Copper-catalyzed Direct Amination of Quinoline *N*-Oxides *via* C-H Bond Activation under Mild Conditions

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Supporting Information

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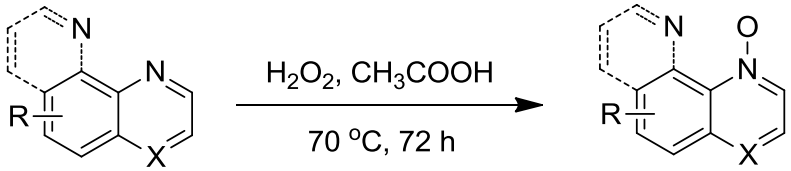
General Information

Chemicals were either purchased or synthesized by standard techniques and all reagents were used directly without further purification. Silica gel was purchased from Qing Dao Hai Yang Chemical Industry Co. ^{1}H and ^{13}C NMR spectra were measured on a 400 MHz Bruker spectrometer (^{1}H 400 MHz, ^{13}C 100 MHz), using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. HRMSESI spectra were obtained on Agilent 6450 spectrometer. The products listed below were determined by ^{1}H, ^{13}C NMR spectra.

General Procedure

1. Synthesis of N-oxides

All of the quinoline-N-oxides were prepared according to literature reported by Hirota and co-workers and slightly modified [1].

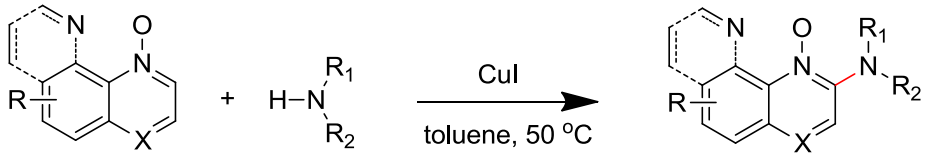


Hydrogen peroxide (30%, 1.4 mL) was added into the solution of the quinoline (10 mmol) in acetic acid (10 mL). The reaction mixture was stirred at 70 ^{o}C for 72 h. The solvent was evaporated under vacuum, and the residue was basified with aqueous solution of sodium carbonate until pH = 9. The resulting mixture was extracted with chloroform (3*20 mL). The organic phase were combined and dried over anhydrous sodium sulphate, filtered and evaporated under vacuum. The residue was purified by flash chromatography (silica gel, EtOAc: methanol 8:1). The product was identified by ^{1}H-NMR and MS spectra and compared to the literature.

2. General catalytic procedure

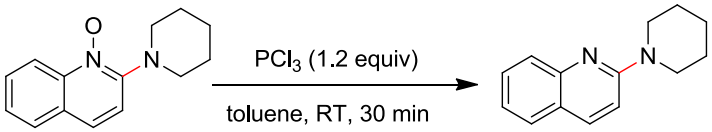
1.6 mmol amine in 1.5 mL toluene was added into the flask charged with 0.2 mmol *N*-oxide, 10 mol% CuI (3.9 mg). The mixture was stirred at 50 ^{o}C for 7 hours, then cooled down to room temperature, diluted with 10 mL CH_2Cl_2 and washed with 10

mL H_2O. The aqueous layer was extracted twice with CH_2Cl_2 (5 mL) and the combined organic phase was dried over Na_2SO_4. After evaporation of the solvents, the residue was purified by silica gel chromatography or thin layer chromatography (TLC) (elute: petroleum ether - EtOAc - Triethylamine).



X = C,N R_1, R_2 = Alkyl R = CH_3, OCH_3, Cl, Br, NO_2

3. General reduction procedure



3aa

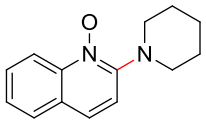
To a stirred mixture of **3aa** (45.6 mg, 0.2 mmol) in toluene (1.0 mL) was dropwise added PCl_3 (21 μL, 0.24 mmol). The reaction mixture was stirred for 30 min at room temperature. Saturated solution of $NaHCO_3$ (5 mL) was added and then stirred for additional 5 min. The aqueous layer was then washed with CH_2Cl_2 (20 mL x 3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give crude product, which was purified by flash column chromatography or thin layer chromatography (TLC) (petroleum ether: EtOAc (5:1) as elute).

References

1. a) Sasaki, K.; Tsurumori, A.; Hirota, T. *J. Chem. Soc., Perkin Trans.* **1998**, *1*, 3851; b) J. L. Wu, X. L. Cui, L. M. Chen, G. J. Jiang, Y. J. Wu, *J. Am. Chem. Soc.* **2009**, *131*, 13888.

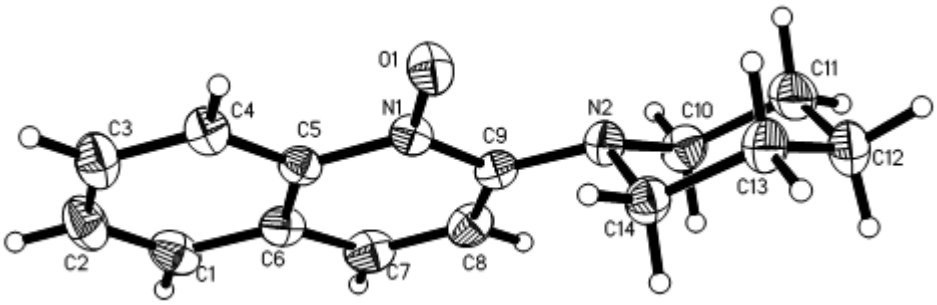
Characterization Data of Products

(3aa) 2-(piperidin-1-yl)quinoline *N*-oxide



Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.590(d, J = 8.4 Hz, 1H), 7.604(m, 2H), 7.533(d, J = 9.09 Hz, 1H), 7.336(m, 1H), 6.967(d, J = 9.16 Hz, 1H), 3.440(t, J = 4.30 Hz, 4H), 1.736(m, 4H), 1.600(m, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 151.071, 141.965, 130.179, 127.447, 126.605, 125.441, 125.149, 118.324, 114.003, 48.611, 25.622, 24.263. HRMS (ESI) Calcd. for $C_{14}H_{16}N_2O$: $[M+H]^+$, 229.1341, Found: m/z 229.1319.

Single crystal of **3aa** was developed successfully and characterized by X-ray diffraction.



Molecular structure of **3aa** (CCDC 973212)

The crystal structure was deposited at the Cambridge Crystallographic Data Centre. The data have been assigned the deposition numbers: CCDC 973212.

Table 1 Crystal data and structure refinement for 201311202a

Identification code	201311202a
Empirical formula	$C_{14}H_{16}N_2O$
Formula weight	228.29
Temperature/K	291.15
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	7.7780(4)
b/Å	11.7072(5)
c/Å	12.9517(6)
α/°	90.00

β/°	90.00
γ/°	90.00
Volume/Å^3	1179.37(10)
Z	4
ρ_{calc}mg/mm^3	1.286
m/mm^{-1}	0.651
F(000)	488.0
Crystal size/mm^3	0.22 × 0.2 × 0.2
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection	10.18 to 144.62 °
Index ranges	-6 ≤ h ≤ 9, -14 ≤ k ≤ 13, -15 ≤ l ≤ 13
Reflections collected	4676
Independent reflections	2271 [R_{int} = 0.0244, R_{sigma} = 0.0349]
Data/restraints/parameters	2271/0/155
Goodness-of-fit on F^2	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0370, wR_2 = 0.0946
Final R indexes [all data]	R_1 = 0.0443, wR_2 = 0.1017
Largest diff. peak/hole / e Å^{-3}	0.13/-0.14
Flack parameter	0.1(3)

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 201311202a. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	1277(2)	8206.6(10)	2674.9(9)	49.0(3)
N1	2047(2)	8309.0(12)	3562.8(10)	38.7(3)
N2	2867(2)	6397.2(12)	3451.4(11)	42.3(3)
C1	2798(3)	10623.0(19)	5461.3(15)	57.4(5)
C2	2054(3)	11516.7(18)	4959.2(18)	63.1(6)
C3	1291(3)	11365.6(17)	3991.3(17)	60.3(5)
C4	1297(3)	10309.5(16)	3531.6(14)	48.0(4)
C5	2060(2)	9383.5(14)	4039.8(13)	39.6(4)
C6	2823(2)	9516.1(17)	5020.3(14)	45.0(4)
C7	3530(3)	8550.7(19)	5511.4(14)	54.7(5)
C8	3527(3)	7527.2(19)	5013.8(16)	50.5(5)
C9	2829(2)	7400.7(14)	4015.8(14)	39.6(4)
C10	3201(3)	5342.3(16)	4031.7(16)	52.8(5)
C11	2846(3)	4309.9(17)	3355.3(19)	64.2(6)

C12	3882(3)	4345.7(17)	2369.7(19)	67.6(6)
C13	3567(3)	5457.4(18)	1802.3(16)	57.5(5)
C14	3904(3)	6469.8(15)	2498.1(14)	48.1(4)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 201311202a. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	66.2(9)	46.7(7)	34.0(6)	-1.0(5)	-12.5(6)	2.6(6)
N1	41.1(7)	43.5(8)	31.6(6)	0.3(6)	-0.6(6)	-2.3(7)
N2	47.9(8)	39.8(7)	39.2(7)	3.4(6)	2.5(7)	1.3(7)
C1	60.2(12)	68.1(13)	43.9(11)	-16.6(9)	5.1(10)	-15.8(11)
C2	80.0(15)	49.6(11)	59.6(12)	-15.2(10)	14.9(13)	-11.4(11)
C3	75.0(15)	44.8(10)	61.2(12)	0.6(9)	12.2(13)	-1.9(11)
C4	54.4(11)	45.8(10)	43.7(9)	0.3(8)	2.7(9)	-2.3(9)
C5	38.0(8)	45.2(9)	35.6(8)	-1.2(7)	5.6(8)	-4.7(8)
C6	42.1(9)	58.3(11)	34.7(8)	-7.0(8)	4.1(8)	-3.9(9)
C7	50.9(11)	77.5(13)	35.7(9)	-4.9(9)	-8.1(9)	0.3(11)
C8	49.1(10)	61.6(11)	40.7(9)	4.0(8)	-7.1(9)	9.0(9)
C9	36.9(8)	46.4(9)	35.5(8)	3.4(7)	1.3(8)	0.7(8)
C10	56.0(12)	48.8(10)	53.6(11)	12.0(9)	-1.6(9)	5.1(9)
C11	62.6(13)	42.4(10)	87.5(17)	12(1)	-9.8(13)	-3.2(10)
C12	70.9(15)	48.1(11)	83.9(15)	-17.8(11)	-6.2(13)	7.9(11)
C13	61.7(12)	56.5(12)	54.3(11)	-12.2(9)	5.5(10)	5.1(11)
C14	50.2(10)	47.1(9)	47(1)	-0.3(8)	8.3(9)	-0.3(9)

Table 4 Bond Lengths for 201311202a.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	N1	1.3019(17)	C4	C5	1.400(3)
N1	C5	1.401(2)	C5	C6	1.411(2)
N1	C9	1.358(2)	C6	C7	1.409(3)
N2	C9	1.384(2)	C7	C8	1.361(3)
N2	C10	1.469(2)	C8	C9	1.410(3)
N2	C14	1.477(2)	C10	C11	1.518(3)
C1	C2	1.361(3)	C11	C12	1.510(3)
C1	C6	1.416(3)	C12	C13	1.514(3)
C2	C3	1.398(3)	C13	C14	1.512(3)
C3	C4	1.372(3)			

Table 5 Bond Angles for 201311202a.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O1	N1	C5	118.38(13)	C5	C6	C1	117.25(18)
O1	N1	C9	121.02(14)	C7	C6	C1	123.89(18)
C9	N1	C5	120.60(14)	C7	C6	C5	118.85(17)
C9	N2	C10	116.56(14)	C8	C7	C6	119.48(17)
C9	N2	C14	113.84(14)	C7	C8	C9	121.83(18)
C10	N2	C14	112.32(15)	N1	C9	N2	116.48(15)
C2	C1	C6	121.12(19)	N1	C9	C8	119.10(17)
C1	C2	C3	120.76(19)	N2	C9	C8	124.42(17)
C4	C3	C2	120.1(2)	N2	C10	C11	110.00(16)
C3	C4	C5	119.67(18)	C12	C11	C10	111.64(18)
N1	C5	C6	119.91(16)	C11	C12	C13	110.35(18)
C4	C5	N1	119.00(15)	C14	C13	C12	110.88(17)
C4	C5	C6	121.09(16)	N2	C14	C13	111.02(16)

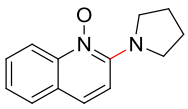
Table 6 Torsion Angles for 201311202a.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O1	N1	C5	C4	-2.0(2)	C5	C6	C7	C8	2.8(3)
O1	N1	C5	C6	177.55(16)	C6	C1	C2	C3	0.1(4)
O1	N1	C9	N2	4.5(2)	C6	C7	C8	C9	-0.2(3)
O1	N1	C9	C8	-174.98(17)	C7	C8	C9	N1	-4.0(3)
N1	C5	C6	C1	179.92(17)	C7	C8	C9	N2	176.61(19)
N1	C5	C6	C7	-1.3(3)	C9	N1	C5	C4	177.60(17)
N2	C10	C11	C12	56.1(2)	C9	N1	C5	C6	-2.8(2)
C1	C2	C3	C4	-0.5(4)	C9	N2	C10	C11	168.6(2)
C1	C6	C7	C8	-178.5(2)	C9	N2	C14	C13	-166.93(17)
C2	C1	C6	C5	0.4(3)	C10	N2	C9	N1	-161.43(16)
C2	C1	C6	C7	-178.2(2)	C10	N2	C9	C8	18.0(3)
C2	C3	C4	C5	0.4(3)	C10	N2	C14	C13	57.8(2)
C3	C4	C5	N1	179.68(19)	C10	C11	C12	C13	-54.8(3)
C3	C4	C5	C6	0.1(3)	C11	C12	C13	C14	54.1(3)
C4	C5	C6	C1	-0.5(3)	C12	C13	C14	N2	-55.5(2)
C4	C5	C6	C7	178.21(19)	C14	N2	C9	N1	65.3(2)
C5	N1	C9	N2	-175.10(15)	C14	N2	C9	C8	-115.2(2)
C5	N1	C9	C8	5.4(3)	C14	N2	C10	C11	-57.5(2)

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 201311202a.

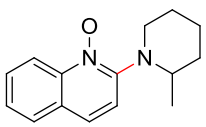
Atom	*x*	*y*	*z*	U(eq)
H1	3297	10741	6105	69
H2	2054	12236	5263	76
H3	780	11982	3658	72
H4	796	10209	2886	58
H7	3995	8612	6171	66
H8	3999	6893	5341	61
H10A	2470	5317	4638	63
H10B	4389	5330	4259	63
H11A	3127	3620	3734	77
H11B	1631	4285	3187	77
H12A	3559	3709	1932	81
H12B	5095	4275	2530	81
H13A	4315	5499	1204	69
H13B	2386	5481	1562	69
H14A	5114	6494	2676	58
H14B	3623	7169	2134	58

(3ab) 2-(pyrrolidin-1-yl)quinoline *N*-oxide



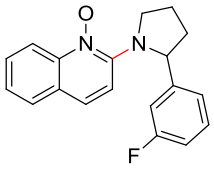
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.520(dd, J = 0.91 Hz, 1H), 7.571(m, 2H), 7.475(d, J = 9.12 Hz, 1H), 7.265(m, 1H), 6.820(d, J = 9.24 Hz, 1H), 3.820(m, 4H), 1.888(m, 4H). ^{13}C NMR (100MHz, $CDCl_3$): 148.719, 142.366, 130.950, 128.185, 127.821, 124.899, 124.266, 118.133, 112.803, 50.920, 25.823. HRMS (ESI) Calcd. for $C_{13}H_{14}N_2O$: $[M+H]^+$, 215.1184, Found: m/z 215.1184.

(3ac) 2-(2-methylpiperidin-1-yl)quinoline *N*-oxide



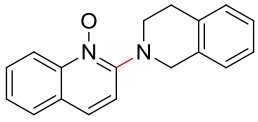
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.671(d, J = 8.81Hz, 1H), 7.696(m, 2H), 7.609(d, J = 9.08 Hz, 1H), 7.451(m, 1H), 7.053(d, J = 9.08 Hz, 1H), 4.805(m, 1H), 3.431(m, 2H), 2.031(m, 1H), 1.786(m, 3H), 1.656(m, 1H), 1.588(m, 1H), 1.171(d, J = 6.81 Hz, 3H). ^{13}C NMR (100MHz, $CDCl_3$): 150.167, 141.432, 129.466, 126.587, 125.569, 124.810, 124.561, 117.799, 114.939, 47.581, 43.417, 29.910, 25.134, 18.506, 14.932. HRMS (ESI) Calcd. for $C_{15}H_{18}N_2O$: $[M+H]^+$, 243.1497, Found: m/z 243.1496.

(3ad) 2-(2-(3-fluorophenyl)pyrrolidin-1-yl)quinoline *N*-oxide



Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.593(d, J = 8.76 Hz, 1H), 7.657(t, J = 7.89 Hz, 1H), 7.612(d, J = 7.69 Hz, 1H), 7.313(d, J = 9.20 Hz, 1H), 7.368(t, J = 7.67 Hz, 1H), 7.184(m, 1H), 7.097(d, J = 7.67 Hz, 1H), 7.016(d, J = 9.86 Hz, 1H), 6.828(m, 2H), 5.284(t, J = 7.45 Hz, 1H), 4.723(m, 1H), 3.955(m, 1H), 2.495(m, 1H), 2.145(m, 1H), 1.944(m, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 161.864-164.314(dd, J = 247.10 Hz), 148.111, 145.658-145.724(dd, J = 6.57 Hz), 142.090, 130.602, 130.328-130.410(dd, J = 8.34 Hz), 127.520, 127.096, 125.097, 124.458, 121.529-121.557(dd, J = 2.89 Hz), 118.137, 114.093-114.304(dd, J = 21.13 Hz), 113.483, 112.834-113.052(dd, J = 21.87 Hz), 640221, 64.204, 52.508, 36.578, 25.075. HRMS (ESI) Calcd. for $C_{19}H_{17}N_2OF$: $[M+H]^+$, 309.1403, Found: m/z 309.1405.

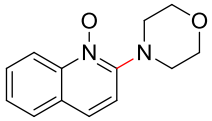
(3ae) 2-(3,4-dihydroisoquinolin-2(1H)-yl)quinoline *N*-oxide



Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.679(d, J = 9.15 Hz, 1H), 7.673(m, 2H), 7.594(d, J = 9.11 Hz, 1H), 7.425(m, 1H), 7.124(m, 5H), 4.737(s, 2H), 4.003(t, J = 5.87 Hz, 2H), 3.055(t, J = 5.79 Hz, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 150.353, 142.125, 134.438, 133.410, 130.597, 128.979, 127.633, 127.006, 126.524,

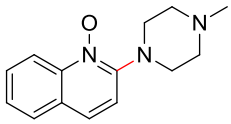
126.142, 126.003, 125.812, 125.383, 118.514, 113.957. HRMS (ESI) Calcd. for $C_{18}H_{16}N_2O$: $[M+H]^+$, 277.1341, Found: m/z 277.1341.

(3af) 4-(quinolin-*N*-oxide-2-yl)morpholine



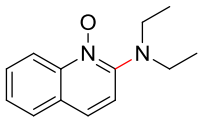
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.600(d, J = 8.75 Hz, 1H), 7.660(m, 3H), 7.425(t, J = 7.18 Hz, 1H), 6.985(d, J = 9.05 Hz, 1H), 3.909(t, J = 4.49 Hz, 4H), 3.553(t, J = 4.64 Hz, 4H). ^{13}C NMR (100MHz, $CDCl_3$): 150.718, 142.551, 131.148, 128.155, 127.496, 126.595, 126.049, 118.983, 113.685, 67.143, 48.251. HRMS (ESI) Calcd. for $C_{13}H_{14}N_2O_2$: $[M+H]^+$, 231.1134, Found: m/z 231.1133.

(3ag) 2-(4-methylpiperazin-1-yl)quinoline *N*-oxide



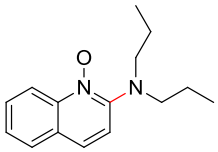
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.621(d, J = 8.79 Hz, 1H), 7.690(m, 2H), 7.626(d, J = 8.79 Hz, 1H), 7.435(t, J = 7.81 Hz, 1H), 7.028(d, J = 9.12 Hz, 1H), 3.610(s, 4H), 2.666(t, J = 4.56 Hz, 4H), 2.340(s, 3H). ^{13}C NMR (100MHz, $CDCl_3$): 150.563, 142.067, 130.634, 127.619, 127.071, 125.948, 125.459, 118.511, 113.686, 54.656, 47.252, 46.014. HRMS (ESI) Calcd. for $C_{14}H_{17}N_3O$: $[M+H]^+$, 244.1450, Found: m/z 244.1447.

(3ah) 2-(N,N-diethylamino)quinolin *N*-oxide



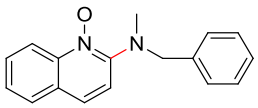
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.636(d, J = 8.67 Hz, 1H), 7.660(m, 2H), 7.574(d, J = 9.18 Hz, 1H), 7.399(t, J = 7.70 Hz, 1H), 7.035(d, J = 9.18 Hz, 1H), 3.693(q, J = 7.04 Hz, 4H), 1.215(t, J = 7.04 Hz, 6H). ^{13}C NMR (100MHz, $CDCl_3$): 149.985, 142.322, 130.336, 127.409, 126.515, 125.403, 124.945, 118.457, 114.902, 44.118, 13.529. HRMS (ESI) Calcd. for $C_{13}H_{16}N_2O$: $[M+H]^+$, 217.1341, Found: m/z 217.1335.

(3ai) 2-(N,N-dipropylamino)quinolin *N*-oxide



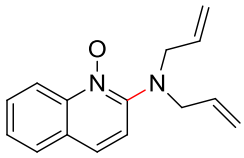
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.619(d, J = 8.74Hz, 1H), 7.634(m, 2H), 7.548(d, J = 9.18 Hz, 1H), 7.378(m, 1H), 7.021(d, J = 9.11Hz, 1H), 3.534(t, J = 7.55 Hz, 4H), 1.592(m, 4H), 0.863(t, J = 7.44 Hz, 6H). ^{13}C NMR (100MHz, $CDCl_3$): 150.497, 142.775, 130.794, 127.878, 127.046, 125.884, 125.442, 118.929, 115.769, 52.754, 22.058, 11.787. HRMS (ESI) Calcd. for $C_{15}H_{20}N_2O$: $[M+H]^+$, 245.1654, Found: m/z 245.1653.

(3aj) 2-(N-benzyl-N-methylamino)quinolin *N*-oxide



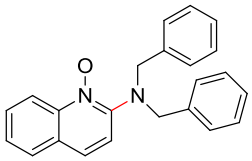
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.711(d, J = 8.80Hz, 1H), 7.684(t, J = 6.80 Hz, 2H), 7.569(d, J = 9.20 Hz, 1H), 7.425(m, 1H), 7.255(m, 5H), 6.967(d, J = 9.2 Hz, 1H), 4.952(s, 2H), 2.992(s, 3H). ^{13}C NMR (100MHz, $CDCl_3$): 150.613, 142.151, 137.683, 130.507, 128.324, 127.611, 127.134, 126.743, 125.710, 125.221, 118.571, 114.450, 54.648, 38.389. HRMS (ESI) Calcd. for $C_{17}H_{16}N_2O$: $[M+H]^+$, 265.1341, Found: m/z 265.1341.

(3ak) 2-(N,N-diallylamino)quinolin *N*-oxide



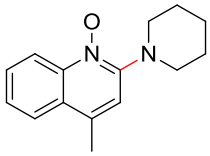
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.661(t, 1H), 7.686(m, 2H), 7.583(d, J = 9.12 Hz, 1H), 7.442(m, 1H), 7.067(d, J = 9.08Hz, 1H), 5.970(m, 2H), 5.225(m, 4H), 4.216(d, J = 5.89 Hz, 4H). ^{13}C NMR (100MHz, $CDCl_3$): 149.739, 142.187, 134.363, 130.444, 127.473, 126.497, 125.655, 125.146, 118.553, 117.859, 115.187, 51.877. HRMS (ESI) Calcd. for $C_{15}H_{16}N_2O$: $[M+H]^+$, 241.1341, Found: m/z 241.1341.

(3al) 2-(N,N-dibenzylamino)quinolin *N*-oxide



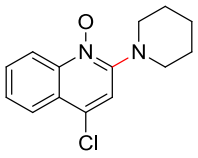
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.800(d, J = 8.82 Hz, 1H), 7.777(m, 2H), 7.537(m, 2H), 7.404(d, J = 7.31 Hz, 4H), 7.306(m, 6H), 7.016(d, J = 9.10 Hz, 1H), 4.839(s, 4H). ^{13}C NMR (100MHz, $CDCl_3$): 149.880, 142.251, 137.386, 130.486, 128.458, 128.153, 127.598, 127.245, 126.290, 126.009, 125.486, 118.758, 115.912, 52.938. HRMS (ESI) Calcd. for $C_{23}H_{20}N_2O$: $[M+H]^+$, 341.1654, Found: m/z 341.1655.

(3ba) 4-methyl-2-(piperidin-1-yl)quinoline *N*-oxide



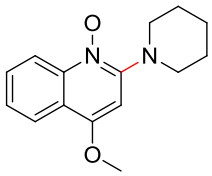
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.677(d, J = 8.71 Hz, 1H), 7.785(d, J = 8.15 Hz, 1H), 7.662(t, J = 7.27 Hz, 1H), 7.434(t, J = 7.23 Hz, 1H) 6.854(s, 1H), 3.503(t, J = 4.34 Hz, 4H), 2.570(s, 3H), 1.789(d, J = 4.78 Hz, 4H), 1.651(d, J = 4.78 Hz, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 150.874, 142.009, 135.417, 130.485, 125.671, 125.287, 124.490, 119.357, 114.813, 49.199, 26.110, 24.780, 18.892. HRMS (ESI) Calcd. for $C_{15}H_{18}N_2O$: $[M+H]^+$, 243.1497, Found: m/z 243.1497.

(3ca) 4-chloro-2-(piperidin-1-yl)quinoline *N*-oxide



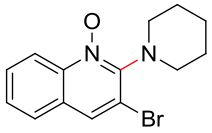
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.682(d, J = 8.73Hz, 1H), 8.053(t, J = 8.3 Hz, 1H), 7.744(m, 1H), 7.753(m, 1H), 7.746(s, 1H), 3.517(t, J = 5.15 Hz, 4H), 1.818(m, 4H), 1.689(m, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 150.804, 142.513, 131.295, 130.901, 126.350, 124.658, 123.045, 119.034, 114.196, 48.873, 25.681, 24.316. HRMS (ESI) Calcd. for $C_{14}H_{15}N_2OCl$: $[M+H]^+$, 263.0951, Found: m/z 263.0949.

(3da) 4-methoxy-2-(piperidin-1-yl)quinoline *N*-oxide



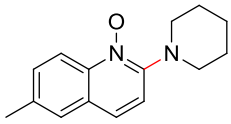
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.532(d, J = 8.70 Hz, 1H), 7.958(d, J = 8.27 Hz, 1H), 7.615(m, 1H), 7.330(m, 1H), 6.240(s, 1H), 3.917(s, 3H), 3.476(t, J = 5.29 Hz, 4H), 1.734(m, 4H), 1.595(m, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 155.330, 151.877, 141.606, 131.180, 124.925, 122.052, 118.442, 118.359, 92.618, 55.893, 49.073, 25.779, 24.383. HRMS (ESI) Calcd. for $C_{15}H_{18}N_2O_2$: $[M+H]^+$, 259.1447, Found: m/z 259.1446.

(3ea) 3-bromo-2-(piperidin-1-yl)quinoline *N*-oxide



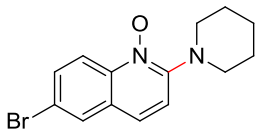
Pale red solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.558(d, J = 8.84 Hz, 1H), 7.905(s, 1H), 7.655(m, 2H), 7.479(m, 1H), 3.413(s, 4H), 1.748(m, 4H), 1.676(s, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 149.603, 141.820, 130.181, 129.855, 127.611, 126.632 126.583, 119.211, 117.140, 49.800, 26.133, 24.103. HRMS (ESI) Calcd. for $C_{14}H_{15}N_2OBr$: $[M+H]^+$, 307.0446, Found: m/z 307.0442.

(3fa) 6-methyl-2-(piperidin-1-yl)quinoline *N*-oxide



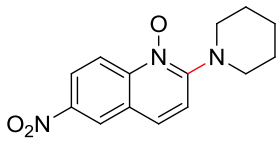
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.516(d, J = 8.85 Hz, 1H), 7.469(m, 3H), 6.974(d, J = 9.03 Hz, 1H), 3.452(t, J = 5.14 Hz, 4H), 2.431(s, 3H), 1.779(m, 4H), 1.645(m, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 150.751, 140.600, 135.485, 132.414, 126.561, 126.217, 125.428, 118.420, 114.033, 48.816, 25.743, 24.421, 21.007. HRMS (ESI) Calcd. for $C_{15}H_{18}N_2O$: $[M+H]^+$, 243.1497, Found: m/z 243.1497.

(3ga) 6-bromo-2-(piperidin-1-yl)quinoline *N*-oxide



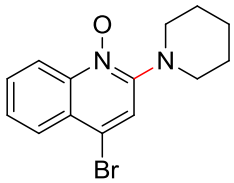
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.528(d, J = 9.34 Hz, 1H), 7.862(d, J = 2.01 Hz, 1H), 7.736(dd, J_1 = 2.06 Hz, J_2 = 9.30 Hz, 1H), 7.568(d, J = 9.10 Hz, 1H), 7.067(d, J = 9.13 Hz, 1H), 3.528(t, J = 5.28 Hz, 4H), 4.082(m, 4H), 2.019(m, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 151.237, 141.011, 133.560, 129.456, 126.359, 125.492, 120.631, 119.376, 115.317, 48.808, 25.756, 24.369. HRMS (ESI) Calcd. for $C_{14}H_{15}N_2OBr$: $[M+H]^+$, 307.0446, Found: m/z 307.0443.

(3ha) 6-nitro-2-(piperidin-1-yl)quinoline *N*-oxide



Pale red solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.724(d, J = 9.50 Hz, 1H), 8.626(d, J = 2.04 Hz, 1H), 8.391(m, 1H), 7.743(d, J = 9.23 Hz, 1H), 7.191(d, J = 9.23 Hz, 1H), 3.651(t, J = 4.08Hz, 4H), 1.807(m, 4H), 1.722(t, J = 5.42Hz, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 152.835, 144.629, 144.409, 127.626, 124.165, 123.871, 123.751, 120.286, 116.387, 48.976, 25.833, 24.269. HRMS (ESI) Calcd. for $C_{15}H_{18}N_2O$: $[M+H]^+$, 274.1192, Found: m/z 274.1188.

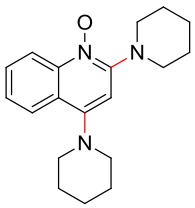
(3ia) 4-bromo-2-(piperidin-1-yl)quinoline *N*-oxide



Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.669(d, J = 8.72 Hz, 1H), 8.010(d, J = 8.23 Hz, 1H), 7.732(m, 1H), 7.529(t, J = 7.73 Hz, 1H), 7.344(s, 1H), 3.513(t, J = 5.19 Hz, 4H), 1.808(q, J = 5.59 Hz, 4H), 1.694(m, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 151.397, 143.020, 131.769, 127.801, 127.093, 124.824, 121.637,

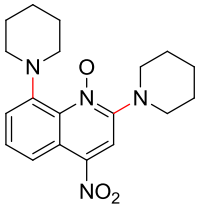
119.500, 118.253, 49.373, 26.176, 24.807. HRMS (ESI) Calcd. for $C_{14}H_{15}N_2OBr$: $[M+H]^+$, 307.0446, Found: m/z 307.0442.

(3ja) 2,4-di(piperidin-1-yl)quinoline *N*-oxide



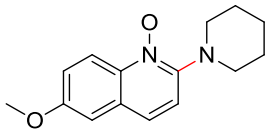
Pale yellow solid; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 8.676(d, J = 8.74 Hz, 1H), 7.922(dd, J_1 = 0.71Hz, J_2 = 8.26 Hz, 1H), 7.665(m, 1H), 7.410(m, 1H), 6.450(s, 1H), 3.536(t, J = 5.12 Hz, 4H), 3.105(t, J = 4.54 Hz, 4H), 1.826(m, 8H), 1.693(t, J = 6.43 Hz, 4H). ^{13}C NMR (100MHz, $CDCl_3$): 151.995, 151.390, 142.751, 130.751, 125.014, 124.274, 121.493, 119.608, 101.986, 54.397, 49.560, 26.524, 26.267, 24.944, 24.770. HRMS (ESI) Calcd. for $C_{19}H2_5N_3O$: $[M+H]^+$, 312.2076, Found: m/z 312.2073.

(3ka) 4-nitro-2,8-di(piperidin-1-yl)quinoline *N*-oxide



Pale red solid; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 8.517(d, J = 9.76 Hz, 1H), 1.943(d, J = 2.58 Hz, 1H), 7.922(s, 1H), 7.495(dd, J_1 = 2.79 Hz, J_2 = 9.82 Hz, 1H), 3.384(m, 8H), 1.835(m, 4H), 1.709(m, 8H). ^{13}C NMR (100MHz, $CDCl_3$): 151.571, 148.459, 138.981, 138.000, 123.190, 120.291, 119.697, 112.174, 10.080, 49.537, 49.391, 25.723, 25.502, 24.398, 34.236. HRMS (ESI) Calcd. for $C_{19}H_{24}N_4O_3$: $[M+H]^+$, 357.1927, Found: m/z 357.1924.

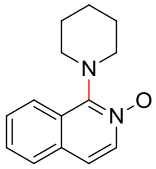
(3la) 6-methoxy-2-(piperidin-1-yl)quinoline *N*-oxide



Pale yellow solid; ^1H NMR (400 MHz, $CDCl_3$) ppm: δ 8.570(d, J = 9.53 Hz, 1H), 7.515(d, J = 9.02 Hz, 1H), 7.312(dd, J_1 = 2.64 Hz, J_2 = 9.43 Hz, 1H), 7.012(d, J = 8.72

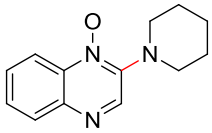
Hz, 2H), 3.875(s, 3H), 3.440(t, J = 4.97 Hz, 4H), 1.806(m, 4H), 1.666(m, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 157.462, 150.204, 127.531, 126.558, 125.704, 122.061, 120.457, 114.677, 106.134, 55.596, 49.003, 25.850, 24.534. HRMS (ESI) Calcd. for $C_{15}H_{18}N_2O_2$: $[M+H]^+$, 259.1447, Found: m/z 259.1446.

(3oa) 1-(piperidin-1-yl)isoquinoline *N*-oxide



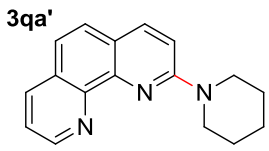
Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.146(d, J = 8.28 Hz, 1H), 7.995(d, J = 7.19 Hz, 1H), 7.692(d, J = 7.66 Hz, 1H), 7.565(m, 1H), 7.510(m, 1H), 7.348(d, J = 7.15 Hz, 1H), 3.320(m, 4H), 1.775(m, 6H). ^{13}C NMR (100MHz, $CDCl_3$): 150.493, 137.589, 130.699, 128.447, 128.277, 127.696, 126.790, 124.247, 119.750, 49.464, 26.422, 24.120. HRMS (ESI) Calcd. for $C_{14}H_{16}N_2O$: $[M+H]^+$, 229.1341, Found: m/z 229.1339.

(3pa) 2-(piperidin-1-yl)quinoxaline *N*-oxide



Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 8.510(s, 1H), 8.484(dd, J_1 = 1.00 Hz, J_2 = 8.44 Hz, 1H). 7.971(dd, J_1 = 1.00 Hz, J_2 = 8.22 Hz, 1H), 7.666(m, 1H), 7.588(m, 1H), 3.534(t, J = 5.15 Hz, 4H), 1.802(m, 4H), 1.700(m, 2H). ^{13}C NMR (100MHz, $CDCl_3$): 145.843, 140.346, 139.890, 137.261, 130.448, 129.570, 128.255, 117.908, 48.656, 25.827, 24.385. HRMS (ESI) Calcd. for $C_{13}H_{15}N_3O$: $[M+H]^+$, 230.1293, Found: m/z 230.1288.

(3qa) 2-(piperidin-1-yl)-1,10-phenanthroline *N*-oxide

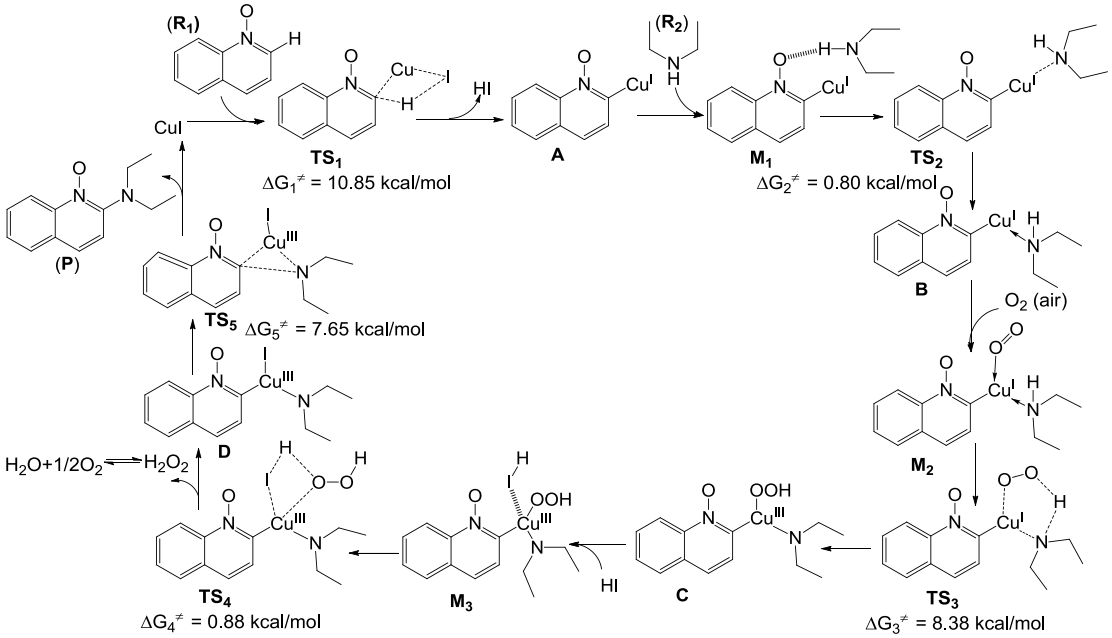


(**3qa** was readily reduced to **3qa'** under air)

Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: δ 9.100(dd, J_1 = 1.52 Hz, J_2 =4.21 Hz, 1H), 8.156(dd, J_1 = 1.52 Hz, J_2 = 8.05 Hz, 1H), 7.952(d, J = 9.13 Hz, 1H), 7.612(d, J = 8.59 Hz, 1H), 7.515(m, 1H), 7.460(d, J = 8.50 Hz,1H), 7.125(d, J = 8.95 Hz, 1H), 3.886(m, 4H), 1.736(m, 6H). ^{13}C NMR (100MHz, $CDCl_3$): 158.55, 149.56, 145.86, 145.48, 137.73, 136.33, 129.70, 126.71, 122.31, 121.99, 121.34, 110.13, 46.47, 26.21, 25.05. HRMS (ESI) Calcd. for $C_{17}H_{17}N_3O$: $[M+H]^+$, 280.1450, Found: m/z 280.1448.

General Computational Calculation Details

DFT calculations were performed using the B3LYP method[1] with the Gaussian09 Program.[2] The 6-31+g* basis set was used for the C, H, O and N, the 6-311g* basis set was used for the Cu and the SDD basis set was used for the I. Firstly, the optimizations at the B3LYP/(6-31+g*, 6-311G*, and SDD) level have been carried out in toluene solvent using the polarizable continuum model[3] (IEF-PCM). Then, frequency calculations at the same level of theory have been performed to identify all of the stationary points as minima (zero imaginary frequencies) or transition states (only one imaginary frequency) and to provide free energies.



Computational Reaction Mechanism

Geometrical Coordinates of the Listed Complexes

CuI

Thermal correction to Gibbs Free Energy = -0.024918 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -1651.908715

Cu	0.00000000	0.00000000	-1.58747400
I	0.00000000	0.00000000	0.86861800

R_1

Thermal correction to Gibbs Free Energy = 0.107790 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -477.011941

C	2.29562800	0.06334100	0.00000000
C	2.02535200	1.44011200	0.00000100
C	-0.03038700	-0.43715200	-0.00000300
C	0.72638200	1.89964800	-0.00000200
H	2.86766000	2.12444100	0.00000400
C	-0.33335100	0.95555400	0.00000000
C	-1.05327000	-1.40753400	-0.00000600
H	0.50391700	2.96241500	0.00000400
C	-1.70466000	1.33235200	0.00000100
C	-2.37256100	-0.99873400	0.00000100
H	-0.77337400	-2.45356800	-0.00001400
C	-2.70106200	0.37903300	0.00000300
H	-1.95151000	2.39097700	0.00000300
H	-3.16570100	-1.74109800	0.00000300
H	-3.74401900	0.68355000	0.00000800
O	1.58500700	-2.12109600	0.00001100
N	1.31087500	-0.85765700	-0.00001100
H	3.29441700	-0.35407000	0.00000500

R_2

Thermal correction to Gibbs Free Energy = 0.119549 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -213.682300

N	-0.01769400	-0.87959500	-0.44372200
H	0.00330500	-1.88337700	-0.59846100
C	-1.33300900	-0.52638400	0.10527000
H	-2.07945400	-1.08932900	-0.46851100
H	-1.43197400	-0.84566500	1.16149500
C	-1.65558400	0.96606700	0.00841500
H	-1.55830100	1.31666200	-1.02539700
H	-2.68343900	1.15092400	0.34456400
H	-0.99106400	1.56831000	0.63800700
C	1.14672200	-0.49045400	0.37040400
H	1.86683700	-1.31842800	0.35212700

H	0.85597200	-0.35547700	1.42776500
C	1.84946300	0.77345300	-0.13768300
H	1.18089900	1.64041100	-0.12867200
H	2.71826000	1.00773900	0.49172200
H	2.19725700	0.62930000	-1.16701800

O_2

Thermal correction to Gibbs Free Energy = -0.015227 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -150.281686

O	0.00000000	0.00000000	0.60743800
O	0.00000000	0.00000000	-0.60743800

A

Thermal correction to Gibbs Free Energy = 0.092675 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -2116.858869

Cu	2.92196000	-0.14927000	0.00001200
C	1.20055700	0.53681200	-0.00001100
C	0.64418700	1.83672100	0.00001100
C	-1.03504800	-0.37232500	-0.00004600
C	-0.71782300	2.05424500	-0.00001400
H	1.32864000	2.67987500	0.00003900
C	-1.59378800	0.93880100	0.00000500
C	-1.86758900	-1.51345800	-0.00002000
H	-1.12813600	3.06094300	-0.00001800
C	-3.01049600	1.06020400	0.00000400
C	-3.23983200	-1.35318100	0.00002400
H	-1.40089800	-2.49061200	-0.00003300
C	-3.81730500	-0.05886900	0.00002800
H	-3.44552500	2.05673300	0.00001600
H	-3.88336700	-2.22890200	0.00003400
H	-4.89867000	0.04908900	0.00004900
O	0.85525900	-1.73910900	0.00002600
N	0.35312300	-0.52273500	-0.00007600

B

Thermal correction to Gibbs Free Energy = 0.233870 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -2330.590940

C	0.49197300	-0.74290400	-0.22655800
C	1.22034700	-1.96033300	-0.16764400
C	2.60588500	0.42432300	0.00542300
C	2.59190900	-2.01870600	-0.03689700
H	0.65145200	-2.88391700	-0.23929400
C	3.32172900	-0.80661100	0.05764100
C	3.28920000	1.65775100	0.09756800

H	3.11869200	-2.96931600	0.00089000
C	4.73542800	-0.75327400	0.20145600
C	4.66419100	1.66870600	0.23622600
H	2.70681600	2.56954400	0.05509800
C	5.39497800	0.45566000	0.28849900
H	5.28819300	-1.68911100	0.24133000
H	5.19036200	2.61719100	0.30654000
H	6.47606700	0.48042800	0.39795400
O	0.58355900	1.56053000	-0.17540600
N	1.21416800	0.40639200	-0.13297400
Cu	-1.35137900	-0.36042100	-0.36849400
N	-3.23593100	0.15357600	-0.48027400
H	-3.39151300	0.41927000	-1.45634500
C	-3.44223000	1.39517500	0.33246400
H	-2.66103200	2.09557800	0.02347200
H	-3.24071400	1.14820400	1.37839700
C	-4.81723200	2.04989900	0.18553300
H	-4.82129500	3.00398600	0.72474600
H	-5.04805800	2.26226400	-0.86637400
H	-5.62496400	1.43602100	0.59767700
C	-4.19490400	-0.95620800	-0.19119300
H	-4.02158200	-1.71754700	-0.95854900
H	-5.22735000	-0.60373800	-0.31146400
C	-4.00238600	-1.56731500	1.19342500
H	-4.21672300	-0.85329600	1.99577600
H	-4.68291500	-2.41731800	1.31630600
H	-2.97491100	-1.92702100	1.32049100

C

Thermal correction to Gibbs Free Energy = 0.236962 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -2480.885098

C	-0.76284000	1.26456800	-0.00512500
C	-1.72757900	2.29054100	0.01411200
C	-2.50264000	-0.42095400	-0.04915500
C	-3.07203500	1.96706200	-0.00130400
H	-1.39860000	3.32406300	0.03944000
C	-3.49206400	0.60782900	-0.03273000
C	-2.84591300	-1.78850600	-0.07895900
H	-3.82828200	2.74810300	0.01124300
C	-4.85465200	0.20536000	-0.04917000
C	-4.18444200	-2.13068600	-0.09214400
H	-2.05991600	-2.53464800	-0.09080600
C	-5.19177500	-1.13264600	-0.07762500
H	-5.62605600	0.97083200	-0.03863200

H	-4.46991300	-3.17850000	-0.11506800
H	-6.23685100	-1.42819400	-0.08946000
O	-0.13591700	-0.86466000	-0.03339200
N	-1.19848100	0.00652600	-0.03188700
Cu	1.09889300	0.63594900	-0.00550700
N	2.78752200	-0.26129200	-0.07835400
O	1.93468400	2.26839800	-0.08695100
H	3.52845400	1.27428100	-0.14315500
C	2.79201300	-1.24775200	-1.16375800
H	2.42072100	-0.74475300	-2.06504600
H	2.10647400	-2.08609500	-0.96180900
C	4.19663200	-1.79965200	-1.46508300
H	4.15343200	-2.44135300	-2.35301900
H	4.89997500	-0.98282400	-1.66354000
H	4.58982400	-2.39992100	-0.63756900
C	3.17309700	-0.80201400	1.23760500
H	3.07397000	0.01885900	1.95900000
H	4.25089600	-1.02774900	1.19724500
C	2.42722400	-2.04225300	1.75589900
H	2.61722100	-2.92696800	1.13779500
H	2.77038700	-2.27031000	2.77245700
H	1.34490400	-1.87886000	1.78607100
O	3.34398400	2.23119800	0.14920200

D

Thermal correction to Gibbs Free Energy = 0.218234 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -2341.397783

C	-0.47949600	0.00933300	-0.53816400
C	-0.99072700	-0.27850500	-1.81549400
C	-2.64632300	-0.23818900	0.42833900
C	-2.33191200	-0.55327400	-1.98259800
H	-0.30900800	-0.30172200	-2.65955200
C	-3.19046500	-0.54176600	-0.85178300
C	-3.45558800	-0.21707800	1.58237400
H	-2.73328900	-0.79196100	-2.96351900
C	-4.58160500	-0.82318300	-0.92970500
C	-4.80372900	-0.49763100	1.46344300
H	-2.99517600	0.01346700	2.53505400
C	-5.37123500	-0.80093100	0.20169600
H	-5.01068400	-1.05880600	-1.90019400
H	-5.43384800	-0.48879500	2.34840700
H	-6.43268000	-1.02043100	0.12790800
O	-0.77104200	0.34562400	1.70512300
N	-1.27769200	0.04722200	0.53992500

Cu	1.31147500	0.38003300	-0.05653400
N	1.46376900	2.16541900	-0.12459200
I	2.29848300	-1.96820300	0.02293200
C	1.04284600	3.00405200	0.99811800
H	-0.05501000	3.01721300	1.06709200
H	1.35321100	4.03625100	0.77460100
C	1.64253400	2.54789300	2.32658000
H	1.36626900	3.25361500	3.11881800
H	1.26302100	1.56219400	2.61087800
H	2.73600900	2.50902300	2.26382300
C	1.42578000	2.84446100	-1.41933100
H	1.74643700	2.13513000	-2.18970000
H	2.20064000	3.62842100	-1.37583000
C	0.08453600	3.48143900	-1.81439800
H	-0.21913500	4.26859800	-1.11733800
H	0.17634800	3.93221500	-2.80923200
H	-0.70737700	2.72614500	-1.84992000

HI

Thermal correction to Gibbs Free Energy = -0.015220 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -12.024000

I	0.00000000	0.00000000	0.03035500
H	0.00000000	0.00000000	-1.60880700

H_2O

Thermal correction to Gibbs Free Energy = 0.003396 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -76.423278

O	0.00000000	0.00000000	0.11783900
H	0.00000000	0.77011700	-0.47135700
H	0.00000000	-0.77011700	-0.47135700

P

Thermal correction to Gibbs Free Energy = 0.228883 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -689.491408

C	-0.72006100	-0.33075100	-0.06319900
C	-0.26762000	-1.68310200	-0.05877700
C	1.58615700	0.37220000	-0.01125300
C	1.06353400	-2.00775600	-0.04289800
H	-1.01089100	-2.46930100	-0.04316100
C	2.03709000	-0.97573700	-0.00327200
C	2.51281000	1.43648300	0.01779800
H	1.37659500	-3.04812700	-0.03414600
C	3.43344500	-1.22102400	0.04498000
C	3.86697200	1.15889200	0.06552600

H	2.13507600	2.45075400	0.00098300
C	4.33527100	-0.17586900	0.07955900
H	3.77922100	-2.25200100	0.05346000
H	4.57956700	1.97899900	0.09271100
H	5.40259800	-0.37569100	0.11652800
O	-0.14085900	1.92007700	-0.20687600
N	0.21848500	0.66850500	-0.09264200
N	-2.05238000	0.00479600	-0.11323100
C	-2.61067500	1.11579600	0.68650800
H	-3.31850600	0.68287200	1.40759300
H	-1.80165700	1.56682500	1.25681800
C	-3.30427700	2.19175400	-0.14931800
H	-3.71042600	2.96526700	0.51439800
H	-2.58485600	2.65518300	-0.82958800
H	-4.14031500	1.79006500	-0.73408000
C	-3.02503900	-0.96004900	-0.63984700
H	-3.79940700	-0.38219600	-1.15760100
H	-2.52948100	-1.55600600	-1.41199900
C	-3.70094200	-1.87677400	0.39337600
H	-4.39436600	-2.55345400	-0.12053600
H	-2.97785300	-2.48710400	0.94524300
H	-4.28116600	-1.30418700	1.12440100

M_1

Thermal correction to Gibbs Free Energy = 0.232090 (Hartree/Particle)

Sum of electronic and thermal Free Energies = -2330.549829

C	0.47172400	-1.28848100	0.16312800
C	1.40441300	-2.02705600	0.93305200
C	2.22197800	0.32824800	-0.27657200
C	2.71402300	-1.62968200	1.10279300
H	1.05659700	-2.94658400	1.39570400
C	3.15325200	-0.42652100	0.49381200
C	2.61017300	1.53395200	-0.90259100
H	3.41068100	-2.21688400	1.69601600
C	4.48109000	0.06882200	0.60920700
C	3.91048300	1.98103600	-0.76729800
H	1.87075800	2.07507200	-1.47946900
C	4.85365400	1.24577300	-0.00667800
H	5.19877300	-0.50143800	1.19416800
H	4.21344100	2.90688100	-1.24900700
H	5.87209700	1.61242200	0.08961700
O	0.06158800	0.58409900	-1.11460200
N	0.91233600	-0.13559600	-0.40322900
Cu	-1.37499300	-1.39969400	-0.22499900

N	-2.96352900	1.34925700	-0.36180900
H	-2.05468600	1.22693700	-0.80752500
C	-2.81221500	1.51216400	1.08790700
H	-1.80527700	1.90637500	1.26194700
H	-2.86265900	0.55103100	1.63439400
C	-3.84824000	2.47212600	1.68155800
H	-3.70529300	2.57115800	2.76529400
H	-3.75781500	3.46373100	1.22429800
H	-4.87198000	2.11531900	1.51320600
C	-3.93677200	0.36203300	-0.80973600
H	-4.19352000	0.56439800	-1.85649600
H	-4.85780500	0.49588300	-0.23156300
C	-3.48961200	-1.11432500	-0.69759900
H	-3.13409400	-1.33372000	0.33737000
H	-4.29961400	-1.83149400	-0.86686500
H	-2.74286100	-1.34490800	-1.48993700

M_2

Thermal correction to Gibbs Free Energy = 0.237826 (Hartree/Particle)

Sum of electronic and thermal Free Energies = -2480.900099

C	-0.77312000	1.13945800	-0.03254800
C	-1.69674700	2.20179100	-0.05246500
C	-2.57638900	-0.46570800	-0.04743500
C	-3.05433400	1.94143900	-0.07049400
H	-1.32041200	3.21988400	-0.05181300
C	-3.52573500	0.60015000	-0.06566000
C	-2.97972400	-1.81805800	-0.04411000
H	-3.77670400	2.75380600	-0.08534100
C	-4.90393300	0.25220100	-0.07921500
C	-4.33021100	-2.10836300	-0.05645200
H	-2.22228000	-2.59284200	-0.03079900
C	-5.29668300	-1.07059900	-0.07408600
H	-5.64314200	1.04905400	-0.09312600
H	-4.65715100	-3.14441400	-0.05314300
H	-6.35327500	-1.32284400	-0.08367800
O	-0.25643500	-1.03675900	-0.00536800
N	-1.24552700	-0.11031200	-0.03123100
Cu	1.08916900	0.62057800	-0.01398600
N	2.90773100	-0.23592500	-0.03419800
O	1.84413300	2.34132100	-0.11142000
H	3.47669300	0.62037400	-0.08270300
C	3.14540000	-1.05152200	-1.25588400
H	2.86425800	-0.42093500	-2.10623400
H	2.44668400	-1.89351900	-1.23972900

C	4.58441100	-1.54209400	-1.43927000
H	4.67587100	-2.04162400	-2.41060800
H	5.29428300	-0.70608000	-1.42368300
H	4.88195800	-2.26116600	-0.66886500
C	3.27138700	-0.89710600	1.25481100
H	3.07075700	-0.15805800	2.03837500
H	4.35227800	-1.08794800	1.27345200
C	2.50307600	-2.18798800	1.52899700
H	2.77214900	-2.98388600	0.82551900
H	2.75005900	-2.54323100	2.53590300
H	1.42087800	-2.03343000	1.47139400
O	2.97997400	2.44695800	0.57323100

M_3

Thermal correction to Gibbs Free Energy = 0.236457 (Hartree/Particle)

Sum of electronic and thermal Free Energies = -2492.881237

C	0.41768000	-0.63013600	-0.57274600
C	0.91090300	-1.37679700	-1.66769100
C	2.67514300	-0.36693700	0.22703900
C	2.25679000	-1.61210000	-1.83792900
H	0.19963200	-1.75087400	-2.39797800
C	3.17555000	-1.11101700	-0.87802000
C	3.54338900	0.15181100	1.21027400
H	2.62492300	-2.17022000	-2.69473600
C	4.57945300	-1.31269200	-0.96363500
C	4.90330200	-0.06575200	1.09080700
H	3.12030500	0.71108500	2.03536700
C	5.42580100	-0.80130800	-0.00082100
H	4.97371900	-1.87764500	-1.80455700
H	5.57867500	0.33290200	1.84285300
H	6.49758000	-0.96122500	-0.07862400
O	0.84120900	0.54432800	1.34916100
N	1.29394600	-0.15685300	0.33759400
Cu	-1.37867900	-0.05241100	-0.28222500
N	-2.14942800	-1.71685300	0.26787700
O	-3.03103600	0.76747000	-0.35927700
C	-1.94490200	-1.96890400	1.70457300
H	-2.78108700	-2.62295700	2.00124100
H	-2.11098100	-1.02214600	2.22833700
C	-0.62801800	-2.60174900	2.16440000
H	-0.66333400	-2.73947600	3.25124800
H	-0.45506000	-3.58492800	1.71385300
H	0.22098900	-1.95148500	1.93947800
C	-1.89593900	-2.86739800	-0.60492300

H	-0.88668500	-3.28044200	-0.48194200
H	-1.98968800	-2.52115600	-1.63960000
C	-2.93488100	-3.98215300	-0.37635400
H	-3.95513900	-3.59543000	-0.47194200
H	-2.78969800	-4.75960600	-1.13486100
H	-2.82881000	-4.44825600	0.60833100
I	-0.48055800	2.82622200	-0.06078700
H	-1.59503800	3.51528800	-1.05368100
O	-4.17544800	-0.08621500	-0.19297600
H	-3.70411400	-0.96119400	-0.03995400

TS_1

Thermal correction to Gibbs Free Energy = 0.094509 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -2128.903367

C	-0.74800700	1.04125300	0.01672100
C	-1.55881300	2.18489400	0.00591900
C	-2.68365000	-0.38740300	0.00506000
C	-2.93505400	2.05118100	-0.00531100
H	-1.09386700	3.16433700	0.00693000
C	-3.52747300	0.76290700	-0.00555100
C	-3.20747300	-1.69713200	0.00673300
H	-3.57373700	2.92978000	-0.01393500
C	-4.93273600	0.54615500	-0.01781400
C	-4.57817500	-1.85855800	-0.00439100
H	-2.52370500	-2.53730700	0.01634200
C	-5.44415100	-0.73424000	-0.01719700
H	-5.59321800	1.40892700	-0.02755100
H	-5.00029700	-2.85920500	-0.00320400
H	-6.51923100	-0.88815000	-0.02654000
O	-0.45001400	-1.19855700	0.02023600
N	-1.32016200	-0.17454500	0.01451300
H	0.87881000	1.70465800	0.01178900
Cu	0.99605100	0.27690000	0.01056300
I	3.49196600	-0.21881500	-0.00827700

TS_2

Thermal correction to Gibbs Free Energy = 0.230223 (Hartree/Particle)
Sum of electronic and thermal Free Energies = -2330.548561

C	0.38917900	-1.20910300	0.14256400
C	1.26476000	-1.97094800	0.95839700
C	2.24071000	0.29037500	-0.30367500
C	2.59031900	-1.64433200	1.14884700
H	0.85570100	-2.85463400	1.44060900
C	3.11081500	-0.48852600	0.51255300

C	2.71357500	1.44883100	-0.96018500
H	3.23823400	-2.25053400	1.77730700
C	4.46252100	-0.06711900	0.64204700
C	4.03440400	1.82592400	-0.80899600
H	2.02059800	2.01205000	-1.57233600
C	4.91685300	1.06491900	-0.00274700
H	5.13270100	-0.65789500	1.26206600
H	4.40054400	2.71552200	-1.31469400
H	5.95268900	1.37533700	0.10544800
O	0.11881500	0.65505100	-1.19073700
N	0.90590200	-0.09824700	-0.44594900
Cu	-1.46448900	-1.27610400	-0.21022000
N	-2.83394900	1.08802900	-0.22524900
H	-2.01724700	1.24077900	-0.80529500
C	-2.75074900	1.47469600	1.17084700
H	-1.69185900	1.62694500	1.41097900
H	-3.09097800	0.64707100	1.81706600
C	-3.54645300	2.73992900	1.52688200
H	-3.46213100	2.96346500	2.59896600
H	-3.17211100	3.60165000	0.96204300
H	-4.61120400	2.61811200	1.29121400
C	-3.93982600	0.31150600	-0.73821300
H	-4.18625800	0.62000600	-1.76196300
H	-4.83107900	0.50858300	-0.13048400
C	-3.63091100	-1.19910800	-0.72265100
H	-3.30331800	-1.49691400	0.29882800
H	-4.47783400	-1.85554600	-0.95436600
H	-2.87164200	-1.43812300	-1.49873700

TS_3

Thermal correction to Gibbs Free Energy = 0.234308 (Hartree/Particle)

Sum of electronic and thermal Free Energies = -2480.886747

C	-0.78600000	1.23436500	0.03871800
C	-1.73772100	2.27148200	0.06423700
C	-2.54203000	-0.42837800	-0.06891600
C	-3.08557100	1.96459400	0.02069600
H	-1.39617300	3.30004000	0.11400000
C	-3.51997300	0.61141000	-0.04705300
C	-2.90103000	-1.79092000	-0.13053700
H	-3.83298300	2.75396100	0.03789500
C	-4.88675100	0.22534700	-0.09368300
C	-4.24288100	-2.11709800	-0.17217800
H	-2.12328100	-2.54558200	-0.14375300
C	-5.23883100	-1.10765300	-0.15425500

H	-5.64927000	0.99963600	-0.08013000
H	-4.53999600	-3.16084800	-0.21984800
H	-6.28695900	-1.39040400	-0.18862900
O	-0.18265700	-0.90255100	-0.02412500
N	-1.23248700	-0.01919000	-0.02044800
Cu	1.06621400	0.60943800	0.07710000
N	2.81148400	-0.21717400	0.02337400
O	1.93195800	2.23523900	0.23302700
H	3.38524300	1.03548300	-0.04216300
C	2.96670400	-1.00300000	-1.21378600
H	2.65760400	-0.35535700	-2.04333100
H	2.28714100	-1.86760700	-1.21134500
C	4.40540000	-1.47451600	-1.47560200
H	4.45856600	-1.94171100	-2.46583100
H	5.10244900	-0.62878600	-1.45946100
H	4.74098500	-2.21363100	-0.74043800
C	3.19177500	-0.92823600	1.25967500
H	3.00795600	-0.23651500	2.09034600
H	4.27946800	-1.09227700	1.23632500
C	2.48182100	-2.26217200	1.52762300
H	2.73664100	-3.02123500	0.77959800
H	2.79087600	-2.64643700	2.50701700
H	1.39345400	-2.14215200	1.53215300
O	3.29890200	2.16267700	-0.11995300

TS_4

Thermal correction to Gibbs Free Energy = 0.236700 (Hartree/Particle)

Sum of electronic and thermal Free Energies = -2492.879842

C	-0.53955300	-0.50526600	0.63379700
C	-1.11134700	-0.88404000	1.86540000
C	-2.72659700	-0.48567700	-0.36904000
C	-2.47266000	-1.05984600	1.99959000
H	-0.45687700	-1.02705500	2.72049500
C	-3.31419500	-0.86290400	0.87254300
C	-3.51401900	-0.27493800	-1.52051800
H	-2.91064200	-1.33669500	2.95479600
C	-4.72621300	-1.02360200	0.91345900
C	-4.88328300	-0.44205200	-1.43725800
H	-3.02210500	0.01696900	-2.44021900
C	-5.49303000	-0.82046800	-0.21595000
H	-5.19016800	-1.31155600	1.85369800
H	-5.49836400	-0.28079200	-2.31834400
H	-6.57142600	-0.94574200	-0.16930400
O	-0.78087500	0.04822100	-1.56209300

N	-1.34100200	-0.31986600	-0.43363100
Cu	1.23444600	-0.06333700	0.09621500
N	1.88764500	-1.85776700	-0.04427500
O	2.85923400	0.66643600	-0.38247400
C	1.29450900	-2.45533200	-1.25229000
H	1.34535000	-1.70907800	-2.05091800
H	0.23469400	-2.69950600	-1.09391800
C	2.03738800	-3.72009700	-1.71871300
H	1.58606500	-4.05087600	-2.66134600
H	3.09804200	-3.51459900	-1.90003600
H	1.95279000	-4.54272800	-1.00205700
C	1.76879300	-2.69725400	1.15819500
H	0.94785100	-3.42379500	1.06452100
H	1.53705800	-2.05978700	2.01640900
C	3.10062300	-3.40427700	1.47079900
H	3.89976700	-2.67008300	1.61689300
H	2.99092600	-3.98173100	2.39793500
H	3.40393500	-4.08978900	0.67493100
I	0.63495300	3.04393500	0.15094100
H	1.71597900	2.66143800	-1.03141000
O	3.87943300	-0.25903200	-0.80542900
H	3.47433700	-1.11346300	-0.47702800

TS_5

Thermal correction to Gibbs Free Energy = 0.219510 (Hartree/Particle)

Sum of electronic and thermal Free Energies = -2341.385587

C	0.44960500	0.36005900	0.41364100
C	0.95567400	0.47838200	1.71866600
C	2.41800200	-0.78399000	-0.29777900
C	2.18999800	-0.04794500	2.03086500
H	0.35161800	0.96372200	2.47756300
C	2.94977200	-0.69511400	1.01969100
C	3.12771500	-1.41946900	-1.33624000
H	2.58107200	0.01611700	3.04222100
C	4.22945100	-1.26541300	1.25506300
C	4.37001400	-1.96131500	-1.06483300
H	2.67655200	-1.47052000	-2.31937600
C	4.92494700	-1.88361500	0.23567800
H	4.64906500	-1.20752400	2.25598300
H	4.92428100	-2.45608100	-1.85730600
H	5.90166500	-2.31747100	0.43041500
O	0.65128900	-0.30663000	-1.76267000
N	1.15721000	-0.23088900	-0.56474200
Cu	-1.36158300	0.46757000	-0.17825500

N	-0.79355100	2.18237700	-0.32996500
I	-2.81472300	-1.58078700	0.11522000
C	-0.15248700	2.68674800	-1.54977100
H	-0.68007200	3.63513300	-1.75163100
H	-0.41556000	2.00014000	-2.35743900
C	1.36243900	2.93615500	-1.59923000
H	1.61116000	3.29856100	-2.60444300
H	1.70446400	3.68336900	-0.88128800
H	1.92097700	2.01162000	-1.43963600
C	-0.92225800	3.07037200	0.83186300
H	-1.30998200	2.46570400	1.65954100
H	-1.74587100	3.75602100	0.57097400
C	0.27233300	3.90257300	1.31540600
H	0.53921800	4.68957600	0.60438400
H	-0.00720000	4.39389600	2.25554000
H	1.15768900	3.28796100	1.50339300

Computational Results

The free energy barriers for all the five steps (**TS_{1-5}**) are 10.85, 0.80, 8.38, 0.88, and 7.65 kcal/mol, which indicates the entire reaction should proceed smoothly.

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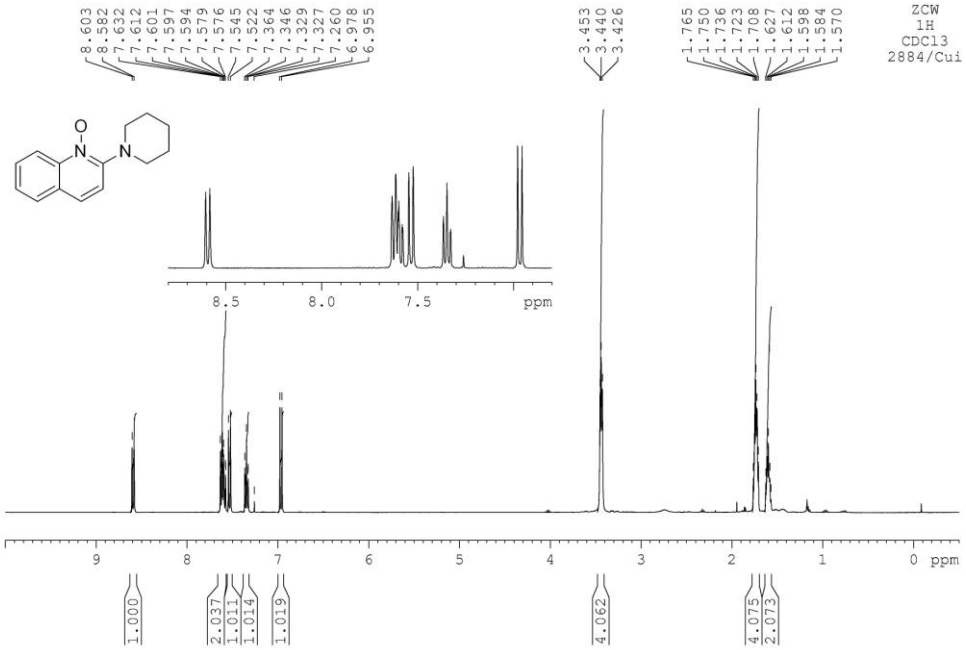
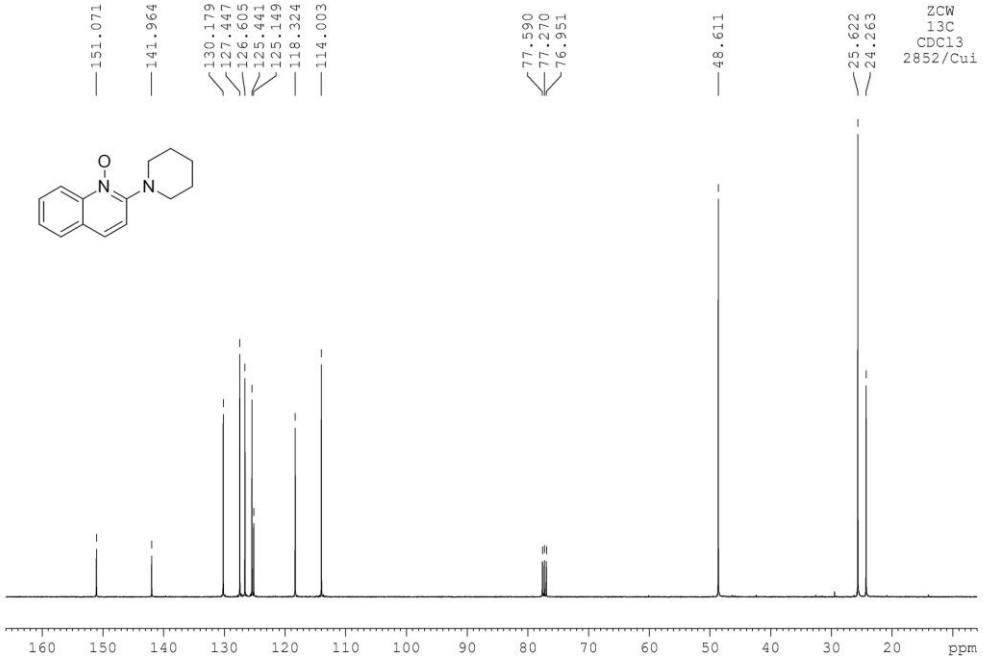
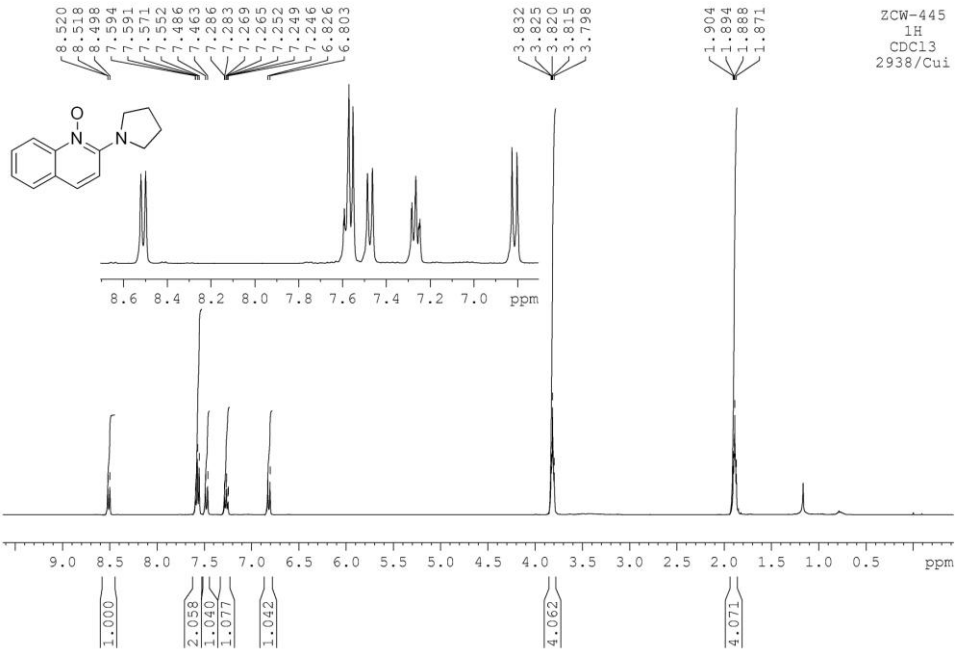
^{1}H NMR and ^{13}C NMR spectra of products



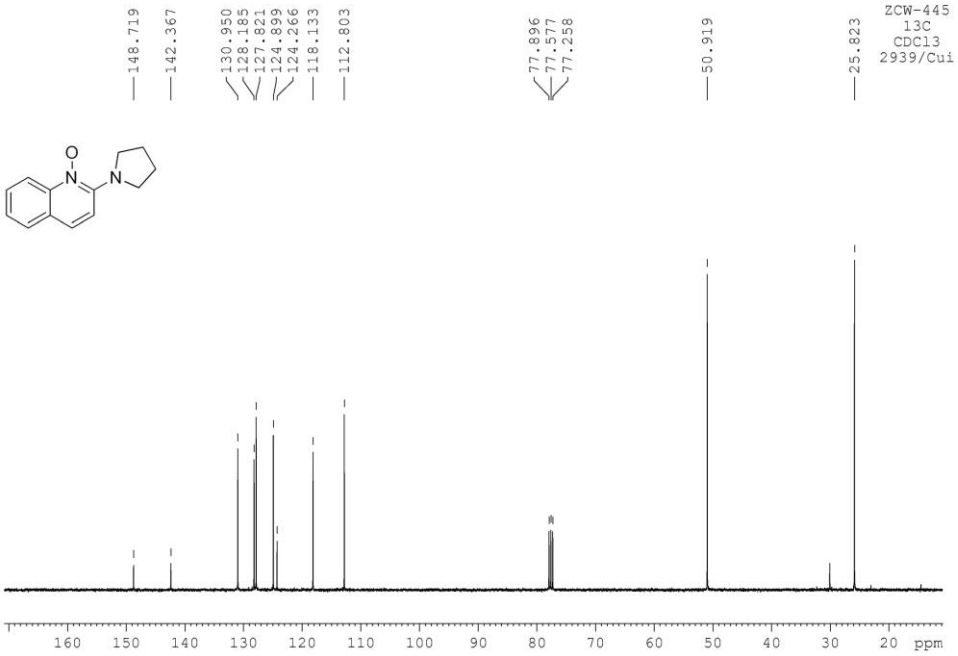
^{1}H NMR spectrum of compound **3aa**



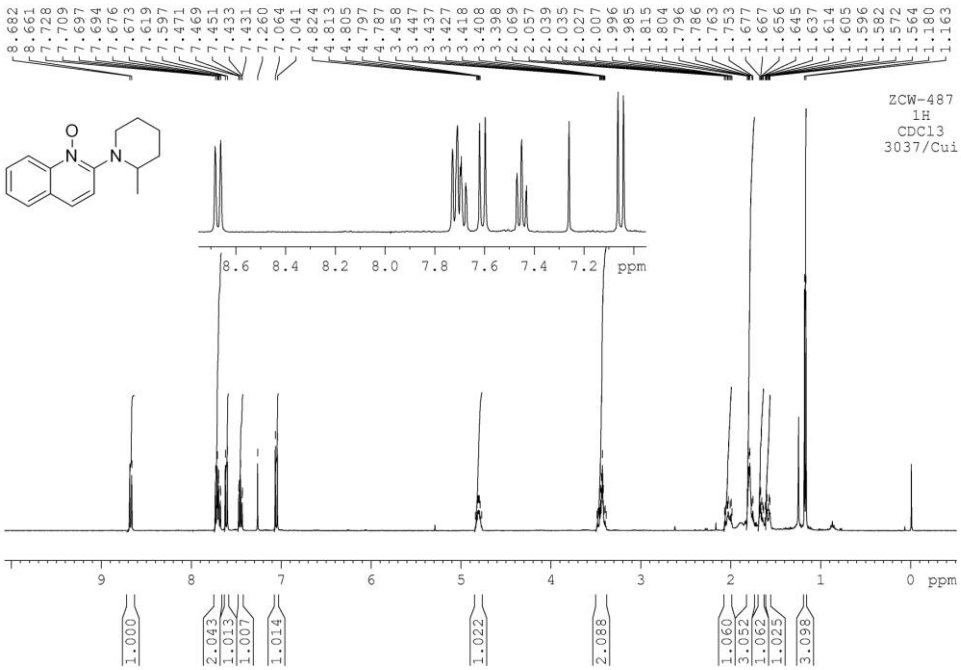
^{13}C NMR spectrum of compound **3aa**



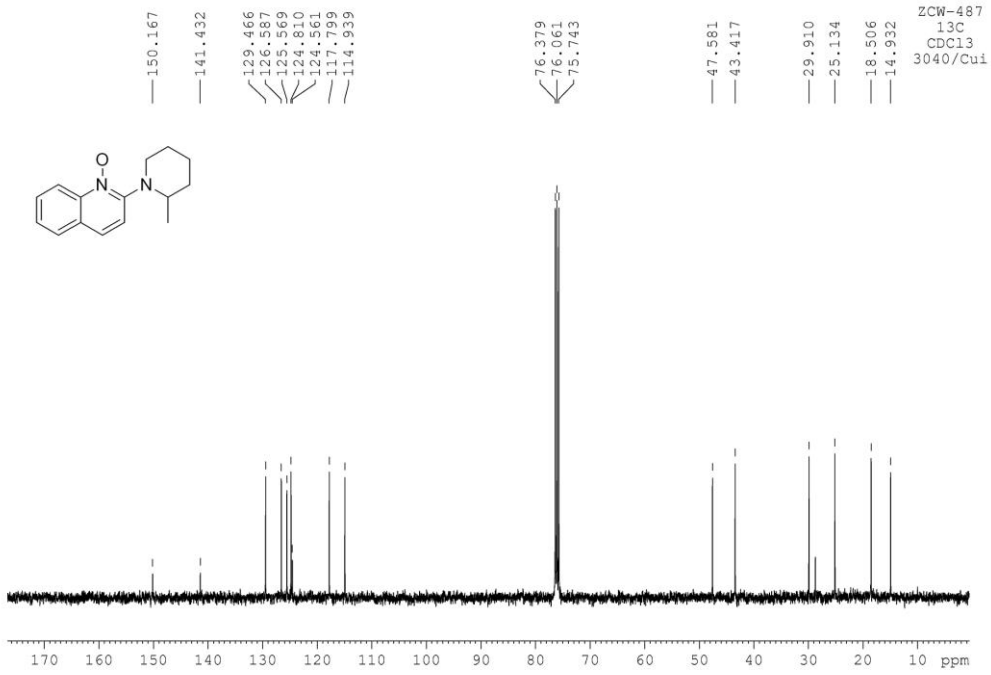
^{1}H NMR spectrum of compound **3ab**



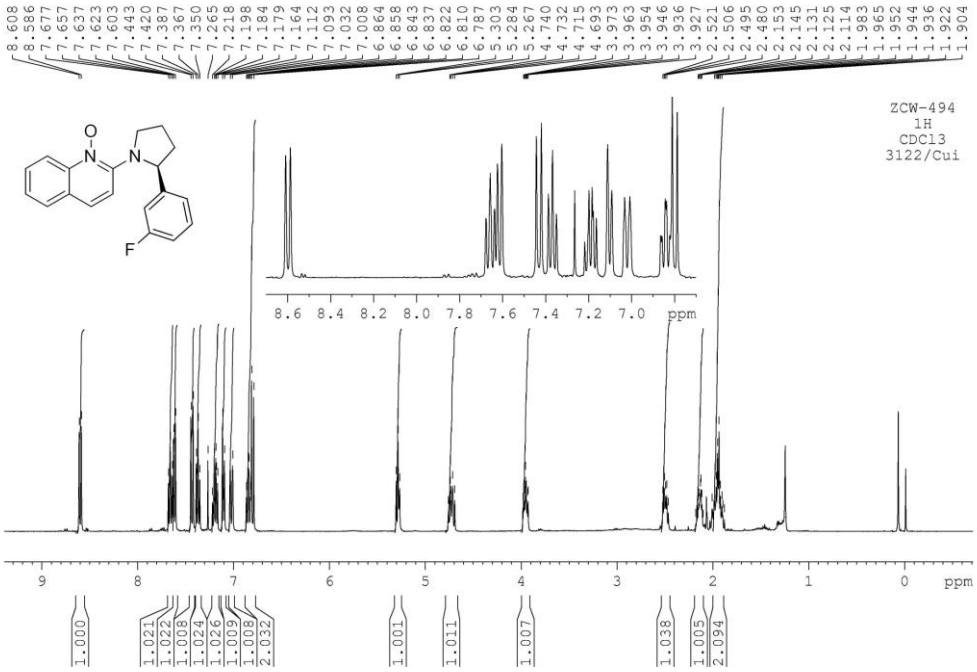
^{13}C NMR spectrum of compound **3ab**



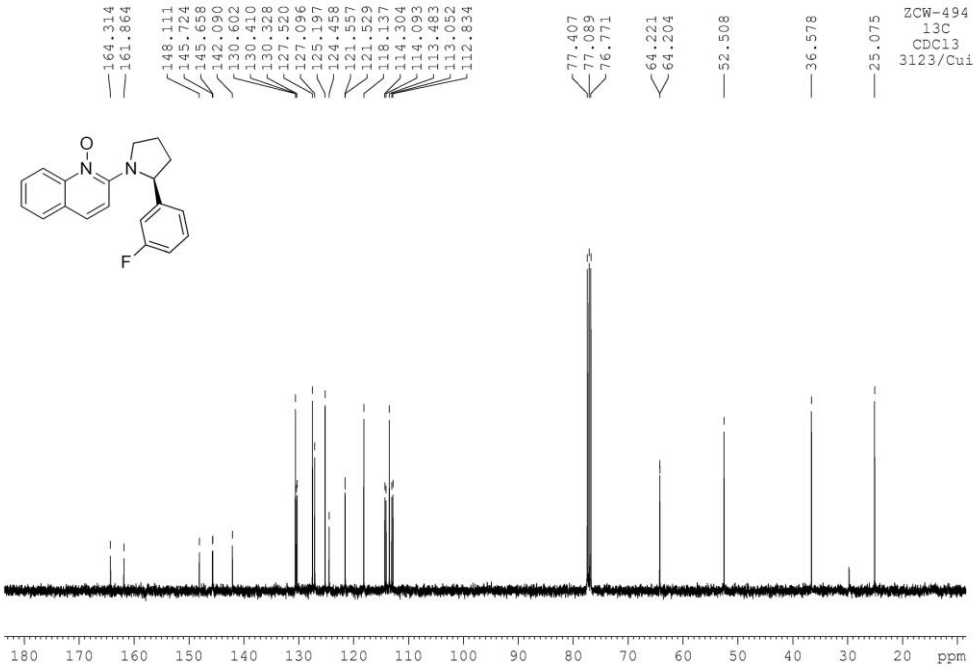
^{1}H NMR spectrum of compound **3ac**



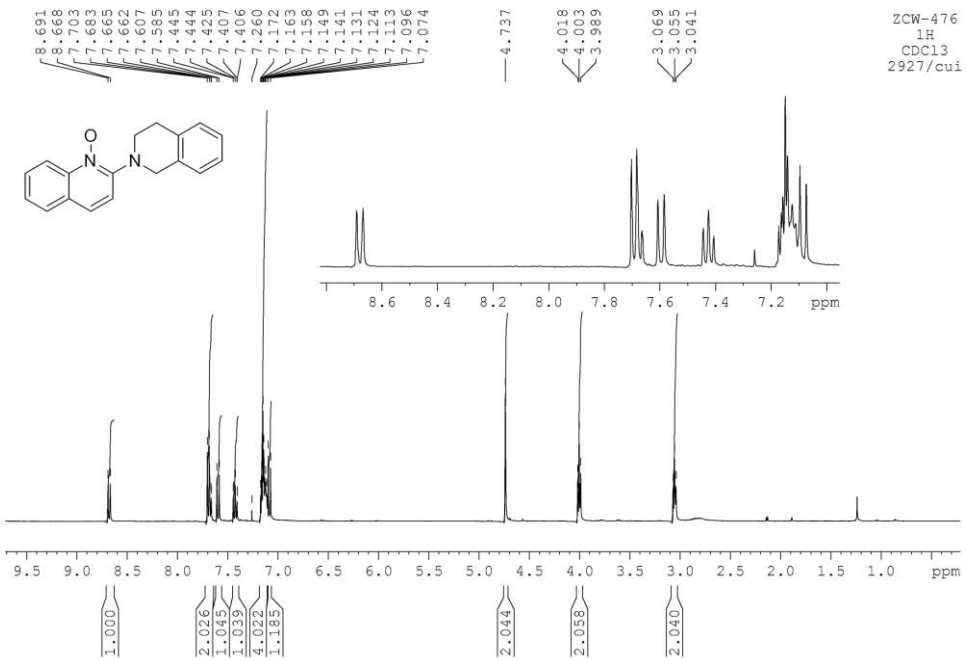
^{13}C NMR spectrum of compound **3ac**



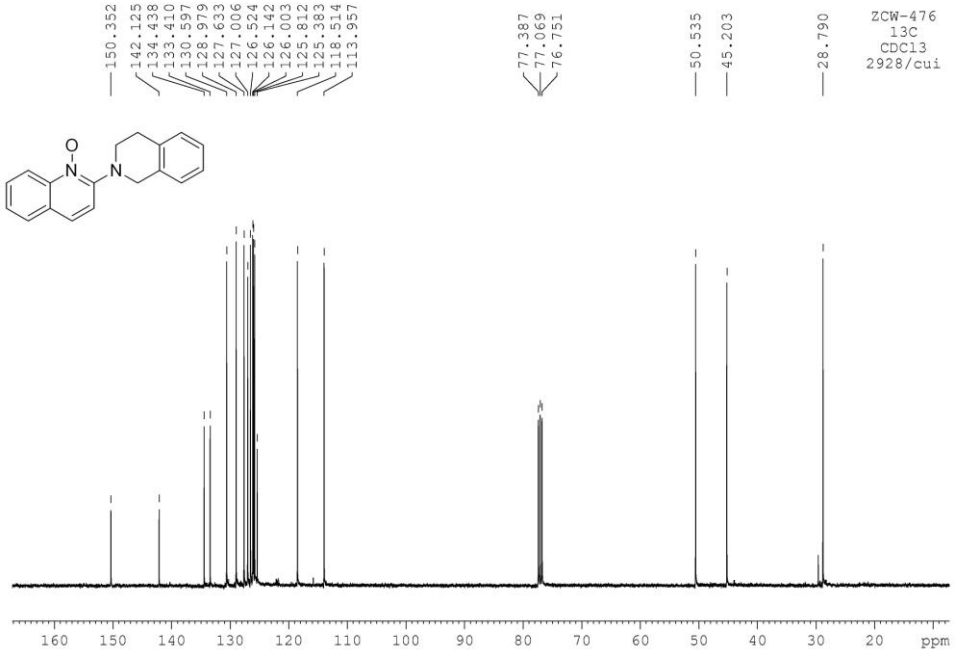
^{1}H NMR spectrum of compound **3ad**



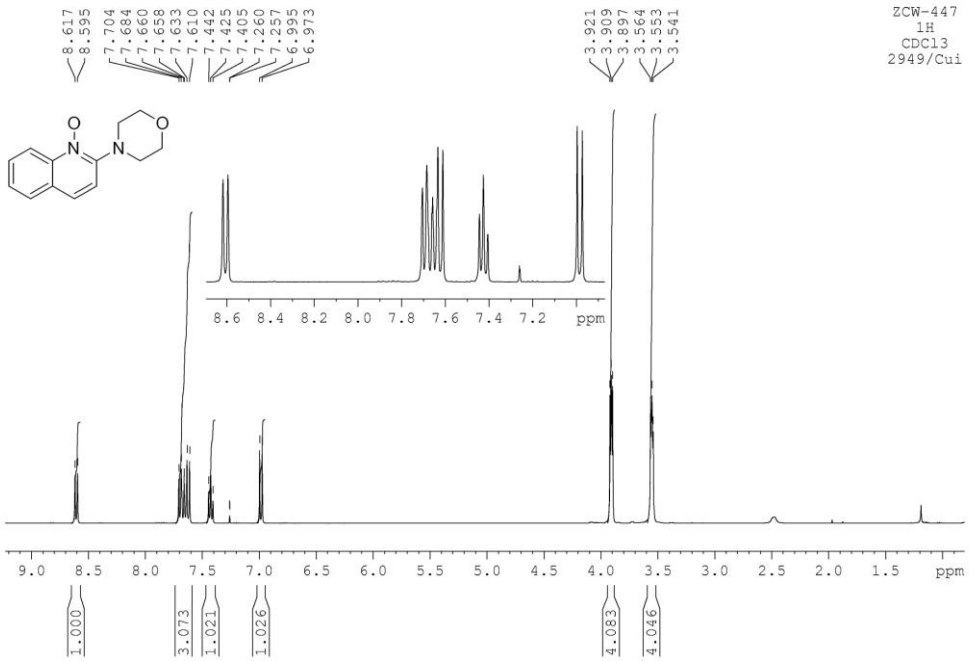
^{13}C NMR spectrum of compound **3ad**



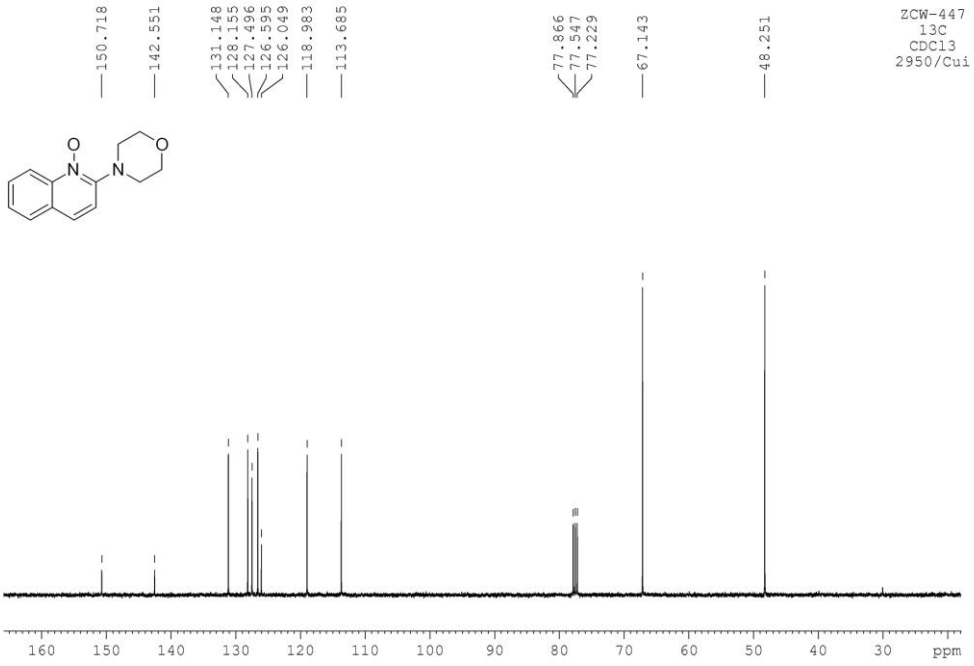
^{1}H NMR spectrum of compound **3ae**



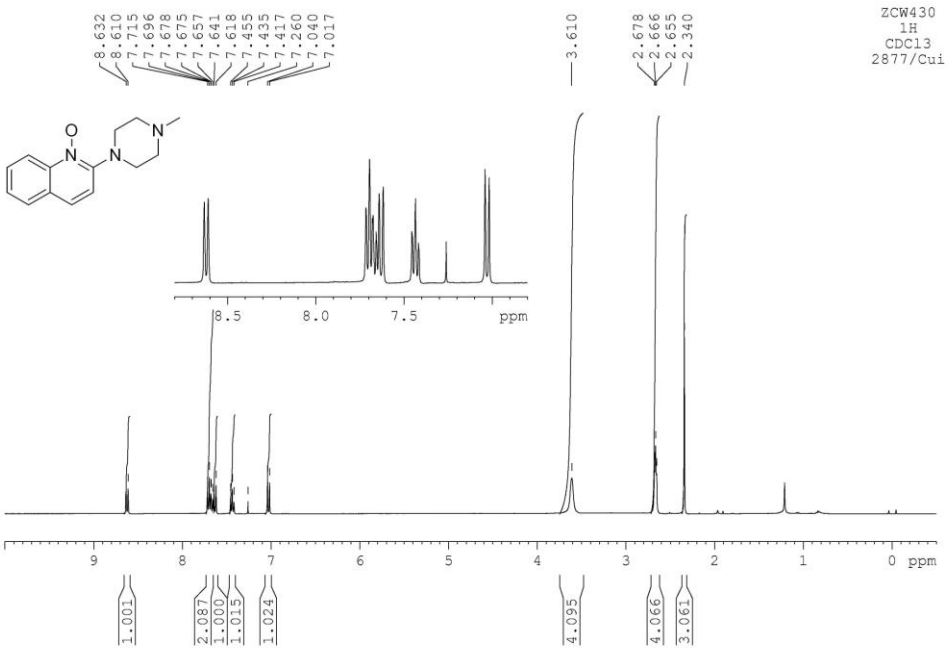
^{13}C NMR spectrum of compound **3ae**



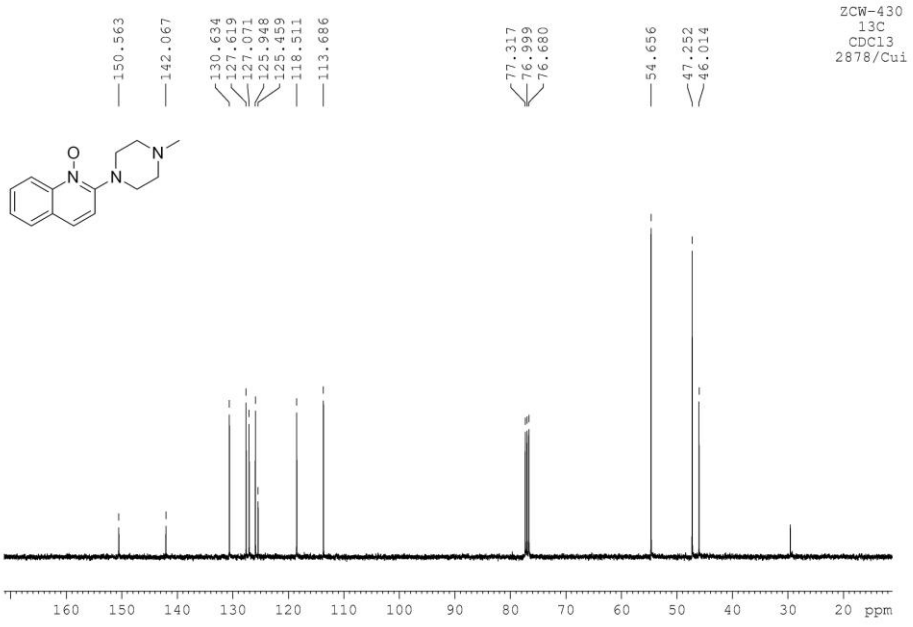
^{1}H NMR spectrum of compound **3af**



^{13}C NMR spectrum of compound **3af**

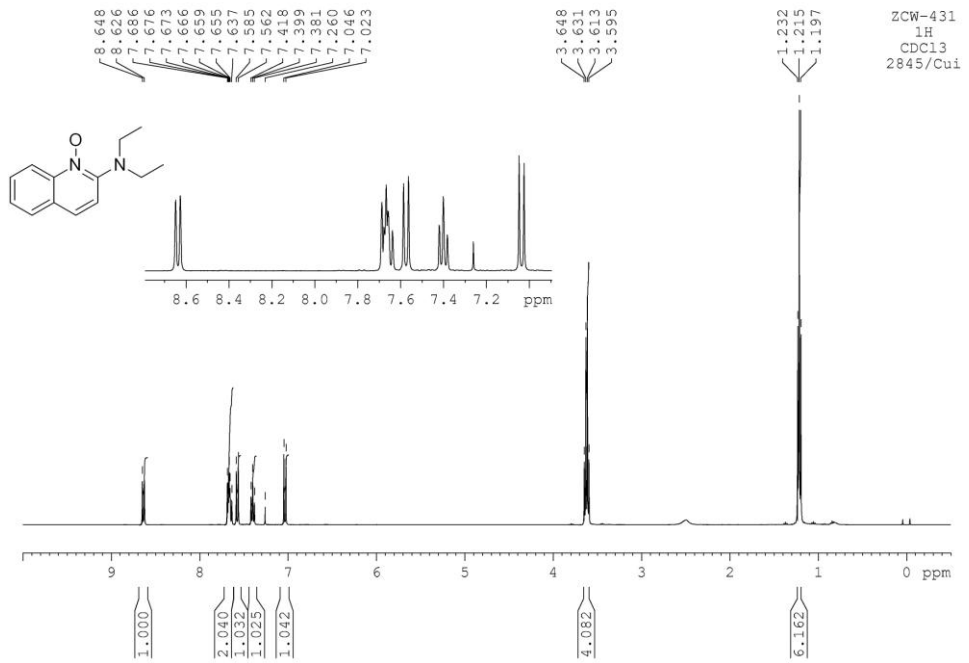


^{1}H NMR spectrum of compound **3ag**

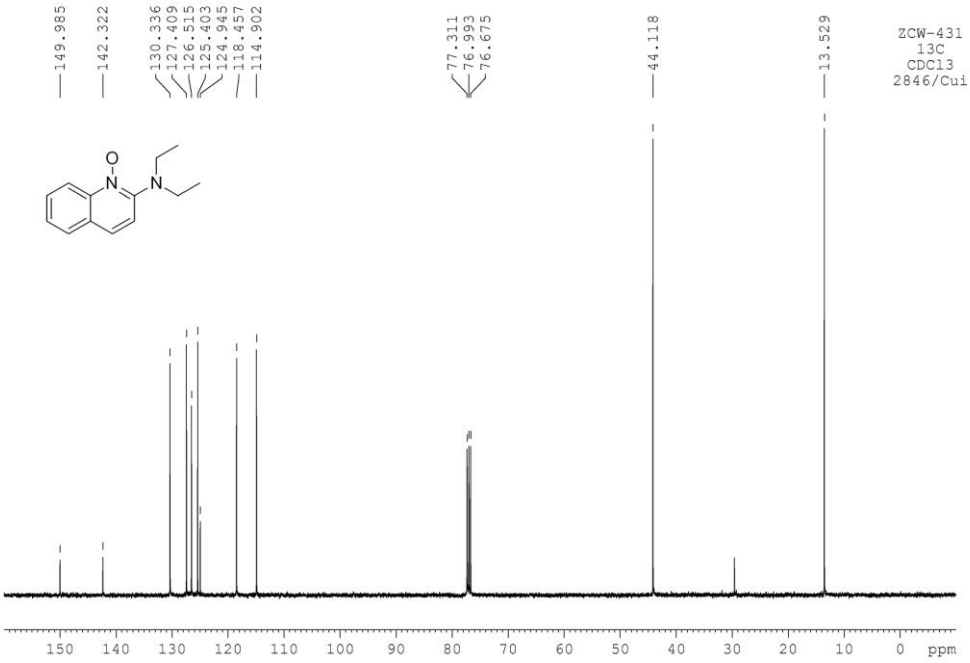


131

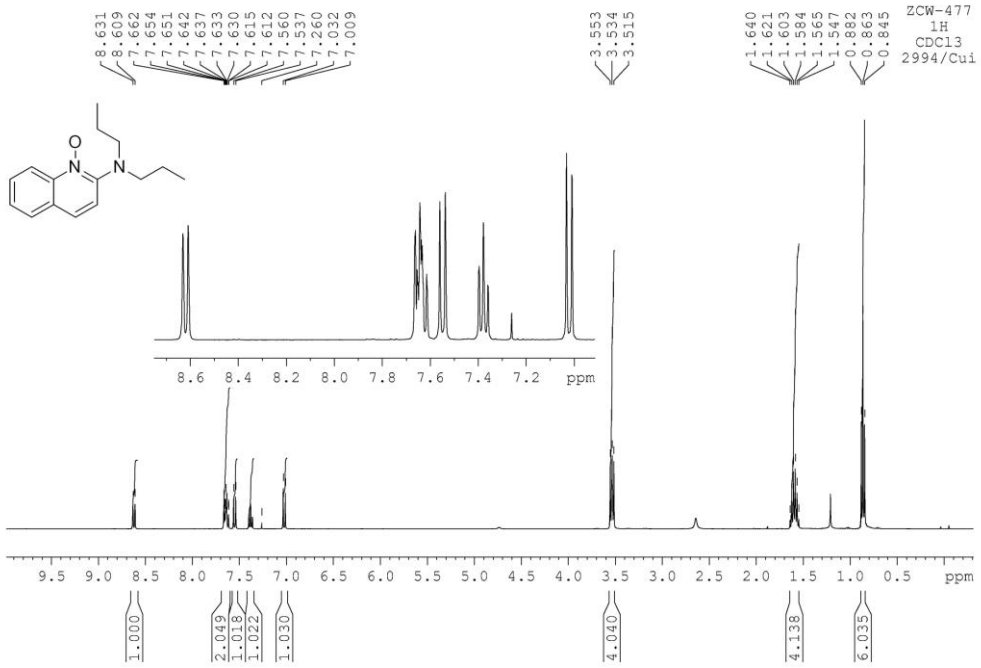
^{13}C NMR spectrum of compound **3ag**



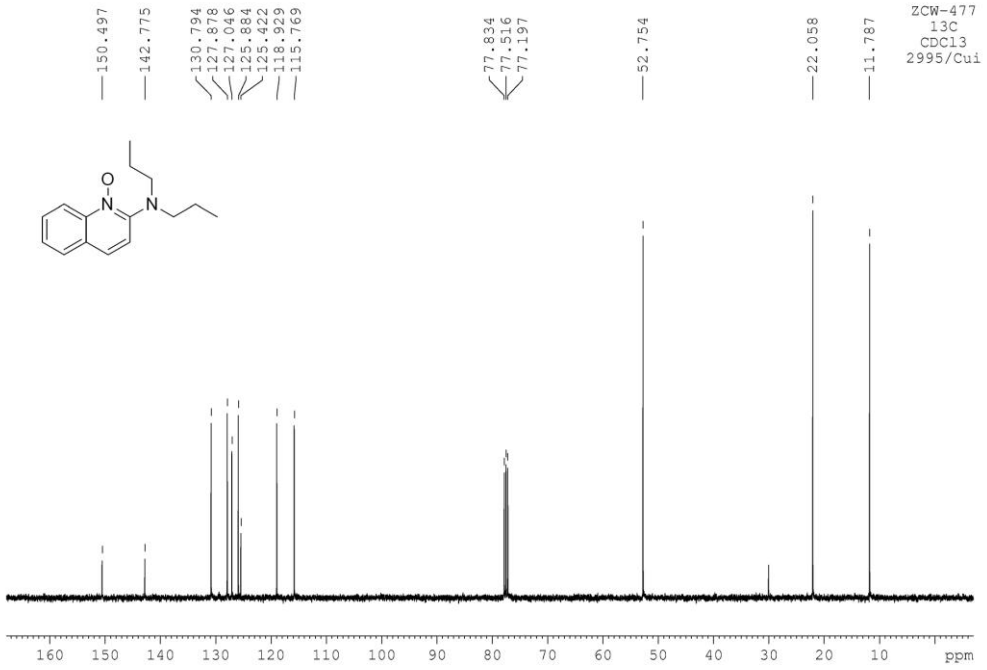
^{1}H NMR spectrum of compound **3ah**



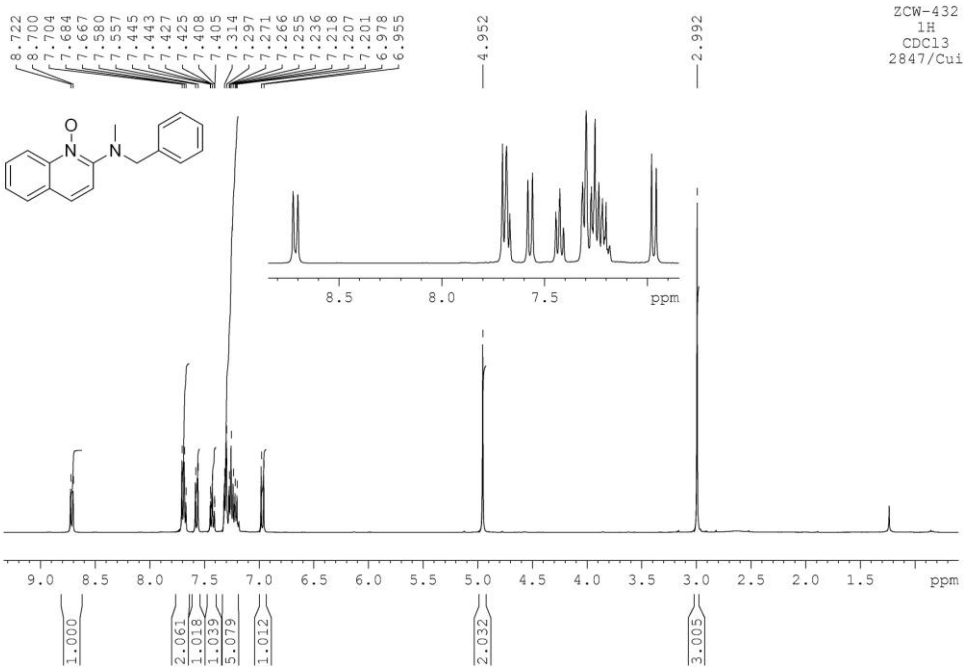
^{13}C NMR spectrum of compound **3ah**



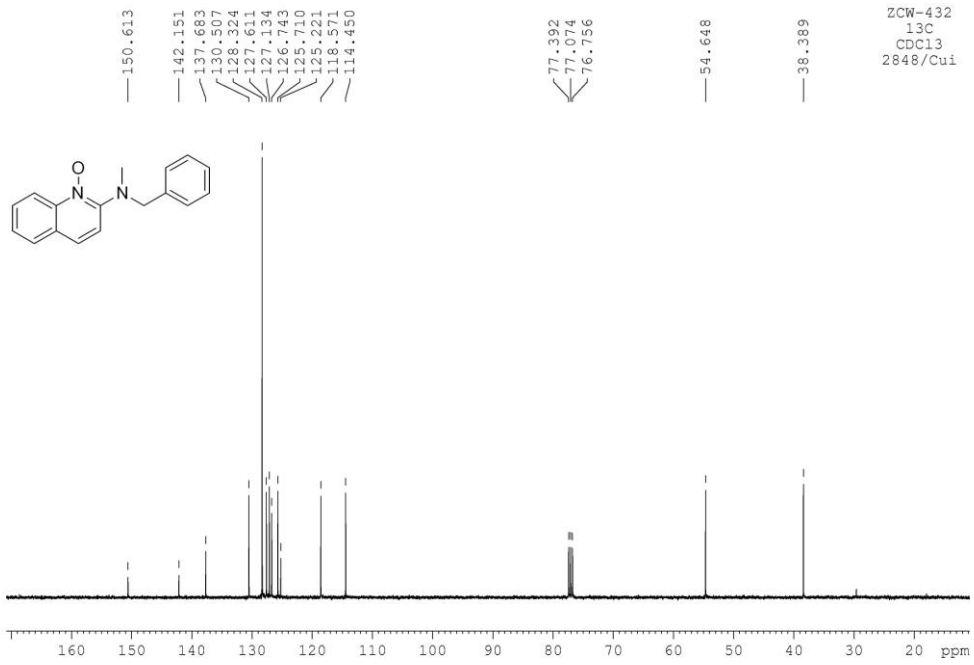
^{1}H NMR spectrum of compound **3ai**



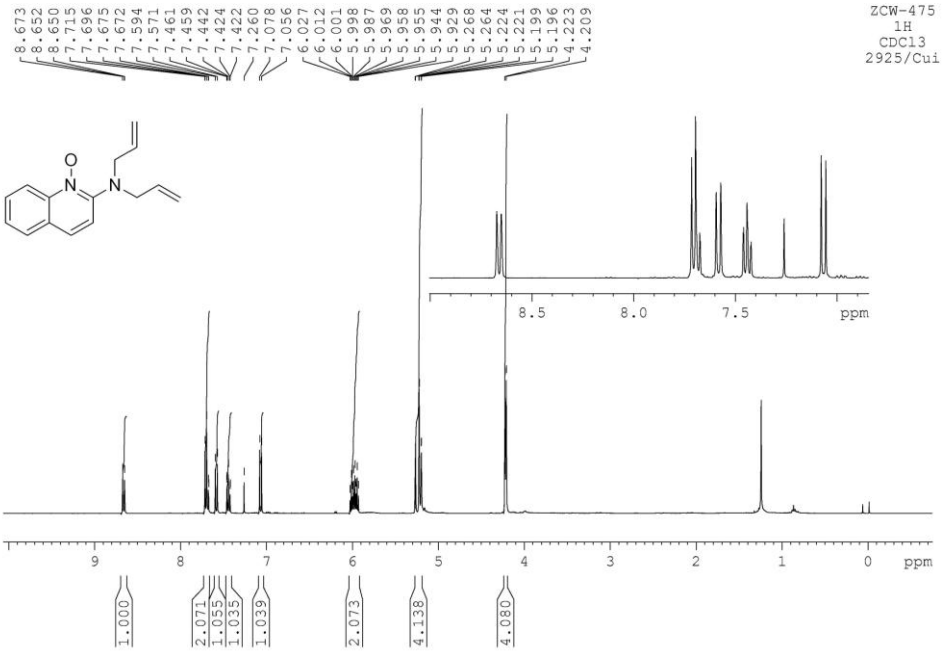
^{13}C NMR spectrum of compound **3ai**



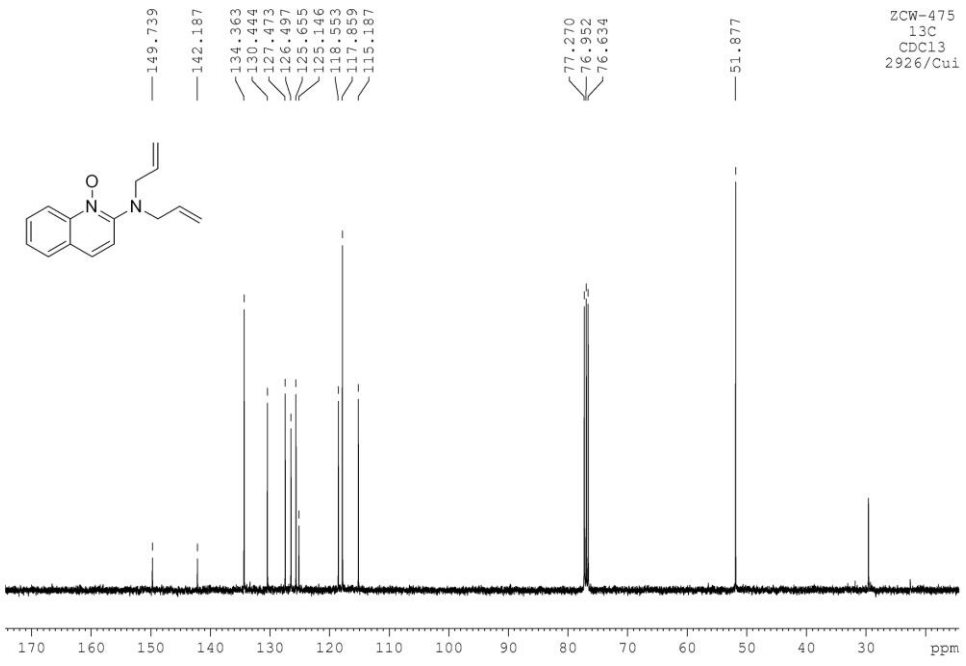
^{1}H NMR spectrum of compound **3aj**



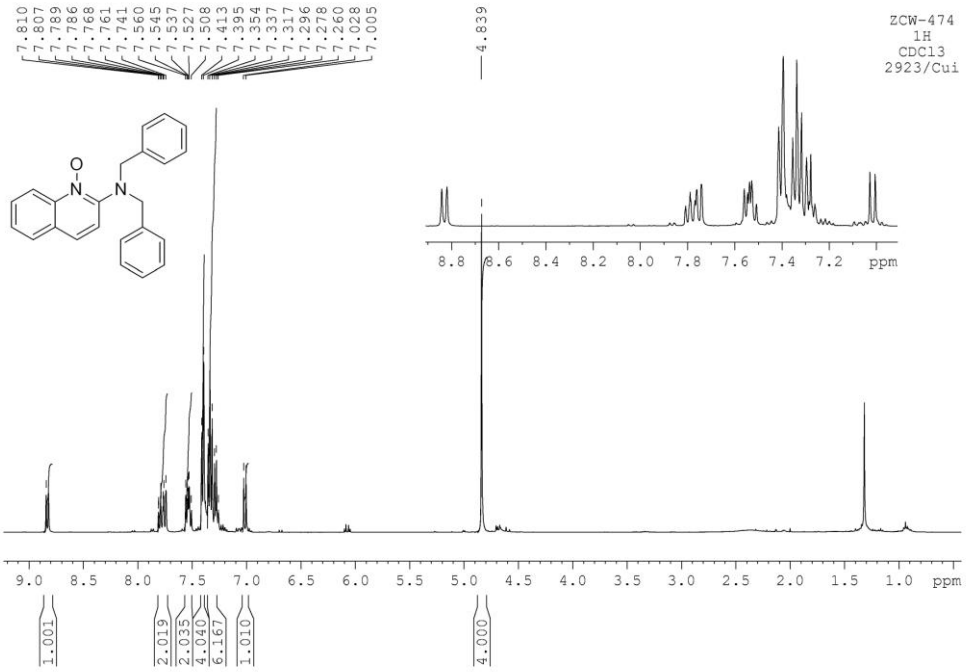
^{13}C NMR spectrum of compound **3aj**



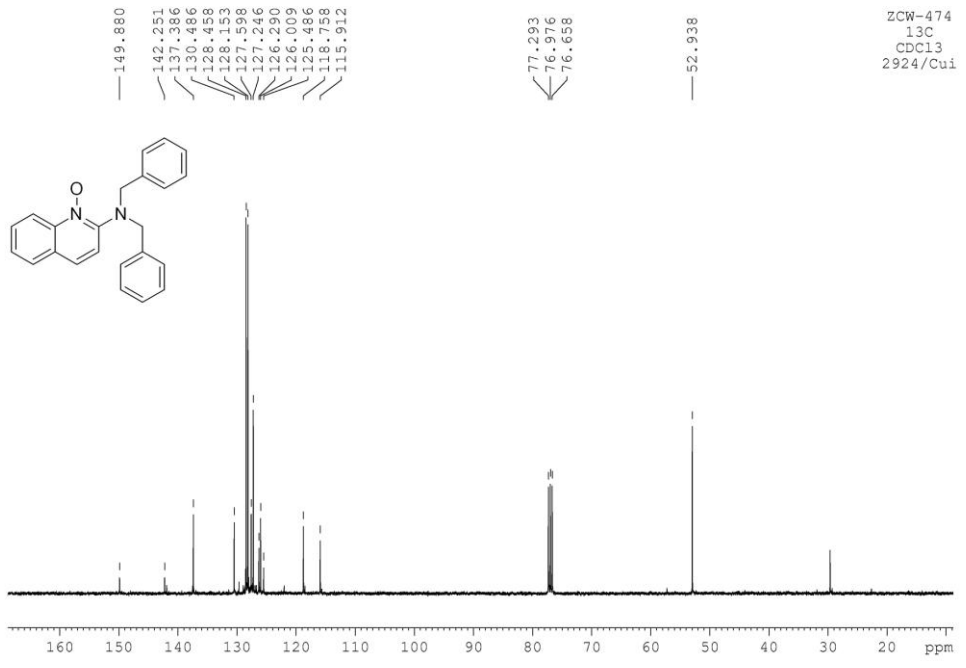
^{1}H NMR spectrum of compound **3ak**



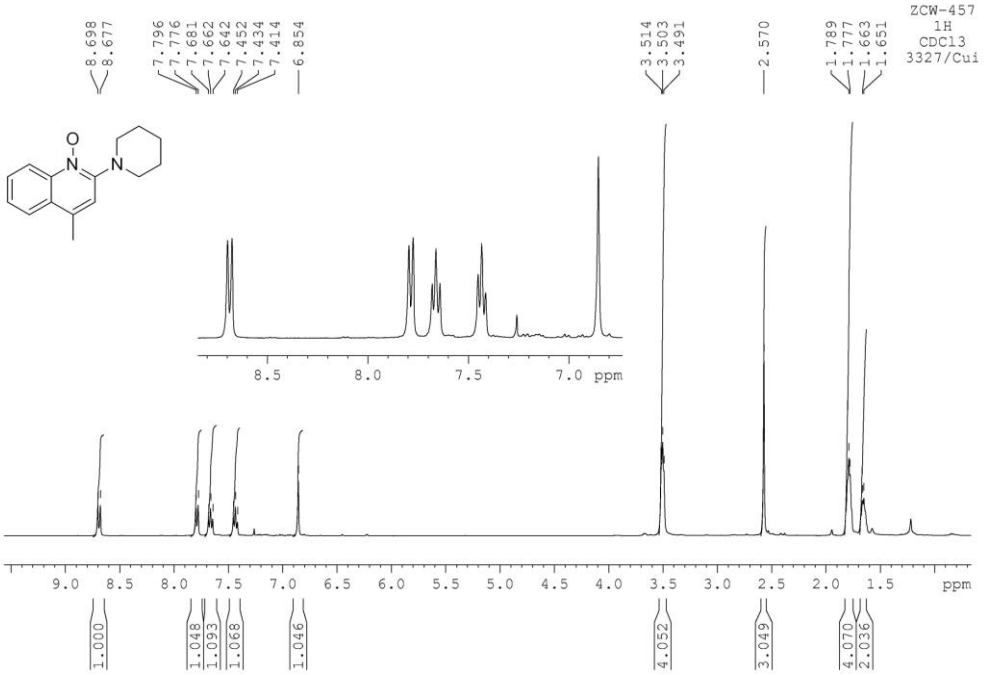
^{13}C NMR spectrum of compound **3ak**



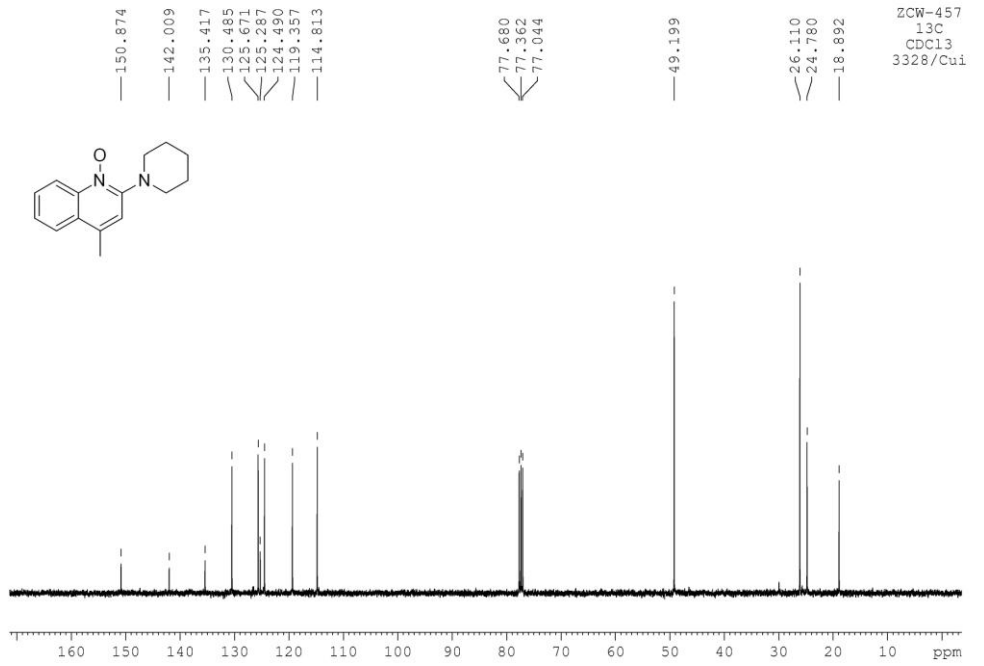
^{1}H NMR spectrum of compound **3al**



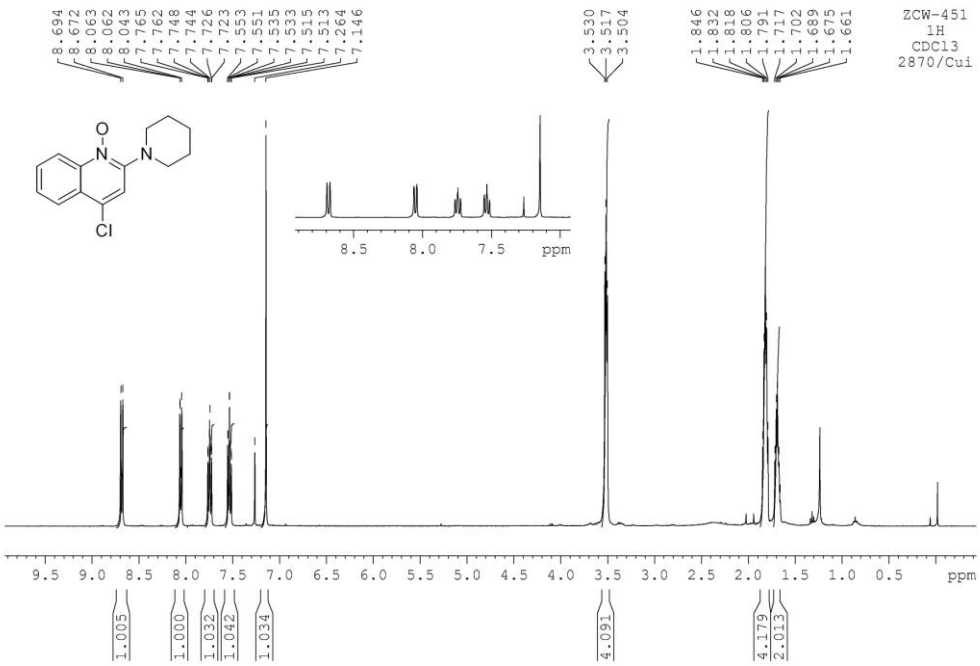
^{13}C NMR spectrum of compound **3al**



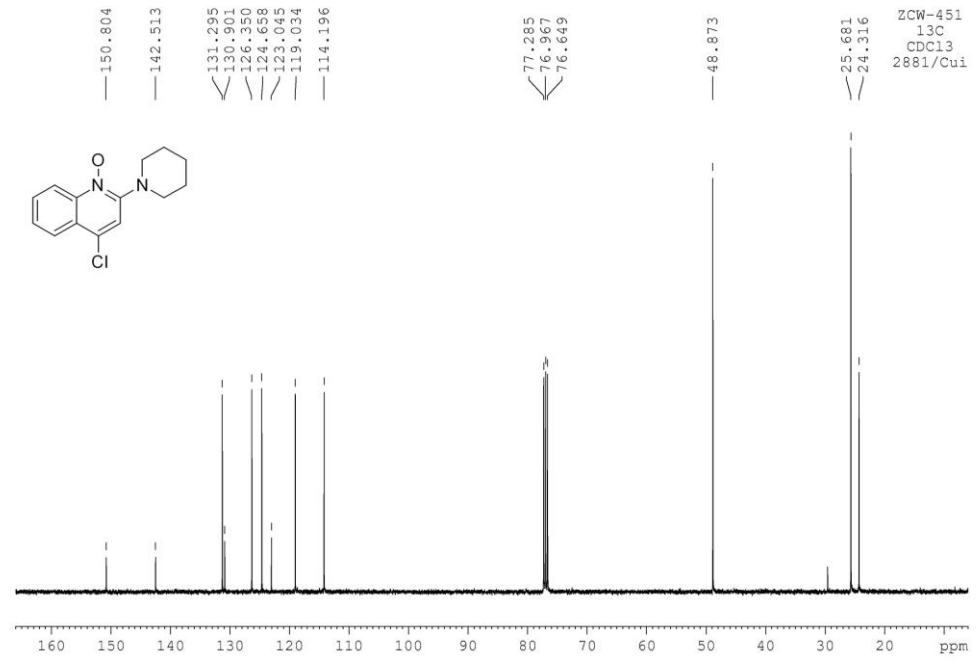
^{1}H NMR spectrum of compound **3ba**



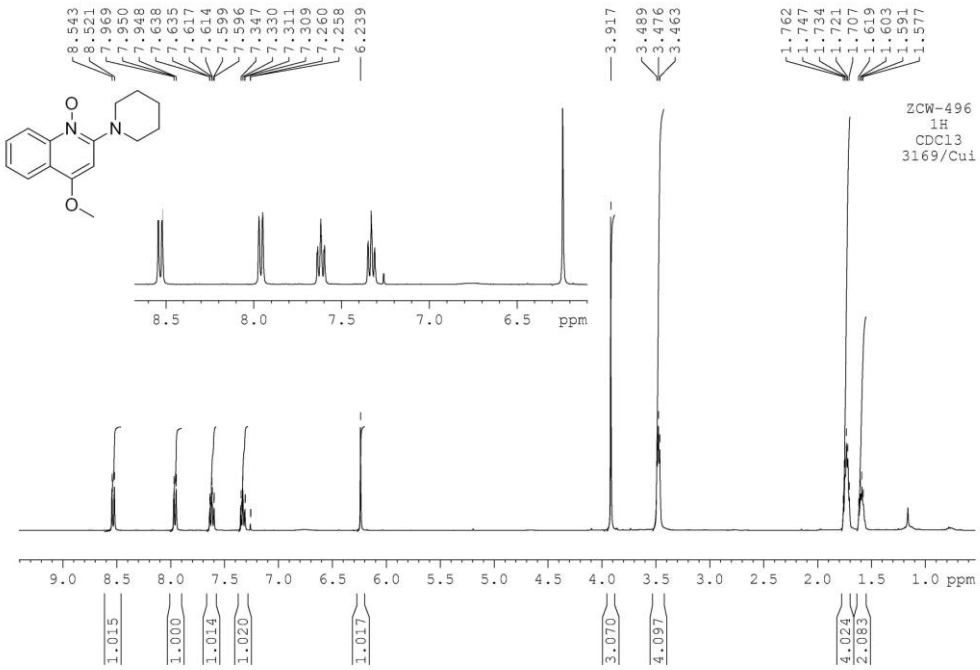
^{13}C NMR spectrum of compound **3ba**



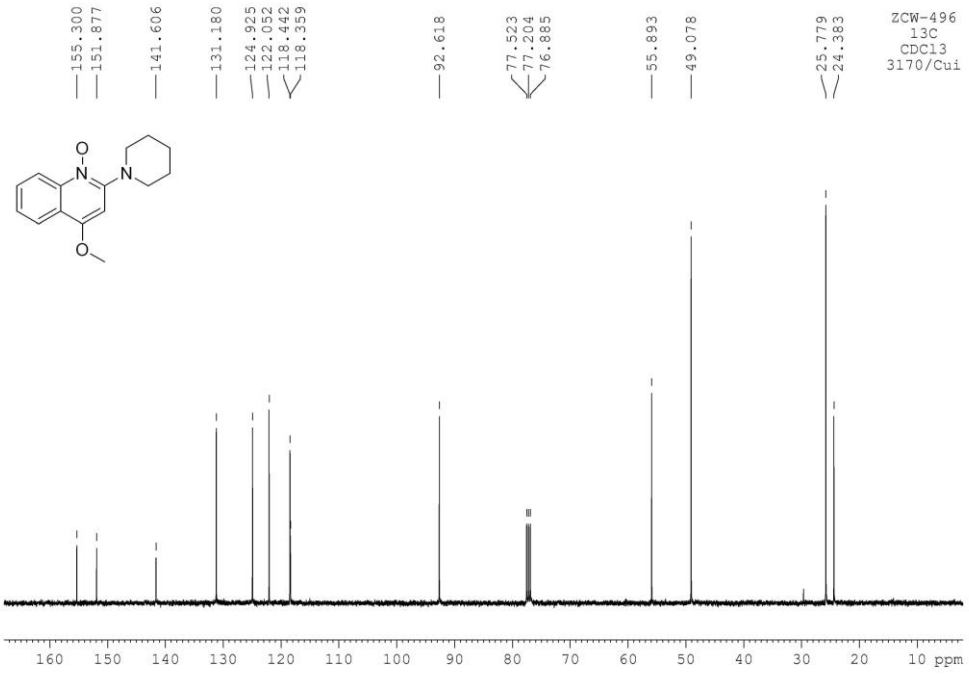
^{1}H NMR spectrum of compound **3ca**



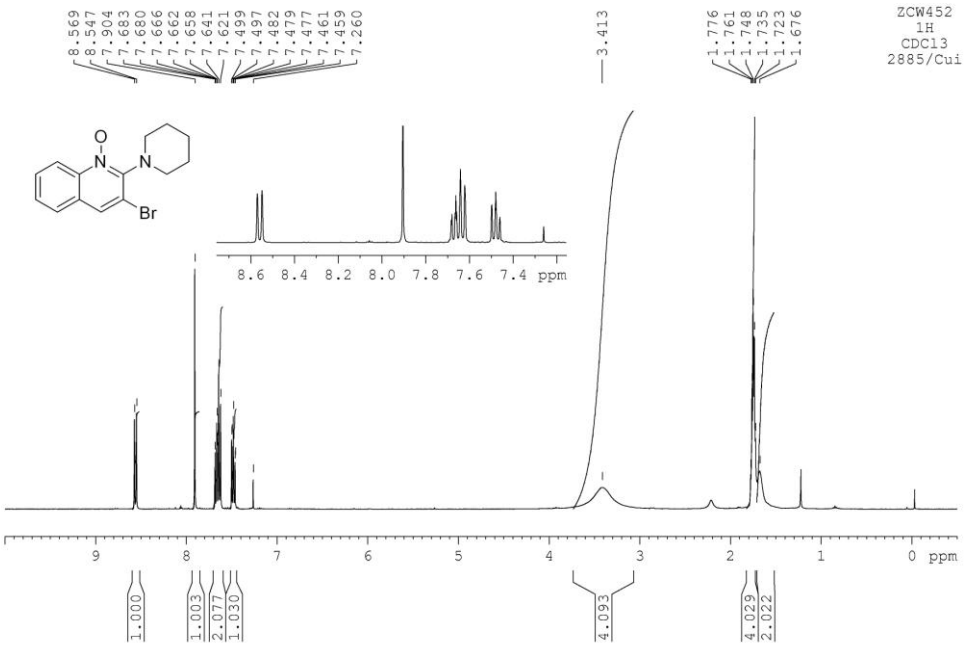
^{13}C NMR spectrum of compound **3ca**



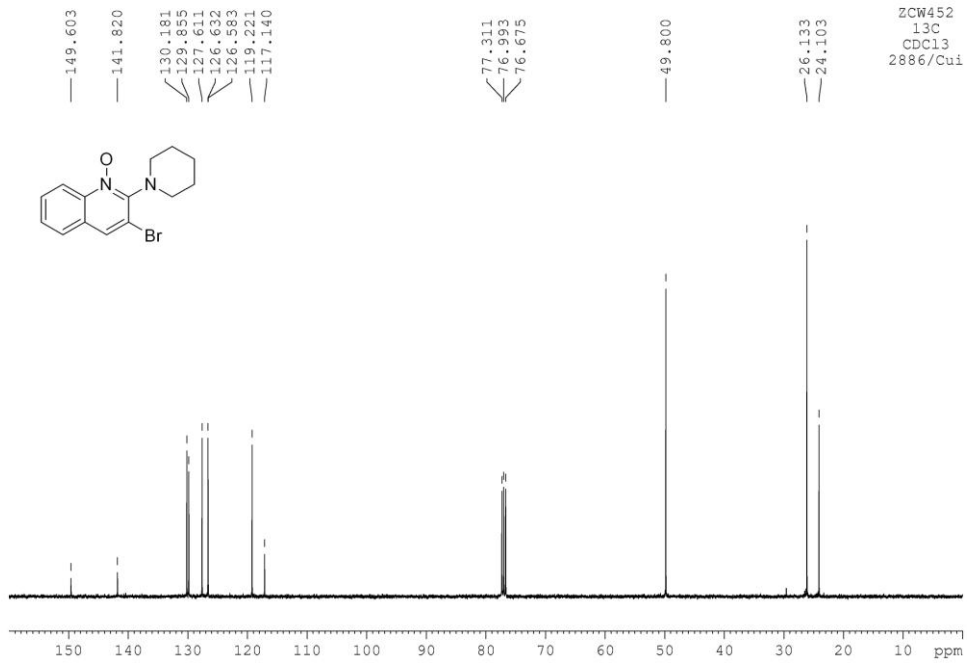
^{1}H NMR spectrum of compound **3da**



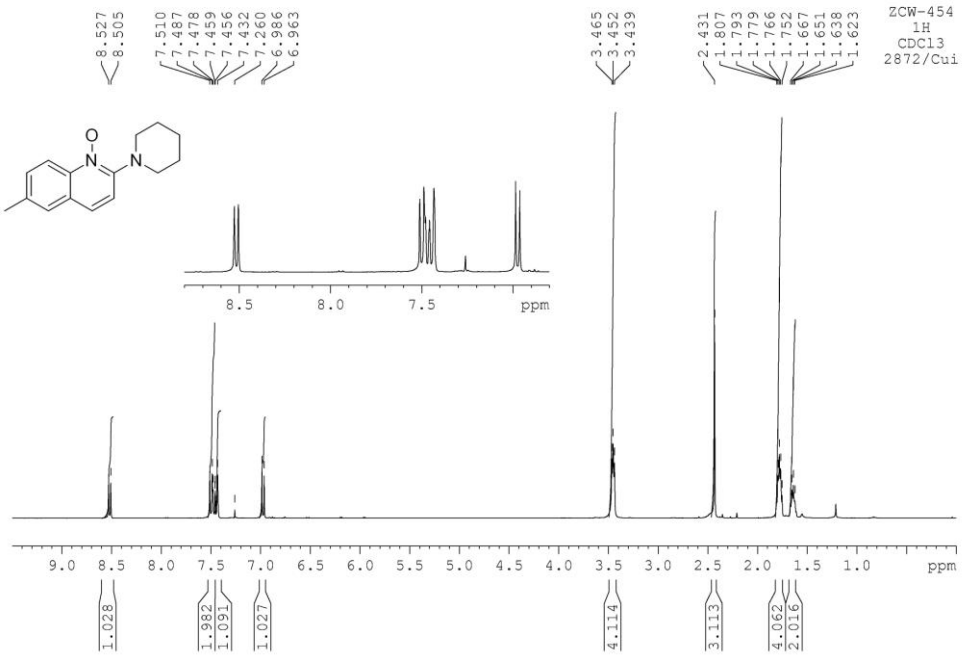
^{13}C NMR spectrum of compound **3da**



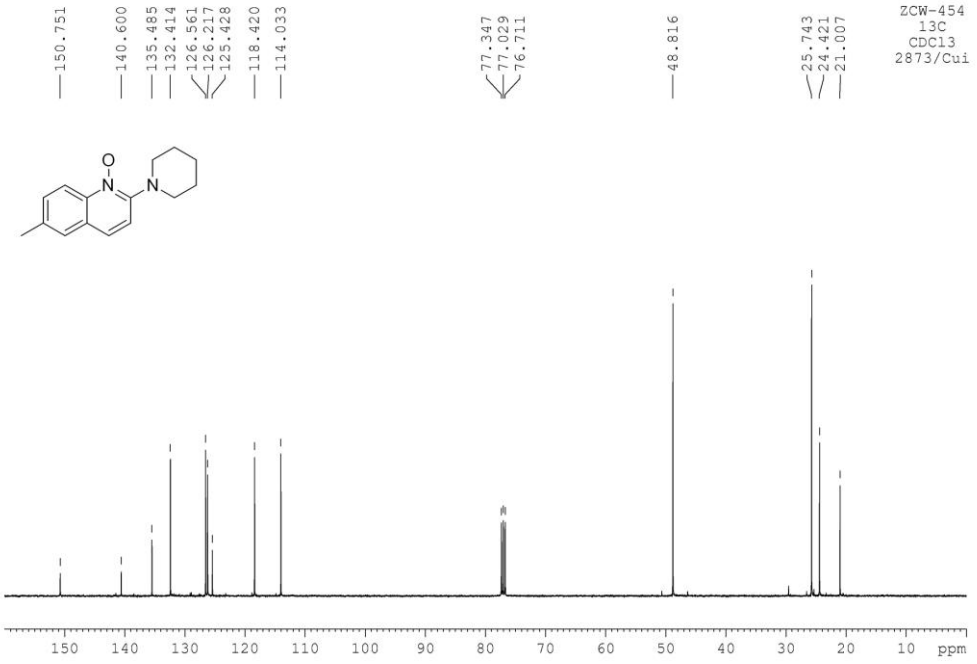
^{1}H NMR spectrum of compound **3ea**



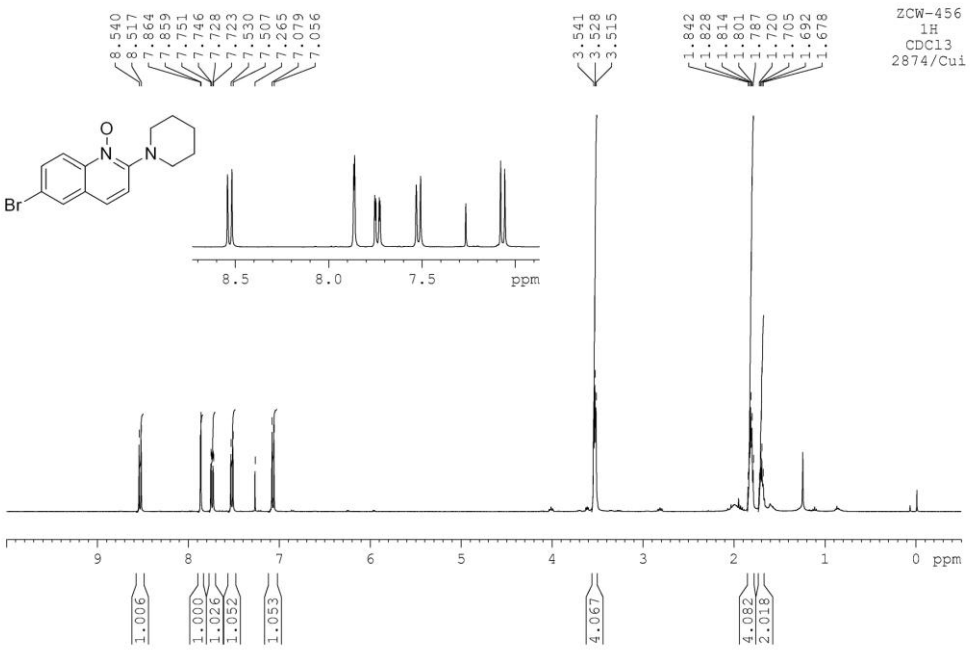
^{13}C NMR spectrum of compound **3ea**



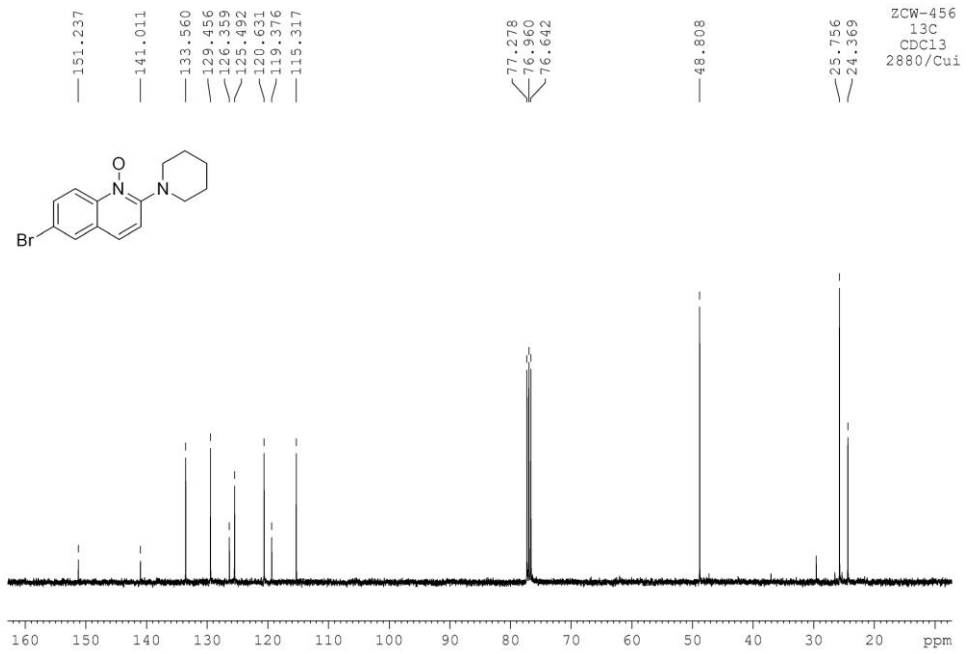
^{1}H NMR spectrum of compound **3fa**



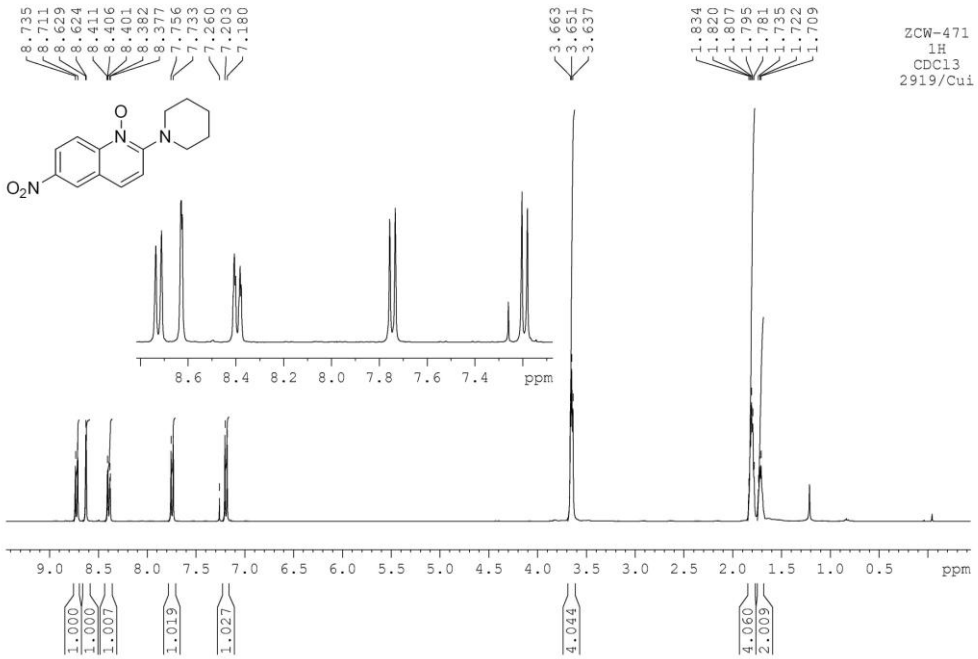
^{13}C NMR spectrum of compound **3fa**



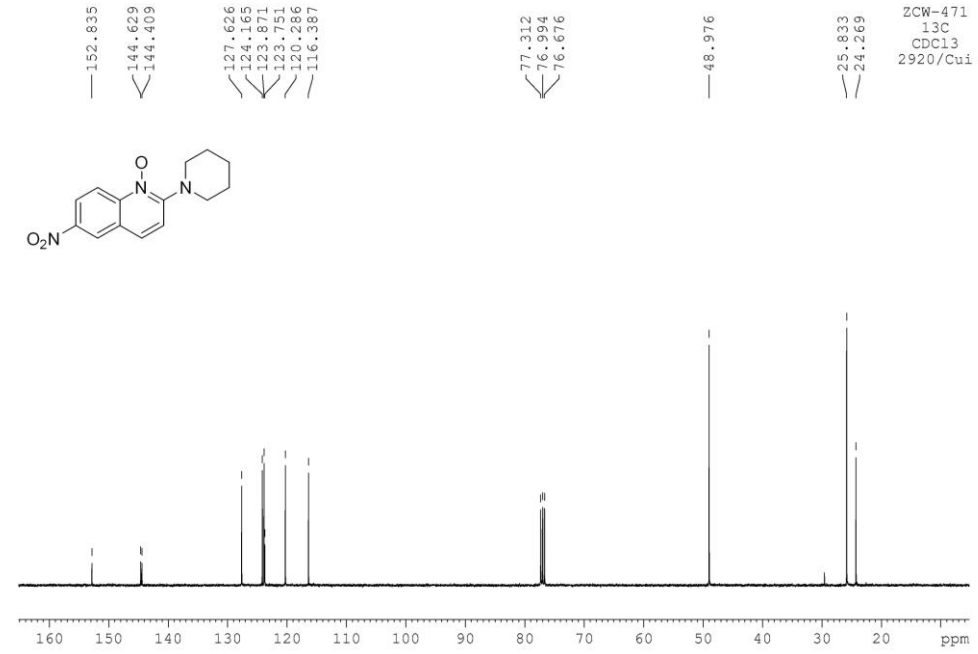
^{1}H NMR spectrum of compound **3ga**



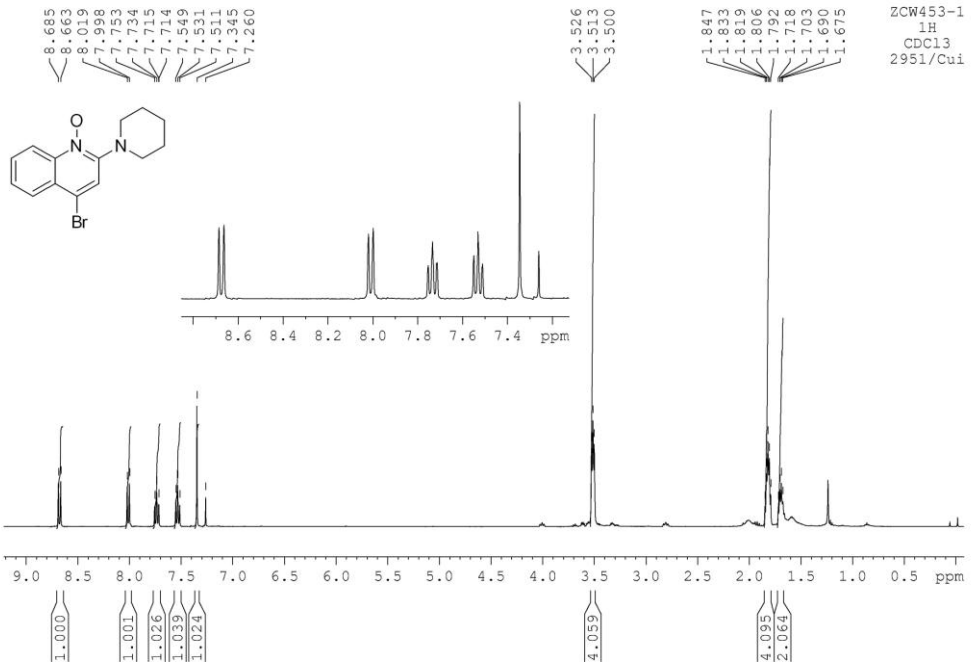
^{13}C NMR spectrum of compound **3ga**



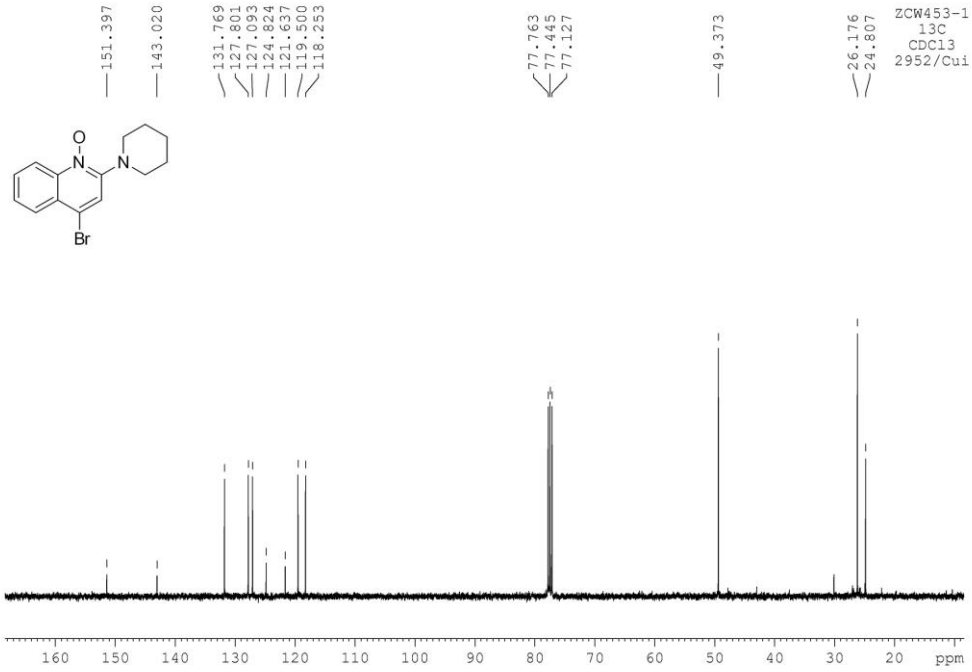
^{1}H NMR spectrum of compound **3ha**



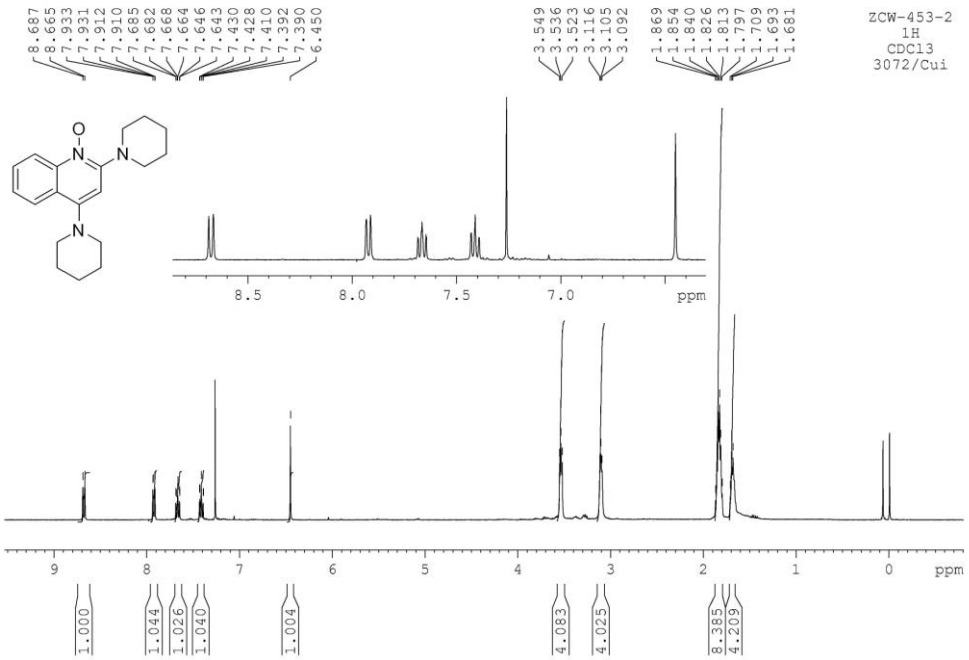
^{13}C NMR spectrum of compound **3ha**



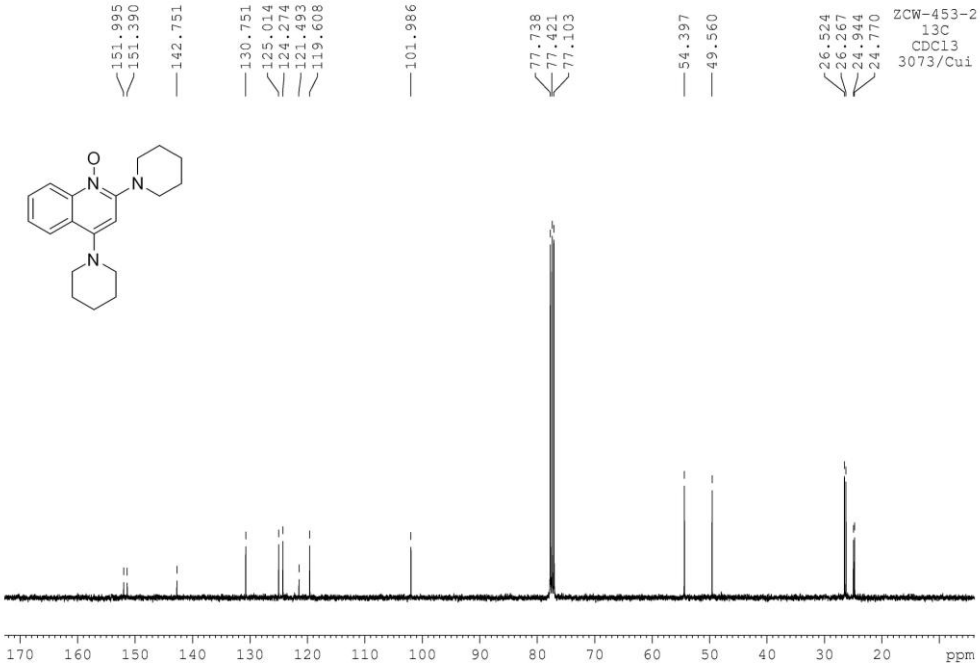
^{1}H NMR spectrum of compound **3ia**



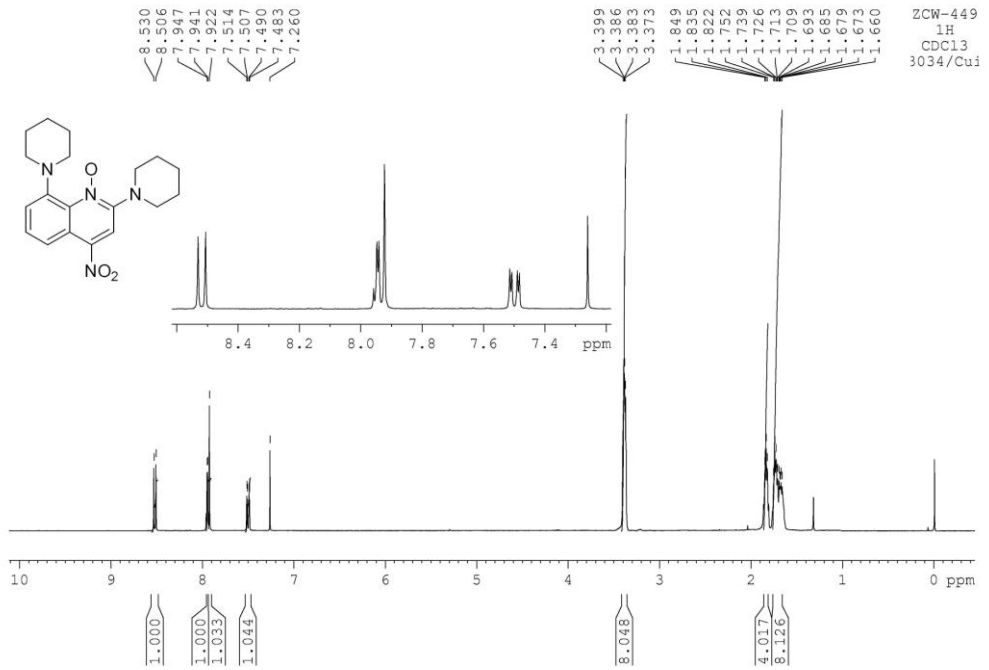
^{13}C NMR spectrum of compound **3ia**



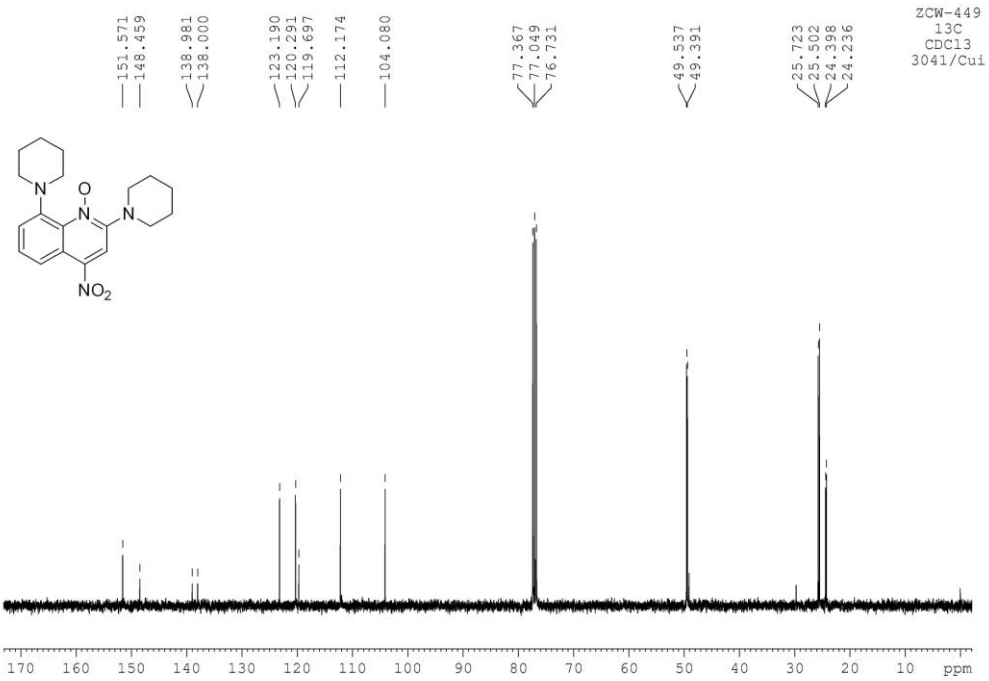
^{1}H NMR spectrum of compound **3ja**



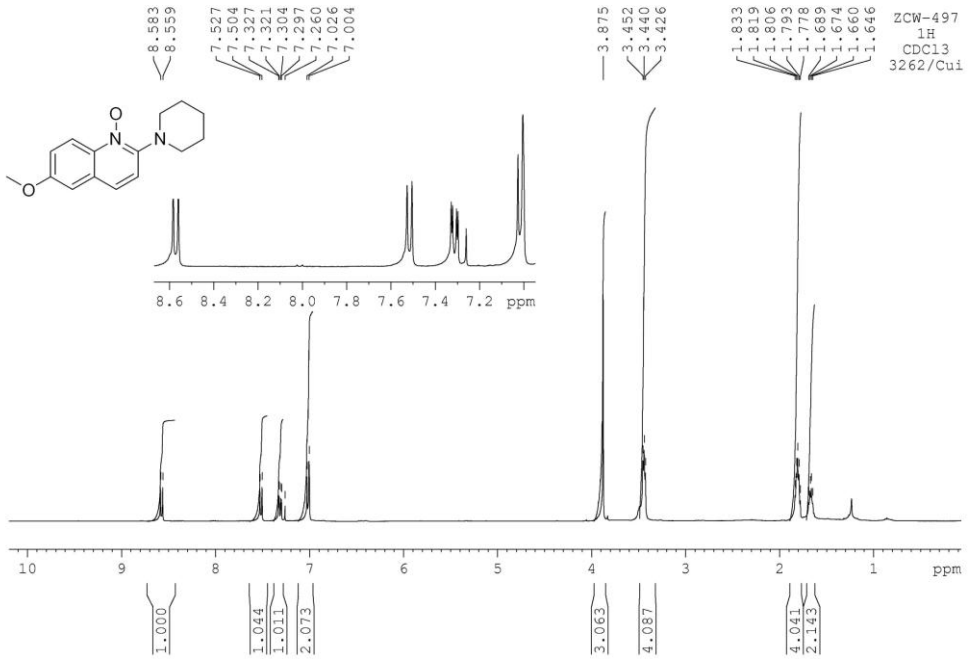
^{13}C NMR spectrum of compound **3ja**



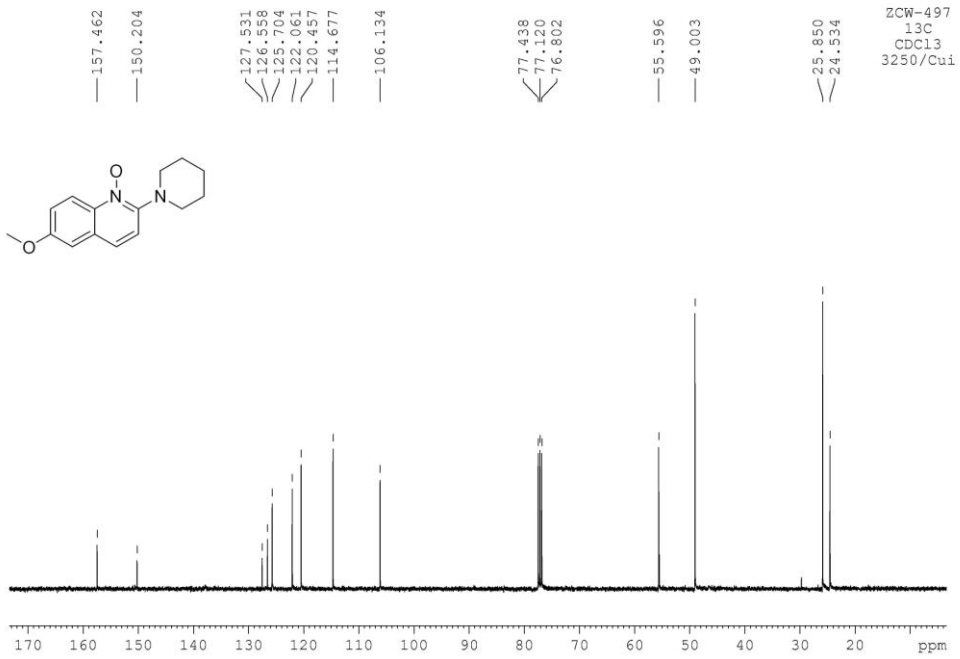
^{1}H NMR spectrum of compound **3ka**



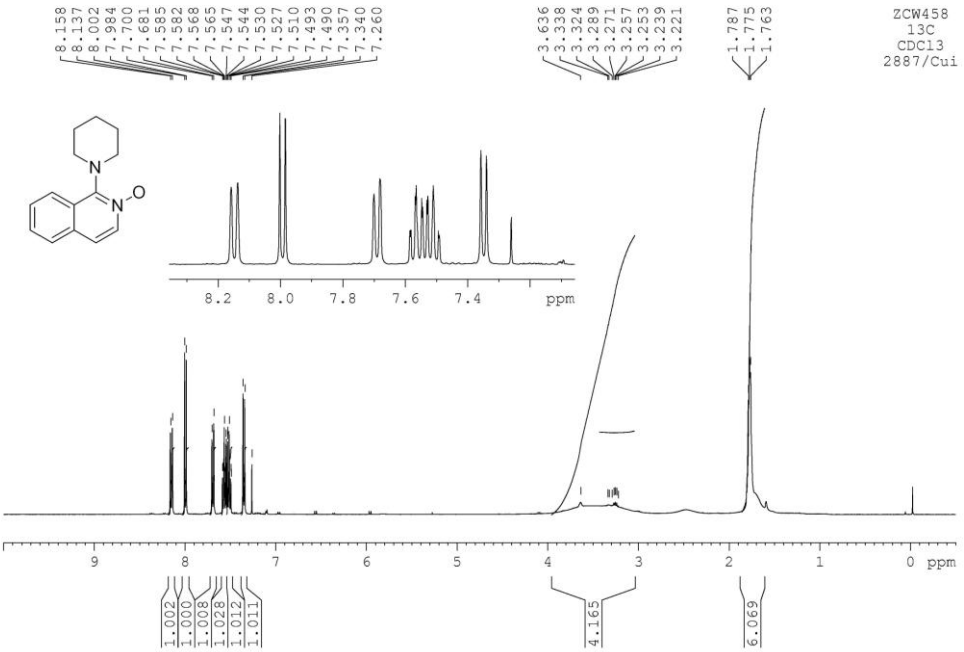
^{13}C NMR spectrum of compound **3ka**



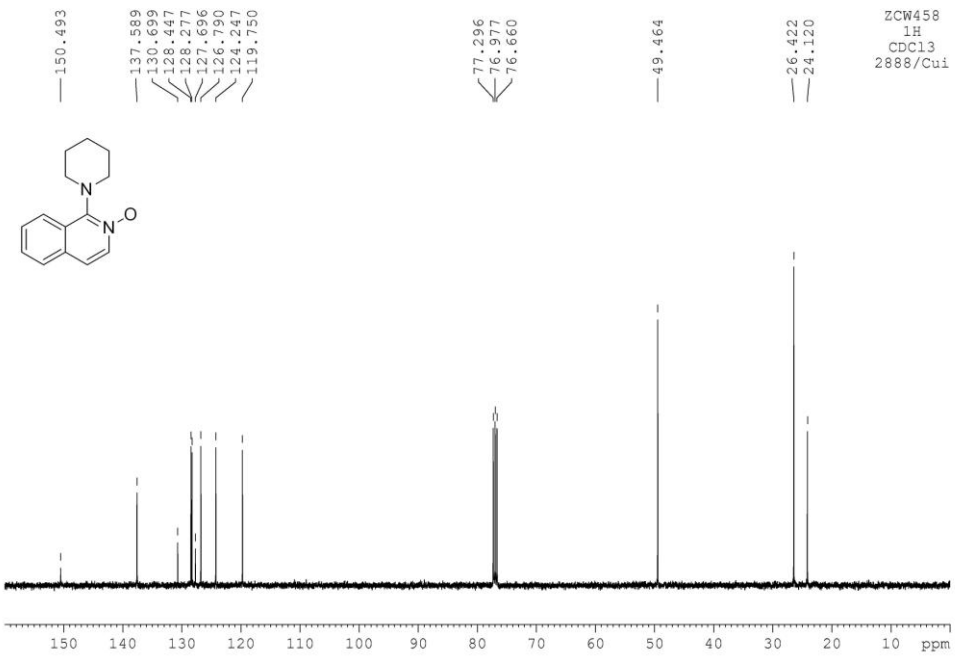
^{1}H NMR spectrum of compound **3la**



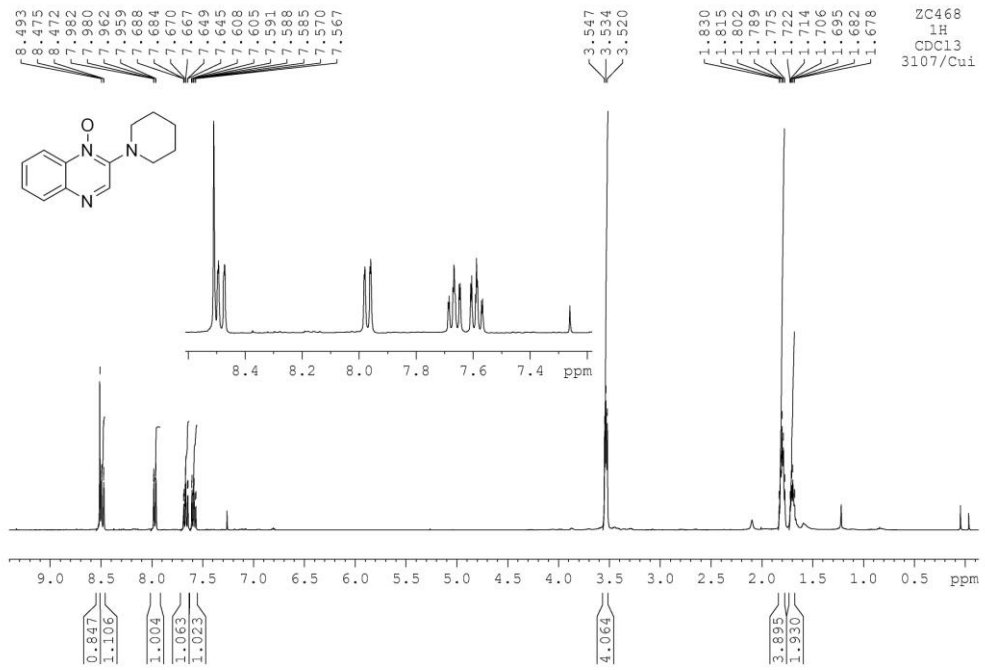
^{13}C NMR spectrum of compound **3la**



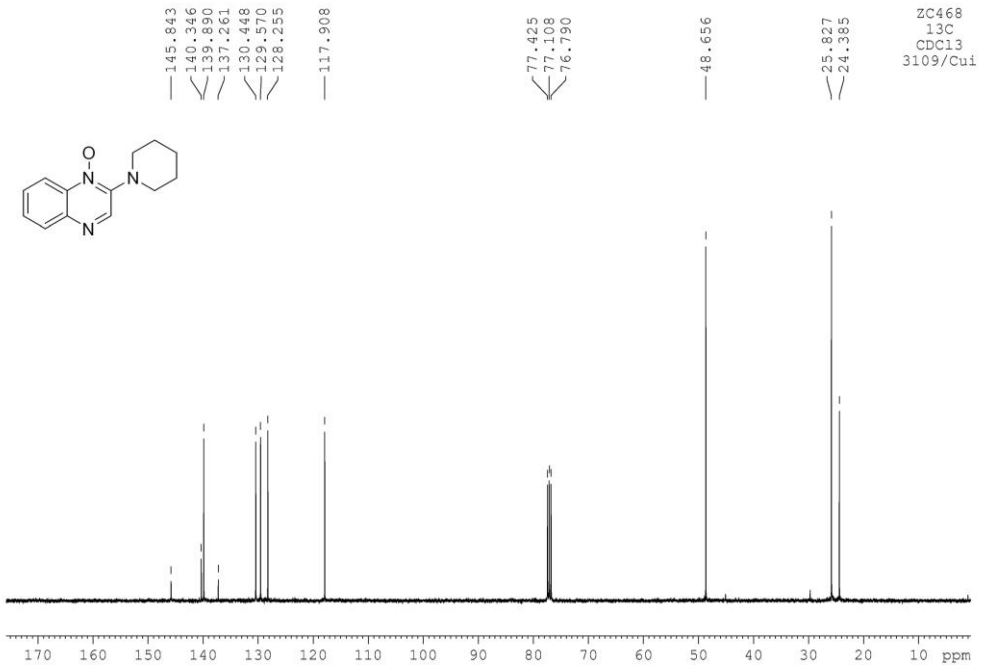
^{1}H NMR spectrum of compound **3oa**



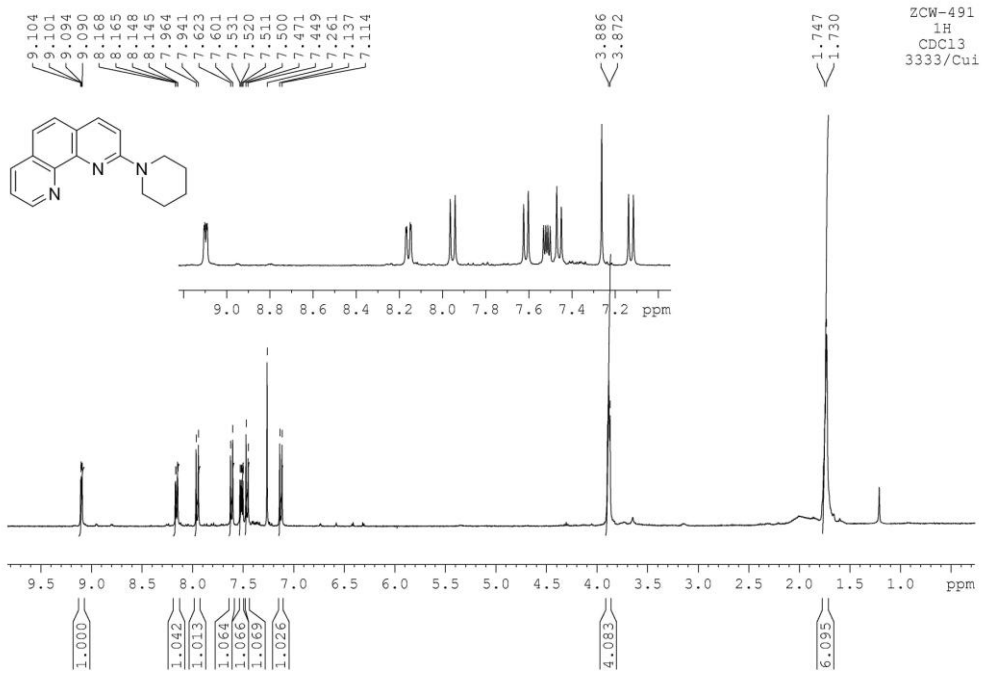
^{13}C NMR spectrum of compound **3oa**



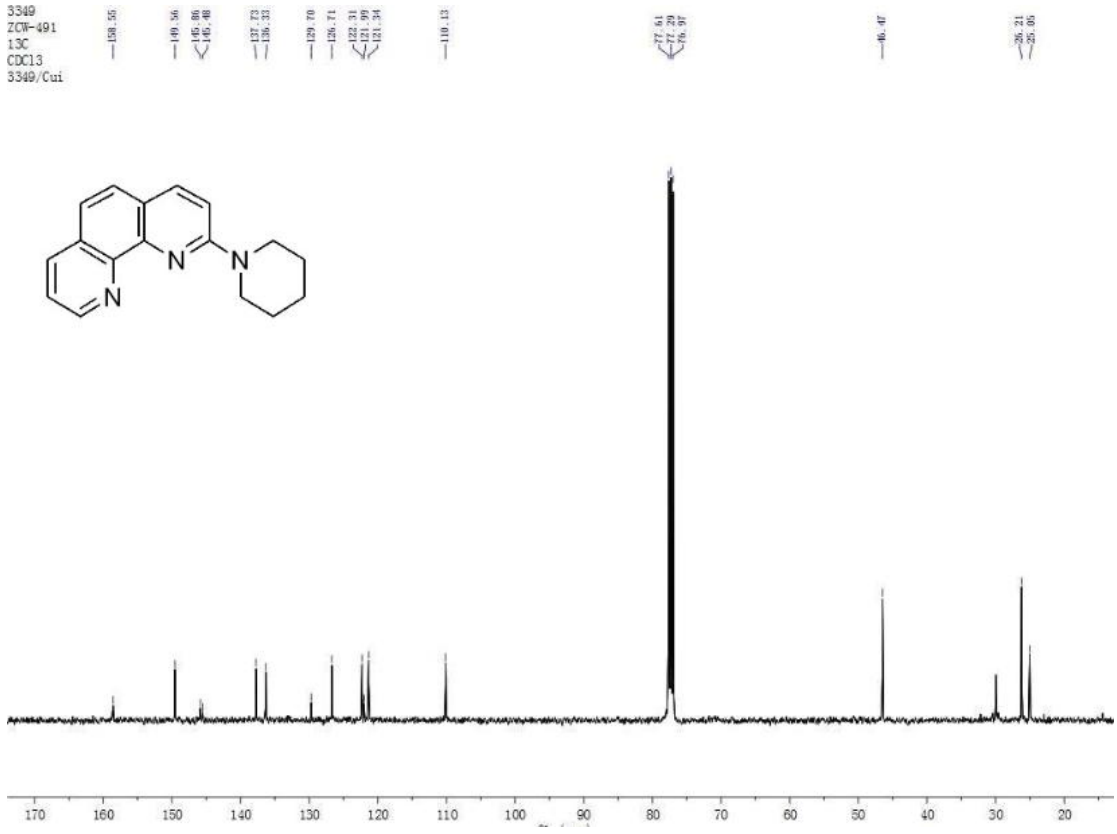
^{1}H NMR spectrum of compound **3pa**



^{13}C NMR spectrum of compound **3pa**



^{1}H NMR spectrum of compound **3qa'**



^{13}C NMR spectrum of compound **3qa'**

(**3qa** was readily reduced to **3qa'** under air)