Electronic Supplementary Material (ESI) for ChemComm.

Supplementary Information

Co(II)/Cu(II)-cocatalyzed oxidative C–H/N–H functionalization of benzamides with ketones: a facile route to isoindolin-1-ones

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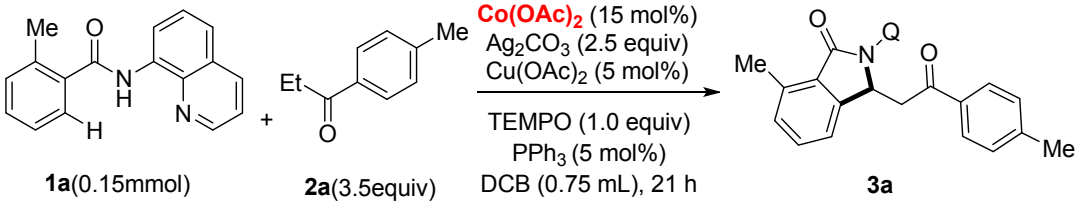
1. General Comments

All other reagents were purchased from TCI, Alfa Aesar, Accela and Adamas used without further purification. DMF and DCE were distilled from CaH_2 under nitrogen and stored under nitrogen. 1,4-Dioxane was distilled from Sodium under nitrogen and stored under nitrogen. ^1H NMR (400 or 600 MHz) and ^{13}C NMR (101 MHz) were obtained on Bruker spectrometer with $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal standard. Chemical shifts were reported in units (ppm) by assigning TMS resonance in the ^1H NMR spectra as 0.00 ppm (chloroform, 7.26 ppm). Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet and m = multiplet), coupling constant (*J* values) in Hz and integration. Chemical shifts for ^{13}C NMR spectra were recorded in ppm from tetramethylsilane using the central peak of $CDCl_3$ (77.00 ppm) as the internal standard. IR-spectra were obtained using the Bruker VERTEX 70 FT-IR spectrometer. The yields reported are the isolated yields.

2. Optimization details for the reaction conditions:

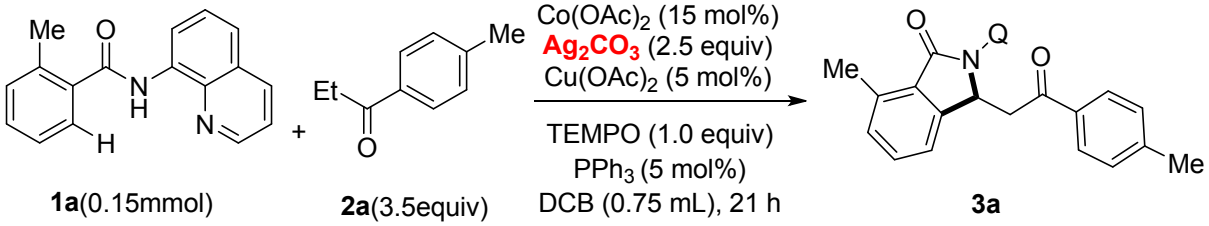
Table S1: Optimization of **cobalt salts**



1a(0.15mmol) + **2a**(3.5equiv) → **3a**

Entry	Cobalt salts	Yield(%)
1	**$Co(OAc)_2$**	**76**
2	$Co(acac)_2$	39
3	$Co(OAc)_2 \cdot 4H_2O$	63
4	$Co(ClO_4)_2 \cdot 6H_2O$	50

Table S2: Optimization of **oxidants**

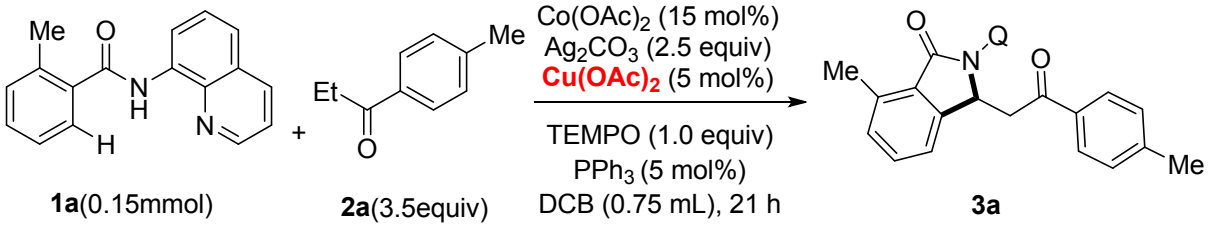


1a(0.15mmol) + **2a**(3.5equiv) → **3a**

Entry	Oxidants	Yield(%)
1	**Ag_2CO_3**	**76**
2	AgOAc	20
3	$AgNO_3$	32
4	Ag_2O	38

5	Ag_2SO_4	52
6	$Mn(OAc)_2.4H_2O$	10

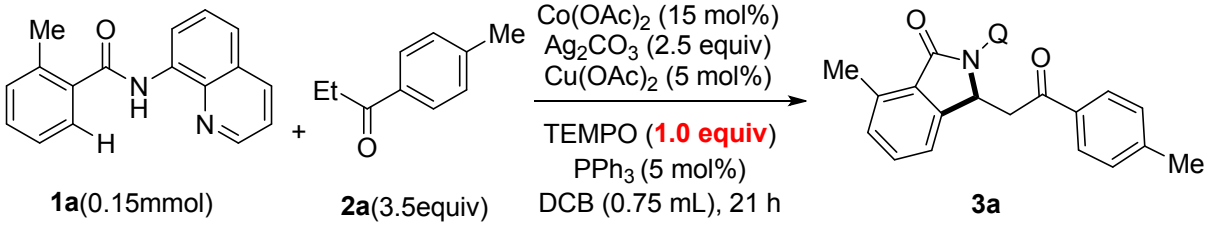
Table S3: Optimization of **copper slats**



1a(0.15mmol) + **2a**(3.5equiv) → **3a**

Entry	Copper salts	Yield(%)
1	**$Cu(OAc)_2$**	**76**
2	$Cu(OTf)_2$	-
3	$Cu(TFA)_2$	-

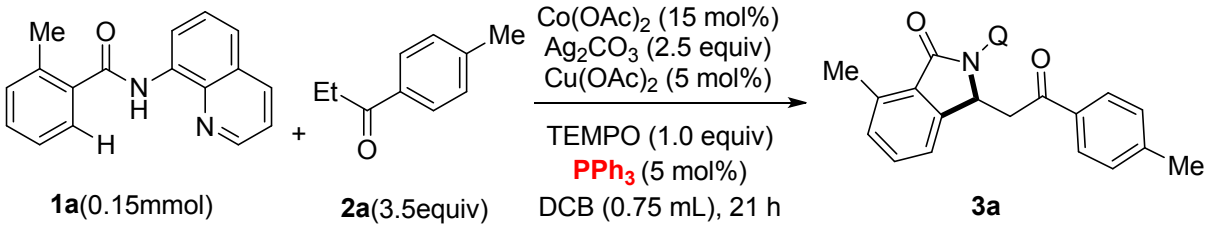
Table S4: Optimization of **the amount of TEMPO**



1a(0.15mmol) + **2a**(3.5equiv) → **3a**

Entry	Equiv.	Yield(%)
1	0.8	66
2	**1.0**	**76**
3	1.2	64

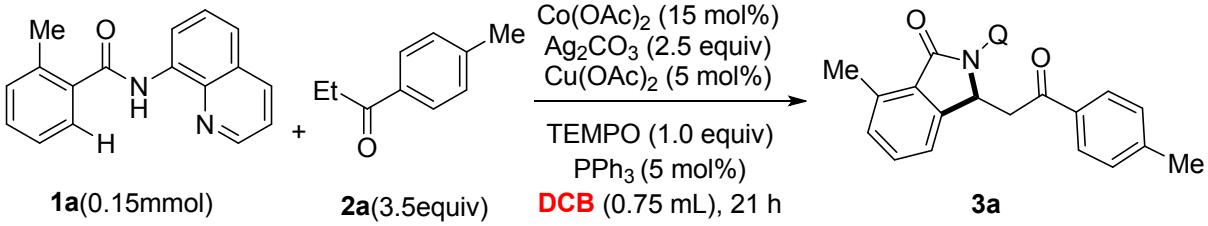
Table S5: Optimization of **ligands**



1a(0.15mmol) **2a**(3.5equiv) **3a**

Entry	Ligands	Yield(%)
1	**P(Ph)$_3$**	**76**
2	2,2'-Bipyridine	51
3	1,10-Phenanthroline	47
4	P(^{t}Bu)$_3$	70

Table S6: Optimization of **solvents**

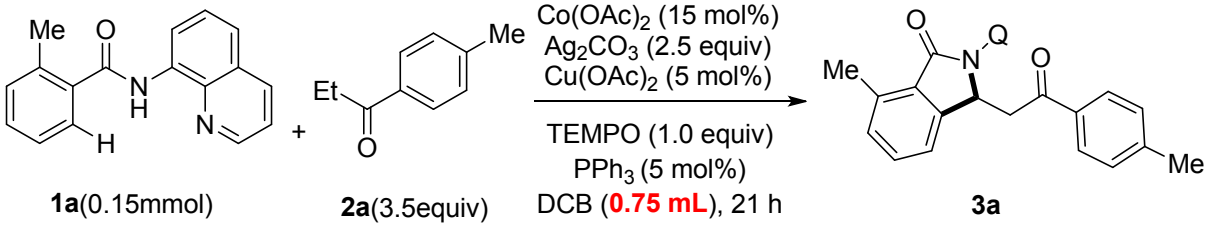


1a(0.15mmol) **2a**(3.5equiv) **3a**

Entry	Solvents	Yield(%
1	**DCB**	**76**
2	PhCl	56
3	DCE	30
4	TFE	-
5	1,4-dioxane	-

6	DMF	-
7	toluene	43
8	$PhCF_3$	50

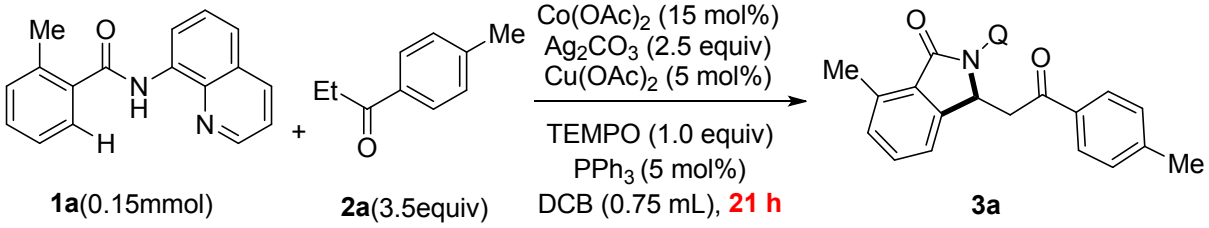
Table S7: Optimization of **the amount of solvent**



1a(0.15mmol) + **2a**(3.5equiv) → **3a**

Entry	mL	Yield(%)
1	0.5	55
2	**0.75**	**76**
3	1.0	63

Table S8: Optimization of **time**



1a(0.15mmol) + **2a**(3.5equiv) → **3a**

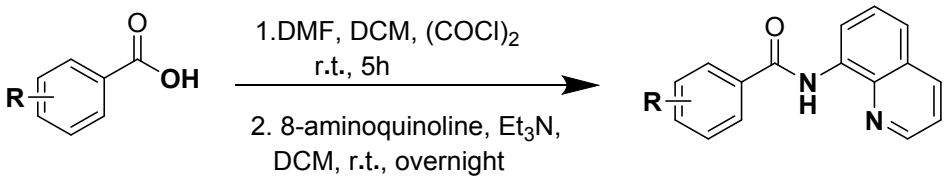
Entry	Time(h)	Yield(%)
1	18	60
2	**21**	**76**
3	24	67

3. General experimental procedures

(1) Synthesis of N-(quinolin-8-yl)benzamides

All amides bearing 8-aminoquinoline moiety were prepared by the reaction of the corresponding acids or acid chlorides with 8-aminoquinoline.[1]

General procedure



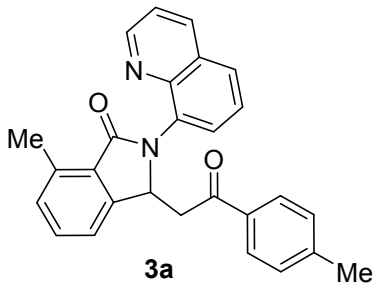
To an oven-dried round bottom flask (100 mL) charged with a magnetic stir-bar was added benzoic acid (10 mmol), DMF (50 μL) and DCM (30 mL). Oxalyl chloride (20 mmol, 1.8 mL) was added drop wise under ice cold condition. The ice bath was removed and the reaction mixture was stirred at room temperature for 5 h. The solvent was then removed by evaporation under reduced pressure, and the resulting residue was dissolved in CH_2Cl_2 (15 mL). After cooling the reaction mixture to 0 °C, another oven-dried round bottom flask (100 mL) charged with a magnetic stir-bar was added 8- aminoquinoline (10 mmol, 1.44 g), Et_3N (20 mmol, 2.8 mL) and DCM (30 mL). To this, a solution of acid chloride in DCM was added dropwise under ice cold condition and was stirred overnight under room temperature. Then, it was treated with water, and extracted

with DCM (3 x 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and the solvent is removed by evaporation under reduced pressure and the residue was purified by column chromatography on silica gel (eluent: EtOAc/PE) to give the desired amides.

(2) General catalytic procedure

In a glove box, a 25 mL Schlenk tube equipped with a stir bar was charged with benzamide (0.15 mmol), $Co(OAc)_2$ (4.1 mg, 15 mol%), Ag_2CO_3 (103.5 mg, 2.5 equiv.), $Cu(OAc)_2$ (1.4 mg, 5 mol%), $P(Ph)_3$ (2.0 mg, 5 mol%), TEMPO (23.5 mg, 1.0 equiv.). The tube was fitted with a rubber septum, and removed out from the glove box. Then ketone (3.5 equiv.) was added through the rubber septum using syringe under the atmosphere of N_2. 1,2-Dichlorobenzene (0.75 mL) was added to the Schlenk tube through the rubber septum using a syringe. The septum was replaced by a Teflon screwcap under N_2 flow. The reaction mixture was stirred at 110 ^oC (pre-heated to 110 ^oC) for 21 h. After cooling down, the solvent was removed in vacuo and the residue was purified by chromatography on silica gel (eluent: EtOAc/PE) to provide the corresponding product.

4. The characterization of products

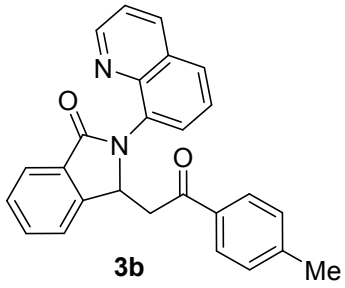


3a

7-methyl-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one (3a). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 43.6 mg, 76%).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.83 – 7.79 (m, 2H), 7.57 (dd, *J* = 7.8, 6.3 Hz, 3H), 7.43-7.37 (m, 2H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.26 – 7.24 (m, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.47 (dd, *J* = 8.1, 4.8 Hz, 1H), 3.36 (dd, *J* = 17.0, 4.8 Hz, 1H), 3.23 (dd, *J* = 17.0, 8.2 Hz, 1H), 2.79 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 169.1, 150.4, 147.2, 145.0, 144.1, 138.3, 136.2, 134.1, 134.0, 131.6, 130.4, 130.3, 129.4, 129.2, 129.0, 128.1, 128.0, 126.3, 121.5, 120.5, 59.0, 42.4, 21.6, 17.6.

IR(KBr) ν 3042, 2920, 2895, 1684, 1605, 1475, 1400, 1200, 798, 688 cm^{-1}.

HRMS (ESI): Calcd for $C_{27}H_{23}N_2O_2$ $[M+H]^+$ 407.1754, Found: 407.1759.

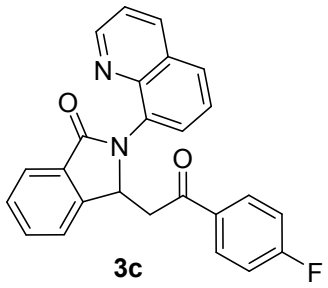


3b

3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one(3b). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 1:1), (eluent: EtOAc/PE: 2/3; 31.8 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 7.86 – 7.81 (m, 2H), 7.61 – 7.50 (m, 6H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 6.55 (dd, *J* = 8.5, 4.6 Hz, 1H), 3.35 (dd, *J* = 17.1, 4.6 Hz, 1H), 3.22 (dd, *J* = 17.1, 8.5 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.0, 168.3, 150.4, 146.6, 144.8, 144.2, 136.3, 134.0, 133.8, 132.0, 130.2, 129.5, 129.2, 128.3, 128.2, 128.0, 126.4, 124.3, 123.2, 121.6, 59.8, 4.1, 21.6.

IR(KBr) ν 3037, 2921, 2896, 1703, 1666, 1605, 1472, 1667, 1399, 1185, 759, 691 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{21}N_2O_2$ $[M+H]^+$ 393.1598, Found: 393.1594.



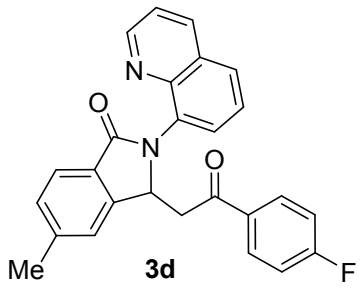
3c

3-(2-(4-fluorophenyl)-2-oxoethyl)-2-(quinolin-8-yl)isoindolin-1-one(3c). The title compound was isolated as an off-white solid (R_f = 0.2

EtOAc/PE 1:1), (eluent: EtOAc/PE: 2/3; 36.8 mg, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.87 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.2 Hz, 1H), 8.00 (d, *J* = 7.4 Hz, 1H), 7.84-7.80 (m, 2H), 7.68 – 7.65 (m, 2H), 7.60 – 7.52 (m, 4H), 7.40 (dd, *J* = 8.3, 4.1 Hz, 1H), 6.98 – 6.96 (m, 2H), 6.55 (dd, *J* = 8.0, 4.9 Hz, 1H), 3.38 (dd, *J* = 17.0, 4.8 Hz, 1H), 3.21 (dd, *J* = 17.0, 8.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.8, 168.2, 165.8 (d, *J* = 256.6 Hz), 150.4, 146.3, 144.7, 136.3, 133.8, 132.9, 132.1, 132.0, 130.6 (d, *J* = 9.4 Hz), 130.3, 129.4, 128.4, 128.2, 126.4, 124.4, 123.1, 121.6, 115.6 (d, *J* = 22.0 Hz), 59.8, 42.1.

IR(KBr) ν 3056, 2924, 2853, 1698, 1595, 1503, 1472, 1395, 1212, 785, 750 cm^{-1}.

HRMS (ESI): Calcd for $C_{25}H_{18}FN_2O_2$ $[M+H]^+$ 397.1347, Found: 397.1346.



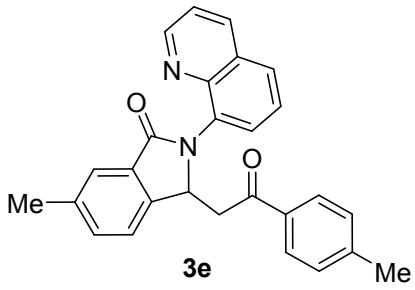
3d

3-(2-(4-fluorophenyl)-2-oxoethyl)-5-methyl-2-(quinolin-8-yl)isoindolin-1-one(3d). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 1:1), (eluent: EtOAc/PE: 2/3; 31.4 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.83 – 7.78 (m, 2H), 7.69 – 7.65 (m, 2H), 7.59 – 7.55 (m, 1H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.33 (d,

J = 7.8 Hz, 2H), 6.97 (t, *J* = 8.6 Hz, 2H), 6.49 (dd, *J* = 7.9, 4.8 Hz, 1H), 3.37 (dd, *J* = 17.1, 4.8 Hz, 1H), 3.20 (dd, *J* = 17.1, 8.0 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.8, 168.4, 165.8 (d, *J* = 256.5 Hz), 150.3, 146.7, 144.7, 142.8, 136.4, 133.9, 132.9, 130.6 (d, *J* = 9.4 Hz), 130.3, 129.4, 128.1, 126.4, 124.2, 123.5, 121.6, 115.6 (d, *J* = 22.0 Hz), 59.5, 42.2, 22.1.

IR(KBr) ν 3061, 2924, 2852, 1688, 1598, 1500, 1401, 1214, 1155, 831, 689 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{20}FN_2O_2$ $[M+H]^+$ 411.1503, Found: 411.1501.



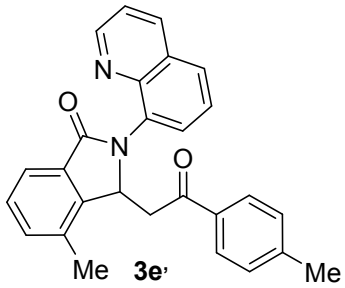
3e

6-methyl-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one (3e). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 1:1), (eluent: EtOAc/PE: 1/3; 27.4 mg, 45%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.88 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.84 (dd, *J* = 7.3, 1.2 Hz, 1H), 7.81 (dd, *J* = 6.2, 1.7 Hz, 2H), 7.59 (d, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.43 – 7.39 (m, 2H), 7.36 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 6.49 (dd, *J* = 8.5, 4.5 Hz, 1H), 3.32 (dd, *J* = 17.0, 4.6 Hz, 1H), 3.19 (dd, *J* = 17.0, 8.6 Hz, 1H), 2.47 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 168.5, 150.4,

144.8, 144.2, 143.8, 138.3, 136.3, 134.1, 134.0, 133.0, 132.1, 130.2, 129.4, 129.2, 128.1, 128.0, 126.4, 124.4, 123.0, 121.6, 59.7, 42.2, 21.6, 21.4.

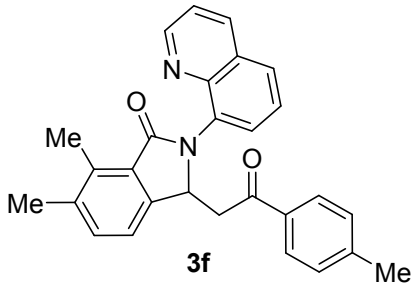
IR(KBr) ν 3034, 2922, 2855, 1700, 1604, 1496, 1395, 1177, 819, 789 cm^{-1}.

HRMS (ESI): Calcd for $C_{27}H_{23}N_2O_2$ $[M+H]^+$ 407.1754, Found: 407.1749.



3e'

4-methyl-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one (3e'). The title compound was isolated in a lower yield, so we could not provide the NMR spectrum. HRMS (ESI): Calcd for $C_{27}H_{23}N_2O_2$ $[M+H]^+$ 407.1754, Found: 407.1752.



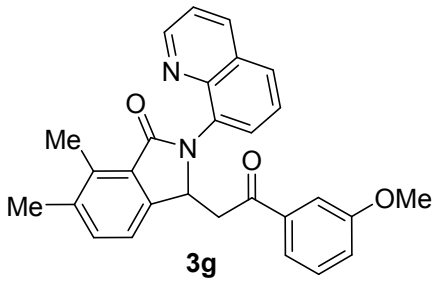
3f

6,7-dimethyl-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one(3f). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 51.7 mg, 82%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 2H), 7.57 (t, *J* = 8.3 Hz, 3H), 7.39 (dd, *J* = 8.3,

4.2 Hz, 1H), 7.31 (d, *J* = 7.7 Hz, 1H), 7.24 (d, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.35 (dd, *J* = 8.0, 4.9 Hz, 1H), 3.34 (dd, *J* = 16.9, 4.9 Hz, 1H), 3.21 (dd, *J* = 16.9, 8.1 Hz, 1H), 2.75 (s, 3H), 2.36 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.2, 169.5, 150.4, 145.0, 144.9, 144.1, 137.5, 137.0, 136.2, 134.3, 134.2, 133.1, 130.5, 129.4, 129.1, 128.7, 128.1, 128.0, 126.3, 121.5, 119.9, 58.4, 42.5, 21.6, 19.3, 13.1.

IR(KBr) ν 3039, 2922, 2861, 1692, 1605, 1474, 1394, 1189, 815, 793 cm^{-1}.

HRMS (ESI): Calcd for $C_{28}H_{25}N_2O_2$ $[M+H]^+$ 421.1911, Found: 421.1906.



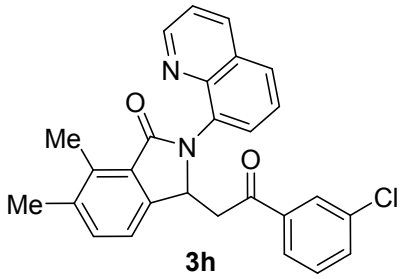
3g

3-(2-(3-methoxyphenyl)-2-oxoethyl)-6,7-dimethyl-2-(quinolin-8-yl)isoindolin-1-one (3g). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 39.9 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, *J* = 2.8 Hz, 1H), 8.18 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.41 (dd, *J* = 8.1, 4.1 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.28-7.18 (m, 4H), 7.02 (d, *J* = 3.1 Hz, 1H), 6.40 – 6.37 (m, 1H), 3.78 (s, 3H), 3.39 (dd, *J* = 17.0, 4.9 Hz, 1H), 3.25 (dd, *J* = 17.0, 7.8 Hz, 1H), 2.78 (s, 3H), 2.39 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 197.4, 169.5, 159.6, 150.4, 145.0, 144.8, 137.9, 137.6, 137.0, 136.2, 134.2, 133.1, 130.5, 129.2, 128.7, 128.1, 126.3,

121.5, 120.6, 119.8, 119.7, 112.0, 58.4, 55.4, 42.8, 19.3, 13.1.

IR(KBr) ν 3018, 2926, 2889, 1688, 1594, 1475, 1399, 1269, 1161, 831, 791 cm^{-1}.

HRMS (ESI): Calcd for $C_{28}H_{25}N_2O_3$ $[M+H]^+$ 437.1860, Found: 437.1855.

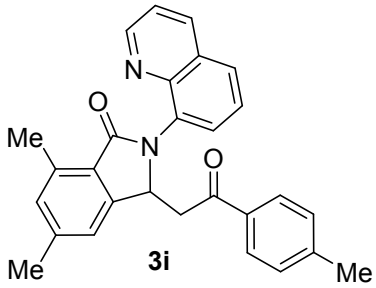


3h

3-(2-(3-chlorophenyl)-2-oxoethyl)-6,7-dimethyl-2-(quinolin-8-yl)isoindolin-1-one(3h). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 37.6 mg, 57%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.85 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.80 – 7.77 (m, 2H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 1.7 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.33 (d, *J* = 7.7 Hz, 1H), 7.24 – 7.20 (m, 2H), 6.35 (t, *J* = 6.3 Hz, 1H), 3.38 (dd, *J* = 16.8, 5.5 Hz, 1H), 3.18 (dd, *J* = 16.8, 7.3 Hz, 1H), 2.75 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl^3$) δ 196.4, 169.4, 150.4, 144.9, 144.5, 138.0, 137.8, 137.2, 136.2, 134.8, 134.1, 133.2, 133.0, 130.5, 129.7, 129.4, 128.7, 128.1, 127.9, 126.3, 125.9, 121.6, 119.7, 58.4, 42.9, 19.3, 13.1.

IR(KBr) ν 3059, 2923, 2889, 1681, 1570, 1476, 1397, 1207, 1024, 797, 690 cm^{-1}.

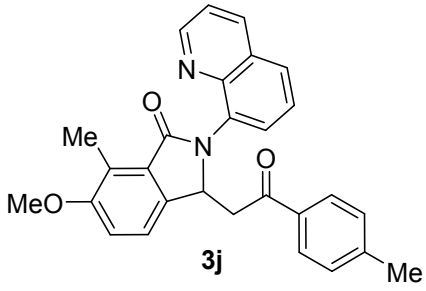
HRMS (ESI): Calcd for $C_{27}H_{22}ClN_2O_2$ $[M+H]^+$ 441.1364, Found: 441.1363.



5,7-dimethyl-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one (3i). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 49.2 mg, 78%).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 2.6 Hz, 1H), 8.15 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.81 – 7.78 (m, 2H), 7.56 (dt, *J* = 7.0, 3.5 Hz, 3H), 7.39 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.11 (dd, *J* = 20.8, 12.8 Hz, 4H), 6.41 (dd, *J* = 7.8, 4.7 Hz, 1H), 3.35 (dd, *J* = 17.1, 4.7 Hz, 1H), 3.23 (dd, *J* = 17.1, 8.1 Hz, 1H), 2.74 (s, 3H), 2.38 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.2, 169.2, 150.4, 147.6, 145.0, 144.1, 142.1, 138.0, 136.3, 134.2, 131.3, 130.4, 129.4, 129.1, 128.8, 128.0, 128.0, 126.5, 126.3, 121.5, 121.0, 58.8, 42.5, 21.8, 21.6, 17.4.

IR(KBr) ν 2921, 2853, 1687, 1606, 1501, 1471, 1363, 1401, 1206, 790, 694 cm^{-1}.

HRMS (ESI): Calcd for $C_{28}H_{25}N_2O_2$ $[M+H]^+$ 421.1911, Found: 421.1916.

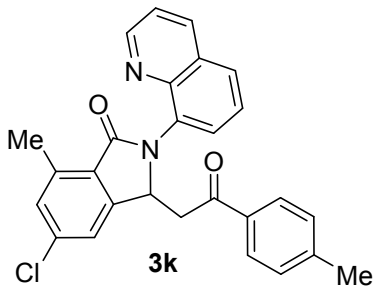


6-methoxy-7-methyl-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-

yl)isoindolin-1-one(3j). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 47.1 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.89 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.81 – 7.79 (m, 2H), 7.57 (t, *J* = 8.3 Hz, 3H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.00 (d, *J* = 8.3 Hz, 1H), 6.34 (dd, *J* = 8.3, 4.6 Hz, 1H), 3.87 (s, 3H), 3.32 (dd, *J* = 16.9, 4.7 Hz, 1H), 3.20 (dd, *J* = 16.9, 8.4 Hz, 1H), 2.68 (s, 3H), 2.33 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 197.4, 169.2, 158.0, 150.4, 145.0, 144.1, 138.8, 136.3, 134.2, 134.2, 130.4, 129.9, 129.4, 129.1, 128.8, 128.1, 128.0, 127.0, 126.3, 121.5, 120.7, 113.7, 58.3, 56.2, 42.8, 21.6, 9.7.

IR(KBr) ν 2951, 2923, 1682, 1608, 1487, 1394, 1365, 1251, 1103, 816, 786 cm^{-1}.

HRMS (ESI): Calcd for $C_{28}H_{25}N_2O_3$ $[M+H]^+$ 437.1860, Found: 437.1865.



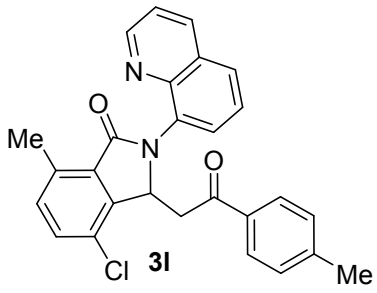
3k

5-chloro-7-methyl-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one(3k). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 34.3 mg, 52%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.88 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.17 – 8.16

(m, 1H), 7.82 – 7.80 (m, 2H), 7.56 – 7.57 (m, 3H), 7.41 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.38 (s, 1H), 7.26 (d, *J* = 5.9 Hz, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.45 (dd, *J* = 8.3, 4.3 Hz, 1H), 3.37 (dd, *J* = 17.4, 4.3 Hz, 1H), 3.22 (dd, *J* = 17.4, 8.4 Hz, 1H), 2.76 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.7, 168.2, 150.5, 148.8, 144.8, 144.3, 134.0, 137.6, 136.3, 133.9, 133.6, 130.5, 130.4, 129.4, 129.2, 128.2, 128.0, 127.6, 126.3, 121.6, 121.1, 58.6, 42.1, 21.6, 17.4.

IR(KBr) ν 3040, 2920, 2852, 1697, 1600, 1500, 1468, 1393, 1188, 794, 689 cm^{-1}.

HRMS (ESI): Calcd for $C_{27}H_{22}ClN_2O_2$ $[M+H]^+$ 441.1364, Found: 441.1360.



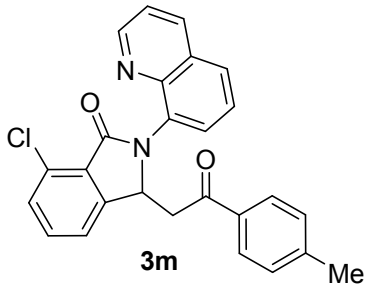
3l

4-chloro-7-methyl-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one(3l). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 30.4 mg, 46%).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.75-7.69 (m, 2H), 7.47 – 7.41 (m, 2H), 7.35 (dd, *J* = 8.2, 5.1 Hz, 3H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.44 (dd, *J* = 6.4, 3.5 Hz, 1H), 3.62 (dd, *J* = 17.2, 6.5 Hz, 1H), 3.56 (dd, *J* = 17.2, 3.6 Hz, 1H), 2.77 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$)

δ 195.9, 168.0, 150.3, 144.8, 143.6, 143.2, 137.1, 136.2, 134.0, 133.6, 132.0, 131.8, 131.6, 130.6, 129.2, 128.9, 128.1, 127.7, 126.2, 125.8, 121.4, 58.7, 39.1, 21.5, 17.1.

IR(KBr) ν 3037, 2919, 2852, 1693, 1602, 1500, 1475, 1403, 1180, 826, 787 cm^{-1}.

HRMS (ESI): Calcd for $C_{27}H_{22}ClN_2O_2$ $[M+H]^+$ 441.1364, Found: 441.1358.



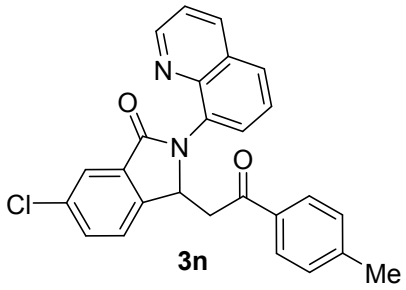
3m

7-chloro-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one(3m). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 25.6 mg, 40%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.88 (dd, *J* = 4.1, 1.7 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.85 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.82 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.59 – 7.56 (m, 3H), 7.46 – 7.44 (m, 3H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.56 (dd, *J* = 8.6, 4.3 Hz, 1H), 3.35 (dd, *J* = 17.2, 4.4 Hz, 1H), 3.20 (dd, *J* = 17.2, 8.6 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.7, 165.9, 150.4, 149.1, 144.7, 144.4, 136.3, 133.9, 133.3, 132.7, 132.1, 130.4, 130.0, 129.4, 129.2, 128.3, 128.0, 126.3, 121.8, 121.6, 58.5, 42.1, 21.6.

IR(KBr) ν 3045, 2924, 2853, 1702, 1602, 1466, 1498, 1394, 1195, 807,

688 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{20}ClN_2O_2$ $[M+H]^+$ 427.1208, Found: 427.1205.

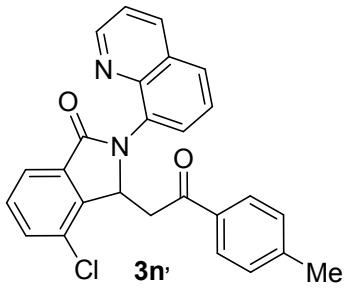


3n

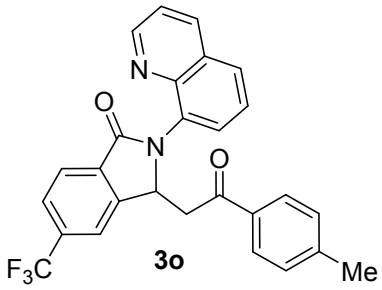
6-chloro-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one (3n). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 32.0 mg, 50%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.89 (dd, *J* = 4.1, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.96 (d, *J* = 1.0 Hz, 1H), 7.85 – 7.82 (m, 2H), 7.61 – 7.57 (m, 3H), 7.51 (d, *J* = 1.2 Hz, 2H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.52 (dd, *J* = 8.9, 4.3 Hz, 1H), 3.34 (dd, *J* = 17.2, 4.3 Hz, 1H), 3.20 (dd, *J* = 17.2, 8.9 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.8, 167.0, 150.5, 144.7, 144.0, 144.4, 136.45, 134.6, 133.9, 133.8, 133.4, 132.1, 130.2, 129.5, 129.2, 128.4, 128.0, 126.4, 124.7, 124.3, 121.7, 59.5, 41.8, 21.6.

IR(KBr) ν 3042, 2922, 2853, 1695, 1602, 1500, 1472, 1402, 1204, 795, 694 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{20}ClN_2O_2$ $[M+H]^+$ 427.1208, Found: 427.1208.



4-chloro-3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one (3n') The title compound was isolated in a lower yield, so we could not provide the NMR spectrum. HRMS (ESI): Calcd for $C_{26}H_{20}ClN_2O_2$ $[M+H]^+$ 427.1208, Found: 427.1204.

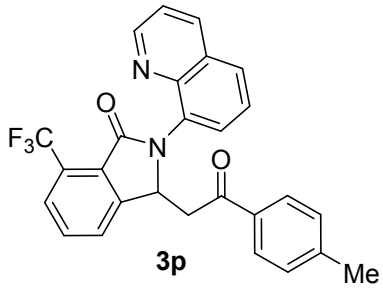


3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)-5-(trifluoromethyl)isoindolin-1-one(3o). The title compound was isolated as an off-white solid (R_f = 0.4 EtOAc/PE 1:1), (eluent: EtOAc/PE: 2/3; 31.1mg, 45%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.89 (dd, *J* = 3.9, 1.3 Hz, 1H), 8.20 – 8.18 (m, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.86 (dd, *J* = 13.5, 6.5 Hz, 3H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.63 – 7.60 (m, 1H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.43 (dd, *J* = 8.3, 4.1 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.60 (dd, *J* = 8.5, 4.2 Hz, 1H), 3.43 (dd, *J* = 17.4, 4.2 Hz, 1H), 3.24 (dd, *J* = 17.4, 8.6 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.5, 167.0, 150.6, 146.9, 144.5, 136.4, 135.4, 134.0, 133.8, 133.7, 133.2, 130.2, 130.0 (CF_3), 129.5, 129.2, 129.0, 128.6, 128.0, 126.4, 125.6 (d, *J* = 3.7

Hz), 125.2 (CF_3), 124.8, 122.5 (CF_3), 121.8, 120.8 (d, J = 3.8 Hz), 59.7, 41.6, 21.6.

IR(KBr) ν 3045, 2923, 2855, 1702, 1606, 1500, 1404, 1329, 1169, 1126, 791, 691 cm^{-1}.

HRMS (ESI): Calcd for $C_{27}H_{20}F_3N_2O_2$ $[M+H]^+$ 461.1471, Found: 461.1469.

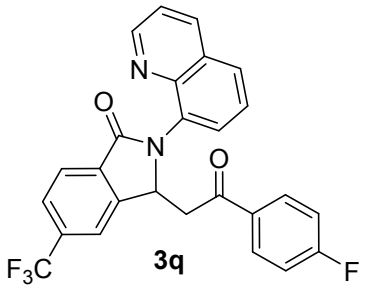


3p

3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)-7-(trifluoromethyl)isoindolin-1-one(3p). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 57.3mg, 83%; **1p** 1.5mmol, **3p** 0.4 g, 58%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.88 (dd, J = 4.2, 1.7 Hz, 1H), 8.18 (dd, J = 8.3, 1.6 Hz, 1H), 7.90 (dd, J = 7.4, 1.2 Hz, 1H), 7.82 (dd, J = 11.1, 4.1 Hz, 3H), 7.64 (t, J = 7.7 Hz, 1H), 7.58 (t, J = 7.7 Hz, 3H), 7.41 (dd, J = 8.3, 4.2 Hz, 1H), 7.13 (d, J = 8.1 Hz, 2H), 6.70 (dd, J = 8.7, 4.1 Hz, 1H), 3.40 (dd, J = 17.3, 4.2 Hz, 1H), 3.24 (dd, J = 17.3, 8.8 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.7, 164.9, 150.4, 148.9, 144.5 (d, J = 6.0 Hz), 136.4, 133.8, 133.1, 131.7, 130.4, 129.4, 129.3 (CF_3), 129.3, 128.3, 128.0, 127.5 (d, J = 34.7 Hz), 127.1, 126.2, 126.0 (d, J = 5.8 Hz), 124.3 (CF_3), 121.6, 121.6 (CF_3), 58.9, 41.9, 21.6.

IR(KBr) ν 3040, 2924, 2854, 1704, 1606, 1503, 1398, 1329, 1148, 806, 697 cm^{-1}.

HRMS (ESI): Calcd for $C_{27}H_{20}F_3N_2O_2$ $[M+H]^+$ 461.1471, Found: 461.1470.



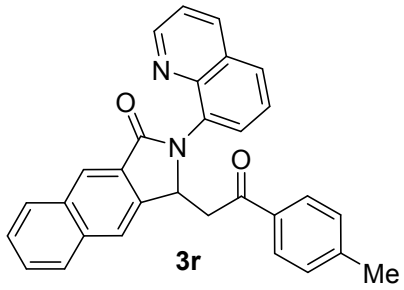
3q

3-(2-(4-fluorophenyl)-2-oxoethyl)-2-(quinolin-8-yl)-5-(trifluoromethyl)isoindolin-1-one(3q). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 34.8mg, 50%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.87 (d, *J* = 2.7 Hz, 1H), 8.18 (d, *J* = 7.4 Hz, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.88 (s, 1H), 7.85 (d, *J* = 7.8 Hz, 2H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.69 (dd, *J* = 8.8, 5.4 Hz, 2H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.43 (dd, *J* = 8.2, 4.1 Hz, 1H), 6.99 (t, *J* = 8.6 Hz, 2H), 6.61 (dd, *J* = 8.1, 4.5 Hz, 1H), 3.45 (dd, *J* = 17.4, 4.5 Hz, 1H), 3.23 (dd, *J* = 17.4, 8.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.2, 167.2, 165.8 (d, *J* = 231.6 Hz), 150.6, 146.7, 144.5, 136.4, 135.4, 133.9 (d, *J* = 32.4 Hz), 133.2, 132.6 (d, *J* = 3.0 Hz), 130.6 (d, *J* = 9.5 Hz), 130.2, 129.5, 128.6, 126.4, 125.7 (d, *J* = 3.7 Hz), 125.2(CF_3), 124.9, 122.5 (CF_3), 121.8, 120.7(d, *J* = 3.9 Hz), 115.7, (d, *J* = 22.1 Hz), 59.7, 41.7.

IR(KBr) ν 3071, 2924, 2852, 1703, 1668, 1596, 1503, 1409, 1329, 1163,

1124, 801, 695 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{17}F_4N_2O_2$ $[M+H]^+$ 465.1221, Found: 465.1228.

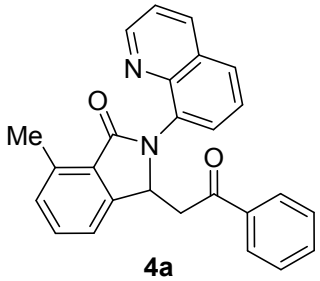


3r

3-(2-oxo-2-(p-tolyl)ethyl)-2-(quinolin-8-yl)-2,3-dihydro-1H-benzo[f]isoindol-1-one(3r). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 38.5mg, 58%). ^1H NMR (600 MHz, $CDCl_3$) δ 9.34 (d, *J* = 8.4 Hz, 1H), 8.88 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.4 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.90 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.82 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.69-7.66 (m, 1H), 7.63 – 7.57 (m, 5H), 7.40 (dd, *J* = 8.3, 4.1 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 6.65 (dd, *J* = 8.3, 4.8 Hz, 1H), 3.43 (dd, *J* = 17.0, 4.8 Hz, 1H), 3.29 (dd, *J* = 17.0, 8.3 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 169.3, 150.4, 147.3, 145.0, 144.2, 136.3, 134.0, 133.9, 133.3, 132.9, 130.4, 129.8, 129.5, 129.2, 128.1, 128.1, 128.0, 126.6, 126.3, 125.8, 125.8, 124.2, 121.6, 120.3, 59.4, 41.9, 21.6.

IR(KBr) ν 3049, 2920, 2852, 1684, 1600, 1500, 1465, 1356, 1398, 1184, 791,751 cm^{-1}.

HRMS (ESI): Calcd for $C_{30}H_{23}N_2O_2$ $[M+H]^+$ 443.1754, Found: 443.1753.

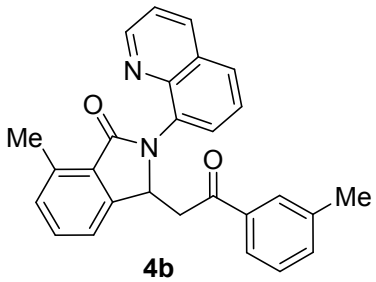


4a

7-methyl-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (4a). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 37.0 mg, 63%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.87 (dd, *J* = 4.1, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.82-7.79 (m, 2H), 7.64 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.57 (dd, *J* = 8.1, 7.5 Hz, 1H), 7.47 – 7.45 (m, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.32 – 7.29 (m, 2H), 7.25 (d, *J* = 7.8 Hz, 1H), 6.48 (dd, *J* = 7.9, 4.9 Hz, 1H), 3.40 (dd, *J* = 17.1, 4.9 Hz, 1H), 3.26 (dd, *J* = 17.1, 8.0 Hz, 1H), 2.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5, 169.1, 150.4, 147.1, 144.9, 138.4, 136.5, 136.2, 134.0, 133.2, 131.6, 130.4, 130.4, 129.4, 129.0, 128.5, 128.1, 127.9, 126.3, 121.5, 120.4, 59.0, 42.5, 17.5.

IR(KBr) ν 3062, 2924, 2855, 1679, 1598, 1502, 1472, 1405, 788, 753, 695 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{21}N_2O_2$ $[M+H]^+$ 393.1598, Found: 393.1598.

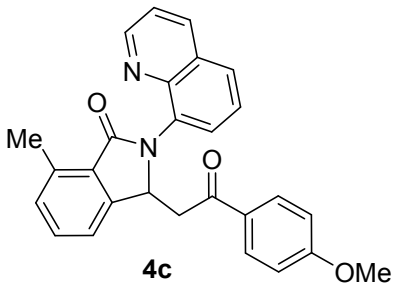


4b

7-methyl-3-(2-oxo-2-(m-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one (4a). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 43.9 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.81 (t, *J* = 6.7 Hz, 2H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.45 – 7.37 (m, 4H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.26 (t, *J* = 7.4 Hz, 2H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.47 (dd, *J* = 7.8, 5.0 Hz, 1H), 3.38 (dd, *J* = 17.0, 4.9 Hz, 1H), 3.24 (dd, *J* = 17.0, 8.0 Hz, 1H), 2.79 (s, 3H), 2.29 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 169.1, 150.4, 147.1, 145.0, 138.4, 138.3, 136.6, 136.2, 134.0, 131.6, 130.4, 130.4, 129.4, 129.0, 128.4, 128.3, 128.1, 126.3, 125.1, 121.5, 120.4, 59.0, 42.6, 21.2, 17.5.

IR(KBr) ν 3062, 2924, 2853, 1686, 1600, 1503, 1474, 1402, 1360, 1183, 783, 686 cm^{-1}.

HRMS (ESI): Calcd for $C_{27}H_{23}N_2O_2$ $[M+H]^+$ 407.1754, Found: 407.1753.



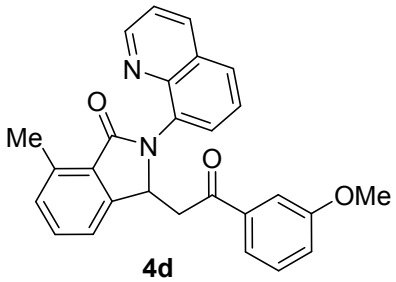
4c

3-(2-(4-methoxyphenyl)-2-oxoethyl)-7-methyl-2-(quinolin-8-yl)isoindolin-1-one (4c). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 1:1), (eluent: EtOAc/PE: 1/3; 31.7 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.82-7.78 (m, 2H), 7.66 – 7.63 (m, 2H), 7.59 – 7.55

(m, 1H), 7.43 – 7.38 (m, 2H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.4 Hz, 1H), 6.79 – 6.76 (m, 2H), 6.45 (dd, *J* = 8.1, 4.8 Hz, 1H), 3.80 (s, 3H), 3.32 (dd, *J* = 16.8, 4.8 Hz, 1H), 3.20 (dd, *J* = 16.8, 8.2 Hz, 1H), 2.79 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 169.1, 163.6, 150.4, 147.2, 145.0, 138.3, 136.2, 134.1, 131.5, 130.4, 130.3, 130.2, 129.7, 129.4, 129.0, 128.1, 126.2, 121.5, 120.5, 113.6, 59.1, 55.5, 42.1, 17.5.

IR(KBr) ν 3041, 2924, 2837, 1687, 1600, 1504, 1469, 1397, 1257, 1173, 789, 687 cm^{-1}.

HRMS (ESI): Calcd for $C_{27}H_{23}N_2O_3$ $[M+H]^+$ 423.1703, Found: 423.1707.



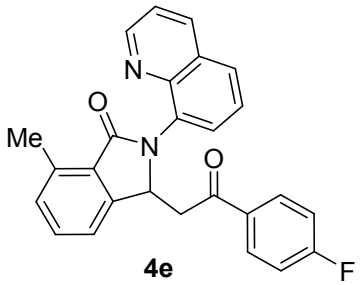
4d

3-(2-(3-methoxyphenyl)-2-oxoethyl)-7-methyl-2-(quinolin-8-yl)isoindolin-1-one (4d). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 33.6 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.82 – 7.79 (m, 2H), 7.59 – 7.55 (m, 1H), 7.44-7.38 (m, 2H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 5.9 Hz, 1H), 7.21 – 7.20 (m, 2H), 7.17 (d, *J* = 1.8 Hz, 1H), 7.02 – 6.99 (m, 1H), 6.46 (dd, *J* = 7.8, 5.0 Hz, 1H), 3.76 (s, 3H), 3.38 (dd, *J* = 17.1, 4.9 Hz, 1H), 3.24 (dd, *J* = 17.1, 7.9 Hz, 1H), 2.79 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 197.3, 169.1, 159.7, 150.4, 147.0, 144.9, 138.4, 137.9, 136.2, 134.0, 131.6, 130.4,

130.4, 129.4, 129.0, 128.1, 126.3, 121.5, 120.6, 120.4, 119.7, 112.0, 59.0, 55.4, 42.7, 17.5.

IR(KBr) ν 3064, 2922, 2840, 1691, 1578, 1479, 1400, 1241, 785, 693 cm^{-1}.

HRMS (ESI): Calcd for $C_{27}H_{23}N_2O_3$ $[M+H]^+$ 423.1703, Found: 423.1702.

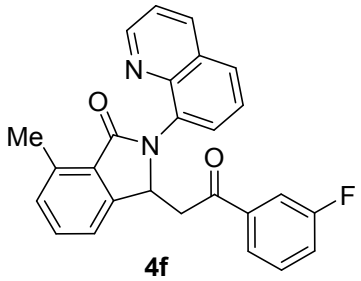


4e

3-(2-(4-fluorophenyl)-2-oxoethyl)-7-methyl-2-(quinolin-8-yl)isoindolin-1-one (4e). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 44.3 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 3.8 Hz, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.80 – 7.78 (m, 2H), 7.65 (dd, *J* = 7.7, 5.8 Hz, 2H), 7.56 (t, *J* = 7.7 Hz, 1H), 7.44-7.37 (m, 2H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 6.9 Hz, 1H), 6.96 (t, *J* = 8.4 Hz, 2H), 6.46 – 6.43 (m, 1H), 3.37 (dd, *J* = 16.9, 4.9 Hz, 1H), 3.21 (dd, *J* = 16.9, 7.7 Hz, 1H), 2.78 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 169.0, 165.7 (d, *J* =256.5 Hz), 150.4, 146.9, 144.9, 138.4, 136.3, 134.0, 133.0 (d, *J* = 2.9 Hz), 131.6, 130.6, 130.5 – 130.4 (m), 129.4, 129.0, 128.1, 126.3, 121.6, 120.3, 115.6 (d, *J* = 22.0 Hz), 59.0, 42.4, 17.5.

IR(KBr) ν 3065, 3013, 2903, 1678, 1576, 1504, 1473, 1401, 1227, 1154, 822, 787 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{20}FN_2O_2$ $[M+H]^+$ 411.1503, Found: 411.1500.

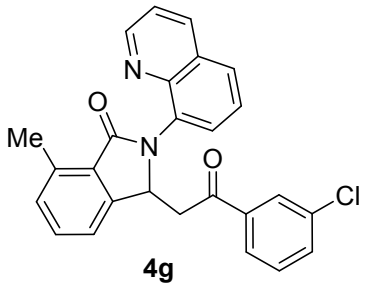


4f

3-(2-(3-fluorophenyl)-2-oxoethyl)-7-methyl-2-(quinolin-8-yl)isoindolin-1-one(4f). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 30.8 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.80 (d, *J* = 7.7 Hz, 2H), 7.57 (dd, *J* = 8.1, 7.5 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.30-7.25 (m, 3H), 7.18-7.13 (m, 1H), 6.46 (dd, *J* = 7.5, 5.3 Hz, 1H), 3.39 (dd, *J* = 17.0, 5.2 Hz, 1H), 3.22 (dd, *J* = 17.0, 7.6 Hz, 1H), 2.79 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3 (d, *J* = 2.1 Hz), 169.0, 162.6 (d, *J* = 249.3 Hz)), 150.4, 146.8, 144.9, 138.6, 138.5, 136.3, 133.9, 131.6, 130.5 (d, *J* = 3.6 Hz), 130.1 (d, *J* = 7.7 Hz), 129.4, 129.0, 128.2, 126.3, 123.6 (d, *J* = 3.0 Hz), 121.6, 120.3, 120.2 (d, *J* = 21.6 Hz), 114.5 (d, *J* = 22.5 Hz), 114.4, 58.9, 42.8, 17.5.

IR(KBr) ν 3068, 2920, 2852, 1687, 1591, 1503, 1477, 1447, 1400, 1240, 792, 685 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{20}FN_2O_2$ $[M+H]^+$ 411.1503, Found: 411.1504.

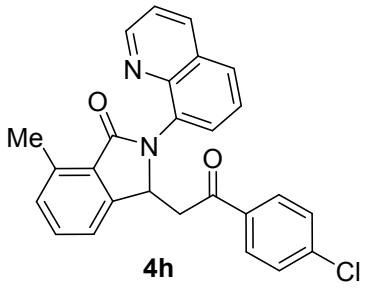


4g

3-(2-(3-chlorophenyl)-2-oxoethyl)-7-methyl-2-(quinolin-8-yl)isoindolin-1-one(4g). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 33.8 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 2H), 7.59 – 7.55 (m, 1H), 7.51 (t, *J* = 1.8 Hz, 1H), 7.49-7.37 (m, 4H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.27 – 7.21 (m, 2H), 6.46 (dd, *J* = 7.1, 5.7 Hz, 1H), 3.40 (dd, *J* = 16.9, 5.4 Hz, 1H), 3.20 (dd, *J* = 16.9, 7.4 Hz, 1H), 2.79 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 169.0, 150.4, 146.7, 144.8, 138.5, 138.0, 136.2, 134.8, 133.9, 133.1, 131.6, 130.5, 130.5, 129.7, 129.4, 129.0, 128.2, 127.9, 126.3, 125.9, 121.6, 120.2, 59.0, 42.8, 17.5.

IR(KBr) ν 3065, 2921, 2851, 1692, 1598, 1503, 1475, 1400, 1211, 784, 689 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{20}ClN_2O_2$ $[M+H]^+$ 427.1208, Found: 427.1211.

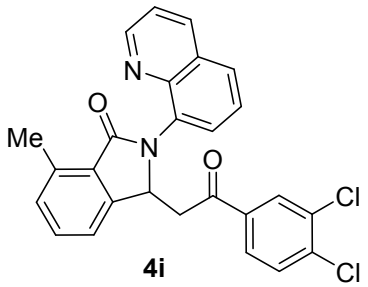


4h

3-(2-(4-chlorophenyl)-2-oxoethyl)-7-methyl-2-(quinolin-8-yl)isoindolin-1-one(4h). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 44.7 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 8.1 Hz, 3H), 7.44 – 7.37 (m, 2H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.25 (dd, *J* = 6.8, 1.8 Hz, 3H), 6.44 (dd, *J* = 7.4, 5.3 Hz, 1H), 3.37 (dd, *J* = 17.0, 5.2 Hz, 1H), 3.21 (dd, *J* = 17.0, 7.6 Hz, 1H), 2.79 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 169.0, 150.4, 146.8, 144.9, 139.7, 138.4, 136.3, 134.8, 134.0, 131.6, 130.5, 130.4, 129.4, 129.2, 129.0, 128.7, 128.2, 126.3, 121.6, 120.3, 59.0, 42.5, 17.5.

IR(KBr) ν 3050, 2920, 2856, 1688, 1591, 1502, 1475, 1401, 1203, 1087, 829, 793 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{20}ClN_2O_2$ $[M+H]^+$ 427.1208, Found: 427.1212.



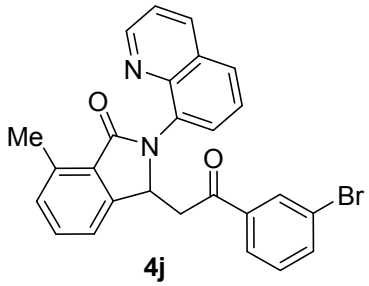
4i

3-(2-(3,4-dichlorophenyl)-2-oxoethyl)-7-methyl-2-(quinolin-8-yl)isoindolin-1-one(4i). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 31.7 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J*

= 8.3, 1.6 Hz, 1H), 7.80 – 7.77 (m, 2H), 7.57 (dd, *J* = 10.1, 5.0 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.35 – 7.31 (m, 2H), 7.27 (d, *J* = 7.7 Hz, 1H), 6.43 (t, *J* = 6.3 Hz, 1H), 3.39 (dd, *J* = 16.7, 5.8 Hz, 1H), 3.18 (dd, *J* = 16.7, 7.0 Hz, 1H), 2.78 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 195.4, 168.9, 150.5, 146.5, 144.8, 138.6, 137.8, 136.26, 135.9, 133.8, 133.1, 131.7, 130.6, 130.5, 129.7, 129.4, 129.0, 128.2, 126.8, 126.32, 121.6, 120.1, 59.1, 42.7, 17.5.

IR(KBr) ν 3066, 2924, 2854, 1683, 1587, 1500, 1469, 1391, 1198, 1032, 783, 691 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{19}Cl_2N_2O_2$ $[M+H]^+$ 461.0818, Found: 461.0817.



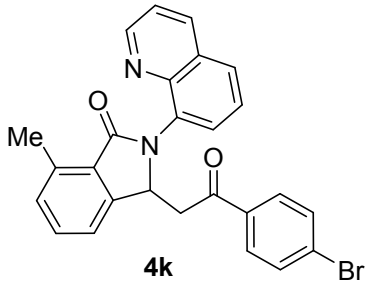
4j

3-(2-(3-bromophenyl)-2-oxoethyl)-7-methyl-2-(quinolin-8-yl)isoindolin-1-one(4j). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 36.0 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.65 (t, *J* = 1.7 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 2H), 7.51 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.26 (t, *J* = 3.7 Hz, 1H), 7.16 (t, *J* = 7.9 Hz, 1H), 6.47 – 6.45 (m, 1H), 3.39 (dd, *J* = 16.9, 5.5

Hz, 1H), 3.20 (dd, *J* = 16.9, 7.2 Hz, 1H), 2.79 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 196.2, 169.0, 150.4, 146.7, 144.8, 138.5, 138.1, 136.2, 136.0, 133.9, 131.6, 130.8, 130.5, 130.5, 130.0, 129.4, 129.0, 128.2, 126.3, 122.8, 121.6, 120.2, 59.0, 42.7, 17.5.

IR(KBr) ν 3062, 2952, 2920, 1684, 1600, 1502, 1473, 1400, 1200, 791, 680 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{20}BrN_2O_2$ $[M+H]^+$ 471.0703, Found: 471.0703.



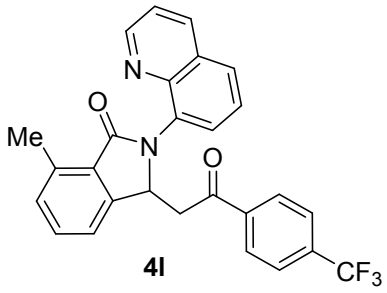
4k

3-(2-(4-bromophenyl)-2-oxoethyl)-7-methyl-2-(quinolin-8-yl)isoindolin-1-one(4k). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 51.5 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.48 – 7.37 (m, 6H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.27 – 7.25 (m, 1H), 6.44 (dd, *J* = 7.4, 5.3 Hz, 1H), 3.37 (dd, *J* = 17.0, 5.2 Hz, 1H), 3.20 (dd, *J* = 17.0, 7.6 Hz, 1H), 2.79 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 196.5, 169.0, 150.4, 146.8, 144.9, 138.5, 136.3, 135.2, 133.9, 131.7, 131.6, 130.5, 130.4, 129.4, 129.3, 129.0, 128.4, 128.2, 126.3, 121.6, 120.3, 59.0, 42.5, 17.5.

IR(KBr) ν 3039, 2922, 2893, 1682, 1580, 1492, 1401, 1206, 833, 795,

695 cm^{-1}.

HRMS (ESI): Calcd for $C_{26}H_{20}BrN_2O_2$ $[M+H]^+$ 471.0703, Found: 471.0701.



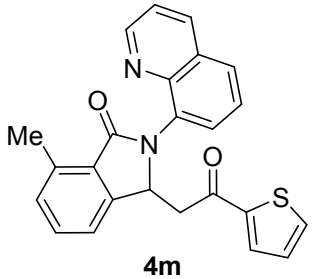
4l

7-methyl-3-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one(4l). The title compound was isolated as an off-white solid (R_f = 0.3 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 24.2 mg, 35%). ^1H NMR (600 MHz, $CDCl_3$) δ 8.84 (dd, *J* = 3.9, 1.3 Hz, 1H), 8.13 (d, *J* = 7.9 Hz, 1H), 7.80 – 7.78 (m, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 8.3 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.38 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 1H), 6.45 (t, *J* = 6.3 Hz, 1H), 3.45 (dd, *J* = 17.0, 5.5 Hz, 1H), 3.27 (dd, *J* = 17.0, 7.2 Hz, 1H), 2.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.7, 169.0, 150.4, 146.6, 139.0, 138.6, 136.3, 134.6, 134.2, 133.9, 131.7, 130.6, 130.5, 129.4, 129.0, 128.2, 128.1, 126.3, *125*.5 (d, *J* = 3.7 Hz), 124.8 (CF_3), 122.1 (CF_3), 121.6, 120.2, 59.0, 42.9, 17.5.

IR(KBr) ν 3040, 2922, 2851, 1689, 1406, 1329, 1163, 1135, 1065, 840, 796, 693 cm^{-1}.

HRMS (ESI): Calcd for $C_{27}H_{20}F_3N_2O_2$ $[M+H]^+$ 461.1471, Found:

461.1470.

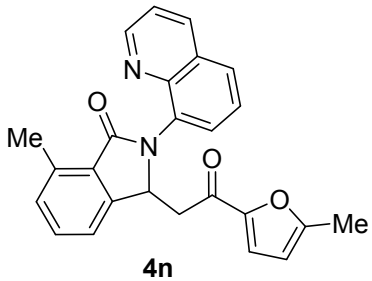


4m

7-methyl-3-(2-oxo-2-(thiophen-2-yl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one(4m). The title compound was isolated as an off-white solid (R_f = 0.4 EtOAc/PE 1:1), (eluent: EtOAc/PE: 1/3; 37.0 mg, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.88 (dd, *J* = 4.1, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.81-7.78 (m, 2H), 7.55 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.52 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.39 (dd, *J* = 8.3, 4.1 Hz, 1H), 7.36 – 7.34 (m, 2H), 7.26 – 7.25 (m, 1H), 6.94 (dd, *J* = 4.9, 3.9 Hz, 1H), 6.44 (dd, *J* = 7.6, 5.4 Hz, 1H), 3.32 (dd, *J* = 16.4, 5.3 Hz, 1H), 3.16 (dd, *J* = 16.4, 7.7 Hz, 1H), 2.79 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 190.0, 169.0, 150.4, 146.7, 144.9, 143.9, 138.4, 136.3, 134.2, 133.9, 132.1, 131.6, 130.4, 130.4, 129.4, 129.0, 128.2, 128.0, 126.2, 121.6, 120.4, 59.0, 43.1, 17.6.

IR(KBr) ν 3085, 2914, 2850, 1687, 1647, 1599, 1499, 1476, 1402, 1204, 1159, 788, 732 cm^{-1}.

HRMS (ESI): Calcd for $C_{24}H_{19}N_2O_2S$ $[M+H]^+$ 399.1162, Found: 399.1167.

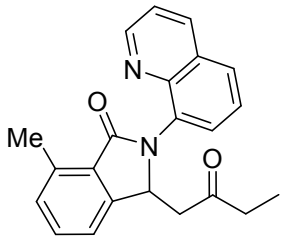


4n

7-methyl-3-(2-(5-methylfuran-2-yl)-2-oxoethyl)-2-(quinolin-8-yl)isoindolin-1-one(4n). The title compound was isolated as an off-white solid (R_f = 0.4 EtOAc/PE 1:1), (eluent: EtOAc/PE: 1/3; 30.3 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, J = 8.3, 1.6 Hz, 1H), 7.81 – 7.78 (m, 2H), 7.56 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.43 – 7.38 (m, 2H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 3.4 Hz, 1H), 6.42 (dd, *J* = 7.6, 5.7 Hz, 1H), 5.99 (dd, *J* = 3.5, 0.8 Hz, 1H), 3.18 (dd, *J* = 16.1, 5.5 Hz, 1H), 3.03 (dd, *J* = 16.1, 7.8 Hz, 1H), 2.78 (s, 3H), 2.26 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 185.2, 169.0, 158.0, 151.1, 150.3, 146.8, 144.9, 138.3, 136.2, 133.9, 131.5, 130.4, 130.4, 129.4, 129.0, 128.0, 126.2, 121.5, 120.4, 119.4, 109.0, 58.9, 42.0, 17.5, 14.0.

IR(KBr) ν 3109, 2922, 1672, 1603, 1509, 1400, 1213, 1045, 822, 787, 689 cm^{-1}.

HRMS (ESI): Calcd for $C_{25}H_{21}N_2O_3$ $[M+H]^+$ 397.1547, Found: 397.1543.



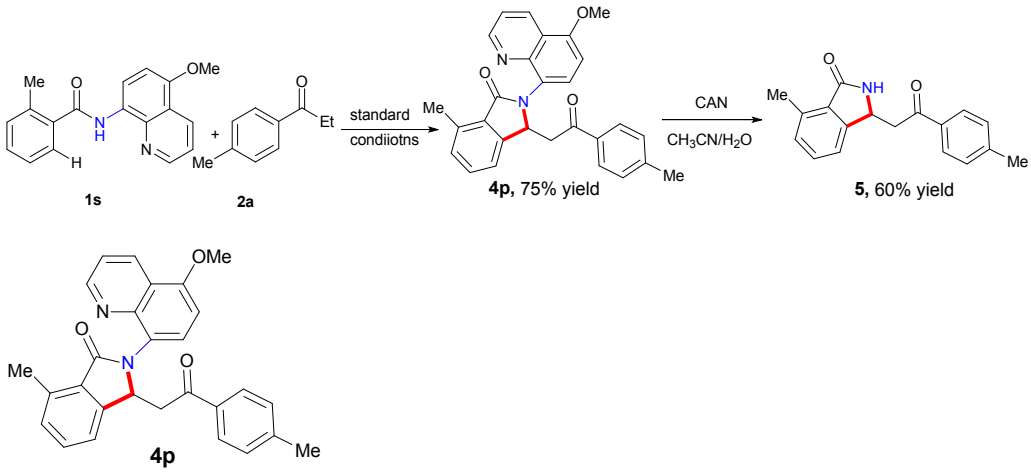
4o

7-methyl-3-(2-oxobutyl)-2-(quinolin-8-yl)isoindolin-1-one(4o). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 19.1 mg, 37%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.86-7.80 (m, 2H), 7.64 – 7.61 (m, 1H), 7.46 – 7.42 (m, 2H), 7.27 (dd, *J* = 12.8, 7.2 Hz, 2H), 6.27 (dd, *J* = 7.7, 5.2 Hz, 1H), 2.83 (dd, *J* = 17.0, 5.1 Hz, 1H), 2.77 (s, 3H), 2.69 (dd, *J* = 17.0, 7.8 Hz, 1H), 2.21-2.06 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 208.5, 169.0, 150.5, 146.9, 144.9, 138.4, 136.3, 134.0, 131.6, 130.4, 130.3, 129.4, 129.0, 128.1, 126.3, 121.6, 120.7, 58.5, 46.0, 36.7, 17.5, 7.3.

IR(KBr) ν 3041, 2925, 1694, 1597, 1498, 1473, 1399, 1197, 795, 693, 622 cm^{-1}.

HRMS (ESI): Calcd for $C_{22}H_{21}N_2O_2$ $[M+H]^+$ 345.1598, Found: 345.1599.

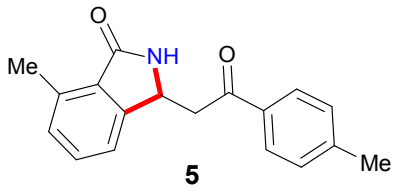
5. Removal of the directing group



2-(5-methoxyquinolin-8-yl)-7-methyl-3-(2-oxo-2-(p-tolyl)ethyl)isoindolin-1-one(4p). The title compound was isolated as an off-white solid (R_f = 0.2 EtOAc/PE 2:3), (eluent: EtOAc/PE: 1/3; 49.0 mg, 75%).^{1}H NMR (600 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.54 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.36 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 8.1 Hz, 2H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.27 (dd, *J* = 7.6, 5.0 Hz, 1H), 3.99 (s, 3H), 3.39 (dd, *J* = 16.9, 5.0 Hz, 1H), 3.22 (dd, *J* = 16.9, 8.0 Hz, 1H), 2.78 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.3, 169.4, 155.1, 150.7, 147.1, 145.5, 144.0, 138.2, 134.2, 131.4, 131.1, 130.7, 130.3, 129.1, 129.1, 128.0, 126.4, 121.6, 120.6, 120.4, 103.8, 59.1, 55.9, 42.3, 21.6, 17.5.

IR(KBr) ν 3130, 1690, 1605, 1593, 1477, 1401, 1272, 1203, 809, 785, 692 cm^{-1}.

HRMS (ESI): Calcd for $C_{28}H_{24}N_2O_3$ $[M+H]^+$ 437.1860, Found: 437.1862.



5

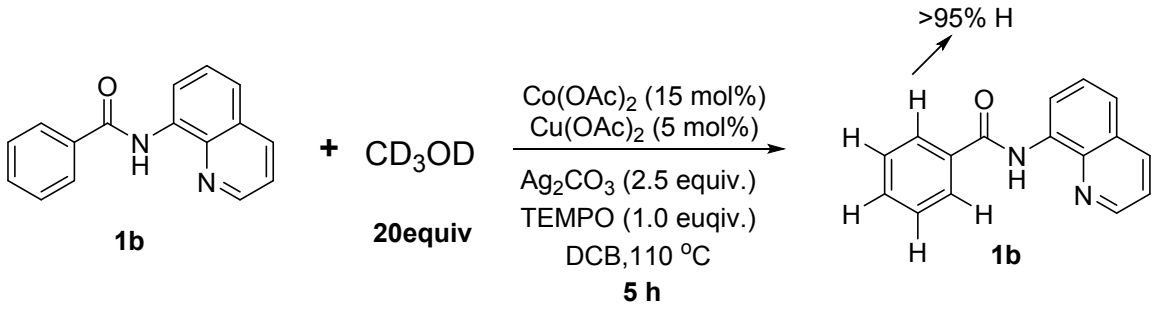
7-methyl-3-(2-oxo-2-(p-tolyl)ethyl)isoindolin-1-one(5). According to the literature,[3] to a solution of **4p** (87.4 mg, 0.2 mmol) in MeCN (2.0 mL) at RT was added solution of CAN (Cerium Diammonium Nitrate) (438 mg, 0.8 mmol, 4 equiv) in H_2O (2.0 mL). Resulting solution was stirred at 40 ^oC for 5 h, H_2O (15 mL) was added and the reaction mixture was extracted with EtOAc (3 x 15 mL). Combined organic phase was washed with 10% Na_2SO_3 solution (2 x 15 mL) and brine (15 mL), dried over $MgSO_4$, filtered, solvent was evaporated. After column chromatography (eluent: EtOAc/PE: 1/4; 34.0 mg; 60%) of an off-white solid was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.2 Hz, 2H), 7.44 (t, J = 7.6 Hz, 1H), 7.28 – 7.25 (m, 3H), 7.22 (d, J = 7.5 Hz, 1H), 6.77 (s, 1H), 5.05 (d, J = 8.7 Hz, 1H), 3.66 (dd, J = 18.0, 3.0 Hz, 1H), 3.04 (dd, J = 18.0, 10.4 Hz, 1H), 2.73 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 170.9, 147.2, 144.8, 138.4, 133.7, 131.5, 130.4, 129.5, 129.0, 128.2, 119.6, 51.7, 44.3, 21.7, 17.3.

IR(KBr) ν 3196, 3089, 2920, 1703, 1679, 1605, 1407, 1374, 1314, 1205, 802, 783 cm^{-1}.

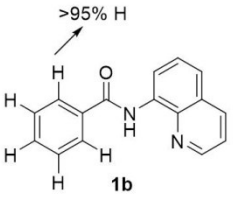
HRMS (ESI): Calcd for $C_{18}H_{17}NO_2$ $[M+H]^+$ 280.1332, Found: 280.1332.

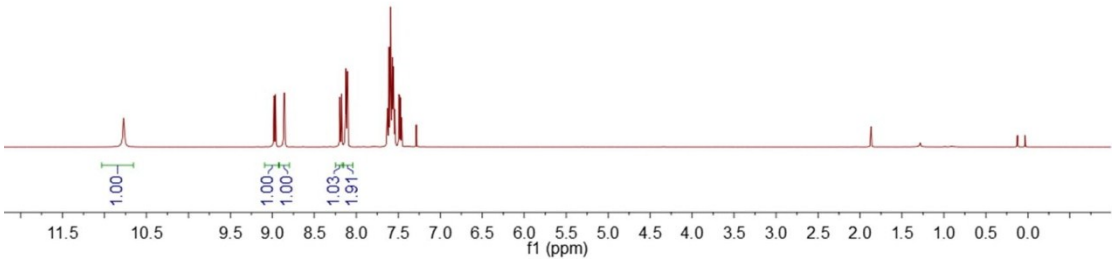
6. Experimental procedures of mechanistic studies

(1) Cobalt-Catalyzed H/D Exchange in 1b with CD_3OD

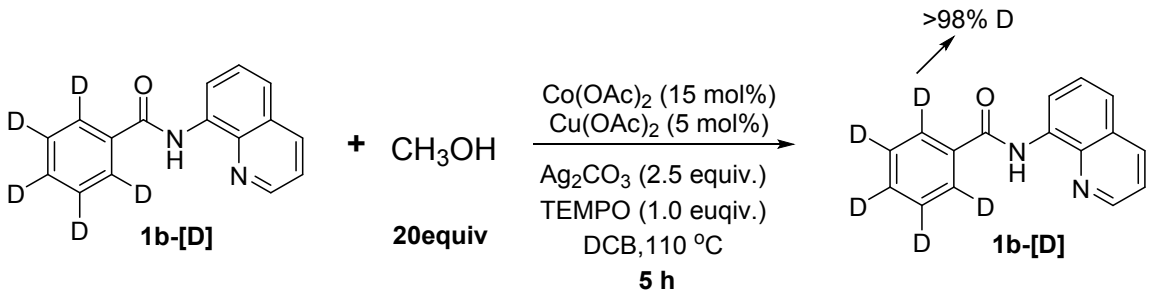


In a glove box, a 25 mL Schlenk tube equipped with a stir bar was charged with **1b** (49.6mg, 0.2 mmol), $Co(OAc)_2$ (5.5 mg, 15 mol%), Ag_2CO_3 (138.0 mg, 2.5 equiv.), $Cu(OAc)_2$ (1.9 mg, 5 mol%), TEMPO (31.3 mg, 1.0 equiv.). The tube was fitted with a rubber septum, and removed out from the glove box. Then CD_3OD (20 equiv.) was added through the rubber septum using syringe under the atmosphere of N_2. 1,2-Dichlorobenzene (1.0 mL) was added to the Schlenk tube through the rubber septum using a syringe. The septum was replaced by a Teflon screwcap under N_2 flow. The reaction mixture was stirred at 110 °C (pre-heated to 110 °C) for 5 h. After cooling down, the solvent was removed in vacuo and the residue was purified by chromatography on silica gel (eluent: EtOAc/PE) to provide the corresponding product, and then analyzed by NMR.



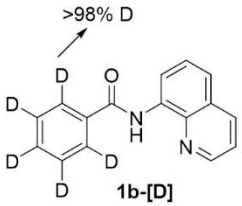


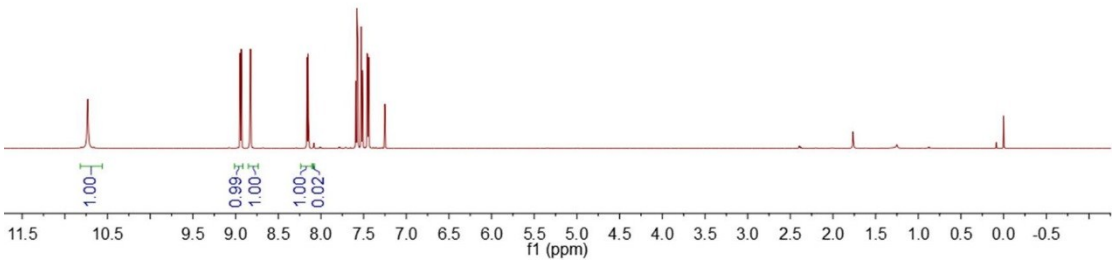
(2) Cobalt-Catalyzed H/D Exchange in 1b-[D] with CH_3OH



In a glove box, a 25 mL Schlenk tube equipped with a stir bar was charged with **1b**-[D] (50.6mg, 0.2 mmol), $Co(OAc)_2$ (5.5 mg, 15 mol%), Ag_2CO_3 (138.0 mg, 2.5 equiv.), $Cu(OAc)_2$ (1.9 mg, 5 mol%), TEMPO (31.3 mg, 1.0 equiv.). The tube was fitted with a rubber septum, and removed out from the glove box. Then CH_3OH (20 equiv.) was added through the rubber septum using a syringe under the atmosphere of N_2. 1,2-Dichlorobenzene (1.0 mL) was added to the Schlenk tube through the rubber septum using syringe. The septum was replaced by a Teflon

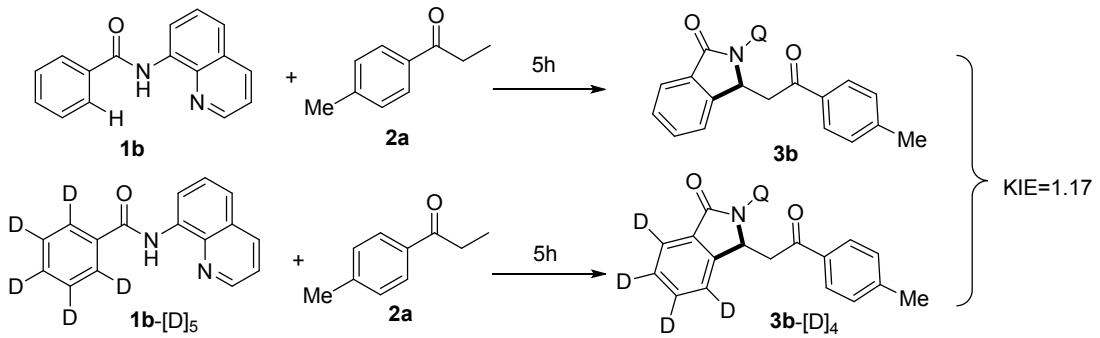
screwcap under N_2 flow. The reaction mixture was stirred at 110 °C (pre-heated to 110 °C) for 5 h. After cooling down, the solvent was removed in vacuo and the residue was purified by chromatography on silica gel (eluent: EtOAc/PE) to provide the corresponding product, and then analyzed by NMR.





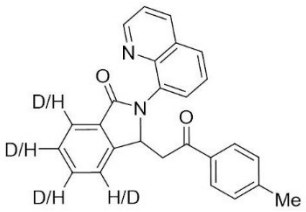
(3) Studies on the Kinetic Isotope Effect.

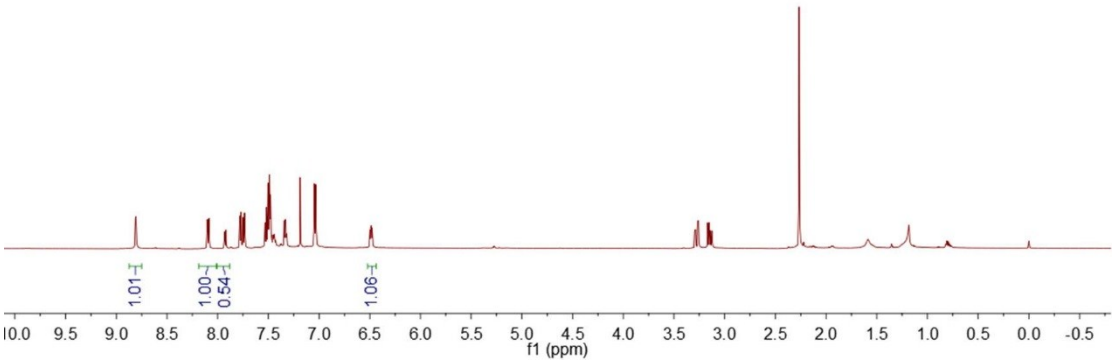
a. Parallel reactions.



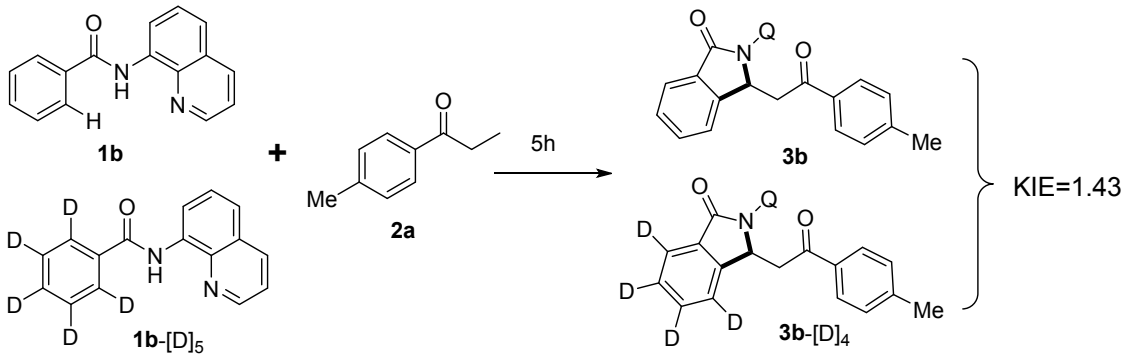
In a glove box, two 25 mL Schlenk tubes equipped with stir bars were

separately added **1b** (49.6 mg, 0.2 mmol), and **1b**-$[D]_5$ (50.6mg, 0.2 mmol). $Co(OAc)_2$ (5.5 mg, 15 mol%), Ag_2CO_3 (138.0 mg, 2.5 equiv.), $Cu(OAc)_2$ (1.9 mg, 5 mol%), TEMPO (31.3 mg, 1.0 equiv.), respectively. The tube was separately fitted with a rubber septum, and removed out from the glove box. Then ketone **2a** (3.5 equiv.) were separately added through the rubber septum using a syringe under the atmosphere of N_2. 1,2-Dichlorobenzene (1.0 mL) was separately added to the Schlenk tube through the rubber septum using syringe. The septum was replaced by a Teflon screwcap under N_2 flow. The reaction mixture was stirred at 110 ^oC (pre-heated to 110 ^oC) for 5 h. After cooling down, the reaction mixture of the two parallel tubes was mixed together. Then the solvent was removed in vacuo and the residue was purified by chromatography on silica gel (eluent: EtOAc/PE) to provide the corresponding products (**3b** and **3b**-d_4), and then analyzed by NMR.



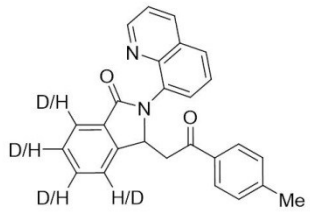


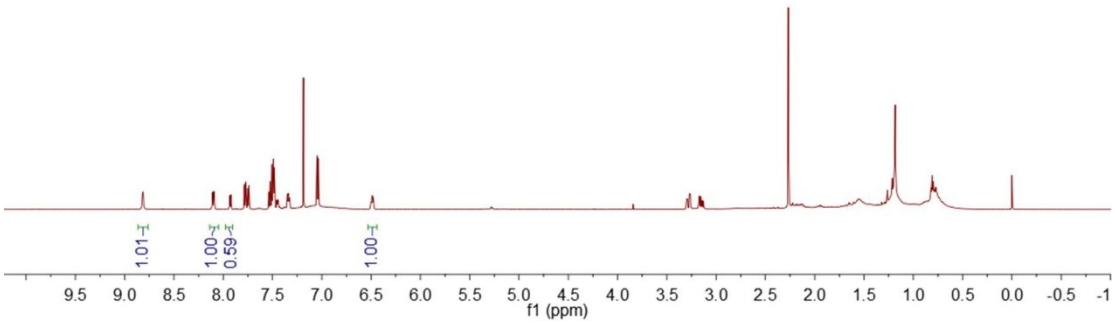
b. Competitive reaction.



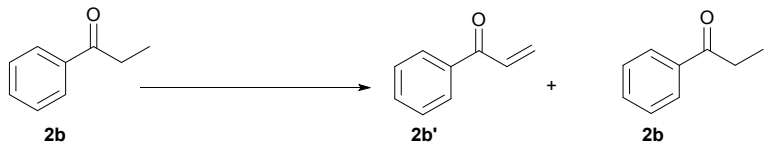
In a glove box, a 25 mL Schlenk tube equipped with a stir bar was charged with **1b** (24.8mg, 0.1 mmol), and **1b**-$[D]_5$ (25.3mg, 0.1 mmol), $Co(OAc)_2$ (5.5 mg, 15 mol%), Ag_2CO_3 (138.0 mg, 2.5 equiv.), $Cu(OAc)_2$ (1.9 mg, 5 mol%), TEMPO (31.3 mg, 1.0 equiv.). The tube was fitted with a rubber septum, and removed out from the glove box. Then ketone **2a** (3.5 equiv.) was added through the rubber septum using syringe under

the atmosphere of N_2. 1,2-Dichlorobenzene (1.0 mL) was added to the Schlenk tube through the rubber septum using a syringe. The septum was replaced by a Teflon screwcap under N_2 flow. The reaction mixture was stirred at 110 °C (pre-heated to 110 °C) for 5 h. After cooling down, the solvent was removed in vacuo and the residue was purified by chromatography on silica gel (eluent: EtOAc/PE) to provide the corresponding products (**3b** and **3b-d$_4$**), and then analyzed by NMR.





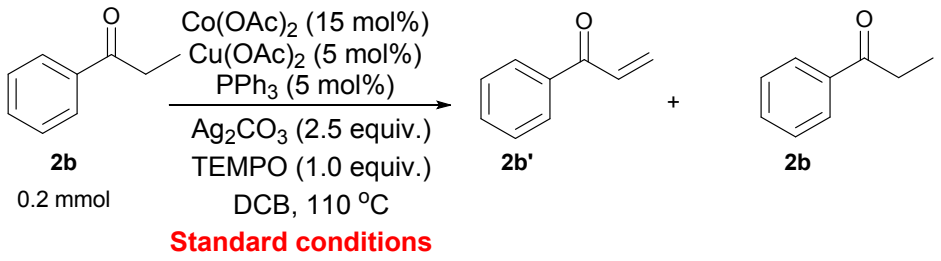
(4) Control experiments about the desaturation of ethyl ketones



In a glove box, a 25 mL Schlenk tube equipped with a stir bar was charged with $Co(OAc)_2$ (15 mol%), Ag_2CO_3 (2.5 equiv.), $Cu(OAc)_2$ (5 mol%), TEMPO (1.0 equiv.). The tube was fitted with a rubber septum,

and removed out from the glove box. Then ketone **2b** (0.2 mmol) was added through the rubber septum using syringe under the atmosphere of N_2. 1,2-Dichlorobenzene (0.75 mL) was added to the Schlenk tube through the rubber septum using a syringe. The septum was replaced by a Teflon screwcap under N_2 flow. The reaction mixture was stirred at 110 ^oC (pre-heated to 110 ^oC) for 21h. After cooling down, the solvent was removed in vacuo and the residue was analyzed by GC-Mass. There is no other compound produced except for **2b'**. The yields of **2b'** and **2b** were determined by GC.

Table S9: Control experiments about the dehydrogenation of ketone **2b**.

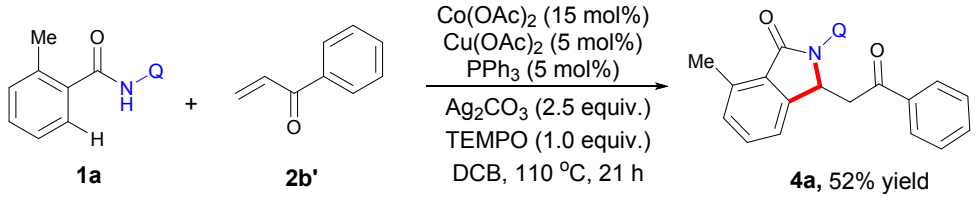


Entry	Conditions	**2b'**(GC yield)	**2b** (GC yield)
1	Standard conditions	68%	32%
2	Without $Co(OAc)_2$	67%	33%
3	Without $Co(OAc)_2$, PPh_3	40%	60%
4	Without $Co(OAc)_2$,TEMPO	No observed	100%
5	Without $Co(OAc)_2$, Ag_2CO_3	23%	77%
6	Without $Co(OAc)_2$, Ag_2CO_3, PPh_3	14%	86%
7	Without $Cu(OAc)_2$	7%	93%

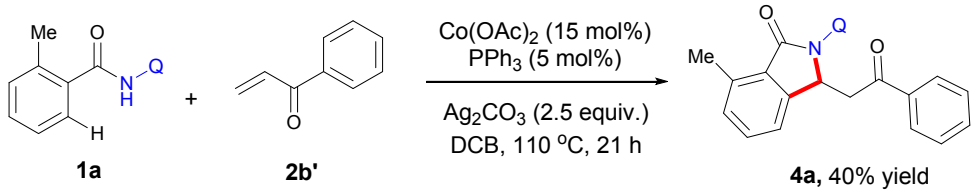
(5) The reaction of 2b' with amide 1a.

In a glove box, a 25 mL Schlenk tube equipped with a stir bar was charged with **1a** (0.15 mmol), $Co(OAc)_2$ (4.1 mg, 15 mol%), Ag_2CO_3 (103.5 mg, 2.5 equiv.), $Cu(OAc)_2$ (1.4 mg, 5 mol%), $P(Ph)_3$ (2.0 mg, 5 mol%), TEMPO (23.5 mg, 1.0 equiv.). The tube was fitted with a rubber septum, and removed out from the glove box. Then **2b'** which was prepared according to literatures[2] (3.5 equiv.) was added through the rubber septum using syringe under the atmosphere of N_2. 1,2-Dichlorobenzene (0.75 mL) was added to the Schlenk tube through the rubber septum using a syringe. The septum was replaced by a Teflon screwcap under N_2 flow. The reaction mixture was stirred at 110 °C (pre-heated to 110 °C) for 21 h. After cooling down, the solvent was removed in vacuo and the residue was purified by chromatography on silica gel (eluent: EtOAc/PE) to provide the corresponding product.

Reaction with standard conditions:



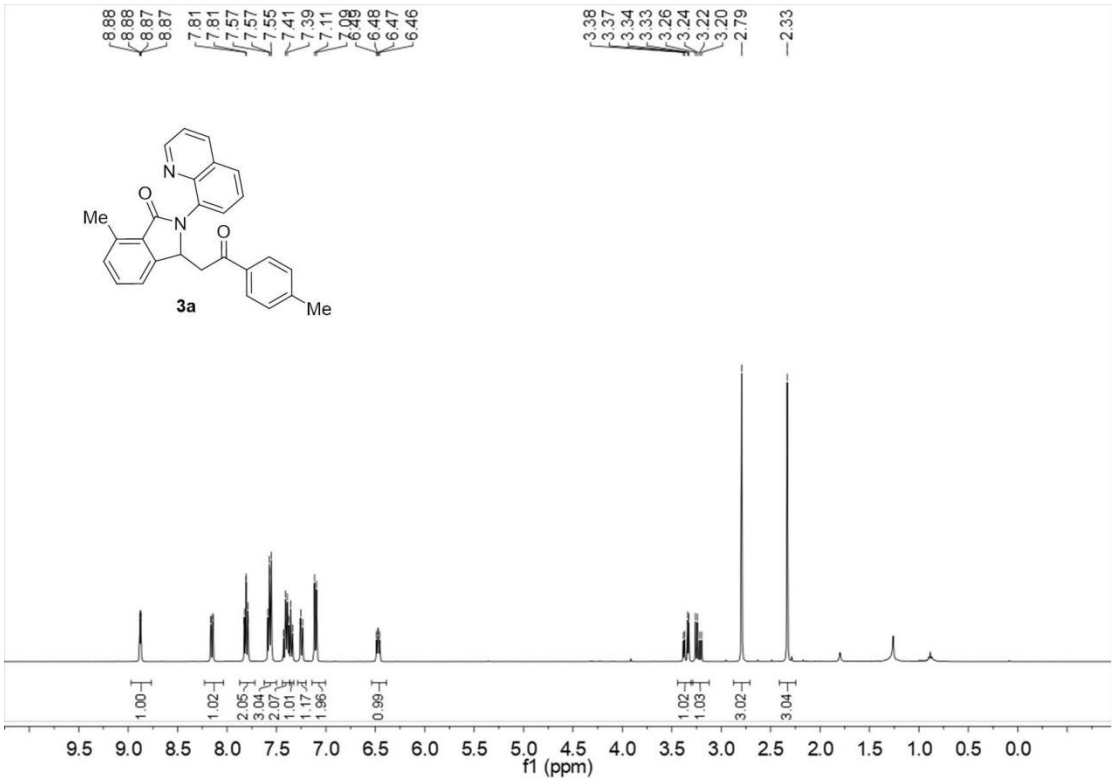
Reaction with conditions without $Cu(OAc)_2$ and TEMPO:

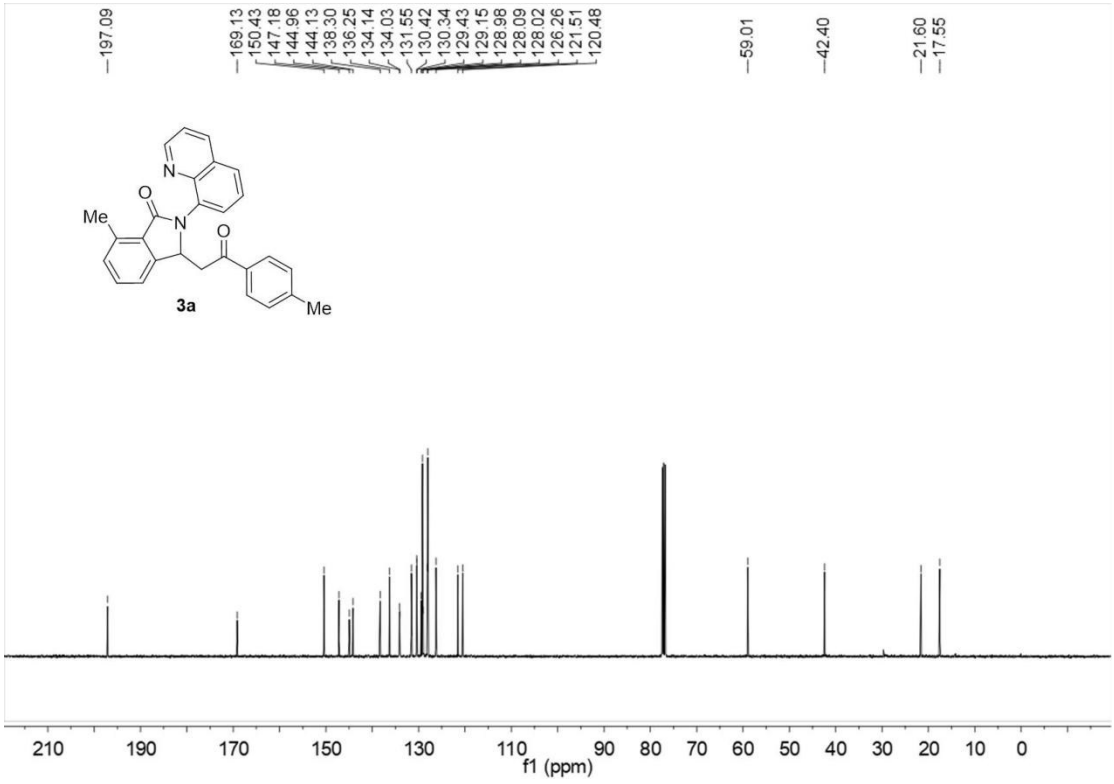


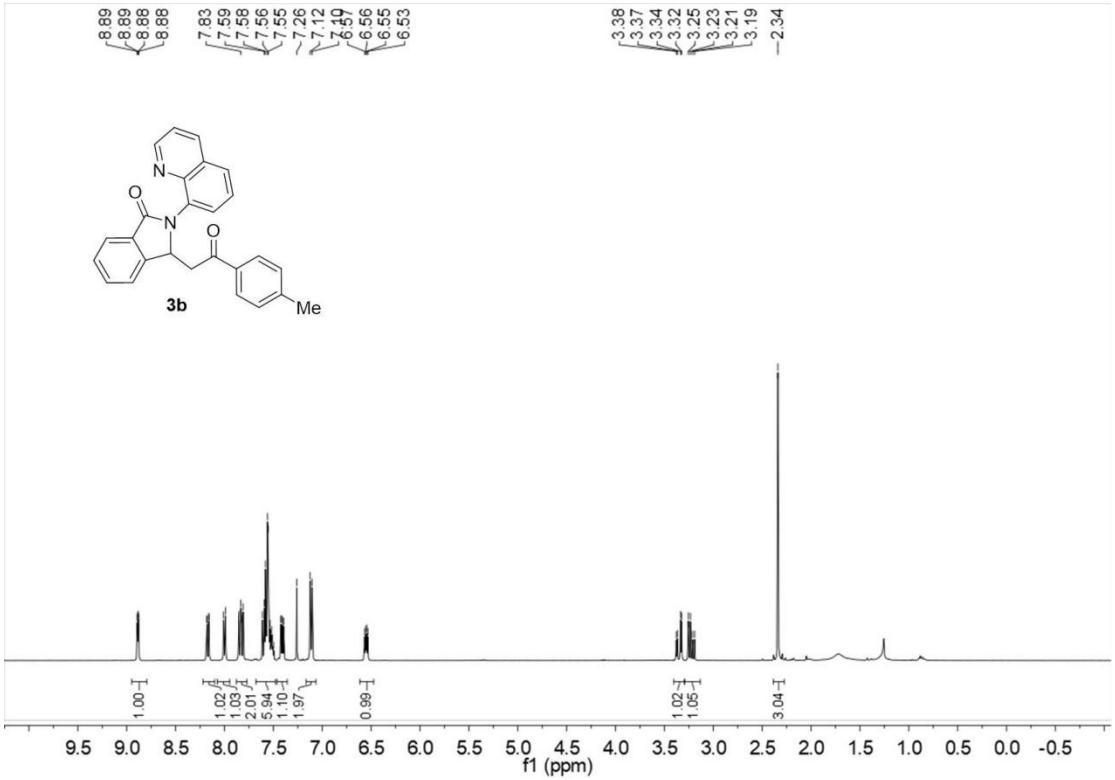
7. Reference

1. (a) Ano, Y.; Tobisu, M.; Chatani, N. *Org. Lett.* **2012**, *14*, 354. (b) Shibata, K.; Chatani, N. *Org. Lett.* **2014**, *16*, 5148.
2. Ma, T.; Fu, X.; Kee, C. W.; Zong, L.; Pan, Y.; Huang, K.-W.; Tan, C.-H. *J. Am. Chem. Soc.* **2011**, 133, 2828.
3. He, G.; Zhang, S. Y.; Nack, W. A.; Li, Q.; Chen, G., *Angew. Chem. Int. Ed.* **2013,** *52*, 1112

8. ^{1}H and ^{13}C NMR spectra



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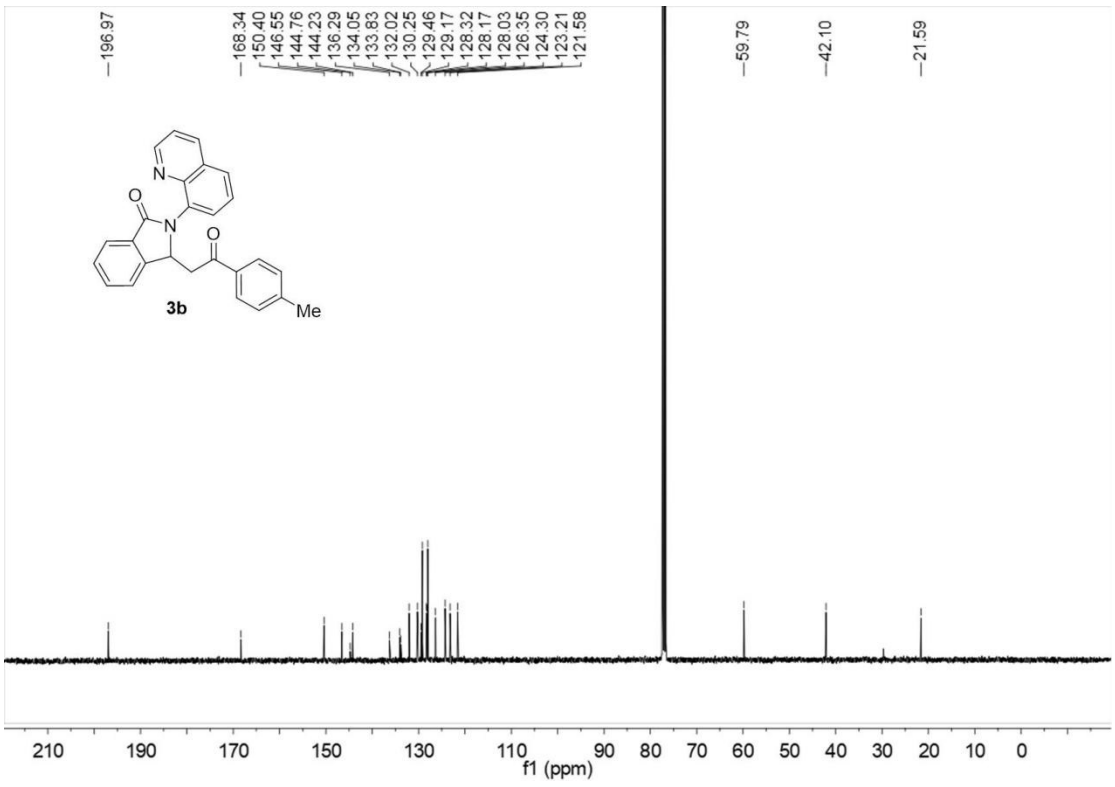
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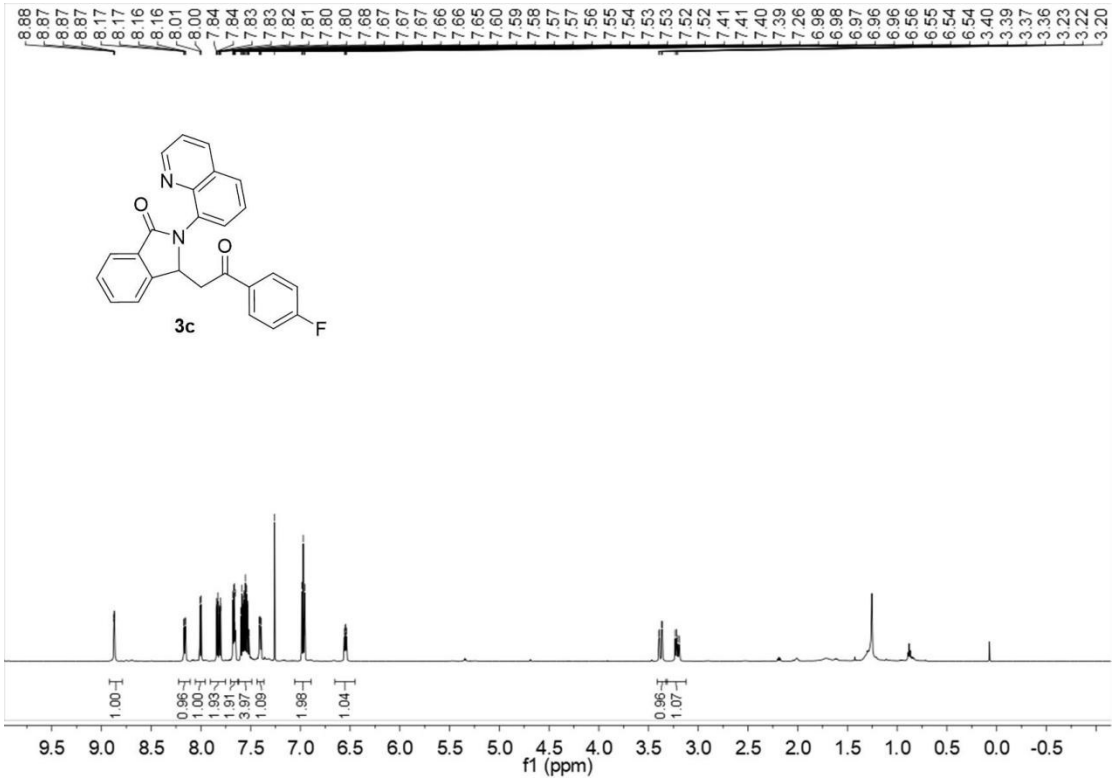
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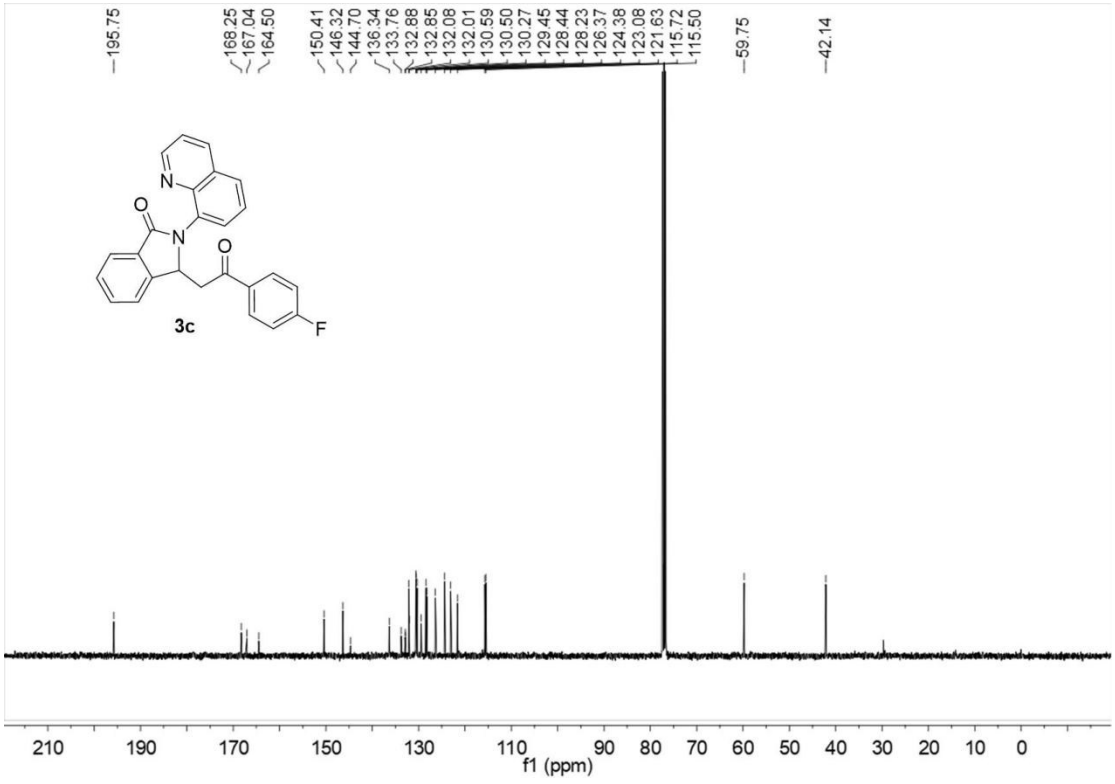
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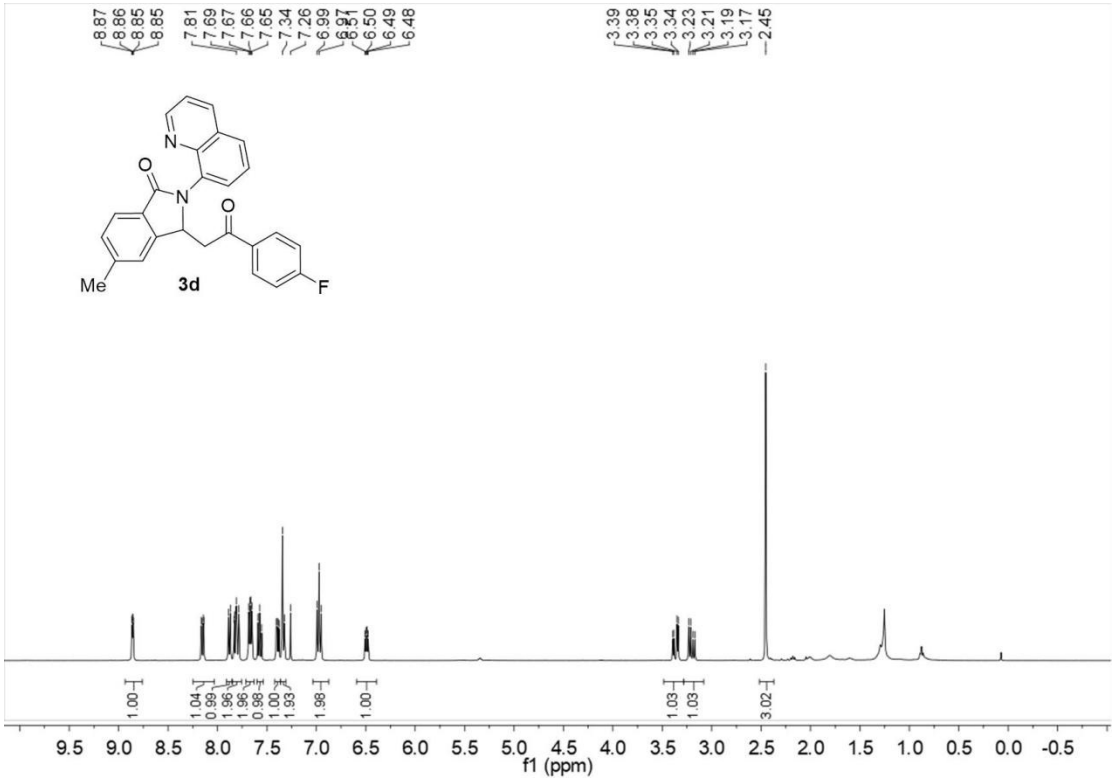
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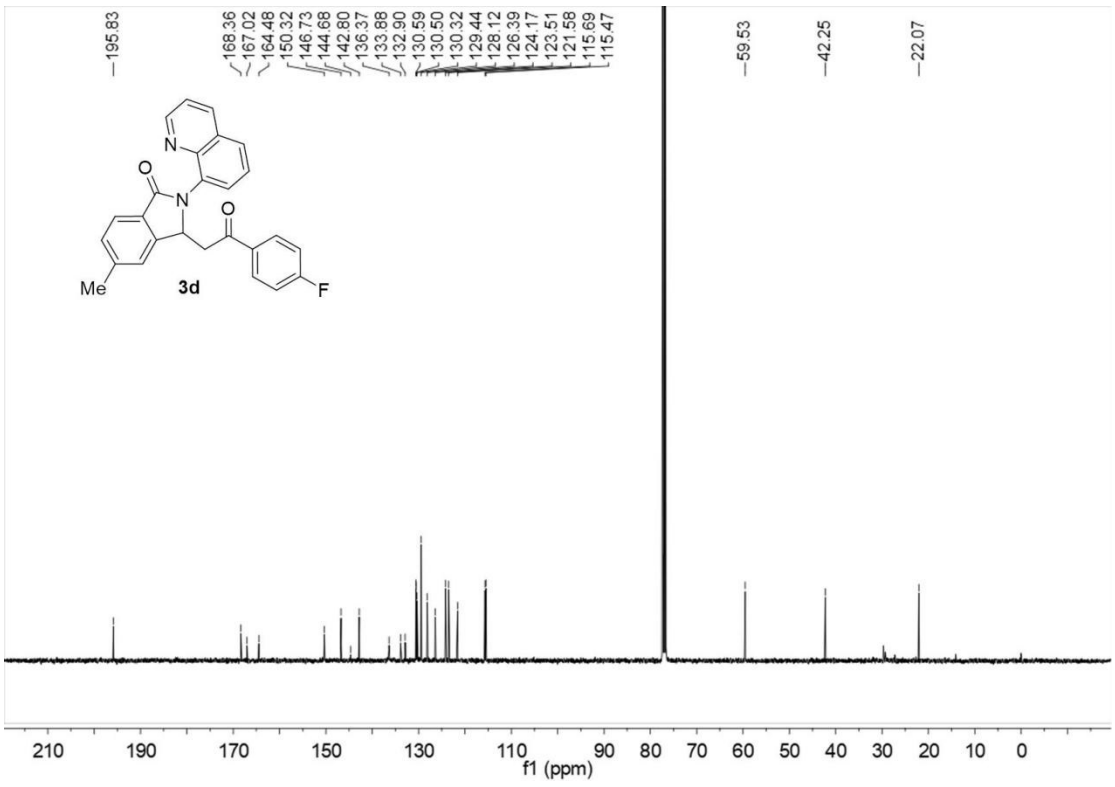
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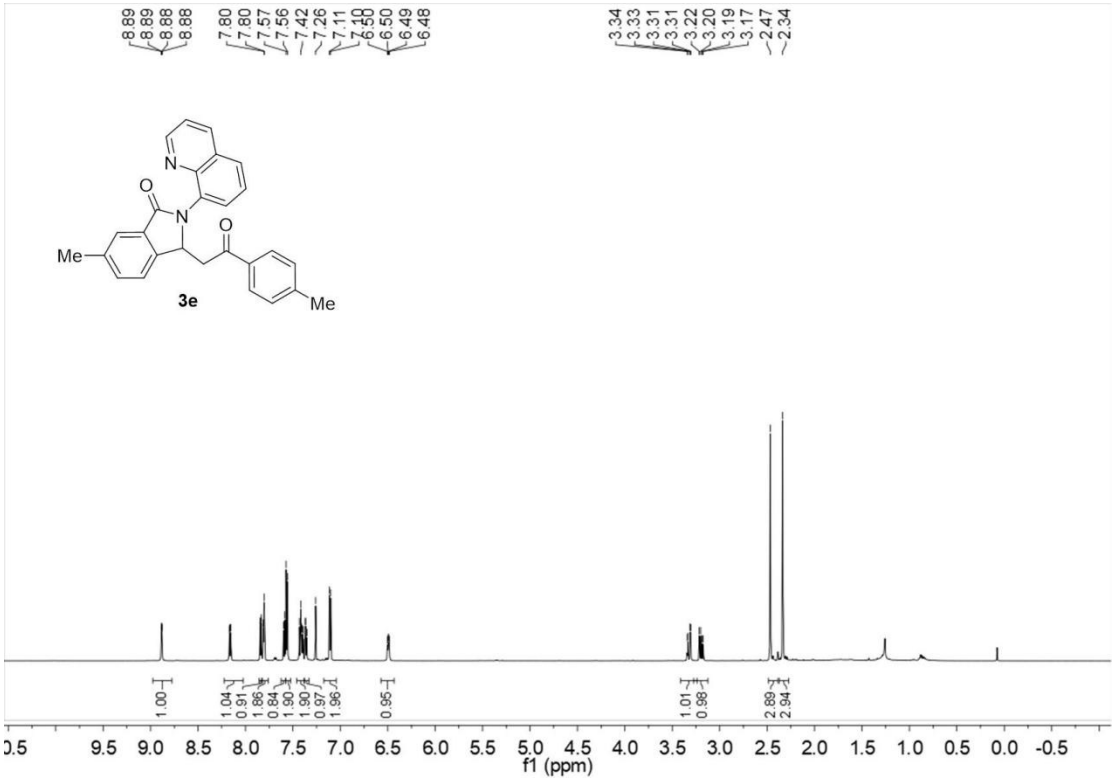
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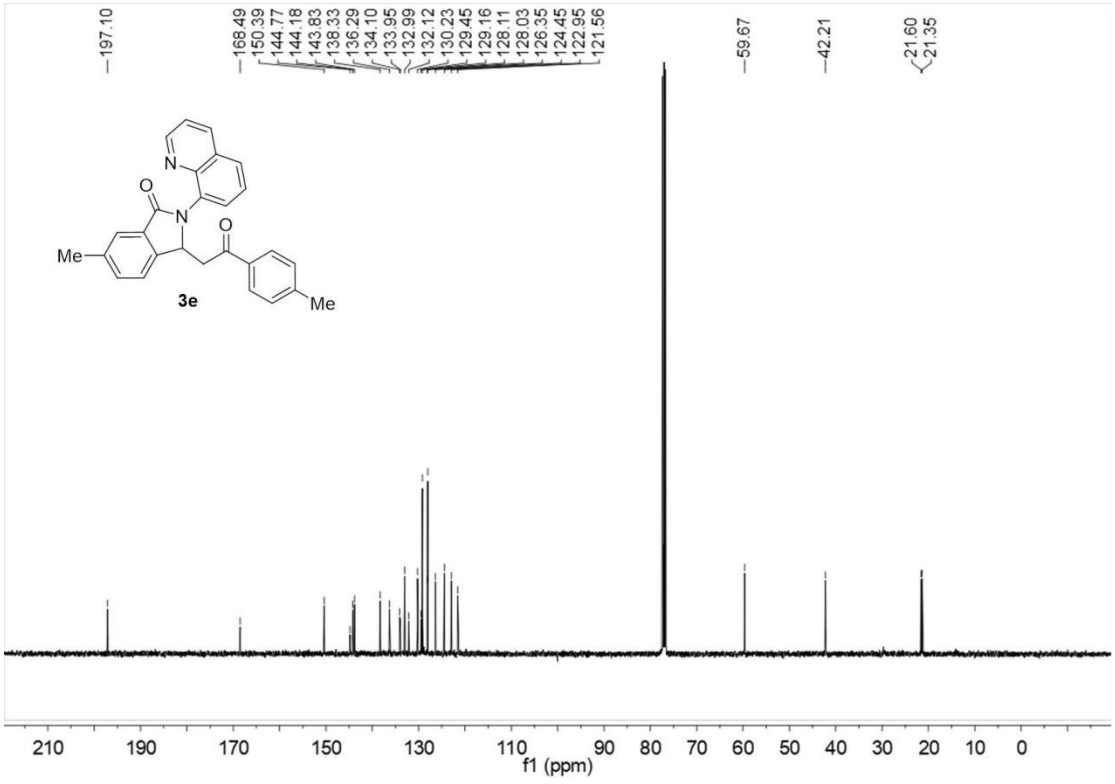
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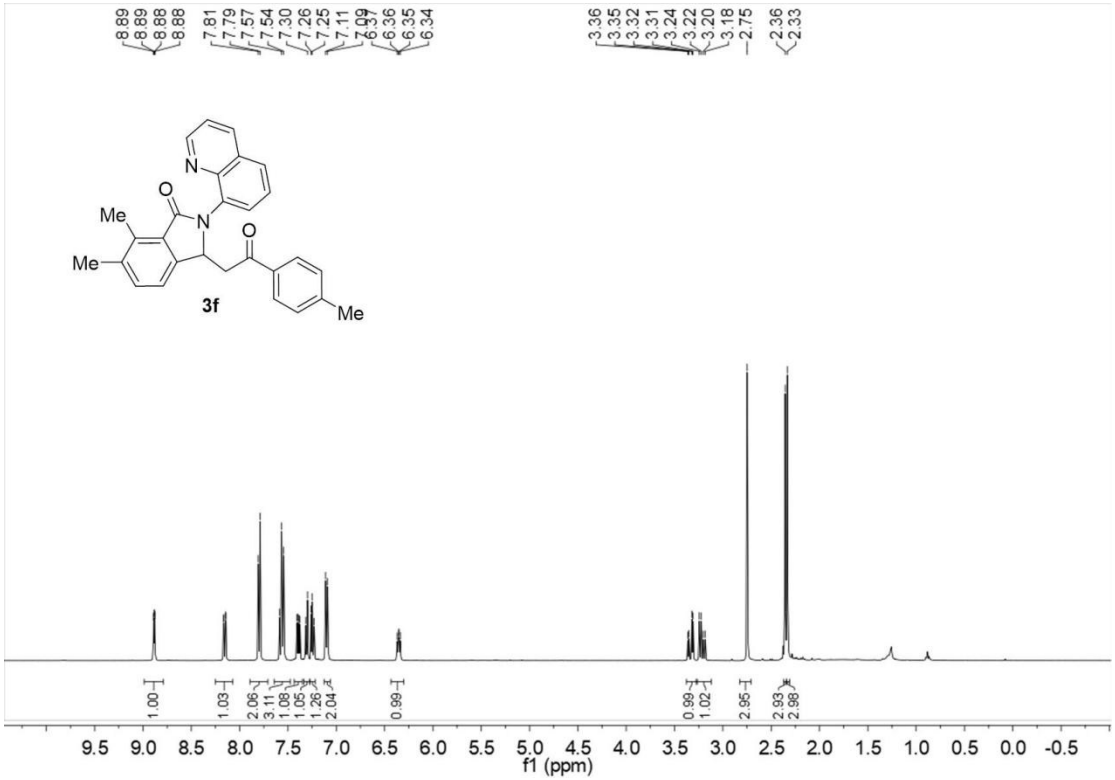
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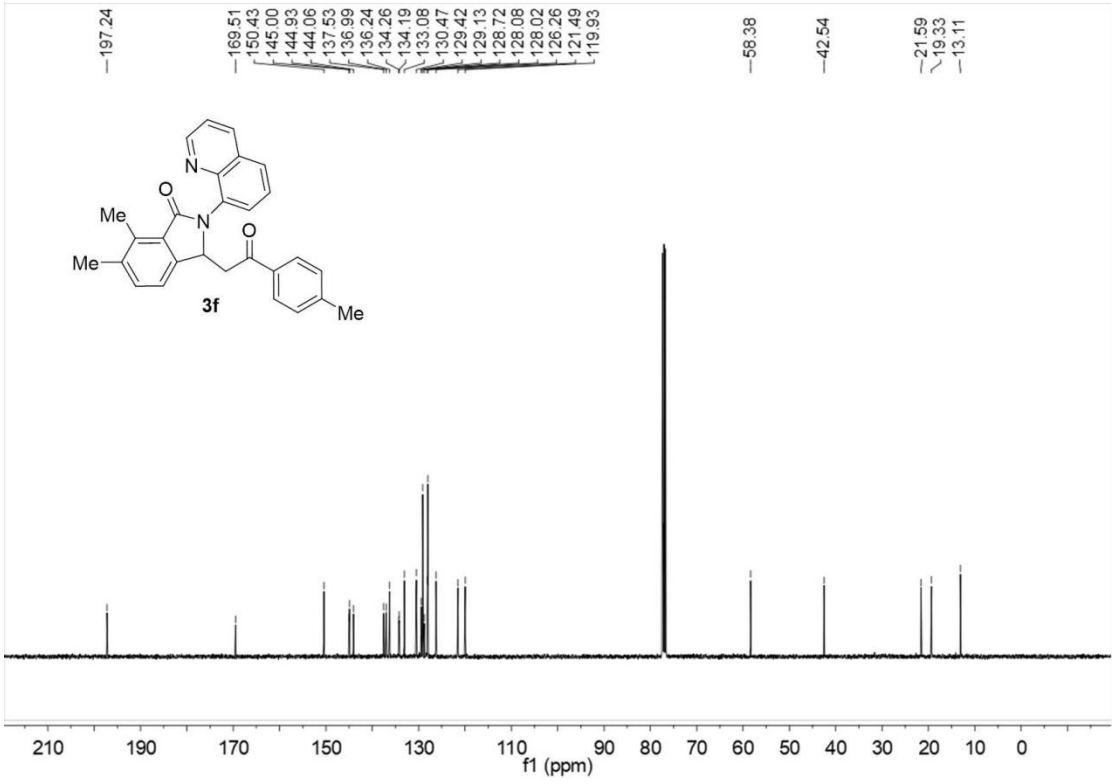
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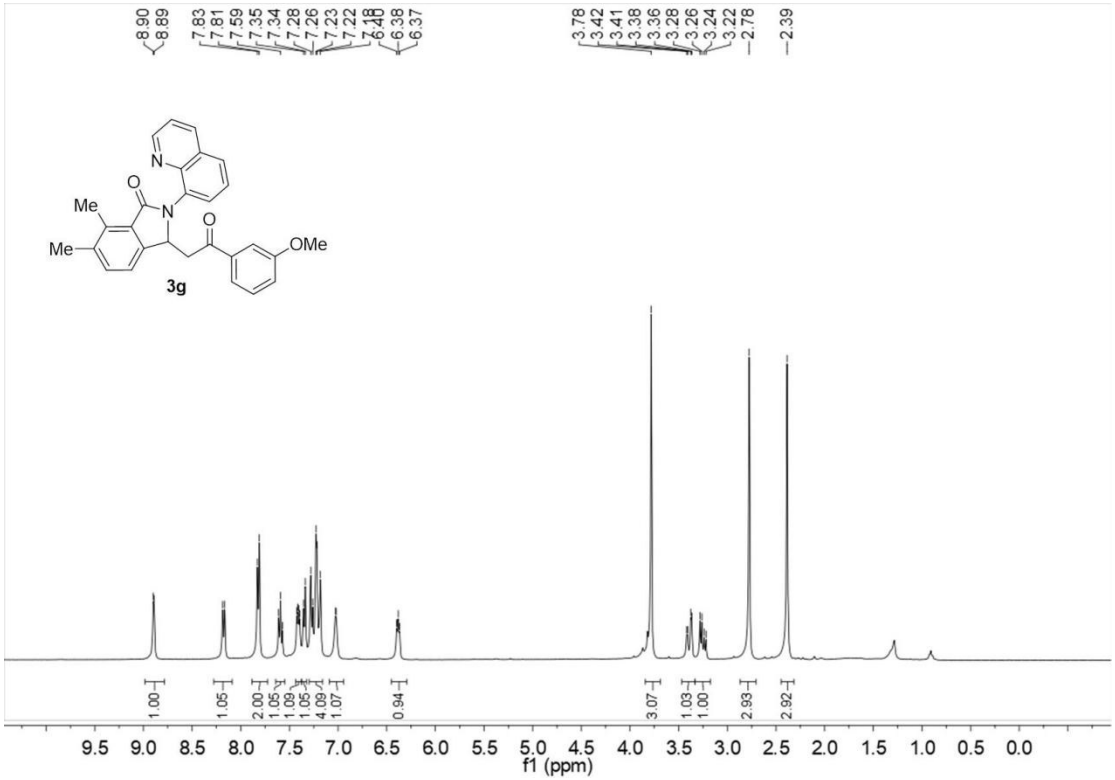
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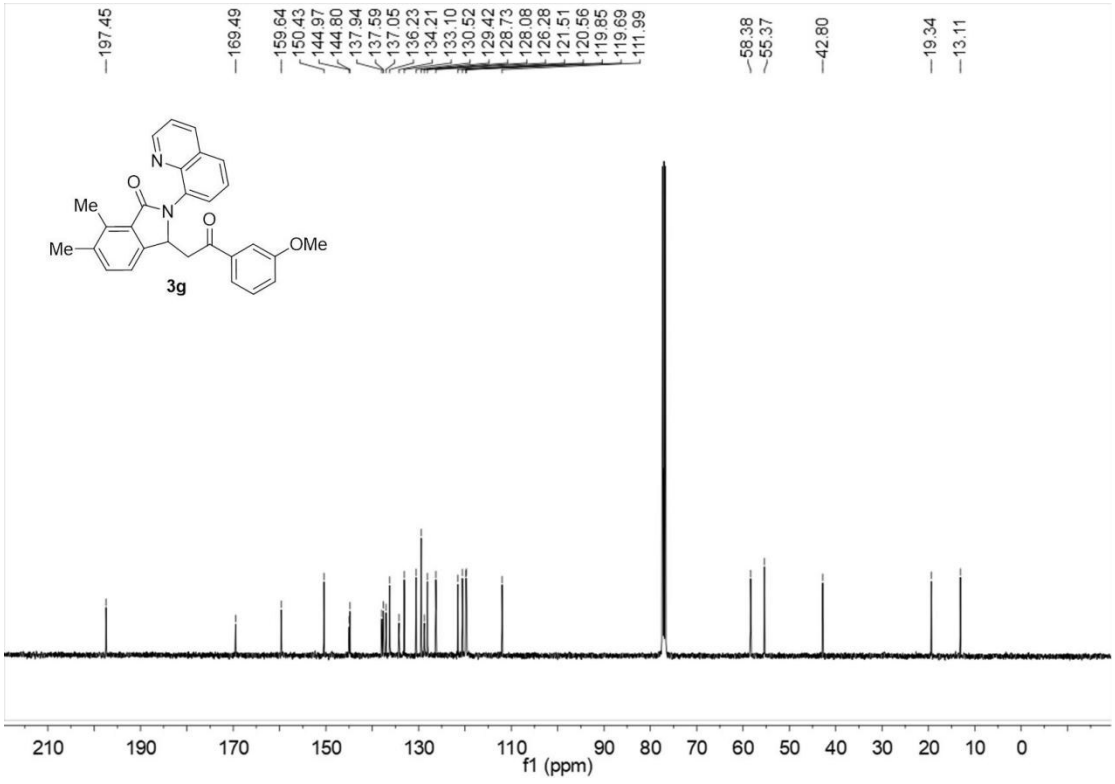
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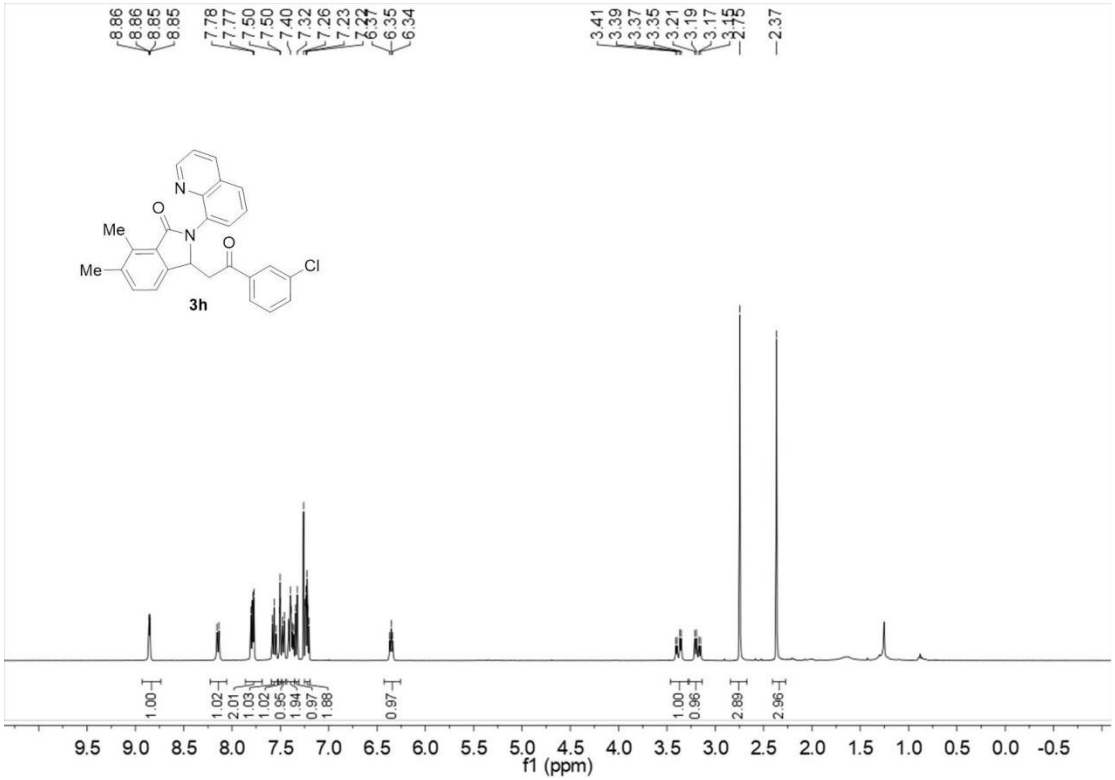
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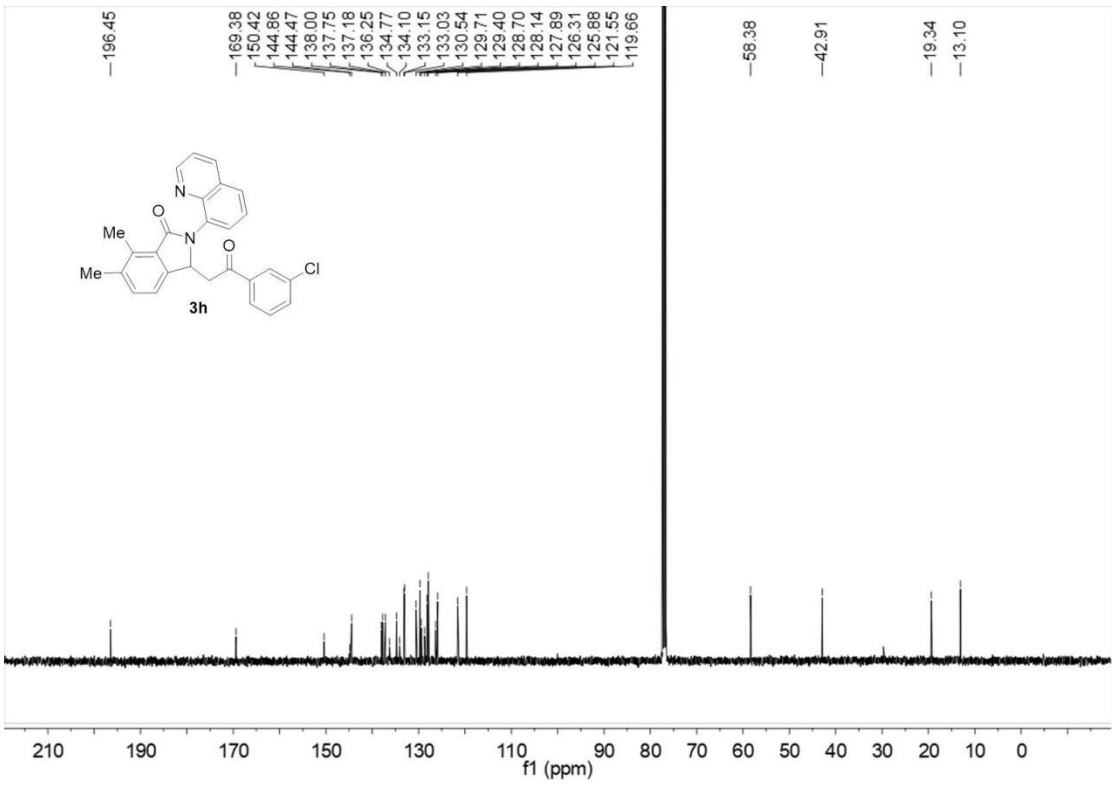
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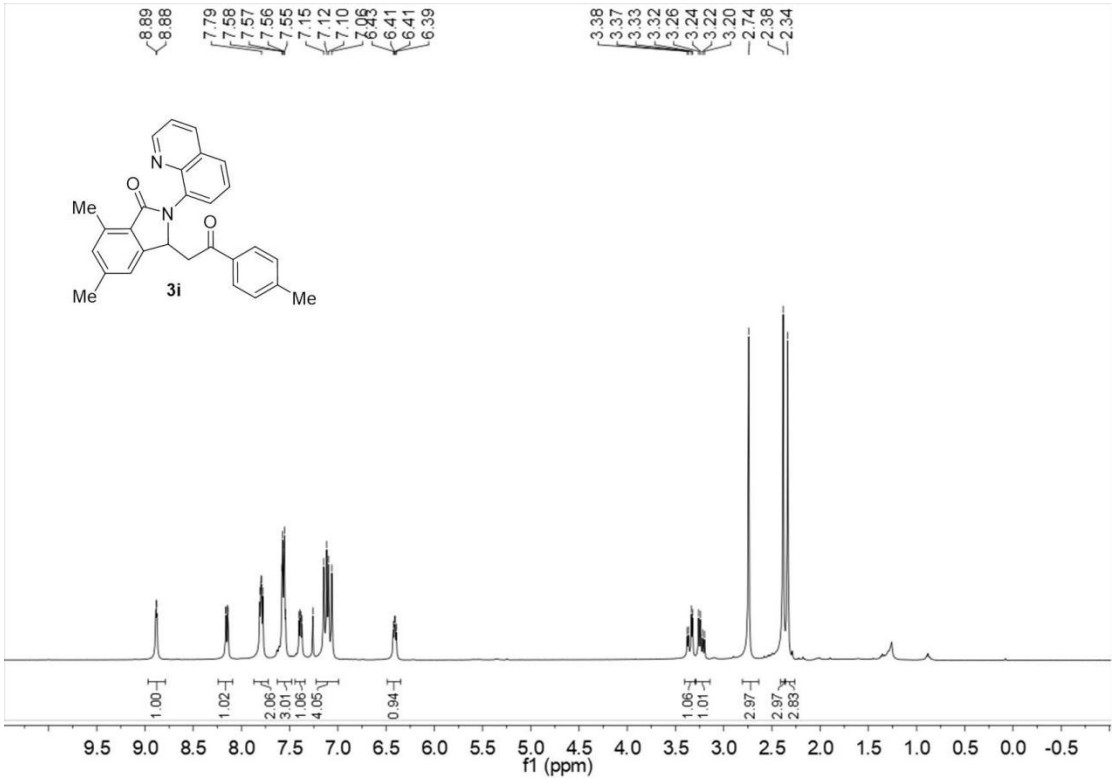
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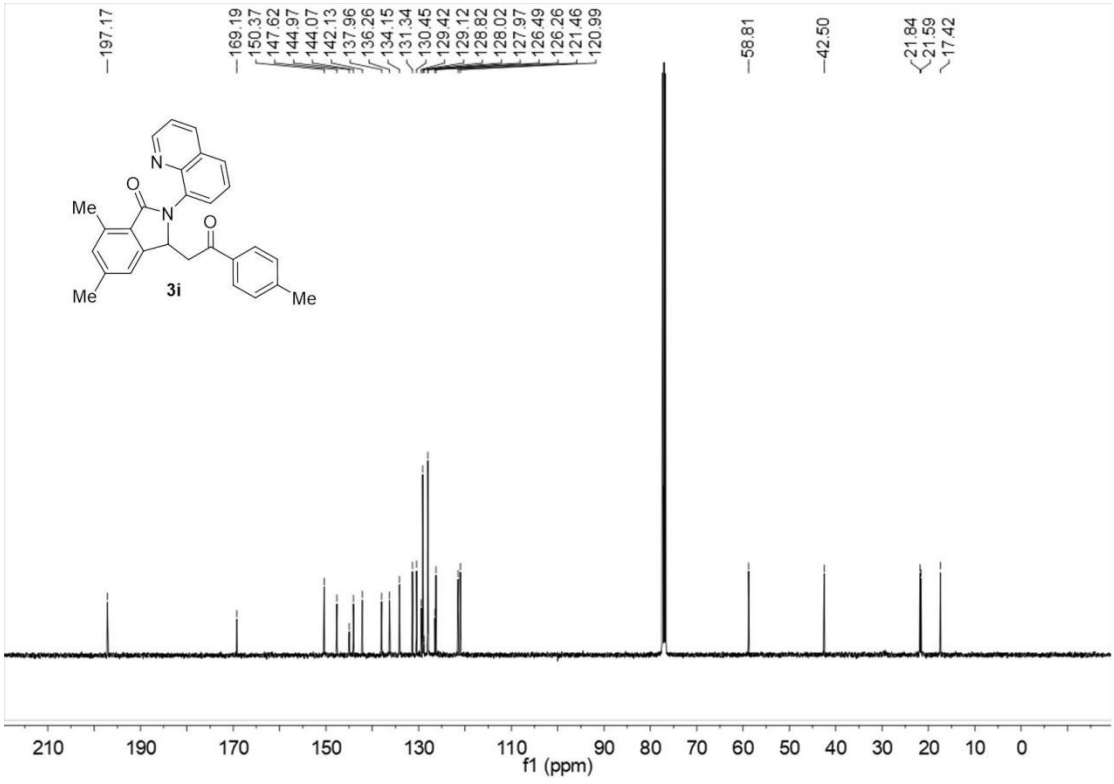
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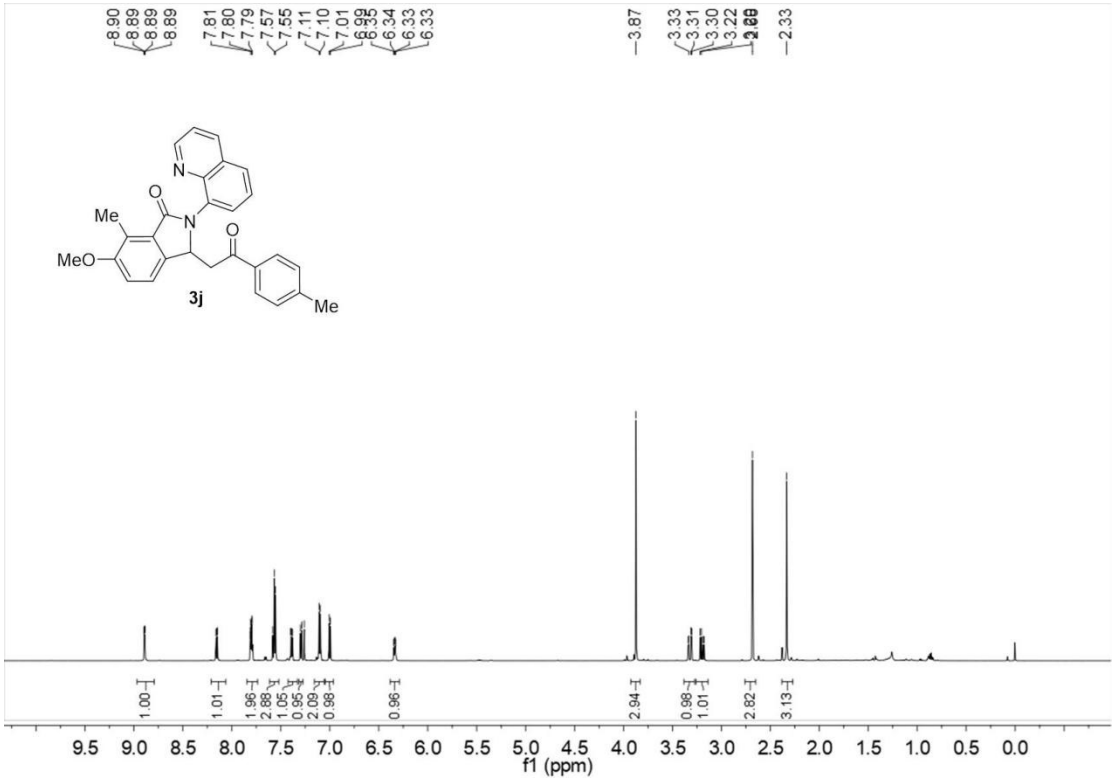
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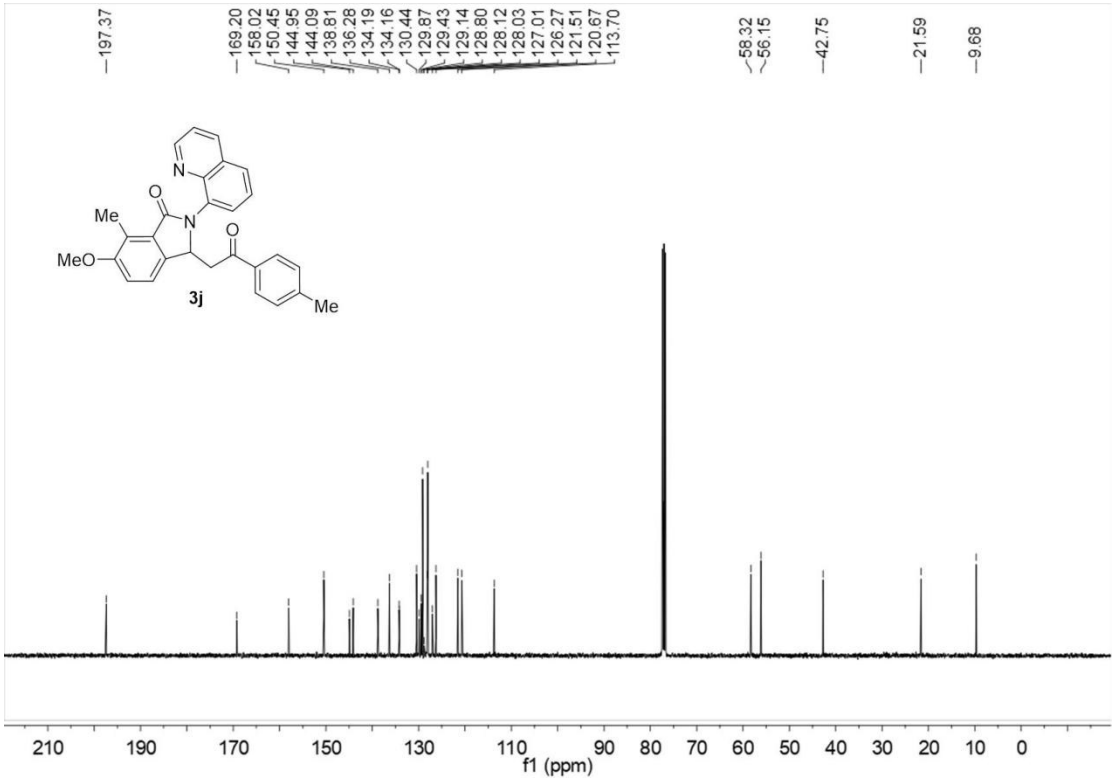
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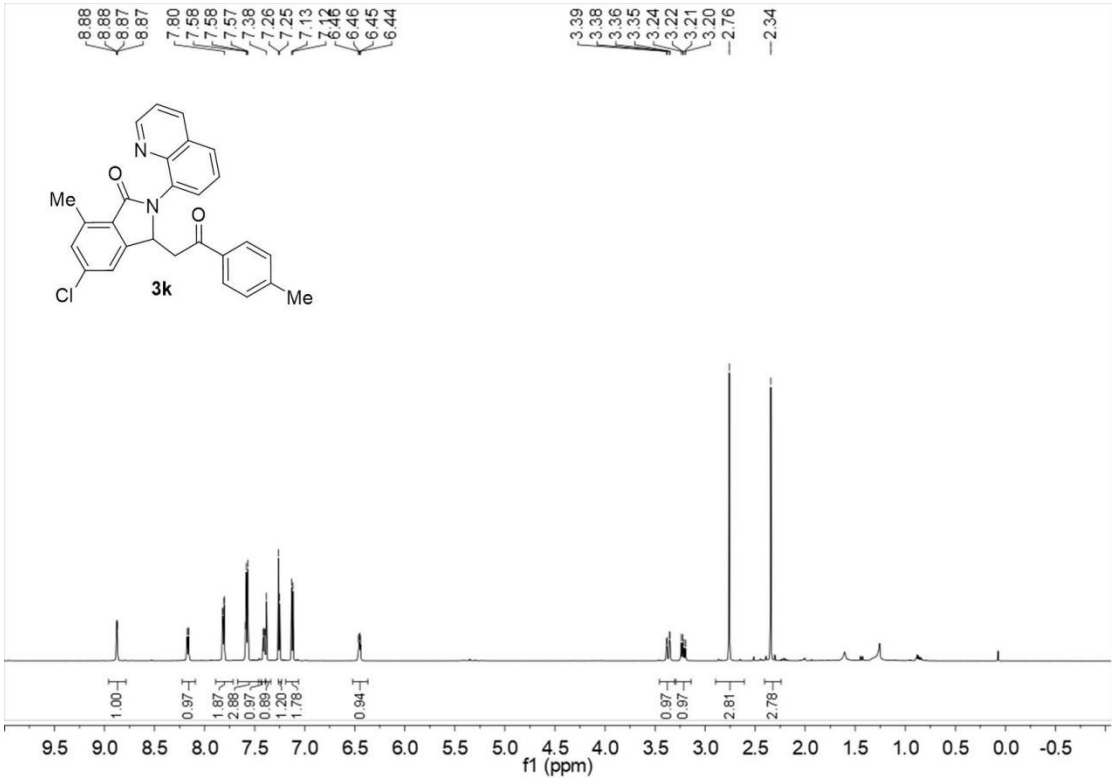
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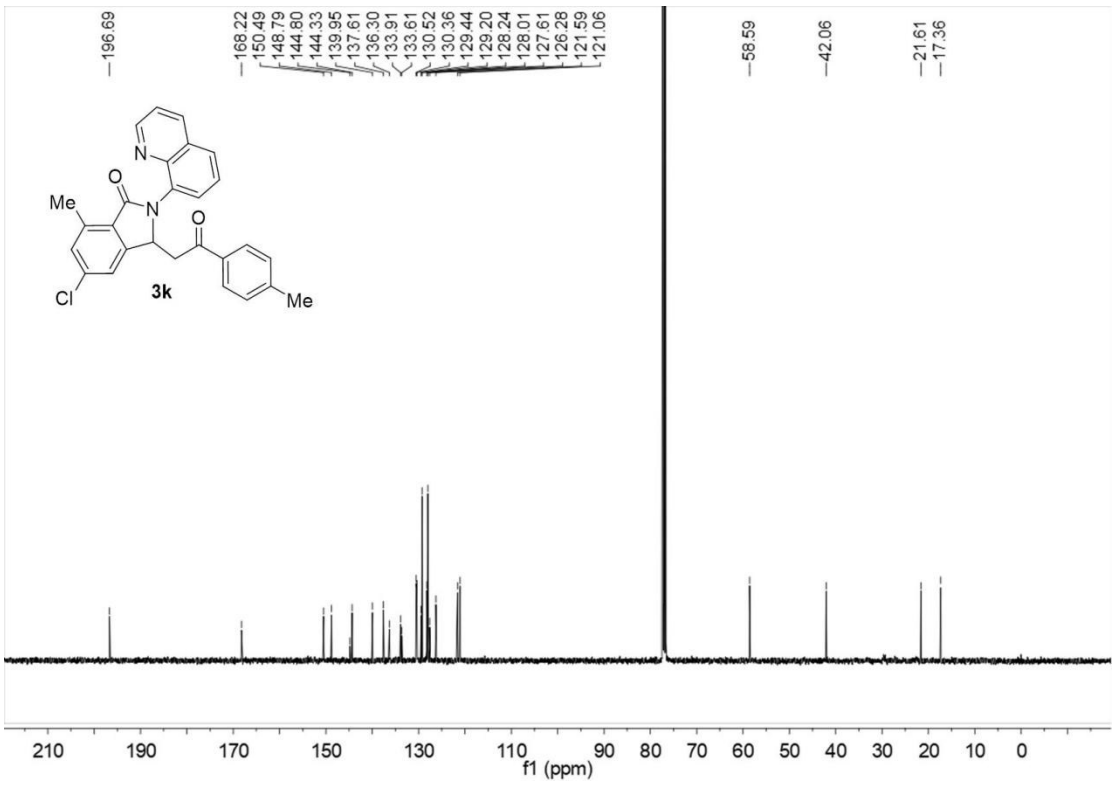
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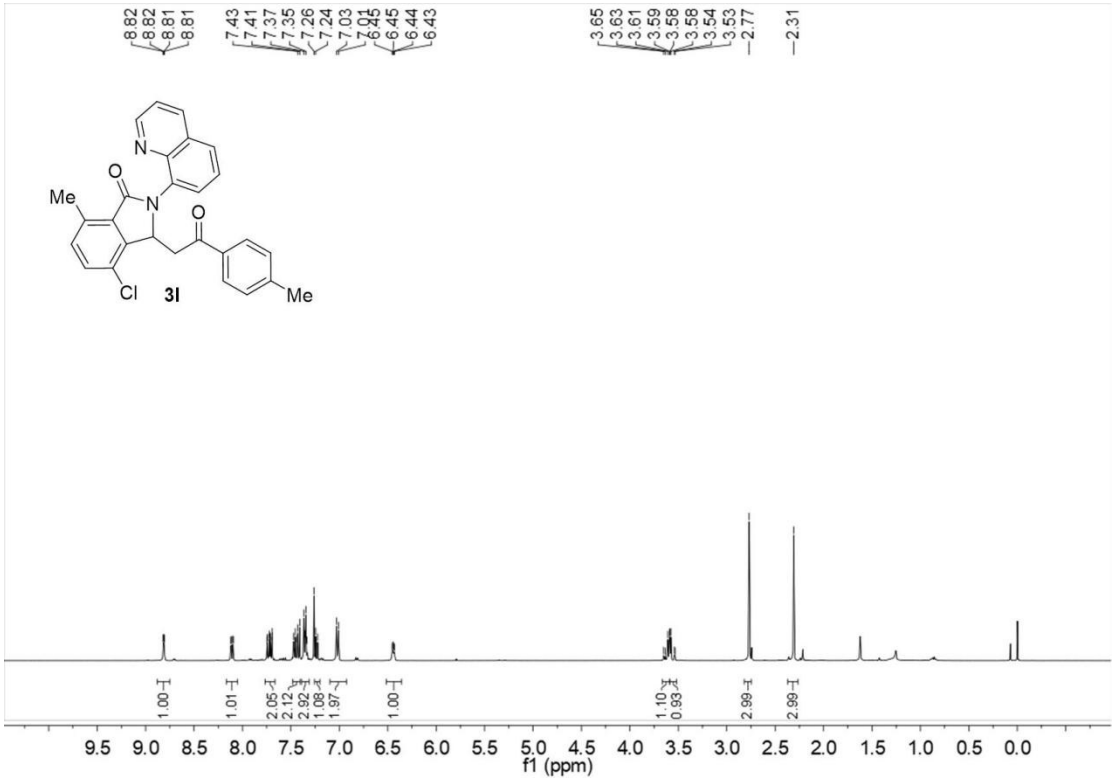
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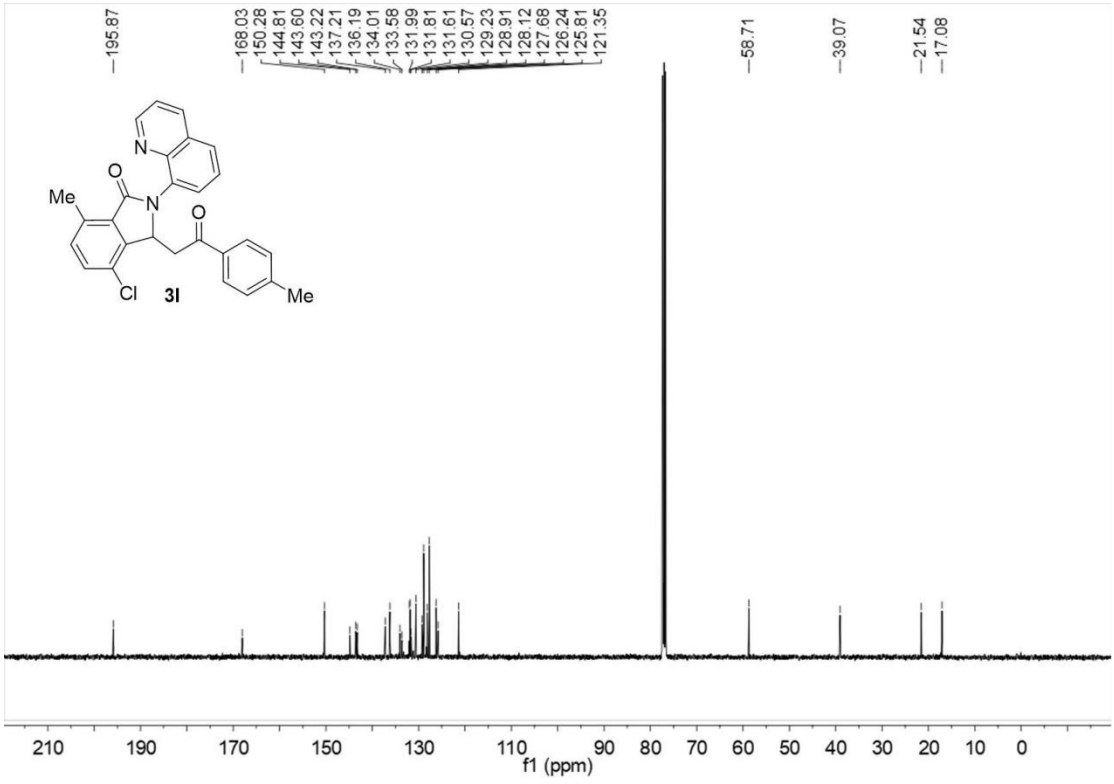
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58.71
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O
Cl
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Me
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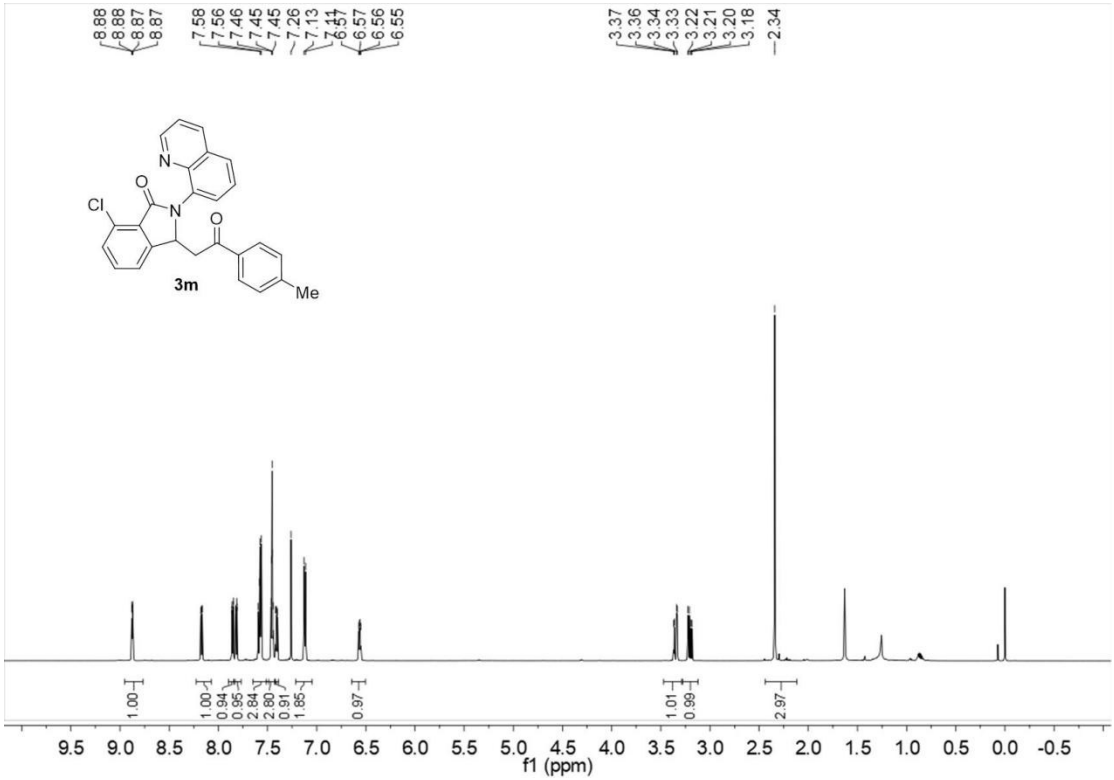
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3.18
2.34
Cl
O
N
O
3m
Me
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1.00
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0.95
2.84
2.80
0.91
1.85
0.97
1.01
0.99
2.97
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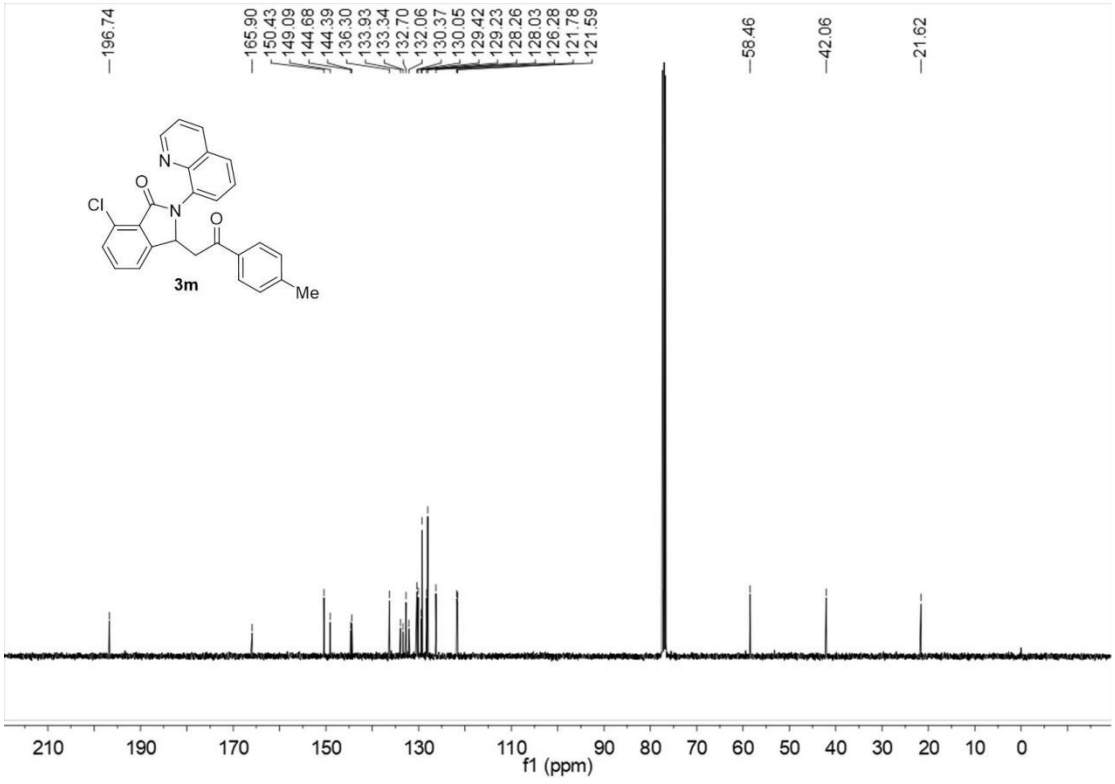
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129.23
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128.03
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121.78
121.59
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N
O
3m
Me
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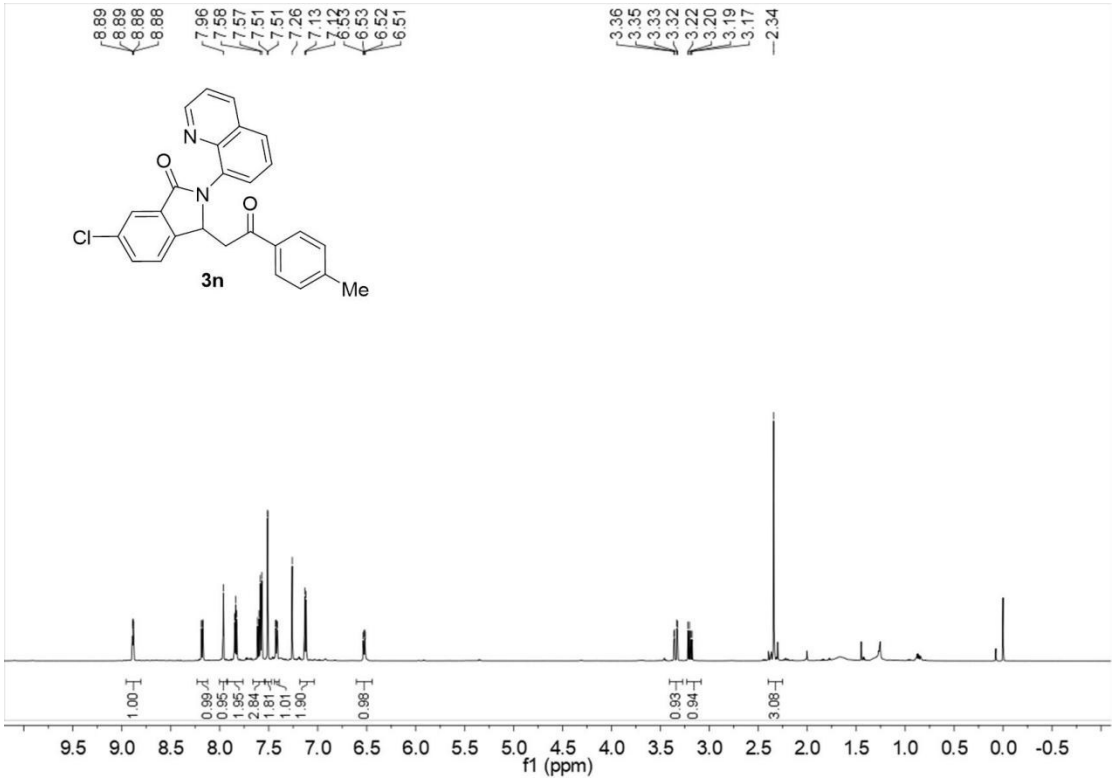
f1 (ppm)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3.32
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3.19
3.17
2.34
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N
O
Cl
3n
Me
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0.95
1.95
2.84
1.81
1.01
1.90
0.98
0.93
0.94
3.08
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
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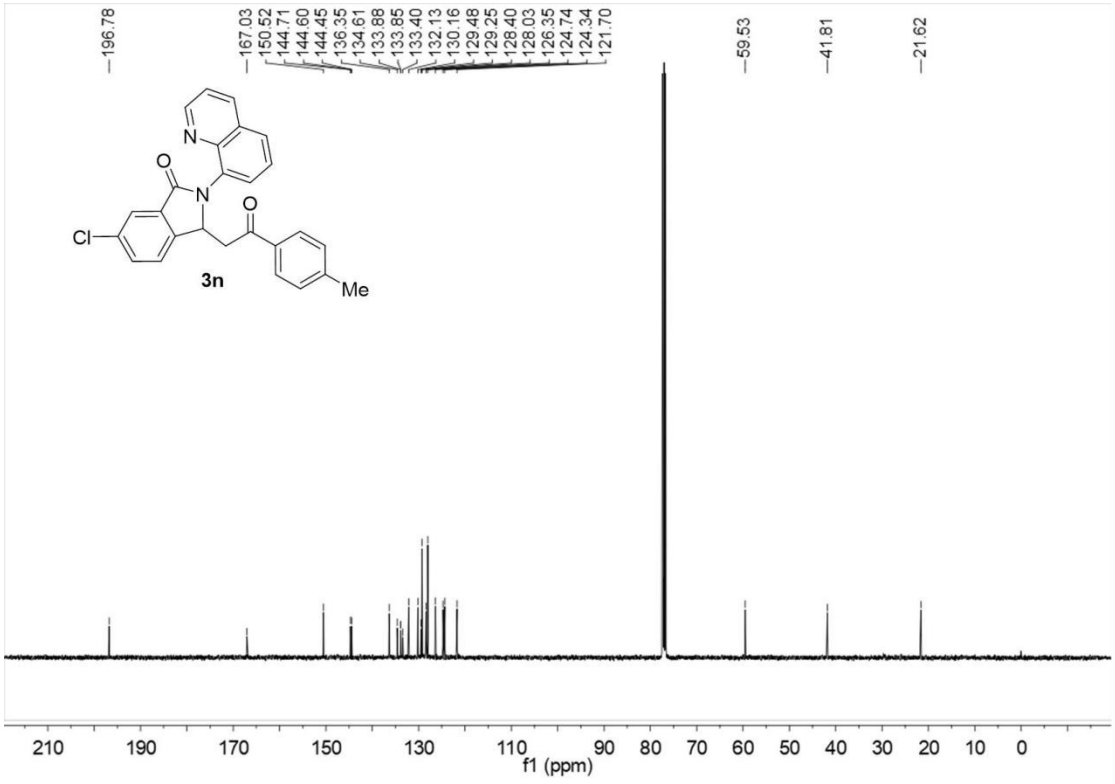
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124.34
121.70
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N
O
Cl
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Me
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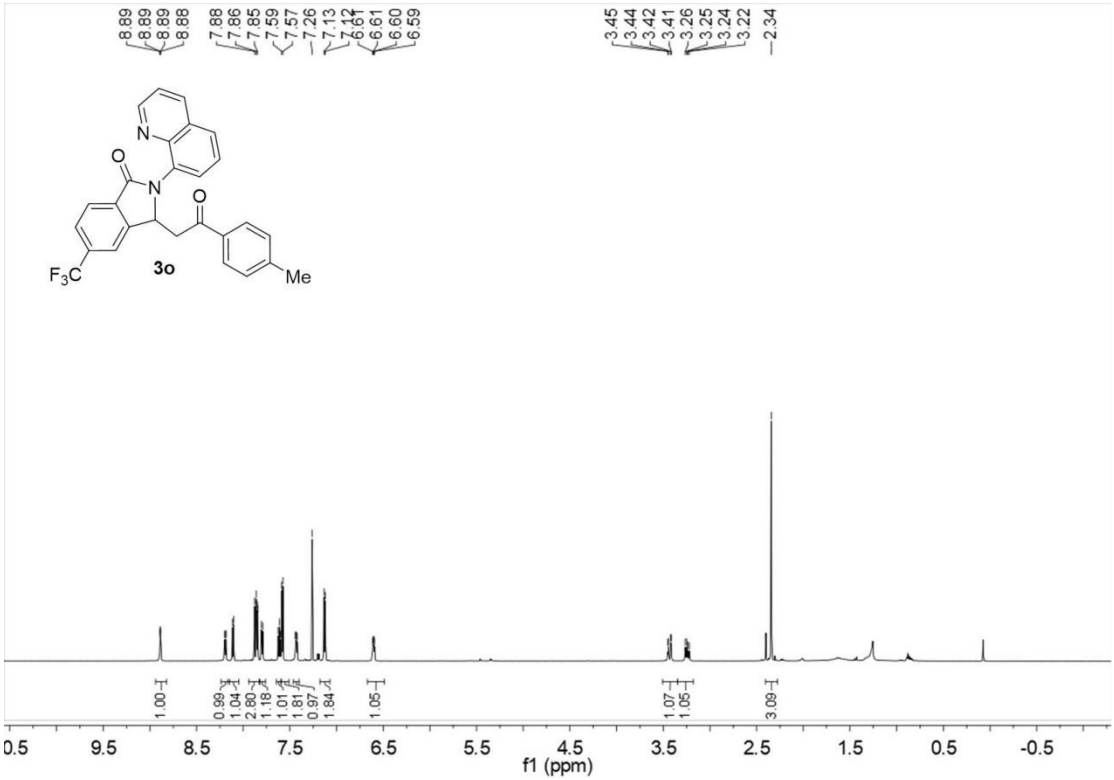
f1 (ppm)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6.59
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3.44
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3.41
3.26
3.25
3.24
3.22
2.34
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1.07
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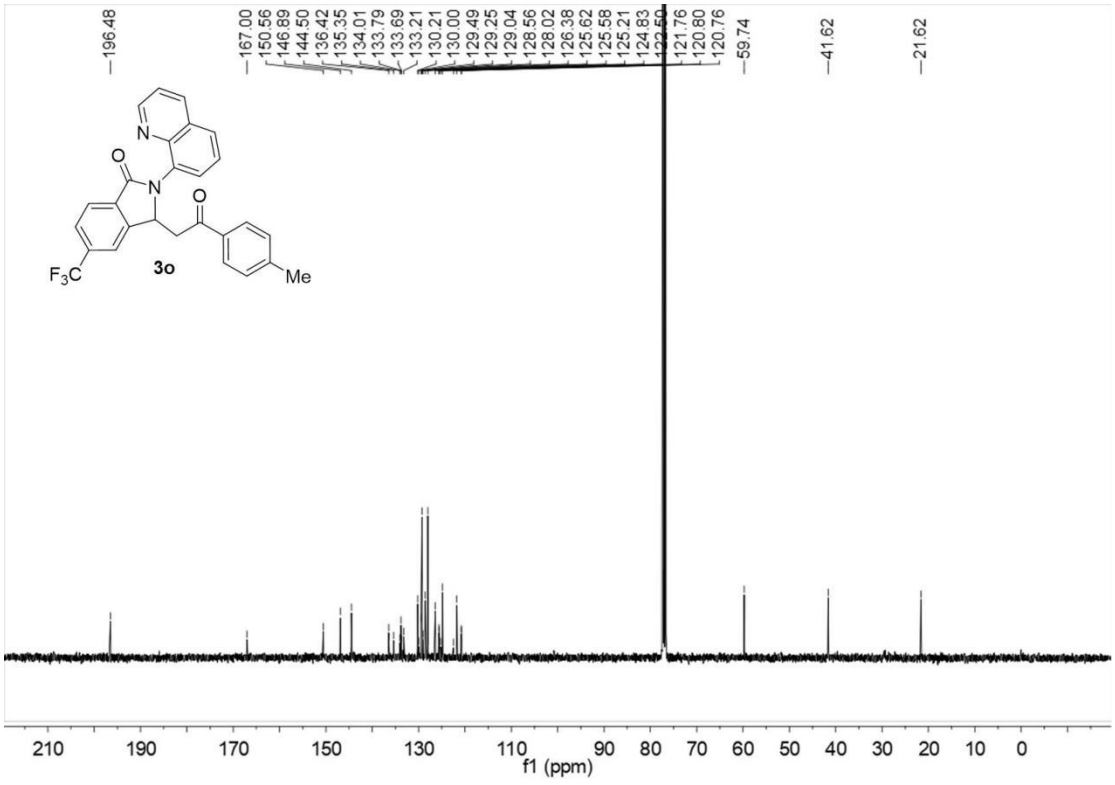
3.09
f1 (ppm)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41.62
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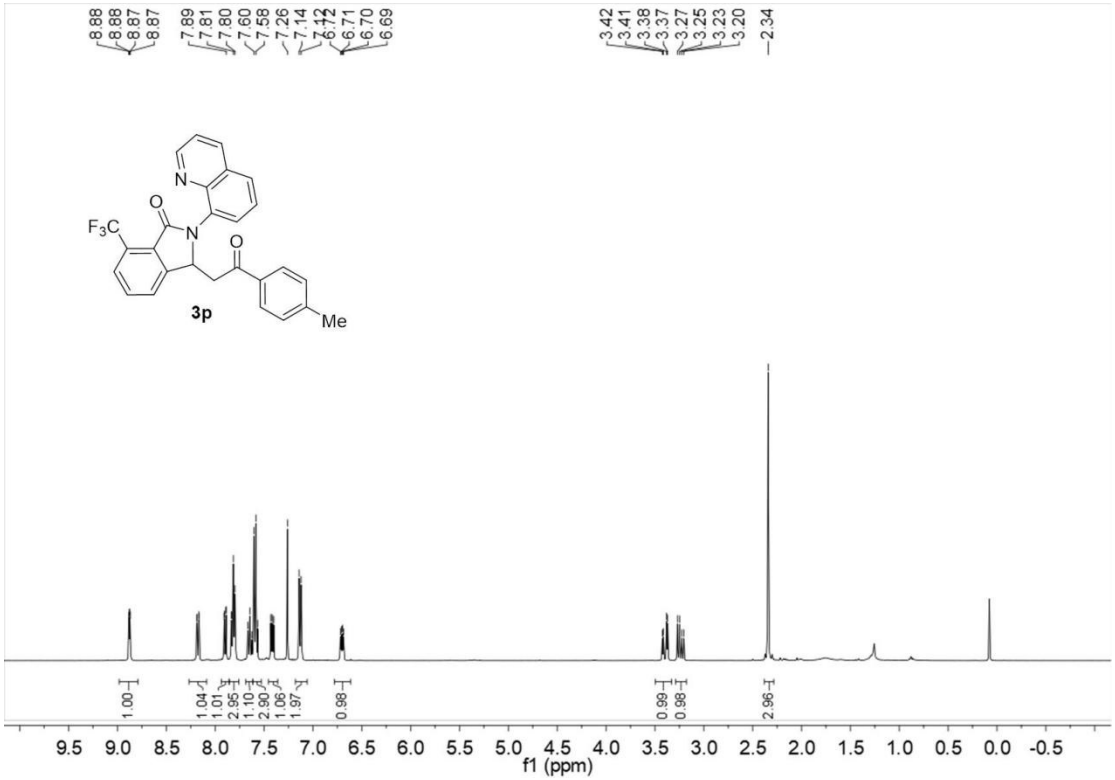
f1 (ppm)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3.37
3.27
3.25
3.23
3.20
2.34
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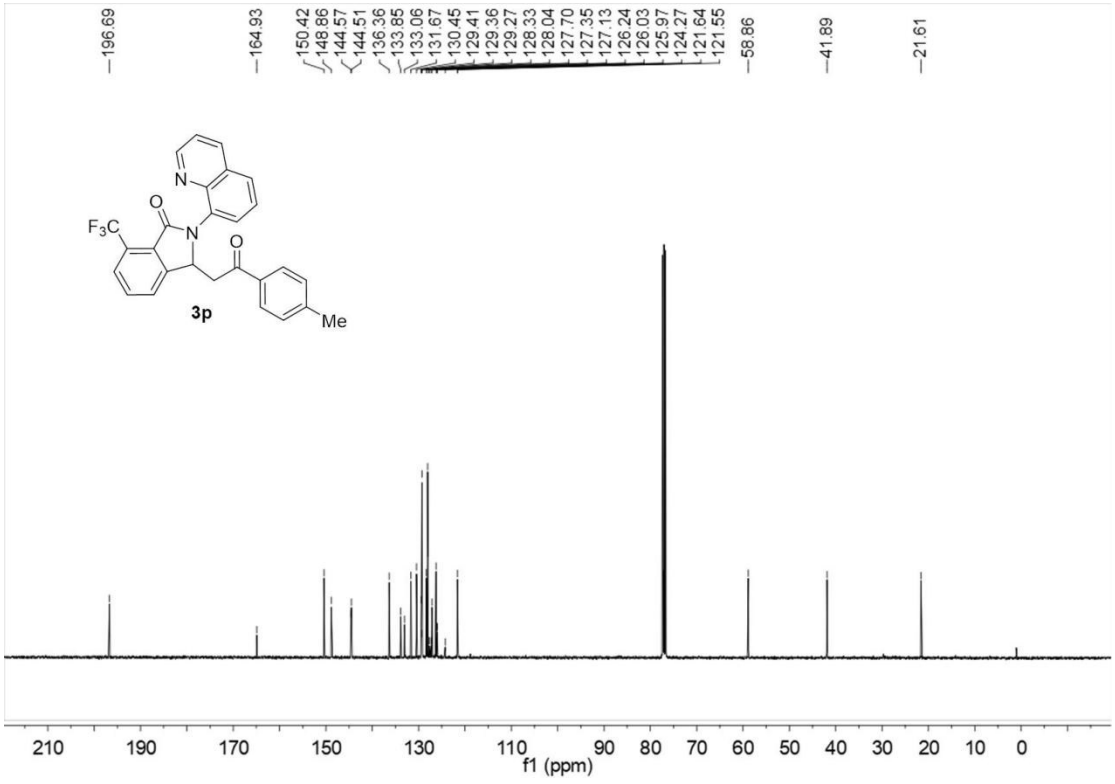
F3C
N
O
3p
Me
1.00
1.04
1.01
2.95
1.10
2.90
1.06
1.97
0.98
0.99
0.98
2.96
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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129.27
128.33
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127.70
127.35
127.13
126.24
126.03
125.97
124.27
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121.55
58.86
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F3C
N
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3p
Me
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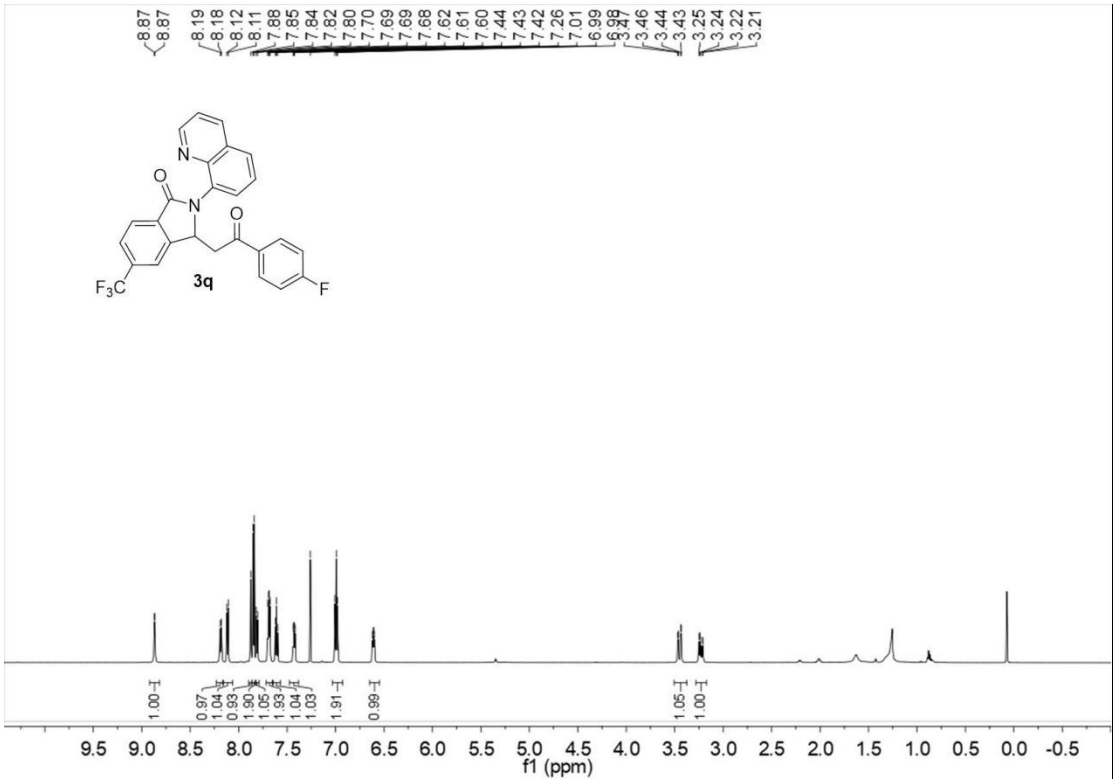
f1 (ppm)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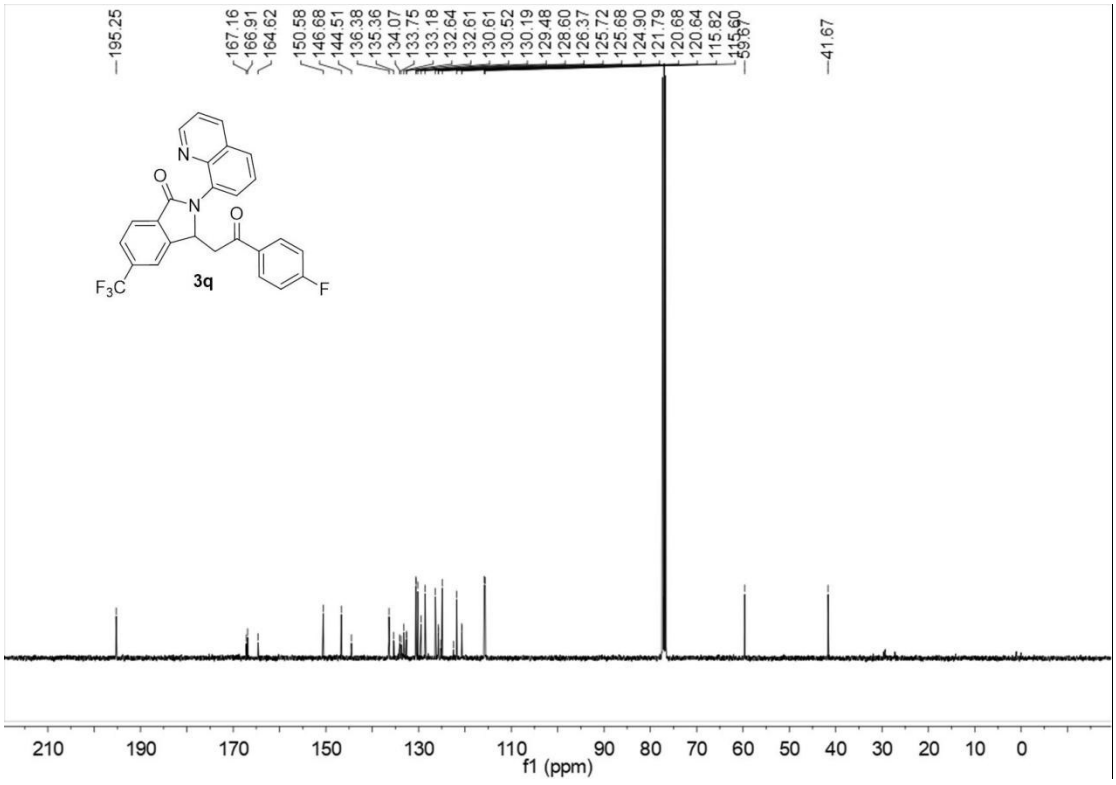
3.25
3.24
3.22
3.21
N
O
N
O
F3C
3q
F
1.00
0.97
1.04
0.93
1.90
1.05
1.93
1.04
1.03
1.91
0.99
1.05
1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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115.60
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F3C
3q
F
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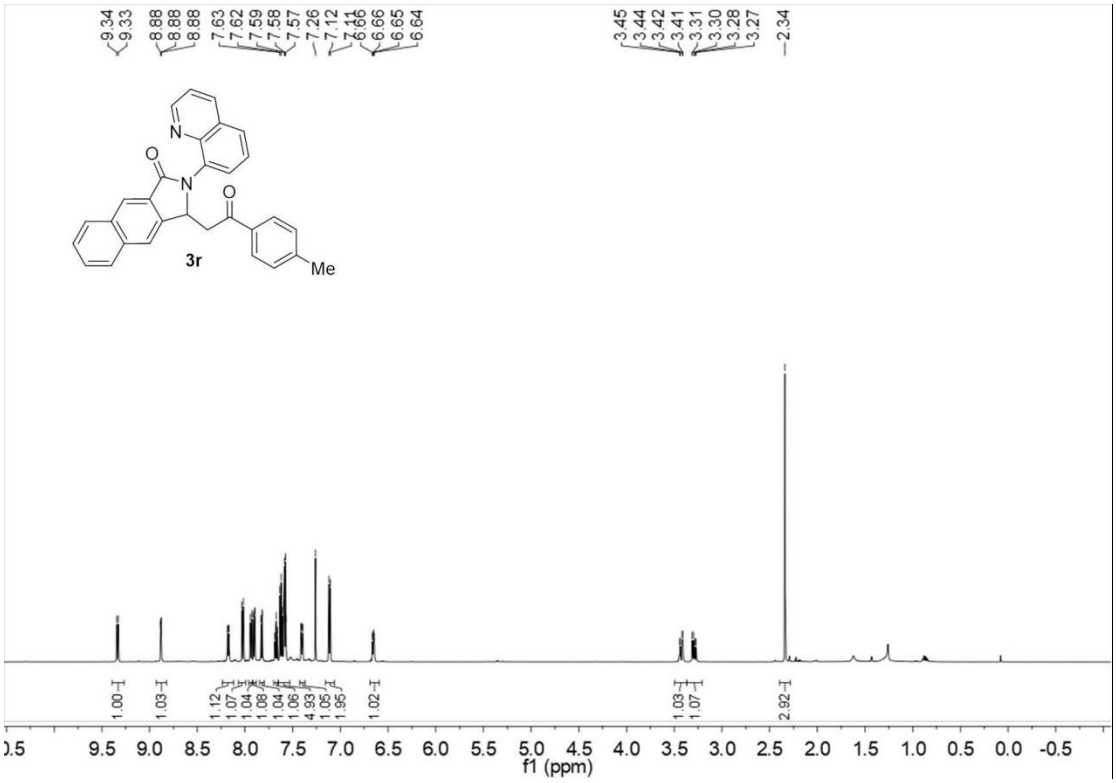
f1 (ppm)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6.64
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3.42
3.41
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3.27
2.34
3r
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1.03
1.12
1.07
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1.03
1.07
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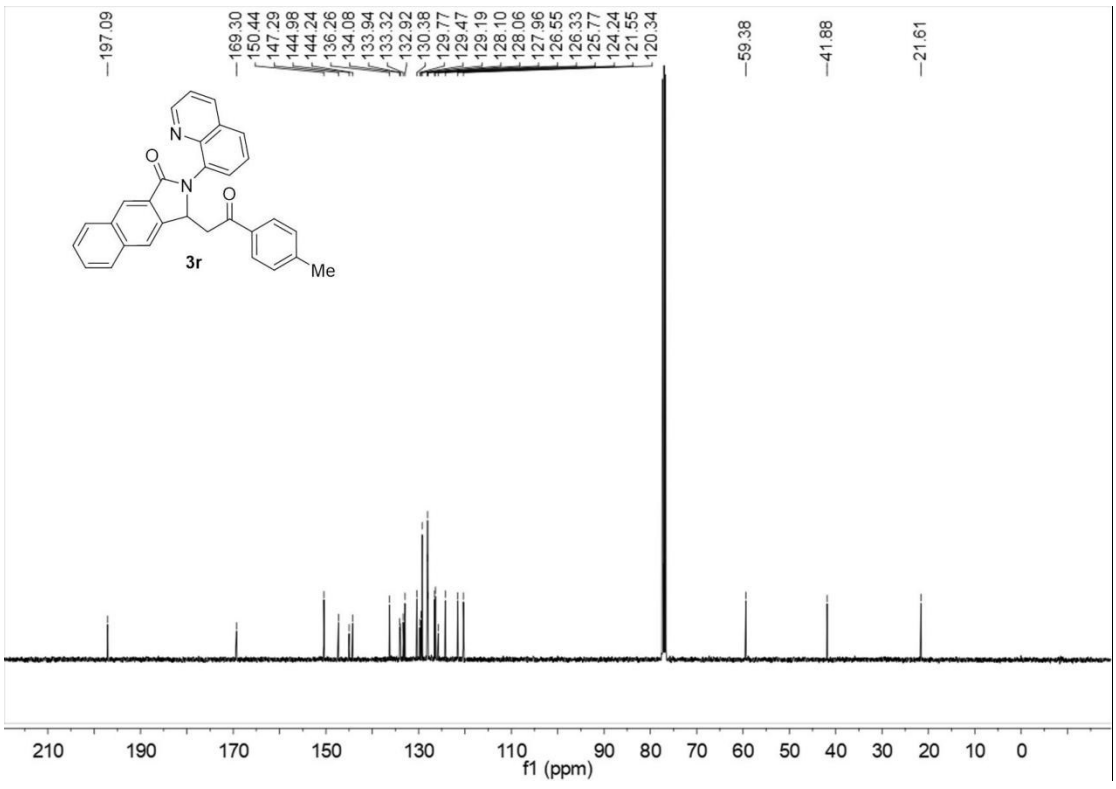
f1 (ppm)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128.06
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41.88
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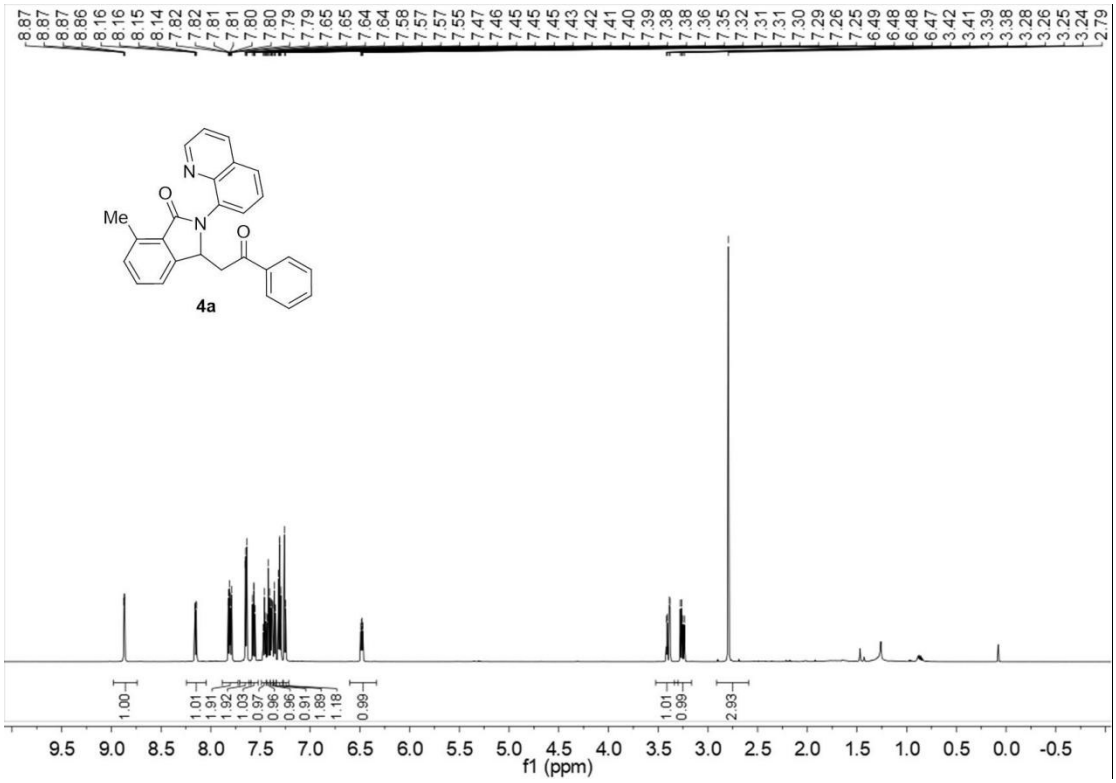
3r
Me
f1 (ppm)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Me
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1.03
0.97
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0.96
0.91
1.89
1.18
0.99
1.01
0.99
2.93
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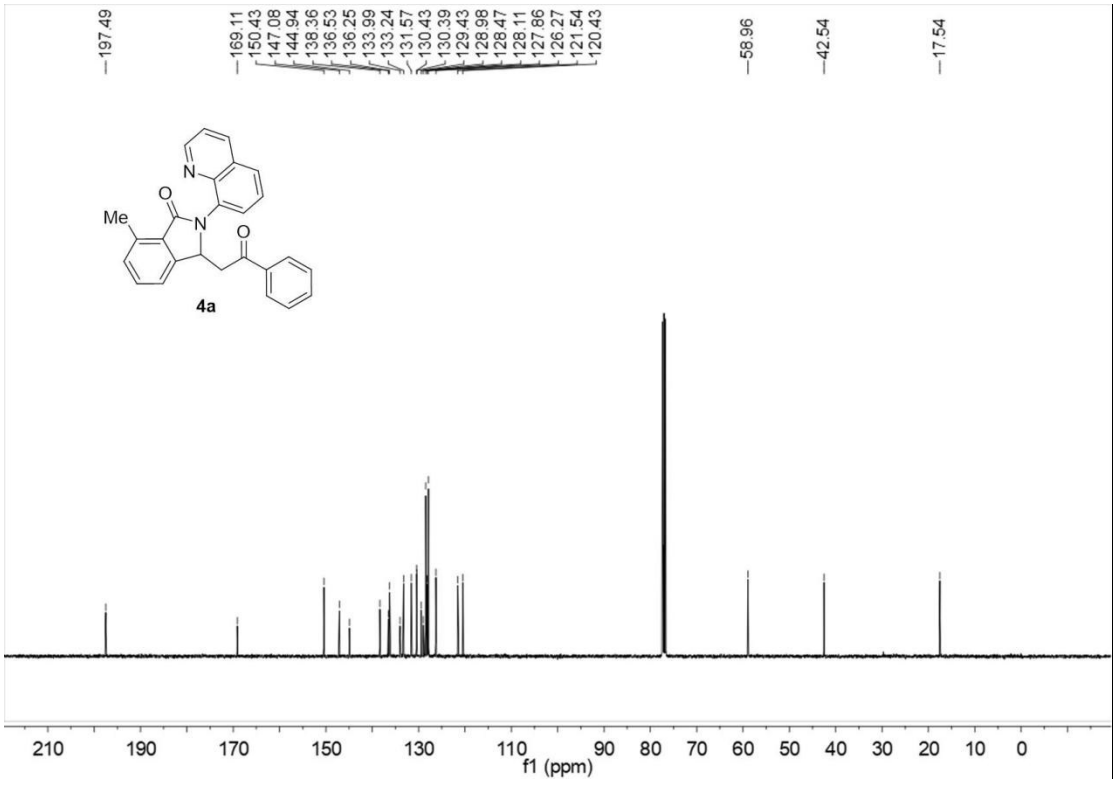
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120.43
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Me
N
O
4a
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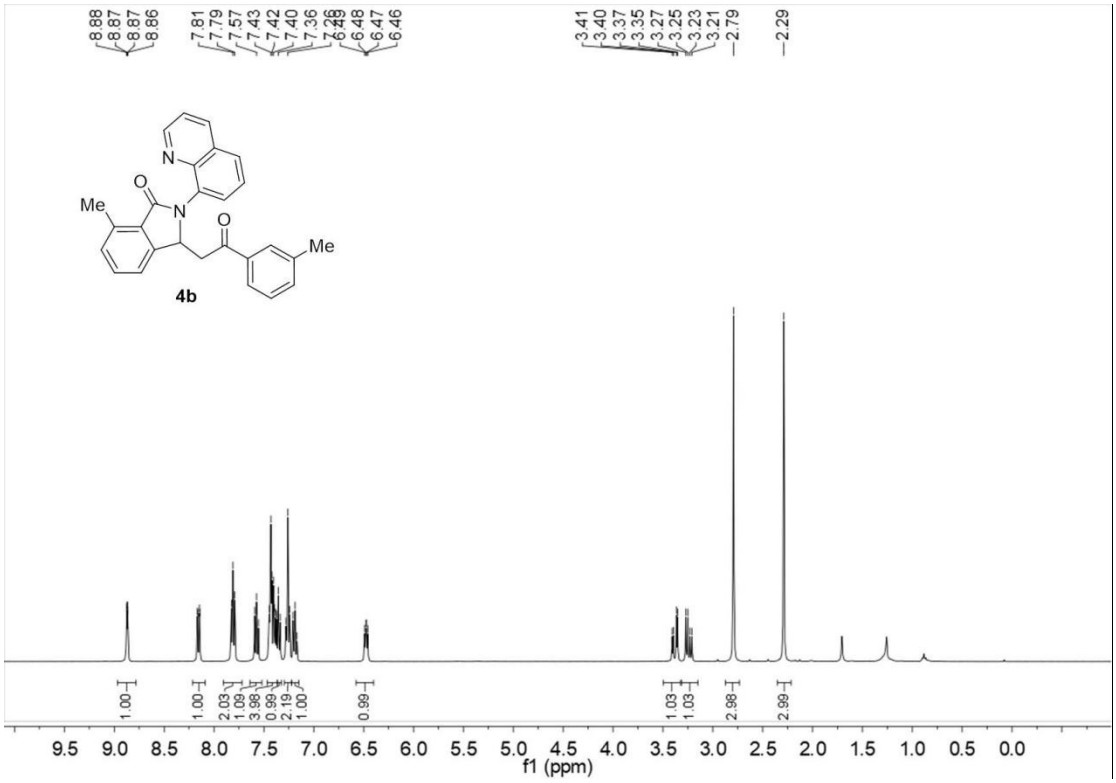
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3.35
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3.25
3.23
3.21
2.79
2.29
Me
Me
4b
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1.00
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1.08
3.98
0.99
2.19
1.00
0.99
1.03
1.03
2.98
2.99
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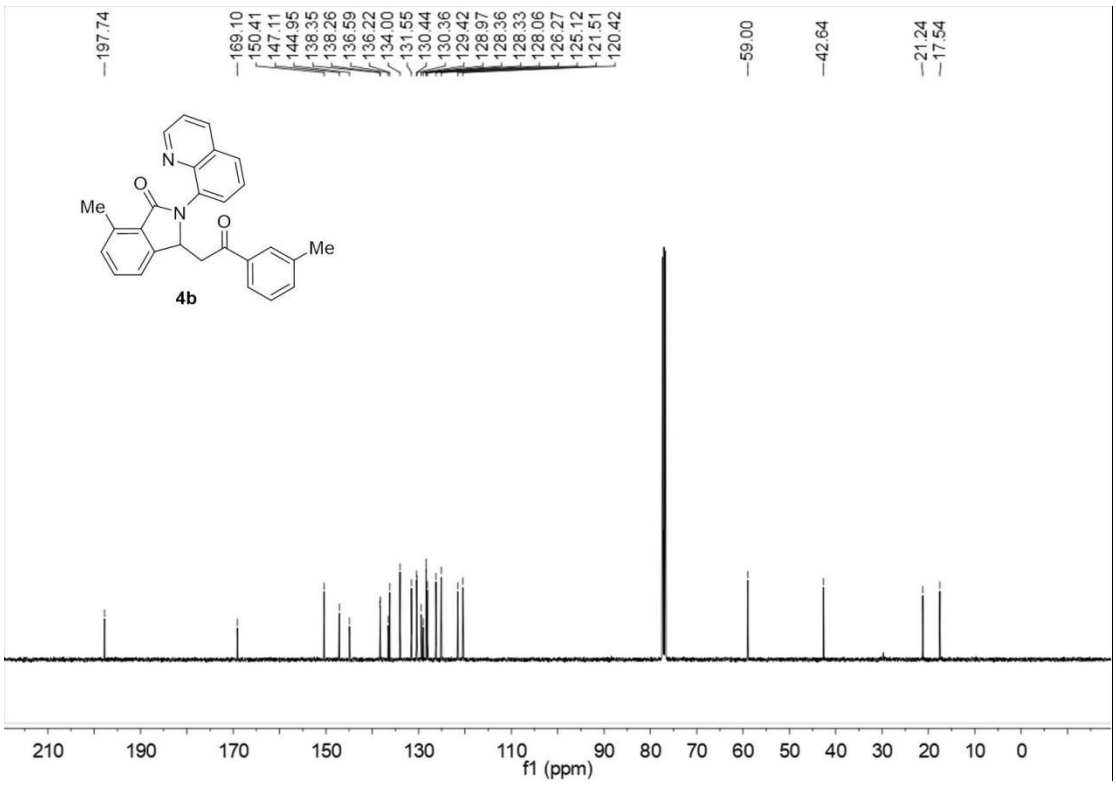
f1 (ppm)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128.97
128.36
128.33
128.06
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125.12
121.51
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21.24
17.54
Me
Me
4b
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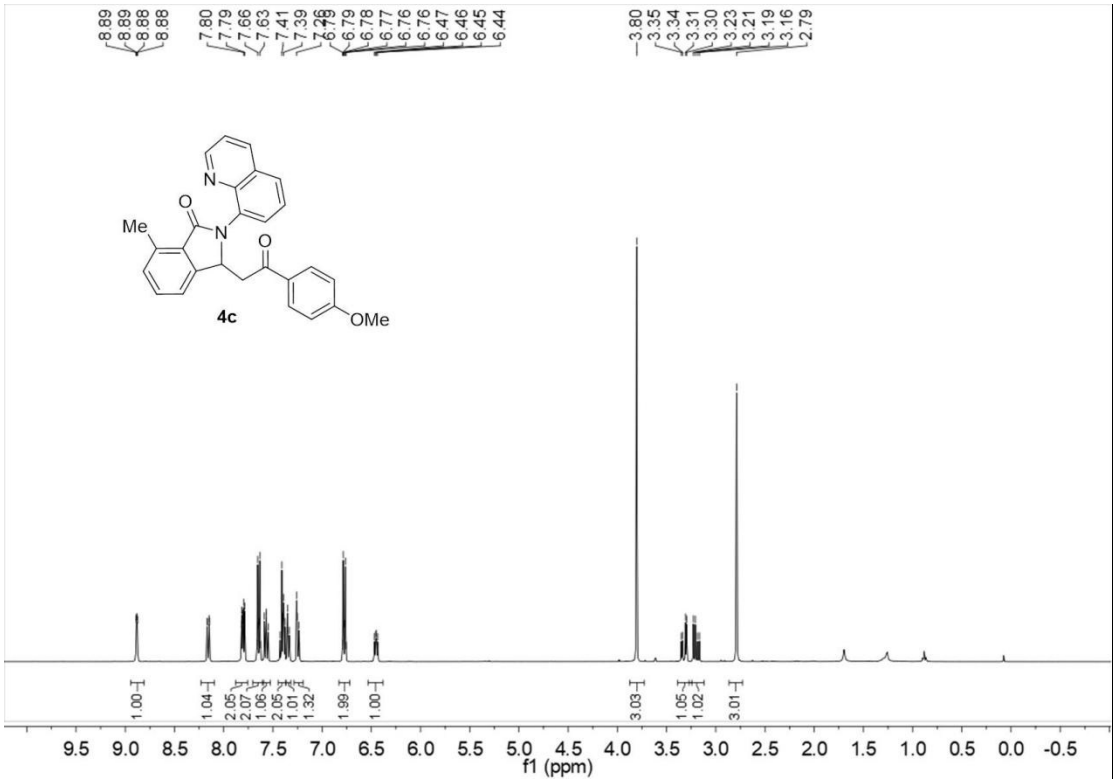
f1 (ppm)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N
O
OMe
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2.05
2.07
1.06
2.05
1.01
1.32
1.99
1.00
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1.05
1.02
3.01
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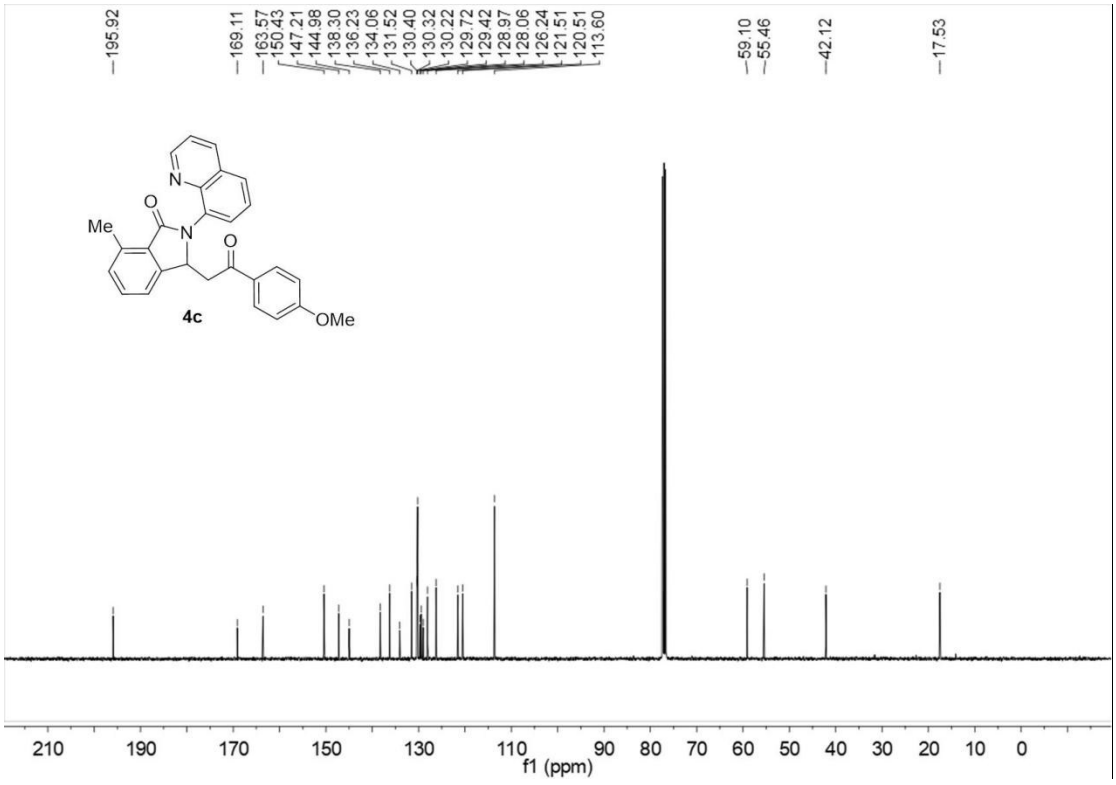
f1 (ppm)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128.97
128.06
126.24
121.51
120.51
113.60
59.10
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Me
O
N
O
OMe
4c
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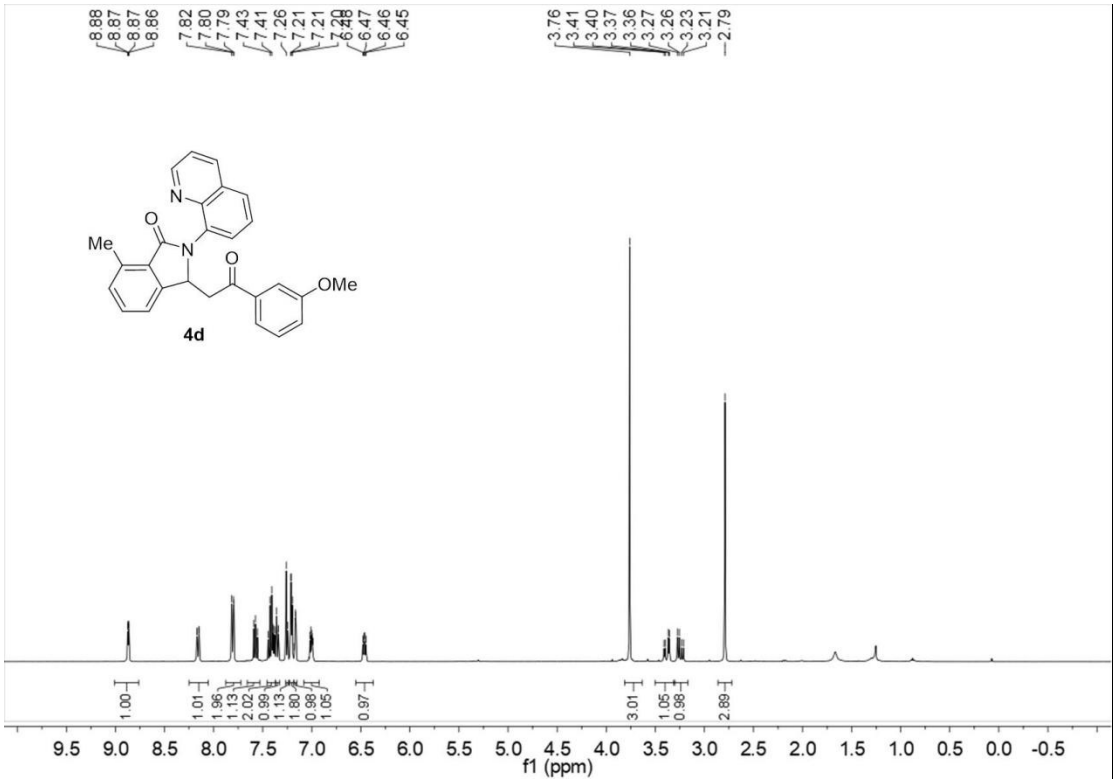
f1 (ppm)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6.46
6.45
3.76
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3.26
3.23
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Me
O
N
O
OMe
4d
1.00
1.01
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2.02
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1.13
1.80
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3.01
1.05
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2.89
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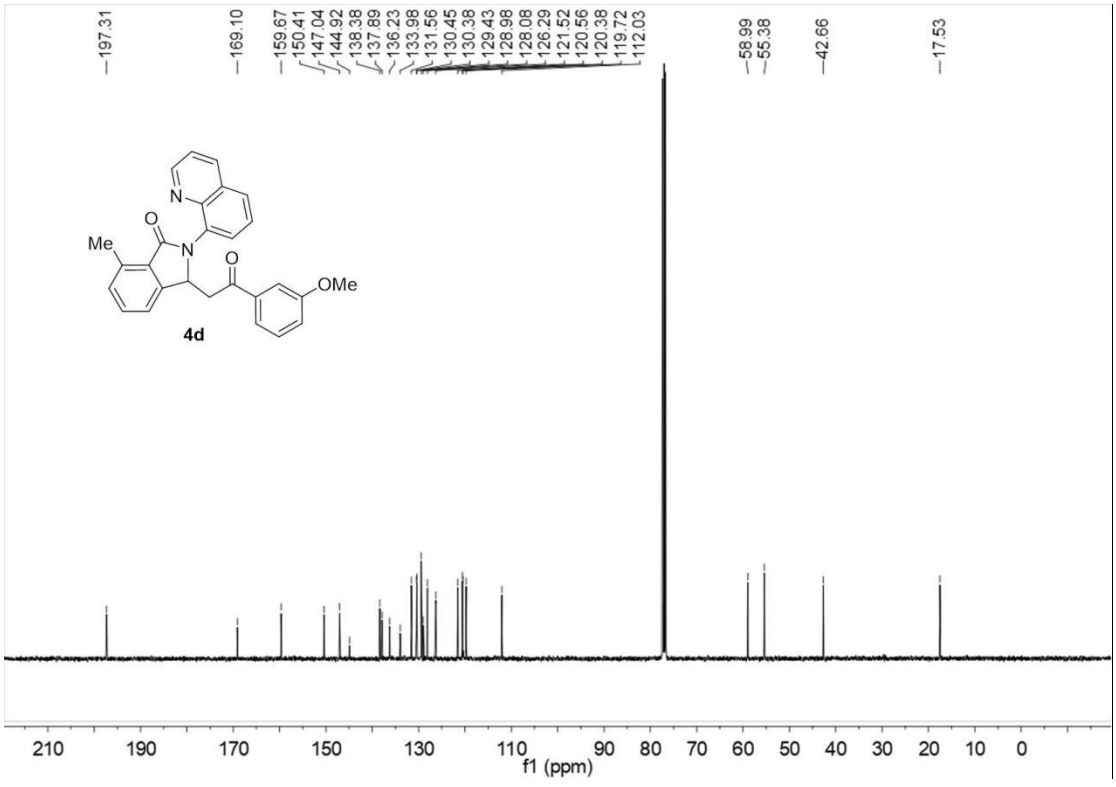
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129.43
128.98
128.08
126.29
121.52
120.56
120.38
119.72
112.03
58.99
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Me
O
N
O
OMe
4d
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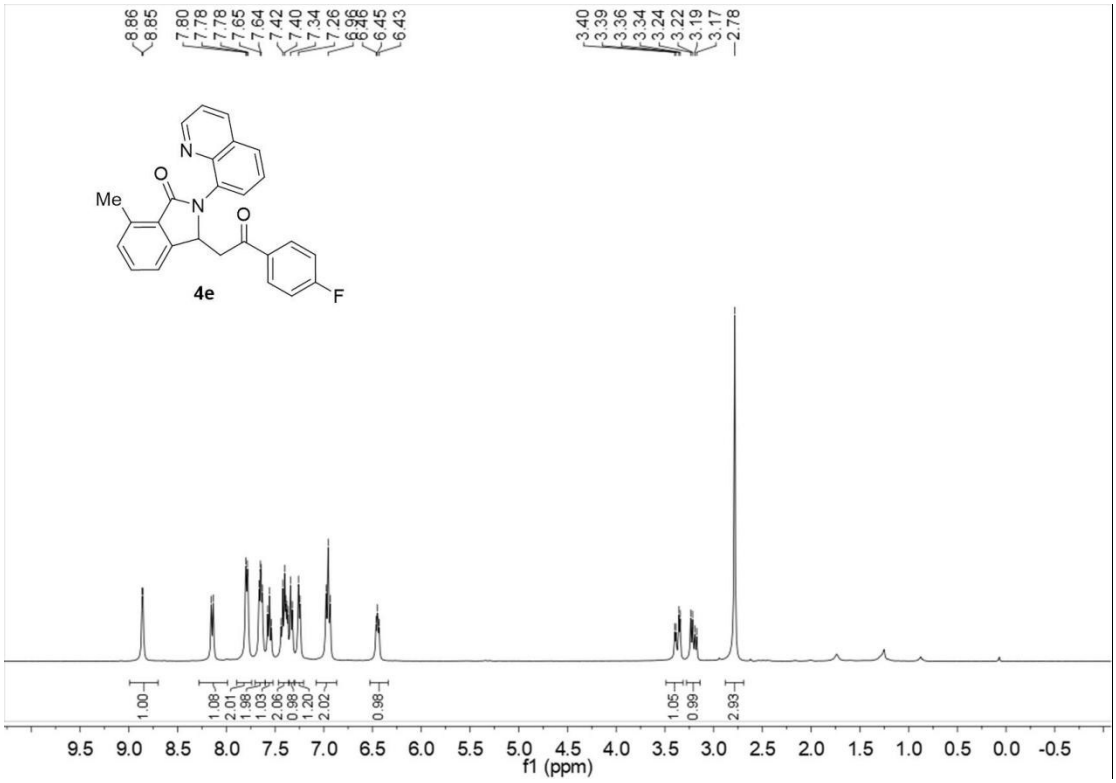
f1 (ppm)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F
4e
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1.08
2.01
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1.03
2.06
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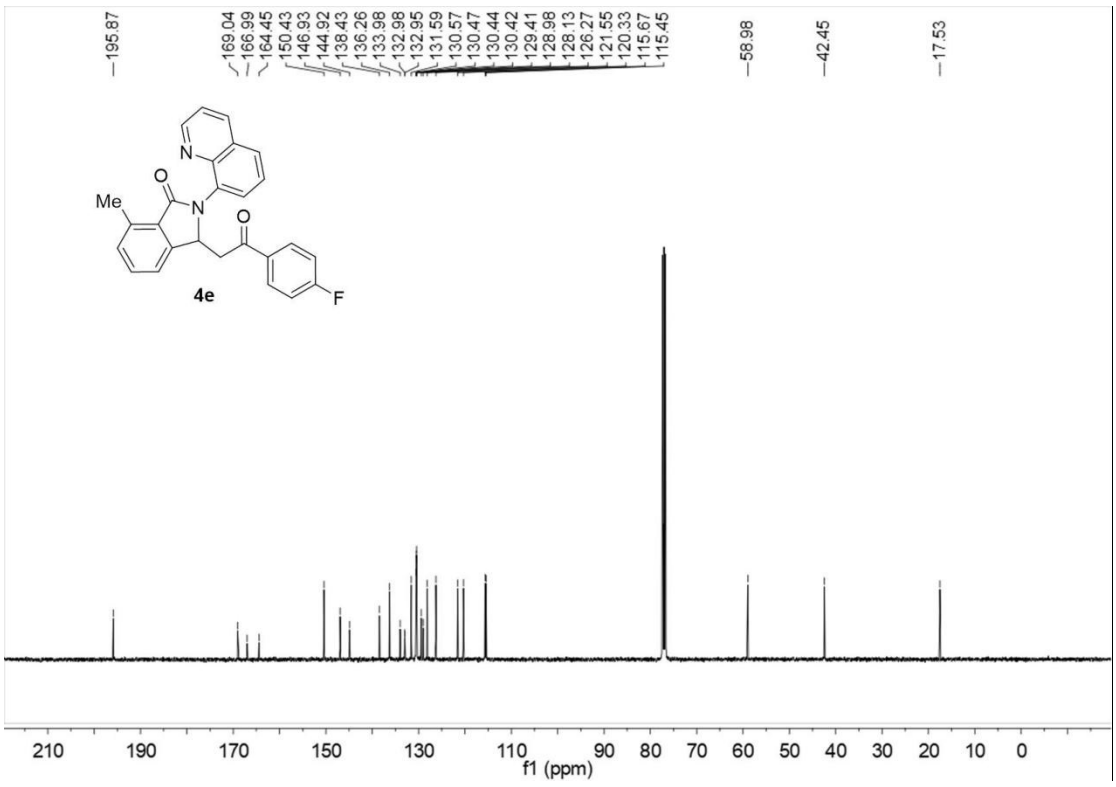
2.02
0.98
1.05
0.99
2.93
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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42.45
17.53
Me
O
N
O
F
4e
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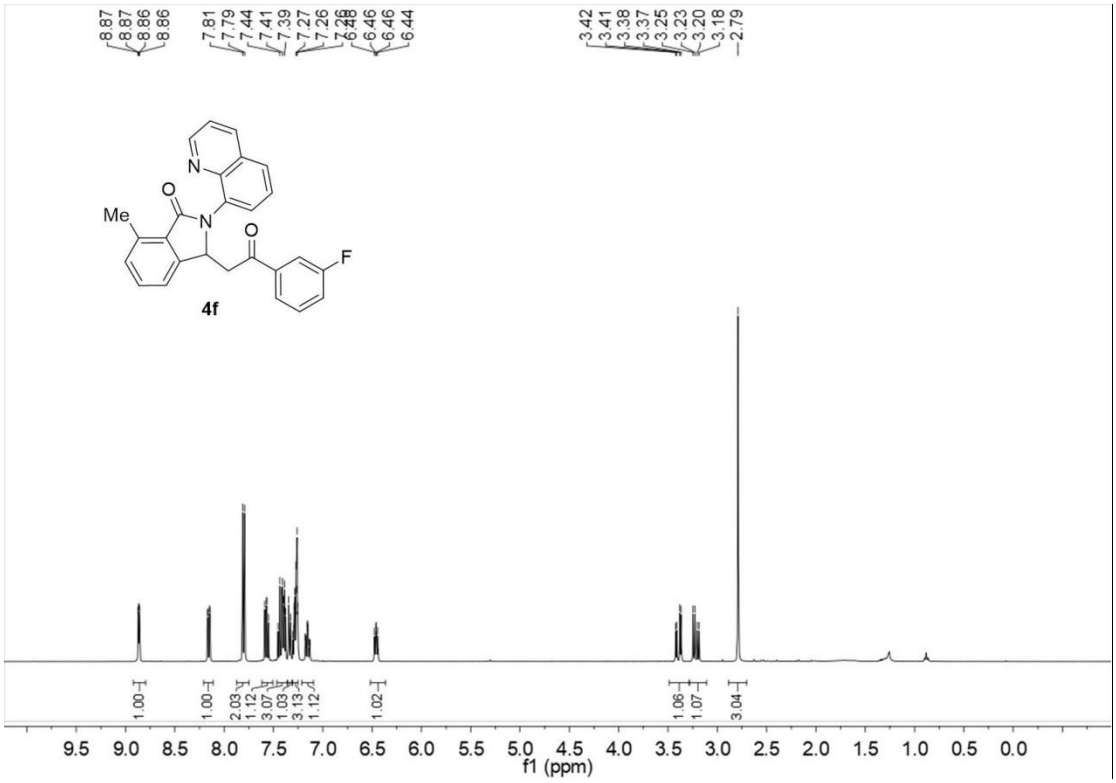
f1 (ppm)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6.44
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3.41
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3.25
3.23
3.20
3.18
2.79
Me
O
N
O
F
4f
1.00
1.00
2.03
1.12
3.07
1.03
3.13
1.12
1.02
1.06
1.07
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
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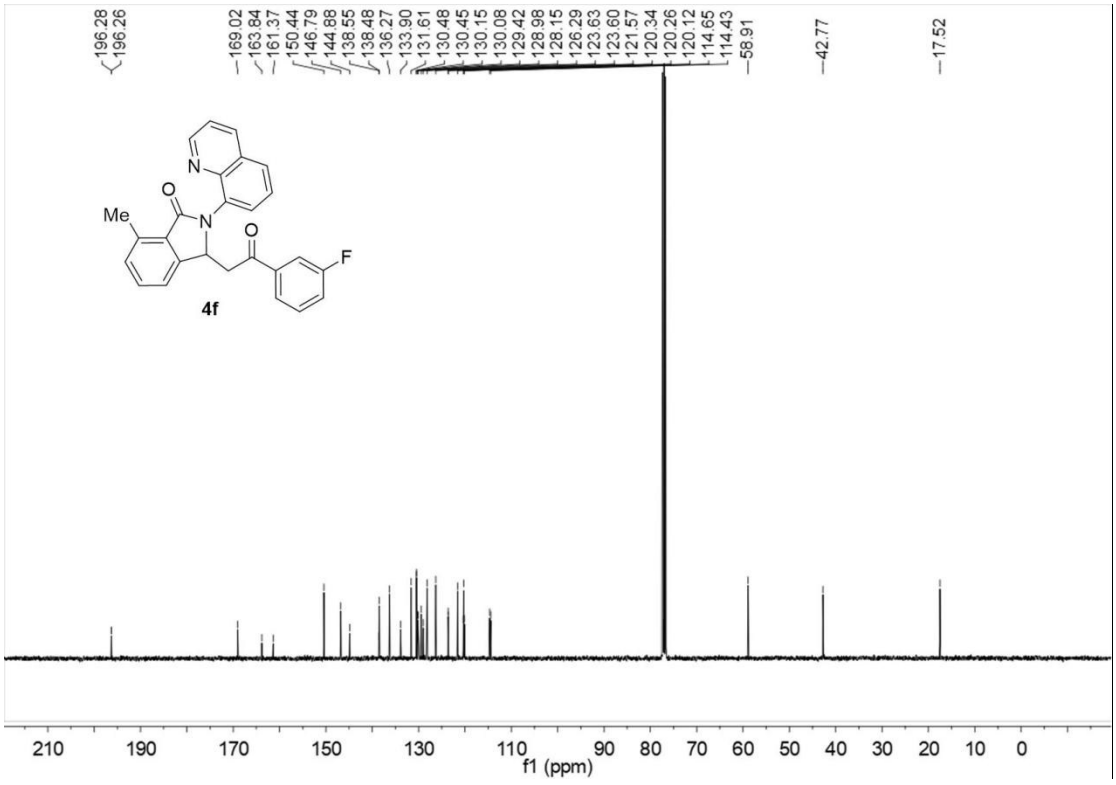
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130.08
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120.26
120.12
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114.43
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O
F
4f
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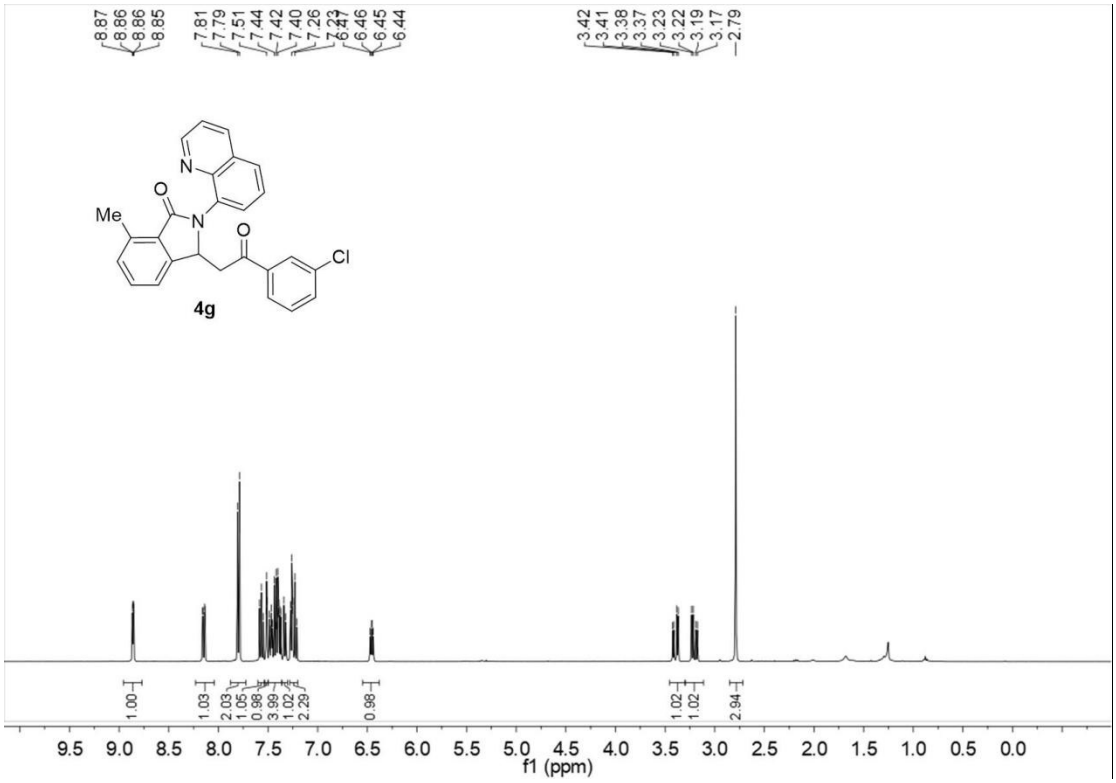
f1 (ppm)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3.22
3.19
3.17
2.79
Me
O
N
O
Cl
4g
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2.03
1.05
0.98
3.99
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2.29
0.98
1.02
1.02
2.94
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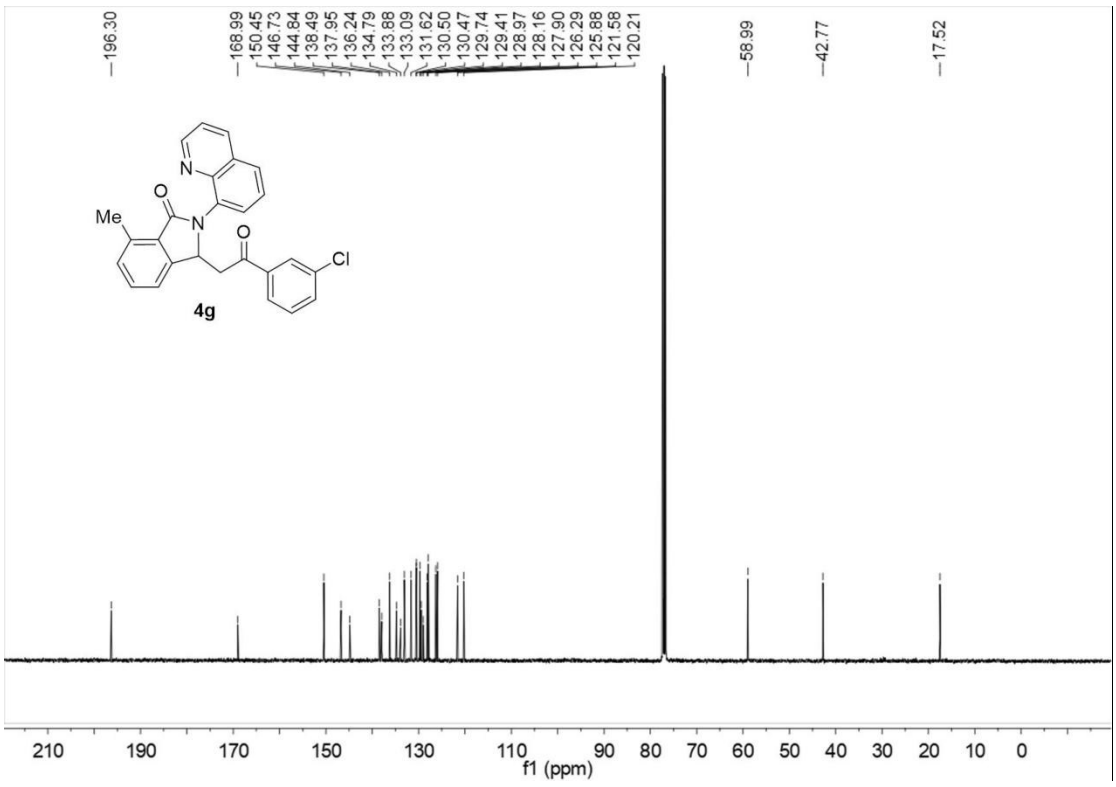
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126.29
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120.21
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N
O
Cl
4g
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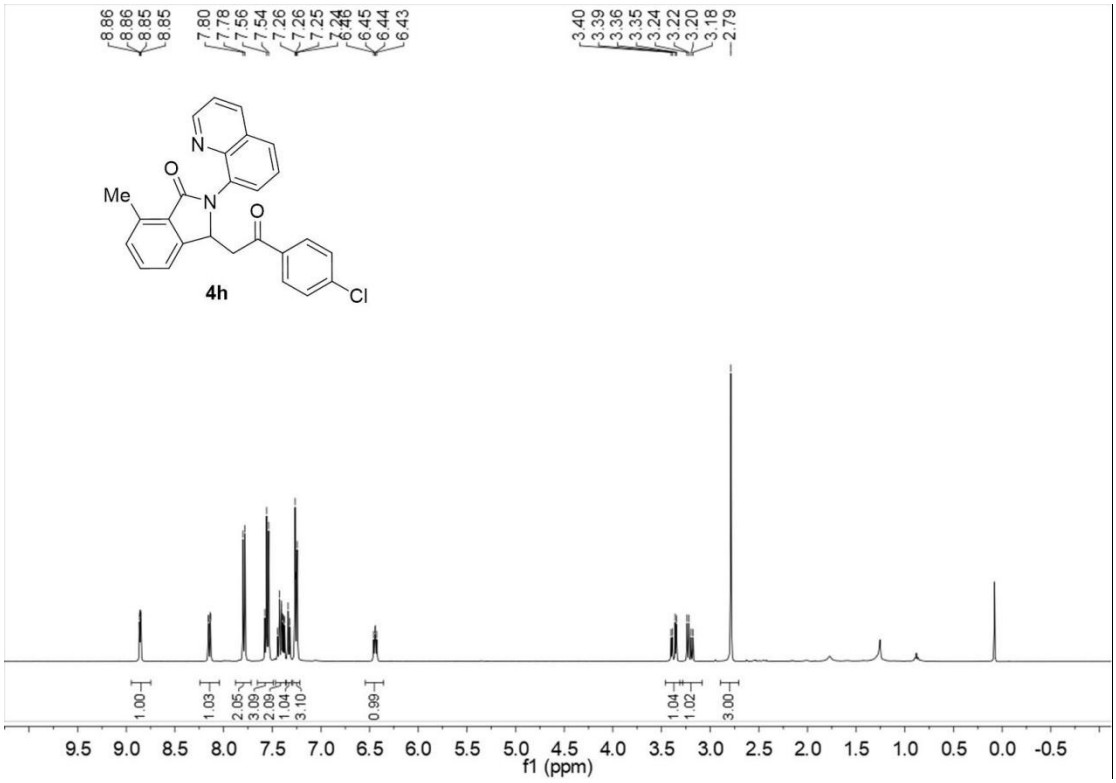
f1 (ppm)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6.43
3.40
3.39
3.36
3.35
3.24
3.22
3.20
3.18
2.79
Me
O
N
O
Cl
4h
1.00
1.03
2.05
3.09
2.09
1.04
3.10
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1.04
1.02
3.00
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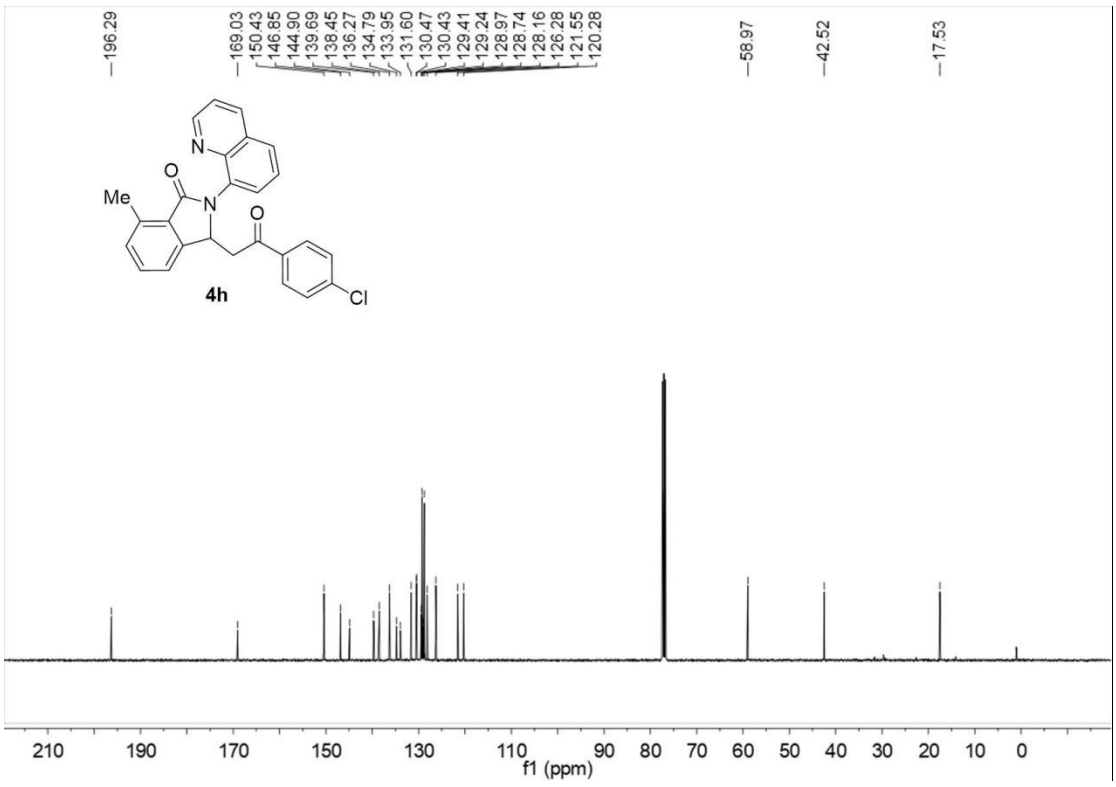
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128.74
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120.28
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N
O
Cl
4h
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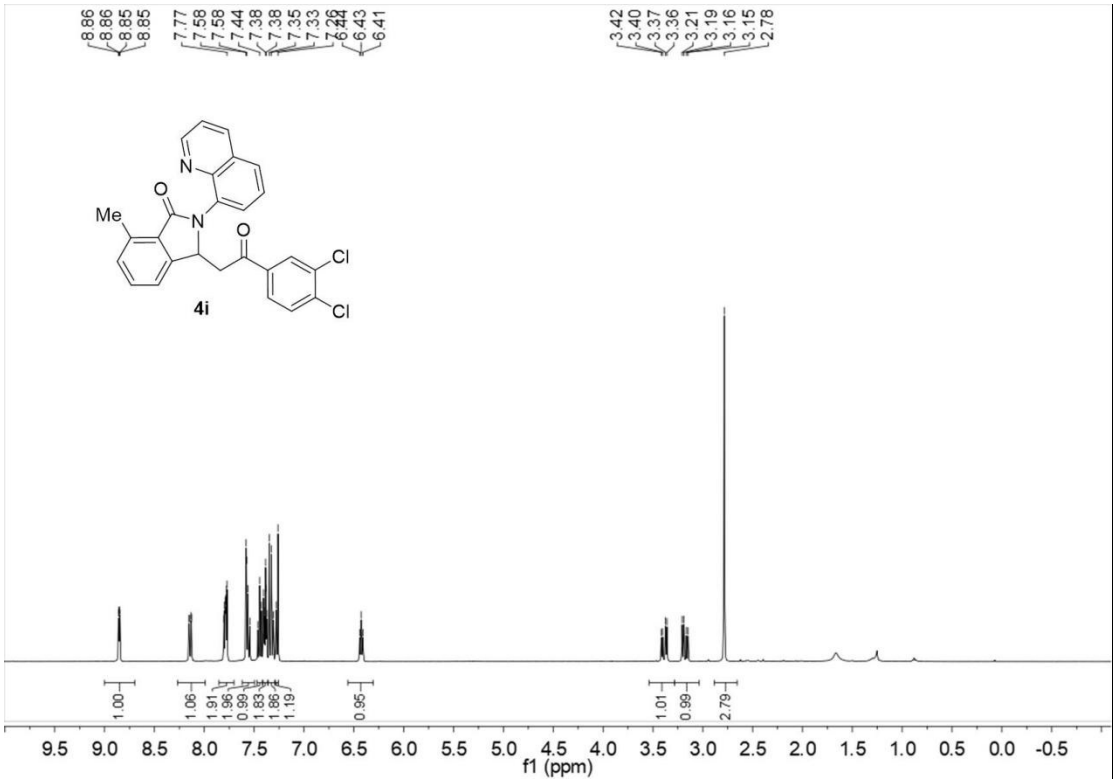
f1 (ppm)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6.43
6.41
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3.37
3.36
3.21
3.19
3.16
3.15
2.78
N
O
Me
N
O
Cl
Cl
4i
1.00
1.06
1.91
1.96
0.99
1.83
1.86
1.19
0.95
1.01
0.99
2.79
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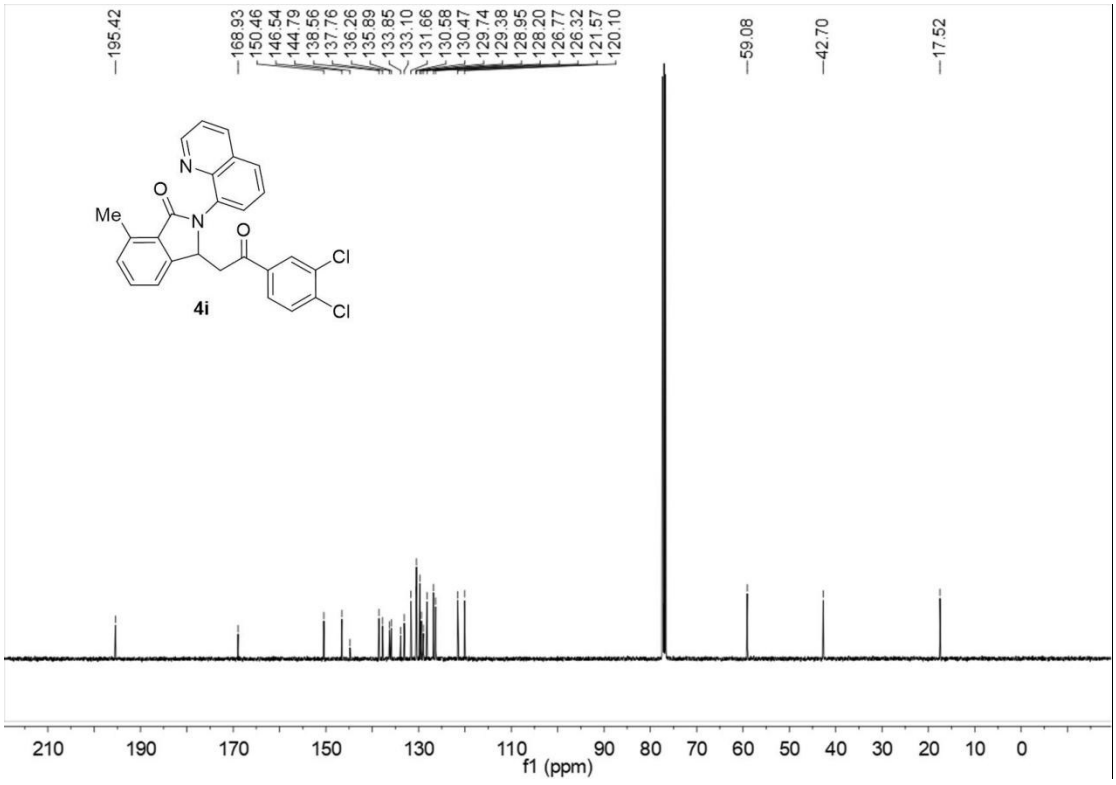
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120.10
59.08
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Me
N
O
Cl
Cl
4i
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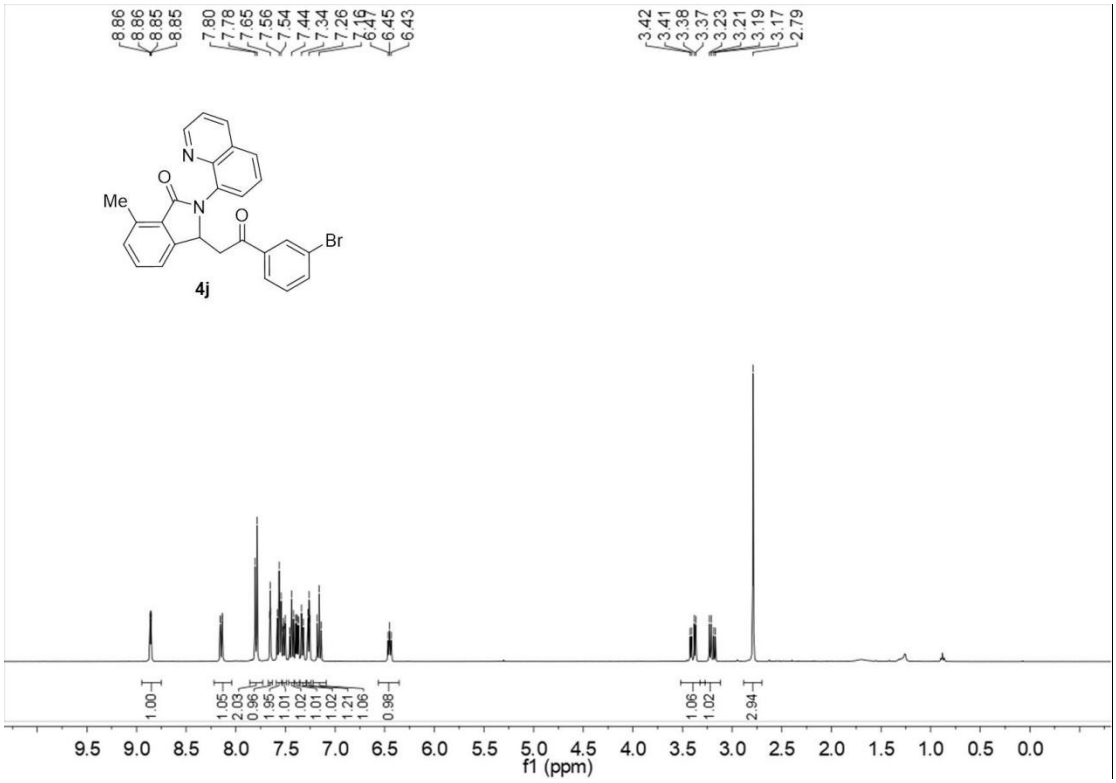
f1 (ppm)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3.23
3.21
3.19
3.17
2.79
N
O
Me
N
O
Br
4j
1.00
1.05
2.03
0.96
1.95
1.01
1.02
1.01
1.02
1.21
1.06
0.98
1.06
1.02
2.94
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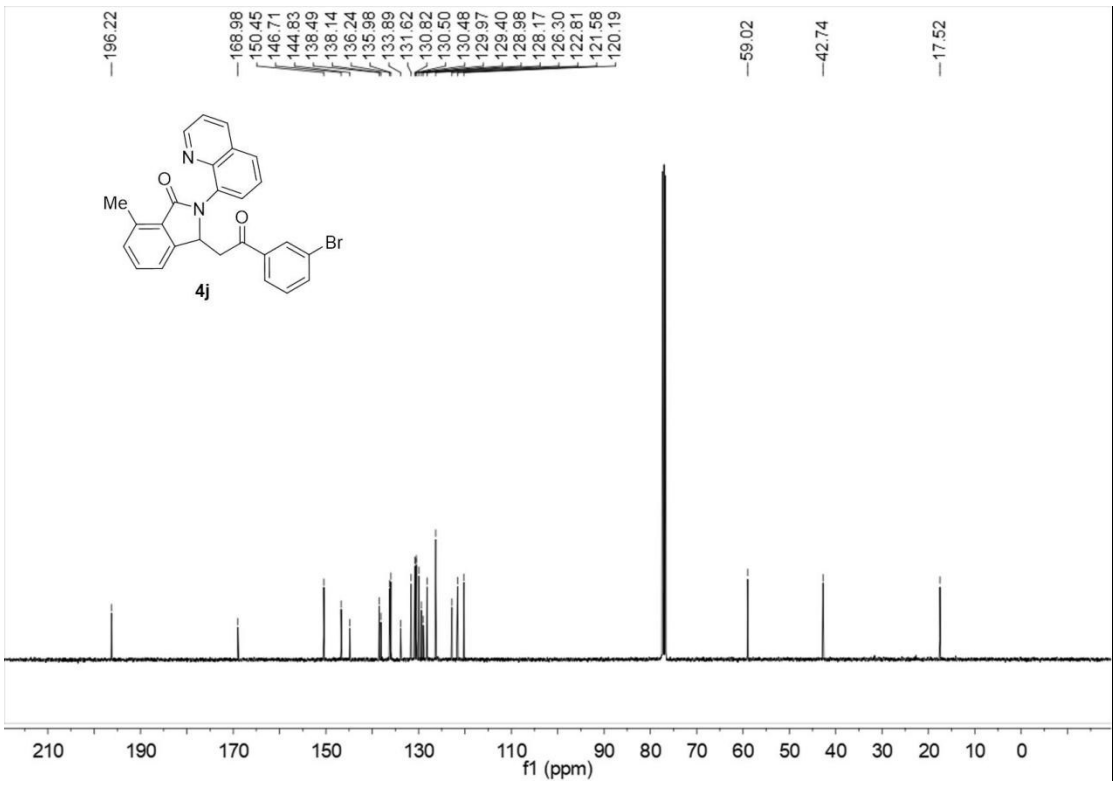
f1 (ppm)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120.19
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Br
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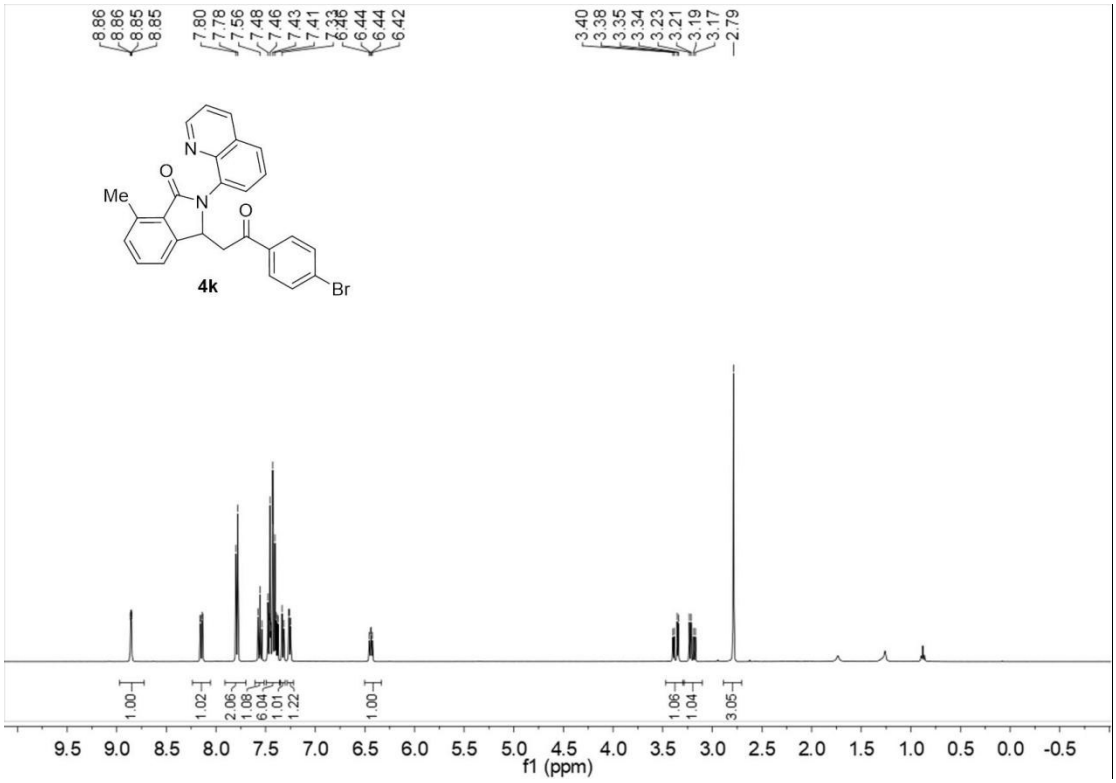
f1 (ppm)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6.42
3.40
3.38
3.35
3.34
3.23
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3.19
3.17
2.79
Me
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O
Br
4k
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1.02
2.06
1.08
6.04
1.01
1.22
1.00
1.06
1.04
3.05
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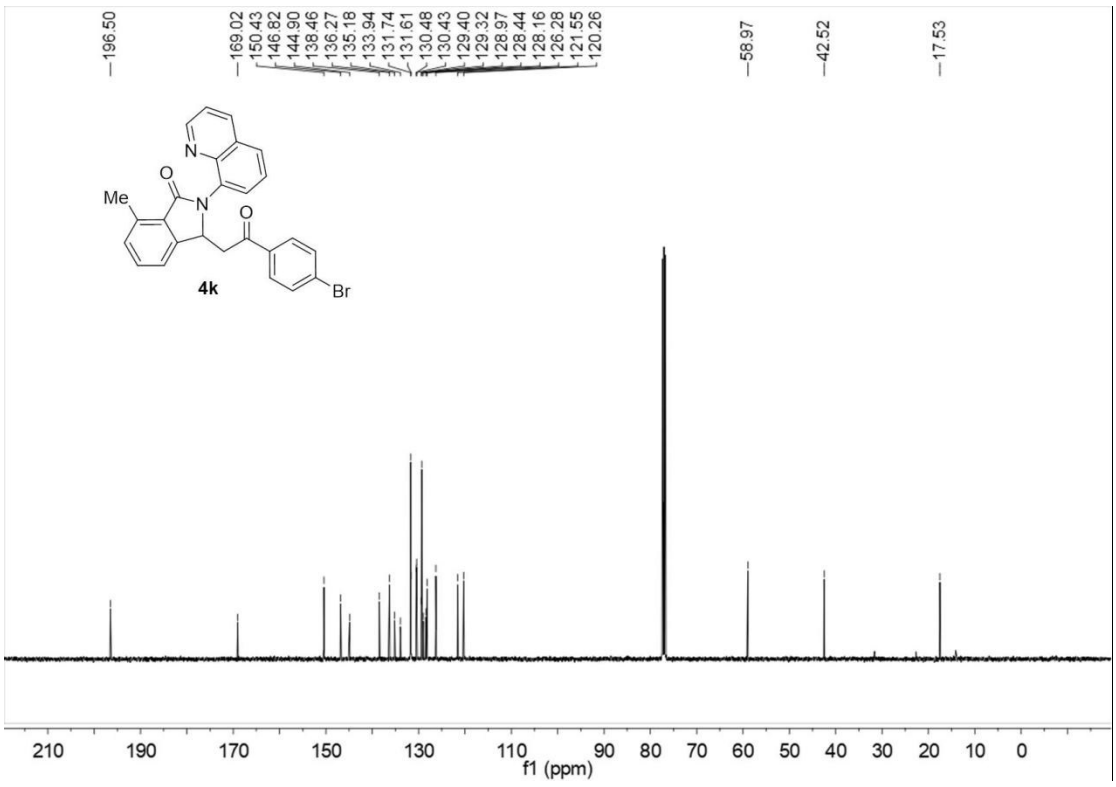
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129.32
128.97
128.44
128.16
126.28
121.55
120.26
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17.53
Me
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N
O
Br
4k
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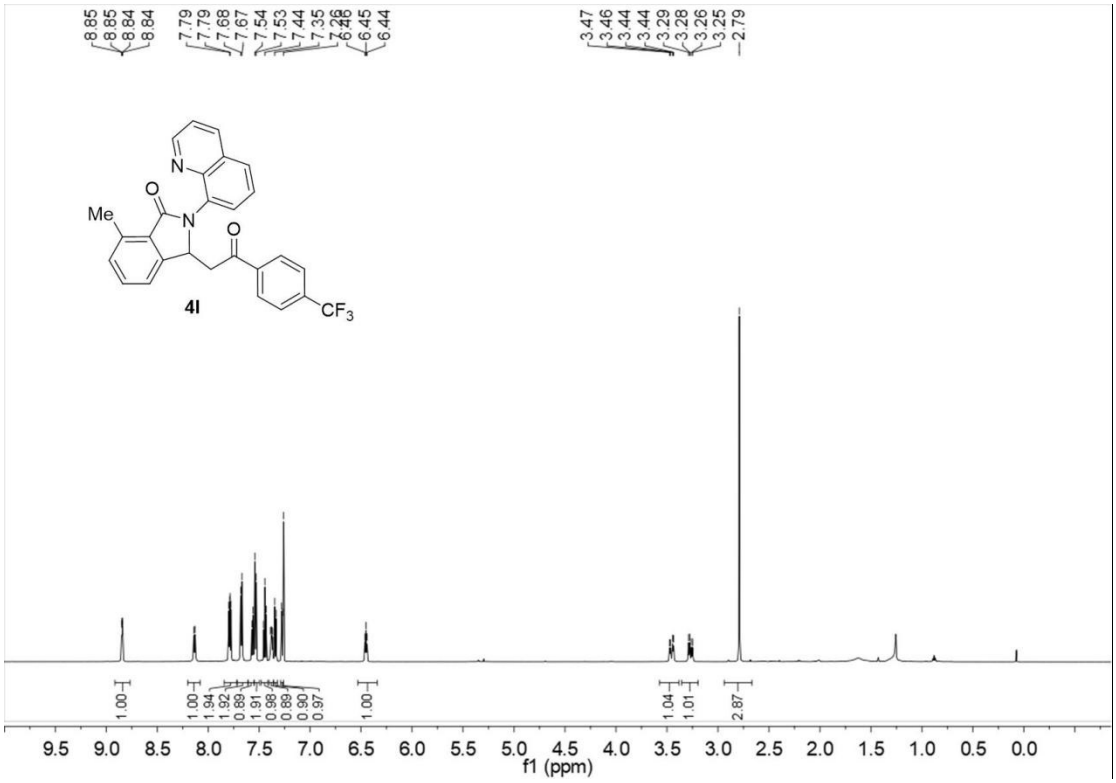
f1 (ppm)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3.46
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3.26
3.25
2.79
Me
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N
O
CF3
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1.91
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0.97
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1.04
1.01
2.87
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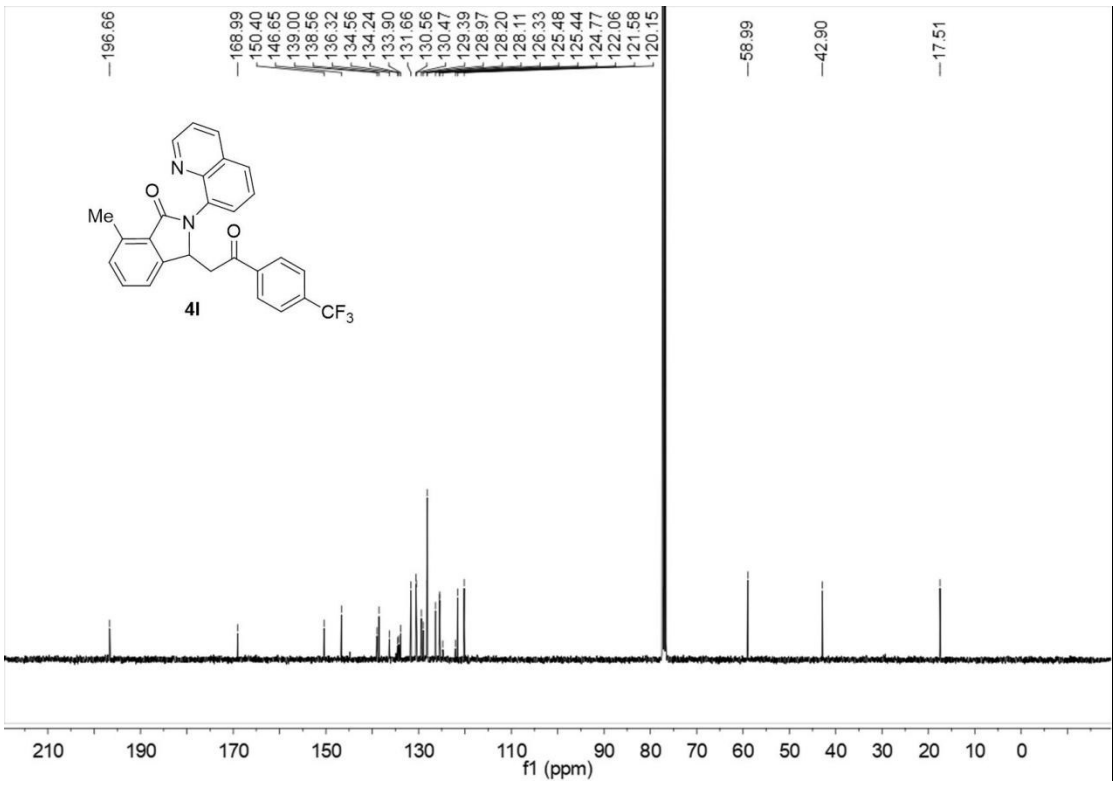
f1 (ppm)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128.20
128.11
126.33
125.48
125.44
124.77
122.06
121.58
120.15
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N
O
CF3
4l
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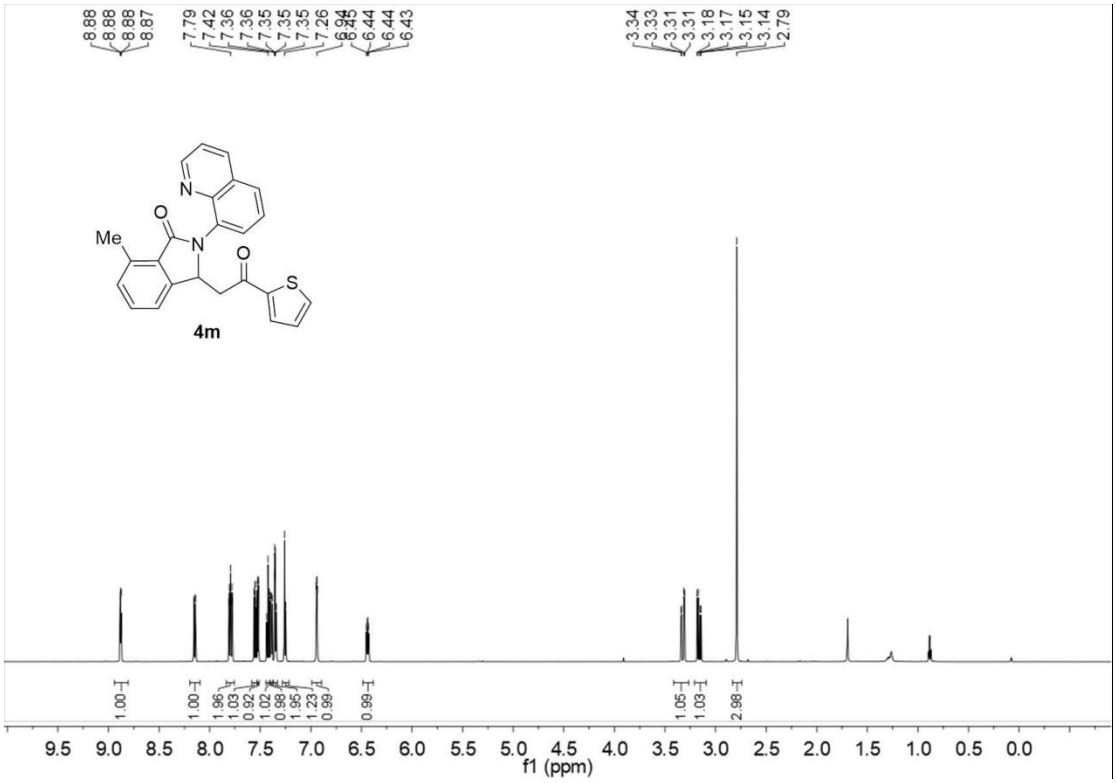
f1 (ppm)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6.43
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3.18
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3.15
3.14
2.79
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O
S
4m
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1.00
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1.02
0.98
1.95
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0.99
1.05
1.03
2.98
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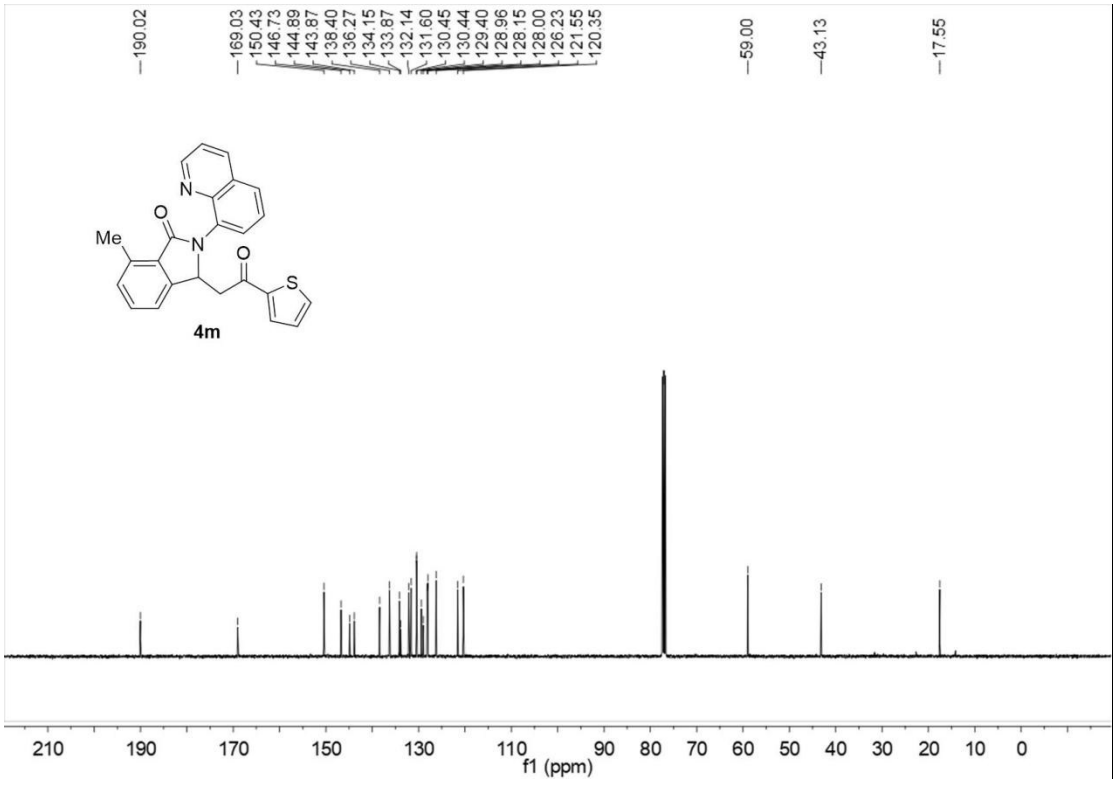
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121.55
120.35
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O
O
S
4m
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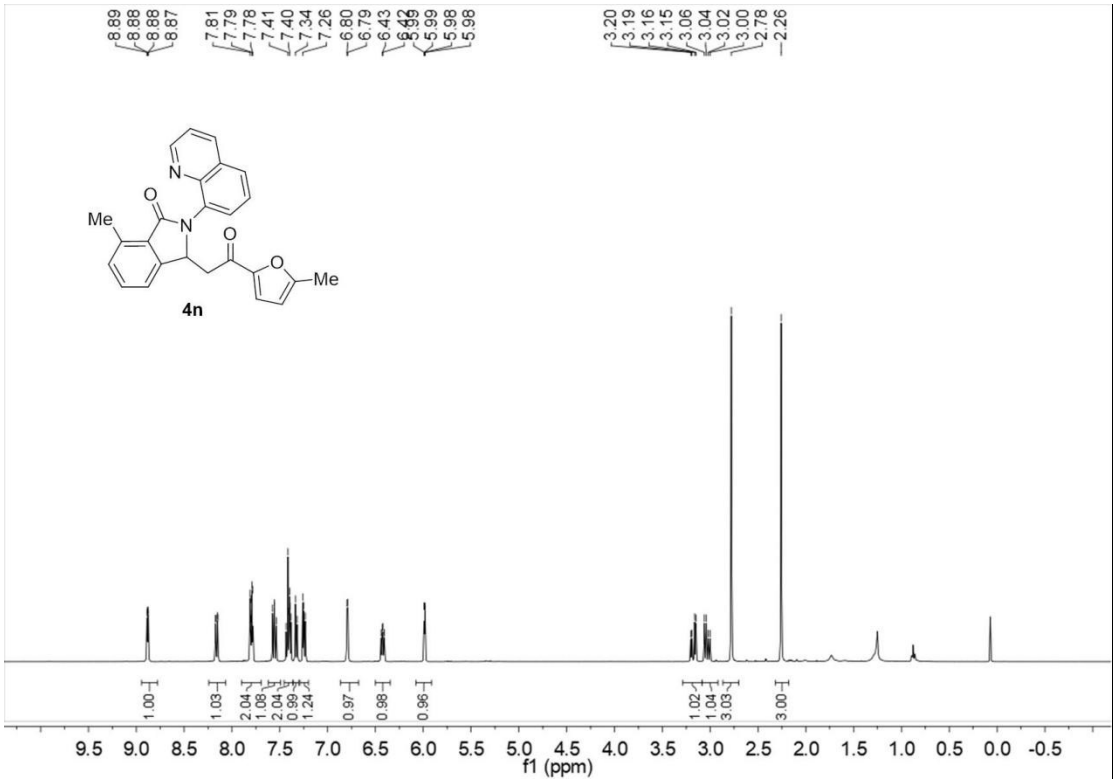
f1 (ppm)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Me
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2.04
1.08
2.04
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0.98
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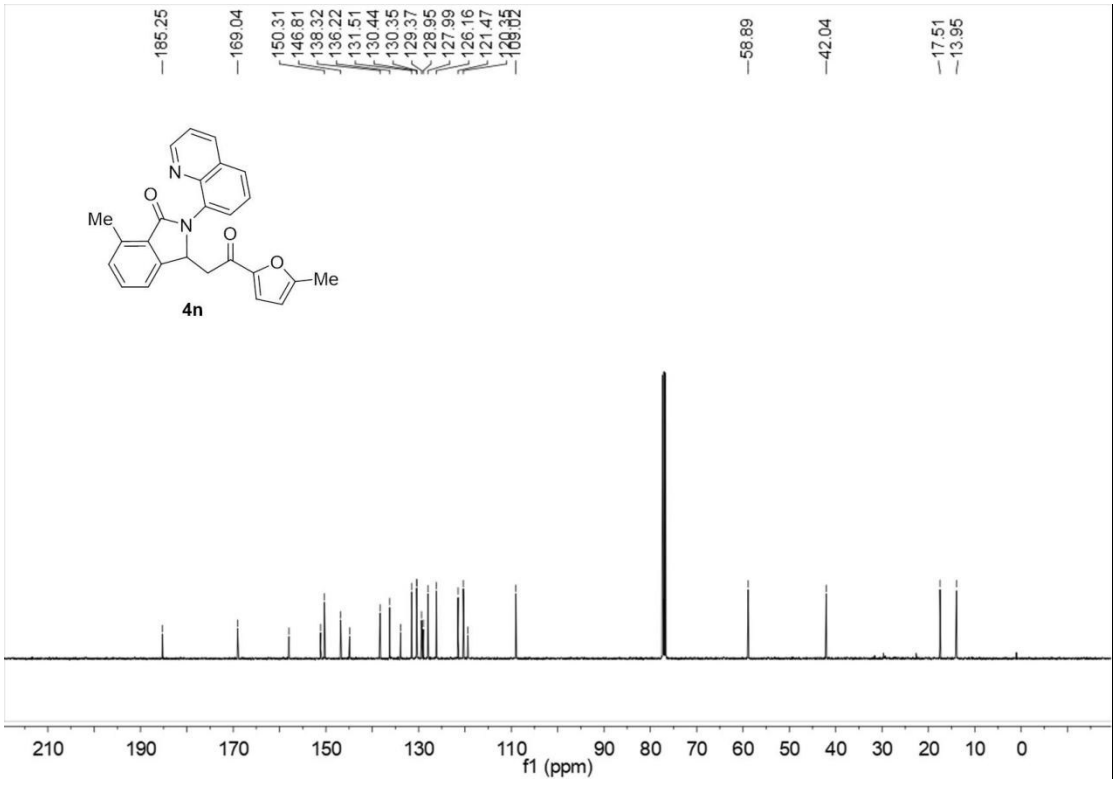
1.04
3.03
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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Me
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O
Me
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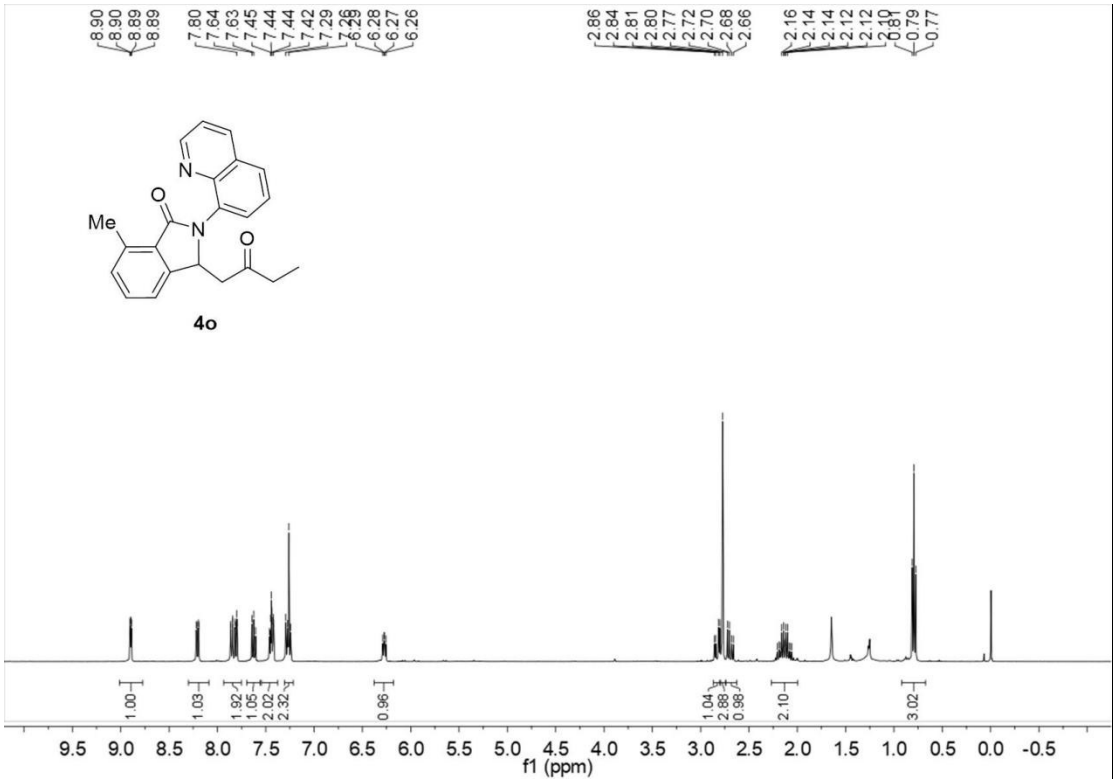
f1 (ppm)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1.04
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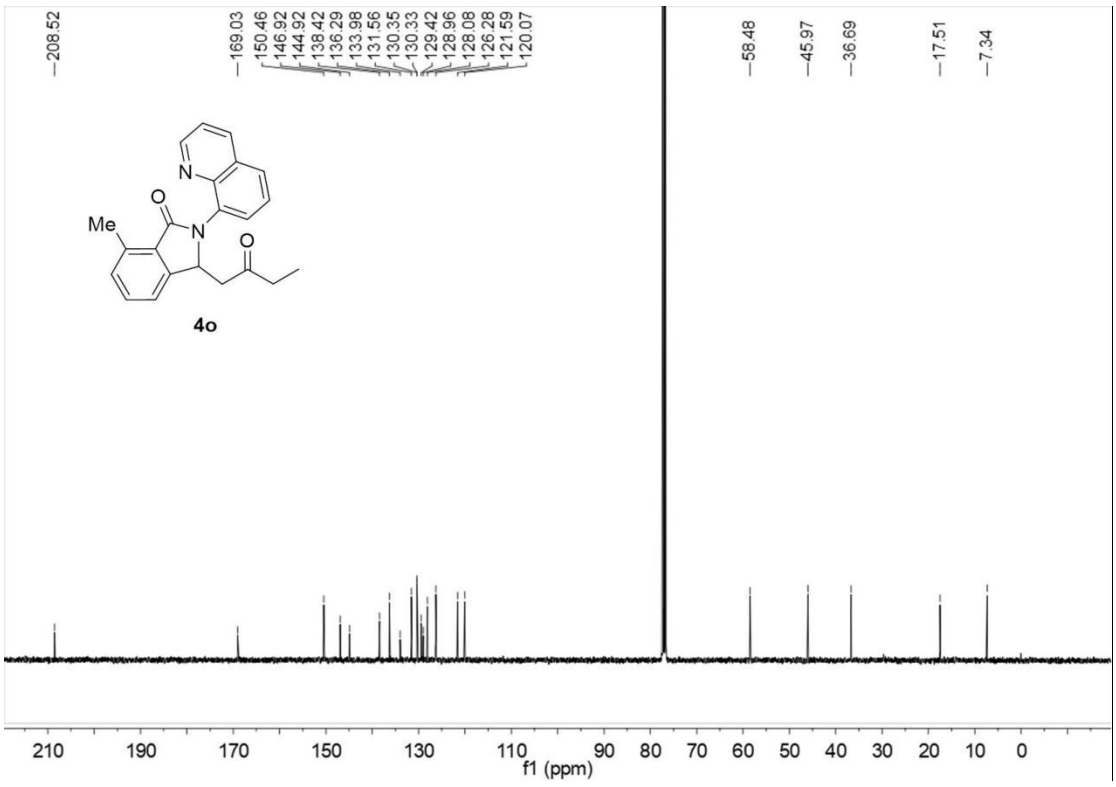
3.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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45.97
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N
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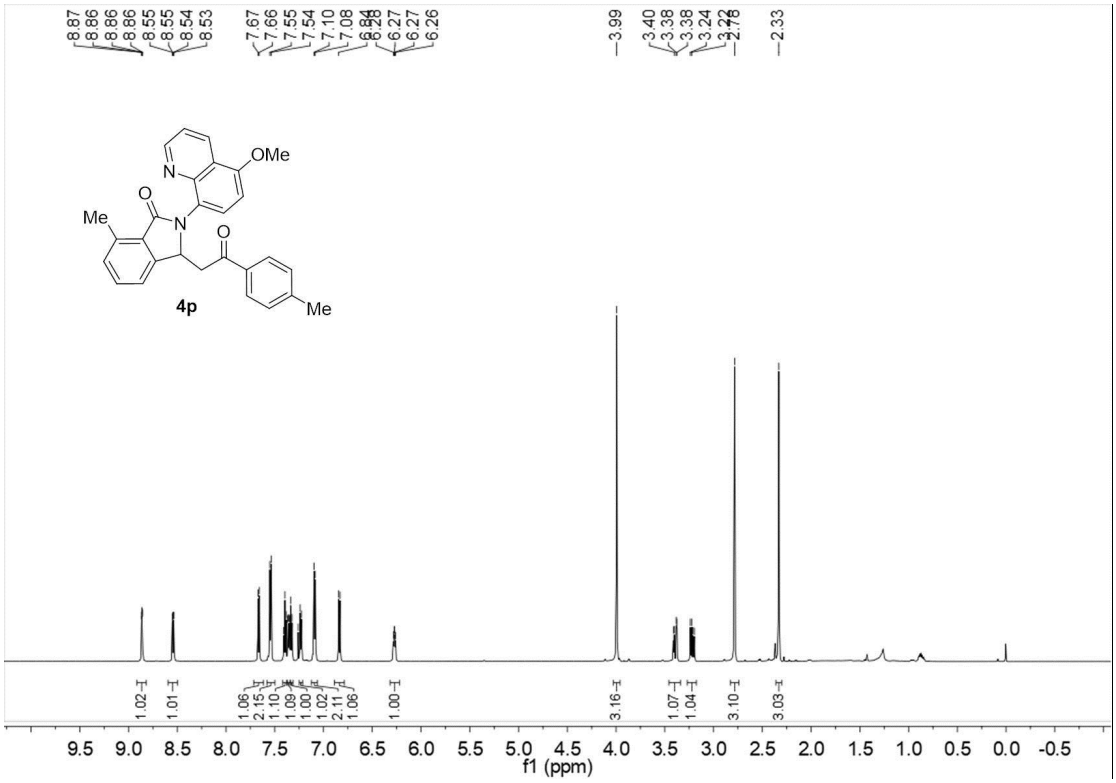
f1 (ppm)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OMe
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Me
N
O
4p
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1.06
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1.09
1.00
1.02
2.11
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1.00
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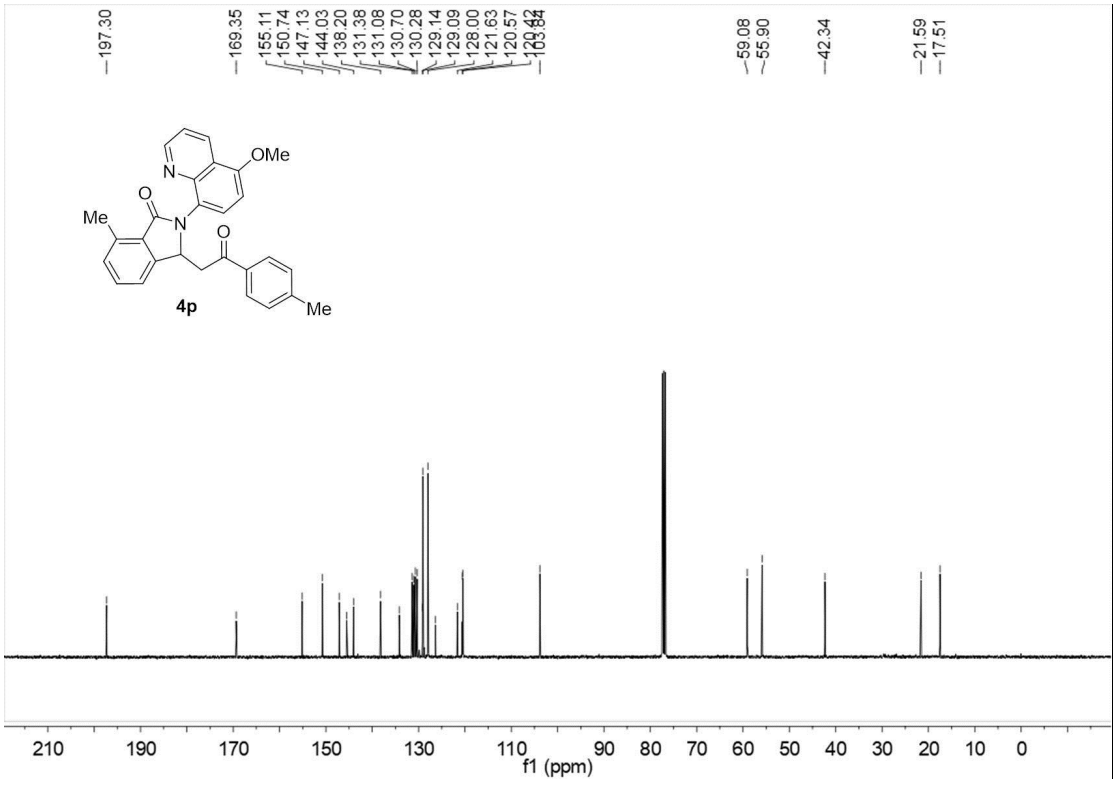
1.04
3.10
3.03
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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O
Me
N
O
4p
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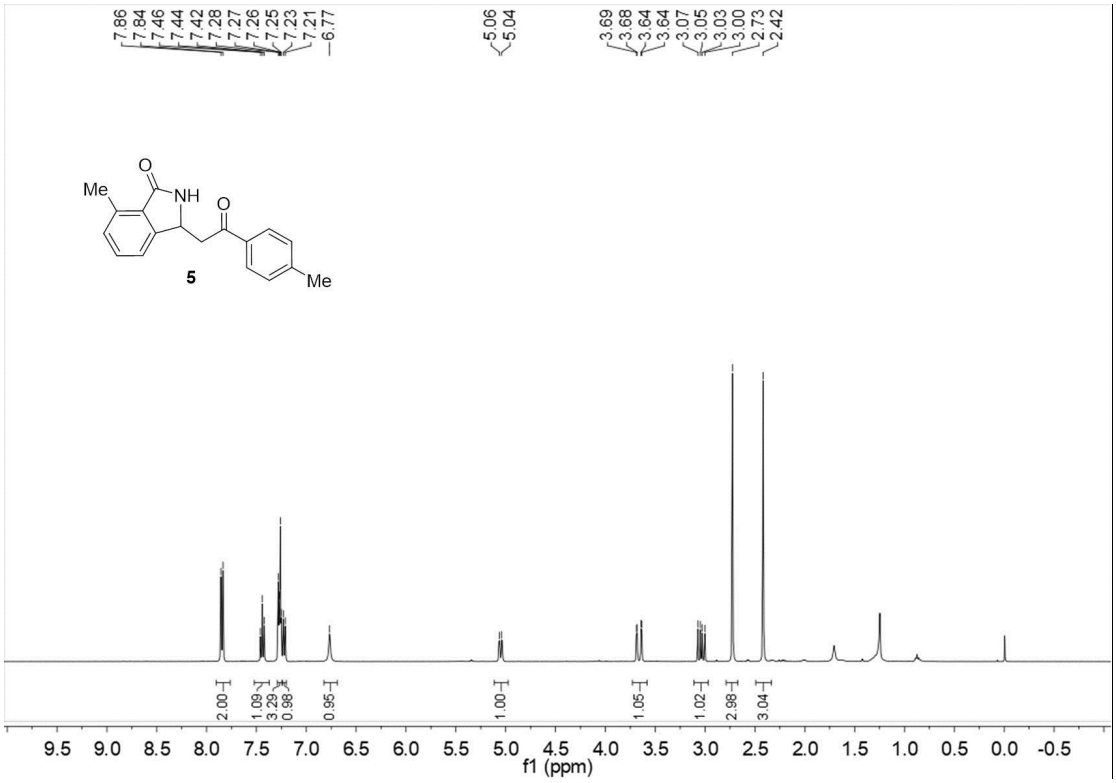
f1 (ppm)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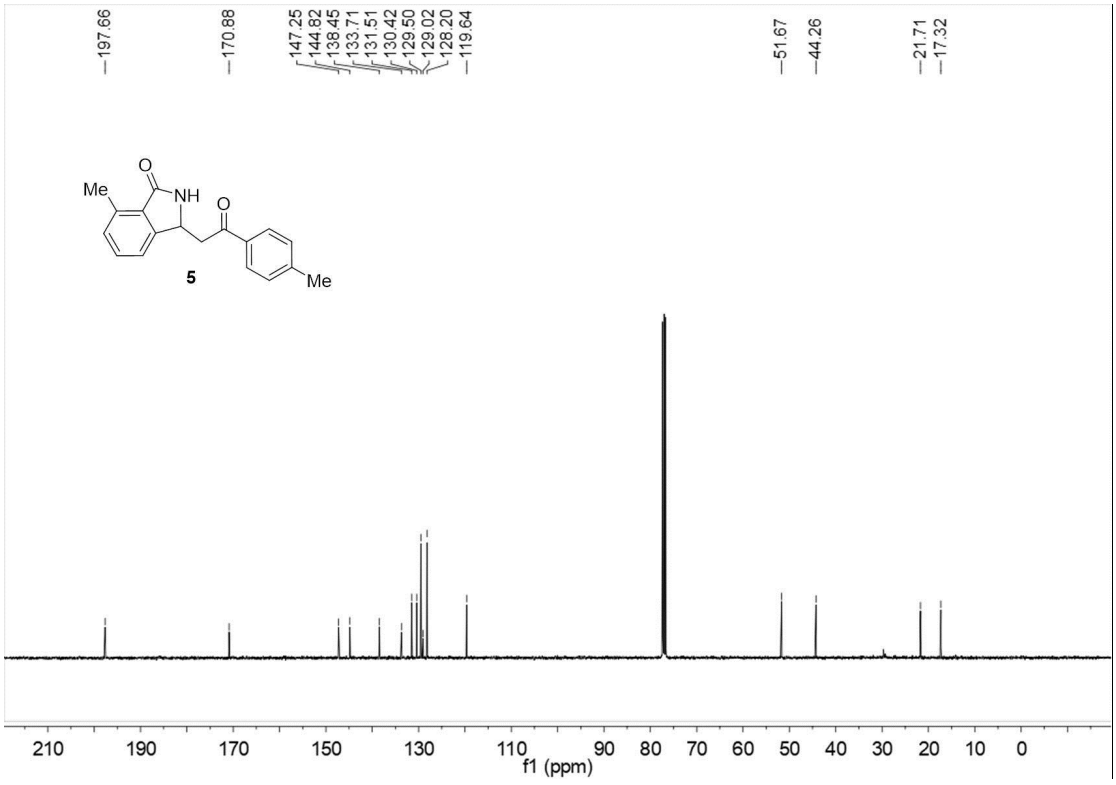
2.98
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


197.66
170.88
147.25
144.82
138.45
133.71
131.51
130.42
129.50
129.02
128.20
119.64
51.67
44.26
21.71
17.32
O
NH
O
Me
Me
5
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)