Supporting Information

Trifunctionalization of Allenes via Cobalt-Catalyzed MHP-Assisted C-H Bond Functionalization and Molecular Oxygen Activation

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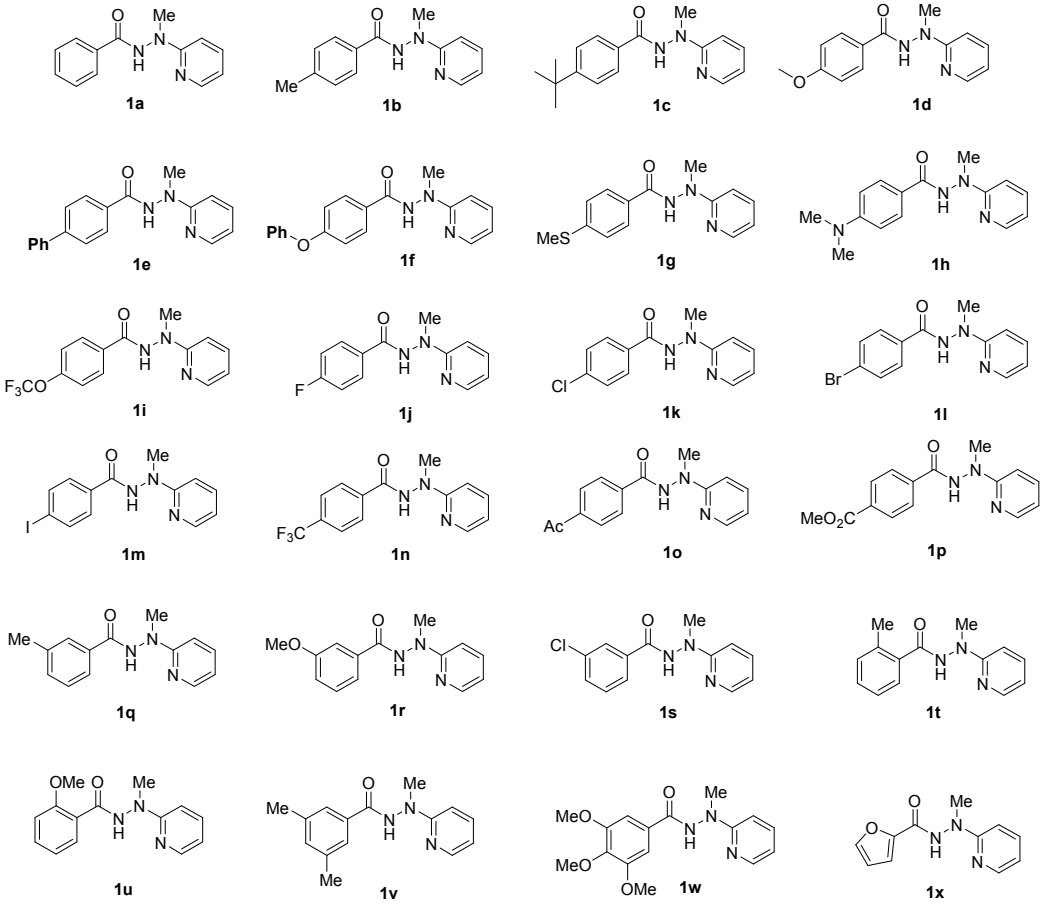
1. Materials and methods

All reactions were carried out under Argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. All the chemicals were purchased commercially, and used without further purification. Dichloromethane and was distilled from calcium hydride. Thin-layer chromatography (TLC) was conducted with 0.25 mm Tsingdao silica gel plates (60F-254) and visualized by exposure to UV light (254 nm) or stained with potassium permanganate. Flash column chromatography was performed on Tsingdao silica gel (200-300 mesh) and neutral/basic aluminum oxide (200-300 mesh). ^{1}H NMR spectra were recorded on Bruker spectrometers (at 400 or 500 MHz) and reported relative to deuterated solvent signals or tetramethylsilane internal standard signals. Data for ^{1}H NMR spectra were reported as follows: chemical shift (δ/ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.), coupling constant (J/Hz) and integration. ^{13}C NMR spectra were recorded on Bruker Spectrometers (100 or 125 MHz). Data for ^{13}C NMR spectra were reported in terms of chemical shift. ^{19}F NMR spectra were recorded on Bruker Spectrometers (376 MHz). High-resolution mass spectrometry (HRMS) was conducted on Bruker Apex IV RTMS. X-ray diffraction was performed on Rigaku Saturn 70 CCD diffractometer using graphite monochromated Cu-Kα radiation at a

temperature of 100 ±1 K.

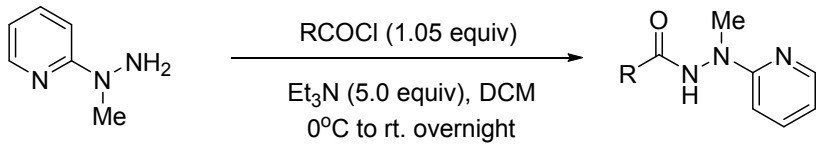
2. General procedure for the synthesis of hydrazides.

Table S1. Scope of hydrazides.



The hydrazides **1a**, **1b**, **1d**, **1j**, **1k**, **1l**, **1m**, **1n**, **1q**, **1t**, **1s**, **1x** were synthesized according to our previous work.[1]

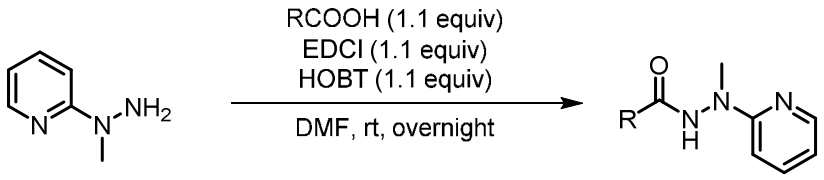
Representative Method A: (**1c**, **1e**, **1i**, **1p**, **1r**, **1u**, **1v**)



To a stirred mixture of 2-(1-methylhydrazinyl)pyridine (1.0 eq, 5mmol) and Et_3N (5.0 eq) in dry CH_2Cl_2 (0.2 to 0.5 M) was added benzoyl

chloride (1.05 eq) dropwise under Ar atmosphere at 0 ^{o}C. Kept the reaction mixture stirred at 0 ^{o}C for about 0.5h, then the resulting mixture was warmed to room temperature and stirred overnight at this temperature. Upon completion of the reaction indicated by TLC, The reaction mixture was washed with H_2O and extracted with CH_2Cl_2 (20ml) for three times. The combined organic phases were washed with brine, dried over with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product.

Representative Method B[3]: (1f, **1g**, **1h**, **1w)**



A mixture of amine (5 mmol), acid (5 mmol), EDCI (5.5 mmol) and HOBT (5.5 mmol) in anhydrous DMF (20 mL) was stirred at room temperature overnight. 100 mL water was added and the mixture was extracted with ethyl acetate three times (20 mL x 3). The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on neutral alumina (eluting with *n*-hexanes/EtOAc = 3:1 to 1:1) to give the desired product.

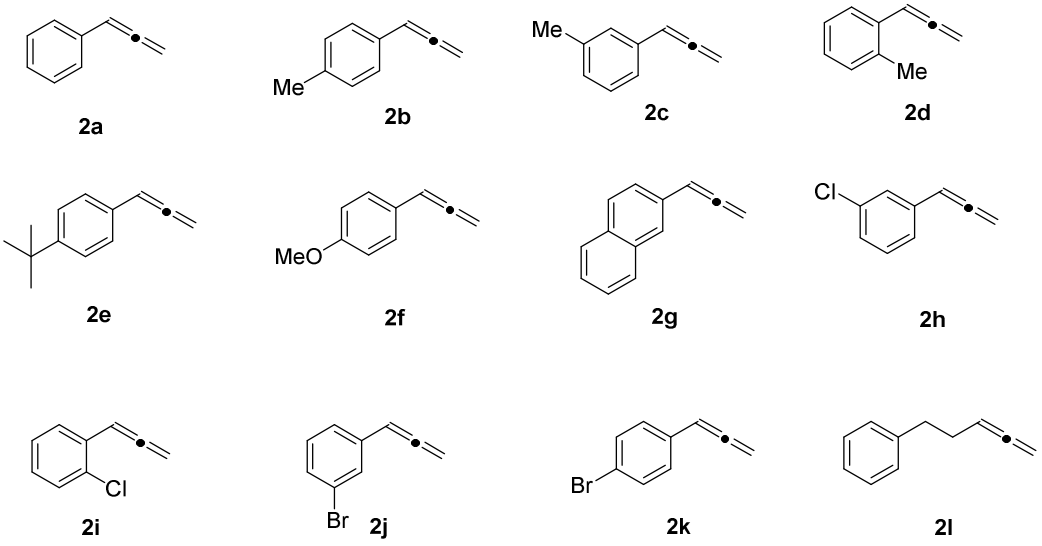
Representative Method C: (1o)

A solution of 4-acetylbenzoic acid (5 mmol) was refluxed in 5 mL $SOCl_2$

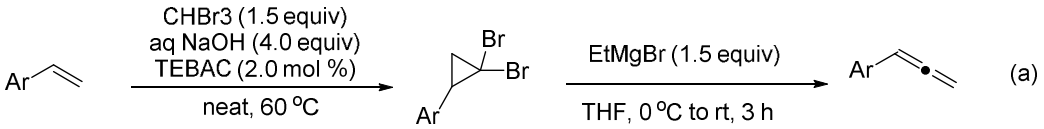
for 2 h and cooled to room temperature. The excess of $SOCl_2$ was removed under vacuum to give corresponding acid choloride. The acid choloride was then re-dissolved in 5 mL dry CH_2Cl_2 and added dropwise to a 20 mL dry CH_2Cl_2 solution containing 2-(1-methylhydrazinyl)pyridine (5 mmol) and Et_3N (25 mmol) at 0 ^oC. After stirring for 6 h at ambient temperature, the resulting mixture was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on neutral alumina (eluting with *n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product.

3. General procedure for the synthesis of allenes

Table S2. Scope of allenes.



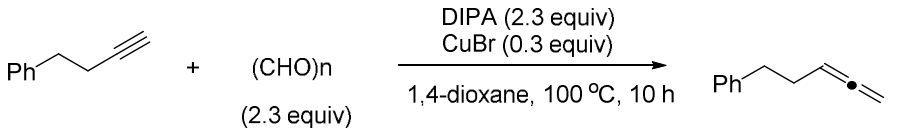
The terminal 1-aryallenes were prepared according to the general general procedure reported by Clavier and coworkers (route a).[4]



(a)

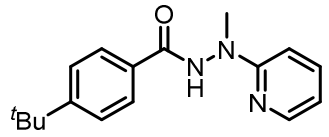
The **2a**,[4] **2b**,[4] **2c**,[5] **2d**,[4] **2e**[6], **2f**,[4] **2g**,[5] **2h**,[5] **2i**,[7] **1j**,[8] **1k**[5] are known compounds.

The allene **2l** was synthesized according to the route outlined in b, the literature method reported by Ma and coworkers.[9]



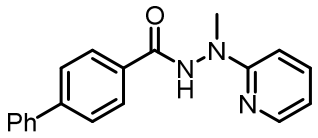
(b)

4. Characterization data for starting materials



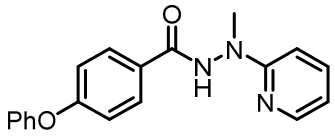
1c

4-(*tert*-Butyl)-*N′*-methyl-*N′*-(pyridin-2-yl)benzohydrazide (1c): Prepared according to method A, purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product **1c** (92% yield) as a white solid, mp 187.8–188.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.62 (br, 1H), 8.20 (d, J = 4.0 Hz, 1H), 7.81 (d, J = 8.5 Hz, 2H), 7.50–7.45 (m, 3H), 6.76 (d, J = 8.5 Hz, 1H), 6.71 (dd, J = 5.0, 6.5 Hz, 1H), 3.43 (s, 3H), 1.35 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.4, 159.4, 155.8, 147.6, 137.6, 129.7, 127.1, 125.7, 114.6, 107.2, 38.9, 35.0, 31.1. HRMS calculated for $C_{17}H_{22}N_3O$ ($M + H^+$): 284.1763, found 284.1757.



1e

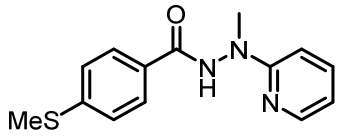
***N′*-Methyl-*N′*-(pyridin-2-yl)-[1,1'-biphenyl]-4-carbohydrazide (1e)**: Prepared according to the general method A, purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product **1e** (92% yield) as a white solid, mp 176.0–178.9 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.83 (br, 1H), 8.22 (d, *J* = 4.0 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 7.5 Hz, 2H), 7.53–7.46 (m, 3H), 7.41 (t, *J* = 7.0 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 1H), 6.73 (dd, *J* = 5.5, 7.0 Hz, 1H), 3.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.3, 159.3, 147.6, 145.0, 139.9, 137.7, 131.2, 129.0, 128.1, 127.8, 127.4, 127.2, 114.8, 107.2, 39.0. HRMS calculated for $C_{19}H_{18}N_3O$ (M + H^+): 304.1450, found 304.1436.



1f

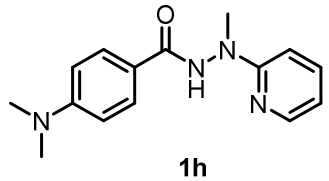
***N′*-Methyl-4-phenoxy-*N′*-(pyridin-2-yl)benzohydrazide (1ae)**: Prepared according to method B, purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product **1f** as a white solid (88% yield), mp 153.8–155 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.79 (br, 1H), 8.18 (d, *J* = 4.5 Hz, 1H), 7.84 (d, *J* = 8.5 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 7.0 Hz, 1H), 7.06 (d,

J = 8.0 Hz, 2H), 6.98 (d, J = 7.5 Hz, 2H), 6.74 (d, J = 8.5 Hz, 1H), 6.70 (t, J = 5.5 Hz, 1H), 3.40 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166,0, 161.1, 159.4, 155.8, 147.6, 137.7, 130.0, 129.3, 126.9, 124.4, 119.9, 117.8, 114.7 107.2, 38.9. HRMS calculated for $C_{19}H_{18}N_3O_2$ (M + H^+): 320.1399, found 320.1391.



1g

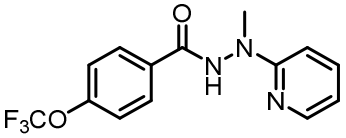
***N′*-Methyl-4-(methylthio)-*N′*-(pyridin-2-yl)benzohydrazide (1g)**: Prepared according to method B, purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product **1g** as a white solid (83% yield), mp 141.0–143.2 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.29 (br, 1H), 8.17–8.16 (m, 1H), 7.73 (d, J = 8.5 Hz, 2H), 7.47–7.43 (m, 1H), 7.14 (d, J = 8.5 Hz, 2H), 6.67-6.70 (m, 2H), 3.34 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2, 159.3, 147.4, 144.3, 137.8, 128.3, 127.7, 125.3, 114.6, 107.2, 38.8, 14.9. HRMS calculated for $C_{14}H_{16}N_3OS$ (M + H^+): 274.1014, found 274.1009.



1h

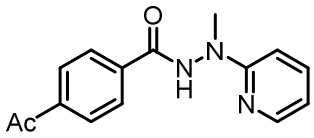
4-(Dimethylamino)-*N′*-methyl-*N′*-(pyridin-2-yl)benzohydrazide (1h): Prepared according to the general method B, purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the

corresponding product **1h** as a white solid (66% yield), mp 184.1–186.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (br, 1H), 8.18 (d, J = 4.0 Hz, 1H), 7.76 (d, J = 9.0 Hz, 2H), 7.42 (t, J = 7.0 Hz, 1H), 6.74 (d, J = 8.5 Hz, 1H), 6.66-6.62 (m, 3H), 3.39 (s, 3H), 3.01 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.6, 159.8, 152.9, 147.5, 137.5, 128.9, 119.0, 114.2, 111.1, 107.2, 40.1, 38.7. HRMS calculated for $C_{15}H_{19}N_4O$ ($M + H^+$): 271.1559, found 271.1553.



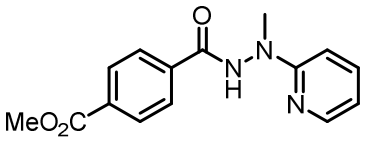
1i

***N′*-Methyl-*N′*-(pyridin-2-yl)-4-(trifluoromethoxy)benzohydrazide (1i)**: Prepared according to method A, purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product **1i** as a white solid (90% yield), mp 117.6–119.6 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.58 (br, 1H), 8.18 (d, J = 4.0 Hz, 1H), 7.88 (d, J = 8.5 Hz, 2H), 7.52–7.49 (m, 1H), 7.12 (d, J = 8.5 Hz, 2H), 6.74–6.70 (m, 2H), 3.36 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.3, 159.1, 151.8, 147.4, 137.9, 130.9, 129.3, 120.6, 120.3 (q, J = 256.6 Hz), 114.9, 107.2, 39.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -57.7. HRMS calculated for $C_{14}H_{13}F_3N_3O_2$ ($M + H^+$): 312.0960, found 312.0946.



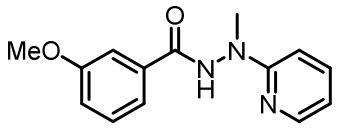
1o

4-Acetyl-*N*′-methyl-*N*′-(pyridin-2-yl)benzohydrazide (1o): Prepared according to the general method C, purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product **1o** as a yellow solid (52% yield over 2 steps), mp 141.4–142.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.51 (br, 1H), 8.16 (d, *J* = 4.0 Hz, 1H), 7.90 (m, 4H), 7.48 (t, *J* = 7.5 Hz, 1H), 6.72-6.70 (m, 2H), 3.35 (s, 3H), 2.59 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.4, 165.8, 159.1, 147.5, 139.5, 137.8, 136.4, 128.5, 127.7, 114.9, 107.2, 38.9, 26.7. HRMS calculated for $C_{15}H_{16}N_3O_2$ ($M + H^+$): 270.1243, found 270.1236.



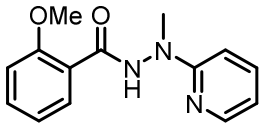
1p

Methyl 4-(2-methyl-2-(pyridin-2-yl)hydrazine-1-carbonyl)benzoate (1p): Prepared according to the general method A, purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product **1h** as a white solid (91% yield), mp 137.0–138.6 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.51 (br, 1H), 8.14 (d, *J* = 4.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.84 (d, *J* = 8.5 Hz, 2H), 7.46-7.42 (m, 1H), 6.69-6.66 (m, 2H), 3.91 (s, 3H), 3.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2, 165.9, 159.1, 147.5, 137.8, 136.3, 133.1, 129.8, 127.4, 114.8, 107.2, 52.4, 38.7. HRMS calculated for $C_{15}H_{16}N_3O_3$ ($M + H^+$): 286.1192, found 286.1186.



1r

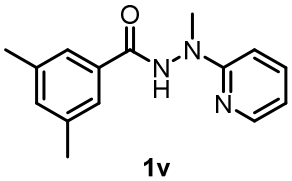
3-Methoxy-*N*′-methyl-*N*′-(pyridin-2-yl)benzohydrazide (1r): Prepared according to the general method A, purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product **1h** as a white solid (81% yield), mp 131.0–132.7 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.77 (br, 1H), 8.20 (d, *J* = 4.5 Hz, 1H), 7.51–7.47 (m, 1H), 7.42–7.40 (m, 2H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.06 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.74 (d, *J* = 8.5 Hz, 1H), 6.72 (dd, *J* = 5.5, 7.0 Hz, 1H), 3.82 (s, 3H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.4, 160.0, 159.3, 147.6, 137.7, 134.0, 129.7, 119.0, 118.5, 114.7, 112.6, 107.2, 55.4, 38.8. HRMS calculated for $C_{14}H_{16}N_3O_2$ ($M + H^+$): 258.1243, found 258.1237.



1u

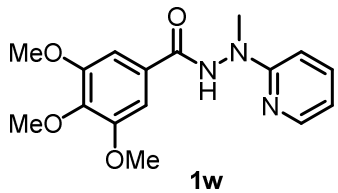
2-Methoxy-*N*'-methyl-*N*'-(pyridin-2-yl)benzohydrazide (1u): Prepared according to the general method A, purified by column chromatography (*n*-hexanes/EtOAc = 2:1 to 1:1) to afford the corresponding product **1u** as a yellow solid (64% yield), mp 112.4–114.1 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.64 (br, 1H), 8.21-8.23 (m, 2H), 7.44–7.53 (m, 2H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 6.78 (d, *J* = 8.5 Hz, 1H), 6.68 (dd, *J* = 5.5, 6.5 Hz, 1H), 4.02 (s, 3H), 3.47 (s, 3H). ^{13}C NMR (125 MHz,

$CDCl_3$): δ 164.9, 159.5, 157.5, 147.6, 137.4, 133.5, 132.6, 121.5, 120.1, 118.5, 114.2, 111.3, 107.1, 56.0, 38.4. HRMS calculated for $C_{14}H_{16}N_3O_2$ ($M + H^+$): 258.1243, found 258.1241.



1v

***N′*,3,5-Trimethyl-*N′*-(pyridin-2-yl)benzohydrazide (1v)**: Prepared according to the general method A, purified by column chromatography (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product **1v** as a white solid (95% yield), mp 164.8–166.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (br, 1H), 8.20 (d, *J* = 4.8 Hz, 1H), 7.50–7.46 (m, 3H), 7.17 (s, 1H), 6.75 (d, *J* = 8.8 Hz, 1H), 6.70 (dd, *J* = 5.2, 6.4 Hz, 1H), 3.41 (s, 3H), 2.35 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 159.3, 147.5, 138.4, 137.6, 133.7, 132.4, 124.9, 114.6, 107.1, 38.7, 21.1. HRMS calculated for $C_{15}H_{18}N_3O$ ($M + H^+$): 256.1450, found 256.1445.



1w

3,4,5-Trimethoxy-*N′*-methyl-*N′*-(pyridin-2-yl)benzohydrazide (1w): Prepared according to the general method B, purified by column chromatography (*n*-hexanes/EtOAc = 2:1 to 1:1) to afford the corresponding product **1w** as a white solid (67% yield), mp 159.0–160.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.15 (br, 1H), 8.19 (d, *J* = 4.5 Hz,

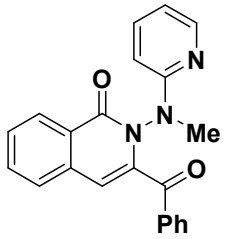
1H), 7.53-7.50 (m, 1H), 7.14 (s, 2H), 6.74-6.70 (m, 2H), 3.83 (s, 3H), 3.75 (s, 6H), 3.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.0, 159.4, 153.0, 147.1, 141.2, 138.0, 127.4, 114.6, 107.2, 104.8, 60.8, 56.2, 39.0. HRMS calculated for $C_{16}H_{20}N_3O_4$ ($M + H^+$): 318.1454, found 318.1435.

5. General procedure for cobalt-catalyzed C(sp^2)-H activation annulation and dioxygen activation approach

To a 25-mL schlenk tube equipped with magnetic stirring bar were added the N'-methyl-N'-(pyridin-2-yl)benzohydrazide (**1a**, 45.4 mg, 0.2 mmol), $Co(OAc)_2{\cdot}4H_2O$ (10.0 mg, 0.04 mmol), Ag_2CO_3 (110.3 mg, 0.4 mmol). The container was sealed, pumped into vacuum, and flushed with O_2 using a blloon for three times. To this tube were sequentially added propa-1,2-dien-1-ylbenzene (**2a**, 93 mg, 0.8 mmol) and the solvent (EtOH, 2 mL). The resulting mixture was stirred for 16 h at 60 ^{o}C, before being cooled down to rt, And the mixture was filtered through a plug of celite, followed by washing with 70 mL of ethyl acetate and the combined organic phases were concentrated under reduced pressure. Then the residue was dissolved in 5 mL DCM and it was followed by addition of DMP (84.8 mg, 0.2 mmol). The resulting reaction mixture was stirred at room temperature for about 1 hour (traced by TLC). The reaction mixture was quenched by addition of saturated $Na_2S_2O_3$ and $NaHCO_3$ solution and stirred for about 20 minutes, and then diluted by 20 mL DCM. The phases were separated, the aqueous phase was extracted with DCM (2 x

25 mL), and the combined organic phases were washed with brine (2 x 30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting sticky oil was purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to give **3aa** (57 mg, 80% yield) as a colorless sticky oil.

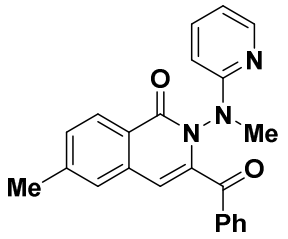
6. Characterization data for products



3aa

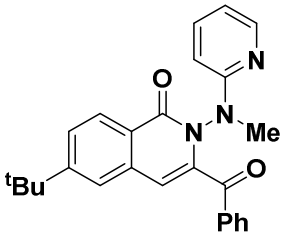
3-Benzoyl-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one:

Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3aa** (57 mg, 80% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 4.0 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 2H), 7.73 (dt, *J* = 1.5 Hz, 7.0 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.55-7.58 (m, 2H), 7.42-7.45 (m, 3H), 6.68 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.65 (s, 1H), 6.51 (d, *J* = 8.5 Hz, 1H), 3.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.0, 161.1, 158.3, 147.7, 142.9, 137.5, 135.9, 135.4, 133.8, 133.2, 130.1, 128.5, 128.3, 128.0, 127.6, 127.0, 115.7, 107.5, 107.0, 38.8. HRMS calculated for $C_{22}H_{18}N_3O_2$ (M + H^+): 356.1399, found 356.1394.



3ba

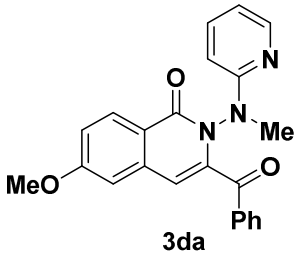
3-Benzoyl-6-methyl-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3ba** (62 mg, 84% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, *J* = 9.0 Hz, 1H), 8.10 (dd, *J* = 1.0, 4.5 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.57 (dt, *J* = 1.5 Hz, 7.5 Hz, 1H), 7.38-7.45 (m, 5H), 6.68 (dd, *J* = 5.0, 6.5 Hz, 1H), 6.59 (s, 1H), 6.48 (d, *J* = 8.5 Hz, 1H), 3.41 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.1, 161.1, 158.4, 147.7, 144.0, 142.9, 137.5, 136.0, 135.5, 133.8, 130.1, 129.8, 128.5, 128.3, 126.9, 125.4, 115.6, 107.5, 107.0, 38.9, 21.8. HRMS calculated for $C_{23}H_{20}N_3O_2$ (M + H^+): 370.1556, found 370.1549.



3ca

3-Benzoyl-6-(tert-butyl)-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by

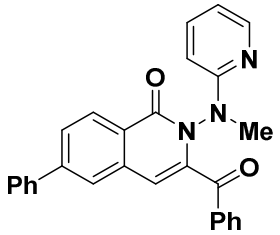
column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3ca** (70 mg, 85% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (d, *J* = 8.5 Hz, 1H), 8.10 (dd, *J* = 1.0, 4.5 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.63 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.56-7.59 (m, 2H), 7.41-7.46 (m, 3H), 6.67 (dd, *J* = 5.0, 6.5 Hz, 1H), 6.66 (s, 1H), 6.49 (d, *J* = 8.5 Hz, 1H), 3.42 (s, 3H), 1.34 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.1, 161.0, 158.4, 157.1, 147.6, 142.7, 137.5, 136.1, 135.3, 133.8, 130.1, 128.5, 128.2, 126.2, 125.3, 123.2, 115.6, 108.2, 107.0, 38.9, 35.3, 31.1. HRMS calculated for $C_{26}H_{26}N_3O_2$ ($M + H^+$): 412.2025, found 412.2020.



3da

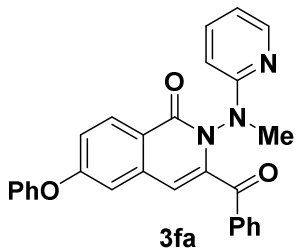
3-Benzoyl-6-methoxy-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3da** (68 mg, 88% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, *J* = 9.0 Hz, 1H), 8.10 (dd, *J* = 1.0, 4.5 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.41-7.45 (m, 3H), 7.12 (dd, *J* = 2.5, 9.0 Hz, 1H), 6.95 (d, *J* = 2.5 Hz, 1H), 6.68 (dd, *J* = 5.0, 7.5 Hz, 1H), 6.50 (s, 1H), 6.48 (d, *J* = 8.5 Hz, 1H), 3.91 (s, 3H), 3.40 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.0, 163.5,

160.8, 158.4, 147.6, 143.4, 137.5, 135.9, 133.8, 130.4, 130.1, 128.5, 121.2, 117.2, 115.6, 108.2, 107.1, 107.0, 55.6, 38.9. HRMS calculated for $C_{23}H_{20}N_3O_3$ ($M + H^+$): 386.1505, found 386.1499.



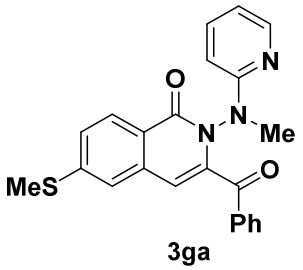
3ea

3-Benzoyl-2-(methyl(pyridin-2-yl)amino)-6-phenylisoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3ea** (71 mg, 82% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 (d, *J* = 9.0 Hz, 1H), 8.11 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.99 (d, *J* = 8.5 Hz, 2H), 7.81 (d, *J* = 2.0 Hz, 1H), 7.79 (s, 1H), 7.67 (dd, *J* = 1.5, 9.0 Hz, 2H), 7.59 (dt, *J* = 1.0, 7.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.42-7.47 (m, 4H), 6.69-6.71 (m, 2H), 6.53 (d, *J* = 8.5 Hz, 1H), 3.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.0, 161.1, 158.3, 147.7, 146.1, 143.3, 139.6, 137.6, 135.9, 135.8, 133.9, 130.1, 129.1, 129.0, 128.5, 127.4, 127.2, 126.4, 125.2, 115.7, 107.6, 107.0, 38.9. HRMS calculated for $C_{28}H_{22}N_3O_2$ ($M + H^+$): 432.1712, found 432.1705.



3fa

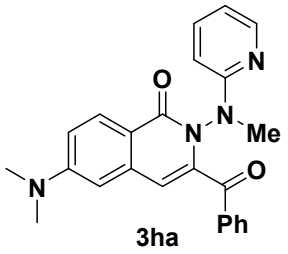
3-Benzoyl-2-(methyl(pyridin-2-yl)amino)-6-phenoxyisoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3fa** (72 mg, 81% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (d, *J* = 9.0 Hz, 1H), 8.11 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 7.81 (d, *J* = 2.0 Hz, 1H), 7.79 (s, 1H), 7.67 (dd, *J* = 1.5, 9.0 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.40-7.46 (m, 5H), 7.20-7.24 (m, 2H), 7.11 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 2.5 Hz, 1H), 6.69 (dd, *J* = 5.5, 7.0 Hz, 1H), 6.51 (d, *J* = 8.5 Hz, 1H), 6.49 (s, 1H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.9, 162.2, 160.7, 158.3, 155.3, 147.7, 143.7, 137.5, 137.4, 135.8, 133.9, 130.8, 130.1, 128.5, 124.9, 122.5, 120.4, 118.9, 115.7, 113.0, 107.0, 106.9, 38.9. HRMS calculated for $C_{28}H_{22}N_3O_3$ ($M + H^+$): 448.1661, found 448.1656.



3ga

3-Benzoyl-2-(methyl(pyridin-2-yl)amino)-6-(methylthio)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by

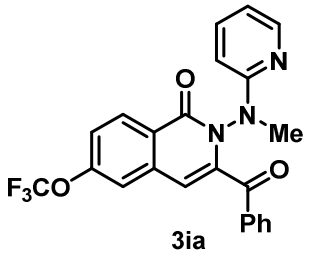
column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3ga** (64 mg, 80% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (d, *J* = 9.0 Hz, 1H), 8.09 (d, *J* = 4.0 Hz, 1H), 7.95 (d, *J* = 7.0 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.41-7.45 (m, 3H), 7.37 (dd, *J* = 2.0, 8.5 Hz, 1H), 7.31 (d, *J* = 1.5 Hz, 1H), 6.68 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.55 (s, 1H), 6.50 (d, *J* = 8.5 Hz, 1H), 3.41 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.9, 160.9, 158.3, 147.6, 146.4, 143.7, 137.5, 135.8, 133.9, 130.1, 128.5, 128.4, 125.6, 124.2, 121.7, 115.7, 108.2, 107.0, 106.7, 38.9, 14.8. HRMS calculated for $C_{23}H_{20}N_3O_2S$ ($M + H^+$): 402.1276, found 402.1270.



3ha

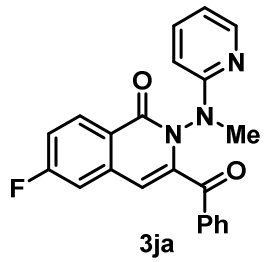
3-Benzoyl-6-(dimethylamino)-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3ha** (59 mg, 74% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23 (d, *J* = 9.0 Hz, 1H), 8.11 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.39-7.47 (m, 3H), 6.93 (dd, *J* = 2.0, 9.0 Hz, 1H), 6.65 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.61 (d, *J* = 2.5 Hz, 1H), 6.52 (s, 1H), 6.46 (d, *J* = 8.5 Hz, 1H), 3.39 (s, 3H), 3.10 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.3,

161.0, 158.8, 153.4, 147.6, 142.9, 137.4, 137.1, 136.2, 133.6, 130.0, 129.8, 128.4, 116.7, 115.3, 113.6, 107.9, 107.1, 106.1, 40.1, 38.9. HRMS calculated for $C_{24}H_{23}N_4O_2$ ($M + H^+$): 399.1821, found 399.1817.



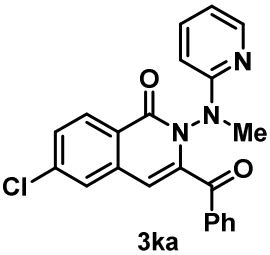
3ia

3-Benzoyl-2-(methyl(pyridin-2-yl)amino)-6-(trifluoromethoxy)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3ia** (67 mg, 76% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46 (d, *J* = 9.0 Hz, 1H), 8.08 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.43-7.47 (m, 3H), 7.41 (s, 1H), 7.36 (d, *J* = 9.0 Hz, 1H), 6.69 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.60 (s, 1H), 6.53 (d, *J* = 8.5 Hz, 1H), 3.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.6, 160.3, 158.0, 152.8, 147.7, 144.6, 137.6, 137.3, 135.6, 134.0, 131.1, 130.1, 128.5, 125.8, 120.4 (q, *J* = 257.6 Hz), 120.3, 117.2, 115.9, 106.9, 106.0, 38.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ -57.5. HRMS calculated for $C_{23}H_{17}F_3N_3O_3$ ($M + H^+$): 440.1222, found 440.1215.



3ja

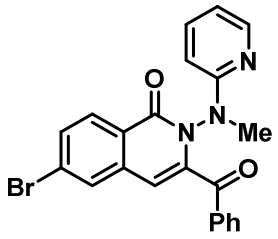
3-Benzoyl-6-fluoro-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3ja** (60 mg, 80% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (dd, *J* = 5.5, 9.0 Hz, 1H), 8.10 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.43-7.47 (m, 3H), 7.22-7.28 (m, 2H), 6.69 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.57 (s, 1H), 6.52 (d, *J* = 8.5 Hz, 1H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.7, 165.8 (d, *J* = 241.9 Hz), 164.7, 160.5, 158.1, 147.7, 144.3, 137.8 (d, *J* = 10.3 Hz), 137.6, 135.6, 134.0, 131.7 (d, *J* = 9.9 Hz), 130.1, 128.5, 124.2, 116.5 (d, *J* = 23.3 Hz), 115.9, 112.0 (d, *J* = 22.1 Hz), 107.0, 106.2, 38.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ -106.6. HRMS calculated for $C_{22}H_{17}FN_3O_2$ (M + H+): 374.1305, found 374.1299.



3ka

3-Benzoyl-6-chloro-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column

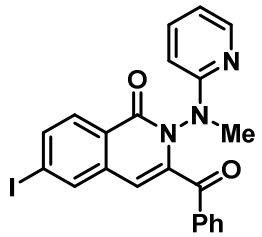
chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3ka** (61 mg, 78% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.33 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 4.0 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 2H), 7.57-7.60 (m, 2H), 7.49 (dd, *J* = 2.0, 8.5 Hz, 1H), 7.43-7.47 (m, 3H), 6.69 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.64 (s, 1H), 6.52 (d, *J* = 8.5 Hz, 1H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.7, 160.6, 158.1, 147.7, 144.3, 139.8, 137.6, 136.8, 135.6, 134.0, 130.2, 130.1, 128.5, 128.4, 126.2, 125.9, 115.9, 107.0, 105.9, 38.9. HRMS calculated for $C_{22}H_{17}ClN_3O_2$ (M + H^+): 390.1009, found 390.1004.



3la

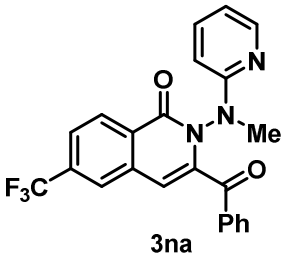
3-Benzoyl-6-bromo-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3la** (67 mg, 77% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (d, *J* = 8.5 Hz, 1H), 8.08 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 1.5 Hz, 1H), 7.64 (dd, *J* = 2.0, 9.0 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.42-7.46 (m, 3H), 6.68 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.53 (s, 1H), 6.52 (d, *J* = 7.5 Hz, 1H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.6, 160.8, 158.0, 147.7,

144.3, 137.6, 136.9, 135.6, 134.0, 131.2, 130.2, 130.1, 129.4, 128.5, 128.4, 126.2, 115.9, 106.9, 105.8, 38.9. HRMS calculated for $C_{22}H_{17}BrN_3O_2$ (M + H^+): 434.0504, found 434.0499.



3ma

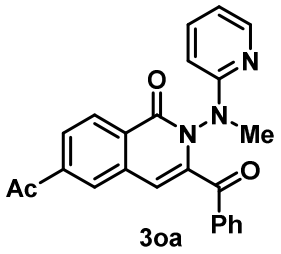
3-Benzoyl-6-iodo-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-on e: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3ma** (75 mg, 78% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08-8.11 (m, 2H), 7.95-7.99 (m, 3H), 7.84 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.42-7.46 (m, 3H), 6.68 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.51-6.53 (m, 2H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.6, 161.0, 158.0, 147.7, 144.1, 137.6, 136.9, 136.8, 135.7, 135.6, 134.0, 130.2, 129.7, 128.5, 126.7, 115.9, 106.9, 105.7, 101.1, 38.9. HRMS calculated for $C_{22}H_{17}IN_3O_2$ (M + H^+): 482.0365, found 482.0360.



3na

3-Benzoyl-2-(methyl(pyridin-2-yl)amino)-6-(trifluoromethyl)isoquino

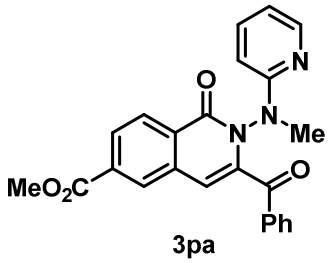
lin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3na** (59 mg, 70% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 5.0 Hz, 1H), 7.98 (d, *J* = 8.5 Hz, 2H), 7.88 (s, 1H), 7.75 (dd, *J* = 1.0, 8.5 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.43-7.48 (m, 3H), 6.70 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.68 (s, 1H), 6.55 (d, *J* = 8.5 Hz, 1H), 3.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.6, 160.5, 157.9, 147.7, 144.6, 137.7, 135.6, 134.9 (q, *J* = 32.8 Hz), 134.1, 130.2, 129.8, 129.5, 128.9 (q, *J* = 60.4 Hz), 128.5, 124.6, 124.2 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 2.9 Hz), 122.4, 116.0, 106.9, 106.4, 38.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.1. HRMS calculated for $C_{23}H_{17}F_3N_3O_2$ ($M + H^+$): 424.1273, found 424.1271.



3oa

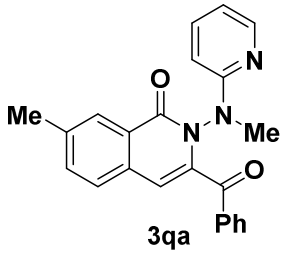
6-Acetyl-3-benzoyl-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3oa** (44 mg, 55% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (d, *J* = 8.5 Hz, 1H), 8.17 (d, *J* = 1.0 Hz, 1H), 8.06-8.09 (m, 2H), 7.97 (d, *J* = 8.5 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.43-7.47 (m, 3H), 6.69-6.71 (m, 2H), 6.54 (d, *J* = 8.5 Hz,

1H), 3.44 (s, 3H), 2.70 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.2, 188.7, 160.7, 158.0, 147.7, 144.0, 140.6, 137.6, 135.7, 135.6, 134.0, 130.3, 130.2, 129.0, 128.5, 127.3, 126.6, 115.9, 107.2, 106.9, 38.9, 26.9. HRMS calculated for $C_{24}H_{20}N_3O_3$ ($M + H^+$): 398.1505, found 398.1502.



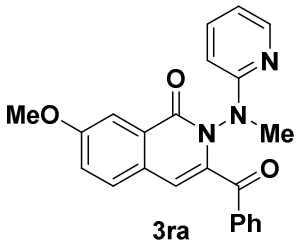
3pa

Methyl-3-benzoyl-2-(methyl(pyridin-2-yl)amino)-1-oxo-1,2-dihydrois oquinoline-6-carboxylate: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3pa** (52 mg, 63% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (d, *J* = 8.5 Hz, 1H), 8.30 (d, *J* = 1.0 Hz, 1H), 8.14 (dd, *J* = 1.5, 8.0 Hz, 1H), 8.09 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.43-7.47 (m, 3H), 6.69-6.71 (m, 2H), 6.53 (d, *J* = 8.5 Hz, 1H), 3.99 (s, 3H), 3.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.7, 166.0, 160.7, 158.0, 147.7, 143.8, 137.6, 135.7, 135.3, 134.3, 134.0, 130.3, 130.2, 128.8, 128.5, 127.9, 115.9, 107.1, 107.0, 52.6, 38.8. HRMS calculated for $C_{24}H_{20}N_3O_4$ ($M + H^+$): 414.1454, found 414.1448.



3qa

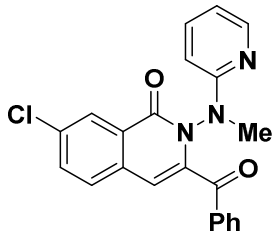
3-Benzoyl-7-methyl-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3qa** (62 mg, 84% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.24 (s, 1H), 8.10 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.95 (d, *J* = 7.0 Hz, 2H), 7.54-7.58 (m, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.41-7.45 (m, 3H), 6.66 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.61 (d, *J* = 2.5 Hz, 1H), 6.64 (s, 1H), 6.48 (d, *J* = 8.5 Hz, 1H), 3.43 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.1, 161.1, 158.4, 147.6, 141.9, 138.6, 137.5, 136.1, 134.6, 133.7, 132.9, 130.1, 128.4, 128.0, 127.6, 127.0, 115.5, 107.9, 107.0, 38.8, 21.5. HRMS calculated for $C_{23}H_{20}N_3O_2$ ($M + H^+$): 370.1556, found 370.1551.



3ra

3-Benzoyl-7-methoxy-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to

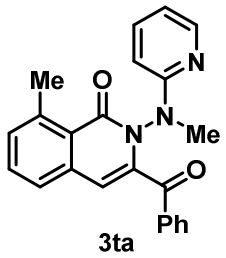
2:1) to afford the corresponding product **3ra** (63 mg, 82% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 7.84 (d, *J* = 2.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.52 (d, *J* = 9.0 Hz, 1H), 7.42-7.48 (m, 3H), 7.32 (dd, *J* = 2.5, 8.5 Hz, 1H), 6.66-6.69 (m, 2H), 6.49 (d, *J* = 8.5 Hz, 1H), 3.92 (s, 3H), 3.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.0, 161.0, 159.9, 158.4, 147.7, 140.5, 137.5, 136.3, 133.6, 130.2, 130.1, 129.2, 129.0, 128.8, 128.4, 123.6, 115.5, 108.5, 106.9, 55.7, 38.8. HRMS calculated for $C_{23}H_{20}N_3O_3$ (M + H^+): 386.1505, found 386.1499.



3sa

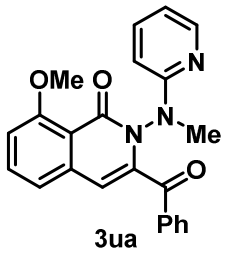
3-Benzoyl-7-chloro-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3sa** (64 mg, 82% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (d, *J* = 2.0 Hz, 1H), 8.09 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.95 (d, *J* = 8.5 Hz, 2H), 7.66 (dd, *J* = 2.0, 8.5 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.43-7.47 (m, 3H), 6.69 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.61 (s, 1H), 6.52 (d, *J* = 9.0 Hz, 1H), 3.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.8, 160.2, 158.0, 147.7, 143.3, 137.6, 135.8, 134.2, 134.0, 133.8, 133.6, 130.1, 128.8, 128.5,

127.9, 115.9, 106.9, 106.6, 38.8. HRMS calculated for $C_{22}H_{17}ClN_3O_2$ (M + H^+): 390.1009, found 390.1005.



3ta

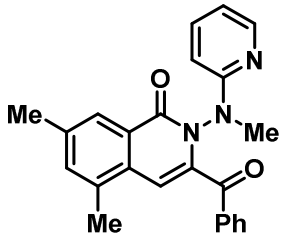
3-Benzoyl-8-methyl-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3ta** (39 mg, 53% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (d, *J* = 4.0 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.53-7.58 (m, 2H), 7.40-7.45 (m, 4H), 7.31 (d, *J* = 7.5 Hz, 1H), 6.66 (dd, *J* = 5.5, 7.0 Hz, 1H), 6.59 (s, 1H), 6.50 (d, *J* = 8.5 Hz, 1H), 3.39 (s, 3H), 2.89 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.9, 161.6, 158.4, 147.7, 142.8, 142.7, 137.5, 137.0, 136.0, 133.7, 132.4, 131.2, 130.1, 128.4, 126.0, 125.5, 115.4, 108.1, 106.9, 38.8, 23.5. HRMS calculated for $C_{23}H_{20}N_3O_2$ (M + H^+): 370.1556, found 370.1550.



3ua

3-Benzoyl-8-methoxy-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column

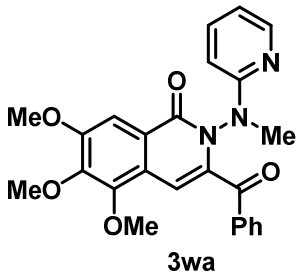
chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3ua** (40 mg, 52% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.57 (dt, *J* = 1.0, 7.5 Hz, 1H), 7.39-7.45 (m, 3H), 7.12 (d, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.65 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.53 (s, 1H), 6.49 (d, *J* = 8.5 Hz, 1H) , 3.97 (s, 3H), 3.37 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.9, 161.3, 159.4, 158.5，147.6, 143.6, 138.5, 137.5, 135.9, 134.0, 133.7, 130.1, 128.4, 119.3, 116.8, 115.5, 109.5, 107.0, 106.8, 56.2, 38.9. HRMS calculated for $C_{23}H_{20}N_3O_3$ ($M + H^+$): 386.1505, found 386.1503.



3va

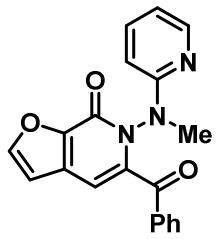
3-Benzoyl-5,7-dimethyl-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3va** (64 mg, 84% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (s, 2H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.40-7.46 (m, 4H), 6.76 (s, 1H), 6.57 (dd, *J* = 1.0, 7.0 Hz, 1H), 6.47 (d, *J* = 8.5 Hz, 1H), 3.40 (s, 3H) , 2.50 (s, 3H) , 2.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.3, 161.3, 158.4, 147.6,

141.5, 138.2, 137.5, 136.2, 135.7, 134.5, 133.7, 131.8, 130.0, 128.4, 127.9, 126.0, 115.6, 107.0, 104.4, 38.8, 21.4, 18.8. HRMS calculated for $C_{24}H_{22}N_3O_2$ ($M + H^+$): 384.1712, found 384.1707.



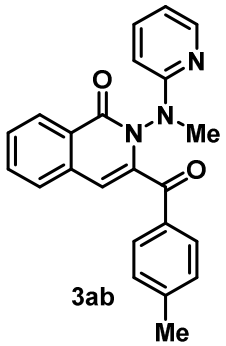
3wa

3-Benzoyl-5,6,7-trimethoxy-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3wa** (76 mg, 85% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.95 (d, *J* = 8.5 Hz, 2H), 7.66 (s, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.41-7.45 (m, 3H), 6.92 (s, 1H), 6.66-6.69 (m, 1H), 6.48 (d, *J* = 8.5 Hz, 1H), 3.99 (s, 3H), 3.97 (s, 3H), 3.96 (s, 3H), 3.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.1, 160.5, 158.4, 154.4, 148.5, 147.6, 146.4, 140.6, 137.5, 136.2, 133.7, 130.1, 128.4, 124.8, 123.8, 115.5, 107.0, 104.6, 102.9, 61.6, 61.0, 56.2, 38.8. HRMS calculated for $C_{25}H_{24}N_3O_5$ ($M + H^+$): 446.1716, found 446.1712.



3xa

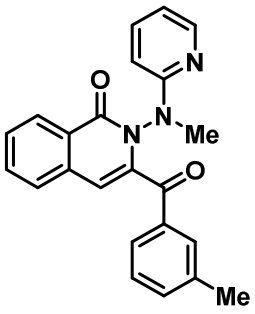
5-Benzoyl-6-(methyl(pyridin-2-yl)amino)furo[2,3-c]pyridin-7(6*H*)-on e: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 4:1 to 2:1) to afford the corresponding product **3xa** (20 mg, 29% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (dd, *J* = 1.5, 5.0 Hz, 1H), 7.89 (dd, *J* = 1.0, 8.5 Hz, 2H), 7.84 (d, *J* = 2.0 Hz, 1H), 7.57 (dt, *J* = 1.0, 7.5 Hz, 1H), 7.41-7.44 (m, 3H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.71 (dd, *J* = 0.5, 5.0 Hz, 1H), 6.61 (s, 1H), 6.45 (d, *J* = 8.5 Hz, 1H), 3.40 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.7, 158.1, 152.4, 149.4, 147.6, 144.9, 144.2, 137.6, 135.9, 133.9, 131.8, 130.4, 128.5, 115.9, 107.9, 107.0, 100.5, 38.1. HRMS calculated for $C_{20}H_{16}N_3O_3$ ($M + H^+$): 346.1192, found 346.1186.



3ab

2-(Methyl(pyridin-2-yl)amino)-3-(4-methylbenzoyl)isoquinolin-1(2*H*) -one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to

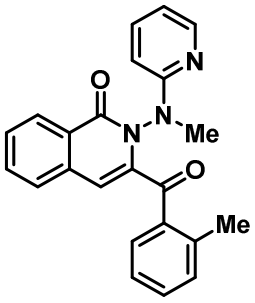
3:1) to afford the corresponding product **3ab** (63 mg, 85% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.0 Hz, 1H), 8.10 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.87 (d, *J* = 8.5 Hz, 2H), 7.73 (dt, *J* = 2.0, 8.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.55 (dt, *J* = 1.0, 8.0 Hz, 1H), 7.42 (dt, *J* = 1.5, 7.0 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.67 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.62 (s, 1H), 6.51 (d, *J* = 8.5 Hz, 1H), 3.44 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.5, 161.1, 158.3, 147.6, 145.1, 143.0, 137.5, 135.4, 133.3, 133.1, 130.3, 129.2, 128.3, 127.9, 127.5, 126.9, 115.6, 107.2, 107.0, 38.8, 21.7. HRMS calculated for $C_{23}H_{20}N_3O_2$ (M + H^+): 370.1556, found 370.1552.



3ac

2-(Methyl(pyridin-2-yl)amino)-3-(3-methylbenzoyl)isoquinolin-1(2*H*) -one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3ac** (65 mg, 88% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 4.0 Hz, 1H), 7.72-7.78 (m, 3H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.44 (dt, *J* = 1.5, 8.5 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H),

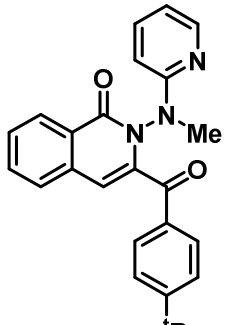
7.32 (t, J = 7.5 Hz, 1H), 6.68 (dd, J = 5.0, 7.0 Hz, 1H), 6.64 (s, 1H), 6.50 (d, J = 8.5 Hz, 1H), 3.42 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.5, 161.1, 158.3, 147.6, 145.1, 143.0, 137.5, 135.4, 133.3, 133.1, 130.3, 129.2, 128.3, 127.9, 127.5, 126.9, 115.6, 107.2, 107.0, 38.8, 21.7. HRMS calculated for $C_{23}H_{20}N_3O_2$ (M + H^+): 370.1556, found 370.1550.



3ad

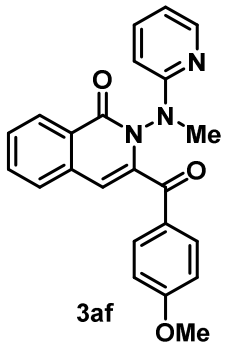
2-(Methyl(pyridin-2-yl)amino)-3-(2-methylbenzoyl)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3ad** (60 mg, 81% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, J = 8.5 Hz, 1H), 8.12 (dd, J = 1.0, 5.0 Hz, 1H), 7.74 (dt, J = 1.0, 8.0 Hz, 1H),7.63 (t, J = 7.0 Hz, 2H), 7.57 (dt, J = 1.0, 8.0 Hz, 1H), 7.41 (dt, J = 2.0, 8.5 Hz, 1H), 7.35 (dt, J = 1.0, 7.5 Hz, 1H), 7.23 (d, J = 7.5 Hz, 1H), 7.18 (d, J = 7.5 Hz, 1H), 6.74 (s, 1H), 6.69 (dd, J = 5.0, 7.0 Hz, 1H), 6.50 (d, J = 8.5 Hz, 1H), 3.25 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.1, 161.2, 158.2, 147.7, 144.1, 139.3, 137.6, 136.3, 135.4, 133.2, 131.9, 131.8, 130.8, 128.4, 128.2, 127.8, 127.3, 125.2, 115.6, 108.2, 106.8, 38.6, 20.3. HRMS

calculated for $C_{23}H_{20}N_3O_2$ (M + H^+): 370.1556, found 370.1552.



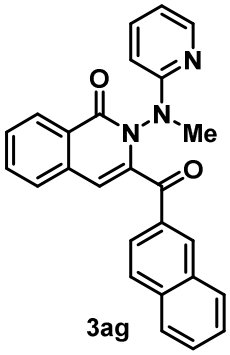
3ae

3-(4-(*tert*-Butyl)benzoyl)-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3ae** (65 mg, 79% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.5 Hz, 1H), 8.11 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.73 (dt, *J* = 1.0, 8.0 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.57 (dt, *J* = 1.0, 7.0 Hz, 1H), 7.42-7.46 (m, 3H), 6.68 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.65 (s, 1H), 6.51 (d, *J* = 8.5 Hz, 1H), 3.45 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.6, 161.2, 158.4, 158.0, 147.6, 143.0, 137.5, 135.5, 133.3, 133.2, 130.2, 128.4, 127.9, 127.6, 127.0, 125.5, 115.6, 107.4, 107.1, 38.8, 35.2, 31.0. HRMS calculated for $C_{26}H_{26}N_3O_2$ (M + H^+): 412.2025, found 412.2017.



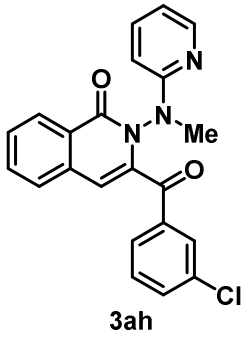
3af

3-(4-Methoxybenzoyl)-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3af** (55 mg, 71% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, *J* = 8.0 Hz, 1H), 8.10 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.97 (dd, *J* = 1.5, 7.0 Hz, 2H), 7.72 (dt, *J* = 1.0, 8.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.55 (dt, *J* = 1.0, 8.0 Hz, 1H), 7.43 (dt, *J* = 2.0, 7.5 Hz, 1H), 6.90 (d, *J* = 9.0 Hz, 2H), 6.67 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.60 (s, 1H), 6.52 (d, *J* = 8.5 Hz, 1H), 3.86 (s, 3H), 3.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.5, 164.4, 161.1, 158.4, 147.6, 143.0, 137.5, 135.5, 133.1, 132.7, 128.6, 128.3, 127.8, 127.4, 126.9, 115.6, 113.8, 107.1, 106.8, 55.5, 38.8. HRMS calculated for $C_{23}H_{20}N_3O_3$ (M + H^+): 386.1505, found 386.1501.



3ag

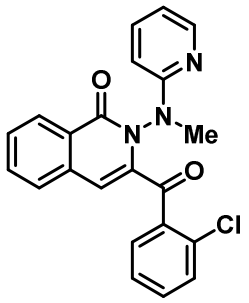
3-(2-Naphthoyl)-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3ag** (69 mg, 85% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.46 (d, *J* = 8.0 Hz, 1H), 8.10 (dd, *J* = 1.0, 5.0 Hz, 1H), 8.02 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.86-7.92 (m, 3H), 7.75 (dt, *J* = 1.5, 8.0 Hz, 1H), 7.57-7.63 (m, 3H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.41 (dt, *J* = 2.0, 7.5 Hz, 1H), 6.71 (s, 1H), 6.63 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.55 (d, *J* = 8.5 Hz, 1H), 3.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 189.0, 161.2, 158.2, 147.6, 143.1, 137.5, 135.9, 135.5, 133.2, 132.1, 129.6, 129.0, 128.6, 128.4, 128.0, 127.8, 127.7, 127.0, 124.6, 115.7, 107.4, 107.0, 38.9. HRMS calculated for $C_{26}H_{20}N_3O_2$ (M + H^+): 406.1556, found 406.1548.



3ah

3-(3-Chlorobenzoyl)-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3ah** (63 mg, 81% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43 (d, *J* = 8.0 Hz, 1H), 8.09

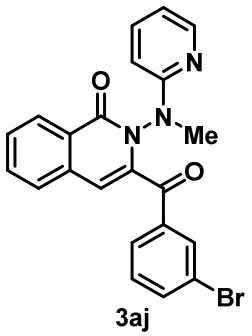
(dd, J = 1.0, 5.0 Hz, 1H), 7.91 (t, J = 1.5 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.75 (dt, J = 1.0, 8.0 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.59 (dt, J = 1.0, 7.5 Hz, 1H), 7.51 (dd, J = 1.0, 8.0 Hz, 1H), 7.46 (dt, J = 1.5, 8.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 6.69 (dd, J = 5.0, 7.0 Hz, 1H), 6.65 (s, 1H), 6.52 (d, J = 8.0 Hz, 1H), 3.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.9, 161.1, 158.0, 147.7, 142.4, 137.6, 137.5, 135.2, 134.7, 133.7, 133.3, 130.1, 129.8, 128.4, 128.2, 128.1, 127.7, 127.1, 115.8, 107.7, 106.9, 38.9. HRMS calculated for $C_{22}H_{17}ClN_3O_2$ (M + H^+): 390.1009, found 390.1003.



3ai

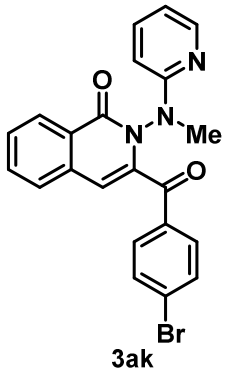
3-(2-Chlorobenzoyl)-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3ai** (67 mg, 86% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, J = 8.0 Hz, 1H), 8.10 (dd, J = 1.0, 5.0 Hz, 1H), 7.74 (dt, J = 1.0, 8.0 Hz, 1H),7.64 (t, J = 7.5 Hz, 2H), 7.59 (dt, J = 1.0, 8.0 Hz, 1H), 7.52 (dd, J = 1.0, 7.5 Hz, 1H), 7.34-7.42 (m, 3H), 7.24 (dt, J = 1.5, 7.5 Hz, 1H), 6.88 (s, 1H), 6.68 (dd, J = 5.0, 7.0 Hz, 1H), 6.39 (d, J = 8.5 Hz, 1H), 3.32 (s, 3H). ^{13}C NMR (125

MHz, $CDCl_3$): δ 188.1, 161.2, 158.0, 147.7, 143.2, 137.5, 136.9, 135.1, 133.3, 132.3, 132.2, 130.8, 130.6, 128.7, 128.4, 128.2, 127.7, 126.5, 115.5, 110.6, 106.8, 38.6. HRMS calculated for $C_{22}H_{17}ClN_3O_2$ ($M + H^+$): 390.1009, found 390.1007.



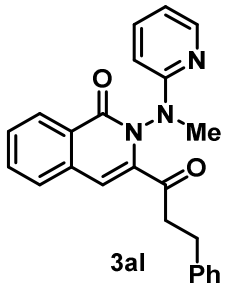
3aj

3-(3-Bromobenzoyl)-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3aj** (59 mg, 68% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.0 Hz, 1H), 8.10-8.11 (m, 2H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.75 (dt, *J* = 1.0, 8.0 Hz, 1H), 7.67 (dd, *J* = 0.5, 8.0 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.46 (dt, *J* = 1.5, 8.5 Hz, 1H), 7.30 (t, *J* = 8.0 Hz, 1H), 6.69 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.64 (s, 1H), 6.52 (d, *J* = 8.5 Hz, 1H), 3.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.8, 161.1, 158.0, 147.7, 142.4, 137.6, 136.6, 135.2, 133.2, 133.0, 130.0, 128.5, 128.4, 128.2, 127.7, 127.1, 122.7, 115.8, 107.6, 106.9, 38.9. HRMS calculated for $C_{22}H_{17}BrN_3O_2$ ($M + H^+$): 434.0504, found 434.0500.



3ak

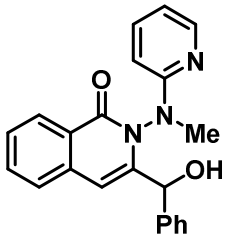
3-(4-Bromobenzoyl)-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one: Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3ak** (63 mg, 73% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 4.0 Hz, 1H), 7.85 (d, *J* = 8.5 Hz, 2H), 7.74 (dt, *J* = 1.0, 8.0 Hz, 1H), 7.56-7.61 (m, 4H), 7.46 (dt, *J* = 2.0, 8.5 Hz, 1H), 6.69 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.62 (s, 1H), 6.52 (d, *J* = 8.5 Hz, 1H), 3.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.1, 161.1, 158.1, 147.7, 142.5, 137.7, 135.2, 134.6, 133.3, 131.8, 131.6, 129.3, 128.4, 128.2, 127.7, 127.1, 115.8, 107.6, 106.9, 38.9. HRMS calculated for $C_{22}H_{17}BrN_3O_2$ (M + H^+): 434.0504, found 434.0500.



3al

2-(Methyl(pyridin-2-yl)amino)-3-(3-phenylpropanoyl)isoquinolin-1(2

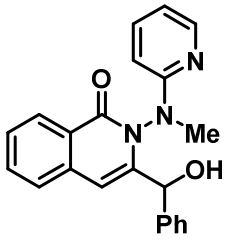
***H*)-one:** Prepared according to the general procedure, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to afford the corresponding product **3al** (43 mg, 56% yield) as a sticky oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.36 (d, *J* = 8.0 Hz, 1H), 8.20 (dd, *J* = 1.0, 5.0 Hz, 1H), 7.71 (dd, *J* = 1.5, 8.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.50-7.56 (m, 2H), 7.14-7.22 (m, 3H), 7.01 (d, *J* = 7.0 Hz, 2H), 6.78 (dd, *J* = 5.0, 7.0 Hz, 1H), 6.62 (s, 1H), 6.51 (d, *J* = 8.5 Hz, 1H), 3.46 (s, 3H), 3.03-3.16 (m, 3H), 2.86-2.97 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.6, 160.8, 158.4, 148.0, 144.0, 137.8, 135.4, 133.2, 128.4, 128.3, 128.2, 128.1, 127.5, 127.2, 126.1, 115.8, 107.0, 106.4, 43.1, 38.8, 29.9. HRMS calculated for $C_{24}H_{22}N_3O_2$ (M + H^+): 384.1712, found 384.1709.



4aa

3-(Hydroxy(phenyl)methyl)-2-(methyl(pyridin-2-yl)amino)isoquinoli n-1(2*H*)-one: Prepared according to the general procedure without further oxidant, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 1.5:1 to 1:1) to afford the corresponding product **4aa** as a foamy solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (d, *J* =

8.0 Hz, 1H), 8.14 (dd, *J* = 1.2, 4.8 Hz, 1H), 7.64 (dt, *J* = 1.2, 8.0 Hz, 1H), 7.50-7.55 (m, 2H), 7.41 (dt, *J* = 0.8, 8.0 Hz, 1H), 7.32-7.37 (m, 5H), 6.78 (dd, *J* = 4.8, 6.8 Hz, 1H), 6.75 (s, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 5.78 (s, 1H), 4.31 (br, 1H), 2.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 159.1, 147.9, 146.9, 140.5, 138.3, 136.4, 132.8, 128.6, 128.2, 127.8, 127.5, 126.6, 126.5, 126.0, 116.2, 107.3, 104.4, 71.6, 38.0. **HRMS** calculated for $C_{24}H_{22}N_3O_2$ ($M + H^+$): 358.1556, found 358.1551.



4aa'

3-(Hydroxy(phenyl)methyl)-2-(methyl(pyridin-2-yl)amino)isoquinoli n-1(2*H*)-one: Prepared according to the general procedure without further oxidant, purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 1.5:1 to 1:1.5) to afford the corresponding product **4aa'** as a foamy solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (d, *J* = 8.0 Hz, 1H), 8.12 (dd, *J* = 1.2, 4.8 Hz, 1H), 7.68 (dt, *J* = 1.2, 8.0 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.44 (dt, *J* = 1.2, 8.0 Hz, 1H), 7.30-7.34 (m, 3H), 7.14-7.23 (m, 3H), 6.81 (s, 1H), 6.71 (dd, *J* = 5.2, 6.8 Hz, 1H), 6.18 (d, *J* = 8.4 Hz, 1H), 5.82 (s, 1H), 4.47 (br, 1H), 3.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 159.1, 147.4, 145.8, 141.3, 137.9, 136.4, 133.0, 128.2, 127.9, 127.4, 126.9, 126.5, 126.4, 126.3, 115.9, 107.5, 106.3, 73.6,

37.6. **HRMS** calculated for $C_{24}H_{22}N_3O_2$ (M + H^+): 358.1556, found 358.1548.

7. Mechanistic studies

(a) To a 25-mL schlenk tube equipped with magnetic stirring bar were added the 3-benzyl-2-(methyl(pyridin-2-yl)amino)isoquinolin-1(2*H*)-one (**7**, 68.2 mg, 0.2 mmol), $Co(OAc)_2 \cdot 4H_2O$ (10.0 mg, 0.04 mmol), Ag_2CO_3 (110.3 mg, 0.4 mmol). The container was sealed, pumped into vacuum, and flushed with O_2 using a blloon for three times. To this tube were sequentially added propa-1,2-dien-1-ylbenzene (**2a**, 93 mg, 0.8 mmol) and the solvent (EtOH, 2 mL). The resulting mixture was stirred for 16 h at 60 ^oC, before being cooled down to rt, And the mixture was filtered through a plug of celite, followed by washing with 70 mL of ethyl acetate and the combined organic phases were concentrated under reduced pressure. The resulting sticky oil was purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 5:1 to 3:1) to give **7** (67 mg, 98% yield) as a colorless foam solid. ^1H NMR (400 MHz, $CDCl_3$): δ 8.32 (dd, *J* = o.4, 8.0 Hz, 1H), 8.24 (m, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.38-7.45 (m, 2H), 7.28-7.30 (m, 2H), 7.19-7.24 (m, 3H), 6.73-6.75 (m, 1H), 6.40 (s, 1H), 6.24 (d, *J* = 8.4 Hz, 1H), 3.92 (s, 2H), 3.36(s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 158.7, 148.0, 144.9, 137.7, 137.0, 136.6, 132.9, 129.1, 128.5, 128.1, 126.8, 126.3, 125.9, 125.8, 115.2, 106.4, 106.2, 38.8, 37.8. **HRMS** calculated for $C_{22}H_{20}N_3O$

$(M + H^+)$: 342.1606, found 342.1600.

(c) To a 25-mL schlenk tube equipped with magnetic stirring bar were added the N'-methyl-N'-(pyridin-2-yl)benzohydrazide (**1a**, 45.4 mg, 0.2 mmol), $Co(OAc)_2 \cdot 4H_2O$ (10.0 mg, 0.04 mmol), Ag_2CO_3 (110.3 mg, 0.4 mmol). The container was sealed, pumped into vacuum, and flushed with O_2 using a blloon for three times. To this tube were sequentially added propa-1,2-dien-1-ylbenzene (**2a**, 93 mg, 0.8 mmol) and the solvent ($EtOH/H_2{}^{18}O$, 3:1, 2 mL). The resulting mixture was stirred for 16 h at 60 ^oC, before being cooled down to rt, And the mixture was filtered through a plug of celite, followed by washing with 70 mL of ethyl acetate. The organic phase was detected by HRMS, and found no ^{18}O labeled 3aa or 4aa (4aa') formed.

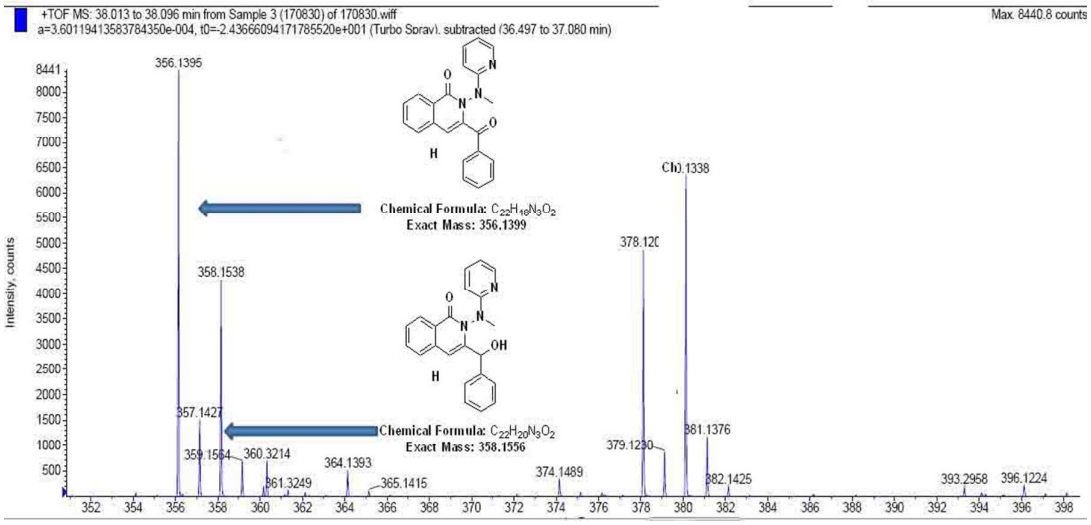


Figure S1. HRMS date of ^{18}O labeled experiment.

(d) To a 25-mL schlenk tube equipped with magnetic stirring bar were added the N'-methyl-N'-(pyridin-2-yl)benzohydrazide (**1a**, 45.4 mg, 0.2

mmol), $Co(OAc)_2 \cdot 4H_2O$ (10.0 mg, 0.04 mmol), Ag_2CO_3 (110.3 mg, 0.4 mmol). The container was sealed, pumped into vacuum, and flushed with O_2 using a blloon for three times. To this tube were sequentially added propa-1,2-dien-1-ylbenzene (**2a**, 93 mg, 0.8 mmol) and the solvent (EtOH, 2 mL). The resulting mixture was stirred for 1 h at 60 ^oC, before being cooled down to rt, And the mixture was filtered through a plug of celite, followed by washing with 70 mL of ethyl acetate. The organic phase was detected by HRMS, and found the peroxy intermediate **6** was formed.

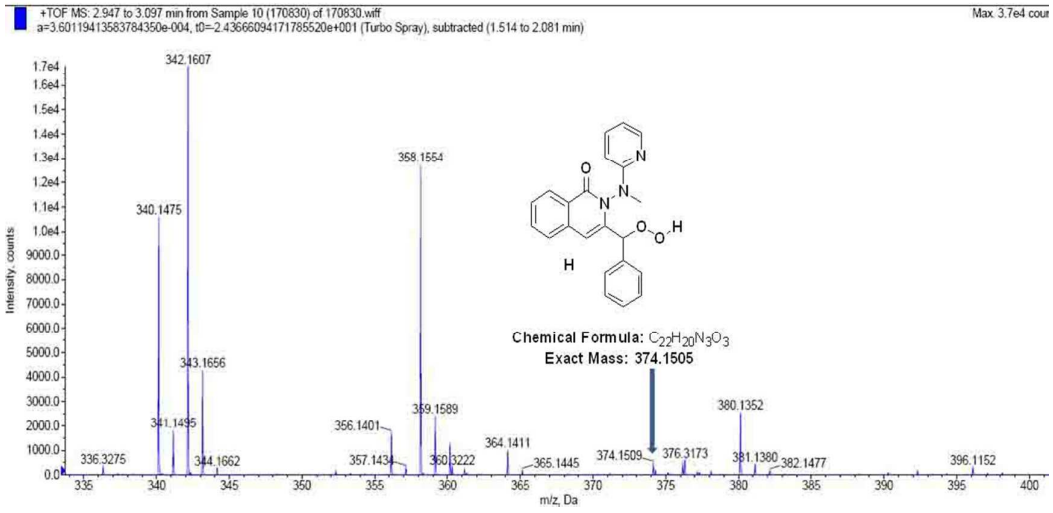
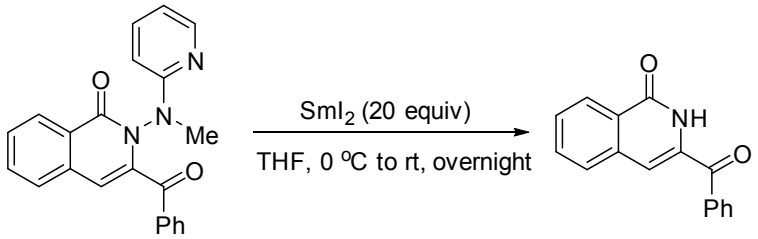


Figure S2. HRMS date of peroxy intermediate.

8. Removal of the directing group[1]



3an **8**

General experiment procedure: An oven-dried 25 mL round bottom

flask was charged with **3aa** (0.1 mmol, 35.5 mg). After purging with Ar three times, 2 mL fresh distilled THF was added, followed by SmI_2 (0.1 M in THF, 10 equiv) was added dropwise at 0 °C. After 5 minutes, the mixture was warmed to rt and stirred overnight. After that the mixture was quenched with 5 mL saturated aqueous $Na_2S_2O_3$ and extracted with DCM, dried over Na_2SO_4, filtered, and concentrated under reduced pressure . Purified by column chromatography on neutral aluminum oxide (*n*-hexanes/EtOAc = 3:1 to 1:1) to afford the corresponding product **8**[10] (15 mg, 60% yield).

3-benzoylisoquinolin-1(2H)-one: ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (br, 1H), 8.39 (d, *J* = 7.2 Hz, 1H), 7.83 (d, *J* = 7.6 Hz, 2H), 7.74 (m, 1H), 7.65-7.69 (m, 3H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.15(s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.9, 161.6, 135.8, 135.6, 133.6, 133.0, 132.8, 129.9, 129.2, 128.6, 128.5, 128.4, 127.9, 116.0.

9. References:

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10. ^{1}H, ^{13}C and ^{19}F NMR Spectra

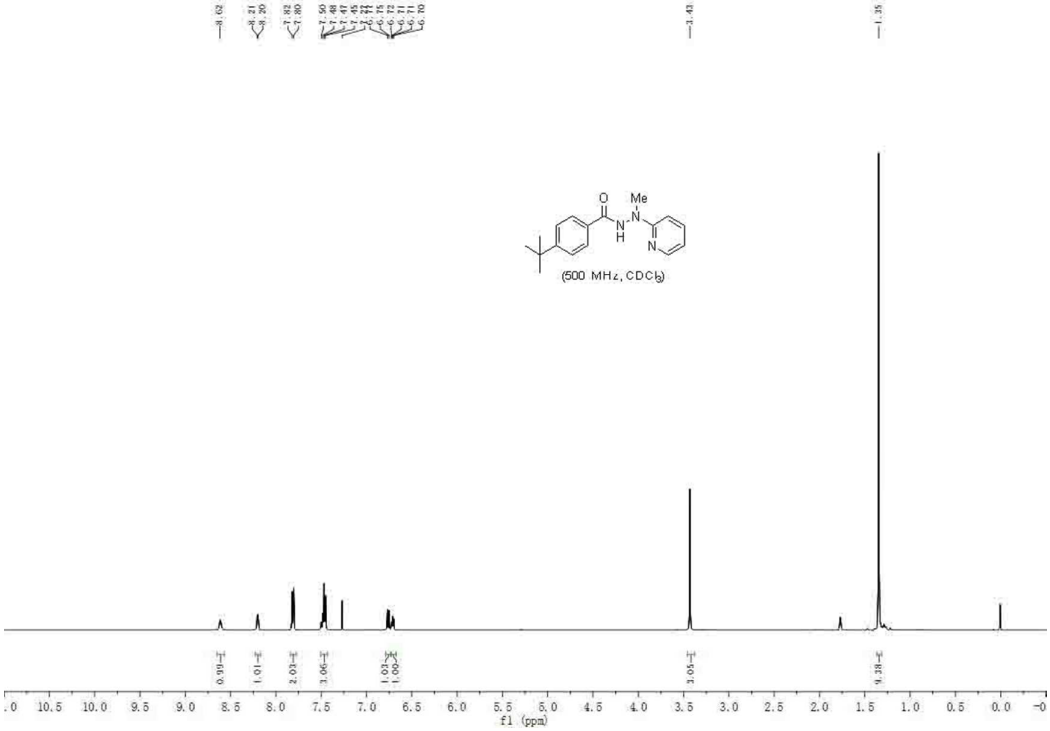


Figure S3. ^{1}H NMR Spectrum of **1c** (500 MHz, $CDCl_3$).

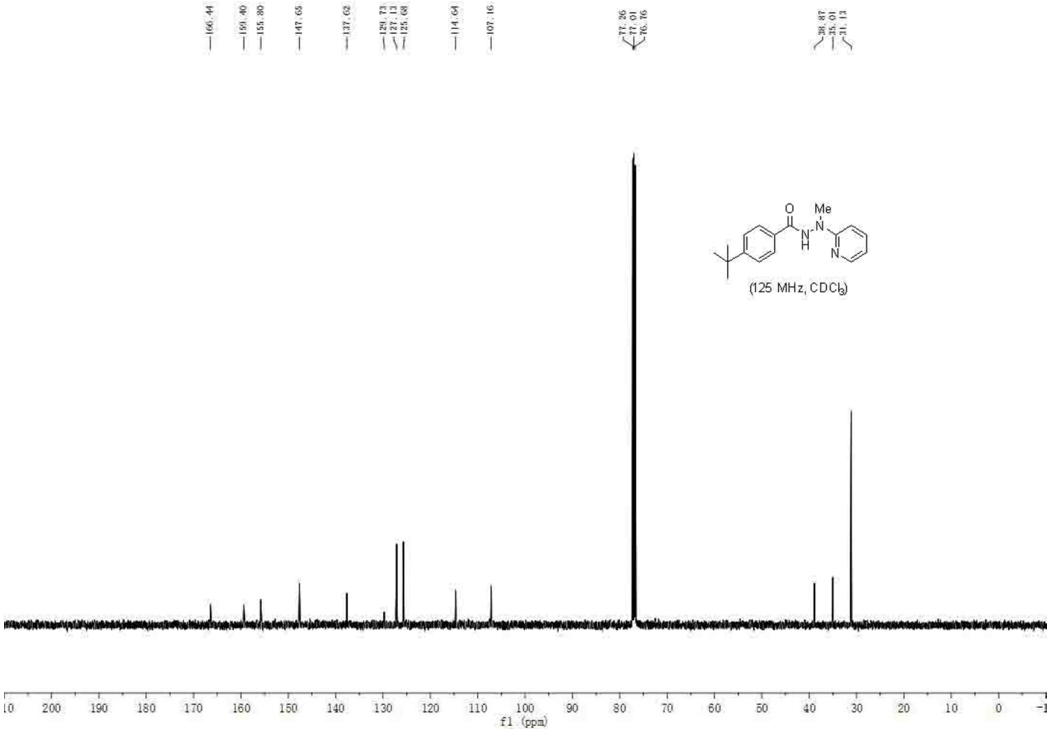


Figure S4. ^{13}C NMR Spectrum of **1c** (125 MHz, $CDCl_3$).

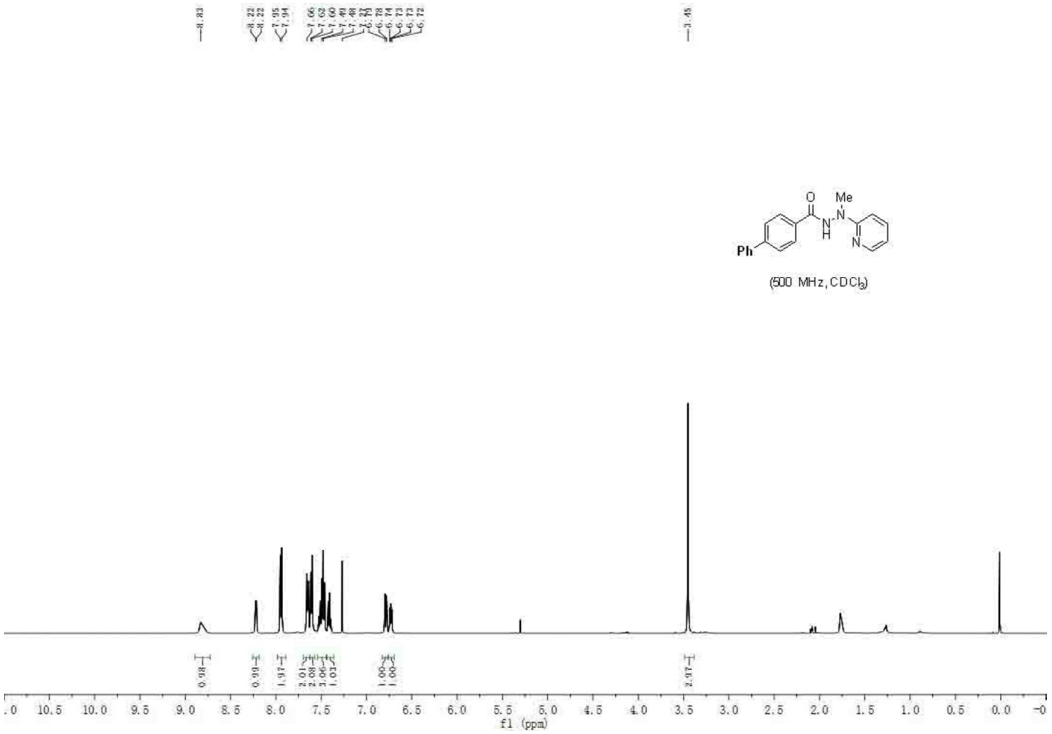


Figure S5. ^{1}H NMR Spectrum of **1e** (500 MHz, $CDCl_3$).

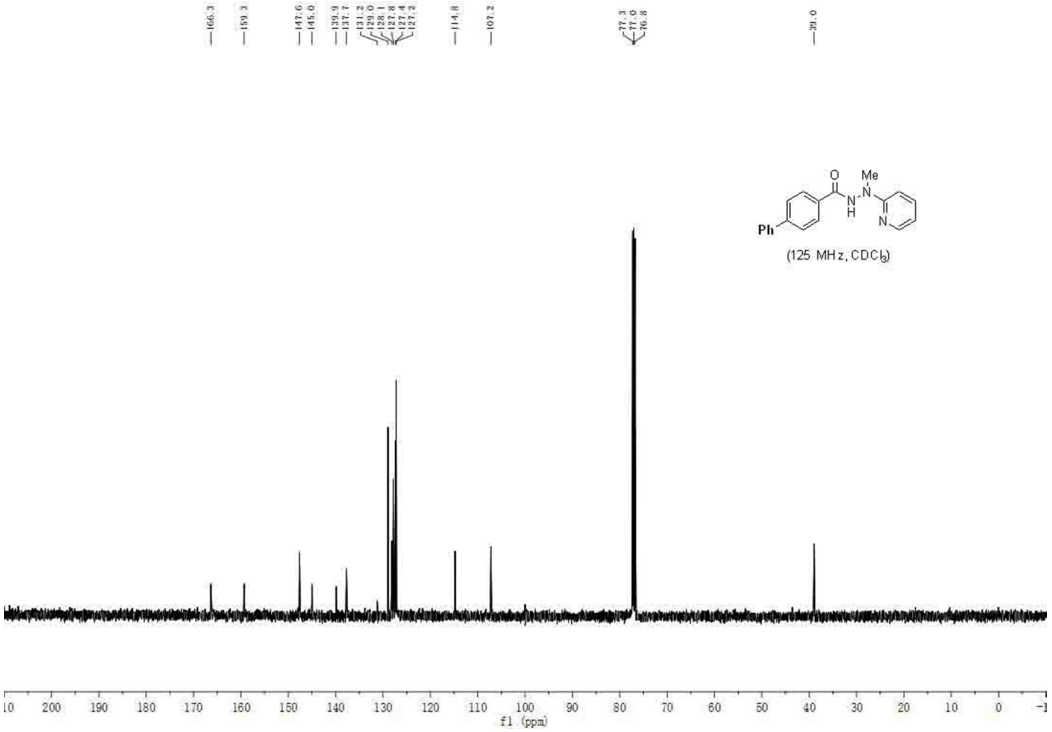


Figure S6. ^{13}C NMR Spectrum of **1e** (125 MHz, $CDCl_3$).

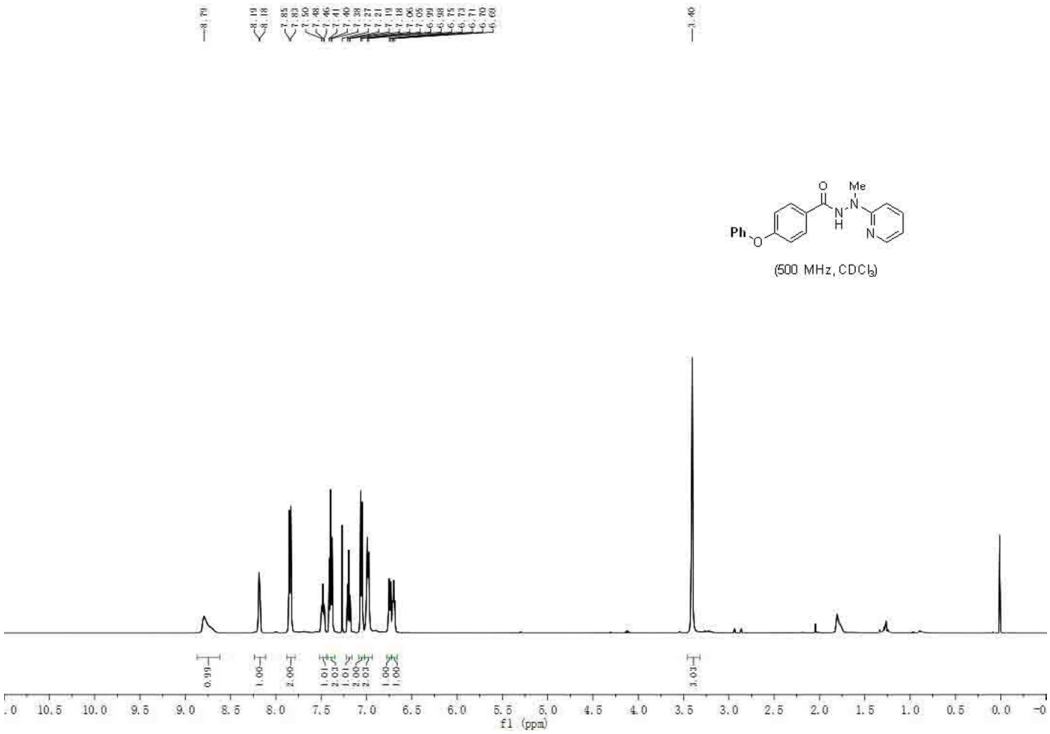


Figure S7. ^{1}H NMR Spectrum of **1f** (500 MHz, $CDCl_3$).

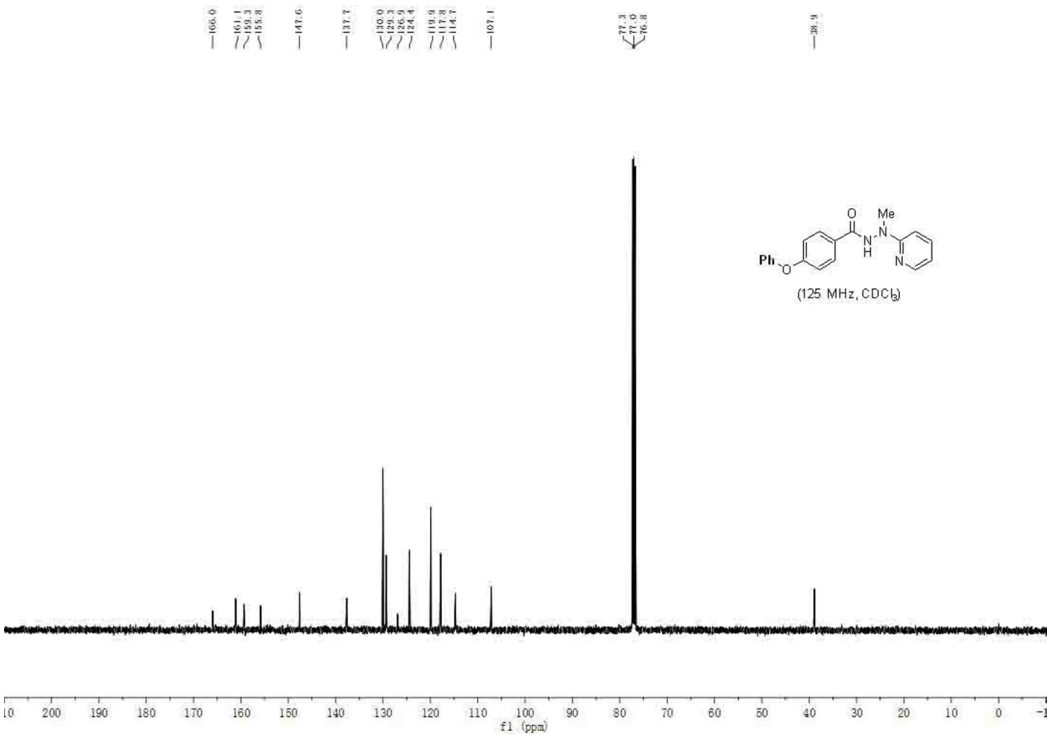


Figure S8. ^{13}C NMR Spectrum of **1f** (125 MHz, $CDCl_3$).

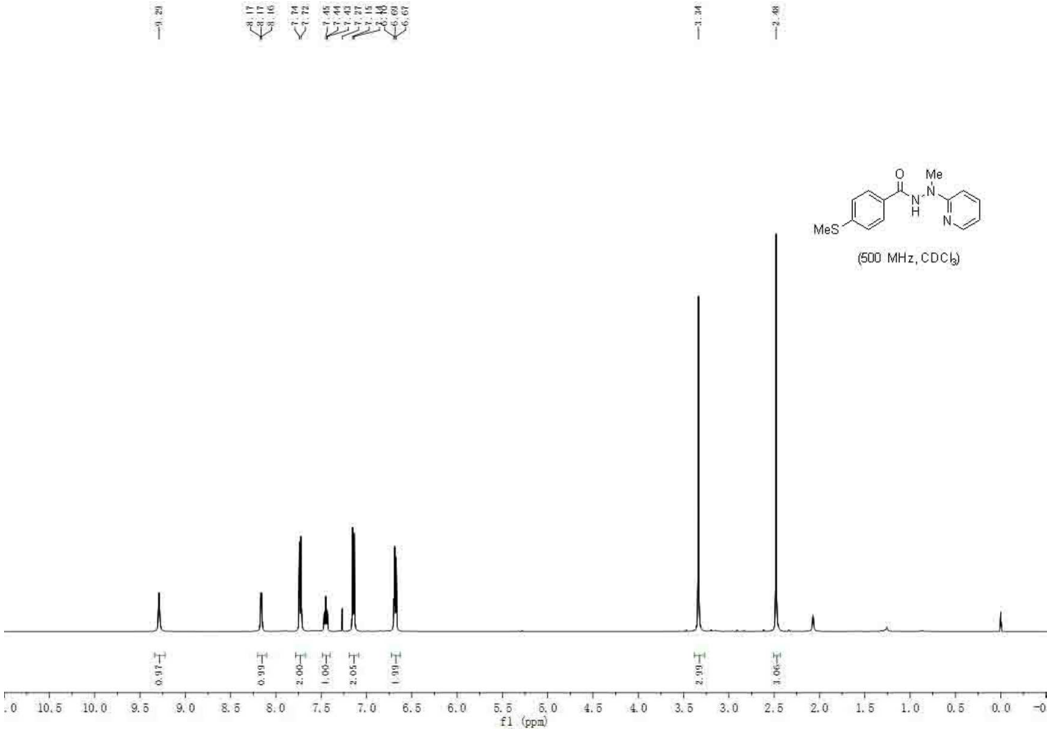


Figure S9. ^{1}H NMR Spectrum of **1g** (500 MHz, $CDCl_3$).

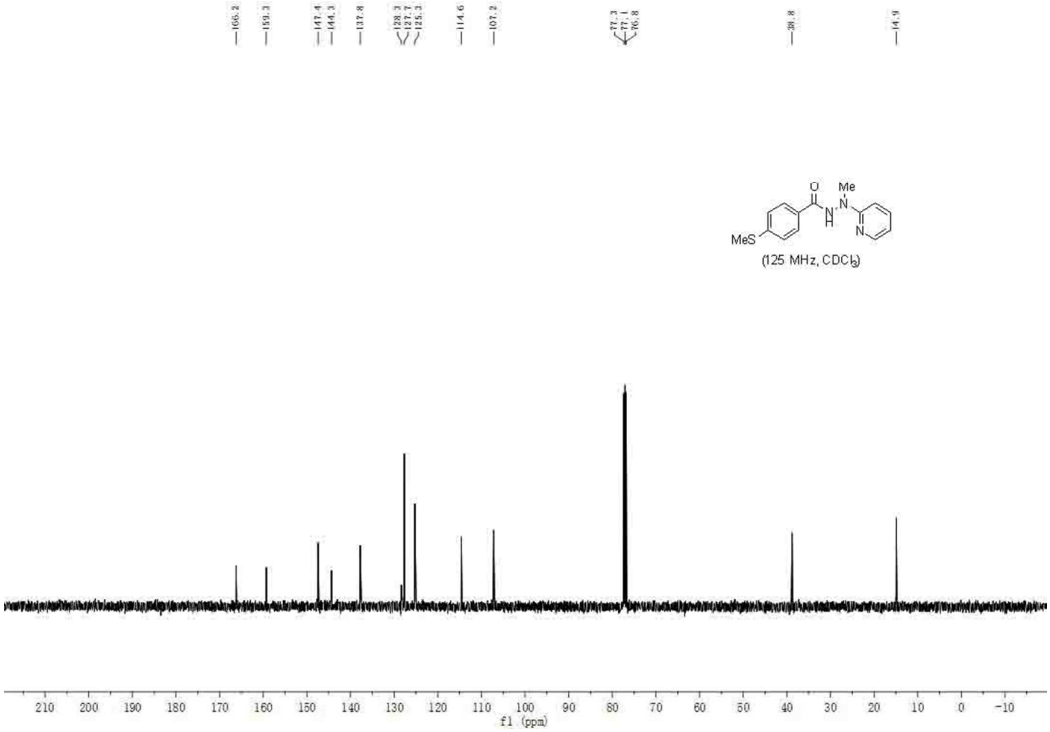


Figure S10. ^{13}C NMR Spectrum of **1g** (125 MHz, $CDCl_3$).

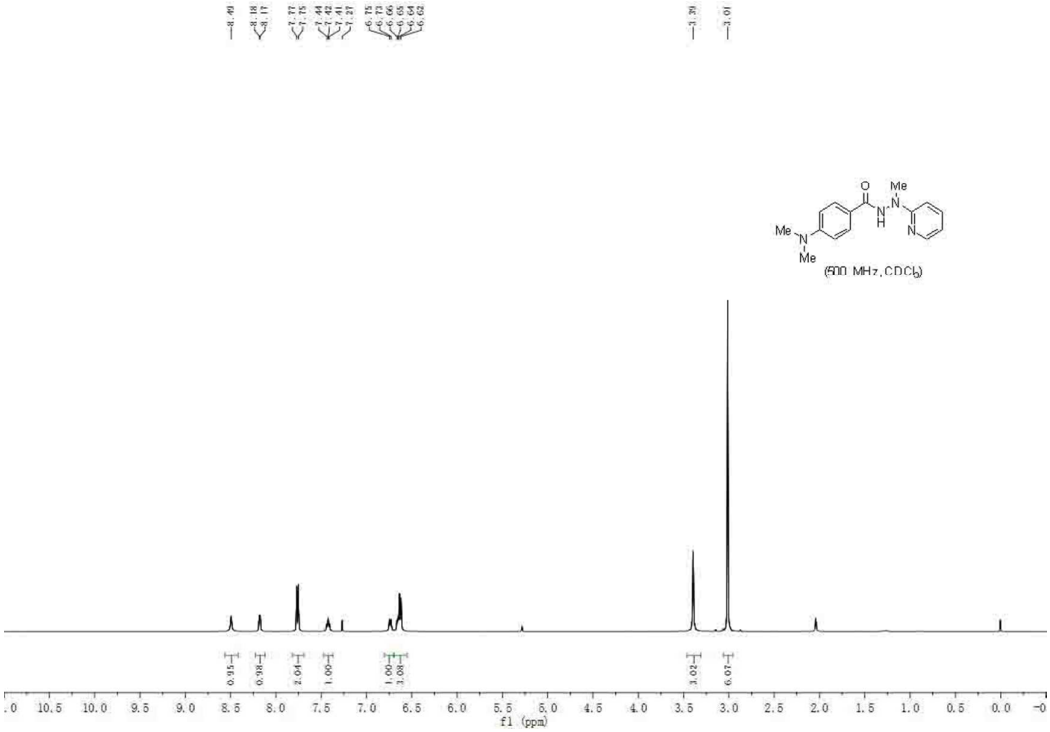


Figure S11. ^{1}H NMR Spectrum of **1h** (500 MHz, $CDCl_3$).

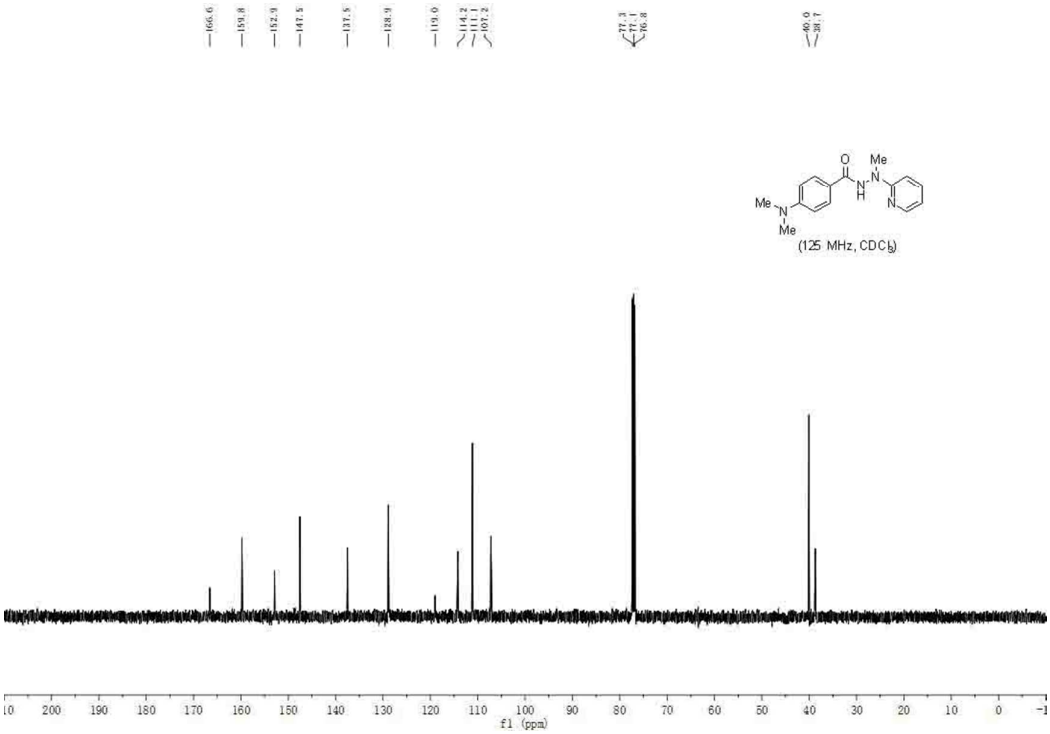


Figure S12. ^{13}C NMR Spectrum of **1h** (125 MHz, $CDCl_3$).

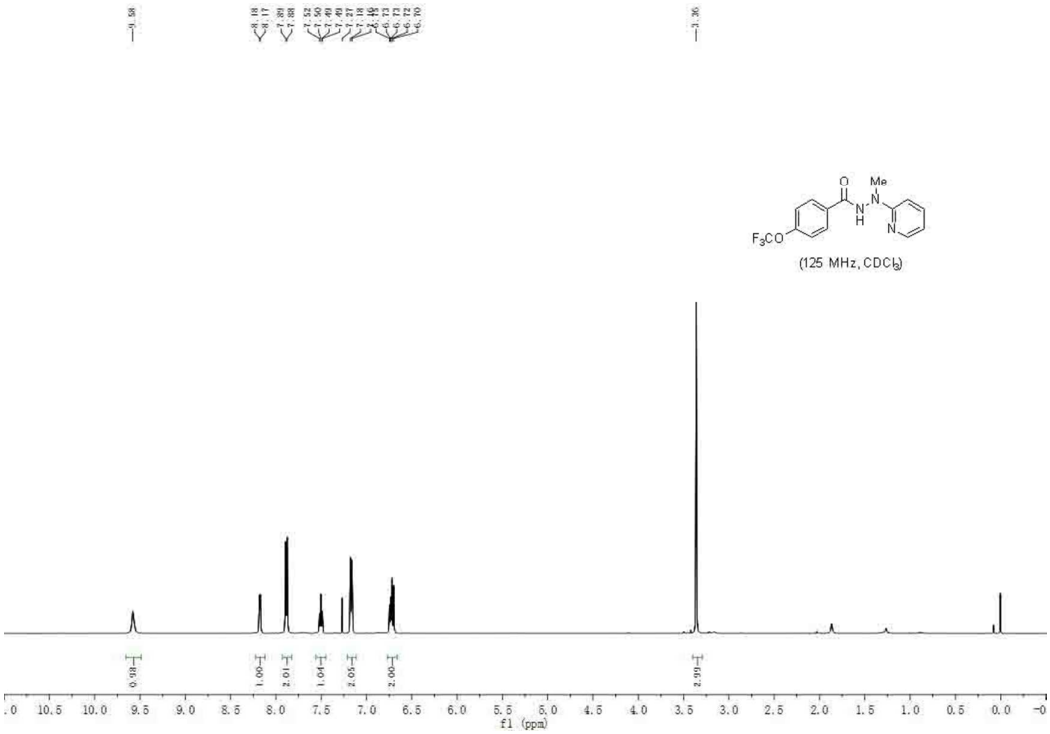


Figure S13. ^{1}H NMR Spectrum of **1i** (500 MHz, $CDCl_3$).

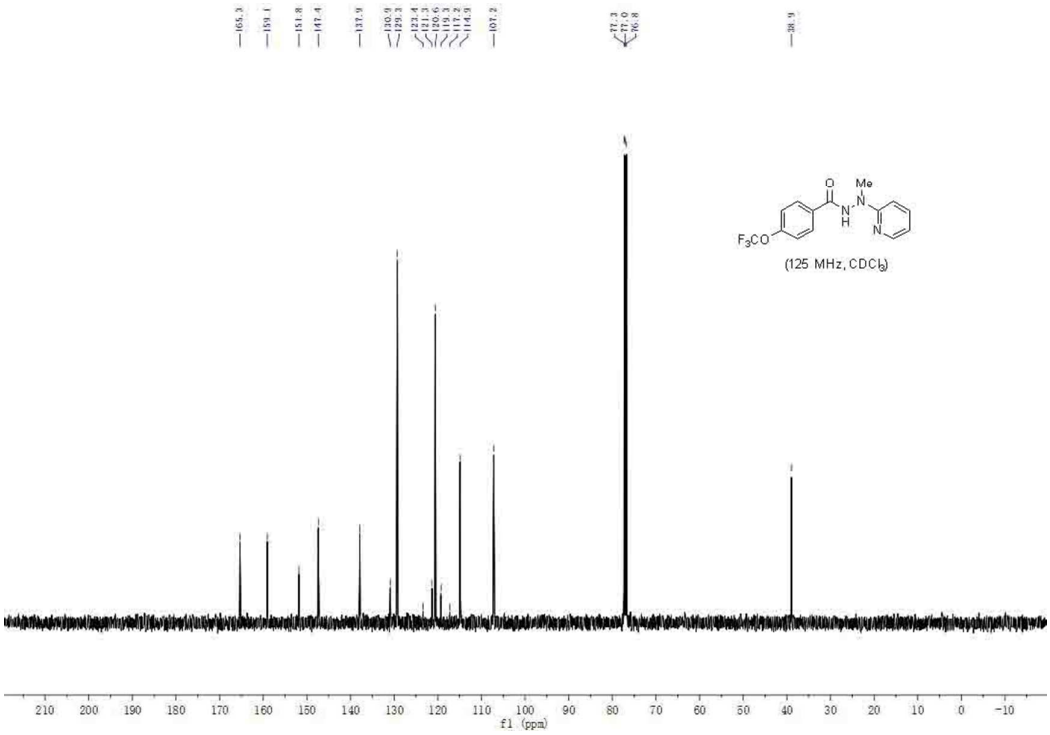


Figure S14. ^{13}C NMR Spectrum of **1i** (125 MHz, $CDCl_3$).

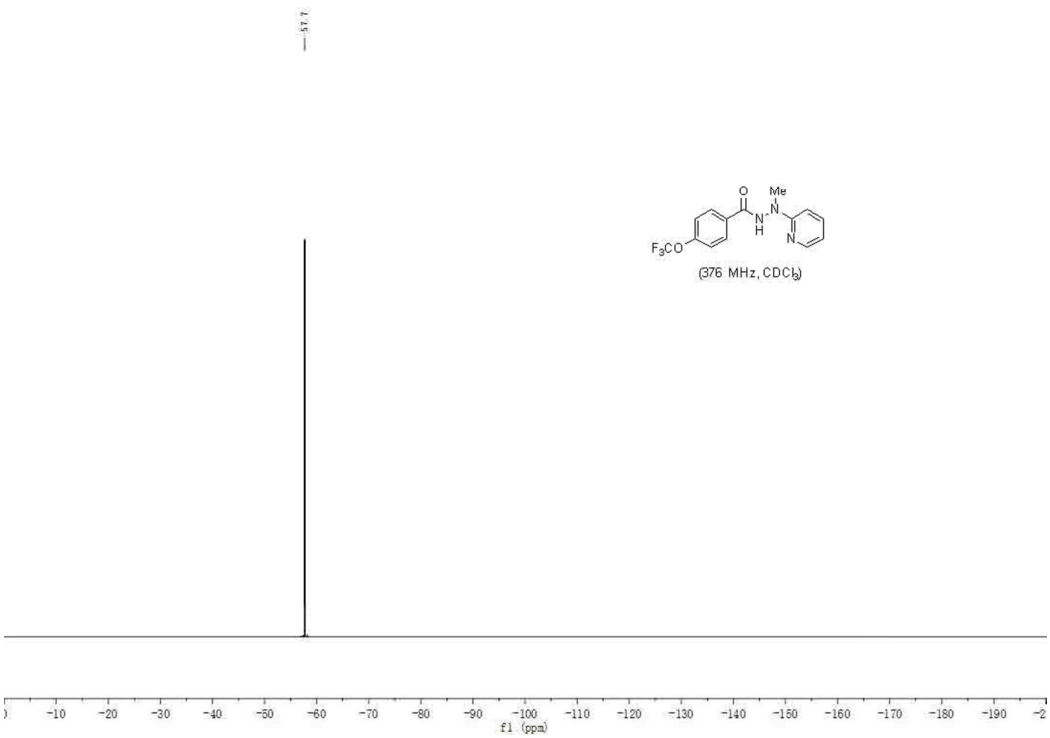


Figure S15. ^{19}F NMR Spectrum of **1i** (376 MHz, $CDCl_3$).

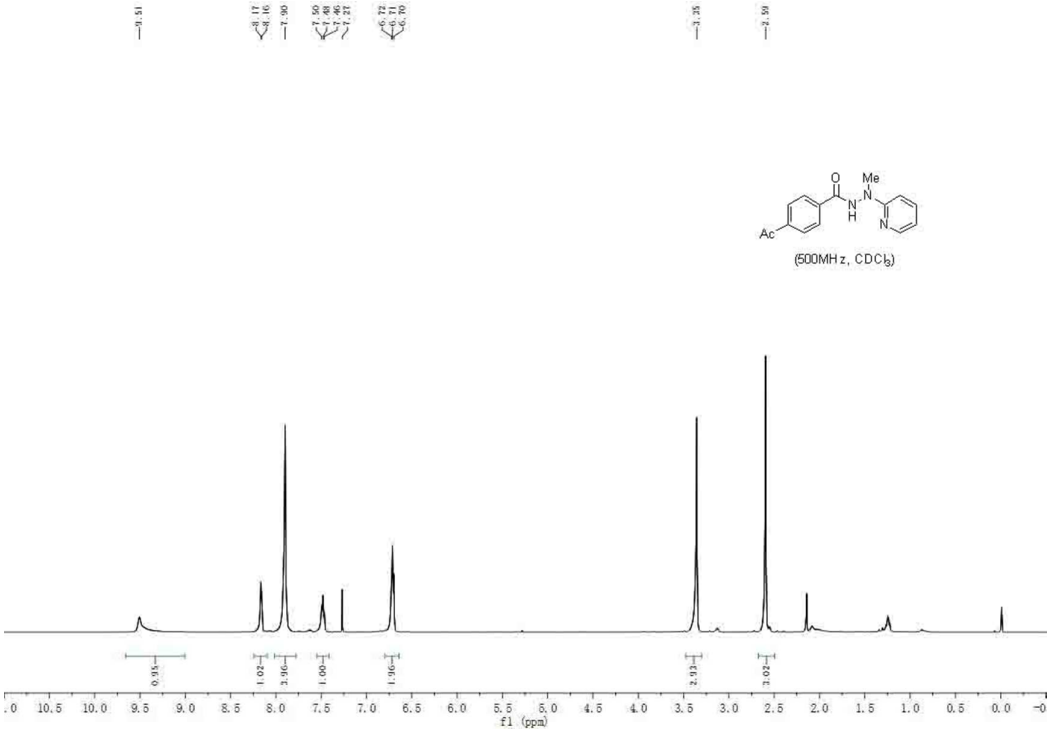


Figure S16. ^{1}H NMR Spectrum of **1o** (500 MHz, $CDCl_3$).

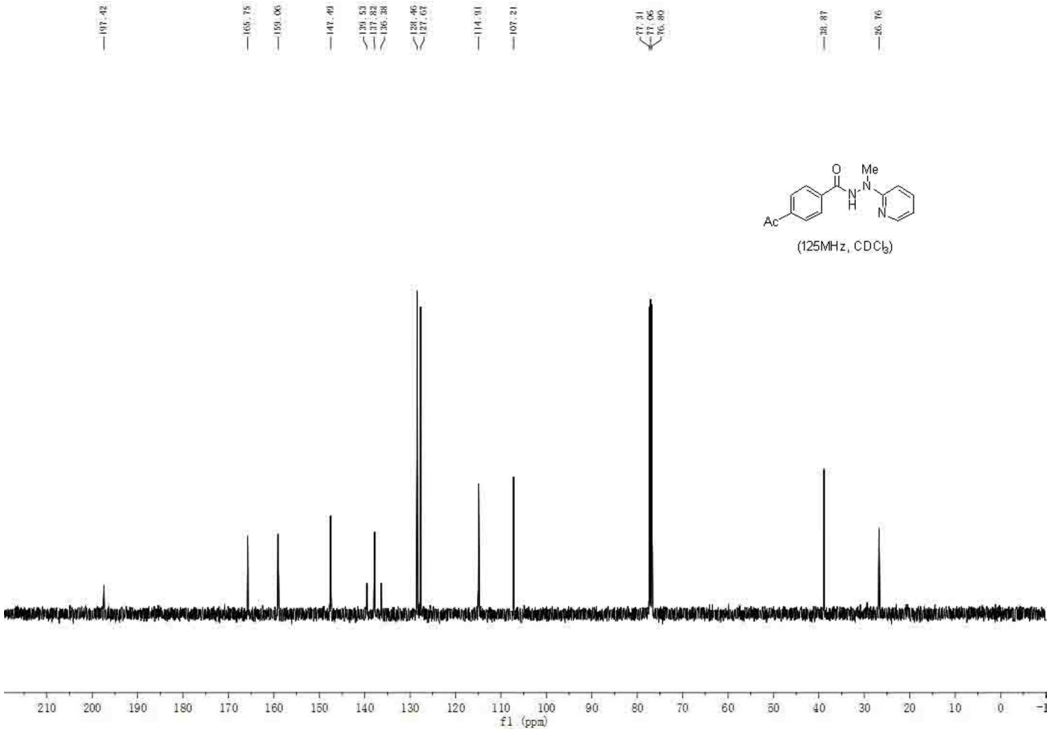


Figure S17. ^{13}C NMR Spectrum of **1o** (125 MHz, $CDCl_3$).

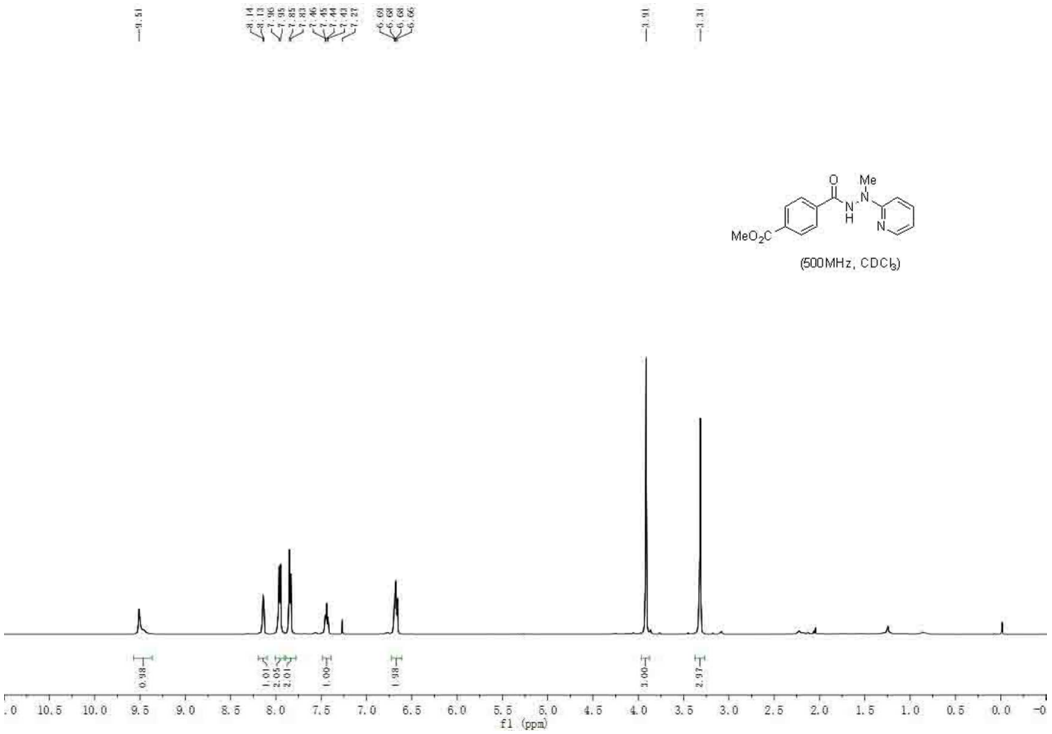


Figure S18. ^{1}H NMR Spectrum of **1p** (500 MHz, $CDCl_3$).

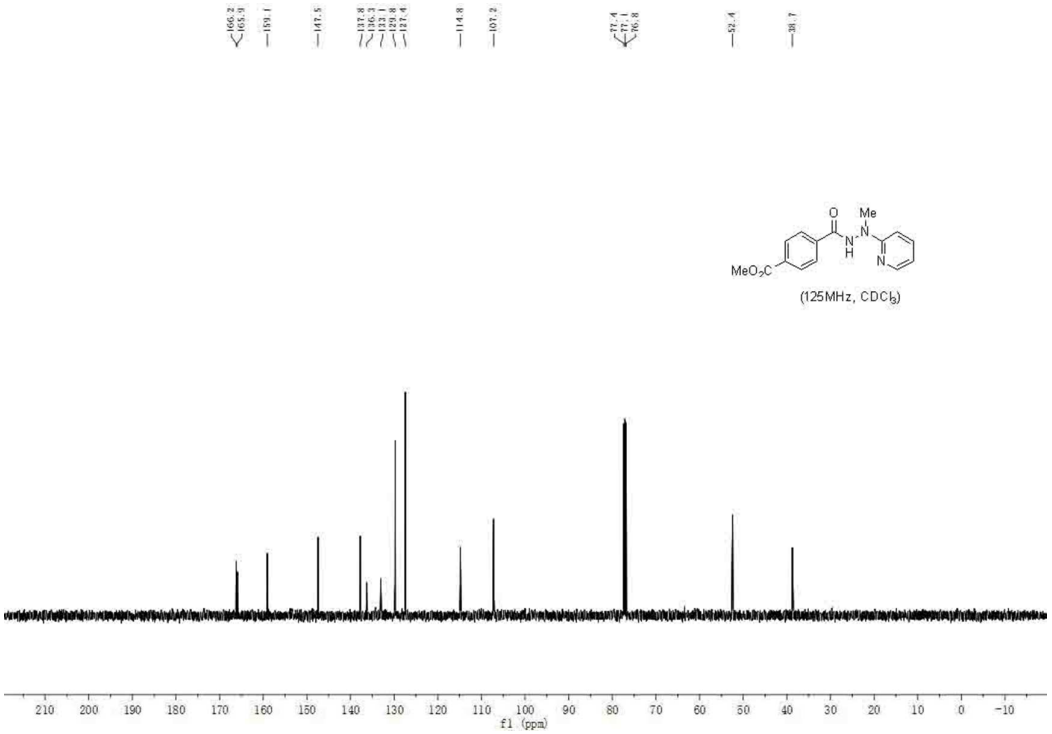


Figure S19. ^{13}C NMR Spectrum of **1p** (125 MHz, $CDCl_3$).

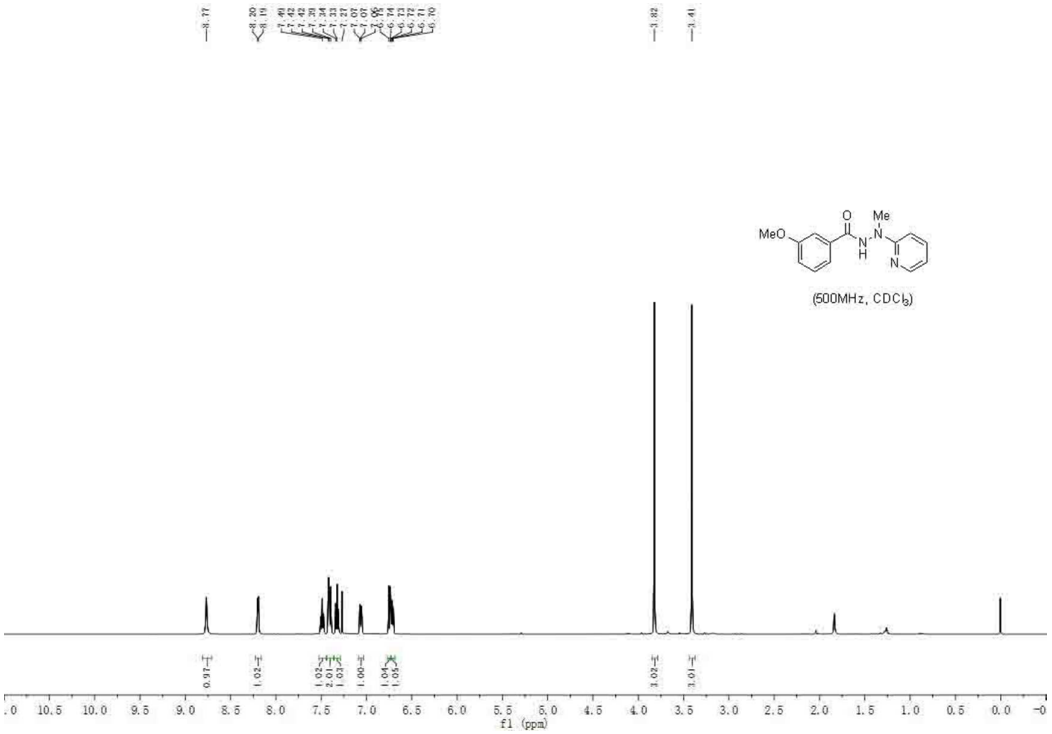


Figure S20. ^{1}H NMR Spectrum of **1r** (500 MHz, $CDCl_3$).

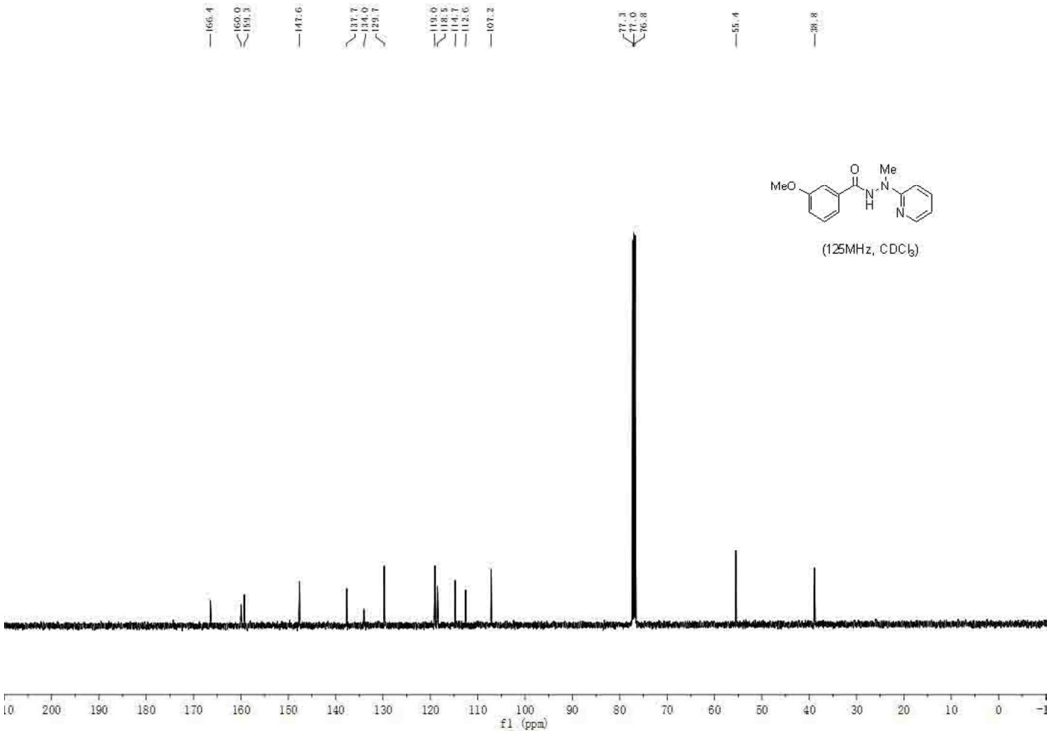


Figure S21. ^{13}C NMR Spectrum of **1r** (125 MHz, $CDCl_3$).

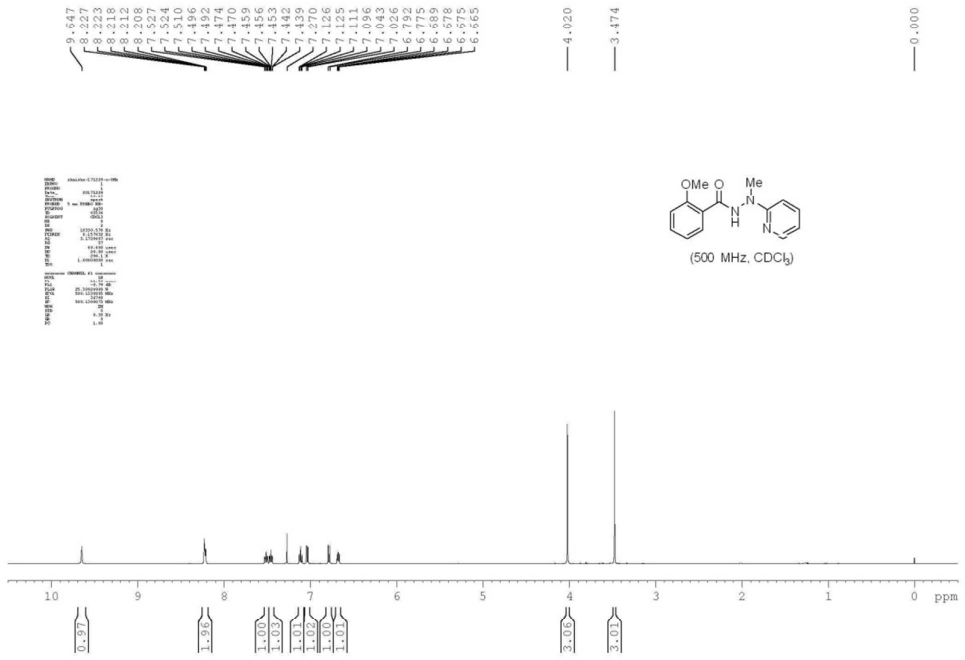


Figure S22. ^{1}H NMR Spectrum of **1u** (500 MHz, $CDCl_3$).

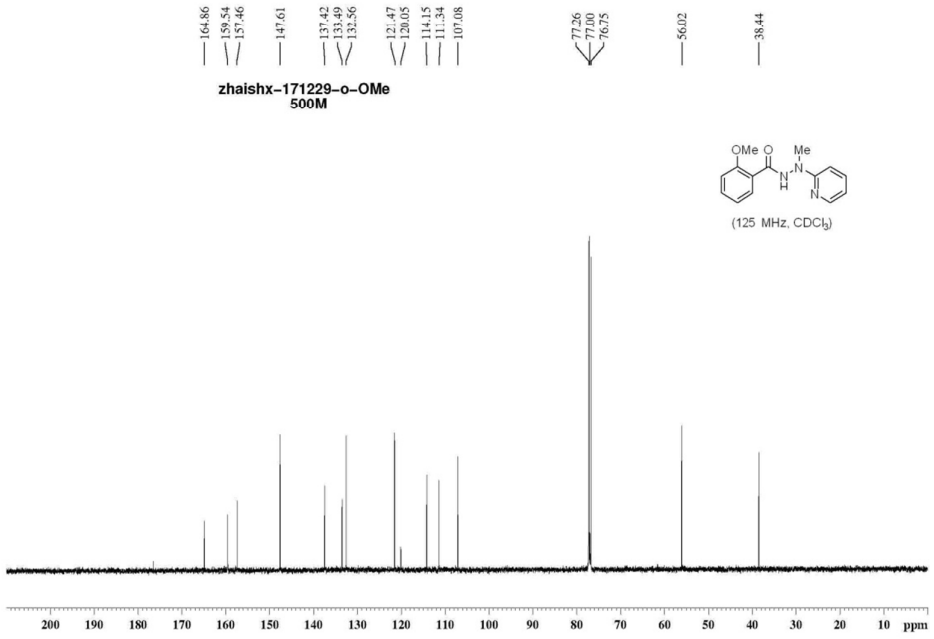


Figure S23. ^{13}C NMR Spectrum of **1u** (125 MHz, $CDCl_3$).

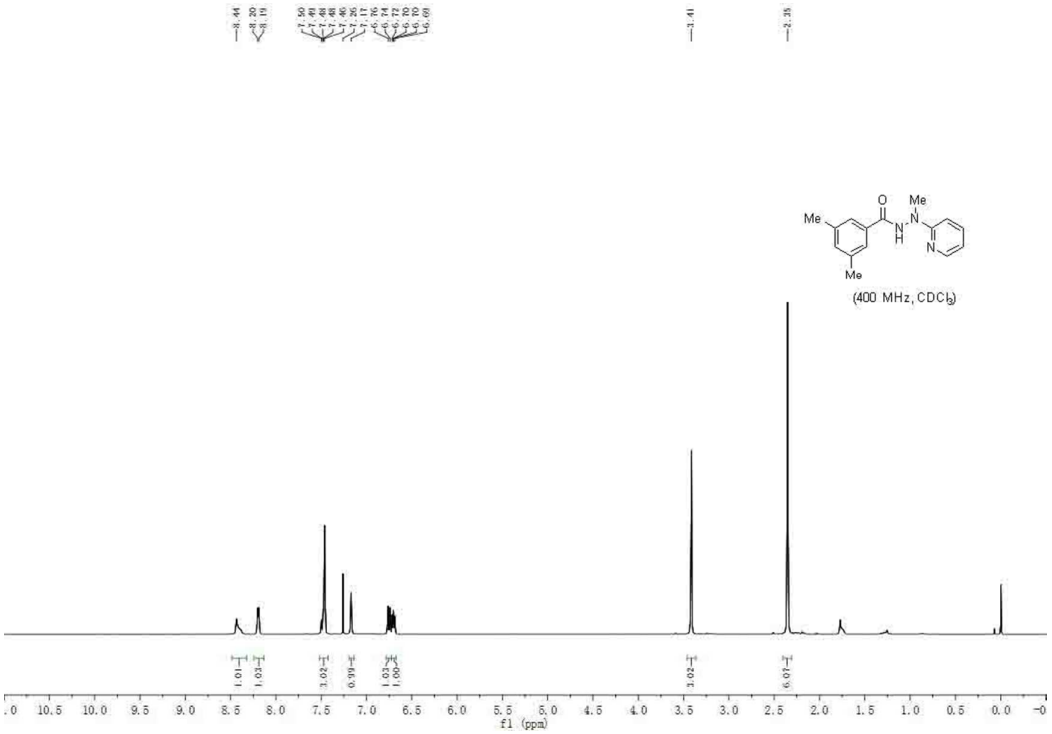


Figure S24. ^{1}H NMR Spectrum of **1v** (500 MHz, $CDCl_3$).

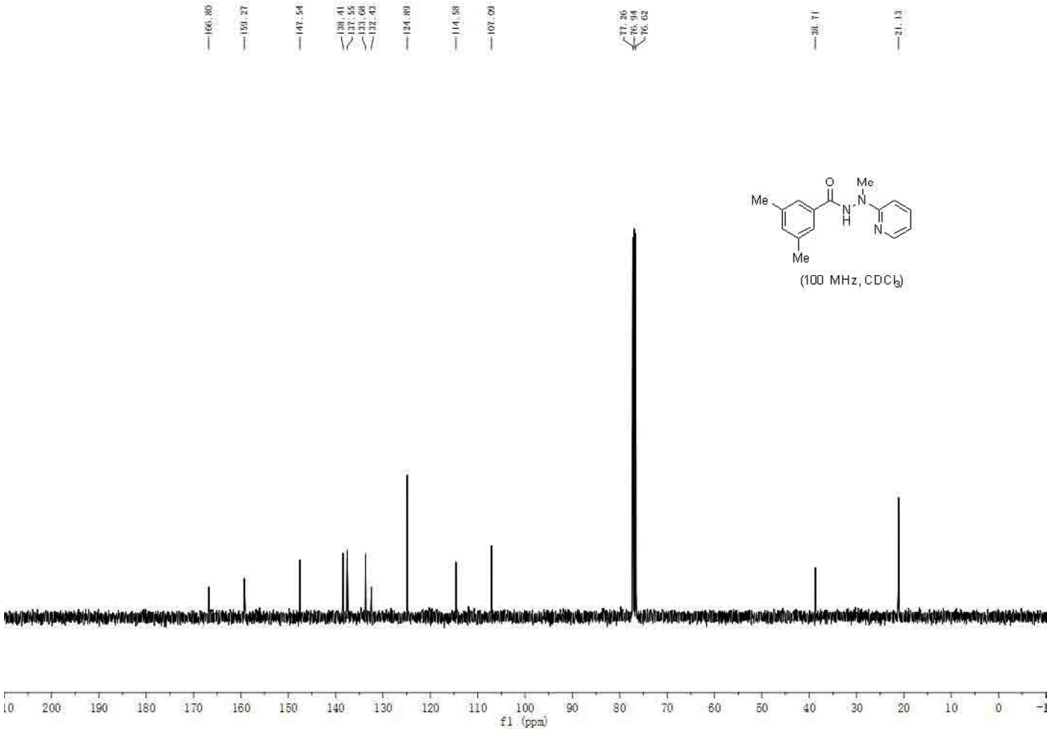


Figure S25. ^{13}C NMR Spectrum of **1v** (125 MHz, $CDCl_3$).

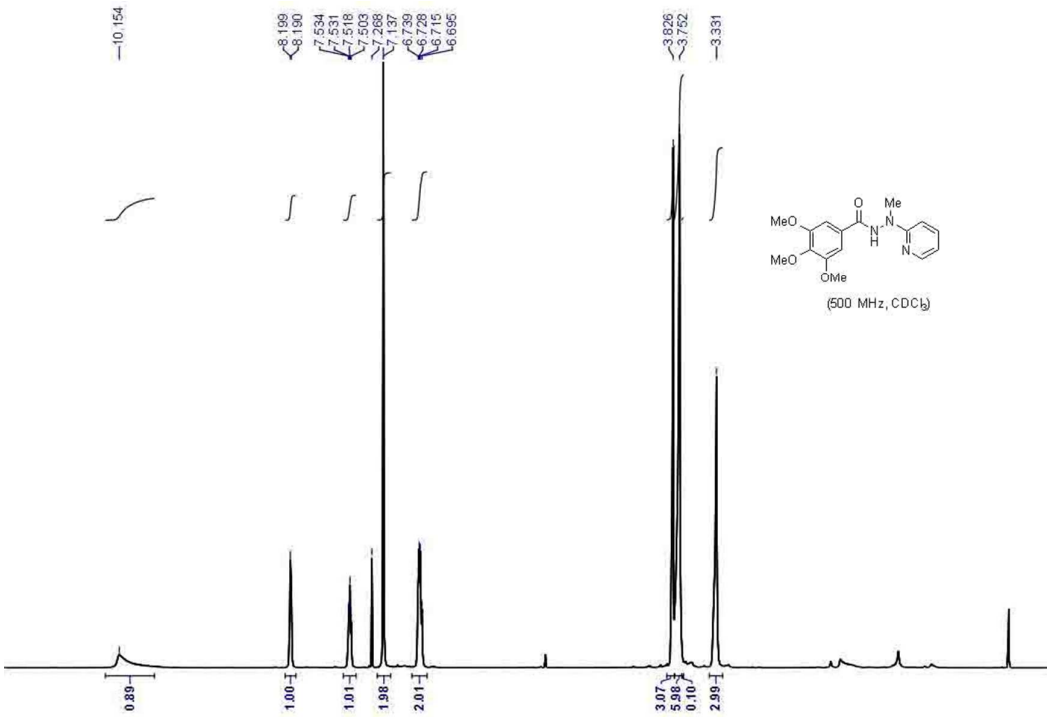


Figure S26. ^{1}H NMR Spectrum of **1w** (500 MHz, $CDCl_3$).

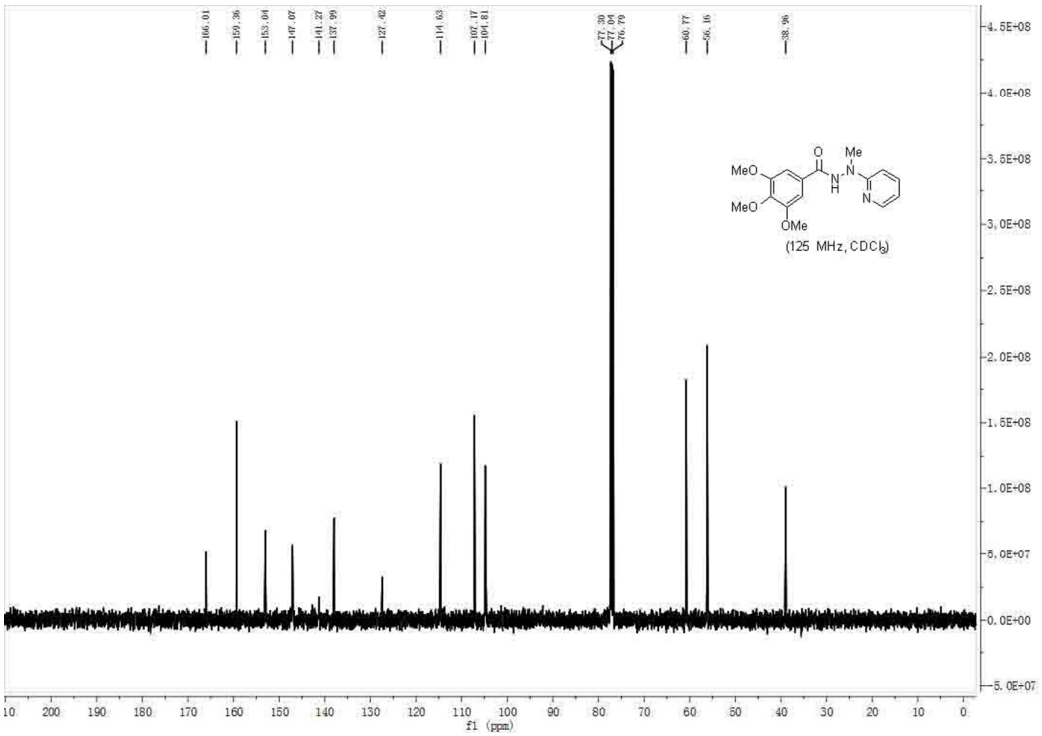


Figure S27. ^{13}C NMR Spectrum of **1w** (125 MHz, $CDCl_3$).

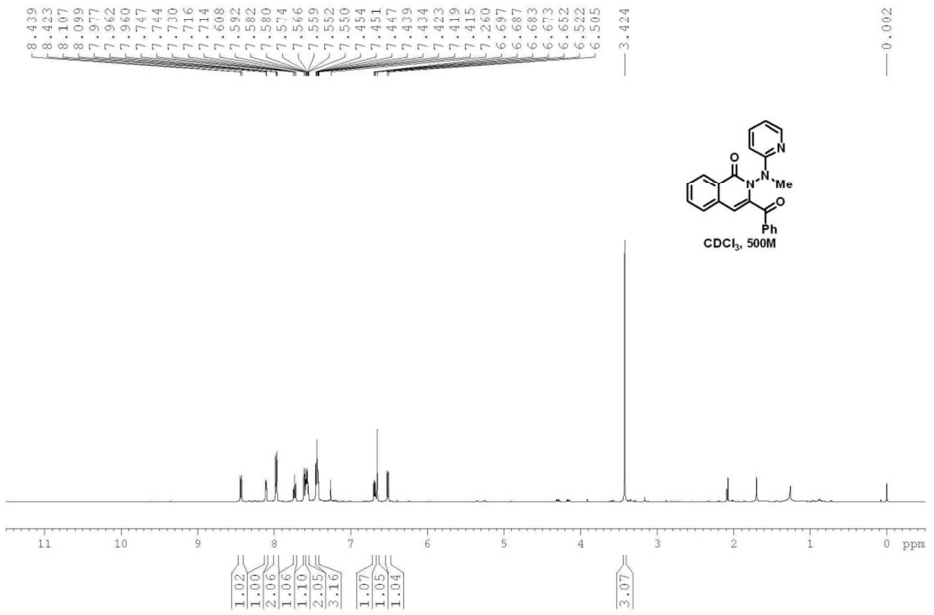


Figure S28. ^{1}H NMR Spectrum of **3aa** (500 MHz, $CDCl_3$).

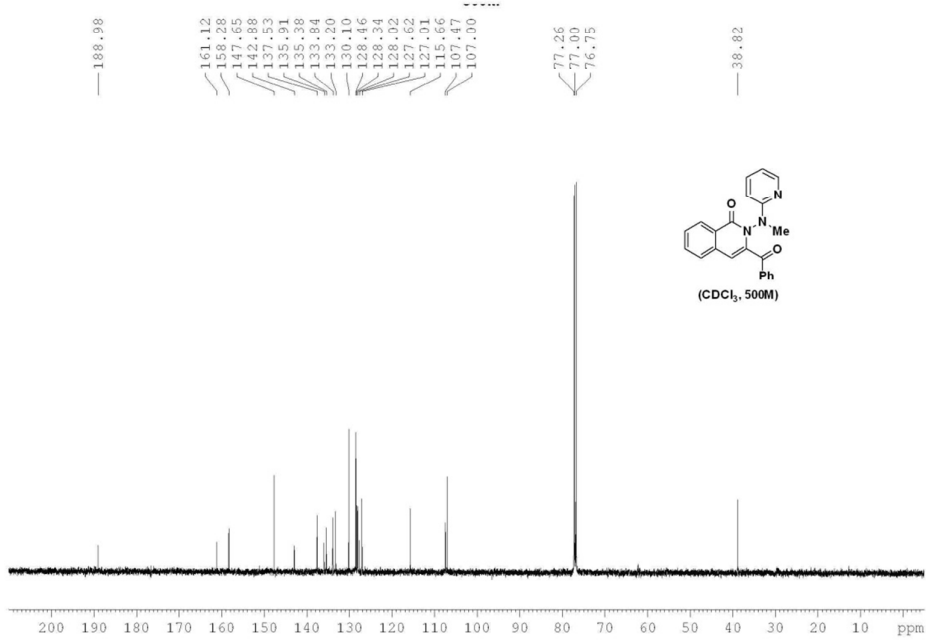


Figure S29. ^{1}H NMR Spectrum of **3aa** (500 MHz, $CDCl_3$).

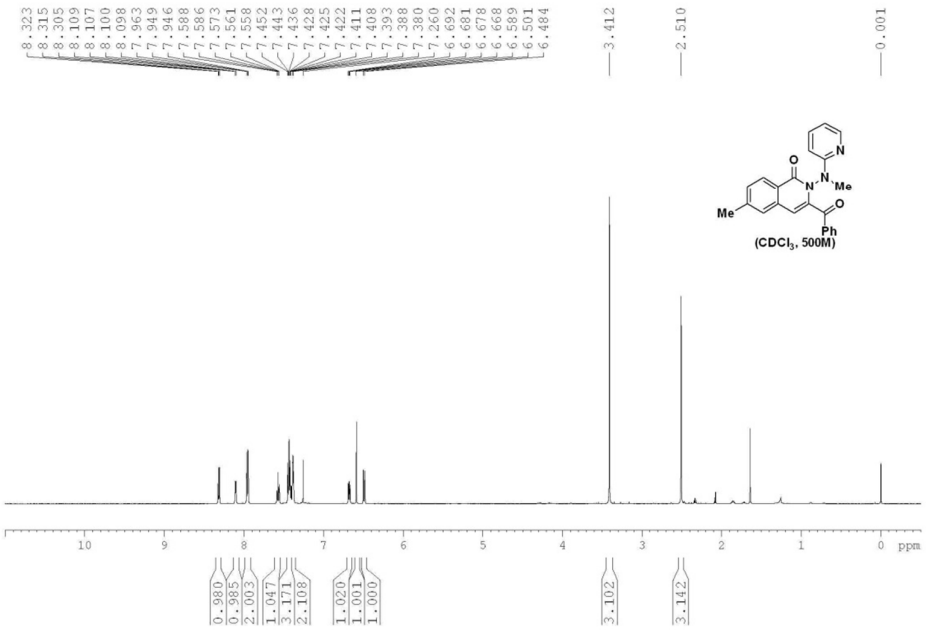


Figure S30. ^{1}H NMR Spectrum of **3ba** (500 MHz, $CDCl_3$).

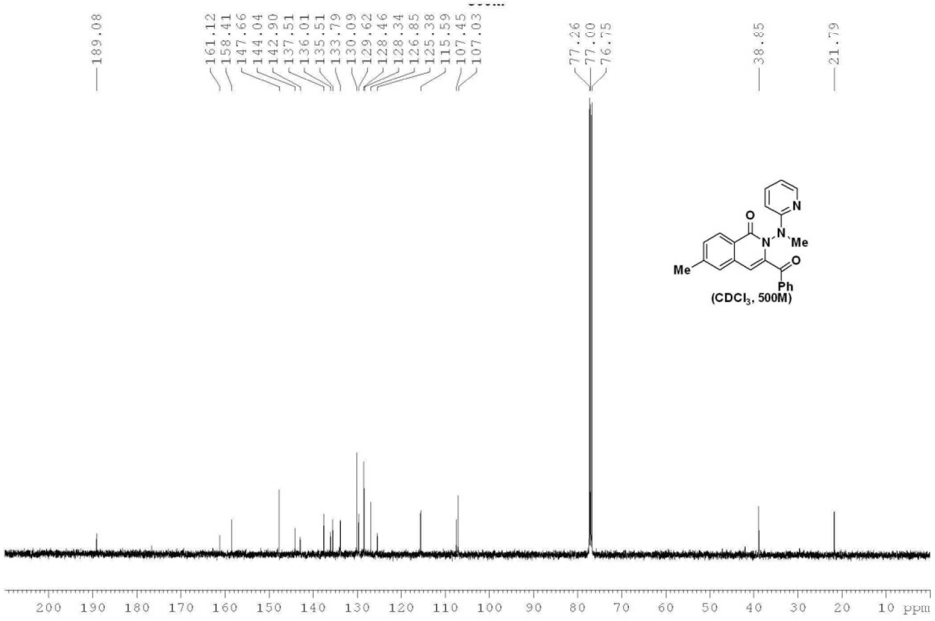


Figure S31. ^{13}C NMR Spectrum of **3ba** (125 MHz, $CDCl_3$).

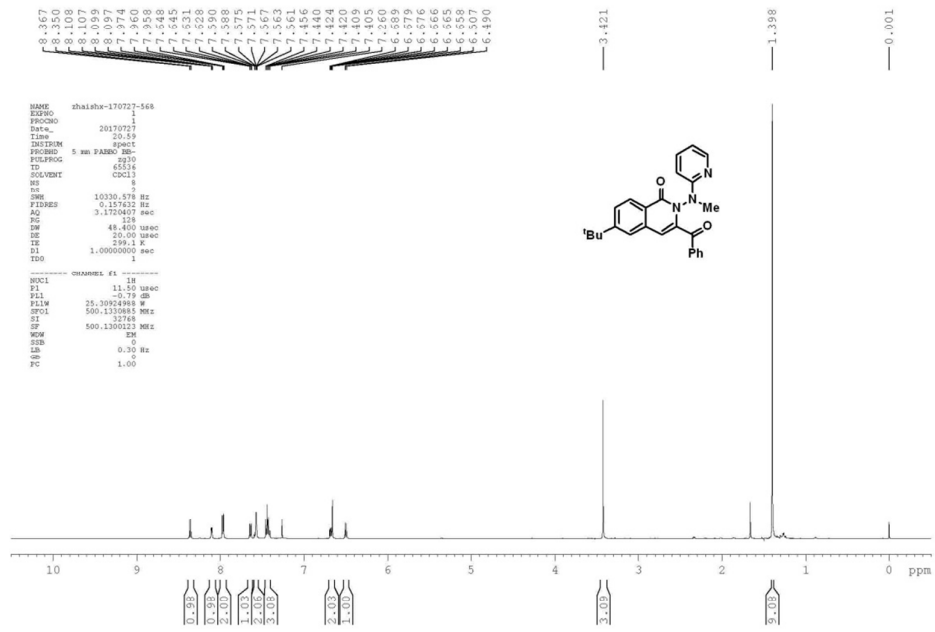


Figure S32. ^{1}H NMR Spectrum of **3ca** (500 MHz, $CDCl_3$).

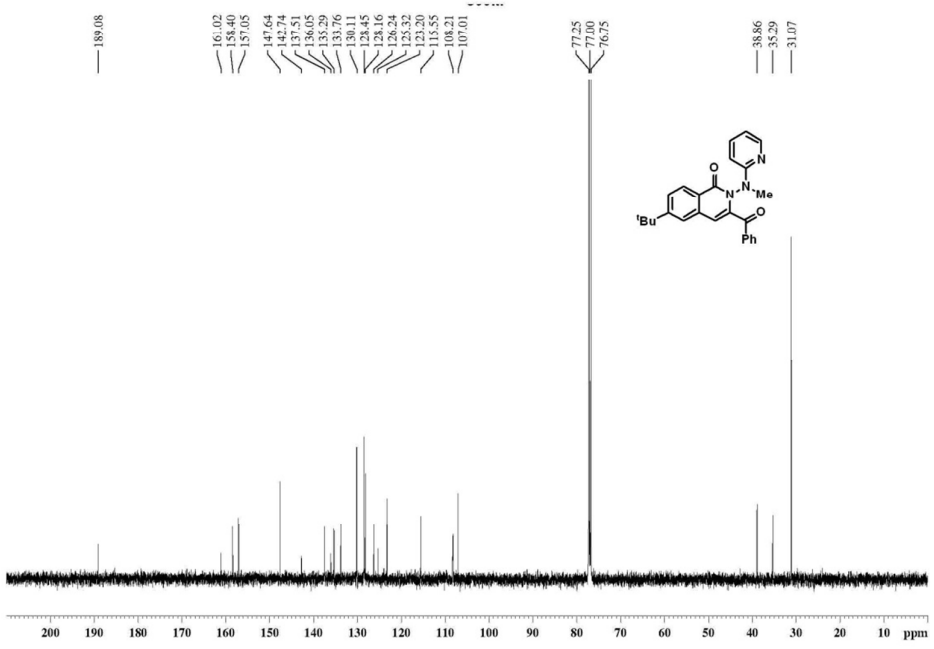


Figure S33. ^{13}C NMR Spectrum of **3ca**(125 MHz, $CDCl_3$).

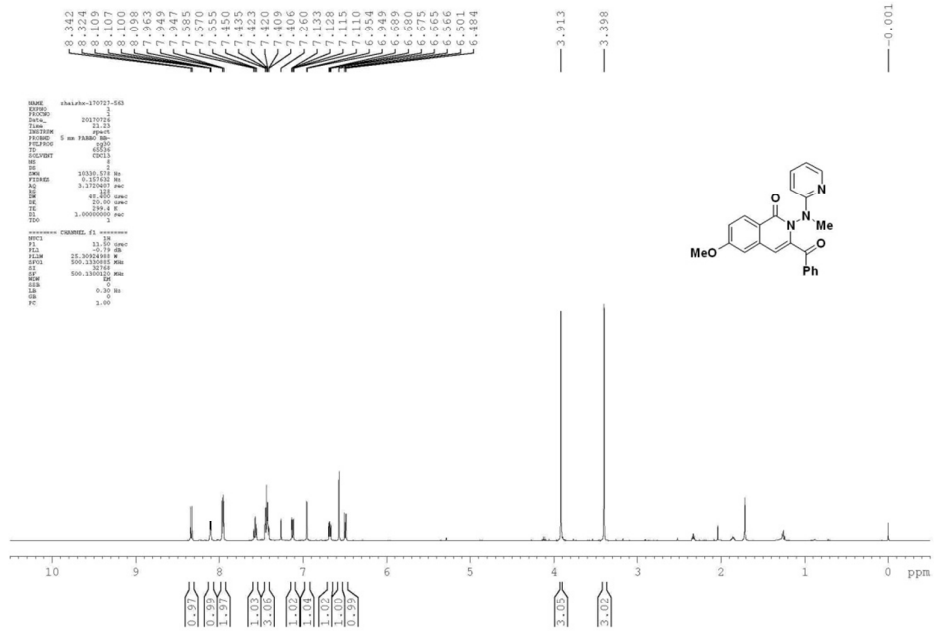


Figure S34. ^{1}H NMR Spectrum of **3da** (500 MHz, $CDCl_3$).

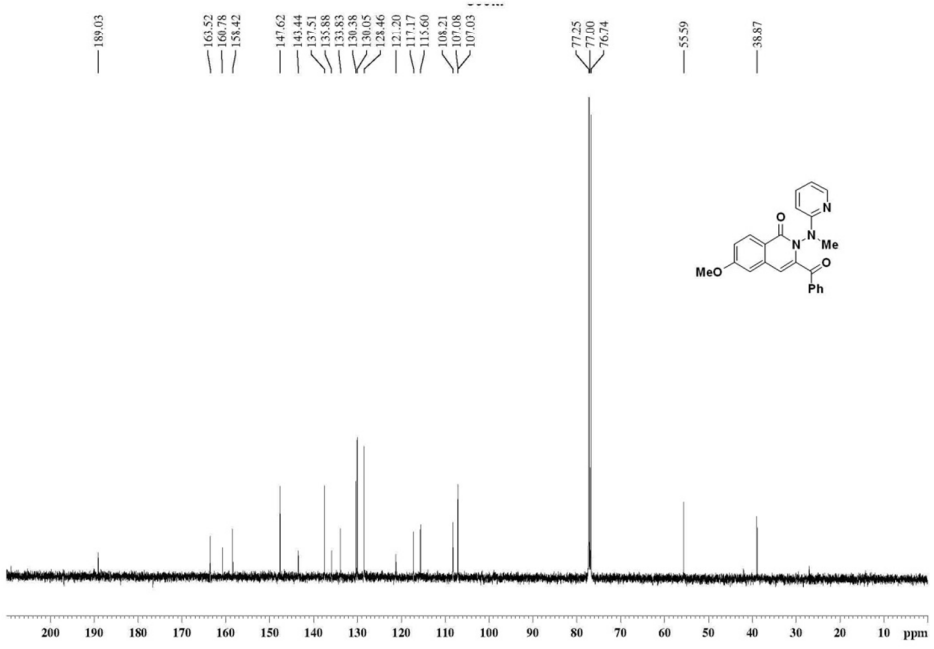


Figure S35. ^{13}C NMR Spectrum of **3da** (125 MHz, $CDCl_3$).

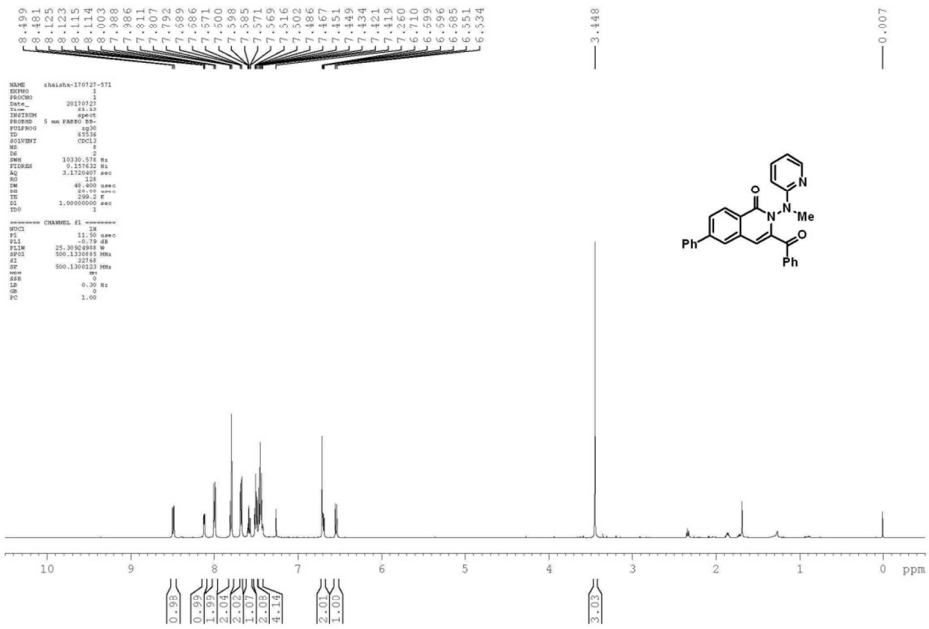


Figure S36. ^{1}H NMR Spectrum of **3ea** (500 MHz, $CDCl_3$).

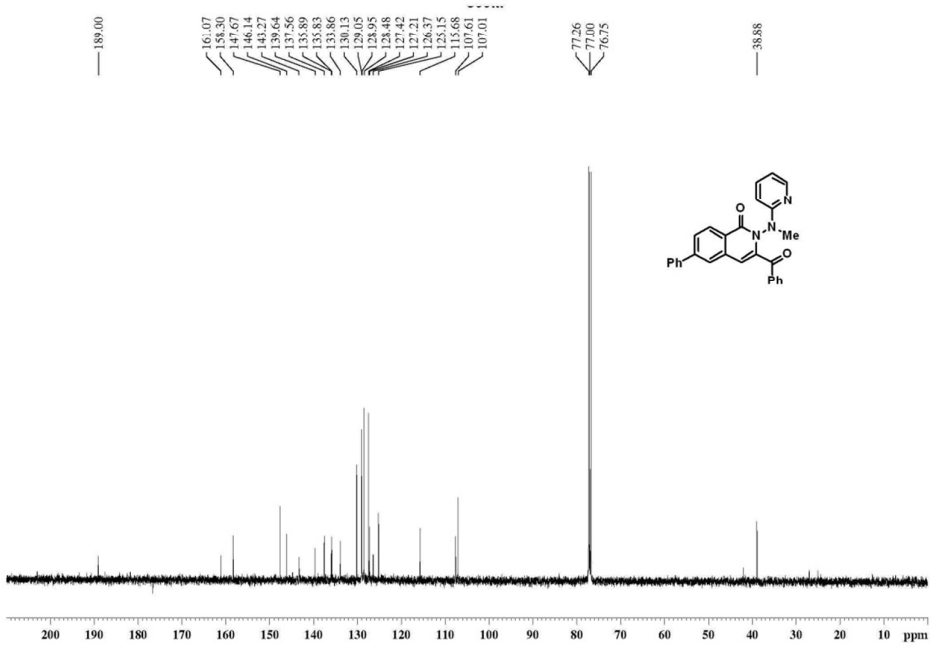


Figure S37. ^{13}C NMR Spectrum of **3ea** (125 MHz, $CDCl_3$).

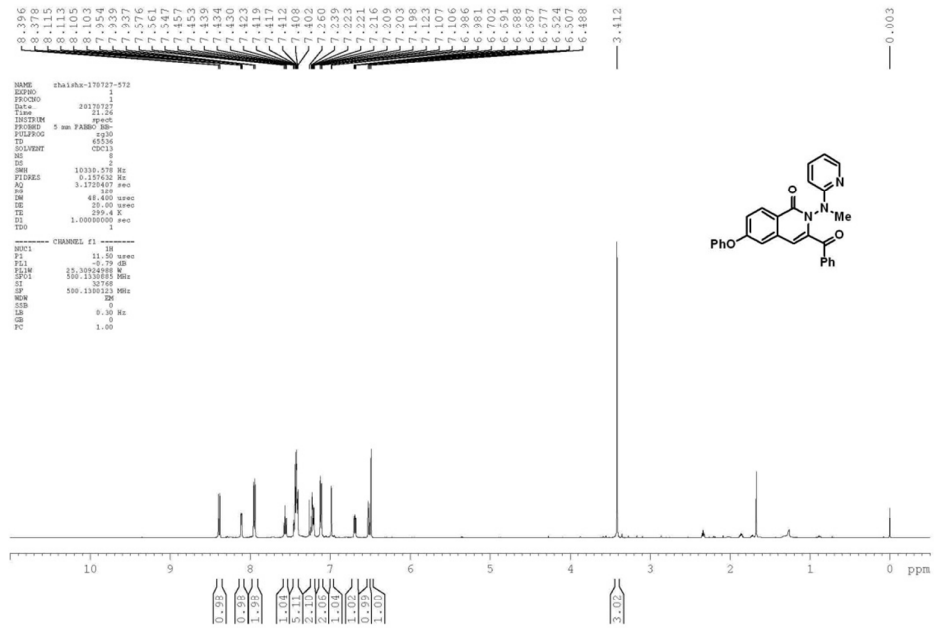


Figure S38. ^{1}H NMR Spectrum of **3fa** (500 MHz, $CDCl_3$).

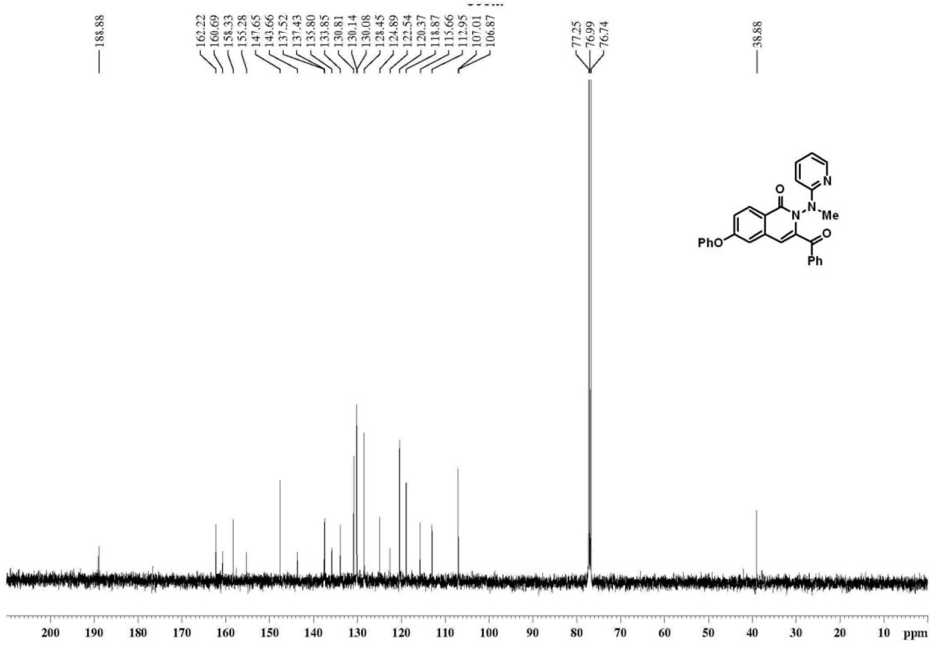


Figure S39. ^{13}C NMR Spectrum of **3fa** (125 MHz, $CDCl_3$).

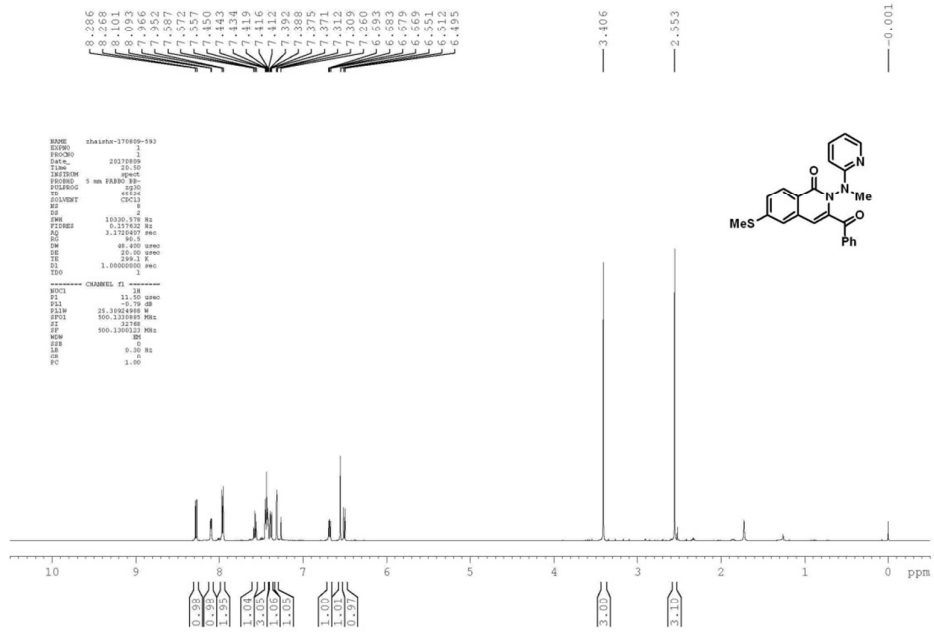


Figure S40. ^{1}H NMR Spectrum of **3ga** (500 MHz, $CDCl_3$).

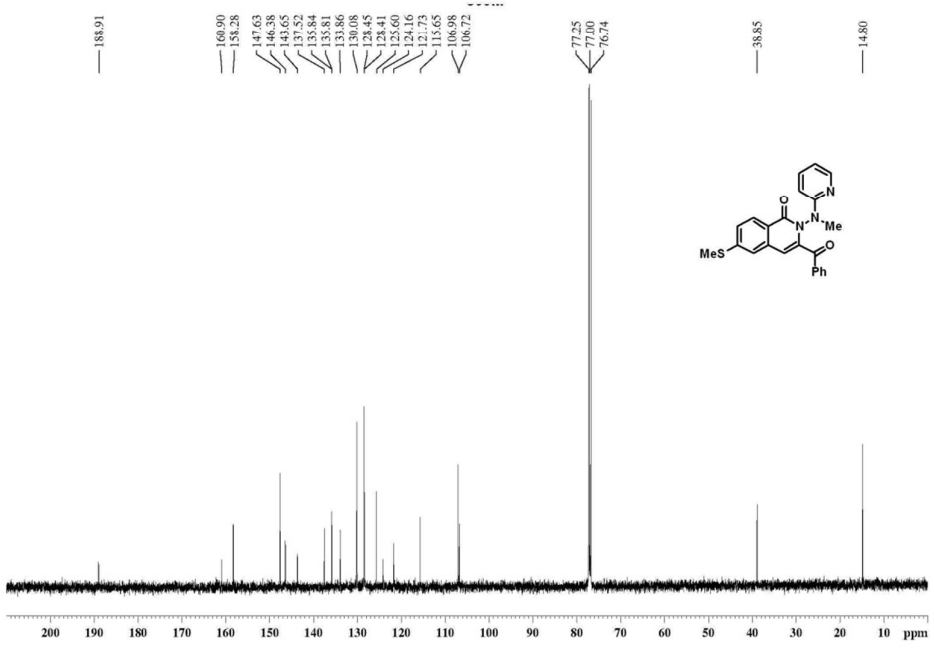


Figure S41. ^{13}C NMR Spectrum of **3ga** (125 MHz, $CDCl_3$).

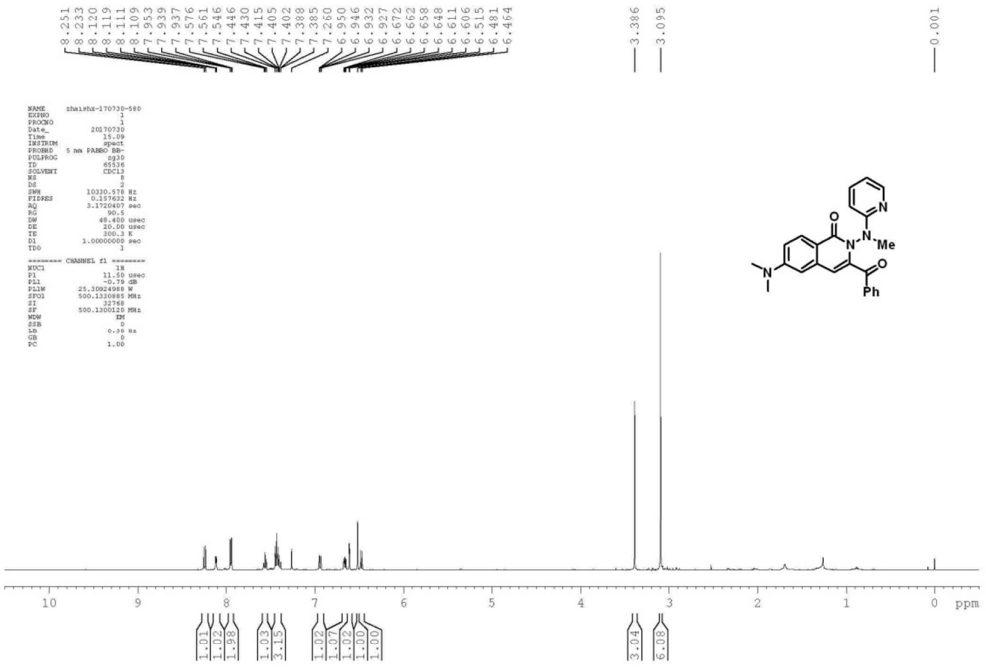


Figure S42. ^{1}H NMR Spectrum of **3ha** (500 MHz, $CDCl_3$).

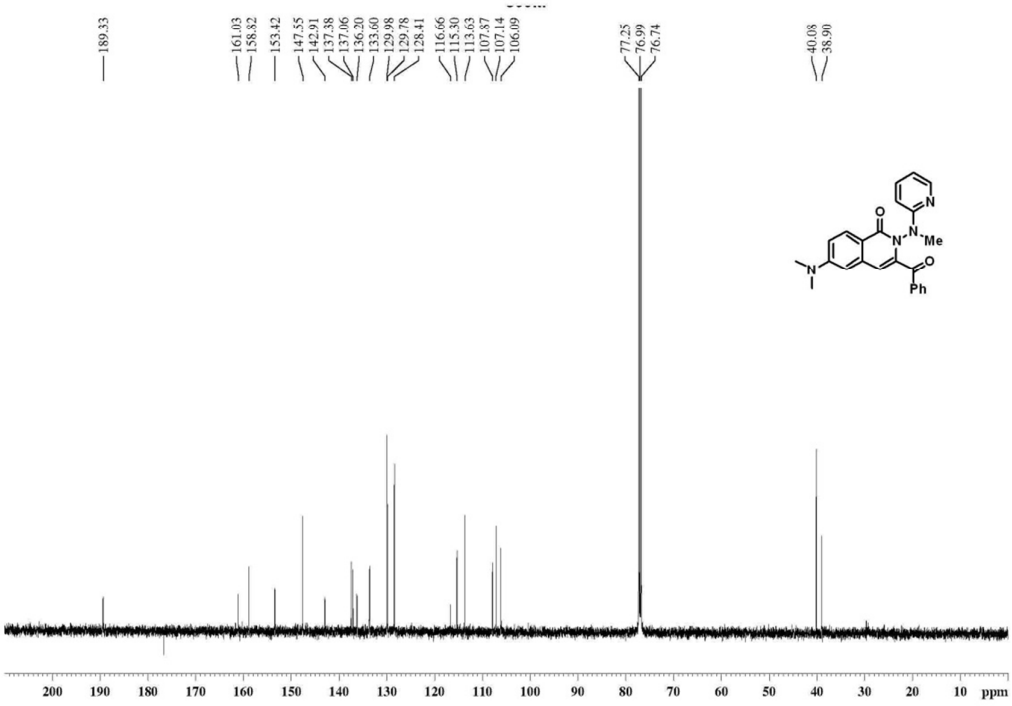


Figure S43. ^{13}C NMR Spectrum of **3ha** (125 MHz, $CDCl_3$).

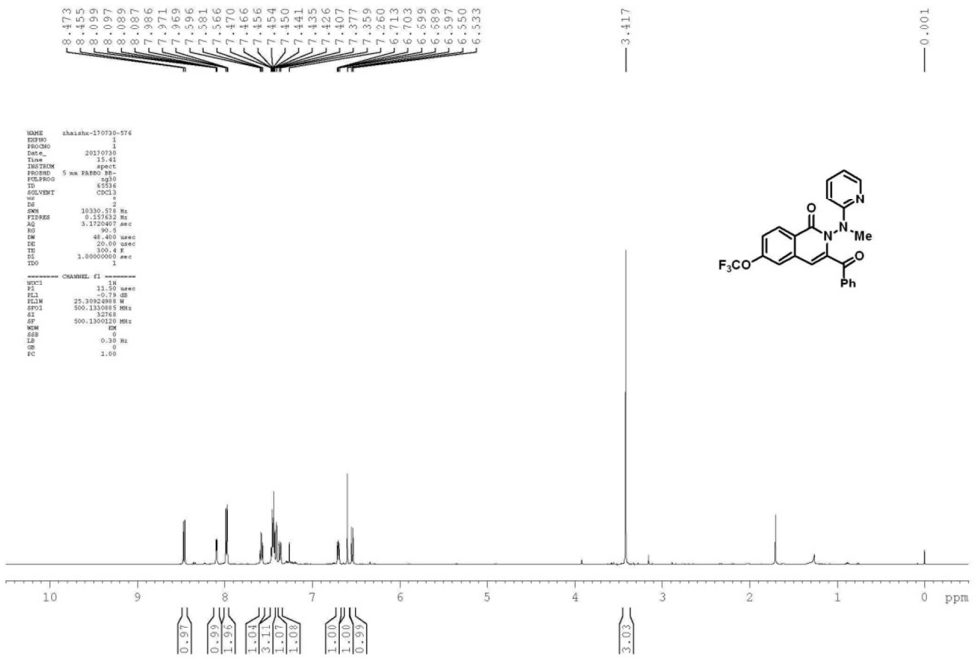


Figure S44. ^{1}H NMR Spectrum of **3ia**(500 MHz, $CDCl_3$).

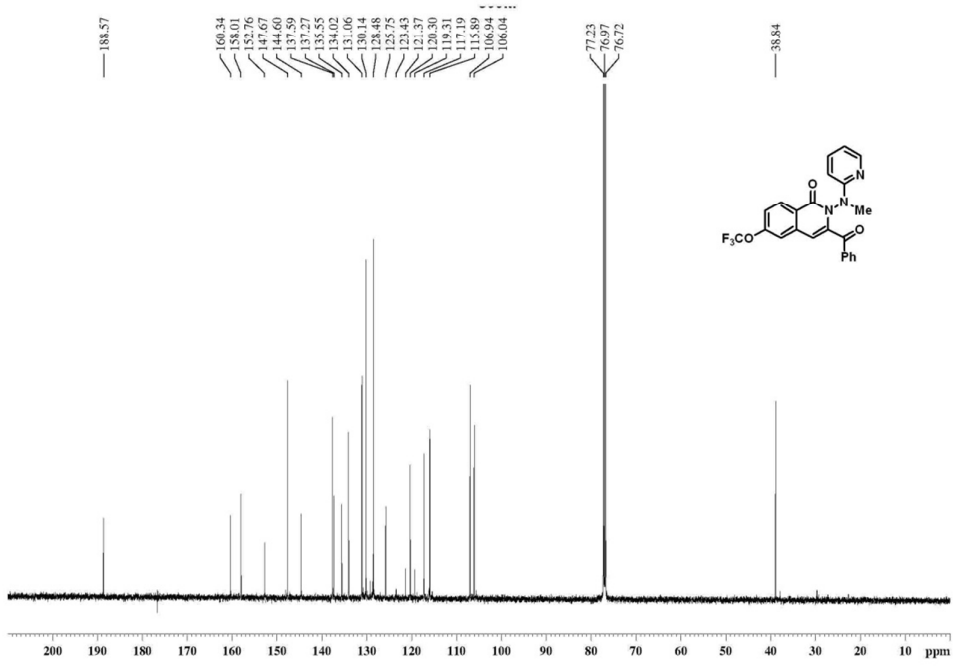


Figure S45. ^{13}C NMR Spectrum of **3ia** (125 MHz, $CDCl_3$).

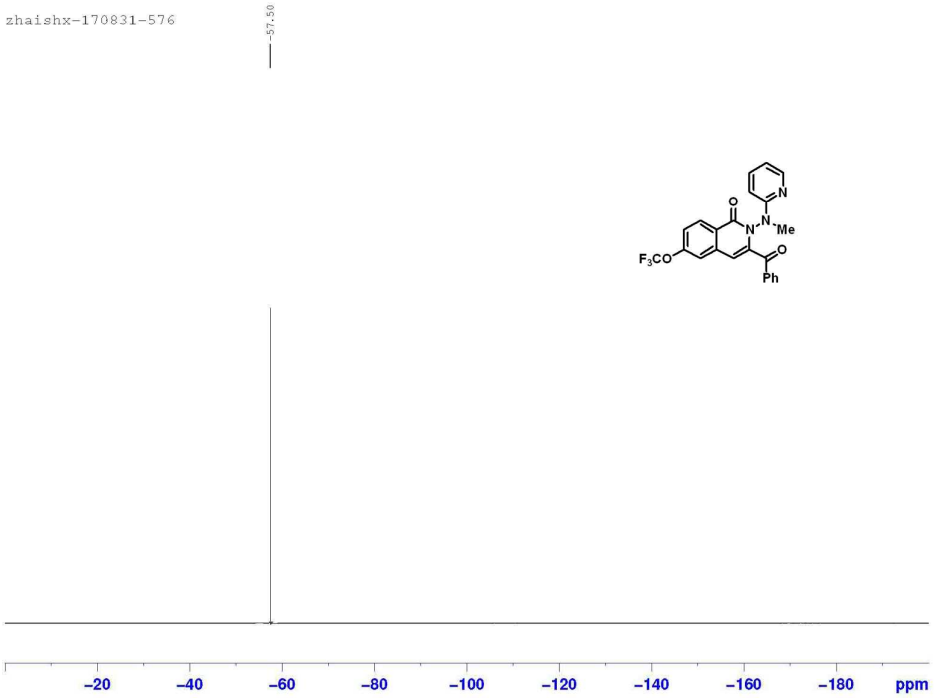


Figure S46. ^{19}F NMR Spectrum of **3ia** (376 MHz, $CDCl_3$).

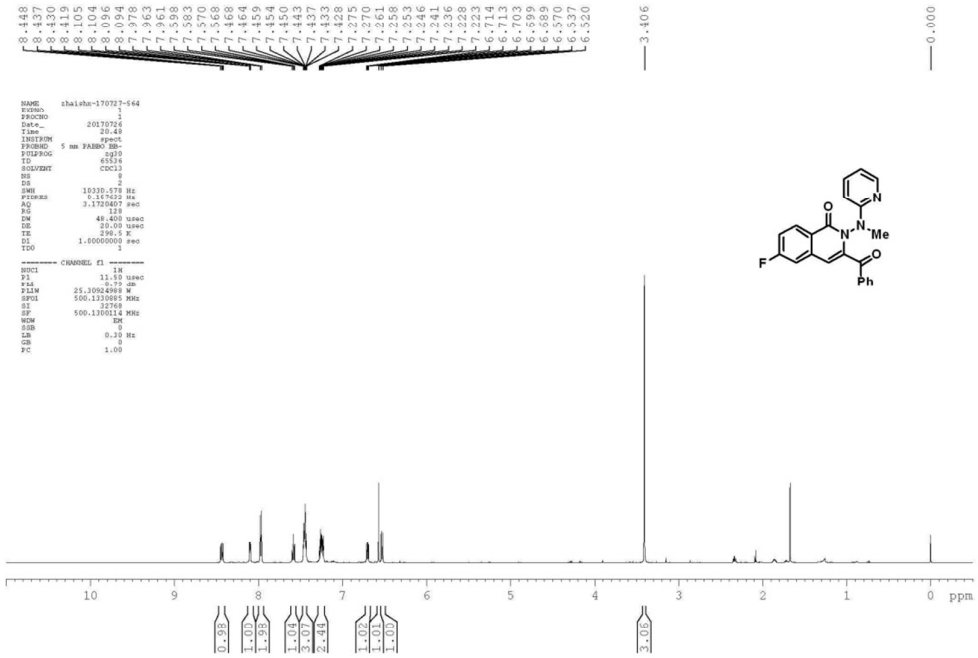


Figure S47. ^{1}H NMR Spectrum of **3ja** (500 MHz, $CDCl_3$).

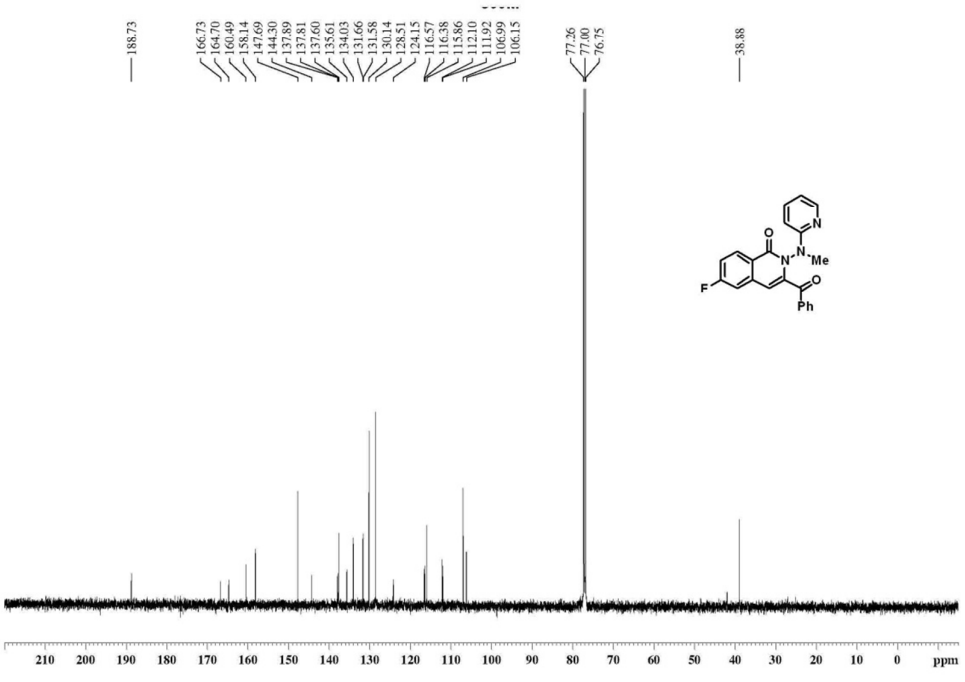


Figure S48. ^{13}C NMR Spectrum of **3ja** (125 MHz, $CDCl_3$).

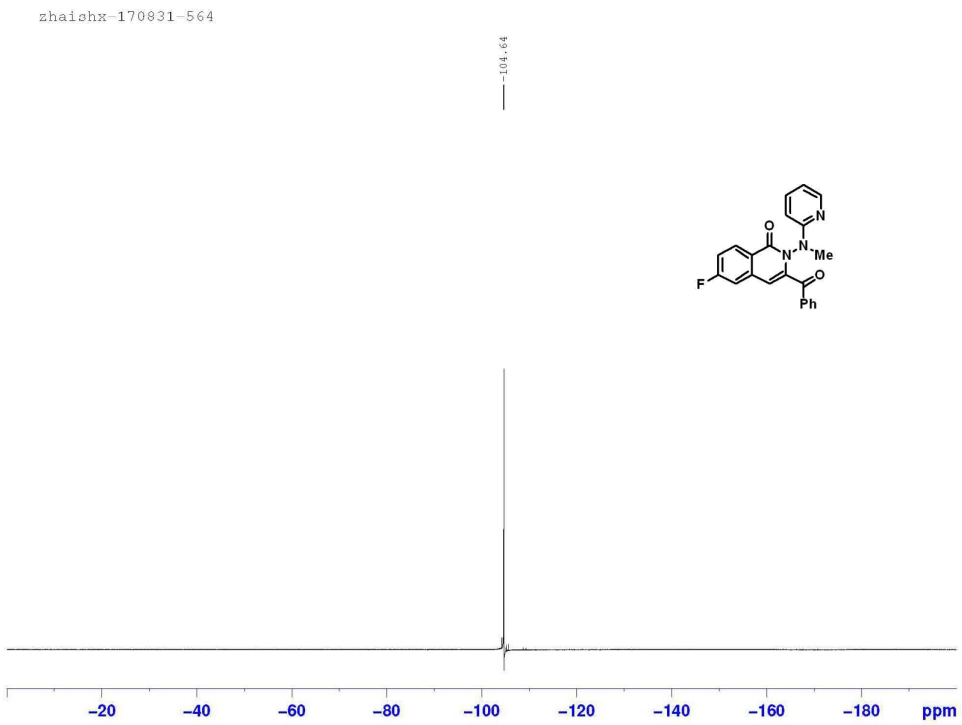


Figure S49. ^{19}F NMR Spectrum of **3ja** (376 MHz, $CDCl_3$).

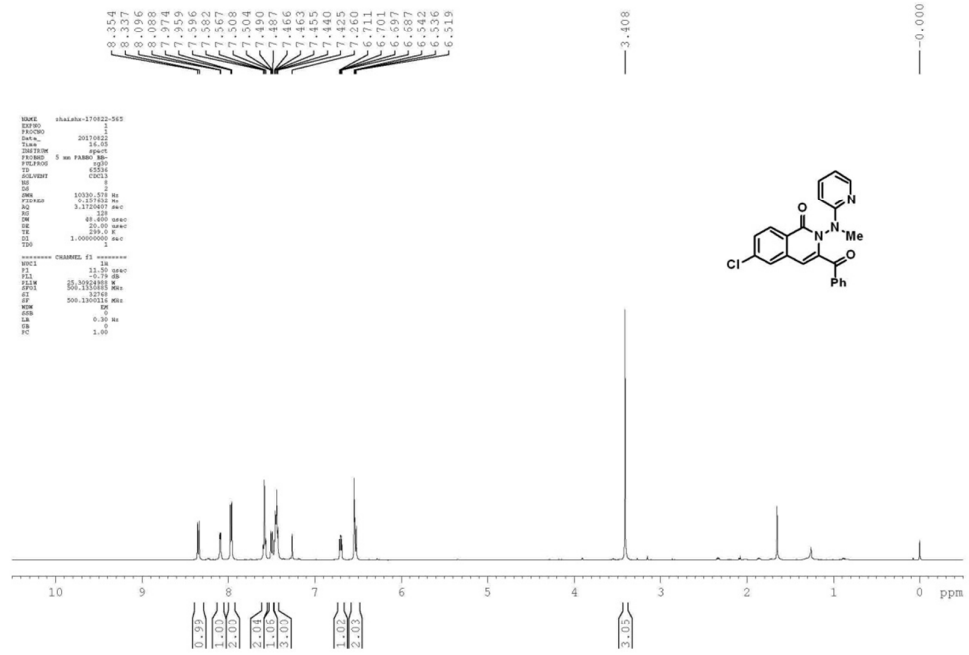


Figure S50. ^{1}H NMR Spectrum of **3ka** (500 MHz, $CDCl_3$).

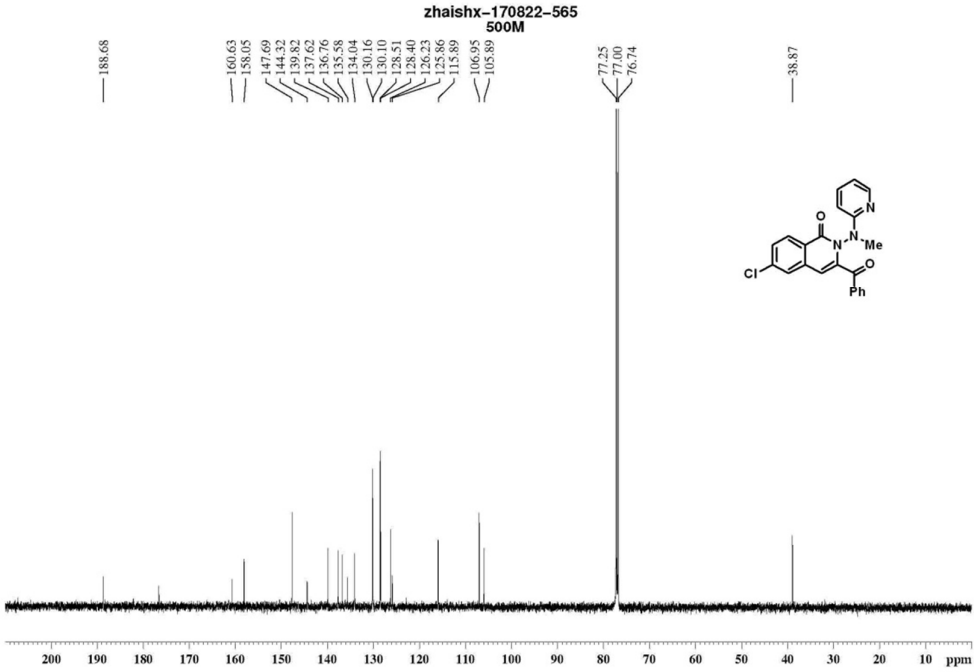


Figure S51. ^{13}C NMR Spectrum of **3ka** (125 MHz, $CDCl_3$).

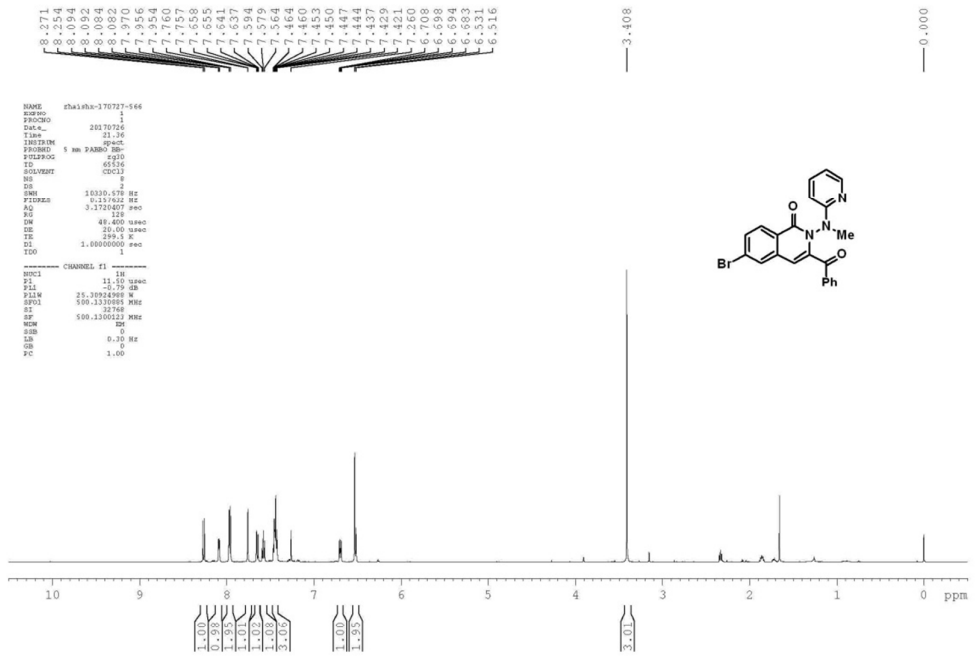


Figure S52. ^{1}H NMR Spectrum of **3la** (500 MHz, $CDCl_3$).

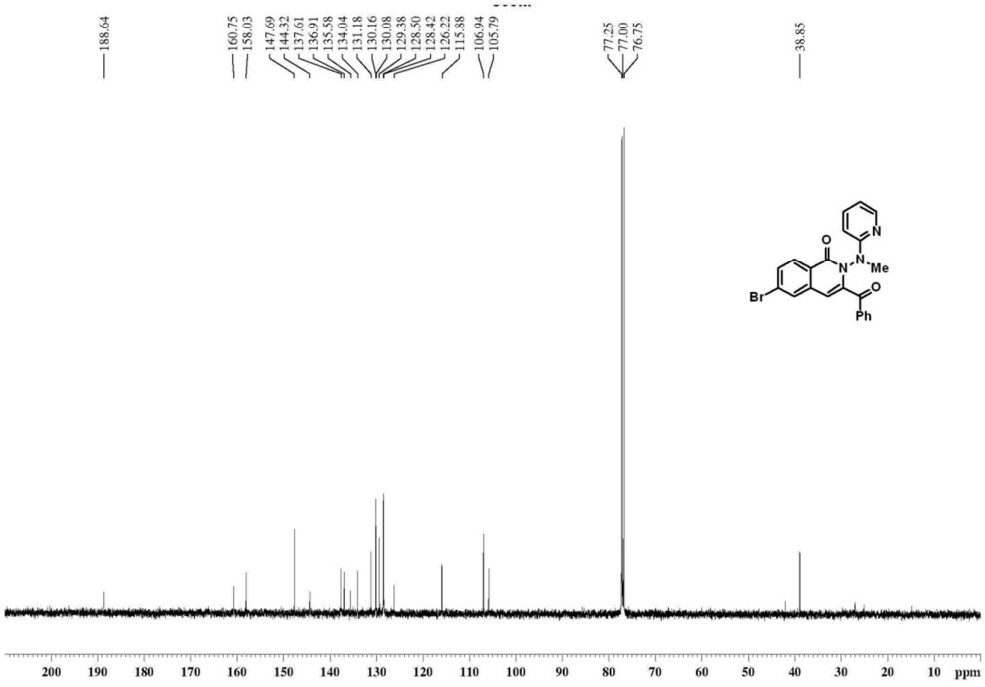


Figure S53. ^{13}C NMR Spectrum of **3la** (125 MHz, $CDCl_3$).

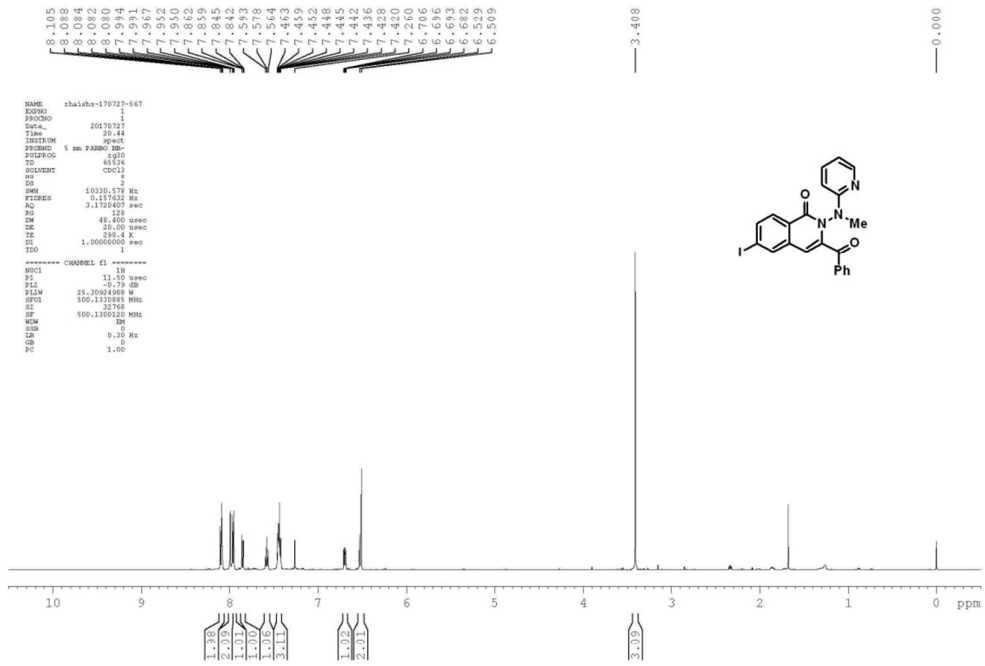


Figure S54. ^{1}H NMR Spectrum of **3ma** (500 MHz, $CDCl_3$).

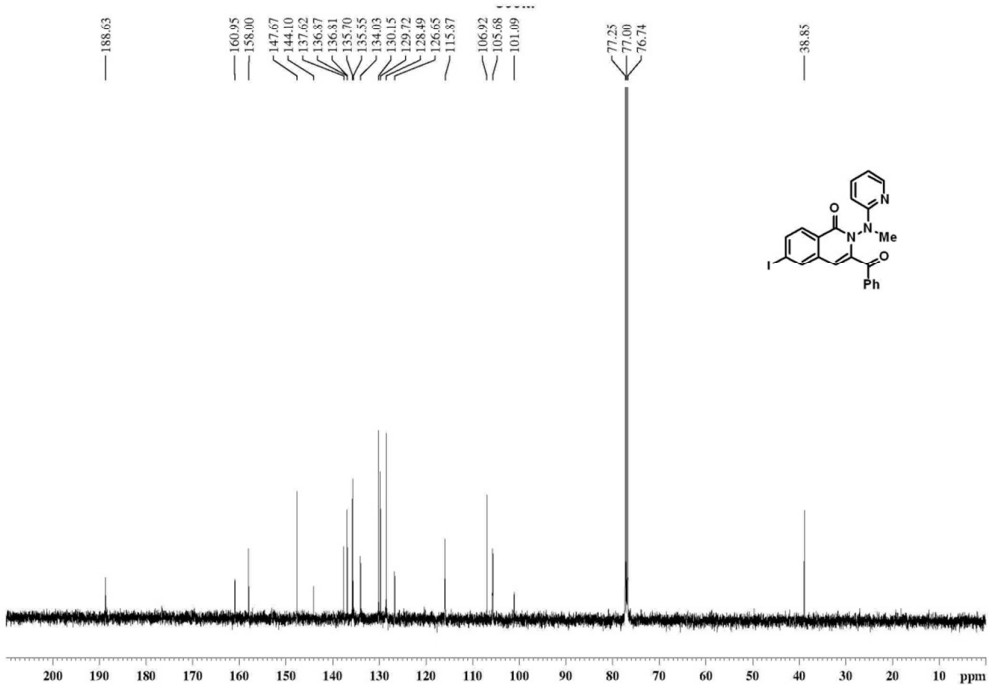


Figure S55. ^{13}C NMR Spectrum of **3ma** (125 MHz, $CDCl_3$).

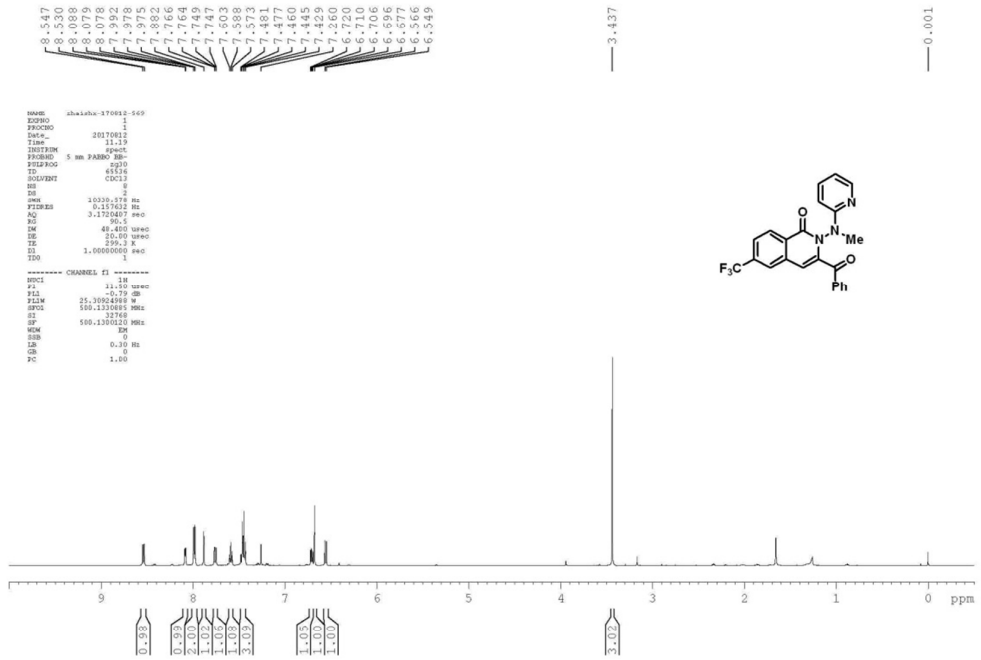


Figure S56. ^{1}H NMR Spectrum of **3na** (500 MHz, $CDCl_3$).

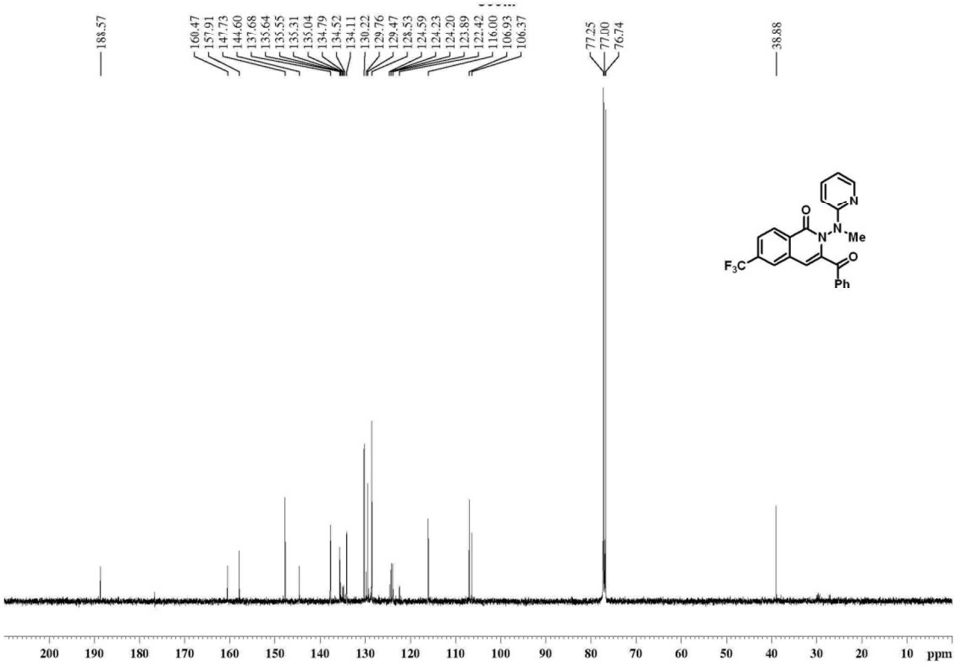


Figure S57. ^{13}C NMR Spectrum of **3na** (125 MHz, $CDCl_3$).

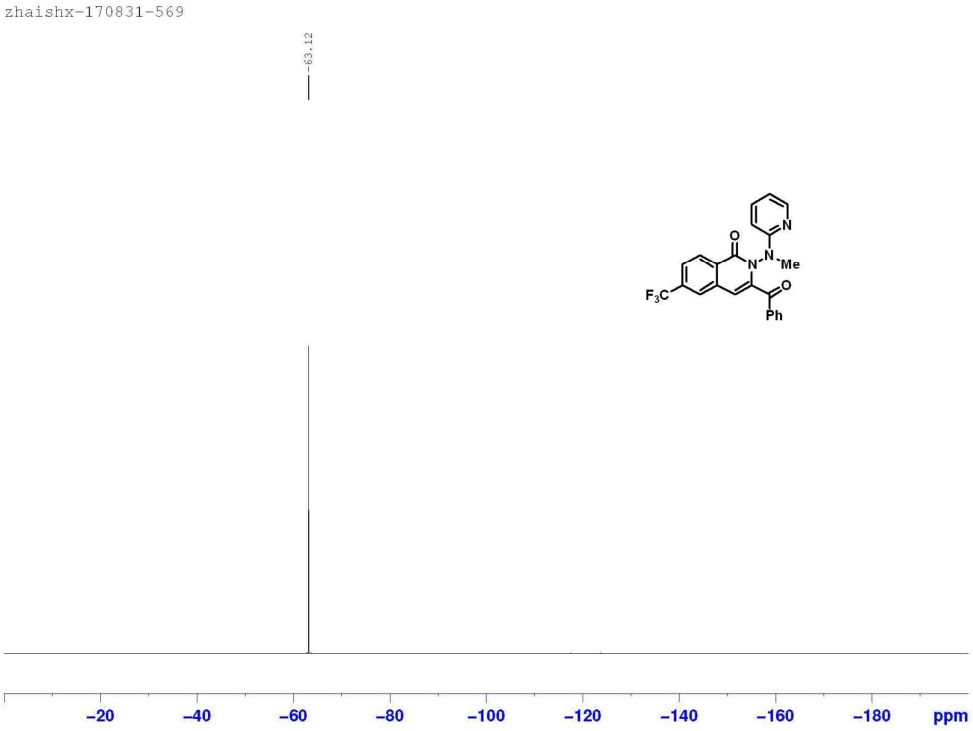


Figure S58. ^{19}F NMR Spectrum of **3na** (376 MHz, $CDCl_3$).

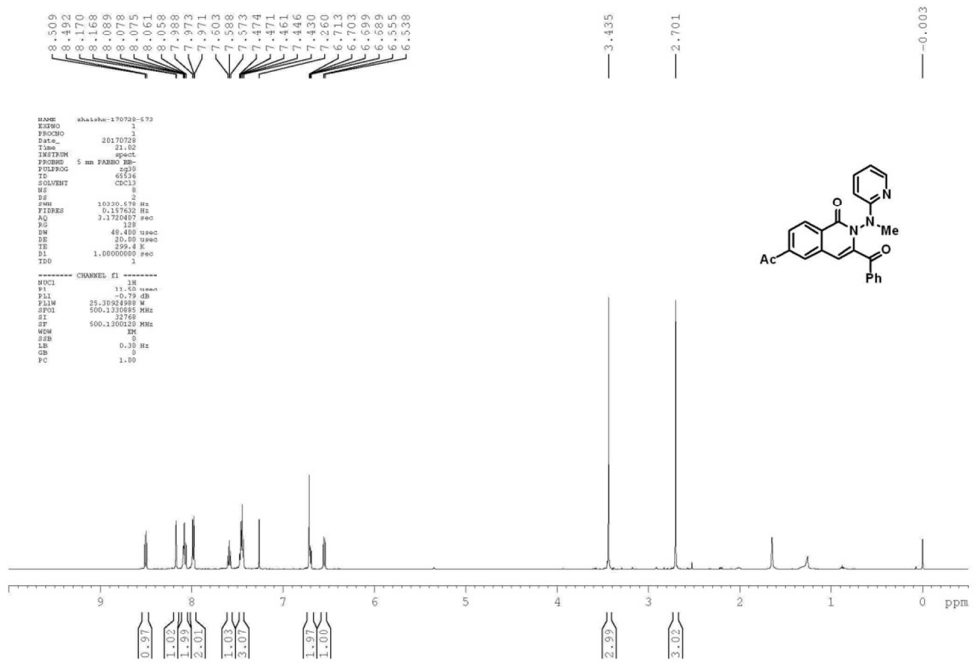


Figure S59. ^{1}H NMR Spectrum of **3oa** (500 MHz, $CDCl_3$).

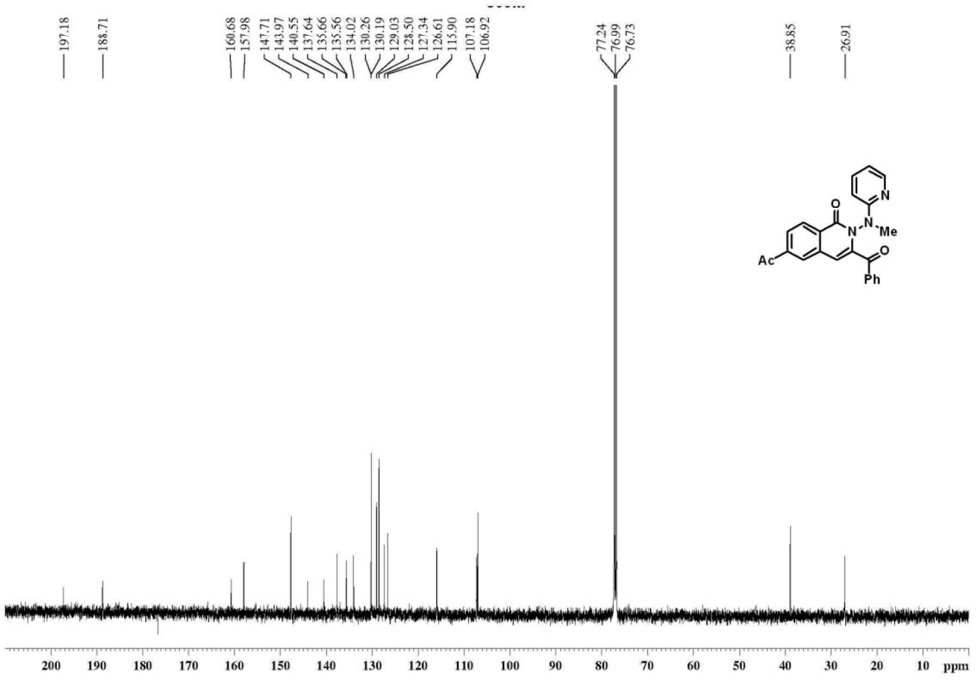


Figure S60. ^{13}C NMR Spectrum of **3oa** (125 MHz, $CDCl_3$).

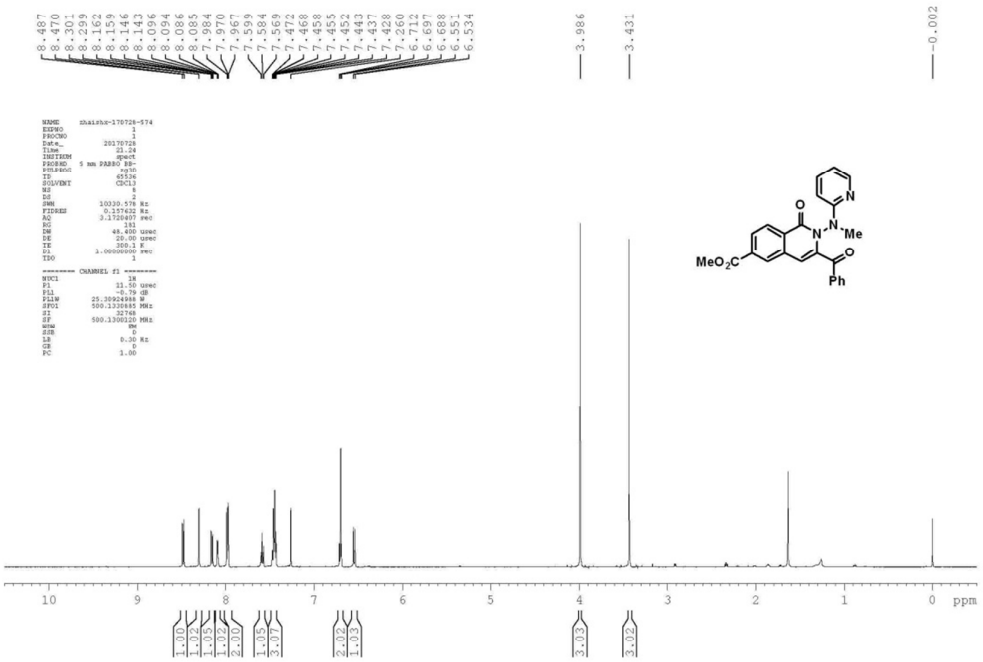


Figure S61. ^{1}H NMR Spectrum of **3pa** (500 MHz, $CDCl_3$).

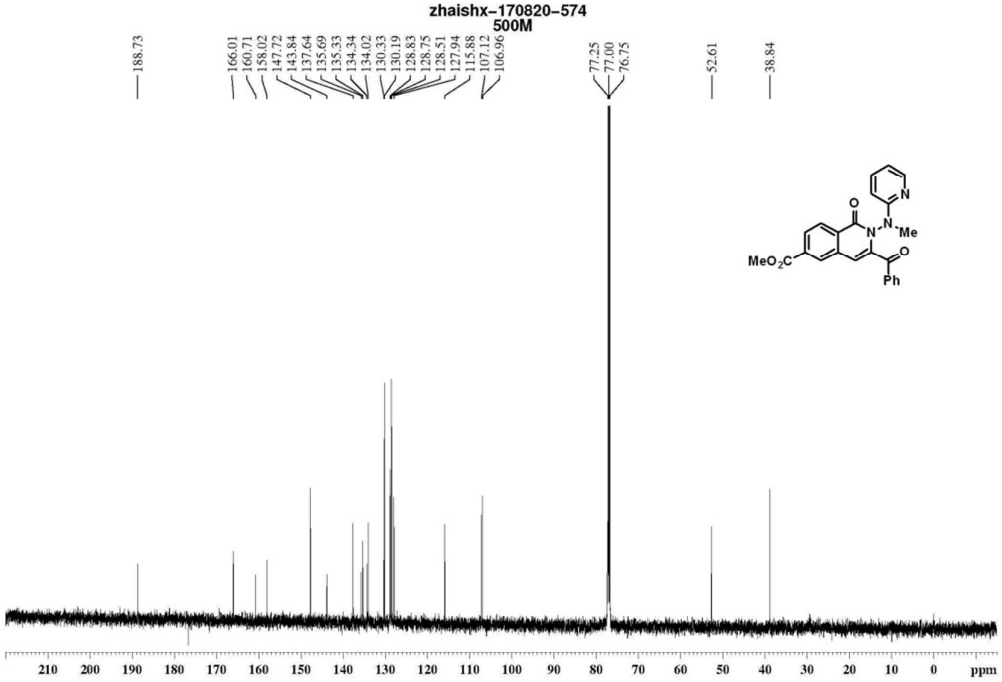


Figure S62. ^{13}C NMR Spectrum of **3pa** (125 MHz, $CDCl_3$).

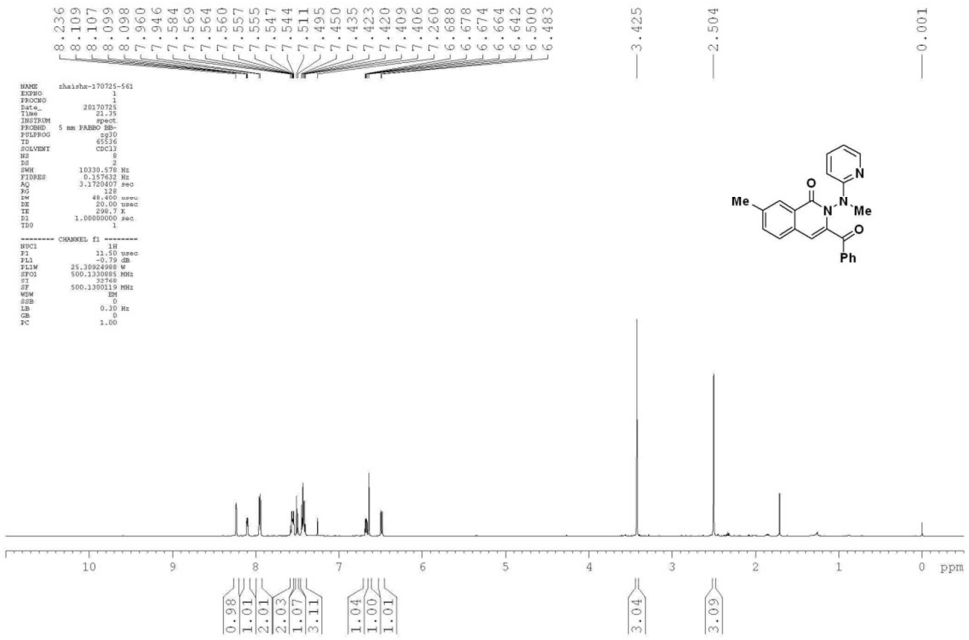


Figure S63. ^{1}H NMR Spectrum of **3qa** (500 MHz, $CDCl_3$).

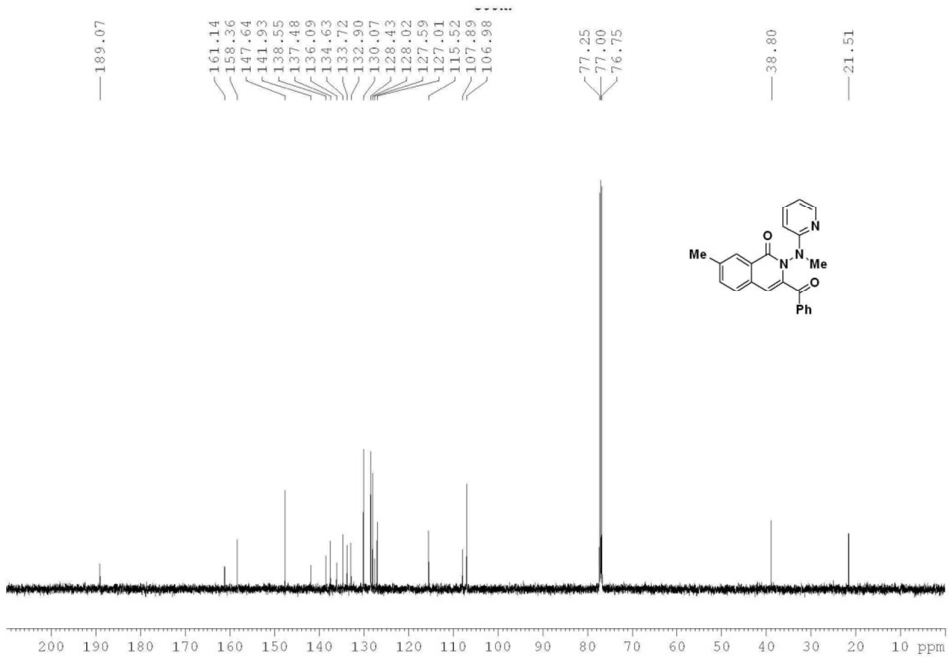


Figure S64. ^{13}C NMR Spectrum of **3qa** (125 MHz, $CDCl_3$).

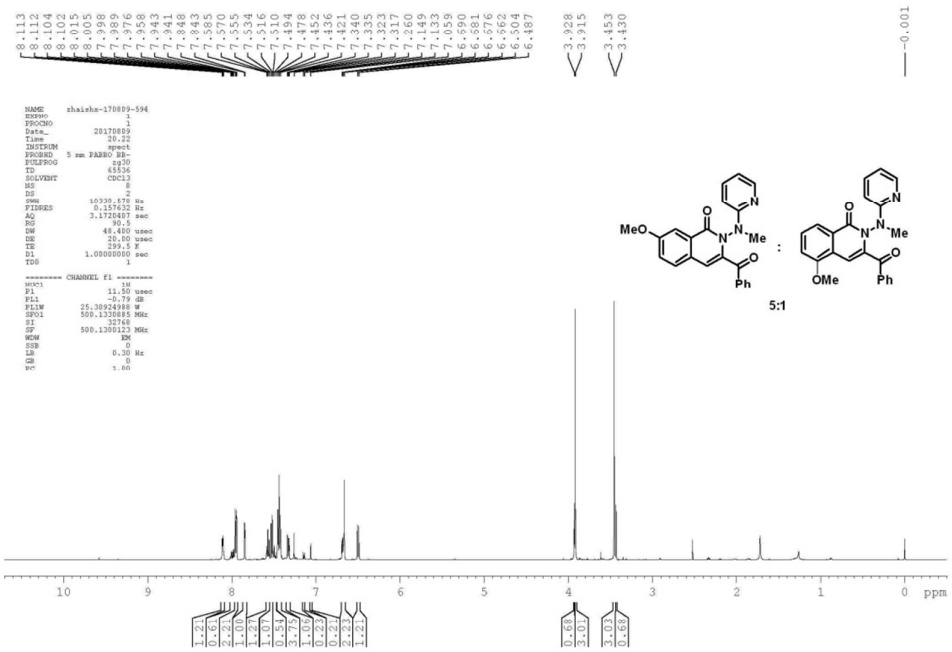


Figure S65. ^{1}H NMR Spectrum of **3ra** (500 MHz, $CDCl_3$).

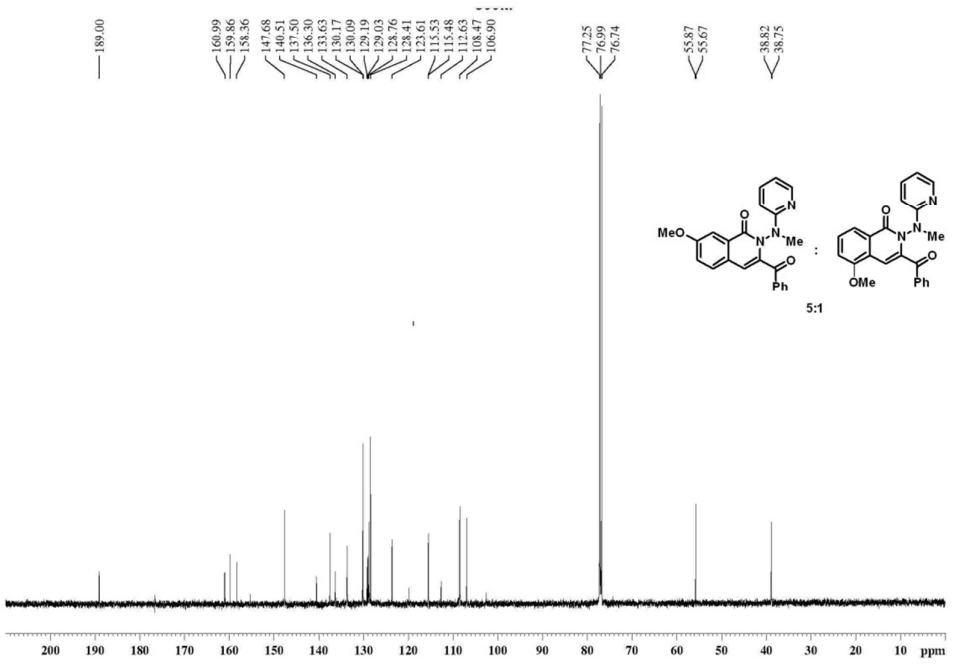


Figure S66. ^{13}C NMR Spectrum of **3ra** (125 MHz, $CDCl_3$).

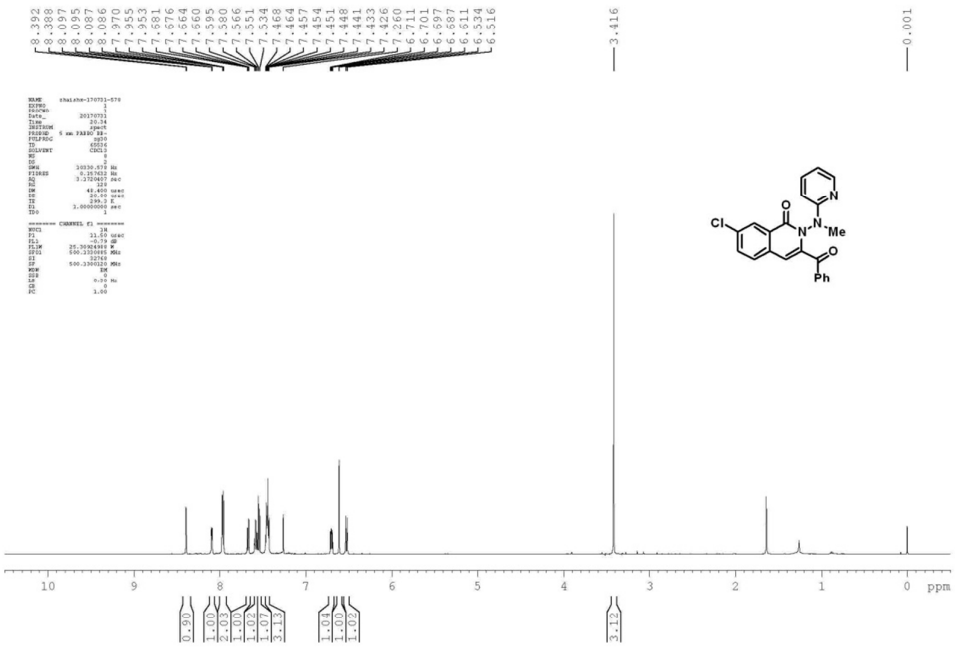


Figure S67. ^{1}H NMR Spectrum of **3sa** (500 MHz, $CDCl_3$).

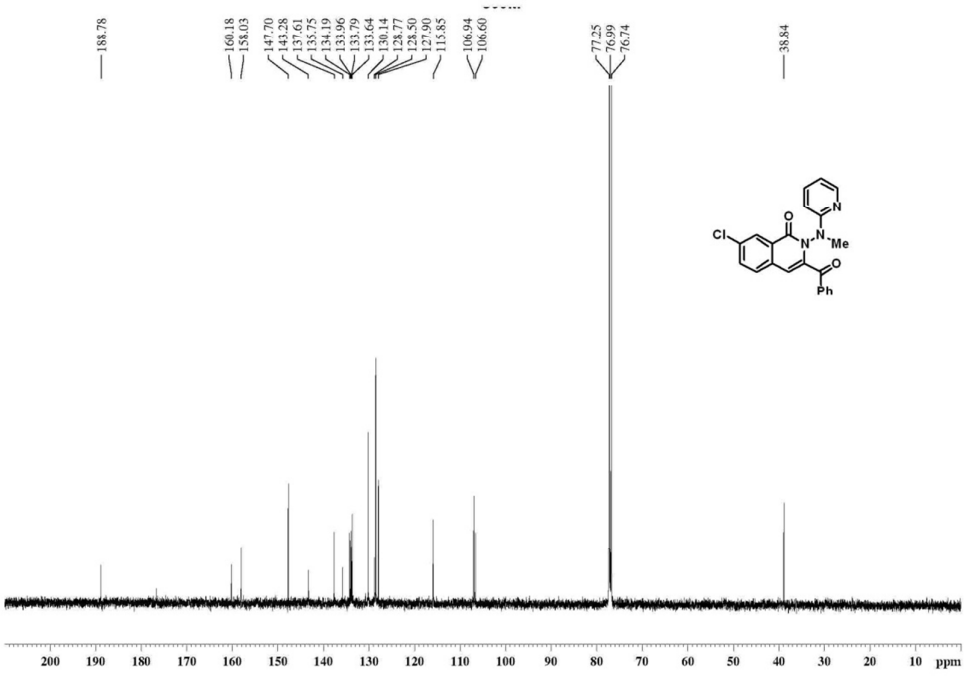


Figure S68. ^{13}C NMR Spectrum of **3sa** (125 MHz, $CDCl_3$).

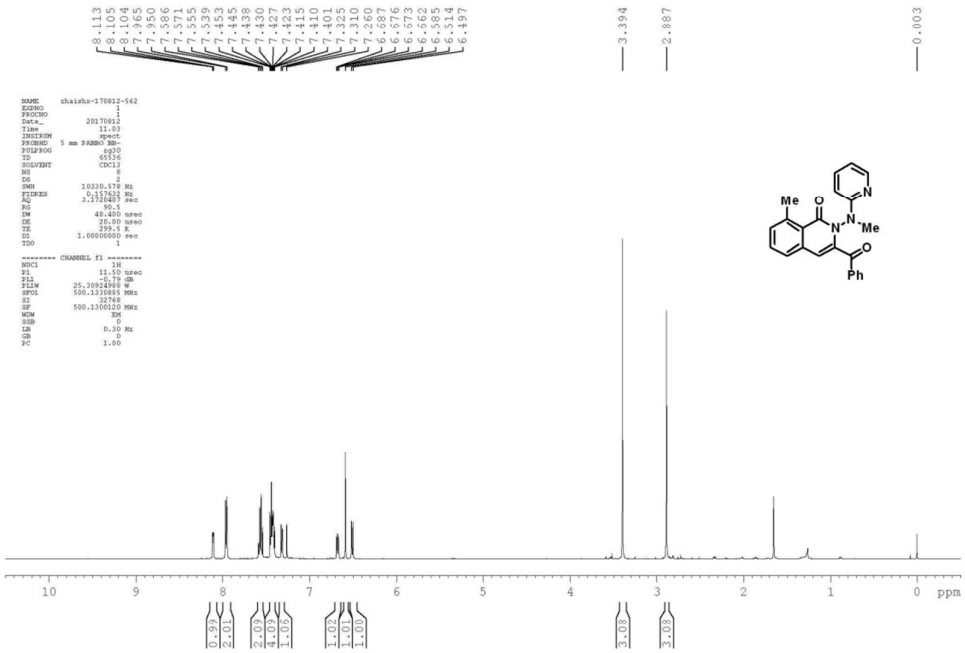


Figure S69. ^{1}H NMR Spectrum of **3ta** (500 MHz, $CDCl_3$).

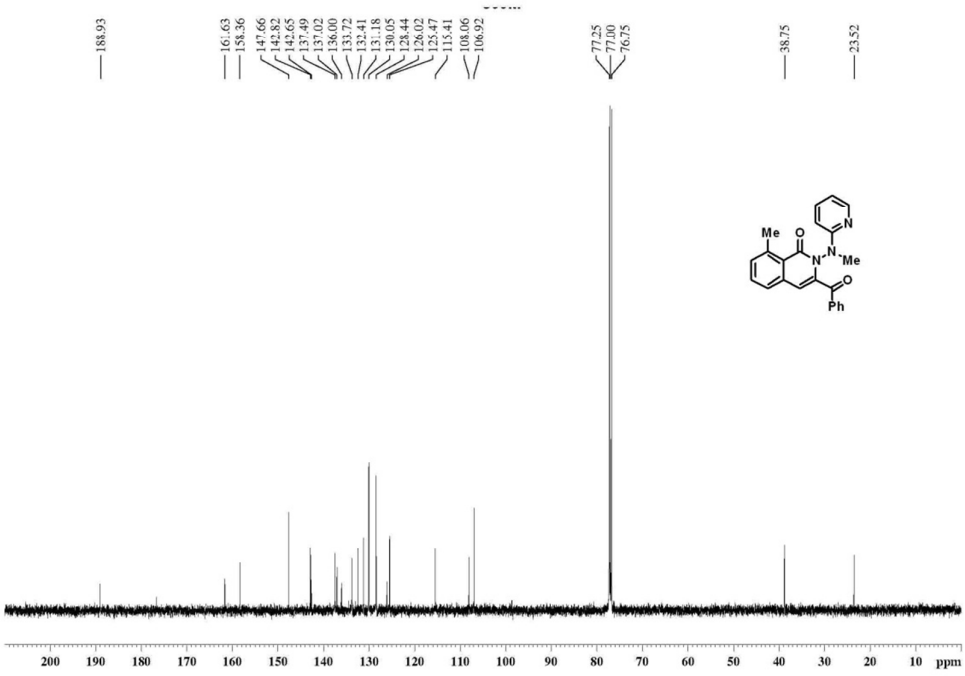


Figure S70. ^{13}C NMR Spectrum of **3ta** (125 MHz, $CDCl_3$).

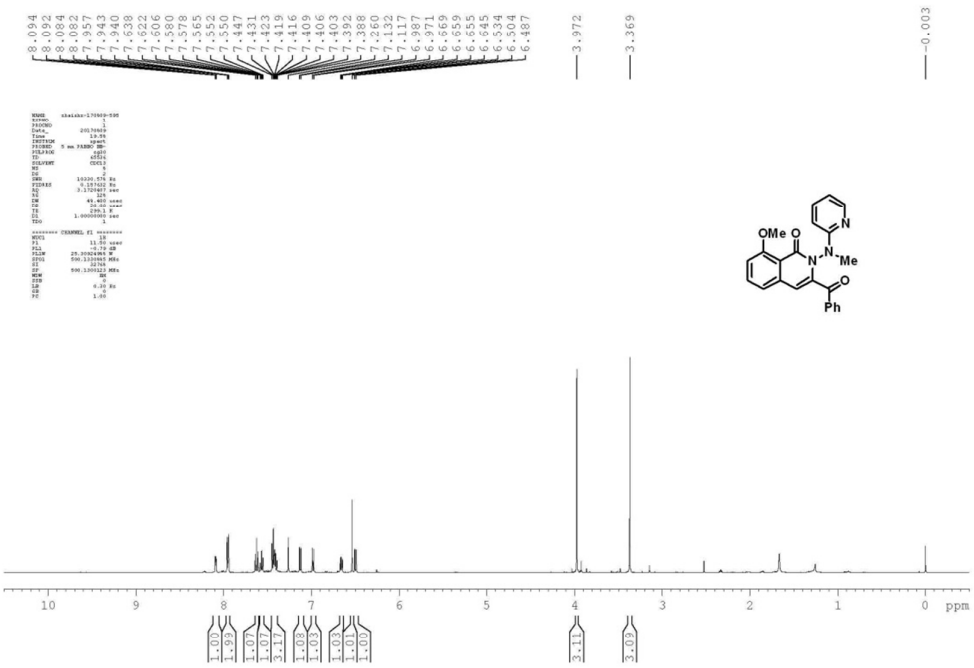


Figure S71. ^{1}H NMR Spectrum of **3ua** (500 MHz, $CDCl_3$).

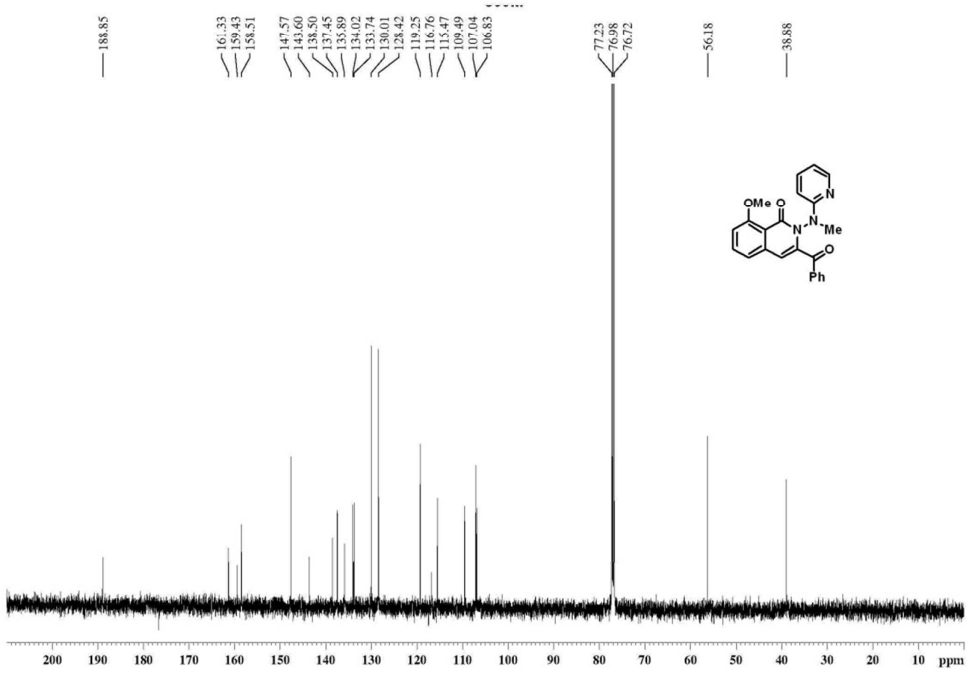


Figure S72. ^{13}C NMR Spectrum of **3ua** (125 MHz, $CDCl_3$).

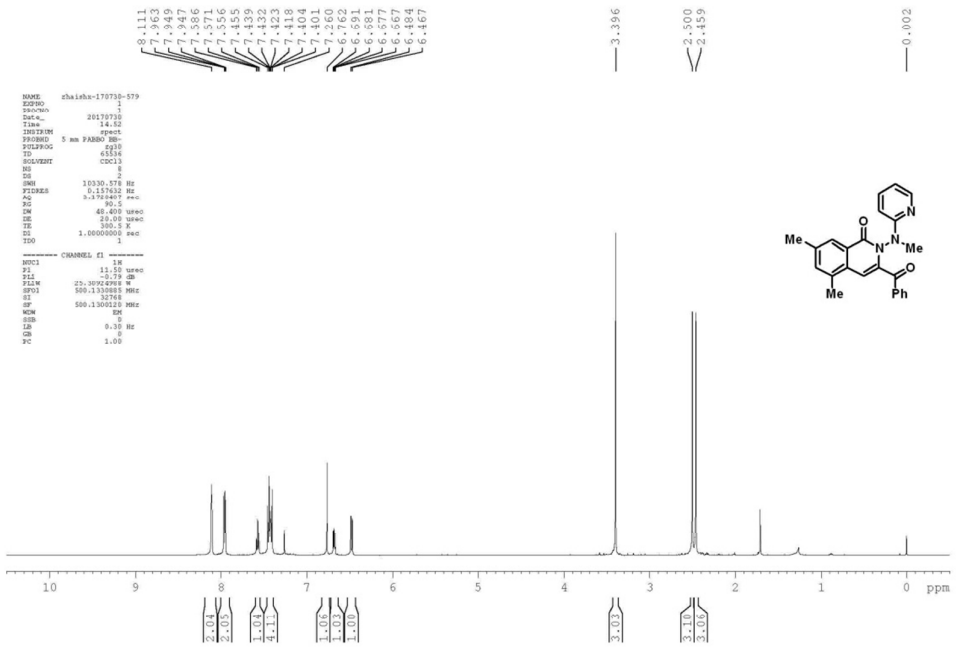


Figure S73. ^{1}H NMR Spectrum of **3va** (500 MHz, $CDCl_3$).

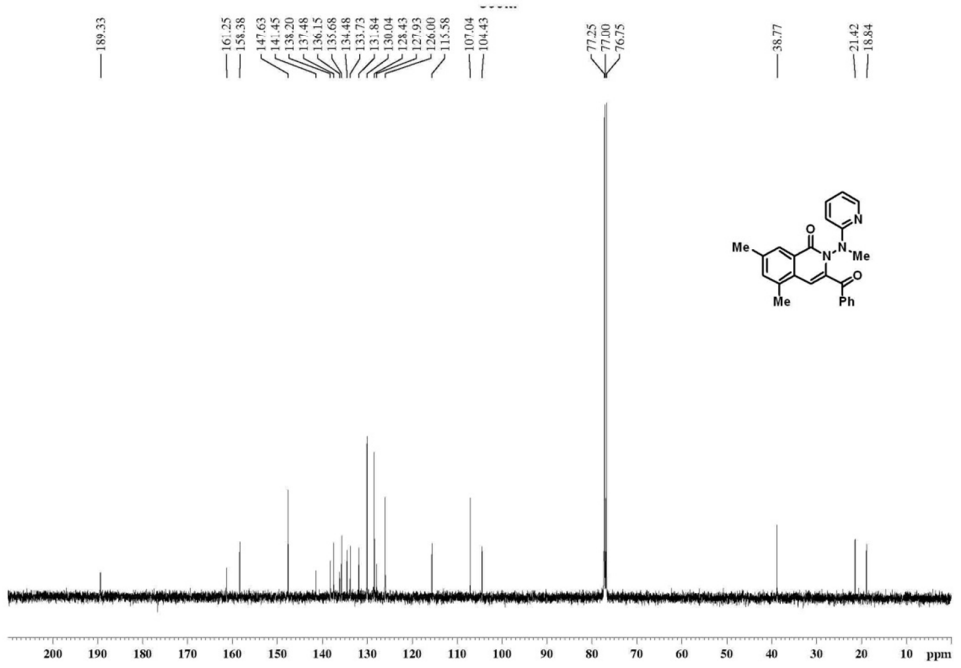


Figure S74. ^{13}C NMR Spectrum of **3va** (125 MHz, $CDCl_3$).

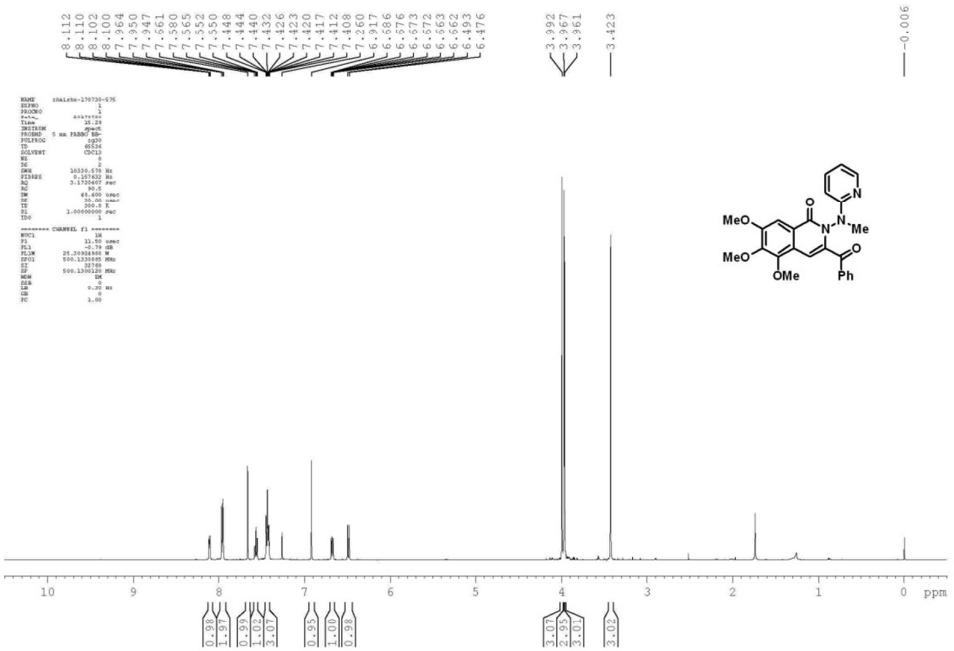


Figure S75. ^{1}H NMR Spectrum of **3wa** (500 MHz, $CDCl_3$).

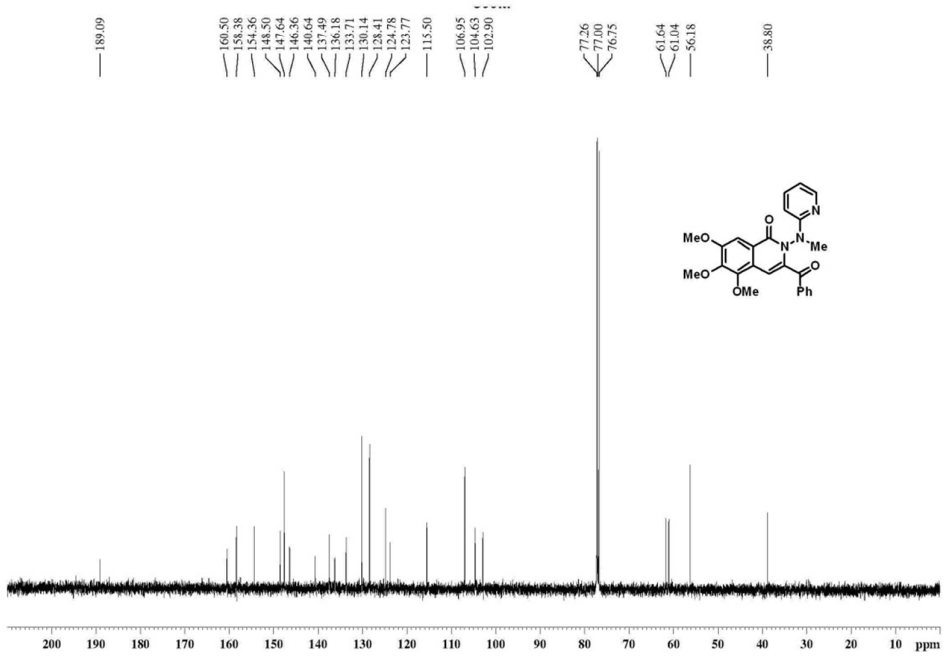


Figure S76. ^{13}C NMR Spectrum of **3wa** (125 MHz, $CDCl_3$).

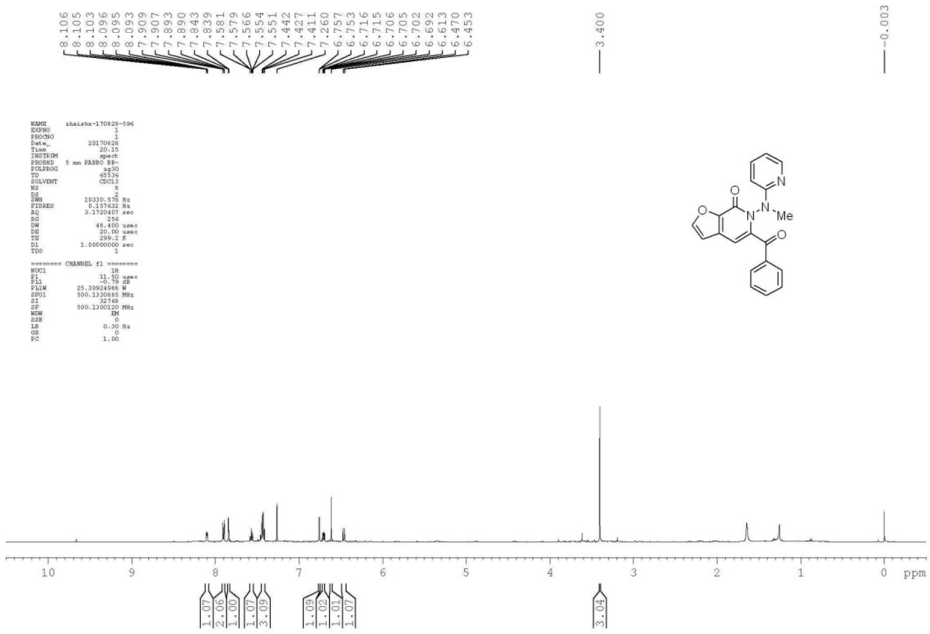


Figure S77. ^{1}H NMR Spectrum of **3xa** (500 MHz, $CDCl_3$).

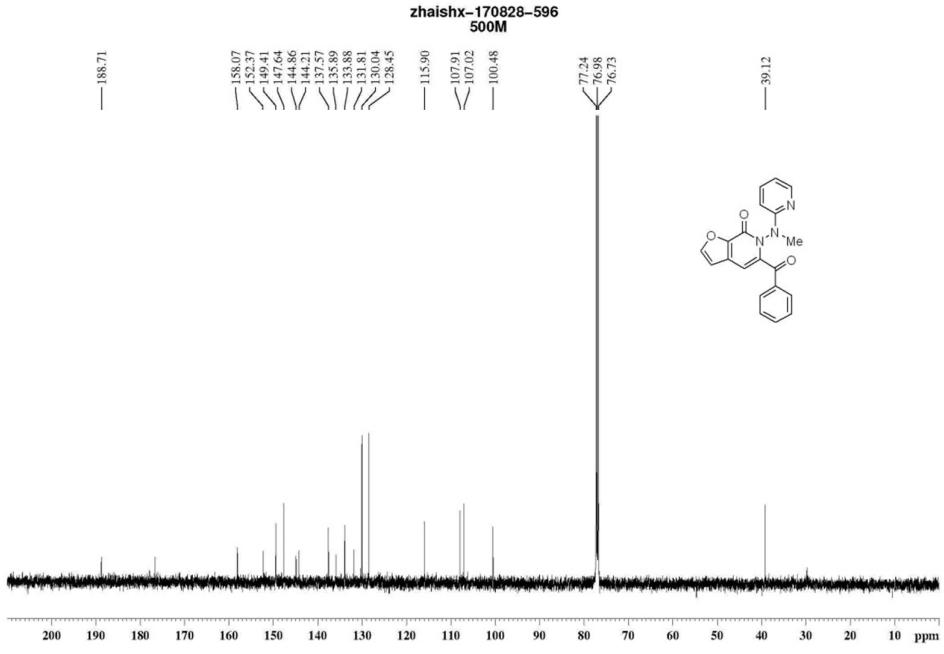


Figure S78. ^{13}C NMR Spectrum of **3xa** (125 MHz, $CDCl_3$).

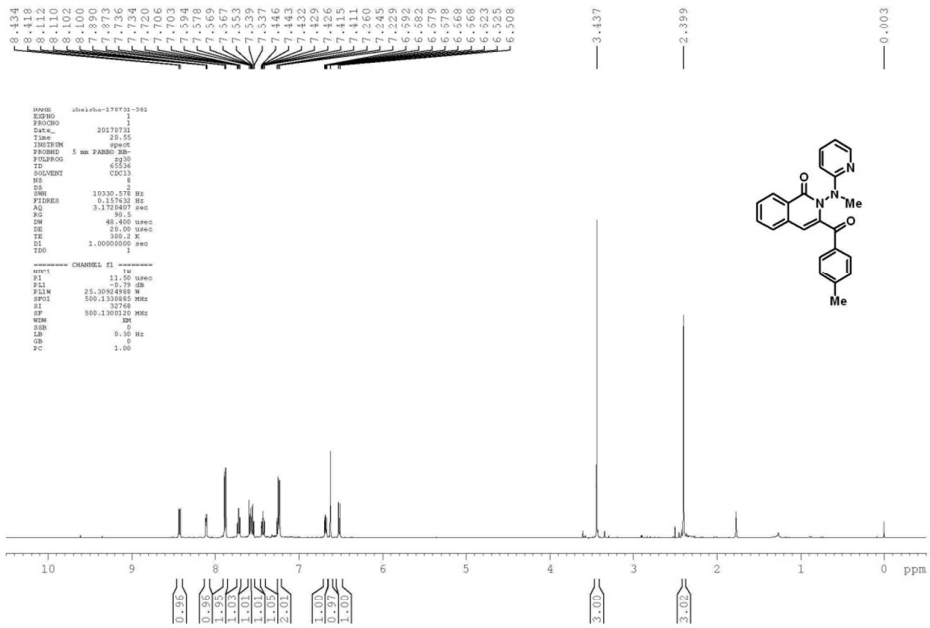


Figure S79. ^{1}H NMR Spectrum of **3ab** (500 MHz, $CDCl_3$).

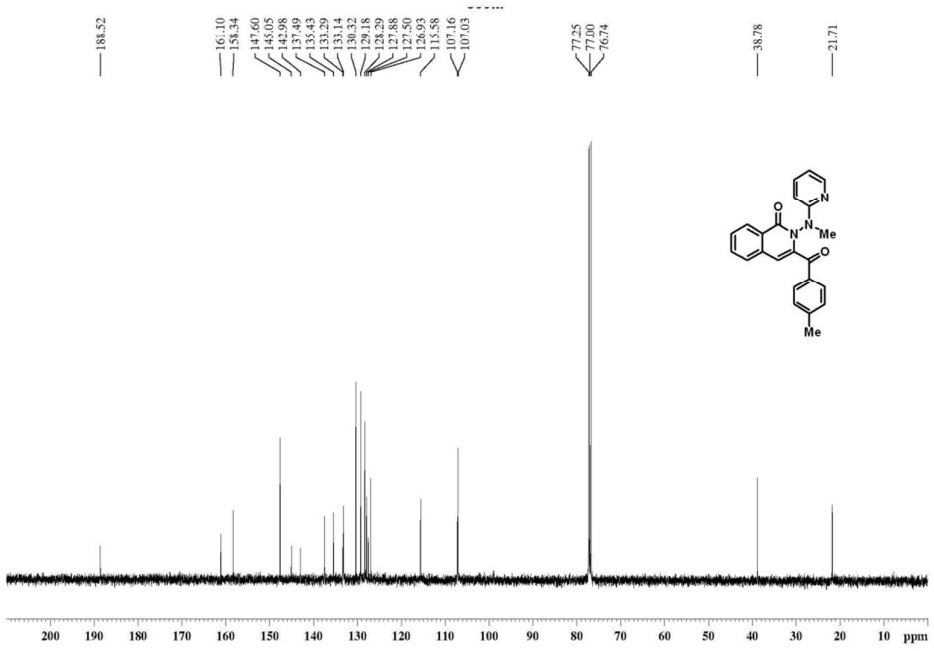


Figure S80. ^{13}C NMR Spectrum of **3ab**(125 MHz, $CDCl_3$).

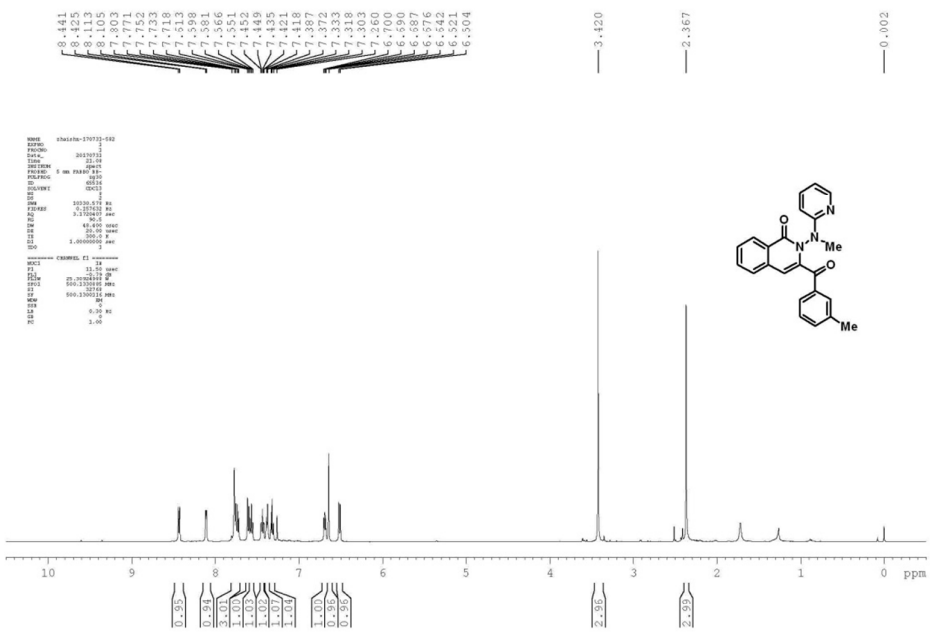


Figure S81. ^{1}H NMR Spectrum of **3ac** (500 MHz, $CDCl_3$).

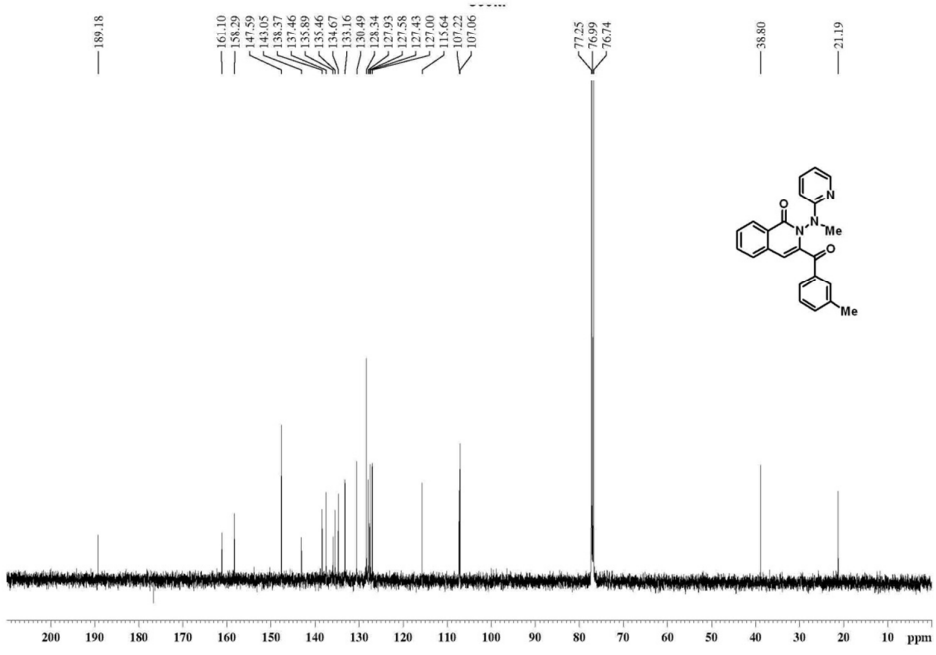


Figure S82. ^{13}C NMR Spectrum of **3ac** (125 MHz, $CDCl_3$).

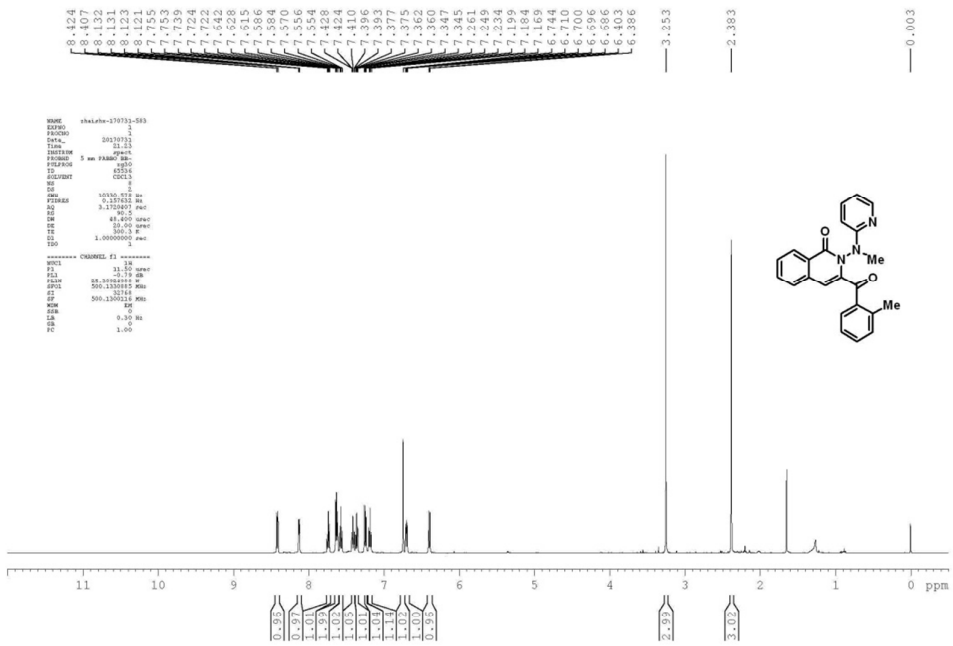


Figure S83. ^{1}H NMR Spectrum of **3ad** (500 MHz, $CDCl_3$).

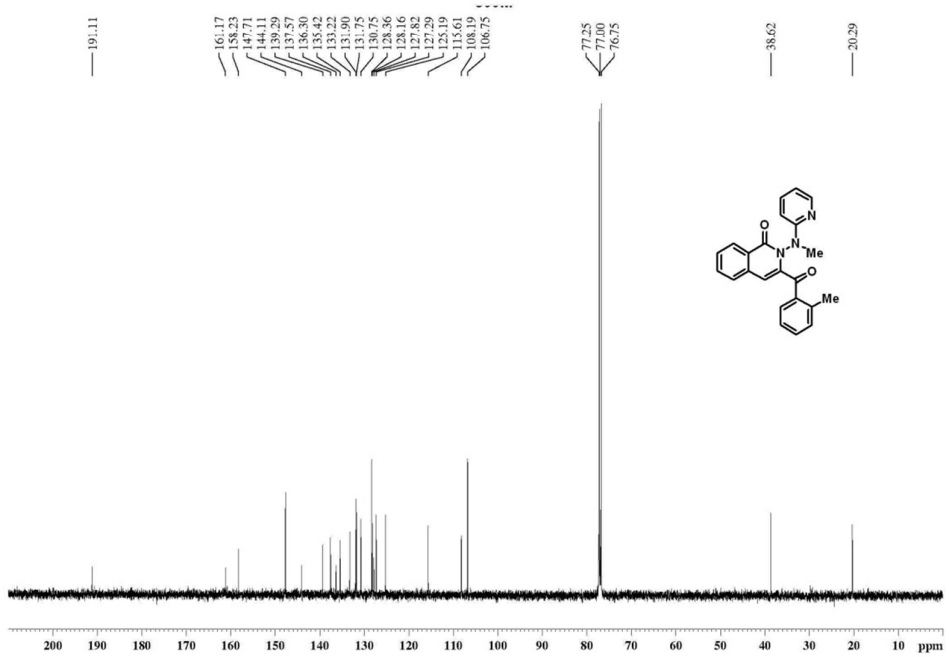


Figure S84. ^{13}C NMR Spectrum of **3ad** (125 MHz, $CDCl_3$).

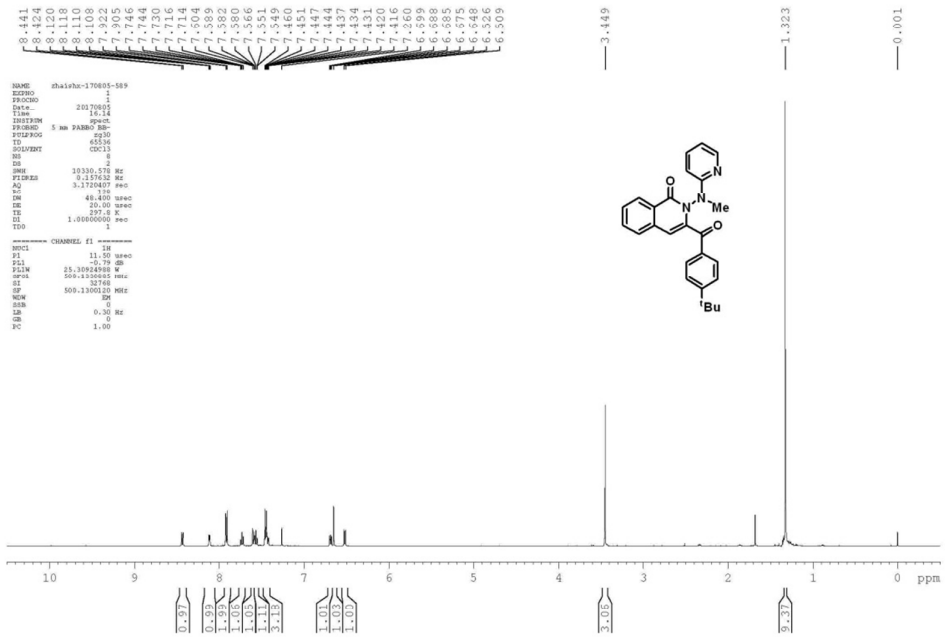


Figure S85. ^{1}H NMR Spectrum of **3ae** (500 MHz, $CDCl_3$).

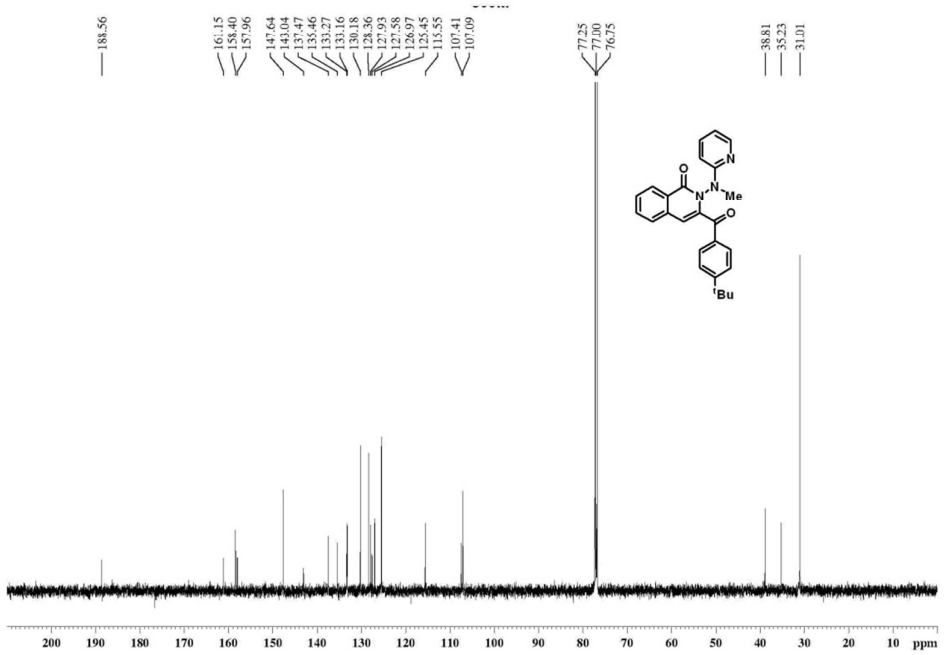


Figure S86. ^{13}C NMR Spectrum of **3ae** (125 MHz, $CDCl_3$).

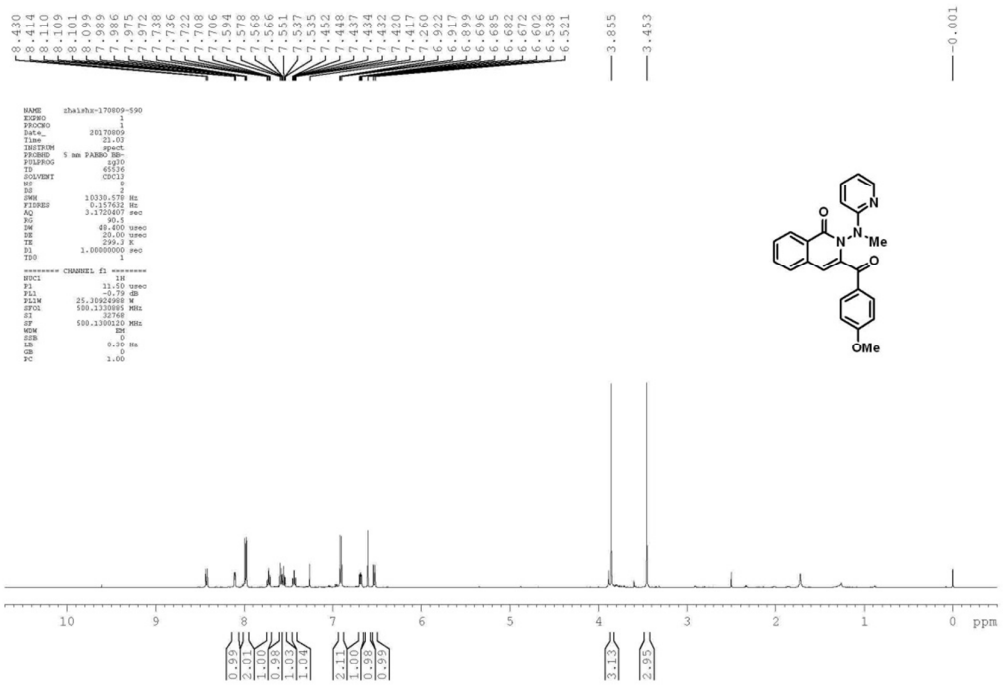


Figure S87. ^{1}H NMR Spectrum of **3af** (500 MHz, $CDCl_3$).

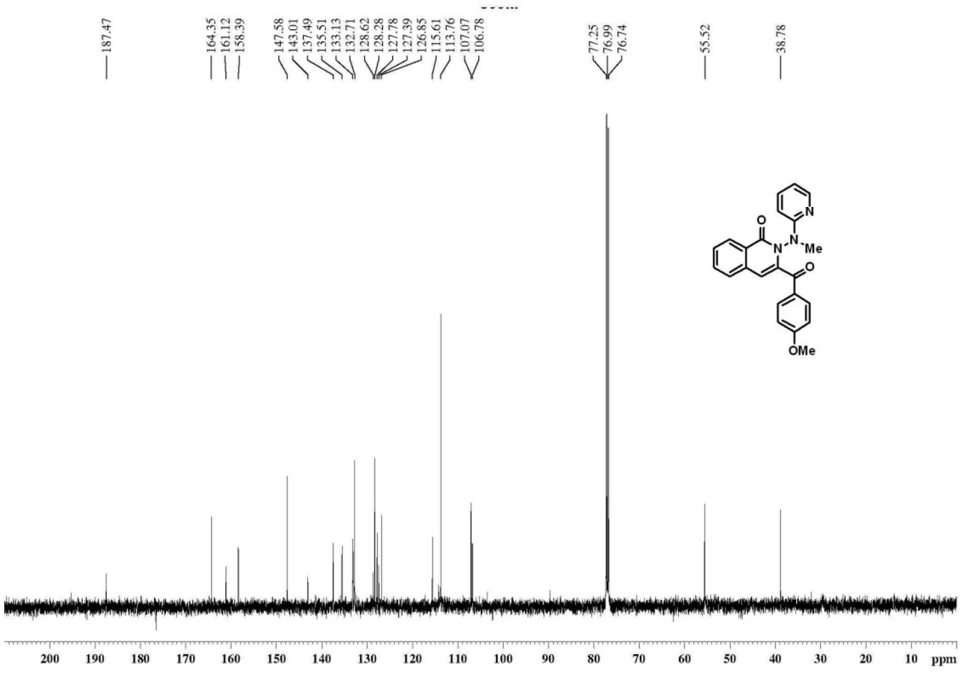


Figure S88. ^{13}C NMR Spectrum of **3af** (125 MHz, $CDCl_3$).

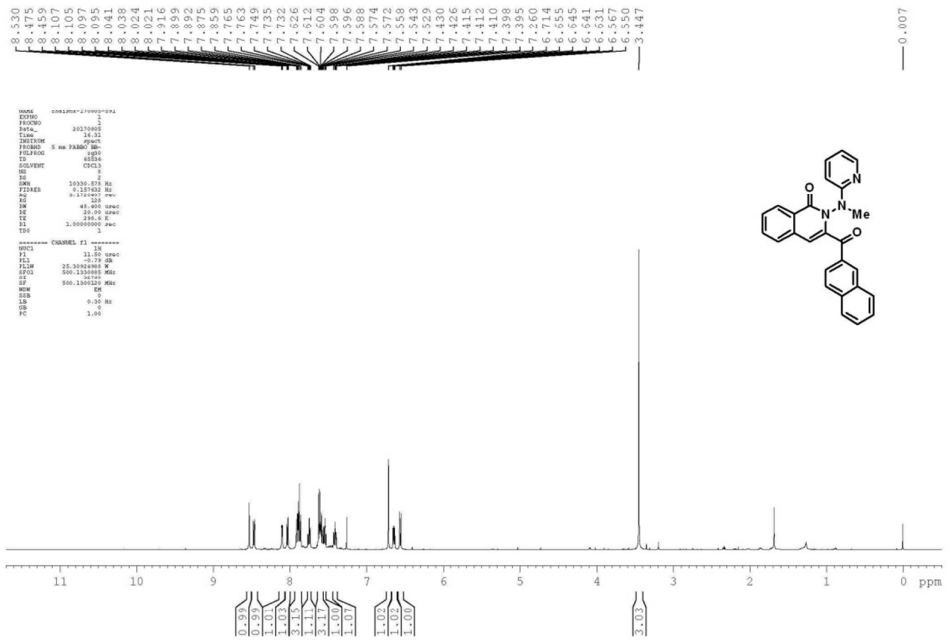


Figure S89. ^{1}H NMR Spectrum of **3ag** (500 MHz, $CDCl_3$).

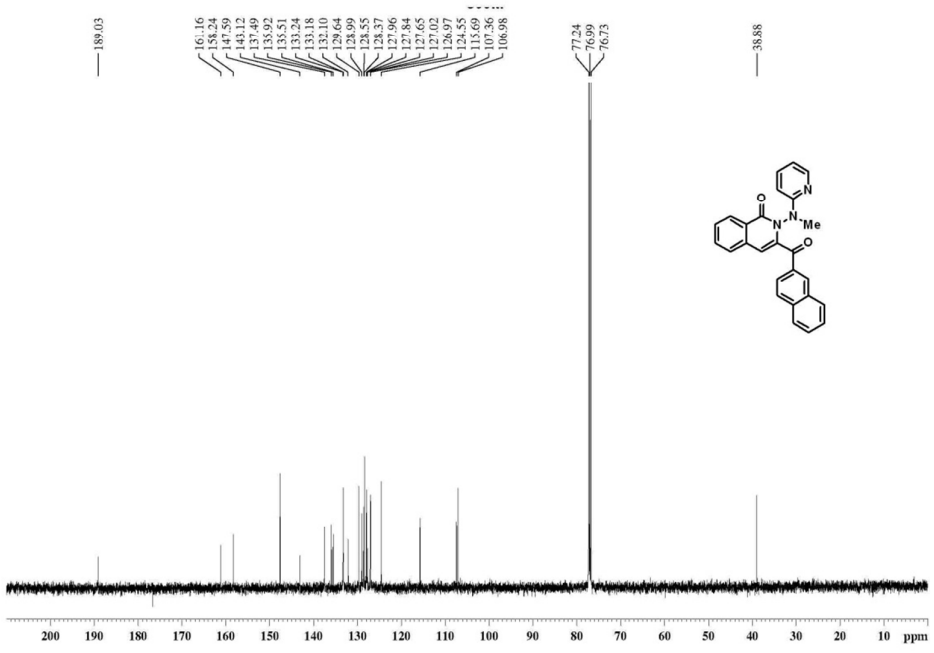


Figure S90. ^{13}C NMR Spectrum of **3ag** (125 MHz, $CDCl_3$).

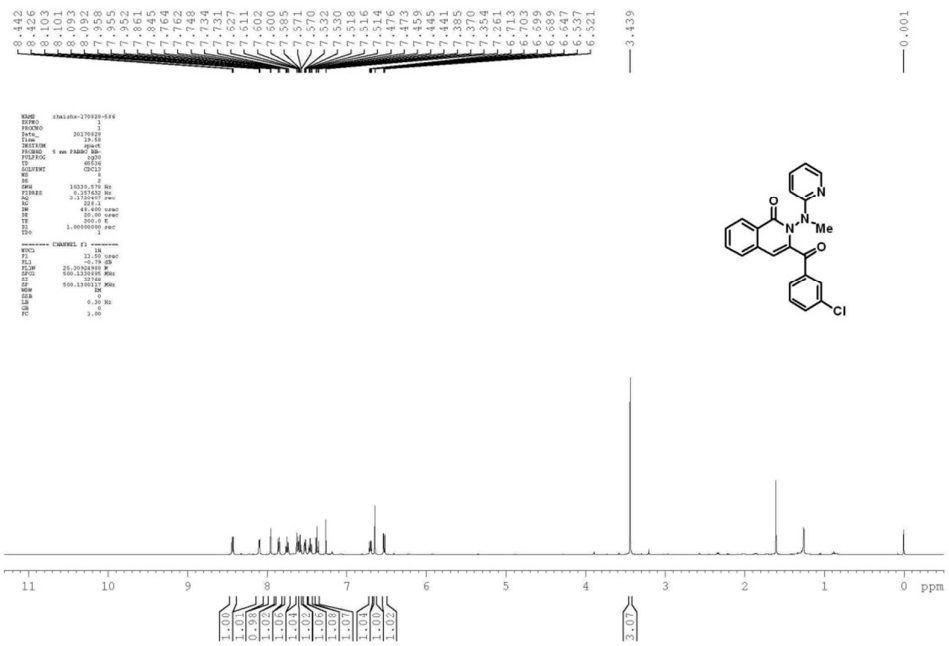


Figure S91. ^{1}H NMR Spectrum of **3ah** (500 MHz, $CDCl_3$).

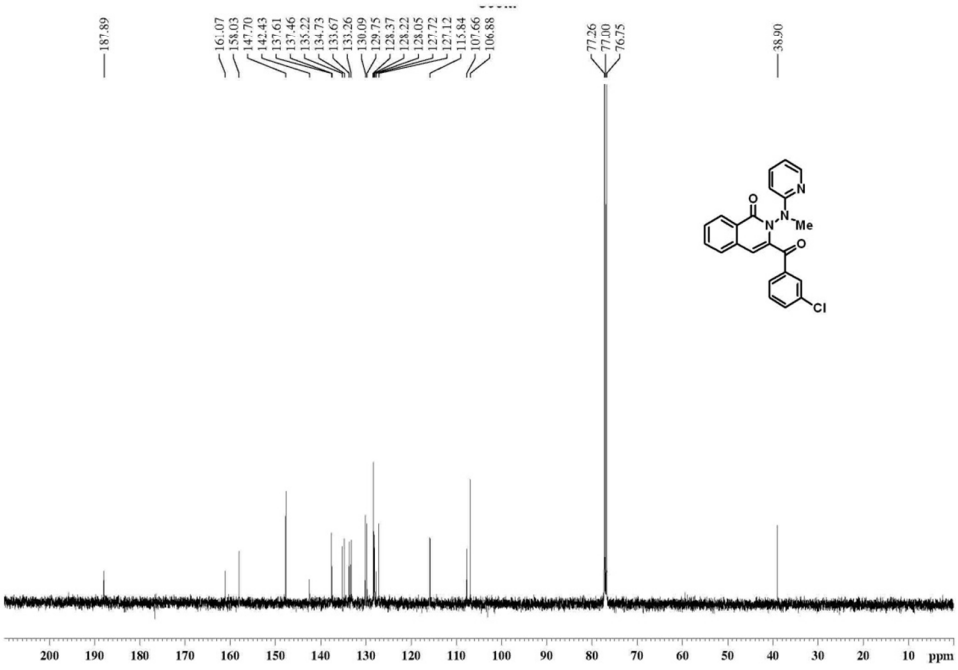


Figure S92. ^{13}C NMR Spectrum of **3ah** (125 MHz, $CDCl_3$).

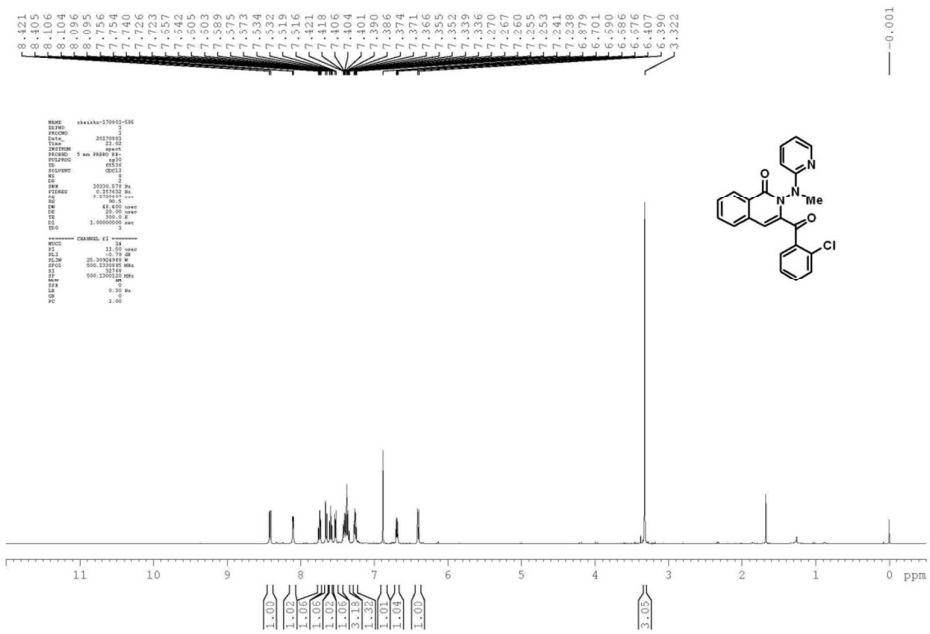


Figure S93. ^{1}H NMR Spectrum of **3ai** (500 MHz, $CDCl_3$).

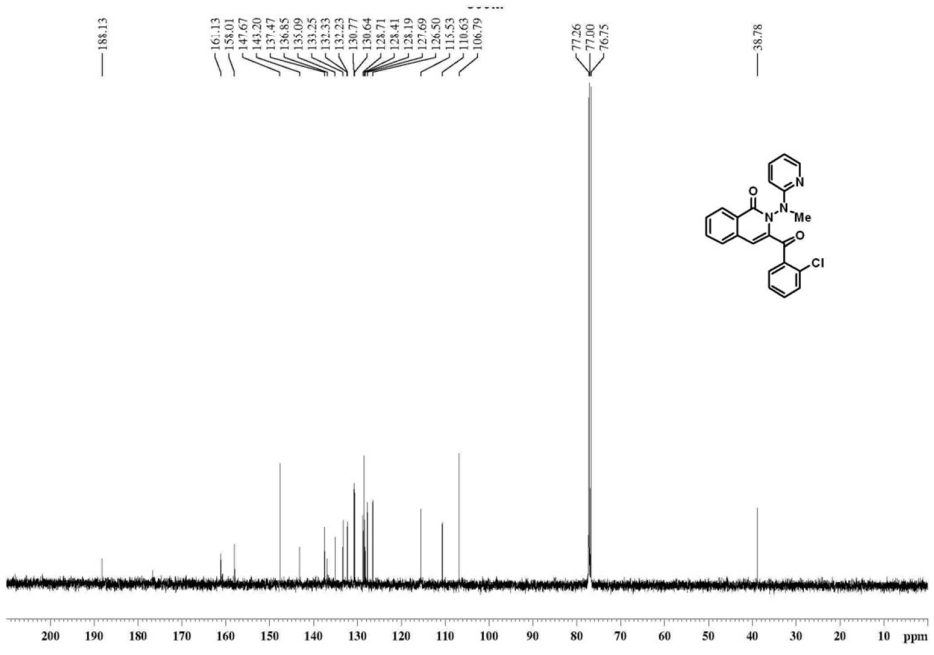


Figure S94. ^{13}C NMR Spectrum of **3ai** (125 MHz, $CDCl_3$).

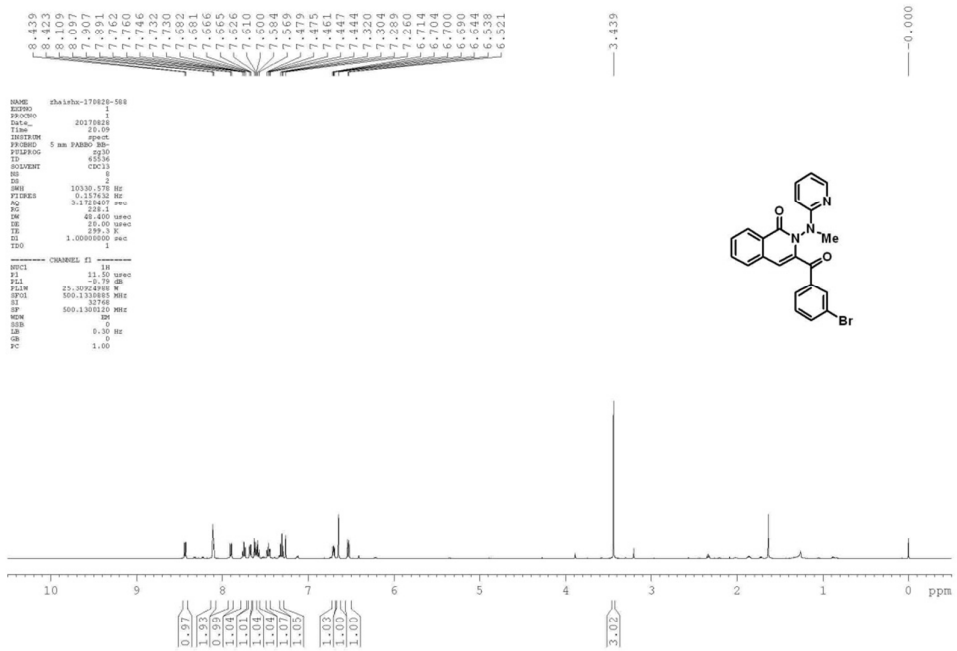


Figure S95. ^{1}H NMR Spectrum of **3aj** (500 MHz, $CDCl_3$).

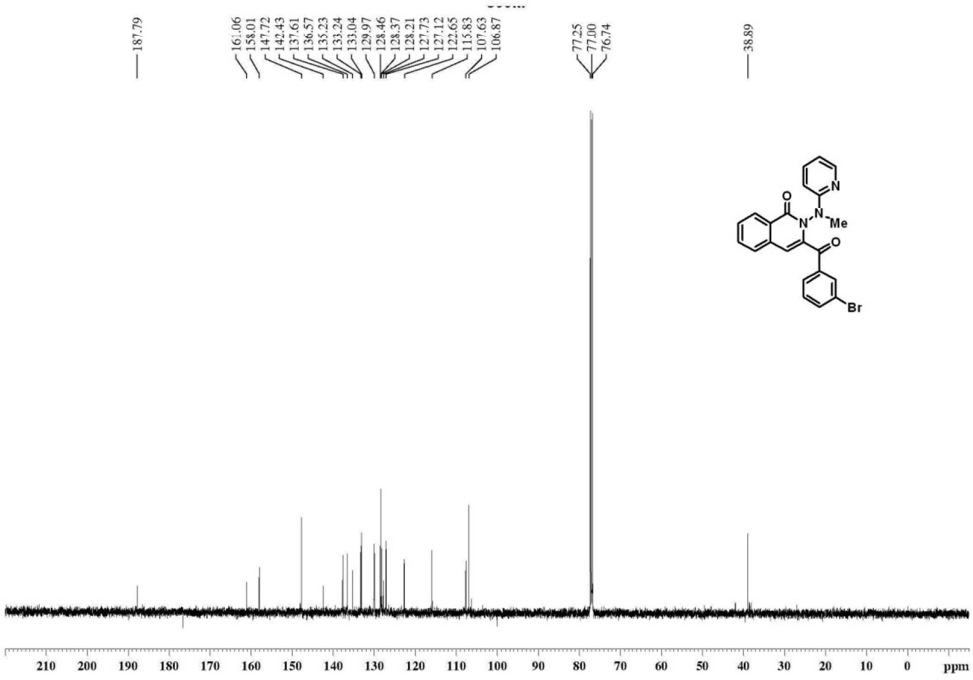


Figure S96. ^{13}C NMR Spectrum of **3aj** (125 MHz, $CDCl_3$).

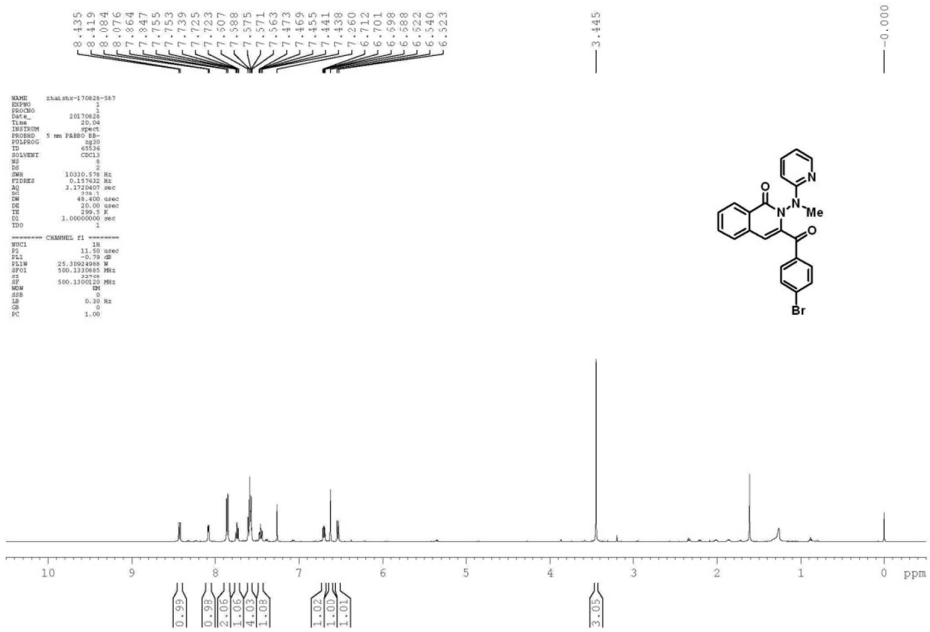


Figure S97. ^{1}H NMR Spectrum of **3ak** (500 MHz, $CDCl_3$).

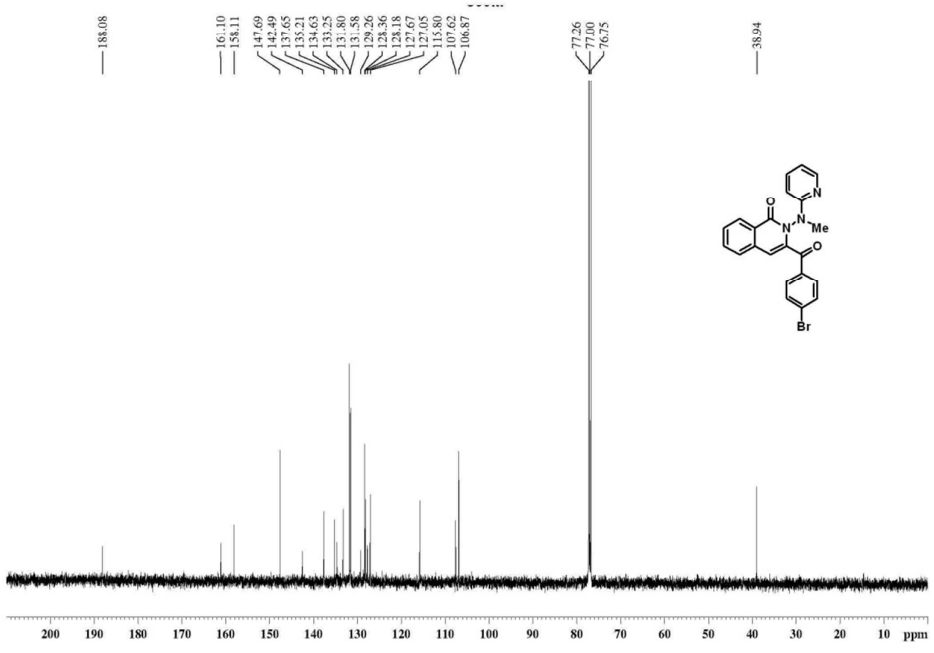


Figure S98. ^{13}C NMR Spectrum of **3ak** (125 MHz, $CDCl_3$).

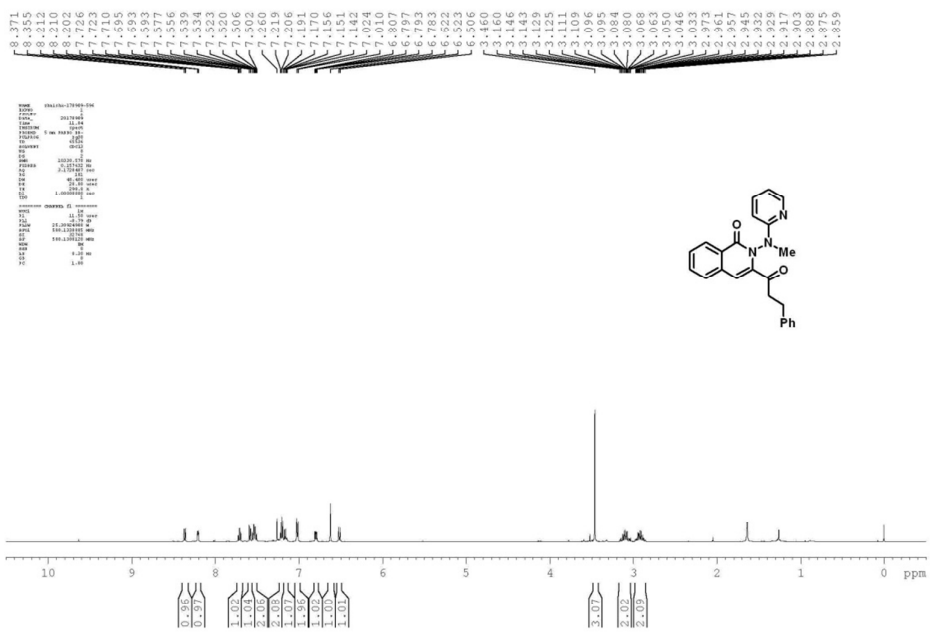


Figure S99. ^{1}H NMR Spectrum of **3al** (500 MHz, $CDCl_3$).

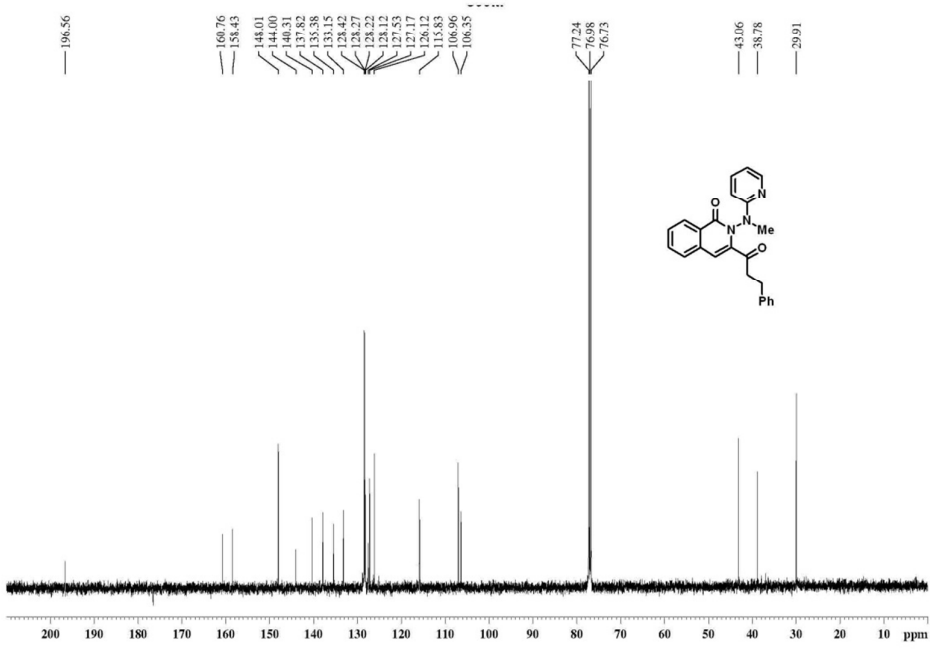


Figure S100. ^{13}C NMR Spectrum of **3al** (125 MHz, $CDCl_3$).

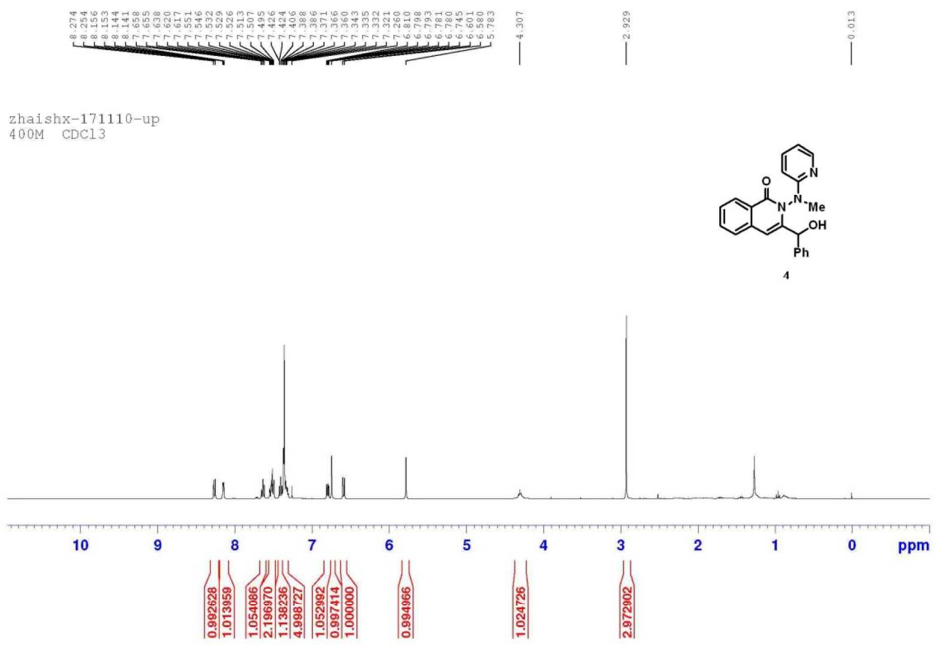


Figure S101. ^{1}H NMR Spectrum of **4** (400 MHz, $CDCl_3$).

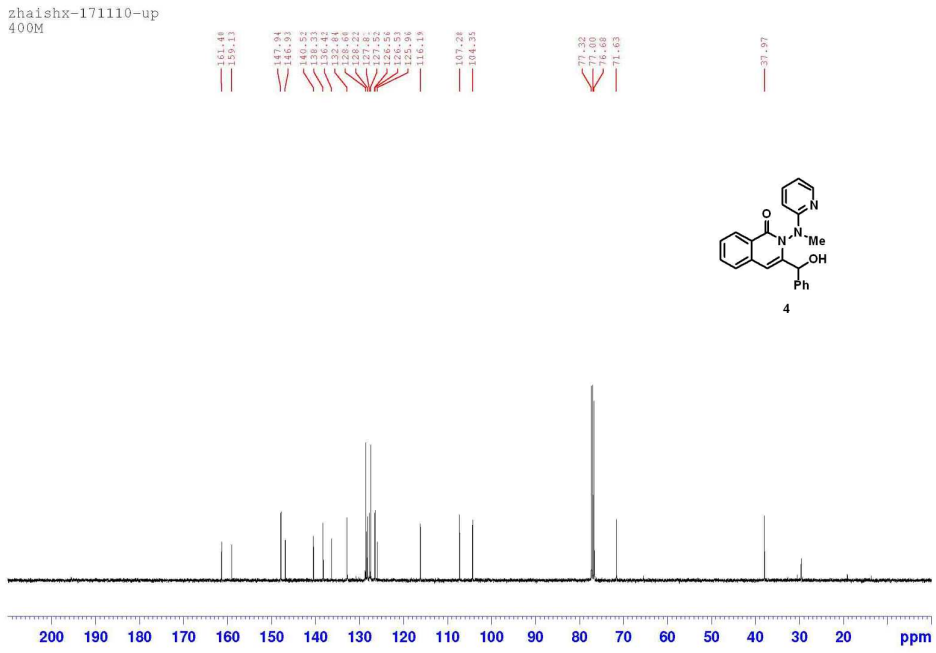


Figure S102. ^{13}C NMR Spectrum of **4** (100 MHz, $CDCl_3$).

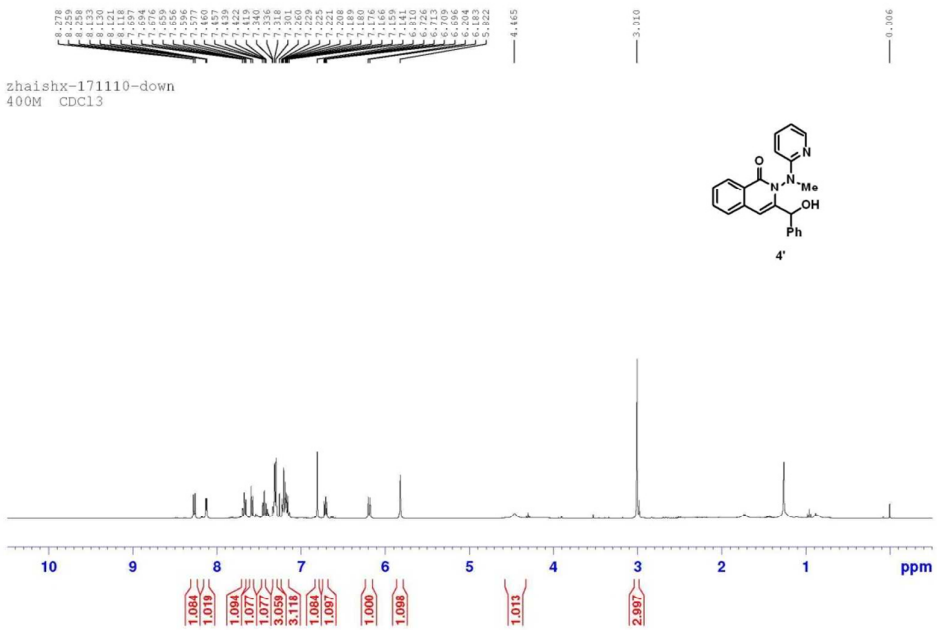


Figure S103. ^{1}H NMR Spectrum of **4'** (400 MHz, $CDCl_3$).

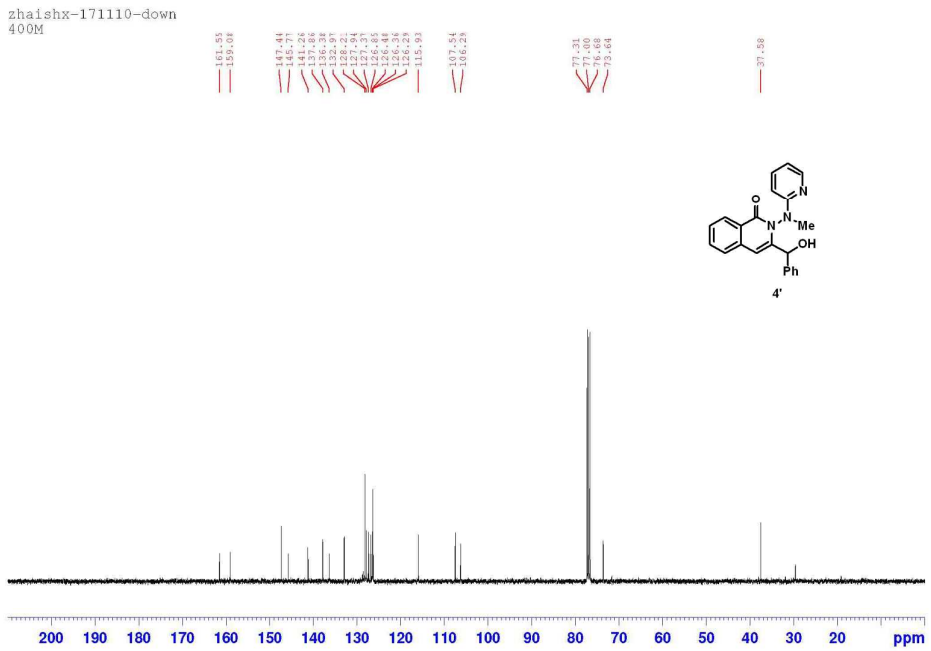


Figure S104. ^{13}C NMR Spectrum of **4'** (100 MHz, $CDCl_3$)

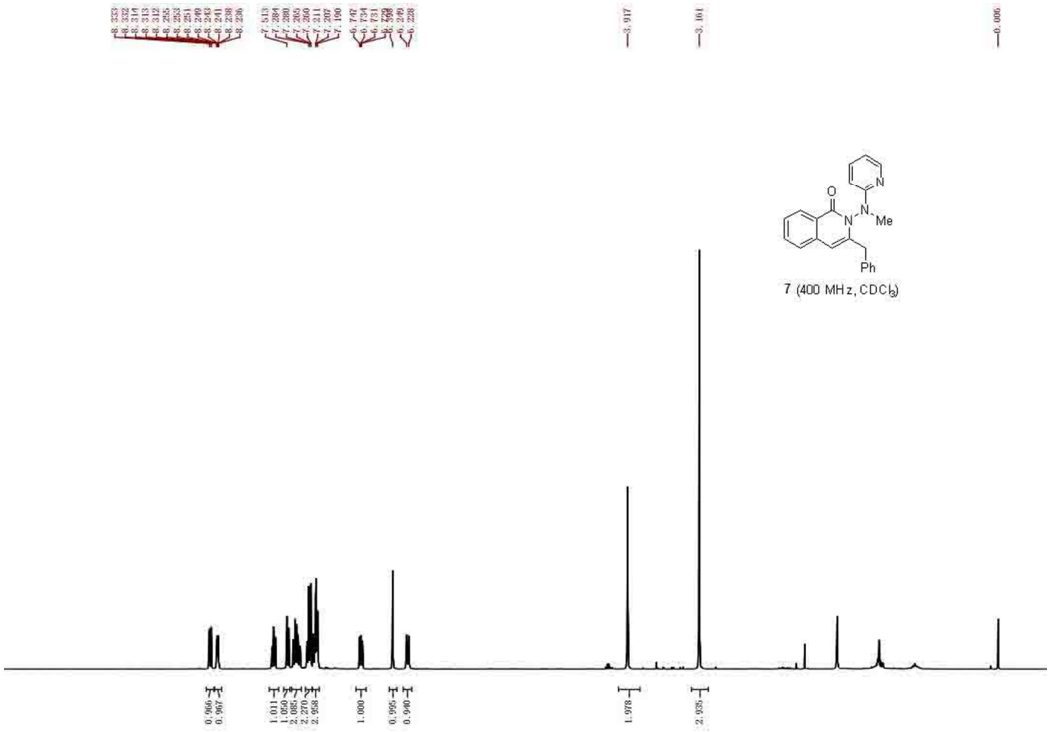


Figure S105. ^{1}H NMR Spectrum of **7** (400 MHz, $CDCl_3$)

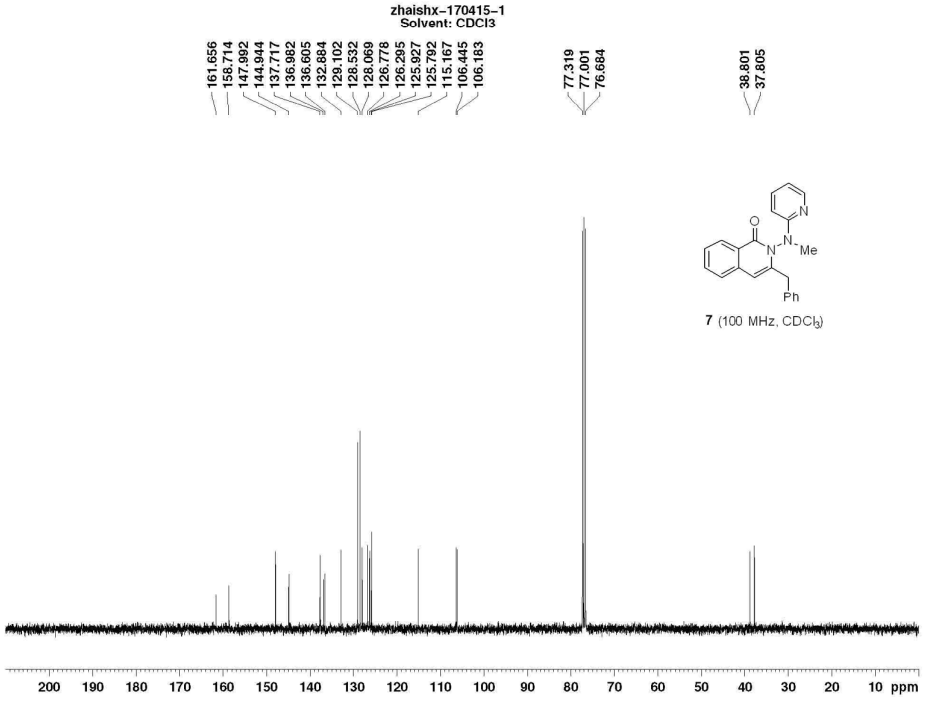


Figure S106. ^{13}C NMR Spectrum of **7** (100 MHz, $CDCl_3$)

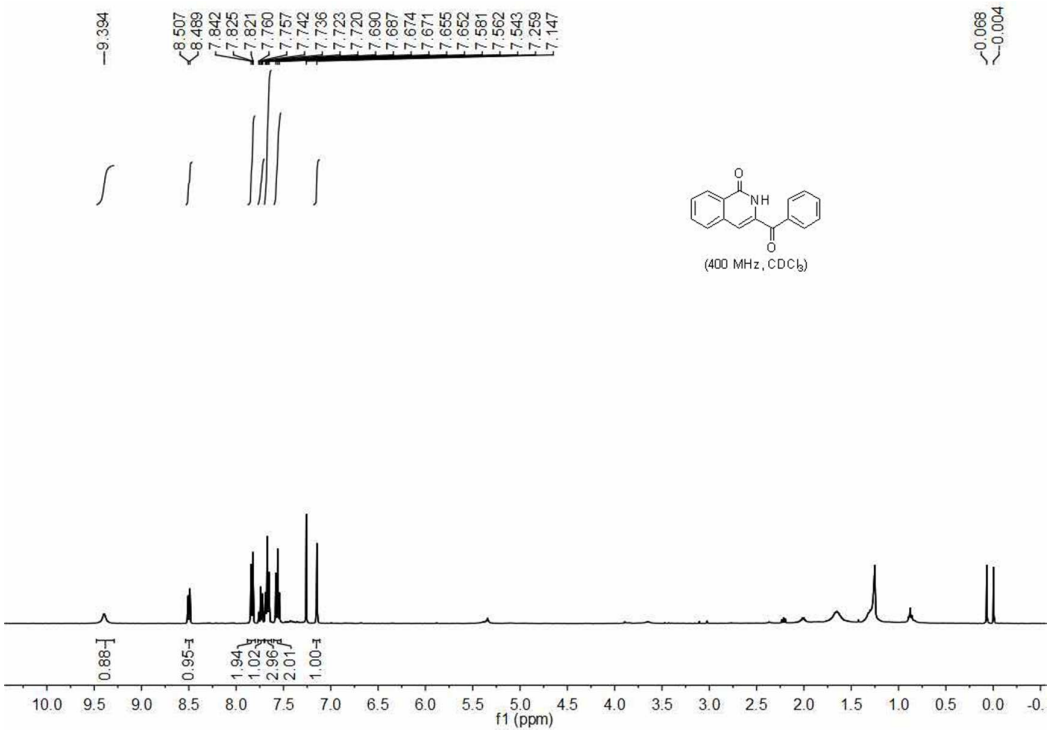


Figure S107. ^{1}H NMR Spectrum of **8** (400 MHz, $CDCl_3$)

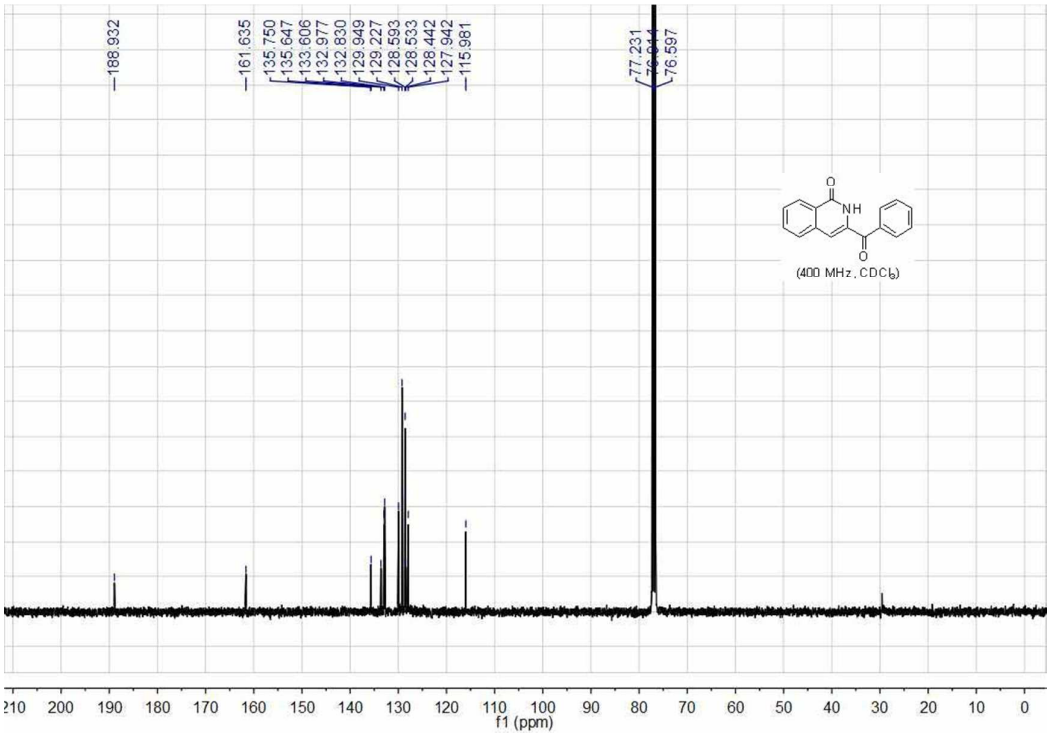


Figure S108. ^{13}C NMR Spectrum of **8** (100 MHz, $CDCl_3$)

11. X-ray Crystallographic Data of Compound **3aa**

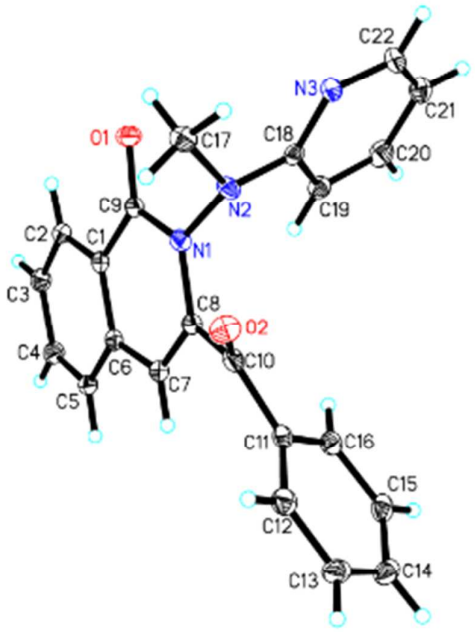
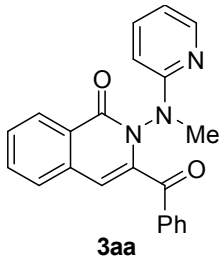


Figure S109. X-ray of compound **3aa** (CCDC:1813669).



3aa

Table S3. Crystal data and structure refinement for **3aa.**

Identification code	exp_975
Empirical formula	$C_{22}H_{17}N_3O_2$
Formula weight	355.38
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	6.0252(3)
b/Å	14.9032(8)
c/Å	19.2088(12)
α/°	90
β/°	93.713(6)
γ/°	90
Volume/Å^3	1721.23(17)
Z	4
ρ_{calc}g/cm^3	1.371
μ/mm^{-1}	0.090
F(000)	744.0
Crystal size/mm^3	0.18 × 0.15 × 0.12
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.25 to 49.988
Index ranges	$-7 \le h \le 5$, $-17 \le k \le 17$, $-22 \le l \le 20$
Reflections collected	9654
Independent reflections	2960 [R_{int} = 0.0637, R_{sigma} = 0.0529]
Data/restraints/parameters	2960/0/245
Goodness-of-fit on F^2	1.042
Final R indexes [I>=2σ (I)]	R_1 = 0.0446, wR_2 = 0.1143
Final R indexes [all data]	R_1 = 0.0543, wR_2 = 0.1252
Largest diff. peak/hole / e Å^{-3}	0.22/-0.26

Table S4. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **3aa**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O(1)	5779.3(18)	1624.5(7)	2475.8(7)	29.0(3)
O(2)	11879.8(18)	3660.2(8)	3414.9(7)	32.6(3)
N(1)	7708(2)	2810.5(9)	2952.9(8)	23.2(3)
N(3)	8649(2)	1231.2(9)	4328.3(8)	24.6(3)
N(2)	8882(2)	2233.2(9)	3423.4(8)	23.7(3)
C(18)	7702(2)	1914.1(10)	3972.8(9)	20.8(4)
C(9)	6050(3)	2436.1(11)	2502.6(9)	22.4(4)
C(6)	4916(3)	4010.5(11)	2205.6(9)	22.5(4)
C(7)	6706(3)	4315.5(11)	2670.3(9)	22.9(4)
C(1)	4625(3)	3082.9(11)	2106.3(9)	22.4(4)
C(8)	8066(2)	3736.1(10)	3027.8(9)	22.0(4)
C(2)	2843(3)	2762.1(11)	1676.6(9)	25.8(4)
C(16)	8194(3)	5149.3(11)	4186.0(9)	26.0(4)
C(11)	9998(3)	4934.6(11)	3800.4(9)	23.5(4)
C(10)	10127(3)	4065.8(11)	3423.1(9)	24.4(4)
C(19)	5716(3)	2315.5(11)	4158(1)	25.7(4)
C(5)	3387(3)	4603.2(11)	1870.2(9)	25.2(4)
C(4)	1598(3)	4274.2(11)	1469.2(10)	28.6(4)
C(22)	7615(3)	925.8(12)	4877.2(10)	30.5(4)
C(3)	1329(3)	3355.6(11)	1368.6(10)	29.5(4)
C(15)	8267(3)	5903.8(12)	4605.2(10)	30.7(4)
C(12)	11838(3)	5506.0(12)	3820.7(10)	28.8(4)
C(17)	10565(3)	1678.7(11)	3113.5(10)	29.0(4)
C(14)	10113(3)	6460.1(12)	4624.5(11)	35.0(5)
C(13)	11876(3)	6267.3(11)	4221.4(11)	33.7(5)
C(20)	4711(3)	1974.6(12)	4721.4(11)	32.9(5)
C(21)	5672(3)	1266.0(12)	5096.6(10)	34.4(5)

Table S5. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **3aa**.

The Anisotropic displacement factor exponent takes the form:

$-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O(1)	34.5(6)	20.2(7)	31.9(8)	0.0(5)	-0.9(6)	0.7(5)
O(2)	25.3(6)	32.4(7)	40.1(9)	-1.8(6)	0.9(6)	4.0(5)
N(1)	25.2(7)	22.6(7)	21.6(9)	3.2(6)	-0.2(6)	2.2(5)
N(3)	27.6(7)	25.3(8)	20.3(8)	1.4(6)	-2.9(6)	1.2(5)
N(2)	23.8(7)	22.9(7)	24.3(9)	6.1(6)	1.6(6)	4.8(5)
C(18)	22.5(8)	19.9(8)	19.5(10)	-3.7(7)	-3.4(7)	-2.4(6)
C(9)	26.3(8)	22.4(9)	19.0(9)	0.3(7)	6.0(7)	0.2(6)
C(6)	26.3(8)	24.4(9)	17.0(9)	-0.3(7)	3.9(7)	-1.4(6)
C(7)	27.9(9)	22.0(8)	19(1)	-0.5(7)	2.5(7)	-1.4(6)
C(1)	27.3(8)	23.9(9)	16.3(9)	-0.7(7)	4.0(7)	0.4(6)
C(8)	24.6(8)	21.7(8)	20(1)	0.2(7)	4.3(7)	-0.3(6)
C(2)	35.8(9)	21.7(9)	19.7(10)	-1.2(7)	0.6(8)	-3.0(7)
C(16)	25.9(8)	28.8(9)	22.6(10)	2.9(8)	-4.2(8)	2.6(7)
C(11)	26.9(9)	25.3(9)	17.3(9)	3.8(7)	-6.1(7)	1.0(6)
C(10)	27.8(9)	25.8(9)	19.3(10)	4.6(7)	-0.9(8)	1.1(7)
C(19)	25.2(8)	25.0(9)	26.5(10)	-2.0(8)	-0.8(8)	3.3(6)
C(5)	34.3(9)	20.9(8)	19.8(10)	0.0(7)	-1.6(8)	0.8(6)
C(4)	32.7(9)	28.0(9)	24.4(11)	0.1(8)	-3.7(8)	3.0(7)
C(22)	39.7(10)	30.7(10)	20.6(10)	4.6(8)	-2.1(9)	0.9(7)
C(3)	33.6(9)	31.3(10)	22.7(11)	-0.3(8)	-5.0(8)	-3.2(7)
C(15)	34.6(10)	34.9(10)	21.8(11)	0.5(8)	-4.3(8)	11.6(7)
C(12)	27.9(9)	30.8(10)	26.8(11)	3.1(8)	-4.6(8)	-0.6(7)
C(17)	26.0(9)	27.8(9)	34.0(11)	3.0(8)	6.6(8)	4.3(7)
C(14)	44.7(11)	27.7(10)	30.3(12)	-3.6(8)	-14.1(9)	6.2(8)
C(13)	35.5(10)	28(1)	35.7(12)	2.1(9)	-11.3(9)	-4.4(7)
C(20)	30.4(9)	36.2(10)	33.1(12)	-6.0(9)	9.4(9)	3.0(7)
C(21)	42.4(11)	37.1(11)	24.7(11)	-0.3(9)	10.3(9)	-1.7(8)

Table S6. Bond Lengths for **3aa.**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O(1)	C(9)	1.2212(19)	C(1)	C(2)	1.396(2)
O(2)	C(10)	1.2181(19)	C(8)	C(10)	1.496(2)
N(1)	N(2)	1.4053(18)	C(2)	C(3)	1.376(2)
N(1)	C(9)	1.395(2)	C(16)	C(11)	1.391(2)
N(1)	C(8)	1.402(2)	C(16)	C(15)	1.382(2)
N(3)	C(18)	1.333(2)	C(11)	C(10)	1.488(2)
N(3)	C(22)	1.339(2)	C(11)	C(12)	1.397(2)
N(2)	C(18)	1.394(2)	C(19)	C(20)	1.372(3)
N(2)	C(17)	1.464(2)	C(5)	C(4)	1.374(2)
C(18)	C(19)	1.404(2)	C(4)	C(3)	1.391(2)
C(9)	C(1)	1.470(2)	C(22)	C(21)	1.367(3)
C(6)	C(7)	1.429(2)	C(15)	C(14)	1.386(3)
C(6)	C(1)	1.405(2)	C(12)	C(13)	1.370(3)
C(6)	C(5)	1.403(2)	C(14)	C(13)	1.385(3)
C(7)	C(8)	1.347(2)	C(20)	C(21)	1.384(3)

Table S7. Bond Angles for **3aa**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C(9)	N(1)	N(2)	117.67(12)	C(7)	C(8)	N(1)	119.59(15)
C(9)	N(1)	C(8)	123.81(13)	C(7)	C(8)	C(10)	120.37(14)
C(8)	N(1)	N(2)	117.94(13)	C(3)	C(2)	C(1)	119.81(15)
C(18)	N(3)	C(22)	117.20(14)	C(15)	C(16)	C(11)	120.05(16)
N(1)	N(2)	C(17)	114.66(14)	C(16)	C(11)	C(10)	121.77(14)
C(18)	N(2)	N(1)	115.82(12)	C(16)	C(11)	C(12)	119.41(16)
C(18)	N(2)	C(17)	121.06(13)	C(12)	C(11)	C(10)	118.52(15)
N(3)	C(18)	N(2)	115.20(13)	O(2)	C(10)	C(8)	121.49(15)
N(3)	C(18)	C(19)	122.63(16)	O(2)	C(10)	C(11)	120.71(14)
N(2)	C(18)	C(19)	122.09(15)	C(11)	C(10)	C(8)	117.72(14)
O(1)	C(9)	N(1)	120.71(15)	C(20)	C(19)	C(18)	117.99(16)
O(1)	C(9)	C(1)	123.76(15)	C(4)	C(5)	C(6)	120.06(15)
N(1)	C(9)	C(1)	115.44(14)	C(5)	C(4)	C(3)	120.63(16)
C(1)	C(6)	C(7)	118.70(15)	N(3)	C(22)	C(21)	124.64(17)
C(1)	C(6)	C(5)	119.00(15)	C(2)	C(3)	C(4)	120.31(16)
C(5)	C(6)	C(7)	122.23(15)	C(16)	C(15)	C(14)	119.84(17)
C(8)	C(7)	C(6)	121.60(15)	C(13)	C(12)	C(11)	120.32(17)
C(6)	C(1)	C(9)	120.76(15)	C(13)	C(14)	C(15)	120.29(17)
C(2)	C(1)	C(9)	118.86(15)	C(12)	C(13)	C(14)	120.02(16)
C(2)	C(1)	C(6)	120.12(15)	C(19)	C(20)	C(21)	120.13(16)
N(1)	C(8)	C(10)	119.50(14)	C(22)	C(21)	C(20)	117.40(17)

Table S8. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for **3aa.**

Atom	*x*	*y*	*z*	U(eq)
H(7)	6938.53	4928.75	2727.31	28
H(2)	2678.88	2149.06	1598.7	31
H(16)	6938.41	4784.95	4161.52	31
H(19)	5101.48	2798.02	3906.27	31
H(5)	3584.48	5219.39	1919.21	30
H(4)	557.77	4669.6	1263.22	34
H(22)	8263.49	448.43	5126.91	37
H(3)	120.54	3141.24	1091.77	35
H(15)	7080.57	6037.79	4873.78	37
H(12)	13043.68	5369.08	3561	35
H(17A)	9845.79	1214.93	2835.05	44
H(17B)	11513.7	1411.86	3477.33	44
H(17C)	11438.95	2045.83	2824.99	44
H(14)	10167.68	6965.18	4909.48	42
H(13)	13086.82	6654.67	4222.52	40
H(20)	3380.08	2220.07	4851.56	40
H(21)	5021.75	1030.51	5482.87	41