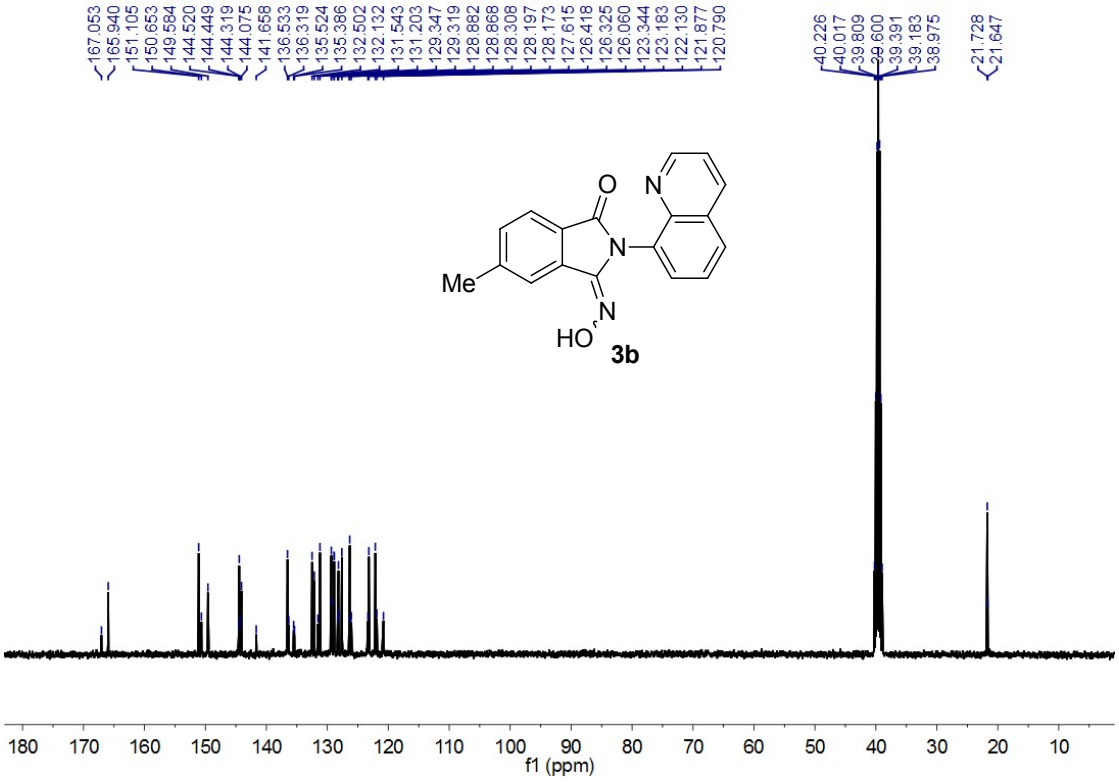
^{13}C NMR Spectrum of **3a**



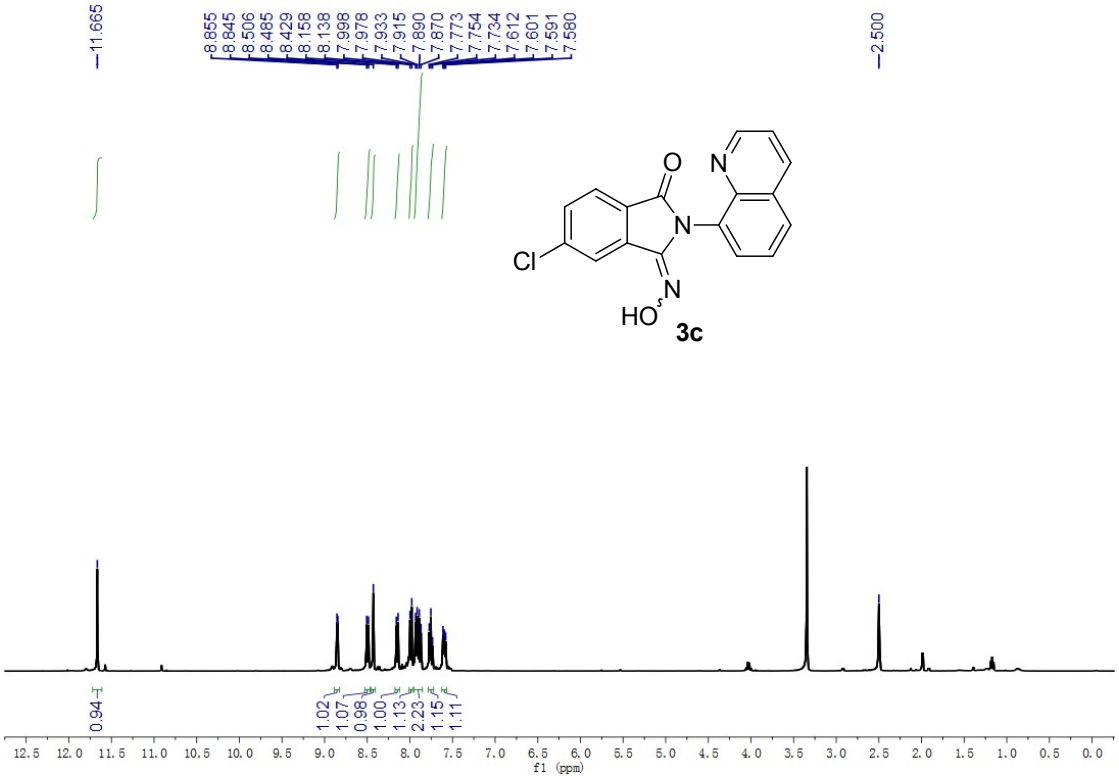
^{1}H NMR Spectrum of **3b**



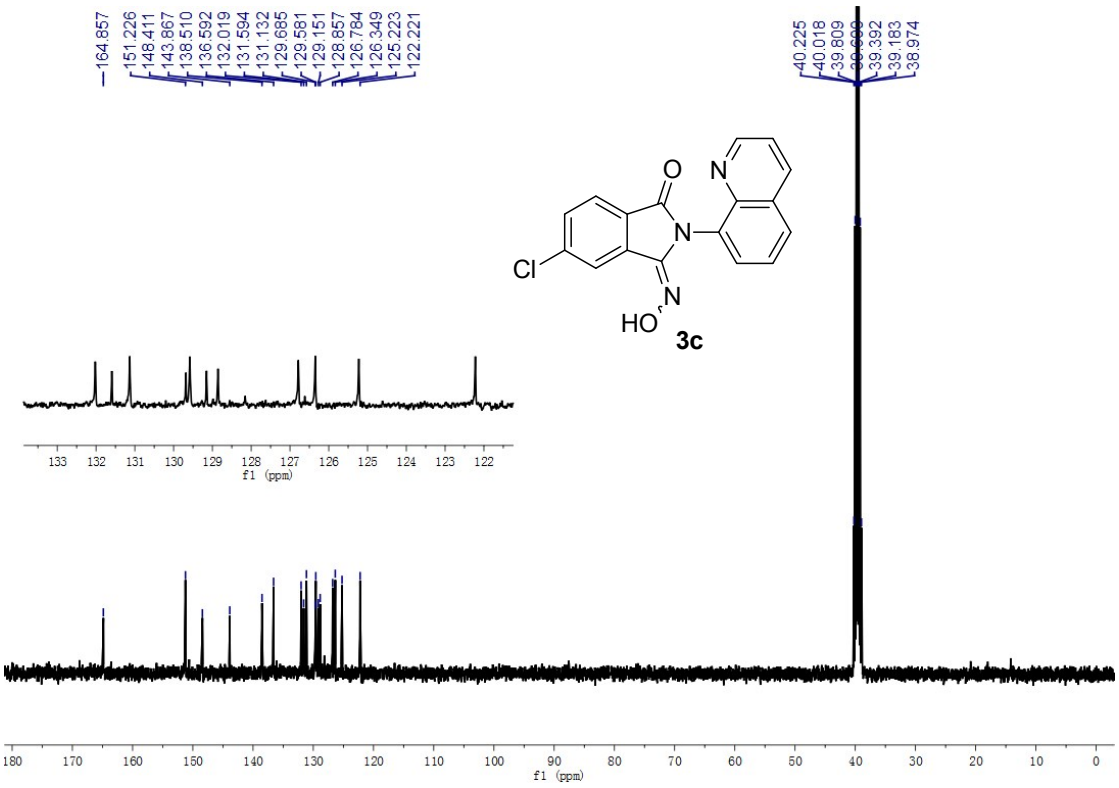
^{13}C NMR Spectrum of **3b**



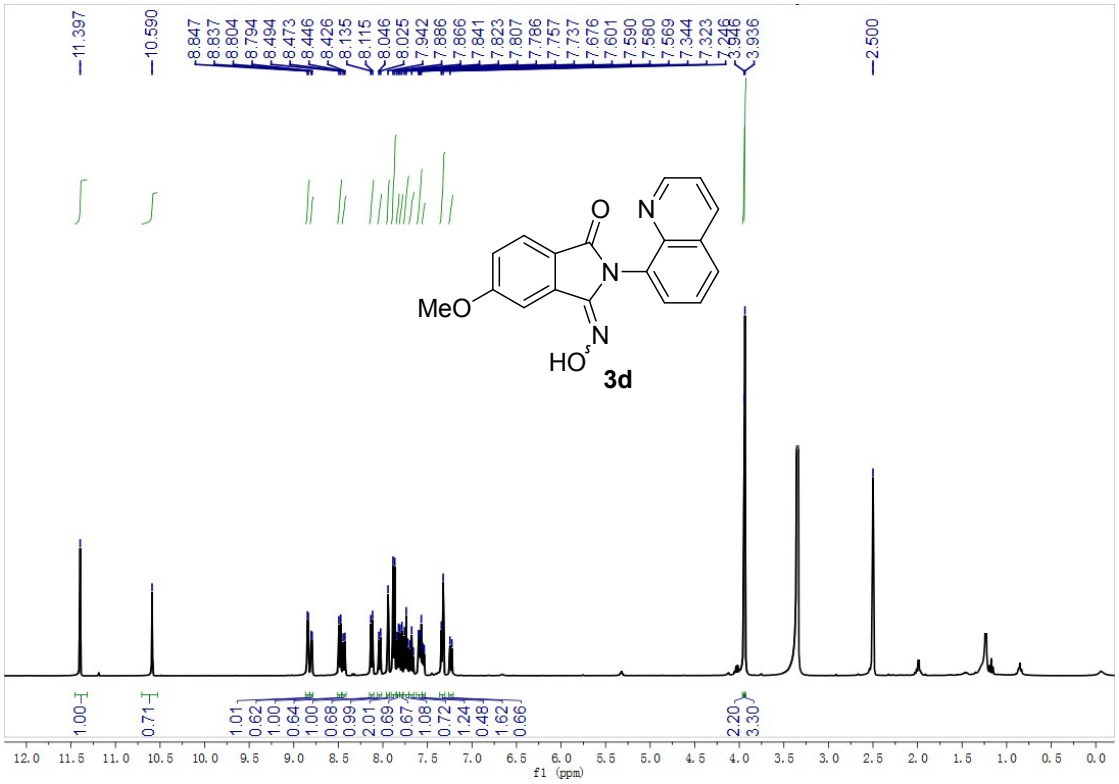
^{1}H NMR Spectrum of **3c**



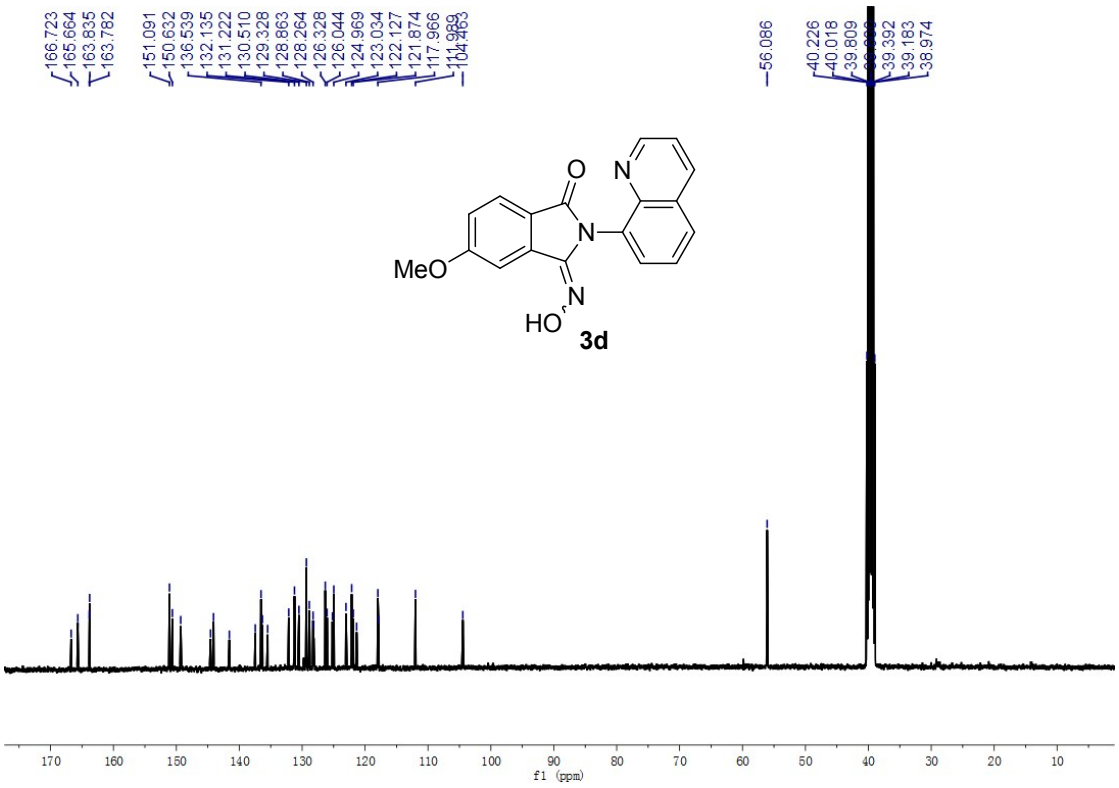
^{13}C NMR Spectrum of **3c**



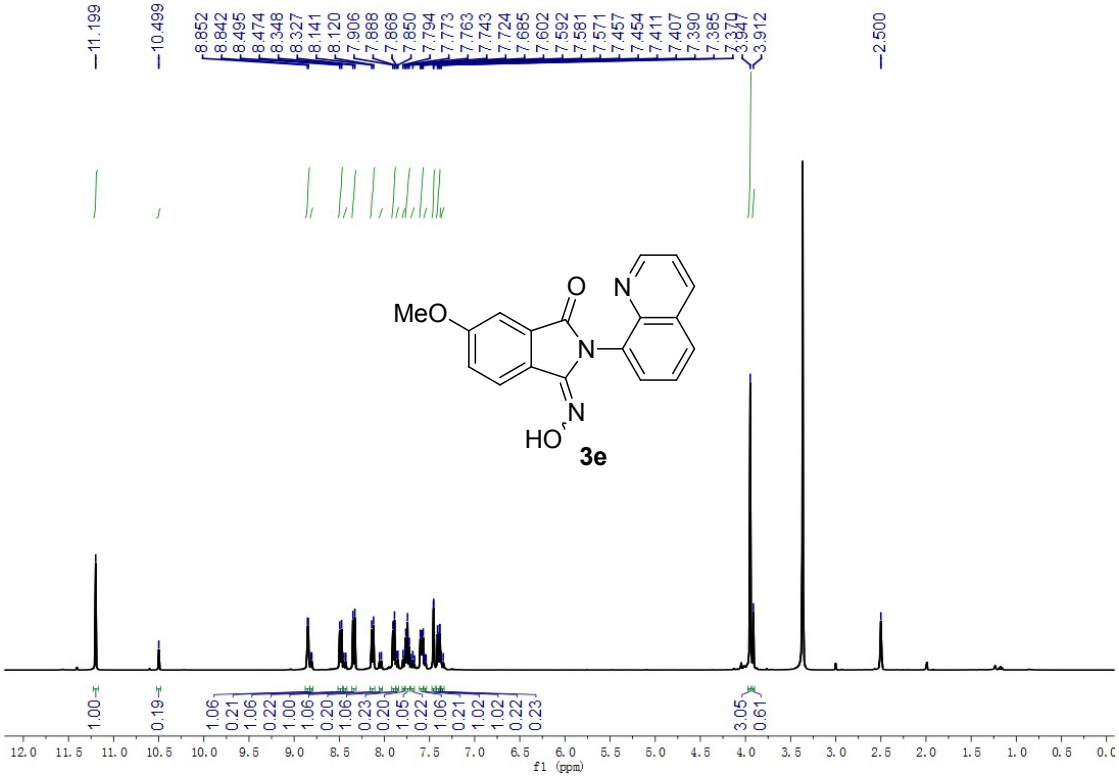
^{1}H NMR Spectrum of **3d**



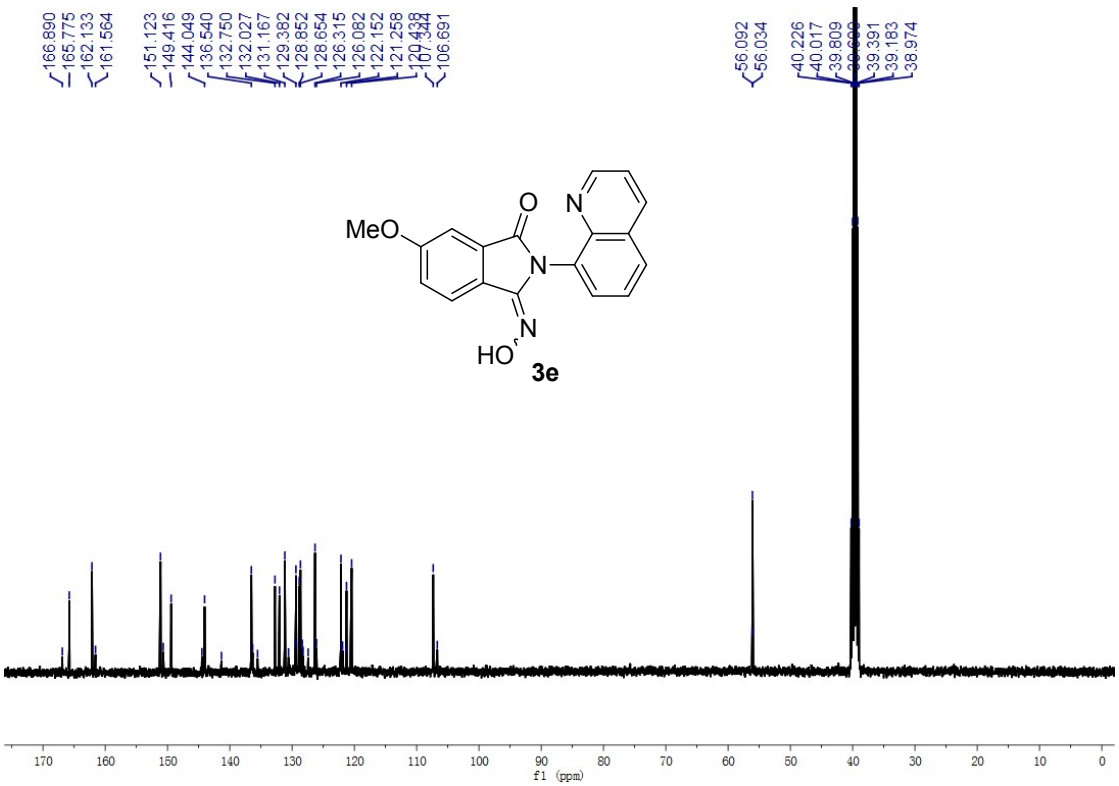
^{13}C NMR Spectrum of **3d**



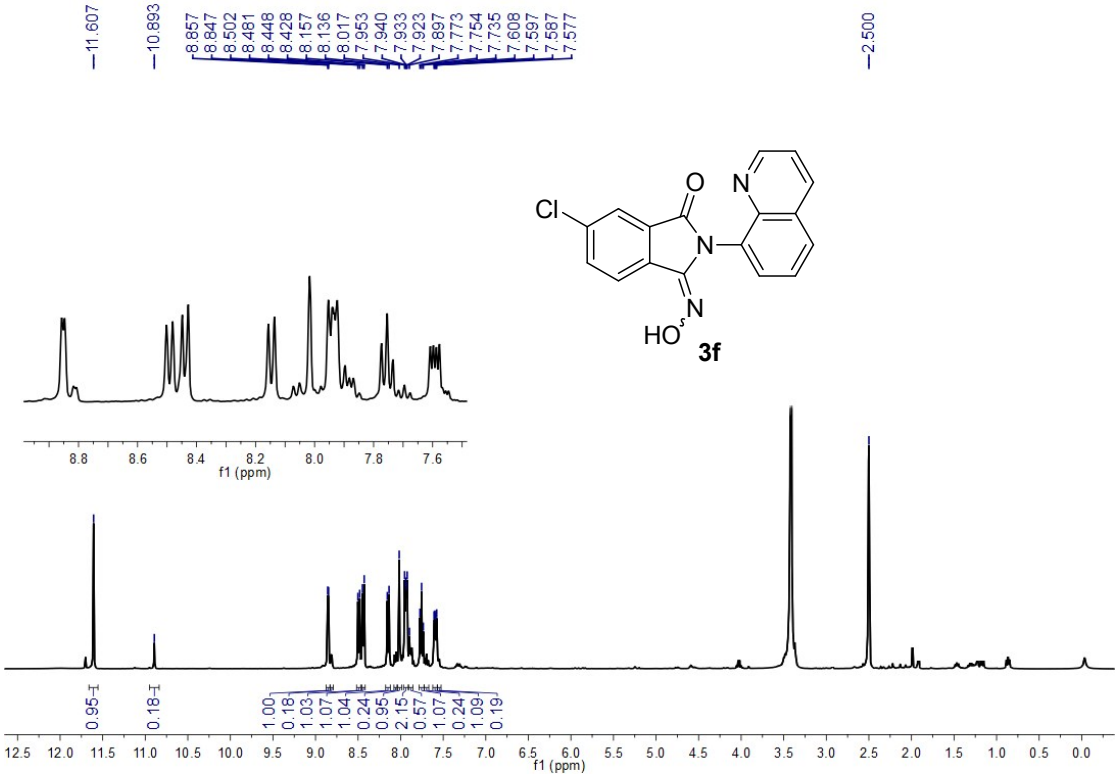
^{1}H NMR Spectrum of **3e**



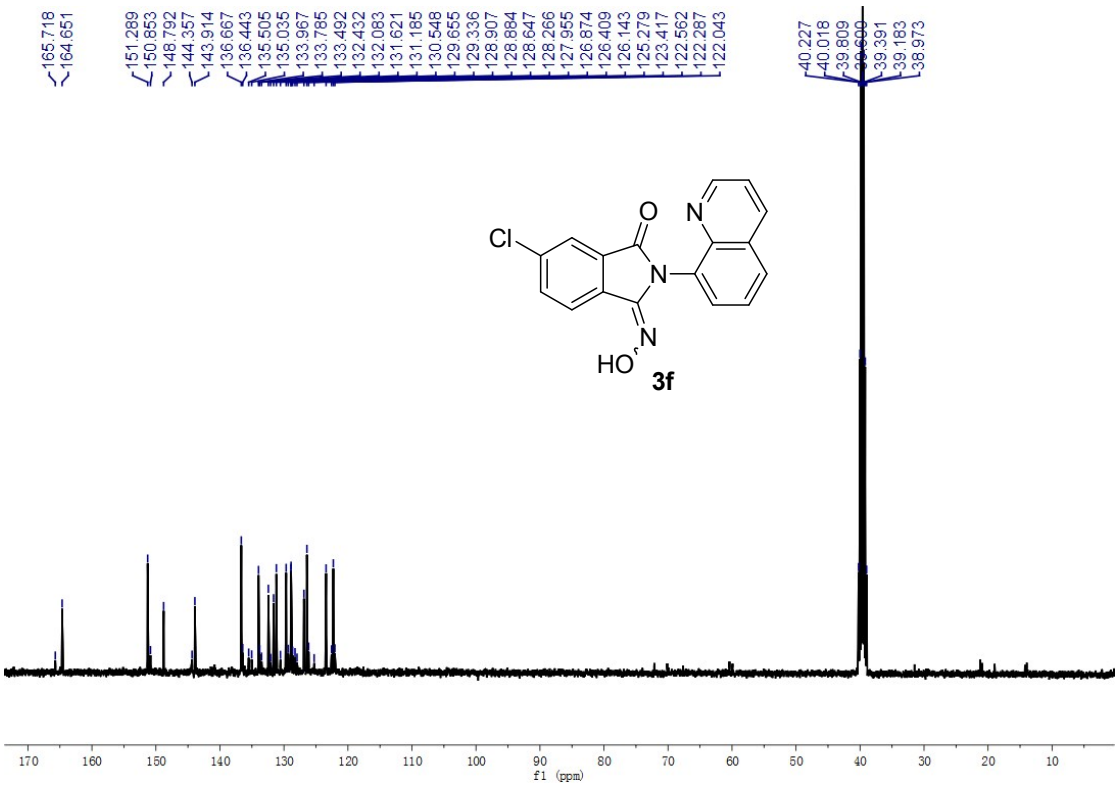
^{13}C NMR Spectrum of **3e**



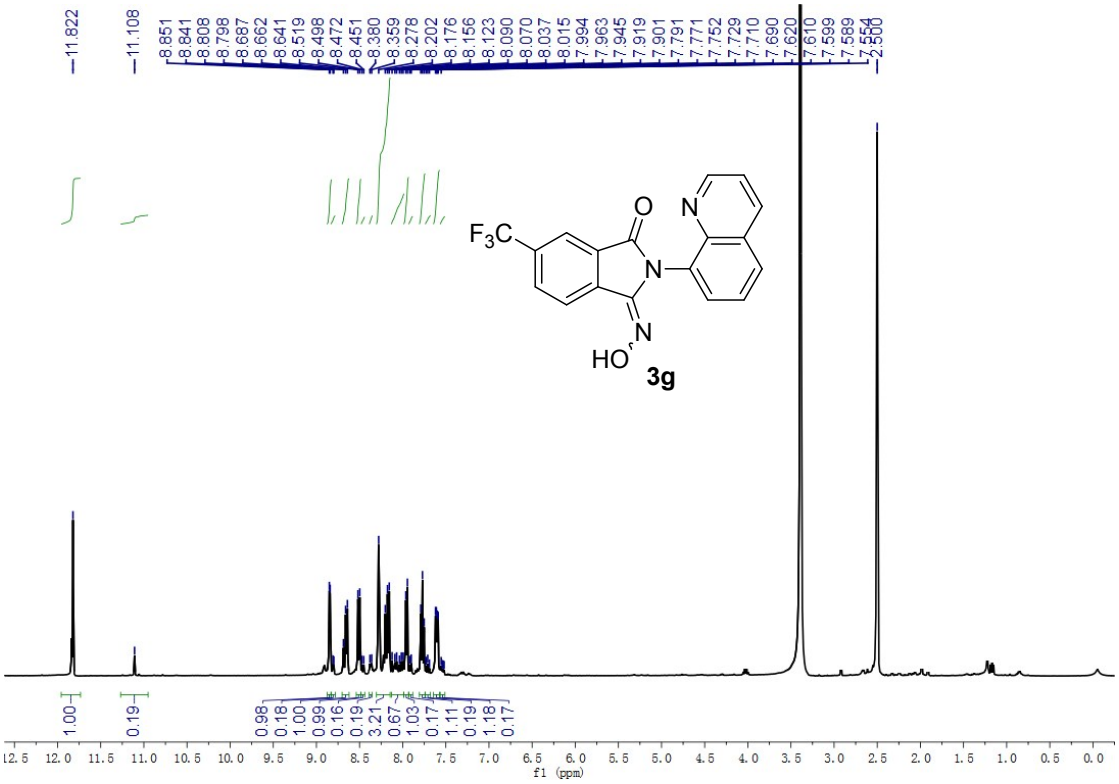
^{1}H NMR Spectrum of **3f**



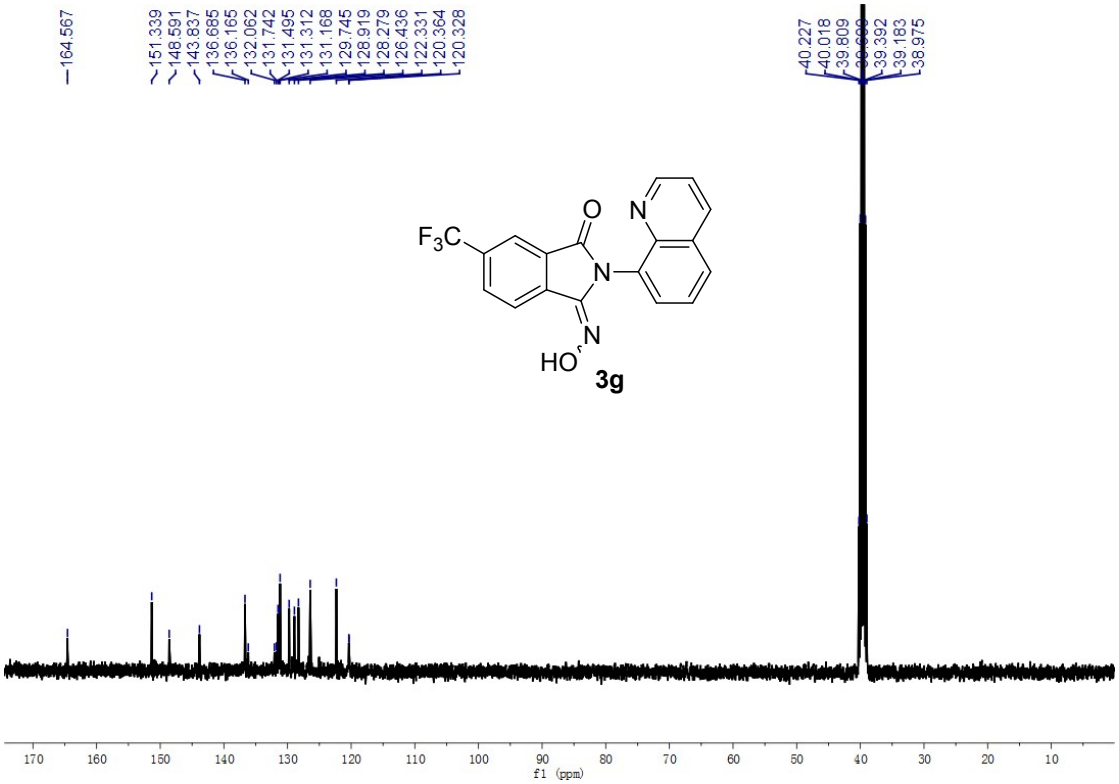
^{13}C NMR Spectrum of **3f**



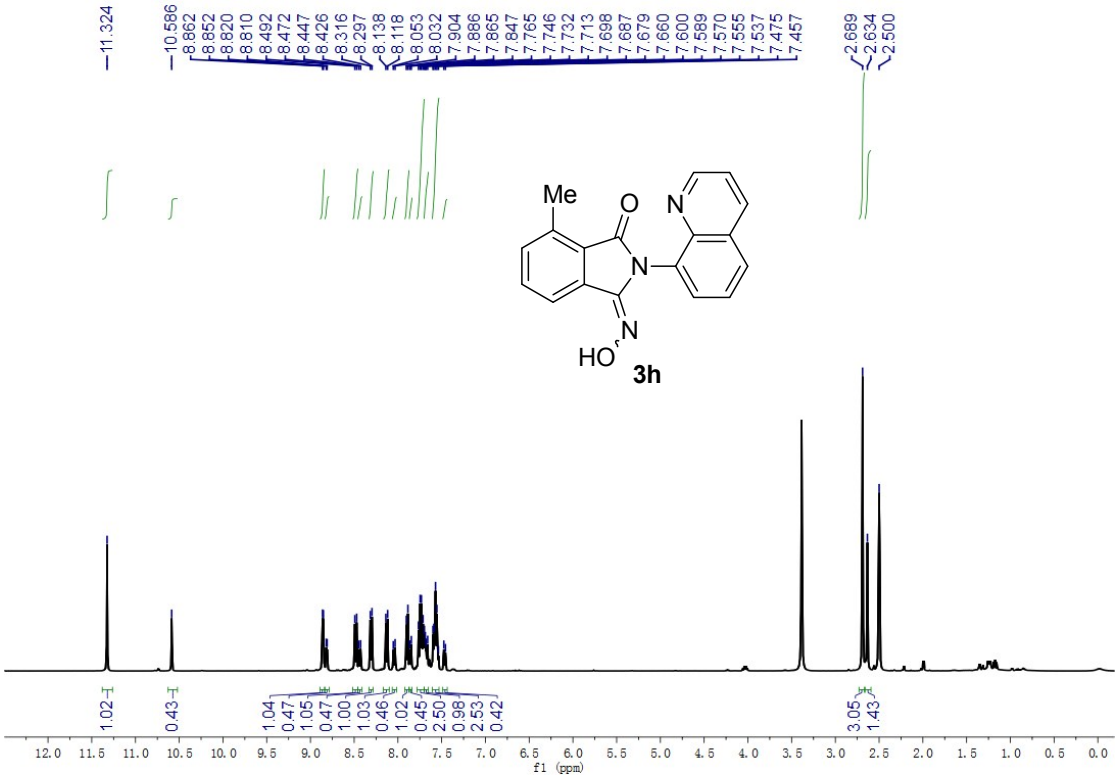
^{1}H NMR Spectrum of **3g**



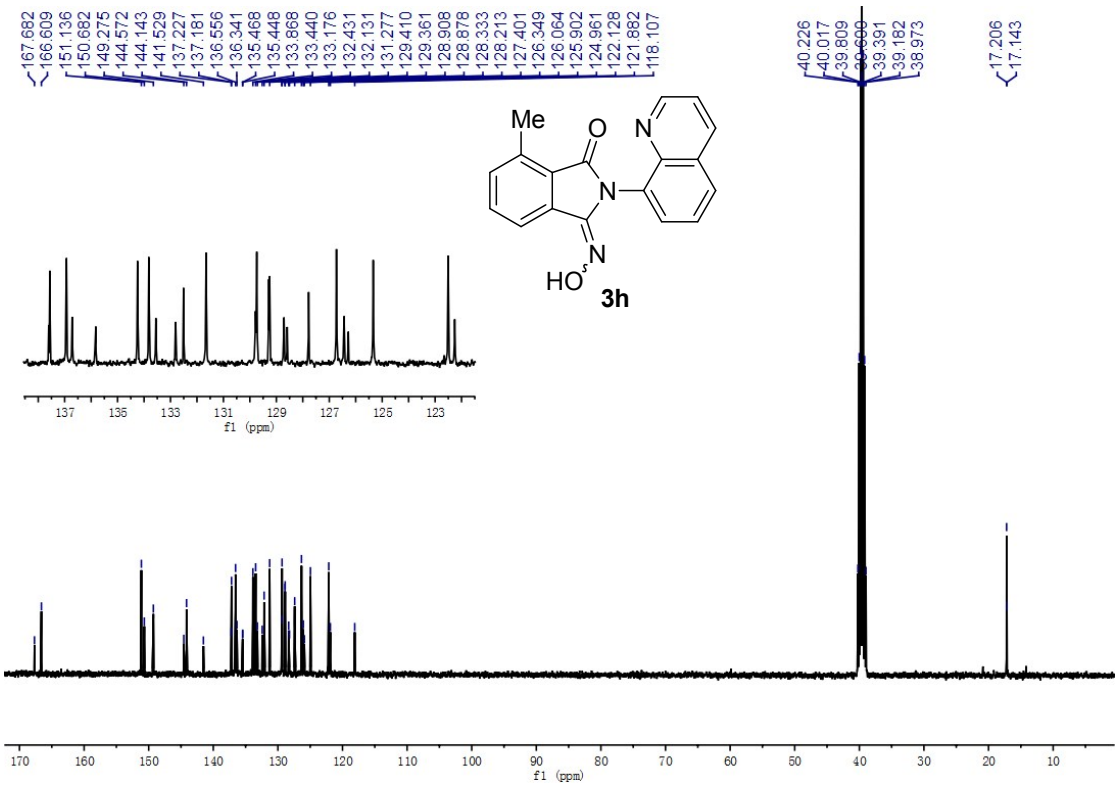
^{13}C NMR Spectrum of **3g**



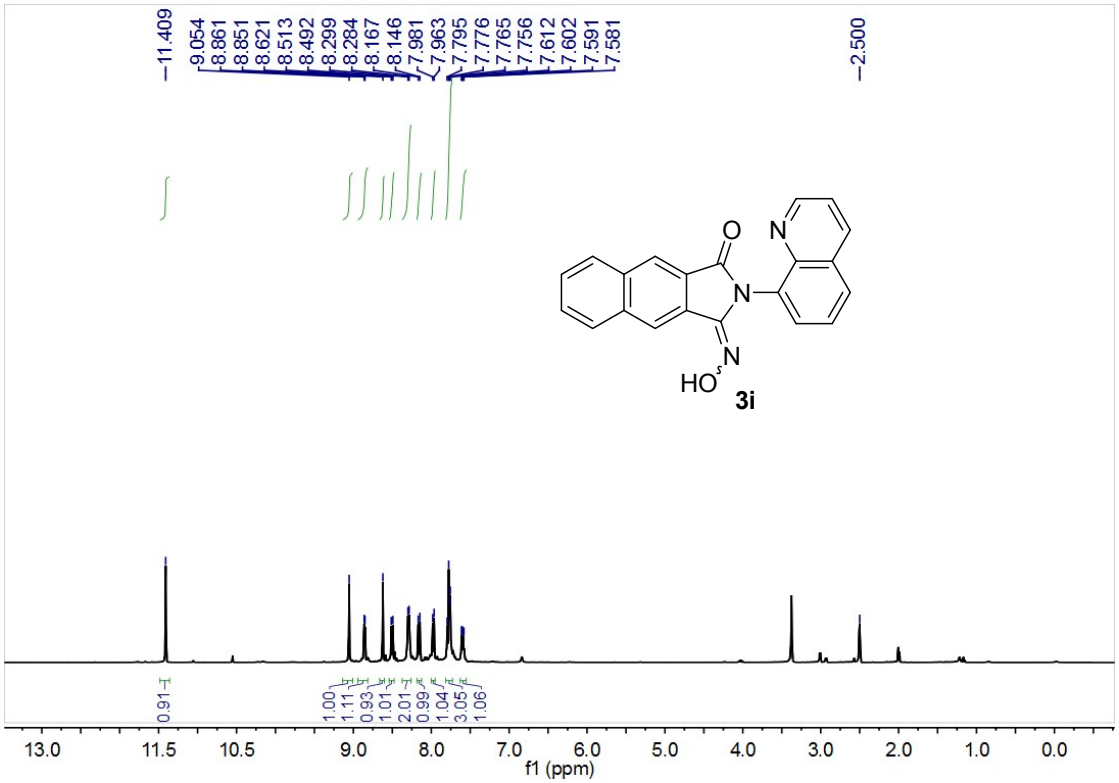
^{1}H NMR Spectrum of **3h**



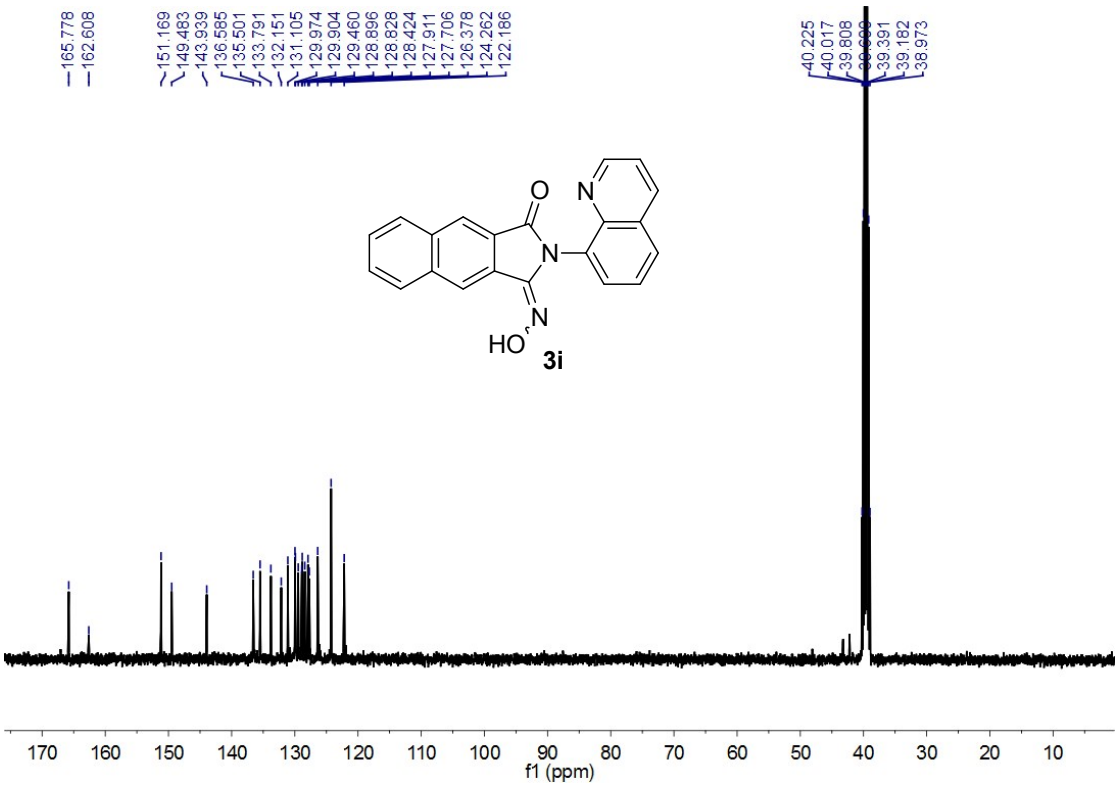
^{13}C NMR Spectrum of **3h**



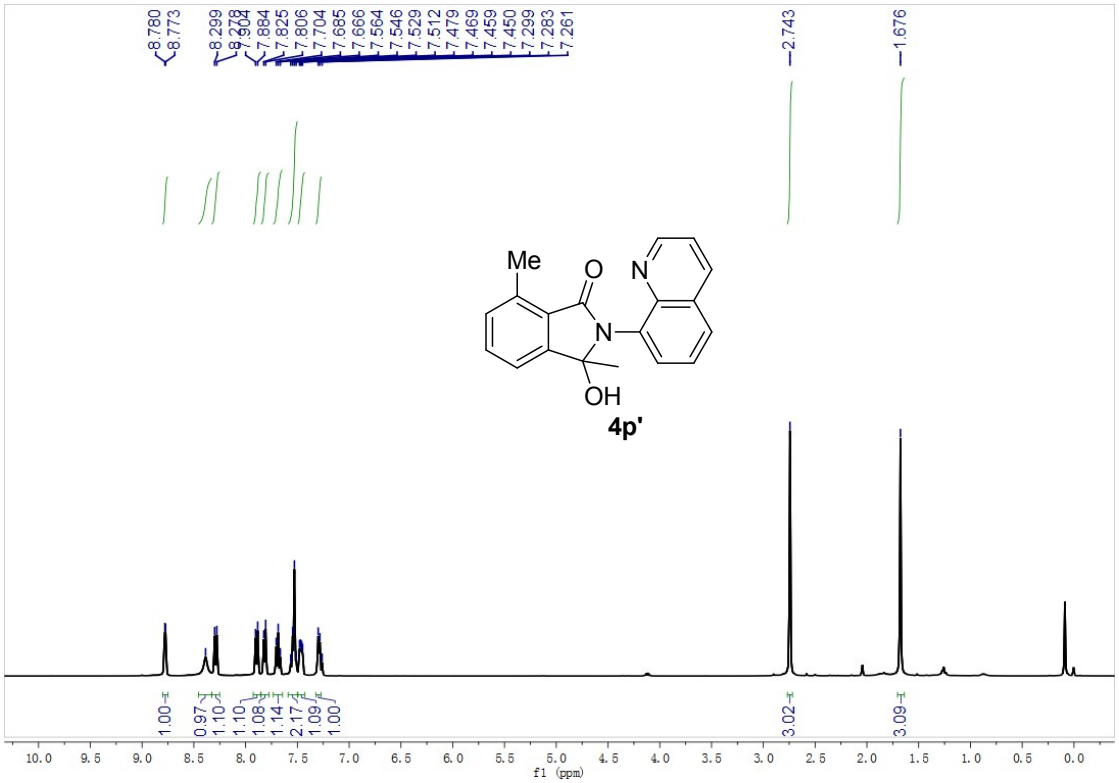
^{1}H NMR Spectrum of **3i**



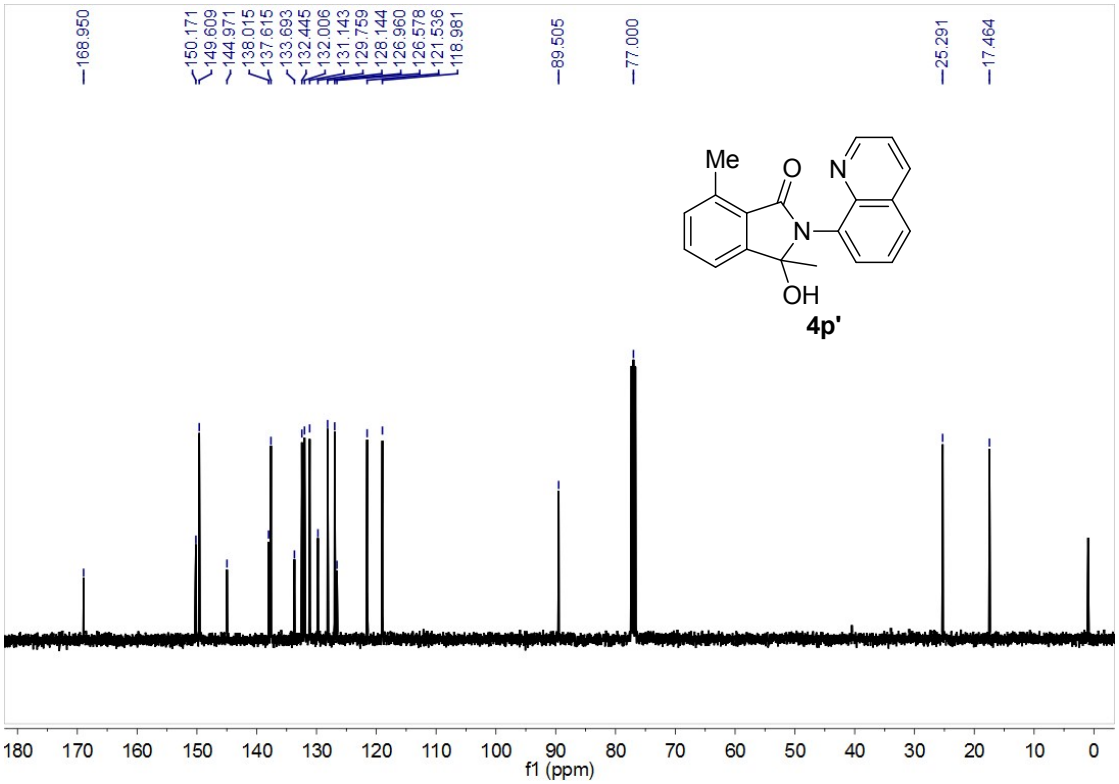
^{13}C NMR Spectrum of **3i**



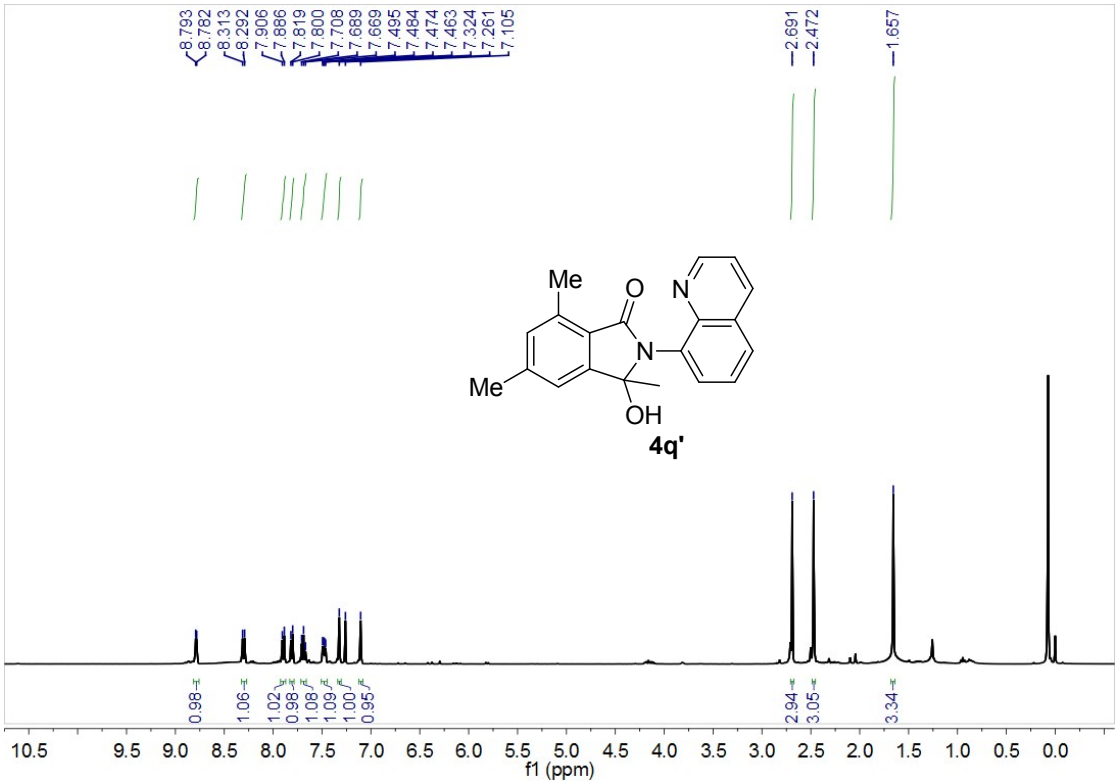
^{1}H NMR Spectrum of **4p'**



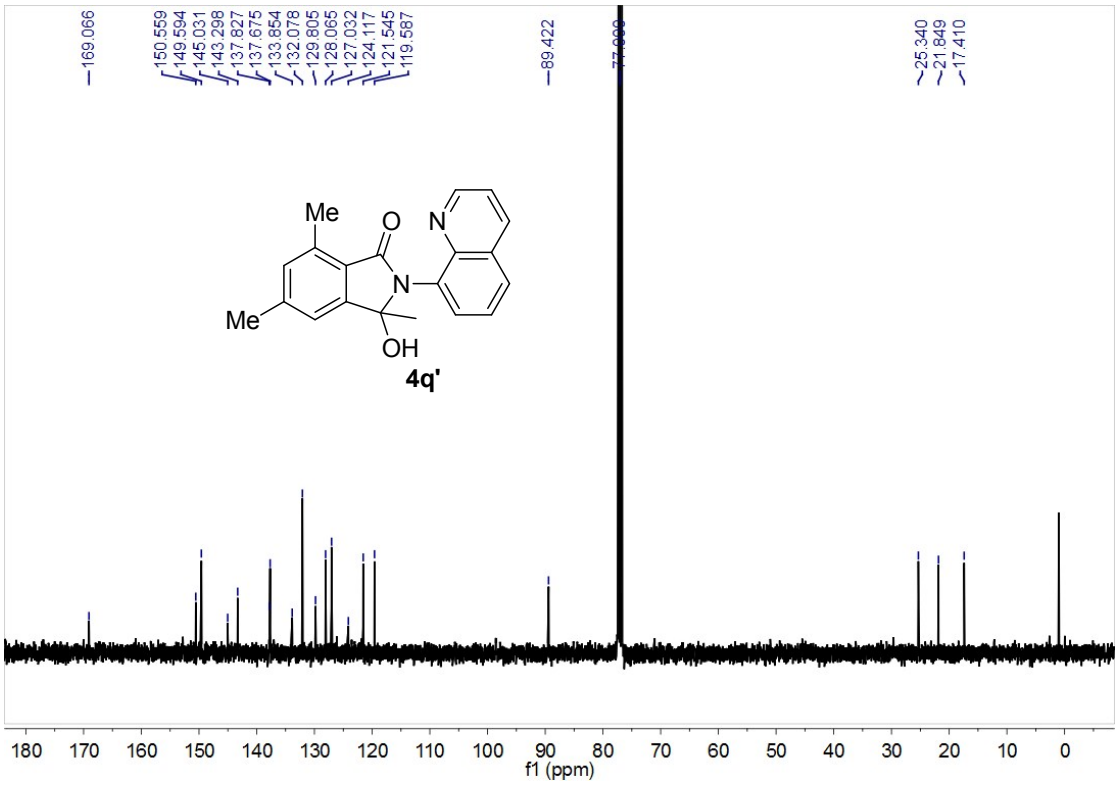
^{13}C NMR Spectrum of **4p'**



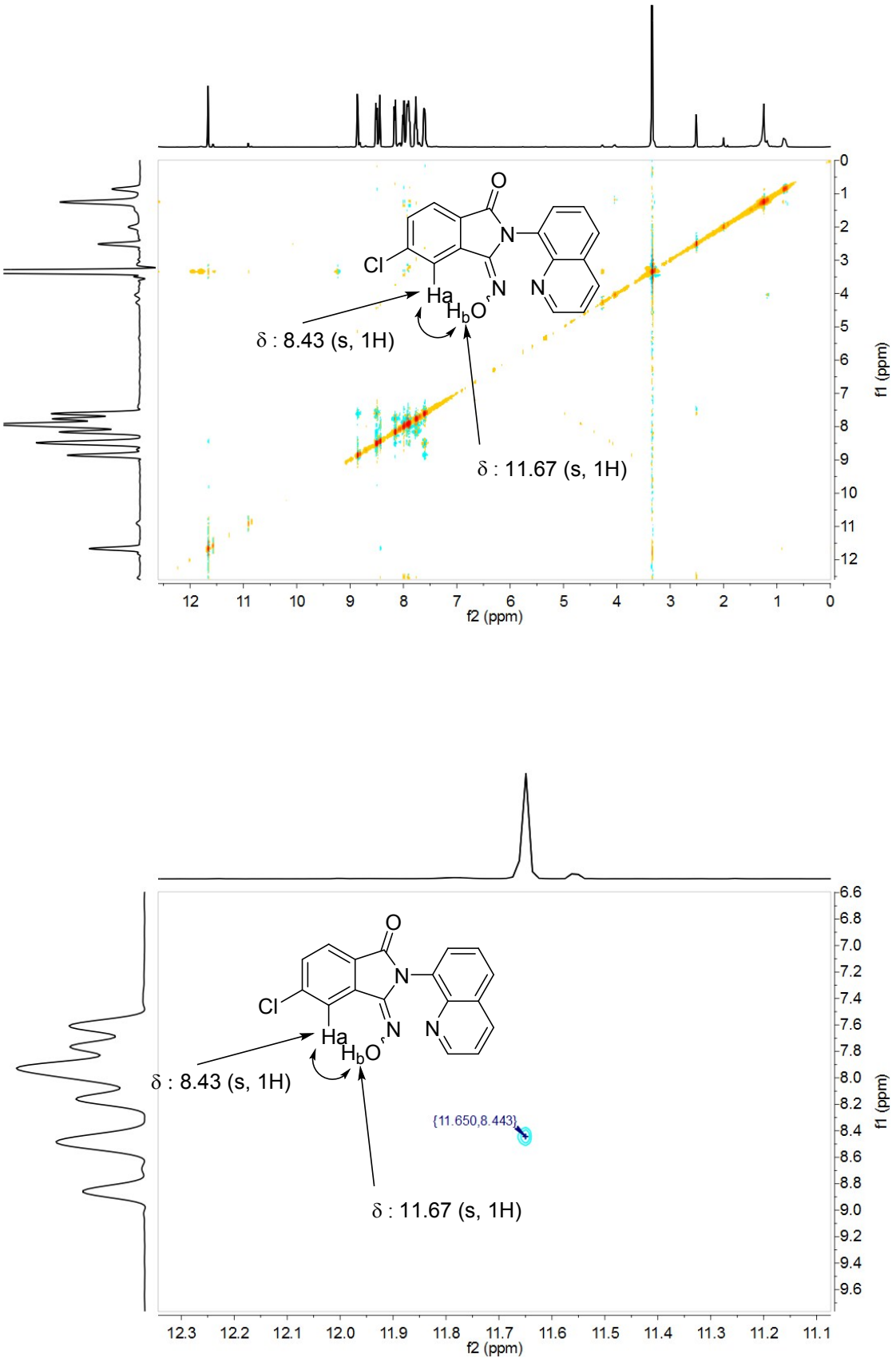
^{1}H NMR Spectrum of **4q'**



^{13}C NMR Spectrum of **4q'**



^{1}H-^{1}H NOESY spectrum of 3c



Partial enlarged view of ^{1}H-^{1}H NOESY spectrum of **3c**