

Supporting Information

Controllable α - or β -Functionalization of α -Diazoketones with Aromatic Amides via Cobalt-Catalyzed C-H Activation: A Regio-selective Approach to Isoindolinones

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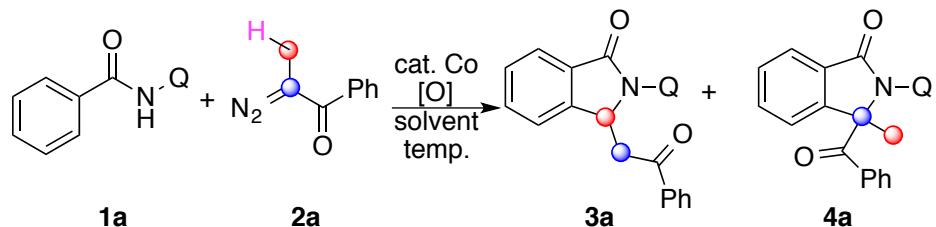
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1. General Details.

All reactions were performed in flame-dried glassware under N₂, and the workup was carried out in N₂, unless otherwise noted. 1,2-dichloroethane (DCE) was dried and distilled from calcium hydride. Column chromatographic purification of products was carried out using silica gel (200~300 mesh). The reagents were used without further purification. ¹H NMR spectra was recorded at 400 MHz, ¹³C NMR spectra was recorded at 100 MHz, and in CDCl₃ (containing 0.03% TMS) solutions. ¹H NMR spectra was recorded with tetramethylsilane (δ = 0.00 ppm) as internal reference; ¹³C NMR spectra was recorded with CDCl₃ (δ = 77.00 ppm) as internal reference. High-resolution mass spectra were performed on a mass spectrometer with a TOF (for EI or ESI) or FT-ICR (for MALDI) analyzer. Single crystal X-ray diffraction data was collected in Bruker SMARTAPEX diffractometers with molybdenum cathodes.

2. Optimization Studies.



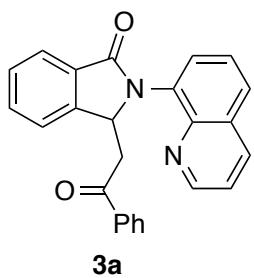
entry	cat. Co (10 mol%)	oxidant 1 (equiv)	oxidant 2 (equiv)	temp. (°C)	solvent	3a yield (%) ^[a]	4a yield (%) ^[a]
1	Co(OAc) ₂	AgOAc (3.0)	-	120	THF	-	-
2	Co(OAc) ₂	Ag ₂ CO ₃ (3.0)	-	120	DCE	35	-
3	Co(OAc) ₂	AgOTf (3.0)	-	120	DCE	27	-
4	Co(OAc) ₂	AgBF ₄ (3.0)	-	120	DCE	-	-
5	Co(OAc) ₂	AgSbF ₆ (3.0)	-	120	DCE	25	-
6	Co(OAc) ₂	AgF (3.0)	-	120	DCE	-	-
7 ^[b]	Co(OAc) ₂	AgOAc (3.0)	-	120	DCE	34	-
8 ^[c]	Co(OAc) ₂	AgOAc (3.0)	-	120	DCE	-	-
9 ^[d]	Co(OAc) ₂	AgOAc (3.0)	-	120	DCE	<10	-
10	Co(OAc) ₂	AgOAc (3.0)	K ₂ S ₂ O ₈ (1.0)	120	DCE	45	-
11 ^[e]	Co(OAc) ₂	AgOAc (3.0)	K ₂ S ₂ O ₈ (1.0)	120	DCE	45	-
12 ^[e]	-	AgOAc (3.0)	TEMPO (1.0)	120	DCE	<5	-
13 ^[e]	Co(OAc) ₂	-	TEMPO (1.0)	120	DCE	<5	-

Reaction conditions: All reactions were carried out using **1a** (0.1 mmol), **2a** (2.0 equiv), in solvent (1.0 mL) under N₂. [a] Isolated yields. [b] PPh₃ (20 mol%). [c] bipy (10 mol%). [d] NaOAc (1.0 equiv). [e] PivOH (1.0 equiv).

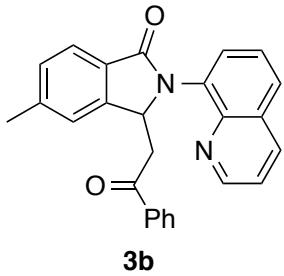
3. Preparation of Products 3 and 4.

Preparation of Products 3:

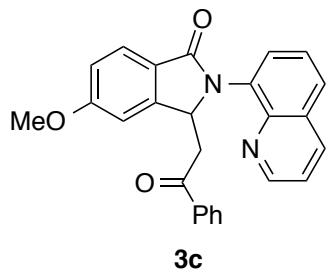
A mixture of N-(quinolin-8-yl)-benzamide (**1a**, 0.1 mmol, 24.8 mg), 2-diazo-1-phenylpropan-1-one (**2a**, 2.0 equiv, 0.2 mmol, 32 mg), Co(OAc)₂ (10 mol%, 0.01 mmol, 1.8 mg), AgOAc (0.3 mmol, 50.1 mg), TEMPO (0.1 mmol, 15.6 mg), PivOH (0.1 mmol, 10.2 mg) and DCE (1.0 ml) were added to a 25 ml sealed tube. The tube was stirred at 130 °C for 12-24h under N₂. Then, the reaction mixture was cooled to room temperature, filtrated and concentrated under reduced pressure directly. The residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate = 6/1-2/1 as the eluent afforded the isoindolinone **3a**.



3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3a): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3a** (35 mg, 93%) as a yellow solid, mp 168-170 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.88 (d, *J*=4.0 Hz, 1H), 8.17 (d, *J*=8.4 Hz, 1H), 8.01 (d, *J*=7.6 Hz, 1H), 7.86-7.79 (m, 2H), 7.65 (d, *J*=8.0 Hz, 2H), 7.61-7.51 (m, 4H), 7.47 (t, *J*=7.6 Hz, 1H), 7.42-7.38 (m, 1H), 7.35-7.29 (m, 2H), 6.61-6.50 (m, 1H), 3.46-3.35 (dd, *J*=4.8, 17.2 Hz, 1H), 3.30-3.21 (dd, *J*=8.4, 17.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 197.8, 168.6, 150.6, 146.6, 144.9, 136.5, 136.5, 133.8, 133.5, 132.2, 132.1, 130.4, 129.5, 128.6, 128.5, 128.3, 128.0, 126.4, 124.4, 123.2, 121.7, 59.5, 41.9; HRMS (ESI) calcd for C₂₅H₁₉N₂O₂ [M+H]⁺: 379.1441, found 379.1449.

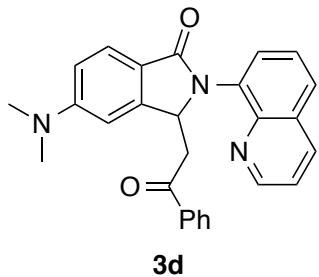


5-methyl-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3b): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3b** (32 mg, 82%) as a yellow solid, mp 156-158 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.86 (d, *J*=2.8 Hz, 1H), 8.16 (d, *J*=6.4 Hz, 1H), 7.88 (d, *J*=7.6 Hz, 1H), 7.84 (d, *J*=7.2 Hz, 1H), 7.80 (d, *J*=8.4 Hz, 1H), 7.66 (d, *J*=8.0 Hz, 2H), 7.61-7.55 (m, 1H), 7.50-7.44 (m, 1H), 7.41-7.37 (m, 1H), 7.37-7.35 (m, 1H), 7.35-7.28 (m, 3H), 6.53-6.50 (dd, *J*=4.4, 8.0 Hz, 1H), 3.42-3.36 (dd, *J*=4.8, 17.2 Hz, 1H), 3.28-3.22 (dd, *J*=8.4, 17.2 Hz, 1H), 2.45 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 198.0, 168.8, 150.7, 147.2, 145.1, 143.0, 136.7, 136.5, 134.1, 133.5, 130.5, 129.6, 129.6, 128.7, 128.3, 128.1, 126.5, 124.3, 123.8, 121.7, 59.4, 42.1, 21.8; HRMS (ESI) calcd for C₂₆H₂₀N₂NaO₂ [M+Na]⁺: 415.1417, found 415.1416.



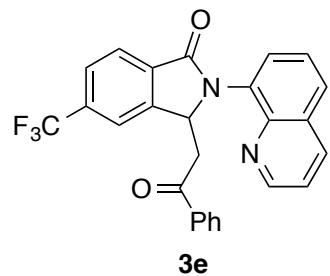
5-methoxy-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3c): Isolation by column chromatography (PE/EtOAc: 2/1) yielded **3d** (35 mg, 85%) as a yellow solid, mp 83-85 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.88 (d, *J*=2.4 Hz, 1H), 8.16 (d, *J*=6.8 Hz, 1H), 7.91 (d, *J*=8.0 Hz, 1H), 7.85 (d, *J*=7.2 Hz, 1H), 7.80 (d, *J*=8.4 Hz, 1H), 7.67 (d, *J*=7.6 Hz, 2H), 7.58 (t, *J*=8.0 Hz, 1H), 7.48 (t, *J*=7.2 Hz, 1H), 7.42-7.38 (m, 1H), 7.32 (t, *J*=7.6 Hz, 2H), 7.12-6.92 (m, 2H), 6.55-6.51 (dd, *J*=4.8, 8.8 Hz, 1H), 3.84 (s, 3H), 3.41-3.36 (dd, *J*=4.4, 16.8 Hz, 1H), 3.37-3.21 (dd, *J*=8.4, 17.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 198.0, 168.5, 163.5, 150.7, 149.1, 145.1, 136.7, 136.5, 134.1, 133.6, 130.5, 129.7, 128.7, 128.2, 128.1, 126.5, 125.9, 124.8, 121.7, 115.3, 108.0, 59.3, 55.5, 42.2; HRMS (ESI) calcd

for $C_{26}H_{20}N_2NaO_3$ $[M+Na]^+$: 431.1366, found 431.1372.



5-(dimethylamino)-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3d):

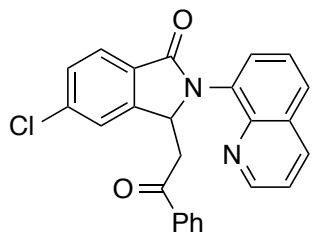
Isolation by column chromatography (PE/EtOAc: 1/1) yielded **3n** (26 mg, 61%) as a brown solid, mp 104-106 °C; 1H NMR (400 MHz, $CDCl_3$): δ 8.88 (s, 1H), 8.14 (d, $J=7.6$ Hz, 1H), 7.87-7.80 (m, 2H), 7.76 (d, $J=8.0$ Hz, 1H), 7.68-7.62 (m, 2H), 7.56 (t, $J=7.6$ Hz, 1H), 7.48-7.44 (m, 1H), 7.39-7.36 (m, 1H), 7.33 (t, $J=7.6$ Hz, 2H), 6.79 (d, $J=6.4$ Hz, 1H), 6.73 (s, 1H), 6.56-6.45(m, 1H), 3.40-3.32 (dd, $J=4.8, 16.8$ Hz, 1H), 3.27-3.21 (dd, $J=8.4, 16.8$ Hz, 1H), 3.01(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.5, 169.3, 153.7, 150.5, 149.1, 145.2, 137.0, 136.4, 134.6, 133.4, 130.5, 129.6, 128.7, 128.1, 127.9, 126.5, 125.5, 121.6, 119.7, 112.2, 105.1, 59.5, 42.7, 40.3; HRMS (ESI) calcd for $C_{27}H_{24}N_3O_2$ $[M+H]^+$: 422.1863, found 422.1870.



3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)-5-(trifluoromethyl)isoindolin-1-one (3e):

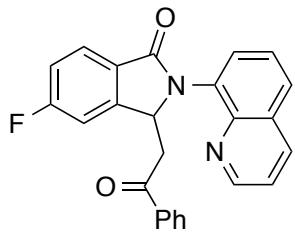
Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3e** (34 mg, 76%) as a white solid, mp 210-213 °C; 1H NMR (400 MHz, $CDCl_3$): δ 8.87 (d, $J=4.0$ Hz, 1H), 8.18 (d, $J=8.0$ Hz, 1H), 8.12 (d, $J=8.0$ Hz, 1H), 7.90 (s, 1H), 7.87-7.83 (m, 2H), 7.82-7.77 (m, 1H), 7.67 (d, $J=8.0$ Hz, 2H), 7.61 (t, $J=8.0$ Hz, 1H), 7.49 (t, $J=7.6$ Hz, 1H), 7.45-7.40 (m, 1H), 7.33 (t, $J=7.6$ Hz, 2H), 6.73-6.53 (m, 1H), 3.55-3.43 (dd, $J=4.4, 17.6$ Hz, 1H), 3.33-3.22 (dd, $J=8.4, 17.6$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.4 167.3, 150.9, 147.1, 144.8,

136.6, 136.4, 135.6, 134.2, 133.9, 133.7, 133.4, 130.4, 129.7, 128.8, 128.0, 126.5, 125.8, 125.8, 125.0, 121.9, 120.9, 120.9, 59.5, 41.5; HRMS (ESI) calcd for $C_{26}H_{17}F_3N_2NaO_2$ $[M+Na]^+$: 469.1134, found 469.1138.



3f

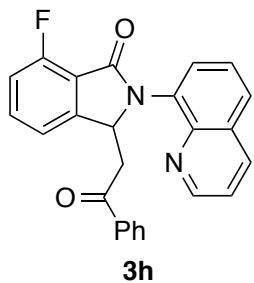
5-chloro-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3f): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3c** (33 mg, 80%) as a white solid, mp 143-145 °C; 1H NMR (400 MHz, $CDCl_3$): δ 8.87 (d, $J=4.4$ Hz, 1H), 8.18 (d, $J=8.8$ Hz, 1H), 7.93 (d, $J=8.0$ Hz, 1H), 7.84 (t, $J=7.2$ Hz, 2H), 7.68 (d, $J=7.6$ Hz, 2H), 7.63-7.57 (m, 2H), 7.49 (t, $J=8.0$ Hz, 2H), 7.44-7.39 (m, 1H), 7.34 (t, $J=7.6$ Hz, 2H), 6.57-6.54 (dd, $J=4.4$, 8.8 Hz, 1H), 3.44-3.39 (dd, $J=4.4$, 17.6 Hz, 1H), 3.28-3.22 (dd, $J=8.8$, 17.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 167.7, 150.8, 148.4, 144.9, 138.6, 136.6, 136.4, 133.7, 133.6, 130.8, 130.4, 129.7, 129.2, 128.8, 128.6, 128.1, 126.5, 125.7, 124.0, 121.9, 59.1, 41.7; HRMS (ESI) calcd for $C_{25}H_{17}ClN_2NaO_2$ $[M+Na]^+$: 435.0871, found 435.0881.



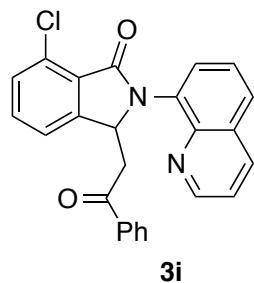
3g

3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)-5-(trifluoromethyl)isoindolin-1-one (3g): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3f** (34 mg, 86%) as a white solid, mp 134-136 °C; 1H NMR (400 MHz, $CDCl_3$): δ 8.88 (d, $J=4.4$ Hz, 1H), 8.18 (d, $J=8.4$ Hz, 1H), 8.01-7.95 (m, 1H), 7.85 (t, $J=7.2$ Hz, 2H), 7.68 (d, $J=7.6$ Hz, 2H), 7.61 (t, $J=7.6$ Hz, 1H), 7.49 (t, $J=7.6$ Hz, 1H), 7.44-7.40 (m, 1H), 7.34 (t, $J=7.6$, 2H), 7.32-7.28 (m, 1H), 7.25-7.19 (m, 1H), 6.64-6.49 (m, 1H), 3.46-3.36 (dd, $J=4.4$, 17.6 Hz, 1H), 3.29-3.20 (dd, $J=8.8$, 17.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 167.7, 167.1, 164.6, 150.8,

149.3, 149.2, 144.9, 136.6, 136.5, 133.7, 133.7, 130.4, 129.7, 128.8, 128.5, 128.3, 128.1, 126.6, 126.5, 121.9, 116.4, 116.2, 111.1, 110.9, 59.2, 59.1, 41.8; HRMS (ESI) calcd for C₂₅H₁₇FN₂NaO₂ [M+Na]⁺: 419.1166, found 419.1170.

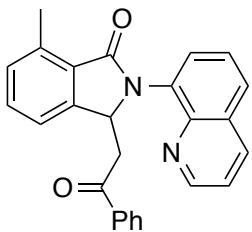


7-fluoro-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3h): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3h** (23 mg, 58%) as a yellow solid, mp 177-179 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.88 (d, J=4.4 Hz, 1H), 8.17 (d, J=8.4 Hz, 1H), 7.89-7.79 (m, 2H), 7.66 (d, J=7.6 Hz, 2H), 7.61-7.57 (m, 1H), 7.55-7.46 (m, 2H), 7.44-7.39 (m, 1H), 7.37-7.30 (m, 3H), 7.21-7.09 (m, 1H), 6.65-6.53 (m, 1H), 3.46-3.35 (dd, J=4.4, 17.2 Hz, 1H), 3.29-3.20 (dd, J=8.4, 17.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 197.6, 165.5, 161.0, 158.4, 150.8, 149.5, 144.9, 136.6, 134.2, 134.1, 133.7, 133.5, 130.6, 129.7, 128.8, 128.5, 128.1, 126.5, 121.8, 119.6, 119.3, 119.3, 115.9, 115.7, 59.2, 41.9; HRMS (ESI) calcd for C₂₅H₁₈FN₂O₂ [M+H]⁺: 397.1347, found 397.1348.



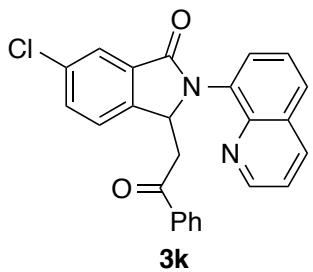
7-chloro-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3i): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3i** (30 mg, 73%) as a yellow solid, mp 243-245 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.89 (d, J=4.0 Hz, 1H), 8.17 (d, J=8.4 Hz, 1H), 7.88-7.80 (m, 2H), 7.65 (d, J=8.0 Hz, 2H), 7.61-7.55 (m, 1H), 7.51-7.44 (m, 4H), 7.43-7.39 (m, 1H), 7.35-7.28 (m, 2H), 6.63-6.46 (m, 1H), 3.45-3.32 (dd, J=4.4, 17.2 Hz, 1H), 3.30-3.16 (dd, J=8.4, 17.6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 197.7, 166.3, 150.7, 149.3, 144.9, 136.6, 136.5, 133.7, 133.5, 133.0, 132.3, 130.6, 130.3, 129.6, 128.7, 128.5,

128.2, 128.1, 126.5, 121.9, 121.8, 58.3, 42.0; HRMS (ESI) calcd for C₂₅H₁₇ClN₂NaO₂ [M+Na]⁺: 435.0871, found 435.0880.



3j

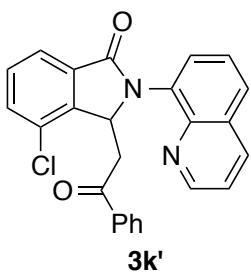
7-methyl-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3j): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3g** (31 mg, 79%) as a yellow solid, mp 176-178 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.87 (d, *J*=4.0 Hz, 1H), 8.15 (d, *J*=8.4 Hz, 1H), 7.81 (t, *J*=6.8 Hz, 2H), 7.64 (d, *J*=8.0 Hz, 2H), 7.57 (t, *J*=8.0 Hz, 1H), 7.46-7.25 (m, 7H), 6.54-6.37 (m, 1H), 3.46-3.33 (dd, *J*=4.8, 16.8 Hz, 1H), 3.31-3.16 (dd, *J*=8.0, 17.2 Hz, 1H), 2.79 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 198.0, 169.5, 150.7, 147.4, 145.2, 138.6, 136.8, 136.5, 134.2, 133.5, 131.8, 130.6, 130.6, 129.6, 129.2, 128.7, 128.3, 128.1, 126.5, 121.7, 120.6, 58.8, 42.3, 17.2; HRMS (ESI) calcd for C₂₆H₂₁N₂O₂ [M+H]⁺: 393.1598, found 393.1602.



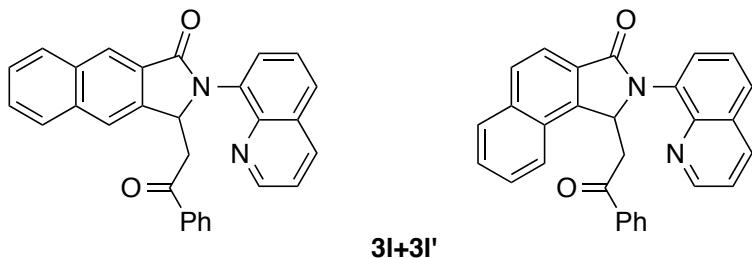
3k

6-chloro-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3k): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3j** (23 mg, 57%) as a yellow solid, mp 179-181 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.89 (d, *J*=4.0 Hz, 1H), 8.18 (d, *J*=6.8 Hz, 1H), 7.97 (s, 1H), 7.87-7.79 (m, 2H), 7.67 (d, *J*=8.0 Hz, 2H), 7.60 (t, *J*=8.0 Hz, 1H), 7.53 (s, 2H), 7.50-7.47 (m, 1H), 7.44-7.40 (m, 1H), 7.33 (t, *J*=8.0 Hz, 2H), 6.63-6.42 (m, 1H), 3.45-3.31 (dd, *J*=4.4, 17.2 Hz, 1H), 3.30-3.15 (dd, *J*=8.4, 17.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 197.7, 167.4, 150.8, 144.9, 144.8, 136.6, 136.5, 134.9, 134.1, 133.7, 133.7, 132.4, 130.4, 129.7, 128.8, 128.7, 128.1, 126.6, 124.9, 124.6, 121.9, 59.4, 41.7; HRMS (ESI)

calcd for C₂₅H₁₈ClN₂O₂ [M+H]⁺: 413.1051, found 413.1055.

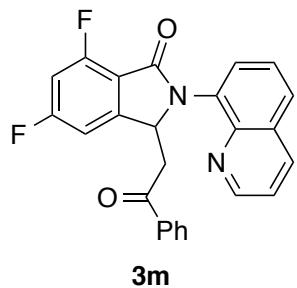


4-chloro-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3'): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3j'** (6 mg, 14%) as a yellow solid, mp 165-167 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.81 (d, *J*=4.0 Hz, 1H), 8.11 (d, *J*=8.0 Hz, 1H), 7.95 (d, *J*=7.6 Hz, 1H), 7.79-7.70 (m, 2H), 7.60-7.55 (m, 1H), 7.54-7.47 (m, 2H), 7.46-7.39 (m, 3H), 7.37-7.33 (m, 1H), 7.23 (t, *J*=7.6 Hz, 2H), 6.64-6.46 (m, 1H), 3.73-3.63 (dd, *J*=6.4, 16.8 Hz 1H), 3.61-3.53 (dd, *J*=3.2, 16.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 196.7, 167.6, 160.4, 150.6, 144.9, 143.1, 136.6, 136.5, 135.3, 133.6, 133.1, 132.7, 130.7, 130.2, 129.5, 129.0, 128.5, 127.7, 126.5, 123.2, 121.7, 59.5, 38.6; HRMS (ESI) calcd for C₂₅H₁₈ClN₂O₂ [M+H]⁺: 413.1051, found 413.1056.



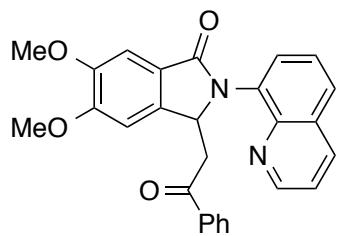
3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)-2,3-dihydro-1H-benzo[f]isoindol-1-one compound with 1-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)-1,2-dihydro-3H-benzo[e]isoindol-3-one (3l+3l'): Isolation by column chromatography (PE/EtOAc: 3/1) yielded (3l+3l') (38 mg, 89%) as a yellow solid, ¹H NMR (400 MHz, CDCl₃): 8.95-8.78 (m, 2H), 8.54 (s, 1H), 8.16 (d, *J*=8.4 Hz, 1H), 8.08-7.96 (m, 7H), 7.90 (d, *J*=7.2 Hz, 2H), 7.85-7.75 (m, 2H), 7.72-7.65 (m, 3H), 7.64-7.51 (m, 5H), 7.48-7.42 (m, 2H), 7.41-7.28 (m, 7H), 7.16 (t, *J*=7.6 Hz, 2H), 6.96-6.84 (m, 1H), 6.75-6.64 (m, 1H), 3.80-3.71 (dd, *J*=7.6, 16.8 Hz, 1H), 3.54-3.43 (m, 2H), 3.39-3.29 (dd, *J*=8.4, 17.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 198.0, 197.2, 169.0, 168.5, 150.7, 150.6, 145.1, 144.9, 144.8, 141.7, 136.7, 136.5,

136.4, 136.3, 135.9, 135.7, 134.2, 134.1, 133.5, 133.3, 133.1, 130.6, 130.5, 130.2, 129.8, 129.7, 129.5, 128.7, 128.5, 128.3, 128.0, 127.8, 127.6, 127.6, 127.5, 126.5, 126.4, 124.8, 123.7, 122.3, 121.8, 121.6, 120.7, 59.6, 59.5, 42.6, 42.5; HRMS (ESI) calcd for C₂₉H₂₁N₂O₂ [M+H]⁺: 429.1598, found 429.1609.



3m

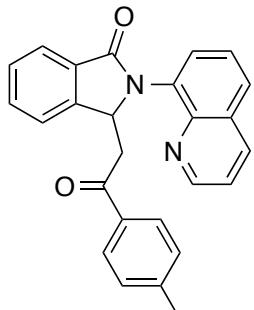
5,7-difluoro-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3m): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3l** (23 mg, 56%) as a yellow solid, mp 197-199 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.88 (d, J=4.4 Hz, 1H), 8.18 (d, J=8.4 Hz, 1H), 7.88-7.81 (m, 2H), 7.69 (d, J=8.0 Hz, 2H), 7.62-7.57 (m, 1H), 7.53-7.47 (m, 1H), 7.45-7.40 (m, 1H), 7.35 (t, J=7.6 Hz, 2H), 7.14(d, J=7.6, 1H), 6.95-6.86 (m, 1H), 6.64-6.55 (m, 1H), 3.44-3.36 (dd, J=4.0, 17.6 Hz, 1H), 3.30-3.21 (dd, J=8.8, 17.6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 197.4, 167.4, 167.3, 164.7, 164.7, 161.4, 161.3, 158.8, 158.7, 151.0, 150.8, 144.9, 136.6, 136.4, 133.9, 133.2, 130.6, 129.7, 128.8, 128.6, 128.1, 126.6, 121.9, 107.5, 107.5, 107.3, 107.3, 104.9, 104.7, 104.6, 104.4, 59.1, 41.7; HRMS (ESI) calcd for C₂₅H₁₇F₂N₂O₂ [M+H]⁺: 415.1253, found 415.1255.



3n

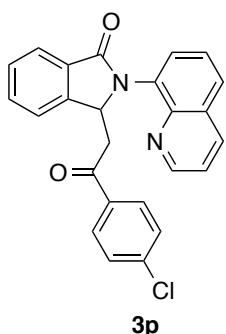
5,6-dimethoxy-3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3n): Isolation by column chromatography (PE/EtOAc: 1/1) yielded **3m** (16 mg, 37%) as a yellow solid, mp 96-98 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.95-8.83 (m, 1H), 8.17 (d, J=8.4 Hz, 1H), 7.89-7.79 (m, 2H), 7.68 (d, J=7.6 Hz, 2H), 7.63-7.57 (m, 1H), 7.51-7.44 (m, 2H), 7.43-7.39 (m, 1H), 7.37-7.30 (m, 2H), 7.05 (s, 1H), 6.54-6.41 (m, 1H), 3.98 (s,

3H), 3.89 (s, 3H), 3.41-3.30 (dd, $J=4.8$, 17.2 Hz, 1H), 3.23-3.17 (dd, $J=8.8$, 17.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 198.4, 168.9, 153.2, 150.7, 150.2, 145.1, 140.6, 136.8, 136.5, 134.2, 133.6, 130.4, 129.7, 128.8, 128.2, 128.1, 126.6, 124.4, 121.8, 105.9, 105.7, 59.3, 56.2, 56.1, 42.3; HRMS (ESI) calcd for $\text{C}_{27}\text{H}_{22}\text{N}_2\text{NaO}_4$ [$\text{M}+\text{Na}]^+$: 461.1472, found 461.1479.



3o

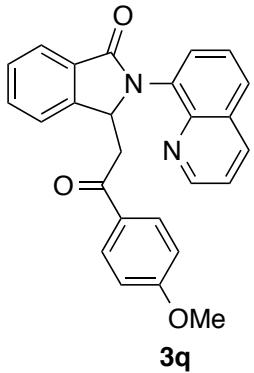
3-(2-oxo-2-(*p*-tolyl)ethyl)-2-(quinolin-8-yl)isoindolin-1-one (3o): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3o** (29 mg, 74%) as a white solid, mp 184-186 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.88 (d, $J=2.4$ Hz, 1H), 8.21-8.13 (m, 1H), 8.00 (d, $J=7.2$ Hz, 1H), 7.89-7.79 (m, 2H), 7.63-7.51 (m, 6H), 7.44-7.37 (m, 1H), 7.11 (d, $J=8.0$ Hz, 2H), 6.61-6.50 (m, 1H), 3.42-3.31 (dd, $J=4.4$, 16.8 Hz, 1H), 3.26-3.17 (dd, $J=8.8$, 17.2 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 197.5, 168.7, 150.7, 146.8, 145.0, 144.5, 136.5, 134.3, 134.0, 132.2, 130.5, 129.7, 129.4, 128.5, 128.4, 128.2, 126.5, 124.5, 123.4, 121.7, 59.7, 41.9, 21.3; HRMS (ESI) calcd for $\text{C}_{26}\text{H}_{21}\text{N}_2\text{O}_2$ [$\text{M}+\text{H}]^+$: 393.1598, found 393.1606.



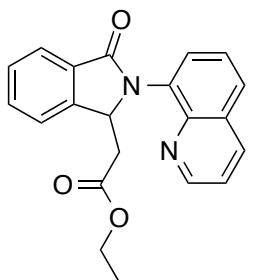
3p

3-(2-(4-chlorophenyl)-2-oxoethyl)-2-(quinolin-8-yl)isoindolin-1-one (3p): Isolation by column chromatography (PE/EtOAc: 3/1) yielded **3p** (33 mg, 80%) as a white solid, mp

177-179 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.87 (d, $J=4.0$ Hz, 1H), 8.16 (d, $J=8.4$ Hz, 1H), 8.00 (d, $J=9.6$ Hz, 1H), 7.86-7.77 (m, 2H), 7.61-7.51 (m, 6H), 7.43-7.36 (m, 1H), 7.26 (d, $J=8.4$ Hz, 2H), 6.60-6.45 (m, 1H), 3.45-3.33 (dd, $J=5.2, 17.2$ Hz, 1H), 3.26-3.16 (dd, $J=7.6, 16.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 196.7, 168.7, 150.8, 146.5, 145.0, 140.1, 136.6, 134.9, 133.9, 132.3, 132.2, 130.5, 129.6, 129.4, 129.0, 128.7, 128.5, 126.6, 124.6, 123.2, 121.8, 59.6, 42.0; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{17}\text{ClN}_2\text{NaO}_2$ [$\text{M}+\text{Na}]^+$: 435.0871, found 435.0873.

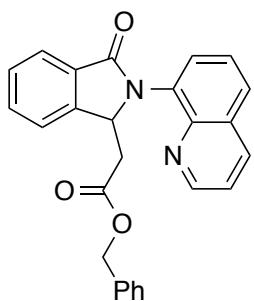


3-(2-(4-methoxyphenyl)-2-oxoethyl)-2-(quinolin-8-yl)isoindolin-1-one (3q): Isolation by column chromatography (PE/EtOAc: 2/1) yielded **3q** (32 mg, 78%) as a brown solid, mp 150-152 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.92-8.86 (m, 1H), 8.20-8.15 (m, 1H), 8.02-7.98 (m, 1H), 7.86-7.80 (m, 2H), 7.68-7.63 (m, 2H), 7.60-7.58 (m, 1H), 7.57-7.51 (m, 3H), 7.43-7.38 (m, 1H), 6.83-6.76 (m, 2H), 6.58-6.49 (m, 1H), 3.81 (s, 3H), 3.37-3.28 (dd, $J=4.4, 16.8$ Hz, 1H), 3.24-3.16 (dd, $J=8.4, 16.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 196.3, 168.8, 164.0, 150.7, 146.9, 145.0, 136.5, 134.0, 132.2, 132.2, 130.4, 129.8, 129.6, 128.5, 128.4, 126.5, 124.5, 123.4, 121.8, 113.8, 59.8, 55.3, 41.6; HRMS (ESI) calcd for $\text{C}_{26}\text{H}_{20}\text{N}_2\text{NaO}_3$ [$\text{M}+\text{Na}]^+$: 431.1366, found 431.1370.



3r

ethyl 2-(3-oxo-2-(quinolin-8-yl)isoindolin-1-yl)acetate (3r): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **3r** (22 mg, 64%) as a white solid, mp 93-95 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.95-8.83 (m, 1H), 8.25-8.16 (m, 1H), 7.99 (d, *J*=7.2 Hz, 1H), 7.91-7.83 (m, 2H), 7.67-7.60 (m, 2H), 7.59-7.52 (m, 2H), 7.47-7.41 (m, 1H), 6.39-6.27 (m, 1H), 3.86-3.76 (m, 2H), 2.81-2.70 (dd, *J*=5.6, 16.0 Hz, 1H), 2.66-2.58 (dd, *J*=6.8, 15.6 Hz, 1H), 0.98 (t, *J*=7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 170.5, 168.7, 150.6, 145.8, 145.0, 136.6, 133.7, 132.4, 132.2, 130.7, 128.6, 128.3, 126.6, 124.5, 122.8, 121.7, 60.5, 59.5, 37.9, 13.5; HRMS (ESI) calcd for C₂₁H₁₈N₂NaO₃ [M+Na]⁺: 369.1210, found 369.1212.



3s

benzyl 2-(3-oxo-2-(quinolin-8-yl)isoindolin-1-yl)acetate (3s): Isolation by column chromatography (PE/EtOAc: 2/1) yielded **3s** (30 mg, 74%) as a yellow solid, mp 53-55 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.90-8.82 (m, 1H), 8.22-8.15 (m, 1H), 8.02-7.93 (m, 1H), 7.87-7.80 (m, 2H), 7.63-7.58 (m, 1H), 7.57-7.55 (m, 1H), 7.54-7.51 (m, 1H), 7.50-7.47 (m, 1H), 7.44-7.39 (m, 1H), 7.33-7.27 (m, 3H), 7.17-7.07 (m, 2H), 6.40-6.27 (m, 1H), 4.86-4.79 (dd, *J*=12.4, 15.6 Hz, 2H), 2.85-2.76 (dd, *J*=5.6, 16.0 Hz, 1H), 2.69-2.61 (dd, *J*=7.6, 16.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 170.4, 168.7, 150.6, 145.6, 145.0, 136.6, 135.4, 133.6, 132.3, 132.3, 130.7, 129.6, 128.7, 128.6, 128.5, 128.5, 128.3, 126.6, 124.6, 122.8, 121.7, 66.4, 59.4, 37.8 ; HRMS (ESI) calcd for C₂₆H₂₀N₂NaO₃ [M+Na]⁺: 431.1374, found 431.1373.

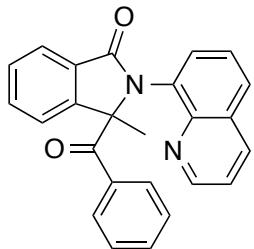
Preparation of Products 4:

A mixture of N-(quinolin-8-yl)-benzamide (**1a**, 0.1 mmol, 24.8 mg), 2-diazo-1-phenylpro-

pan-1-one (**2a**, 2.0 equiv, 0.2 mmol, 32 mg), Co(acac)₂ (10 mol%, 0.01 mmol, 2.6 mg), TBHP (0.2 mmol, 34 uL, 6M in decane) and DCE (1.0 ml) were added to a 25 ml sealed tube. The tube was stirred at 30 °C for 5 h under N₂. Then, the reaction mixture was cooled to room temperature, filtrated and concentrated under reduced pressure directly. The residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate = 6/1-2/1 as the eluent afforded the isoindolinones **4a**.

The 1.0 mmol scale reaction for the preparation of **4b**:

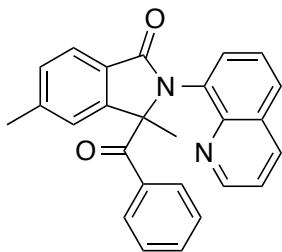
A mixture of 4-methyl-N-(quinolin-8-yl)benzamide (**1b**, 1.0 mmol, 262.1 mg), 2-diazo-1-phenylpropan-1-one (**2a**, 2.0 equiv, 2.0 mmol, 320 mg), Co(acac)₂ (10 mol%, 0.1 mmol, 26 mg), TBHP (2.0 mmol, 340 uL, 6M in decane) and DCE (10.0 ml) were added to a 50 ml sealed tube. The tube was stirred at 30 °C for 5 h under N₂. Then, the reaction mixture was cooled to room temperature, filtrated and concentrated under reduced pressure directly. The residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate = 6/1-2/1 as the eluent afforded the isoindolinones **4b** (281 mg, 72%).



4a

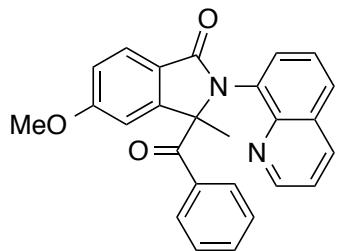
3-benzoyl-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4a): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4a** (34 mg, 91%) as a yellow solid, mp 105-107 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.64 (d, *J*=4.0 Hz, 1H), 8.16 (d, *J*=8.4 Hz, 1H), 8.02 (d, *J*=7.6 Hz, 1H), 7.79 (m, *J*=8.0 Hz, 1H), 7.70 (d, *J*=7.6 Hz, 1H), 7.63-7.57 (m, 3H), 7.54-7.50 (m, 2H), 7.44 (d, *J*=7.2 Hz, 1H), 7.38-7.35 (m, 1H), 7.33-7.29 (m, 1H), 7.22-7.16 (m, 2H), 1.67 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 196.2, 170.2, 148.6, 147.3, 143.1, 137.1, 136.5, 134.2, 133.2, 131.8, 131.5, 129.3, 129.3, 129.1, 128.4, 128.2, 127.7, 126.7, 125.1,

122.5, 121.8, 76.2, 21.8; HRMS (ESI) calcd for C₂₅H₁₉N₂O₂ [M+H]⁺: 379.1441, found 379.1445.



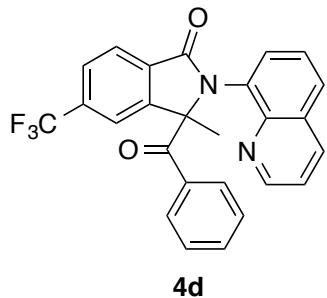
4b

3-benzoyl-3,5-dimethyl-2-(quinolin-8-yl)isoindolin-1-one (4b): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4b** (37 mg, 95%) as a brown solid, mp 205-207 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.63 (d, J=4.4 Hz, 1H), 8.16 (d, J=6.8 Hz, 1H), 7.91 (d, J=7.6 Hz, 1H), 7.78 (d, J=8.4 Hz, 1H), 7.68 (d, J=7.6 Hz, 1H), 7.62 (d, J=8.0 Hz, 2H), 7.51 (t, J=8.0 Hz, 1H), 7.40-7.31 (m, 3H), 7.27-7.19 (m, 3H), 2.43 (s, 3H), 1.64 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 196.5, 170.3, 148.5, 147.7, 144.2, 143.3, 137.3, 136.5, 134.5, 131.8, 130.5, 129.3, 129.2, 129.0, 128.4, 128.2, 127.5, 126.7, 124.9, 122.9, 121.8, 76.1, 22.0, 21.7; HRMS (ESI) calcd for C₂₆H₂₁N₂O₂ [M+H]⁺: 393.1598, found 393.1604.



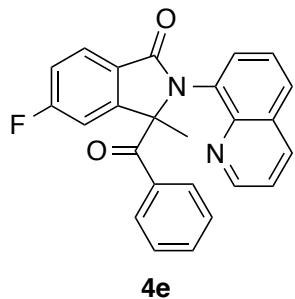
4c

3-benzoyl-5-methoxy-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4c): Isolation by column chromatography (PE/EtOAc: 2/1) yielded **4c** (36 mg, 90%) as a brown solid, mp 221-223 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.61 (s, 1H), 8.15 (d, J=8.4 Hz, 1H), 7.92 (d, J=8.4 Hz, 1H), 7.80-7.71 (m, 2H), 7.65 (d, J=8.0 Hz, 2H), 7.55-7.49 (m, 1H), 7.39-7.31 (m, 2H), 7.24-7.17 (m, 2H), 7.03 (d, J=6.4 Hz, 1H), 6.89 (s, 1H), 3.84 (s, 3H), 1.65 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 196.3, 170.0, 164.2, 149.8, 148.3, 143.1, 137.3, 136.5, 134.5, 131.8, 129.3, 129.2, 128.4, 128.1, 127.3, 126.7, 126.6, 124.1, 121.8, 116.4, 106.6, 76.0, 55.7, 22.1; HRMS (ESI) calcd for C₂₆H₂₁N₂O₃ [M+H]⁺: 409.1547, found 409.1549.

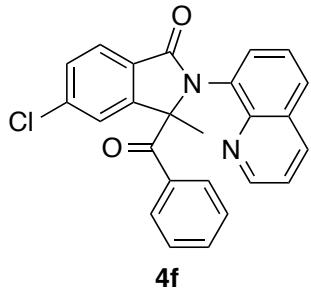


3-benzoyl-3-methyl-2-(quinolin-8-yl)-5-(trifluoromethyl)isoindolin-1-one (4d):

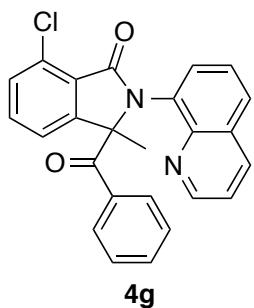
Isolation by column chromatography (PE/EtOAc: 2/1) yielded **4h** (32 mg, 73%) as a brown solid, mp 135-137 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.64 (d, *J*=3.2 Hz, 1H), 8.19 (d, *J*=8.0 Hz, 1H), 8.11 (d, *J*=8.0 Hz, 1H), 7.86-7.78 (m, 2H), 7.75-7.70 (m, 2H), 7.60-7.54 (m, 3H), 7.42-7.38 (m, 1H), 7.37-7.32 (m, 1H), 7.23-7.17 (m, 2H), 1.70 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 195.2, 168.7, 148.6, 147.8, 142.8, 136.9, 136.7, 135.2, 134.8, 134.7, 133.7, 132.1, 129.3, 129.2, 128.6, 128.2, 128.0, 126.8, 126.6, 126.6, 125.7, 125.0, 122.3, 122.1, 119.8, 119.8, 76.4, 21.7; HRMS (ESI) calcd for C₂₆H₁₈F₃N₂O₂ [M+H]⁺: 447.1315, found 447.1321.



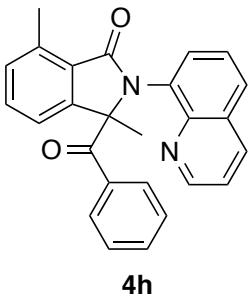
3-benzoyl-5-fluoro-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4e): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4g** (33 mg, 83%) as a yellow solid, mp 148-150 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.62 (d, *J*=3.6 Hz, 1H), 8.17 (d, *J*=8.4 Hz, 1H), 8.02-7.96 (m, 1H), 7.80 (d, *J*=8.4 Hz, 1H), 7.75 (d, *J*=7.6 Hz, 1H), 7.62 (d, *J*=8.0 Hz, 2H), 7.57-7.52 (m, 1H), 7.40-7.36 (m, 1H), 7.36-7.31 (m, 1H), 7.25-7.18 (m, 3H), 7.12 (d, *J*=7.6 Hz, 1H), 1.66 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 195.4, 169.1, 167.5, 164.9, 150.0, 149.9, 148.4, 142.9, 137.0, 136.6, 134.0, 132.0, 129.3, 129.2, 128.5, 128.1, 127.6, 127.3, 127.2, 126.8, 121.9, 117.3, 117.1, 110.0, 109.8, 75.9, 21.8; HRMS (ESI) calcd for C₂₅H₁₈FN₂O₂ [M+H]⁺: 397.1347, found 397.1353.



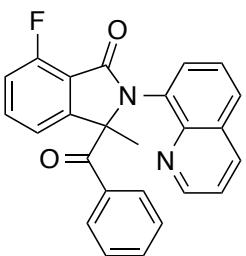
3-benzoyl-5-chloro-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4f): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4d** (38 mg, 93%) as a brown solid, mp 192-194 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.62 (d, *J*=4.4 Hz, 1H), 8.17 (d, *J*=8.4 Hz, 1H), 7.93 (d, *J*=8.0 Hz, 1H), 7.80 (d, *J*=8.0 Hz, 1H), 7.72 (d, *J*=7.6 Hz, 1H), 7.62 (d, *J*=7.6 Hz, 2H), 7.56-7.48 (m, 2H), 7.44 (s, 1H), 7.40-7.33 (m, 2H), 7.25-7.18 (m, 2H), 1.65 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 195.3, 169.1, 149.0, 148.5, 142.9, 139.6, 136.9, 136.6, 133.9, 132.0, 130.0, 129.3, 129.2, 128.5, 128.1, 127.7, 126.7, 126.3, 122.9, 121.9, 76.0, 21.8; HRMS (ESI) calcd for C₂₅H₁₈ClN₂O₂ [M+H]⁺: 413.1051, found 413.1052.



3-benzoyl-7-chloro-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4g): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4f** (30 mg, 73%) as a yellow solid, mp 193-195 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.60 (d, *J*=4.4 Hz, 1H), 8.17 (d, *J*=8.4 Hz, 1H), 7.80 (d, *J*=8.4 Hz, 2H), 7.63 (d, *J*=8.0 Hz, 2H), 7.56-7.52 (m, 1H), 7.48-7.43 (m, 2H), 7.39-7.32 (m, 3H), 7.25-7.19 (m, 2H), 1.66 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 195.3, 167.6, 149.8, 148.3, 142.9, 137.0, 136.5, 133.9, 133.7, 132.7, 131.9, 131.0, 129.2, 129.2, 128.5, 128.2, 127.6, 127.4, 126.7, 121.9, 121.1, 75.0, 22.1; HRMS (ESI) calcd for C₂₅H₁₈ClN₂O₂ [M+H]⁺: 413.1051, found 413.1061.

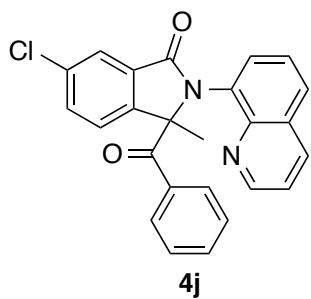


3-benzoyl-3,7-dimethyl-2-(quinolin-8-yl)isoindolin-1-one (4h): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4e** (36mg, 96%) as a brown solid, mp 146-148 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.64 (d, *J*=4.0 Hz, 1H), 8.19-8.14 (m, 1H), 7.78 (d, *J*=8.4 Hz, 1H), 7.66 (d, *J*=7.6 Hz, 1H), 7.60 (d, *J*=7.6 Hz, 2H), 7.52-7.48 (m, 1H), 7.45-7.41 (m, 1H), 7.38-7.31 (m, 2H), 7.27-7.20 (m, 4H), 2.81 (s, 3H), 1.65 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 196.7, 170.8, 148.7, 148.0, 143.5, 139.3, 137.4, 136.5, 134.5, 132.6, 131.7, 131.4, 129.3, 129.2, 128.6, 128.5, 128.4, 127.6, 126.6, 121.8, 120.0, 75.3, 22.2, 17.2; HRMS (ESI) calcd for C₂₆H₂₁N₂O₂ [M+H]⁺: 393.1598, found 393.1599.

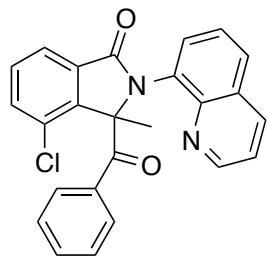


4i

3-benzoyl-7-fluoro-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4i): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4i** (22 mg, 55%) as a white solid, mp 141-143 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.61 (s, 1H), 8.17 (d, *J*=7.6 Hz, 1H), 7.80 (d, *J*=8.4 Hz, 1H), 7.75 (d, *J*=7.6 Hz, 1H), 7.65 (d, *J*=7.6 Hz, 2H), 7.56-7.50 (m, 2H), 7.41-7.33 (m, 2H), 7.26-7.21 (m, 3H), 7.14 (t, *J*=8.8 Hz, 1H), 1.66 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 195.5, 166.9, 161.0, 158.4, 150.0, 148.4, 143.0, 137.0, 136.6, 135.1, 135.1, 133.8, 132.0, 129.3, 129.2, 128.5, 128.3, 127.7, 126.8, 121.9, 118.9, 118.8, 118.6, 118.5, 116.7, 116.5, 75.9, 22.1; HRMS (ESI) calcd for C₂₅H₁₈FN₂O₂ [M+H]⁺: 397.1347, found 397.1345.

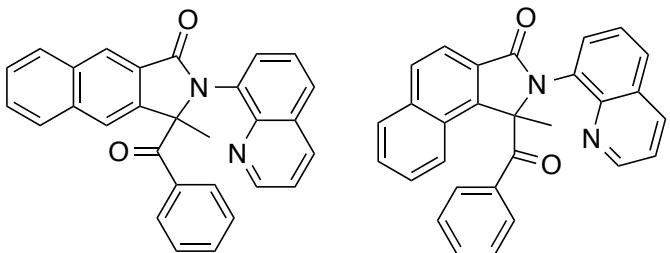


3-benzoyl-6-chloro-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4j): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4j** (23 mg, 55%) as a yellow solid, mp 89-91 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.62 (s, 1H), 8.18 (d, *J*=8.4 Hz, 1H), 7.93 (s, 1H), 7.81 (d, *J*=8.0 Hz, 1H), 7.71 (d, *J*=7.6 Hz, 1H), 7.60 (d, *J*=7.6 Hz, 2H), 7.56-7.51 (m, 2H), 7.41-7.33 (m, 3H), 7.25-7.18 (m, 2H), 1.65 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 195.6, 168.8, 148.6, 145.6, 142.9, 137.0, 136.6, 135.7, 133.9, 133.4, 133.3, 132.0, 129.3, 129.2, 128.5, 128.1, 127.8, 126.7, 125.2, 123.8, 122.0, 76.0, 21.8; HRMS (ESI) calcd for C₂₅H₁₈ClN₂O₂ [M+H]⁺: 413.1051, found 413.1051.



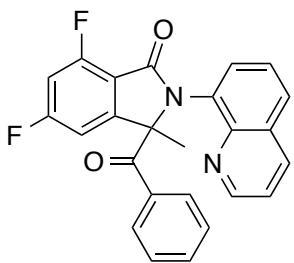
4j'

3-benzoyl-4-chloro-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4j'): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4j'** (8 mg, 20%) as a yellow solid, mp 224-226 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.74 (s, 1H), 8.18 (d, *J*=8.4 Hz, 1H), 8.02 (d, *J*=7.2 Hz, 1H), 7.87 (d, *J*=8.0 Hz, 1H), 7.67 (d, *J*=8.0 Hz, 2H), 7.54-7.47 (m, 3H), 7.43-7.38 (m, 3H), 7.29-7.25 (m, 2H), 1.76 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 195.2, 168.7, 150.4, 145.2, 145.0, 136.9, 136.4, 1341, 133.8, 133.5, 132.7, 130.9, 130.1, 129.7, 129.5, 129.4, 128.9, 128.6, 126.4, 123.9, 122.0, 74.6, 18.9; HRMS (ESI) calcd for C₂₅H₁₈ClN₂O₂ [M+H]⁺: 413.1051, found 413.1063.



4k+4k'

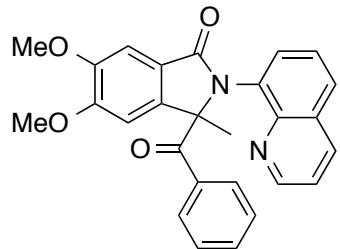
1-benzoyl-1-methyl-2-(quinolin-8-yl)-1,2-dihydro-3*H*-benzo[*e*]isoindol-3-one compound with 3-benzoyl-3-methyl-2-(quinolin-8-yl)-2,3-dihydro-1*H*-benzo[*f*]isoindol-1-one (4k:4k'): Isolation by column chromatography (PE/EtOAc: 5/1) yielded **4k+4k'** (38 mg, 88%) as a yellow solid; ¹H NMR (400 MHz, CDCl₃): δ 8.74-8.69 (m, 0.5H), 8.68-8.65 (m, 1H), 8.59 (s, 1H), 8.20-8.14 (m, 1.67H), 8.13-8.08 (m, 0.69H), 8.08-8.03 (m, 1.35H), 8.02-7.95 (m, 1.32H), 7.92-7.86 (m, 2.29H), 7.85-7.78 (m, 1.82H), 7.69-7.61 (m, 4.45H), 7.61-7.56 (m, 2.92H), 7.55-7.48 (m, 2.56H), 7.41-7.34 (m, 1.86H), 7.33-7.24 (m, 2.11H), 7.21-7.12 (m, 3.28H), 1.87 (s, 1.44H), 1.76 (s, 3.59H); ¹³C NMR (100 MHz, CDCl₃): δ 197.6, 196.7, 170.5, 170.0, 149.6, 148.8, 145.5, 144.4, 143.5, 142.2, 137.1, 137.0, 136.5, 136.4, 136.3, 136.0, 134.4, 134.3, 133.6, 132.5, 131.9, 130.8, 129.9, 129.8, 129.7, 129.5, 129.4, 129.3, 129.1, 129.0, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.0, 127.9, 127.9, 127.5, 127.1, 126.7, 126.5, 125.9, 123.8, 121.9, 121.9, 121.8, 120.9, 76.2, 76.1, 22.6, 21.9; HRMS (ESI) calcd for C₂₉H₂₁N₂O₂ [M+H]⁺: 429.1598, found 429.1595.



4l

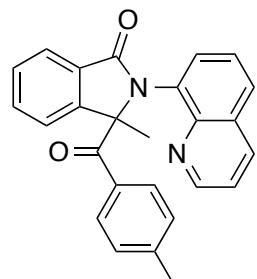
3-benzoyl-5,7-difluoro-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4l): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4l** (39 mg, 95%) as a brown solid, mp 173-175 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.60 (d, *J*=2.8 Hz, 1H), 8.18 (d, *J*=6.8 Hz, 1H), 7.85-7.78 (m, 2H), 7.67 (d, *J*=8.0 Hz, 2H), 7.55 (t, *J*=8.0 Hz, 1H), 7.43-7.35 (m, 2H), 7.28-

7.23 (m, 2H), 6.95 (d, $J=7.6$ Hz, 1H), 6.92-6.86 (m, 1H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 194.5, 167.8, 167.7, 166.0, 165.2, 165.1, 161.5, 161.4, 158.9, 158.7, 151.7, 151.6, 148.3, 142.7, 136.8, 136.6, 133.5, 132.1, 129.3, 129.2, 128.6, 128.1, 127.7, 126.8, 122.0, 115.4, 115.2, 106.5, 106.3, 106.2, 105.7, 105.5, 105.2, 76.0, 22.1; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{16}\text{F}_2\text{N}_2\text{O}_2$ [$\text{M}+\text{H}]^+$: 415.1253, found 415.1255.



4m

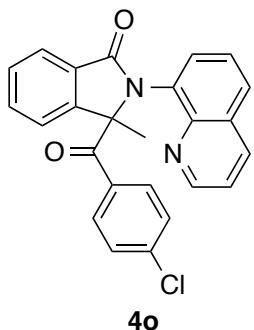
3-benzoyl-5,6-dimethoxy-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4m): Isolation by column chromatography (PE/EtOAc: 1/1) yielded **4m** (40 mg, 91%) as a yellow solid, mp 186-188 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.63 (d, $J=2.8$ Hz, 1H), 8.16 (d, $J=6.8$ Hz, 1H), 7.80-7.72 (m, 2H), 7.63 (d, $J=8.0$ Hz, 2H), 7.57-7.51 (m, 1H), 7.46 (s, 1H), 7.39-7.31 (m, 2H), 7.21 (t, $J=7.6$ Hz, 2H), 6.86 (s, 1H), 3.97 (s, 3H), 3.92 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 196.7, 170.4, 154.2, 150.8, 148.3, 143.0, 141.0, 137.4, 136.5, 134.5, 131.7, 129.3, 129.1, 128.4, 127.9, 127.2, 126.7, 123.9, 121.8, 106.2, 104.0, 75.8, 56.3, 56.1, 21.9; HRMS (ESI) calcd for $\text{C}_{27}\text{H}_{23}\text{N}_2\text{O}_4$ [$\text{M}+\text{H}]^+$: 439.1652, found 439.1658.



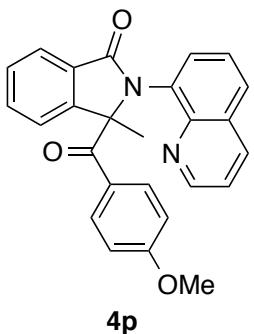
4n

3-methyl-3-(4-methylbenzoyl)-2-(quinolin-8-yl)isoindolin-1-one (4n): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4n** (35 mg, 90%) as a yellow solid, mp 178-180 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.67 (s, 1H), 8.15 (d, $J=8.4$ Hz, 1H), 8.04 (d, $J=7.6$ Hz, 1H), 7.79 (d, $J=8.0$ Hz, 1H), 7.61-7.49 (m, 6H), 7.42 (d, $J=7.6$ Hz, 1H), 7.39-

7.35 (m, 1H), 7.01 (d, $J=8.0$ Hz, 2H), 2.26 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 196.2, 170.1, 149.0, 147.7, 143.6, 142.7, 136.4, 134.4, 134.3, 133.2, 131.6, 129.4, 129.3, 129.2, 128.4, 127.9, 126.6, 125.2, 122.4, 121.8, 76.2, 22.0, 21.1; HRMS (ESI) calcd for $\text{C}_{26}\text{H}_{21}\text{N}_2\text{O}_2$ [$\text{M}+\text{H}]^+$: 393.1598, found 393.1594.

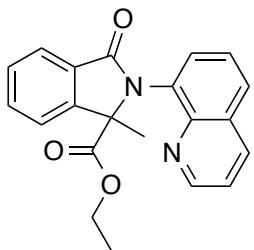


3-(4-chlorobenzoyl)-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4o): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4o** (29 mg, 71%) as a yellow solid, mp 186-188 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.56 (s, 1H), 8.19 (d, $J=7.2$ Hz, 1H), 7.98 (d, $J=7.8$ Hz, 1H), 7.93 (d, $J=7.8$ Hz, 1H), 7.81 (d, $J=8.4$ Hz, 1H), 7.64-7.53 (m, 5H), 7.43 (d, $J=7.8$ Hz, 1H), 7.41-7.37 (m, 1H), 7.12 (d, $J=8.4$ Hz, 2H), 1.66 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 194.4, 170.1, 147.8, 147.0, 142.4, 137.7, 136.7, 135.7, 133.9, 133.4, 131.4, 130.7, 129.5, 129.2, 128.5, 127.9, 127.2, 126.9, 125.1, 122.6, 122.0, 76.1, 21.8; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{18}\text{ClN}_2\text{O}_2$ [$\text{M}+\text{H}]^+$: 413.1051, found 413.1050.



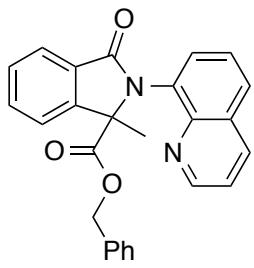
3-(4-methoxybenzoyl)-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4p): Isolation by column chromatography (PE/EtOAc: 2/1) yielded **4p** (35 mg, 85%) as a yellow solid, mp 180-182 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.75-8.68 (m, 1H), 8.19-8.14 (m, 1H), 8.10-8.05 (m, 1H), 7.82-7.78 (m, 1H), 7.66 (d, $J=8.8$ Hz, 2H), 7.60-7.54 (m, 2H), 7.52-7.45 (m, 2H), 7.44-7.41 (m, 1H), 7.39-7.36 (m, 1H), 6.76-6.71 (m, 2H), 3.75 (s, 3H), 1.66 (s, 3H);

¹³C NMR (100 MHz, CDCl₃): δ 195.2, 170.1, 162.8, 149.4, 148.1, 144.0, 136.4, 134.5, 133.2, 131.6, 131.4, 129.4, 129.4, 129.3, 128.6, 128.2, 126.5, 125.2, 122.4, 121.8, 113.7, 76.1, 55.1, 22.1; HRMS (ESI) calcd for C₂₆H₂₁N₂O₃ [M+H]⁺: 409.1547, found 409.1548.



4q

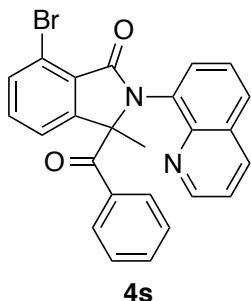
ethyl 1-methyl-3-oxo-2-(quinolin-8-yl)isoindoline-1-carboxylate (4q): Isolation by column chromatography (PE/EtOAc: 5/1) yielded **4q** (21 mg, 61%) as a yellow solid, mp 57-59 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.82 (d, J=2.8 Hz, 1H), 8.19 (d, J=6.8 Hz, 1H), 8.00 (d, J=7.2 Hz, 1H), 7.96 (d, J=7.6 Hz, 1H), 7.87 (d, J=8.0 Hz, 1H), 7.67-7.55 (m, 4H), 7.43-7.36 (m, 1H), 4.24-4.14 (m, 2H), 1.68 (s, 3H), 1.18 (t, J=7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 171.8, 169.6, 150.4, 147.1, 145.4, 136.4, 134.7, 132.5, 131.6, 130.2, 129.6, 129.2, 128.8, 126.5, 124.8, 121.7, 71.3, 61.9, 20.4, 13.6; HRMS (ESI) calcd for C₂₁H₁₉N₂O₃ [M+H]⁺: 347.1390, found 347.1384.



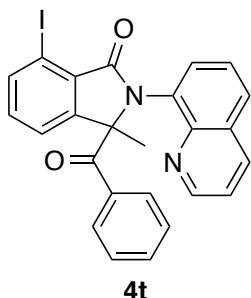
4r

benzyl 1-methyl-3-oxo-2-(quinolin-8-yl)isoindoline-1-carboxylate (4r): Isolation by column chromatography (PE/EtOAc: 2/1) yielded **4r** (17 mg, 41%) as a brown solid, mp 66-68 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.79-8.73 (m, 1H), 8.16 (d, J=6.4 Hz, 1H), 8.01 (d, J=6.4 Hz, 1H), 7.82 (d, J=8.0 Hz, 1H), 7.76 (d, J=7.6 Hz, 1H), 7.61-7.56 (m, 2H), 7.51-7.45 (m, 2H), 7.38-7.35 (m, 1H), 7.30-7.26 (m, 3H), 7.18-7.13 (m, 2H), 5.21 (d, J=12.4 Hz, 1H), 5.18 (d, J=12.4 Hz, 1H), 1.68 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 171.5, 169.5, 150.2, 146.9, 145.1, 136.4, 135.4, 134.4, 132.5, 131.6, 130.0, 129.5, 129.3, 128.7, 128.6,

128.5, 128.3, 126.5, 124.8, 121.7, 121.7, 71.2, 67.4, 20.2; HRMS (ESI) calcd for C₂₆H₂₁N₂O₃ [M+H]⁺: 409.1547, found 409.1545.



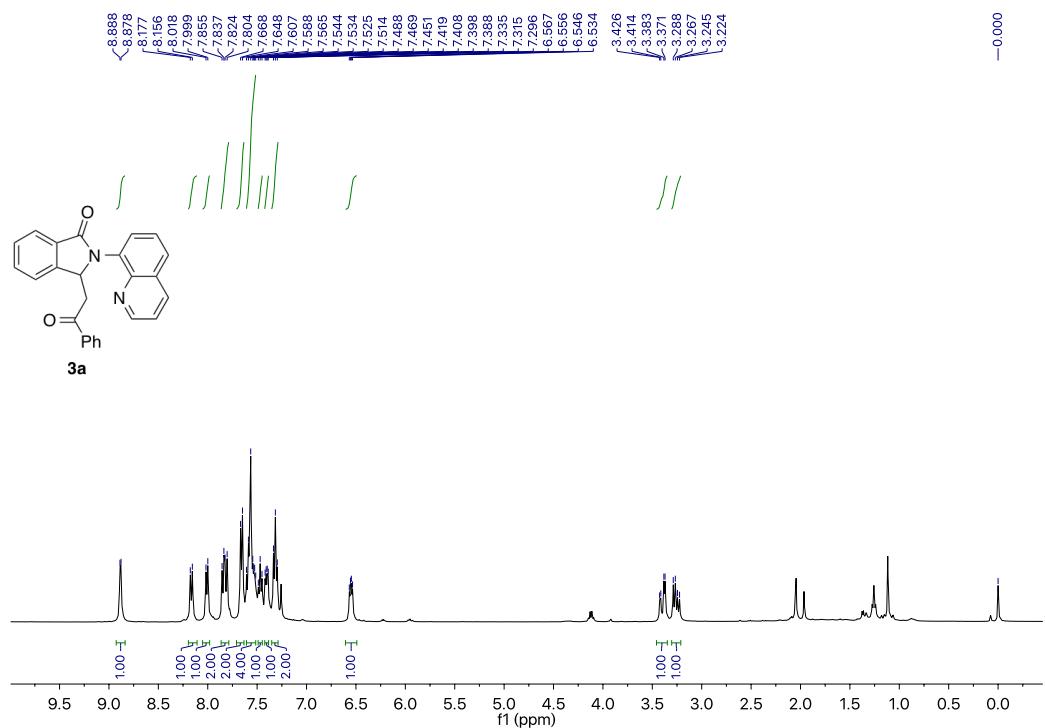
3-benzoyl-7-bromo-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4s): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4s** (34 mg, 74%) as a colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 8.60 (d, *J*=4.4 Hz, 1H), 8.18 (d, *J*=8.0 Hz, 1H), 7.80 (d, *J*=8.0 Hz, 2H), 7.66-7.61 (m, 3H), 7.54 (t, *J*=8.0 Hz, 1H), 7.41-7.33 (m, 4H), 7.22 (t, *J*=7.6 Hz, 2H), 1.66 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 195.3, 167.9, 150.0, 148.3, 142.8, 137.0, 136.6, 134.4, 133.9, 131.9, 129.2, 128.9, 128.5, 128.3, 127.6, 126.7, 121.9, 121.7, 120.2, 74.8, 22.1; HRMS (ESI) calcd for C₂₅H₁₈BrN₂O₂ [M+H]⁺: 457.0546, found 457.0544.



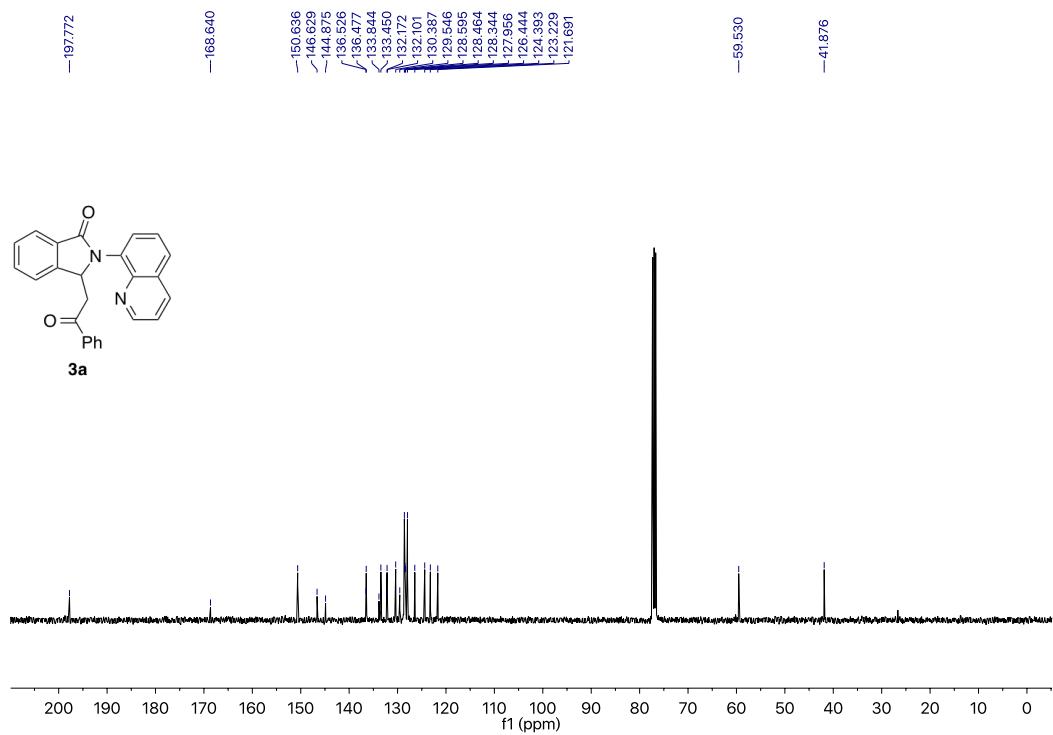
3-benzoyl-7-iodo-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4t): Isolation by column chromatography (PE/EtOAc: 4/1) yielded **4t** (40 mg, 79%) as a colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 8.61 (d, *J*=8.0 Hz, 1H), 8.21-8.15 (m, 1H), 7.96 (d, *J*=7.6 Hz, 1H), 7.80 (d, *J*=8.0 Hz, 2H), 7.59 (d, *J*=8.0 Hz, 2H), 7.52 (t, *J*=8.0 Hz, 1H), 7.43-7.32 (m, 3H), 7.26-7.19 (m, 3H), 1.66 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 195.2, 168.3, 149.8, 148.3, 142.8, 141.0, 137.0, 136.5, 133.9, 133.9, 131.9, 131.2, 129.2, 128.5, 128.3, 127.6, 126.7, 122.5, 121.9, 91.1, 74.4, 22.0; HRMS (ESI) calcd for C₂₅H₁₈IN₂O₂ [M+H]⁺: 505.0408, found 505.0407.

4. NMR spectra of all new compounds.

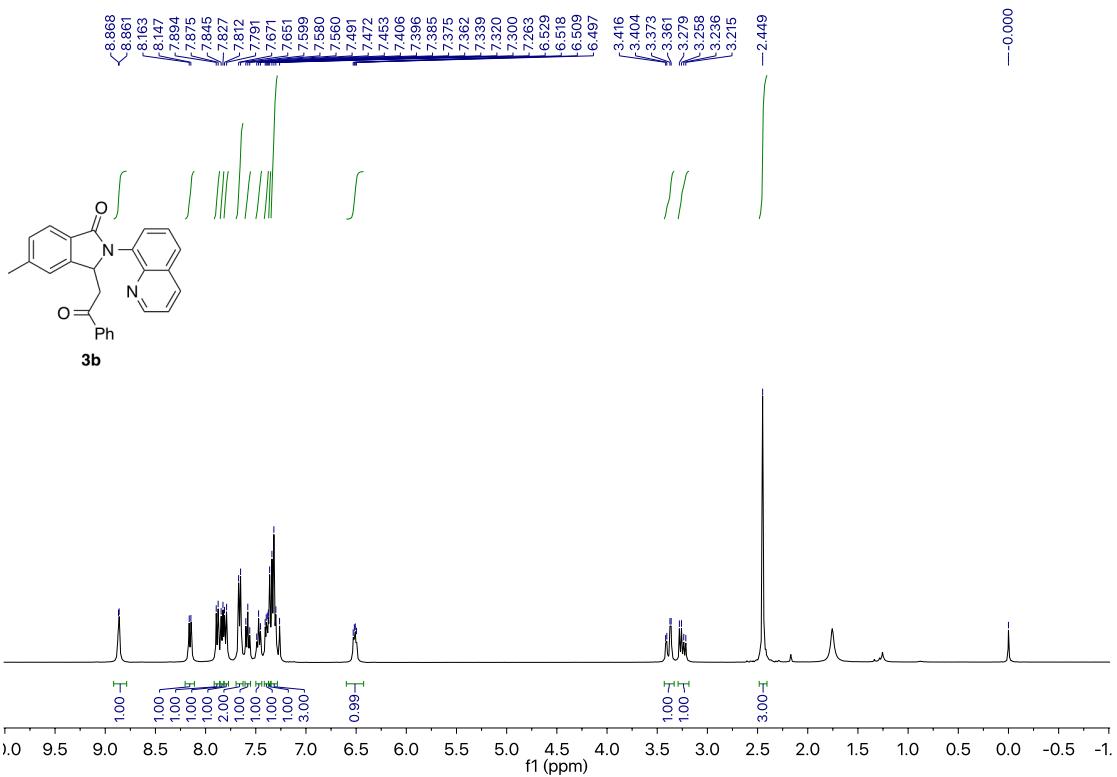
^1H NMR (400 MHz, CDCl_3)



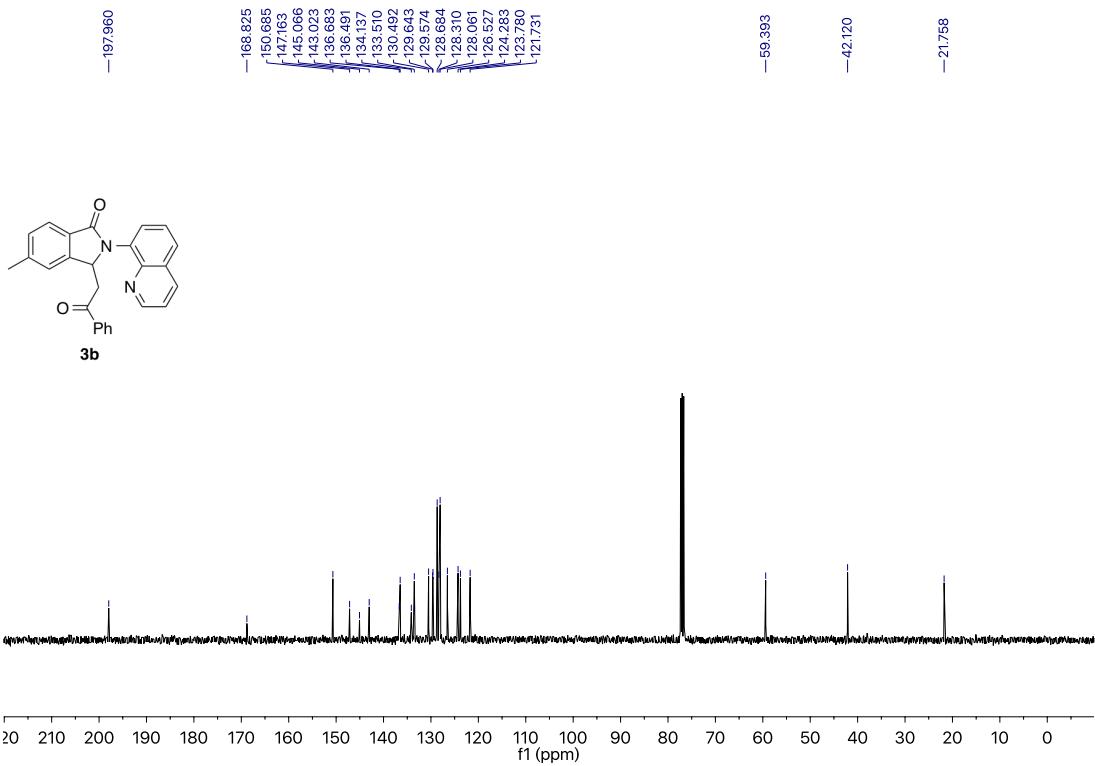
^{13}C NMR (100 MHz, CDCl_3)



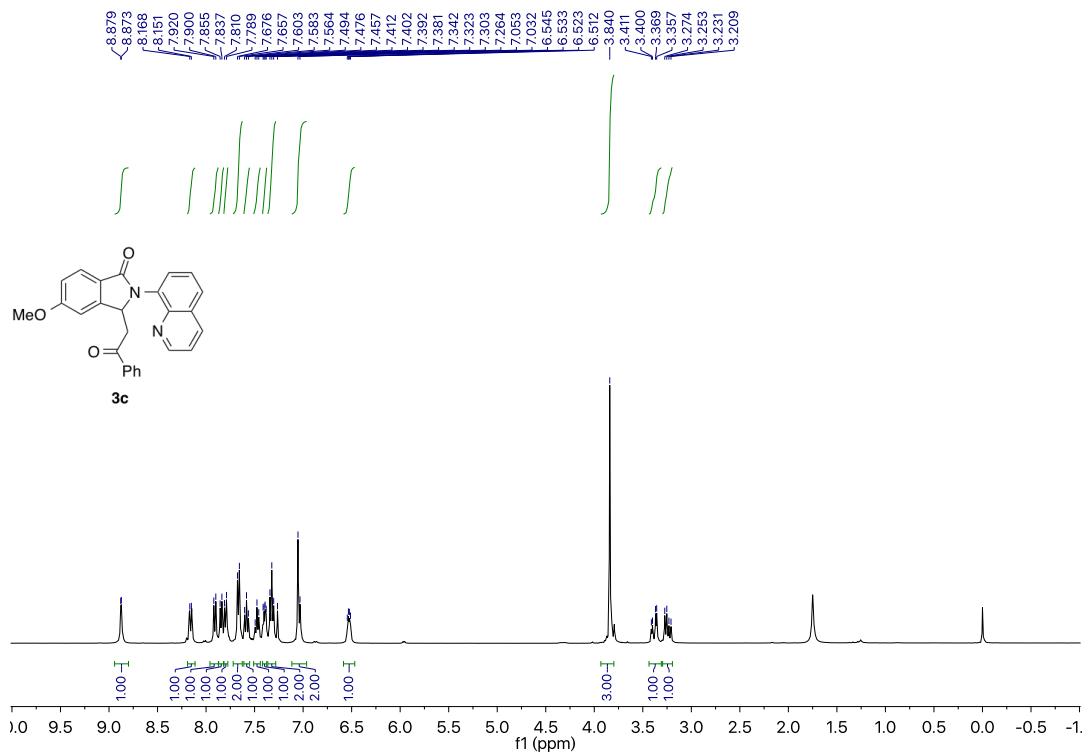
¹H NMR (400 MHz, CDCl₃)



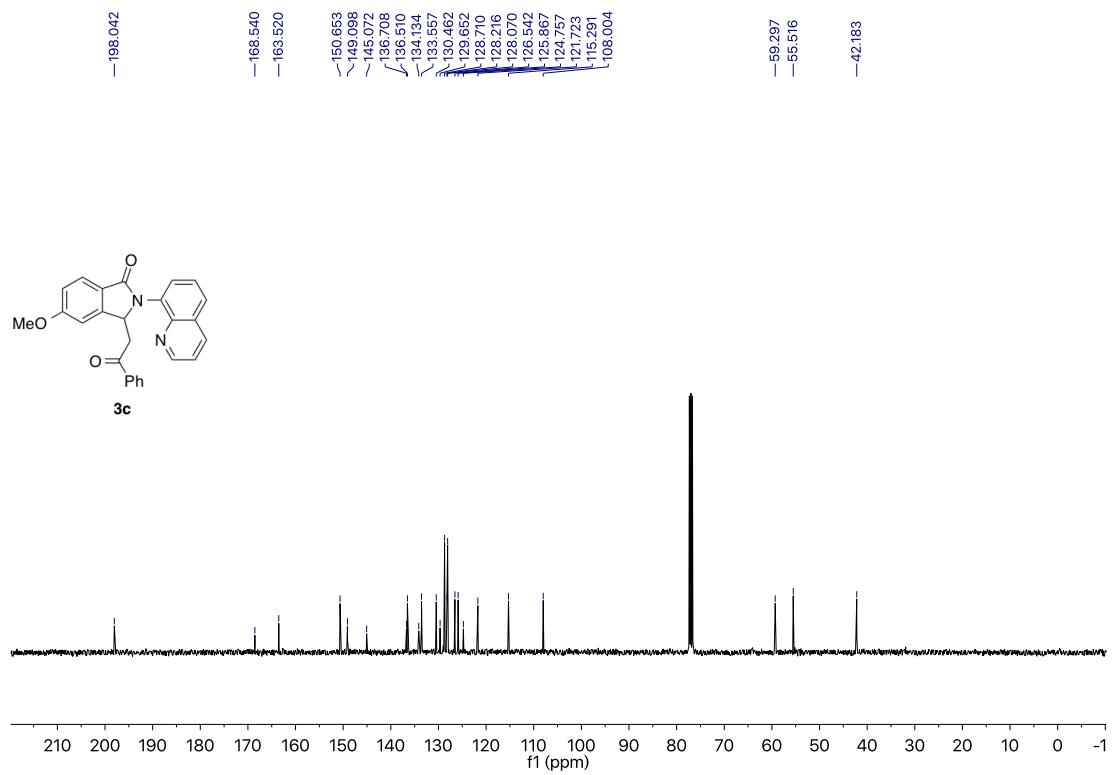
¹³C NMR (100 MHz, CDCl₃)



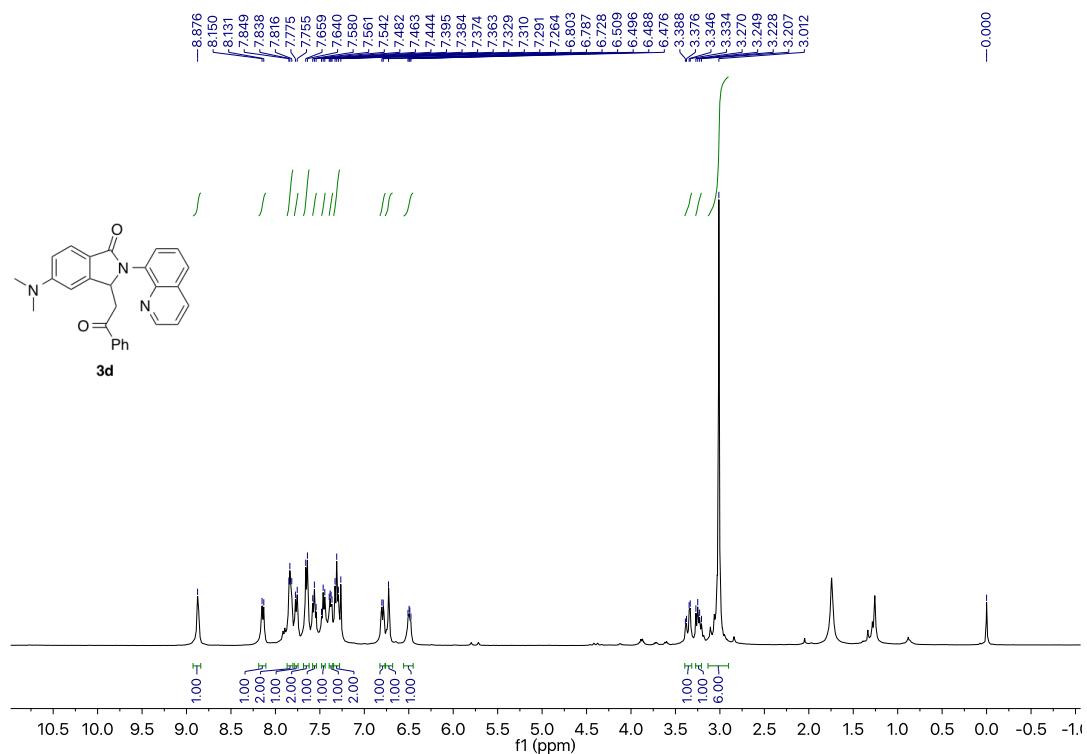
¹H NMR (400 MHz, CDCl₃)



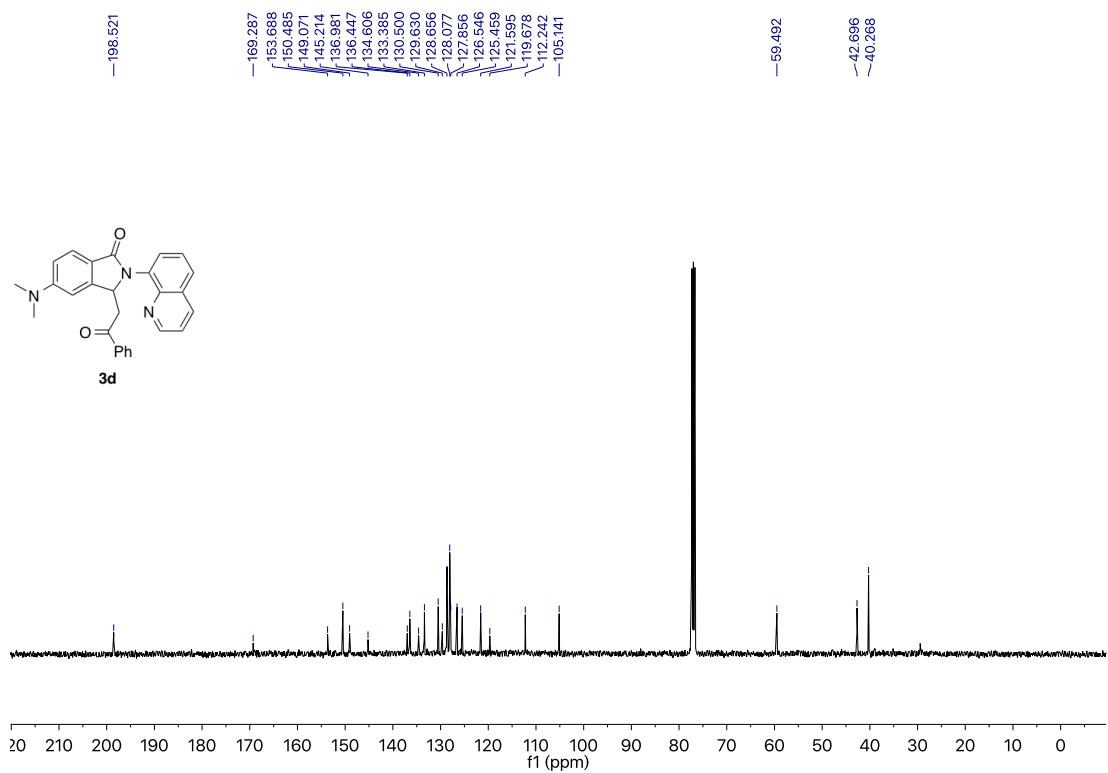
¹³C NMR (100 MHz, CDCl₃)



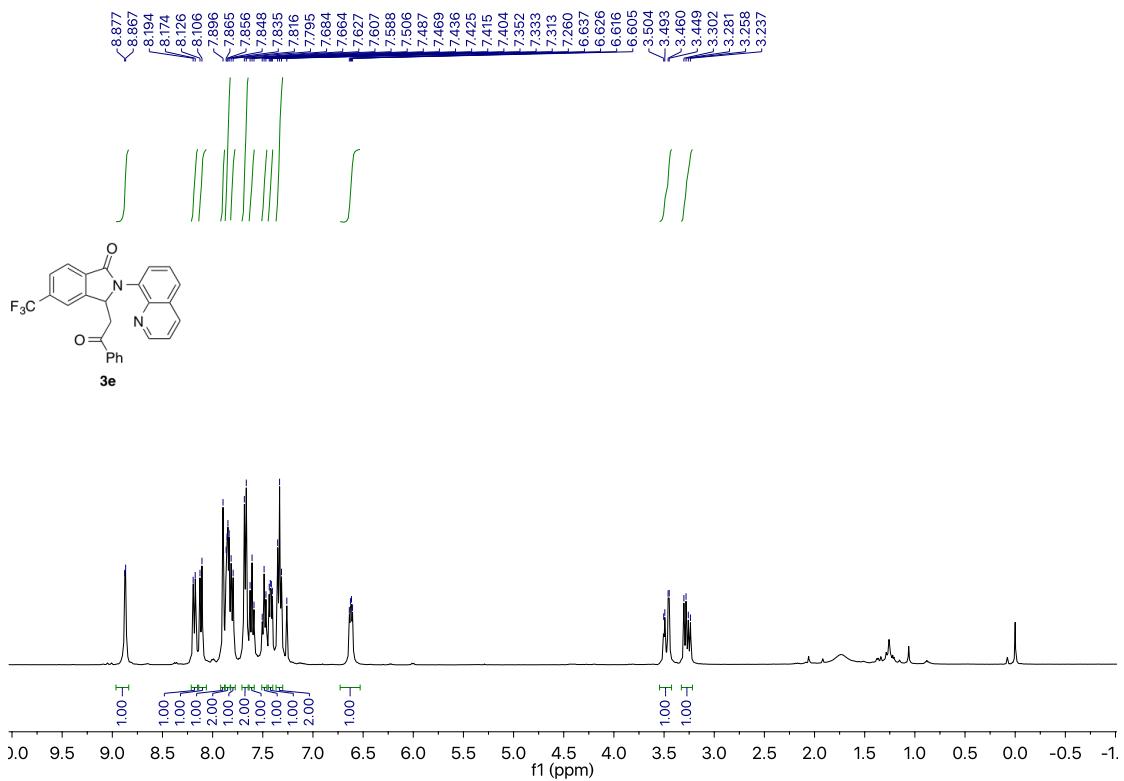
¹H NMR (400 MHz, CDCl₃)



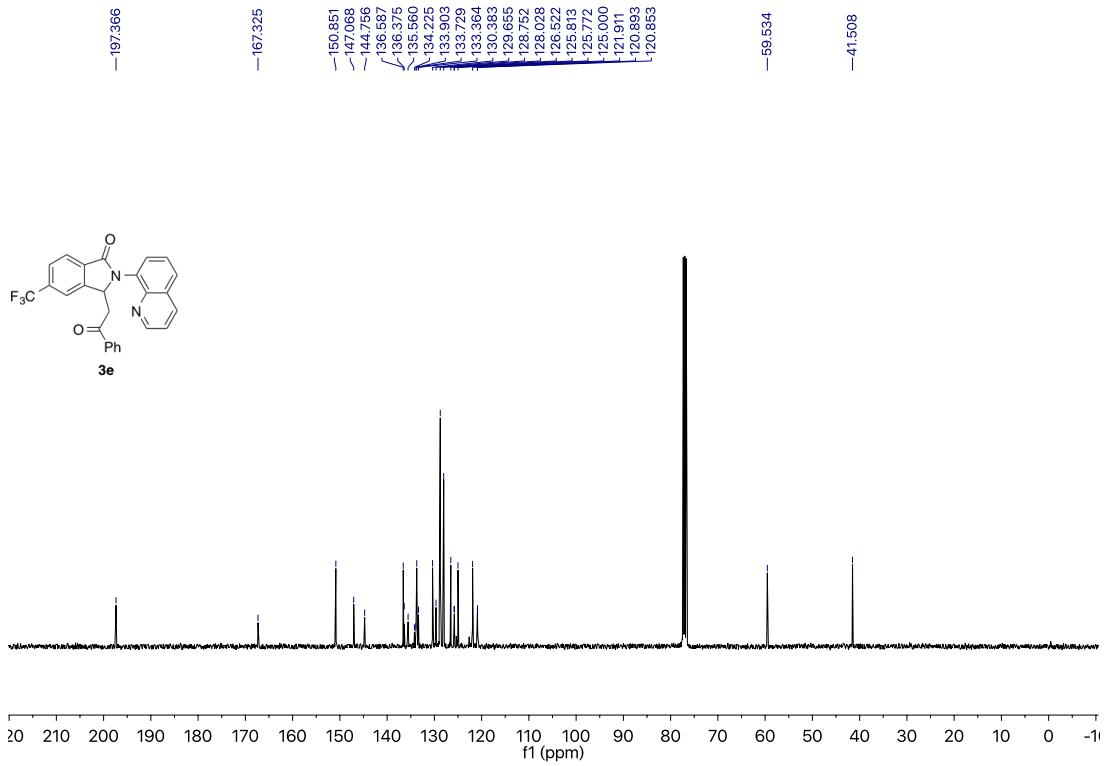
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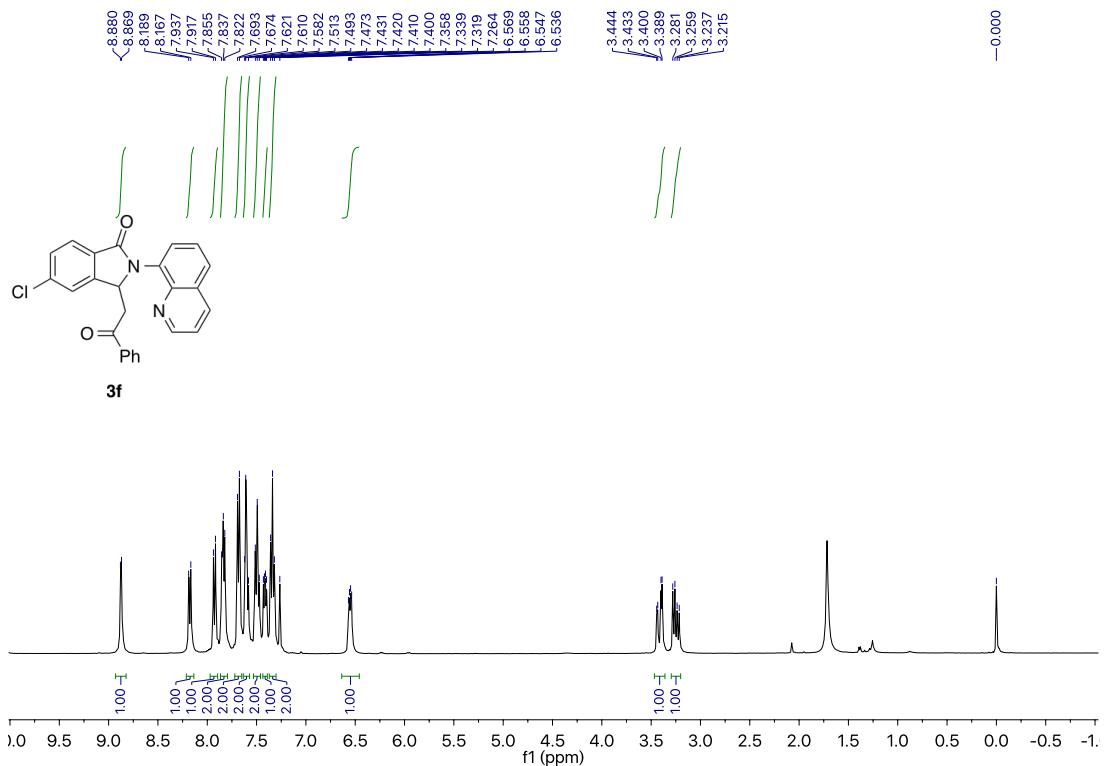
¹H NMR (400 MHz, CDCl₃)



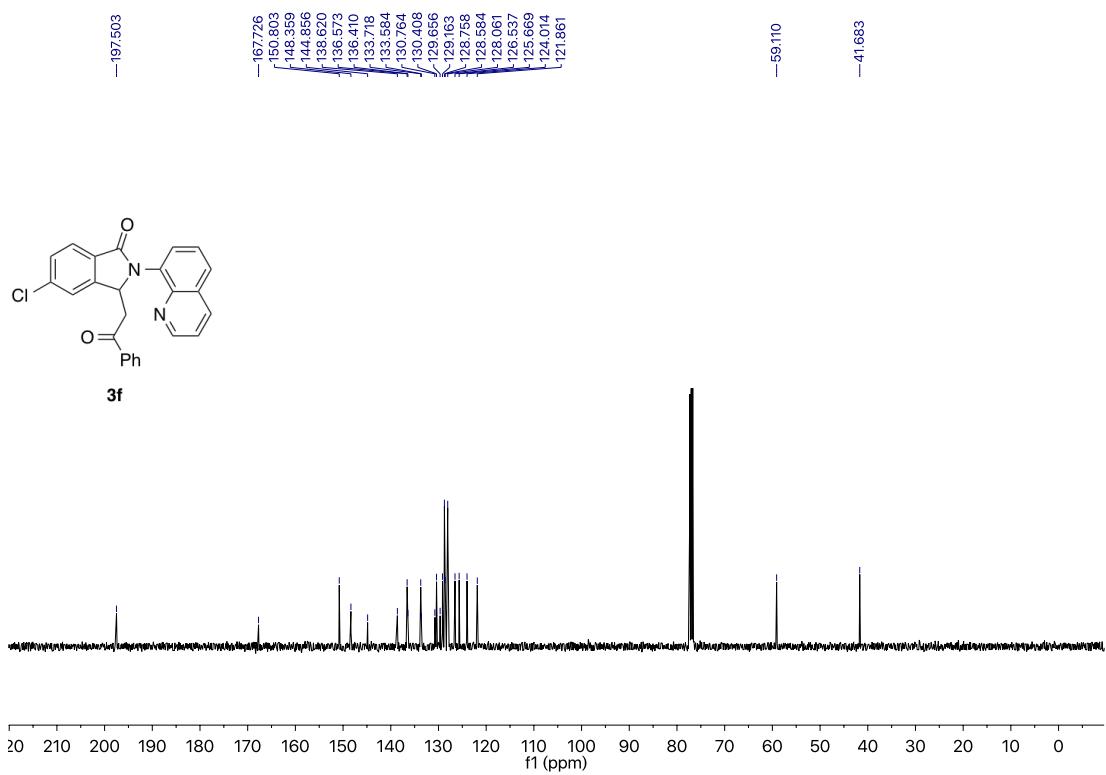
¹³C NMR (100 MHz, CDCl₃)



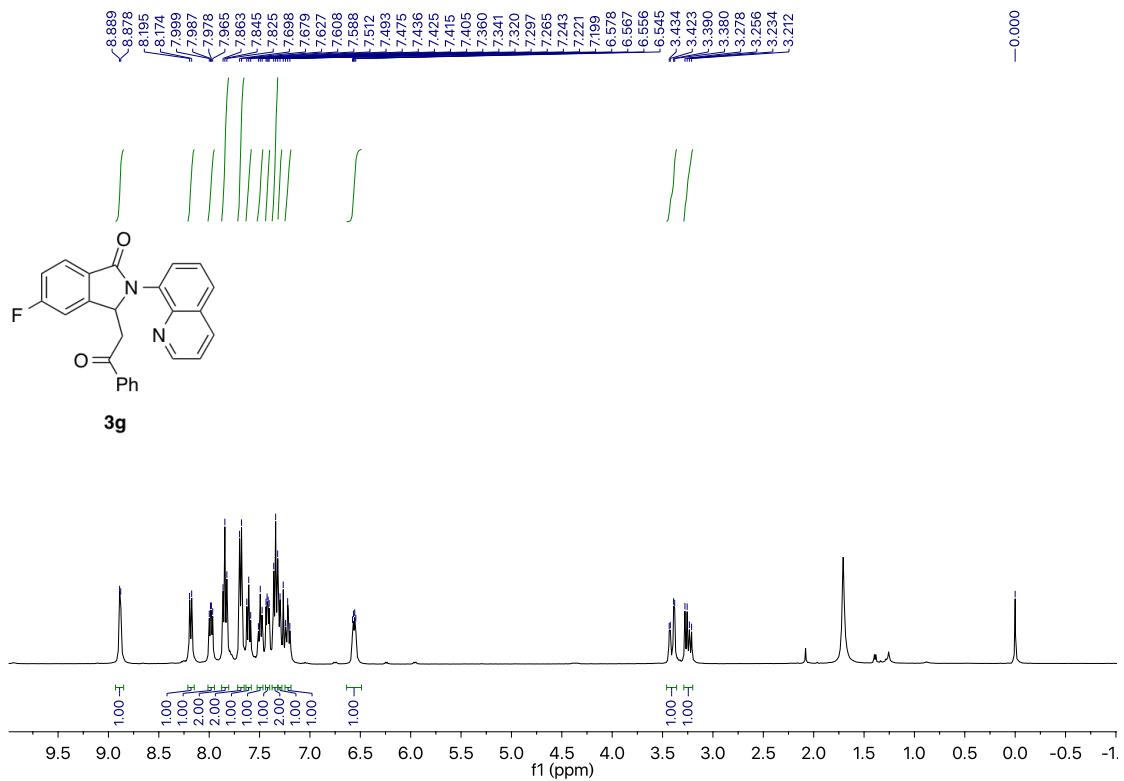
¹H NMR (400 MHz, CDCl₃)



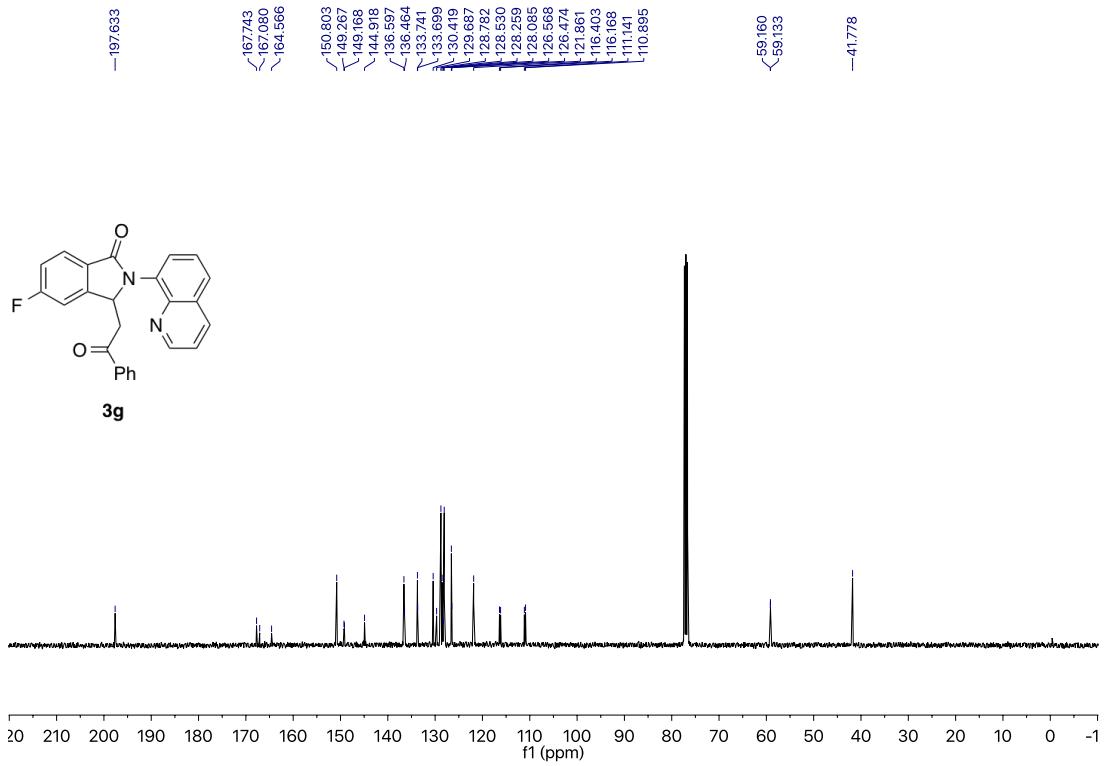
¹³C NMR (100 MHz, CDCl₃)



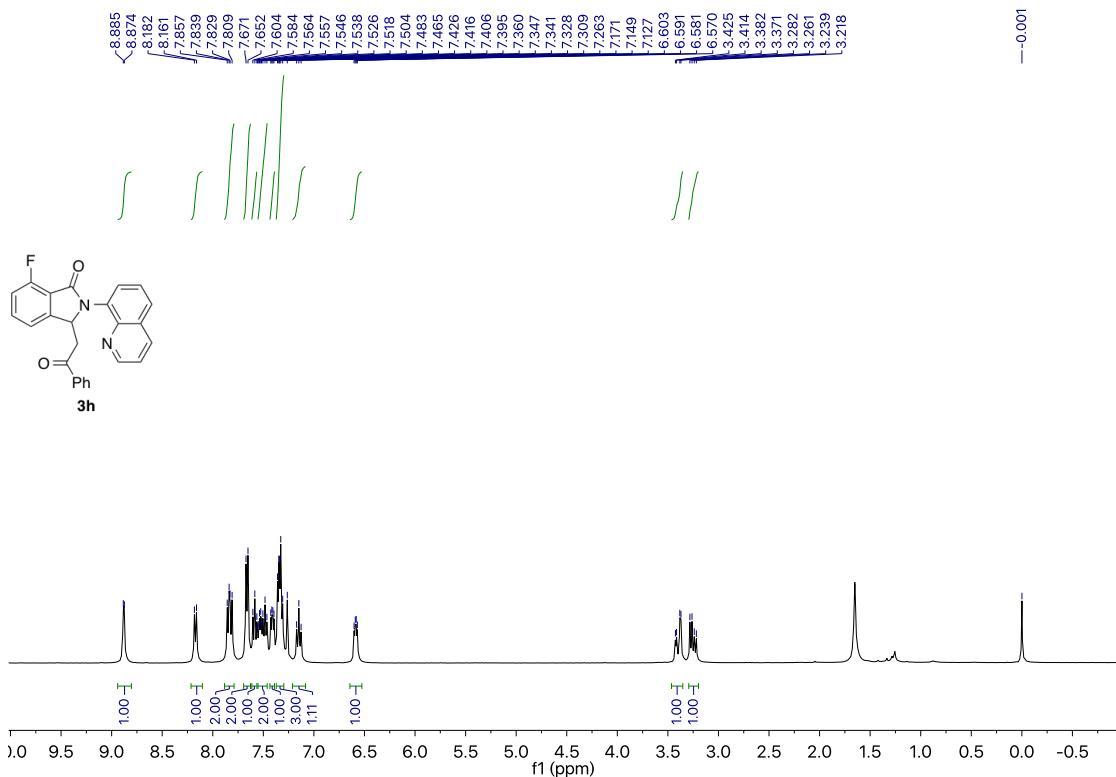
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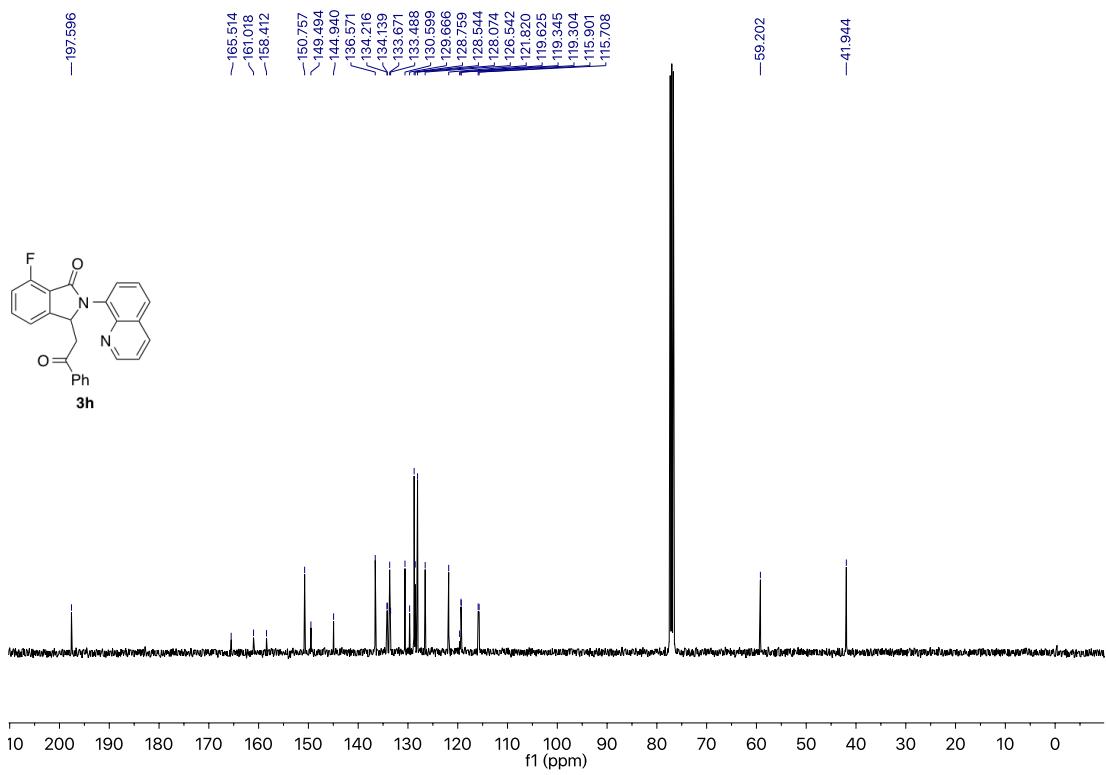
¹³C NMR (100 MHz, CDCl₃)



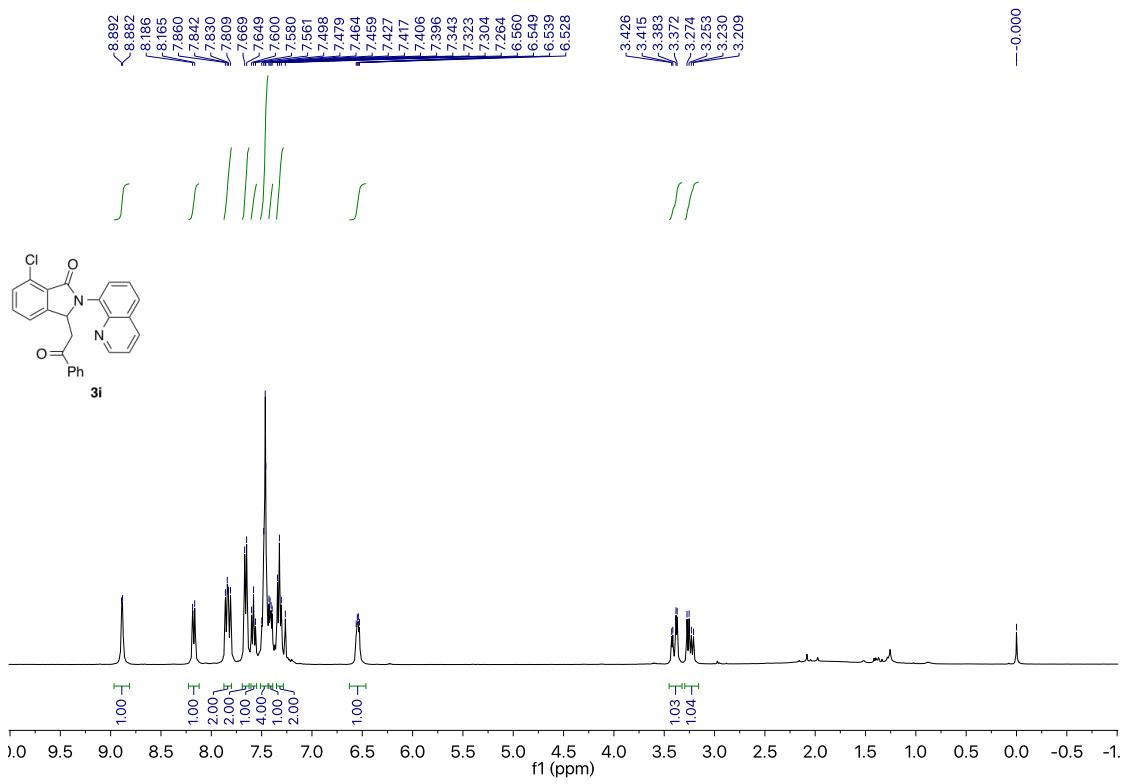
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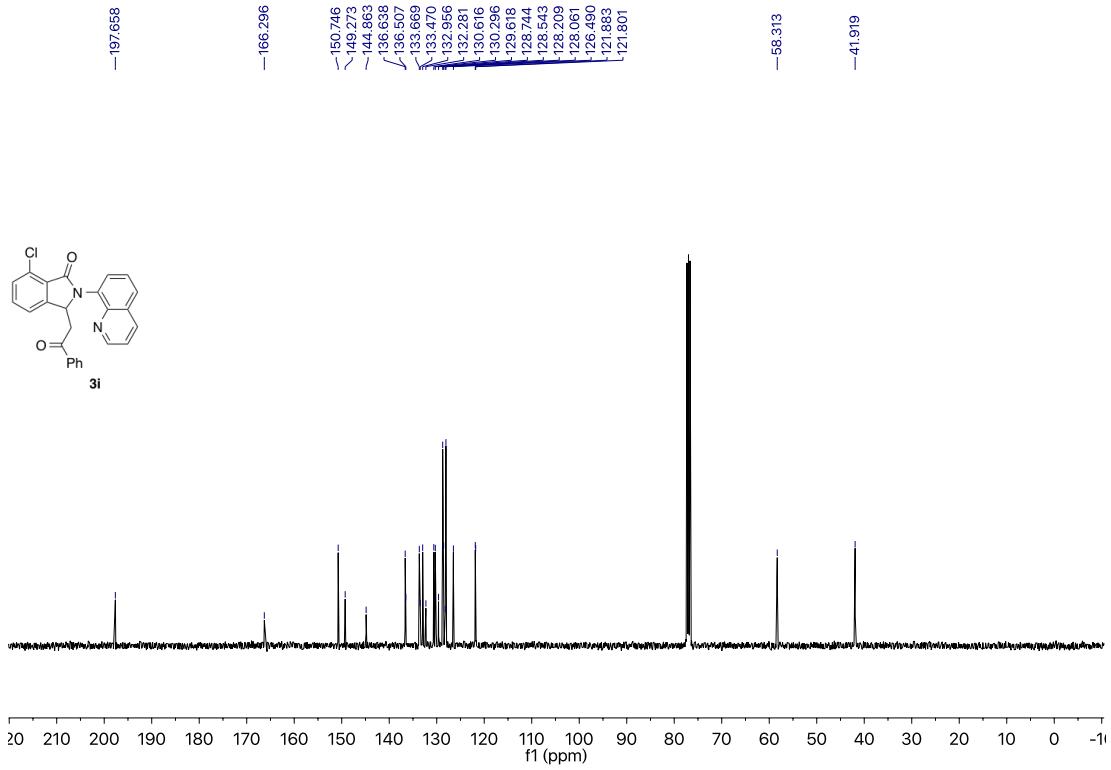
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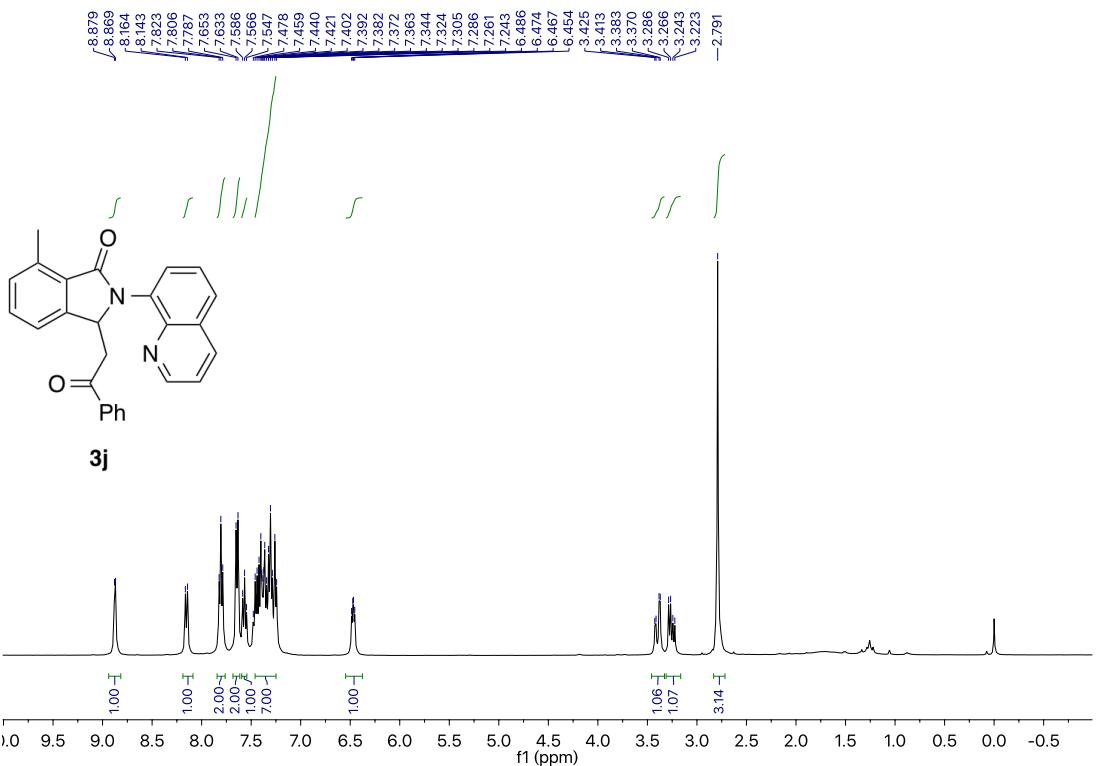
¹H NMR (400 MHz, CDCl₃)



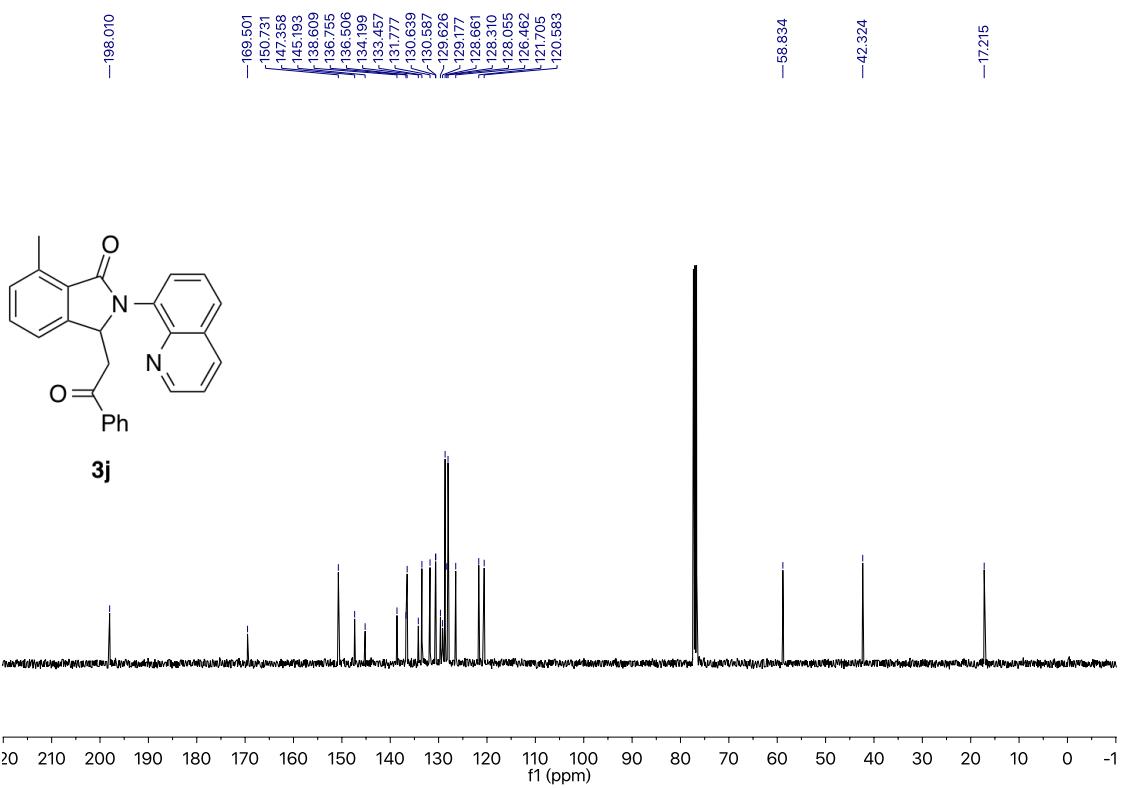
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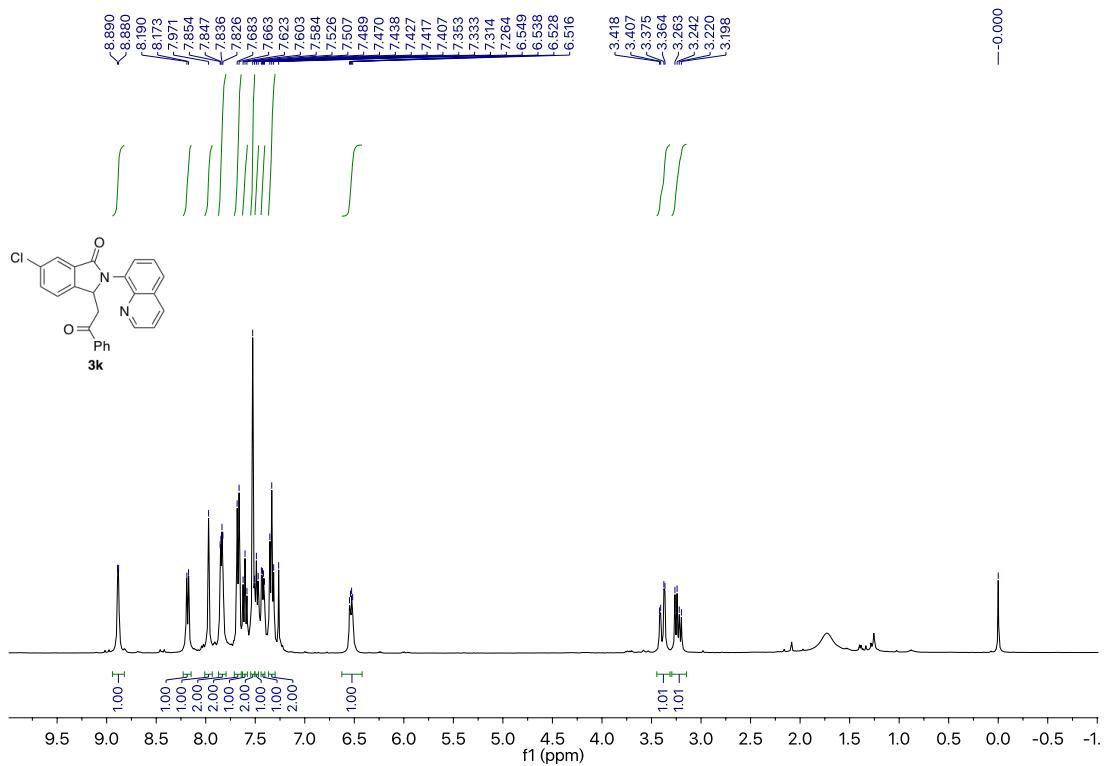
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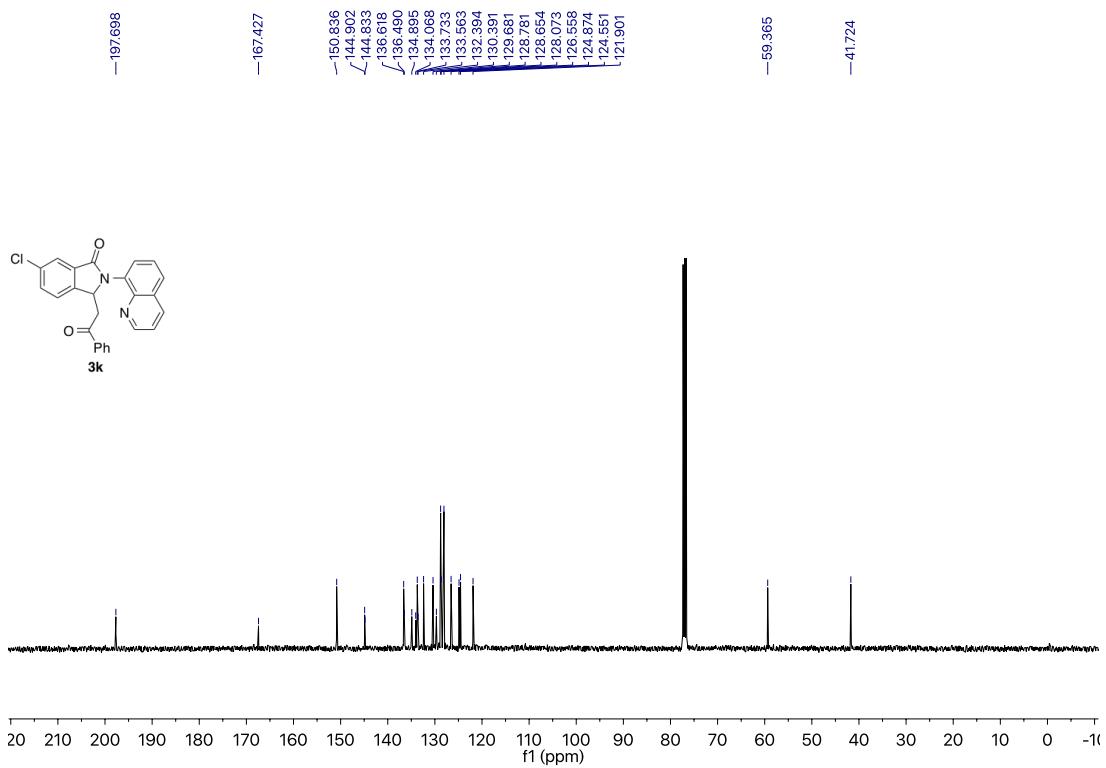
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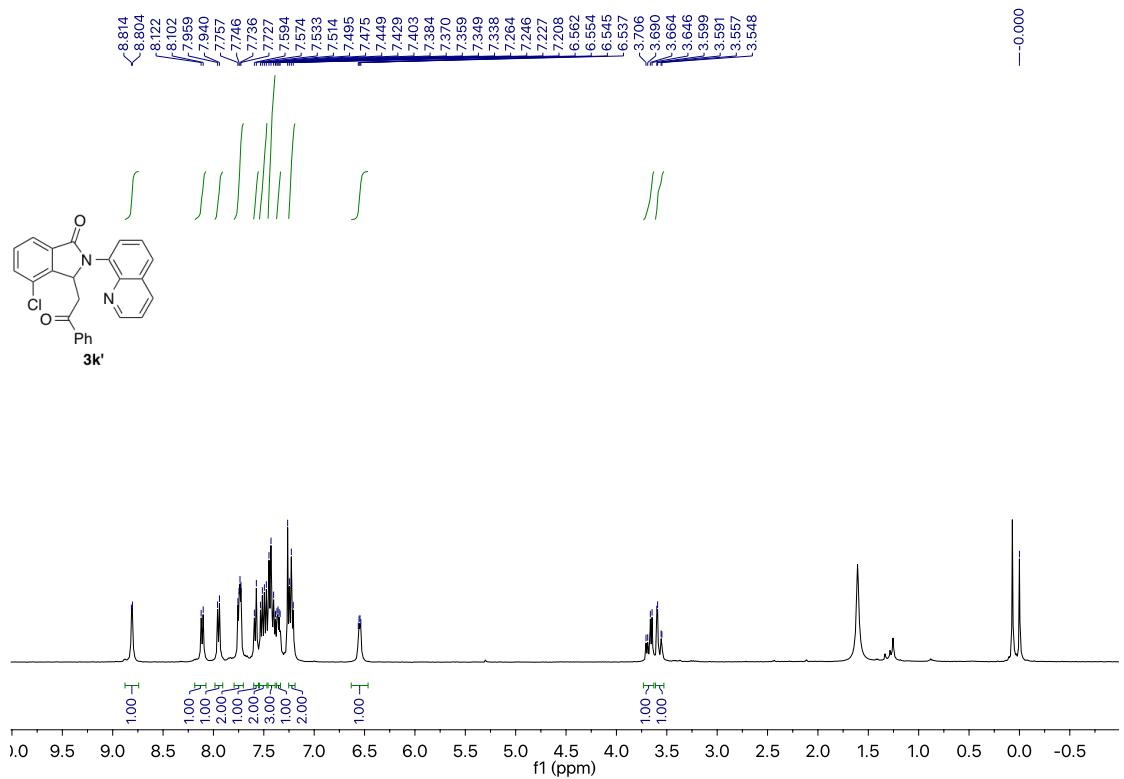
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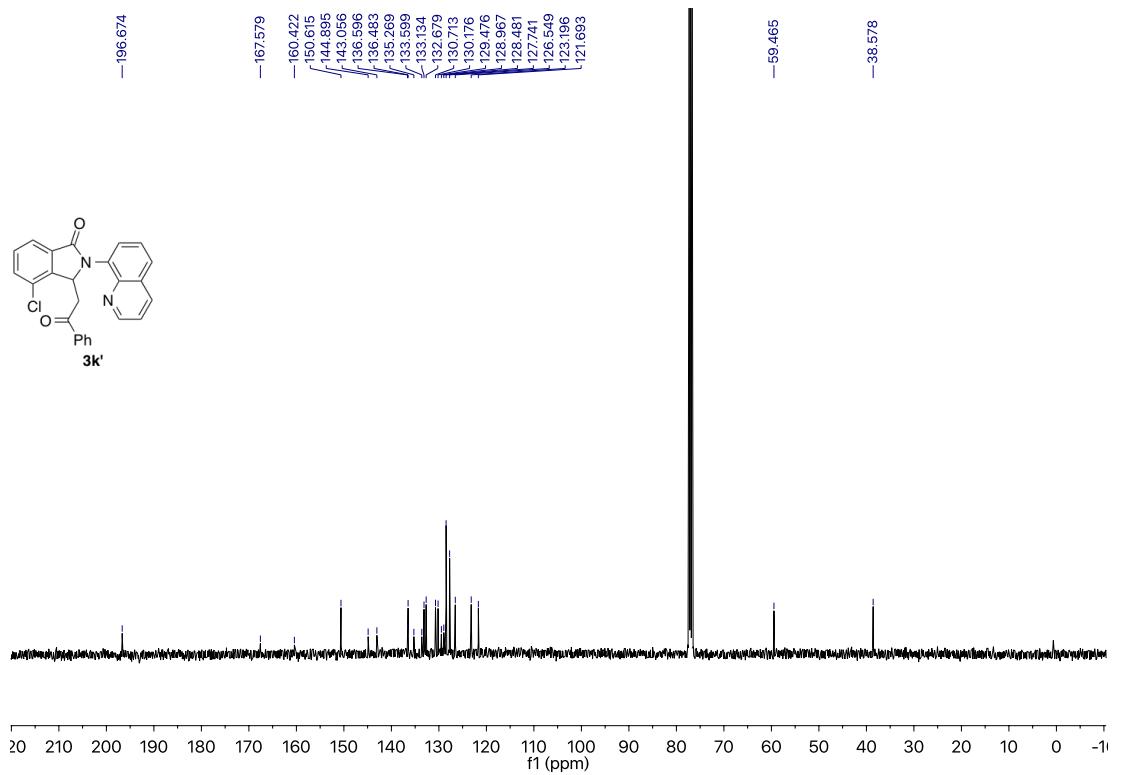
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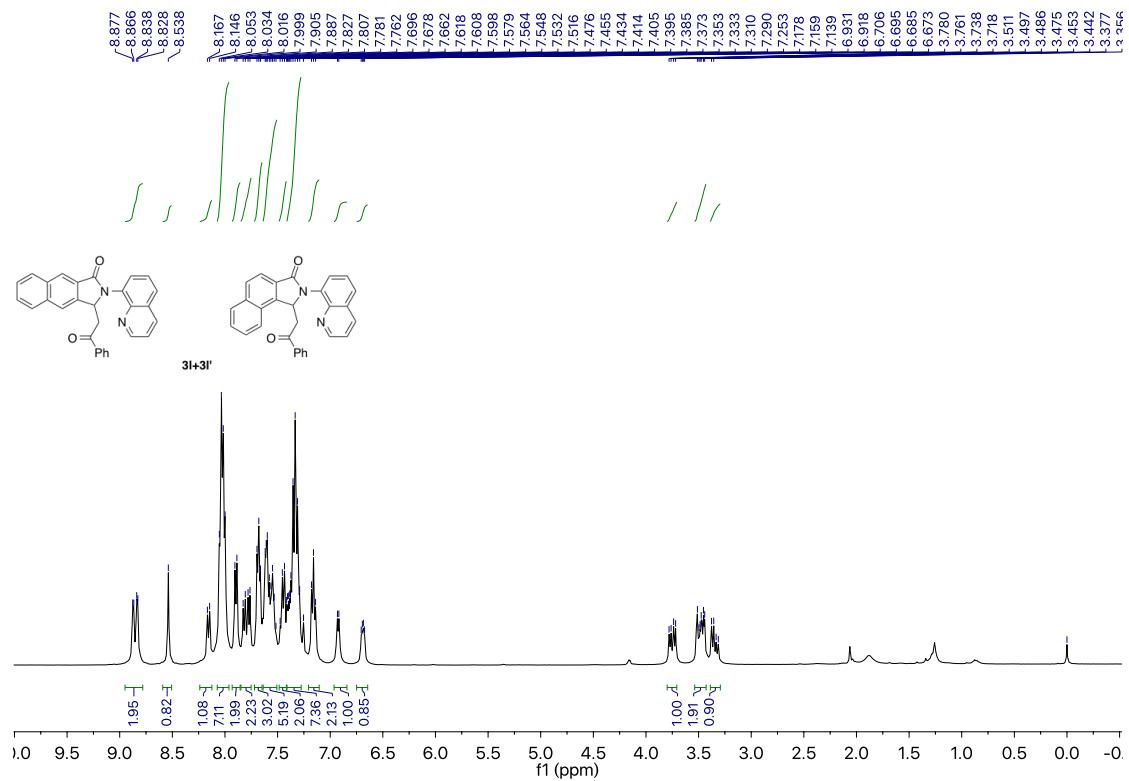
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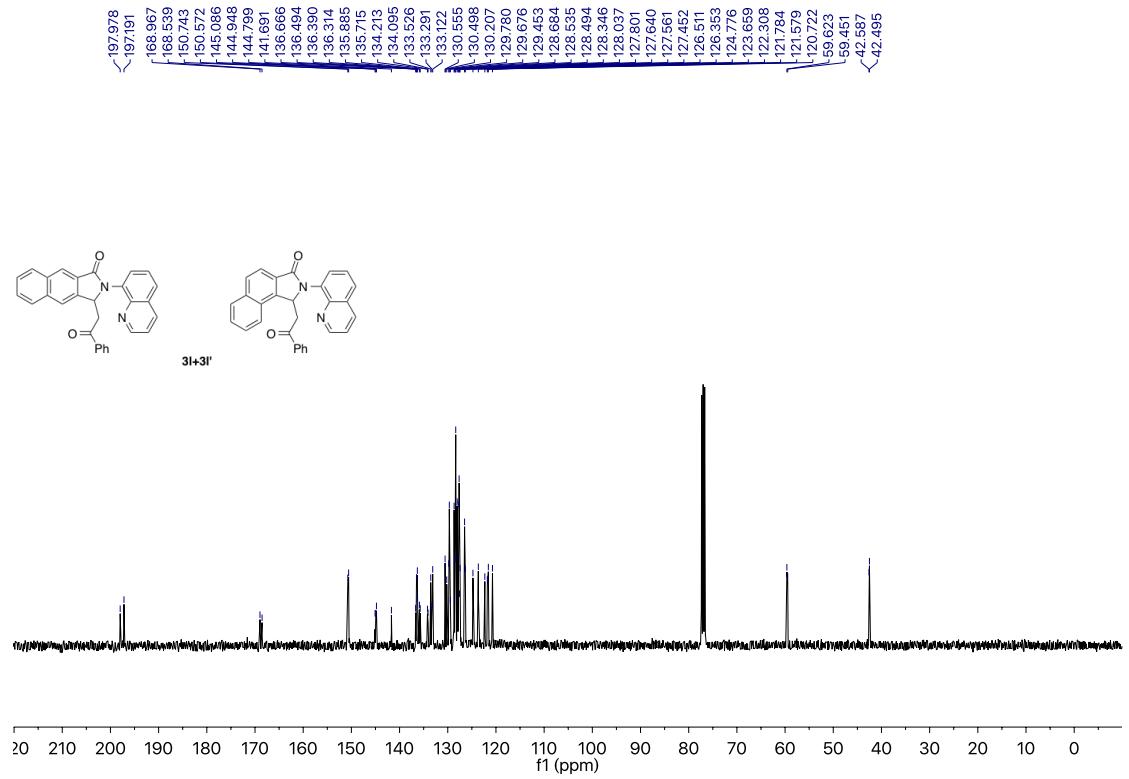
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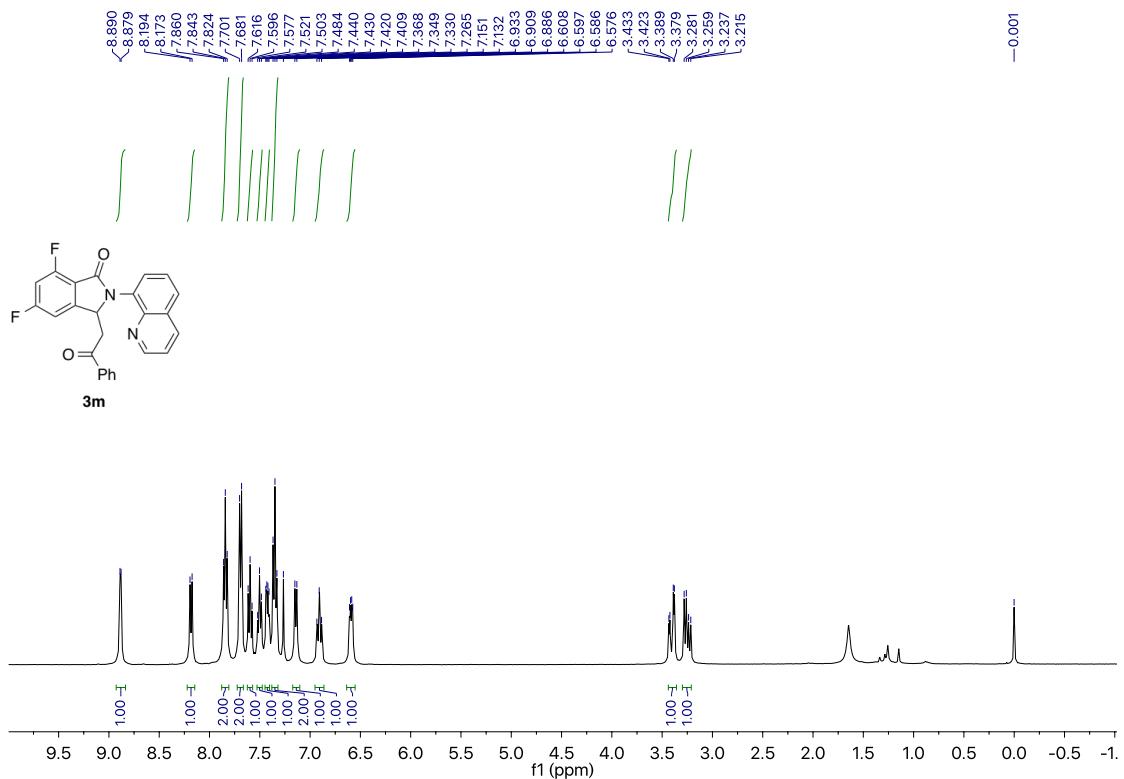
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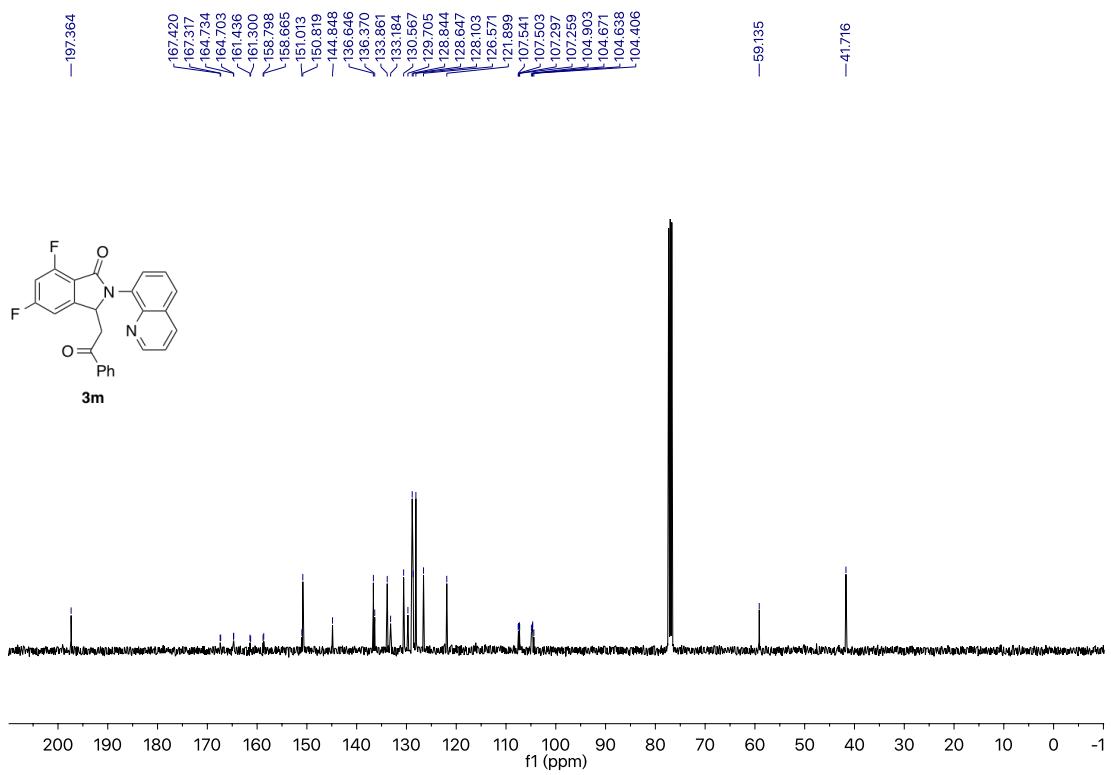
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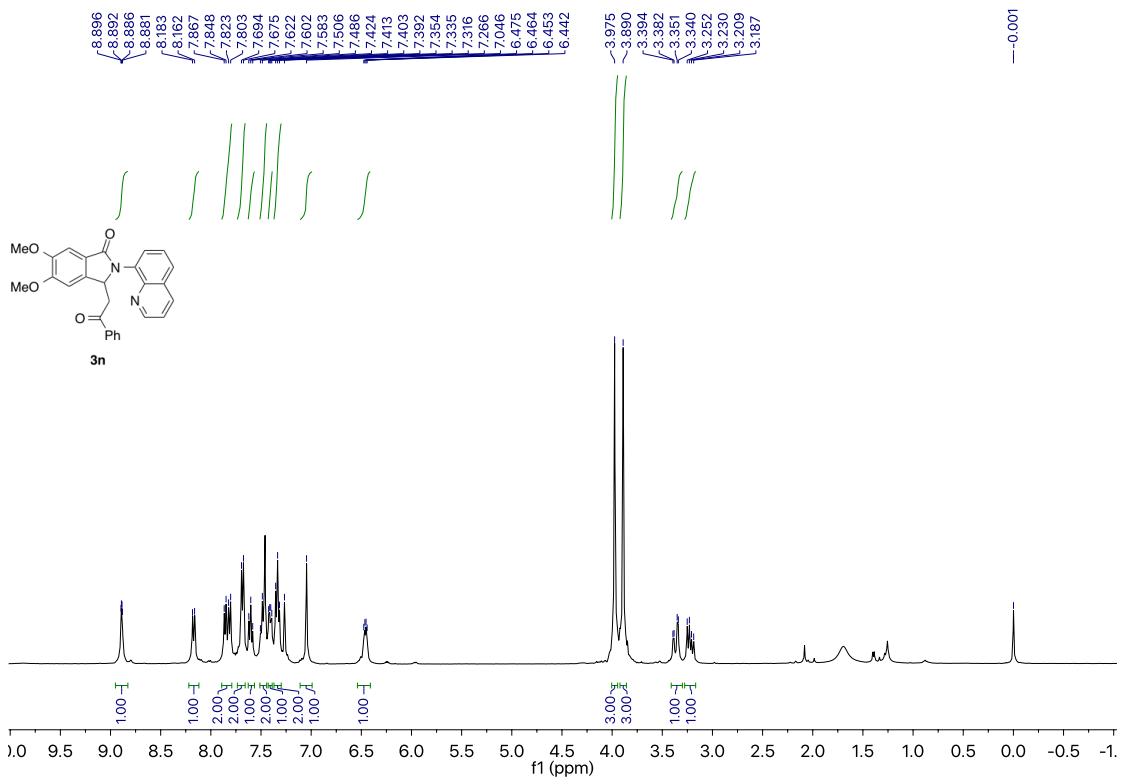
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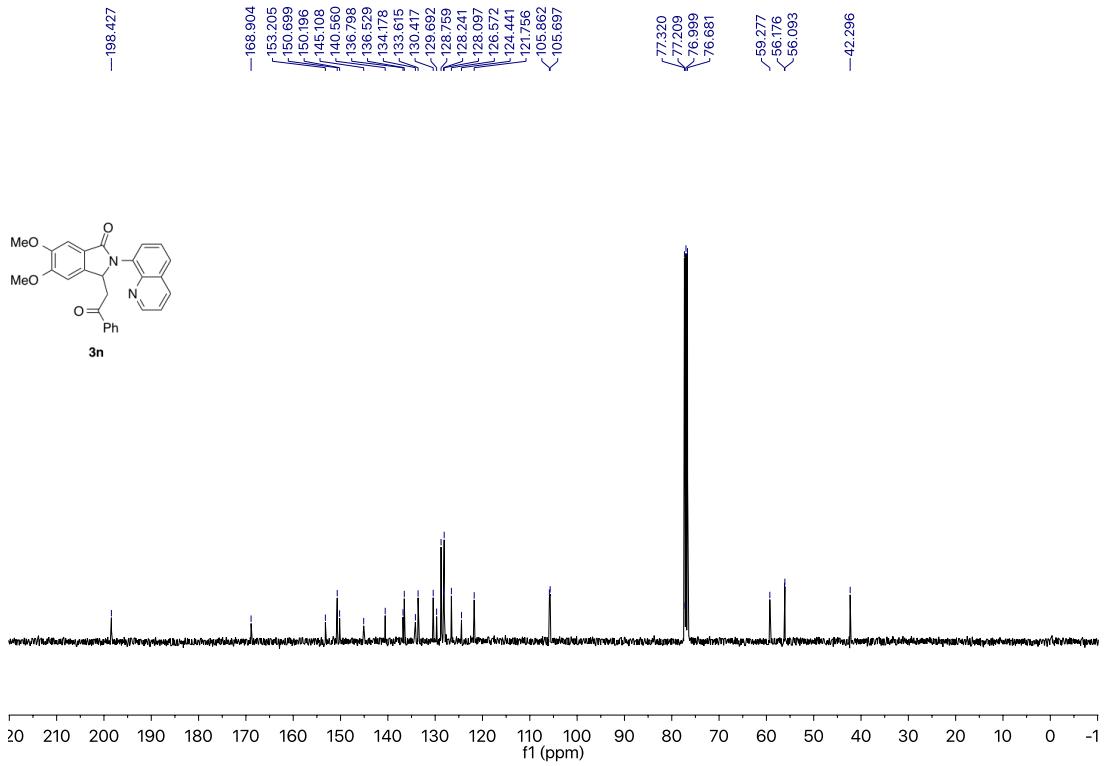
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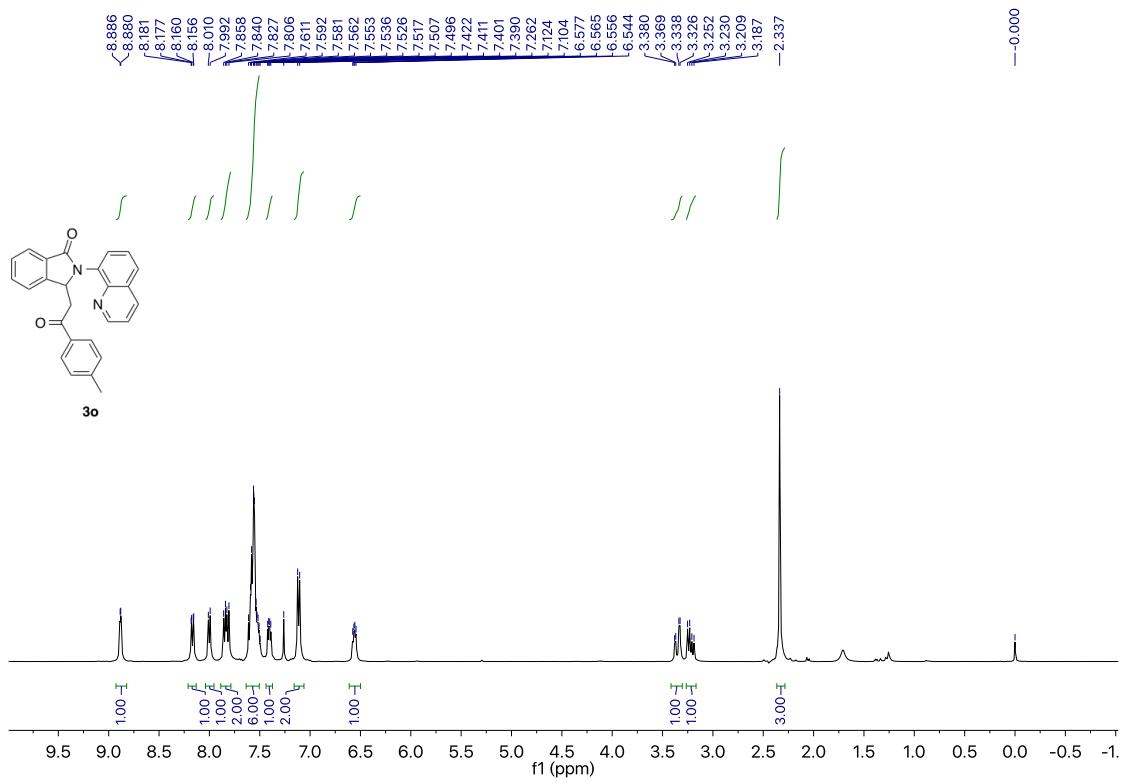
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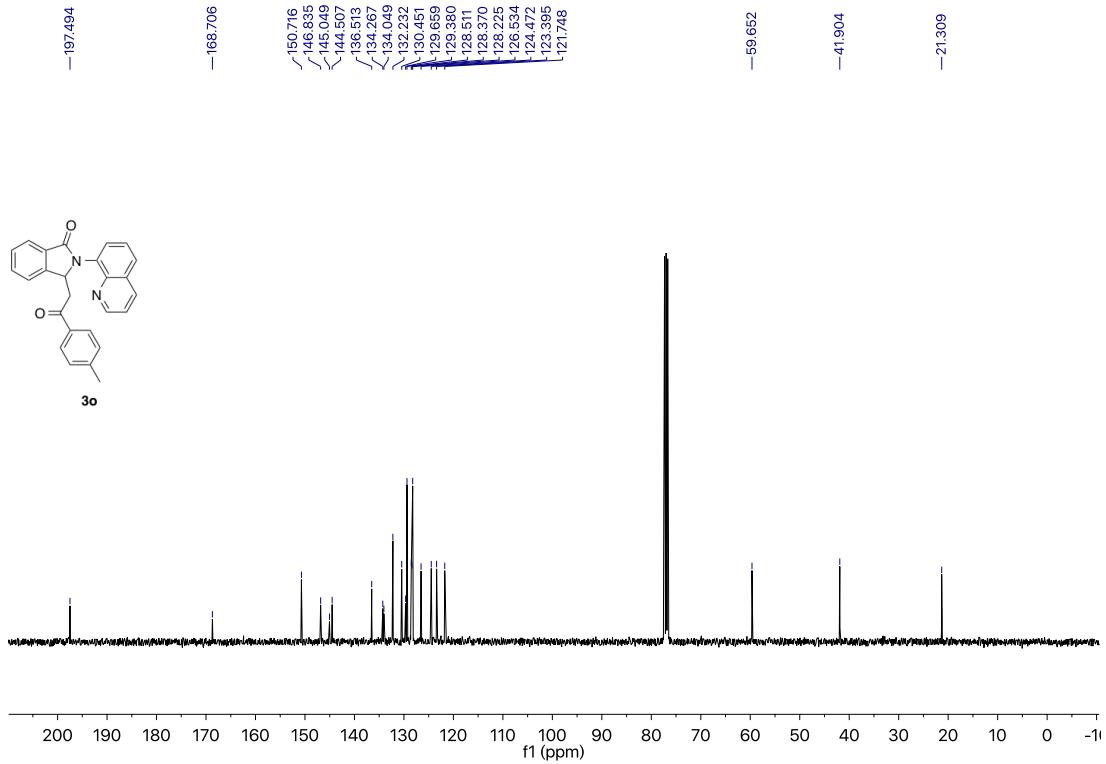
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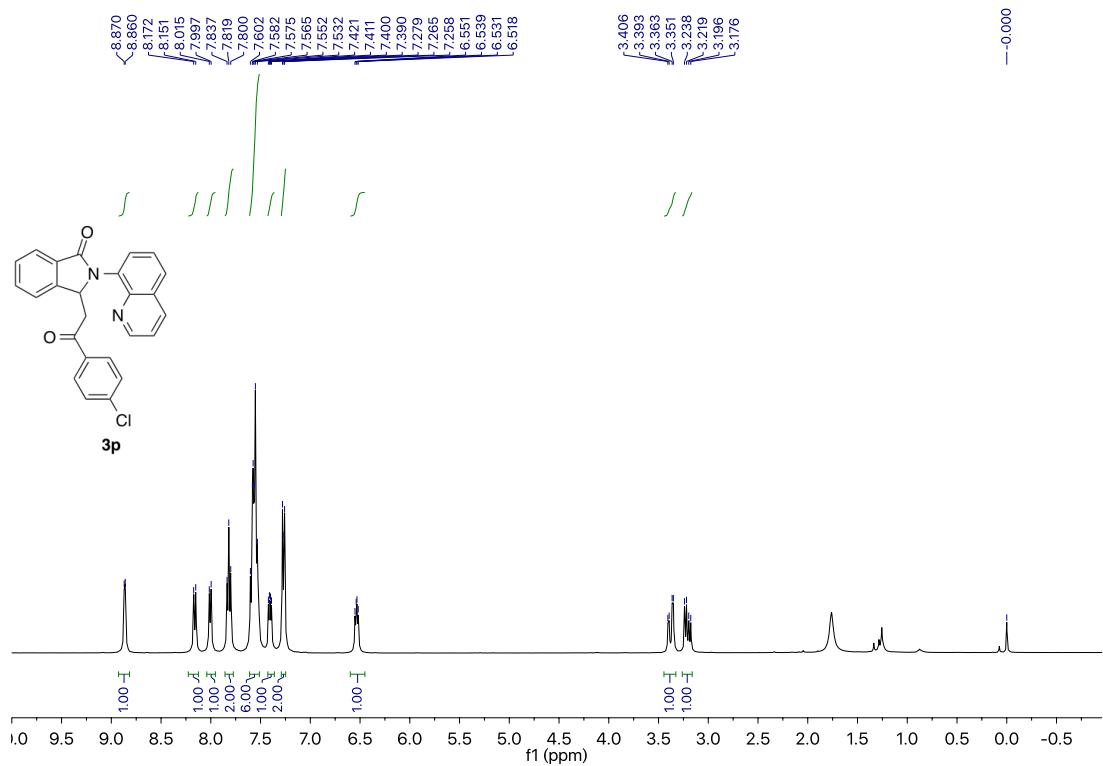
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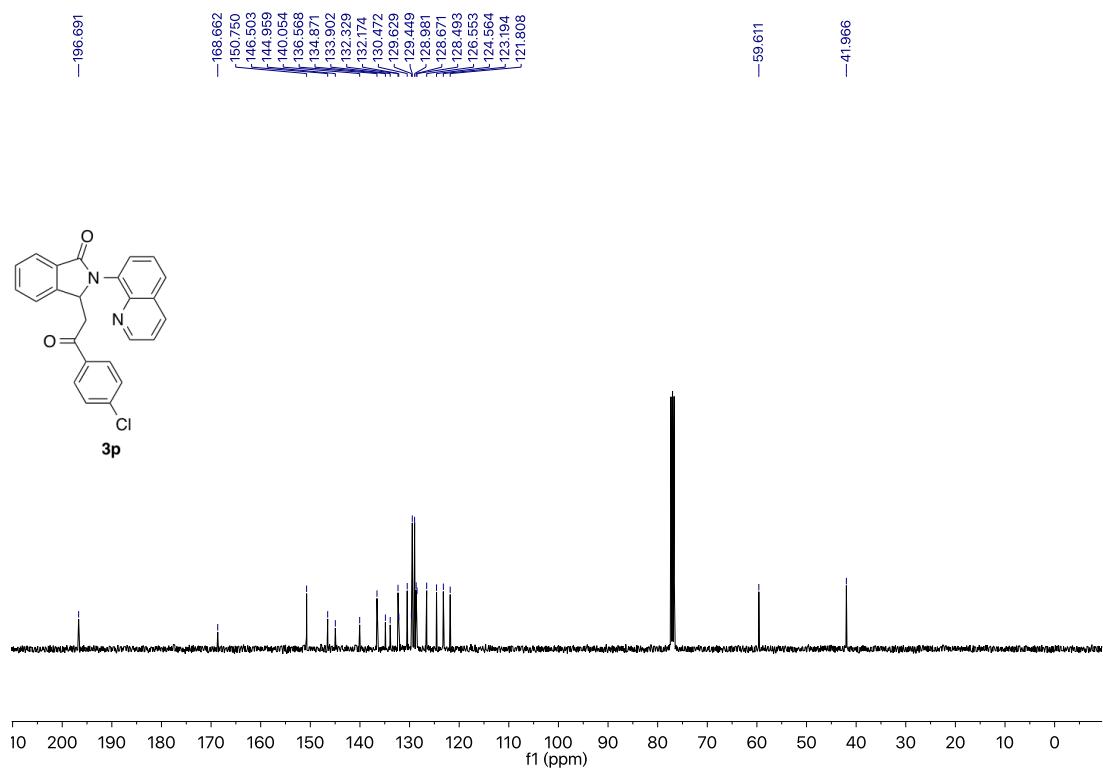
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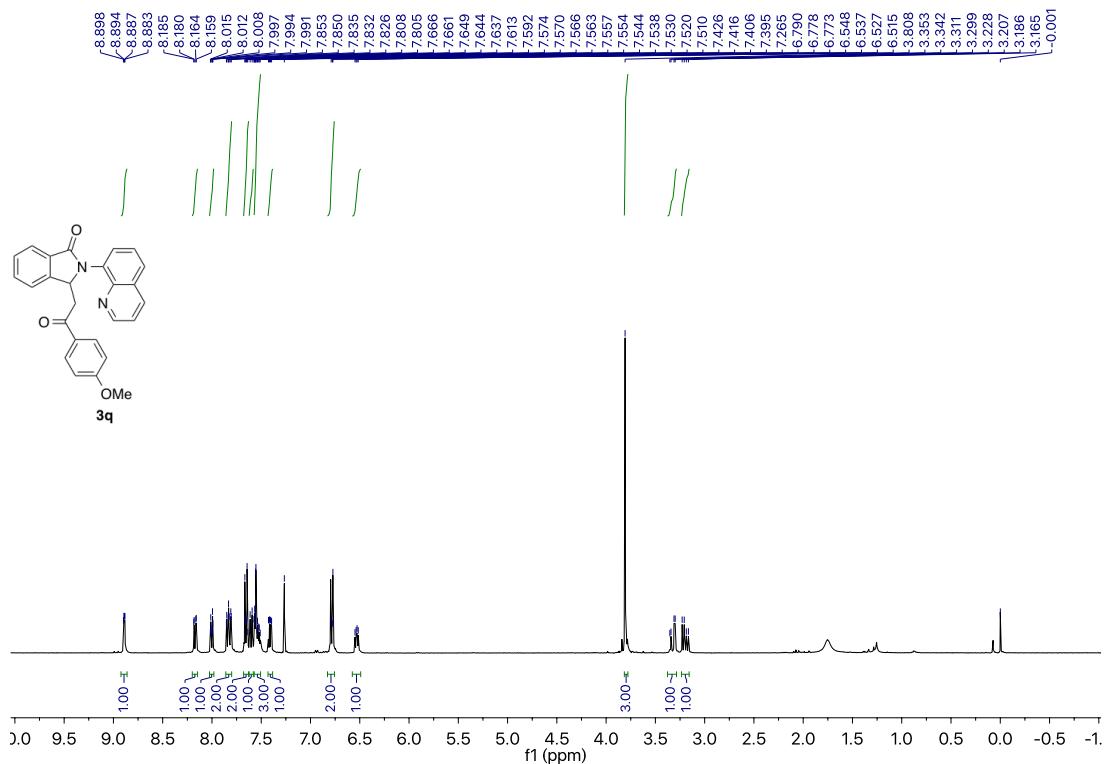
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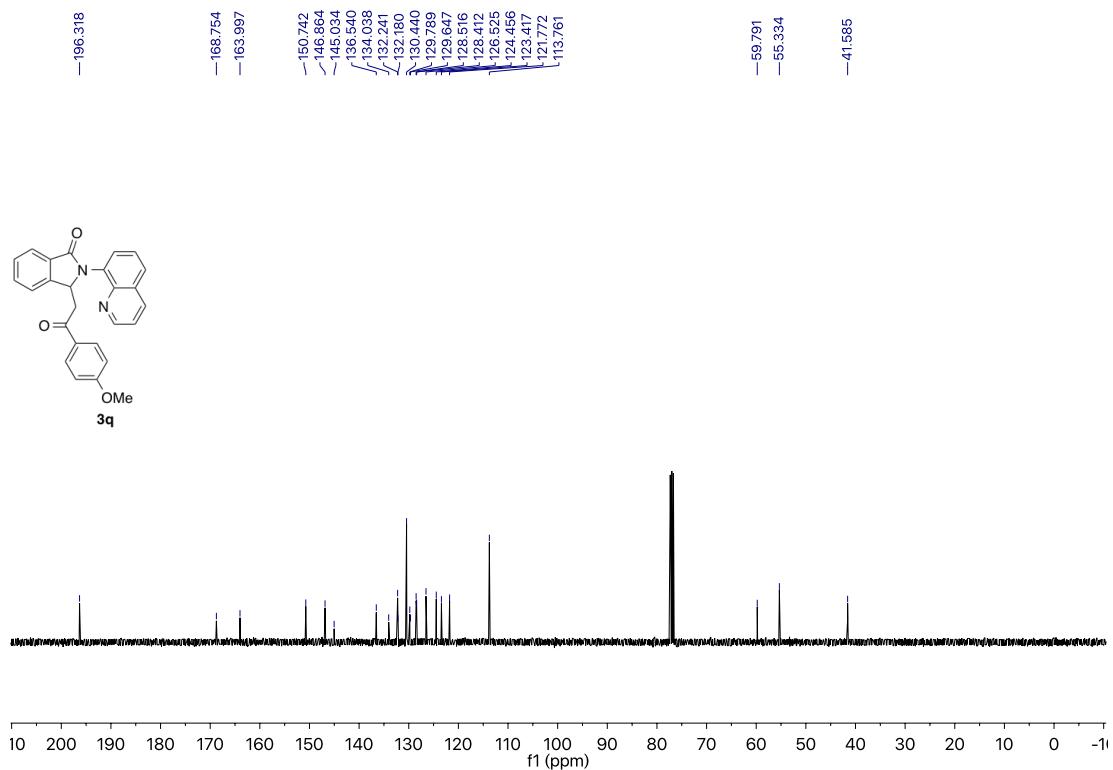
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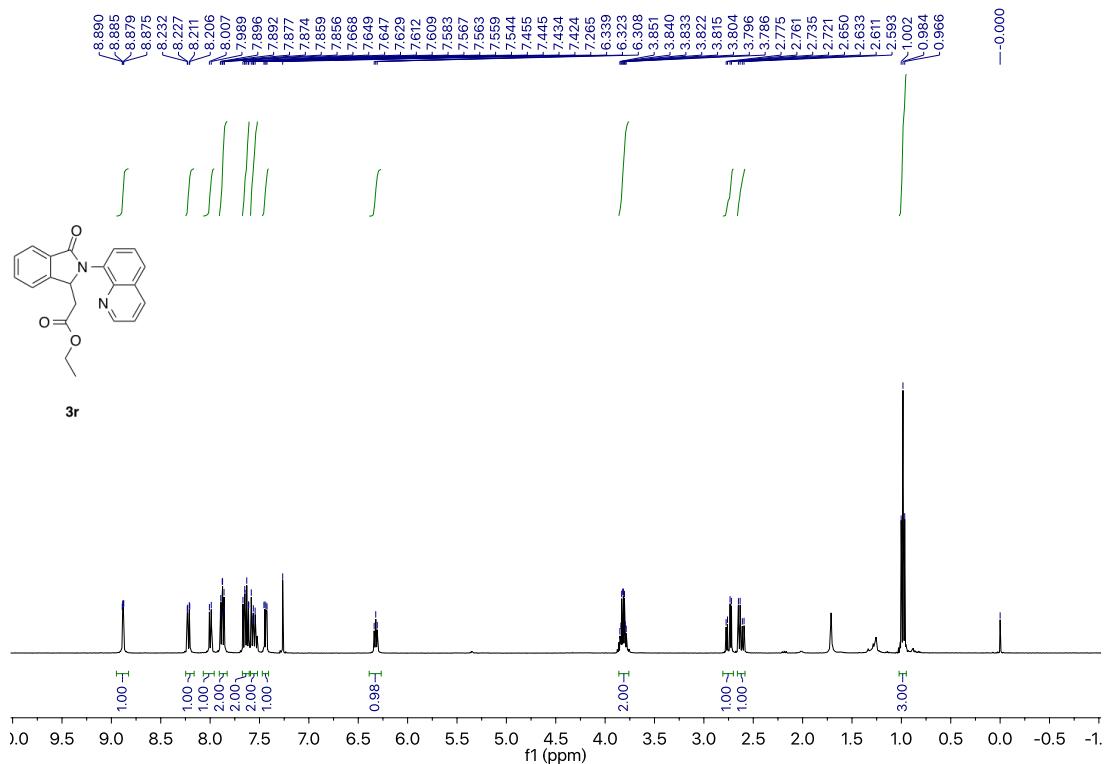
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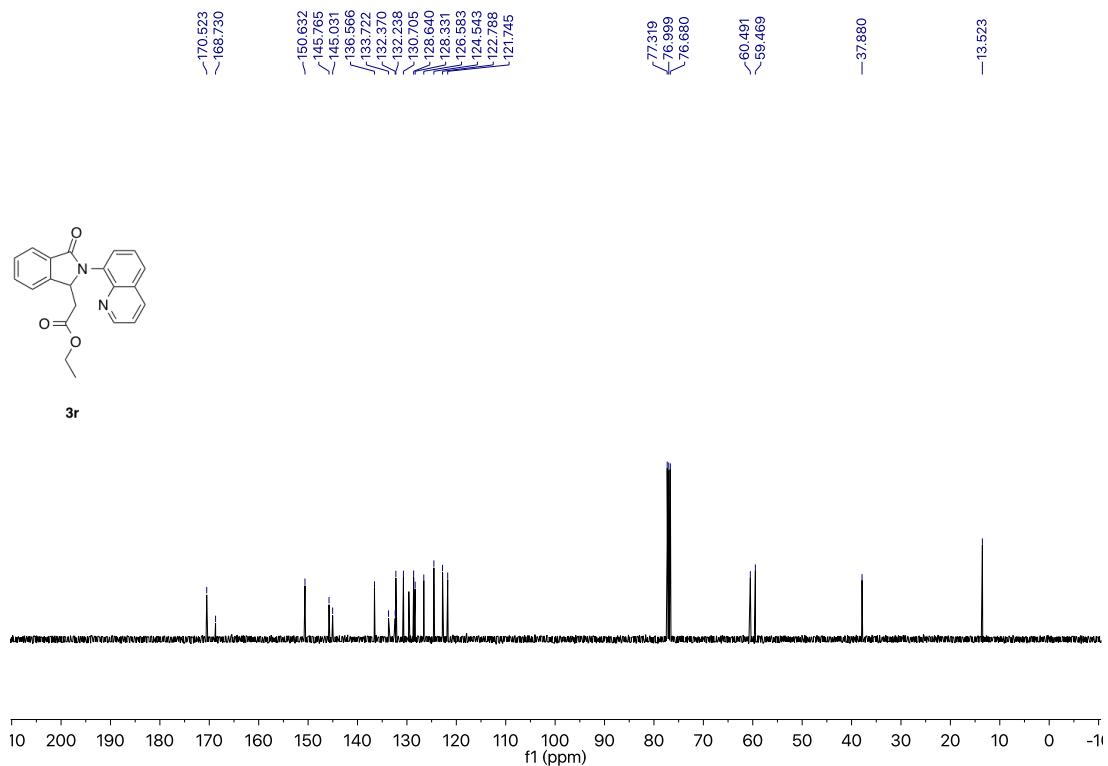
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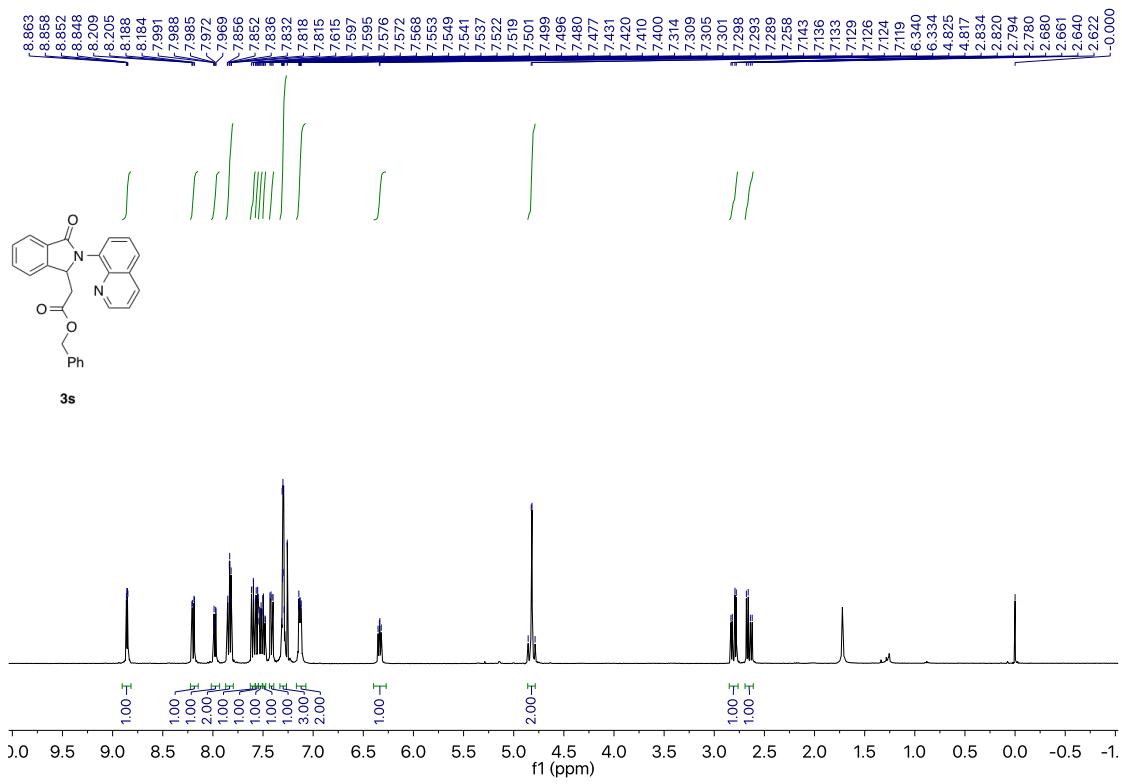
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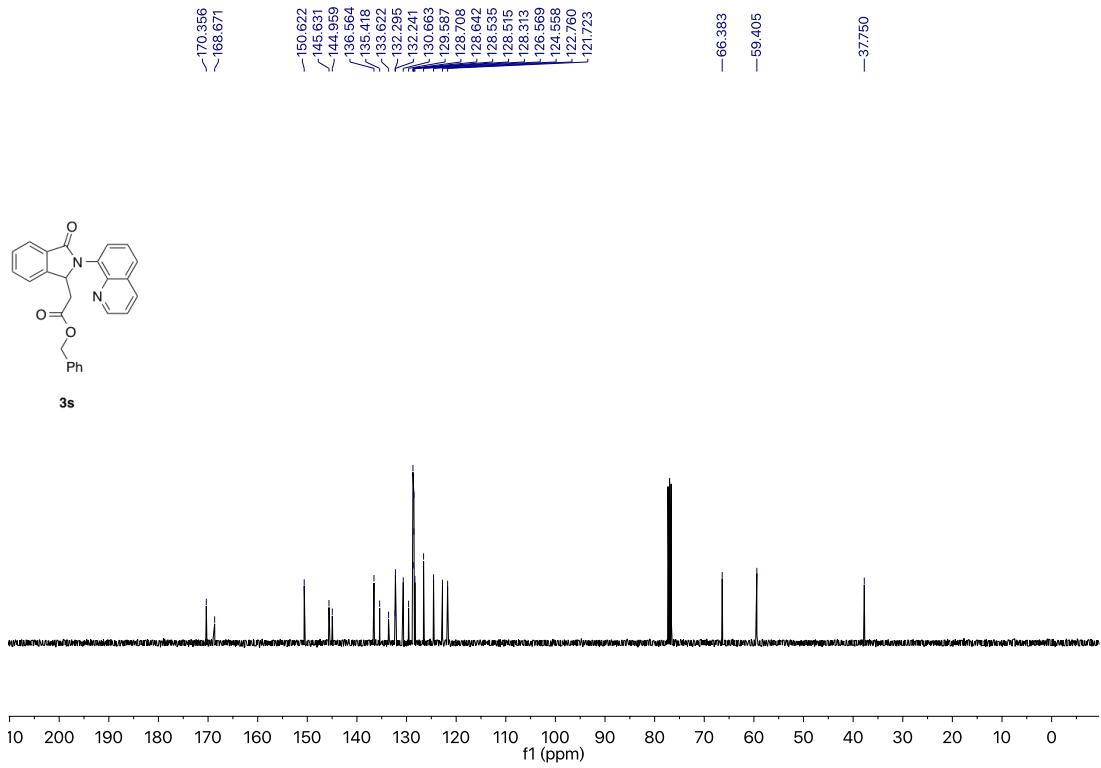
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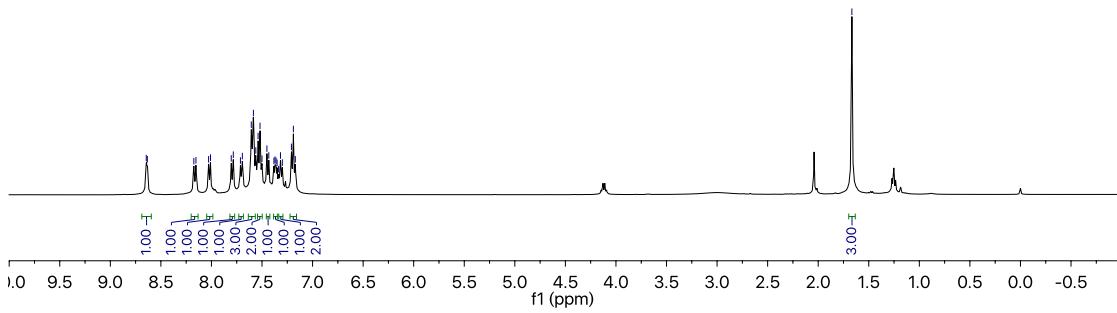
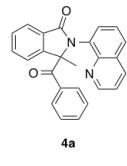
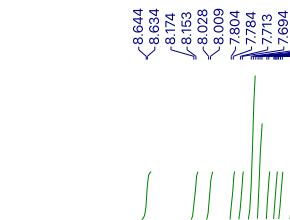
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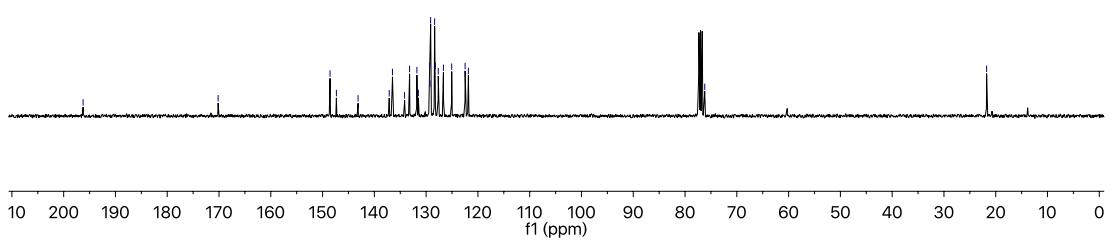
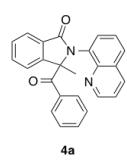
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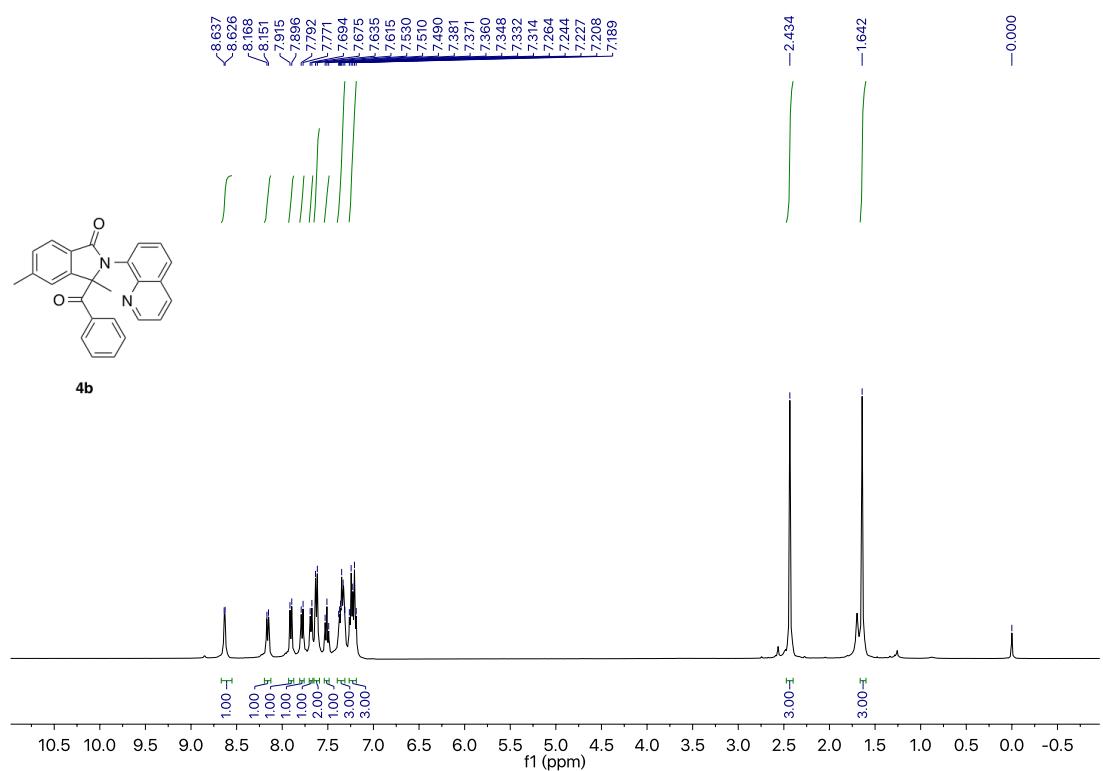
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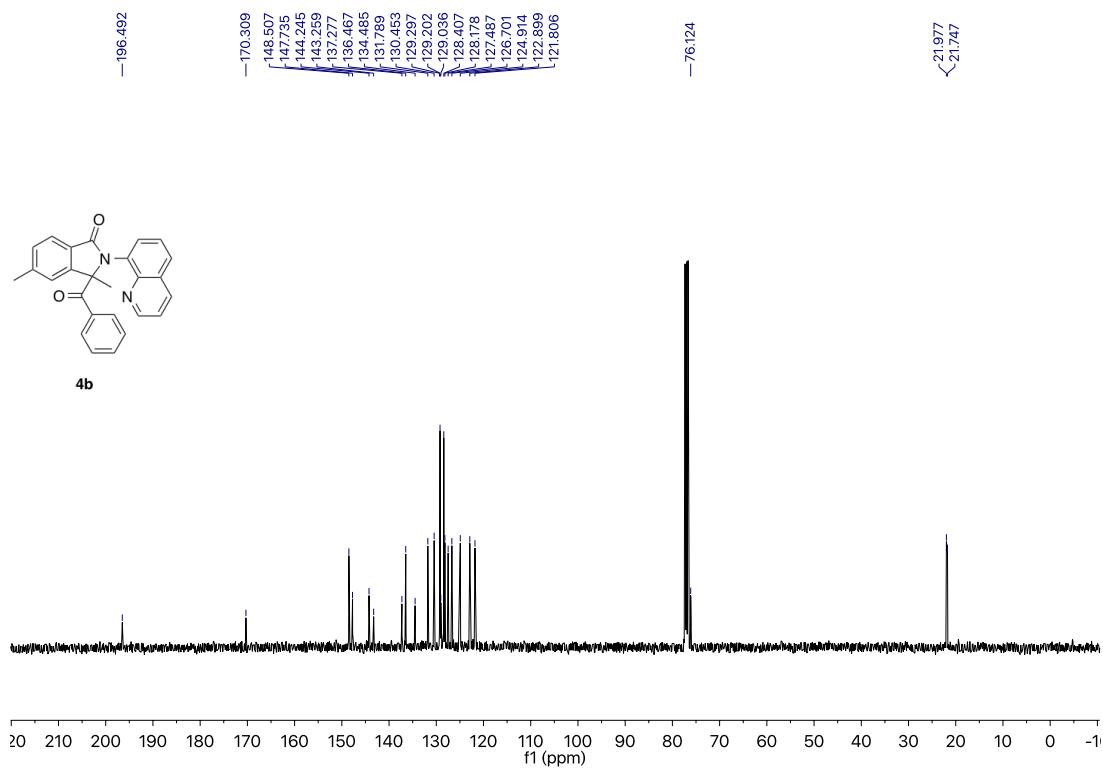
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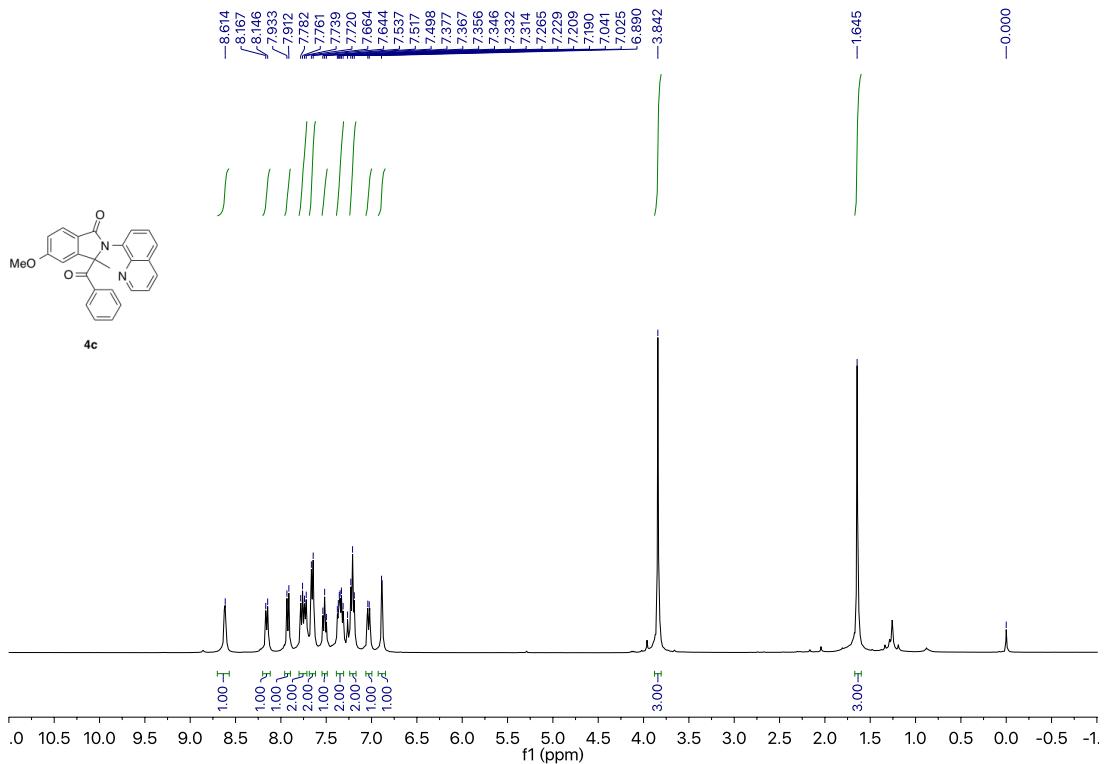
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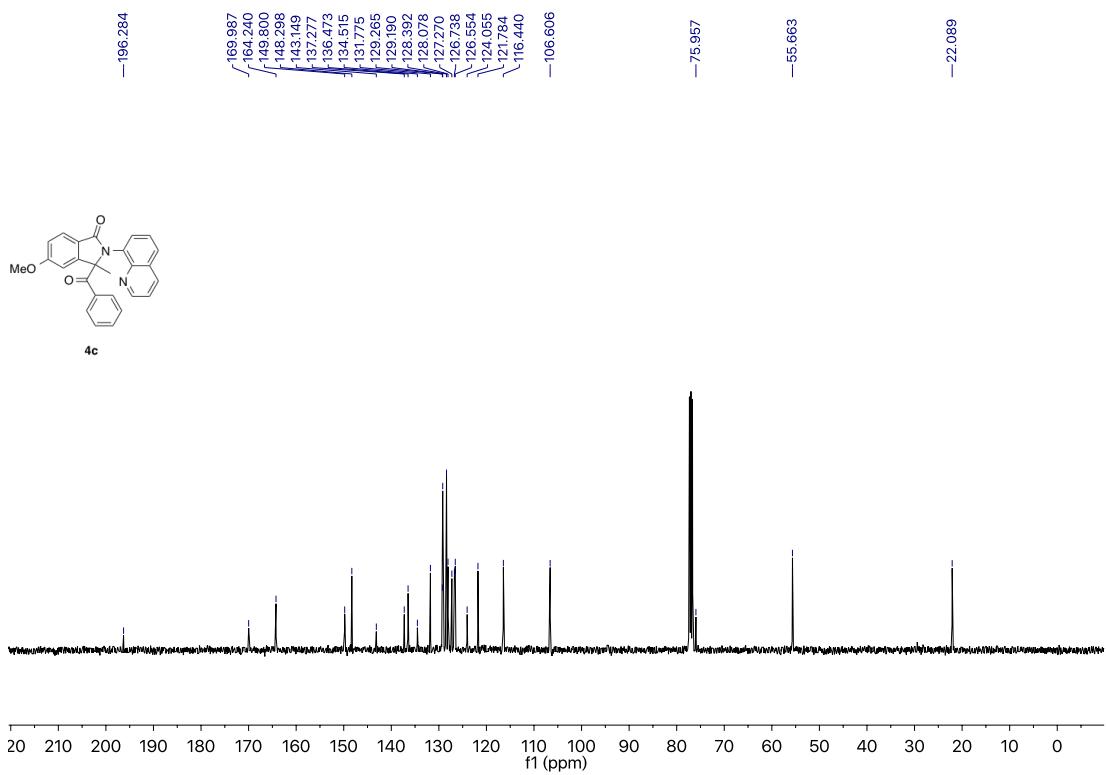
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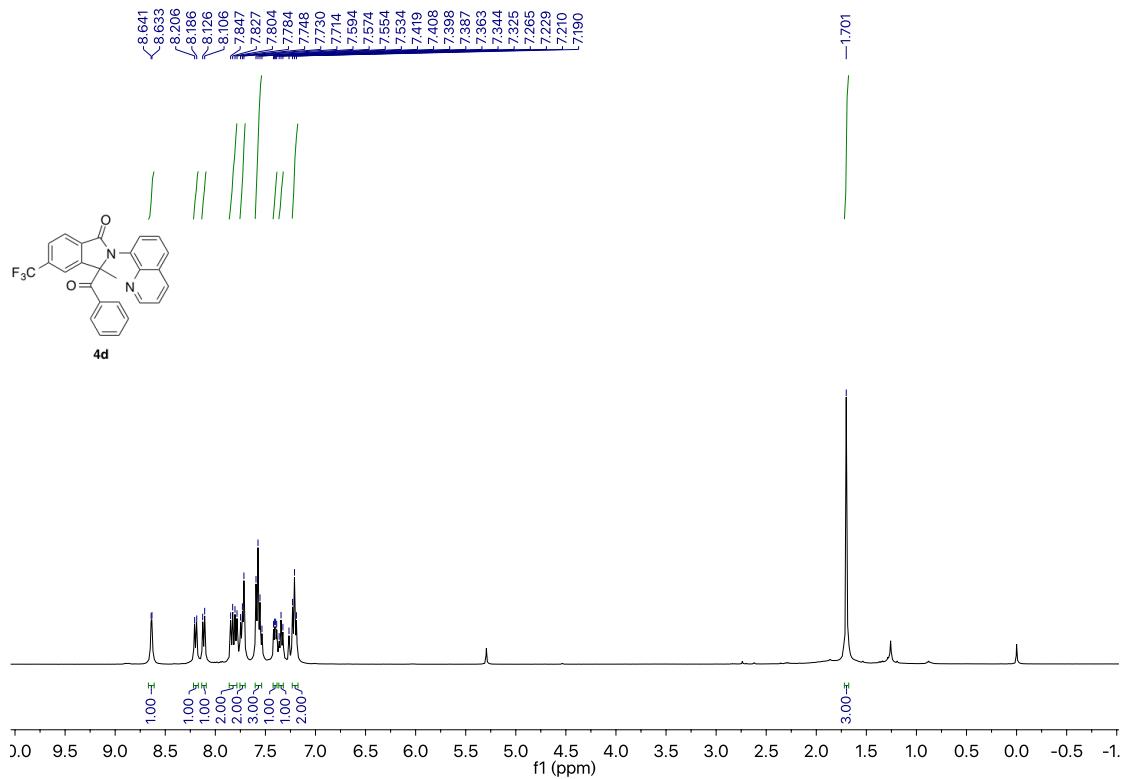
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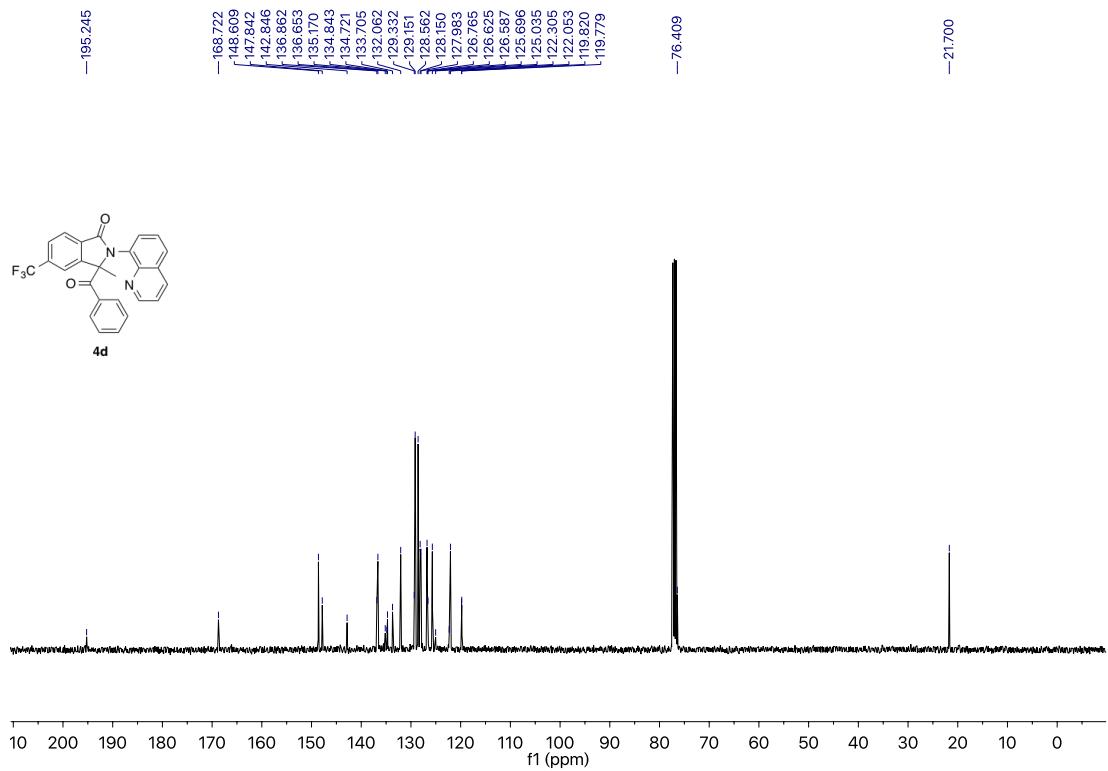
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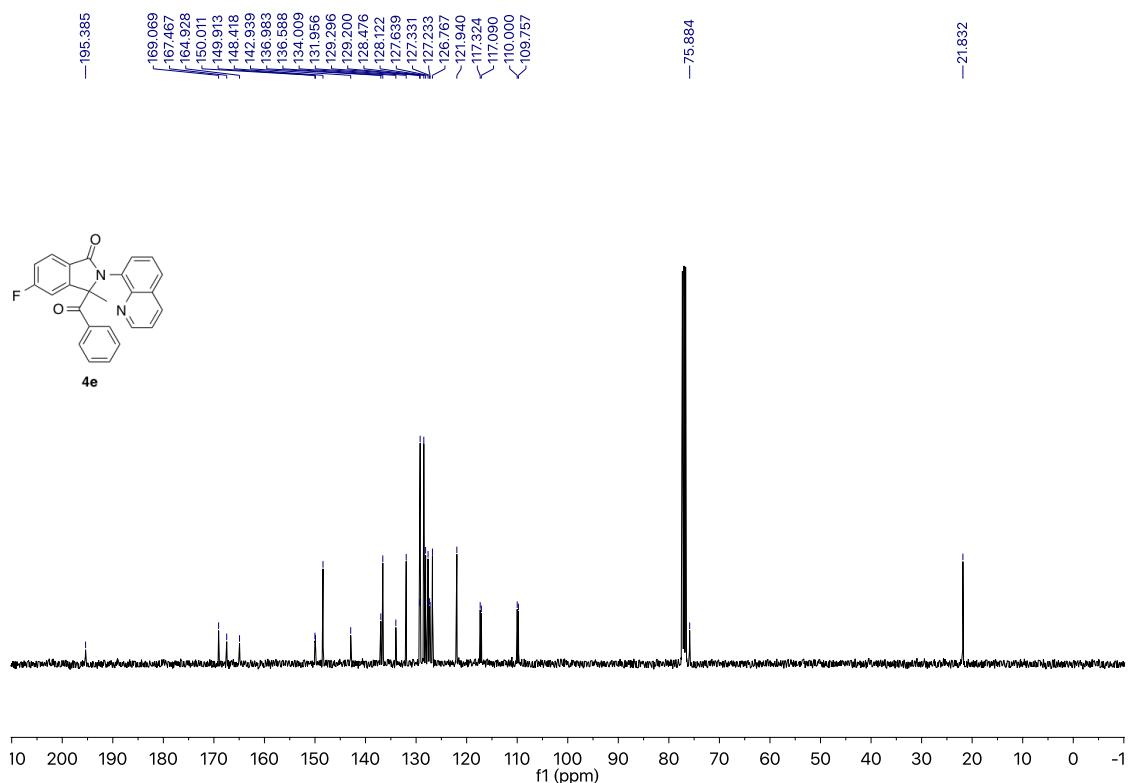
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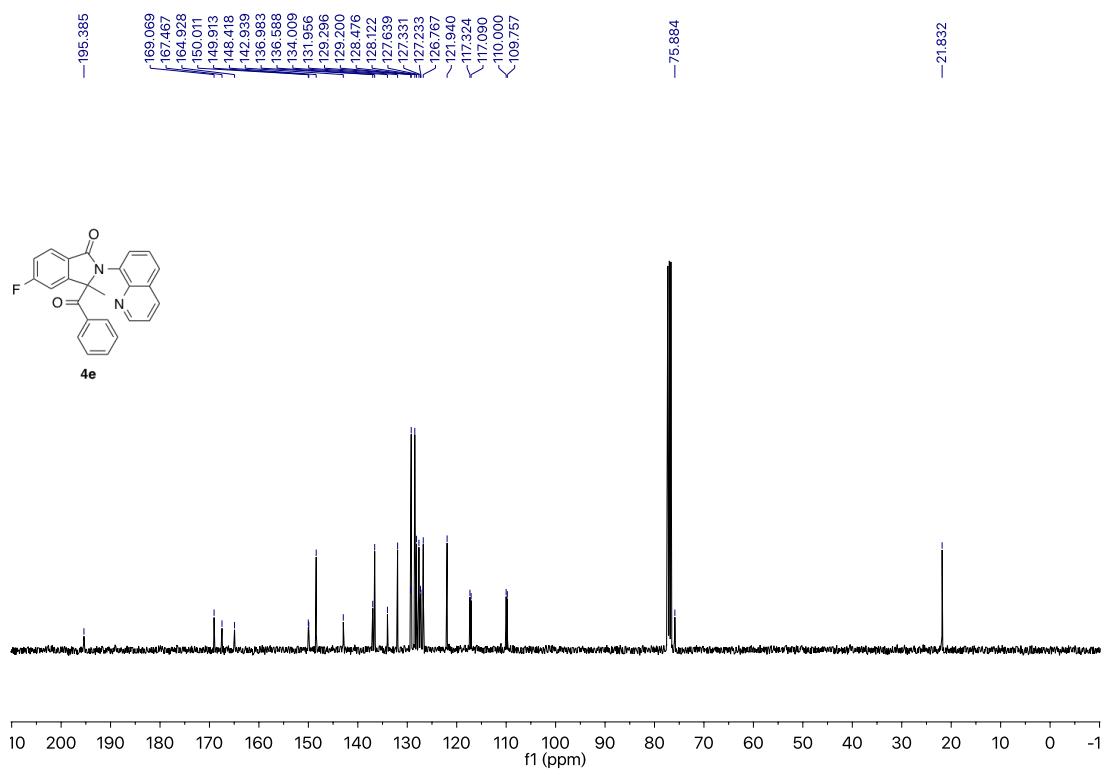
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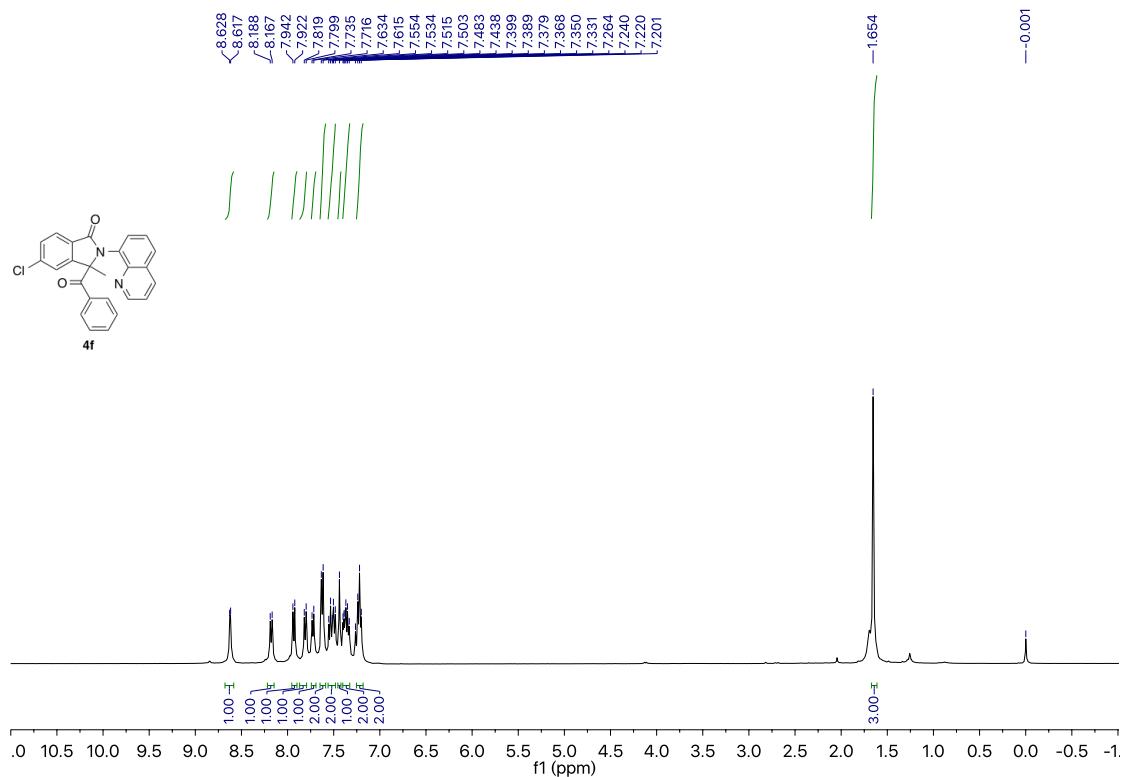
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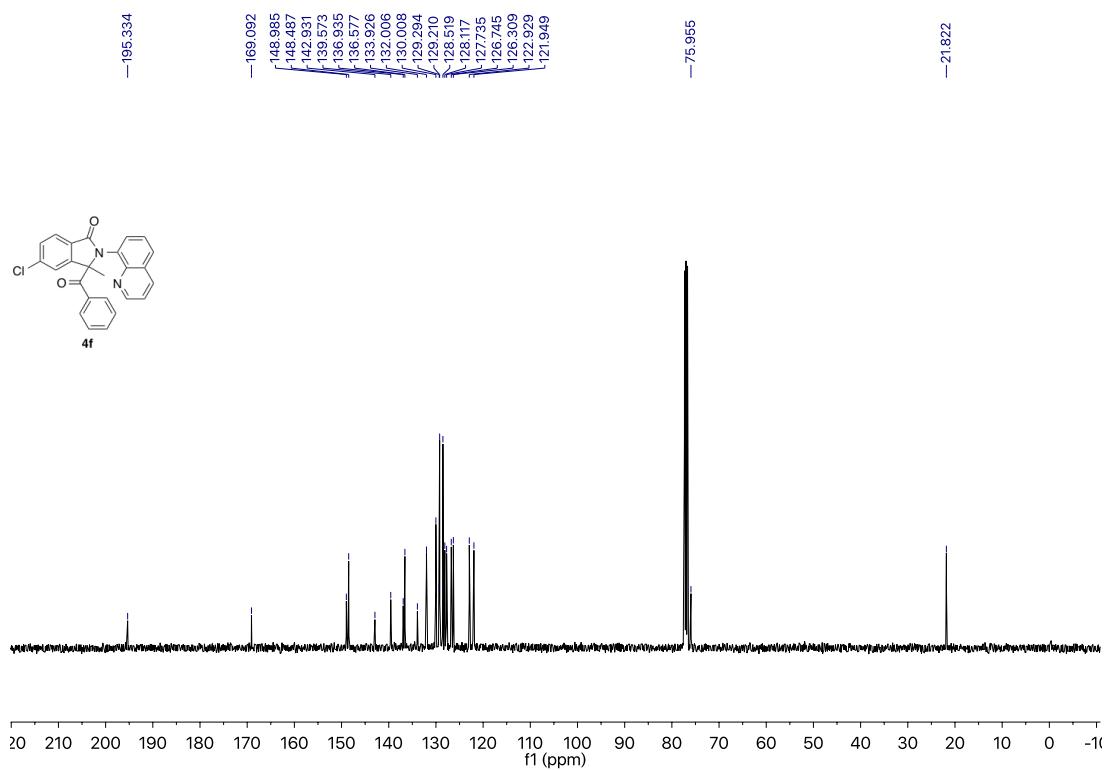
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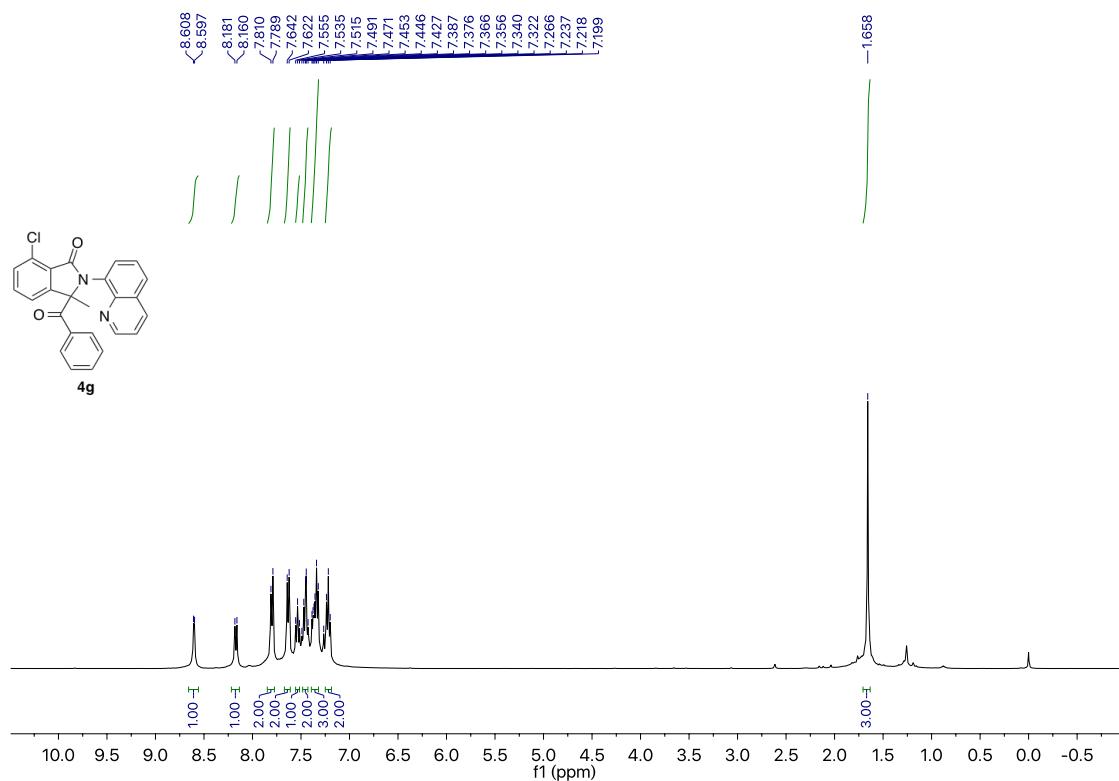
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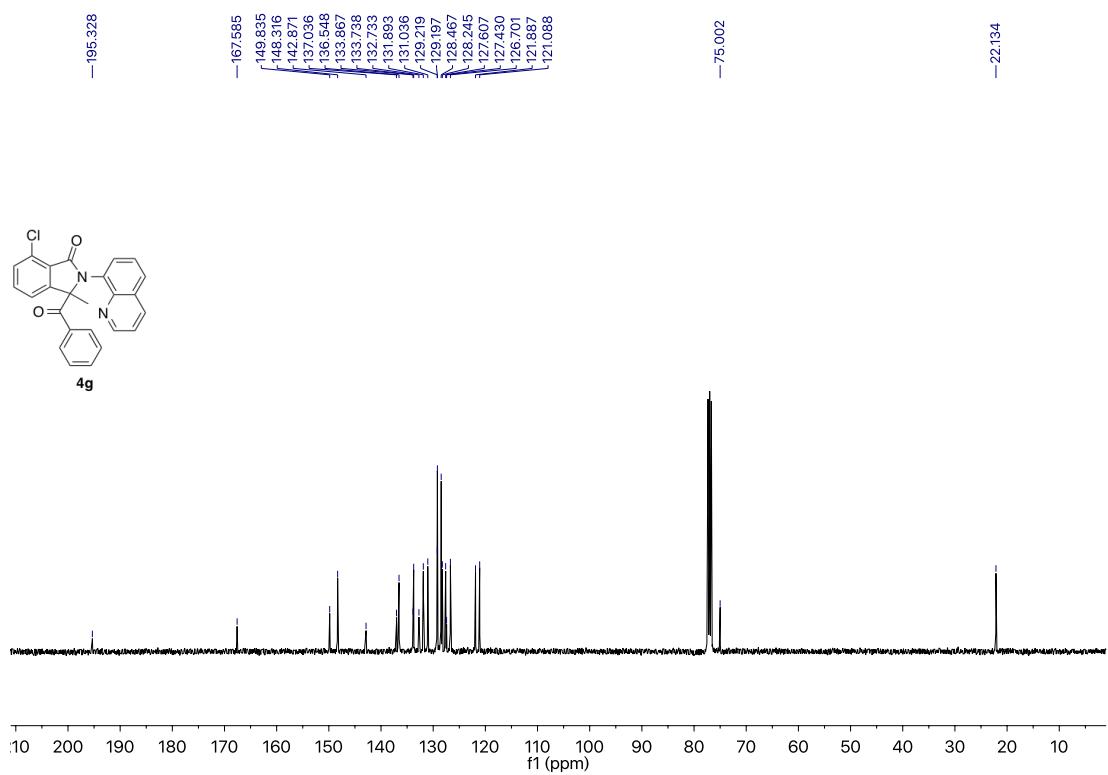
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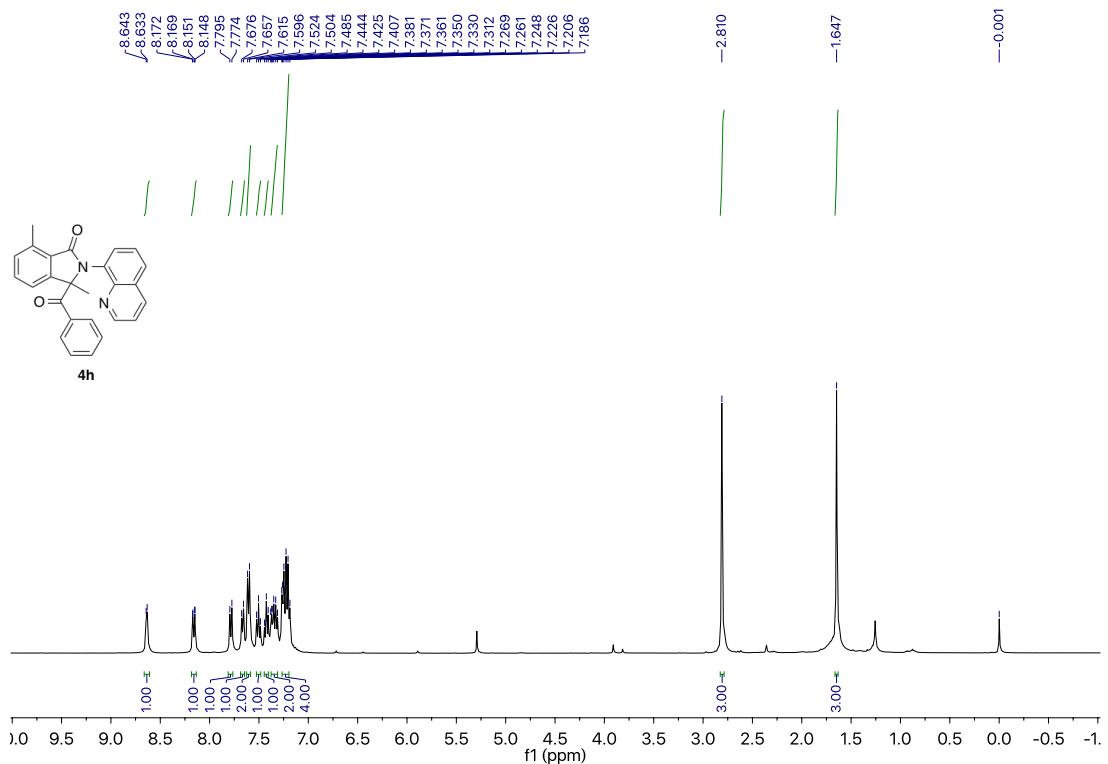
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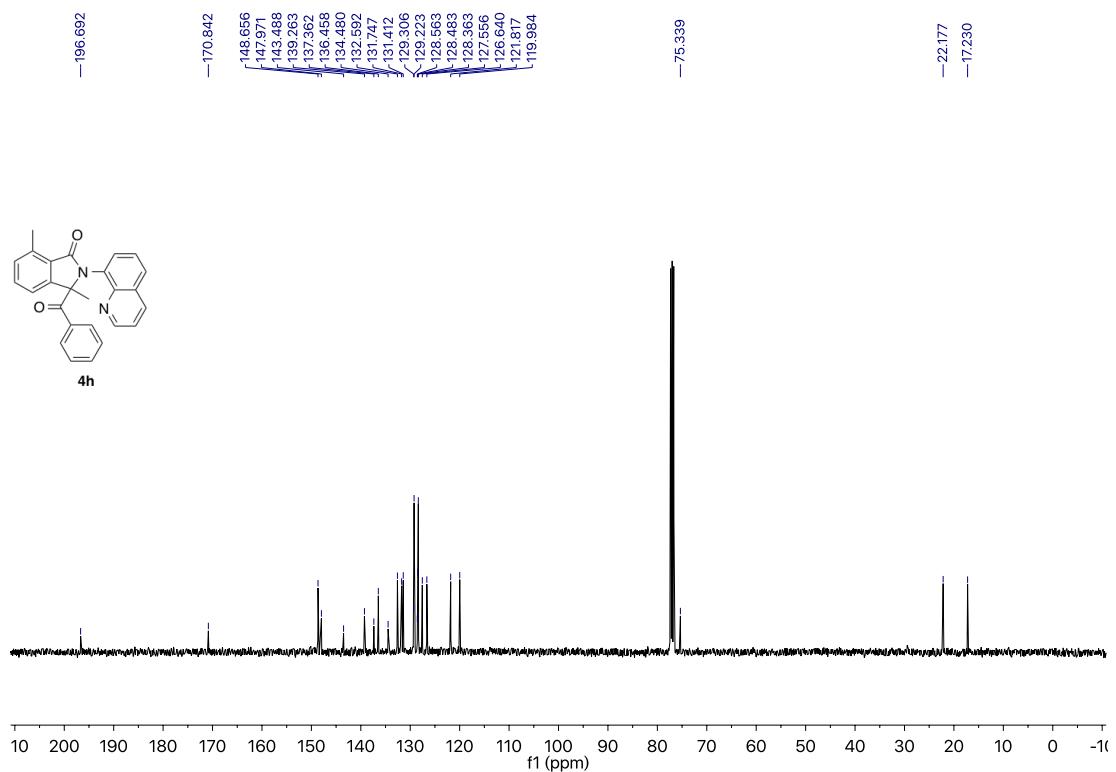
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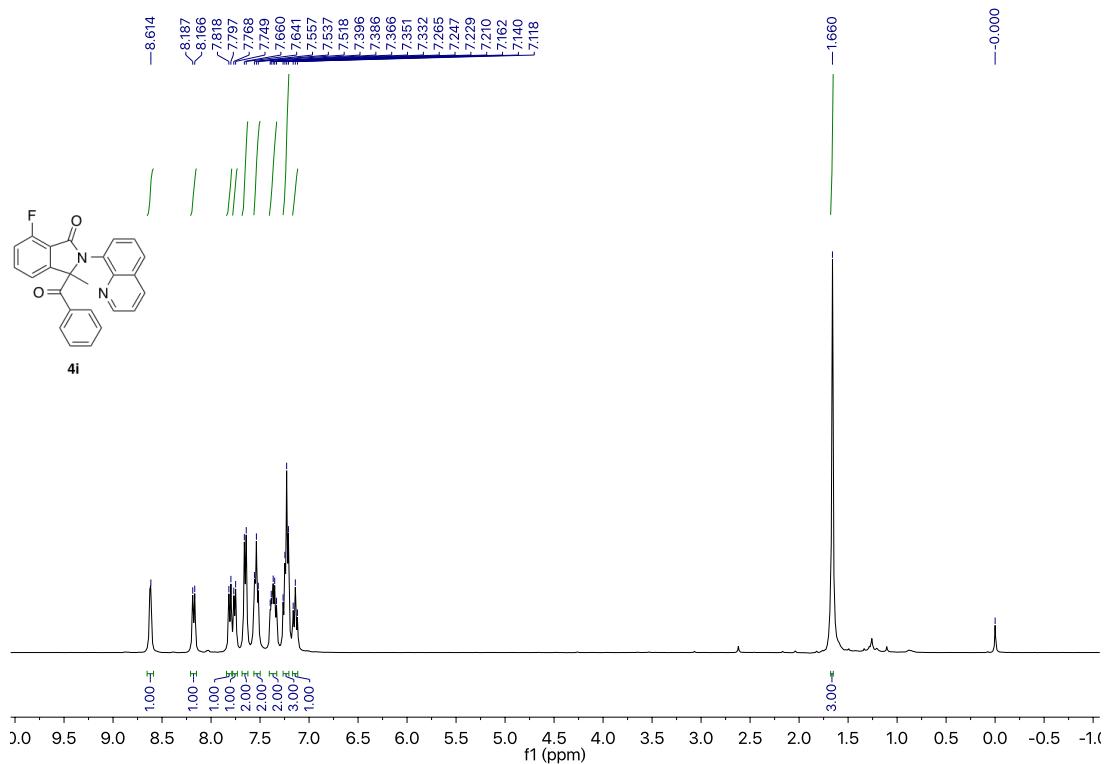
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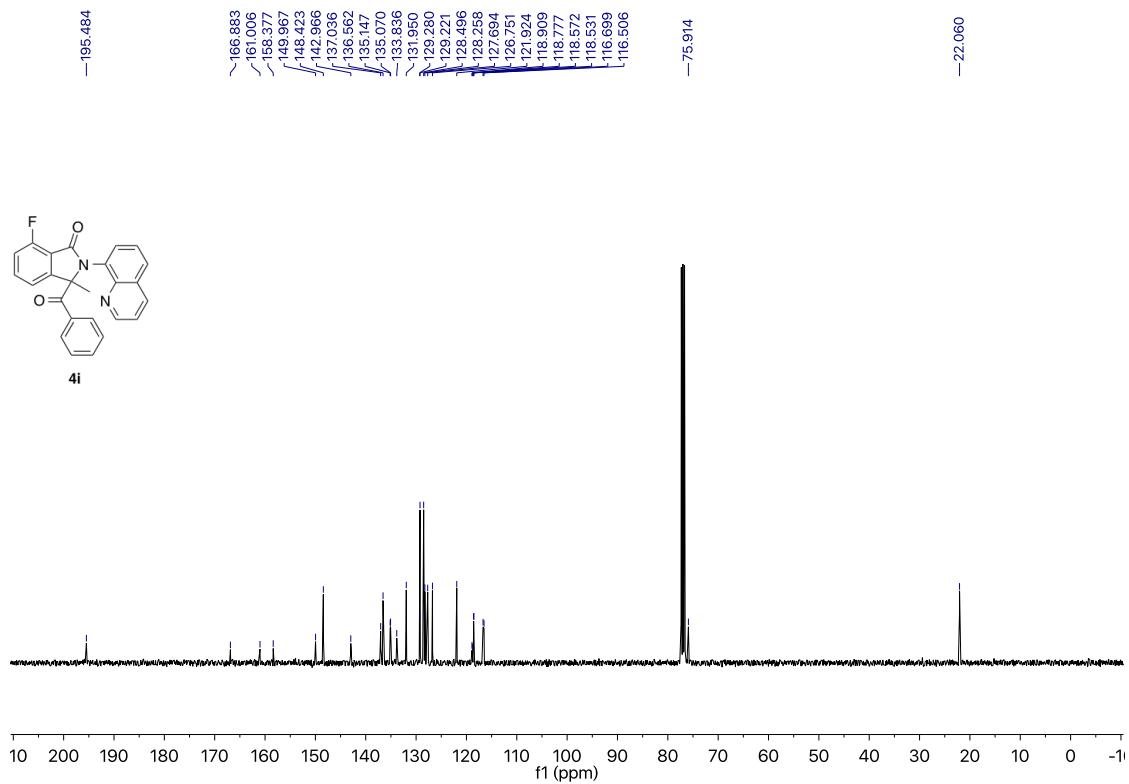
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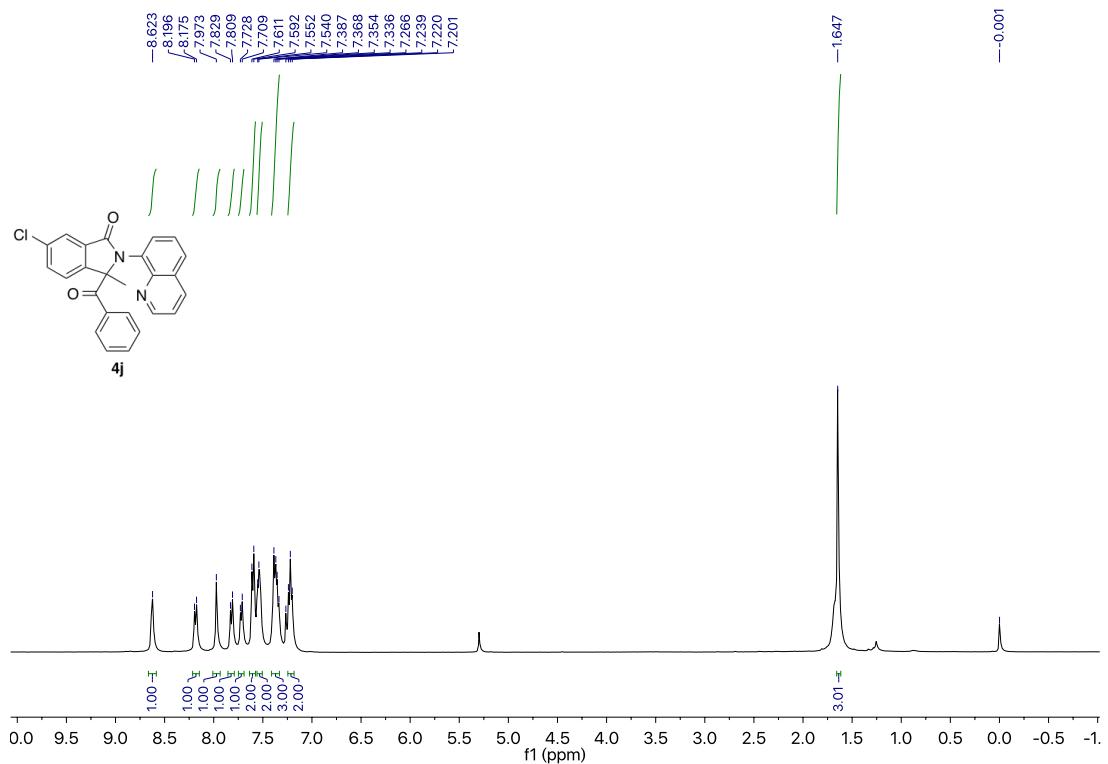
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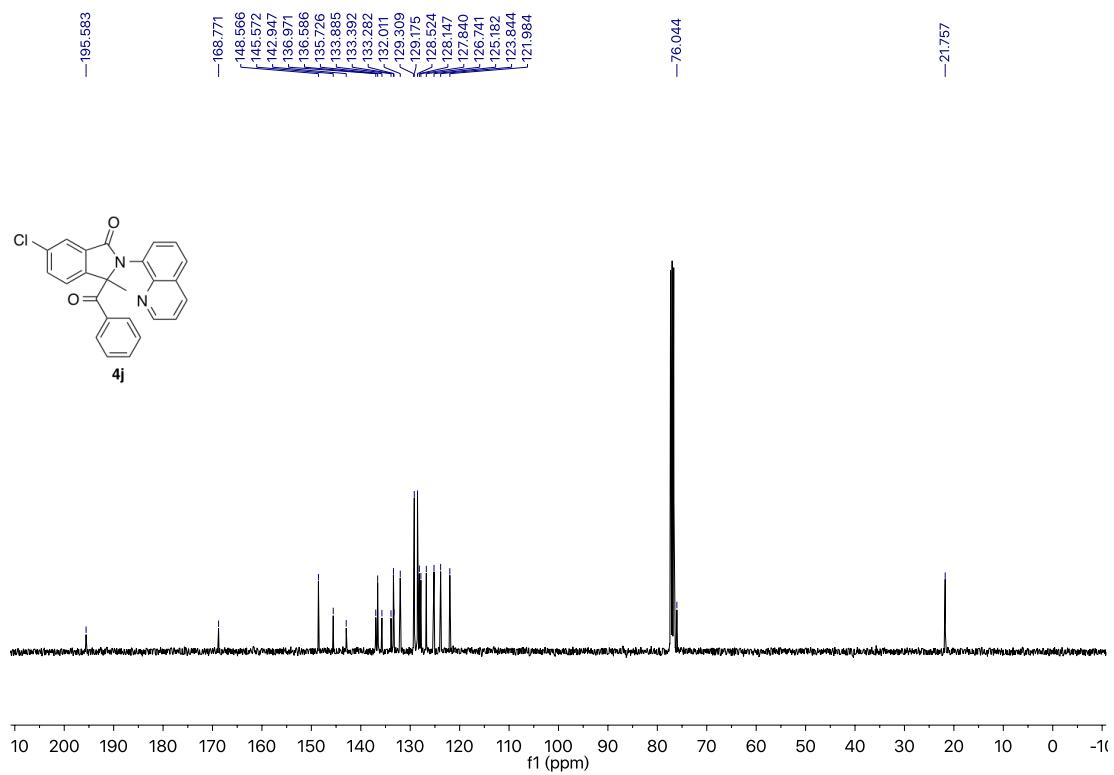
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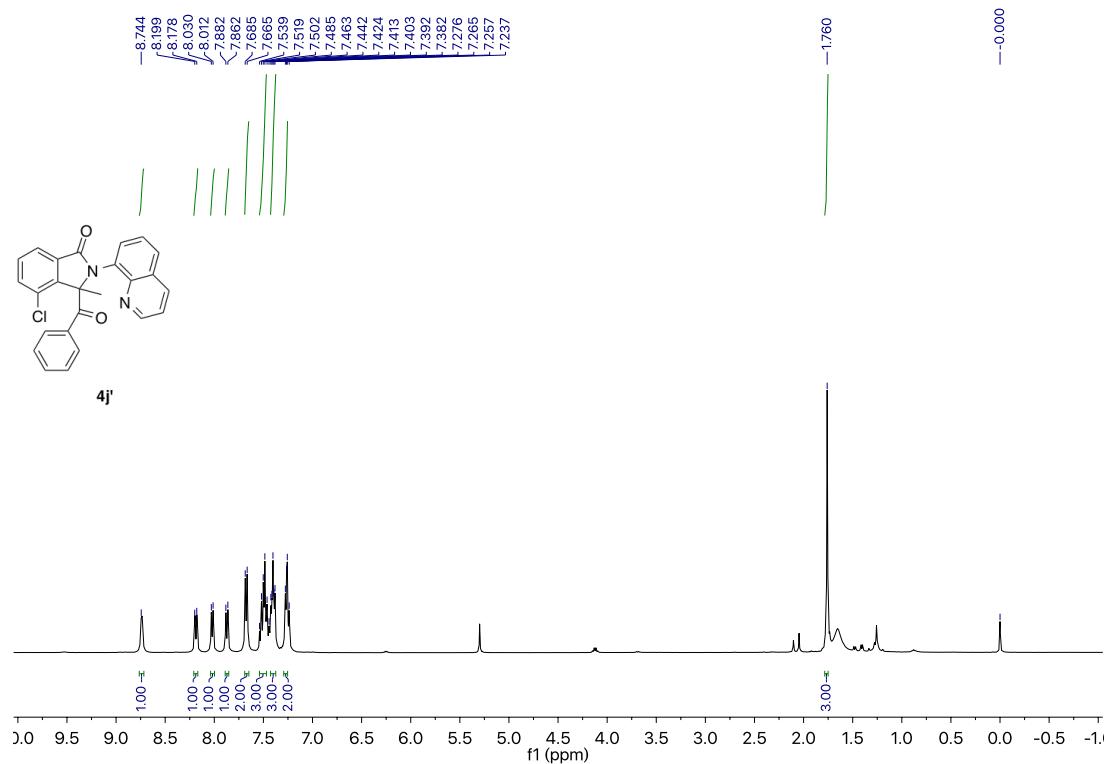
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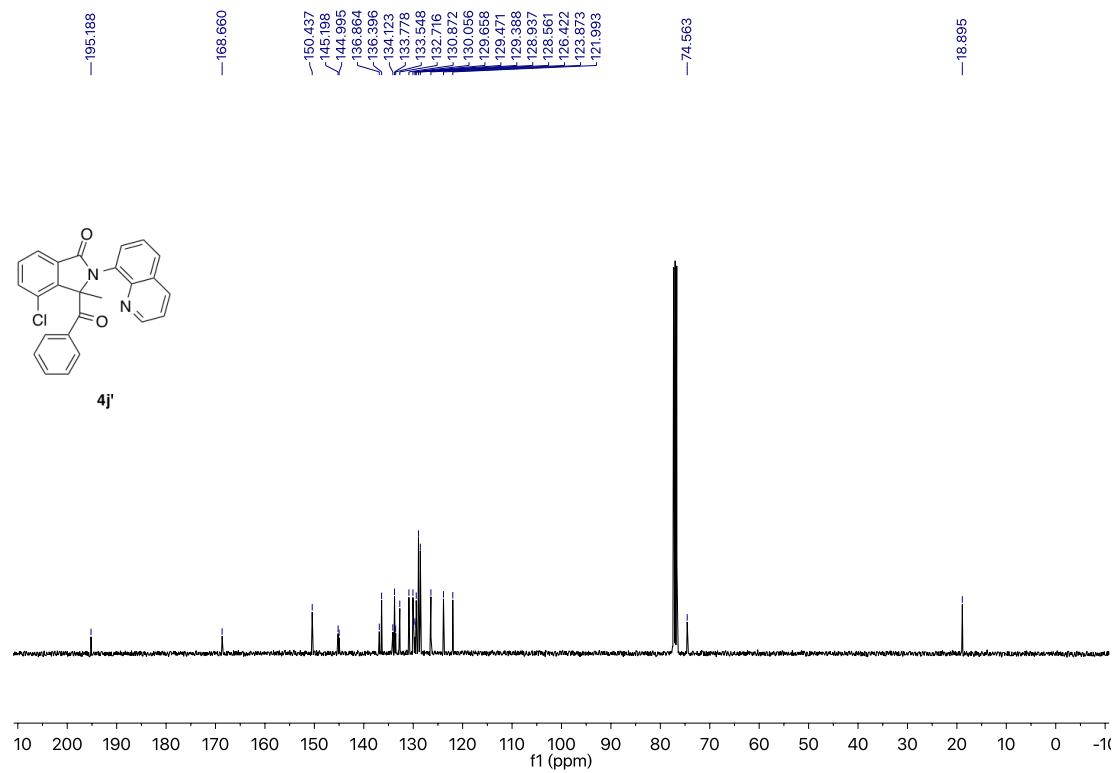
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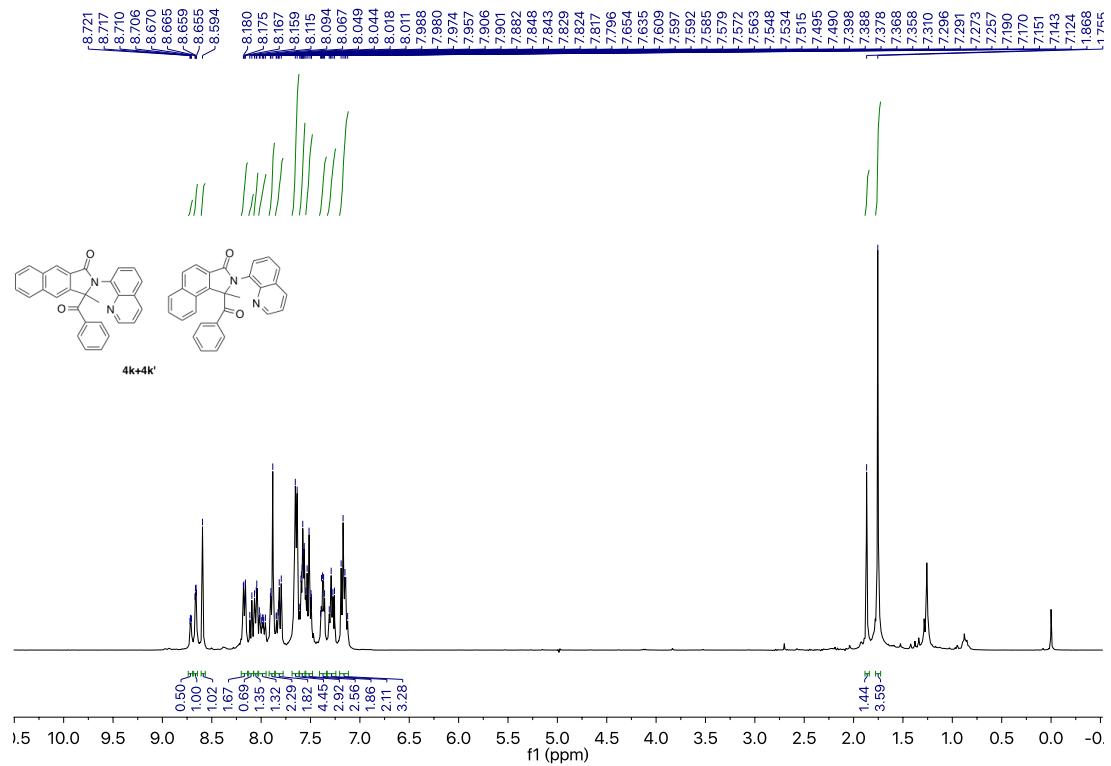
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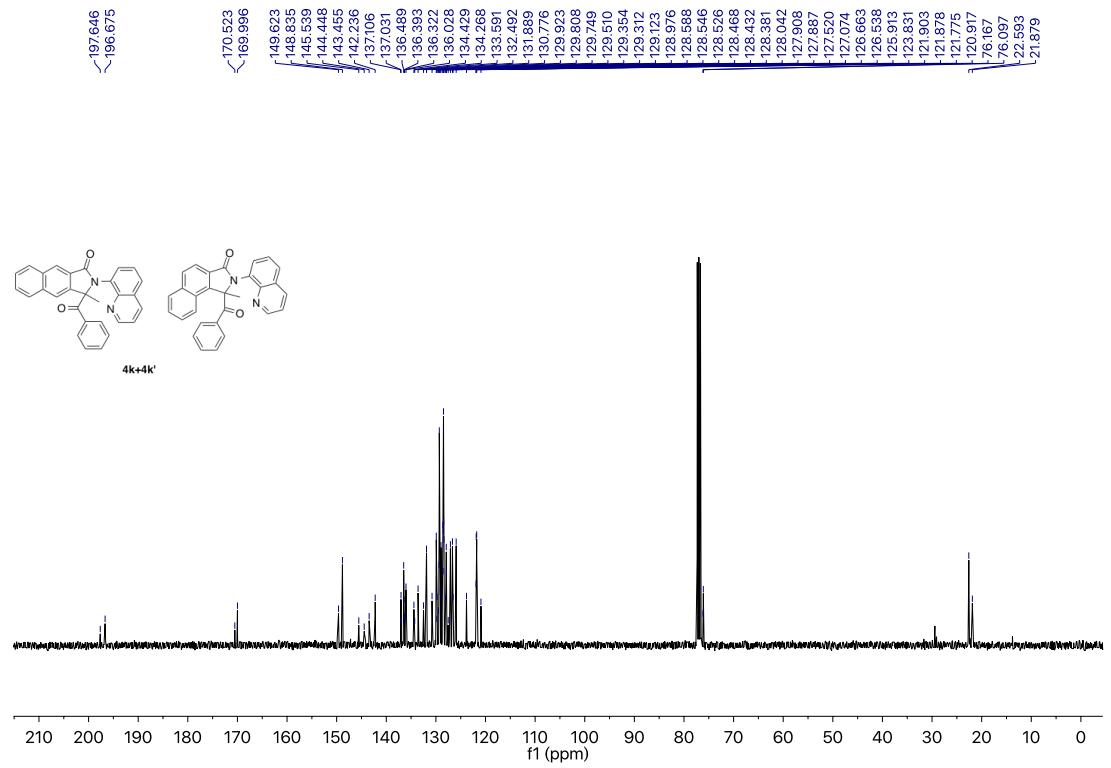
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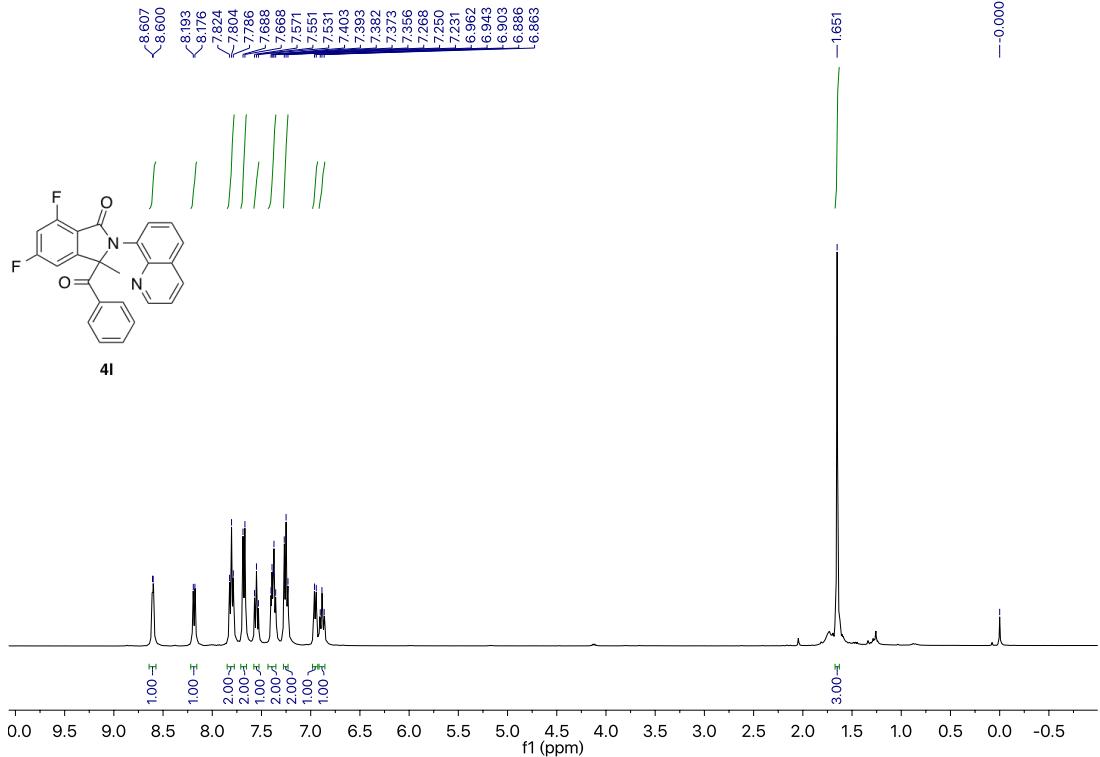
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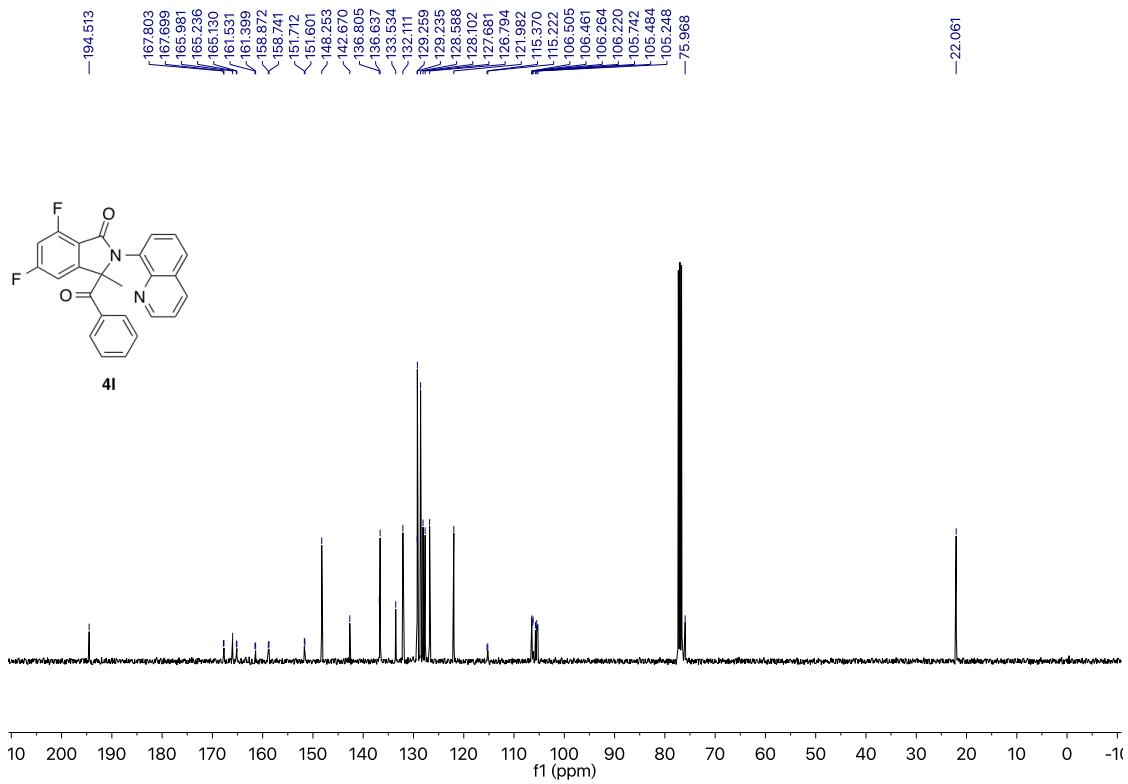
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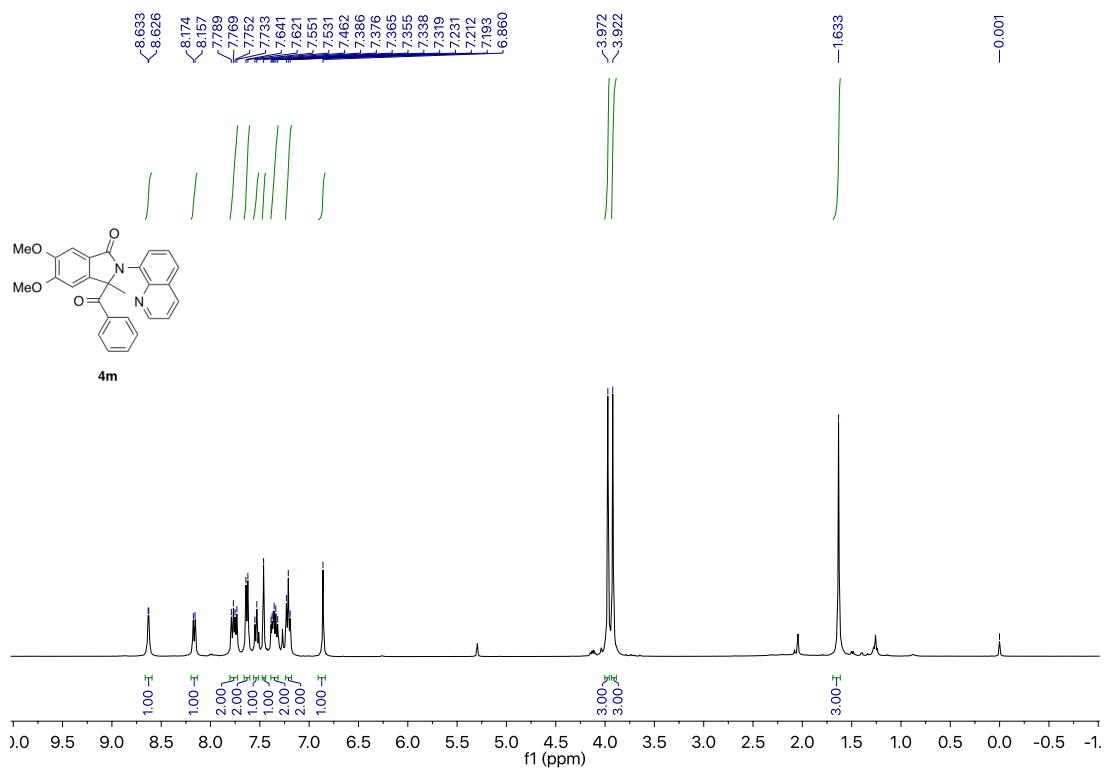
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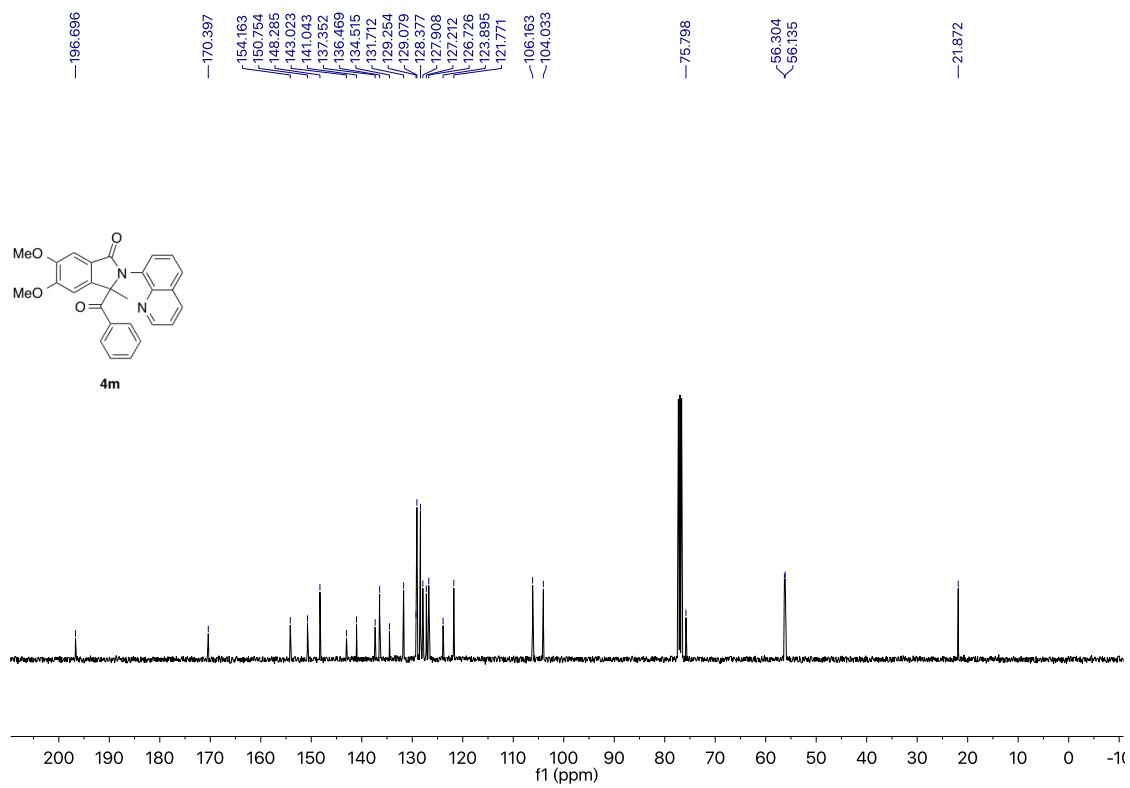
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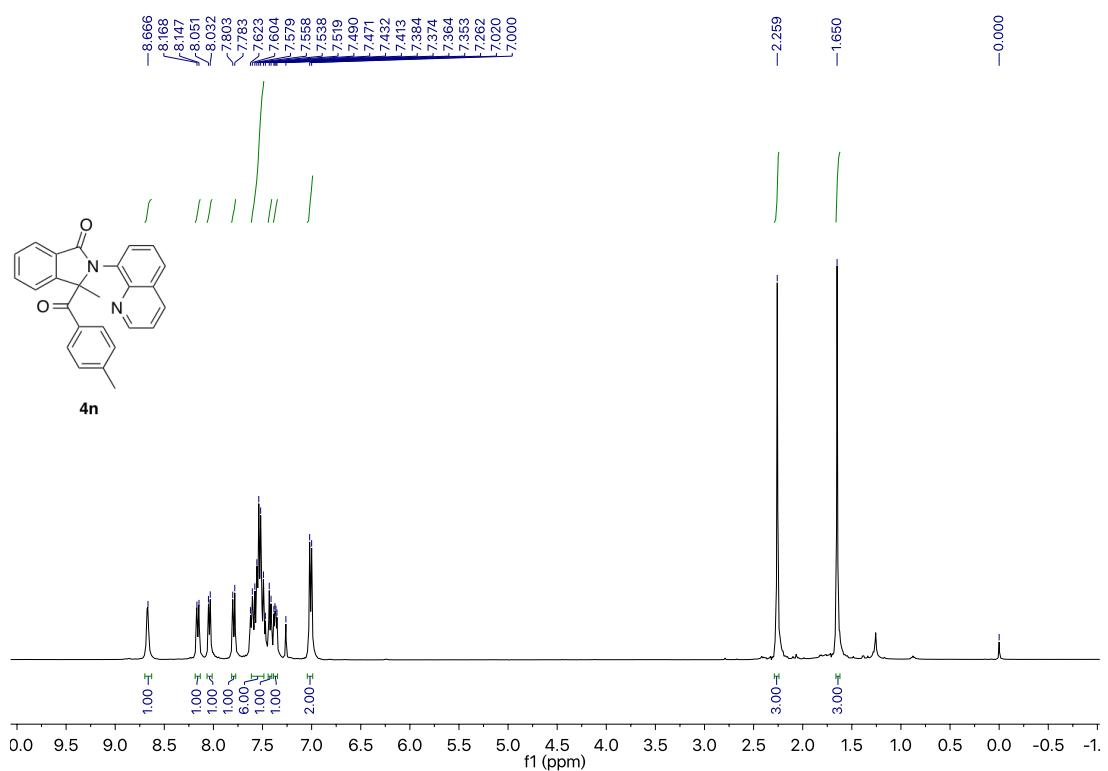
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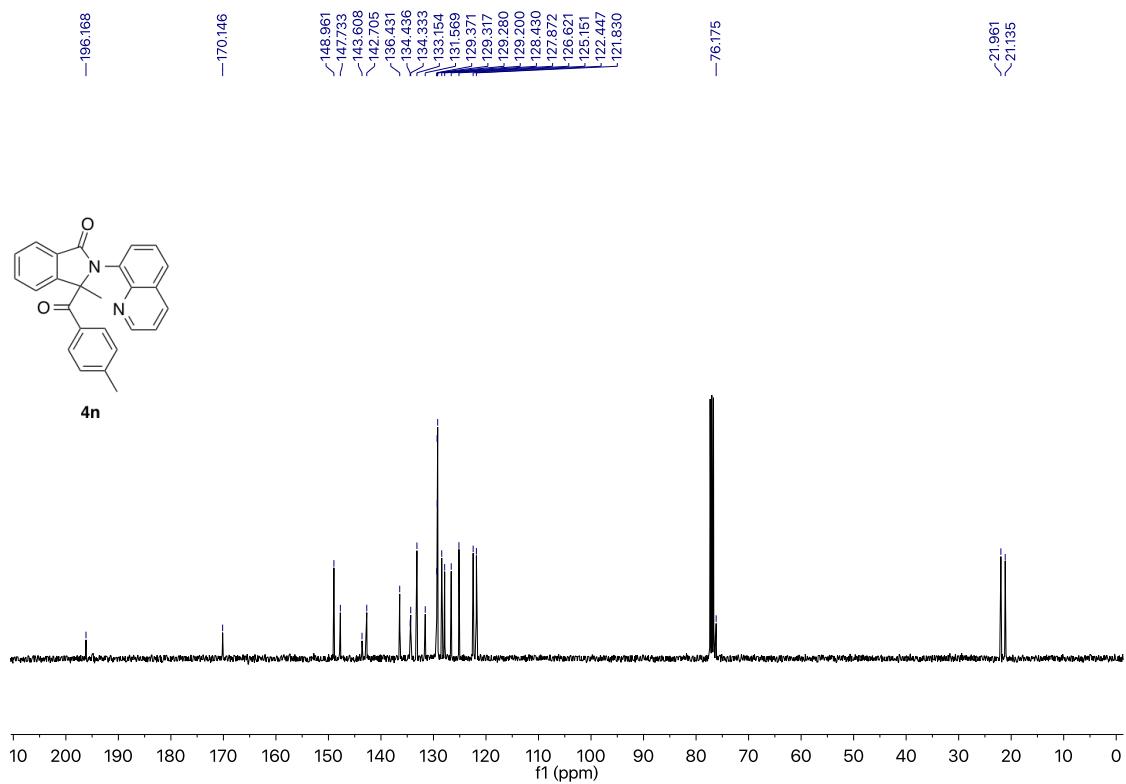
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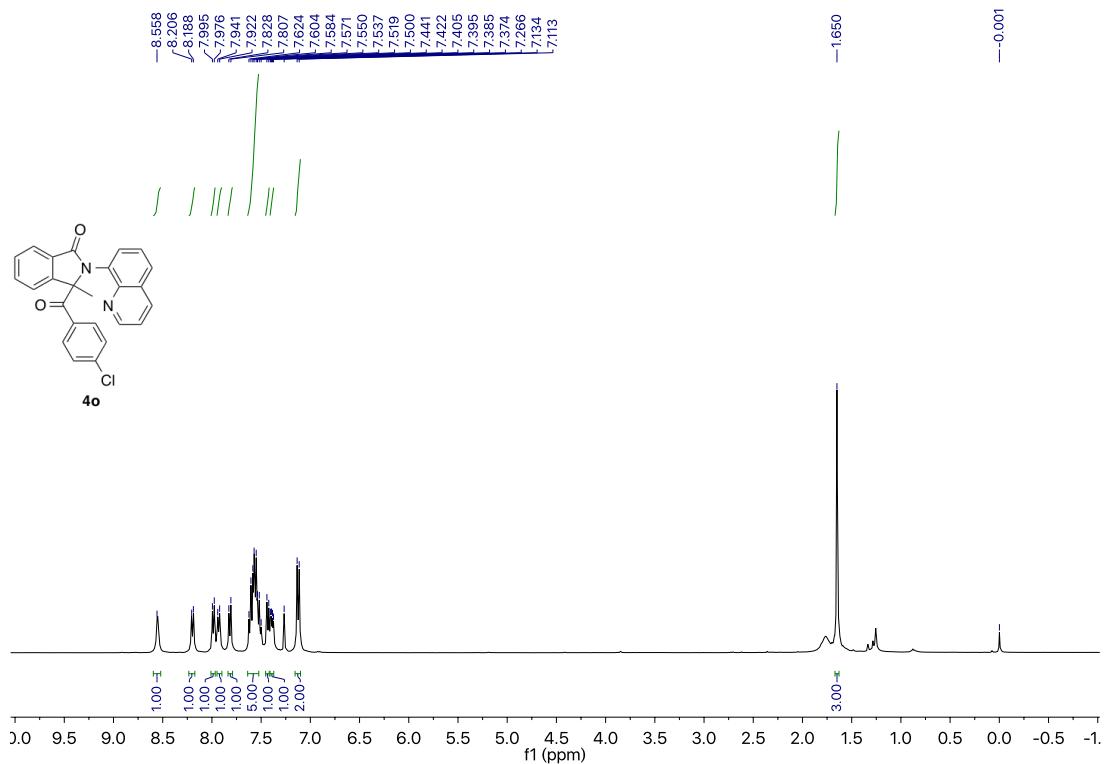
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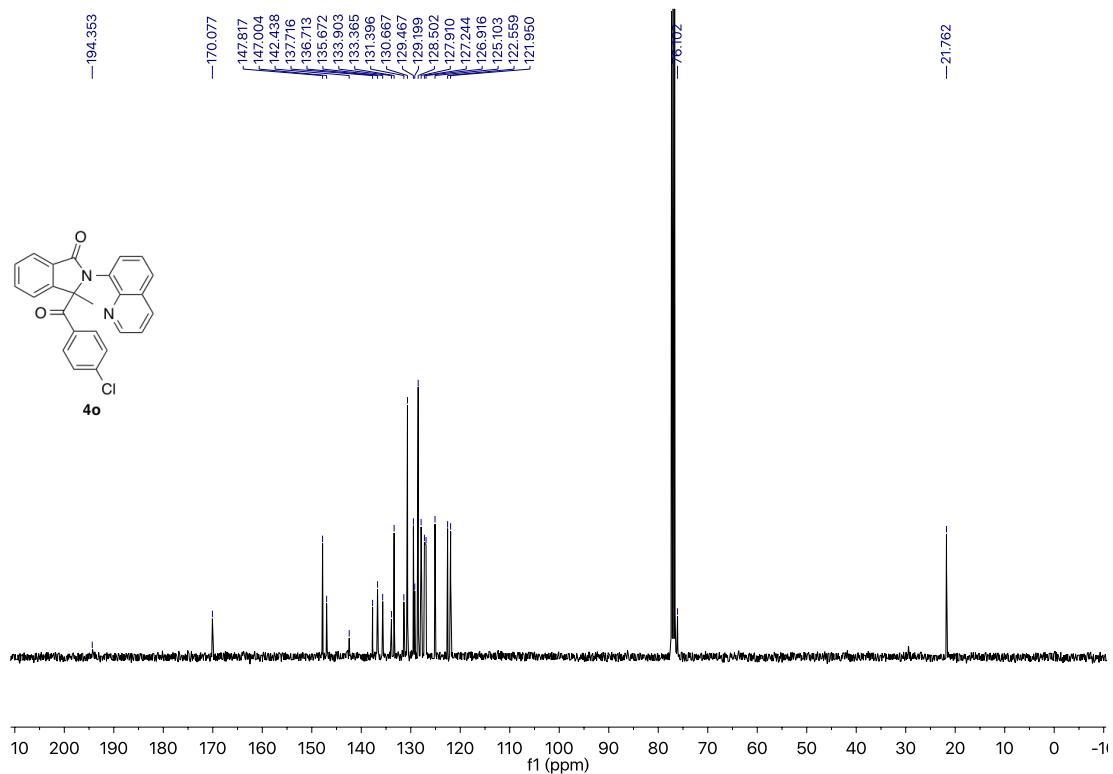
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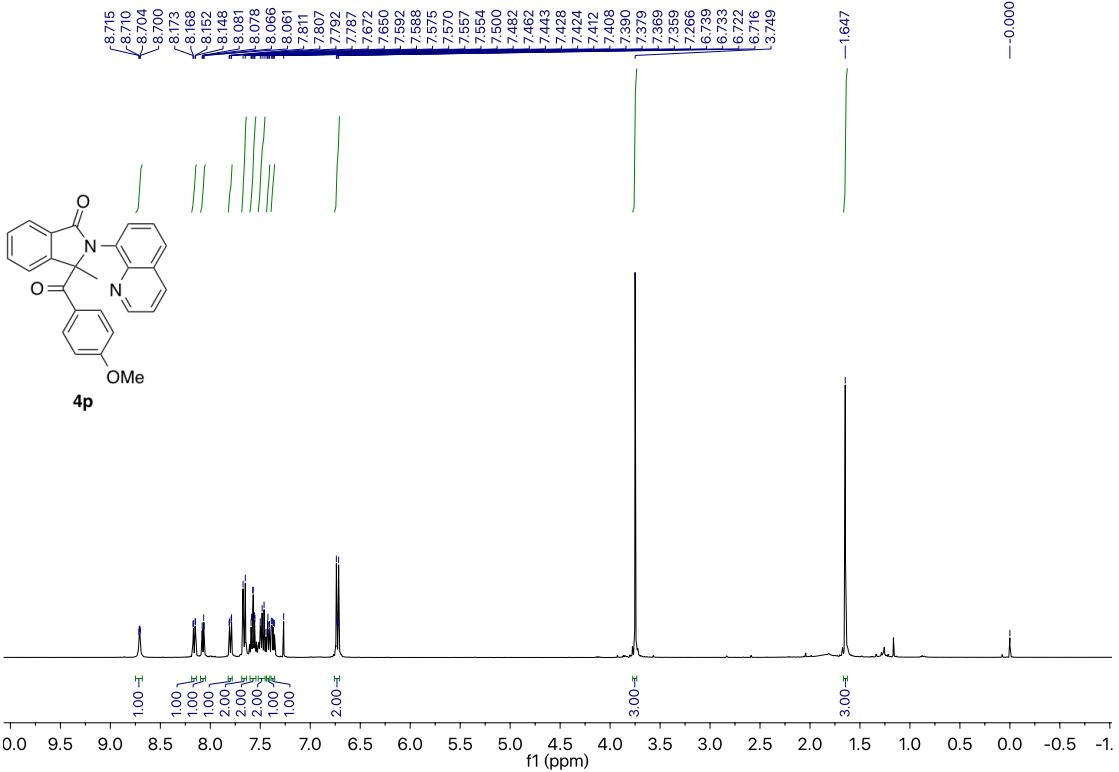
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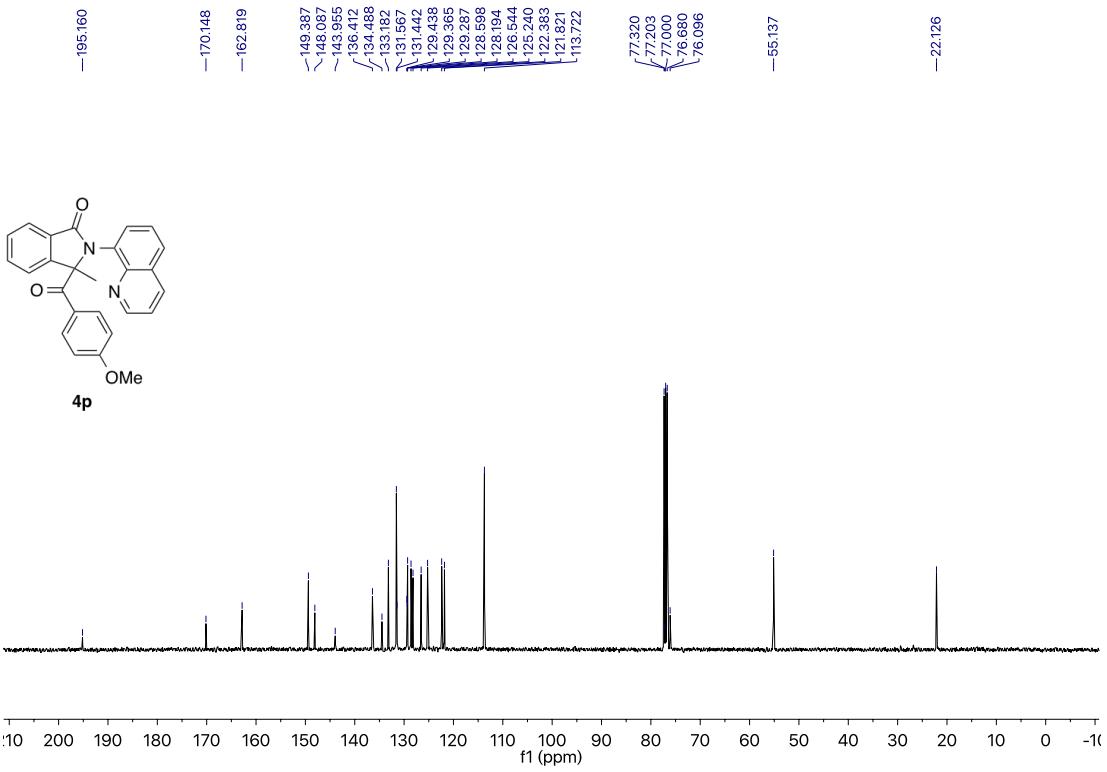
¹³C NMR (100 MHz, CDCl₃)



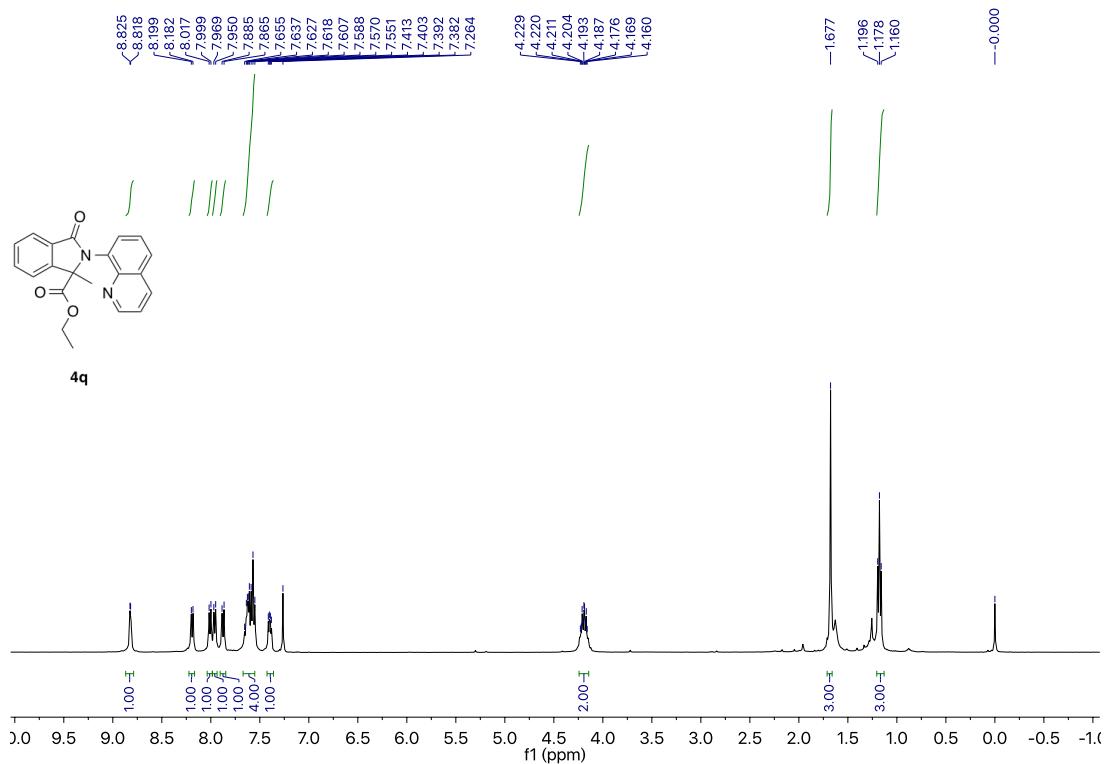
¹H NMR (400 MHz, CDCl₃)



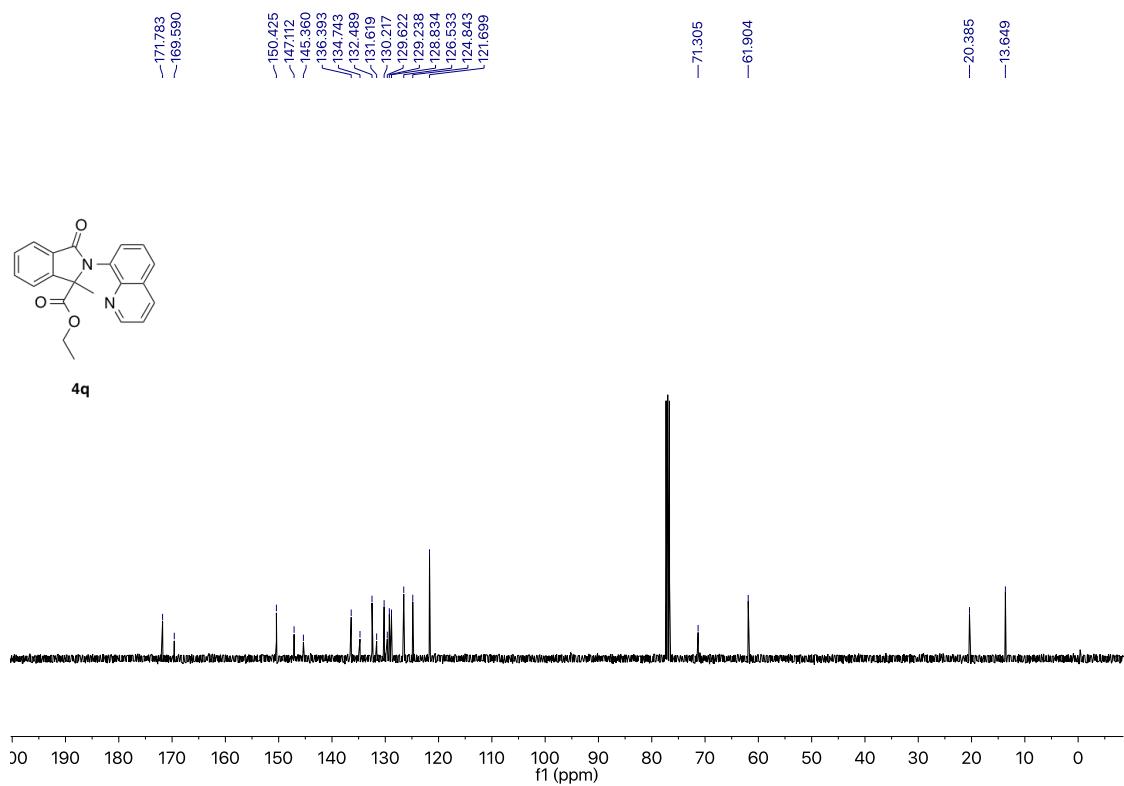
¹³C NMR (100 MHz, CDCl₃)



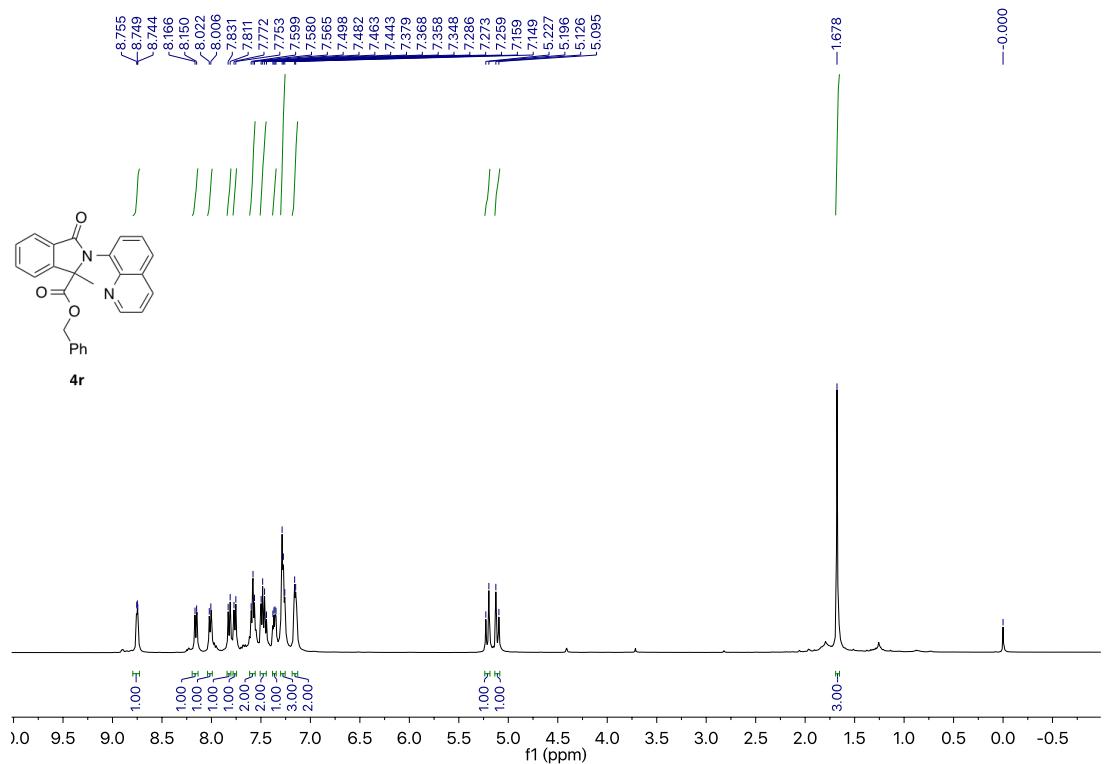
¹H NMR (400 MHz, CDCl₃)



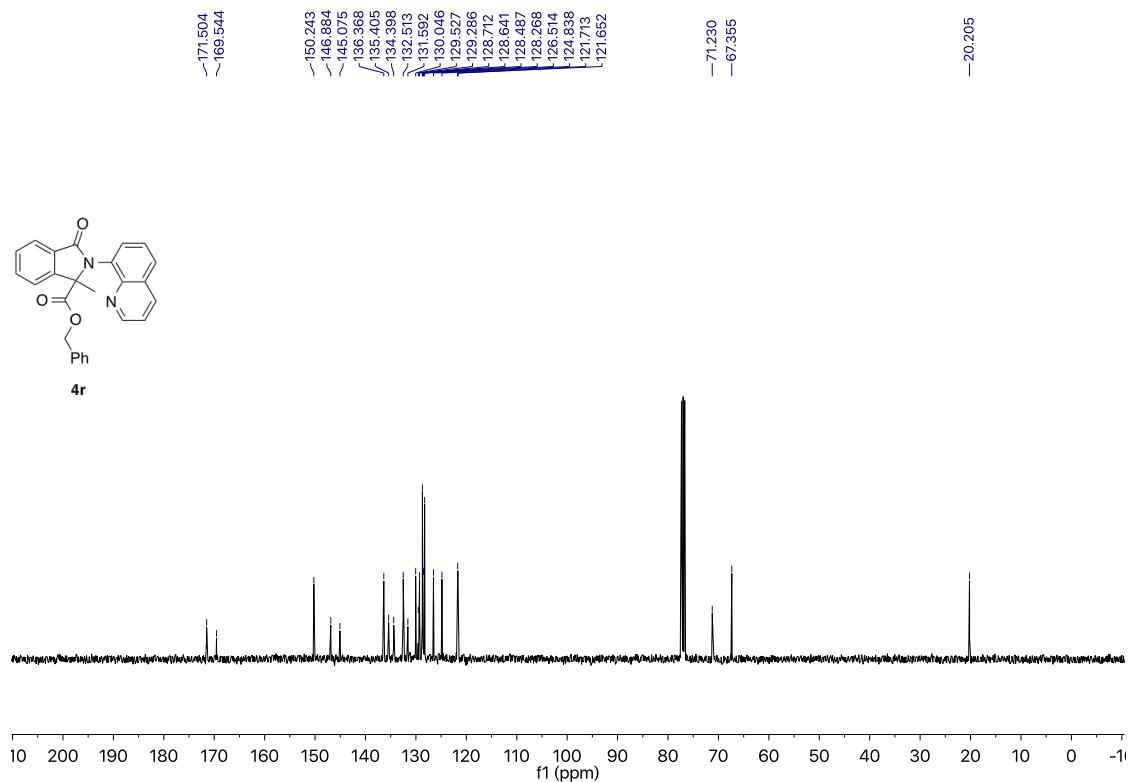
¹³C NMR (100 MHz, CDCl₃)



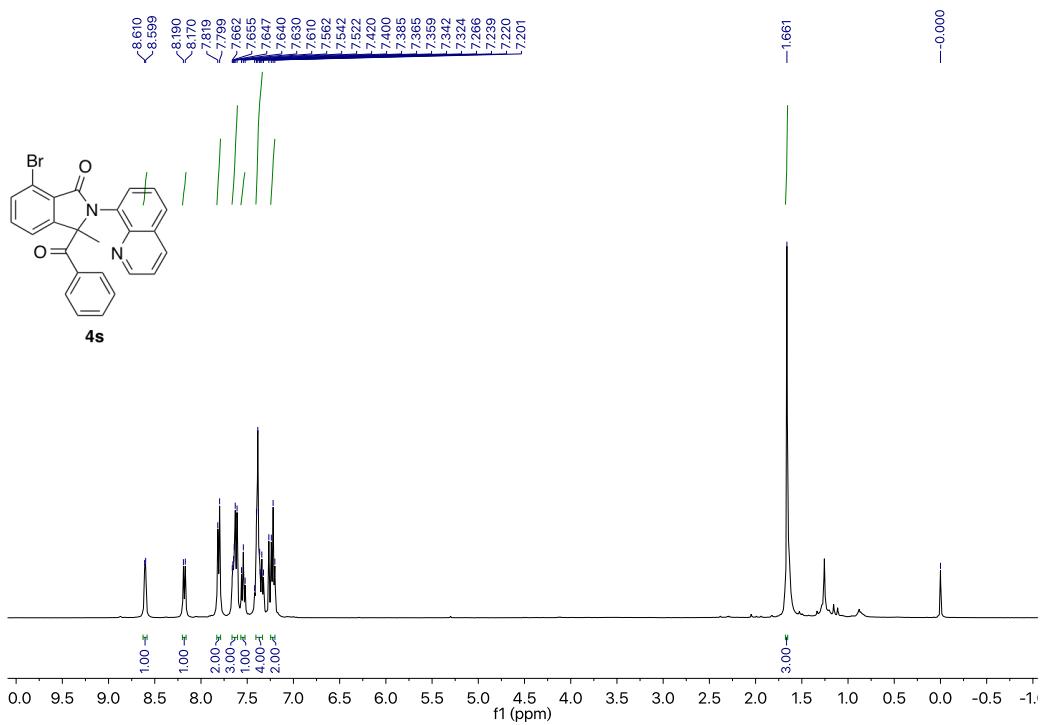
¹H NMR (400 MHz, CDCl₃)



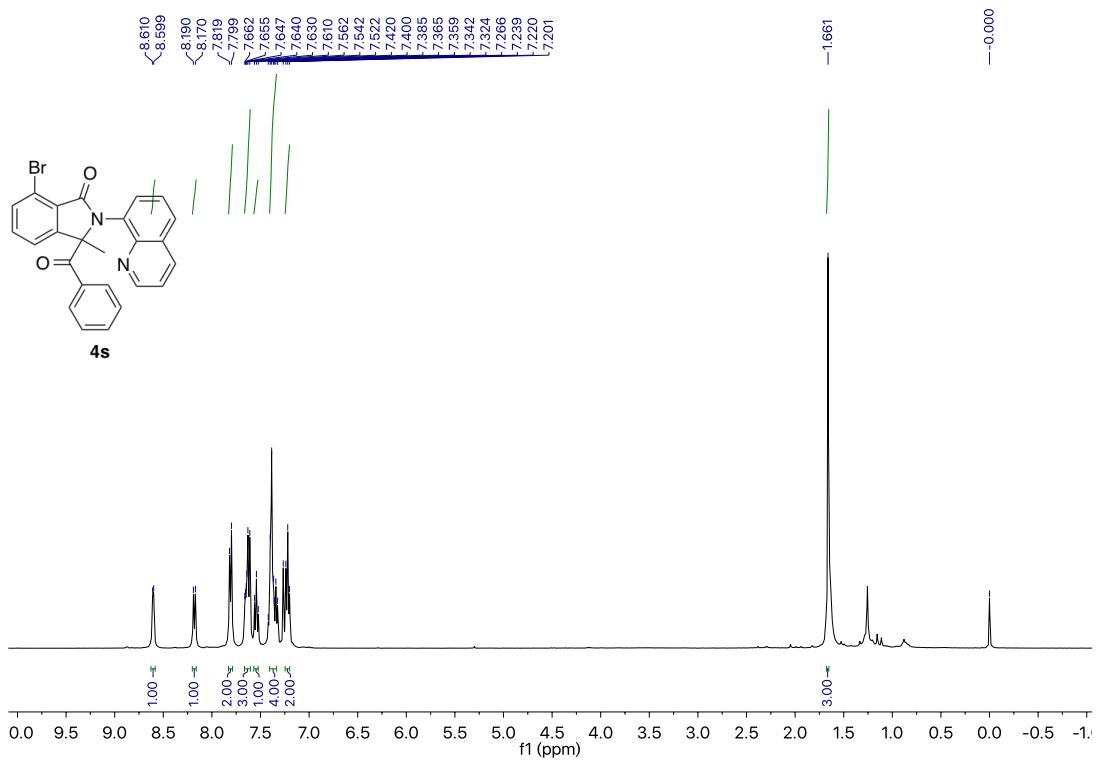
¹³C NMR (100 MHz, CDCl₃)



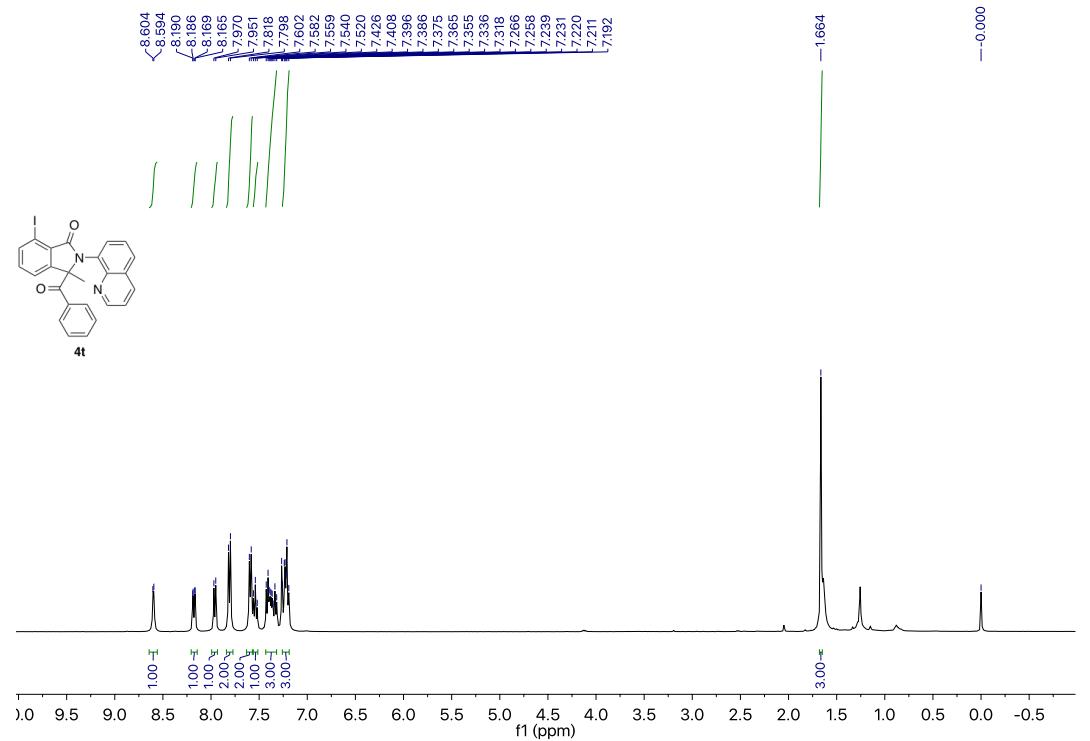
¹H NMR (400 MHz, CDCl₃)



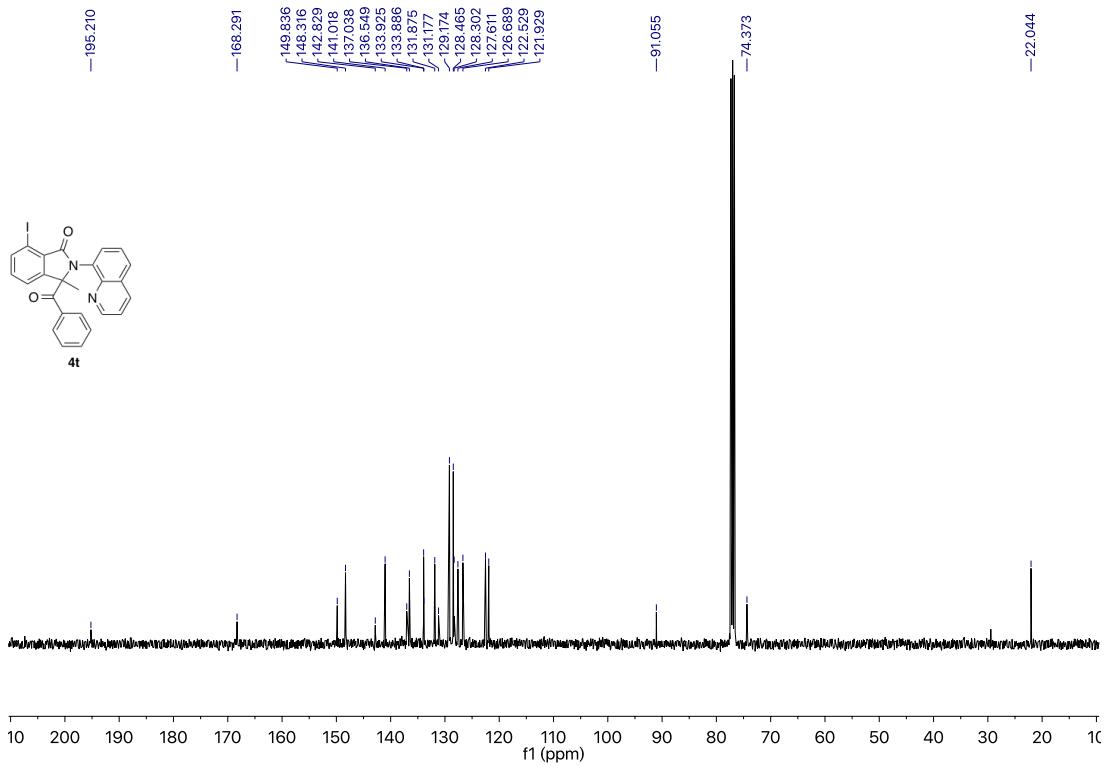
¹³C NMR (100 MHz, CDCl₃)



¹H NMR (400 MHz, CDCl₃)

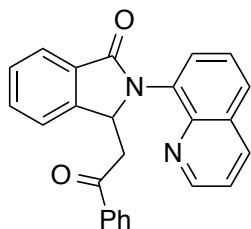


¹³C NMR (100 MHz, CDCl₃)



5. X-ray Crystallography of Compound 3a.

3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoindolin-1-one (3a, CCDC-1922682)

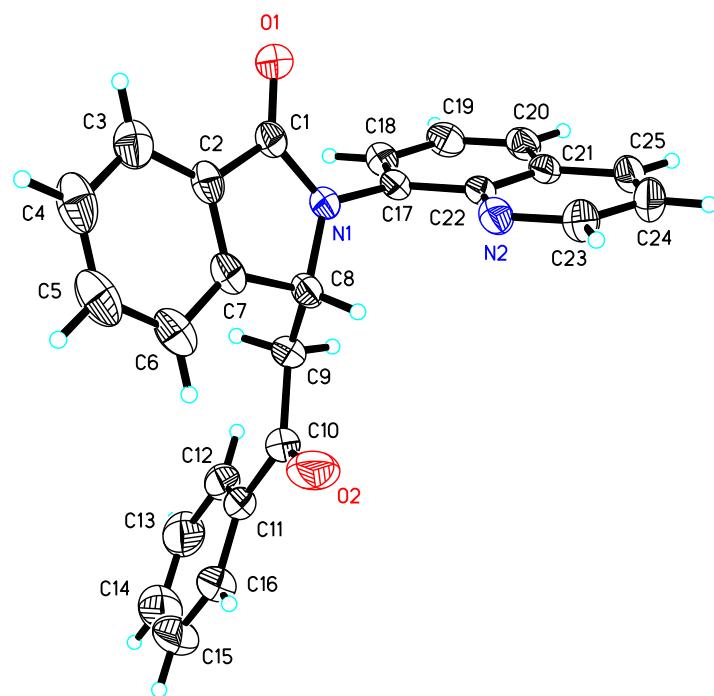


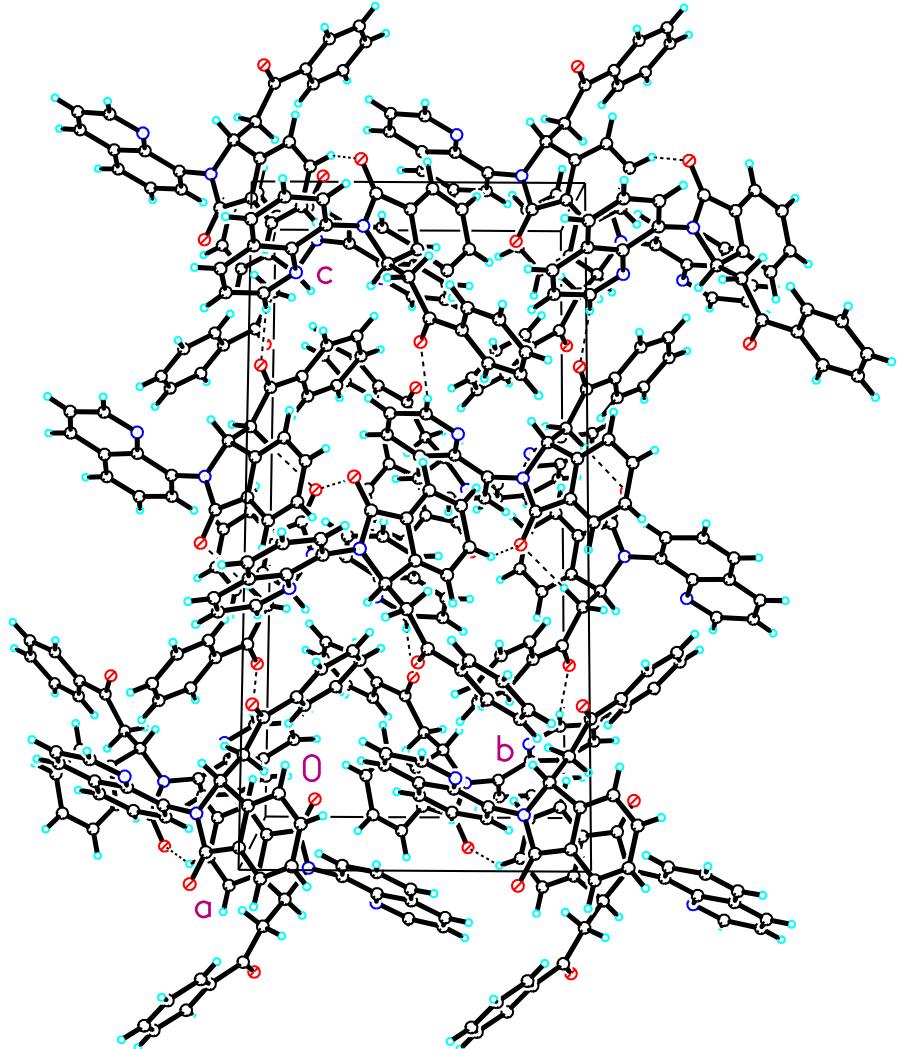
3a

Table S1. Crystal data and structure refinement for **3a**

Identification code	3a	
Empirical formula	C ₂₅ H ₁₈ N ₂ O ₂	
Formula weight	378.41	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 17.2010(8) Å b = 10.7246(3) Å c = 22.2115(9) Å	α= 90°. β= 104.5160(10)°. γ = 90°
Volume	3966.6(3) Å ³	
Z	8	
Density (calculated)	1.267 Mg/m ³	
Absorption coefficient	0.081 mm ⁻¹	
F(000)	1584	
Crystal size	0.180 x 0.150 x 0.080 mm ³	
Theta range for data collection	2.259 to 26.000°	
Index ranges	-21<=h<=21, -11<=k<=13, -27<=l<=27	

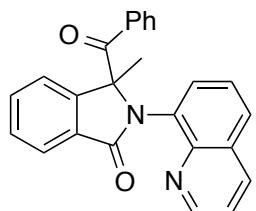
Reflections collected	26409
Independent reflections	7752 [$R(\text{int}) = 0.0924$]
Completeness to theta = 26.000°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.4288
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7752 / 0 / 524
Goodness-of-fit on F^2	1.043
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0636$, $wR_2 = 0.1580$
R indices (all data)	$R_1 = 0.1088$, $wR_2 = 0.1972$
Extinction coefficient	0.019(2)
Largest diff. peak and hole	0.195 and -0.222 e. \AA^{-3}





6. X-ray Crystallography of Compound 4a.

3-benzoyl-3-methyl-2-(quinolin-8-yl)isoindolin-1-one (4a, CCDC-1922684)



4a

Table S2. Crystal data and structure refinement for **4a**

Identification code	4a	
Empirical formula	C ₂₅ H ₁₈ N ₂ O ₂	
Formula weight	378.41	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 9.9072(8) Å b = 12.9383(3) Å c = 15.3549(9) Å	α= 90°. β= 104.5160(10)°. γ = 90°
Volume	1956.4(2) Å ³	
Z	4	
Density (calculated)	1.285 Mg/m ³	
Absorption coefficient	0.082 mm ⁻¹	
F(000)	792	
Crystal size	0.200 x 0.170 x 0.130 mm ³	
Theta range for data collection	3.193 to 25.999°	
Index ranges	-12<=h<=9, -15<=k<=15, -18<=l<=18	
Reflections collected	10503	

Independent reflections	3784 [$R(\text{int}) = 0.0209$]
Completeness to theta = 26.000°	98.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6334
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3784 / 0 / 264
Goodness-of-fit on F^2	1.017
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0383$, $wR_2 = 0.0891$
R indices (all data)	$R_1 = 0.0512$, $wR_2 = 0.0985$
Extinction coefficient	0.025(6)
Largest diff. peak and hole	0.139 and -0.111 e. \AA^{-3}

