Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Copper(II) Catalyzed Domino Synthesis of Quinoline Derivatives from Arylamines and Alkynes

Huimin Dai, Chun-Xiao Li, Chao Yu, Zihao Wang, Hong Yan* and Changsheng Lu*

State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing University, Jiangsu 210023, China

Table of Contents

I. General Remarks

Analytical thin layer chromatography (TLC) was performed on silica gel GF254 plates. Flash column chromatography was undertaken on silica gel (200–300 mesh). ^{1}H NMR was performed on Bruker DRX 500 or 400 MHz at ambient temperature. Data was recorded as follows: chemical shift in ppm from solvent resonance employed as their internal standard (deuterochloroform at 7.26 ppm) on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; brs = broad singlet), coupling constant (Hz), integration, and assignment. ^{13}C NMR was recorded on 125 or 100 MHz at ambient temperature and fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.00 ppm of *d*–chloroform. High resolution mass spectra were measured on Agilent-G6540 UHD Accurate-MassQ-TOF. In experiments that required, all the solvents were used without any purification. Other simple chemicals were analytical-pure grade and obtained commercially.

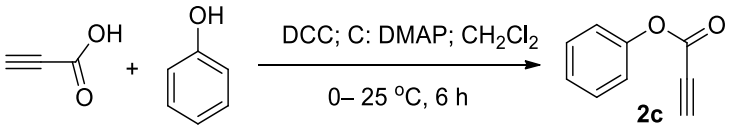
X-ray Crystallography X-ray diffraction data was collected on a Bruker SMART Apex II CCD diffractometer by means of graphitemonochromated Mo Kα (λ = 0.71073 Å) radiation at 296 K. During the collection of the intensity data, no significant decay was observed. The intensities were corrected for Lorentz polarization effects and empirical absorption by using the SADABS program.[S1] All non-hydrogen atom positions were determined utilizing the difference Fourier synthesis. Hydrogen atoms were placed at geometrically calculated positions, which were refined using a riding model. The structures were solved by direct methods with the SHELXL-97 program.[S2] All calculations were performed by applying the Bruker SMART program. Crystallographic data (CCDC No. 1014545) of **3ac** is in Table S1.

II. General procedure for preparing 2,4-disubstituted quinolines

To a tube which contained 4.0 mL acetonitrile solution of arylamine (0.4 mmol), $Cu(OAc)_2{\cdot}H_2O$ (40.0 mg, 0.2 mmol), $Ca(OAc)_2$ H_2O (155.1 mg, 0.88 mmol) and *n*-Bu_4NOAc (12.1 mg, 0.04 mmol), alkyne (1.2 mmol) was added. The tube was capped and let it stirred at room temperature for 5 min. Then $Na_2S_2O_8$ (95.2 mg, 0.4 mmol) was added. The reaction was kept at room temperature for another 12 h, then the mixture was filtered and the filtrate was evaporated under reduced pressure. The residue was purified immediately by column chromatography on silica gel to produce pure products (ethyl acetate and petrol ether as the eluent).

III. Preparation of alkynes 2c, 2e-h

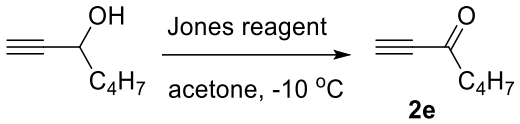
3.1 Synthesis of alkynes 2c



To the solution of phenol (0.94 g, 10 mmol) and propiolic acid (0.65 g, 9.25 mmol) in CH_2Cl_2 (5.0 mL) at 0 °C was added the solution of dicyclohexylcarbodiimide (1.91 g, 9.25 mmol) and 4-dimethylaminopyridine (0.0113 g, 0.0925 mmol) in CH_2Cl_2 (5.0 mL) over 1 h. The reaction was stirred for an additional 5 h. The mixture was then filtered, and washed with ether. Following evaporation of the solvents, the crude product was purified by silica gel chromatography (petrol ether/ethyl acetate =

95/5). Oil. Yield: 1.01 g, 6.94 mmol, 75%. The NMR data are consistent with the literature.[S3]

3.2 Synthesis of alkynes 2e



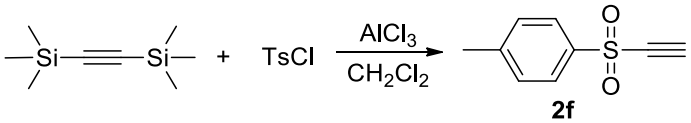
2e

Jones reagent (0.75 mL, 1.2 equiv) was dropwise added to a solution of propargylic alcohol (0.56 g, 5.09 mmol) in acetone at -10 ℃, which left a persistent yellow tint after 30 min. Excess Jones reagent was quenched by the addition of 2-propanol (0.10 mL), and stirring continued for another 15 min at the same temperature. The reaction was filtered through Celite and dried ($MgSO_4$), and the solvent was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (10% ethyl acetate in hexane) to give the product as a volatile colorless liquid (401.8 mg, 3.72 mmol, 73%). The NMR data are consistent with the literature.[S4]

3.3 Synthesis of arylsulfonyl ethylene 2f and 2g[S5,S6]

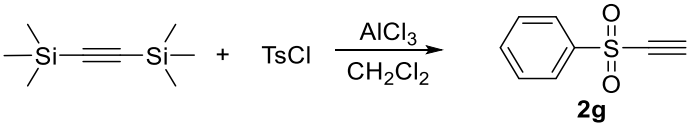
In a three-necked, round bottomed flask (50 mL, flame-dried) fitted with a nitrogen inlet and glass stoppers was filled with dry dichloromethane (10.0 mL) and freshly powdered anhydrous aluminum chloride (0.74 g, 5.5 mmol). After the addition of sulfonyl chloride (5.5 mmol), the resulting dark-brown mixture was shaken occasionally for 20 min at room temperature.

A three-necked, round-bottomed flask (100 mL) equipped with a 25-mL addition funnel and a Teflon coated stirring bar was flame-dried under a stream of dry nitrogen. The flask was charged with bis(trimethylsilyl)acetylene (0.85 g, 5 mmol) and dry dichloromethane (5.0 mL) and the solution was cooled to 0 ℃ in an ice–water bath. The sulfonyl chloride–aluminum chloride complex was quickly filtered through a glass wool plug into the addition funnel. The residue was washed rapidly with an additional 5.0 mL of dry dichloromethane and the funnel was quickly stoppered. The complex was added dropwise during 1 h to the cold (0 ℃), magnetically stirred silylacetylene solution. On completion of the addition, the reaction mixture was allowed to warm to room temperature and was stirred for an additional 12 h. The mixture was hydrolyzed by pouring into a slurry of 20% hydrochloric acid (5.0 mL) and ice (5 g). The organic layer was separated, washed twice with water (7.0 mL), and dried over anhydrous sodium sulfate. Removal of solvent in a rotary evaporator gave the crude product, which was purified by silica gel chromatography using 10% ethyl acetate in petroleum ether as eluent.



2f

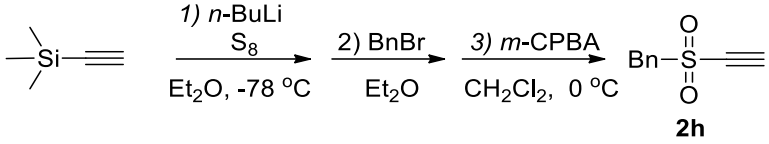
Yellow solid. Yield: 6245 mg, 3.465 mmol, 63%. The NMR data are consistent with the literature[S5].



2g

Yellow solid. Yield: 4479 mg, 2.695 mmol, 49%. The NMR data are consistent with the literature[S6].

3.4 Synthesis of benzylsulfonyl ethylene 2h



(1) To a solution of trimethylsilylacetylene (1.5 g, 15.27 mmol) in anhydrous ether (20 mL) under argon atmosphere was added a 2.4 M solution of *n*-BuLi in hexane (6.7 mL, 16 mmol) at –78 ℃. After 10 min, sulfur powder (480 mg, 15 mmol) was added and the reaction was warmed up to room temperature and was stirred for another hour. (2) Benzyl bromide (1.9 mL, 16 mmol) was added to the mixture and the reaction was kept for another 2 h. Removed the solvent under reduced pressure and dissolved the residue with petrol ether. Then the solution was quickly filtered through celite and the solvent was removed under reduced pressure. (3) The residue was dissolved in DCM (20 mL) and *m*-CPBA (40 mmol) was added to the solution at 0 °C. Once the material was consumed (monitored by TLC), the crude mixture was treated with 10 mL of saturated solution of Na_2SO_3 and then washed with a saturated solution of Na_2CO_3 (3 × 15 mL). The organic layer was dried with Na_2SO_4 and then concentrated under reduced pressure. The residue was purified by chromatography 10% ethyl acetate in petroleum ether as eluent. The NMR data are consistent with the literature[S7]. Yield: 1.3787 g, 7.65 mmol, 51%.

IV. Control experiments

4.1 Terminal deuteration of methyl propiolate[S8]

A flame-dried 10-mL round bottomed flask was charged with alkyne (0.3 mL) and potassium carbonate (700 mg) in dry acetonitrile (5.0 mL). The mixture was allowed to stir under an atmosphere of N_2 for 30 min, to which D_2O (2.0 mL, around 40 equiv.) was added then, and left to stir for 1 h. The resulting crude reaction mixture was diluted with dichloromethane (5.0 mL) and transferred to a separating funnel. The organic layer was separated, dried with $MgSO_4$, and filtered. The solution of deuterated methyl propiolate was distilled under vacuum, giving 95% yield and 94% deuteration.

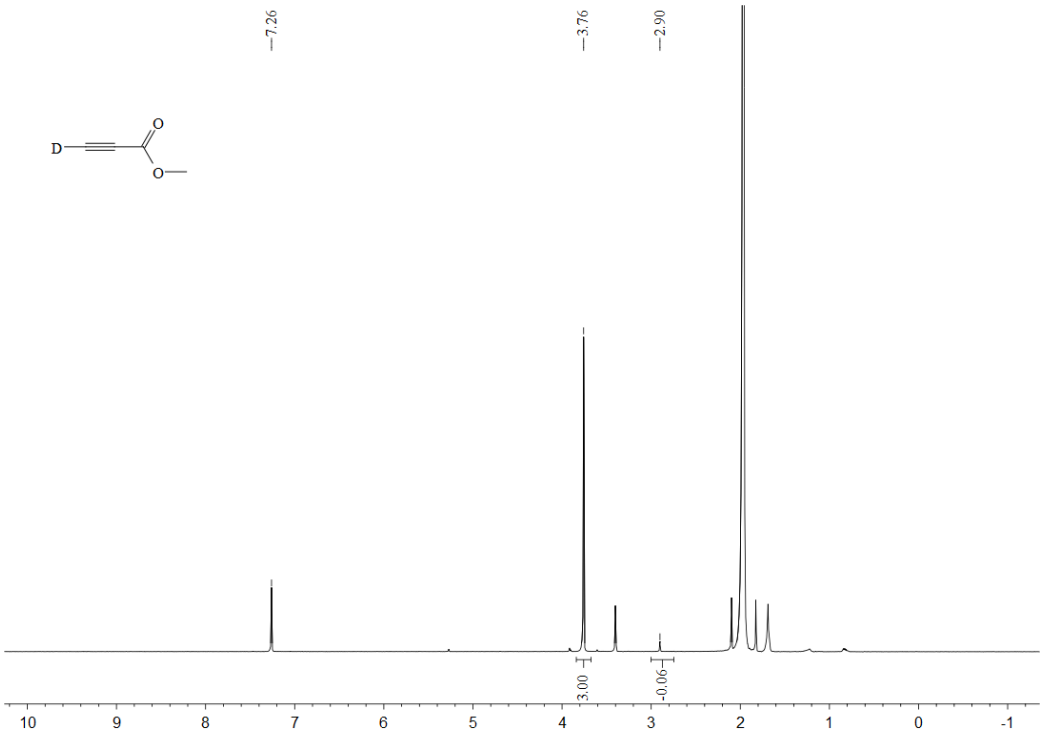


Figure S1. ^{1}H NMR of deuterated methyl propiolate in $CDCl_3$ (500 MHz)

4.2 Deuterium control experiment

The deuterated methyl propiolate was washed with deionized water, dried with $MgSO_4$, and then filtered. The product **3aa** was obtained by following the standard quinoline preparation from 1-Naphythylamine (**1a**) and **D-2a**, and the ^{1}H NMR spectrum is shown in Figure S2.

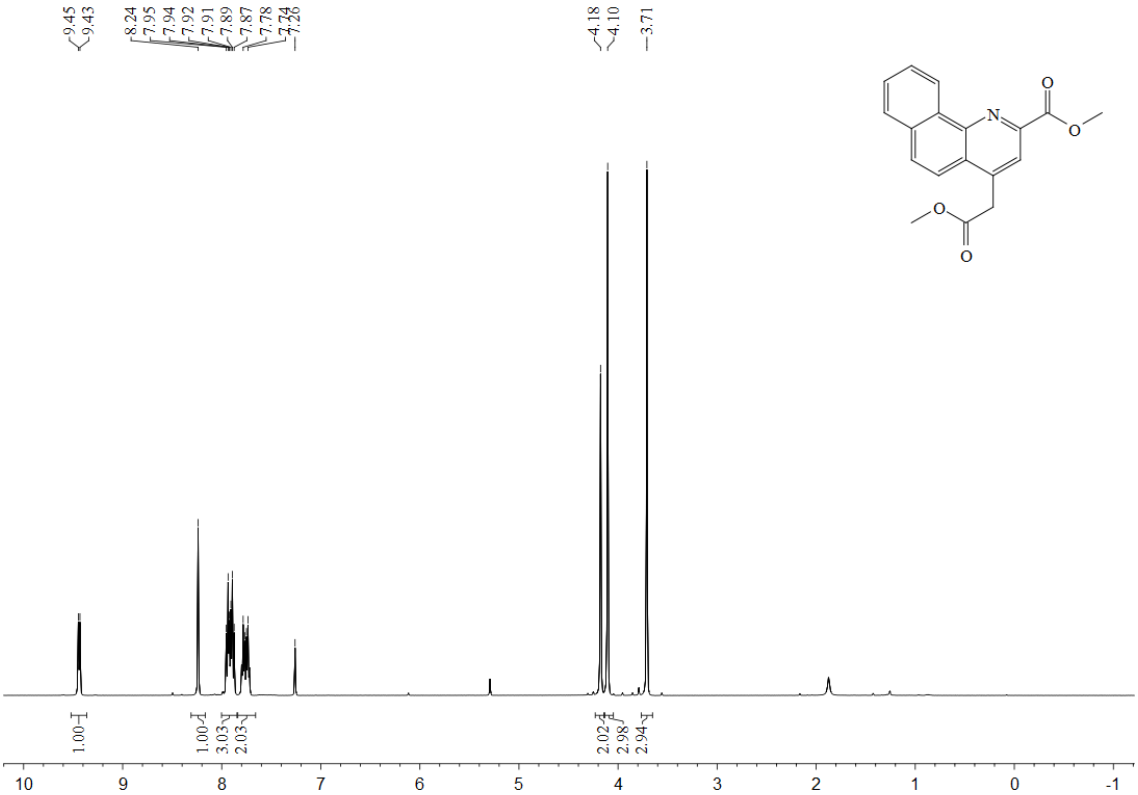


Figure S2. 3aa preparation from 1-naphythylamine and *d*-methyl propiolate **D-2a** in acetonitrile

Follow the standard procedure to prepare quinoline with methyl propionate, 1-naphythylamine and 2 drops of heavy water. The ^{1}H NMR spectrum of the product is shown in Figure S3.

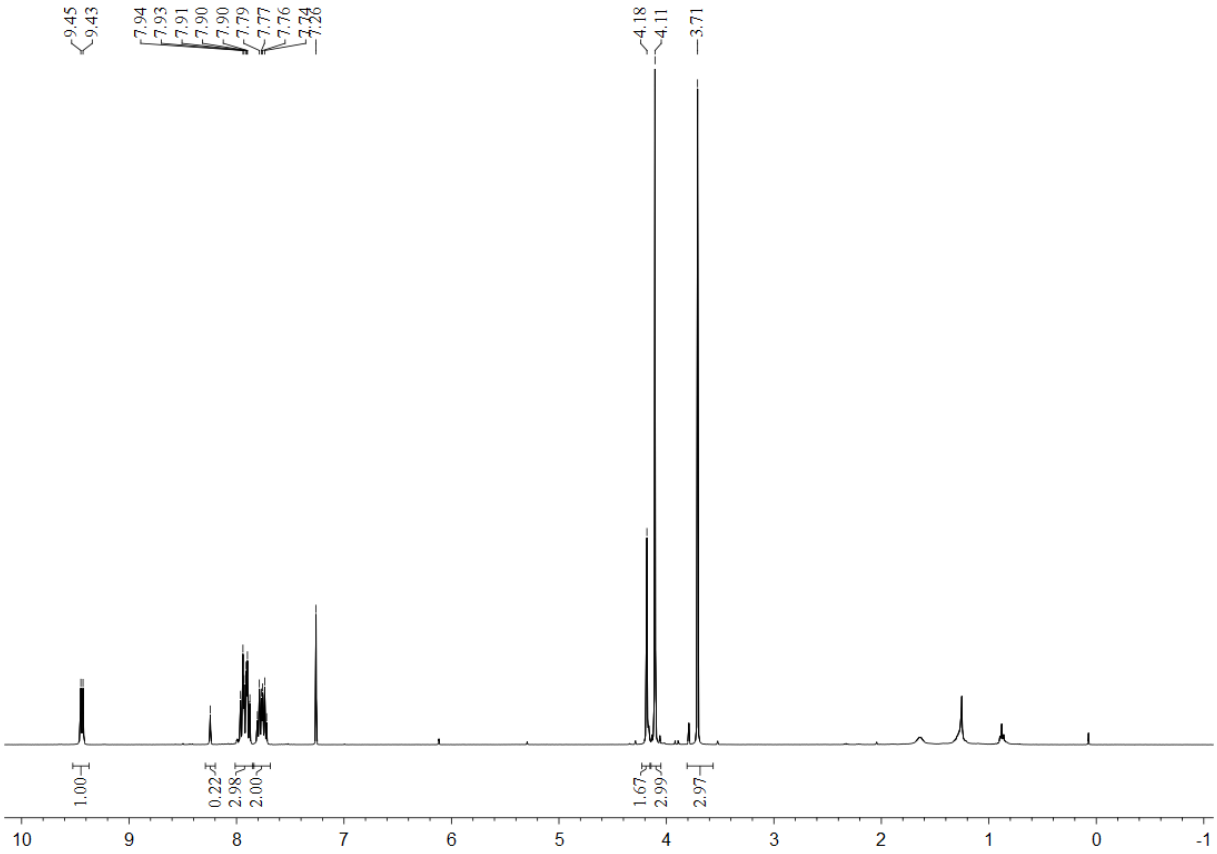
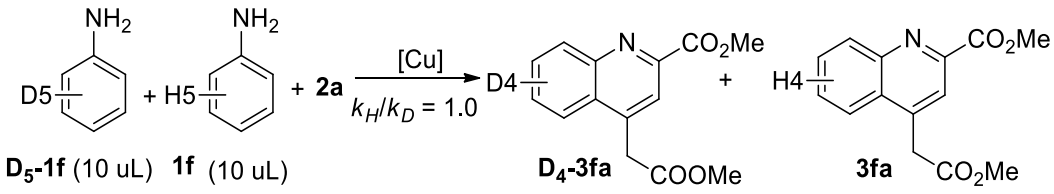


Figure S3. **D-3aa** preparation from 1-naphythylamine and methyl propionate in D_2O-contained acetonitrile

4.3 KIE effect of arylamine 1f

To the 6.0 mL acetonitrile solution of arylamine (**1f**: 10.0 μL; **D$_5$-1f**: 10.0 μL), $Cu(OAc)_2{\cdot}H_2O$ (21.9 mg, 0.11 mmol), $Ca(OAc)_2{\cdot}H_2O$ (85.3 mg, 0.484 mmol) and *n*-Bu_4NOAc (6.6 mg, 0.022 mmol), the alkyne **2a** (54.0 μL) was added. The mixture was stirred at room temperature for 5 minutes, and then $Na_2S_2O_8$ (52.4 mg, 0.22 mmol) was added. At last, the reaction was left at room temperature for another 12h, and then filtered. The filtrate was evaporated under reduced pressure. The resulting residue was immediately purified by column chromatography on silica gel to produce **3fa** and **D$_4$-3fa** (petrol ether/ethyl acetate = 5/1).



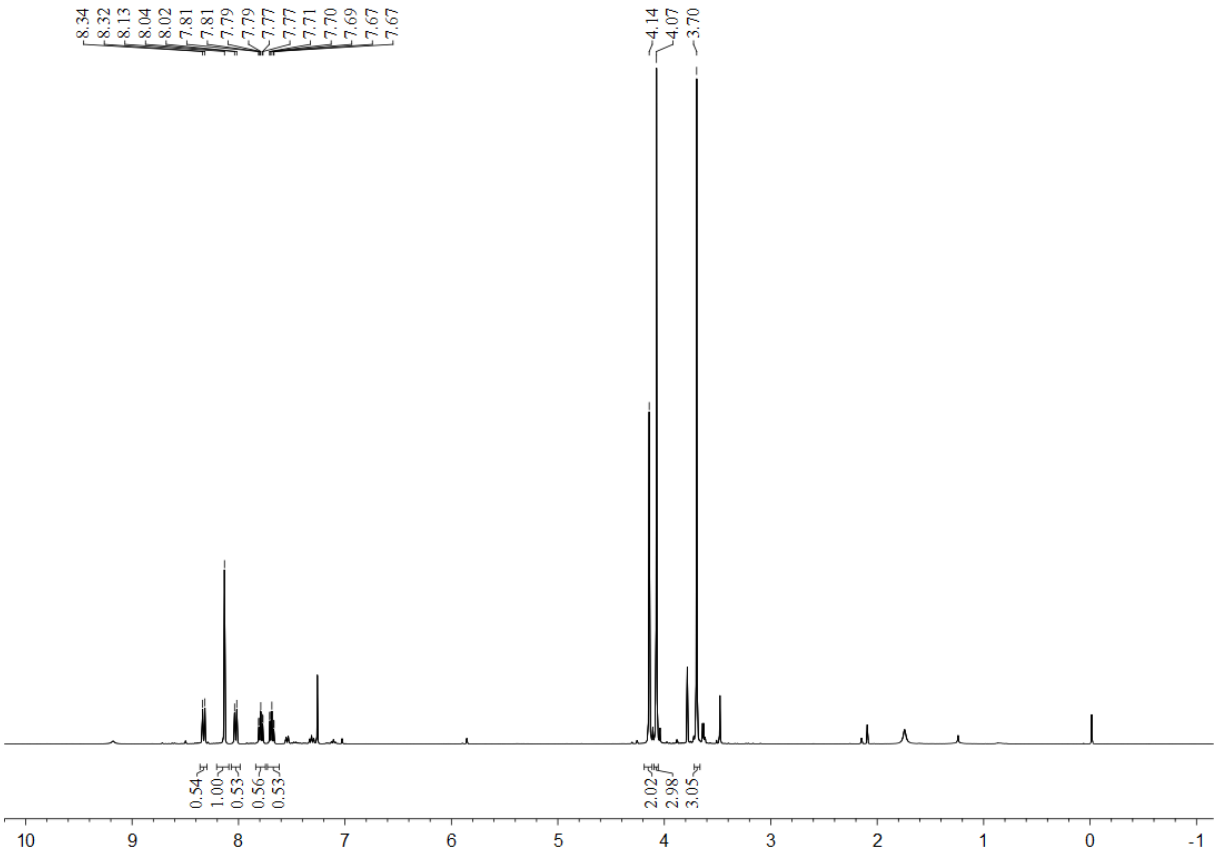
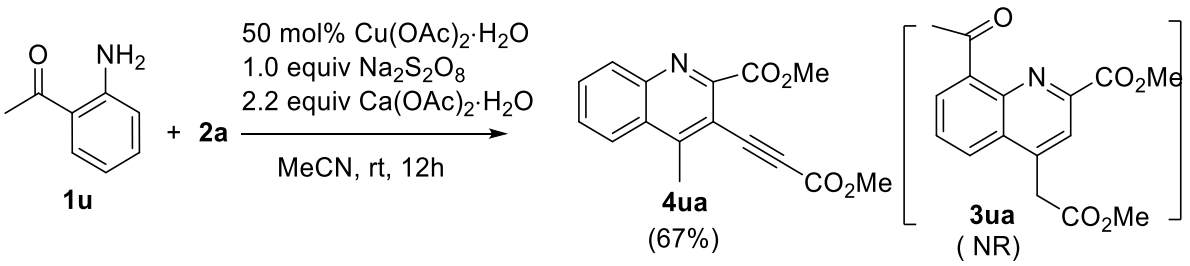


Figure S4. Quinolines **3fa** and **D_4-3fa** preparation from anilines (**1f**:**D_5-1f** = 1:1).

4.4 Reaction between 1-(2-aminophenyl)ethanone and methyl propiolate

4ua was separated instead of **3ua** by following the standard procedure of the quinoline preparation from **1u** and **2a**.



4.5 EPR Experiments

The EPR spectra were collected as follows:

An oven dried 10 mL reaction flask was fitted with a magnetic stirring bar and open to air. At 25 ^{o}C, MeCN (4 mL), $Cu(OAc)_2H_2O$ (40 mg, 0.2 mmol) were added into the flask. After filtration, the sample was taken out into a thin tube and frozen by liquid nitrogen. EPR was recorded at 90 K on EPR spectrometer operated at 9.444 GHz. Typical spectrometer parameters are shown as follows, scan range: 2000 G; conter field set: 3357; time onstant: 163.8 ms; scan time: 81.92 s; modulation amplitude: 4.0 G; modulation frequency: 100 kHz; receiver gain: 1.00 x 10^3, microwave power: 1.797 mW. Methyl propiolate (1.2 mmol, 3 equiv) was added to the solution of $Cu(OAc)_2$ in MeCN at room temperature. After 30 min, the solution was taken out into a thin tube and frozen by liquid nitrogen. After the test

of EPR, the reaction mixture was examined by GC-MS. The alkyne homocoupling product **5a** was observed.

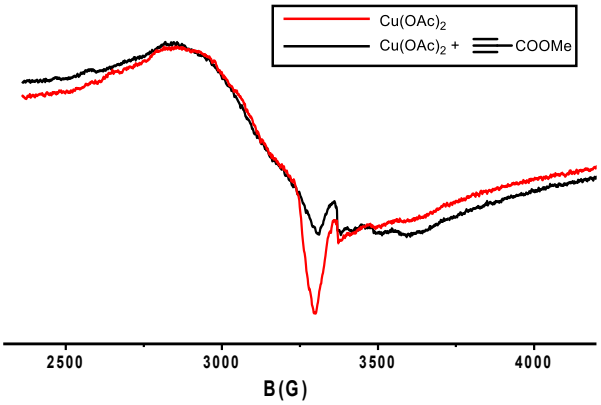


Figure S5 EPR spectra of $Cu(OAc)_2$ without (red) and with (black) alkyne at 90 K.

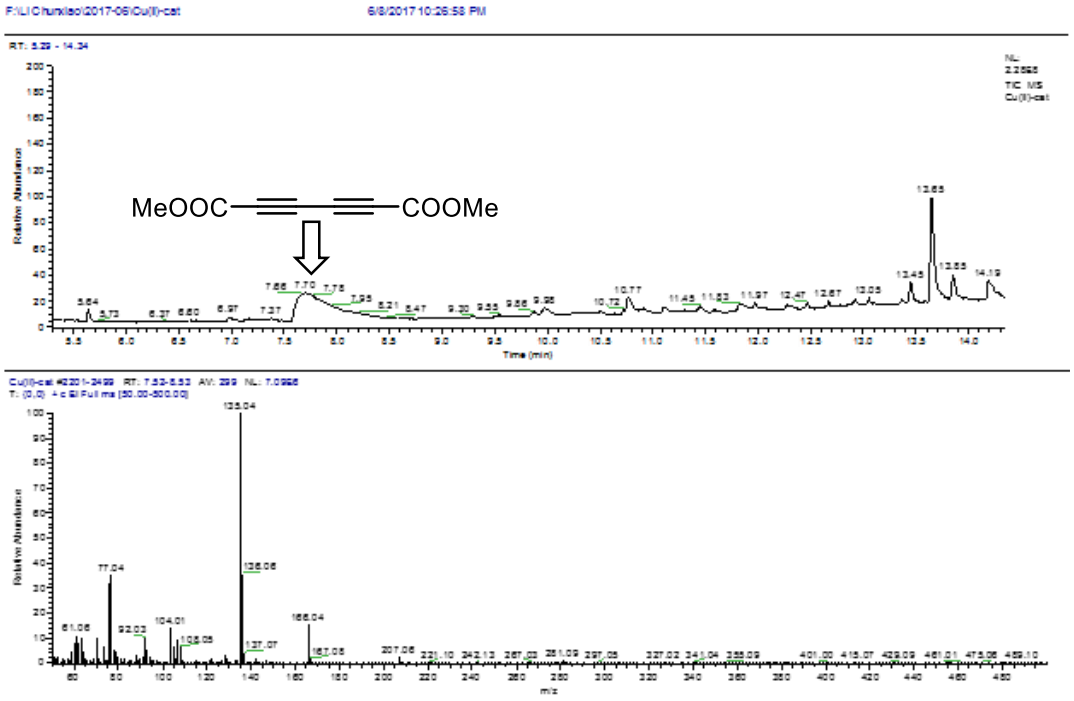


Figure S6 GC-MS of reaction system

As shown in Figure S5, compared to $Cu(OAc)_2$, reaction mixture with 3 equiv methyl propiolate exhibited a damping signal, indicating that the concentration of Cu(II) has decreased. Combined with the result of GC-MS, the catalytic cycle A in Scheme 3 seems to be possible.

V. Crystal structure of 3ac

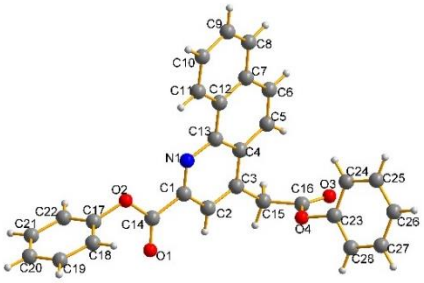


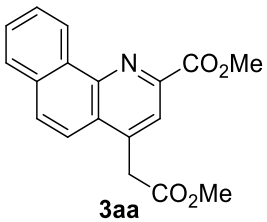
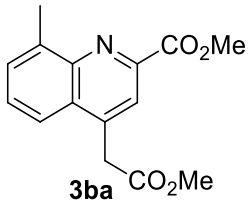
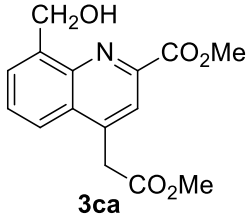
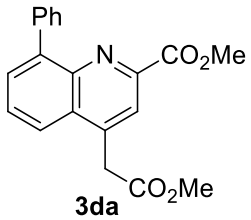
Figure S7. Crystal structure of **3ac**.

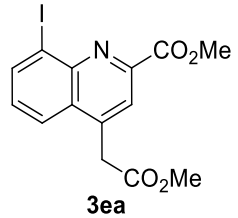
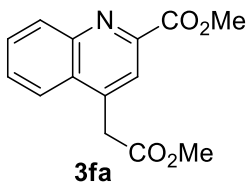
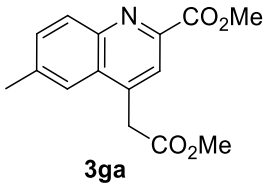
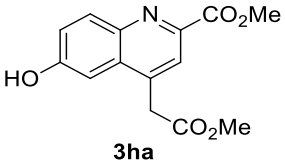
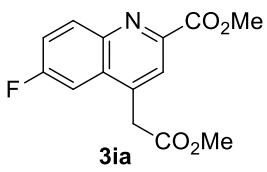
Table S1. Crystallographic data of compounds **3ac**

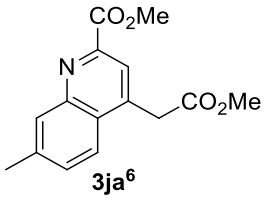
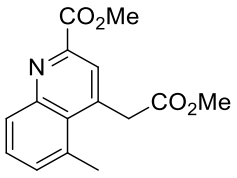
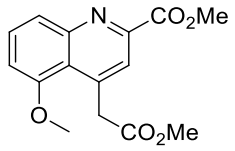
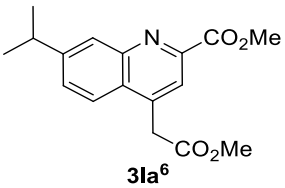
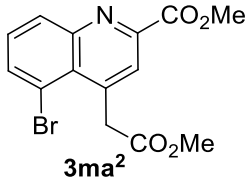
	3ac
Chemical formula	$C_{28}H_{19}NO_4$
Crystal size	0.24 × 0.17 × 0.12
Molecular weight	433.44
Temperature(K)	296(2)
Radiation	Mo-Kα(0.71073 Å)
Crystal system	Triclinic
Space group	*P*-1
a (Å)	5.902(3)
b (Å)	14.138(7)
c (Å)	14.345(8)
α (°)	67.772(8)
β (°)	85.634(8)
γ (°)	89.402(9)
V (Å^3)	1104.6(10)
Z	2
D_c (g cm^{-3})	1.303
μ (mm^{-1}) absort.coeff	0.088
F (000)	452
θ rang (deg)	1.54-25.00
Reflections collected	6078 (R_{int} = 0.0291)
Indep. reflns	3828
Refns obs. [$I > 2\sigma(I)$]	3206
Data /restr./paras	3828/0/298
Goodness-of-fit on F^2	1.075
R_1, wR_2 [$I > 2\sigma(I)$]	0.0460/0.1147
R1/*w*R2 (all data)	0.0387/0.1107
larg.peak/hole (e·Å^{-3})	0.127/–0.173

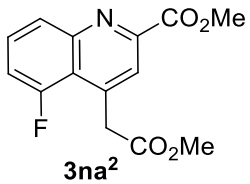
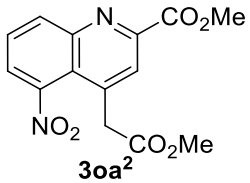
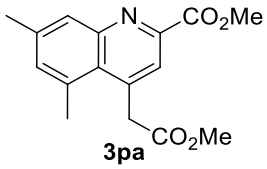
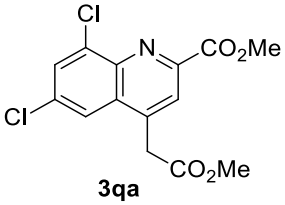
VI. Characterization data for products

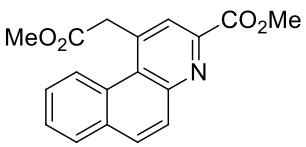
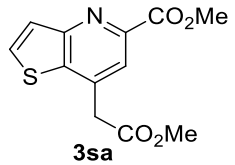
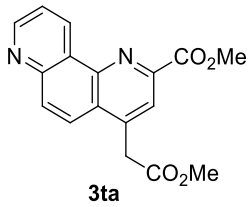
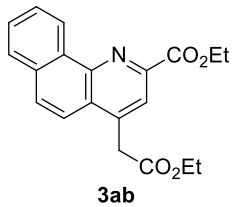
 **5a**	**dimethyl hexa-2,4-diynedioate** White oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.83 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 152.07, 72.27, 68.08, 53.45.

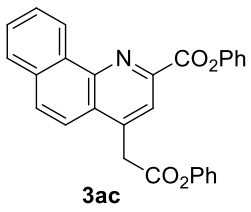
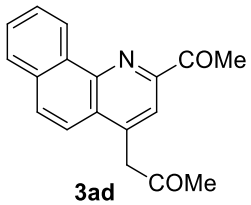
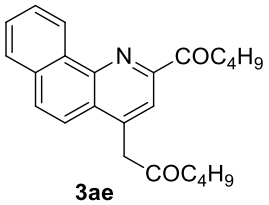
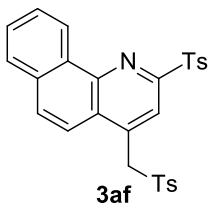
 **3aa**	**dethyl 4-(2-methoxy-2-oxoethyl)benzo[h]quinoline-2-carboxylate** Yield: 100.2 mg, 0.324 mmol, 81%. White solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.44 (d, *J* = 8.0 Hz, 1H), 8.24 (s, 1H), 7.94 (d, *J* = 9.1 Hz, 1H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.88 (d, *J* = 9.1 Hz, 1H), 7.78 (t, *J* = 7.5 Hz, 1H), 7.74 (t, *J* = 7.3 Hz, 1H), 4.18 (s, 2H), 4.10 (s, 3H), 3.71 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.24, 166.09, 146.44, 145.91, 140.87, 133.34, 131.83, 130.52, 128.86, 127.75, 127.72, 127.18, 125.36, 123.78, 120.41, 52.96, 52.50, 38.58. **HRMS** (ESI) calc for $C_{18}H_{16}NO_4$ $(M+H)^+$ (310.1074) found (310.1075); $C_{18}H_{15}NO_4Na$ $(M+Na)^+$ (332.0893) found (332.0894). m.p. 84.8-85.4 °C
 **3ba**	**methyl 4-(2-methoxy-2-oxoethyl)-8-methylquinoline-2-carboxylate** Yield: 86.4 mg, 0.316 mmol, 79%. White solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 6.6 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 4.13 (s, 2H), 4.06 (s, 3H), 3.70 (s, 3H), 2.90 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.34, 166.12, 147.00, 146.38, 141.31, 139.64, 130.25, 128.72, 128.59, 122.30, 121.24, 52.96, 52.45, 38.61, 18.26. **HRMS** (ESI) calc for $C_{15}H_{16}NO_4$ $(M+H)^+$ (274.1074) found (274.1073); $C_{15}H_{15}NO_4Na$ $(M+Na)^+$ (296.0893) found (296.0897). m.p. 85.7-86.4 °C
 **3ca**	**methyl-(hydroxymethyl)-4-(2-methoxy-2-oxoethyl)quinoline-2-carboxylate** Yield: 79.8 mg, 0.276 mmol, 69%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.96 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.76 – 7.54 (m, 2H), 5.23 (s, 2H), 5.16 (brs, 1H), 4.15 (s, 2H), 4.05 (s, 3H), 3.70 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.00, 165.36, 146.56, 145.89, 142.32, 140.14, 128.91, 128.88, 128.53, 123.02, 122.43, 64.77, 53.03, 52.54, 38.58. **HRMS** (ESI) calc for $C_{15}H_{16}NO_5$ $(M+H)^+$ (290.1023) found (290.1022); $C_{15}H_{15}NO_5Na$ $(M+Na)^+$ (312.0842) found (312.0840). m.p. 133.2-134.1 °C
 **3da**	**methyl 4-(2-methoxy-2-oxoethyl)-8-phenylquinoline-2-carboxylate** Yield: 99.3 mg, 0.296 mmol, 74%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.03 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.87 (dd, *J* = 7.2, 1.4 Hz, 1H), 7.83 (dd, *J* = 7.3, 2.2 Hz, 2H), 7.75 (dd, *J* = 8.4, 7.2 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 1H), 4.18 (s, 2H), 3.97 (s, 3H), 3.73 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.32, 166.06, 147.08, 145.37, 142.39, 141.31, 138.61, 131.22, 130.93, 128.93, 128.78, 127.82, 127.57, 122.84, 122.39, 52.85, 52.51, 38.75. **HRMS** (ESI) calc for $C_{20}H_{18}NO_4$ $(M+H)^+$ (336.1230) found (336.1229); $C_{20}H_{17}NO_4Na$ $(M+Na)^+$ (358.1050) found (358.1051). m.p. 119.5-120.1 °C

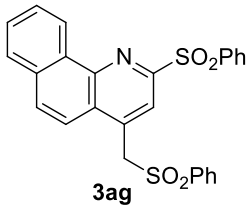
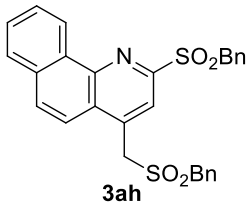
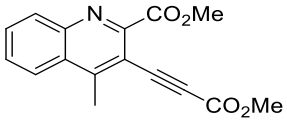
 **3ea**	**methyl 8-iodo-4-(2-methoxy-2-oxoethyl) quinoline-2-carboxylate** Yield: 112.5 mg, 0.292 mmol, 73%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.44 (dd, *J* = 7.4, 0.9 Hz, 1H), 8.16 (s, 1H), 8.03 (dd, *J* = 8.4, 0.9 Hz, 1H), 7.39 (dd, *J* = 8.4, 7.4 Hz, 1H), 4.15 (s, 2H), 4.08 (s, 3H), 3.70 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.89, 165.44, 148.40, 146.70, 142.39, 141.03, 129.93, 129.22, 124.30, 123.46, 105.92, 53.27, 52.61, 38.27. **HRMS** (ESI) calc for $C_{14}H_{13}INO_4$ $(M+H)^+$ (385.9884) found (385.9882); $C_{14}H_{12}INO_4Na$ $(M+Na)^+$ (407.9703) found (407.9706). m.p. 106.9-107.4 °C
 **3fa**	**methyl 4-(2-methoxy-2-oxoethyl)-8-methylquinoline-2-carboxylate** Yield: 79.9 mg, 0.308 mmol, 77%. White solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.4 Hz, 1H), 8.13 (s, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 4.14 (s, 2H), 4.08 (s, 3H), 3.70 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.07, 165.73, 147.69, 147.54, 141.62, 131.45, 130.21, 129.05, 128.58, 123.45, 122.51, 53.19, 52.48, 38.32. **HRMS** (ESI) calc for $C_{14}H_{14}NO_4$ $(M+H)^+$ (260.0917) found (260.0920); $C_{14}H_{13}NO_4Na$ $(M+Na)^+$ (282.0737) found (282.0740). m.p. 94.5-95.5 °C
 **3ga**	**methyl 4-(2-methoxy-2-oxoethyl)-6-methylquinoline-2-carboxylate** Yield: 88.5 mg, 0.324 mmol, 81%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.7 Hz, 1H), 8.10 (s, 1H), 7.76 (s, 1H), 7.62 (dd, *J* = 8.7, 1.7 Hz, 1H), 4.11 (s, 2H), 4.06 (s, 3H), 3.70 (s, 3H), 2.58 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.19, 165.81, 146.55, 146.25, 140.67, 139.53, 132.58, 131.08, 128.61, 122.59, 122.28, 53.13, 52.46, 38.23, 22.14. **HRMS** (ESI) calc for $C_{15}H_{16}NO_4$ $(M+H)^+$ (274.1074) found (274.1077), $C_{15}H_{15}NO_4Na$ $(M+Na)^+$ (296.0893) found (296.0896). m.p. 97.3-98.1 °C
 **3ha**	**methyl-6-hydroxy-4-(2-methoxy-2-oxoethyl)quinoline-2-carboxylate** Yield: 80.4 mg, 0.292 mmol, 73%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 9.2 Hz, 1H), 8.08 (s, 1H), 7.40 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.32 (d, *J* = 2.6 Hz, 1H), 4.04 (s, 3H), 4.03 (s, 2H), 3.68 (s, 3H), 1.71 (brs, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.41, 165.86, 156.82, 144.69, 143.28, 139.55, 133.02, 130.33, 122.94, 122.80, 105.26, 53.09, 52.57, 38.57. **HRMS** (ESI) calc for $C_{14}H_{14}NO_5$ $(M+H)^+$ (276.0866) found (276.0861); $C_{14}H_{13}NO_5Na$ $(M+Na)^+$ (298.0686) found (298.0681). m.p. 116.8-117.4 °C
 **3ia**	**methyl 6-fluoro-4-(2-methoxy-2-oxoethyl)quinoline-2-carboxylate** Yield: 87.6 mg, 0.316 mmol, 79%. White solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.37 (dd, *J* = 9.0, 5.6 Hz, 1H), 8.16 (s, 1H), 7.64 (d, *J* = 9.4 Hz, 1H), 7.58 (t, *J* = 8.5 Hz, 1H), 4.09 (s, 2H), 4.08 (s, 3H), 3.73 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.78, 165.51, δ 162.10 (d, $J_{C\text{-}F}$ = 252.6 Hz), 146.96, 144.83, 141.19, 134.15 (d, $J_{C\text{-}F}$ = 9.6 Hz), 129.73, 123.17,

	120.82 (d, $J_{C\text{-}F}$ = 25.9 Hz), 107.38 (d, $J_{C\text{-}F}$ = 23.0 Hz), 53.29, 52.64, 38.38. **HRMS** (ESI) calc for $C_{14}H_{13}FNO_4$ $(M+H)^+$ (278.0823) found (278.0823); $C_{14}H_{12}FNO_4Na$ $(M+Na)^+$ (300.0643) found (300.0647). m.p. 102.0-102.5 °C
 **3ja^6**  **3ja^2**	**3ja^6 methyl 4-(2-methoxy-2-oxoethyl)-7-methylquinoline-2-carboxylate** **3ja^2 methyl 4-(2-methoxy-2-oxoethyl)-5-methylquinoline-2-carboxylate** Yield: 89.6 mg, 0.328 mmol, 82% (**3ja^6**:**3ja^2** = 1:1). White solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.4 Hz, 1H), 8.15 (s, 1H), 8.06 (s, 1H), 8.00 (s, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.43 (d, *J* = 6.8 Hz, 1H), 4.34 (s, 2H), 4.11 (s, 2H), 4.06 (s, 6H), 3.72 (s, 3H), 3.69 (s, 3H), 2.84 (s, 3H), 2.57 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.85, 170.12, 165.74, 165.66, 149.67, 147.79, 147.34, 146.54, 142.20, 141.49, 140.83, 134.22, 132.48, 131.41, 130.69, 130.17, 129.48, 128.97, 126.70, 124.89, 123.11, 121.78, 53.14 (2C), 52.49, 52.46, 42.12, 38.32, 24.59, 21.65. **HRMS** (ESI) calc for $C_{15}H_{16}NO_4$ $(M+H)^+$ (274.1074) found (274.1076), $C_{15}H_{16}NO_4$ $(M+Na)^+$ (296.0893) found (296.0896). (Note: **3ja^6** and **3ja^2** were not separated)
 **3ka^2**	**methyl 7-methoxy-4-(2-methoxy-2-oxoethyl)quinoline-2-carboxylate** Yield: 74.0 mg, 0.256 mmol, 64%. White solid. **^{1}H NMR** (400 MHz, CDCl3) δ 7.92 (s, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 4.24 (s, 2H), 4.06 (s, 3H), 3.91 (s, 3H), 3.69 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.08, 165.80, 156.12, 149.74, 147.66, 142.06, 129.84, 123.97, 123.85, 121.47, 107.39, 55.35, 53.18, 51.96, 43.26. **HRMS** (ESI) calc for $C_{15}H_{16}NO_5$ $(M+H)^+$ (290.1023) found (290.1027); $C_{15}H_{15}NNaO_5$ $(M+Na)^+$ (312.0842) found (312.0845). m.p. 116.9-117.5 °C
 **3la^6**	**methyl 7-isopropyl-4-(2-methoxy-2-oxoethyl)quinoline-2-carboxylate** Yield: 98.8 mg, 0.328 mmol, 82%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 1.8 Hz, 1H), 8.08 (s, 1H), 7.96 (d, *J* = 8.7 Hz, 1H), 7.59 (dd, *J* = 8.7, 1.8 Hz, 1H), 4.12 (s, 2H), 4.07 (s, 3H), 3.70 (s, 3H), 3.13 (hept, *J* = 6.9 Hz, 1H), 1.36 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.26, 165.96, 151.35, 148.15, 147.43, 141.15, 129.50, 127.59, 126.99, 123.21, 121.85, 53.19, 52.50, 38.32, 34.12, 23.59. **HRMS** (ESI) calc for $C_{17}H_{20}NO_4$ $(M+H)^+$ (302.1387) found (302.1389); $C_{17}H_{19}NO_4Na$ $(M+Na)^+$ (324.1206) found (324.1209). m.p. 94.0-94.6 °C
 **3ma^2**	**methyl 5-bromo-4-(2-methoxy-2-oxoethyl)quinoline-2-carboxylate** Yield: 67.6 mg, 0.2 mmol, 50%. White solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 6.7 Hz, 1H), 8.05 (s, 1H), 7.97 (d, *J* = 6.7 Hz, 1H), 7.57 (t, *J* = 6.7 Hz, 1H), 4.62 (s, 2H), 4.08 (s, 3H), 3.74 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.78, 165.21, 149.87, 147.44, 142.49,

	135.95, 132.34, 129.88, 128.08, 126.24, 118.01, 53.32, 52.47, 42.33. **HRMS** (ESI) calc for $C_{14}H_{13}BrNO_4$ $(M+H)^+$ (338.0022) found (338.0021); $C_{14}H_{12}BrNO_4Na$ $(M+Na)^+$ (359.9842) found (359.9843). m.p. 130.7-131.3 ^oC
 **3na²**	**methyl 5-fluoro-4-(2-methoxy-2-oxoethyl)quinoline-2-carboxylate** Yield: 64.3 mg, 0.232 mmol, 58%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.5 Hz, 1H), 8.04 (s, 1H), 7.71 (dd, *J* = 8.2, 5.7 Hz, 1H), 7.33 (dd, *J* = 7.8, 12.4 Hz, 1H), 4.26 (d, *J* = 5.0 Hz, 2H), 4.09 (s, 3H), 3.73 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.45, 165.42, 158.46 (d, $J_{C\text{-}F}$ = 255.1 Hz), 149.32 (d, $J_{C\text{-}F}$ = 2.3 Hz), 148.32 (d, $J_{C\text{-}F}$ = 1.8 Hz), 140.28, 129.60 (d, $J_{C\text{-}F}$ = 9.9 Hz), 127.70 (d, $J_{C\text{-}F}$ = 4.1 Hz), 124.14 (d, $J_{C\text{-}F}$ = 1.3 Hz), 119.68 (d, $J_{C\text{-}F}$ = 12.0 Hz), 113.72 (d, $J_{C\text{-}F}$ = 22.6 Hz), 53.36, 52.34, 41.15 (d, $J_{C\text{-}F}$ = 9.8 Hz). **HRMS** (ESI) calc for $C_{14}H_{13}FNO_4$ $(M+H)^+$ (278.0823) found (278.0824); $C_{14}H_{12}FNO_4Na$ $(M+Na)^+$ (300.0643) found (300.0645). m.p. 124.6-125.3 ^oC
 **3oa²**	**methyl 4-(2-methoxy-2-oxoethyl)-5-nitroquinoline-2-carboxylate** Yield: 62.1 mg, 0.204 mmol, 51%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 8.4, 1.3 Hz, 1H), 8.22 (s, 1H), 7.96 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.82 (dd, *J* = 8.4, 7.6 Hz, 1H), 4.10 (s, 3H), 4.04 (s, 2H), 3.73 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.69, 164.85, 148.68, 148.53, 147.64, 139.92, 136.43, 128.27, 126.81, 125.44, 120.92, 53.54, 52.70, 39.48. **HRMS** (ESI) calc for $C_{14}H_{13}N_2O_6$ $(M+H)^+$ (305.0768) found (305.0764), $C_{14}H_{12}N_2O_6Na$ $(M+Na)^+$ (327.0588) found (327.0587). m.p. 140.1-140.8 ^oC
 **3pa**	**methyl 4-(2-methoxy-2-oxoethyl)-5, 7-dimethylquinoline-2- carboxylate** Yield: 96.5 mg, 0.336 mmol, 84%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.94 (s, 1H), 7.28 (s, 1H), 4.32 (s, 2H), 4.06 (s, 3H), 3.72 (s, 3H), 2.81 (s, 3H), 2.49 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.99, 165.89, 150.10, 146.57, 141.76, 139.61, 134.88, 133.71, 129.63, 127.02, 124.17, 53.09, 52.49, 42.06, 24.48, 21.18. **HRMS** (ESI) calc for $C_{16}H_{18}NO_4$ $(M+H)^+$ (288.1230) found (288.1231); $C_{16}H_{17}NO_4Na$ $(M+Na)^+$ (310.1050) found (310.1050). m.p. 82.5-83.6 ^oC
 **3qa**	**methyl 6, 8-dichloro-4-(2-methoxy-2-oxoethyl) quinoline-2-carboxylate** Yield: 82.7 mg, 0.252 mmol, 63%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.94 (d, *J* = 2.1 Hz, 1H), 7.91 (d, *J* = 2.1 Hz, 1H), 4.11 (s, 2H), 4.08 (s, 3H), 3.74 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.49, 165.31, 148.08, 142.89, 141.49, 136.85, 134.62, 131.13, 130.19, 124.24, 121.81, 53.42, 52.78, 38.36. **HRMS** (ESI) calc for $C_{14}H_{12}Cl_2NO_4$ $(M+H)^+$ (328.0138) found (328.0137), $C_{14}H_{11}Cl_2NO_4Na$ $(M+Na)^+$ (349.9957) found (349.9959). m.p. 104.9-105.6 ^oC

 **3ra**	**methyl 1-(2-methoxy-2-oxoethyl)benzo[f]quinoline-3-carboxylate** Yield: 95.3 mg, 0.308 mmol, 77%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.58 – 8.49 (m, 1H), 8.22 (s, 1H), 8.12 (d, *J* = 9.0 Hz, 1H), 7.99 (d, *J* = 9.0 Hz, 1H), 7.98 – 7.91 (m, 1H), 7.74 – 7.65 (m, 2H), 4.49 (s, 2H), 4.09 (s, 3H), 3.75 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.47, 165.72, 149.70, 145.85, 141.41, 133.63, 132.09, 129.30 (2C), 129.09, 127.96, 127.63, 127.09, 126.99, 126.03, 53.16, 52.66, 43.34. **HRMS** (ESI) calc for $C_{18}H_{16}NO_4$ $(M+H)^+$ (310.1074) found (310.1073); $C_{18}H_{15}NO_4Na$ $(M+Na)^+$ (332.0893) found (332.0892). m.p. 91.5-92.4 ^oC
 **3sa**	**methyl 7-(2-methoxy-2-oxoethyl)thieno[3,2-b]pyridine-5-carboxylate** Yield: 71.1 mg, 0.268 mmol, 67%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.83 (d, *J* = 5.6 Hz, 1H), 7.73 (d, *J* = 5.6 Hz, 1H), 4.04 (s, 3H), 3.96 (s, 2H), 3.72 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.12, 165.95, 156.41, 146.06, 138.23, 136.94, 131.72, 126.20, 120.43, 53.06, 52.56, 39.75. **HRMS** (ESI) calc for $C_{12}H_{12}NO_4S$ $(M+H)^+$ (266.0482) found (266.0481); $C_{12}H_{11}NO_4SNa$ $(M+Na)^+$ (288.0301) found (288.0303). m.p. 117.6-118.3 ^oC
 **3ta**	**methyl 4-(2-methoxy-2-oxoethyl)-1,7-phenanthroline-2-carboxylate** Yield: 67.0 mg, 0.216 mmol, 54%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.05 (d, *J* = 4.4 Hz, 1H), 9.04 (d, *J* = 8.6 Hz, 1H), 8.44 (d, *J* = 9.3 Hz, 1H), 8.37 (d, *J* = 9.3 Hz, 1H), 8.31 (s, 1H), 7.68 (dd, *J* = 8.6, 4.4 Hz, 1H), 4.48 (s, 2H), 4.11 (s, 3H), 3.77 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.99, 165.38, 149.38, 149.18, 148.53, 147.09, 141.98, 135.62, 135.61, 134.14, 132.33, 126.69, 124.87, 121.33, 53.37, 52.92, 43.04. **HRMS** (ESI) calc for $C_{17}H_{15}N_2O_4$ $(M+H)^+$ (311.1026) found (311.1027); $C_{17}H_{14}N_2O_4Na$ $(M+Na)^+$ (333.0846) found (333.0849). m.p. 147.9-148.5 ^oC
 **3ab**	**ethyl 4-(2-ethoxy-2-oxoethyl)benzo[h]quinoline-2-carboxylate** Yield: 110.67 mg, 0.328 mmol, 82%. White solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.46 (d, *J* = 8.1 Hz, 1H), 8.23 (s, 1H), 7.96 – 7.89 (m, 3H), 7.79 (t, *J* = 7.3 Hz, 1H), 7.74 (t, *J* = 7.3 Hz, 1H), 4.57 (q, *J* = 7.1 Hz, 2H), 4.21 – 4.15 (m, 2H), 4.16 (s, 2H), 1.53 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.84, 165.59, 146.45, 146.28, 141.02, 133.35, 131.94, 130.42, 130.32, 128.79, 127.68, 127.14, 125.46, 123.70, 120.52, 61.97, 61.48, 38.92, 14.38, 14.09. **HRMS** (ESI) calc for $C_{20}H_{20}NO_4$ $(M+H)^+$ (338.1387) found (338.1388); $C_{20}H_{19}NO_4Na$ $(M+Na)^+$ (360.1206) found (360.1211). m.p. 131.0-131.6 ^oC

 **3ac**	**phenyl 4-(2-oxo-2-phenoxyethyl)benzo[h]quinoline-2-carboxylate** Yield: 145.6 mg, 0.336 mmol, 84%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.53 (d, *J*= 7.3 Hz, 1H), 8.48 (s, 1H), 8.04 (s, 2H), 7.97 (d, *J*= 7.5 Hz, 1H), 7.82 (t, *J*= 7.6 Hz, 1H), 7.78 (t, *J*= 7.6 Hz, 1H), 7.50 (t, *J*= 7.9 Hz, 2H), 7.38 (d, *J*= 7.6 Hz, 2H), 7.36 – 7.30 (m, 3H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.04 (d, *J*= 7.6 Hz, 2H), 4.46 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.37, 164.19, 151.18, 150.38, 146.68, 145.49, 140.53, 133.39, 131.91, 131.09, 129.57, 129.47, 129.06, 127.99, 127.82, 127.39, 126.17, 126.11, 125.47, 124.24, 121.73, 121.22, 120.26, 38.97. **HRMS** (ESI) calc for $C_{28}H_{20}NO_4$ $(M+H)^+$ (434.1387) found (434.1388). $C_{28}H_{19}NO_4Na$ $(M+Na)^+$ (456.1206) found (456.1208). m.p. 93.8-94.7 ^{o}C
 **3ad**	**1-(2-acetylbenzo[h]quinolin-4-yl)propan-2-one** Yield: 98.7 mg, 0.356 mmol, 89%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.40 (d, *J* = 8.0 Hz, 1H), 8.13 (s, 1H), 7.94 (d, *J* = 8.8 Hz, 2H), 7.83 – 7.72 (m, 3H), 4.25 (s, 2H), 3.00 (s, 3H), 2.24 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 204.12, 200.73, 151.19, 145.83, 141.14, 133.38, 131.94, 130.50, 128.75, 127.89, 127.71, 127.58, 124.87, 120.76, 120.58, 48.53, 29.59, 25.70. **HRMS** (ESI) calc for $C_{18}H_{16}NO_2$ $(M+H)^+$ (278.1176) found (278.1179); $C_{18}H_{15}NO_2Na$ $(M+Na)^+$ (300.0995) found (300.0993). m.p. 109.4-110.4 ^{o}C
 **3ae**	**1-(2-pentanoylbenzo[h]quinolin-4-yl)hexan-2-one** Yield: 127.2 mg, 0.352 mmol, 88%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.38 (d, *J* = 8.1 Hz, 1H), 8.10 (s, 1H), 7.92 (d, *J* = 7.0 Hz, 1H), 7.91 (d, *J* = 7.0 Hz, 1H), 7.86 – 7.66 (m, 3H), 4.23 (s, 2H), 3.53 (t, *J* = 7.5 Hz, 2H), 2.52 (t, *J* = 7.4 Hz, 2H), 1.92 – 1.78 (m, 2H), 1.64 – 1.44 (m, 4H), 1.32 – 1.13 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H), 0.86 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.51, 202.93, 151.01, 145.71, 141.34, 133.37, 131.99, 130.23, 128.64, 127.85, 127.63, 127.59, 124.85, 120.92, 120.77, 47.70, 42.06, 37.39, 26.62, 25.74, 22.67, 22.15, 14.05, 13.77. **HRMS** (ESI) calc for $C_{24}H_{28}NO_2$ $(M+H)^+$ (362.2115) found (362.2110); $C_{24}H_{27}NO_2Na$ $(M+Na)^+$ (384.1934) found (384.1929). m.p. 89.1-89.6 ^{o}C
 **3af**	**2-tosyl-4-(tosylmethyl)benzo[h]quinoline** Yield: 184.6 mg, 0.368 mmol, 92%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.15 – 9.04 (m, 1H), 8.01 (d, *J* = 8.3 Hz, 2H), 7.85 – 7.83 (m, 3H), 7.74 – 7.71 (m, 3H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 4.87 (s, 2H), 2.46 (s, 3H), 2.42 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.08, 146.93, 145.82, 144.91, 136.71, 135.92, 134.07, 133.49, 131.29, 130.95, 130.00, 129.69, 129.58, 129.18, 128.61, 128.01, 127.79, 126.99, 125.24, 121.04, 120.47, 59.43, 21.70, 21.66. **HRMS** (ESI) calc for $C_{28}H_{24}NO_4S_2$ $(M+H)^+$ (502.1141) found

	(502.1141); $C_{28}H_{23}NO_4S_2Na$ $(M+Na)^+$ (524.0961) found (524.0962). m.p. 146.8-147.5 °C
 **3ag**	**2-(phenylsulfonyl)-4-((phenylsulfonyl)methyl)benzo[h]quinoline** Yield: 172.3 mg, 0.364 mmol, 91%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.18 – 9.04 (m, 1H), 8.14 (d, *J* = 7.1 Hz, 2H), 7.99 – 7.86 (m, 3H), 7.84 – 7.71 (m, 3H), 7.67 (t, *J* = 7.4 Hz, 2H), 7.63 (d, *J* = 7.4 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 2H), 7.45 (t, *J* = 7.9 Hz, 2H), 4.91 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.82, 146.98, 138.83, 136.98, 136.55, 134.54, 133.85, 133.49, 131.51, 130.92, 129.68, 129.41, 129.19, 129.06, 128.59, 128.11, 127.85, 127.04, 125.24, 121.16, 120.34, 59.36. **HRMS** (ESI) calc for $C_{26}H_{20}NO_4S_2$ $(M+H)^+$ (474.0828) found (474.0823); $C_{26}H_{19}NO_4S_2Na$ $(M+Na)^+$ (496.0648) found (496.0645). m.p. 132.1-132.7 °C
 **3ah**	**(((2-(benzoylsulfonyl)benzo[h]quinolin-4-yl)methyl)sulfonyl)(phenyl)methanone** Yield: 182.6 mg, 0.364 mmol, 91%. White solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.38 (dd, *J* = 6.6, 2.9 Hz, 1H), 8.03 (d, *J* = 9.1 Hz, 1H), 7.98 (dd, *J* = 7.2, 1.9 Hz, 1H), 7.90 (s, 1H), 7.90 – 7.77 (m, 3H), 7.49 – 7.39 (m, 3H), 7.36 (dd, *J* = 6.7, 2.9 Hz, 2H), 7.25 – 7.11 (m, 5H), 4.89 (s, 2H), 4.59 (s, 2H), 4.13 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.76, 146.97, 135.95, 133.71, 131.86, 131.13, 130.88, 130.77, 129.93, 129.58, 129.37, 128.77, 128.75, 128.32, 128.05, 127.85, 127.47, 126.88, 125.29, 122.06, 120.79, 59.37, 58.51, 54.17. **HRMS** (ESI) calc for $C_{28}H_{24}NO_4S_2$ $(M+H)^+$ (502.1141) found (502.1132); $C_{28}H_{23}NO_4S_2Na$ $(M+Na)^+$ (524.0961) found (524.0953). m.p. 122.0-122.5 °C
 **4ua**	**methyl-(3-methoxy-3-oxoprop-1-yn-1-yl)-4-methylquinoline-2-carboxy-late** Yield: 75.9 mg, 0.268 mmol, 67%. White solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.84 (dd, *J* = 8.4, 7.1 Hz, 1H), 7.72 (dd, *J* = 8.4, 7.1 Hz, 1H), 4.09 (s, 3H), 3.88 (s, 3H), 2.96 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 165.35, 154.15, 152.25, 150.03, 145.86, 131.60, 131.02, 129.08, 127.24, 124.21, 112.24, 89.74, 81.30, 53.24, 52.92, 17.02. **HRMS** (ESI) calc for $C_{16}H_{14}NO_4$ $(M+H)^+$ (284.0917) found (284.0921); $C_{16}H_{13}NO_4Na$ $(M+Na)^+$ (306.0737) found (306.0737). m.p. 130.8-131.8 °C

VII. References

[S1] G. M. Sheldrick, SADABS, *A Program for Empirical Absorption Correction*; University of Göttingen; Göttingen, Germany, **1998**.

[S2] G. M. Sheldrick, SHELXL-97, *Program for the Refinement of Crystal Structures*; University of Göttingen; Göttingen, Germany, **1997**.

[S3] P. V. Ramachandran, M. T. Rudd and M. Vankat Ram Reddy, *Tetrahedron Lett.* 2005, **46**, 2547.

[S4] B. D. Schwartz, P. Y. Hayes, W. Kitching and J. J. De Voss. *J. Org. Chem.* 2005, **70**, 3054.

[S5] L. Waykole and L. A. Paquette, *Org. Synth.* 1989, **67**, 149.

[S6] Z.-M. Chen and M. L. Trudell, *Synth. Commun.* 1994, **24**, 3149.

[S7] K. Steffen and H. Gerhard, *Chem. Ber.* 1987, **120**, 71.

[S8] S. P. Bew, G. D. Hiatt-Gipson, J. A. Lovell and C. Poullaine, *Org. Lett.* 2012, **14**, 456.

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

Figure S6. ^{1}H NMR spectrum of Compound **3aa** ($CDCl_3$, 500 MHz)

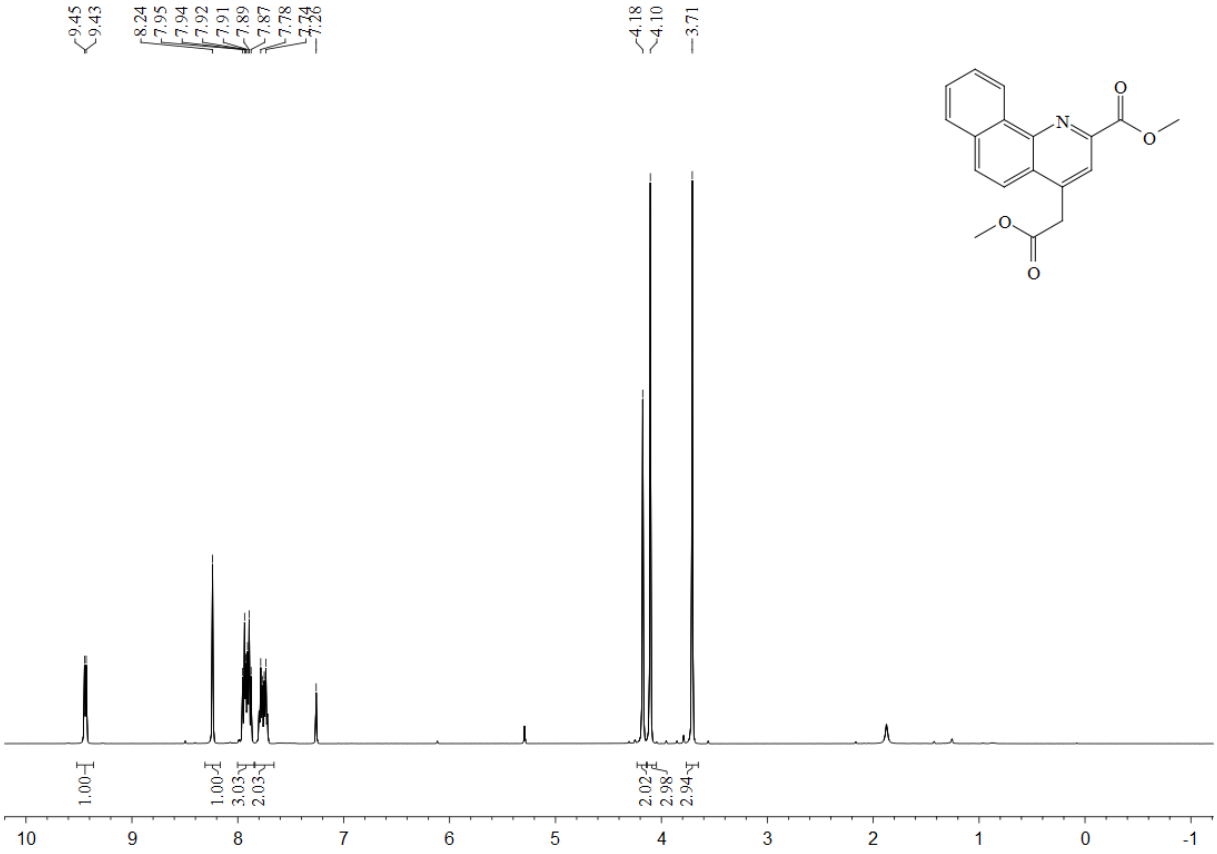


Figure S7. ^{13}C NMR spectrum of Compound **3aa** ($CDCl_3$, 125 MHz)

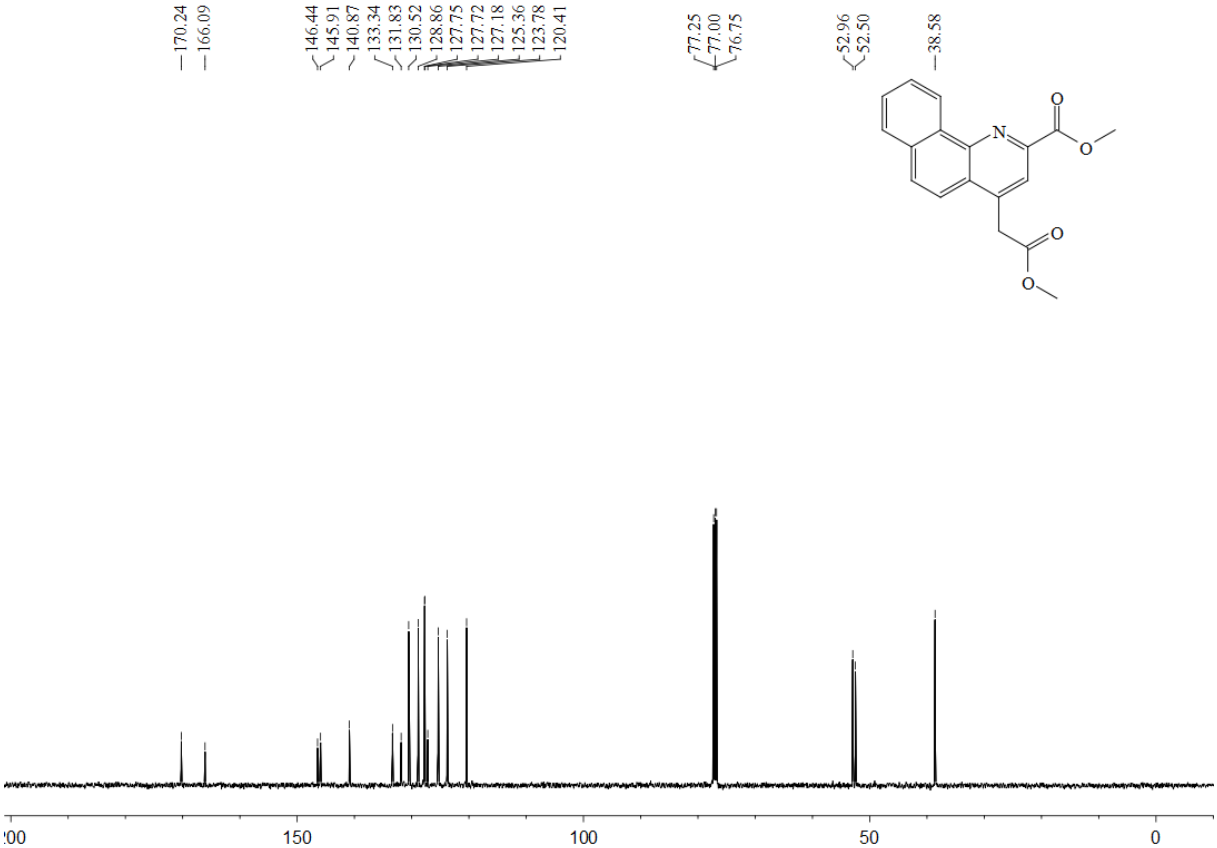


Figure S8. ^{1}H NMR spectrum of Compound **3ba** ($CDCl_3$, 500 MHz)

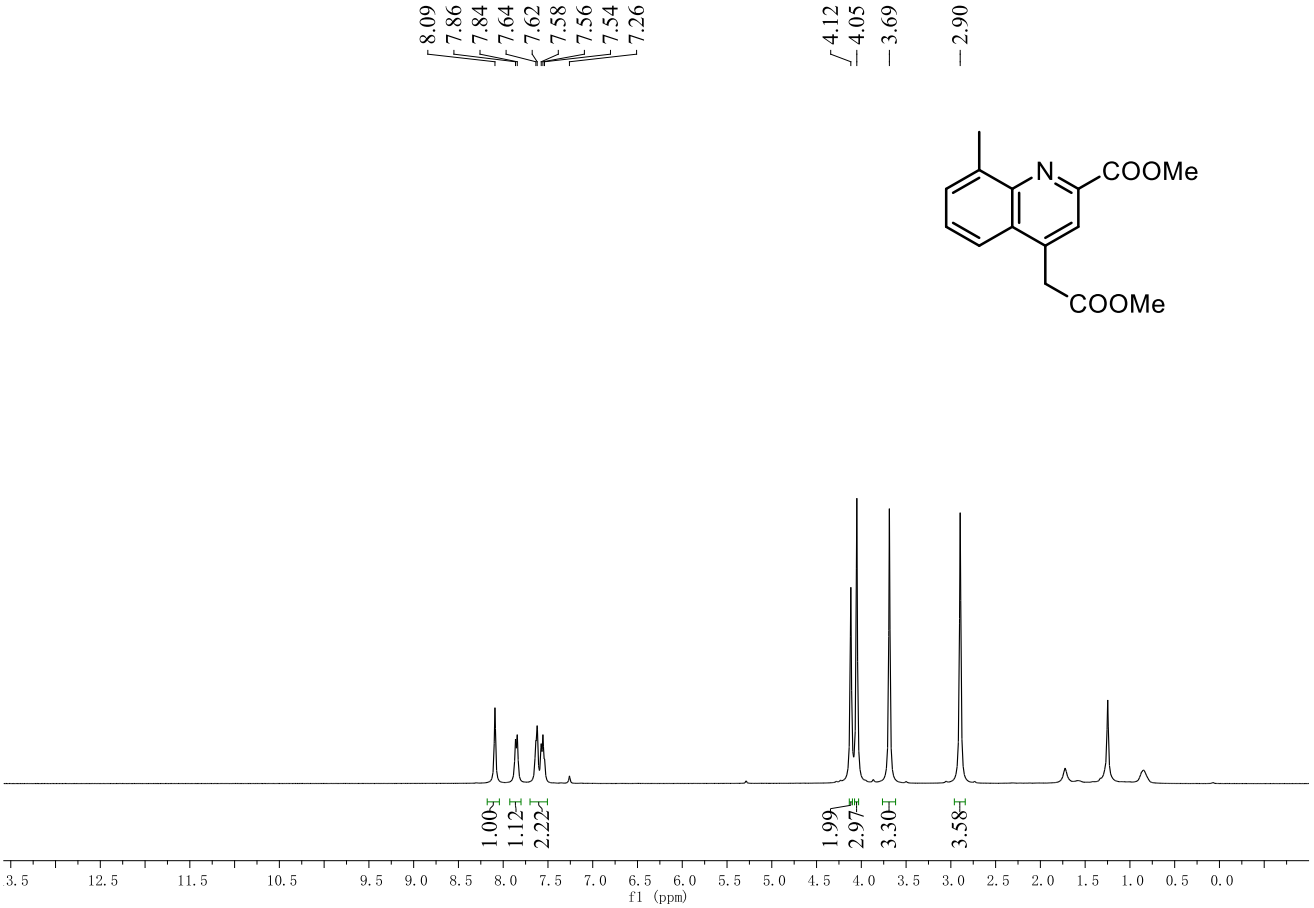


Figure S9. ^{13}C NMR spectrum of Compound **3ba** ($CDCl_3$, 125 MHz)

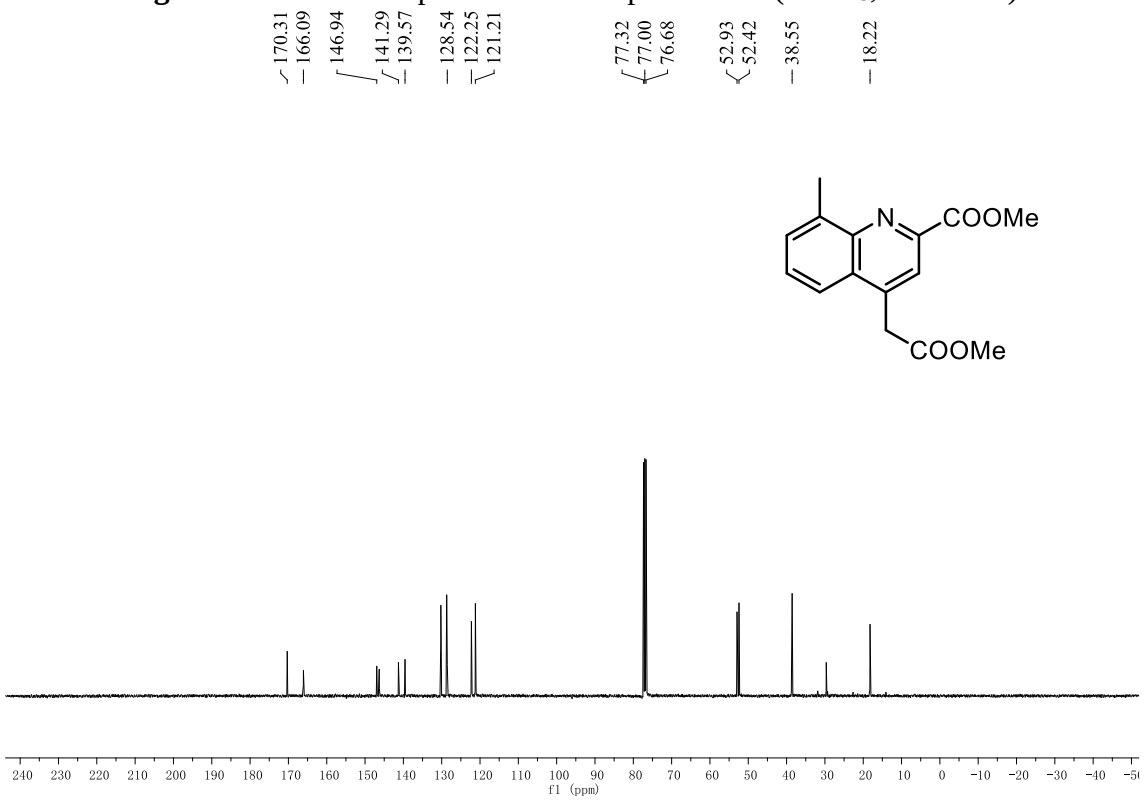


Figure S10. ^{1}H NMR spectrum of Compound **3ca** ($CDCl_3$, 400 MHz)

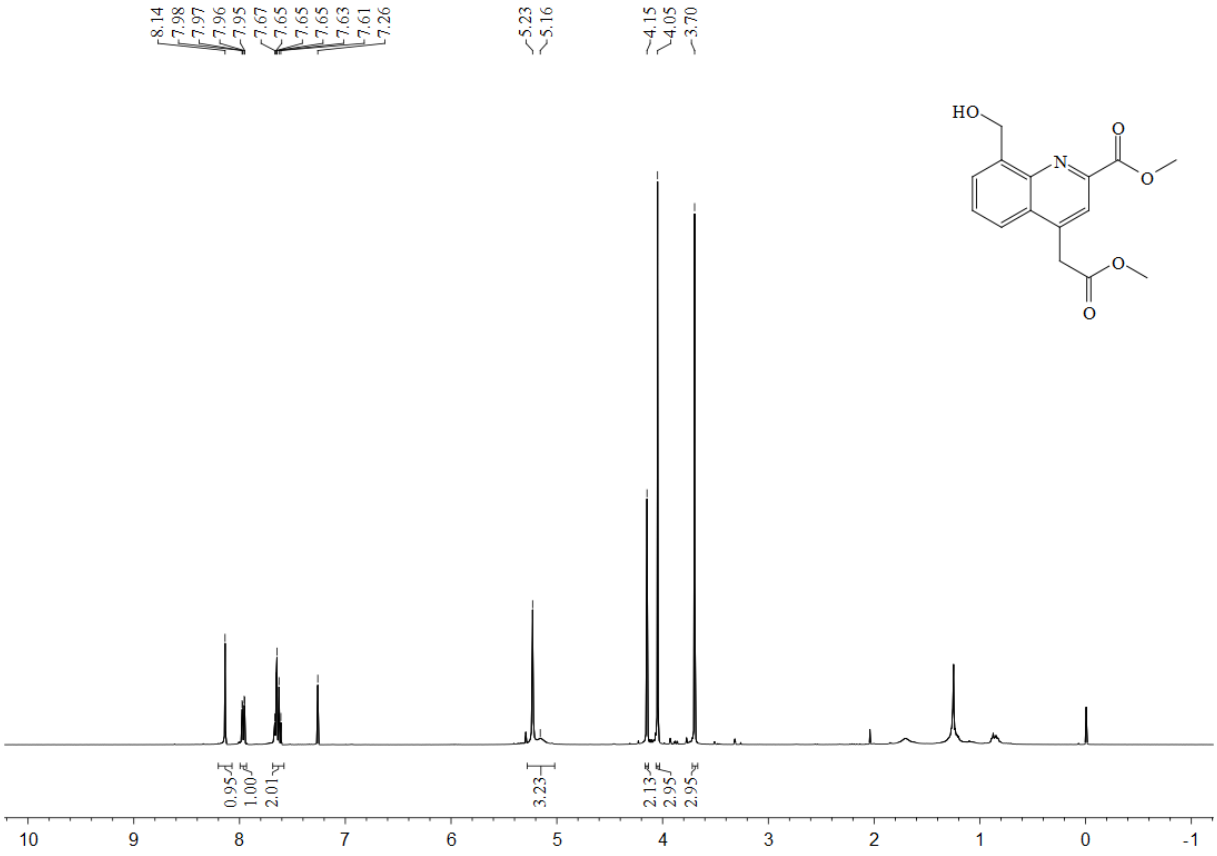


Figure S11. ^{13}C NMR spectrum of Compound **3ca** ($CDCl_3$, 125 MHz)

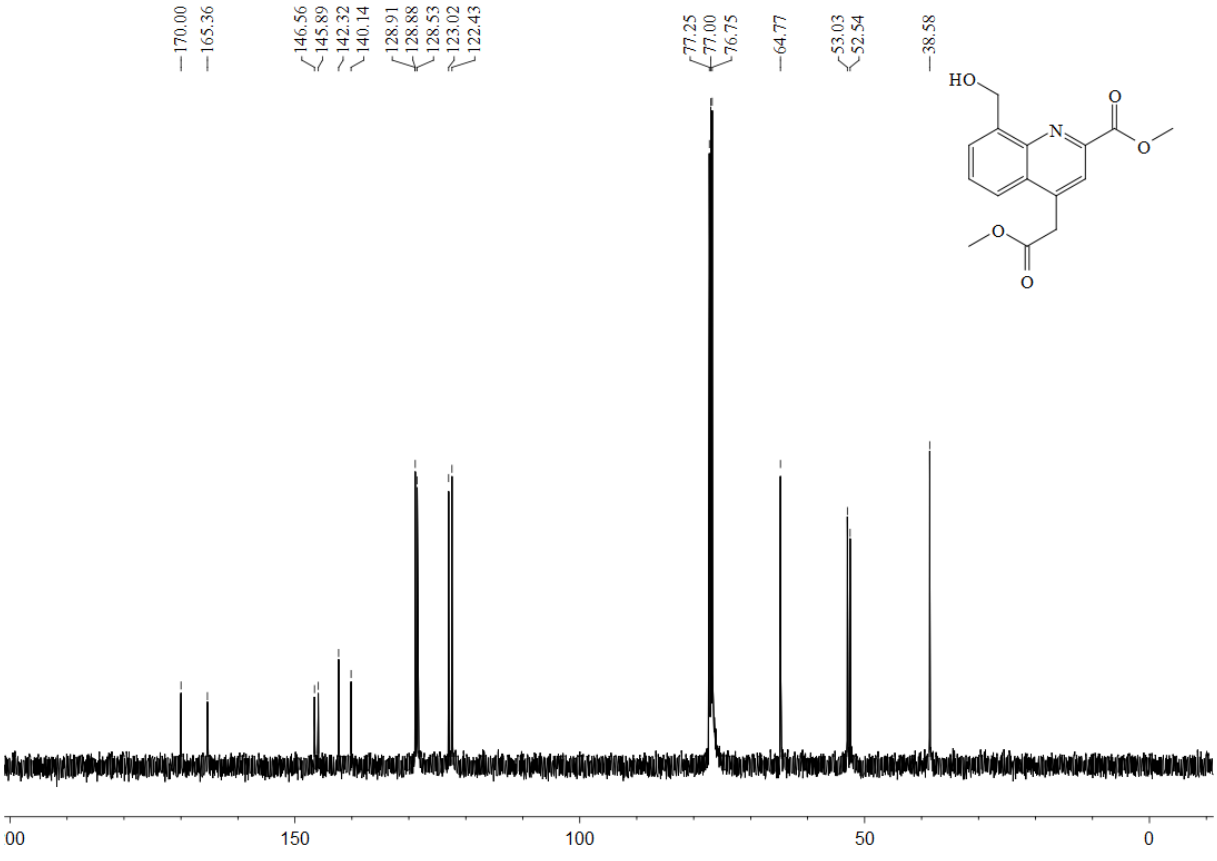


Figure S12. ^{1}H NMR spectrum of Compound **3da** ($CDCl_3$, 400 MHz)

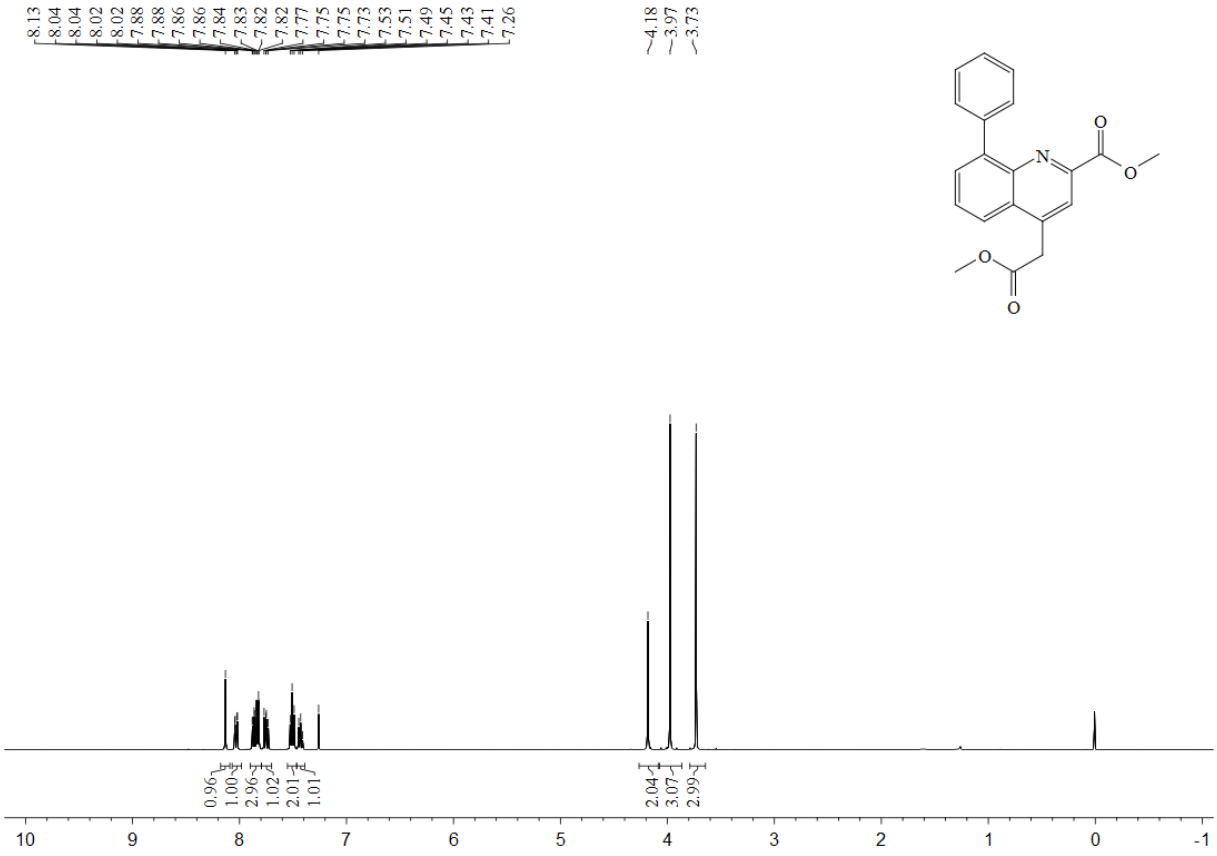


Figure S13. ^{13}C NMR spectrum of Compound **3da** ($CDCl_3$, 100 MHz)

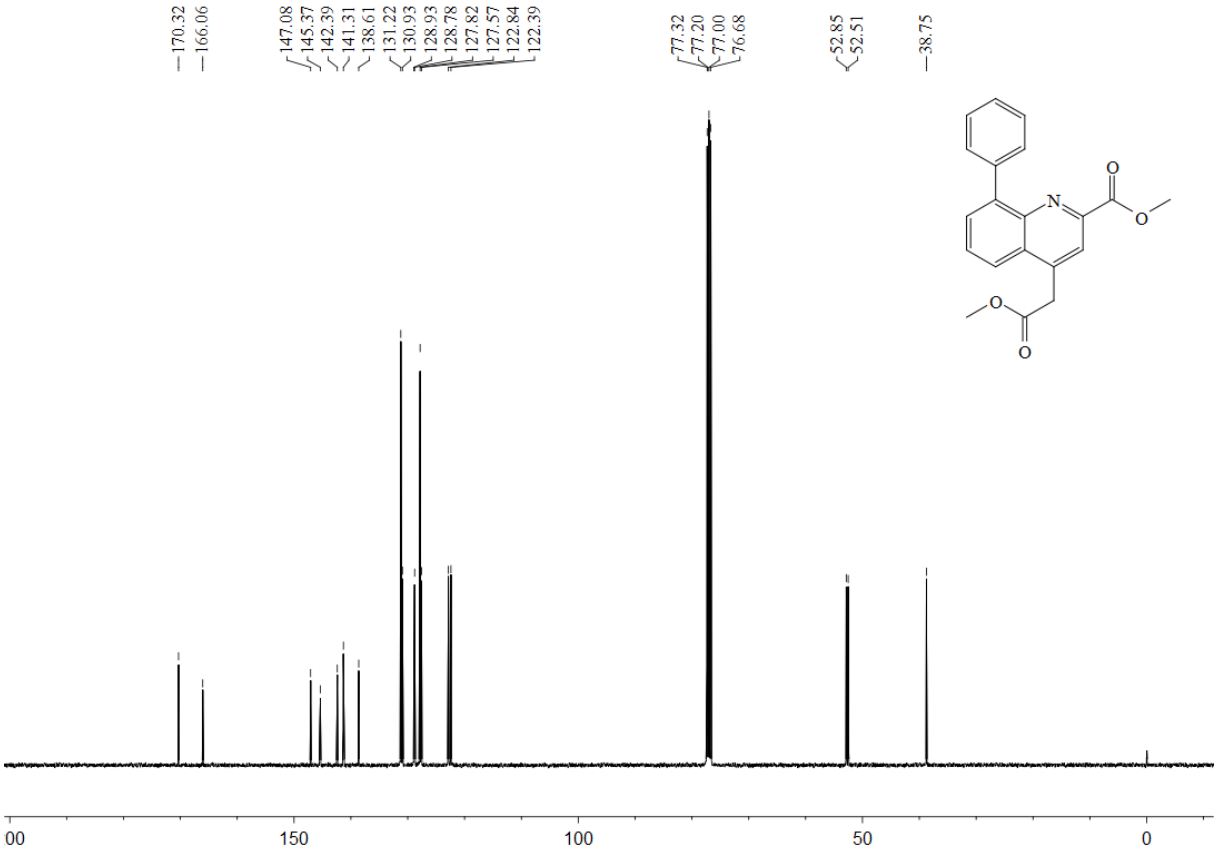


Figure S14. ^{1}H NMR spectrum of Compound **3ea** ($CDCl_3$, 400 MHz)

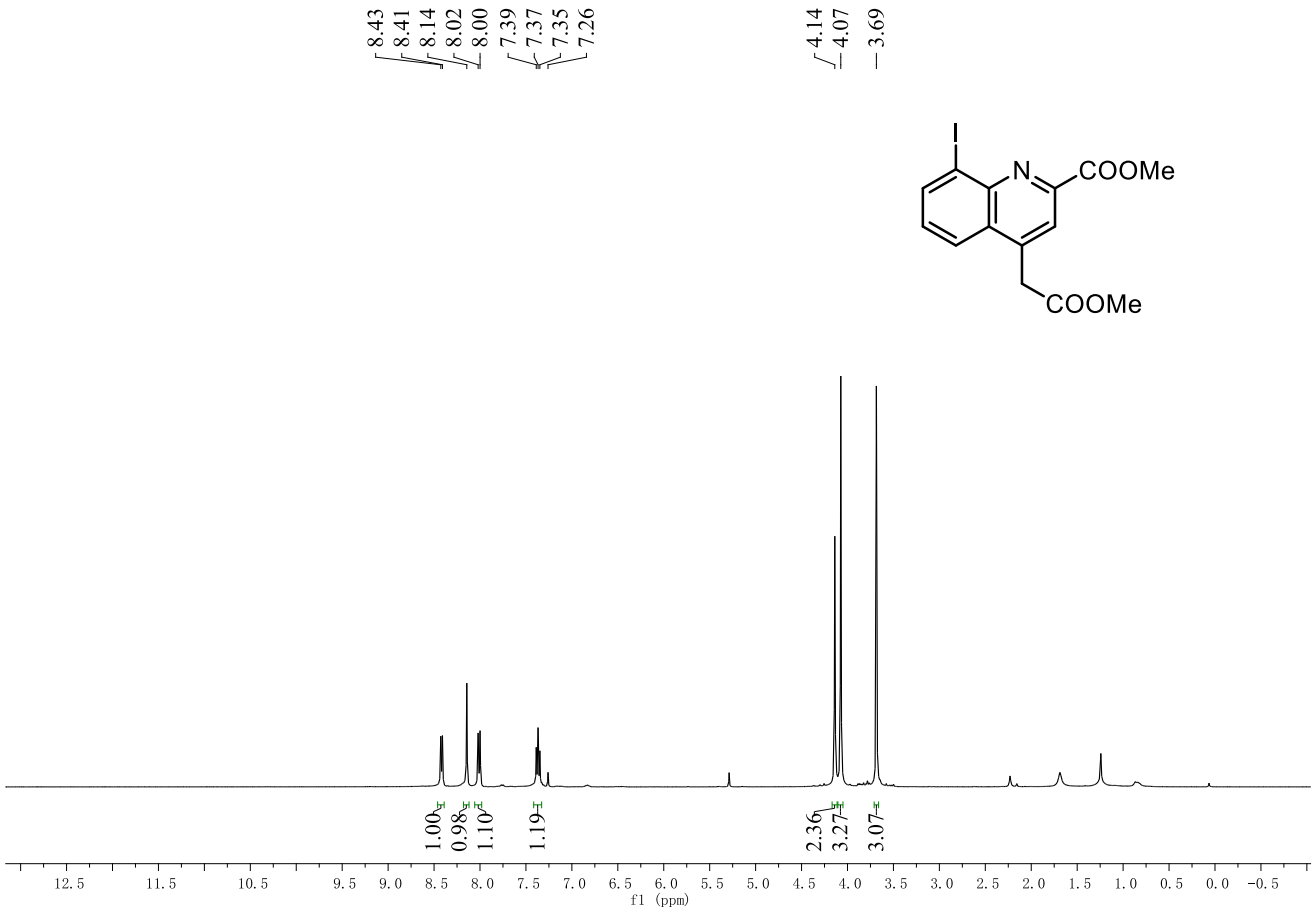


Figure S15. ^{13}C NMR spectrum of Compound **3ea** ($CDCl_3$, 100 MHz)

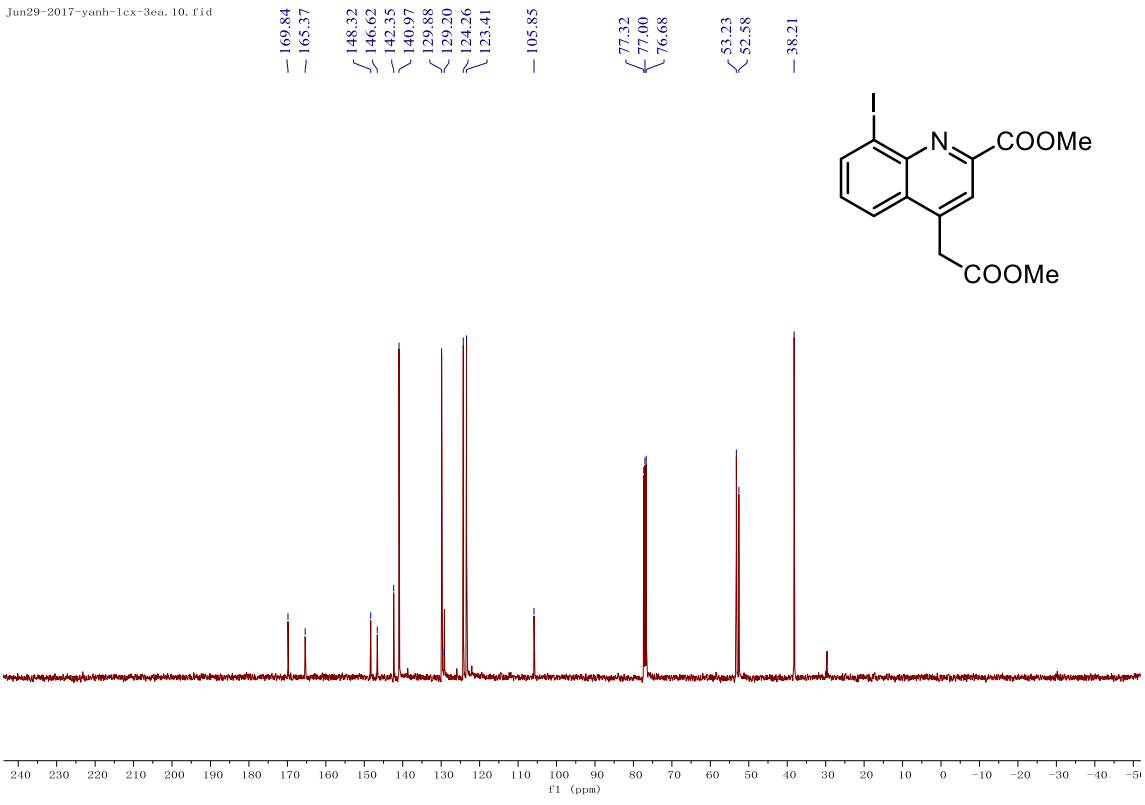


Figure S16. ^{1}H NMR spectrum of Compound **3fa** ($CDCl_3$, 500 MHz)

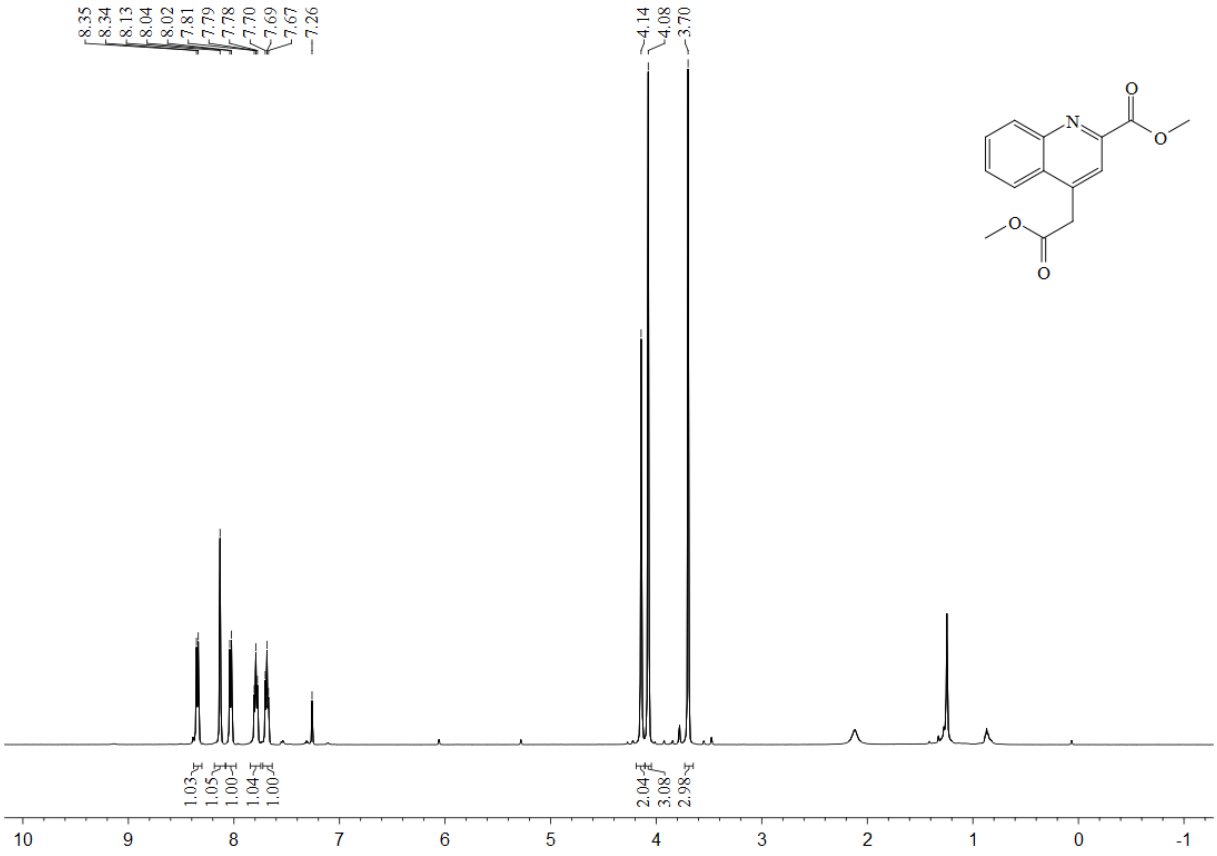


Figure S17. ^{13}C NMR spectrum of Compound **3fa** ($CDCl_3$, 125 MHz)

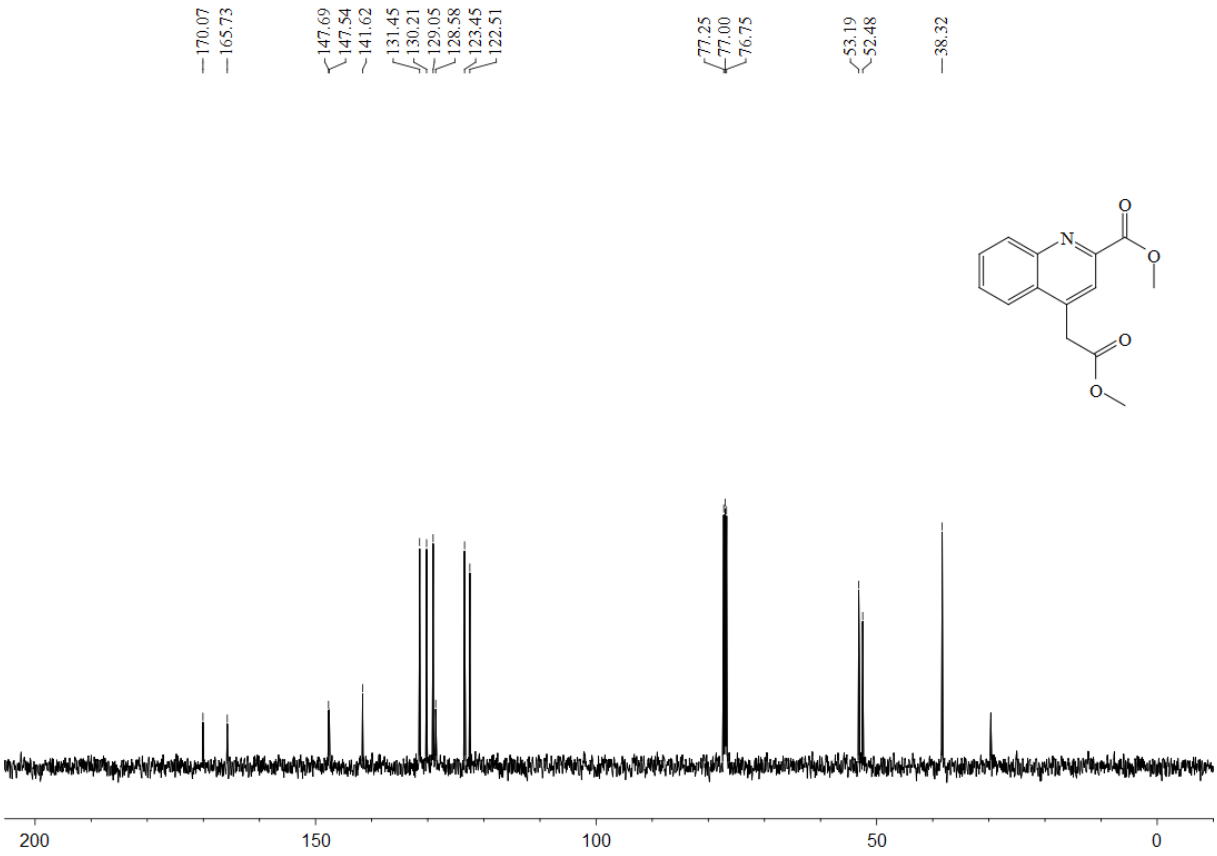


Figure S18. ^{1}H NMR spectrum of Compound **3ga** ($CDCl_3$, 400 MHz)

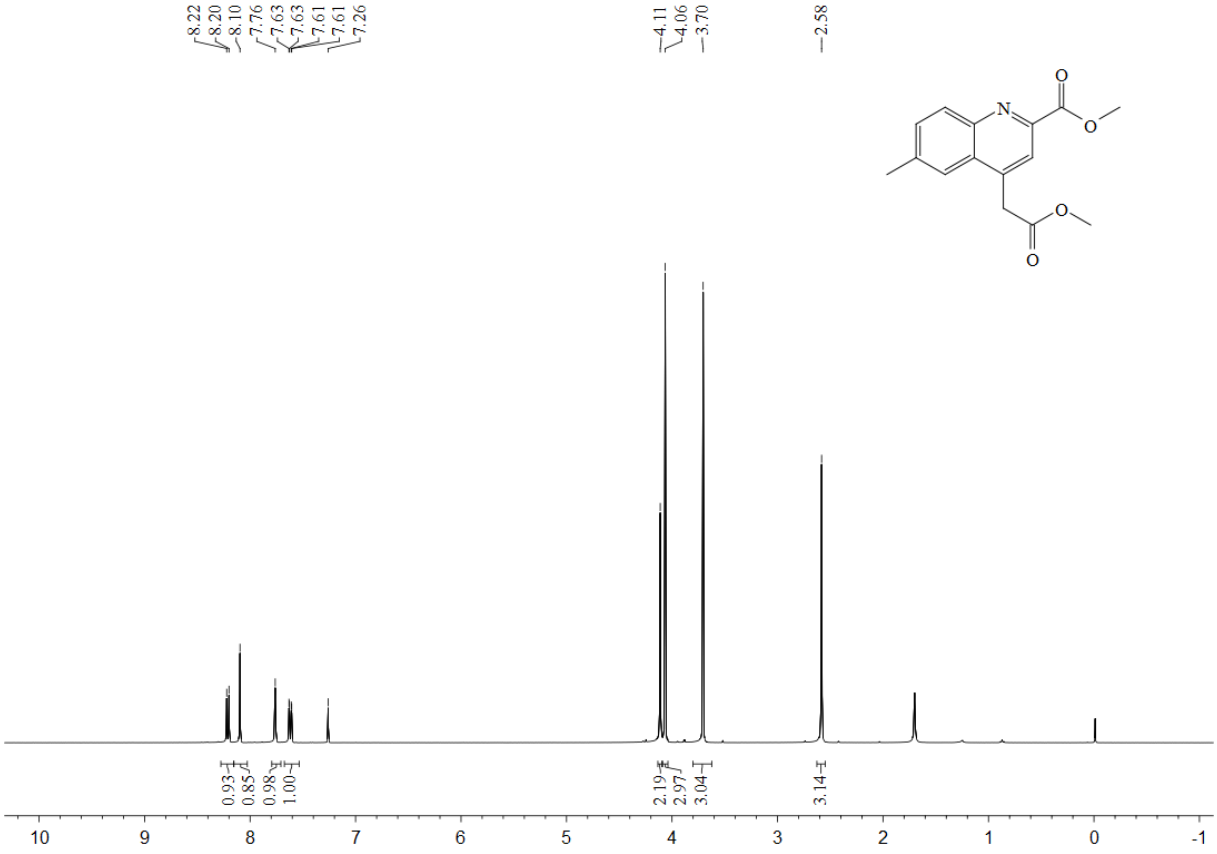


Figure S19. ^{13}C NMR spectrum of Compound **3ga** ($CDCl_3$, 125 MHz)

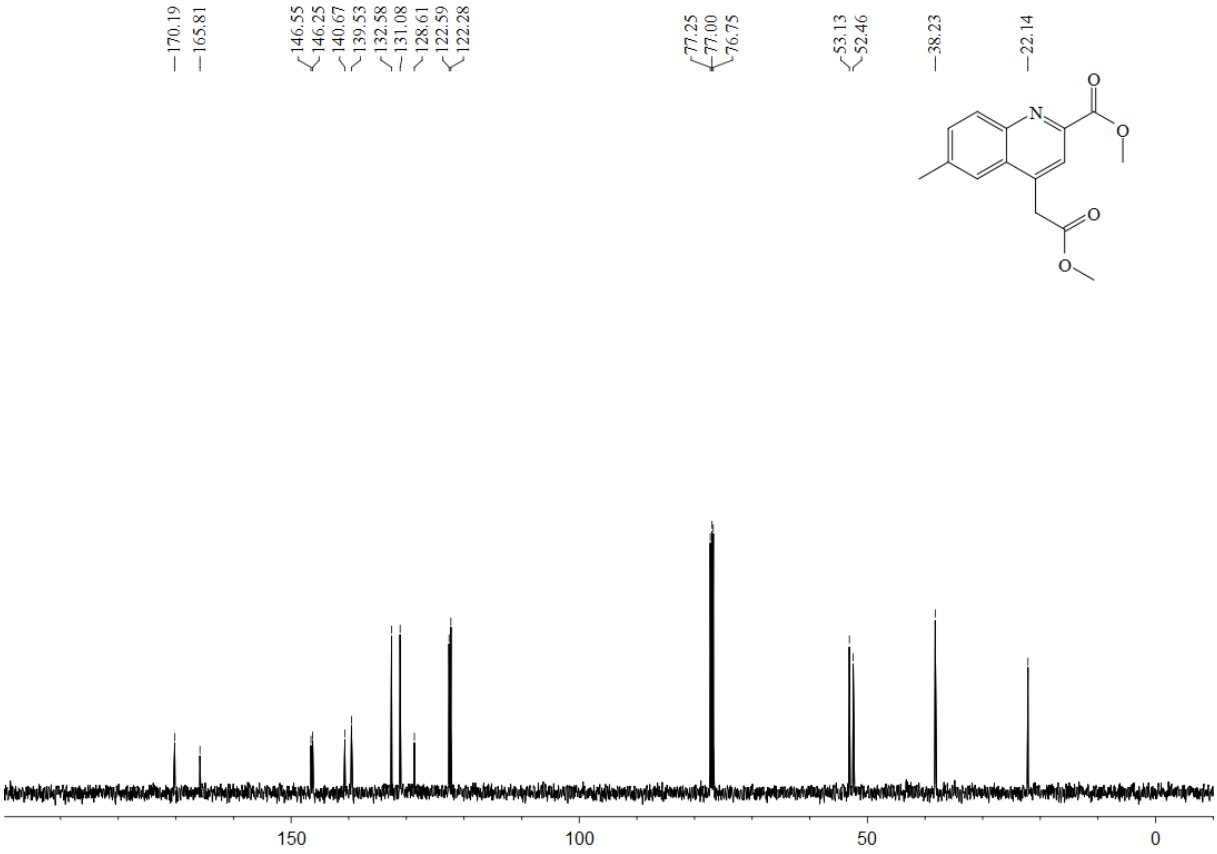


Figure S20. ^{1}H NMR spectrum of Compound **3ha** ($CDCl_3$, 400 MHz)

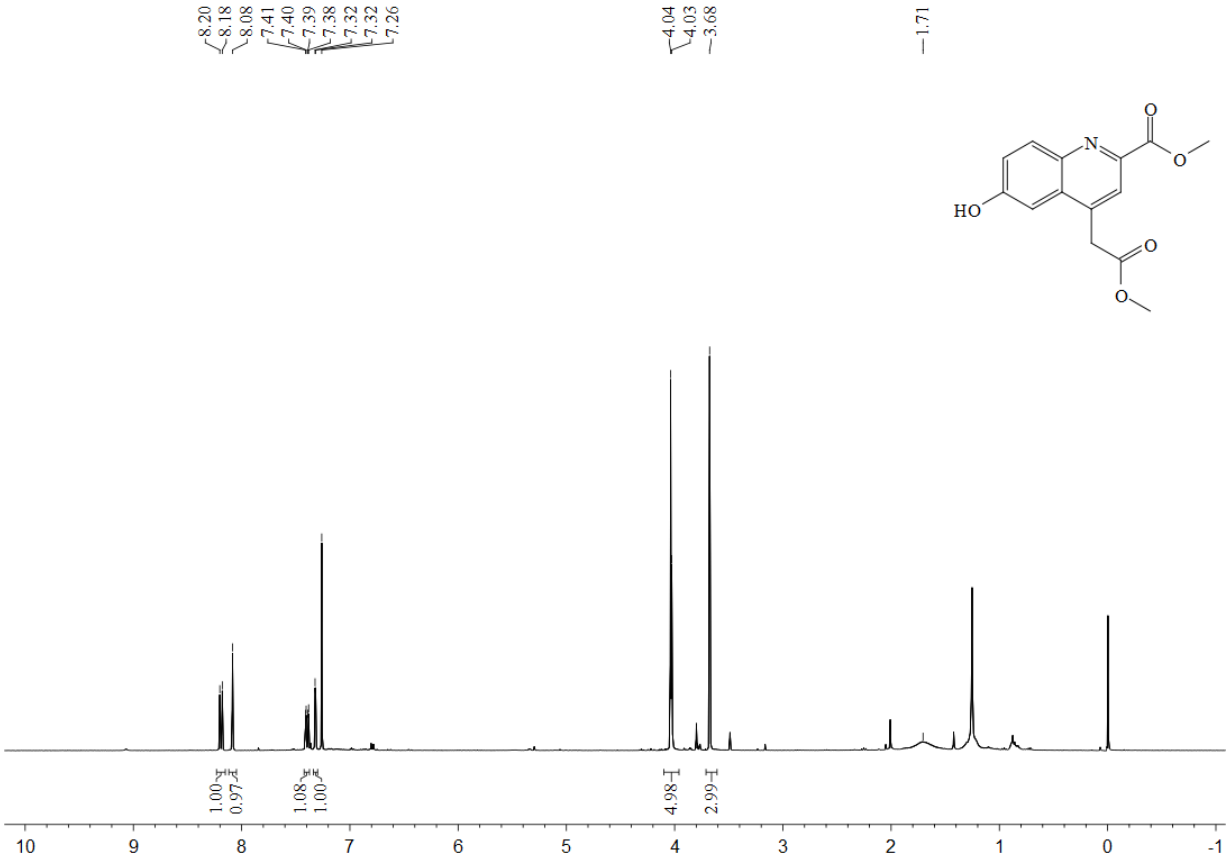


Figure S21. ^{13}C NMR spectrum of Compound **3ha** ($CDCl_3$, 100 MHz)

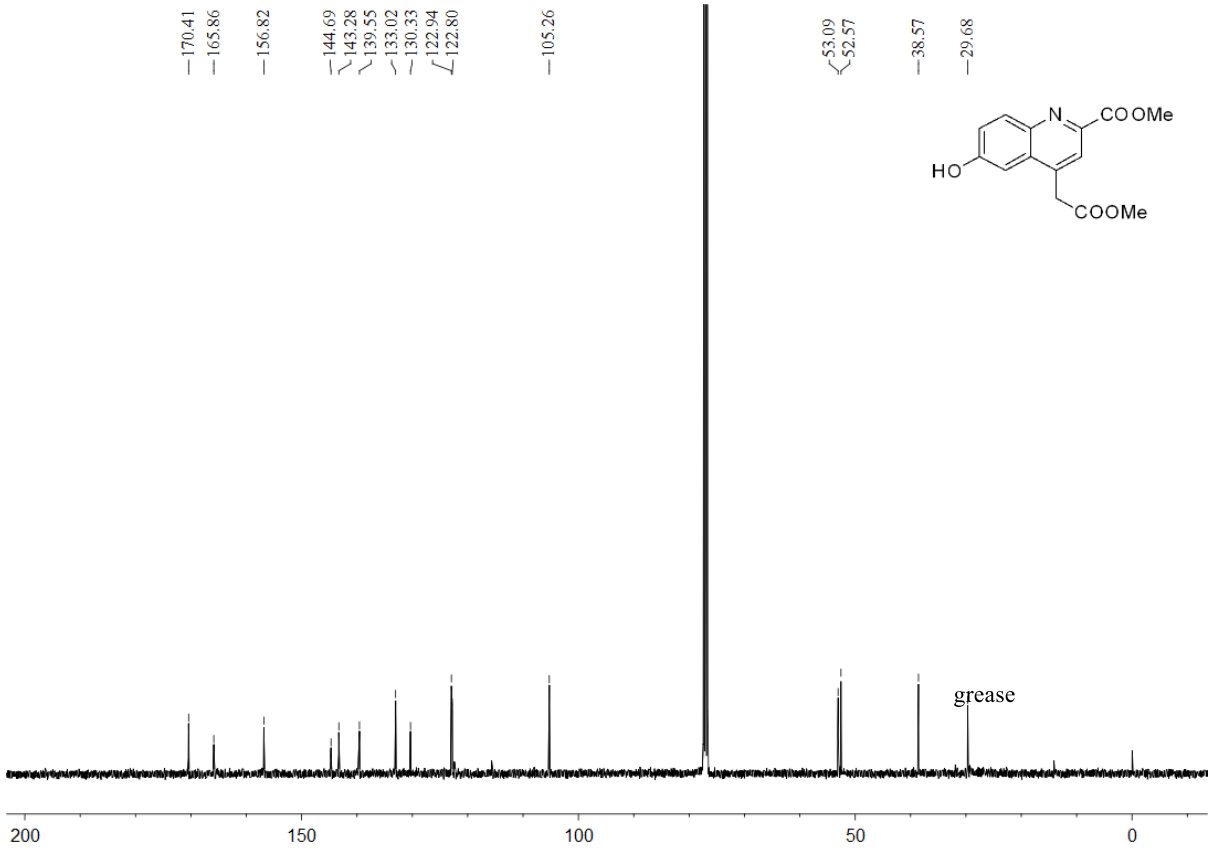


Figure S22. ^{1}H NMR spectrum of Compound **3ia** ($CDCl_3$, 500 MHz)

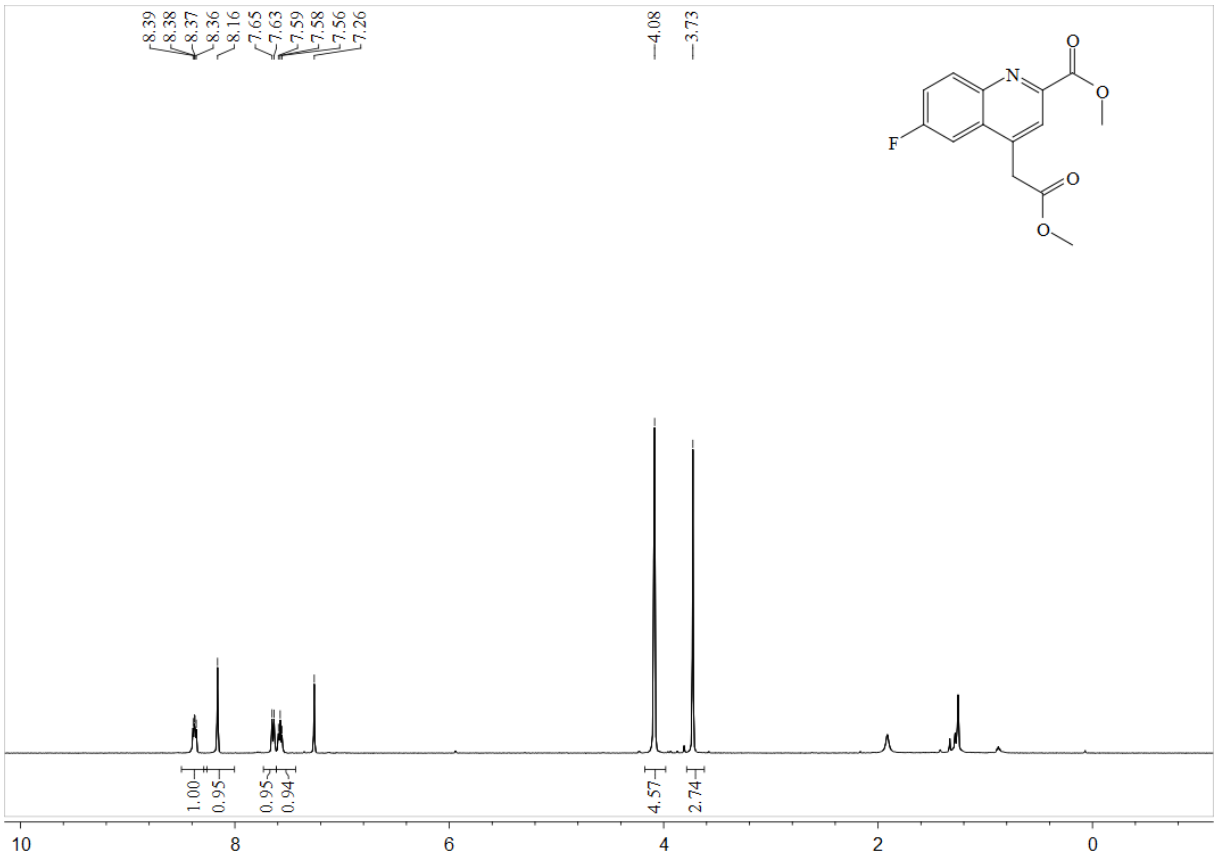


Figure S23. ^{13}C NMR spectrum of Compound **3ia** ($CDCl_3$, 125 MHz)

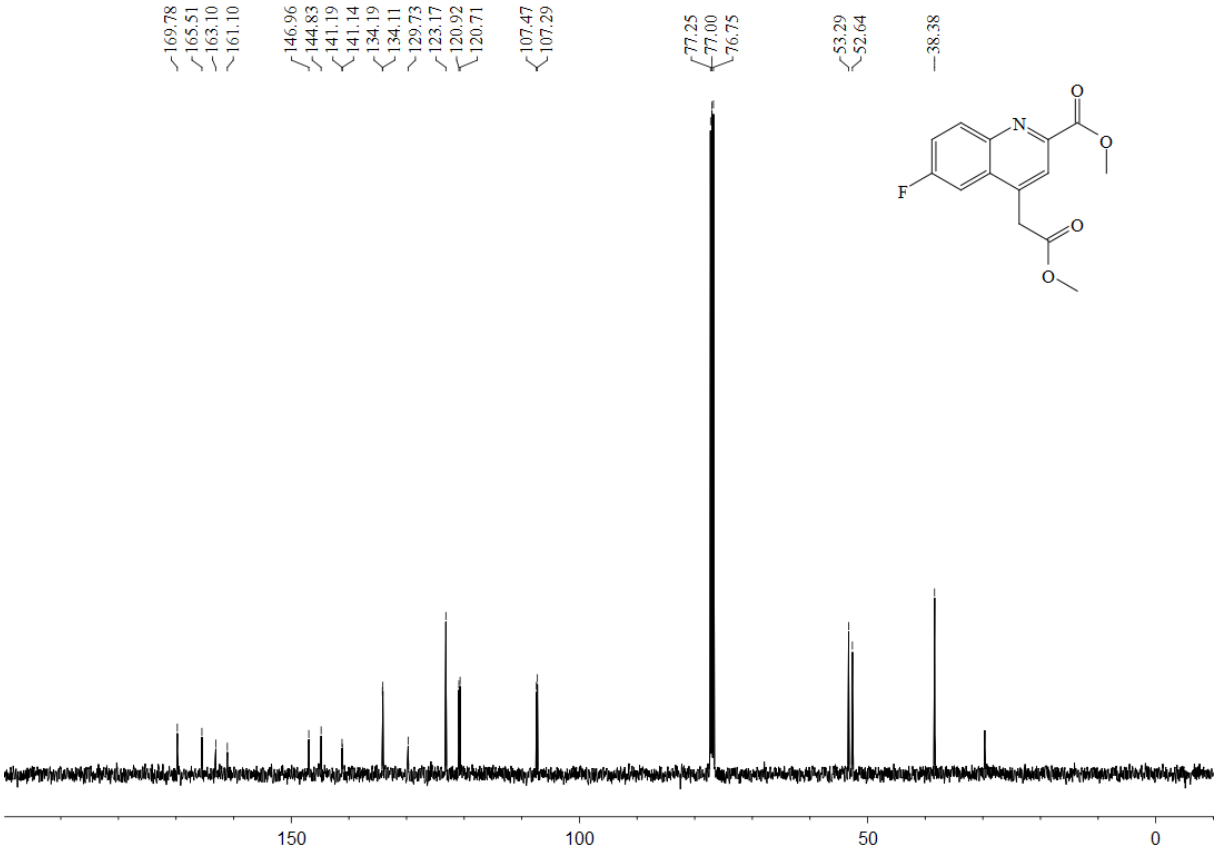


Figure S24. ^{1}H NMR spectrum of Compound **3ja**[6] and **3ja**[2] ($CDCl_3$, 500 MHz)

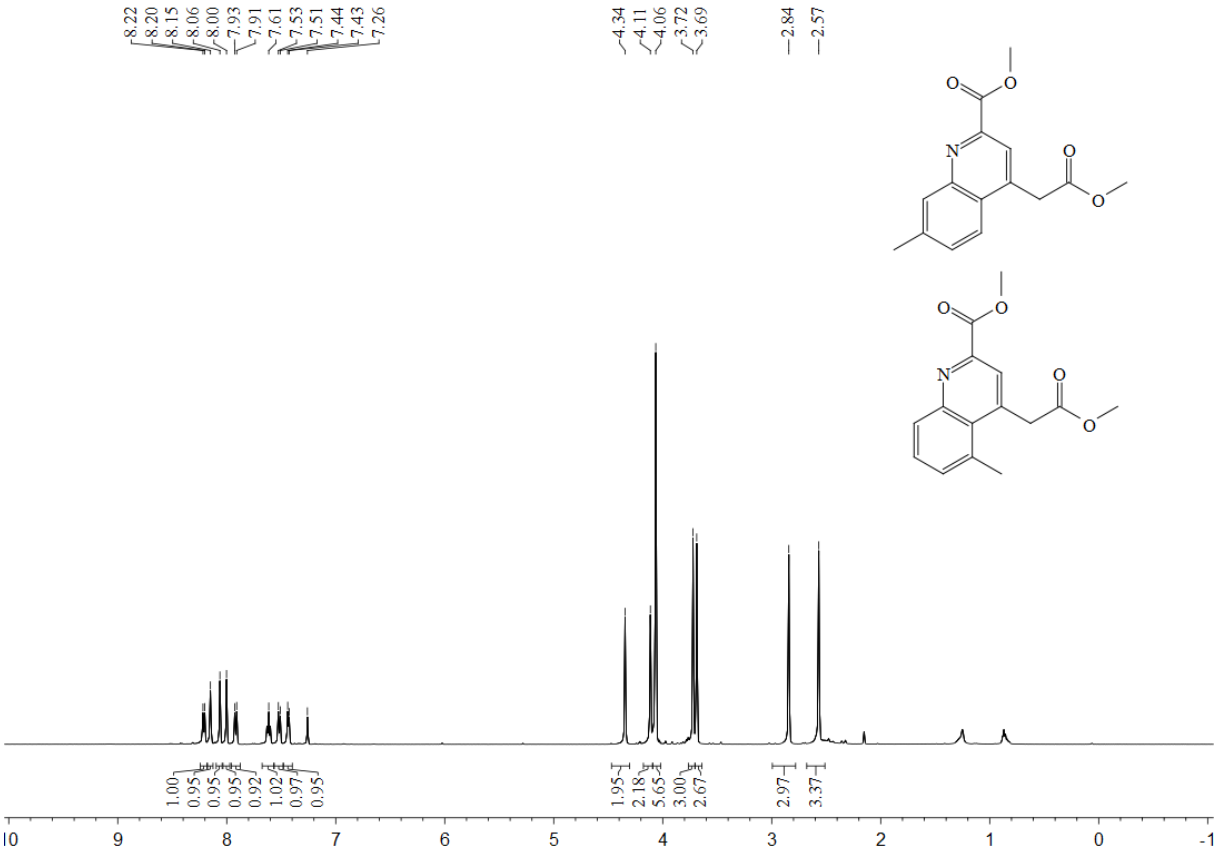


Figure S25. ^{13}C NMR spectrum of Compound **3ja**[6] and **3ja**[2] ($CDCl_3$, 125 MHz)

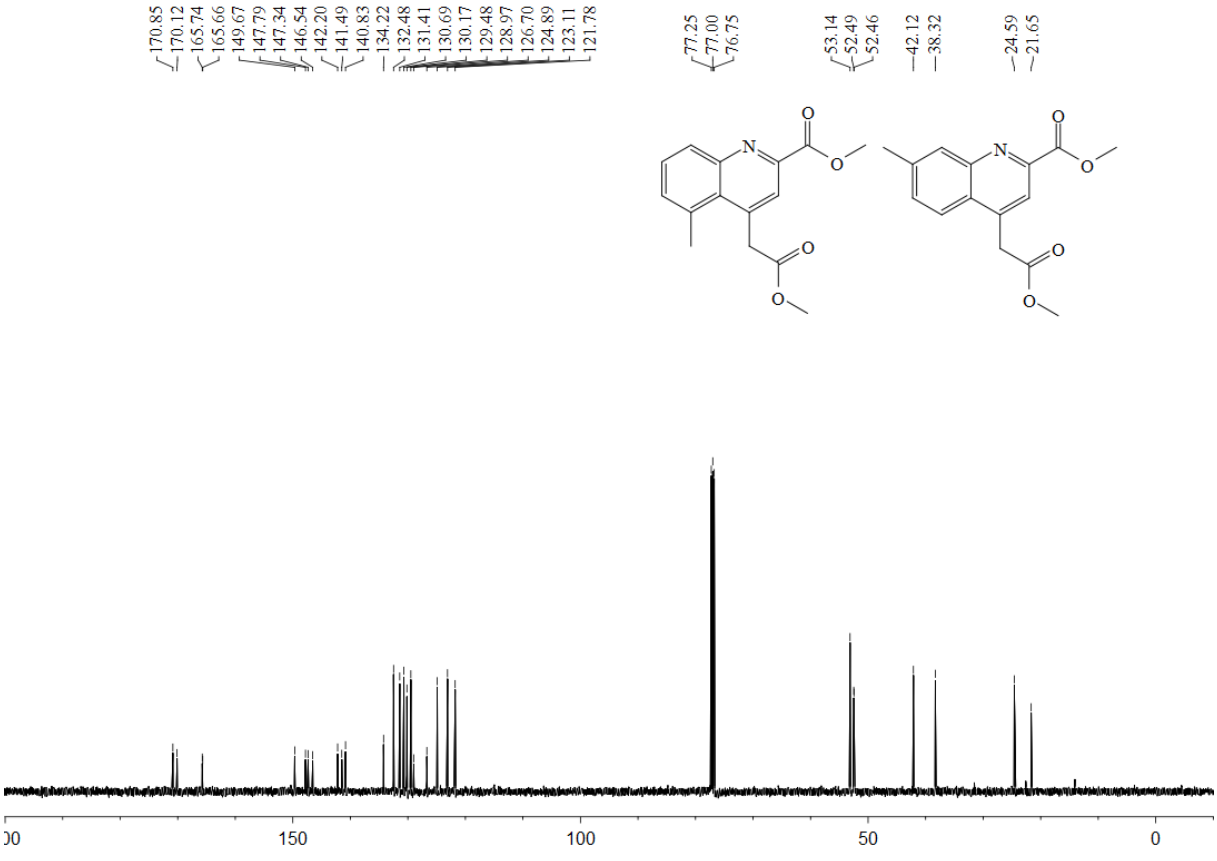


Figure S26. ^{1}H NMR spectrum of Compound **3ka**^{2} ($CDCl_3$, 400 MHz)

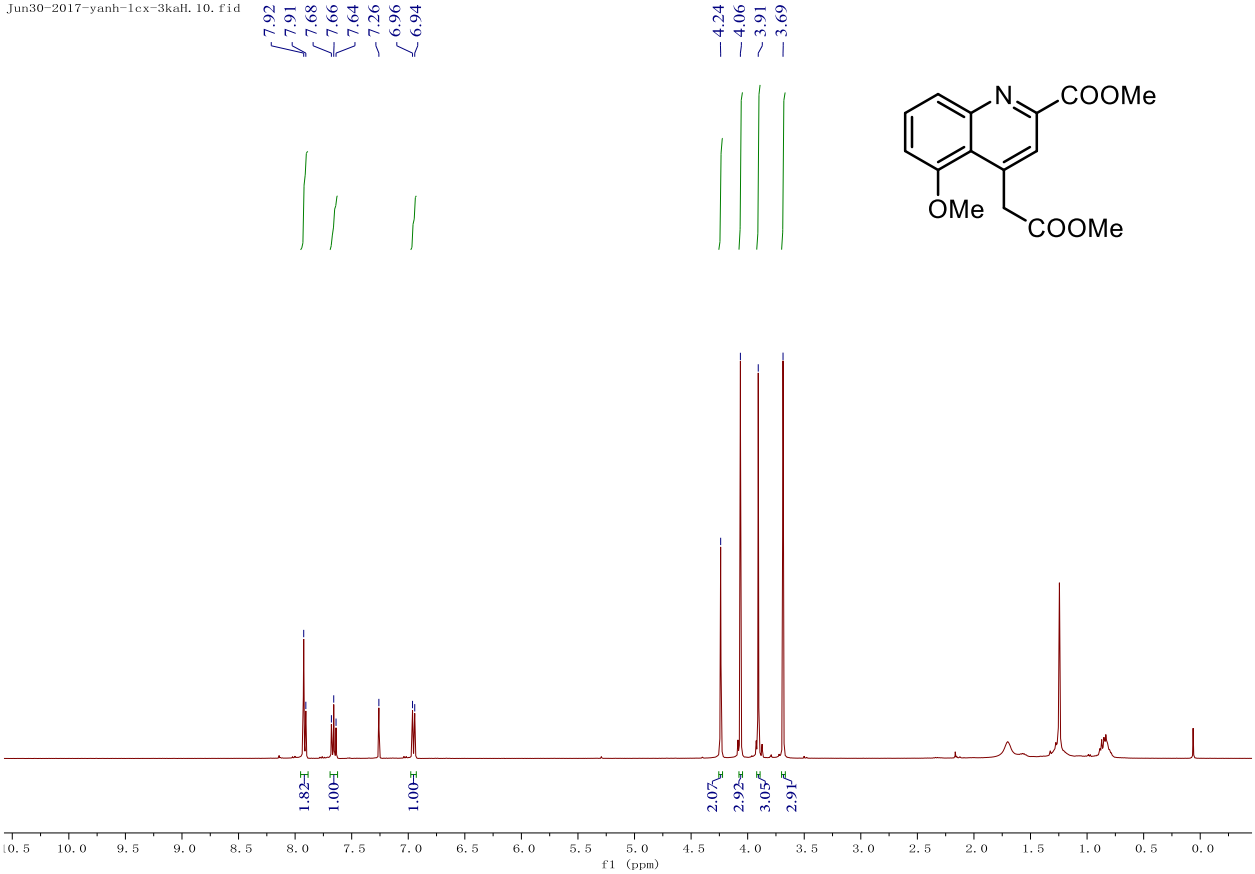


Figure S27. ^{13}C NMR spectrum of Compound **3ka**^{2} ($CDCl_3$, 100 MHz)

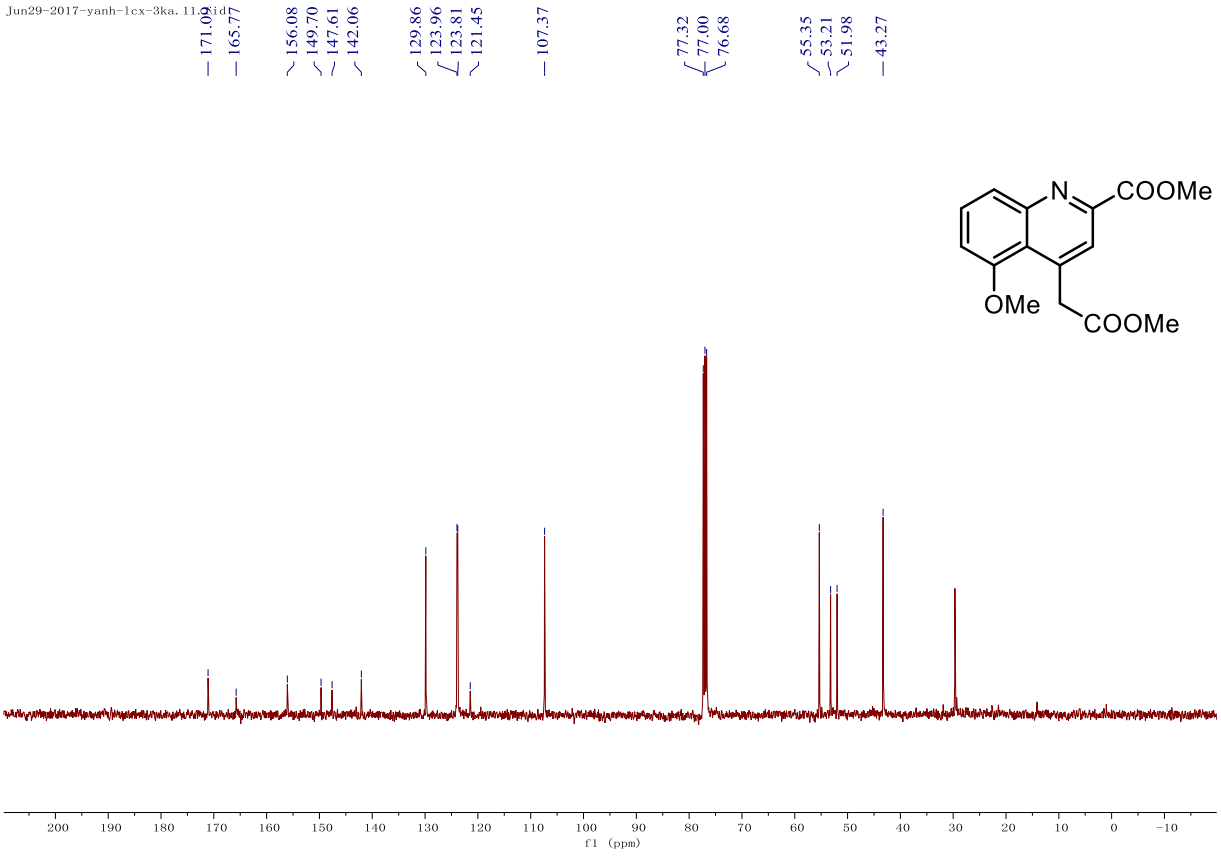


Figure S28. ^{1}H NMR spectrum of Compound **3la**[6] ($CDCl_3$, 400 MHz)

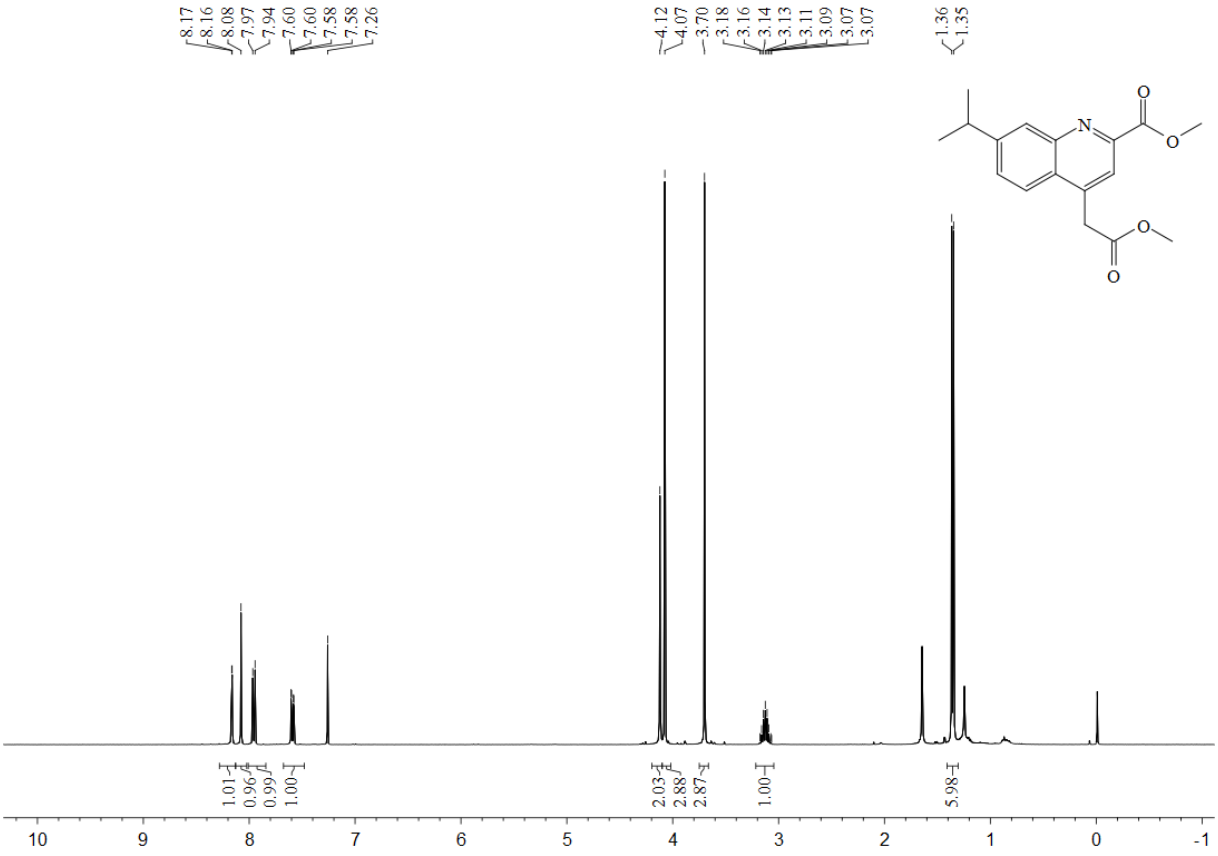


Figure S29. ^{13}C NMR spectrum of Compound **3la**[6] ($CDCl_3$, 100 MHz)

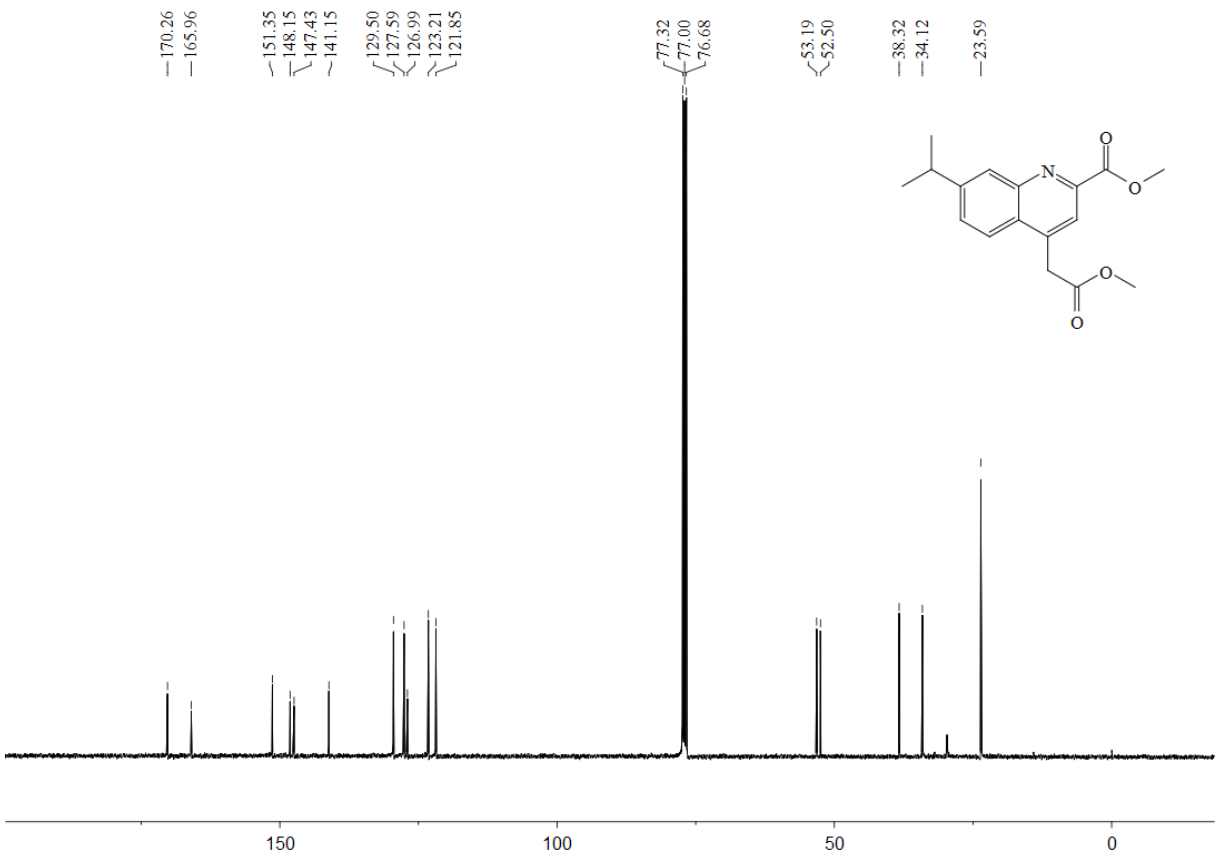


Figure S30. ^{1}H NMR spectrum of Compound **3ma²** ($CDCl_3$, 500 MHz)

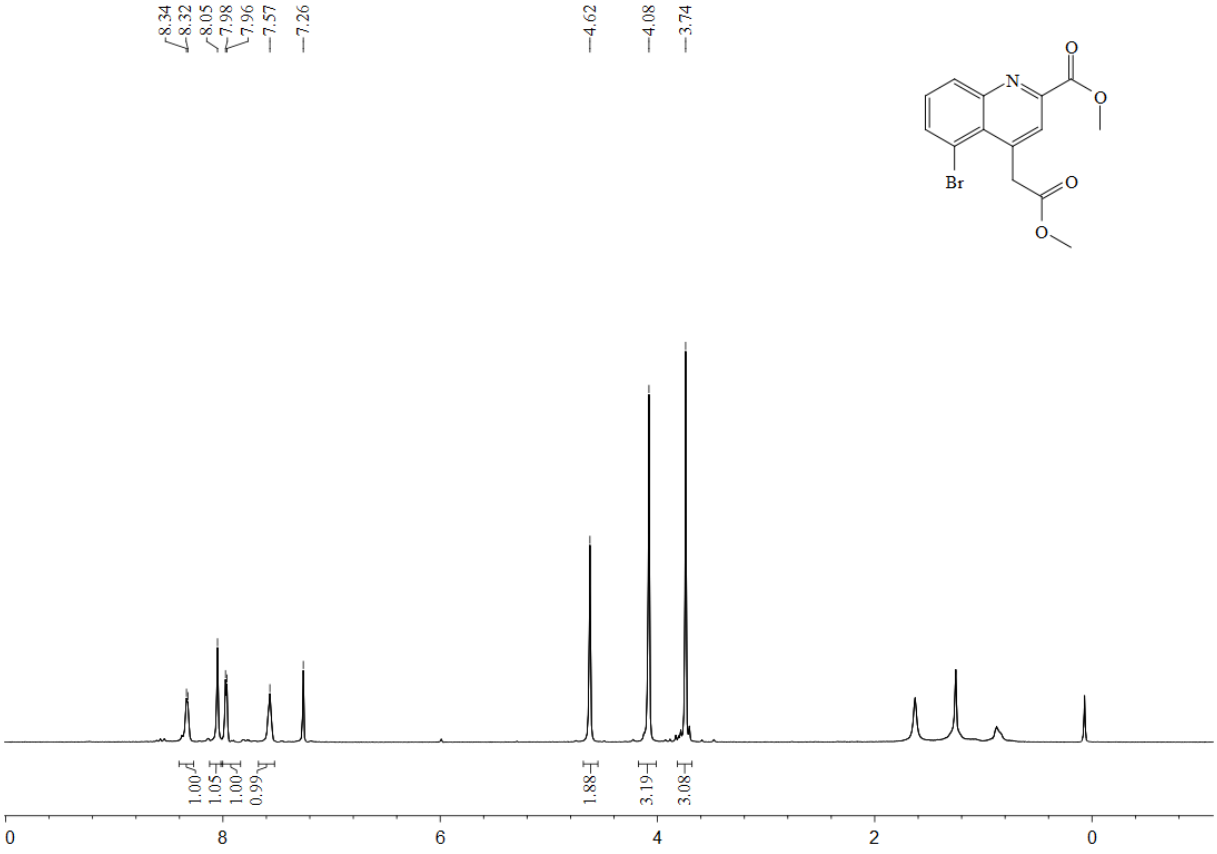


Figure S31. ^{13}C NMR spectrum of Compound **3ma²** ($CDCl_3$, 125 MHz)

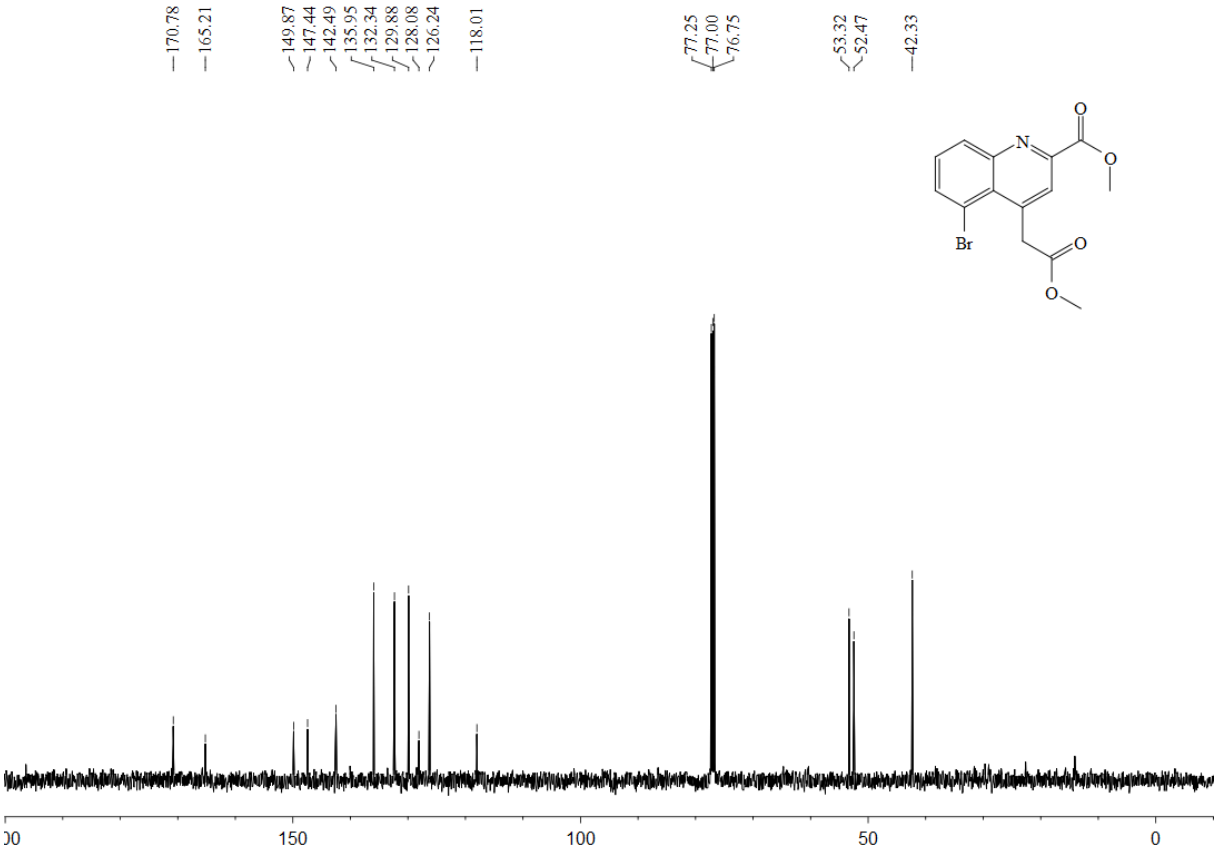


Figure S32. ^{1}H NMR spectrum of Compound **3na**[2] ($CDCl_3$, 400 MHz)

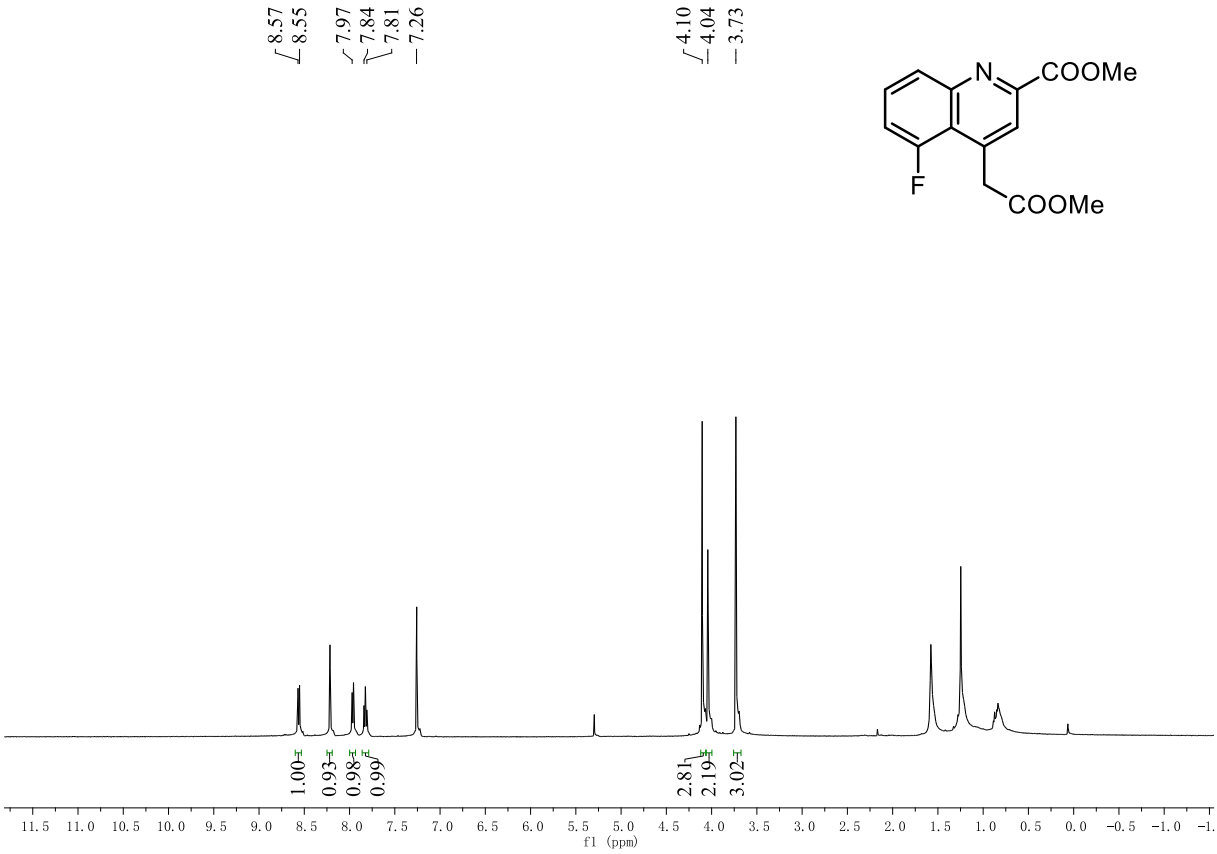


Figure S33. ^{13}C NMR spectrum of Compound **3na**[2] ($CDCl_3$, 100 MHz)

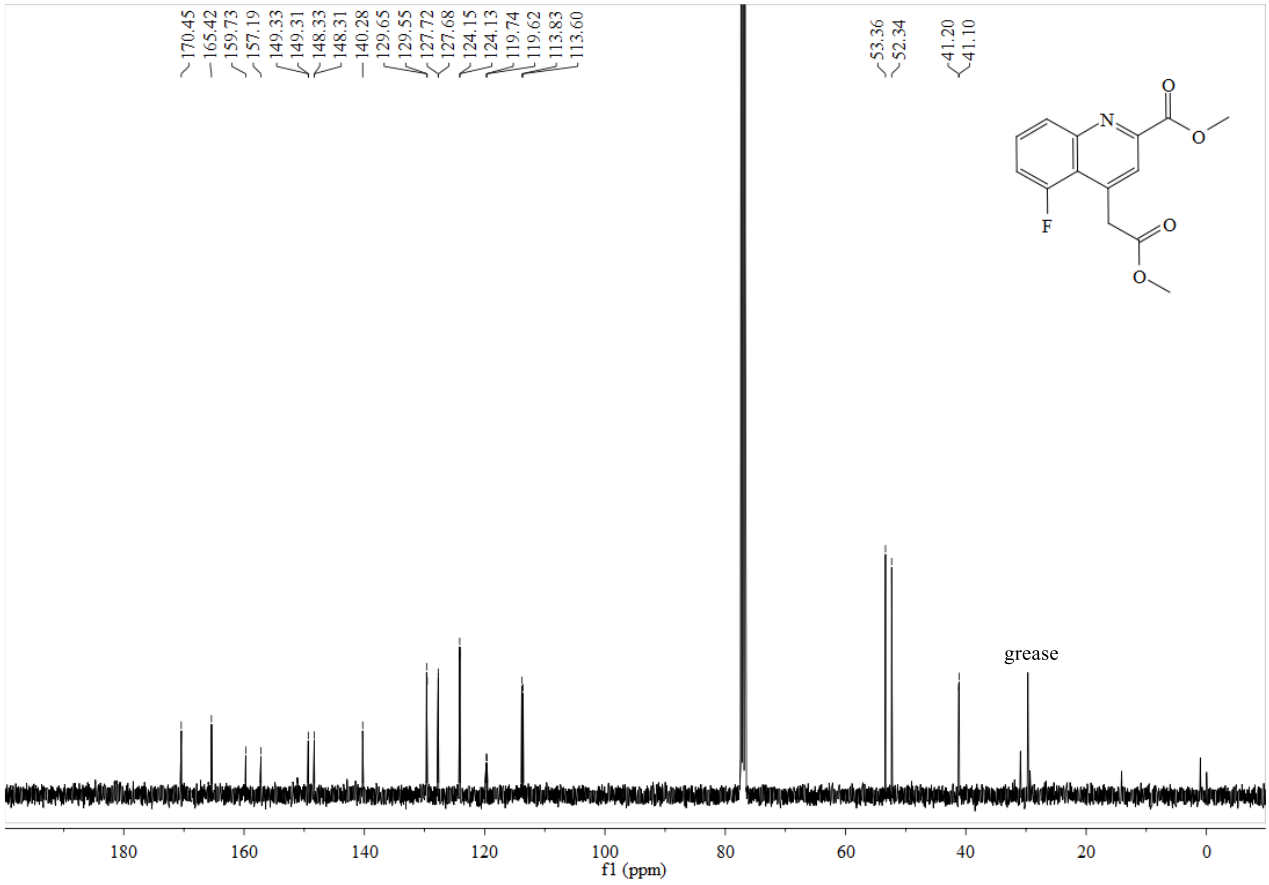


Figure S34. ^{1}H NMR spectrum of Compound **3oa**[2] ($CDCl_3$, 400 MHz)

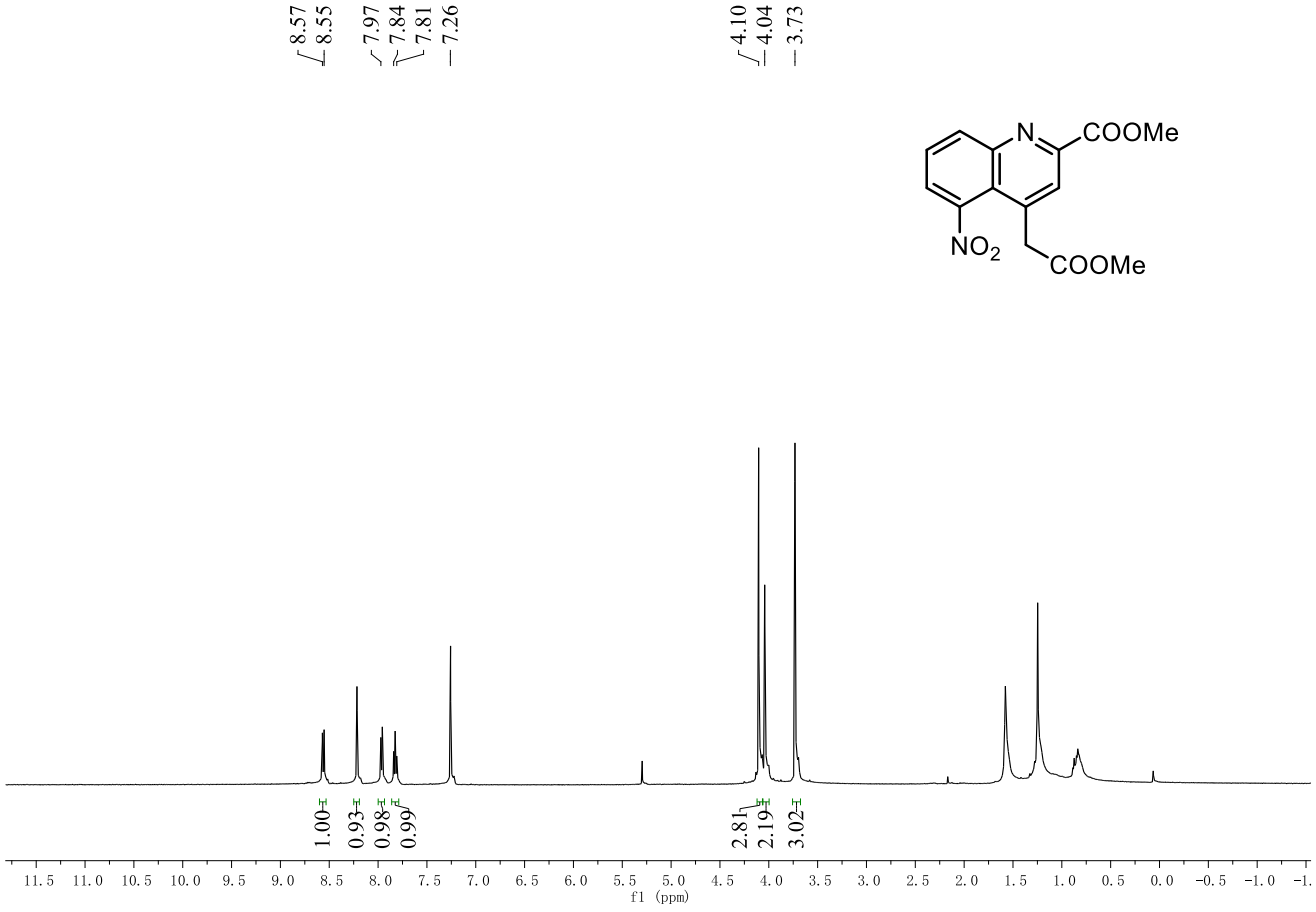


Figure S35. ^{13}C NMR spectrum of Compound **3oa**[2] ($CDCl_3$, 100 MHz)

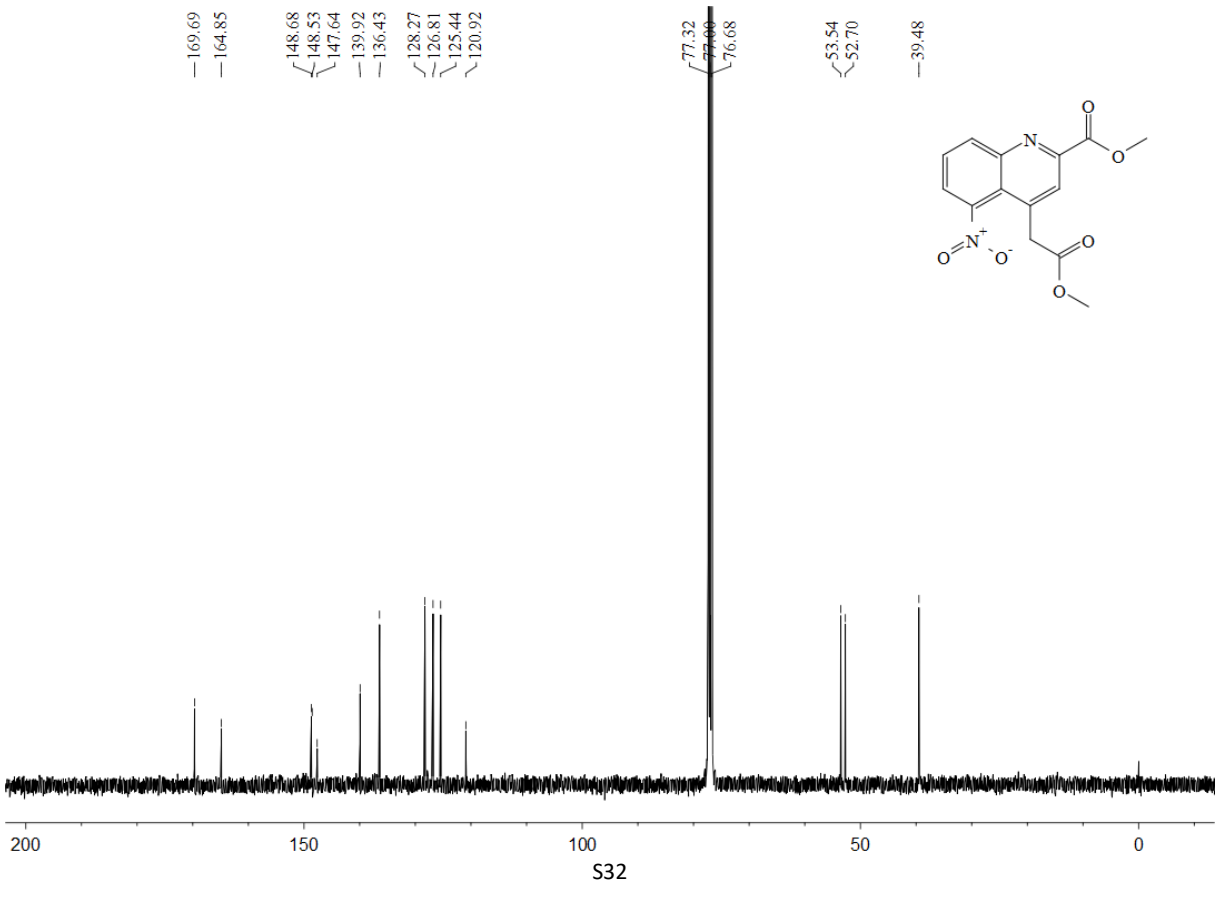


Figure S36. ^{1}H NMR spectrum of Compound **3pa** ($CDCl_3$, 400 MHz)

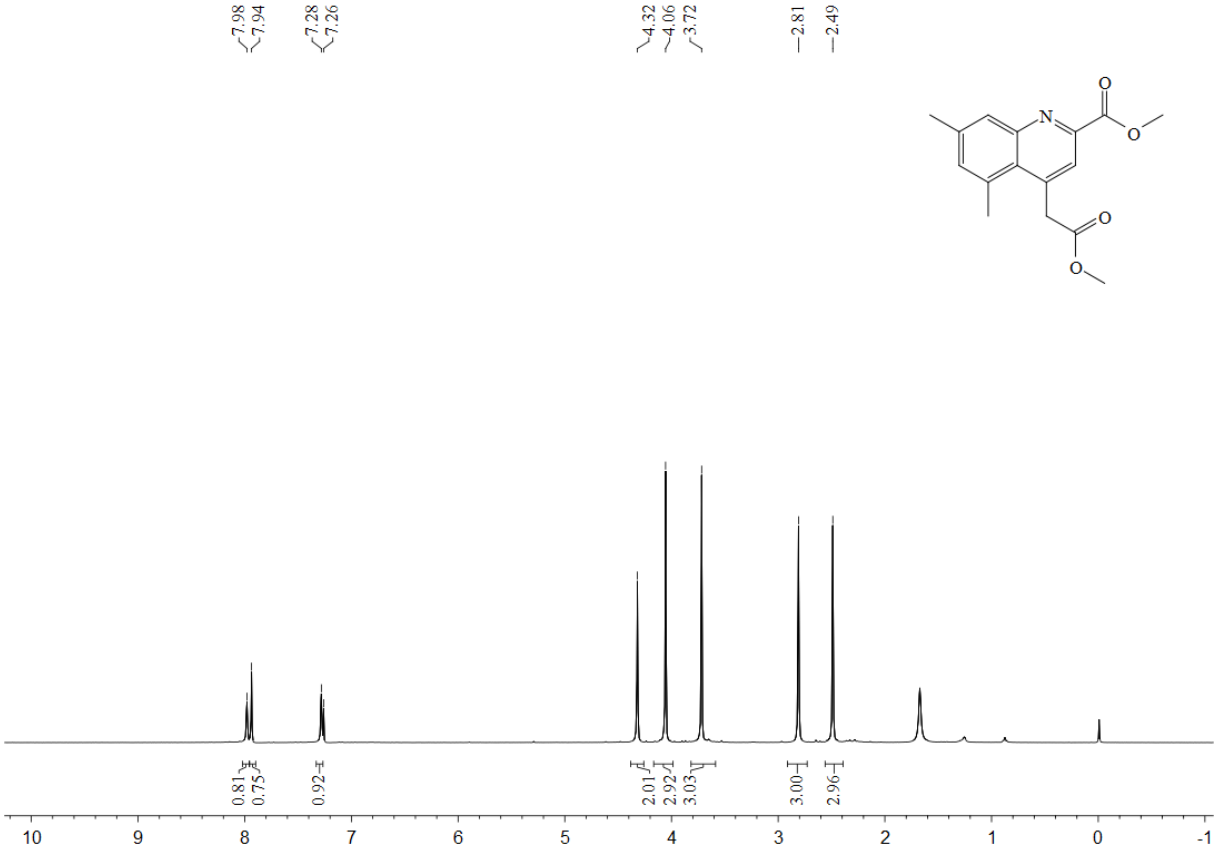


Figure S37. ^{13}C NMR spectrum of Compound **3pa** ($CDCl_3$, 100 MHz)

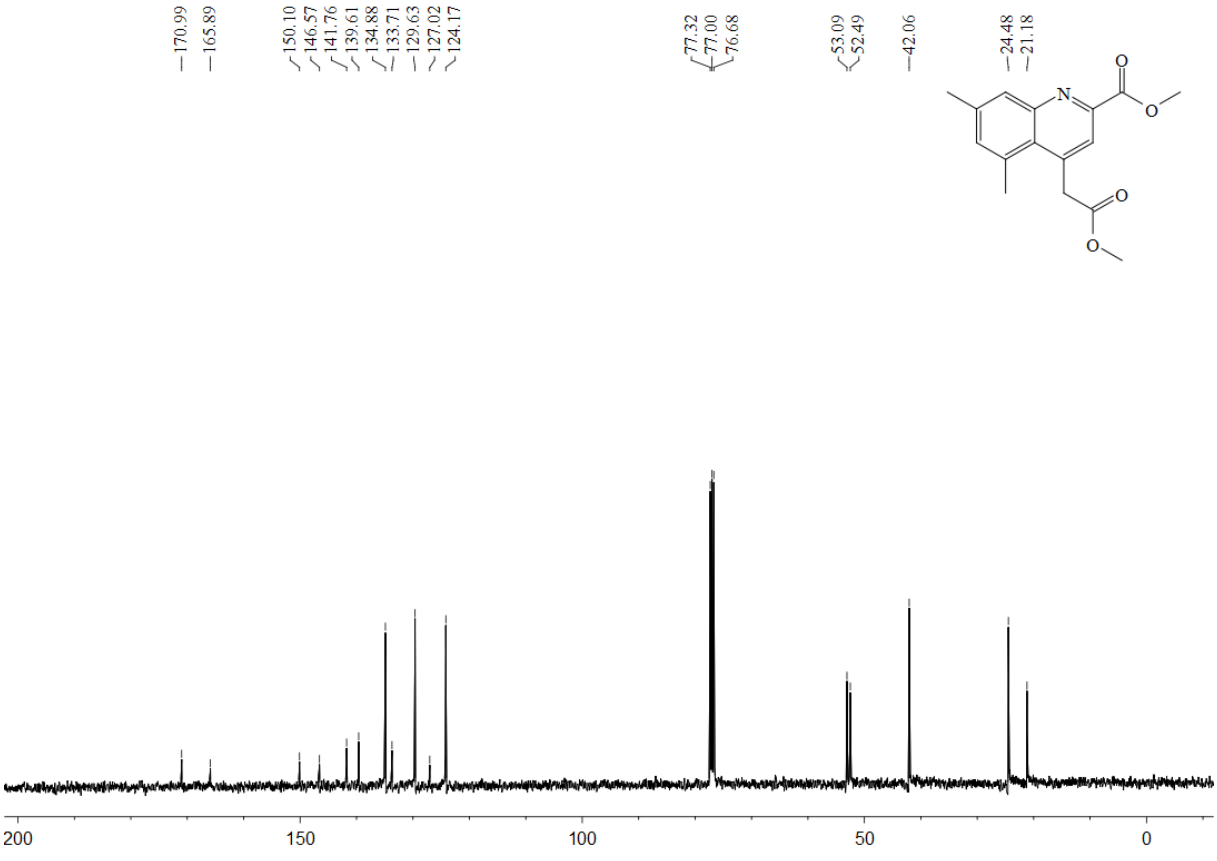


Figure S38. ^{1}H NMR spectrum of Compound **3qa** ($CDCl_3$, 400 MHz)

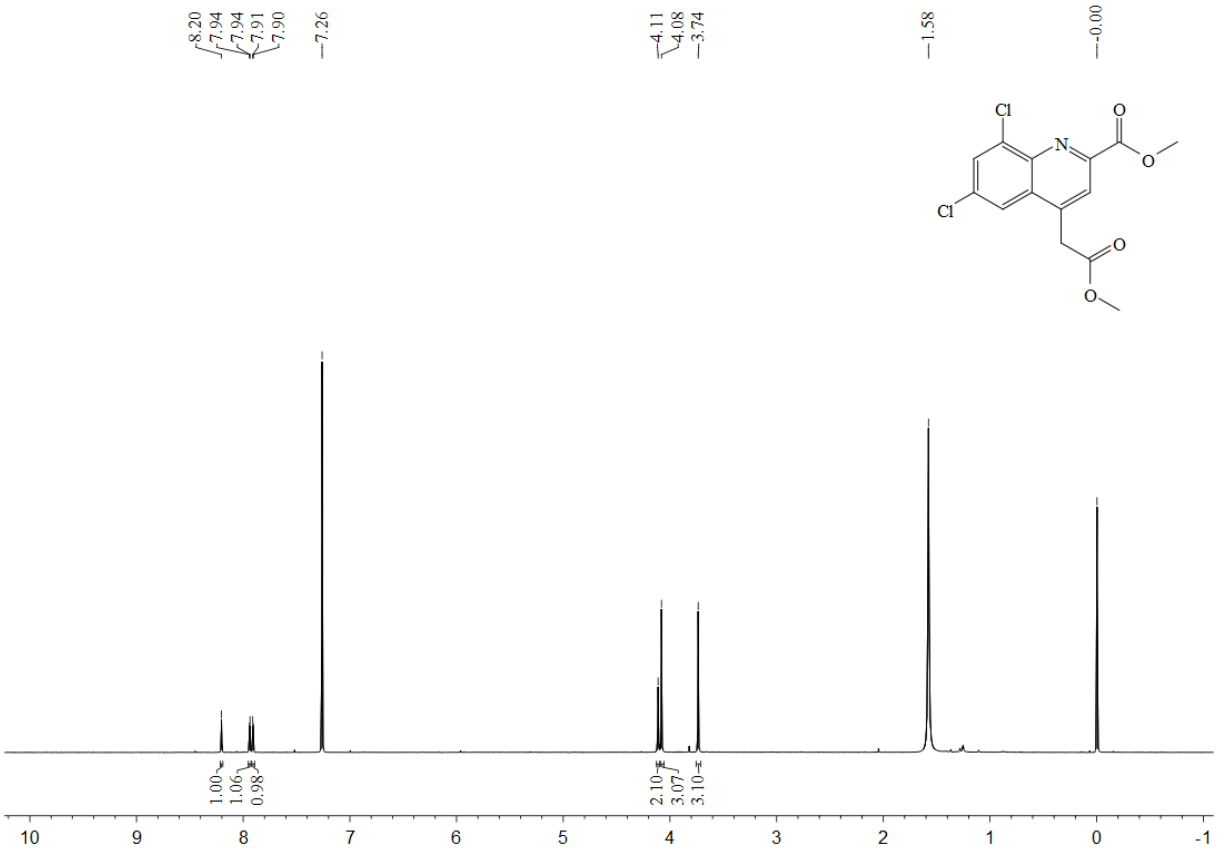


Figure S39. ^{13}C NMR spectrum of Compound **3qa** ($CDCl_3$, 100 MHz)

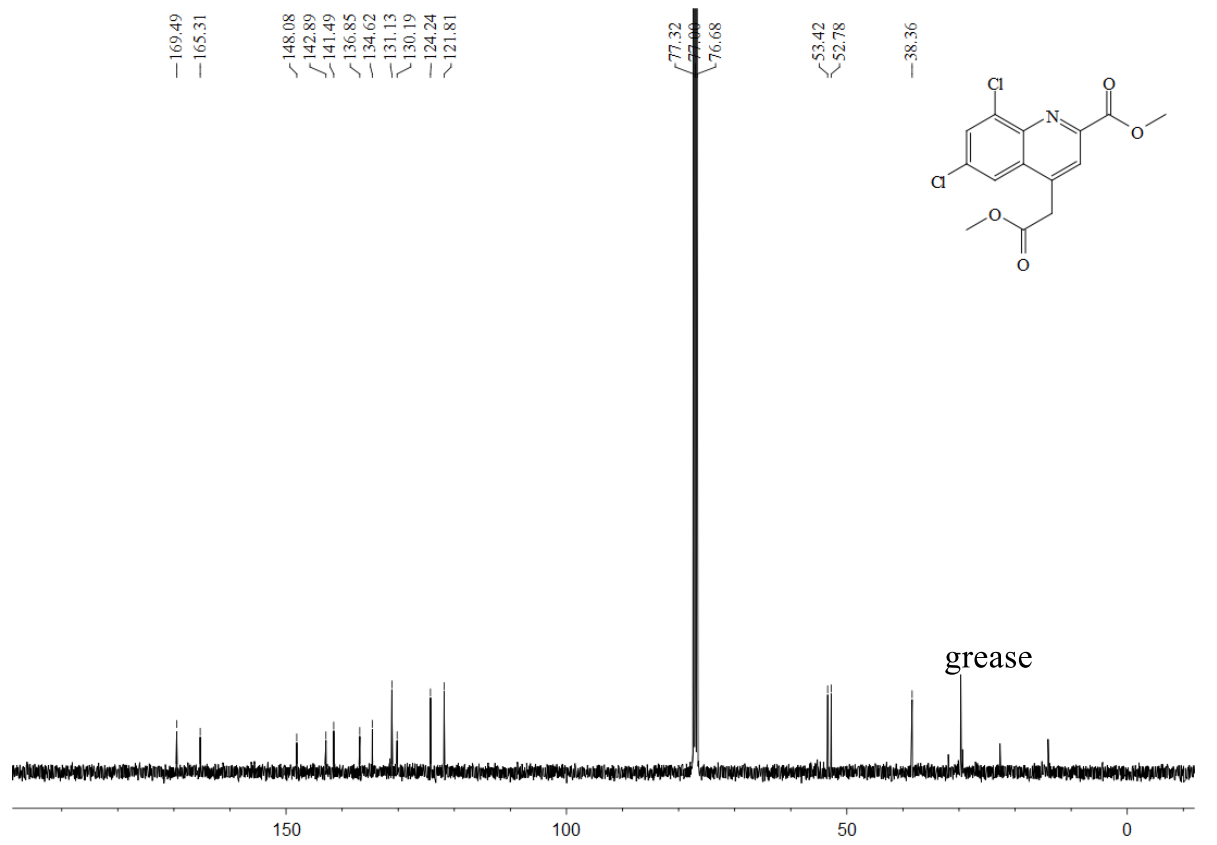


Figure S40. ^{1}H NMR spectrum of Compound **3ra** ($CDCl_3$, 400 MHz)

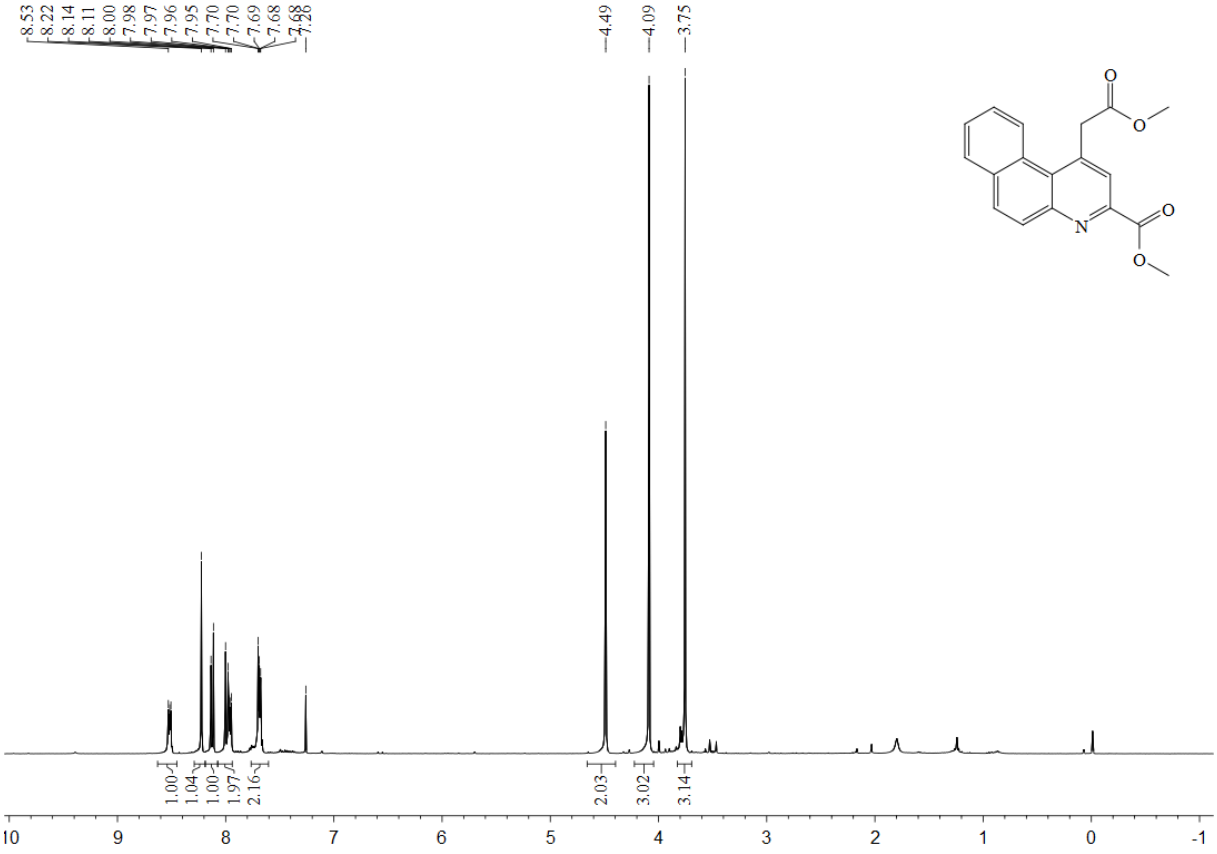


Figure S41. ^{13}C NMR spectrum of Compound **3ra** ($CDCl_3$, 100 MHz)

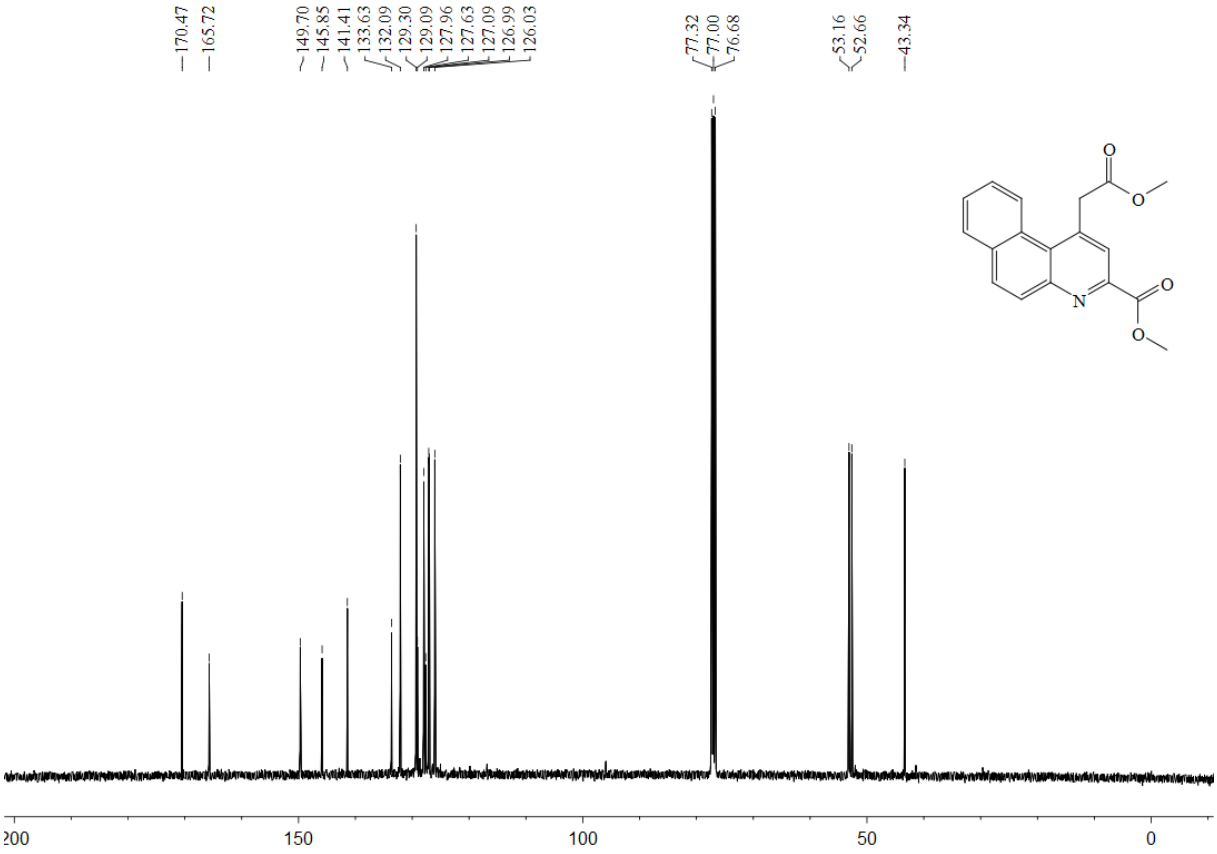


Figure S42. NOESY spectrum of Compound **3ra** ($CDCl_3$, 400 MHz)

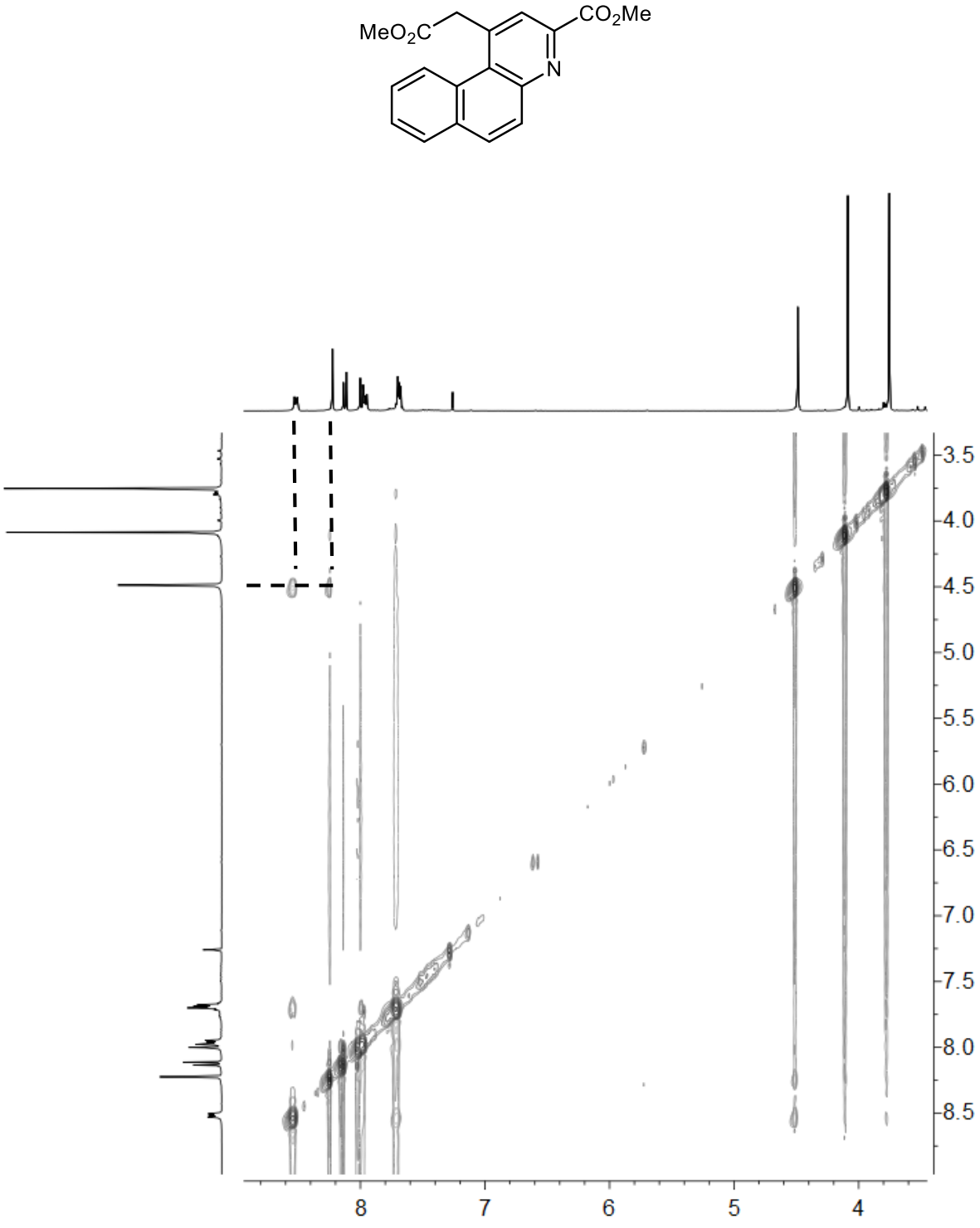


Figure S43. ^{1}H NMR spectrum of Compound **3sa** ($CDCl_3$, 400 MHz)

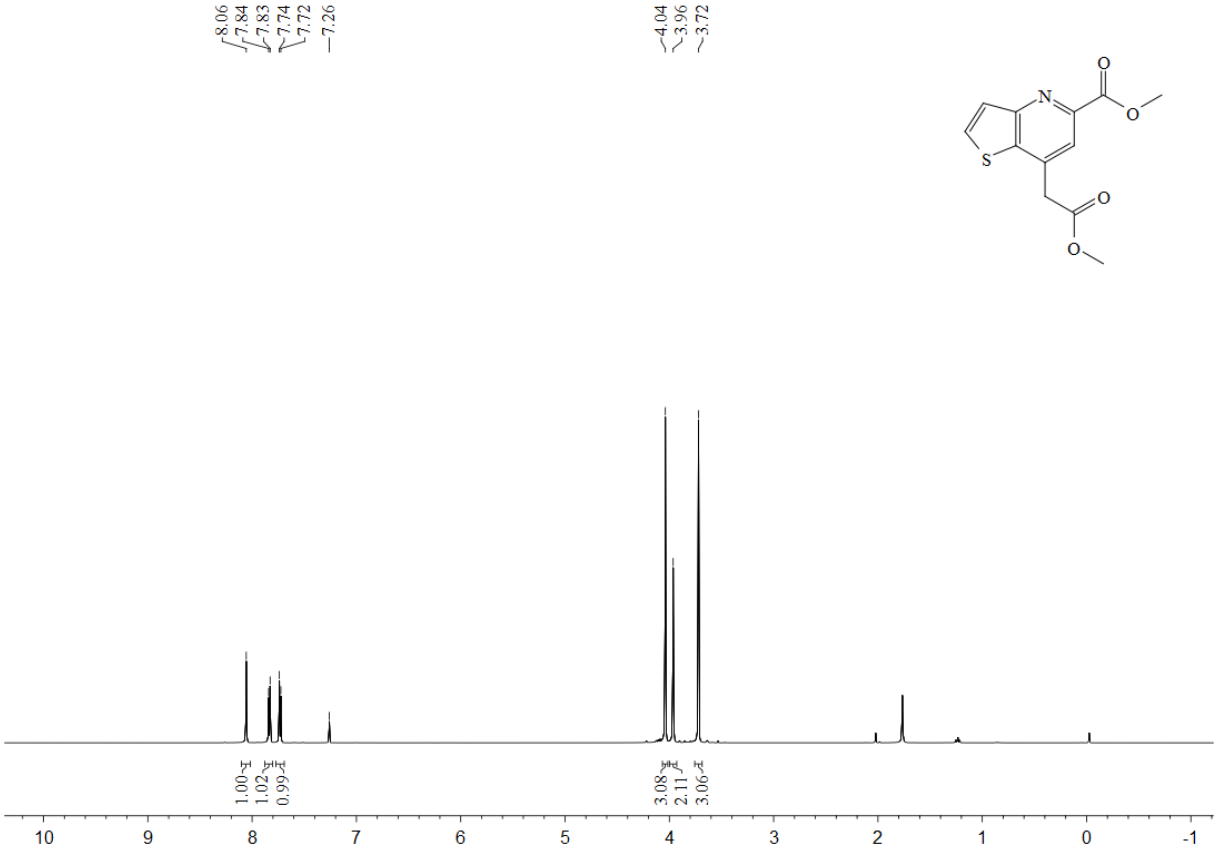


Figure S44. ^{13}C NMR spectrum of Compound **3sa** ($CDCl_3$, 100 MHz)

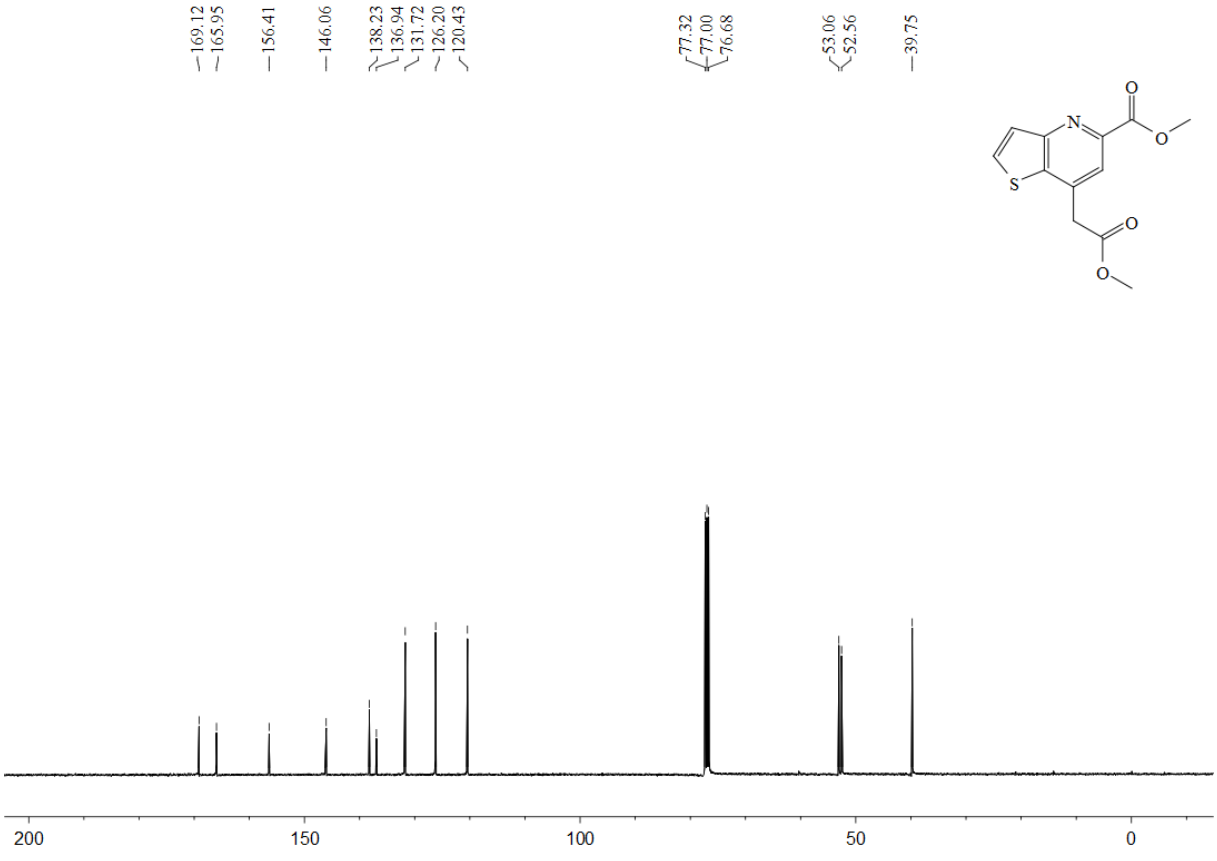


Figure S45. ^{1}H NMR spectrum of Compound **3ta** ($CDCl_3$, 400 MHz)

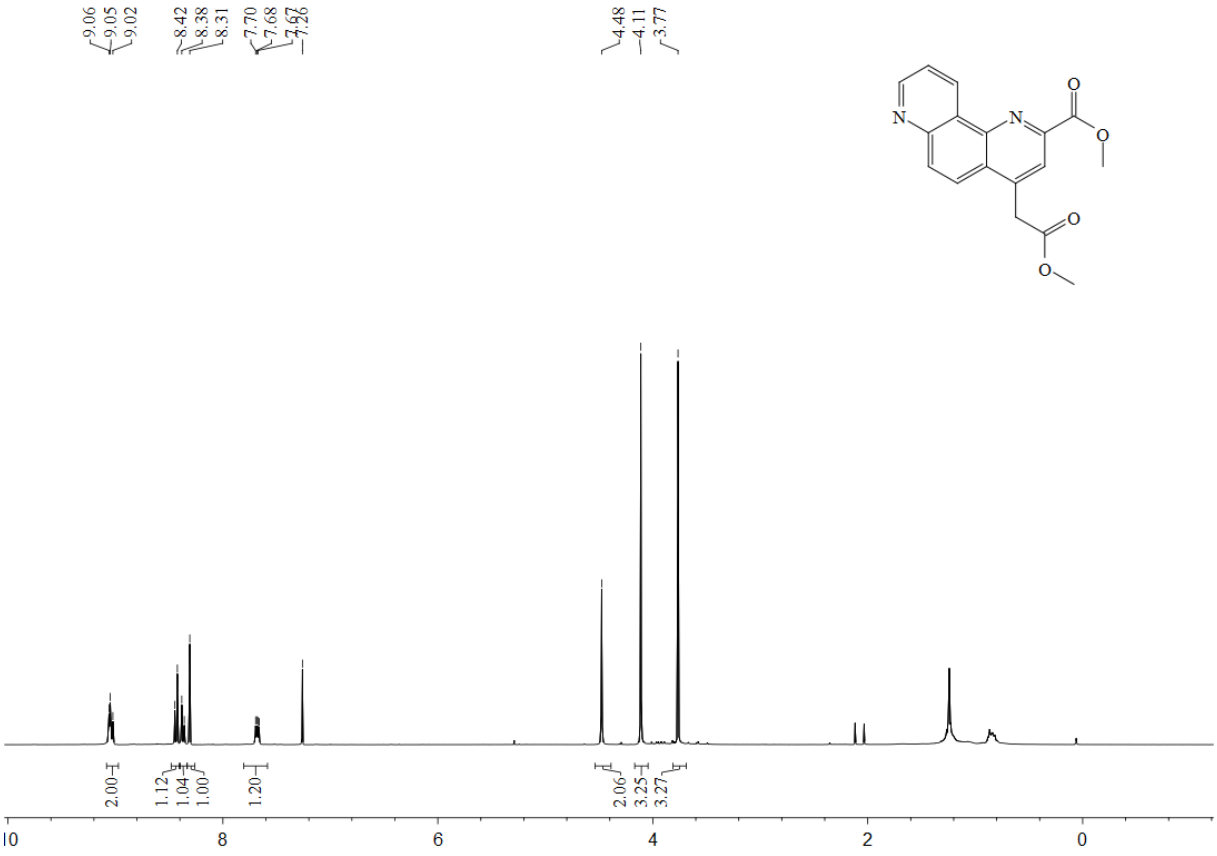


Figure S46. ^{13}C NMR spectrum of Compound **3ta** ($CDCl_3$, 100 MHz)

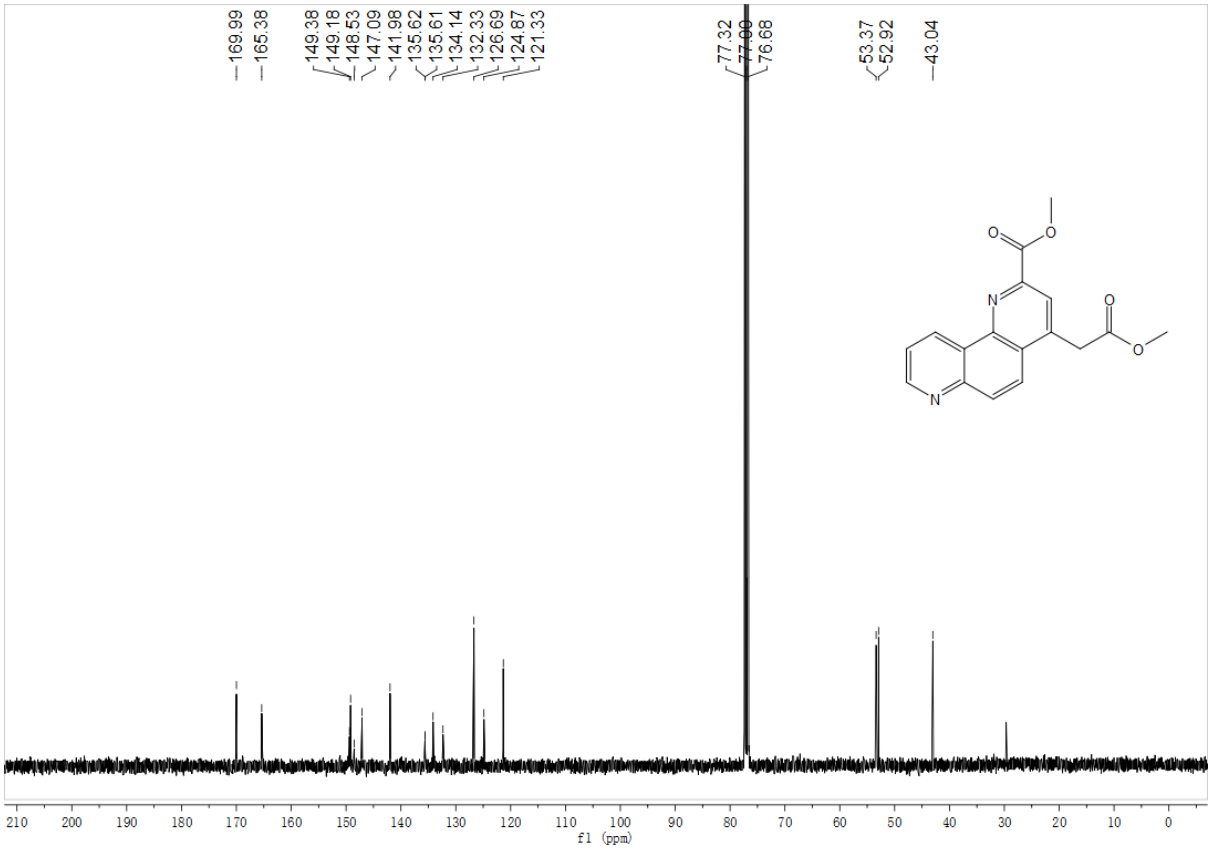


Figure S47. ^{1}H NMR spectrum of Compound **3ab** ($CDCl_3$, 500 MHz)

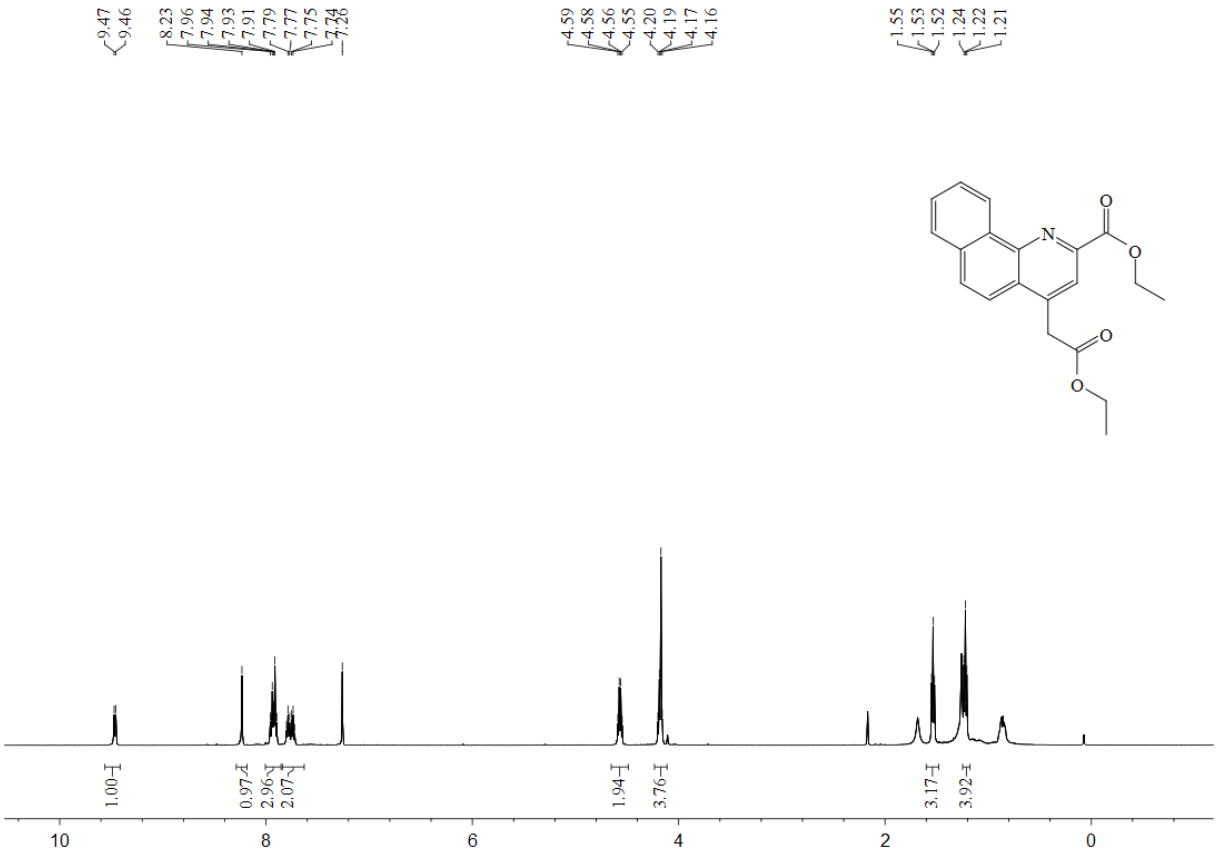


Figure S48. ^{13}C NMR spectrum of Compound **3ab** ($CDCl_3$, 125 MHz)

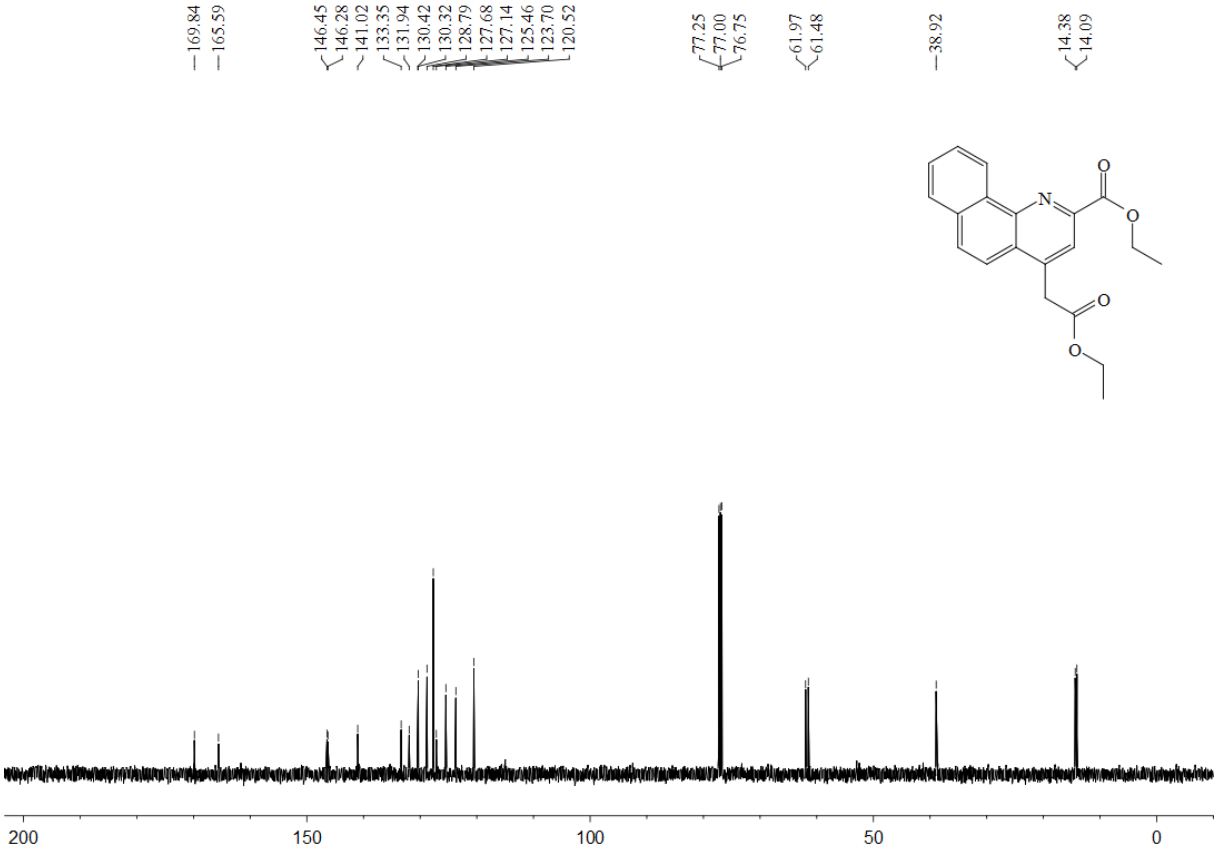


Figure S49. ^{1}H NMR spectrum of Compound **3ac** ($CDCl_3$, 400 MHz)

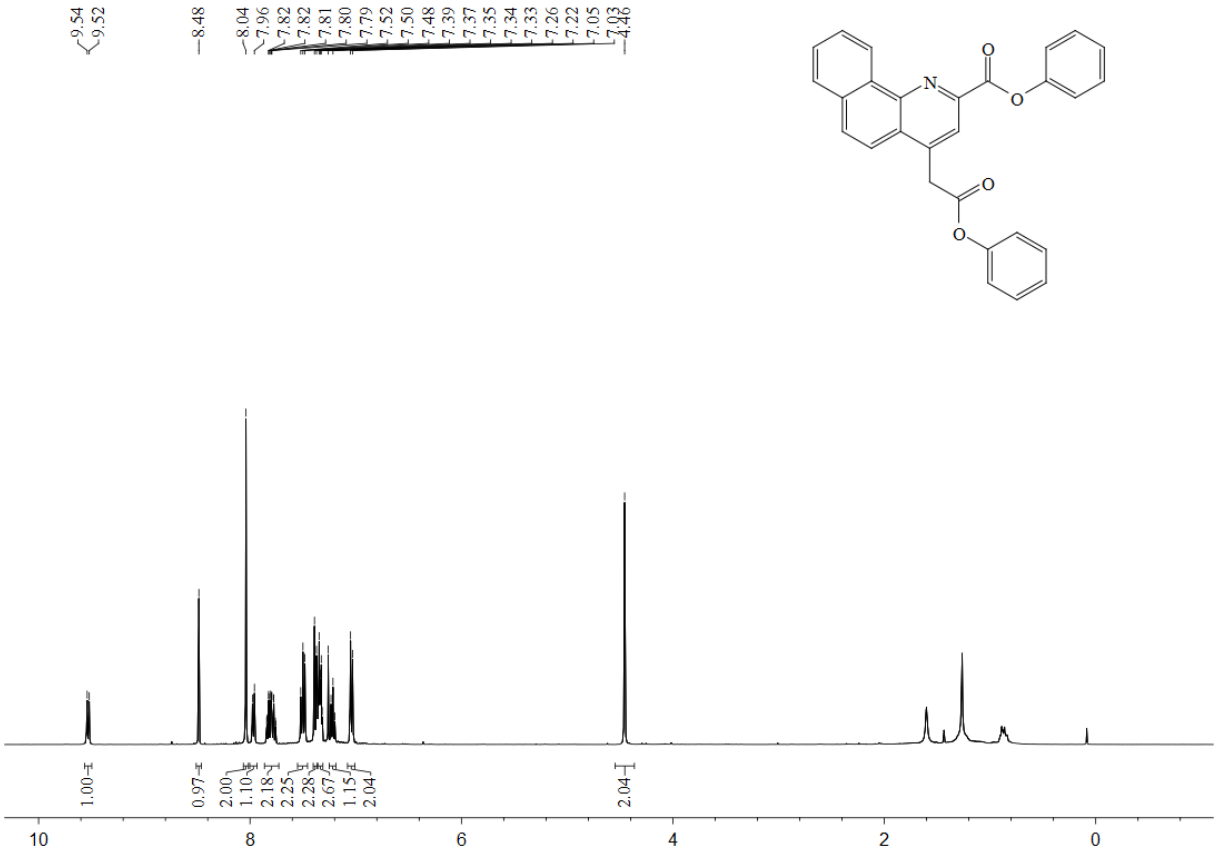


Figure S50. ^{13}C NMR spectrum of Compound **3ac** ($CDCl_3$, 100 MHz)

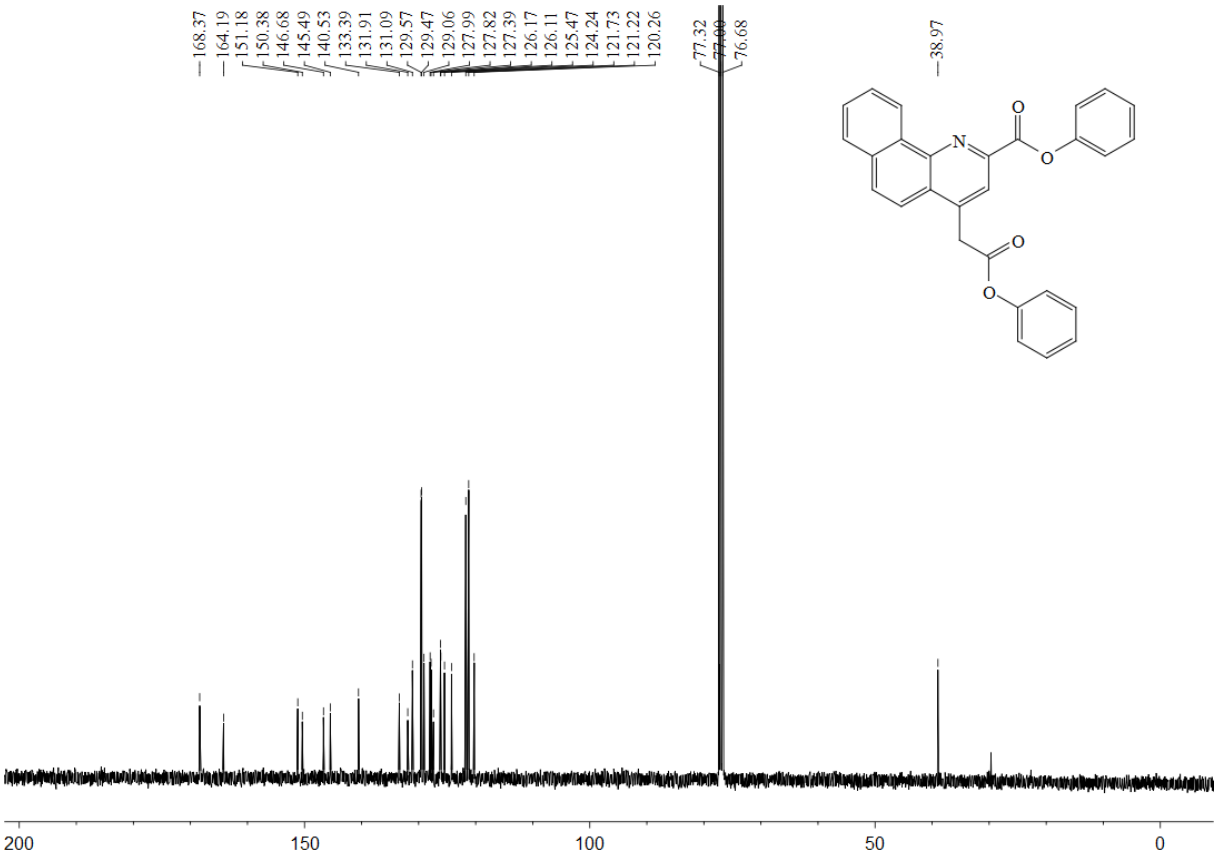


Figure S51. ^{1}H NMR spectrum of Compound **3ad** ($CDCl_3$, 400 MHz)

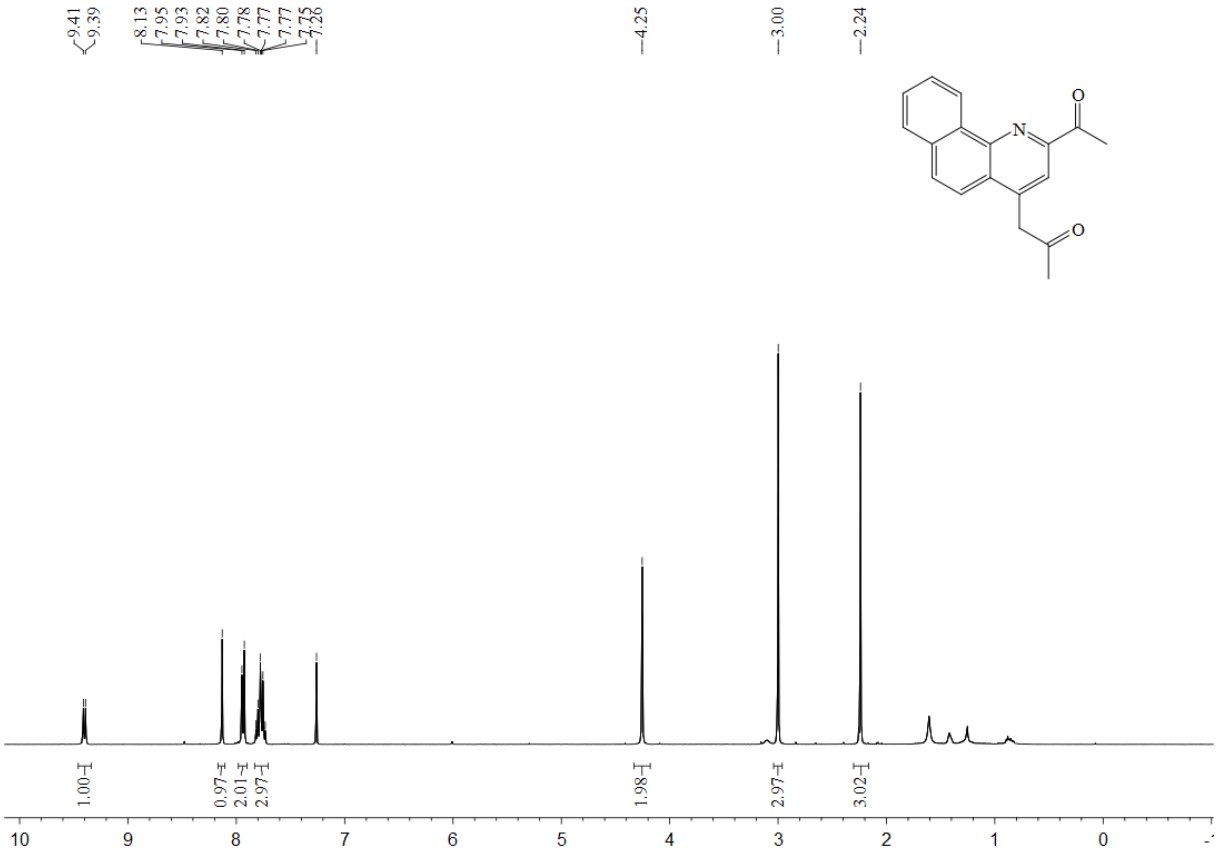


Figure S52. ^{13}H NMR spectrum of Compound **3ad** ($CDCl_3$, 100 MHz)

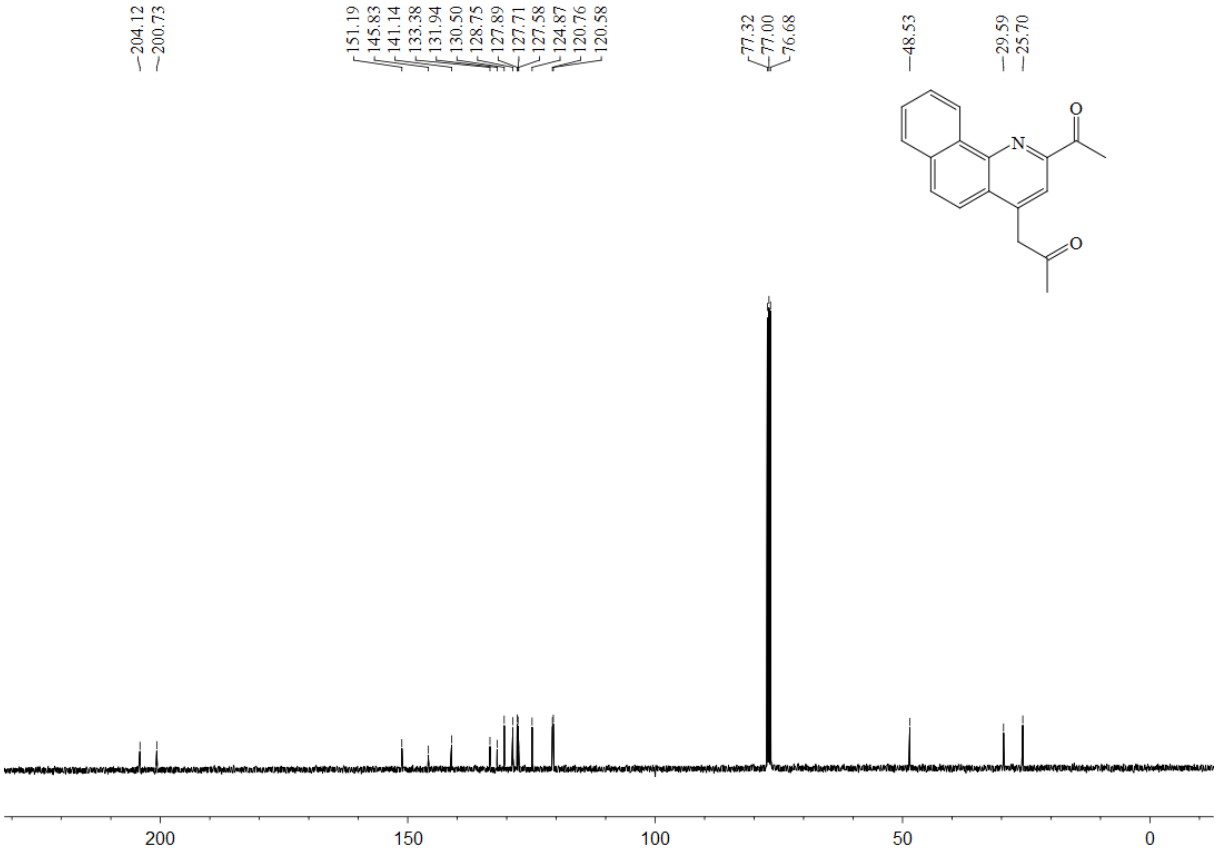


Figure S53. ^{1}H NMR spectrum of Compound **3ae** ($CDCl_3$, 400 MHz)

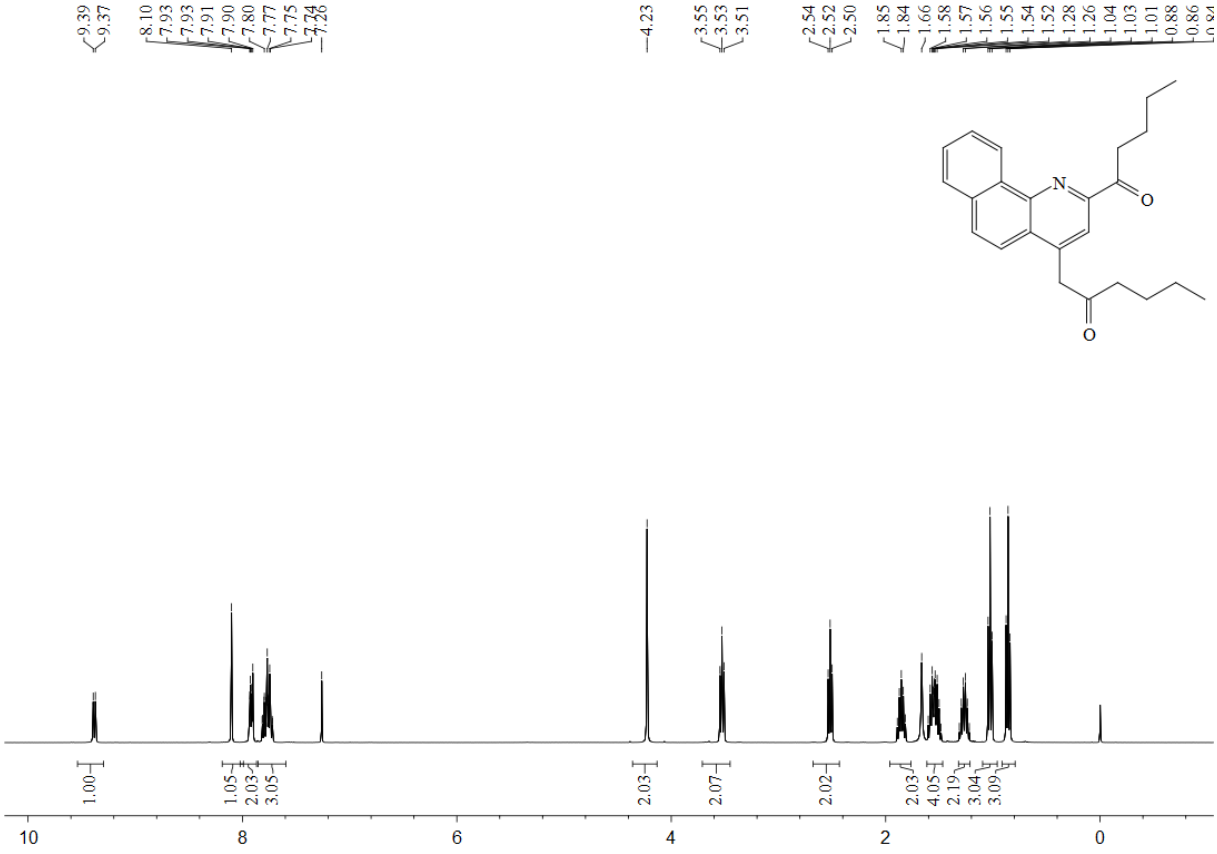


Figure S54. ^{1}H NMR spectrum of Compound **3ae** ($CDCl_3$, 100 MHz)

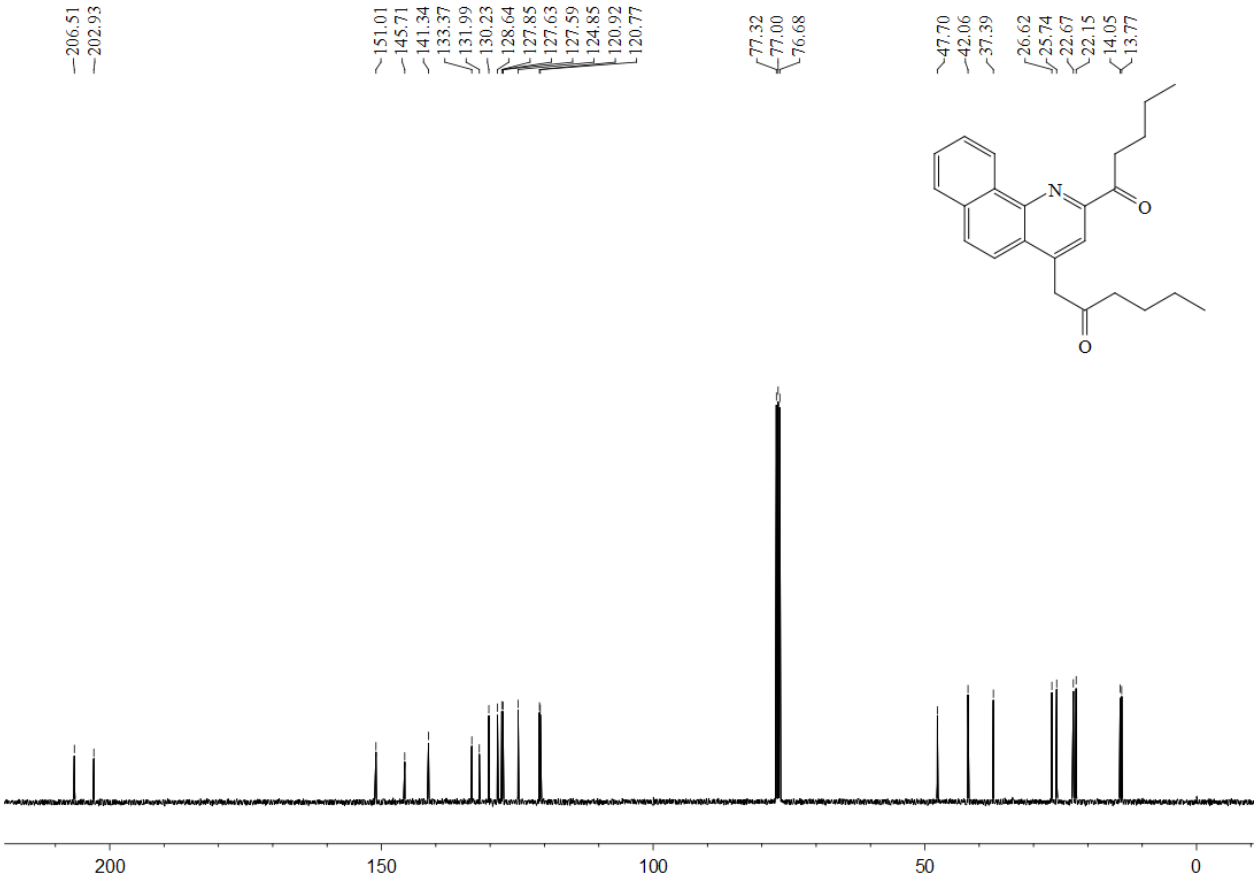


Figure S55. ^{1}H NMR spectrum of Compound **3af** ($CDCl_3$, 400 MHz)

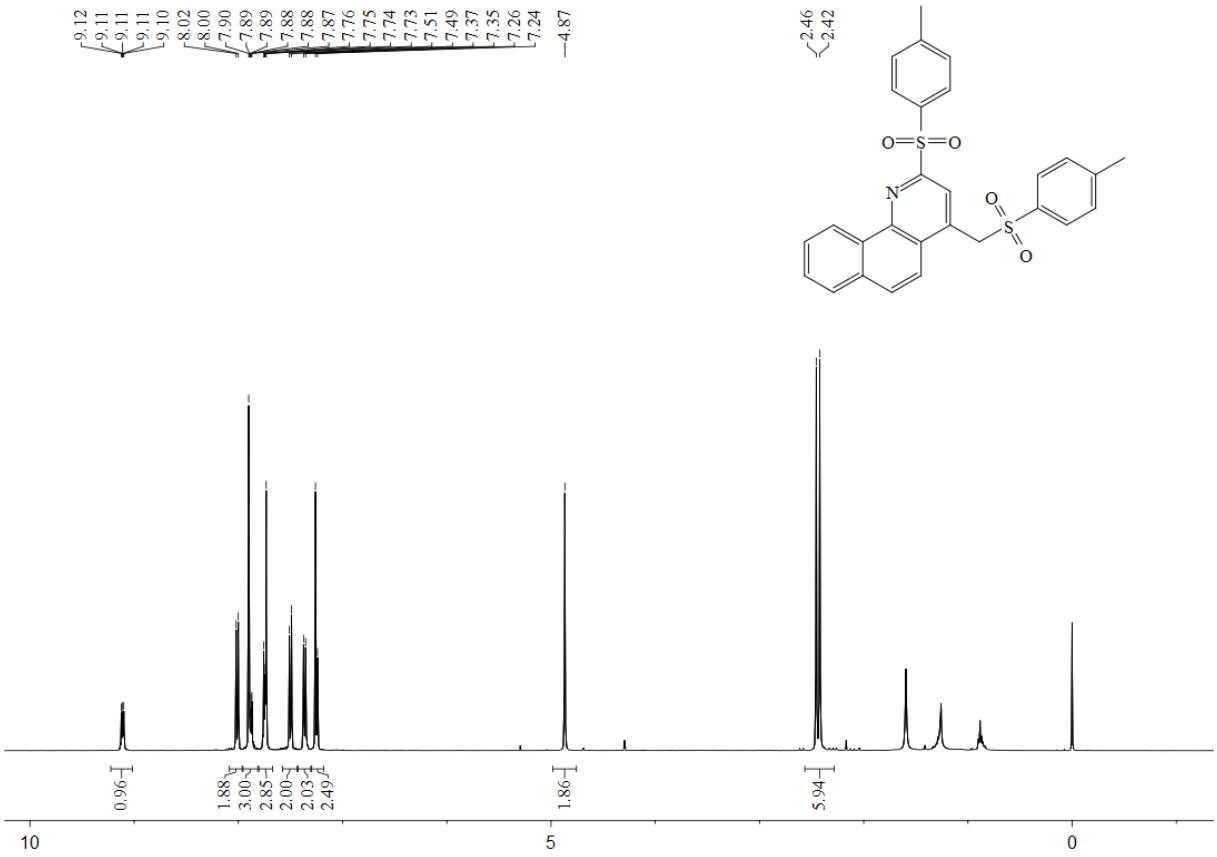


Figure S56. ^{13}C NMR spectrum of Compound **3af** ($CDCl_3$, 100 MHz)

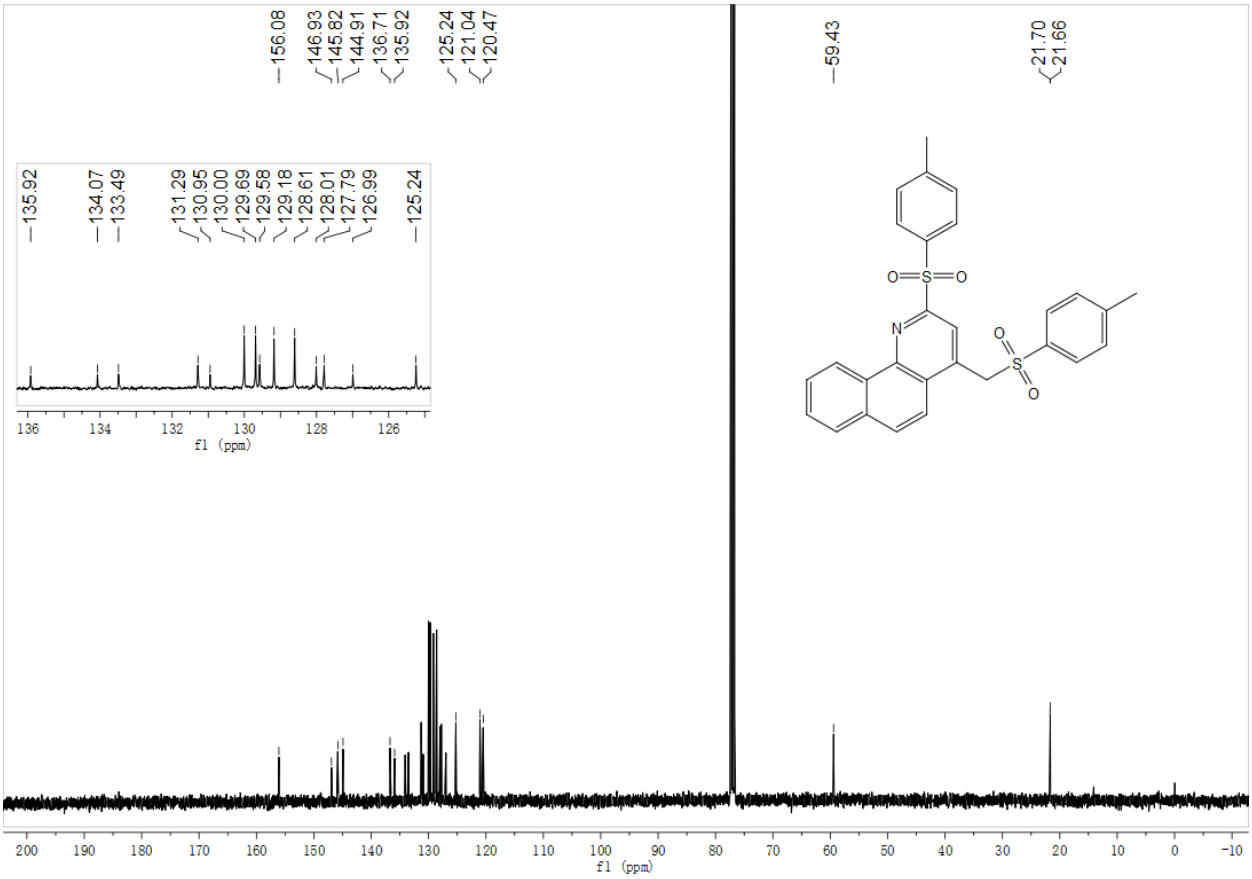


Figure S57. ^{1}H NMR spectrum of Compound **3ag** ($CDCl_3$, 400 MHz)

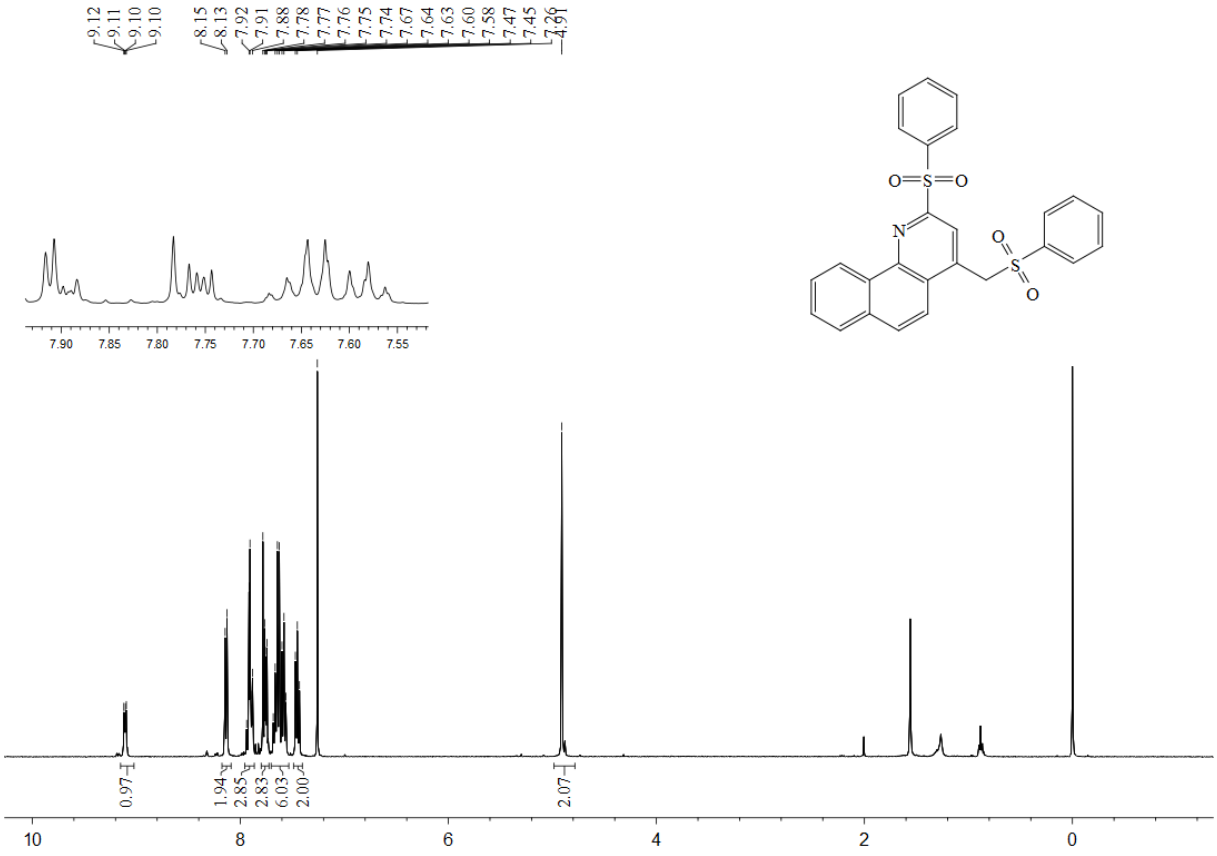


Figure S58. ^{13}C NMR spectrum of Compound **3ag** ($CDCl_3$, 100 MHz)

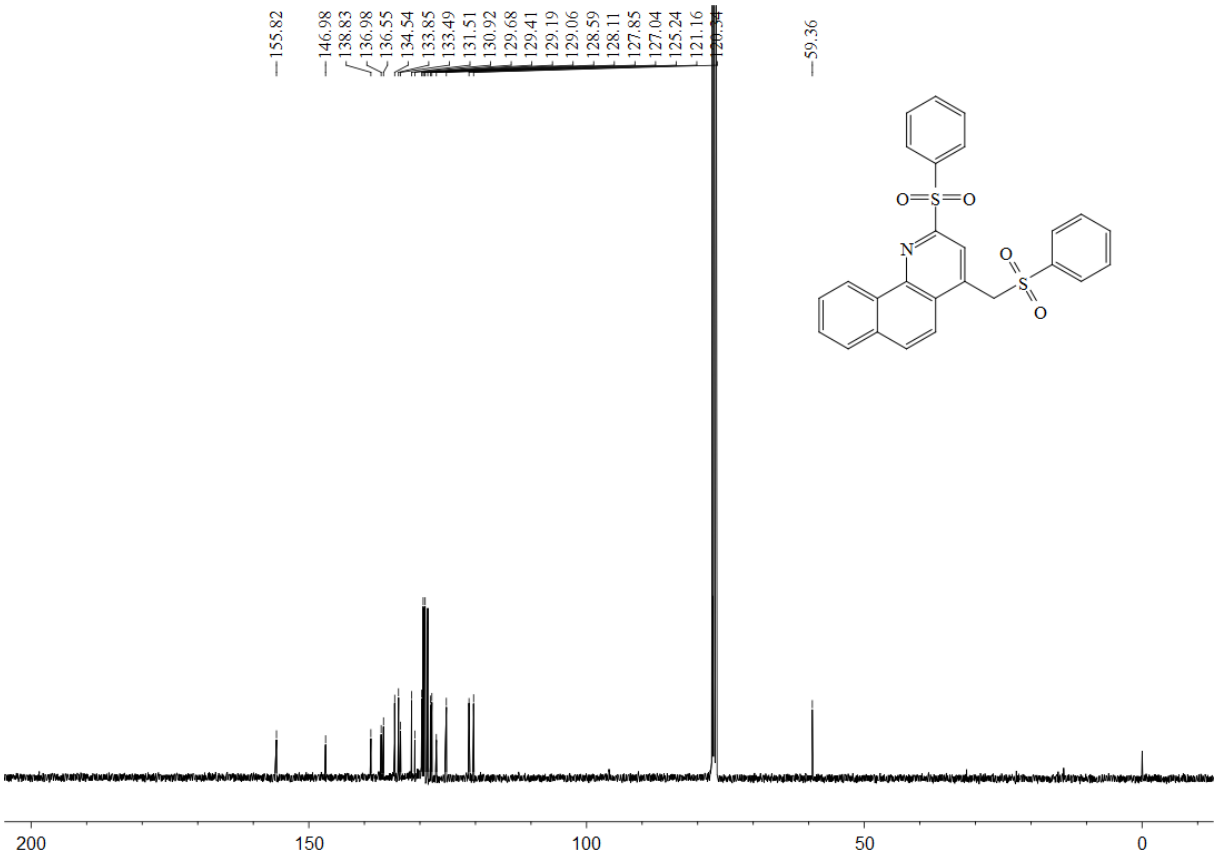


Figure S59. ^{1}H NMR spectrum of Compound **3ah** ($CDCl_3$, 400 MHz)

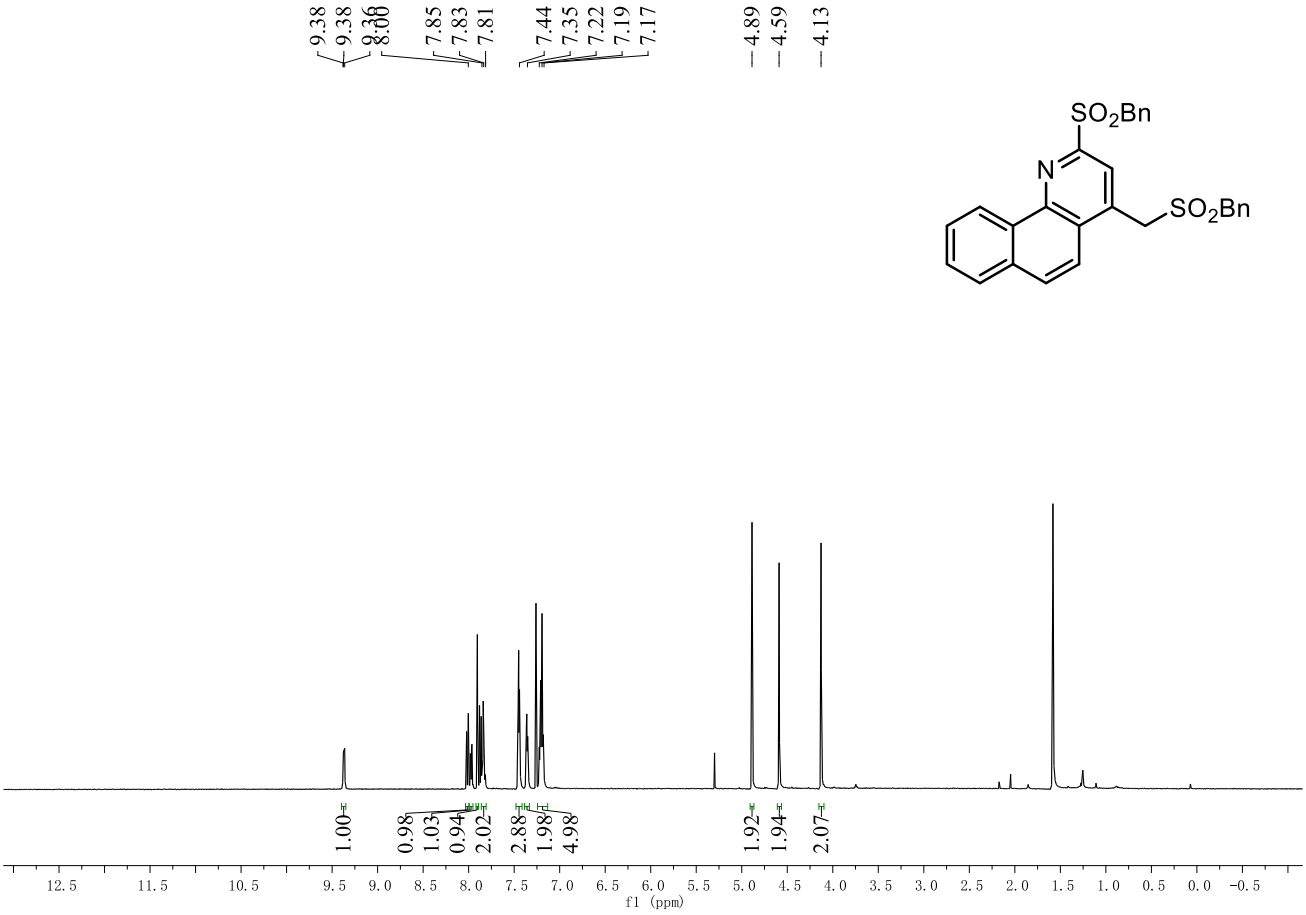


Figure S60. ^{13}C NMR spectrum of Compound **3ah** ($CDCl_3$, 100 MHz)

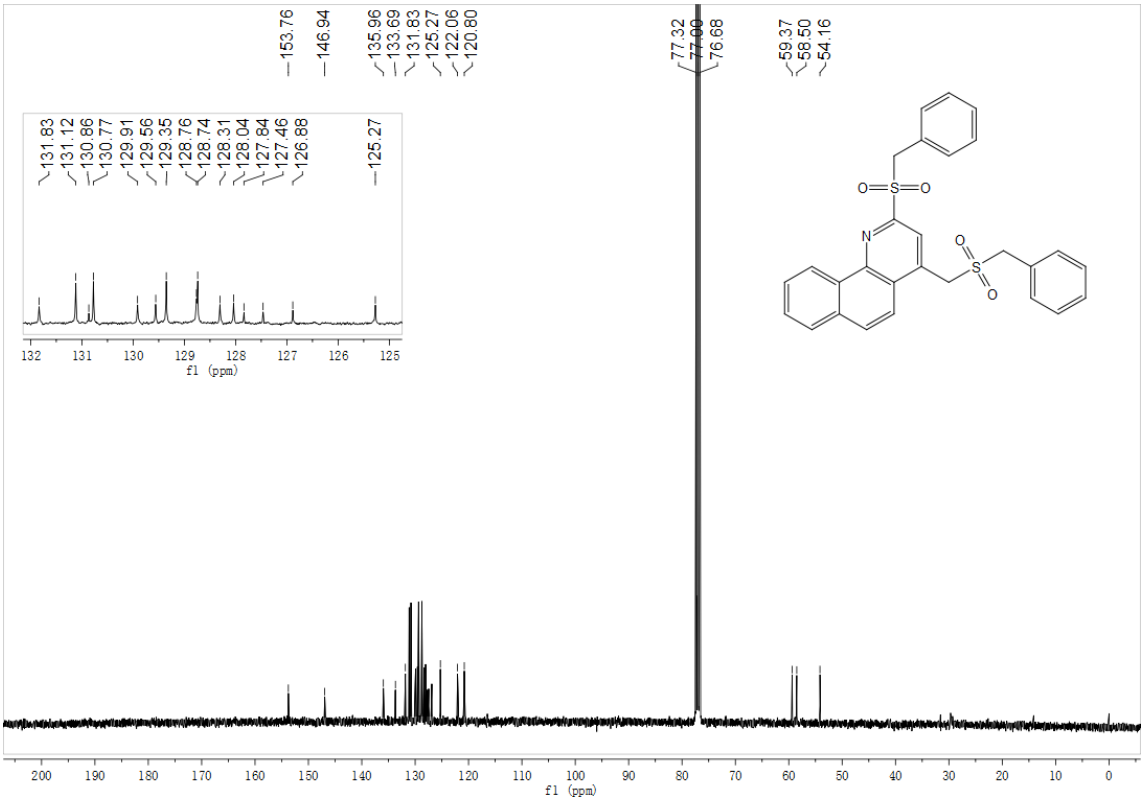


Figure S61. ^{1}H NMR spectrum of Compound **4ua** ($CDCl_3$, 500 MHz)

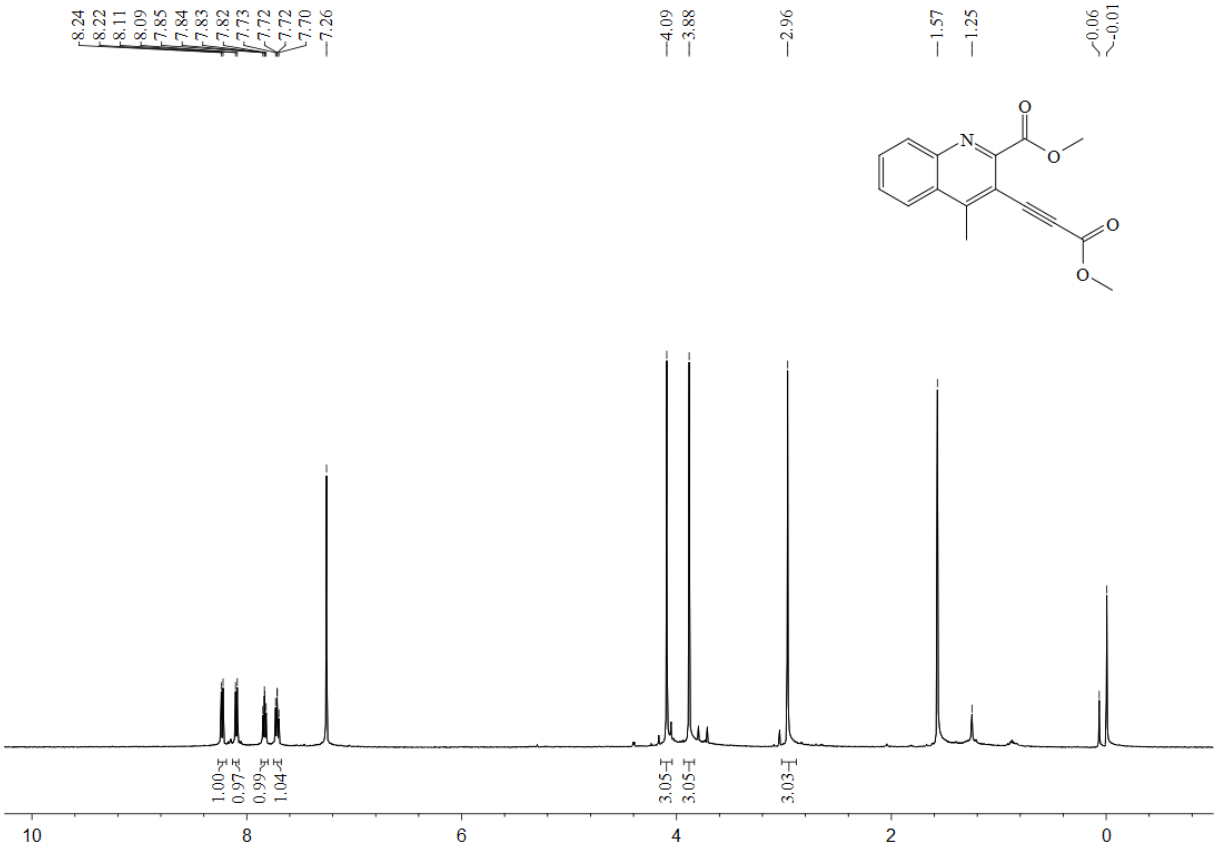


Figure S62. ^{13}C NMR spectrum of Compound **4ua** ($CDCl_3$, 125 MHz)