Supporting information

Transition Metal-Free *α*-Methylation of 1,8-Naphthyridine Derivatives Using DMSO as Methylation Reagent

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1. General information

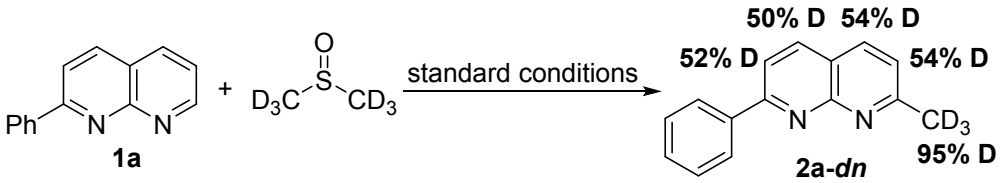
All the obtained products were characterized by melting points (m.p), ^{1}H-NMR, ^{13}C-NMR. Melting points were measured on an Electrothemal SGW-X4 microscopy digital melting point apparatus and are uncorrected; ^{1}H-NMR and ^{13}C-NMR spectra were obtained on Bruker-400/500 and referenced to 7.26 ppm for chloroform solvent with TMS as internal standard (0 ppm). Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), multiplet (m); TLC was performed using commercially prepared 100-400 mesh silica gel plates (GF254), and visualization was effected at 254 nm; Unless otherwise stated, all the reagents were purchased from commercial sources (J&K Chemic, TCI, Fluka, Acros, SCRC), used without further purification.

2. Typical procedure for the synthesis of 2a

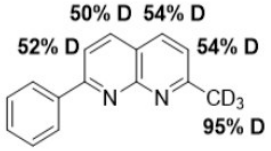
In a Schlenk tube of 25mL, 2-phenyl-1,8-naphthyridine **1a** (41.2 mg, 0.2 mmol), *t*-BuONa (0.4 mmol, 2.0 equiv), and 1-phenylethanol (0.2 mmol, 1 equiv) were dissolved in DMSO (2 mL) under visible light irradiation (blue LEDs, 3W) and stirred at 100 ° C for 8 h, irradiation was conducted in a photochemical reactor equipped with visible light irradiation (420 nm<λ<780 nm). After completion of the reaction, the resulting solution was cooled to room temperature; the solution was diluted with ethyl acetate (10 mL), washed with water (5 mL), extracted with ethyl acetate (3×5 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by preparative TLC on silica gel to give the desired product (**2a**).

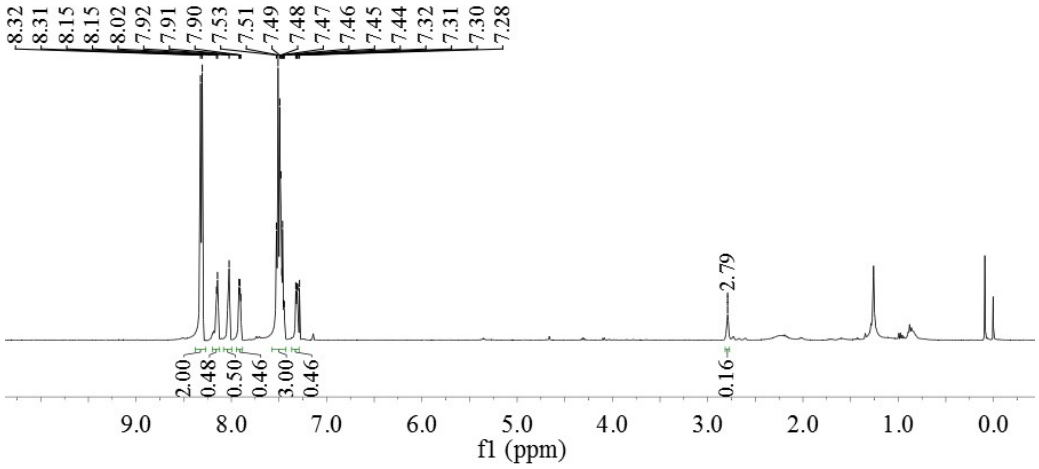
Reaction device

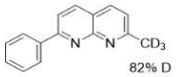
3. Deuterium labeling experiment

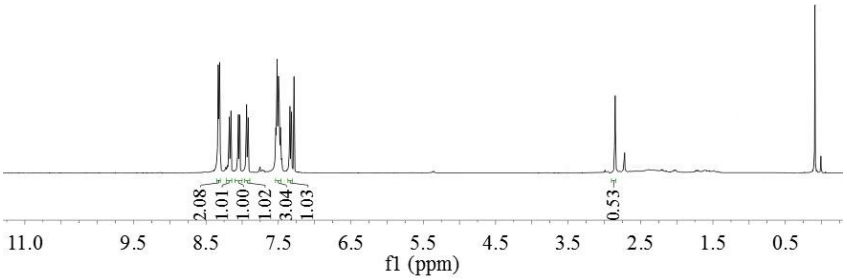


^{1}H- NMR spectrum of deuterated product

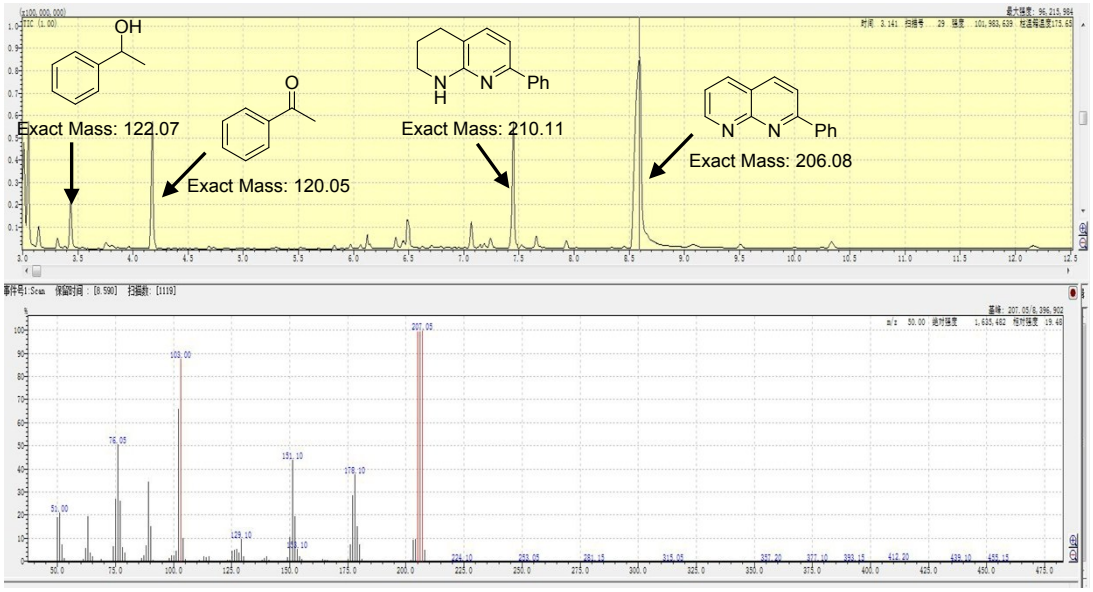




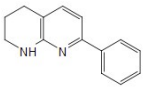


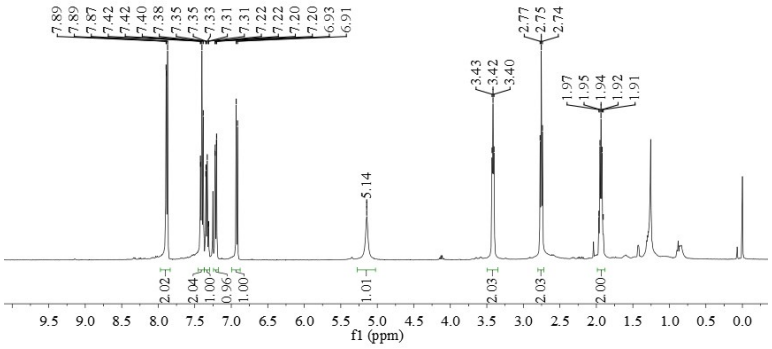


Detection of reaction by-products by GC-MS analysis



^{1}H- NMR spectrum of by-products 1a’





4. Crystal data and structure refinement for compound 2q (CCDC: 1918670)

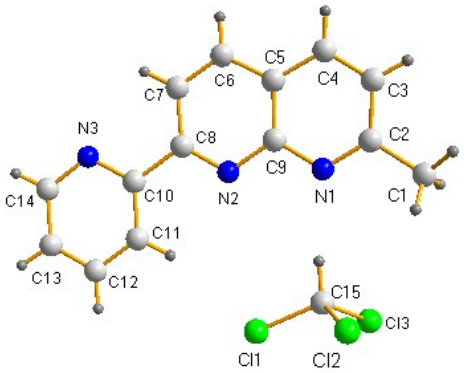


Figure 1. ORTEP drawing of **2q** with the numbering scheme.

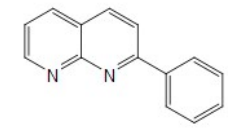
Table S1. Crystal data and structure refinement for **2q**.

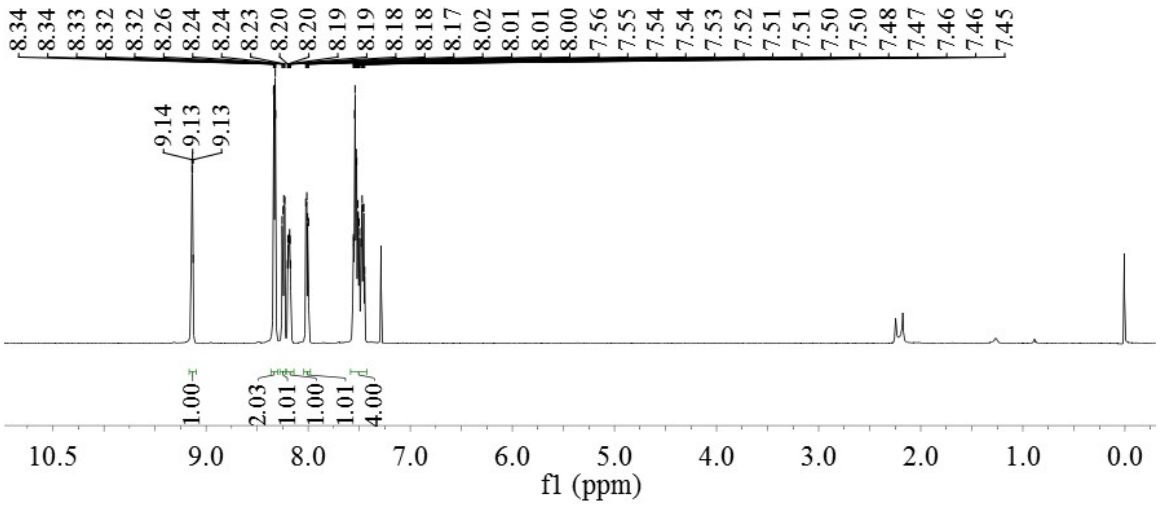
Identification code	2q	
Empirical formula	C15 H12 Cl3 N3	
Formula weight	340.63	
Temperature	296.15 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pnma	
Unit cell dimensions	a = 10.485(4) Å	α= 90°.
	b = 6.832(3) Å	β= 90°.
	c = 21.082(8) Å	γ = 90°.
Volume	1510.2(10) $Å^3$	
Z	4	
Density (calculated)	1.498 Mg/m^3	
Absorption coefficient	0.602 mm^{-1}	
F(000)	696	
Crystal size	0.21 x 0.20 x 0.19 mm^3	
Theta range for data collection	1.932 to 27.499°.	
Index ranges	-13<=h<=13, -8<=k<=8, -26<=l<=27	
Reflections collected	16256	
Independent reflections	1865 [R(int) = 0.0384]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.6696	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1865 / 0 / 125	

Goodness-of-fit on F^2	1.063
Final R indices [I>2sigma(I)]	R1 = 0.0653, wR2 = 0.1794
R indices (all data)	R1 = 0.0787, wR2 = 0.1961
Extinction coefficient	n/a
Largest diff. peak and hole	0.483 and -0.759 e.$Å^{-3}$

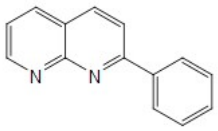
5. NMR spectra of products

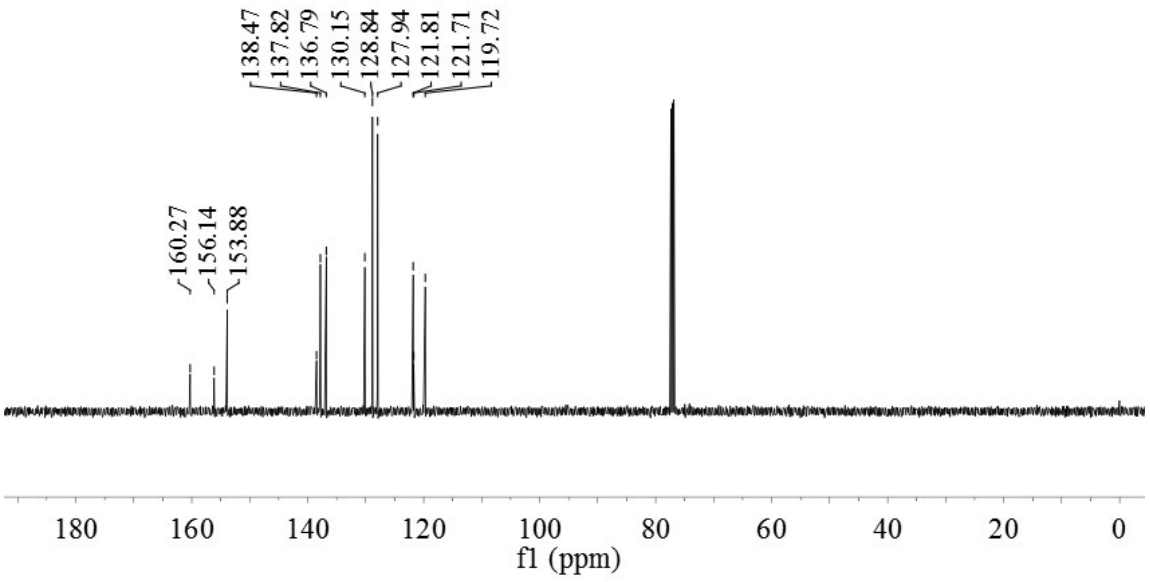
^{1}H NMR Spectrum for 1a ($CDCl_3$, 400 MHz)



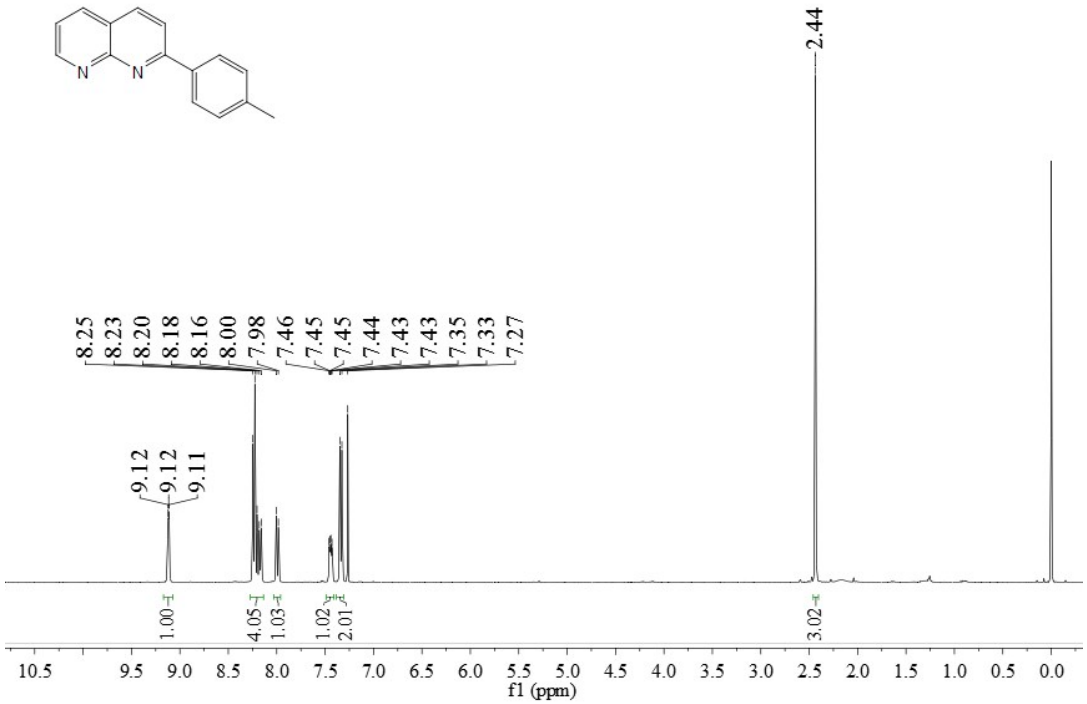


^{13}C NMR Spectrum for 1a ($CDCl_3$, 101 MHz)

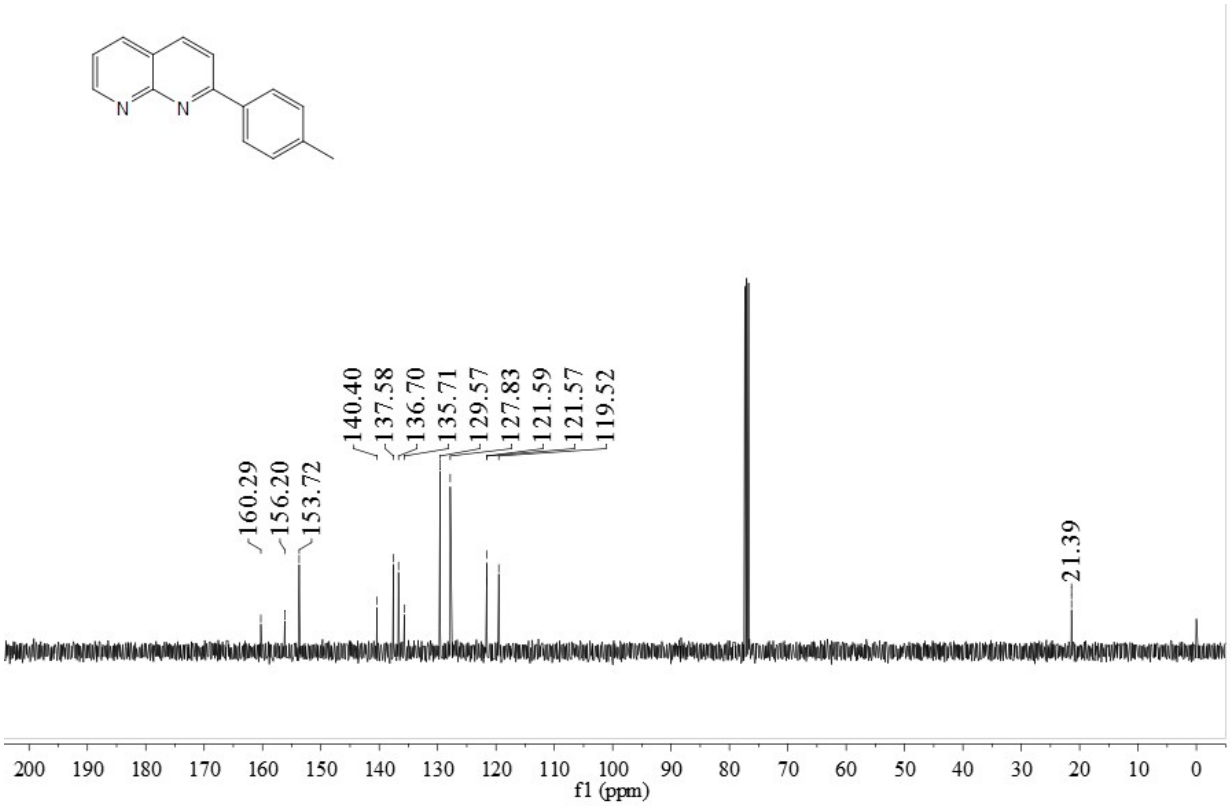




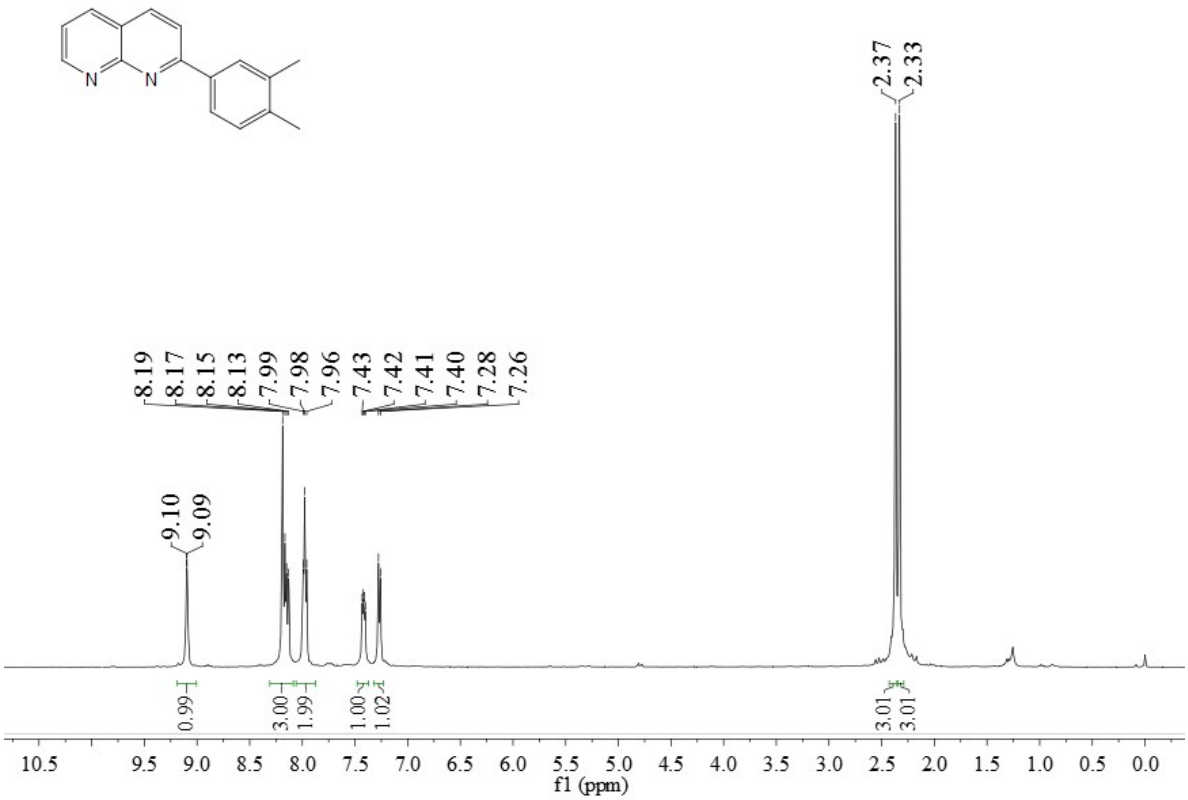
^{1}H NMR Spectrum for 1b ($CDCl_3$, 400 MHz)



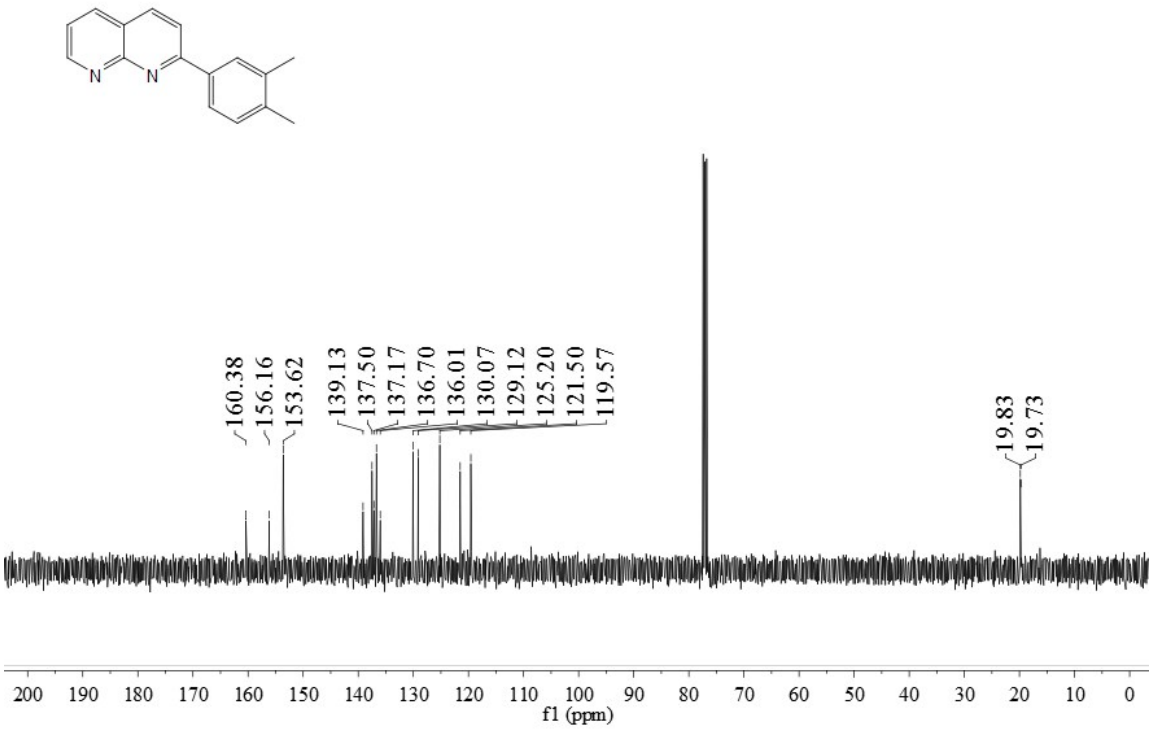
^{13}C NMR Spectrum for 1b ($CDCl_3$, 101 MHz)



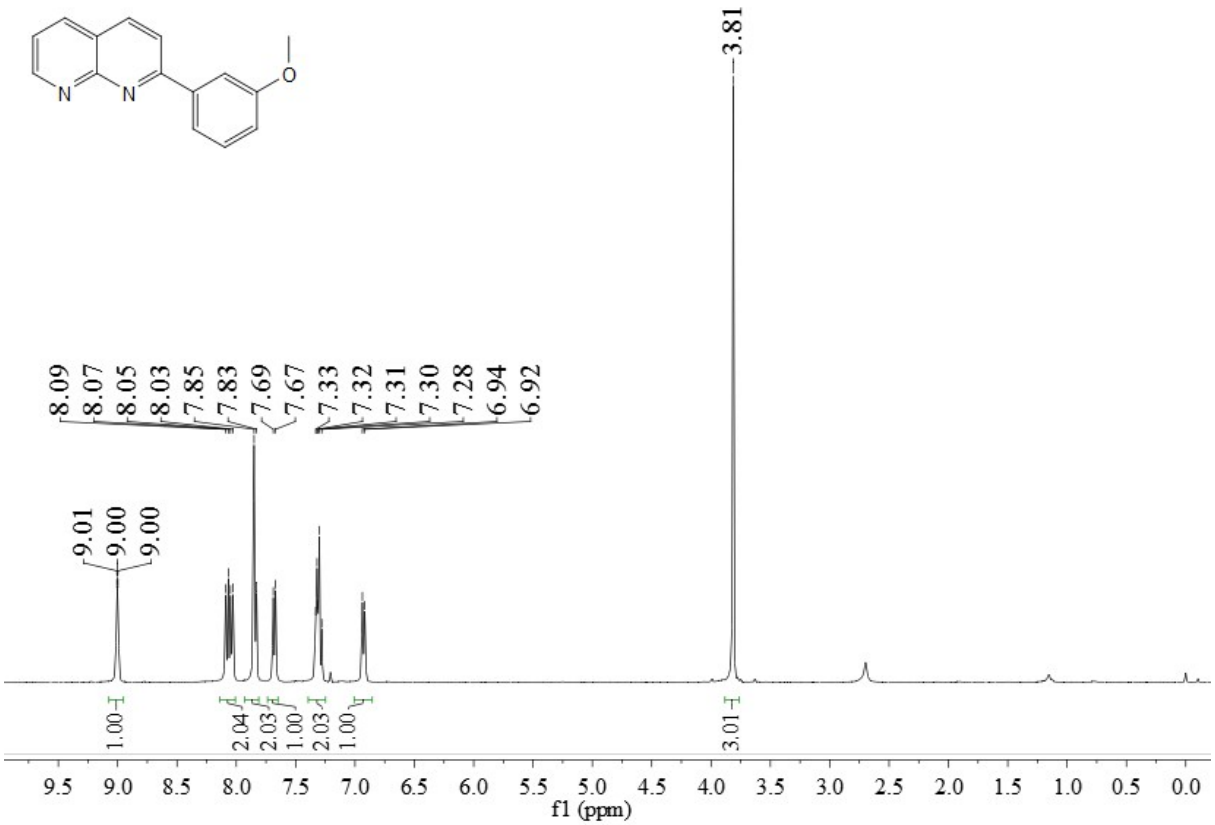
^{1}H NMR Spectrum for 1c ($CDCl_3$, 400 MHz)



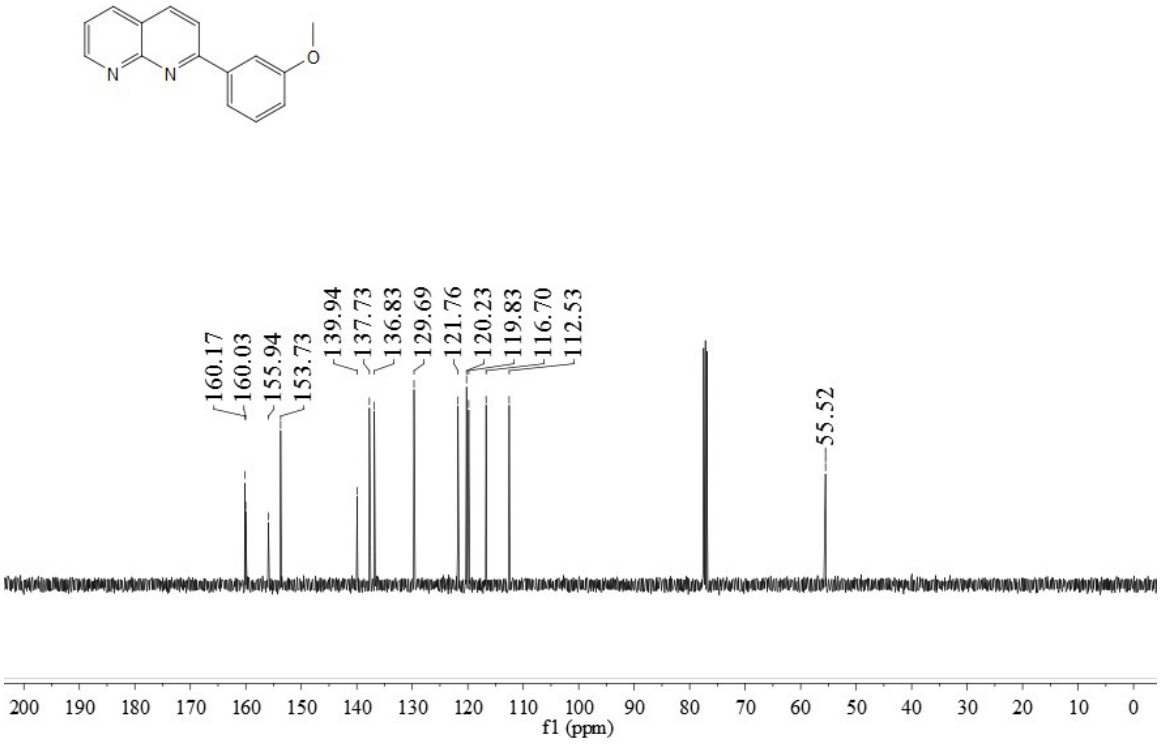
^{13}C NMR Spectrum for 1c ($CDCl_3$, 101 MHz)



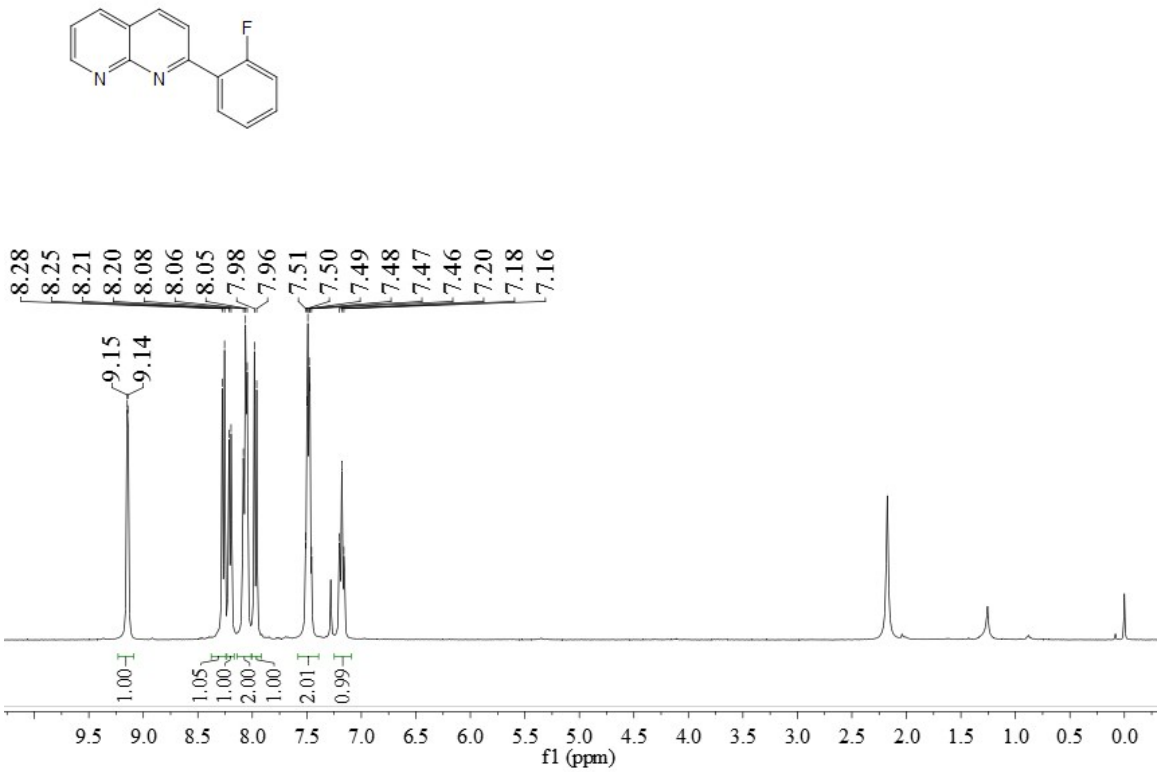
^{1}H NMR Spectrum for 1d ($CDCl_3$, 400 MHz)



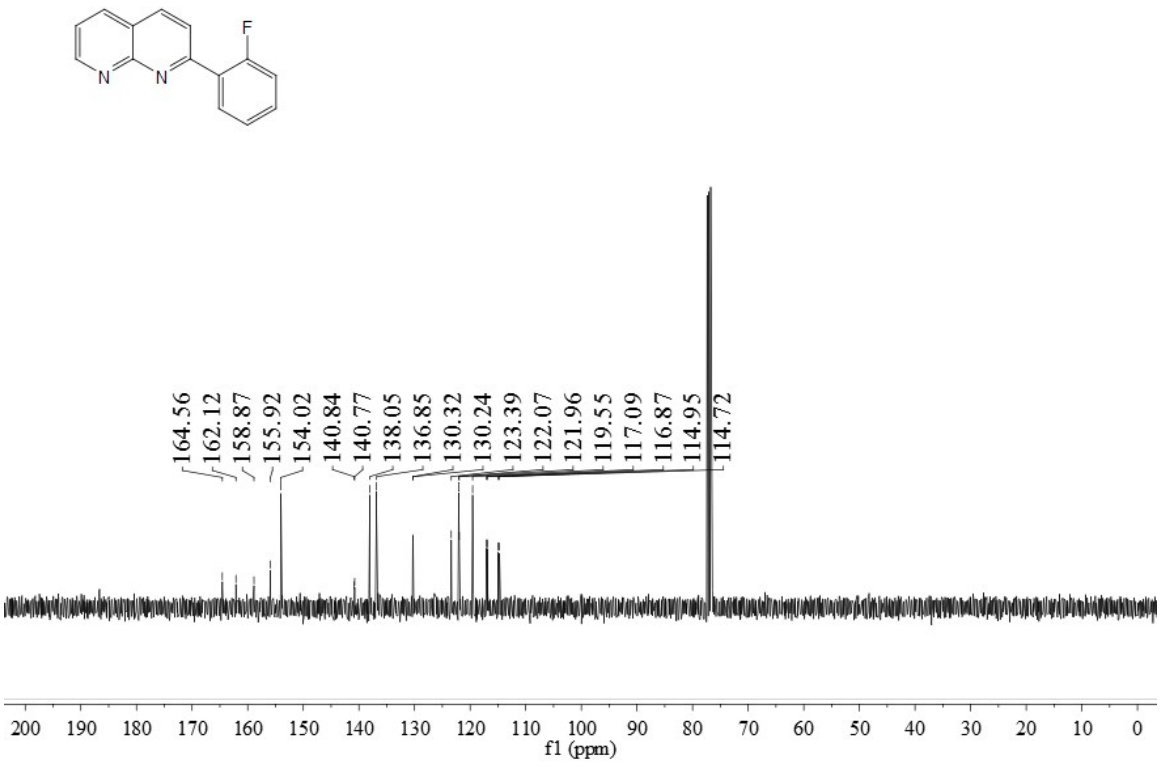
^{13}C NMR Spectrum for 1d ($CDCl_3$, 101 MHz)



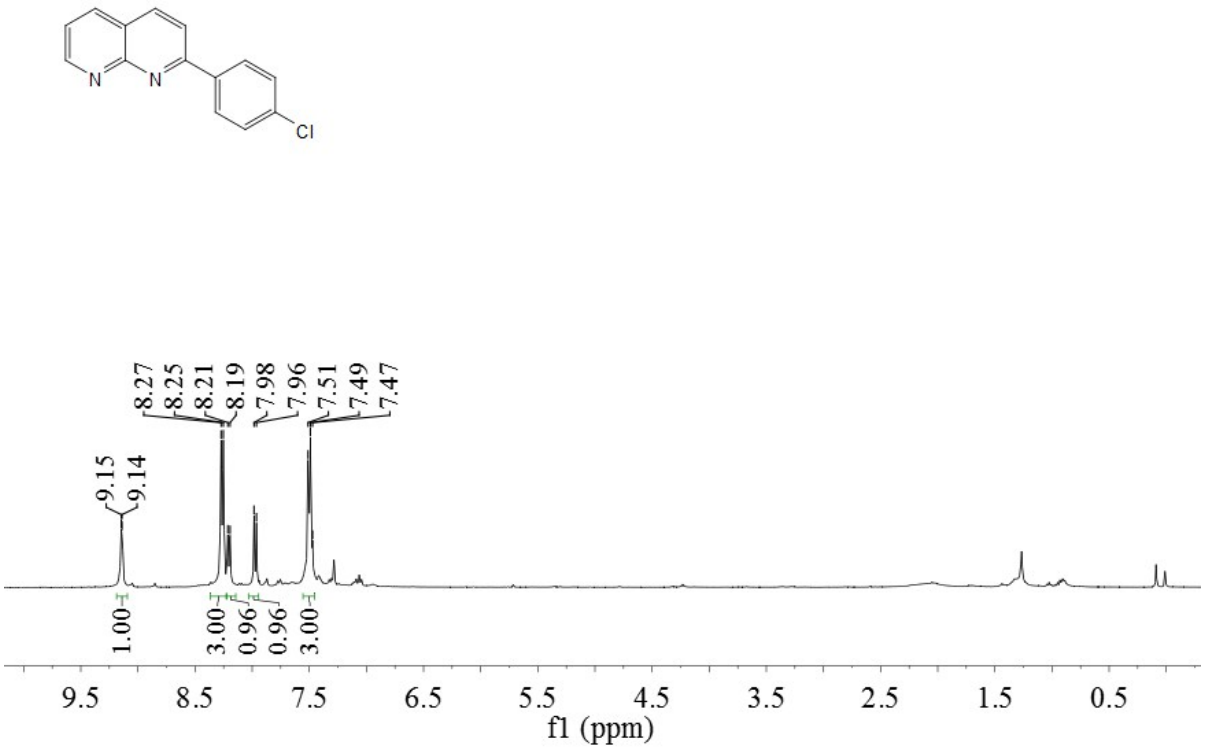
^{1}H NMR Spectrum for 1e ($CDCl_3$, 400 MHz)



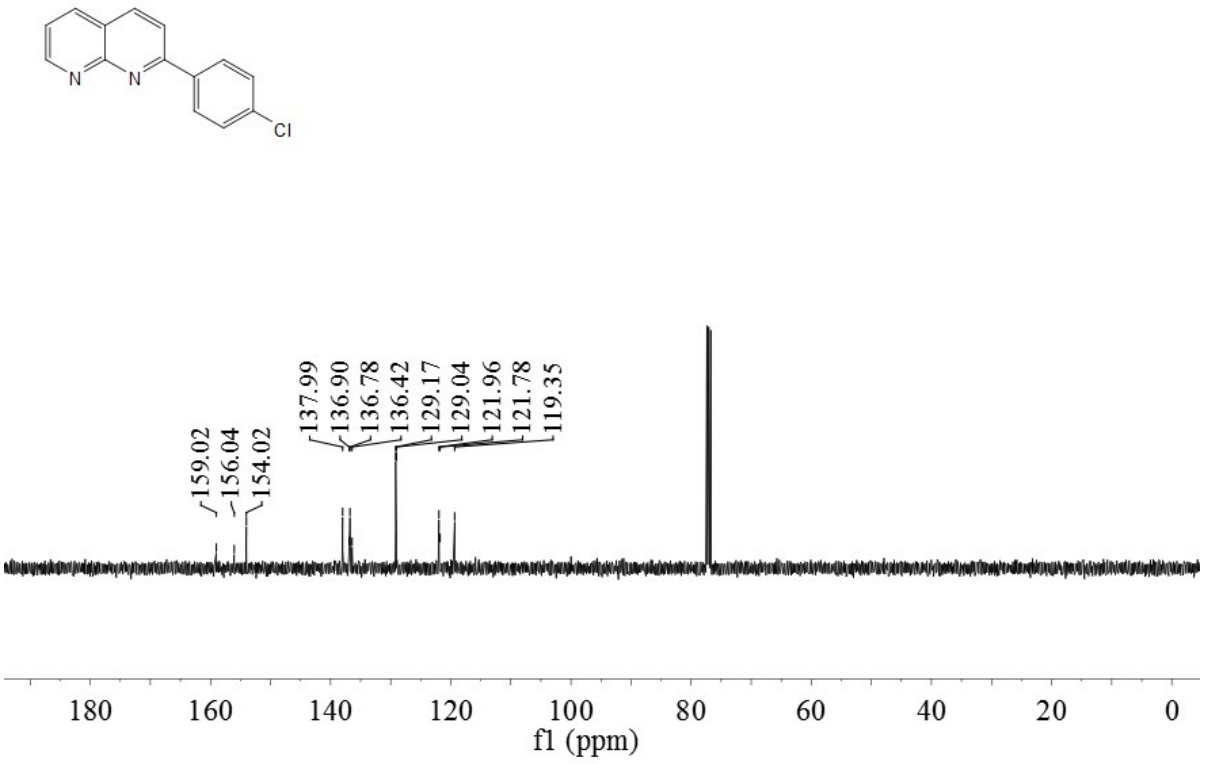
^{13}C NMR Spectrum for 1e ($CDCl_3$, 101 MHz)



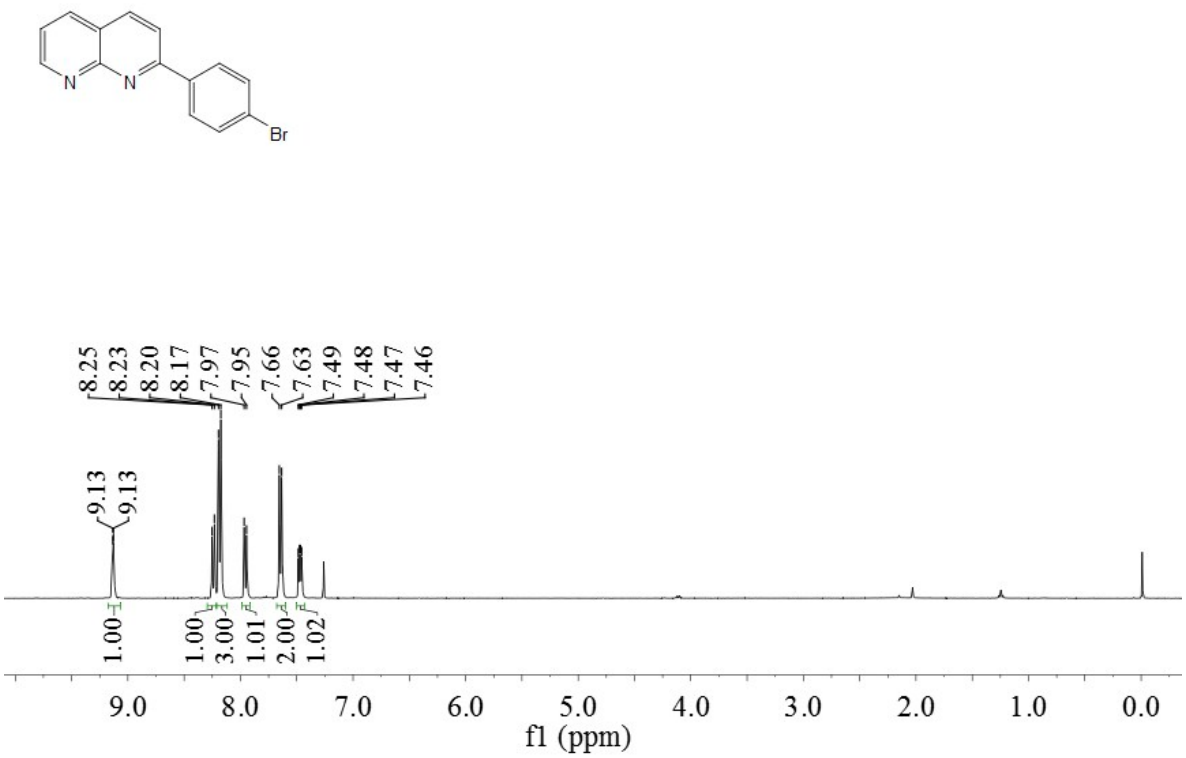
^{1}H NMR Spectrum for 1f ($CDCl_3$, 400 MHz)



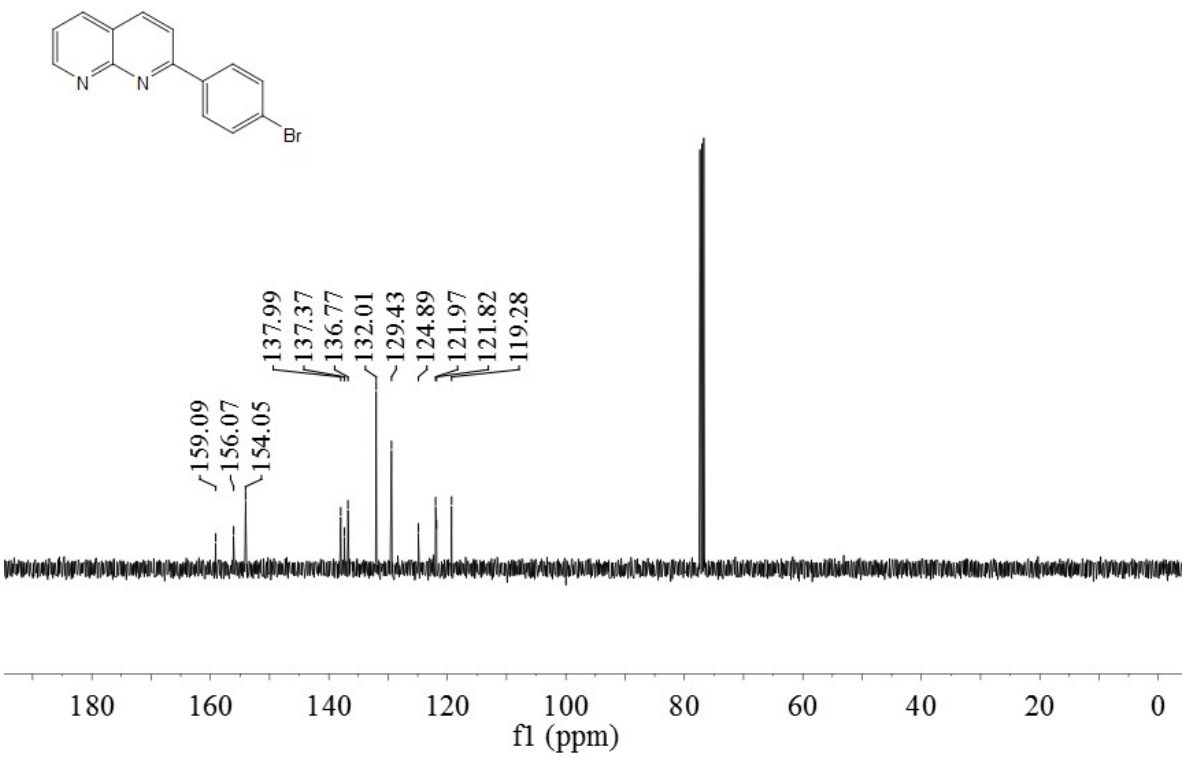
^{13}C NMR Spectrum for 1f ($CDCl_3$, 101 MHz)



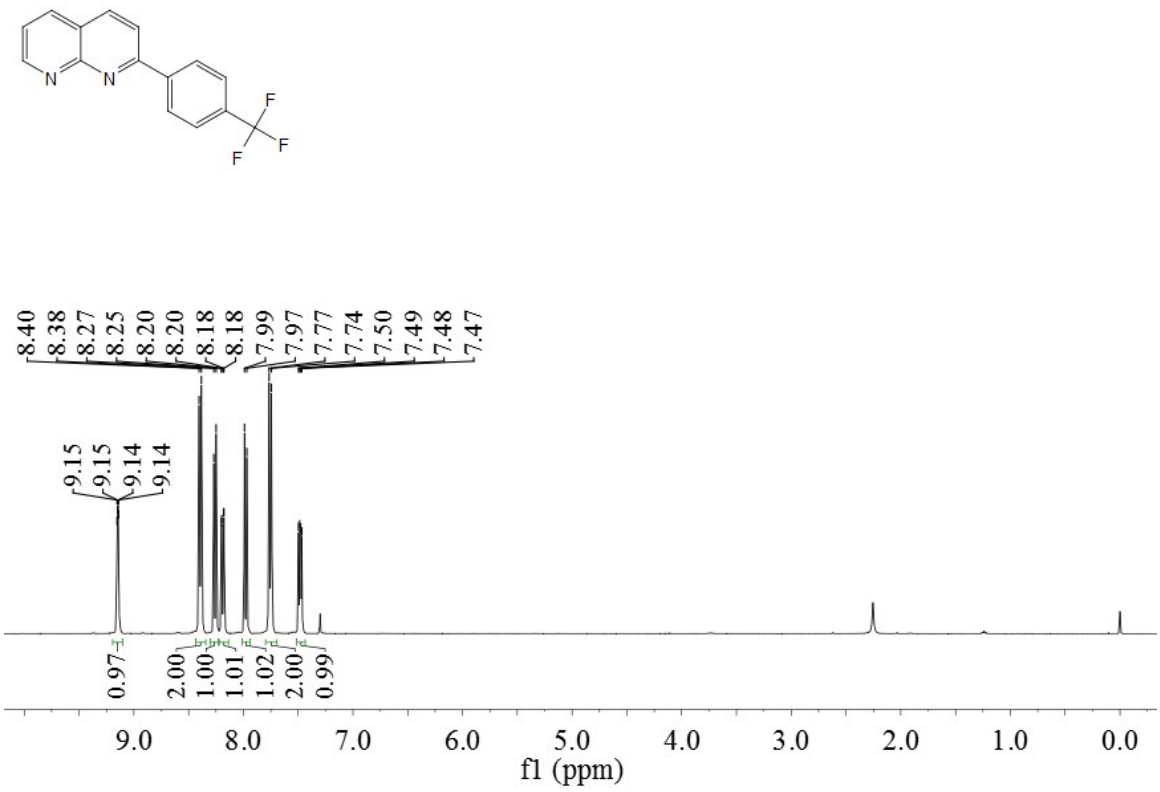
^{1}H NMR Spectrum for 1g ($CDCl_3$, 400 MHz)



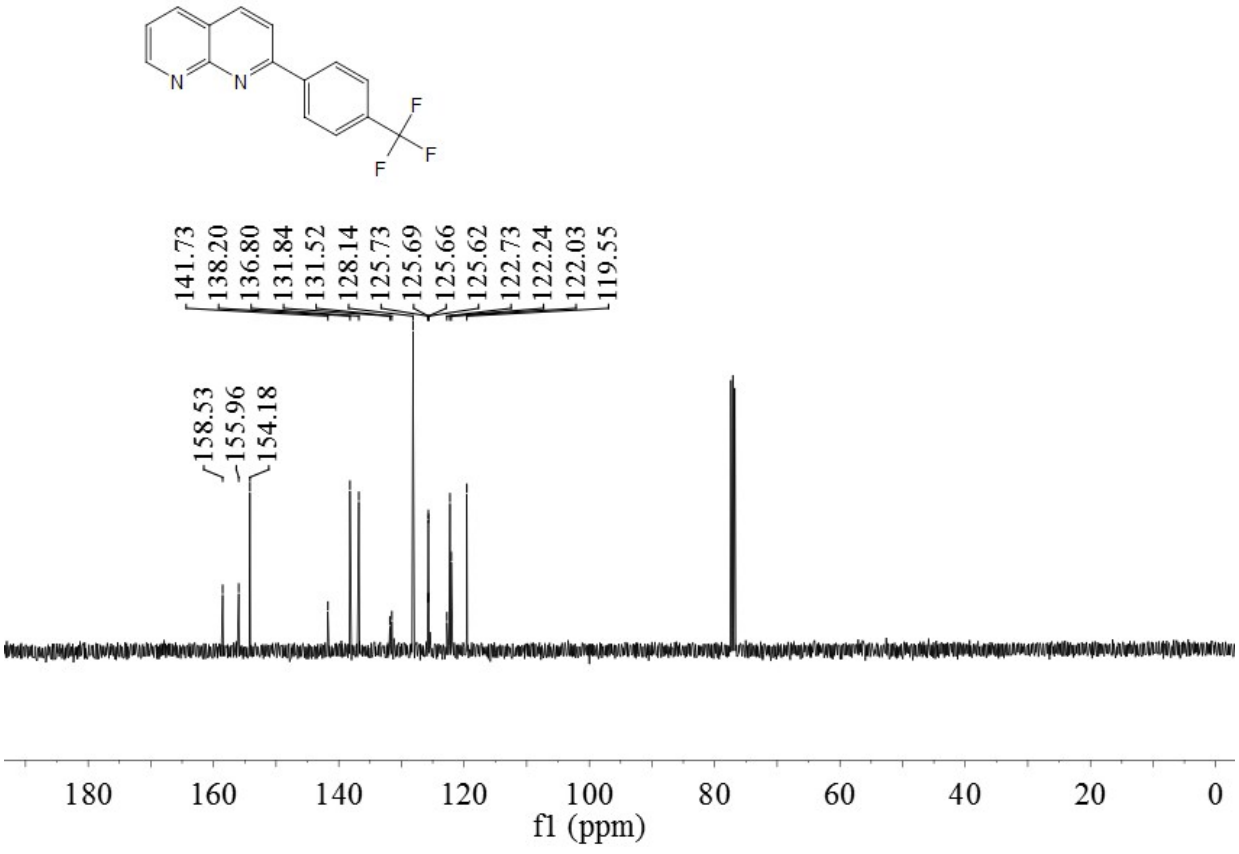
^{13}C NMR Spectrum for 1g ($CDCl_3$, 101 MHz)



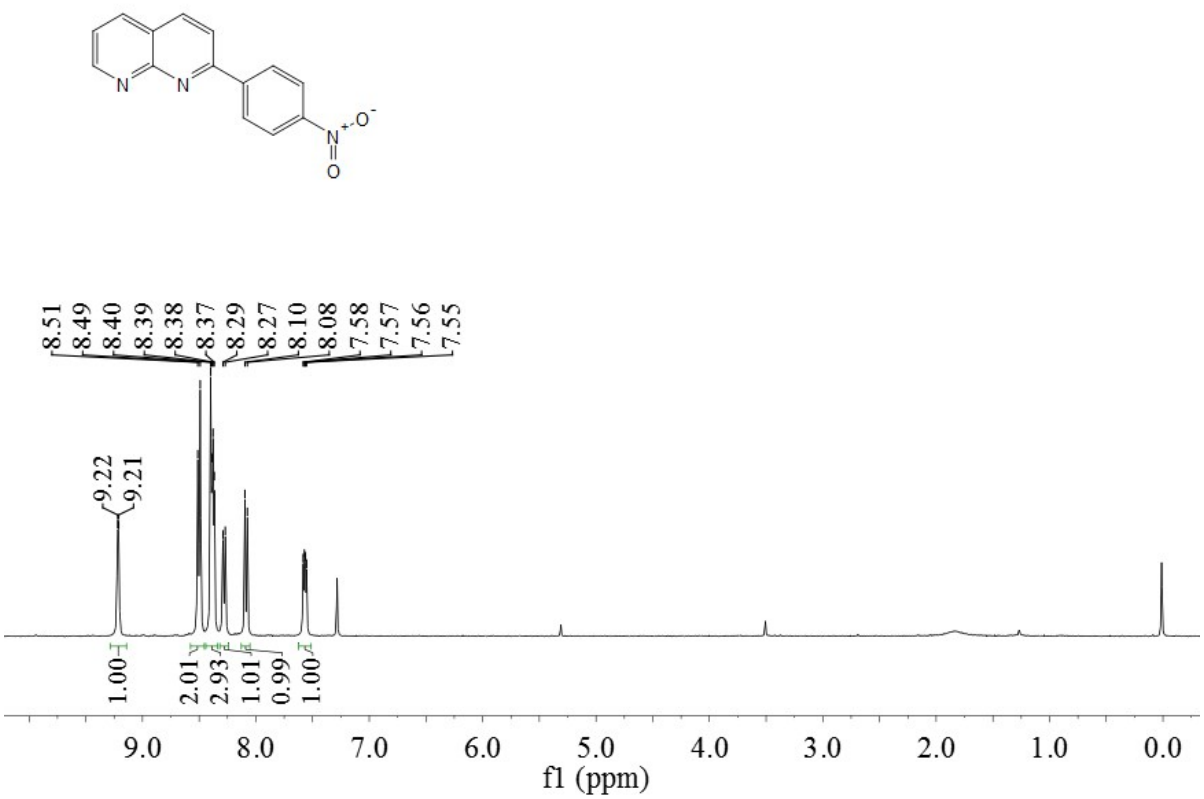
^{1}H NMR Spectrum for 1i ($CDCl_3$, 400 MHz)



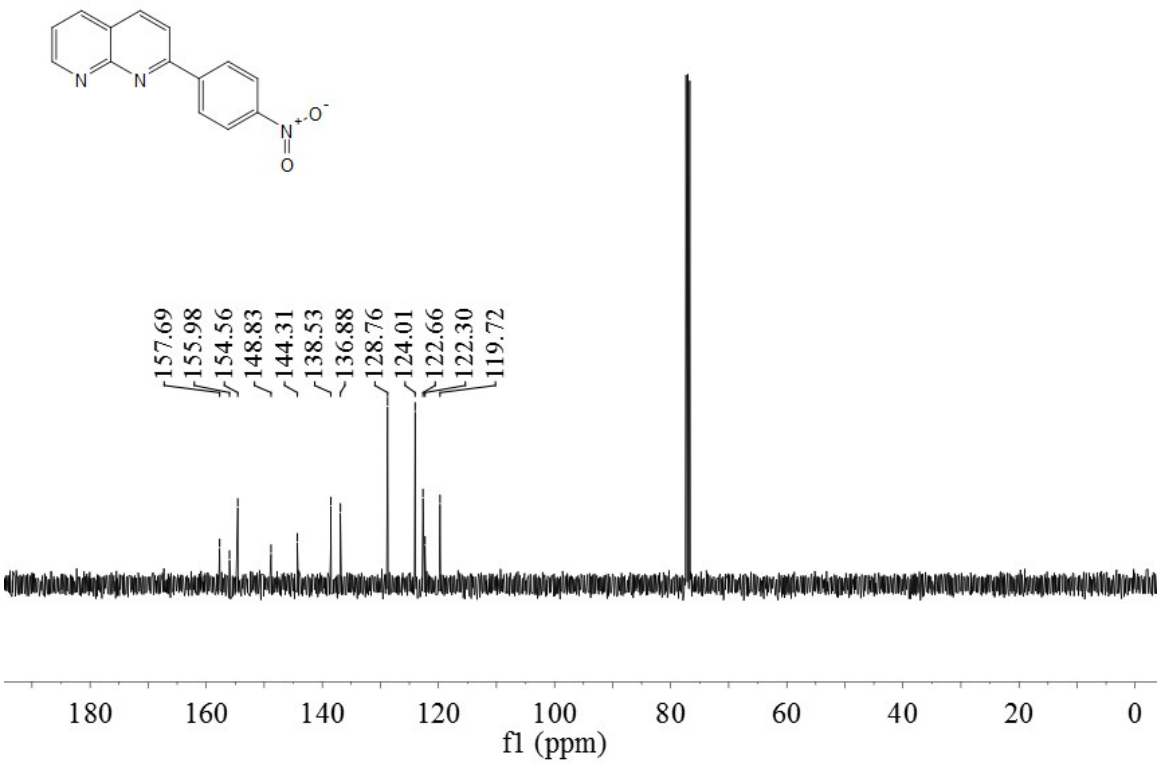
^{13}C NMR Spectrum for 1i ($CDCl_3$, 101 MHz)



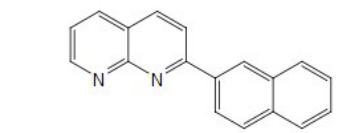
^{1}H NMR Spectrum for 1j ($CDCl_3$, 400 MHz)

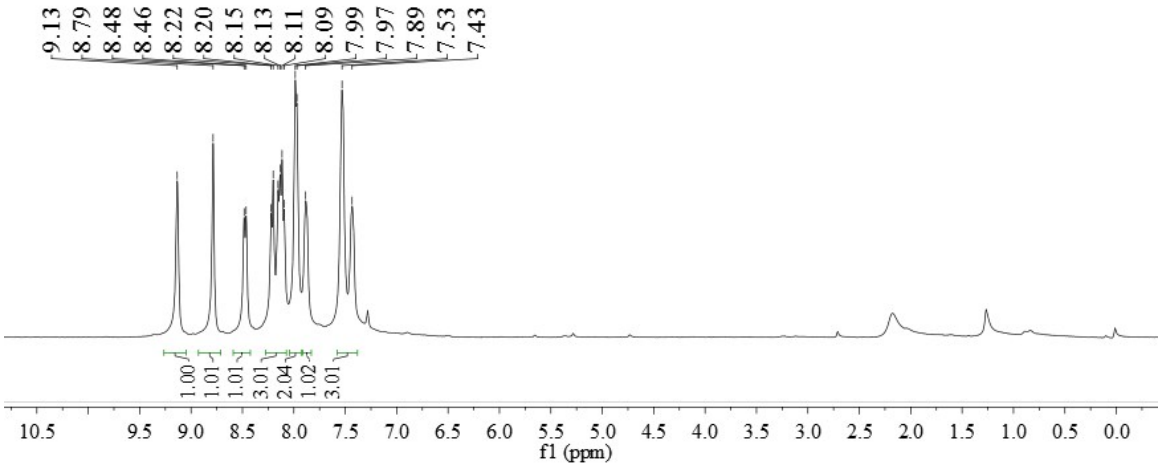


^{13}C NMR Spectrum for 1j ($CDCl_3$, 101 MHz)

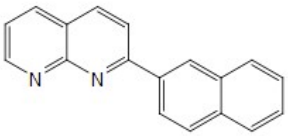


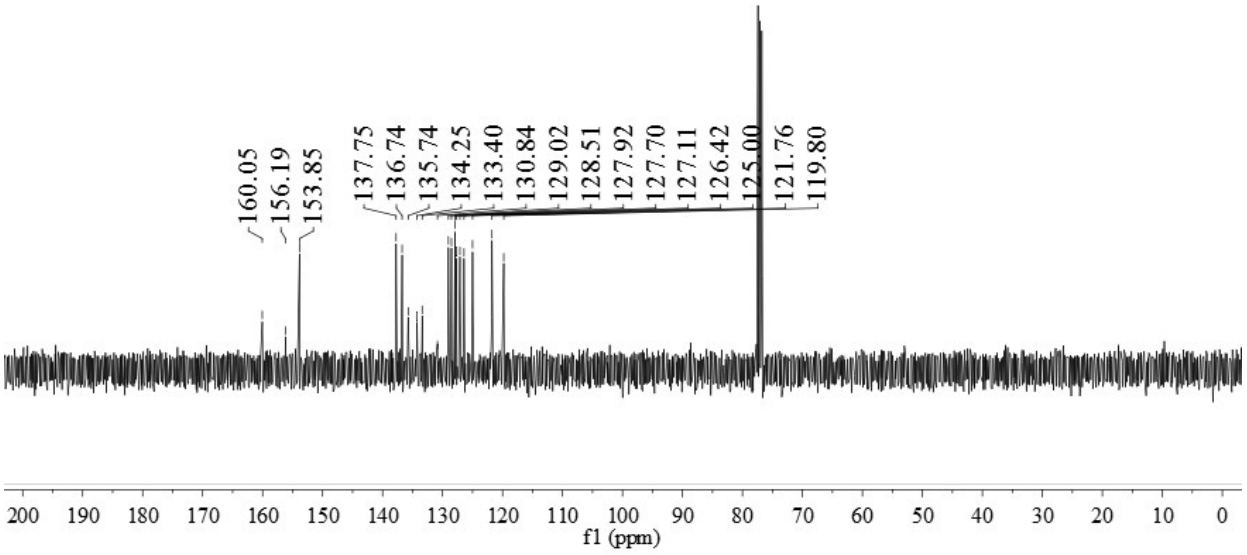
^{1}H NMR Spectrum for 1k ($CDCl_3$, 400 MHz)



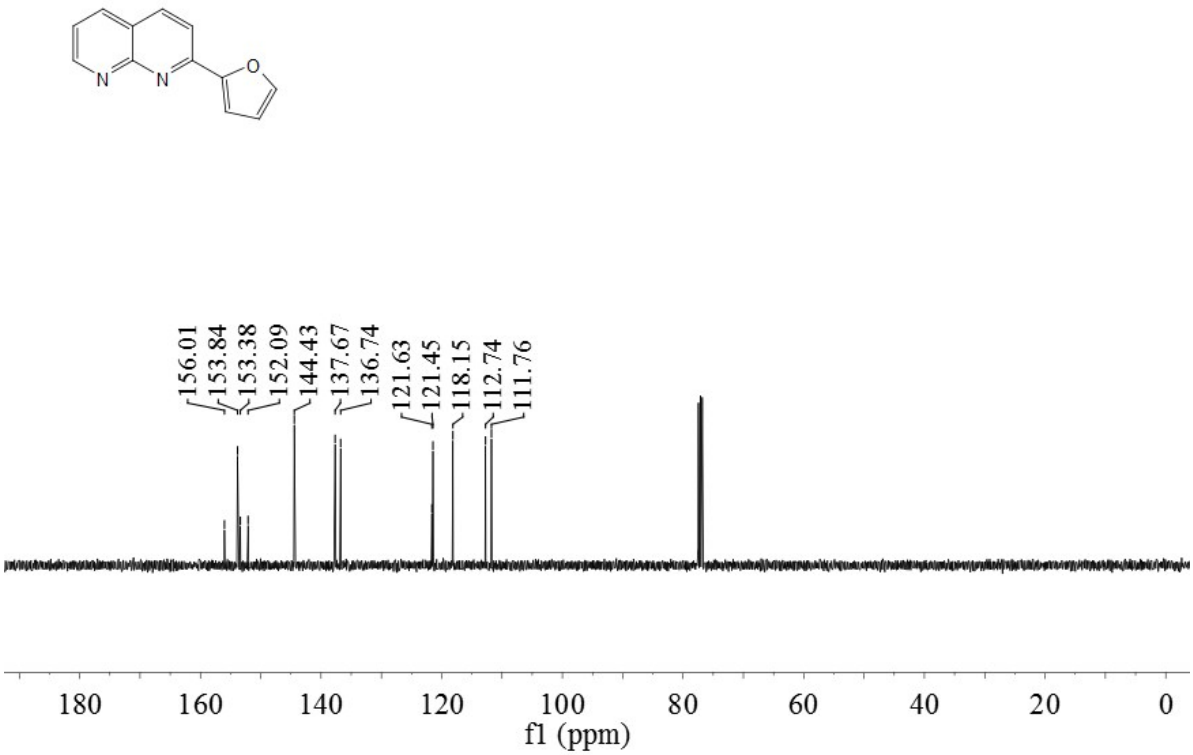


^{13}C NMR Spectrum for 1k ($CDCl_3$, 101 MHz)

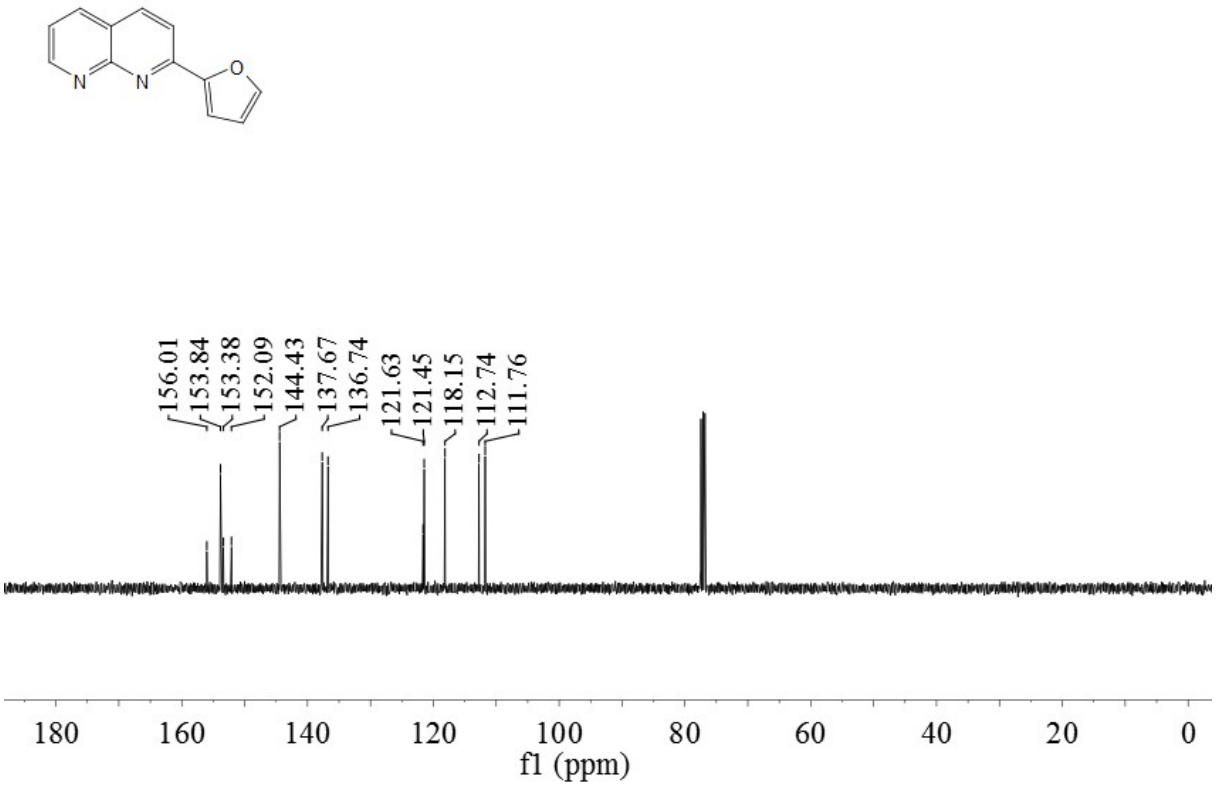




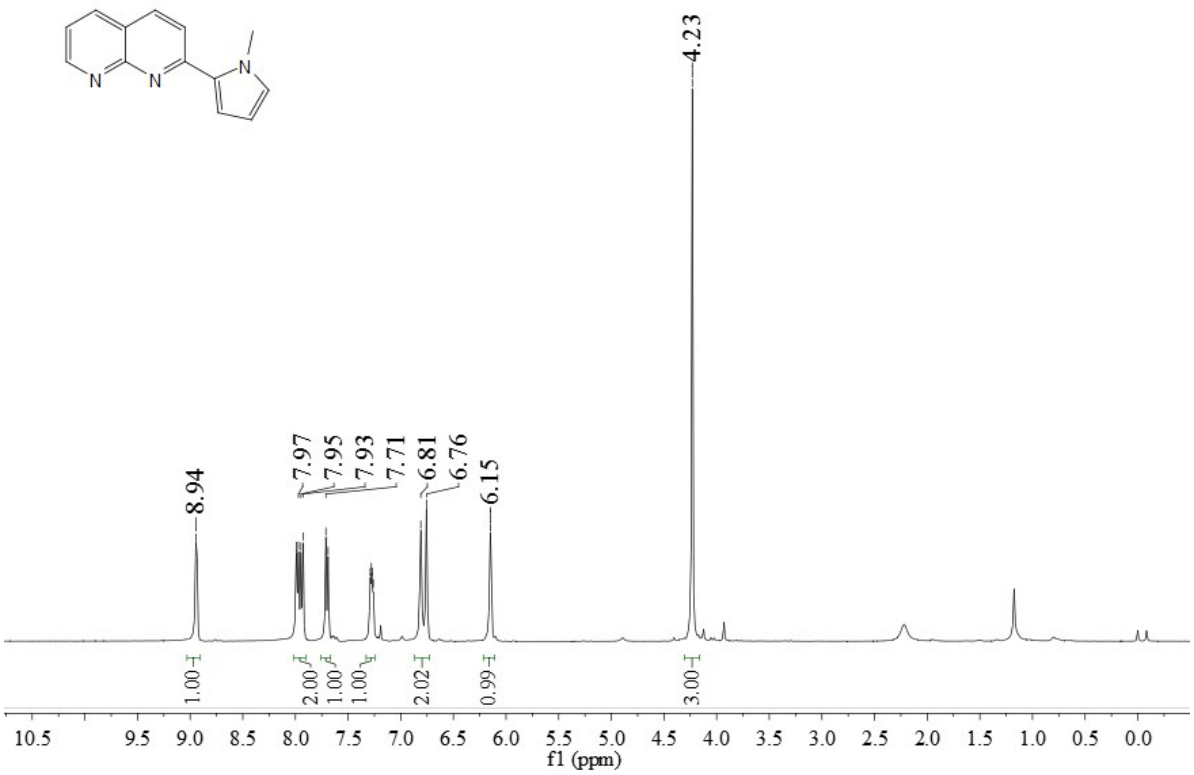
^{1}H NMR Spectrum for 1l ($CDCl_3$, 400 MHz)



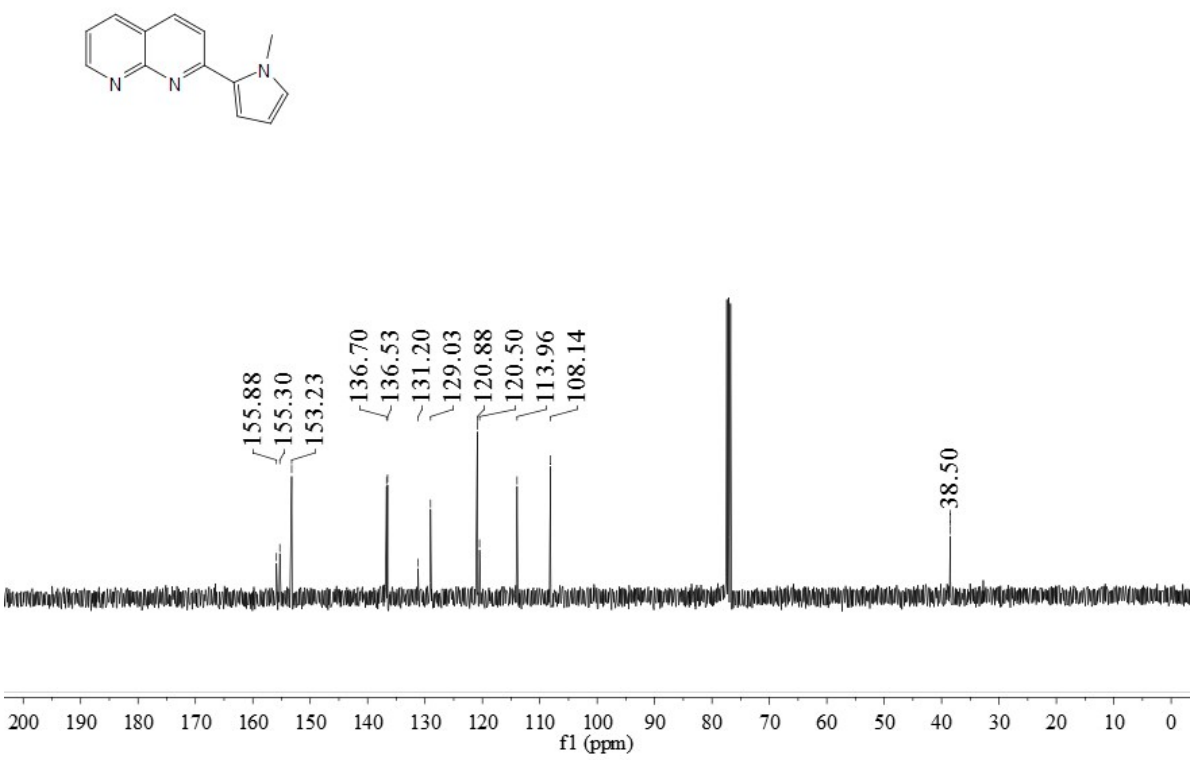
^{13}C NMR Spectrum for 1l ($CDCl_3$, 101 MHz)



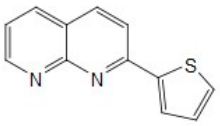
^{1}H NMR Spectrum for 1m ($CDCl_3$, 400 MHz)

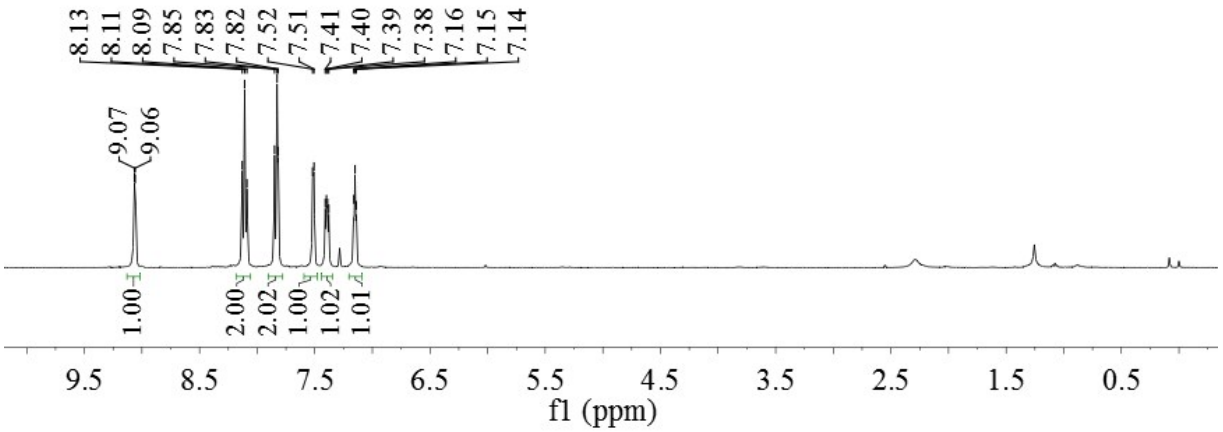


^{13}C NMR Spectrum for 1m ($CDCl_3$, 101 MHz)

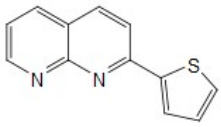


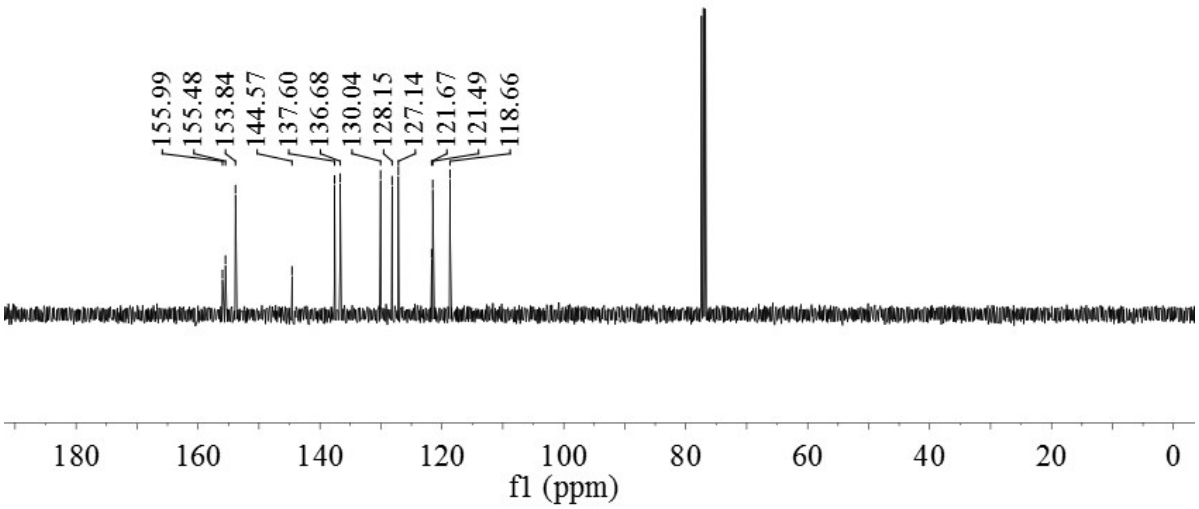
^{1}H NMR Spectrum for 1n ($CDCl_3$, 400 MHz)



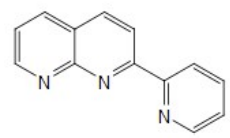


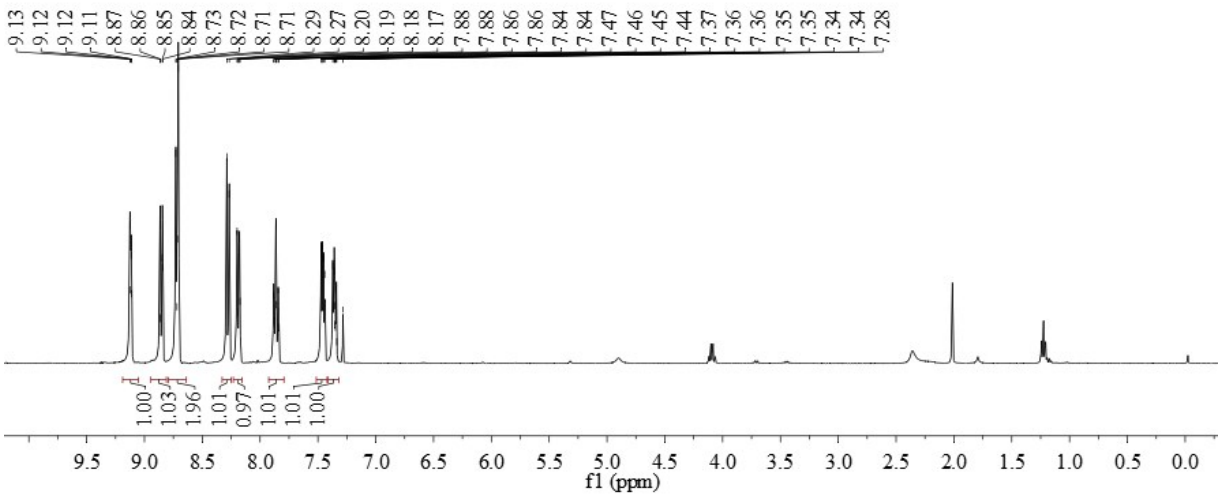
^{13}C NMR Spectrum for 1n ($CDCl_3$, 101 MHz)



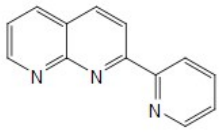


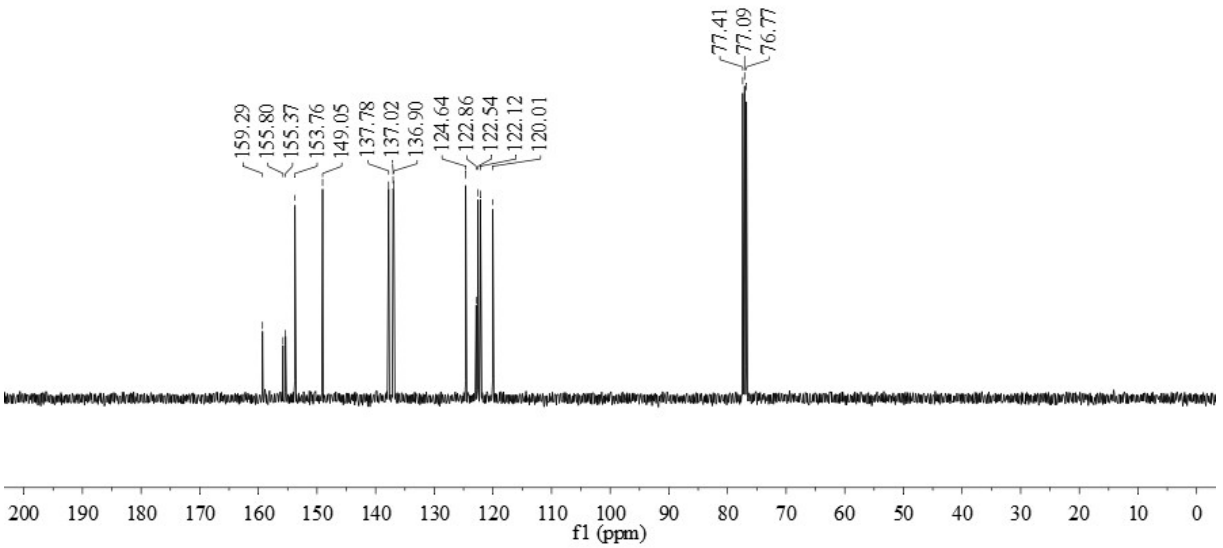
^{1}H NMR Spectrum for 1q ($CDCl_3$, 400 MHz)



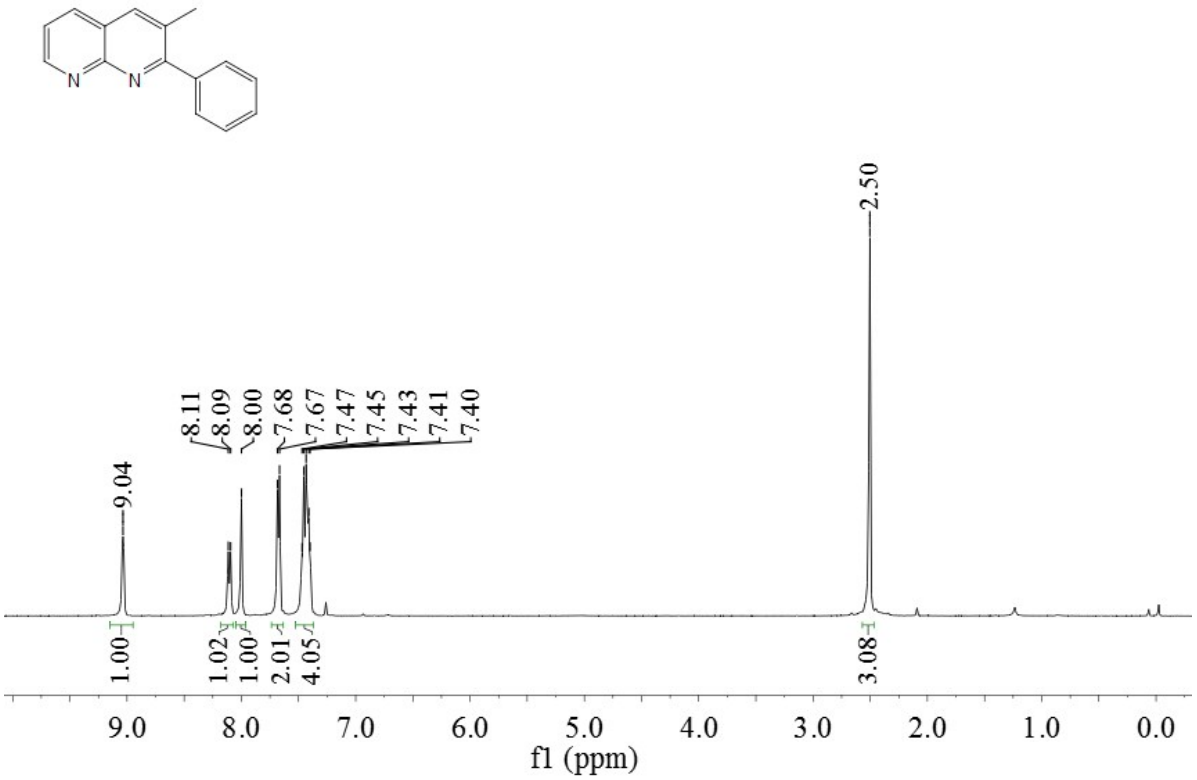


^{13}C NMR Spectrum for 1q ($CDCl_3$, 101 MHz)

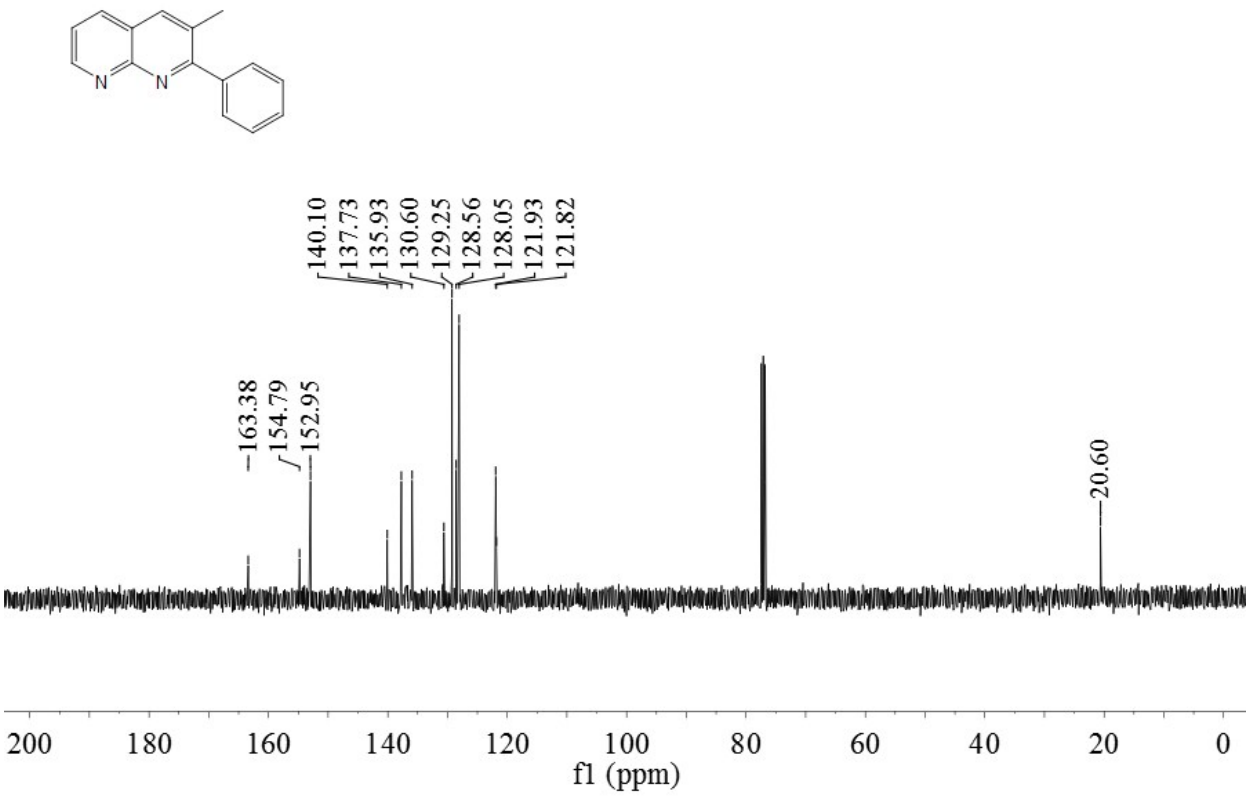




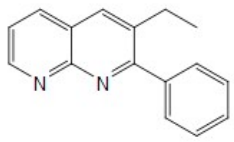
^{1}H NMR Spectrum for 1r ($CDCl_3$, 400 MHz)

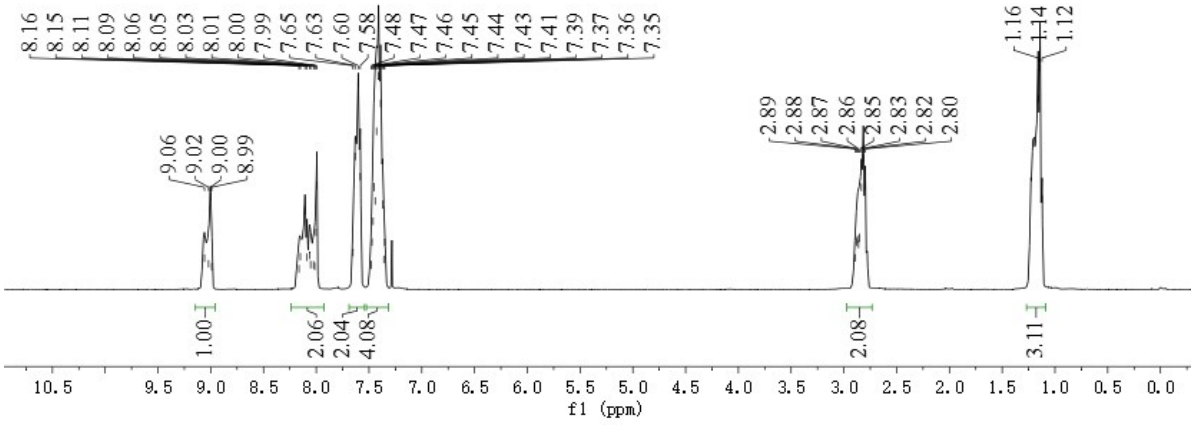


^{13}C NMR Spectrum for 1r ($CDCl_3$, 101 MHz)

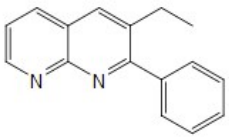


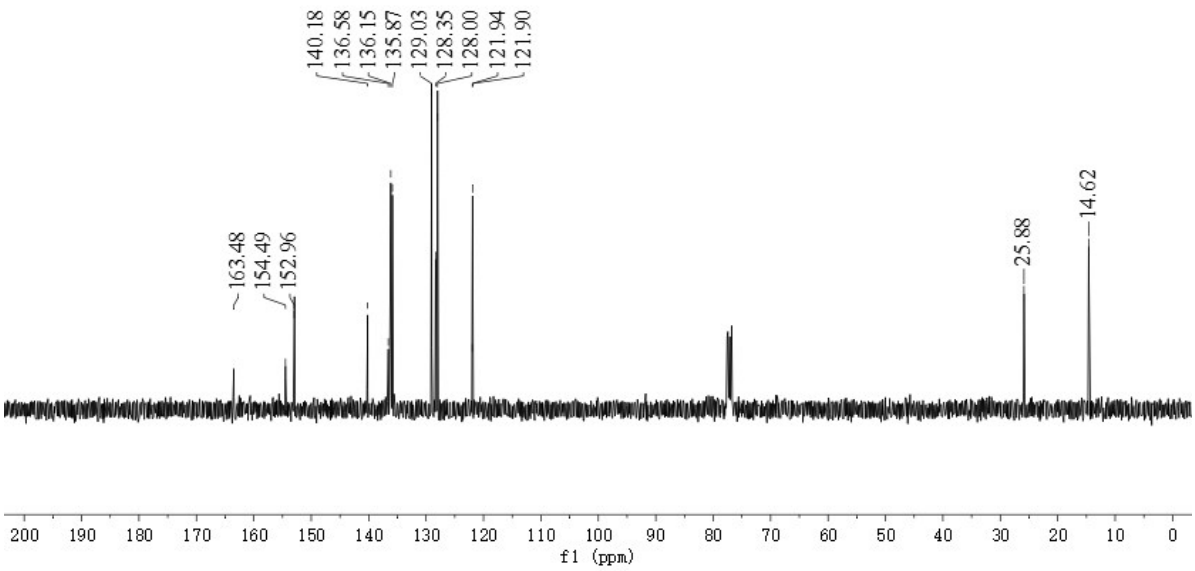
^{1}H NMR Spectrum for 1s ($CDCl_3$, 400 MHz)



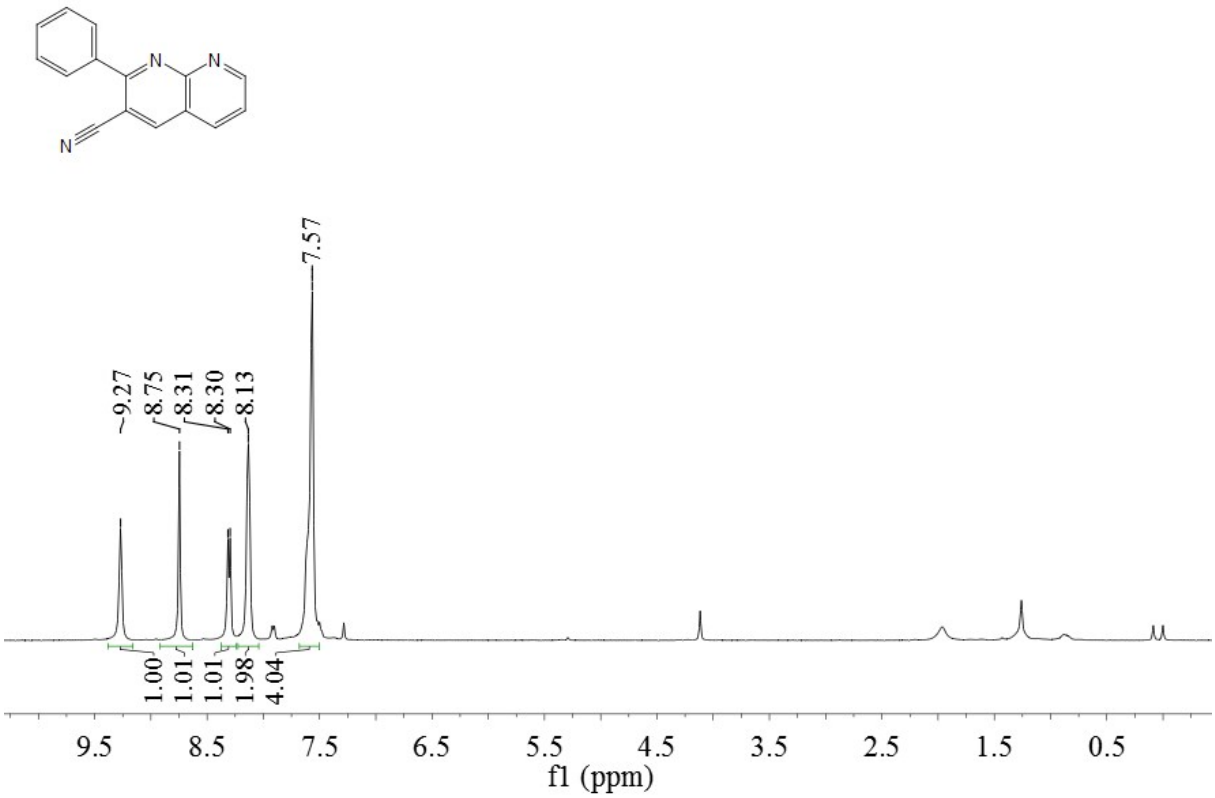


^{13}C NMR Spectrum for 1s ($CDCl_3$, 101 MHz)

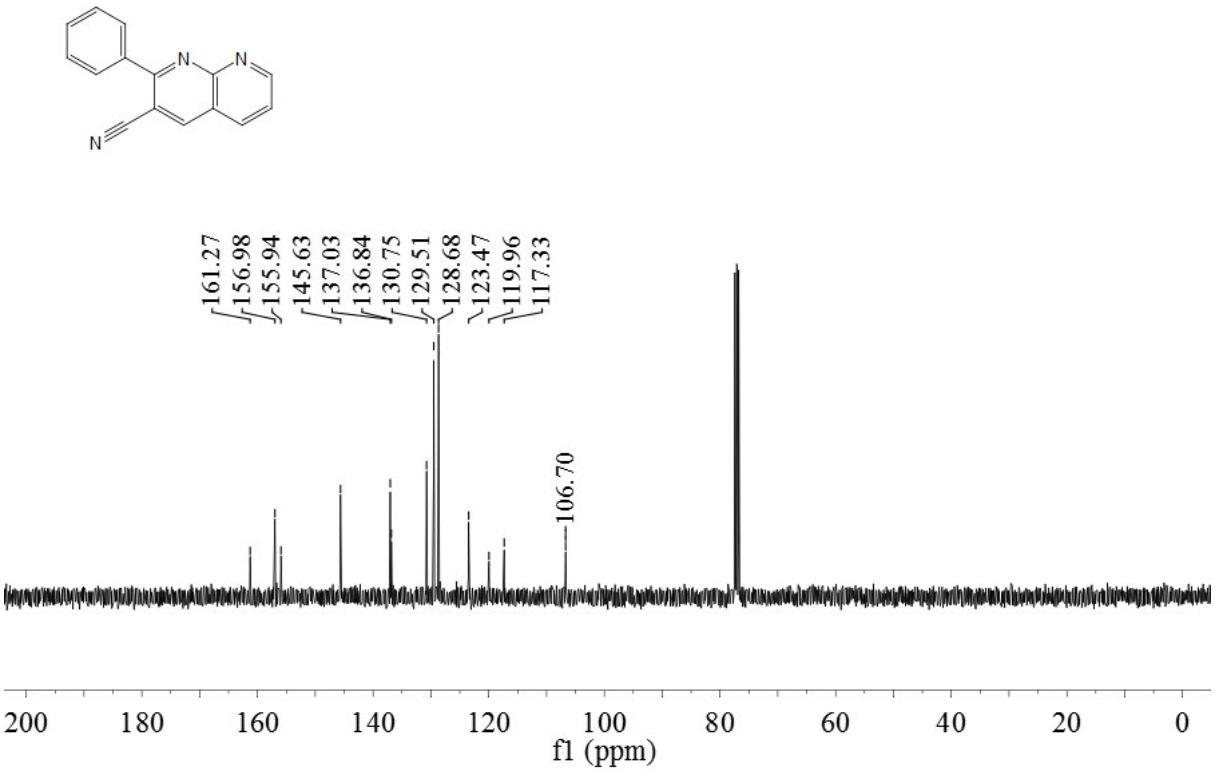




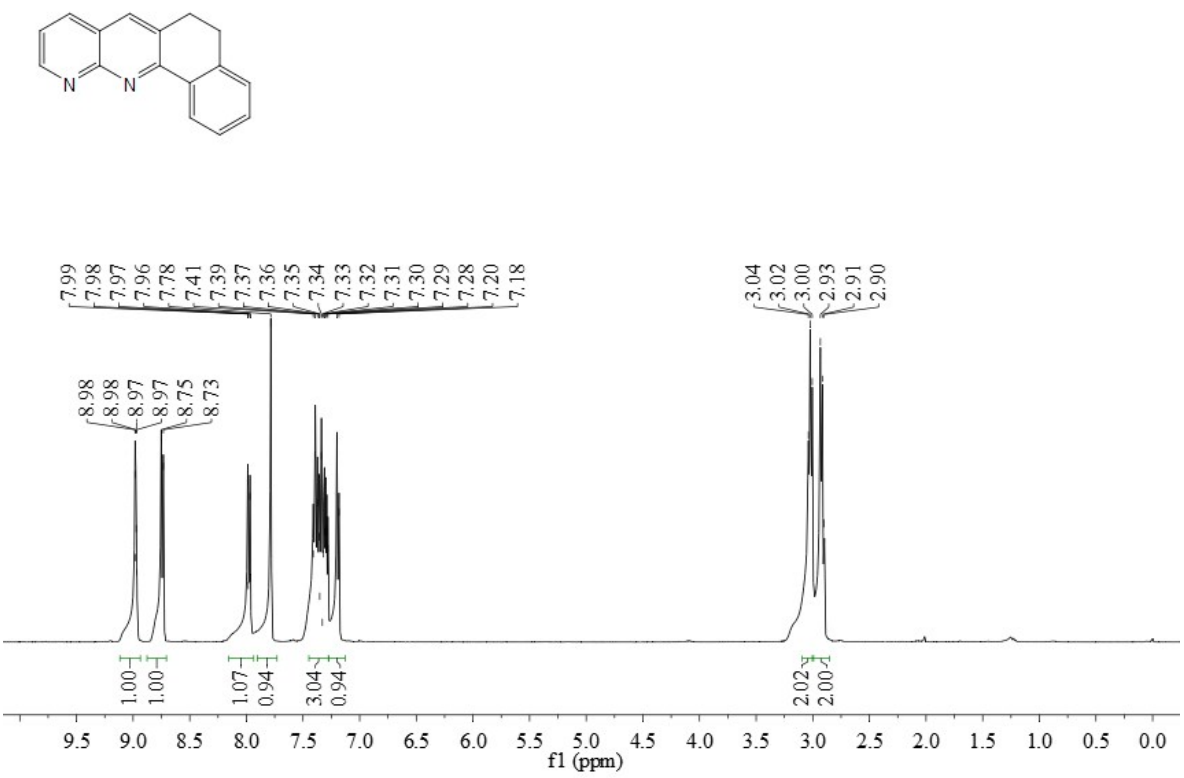
^{1}H NMR Spectrum for 1u ($CDCl_3$, 400 MHz)



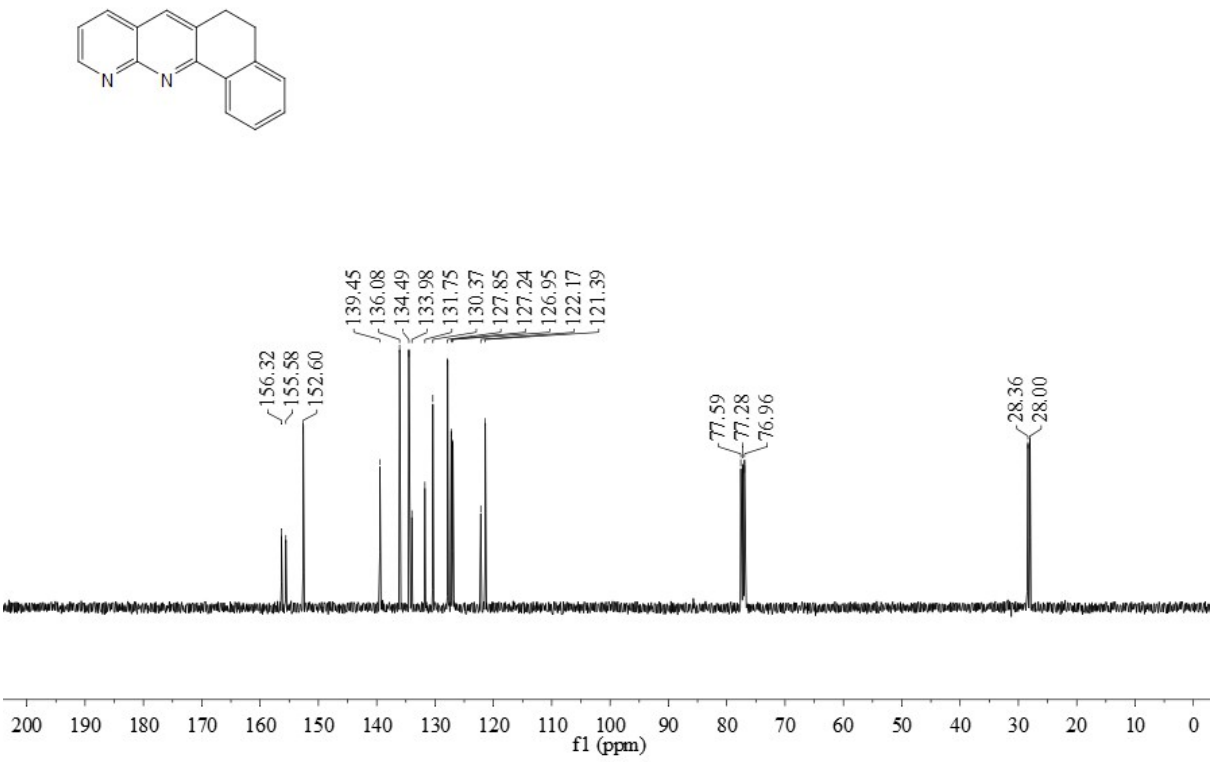
^{13}C NMR Spectrum for 1u ($CDCl_3$, 101 MHz)



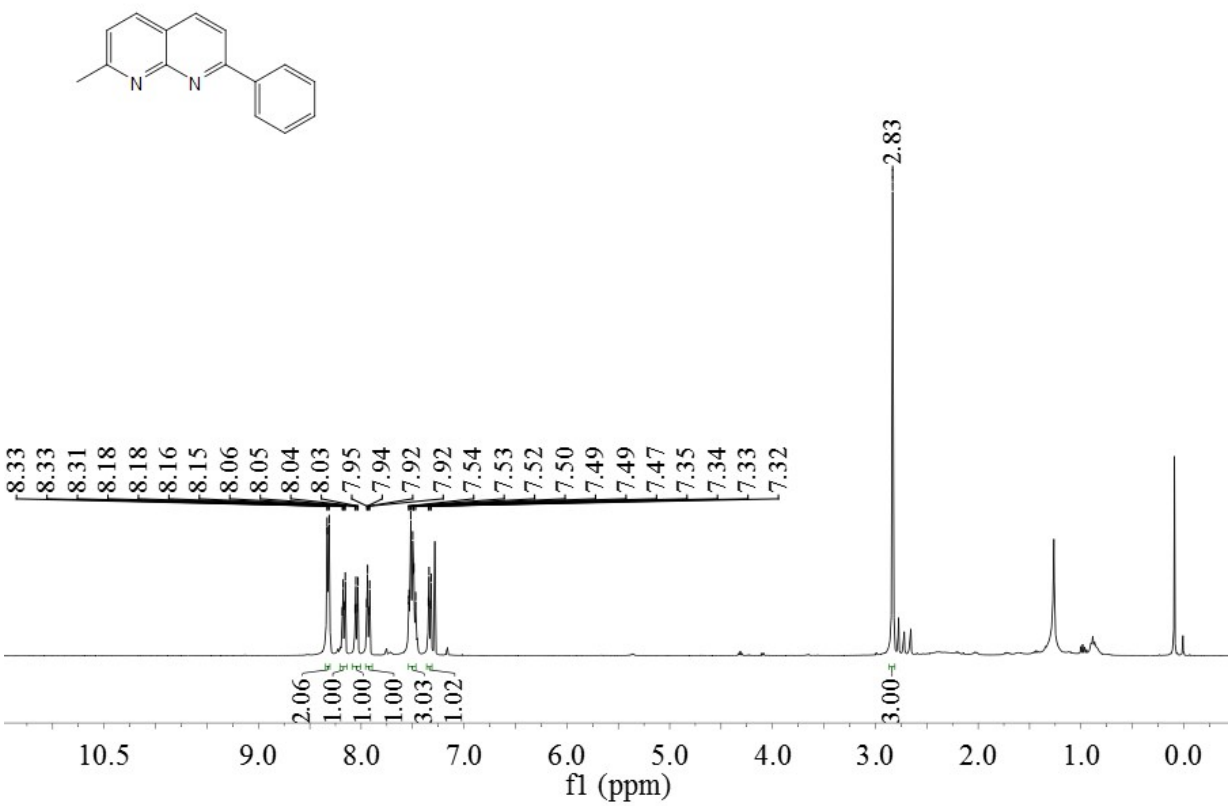
^{1}H NMR Spectrum for 1v ($CDCl_3$, 400 MHz)



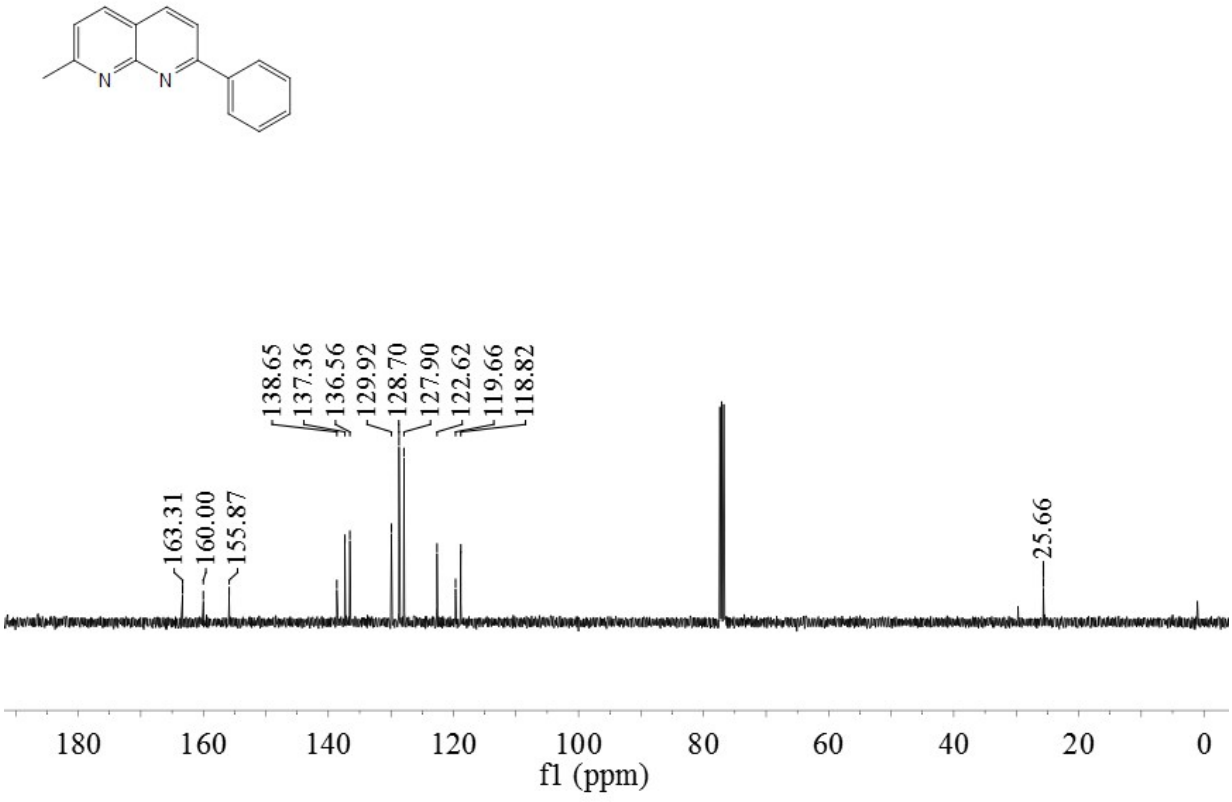
^{13}C NMR Spectrum for 1v ($CDCl_3$, 101 MHz)



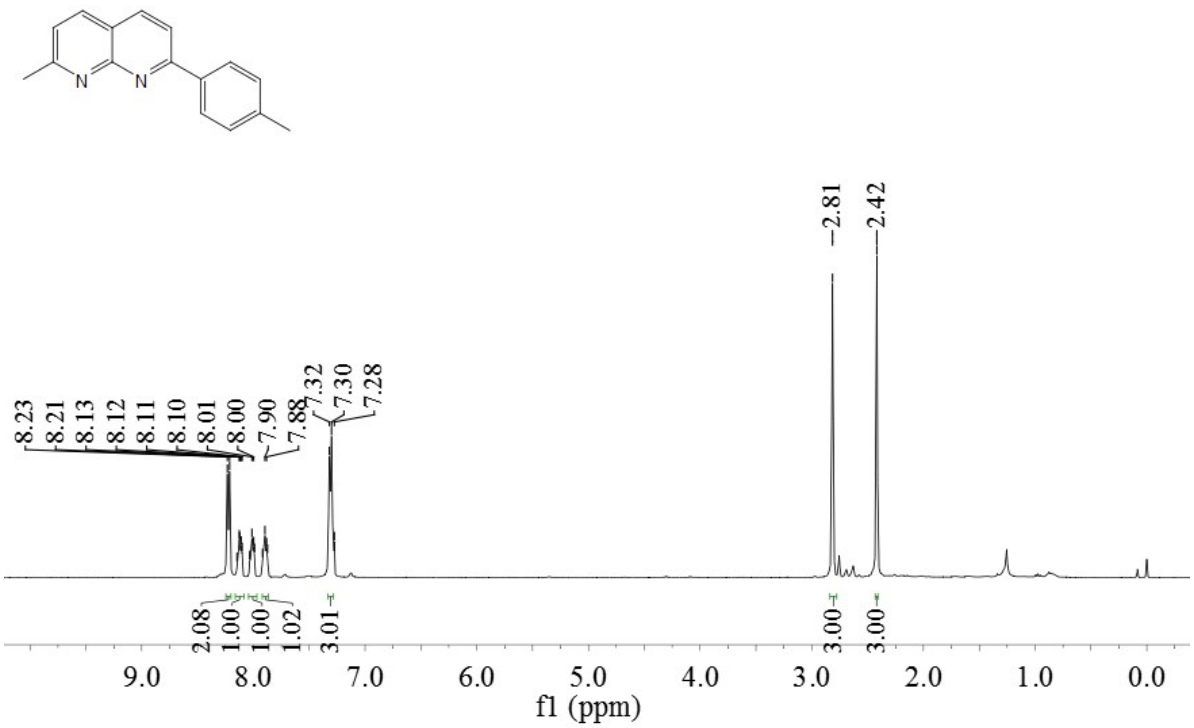
^{1}H NMR Spectrum for 2a ($CDCl_3$, 500 MHz)



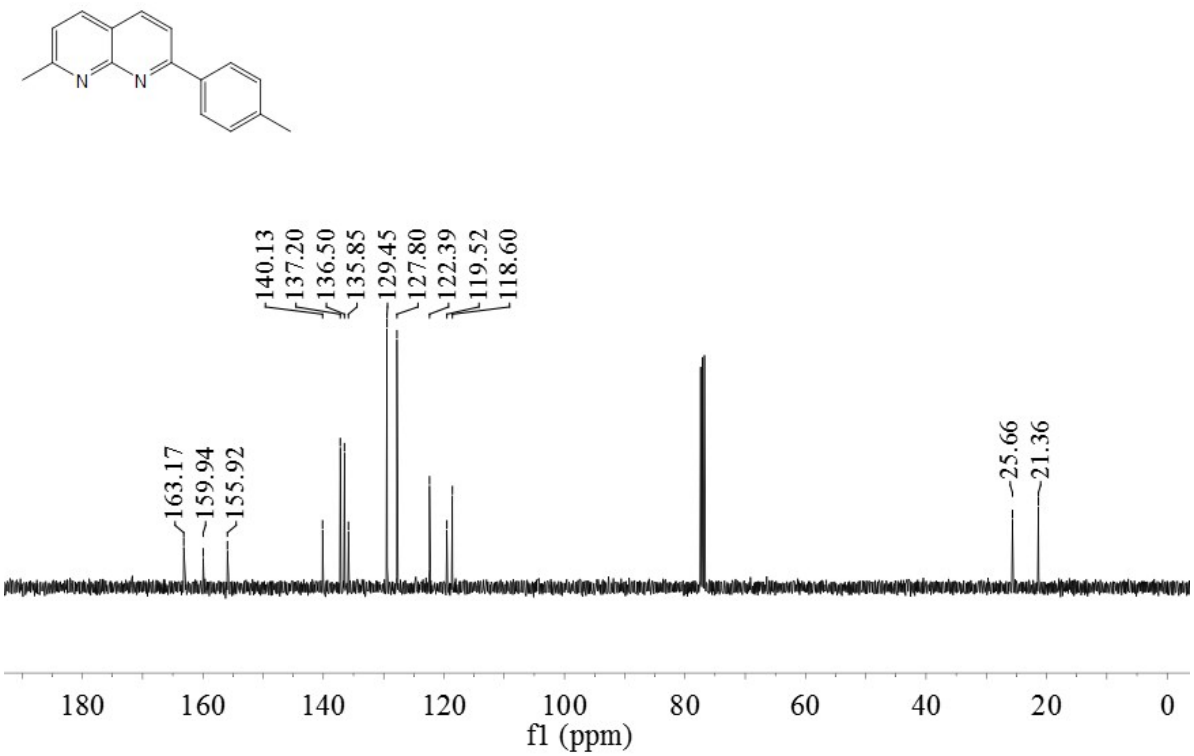
^{13}C NMR Spectrum for 2a ($CDCl_3$, 126 MHz)



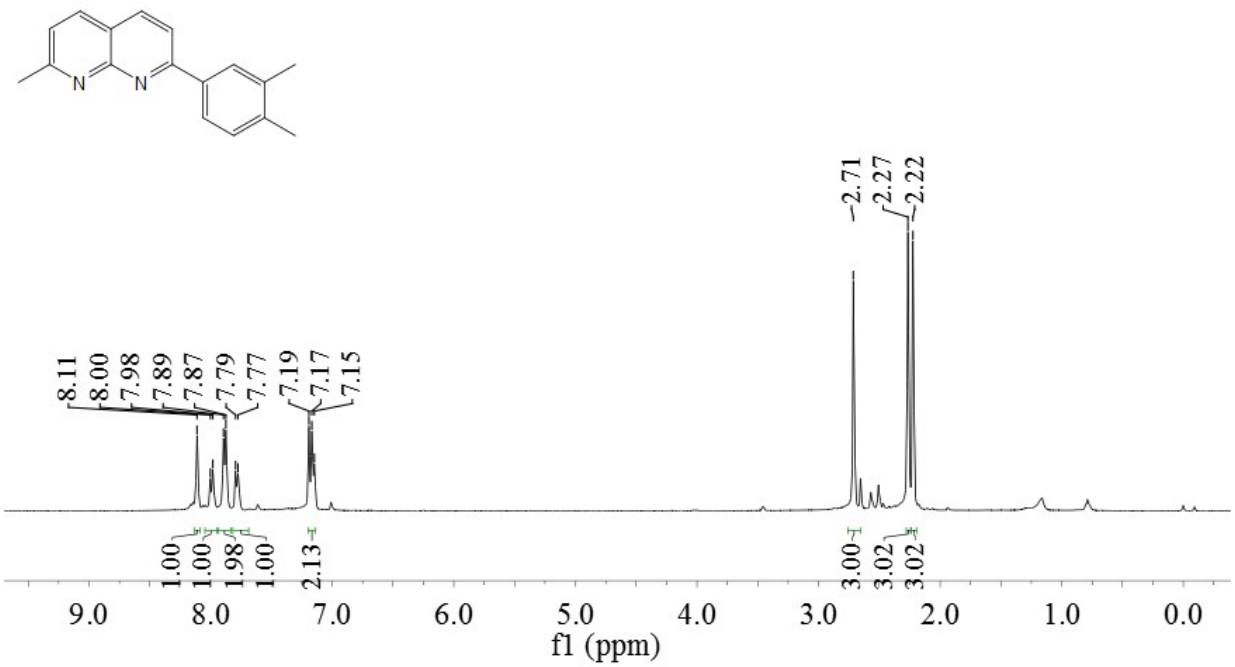
^{1}H NMR Spectrum for 2b ($CDCl_3$, 500 MHz)



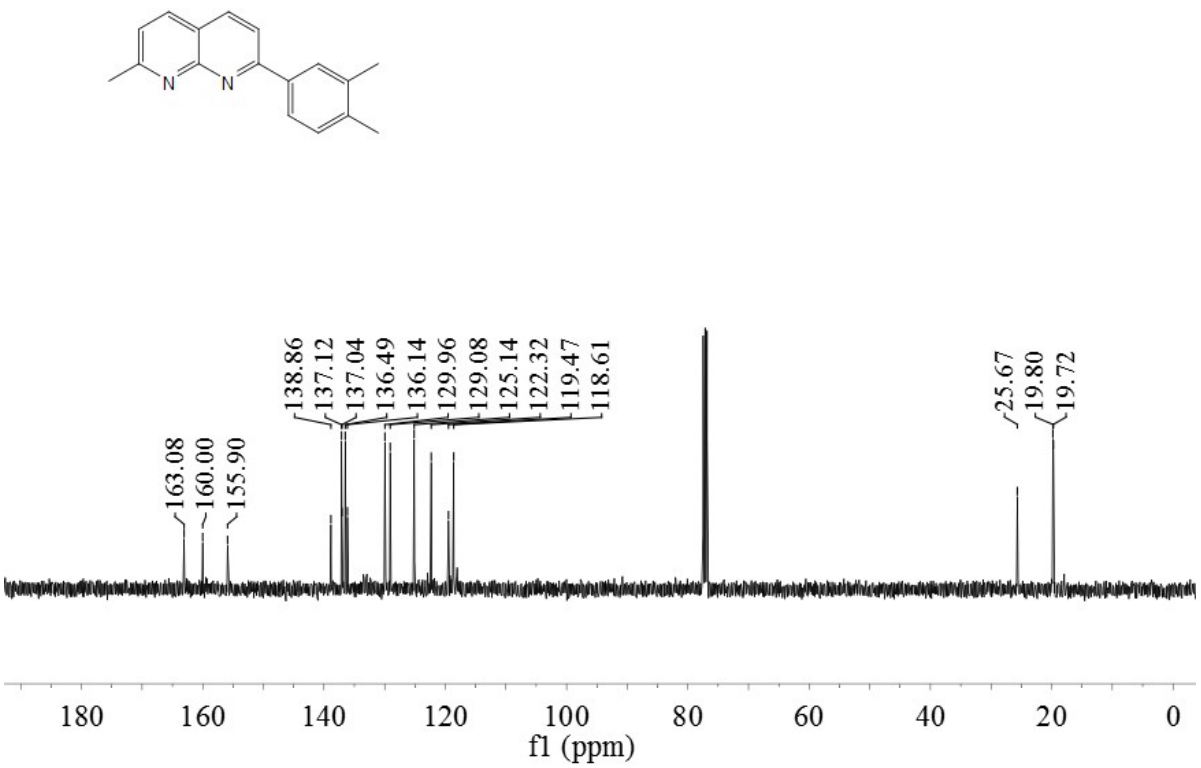
^{13}C NMR Spectrum for 2b ($CDCl_3$, 126 MHz)



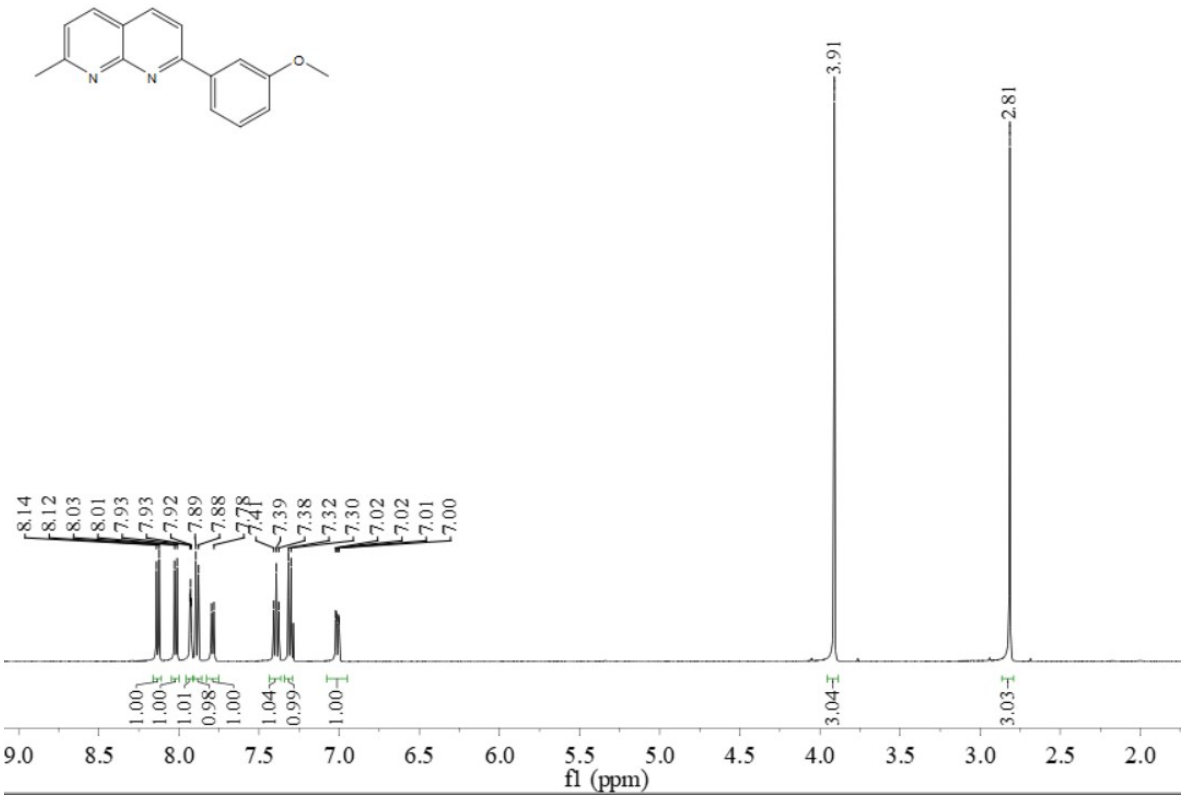
^{1}H NMR Spectrum for 2c ($CDCl_3$, 500 MHz)



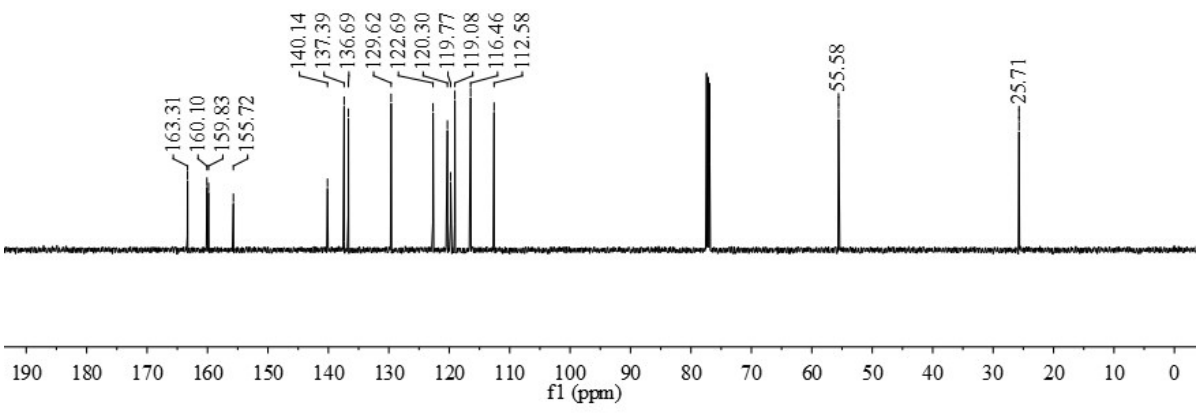
^{13}C NMR Spectrum for 2c ($CDCl_3$, 126 MHz)



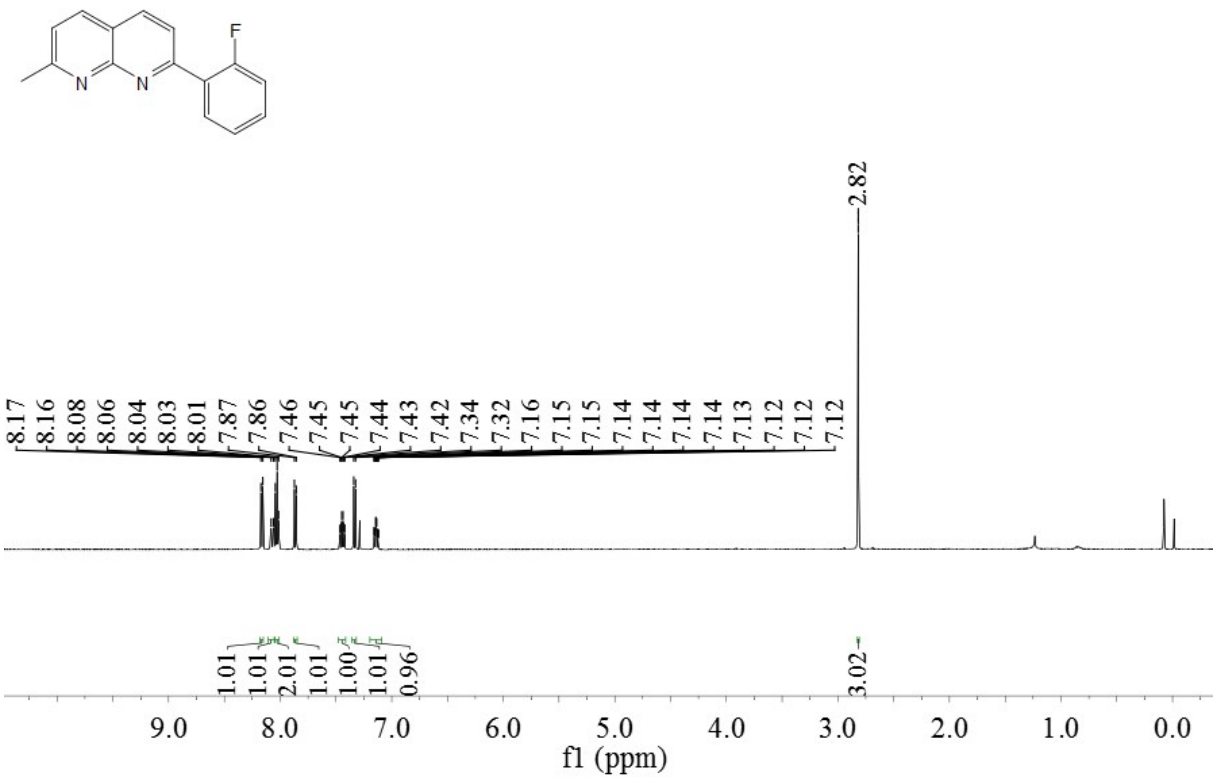
^{1}H NMR Spectrum for 2d ($CDCl_3$, 500 MHz)



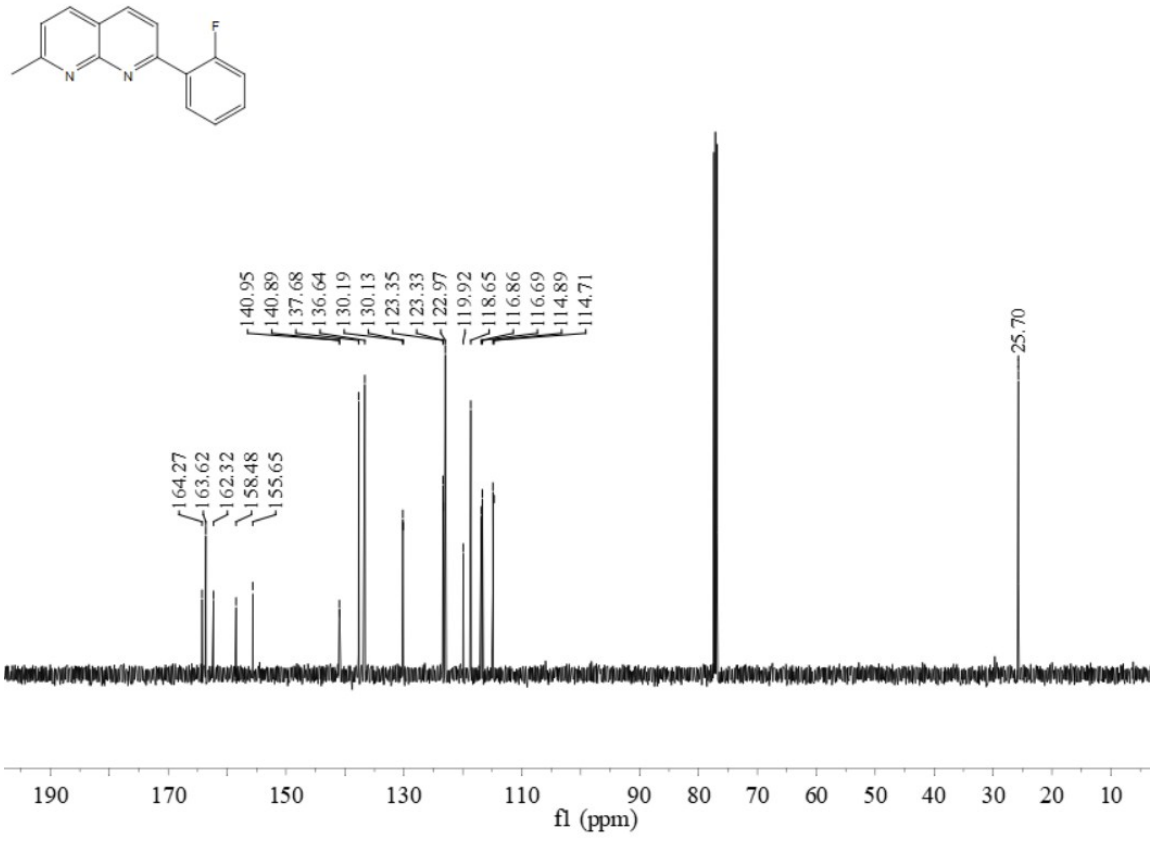
^{13}C NMR Spectrum for 2d ($CDCl_3$, 126 MHz)



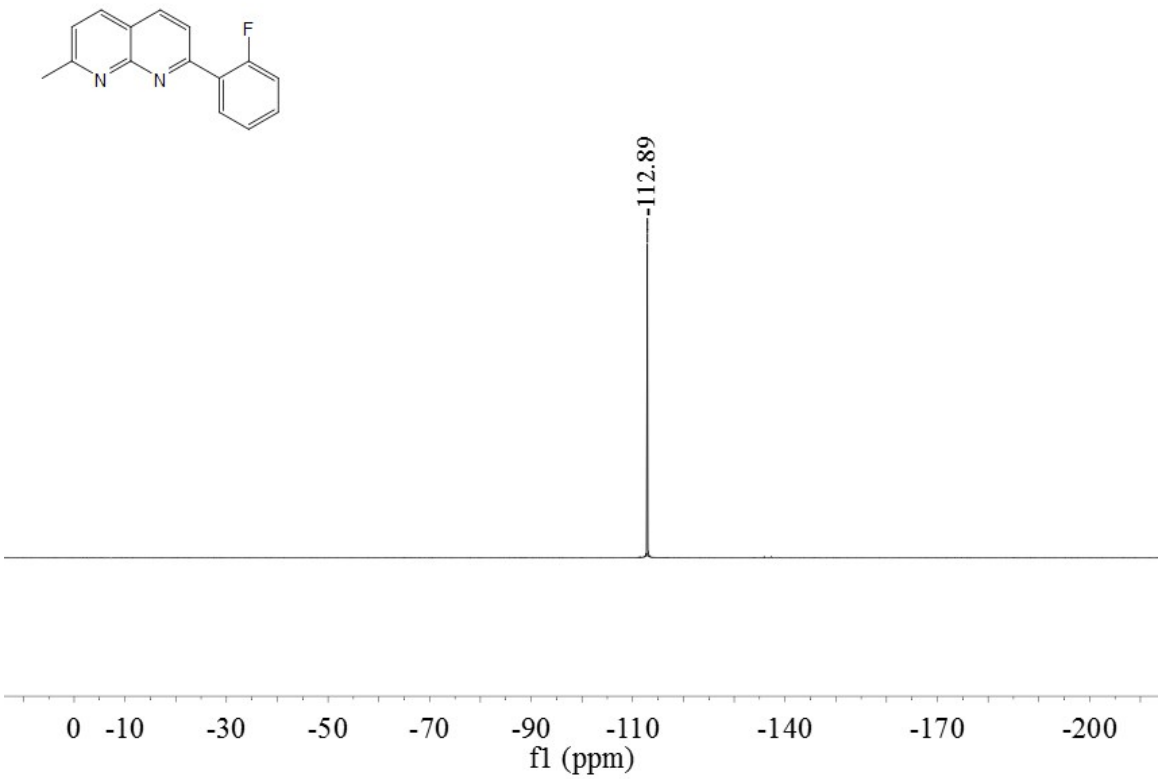
^{1}H NMR Spectrum for 2e ($CDCl_3$, 500 MHz)



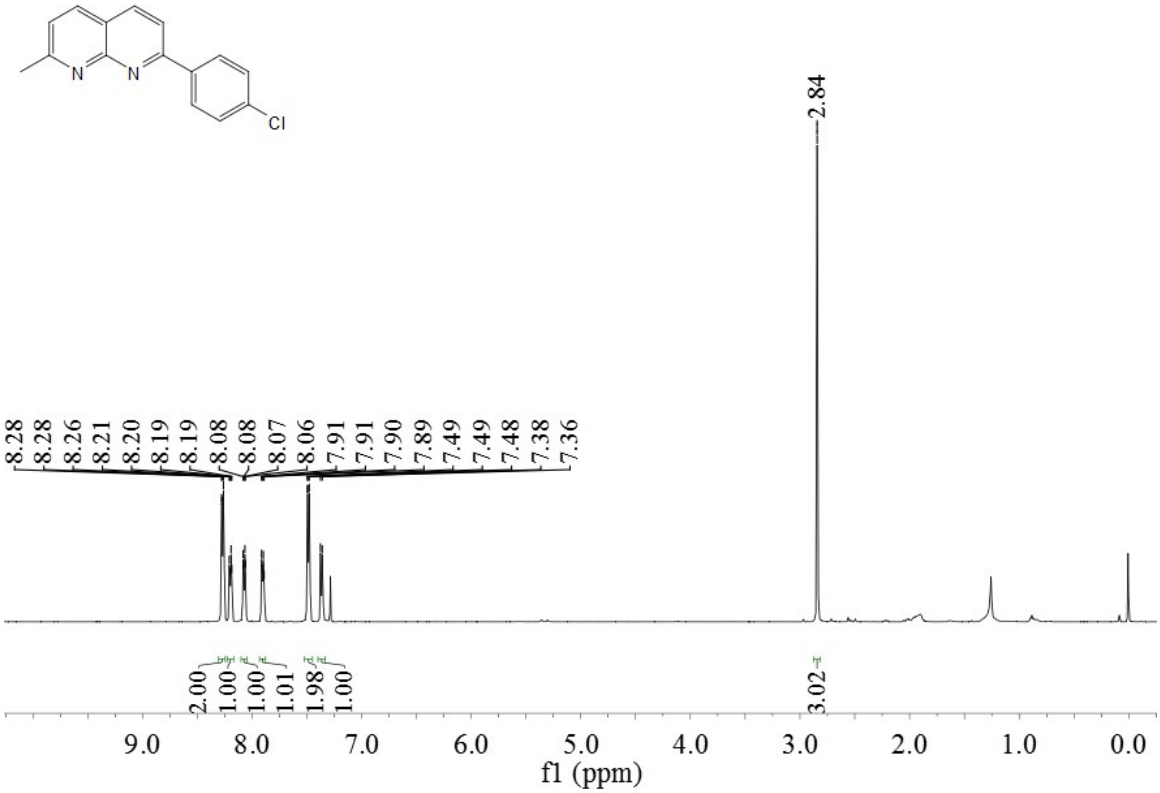
^{13}C NMR Spectrum for 2e ($CDCl_3$, 126 MHz)



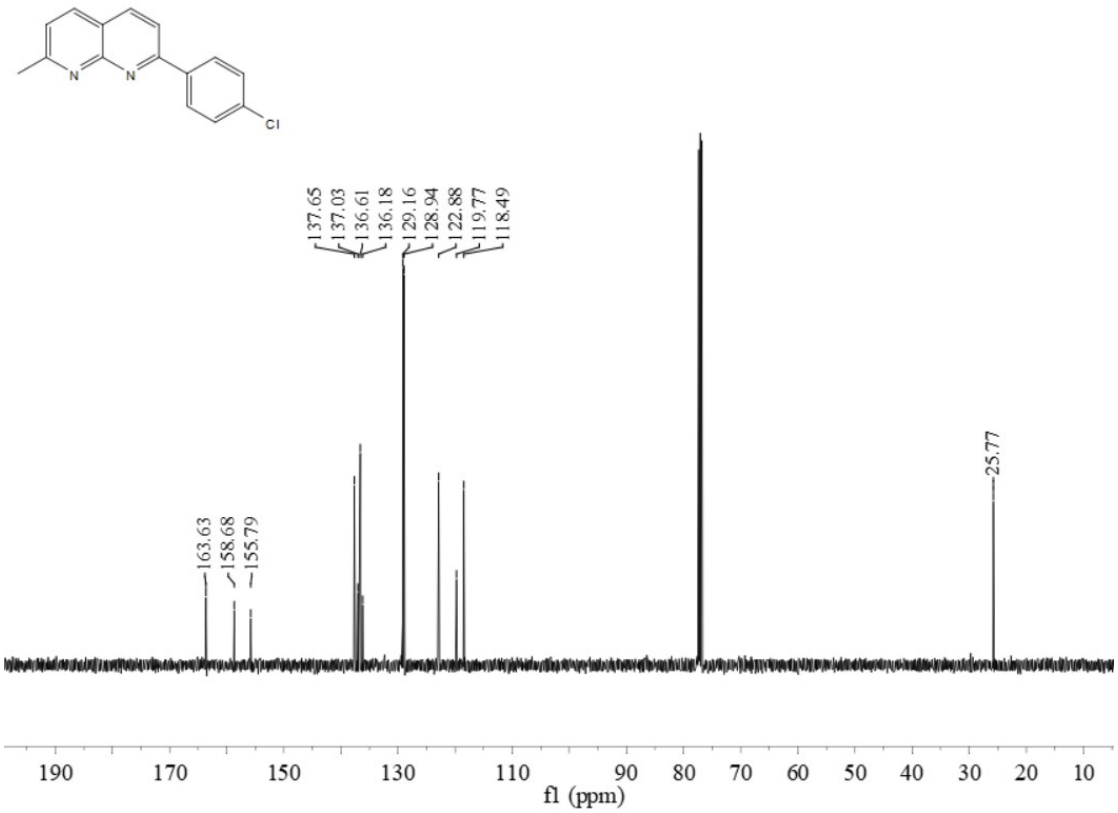
^{19}F NMR (471 MHz, $CDCl_3$)



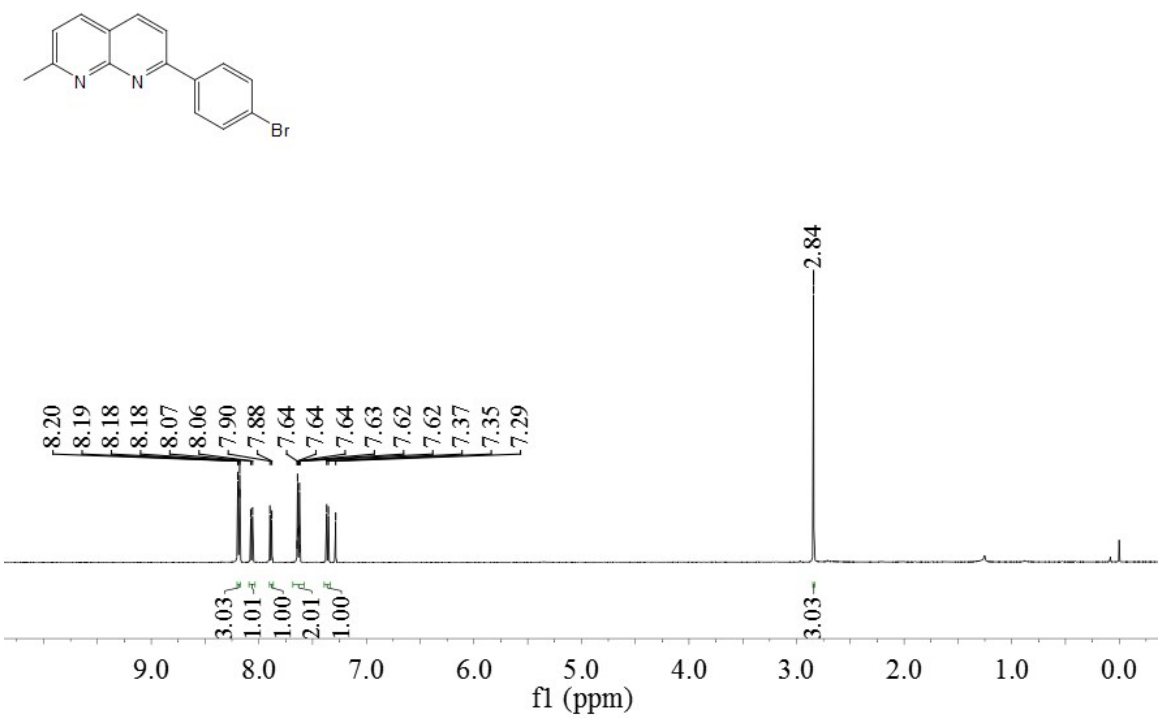
^{1}H NMR Spectrum for 2f ($CDCl_3$, 500 MHz)



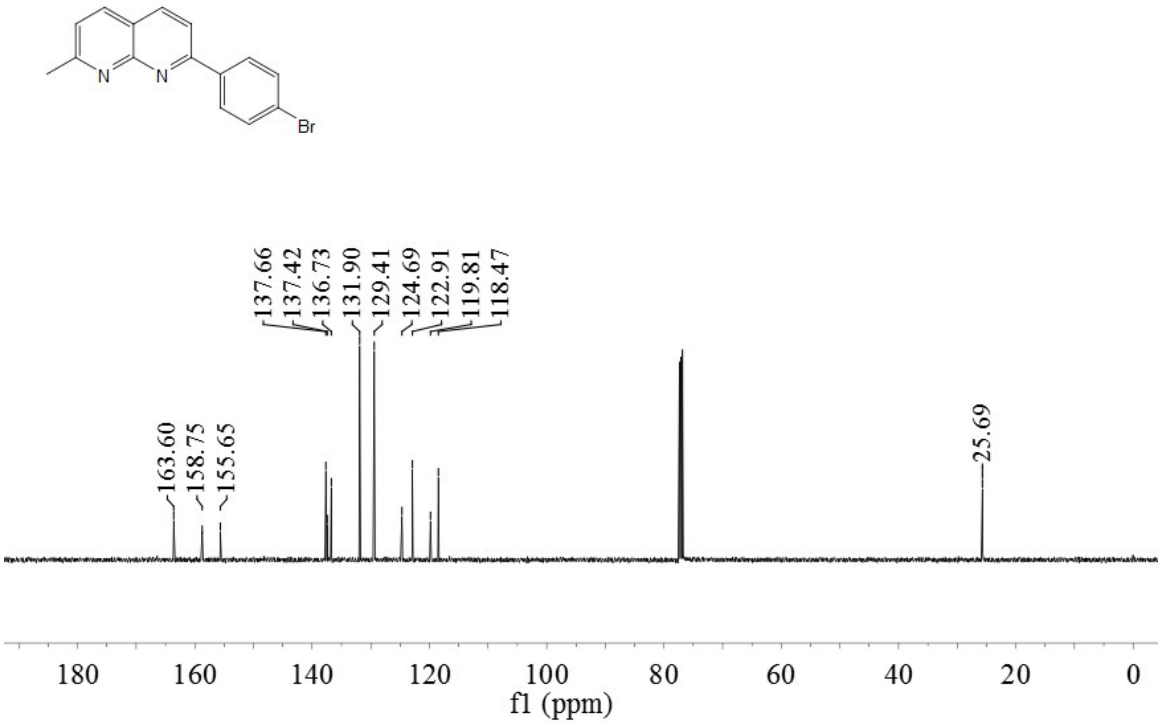
^{13}C NMR Spectrum for 2f ($CDCl_3$, 126 MHz)



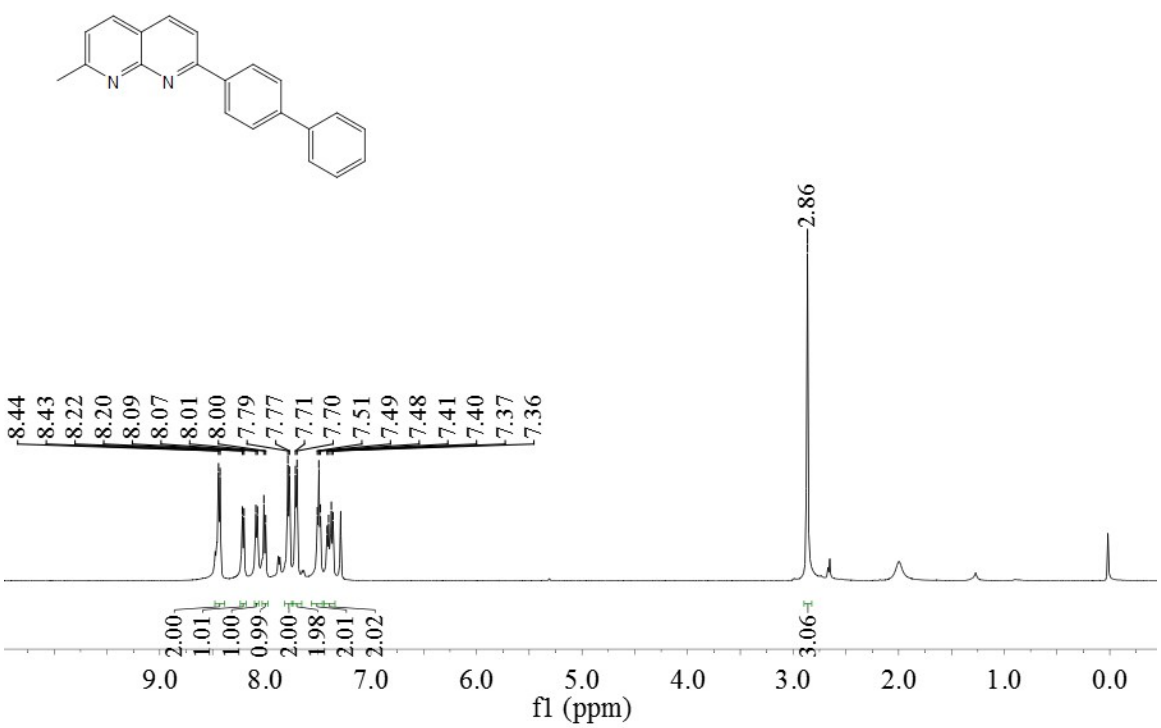
^{1}H NMR Spectrum for 2g ($CDCl_3$, 500 MHz)



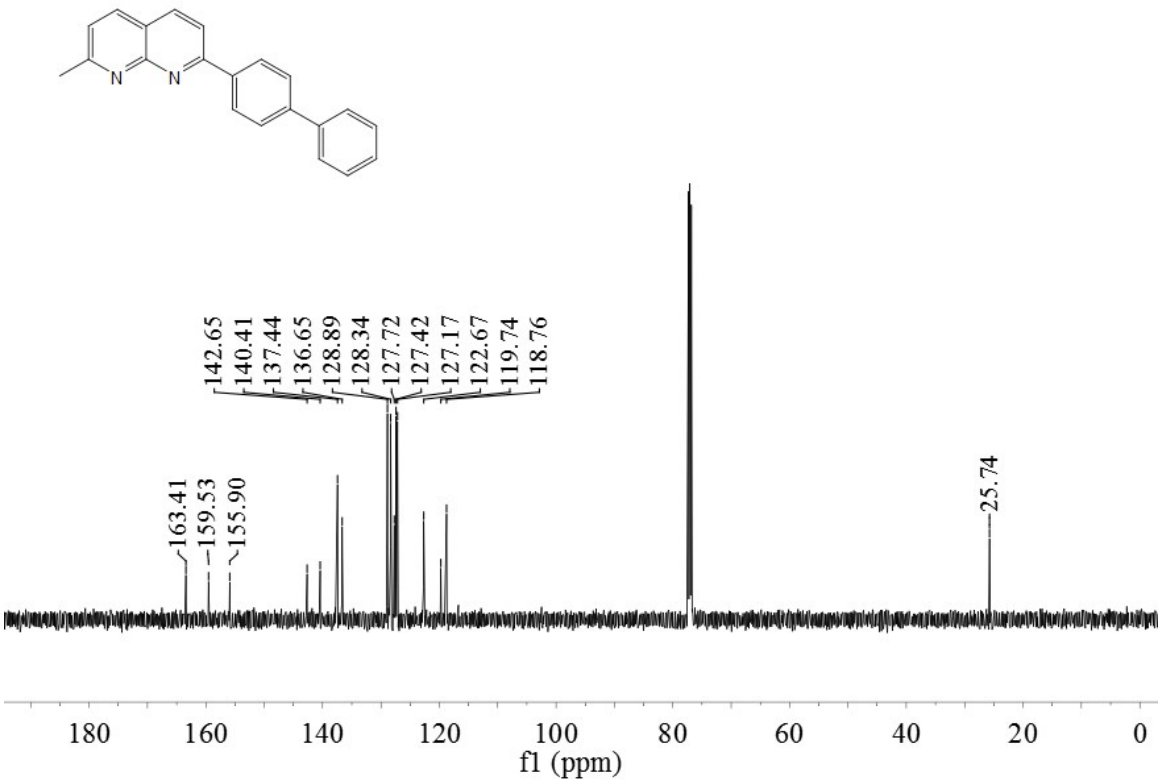
^{13}C NMR Spectrum for 2g ($CDCl_3$, 126 MHz)



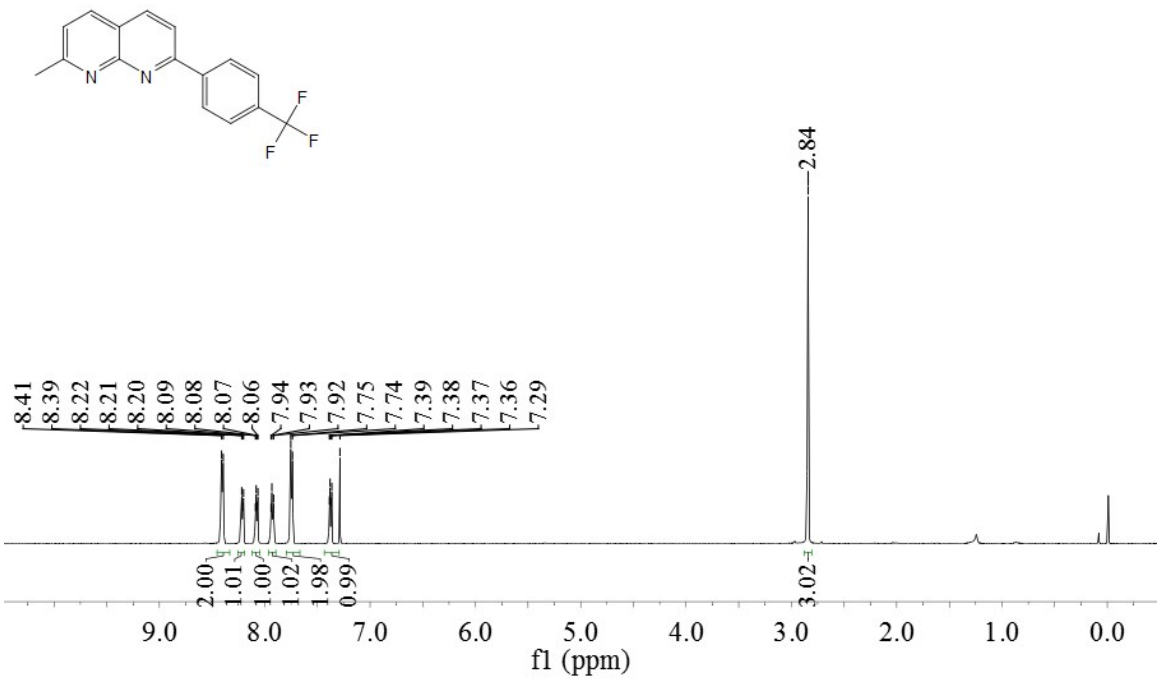
^{1}H NMR Spectrum for 2h ($CDCl_3$, 500 MHz)



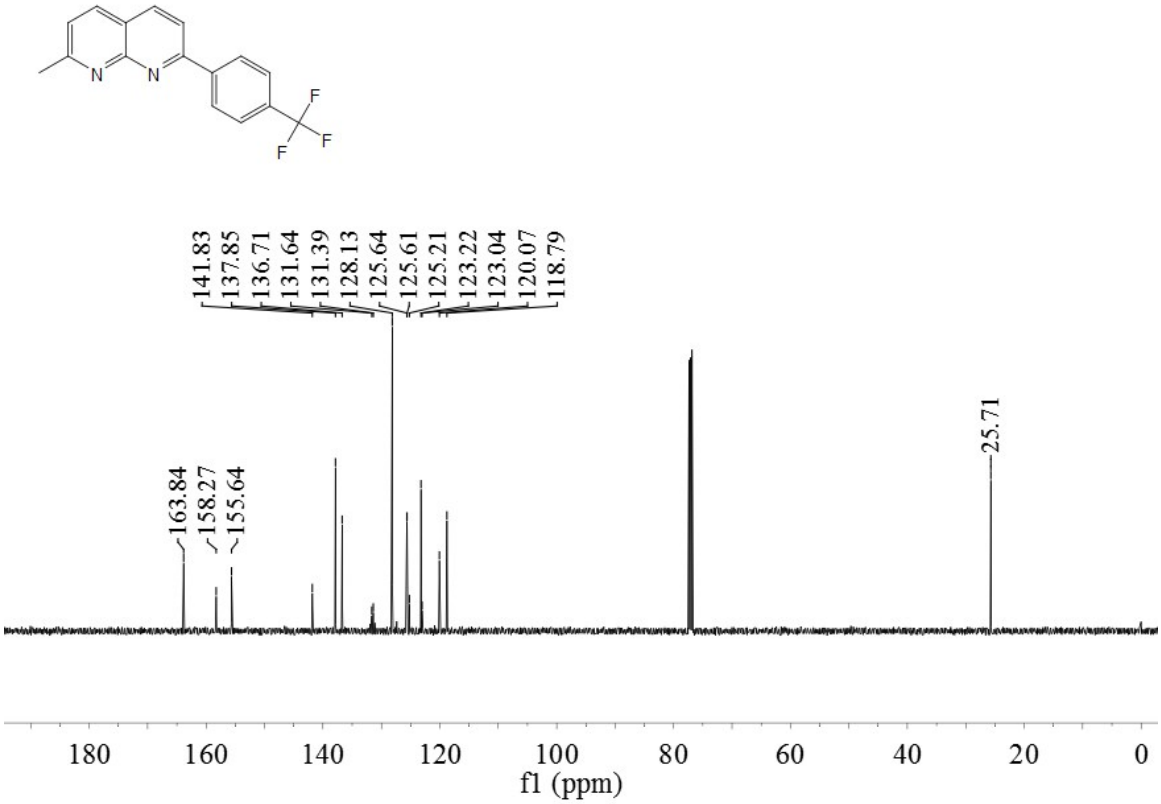
^{13}C NMR Spectrum for 2h ($CDCl_3$, 126 MHz)



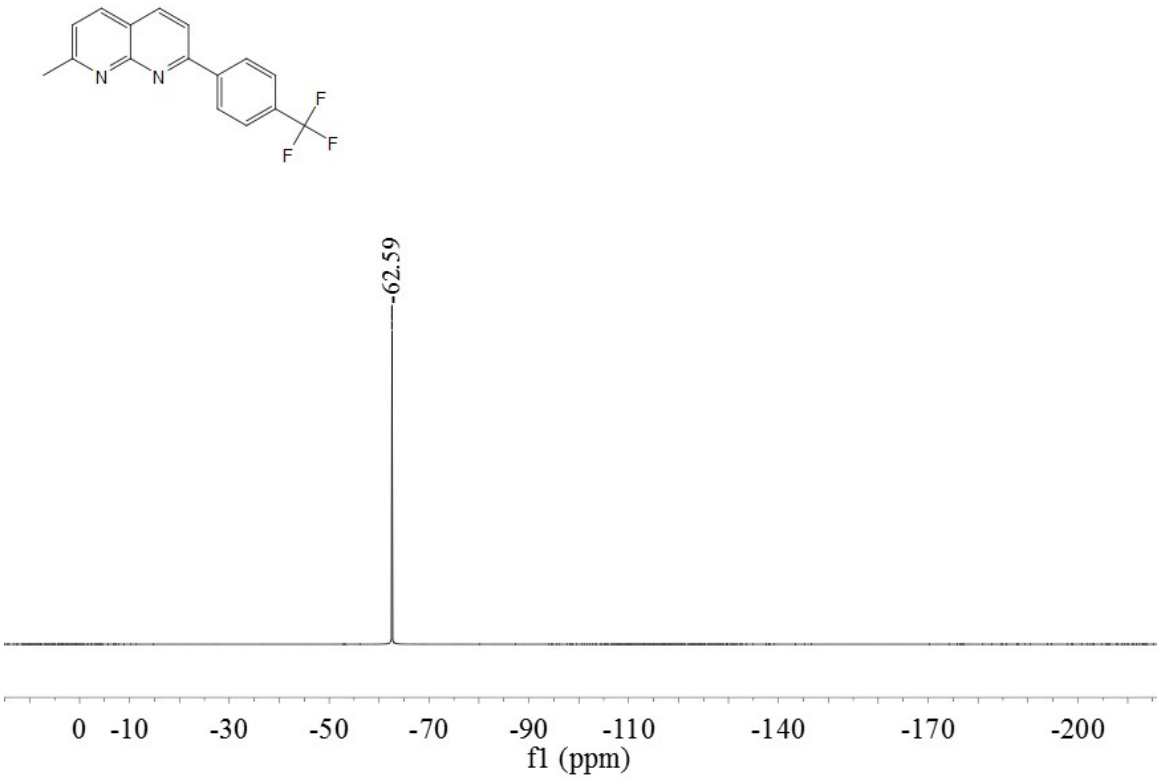
^{1}H NMR Spectrum for 2i ($CDCl_3$, 500 MHz)



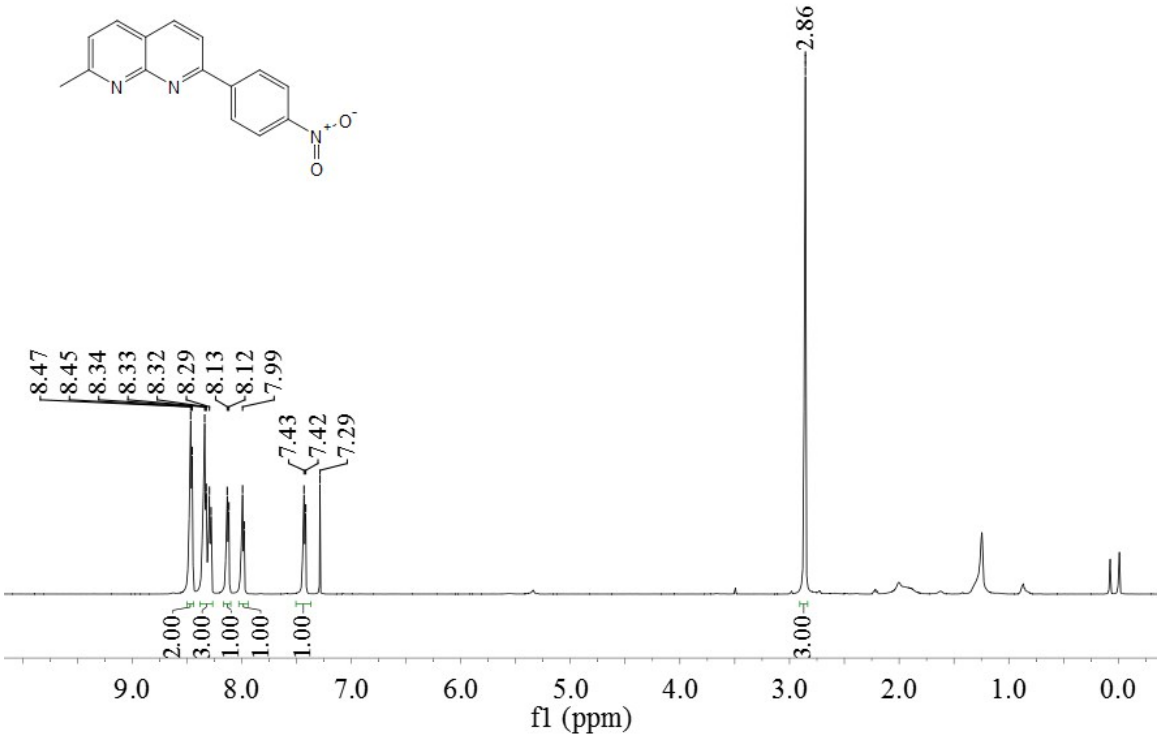
^{13}C NMR Spectrum for 2i ($CDCl_3$, 126 MHz)



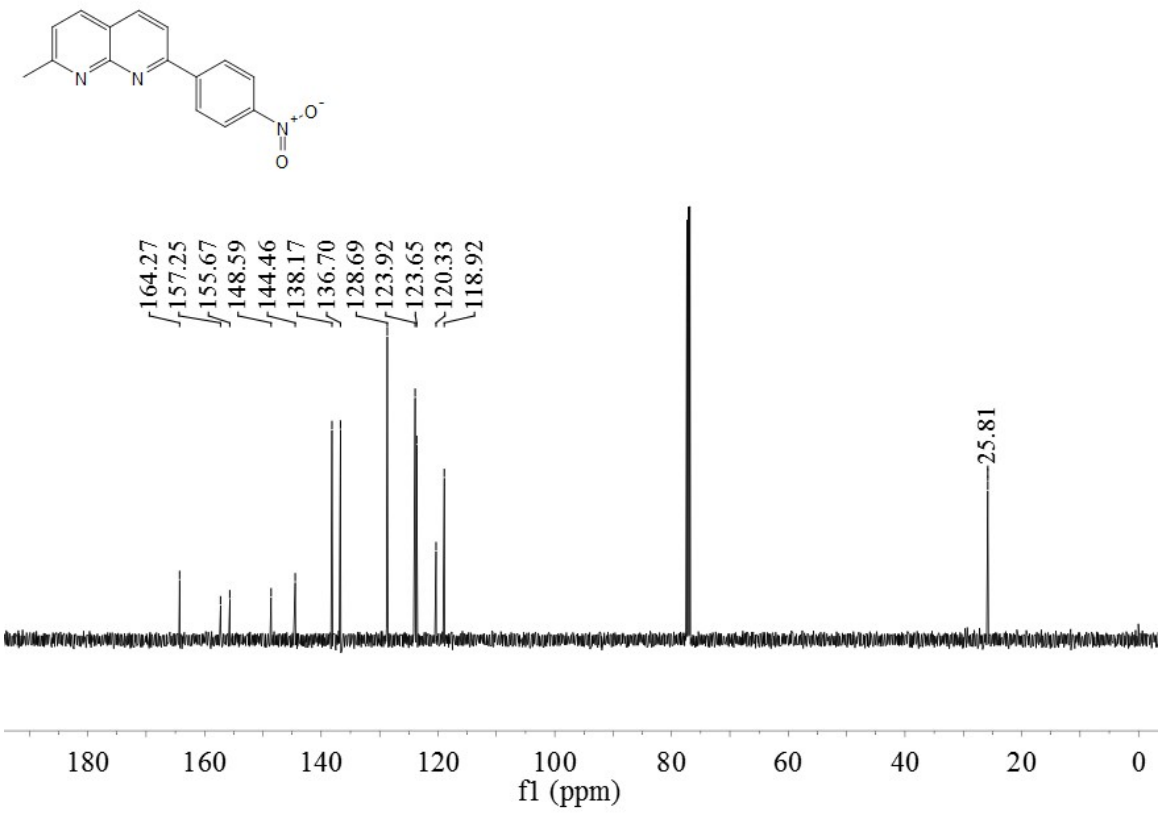
^{19}F NMR (471 MHz, $CDCl_3$)



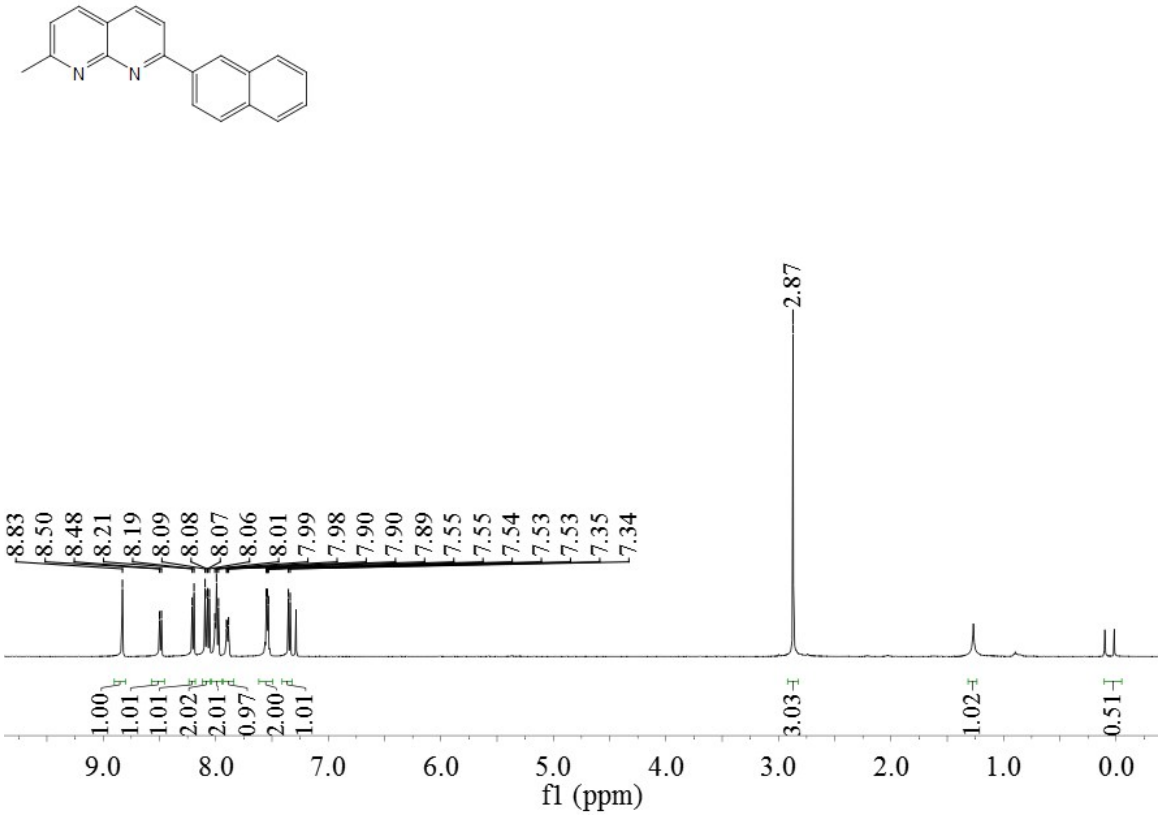
^{1}H NMR Spectrum for 2j ($CDCl_3$, 500 MHz)



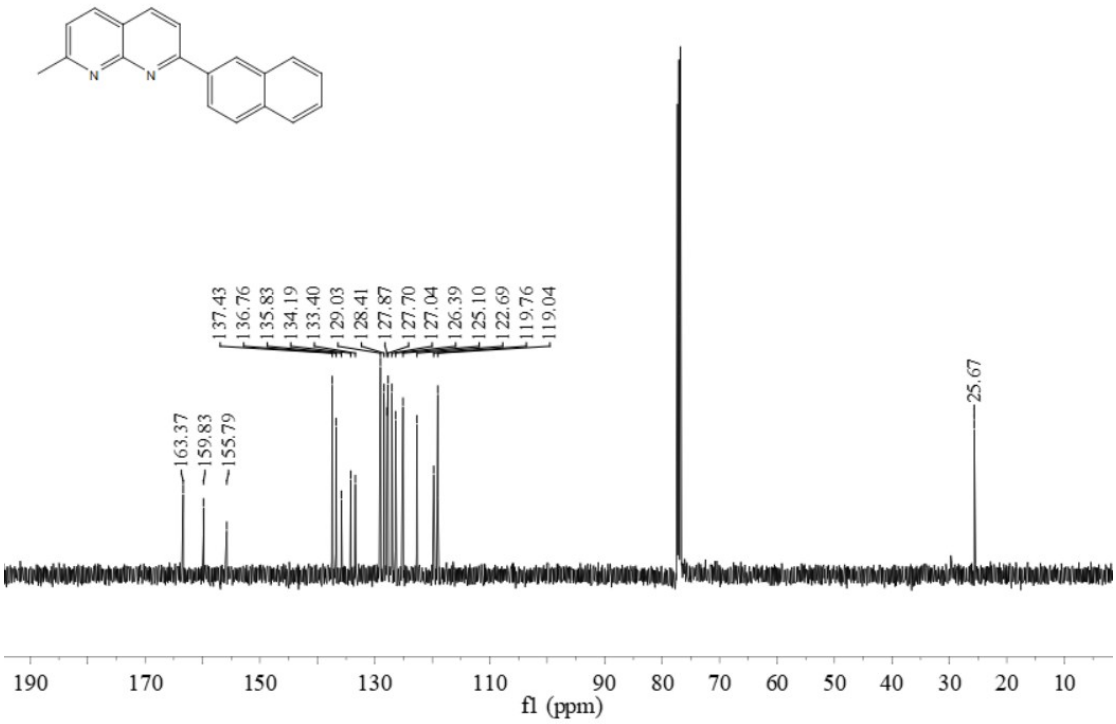
^{13}C NMR Spectrum for 2j ($CDCl_3$, 126 MHz)



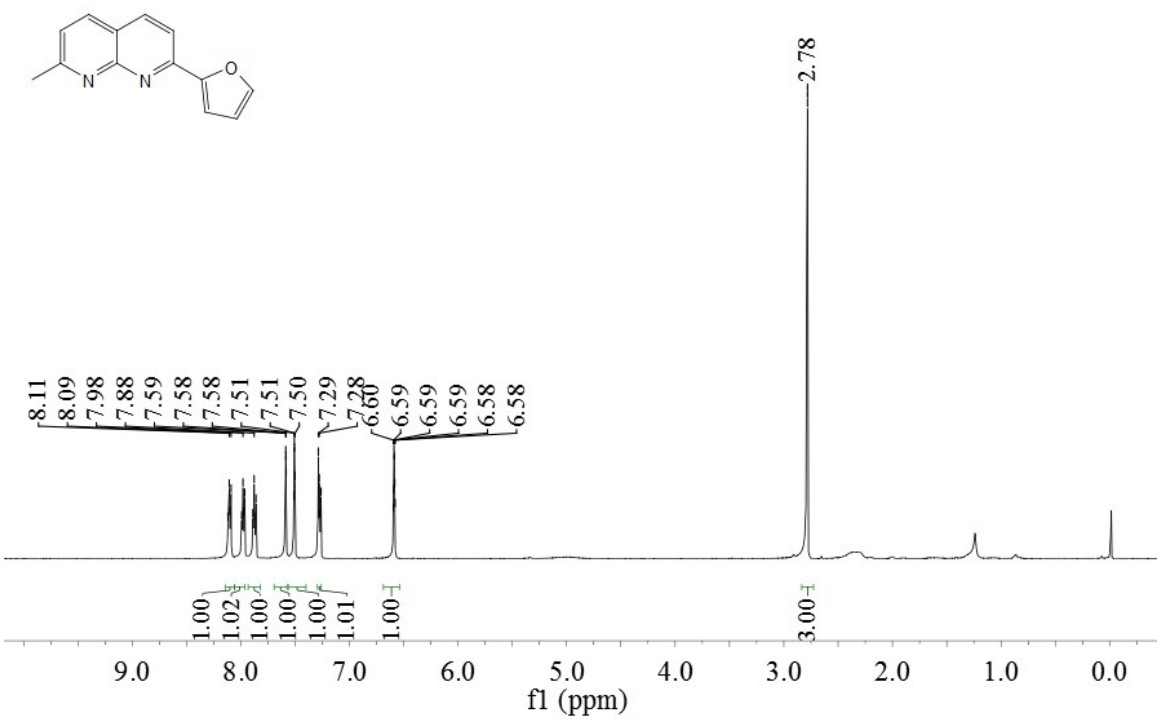
^{1}H NMR Spectrum for 2k ($CDCl_3$, 500 MHz)



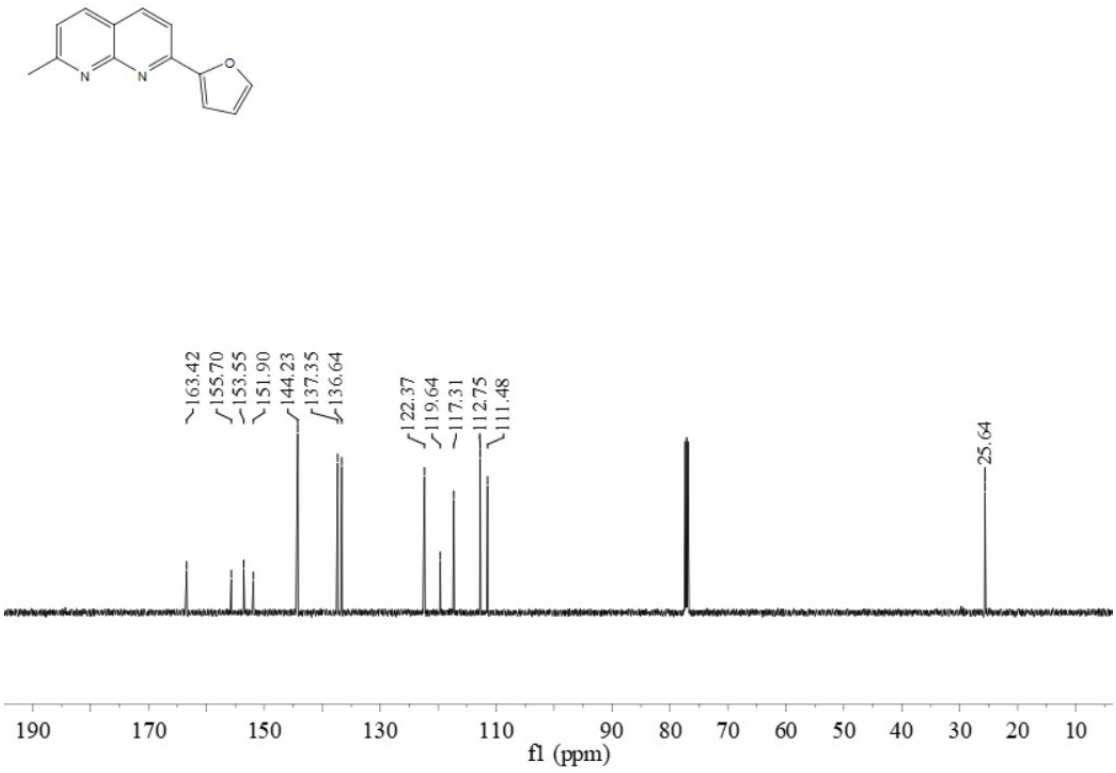
^{13}C NMR Spectrum for 2k ($CDCl_3$, 126 MHz)



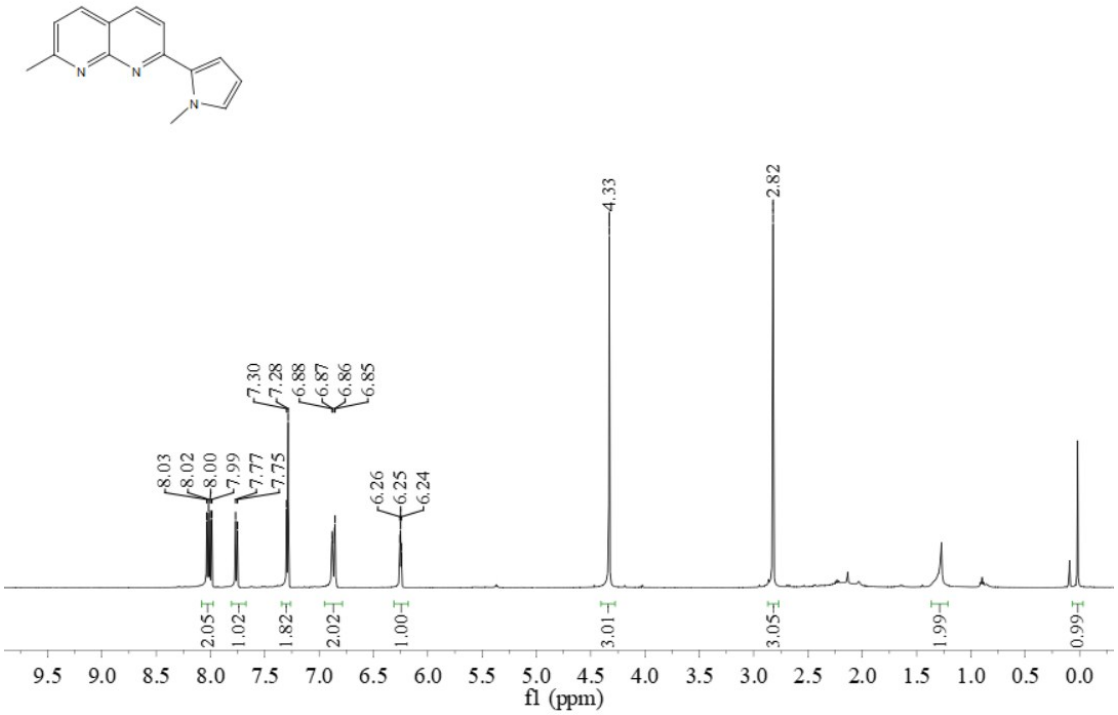
^{1}H NMR Spectrum for 2l ($CDCl_3$, 500 MHz)



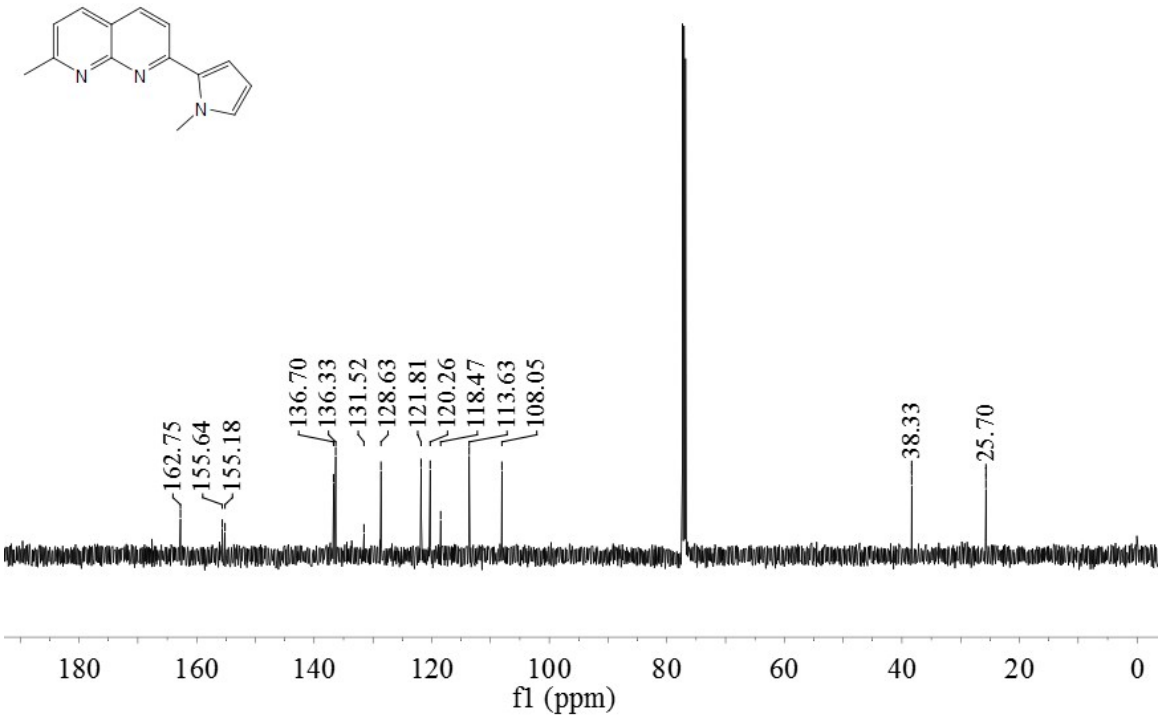
^{13}C NMR Spectrum for 2l ($CDCl_3$, 126 MHz)



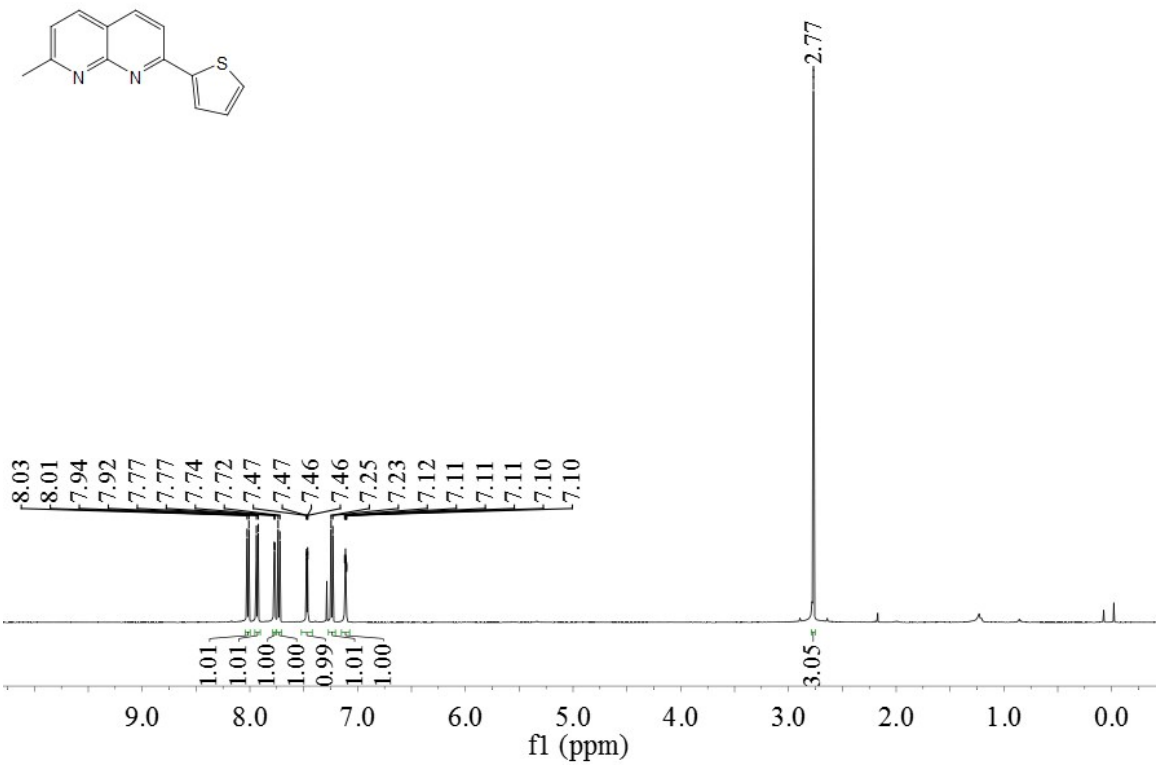
^{1}H NMR Spectrum for 2m ($CDCl_3$, 500 MHz)



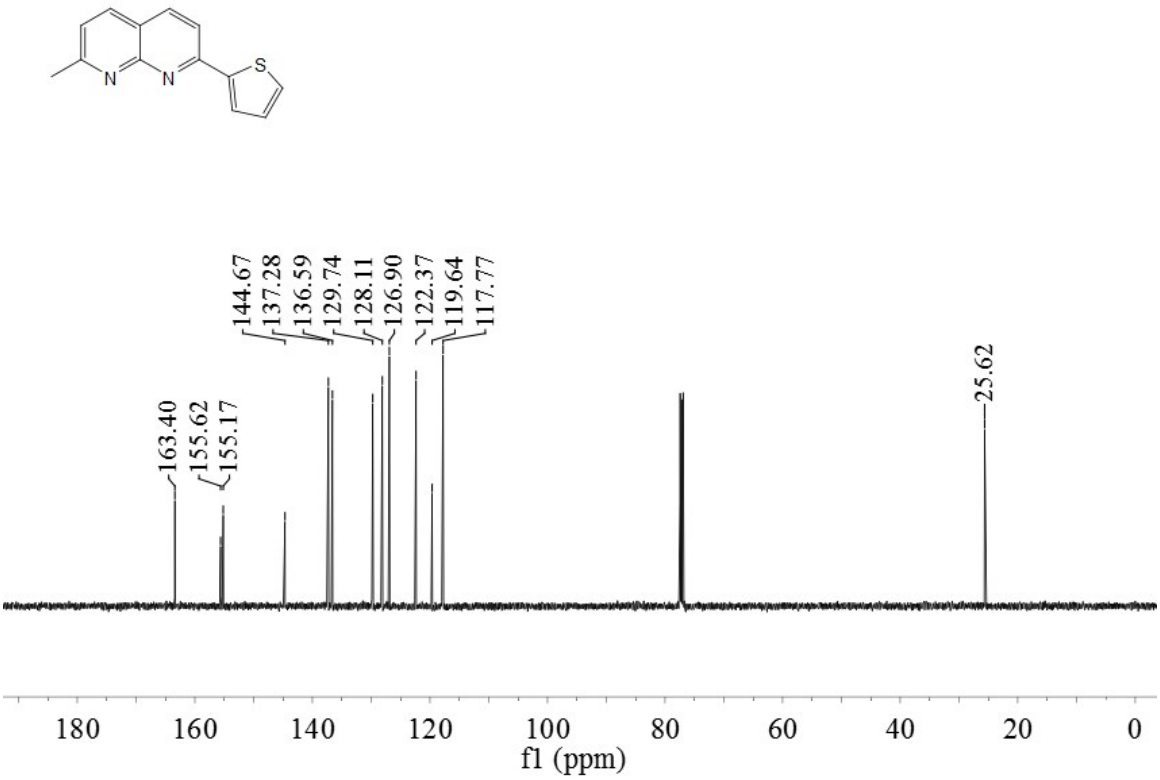
^{13}C NMR Spectrum for 2m ($CDCl_3$, 126 MHz)



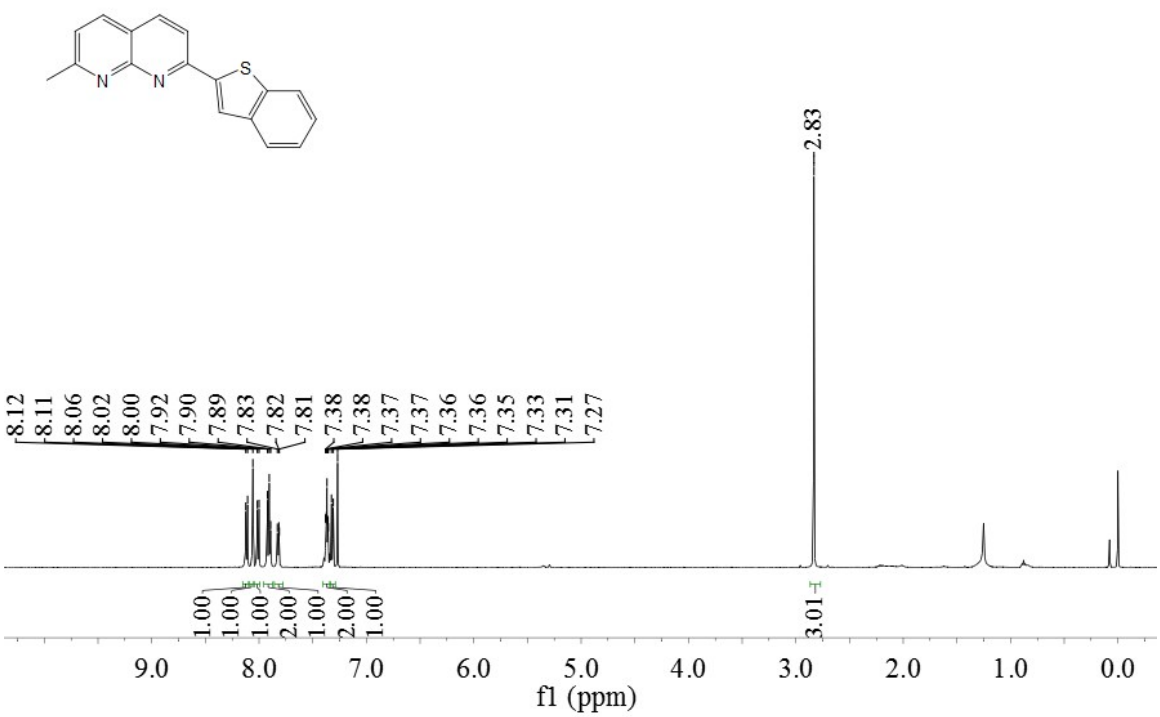
^{1}H NMR Spectrum for 2n ($CDCl_3$, 500 MHz)



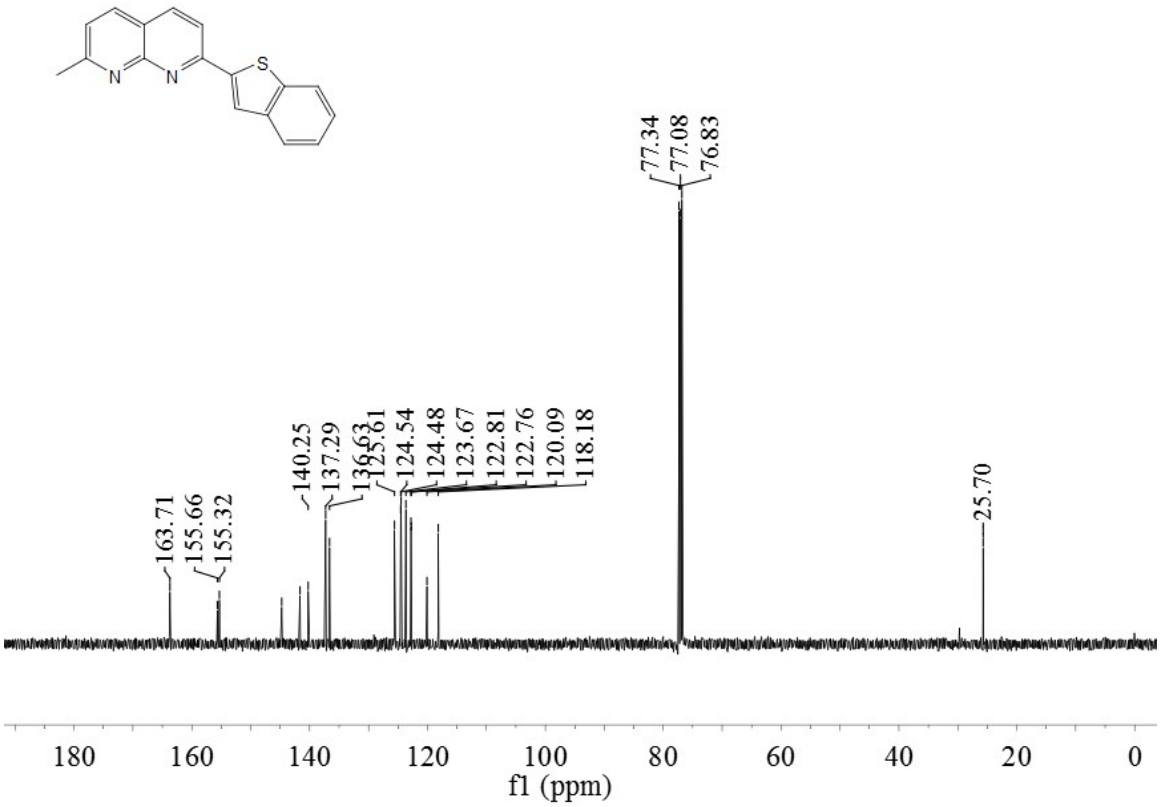
^{13}C NMR Spectrum for 2n ($CDCl_3$, 126 MHz)



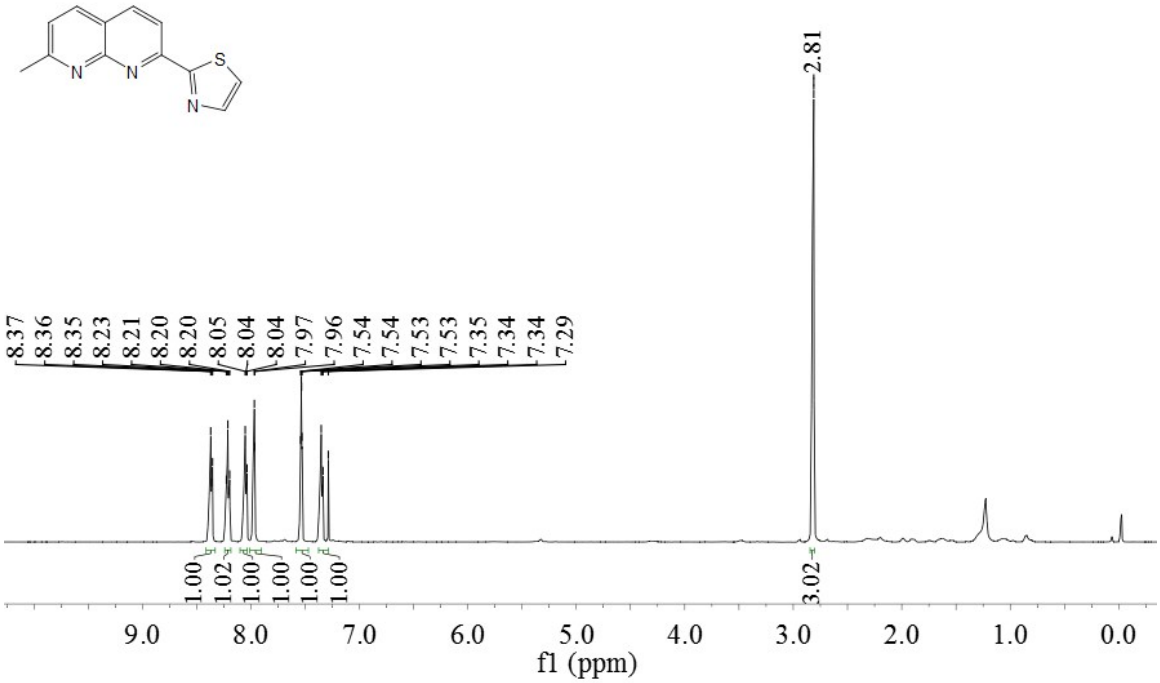
^{1}H NMR Spectrum for 2o ($CDCl_3$, 500 MHz)



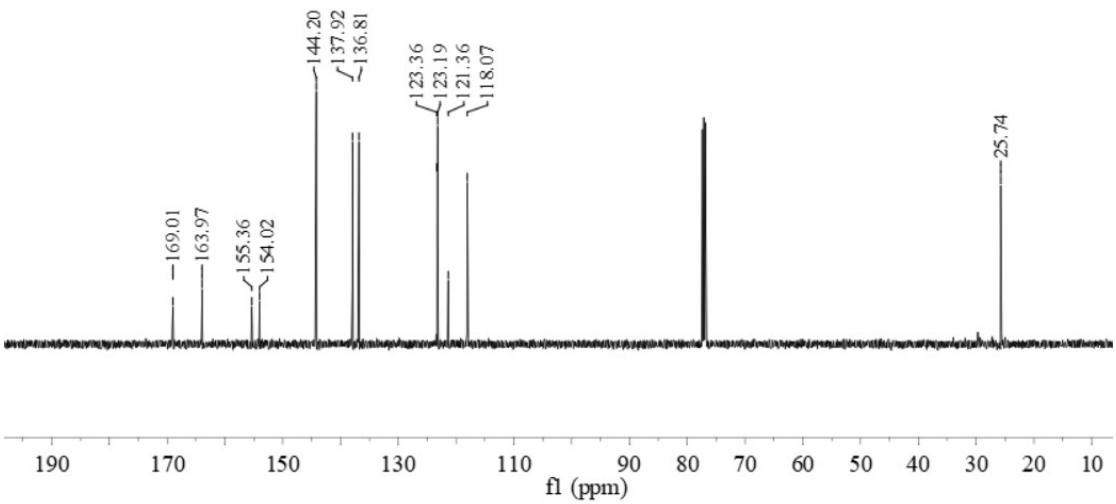
^{13}C NMR Spectrum for 2o ($CDCl_3$, 126 MHz)



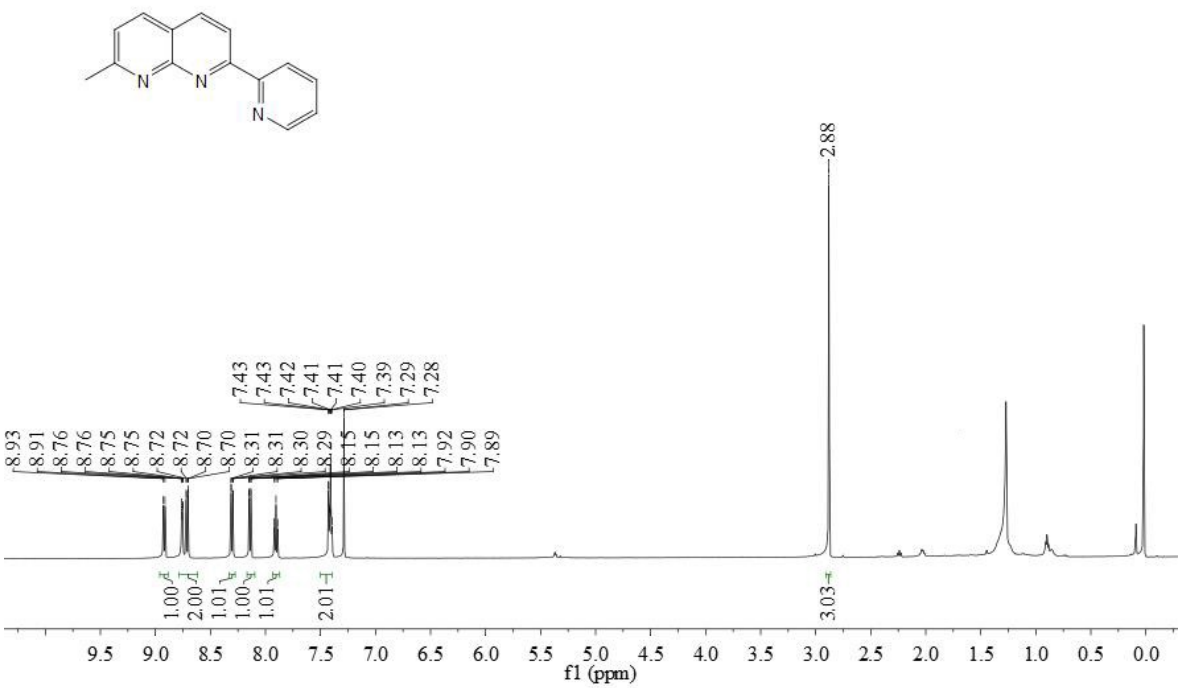
^{1}H NMR Spectrum for 2p ($CDCl_3$, 500 MHz)



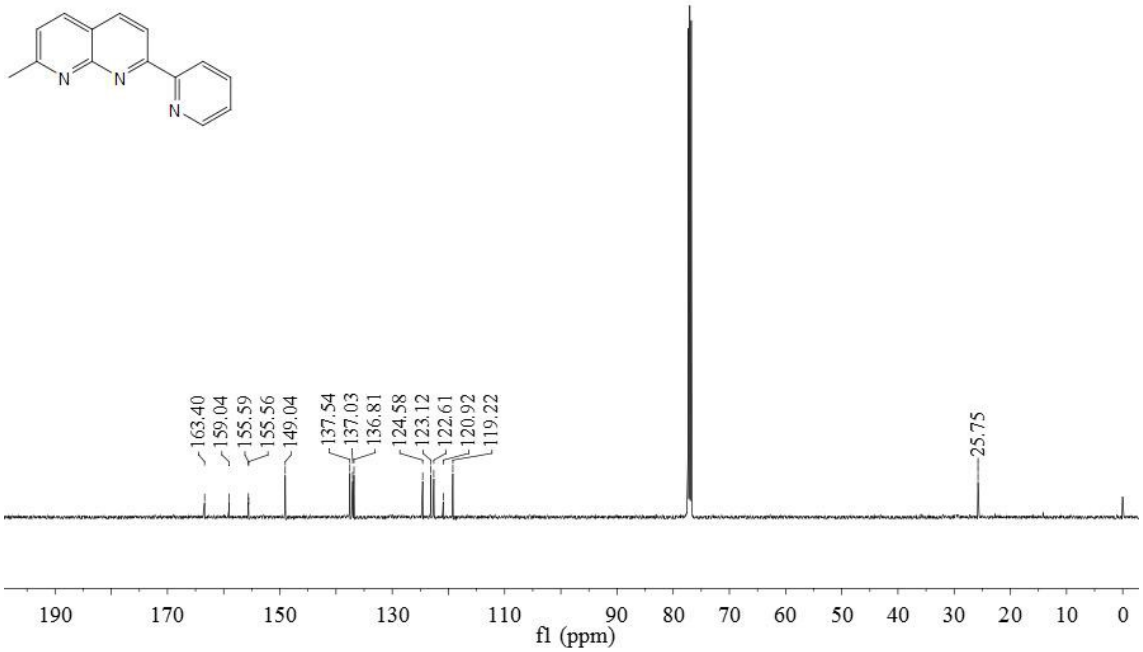
^{13}C NMR Spectrum for 2p ($CDCl_3$, 126 MHz)



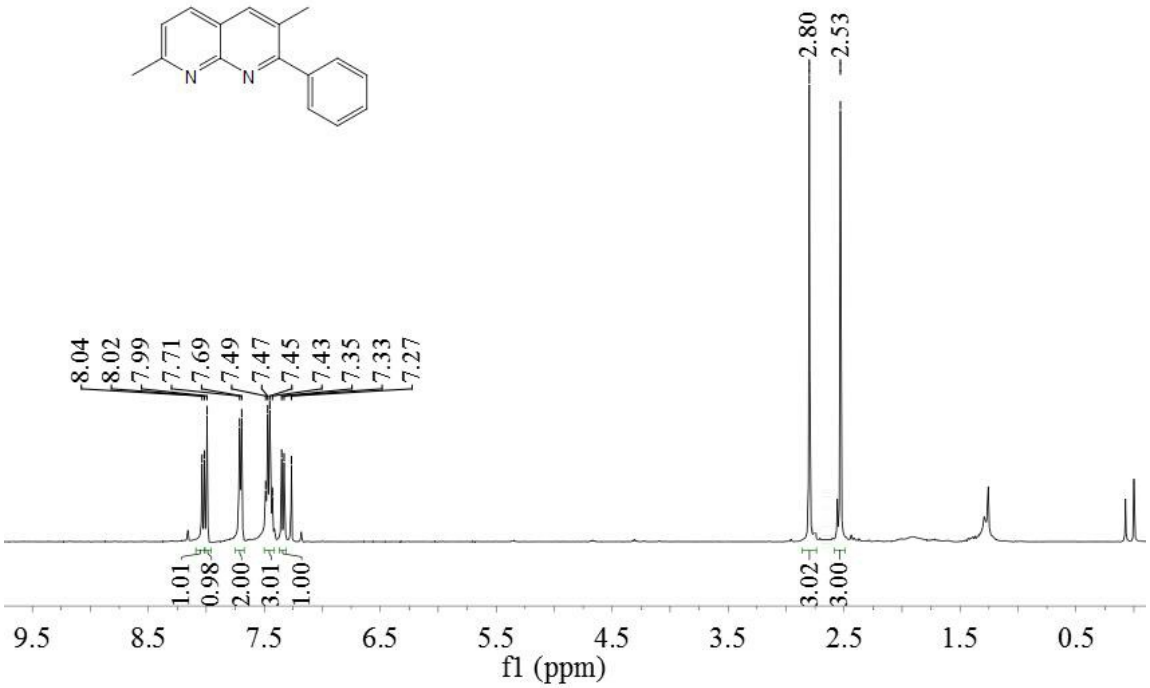
^{1}H NMR Spectrum for 2q ($CDCl_3$, 500 MHz)



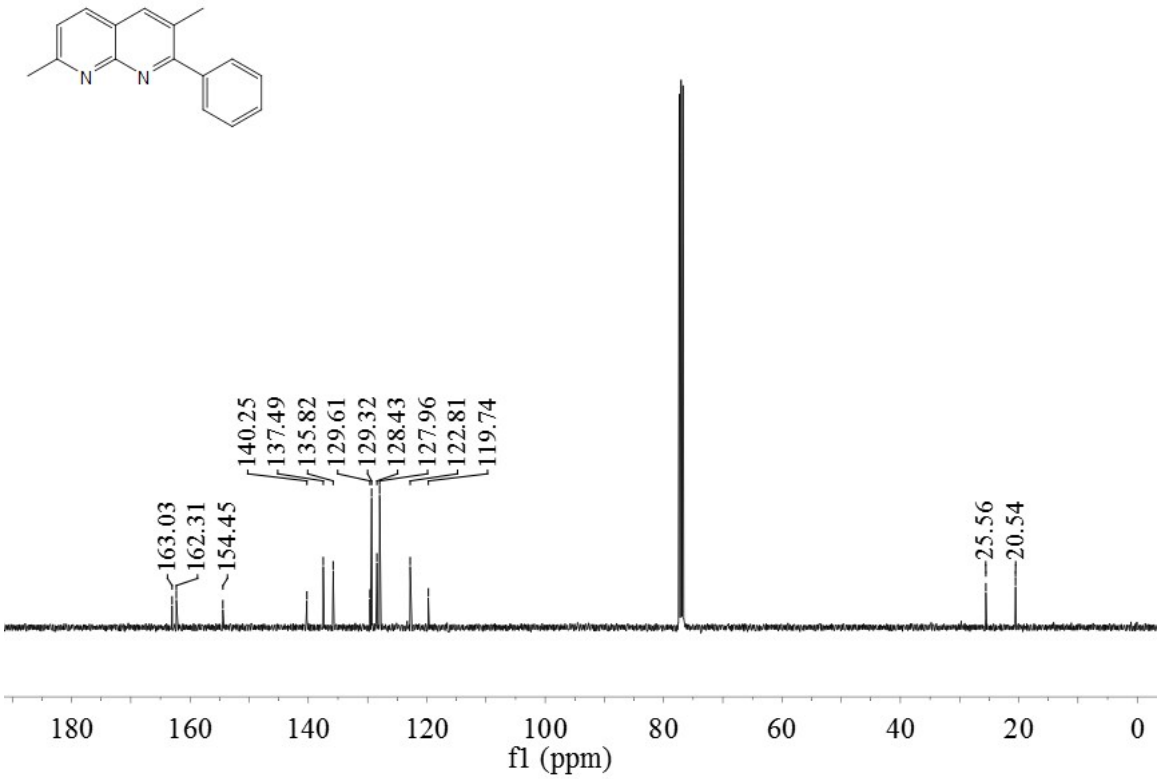
^{13}C NMR Spectrum for 2q ($CDCl_3$, 126 MHz)



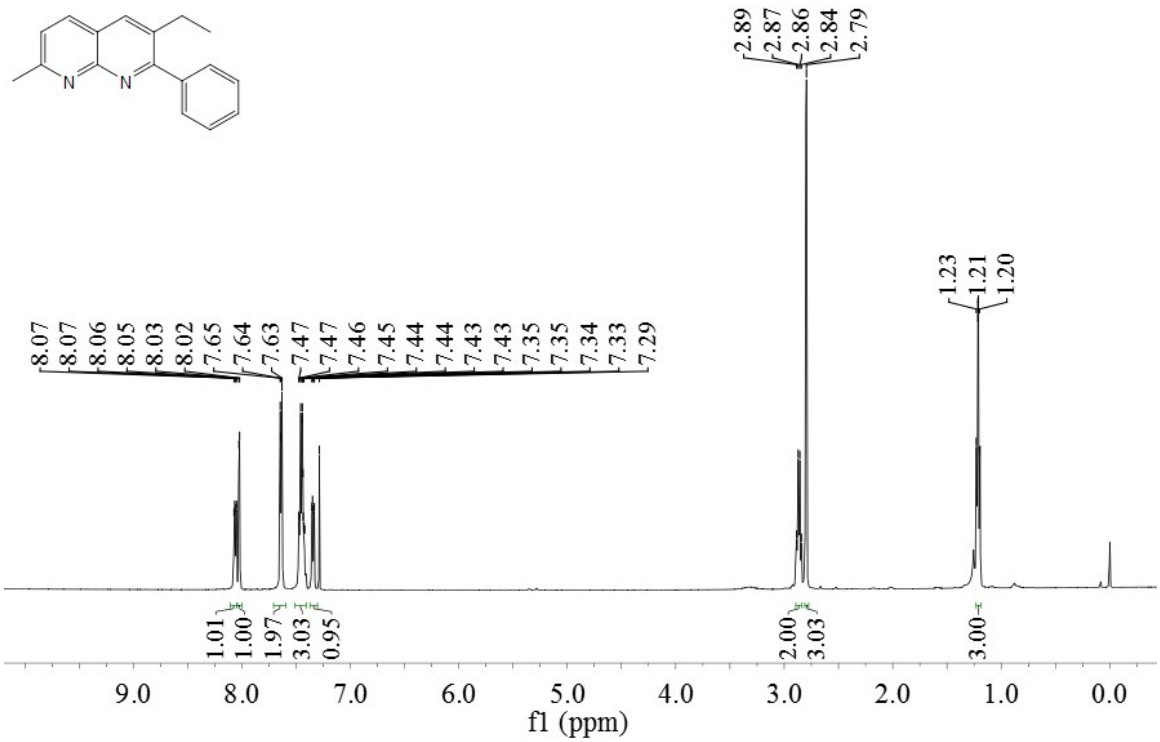
^{1}H NMR Spectrum for 2r ($CDCl_3$, 500 MHz)



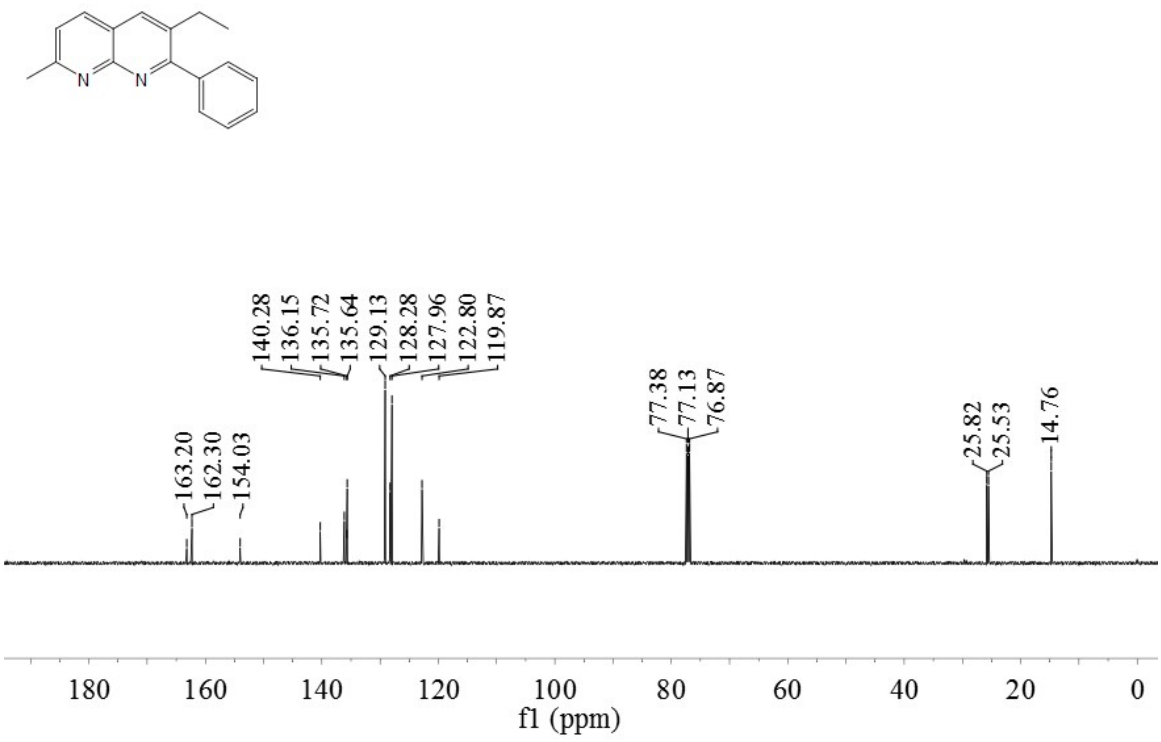
^{13}C NMR Spectrum for 2r ($CDCl_3$, 126 MHz)



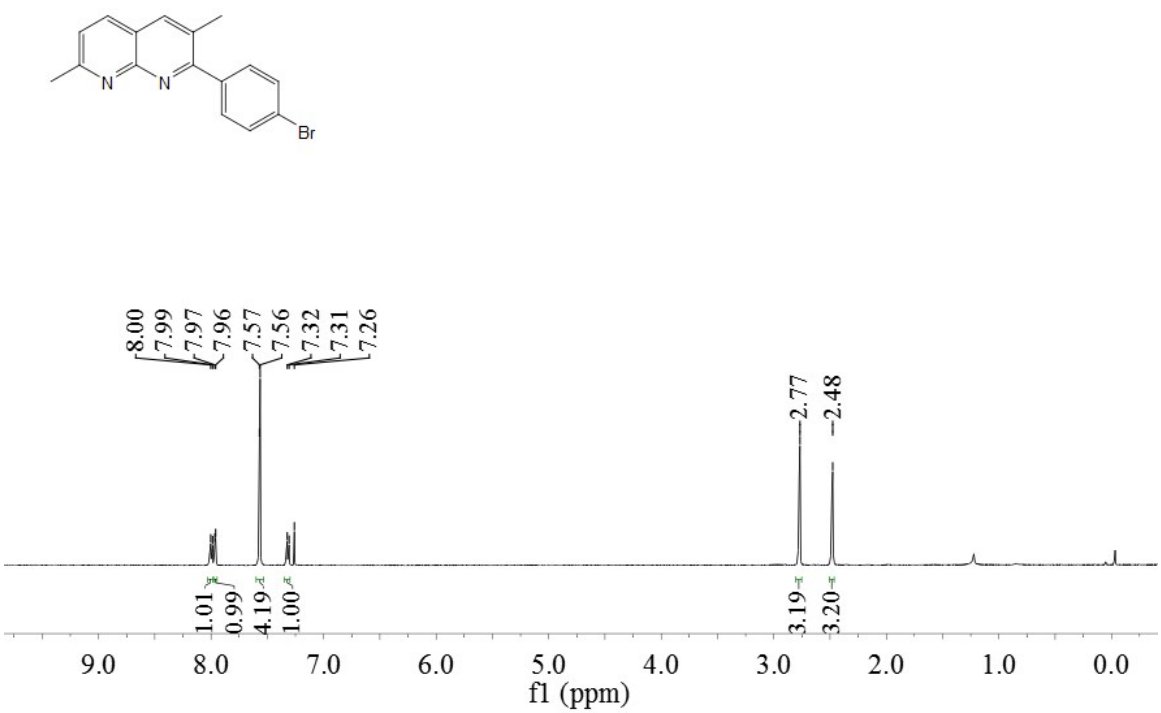
^{1}H NMR Spectrum for 2s ($CDCl_3$, 500 MHz)



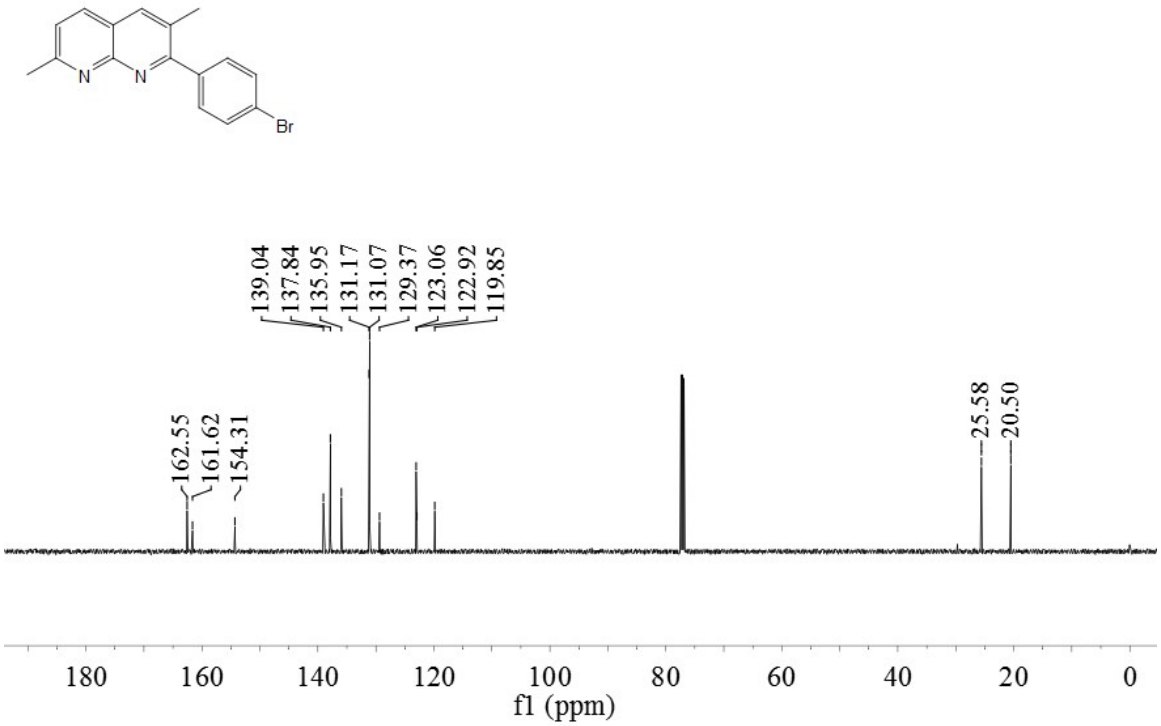
^{13}C NMR Spectrum for 2s ($CDCl_3$, 126 MHz)



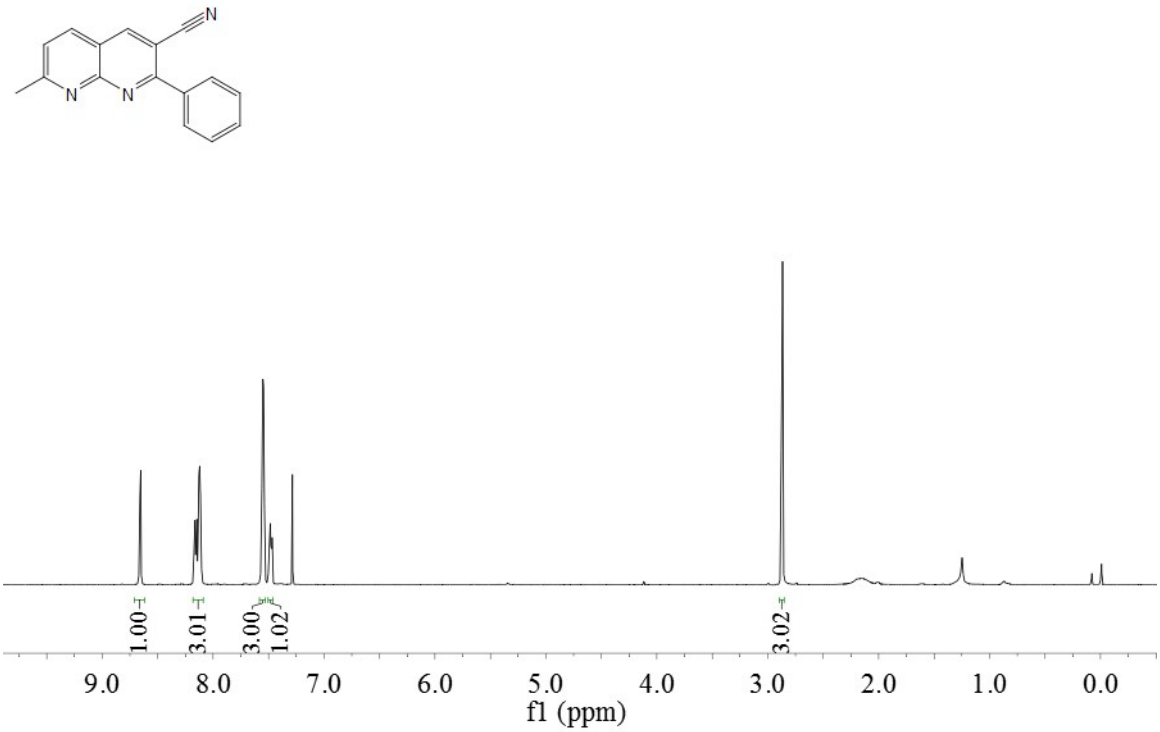
^{1}H NMR Spectrum for 2t ($CDCl_3$, 500 MHz)



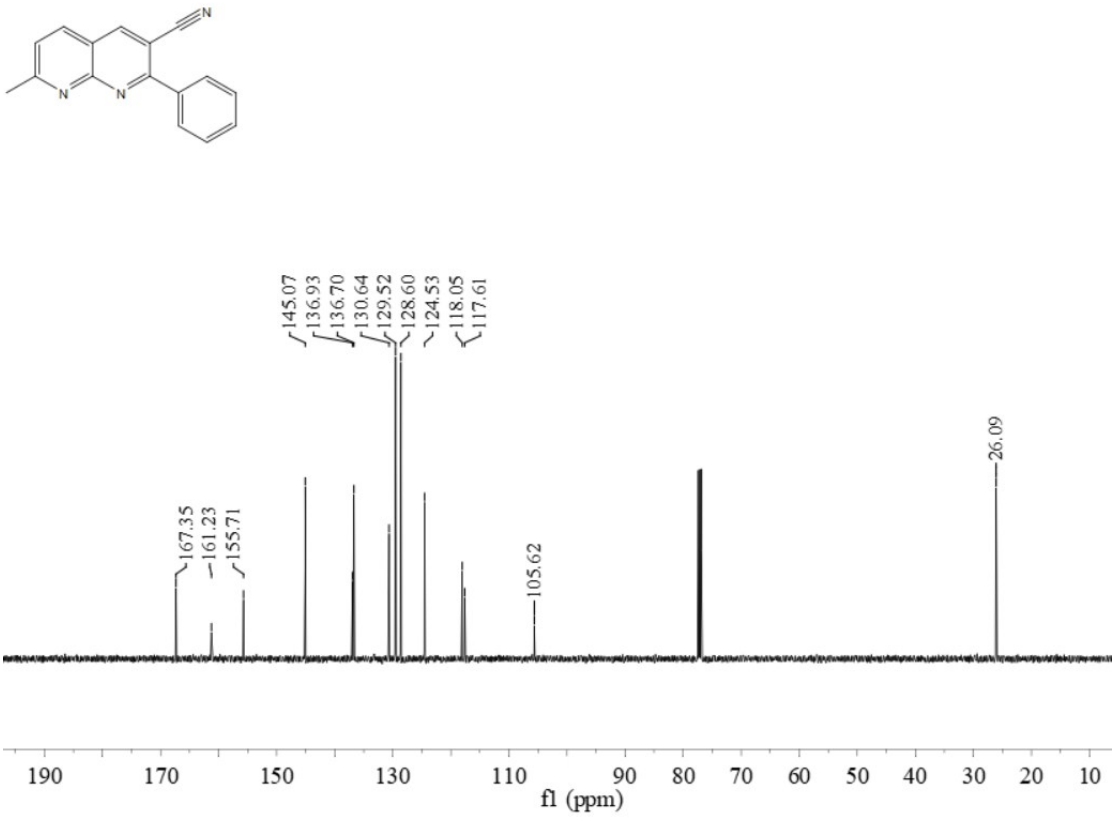
^{13}C NMR Spectrum for 2t ($CDCl_3$, 126 MHz)



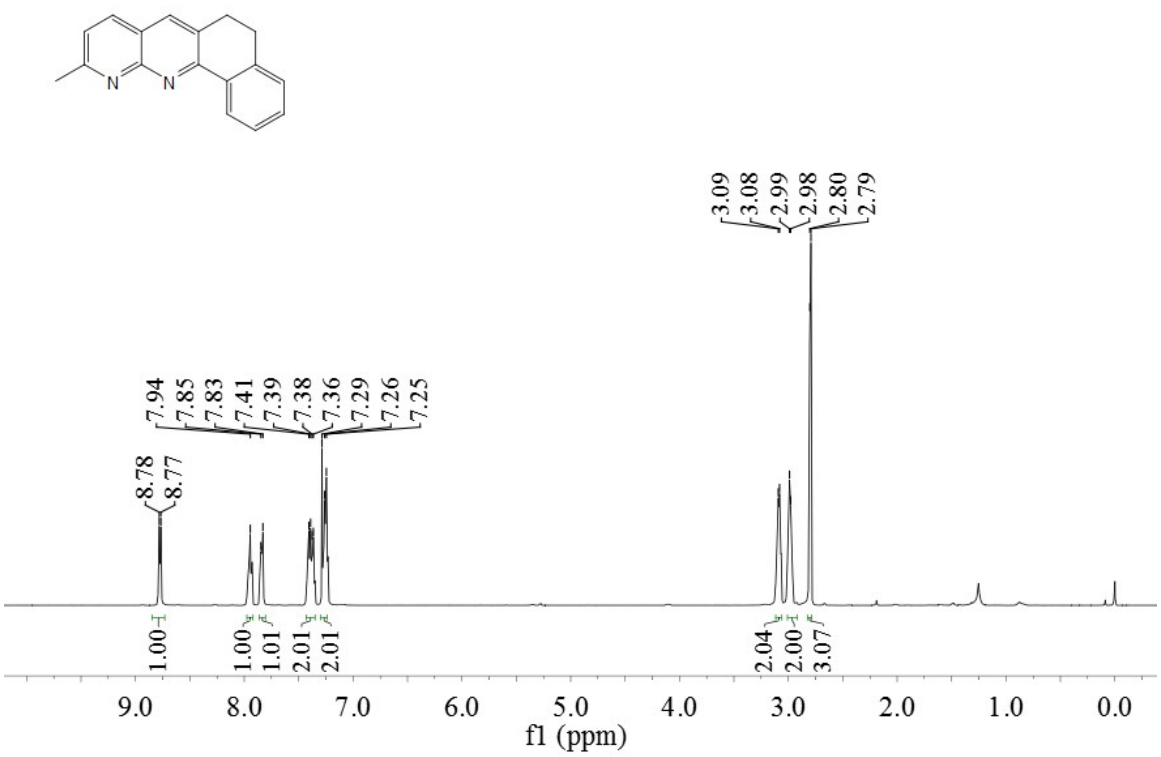
^{1}H NMR Spectrum for 2u ($CDCl_3$, 500 MHz)



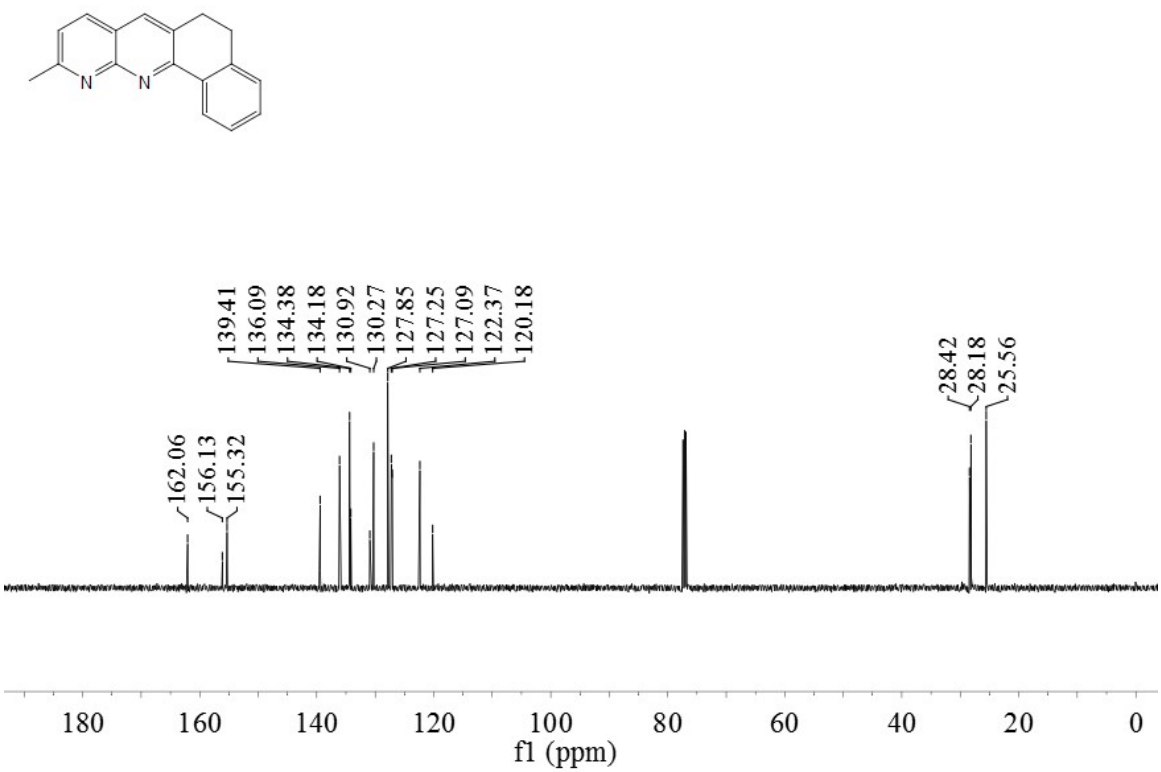
^{13}C NMR Spectrum for 2u ($CDCl_3$, 126 MHz)



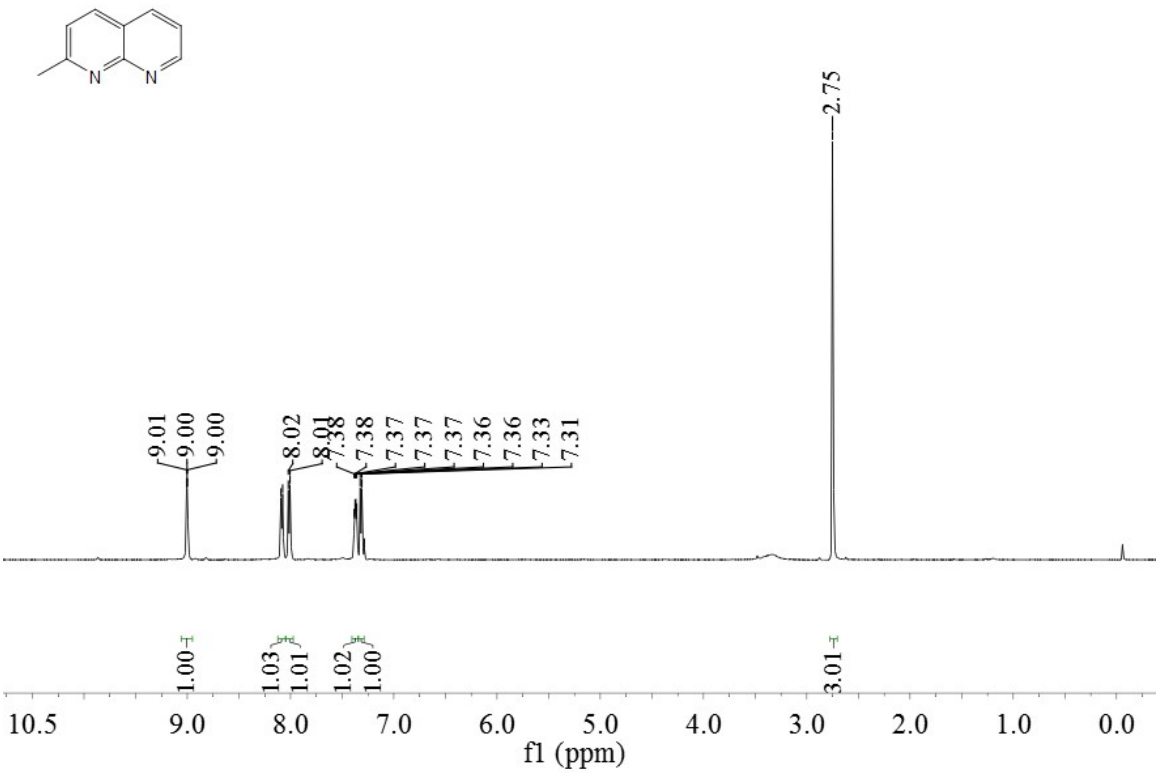
^{1}H NMR Spectrum for 2v ($CDCl_3$, 500 MHz)



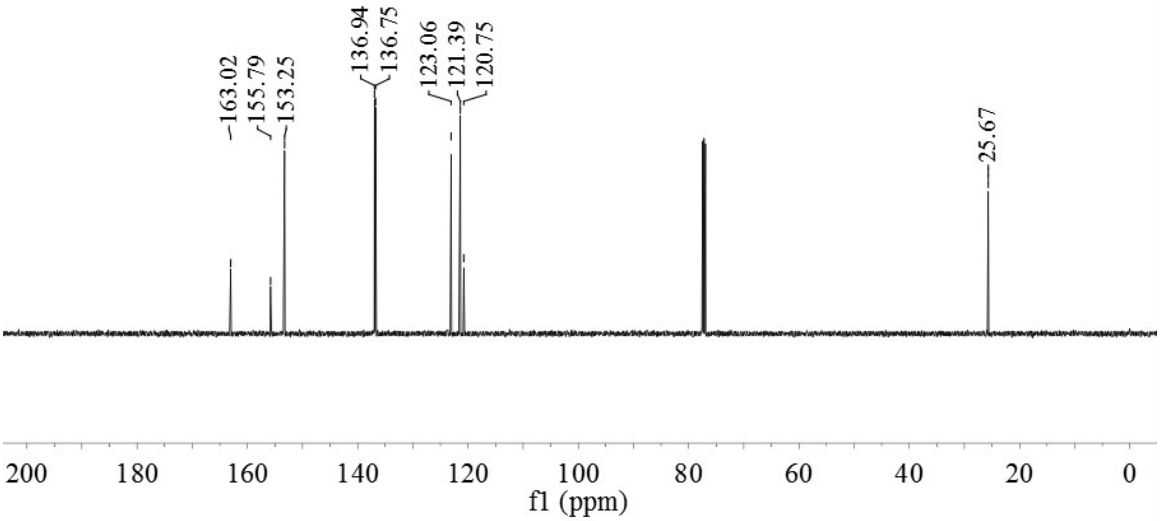
^{13}C NMR Spectrum for 2v ($CDCl_3$, 126 MHz)



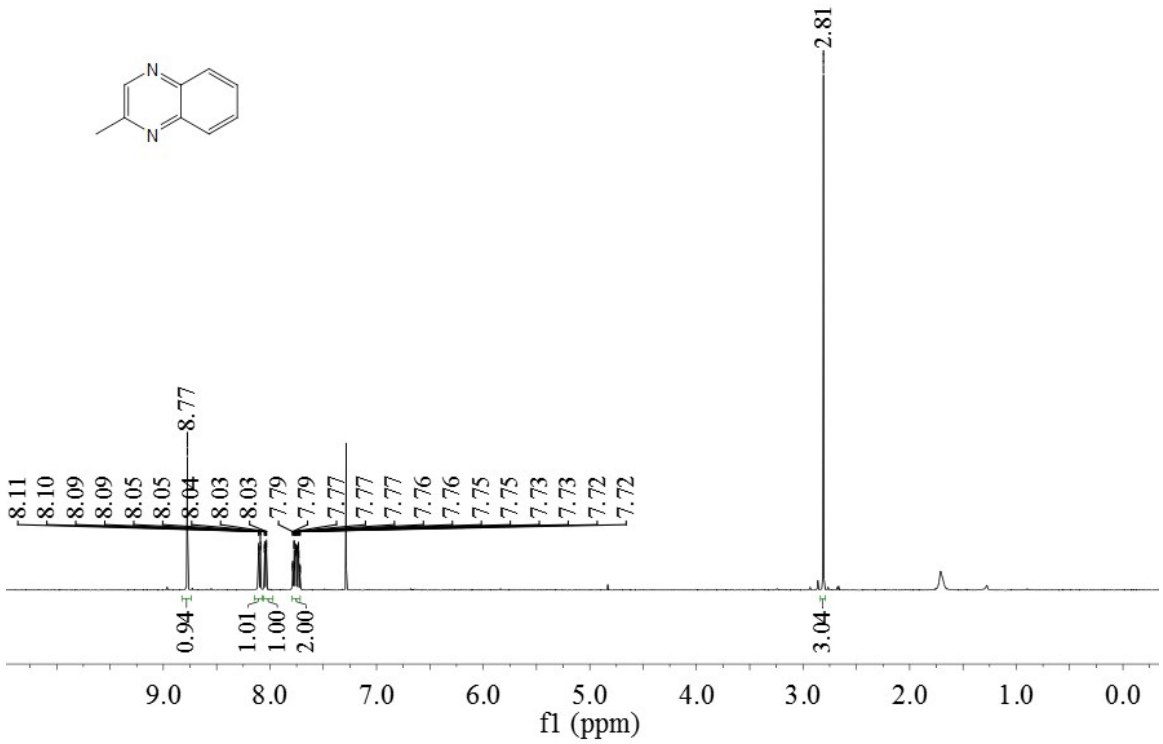
^{1}H NMR Spectrum for 2w ($CDCl_3$, 500 MHz)



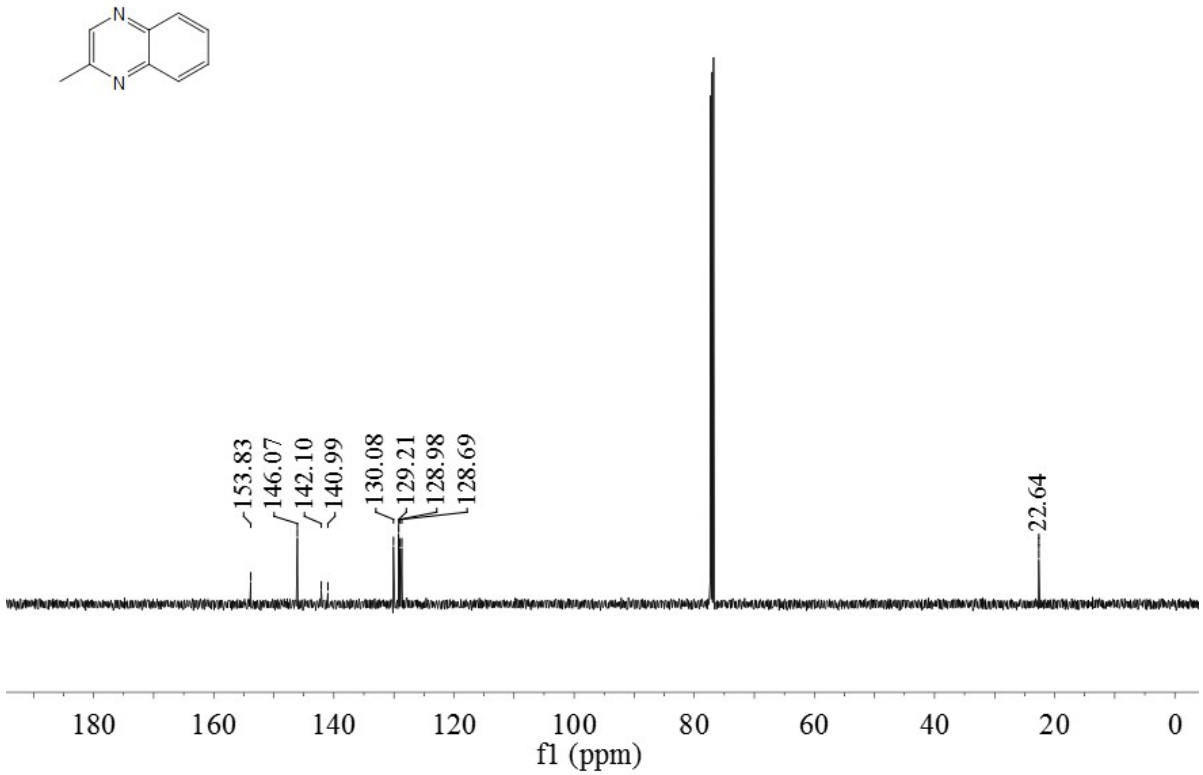
^{13}C NMR Spectrum for 2w ($CDCl_3$, 126 MHz)



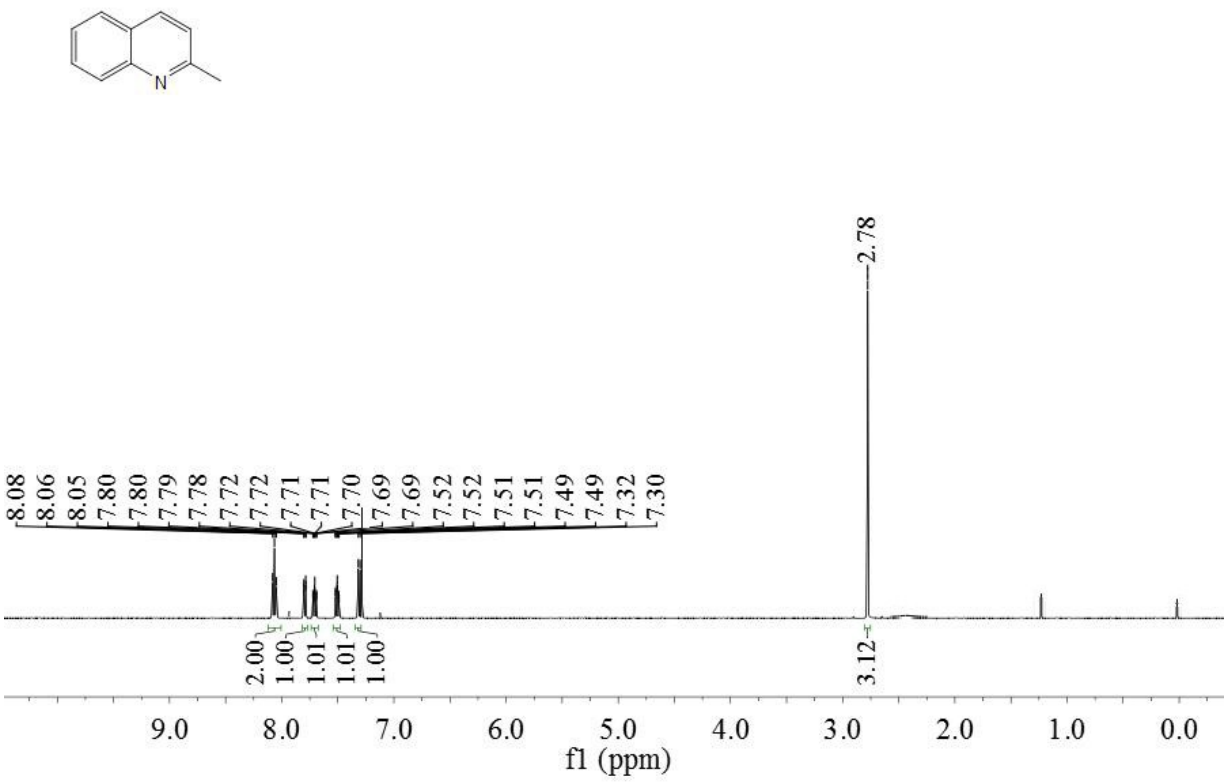
^{1}H NMR Spectrum for 2x ($CDCl_3$, 500 MHz)



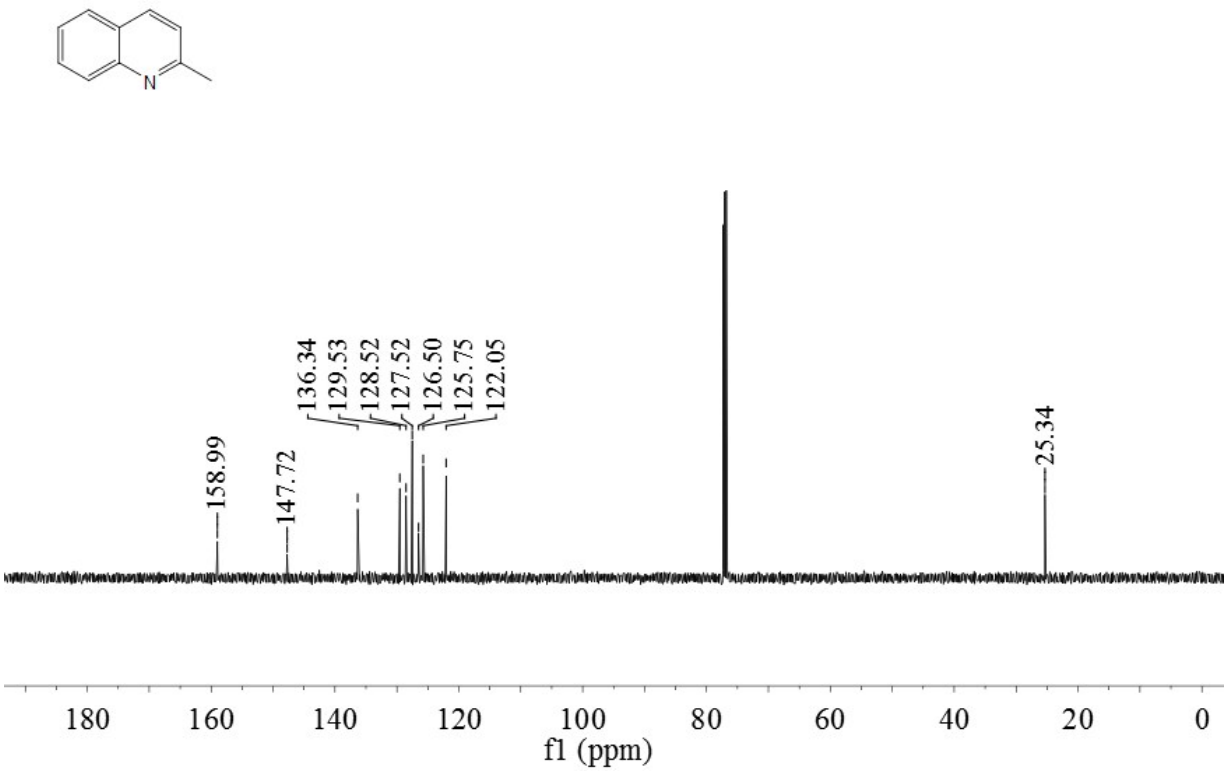
^{13}C NMR Spectrum for 2x ($CDCl_3$, 126 MHz)



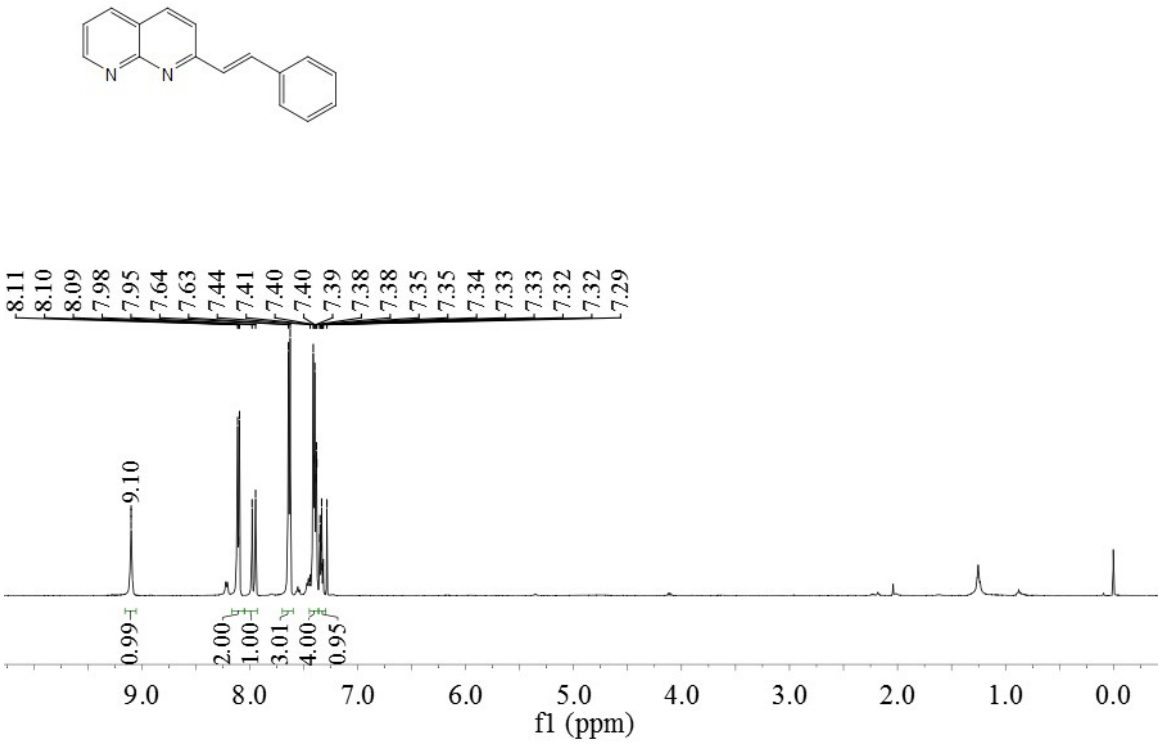
^{1}H NMR Spectrum for 2z ($CDCl_3$, 500 MHz)



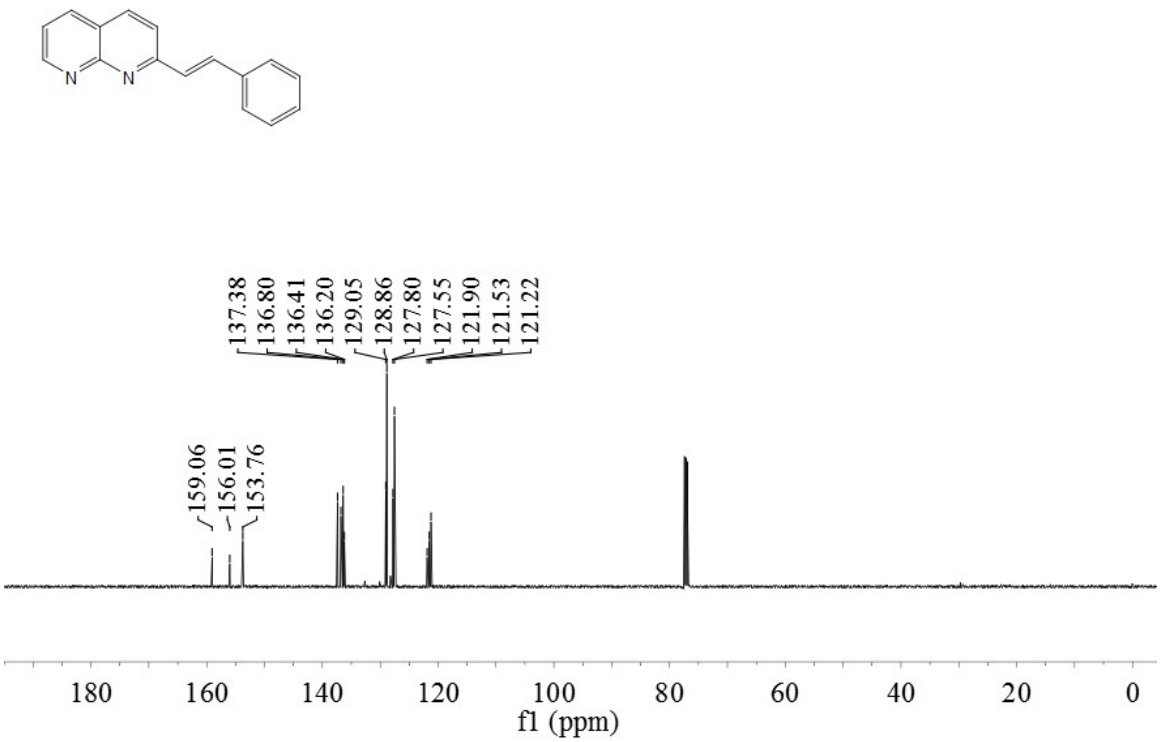
^{13}C NMR Spectrum for 2z ($CDCl_3$, 126 MHz)



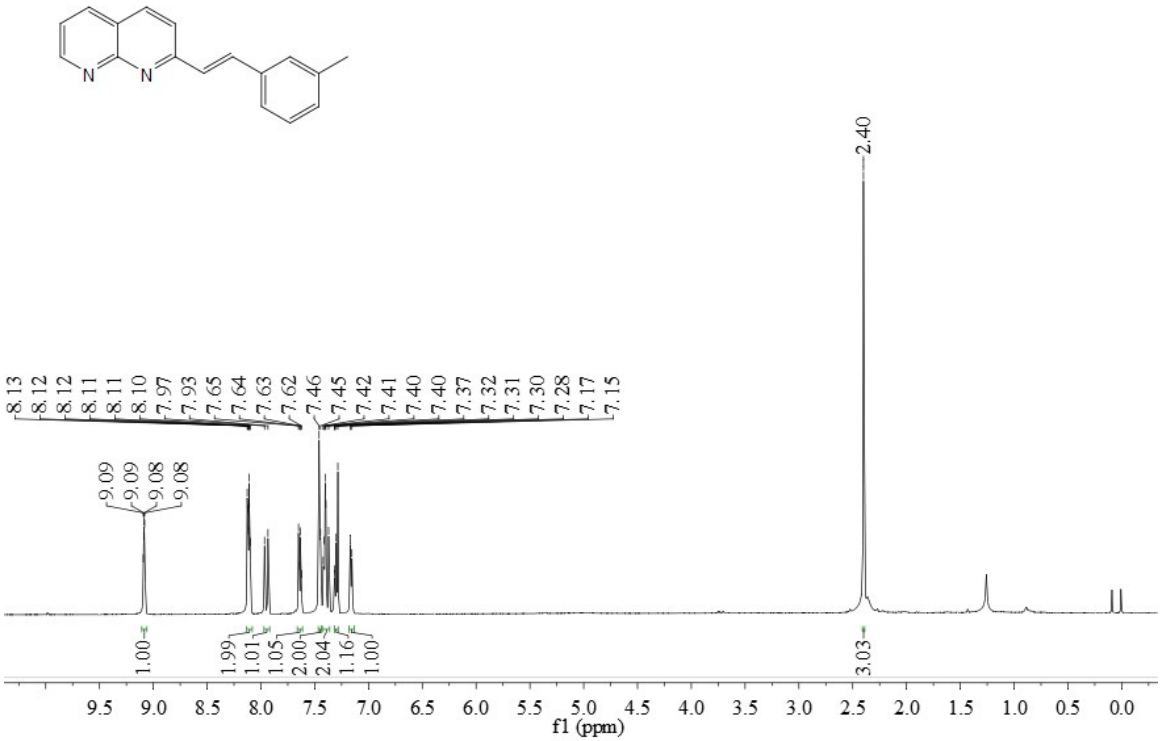
^{1}H NMR Spectrum for 3a ($CDCl_3$, 500 MHz)



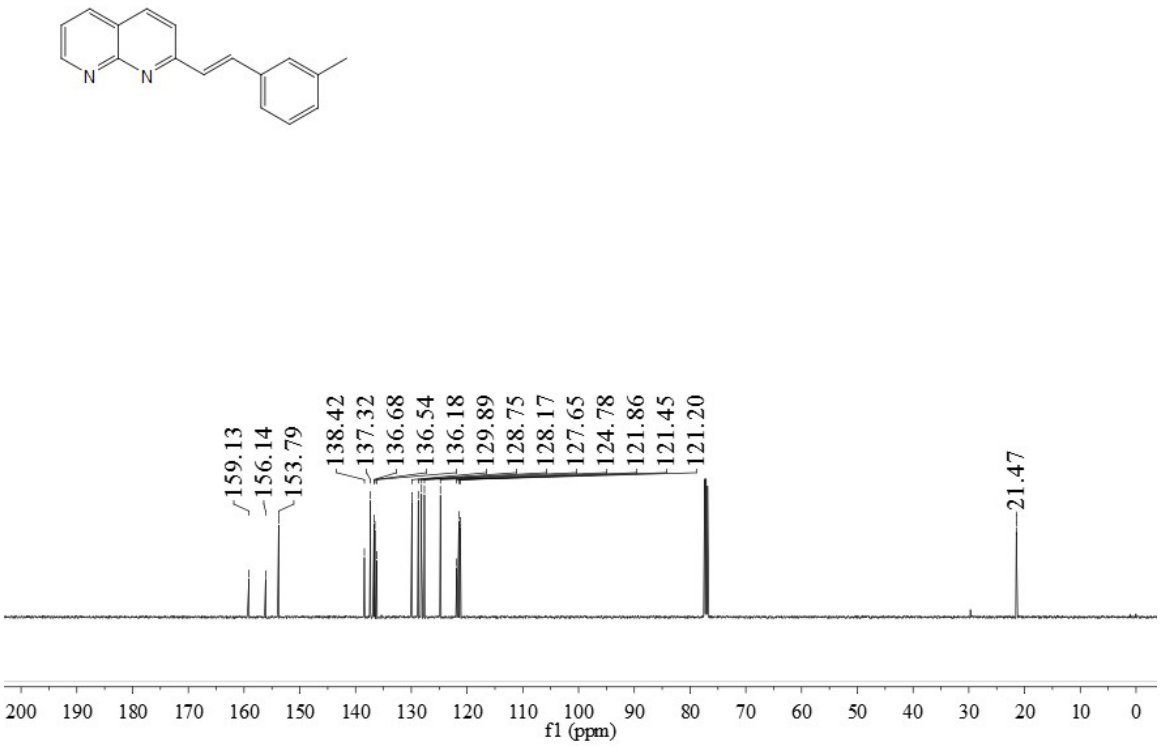
^{13}C NMR Spectrum for 3a ($CDCl_3$, 126 MHz)



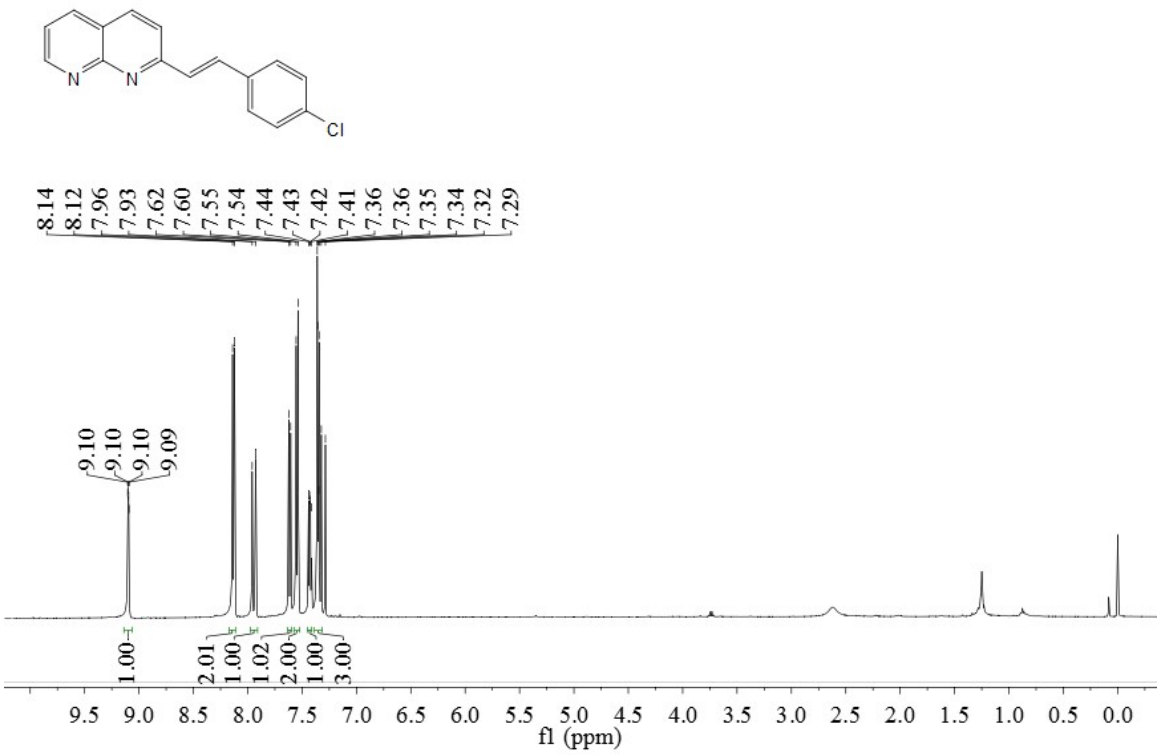
^{1}H NMR Spectrum for 3b ($CDCl_3$, 500 MHz)



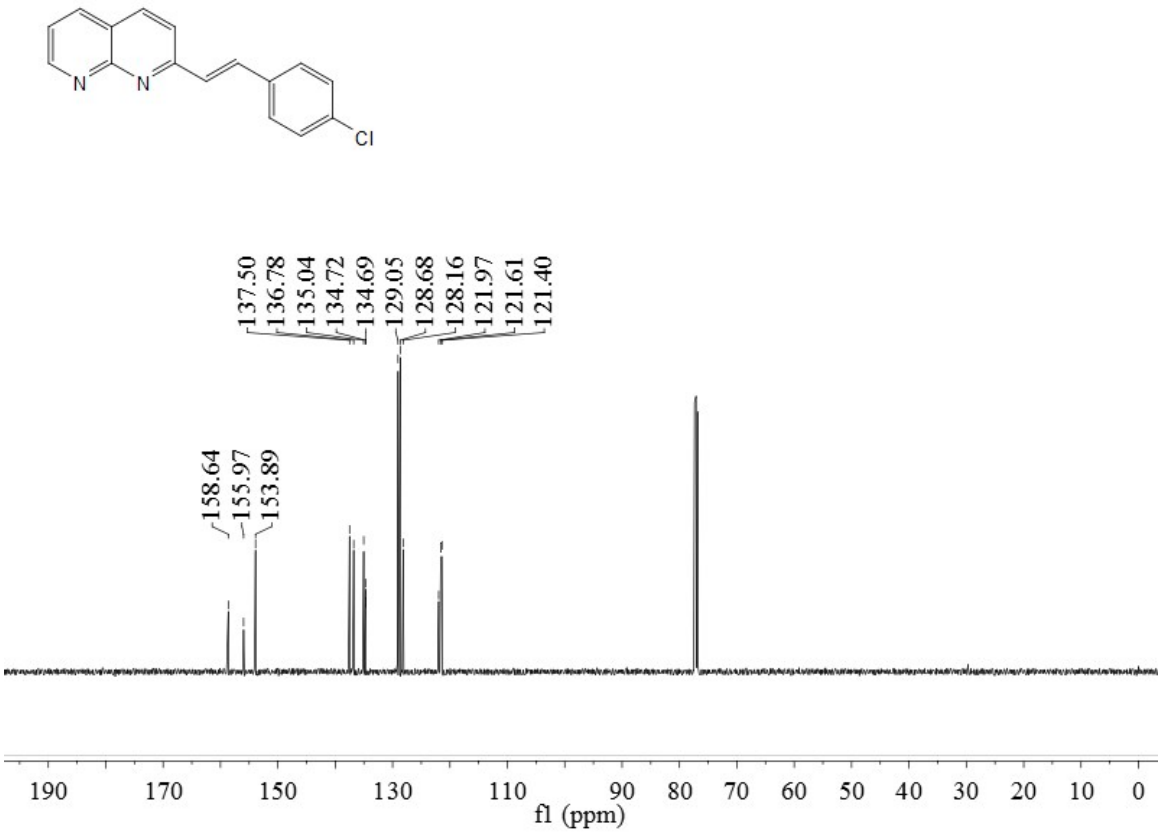
^{13}C NMR Spectrum for 3b ($CDCl_3$, 126 MHz)



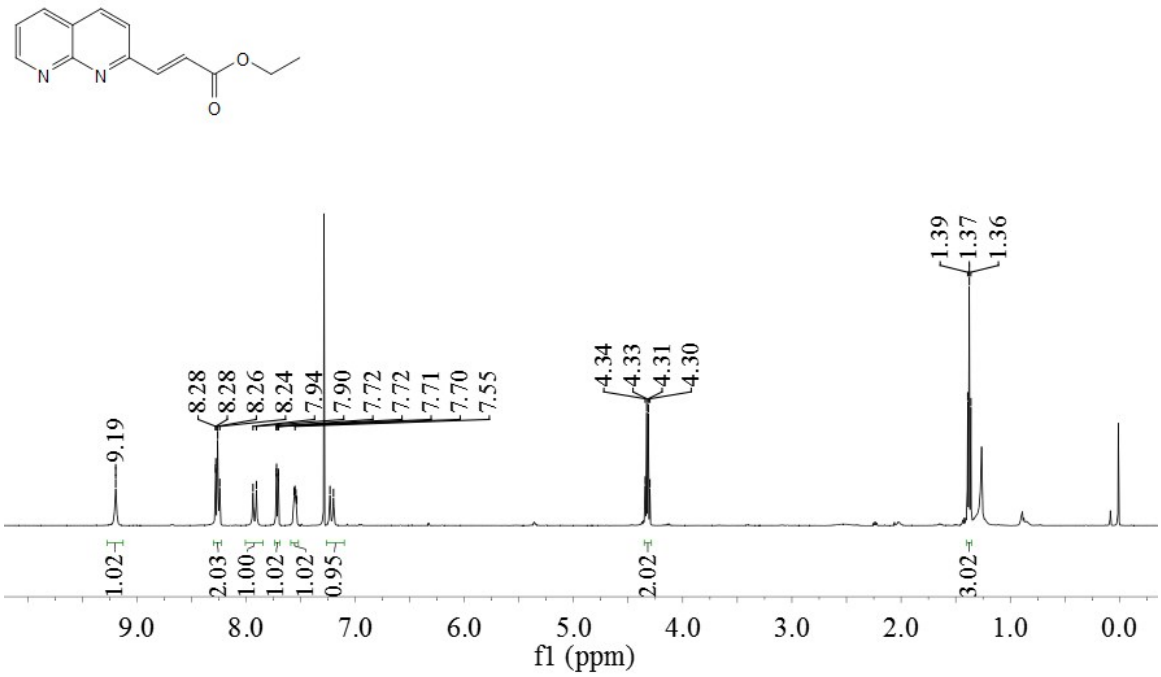
^{1}H NMR Spectrum for 3c ($CDCl_3$, 500 MHz)



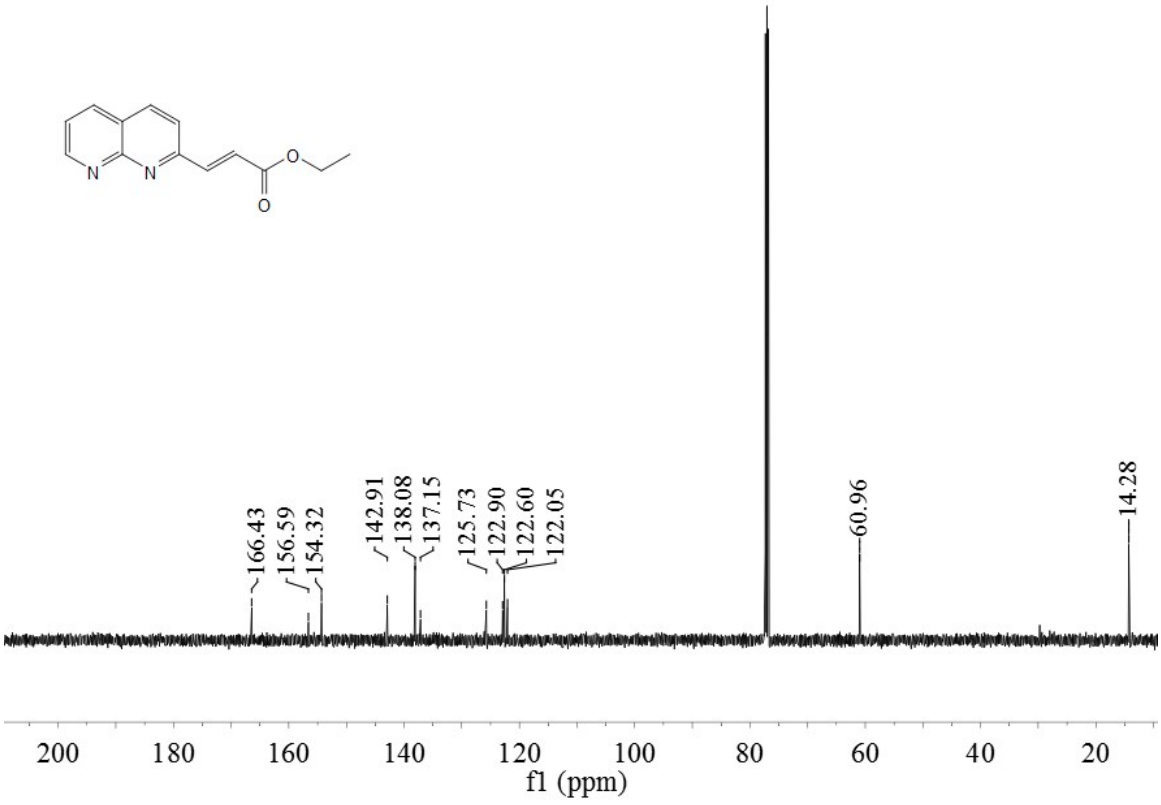
^{13}C NMR Spectrum for 3c ($CDCl_3$, 126 MHz)



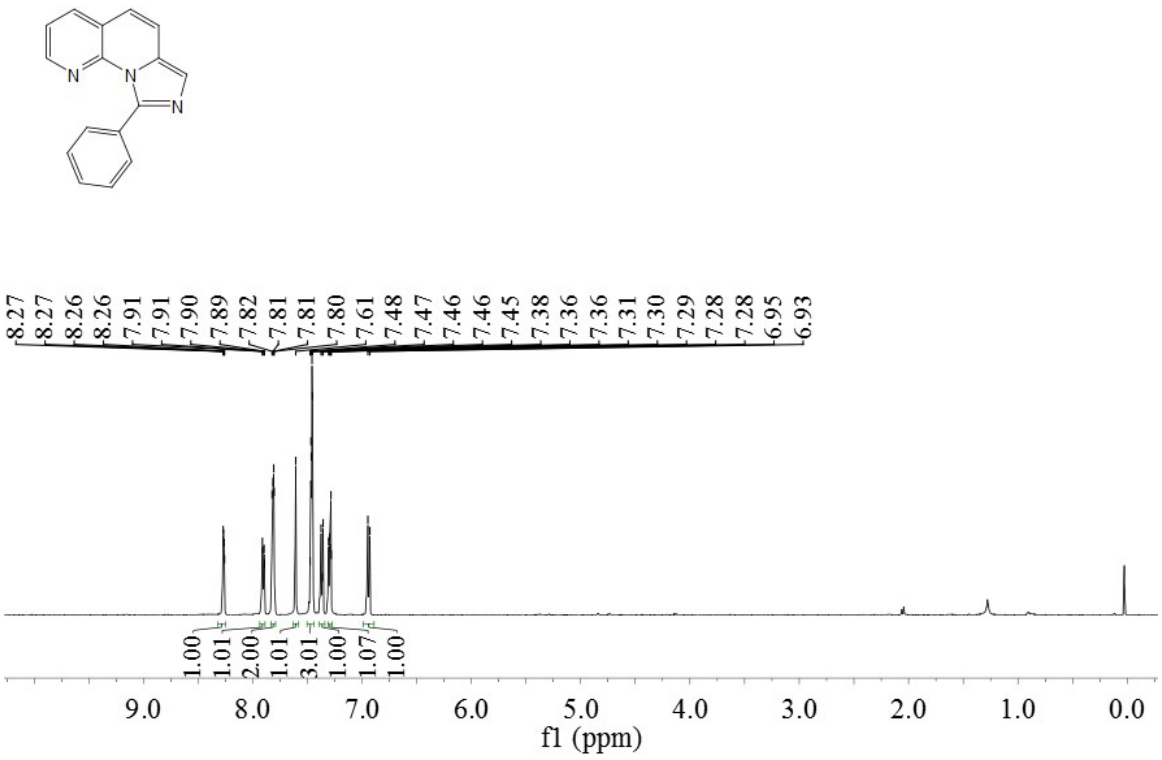
^{1}H NMR Spectrum for 3d ($CDCl_3$, 500 MHz)



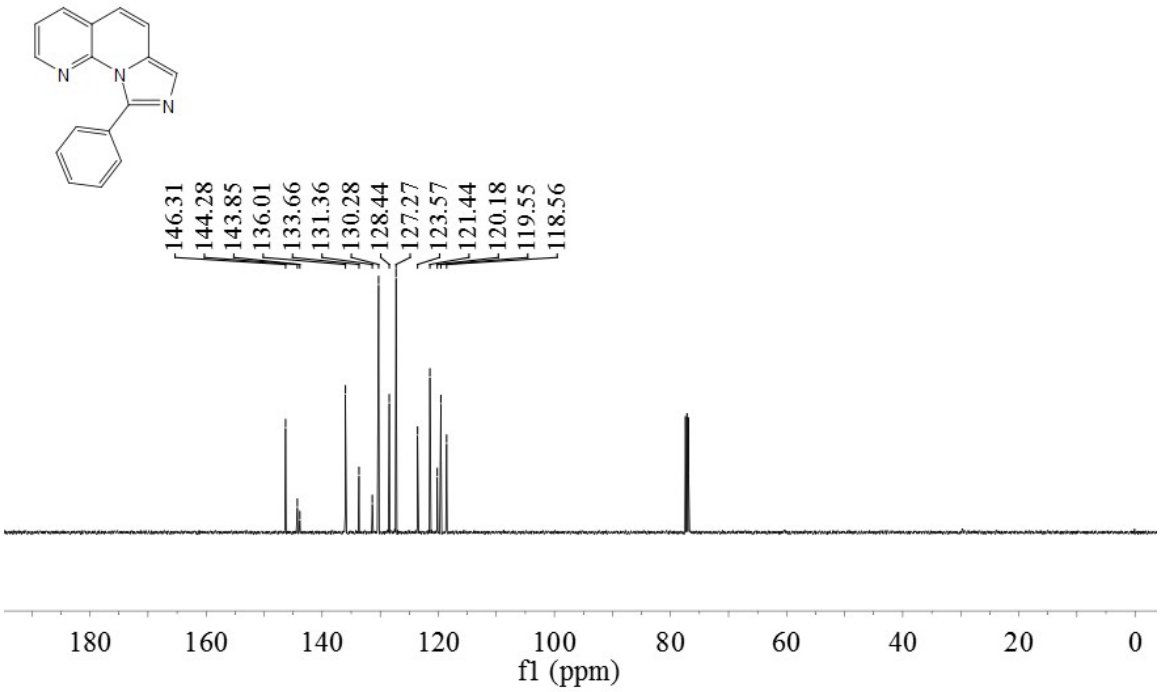
^{13}C NMR Spectrum for 3d ($CDCl_3$, 126 MHz)



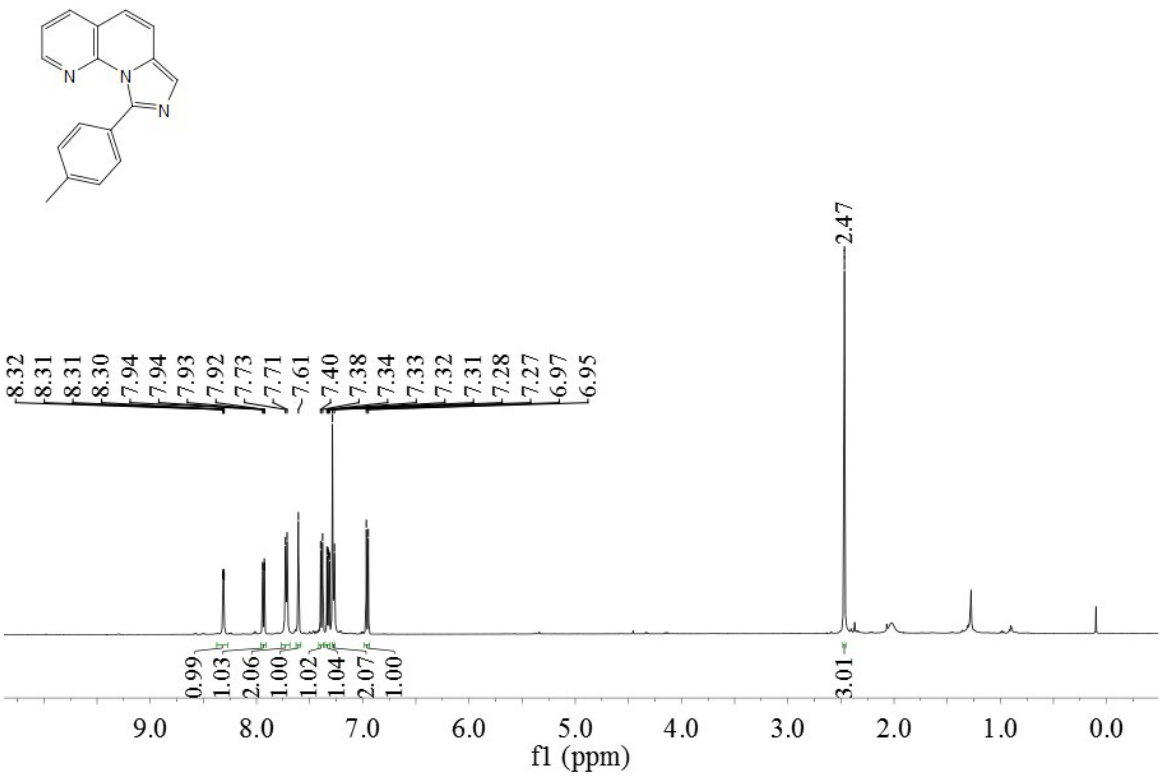
^{1}H NMR Spectrum for 4a ($CDCl_3$, 500 MHz)



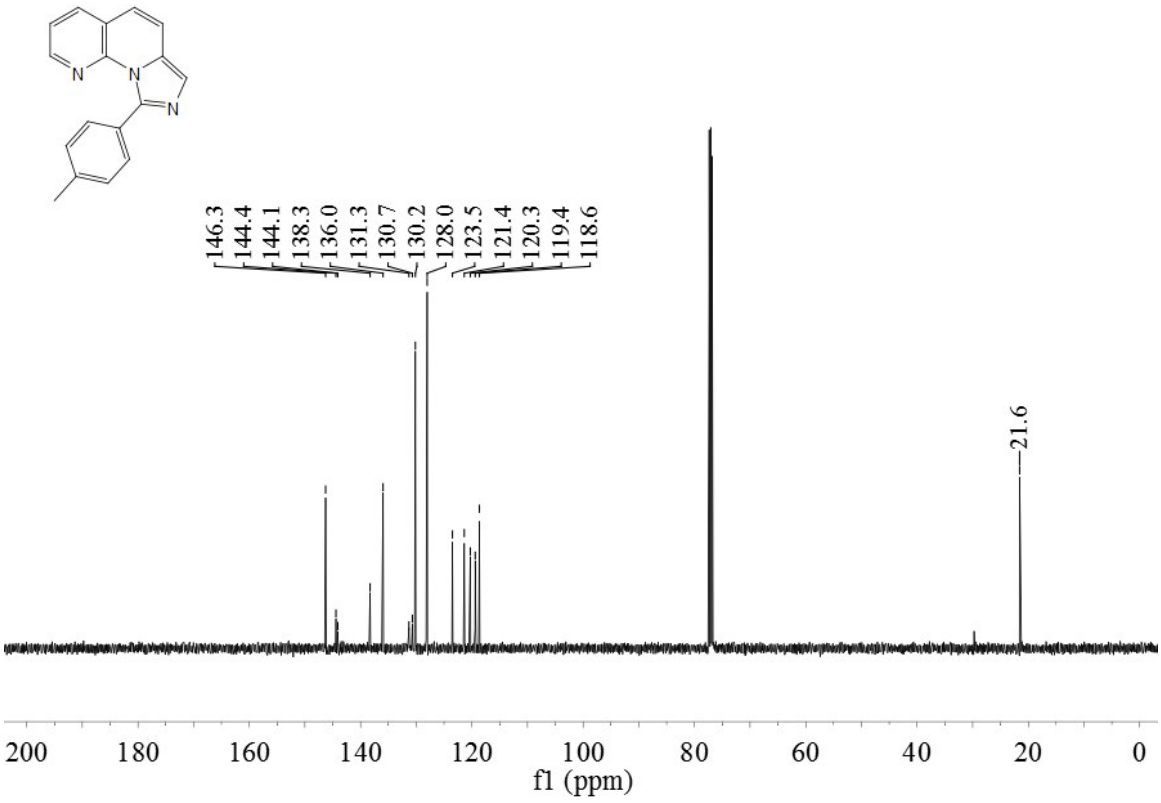
^{13}C NMR Spectrum for 4a ($CDCl_3$, 126 MHz)



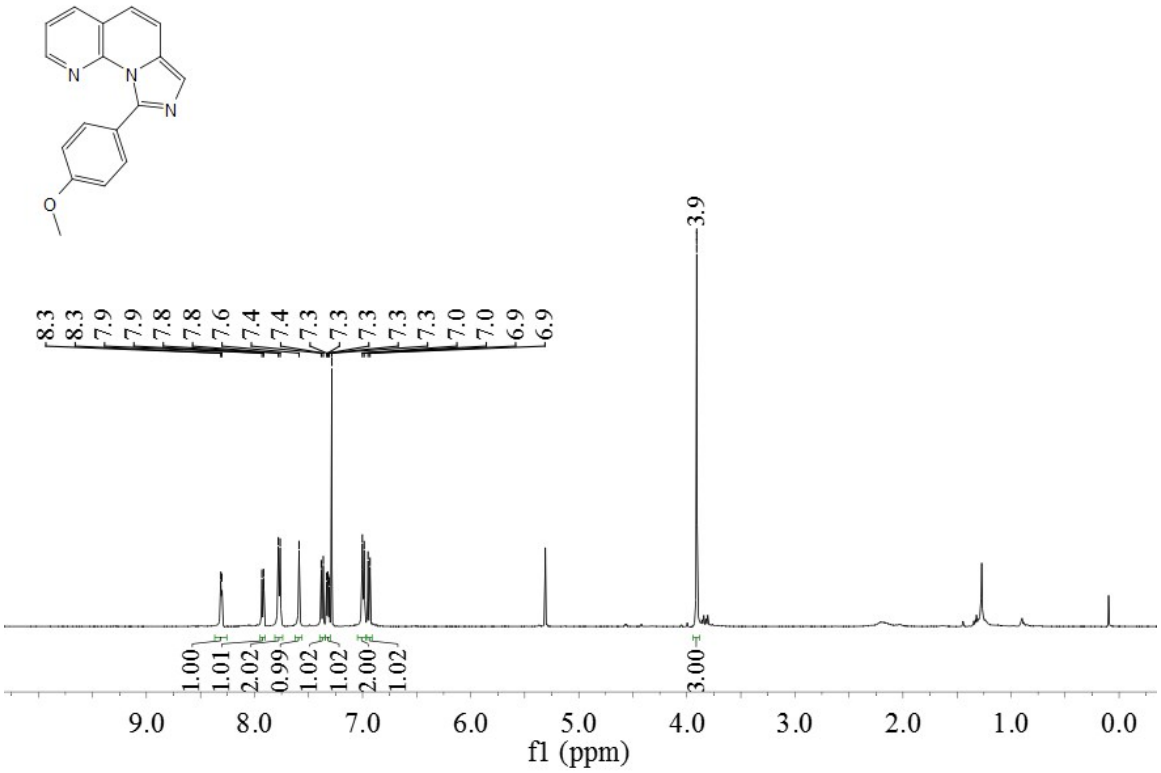
^{1}H NMR Spectrum for 4b ($CDCl_3$, 500 MHz)



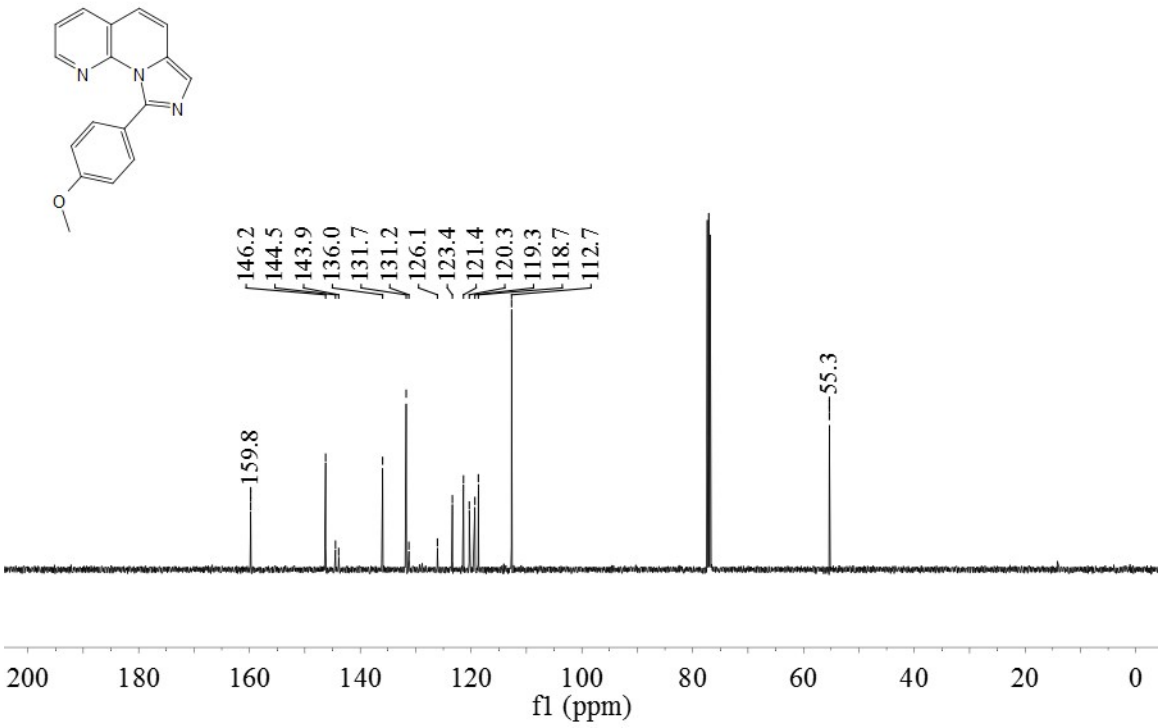
^{13}C NMR Spectrum for 4b ($CDCl_3$, 126 MHz)



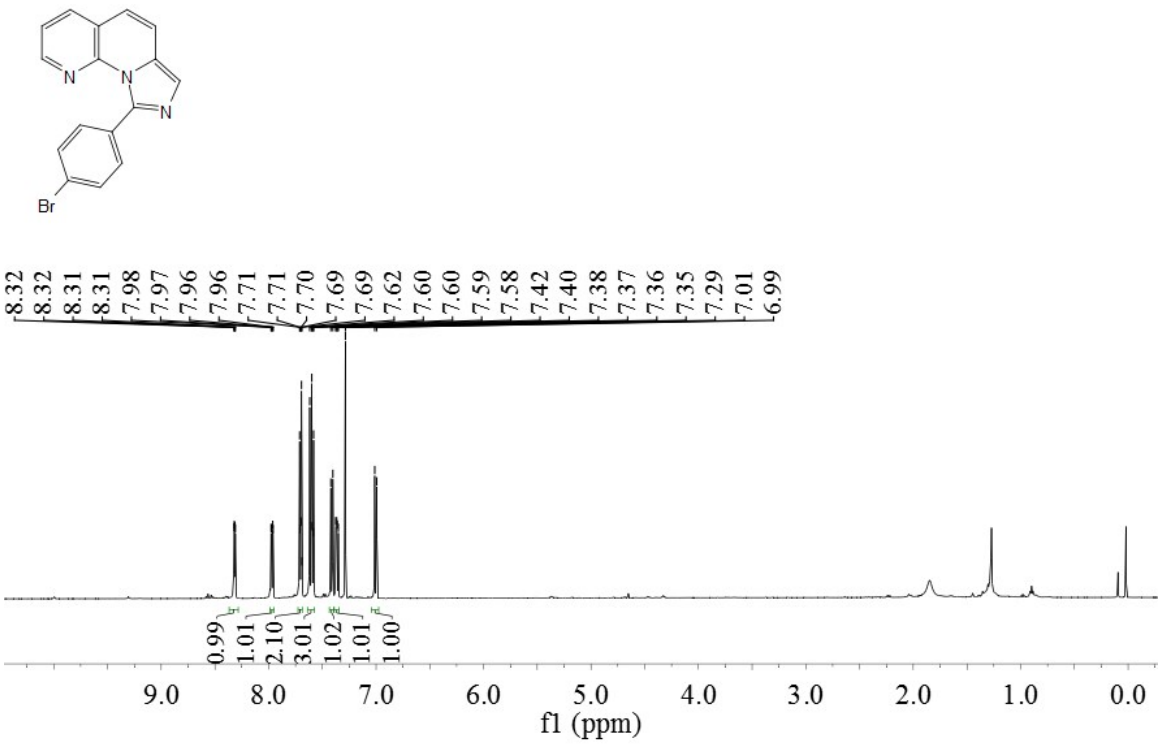
^{1}H NMR Spectrum for 4c ($CDCl_3$, 500 MHz)



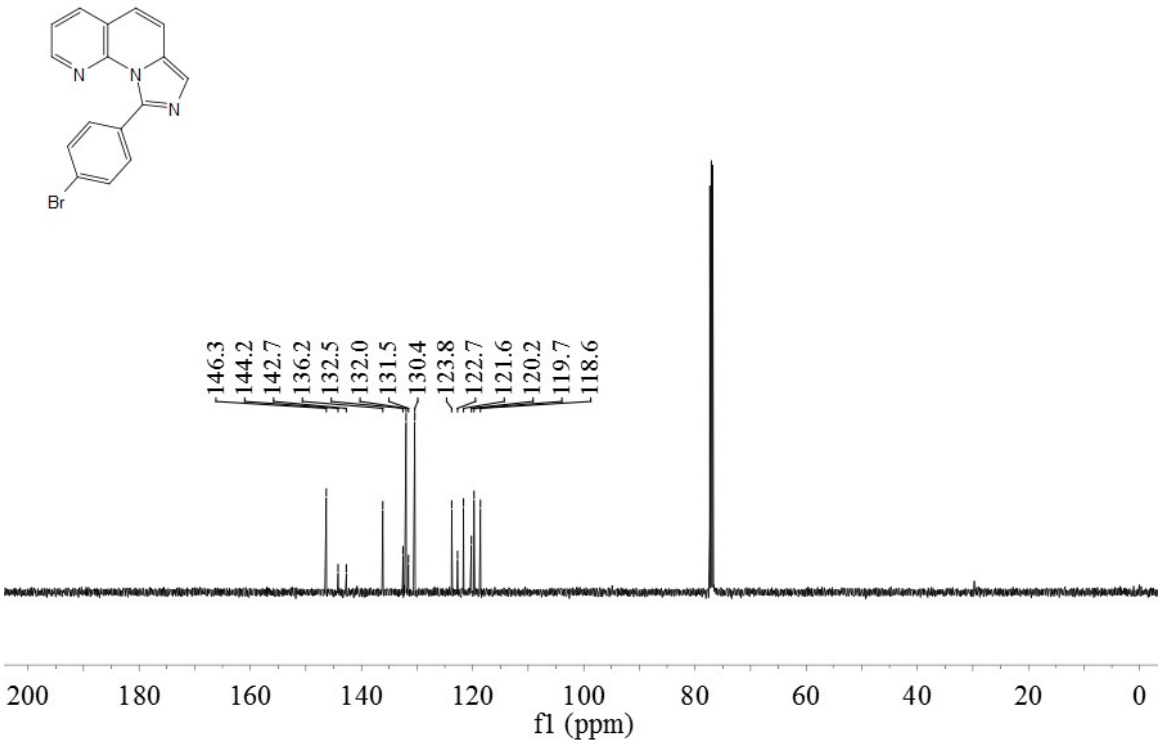
^{13}C NMR Spectrum for 4c ($CDCl_3$, 126 MHz)



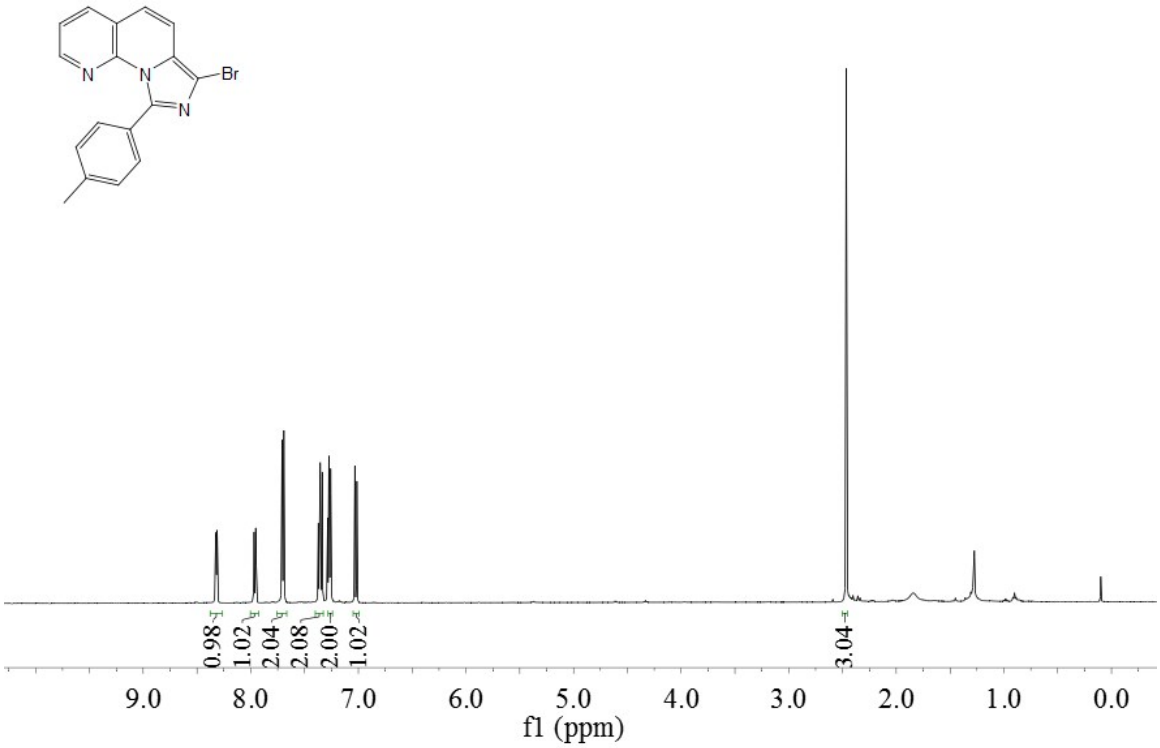
^{1}H NMR Spectrum for 4d ($CDCl_3$, 500 MHz)



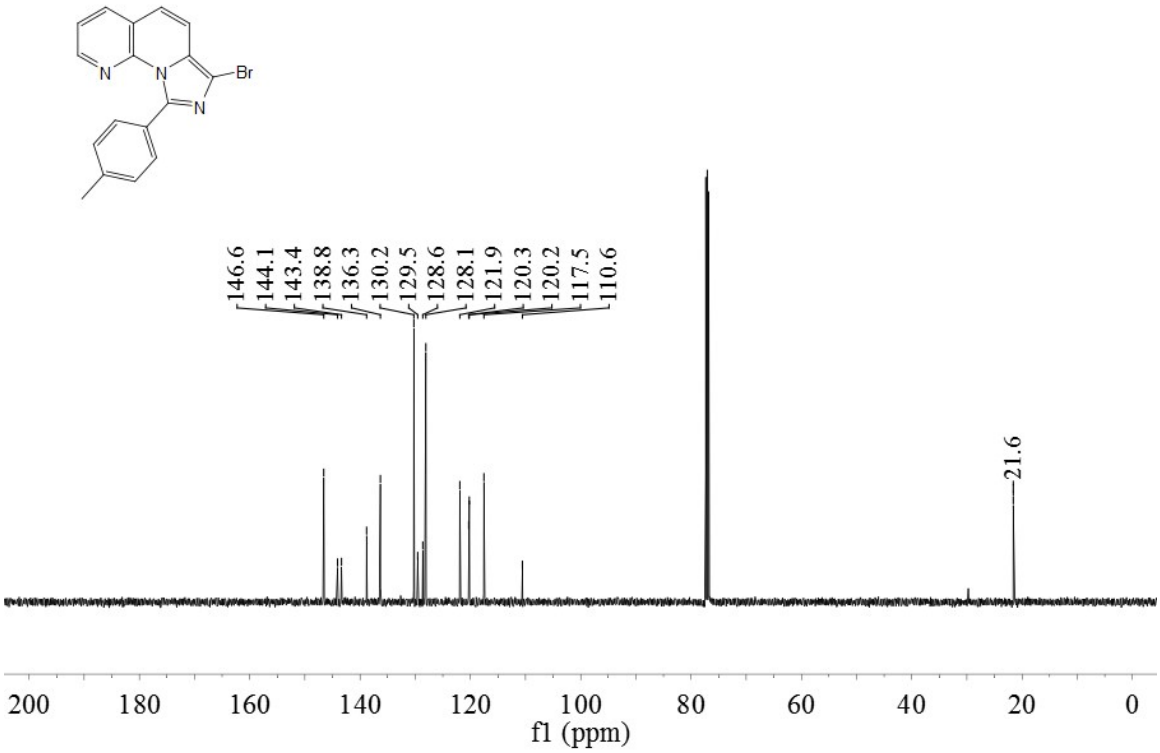
^{13}C NMR Spectrum for 4d ($CDCl_3$, 126 MHz)



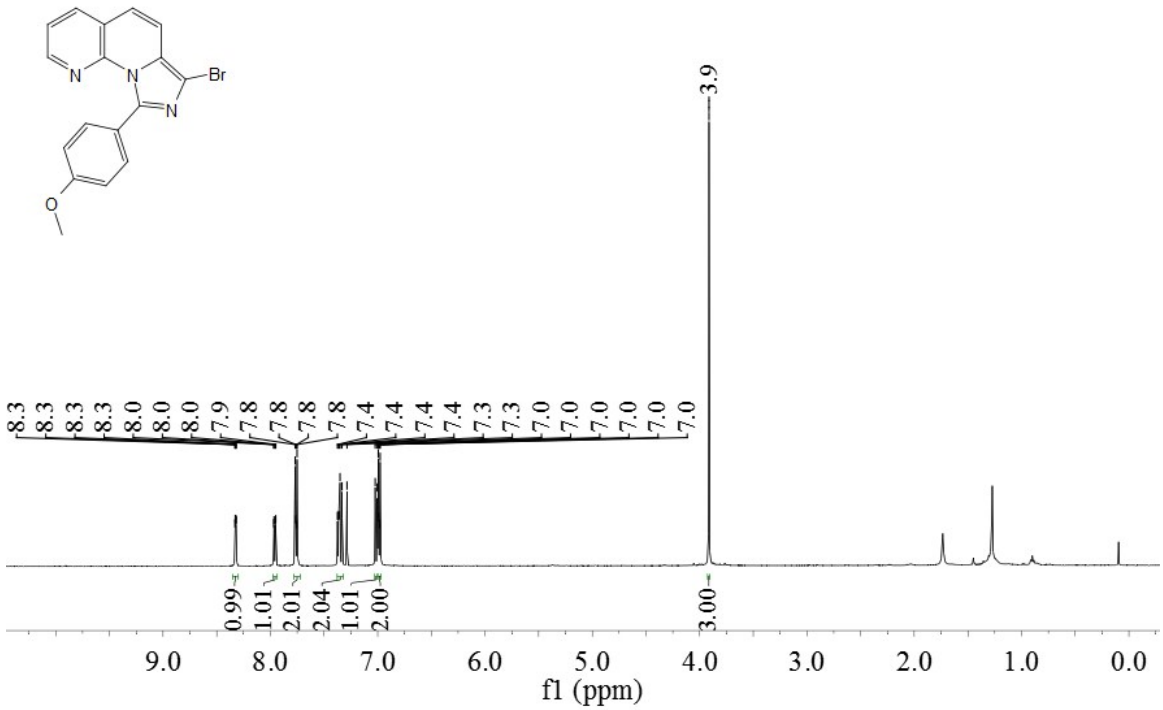
^{1}H NMR Spectrum for 5a ($CDCl_3$, 500 MHz)



^{13}C NMR Spectrum for 5a ($CDCl_3$, 126 MHz)



^{1}H NMR Spectrum for 5b ($CDCl_3$, 500 MHz)



^{13}C NMR Spectrum for 5b ($CDCl_3$, 126 MHz)