Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Electronic Supporting Information

for

Palladium-Catalyzed C−H Amination Using Aluminum Nitrate as the Oxidant

Kai Jia,‡ Yuan Xue,‡ Daoquan Tu*, Jun Luo* and Chao Jiang*

School of Chemistry and Chemical Engineering, Nanjing University of Science and Technology, Nanjing, Jiangsu 210094, China.

The Research Academy of Jiangsu Hansoh Pharmaceutical Co., Ltd., Dongjin Road, Huaguoshan Avenue, Lianyungang, Jiangsu 222069, China.

Email: chaojiang@njust.edu.cn, luojun@njust.edu.cn, tudq@hspharm.com

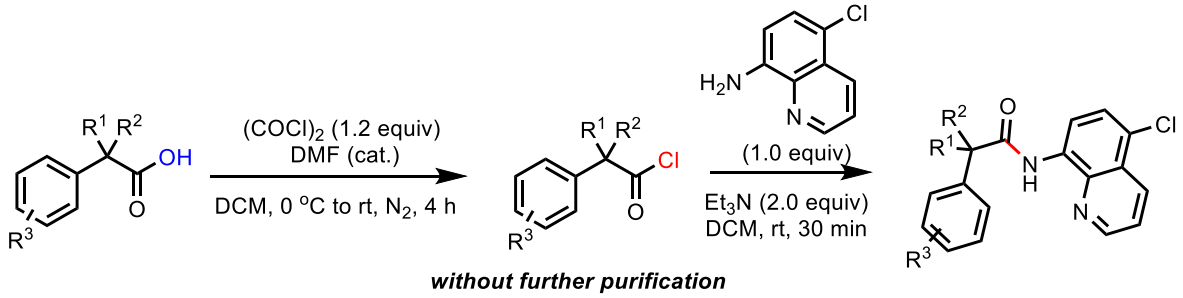
Table of content

General Information

All reagents and metal catalysts were obtained from commercial sources without further purification. Analytical thin layer chromatography was performed on 0.5 mm silica gel. Visualization was carried out with UV light. Silica gel 60H (200-300 mesh) manufactured by Qingdao Haiyang Chemical Group Co. (China) was used for general chromatography. ^{1}H NMR was recorded on Bruker AV-500 instrument (500 MHz) or Bruker AMX-400 instrument (400MHz). Chemical shifts were quoted in parts per million (ppm) referenced to 0.0 ppm for tetramethylsilane. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, *J*, were reported in Hertz unit (Hz). ^{13}C NMR spectra were recorded on Bruker AV-500 instrument (126 MHz) or Bruker AMX-400 instrument (101 MHz) and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to either the center line of a triplet at 77.16 ppm of chloroform-d_1 or the center line of a multiplet at 39.52 ppm of DMSO-d_6. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

Experimental Section

Preparation of Substrate



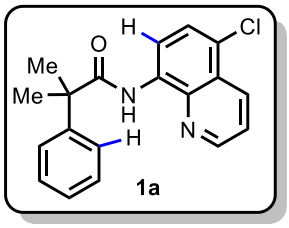
without further purification

General procedure:

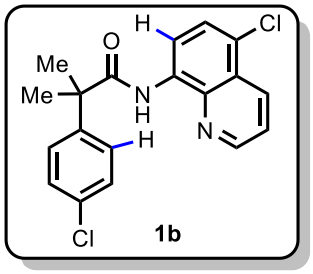
Step 1: To a 100 mL round bottom flask under a nitrogen atmosphere was added carboxylic acid[1] (10 mmol, 1.0 equiv) and 50 mL dichloromethane. To the resulting stirred solution was added oxalyl chloride (1 mL, 12 mmol. 1.2 equiv) and 3 drops DMF. The mixture was stirred at room temperature for 4 hours until all gas evolution ceased, which was used for the next step without any further purification.

Step 2: To a solution of 5-chloro-8-aminoquinoline[2] (1.96 g, 10.0 mmol) and NEt_3 (2.8 mL, 20.0 mmol, 2.0 equiv) in dichloromethane (10 mL), the solution of fresh prepared acid chloride was added dropwise. The resulting mixture was stirred at room temperature for 30 min. Then, the mixture was quenched with H_2O (50 mL) and 1M HCl (30 mL), and was extracted with 100mL dichloromethane for three times. The organic layer was dried over Na_2SO_4. After

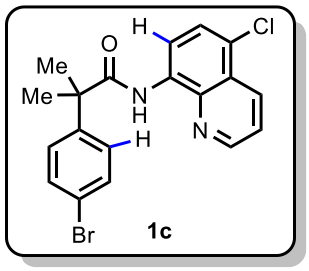
filtration and evaporation, the amide was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1).



***N*-(5-chloroquinolin-8-yl)-2-methyl-2-phenylpropanamide** (**1a**): White solid. Yield: 89%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.70 (d, *J* = 8.4 Hz, 1H), 8.63 (d, *J* = 4.1 Hz, 1H), 8.48 (d, *J* = 8.5 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 7.9 Hz, 2H), 7.46 (dd, *J* = 8.4, 4.1 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 1H), 1.78 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 148.6, 144.7, 139.2, 134.0, 133.1, 128.9, 127.2, 127.1, 126.4, 125.8, 124.0, 122.2, 115.9, 48.4, 27.0. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{18}ClN_2O$ $[M+H]^+$ 325.1107, found 325.1106.

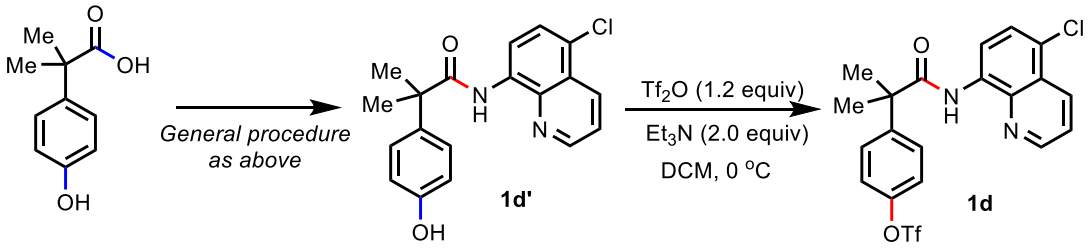


2-(4-chlorophenyl)-*N*-(5-chloroquinolin-8-yl)-2-methylpropanamide (**1b**): White solid. Yield: 80%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.75 – 8.62 (m, 2H), 8.50 (d, *J* = 8.5 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.49 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.46 (d, *J* = 8.6 Hz, 2H), 7.37 (d, *J* = 8.6 Hz, 2H), 1.75 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 148.7, 143.3, 139.1, 133.8, 133.3, 133.1, 129.0, 127.8, 127.2, 125.8, 124.3, 122.3, 116.0, 48.1, 26.9. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{17}Cl_2N_2O$ $[M+H]^+$ 359.0718, found 359.0714.



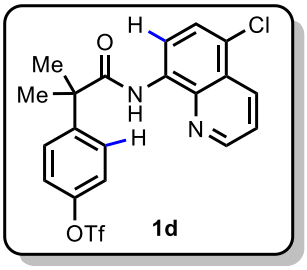
2-(4-bromophenyl)-*N*-(5-chloroquinolin-8-yl)-2-methylpropanamide (**1c**): White solid. Yield: 75%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.68 (dd, *J* = 4.9, 3.5 Hz, 2H), 8.50 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.54 – 7.47 (m, 3H), 7.40 (d, *J* = 8.6 Hz, 2H), 1.75 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 148.7, 143.9, 139.1, 133.8, 133.2, 131.9, 128.2, 127.1, 125.8, 124.3, 122.3, 121.2, 116.0, 48.2, 26.9. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{17}BrClN_2O$ $[M+H]^+$ 403.0213, found 403.0215.

The procedure for the synthesis of substrate (**1d**)

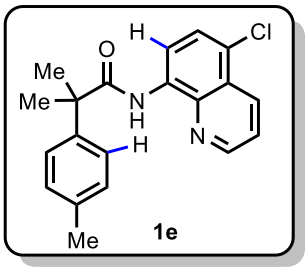


Following the general procedure, compound **1d'** was synthesized smoothly. Under argon, a 100 mL Schlenk flask was charged successively with **1d'** (1.0 mmol), dry DCM (5 mL) and

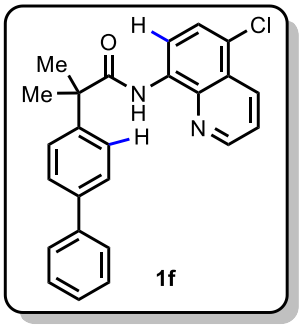
Et_3N (2.0 mmol). The solution was cooled to 0 °C in an ice bath, and treated with dropwise addition of triflic anhydride (1.2 mmol). The resulting mixture was slowly warmed up to 25 °C and kept stirred for additional 5 hours. At the end of the reaction (monitored by TLC), the mixture was passed through a pad of silica gel with 1:30 ethyl acetate/hexane washings, until no more aryl triflate was eluted out. The filtrate was concentrated on a rotary evaporator and the residue was subjected to flash silica gel chromatography to afford the desired aryl triflate **1d**.



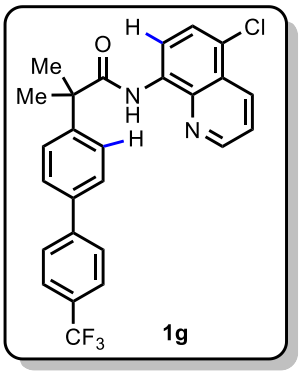
4-(1-((5-chloroquinolin-8-yl)amino)-2-methyl-1-oxopropan-2-yl)phenyl trifluoromethanesulfonate (**1d**): pale yellow oil. Yield: 62%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.66 (dd, *J* = 12.4, 5.7 Hz, 2H), 8.50 (d, *J* = 8.4 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.49 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.32 (d, *J* = 8.7 Hz, 2H), 1.79 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 148.8, 148.6, 145.4, 139.2, 133.6, 133.3, 128.5, 127.1, 125.9, 124.5, 122.4, 121.7, 120.1, 117.5, 116.0, 48.3, 27.0. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{17}ClF_3N_2O_4S$ $[M+H]^+$ 473.0550, found 473.0552.



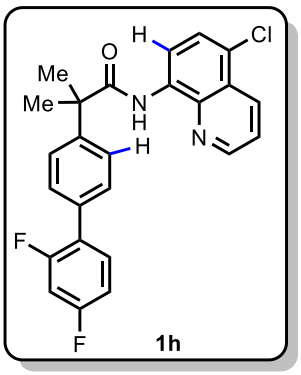
***N*-(5-chloroquinolin-8-yl)-2-methyl-2-(p-tolyl)propanamide** (**1e**): white solid. Yield: 71%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.70 (d, *J* = 8.4 Hz, 1H), 8.64 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.47 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.46 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 2.36 (s, 3H), 1.76 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 148.6, 141.7, 139.2, 136.8, 134.0, 133.1, 129.6, 127.2, 126.2, 125.8, 124.0, 122.2, 115.9, 48.1, 27.0, 21.1. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{20}ClN_2O$ $[M+H]^+$ 339.1264, found 339.1260.



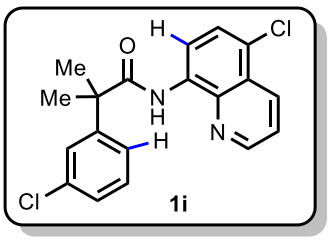
2-([1,1'-biphenyl]-4-yl)-*N*-(5-chloroquinolin-8-yl)-2-methylpropanamide (**1f**): White solid. Yield: 86%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.71 (d, *J* = 8.4 Hz, 1H), 8.62 (d, *J* = 4.1 Hz, 1H), 8.49 (d, *J* = 8.5 Hz, 1H), 7.65 – 7.57 (m, 7H), 7.47 – 7.43 (m, 3H), 7.35 (t, *J* = 7.3 Hz, 1H), 1.82 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.8, 148.6, 143.8, 140.7, 140.0, 139.2, 134.0, 133.2, 128.9, 127.5, 127.4, 127.2, 127.1, 126.9, 125.9, 124.1, 122.2, 116.0, 48.3, 27.0. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{22}ClN_2O$ $[M+H]^+$ 401.1421, found 401.1420.



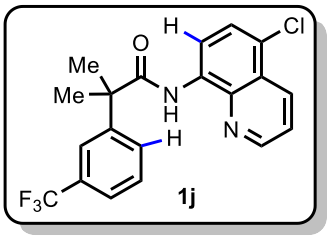
***N*-(5-chloroquinolin-8-yl)-2-methyl-2-(4'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl)propenamide** (**1g**): White solid. Yield: 56%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.72 (d, *J* = 8.4 Hz, 1H), 8.63 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.50 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.70 (s, 4H), 7.64 (s, 4H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.47 (dd, *J* = 8.5, 4.2 Hz, 1H), 1.83 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 148.6, 144.9, 144.2, 139.2, 138.5, 133.9, 133.2, 129.4 (d, *J* = 32.6 Hz), 127.7, 127.3, 127.2, 127.1, 125.9, 125.8 (q, *J* = 3.8 Hz), 124.2, 122.2, 116.0, 48.3, 26.9. HRMS (ESI-TOF) *m/z* calcd for $C_{26}H_{21}ClF_3N_2O$ $[M+H]^+$ 469.1295, found 469.1293.



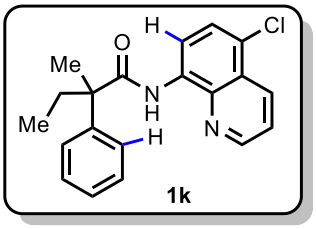
***N*-(5-chloroquinolin-8-yl)-2-(2',4'-difluoro-[1,1'-biphenyl]-4-yl)-2-methylpropanamide** (**1h**): Yellow oil. Yield: 68%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.71 (d, *J* = 8.4 Hz, 1H), 8.62 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.46 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 3H), 7.47 – 7.37 (m, 2H), 6.98 – 6.88 (m, 2H), 1.82 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 161.1 (ddd, *J* = 262.4, 249.7, 11.6 Hz), 148.6, 144.3, 139.2, 133.9, 133.8, 133.2, 131.4 (dd, *J* = 9.5, 5.0 Hz), 129.4 (d, *J* = 2.8 Hz), 127.2, 126.7, 125.9, 124.9 (dd, *J* = 13.9, 3.8 Hz), 124.2, 122.2, 116.0, 111.7 (d, *J* = 17.4 Hz), 104.8 – 104.2 (m), 48.3, 27.0. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{20}ClF_2N_2O$ $[M+H]^+$ 437.1232, found 437.1230.



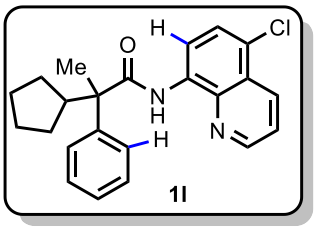
2-(3-chlorophenyl)-*N*-(5-chloroquinolin-8-yl)-2-methylpropanamide (**1i**): White solid. Yield: 86%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.74 – 8.64 (m, 2H), 8.49 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.53 (s, 1H), 7.49 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.35 – 7.27 (m, 2H), 1.76 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 148.7, 146.9, 139.2, 134.8, 133.8, 133.2, 130.1, 127.4, 127.1, 126.7, 125.9, 124.8, 124.3, 122.3, 116.0, 48.4, 26.9. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{17}Cl_2N_2O$ $[M+H]^+$ 359.0718, found 359.0716.



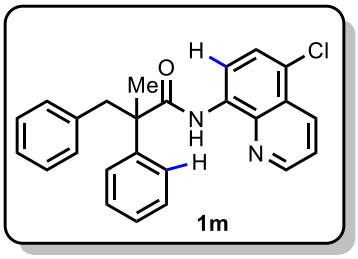
***N*-(5-chloroquinolin-8-yl)-2-methyl-2-(3-(trifluoromethyl)phenyl)propanamide** (**1j**): Yellow oil, 88%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.73 – 8.58 (m, 2H), 8.49 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.81 (s, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.58 (t, *J* = 7.0 Hz, 2H), 7.54 – 7.46 (m, 2H), 1.81 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 148.6, 145.8, 139.0, 133.6, 133.1, 131.2 (q, *J* = 32.1 Hz), 130.2, 129.4, 127.0, 125.7, 124.3, 124.1 (q, *J* = 3.7 Hz), 123.0 (q, *J* = 3.8 Hz), 122.2, 116.0, 48.4, 26.8. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{17}ClF_3N_2O$ $[M+H]^+$ 393.0982, found 393.0980.



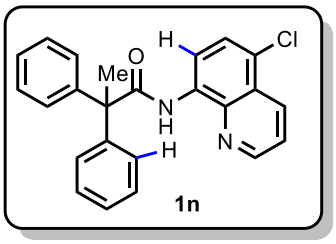
***N*-(5-chloroquinolin-8-yl)-2-methyl-2-phenylbutanamide** (**1k**): White solid. Yield: 88%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.71 (d, *J* = 8.4 Hz, 1H), 8.64 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.48 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.47 (td, *J* = 8.6, 2.7 Hz, 3H), 7.39 (t, *J* = 7.7 Hz, 2H), 7.30 (d, *J* = 7.3 Hz, 1H), 2.28 (dq, *J* = 14.7, 7.4 Hz, 1H), 2.19 (dq, *J* = 14.7, 7.4 Hz, 1H), 1.73 (s, 3H), 0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 148.6, 143.7, 139.2, 134.0, 133.1, 128.8, 127.2, 127.1, 126.9, 125.8, 124.0, 122.2, 115.9, 52.3, 31.7, 23.0, 9.1. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{20}ClN_2O$ $[M+H]^+$ 339.1264, found 339.1266.



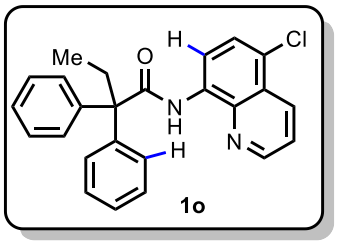
***N*-(5-chloroquinolin-8-yl)-2-cyclopentyl-2-phenylpropanamide** (**1l**): White solid. Yield: 78%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.71 (d, *J* = 8.4 Hz, 1H), 8.67 (d, *J* = 3.9 Hz, 1H), 8.46 (d, *J* = 8.4 Hz, 1H), 7.54 (dd, *J* = 10.7, 8.6 Hz, 3H), 7.45 (dd, *J* = 8.4, 4.1 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.27 (d, *J* = 7.0 Hz, 1H), 3.07 – 2.94 (m, 1H), 1.96 – 1.86 (m, 1H), 1.74 (s, 3H), 1.65 – 1.51 (m, 6H), 1.34 – 1.25 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 148.6, 144.0, 139.2, 134.1, 133.2, 128.6, 127.2, 127.0, 126.9, 125.8, 123.8, 122.2, 115.9, 54.3, 46.4, 28.6, 28.3, 26.0, 25.8, 19.2. HRMS (ESI-TOF) *m/z* calcd for $C_{23}H_{24}ClN_2O$ $[M+H]^+$ 379.1577, found 379.1573.



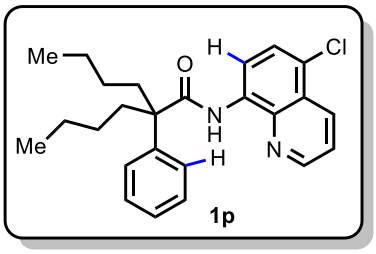
***N*-(5-chloroquinolin-8-yl)-2-methyl-2,3-diphenylpropanamide** (**1m**): White solid. Yield: 72%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.74 (d, J = 8.4 Hz, 1H), 8.64 – 8.57 (m, 1H), 8.49 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.47 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.42 (d, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.32 (d, *J* = 7.3 Hz, 1H), 7.12 (q, *J* = 5.1 Hz, 3H), 6.90 – 6.84 (m, 2H), 3.60 (d, *J* = 13.4 Hz, 1H), 3.40 (d, *J* = 13.4 Hz, 1H), 1.68 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 148.6, 142.9, 139.2, 137.5, 133.9, 133.2, 130.7, 128.7, 127.8, 127.3, 127.3, 127.2, 126.4, 125.7, 124.1, 122.2, 116.0, 52.9, 45.2, 22.9. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{22}ClN_2O$ $[M+H]^+$ 401.1421, found 401.1420.



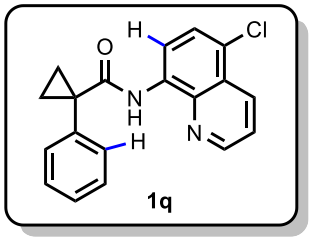
***N*-(5-chloroquinolin-8-yl)-2,2-diphenylpropanamide** (**1n**): White solid. Yield: 90%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.81 (d, *J* = 8.4 Hz, 1H), 8.57 – 8.51 (m, 1H), 8.47 (d, *J* = 8.5 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.44 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.41 – 7.35 (m, 8H), 7.35 – 7.28 (m, 2H), 2.17 (s, 3H). The spectral data of the starting material was in accordance with the reported in the literature[3].



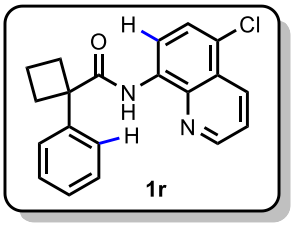
***N*-(5-chloroquinolin-8-yl)-2,2-diphenylbutanamide** (**1o**): White solid. Yield: 81%**.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.74 (d, *J* = 8.4 Hz, 1H), 8.59 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.47 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.49 – 7.42 (m, 5H), 7.37 (t, *J* = 7.7 Hz, 4H), 7.30 (t, *J* = 7.3 Hz, 2H), 2.63 (d, *J* = 7.3 Hz, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 148.6, 142.9, 139.3, 134.0, 133.1, 129.3, 128.4, 127.1, 127.0, 125.8, 124.1, 122.2, 115.9, 62.6, 31.5, 10.2. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{22}ClN_2O$ $[M+H]^+$ 401.1421, found 401.1420.



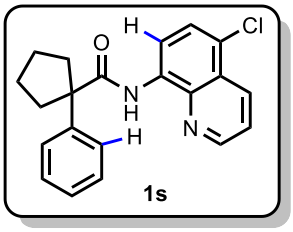
2-butyl-*N*-(5-chloroquinolin-8-yl)-2-phenylhexanamide (**1p**): White solid. Yield: 86%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.70 (d, *J* = 8.4 Hz, 1H), 8.64 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.48 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.49 – 7.42 (m, 3H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.29 – 7.24 (m, 1H), 2.16 (ddt, *J* = 18.4, 13.7, 6.9 Hz, 4H), 1.33 (t, *J* = 6.8 Hz, 4H), 1.22 – 1.16 (m, 2H), 1.16 – 1.09 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 148.6, 143.4, 139.2, 134.1, 133.1, 128.6, 127.2, 127.1, 126.9, 125.8, 123.8, 122.1, 115.9, 55.4, 34.8, 26.2, 23.3, 14.0. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{30}ClN_2O$ $[M+H]^+$ 409.2047, found 409.2049.



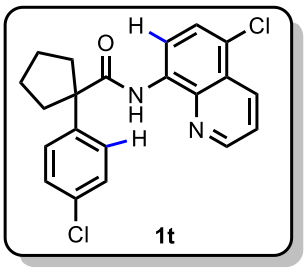
***N*-(5-chloroquinolin-8-yl)-1-phenylcyclopropane-1-carboxamide** (**1q**): White solid. Yield: 65%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.64 (d, *J* = 8.4 Hz, 1H), 8.47 (d, *J* = 3.9 Hz, 1H), 8.44 (d, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 7.2 Hz, 2H), 7.45 (d, *J* = 7.1 Hz, 1H), 7.41 (dd, *J* = 8.5, 4.2 Hz, 1H), 1.79 – 1.75 (m, 2H), 1.25 (dd, *J* = 6.7, 3.7 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 148.5, 139.2, 139.1, 134.0, 133.0, 131.4, 129.2, 128.2, 127.1, 125.7, 124.0, 122.1, 115.6, 32.0, 16.4. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{16}ClN_2O$ $[M+H]^+$ 323.0951, found 323.0953.



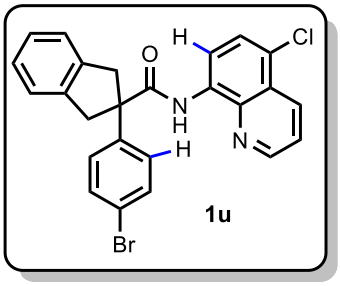
***N*-(5-chloroquinolin-8-yl)-1-phenylcyclobutane-1-carboxamide** (**1r**): White solid. Yield: 75%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.73 – 8.65 (m, 2H), 8.48 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.52 – 7.45 (m, 3H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 1H), 3.03 (ddd, *J* = 11.9, 9.1, 5.4 Hz, 2H), 2.71 – 2.61 (m, 2H), 2.28 – 2.16 (m, 1H), 2.03 – 1.93 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 148.6, 144.2, 139.2, 134.0, 133.2, 128.9, 127.1, 127.0, 126.4, 125.8, 124.0, 122.2, 115.8, 54.5, 32.3, 16.7. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{18}ClN_2O$ $[M+H]^+$ 337.1108, found 337.1106.



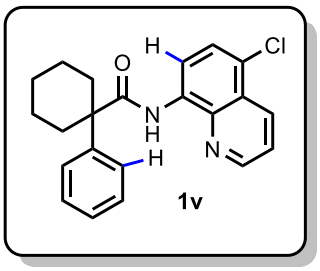
***N*-(5-chloroquinolin-8-yl)-1-phenylcyclopentane-1-carboxamide** (**1s**): White solid. Yield: 77%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.68 (dd, *J* = 4.2, 1.3 Hz, 1H), 8.65 (d, *J* = 8.4 Hz, 1H), 8.46 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.54 (dd, *J* = 7.7, 6.3 Hz, 3H), 7.46 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 2.78 – 2.69 (m, 2H), 2.19 (dt, *J* = 13.3, 6.8 Hz, 2H), 1.94 – 1.86 (m, 2H), 1.83 – 1.75 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 148.6, 143.7, 139.2, 134.1, 133.1, 128.9, 127.1, 127.1, 127.0, 125.8, 123.9, 122.2, 115.8, 61.0, 36.7, 24.0. HRMS (ESI-TOF) *m/z* calcd for $C_{21}H_{20}ClN_2O$ $[M+H]^+$ 351.1264, found 351.1260.



1-(4-chlorophenyl)-*N*-(5-chloroquinolin-8-yl)cyclopentane-1-carboxamide (**1t**): White solid. Yield: 78%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.72 (d, *J* = 4.0 Hz, 1H), 8.63 (d, *J* = 8.4 Hz, 1H), 8.49 (d, *J* = 8.5 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.52 – 7.44 (m, 3H), 7.35 (d, *J* = 8.4 Hz, 2H), 2.71 (dd, *J* = 11.5, 5.5 Hz, 2H), 2.19 – 2.08 (m, 2H), 1.89 (dd, *J* = 7.0, 4.4 Hz, 2H), 1.79 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 148.7, 142.3, 139.1, 133.9, 133.2, 133.0, 129.0, 128.4, 127.1, 125.8, 124.1, 122.3, 115.8, 60.6, 36.7, 23.9. HRMS (ESI-TOF) *m/z* calcd for $C_{21}H_{19}Cl_2N_2O$ $[M+H]^+$ 385.0874, found 385.0870.

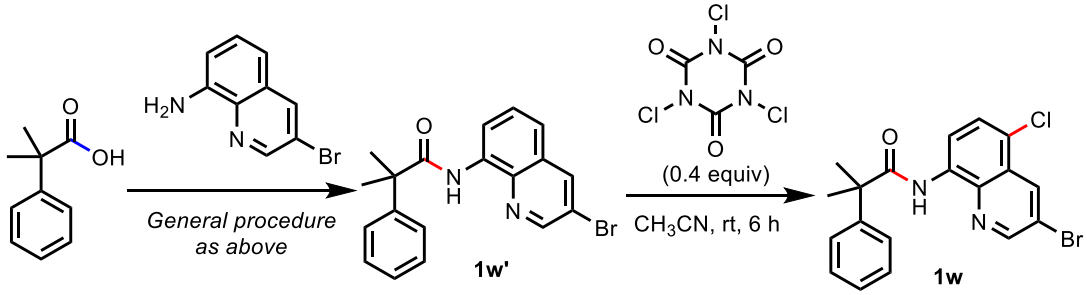


2-(4-bromophenyl)-*N*-(5-chloroquinolin-8-yl)-2,3-dihydro-1H-indene-2-carboxamide (**1u**): White solid. Yield: 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 8.74 (dd, *J* = 4.2, 1.3 Hz, 1H), 8.61 (d, *J* = 8.4 Hz, 1H), 8.51 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.56 – 7.48 (m, 3H), 7.47 (s, 1H), 7.40 (d, *J* = 8.5 Hz, 2H), 7.29 (dd, *J* = 5.1, 3.4 Hz, 2H), 7.19 (dd, *J* = 5.5, 3.2 Hz, 2H), 4.04 (d, *J* = 15.6 Hz, 2H), 3.52 (d, *J* = 15.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 148.7, 142.5, 140.7, 139.1, 133.7, 133.3, 132.0, 128.6, 127.1, 127.0, 125.8, 124.3, 124.3, 122.3, 121.3, 116.1, 60.9, 43.3. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{19}BrClN_2O$ $[M+H]^+$ 477.0369, found 477.0373.

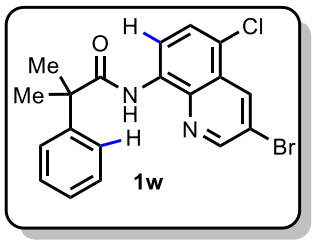


***N*-(5-chloroquinolin-8-yl)-1-phenylcyclohexane-1-carboxamide** (**1v**): White solid. Yield: 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.79 – 8.68 (m, 2H), 8.52 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.59 (dd, *J* = 13.8, 5.1 Hz, 3H), 7.51 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.42 (dd, *J* = 10.6, 5.0 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 1H), 2.60 – 2.49 (m, 2H), 2.26 – 2.14 (m, 2H), 1.81 – 1.61 (m, 5H), 1.48 (ddd, *J* = 16.7, 8.2, 4.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 148.6, 143.3, 139.2, 134.0, 133.2, 129.0, 127.2, 126.9, 126.6, 125.8, 123.9, 122.2, 115.9, 52.4, 34.6, 25.9, 23.1. HRMS (ESI-TOF) *m/z* calcd for $C_{22}H_{22}ClN_2O$ $[M+H]^+$ 365.1421, found 365.1424.

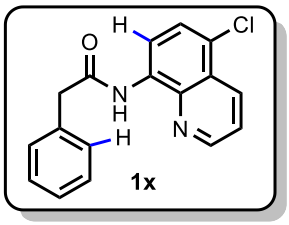
The procedure for the synthesis of substrate (**1w**)



Following the general procedure, compound **1w'** was synthesized smoothly. To a solution of compound **1w'** (1 mmol, 368 mg) in CH_3CN (10 mL), TCCA (0.4 mmol, 93 mg) was added stirred at room temperature for 6 h. At the end of the reaction (monitored by TLC), the mixture was concentrated on a rotary evaporator and the residue was subjected to flash silica gel chromatography to afford the desired substrate **1w**.



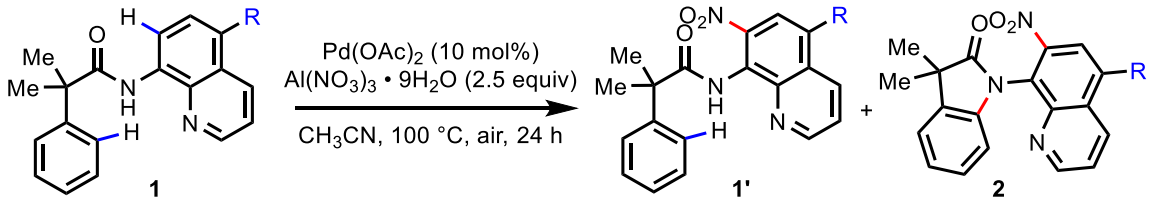
***N*-(3-bromo-5-chloroquinolin-8-yl)-2-methyl-2-phenylpropanamide** (**1w**): White solid. Yield: 60%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.53 (s, 1H), 8.70 (d, *J* = 8.5 Hz, 1H), 8.59 (q, *J* = 2.2 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 1H), 7.51 (dd, *J* = 8.3, 0.9 Hz, 2H), 7.41 (dd, *J* = 10.5, 5.0 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 1H), 1.76 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 149.7, 144.4, 137.1, 134.5, 134.2, 129.0, 128.4, 127.3, 126.6, 126.4, 122.8, 118.9, 116.3, 48.5, 26.9. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{17}BrClN_2O$ $[M+H]^+$ 403.0213, found 403.0210.



***N*-(5-chloroquinolin-8-yl)-2-phenylacetamide** (**1x**): White solid. Yield: 79%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.77 – 8.64 (m, 2H), 8.51 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.51 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.42 (q, *J* = 7.4 Hz, 4H), 7.35 (d, *J* = 6.6 Hz, 1H), 3.89 (s, 2H). The spectral data of the starting material was in accordance with the reported in the literature[4].

Optimization of Reaction Conditions

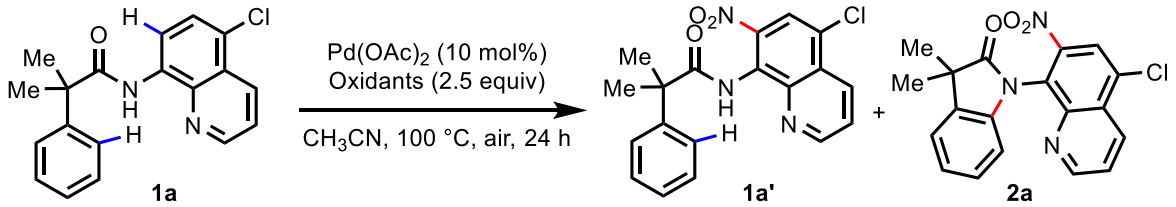
Table S1. Screening of directing groups[a,b]



Entry	Change from above condition	Recover yield [%] (**1**)	Yield [%] (**1'/2**)
1	**1a** R = Cl	0	trace/80[c]
2	**1aa** R = H	90	trace/0
3	**1ab** R = OCH_3	0	trace/0
4	**1ac** R = NO_2	45	8/0

[a]**Conditions**: Substrate **1** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol %), $Al(NO_3)_3·9H_2O$ (2.5 equiv), CH_3CN (2 mL), 100 ℃, under air, 24 h. [b]The yields were detected by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard. [c]Isolated yield.

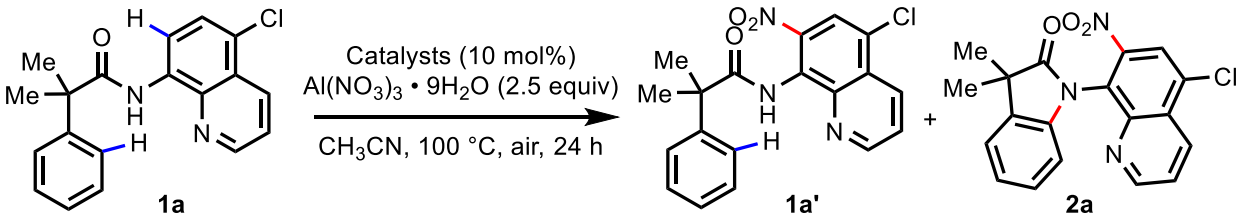
Table S2. Screening of the oxidants[a,b]



Entry	Oxidants	Recover yield [%] (**1**)	Yield [%] (**1'/2**)
1	$Al(NO_3)_3·9H_2O$	0	trace/80[c]
2	$Fe(NO_3)_3·9H_2O$	10	75c/trace
3	$Cu(NO_3)_3·3H_2O$	15	42/0
4	*t*-BuONO	0	70/trace
5	$Co(NO_3)_2·6H_2O$	24	45/0
6	CAN[d]	0	0/0

[a]**Conditions**: Substrate **1a** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol %), oxidants (2.5 equiv), CH_3CN (2 mL), 100 ℃, under air, 24 h. [b]The yields were detected by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard. [c]Isolated yield. [d]CAN = ceric ammonium nitrate.

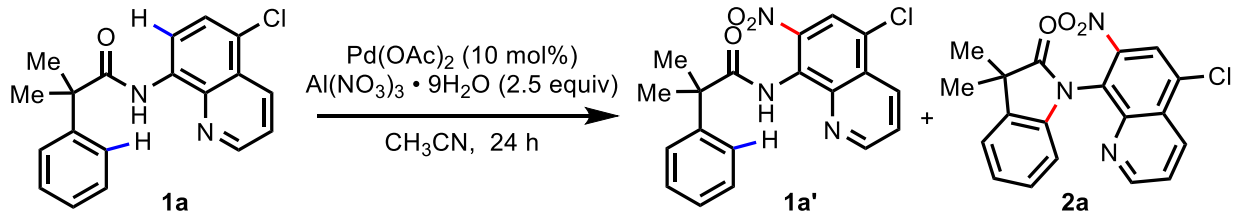
Table S3. Screening of metal catalysts[a,b]



Entry	Catalysts	Yield [%] (**1'/2**)
1	$Pd(OAc)_2$	trace/80[c]
2	$PdCl_2$	0/75
3	$Pd(TFA)_2$	0/60
4	$Cu(OAc)_2$	30/0
5	$Co(OAc)_2$	35/0
6	$Ni(acac)_2$	25/0
7	without catalyst	55/0

[a]**Conditions**: Substrate **1a** (0.2 mmol, 1.0 equiv), catalysts (10 mol %), $Al(NO_3)_3 \cdot 9H_2O$ (2.5 equiv), CH_3CN (2 mL), 100 ℃, under air, 24 h. [b]The yields were detected by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard. [c]Isolated yield.

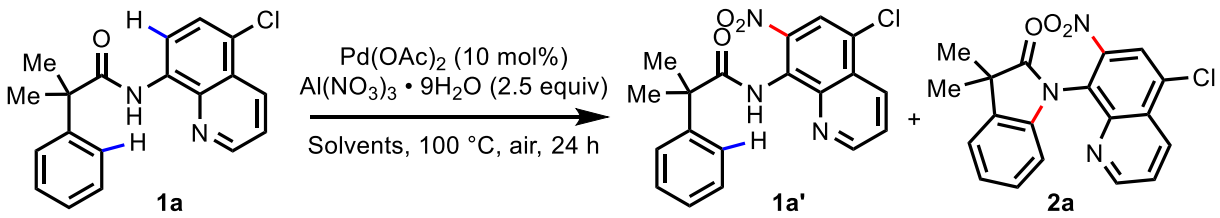
Table S4. Optimization of temperature and atmosphere[a,b]



Entry	Temperature [℃]	Atmosphere	Yield [%] (**1'/2**)
1	100	air	trace/80[c]
2	80	air	30/46
3	90	air	20/55
4	110	air	trace/78[c]
5	100	O_2	trace/80
6	100	Ar	trace/78

[a]**Conditions**: Substrate **1a** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol %), $Al(NO_3)_3 \cdot 9H_2O$ (2.5 equiv), CH_3CN (2 mL), 24 h. [b]The yields were detected by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard. [c]Isolated yield.

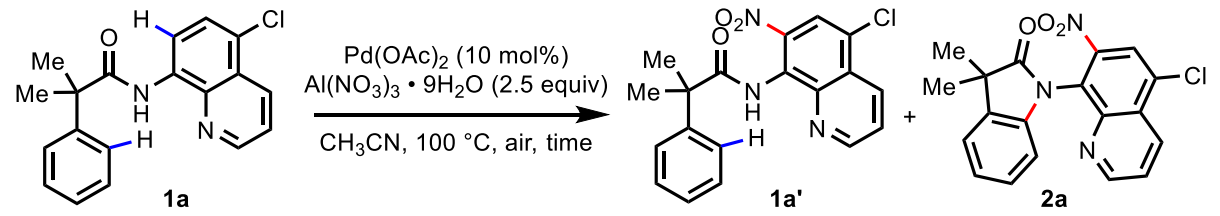
Table S5. Optimization of solvents[a,b]



Entry	Solvents	Yield [%] (**1'/2**)
1	CH_3CN	trace/80[c]
2	DCE	70/0
3	1,4-dioxane	30/0
4	Toluene	40/0
5	DMSO	23/0
6	DMF	20/0
7	HFIP	0/0
8	CH_3CN/H_2O (v:v=2:1)	0/trace

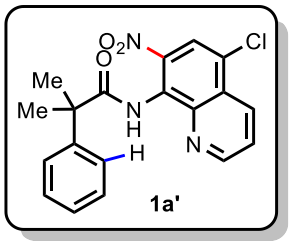
[a]**Conditions**: Substrate **1a** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol %), $Al(NO_3)_3 \cdot 9H_2O$ (2.5 equiv), solvent (2 mL), 100 ℃, under air, 24 h. [b]The yields were detected by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard. [c]Isolated yield.

Table S6. Optimization of reaction time and stoichiometric quantity[a,b]

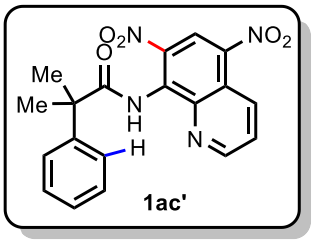


Entry	Time [h]	$Al(NO_3)_3 \cdot 9H_2O$ (equiv)	Yield [%] (**1'/2**)
1	24	2.5	trace/80[c]
2	12	2.5	45/40
3	18	2.5	40/48
4	30	2.5	0/75
5	24	1.0	85/10
6	24	1.5	70/20
7	24	2.0	20/55
8	24	3.0	0/76

[a]**Conditions**: Substrate **1a** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol %), CH_3CN (2 mL), 100 ℃, under air. [b]The yields were detected by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard. [c]Isolated yield.

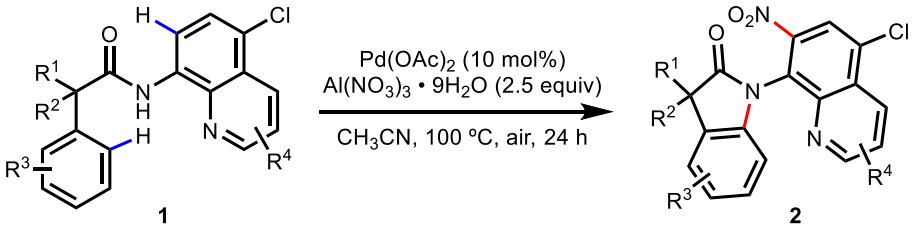


***N*-(5-chloro-7-nitroquinolin-8-yl)-2-methyl-2-phenylpropanamide** (**1a'**): Yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.39 (s, 1H), 8.73 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.54 (dd, *J* = 8.5, 1.5 Hz, 1H), 8.07 (s, 1H), 7.63 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.36 (t, *J* = 7.3 Hz, 1H), 1.74 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 150.6, 143.9, 141.1, 139.6, 133.4, 129.0, 127.6, 127.5, 127.4, 126.6, 125.9, 124.5, 121.8, 48.2, 26.6. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{17}ClN_3O_3$ $[M+H]^+$ 370.0958, found 370.0953.

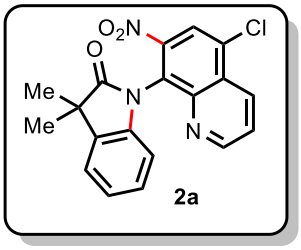


***N*-(5,7-dinitroquinolin-8-yl)-2-methyl-2-phenylpropanamide** (**1ac'**): Yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.83 (s, 1H), 9.21 (d, *J* = 8.8 Hz, 1H), 8.98 (s, 1H), 8.74 (d, *J* = 4.0 Hz, 1H), 7.76 (dd, *J* = 8.8, 4.2 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.1 Hz, 1H), 1.75 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3, 150.1, 144.1, 140.7, 140.4, 136.2, 129.4, 128.9, 128.2, 127.4, 126.6, 123.7, 122.6, 122.1, 48.2, 26.6. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{17}N_4O_5$ $[M+H]^+$ 381.1199, found 381.1198.

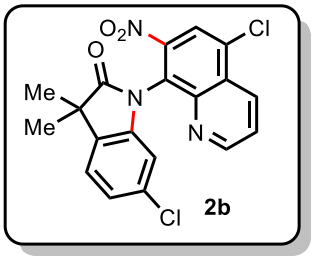
Procedure for the Palladium Catalyzed C(sp^2)−H Amidation



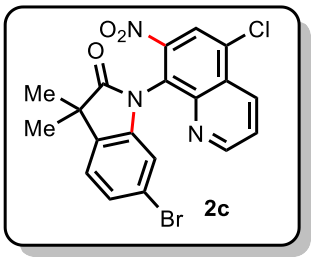
General Procedure: In a 25 mL sealed tube, equipped with a stir bar, was charged with substrates **1** (0.1 mmol), $Pd(OAc)_2$ (10 mol %), $Al(NO_3)_3{\cdot}9H_2O$ (0.25 mmol, 93.8 mg) and CH_3CN (2 mL). The tube was capped, and then the reaction mixture was stirred at 100 ˚C for 24 h. Upon completion, ethyl acetate was added to dilute the mixture and then filtered through a pad of silica gel. The solvent was evaporated under reduced pressure and then purified by column chromatography on silica gel with a gradient eluent of petroleum ether and ethyl acetate to obtain the pure product.



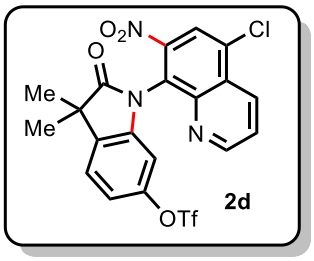
1-(5-chloro-7-nitroquinolin-8-yl)-3,3-dimethylindolin-2-one (**2a**): Yellow solid. Yield: 80%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.69 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.34 (s, 1H), 7.70 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.37 – 7.30 (m, 1H), 7.15 – 7.07 (m, 2H), 6.32 – 6.25 (m, 1H), 1.61 (s, 3H), 1.56 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.2, 153.4, 146.8, 144.9, 142.7, 135.6, 133.6, 133.4, 129.7, 127.5, 126.8, 124.9, 123.2, 122.7, 121.7, 109.6, 44.8, 24.7, 24.4. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{15}ClN_3O_3$ $[M+H]^+$ 368.0802, found 368.0805.



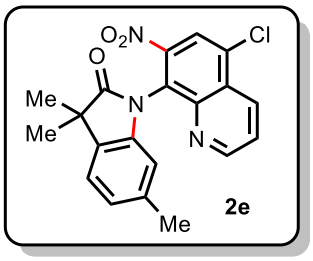
6-chloro-1-(5-chloro-7-nitroquinolin-8-yl)-3,3-dimethylindolin-2-one (**2b**): Yellow solid. Yield: 72%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (d, *J* = 4.0 Hz, 1H), 8.71 (d, *J* = 8.6 Hz, 1H), 8.36 (s, 1H), 7.73 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 1H), 6.27 (s, 1H), 1.59 (s, 3H), 1.54 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.0, 153.6, 146.7, 144.7, 143.8, 134.1, 134.0, 133.5, 133.2, 129.8, 126.1, 125.1, 123.6, 123.1, 121.8, 110.4, 44.5, 24.6, 24.2. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{14}Cl_2N_3O_3$ $[M+H]^+$ 402.0412, found 402.0415.



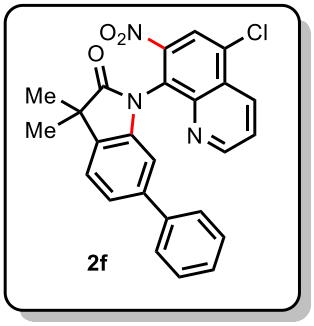
6-bromo-1-(5-chloro-7-nitroquinolin-8-yl)-3,3-dimethylindolin-2-one (**2c**): Yellow solid. Yield: 65%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 – 8.97 (m, 1H), 8.70 (d, *J* = 8.6 Hz, 1H), 8.36 (s, 1H), 7.73 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.25 (dd, *J* = 9.8, 1.8 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 6.42 (s, 1H), 1.59 (s, 3H), 1.54 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 180.5, 154.6, 147.3, 144.5, 144.3, 134.5, 134.0, 133.7, 129.7, 126.4, 126.1, 125.4, 125.2, 122.2, 120.9, 113.7, 44.4, 24.4, 24.1. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{14}BrClN_3O_3$ $[M+H]^+$ 445.9907, found 445.9905.



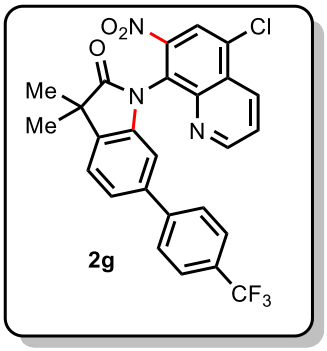
1-(5-chloro-7-nitroquinolin-8-yl)-3,3-dimethyl-2-oxoindolin-6-yl trifluoromethanesulfonate (**2d**): Yellow solid. Yield: 78%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.72 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.36 (s, 1H), 7.74 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.02 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.21 (d, *J* = 2.2 Hz, 1H), 1.60 (s, 3H), 1.55 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.6, 153.4, 148.8, 146.6, 144.4, 144.2, 135.5, 134.3, 133.6, 129.8, 125.4, 125.1, 123.7, 121.8, 115.5, 104.2, 44.5, 24.5, 24.2. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{14}ClF_3N_3O_6S$ $[M+H]^+$ 516.0244, found 516.0240.



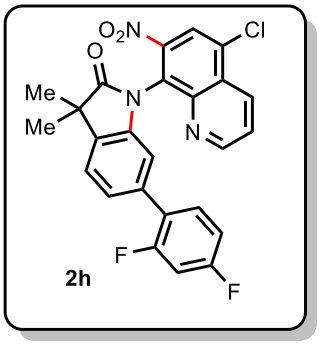
1-(5-chloro-7-nitroquinolin-8-yl)-3,3,6-trimethylindolin-2-one (**2e**): Yellow solid. Yield: 65%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (d, *J* = 3.9 Hz, 1H), 8.70 (d, *J* = 8.5 Hz, 1H), 8.35 (s, 1H), 7.71 (dd, *J* = 8.5, 4.0 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.09 (s, 1H), 2.19 (s, 3H), 1.59 (s, 3H), 1.54 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.5, 153.4, 146.8, 145.0, 142.8, 137.6, 133.6, 133.4, 132.8, 129.7, 127.0, 124.9, 123.8, 122.4, 121.7, 110.3, 44.6, 24.8, 24.4, 21.6. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{17}ClN_3O_3$ $[M+H]^+$ 382.0958, found 382.0956.



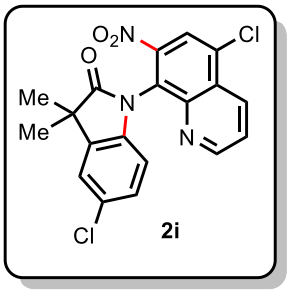
1-(5-chloro-7-nitroquinolin-8-yl)-3,3-dimethyl-6-phenylindolin-2-one (**2f**): Yellow oil. Yield: 73%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (d, *J* = 2.6 Hz, 1H), 8.70 (d, *J* = 8.5 Hz, 1H), 8.36 (s, 1H), 7.70 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.39 (dd, *J* = 15.6, 7.6 Hz, 3H), 7.32 (dd, *J* = 12.5, 7.1 Hz, 3H), 7.26 (t, *J* = 7.1 Hz, 1H), 6.46 (s, 1H), 1.66 (s, 3H), 1.60 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.3, 153.5, 146.9, 145.0, 143.3, 141.3, 141.1, 134.7, 133.8, 133.4, 129.7, 128.6, 127.4, 127.2, 126.7, 124.9, 122.9, 122.3, 121.8, 108.5, 44.7, 24.8, 24.4. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{19}ClN_3O_3$ $[M+H]^+$ 444.1115, found 444.1112.



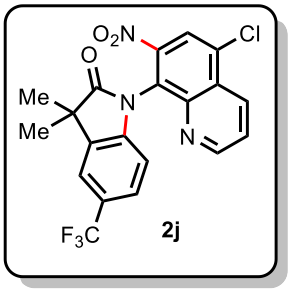
1-(5-chloro-7-nitroquinolin-8-yl)-3,3-dimethyl-6-(4-(trifluoromethyl)phenyl)indolin-2-one (**2g**): Yellow oil, Yield: 85%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.71 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.36 (s, 1H), 7.72 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.33 (dd, *J* = 7.7, 1.5 Hz, 1H), 6.46 (s, 1H), 1.66 (s, 3H), 1.60 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.2, 153.5, 146.9, 144.9, 144.5, 143.5, 139.8, 135.7, 133.9, 133.5, 129.8, 128.4, 127.5, 126.5, 125.6 (dd, *J* = 7.6, 3.8 Hz), 125.0, 123.2, 122.5, 121.8, 108.6, 44.7, 24.7, 24.4. HRMS (ESI-TOF) *m/z* calcd for $C_{26}H_{18}ClF_3N_3O_3$ $[M+H]^+$ 512.0989, found 512.0987.



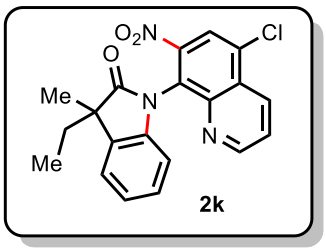
1-(5-chloro-7-nitroquinolin-8-yl)-6-(2,4-difluorophenyl)-3,3-dimethylindolin-2-one (**2h**): Yellow oil, Yield: 82%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (d, *J* = 3.0 Hz, 1H), 8.69 (d, *J* = 8.5 Hz, 1H), 8.34 (s, 1H), 7.71 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.27 – 7.21 (m, 2H), 6.81 (dt, *J* = 19.4, 8.4 Hz, 2H), 6.40 (s, 1H), 1.65 (s, 3H), 1.59 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.2, 160.9 (ddd, *J* = 262.5, 249.8, 11.7 Hz), 153.4, 146.8, 144.8, 142.9, 135.2, 134.5, 133.8, 133.4, 131.5 (dd, *J* = 9.5, 4.8 Hz), 129.7, 126.5, 125.0, 124.0, 122.7, 121.7, 111.7 – 111.2 (m), 110.3 (d, *J* = 2.8 Hz), 104.5 – 104.0 (m), 44.8, 24.7, 24.4. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{17}ClF_2N_3O_3$ $[M+H]^+$ 480.0927, found 480.0924.



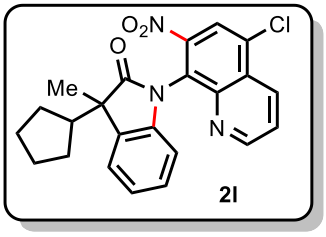
5-chloro-1-(5-chloro-7-nitroquinolin-8-yl)-3,3-dimethylindolin-2-one (**2i**): Yellow solid. Yield: 77%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (d, *J* = 2.7 Hz, 1H), 8.70 (d, *J* = 8.6 Hz, 1H), 8.34 (d, *J* = 3.9 Hz, 1H), 7.72 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.31 (d, *J* = 1.8 Hz, 1H), 7.08 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.22 (d, *J* = 8.3 Hz, 1H), 1.60 (s, 3H), 1.55 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.6, 153.5, 146.7, 144.7, 141.3, 137.2, 133.9, 133.5, 129.7, 128.5, 127.5, 126.3, 125.0, 123.3, 121.7, 110.8, 45.1, 24.6, 24.2. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{14}Cl_2N_3O_3$ $[M+H]^+$ 402.0412, found 402.0415.



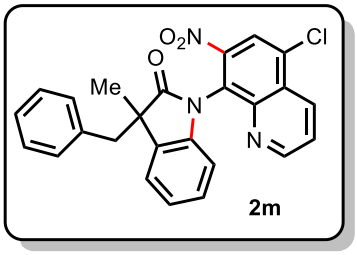
1-(5-chloro-7-nitroquinolin-8-yl)-3,3-dimethyl-5-(trifluoromethyl)indolin-2-one (**2j**): Yellow oil. Yield: 51%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (d, *J* = 3.4 Hz, 1H), 8.72 (d, *J* = 8.5 Hz, 1H), 8.37 (s, 1H), 7.73 (dd, *J* = 8.5, 4.0 Hz, 1H), 7.57 (s, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 6.36 (d, *J* = 8.2 Hz, 1H), 1.63 (s, 3H), 1.58 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.8, 153.5, 146.7, 145.6, 144.7, 136.1, 134.2, 133.5, 129.8, 126.0, 125.6 (d, *J* = 9.4 Hz), 125.3 (d, *J* = 4.4 Hz), 125.1, 121.8, 119.9 (dd, *J* = 7.5, 3.5 Hz), 109.6, 44.8, 24.5, 24.2. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{14}ClF_3N_3O_3$ $[M+H]^+$ 436.0676, found 436.0672.



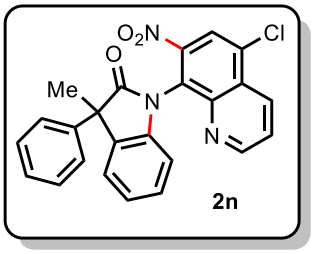
1-(5-chloro-7-nitroquinolin-8-yl)-3-ethyl-3-methylindolin-2-one (**2k**): Yellow solid. Yield: 45%.^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 – 8.92 (m, 1H), 8.68 (dd, *J* = 8.6, 1.1 Hz, 1H), 8.31 (s, 1H), 7.68 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.30 (dd, *J* = 5.5, 2.9 Hz, 1H), 7.15 – 7.08 (m, 2H), 6.31 (dd, *J* = 5.8, 2.8 Hz, 1H), 2.10 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.95 (dq, *J* = 14.8, 7.5 Hz, 1H), 1.60 (s, 3H), 0.86 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.0, 153.4, 147.5, 144.8, 143.7, 133.9, 133.8, 133.4, 129.7, 127.5, 126.8, 124.8, 123.1, 123.0, 121.5, 109.4, 49.7, 31.3, 24.5, 9.1. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{17}ClN_3O_3$ $[M+H]^+$ 382.0958, found 382.0955.



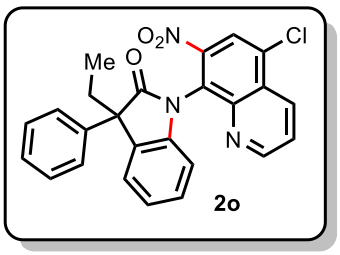
1-(5-chloro-7-nitroquinolin-8-yl)-3-cyclopentyl-3-methylindolin-2-one (**2l**): Yellow oil, Yield: 57%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.94 (d, *J* = 3.9 Hz, 1H), 8.67 (d, *J* = 8.6 Hz, 1H), 8.29 (s, 1H), 7.67 (dd, *J* = 8.5, 4.0 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.14 – 7.04 (m, 2H), 6.30 (d, *J* = 6.8 Hz, 1H), 2.46 (dt, *J* = 17.1, 8.5 Hz, 1H), 1.85 (d, *J* = 5.1 Hz, 1H), 1.79 – 1.73 (m, 1H), 1.65 (s, 3H), 1.63 – 1.52 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.3, 153.4, 147.9, 144.7, 143.8, 133.9, 133.8, 133.4, 129.7, 127.4, 126.6, 124.8, 123.7, 122.8, 121.3, 109.3, 50.7, 47.7, 27.8, 27.1, 25.2, 25.1, 23.3. HRMS (ESI-TOF) *m/z* calcd for $C_{23}H_{21}ClN_3O_3$ $[M+H]^+$ 422.1271, found 422.1271.



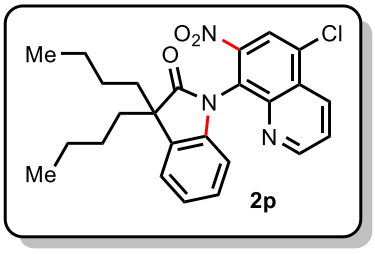
3-benzyl-1-(5-chloro-7-nitroquinolin-8-yl)-3-methylindolin-2-one (**2m**): Yellow solid. Yield: 55%.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (dd, *J* = 4.0, 1.5 Hz, 1H), 8.64 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.31 (s, 1H), 7.64 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.20 – 7.13 (m, 4H), 7.09 – 7.04 (m, 4H), 6.20 – 6.11 (m, 1H), 3.30 (d, *J* = 13.4 Hz, 1H), 3.24 (d, *J* = 13.3 Hz, 1H), 1.62 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.9, 153.0, 146.3, 144.8, 143.2, 136.4, 133.4, 133.1, 133.0, 130.7, 129.8, 129.5, 128.1, 127.8, 127.6, 126.5, 126.4, 124.7, 123.9, 122.7, 121.7, 109.6, 50.2, 43.8, 23.5. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{19}ClN_3O_3$ $[M+H]^+$ 444.1115, found 444.1113.



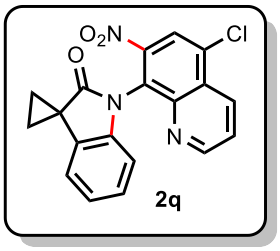
1-(5-chloro-7-nitroquinolin-8-yl)-3-methyl-3-phenylindolin-2-one (**2n**): Yellow solid. Yield: 53%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (dd, *J* = 4.0, 1.4 Hz, 1H), 8.69 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.37 (s, 1H), 7.70 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.62 (d, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.27 (d, *J* = 7.4 Hz, 1H), 7.23 – 7.19 (m, 1H), 7.15 – 7.06 (m, 2H), 6.34 (d, *J* = 7.3 Hz, 1H), 1.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.3, 153.4, 146.6, 145.0, 143.1, 140.9, 135.7, 133.8, 133.4, 129.7, 128.6, 128.2, 128.1, 127.8, 127.3, 127.1, 126.7, 125.0, 124.2, 123.5, 121.8, 109.7, 52.9, 22.8. HRMS (ESI-TOF) *m/z* calcd for $C_{24}H_{17}ClN_3O_3$ $[M+H]^+$ 430.0958, found 430.0955.



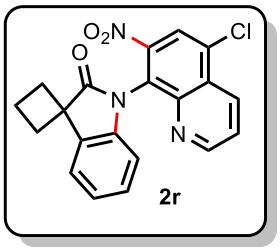
1-(5-chloro-7-nitroquinolin-8-yl)-3-ethyl-3-phenylindolin-2-one (**2o**): Yellow solid. Yield: 58%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.69 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.31 (s, 1H), 7.70 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.51 – 7.44 (m, 2H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.32 – 7.26 (m, 2H), 7.19 – 7.13 (m, 2H), 6.36– 6.34 (m, 1H), 2.70 – 2.63 (m, 1H), 2.47 – 2.40 (m, 1H), 1.08 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.6, 153.2, 147.0, 144.9, 144.3, 134.0, 133.8, 133.4, 132.5, 129.7, 128.6, 127.9, 127.6, 127.4, 126.8, 125.1, 124.9, 123.2, 121.7, 109.6, 58.0, 31.0, 9.3. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{19}ClN_3O_3$ $[M+H]^+$ 444.1115, found 444.1113.



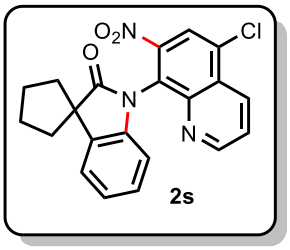
3,3-dibutyl-1-(5-chloro-7-nitroquinolin-8-yl)indolin-2-one (**2p**): Yellow solid. Yield: 81%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.93 (dd, *J* = 4.0, 1.3 Hz, 1H), 8.68 (dd, *J* = 8.6, 1.3 Hz, 1H), 8.29 (s, 1H), 7.68 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.13 – 7.09 (m, 2H), 6.39 – 6.20 (m, 1H), 2.04 – 1.85 (m, 4H), 1.58 – 1.51 (m, 1H), 1.36 – 1.10 (m, 7H), 0.86 (dd, *J* = 15.7, 7.4 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.5, 152.9, 147.4, 144.9, 144.2, 133.6, 133.3, 132.8, 129.5, 127.3, 126.8, 124.7, 123.2, 122.8, 121.5, 109.2, 53.7, 38.7, 38.1, 26.8, 26.3, 23.2, 23.1, 14.2, 13.8. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{27}ClN_3O_3$ $[M+H]^+$ 452.1741, found 452.1740.



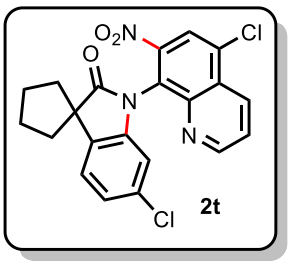
1'-(5-chloro-7-nitroquinolin-8-yl)spiro[cyclopropane-1,3'-indolin]-2'-one (**2q**): Yellow solid. Yield: 40%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (d, *J* = 3.0 Hz, 1H), 8.77 – 8.61 (m, 1H), 8.33 (s, 1H), 7.72 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.11 – 7.07 (m, 2H), 6.96 (dd, *J* = 5.4, 3.1 Hz, 1H), 6.36 (dd, *J* = 5.7, 2.9 Hz, 1H), 1.95 – 1.87 (m, 2H), 1.75 – 1.67 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.1, 153.4, 146.8, 145.0, 143.4, 133.6, 133.4, 130.6, 129.6, 126.6, 124.8, 122.9, 121.8, 118.7, 109.7, 27.8, 20.5, 20.0. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{13}ClN_3O_3$ $[M+H]^+$ 366.0645, found 366.0647.



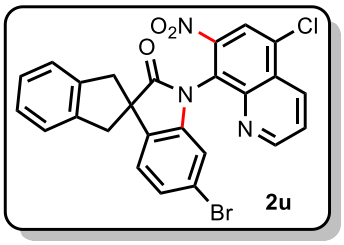
1'-(5-chloro-7-nitroquinolin-8-yl)spiro[cyclobutane-1,3'-indolin]-2'-one (**2r**): Yellow solid. Yield: 65%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.70 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.34 (s, 1H), 7.71 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.63 (d, *J* = 6.8 Hz, 1H), 7.15 (dt, *J* = 7.5, 3.8 Hz, 1H), 7.09 (td, *J* = 7.7, 1.2 Hz, 1H), 6.24 (d, *J* = 7.7 Hz, 1H), 2.85 – 2.76 (m, 2H), 2.63 – 2.52 (m, 2H), 2.48 – 2.39 (m, 1H), 2.32 – 2.22 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.5, 153.3, 146.6, 145.0, 142.9, 133.9, 133.4, 129.6, 127.6, 126.9, 124.9, 123.4, 122.8, 121.8, 109.4, 48.8, 32.3, 31.4, 16.8. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{15}ClN_3O_3$ $[M+H]^+$ 380.0802, found 380.0797.



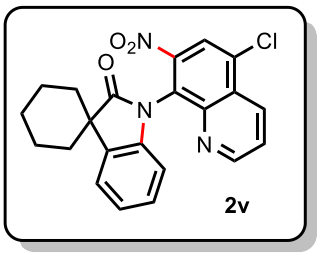
1'-(5-chloro-7-nitroquinolin-8-yl)spiro[cyclopentane-1,3'-indolin]-2'-one (**2s**): Yellow solid. Yield: 75%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.69 (d, *J* = 8.1 Hz, 1H), 8.34 (s, 1H), 7.71 (d, *J* = 5.7 Hz, 1H), 7.33 (d, *J* = 6.8 Hz, 1H), 7.12 – 7.06 (m, 2H), 6.26 (d, *J* = 7.0 Hz, 1H), 2.39 – 2.33 (m, 2H), 2.12 – 2.05 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.0, 153.3, 146.7, 145.0, 142.9, 136.4, 133.5, 133.4, 129.6, 127.2, 127.0, 124.9, 123.3, 122.7, 121.8, 109.4, 54.5, 38.9, 38.7, 26.8, 26.7. HRMS (ESI-TOF) *m/z* calcd for $C_{21}H_{17}ClN_3O_3$ $[M+H]^+$ 394.0958, found 394.0956.



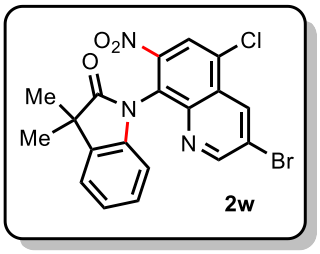
6'-chloro-1'-(5-chloro-7-nitroquinolin-8-yl)spiro[cyclopentane-1,3'-indolin]-2'-one (**2t**): Yellow solid. Yield: 78%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (d, *J* = 3.5 Hz, 1H), 8.70 (d, *J* = 8.5 Hz, 1H), 8.36 (d, *J* = 4.8 Hz, 1H), 7.72 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.07 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.25 (s, 1H), 2.38 – 2.32 (m, 2H), 2.12 – 2.02 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.9, 153.5, 146.6, 144.7, 144.0, 134.7, 133.9, 133.5, 132.9, 129.7, 126.3, 125.1, 123.6, 123.2, 121.8, 110.2, 54.1, 38.8, 38.7, 26.8, 26.6. HRMS (ESI-TOF) *m/z* calcd for $C_{21}H_{16}Cl_2N_3O_3$ $[M+H]^+$ 428.0569, found 428.0573.



6'-bromo-1'-(5-chloro-7-nitroquinolin-8-yl)-1,3-dihydrospiro[indene-2,3'-indolin]-2'-one (**2u**): Yellow solid. Yield: 60%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.07 (d, *J* = 2.9 Hz, 1H), 8.73 (d, *J* = 7.7 Hz, 1H), 8.39 (s, 1H), 7.76 (dd, *J* = 8.6, 4.0 Hz, 1H), 7.28 (dd, *J* = 16.2, 6.2 Hz, 4H), 7.08 (d, *J* = 7.0 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.42 (s, 1H), 3.77 (t, *J* = 15.0 Hz, 2H), 3.37 (d, *J* = 15.8 Hz, 1H), 3.31 (d, *J* = 15.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.9, 153.7, 146.6, 144.7, 143.9, 140.9, 140.8, 134.9, 134.2, 133.6, 129.8, 127.3, 127.2, 126.3, 125.2, 124.9, 124.8, 124.6, 123.3, 121.9, 121.3, 113.1, 54.4, 44.5, 44.1, 43.9. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{16}BrClN_3O_3$ $[M+H]^+$ 520.0064, found 520.0062.

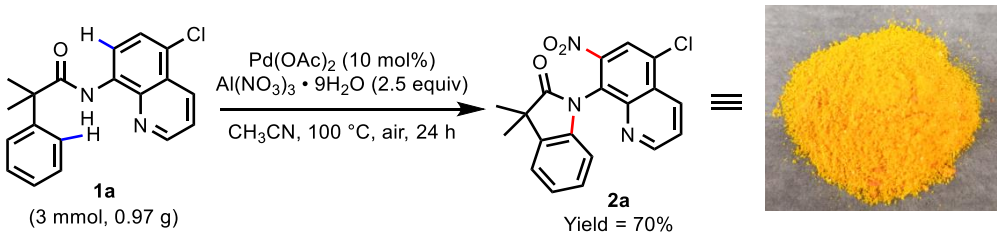


1'-(5-chloro-7-nitroquinolin-8-yl)spiro[cyclohexane-1,3'-indolin]-2'-one (**2v**): Yellow solid. Yield: 78%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 – 8.95 (m, 1H), 8.69 (d, *J* = 8.6 Hz, 1H), 8.33 (s, 1H), 7.70 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.56 (dd, *J* = 5.3, 3.3 Hz, 1H), 7.10 (dt, *J* = 7.7, 3.8 Hz, 2H), 6.27 (dd, *J* = 5.5, 3.4 Hz, 1H), 2.13 – 1.95 (m, 4H), 1.95 – 1.88 (m, 1H), 1.85 – 1.80 (m, 3H), 1.75 – 1.65 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.4, 153.4, 146.8, 144.9, 142.9, 135.2, 133.5, 133.4, 129.6, 127.3, 126.8, 124.9, 124.1, 122.7, 121.7, 109.6, 47.9, 33.4, 33.0, 25.3, 21.2, 21.1. HRMS (ESI-TOF) *m/z* calcd for $C_{22}H_{19}ClN_3O_3$ $[M+H]^+$ 408.1115, found 408.1118.



1-(3-bromo-5-chloro-7-nitroquinolin-8-yl)-3,3-dimethylindolin-2-one (**2w**): Yellow solid. Yield: 71%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97 (d, *J* = 2.1 Hz, 1H), 8.84 (d, *J* = 2.1 Hz, 1H), 8.37 (s, 1H), 7.38 – 7.30 (m, 1H), 7.14 – 7.09 (m, 2H), 6.27 (d, *J* = 7.4 Hz, 1H), 1.60 (s, 3H), 1.55 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.1, 154.7, 146.7, 143.1, 142.5, 135.6, 134.9, 132.4, 130.4, 127.6, 127.1, 123.3, 123.0, 122.8, 122.7, 109.5, 44.8, 24.7, 24.4. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{14}BrClN_3O_3$ $[M+H]^+$ 445.9907, found 445.9908.

Scale up Experiment on Gram Scale



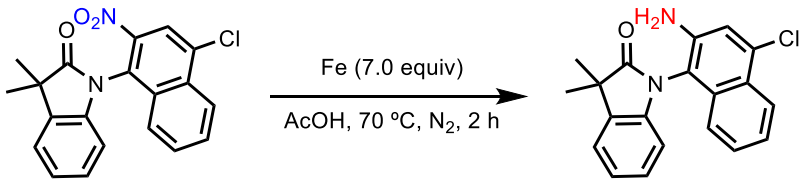
1a
(3 mmol, 0.97 g)

2a
Yield = 70%

In a 100 mL sealed tube, equipped with a stir bar, was charged with substrates **1a** (0.97 g, 3 mmol), $Pd(OAc)_2$ (67.2 mg, 10 mol %), $Al(NO_3)_3{\cdot}9H_2O$ (2.82 g, 7.5 mmol) and CH_3CN (30 mL). The tube was capped, and then the reaction mixture was stirred at 100 ˚C for 24 h. Upon completion, ethyl acetate was added to dilute the mixture and then filtered through a pad of silica gel. The solvent was evaporated under reduced pressure and then purified by column chromatography on silica gel with a gradient eluent of petroleum ether and ethyl acetate to obtain the pure product **2a** as a yellow solid (0.77 g, isolated yield: 70%)

Procedure of Auxiliary Removal and Derivatization

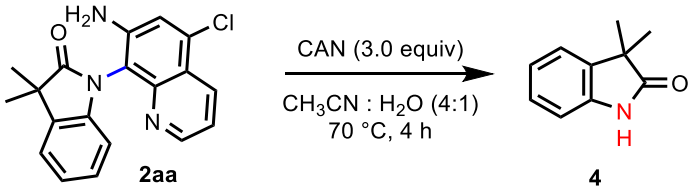
1-(7-amino-5-chloroquinolin-8-yl)-3,3-dimethylindolin-2-one (**2aa**)



2a **2aa**

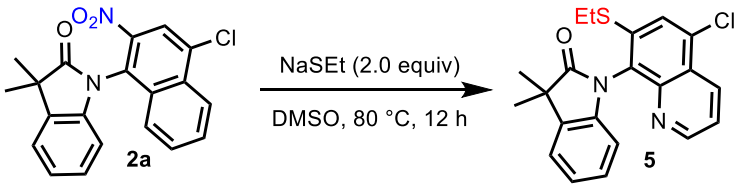
Oxindole **2a** (0.2 mmol, 73 mg) was dissolved in 10 mL of acetic acid, and the iron powder (1.4 mmol, 78.4 mg,) was added to the solution. The mixture was heated to 70 °C for 2 h under nitrogen. The reaction was filtered through a Celite pad, and washed with ethyl acetate. The filtrate was basified by 4M NaOH aq. until pH = 10, extracted with ethyl acetate for three times. The combined organic layer was washed with brine and dried by anhydrous Na_2SO_4, and concentrated in vacuo. The resulting crude amine was purified by column chromatography on silica gel with a gradient eluent of petroleum ether and ethyl acetate to give **2aa** as a white solid in 95% isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.37 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.33 (dd, *J* = 6.7, 1.8 Hz, 1H), 7.27 – 7.20 (m, 2H), 7.14 – 7.02 (m, 2H), 6.37 (dd, *J* = 6.2, 2.5 Hz, 1H), 4.24 (s, 2H), 1.66 (s, 3H), 1.58 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 181.5, 152.0, 147.9, 146.8, 143.6, 136.4, 132.8, 131.6, 127.8, 123.0, 122.4, 119.2, 119.0, 118.4, 109.5, 109.3, 44.3, 25.8, 24.1. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{17}ClN_3O$ $[M+H]^+$ 338.1060, found 338.1063.

3,3-dimethylindolin-2-one (**4**)



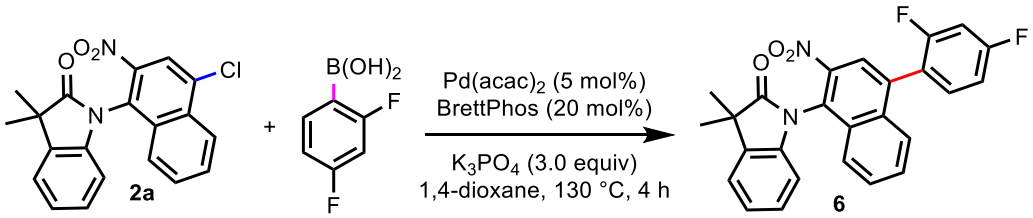
In a 25 mL sealed tube, a mixture of **2aa** (0.1 mmol, 34 mg) and CAN (0.3 mmol, 164 mg) dissolved in CH_3CN (4 mL) and H_2O (1 mL) was stirred in oil bath at 70 °C for 4 h. Then, the mixture was quenched with H_2O (20 mL) and extracted with ethyl acetate (20 mL) for three times. The organic layer was dried over Na_2SO_4. After filtration and evaporation, the crude product was purified by column chromatography on silica gel to give **4** as a white solid in 62 % yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.22 – 7.18 (m, 2H), 7.06 (t, *J* = 8.0 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 1.41 (s, 6H). The ^{1}HNMR spectral data was in accordance with the reported data in the literature.[6]

1-(5-chloro-7-(ethylthio)quinolin-8-yl)-3,3-dimethylindolin-2-one (**5**)



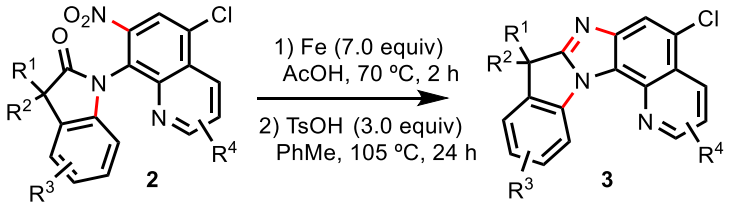
A mixture of **2a** (0.1 mmol, 36.7 mg), NaSEt (0.2 mmol, 16.8 mg), and DMSO (2 mL) was stirred in a reaction tube at 80 °C for 12 h. The resulting mixture was then quenched with water. The mixture was extracted with ethyl acetate for three times, and the combined organic layer was dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel to give **5** as a grey solid in 85% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.51 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.70 (s, 1H), 7.43 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.33 (dd, *J* = 5.6, 3.0 Hz, 1H), 7.12 – 7.05 (m, 2H), 6.25 (dd, *J* = 5.0, 3.8 Hz, 1H), 3.10 – 2.96 (m, 2H), 1.63 (s, 3H), 1.59 (s, 3H), 1.34 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.2, 152.3, 145.5, 142.7, 140.9, 135.9, 133.1, 132.9, 127.5, 125.1, 124.8, 122.6, 122.6, 121.7, 109.4, 44.8, 26.5, 25.0, 24.6, 14.0. HRMS (ESI-TOF) *m/z* calcd for $C_{21}H_{20}ClN_2OS$ $[M+H]^+$ 383.0985, found 383.0981.

1-(5-(2,4-difluorophenyl)-7-nitroquinolin-8-yl)-3,3-dimethylindolin-2-one (**6**)



A mixture of **2a** (0.2 mmol, 73.4 mg), $Pd(acac)_2$ (5 mol %, 3.4 mg), BrettPhos (20 mol %, 21.5 mg), boronic acid (0.3 mmol, 57.0 mg), K_3PO_4 (0.6 mmol, 127.2 mg) in 1,4-dioxane (3 mL) was stirred at 130 °C in a 25 mL sealed tube for 4 h. After completed, cooling to room temperature, the opaque solution was filtered through Celite and the filtrate was concentrated in vacuo. Column purification (5:1 petroleum ether /ethyl acetate) gave **6** as a yellow oil (Yield: 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 – 8.93 (m, 1H), 8.18 (s, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.56 (dd, *J* = 8.6, 4.0 Hz, 1H), 7.47 (dd, *J* = 14.7, 8.2 Hz, 1H), 7.40 – 7.31 (m, 1H), 7.19 – 7.01 (m, 4H), 6.38 (d, *J* = 37.1 Hz, 1H), 1.64 (s, 3H), 1.58 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.4, 164.7 (d, *J* = 11.6 Hz), 162.7 (d, *J* = 11.4 Hz), 152.8, 146.7, 144.6, 142.9, 135.7 (d, *J* = 19.8 Hz), 134.5, 133.0, 130.4, 127.5, 124.3, 123.1 (d, *J* = 7.4 Hz), 122.6, 120.6 (d, *J* = 12.4 Hz), 112.6, 112.4, 109.9, 109.7, 104.8, 104.6, 44.9, 24.7, 24.4. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{18}F_2N_3O_3$ $[M+H]^+$ 446.1316, found 446.1314.

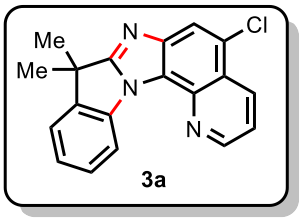
Procedure for the Synthesis of Novel Polycyclic Compounds



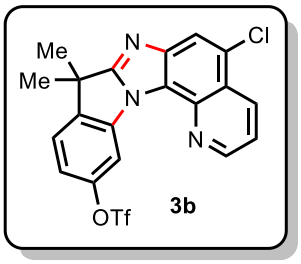
General procedure:

Step 1: Oxindole substrates **2** (0.2 mmol) was dissolved in 10 mL of acetic acid, and the iron powder (1.4 mmol, 78.4 mg) was added to the solution. The mixture was heated to 70 °C for 2 h under nitrogen. The reaction was filtered through a Celite pad, and washed with ethyl acetate. The filtrate was basified by 4M NaOH aq. until pH = 10, extracted with ethyl acetate for three times. The combined organic layer was washed with brine and dried by anhydrous Na_2SO_4, and concentrated in vacuo. The resulting crude amine was used for next step without further purification.

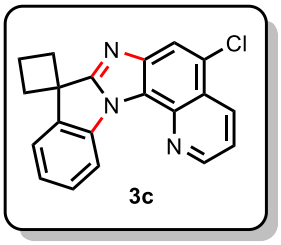
Step 2: Crude amine was dissolved in 10 mL toluene, and $TsOH \cdot H_2O$ (0.6 mmol, 114 mg) was added to the solution. The mixture was heated to 105 °C for 24 h. After the reaction completed, diluted with 30 mL ethyl acetate, the solution was basified by 1N NaOH aq. until pH = 10, extracted with ethyl acetate for three times. The combined organic layer was washed with brine and dried by anhydrous Na_2SO_4, and concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel.



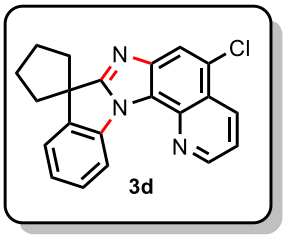
5-chloro-8,8-dimethyl-8*H*-indolo[1',2':1,2]imidazo[4,5-h]quinoline (**3a**): White solid. Yield: 86%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.40 (d, *J* = 7.9 Hz, 1H), 9.07 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.71 (dd, *J* = 8.5, 1.5 Hz, 1H), 8.07 (s, 1H), 7.57 – 7.49 (m, 2H), 7.46 (d, *J* = 7.1 Hz, 1H), 7.32 (td, *J* = 7.5, 0.8 Hz, 1H), 1.73 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 149.1, 146.7, 143.5, 137.9, 133.6, 128.3, 125.8, 125.5, 125.3, 123.1, 122.9, 121.1, 120.1, 116.7, 40.5, 26.0. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{15}ClN_3$ $[M+H]^+$ 320.0955, found 320.0953.



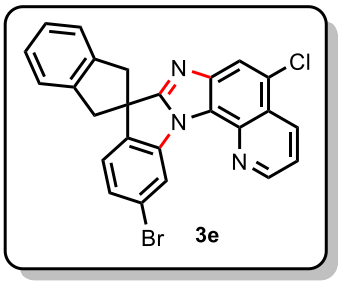
5-chloro-8,8-dimethyl-8*H*-indolo[1',2':1,2]imidazo[4,5-h]quinolin-11-yl trifluoromethanesulfonate (**3b**): White solid. Yield: 72%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (s, 1H), 9.05 (d, *J* = 3.7 Hz, 1H), 8.74 (d, *J* = 8.4 Hz, 1H), 8.07 (s, 1H), 7.60 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.51 (d, *J* = 8.2 Hz, 1H), 7.22 (d, *J* = 7.3 Hz, 1H), 1.75 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 149.5, 149.3, 146.9, 143.6, 139.0, 137.8, 134.0, 126.3, 125.6, 124.1, 123.6, 121.2, 120.7, 118.0, 110.7, 40.8, 25.8. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{14}ClF_3N_3O_3S$ $[M+H]^+$ 468.0396, found 468.0395.



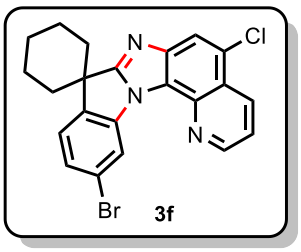
5'-chlorospiro[cyclobutane-1,8'-indolo[1',2':1,2]imidazo[4,5-h]quinoline] (**3c**): White solid. Yield: 87%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (d, *J* = 7.9 Hz, 1H), 9.03 – 8.99 (m, 1H), 8.66 (d, *J* = 8.5 Hz, 1H), 8.08 (s, 1H), 7.74 (d, *J* = 7.4 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 2.96 – 2.89 (m, 2H), 2.80 – 2.63 (m, 3H), 2.46 – 2.36 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2, 149.2, 146.9, 141.9, 138.1, 137.9, 133.7, 128.4, 125.9, 125.5, 123.2, 121.2, 120.4, 116.3, 44.6, 33.1, 17.0. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{15}ClN_3$ $[M+H]^+$ 332.0955, found 332.0952.



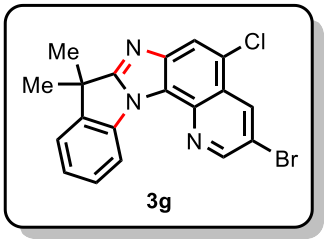
5'-chlorospiro[cyclopentane-1,8'-indolo[1',2':1,2]imidazo[4,5-h]quinoline] (**3d**): White solid. Yield: 80%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.39 (d, *J* = 7.9 Hz, 1H), 9.05 (dd, *J* = 4.2, 1.3 Hz, 1H), 8.69 (dd, *J* = 8.5, 1.3 Hz, 1H), 8.08 (s, 1H), 7.55 – 7.39 (m, 3H), 7.29 (t, *J* = 7.5 Hz, 1H), 2.43 – 2.32 (m, 4H), 2.24 – 2.14 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.1, 149.2, 147.0, 143.8, 138.3, 138.0, 133.7, 128.1, 125.8, 125.4, 123.2, 123.2, 121.2, 120.1, 116.4, 50.4, 39.4, 26.6. HRMS (ESI-TOF) *m/z* calcd for $C_{21}H_{17}ClN_3$ $[M+H]^+$ 346.1111, found 346.1106.



11'-bromo-5'-chloro-1,3-dihydrospiro[indene-2,8'-indolo[1',2':1,2]imidazo[4,5-h]quinoline] (**3e**): White solid. Yield: 83%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.62 (d, *J* = 1.7 Hz, 1H), 9.11 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.73 (dd, *J* = 8.5, 1.4 Hz, 1H), 8.05 (s, 1H), 7.58 (dd, *J* = 8.5, 4.3 Hz, 1H), 7.33 (dq, *J* = 6.3, 4.1 Hz, 4H), 7.26 – 7.25 (m, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 3.93 (d, *J* = 15.8 Hz, 2H), 3.38 (d, *J* = 15.8 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.4, 149.5, 146.9, 142.7, 140.8, 138.8, 137.8, 133.9, 128.4, 127.4, 126.1, 125.9, 124.8, 123.6, 123.4, 122.0, 121.2, 120.5, 119.9, 50.0, 44.9. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{16}BrClN_3$ $[M+H]^+$ 472.0216, found 472.0218.

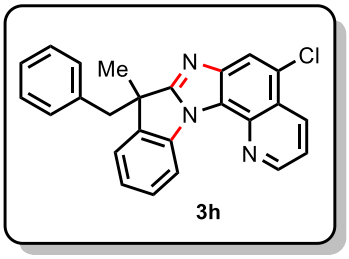


5'-chlorospiro[cyclohexane-1,8'-indolo[1',2':1,2]imidazo[4,5-h]quinoline] (**3f**): White solid. Yield: 78%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.46 (d, *J* = 8.2 Hz, 1H), 9.06 (d, *J* = 4.0 Hz, 1H), 8.70 (d, *J* = 8.5 Hz, 1H), 8.14 (s, 1H), 7.56 – 7.47 (m, 3H), 7.30 (t, *J* = 7.5 Hz, 1H), 2.43 – 2.31 (m, 2H), 2.06 – 1.93 (m, 3H), 1.85 (d, *J* = 10.2 Hz, 4H), 1.65 – 1.55 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2, 149.1, 146.8, 143.3, 138.0, 138.0, 133.7, 128.1, 125.7, 125.3, 125.1, 123.5, 123.2, 121.4, 120.1, 116.6, 44.7, 35.0, 25.6, 22.0. HRMS (ESI-TOF) *m/z* calcd for $C_{22}H_{19}ClN_3$ $[M+H]^+$ 360.1268, found 360.1265.



3g

3-bromo-5-chloro-8,8-dimethyl-8*H*-indolo[1',2':1,2]imidazo[4,5-h] quinoline (**3g**): White solid. Yield: 85%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.25 (d, *J* = 7.9 Hz, 1H), 9.08 (d, *J* = 2.1 Hz, 1H), 8.87 (d, *J* = 2.2 Hz, 1H), 8.10 (s, 1H), 7.53 – 7.44 (m, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 1.73 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 150.2, 147.1, 143.5, 137.7, 136.0, 135.5, 128.4, 125.7, 125.6, 124.5, 124.3, 123.1, 122.3, 116.5, 40.6, 26.0. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{14}BrClN_3$ $[M+H]^+$ 398.0060, found 398.0063.



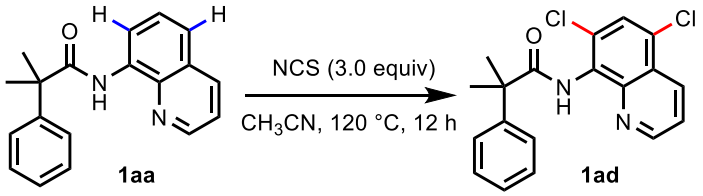
3h

8-benzyl-5-chloro-8-methyl-8*H*-indolo[1',2':1,2]imidazo[4,5-h]quinoline (**3h**): White solid. Yield: 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (d, *J* = 7.9 Hz, 1H), 8.97 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.66 (dd, *J* = 8.5, 1.4 Hz, 1H), 8.11 (s, 1H), 7.51 – 7.36 (m, 3H), 7.29 (t, *J* = 7.5 Hz, 1H), 6.96 – 6.86 (m, 3H), 6.82 – 6.76 (m, 2H), 3.50 (d, *J* = 13.3 Hz, 1H), 3.40 (d, *J* = 13.2 Hz, 1H), 1.83 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 149.1, 146.6, 140.8, 138.5, 137.9, 135.9, 133.6, 129.8, 128.4, 127.6, 126.5, 125.7, 125.5, 124.9, 124.0, 123.2, 121.2, 120.1, 116.5, 46.0, 45.7, 24.6. HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{19}ClN_3$ $[M+H]^+$ 396.1268, found 396.1265.

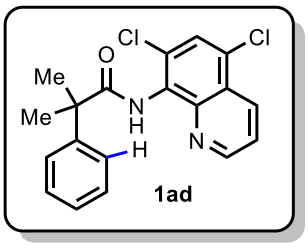
Procedure for Mechanism Studies

Preparation of the Required Substrate

The procedure for the synthesis of substrate **1ad**

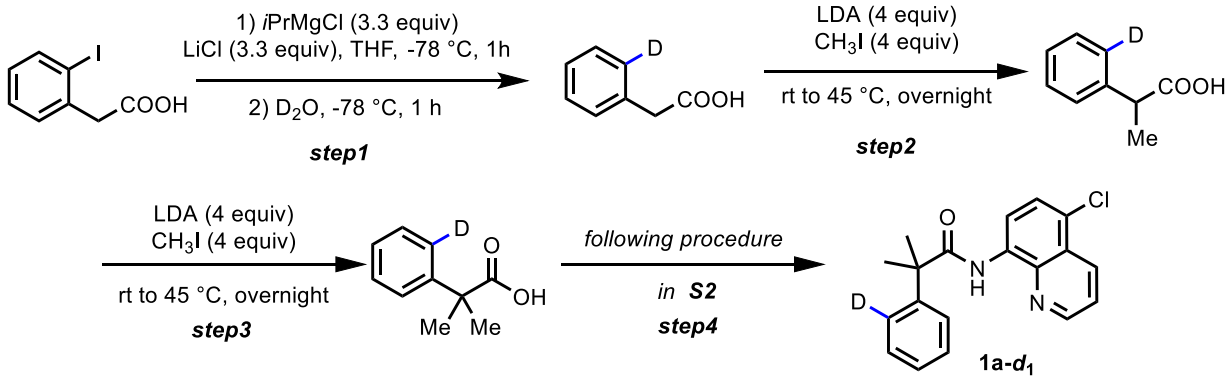


To a solution of **1aa** (1 mmol, 290 mg) and NCS (3 mmol, 400 mg) in CH_3CN (10 mL) was stirred at 120 °C for 12 h. The solvents were removed under reduced pressure. The crude mixture was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1).



***N*-(5,7-dichloroquinolin-8-yl)-2-methyl-2-phenylpropanamide** (**1ad**): White solid. Yield: 80%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.46 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.98 (s, 1H), 7.66 (s, 1H), 7.61 (d, *J* = 7.4 Hz, 2H), 7.50 – 7.41 (m, 3H), 7.34 (t, *J* = 7.3 Hz, 1H), 1.78 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.7, 150.6, 144.8, 143.9, 133.0, 131.5, 129.9, 128.8, 128.6, 128.2, 127.3, 126.9, 125.0, 122.1, 48.3, 48.3, 27.2, 27.1. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{17}Cl_2N_2O$ $[M+H]^+$ 359.0718, found 359.0716.

Preparation of Deuterium-labeled Substrate **1a-*d*$_1$**



Step 1: In a 100 mL flask, 2-(2-iodophenyl)acetic acid (2.6 g, 10 mmol) was dissolved in THF (30 mL), then anhydrous LiCl (1.4 g, 33 mmol), *i*PrMgCl (16.5 mL, 2 M in THF, 33 mmol.) was added at -78 °C under N_2 atmosphere. After being stirred at the same temperature for 1 h, D_2O (4.0 mL) was added dropwise to the reaction mixture under -78 °C and the temperature was gradually raised to room temperature, and the mixture was stirred for another 1 h. The HCl (2.0 M, 10 mL) was added then extracted with ether (3×50 mL), dried with anhydrous Na_2SO_4,

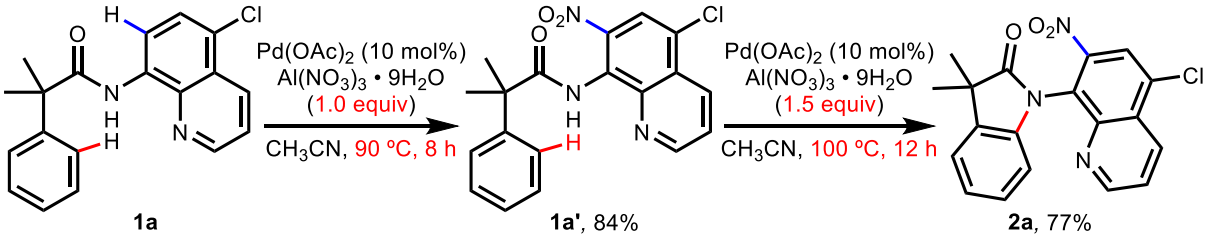
solvent was evaporated in Rota-evaporator. The residue was purified by silica gel chromatography (2%–10% ethyl acetate /petroleum ether) to provide corresponding deuterium-labeled acid.

Step 2: Followed by the reported procedure[5] to provide the mono-methylation deuterium-labeled acid.

Step 3*:* Repeat the step 2 to provide the di-methylation deuterium-labeled acid.

Step 4: Followed by the general procedure for preparation of substrate to provide the **1a-*d*$_1$**.

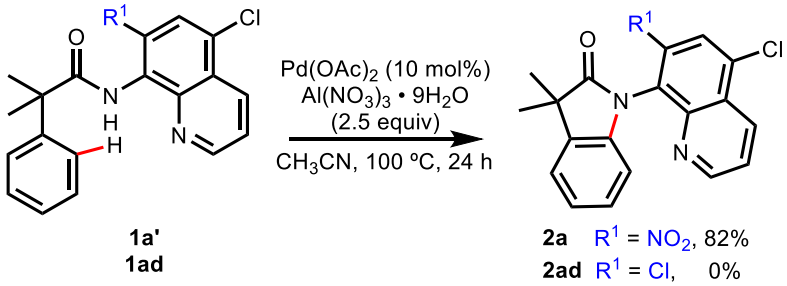
Stepwise Control of the Reaction



Step 1: In a 25 mL sealed tube, equipped with a stir bar, was charged with substrate **1a** (0.1 mmol), $Pd(OAc)_2$ (10 mol %), $Al(NO_3)_3{\cdot}9H_2O$ (0.1 mmol, 37.5 mg), and CH_3CN (2 mL). The tube was capped, and then the reaction mixture was stirred at 90 ˚C for 8 h. Upon completion, ethyl acetate was added to dilute the mixture and then filtered through a pad of silica gel. The solvent was evaporated under reduced pressure and then purified by column chromatography on silica gel with a gradient eluent of petroleum ether and ethyl acetate to obtain the nitrified intermediate **1a'** in 84% yield.

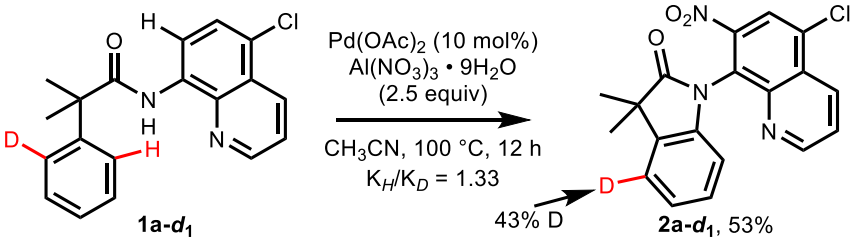
Step 2: The previously obtained **1a'** was mixed with $Pd(OAc)_2$ (10 mol %), $Al(NO_3)_3{\cdot}9H_2O$ (0.15 mmol, 56.3 mg) and CH_3CN (2 mL) in a clean 25mL sealed tube equipped with a stir bar. The tube was capped, and then the reaction mixture was stirred at 100 ˚C for 12 h. Then, ethyl acetate was added to dilute the mixture and then filtered through a pad of silica gel. The solvent was evaporated under reduced pressure and then purified by column chromatography on silica gel with petroleum ether and ethyl acetate to obtain the oxindole **2a** in 77% yield.

Directing Group Modification Control Reaction



The directing group modification control experiment followed the procedure for the palladium catalyzed C(sp^2)−H amidation.

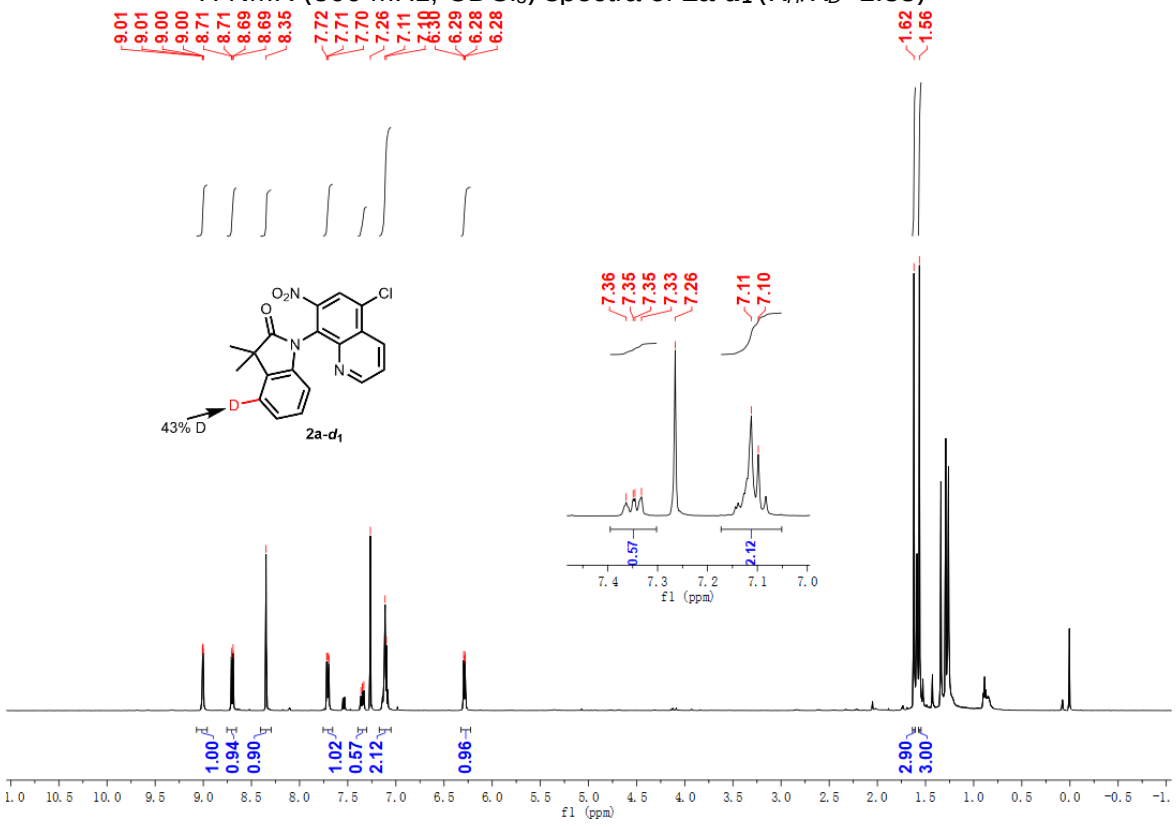
Intramolecular Competition KIE Study



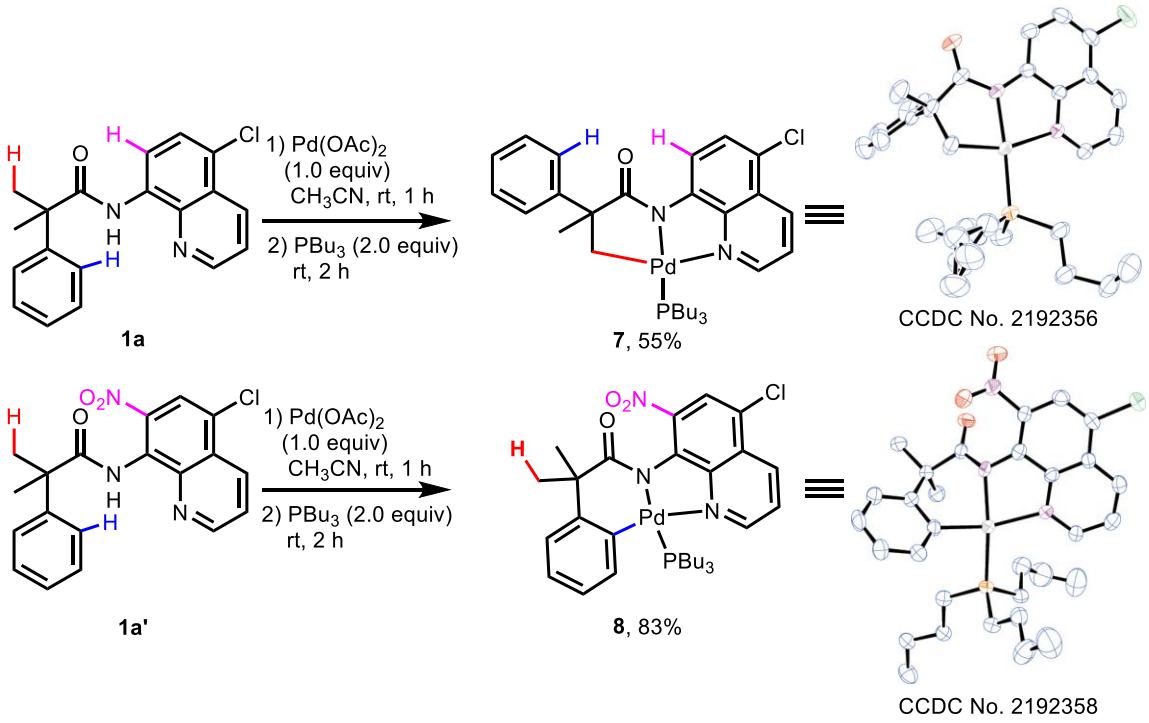
1a-*d*$_1$ **2a-*d*$_1$**, 53%

In a 25 mL sealed tube, equipped with a stir bar, was charged with substrates **1a-*d*$_1$** (0.1 mmol), $Pd(OAc)_2$ (10 mol %), $Al(NO_3)_3{\cdot}9H_2O$ (0.25 mmol, 93.8 mg) and CH_3CN (2 mL). The tube was capped, and then the reaction mixture was stirred at 100 ˚C for 12 h. Then, ethyl acetate was added to dilute the mixture and then filtered through a pad of silica gel. The solvent was evaporated under reduced pressure and then purified by column chromatography on silica gel with a gradient eluent of petroleum ether and ethyl acetate to obtain the product **2a-*d*$_1$** in 53% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.70 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.35 (s, 1H), 7.71 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.35 (dd, *J* = 8.6, 6.8 Hz, 0.57H), 7.17 – 7.05 (m, 2H), 6.29 (dd, *J* = 7.1, 1.6 Hz, 1H), 1.62 (s, 3H), 1.56 (s, 3H). The KIE value was calculated as k_H/k_D = 1.33

^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2a-*d*$_1$** (K_H/K_D=1.33)

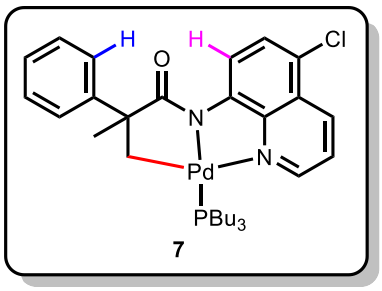


Characterization of C-H insertion palladium complexes

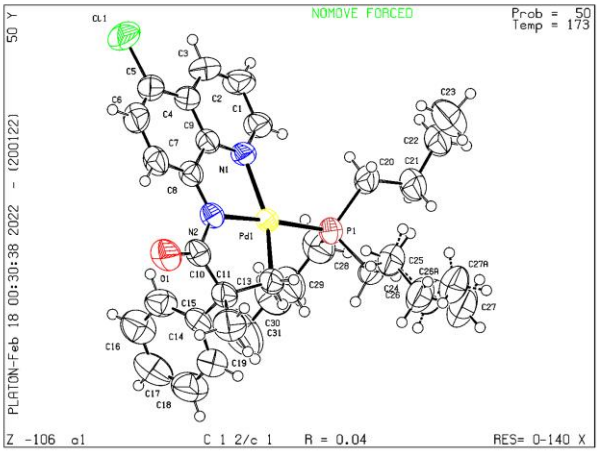


Procedure for the synthesis of palladium complexes:

The acetonitrile solution of substrate **1** (0.2 mmol) and $Pd(OAc)_2$ (0.2 mmol, 45 mg) was placed in a 25mL sealed tube equipped with a stir bar, covered with a stopper and stirred for 1 hour at room temperature. After complete substrate transformation, PBu_3 (0.4 mmol, 81 mg) was added to the mixture and stirred for 2 hours at room temperature. After the reaction, the mixture was filtered through a pad of Celite and washed with a small amount of ethyl acetate. The filtrate was concentrated under *vacuum* and then purified by PLC (20% ethyl acetate/ petroleum ether) to obtain the desired palladium complex. The obtained palladium complexes were recrystallized with a mixture of hexane and dichloromethane for X-ray single crystal diffraction analysis.



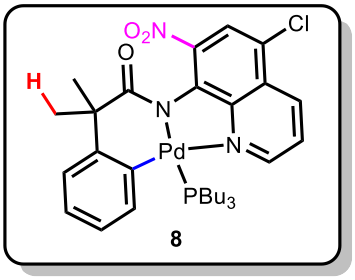
Characterization of complex **7**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.15 (d, *J* = 8.6 Hz, 1H), 8.63 (dd, *J* = 8.5, 1.4 Hz, 1H), 8.46 – 8.40 (m, 1H), 7.71 – 7.63 (m, 2H), 7.57 (d, *J* = 8.6 Hz, 1H), 7.45 (dd, *J* = 8.5, 4.7 Hz, 1H), 7.28 – 7.23 (m, 2H), 7.13 (t, *J* = 7.3 Hz, 1H), 1.97 (dd, *J* = 9.6, 4.0 Hz, 1H), 1.91 (dd, *J* = 9.5, 7.6 Hz, 1H), 1.72 (dt, *J* = 14.7, 5.4 Hz, 9H), 1.53 (qd, *J* = 12.9, 6.0 Hz, 6H), 1.43 (dt, *J* = 14.3, 7.2 Hz, 6H), 0.92 (t, *J* = 7.3 Hz, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.1, 149.6, 148.6, 147.3, 146.8, 135.2, 129.2, 127.8 (d, *J* = 13.1 Hz), 126.4, 125.5, 121.1, 120.4, 120.0, 59.4, 29.8 (d, *J* = 6.2 Hz), 29.2, 26.6, 24.5 (d, *J* = 13.1 Hz), 23.3, 23.0, 13.8. HRMS (ESI-TOF) *m/z* calcd for $C_{31}H_{42}ClN_2OPPd$ $[M+H]^+$ 631.1836, found 631.1832.



Crystal data and structure refinement for 7. (CCDC 2192356)

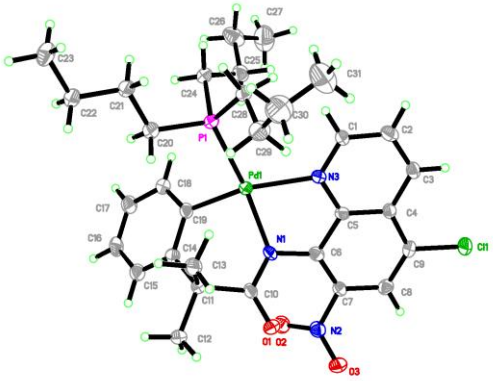
Report date	2022-01-10	
Identification code	A1	
Empirical formula	$C_{31}\,H_{42}\,Cl\,N_2\,O\,P\,Pd$	
Formula weight	631.48	
Temperature	173.00 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 36.933(10) Å	α = 90°
	b = 9.895(3) Å	β = 108.846(9)°
	c = 18.155(5) Å	γ = 90°
Volume	6279(3) $Å^3$	
Z	8	
Density (calculated)	1.366 g/cm^3	
Absorption coefficient	0.752 mm^{-1}	
F(000)	2624.0	
Crystal size	0.12 × 0.11 × 0.1 mm^3	
Theta range for data collection	4.278 to 54.938°	

Index ranges	-45≤h≤47, -12≤k≤12, -23≤l≤23
Reflections collected	42235
Independent reflections	7144 [R_{int} = 0.0450, R_{sigma} = 0.0309]
Completeness to theta = 53.594°	99.4%
Refinement method	Full-matrix least-squaares on F^2
Data / restraints / parameters	7144/56/358
Goodness-of-fit on F^2	1.033
Final R indices [I>2sigma(I)]	R_1 = 0.0381, wR_2 = 0.0915
R indices (all data)	R_1 = 0.0582, wR_2 = 0.1043
Extinction coefficient	n/a
Largest diff. peak and hole	0.64 and -0.47 e·Å^{-3}



8

Characterization of complex **8**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (dd, *J* = 8.5, 1.0 Hz, 1H), 8.61 (d, *J* = 4.4 Hz, 1H), 8.10 (s, 1H), 7.68 (dd, *J* = 8.5, 4.8 Hz, 1H), 7.24 – 7.16 (m, 2H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.90 (t, *J* = 6.8 Hz, 1H), 2.21 (s, 3H), 1.84 (dd, *J* = 16.8, 8.6 Hz, 6H), 1.75 (s, 3H), 1.58 (dd, *J* = 13.7, 7.8 Hz, 3H), 1.52 – 1.43 (m, 3H), 1.35 (qd, *J* = 14.4, 7.1 Hz, 6H), 0.83 (t, *J* = 7.3 Hz, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.9, 149.8, 148.5, 147.6, 145.3 (d, *J* = 6.7 Hz), 144.5, 141.8, 135.8, 135.3 (d, *J* = 12.2 Hz), 129.4, 125.7 (d, *J* = 4.2 Hz), 124.9, 124.4, 124.1, 123.8, 121.0, 51.7, 36.7, 26.9, 25.9, 25.0, 24.8, 24.4 (d, *J* = 13.5 Hz), 13.6. HRMS (ESI-TOF) *m/z* calcd for $C_{31}H_{41}ClN_3O_3PPd$ $[M+H]^+$ 676.1687, found 676.1683.



Crystal data and structure refinement for 8. (CCDC 2192358)

Report date	2019-11-29	
Identification code	20191129ZH_NLG_JC_0m_a	
Empirical formula	$C_{64}H_{86}Cl_7N_6O_6P_2Pd_2$	
Formula weight	1558.27	
Temperature	190(2) K	
Wavelength	1.34139 Å	
Crystal system	monoclinic	
Space group	P 1 21/n 1 (14)	
Unit cell dimensions	a = 10.4357(2) Å	α = 90°
	b = 18.1956(4) Å	β = 91.6550(10)°
	c = 36.8424(7) Å	γ = 90°
Volume	6992.9(2) $Å^3$	
Z	4	
Density (calculated)	1.480 g/cm^3	
Absorption coefficient	5.017 mm^{-1}	
F(000)	3204	
Crystal size	0.12 × 0.11 × 0.08 mm^3	

Theta range for data collection	2.087 to 53.939°
Index ranges	-12≤h≤12, -21≤k≤21, -44≤l≤44
Reflections collected	63633
Independent reflections	12801 [R_{int} = 0.0880]
Completeness to theta = 53.594°	99.9%
Refinement method	Full-matrix least-squaares on F^2
Data / restraints / parameters	12801/0/794
Goodness-of-fit on F^2	1.024
Final R indices [I>2sigma(I)]	R_{obs} = 0.0668, wR_{obs} = 0.1605
R indices (all data)	R_{all} = 0.1084, wR_{all} = 0.1854
Extinction coefficient	n/a
Largest diff. peak and hole	2.290 and -1.429 e·$Å^{-3}$

References

1. (a) Yang, M.; Jiang, X.; Shi, W.-J.; Zhu, Q.-L.; Shi, Z.-J. *Org. Lett.* **2013***, 15,* 690–693; (b) Cheng, X.-F.; Li, Y.; Su, Y.-M.; Yin, F.; Wang, J.-Y.; Sheng, J.; Vora, H. U.; Wang, X.-S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013***, 135,* 1236–1239; (c) Crowley, D. C.; Lynch, D.; Maguire, A. R. *J. Org. Chem*. **2018**, *83*, 3794–3805.

2. Motati, D. R.; Uredia, D.; Watkins, E. B. *Chem. Sci.,* **2018***, 9,* 1782–1788.

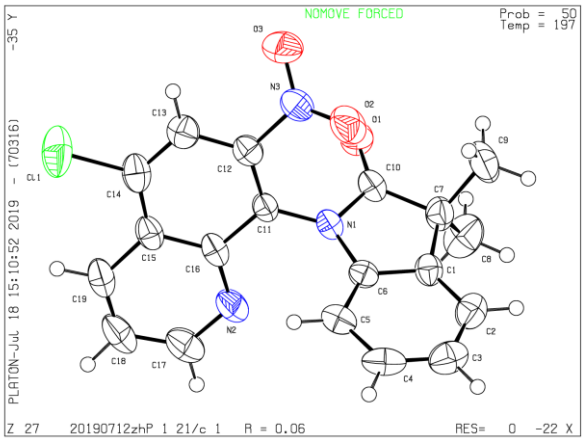
3. He, G.; Zhang, S.-Y.; Nack, W. A.; Li, Q.; Chen, G. *Angew. Chem. Int. Ed.* **2013**, *52*, 11124 –11128.

4. Du, Y.; Liu, Y.; Wan, J.-P. *J. Org. Chem.* **2018**, *83*, 3403−3408.

5. Barczak, N. T.; Jarvo, E. J. *Chem. Eur. J.* **2011**, *17*, 12912–12916.

6. Wasa, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14058–14059.

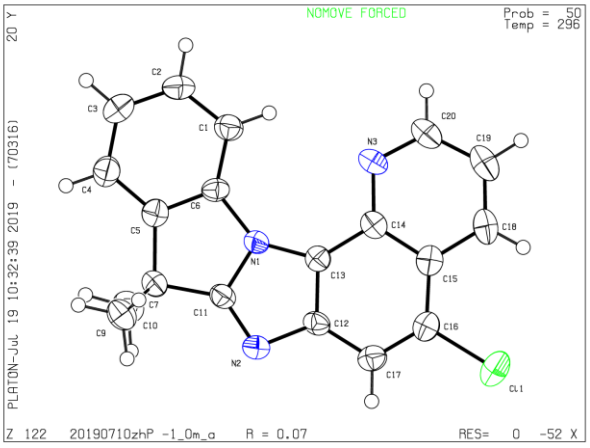
X-Ray Crystallographic Data of 2a and 3a



Crystal data and structure refinement for 2a. (CCDC 2192355)

Report date	2019-07-12	
Identification code	20190712zh_jc2_0m_a	
Empirical formula	$C_{19}H_{14}ClN_3O_3$	
Formula weight	367.78	
Temperature	197 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 10.885(7) Å	α = 90°
	b = 10.488(6) Å	β = 93.959(11)°
	c = 14.783(9) Å	γ = 90°
Volume	1683.7(17) $Å^3$	
Z	4	
Density (calculated)	1.451 g/cm^3	
Absorption coefficient	0.252 mm^{-1}	
F(000)	760	
Crystal size	0.12 × 0.08 × 0.06 mm^3	

Theta range for data collection	1.875 to 25.219°
Index ranges	-8≤h≤13, -12≤k≤11, -17≤l≤17
Reflections collected	8952
Independent reflections	3025 [R_{int} = 0.0750]
Completeness to theta = 53.594°	99.8%
Refinement method	Full-matrix least-squaares on F^2
Data / restraints / parameters	3025/0/237
Goodness-of-fit on F^2	1.039
Final R indices [I>2sigma(I)]	R_{obs} = 0.0639, wR_{obs} = 0.1513
R indices (all data)	R_{all} = 0.1025, wR_{all} = 0.1908
Extinction coefficient	n/a
Largest diff. peak and hole	0.308 and -0.332 e·Å^{-3}



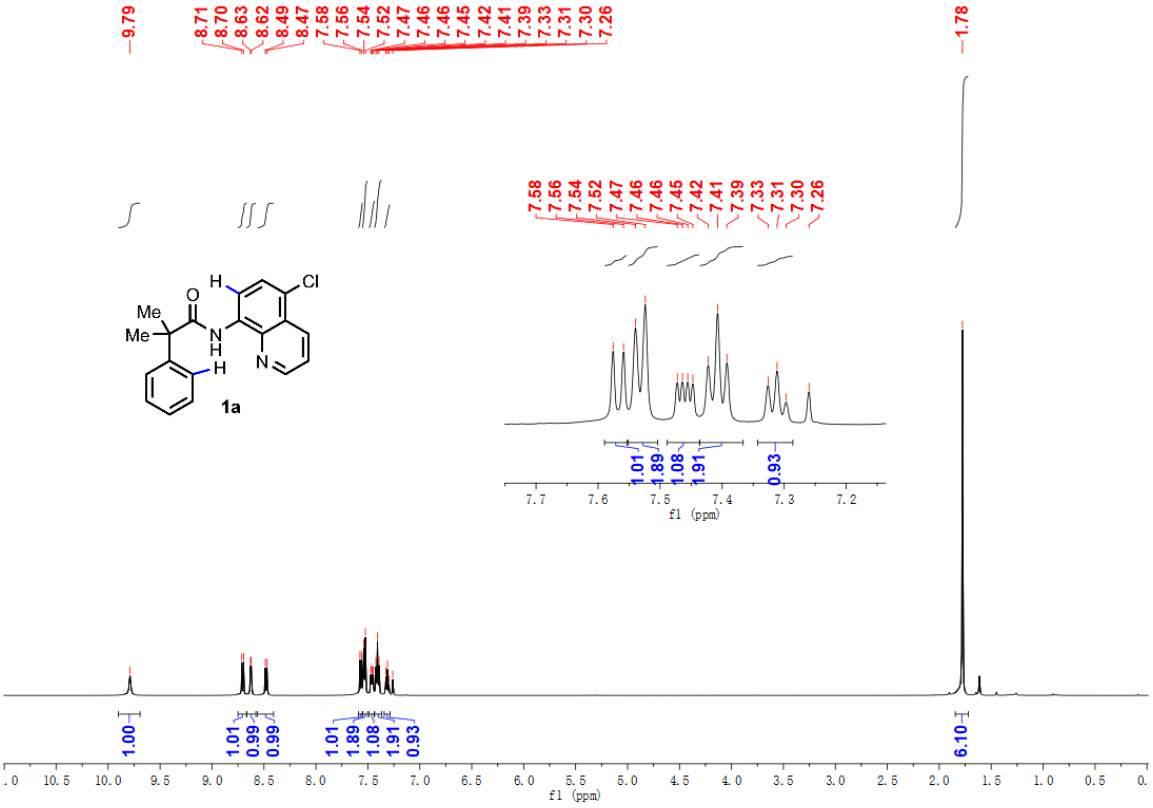
Crystal data and structure refinement for 3a. (CCDC 2192357)

Report date	2019-07-10
Identification code	20190710zh_jc3_0m_a
Empirical formula	$C_{19}H_{14}ClN_3$
Formula weight	319.78
Temperature	296.15 K
Wavelength	0.71073 Å

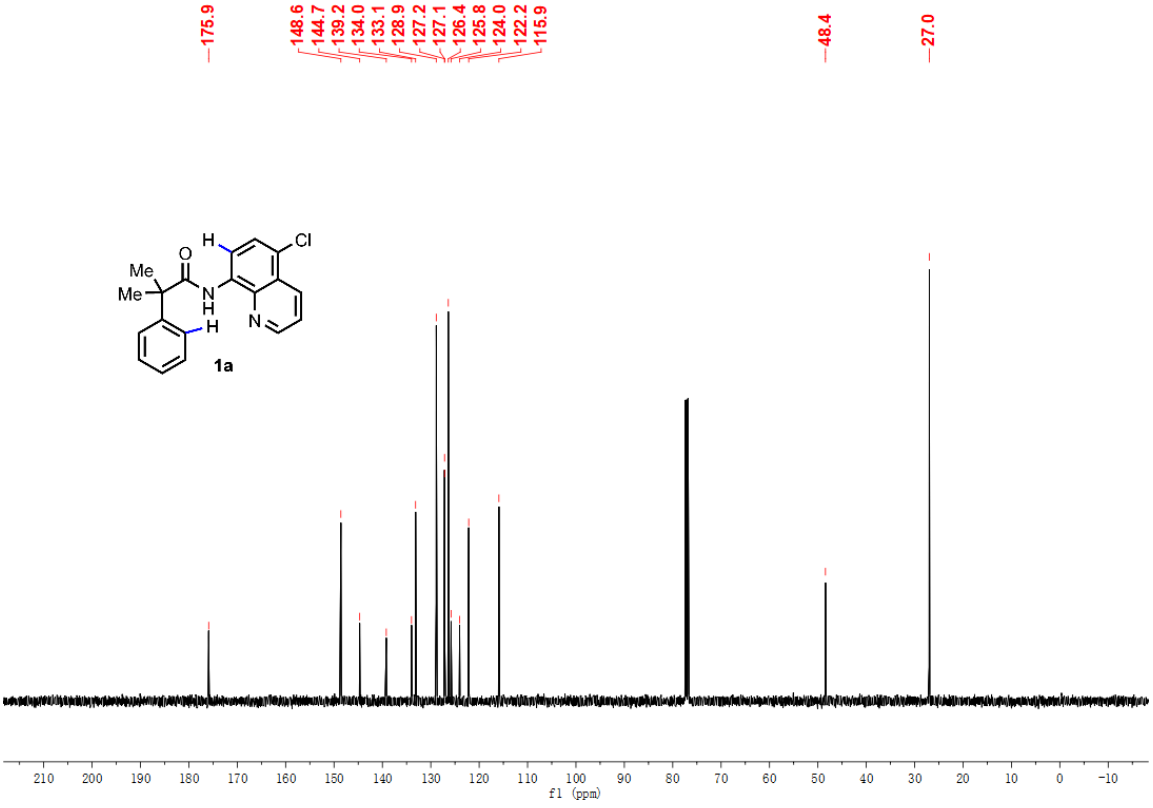
Crystal system	triclinic	
Space group	P -1 (2)	
Unit cell dimensions	a = 8.476(6) Å	α = 86.626(10)°
	b = 8.865(6) Å	β = 77.299(10)°
	c = 10.558(7) Å	γ = 80.134(12)°
Volume	762.3(9) $Å^3$	
Z	2	
Density (calculated)	1.393 g/cm^3	
Absorption coefficient	0.253 mm^{-1}	
F(000)	332	
Crystal size	0.15 × 0.06 × 0.04 mm^3	
Theta range for data collection	1.978 to 27.367°	
Index ranges	-10≤h≤7, -11≤k≤10, -13≤l≤12	
Reflections collected	4996	
Independent reflections	3409 [R_{int} = 0.0407]	
Completeness to theta = 53.594°	99.6%	
Refinement method	Full-matrix least-squaares on F^2	
Data / restraints / parameters	3409/0/210	
Goodness-of-fit on F^2	1.006	
Final R indices [I>2sigma(I)]	R_{obs} = 0.0677, wR_{obs} = 0.1729	
R indices (all data)	R_{all} = 0.0951, wR_{all} = 0.2020	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.359 and -0.543 $e·Å^{-3}$	

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

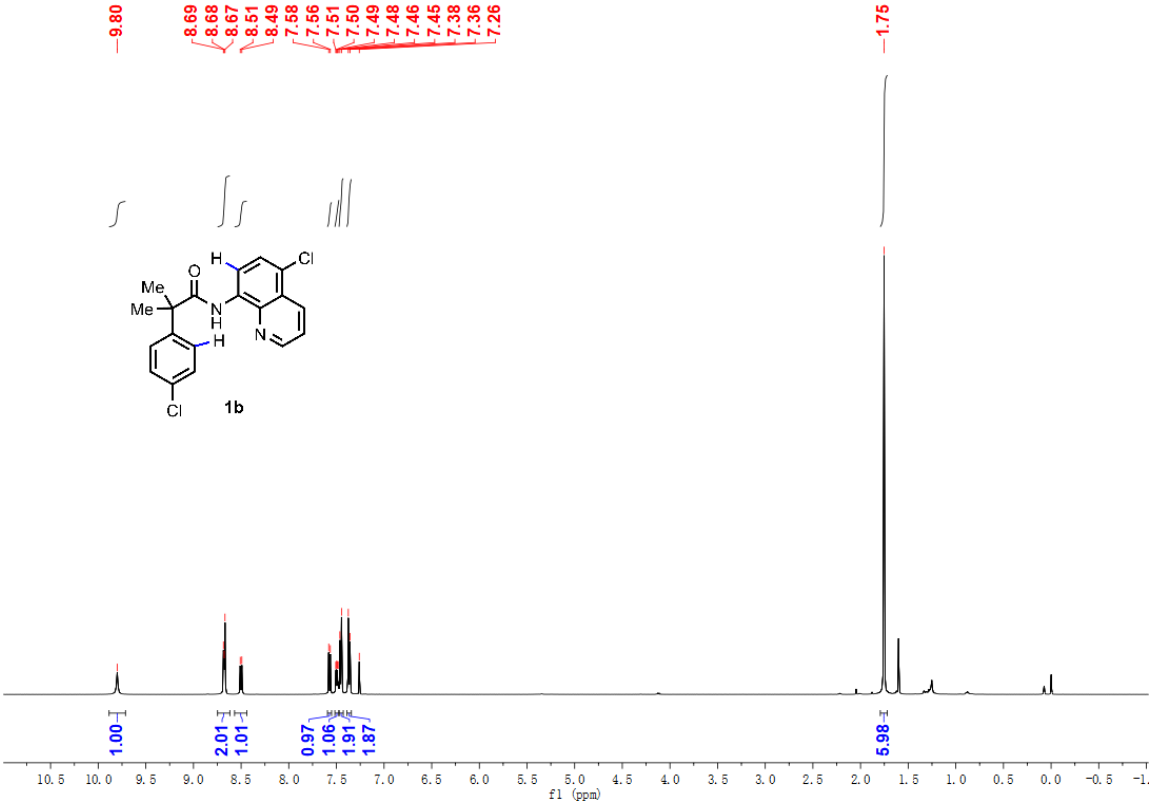
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1a**



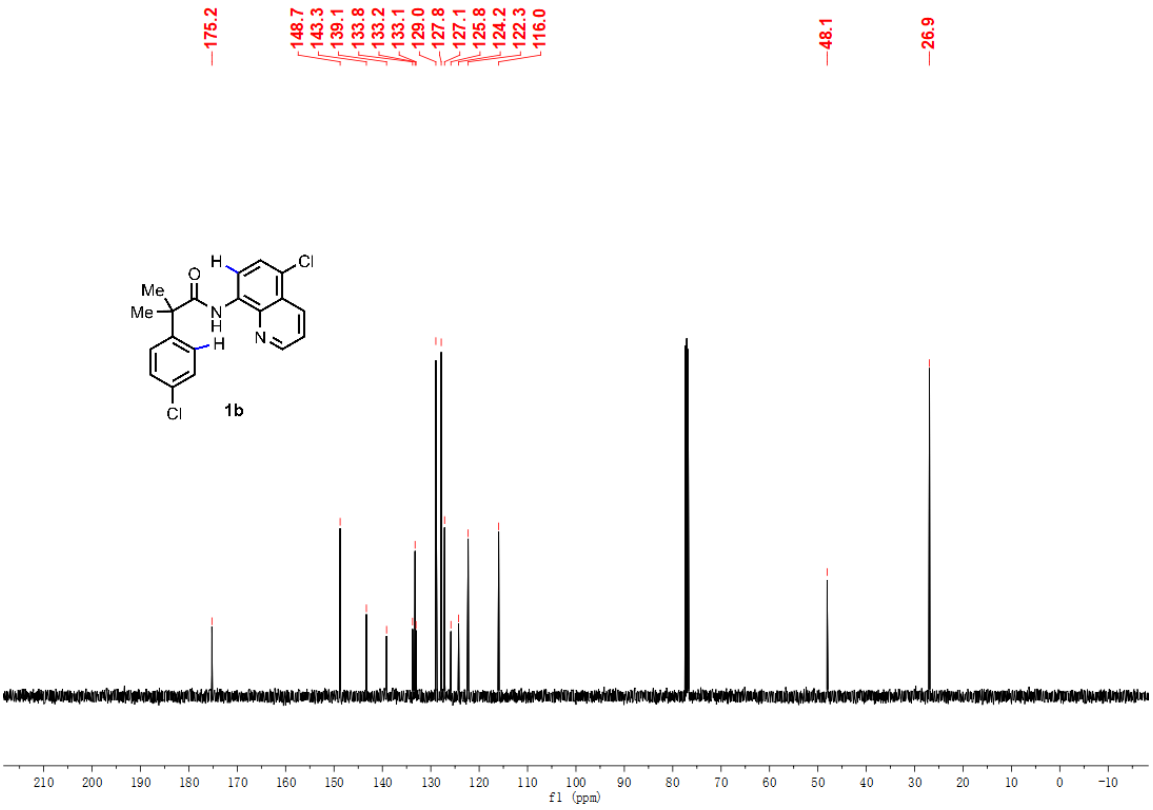
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1a**



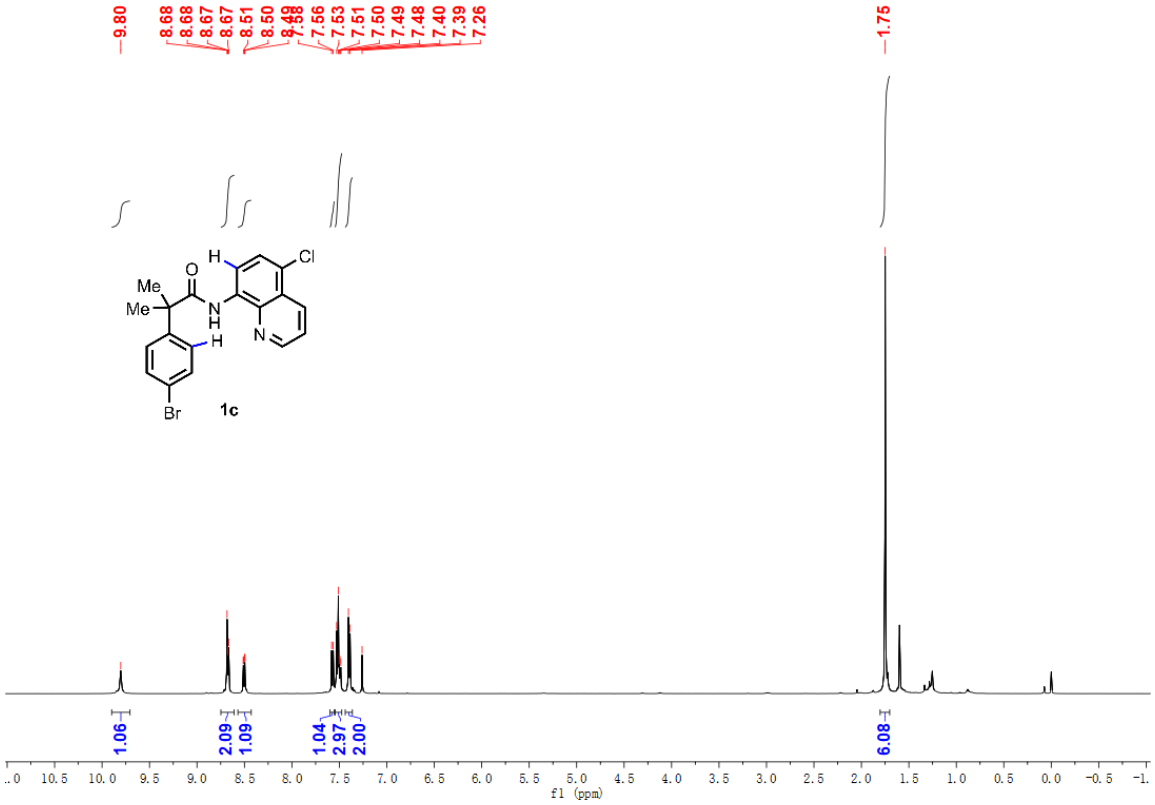
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1b**



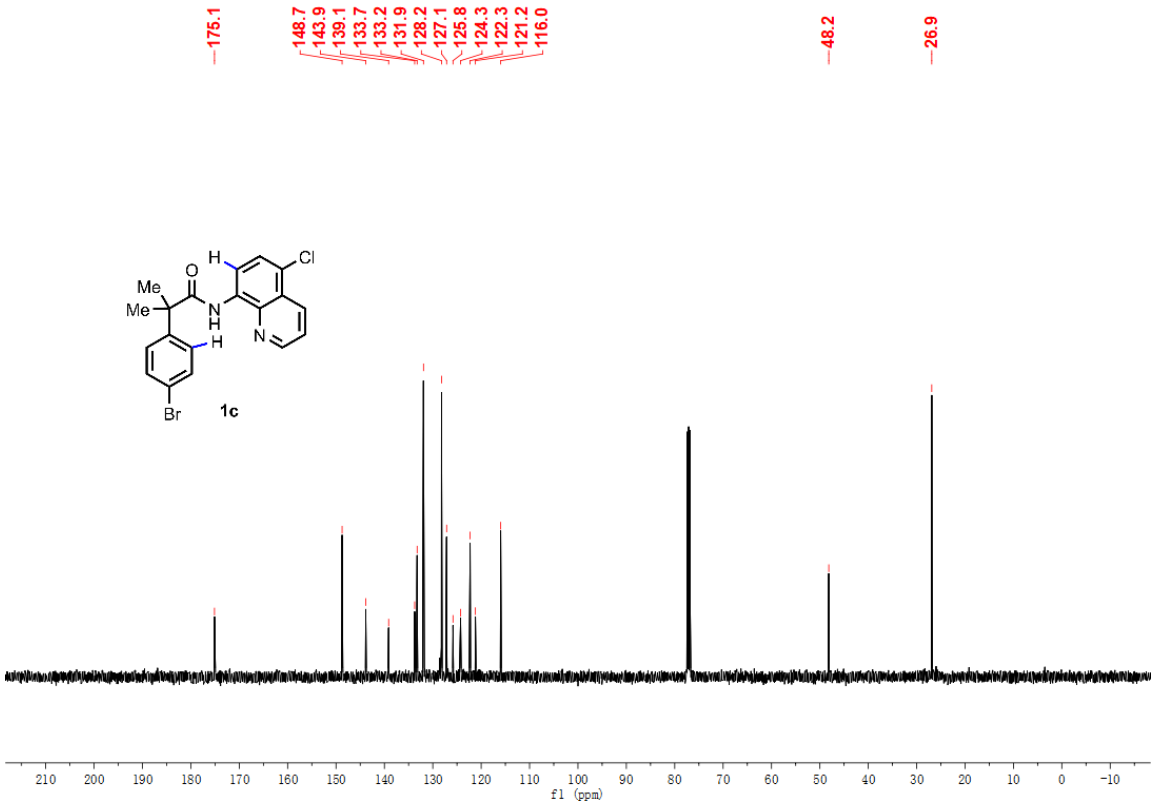
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1b**



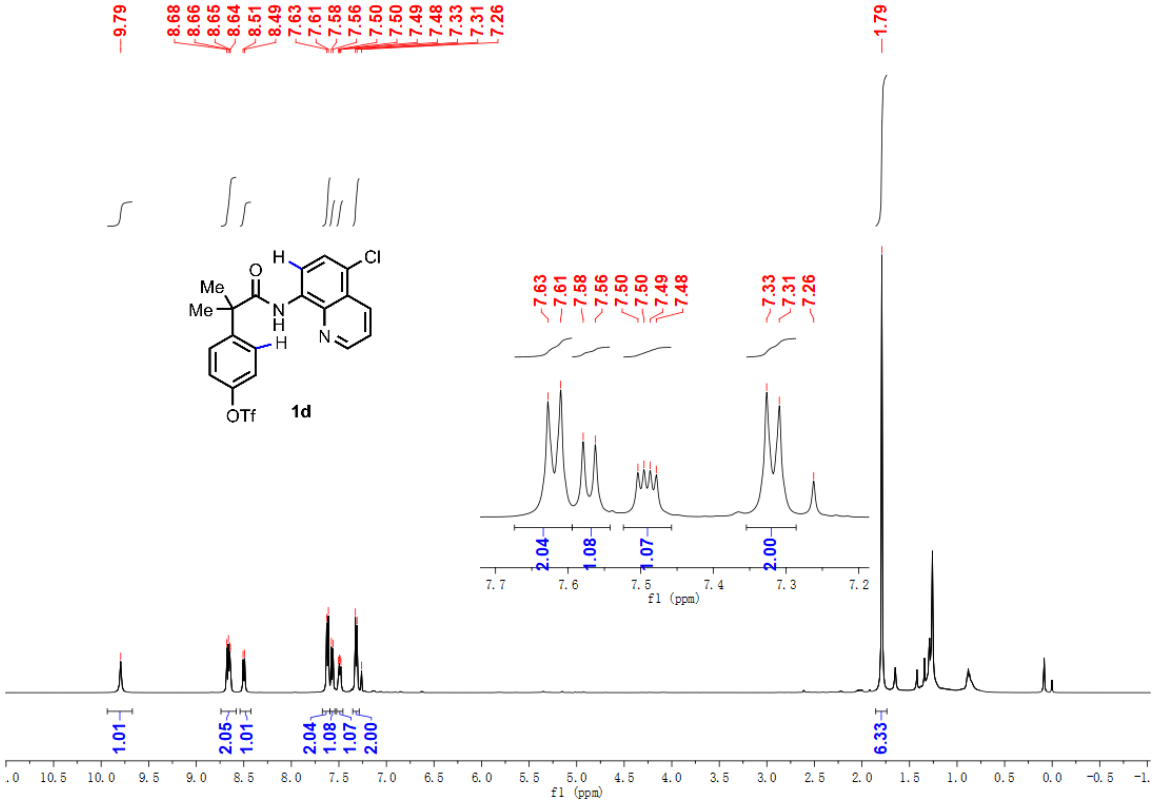
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1c**



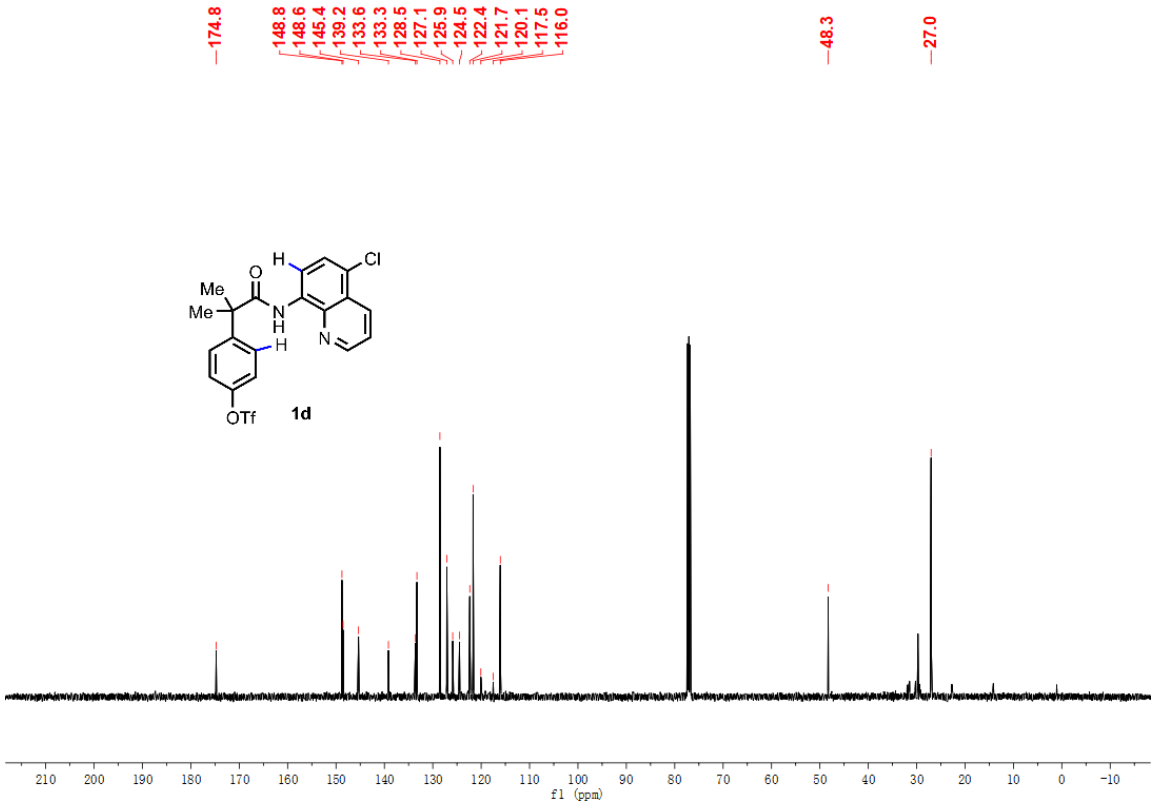
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1c**



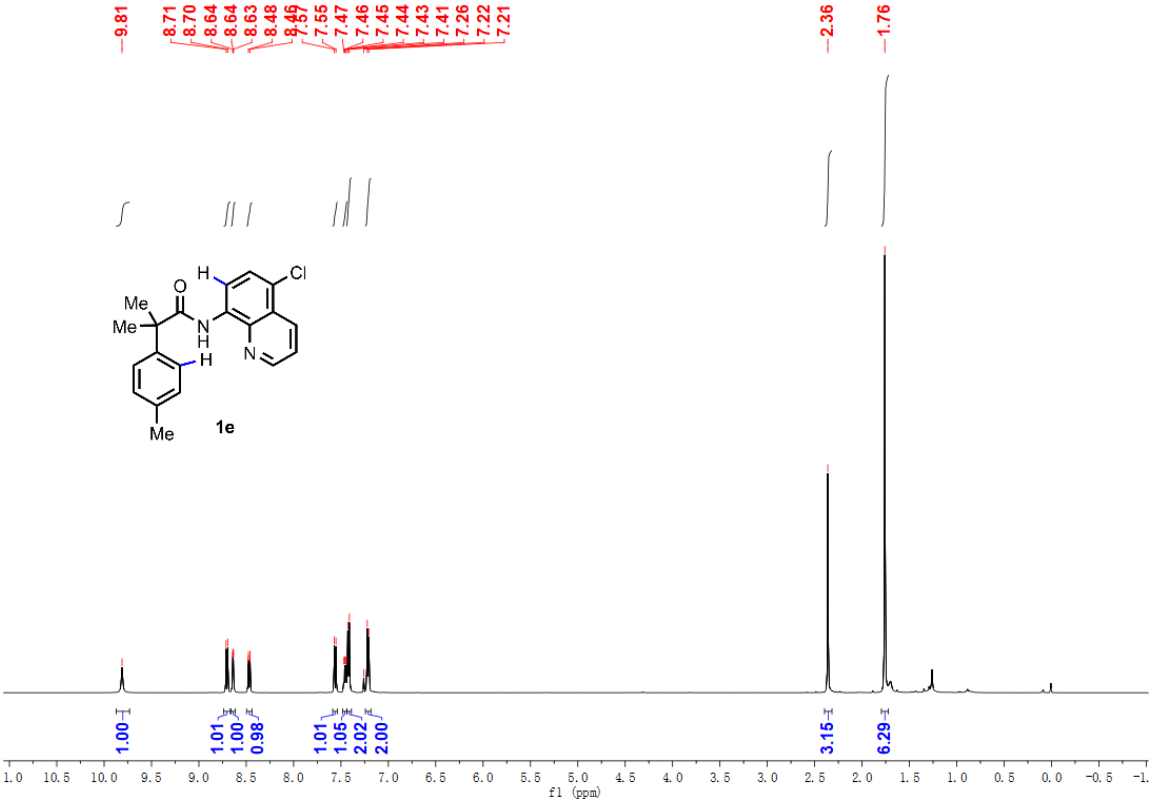
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1d**



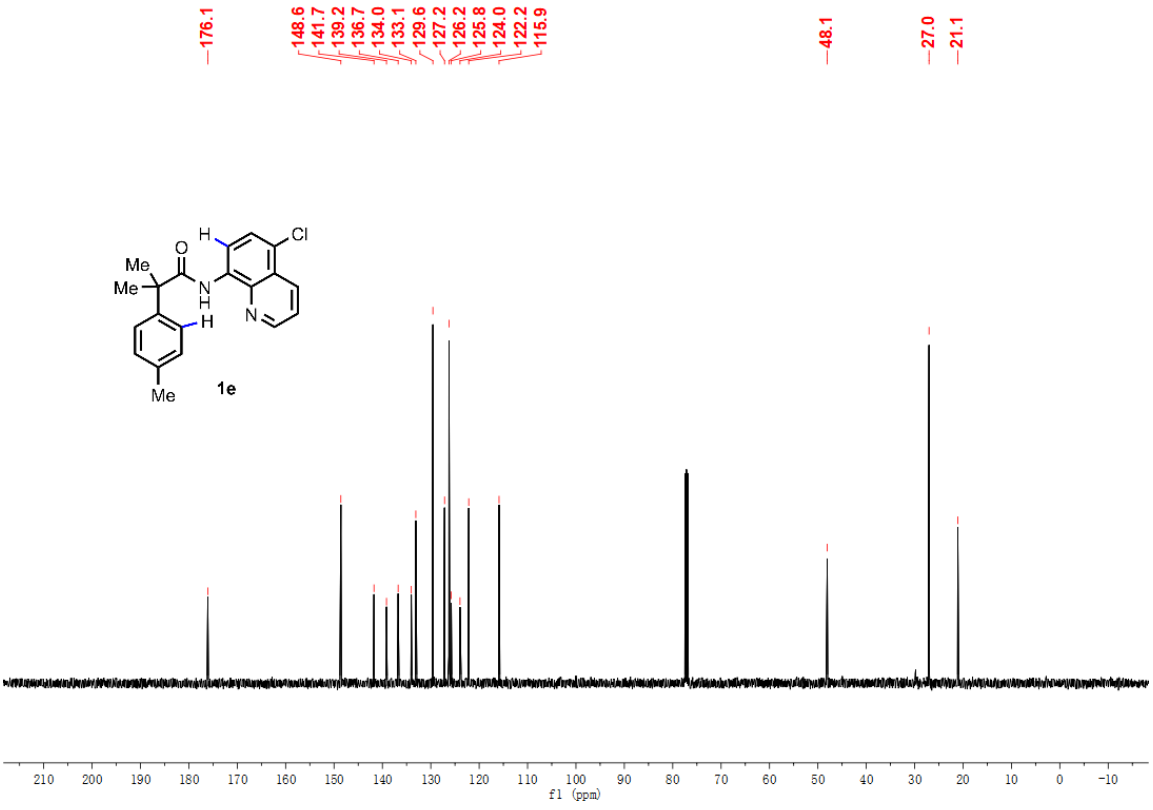
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1d**



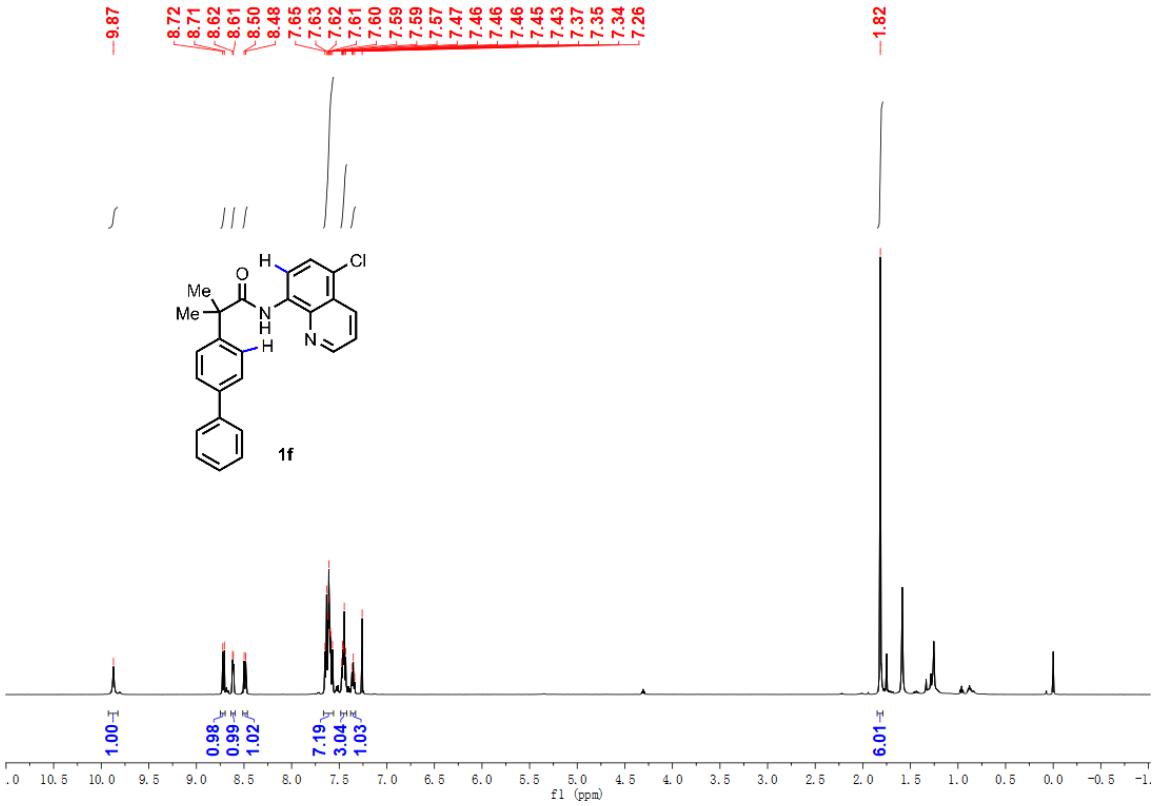
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1e**



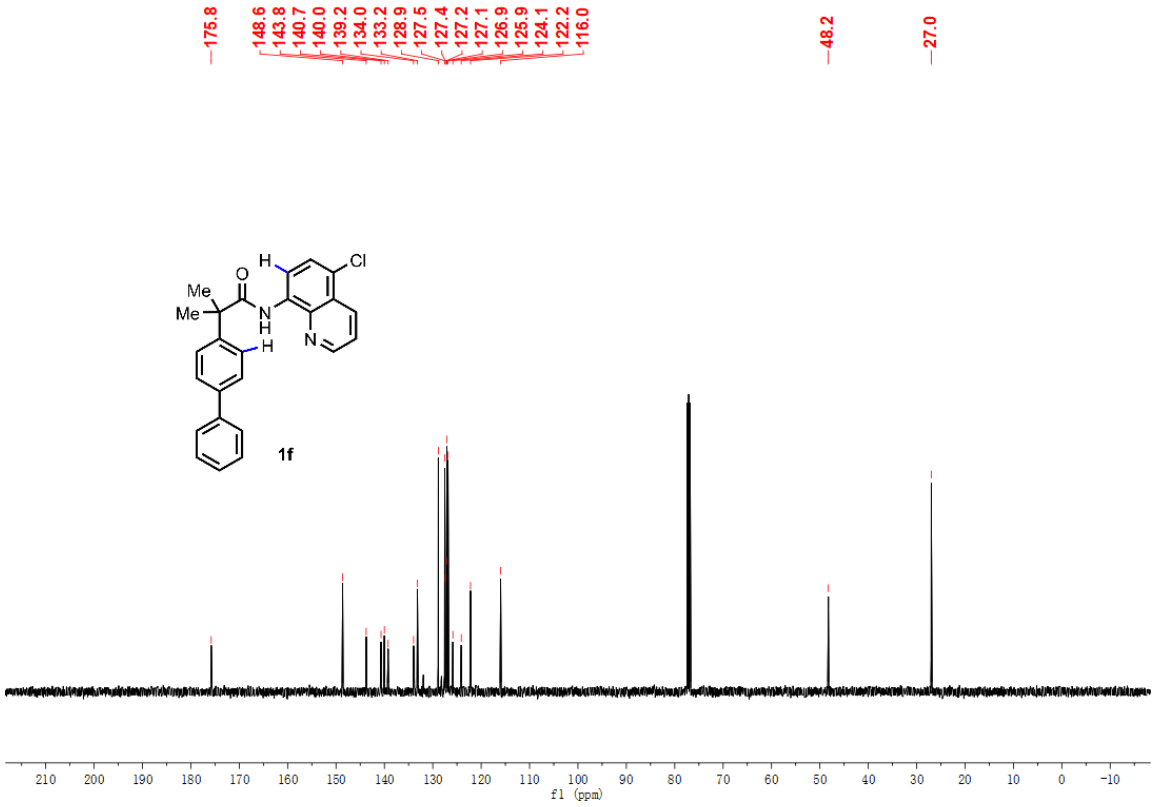
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1e**



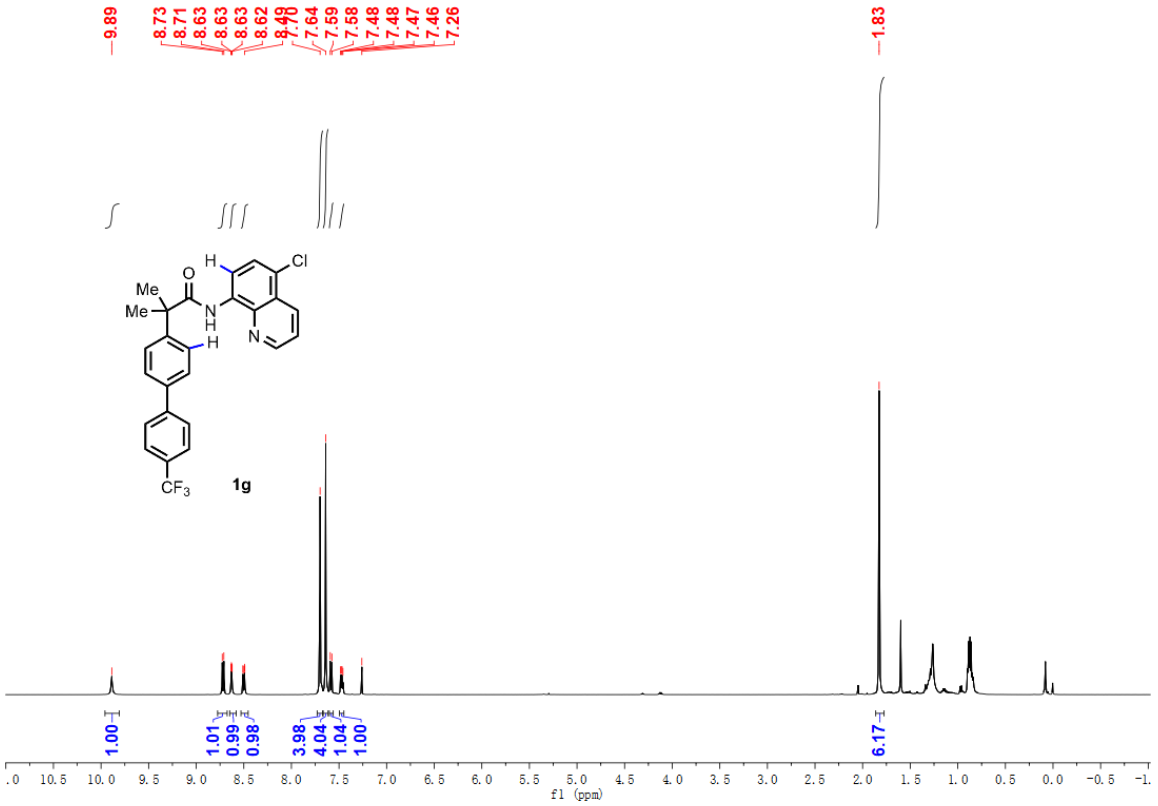
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1f**



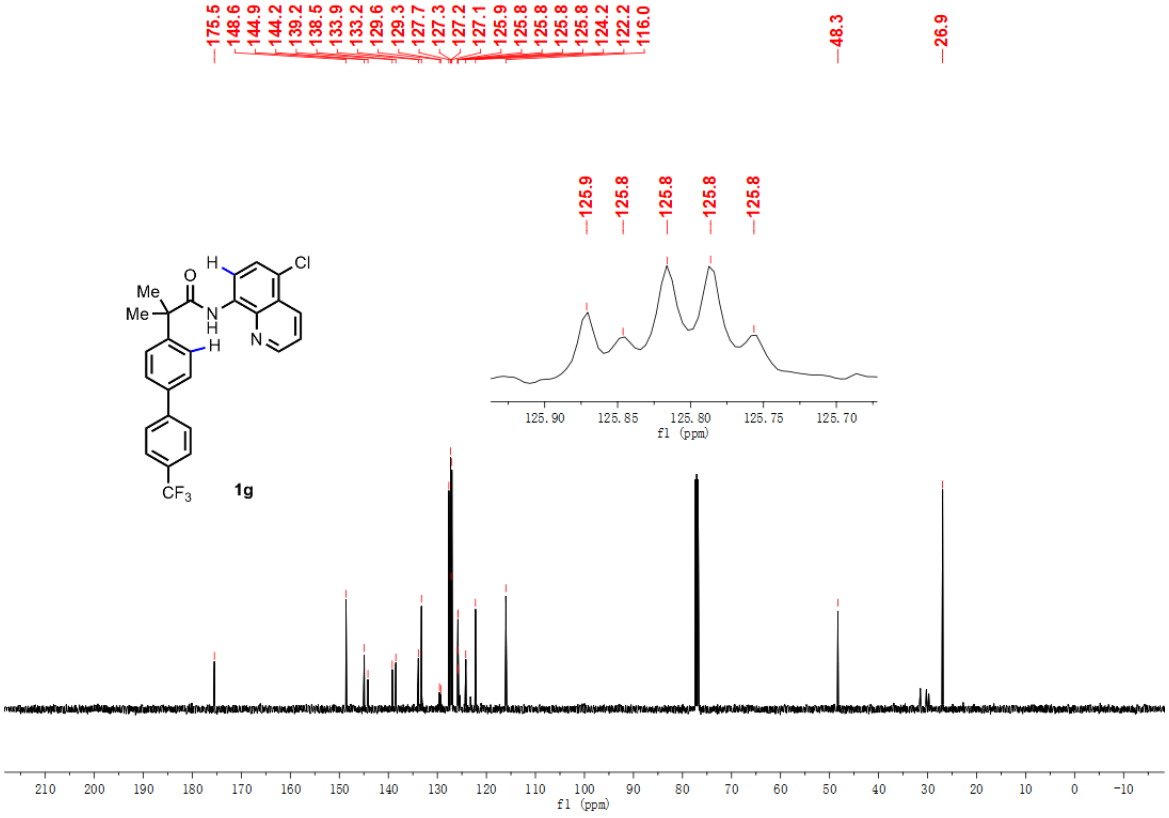
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1f**



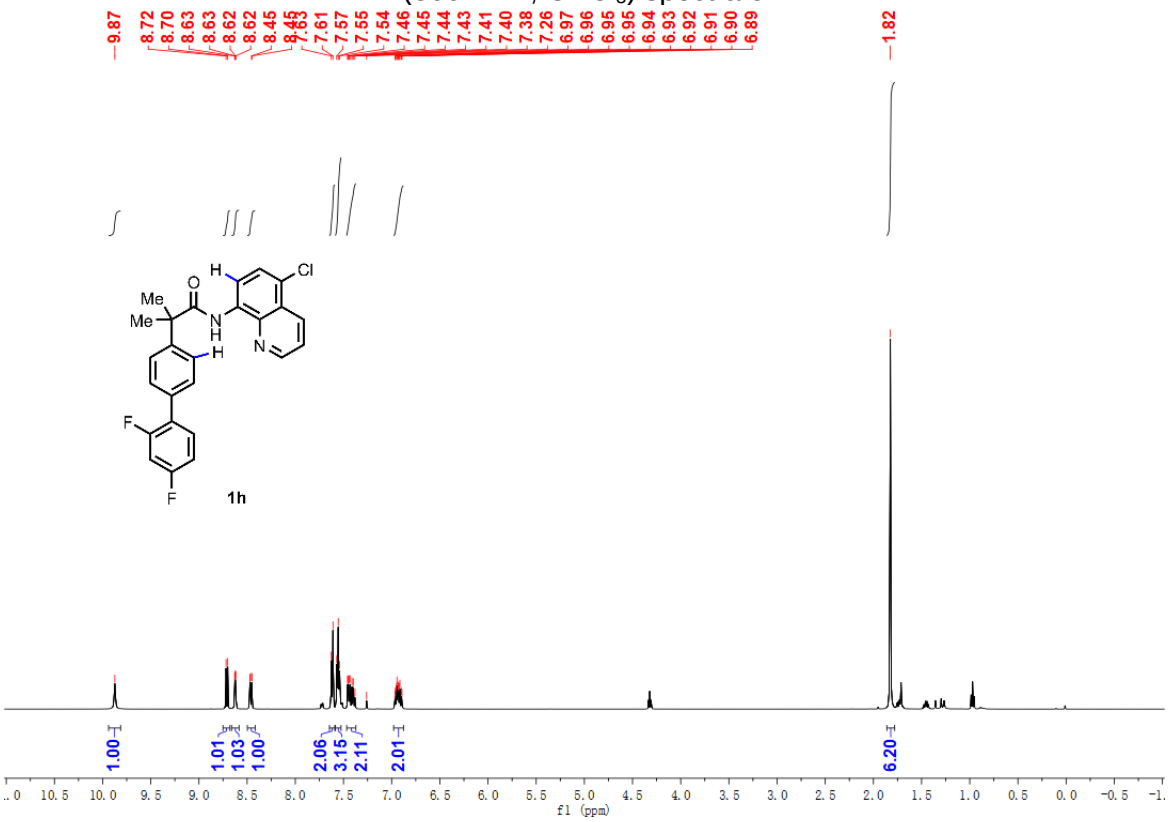
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1g**



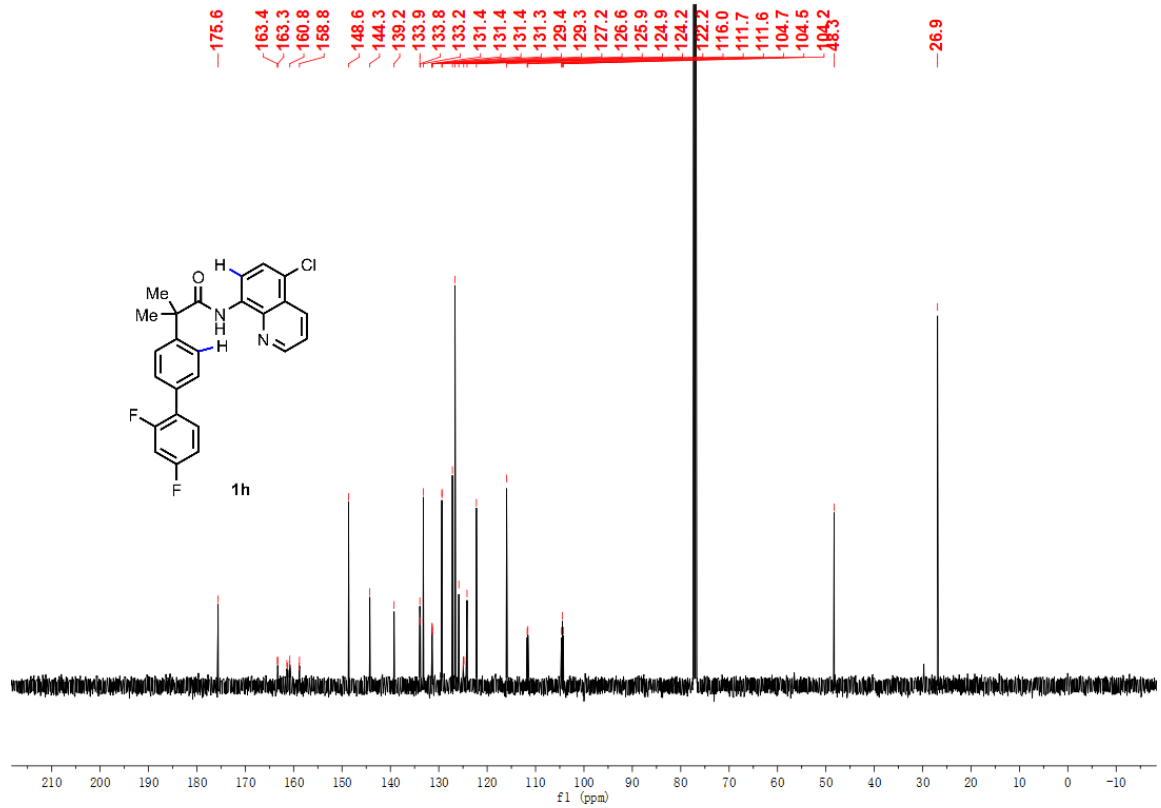
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1g**



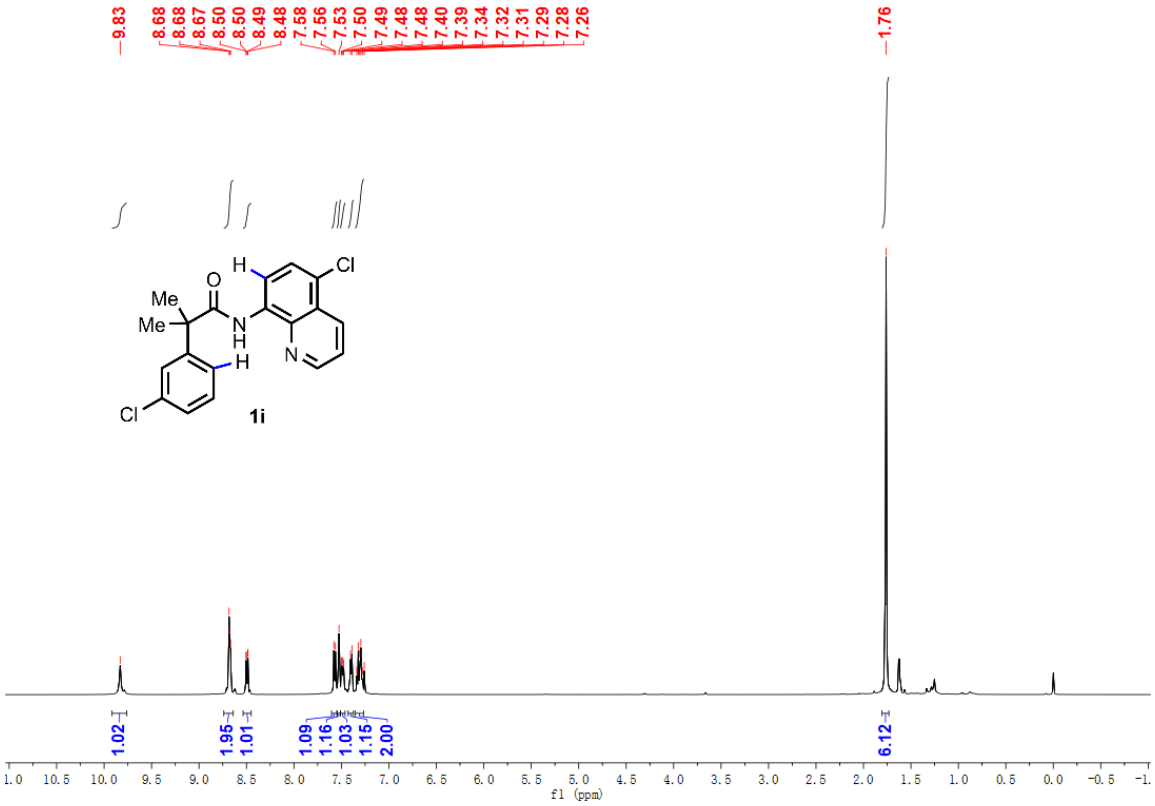
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1h**



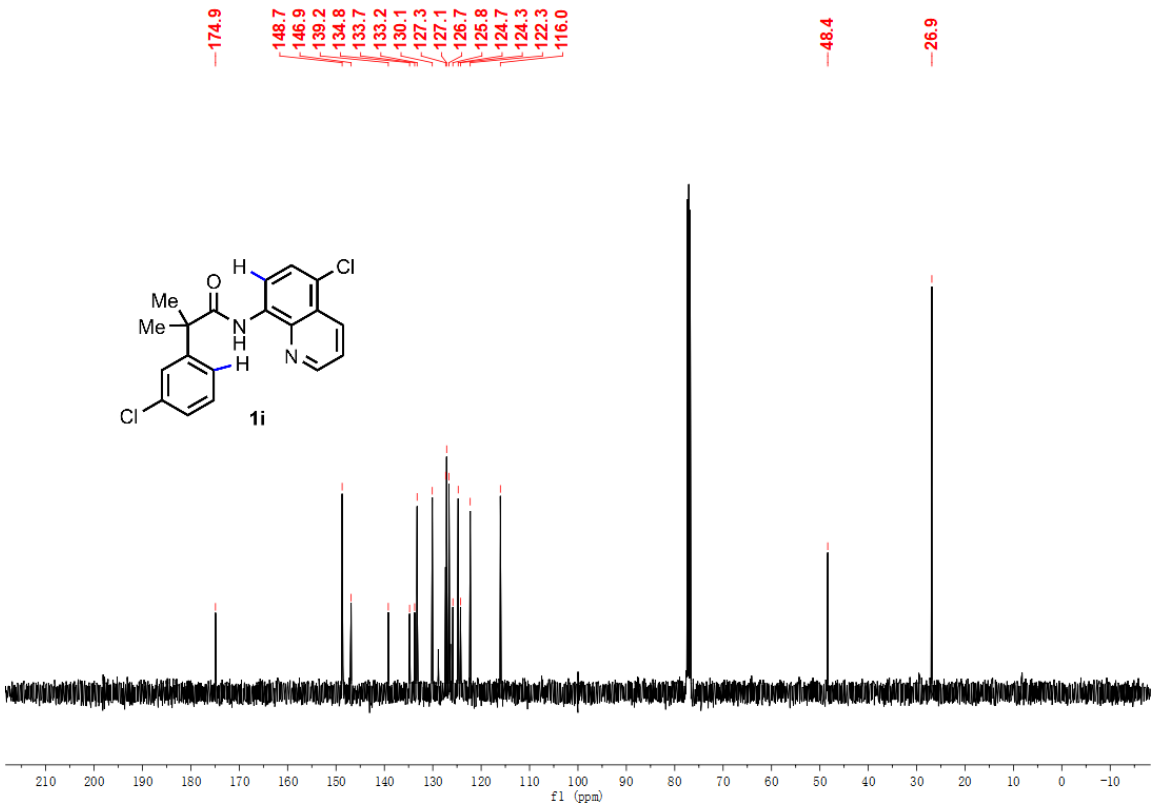
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1h**



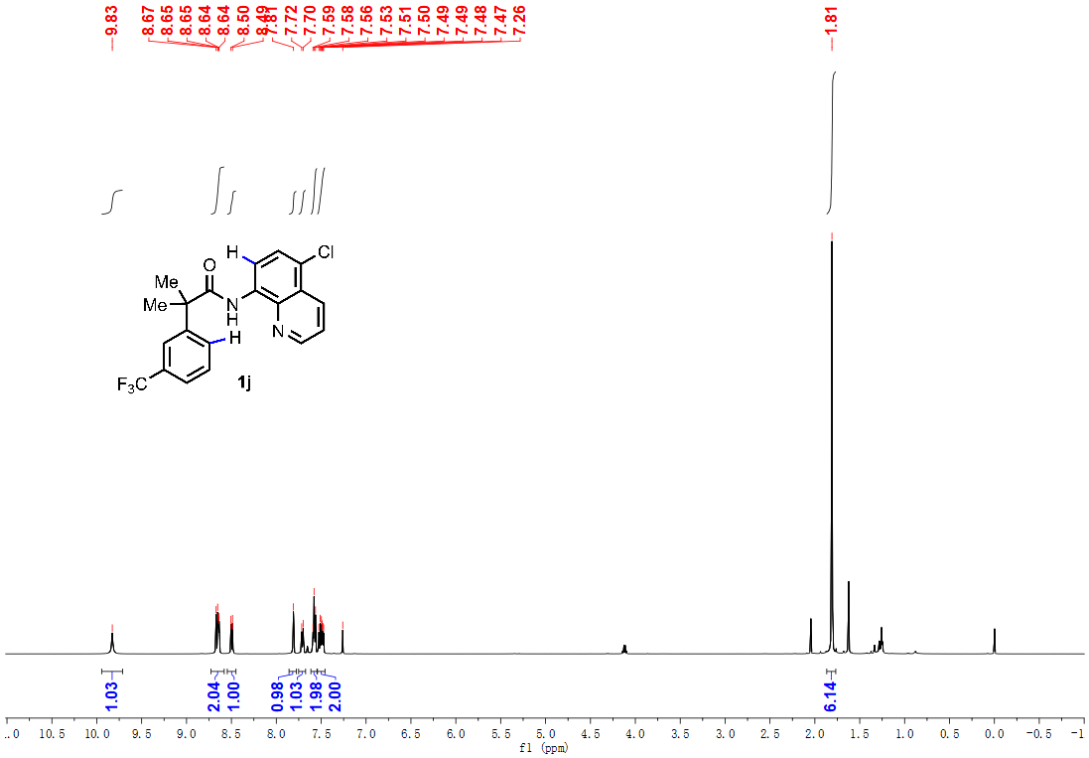
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1i**



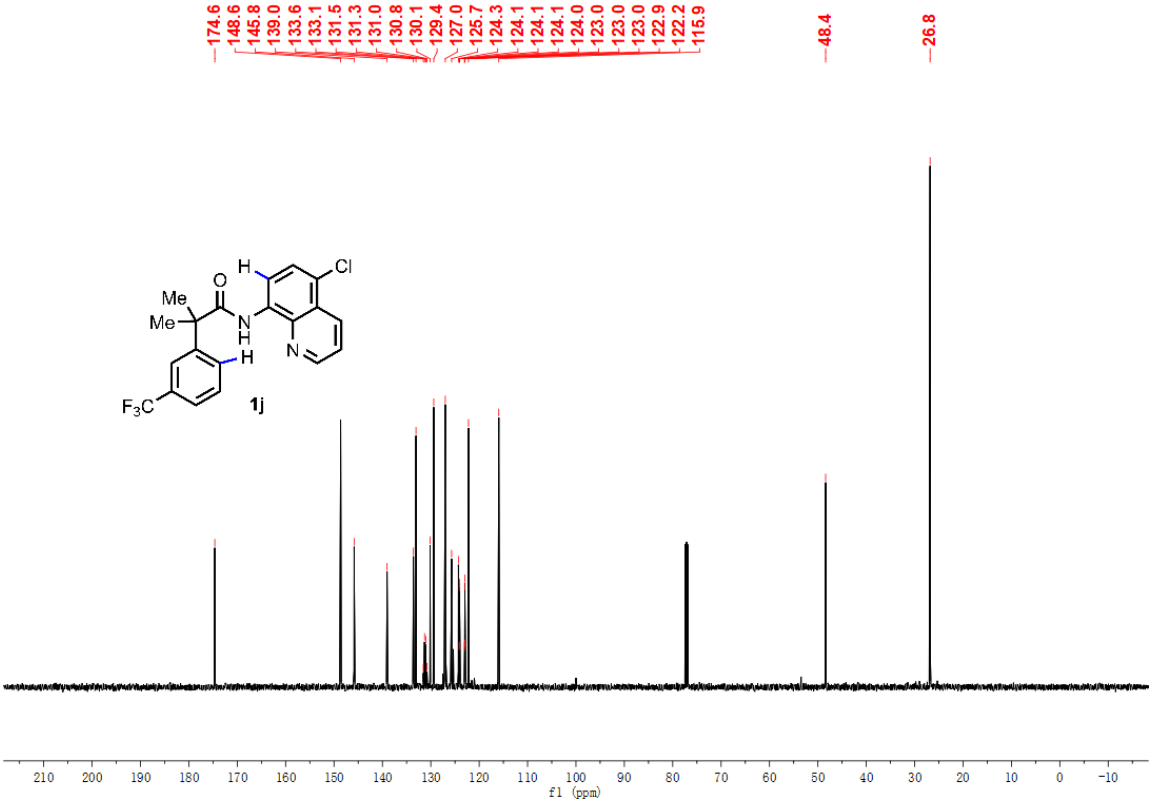
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1i**



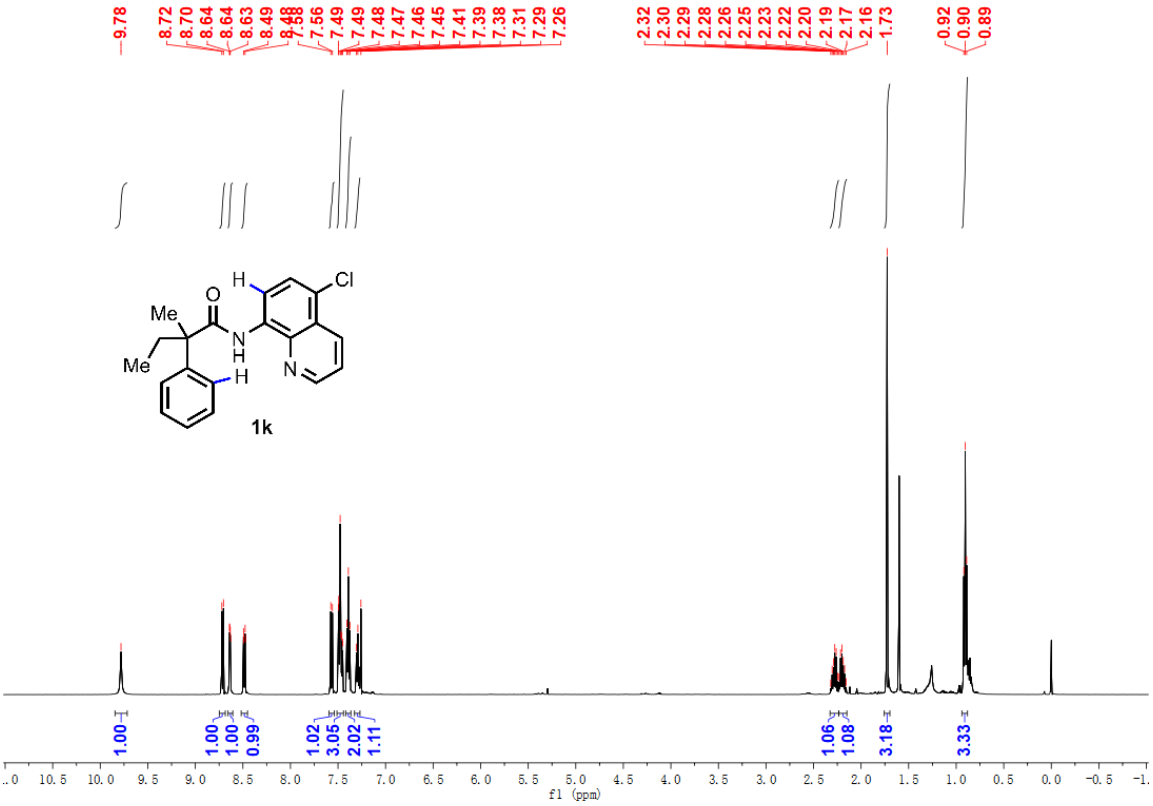
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1j**



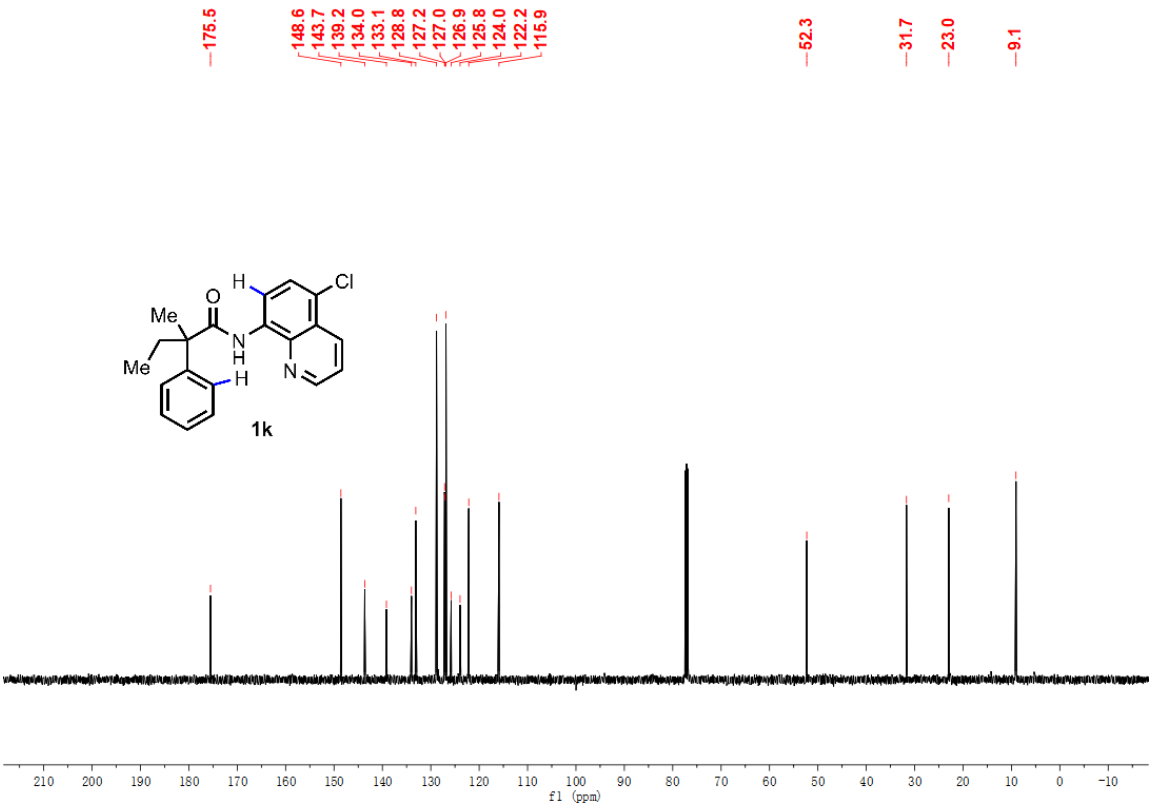
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1j**



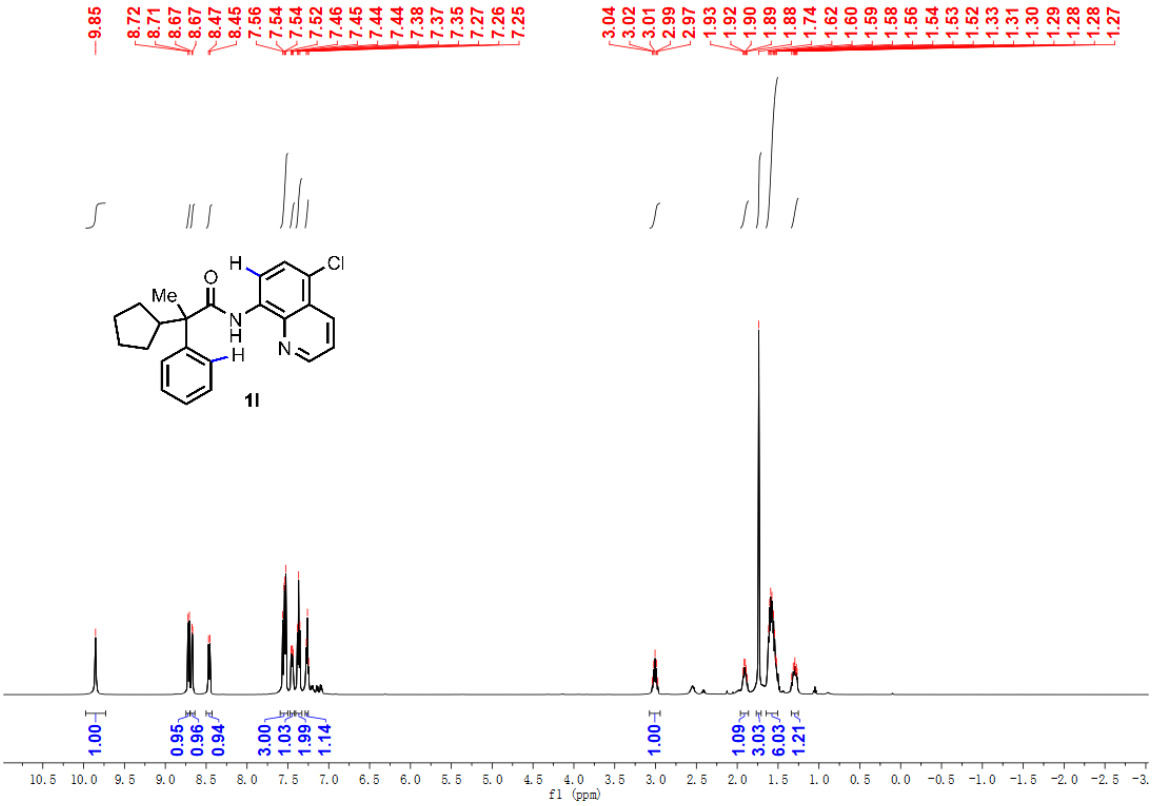
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1k**



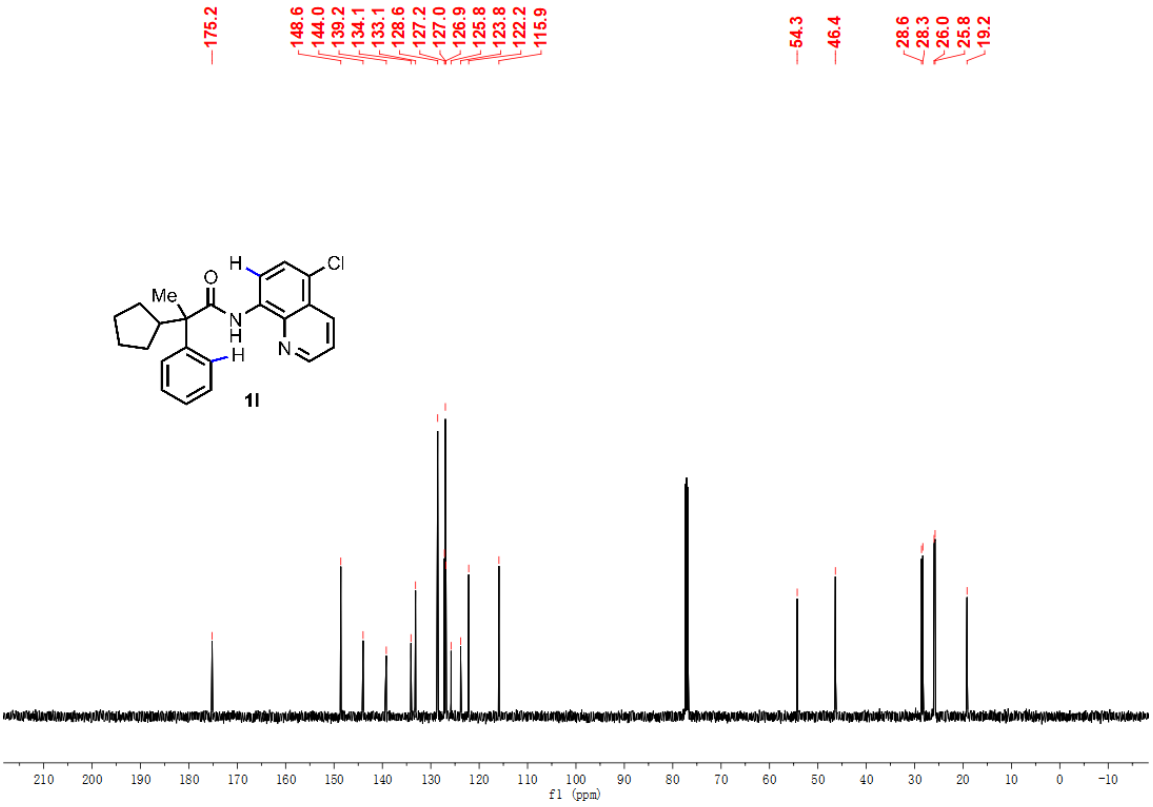
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1k**



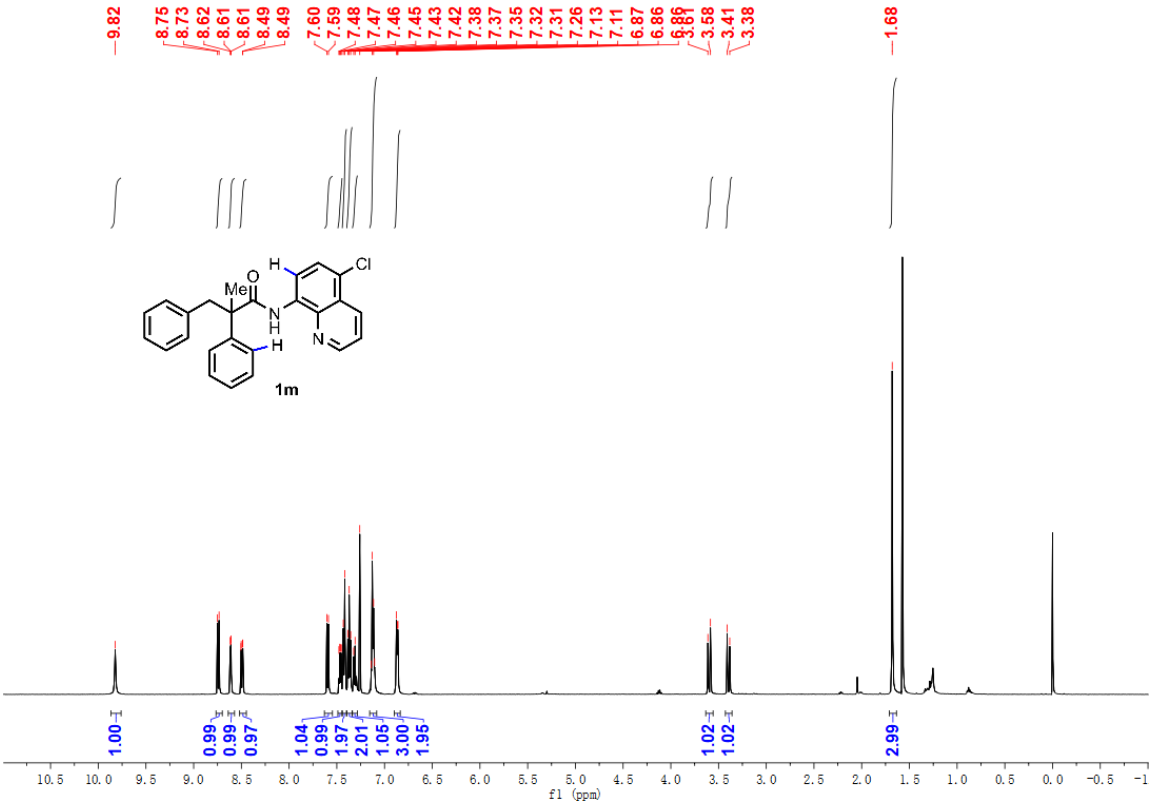
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1l**



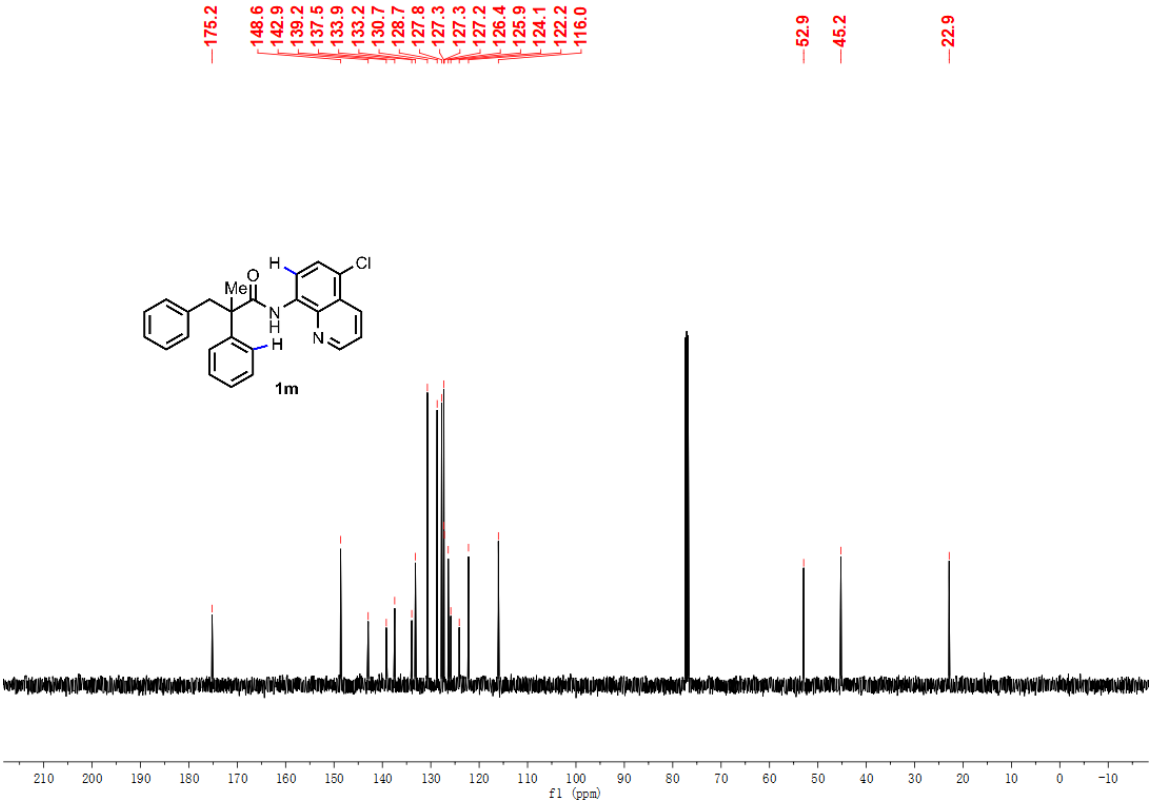
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1l**



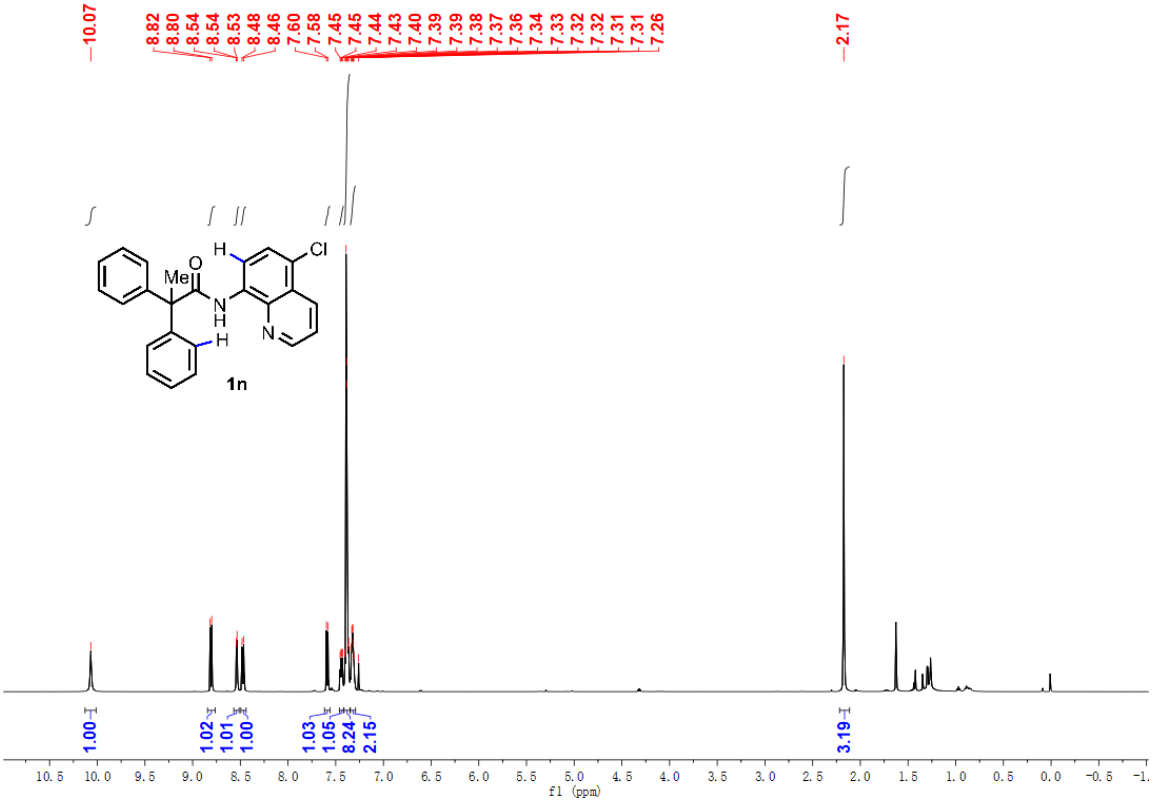
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1m**



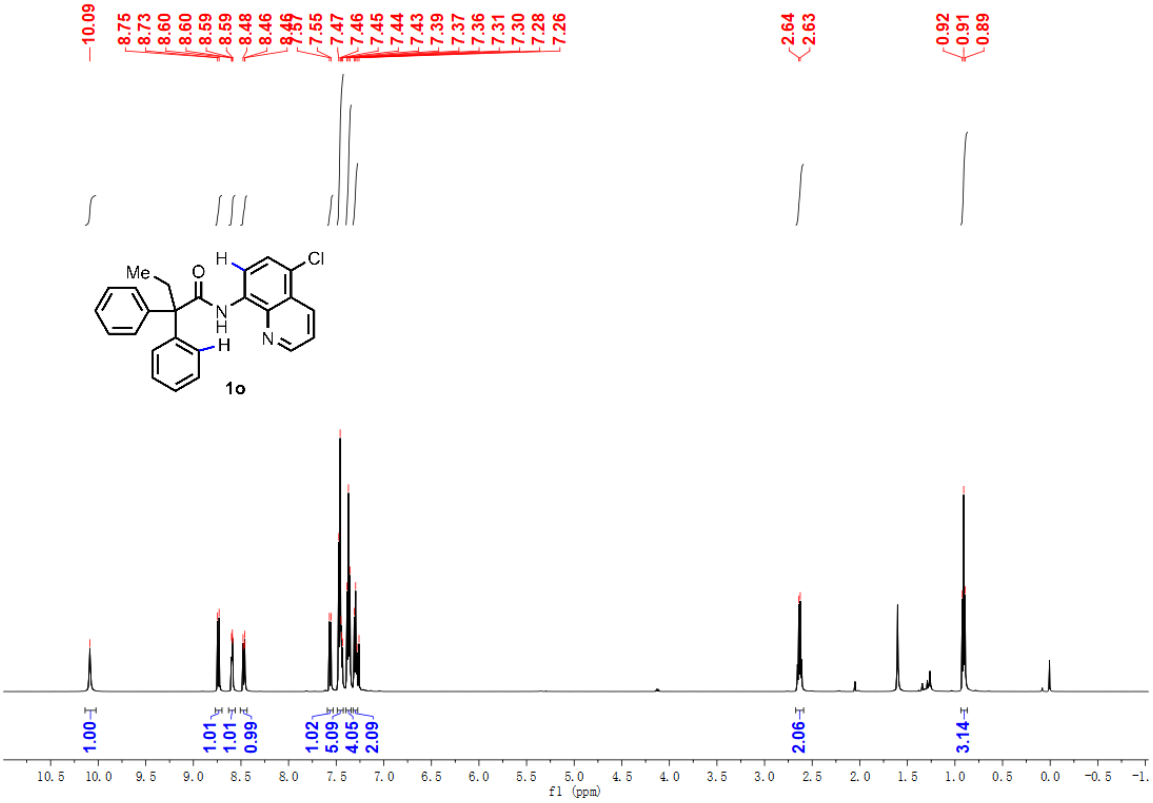
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1m**



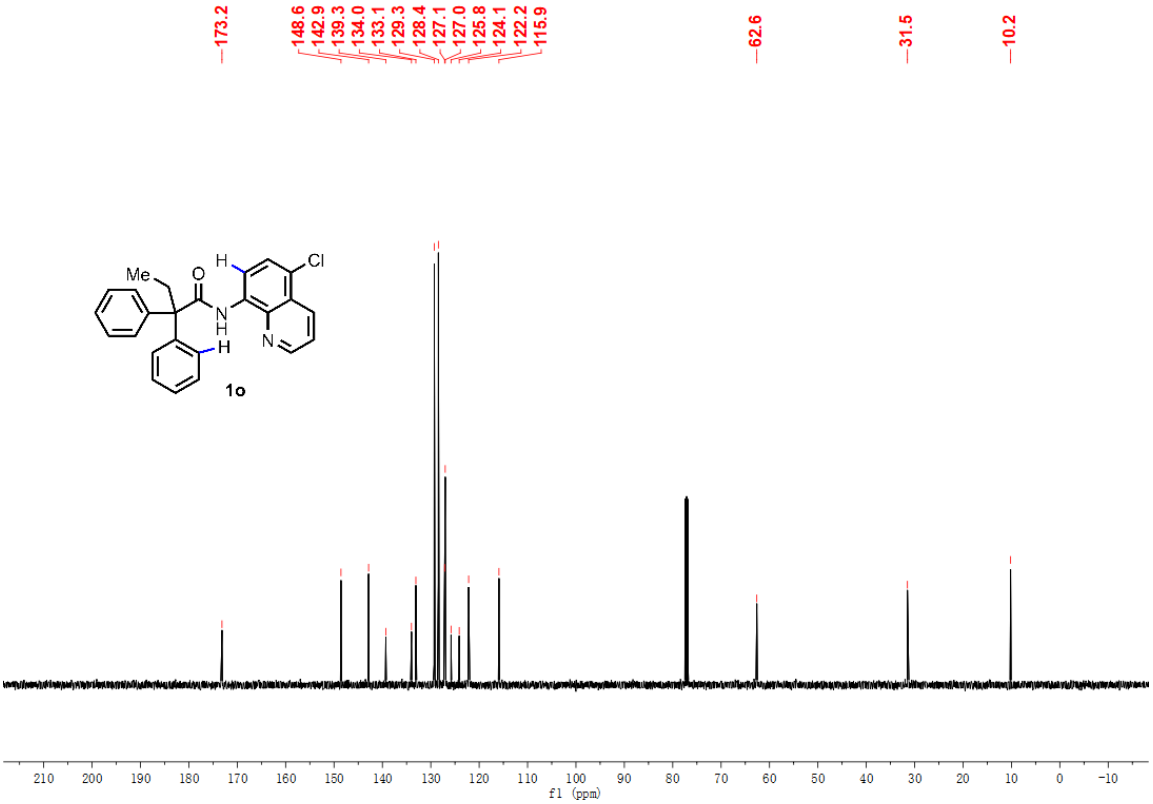
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1n**



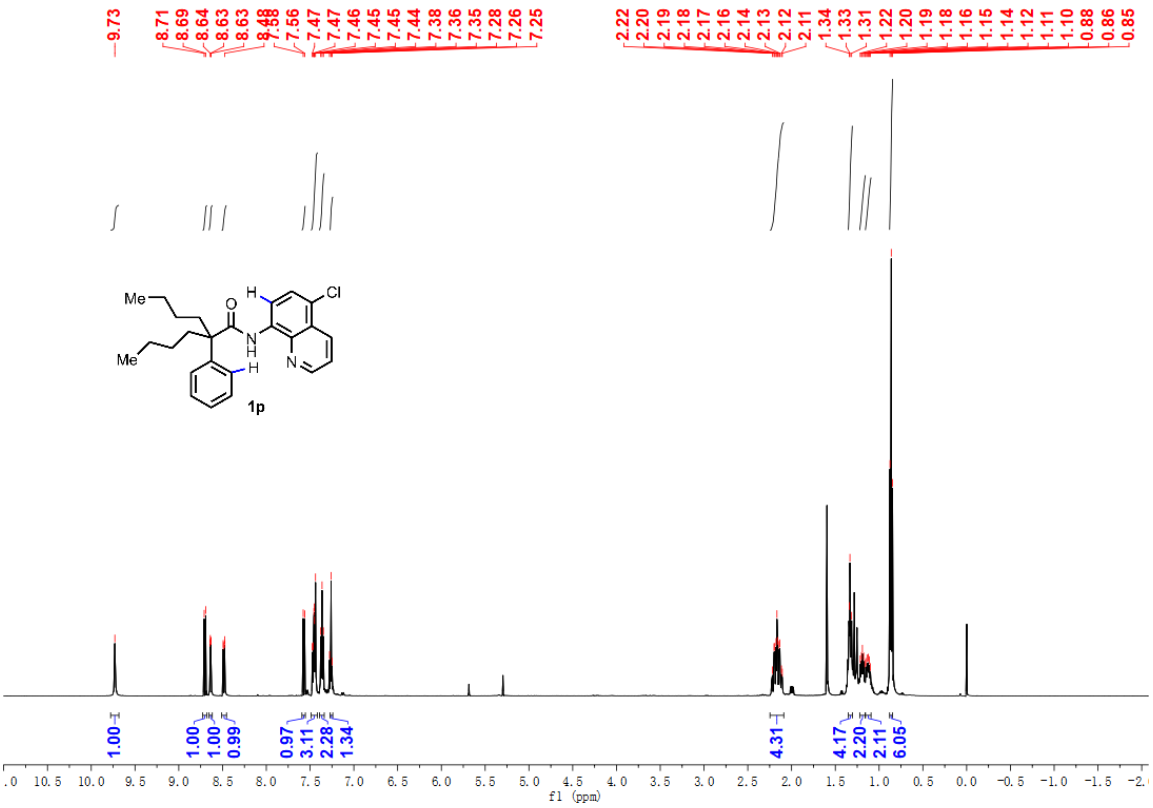
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1o**



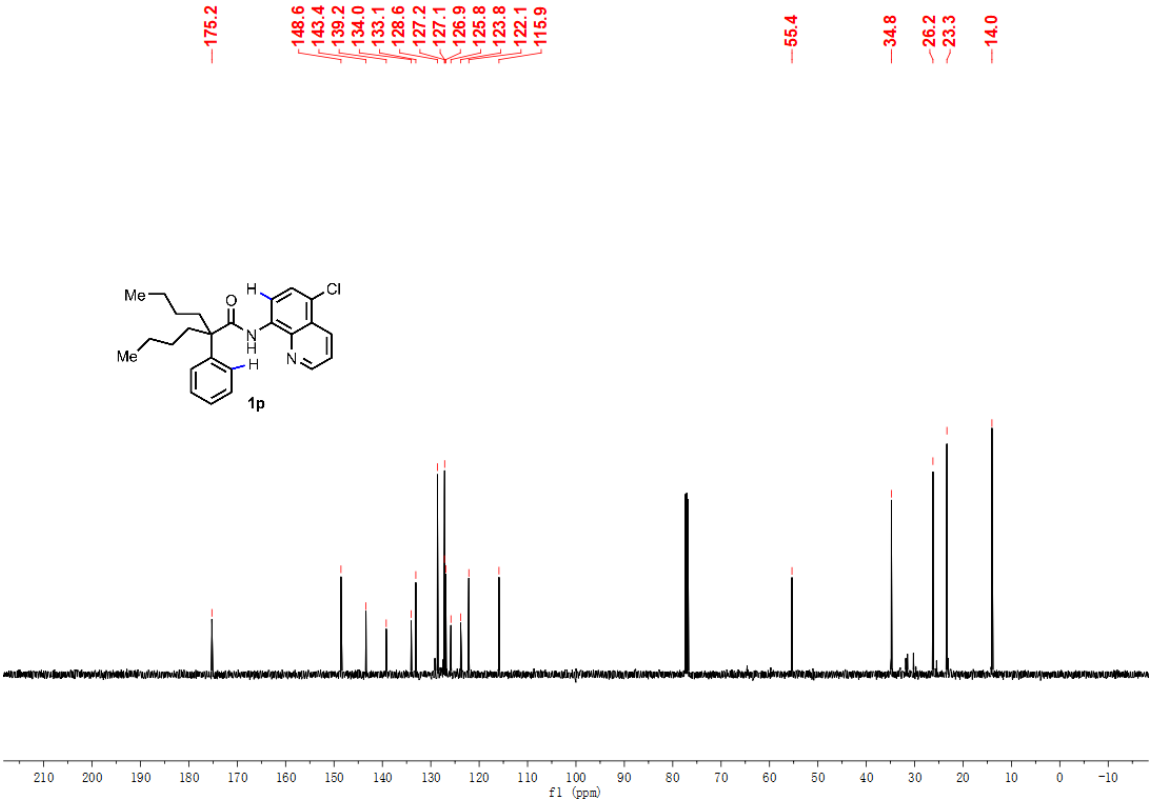
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1o**



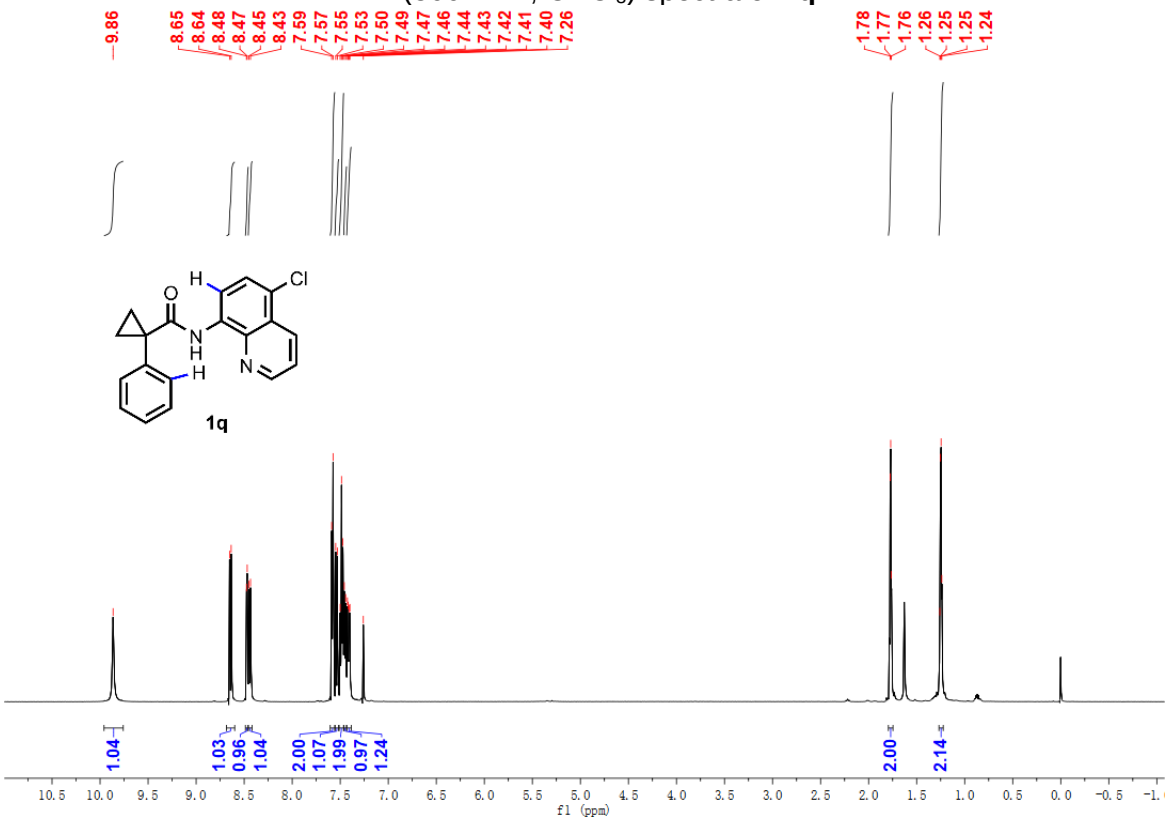
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1p**



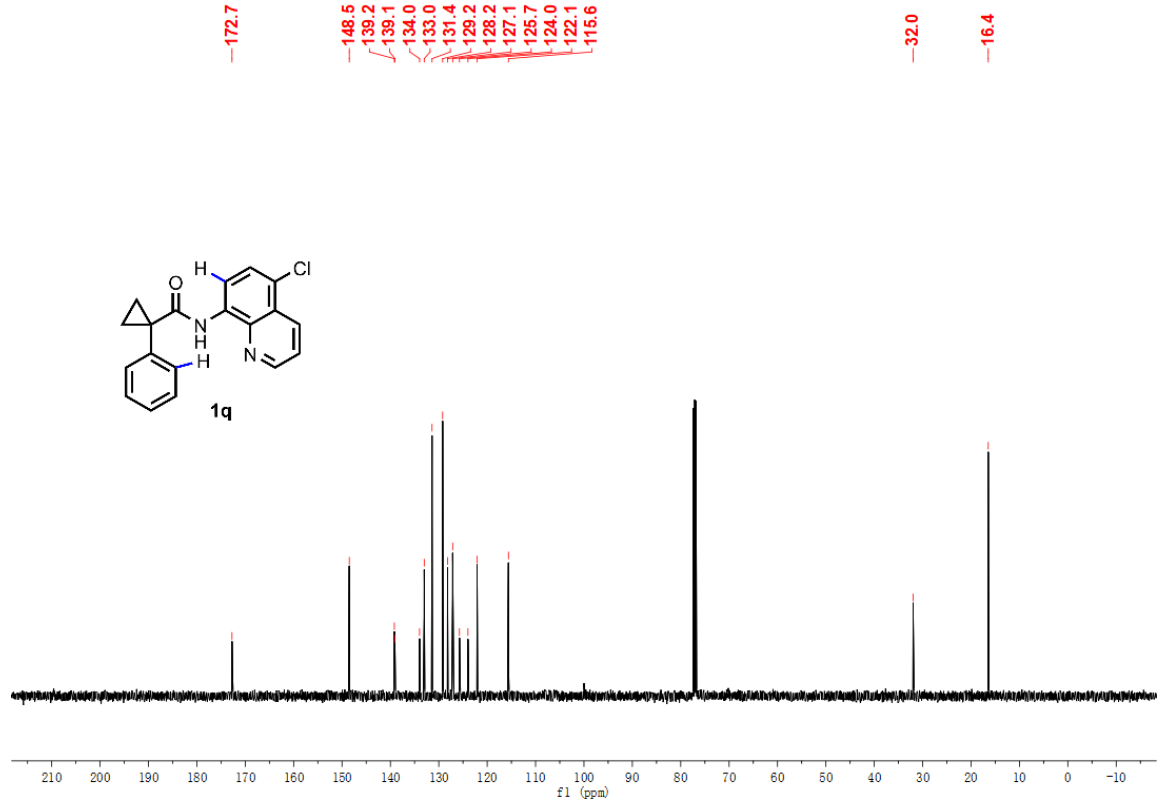
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1p**



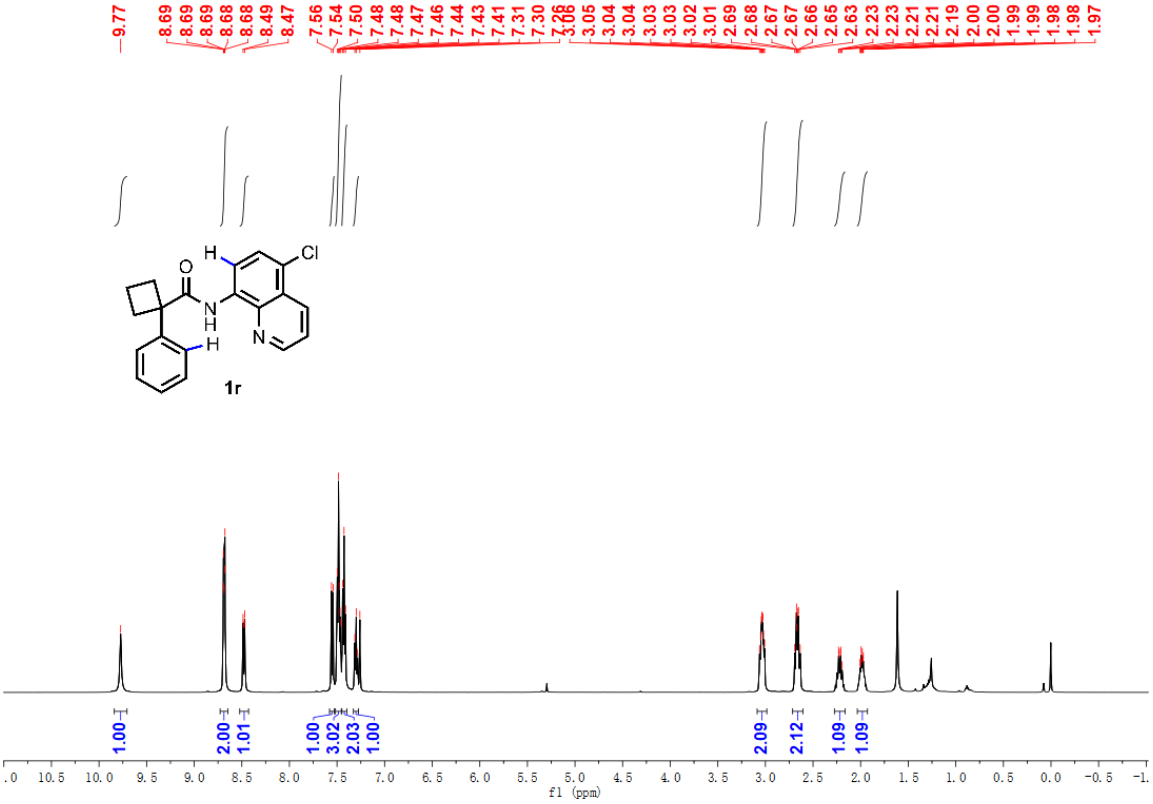
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1q**



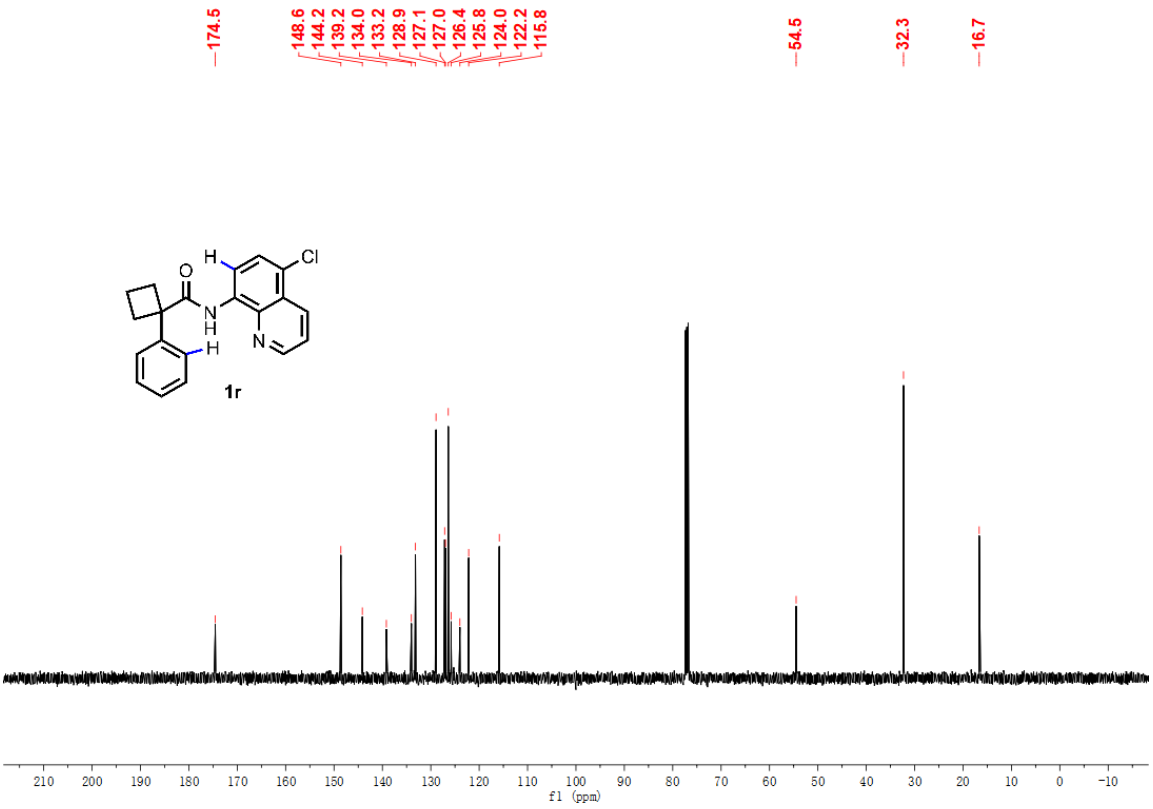
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1q**



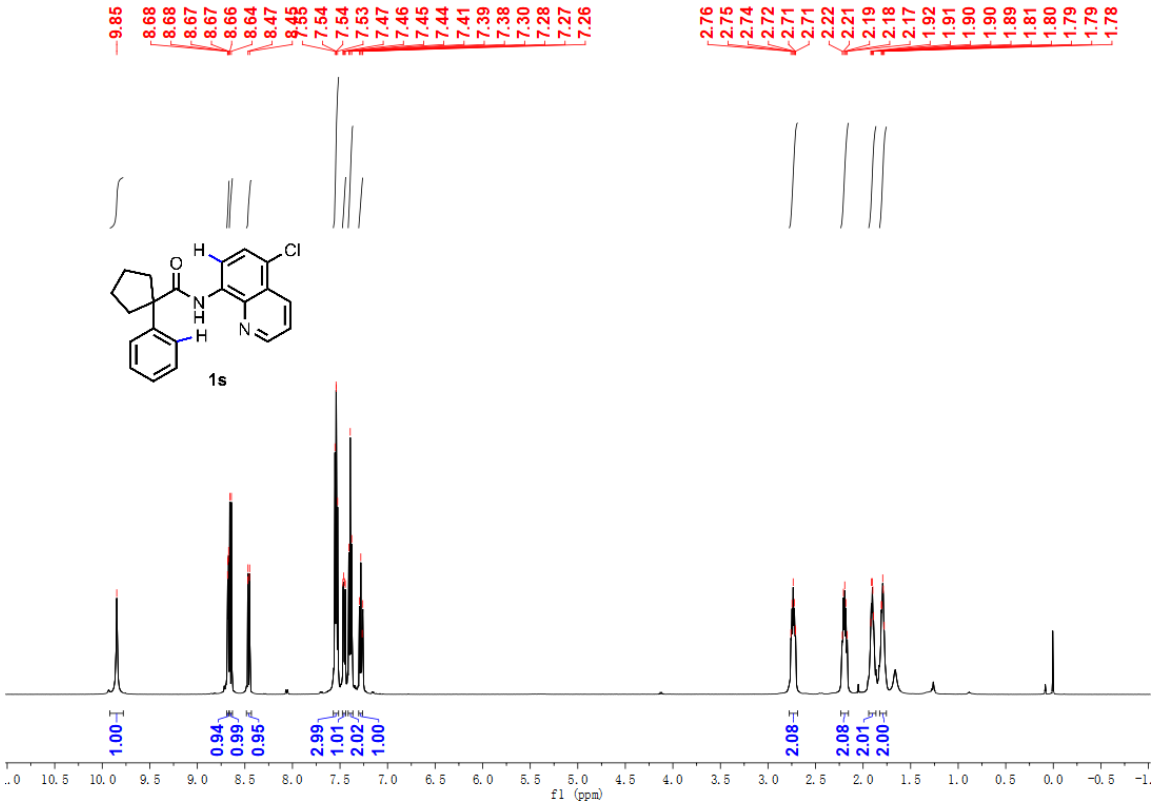
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1r**



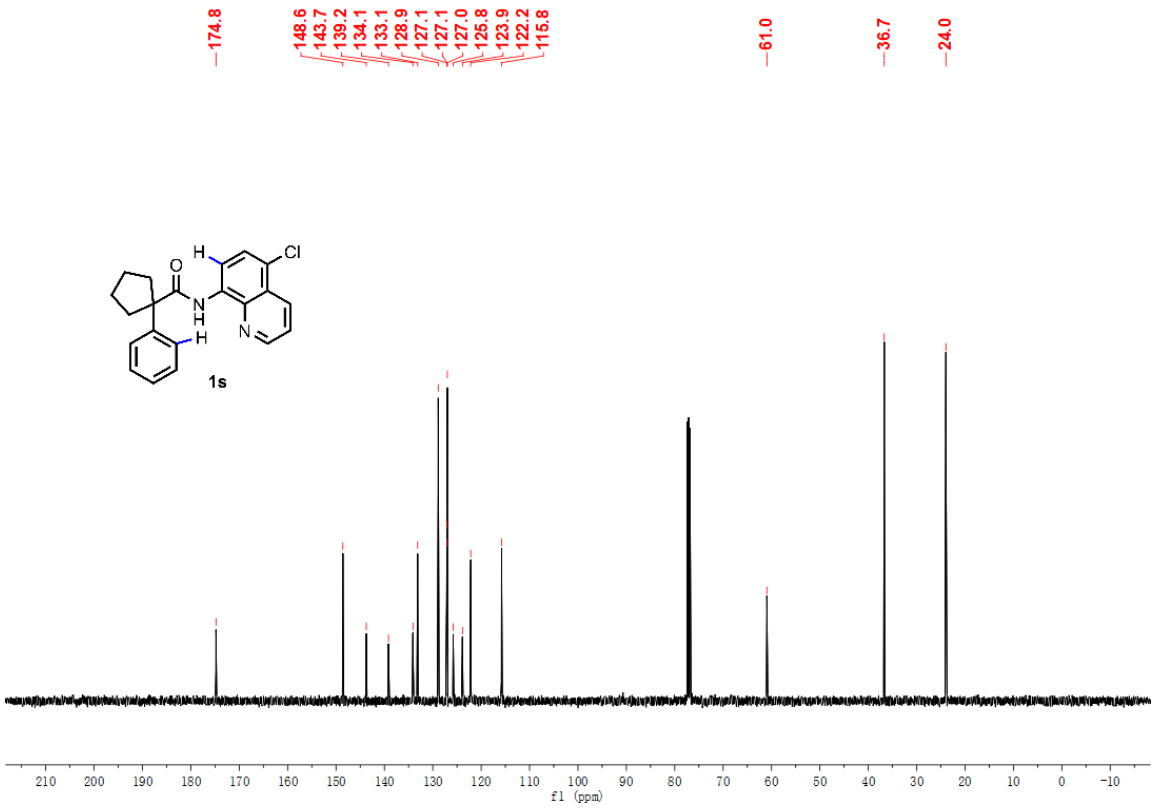
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1r**



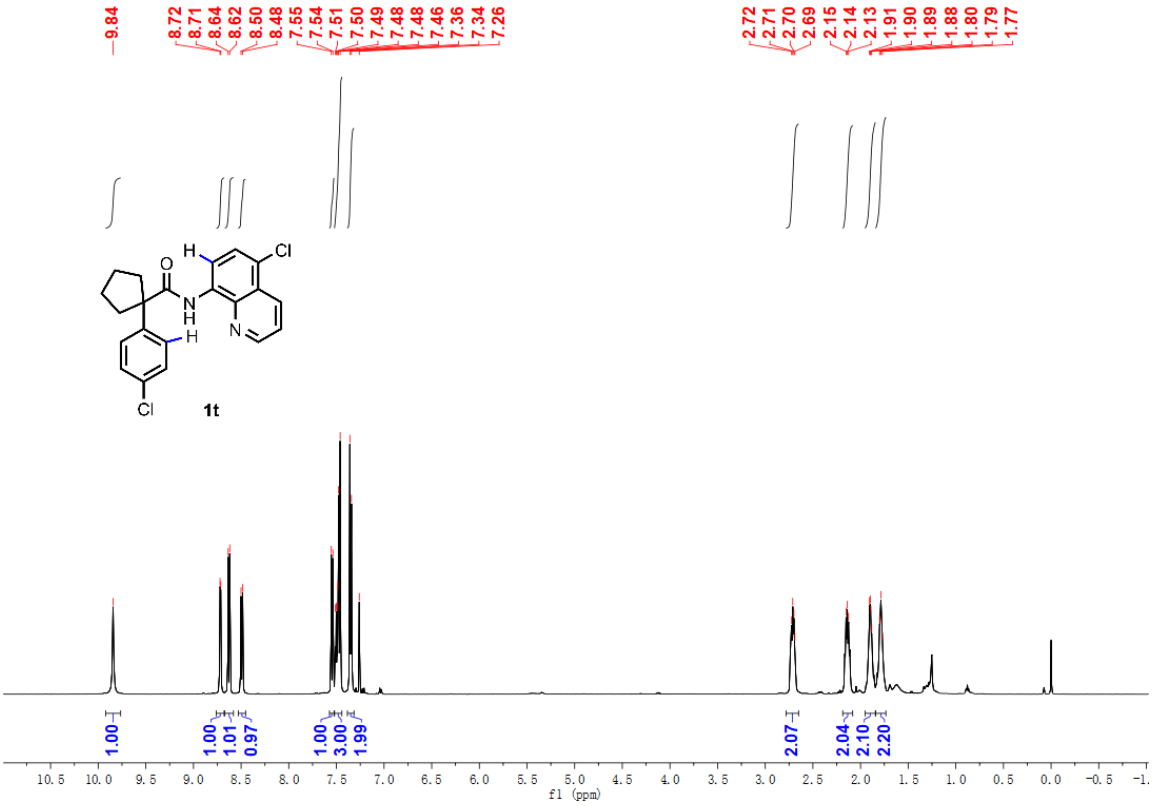
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1s**



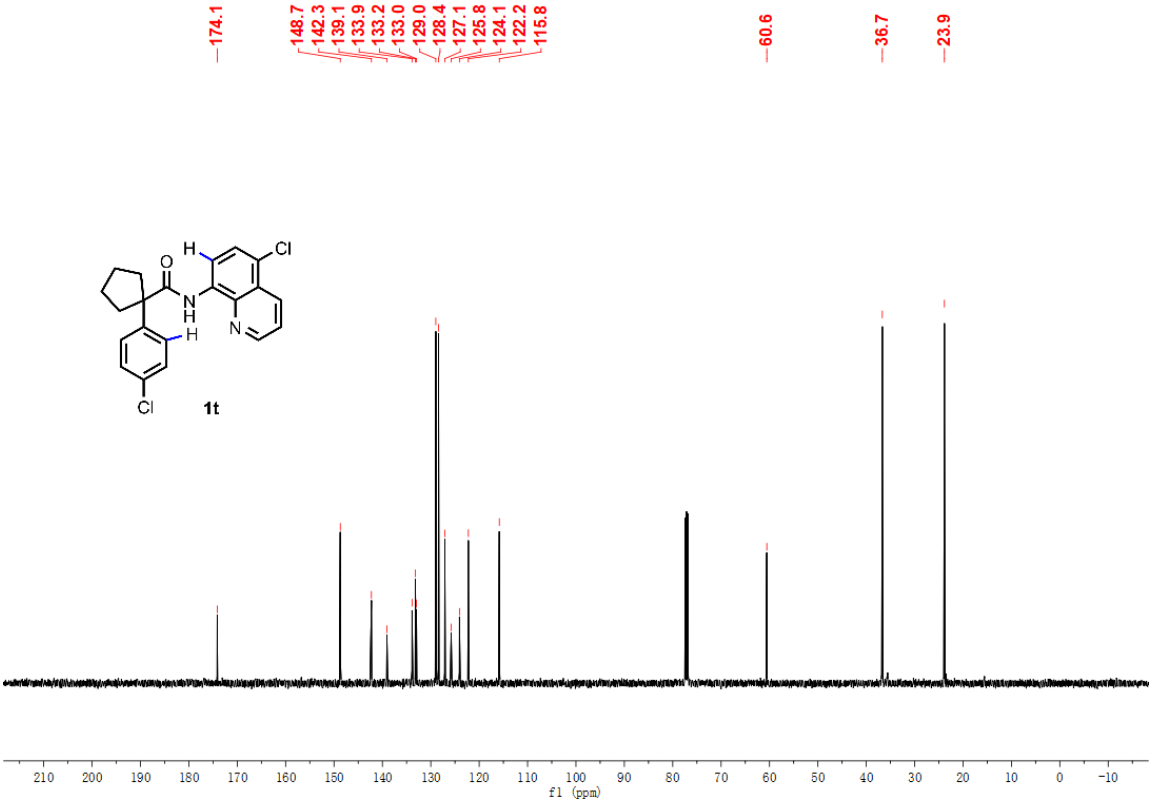
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1s**



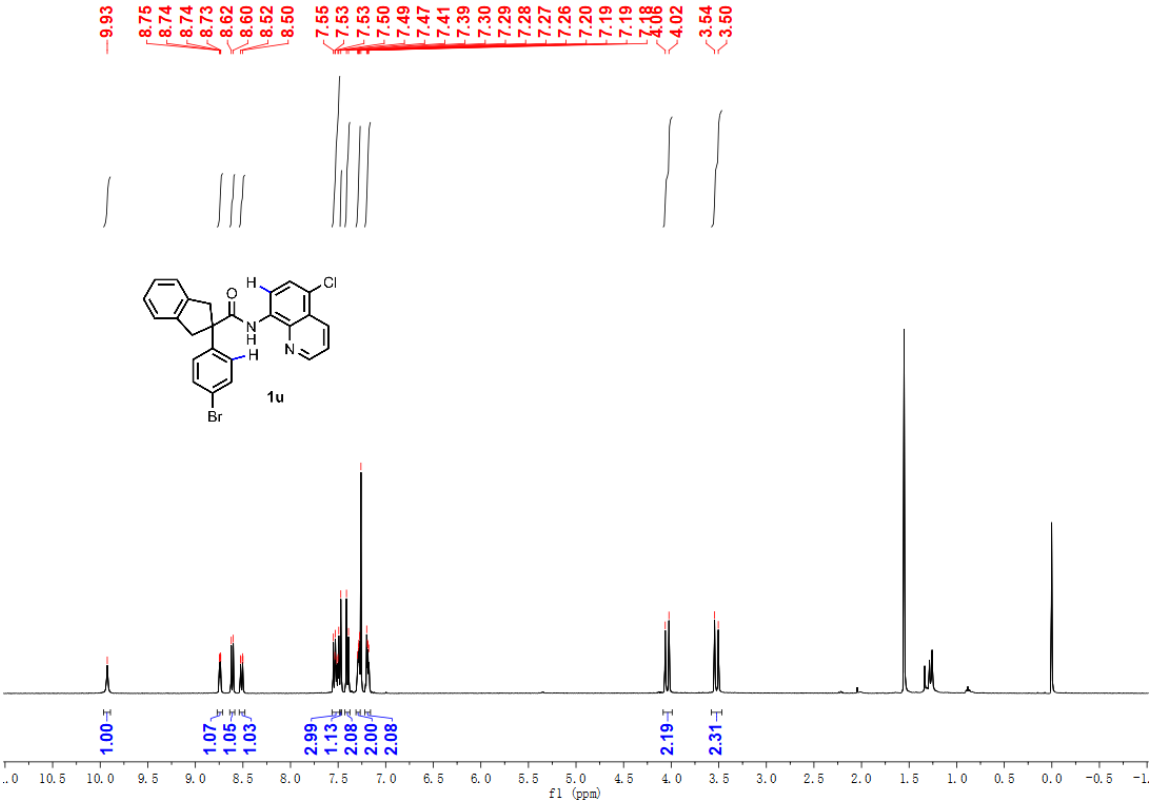
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1t**



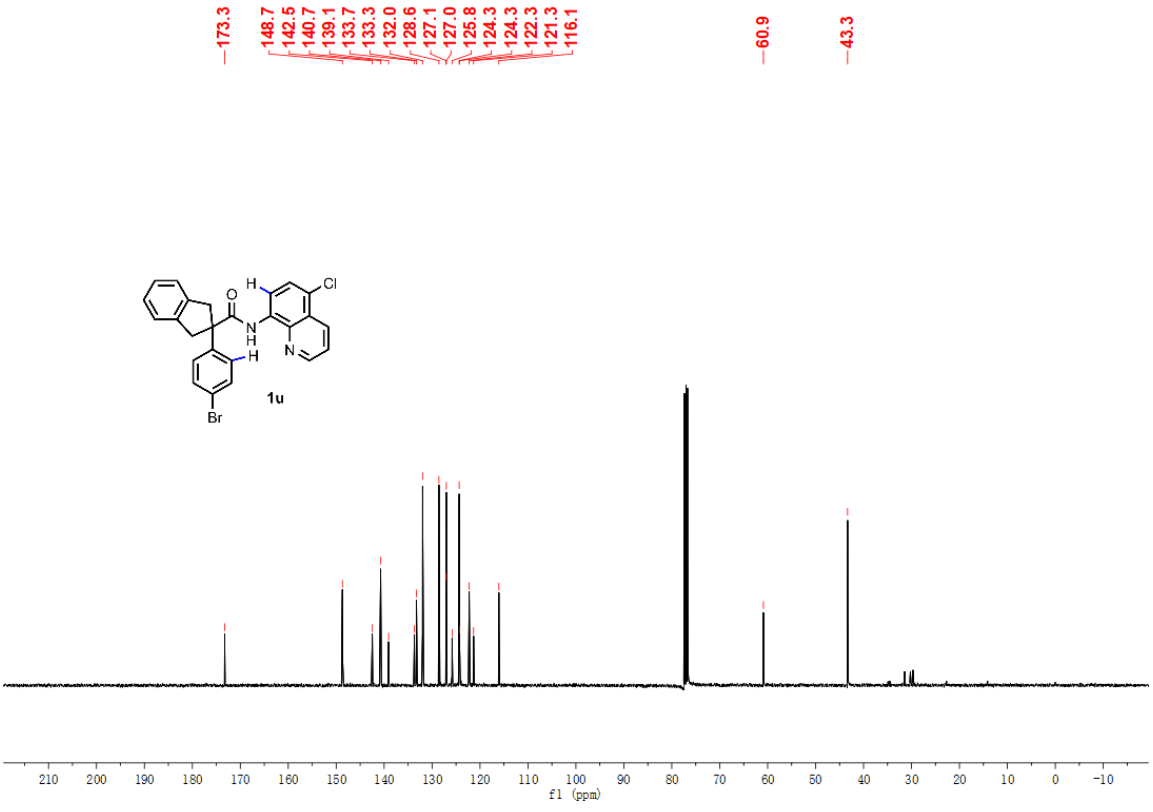
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1t**



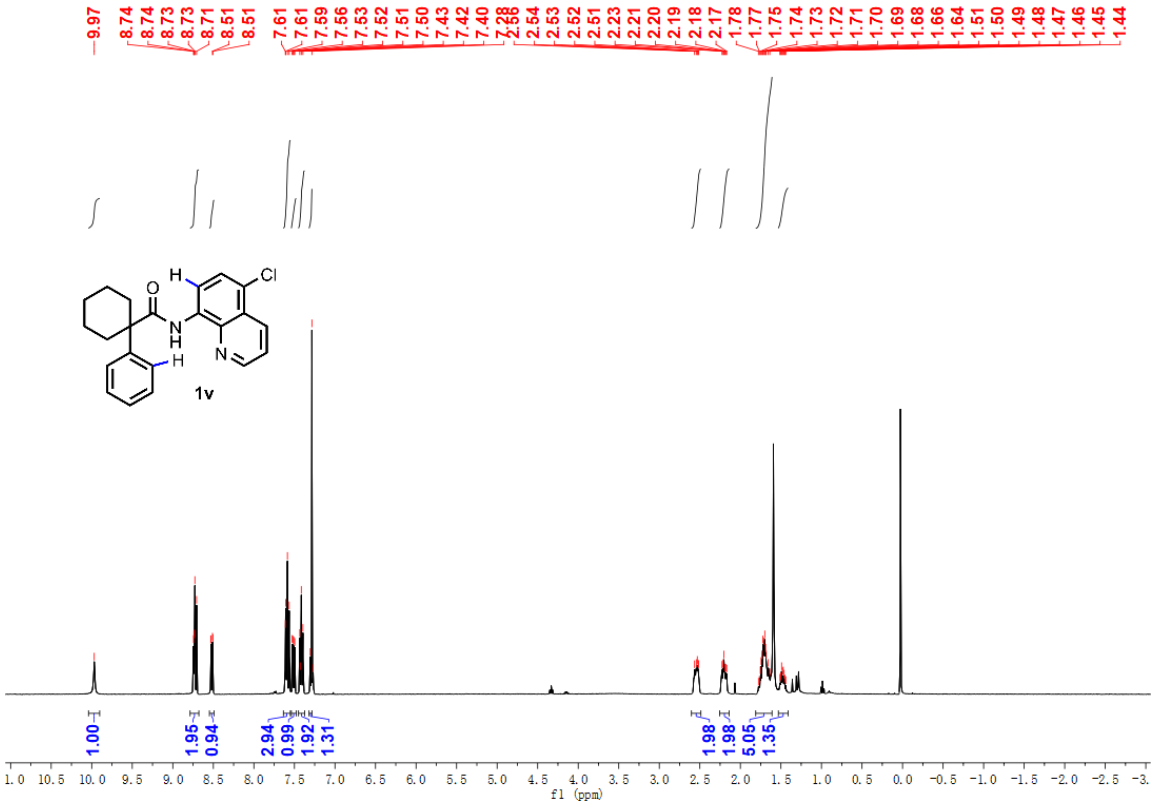
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **1u**



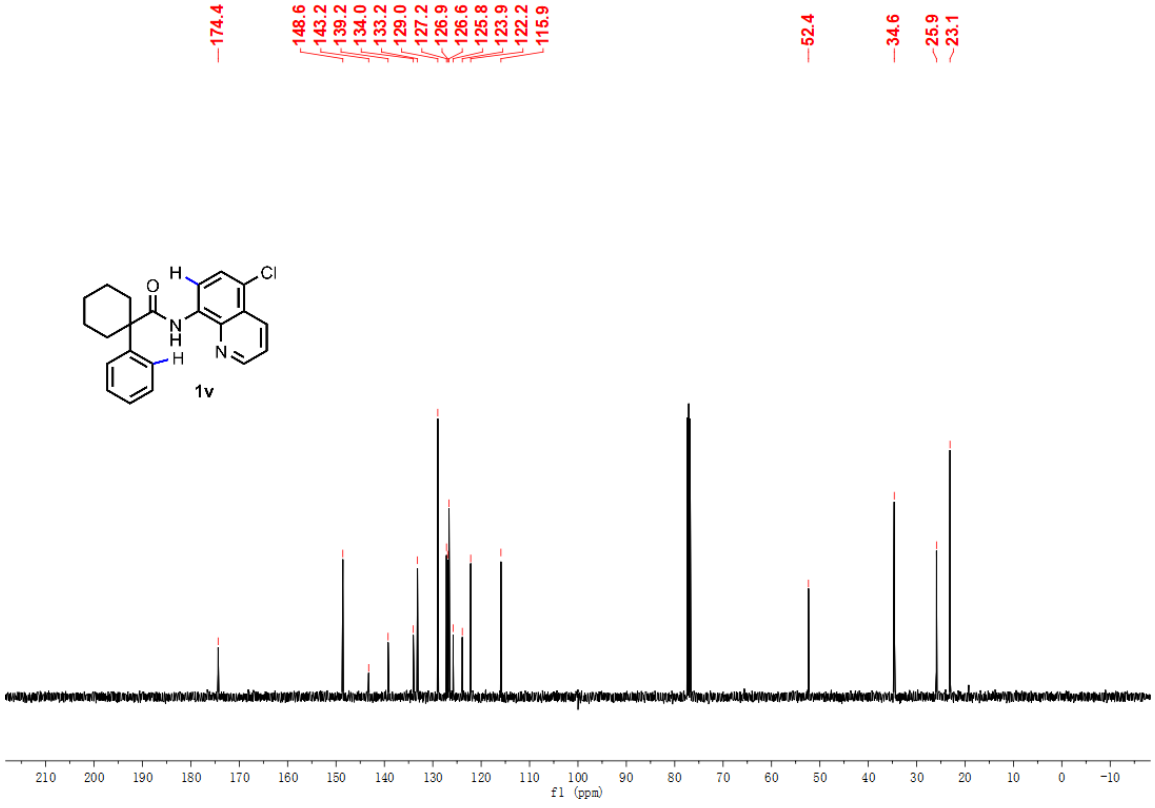
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **1u**



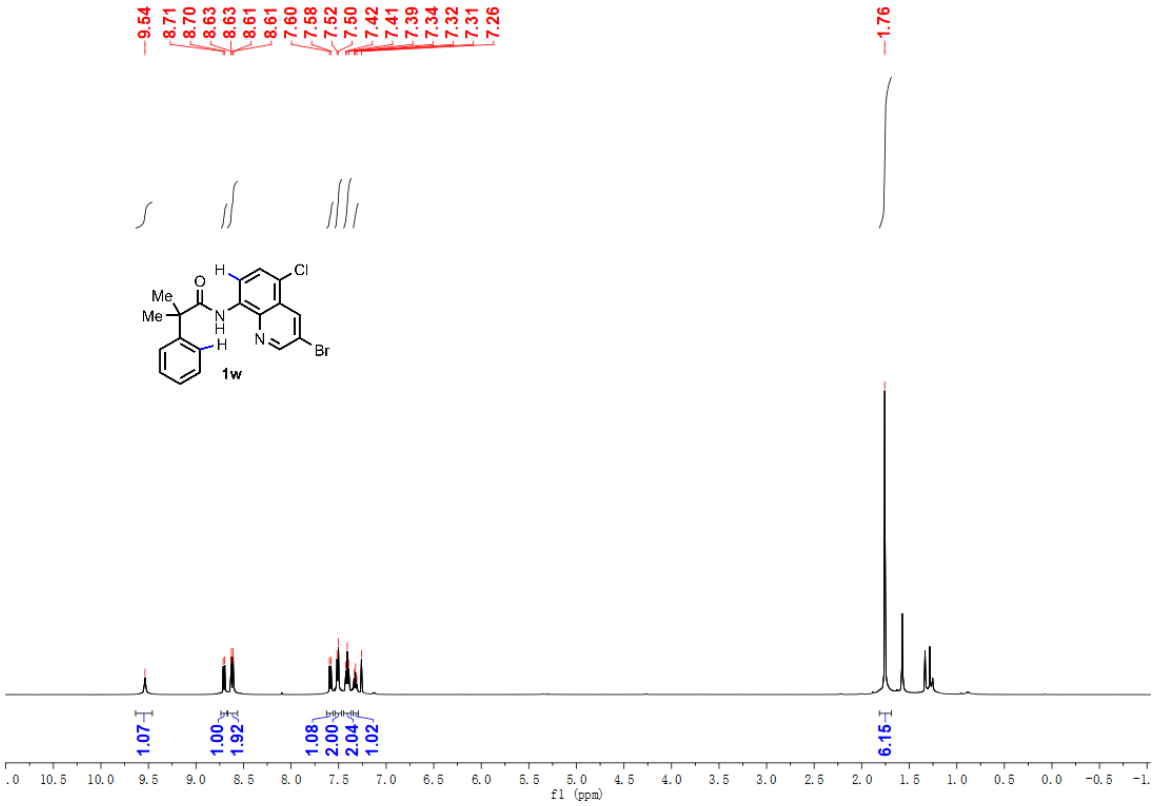
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **1v**



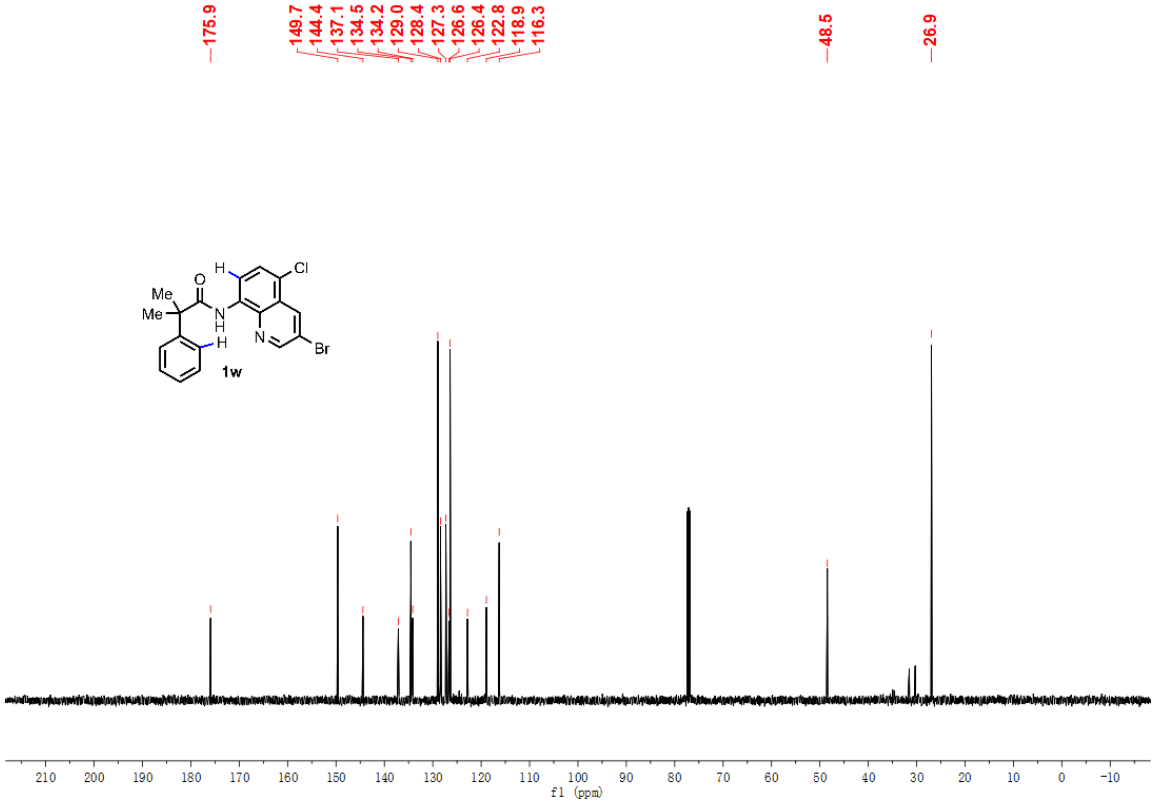
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1v**



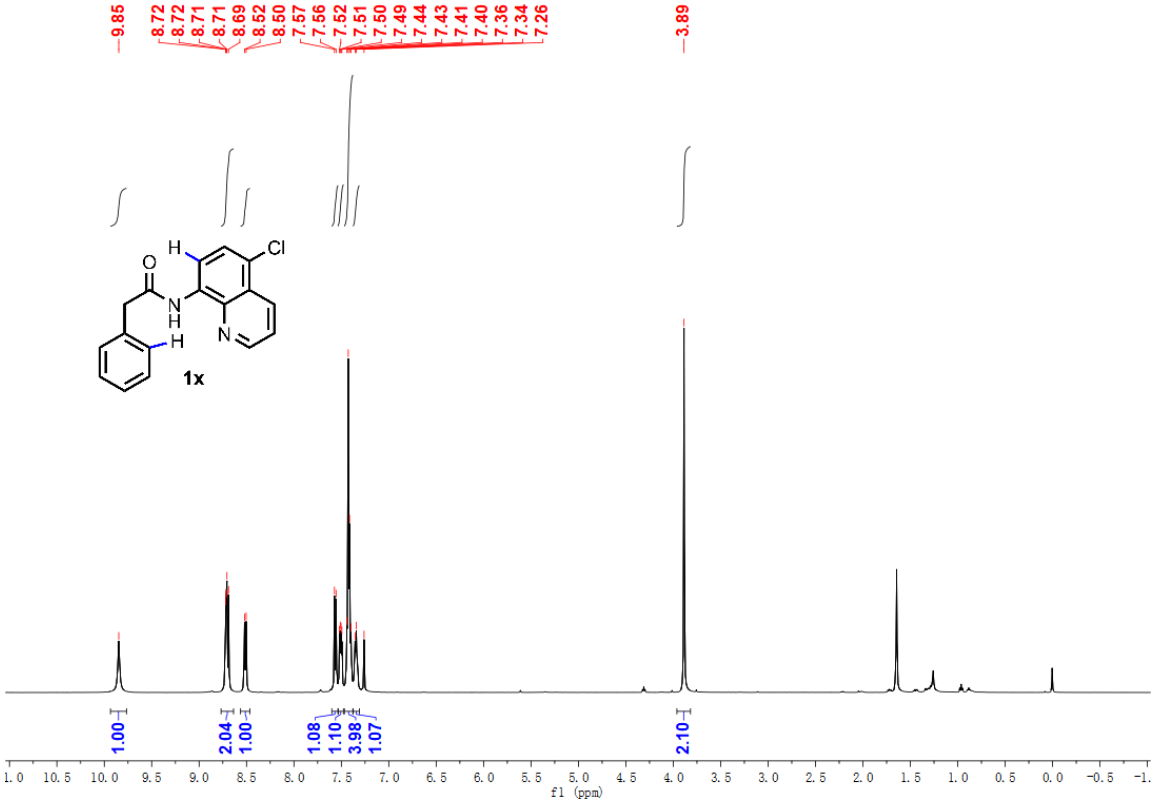
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1w**



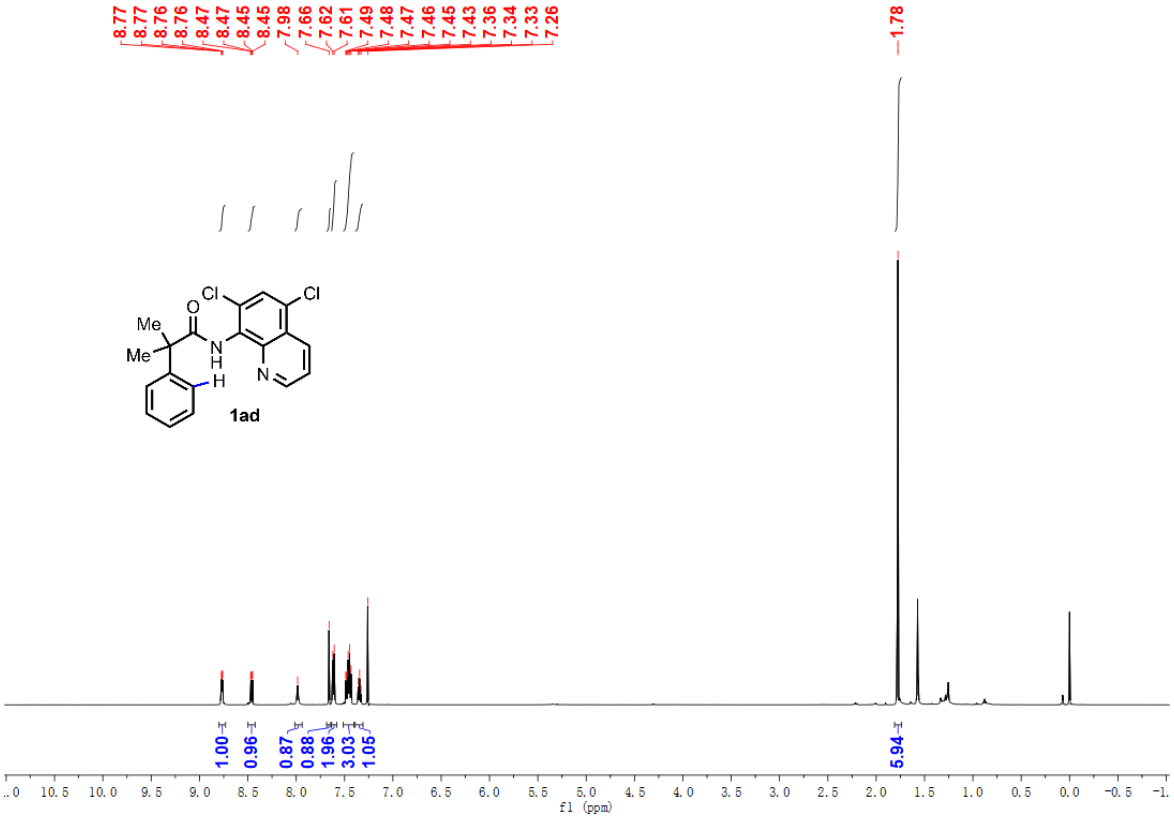
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1w**



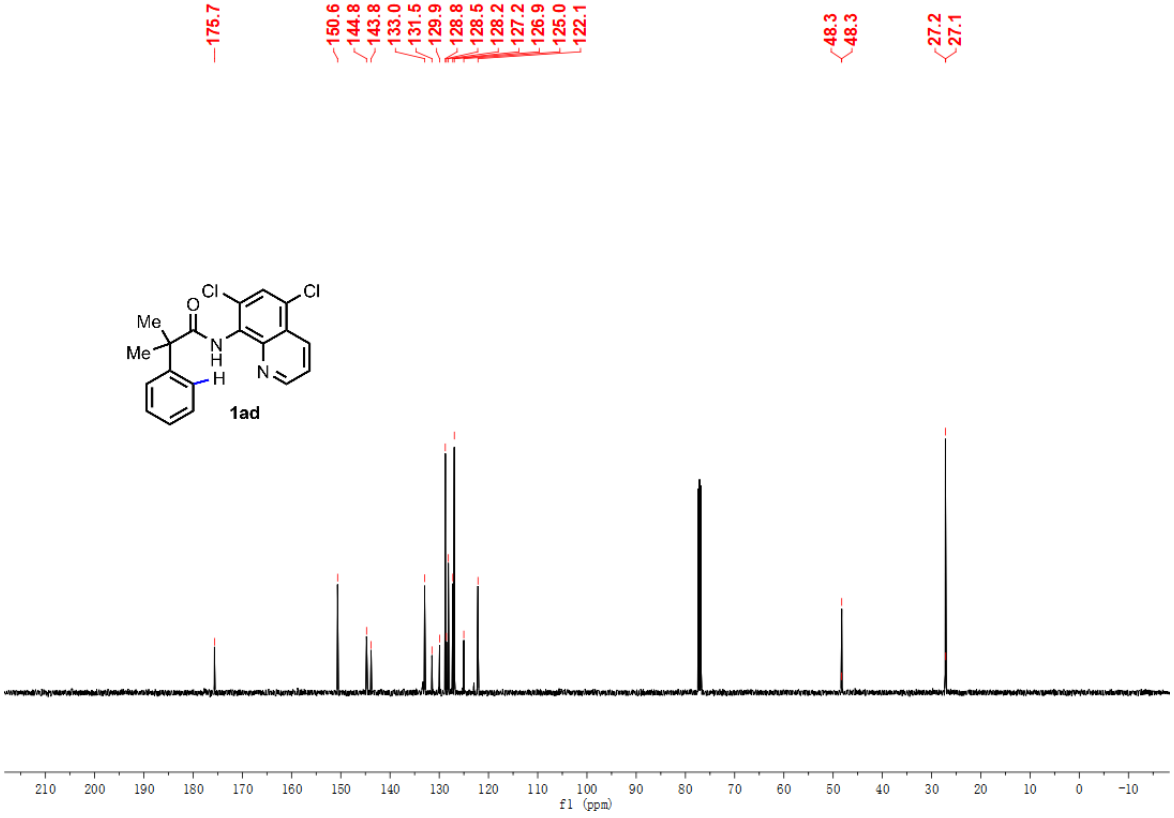
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1x**



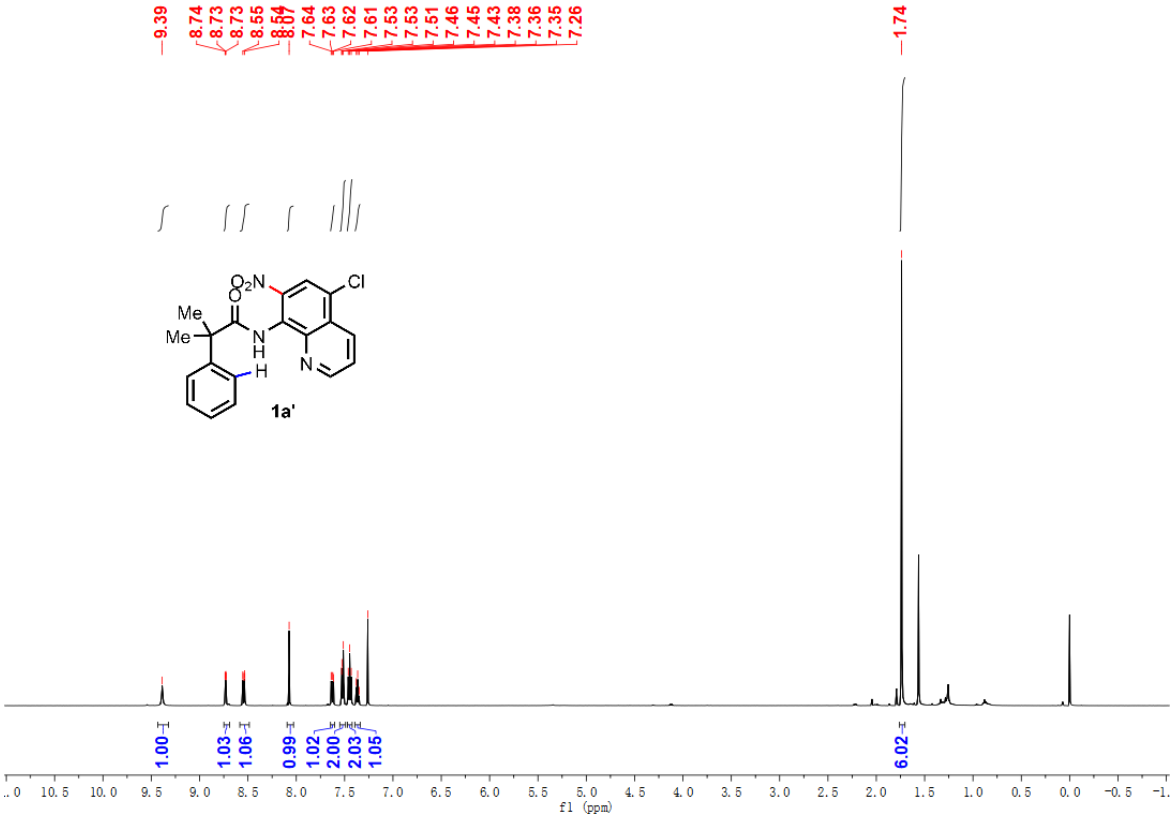
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1ad**



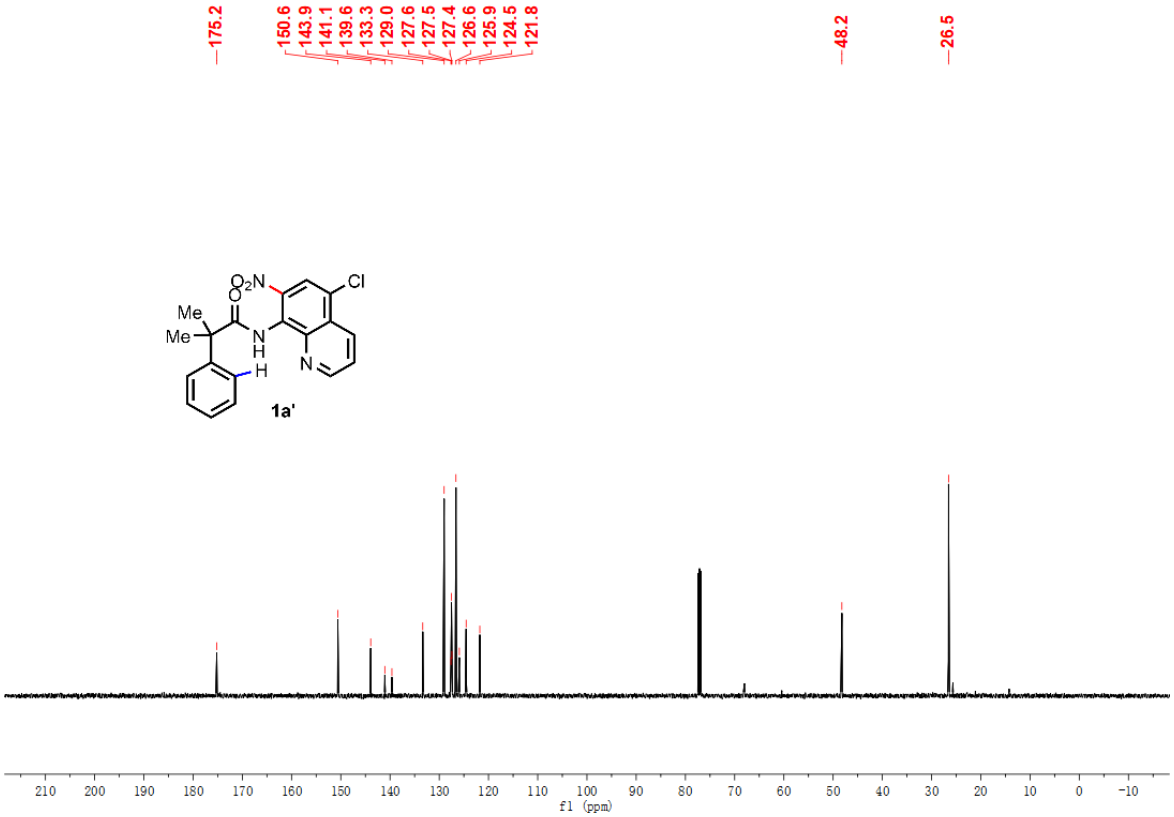
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1ad**



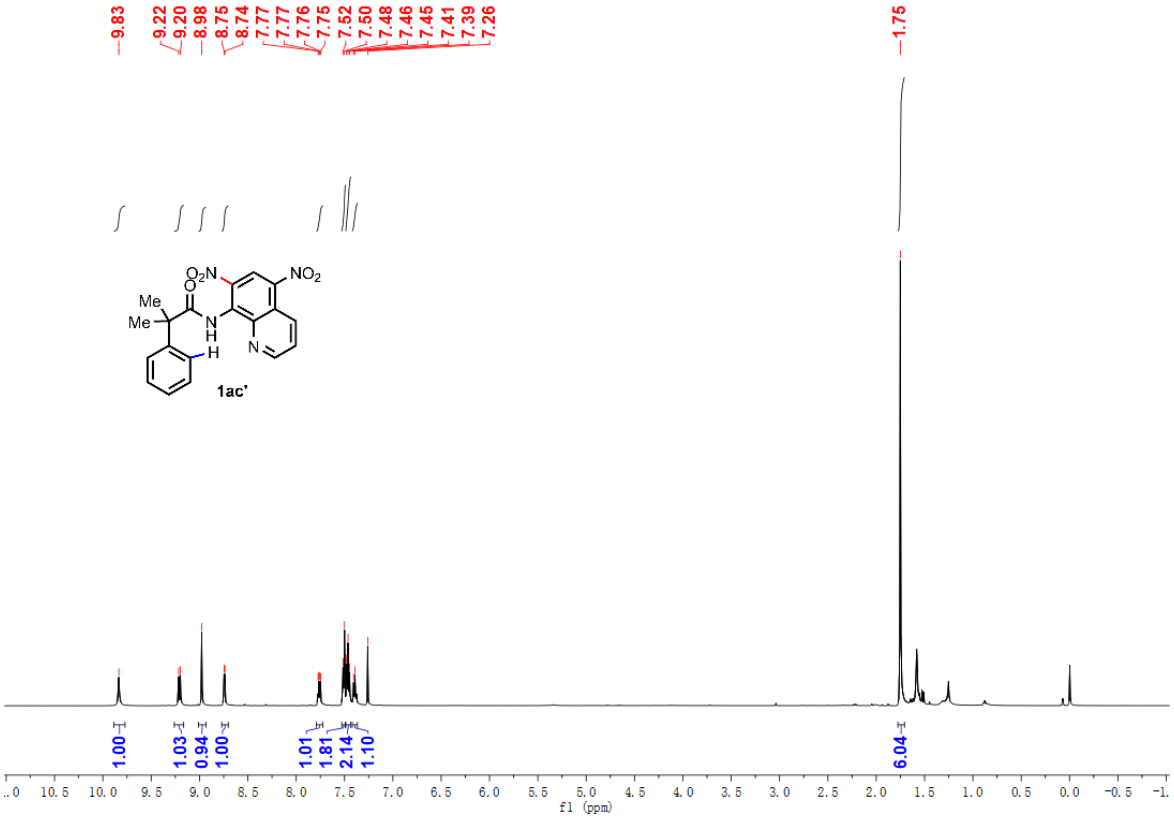
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1a'**



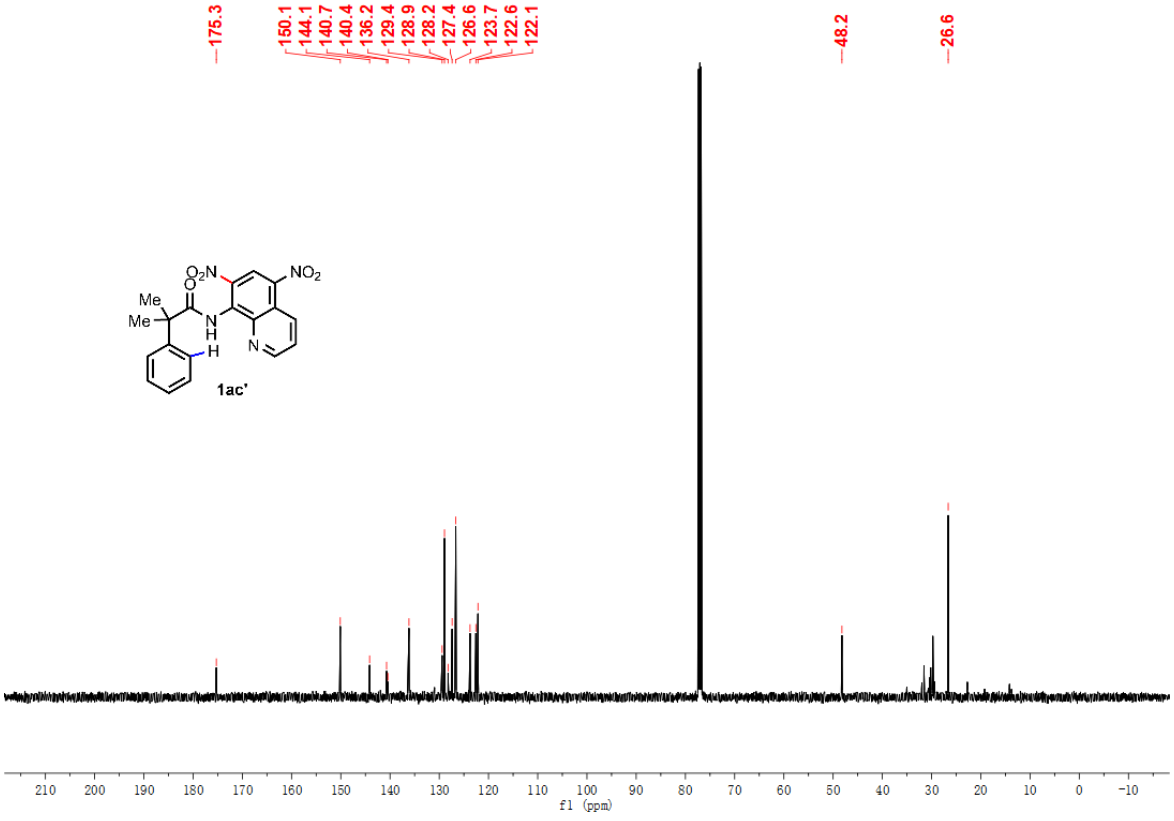
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1a'**



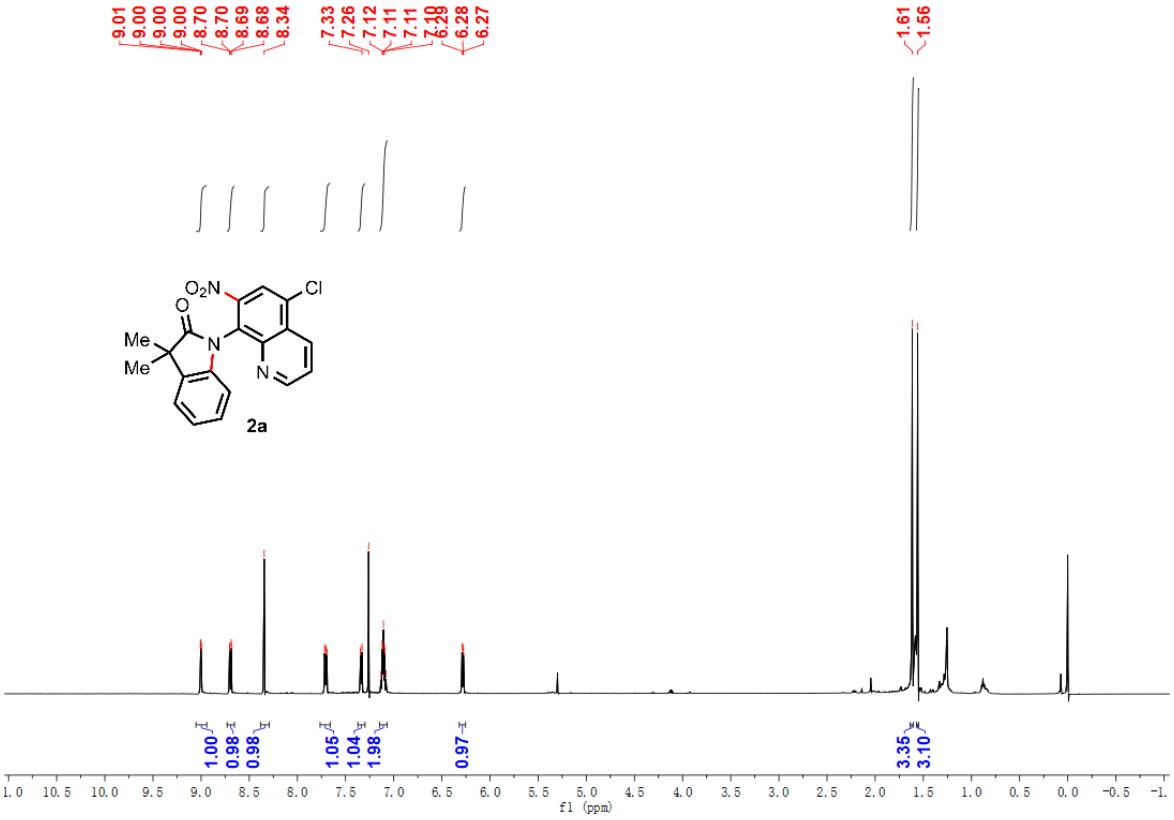
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **1ac'**



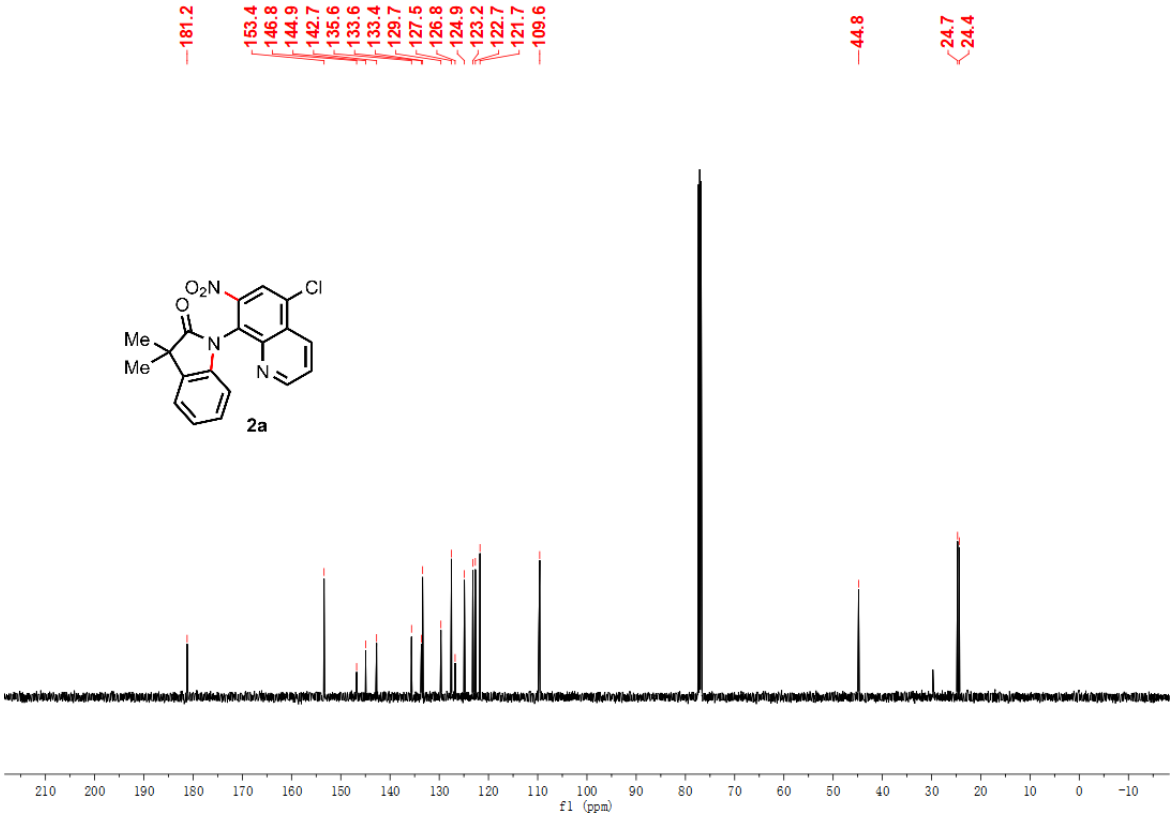
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **1ac'**



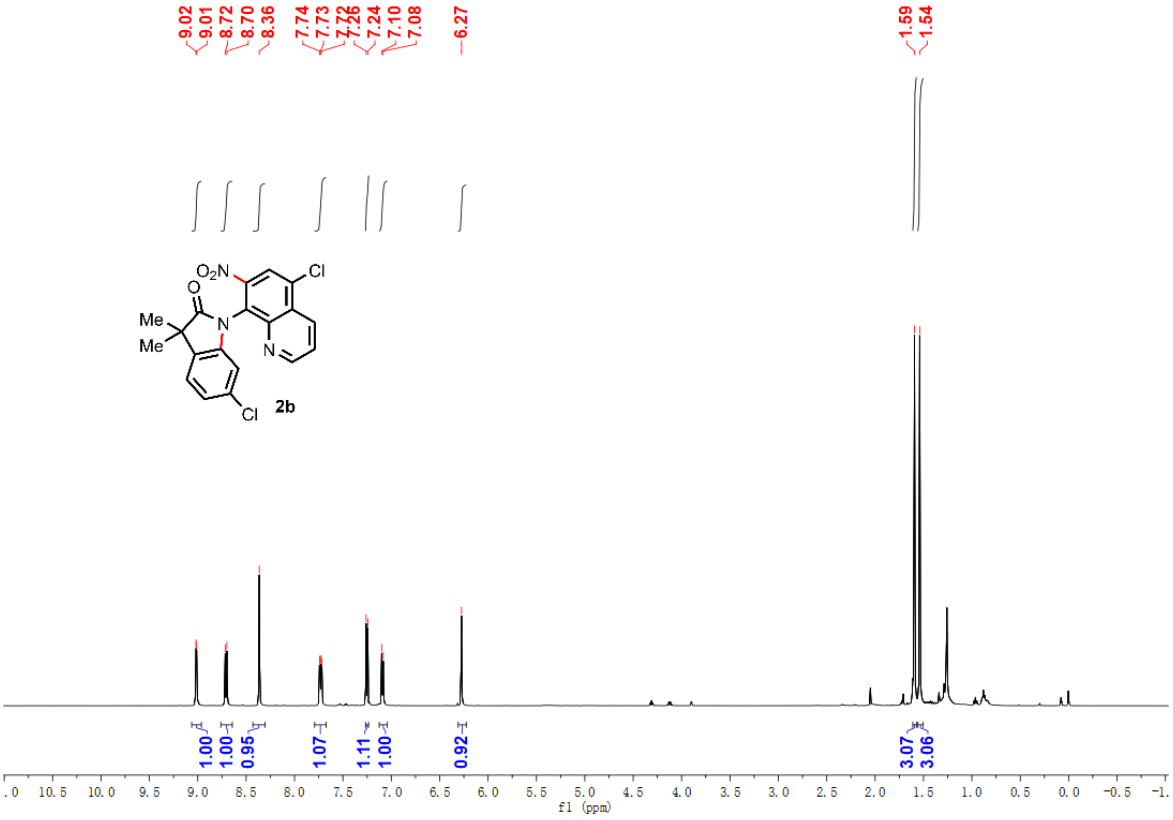
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2a**



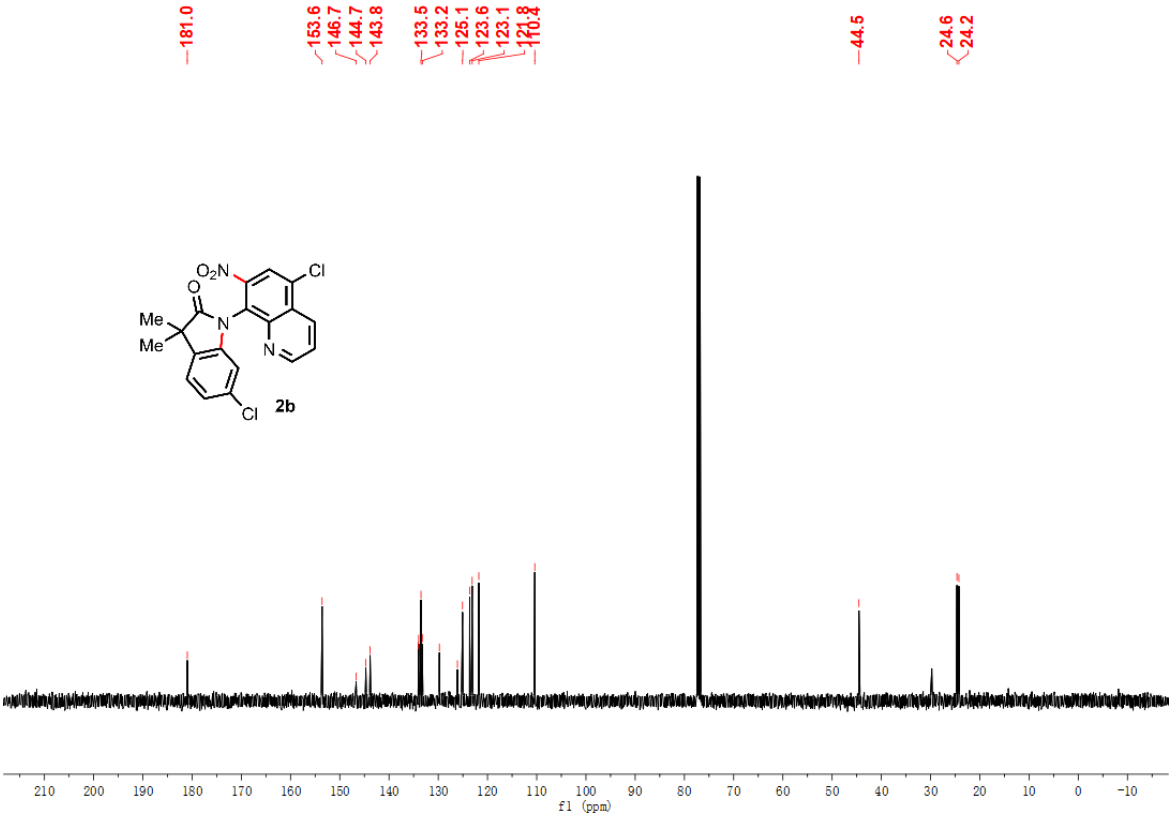
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2a**



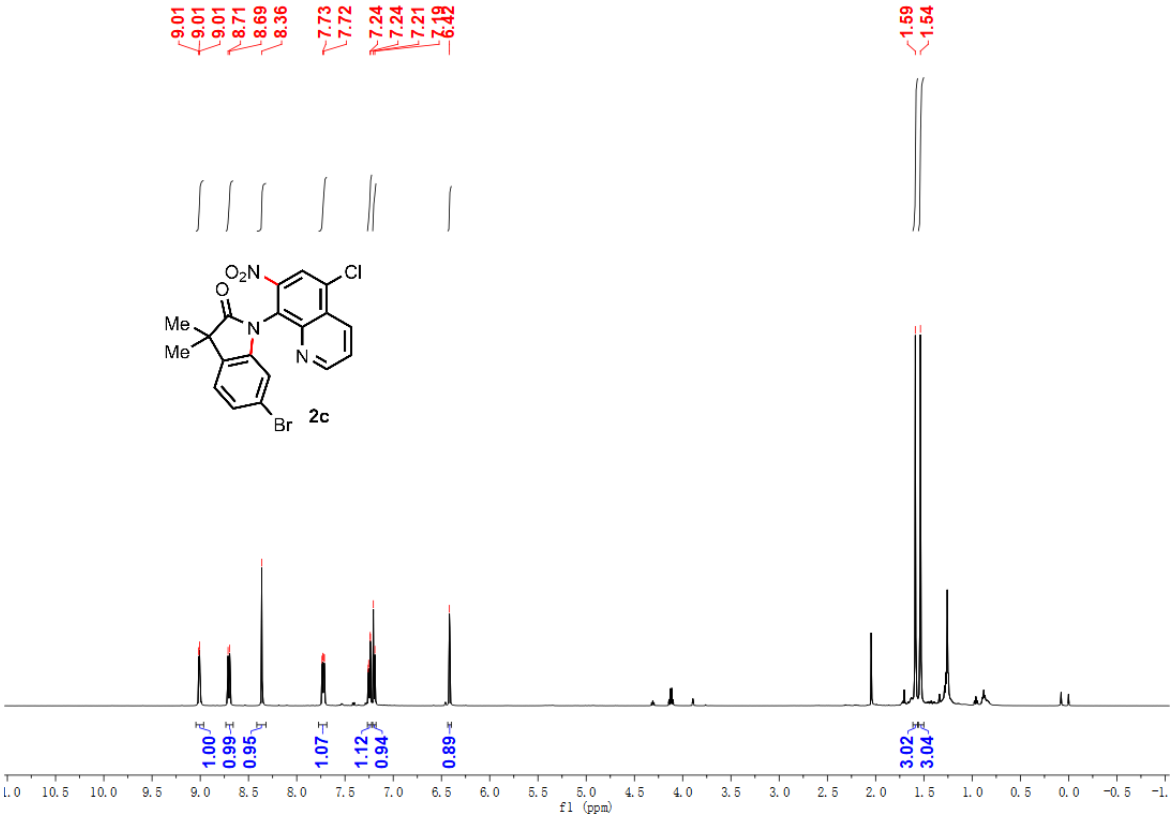
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2b**



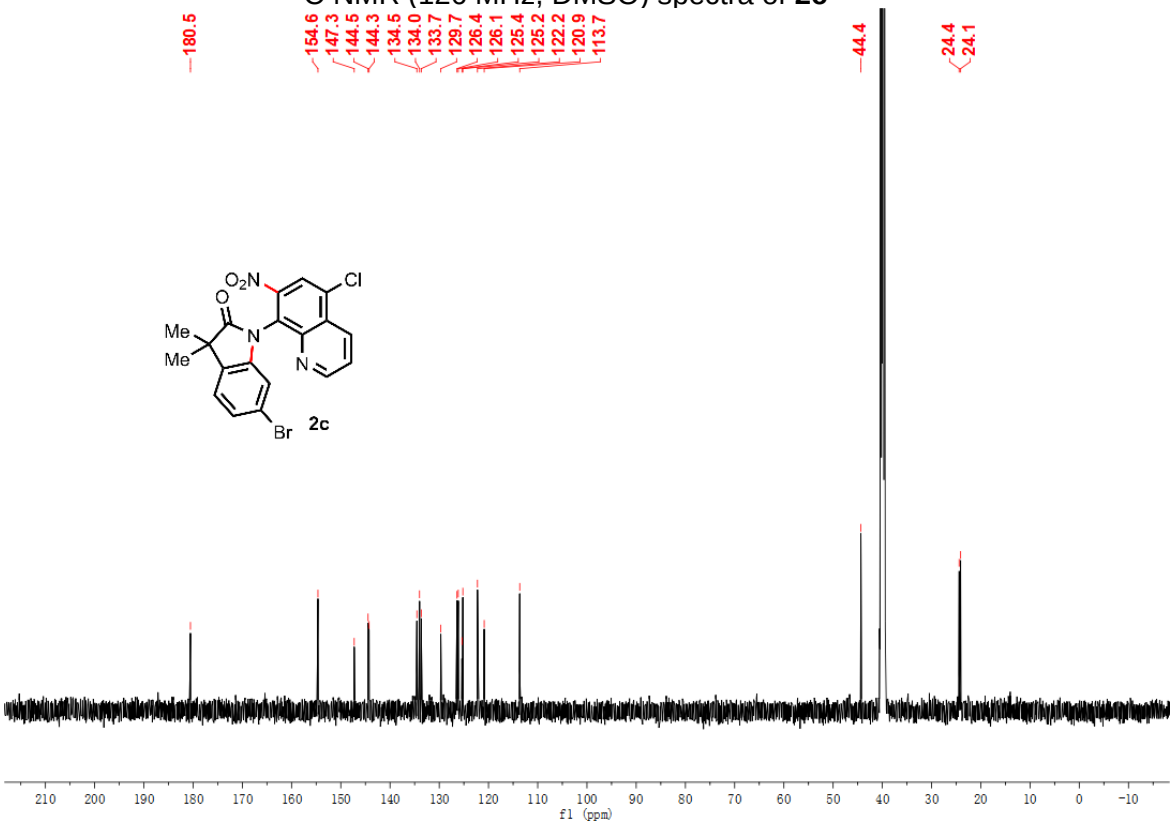
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2b**



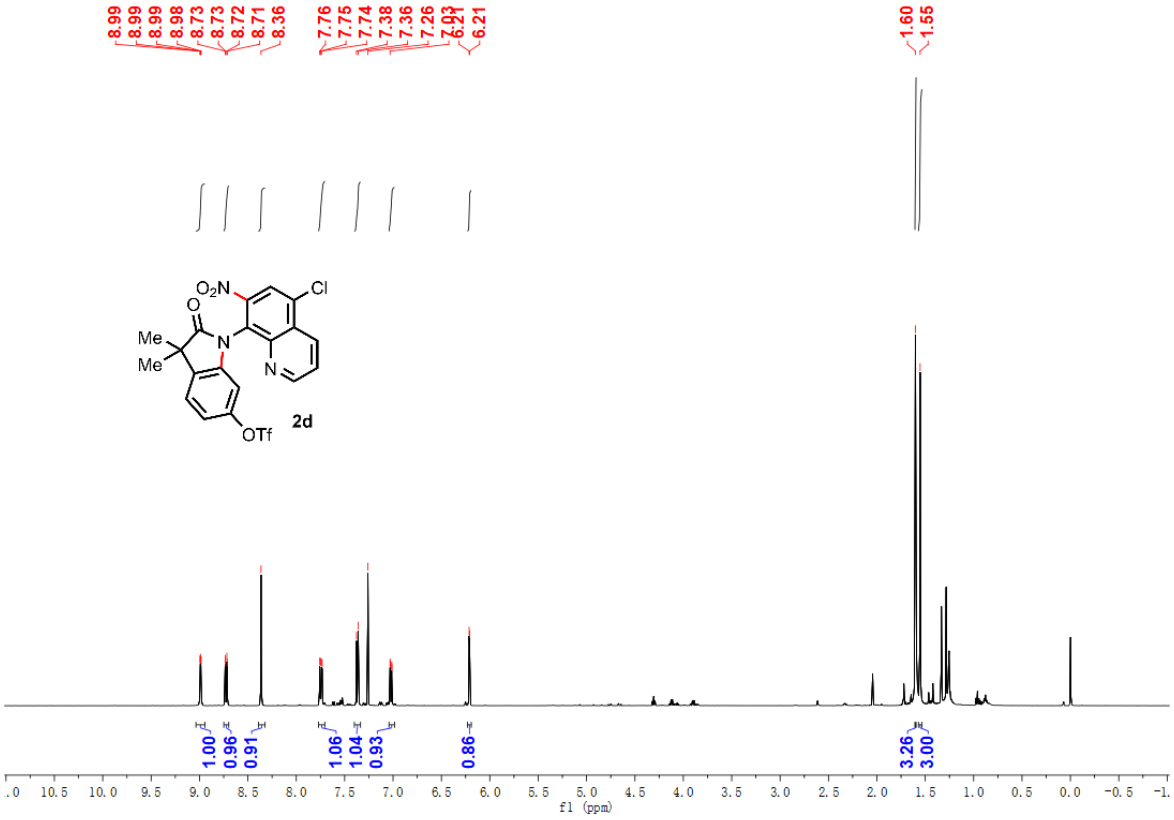
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2c**



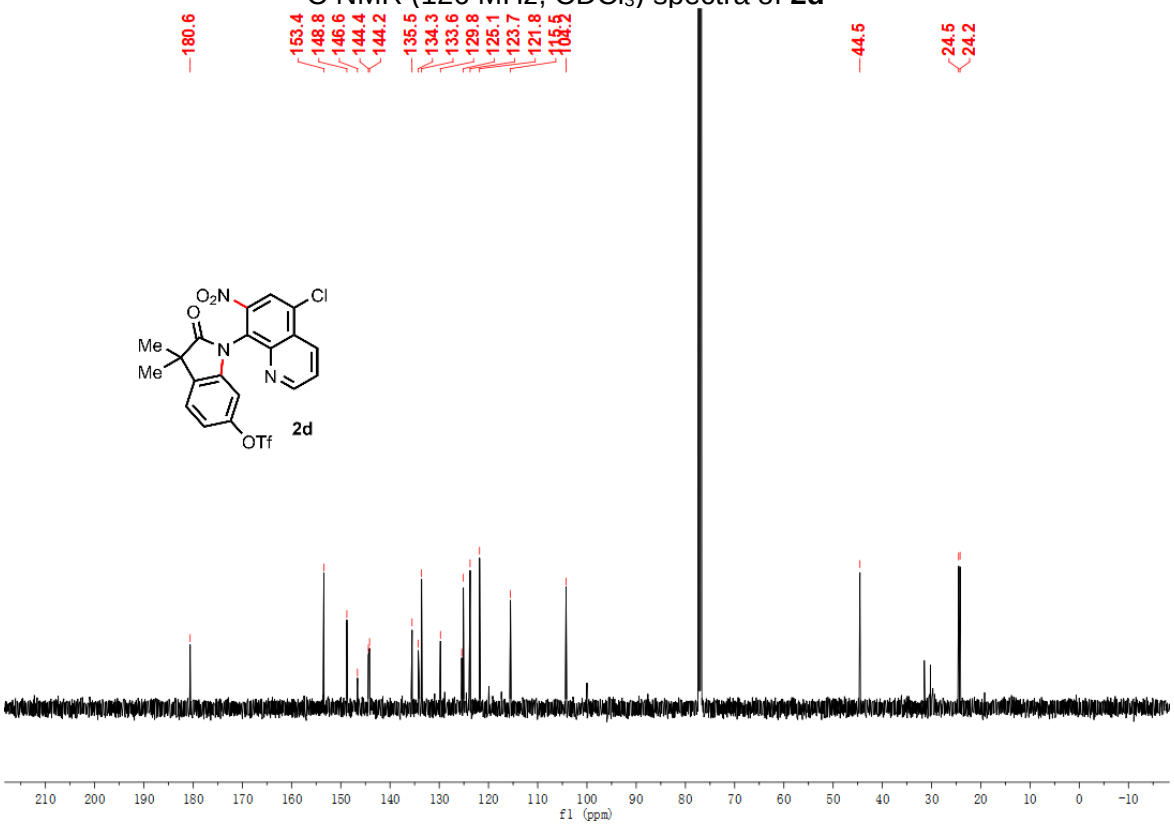
^{13}C NMR (126 MHz, DMSO) spectra of **2c**



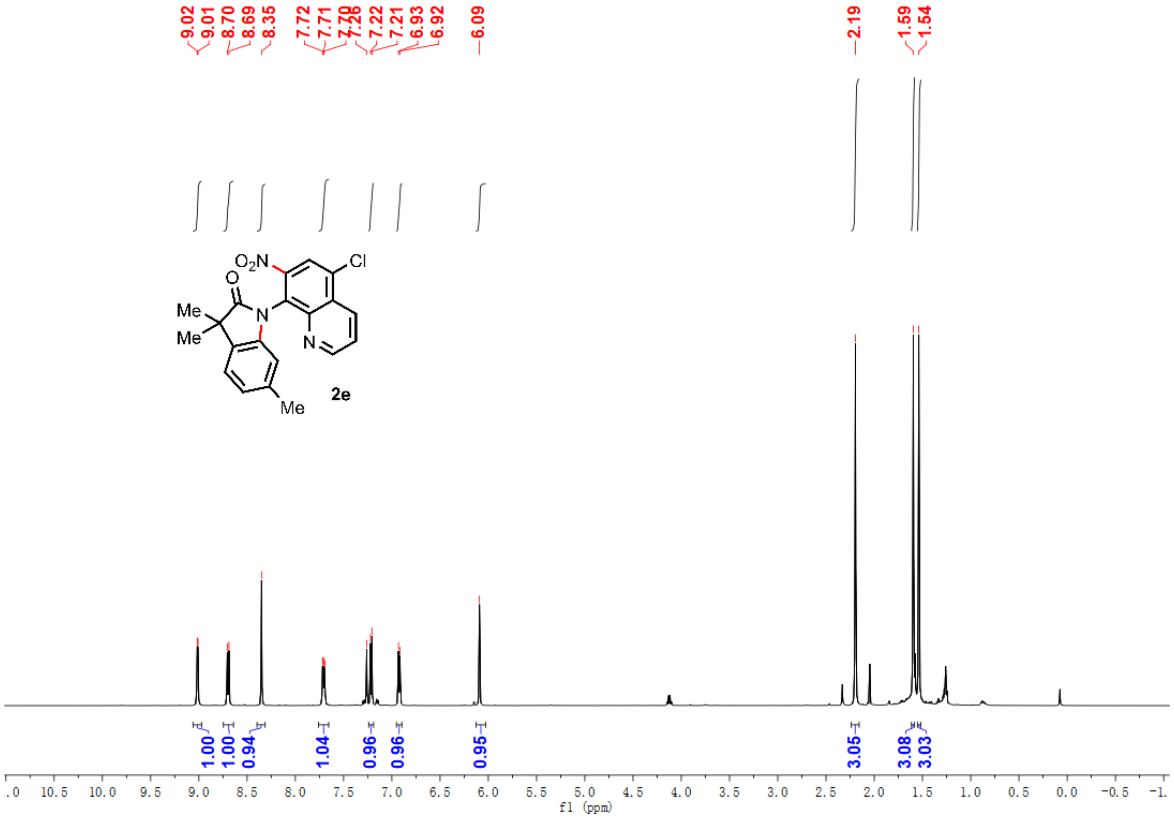
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2d**



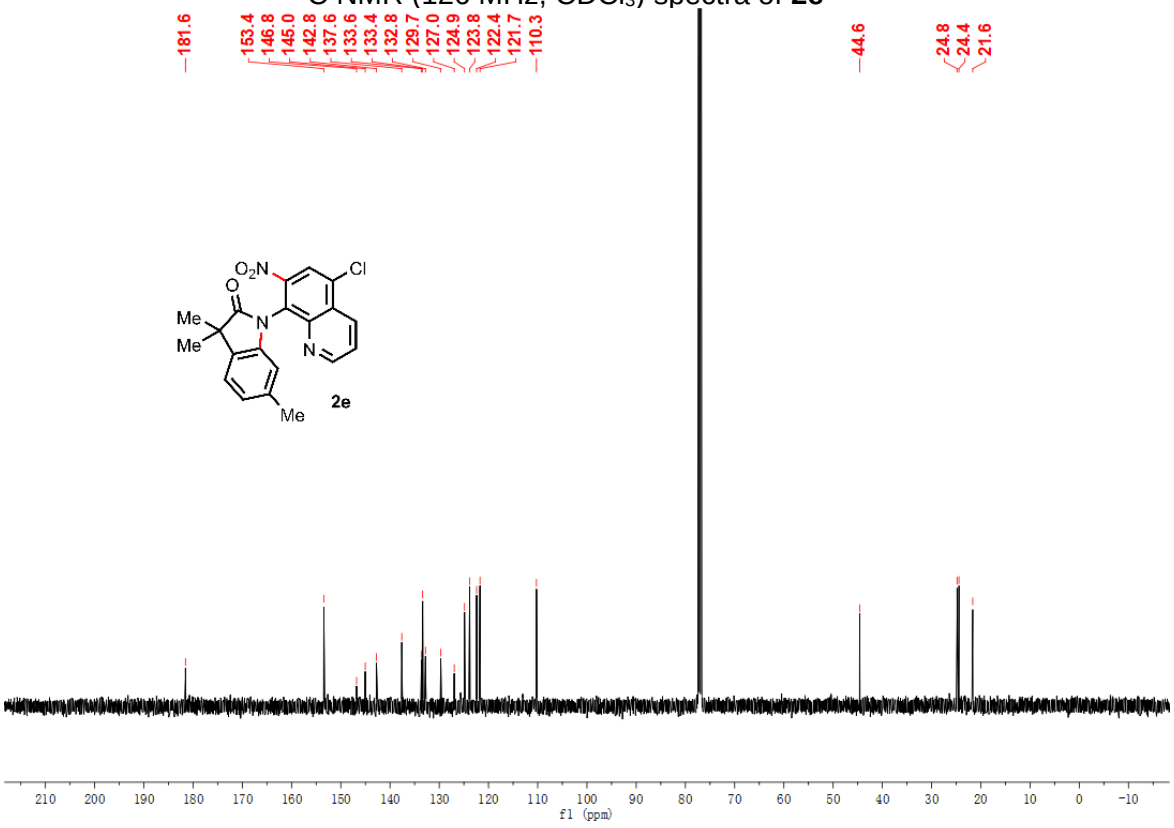
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2d**



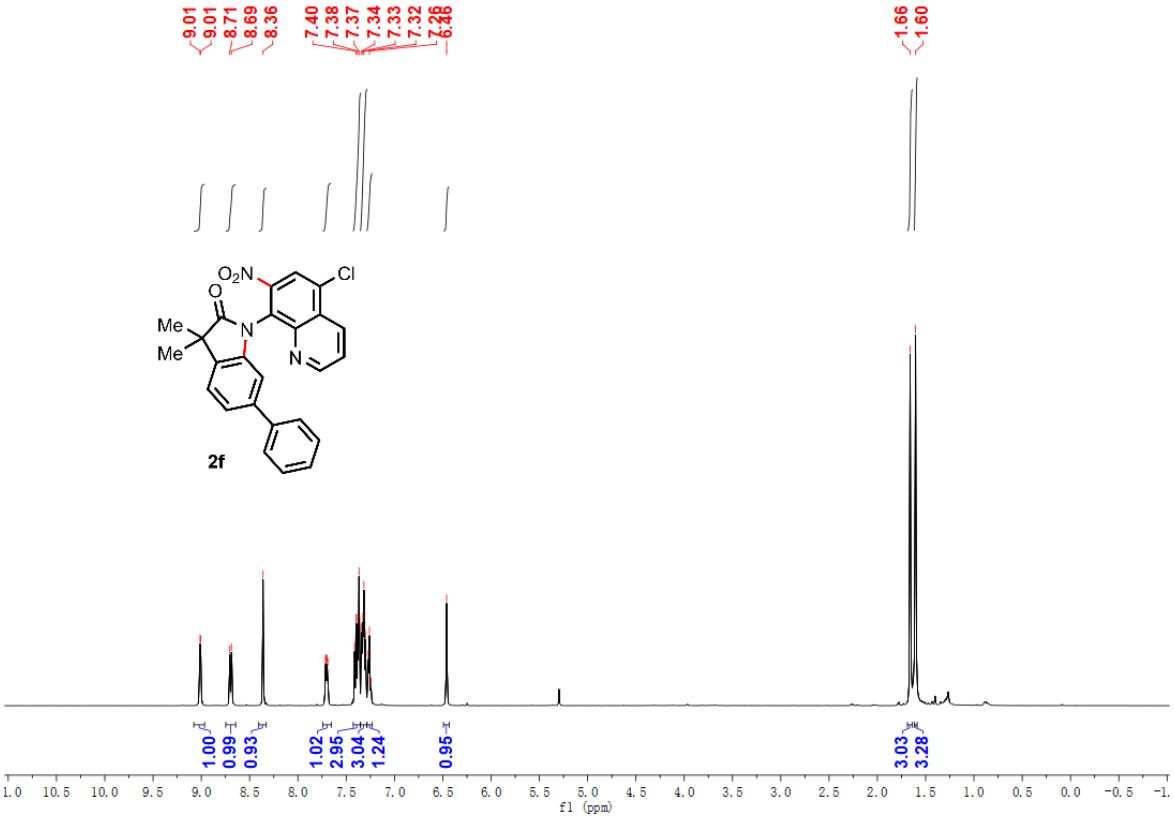
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2e**



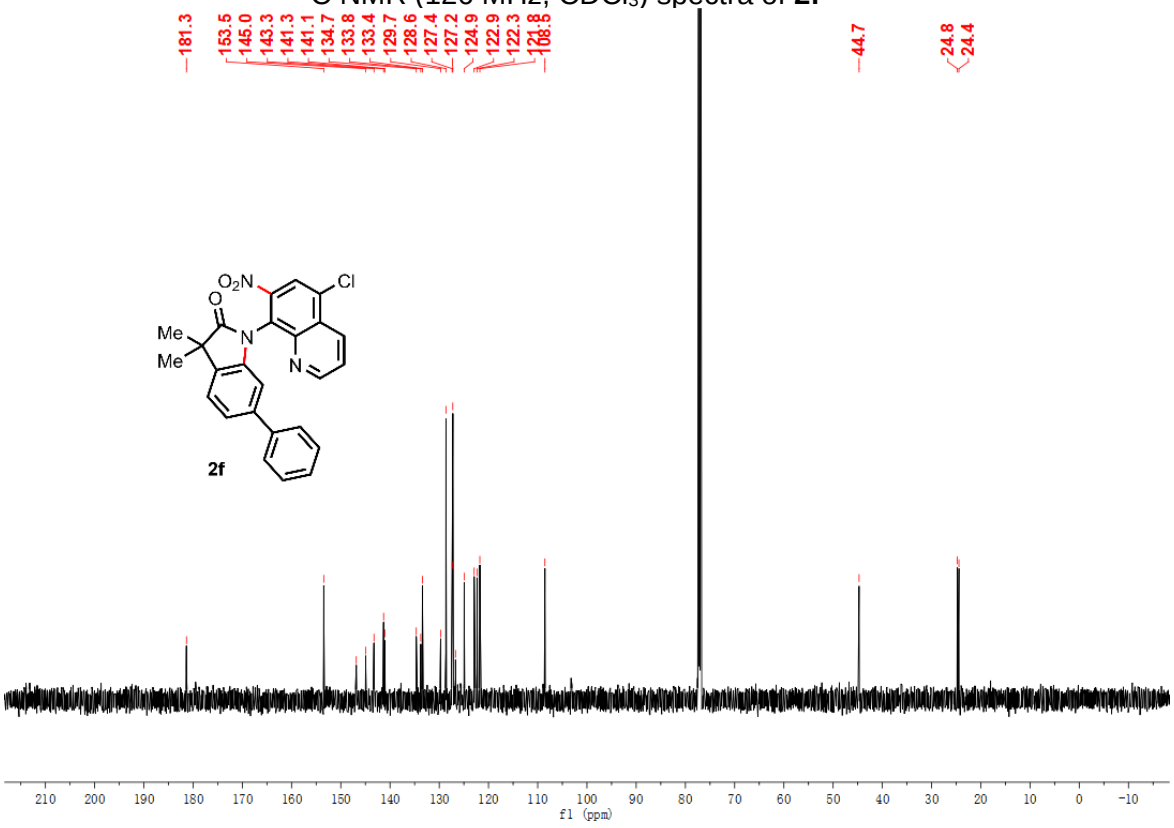
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2e**



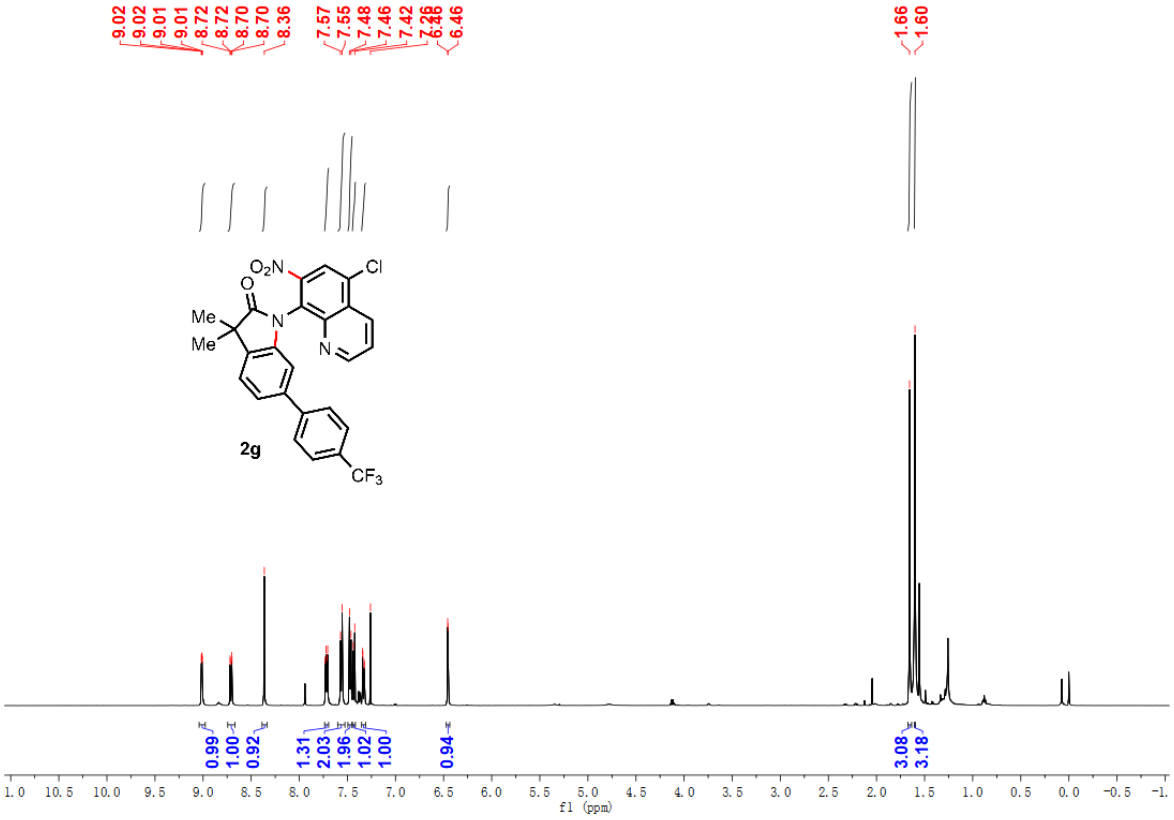
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2f**



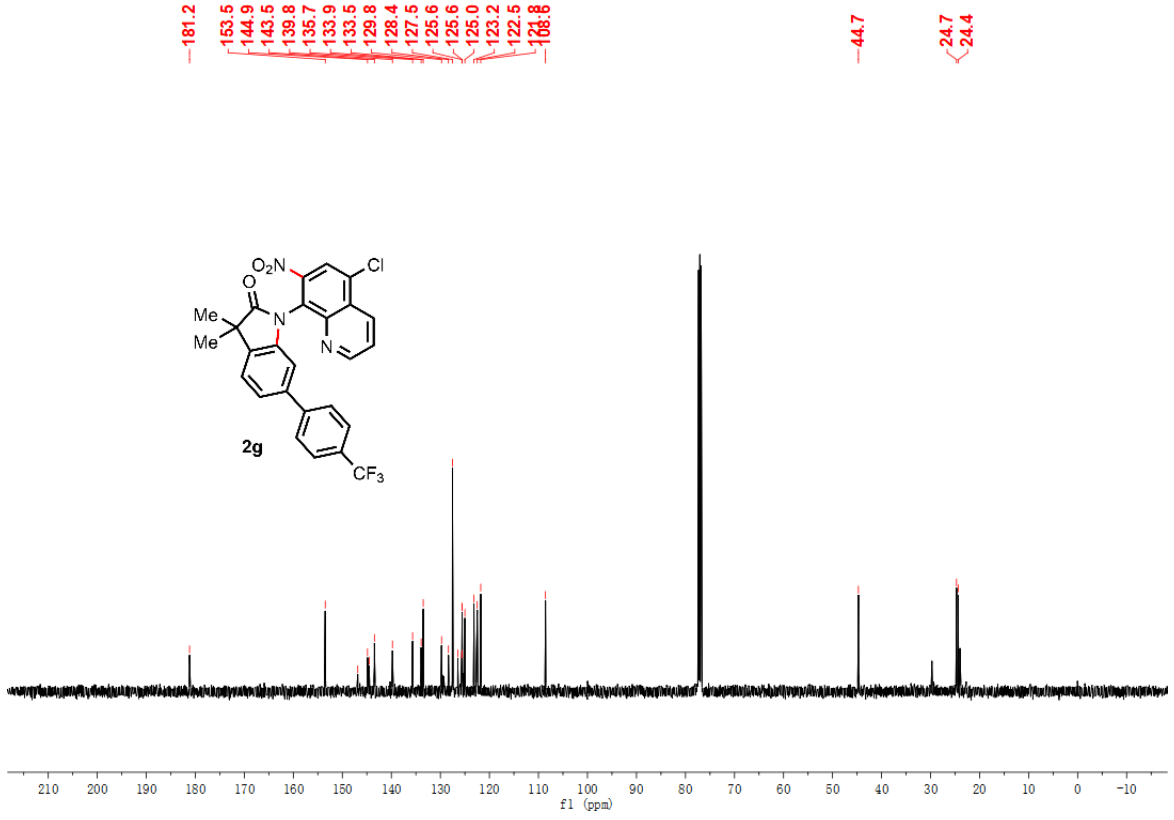
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2f**



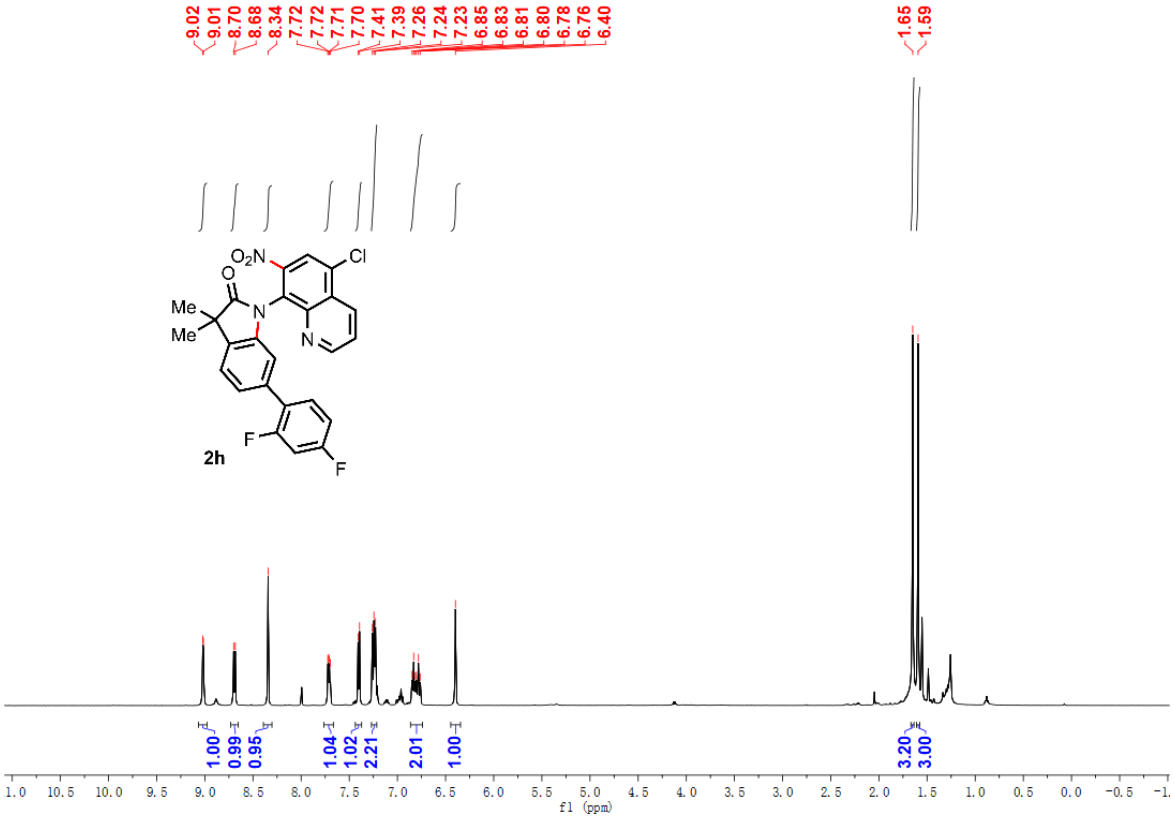
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2g**



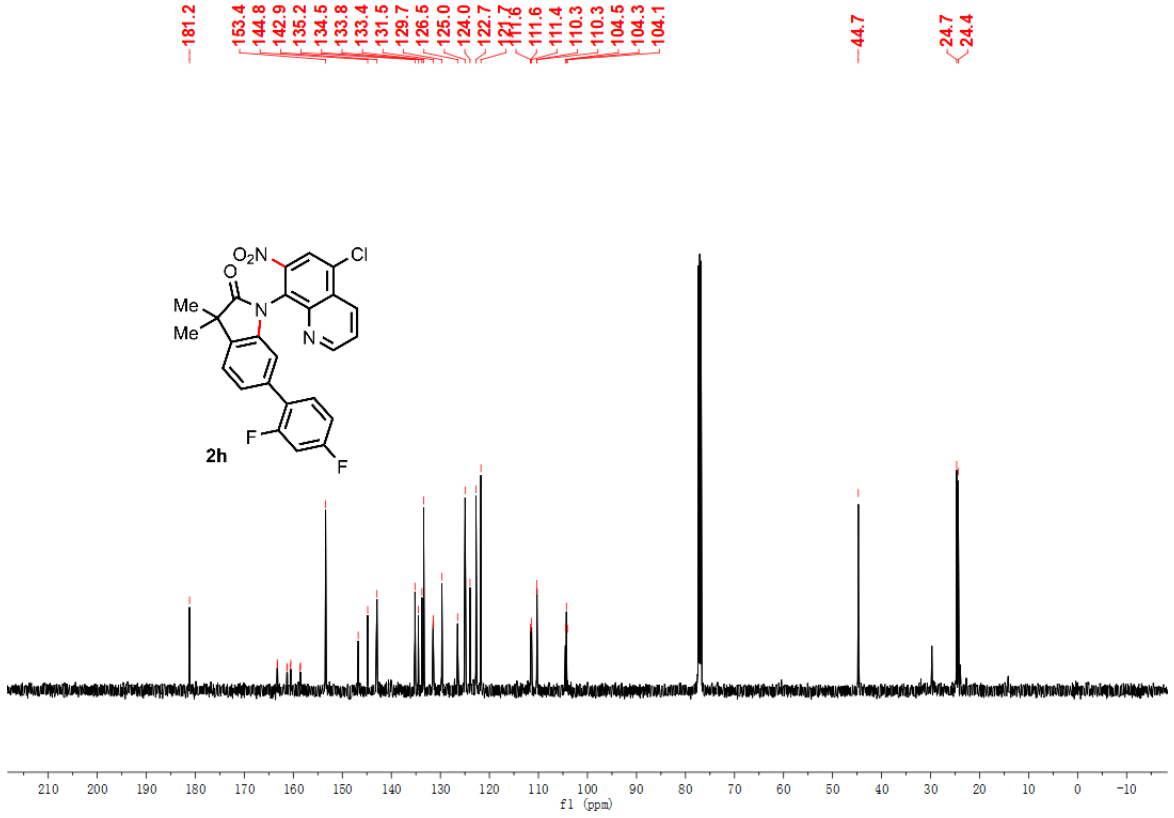
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2g**



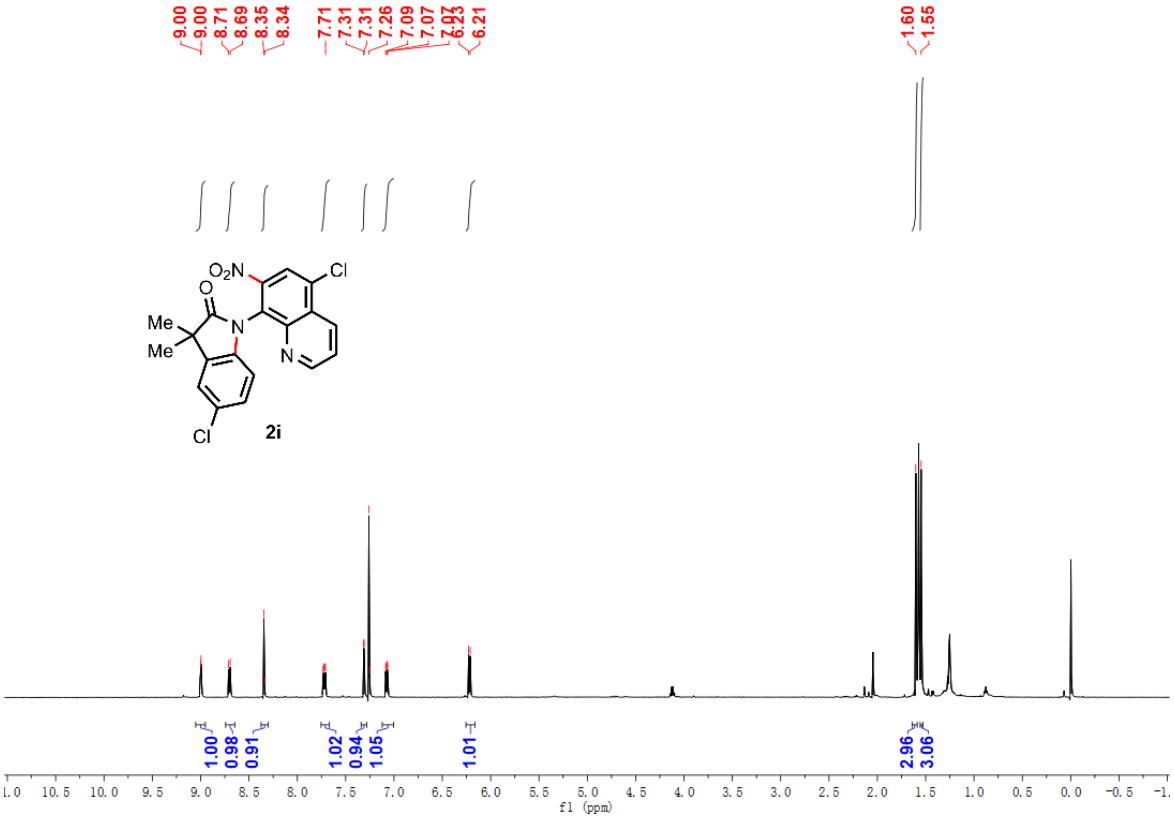
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2h**



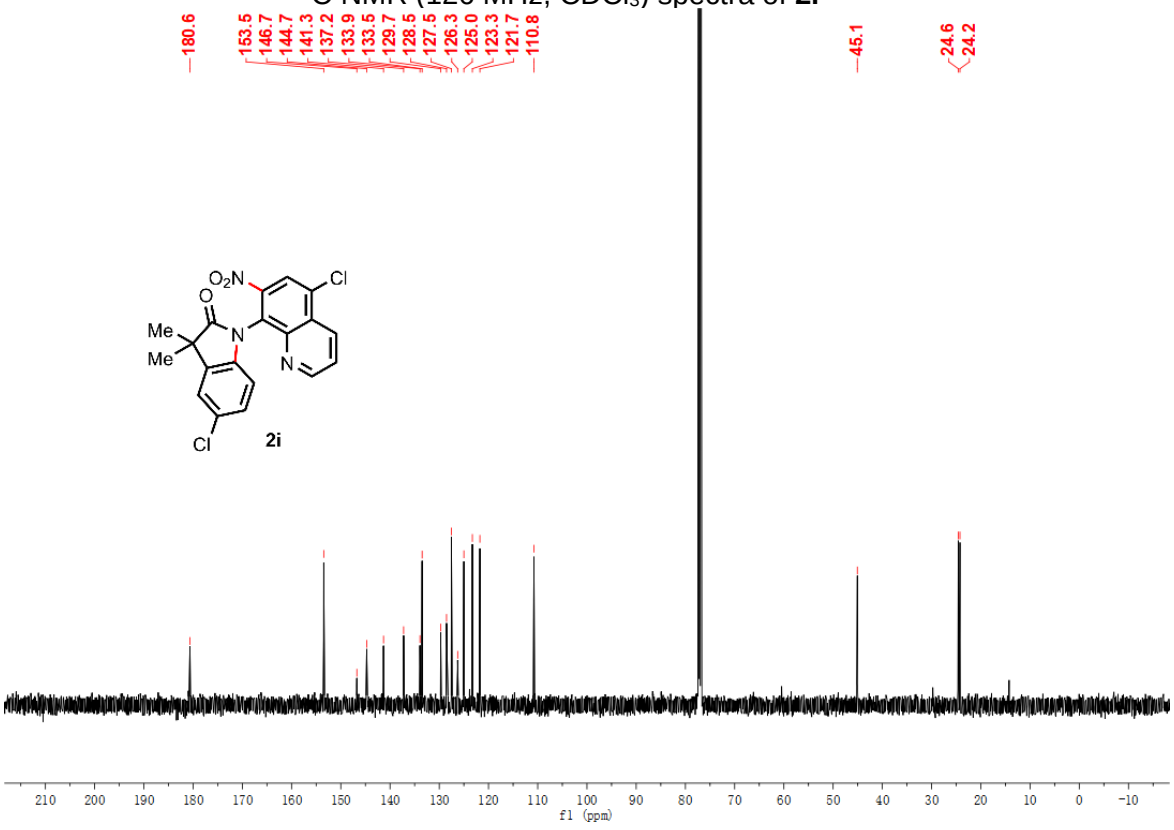
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2h**



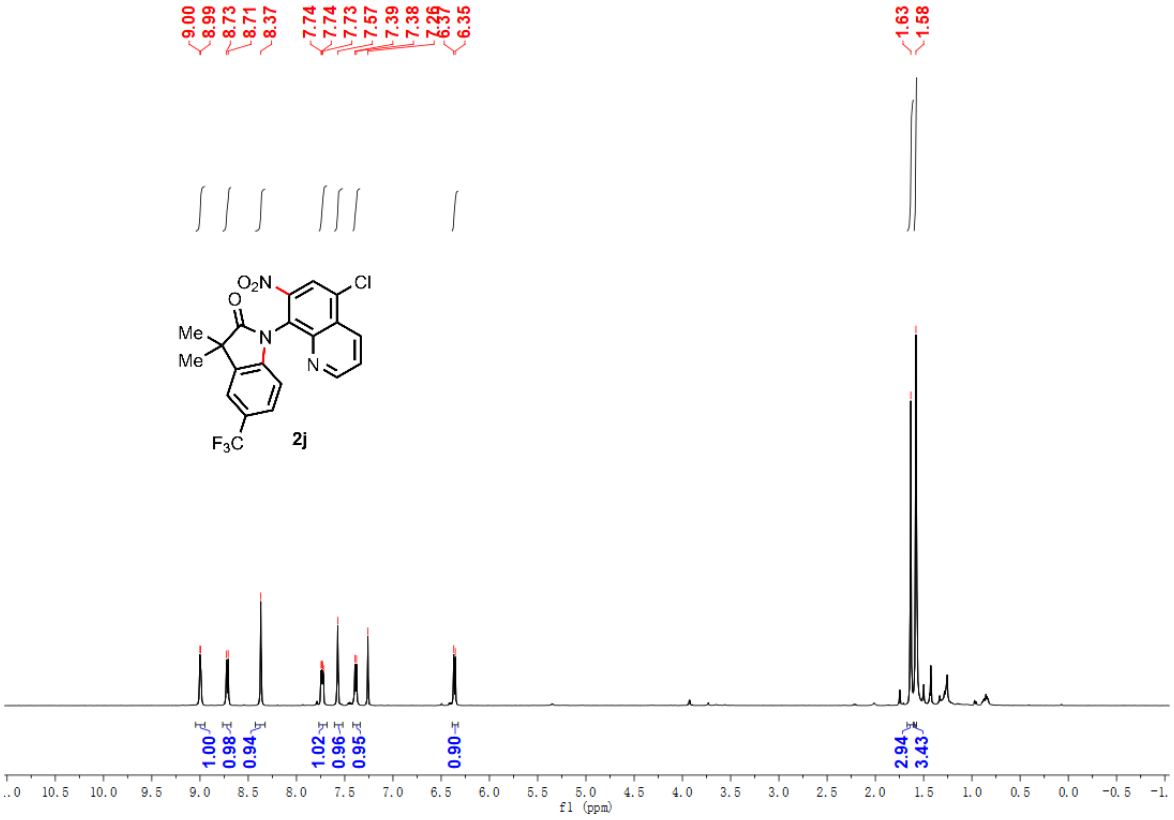
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2i**



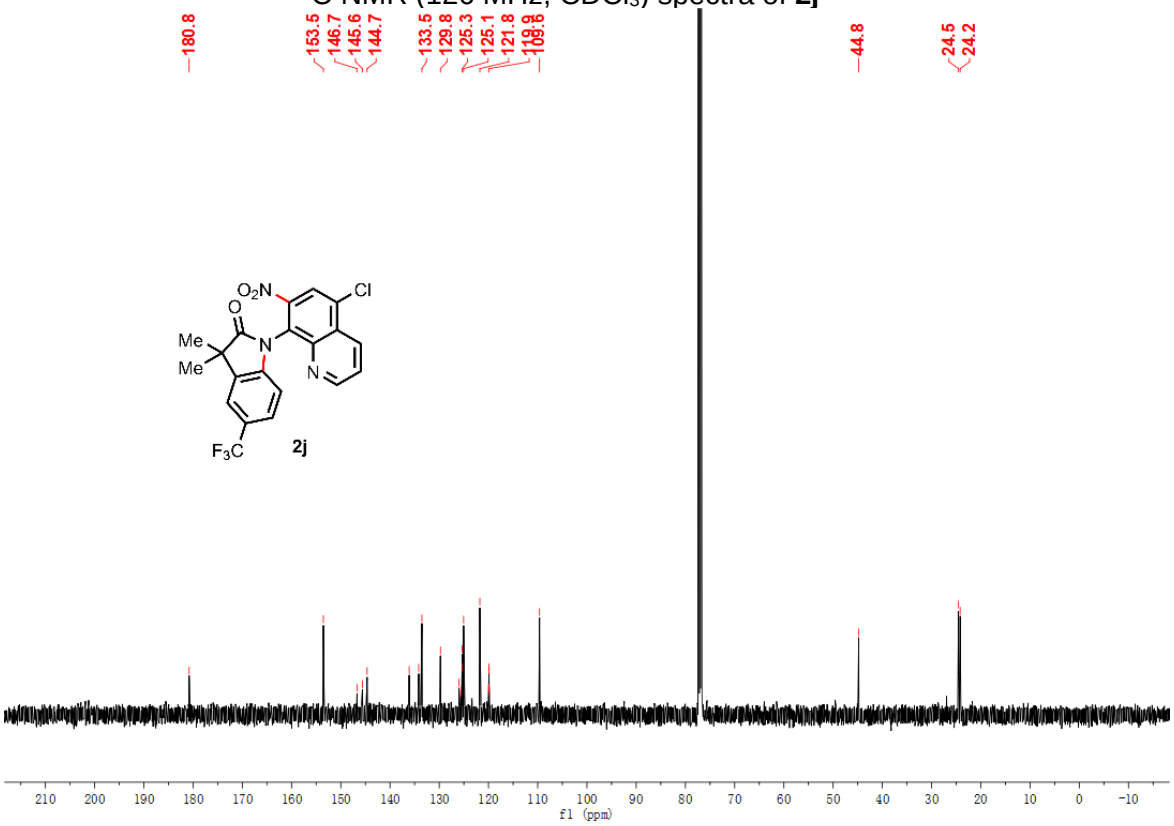
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2i**



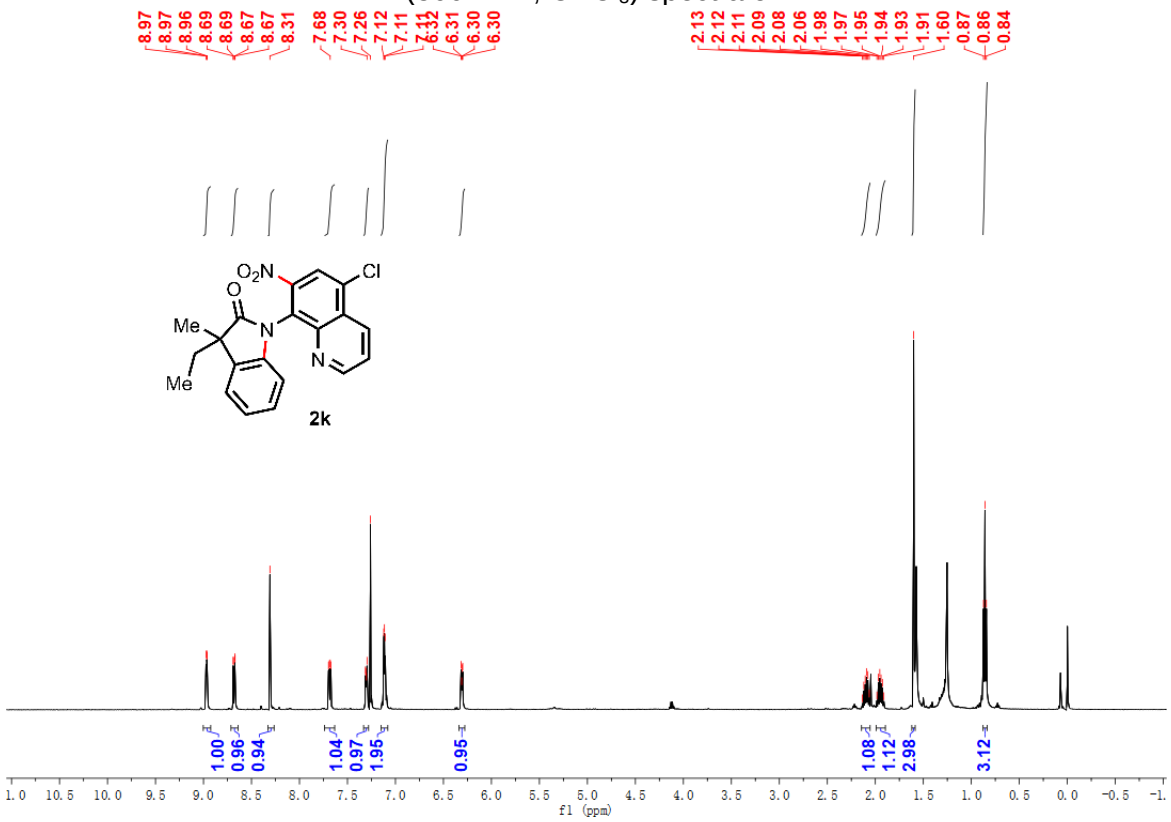
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2j**



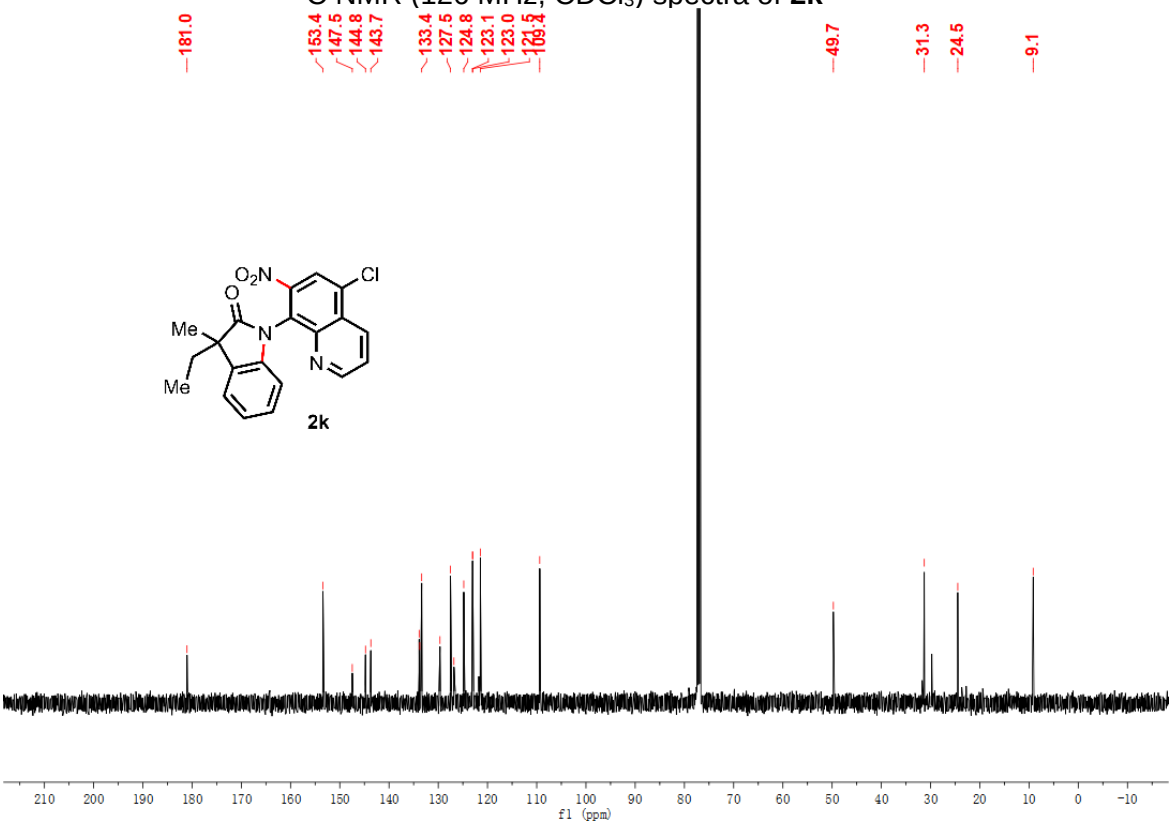
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2j**



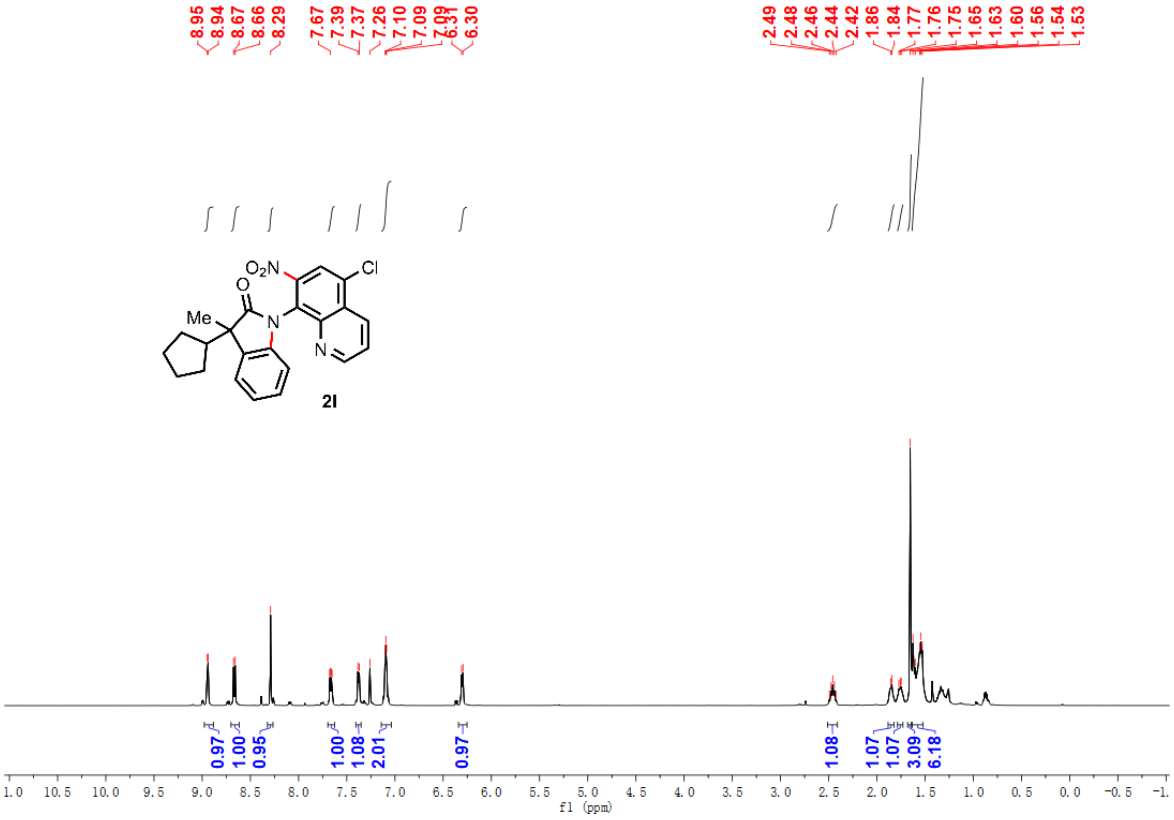
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2k**



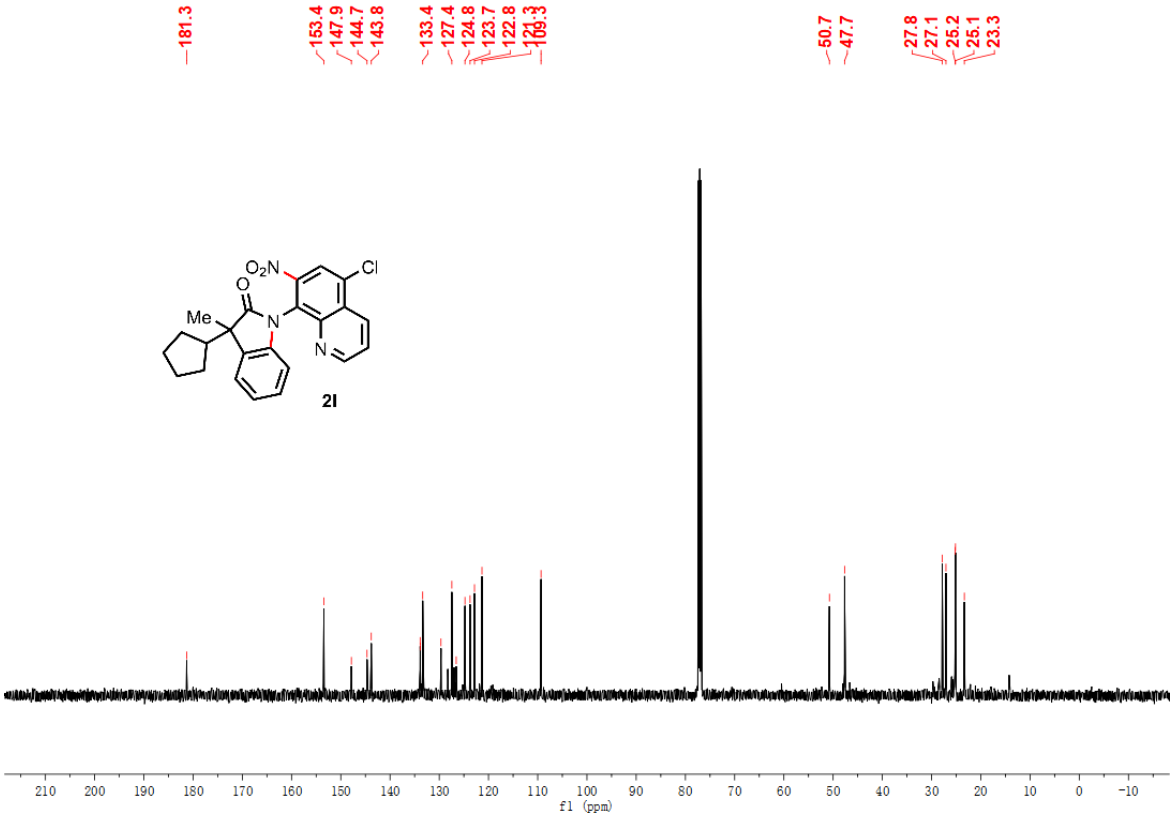
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2k**



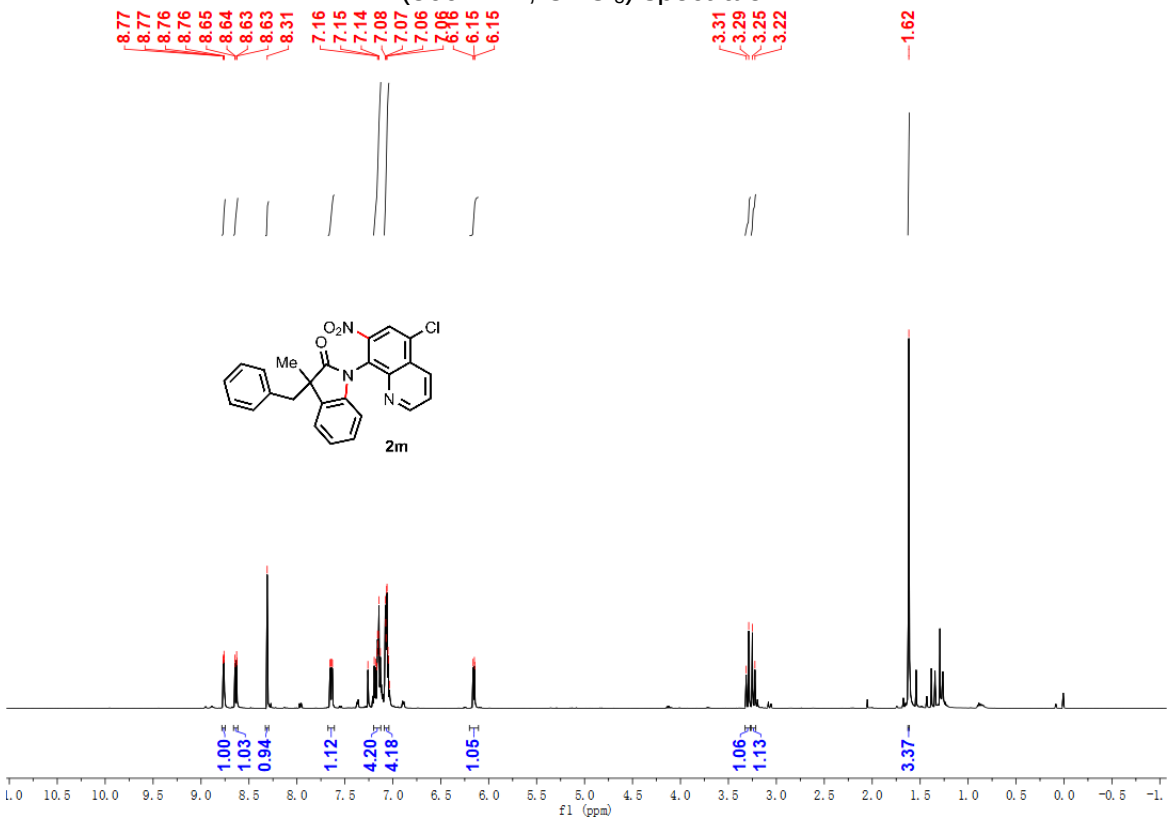
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2l**



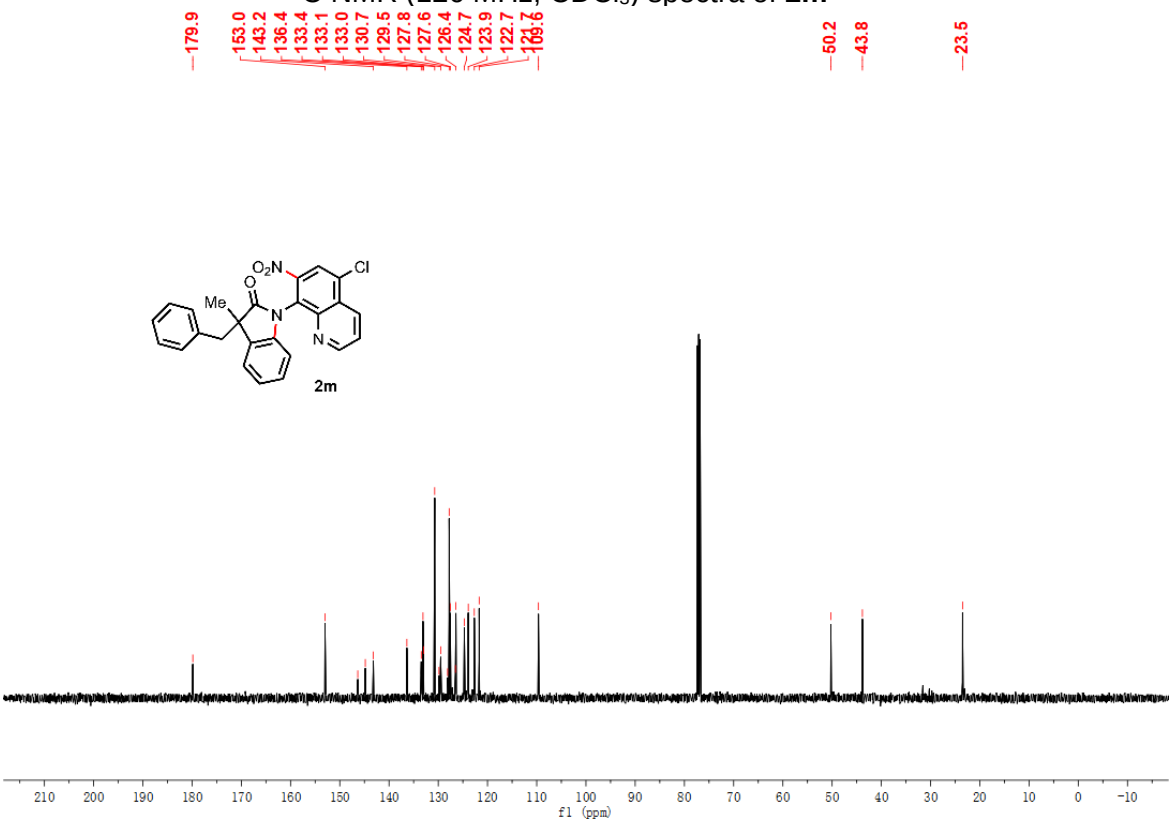
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2l**



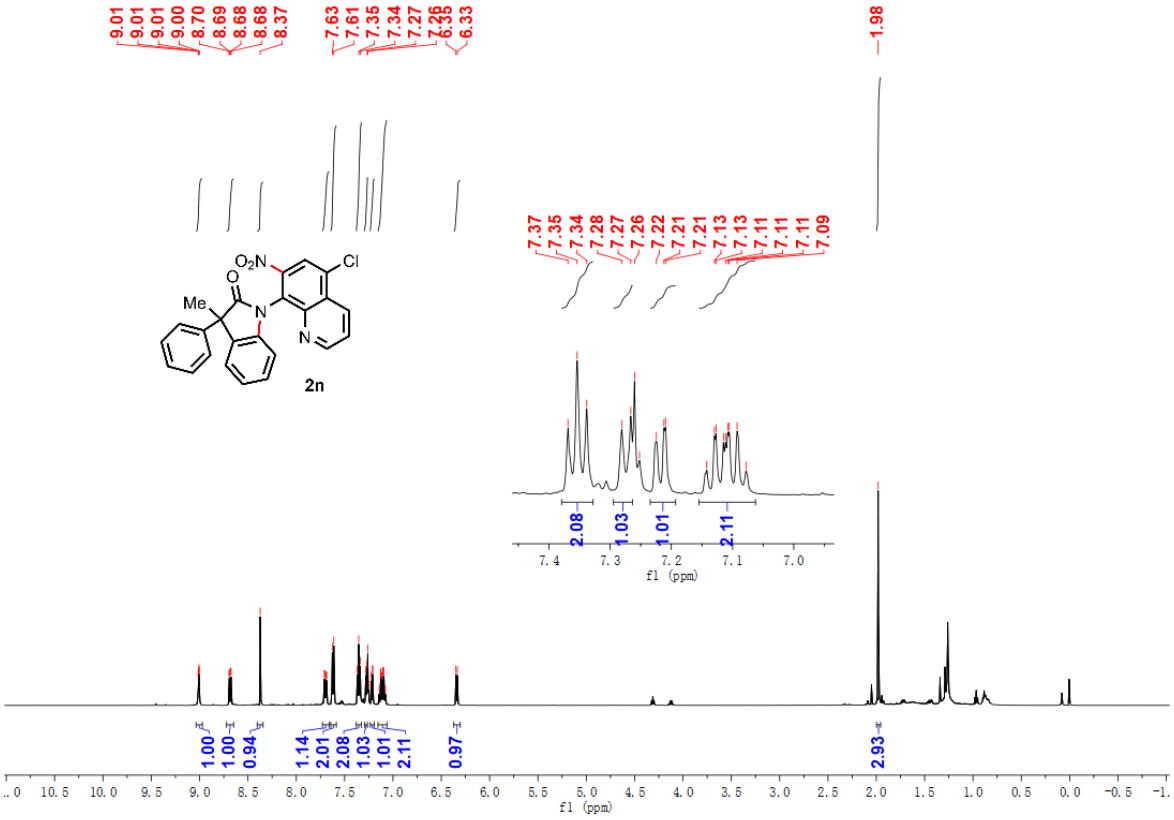
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2m**



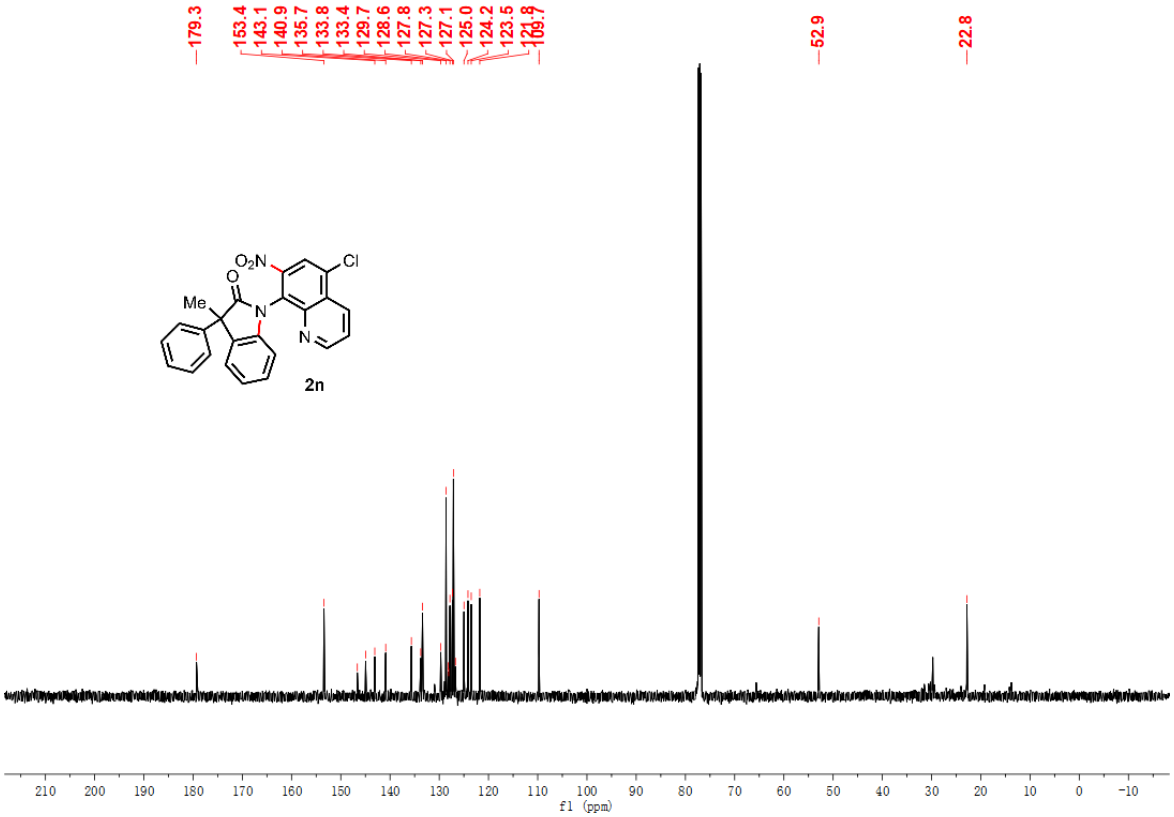
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2m**



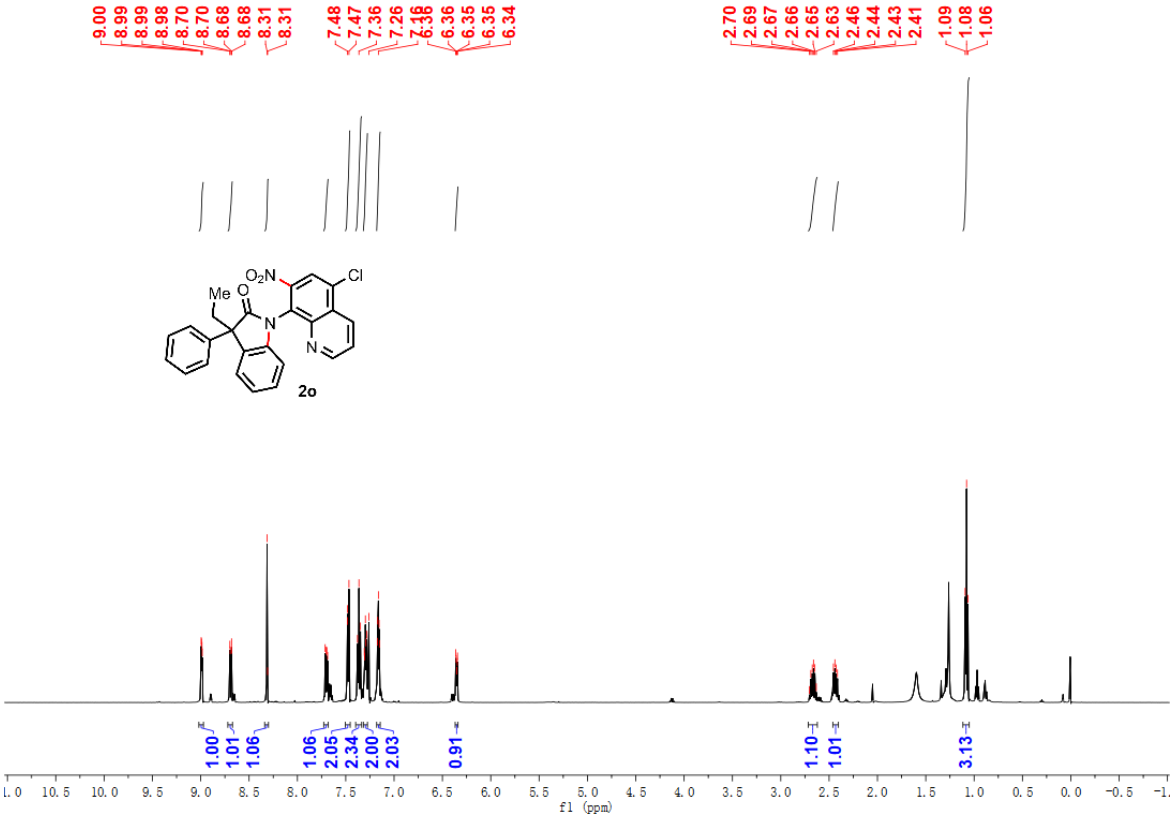
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2n**



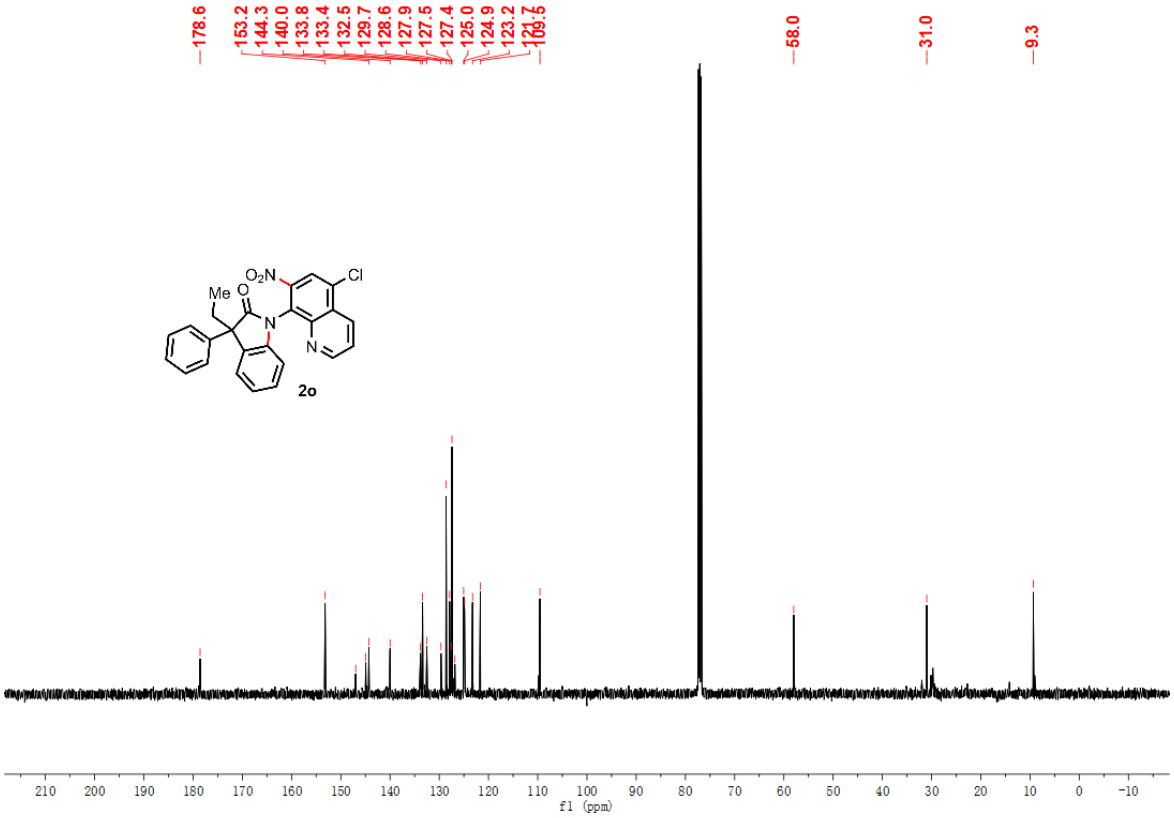
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2n**



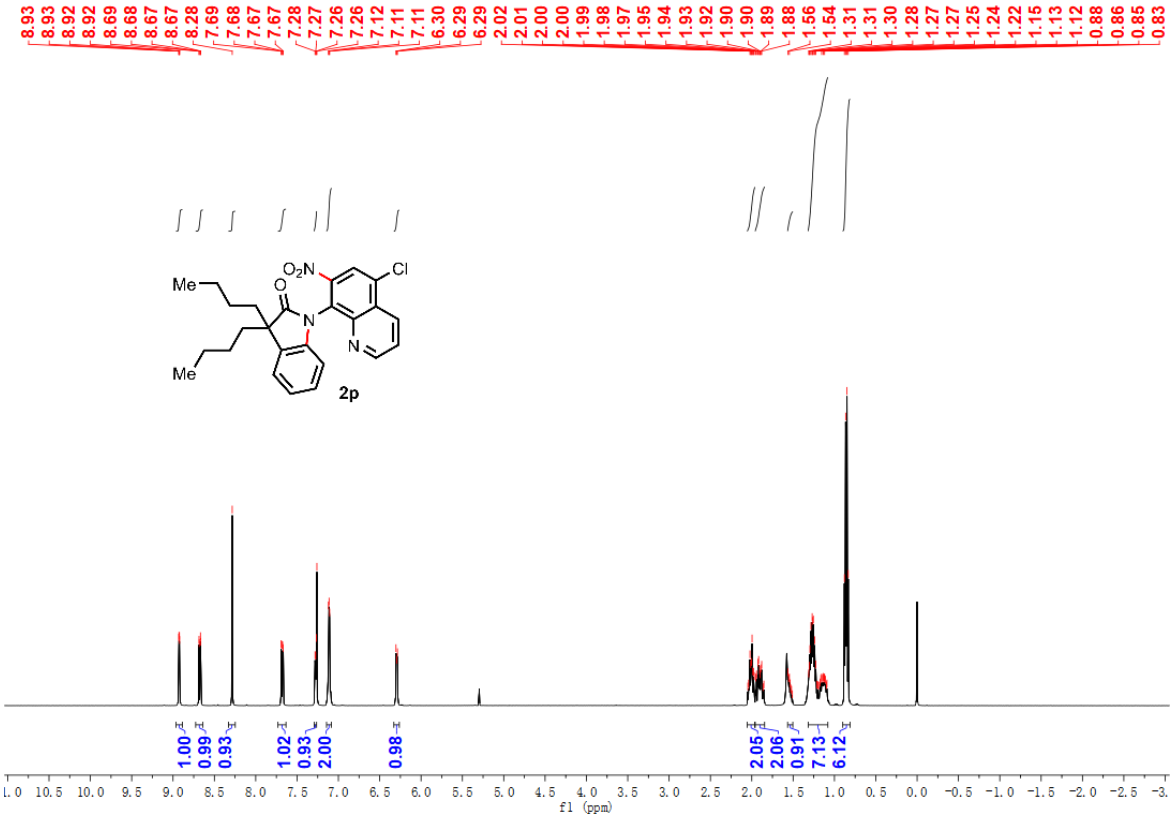
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2o**



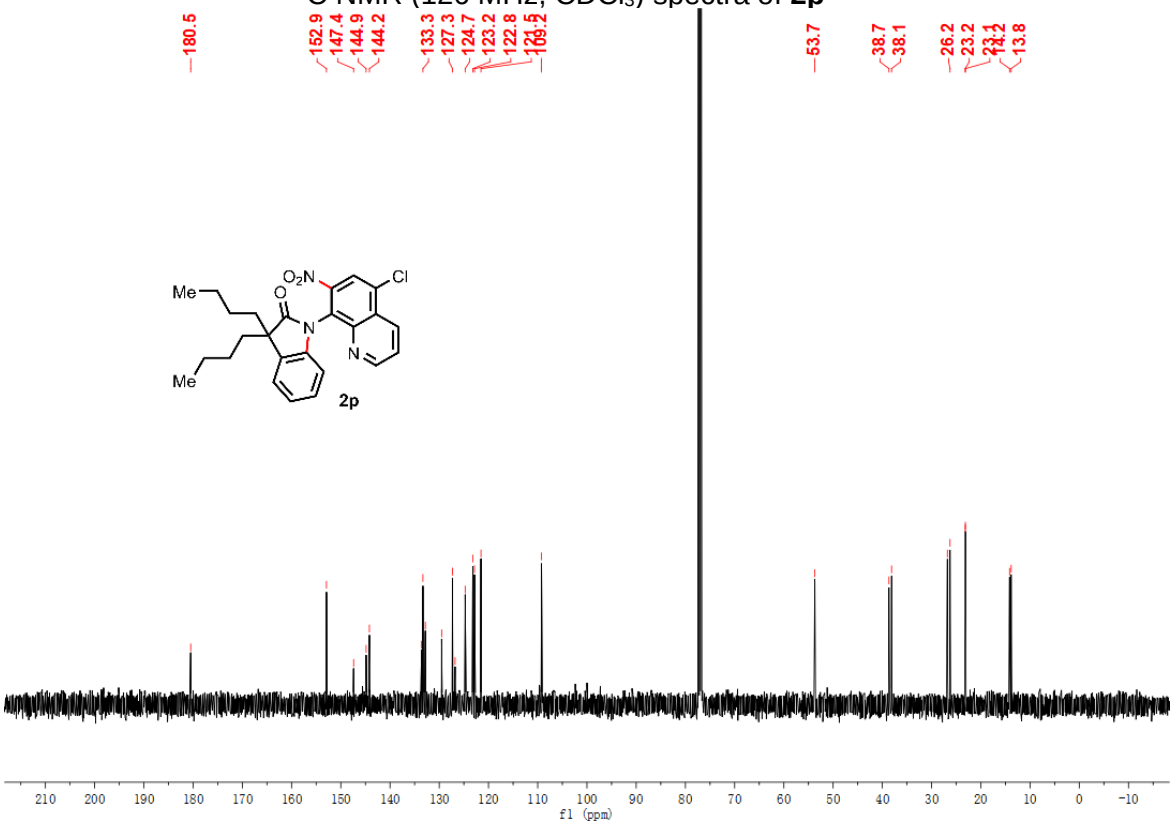
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2o**



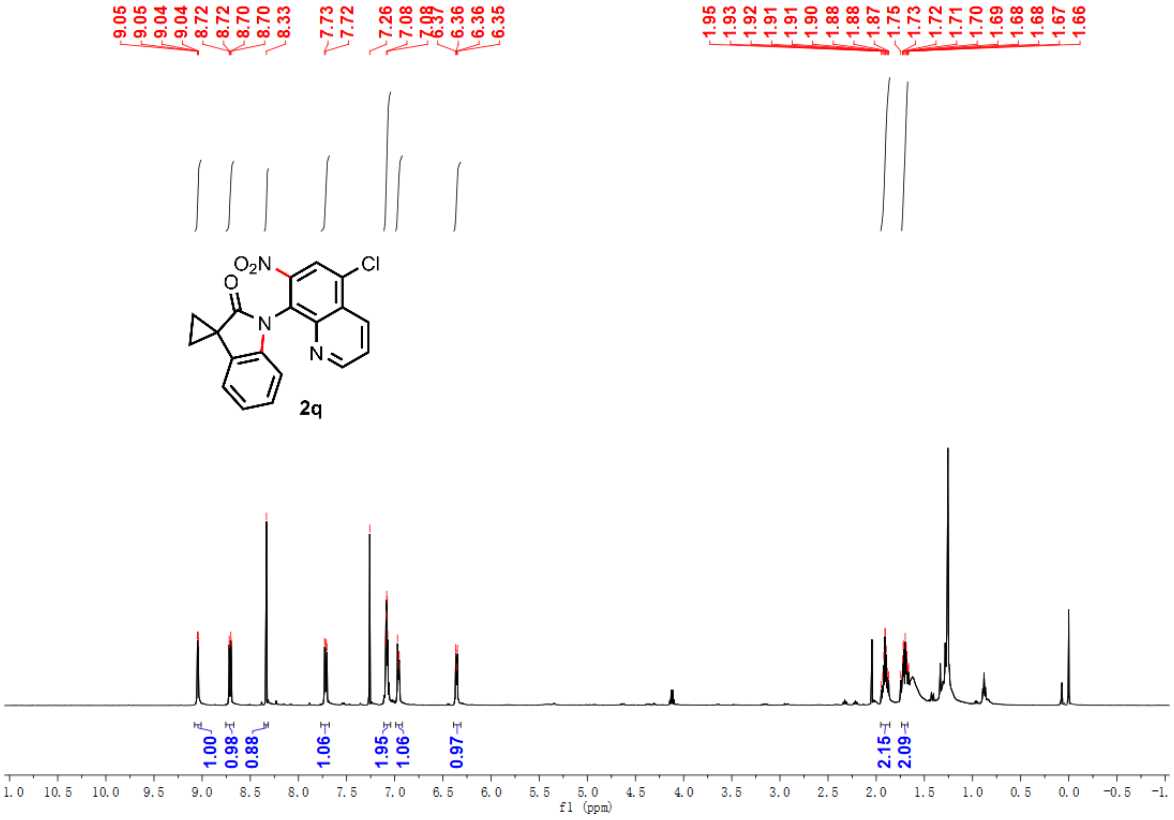
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2p**



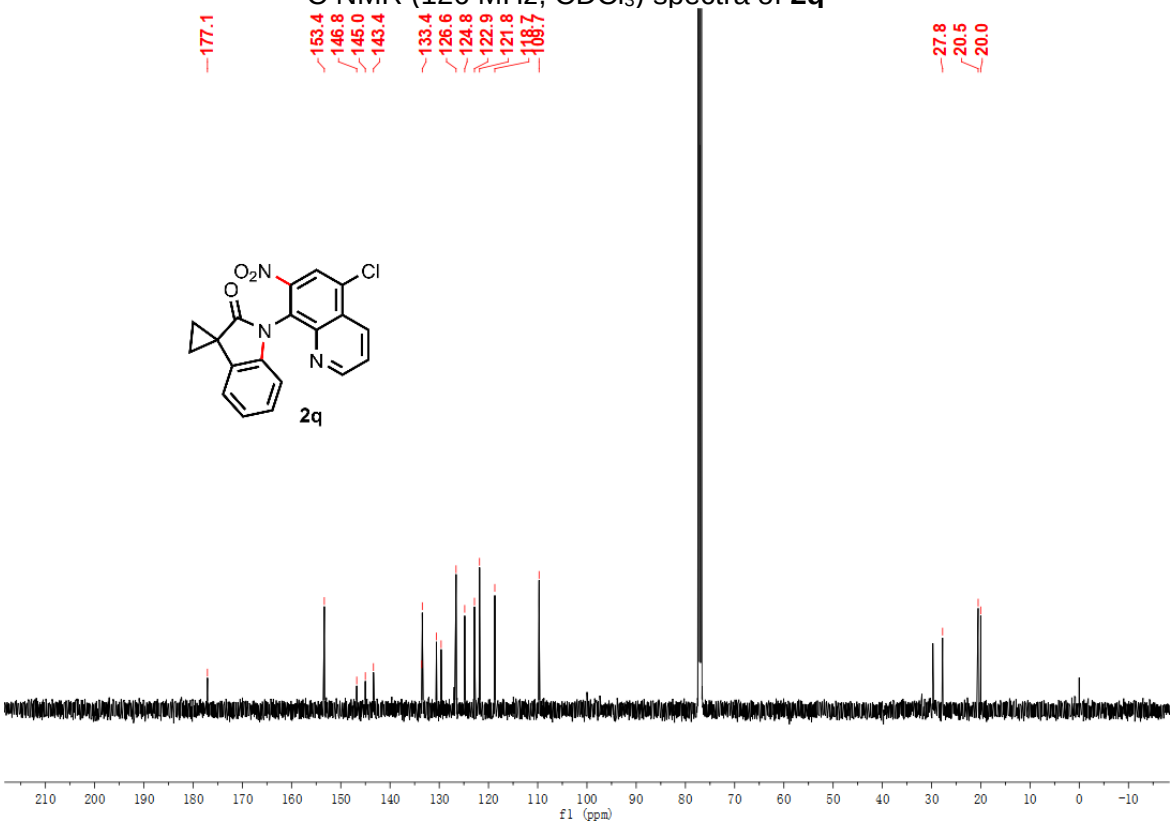
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2p**



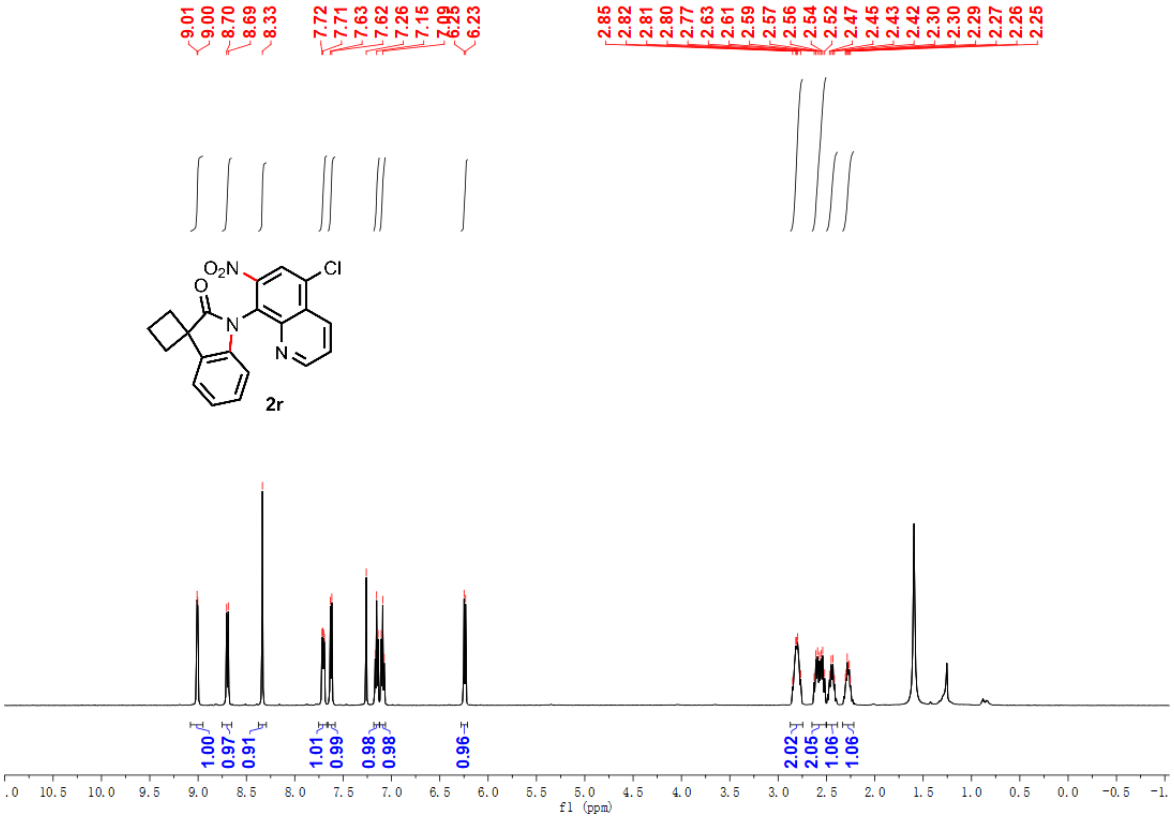
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2q**



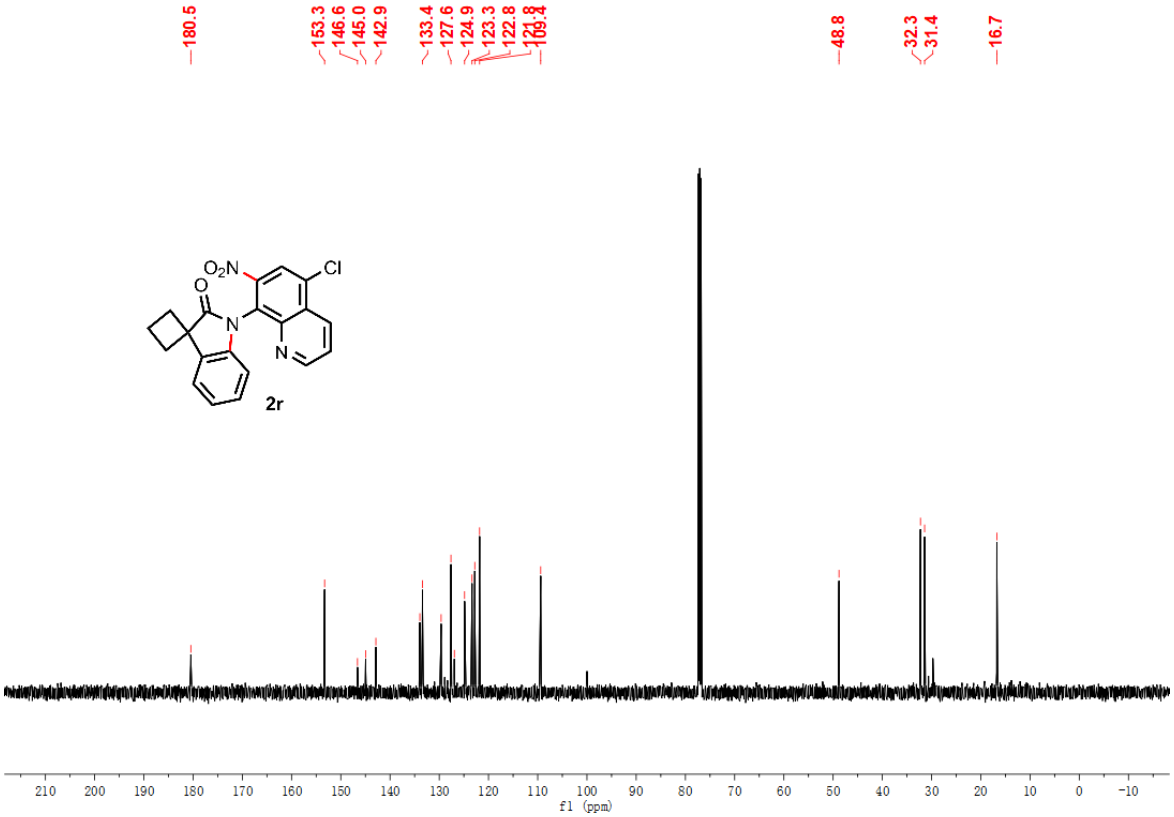
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2q**



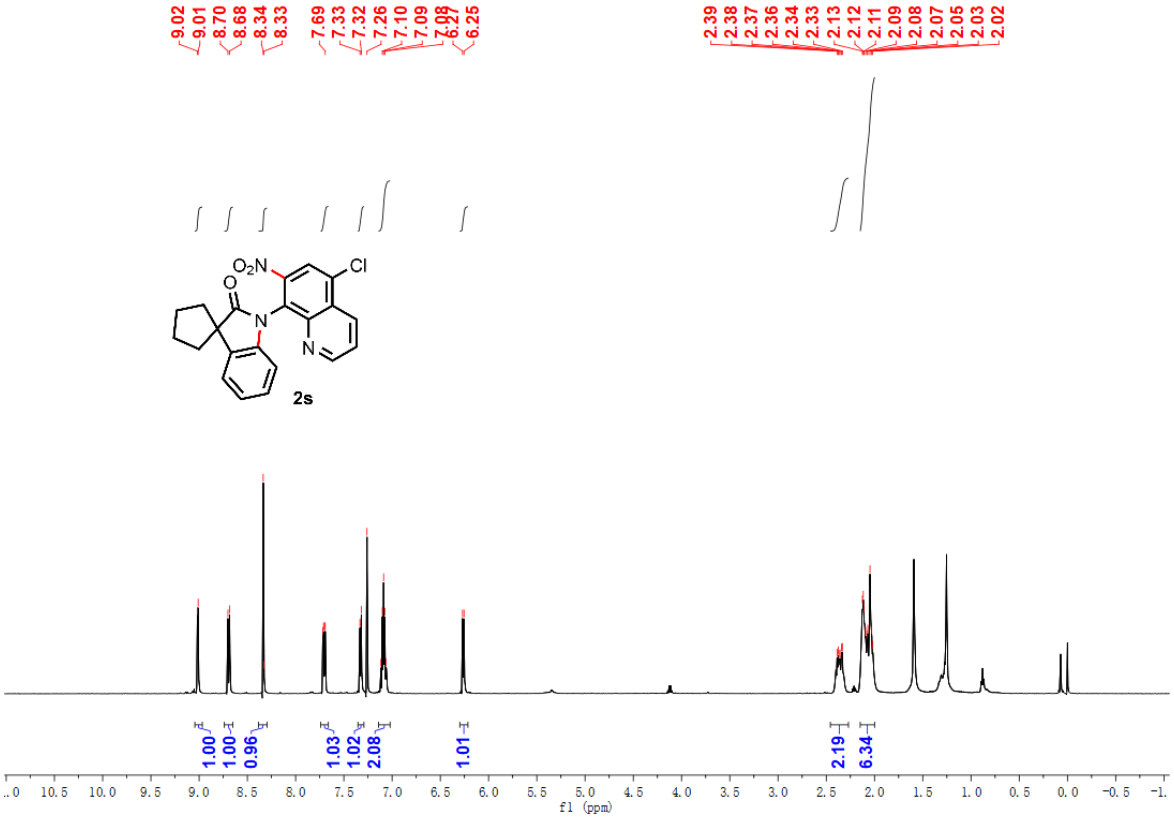
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2r**



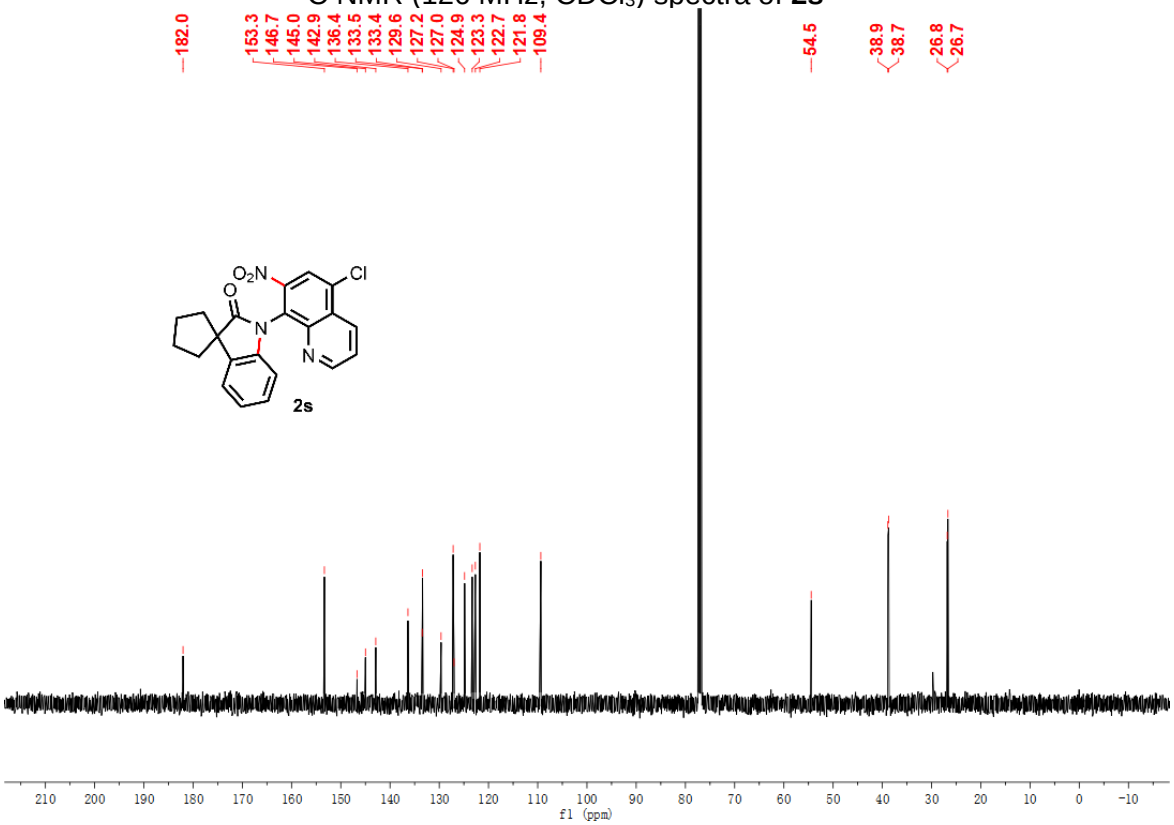
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2r**



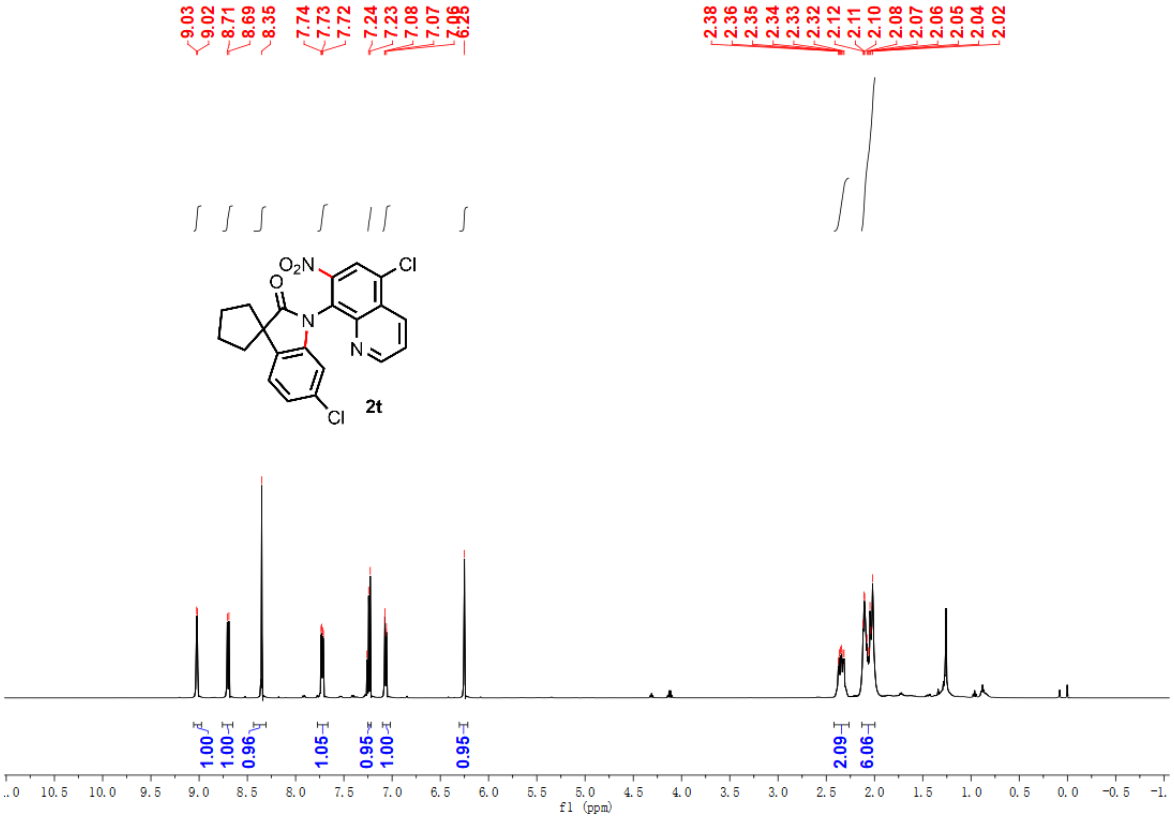
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2s**



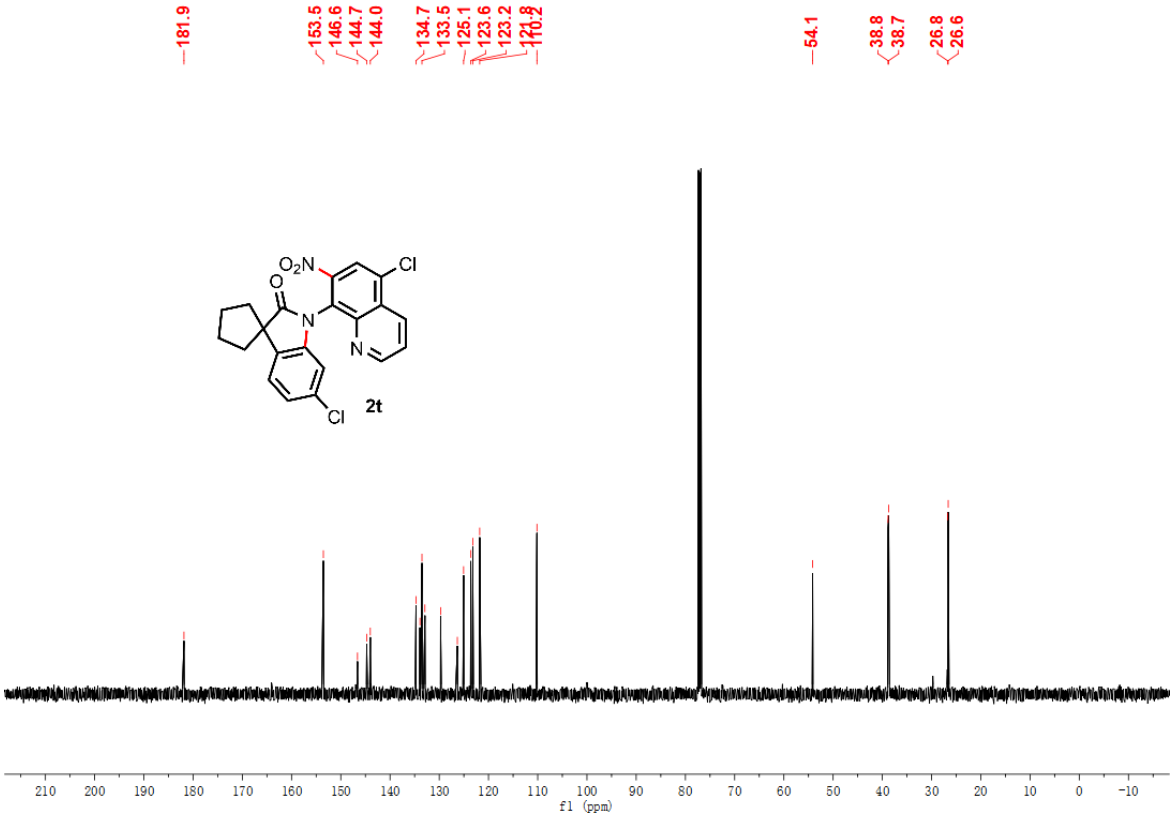
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2s**



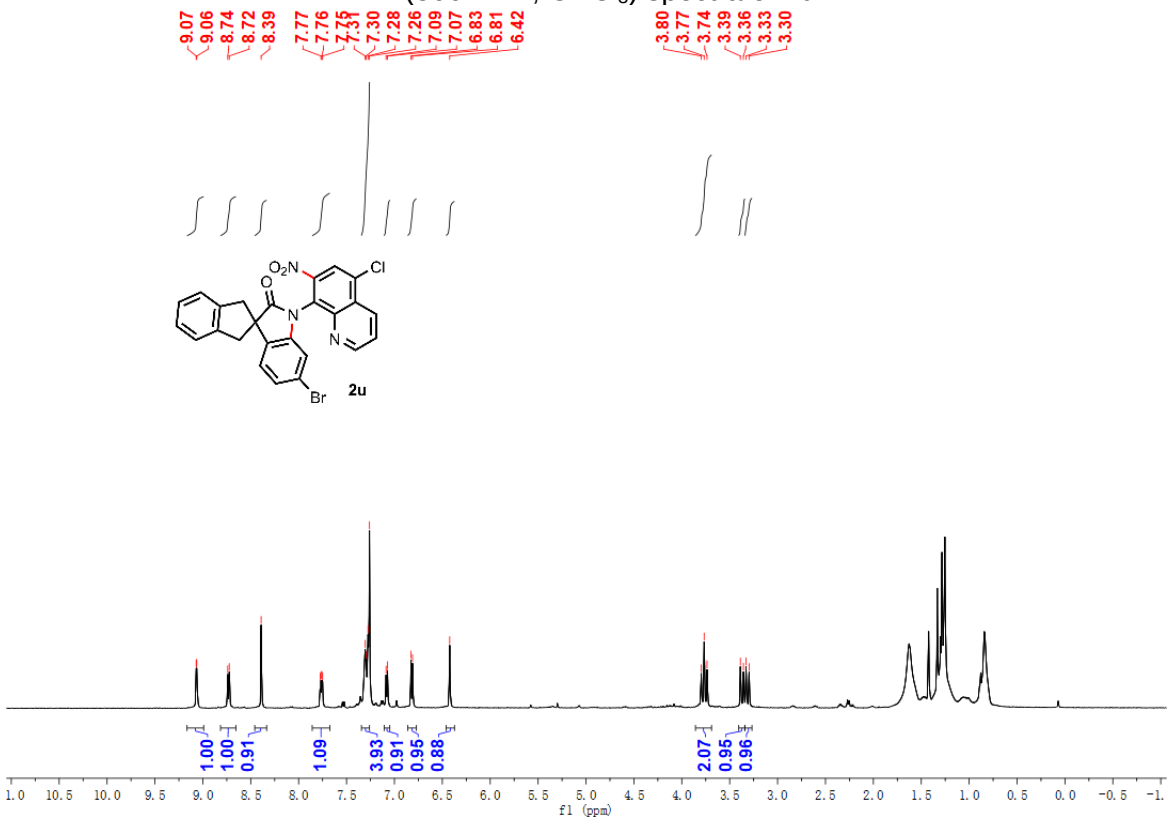
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2t**



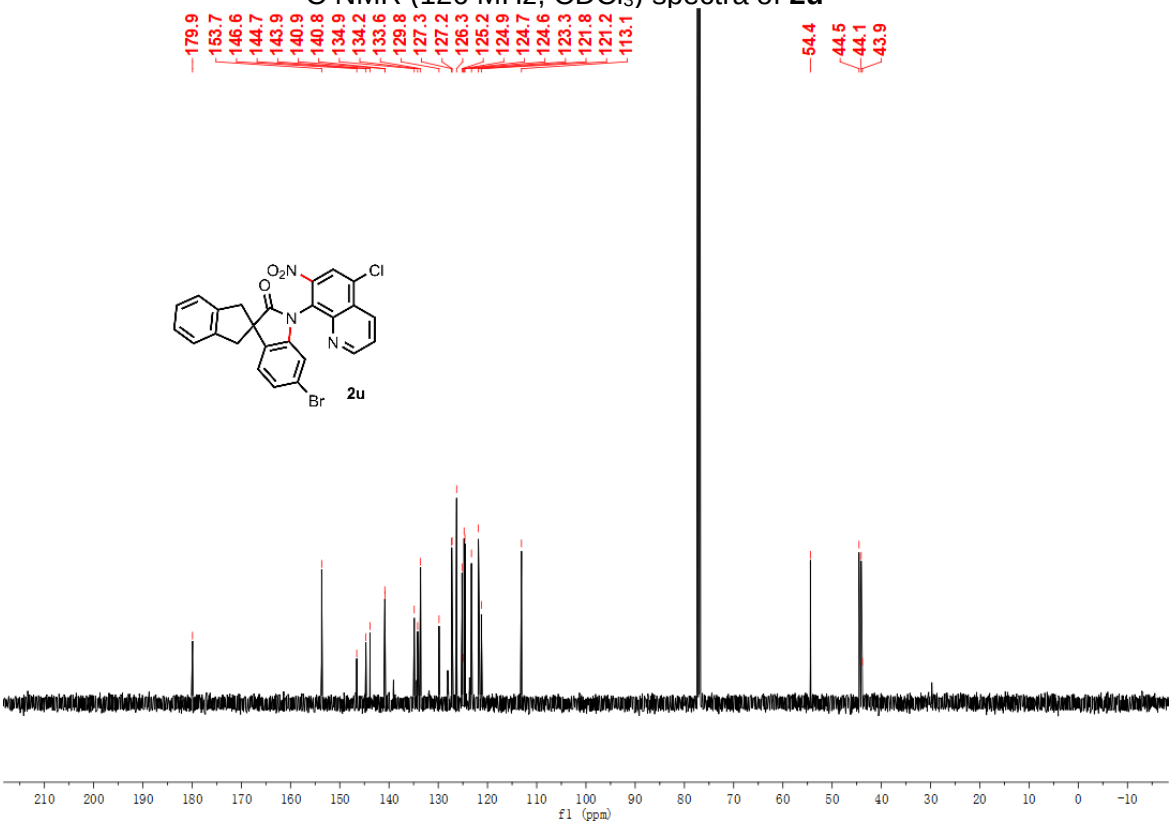
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2t**



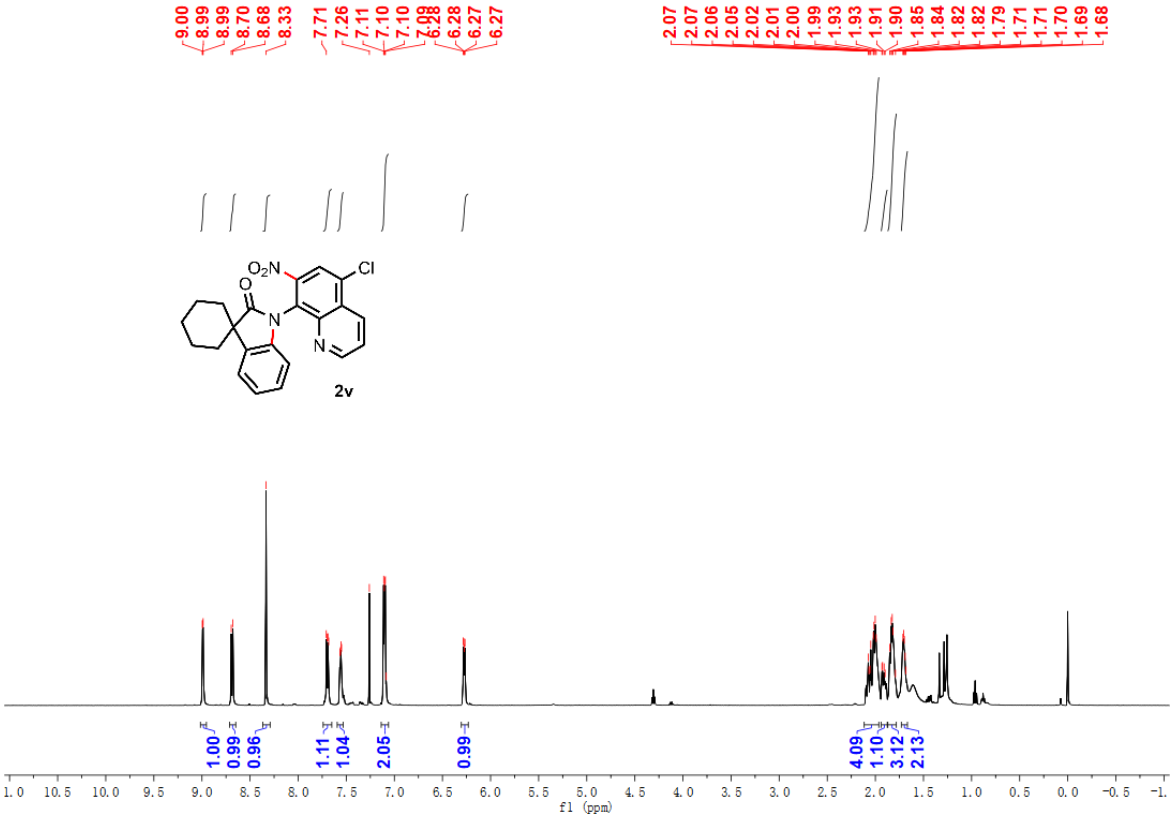
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2u**



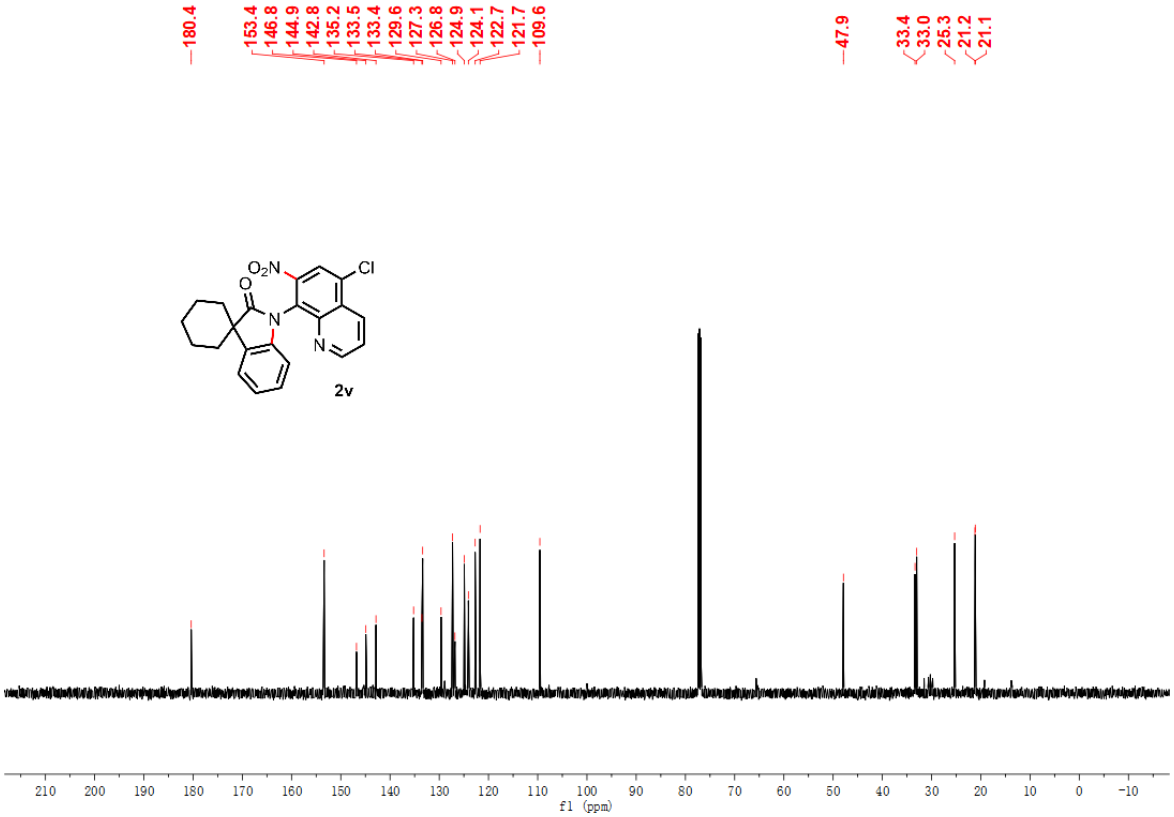
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2u**



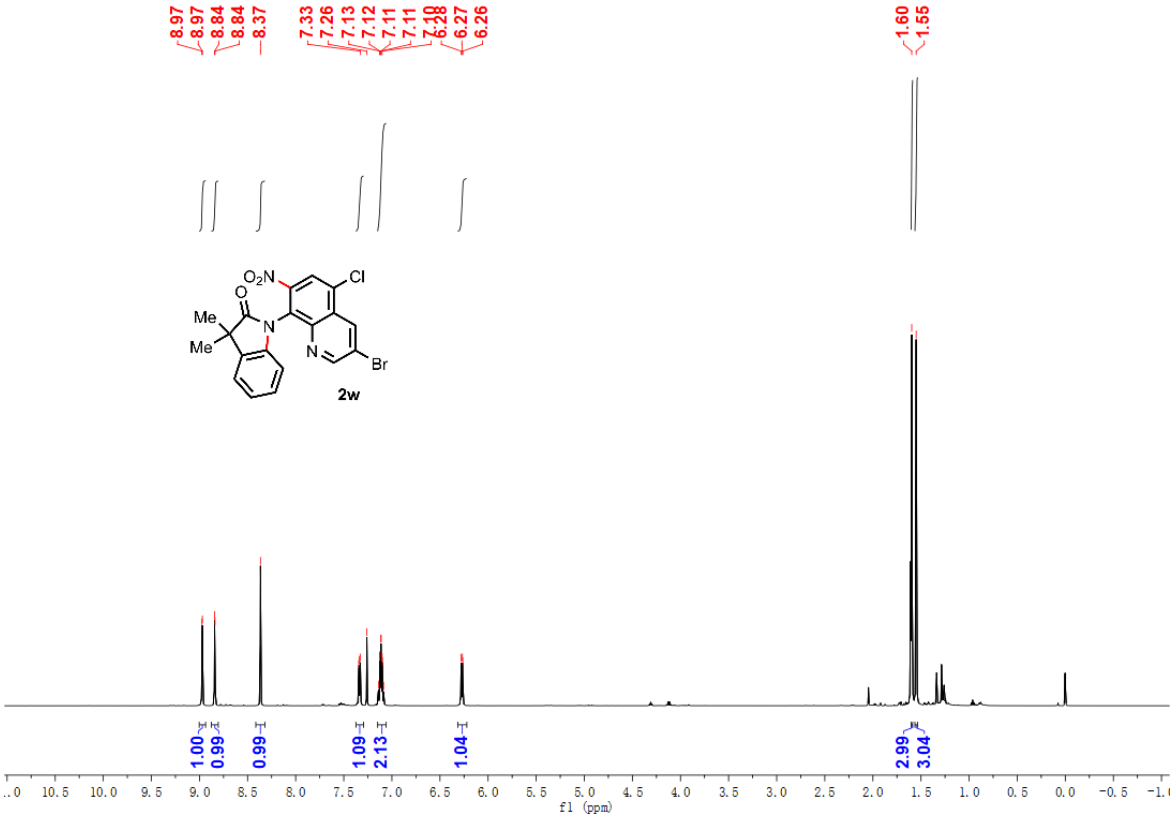
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2v**



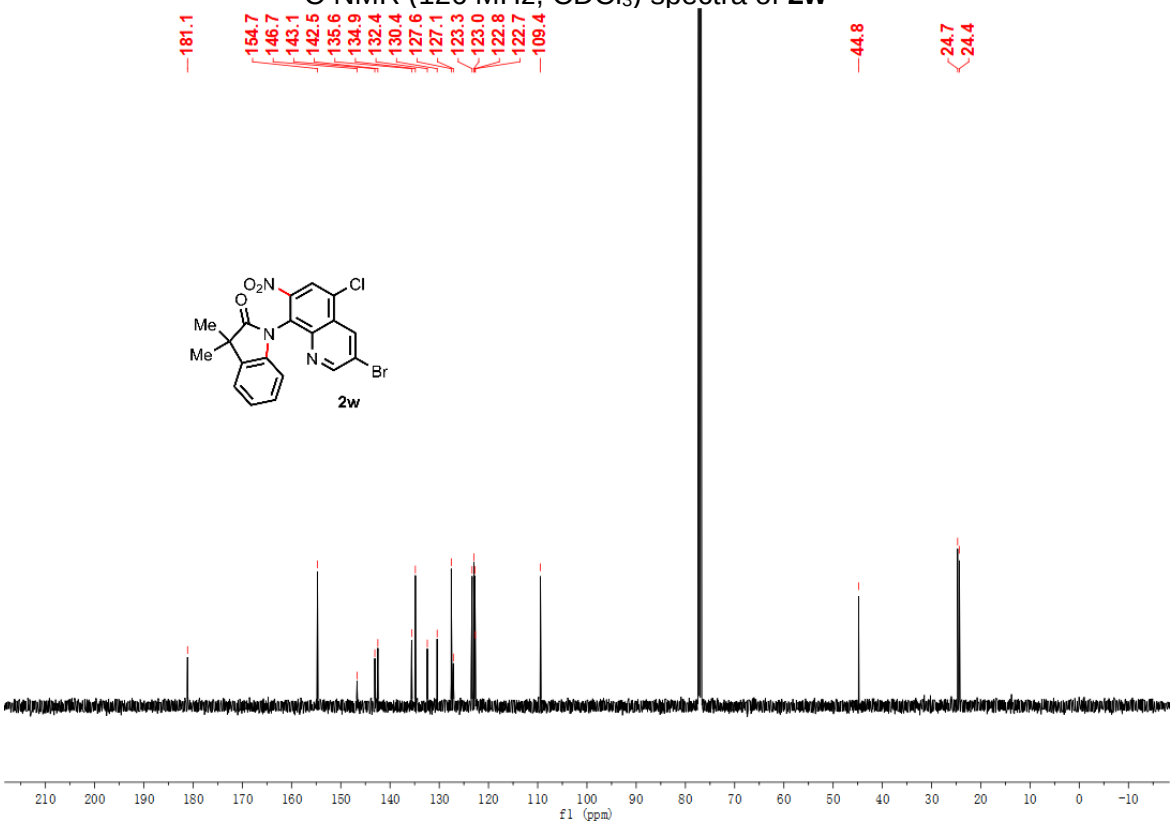
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2v**



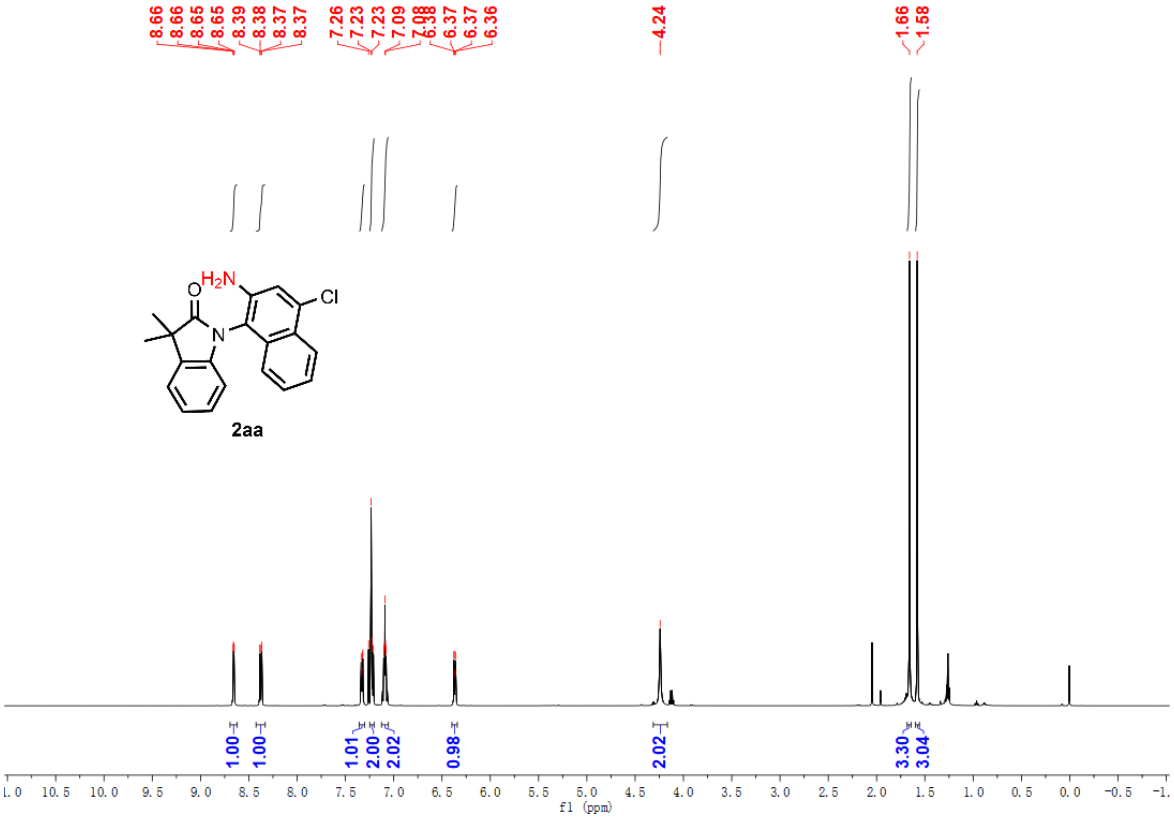
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2w**



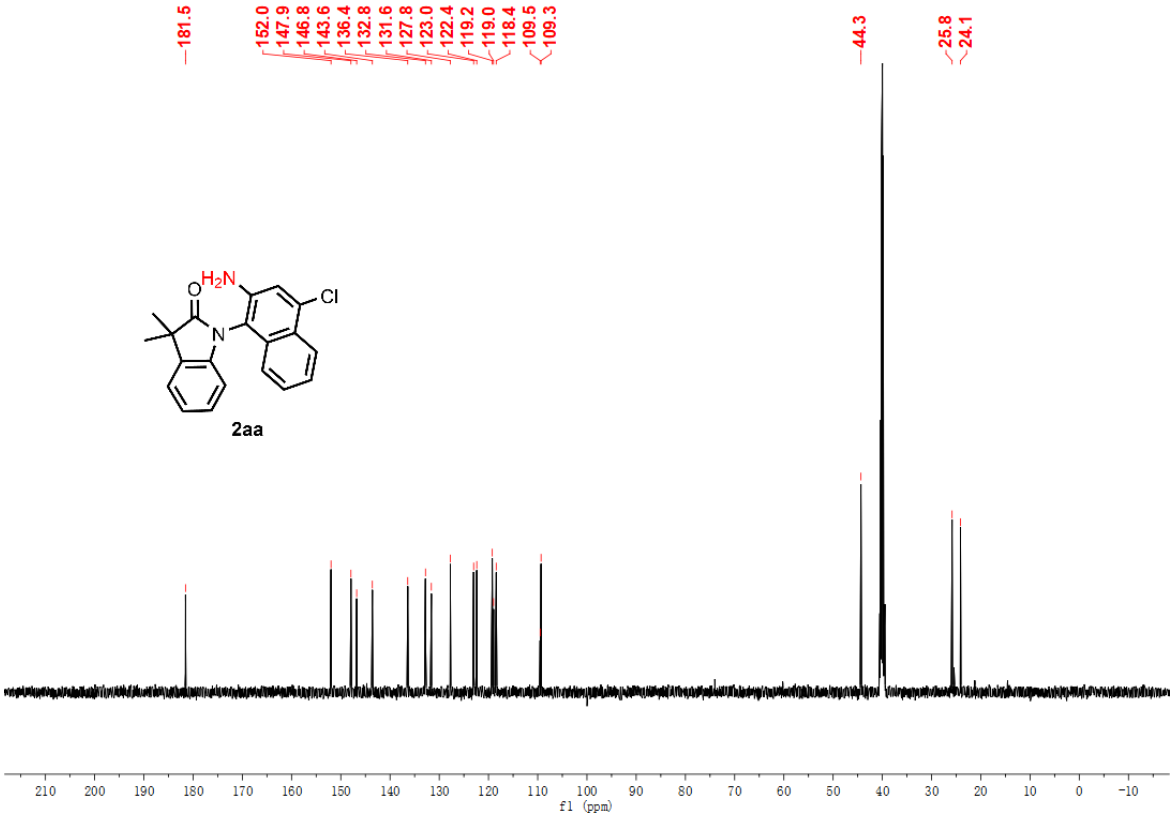
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **2w**



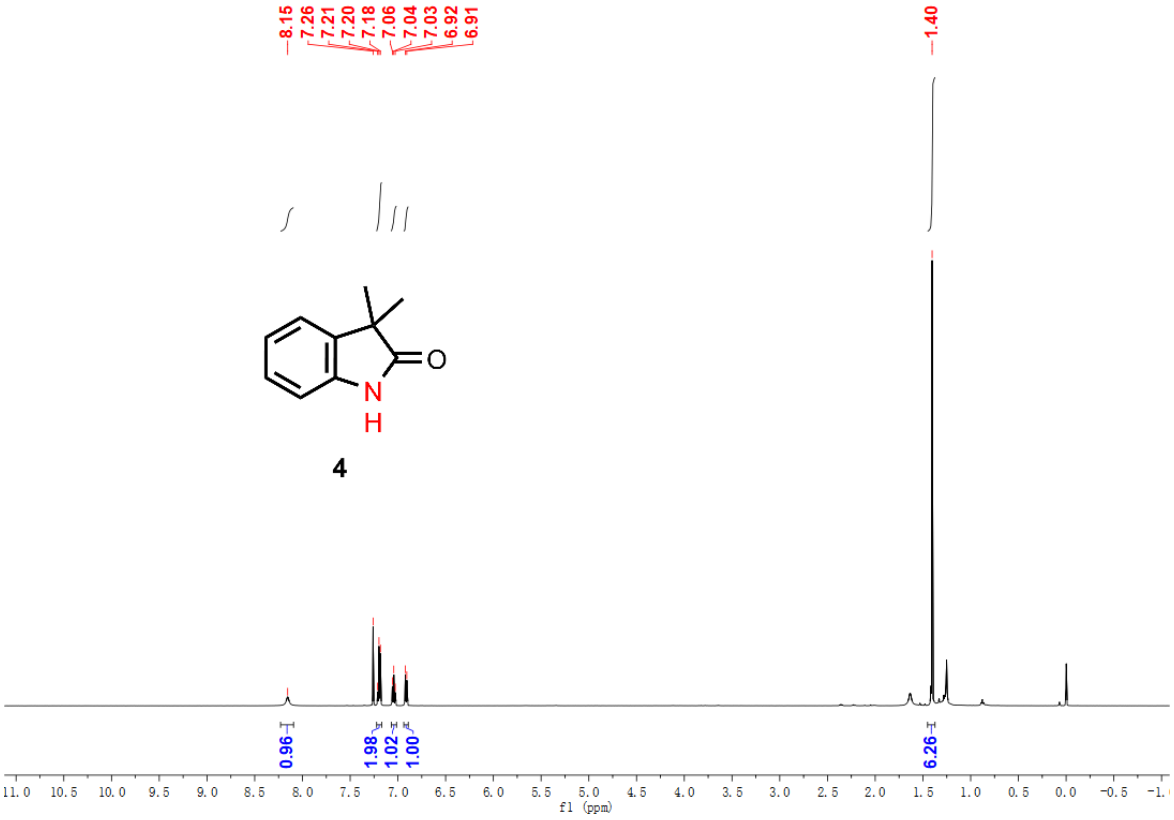
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **2aa**



^{13}C NMR (126 MHz, DMSO) spectra of **2aa**

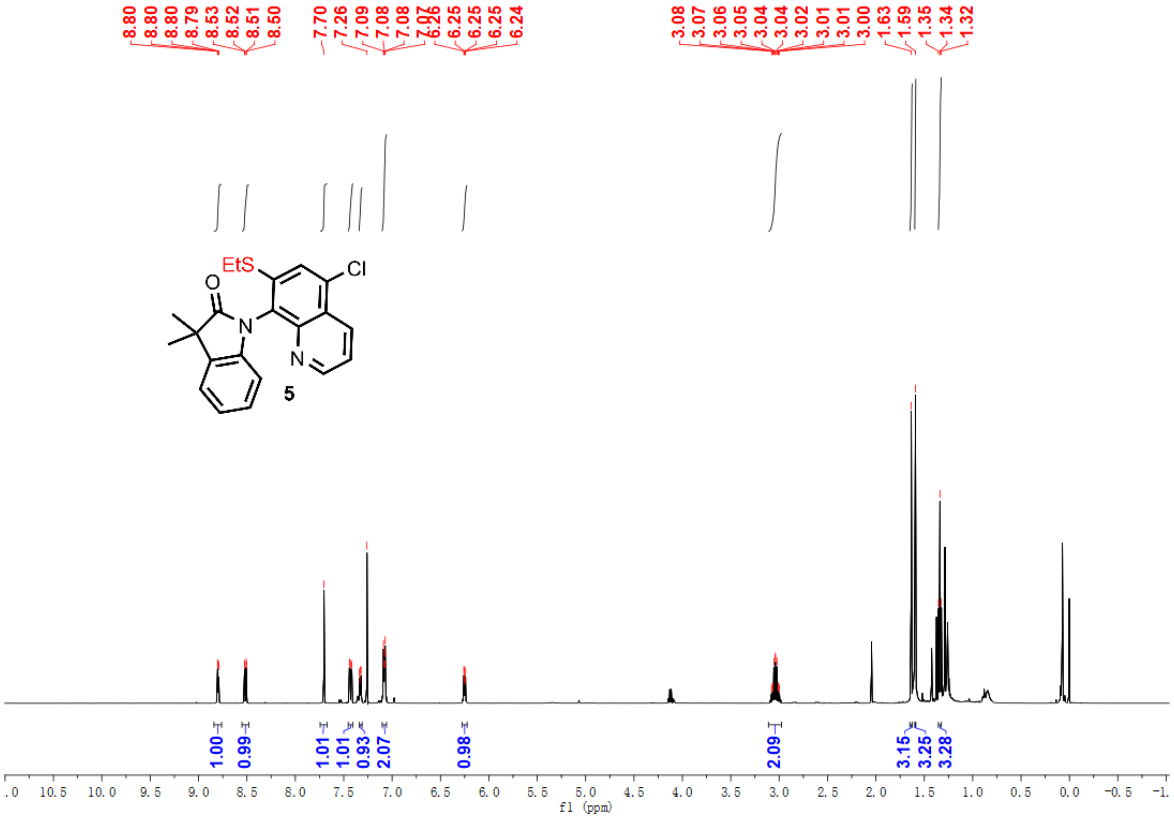


^{1}H NMR (500 MHz, $CDCl_3$) spectra of **4**

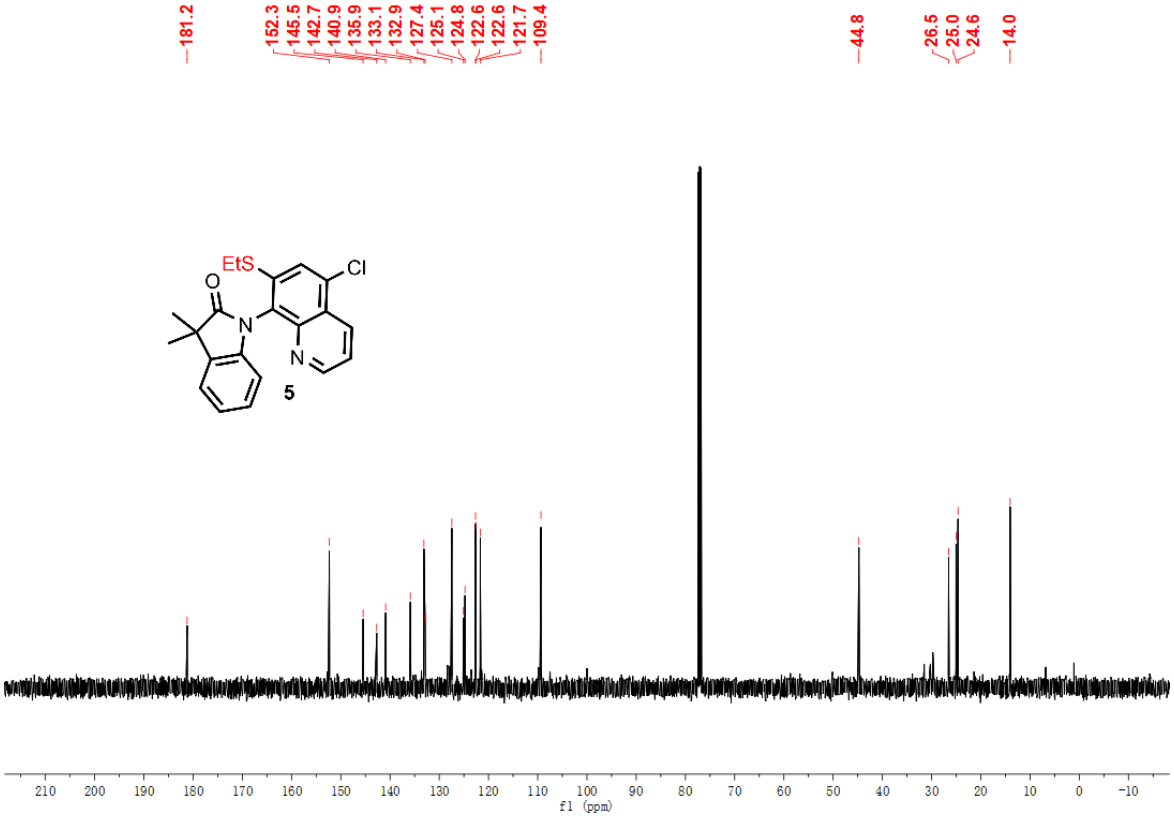


4

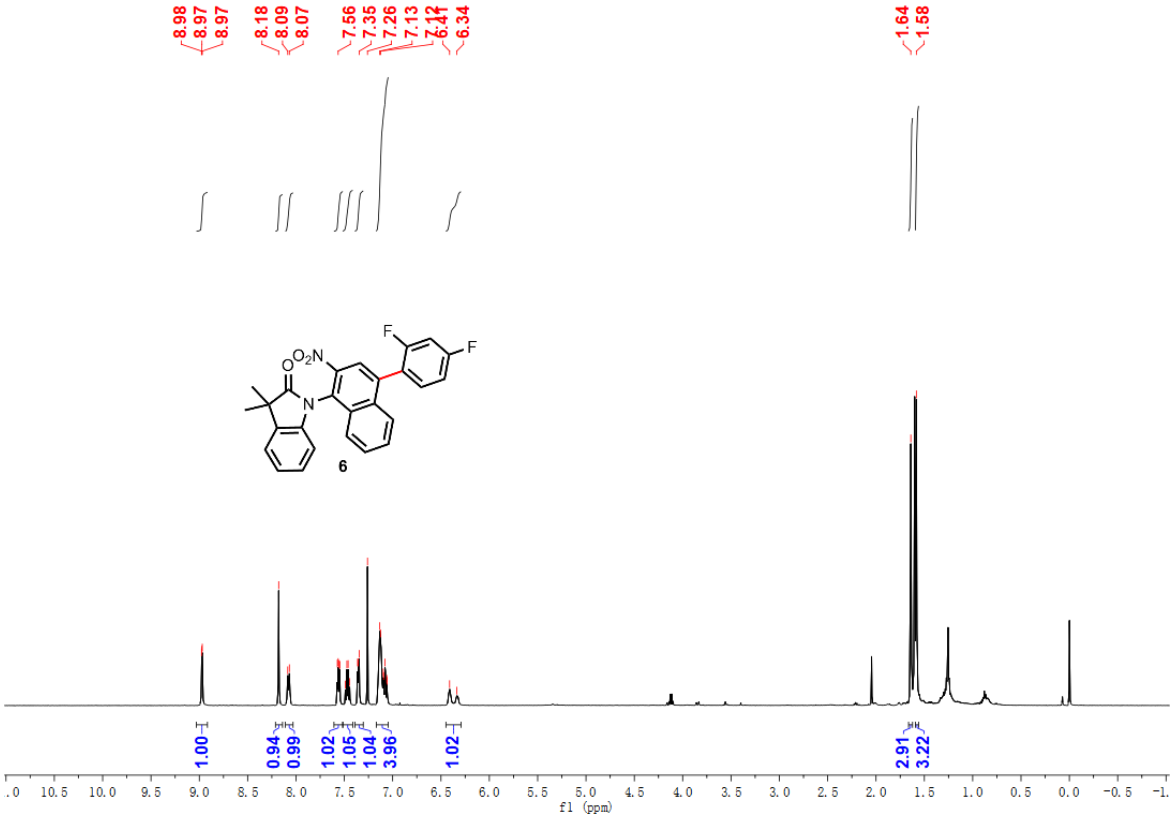
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **5**



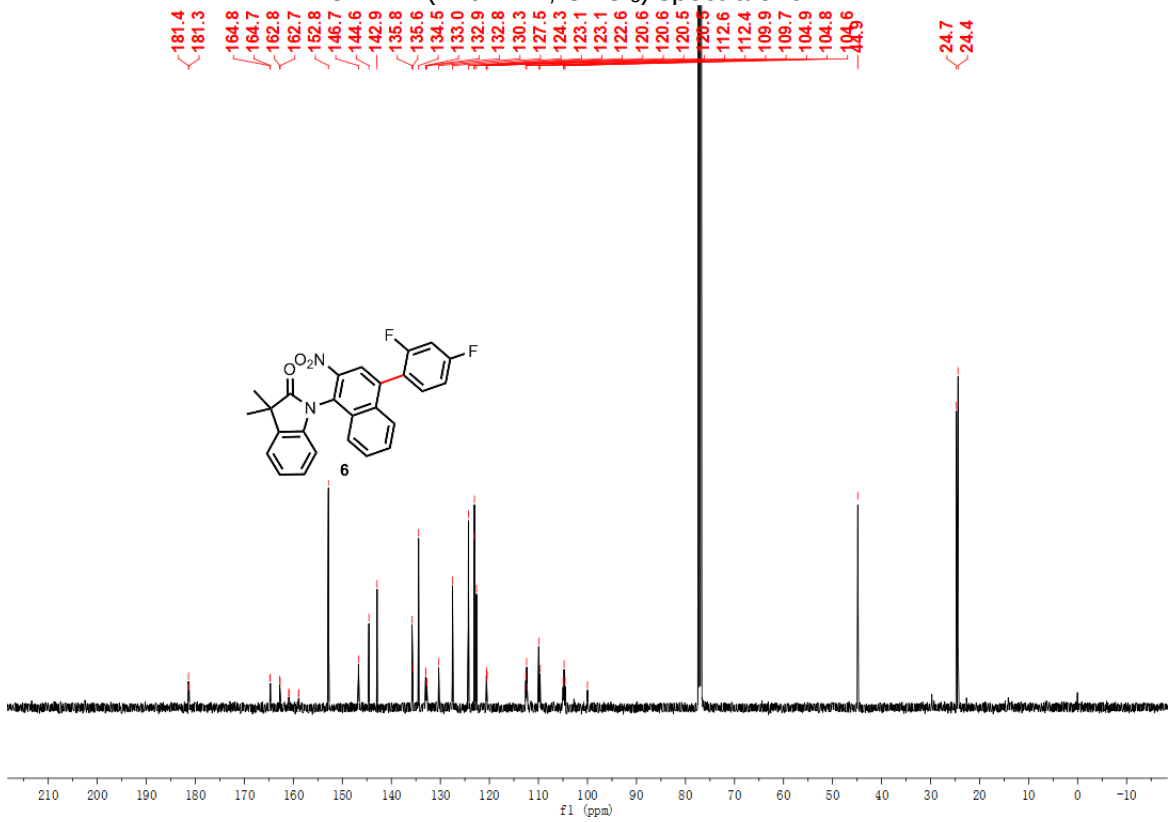
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **5**



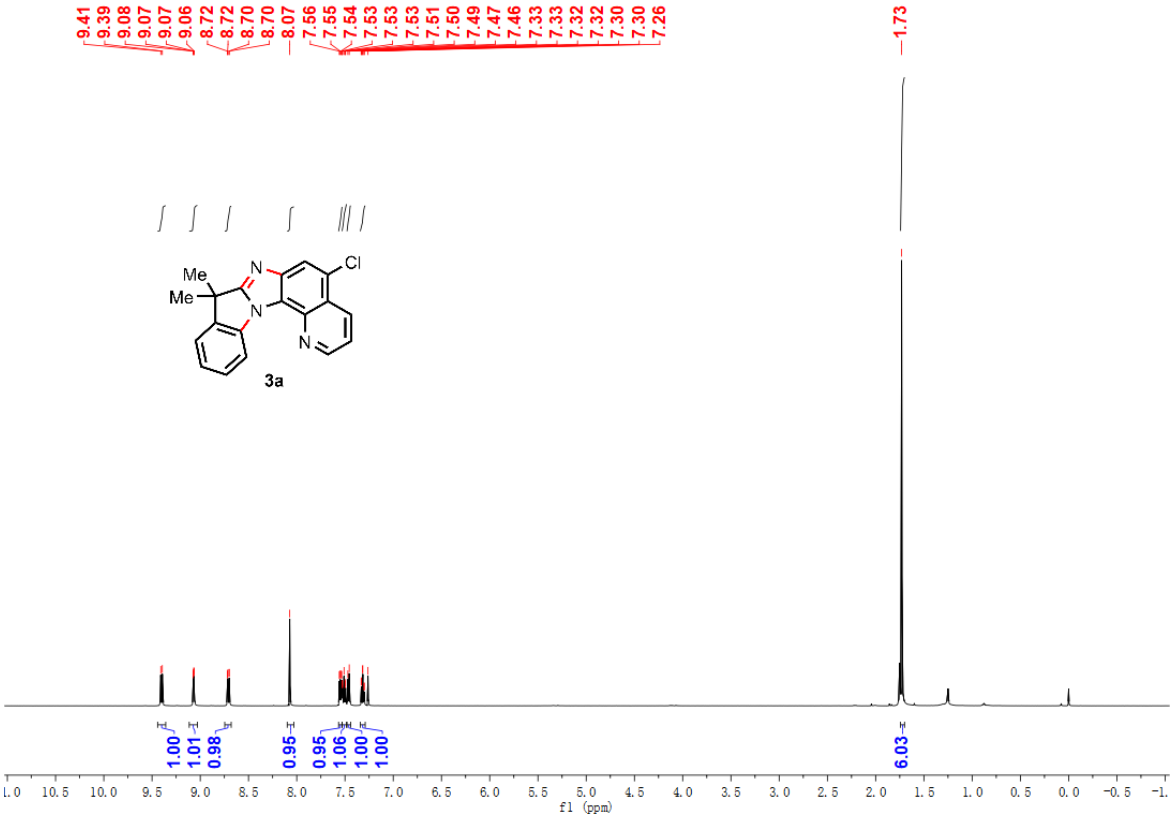
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **6**



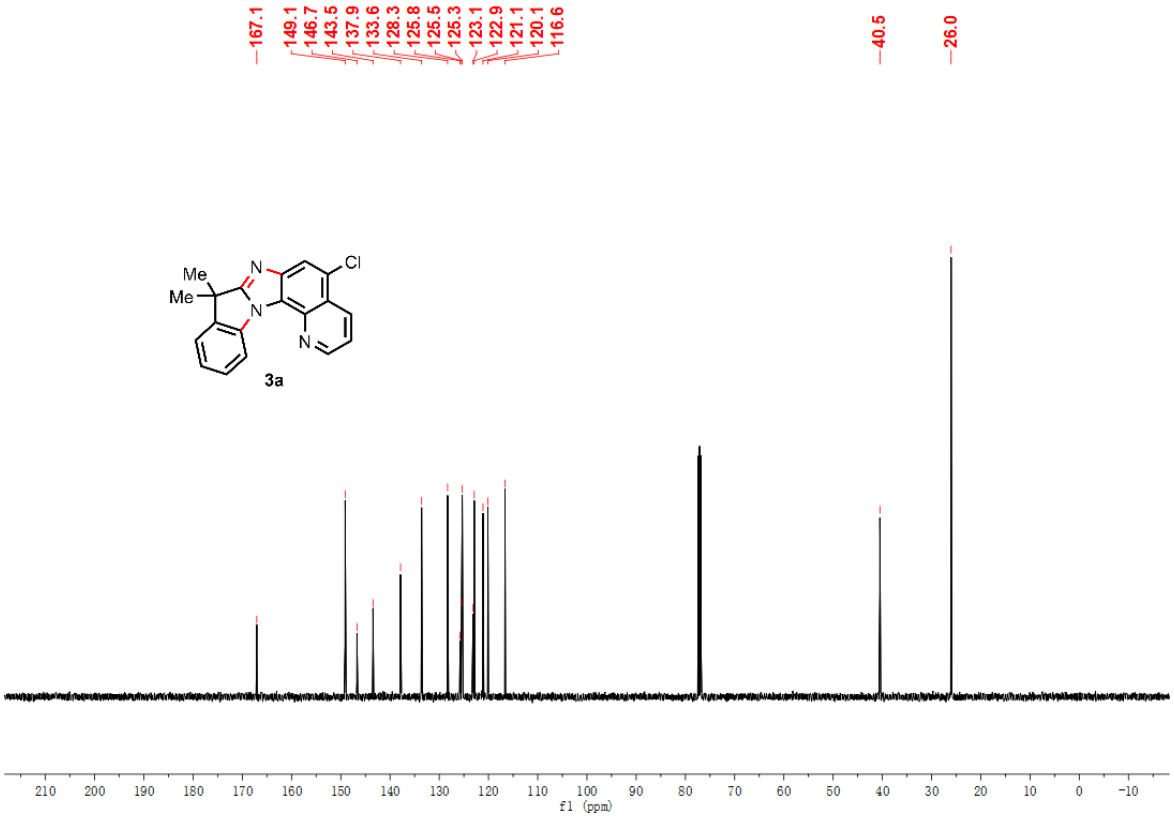
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **6**



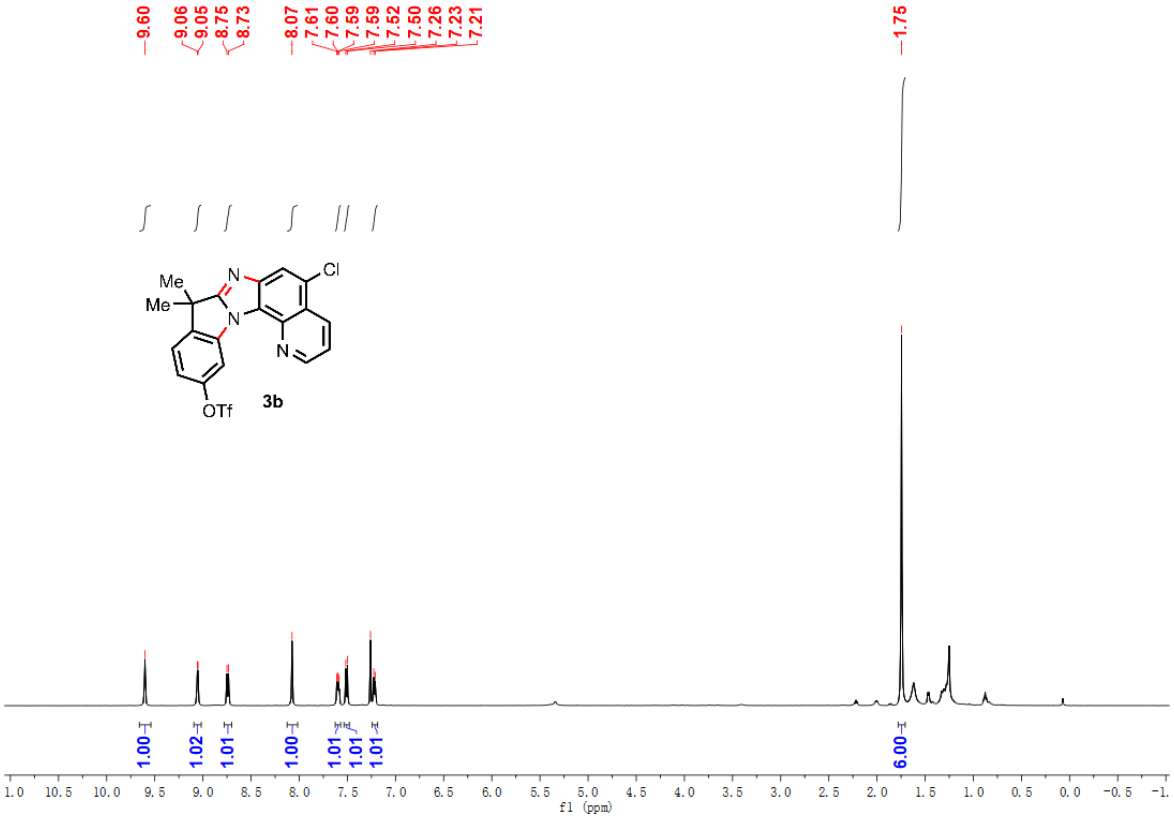
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **3a**



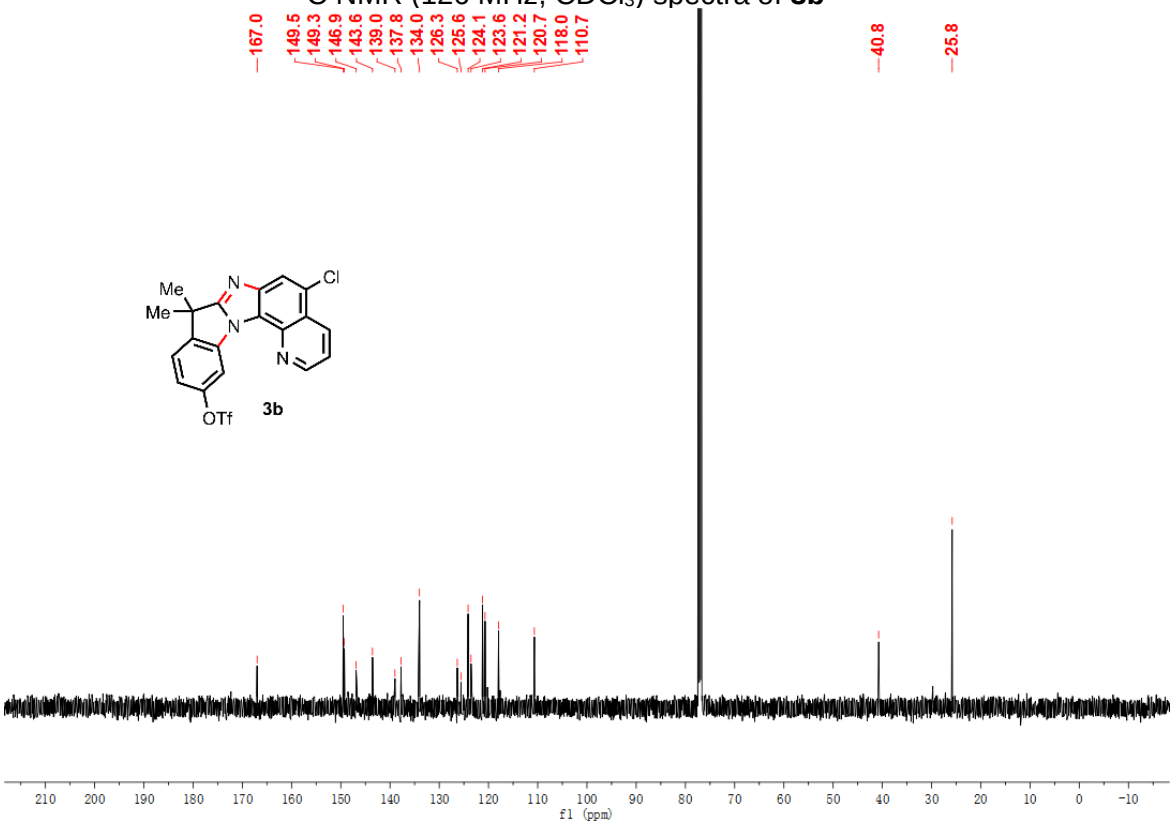
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **3a**



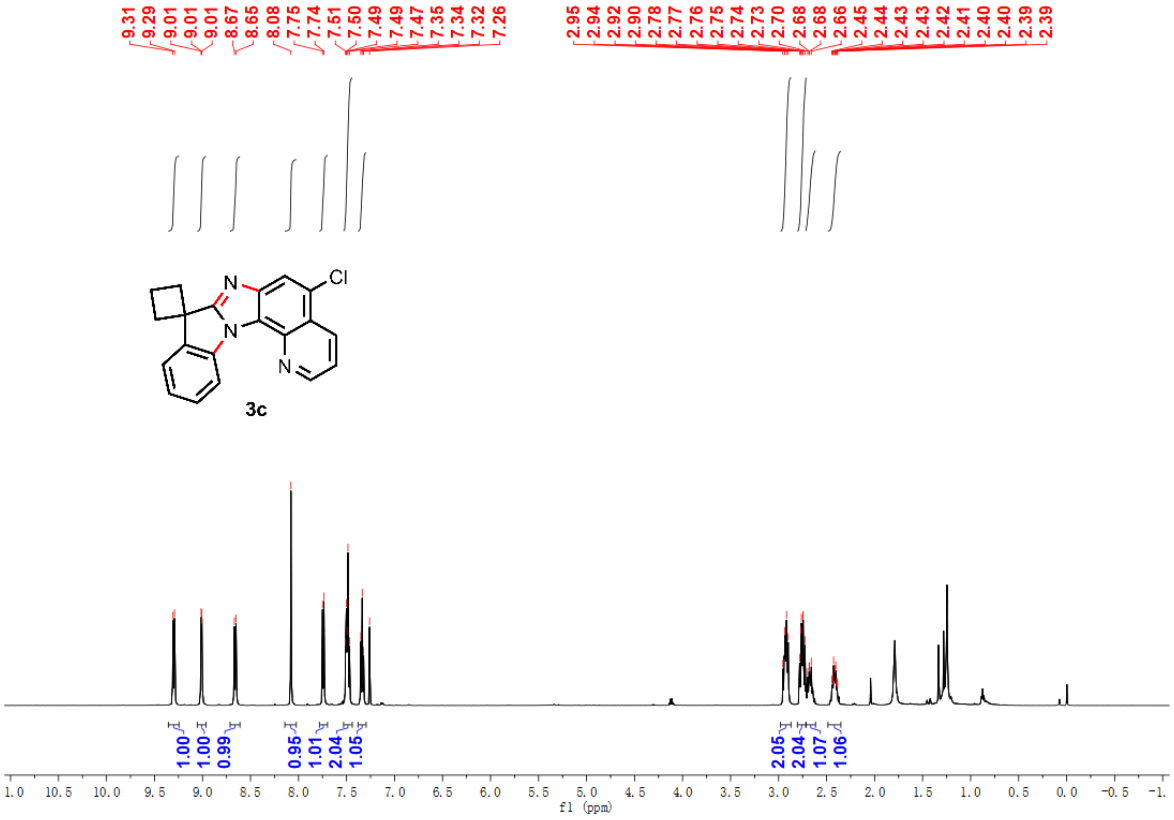
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **3b**



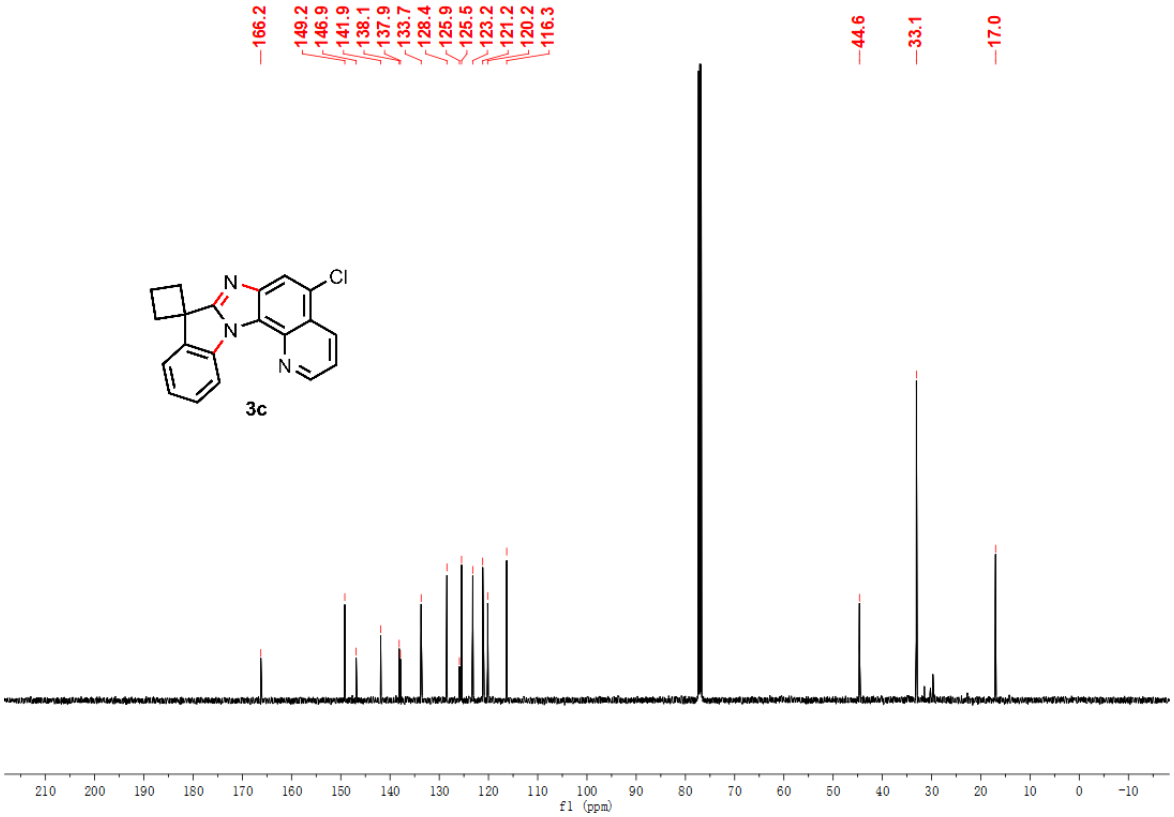
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **3b**



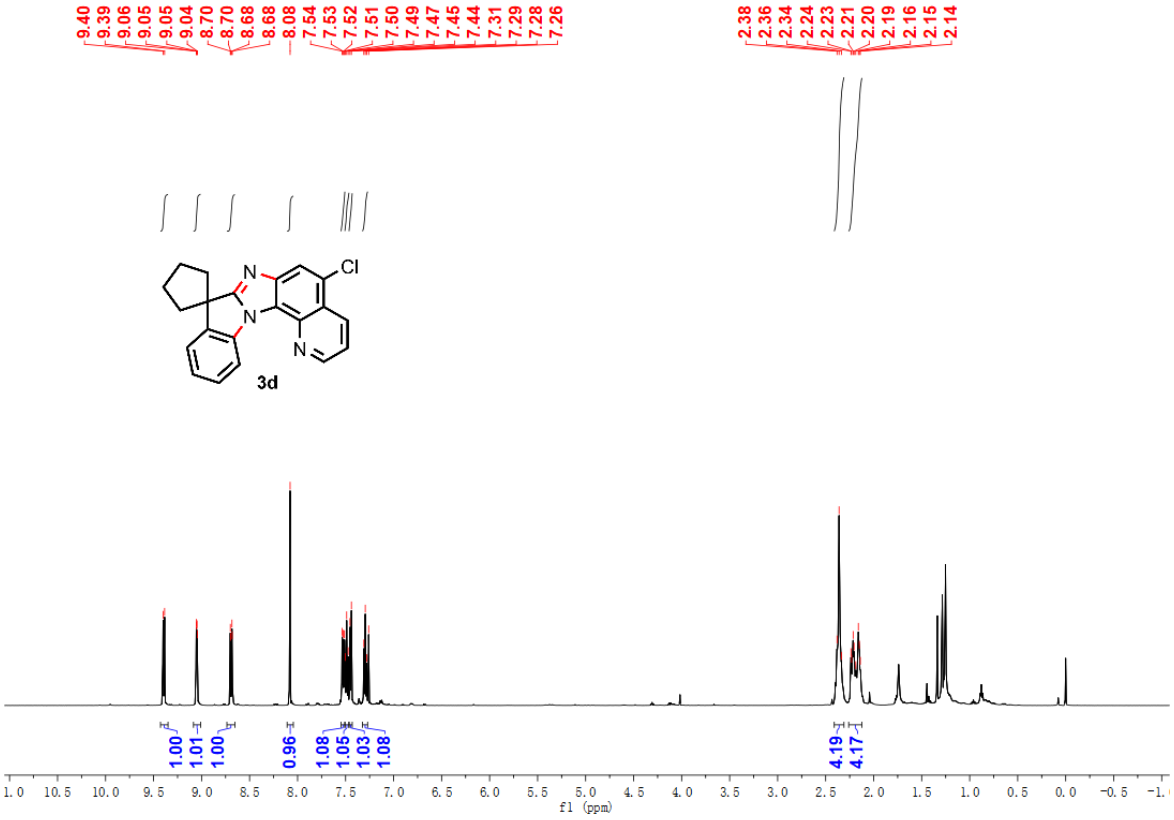
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **3c**



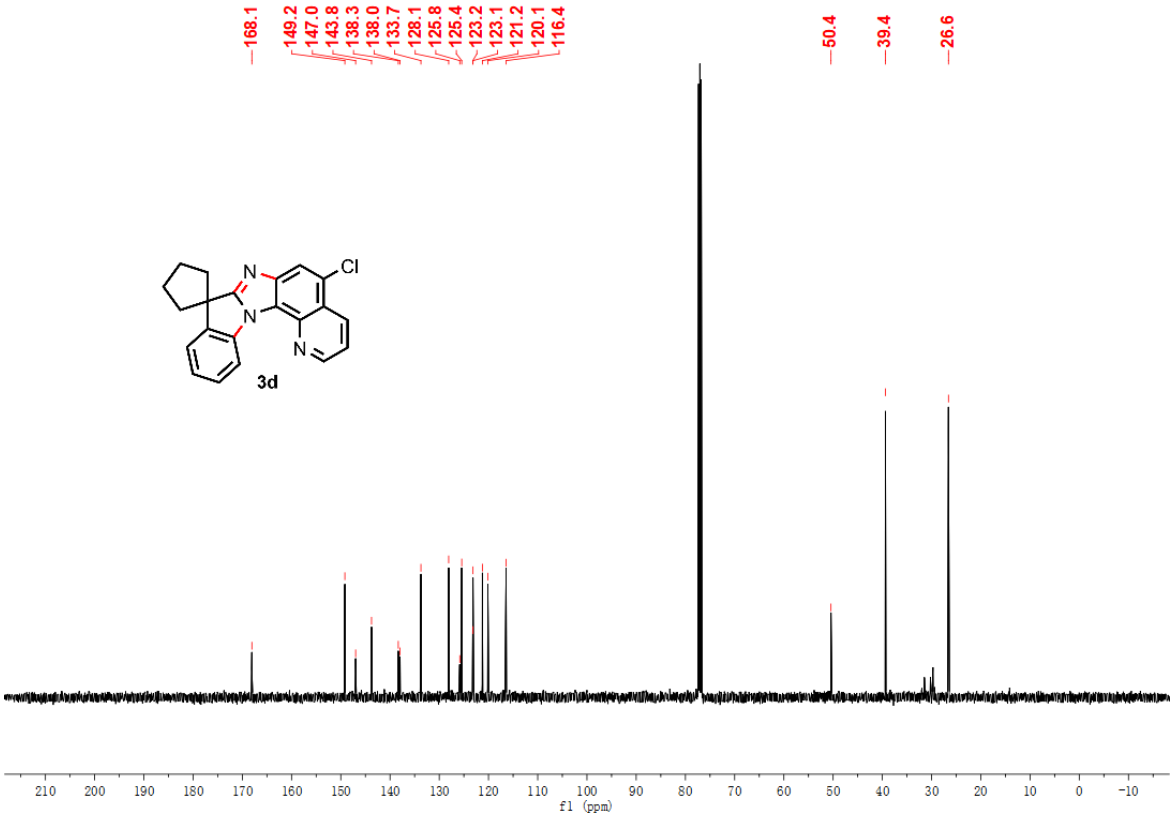
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **3c**



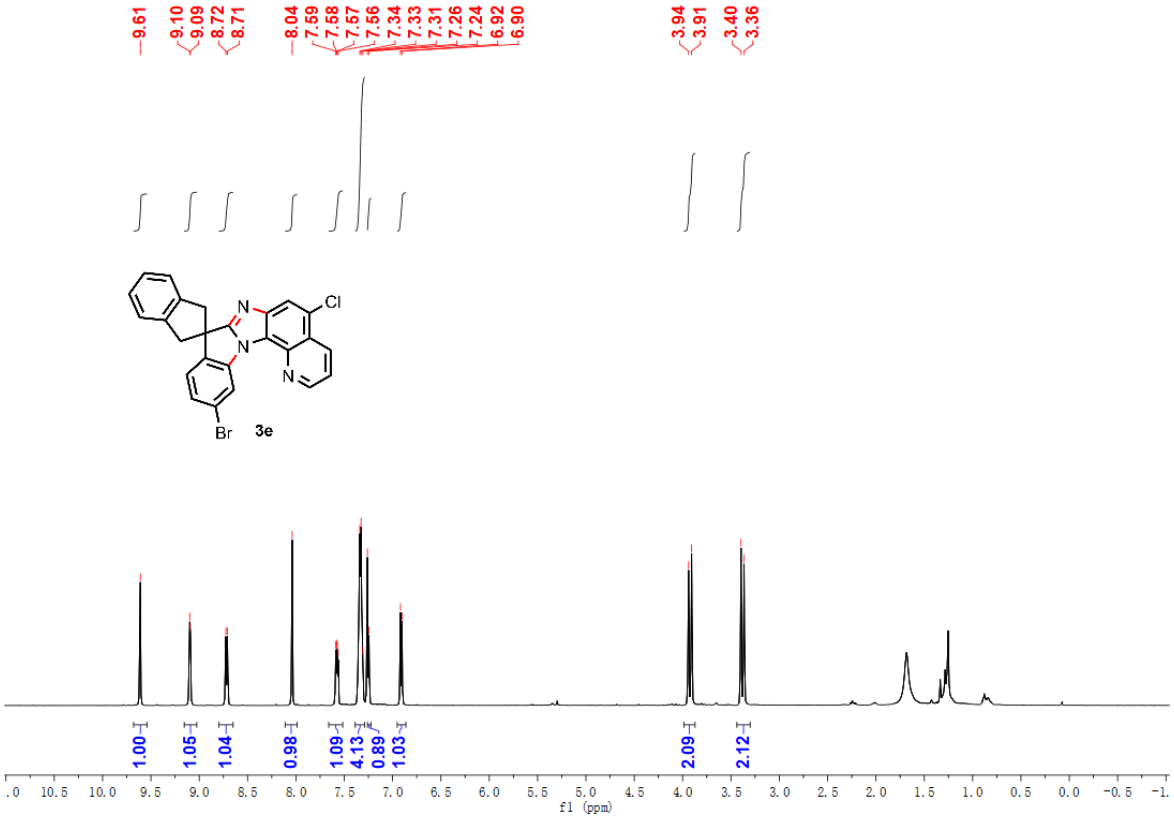
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **3d**



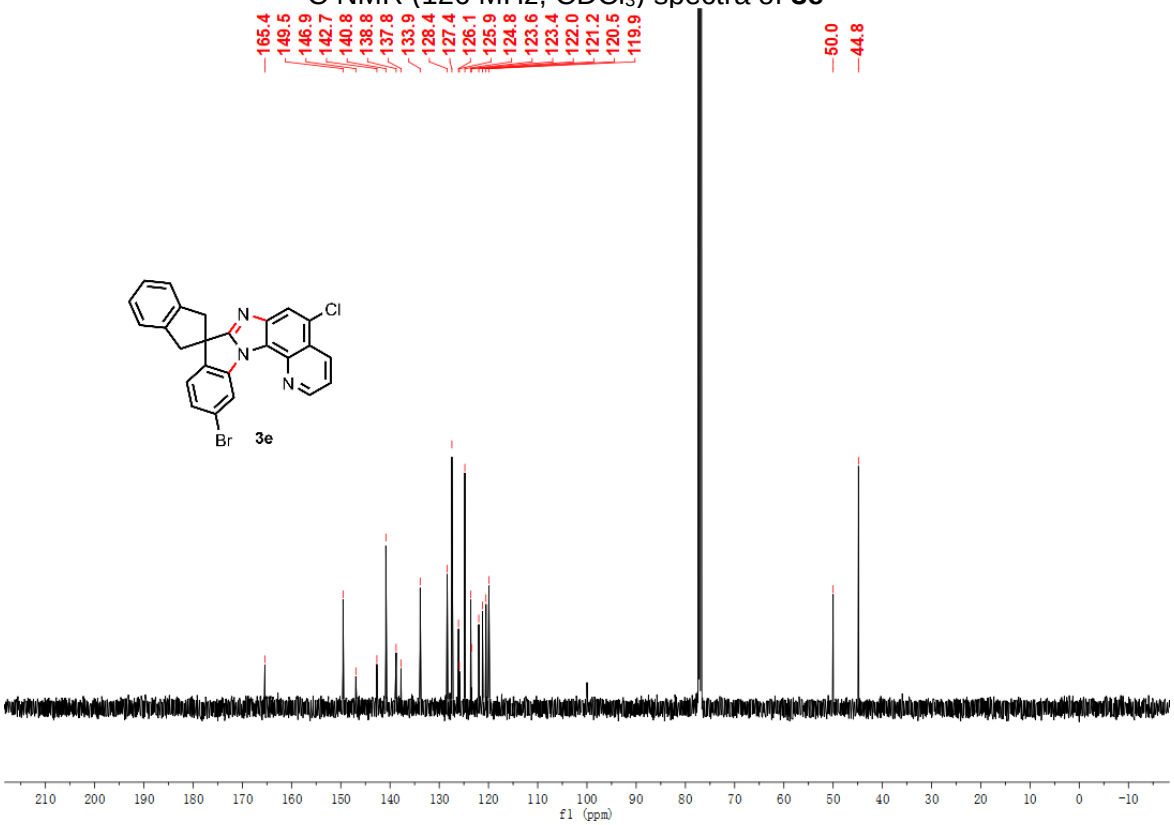
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **3d**



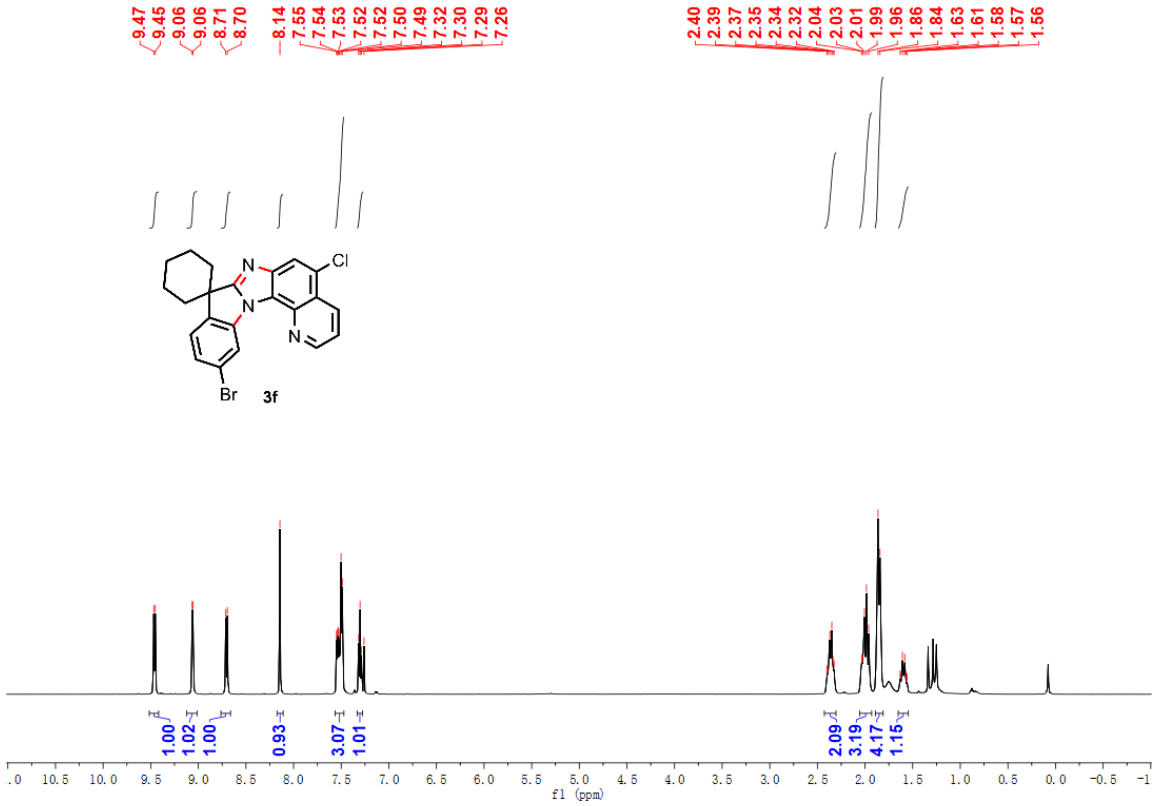
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **3e**



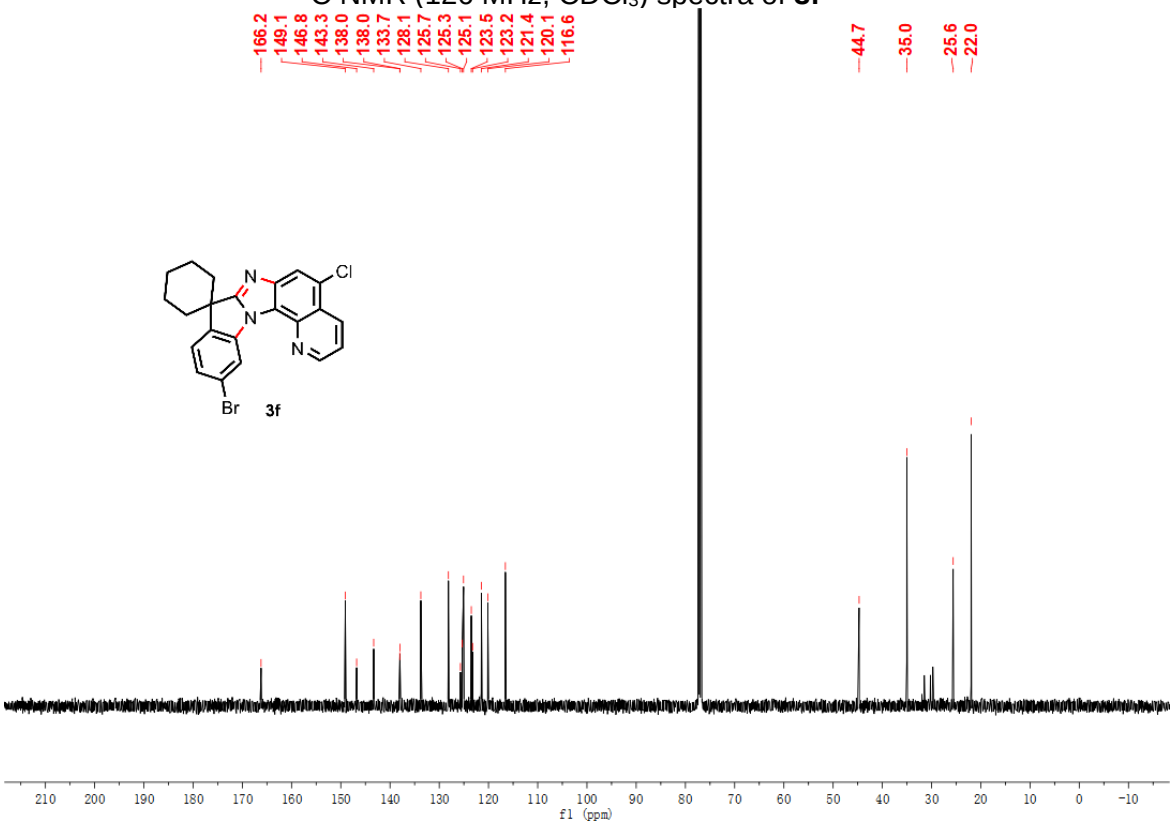
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **3e**



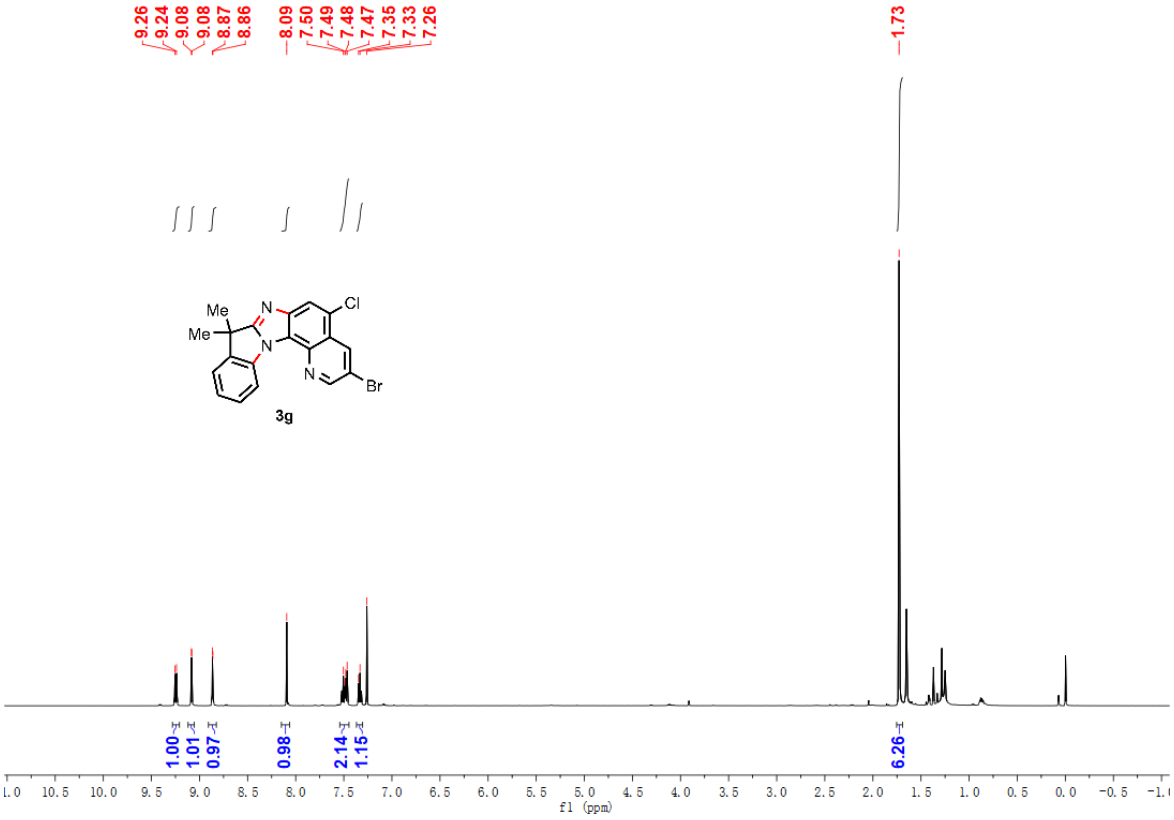
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **3f**



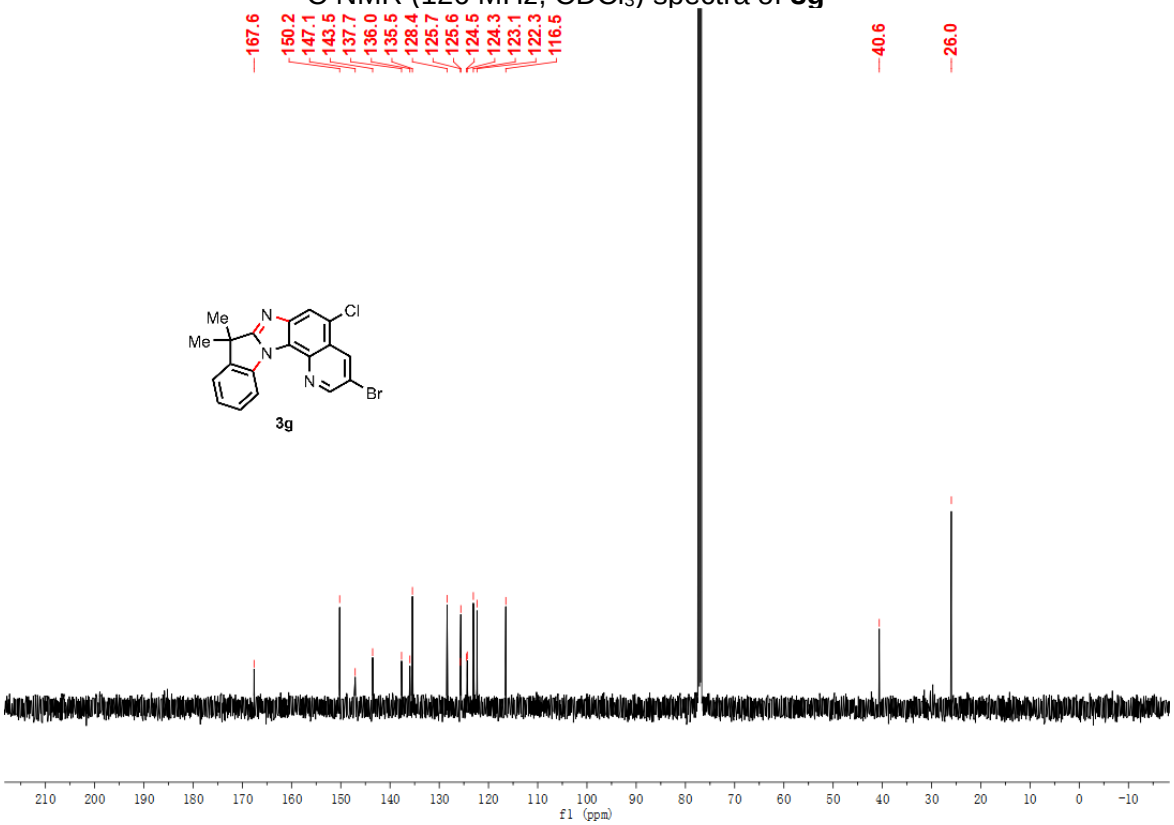
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **3f**



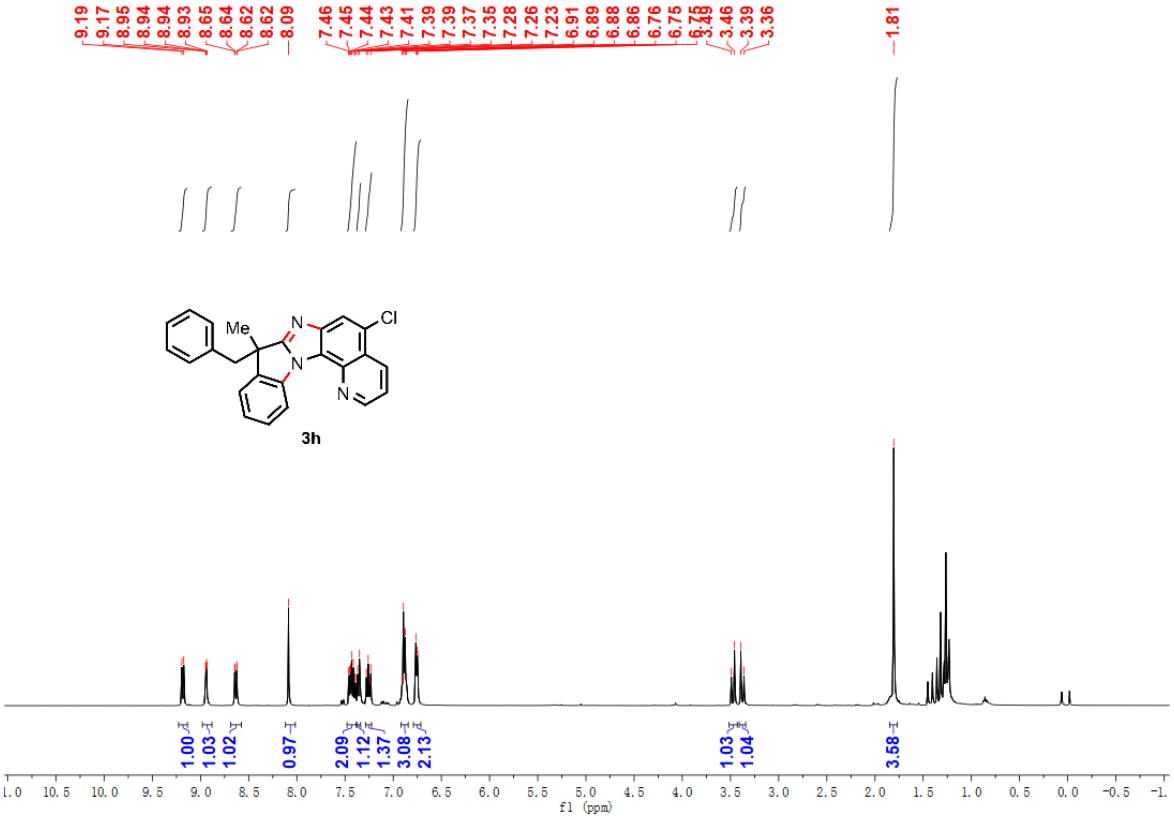
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **3g**



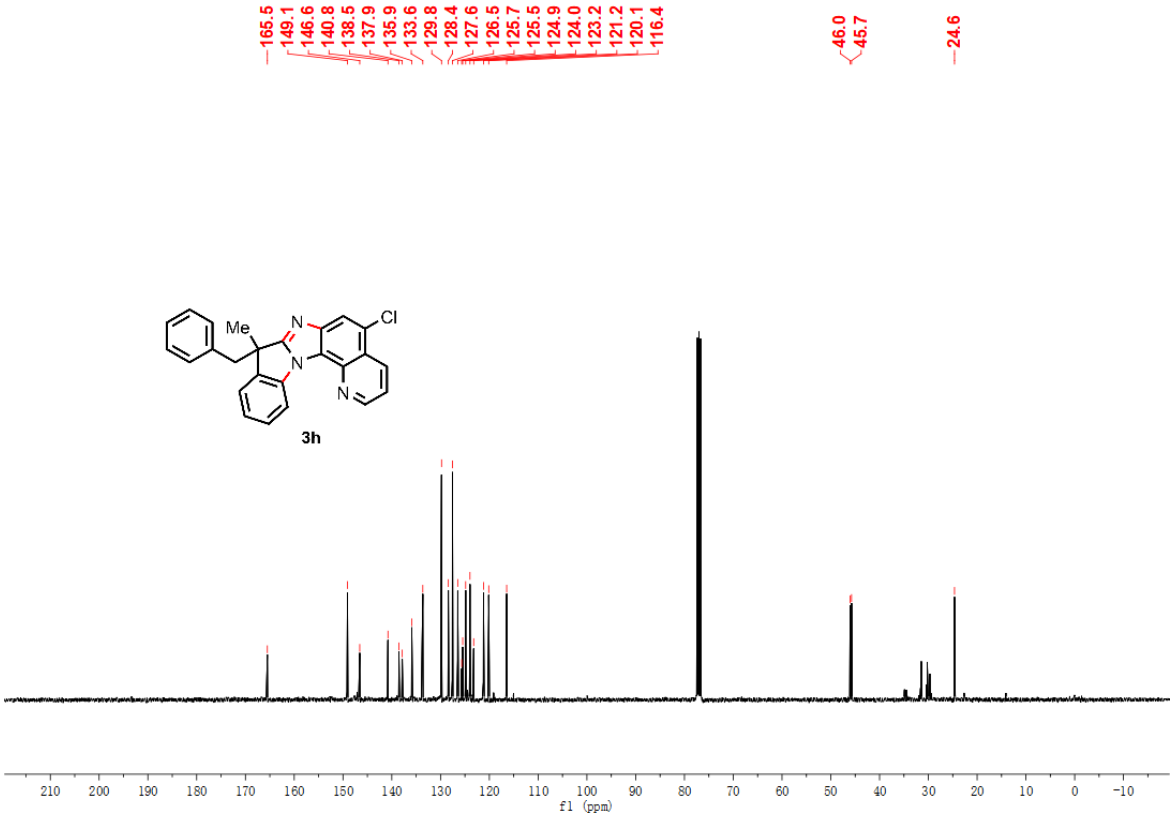
^{13}C NMR (126 MHz, $CDCl_3$) spectra of **3g**



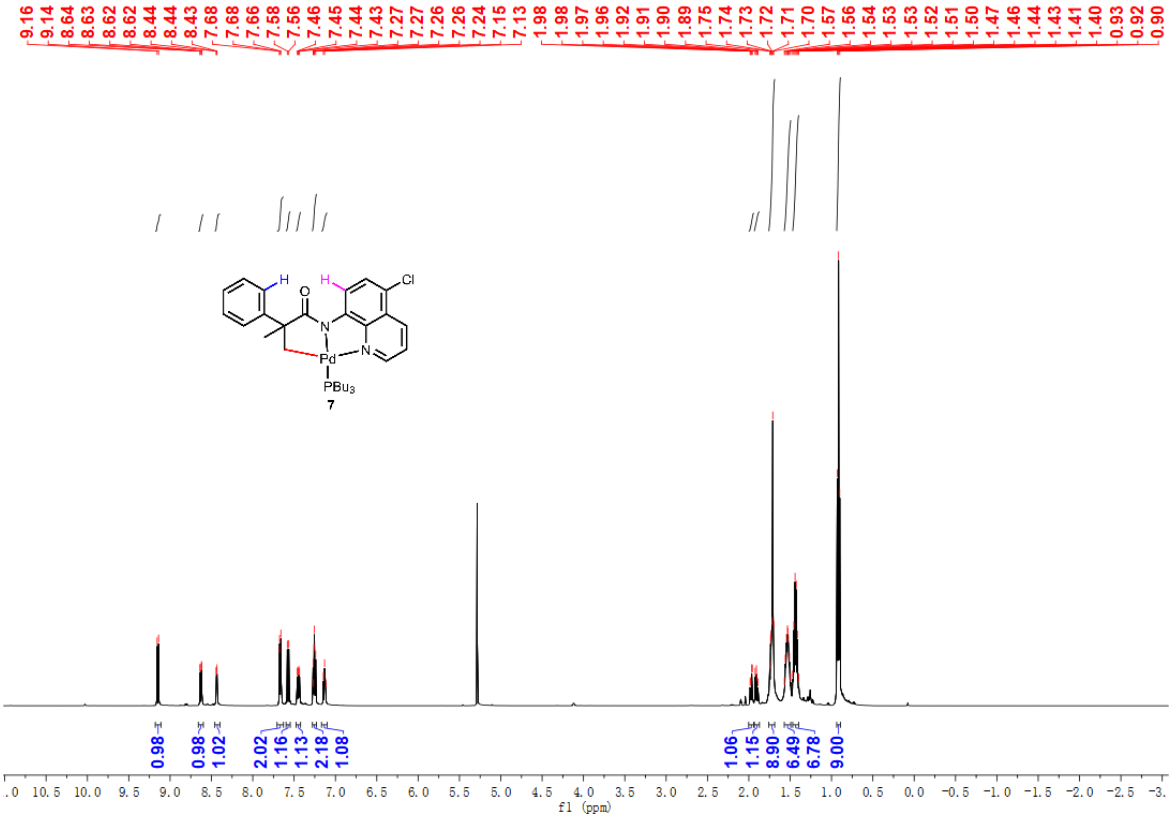
^{1}H NMR (400 MHz, $CDCl_3$) spectra of **3h**



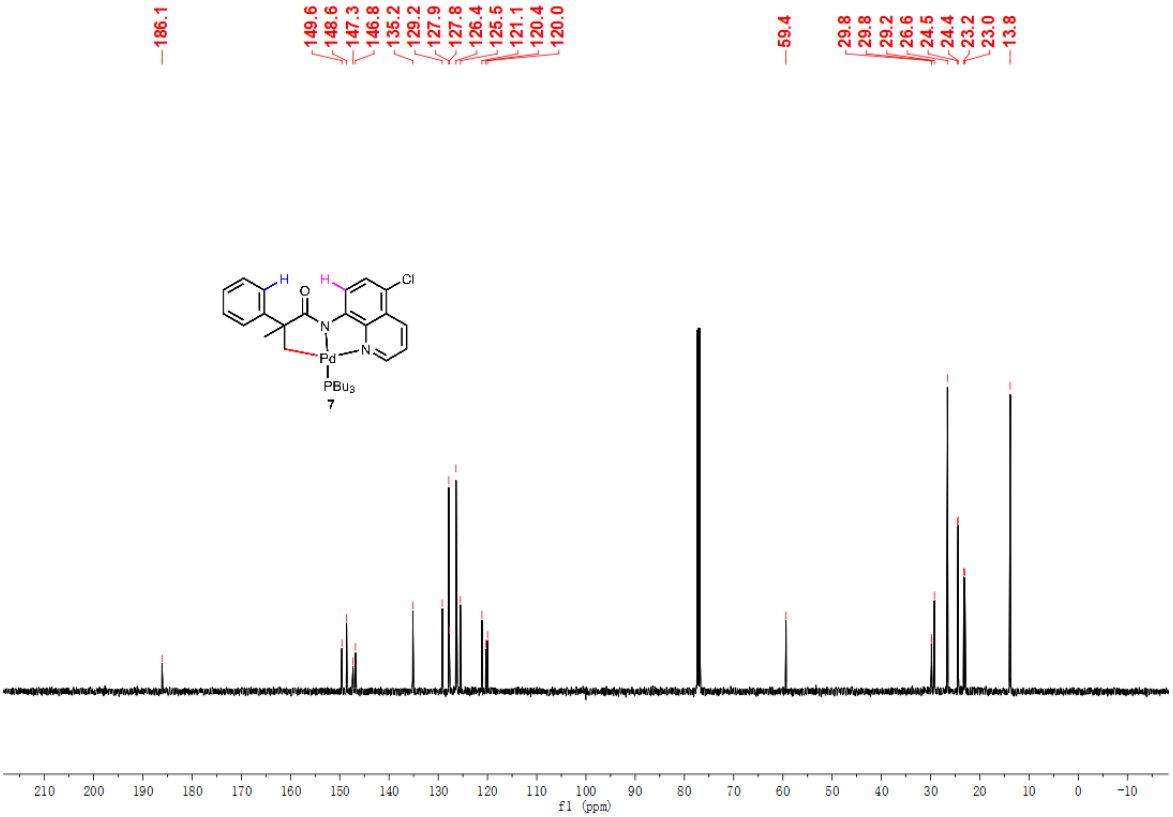
^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3h**



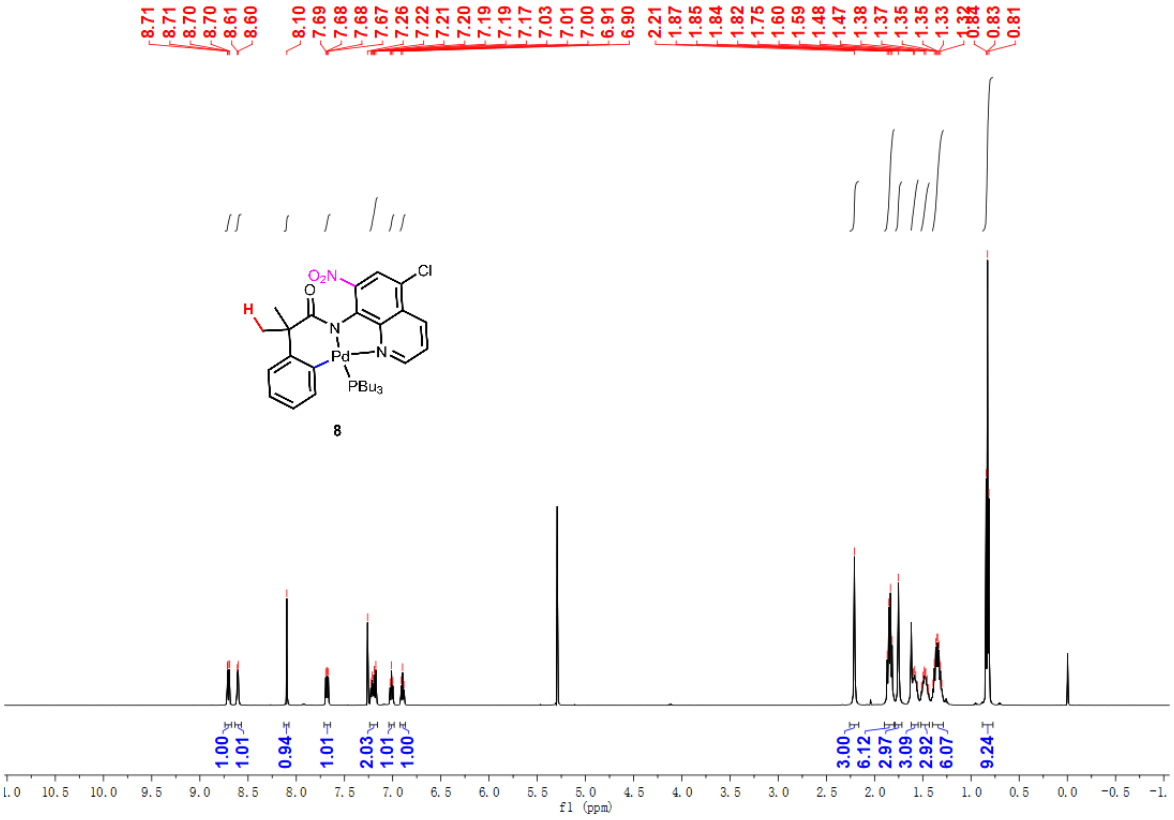
^{1}H NMR (500 MHz, $CDCl_3$) spectra of **7**



^{13}C NMR (126 MHz, $CDCl_3$) spectra of **7**



^{1}H NMR (500 MHz, $CDCl_3$) spectra of **8**



^{13}C NMR (126 MHz, $CDCl_3$) spectra of **8**