

## **Palladium-catalysed imidoylative difunctionalization of allenes: access to quinolines and indeno[1,2-b]quinolines**

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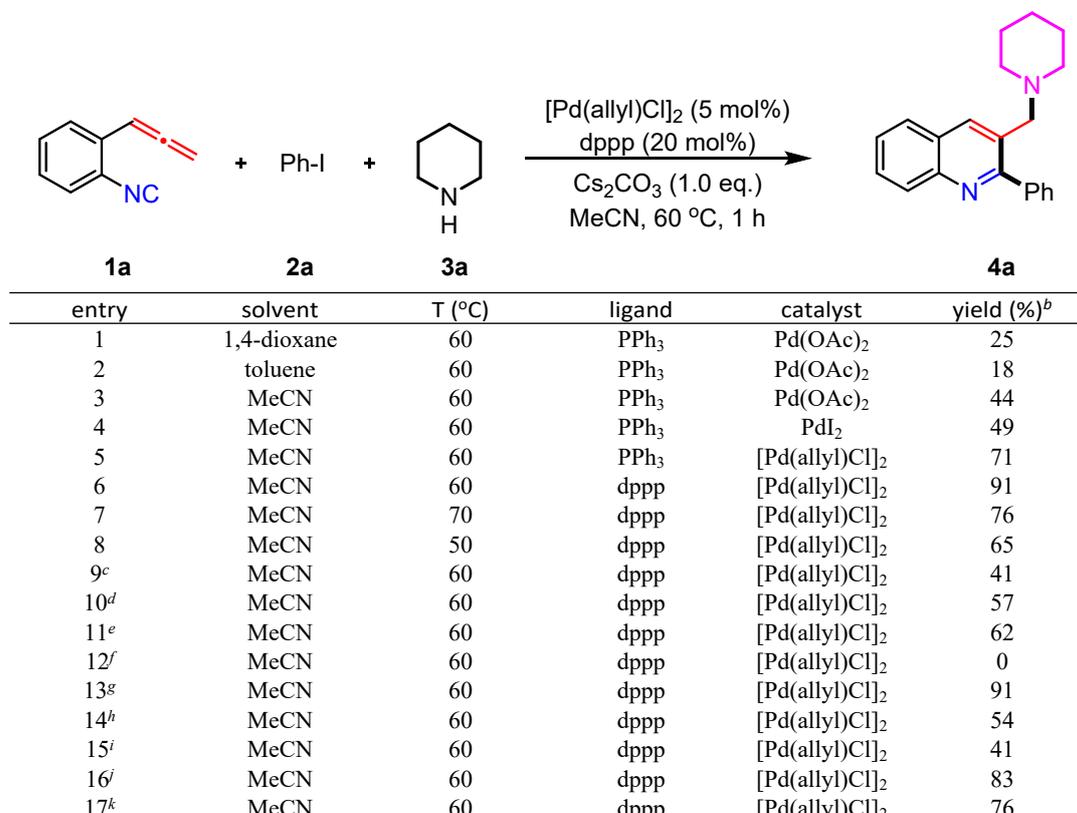
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## 1. General Information

Unless otherwise noted, all reagents and materials were purchased from Energy Chemical, Bide Pharm suppliers and used as received unless otherwise noted. All reactions were carried out in flame-dried glassware under Argon atmosphere. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (bp. 30-60 °C). NMR spectra were recorded on a AVANCE NEO 400 MHz and AVANCE IIT HD 500 MHz NMR spectrometers. Chemical shift values for protons are reported in parts per million (ppm,  $\delta$  scale) downfield from tetramethylsilane and are referenced to residual proton of Chloroform-d ( $\delta$  7.26). Chemical shifts for carbons are reported in parts per million (ppm,  $\delta$  scale) downfield from tetramethylsilane and are referenced to the carbon resonance of Chloroform-d ( $\delta$  77.16). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublet of doublets); dt (doublet of triplets); td (triplet of doublets); m (multiplets). Coupling constants are reported as a  $J$  value in Hz. Mass spectra were obtained on a Agilent 6200 Accurate-Mass Q-TOF LC/MS with ESI mode.

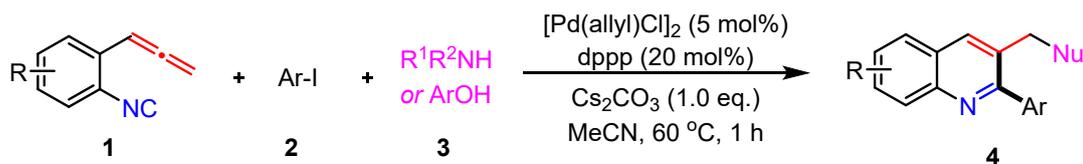
## 2. Optimization of the Reaction Conditions<sup>a</sup>



<sup>a</sup>Reaction conditions: **1a** (0.10 mmol), **2a** (0.15 mmol), **3a** (0.15 mmol), [Pd(allyl)Cl]<sub>2</sub> (5 mol%), dppp (20 mol%), Cs<sub>2</sub>CO<sub>3</sub> (0.10 mmol), 60 °C, in Ar. A solution of **1a** in MeCN (1.0 mL) was added to the reaction mixture (in 1.0 mL MeCN) *via* a syringe pump within 1 h. <sup>b</sup>Yield of isolated products. <sup>c</sup>dppp (10 mol%). <sup>d</sup>[Pd(allyl)Cl]<sub>2</sub> (2.5 mol%), dppp (10 mol%). <sup>e</sup>**1a** (0.10 mmol), **2a** (0.10 mmol), **3a** (0.10 mmol). <sup>f</sup>PhBr used instead of PhI. <sup>g</sup>**1a** (0.10 mmol), **2a** (0.20 mmol), **3a** (0.20 mmol). <sup>h</sup>**1a** (0.15 mmol), **2a** (0.10 mmol), **3a** (0.15 mmol). <sup>i</sup>**1a** (0.15 mmol), **2a** (0.15 mmol), **3a** (0.10 mmol). <sup>j</sup>MeCN (1.0 mL). <sup>k</sup>MeCN (3.0 mL).

## 3. Experimental Procedures

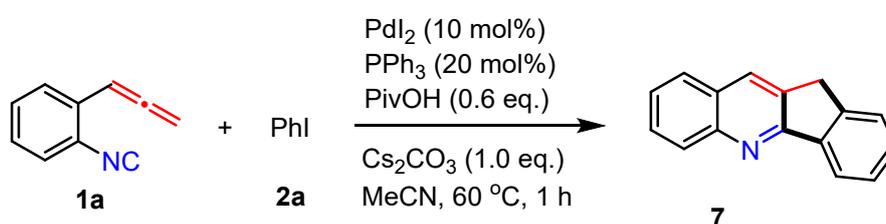
### 3.1 General Procedure for the Three-component Cyclization Reaction



An oven-dried 25 mL schlenk tube charged with [Pd(allyl)Cl]<sub>2</sub> (0.005 mmol, 5 mol%), dppp (0.02 mmol, 20 mol%) and Cs<sub>2</sub>CO<sub>3</sub> (0.1 mmol, 1.0 equiv.) was refilled

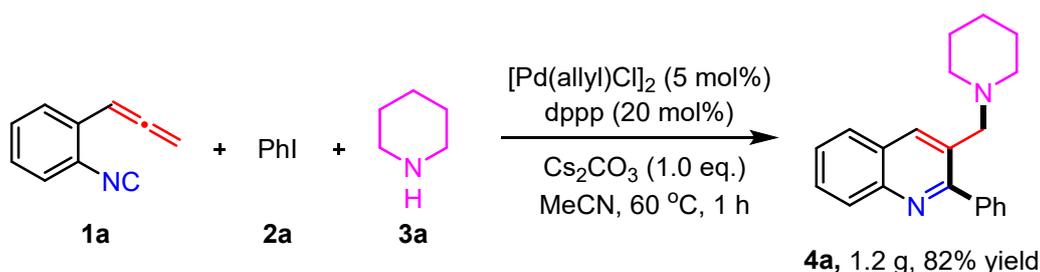
with argon for 3 times. Then a solution of **2** (0.15 mmol, 1.5 equiv.) and **3** (0.15 mmol, 1.5 equiv.) in 1.0 mL of MeCN was added by syringe and the tube was placed in a 60 °C oil-bath. A solution of **1** (0.1 mmol, 1.0 equiv.) in 1.0 mL of MeCN was added dropwise with a syringe pump to the reaction mixture. The addition was finished within 1 h. The reaction mixture was cooled to room temperature, quenched with water (10 mL), and then extracted with EA (10 mL×3). The organic layer was washed with brine and dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporating under reduced pressure, the residue was purified using flash column chromatography with silica gel to give product **4**.

### 3.2 Synthesis of indenoquinoline



An oven-dried 25 mL schlenk tube charged with PdI<sub>2</sub> (0.01 mmol, 5 mol%), PPh<sub>3</sub> (0.02 mmol, 20 mol%), Cs<sub>2</sub>CO<sub>3</sub> (0.1 mmol, 1.0 equiv.) and PivOH (0.06 mmol, 0.6 equiv.) was refilled with argon for 3 times. Then a solution of **2a** (0.15 mmol, 1.5 equiv.) in 1.0 mL of MeCN was added by syringe and the tube was placed in a 60 °C oil-bath. A solution of **1a** (0.1 mmol, 1.0 equiv.) in 1.0 mL of MeCN was added dropwise with a syringe pump to the reaction mixture. The addition was finished within 1 h. The reaction mixture was cooled to room temperature, quenched with water (10 mL), and then extracted with EA (10 mL×3). The organic layer was washed with brine and dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporating under reduced pressure, the residue was purified using flash column chromatography with silica gel to give product **7**.

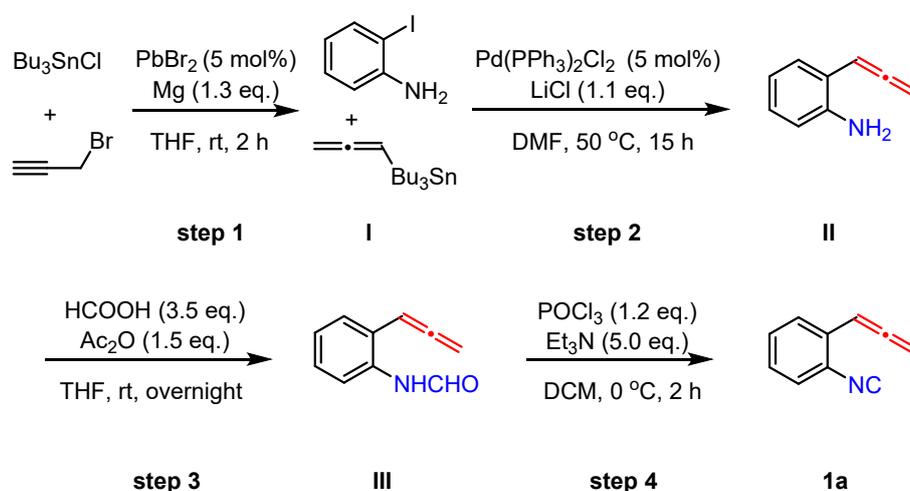
### 3.3 General Procedure for the Gram-Scale Synthesis



An oven-dried 150 mL schlenk tube charged with [Pd(allyl)Cl]<sub>2</sub> (0.25 mmol, 5

mol%), dppp (1 mmol, 20 mol%) and Cs<sub>2</sub>CO<sub>3</sub> (5 mmol, 1.0 equiv.) was refilled with argon for 3 times. Then a solution of **2a** (7.5 mmol, 1.5 equiv.) and **3a** (7.5 mmol, 1.5 equiv.) in 30 mL of MeCN was added by syringe and the tube was placed in a 60 °C oil-bath. A solution of **1a** (5 mmol, 1.0 equiv.) in 30 mL of MeCN was added dropwise with a syringe pump to the reaction mixture. The addition was finished within 1 h. The reaction mixture was cooled to room temperature, quenched with water (10 mL), and then extracted with EA (30 mL×3). The organic layer was washed with brine and dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporating under reduced pressure, the residue was purified using flash column chromatography with silica gel to give product **4a**.

### 3.4 Preparation of Allenyl Isocyanides<sup>[1]</sup>



**Step 1:** To a mixture of tributyltin chloride (10 mmol), lead bromide (5 mol%) and magnesium powder (1.3 equiv.) was added a solution of dried THF (0.5 M) under Ar. The reaction mixture was stirred at 0 °C, and 3-bromopropyne (1.3 equiv.) was slowly added. Then the reaction was allowed to return to room temperature and stirred for another 2 h. Then the reaction was quenched with water (10 mL), and then the waste residue produced was filtered out by diatomaceous earth, and extracted with EA (20 mL×3). The organic layer was washed with brine and dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporating under reduced pressure, the residue was purified using flash column chromatography with silica gel to give compound **I**.

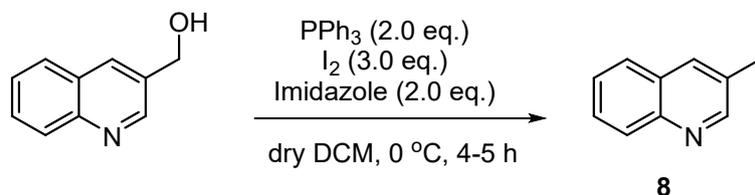
**Step 2:** To a mixture of *o*-iodoaniline (5 mmol), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (5 mol%) and LiCl (1.1 equiv.) was added a solution of dried DMF (0.5 M) under Ar. The reaction mixture was stirred at 50 °C, and compound **I** (1.3 equiv.) was added, followed by continued reaction for 15 h. Then the reaction was quenched with a large amount of water (100 mL) and extracted with EA (50 mL×3). The organic layer was washed with brine and dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporating under reduced pressure, the residue was purified using flash column chromatography with silica gel to give compound **II**.

**Step 3:** Under an argon atmosphere, product **II** was dissolved in dry THF (0.5 M), followed by the addition of a pre-mixed solution of formic acid and acetic anhydride (prepared by stirring for 30 min). The reaction mixture was stirred at room temperature

for 12 h. Upon completion, a saturated aqueous sodium bicarbonate solution was slowly added dropwise with stirring until gas evolution ceased. The mixture was extracted with EA (30 mL×3), The organic layer was washed with brine and dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporating under reduced pressure, the residue was purified using flash column chromatography with silica gel to give compound **III**.

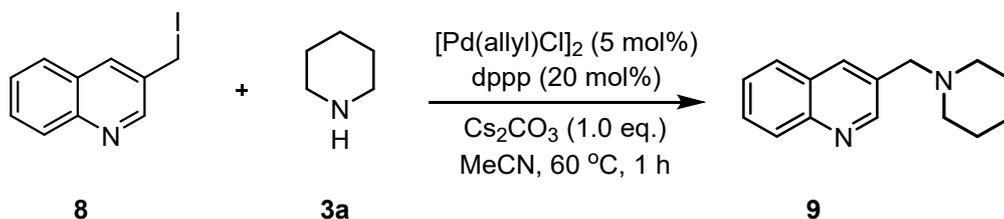
**Step 4:** Under an argon atmosphere, product **III** was dissolved in dry DCM (0.2 M), followed by the addition of Et<sub>3</sub>N (5.0 equiv.) at 0 °C. Then, POCl<sub>3</sub> (1.2 equiv.) was added dropwise slowly, and the reaction was continued at 0 °C for 2 h. The mixture was quenched by the slow addition of saturated aqueous sodium bicarbonate solution at 0 °C and extracted with DCM (20 mL×3). The organic layer was washed with brine and dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporating under reduced pressure, the residue was purified using flash column chromatography with silica gel to give compound **1**.

### 3.5 Preparation of 3-(iodomethyl)quinoline<sup>[2]</sup>



Add quinolin-3-ylmethanol (0.3 mmol) to a stir solution of PPh<sub>3</sub> (2.0 equiv.), I<sub>2</sub> (3.0 equiv.) and imidazole (2.0 equiv.) in dry CH<sub>2</sub>Cl<sub>2</sub> (5 ml). The reaction was continued at 0 °C for 4-5 h. Check the completion of the reaction by TLC analysis. Purify the crude product by column chromatography (petroleum ether/ethyl acetate, 2:1) to give compound **8**.

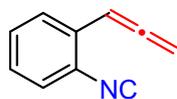
### 3.6 Synthesis of 3-(piperidin-1-ylmethyl)quinoline



An oven-dried 150 mL schlenk tube charged with [Pd(allyl)Cl]<sub>2</sub> (0.005 mmol, 5 mol%), dppp (0.02 mmol, 20 mol%) and Cs<sub>2</sub>CO<sub>3</sub> (0.1 mmol, 1.0 equiv.) was refilled with argon for 3 times. Then a solution of **8** (0.1 mmol, 1.0 equiv.) and **3a** (0.15 mmol, 1.5 equiv.) in 2.0 mL of MeCN was added by syringe and the tube was placed in a 60 °C oil-bath and react for 1 h. The reaction mixture was cooled to room temperature, quenched with water (5 mL), and then extracted with EA (5 mL×3). The organic layer was washed with brine and dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporating under reduced pressure, the residue was purified using flash column chromatography with silica gel to give product **9**.



## 4. Characterization Data for the compounds



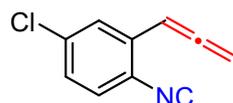
### 1-isocyano-2-(propa-1,2-dien-1-yl)benzene (**1a**)

**1a** was prepared from **III** (1.5 mmol) by step 3. The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:30) to give **1a** (174.5 mg, 82%) as a yellow oil.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43–7.26 (m, 4H), 6.89–6.83 (m, 1H), 5.01 (d,  $J = 5.9$  Hz, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  212.4, 165.0, 137.3, 133.4, 131.1, 102.5, 92.7, 81.4.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{10}\text{H}_8\text{N}$ : 142.0651, found: 142.0644.



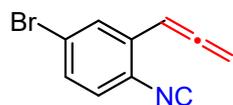
### 4-chloro-1-isocyano-2-(propa-1,2-dien-1-yl)benzene (**1b**)

**1b** was prepared from **III** (1.6 mmol) by step 3. The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:30) to give **1b** (246.1 mg, 88%) as a yellow solid, mp = 68–69 °C.

$^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 (d,  $J = 2.5$  Hz, 1H), 7.26 (d,  $J = 8.3$  Hz, 1H), 7.23–7.07 (m, 1H), 6.44 (t,  $J = 6.7$  Hz, 1H), 5.31 (d,  $J = 6.9$  Hz, 2H).

$^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  211.0, 168.5, 135.5, 132.5, 128.3, 127.7, 127.3, 88.6, 80.5.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{10}\text{H}_7\text{ClN}$ : 176.0262, found: 176.0258.



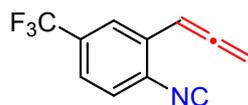
### 4-bromo-1-isocyano-2-(propa-1,2-dien-1-yl)benzene (**1c**)

**1c** was prepared from **III** (1.5 mmol) by step 3. The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:30) to give **1c** (293.5 mg, 89%) as a yellow solid, mp = 70–71 °C.

$^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57 (t,  $J = 2.7$  Hz, 1H), 7.29 (dd,  $J = 8.5, 2.3$  Hz, 1H), 7.17 (d,  $J = 8.4$  Hz, 1H), 6.41 (t,  $J = 6.8$  Hz, 1H), 5.31 (d,  $J = 6.8$  Hz, 2H).

$^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  210.9, 168.8, 132.5, 130.5, 130.2, 128.3, 123.5, 88.4, 80.5.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{10}\text{H}_7\text{BrN}$ : 219.9756, found: 219.9763.



### 1-isocyano-2-(propa-1,2-dien-1-yl)-4-(trifluoromethyl)benzene (**1d**)

**1d** was prepared from **III** (1.3 mmol) by step 3. The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:30) to give **1d** (252.4 mg, 93%) as a yellow solid, mp = 62–63 °C.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.73 (s, 1H), 7.44 (d, *J* = 1.4 Hz, 2H), 6.52 (t, *J* = 6.8 Hz, 1H), 5.35 (d, *J* = 6.9 Hz, 2H).

<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 211.1, 170.1, 131.8, 131.5 (q, *J* = 33.2 Hz), 127.8, 124.6 (q, *J* = 4.0 Hz), 124.2 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 273.4 Hz), 88.6, 80.7.

<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -63.17.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>11</sub>H<sub>7</sub>F<sub>3</sub>N: 210.0525, found: 210.0521.



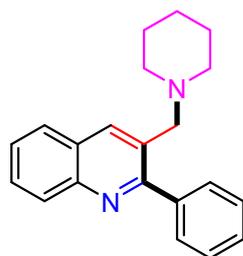
### 1-chloro-2-isocyano-3-(propa-1,2-dien-1-yl)benzene (**1e**)

**1e** was prepared from **III** (1.2 mmol) by step 3. The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:30) to give **1e** (182.6 mg, 87%) as a yellow solid, mp = 60–61 °C.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.36 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.29–7.21 (m, 2H), 6.45 (t, *J* = 6.8 Hz, 1H), 5.28 (d, *J* = 6.8 Hz, 2H).

<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 211.1, 172.2, 132.7, 131.3, 129.5, 127.7, 125.6, 89.2, 80.1.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>10</sub>H<sub>7</sub>ClN: 176.0262, found: 176.0266.



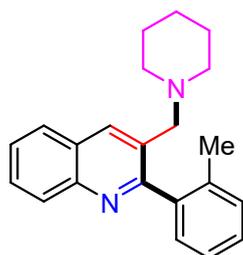
### 2-phenyl-3-(piperidin-1-ylmethyl)quinoline (**4a**)

27.5 mg, 91% yield, yellow solid, mp = 98–99 °C, R<sub>f</sub> = 0.4 (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4a**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.31 (s, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 7.89–7.83 (m, 1H), 7.73–7.63 (m, 3H), 7.56–7.51 (m, 1H), 7.51–7.39 (m, 3H), 3.53 (s, 2H), 2.36 (s, 4H), 1.60–1.51 (m, 4H), 1.47–1.36 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 160.9, 146.9, 140.8, 137.0, 130.3, 129.3, 129.3, 129.2, 128.2, 128.1, 127.4, 127.4, 126.4, 60.4, 54.3, 26.1, 24.4.

**HRMS (ESI) m/z:**  $[M + H]^+$  Calcd for  $C_{21}H_{23}N_2$ : 303.1856, found: 303.1858.



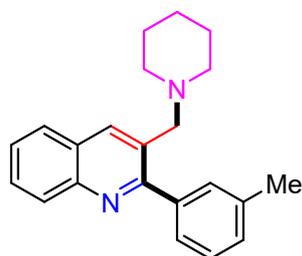
### 3-(piperidin-1-ylmethyl)-2-(o-tolyl)quinoline (**4b**)

15.2 mg, 48% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4b**.

$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.30 (s, 1H), 8.14 (d,  $J = 8.4$  Hz, 1H), 7.82 (d,  $J = 8.1$  Hz, 1H), 7.71–7.62 (m, 1H), 7.58–7.48 (m, 2H), 7.42 (d,  $J = 7.6$  Hz, 1H), 7.36–7.29 (m, 1H), 7.26 (s, 1H), 3.51 (s, 2H), 2.42 (s, 3H), 2.40 (s, 4H), 1.64–1.52 (m, 4H), 1.50–1.40 (m, 2H).

$^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  161.4, 147.0, 140.9, 137.9, 137.1, 131.3, 129.6, 129.3, 129.1, 128.8, 127.7, 127.3, 127.2, 126.2, 126.1, 60.4, 54.2, 26.2, 24.3, 21.0.

**HRMS (ESI) m/z:**  $[M + H]^+$  Calcd for  $C_{22}H_{25}N_2$ : 317.2012, found: 317.2014.



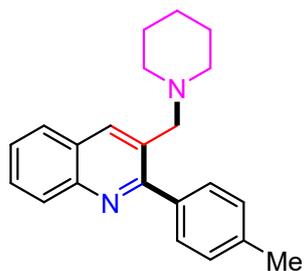
### 3-(piperidin-1-ylmethyl)-2-(m-tolyl)quinoline (**4c**)

27.5 mg, 92% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4c**.

$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.31 (s, 1H), 8.18 (d,  $J = 8.4$  Hz, 1H), 7.88 (d,  $J = 8.1$  Hz, 1H), 7.75–7.67 (m, 1H), 7.62–7.50 (m, 2H), 7.48 (d,  $J = 7.6$  Hz, 1H), 7.42–7.34 (m, 1H), 7.26 (s, 1H), 3.55 (s, 2H), 2.46 (s, 3H), 2.41 (s, 4H), 1.66–1.53 (m, 4H), 1.51–1.40 (m, 2H).

$^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  161.1, 146.9, 140.6, 137.7, 137.0, 130.3, 130.0, 129.3, 129.2, 128.9, 127.9, 127.4, 127.3, 126.3, 126.3, 60.4, 54.3, 26.1, 24.4, 21.6.

**HRMS (ESI) m/z:**  $[M + H]^+$  Calcd for  $C_{22}H_{25}N_2$ : 317.2012, found: 317.2014.



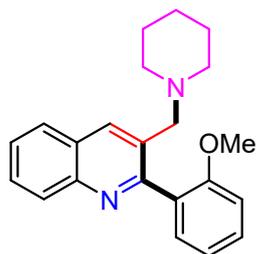
### 3-(piperidin-1-ylmethyl)-2-(p-tolyl)quinoline (4d)

29.4 mg, 93% yield, yellow solid, mp = 124–125 °C, Rf = 0.4 (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4d**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.30 (s, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.89–7.82 (m, 1H), 7.72–7.64 (m, 1H), 7.62–7.55 (m, 2H), 7.55–7.49 (m, 1H), 7.29 (s, 2H), 3.54 (s, 2H), 2.43 (s, 3H), 2.38 (s, 4H), 1.60–1.53 (m, 4H), 1.48–1.38 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 160.8, 146.9, 138.0, 137.8, 136.9, 130.3, 129.3, 129.2, 129.1, 128.8, 127.4, 127.3, 126.2, 60.4, 54.4, 26.1, 24.4, 21.4.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>25</sub>N<sub>2</sub>: 317.2012, found: 317.2019.



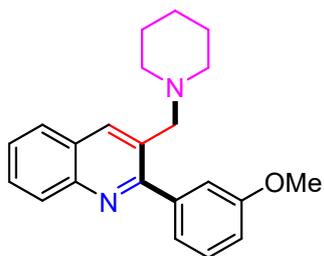
### 2-(2-methoxyphenyl)-3-(piperidin-1-ylmethyl)quinoline (4e)

14 mg, 42% yield, yellow oil, Rf = 0.4 (PE/EA = 3:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) to give **4e**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.31 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.72–7.65 (m, 1H), 7.64–7.60 (m, 2H), 7.51–7.20 (m, 3H), 3.82 (s, 3H), 3.53 (s, 2H), 2.38 (s, 4H), 1.63–1.56 (m, 4H), 1.46–1.42 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 161.1, 159.2, 146.9, 141.9, 136.9, 130.3, 129.4, 129.1, 129.0, 127.1, 126.9, 121.3, 114.2, 114.1, 60.3, 54.6, 54.3, 26.4, 24.0.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>25</sub>N<sub>2</sub>O: 333.1961, found: 333.1965.



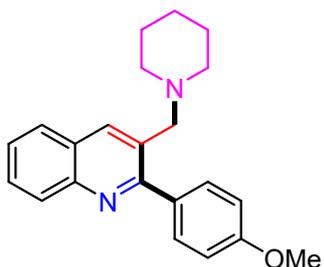
#### 2-(3-methoxyphenyl)-3-(piperidin-1-ylmethyl)quinoline (4f)

28.9 mg, 87% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 3:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) to give **4f**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.30 (s, 1H), 8.14 (d,  $J = 8.5$  Hz, 1H), 7.86 (d,  $J = 8.1$  Hz, 1H), 7.72–7.65 (m, 1H), 7.57–7.49 (m, 1H), 7.41–7.34 (m, 1H), 7.27–7.20 (m, 2H), 7.03–6.95 (m, 1H), 3.86 (s, 3H), 3.53 (s, 2H), 2.37 (s, 4H), 1.60–1.51 (m, 4H), 1.47–1.38 (m, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.6, 159.4, 146.8, 142.0, 137.1, 130.3, 129.3, 129.2, 129.1, 127.4, 126.4, 121.8, 114.6, 114.2, 60.4, 55.4, 54.4, 26.1, 24.4.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}$ : 333.1961, found: 333.1960.



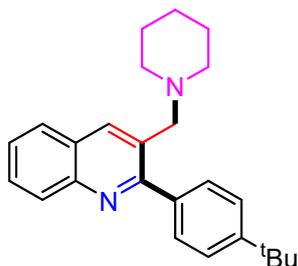
#### 2-(4-methoxyphenyl)-3-(piperidin-1-ylmethyl)quinoline (4g)

29.2 mg, 88% yield, yellow solid, mp = 95–96 °C,  $R_f = 0.4$  (PE/EA = 3:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) to give **4g**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.26 (s, 1H), 8.16–8.10 (m, 1H), 7.86–7.81 (m, 1H), 7.72–7.63 (m, 3H), 7.54–7.47 (m, 1H), 7.05–6.97 (m, 2H), 3.88 (s, 3H), 3.53 (s, 2H), 2.38 (s, 4H), 1.61–1.54 (m, 4H), 1.47–1.38 (m, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.5, 159.7, 147.0, 137.2, 133.2, 130.8, 130.3, 129.2, 129.1, 127.4, 127.2, 126.2, 113.5, 60.6, 55.4, 54.3, 26.1, 24.4.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}$ : 333.1961, found: 333.1966.



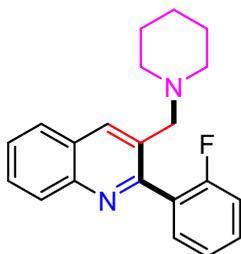
### 2-(4-(tert-butyl)phenyl)-3-(piperidin-1-ylmethyl)quinoline (4h)

33 mg, 92% yield, yellow solid, mp = 75–76 °C, R<sub>f</sub> = 0.4 (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4h**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.31 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.87–7.83 (m, 1H), 7.70–7.66 (m, 1H), 7.65–7.61 (m, 2H), 7.53–7.47 (m, 3H), 3.58 (s, 2H), 2.39 (s, 4H), 1.61–1.54 (m, 4H), 1.46–1.42 (m, 2H), 1.39 (s, 9H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 160.8, 151.1, 147.0, 137.8, 137.0, 136.8, 130.4, 129.3, 129.2, 129.1, 129.0, 127.4, 127.3, 126.2, 125.1, 60.4, 54.4, 34.7, 31.4, 26.1, 24.4.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>25</sub>H<sub>31</sub>N<sub>2</sub>: 359.2482, found: 359.2484.



### 2-(2-fluorophenyl)-3-(piperidin-1-ylmethyl)quinoline (4i)

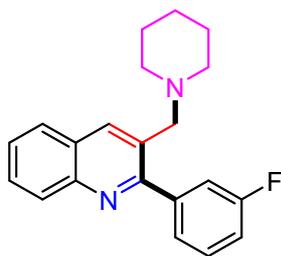
31 mg, 97% yield, yellow oil, R<sub>f</sub> = 0.4 (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4i**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.35 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.75–7.66 (m, 1H), 7.59–7.53 (m, 1H), 7.53–7.40 (m, 2H), 7.30–7.24 (m, 1H), 7.21–7.12 (m, 1H), 3.48 (s, 2H), 2.32–2.22 (m, 4H), 1.53–1.45 (m, 4H), 1.43–1.35 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 161.1, 158.6, 155.9, 146.9, 136.1, 131.8, 131.2 (d, *J* = 3.6 Hz), 130.1 (d, *J* = 8.0 Hz), 129.3 (d, *J* = 8.8 Hz), 128.6 (d, *J* = 16.4 Hz), 127.8, 127.5, 126.7, 124.2 (d, *J* = 3.5 Hz), 115.5 (d, *J* = 21.8 Hz), 59.9 (d, *J* = 3.0 Hz), 54.4, 26.0, 24.3.

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -110.93.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>22</sub>FN<sub>2</sub>: 321.1762, found: 321.1756.



### 2-(3-fluorophenyl)-3-(piperidin-1-ylmethyl)quinoline (4j)

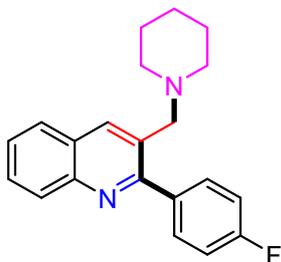
26.9 mg, 84% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4j**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H), 8.14 (d,  $J = 8.4$  Hz, 1H), 7.86 (d,  $J = 8.1$  Hz, 1H), 7.75–7.67 (m, 1H), 7.61–7.52 (m, 2H), 7.50 (d,  $J = 7.6$  Hz, 1H), 7.47–7.38 (m, 1H), 7.19–7.09 (m, 1H), 3.49 (s, 2H), 2.49–2.22 (m, 4H), 1.59–1.51 (m, 4H), 1.48–1.38 (m, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  163.8, 161.3, 159.5 (d,  $J = 2.1$  Hz), 146.9, 142.8 (d,  $J = 7.9$  Hz), 137.6, 130.0, 129.6 (d,  $J = 8.1$  Hz), 129.4 (d,  $J = 14.0$  Hz), 127.4, 127.4, 126.7, 125.2 (d,  $J = 2.9$  Hz), 116.7 (d,  $J = 22.6$  Hz), 115.1 (d,  $J = 21.1$  Hz), 60.5, 54.2, 26.0, 24.4.

$^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -113.56.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{21}\text{H}_{22}\text{FN}_2$ : 321.1762, found: 321.1760.



### 2-(4-fluorophenyl)-3-(piperidin-1-ylmethyl)quinoline (4k)

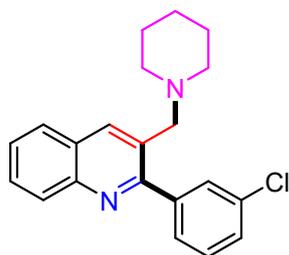
26 mg, 81% yield, yellow solid, mp = 102–103 °C,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4k**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24 (s, 1H), 8.13 (d,  $J = 8.5$  Hz, 1H), 7.89–7.82 (m, 1H), 7.77–7.66 (m, 3H), 7.58–7.51 (m, 1H), 7.21–7.11 (m, 2H), 3.48 (s, 2H), 2.49–2.27 (m, 4H), 1.59–1.50 (m, 4H), 1.48–1.39 (m, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  164.2, 161.7, 159.9, 146.9, 137.5, 136.8 (d,  $J = 3.5$  Hz), 131.3 (d,  $J = 8.0$  Hz), 130.1, 129.4, 129.2, 127.4, 127.3, 126.5, 115.1, 114.9, 60.6, 54.2, 26.1, 24.4.

$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -113.93.

HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{21}\text{H}_{22}\text{FN}_2$ : 321.1762, found: 321.1769.



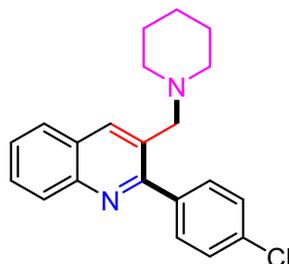
#### 2-(3-chlorophenyl)-3-(piperidin-1-ylmethyl)quinoline (4l)

30 mg, 89% yield, yellow solid, mp = 131–132 °C,  $R_f$  = 0.4 (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4l**.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.21 (s, 1H), 8.14 (d,  $J$  = 8.5 Hz, 1H), 7.91 (d,  $J$  = 2.1 Hz, 1H), 7.89–7.82 (m, 1H), 7.75–7.67 (m, 1H), 7.65–7.59 (m, 1H), 7.59–7.52 (m, 1H), 7.45–7.38 (m, 2H), 3.46 (s, 2H), 1.63–1.53 (m, 4H), 1.49–1.40 (m, 2H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  159.5, 146.9, 142.4, 137.7, 134.0, 130.0, 129.8, 129.5, 129.3, 128.3, 127.7, 127.4, 127.3, 126.7, 60.6, 54.1, 26.0, 24.4.

HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{21}\text{H}_{22}\text{ClN}_2$ : 337.1466, found: 337.1468.



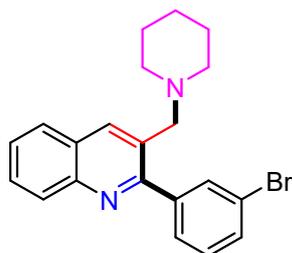
#### 2-(4-chlorophenyl)-3-(piperidin-1-ylmethyl)quinoline (4m)

26 mg, 77% yield, yellow solid, mp = 125–126 °C,  $R_f$  = 0.4 (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4m**.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H), 8.12 (d,  $J$  = 8.4 Hz, 1H), 7.88–7.83 (m, 1H), 7.73–7.67 (m, 3H), 7.57–7.52 (m, 1H), 7.47–7.42 (m, 2H), 3.48 (s, 2H), 2.37 (s, 4H), 1.58–1.51 (m, 4H), 1.46–1.38 (m, 2H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  159.7, 147.0, 139.1, 137.6, 134.4, 130.9, 130.0, 129.4, 129.3, 128.2, 127.4, 127.3, 126.6, 60.5, 54.2, 26.0, 24.4.

HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{21}\text{H}_{22}\text{ClN}_2$ : 337.1466, found: 337.1464.



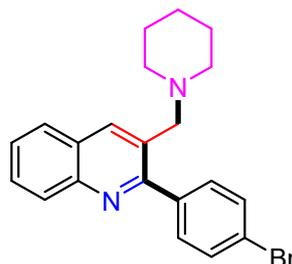
### 2-(3-bromophenyl)-3-(piperidin-1-ylmethyl)quinoline (**4n**)

36.9 mg, 97% yield, yellow solid, mp = 105–106 °C, Rf = 0.4 (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4n**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.19 (s, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 8.10 (d, *J* = 2.0 Hz, 1H), 7.87–7.82 (m, 1H), 7.73–7.66 (m, 2H), 7.59–7.52 (m, 2H), 7.38–7.32 (m, 1H), 3.45 (s, 2H), 2.39 (s, 4H), 1.60–1.53 (m, 4H), 1.49–1.40 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 159.4, 147.0, 142.7, 137.8, 132.7, 131.2, 130.0, 129.6, 129.5, 129.3, 128.1, 127.4, 127.3, 126.7, 122.2, 60.6, 54.1, 26.1, 24.4.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>22</sub>BrN<sub>2</sub>: 381.0961, found: 381.0958.



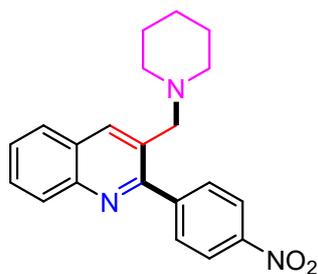
### 2-(4-bromophenyl)-3-(piperidin-1-ylmethyl)quinoline (**4o**)

27.8 mg, 73% yield, yellow solid, mp = 142–143 °C, Rf = 0.4 (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4o**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.24 (s, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.88–7.83 (m, 1H), 7.72–7.68 (m, 1H), 7.67–7.63 (m, 2H), 7.63–7.58 (m, 2H), 7.58–7.52 (m, 1H), 3.48 (s, 2H), 2.37 (s, 4H), 1.58–1.50 (m, 4H), 1.48–1.38 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 159.7, 147.0, 139.6, 137.6, 131.2, 130.0, 129.5, 129.3, 127.4, 127.3, 126.6, 122.7, 60.5, 54.2, 26.0, 24.4.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>22</sub>BrN<sub>2</sub>: 381.0961, found: 381.0966.



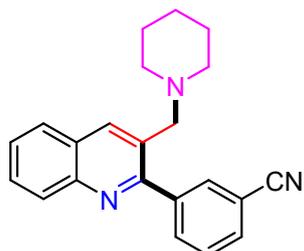
### 2-(4-nitrophenyl)-3-(piperidin-1-ylmethyl)quinoline (4p)

26 mg, 75% yield, yellow solid, mp = 151–152 °C, Rf = 0.4 (PE/EA = 2:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:3) to give **4p**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.37–8.29 (m, 2H), 8.22 (s, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 8.03–7.95 (m, 2H), 7.91–7.84 (m, 1H), 7.77–7.69 (m, 1H), 7.63–7.54 (m, 1H), 3.45 (s, 2H), 2.34 (s, 4H), 1.55–1.47 (m, 4H), 1.47–1.38 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 158.6, 147.7, 147.3, 147.0, 138.1, 130.5, 129.9, 129.8, 129.4, 127.4, 127.4, 127.2, 123.2, 60.6, 54.1, 26.0, 24.3.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>21</sub>H<sub>22</sub>N<sub>3</sub>O<sub>2</sub>: 348.1707, found: 348.1706.



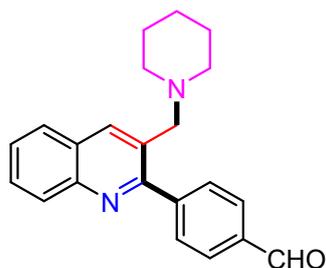
### 3-(3-(piperidin-1-ylmethyl)quinolin-2-yl)benzonitrile (4q)

27 mg, 83% yield, yellow solid, mp = 133–134 °C, Rf = 0.4 (PE/EA = 2:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:3) to give **4q**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.36–8.29 (m, 1H), 8.18 (s, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 8.08–8.01 (m, 1H), 7.90–7.83 (m, 1H), 7.76–7.69 (m, 2H), 7.62–7.55 (m, 2H), 3.43 (s, 2H), 2.38 (s, 4H), 1.61–1.52 (m, 4H), 1.48–1.38 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 158.7, 147.1, 141.9, 138.3, 134.0, 133.6, 131.7, 129.8, 129.3, 128.9, 127.4, 127.3, 127.0, 119.0, 112.1, 60.7, 54.0, 26.0, 24.3.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>22</sub>N<sub>3</sub>: 328.1808, found: 328.1815.



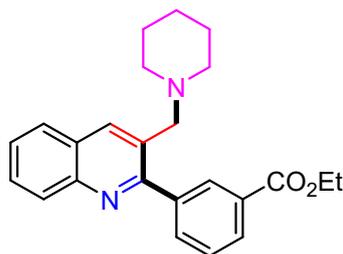
#### 4-(3-(piperidin-1-ylmethyl)quinolin-2-yl)benzaldehyde (**4r**)

28 mg, 85% yield, yellow solid, mp = 104–105 °C, Rf = 0.4 (PE/EA = 3:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) to give **4r**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 10.13 (s, 1H), 8.28 (s, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 8.05–7.98 (m, 2H), 7.96–7.86 (m, 3H), 7.76–7.70 (m, 1H), 7.63–7.55 (m, 1H), 3.51 (s, 2H), 2.48–2.23 (m, 4H), 1.58–1.50 (m, 4H), 1.46–1.37 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 192.3, 159.5, 146.9, 146.9, 137.7, 135.8, 130.1, 130.0, 129.6, 129.5, 129.3, 127.4, 127.4, 126.9, 60.5, 54.1, 26.0, 24.3.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>23</sub>N<sub>2</sub>O: 331.1805, found: 331.1801.



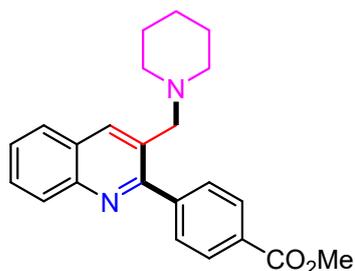
#### ethyl 3-(3-(piperidin-1-ylmethyl)quinolin-2-yl)benzoate (**4s**)

24.4 mg, 65% yield, yellow oil, Rf = 0.4 (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4s**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.43–8.38 (m, 1H), 8.26 (s, 1H), 8.17–8.11 (m, 2H), 7.93–7.85 (m, 2H), 7.74–7.68 (m, 1H), 7.59–7.53 (m, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.48 (s, 2H), 2.35 (s, 4H), 1.58–1.50 (m, 4H), 1.44–1.36 (m, 5H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 166.6, 160.0, 147.0, 141.0, 137.5, 133.8, 130.5, 130.3, 129.4, 129.4, 129.3, 128.1, 127.4, 127.4, 126.6, 61.0, 60.6, 54.2, 26.0, 24.4, 14.4.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>24</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub>: 375.2067, found: 375.2065.



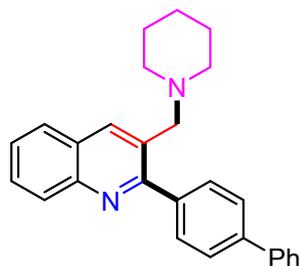
**methyl 4-(3-(piperidin-1-ylmethyl)quinolin-2-yl)benzoate (4t)**

24.5 mg, 68% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4t**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H), 8.20–8.07 (m, 3H), 7.90–7.83 (m, 1H), 7.83–7.76 (m, 2H), 7.75–7.66 (m, 1H), 7.60–7.51 (m, 1H), 3.96 (s, 3H), 3.47 (s, 2H), 2.33 (s, 4H), 1.53 (s, 4H), 1.45–1.36 (m, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.6, 159.4, 146.8, 142.0, 137.1, 130.3, 129.3, 129.2, 129.1, 127.4, 126.4, 121.8, 114.6, 114.2, 60.4, 55.4, 54.4, 26.1, 24.4.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_2$ : 361.1911, found: 361.1910.



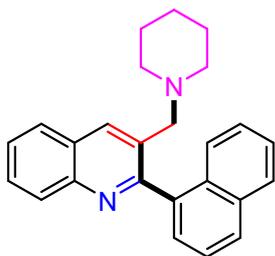
**2-([1,1'-biphenyl]-4-yl)-3-(piperidin-1-ylmethyl)quinoline (4u)**

34 mg, 90% yield, yellow solid, mp = 78–79 °C,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4u**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.18 (d,  $J = 8.5$  Hz, 1H), 7.88 (d,  $J = 8.2$  Hz, 1H), 7.84–7.78 (m, 2H), 7.75–7.67 (m, 5H), 7.58–7.52 (m, 1H), 7.52–7.45 (m, 2H), 7.43–7.36 (m, 1H), 3.61 (s, 2H), 2.42 (s, 4H), 1.62–1.53 (m, 4H), 1.48–1.38 (m, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.5, 147.0, 141.0, 141.0, 139.7, 137.2, 130.2, 129.8, 129.3, 128.9, 127.5, 127.4, 127.3, 127.2, 126.9, 126.4, 60.5, 54.3, 26.0, 24.4.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{27}\text{H}_{27}\text{N}_2$ : 379.2169, found: 379.2164.



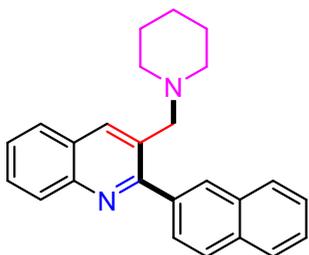
#### 2-(naphthalen-1-yl)-3-(piperidin-1-ylmethyl)quinoline (4v)

22.2 mg, 63% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4v**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.44 (s, 1H), 8.16 (d,  $J = 8.5$  Hz, 1H), 7.96–7.89 (m, 3H), 7.76–7.70 (m, 1H), 7.61–7.55 (m, 2H), 7.54–7.45 (m, 2H), 7.37–7.29 (m, 2H), 3.31 (s, 2H), 2.20 (s, 4H), 1.47–1.39 (m, 4H), 1.33–1.27 (m, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.1, 146.9, 137.9, 136.0, 133.6, 131.9, 129.4, 129.3, 128.4, 128.3, 127.7, 127.6, 126.6, 126.5, 126.3, 125.9, 125.6, 125.3, 59.8, 54.3, 25.9, 24.2.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{25}\text{H}_{25}\text{N}_2$ : 353.2012, found: 353.2007.



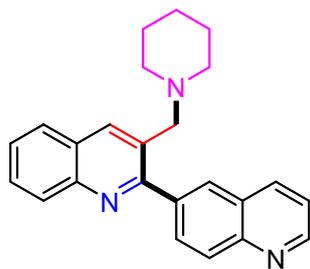
#### 2-(naphthalen-2-yl)-3-(piperidin-1-ylmethyl)quinoline (4w)

32 mg, 91% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4w**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.54 (s, 1H), 8.26 (d,  $J = 8.5$  Hz, 1H), 8.11–7.94 (m, 3H), 7.86–7.78 (m, 1H), 7.73–7.66 (m, 2H), 7.64–7.54 (m, 2H), 7.52–7.35 (m, 2H), 3.40 (s, 2H), 2.30 (s, 4H), 1.61–1.45 (m, 4H), 1.45–1.35 (m, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.9, 147.1, 138.1, 137.4, 133.2, 133.2, 130.5, 129.4, 129.3, 129.0, 128.6, 127.8, 127.7, 127.5, 127.4, 127.3, 126.5, 126.4, 126.2, 60.7, 54.3, 26.2, 24.5.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{25}\text{H}_{25}\text{N}_2$ : 353.2012, found: 353.2008.



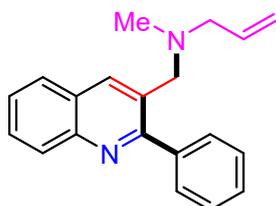
### 3-(piperidin-1-ylmethyl)-2,6'-biquinoline (4x)

28 mg, 80% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 3:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) to give **4x**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.99–8.93 (m, 1H), 8.33–8.08 (m, 6H), 7.91–7.84 (m, 1H), 7.76–7.67 (m, 1H), 7.60–7.52 (m, 1H), 7.48–7.41 (m, 1H), 3.52 (s, 2H), 2.37 (s, 4H), 1.59–1.52 (m, 4H), 1.47–1.38 (m, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.1, 150.8, 148.0, 147.0, 138.9, 137.7, 136.7, 131.1, 130.2, 129.5, 129.3, 129.0, 128.8, 128.0, 127.4, 127.3, 126.7, 121.5, 60.7, 54.2, 26.0, 24.4.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{24}\text{H}_{24}\text{N}_3$ : 354.1965, found: 354.1966.



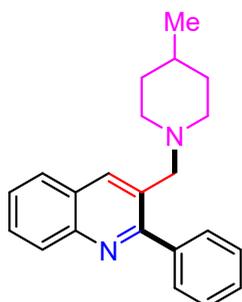
### N-methyl-N-((2-phenylquinolin-3-yl)methyl)prop-2-en-1-amine (4y)

19 mg, 66% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4y**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.38 (s, 1H), 8.15 (d,  $J = 8.5$  Hz, 1H), 7.87 (d,  $J = 8.2$  Hz, 1H), 7.73–7.67 (m, 1H), 7.65–7.59 (m, 2H), 7.56–7.44 (m, 4H), 5.80 (m, 1H), 5.14 (dd,  $J = 18.5, 13.6$  Hz, 2H), 3.62 (s, 2H), 3.01 (d,  $J = 6.4$  Hz, 2H), 2.18 (s, 3H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.6, 146.9, 140.5, 137.0, 135.5, 130.5, 129.3, 129.3, 129.2, 128.2, 128.2, 127.4, 126.5, 117.7, 60.5, 58.4, 41.9.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{20}\text{H}_{21}\text{N}_2$ : 289.1699, found: 289.1691.



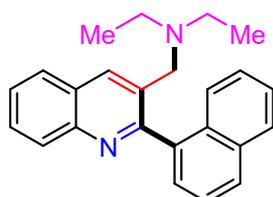
### 3-((4-methylpiperidin-1-yl)methyl)-2-phenylquinoline (4z)

27.9 mg, 88% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4z**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.33 (s, 1H), 8.22–8.10 (m, 1H), 7.92–7.81 (m, 1H), 7.75–7.66 (m, 1H), 7.65–7.58 (m, 2H), 7.56–7.52 (m, 2H), 7.36–7.25 (m, 2H), 3.57 (s, 2H), 2.46 (s, 3H), 2.45–2.32 (m, 4H), 1.65–1.53 (m, 4H), 1.47–1.44 (m, 1H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.8, 146.9, 138.0, 137.8, 136.9, 129.3, 129.2, 129.1, 128.8, 127.4, 127.3, 126.2, 60.4, 54.3, 26.0, 24.4, 21.4.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{22}\text{H}_{25}\text{N}_2$ : 317.2012, found: 317.2016.



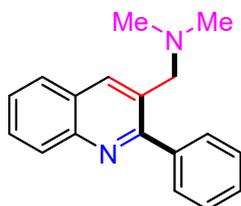
### N-ethyl-N-((2-(naphthalen-1-yl)quinolin-3-yl)methyl)ethanamine (4aa)

24.4 mg, 72% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4aa**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.53 (s, 1H), 8.17 (d,  $J = 8.4$  Hz, 1H), 8.00–7.89 (m, 3H), 7.74–7.69 (m, 1H), 7.61–7.57 (m, 2H), 7.54–7.45 (m, 2H), 7.39–7.28 (m, 2H), 3.40 (s, 2H), 2.37 (q,  $J = 7.1$  Hz, 4H), 0.82 (t,  $J = 7.1$  Hz, 6H).

$^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  159.9, 146.9, 138.1, 135.9, 133.7, 133.5, 131.9, 129.4, 129.1, 128.4, 128.3, 127.9, 127.5, 126.6, 126.4, 126.3, 125.9, 125.6, 125.4, 54.4, 47.1, 11.9.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{24}\text{H}_{25}\text{N}_2$ : 341.2012, found: 341.2006.



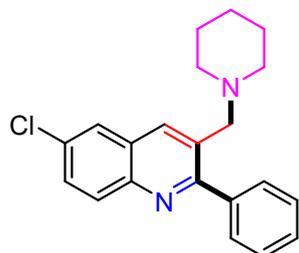
### N,N-dimethyl-1-(2-phenylquinolin-3-yl)methanamine (4ab)

16.2 mg, 62% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4ab**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.43 (s, 1H), 8.25–8.10 (m, 1H), 7.96–7.86 (m, 1H), 7.77–7.70 (m, 1H), 7.70–7.63 (m, 2H), 7.60–7.47 (m, 4H), 3.64 (s, 2H), 2.29 (s, 6H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  161.1, 152.0, 142.2, 134.8, 133.4, 131.8, 130.8, 129.3, 126.3, 124.2, 121.6, 120.3, 118.0, 111.1, 60.2, 32.7.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{18}\text{H}_{19}\text{N}_2$ : 263.1543, found: 263.1549.



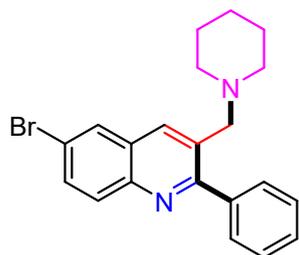
**6-chloro-2-phenyl-3-(piperidin-1-ylmethyl)quinoline (4ac)**

22.8 mg, 68% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4ac**.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.23 (s, 1H), 8.07 (d,  $J = 8.9$  Hz, 1H), 7.85 (s, 1H), 7.78–7.56 (m, 3H), 7.55–7.40 (m, 3H), 3.51 (s, 2H), 2.36 (s, 4H), 1.75–1.38 (m, 6H).

$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  161.1, 145.3, 140.4, 136.0, 132.1, 131.7, 131.0, 130.2, 129.3, 128.5, 128.3, 128.1, 126.1, 60.4, 54.5, 26.2, 24.5.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{21}\text{H}_{22}\text{ClN}_2$ : 337.1466, found: 337.1458.



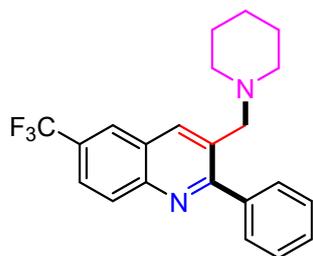
**6-bromo-2-phenyl-3-(piperidin-1-ylmethyl)quinoline (4ad)**

32.7 mg, 87% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4ad**.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.22 (s, 1H), 8.06–7.95 (m, 2H), 7.74 (dd,  $J = 8.9, 2.2$  Hz, 1H), 7.70–7.61 (m, 2H), 7.53–7.40 (m, 3H), 3.51 (s, 2H), 2.35 (s, 4H), 1.59–1.51 (m, 4H), 1.46–1.37 (m, 2H).

$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  161.2, 145.5, 140.3, 135.9, 132.7, 131.6, 131.1, 129.5, 129.2, 128.6, 128.5, 128.2, 120.2, 60.4, 54.5, 26.2, 24.4.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{21}\text{H}_{22}\text{BrN}_2$ : 381.0961, found: 381.0952.



**2-phenyl-3-(piperidin-1-ylmethyl)-6-(trifluoromethyl)quinoline (4ae)**

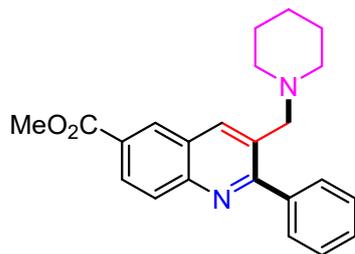
32 mg, 87% yield, yellow oil,  $R_f = 0.5$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4ae**.

$^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.42 (s, 1H), 8.25 (d,  $J = 8.8$  Hz, 1H), 8.19 (s, 1H), 7.86 (dd,  $J = 8.9, 2.0$  Hz, 1H), 7.71–7.65 (m, 2H), 7.53–7.42 (m, 3H), 3.54 (s, 2H), 2.37 (s, 4H), 1.61–1.51 (m, 4H), 1.47–1.38 (m, 2H).

$^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  163.0, 147.9, 140.2, 137.7, 132.2, 130.6, 129.3, 128.7, 128.3, 128.1, 126.4, 125.5 (q,  $J = 4.2$  Hz), 124.9 (q,  $J = 2.9$  Hz), 124.3 (q,  $J = 272.2$  Hz), 60.4, 54.5, 26.2, 24.4.

$^{19}\text{F NMR}$  (471 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.19.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{22}\text{H}_{22}\text{F}_3\text{N}_2$ : 371.1730, found: 371.1737.



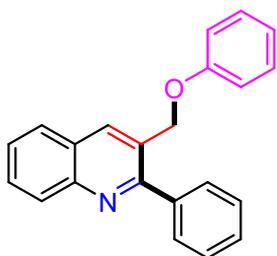
**methyl 2-phenyl-3-(piperidin-1-ylmethyl)quinoline-6-carboxylate (4af)**

28 mg, 78% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 4:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) to give **4af**.

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H), 8.20–8.07 (m, 3H), 7.90–7.83 (m, 1H), 7.83–7.76 (m, 2H), 7.75–7.66 (m, 1H), 7.60–7.51 (m, 1H), 3.96 (s, 3H), 3.47 (s, 2H), 2.33 (s, 4H), 1.53 (s, 4H), 1.45–1.36 (m, 2H).

$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.6, 159.4, 146.8, 141.9, 137.1, 130.1, 129.3, 129.3, 129.2, 127.4, 127.4, 126.4, 121.8, 114.6, 114.2, 60.3, 55.4, 54.4, 26.0, 24.3.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_2$ : 361.1911, found: 361.1919.



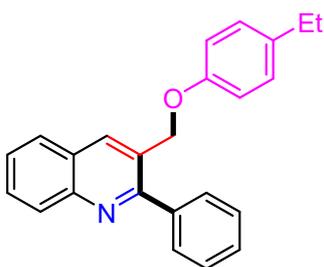
### 3-(phenoxy)methyl-2-phenylquinoline (4ag)

30.1 mg, 97% yield, yellow oil,  $R_f = 0.5$  (PE/EA = 10:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) to give **4ag**.

$^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.45 (s, 1H), 8.19 (d,  $J = 8.5$  Hz, 1H), 7.89 (dd,  $J = 8.2, 1.4$  Hz, 1H), 7.77–7.71 (m, 1H), 7.70–7.65 (m, 2H), 7.60–7.54 (m, 1H), 7.52–7.44 (m, 3H), 7.31–7.27 (m, 2H), 7.01–6.95 (m, 1H), 6.94–6.90 (m, 2H), 5.14 (d,  $J = 0.9$  Hz, 2H).

$^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  159.2, 158.4, 147.6, 139.8, 136.7, 130.1, 129.7, 129.5, 129.0, 128.9, 128.7, 128.5, 127.7, 127.4, 126.9, 121.5, 115.0, 67.6.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{22}\text{H}_{18}\text{NO}$ : 312.1383, found: 312.1376.



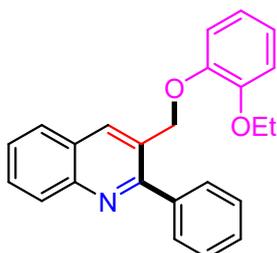
### 3-((4-ethylphenoxy)methyl)-2-phenylquinoline (4ah)

30 mg, 89% yield, yellow oil,  $R_f = 0.5$  (PE/EA = 10:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) to give **4ah**.

$^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.44 (s, 1H), 8.18 (d,  $J = 8.5$  Hz, 1H), 7.89 (dd,  $J = 8.1, 1.5$  Hz, 1H), 7.78–7.70 (m, 1H), 7.70–7.64 (m, 2H), 7.60–7.53 (m, 1H), 7.52–7.44 (m, 3H), 7.10 (d,  $J = 8.6$  Hz, 2H), 6.84 (d,  $J = 8.6$  Hz, 2H), 5.12 (d,  $J = 0.9$  Hz, 2H), 2.59 (q,  $J = 7.6$  Hz, 2H), 1.21 (t,  $J = 7.6$  Hz, 3H).

$^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  159.2, 156.5, 137.3, 136.7, 130.0, 129.5, 129.0, 128.9, 128.8, 128.8, 128.7, 127.8, 127.4, 126.8, 115.0, 67.9, 28.1, 16.0.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{24}\text{H}_{22}\text{NO}$ : 340.1696, found: 340.1688.



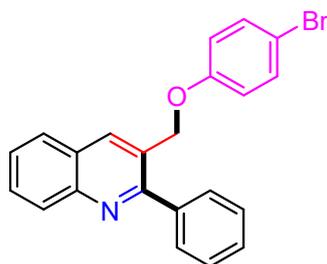
### 3-((2-ethoxyphenoxy)methyl)-2-phenylquinoline (4ai)

34.3 mg, 97% yield, yellow oil, R<sub>f</sub> = 0.4 (PE/EA = 6:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:15) to give **4ai**.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.52 (s, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.77–7.63 (m, 3H), 7.60–7.41 (m, 4H), 6.99–6.86 (m, 2H), 6.85–6.77 (m, 2H), 5.20 (s, 2H), 4.10 (q, *J* = 7.4, 6.9 Hz, 2H), 1.45 (t, *J* = 7.0 Hz, 3H).

<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 159.1, 149.6, 148.2, 147.5, 139.9, 136.5, 129.8, 129.5, 129.0, 129.0, 128.8, 128.6, 127.8, 127.4, 126.7, 122.4, 121.0, 115.7, 113.7, 69.2, 64.5, 15.1.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>24</sub>H<sub>22</sub>NO<sub>2</sub>: 356.1645, found: 356.1642.



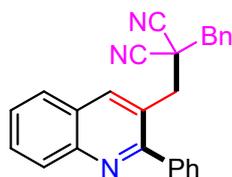
### 3-((4-bromophenoxy)methyl)-2-phenylquinoline (4aj)

29.1 mg, 75% yield, yellow oil, R<sub>f</sub> = 0.5 (PE/EA = 10:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) to give **4aj**.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.41 (s, 1H), 8.19 (d, *J* = 8.1 Hz, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.82–7.71 (m, 1H), 7.69–7.55 (m, 3H), 7.53–7.42 (m, 3H), 7.41–7.30 (m, 2H), 6.92–6.65 (m, 2H), 5.10 (d, *J* = 4.7 Hz, 2H).

<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 159.2, 157.4, 147.5, 139.6, 136.9, 132.5, 130.3, 129.4, 129.0, 128.9, 128.7, 128.0, 127.7, 127.3, 127.0, 116.8, 113.7, 67.9.

HRMS (ESI) *m/z*: [M + H]<sup>+</sup> Calcd for C<sub>22</sub>H<sub>17</sub>BrNO: 390.0488, found: 390.0480.



### 2-benzyl-2-((2-phenylquinolin-3-yl)methyl)malononitrile (6a)

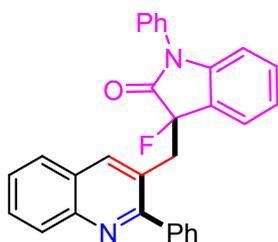
12.9 mg, 35% yield, yellow oil, R<sub>f</sub> = 0.4 (PE/EA = 2:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:3) to give **6a**.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.54 (s, 1H), 8.19 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.79 (t, *J* = 7.7 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.53–7.46 (m, 6H), 7.34–7.32 (m, 2H), 7.24–7.20 (m, 2H), 3.60 (s, 2H), 2.99 (s, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 160.5, 147.6, 139.5, 138.5, 131.6, 130.8, 130.3, 129.7,

129.6, 129.1, 129.0, 128.9, 128.8, 127.8, 127.4, 127.0, 124.1, 115.0, 43.4, 40.6, 38.7.

**HRMS (ESI) m/z:**  $[M + H]^+$  Calcd for  $C_{26}H_{20}N_3$ : 374.1652, found: 374.1654.



### 3-fluoro-3-((2-(4-fluorophenyl)quinolin-3-yl)methyl)-1-phenylindolin-2-one (6b)

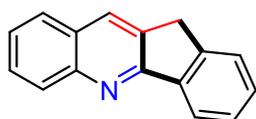
29.8 mg, 65% yield, colorless oil,  $R_f = 0.4$  (PE/EA = 3:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) to give **6b**.

**$^1H$  NMR** (500 MHz,  $CDCl_3$ )  $\delta$  8.37 (s, 1H), 8.11 (d,  $J = 8.5$  Hz, 1H), 7.82 (d,  $J = 7.9$  Hz, 1H), 7.74 (m, 1H), 7.58 (t,  $J = 7.2$  Hz, 1H), 7.49–7.34 (m, 3H), 7.24–7.12 (m, 3H), 7.09–7.02 (m, 4H), 6.89 (t,  $J = 7.5$  Hz, 1H), 6.56 (dd,  $J = 15.2, 7.7$  Hz, 2H), 3.97 (t,  $J = 14.3$  Hz, 1H), 3.62 (dd,  $J = 22.5, 14.4$  Hz, 1H).

**$^{13}C$  NMR** (126 MHz,  $CDCl_3$ )  $\delta$  172.0 (d,  $J = 21.0$  Hz), 163.8, 161.9, 159.9, 143.7 (d,  $J = 5.3$  Hz), 139.2, 133.3, 131.3 (d,  $J = 8.2$  Hz), 131.2 (d,  $J = 2.7$  Hz), 130.2, 129.9, 129.3, 128.7, 127.6, 127.1, 126.3, 125.6, 124.7 (d,  $J = 14.2$  Hz), 124.5, 123.7, 115.4 (d,  $J = 21.6$  Hz), 110.0, 94.1, 92.5, 37.4 (d,  $J = 28.6$  Hz), 29.8.

**$^{19}F$  NMR** (471 MHz,  $CDCl_3$ )  $\delta$  -113.42, -155.20.

**HRMS (ESI) m/z:**  $[M + H]^+$  Calcd for  $C_{30}H_{21}F_2N_2O$ : 463.1616, found: 463.1618.



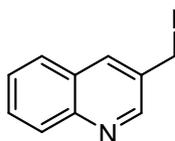
### 11H-indeno[1,2-b]quinoline (7)

10.7 mg, 50% yield, yellow oil,  $R_f = 0.5$  (PE/EA = 6:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:12) to give **7**.

**$^1H$  NMR** (500 MHz,  $CDCl_3$ )  $\delta$  8.32 (dd,  $J = 6.6, 2.0$  Hz, 1H), 8.26–8.14 (m, 2H), 7.82 (dd,  $J = 8.1, 1.4$  Hz, 1H), 7.72–7.68 (m, 1H), 7.61 (dd,  $J = 7.2, 1.5$  Hz, 1H), 7.53–7.49 (m, 3H), 4.04 (s, 2H).

**$^{13}C$  NMR** (126 MHz,  $CDCl_3$ )  $\delta$  161.8, 148.1, 145.3, 140.4, 134.8, 131.4, 130.2, 129.2, 129.0, 127.9, 127.7, 127.5, 125.8, 125.6, 122.3, 34.2.

**HRMS (ESI) m/z:**  $[M + H]^+$  Calcd for  $C_{16}H_{12}N$ : 218.0964, found: 218.0956.



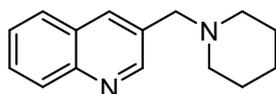
### 3-(iodomethyl)quinoline (8)

53.9 mg, 67% yield, yellow oil,  $R_f = 0.4$  (PE/EA = 3:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:4) to give **8**.

$^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.90 (d,  $J = 2.4$  Hz, 1H), 8.11–8.02 (m, 2H), 7.74 (dd,  $J = 8.2, 1.4$  Hz, 1H), 7.71–7.64 (m, 1H), 7.56–7.46 (m, 1H), 4.57 (s, 2H).

$^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  151.3, 147.4, 134.9, 132.4, 129.9, 129.4, 127.7, 127.6, 127.3, 1.4.

**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{10}\text{H}_9\text{IN}$ : 269.9774 found: 269.9769.



### quinolin-3-ylmethanol (9)

10.2 mg, 46% yield, yellow oil,  $R_f = 0.3$  (PE/EA = 2:1, v/v). The product was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:3) to give **9**.

$^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.88 (d,  $J = 2.2$  Hz, 1H), 8.14–8.01 (m, 2H), 7.79 (dd,  $J = 8.2, 1.4$  Hz, 1H), 7.71–7.63 (m, 1H), 7.56–7.49 (m, 1H), 3.65 (s, 2H), 2.43 (s, 4H), 1.65–1.53 (m, 4H), 1.49–1.36 (m, 2H).

$^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  152.4, 147.6, 135.7, 131.5, 129.3, 129.1, 128.1, 127.7, 126.7, 61.3, 54.7, 26.0, 24.4.

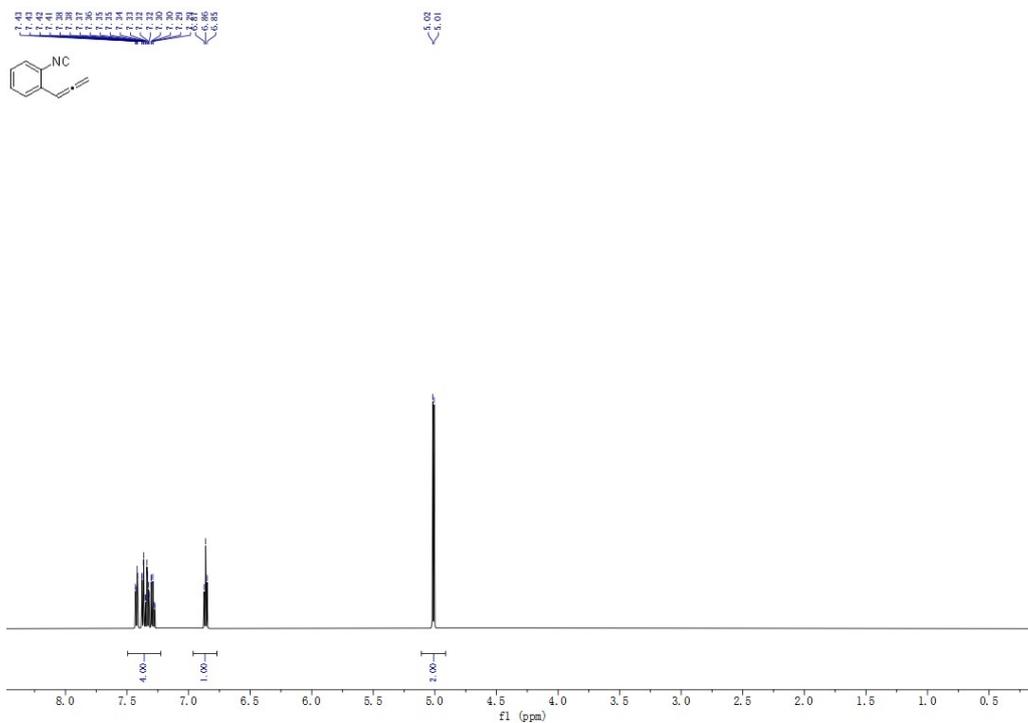
**HRMS (ESI) m/z:**  $[\text{M} + \text{H}]^+$  Calcd for  $\text{C}_{15}\text{H}_{19}\text{N}_2$ : 227.1543 found: 227.1551.

## 5. References

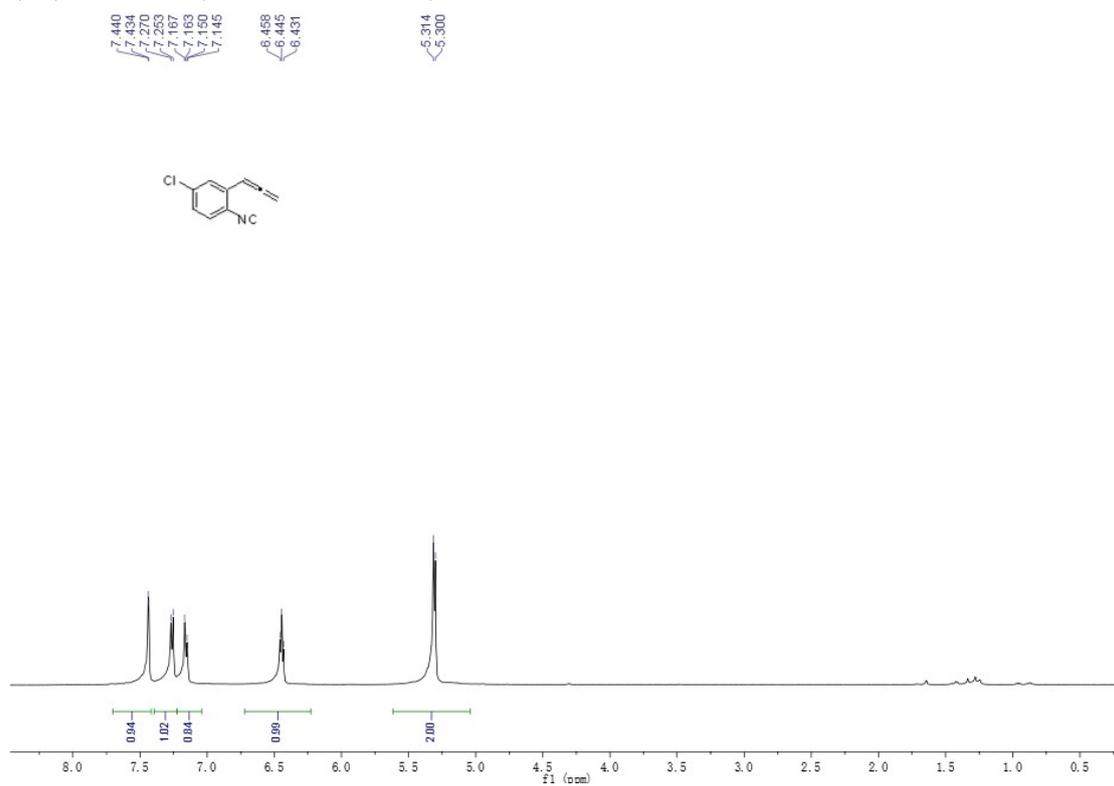
- [1] Kanbayashi, N.; Okamura, T.; Onitsuka, K. Living Cyclocopolymerization through Alternating Insertion of Isocyanide and Allene via Controlling the Reactivity of the Propagation Species: Detailed Mechanistic Investigation. *J. Am. Chem. Soc.* **2019**, *141*, 15307-15317.
- [2] Aravinda, T.; Bhojya Naik, H. S.; Prakash Naik, H. R. 1,2,3-Triazole Fused Quinoline-Peptidomimetics: Studies on Synthesis, DNA Binding and Photonuclease Activity. *Int. J. Pept. Res. Ther.* **2009**, *15*, 273–279.

## 6. Copies of the $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and $^{19}\text{F}$ NMR Spectra

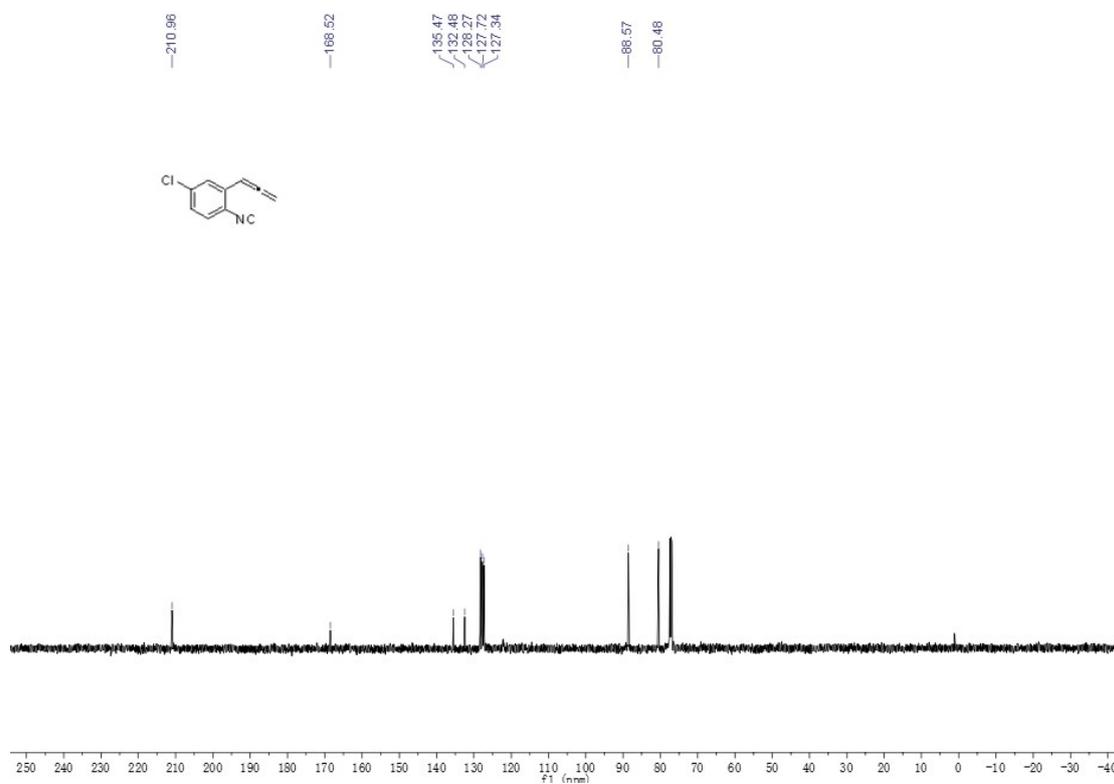
### (1a) $^1\text{H}$ NMR (400 MHz, $\text{CDCl}_3$ )



**(1b)**  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



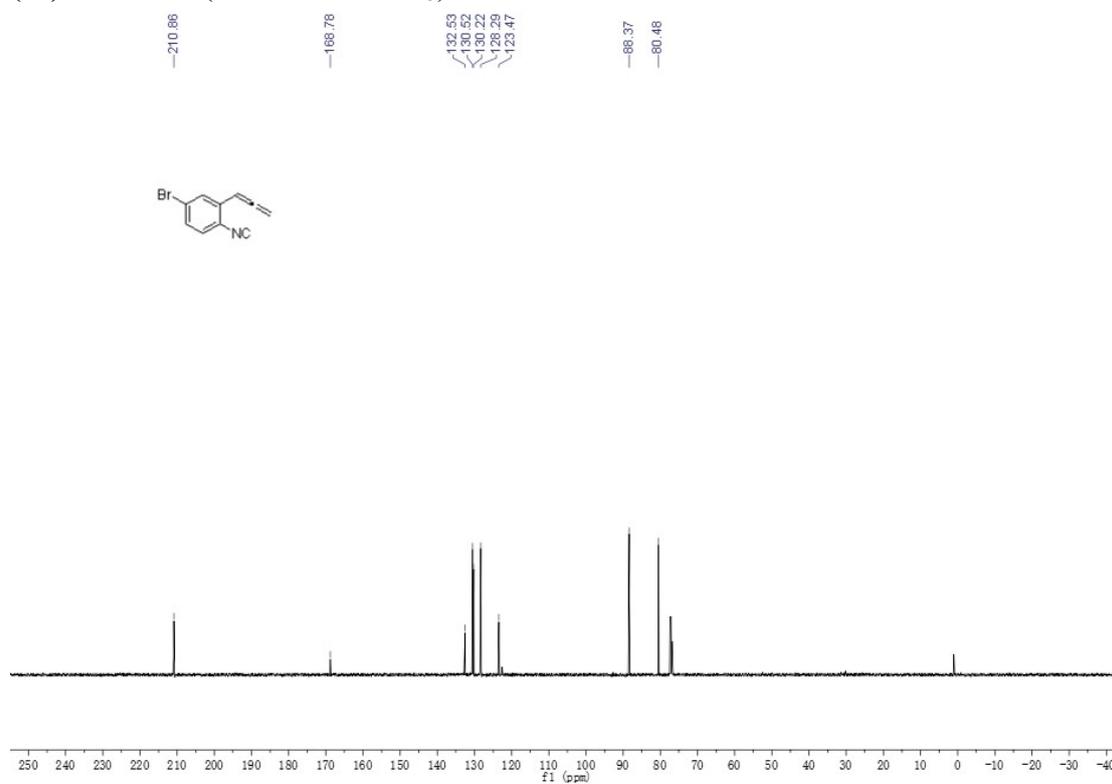
**(1b)**  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



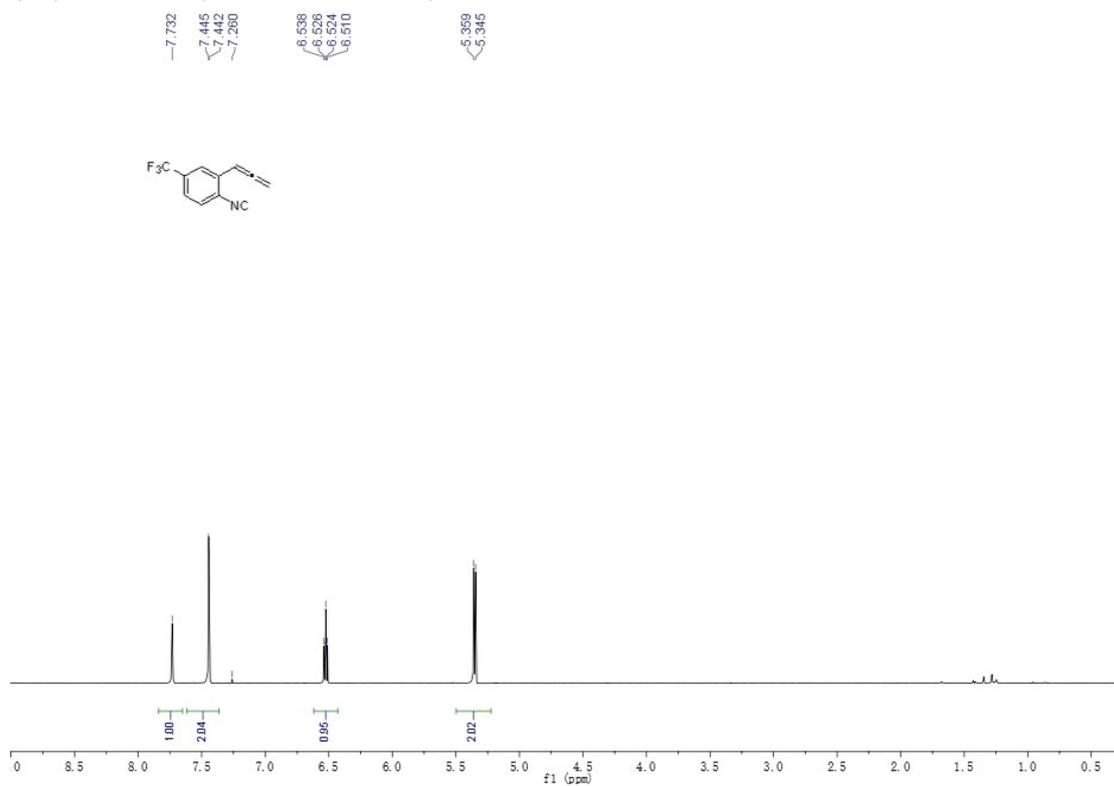
(1c)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



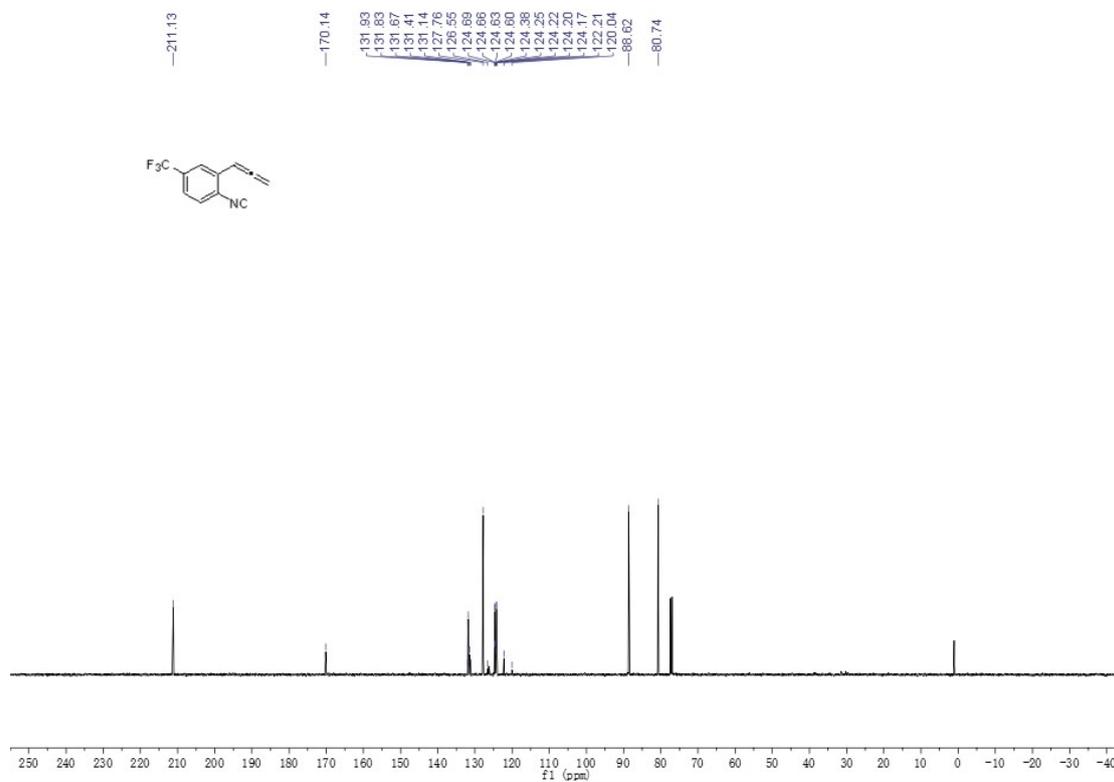
(1c)  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



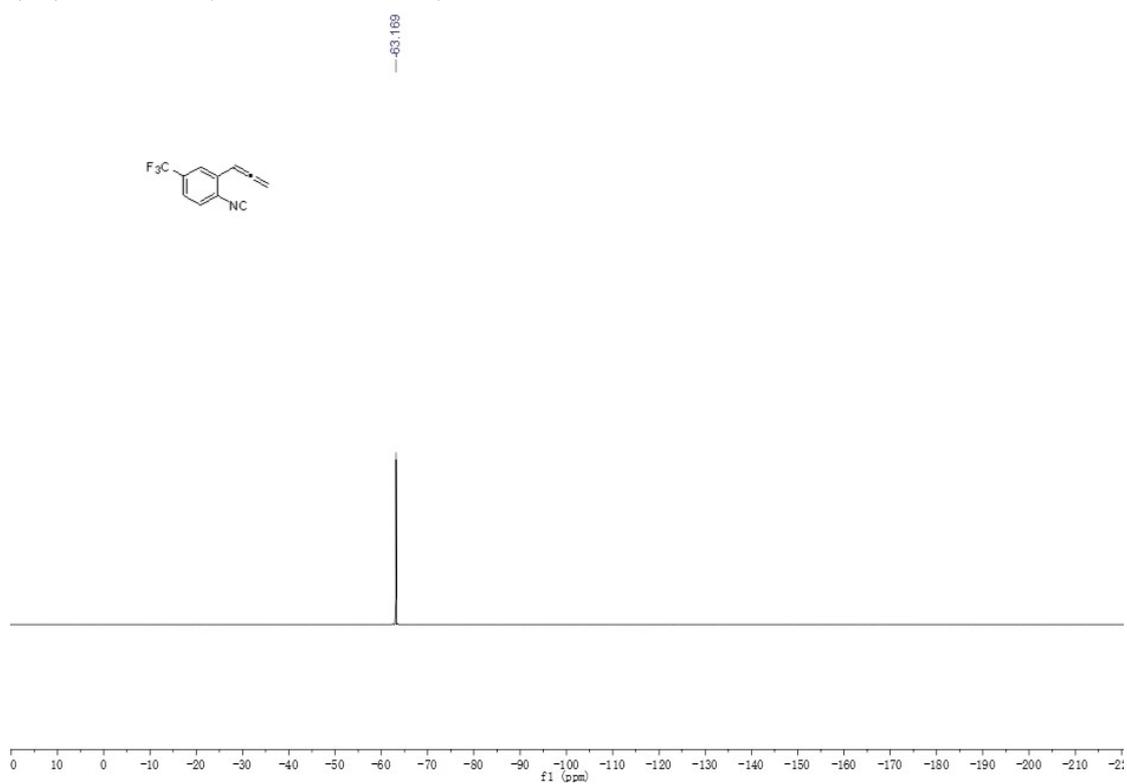
(1d) <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)



(1d) <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)



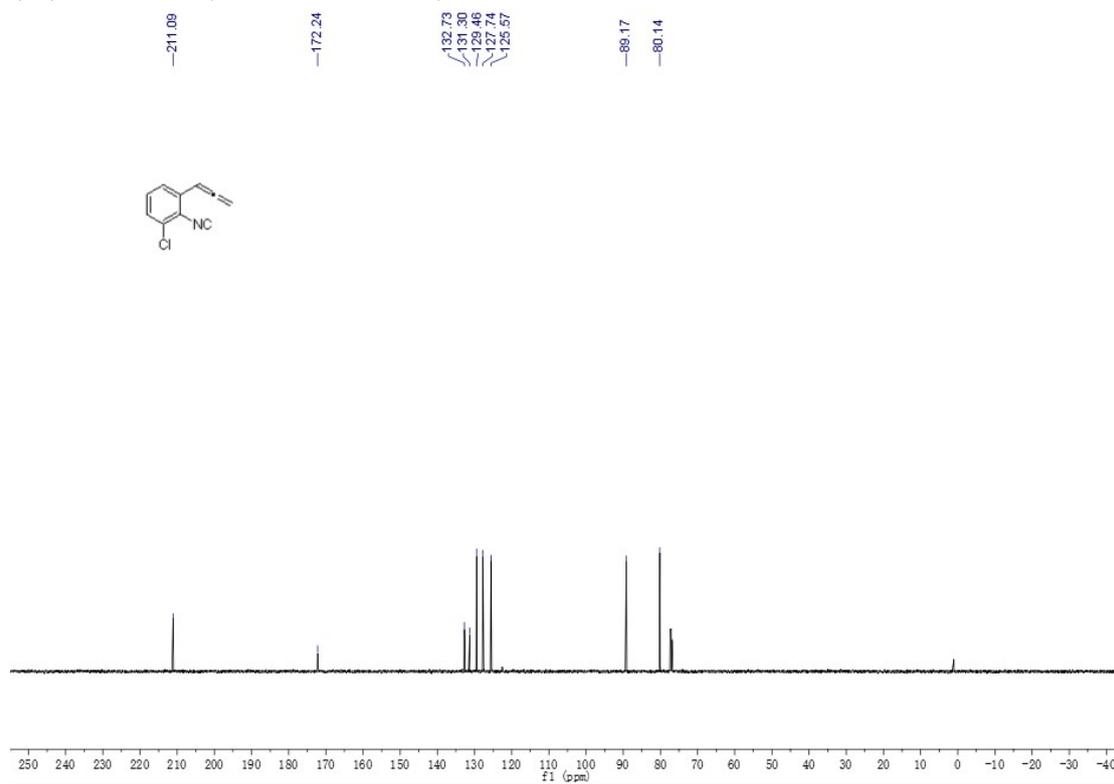
(1d)  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )



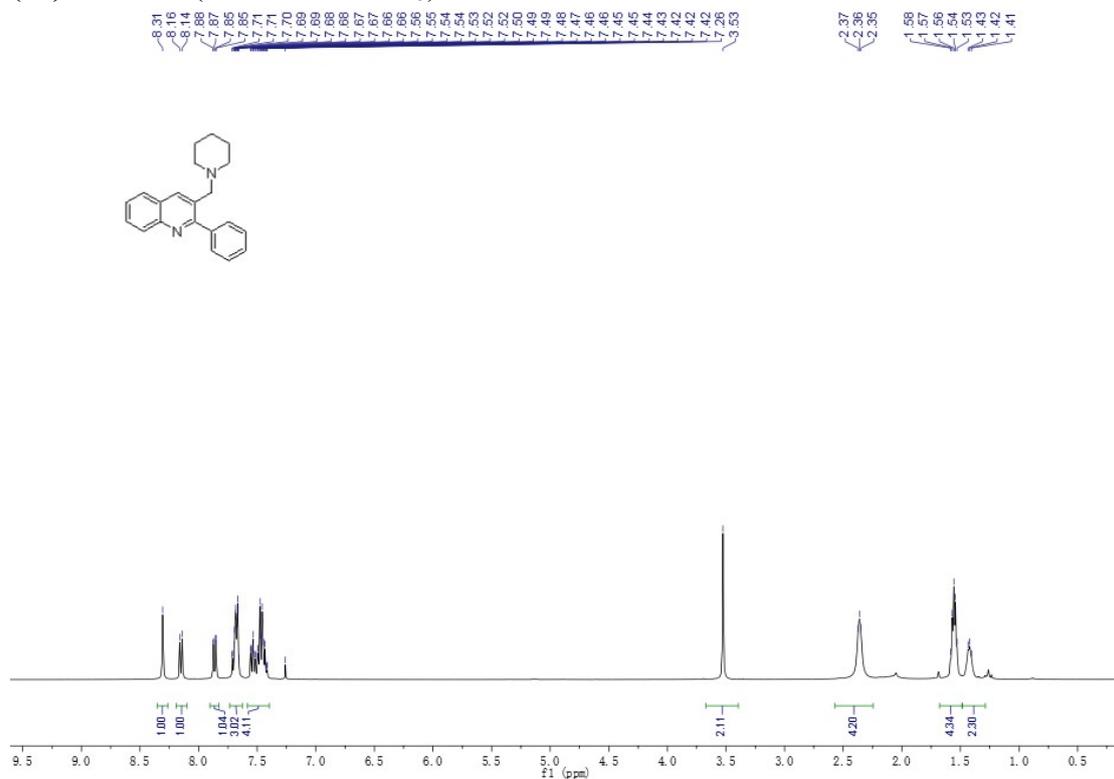
(1e)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



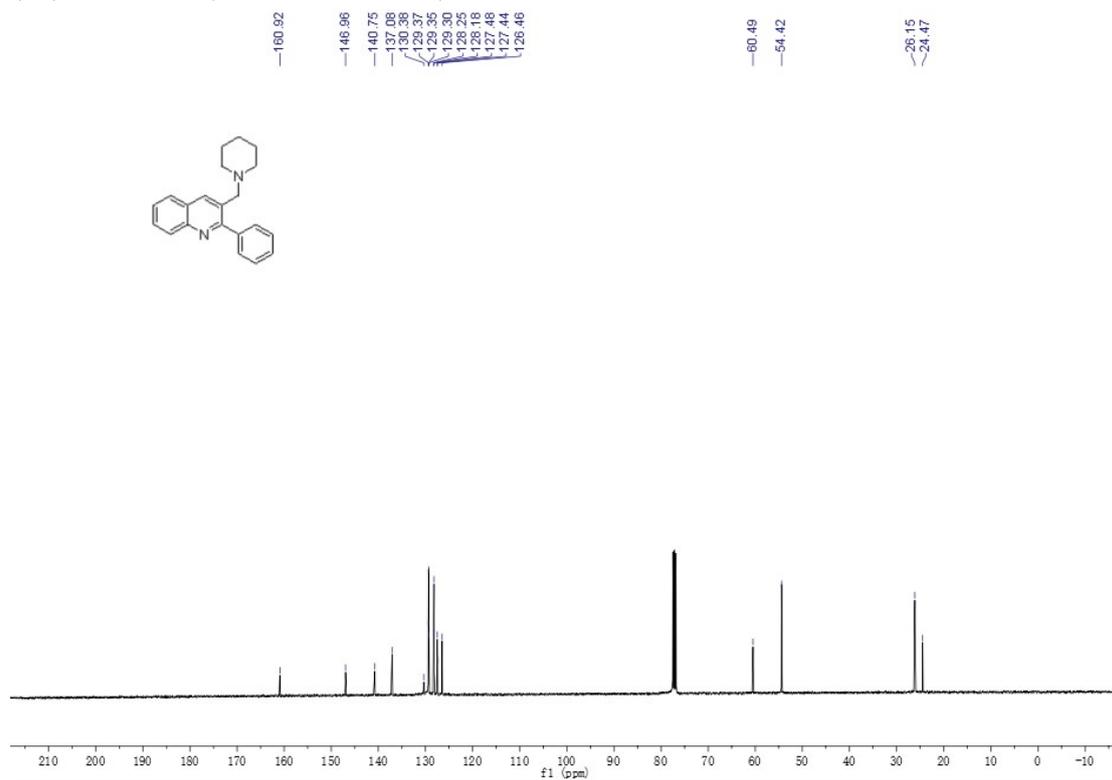
(1e)  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



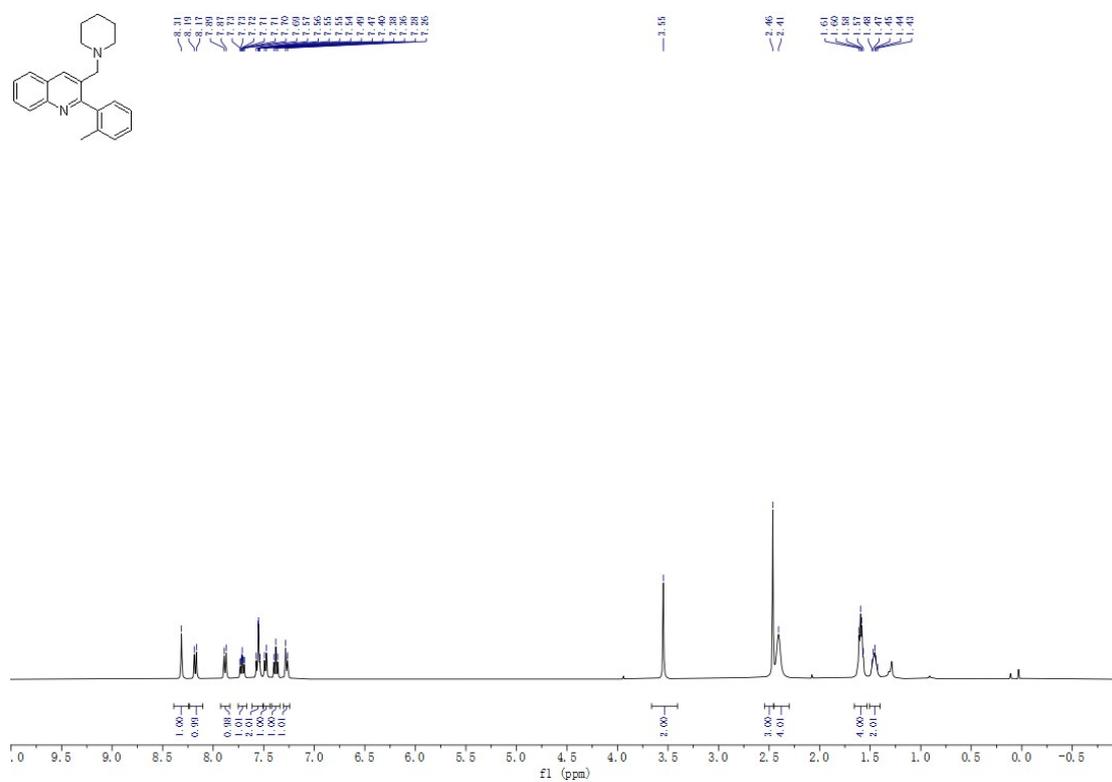
(4a)  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



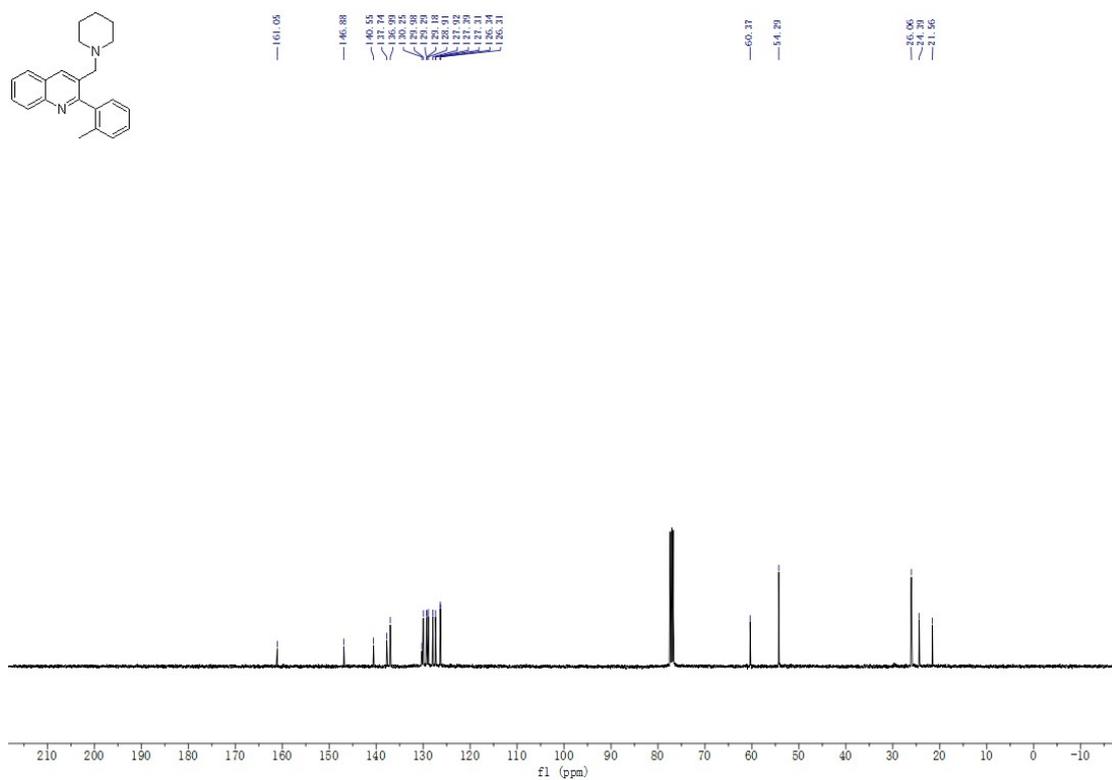
(4a)  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



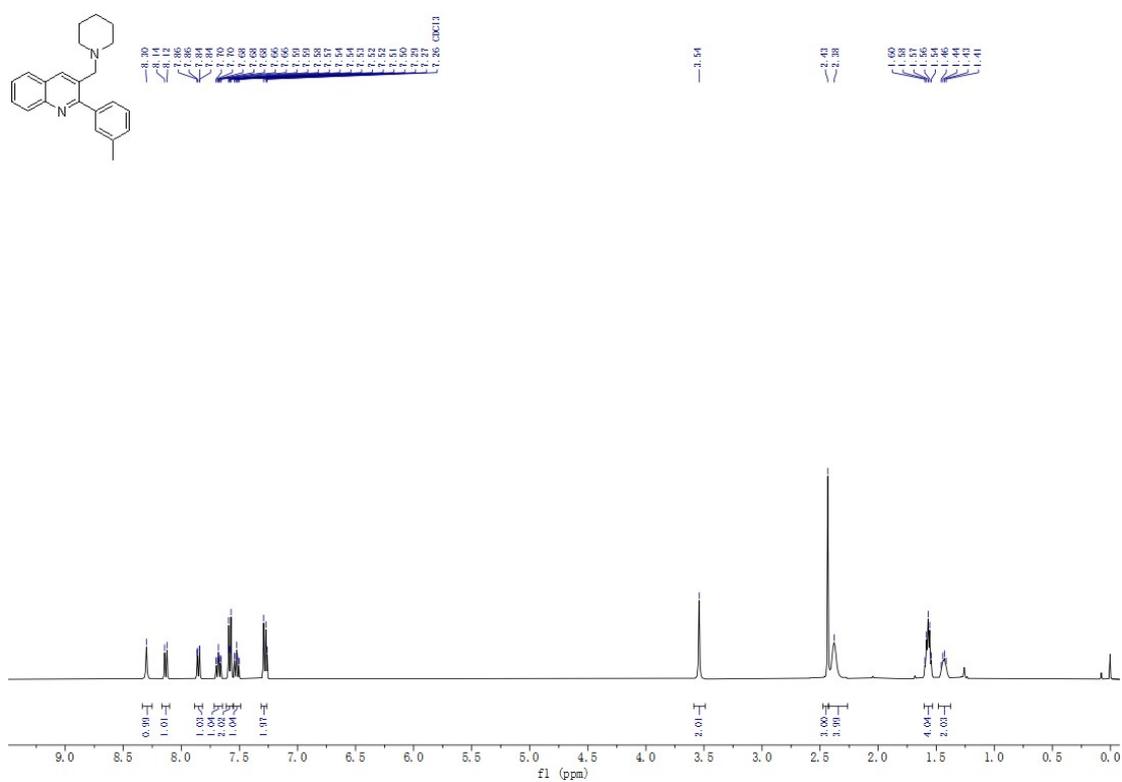
(4b)  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



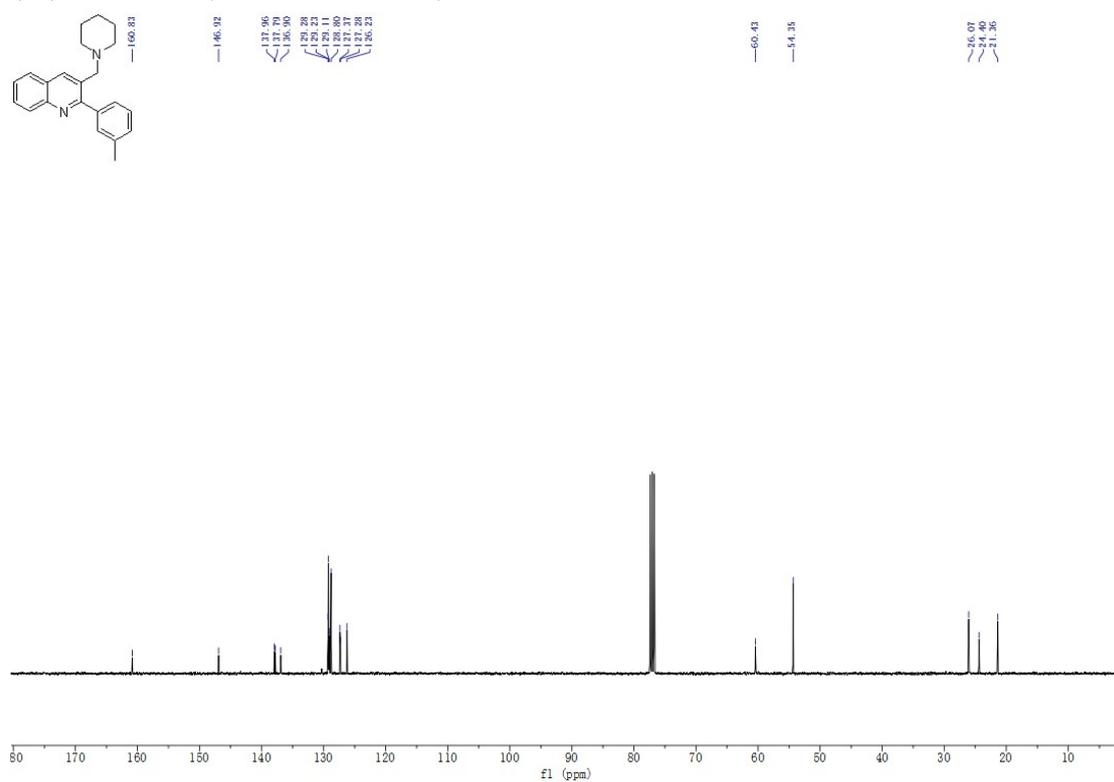
**(4b)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



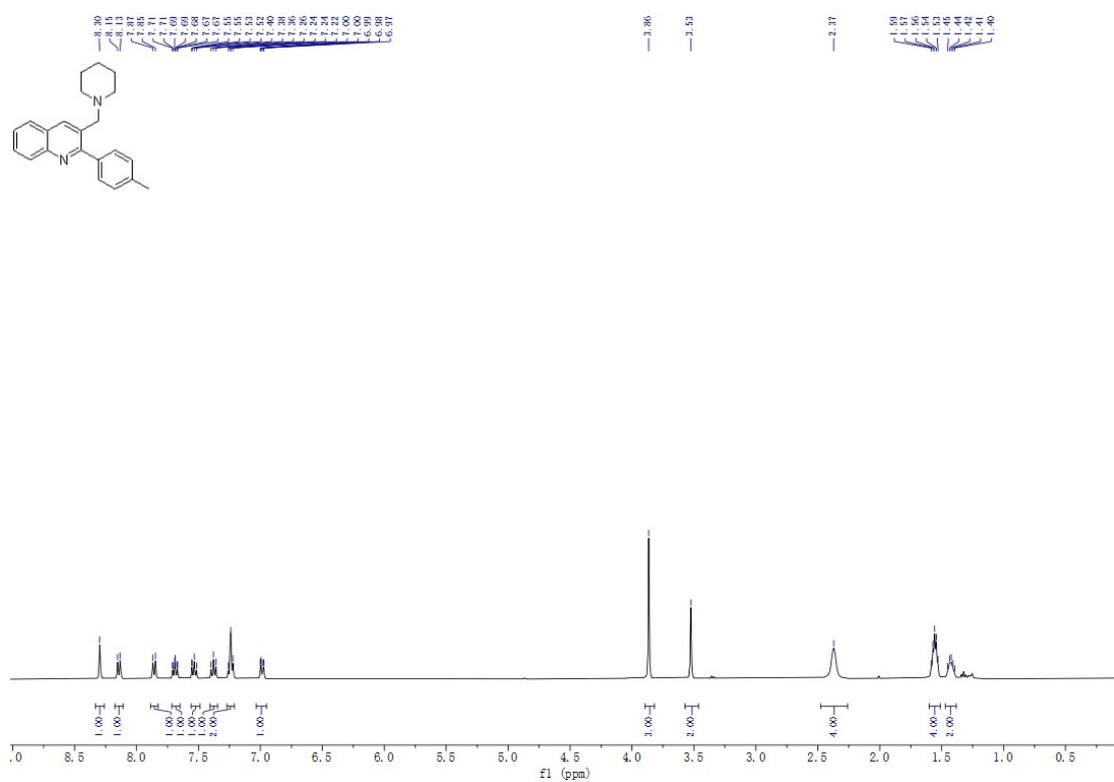
**(4c)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



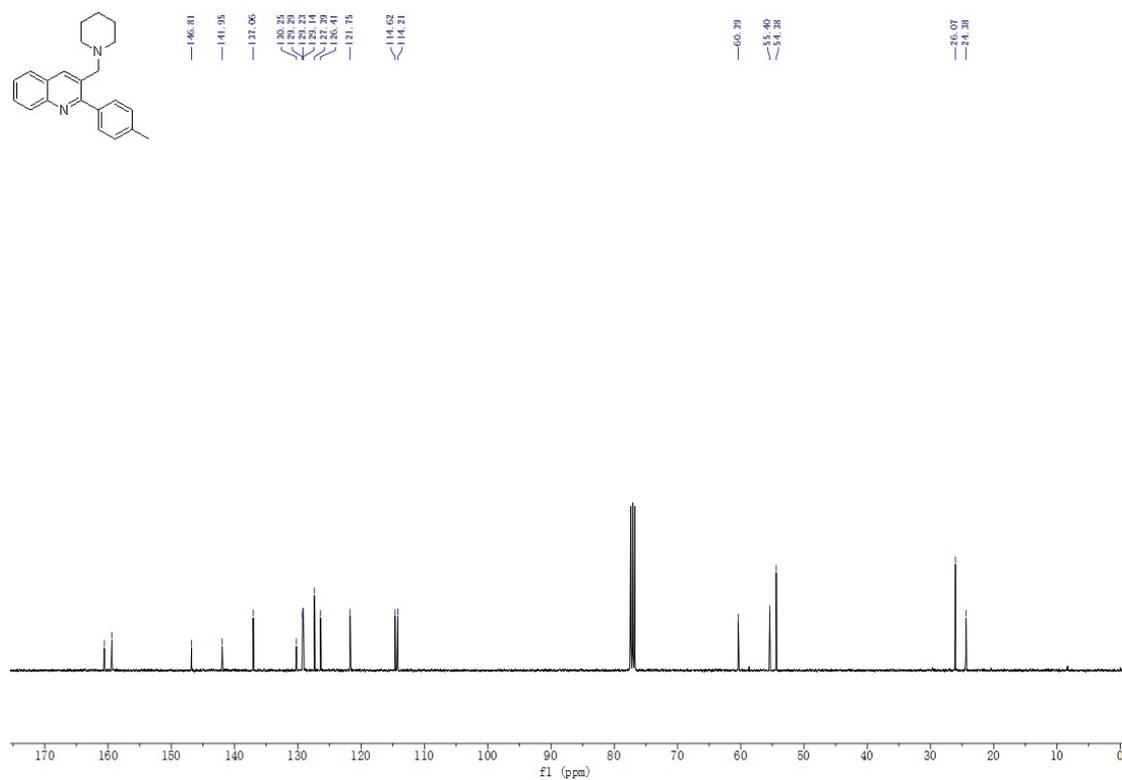
(4c)  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



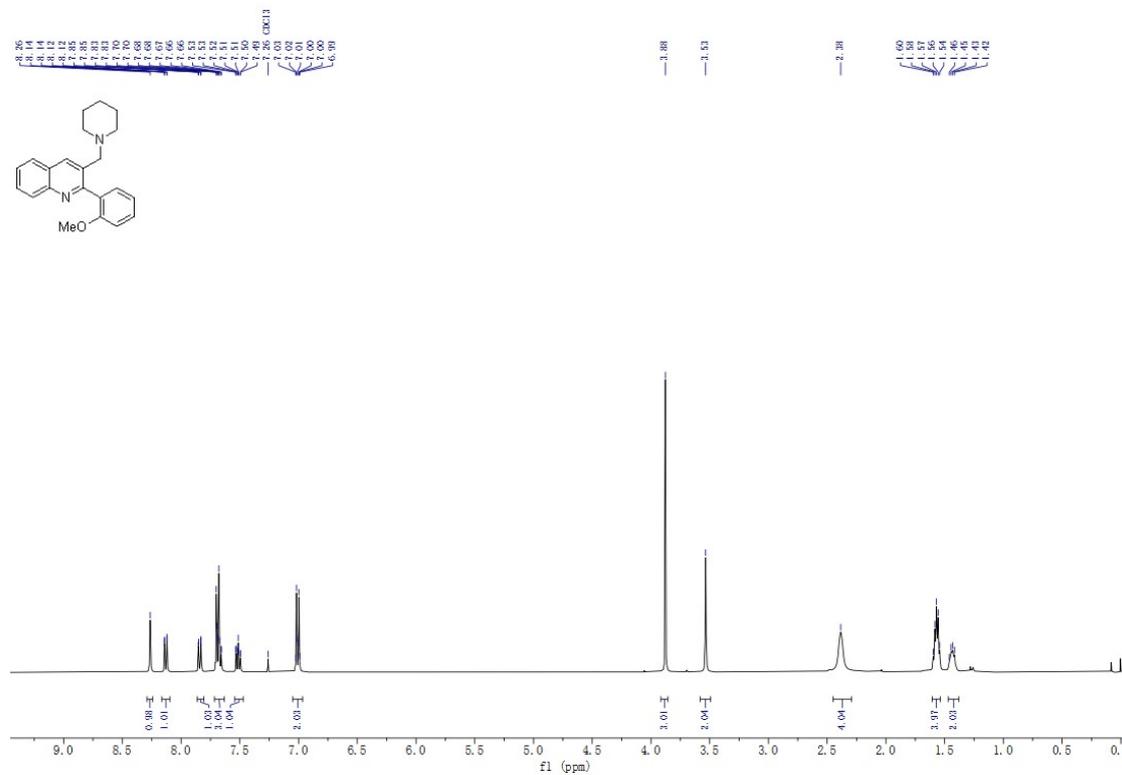
(4d)  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



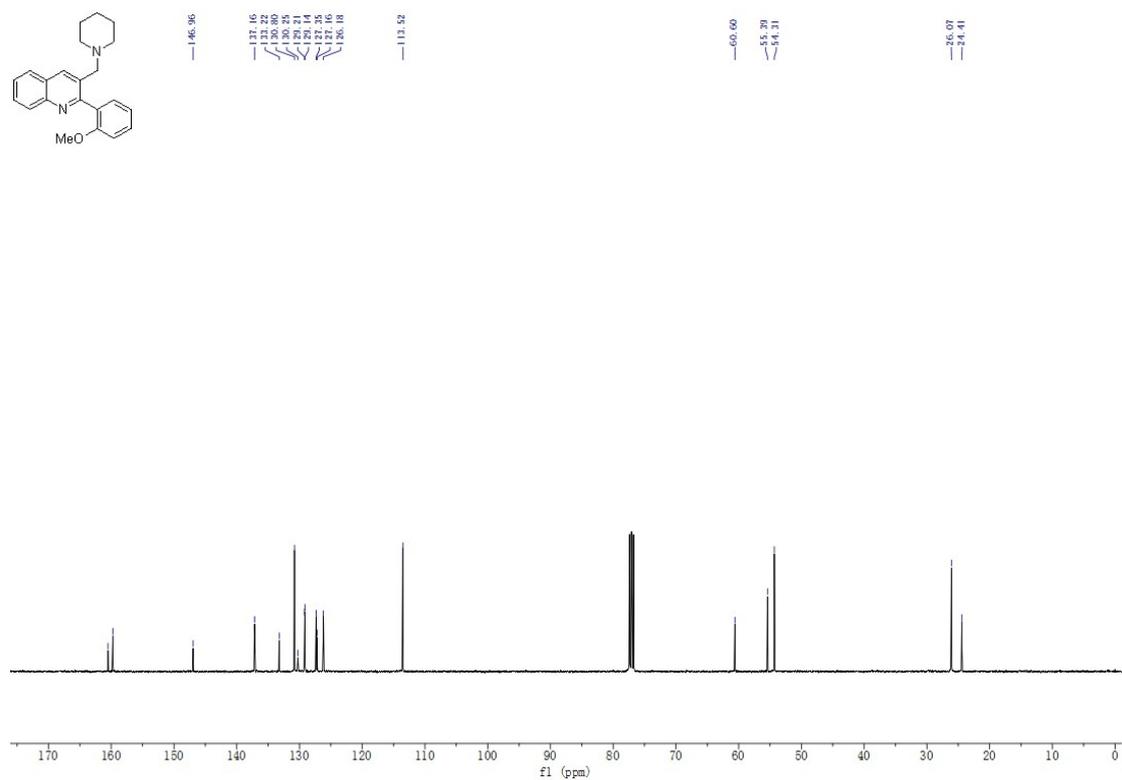
**(4d)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



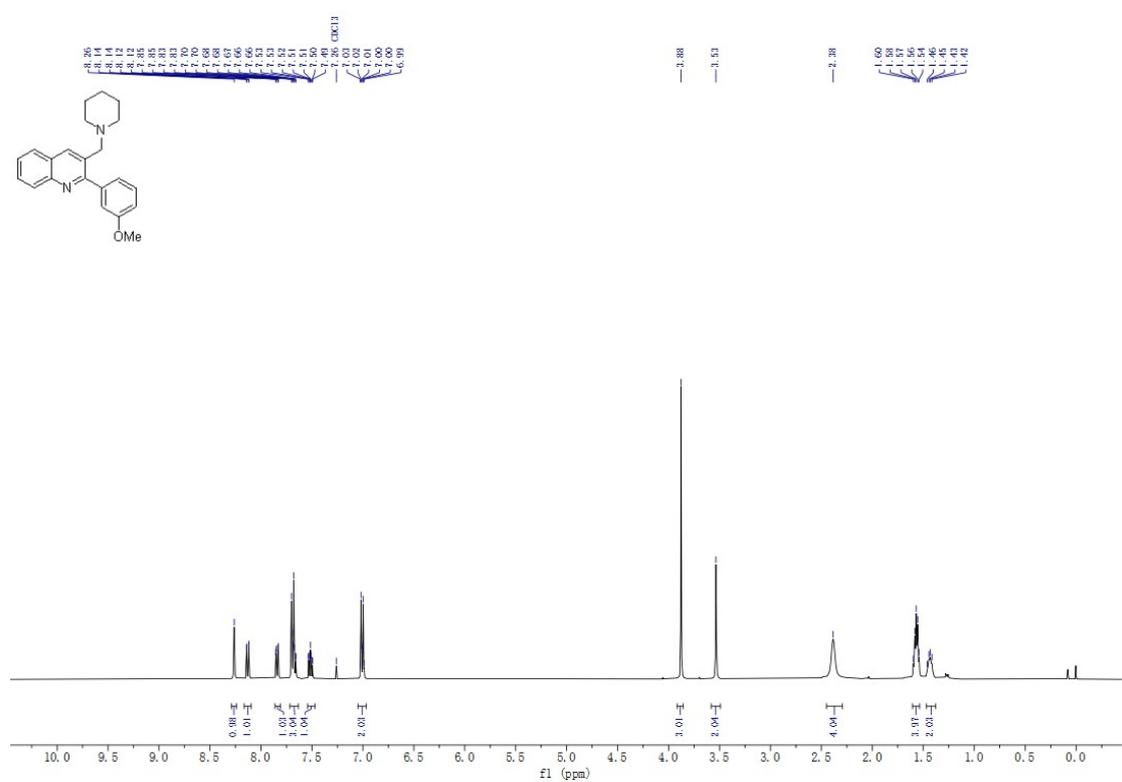
**(4e)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



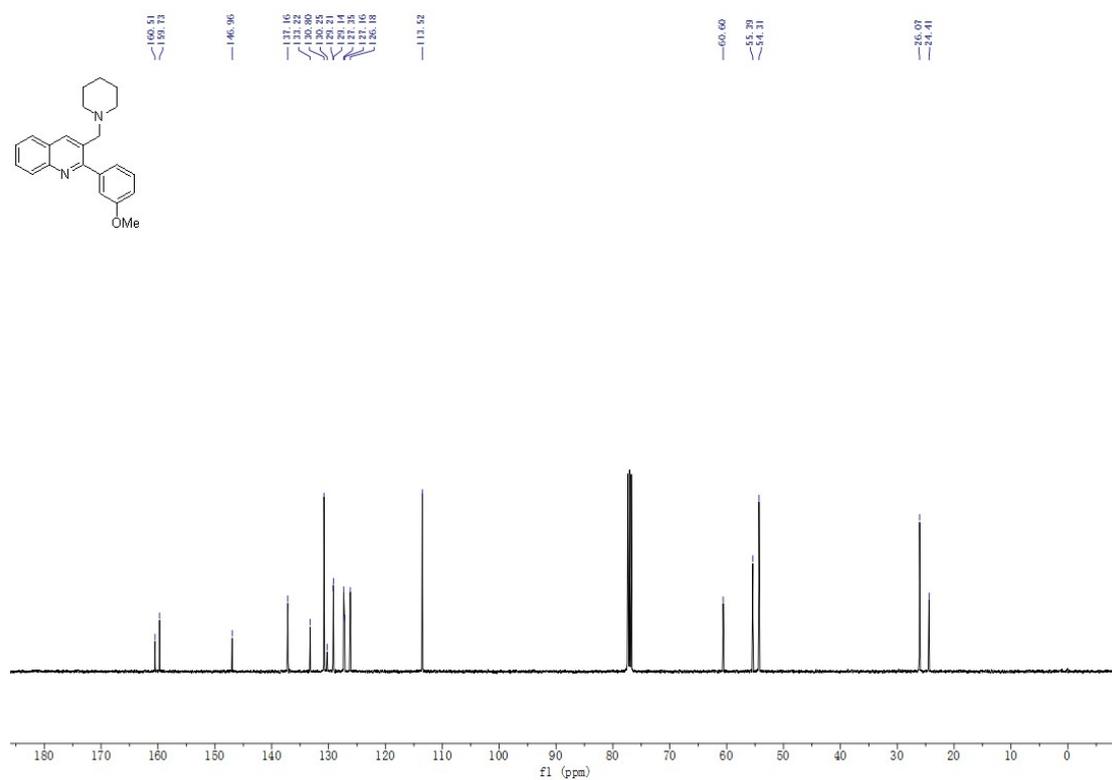
**(4e)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



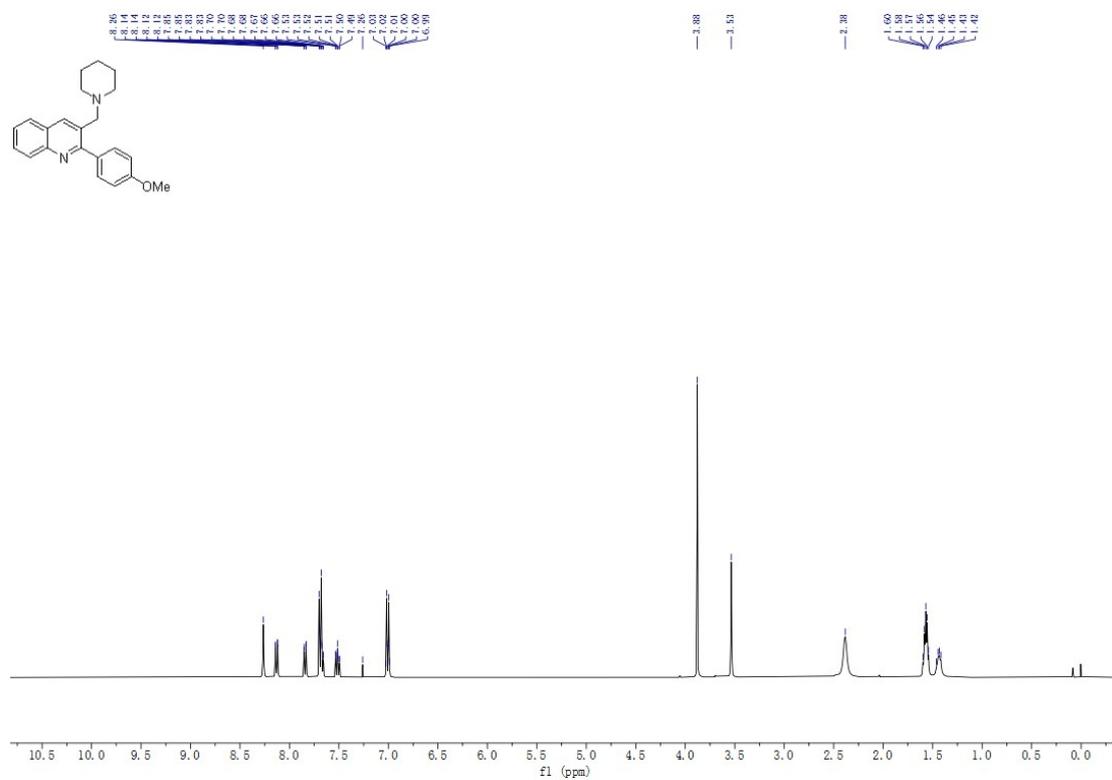
**(4f)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



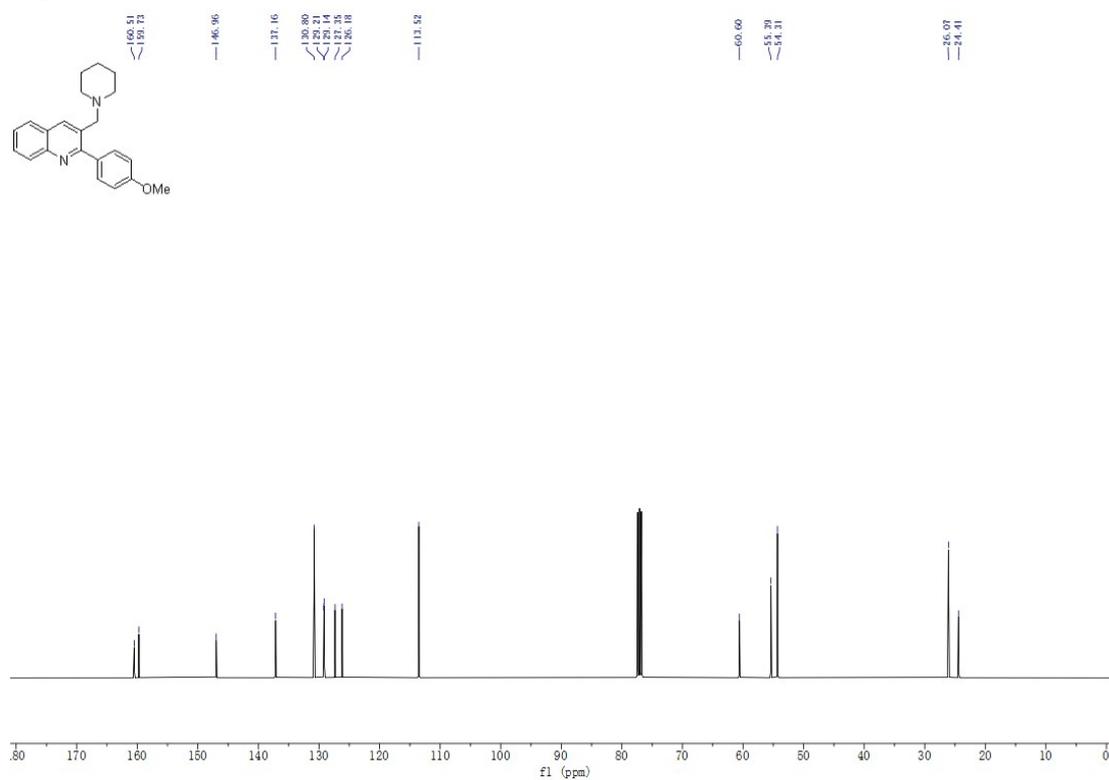
(4f) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



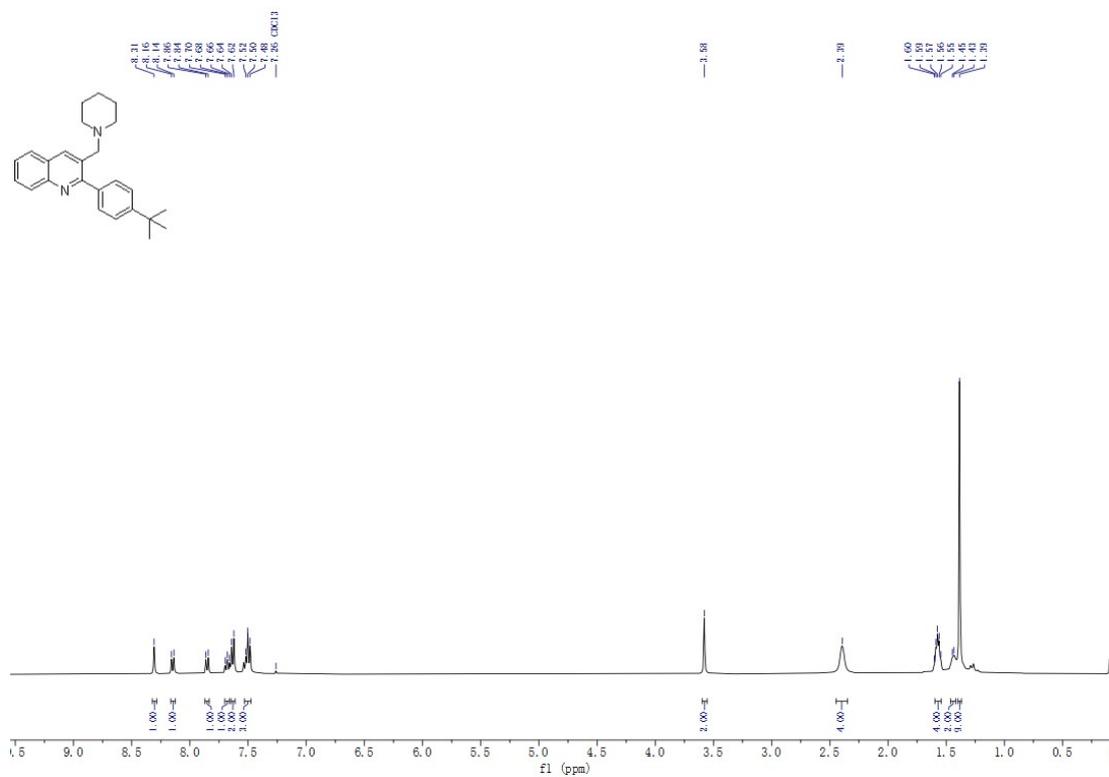
(4g) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



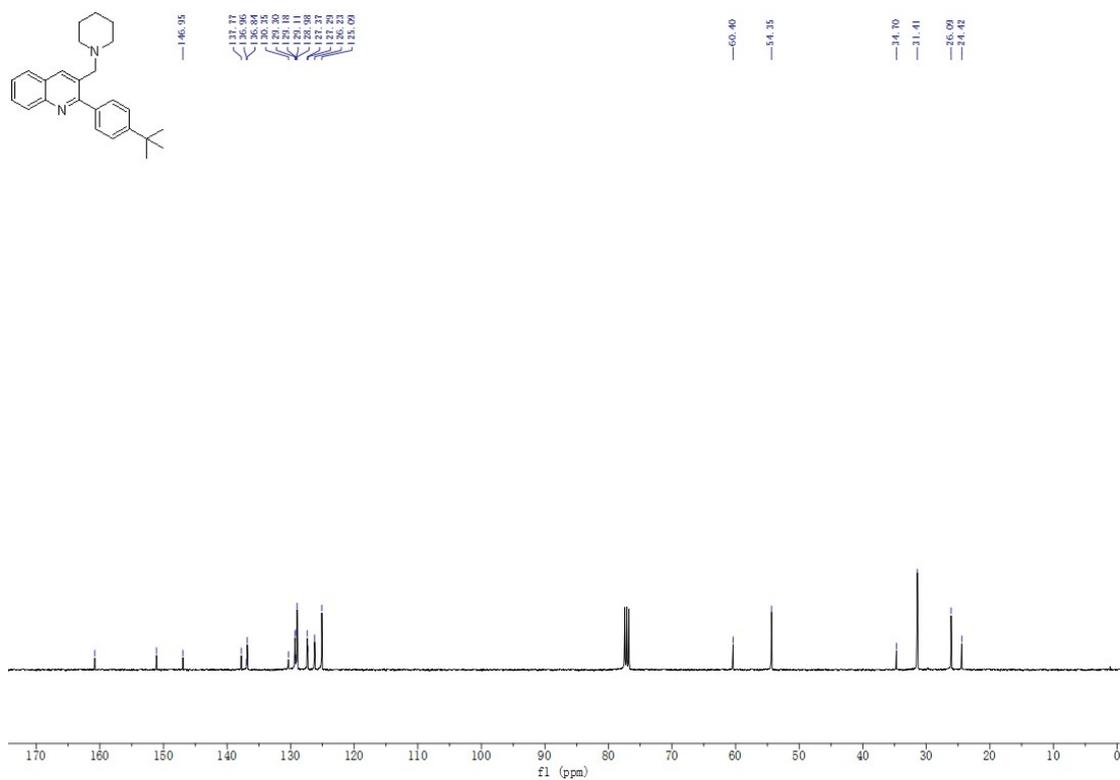
**(4g)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



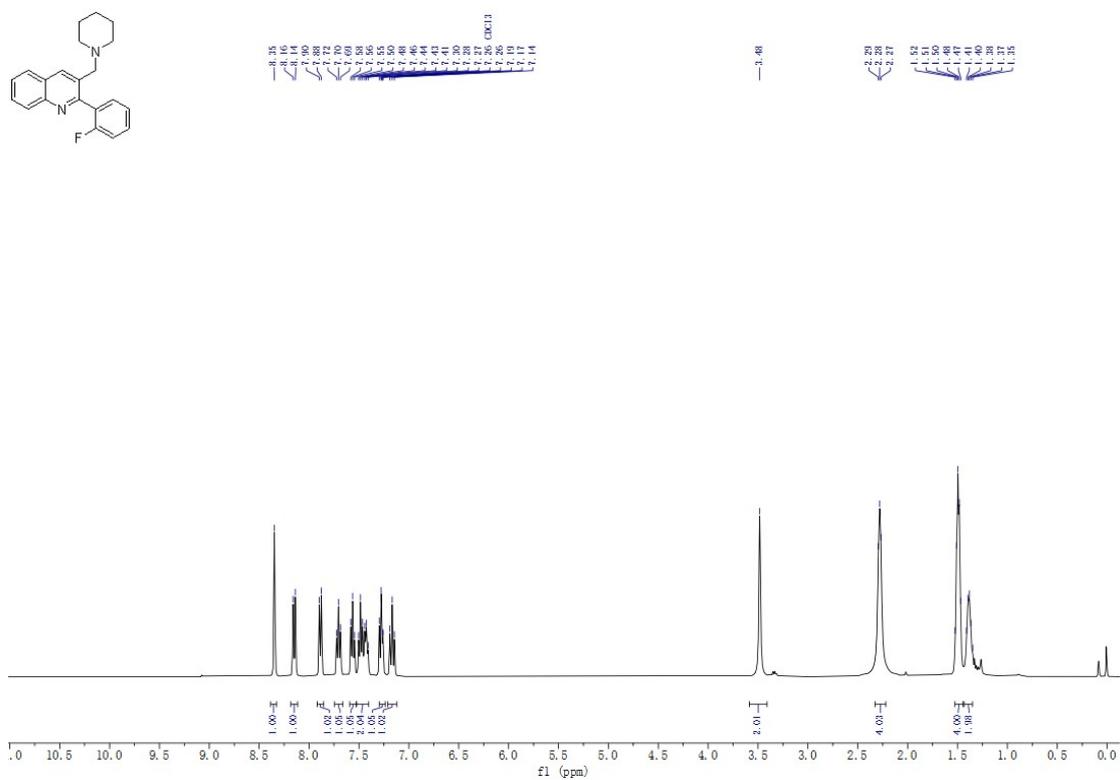
**(4h)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



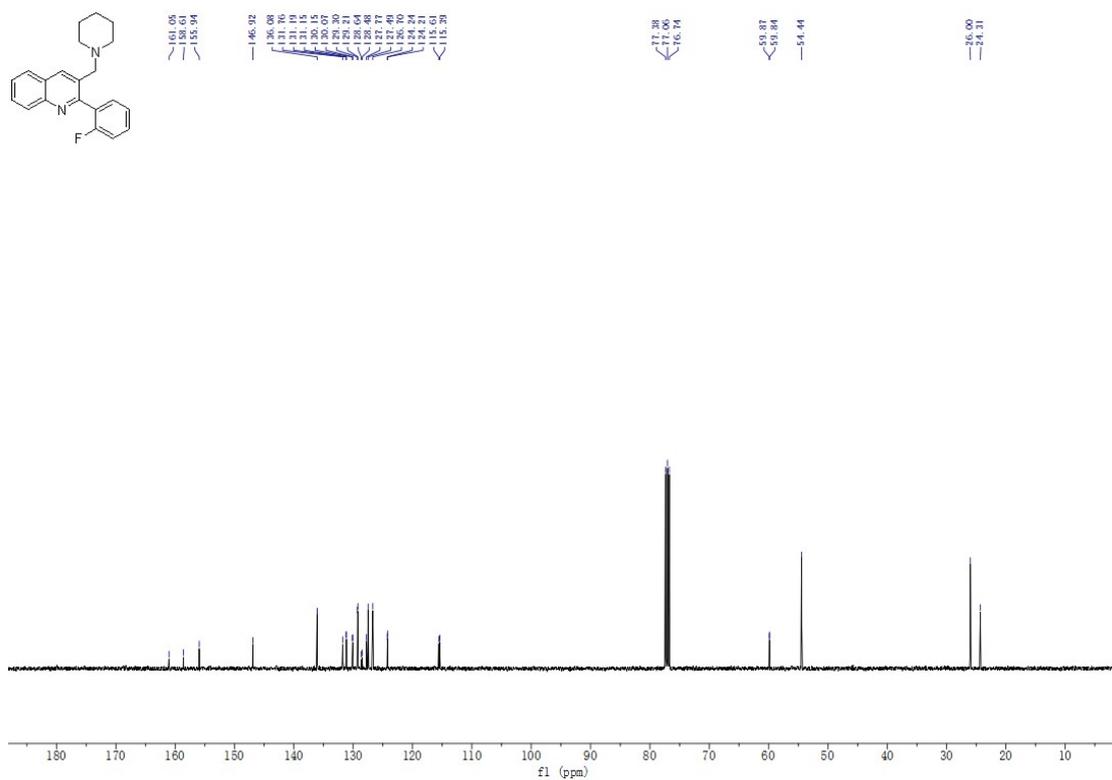
**(4h)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



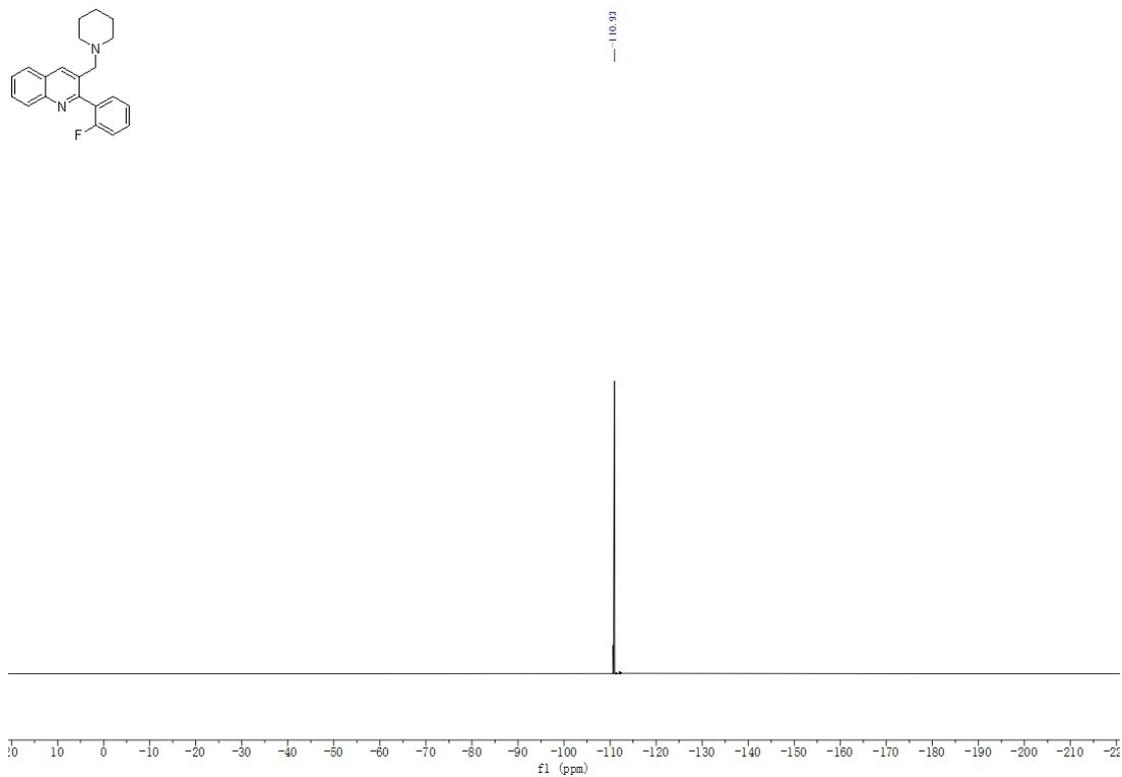
**(4i)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



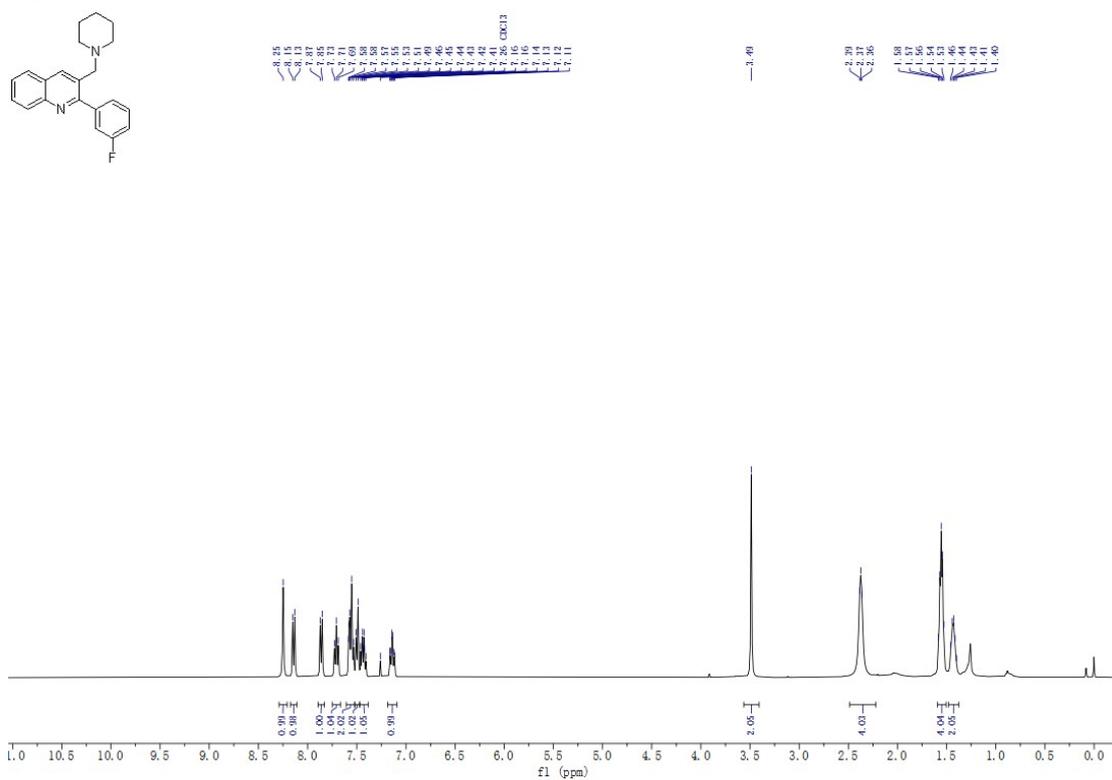
**(4i)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



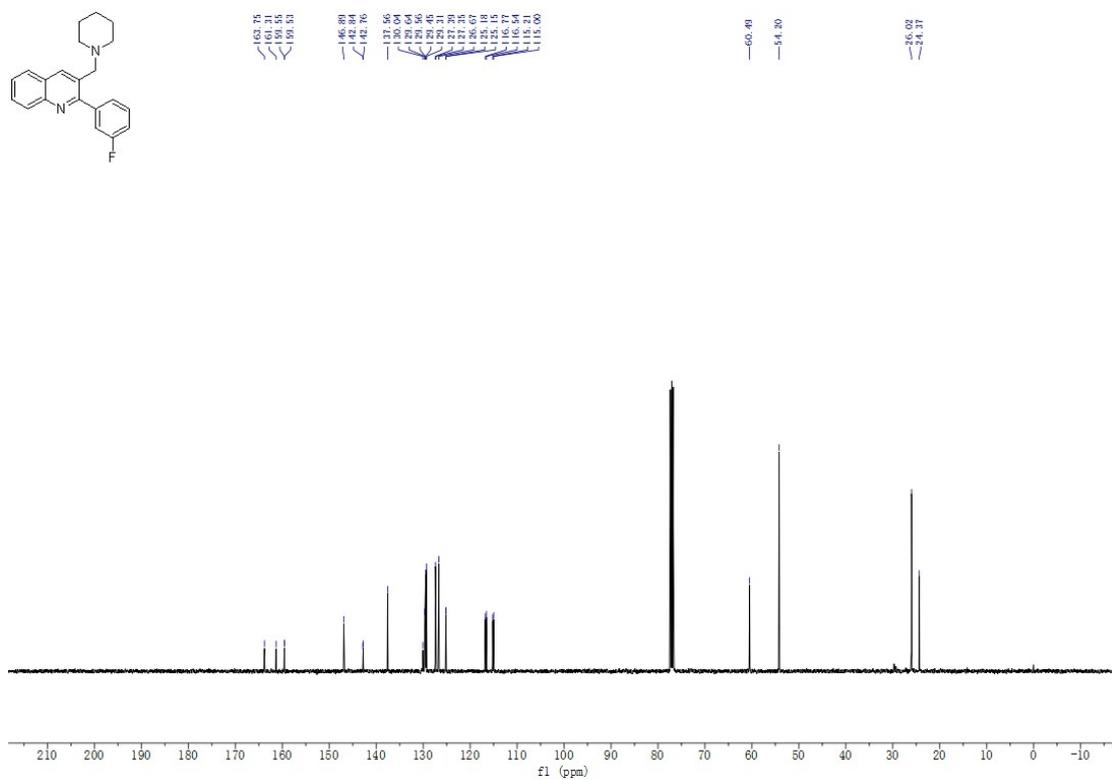
**(4i)**  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )



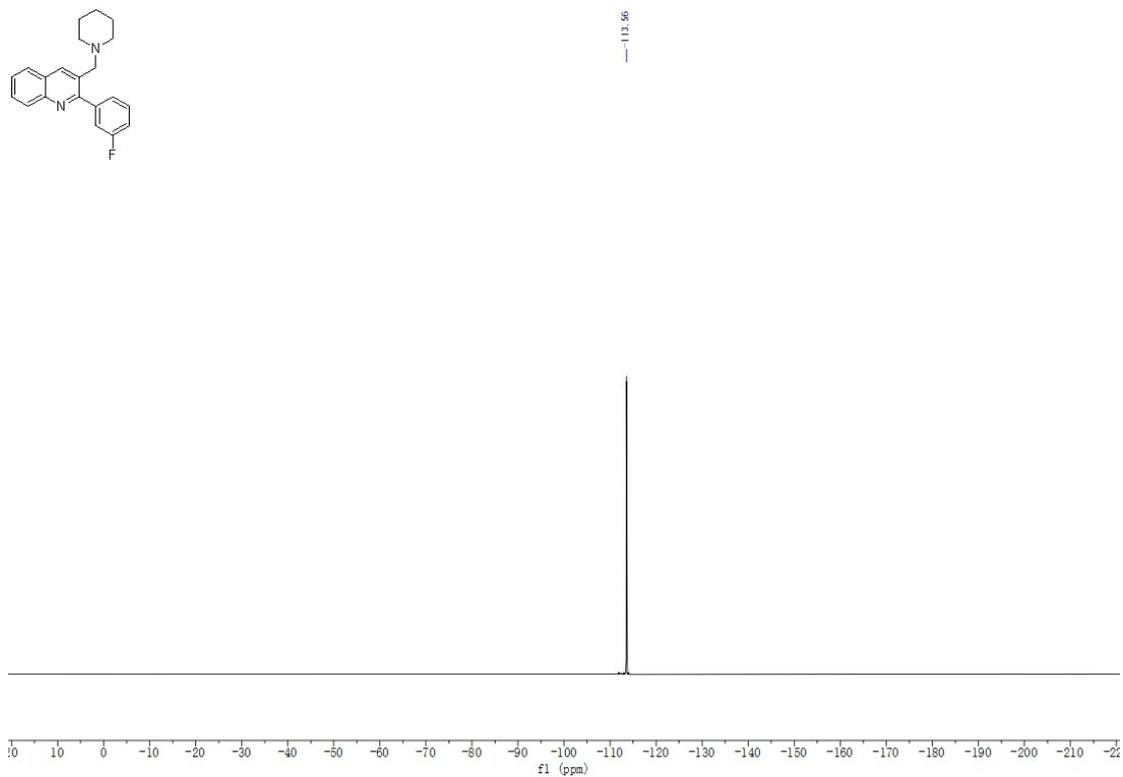
**(4j)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



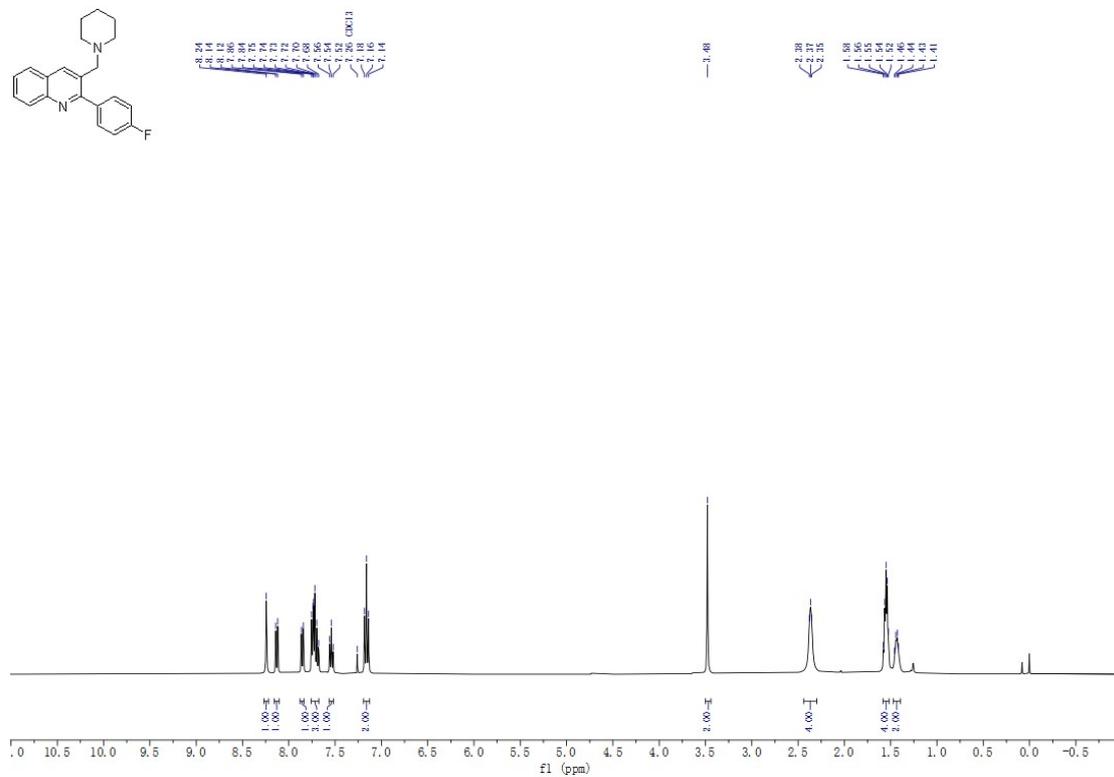
**(4j)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



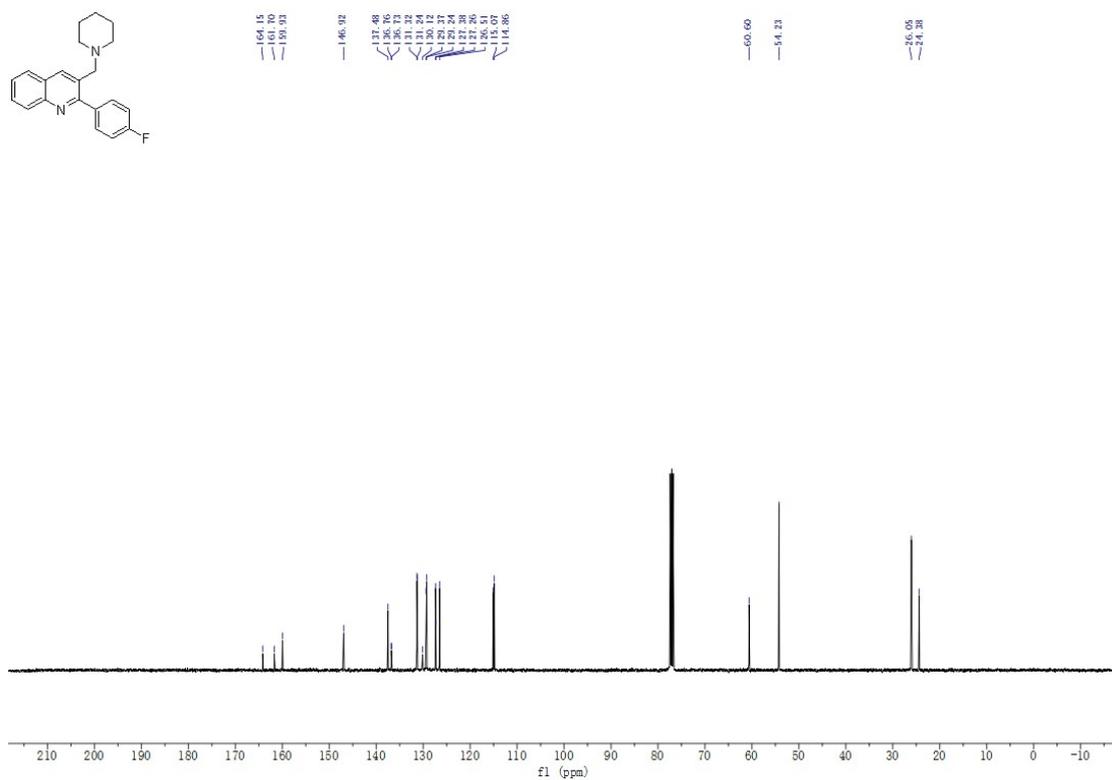
**(4j)**  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )



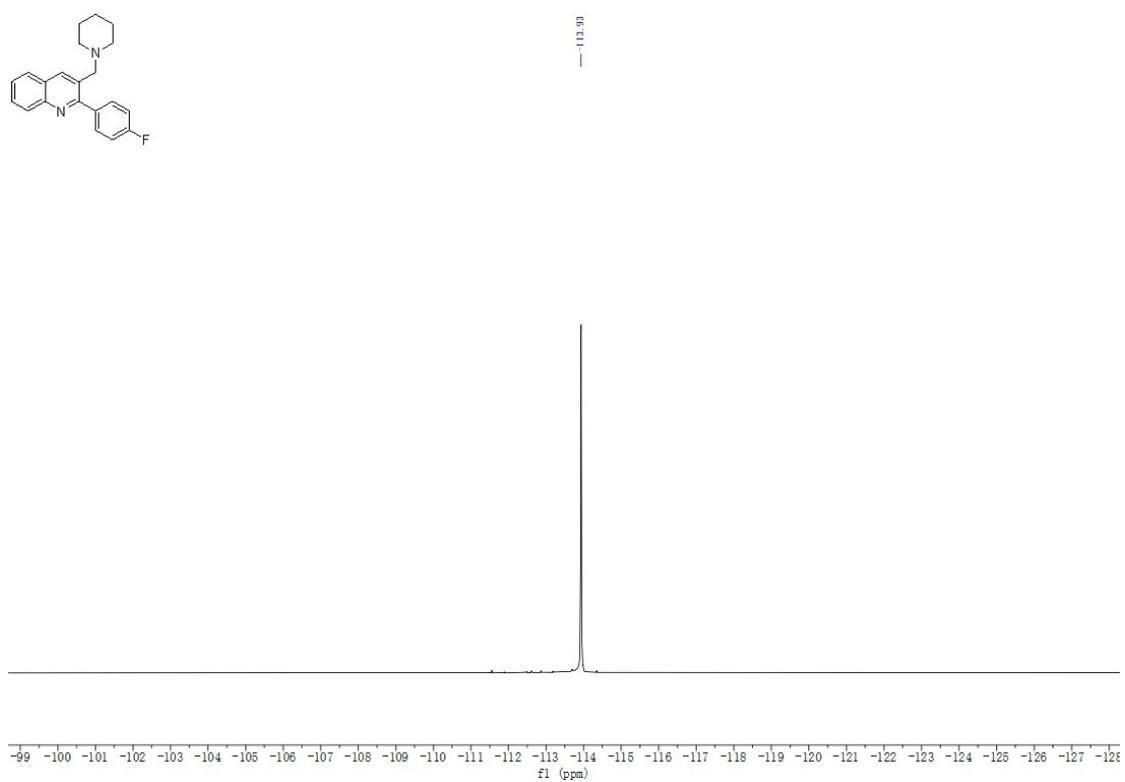
**(4k)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



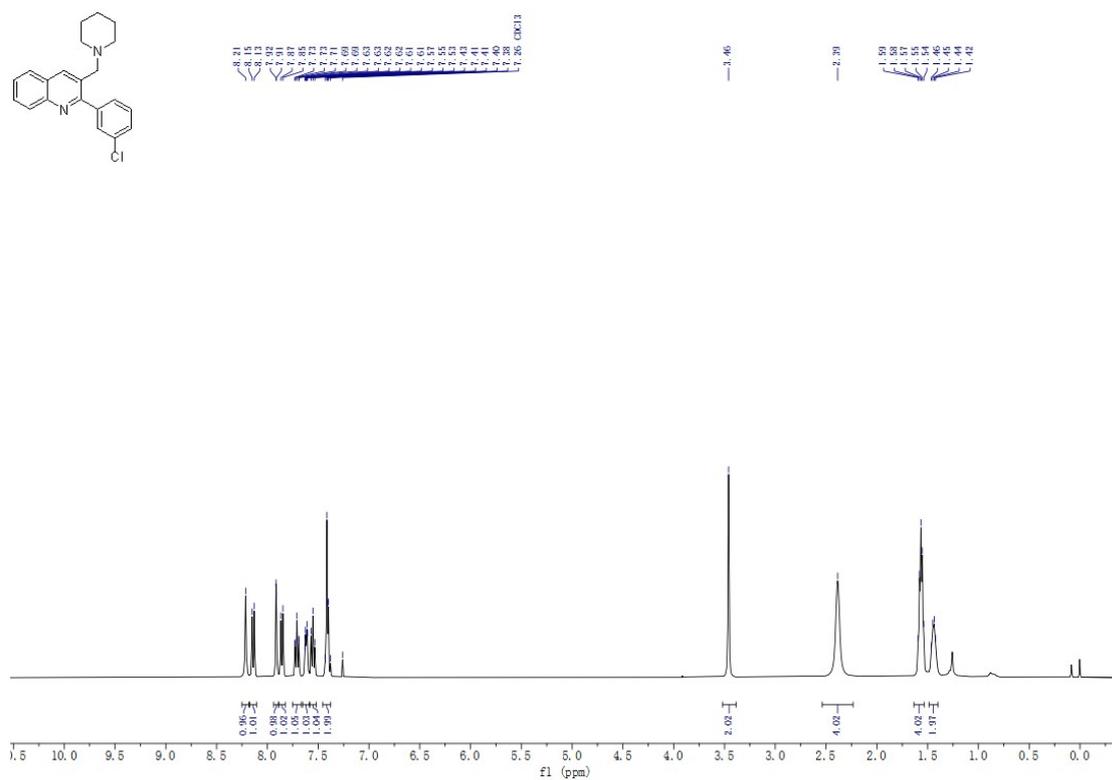
**(4k)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



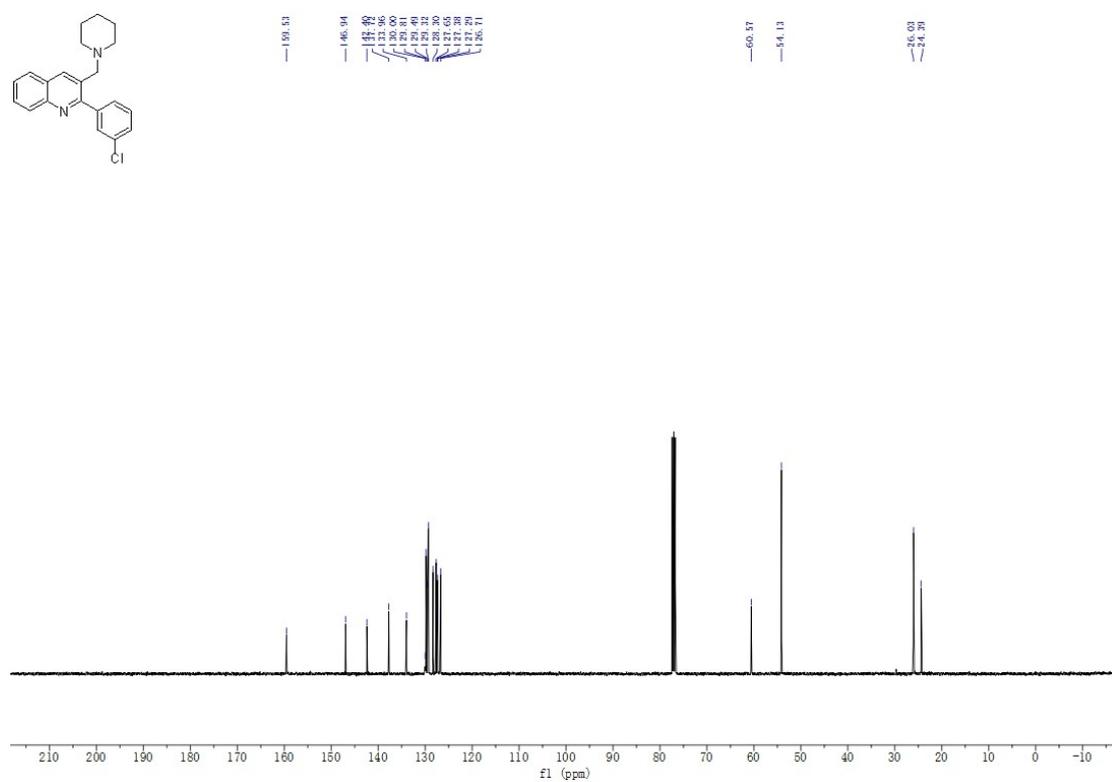
**(4k)**  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )



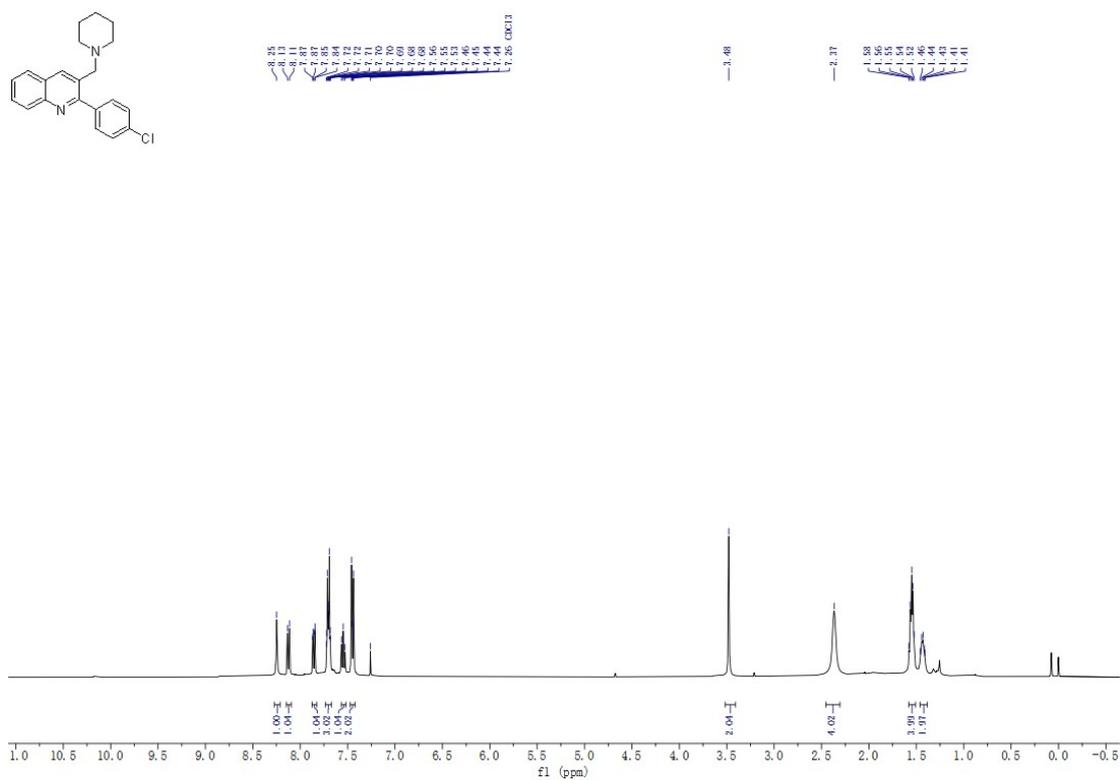
**(41)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



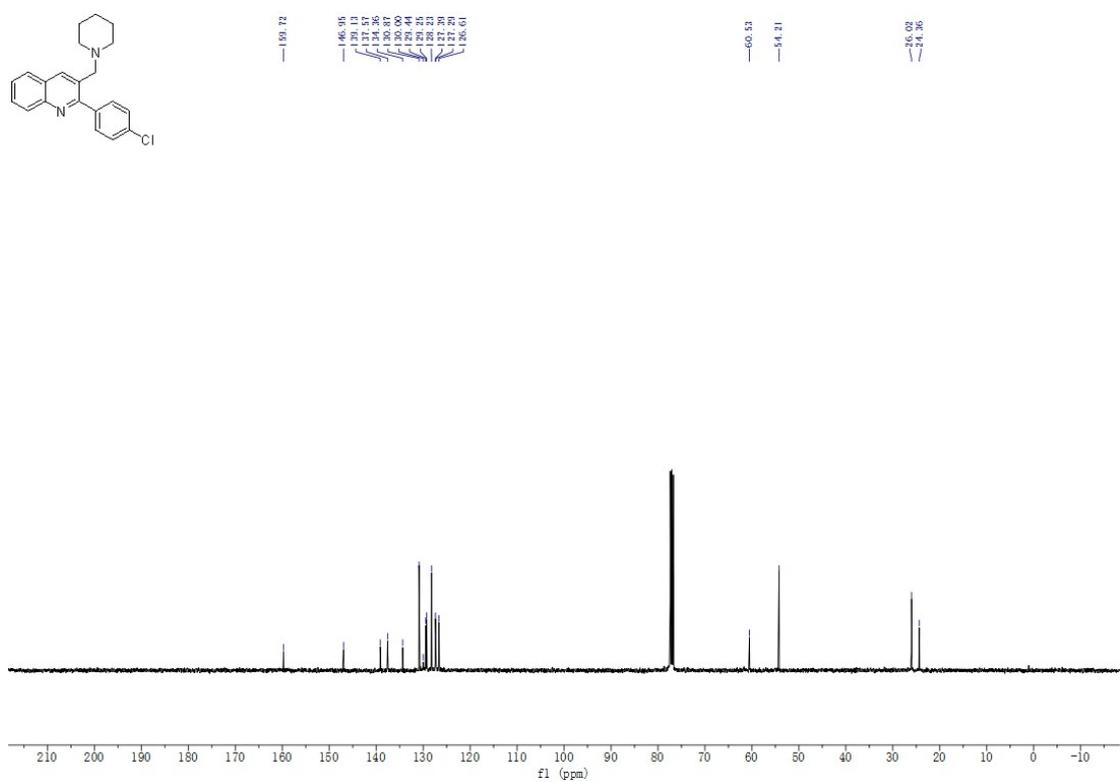
**(41)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



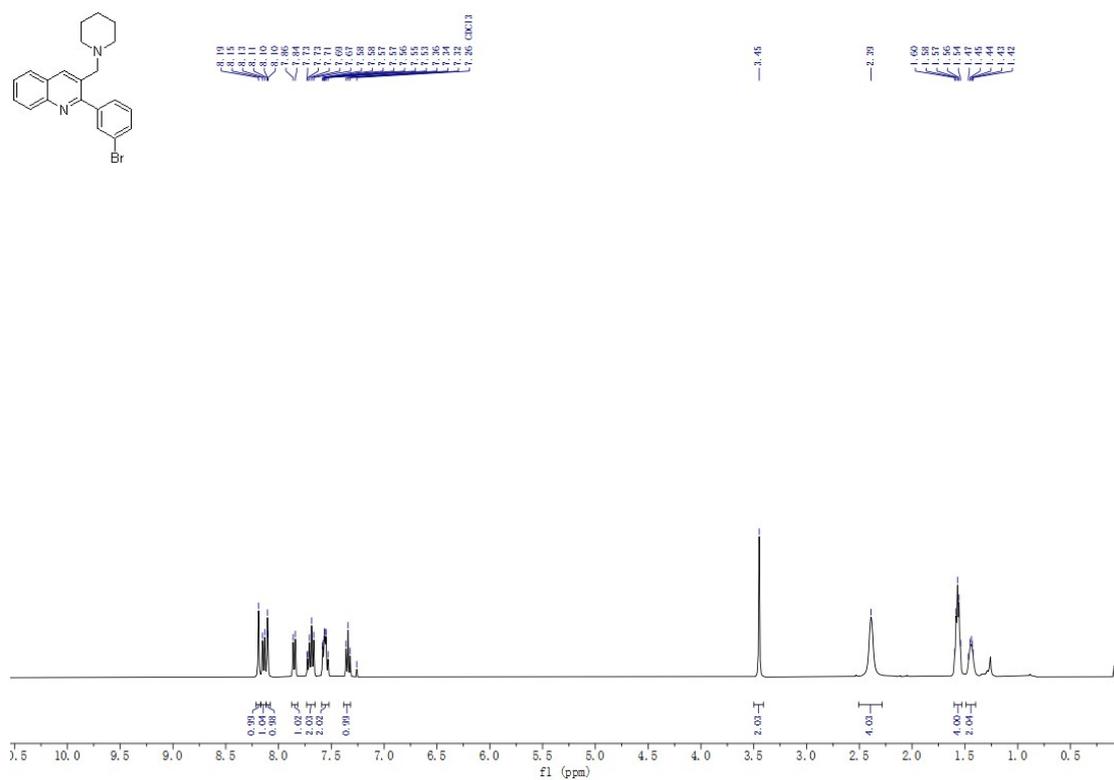
**(4m)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



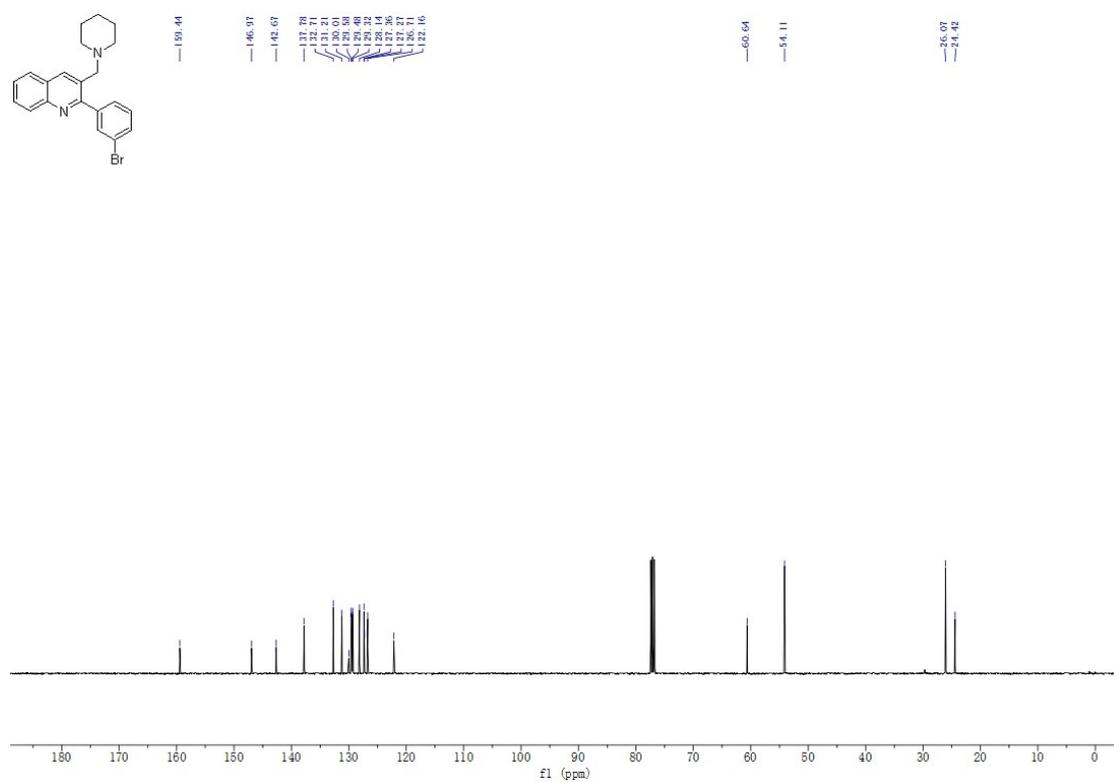
**(4m)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



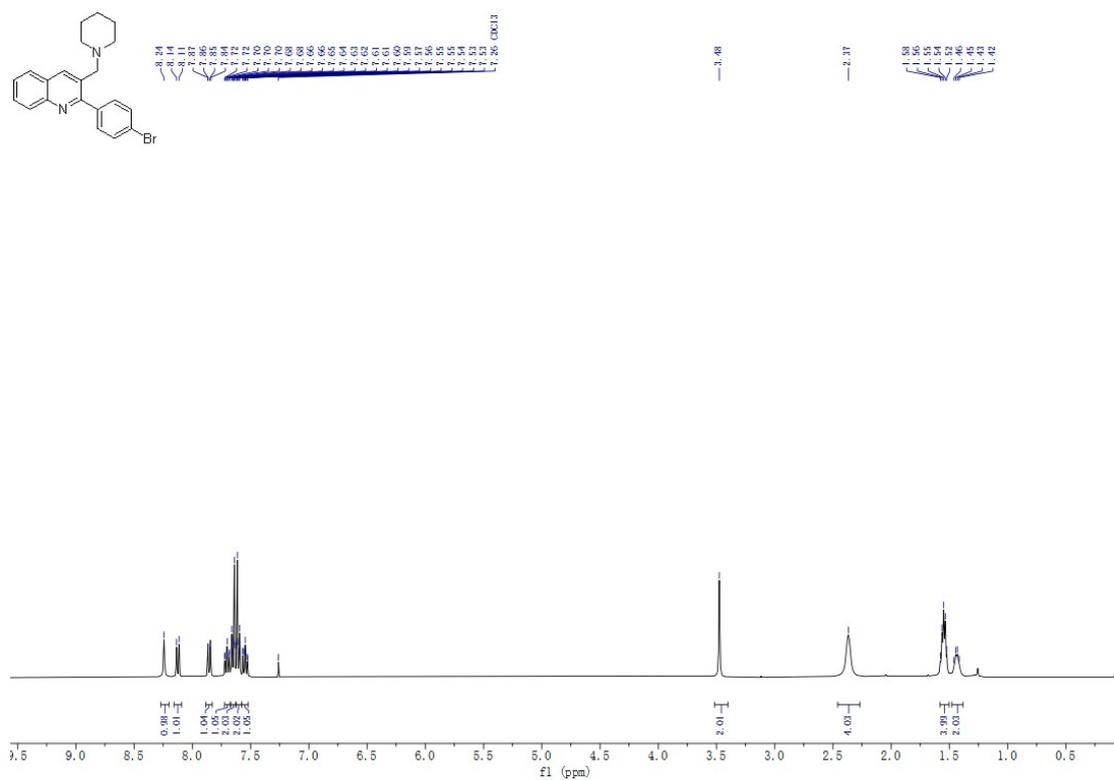
(4n) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



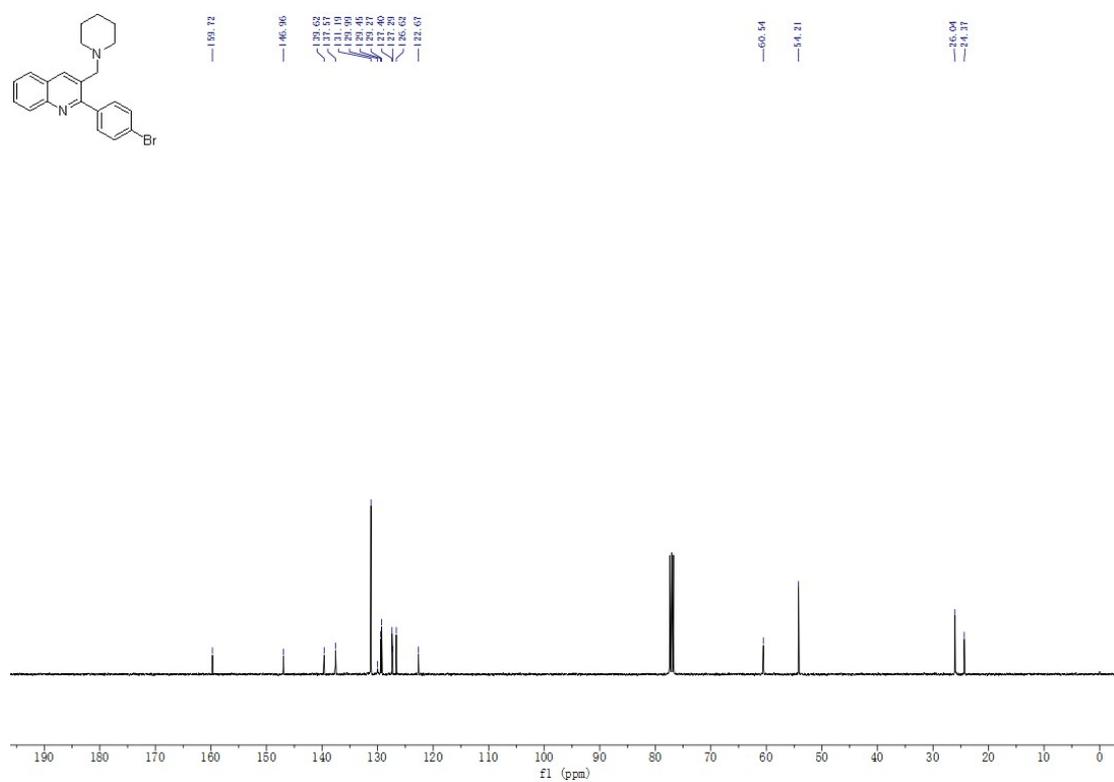
(4n) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



**(4o)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

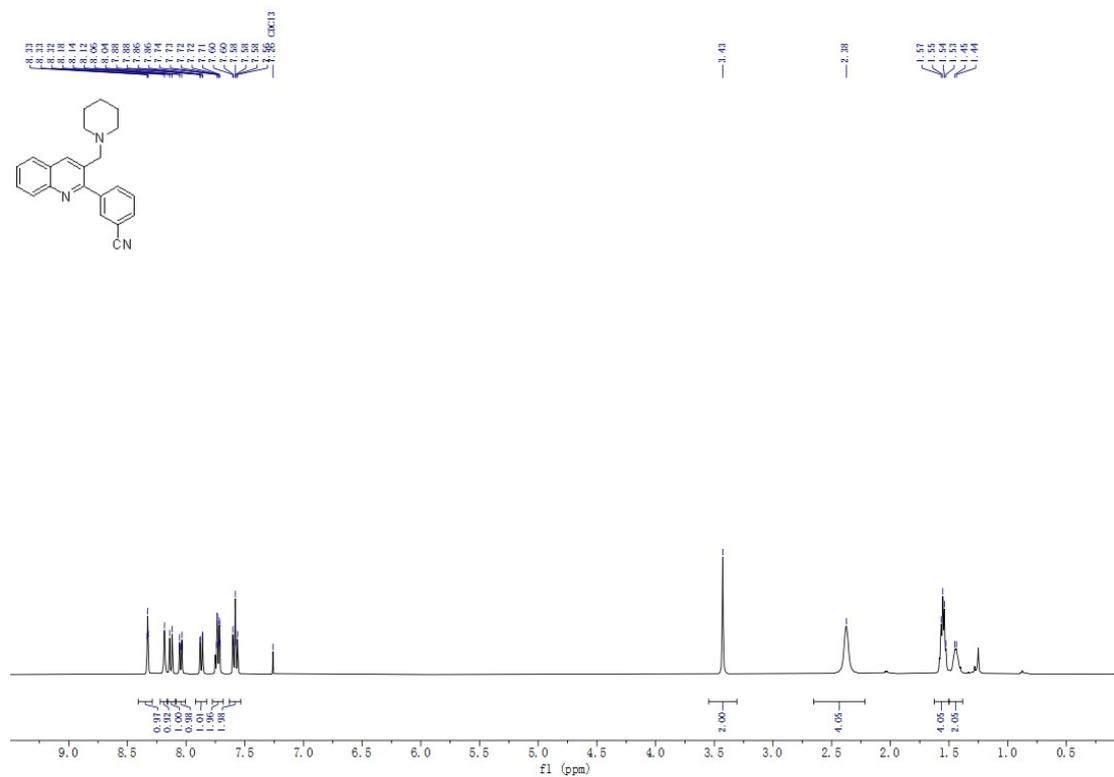


**(4o)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )

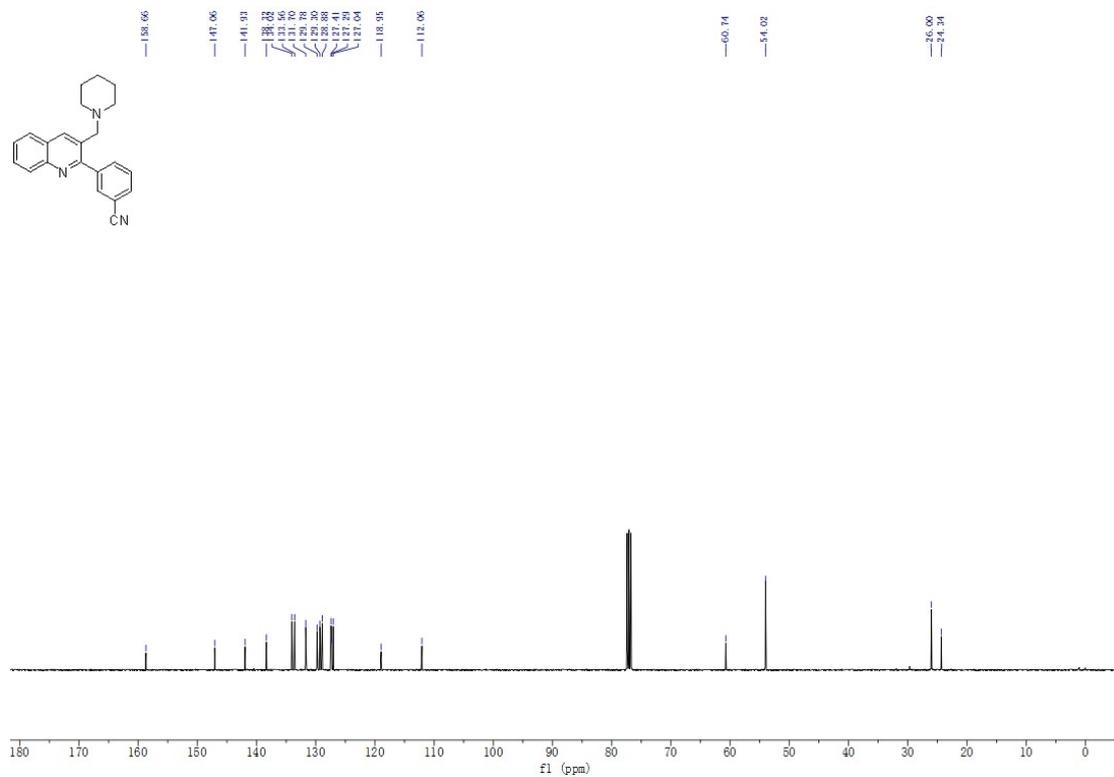




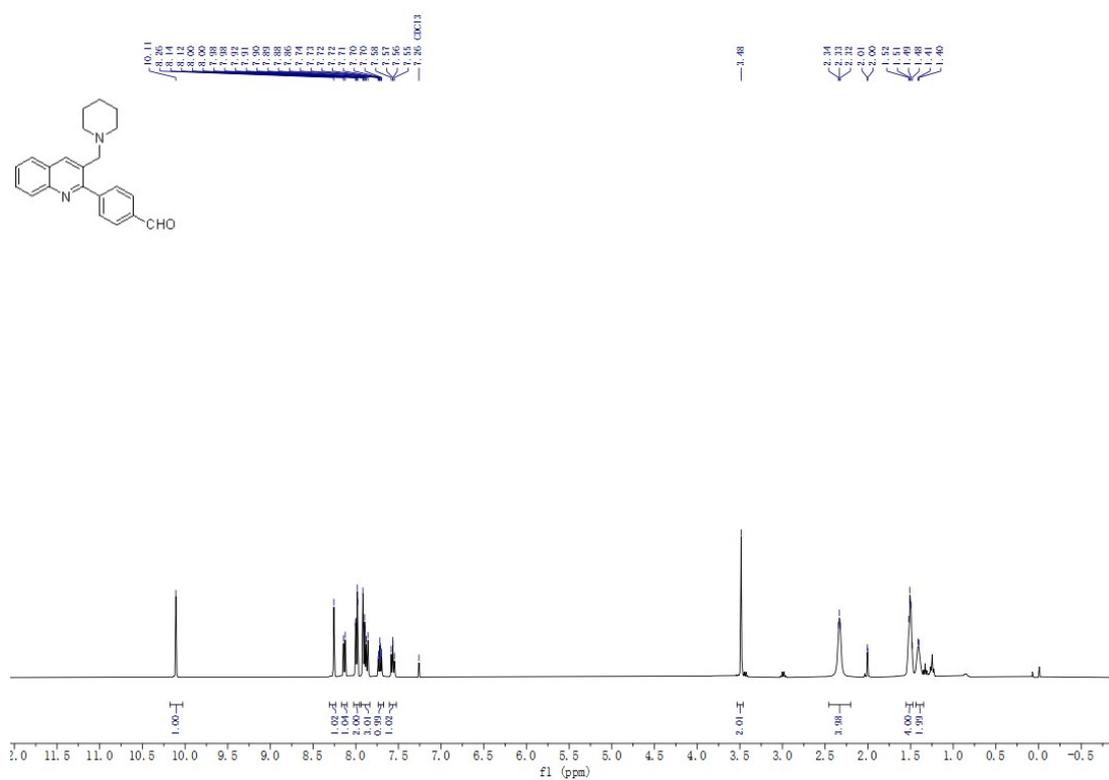
(4q) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



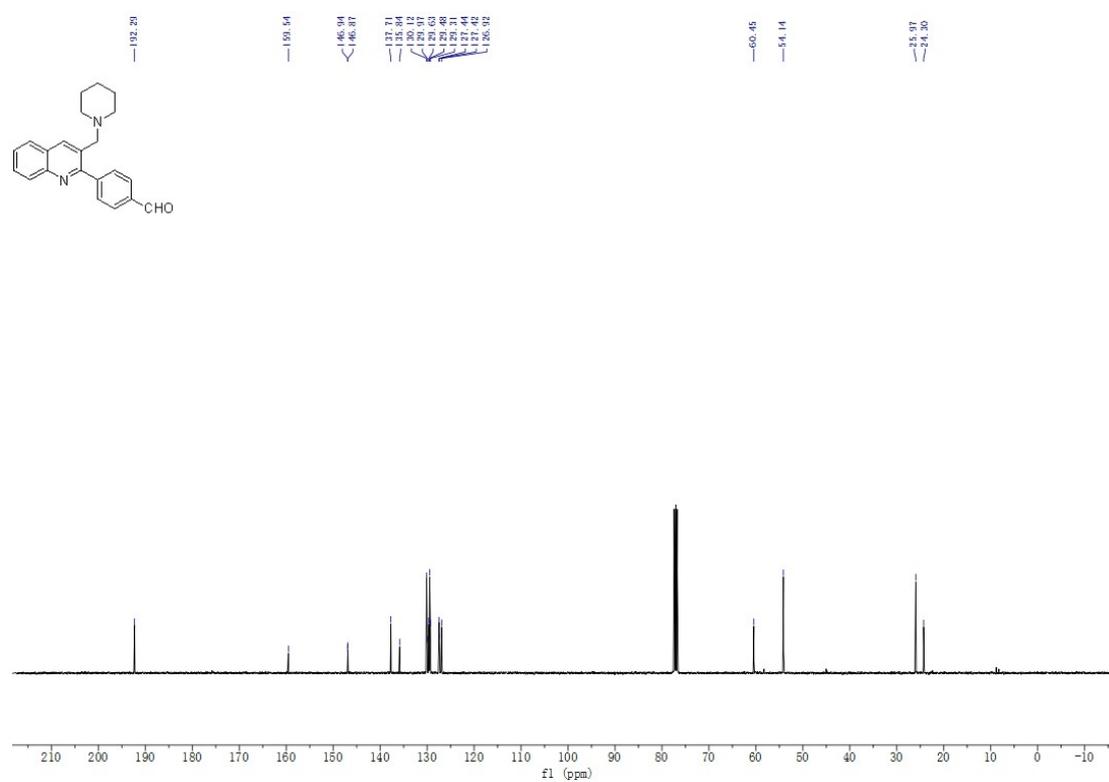
(4q) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



(4r) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

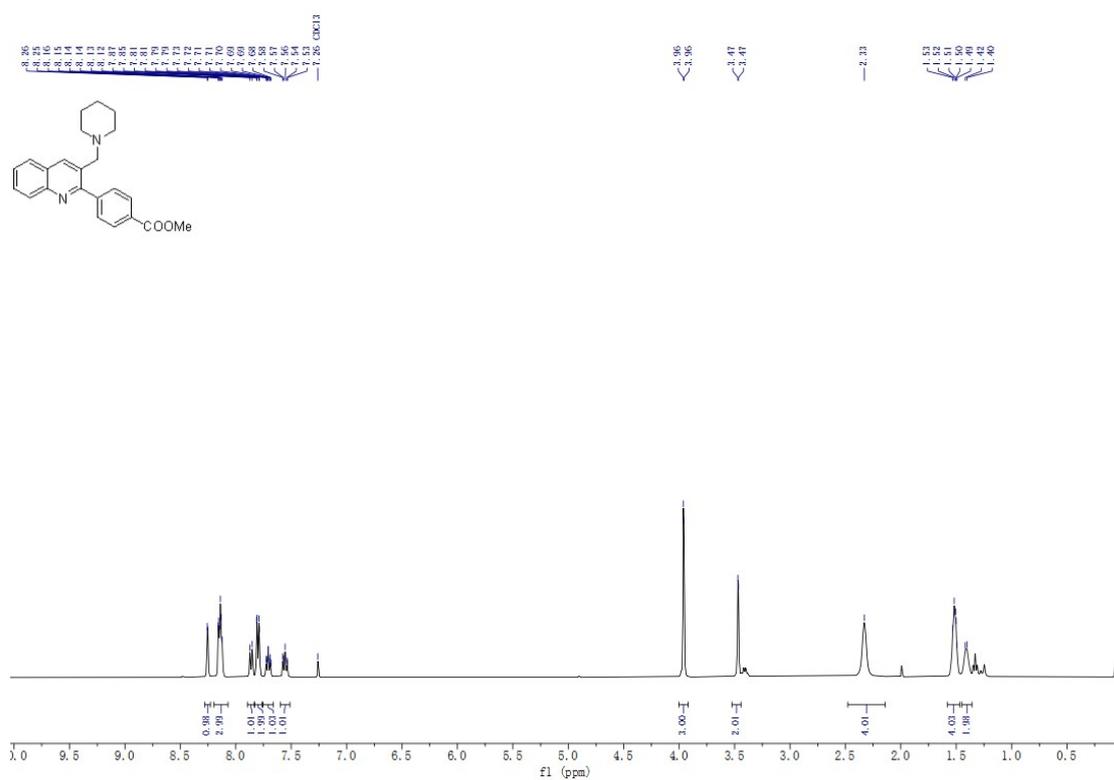


(4r) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)

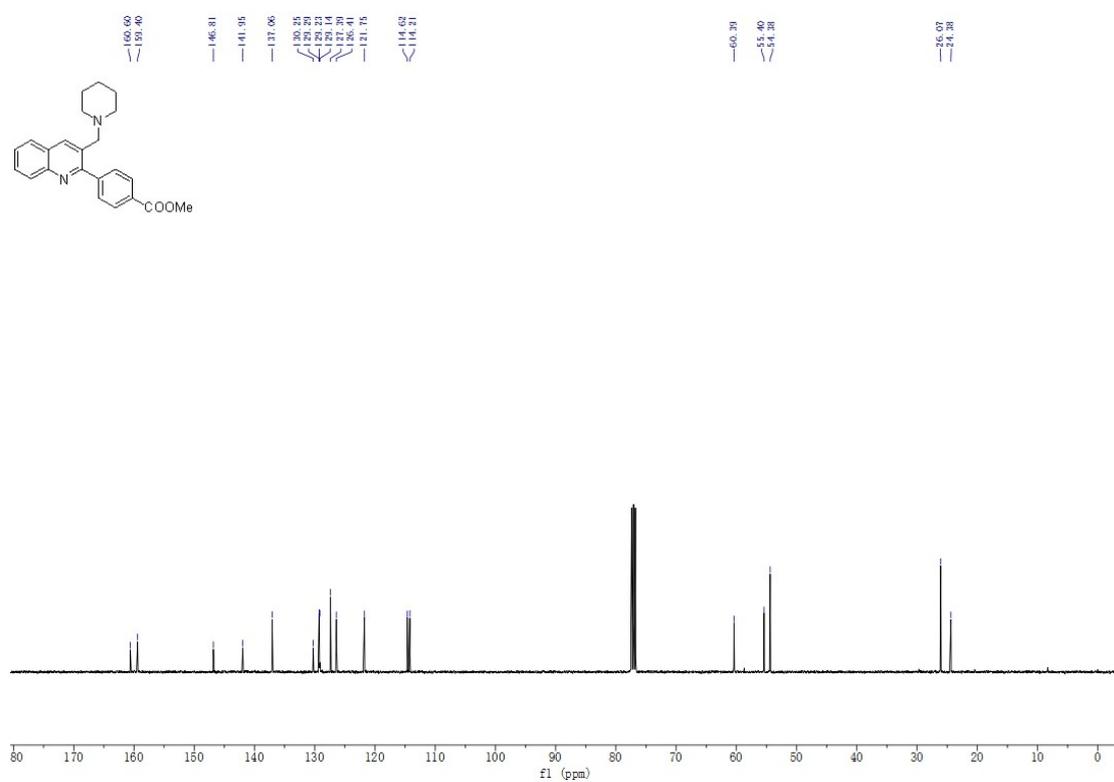




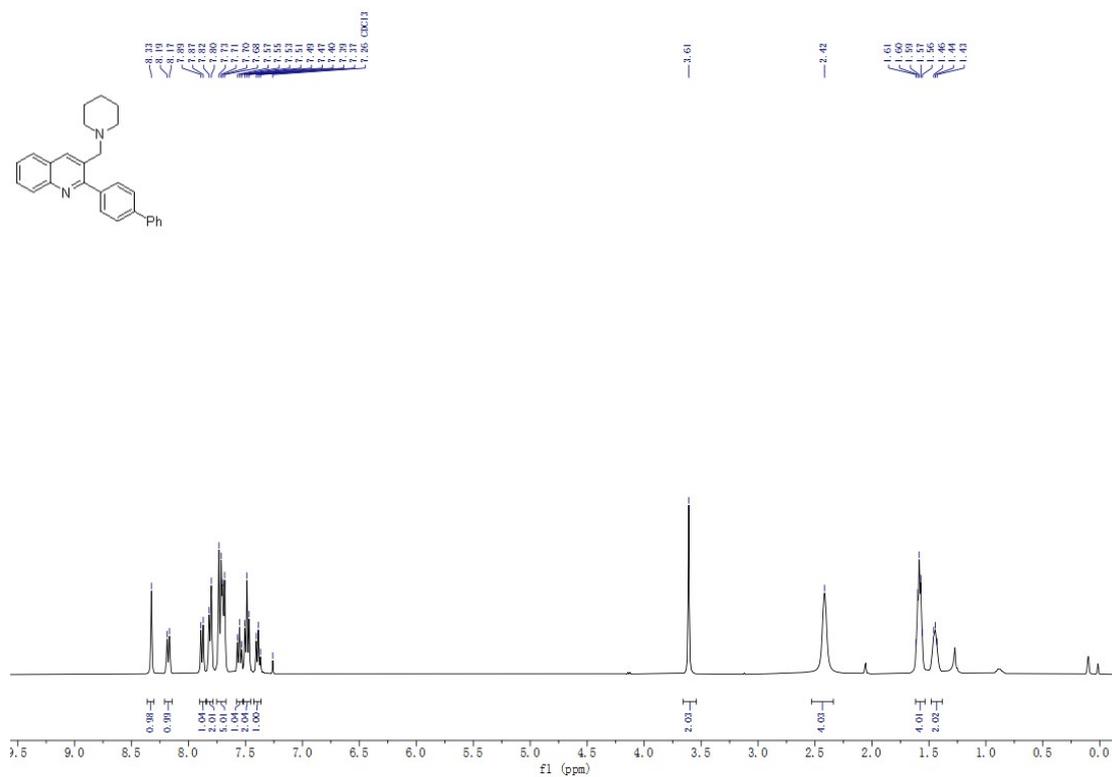
(4t) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



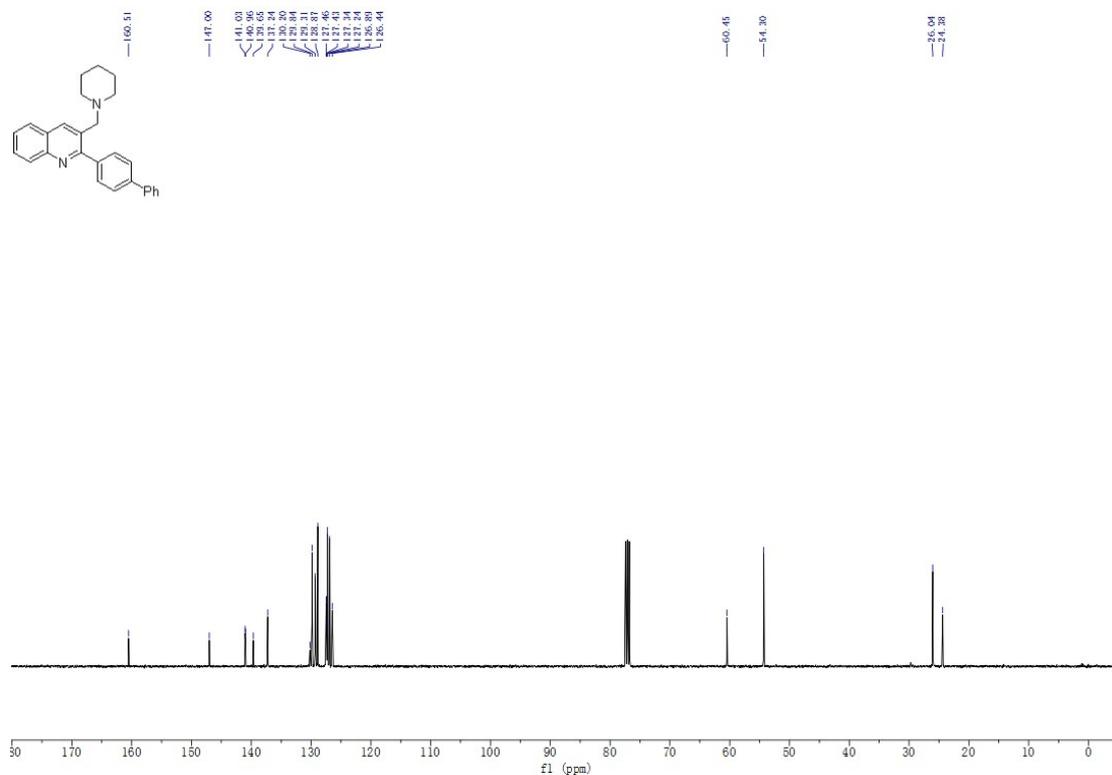
(4t) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



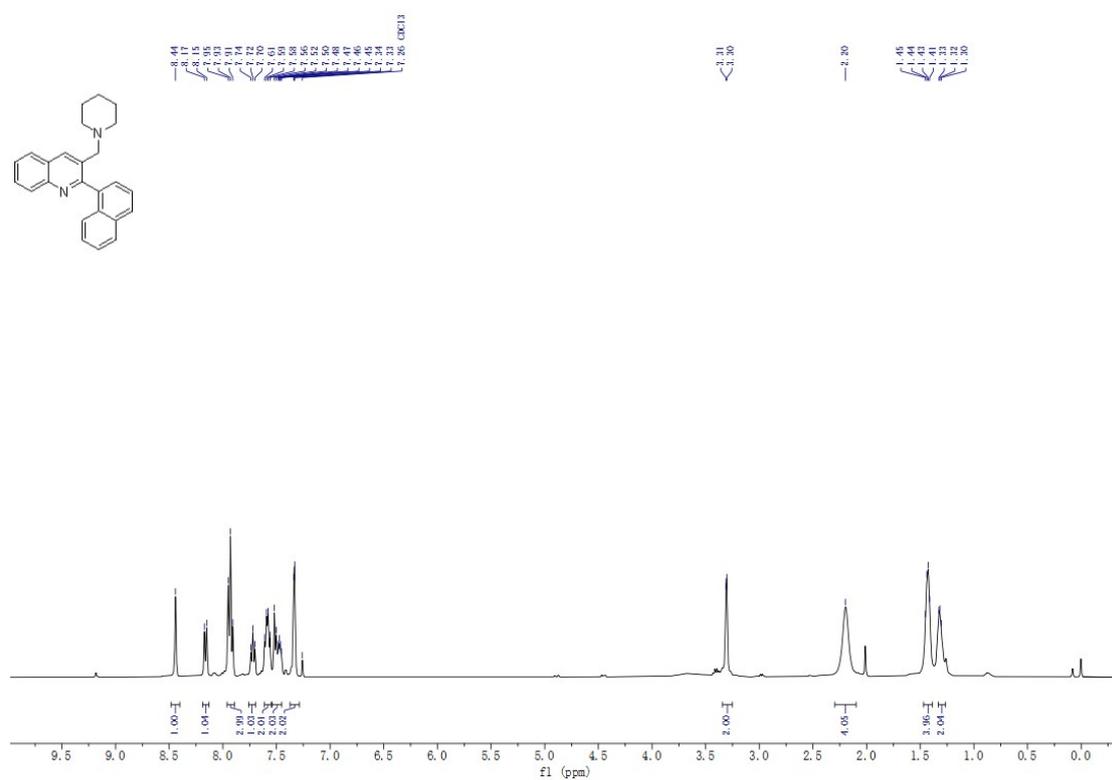
(4u)  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



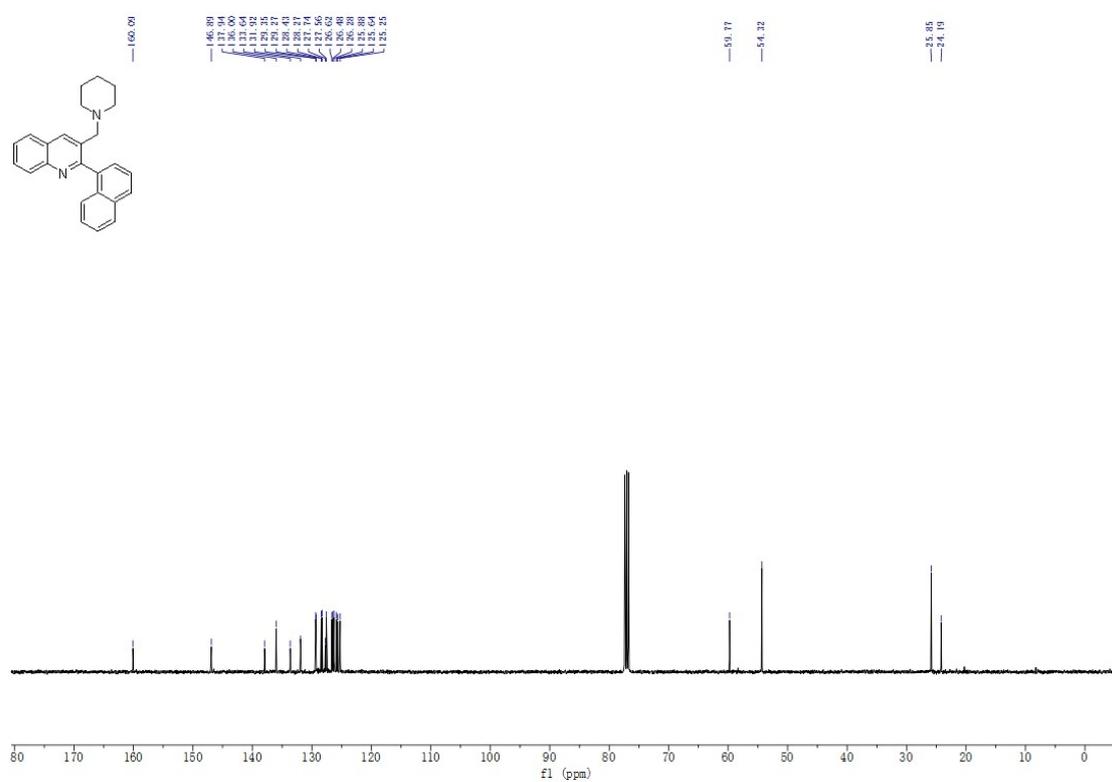
(4u)  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



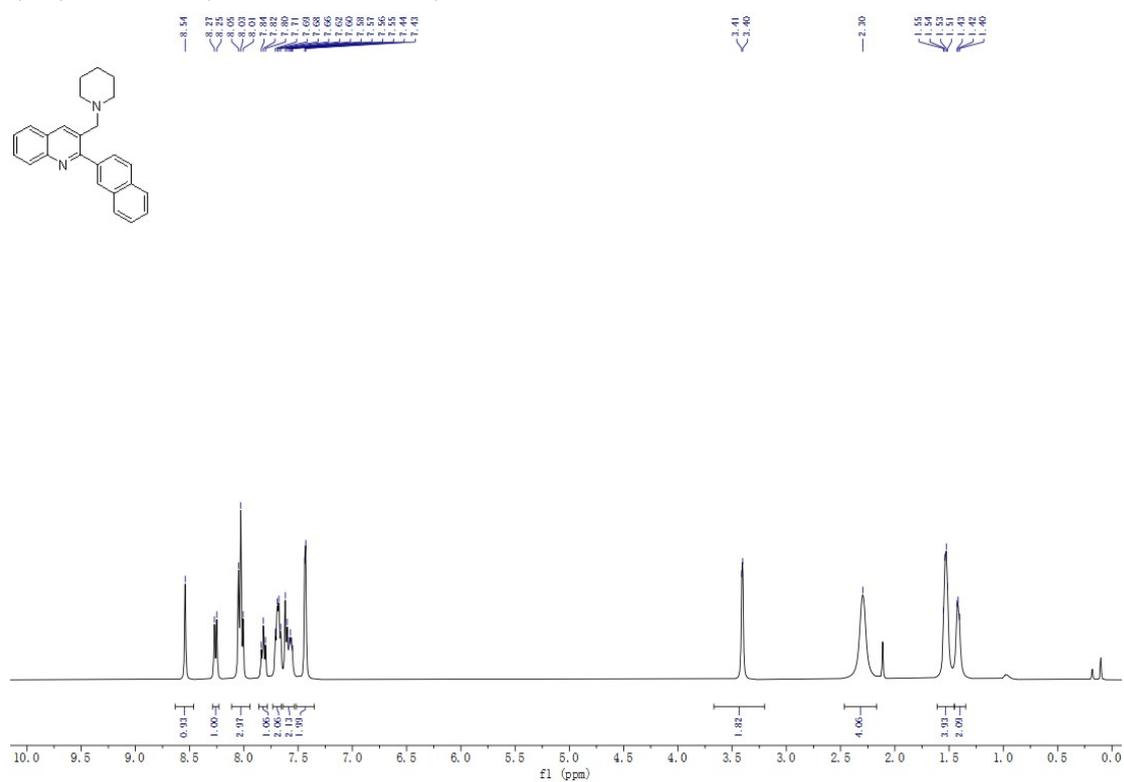
(4v) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



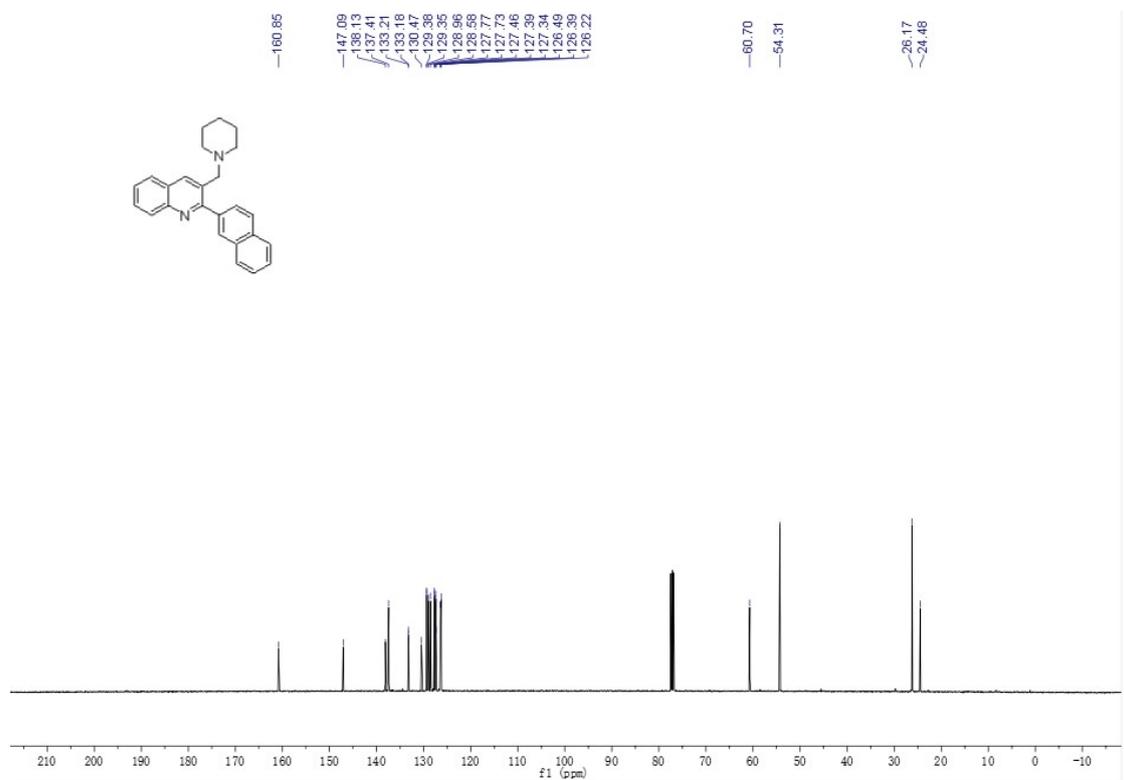
(4v) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



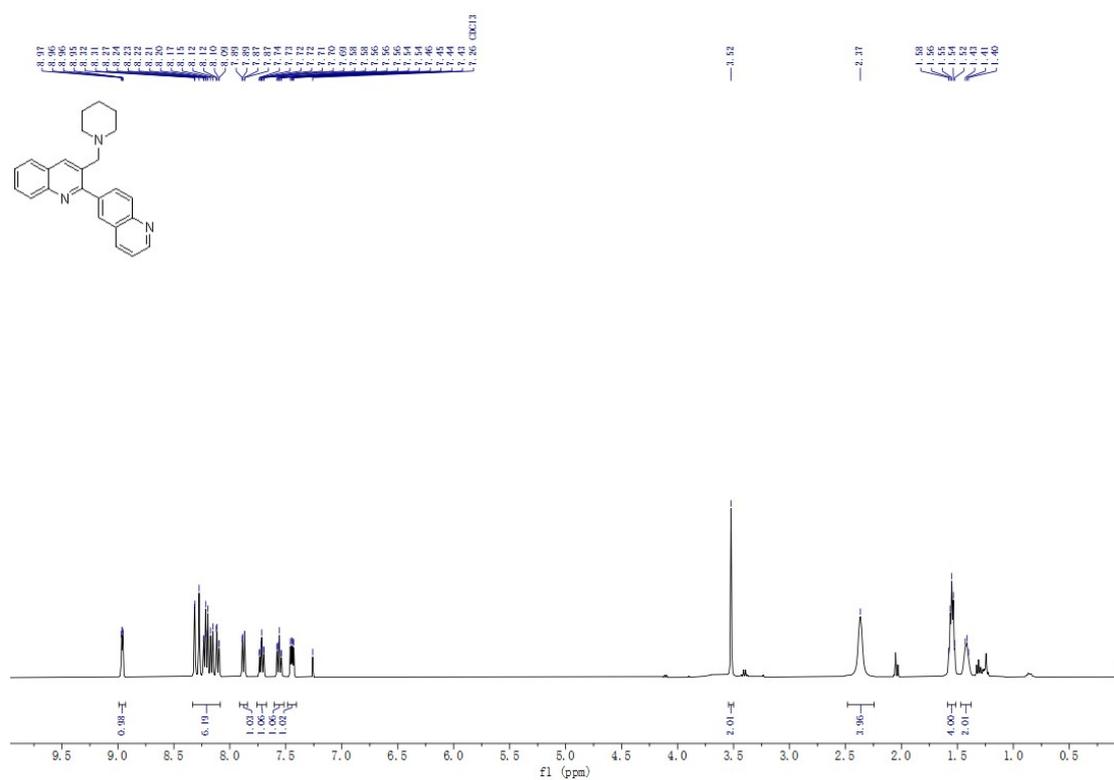
**(4w)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



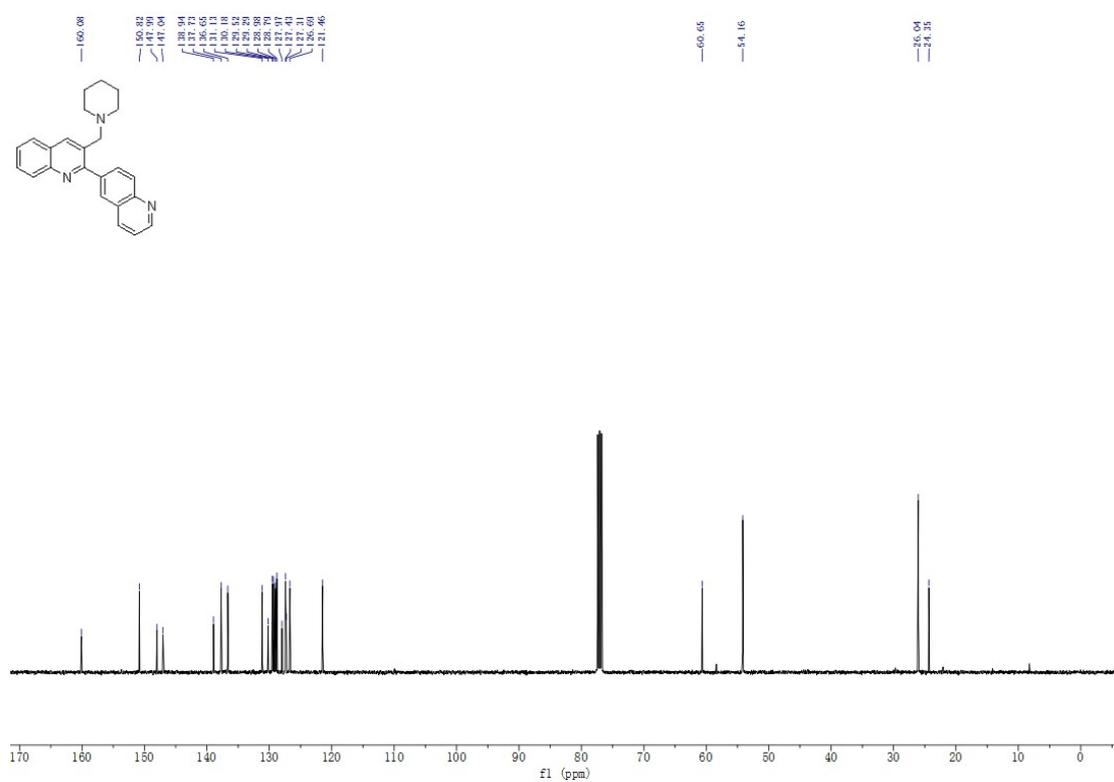
**(4w)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



(4x) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

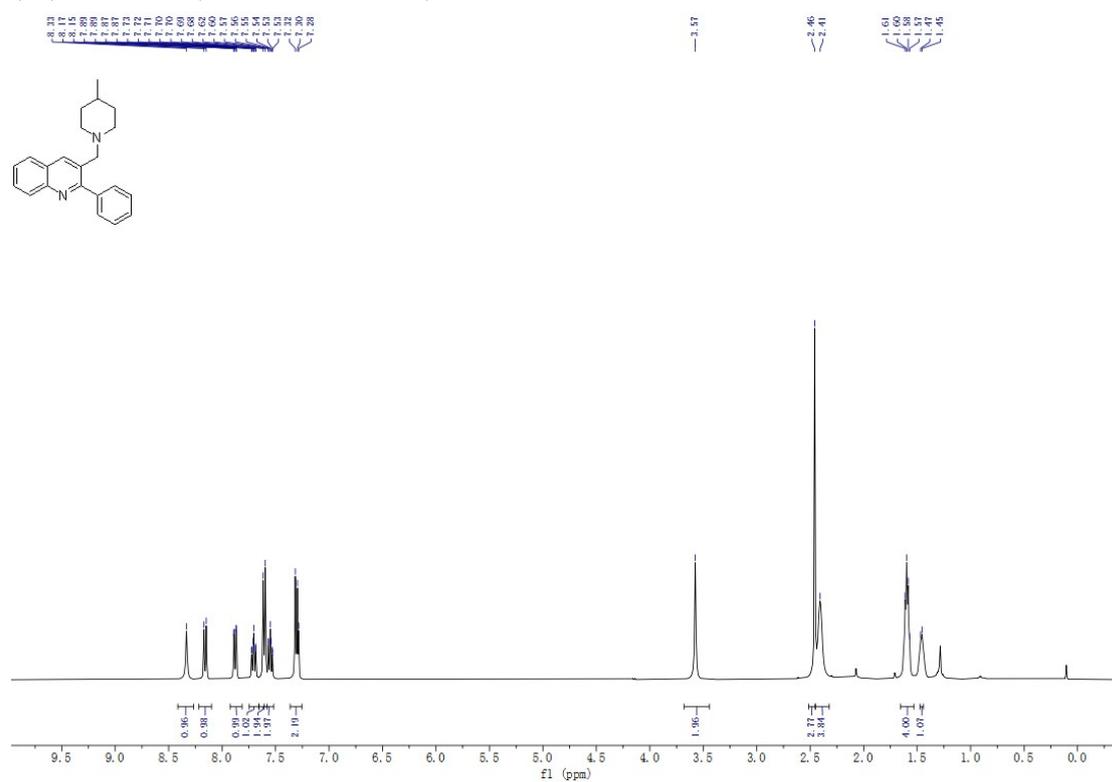


(4x) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)

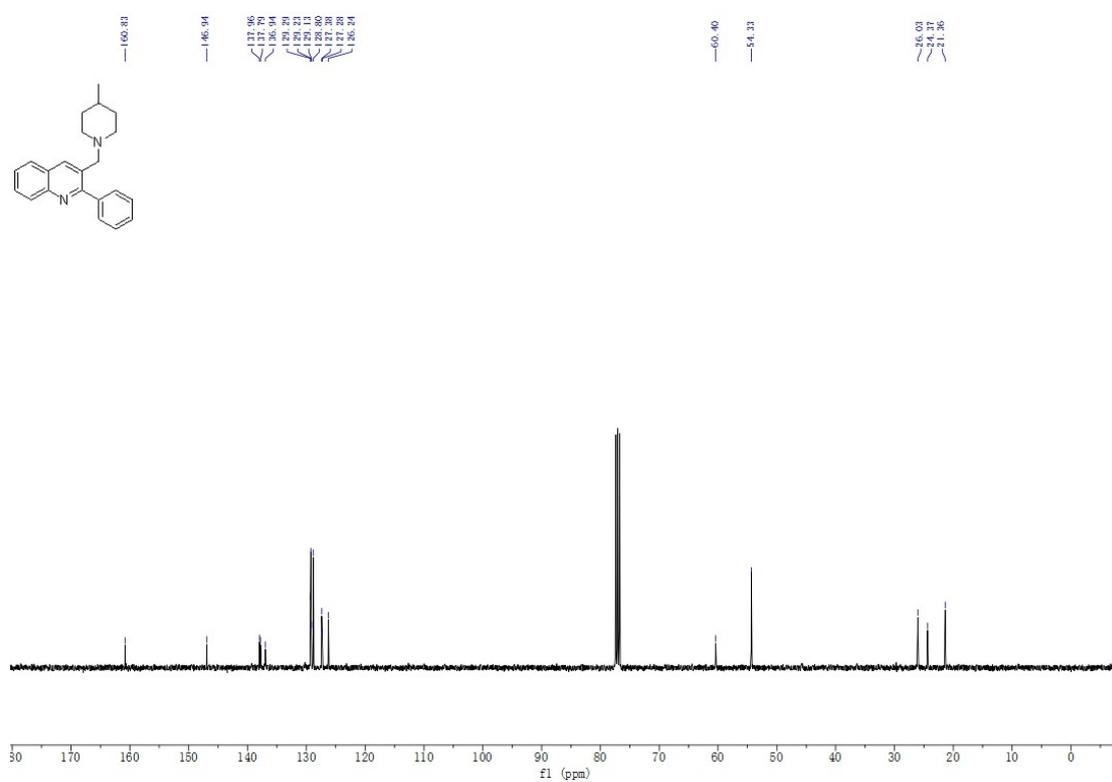




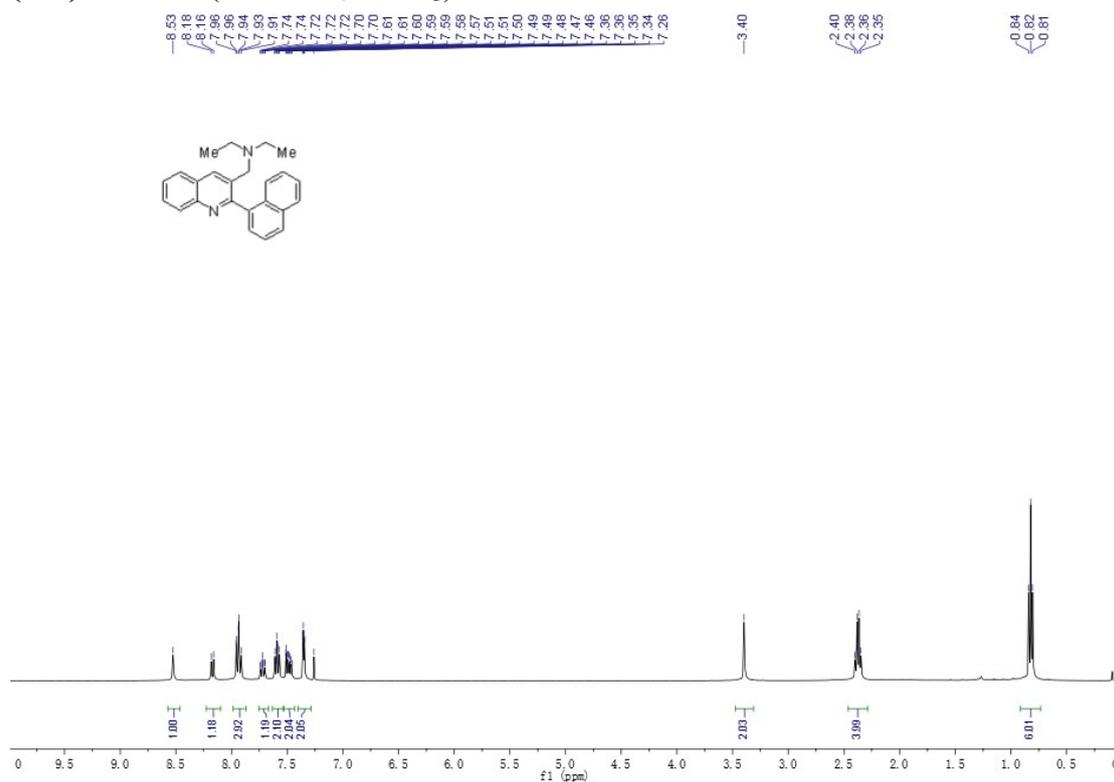
**(4z)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



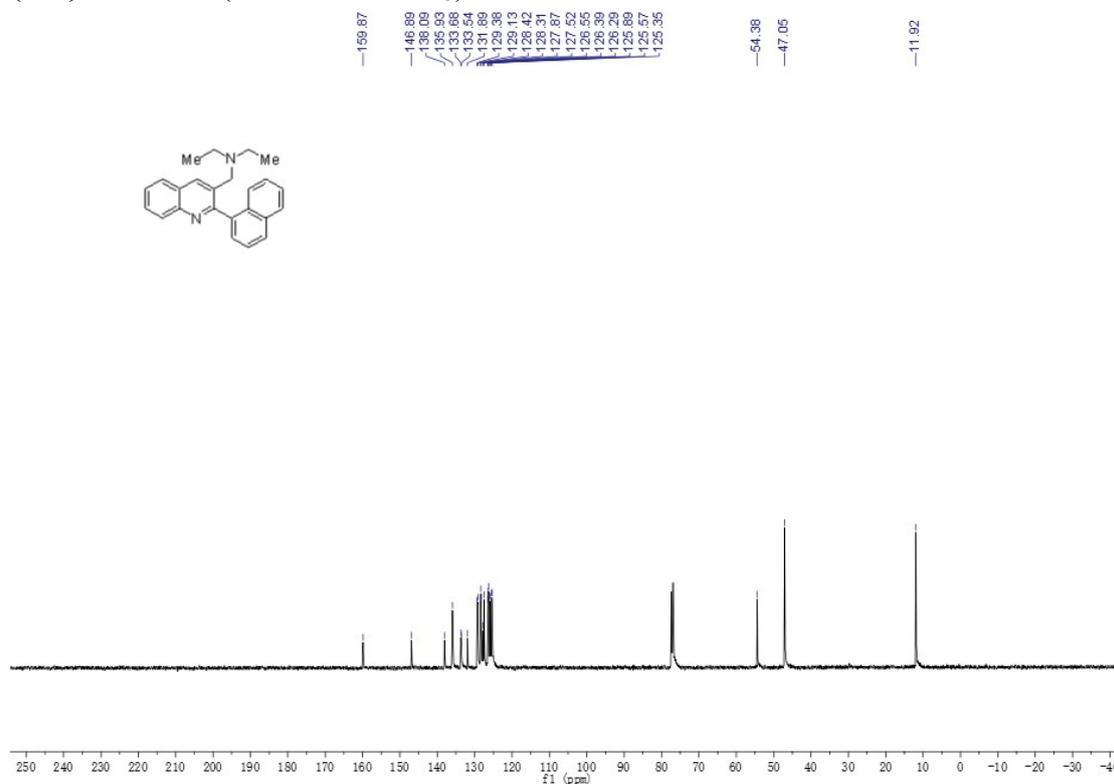
**(4z)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



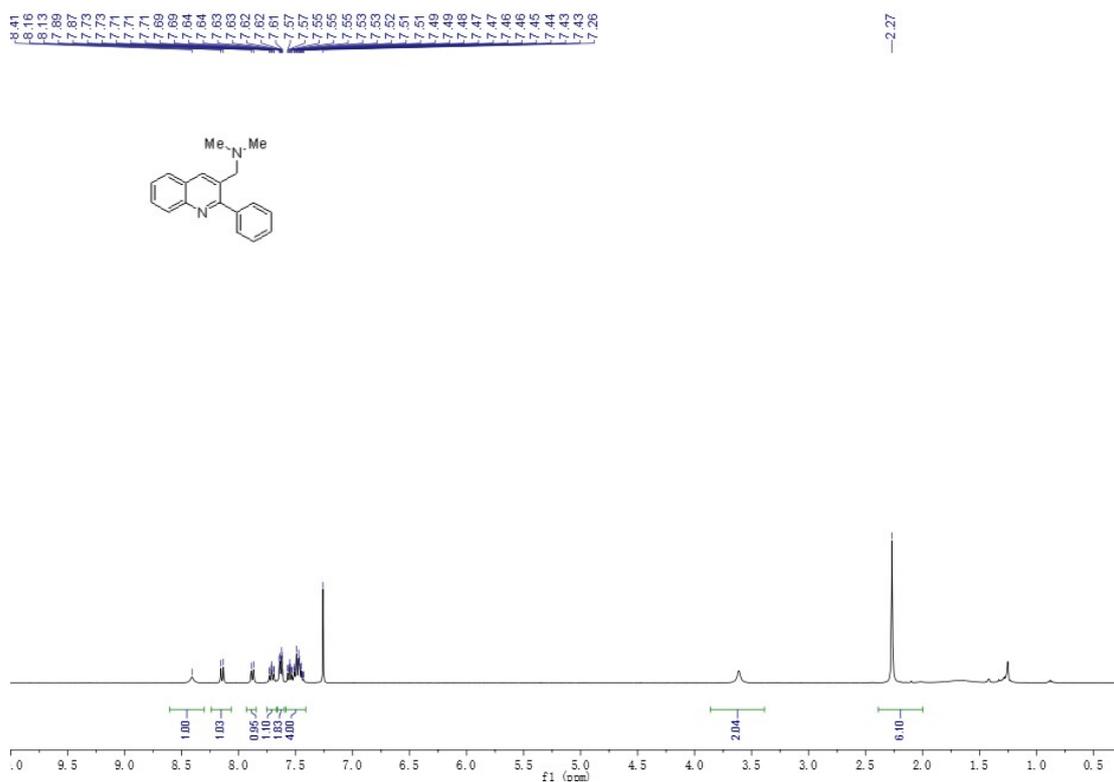
(4aa) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



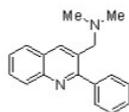
(4aa) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



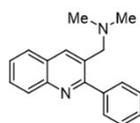
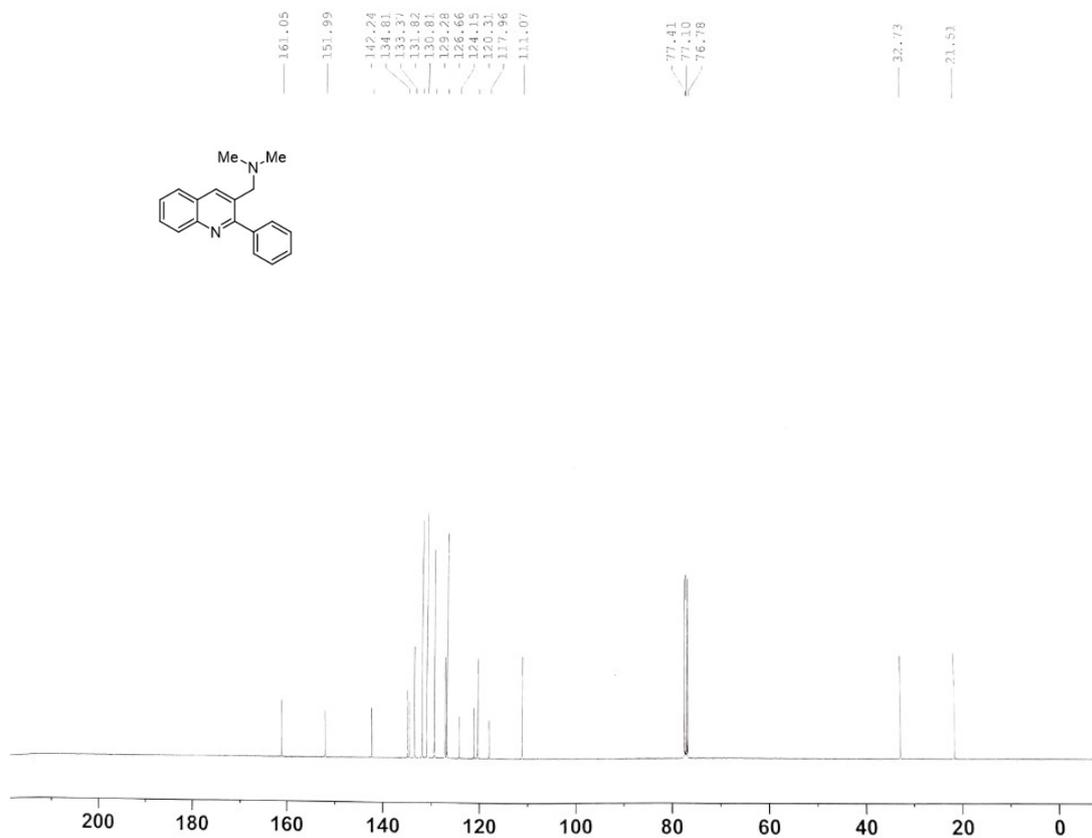
**(4ab)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



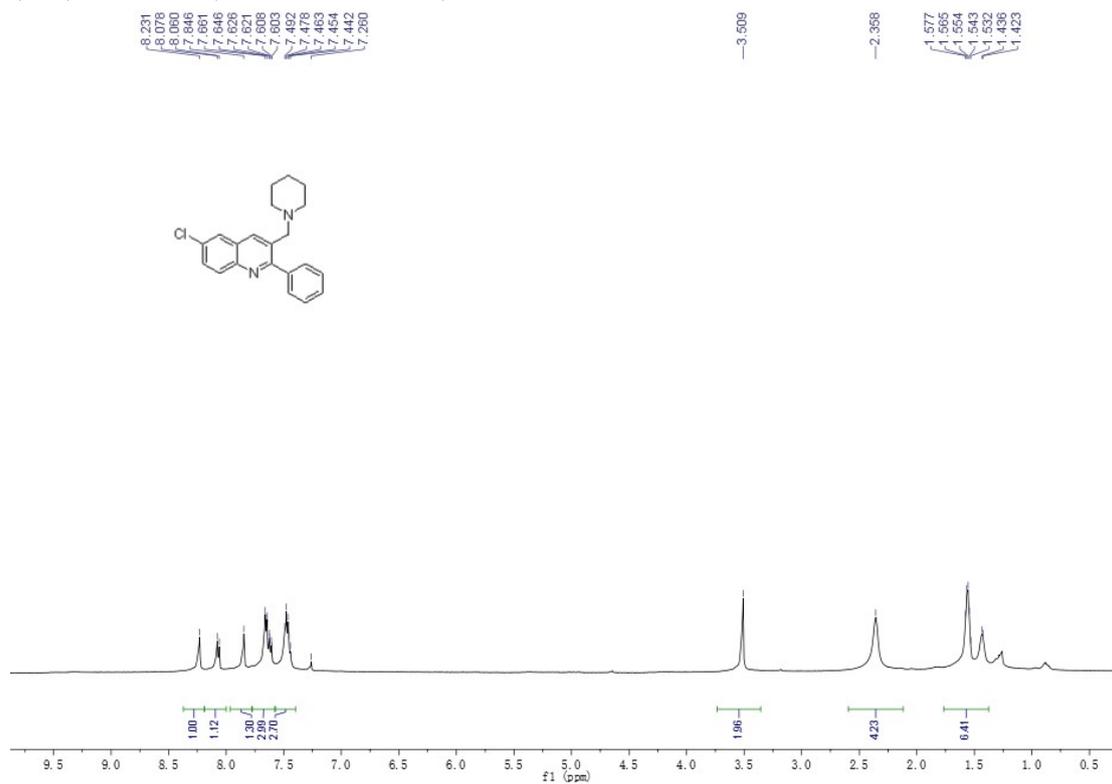
-2.27



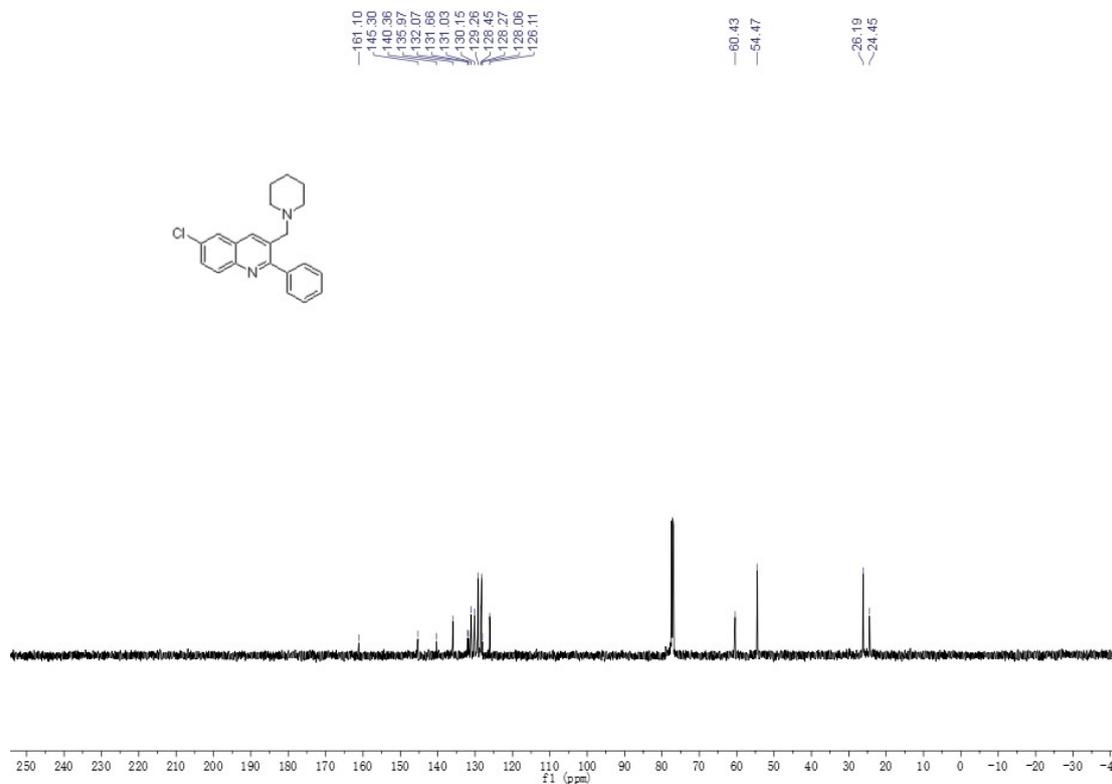
**(4ab)**  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



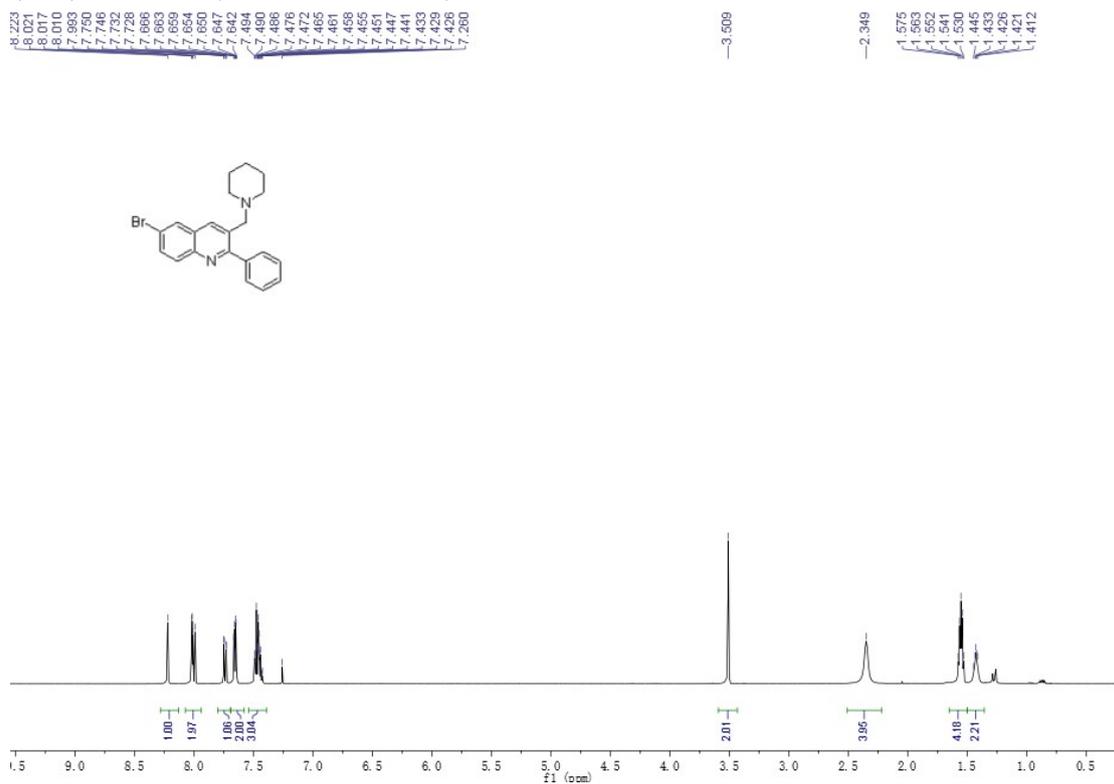
(4ac)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



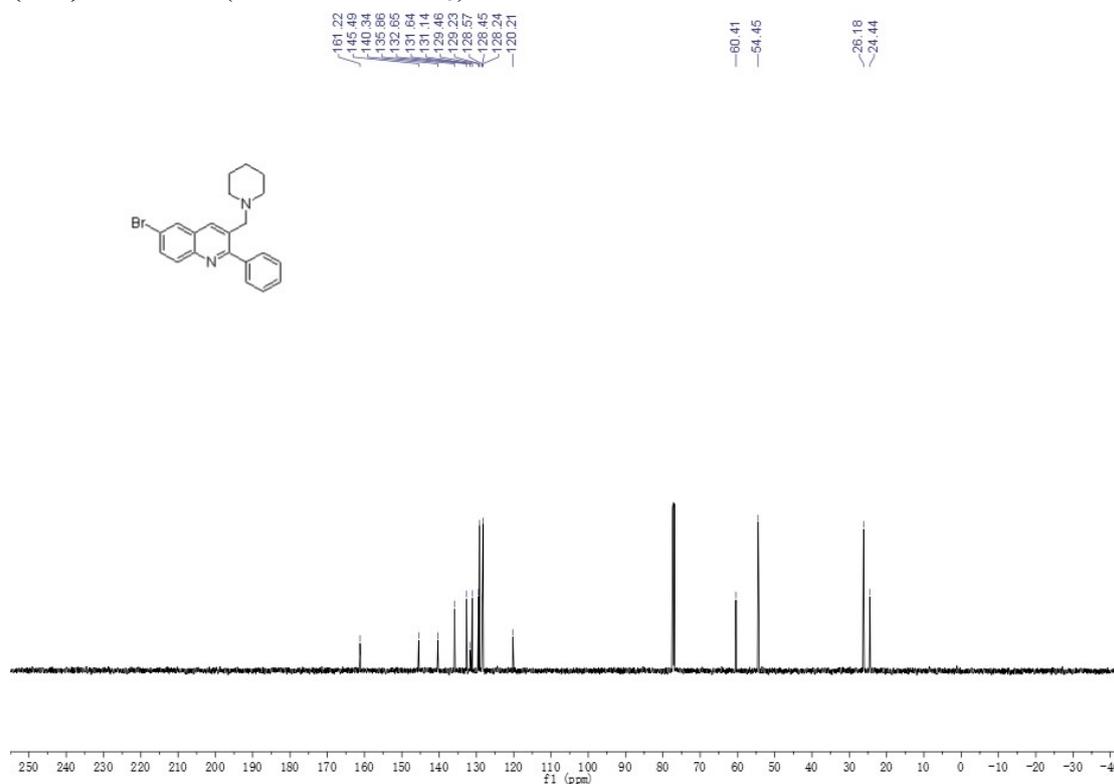
(4ac)  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



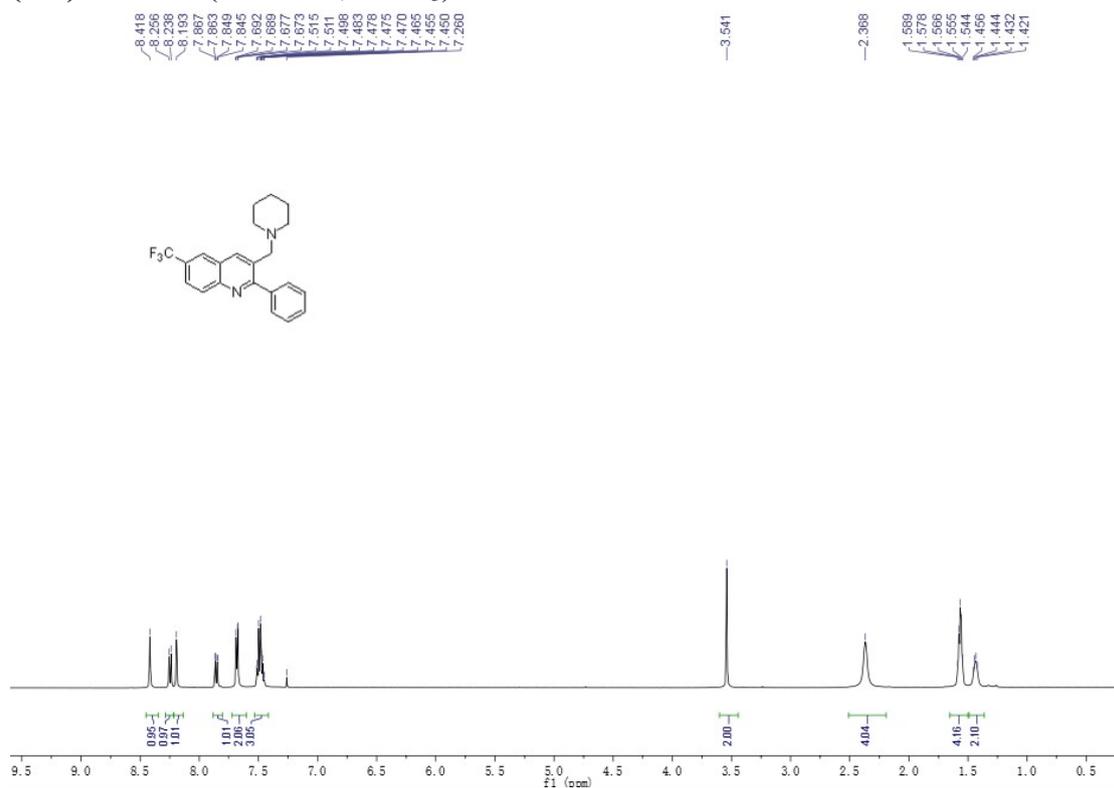
**(4ad)**  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



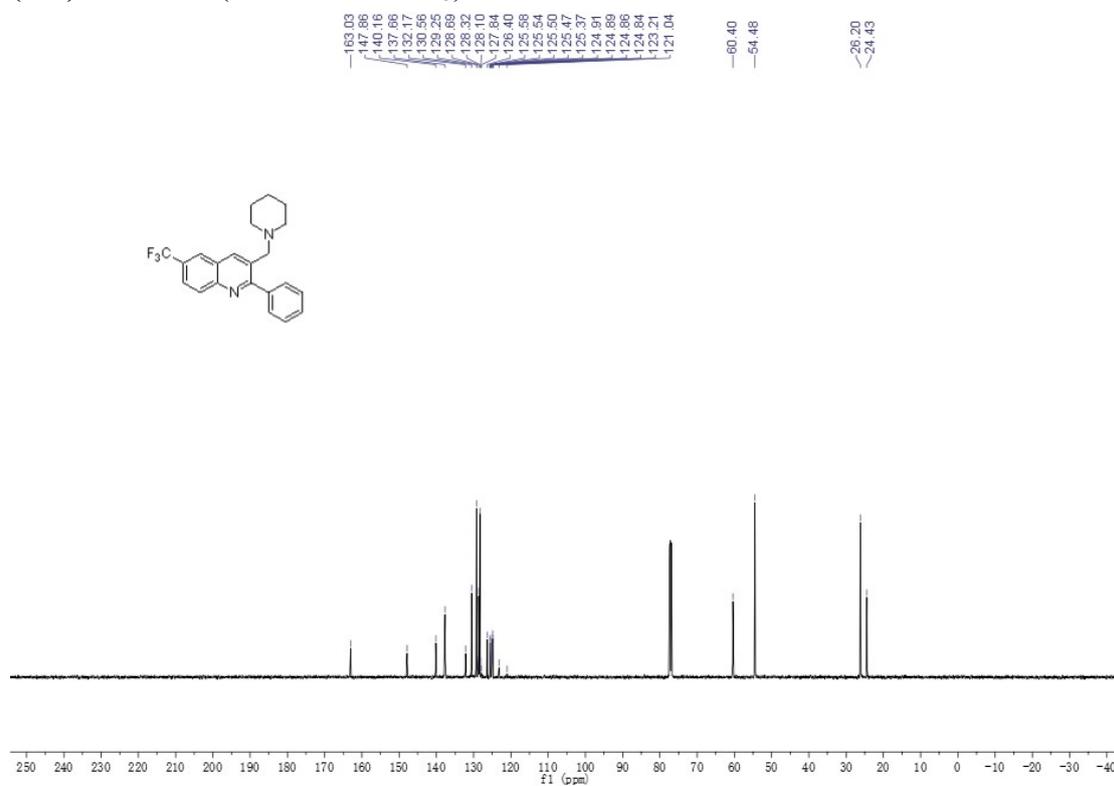
**(4ad)**  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



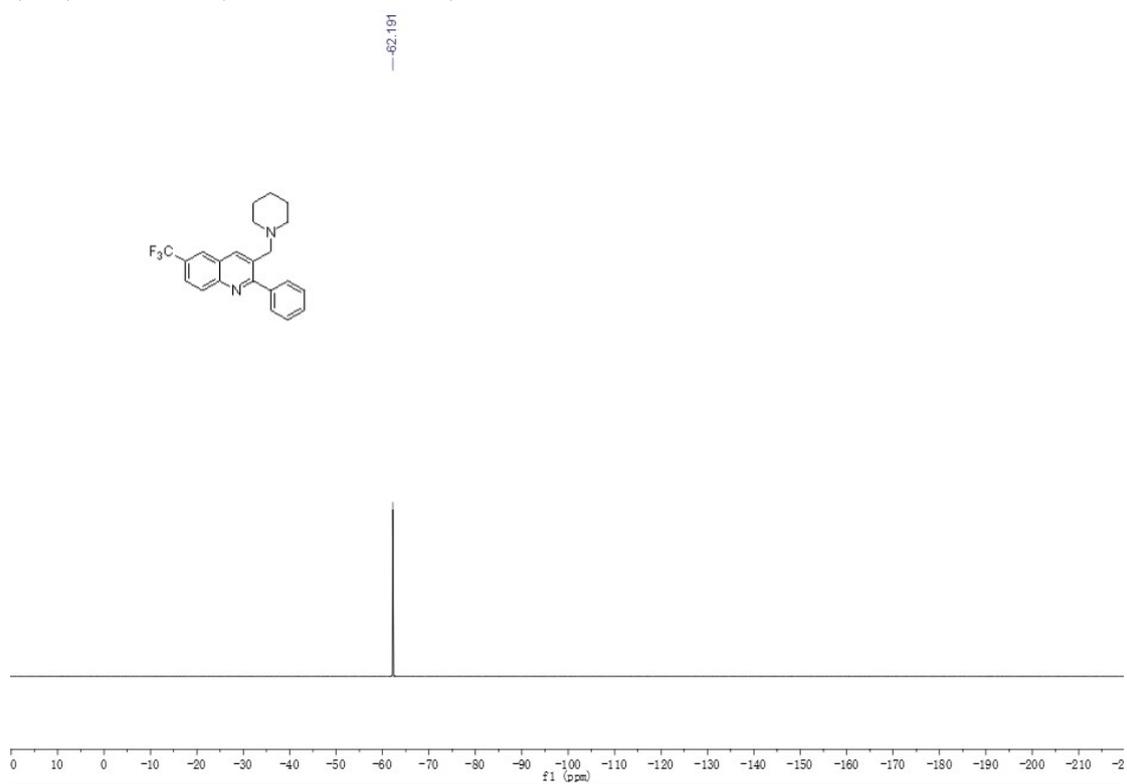
(4ae)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



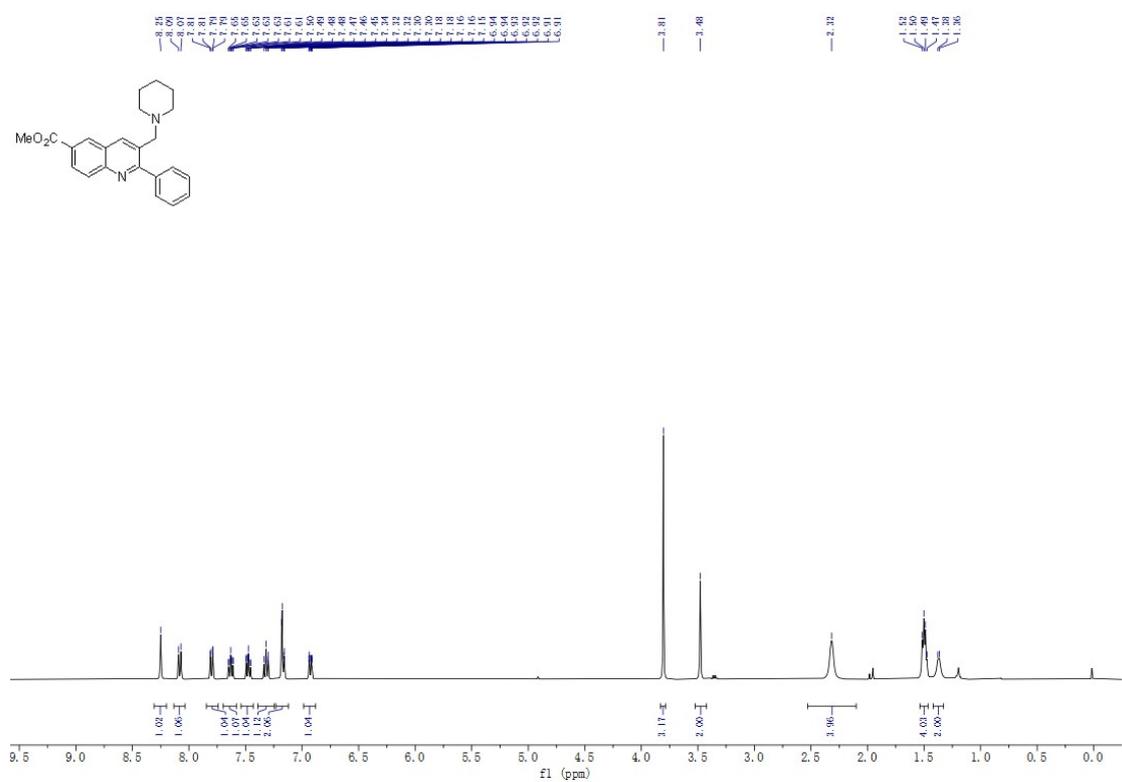
(4ae)  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



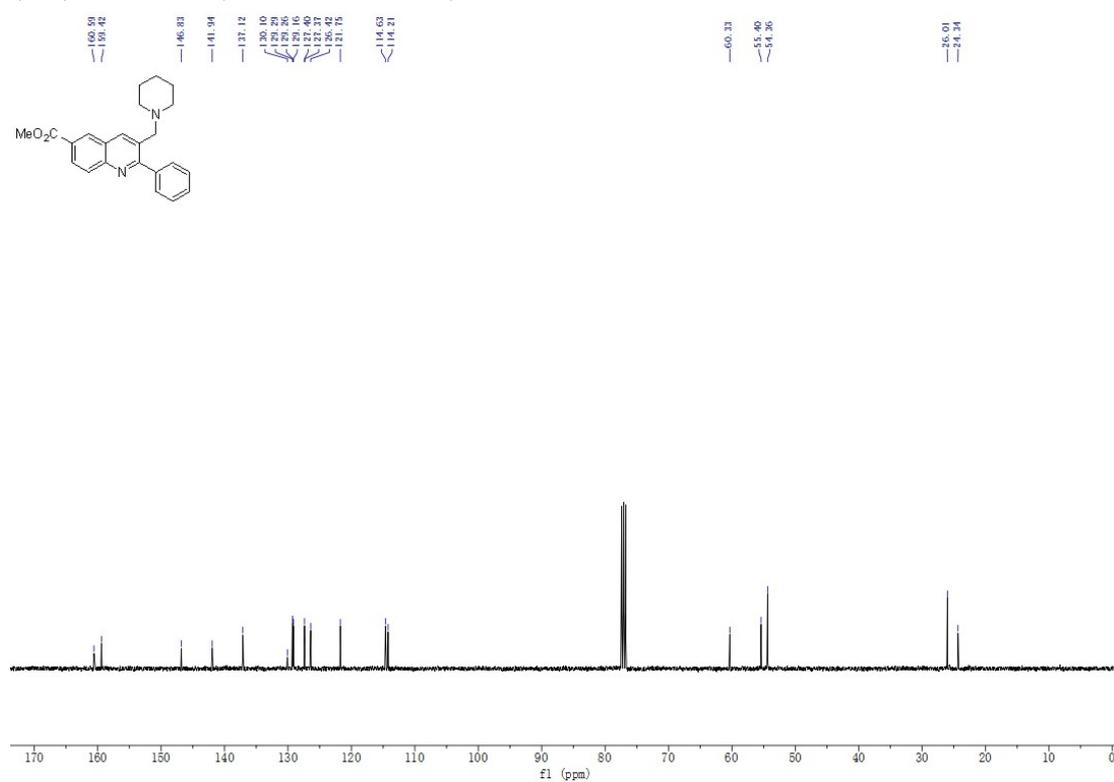
**(4ae)**  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )



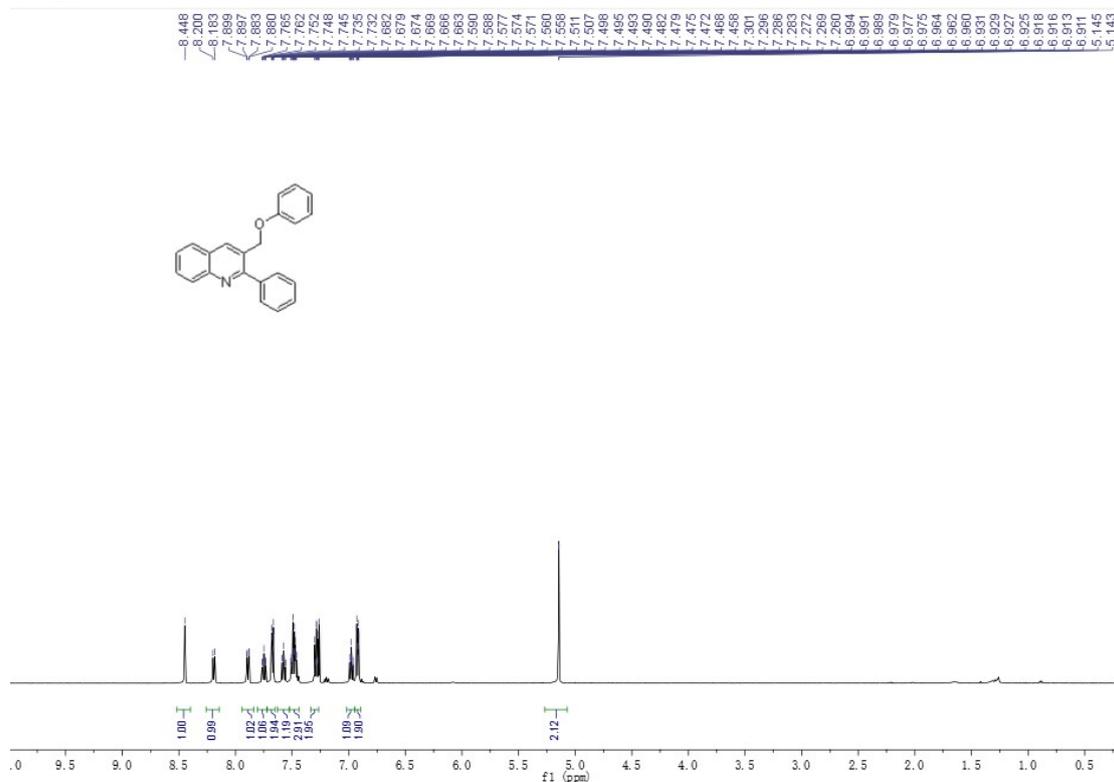
**(4af)**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



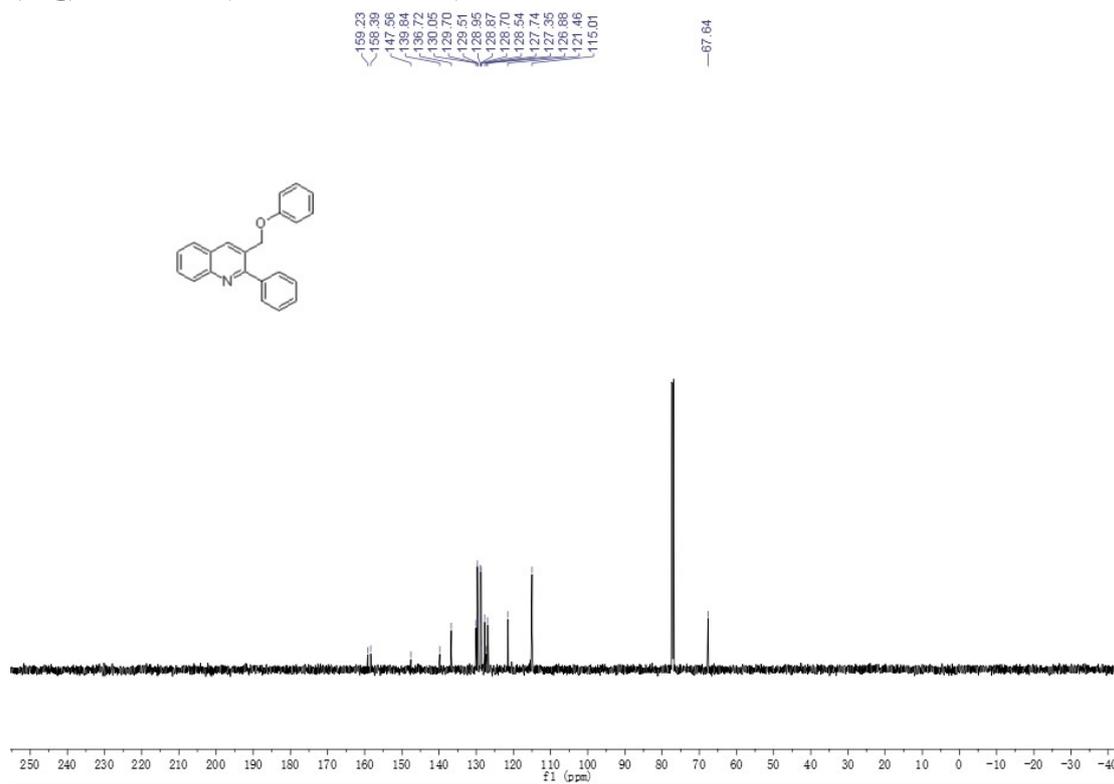
(4af) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



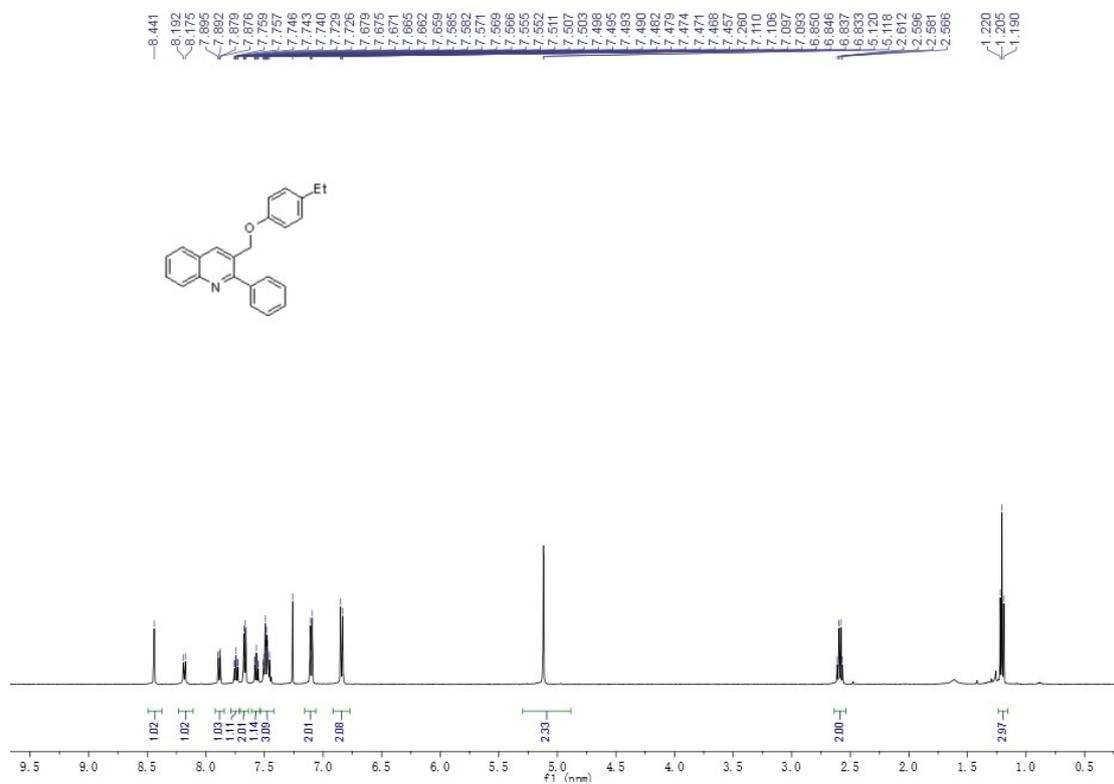
(4ag) <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)



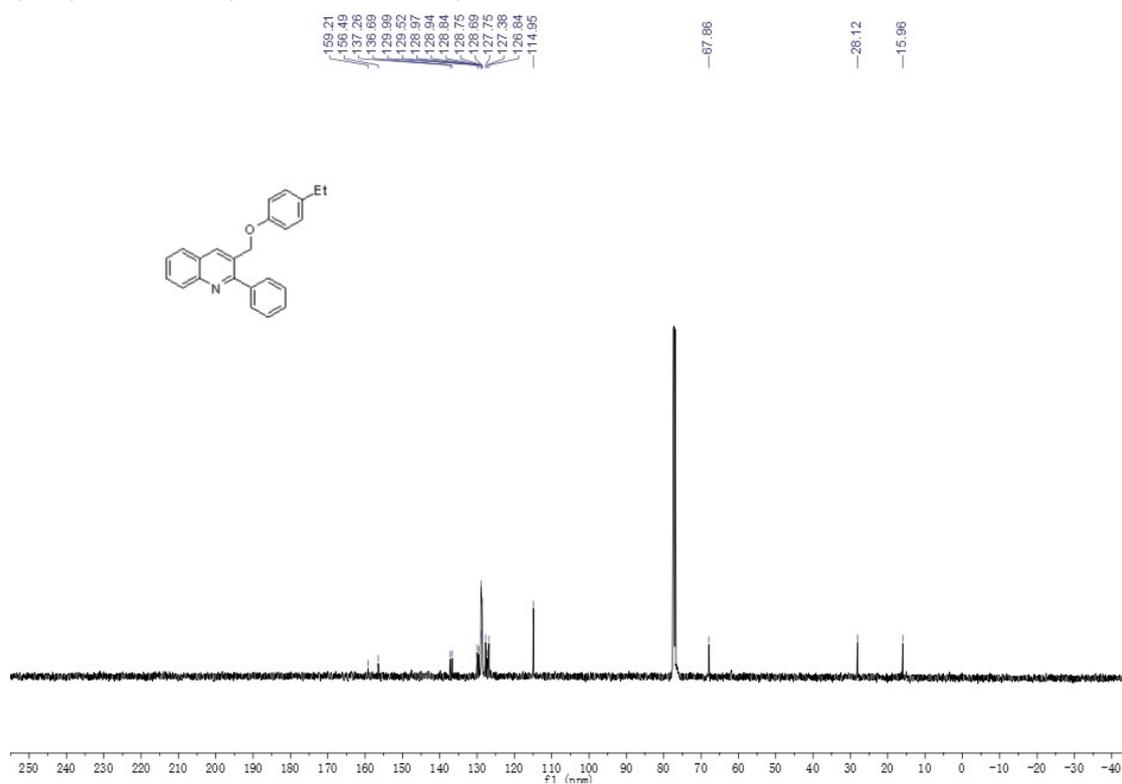
(4ag)  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



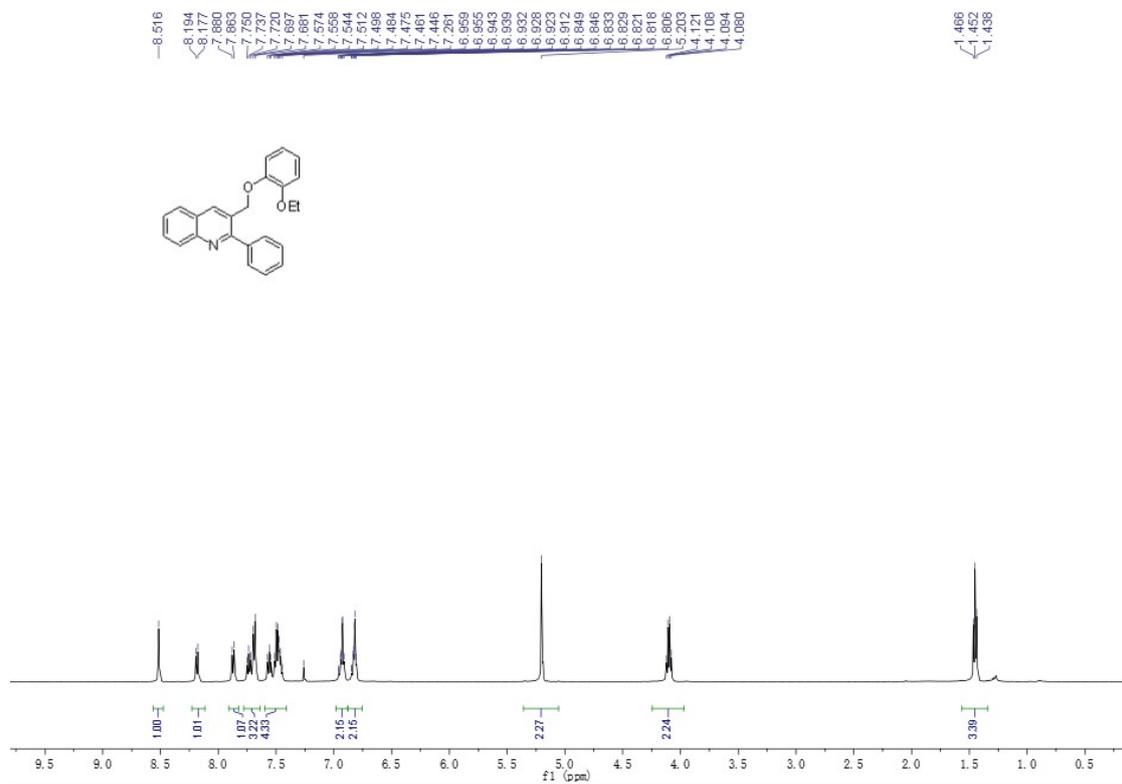
(4ah)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



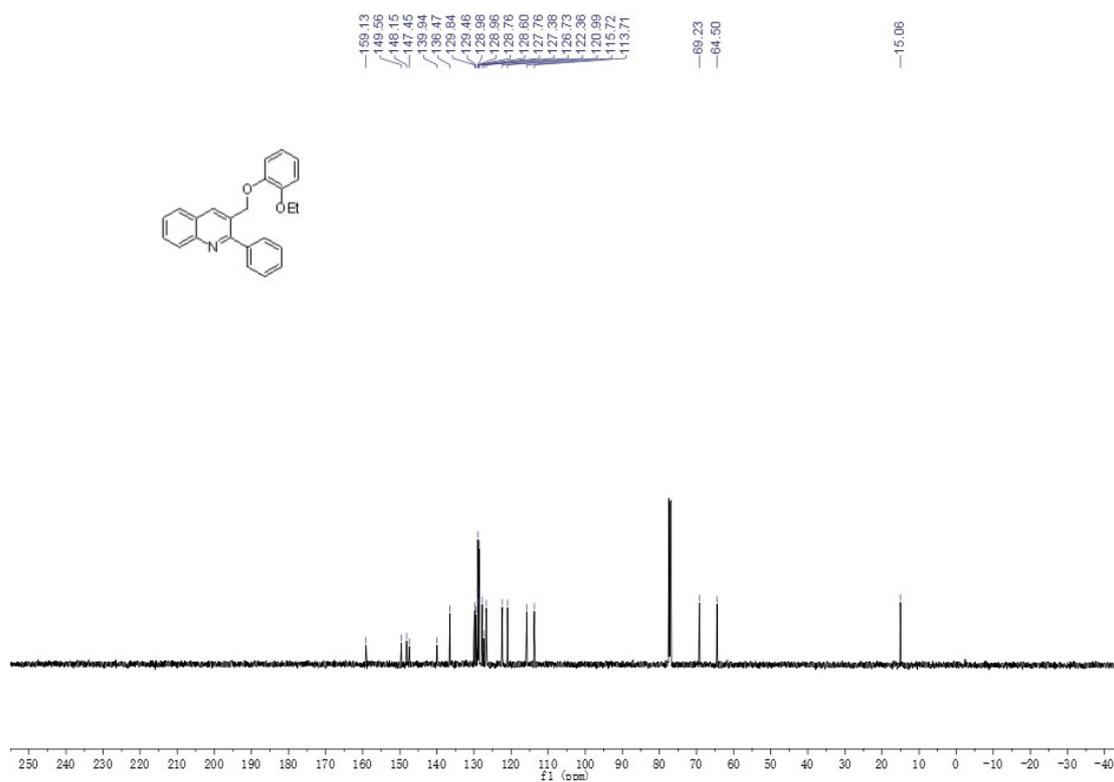
(4ah) <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)



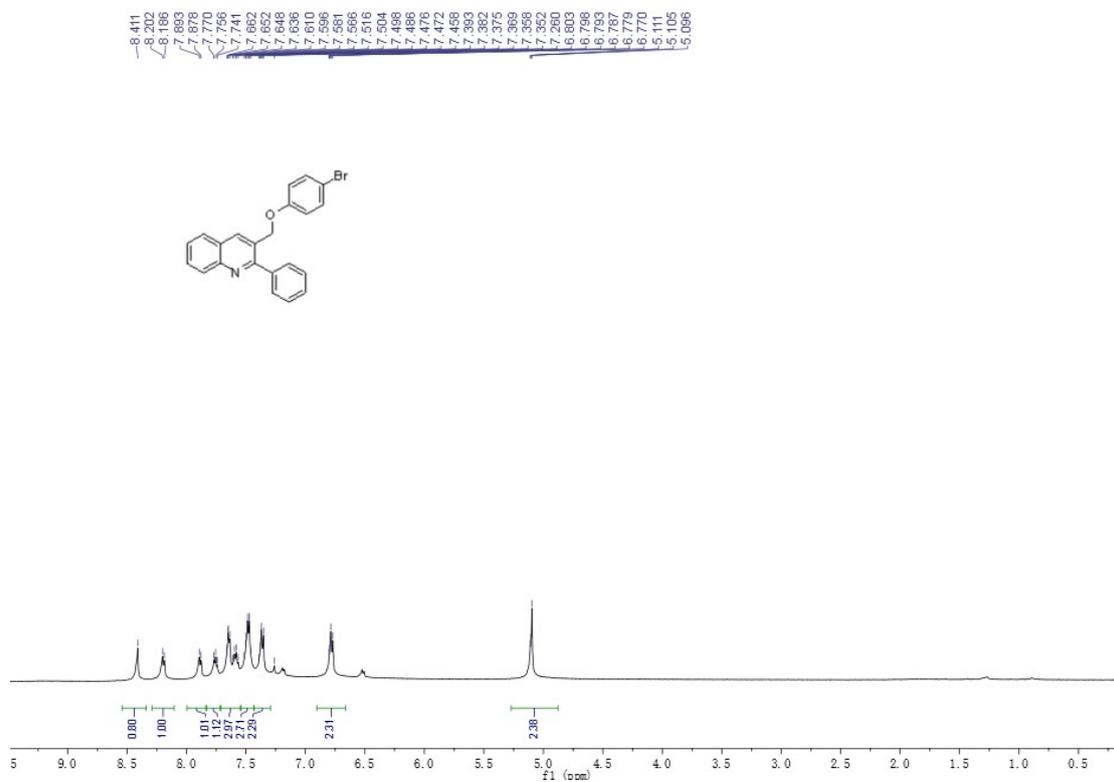
(4ai) <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)



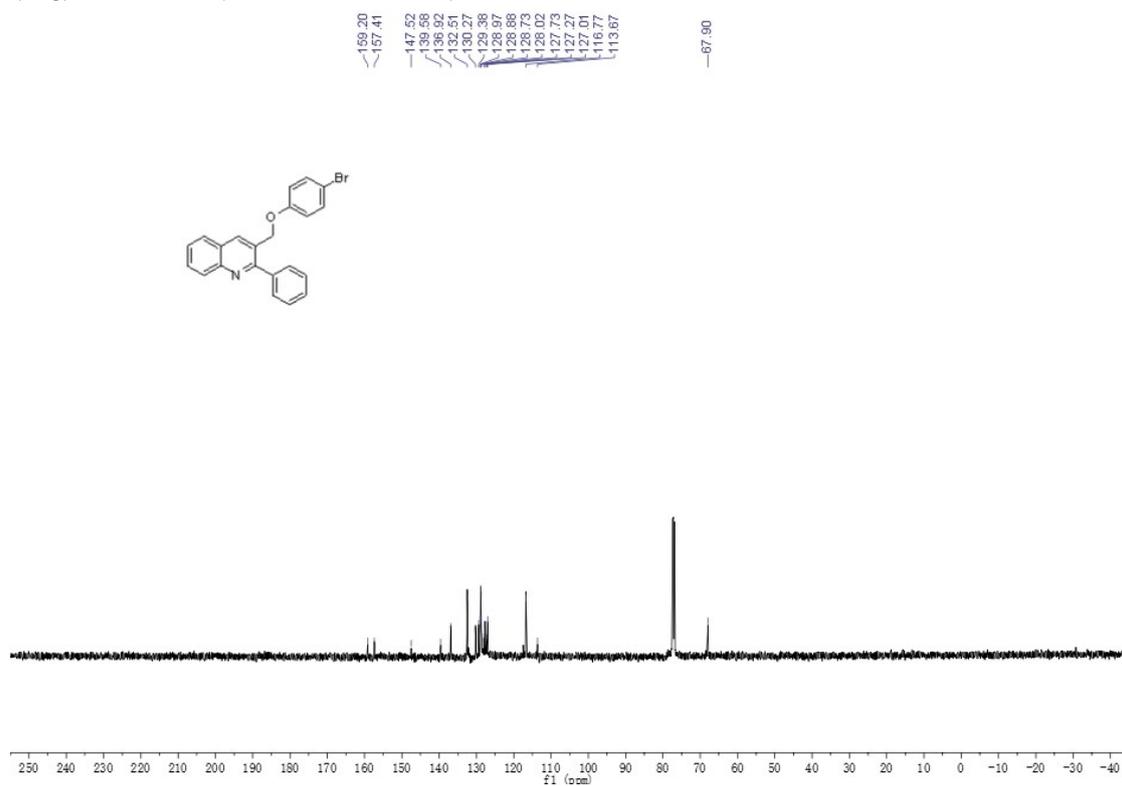
**(4ai)**  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



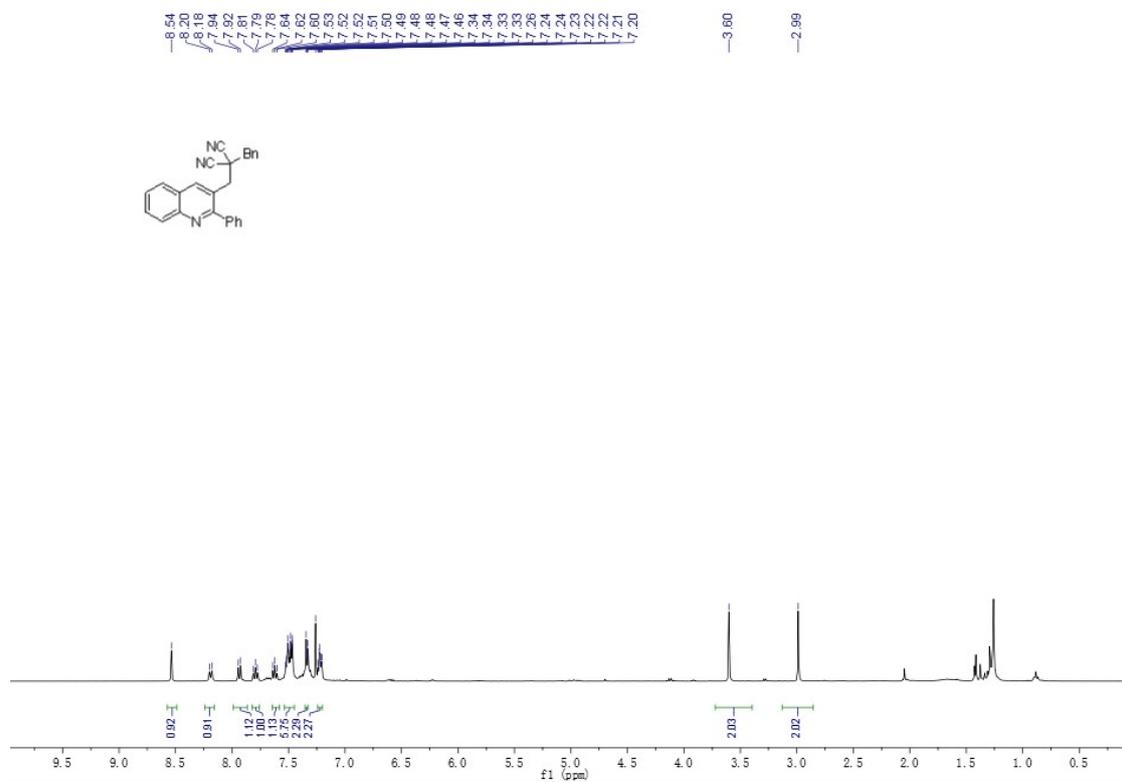
**(4aj)**  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



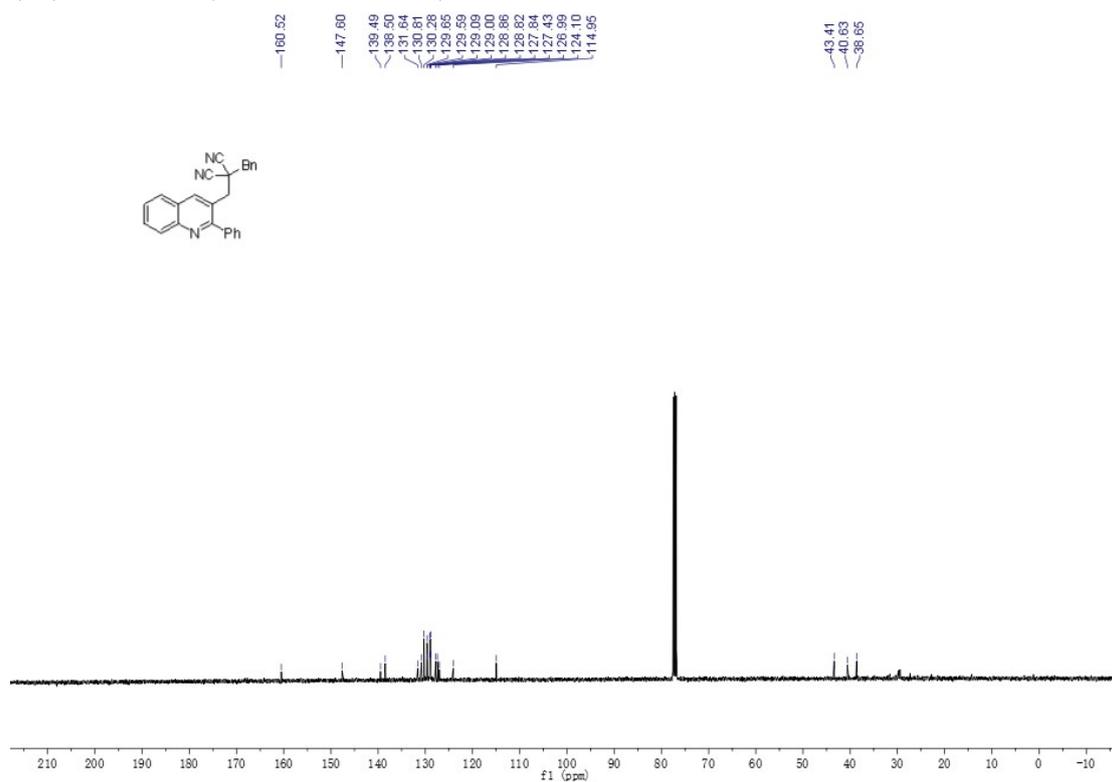
(4aj)  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



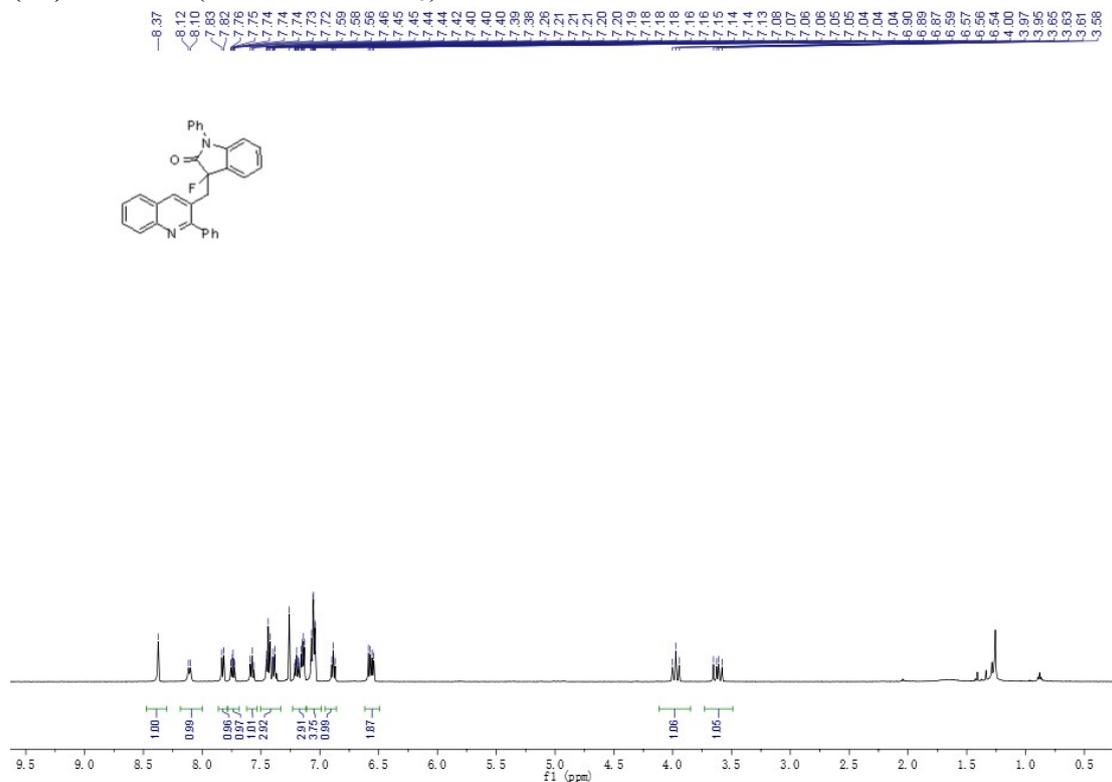
(6a)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



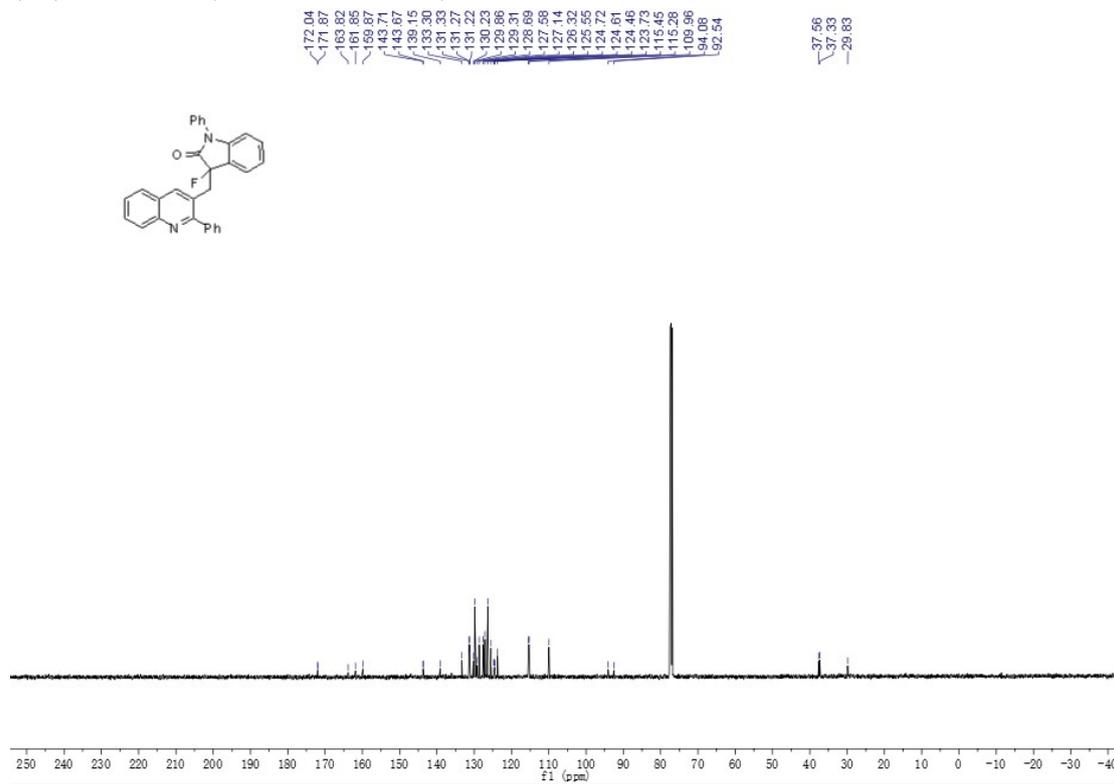
(6a)  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



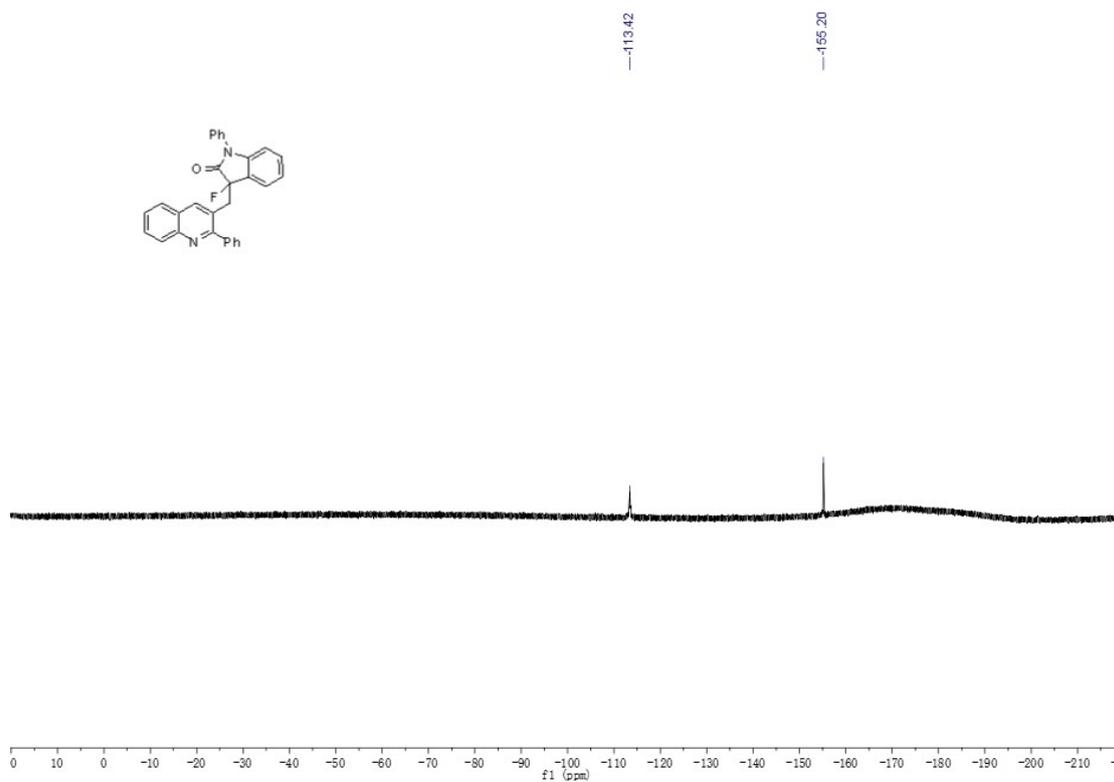
(6b)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



**(6b)**  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )

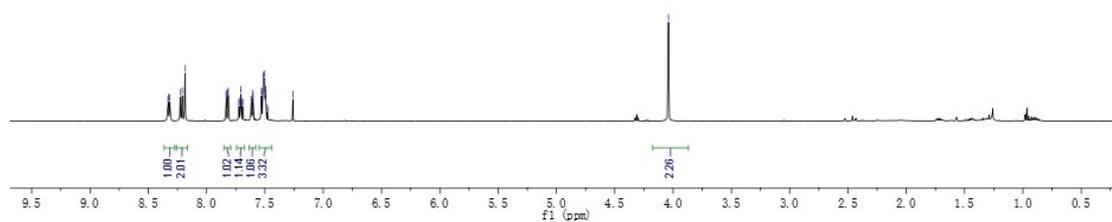
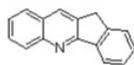


**(6b)**  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )



(7)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )

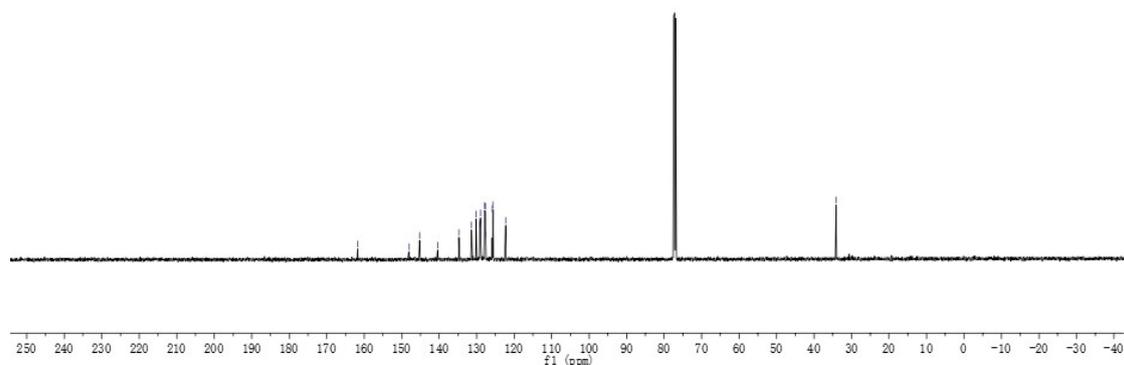
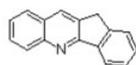
8.33  
8.33  
8.32  
8.31  
8.23  
8.19  
7.83  
7.82  
7.81  
7.72  
7.71  
7.70  
7.69  
7.68  
7.62  
7.61  
7.61  
7.60  
7.53  
7.53  
7.52  
7.52  
7.51  
7.51  
7.50  
7.50  
7.49  
7.49  
7.48  
7.48  
7.04



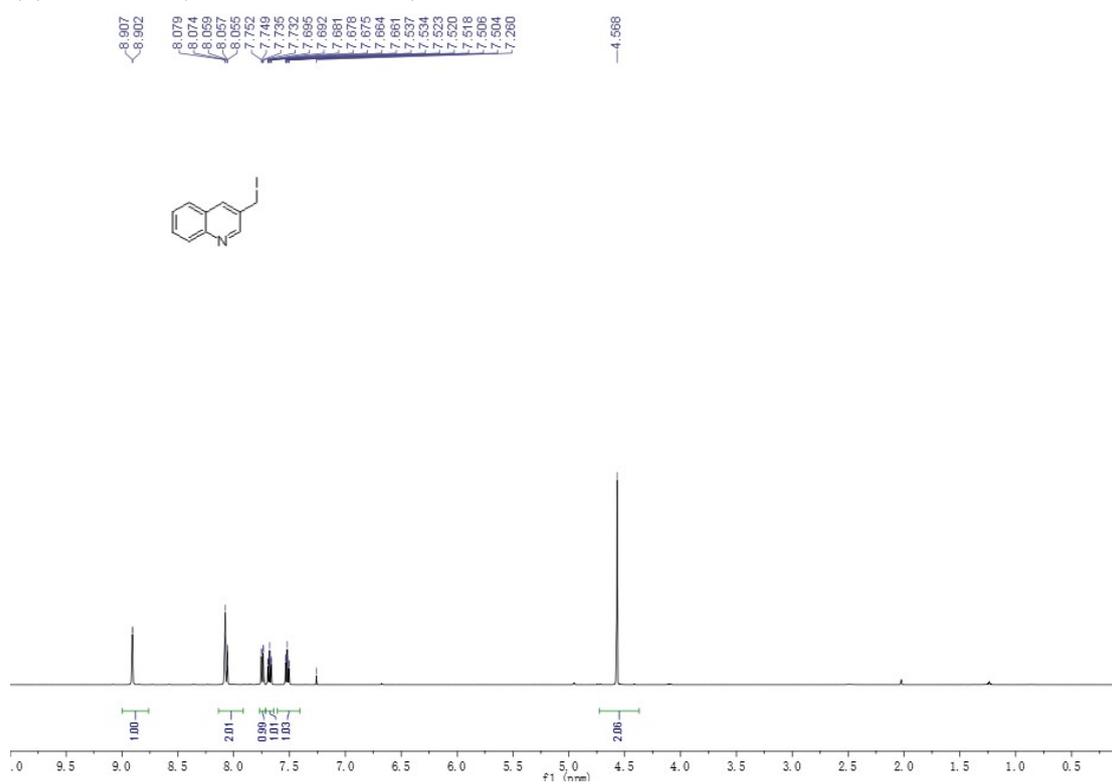
(7)  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )

181.77  
148.10  
145.25  
140.43  
134.76  
131.37  
130.15  
129.18  
129.00  
127.61  
127.59  
125.84  
125.60  
122.27

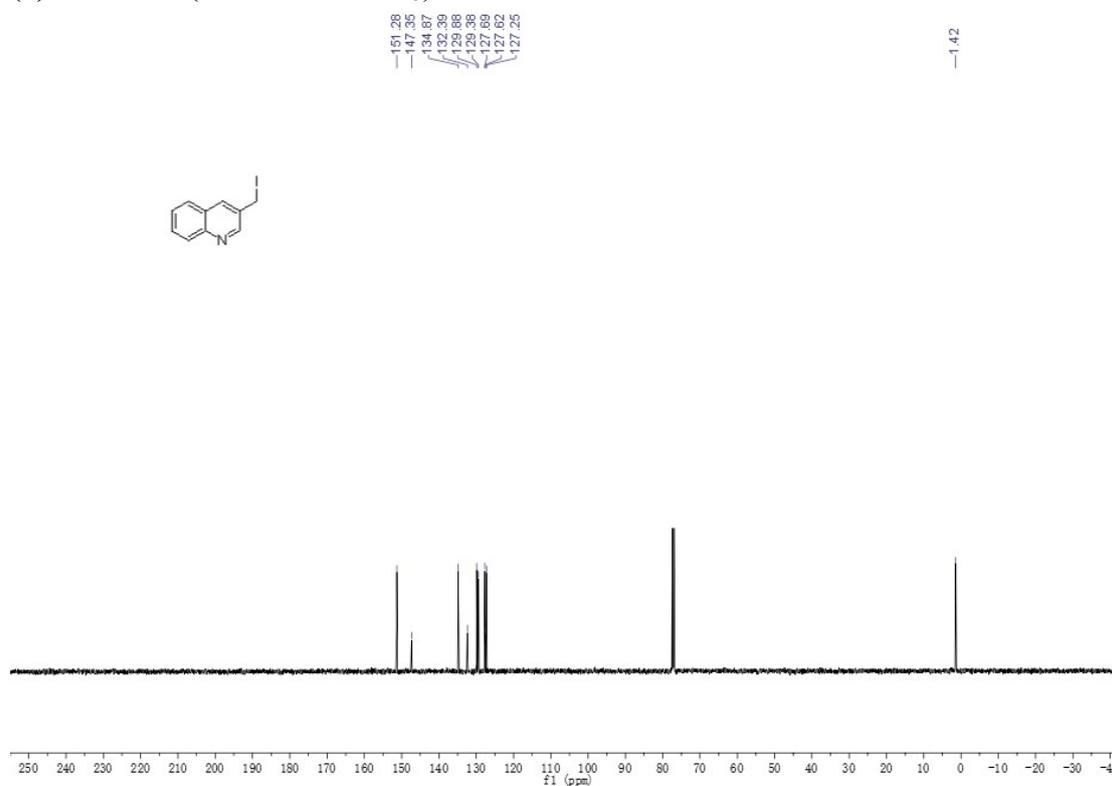
34.16



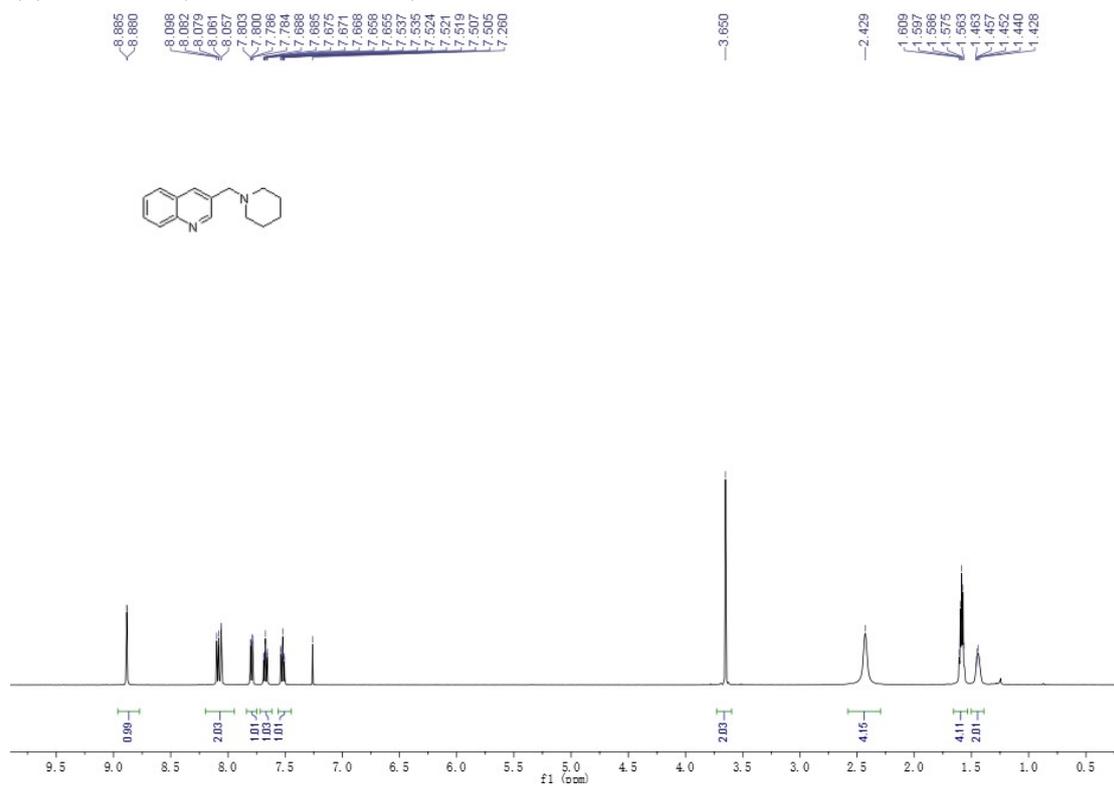
(8)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



(8)  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



(9)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



(9)  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )

