# Supplementary Materials

# $C_3$-Alkylation of Imidazo[1,2-a]pyridines via Three-Component Aza-Friedel–Crafts Reaction Catalyzed by $Y(OTf)_3$

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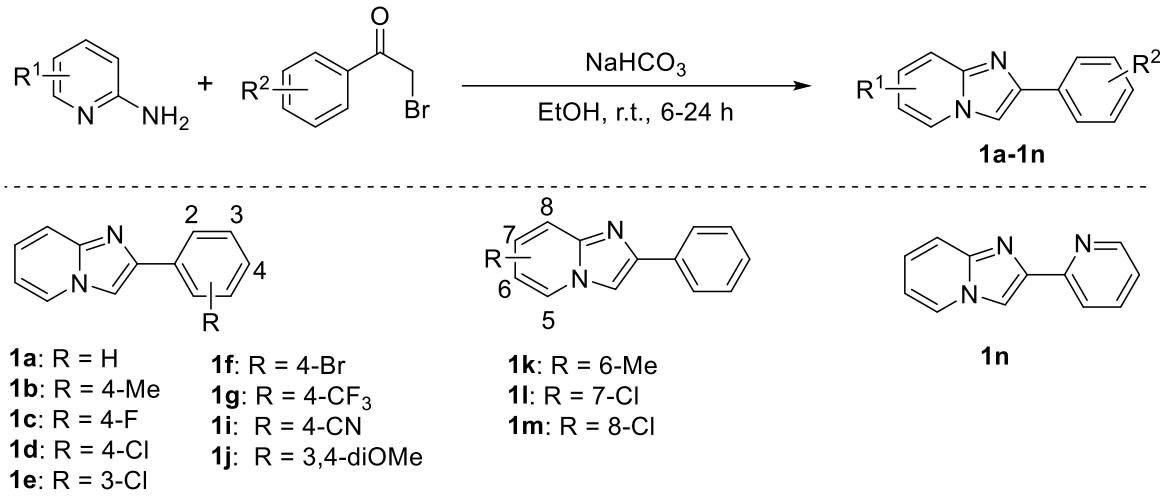
## General Information

Melting point (m.p.) was performed on a Büchi Melting Point B-545 instrument without correcting. The data of $^{1}H$, $^{13}C$ and $^{19}F$ NMR spectra were collected on a BRUKER DRX-400 spectrometer using tetramethylsilane (TMS) as an internal standard.

High-resolution mass spectra (HRMS) were obtained with a LCMS-IT-TOF mass spectrometer. Single-crystal X-ray analysis was obtained using Bruker APEX2 Smart CCD. TLC was performed on commercially prepared 100-400 mesh silica gel plates (GF254) and visualization was detected at 254 or 365 nm.

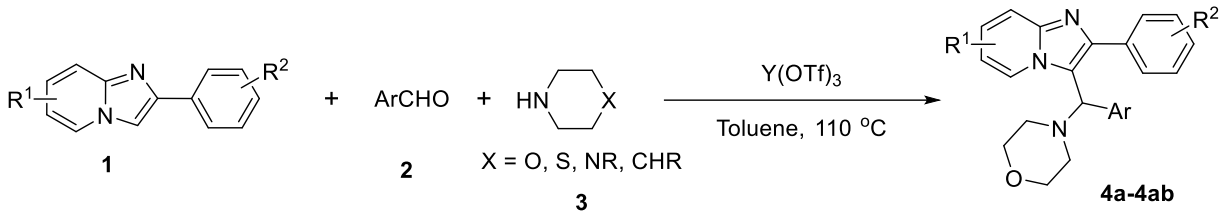
All reagents and solvents were purchased from commercial sources and used without further purification. 2-Substituted imidazo[1,2-a]pyridines **1** were synthesized from 2-bromoacetophenones and various 2-aminopyridines (see the following for details) [1,2].

## Experimental Procedure for Compounds 1a-1n




Compounds **1a**-**1n** were synthesized according to the reported procedure [1,2]. $NaHCO_3$ (24 mmol, 1.2 equiv.) was added to the ethanol solution containing 2-bromoacetophenones (20 mmol, 1.0 equiv) and 2-aminopyridines (22 mmol, 1.1 equiv.). Then, the reaction mixture was stirred at room temperature for 6-24 hours. After completion of the reaction, the resulting mixture was diluted with water (15 mL) and extracted with ether (3 × 20 mL). The combined organic layer was washed with brine (25 mL) and dried with anhydrous $MgSO_4$, then concentrated under vacuum. The analytically pure 2-arylimidazo[1,2-a]pyridines **1a**-**1n** were obtained by silica gel column with petroleum ether/EtOAc as the eluent with 50-90% yields.

## Experimental Procedure for Compounds 4a-4ab




A mixture of imidazo[1,2-a]pyridine **1** (0.2 mmol, 1.0 equiv.), aromatic aldehyde **2** (0.3 mmol, 1.5 equiv.), cycloamine **3** (0.4 mmol, 2 equiv.) and $Y(OTf)_3$ (0.04 mmol, 0.2 equiv.) in toluene (1.0 mL) was stirred at 110 °C for 12 h. After the completion of the reaction, the reaction mixture was quenched with $H_2O$ (15 mL) and extracted with ethyl acetate (3 × 15 mL). Then, the organic layer was dried over anhydrous $Na_2SO_4$. After filtration and evaporation of the solvents under reduced pressure, the crude product was purified by column chromatography on silica gel to afford the desired product **4**.

## Data of Single-crystal X-ray Analysis

**Table S1**. Crystal data and structure refinement for **4a**

| Compound | **4a** |
|---|---|
| Empirical formula | $C_{25}H_{26}N_3O$ |
| Formula weight | 382.49 |
| Temperature/K | 293(2) |
| Crystal system | Monoclinic |
| Space group | *C2/c* |
| *a* (Å) | 28.454(9) |
| *b* (Å) | 16.626(4) |
| *c* (Å) | 11.930(3) |
| *α* (°) | 90 |
| *β* (°) | 101.57(3) |
| *γ* (°) | 90 |
| Volume(Å$^3$) | 5529(2) |
| *Z* | 8 |
| $\rho_{calc}$g/cm$^3$ | 0.924 |
| μ /mm$^{-1}$ | 0.057 |
| *F* (000) | 1640.0 |
| Crystal size/mm$^3$ | 0.08 * 0/06 * 0.04 |
| Radiation | MoKα (λ = 0.71073) |
| 2Θ range for data collection/° | 4.726 to 58.182 |
| Index ranges | -22≤h≤37, -22≤k≤19, -16≤l≤ 15 |
| Reflections collected | 12814 |
| Independent reflections | 6361 [Rint = 0.0714, Rsigma = 0.1707] |
| Data/restraints/parameters | 6361/0/263 |
| Goodness-of-fit on F2 | 0.975 |
| Final R indexes [I>=2σ (I)] | R1 = 0.1019, wR2 = 0.2316 |
| *Final R indexes [all data]* | R1 = 0.2011, wR2 = 0.2862 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.24/-0.26 |

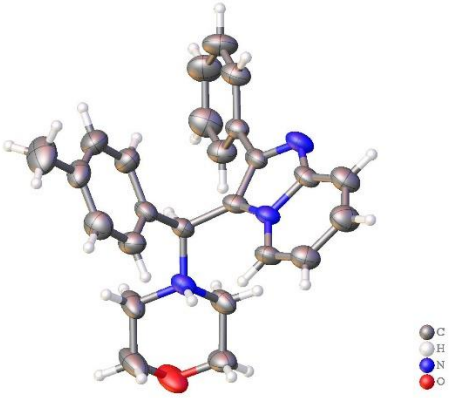
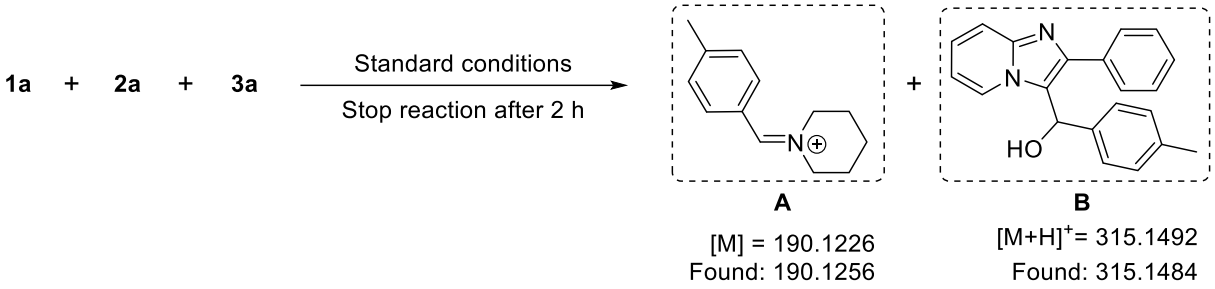



**Figure S1**. The molecular structure of compound **4a**.

## Mechanism investigation



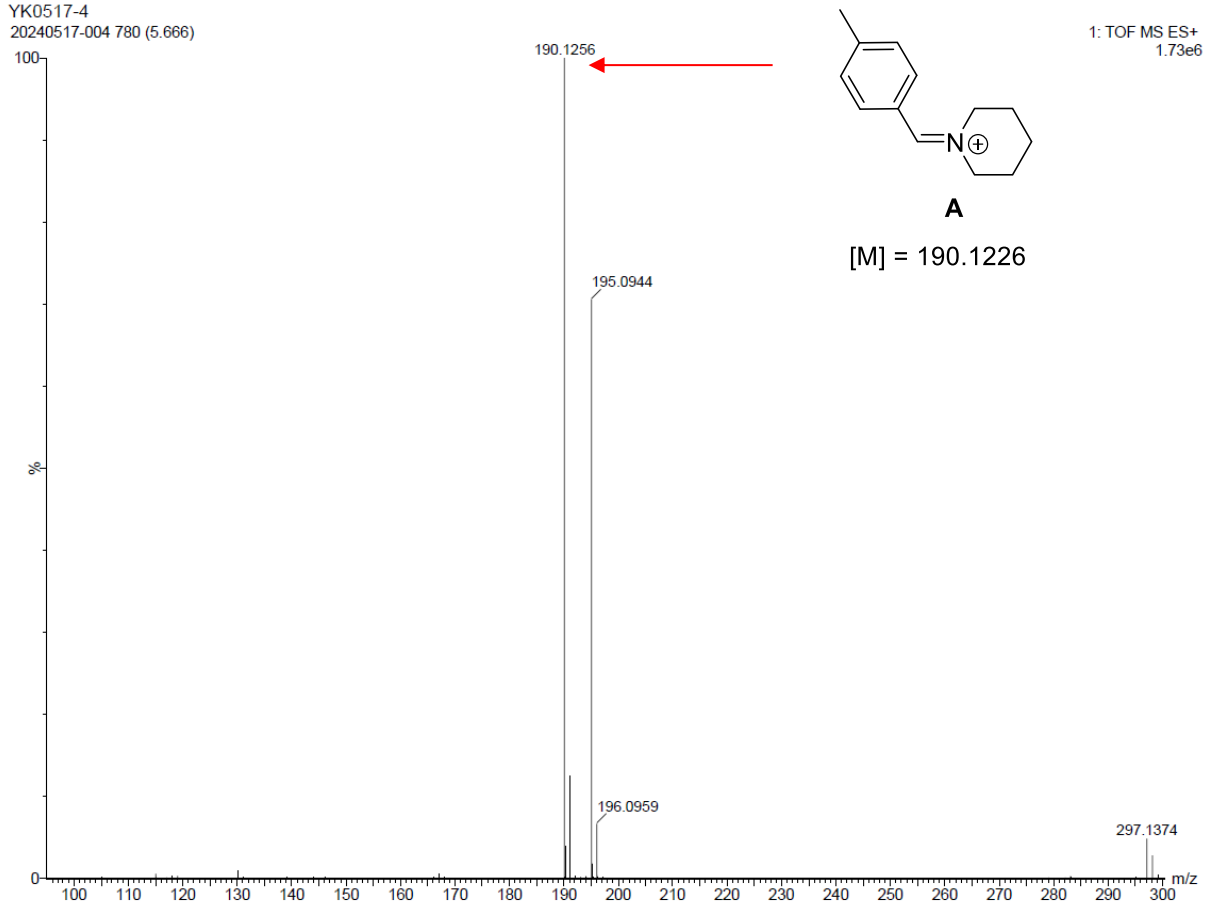




**Figure S2**. ESI-HRMS spectrum of imine **A**.

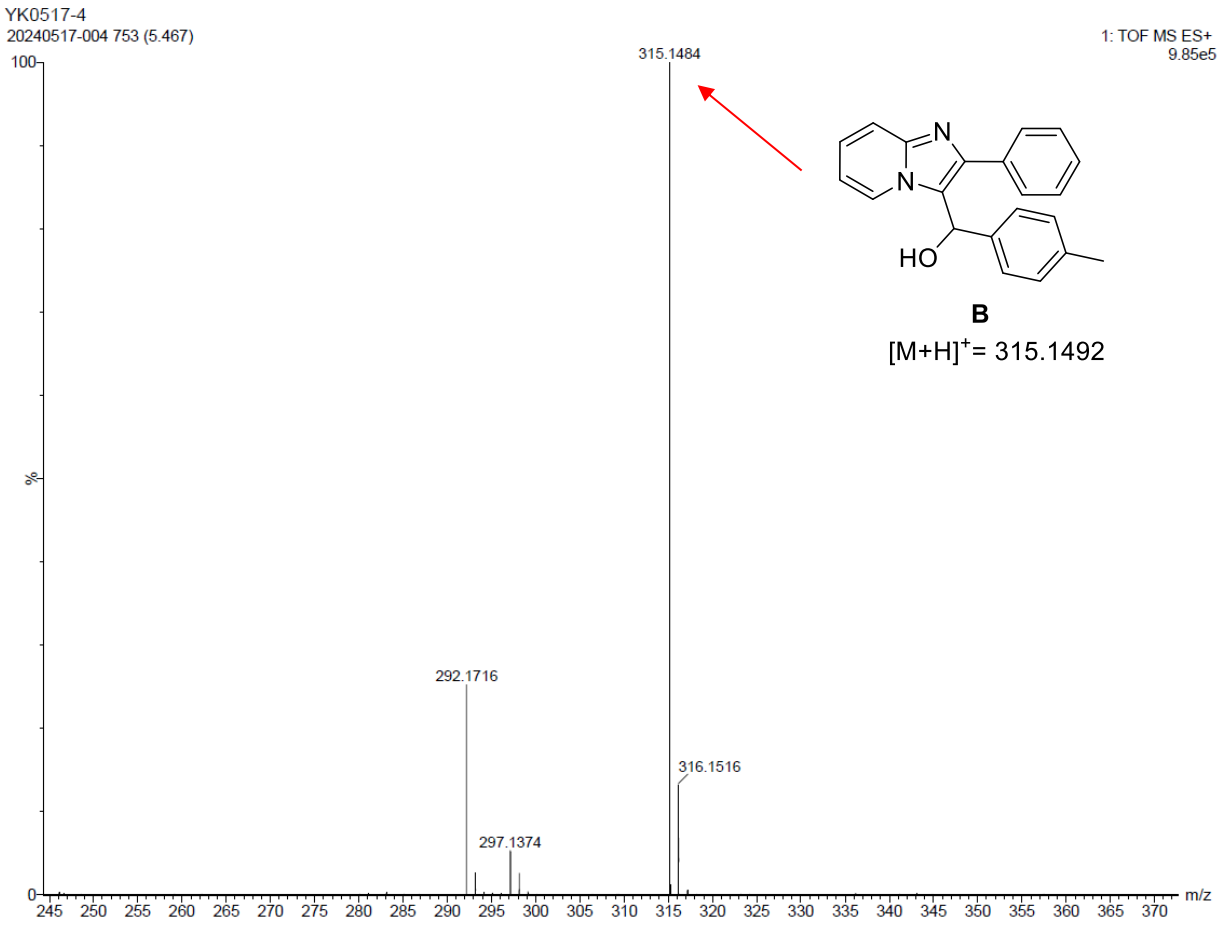
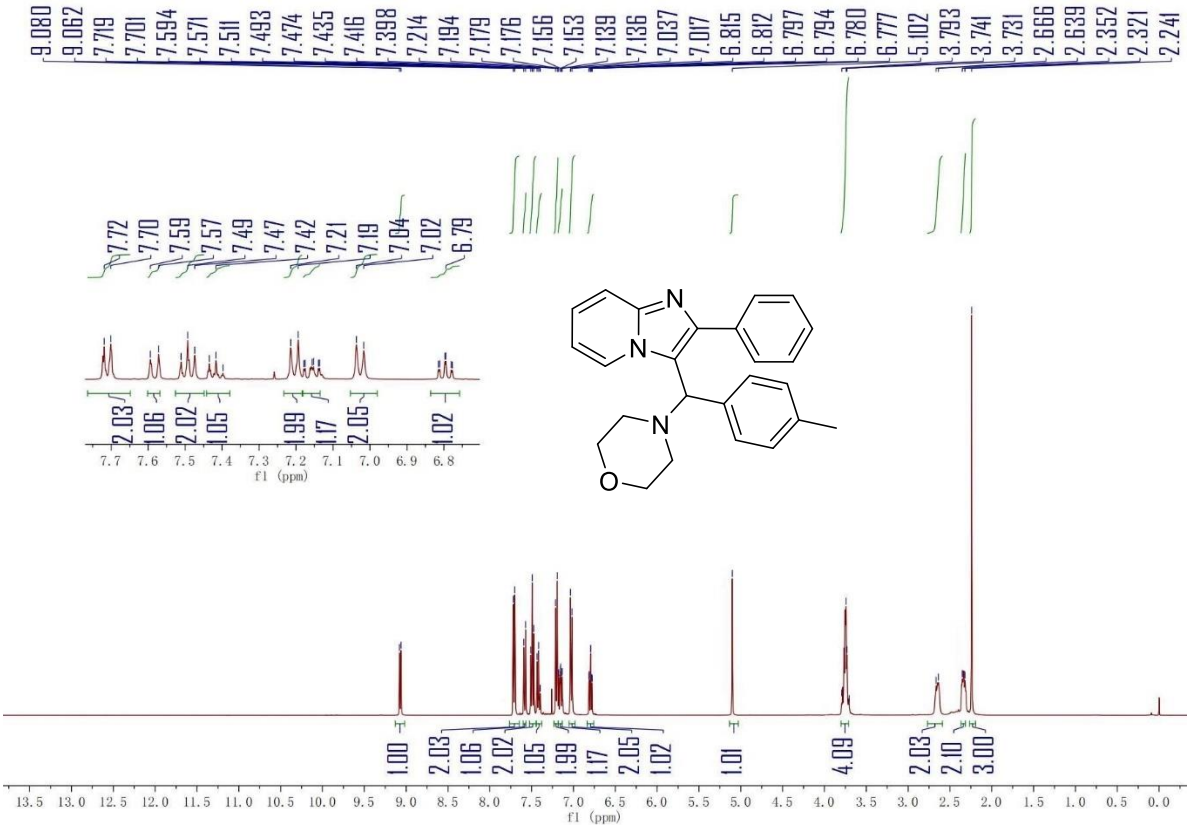
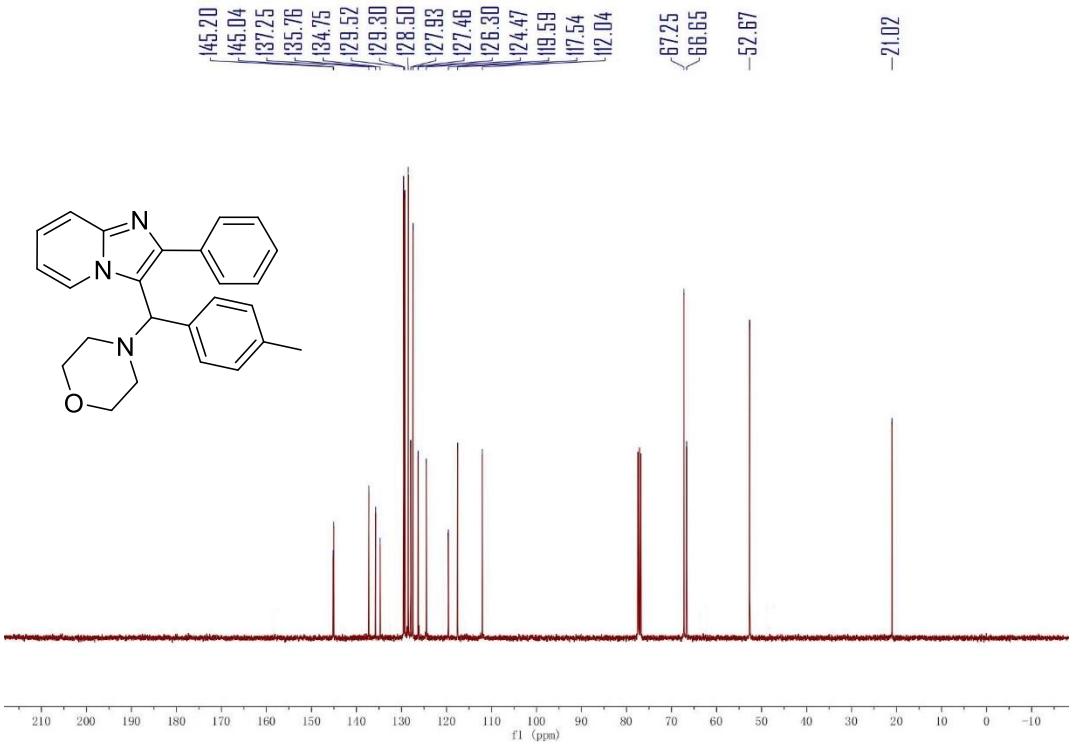



**Figure S3.** ESI-HRMS spectrum of benzyl alcohol **B**.

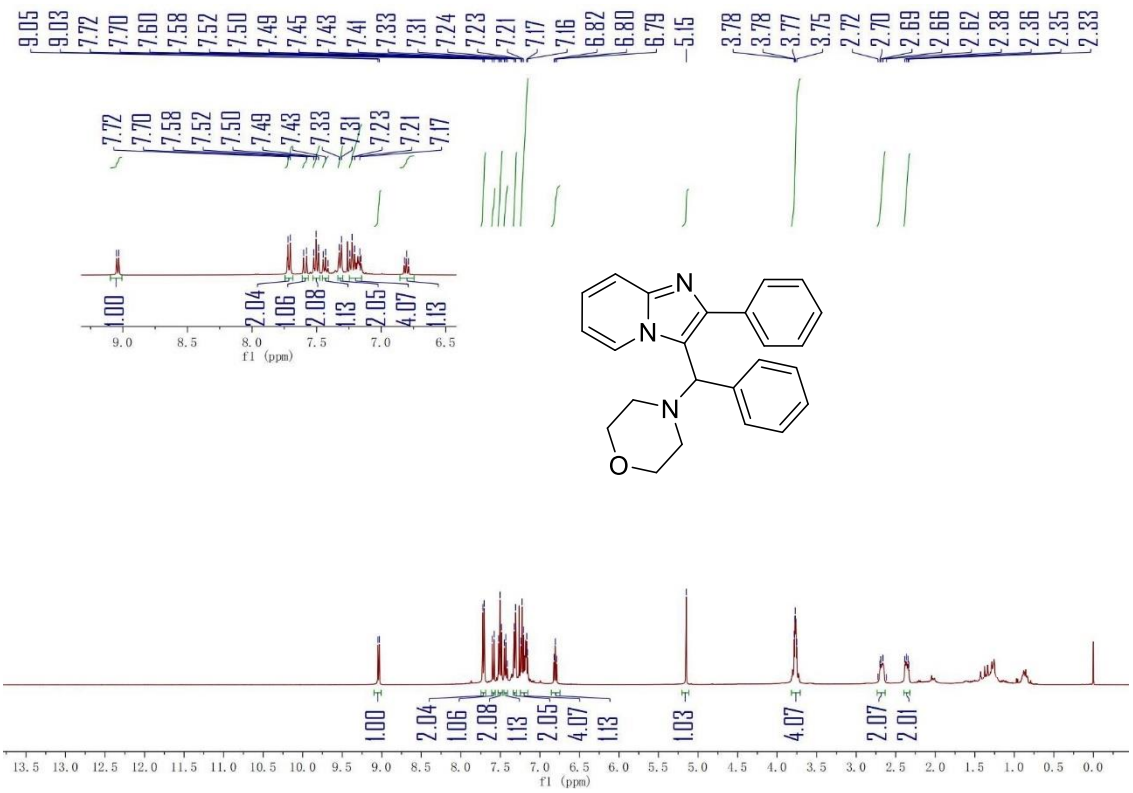
## NMR Spectra for All Compounds 4a-4ab



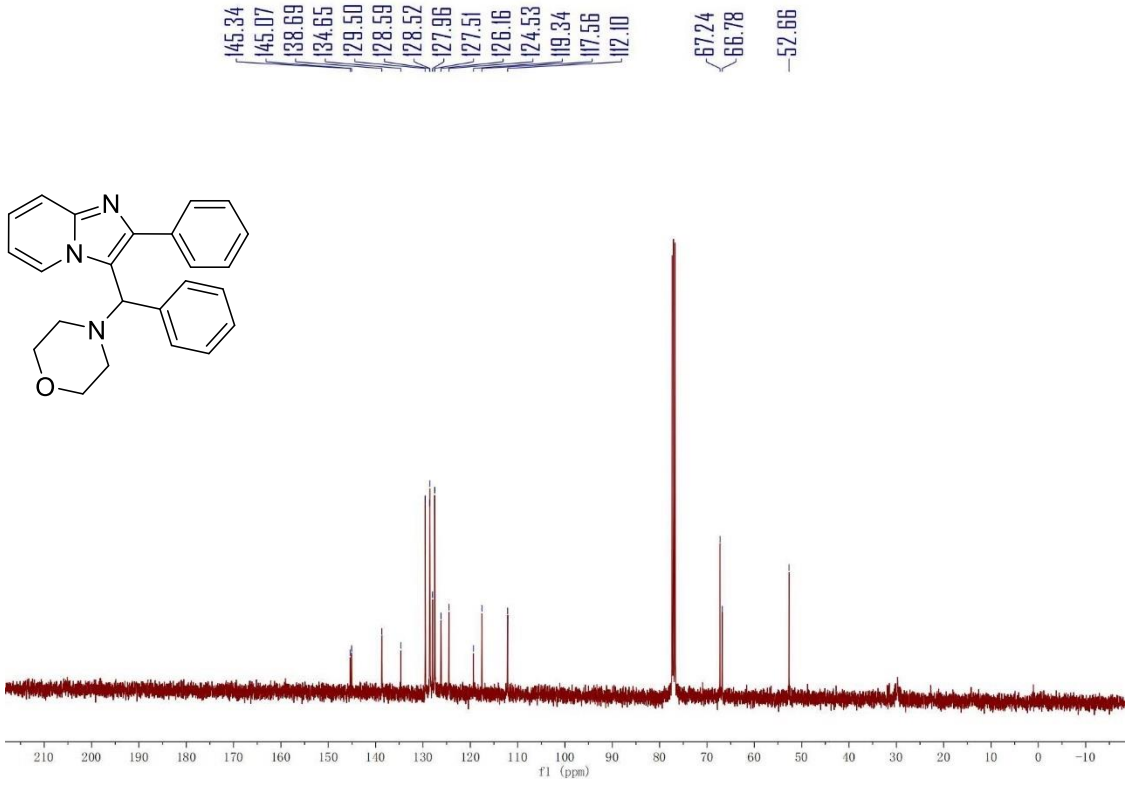
$^{1}$H NMR spectrum of compound **4a**



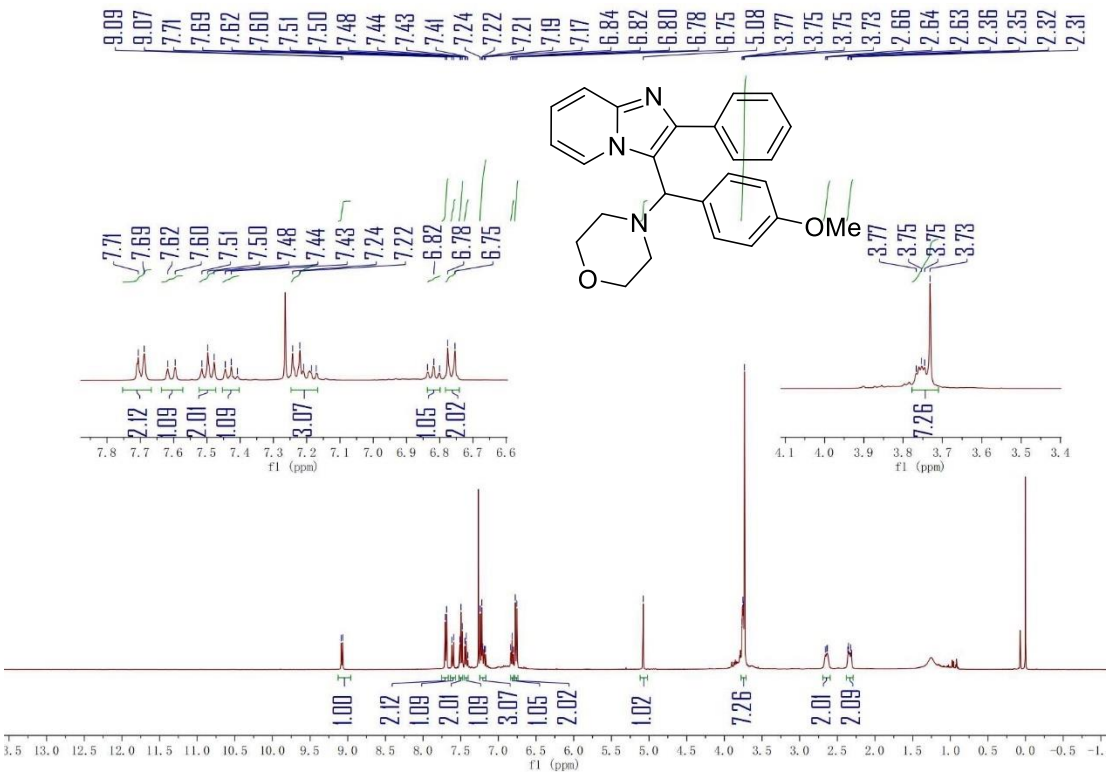
$^{13}$C NMR spectrum of compound **4a**



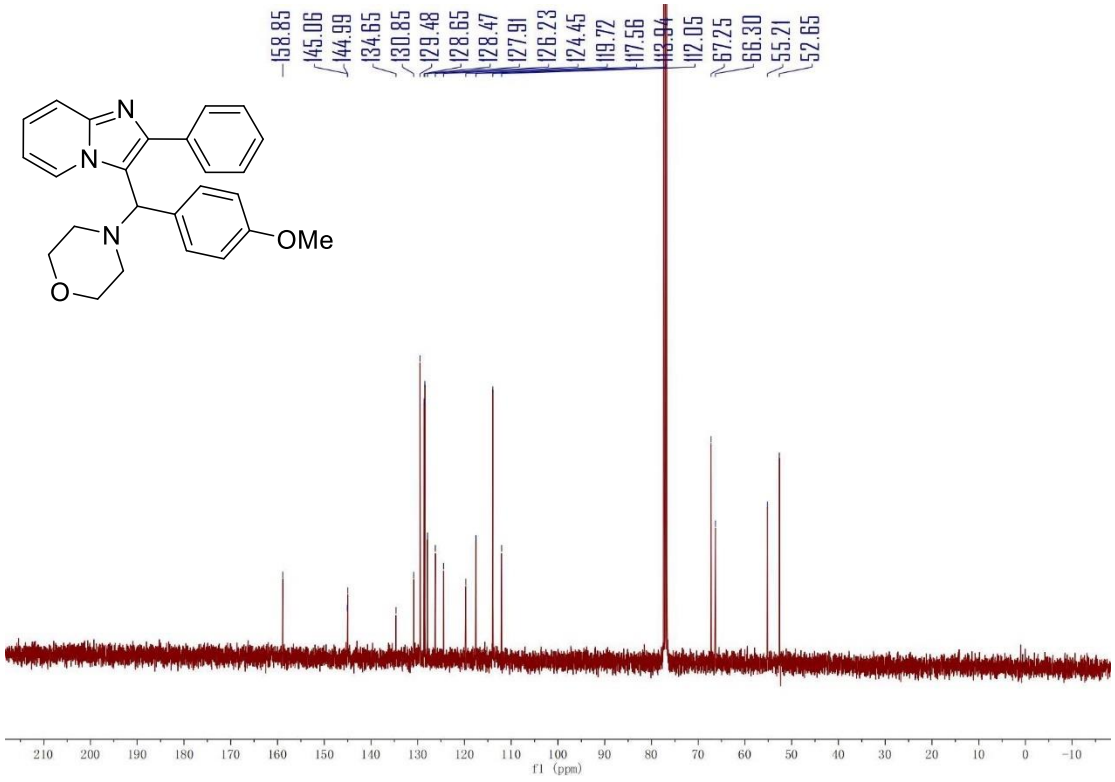
$^{1}$H NMR spectrum of compound **4b**



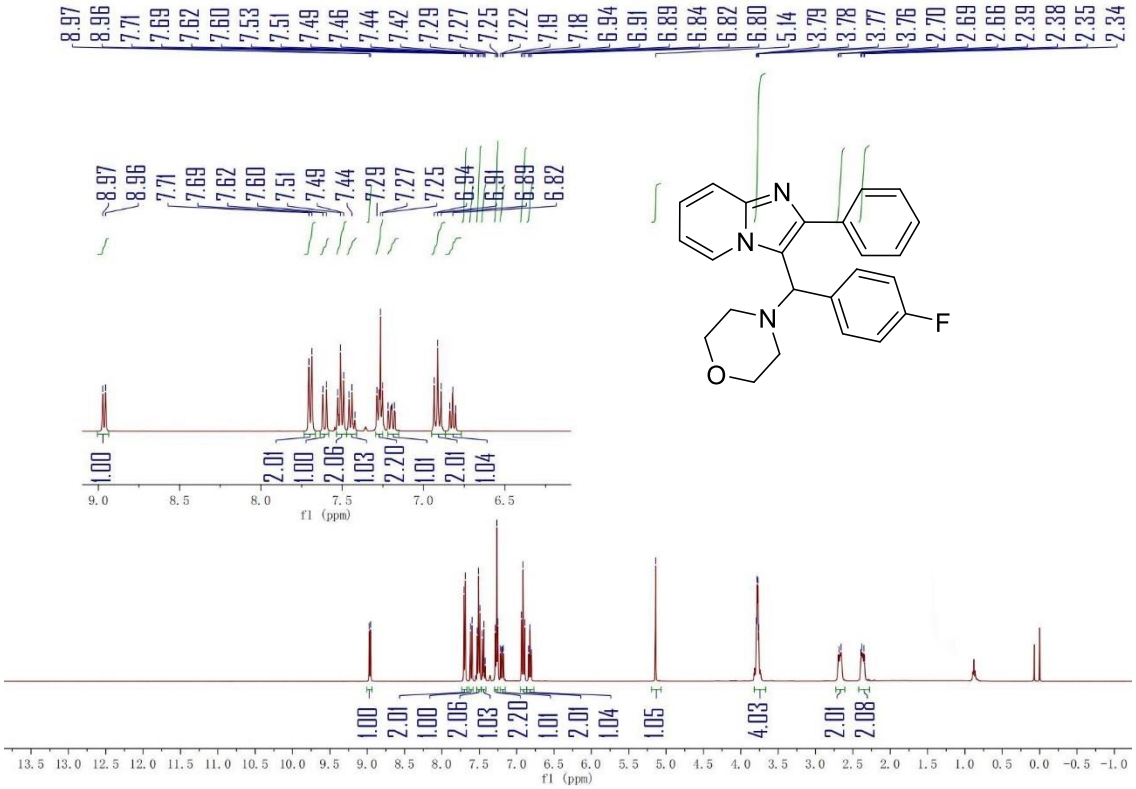
$^{13}$C NMR spectrum of compound **4b**



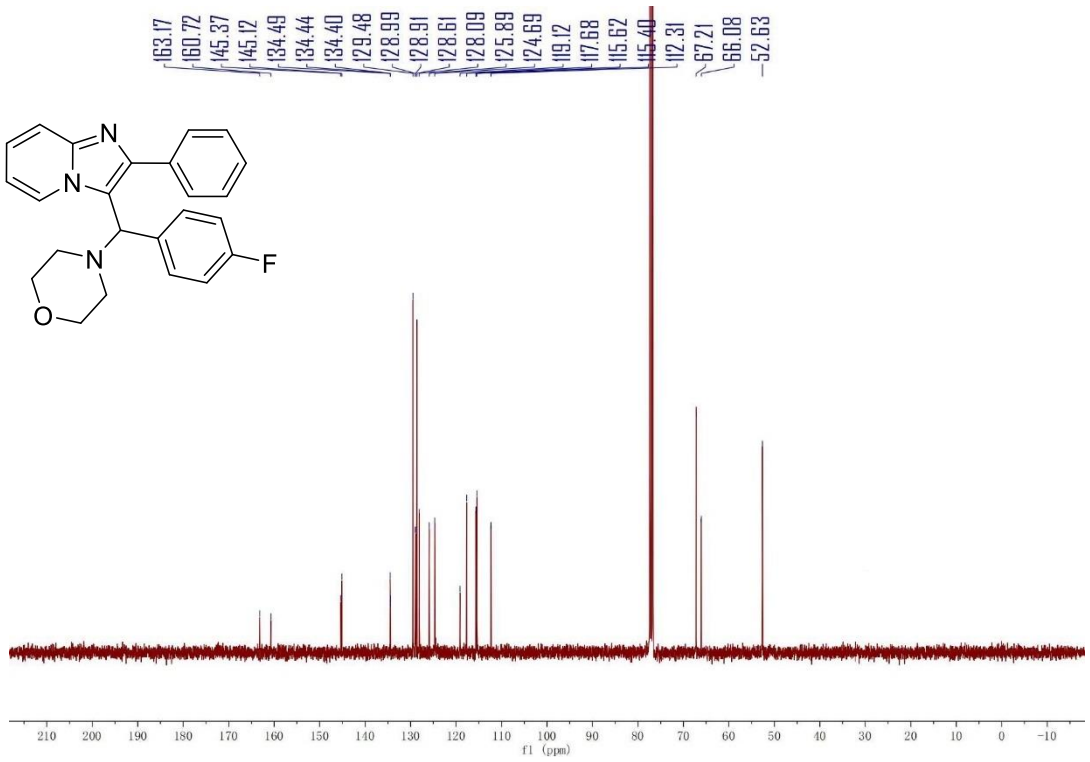

$^{1}$H NMR spectrum of compound **4c**



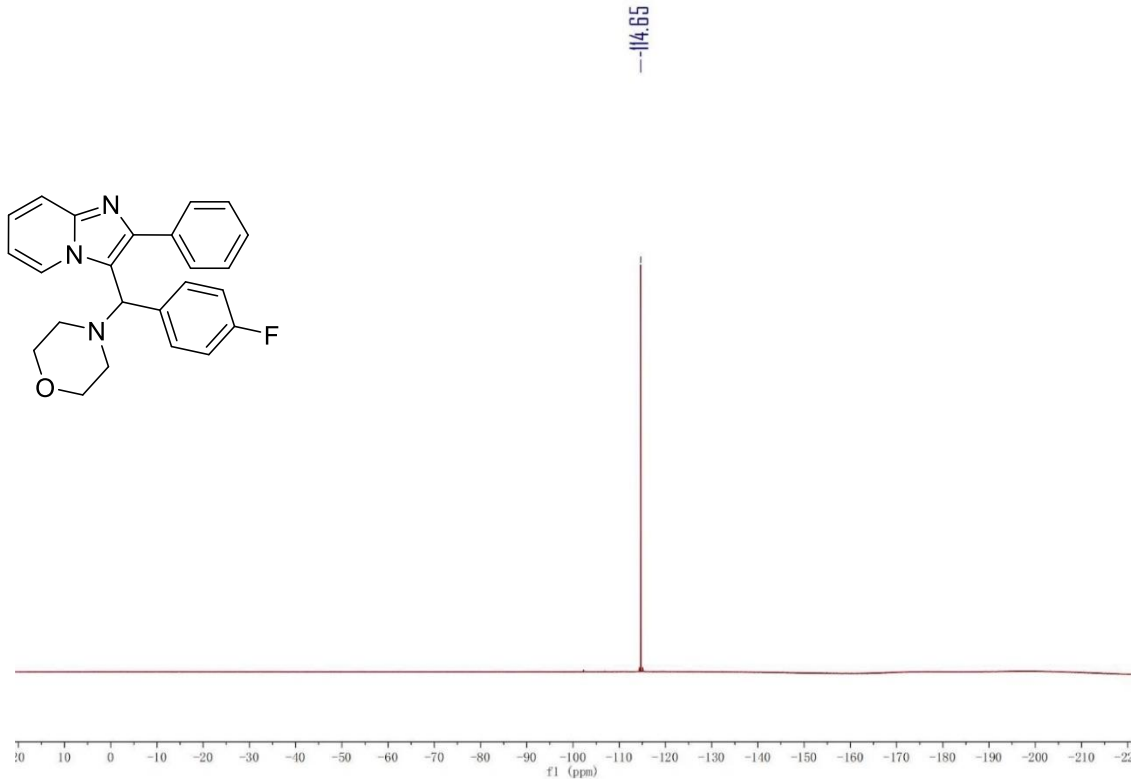

$^{13}$C NMR spectrum of compound **4c**



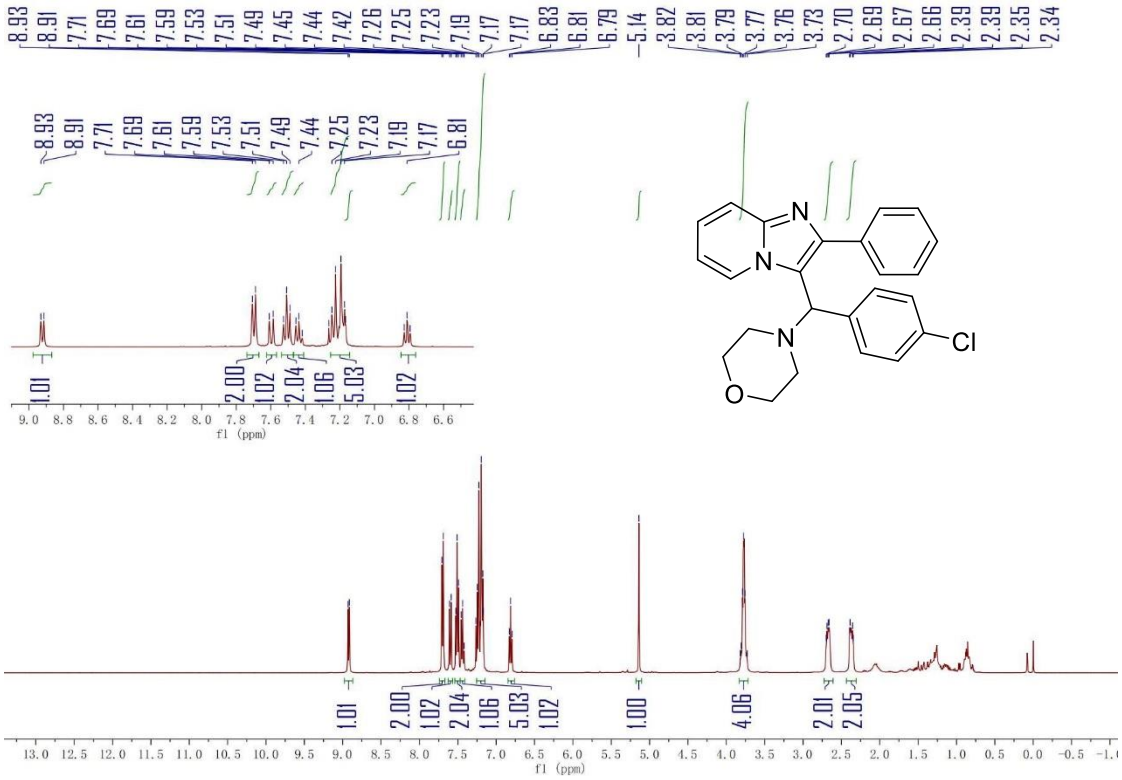
$^{1}$H NMR spectrum of compound **4d**



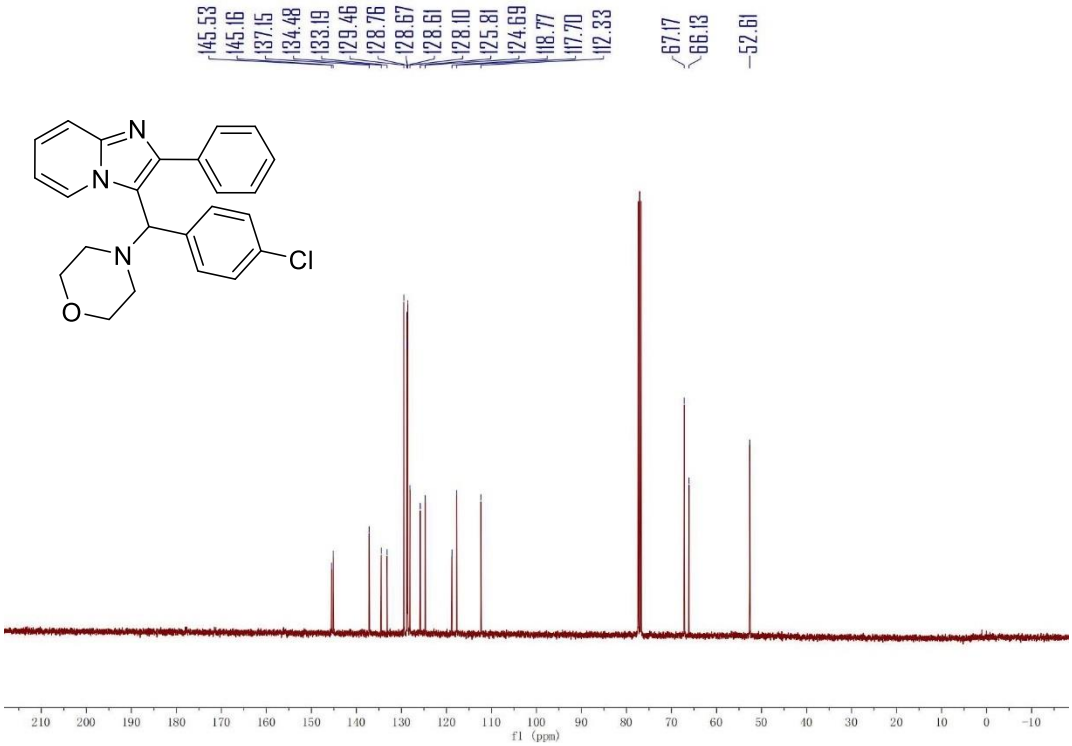
$^{13}$C NMR spectrum of compound **4d**



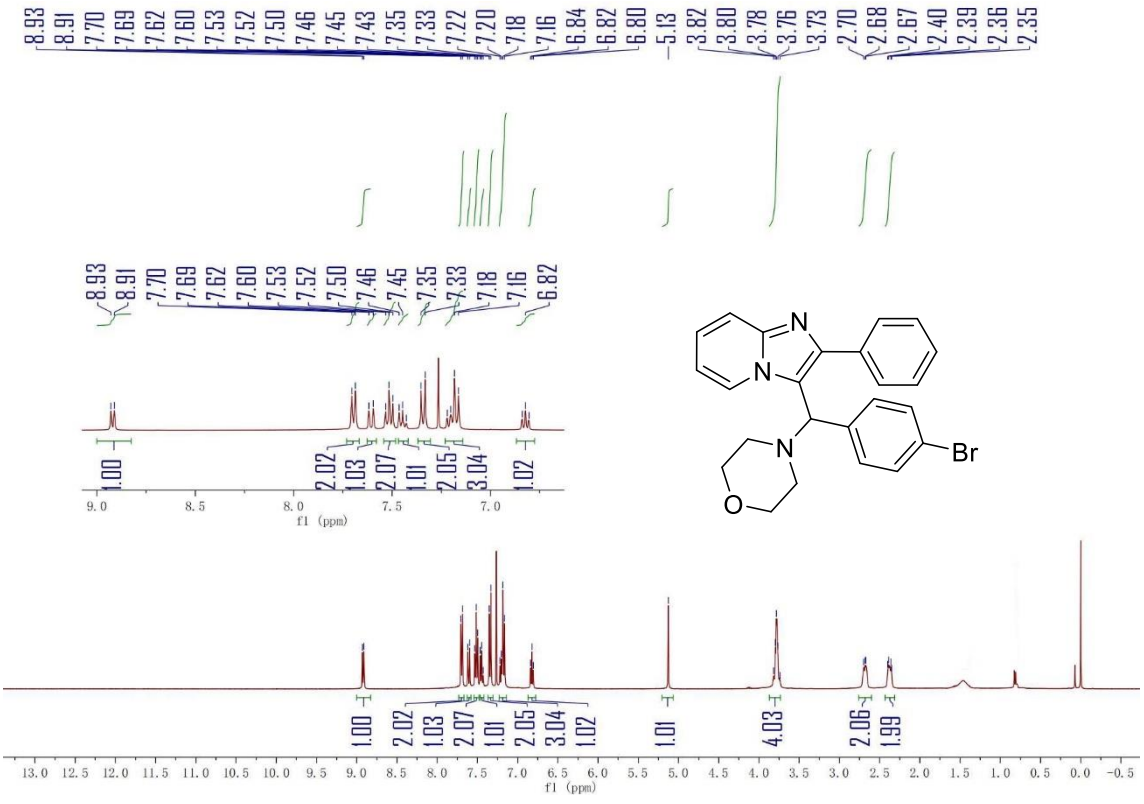

$^{19}$F NMR spectrum of compound **4d**



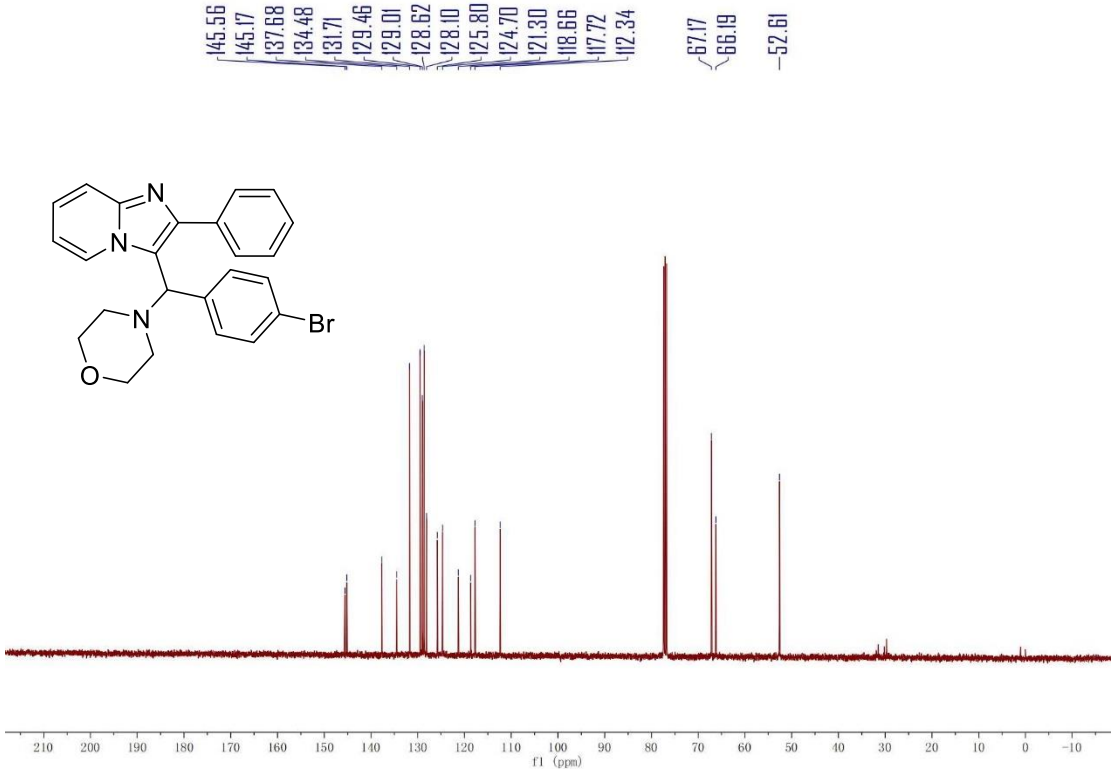

$^{1}$H NMR spectrum of compound **4e**



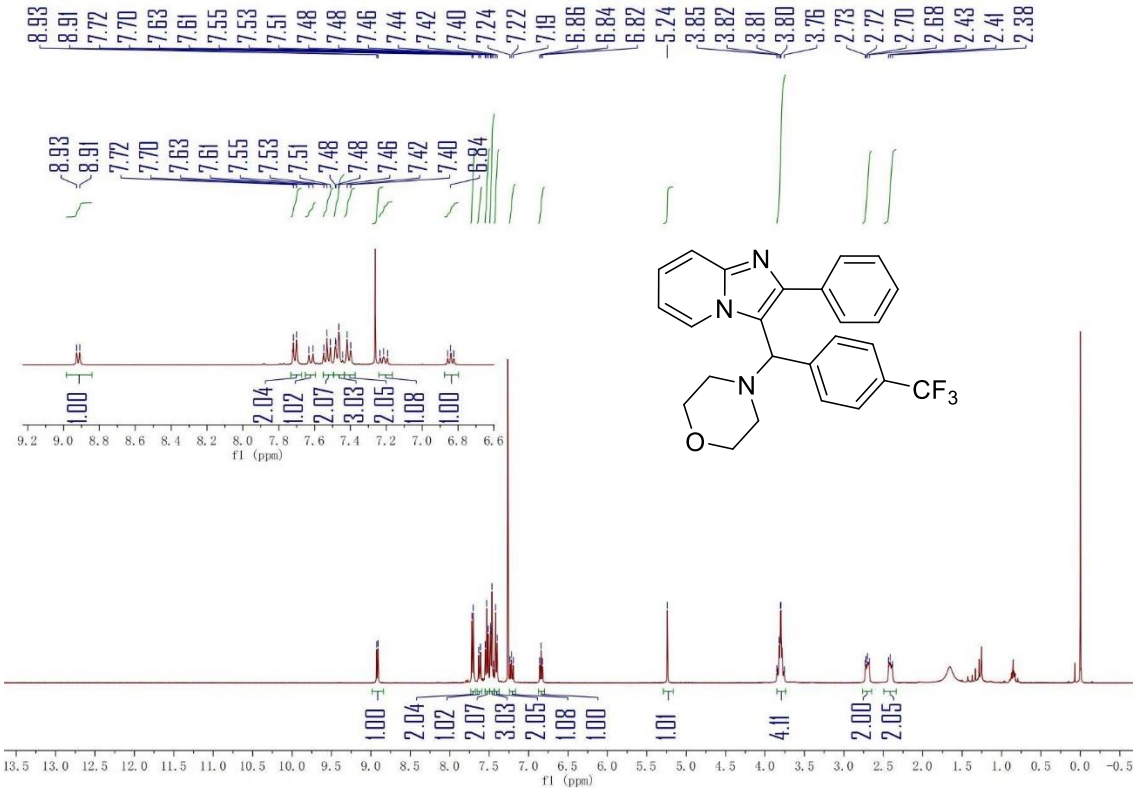

$^{13}$C NMR spectrum of compound **4e**



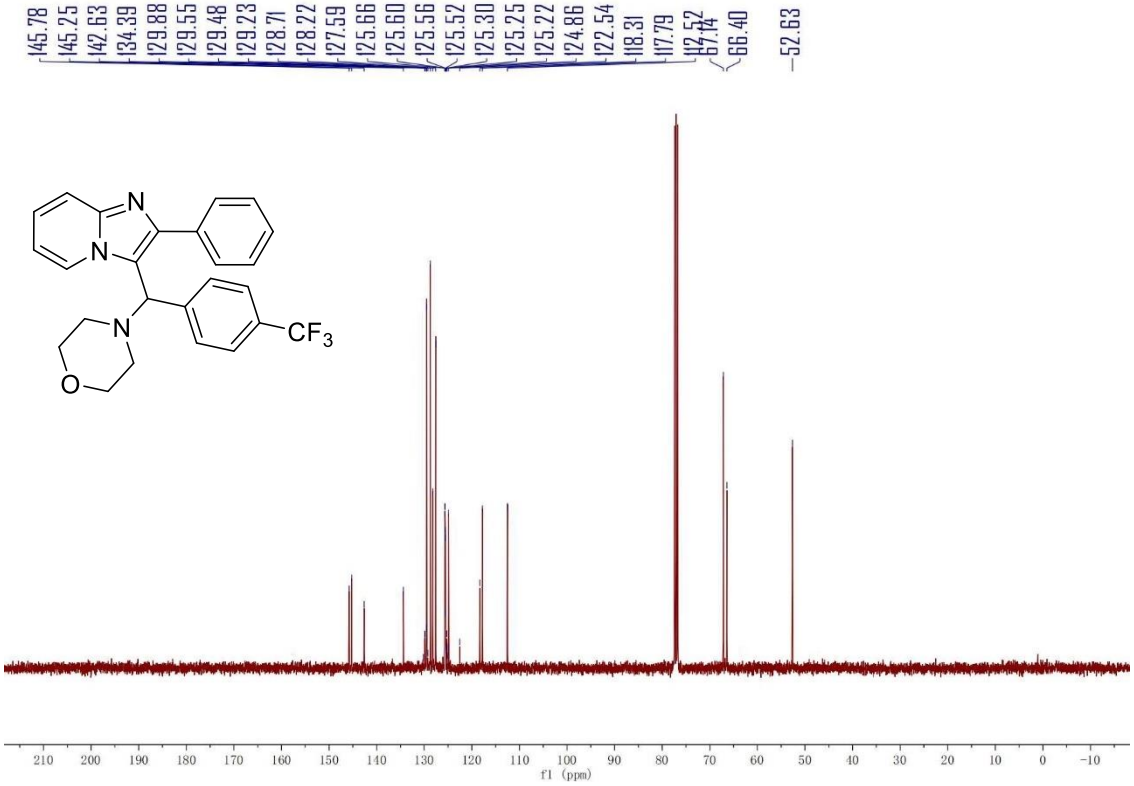

$^{1}$H NMR spectrum of compound **4f**



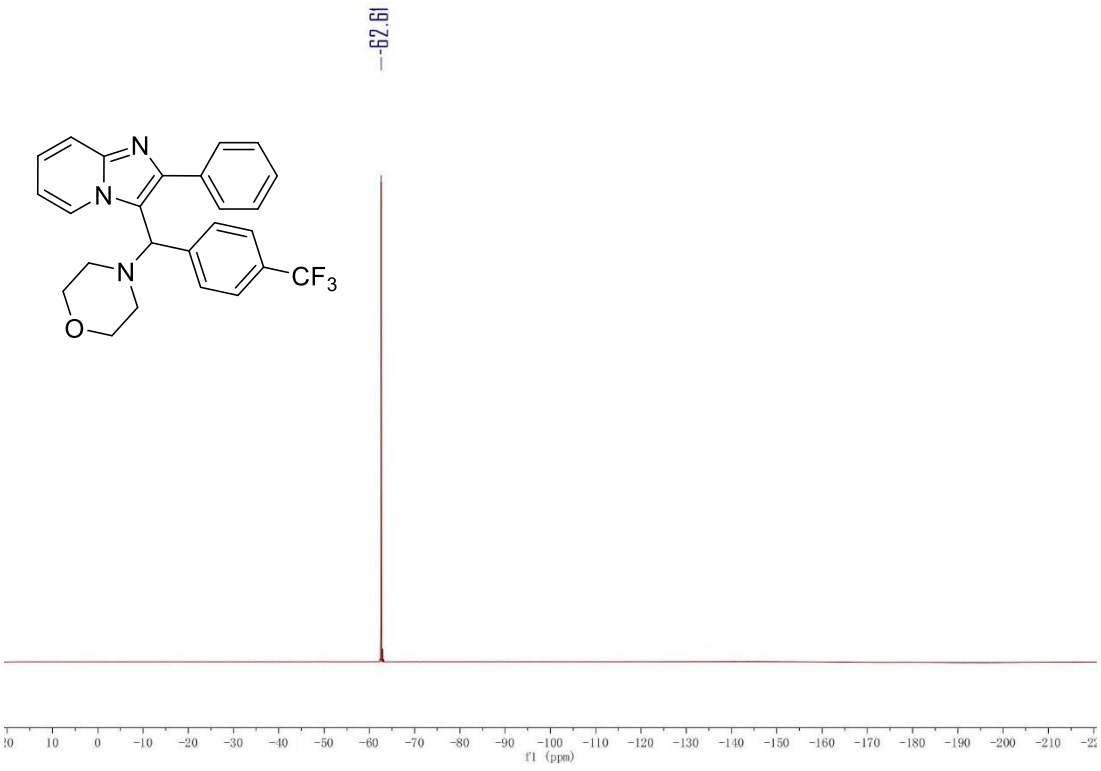

$^{13}$C NMR spectrum of compound **4f**



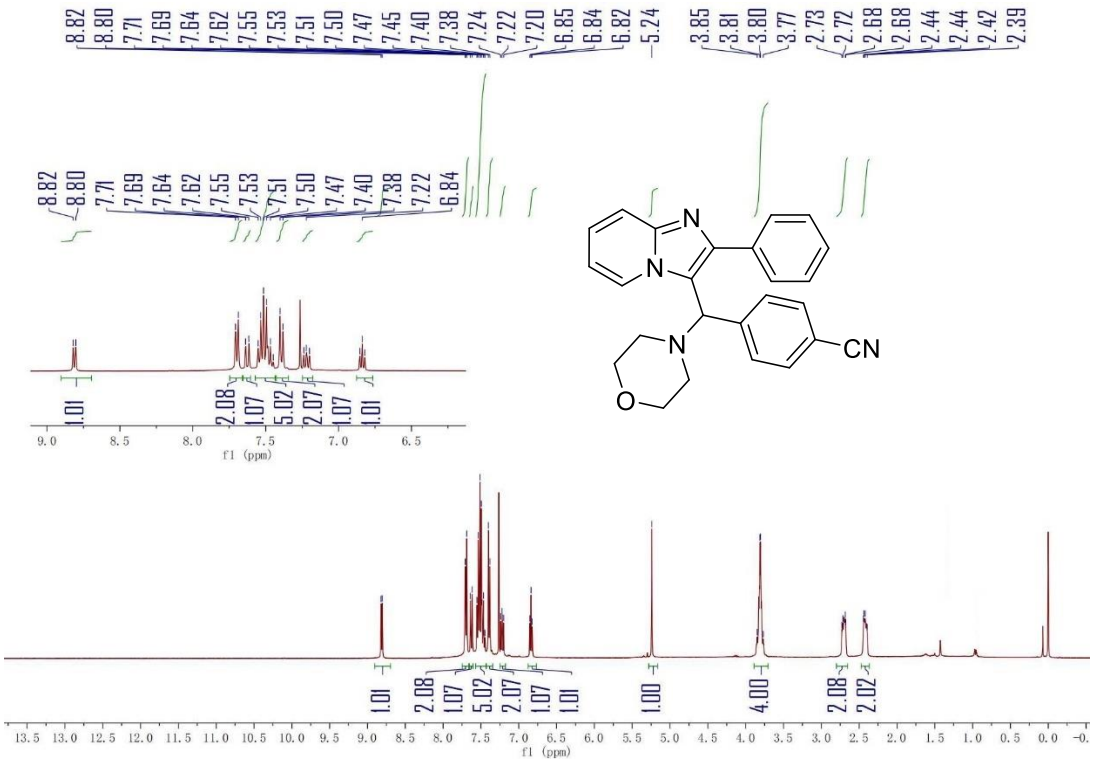

$^{1}$H NMR spectrum of compound **4g**



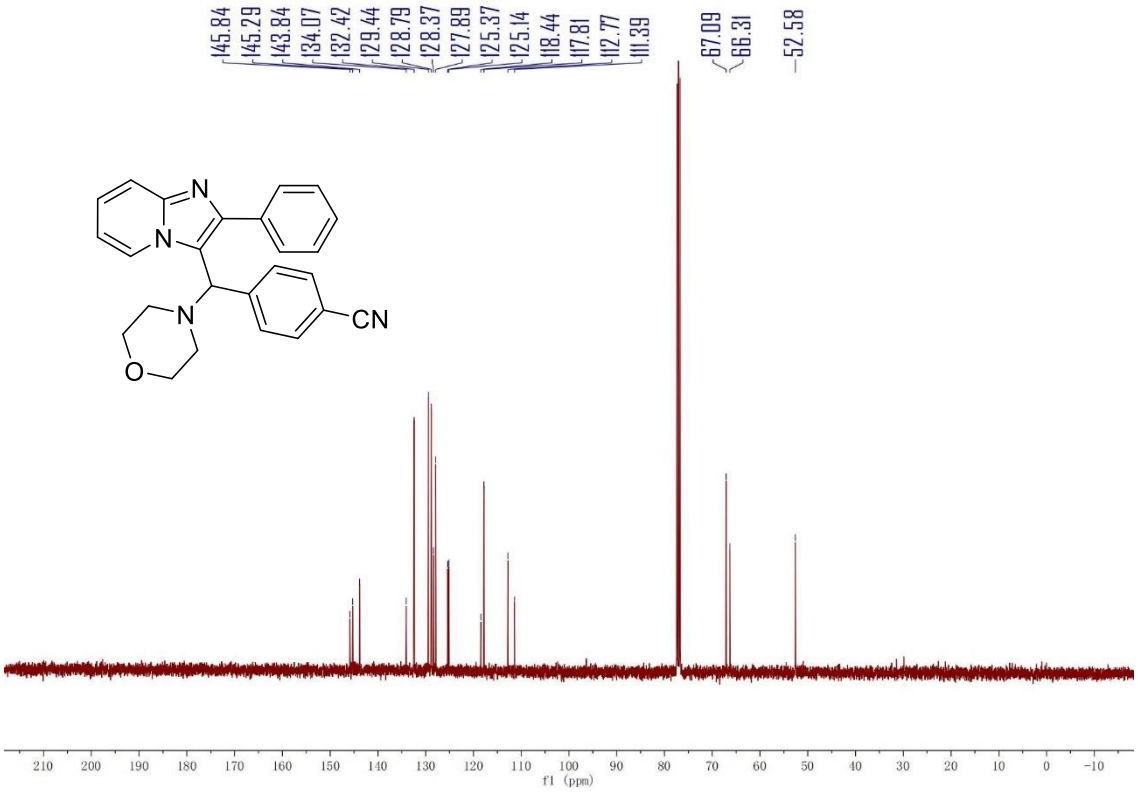

$^{13}$C NMR spectrum of compound **4g**



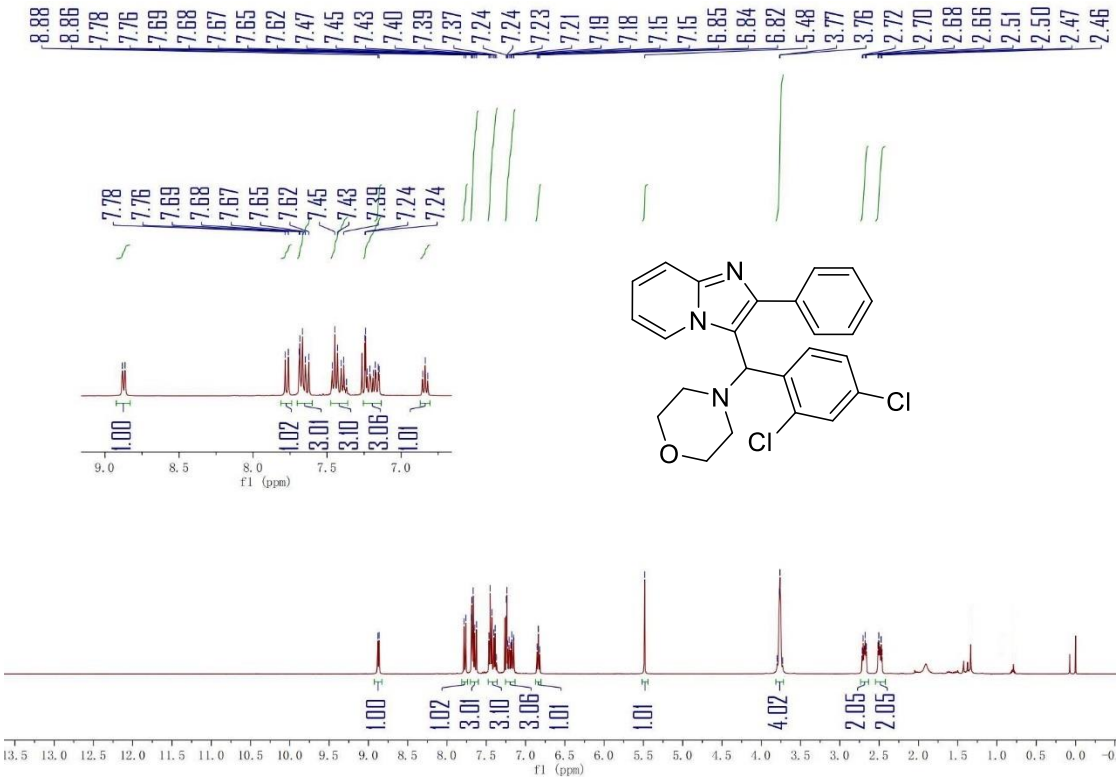

$^{19}$F NMR spectrum of compound **4g**



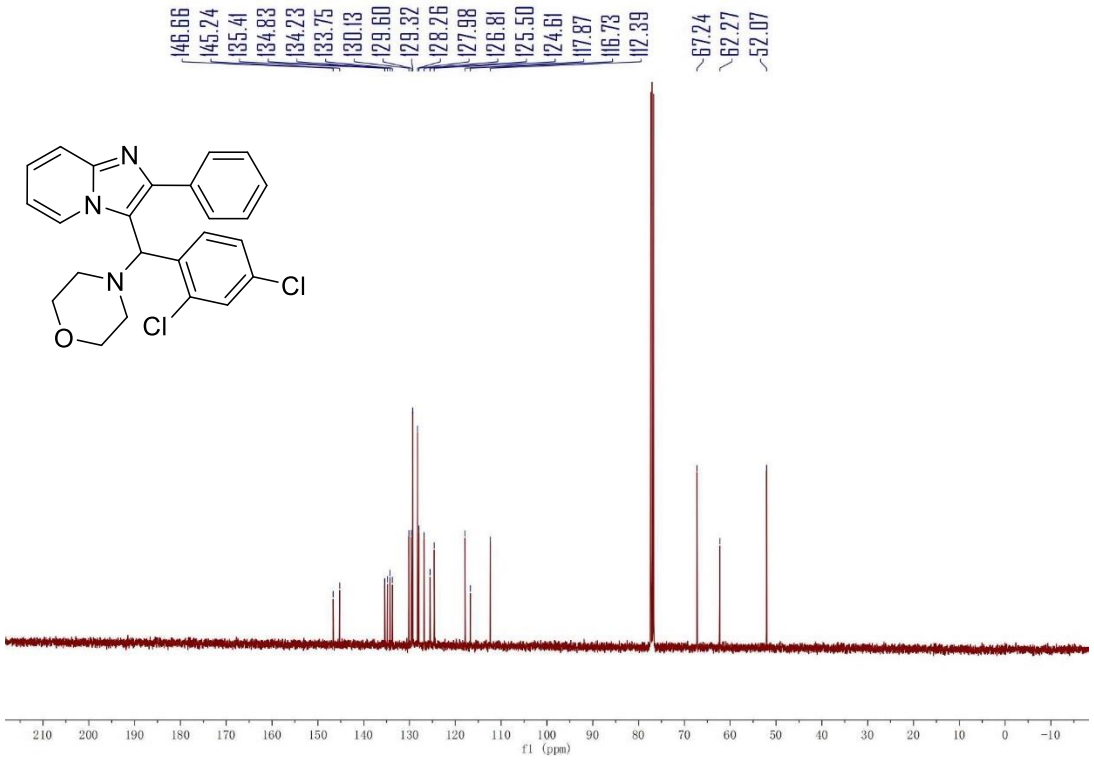

$^{1}$H NMR spectrum of compound **4h**



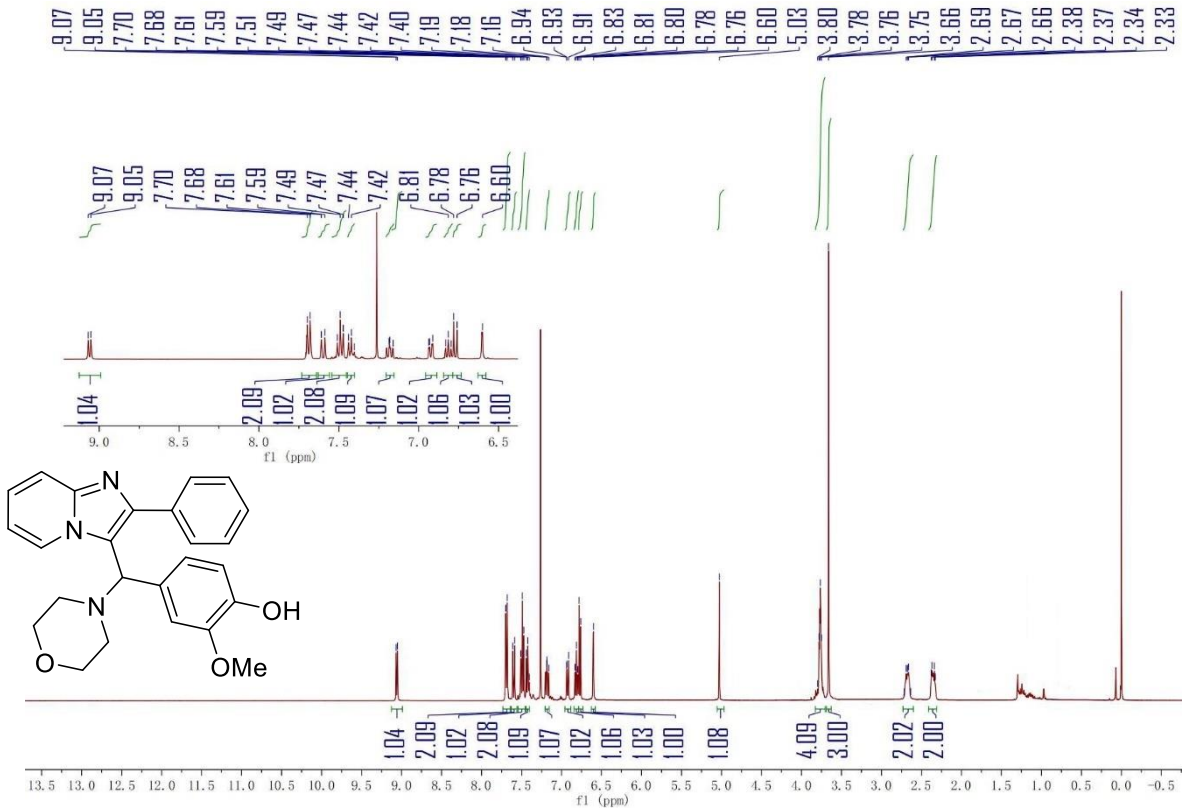

$^{13}$C NMR spectrum of compound **4h**



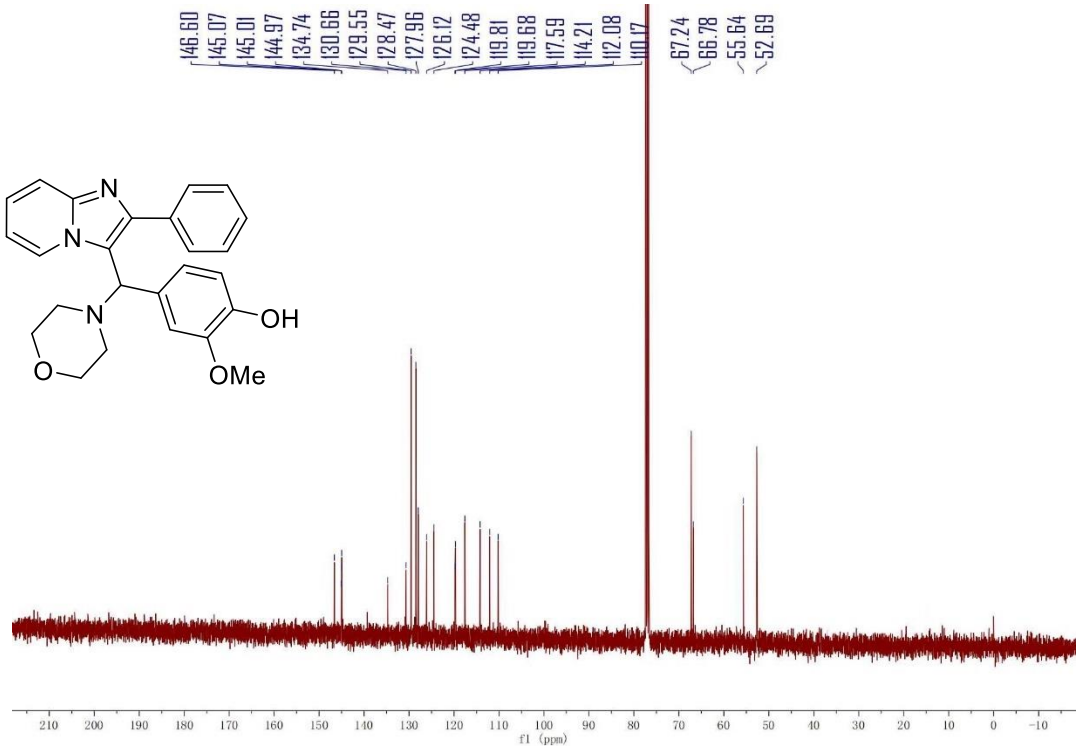

$^{1}$H NMR spectrum of compound **4i**



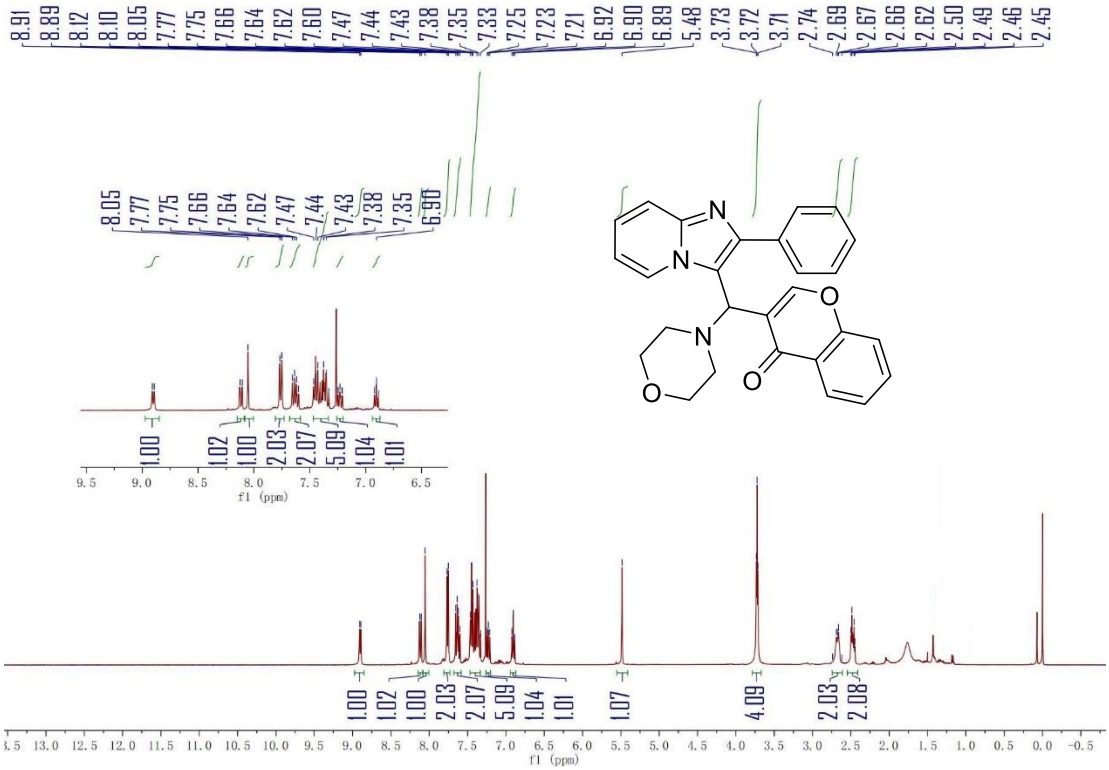

$^{13}$C NMR spectrum of compound **4i**



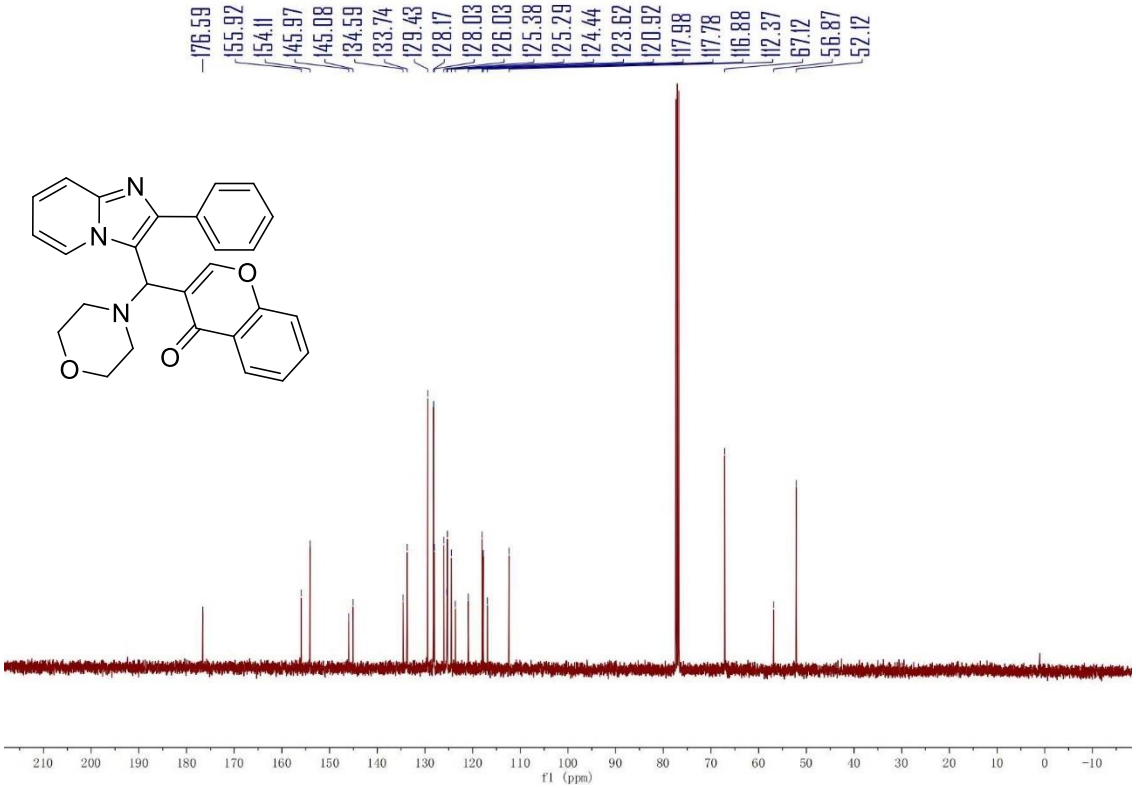

$^{1}$H NMR spectrum of compound **4j**



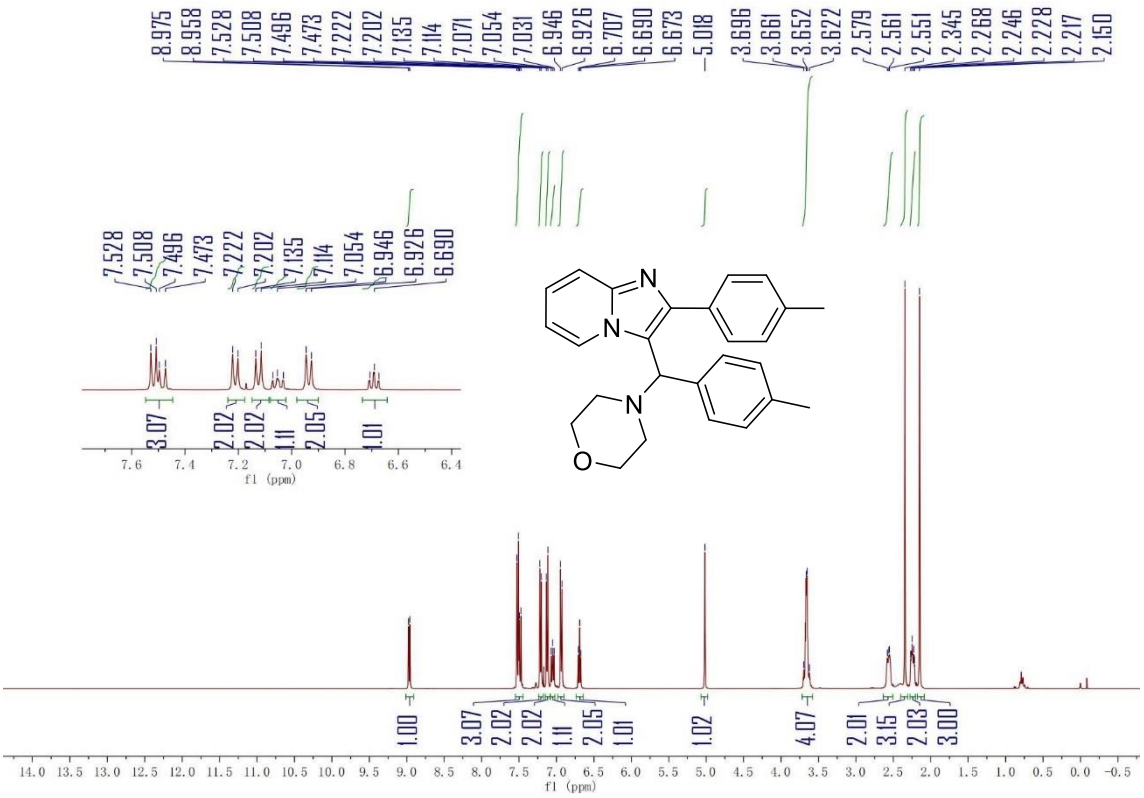

$^{13}$C NMR spectrum of compound **4j**



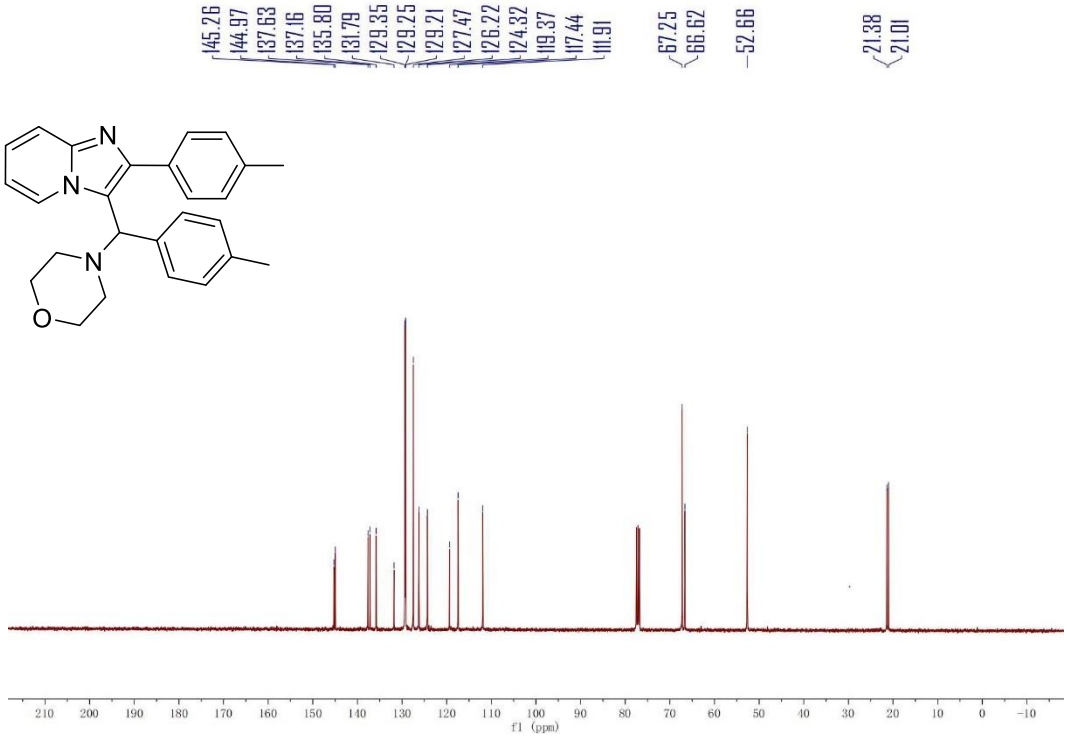
$^{1}$H NMR spectrum of compound **4k**



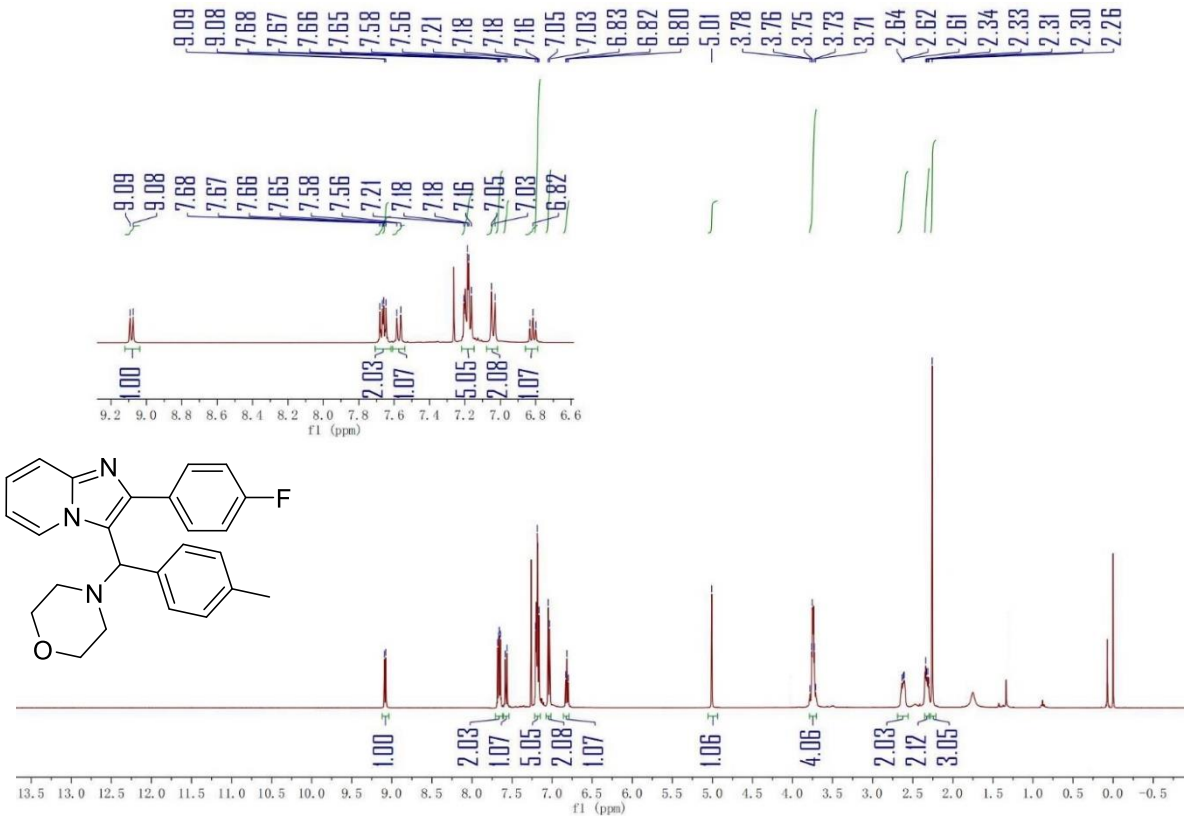
$^{13}$C NMR spectrum of compound **4k**



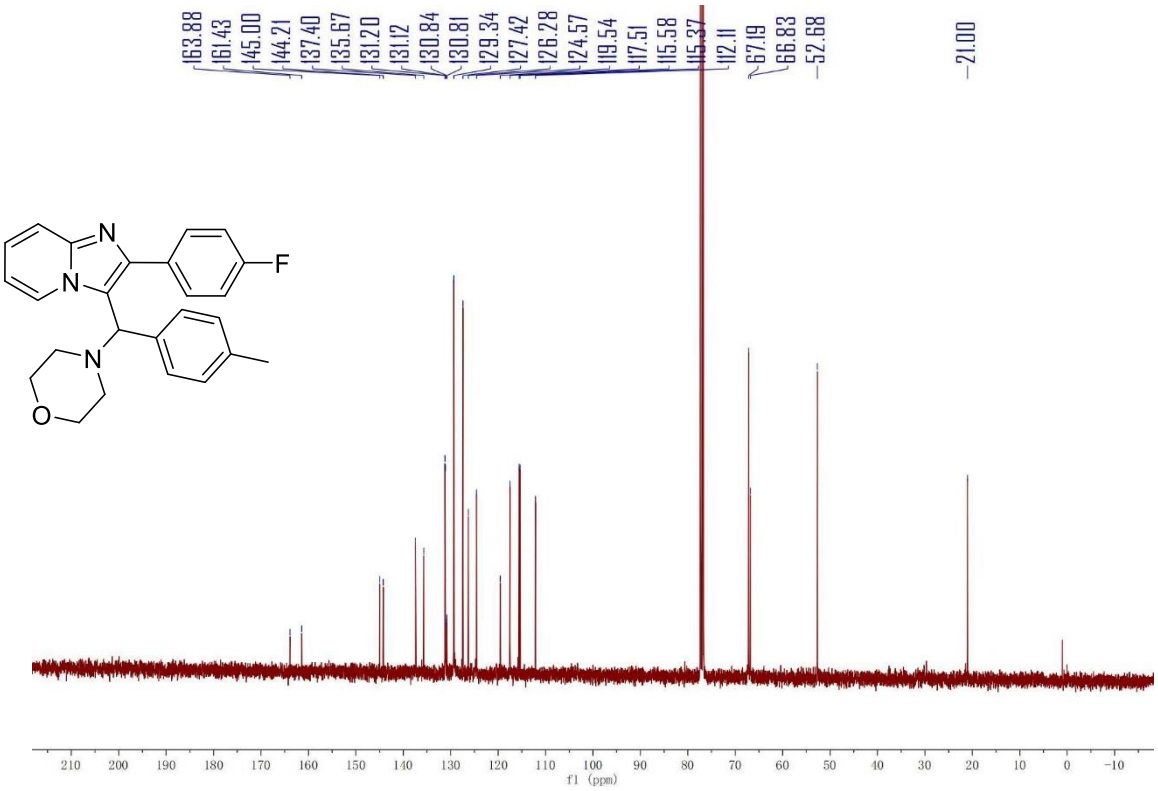

$^{1}$H NMR spectrum of compound **4l**



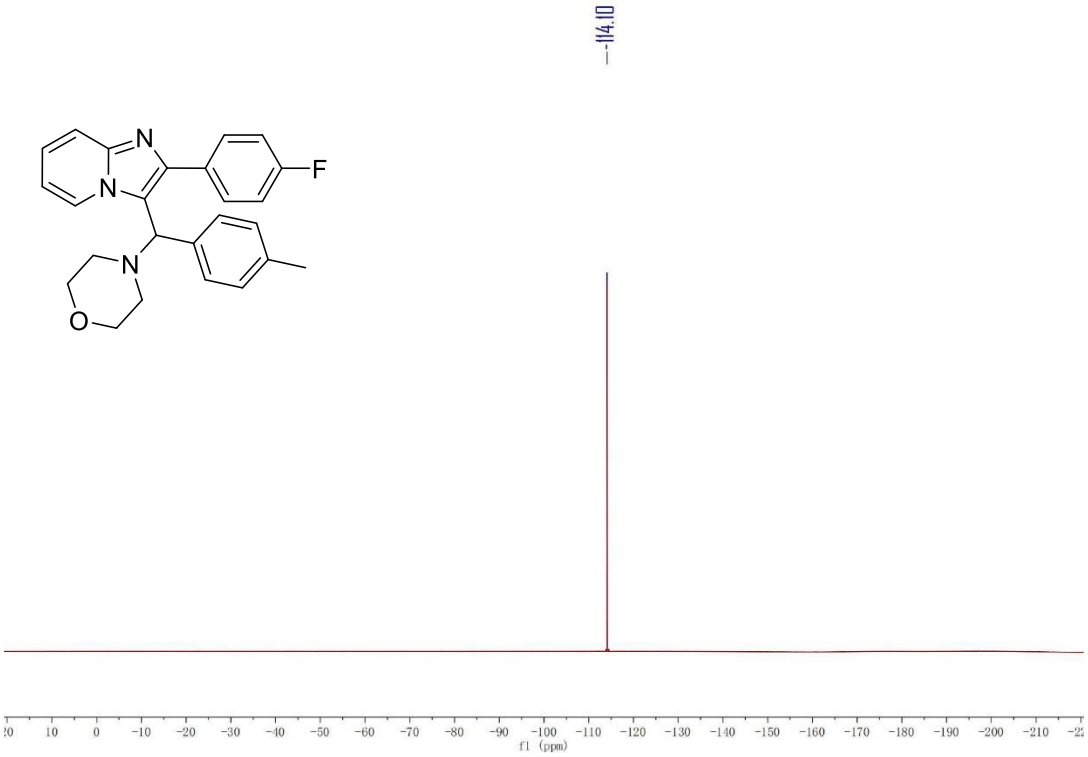

$^{13}$C NMR spectrum of compound **4l**



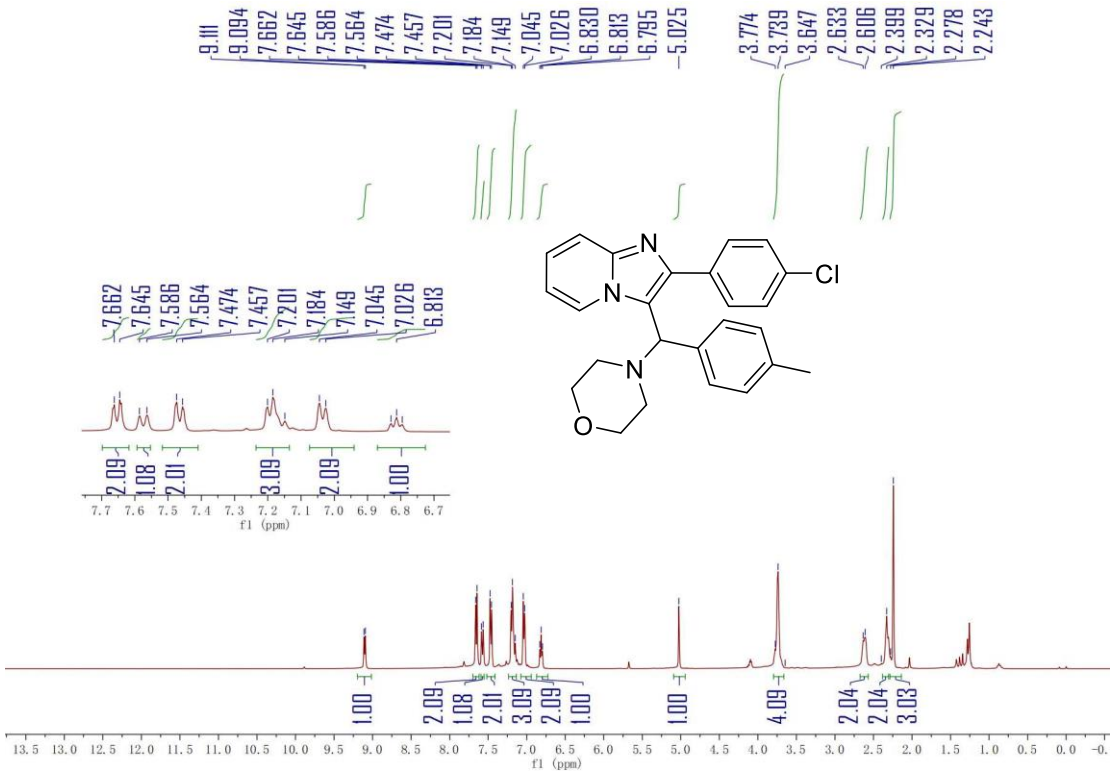
$^{1}$H NMR spectrum of compound **4m**



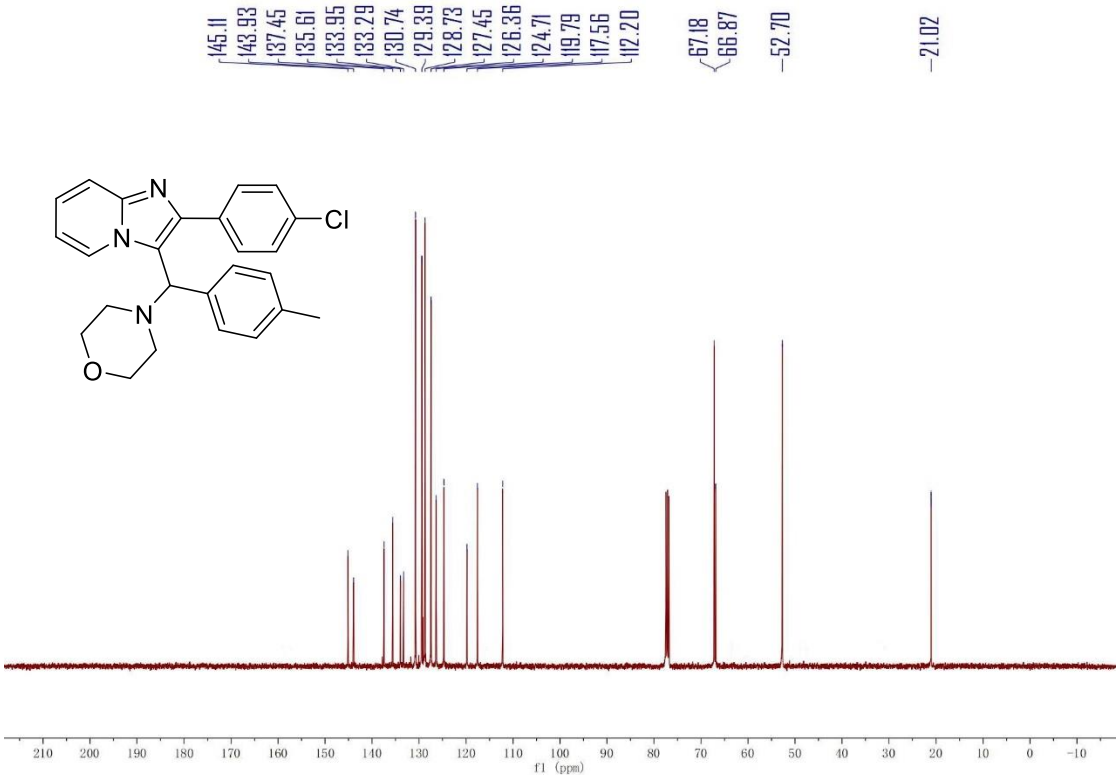
$^{13}$C NMR spectrum of compound **4m**



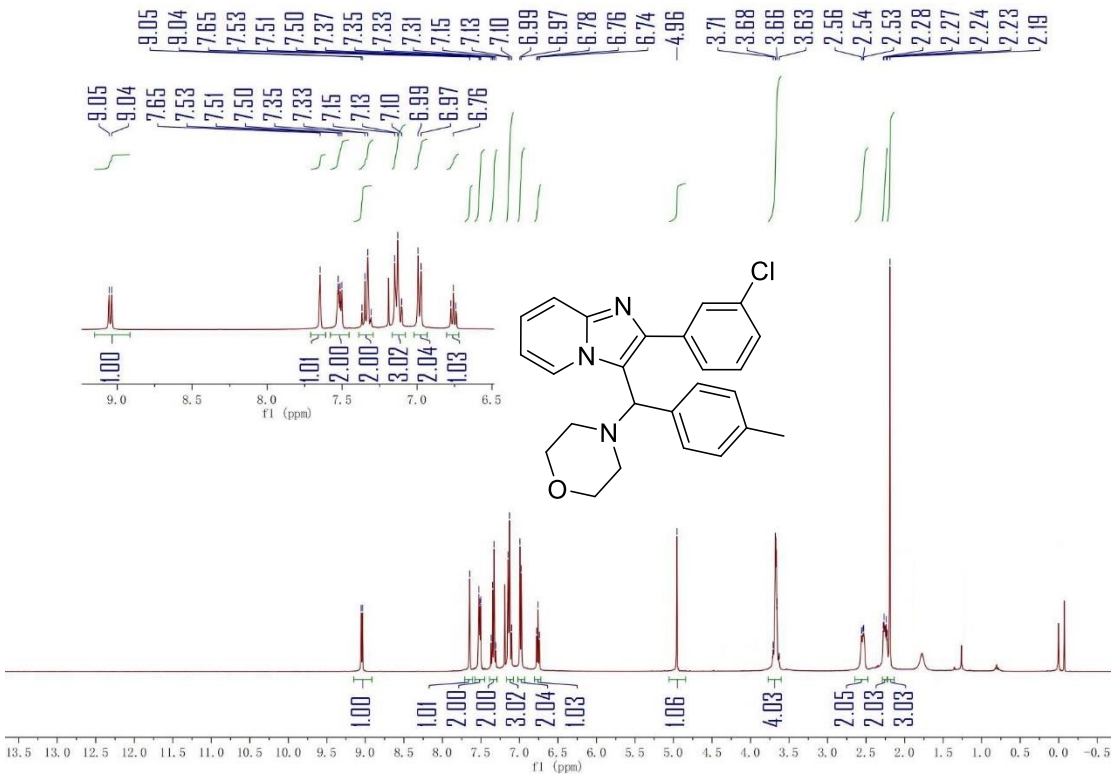

$^{19}$F NMR spectrum of compound **4m**



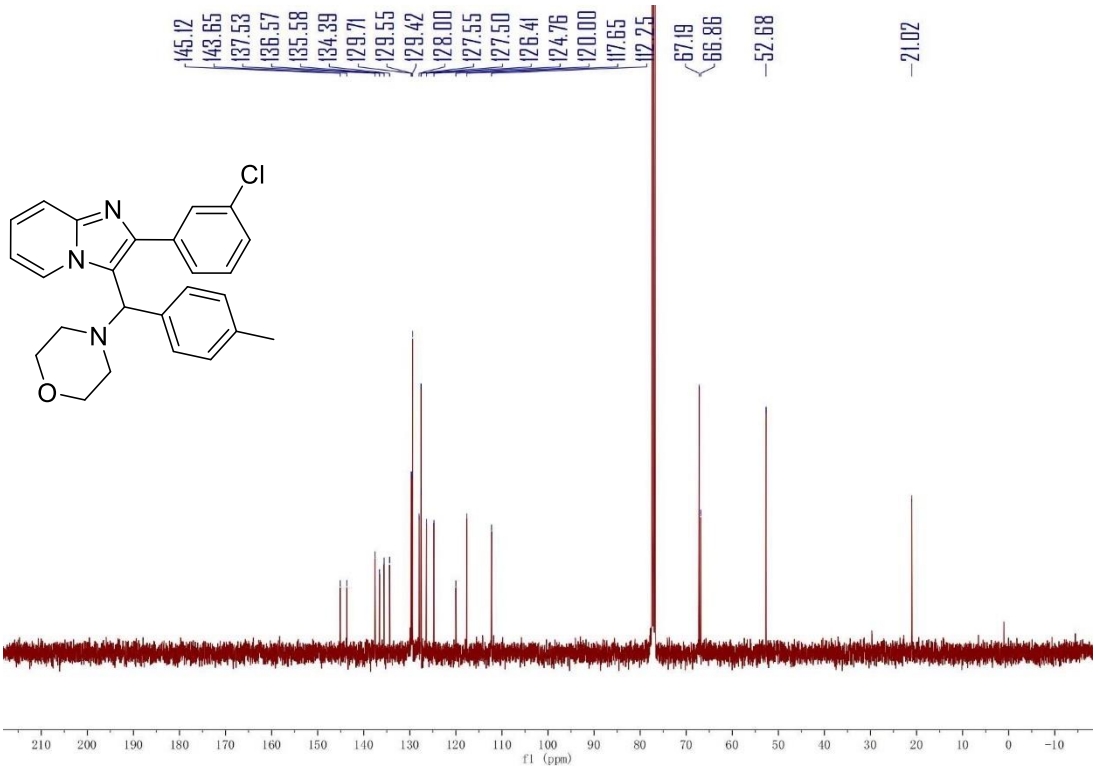

$^{1}$H NMR spectrum of compound **4n**



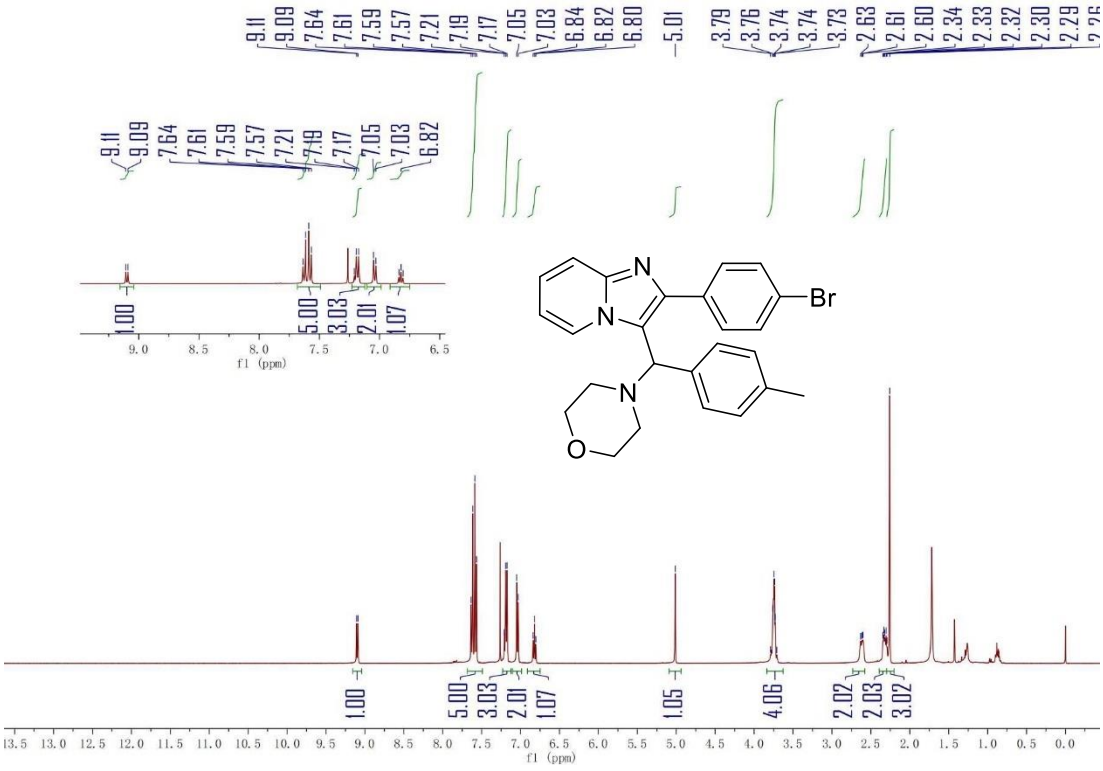

$^{13}$C NMR spectrum of compound **4n**



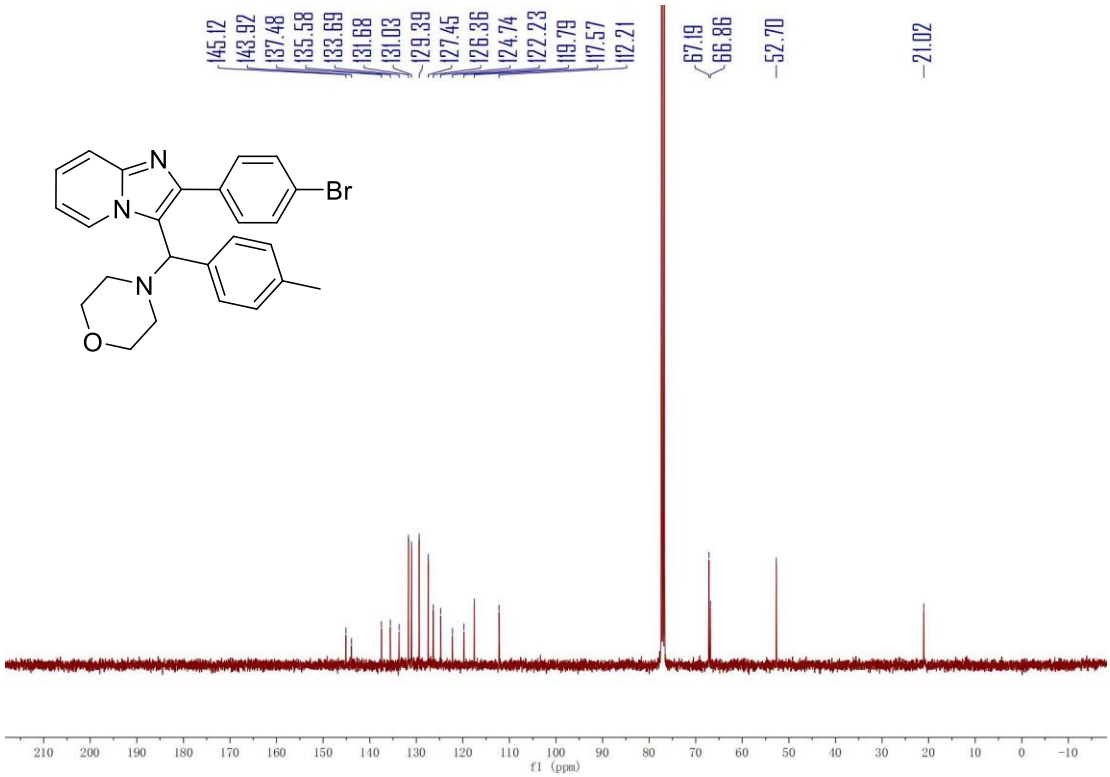

$^{1}$H NMR spectrum of compound **4o**



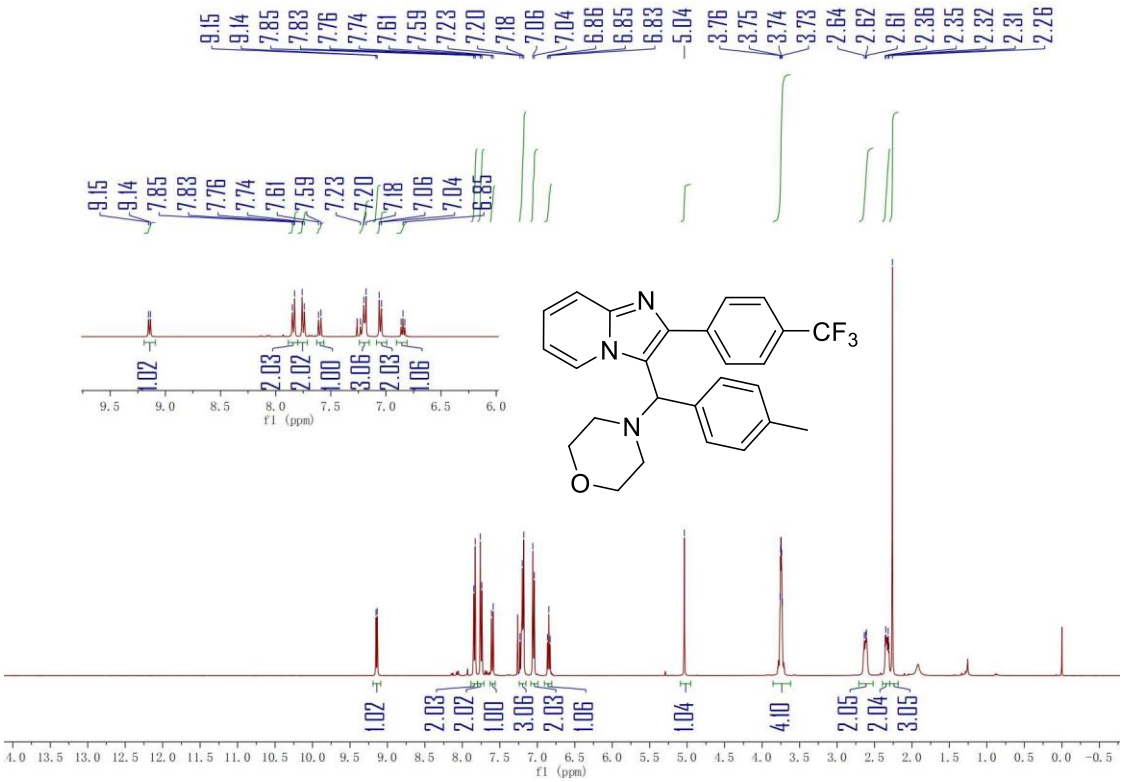

$^{13}$C NMR spectrum of compound **4o**



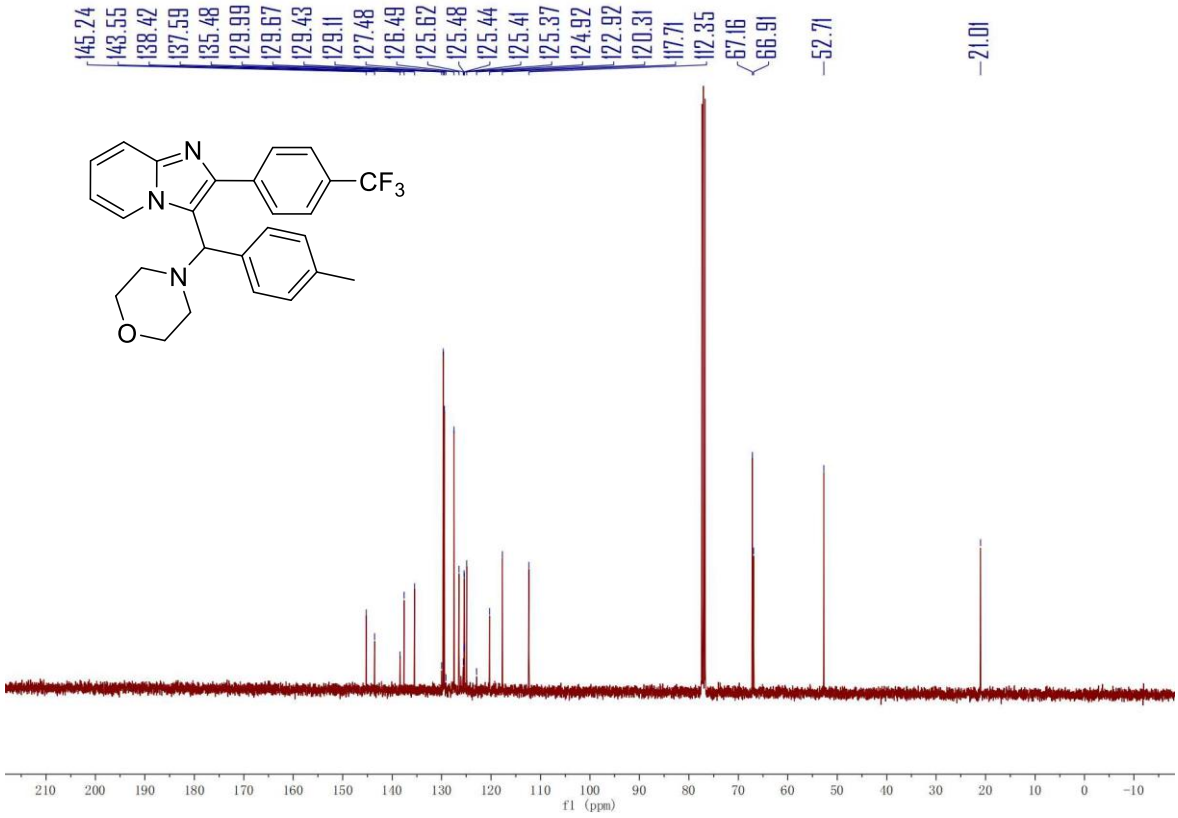

$^{1}$H NMR spectrum of compound **4p**



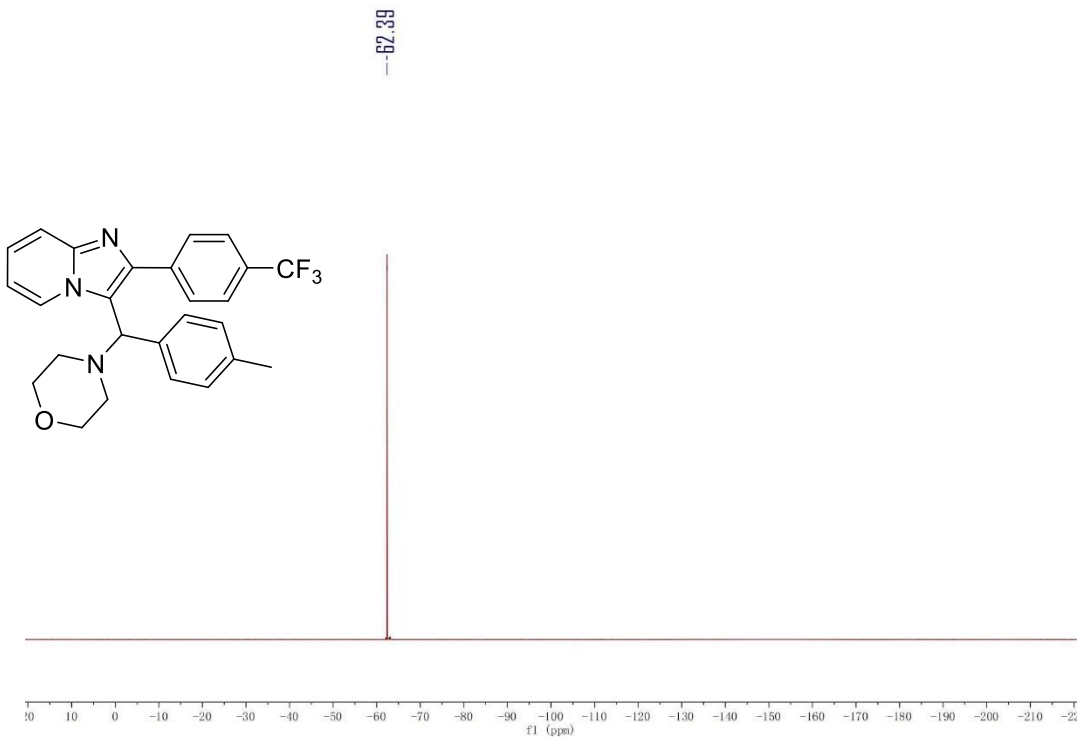

$^{13}$C NMR spectrum of compound **4p**



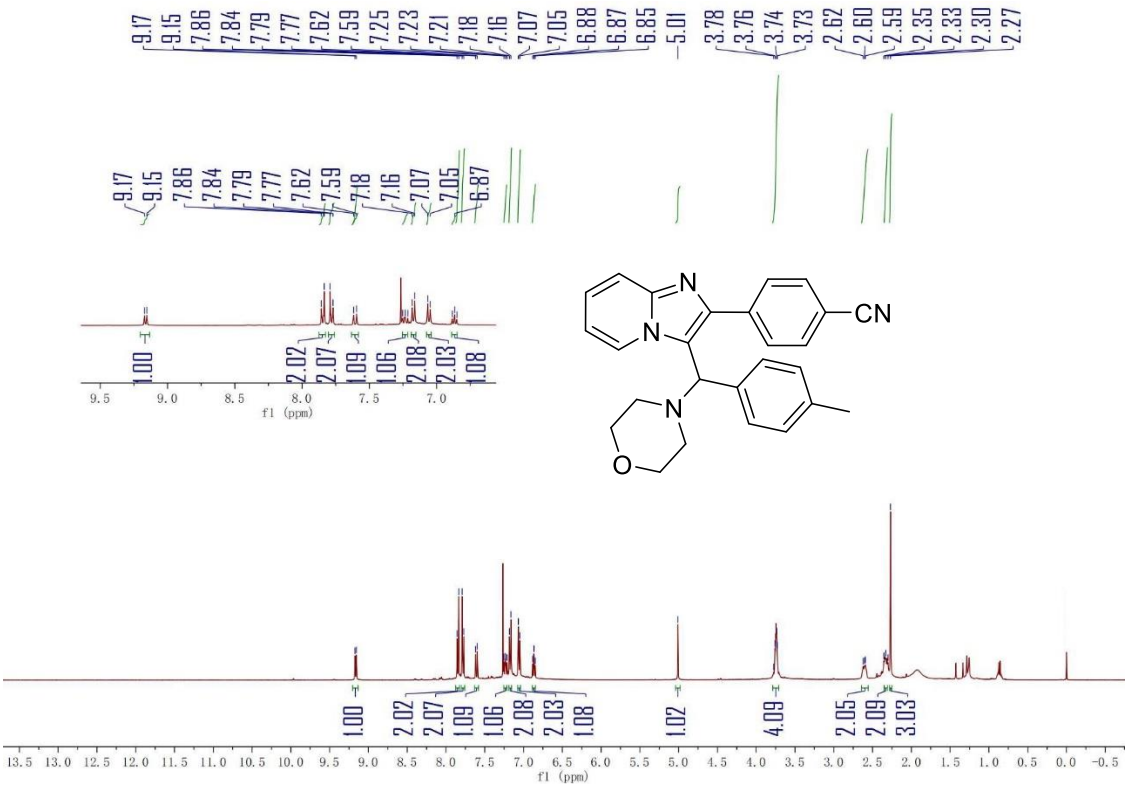

$^{1}$H NMR spectrum of compound **4q**



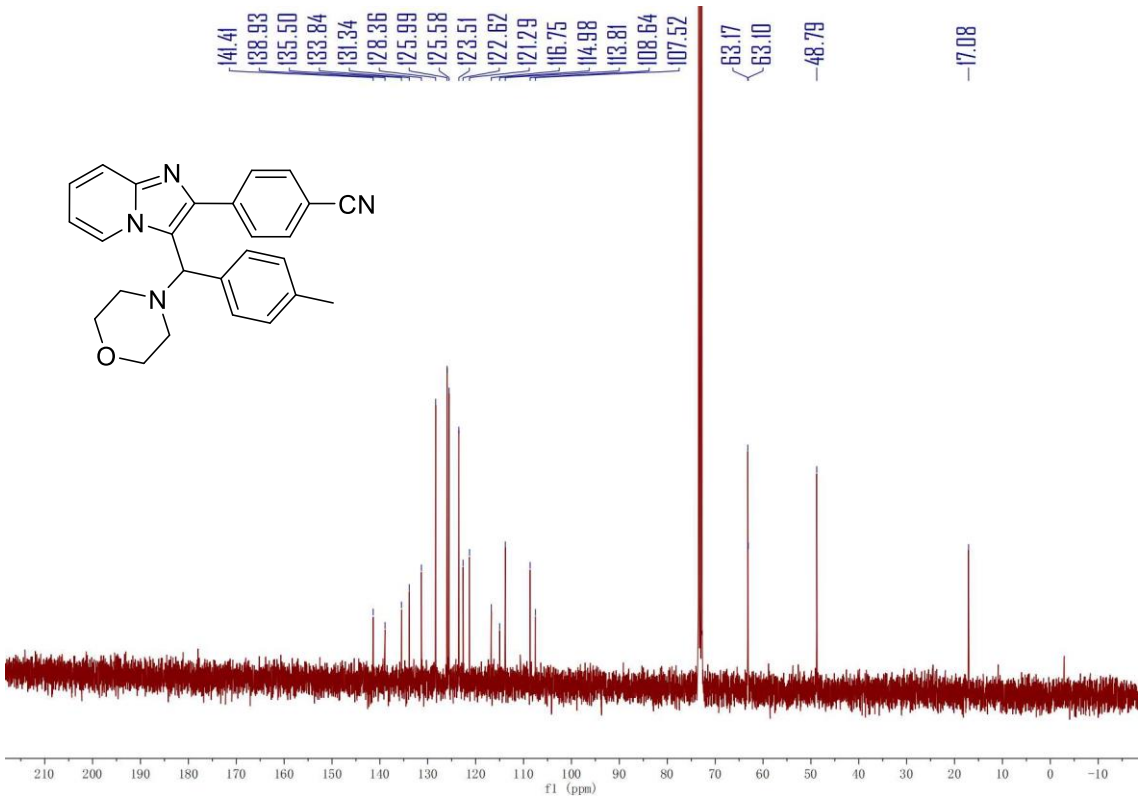

$^{13}$C NMR spectrum of compound **4q**



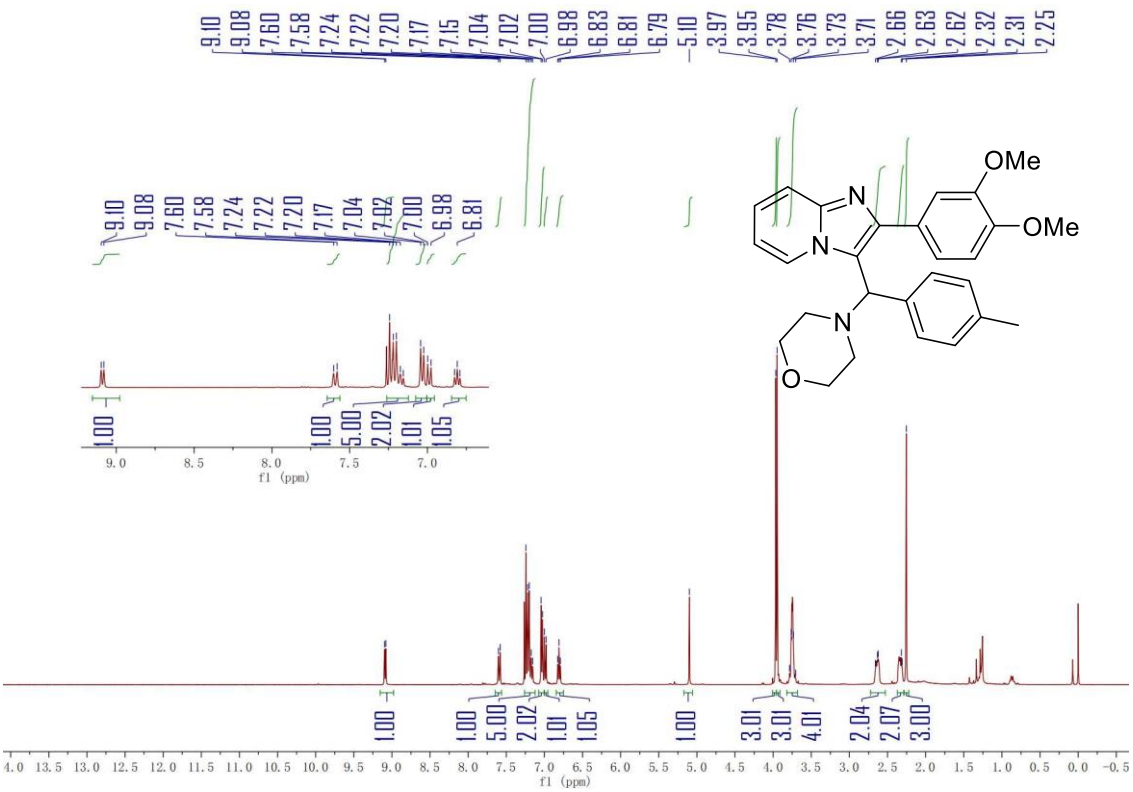

$^{19}$F NMR spectrum of compound **4q**



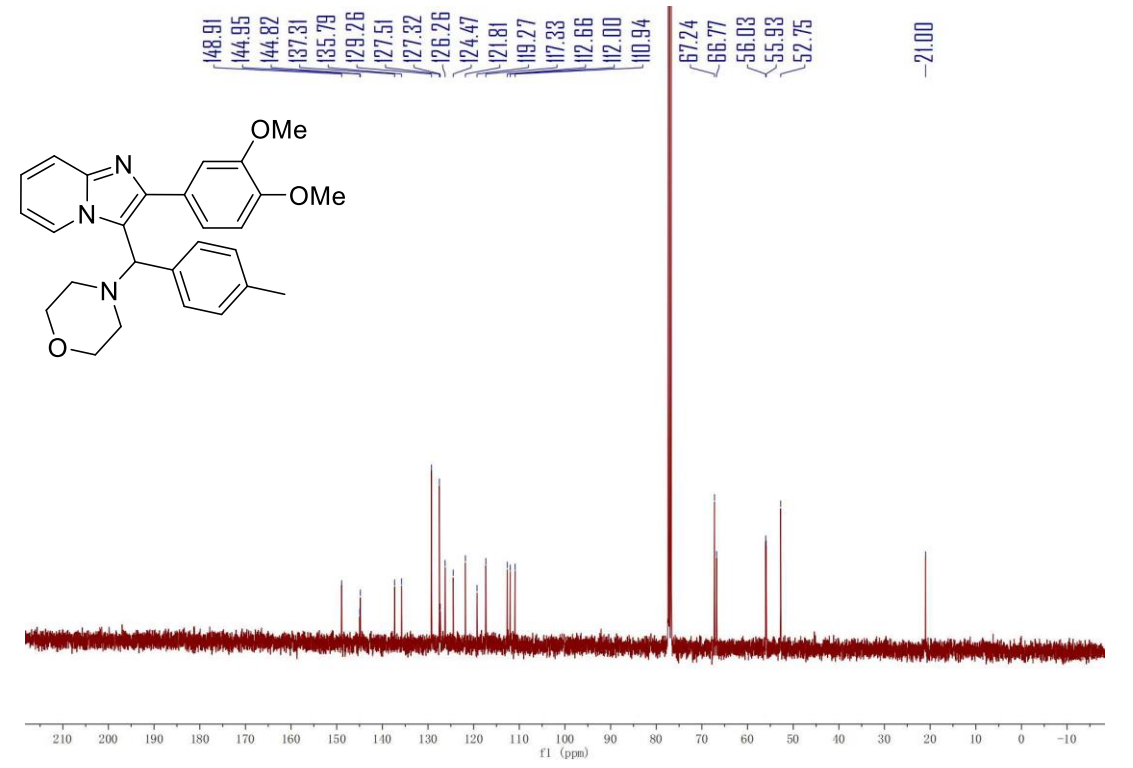

$^{1}$H NMR spectrum of compound **4r**



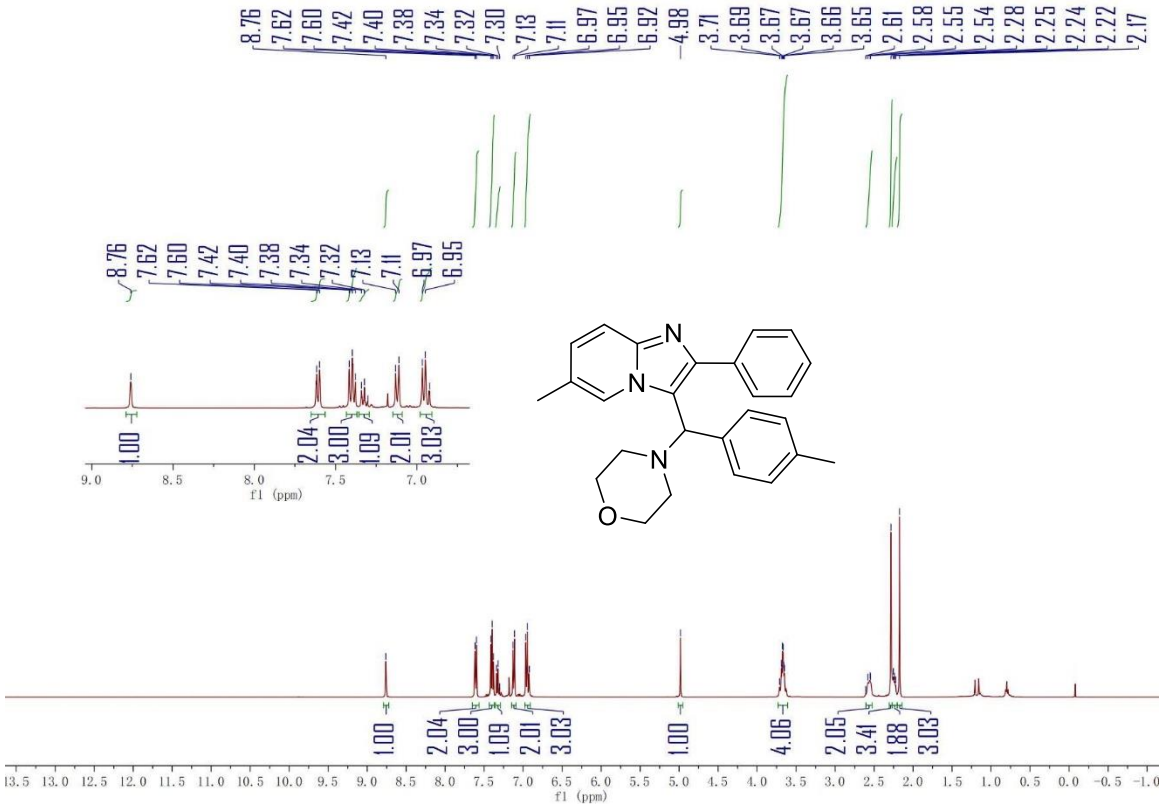

$^{13}$C NMR spectrum of compound **4r**



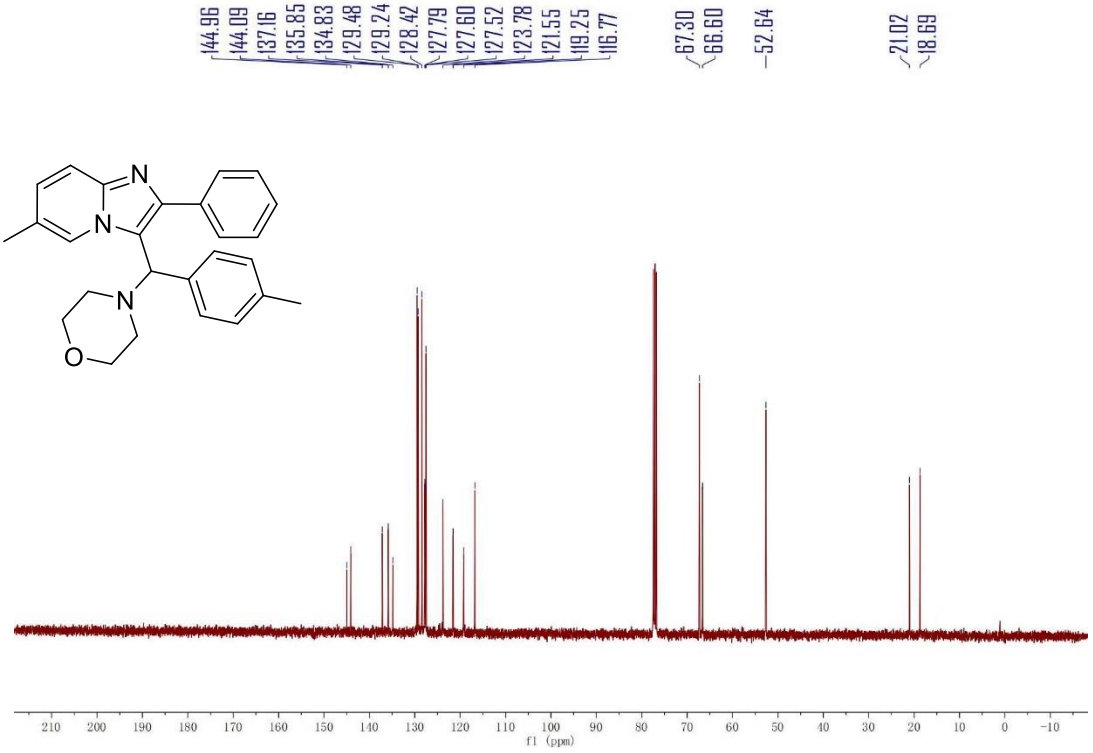

$^{1}$H NMR spectrum of compound **4s**



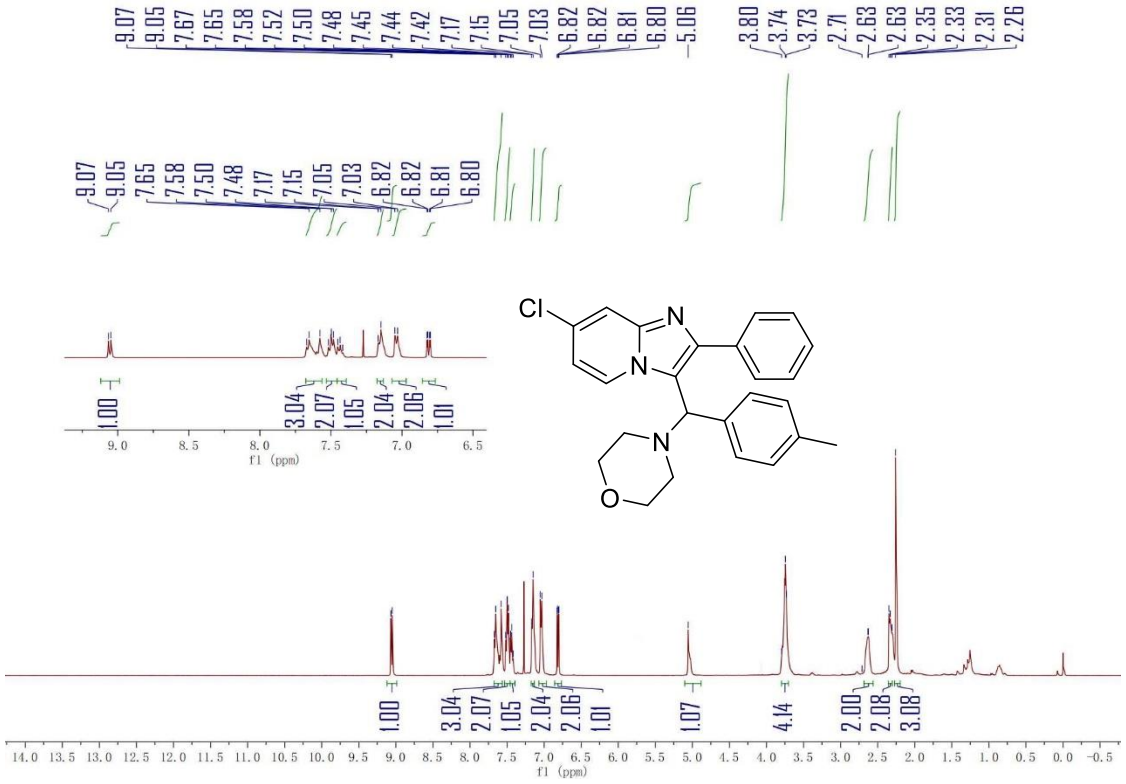

$^{13}$C NMR spectrum of compound **4s**



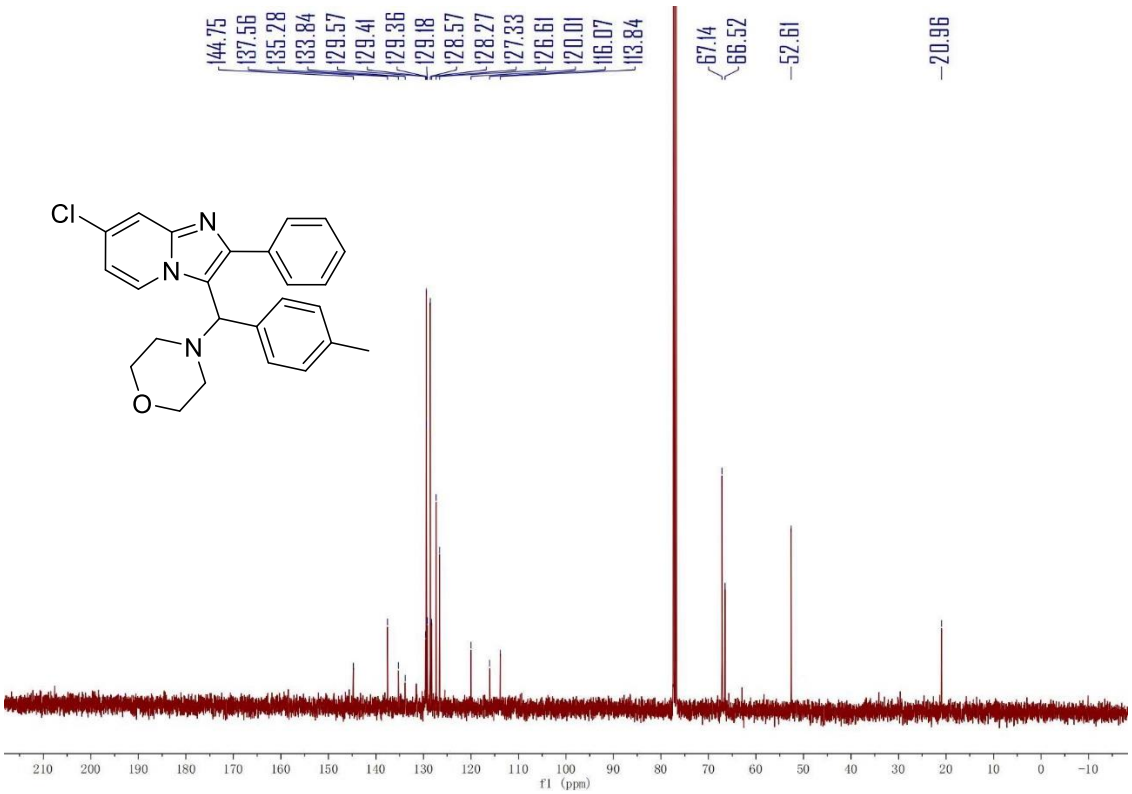
$^{1}$H NMR spectrum of compound **4t**



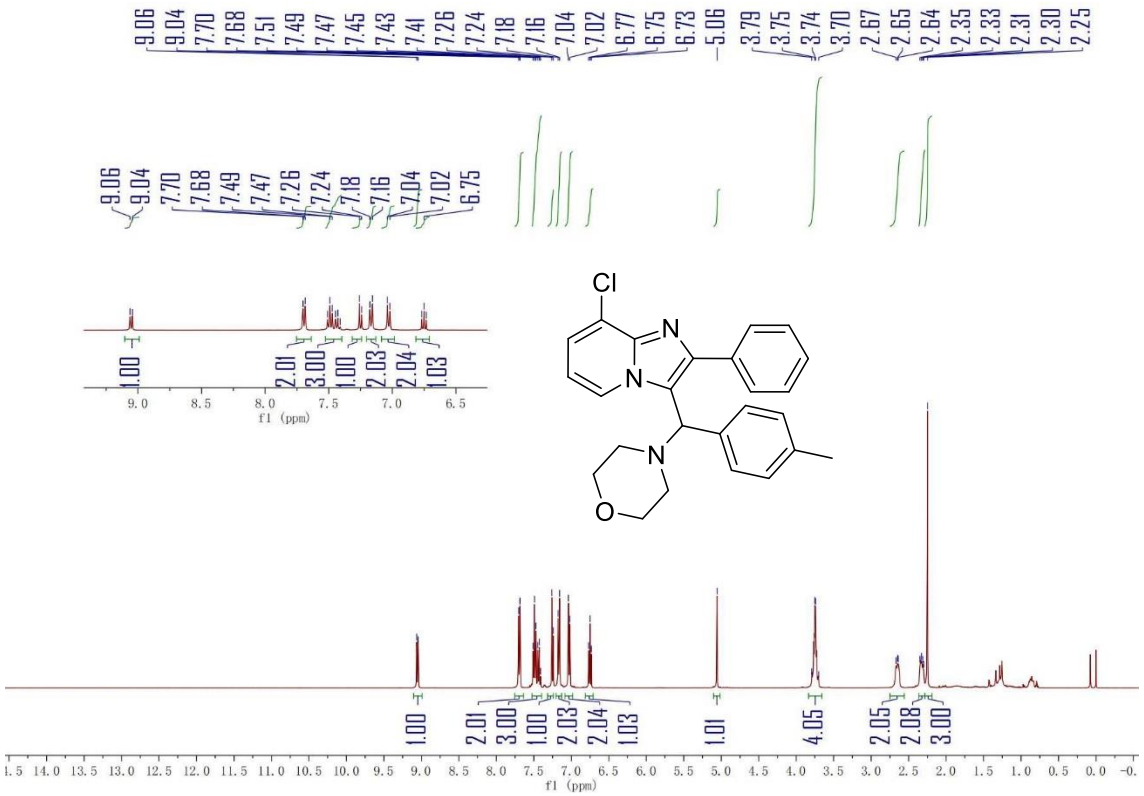
$^{13}$C NMR spectrum of compound **4t**



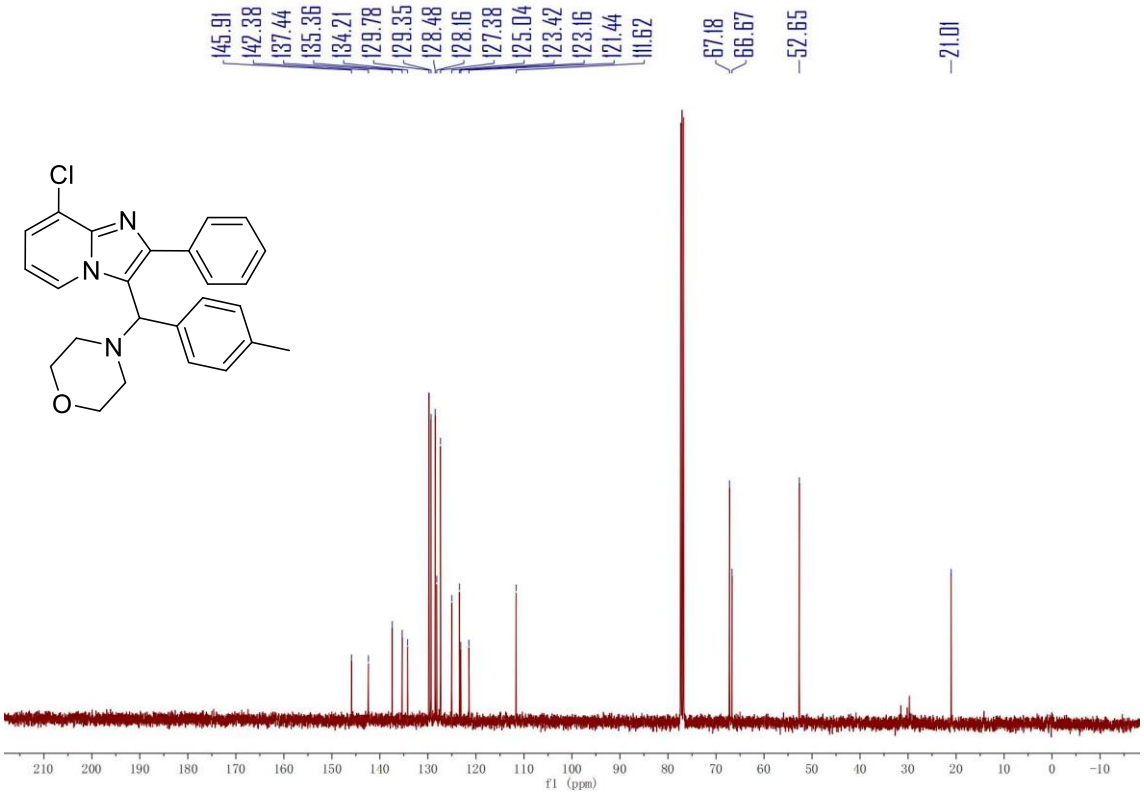

$^{1}$H NMR spectrum of compound **4u**



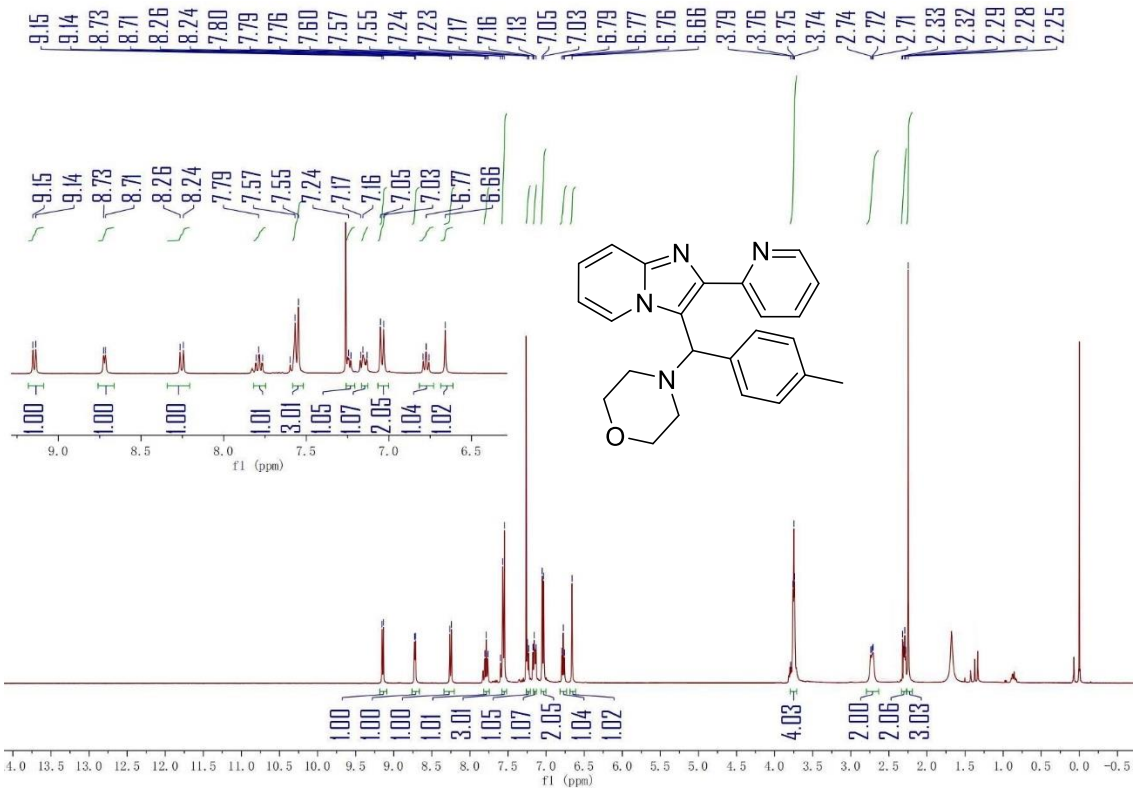

$^{13}$C NMR spectrum of compound **4u**



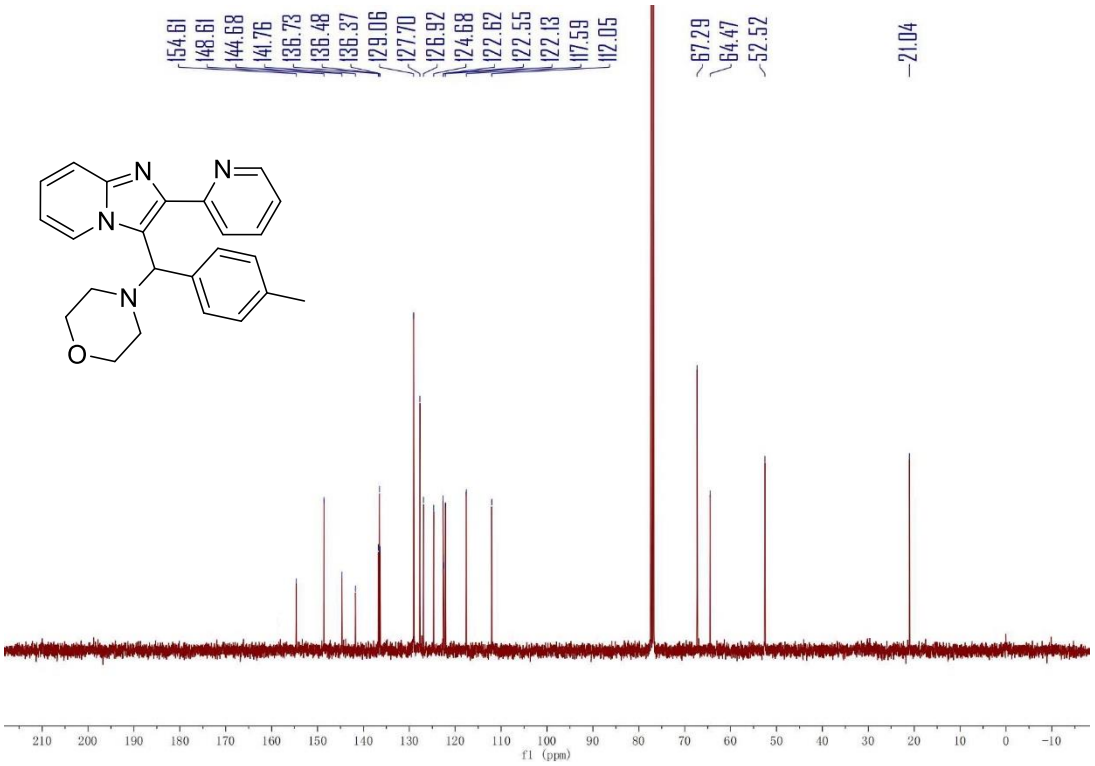

$^{1}$H NMR spectrum of compound **4v**



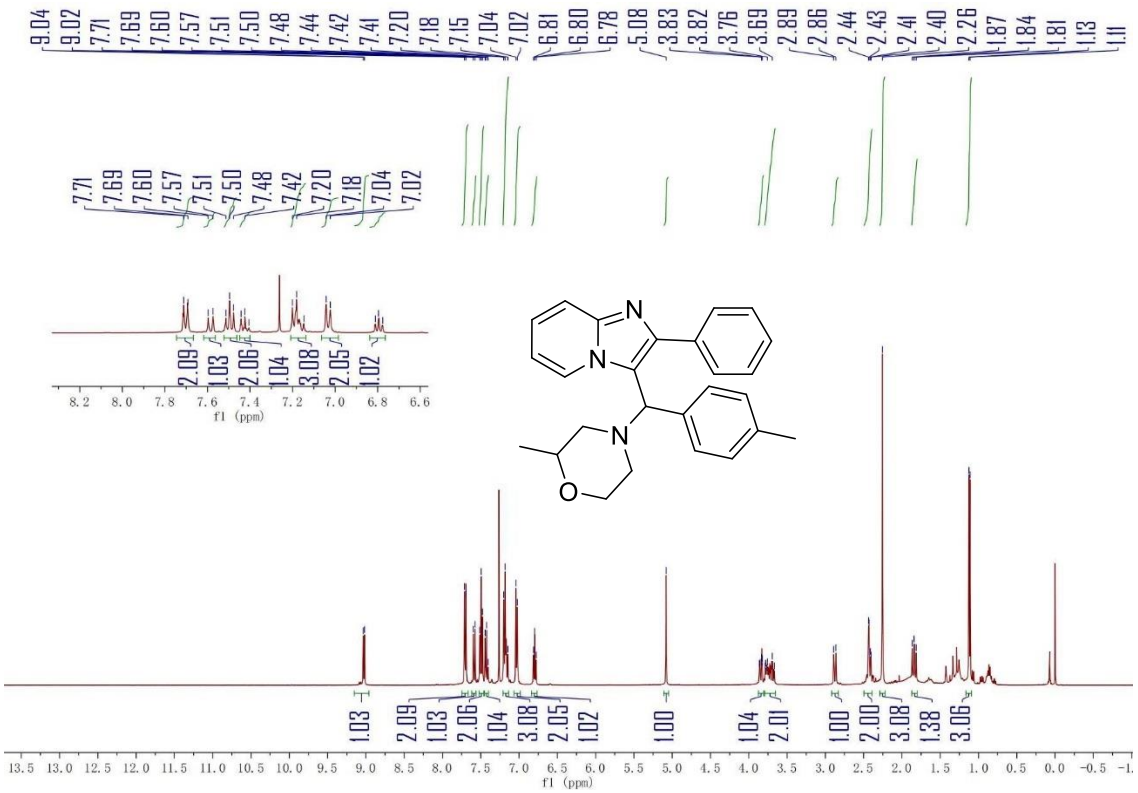

$^{13}$C NMR spectrum of compound **4v**



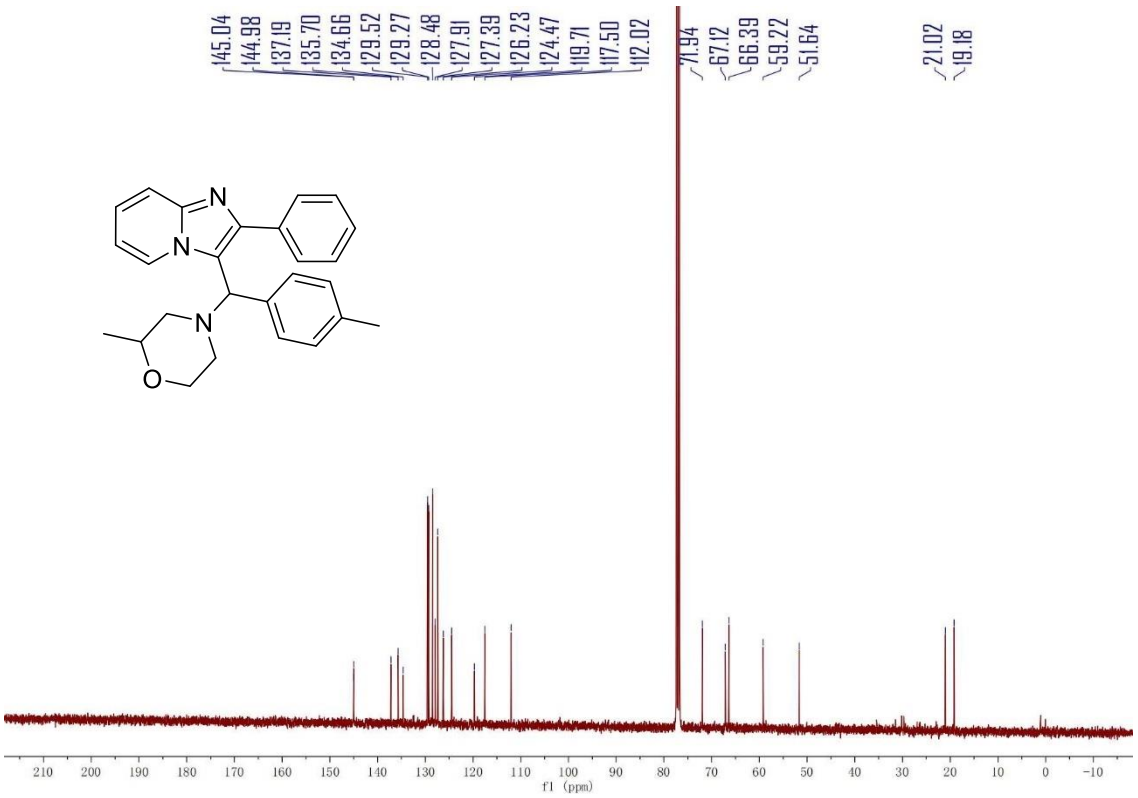
$^{1}$H NMR spectrum of compound **4w**



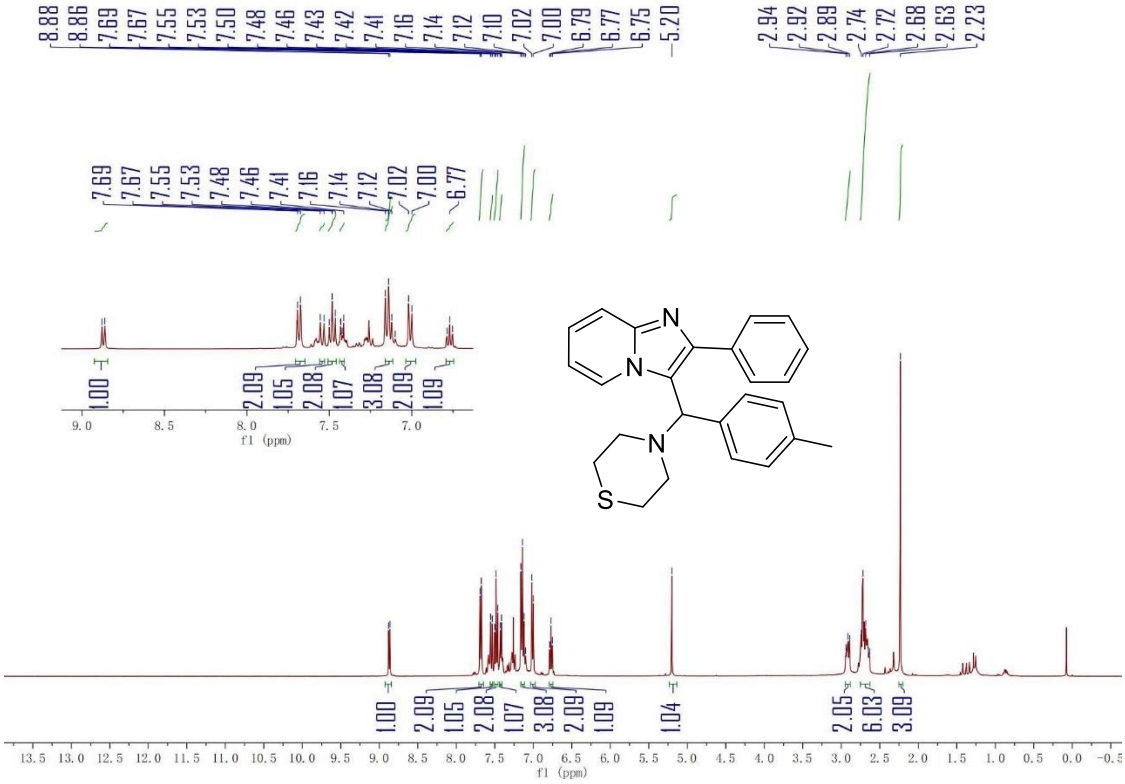
$^{13}$C NMR spectrum of compound **4w**



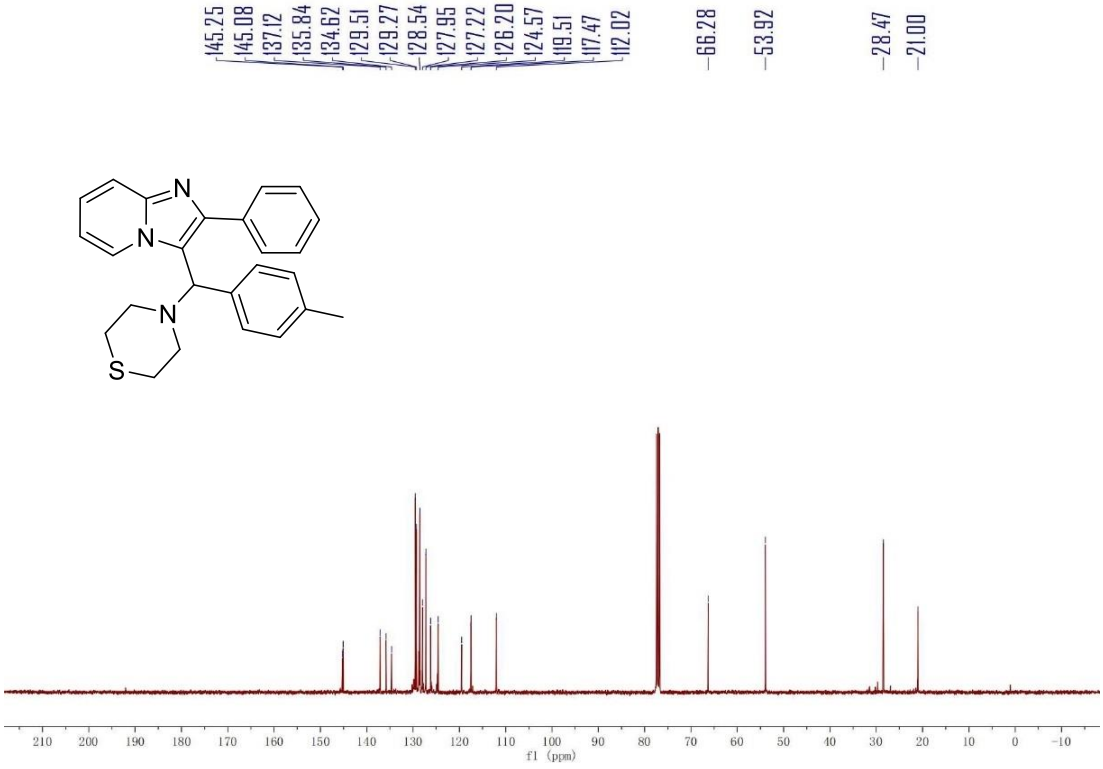
$^{1}$H NMR spectrum of compound **4x**



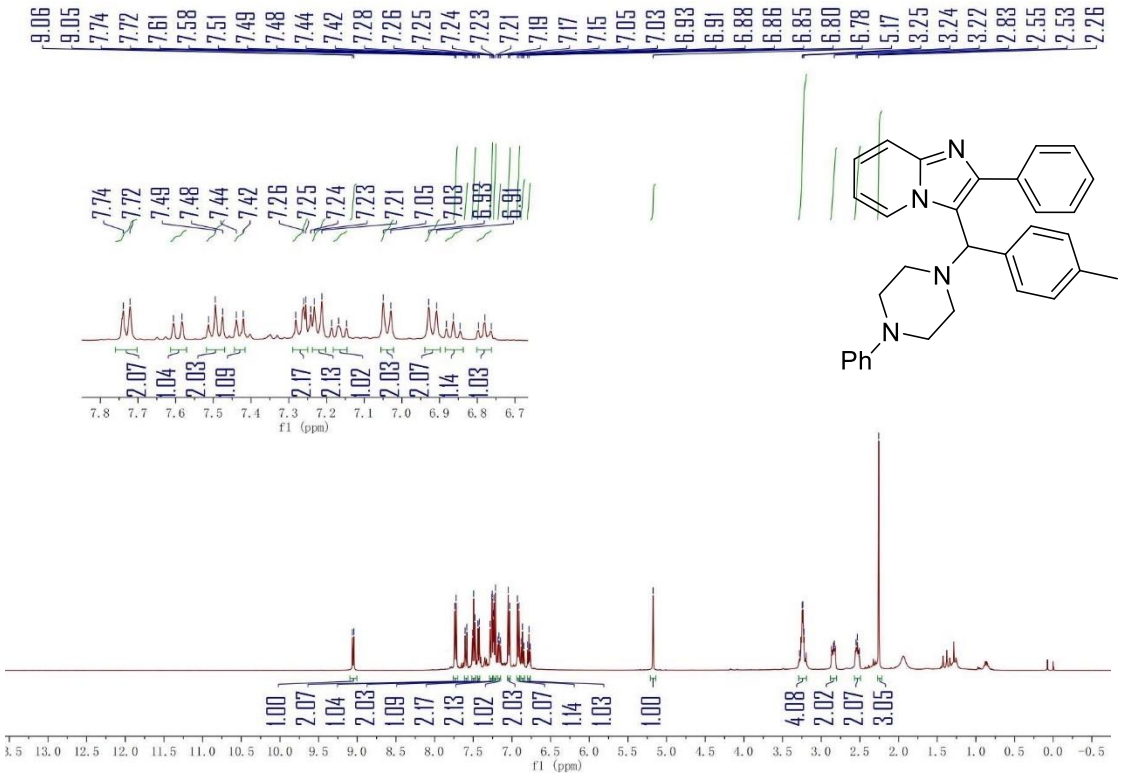
$^{13}$C NMR spectrum of compound **4x**



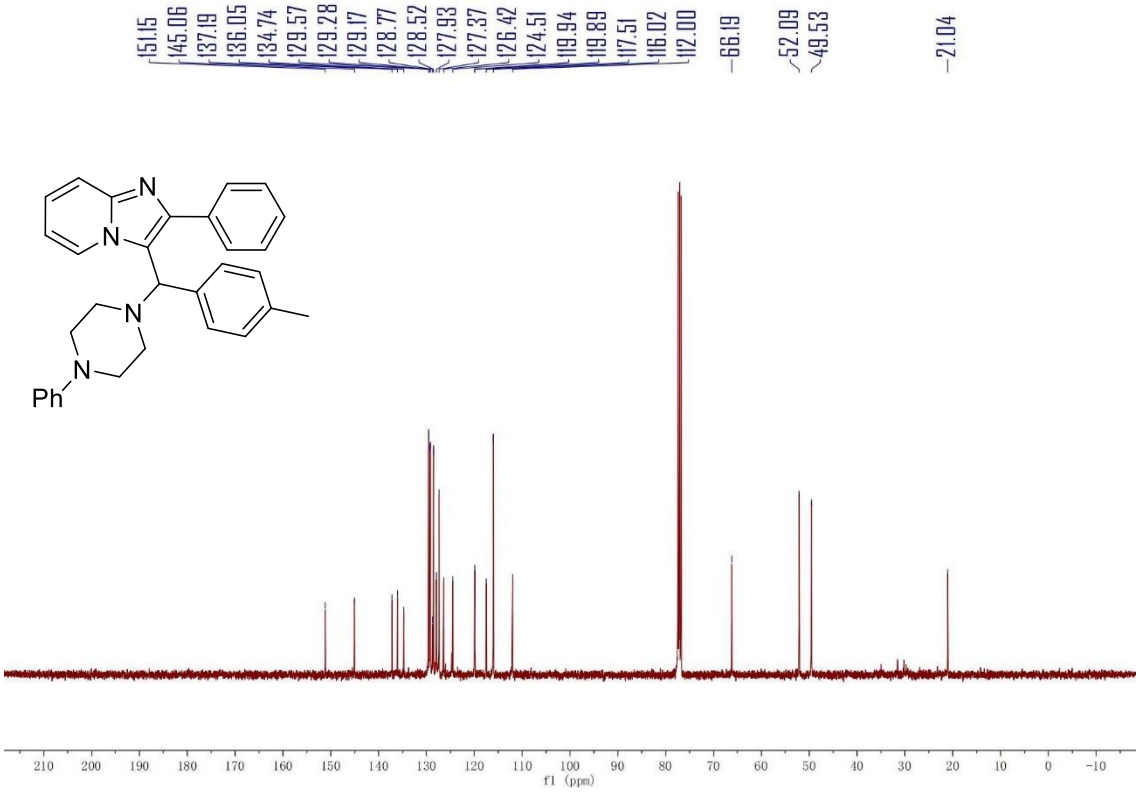
$^{1}$H NMR spectrum of compound **4y**



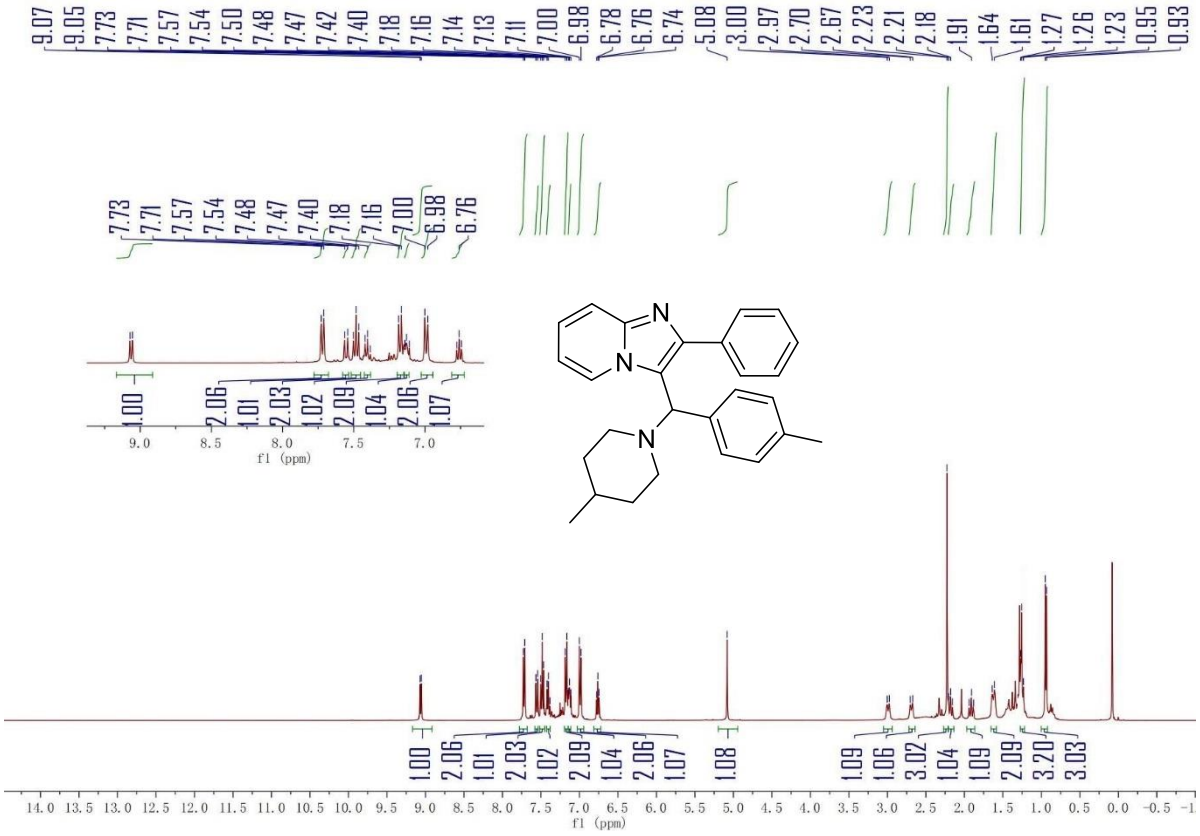
$^{13}$C NMR spectrum of compound **4y**



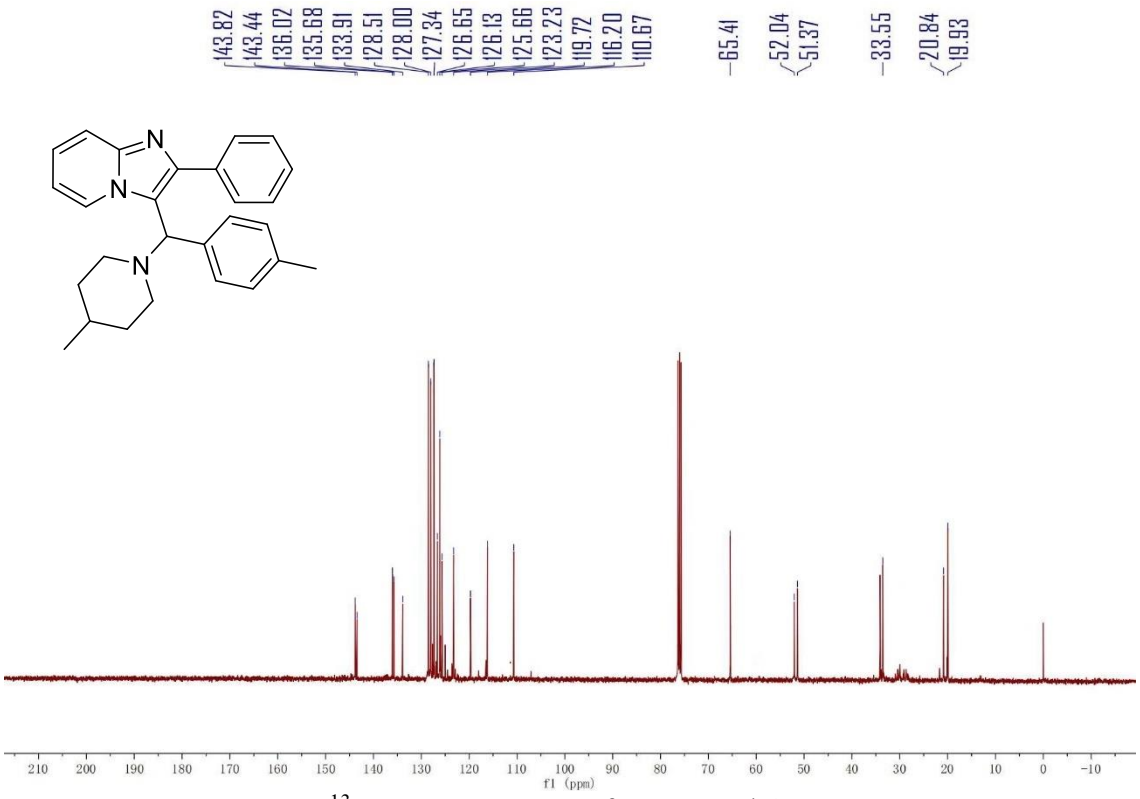
$^{1}$H NMR spectrum of compound **4z**



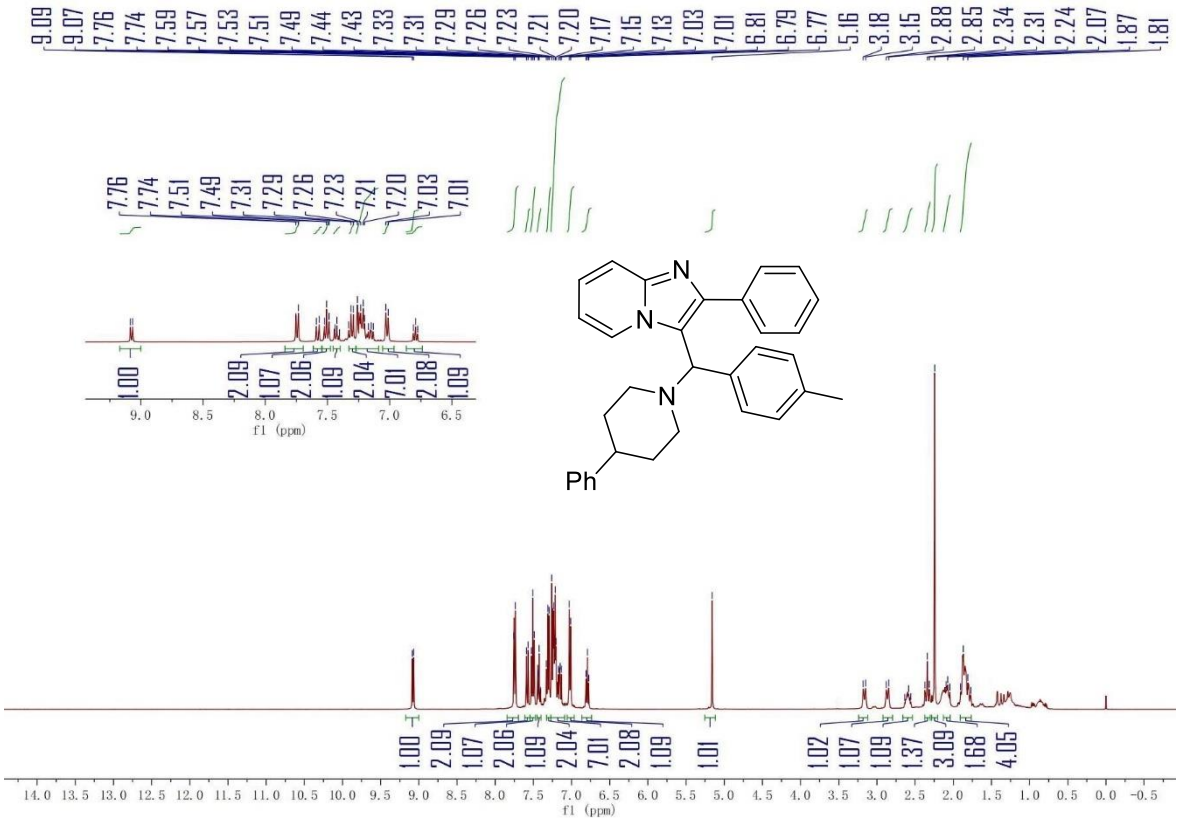
$^{13}$C NMR spectrum of compound **4z**



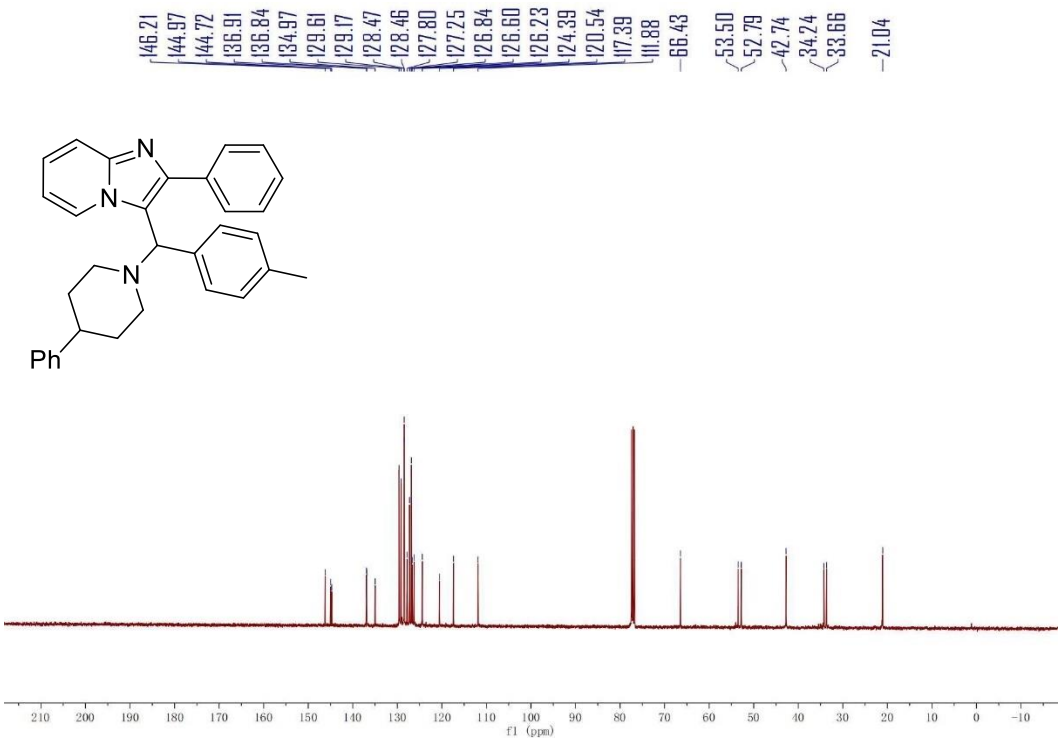
$^{1}$H NMR spectrum of compound **4aa**



$^{13}$C NMR spectrum of compound **4aa**




$^{1}$H NMR spectrum of compound **4ab**




$^{13}$C NMR spectrum of compound **4ab**

## References


[1] Obermayer, D.; Znidar, D.; Glotz, G.; Stadler, A.; Dallinger, D.; Kappe, C. O. Design and performance validation of a conductively heated sealed-vessel reactor for organic Synthesis. *J. Org. Chem*. **2016**, *81*, 11788-11801.

[2] Ghosh, P.; Ganguly, B.; Kar, B.; Dwivedi, S.; Das, S. Green procedure for highly efficient, rapid synthesis of imidazo[1,2-a]pyridine and its late stage functionalization. *Synth. Commun*. **2018**, *48*, 1076.