Cu-Catalyzed Domino Route to Imidazo[1,2-*a*]pyridines

M.Sc. Thesis

By

Ram Kumar

DISCIPLINE OF CHEMISTRY

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Cu-Catalyzed Domino Route to Imidazo[1,2-*a*]pyridines

A THESIS

Submitted in partial fulfillment of the
requirements for the award of the degree
of
Master of Science

by

Ram Kumar

DISCIPLINE OF CHEMISTRY

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CANDIDATE'S DECLARATION

I hereby certify that the work which is being presented in the thesis entitled **Cu-Catalyzed Domino Route to imidazo[1,2-*a*]pyridines** in the partial fulfillment of the requirements for the award of the degree of **MASTER OF SCIENCE** and submitted in the **DISCIPLINE OF CHEMISTRY, Indian Institute of Technology Indore**, is an authentic record of my own work carried out during the period from July 2018 to June 2019 under the supervision of **Dr. Sampak Samanta**, Associate Professor, IIT Indore.

The matter presented in this thesis has not been submitted by me for the award of any other degree of this or any other institute.

Ram kumar

This is to certify that the above statement made by the candidate is correct to the best of my/our knowledge.

Dr. Sampak Samanta

Ram kumar has successfully given his M.Sc. Oral Examination held on 1/7/2019

Signature of Supervisor of M.Sc. thesis	Convener, DPGC
Date:	Date:
Signature of PSPC Member	Signature of PSPC Member
Dr. Chelvam Venkatesh	Dr. Shaikh M. Mobin
Date:	Date:

Dedicated to My LOVELY Family…….

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I want to extend my thanks to my batch mates who were always there with me and never let me down during my bad time. Last but not least I would like to pay sincere gratitude to my loving parents for their continuous help and moral support throughout my project work.

Ram Kumar

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Abstract

A new route to imidazo[*1,2-a*]pyridines by using copper-catalyzed one-pot reaction of oxime acetates with 2-aminopyridines has been demonstrated. The importance of the present protocol is (1) low cost catalyst loading; (2) easily available starting materials; and (3) absence of stoichiometric external oxidants. Hence, this domino strategy provides an excellent alternative over previous approaches in the synthesis of imidazo[1,2-*a*]pyridines.

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ACRONYMS

DMSO	Dimethyl sulphoxide
DCM	Dichloromethane
NEt_3	Triethyl amine
$CDCl_3$	Chloroform-D
DMF	*N*,*N*-dimethyl formamide
THF	Tetrahydrofuran
DABCO	1,4-Diazabicyclo [2,2,2]octane
DBU	1,8-Diazaicyclo [5,4,0]undec-7-ene
IPs	Imidazo[1,2-*a*]pyridine
CH_3CN	Acetonitrile
CH_3OH	Methanol
EtOAc	Ethyl acetate
HRMS	High Resolution Mass Spectrometry
NMR	Nuclear magnetic resonance spectroscopy
^{1}H NMR	Proton NMR spectroscopy
^{13}C NMR	Carbon-13 NMR spectroscopy
IR	Infrared spectroscopy
M	Molar
Ppm	Parts per million

SYMBOLS/UNITS

Λ	Wavelength
Δ	Chemical shift
Nm	Nanometer
°C	Degree Celsius
Mmol	Milli mole
M	Molar
G	Gram
H	Hour
J	Coupling constant
nM	Nano molar
Ml	Milli litre
Dd	Doublet of doublet
Hz/MHz	Hertz/Mega Hertz
R_f	Retention factor
Ppm	Parts per million

Chapter-1

INTRODUCTION

1.1. General Introduction:

In recent years, efficient synthesis of imidazo[1,2-*a*]pyridines has gained much interest in synthetic organic and medicinal chemistry because these moieties are found in a large number of bioactive natural molecules. Furthermore, they constitute several marketable drugs such as telcagepant, tentoparazole, soraparazan, miroprofen, zolpidem, minodernic acid etc. In addition, several imidazopyridines derivatives exhibited broad spectrum of biological activities including antiviral, analgesic, anthelmintic, antifungal, antibacterial, antiprotozoal etc. Moreover, they also play an important role as reactive intermediates *[1-6]*.

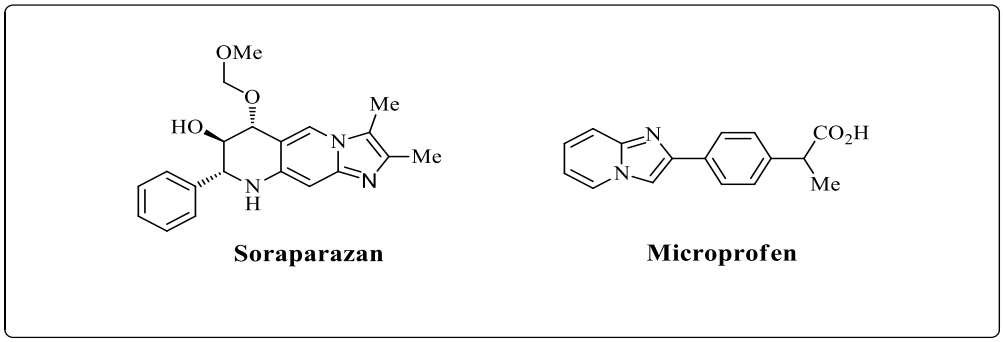


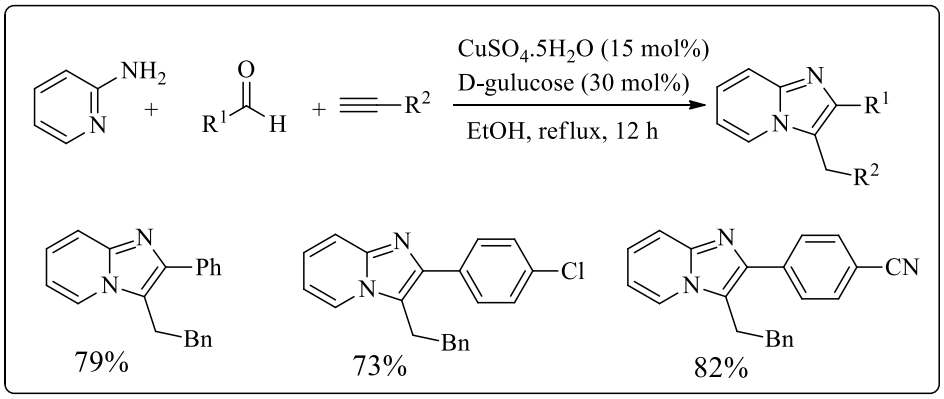
Figure 1: Representative examples of some biologically active heterocycles possessing an imidazopyridine moiety *[6]*.

Therefore, many powerful synthetic strategies have been developed to synthesize the imidazo[1,2-*a*]pyridines via multicomponent, oxidative coupling and tandem reactions. All these methods involve expensive metal-salts like Pd, Au etc. Therefore, it is a great idea to use a commercially available cheap catalyst for the synthesis of abovementioned heterocycles from simple substances.

Some of the recent reports have been described in the next section.

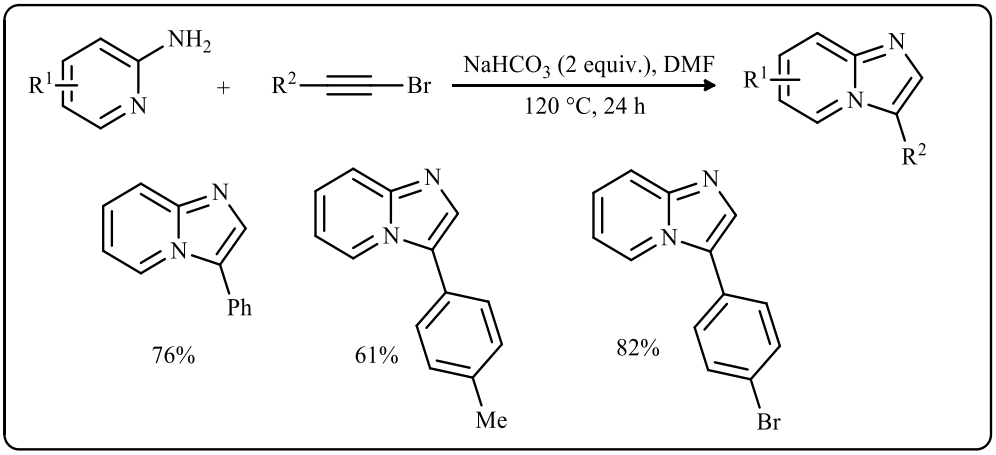
1.2. Literature survey:

In 2012, Shankar *et al*. developed one-pot synthesis of a series of imidazopyridines by mixing 2-aminopyridine, aldehydes and aryl-acetylenes in the presence $CuSO_4$ as a powerful catalyst *[16]*.



Scheme 1. Three component synthesis of imidazopyridines derivatives.

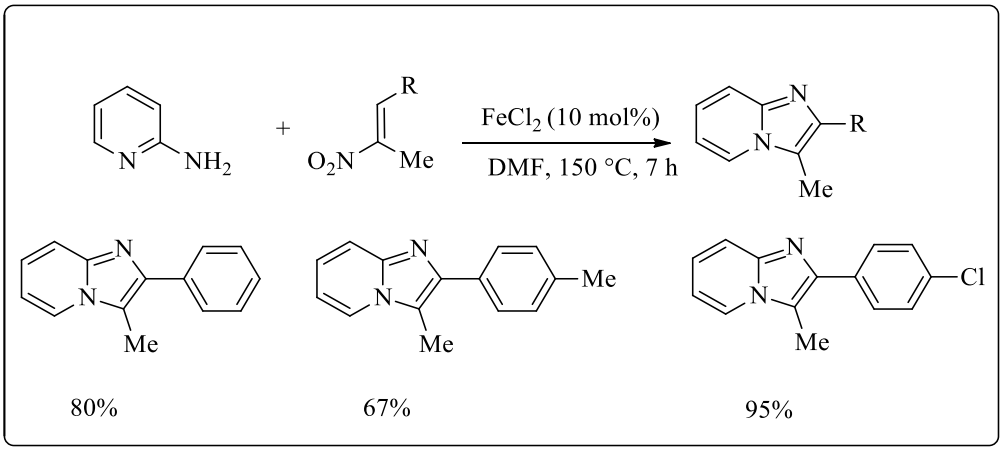
In 2011, Zhou *et al*. reported an efficient method for the synthesis of 3-arylimidazo[1,2-*a*]pyridines via catalyst-free cascade process from 2-aminopyridine and 1-bromo-2-phenylacetylene and 1,1-dibromo-2-phenylethene *[17]*.



Scheme 2. Synthesis of imidazopyridines using 1-bromo-2-phenyl acetylene derivatives and 2-aminopyridines.

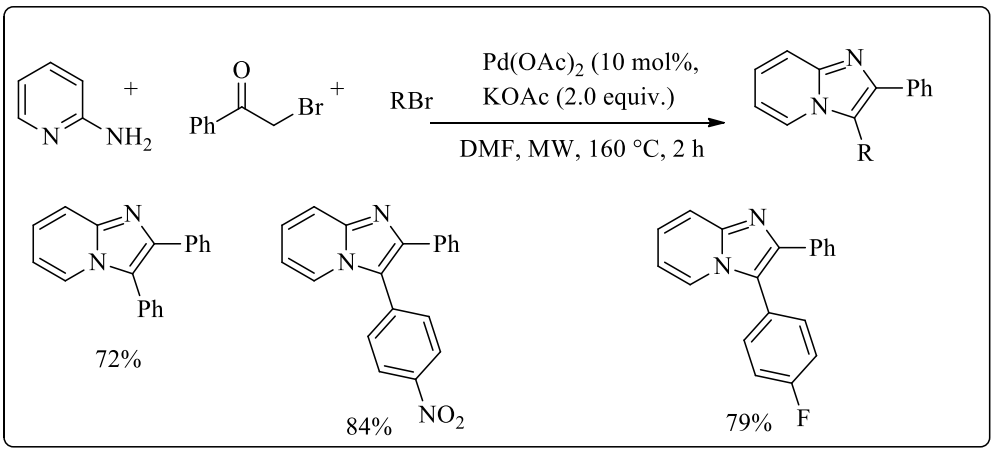
In 2012, Huang and his group revealed a new methodology for the synthesis of 3-methyl-2-arylimidazo[1,2-*a*] pyridines from 2-

aminopyridine and 2-methyl-nitrolefines derivatives using $FeCl_2$ as a catalyst. This methodology facilitates the easy access to the correspond products in good to excellent yields *[18]*.



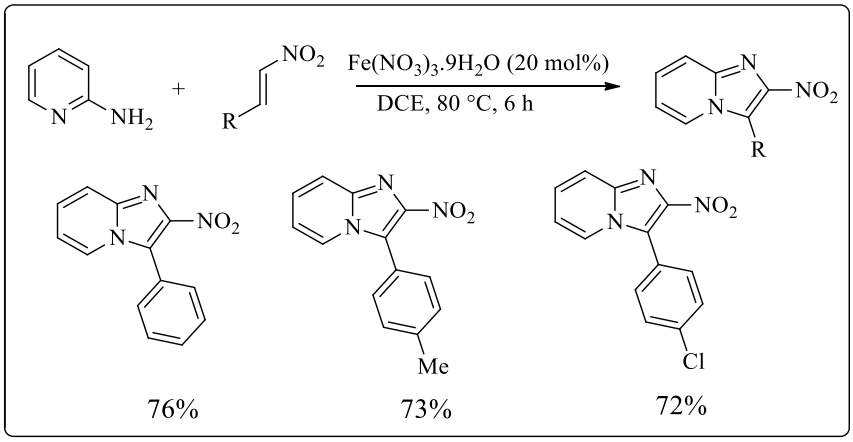
Scheme 3. Synthesis of 3-methyl-2-arylimidazo[1,2-*a*] pyridines under $FeCl_2$ catalyzed system.

In 2014, Li and his colleagues developed the three component synthesis of 2,3-diarylimidazo[1,2-a]pyridines involving 2-aminopyridine, phenacyl bromides and alkylbromides as the starting materials in the presence of Pd $(OAc)_2$ as a catalyst under MW irradiation. All the desired products were obtained in good to moderate yields *[20]*.



Scheme 4. Pd (II) catalyzed three component synthesis of imidazopyridines.

In 2014, Hajra *et al*. reported a regioselective synthesis of imidazo[1,2-*a*] pyridines derivatives using 20 mol% of $Fe(NO_3)_3.9H_2O$ as a catalyst.This reaction involves nitro-alkenes and 2-aminopyridines as simple starting materials *[21]*.

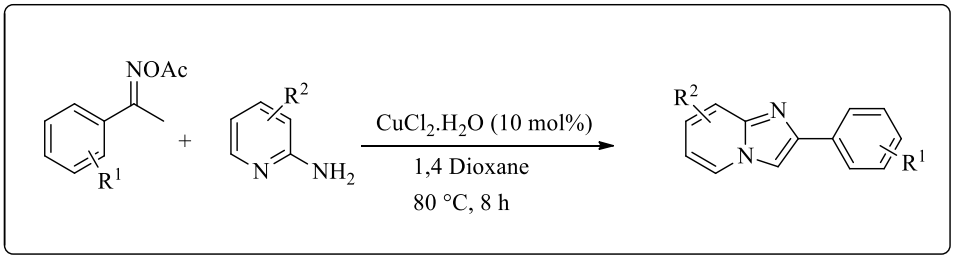


Scheme 5. Fe (II)-catalyzed one pot economy approach to imidazopyridines.

1.3. Aim of the Present Work:

In view of their great significance, the synthesis of bioactive imidazo[1,2-*a*]pyridines (IPs) has gained considerable interest in recent years. In this framework, numerous approaches for the preparation of functionalized IPs have been developed. Although the reported methods are useful to synthesize the title scaffolds they encounter some drawbacks like harsh reaction conditions, expensive metal-salts, high catalyst loading, long reaction times, and low yields of products due to the formation of large amounts of by-products. Because of those intrinsic defects, development of a simple, efficient methodology with broad substrate scope under mild condition is very important.

Herein, we wish to report a new route to imidazo[1,2-*a*]pyridine derivatives via copper-catalyzed annulation reaction of 2-aminopyridines with oxime acetates as shown in Scheme 6.



Scheme 6. Synthesis of imidazo[1,2-*a*]pyridine derivatives.

Chapter-2

Experimental section

2.1. Materials and Instrumentation

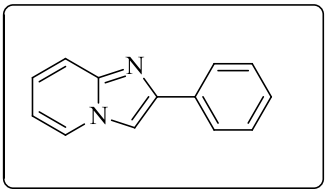
Chemicals were used as received unless otherwise indicated. All reactions were carried out under air and monitored by TLC using Merck 60 F254 pre coated silica gel plate (0.25 mm thickness) and the products were visualized by UV detection. All the oxygen or moisture sensitive reactions were carried out under argon atmosphere. Column chromatography was carried out with silica gel (100-200 mesh). ^{1}H NMR spectra were recorded using a Brukar AV 400 MHz spectrometer. Chemical shifts are reported in delta (δ) units, expressed in parts per million (ppm) downfield from tetramethylsilane (TMS) using residual protonated solvent as an internal standard {$CDCl_3$, 7.26 ppm}. ^{13}C NMR spectra were recorded using a 100 MHz spectrometer. Chemical shifts are reported in delta (δ) units, expressed in parts per million (ppm) downfield from tetramethylsilane (TMS) using the solvent as internal standard {$CDCl_3$, 77.03 ppm}.Multiplicity have been described as “s = singlet; d = doublet; t = triplet and m = multiplet.” The LCMS spectra of the compounds were recorded by using Bruker Daltonics MicroTOF-Q II mass spectrometer using methanol as solvent. Compounds were named by using Chem draw Ultra 11.0.

2.2. General procedure for synthesis of imidazo[1,2-*a*] pyridines:

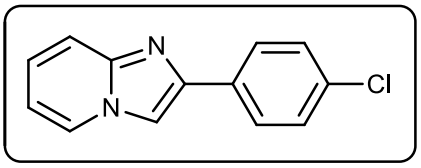
To a solution of 2-aminopyridine (1 mmol) and oxime acetate (1 mmol) in a 5 mL round bottom flask was added $CuCl_2.2H_2O$ (10 mol %) followed by 1 mL 1,4-dioxane. The reaction mixture was heated at 80 °C for 8 h. The progress of reaction was monitored by TLC. After completion of the reaction, 1 mL of water was added to the reaction mixture and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over anhydrous $MgSO_4$, filtered and was concentrated in rotary evaporator under reduced pressure. The crude product was purified by column chromatography over silica gel (100-200 mesh) using 1:4 of mixture of ethyl acetate and hexane to obtain imidazo[1,2-*a*]pyridine.

All the imidazo[1,2-*a*]pyridine derivatives were characterized by corresponding spectroscopic techniques (^{1}H NMR, ^{13}C NMR and LCMS).

2-Phenylimidazo[1,2-*a*]pyridine (3aa) : White solid, yield 82% (159 mg); mp 134-136 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 6.8 Hz, 1H), 7.97 (d, J = 7.2 Hz, 2H), 7.87 (s, 1H), 7.68 (d, J = 9.1 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.34 (t, J = 7. 4 Hz, 1H), 7.17 – 7.23 (m, 1H), 6.81 (t, J = 6.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 145.5, 133.5, 128.7, 128.5, 126.1, 125.6, 124.8, 117.5, 112.6, 108.1 ppm; LC-MS (ESI) m/z calcd for $C_{13}H_{10}N_2$ $[M+Na]^+$ 217.2211, found 217.0864.

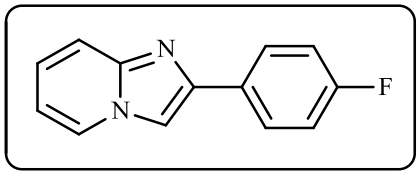


2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridine (3ab): Yellow solid; yield 78% (178 mg); mp 210-212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 4.2 Hz, 1H), 7.83–7.96 (m, 3H), 7.68 (d, J = 8.6 Hz, 1H), 7.41 (d, J = 7.0 Hz, 2H), 7.23 (s, 1H), 6.83 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$)



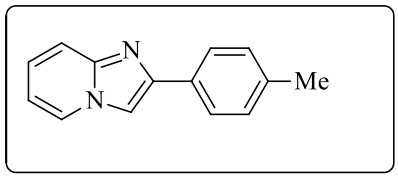
δ 145.6, 144.3, 133.7, 132.1, 128.9, 127.3, 125.6, 125.1, 117.5, 112.7, 108.22 ppm; LC-MS (ESI) m/z calcd for $C_{13}H_9ClN_2$ $[M+Na]^+$ 251.0347, found 251.0489.

2-(4-Fluorophenyl)imidazo[1,2-*a*]pyridine (3ac): Light pink solid; yield



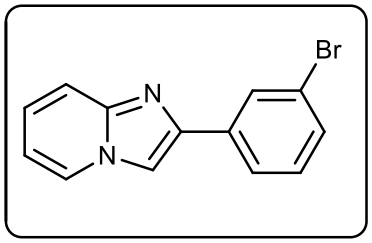
76% (161 mg); mp 175-177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 6.7 Hz, 1H), 7.94 (dd, J = 8.4, 5.5 Hz, 2H), 7.82 (s, 1H), 7.69 (d, J = 9.0 Hz, 1H), 7.19 – 7.25 (m, 1H), 7.13 (t, J = 8.6 Hz, 2H), 6.83 (t, J = 6.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8 (d, J= 249.3 Hz), 145.58, 144.93, 129.9 (d, J= 3 Hz), 127.7 (d, J= 8.1 Hz), 125.59, 124.84, 117.49, 115.7 (d, J= 21.4 Hz), 112.54, 107.80 ppm; LCMS (ESI) m/z calcd for $C_{13}H_{10}FN_2$ $[M+Na]^+$ 235.0642, found 235.0759.

2-(4-Methylphenyl)imidazo[1,2-*a*]pyridine (3ad): White solid, yield



84% (174 mg); mp 145-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 6.6 Hz, 1H), 7.75 – 7.89 (m, 3H), 7.66 (d, J = 9.0 Hz, 1H), 7.24 (s, 2H), 7.18 (t, J = 7.7 Hz, 1H), 6.78 (t, J = 6.5 Hz, 1H), 2.39 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 145.4, 138.0, 130.6, 129.4, 125.9, 125.5, 124.8, 117.3, 112.5, 107.7, 21.3 ppm; LCMS (ESI) m/z calcd for $C_{14}H_{12}N_2$ $[M+H]^+$ 209.1074, found 209.1152.

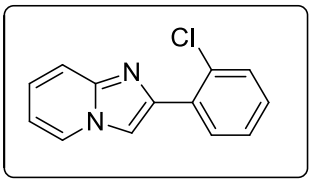
2-(3-Bromophenyl)imidazo[1,2-*a*]pyridine (3ae): yellow solid; yield



80% (217 mg); mp 200-203 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.15 (m, 2H), 7.87 (d, J = 9.2 Hz, 2H), 7.64 (d, J = 9.1 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.30 (t, J = 7.9 Hz, 1H), 7.20 (dd, J = 11.4, 4.4 Hz, 1H), 6.80 (t, J = 6.6 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 144.2, 135.8, 130.8, 130.3, 129.1, 125.7, 125.1, 124.5, 122.9, 117.6, 112.7, 108.5.

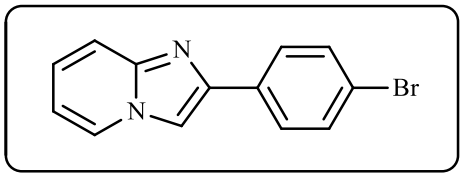
LCMS (ESI) m/z calcd for $C_{13}H_9{}^{79}BrN_2$ $[M+H]^+$ 273.0022, found 273.0039 ; m/z calcd for $C_{13}H_9{}^{81}BrN_2$ $[M+H]^+$ 275.0002, found 275.0019

2-(2-Chlorophenyl)imidazo[1,2-*a*]pyridine (3af): Black Solid; yield



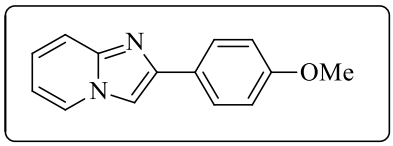
73% (166 mg); mp 198-200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 1.3 Hz, 1H), 8.28 (s, 1H), 8.14 (d, J = 6.8 Hz, 1H), 7.65 (d, J = 9.1 Hz, 1H), 7.47 (d, J = 7.9 Hz, 1H), 7.38 (t, J = 7.2 Hz, 1H), 7.28 (d, J = 1.4 Hz, 1H), 7.16 – 7.25 (m, 1H), 6.79 (t, J = 6.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ- 144.4, 141.7, 132.2, 131.7, 130.9, 130.3, 128.6, 127.1, 125.8, 124.9, 117.5, 112.5, 112.4 ppm; LCMS (ESI) m/z calcd for $C_{13}H_9ClN_2$ $[M+Na]^+$ 251.0347, found 251.0489.

2-(4-Bromophenyl)imidazo[1,2-*a*]pyridine (3ag): White solid; yield



78% (213 mg); mp 211-213 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 6.0 Hz, 1H), 7.87–7.7-(m, 3H), 7.65 (d, J = 8.9 Hz, 1H), 7.55 (d, J = 7.5 Hz, 2H), 7.20 (t, J = 7.3 Hz, 1H), 6.80 (d, J = 5.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$); δ 145.6, 144.4, 132.5, 131.9, 127.6, 125.7, 125.3, 122.1, 117.5, 112.8, 108.3 ppm; LCMS (ESI) m/z calcd for $C_{13}H_9{}^{79}BrN_2$ $[M+H]^+$ 273.0022, found 273.0037; m/z calcd for $C_{13}H_9{}^{81}BrN_2$ $[M+H]^+$ 275.0019, found 275.0026.

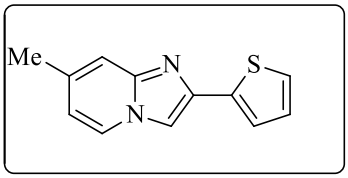
2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyridine (3ah): White solid; yield



85% (190 mg); mp 134-136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.38 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 4.1 Hz, 1H), 7.90 (d, J = 8.7 Hz, 2H), 7.75 (t, J = 7.4 Hz, 1H), 7.03 – 7.09 (m, 1H), 6.99 (d, J = 8.7 Hz, 2H), 3.88 (s, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 162.7, 151.8 147.8, 138.5, 129.2, 126.4, 119.7, 114.1, 114.1, 114.0, 55.51 ppm; LCMS (ESI) m/z calcd for $C_{14}H_{12}N_2O$ $[M+H]^+$ 225.1023, found 225.1004.

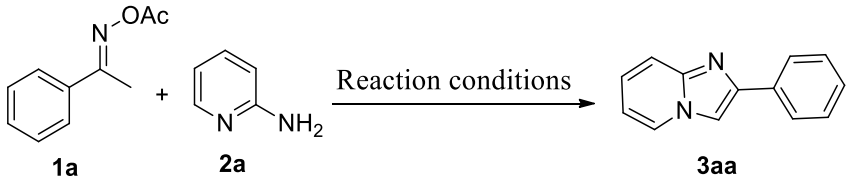
7-Methyl-2-(thiophen-2-yl)imidazo[1,2-*a*]pyridine (3ai): Light yellow solid; yield 78% (166 mg); mp 140-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 6.4 Hz, 1H), 7.69 (s, 1H), 7.49 (d, *J* = 2.1 Hz, 1H), 7.39 (s, 1H), 7.29 (d, *J* = 5.0 Hz, 1H), 7.08 (dd, *J* = 4.6, 3.5 Hz, 1H), 6.59 (d, *J* = 6.8 Hz, 1H), 2.39 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 140.3, 137.3, 136.2, 127.7, 124.9. 124.6, 123.7, 115.6, 115.4, 106.9, 21.4 ppm; LCMS (ESI) m/z calcd for $C_{12}H_{10}N_2S$ $[M+H]^+$ 215.0408, found 215.0324.



CHAPTER 3

Results and Discussion:

Table: 1 Optimization of reaction at different conditions[a,b]



Entry	**Solvent**	**Catalyst (10 mol%)**	**Temp (°C)**	**Time (h)**	**Yield (%)[b]**
1	Toluene	$CuBr_2$	80	8	35
2	Toluene	$Cu(OAc)_2.H_2O$	80	8	62
3	Toluene	$Cu(OTf)_2$	80	8	15
4	Toluene	CuBr	80	8	26
5	Toluene	$CuCl_2.2H_2O$	80	8	72
6	THF	$CuCl_2.2H_2O$	25	8	0
7	THF	$CuCl_2.2H_2O$	50	8	25
8	THF	$CuCl_2.2H_2O$	60	8	50
9	THF	$CuCl_2.2H_2O$	80	8	70
10	1,4-Dioxane	$CuCl_2.2H_2O$	25	8	0
11	1,4-Dioxane	$CuCl_2.2H_2O$	50	8	40
12	**1,4-Dioxane**	**$CuCl_2.2H_2O$**	**80**	**8**	**82**
13	1,4-Dioxane	$CuCl_2.2H_2O$	100	8	70
14	Acetonitrile	$CuCl_2.2H_2O$	80	8	45

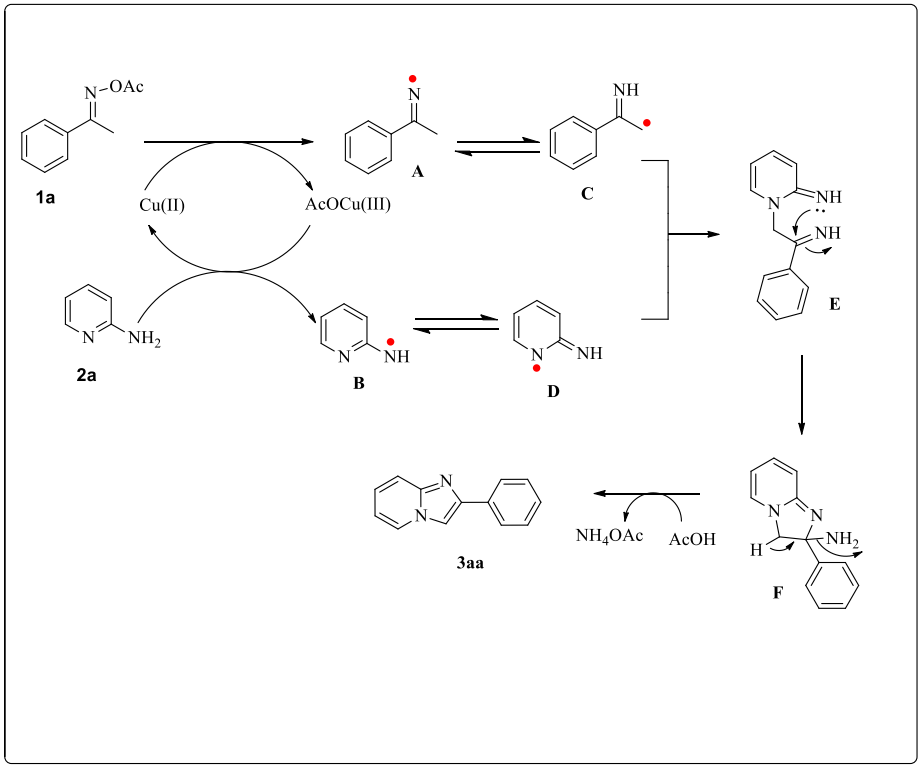
[a]All the reactions were carried out with **1a** (1 mmol), **2a** (1 mmol) and catalyst (10 mol%) in solvent (1 mL) for 8 h.

[b]Isolated yield after column chromatography.

Our investigation was commenced by stirring the (*E*) acetophenone O-acetyl oxime (**1a**) and 2-aminopyridine (**2a**) at 80 °C in the presence of toluene using 10 mol% of $CuBr_2$ as a catalyst. After 8 h, we isolated 2-phenylimidazo[1,2-*a*]pyridine (**3aa**) as our desired product in 35% yield. (entry 1). To improve the yield of the product (**3aa**) several other copper salts like $Cu(OAc)_2.H_2O$, CuBr, $Cu(OTf)_2$, $CuCl_2.2H_2O$ were examined for this reaction. Among these salts, $CuCl_2.2H_2O$ enhances the result (yield 72%) (entry 5). After selection of the best catalyst, next we proceeded further to optimize the reaction in different solvents like THF, 1,4-dioxane, ACN in the presence of $CuCl_2.2H_2O$ as catalyst. After screening the various catalysts and solvents, we can conclude that combination of $CuCl_2.2H_2O$ as a catalyst and 1,4-dioxane as a solvent found to be best reaction condition for the synthesis of desired scaffold in 82% yield (entry 12). The reaction was unsuccessful at room temperature (entry 10).

3.1. Plausible Reaction Mechanism

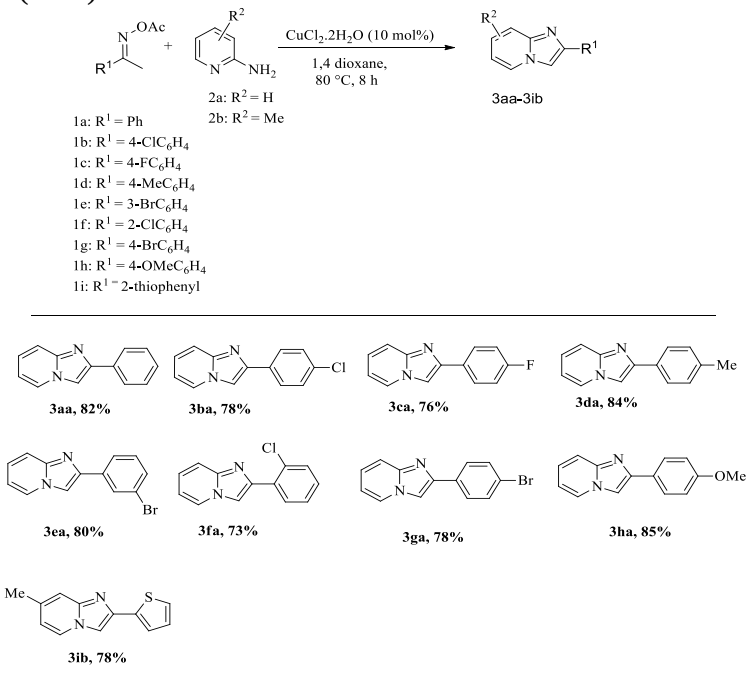
A plausible reaction mechanism is outlined in scheme 7. Initially, iminium radical **A** was generated by oxidation of Cu (II) to AcOCu (III), and this radical was rapidly tautomerized to **C**. Radical **B** was then formed via a single-electron-transfer (SET) process between AcOCu (III) and , releasing AcOH and regenerating the Cu (II) species back to the catalytic cycle. Then **B** underwent tautomerization to give **D** and subsequently, the intermediate product **E** was produced by the radical coupling reaction of **C** and **D**. **E** undergoes intramolecular cyclization to give cyclized product **F**, followed by elimination of ammonium acetate to afford the desired product imidazo[1,2-*a*]pyridine (**3aa**).



Scheme 7. Plausible mechanism of the reaction

3.2. Substrate scope and generality of reaction condition:

After successfully developing a simple one pot synthesis of **3aa**, we examined the generality and scope of this annulation process by reacting several kinds of oxime acetates and 2-aminopyridines to prepare a group of imidazo[1,2-*a*]pyridines as shown in scheme-8. Both electron rich (OMe, Me) and electron withdrawing halogen atoms (F, Cl, Br) on the aryl ring of oxime acetate underwent spotless reaction with 2-aminopyridine in the present catalytic system to afford the corresponding imidazo[1,2-*a*]pyridine derivatives in excellent yields (73-85%). It should be noted that electron withdrawing halogen atoms provided slightly lower yields as compared to electron donating substituents. Interestingly, this method is also equally applicable for heterocycle-substituted oxime acetate. For example, the compound **2b** reacted smoothly with **1i** to produce the corresponding thiophenyl-substituted imidazopyridine **3ib** (78%).



Scheme 8. List of derivatives of imidazo[1,2-*a*]pyridines.

Chapter 4

Conclusion

In this work, we have successfully synthesized an array of pharmaceutically important imidazo[1,2-*a*]pyridines scaffolds via annulation of oxime acetates and 2-aminopyridines in the presence of $CuCl_2.2H_2O$ catalyst. In addition this methodology delivers aforementioned compounds in excellent yields with the use of easily commercially available starting materials under mild conditions. Various functional groups of oxime acetates and aminopyridines can be tolerated under our established conditions.

APPENDIX A

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

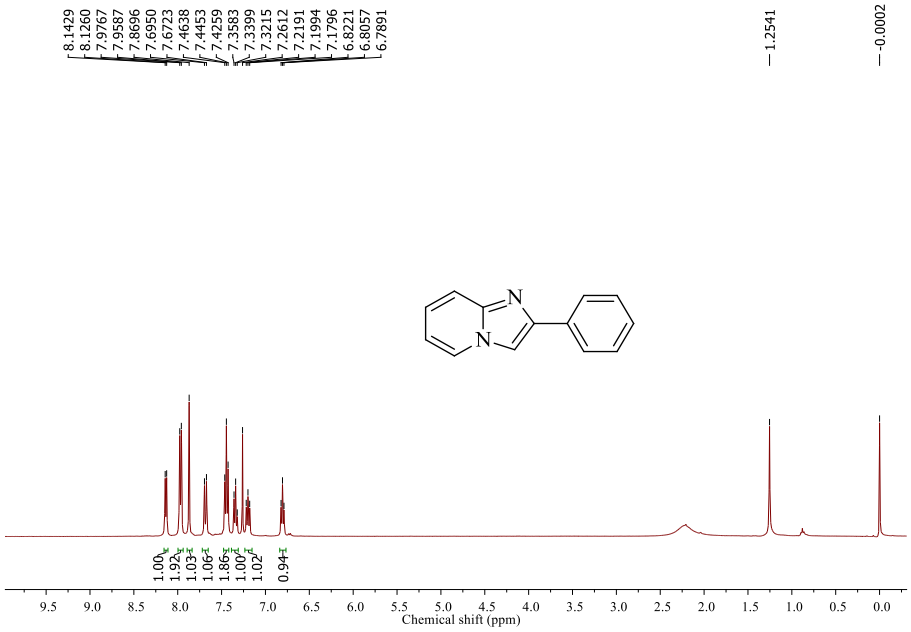


Figure 3. 400 MHz ^{1}H-NMR of **3aa** in $CDCl_3$

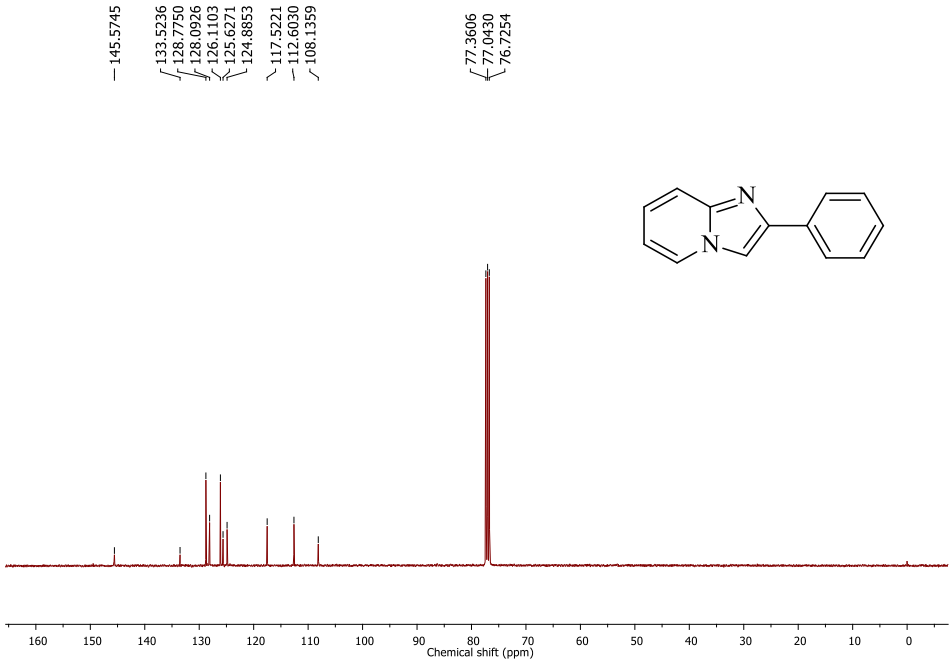


Figure 4. 100 MHz ^{13}C-NMR of **3aa** in $CDCl_3$

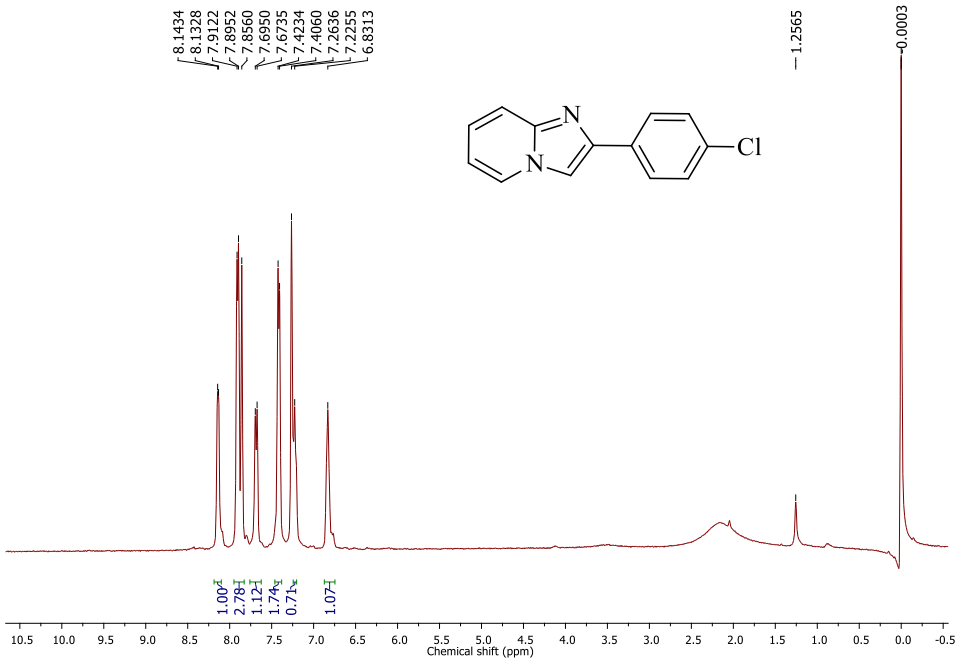


Figure 5. 400 MHz ^{1}H-NMR of **3ba** in $CDCl_3$

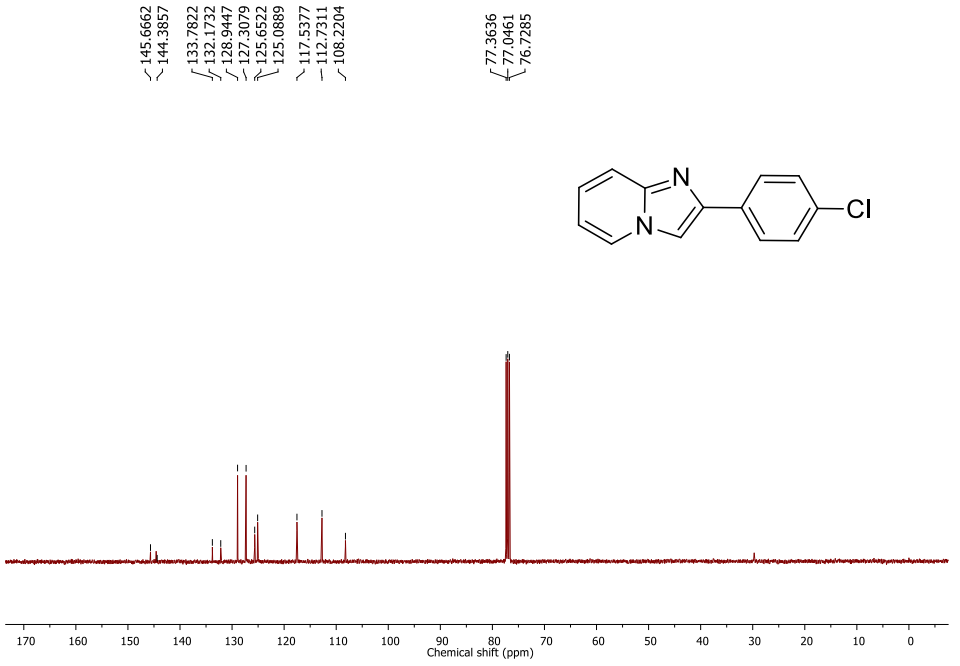


Figure 6. 100 MHz ^{13}C-NMR of **3ba** in $CDCl_3$.

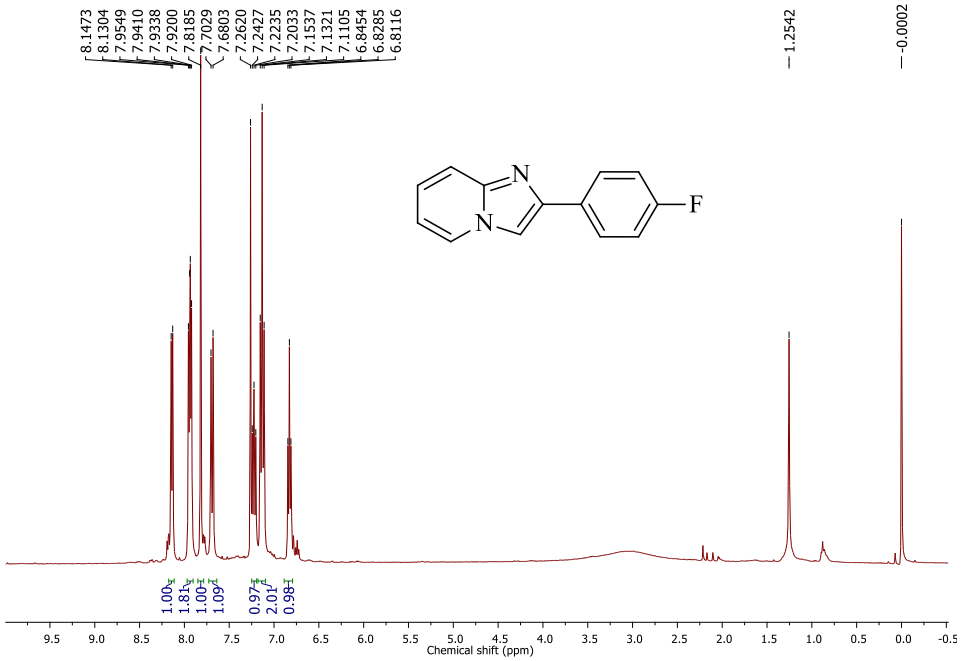


Figure 7. 400 MHz ^{1}H-NMR of **3ca** in $CDCl_3$

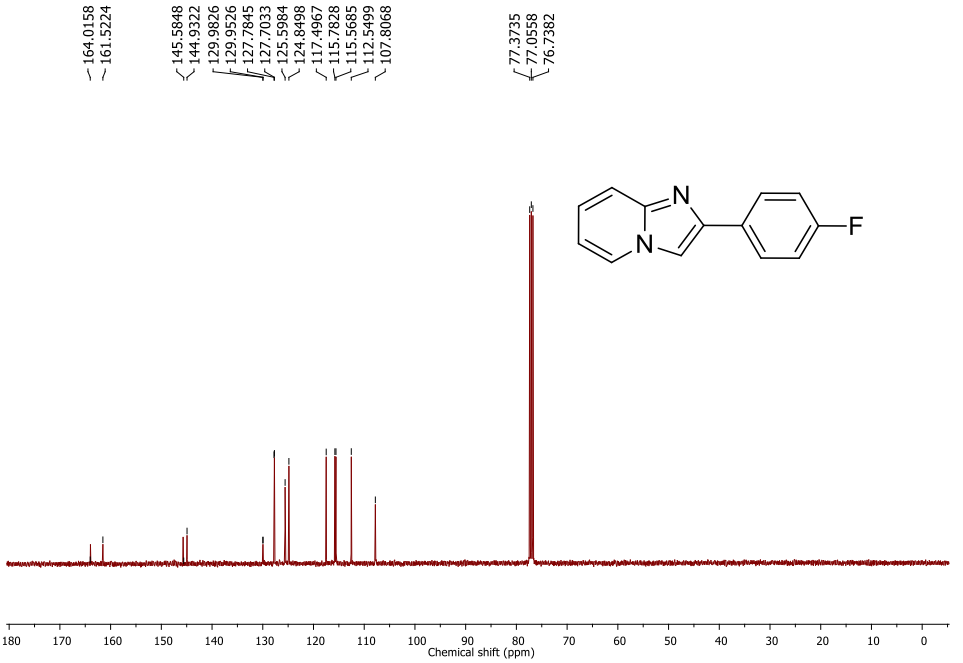


Figure 8. 100 MHz ^{13}C-NMR of **3ca** in $CDCl_3$

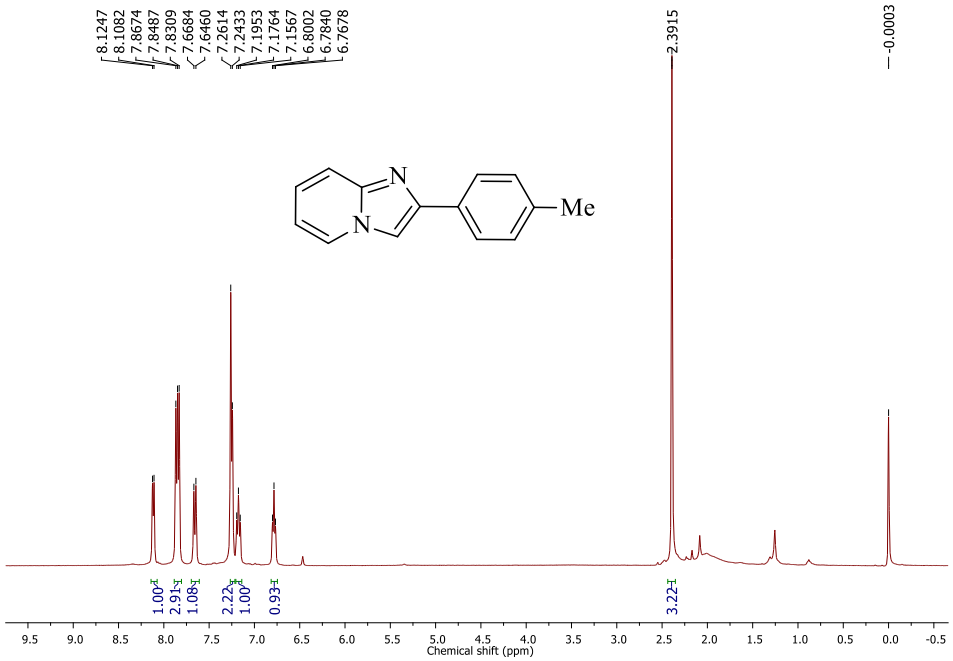


Figure 11. 400 MHz H-NMR of **3da** in $CDCl_3$.

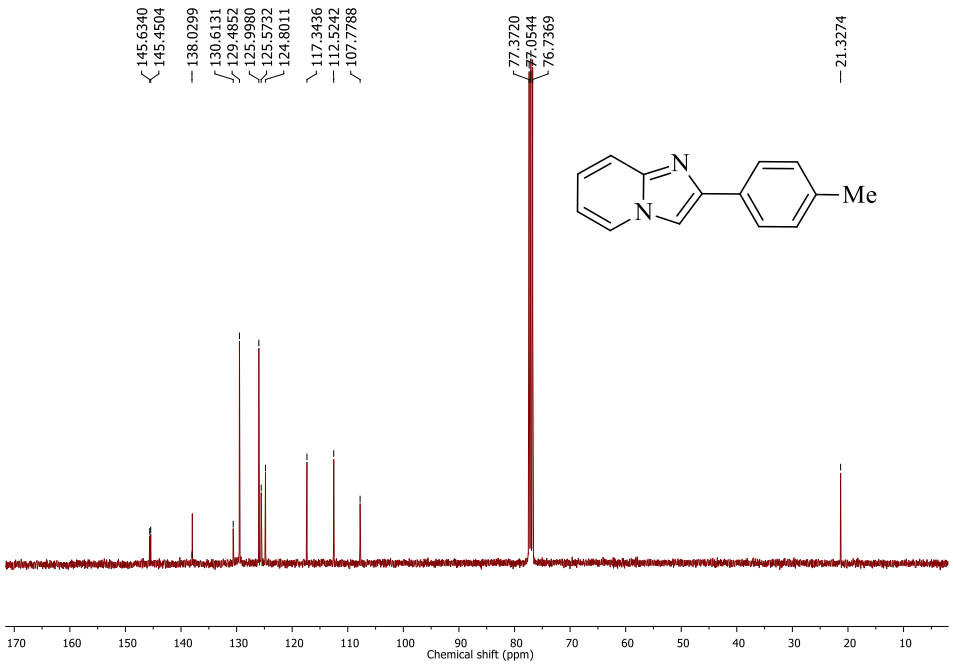


Figure 12. 100 MHz ^{13}C-NMR of **3da** in $CDCl_3$.

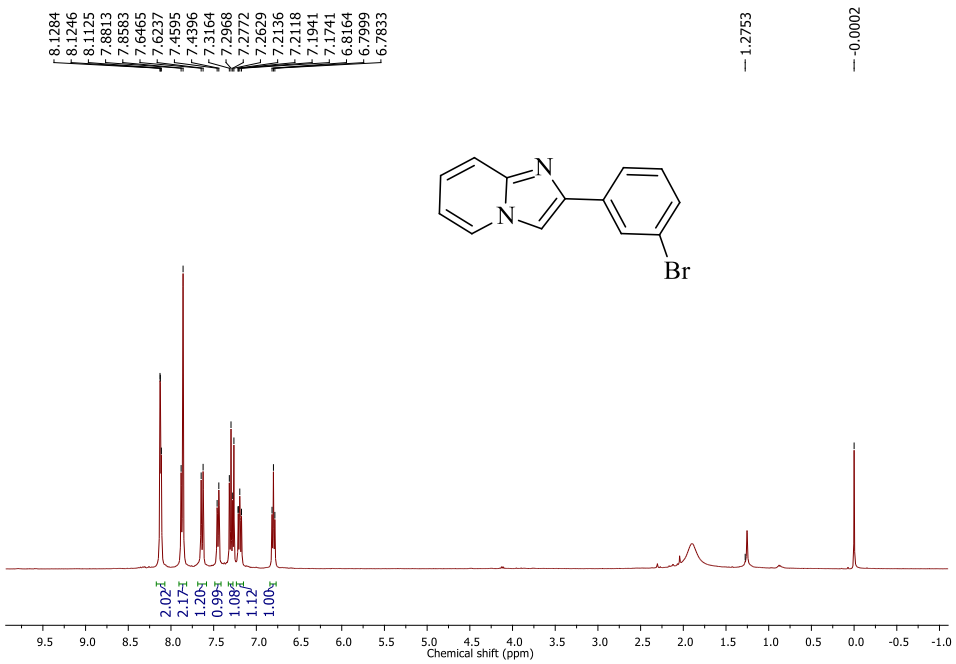


Figure 13. 400 MHz ^{1}H-NMR of **3ea** in $CDCl_3$.

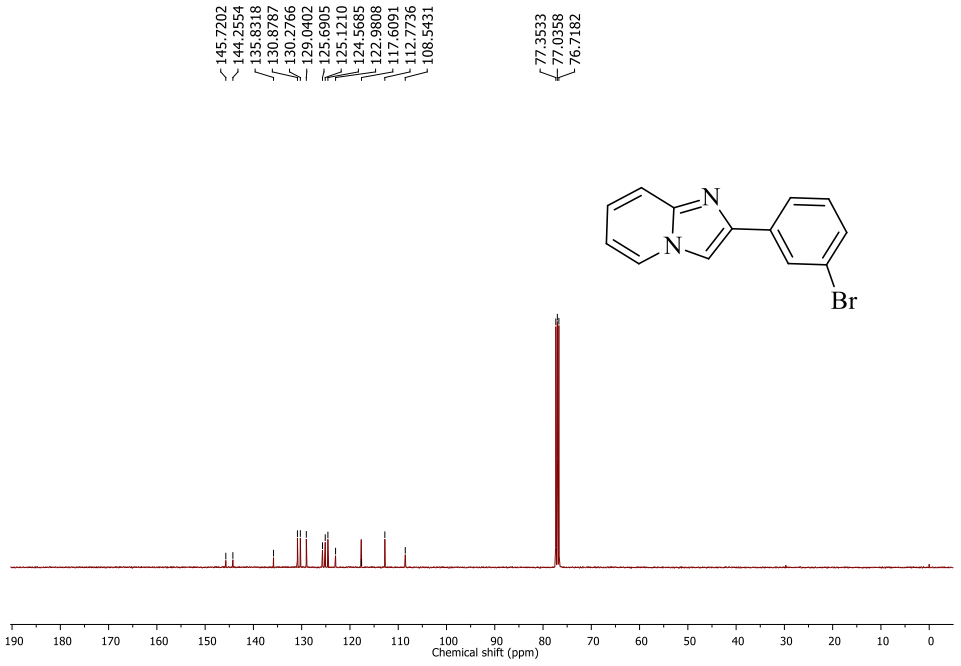


Figure 14. 100 MHz ^{13}C-NMR of **3ea** in $CDCl_3$.

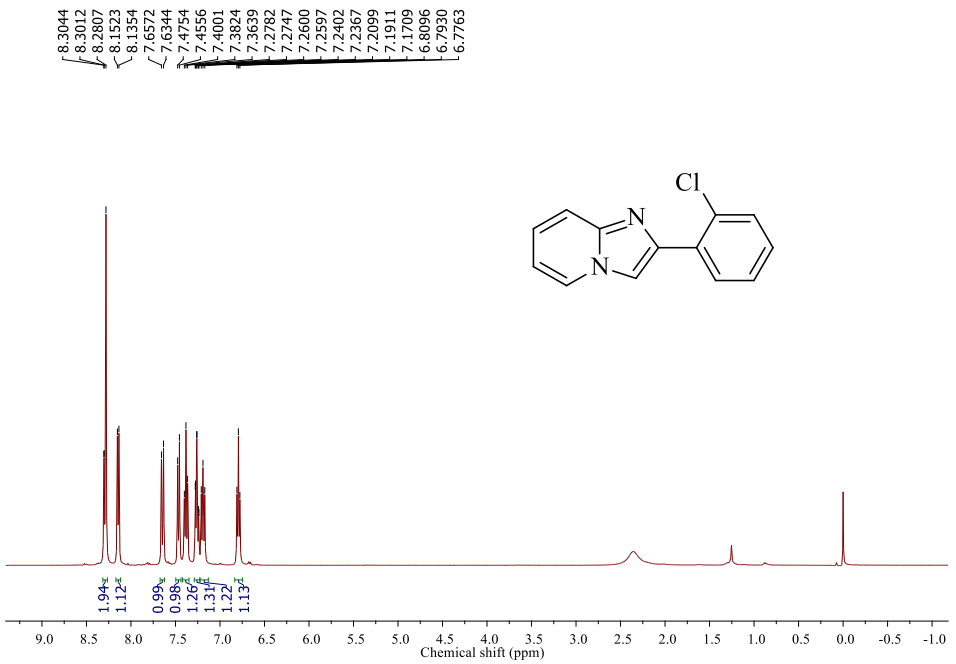


Figure 15. 400 MHz ^{1}H-NMR of **3fa** in $CDCl_3$

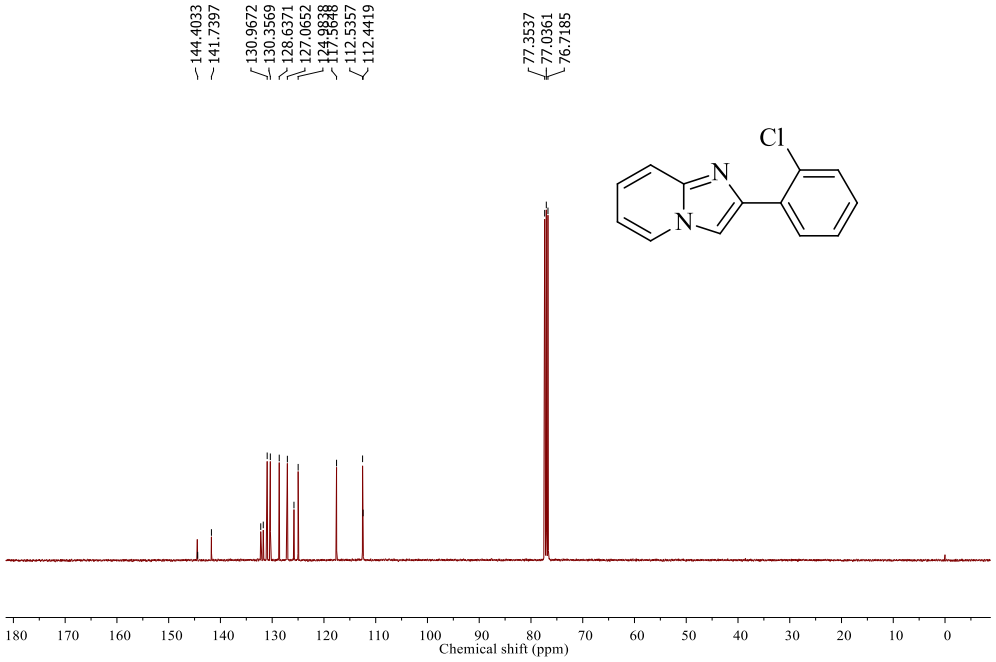


Figure 16. 100 MHz ^{13}C-NMR of **3fa** in $CDCl_3$

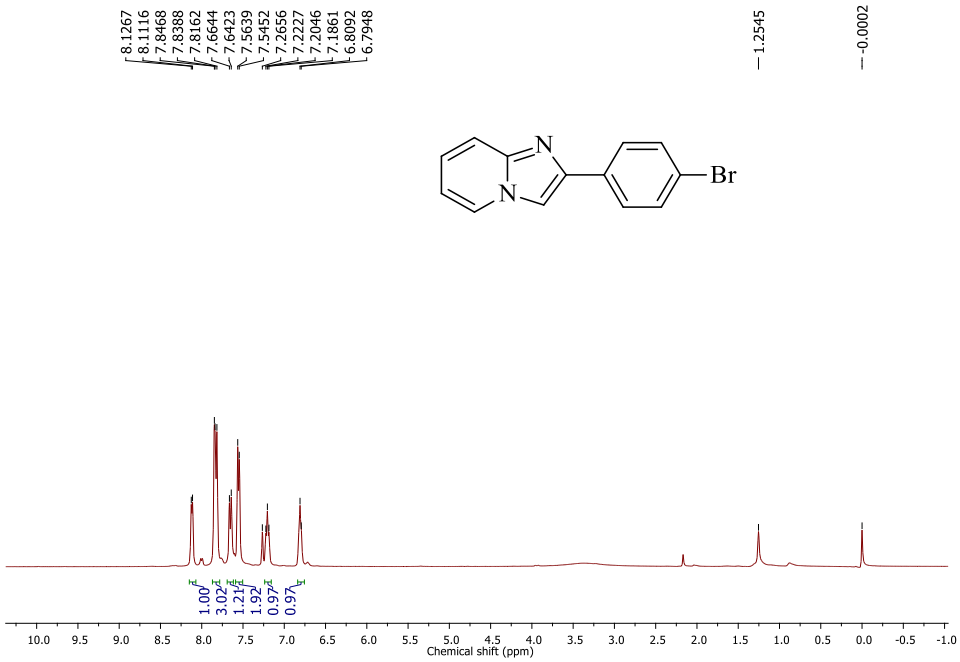


Figure 17. 400 MHz ^{1}H-NMR of **3ga** in $CDCl_3$

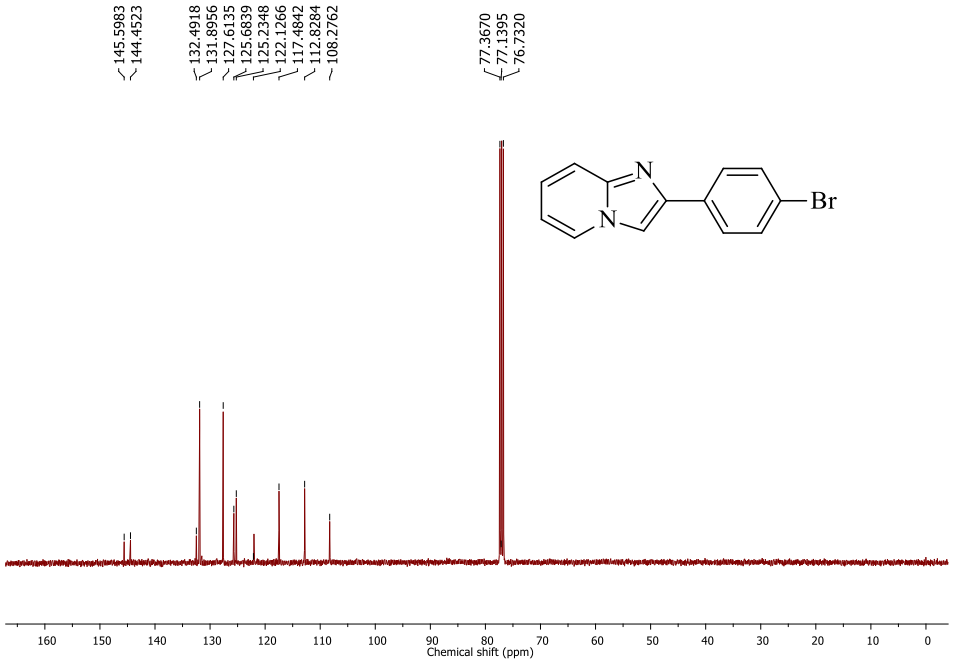


Figure 18. 100 MHz ^{13}C-NMR of **3ga** in $CDCl_3$

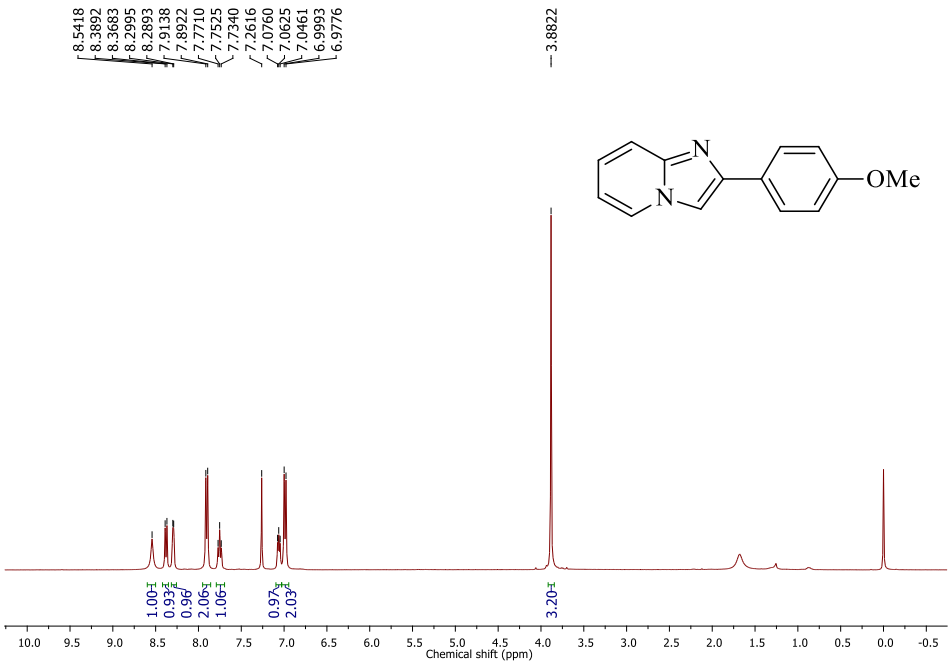


Figure 19. 400 MHz ^{1}H-NMR of **3ha** in $CDCl_3$

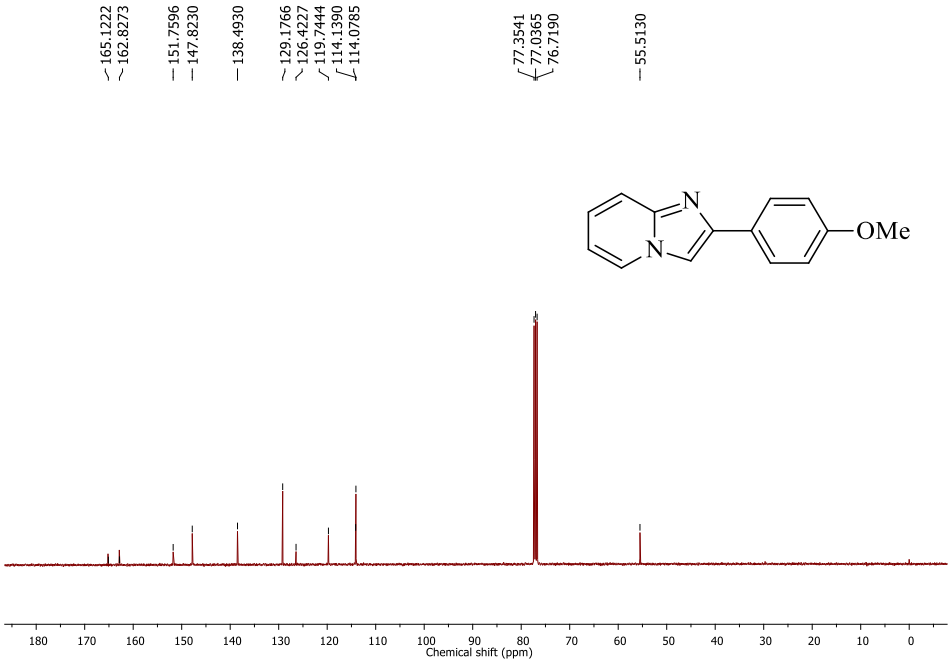


Figure 20. 100 MHz ^{13}C-NMR of **3ha** in $CDCl_3$

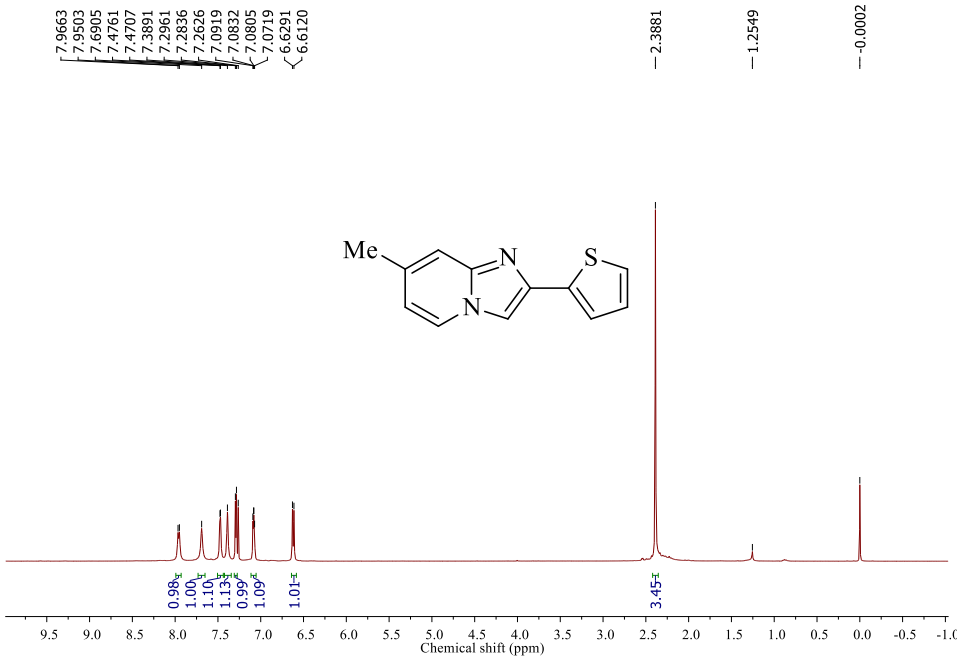


Figure 21. 400 MHz ^{1}H-NMR of **3ib** in $CDCl_3$

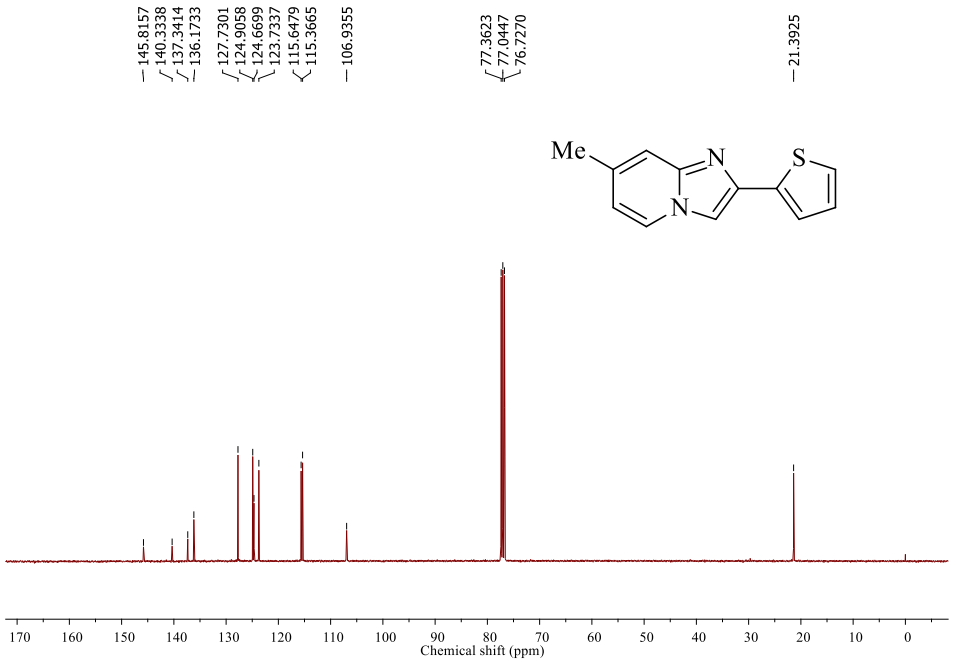


Figure 22. 100 MHz ^{13}C-NMR of **3ib** in $CDCl_3$

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