Electronic Supplementary Information

Hydride Transfer-initiated Synthesis of 3-Functionalized Quinolines by Deconstruction of Isoquinoline Derivatives

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1. General information

All the obtained products were characterized by ^{1}H-NMR, ^{13}C-NMR and mass spectra (MS), high-resolution mass spectra (HRMS), and melting points (m.p.). The NMR spectra were recorded on Bruker spectrometer (^{1}H at 500 MHz, ^{13}C at 126 MHz and ^{19}F at 471 MHz). Chemical shifts (δ) were given in ppm with reference to solvent signals [^{1}H NMR: $CDCl_3$ (7.26); ^{13}C NMR: $CDCl_3$ (77.16); ^{1}H NMR: DMSO-d_6 (2.50); ^{13}C NMR: DMSO-d_6 (40.01); ^{1}H NMR: CD_3OD (3.31); ^{13}C NMR: CD_3OD (49.00)]. ^{1}H NMR data are reported as followed: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz), and integration. High-resolution mass spectra (HRMS) were recorded on a thermo scientific Q Exactive Ultimate 3000 UPLC. Melting points were measured on a BUCHI Melting Point M-565. Column chromatography was performed on silica gel (200-300 mesh). TLC was performed using commercially prepared 1600-2000 mesh silica gel plates (GF254), and visualization was effected with short wavelength UV light (254 nm).

All the reagents were purchased from Bide Pharmatech Ltd. and Energy Chemical. All solvents were purchased from Greagent (Shanghai Titansci incorporated company) and used without further purification.

2. Experimental Section

2.1. Substrates preparation.

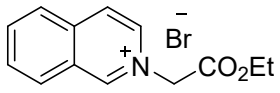
(1) Synthesis of isoquinolinium salts (1a-1n, 1p)[1]:

Method 1: Synthesis of compound **1a**: isoquinoline (3 mmol), ethyl bromoacetate or benzyl bromide (4.5 mmol) and acetone (3 mL) were introduced in a flask (50 mL). And it was stirred at room temperature for 24 hours. Then, the solvent was removed. The reaction mixture was washed with small amount of diethyl ether and finally dried under vacuum to get **1a**.

Method 2: Synthesis of compound **1i**: 6-phenylisoquinoline (3 mmol), ethyl bromoacetate (4.5 mmol) and toluene (3 mL) were introduced in a flask (50 mL). And it was stirred at 100 °C for 24 hours. Then, the solvent was removed. The reaction mixture was washed with small amount of diethyl ether and finally dried under vacuum to get **1i**.

Method 3: Synthesis of compound **1o**[2]: The oven-dried round-bottom flask were charged with CH_3CN (15 mL), isoquinoline (5mmol, 1.0equiv), CH_3I (10 mmol, 2.0 eq). The reaction mixture was refluxed for 12 hours, and then cooled to room temperature. When ethyl acetate was added to the system, the isoquinoline salt precipitated quickly as a solid, which was filtered and washed with ethyl acetate to give pure product **1o**.

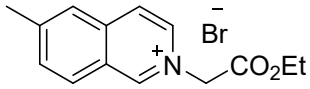
(1) 2-(2-ethoxy-2-oxoethyl)isoquinolin-2-ium bromide (**1a**)[1]



Method 1, White solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.22 (d, J = 10.0 Hz, 1H), 8.85 (d, J = 5.0 Hz, 1H), 8.70 (d, J = 5.0 Hz, 1H), 8.53 (d, J = 10.0 Hz, 1H), 8.40 (d, J = 10.0 Hz, 1H), 8.31 (t, J = 10.0 Hz, 1H), 8.10 (t, J = 10.0 Hz, 1H), 5.90 (d, J = 5.0 Hz, 2H), 4.26 (q, J = 10.0 Hz, 2H), 1.26 (t, J = 5.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.47, 151.72, 137.62, 137.25, 136.12, 131.42, 130.60, 127.35, 126.64,

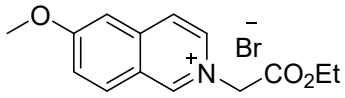
125.38, 62.31, 60.14, 13.93. HRMS (ESI): Calcd. for $C_{13}H_{14}NO_2$ $[M\text{-}Br]^+$: 216.1025; found: 216.1017.

(2) 2-(2-ethoxy-2-oxoethyl)-6-methylisoquinolin-2-ium bromide (**1b**)[1]



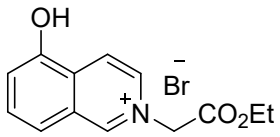
Method 1, Brown solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.08 (s, 1H), 8.76 (d, J = 5.0 Hz, 1H), 8.53 (d, J = 5.0 Hz, 1H), 8.42 (d, J = 10.0 Hz, 1H), 8.16 (s, 1H), 7.94 (d, J = 10.0 Hz, 1H), 5.84 (s, 2H), 4.25 (q, J = 10.0 Hz, 2H), 2.66 (s, 3H), 1.26 (t, J = 10.0 Hz 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.63, 150.95, 149.51, 137.45, 136.20, 133.59, 130.32, 126.13, 125.01, 124.47, 62.29, 59.91, 22.31, 13.96. HRMS (ESI): Calcd. For $C_{14}H_{16}NO_2$ $[M\text{-}Br]^+$: 230.1181; found: 230.1173.

(3) 2-(2-ethoxy-2-oxoethyl)-6-methoxyisoquinolin-2-ium bromide (**1c**)[1]



Method 1, White solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 8.67 (d, J = 10.0 Hz, 1H), 8.42 (d, J = 10.0 Hz, 1H), 8.39 (d, J = 5.0 Hz, 1H), 7.82 (s, 1H), 7.66 (d, J = 10.0 Hz, 1H), 5.78 (s, 2H), 4.24 (q, J = 5.0 Hz, 2H), 4.06 (s, 3H), 1.25 (t, J = 5.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.79, 166.04, 149.62, 140.29, 136.30, 132.58, 124.19, 123.31, 122.06, 106.01, 62.23, 59.45, 56.80, 13.96. HRMS (ESI): Calcd. for $C_{14}H_{16}NO_3$ $[M\text{-}Br]^+$: 246.1130; found: 246.1121.

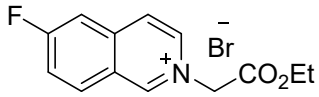
(4) 2-(2-ethoxy-2-oxoethyl)-5-hydroxyisoquinolin-2-ium bromide (**1d**)[1]



Method 1, Orange solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.50 (s, 1H), 10.14 (s, 1H), 8.72 (d, J = 10.0 Hz, 1H), 8.57 (d, J = 5.0 Hz, 1H), 7.87 – 7.89 (m, 2H), 7.65 (d, J = 5.0 Hz, 1H), 5.89 (s, 2H), 4.23 (q, J = 10.0, 2H), 1.24 (t, J = 10.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.55, 153.01, 151.23, 134.95, 132.64, 128.20,

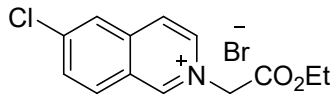
127.73, 120.45, 120.38, 118.96, 62.32, 60.08, 13.97. HRMS (ESI): Calcd. for $C_{13}H_{14}NO_3$ $[M\text{-}Br]^+$: 232.0974; found: 232.0965.

(5) 2-(2-ethoxy-2-oxoethyl)-6-fluoroisoquinolin-2-ium bromide (**1e**)[1]



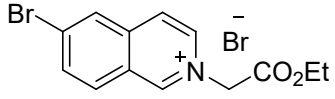
Method 1, Brown solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.22 (s, 1H), 8.85 (d, J = 5.0 Hz, 1H), 8.70 – 8.65 (m, 2H), 8.28 (t, J = 5.0 Hz, 1H), 8.06 – 8.02 (m, 1H), 5.87 (s, 2H), 4.25 (q, J = 10.0 Hz, 2H), 1.26 (t, J = 10.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.03 (d, J = 260.8 Hz), 166.95, 151.97, 140.29 (d, J = 12.6 Hz), 137.30, 135.47 (d, J = 11.3 Hz), 125.29 (d, J = 6.3 Hz), 124.68, 122.71 (d, J = 26.5 Hz), 112.20 (d, J = 22.7 Hz), 62.86, 60.59, 14.44. ^{19}F NMR (471 MHz, DMSO-d_6) δ -94.70. HRMS (ESI): Calcd. for $C_{13}H_{13}FNO_2$ $[M\text{-}Br]^+$: 234.0930; found: 234.0921.

(6) 2-(2-ethoxy-2-oxoethyl)-6-chloroisoquinolin-2-ium bromide (**1f**)[1]



Method 1, Yellow solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.18 (s, 1H), 8.85 (d, J = 5.0 Hz, 1H), 8.62 (d, J = 5.0 Hz, 1H), 8.59 – 8.58 (m, 2H), 8.13 (d, J = 5.0 Hz, 1H), 5.85 (s, 2H), 4.26 (q, J = 5.0 Hz, 2H), 1.26 (t, J = 5.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.35, 151.78, 142.65, 138.08, 137.22, 132.77, 132.12, 126.42, 125.21, 124.50, 62.38, 60.22, 13.94. HRMS (ESI): Calcd. for $C_{13}H_{13}ClNO_2$ $[M\text{-}Br]^+$: 250.0635; found: 250.0625.

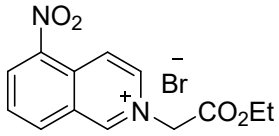
(7) 2-(2-ethoxy-2-oxoethyl)-6-bromoisoquinolin-2-ium bromide (**1g**)[1]



Method 1, Brown solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.22 (s, 1H), 8.87 (d, J = 10.0 Hz, 1H), 8.75 (s, 1H), 8.62 (d, J = 10.0 Hz, 1H), 8.48 (d, J = 10.0 Hz, 1H), 8.23 (d, J = 5.0 Hz, 1H), 5.87 (s, 2H), 4.25 (q, J = 5.0 Hz, 2H), 1.26 (t, J = 5.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.34, 151.99, 138.10, 137.26, 134.73, 132.50,

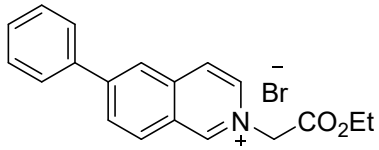
132.44, 129.74, 125.40, 124.39, 62.38, 60.26, 13.96. HRMS (ESI): Calcd. for $C_{13}H_{13}BrNO_2$ $[M\text{-}Br]^+$: 294.0130; found: 294.0119.

(8) 2-(2-ethoxy-2-oxoethyl)-5-nitroisoquinolin-2-ium bromide (**1h**)[1]



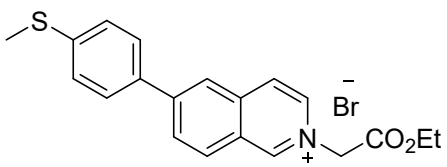
Method 1, Brown solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.44 (s, 1H), 9.11 (d, J = 7.8 Hz, 1H), 9.08 (d, J = 7.2 Hz, 1H), 9.02 (d, J = 7.2 Hz, 1H), 8.95 (d, J = 8.2 Hz, 1H), 8.29 (t, J = 8.0 Hz, 1H), 5.93 (s, 2H), 4.28 (q, J = 7.0 Hz, 2H), 1.28 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.14, 152.82, 144.17, 138.83, 137.80, 135.04, 130.91, 129.71, 127.56, 121.47, 62.46, 60.39, 13.94. HRMS (ESI): Calcd. for $C_{13}H_{13}N_2O_4$ $[M\text{-}Br]^+$: 261.0875; found: 261.0868.

(9) 2-(2-ethoxy-2-oxoethyl)-6-phenylisoquinolin-2-ium bromide (**1i**)[1]



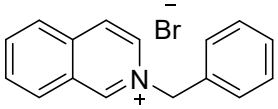
Method 2, White solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.14 (s, 1H), 8.81 (d, J = 5.0 Hz, 1H), 8.73 (s, 1H), 8.66 (d, J = 10.0 Hz, 1H), 8.60 (d, J = 10.0 Hz, 1H), 8.44 (d, J = 10.0 Hz, 1H), 7.98 (d, J = 10.0 Hz, 2H), 7.61 (t, J = 10.0 Hz, 2H), 7.57 (d, J = 5.0 Hz, 1H), 5.87 (s, 2H), 4.27 (q, J = 5.0 Hz, 2H), 1.28 (t, J = 10.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.55, 151.18, 148.26, 137.81, 137.48, 136.45, 131.28, 130.38, 129.90, 129.42 , 127.85, 125.80, 125.37, 124.31, 62.34, 60.07, 13.95. HRMS (ESI): Calcd. for $C_{19}H_{18}NO_2$ $[M\text{-}Br]^+$: 292.1338; found: 292.1326.

(10) 2-(2-ethoxy-2-oxoethyl)-6-(4-(methylthio)phenyl)isoquinolin-2-ium bromide (**1j**)[1]



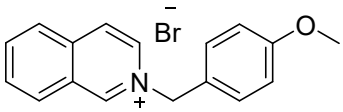
Method 2, Yellow solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.03 (d, J = 10.0 Hz, 1H), 8.75 (d, J = 5.0 Hz, 1H), 8.70 (s, 1H), 8.61 (d, J = 5.0 Hz, 1H), 8.57 (d, J = 10.0 Hz, 1H), 8.45 (d, J = 10.0 Hz, 1H), 7.97 – 7.95 (m, 2H), 7.48 (d, J = 10.0 Hz, 2H), 5.81 (t, J = 5.0 Hz, 2H), 4.27 (q, J = 5.0 Hz, 2H), 2.57 (s, 3H), 1.28 (t, J = 10.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.58, 150.97, 147.65, 141.44, 137.89, 136.44, 133.41, 131.29, 129.99, 128.18, 126.20, 125.69, 125.24, 123.49, 62.34, 60.03, 14.24, 13.95. HRMS (ESI): Calcd. for $C_{20}H_{20}NO_2S$ $[M\text{-}Br]^+$: 338.1215; found: 338.1203.

(11) 2-benzylisoquinolin-2-ium bromide (**1k**)[1]



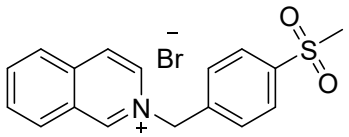
Method 1, White solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.49 (s, 1H), 8.91 (d, J =5.0 Hz, 1H), 8.63 (d, J = 10.0 Hz, 1H), 8.55 (d, J = 10.0 Hz, 1H), 8.35 (d, J = 5.0 Hz, 1H), 8.25 (t, J = 10.0 Hz, 1H), 8.07 (t, J = 10.0 Hz, 1H), 7.66 (s, 1H), 7.65 (s, 1H), 7.45 – 7.39 (m, 3H), 6.06 (s, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 150.12, 137.05, 136.98, 134.73, 134.30, 131.25, 130.51, 129.24, 129.11, 128.90, 127.29, 127.23, 126.23, 63.08. HRMS (ESI): Calcd. for $C_{16}H_{14}N$ $[M-Br]^+$: 220.1126; found: 220.1116.

(12) 2-(4-methoxybenzyl)isoquinolin-2-ium bromide (**1l**)[1]



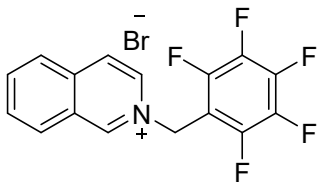
Method 1, White solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.46 (d, J = 25.0 Hz, 1H), 8.91 (t, J = 5.0 Hz, 1H), 8.62 (d, J = 5.0 Hz, 1H), 8.55 (d, J = 10.0 Hz, 1H), 8.36 (d, J = 5.0 Hz, 1H), 8.26 (t, J = 5.0 Hz, 1H), 8.08 (t, J = 10.0, 5.0 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.31 (d, J = 5.0 Hz, 1H), 7.19 (d, J = 5.0 Hz, 1H), 6.98 (d, J = 5.0 Hz, 1H), 6.00 (d, J = 5.0 Hz, 2H), 3.76 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 159.61, 150.14, 137.07, 137.00, 135.59, 134.73, 131.25, 130.55, 130.33, 127.30, 127.24, 126.19, 120.93, 114.87, 114.72, 63.08, 55.30. HRMS (ESI): Calcd. for $C_{17}H_{16}NO$ $[M-Br]^+$: 250.1232; found: 250.1222.

(13) 2-(4-methylsulfonylbenzyl)isoquinolin-2-ium bromide (**1m**)[1]

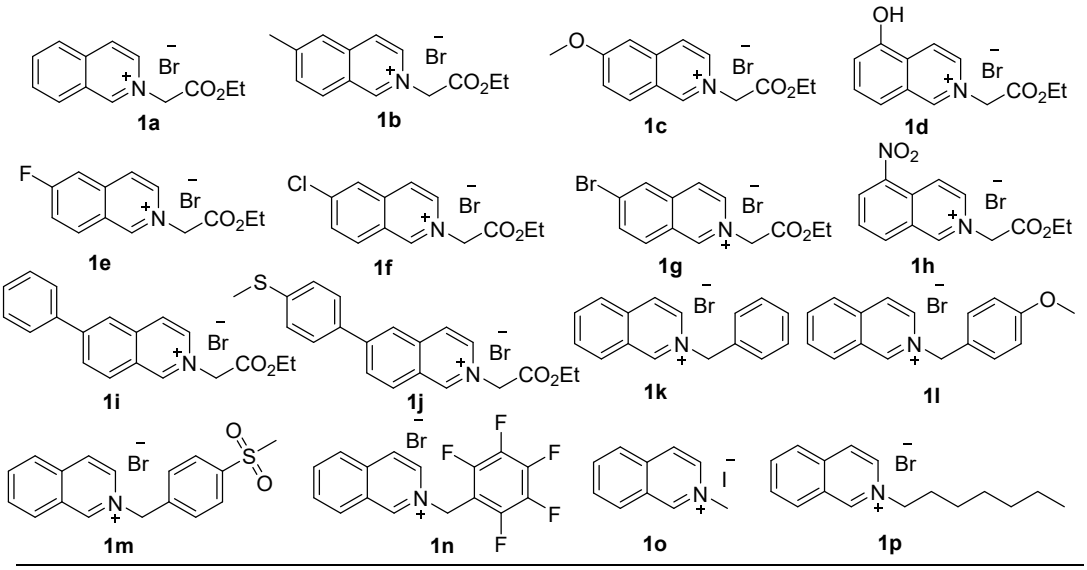


Method 1, White solid, ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.50 (d, J = 5.0 Hz, 1H), 8.93 (d, J = 5.0 Hz, 1H), 8.66 (d, J = 10.0 Hz, 1H), 8.56 (d, J = 5.0 Hz, 1H), 8.38 (d, J = 10.0 Hz, 1H), 8.28 (t, J = 10.0 Hz, 1H), 8.09 (t, J = 10.0 Hz, 1H), 7.99 (d, J = 10.0 Hz, 2H), 7.89 (s, 1H) 7.90 (s, 1H), 6.21 (s, 2H), 3.23 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 150.66, 141.38, 139.68, 137.25, 137.13, 134.89, 131.34, 130.65, 129.78, 127.64, 127.34, 127.31, 126.37, 62.20, 43.33. HRMS (ESI): Calcd. for $C_{17}H_{16}NO_2S$ $[M-Br]^+$: 298.0902; found: 298.0892.

(14) 2-((perfluorophenyl)methyl)isoquinolin-2-ium bromide (**1n**)[1]



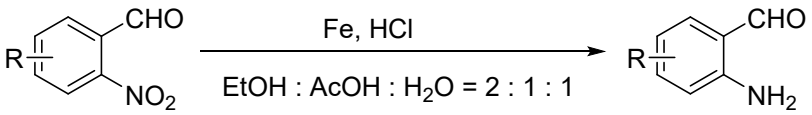
Method 1, White solid, ^{1}H NMR (500 MHz, CD_3OD) δ 10.17 (s, 1H), 8.75 (d, J = 6.8 Hz, 1H), 8.64 (d, J = 8.4 Hz, 1H), 8.61 (d, J = 6.9 Hz, 1H), 8.37 (d, J = 8.3 Hz, 1H), 8.30 (t, J = 7.6 Hz, 1H), 8.11 (t, J = 7.6 Hz, 1H), 6.30 (s, 2H). ^{13}C NMR (126 MHz, CD_3OD) δ 151.65, 148.55 – 148.33 (m), 146.56 – 145.05 (m), 143.21 – 143.01 (m), 140.49 - 140.21 (m), 139.38, 139.09, 138.50 – 138.23 (m), 135.76, 132.88, 132.06, 129.29, 128.63, 128.12, 108.58 (td, J = 17.2, 4.0 Hz), 53.10. ^{19}F NMR (471 MHz, DMSO-d_6) δ -139.69 (dd, J = 23.3, 6.6 Hz), -152.34 (d, J = 21.3 Hz), -161.63 (dd, J = 30.6, 14.7 Hz). HRMS (ESI): Calcd. for $C_{16}H_9F_5N$ $[M-Br]^+$: 216.1025; found: 216.1017.



Scheme S1 Various isoquinolinium salts employed for the reaction.

(2) Synthesis of 2-aminobenzaldehyde derivatives 2

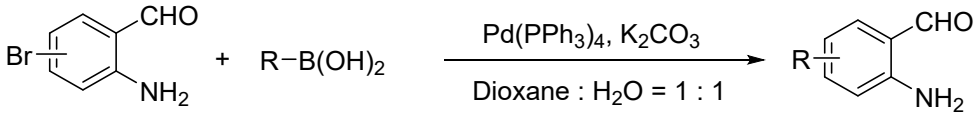
Method 1[3]**:**



Scheme S2 Synthesis of 2-aminobenzaldehyde derivatives.

A mixture of 2-nitro carbonyl compounds (3 mmol), iron powder (20 mmol), HCl (2 drops), and a mixture of EtOH, HOAc and H_2O (2 : 2 : 1 = 10 mL : 10 mL : 5 mL) were refluxed for 15 min and then stirred at 25 °C for 25 minutes. The solution was filtered, diluted with water (20 mL), and extracted with CH_2Cl_2 (3 x 30 mL). The organic layer was washed with saturated $NaHCO_3$ (2 x 30 mL) and H_2O (2 x 30 mL), dried using anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel to provide the corresponding 2-amino carbonyl compounds with high purity. 2-aminobenzaldehydes (**2b**, **2i**, **2j**, **2o**) were obtained were shown in Scheme S2.

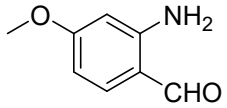
Method 2[4]**:**



Scheme S3 Synthesis of 2-aminobenzaldehyde derivatives.

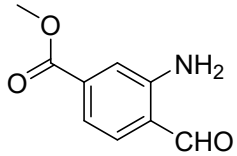
The 2-amino-5-bromobenzaldehyde (2 mmol), *p*-tolylboronic acid (2.4 mmol), K_2CO_3 (6 mmol), $Pd(PPh_3)_4$ (5 mol %), 2.5 mL dioxane and 2.5 mL H_2O were taken in a 50 mL Schlenk tube. The tube was evacuated and backfilled with N_2 for three times. The mixture was stirred at 100 °C for 3 h. The reaction mixture was poured into 20 mL of ethyl acetate and the organic layer was separated. The organic layer was washed with 1M HCl and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by chromatography on silica gel to afford the coupling product. 2-aminobenzaldehydes derivatives (**2l**, **2m, 2n**) were obtained were shown in Scheme S3.

(1) 2-amino-4-methoxybenzaldehyde (**2b**)[3]



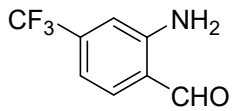
Method 1, ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.63 (s, 1H), 7.41 (d, J = 9.2 Hz, 1H), 7.20 (s, 2H), 6.25 – 6.21 (m, 2H), 3.75 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 191.60, 164.72, 153.02, 137.60, 112.92, 104.30, 97.67, 55.15.

(2) methyl 3-amino-4-formylbenzoate (**2i**)[3]



Method 1, ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 7.68 (d, J = 8.2 Hz, 1H), 7.42 (s, 1H), 7.29 (s, 2H), 7.13 (d, J = 8.2 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 194.21, 165.87, 150.25, 135.88, 134.68, 119.79, 117.21, 114.46, 52.38.

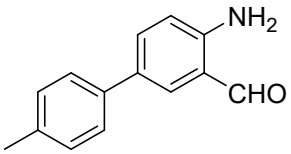
(3) 2-amino-4-(trifluoromethyl)benzaldehyde (**2j**)[3]



Method 1, ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 7.74 (d, J = 7.9 Hz, 1H), 7.42 (s, 2H), 7.13 (s, 1H), 6.85 (d, J = 8.0 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ

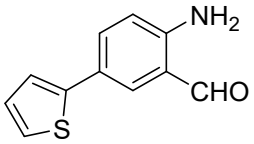
194.06, 150.39, 136.83, 134.30 (d, J = 31.6 Hz), 124.81, 122.64, 119.43, 112.75 – 112.68 (m), 110.28 (d, J = 3.2 Hz). ^{19}F NMR (471 MHz, DMSO) δ -62.89.

(4) 2-amino-4-(*p*-tolyl))benzaldehyde (**2l**)[4]



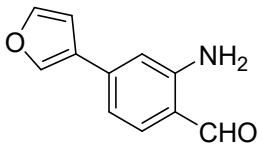
Method 2, ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.07 (s, 1H), 8.81 (d, J = 2.2 Hz, 1H), 8.70 (dd, J = 8.6, 2.2 Hz, 1H), 8.56 (d, J = 8.2 Hz, 2H), 8.38 – 8.35 (m, 2H), 7.85 (d, J = 8.6 Hz, 1H), 3.51 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.33, 149.10, 137.22, 136.62, 134.06, 133.71, 129.84, 129.72, 126.16, 119.16, 116.75, 21.19.

(5) 2-amino-5-(thiophen-2-yl)benzaldehyde (**2m**)[4]



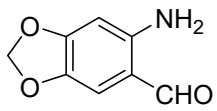
Method 2, ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 7.69 (s, 1H), 7.56 (d, J = 8.6 Hz, 1H), 7.21 (d, J = 5.0 Hz, 1H), 7.18 (d, J = 2.8 Hz, 1H), 7.07 – 7.04 (m, 1H), 6.67 (d, J = 8.6 Hz, 1H), 6.21 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.01, 149.29, 143.67, 133.17, 132.79, 128.08, 123.61, 123.46, 121.77, 118.76, 116.75.

(6) 2-amino-4-(furan-3-yl)benzaldehyde (**2n**)[4]

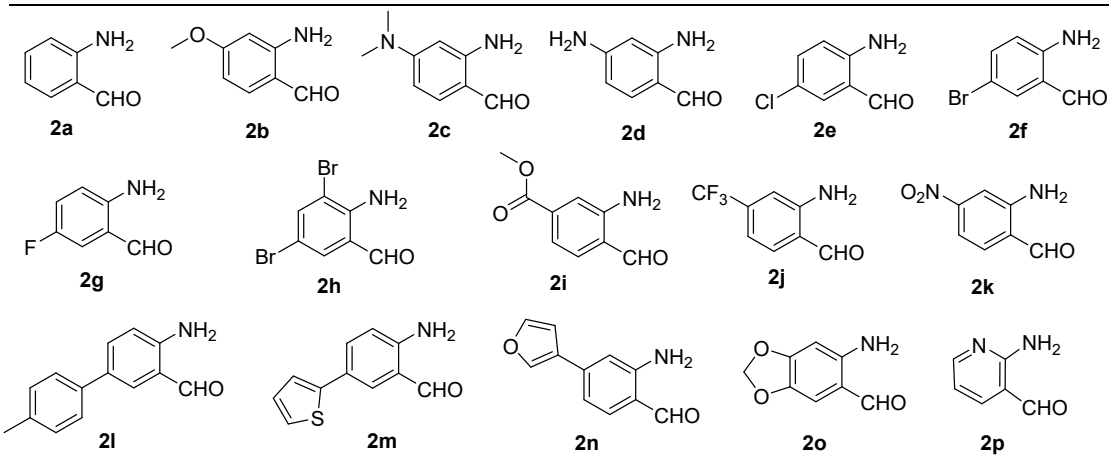


Method 2, ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.79 (s, 1H), 7.51 – 7.45 (m, 2H), 7.47 (d, J = 8.2 Hz, 1H), 6.88 (dd, J = 8.2, 1.0 Hz, 1H), 6.75 (s, 1H), 6.69 (s, 1H), 6.18 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.32, 150.41, 144.13, 140.18, 139.23, 136.44, 125.81, 117.97, 114.54, 112.63, 108.76.

(7) 6-aminobenzo[*d*][1,3]dioxole-5-carbaldehyde (**2o**)[3]



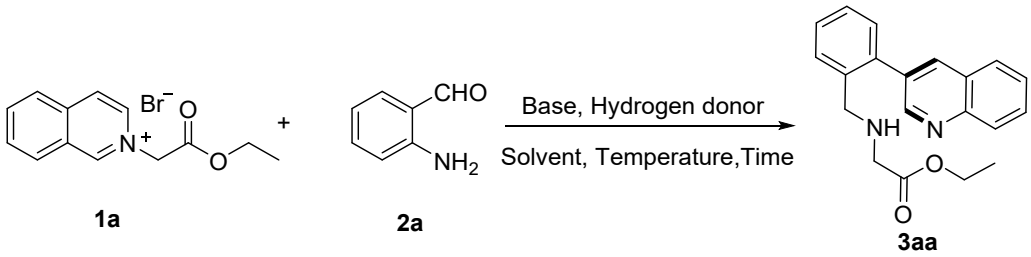
Method 1, ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.54 (s, 1H), 7.25 (s, 2H), 6.99 (s, 1H), 6.31 (s, 1H), 5.96 (s, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 190.47, 153.54, 150.12, 138.09, 110.95, 110.65, 101.26, 95.17.



Scheme S4. Substrates employed for the reaction.

2.2. Detailed Optimization Studies

Table S1. Screening of hydrogen donor.[a]



Entry	Hydrogen donor	Base	Yield (%)[b]
1	1,1,3,3-Tetramethyldisiloxane	Cs_2CO_3	5
2	$(EtO)_3SiH$	Cs_2CO_3	27
3	Et_2SiH_2	Cs_2CO_3	<5
4	Et_3SiH	Cs_2CO_3	Trace
5	$PhSiH_3$	Cs_2CO_3	50[c]
6	HBpin	Cs_2CO_3	Trace
7	$(EtO)_3SiH$	Cs_2CO_3	Trace
8	Polymethylhydrosiloxane	Cs_2CO_3	Trace

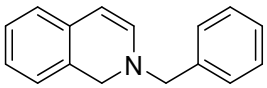
[a]Unless otherwise stated, all the reactions were performed with **1a** (0.2 mmol), **2a** (0.2 mmol), hydrogen donor (1 equiv.), additive (0.5 equiv), *t*-AmOH (1.0 mL) at 85 °C for 16 h. [b]GC yield using hexadecane as an internal standard. [c]0.5 equiv. $PhSiH_3$.

2.3. Typical procedure for the synthesis of 3aa

Under N_2 atmosphere, 2-(2-ethoxy-2-oxoethyl)isoquinolin-2-ium bromide **1a** (0.3 mmol), 2-aminobenzaldehyde **2a** (0.2 mmol), Cs_2CO_3 (50 mol %), $PhSiH_3$ (75 mol %) and *t*-AmOH (1.0 mL) were introduced in a Schlenk tube, successively. Then the Schlenk tube was closed and the resulting mixture was stirred at 85 °C oil bath for 20 h. After cooling down to room temperature, the resulting mixture was filtrated, extracted with ethyl acetate, washed with 5% Na_2CO_3 solution, dried with anhydrous Na_2SO_4, and then concentrated by removing the solvent under vacuum. Finally, the residue was purified by preparative TLC on silica, eluting with petroleum ether (PE) : ethyl acetate (EA) = 2 : 1 (v/v) to give *N*-(2-(quinolin-3-yl)benzyl)glycine ethyl ester **3aa.**

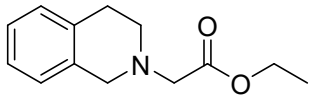
3. Control experiments

(1) Synthesis of 2-benzyl-1,2-dihydroisoquinoline (1k-1)[1]



To a suspension of 1-benzylisoquinolin-1-ium bromide **1k** (3.0 mmol) in 25 mL of THF was slowly added lithium aluminium hydride (3.0 mmol) at room temperature. The reaction was stirred at room temperature for 20 minutes, then slowly quenched with 0.1 mL of water and stirred for additional 10 minutes. To the reaction was added 0.2 mL 10% sodium hydroxide solution and stirred at room temperature for additional 10 minutes. The reaction was added 5% Na_2CO_3 solution and the resulting mixture was extracted with ethyl acetate, dried with anhydrous Na_2SO_4, and then concentrated by removing the solvent under vacuum to give the unstable crude 1-benzyl-1,2-dihydroisoquinoline as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 4H), 7.22 (td, *J* = 6.6, 6.2, 2.6 Hz, 1H), 7.03 (t, *J* = 7.8 Hz, 1H), 6.89 (td, *J* = 7.4, 1.2 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.76 (d, *J* = 7.4 Hz, 1H), 6.17 (d, *J* = 7.4 Hz, 1H), 5.26 (d, *J* = 7.4 Hz, 1H), 4.13 (s, 2H), 4.03 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.0, 137.4, 134.0, 128.8, 128.3, 127.7, 127.7, 125.7, 124.9, 122.9, 98.3, 59.4, 51.1.

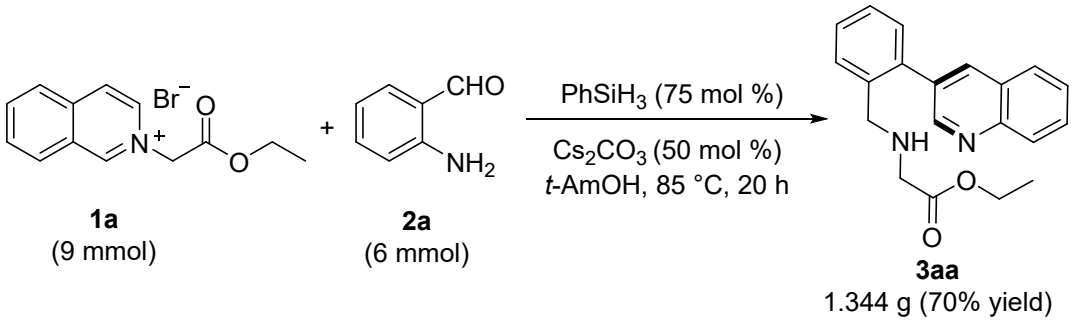
(2) Synthesis of ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (1a-2)[5]



A dried 250 mL round bottom flask was equipped with a magnetic stir bar and charged with 1,2,3,4-tetrahydroisoquinoline (30 mmol), Na_2CO_3 (20 mmol), and THF (60 mL). Then, ethyl bromoacetate (40 mmol) was added, and the resulting mixture appeared as a pale yellow emulsion. The reaction was stirred at room temperature overnight. After 1,2,3,4-tetrahydroisoquinoline was completely consumed as indicated by TLC, ethyl acetate and water were added to the reaction. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After the organic phase was filtered and concentrated, the residue was purified by column chromatography, eluting with PE : EA (20: 1 to 5:1) to give **1a-2** as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 – 7.05 (m, 3H), 7.00 (d, *J* = 6.4 Hz, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 2H), 3.41 (s, 2H), 2.96 – 2.91 (m, 2H), 2.91 – 2.87 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.58, 134.37, 133.94, 128.79, 126.58, 126.27, 125.73, 60.73, 59.21, 55.41, 50.75, 29.01, 14.38.

4. Synthetic applications

(1) One-pot gram scale synthesis of compound 3aa



1a
(9 mmol)

2a
(6 mmol)

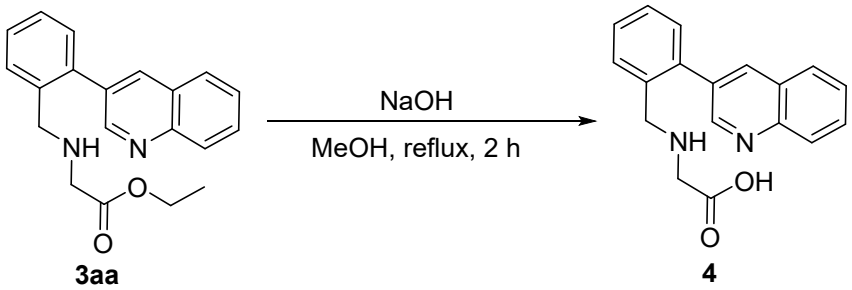
3aa
1.344 g (70% yield)

Scheme S5. Synthesis of compound **3aa**.

Under N_2 atmosphere, 2-(2-ethoxy-2-oxoethyl)isoquinolin-2-ium bromide **1a** (9 mmol), 2-aminobenzaldehyde **2a** (6 mmol), Cs_2CO_3 (50 mol%), $PhSiH_3$ (75 mol%) and *t*-AmOH (30.0 mL) were introduced successively in a Schlenk tube (100 mL) equipped with a magnetic stirrer bar. Then the Schlenk tube was closed and the resulting mixture was stirred at 85 °C oil bath for 24 h. After cooling down to room

temperature, the resulting mixture was extracted with ethyl acetate, washed with 5% Na_2CO_3 solution, dried with anhydrous Na_2SO_4, and then concentrated by removing the solvent under vacuum. Finally, the residue was purified by column chromatography, eluting with PE : EA = 5 : 1 (v/v) to give **3aa** (1.344 g, 70% yield).

(2) Synthesis of amino acid 4[6]



3aa **4**

Scheme S6. Synthesis of amino acid 4

Compound **3aa** (0.2 mmol) was dissolved in methanol (2 mL) and added 3N NaOH (aq) (0.1 mL, 0.3 mmol). The reaction was stirred at room temperature for 2 hours and monitored by TCL. The resulting mixture was filtered and concentrated under vacuum. The residue was directly purified by preparative TLC on silica, eluting with dichloromethane : methanol = 3 : 1 (v/v) to give amino acid **4** (95%) as yellow-orange solid. ^{1}H NMR (500 MHz,DMSO-d_6) δ 8.92 (s, 1H), 8.49 (s, 1H), 8.08 (d, J = 8.6 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 7.4 Hz, 1H), 7.81 (t, J = 7.6 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.60 – 7.51 (m, 2H), 7.45 (d, J = 7.0 Hz, 1H), 4.22 (s, 2H), 3.69 (s, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.75, 151.01, 146.63, 138.66, 136.10, 132.47, 130.94, 130.42, 130.09, 129.81, 128.90, 128.66, 128.51, 127.20, 127.02, 47.02, 46.91. HRMS (ESI): Calcd. for $C_{18}H_{16}N_2O_2$ $[M+H]^+$: 293.1285; found: 293.1280.

6. Reference

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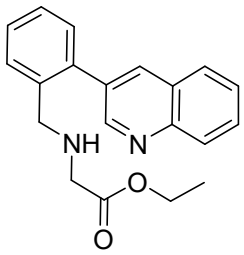
6 H. Neelakantan, H.-Y. Wang, V. Vance, J. D. Hommel, S. F. McHardy and S. J. Watowich, *J. Med. Chem.*, 2017, **60**, 5015.

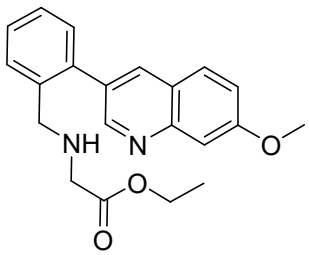
7. Analytic data of the obtained compounds

(1) ethyl (2-(quinolin-3-yl)benzyl)glycinate (3aa)



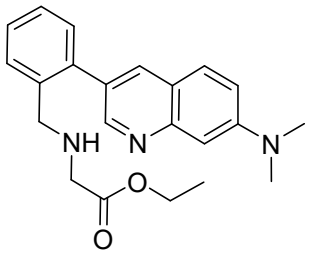
Yellow oil, 57.6 mg (90%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.24 (s, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.34 (d, *J* = 7.4 Hz, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.74 (s, 2H), 3.31 (s, 2H), 1.17 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.32, 151.43, 147.15, 138.35, 137.57, 135.67, 134.04, 130.62, 129.68, 129.54, 129.28, 128.48, 128.07, 127.71, 127.56, 126.98, 60.76, 50.81, 50.31, 14.20. HRMS (ESI): Calcd. for $C_{20}H_{20}N_2O_2$ $[M+H]^+$: 321.1598; found: 321.161202.

(2) ethyl (2-(7-methoxyquinolin-3-yl)benzyl)glycinate (3ab)



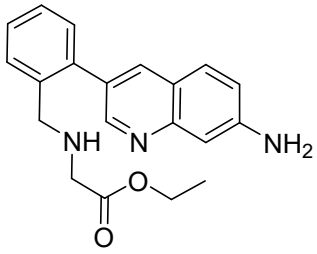
Yellow oil, 55.4 mg (79%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.15 (s, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.46 (s, 1H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.32 (d, *J* = 7.2 Hz, 1H), 7.22 (d, *J* = 9.0 Hz, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.96 (s, 3H), 3.73 (s, 2H), 3.31 (s, 2H), 1.17 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.32, 160.84, 151.42, 148.82), 138.52, 137.55, 135.47, 131.94, 130.64, 129.63, 129.07 , 128.27, 127.51, 122.90, 120.22, 107.15, 60.75, 55.60, 50.82, 50.31, 14.20. HRMS (ESI): Calcd. for $C_{21}H_{22}N_2O_3$ $[M+H]^+$: 351.1703; found: 351.1700.

(3) ethyl (2-(7-(dimethylamino)quinolin-3-yl)benzyl)glycinate (3ac)



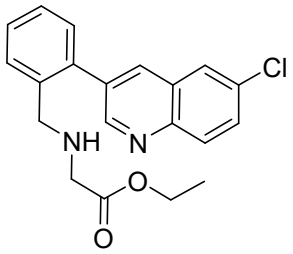
Dark brown oil, 44.3 mg (61%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.05 (s, 1H), 7.68 (d, *J* = 9.0 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.39 – 7.31 (m, 3H), 7.22 – 7.19 (m, 2H), 4.07 (q, *J* = 7.2 Hz, 2H), 3.76 (s, 2H), 3.31 (s, 2H), 3.11 (s, 6H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.31, 151.46, 151.17, 148.72, 138.87, 137.51, 135.52, 130.65, 129.98, 129.52, 128.67, 128.02, 127.46, 120.33, 116.79, 106.37, 60.76, 50.81, 50.31, 40.57, 14.21. HRMS (ESI): Calcd. for $C_{22}H_{25}N_3O_2$ $[M+H]^+$: 364.2020; found: 364.2017.

(4) ethyl (2-(7-aminoquinolin-3-yl)benzyl)glycinate (3ad)



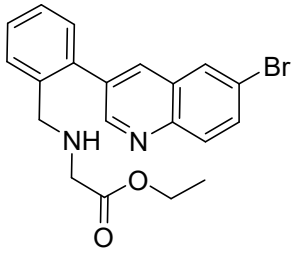
Dark brown oil, 56.3 mg (84%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.03 (s, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.53 (d, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.24 (s, 1H), 6.98 (d, *J* = 8.6 Hz, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.74 (s, 2H), 3.30 (s, 2H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.30, 151.20, 148.70, 148.20, 138.67, 137.46, 135.63, 130.57, 130.43, 129.51, 129.17, 128.04, 127.42, 121.51, 119.15, 108.57, 60.72, 50.74, 50.25, 14.15. HRMS (ESI): Calcd. for $C_{20}H_{21}N_3O_2$ $[M+H]^+$: 336.1707; found: 336.1704.

(5) ethyl (2-(6-chloroquinolin-3-yl)benzyl)glycinate (3ae)



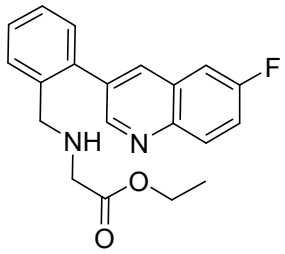
Yellow oil, 58.8 mg (83%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.18 (s, 1H), 8.07 (d, *J* = 9.0 Hz, 1H), 7.83 (s, 1H), 7.64 (d, *J* = 9.0 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.32 (d, *J* = 7.4 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.71 (s, 2H), 3.32 (s, 2H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.35, 151.72, 145.52, 137.95, 137.55, 134.93, 134.72, 132.70, 130.92, 130.54, 130.42, 129.89, 128.69, 128.36, 127.68, 126.70, 60.82, 50.87, 50.30, 14.22. HRMS (ESI): Calcd. for $C_{20}H_{19}ClN_2O_2$ $[M+H]^+$: 355.1208; found: 355.1205.

(6) ethyl (2-(6-bromoquinolin-3-yl)benzyl)glycinate (3af)



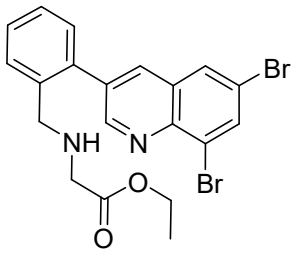
Yellow oil, 69.3 mg (87%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.18 (s, 1H), 8.00 (d, *J* = 9.8 Hz, 2H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.32 (d, *J* = 7.4 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.71 (s, 2H), 3.32 (s, 2H), 1.19 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.36, 151.86, 145.72, 137.93, 137.56, 134.91, 134.63, 132.96, 131.03, 130.56, 130.08, 129.91, 128.87, 128.71, 127.70, 120.88, 60.83, 50.88, 50.31, 14.24. HRMS (ESI): Calcd. for $C_{20}H_{19}BrN_2O_2$ $[M+H]^+$: 399.0703; found: 399.0701.

(7) ethyl (2-(6-fluoroquinolin-3-yl)benzyl)glycinate (3ag)



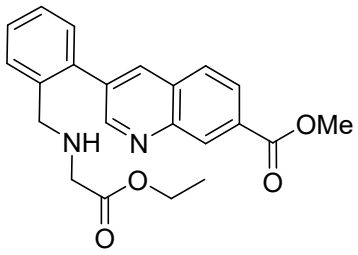
Yellow oil, 33.1 mg (49%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.22 (s, 1H), 8.14 (dd, *J* = 9.0, 5.4 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.48 – 7.41 (m, 2H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.73 (s, 2H), 3.32 (s, 2H), 1.19 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.39, 160.82 (d, *J* = 249.48 Hz), 150.86 (d, *J* = 2.5 Hz), 144.31, 138.08, 137.59, 135.07 (d, *J* = 5.0 Hz), 134.83, 131.84 (d, *J* = 8.8 Hz), 130.60, 129.87, 128.69 , 128.47 (d, *J* = 10.1 Hz), 127.69, 119.80 (d, *J* = 25.2 Hz), 111.04 (d, *J* = 21.4 Hz), 60.85, 50.89, 50.35, 14.25. ^{19}F NMR (471 MHz, $CDCl_3$) δ -112.85 (dd, *J* = 14.0, 8.2 Hz). HRMS (ESI): Calcd. for $C_{20}H_{19}FN_2O_2$ $[M+H]^+$: 339.1503; found: 339.1507.

(8) ethyl (2-(6,8-dibromoquinolin-3-yl)benzyl)glycinate (3ah)



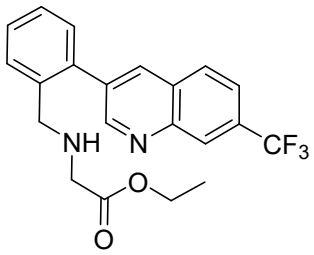
Yellow oil, 68.5 mg (72%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.22 (s, 1H), 8.14 (s, 1H), 7.99 (s, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 7.4 Hz, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.69 (s, 2H), 3.31 (s, 2H), 1.19 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.32, 152.54, 143.01, 137.53, 137.32, 135.79, 135.24, 133.91, 130.53, 130.03, 129.66, 128.94, 127.82, 125.75, 120.24, 60.87, 50.89, 50.27, 14.24. HRMS (ESI): Calcd. for $C_{20}H_{18}Br_2N_2O_2$ $[M+H]^+$: 476.9808; found: 476.9807.

(9) methyl 3-(2-(((2-ethoxy-2-oxoethyl)amino)methyl)phenyl)quinoline-7-carboxylate (3ai)



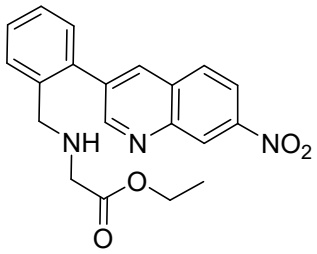
Yellow oil, 69.6 mg (92%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.84 (s, 1H), 8.28 (s, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.99 (s, 3H), 3.72 (s, 2H), 3.31 (s, 2H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.31, 166.82, 152.53, 146.43, 137.90, 137.53, 135.83, 135.31, 131.90, 130.88, 130.53, 130.18, 129.90, 128.75, 128.36, 127.69, 126.44, 60.78, 52.54, 50.84, 50.27, 14.20. HRMS (ESI): Calcd. for $C_{22}H_{22}N_2O_4$ $[M+H]^+$: 379.1652; found: 379.1647.

(10) ethyl (2-(7-(trifluoromethyl)quinolin-3-yl)benzyl)glycinate (3aj)



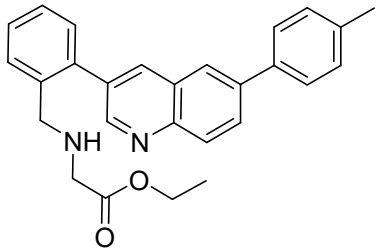
Yellow oil, 39.6 mg (51%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.46 (s, 1H), 8.35 (s, 1H), 8.00 (d, *J* = 8.6 Hz, 1H), 7.76 (d, *J* = 8.6 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 7.4 Hz, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.72 (s, 2H), 3.33 (s, 2H), 1.19 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.39, 152.98, 146.14, 137.68 (d, *J* = 31.5 Hz), 136.04, 135.50, 131.40 (t, *J* = 32.8 Hz), 130.61, 130.05, 129.38, 128.28, 128.92, 127.82, 127.20 (d, *J* = 4.4 Hz), 124.08 (d, *J* = 273.4 Hz), 122.69 (d, *J* = 2.9 Hz), 60.89, 50.94, 50.33, 14.24. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.57 (s). HRMS (ESI): Calcd. for $C_{21}H_{19}F_3N_2O_2$ $[M+H]^+$: 389.1471; found: 389.1468.

(11) ethyl (2-(7-nitroquinolin-3-yl)benzyl)glycinate (3ak)



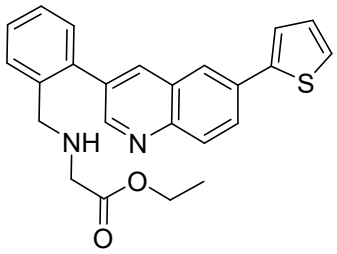
Dark brown oil, 35.8 mg (49 %), ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (s, 1H), 9.05 (s, 1H), 8.44 (s, 1H), 8.36 (d, *J* = 9.0 Hz, 1H), 8.04 (d, *J* = 9.0 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 8.2 Hz, 1H), 7.44 (t, *J* = 6.7 Hz, 1H), 7.38 (d, *J* = 7.4 Hz, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.74 (s, 2H), 3.35 (s, 2H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.38, 154.04, 148.11, 146.04, 137.60, 137.48, 137.16, 135.40, 131.05, 130.58, 130.28, 129.77, 129.16, 127.96, 125.74, 120.51, 60.91, 51.06, 50.36, 14.29. HRMS (ESI): Calcd. for $C_{20}H_{19}N_3O_4$ $[M+H]^+$: 366.1448; found: 366.1448.

(12) ethyl (2-(6-(*p*-tolyl)quinolin-3-yl)benzyl)glycinate (3al)



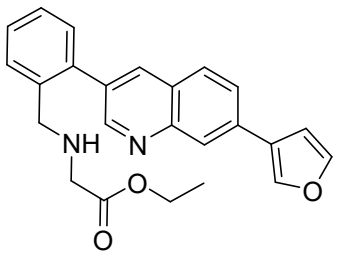
Yellow oil, 62.4 mg (76%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.28 (s, 1H), 8.21 (d, *J* = 8.8 Hz, 1H), 8.02 (s, 1H), 8.00 (d, *J* = 8.8 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.46 – 7.42 (m, 1H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.37 (d, *J* = 7.4 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.78 (s, 2H), 3.34 (s, 2H), 2.42 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.29, 151.18, 146.43, 139.68, 138.38, 137.71, 137.55, 137.43 135.79, 134.36, 130.58, 129.76, 129.71, 129.59, 129.24, 128.48, 127.94, 127.57, 127.31, 125.32, 60.75, 50.83, 50.31, 21.19, 14.19. HRMS (ESI): Calcd. for $C_{27}H_{26}N_2O_2$ $[M+H]^+$: 411.2067; found: 411.2064.

(13) ethyl (2-(6-(thiophen-2-yl)quinolin-3-yl)benzyl)glycinate (3am)



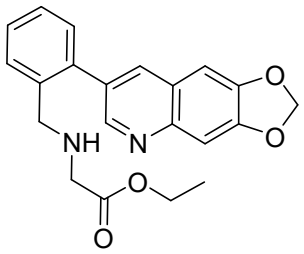
Yellow oil, 68.4 mg (85%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.23 (s, 1H), 8.14 (d, *J* = 8.8 Hz, 1H), 8.04 (s, 1H), 8.00 (d, *J* = 8.8 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 2.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.35 – 7.34 (m, 2H), 7.12 (t, *J* = 4.0 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.76 (s, 2H), 3.33 (s, 2H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.33, 151.28, 146.57, 143.53, 138.24, 137.56, 135.58, 134.66, 132.98, 130.56, 129.84, 129.75, 128.54, 128.38, 128.05, 128.02, 127.59, 125.81, 124.20, 123.98, 60.78, 50.83, 50.32, 14.21. HRMS (ESI): Calcd. for $C_{24}H_{22}N_2O_2S$ $[M+H]^+$: 403.1475; found: 403.1494.

(14) ethyl (2-(7-(furan-3-yl)quinolin-3-yl)benzyl)glycinate (3an)



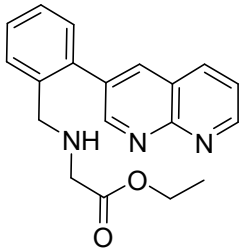
Yellow oil, 48.7 mg (63%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.23 (d, *J* = 15.0 Hz, 2H), 7.91 (s, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 7.4 Hz, 1H), 7.54 (s, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 7.4 Hz, 1H), 6.88 (s, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.76 (s, 2H), 3.33 (s, 2H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.35, 151.91, 147.61, 144.21, 139.56, 138.37, 137.60, 135.42, 133.77, 133.71, 130.62, 129.76, 128.56, 126.50, 127.61, 126.75, 126.12, 125.49, 125.12, 108.90, 60.80, 50.88, 50.36, 14.23. HRMS (ESI): Calcd. for $C_{24}H_{22}N_2O_3$ $[M+H]^+$: 387.1703; found: 387.1705.

(15) ethyl (2-([1,3]dioxolo[4,5-g]quinolin-7-yl)benzyl)glycinate (3ao)



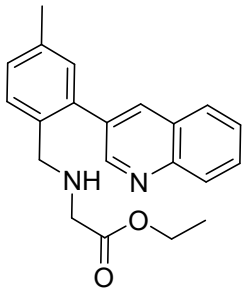
Yellow oil, 40.1 mg (40.1%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.04 (s, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.41 (s, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.07 (s, 1H), 6.10 (s, 2H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.73 (s, 2H), 3.31 (s, 2H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.37, 150.84, 148.87, 148.24, 145.42, 138.49, 137.52, 134.80, 132.47, 130.60, 129.63, 128.30, 127.51, 124.78, 105.67, 103.00, 101.86, 60.81, 50.82, 50.34, 14.23. HRMS (ESI): Calcd. for $C_{21}H_{20}N_2O_4$ $[M+H]^+$: 365.1496; found: 365.1493.

(16) ethyl (2-(1,8-naphthyridin-3-yl)benzyl)glycinate (3ap)



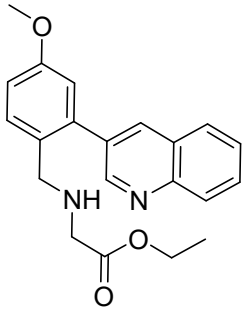
Yellow oil, 30.2 mg (30.2%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.16 (s, 1H), 9.11 (s, 1H), 8.36 – 8.21 (m, 2H), 7.59 – 7.49 (m, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.33 (d, *J* = 6.8 Hz, 1H), 4.07 (q, *J* = 7.2 Hz, 2H), 3.71 (s, 2H), 3.31 (s, 2H), 1.17 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.27, 155.23, 154.70, 153.55, 137.48, 137.60, 136.69, 135.24, 130.60, 129.95, 128.81, 127.74, 122.55, 122.28, 60.83, 50.91, 50.28, 14.21. HRMS (ESI): Calcd. for $C_{19}H_{19}N_3O_2$ $[M+H]^+$: 322.1550; found: 322.1647.

(17) ethyl (4-methyl-2-(quinolin-3-yl)benzyl)glycinate (3ba)



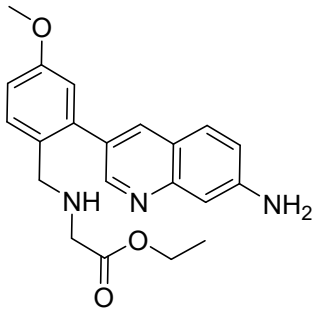
Yellow oil, 50.8 mg (76%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.23 (s, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.16 (s, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.70 (s, 2H), 3.30 (s, 2H), 2.39 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.35, 151.46, 147.09, 138.22, 137.25, 135.63, 134.54, 134.19, 131.29, 129.76, 129.48, 129.23, 129,19, 128.06, 127.73, 126.95, 60.74, 50.50, 50.25, 21.12, 14.19. HRMS (ESI): Calcd. for $C_{21}H_{22}N_2O_2$ $[M+H]^+$: 335.1754; found: 335.1752.

(18) ethyl (4-methoxy-2-(quinolin-3-yl)benzyl)glycinate (3ca)



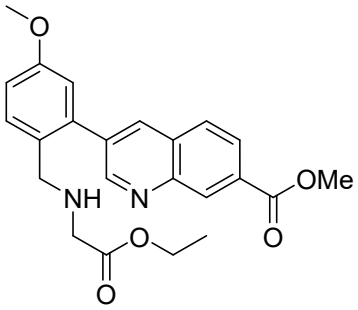
Yellow oil, 62.3 mg (89%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.25 (s, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 8.6 Hz, 1H), 6.95 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.87 (d, *J* = 2.6 Hz, 1H), 4.05 (q, *J* = 7.2 Hz, 2H), 3.82 (s, 3H), 3.66 (s, 2H), 3.29 (s, 2H), 1.15 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.36, 158.74, 151.29, 147.17, 139.57, 135.63, 133.98, 131.18, 129.77, 129.57, 129.23, 128.09, 127.66, 126.99, 115.97, 113.85, 60.73, 55.44, 50.17, 50.18, 14.18. HRMS (ESI): Calcd. for $C_{21}H_{22}N_2O_3$ $[M+H]^+$: 351.1703; found: 351.1702.

(19) ethyl (4-nitro-2-(7-amino-quinolin-3-yl)benzyl)glycinate (3cd)



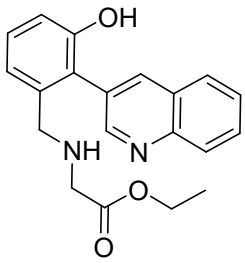
Dark brown oil, 47.5 mg (65%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.05 (s, 1H), 7.62 (d, *J* = 8.6 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.24 (s, 1H), 6.99 (d, *J* = 8.6 Hz, 1H), 6.91 (d, *J* = 8.6 Hz, 1H), 6.84 (s, 1H), 4.05 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 3.66 (s, 2H), 3.28 (s, 2H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.37, 158.70, 151.13, 148.77, 148.22, 139.98, 135.63, 131.04, 130.47, 129.73, 129.25, 121.53, 119.20, 115.90, 113.56, 108.65, 60.75, 55.43, 50.18, 14.19. HRMS (ESI): Calcd. for $C_{21}H_{23}N_3O_3$ $[M+H]^+$: 366.1812; found: 366.1808.

(20) Methyl 3-(2-(((2-ethoxy-2-oxoethyl)amino)methyl)-5-methoxyphenyl)quinoline-7-carboxylate (3ci)



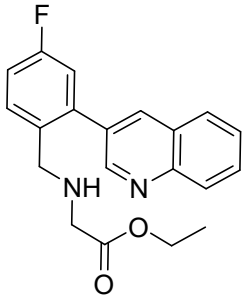
Yellow oil, 54.7 mg (67%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.83 (s, 1H), 8.30 (s, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.45 (d, *J* = 8.6 Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 1H), 6.87 (s, 1H), 4.05 (q, *J* = 7.2 Hz, 2H), 3.99 (s, 3H), 3.81 (s, 3H), 3.64 (s, 2H), 3.29 (s, 2H), 1.15 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.35, 166.82, 158.84, 152.43, 146.48, 139.13, 135.79, 135.29, 131.88, 131.40, 130.92, 130.15, 129.72, 128.39, 126.44, 115.91, 114.11, 60.76, 55.47, 52.53, 50.24, 50.15, 14.19. HRMS (ESI): Calcd. for $C_{23}H_{24}N_2O_5$ $[M+H]^+$: 409.1758; found: 409.1756.

(21) ethyl (3-hydroxy-2-(quinolin-3-yl)benzyl)glycinate (3da)



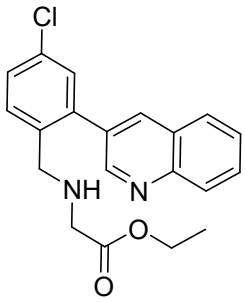
Yellow oil, 36.3 mg (54 %), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.15 (s, 1H), 8.00 (d, *J* = 8.6 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 8.2 Hz, 1H), 4.00 (q, *J* = 7.2 Hz, 2H), 3.49 (s, 2H), 3.20 (s, 2H), 1.12 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.21, 155.05, 152.27, 146.24, 139.14, 137.81, 129.77, 129.60, 128.35, 128.08, 127.91, 126.96, 125.09, 120.63, 115.40, 60.86, 50.89, 50.09, 14.17. HRMS (ESI): Calcd. for $C_{20}H_{20}N_2O_3$ $[M+H]^+$: 337.1547; found: 337.1547.

(22) ethyl (4-fluoro-2-(quinolin-3-yl)benzyl)glycinate (3ea)



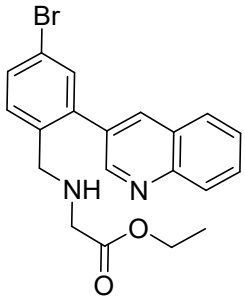
Yellow oil, 51.4 mg (76%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.95 (s, 1H), 8.24 (s, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.54 (dd, *J* = 8.4, 6.0 Hz, 1H), 7.12 – 7.08 (m, 1H), 7.05 (dd, *J* = 9.2, 2.6 Hz, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.68 (s, 2H), 3.29 (s, 2H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.30, 161.77 (d, *J* = 247.0 Hz), 150.94, 147.32, 140.26 (d, *J* = 7.9 Hz), 135.75, 133.50 (d, *J* = 3.1 Hz), 132.98, 131.56 (d, *J* = 8.3 Hz), 129.84, 129.31, 128.12, 127.58, 127.17, 117.27 (d, *J* = 21.4 Hz), 115.23 (d, *J* = 21.4 Hz), 60.82, 50.20, 50.14, 14.19. ^{19}F NMR (471 MHz, $CDCl_3$) δ -114.96 (s). HRMS (ESI): Calcd. for $C_{20}H_{19}FN_2O_2$ $[M+H]^+$: 339.1503; found: 339.1503.

(23) ethyl (4-chloro-2-(quinolin-3-yl)benzyl)glycinate (3fa)



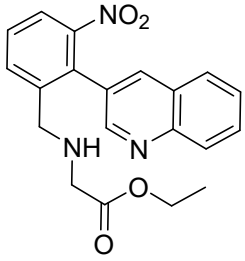
Yellow oil, 45.3 mg (64%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.20 (s, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.33 (s, 1H), 4.06 (q, *J* = 7.1 Hz, 2H), 3.68 (s, 2H), 3.29 (s, 2H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.26, 150.89, 147.33, 139.99, 136.19, 135.77, 133.15, 132.76, 131.07, 130.36, 129.87, 129.32, 128.47, 128.10, 127.58, 127.20, 60.84, 50.20, 14.19. HRMS (ESI): Calcd. for $C_{20}H_{19}ClN_2O_2$ $[M+H]^+$: 355.1208; found: 355.1204.

(24) ethyl (4-bromo-2-(quinolin-3-yl)benzyl)glycinate (3ga)



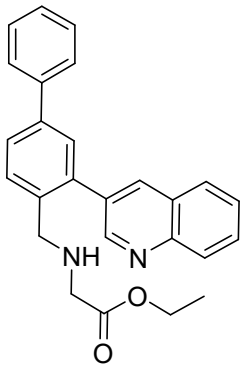
Yellow oil, 51.0 mg (64%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.20 (s, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.74 (t, *J* = 7.8 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 8.2 Hz, 1H), 7.49 (s, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.67 (s, 2H), 3.29 (s, 2H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.25, 150.90, 147.35, 140.33, 136.72, 135.78, 133.24, 132.66, 131.44, 131.32, 129.89, 129.34, 128.11, 127.59, 127.21, 121.21, 60.86, 50.26, 50.21, 14.21. HRMS (ESI): Calcd. for $C_{20}H_{19}BrN_2O_2$ $[M+H]^+$: 399.0703; found: 399.0708.

(25) ethyl (3-nitro-2-(quinolin-3-yl)benzyl)glycinate (3ha)



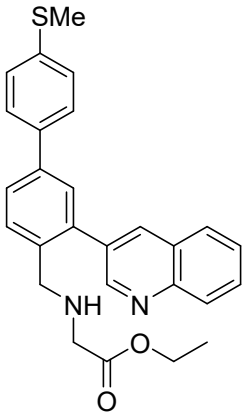
Dark brown oil, 10.2 mg (14%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.17 (d, *J* = 8.6 Hz, 1H), 8.03 (s, 1H), 7.90 – 7.8 (m, 2H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.78 (t, *J* = 7.8 Hz, 1H), 7.61 – 7.57 (m, 2H), 4.05 (q, *J* = 7.2 Hz, 2H), 3.56 (s, 2H), 3.22 (d, *J* = 5.0 Hz, 2H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.13, 150.59, 150.41, 147.54, 141.58, 135.31, 133.13, 132.14, 130.21, 129.54, 129.30, 128.51, 128.12, 127.43, 127.36, 123.00, 61.00, 50.60, 50.27, 14.24. HRMS (ESI): Calcd. for $C_{20}H_{19}N_3O_4$ $[M+H]^+$: 366.1448; found: 366.1459.

(26) ethyl (4-phenyl-2-(quinolin-3-yl)benzyl)glycinate (3ia)



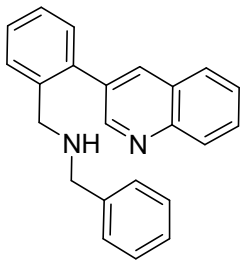
Yellow oil, 62.9 mg (79%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.29 (s, 1H), 8.18 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 7.8 Hz, 1H), 7.67 (s, 2H), 7.63 (d, *J* = 7.4 Hz, 2H), 7.59 (t, *J* = 7.0 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 2H), 3.36 (s, 2H), 1.19 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.31, 151.39, 147.25, 140.51, 140,37, 138.82, 136.62, 135.72, 134.03, 130.22, 129.60, 129.33, 128.93, 128.08, 127.73, 127.61, 127.15, 127.08, 127.03, 60.77, 50.55, 50.32, 14.20. HRMS (ESI): Calcd. for $C_{26}H_{24}N_2O_2$ $[M+H]^+$: 397.1911; found: 397.1909.

(27) ethyl (4-(4-(methylthio)phenyl)-2-(quinolin-3-yl)benzyl)glycinate (3ja)



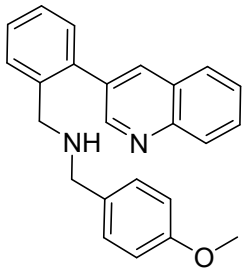
Yellow oil, 50.4 mg (57%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.28 (s, 1H), 8.17 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.66 – 7.62 (m, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.57 – 7.54 (m, 3H), 7.32 (d, *J* = 8.2 Hz, 2H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.78 (s, 2H), 3.34 (s, 2H), 2.50 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.34, 151.36, 147.25, 139.81, 138.89, 138.14, 137.09, 136.58, 135.74, 134.00, 130.28, 129.64, 129.31, 128.97, 128.10, 127.73, 127.46, 127.07, 127.01, 126.74, 60.80, 50.55, 50.32, 15.87, 14.22. HRMS (ESI): Calcd. for $C_{27}H_{26}N_2O_2S$ $[M+H]^+$: 443.1788; found: 443.1782.

(28) N-benzyl-2-(quinolin-3-yl)benzyl amine (3ka)



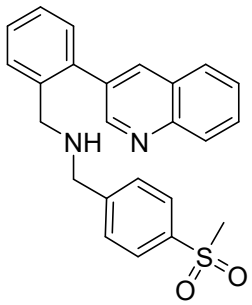
Yellow oil, 45.4 mg (70%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.24 (s, 1H), 8.19 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.76 (t, *J* = 7.8 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.44 (t, *J* = 6.8 Hz, 1H), 7.40 (t, *J* = 6.8 Hz, 1H), 7.36 (d, *J* = 7.4 Hz, 1H), 7.21 – 7.14 (m, 5H), 3.77 (s, 2H), 3.72 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.39, 147.18, 140.02, 138.36, 138.26, 135.57, 134.18, 130.61, 129.76, 129.53, 129.33, 128.44, 128.35, 128.07, 128.03, 127.72, 127.45, 126.99, 126.97, 53.61, 51.03. HRMS (ESI): Calcd. for $C_{20}H_{19}N_3O_4$ $[M+H]^+$: 325.1699; found: 325.1695.

(29) N-(4-methoxybenzyl)-2-(quinolin-3-yl)benzyl amine (3la)



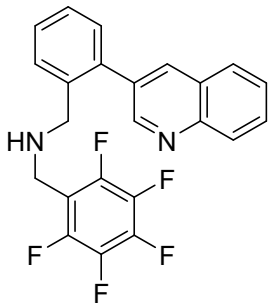
Yellow oil, 46.8 mg (66 %), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.23 (s, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.77 – 7.74 (m, 1H), 7.61 – 7.57 (m, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 6.79 – 6.76 (m, 2H), 6.71 (dd, *J* = 8.1, 2.3 Hz, 1H), 3.78 (s, 2H), 3.73 (s, 3H), 3.69 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.74, 151.41, 147.21, 141.63, 138.37, 138.16, 135.57, 134.17, 130.64, 129.75, 129.53, 129.38, 129.35, 128.46, 128.09, 127.73, 127.49, 126.99, 120.35, 113.61, 112.54, 55.21, 53.53, 50.96. HRMS (ESI): Calcd. for $C_{24}H_{22}N_2O$ $[M+H]^+$: 355.1805; found: 355.1801.

(30) N-(4-methylsulfonylbenzyl)-2-(quinolin-3-yl)benzyl amine (3ma)



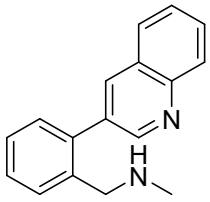
Yellow oil, 57.9 mg (72 %), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.17 (s, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.44 – 7.36 (m, 2H), 7.35 – 7.30 (m, 3H), 3.76 (s, 2H), 3.72 (s, 2H), 2.94 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.27, 147.07, 146.60, 138.93, 138.35, 137.75, 135.41, 134.12, 130.64, 129.70, 129.67, 129.23, 128.65, 128.50, 127,94, 127.62, 127.33, 127.16, 52.83, 51.05, 44.50. HRMS (ESI): Calcd. for $C_{24}H_{22}N_2O_2S$ $[M+H]^+$: 403.1475; found: 403.1482.

(31) N-((perfluorophenyl)methyl)-benzyl)-2-(quinolin-3-yl)benzyl amine (3na)



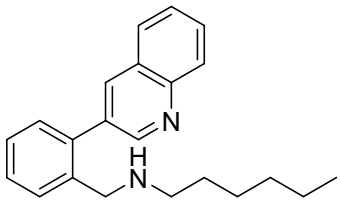
White solid, m.p. 94-95 ºC, 60.5 mg (73%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.14 (d, *J* = 8.8 Hz, 2H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 7.4 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.33 (d, *J* = 7.2 Hz, 1H), 3.80 (s, 2H), 3.70 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.13, 147.13, 146.08, 144.14, 141.33, 139.31 – 138.25 (m), 138.48, 137.24, 136.21, 135.30, 133.76, 130.68, 129.88, 129.70, 129.29, 128.54, 127.85, 127.81, 127.47, 127.15, 112.92, 50.67, 40.24. ^{19}F NMR (471 MHz, $CDCl_3$) δ -144.31 (dd, *J* = 22.9, 8.5 Hz), -155.08 (s), -155.12 (s), -155.15 (d, *J* = 20.8 Hz), -161.91 (td, *J* = 22.3, 8.6 Hz). HRMS (ESI): Calcd. for $C_{23}H_{15}F_5N_2$ $[M+H]^+$: 415.1228; found: 415.1223.

(32) N-methyl-1-(2-(quinolin-3-yl)phenyl)methanamine (3oa)



Yellow oil, 18.0 mg (36 %), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.22 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 7.8 Hz, 1H), 7.61 – 7.59 (m, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.36 (d, *J* = 7.4 Hz, 1H), 3.76 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.36, 147.26, 138.36, 137.02, 135.74, 134.07, 130.73, 129.72, 129.62, 129.38, 128.63, 128.12, 127.78, 127.71, 127.17, 52.93, 35.70. MS (EI): m/z 248.3 $[M]^+$.

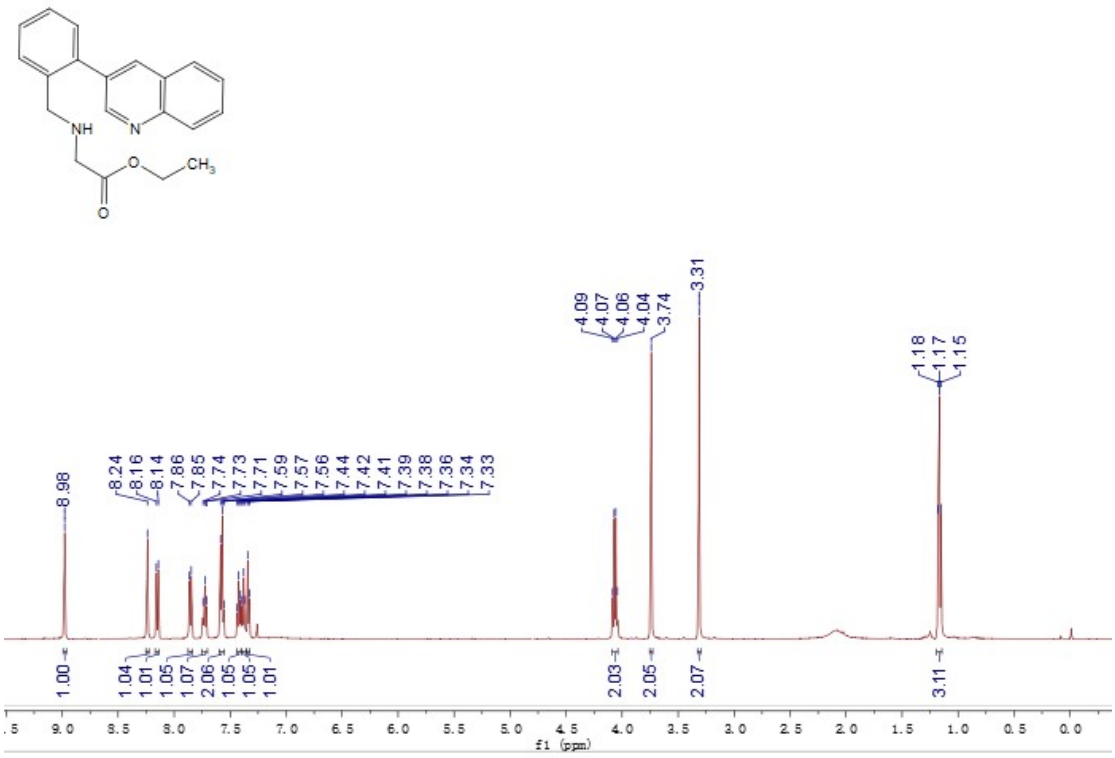
(33) N-(2-(quinolin-3-yl)benzyl)hexan-1-amine (3pa)



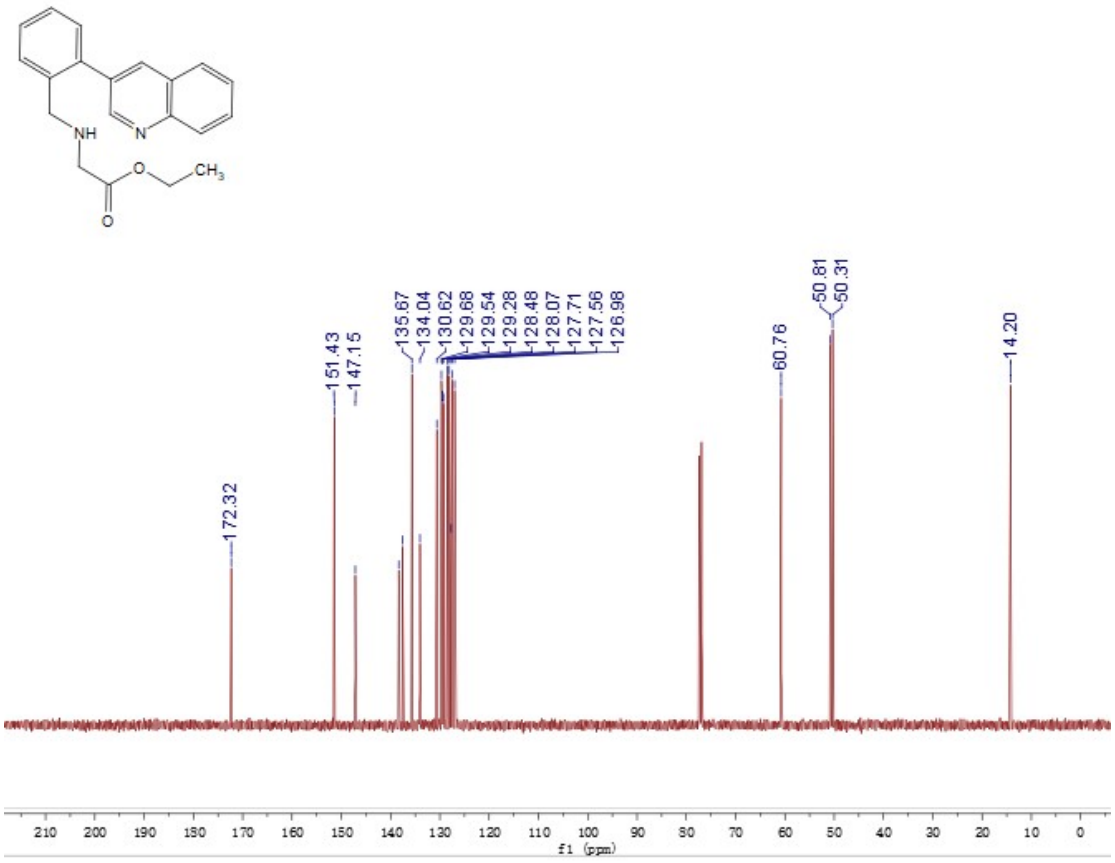
Yellow oil, 53.7mg (84 %), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.26 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.73 (t, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 7.4 Hz, 3H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 3.75 (s, 2H), 2.51 (t, *J* = 7.4 Hz, 2H), 1.41 – 1.36 (m, 2H), 1.23 – 1.15 (m, 6H), 0.82 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.23, 146.06, 137.12, 136.67, 134.54, 132.98, 129.47, 128.53, 128.44, 128.20, 127.37, 126.90, 126.60, 126.36, 125.92, 50.14, 48.36, 30.60, 28.55, 25.86, 21.49, 12.98. MS (EI): m/z 318.4 $[M]^+$.

8. NMR spectra

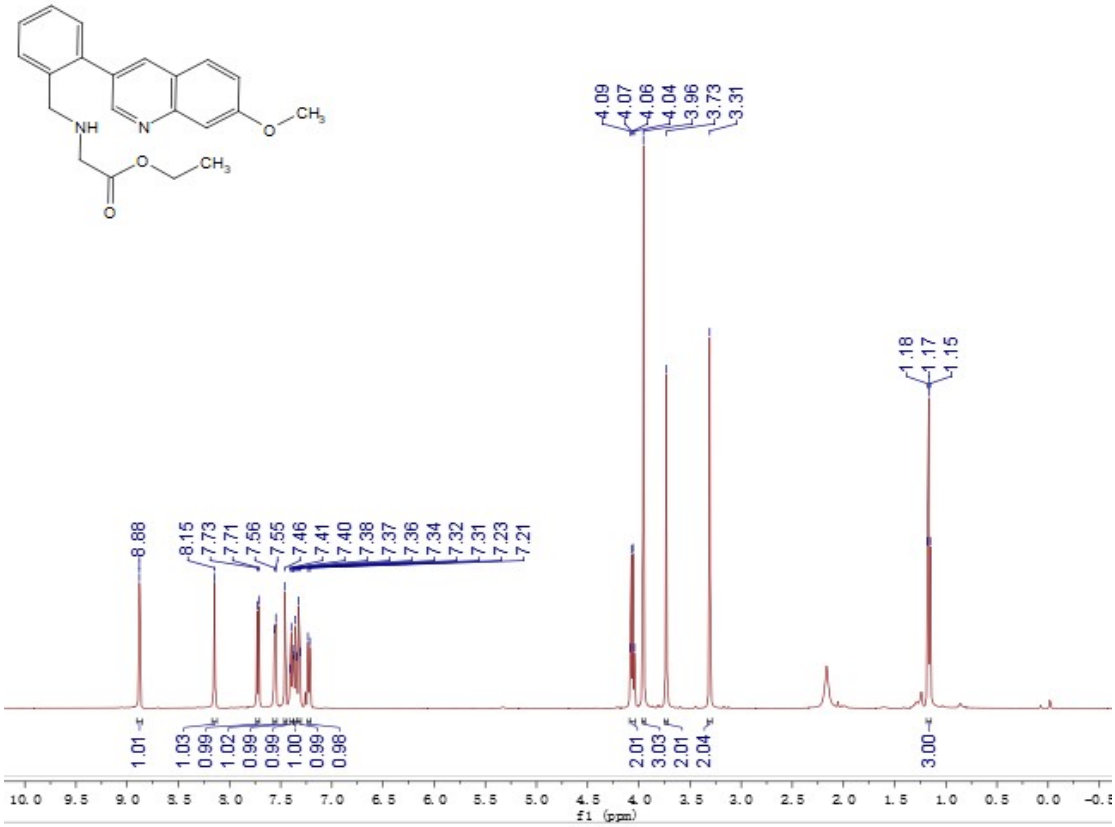
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3aa



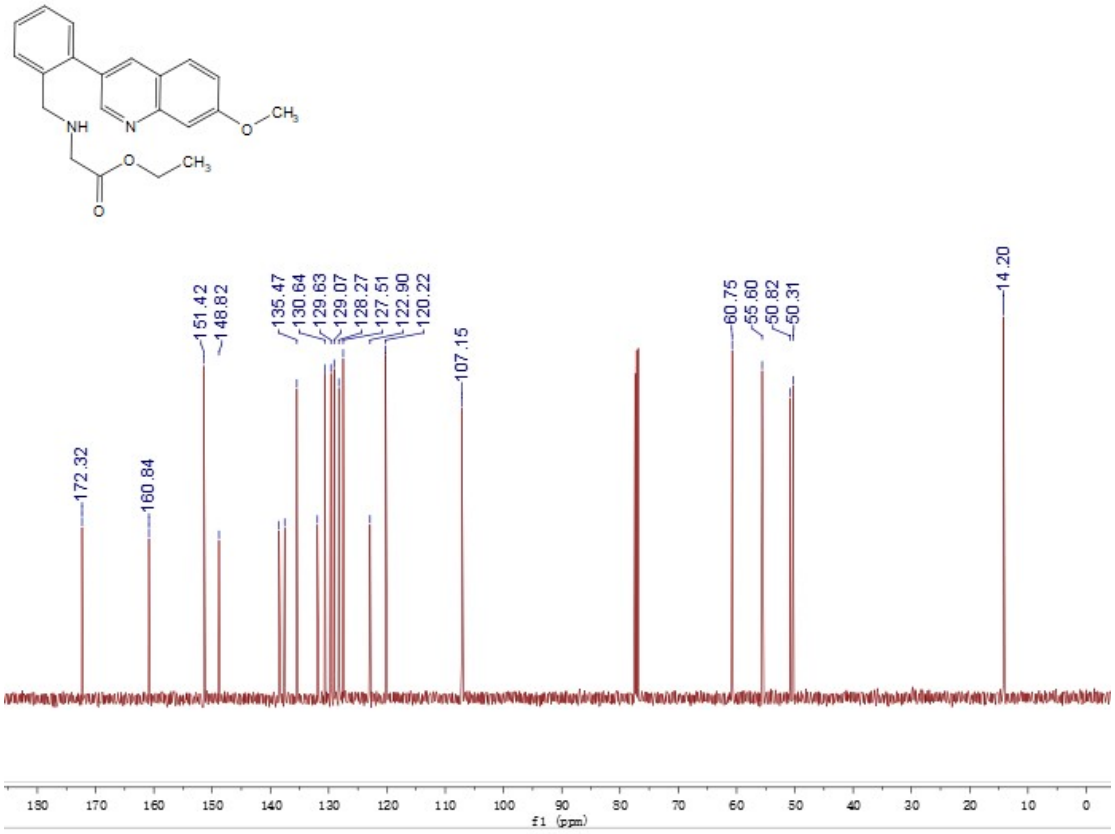
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3aa



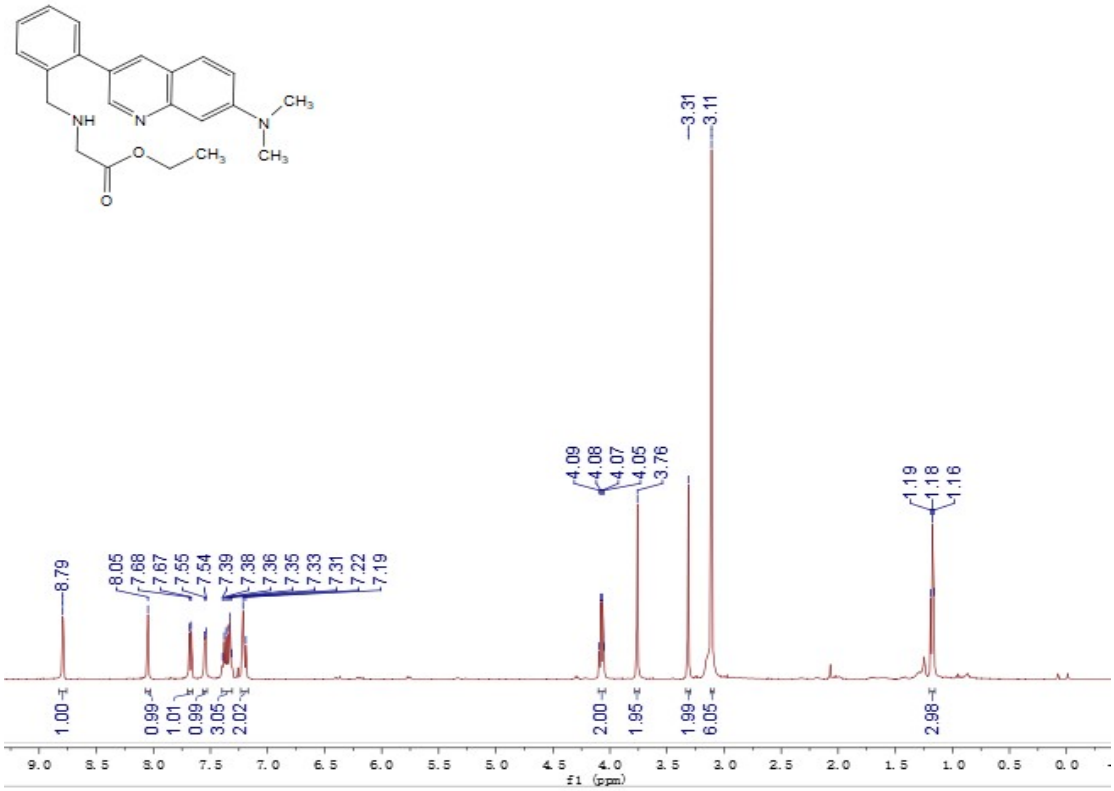
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ab



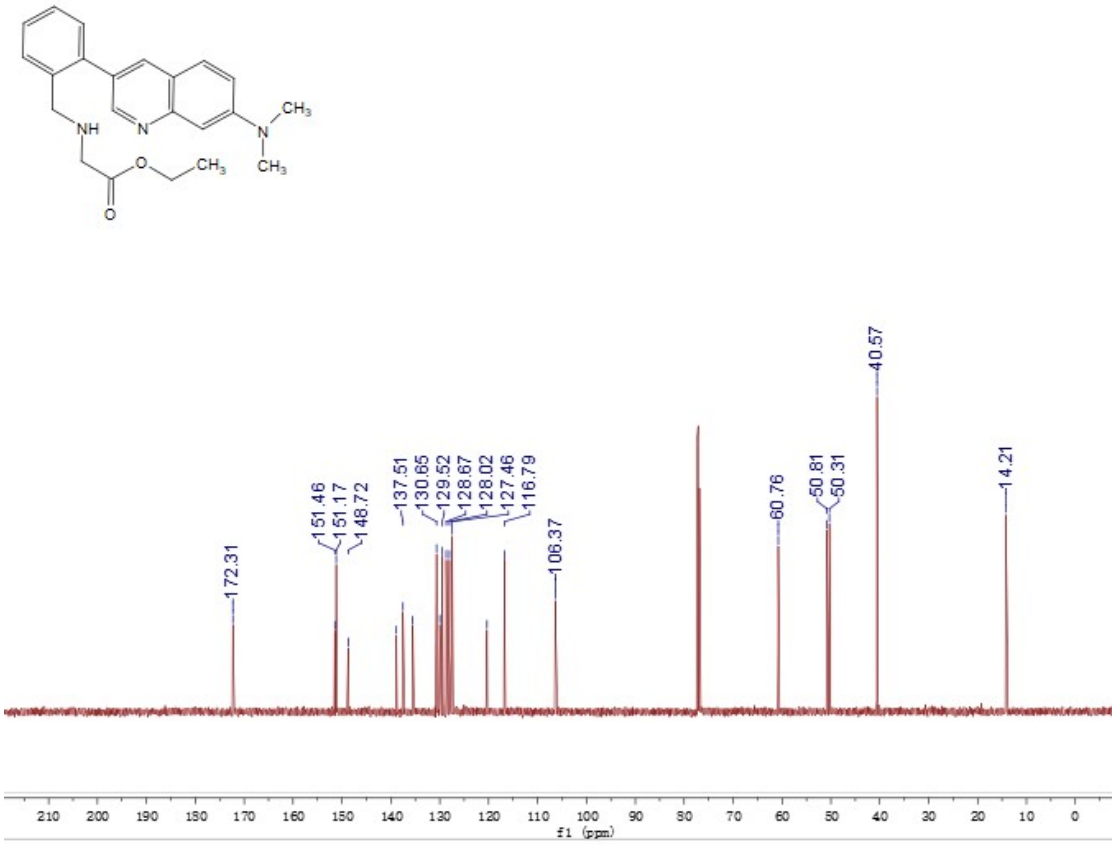
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ab



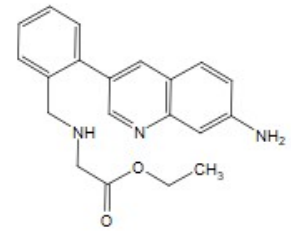
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ac

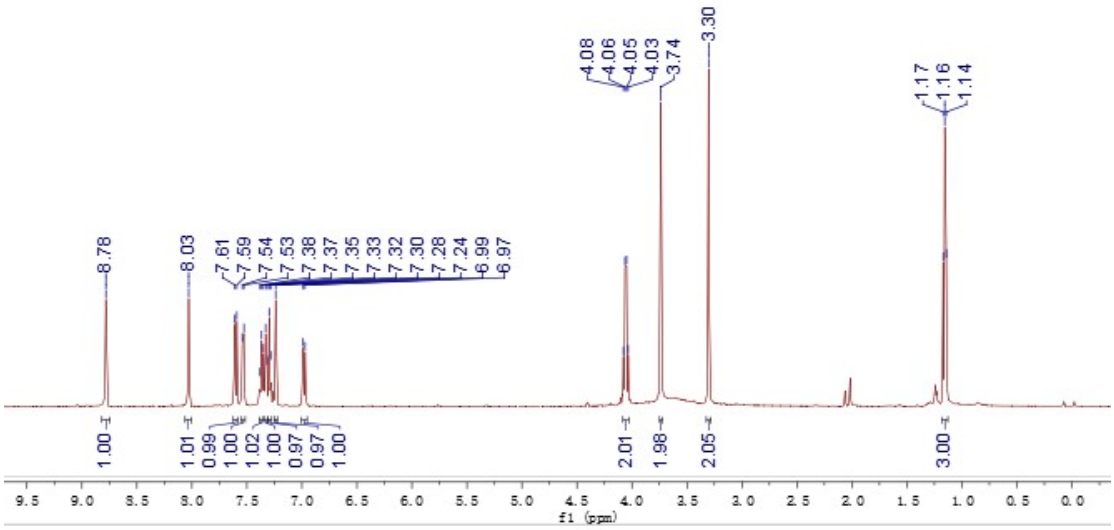


^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ac

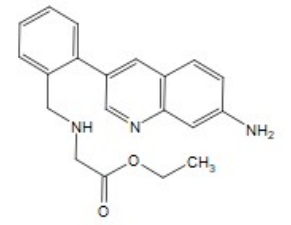


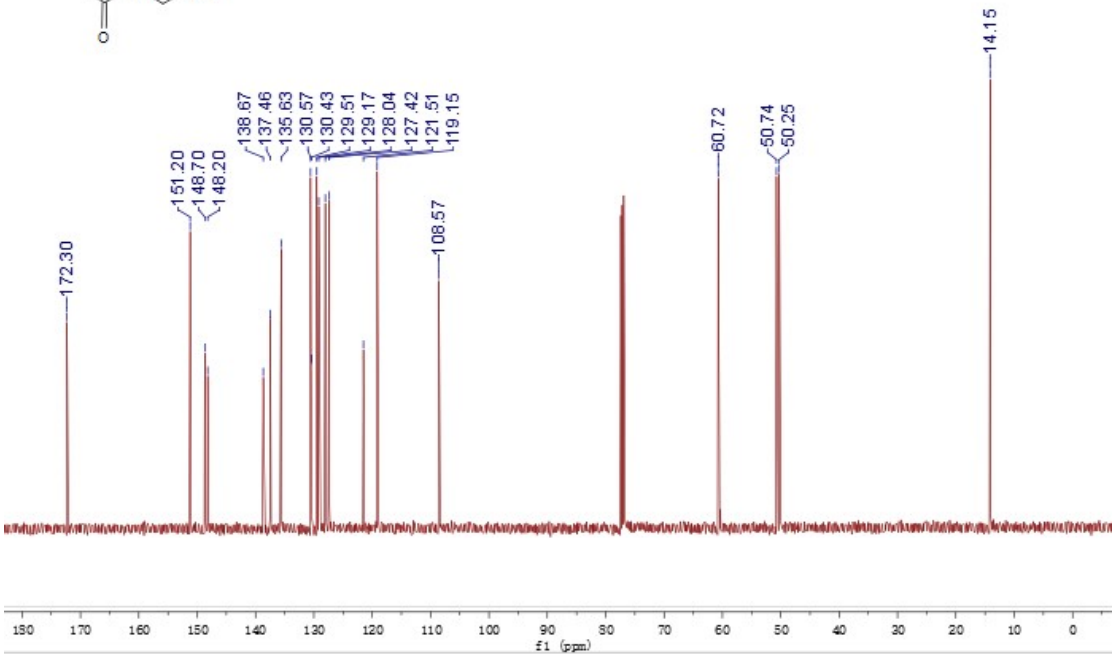
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ad



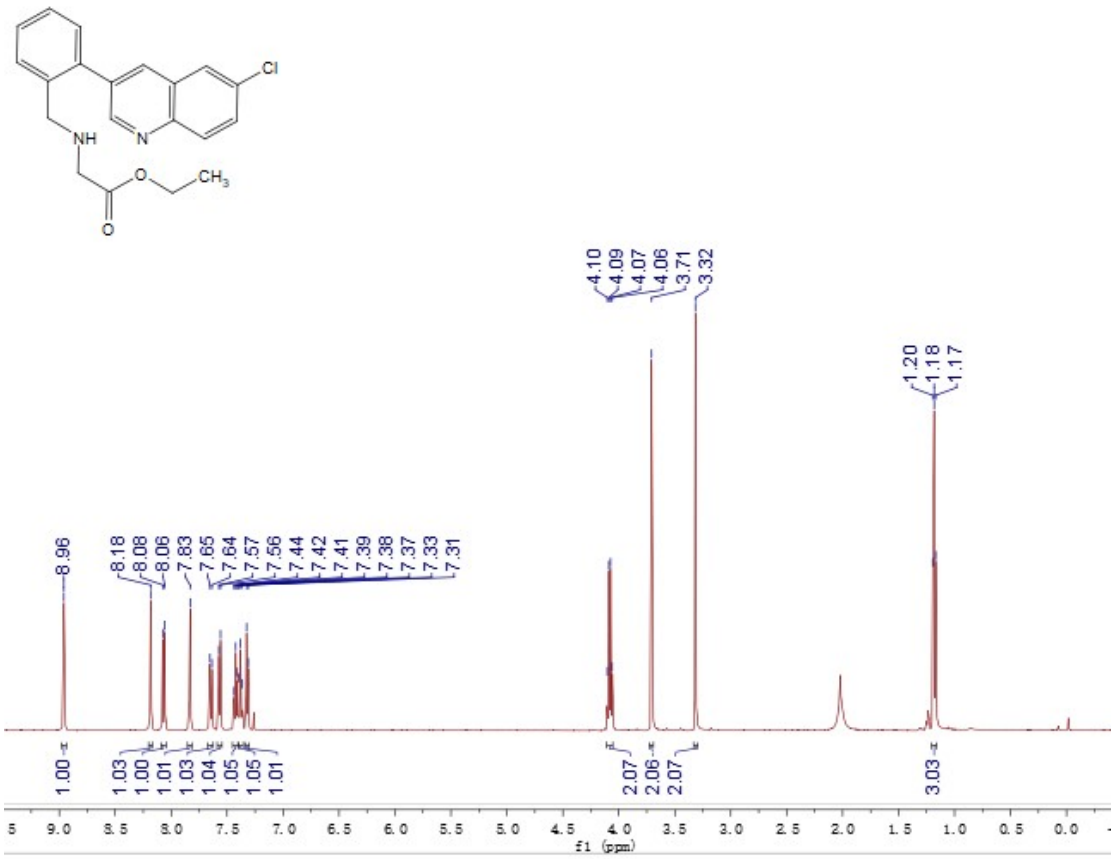


^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ad

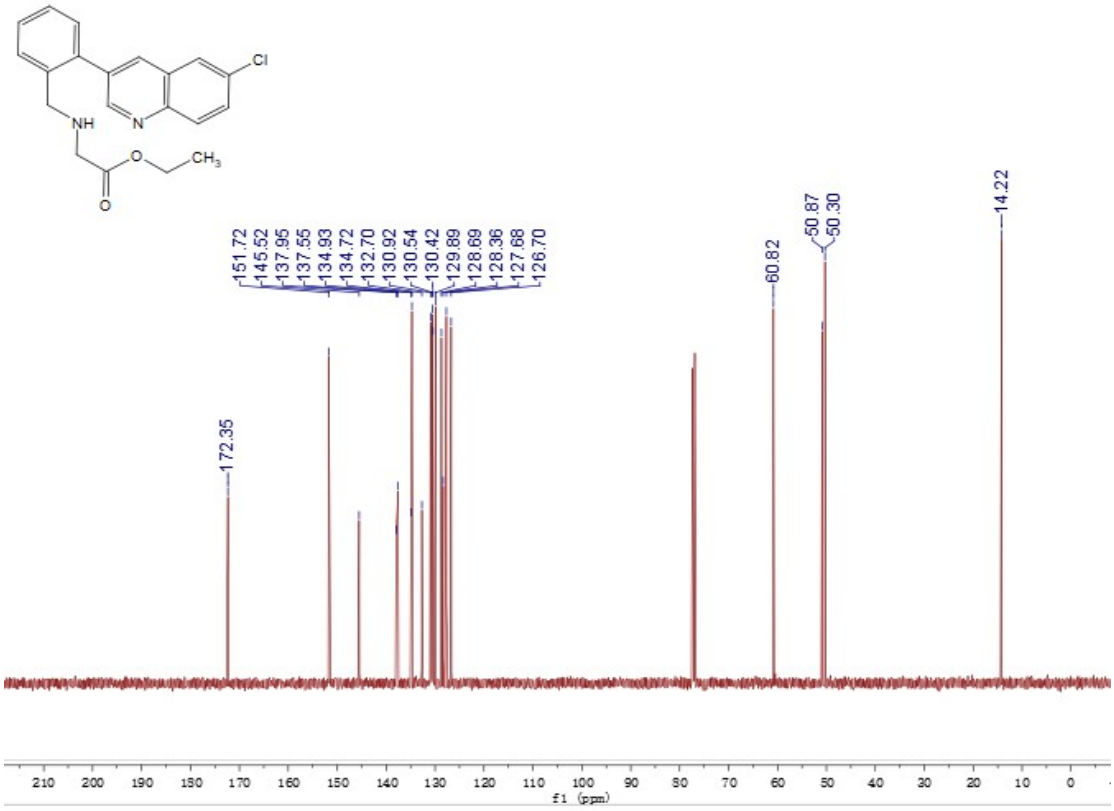




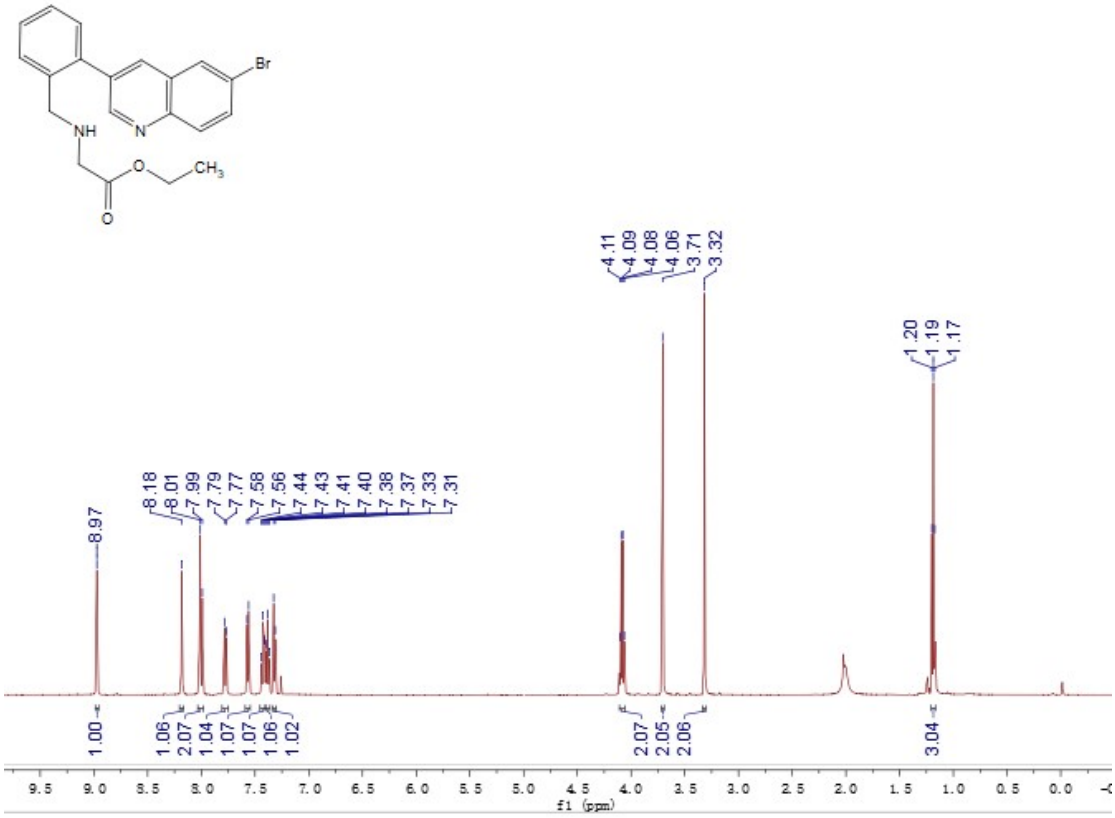
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ae



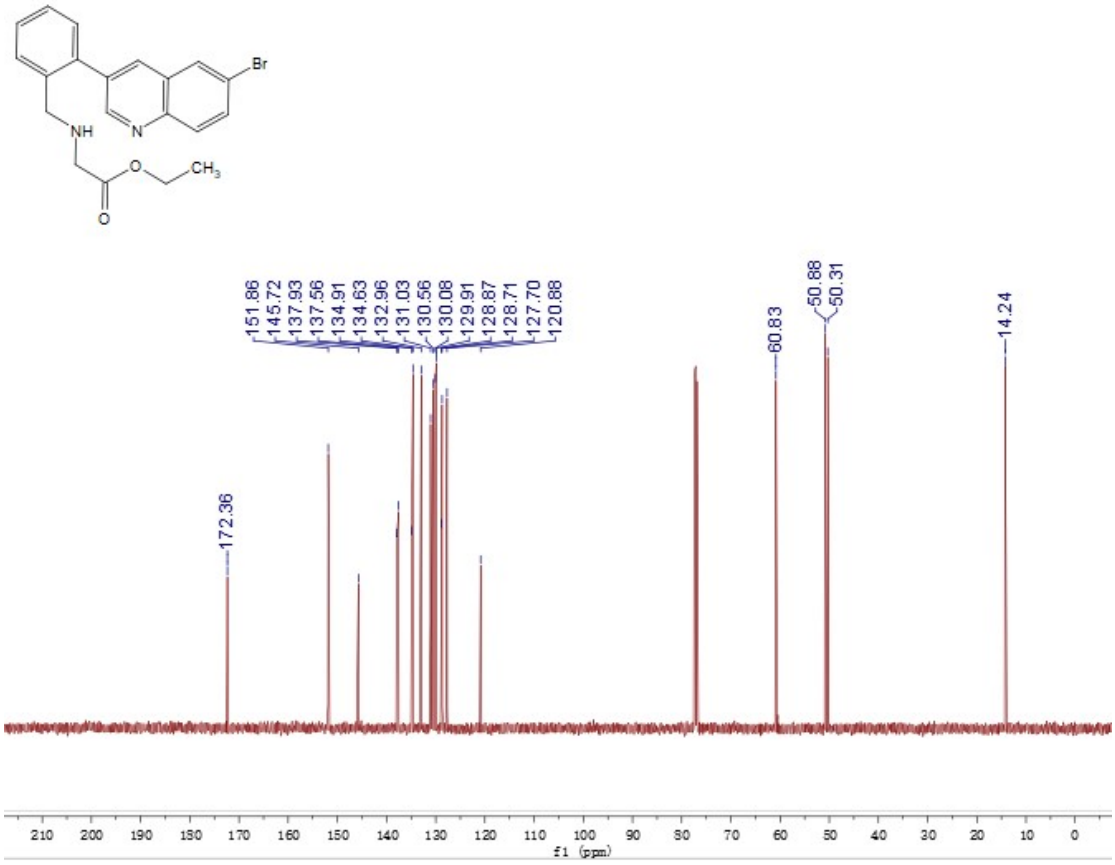
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ae



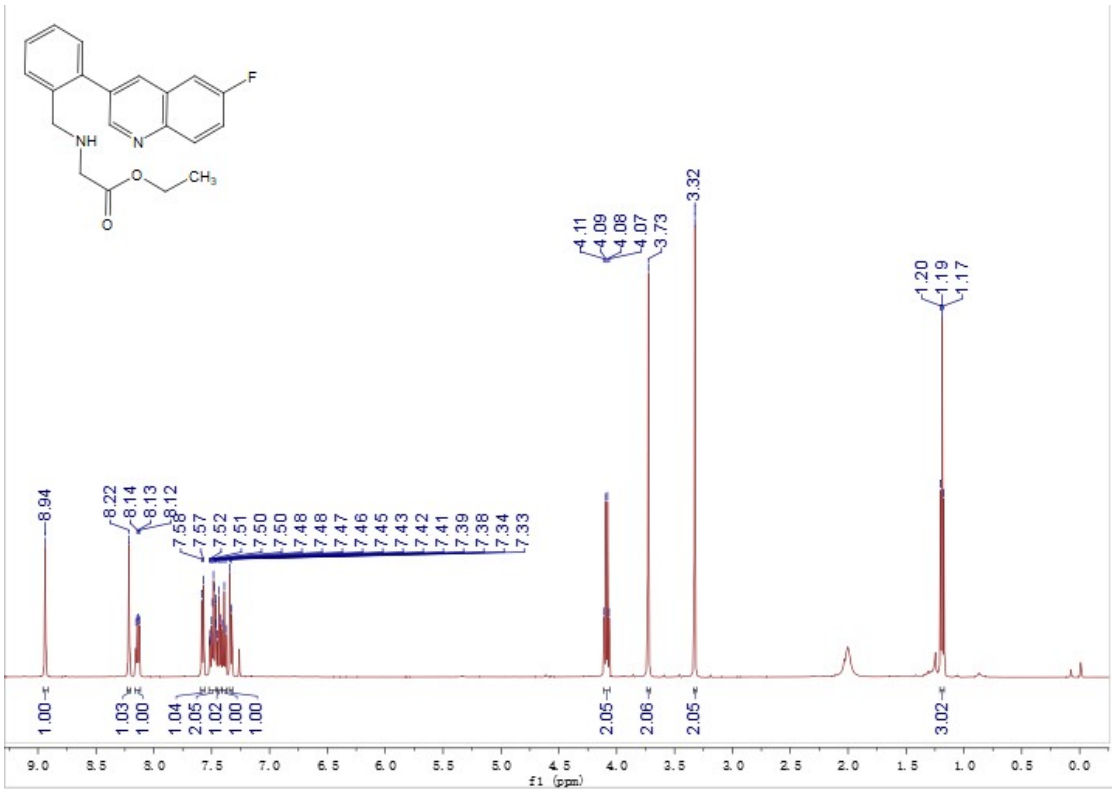
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3af



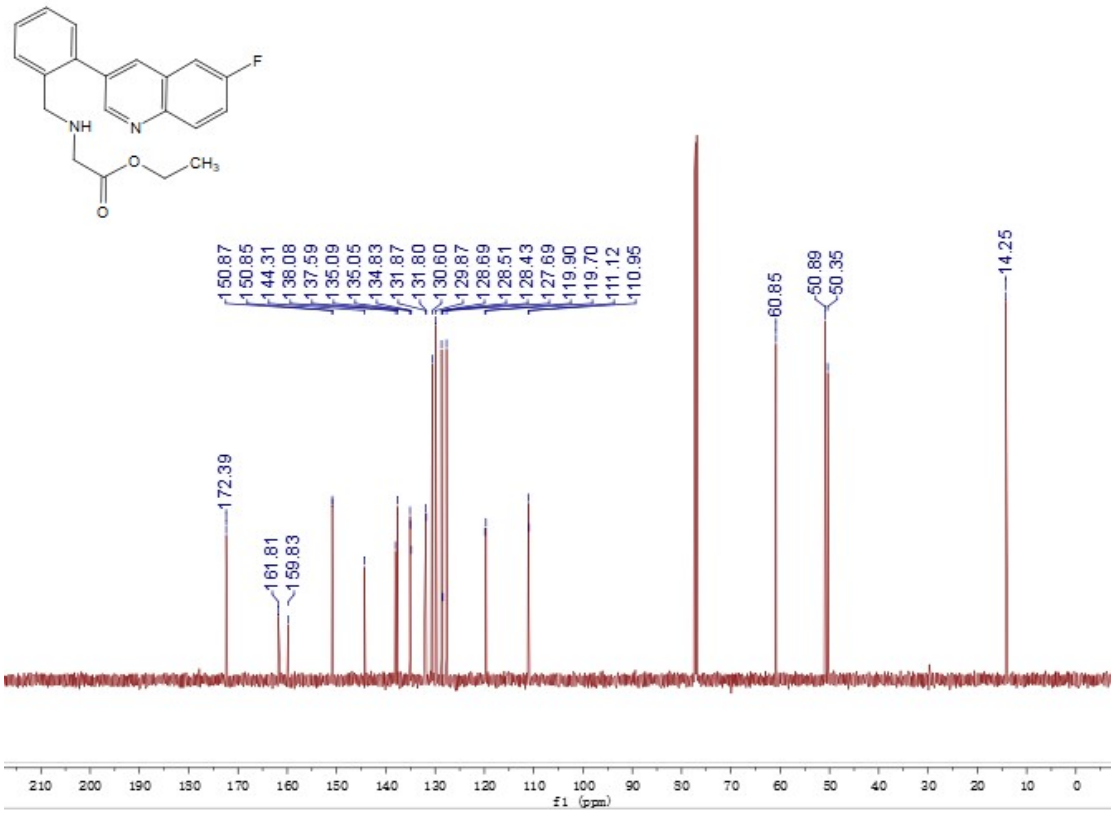
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3af



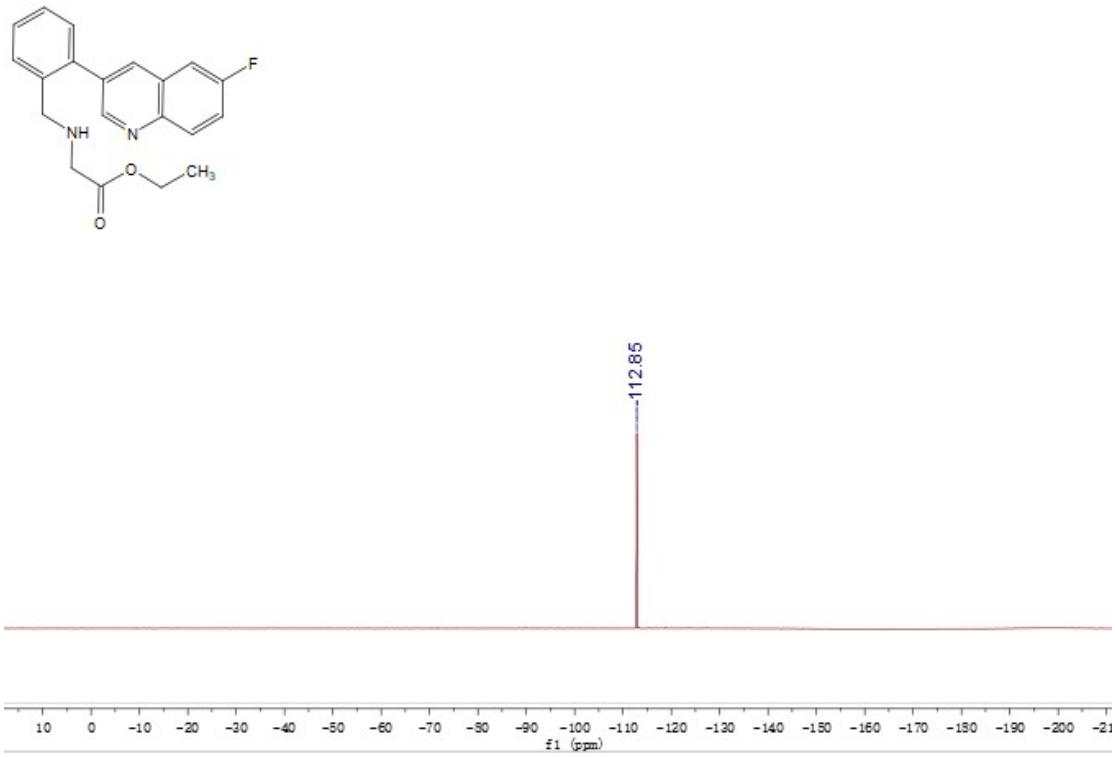
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ag



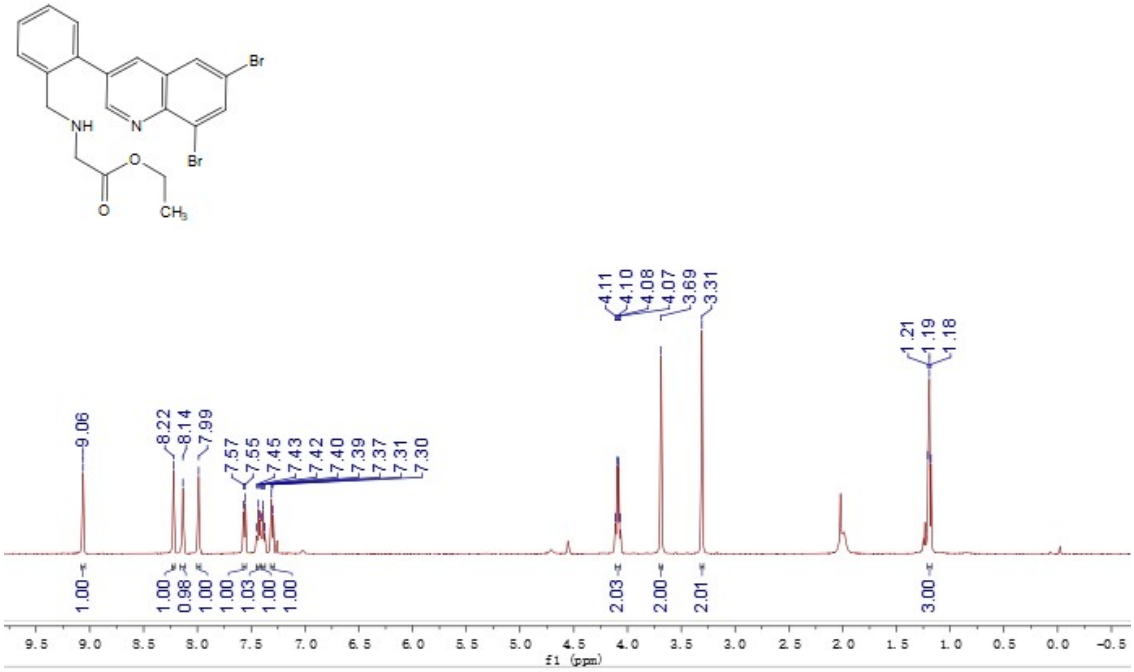
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ag



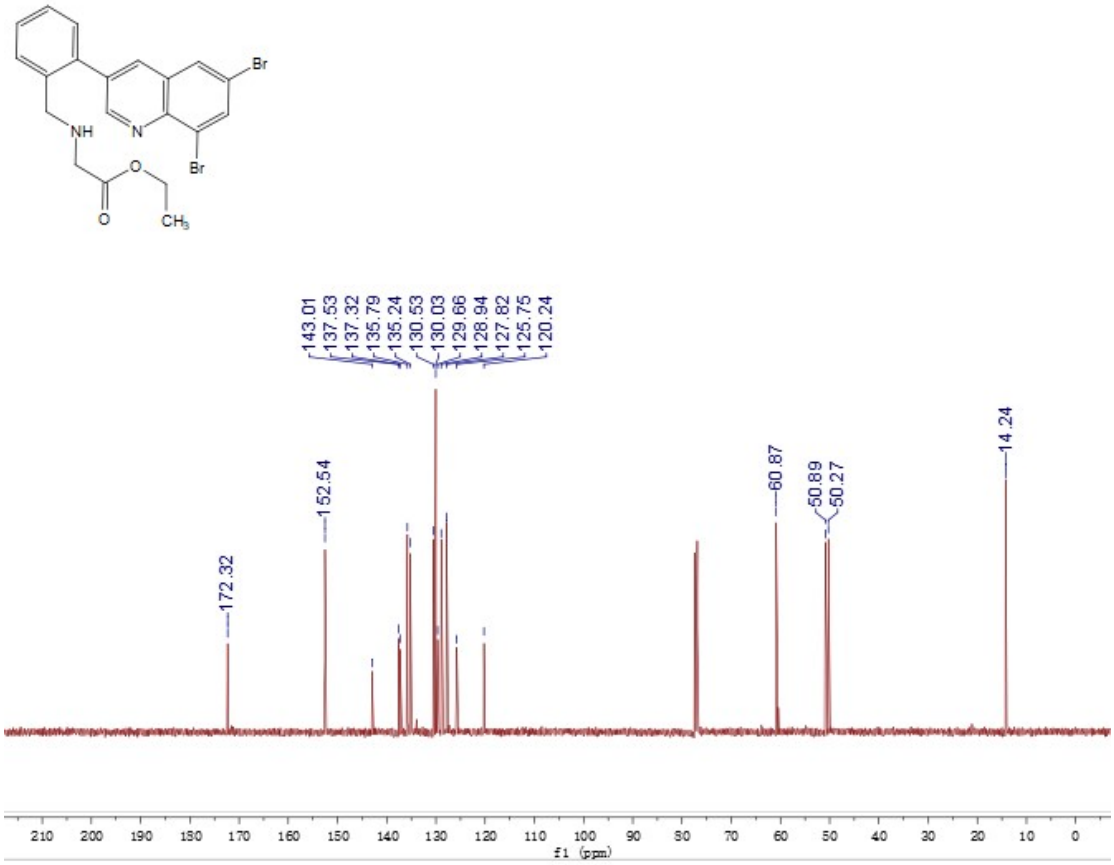
^{19}F-NMR (471 MHz, $CDCl_3$) spectrum of 3ag



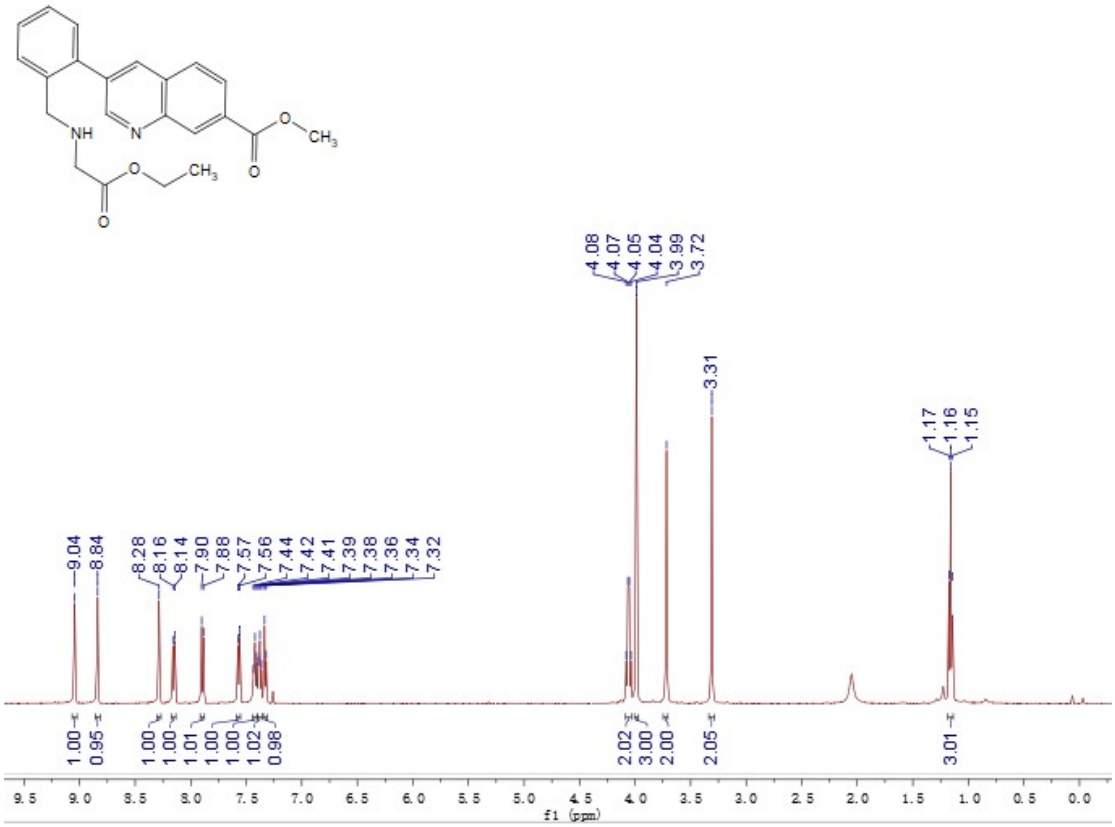
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ah



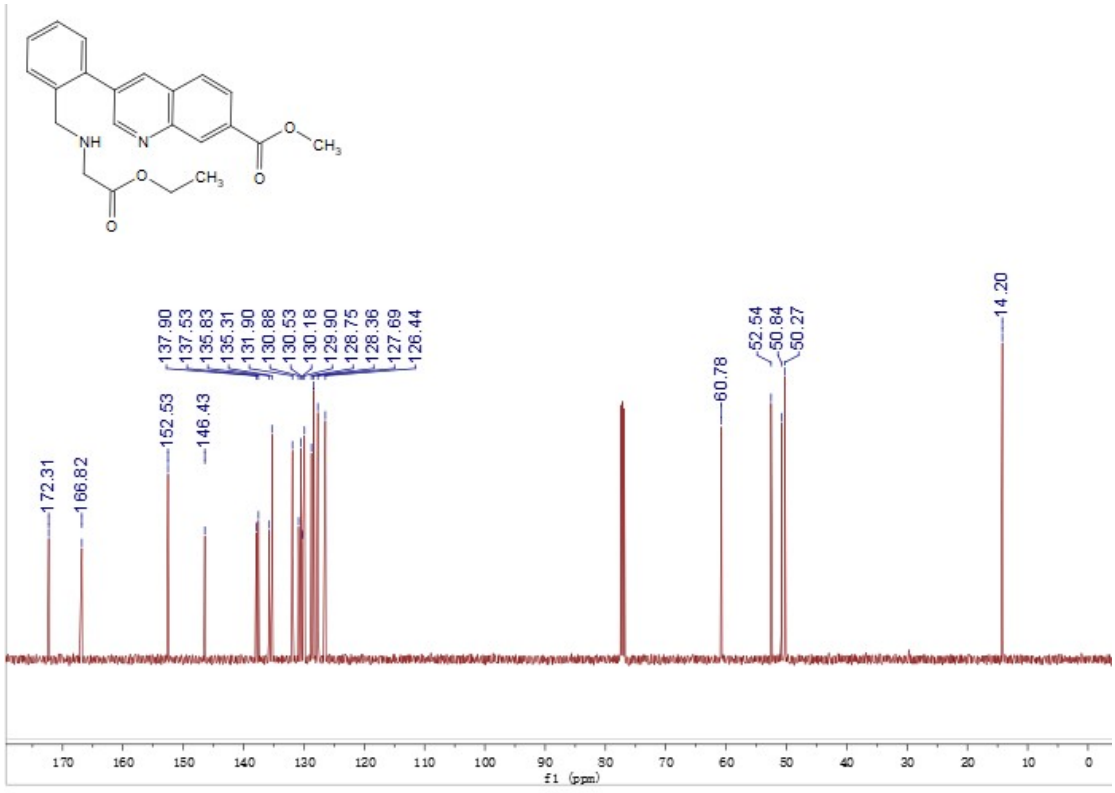
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ah



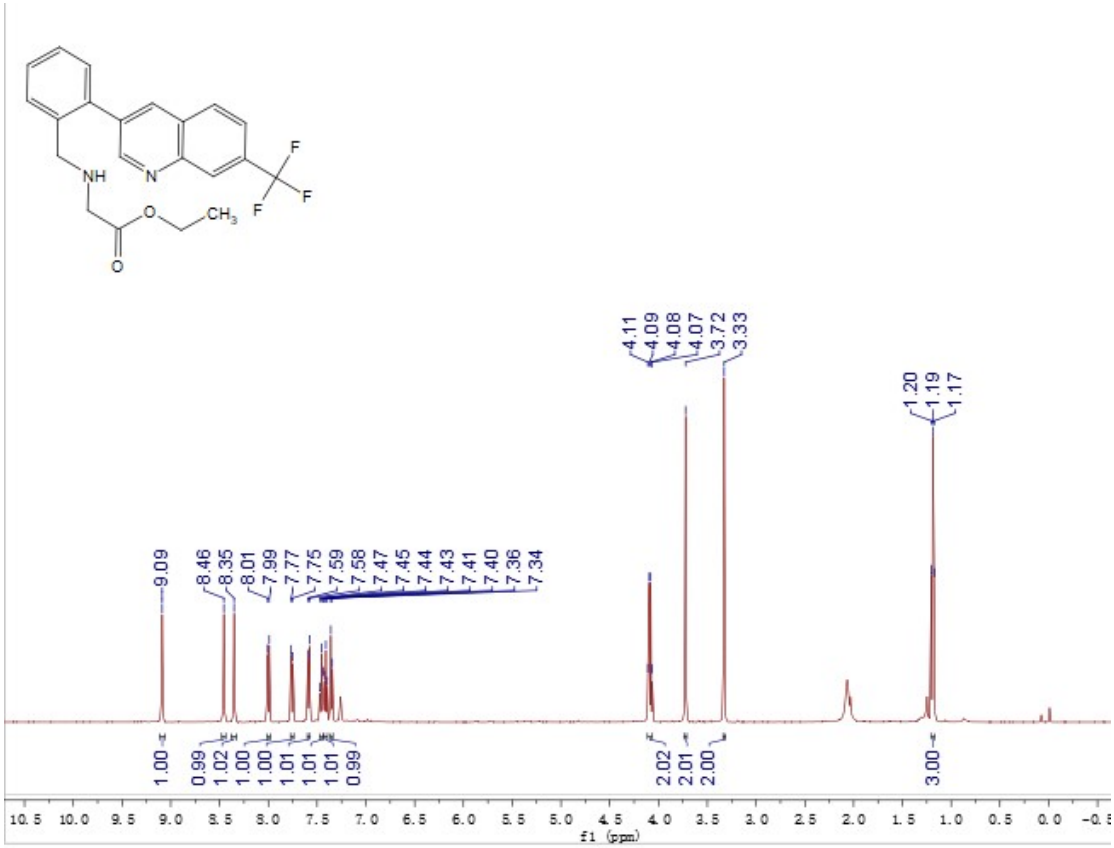
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ai



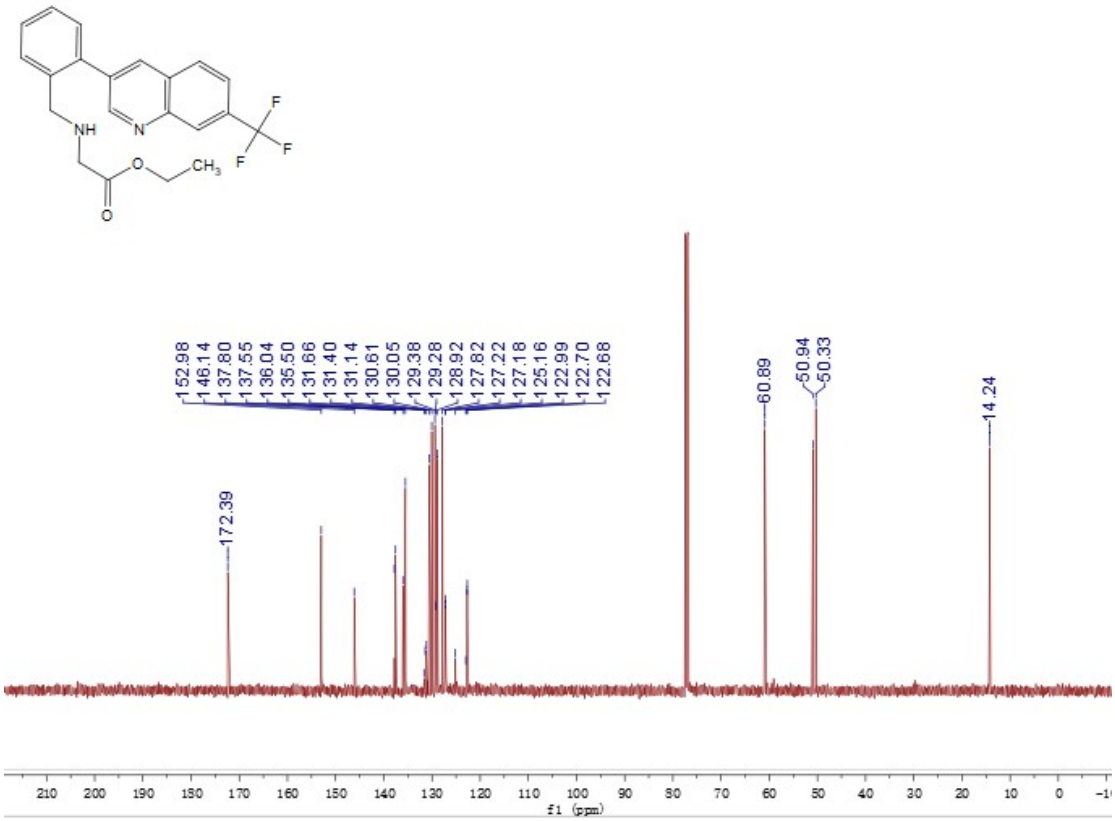
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ai



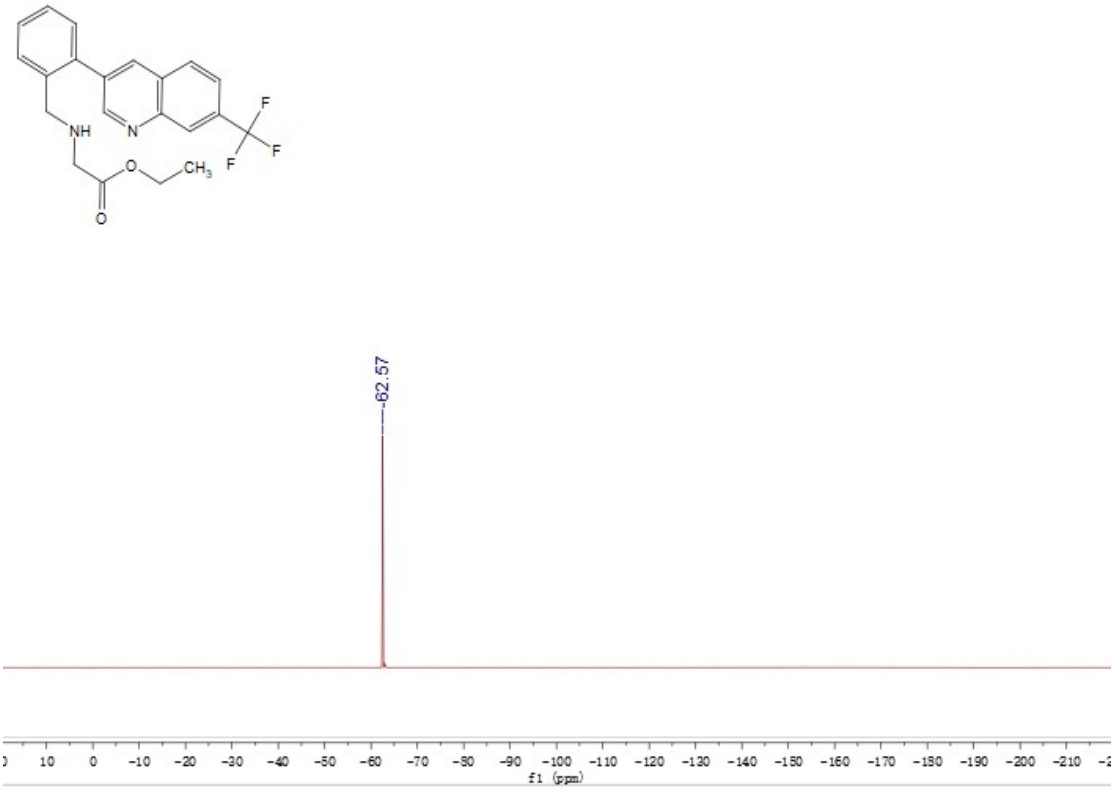
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3aj



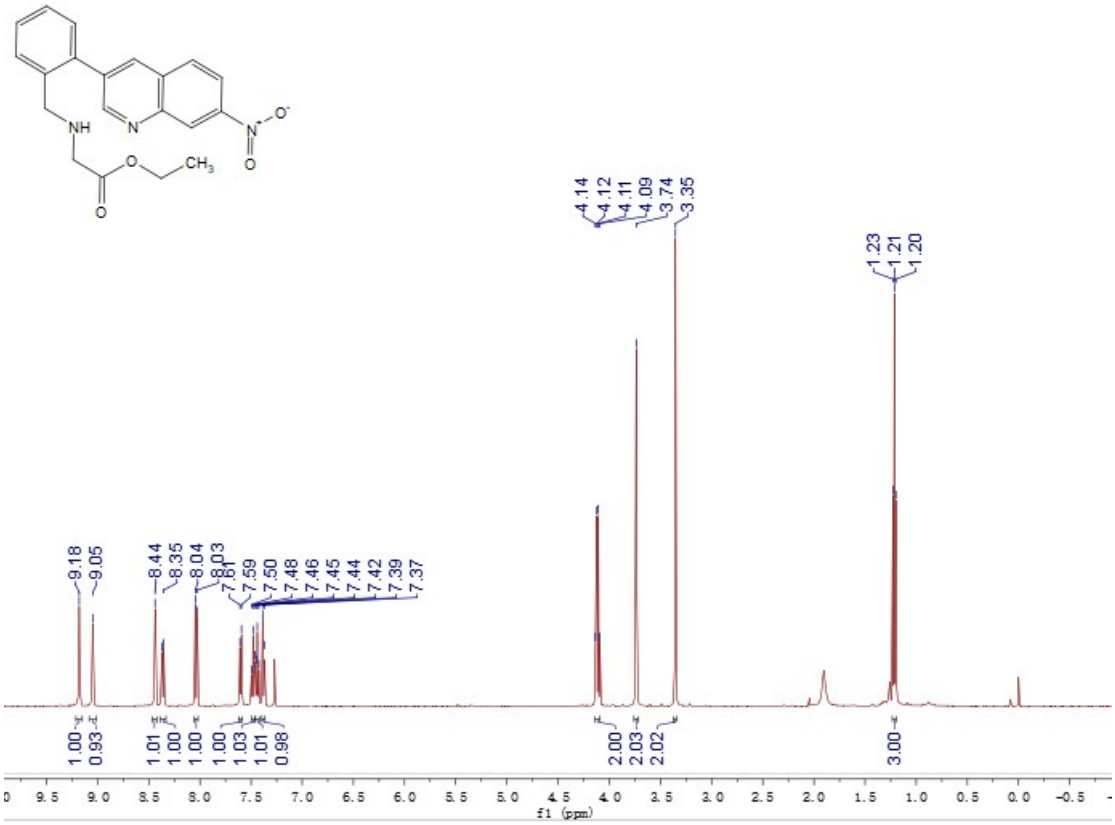
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3aj



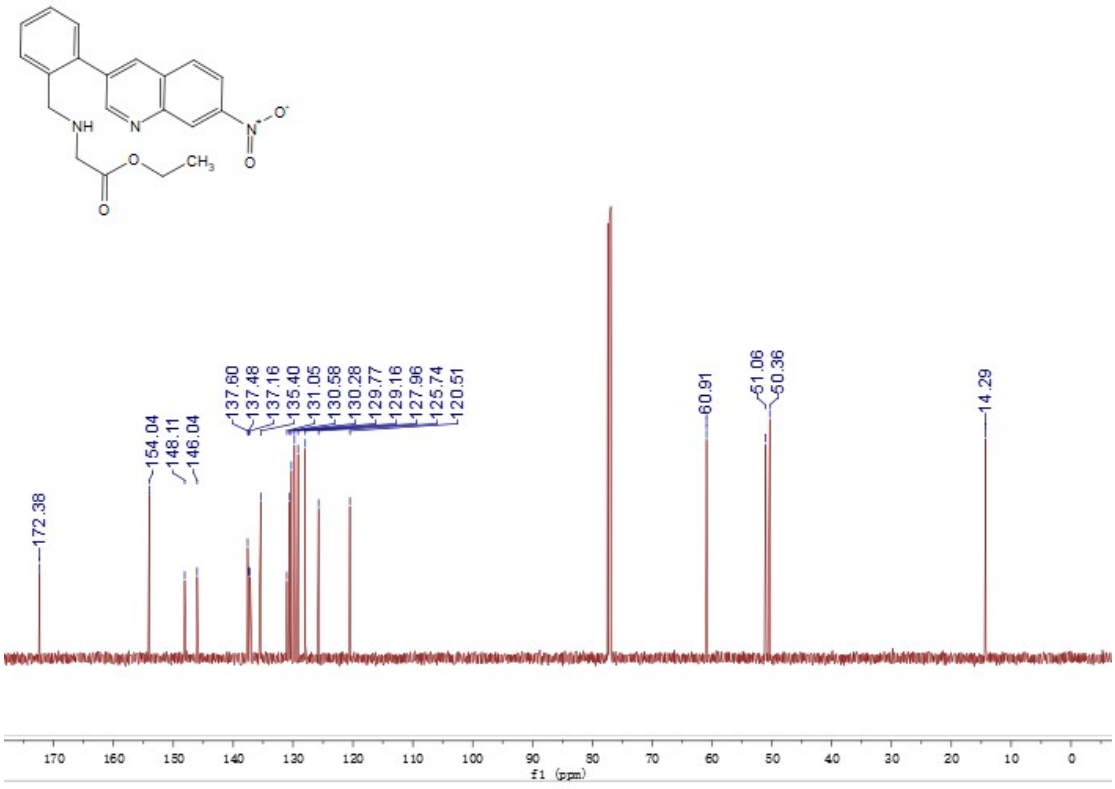
^{19}F-NMR (471 MHz, $CDCl_3$) spectrum of 3aj



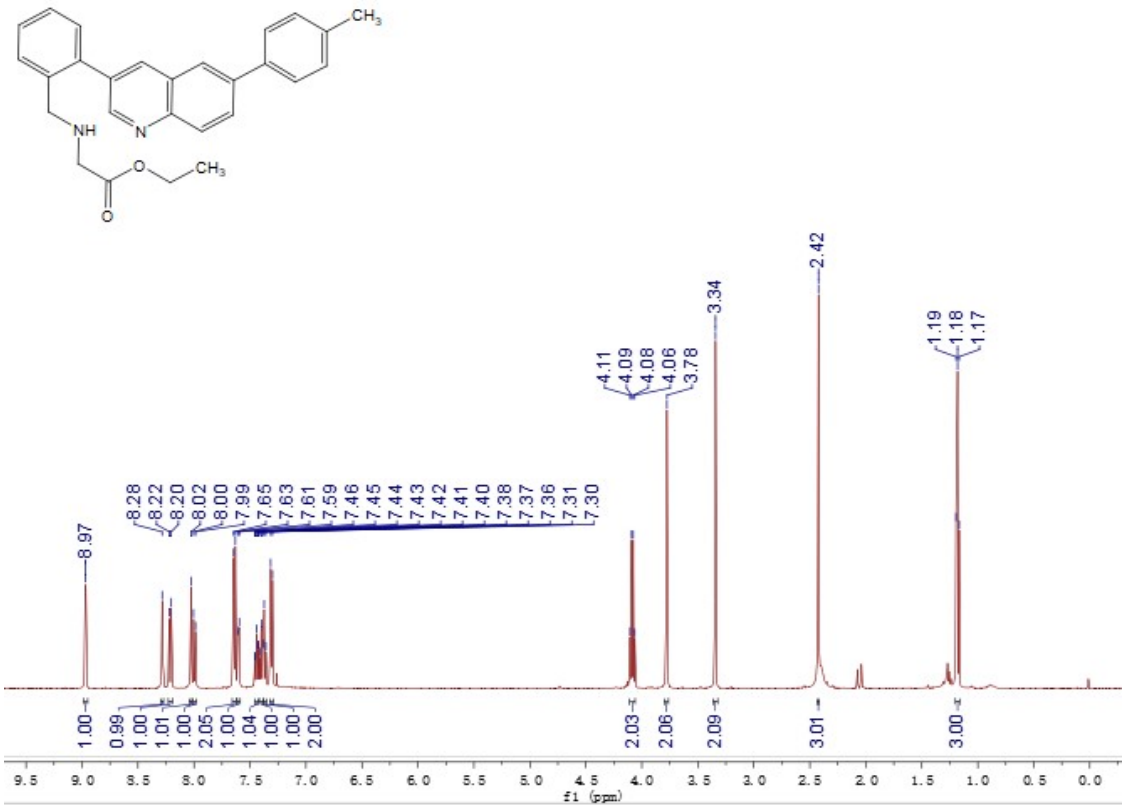
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ak



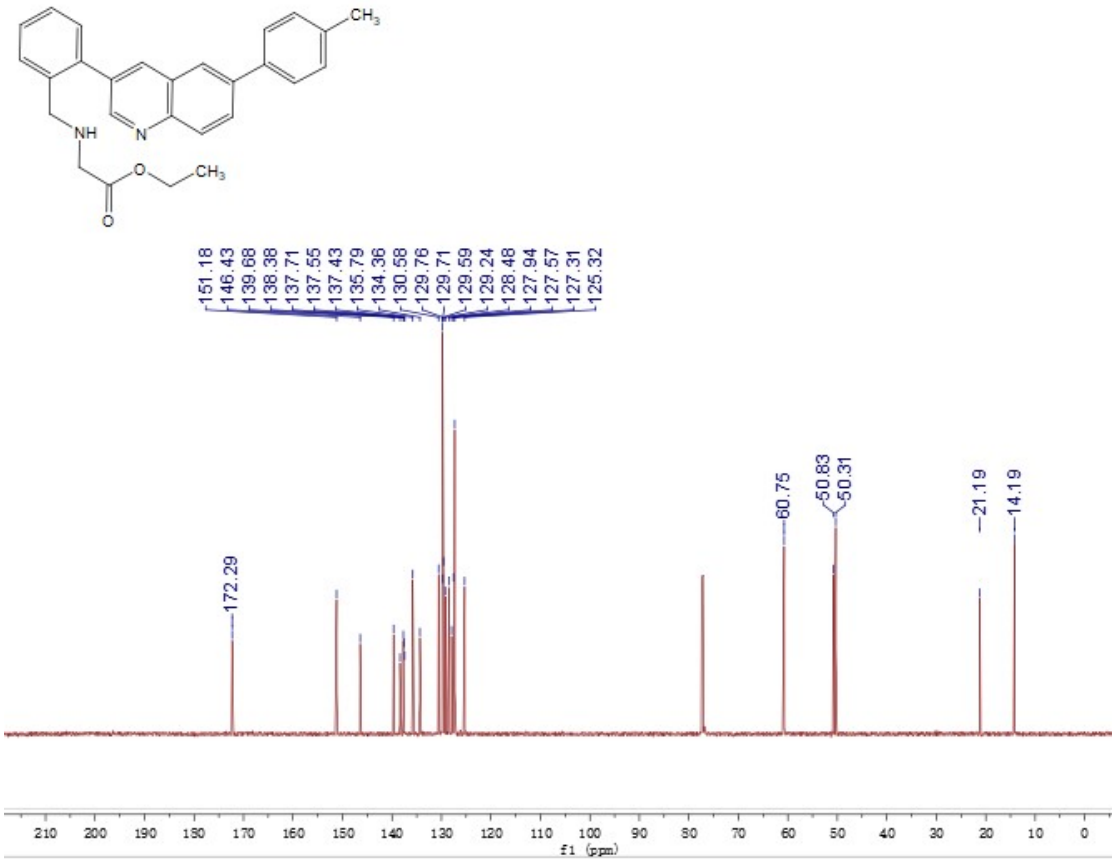
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ak



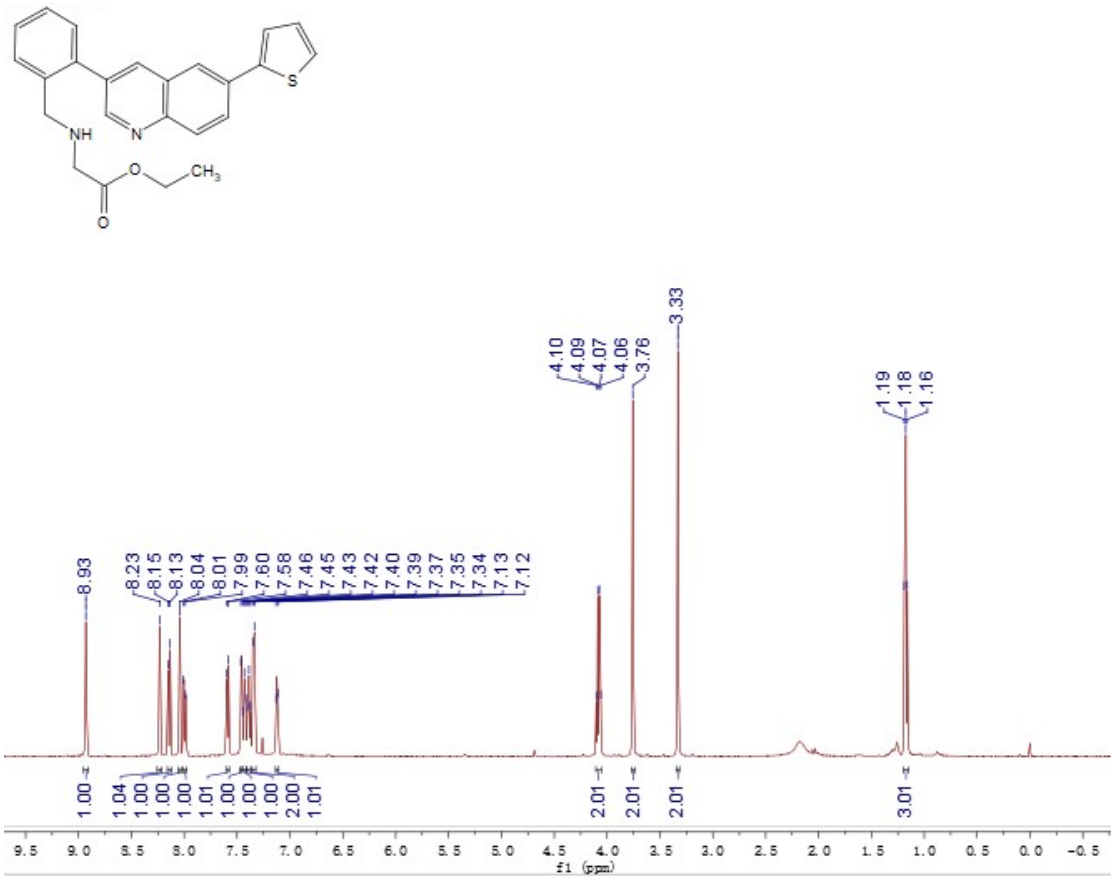
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3al



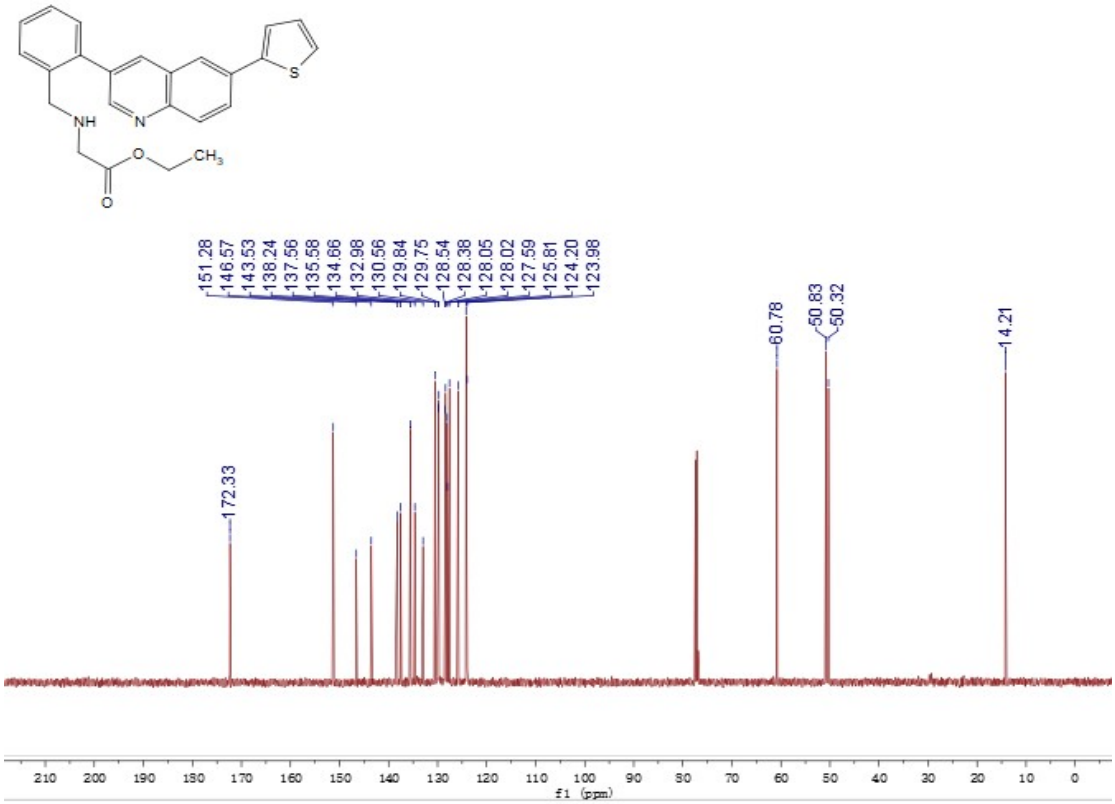
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3al



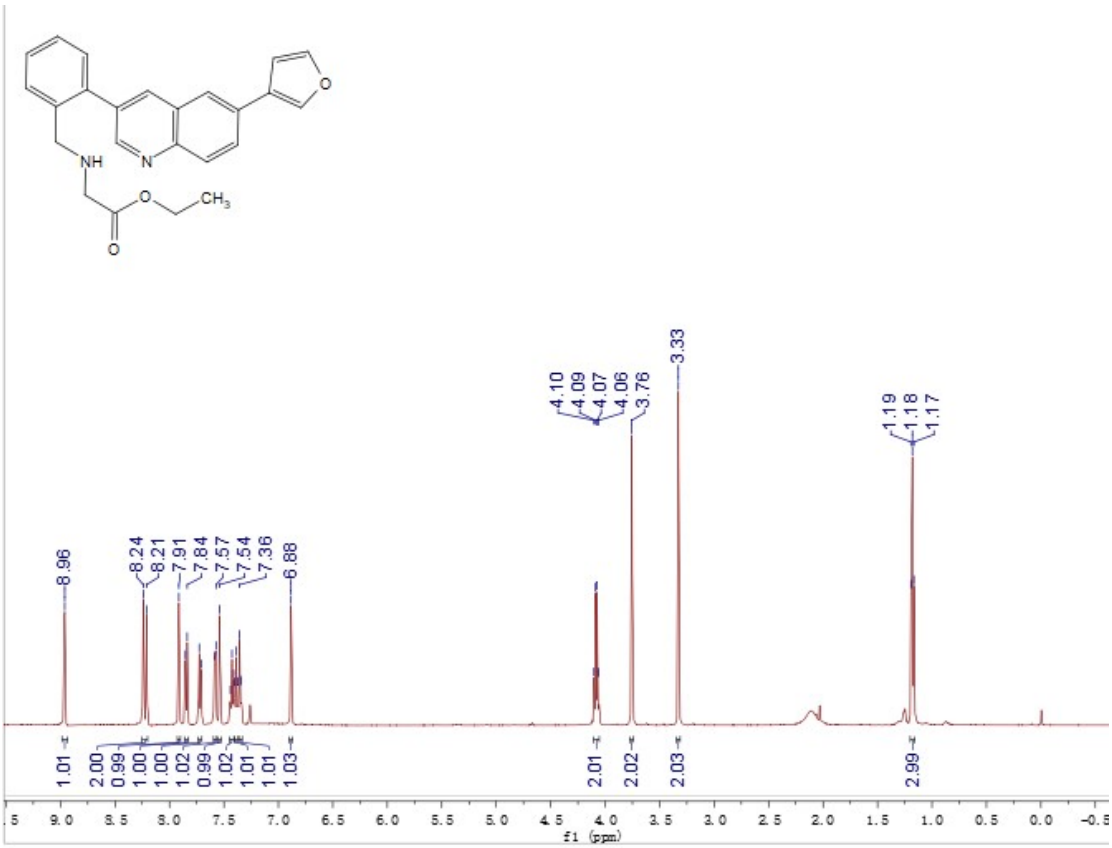
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3am



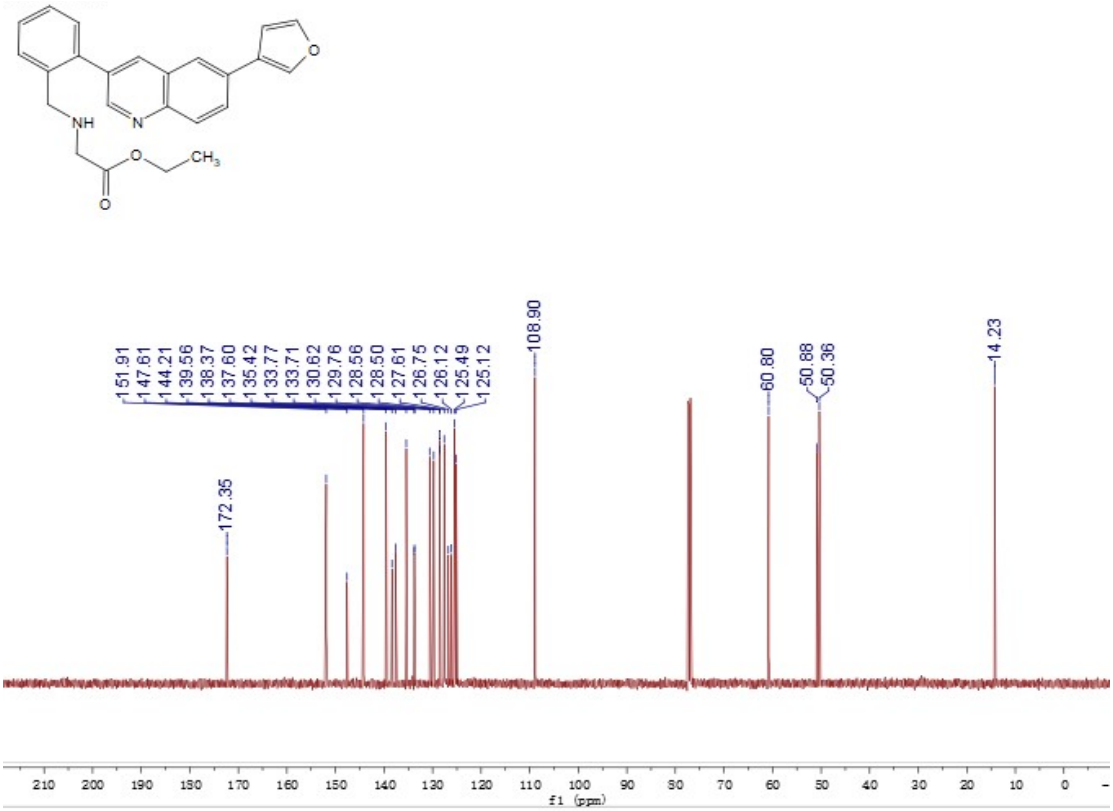
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3am



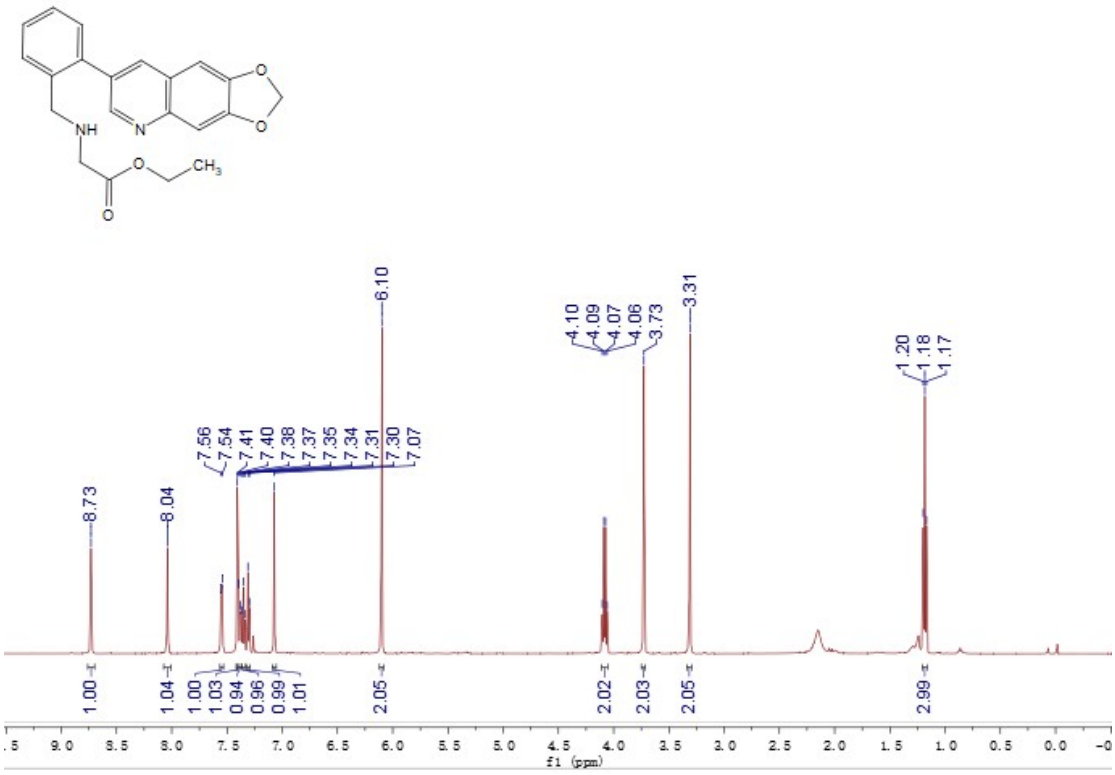
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3an



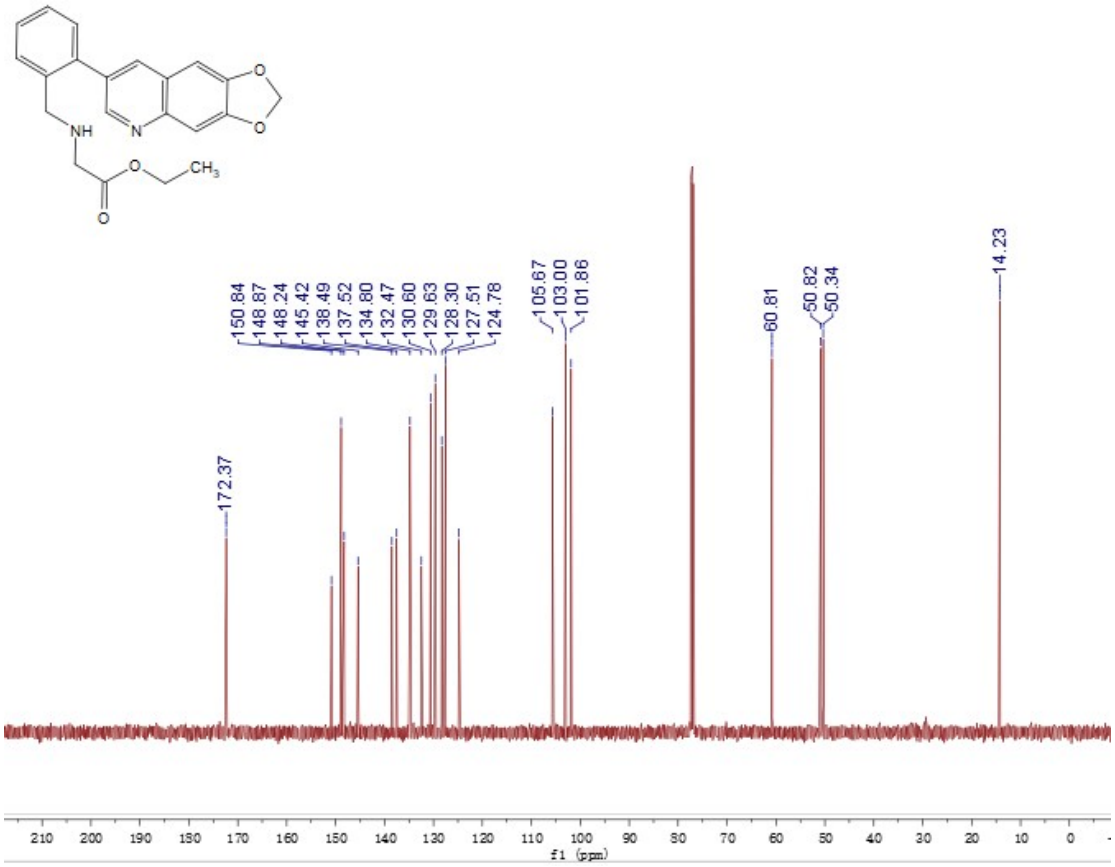
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3an



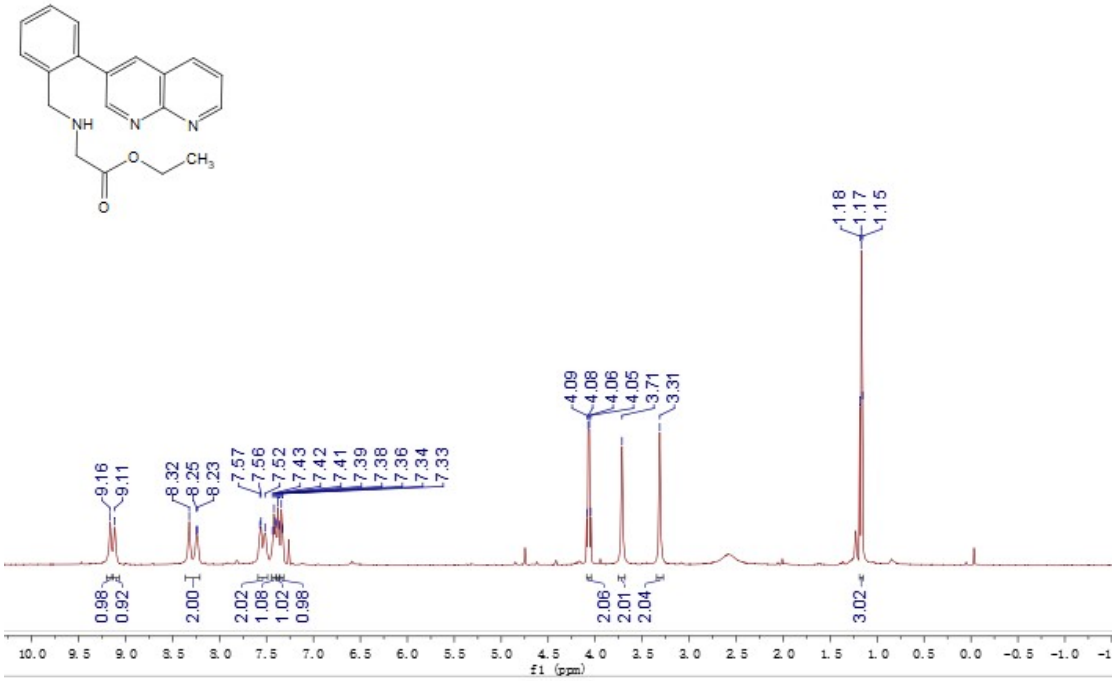
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ao



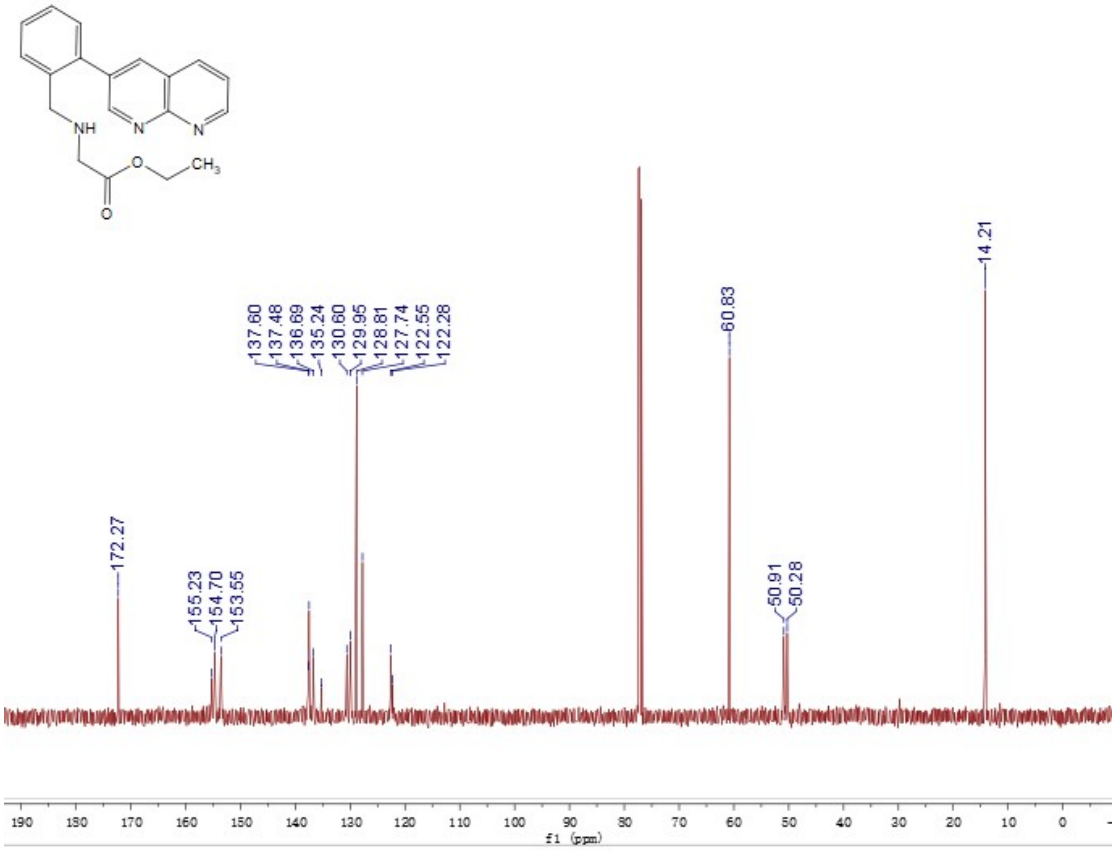
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ao



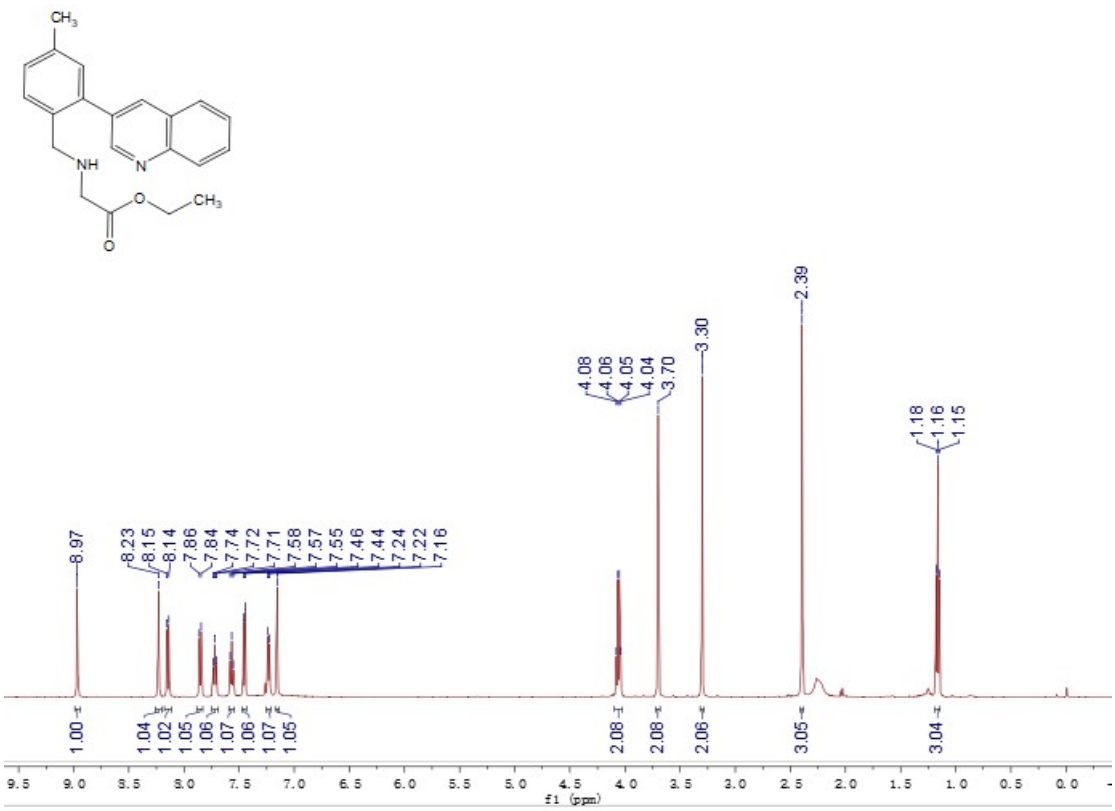
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ap



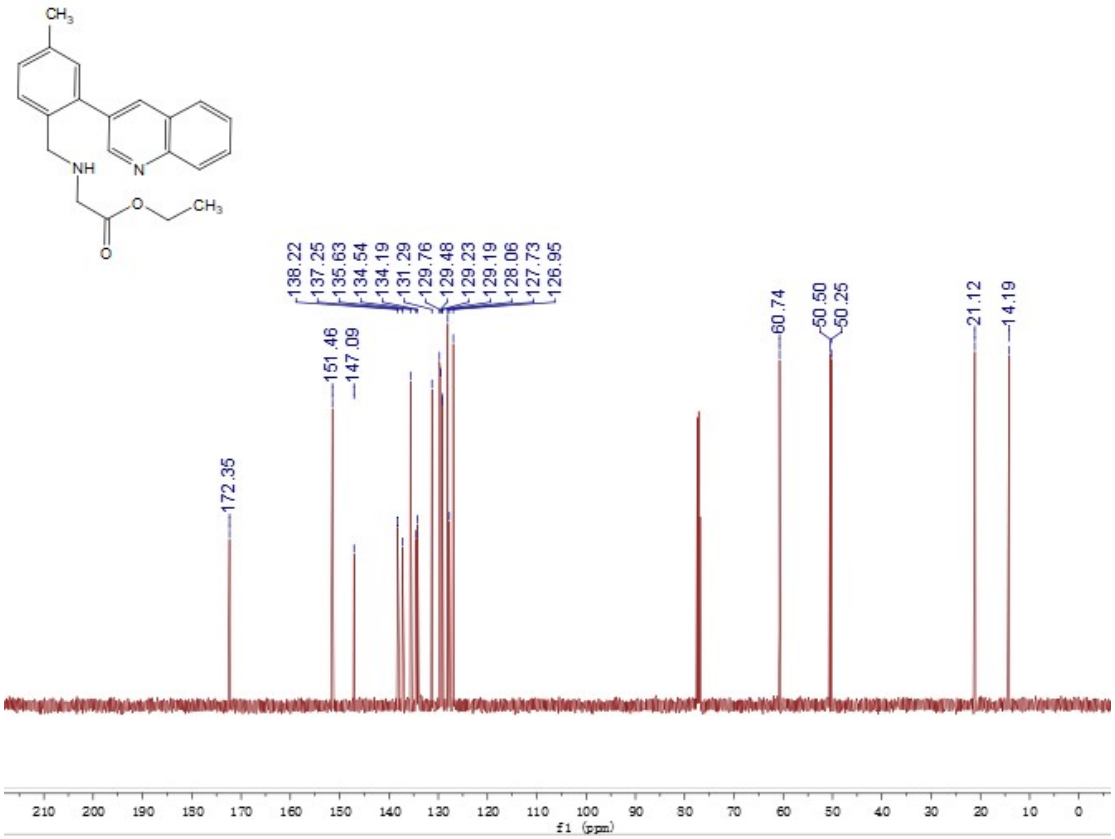
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ap



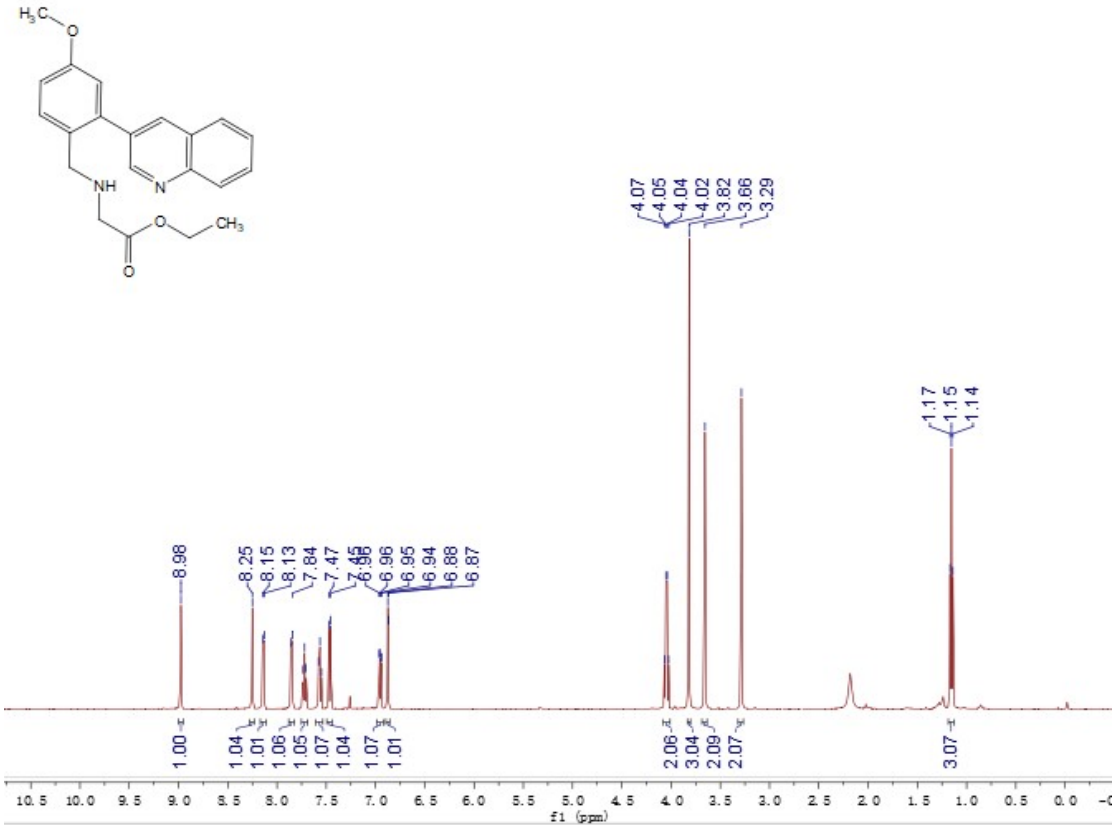
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ba



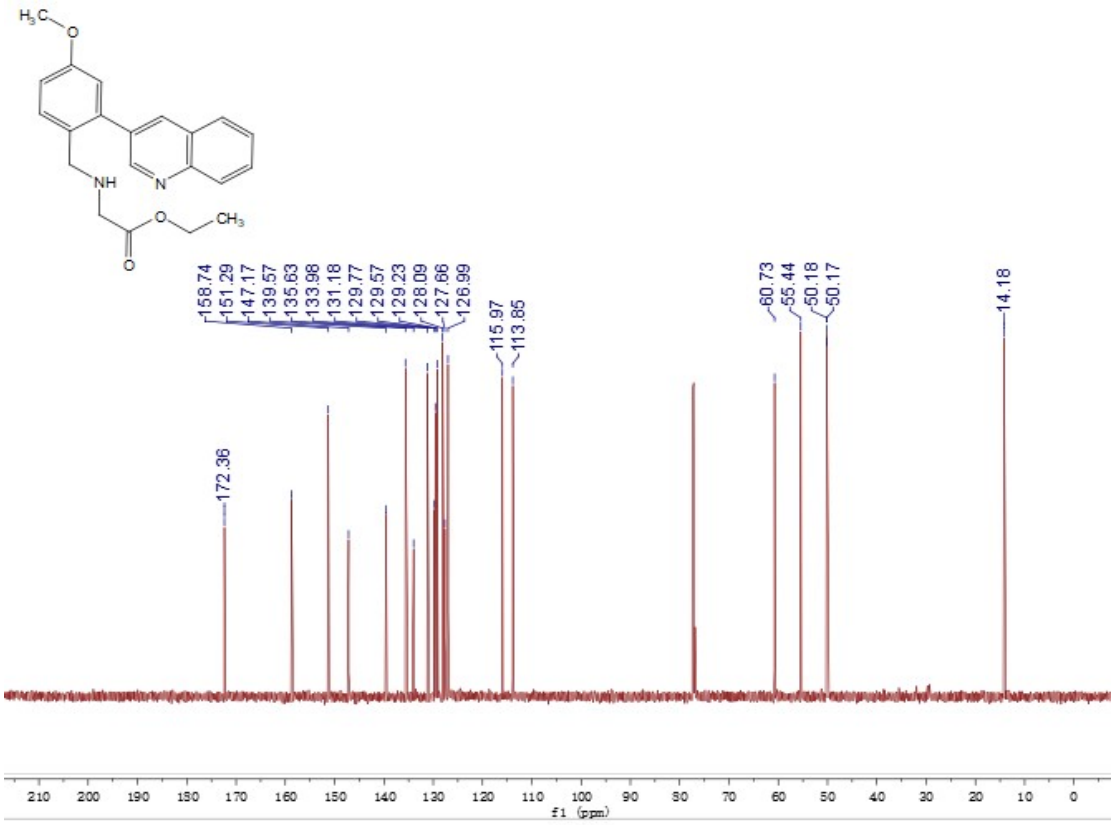
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ba



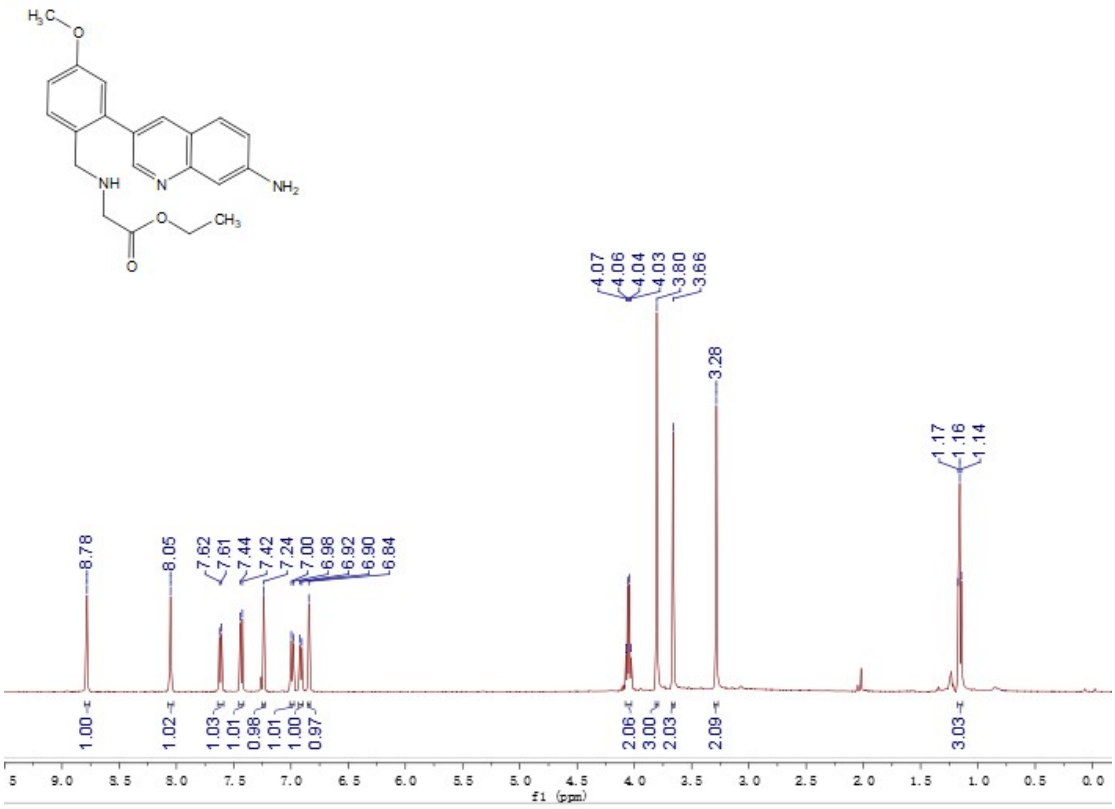
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum 3ca



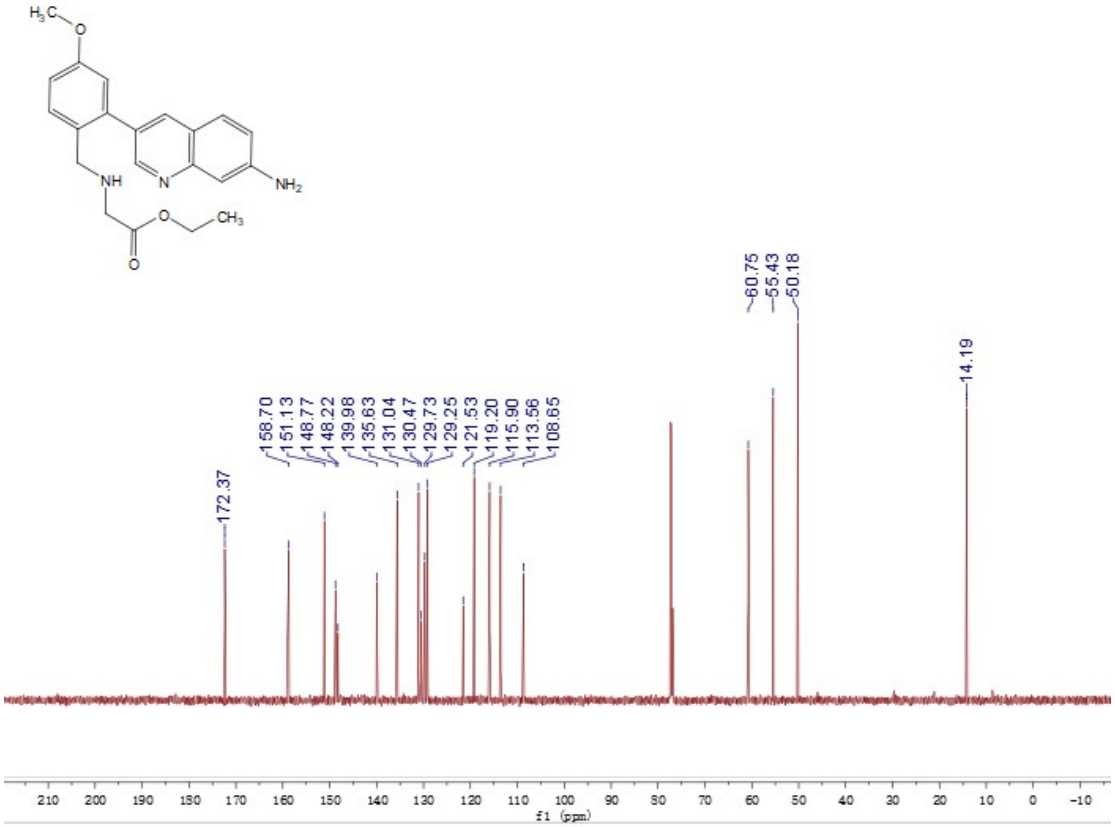
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ca



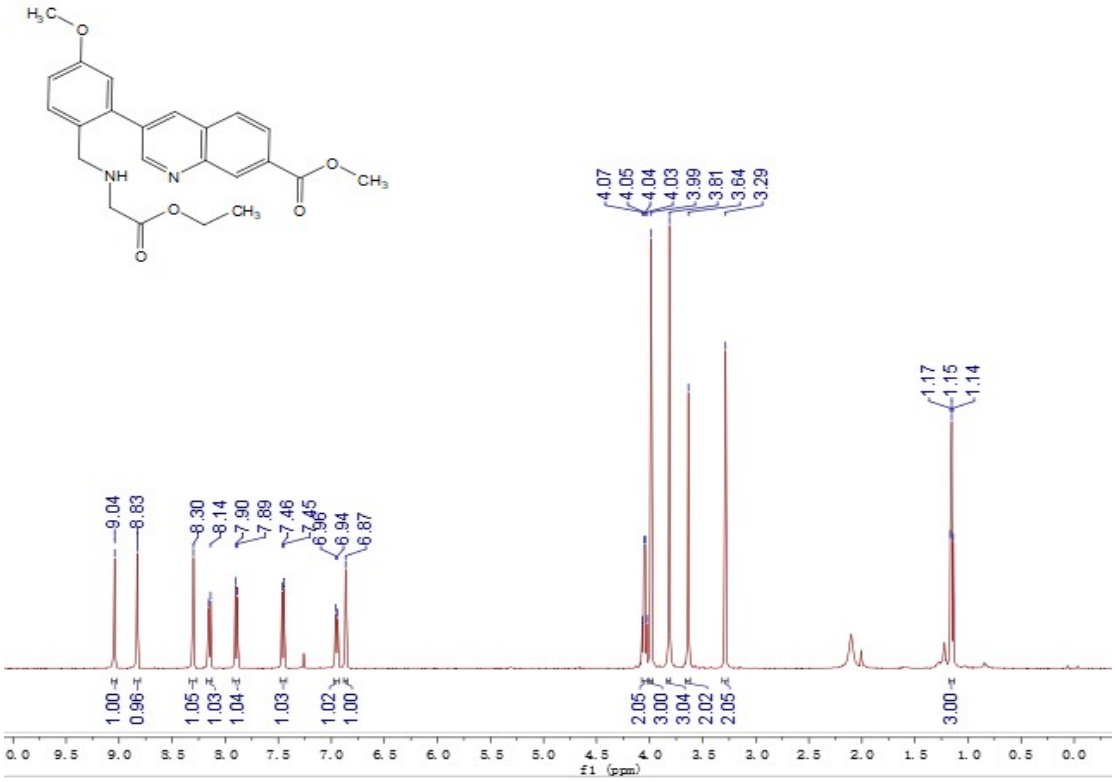
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3cd



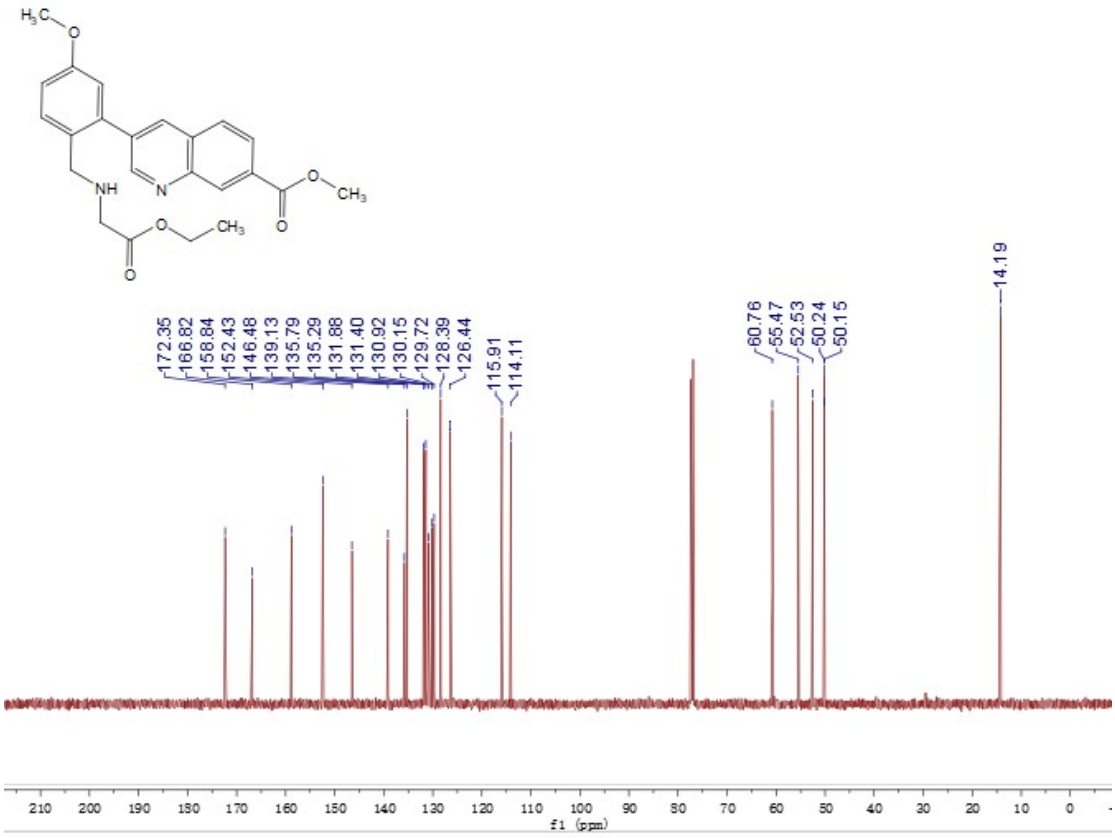
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3cd



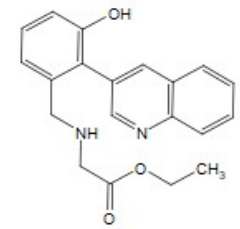
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ci

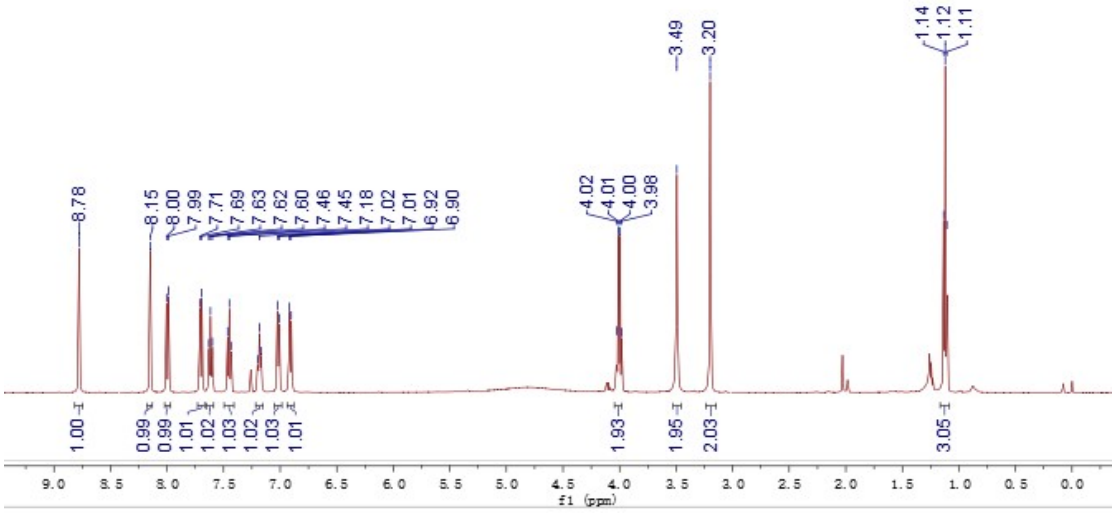


^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ci

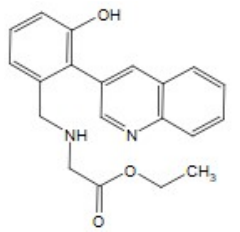


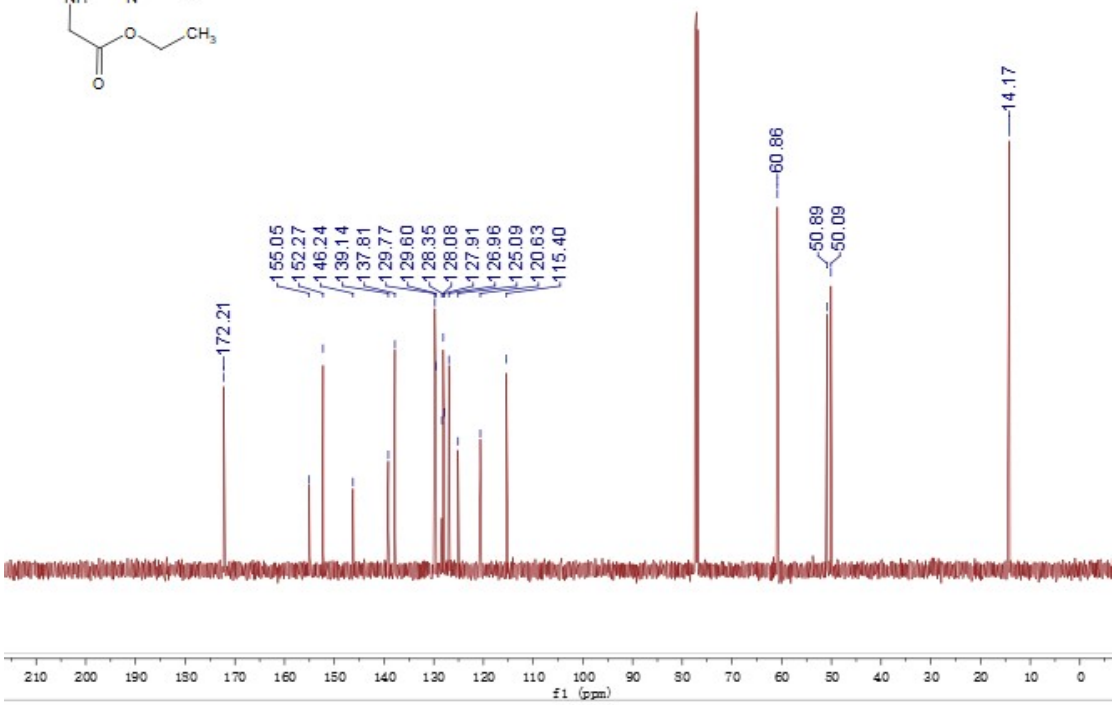
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3da



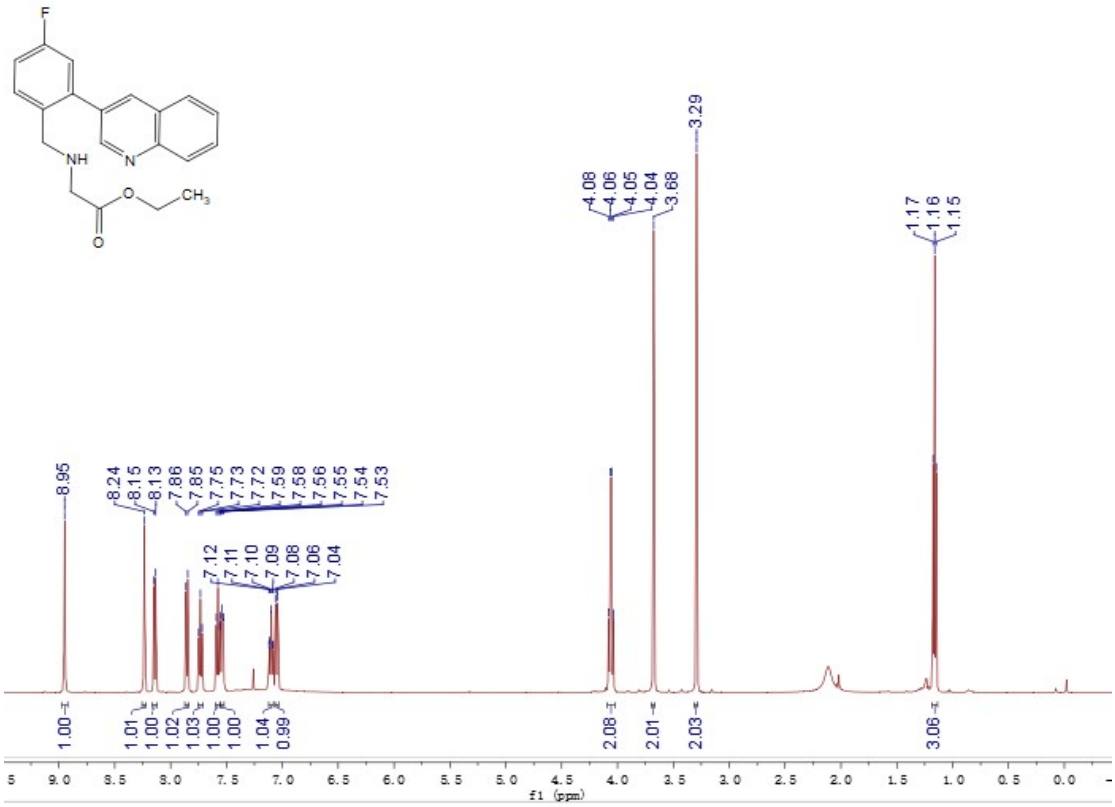


^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3da

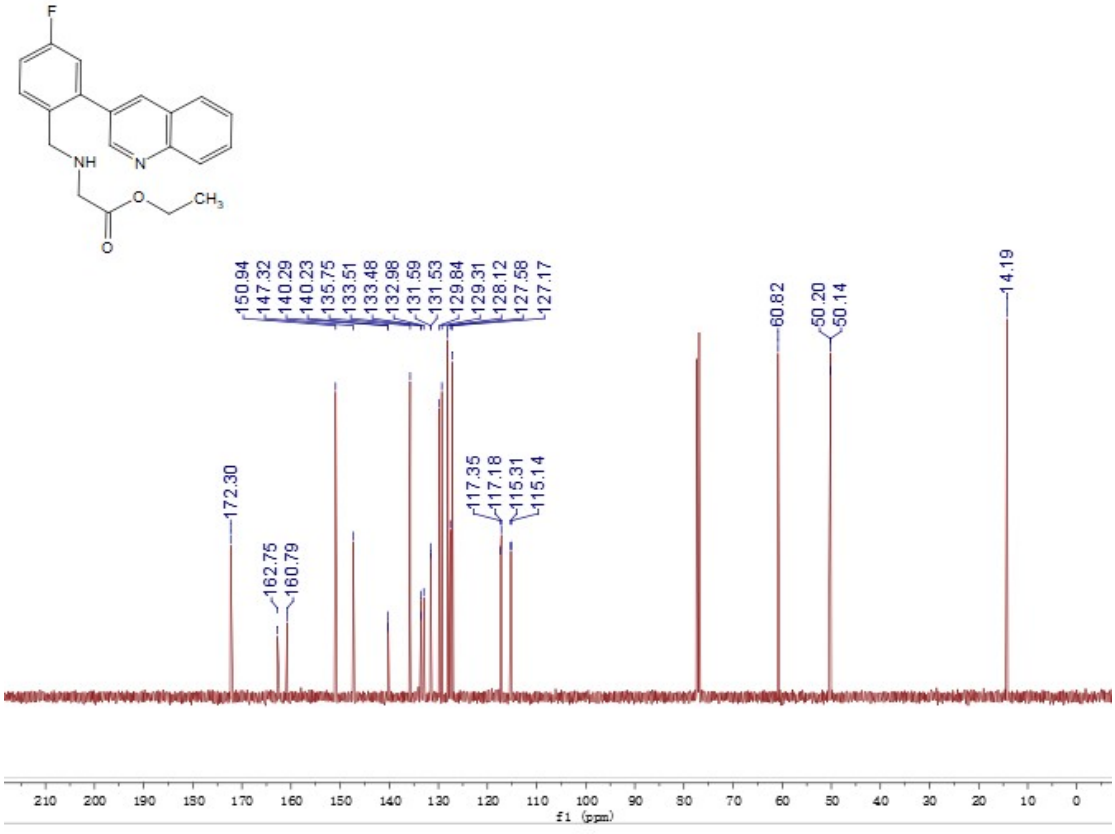




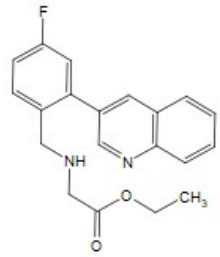
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ea

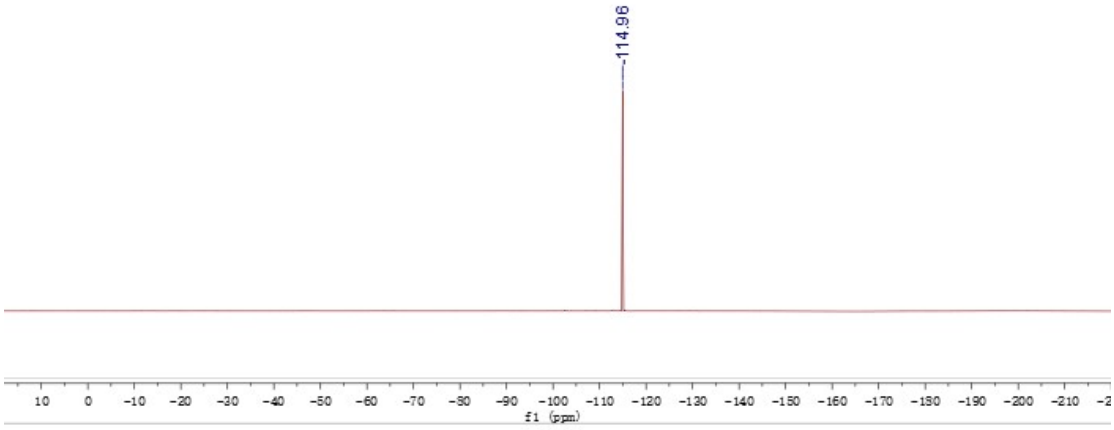


^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ea

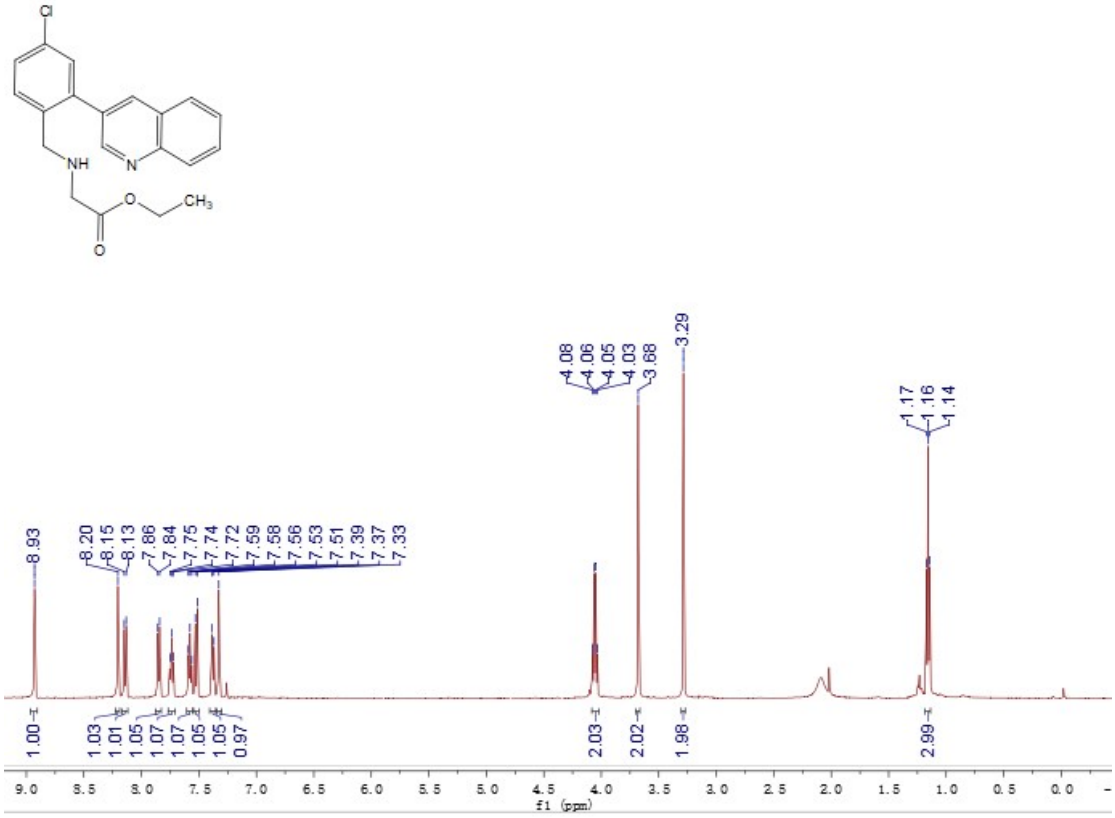


^{19}F-NMR (471 MHz, $CDCl_3$) spectrum of 3ea

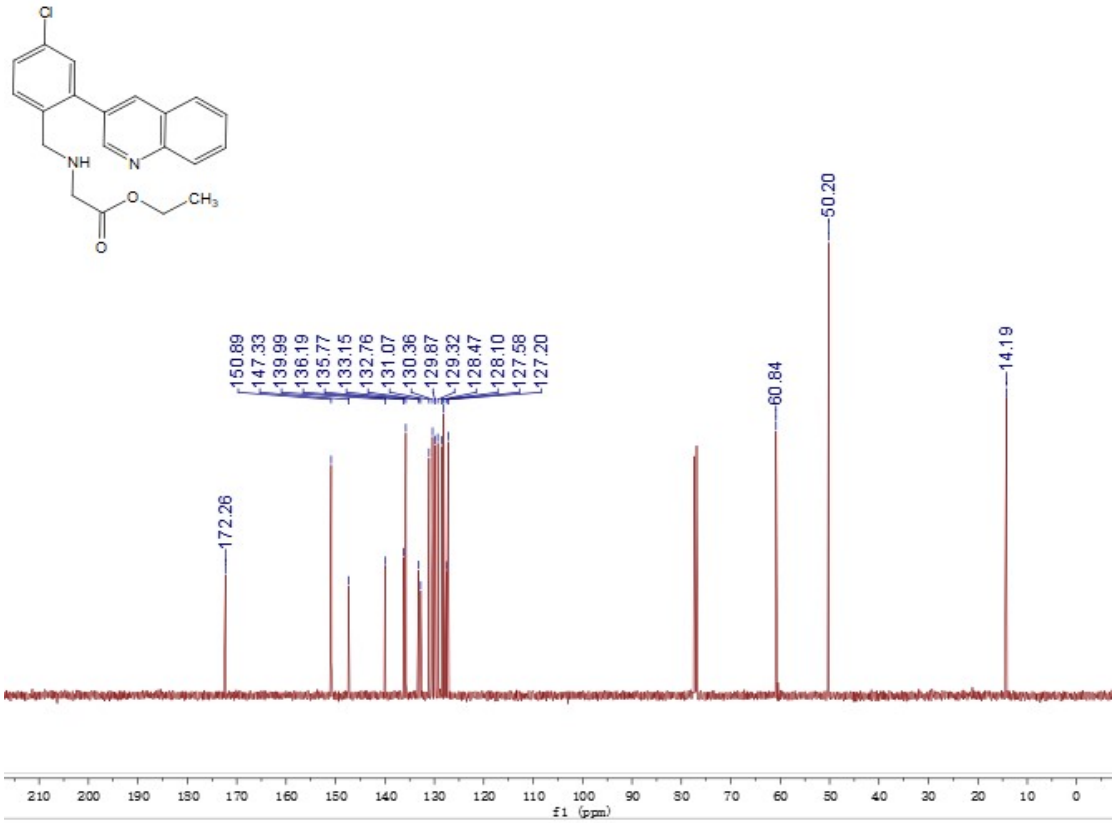

F
NH
N
O
CH3
O


-114.96
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

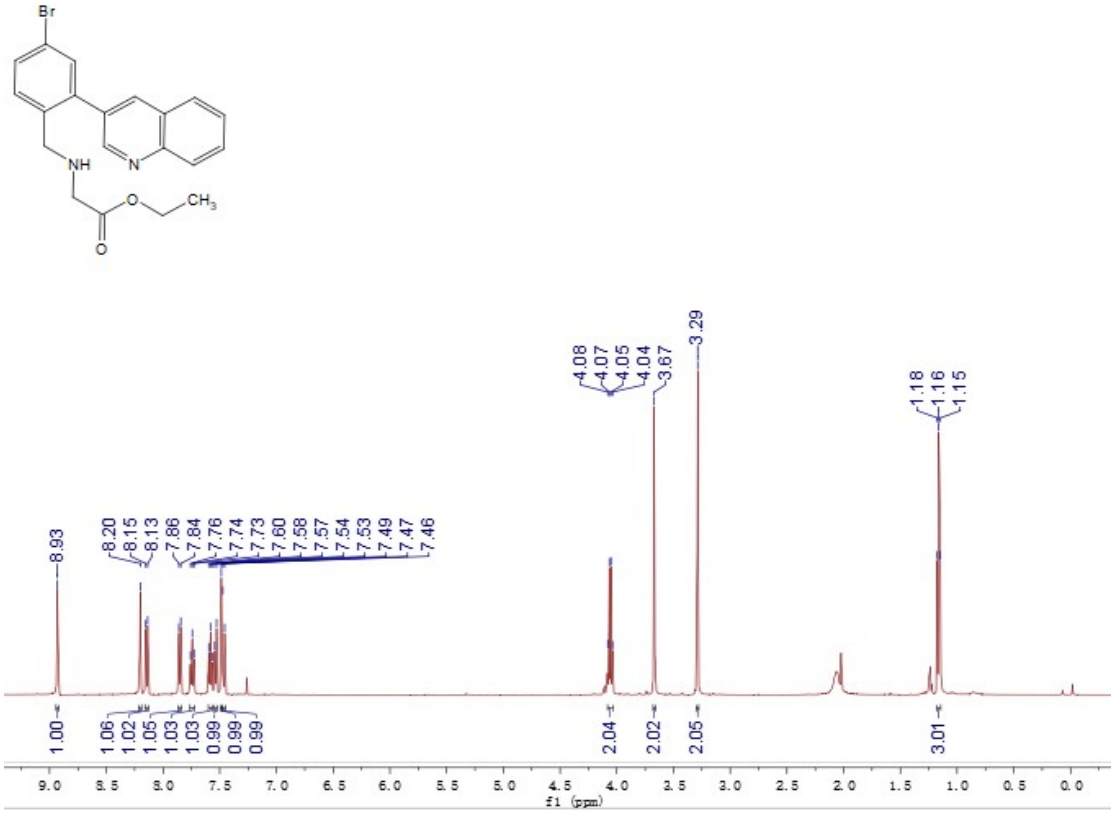
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3fa



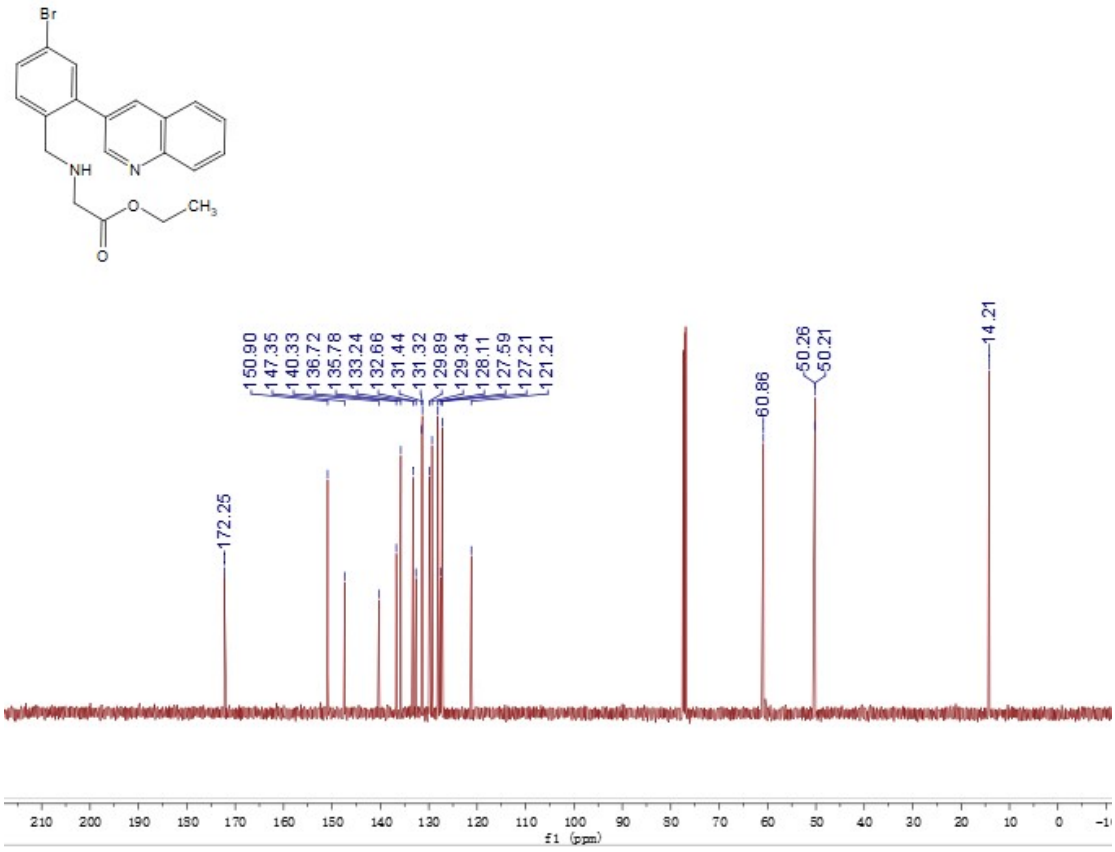
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3fa



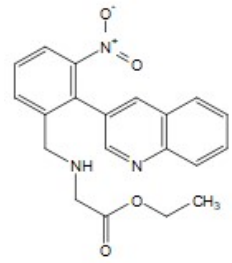
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ga

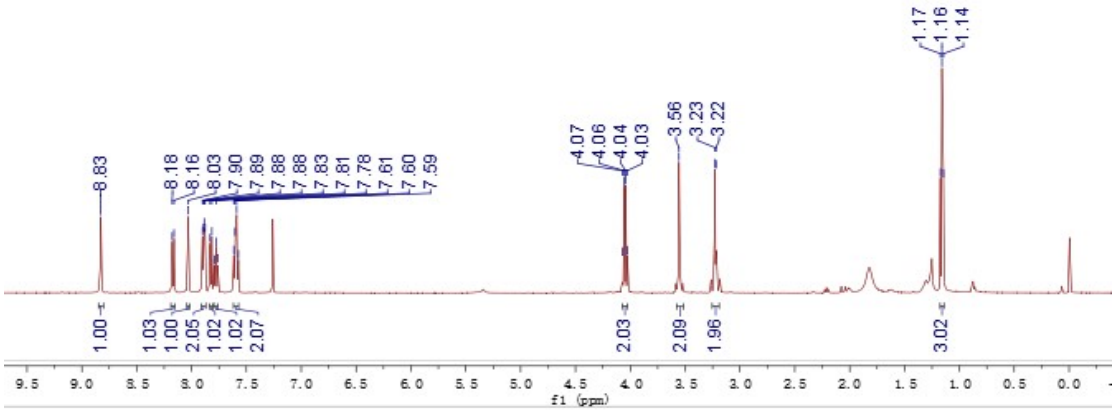


^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ga

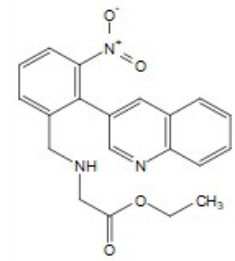


^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ha

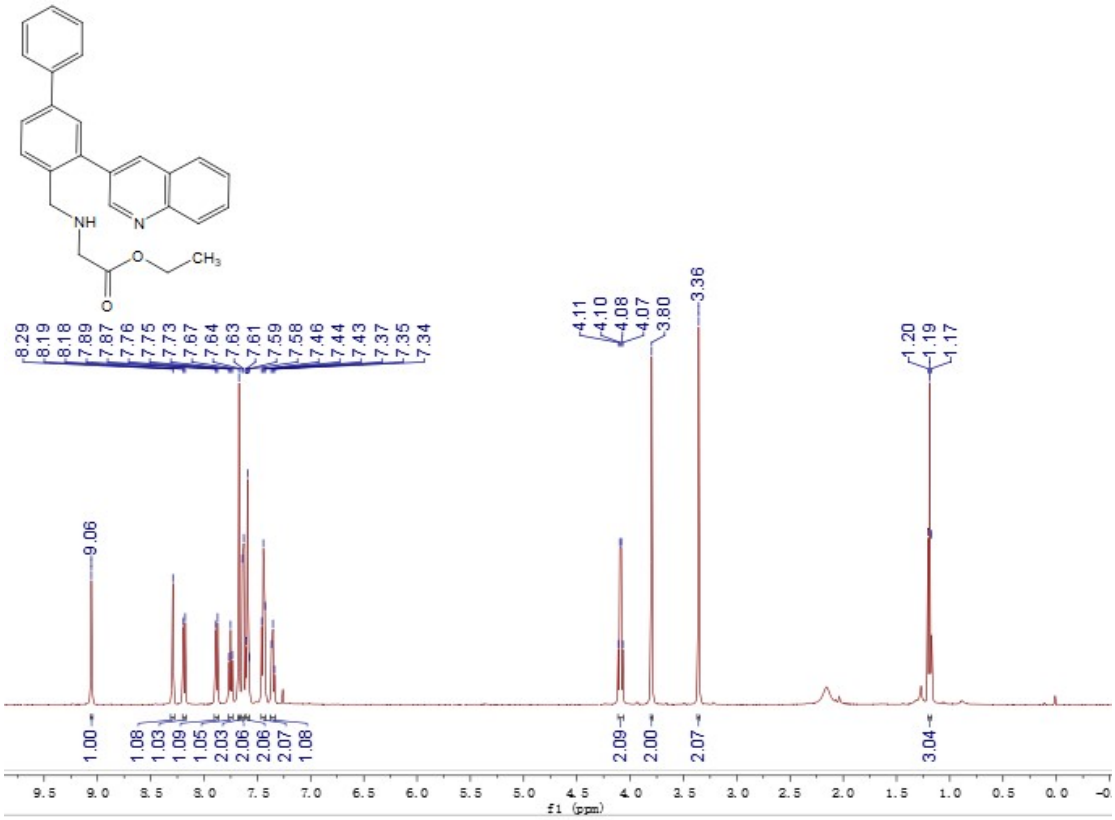




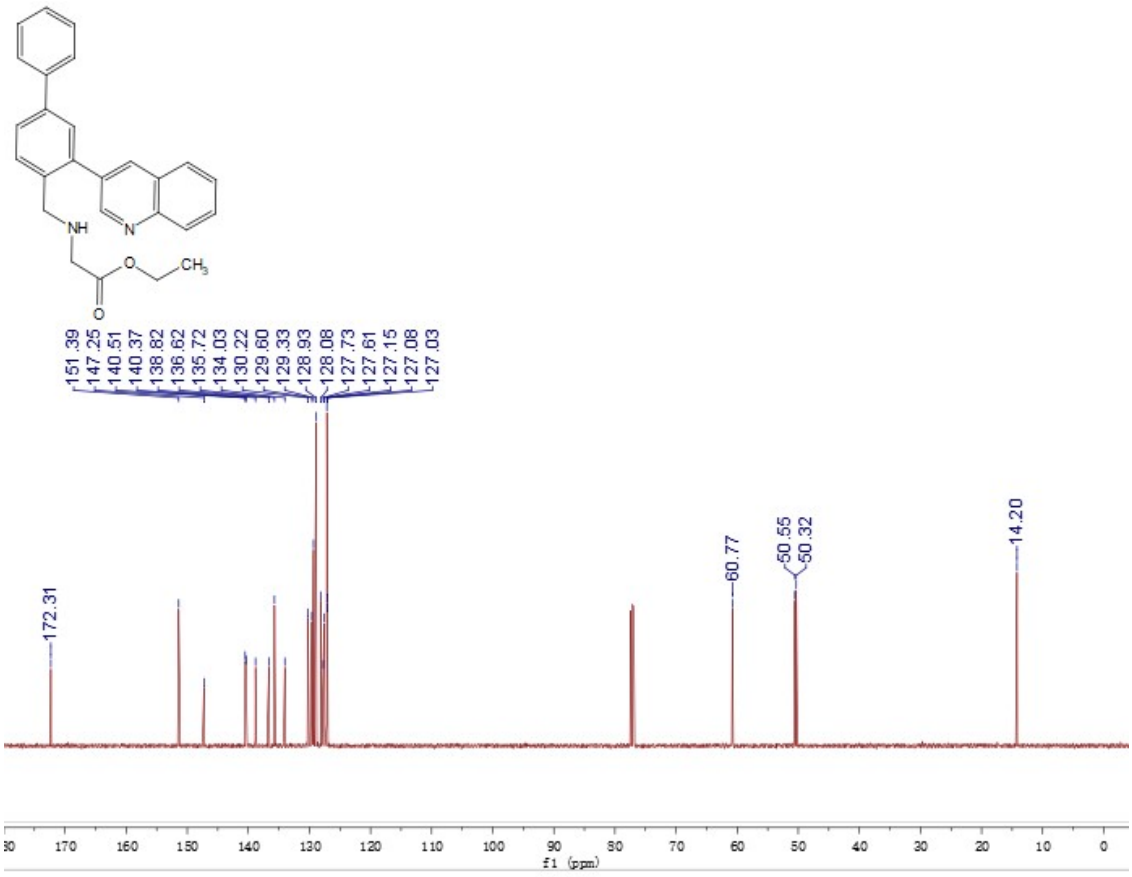
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ha



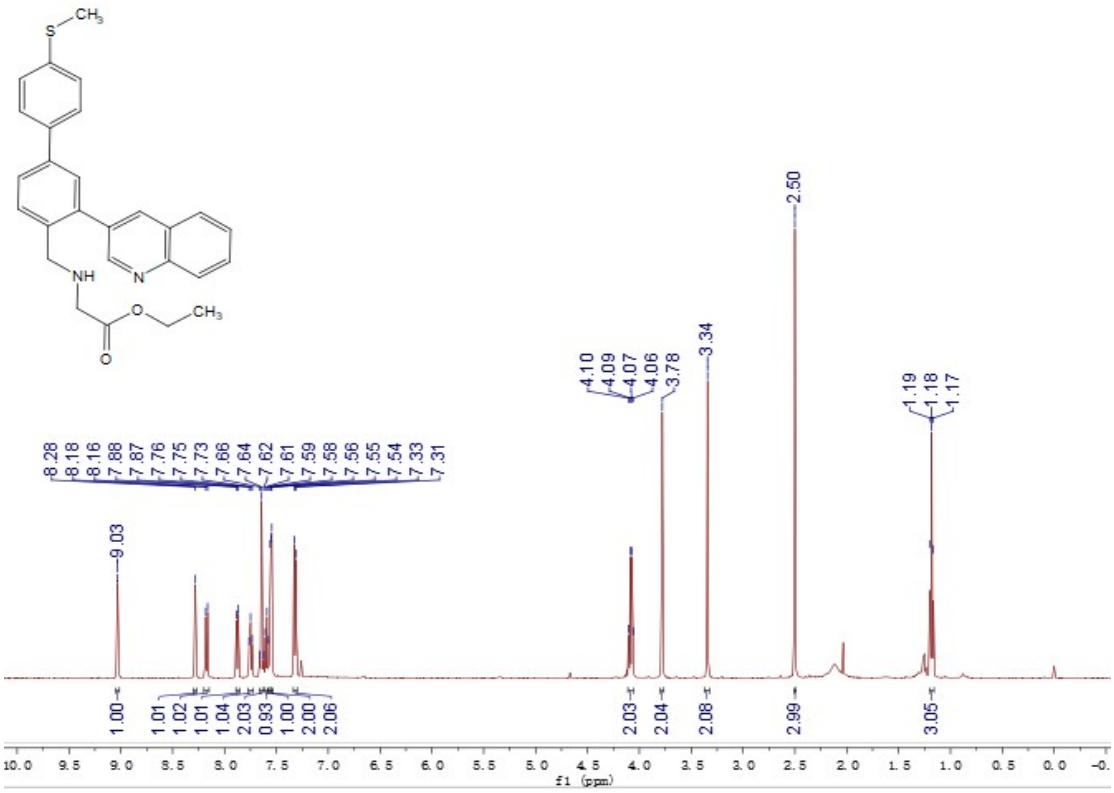
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ia



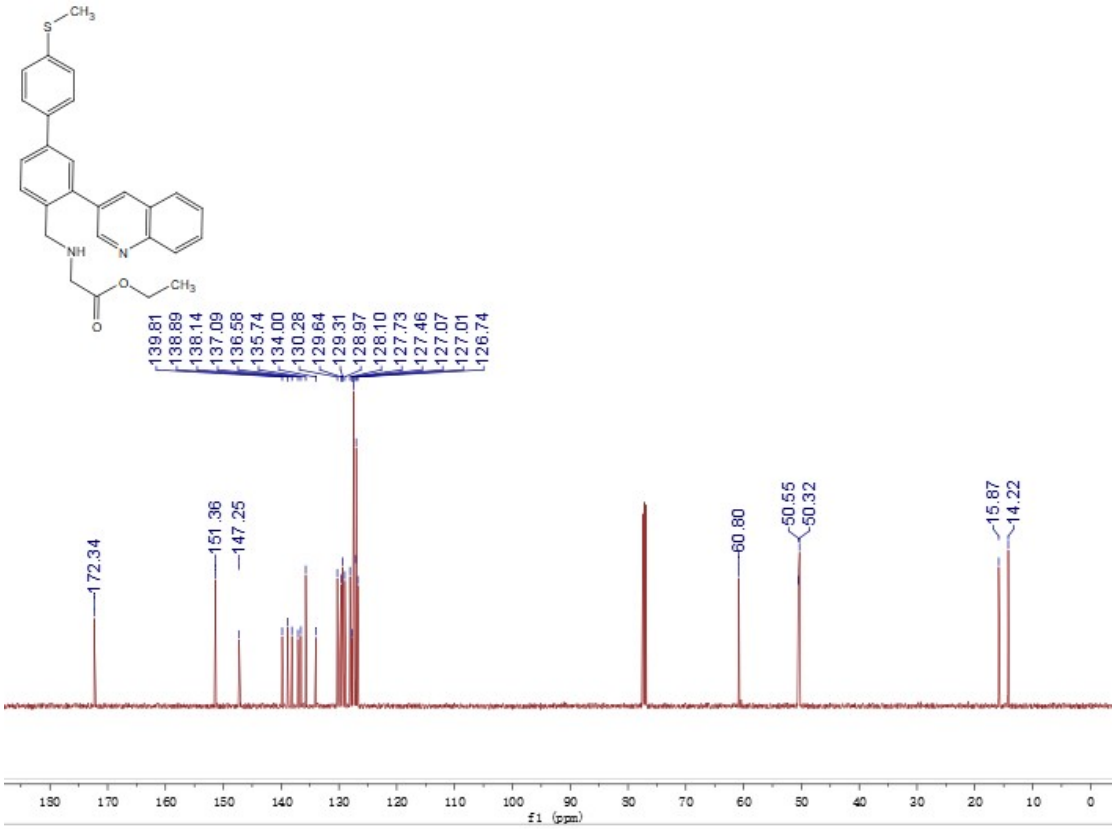
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum 3ia



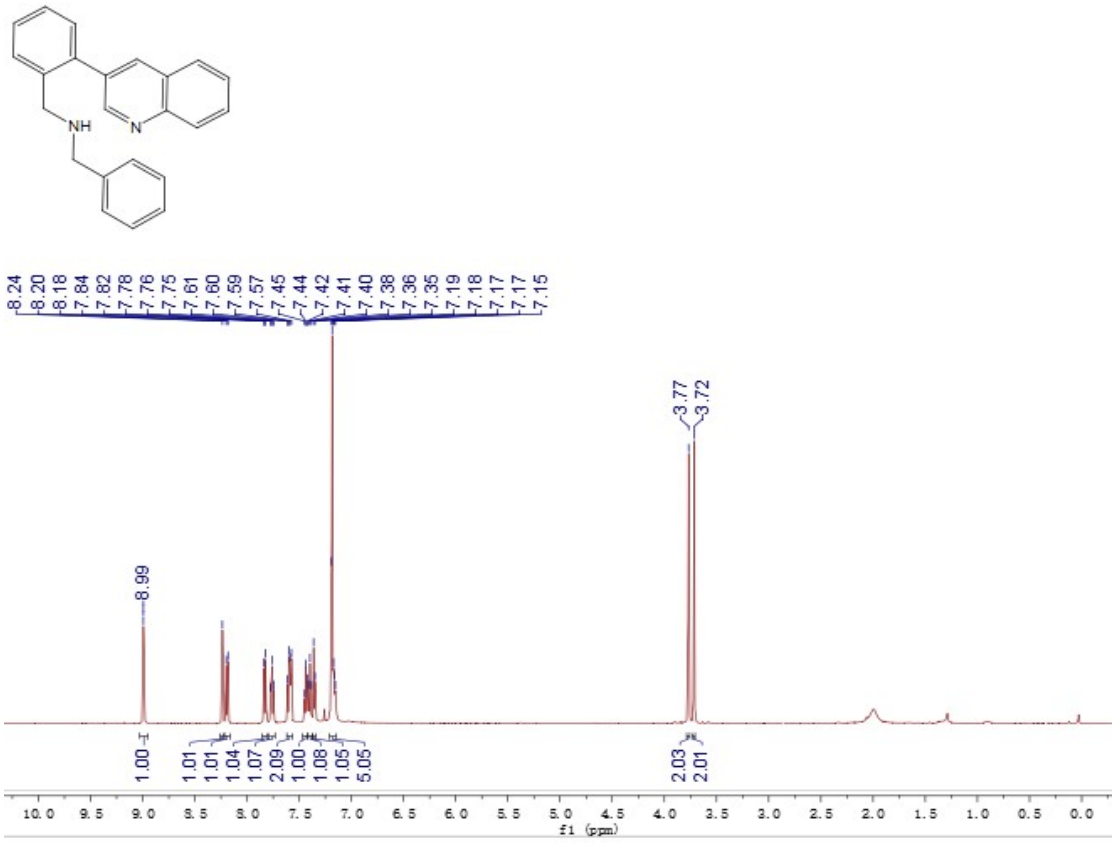
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ja



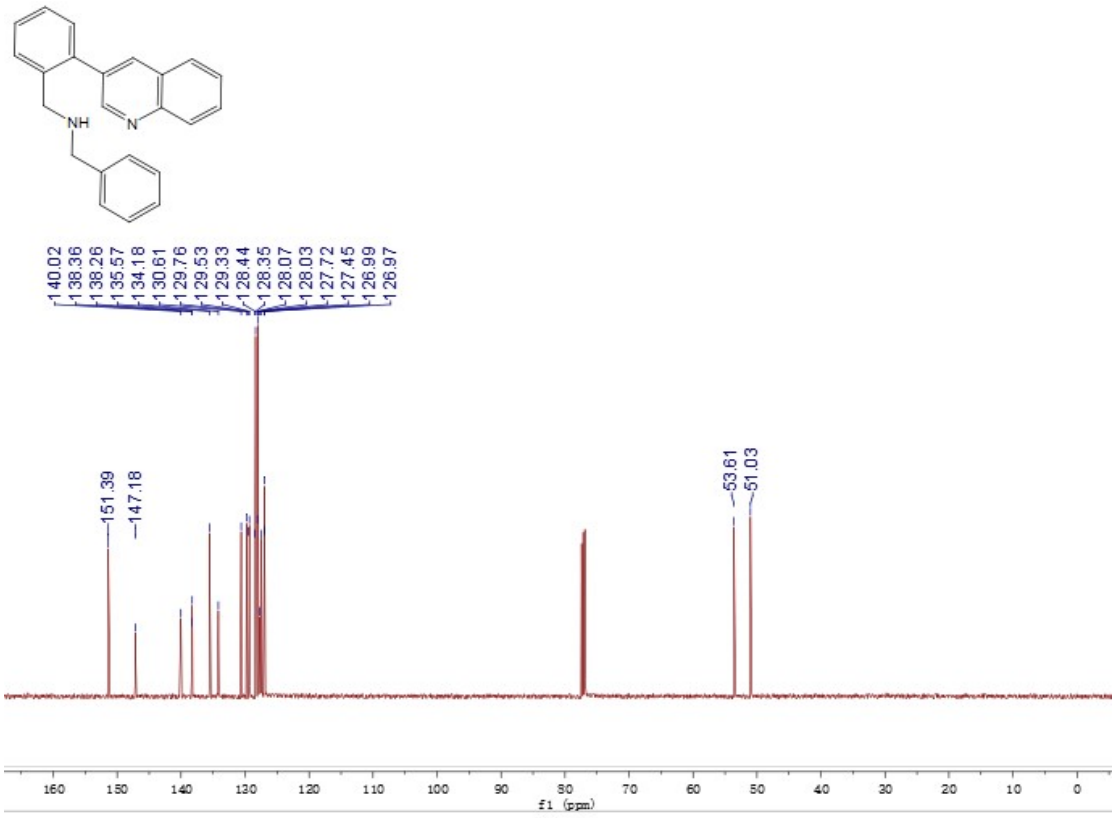
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ja



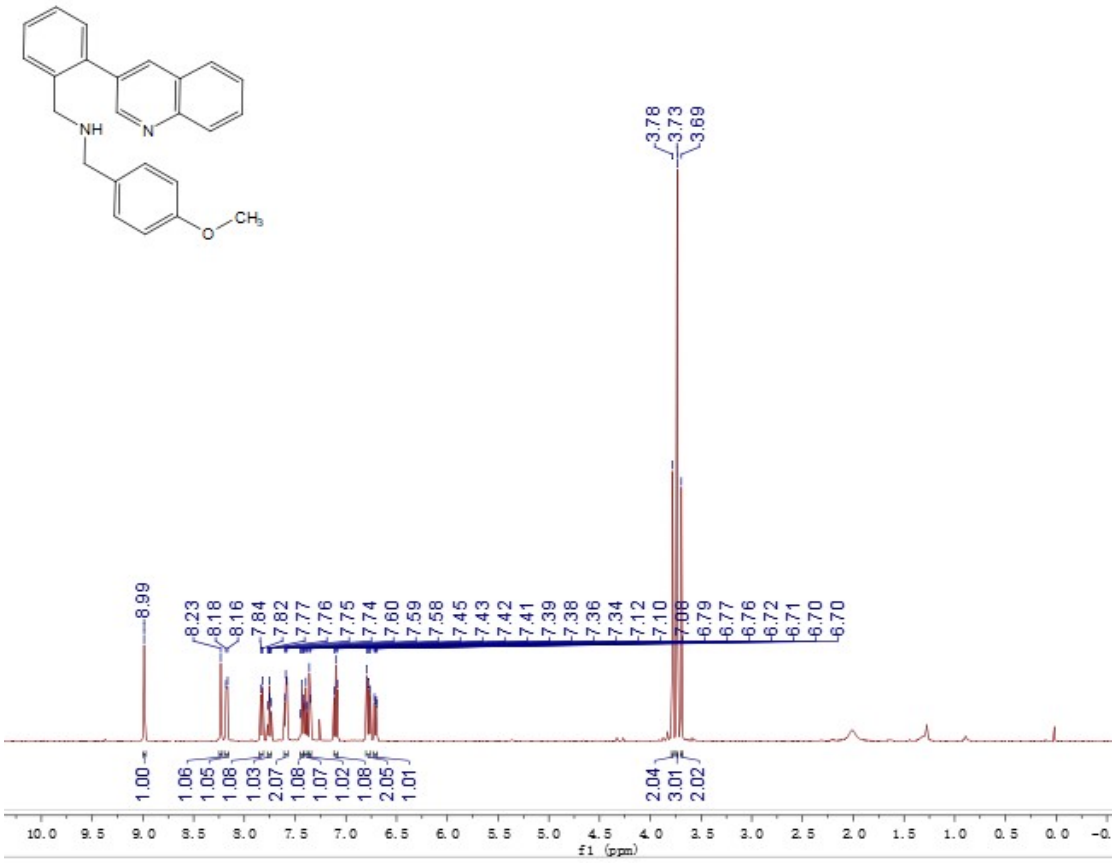
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ka



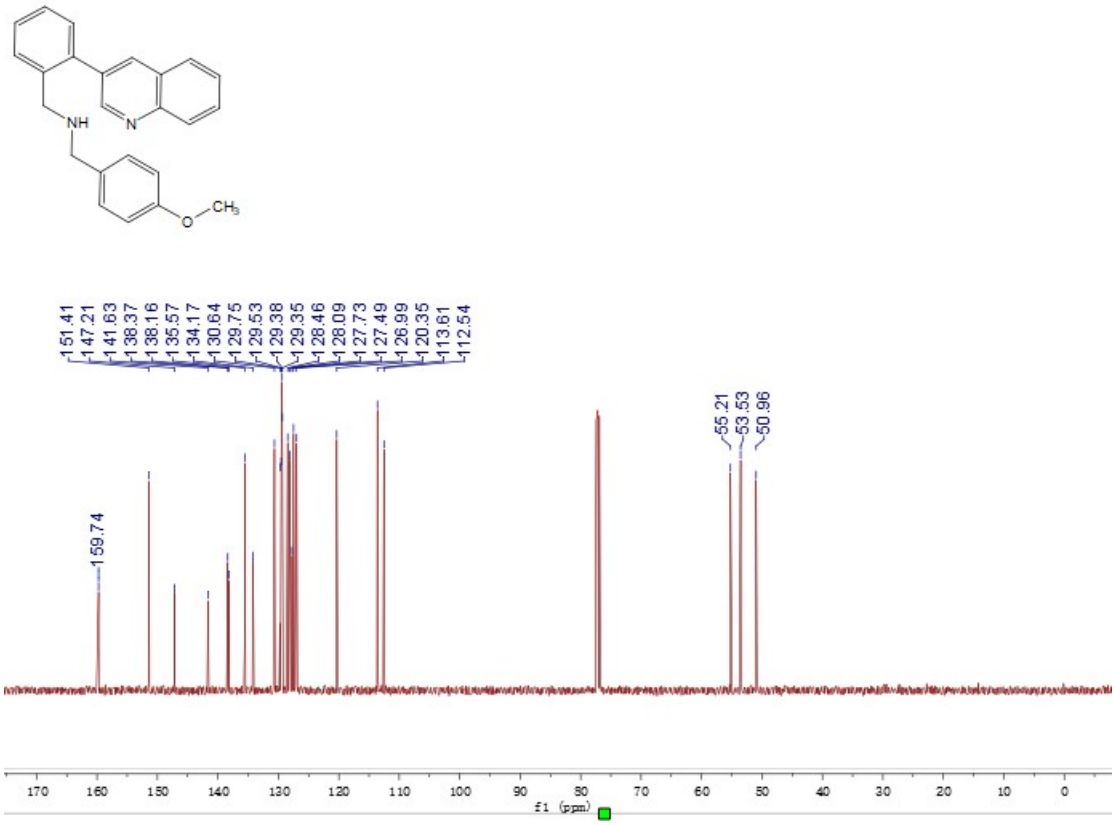
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ka



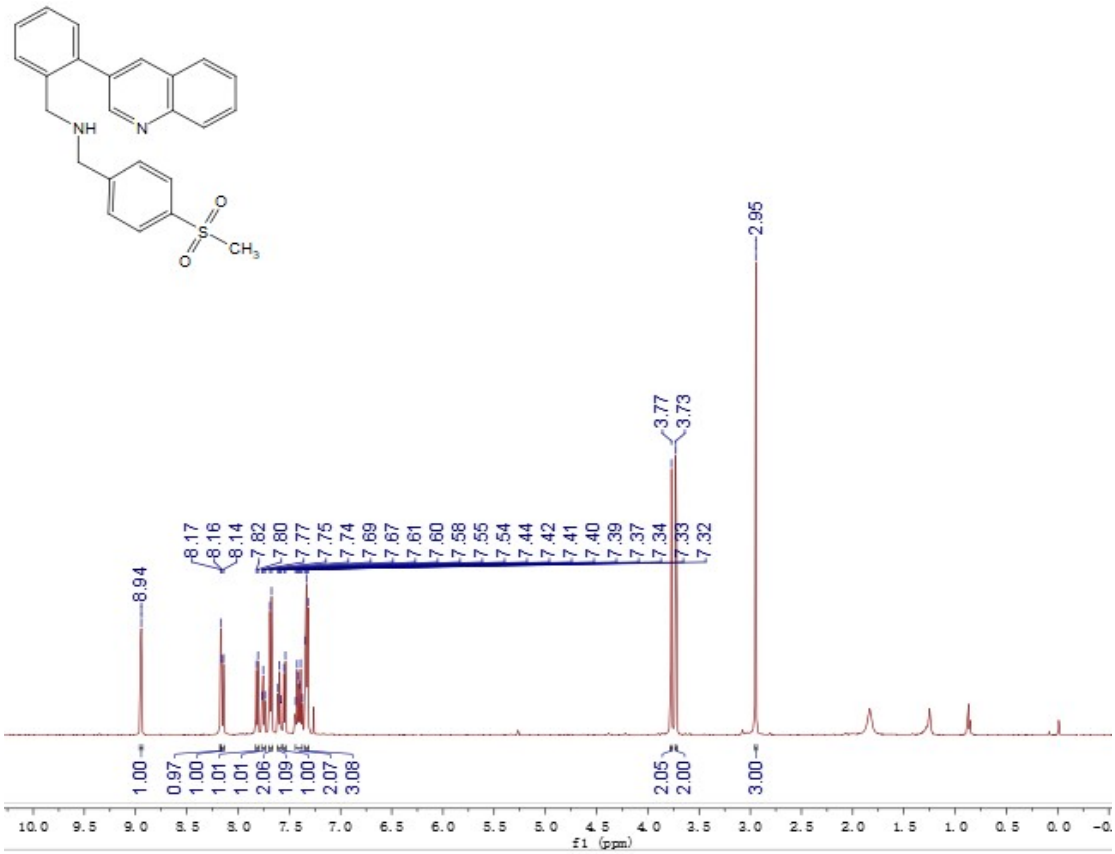
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3la



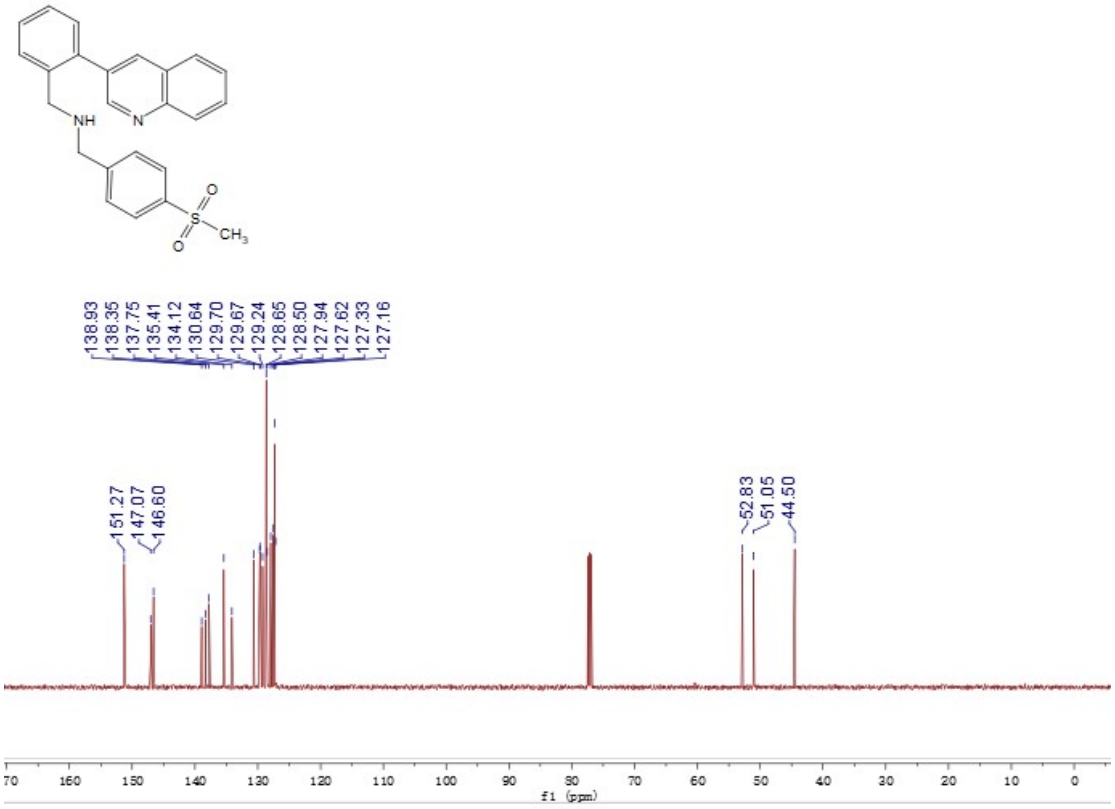
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3la



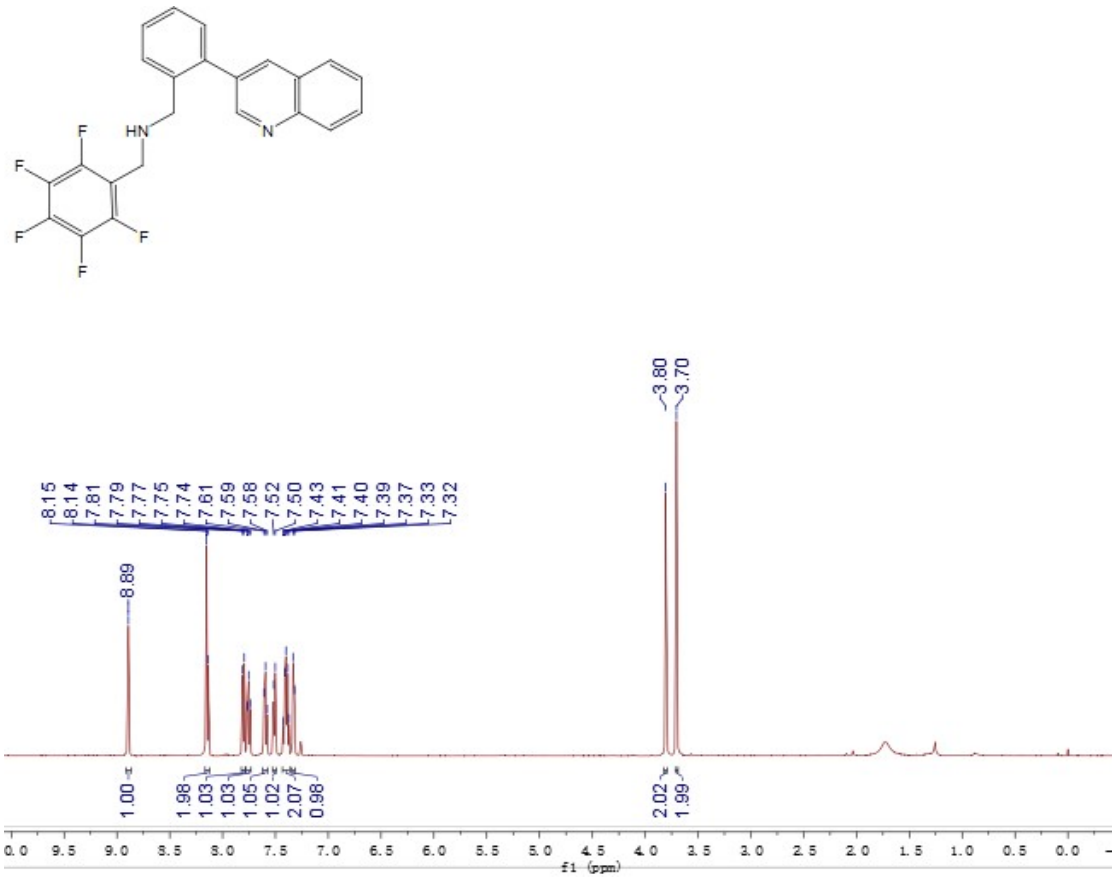
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3ma



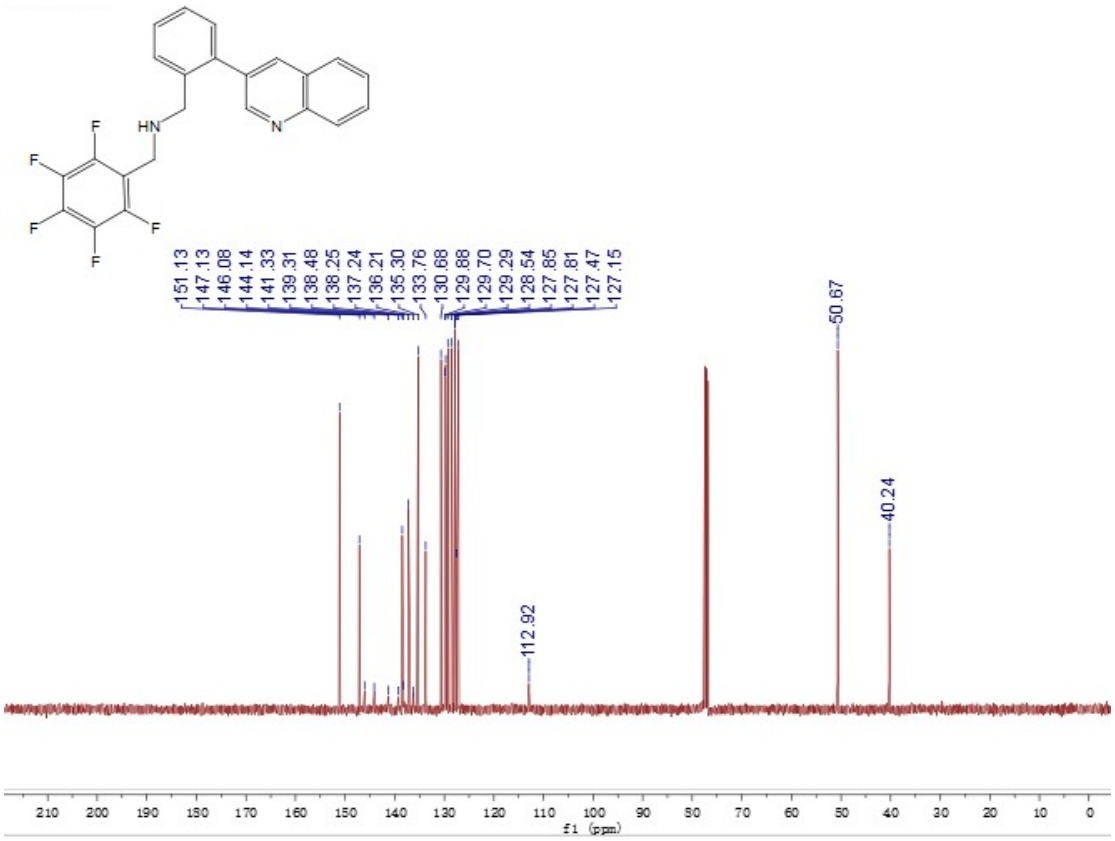
^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3ma



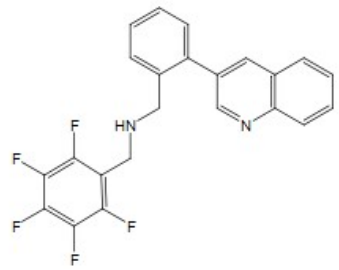
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3na

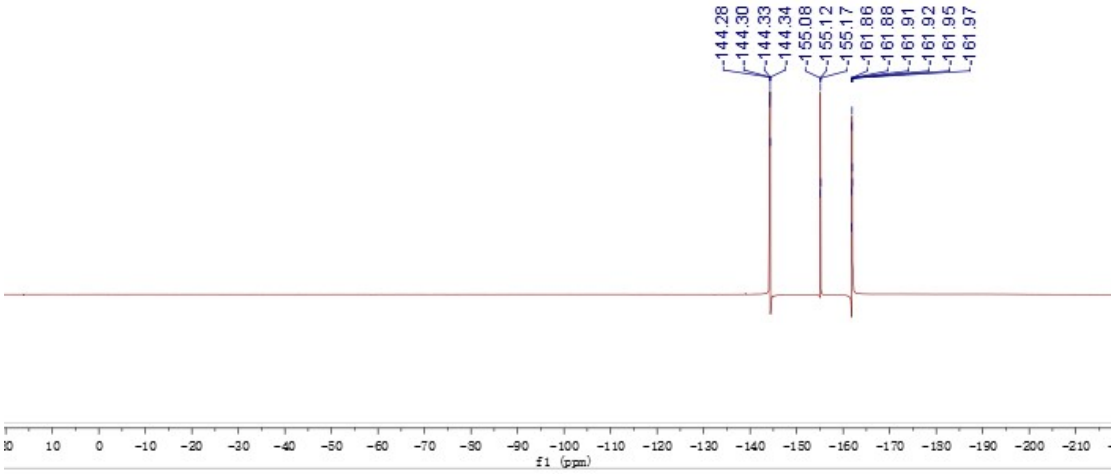


^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3na

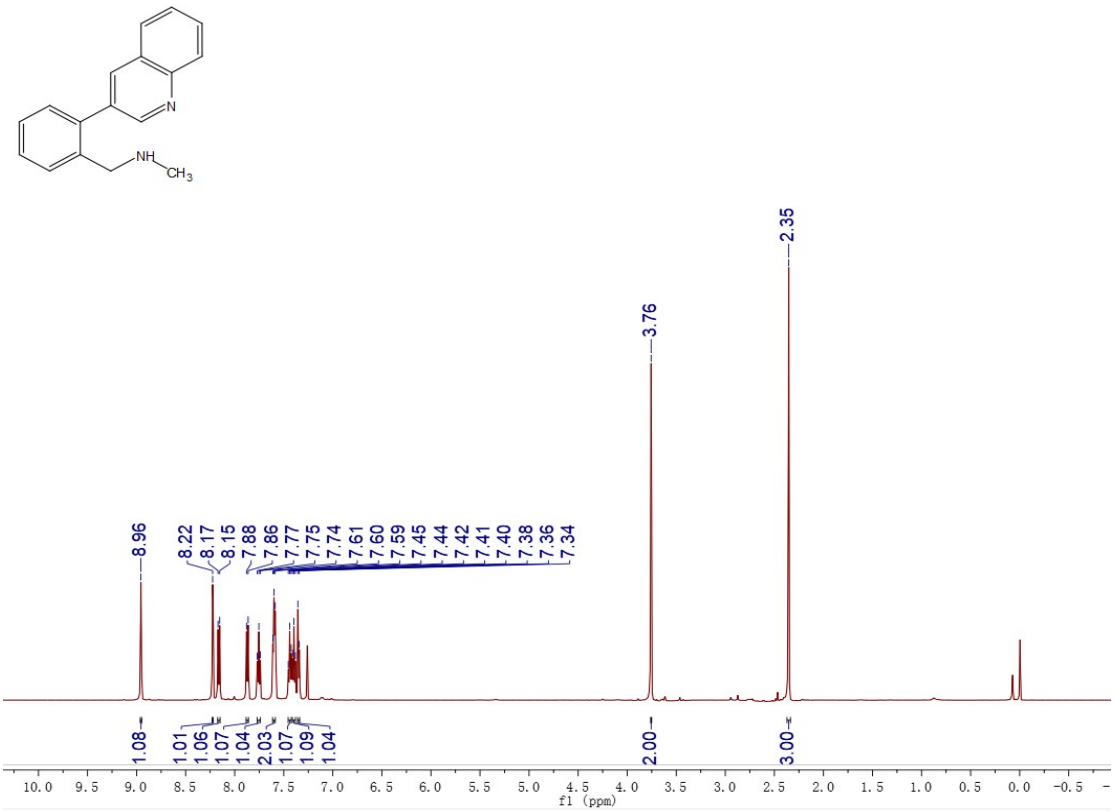


^{19}F-NMR (471 MHz, $CDCl_3$) spectrum of 3na

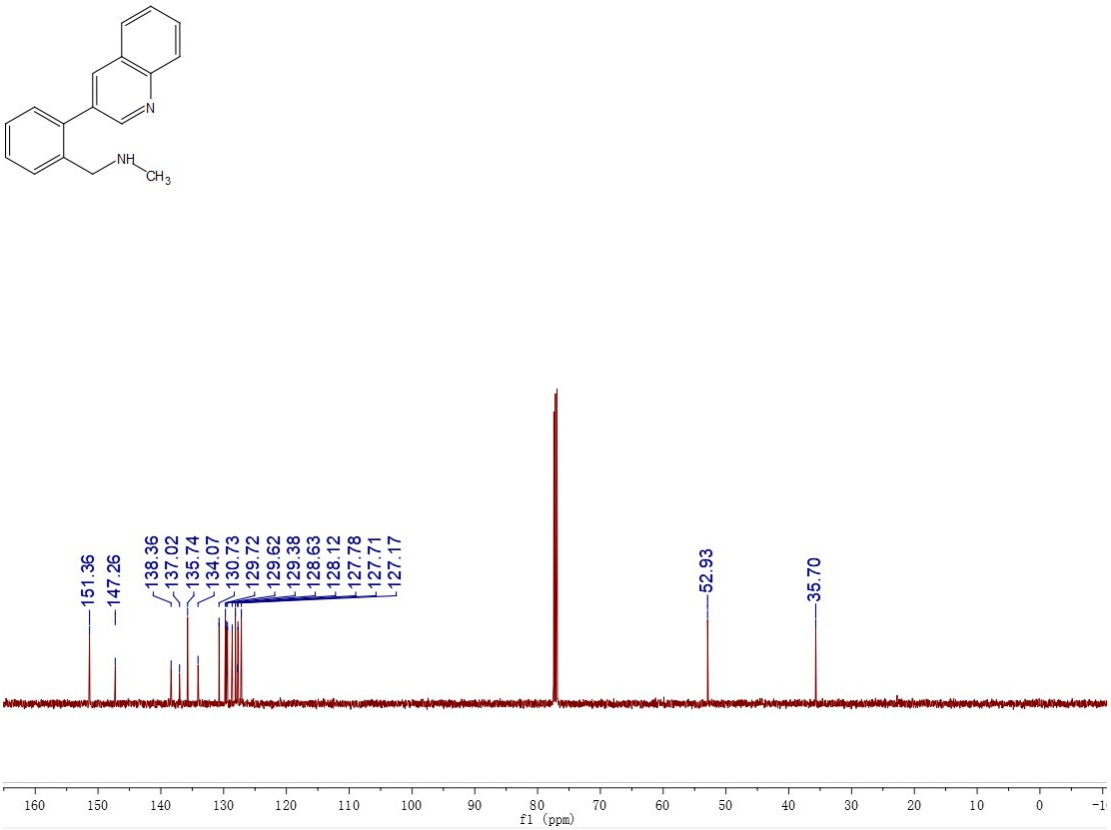

F
HN
F
F
F
F
N


-144.28
-144.30
-144.33
-144.34
-155.08
-155.12
-155.17
-161.86
-161.88
-161.91
-161.92
-161.95
-161.97
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

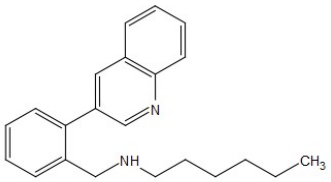
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3oa

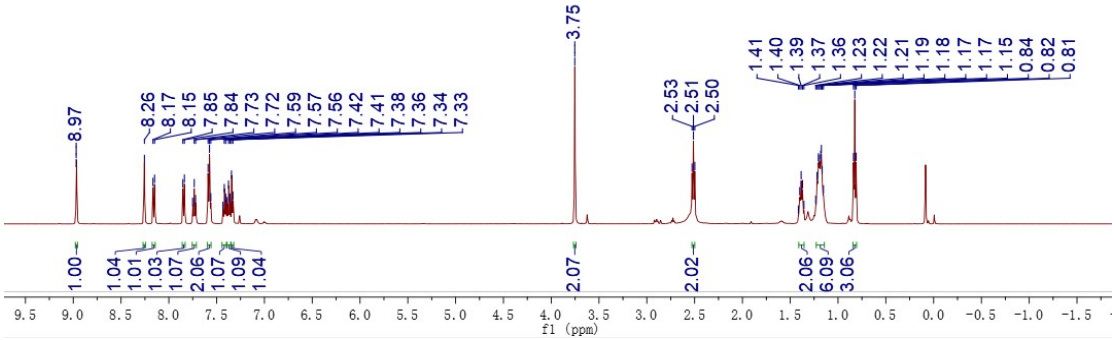


^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3oa

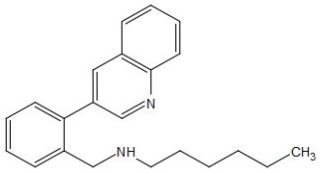


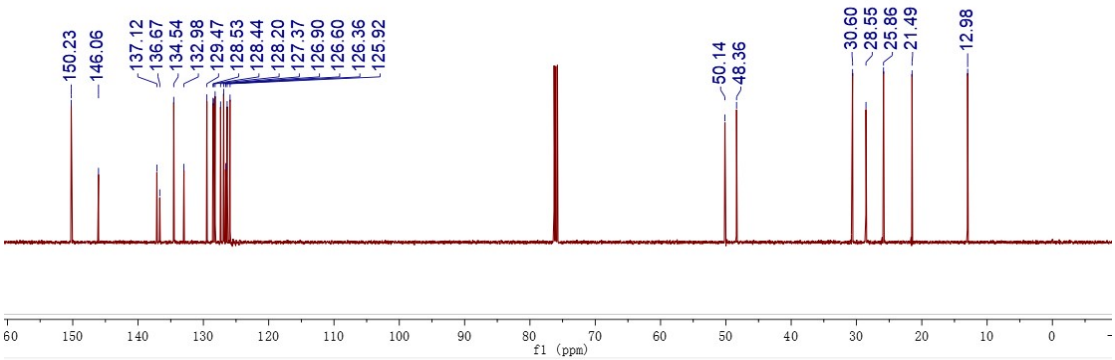
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 3pa



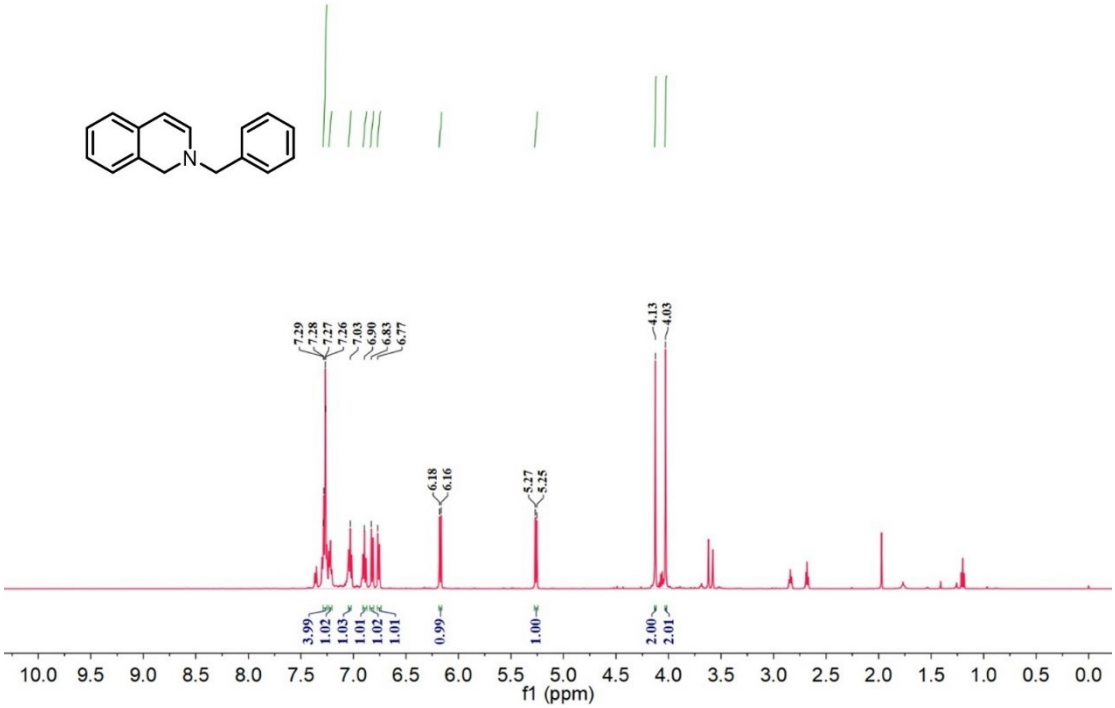


^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 3pa

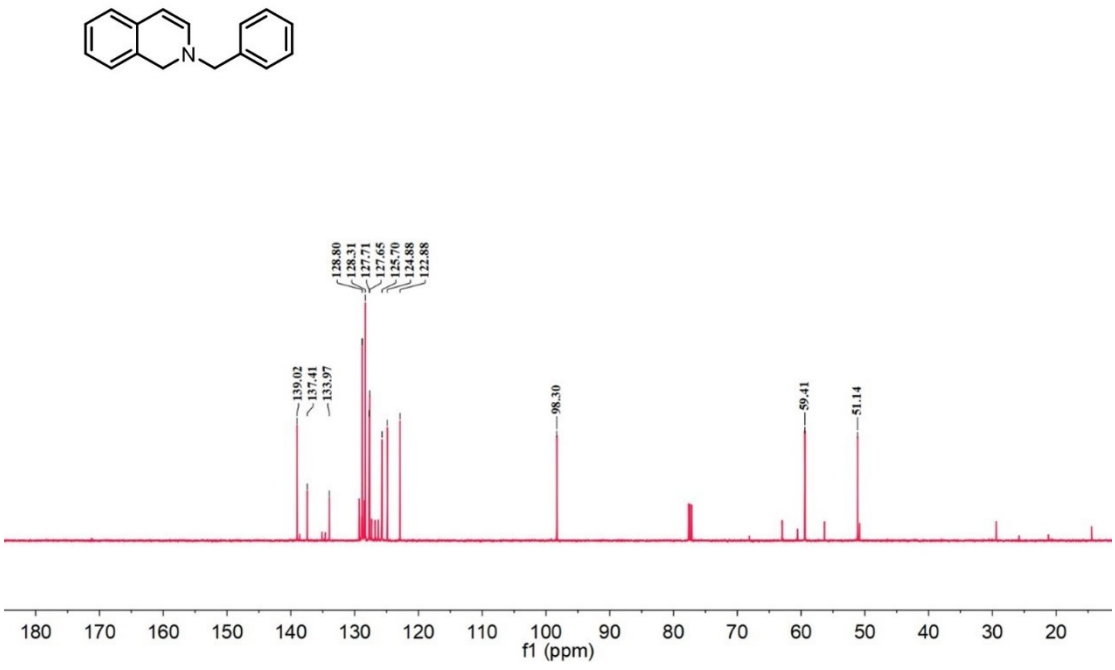




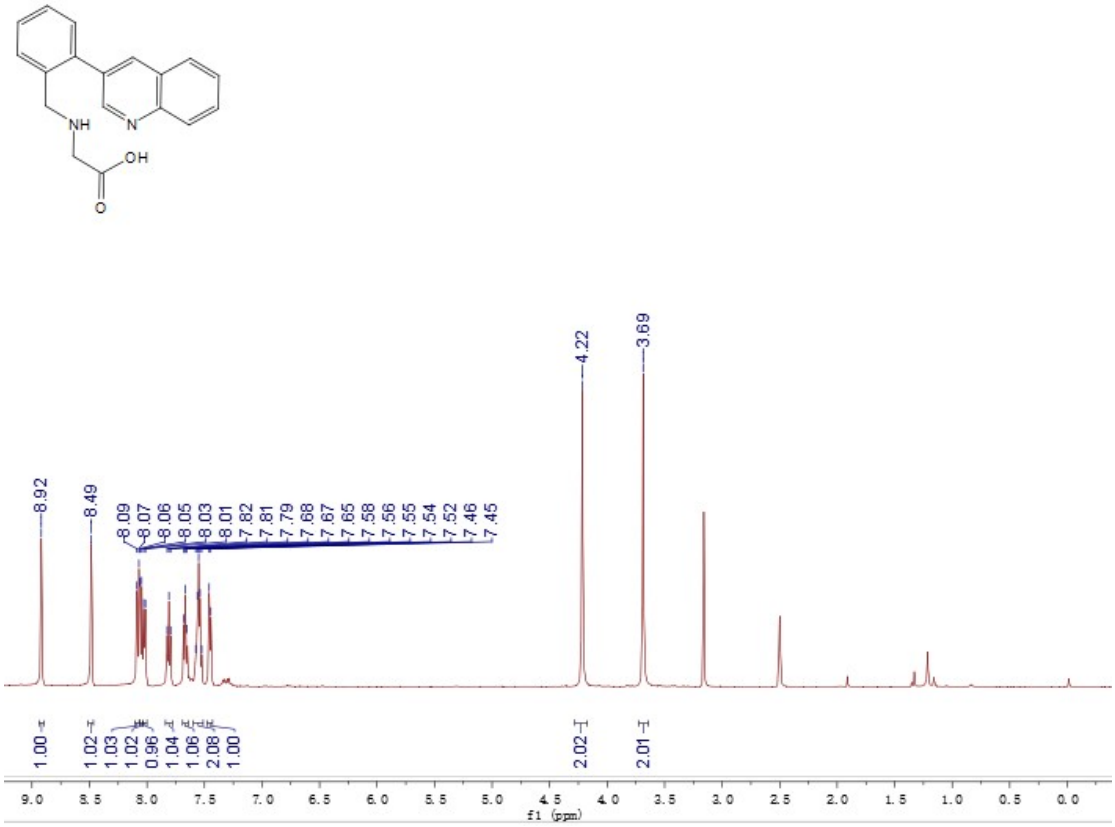
^{1}H-NMR (500 MHz, $CDCl_3$) spectrum of 1k-1



^{13}C-NMR (126 MHz, $CDCl_3$) spectrum of 1k-1



^{1}H-NMR (500 MHz, DMSO-d_6) spectrum of 4



^{13}C-NMR (126 MHz, DMSO-d_6) spectrum of 4