

Investigation on Metal and Halogen Dependent Cyclization of Schiff base or Reduced Schiff base Precursor into Fluorescent Pyrido[1,2-a]quinoxalin-11-ylum Derivatives

*A
Thesis Submitted
In Partial Fulfillment of the Requirement
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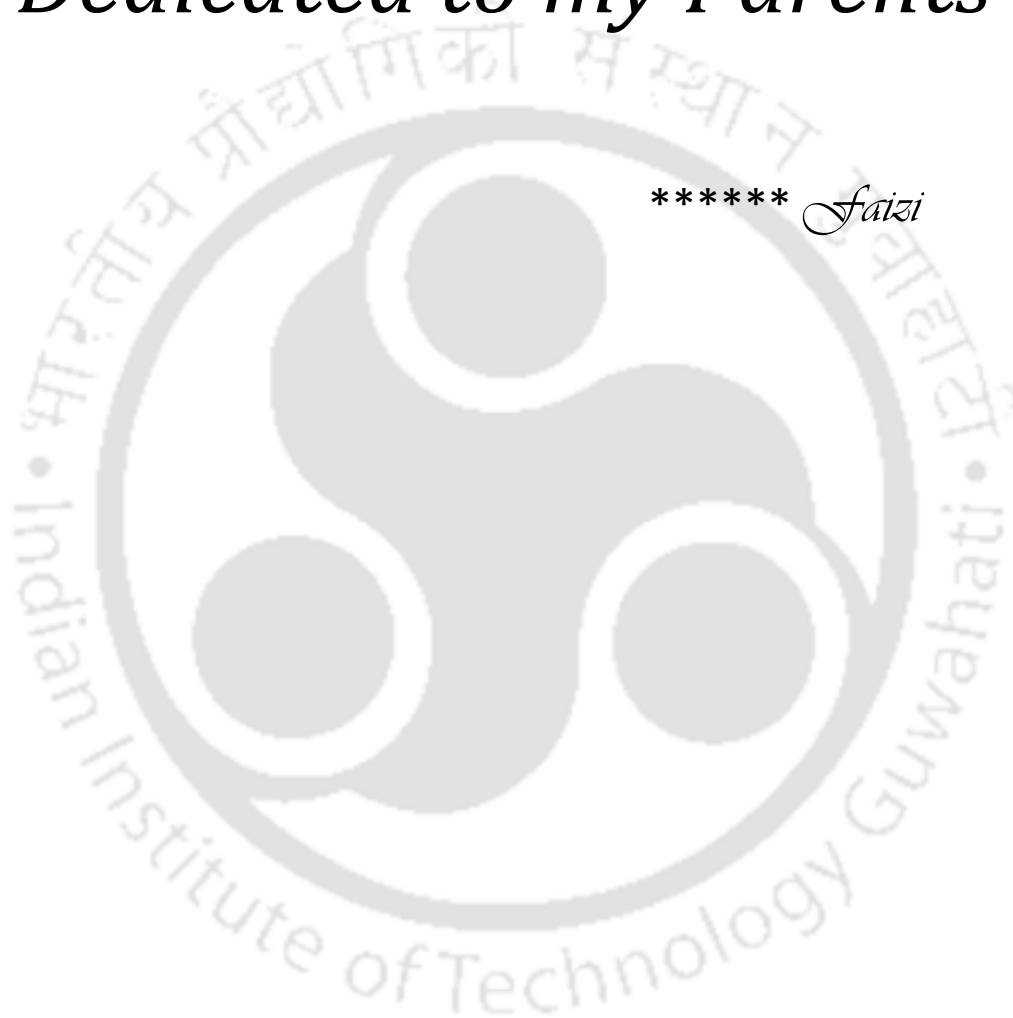
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Dedicated to my Parents

***** *Faizi*





STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology Guwahati, India under the supervision of Prof. Manabendra Ray, Professor, Department of Chemistry, Indian Institute of Technology Guwahati, India.

In keeping with the general practice of reporting observations, due acknowledgements have been made wherever the work described is based on the findings of other investigations.

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CERTIFICATE

This is to certify that Mr. Md. Serajul Haque Faizi has been working under my supervision since July 2007. I am forwarding his thesis, entitled, “**Investigation on metal and halogen dependent cyclization of Schiff base or reduced Schiff base precursor into fluorescent pyrido[1,2-a]quinoxalin-11-ylum derivatives**” being submitted for the degree of Doctorate of Philosophy of this Institute. I certify that he has fulfilled all the requirements according to the rules of this Institute, and that the investigations embodied in this thesis have not been submitted elsewhere for a degree.

October - 2012
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Prof. Manabendra Ray
Supervisor

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Md. Serajul Haque Faizi

Abstract

Quinoxalines are an important class of heterocyclic compounds used as dyes, pharmaceuticals and the moiety is present in a number of antibiotics.¹ Previously, the synthesis of a new tricyclic quinoxaline derivative, pyrido[1,2-*a*]quinoxalin-11-ylum perchlorate [**P**¹] ClO_4 , formed by Cu(II) mediated cyclization of a simple Schiff base precursor was published by *Koner and Ray*.² Structurally, only three other tricyclic heterocycles with similar structure are known (Figure 1). The 3-5 benzo[*e*]pyrido[2,1-*c*][1,2,4]triazin-11-ium (**I**) salts reported by *Goswami et al.* are highly fluorescent and shows strong binding with calf thymus DNA.³ *Goswami and Adak* reported synthesis of cyclic pyrido[1,2-*a*]quinoxaline phosphate (**II**) by phosphorylation of the quinoxaline derivative of sugar precursor with $(\text{PhO})\text{P}(\text{O})\text{Cl}_2$.⁴ Pyrido[1,2-*a*]quinoxalinium ions (**III**) reported by *Chernavskaya et al.*⁵ and structurally characterized by *Duffy et al.*⁶ showed antimicrobial activity as well as pH sensitive fluorescence. None of these syntheses involves metal ion and syntheses were not trivial.

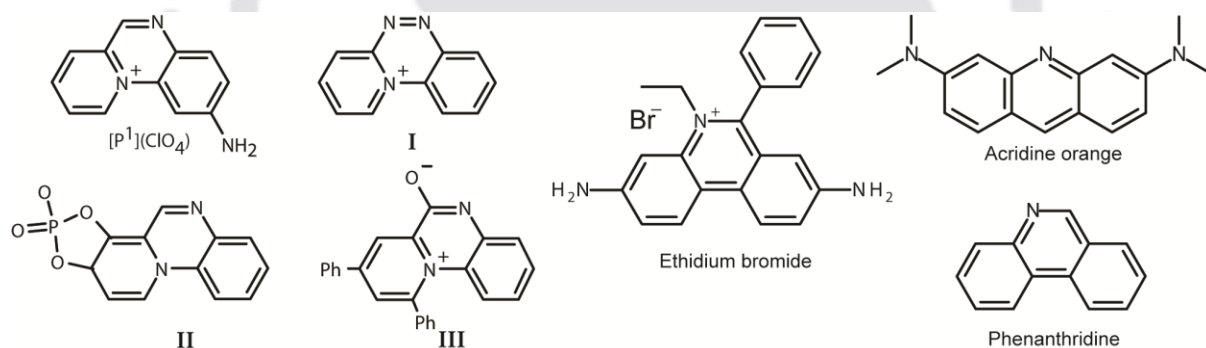


Figure 1. Reported structures of tricyclic heterocycles and fluorescent dyes

Compound [**P**¹] ClO_4 as well as **I** are fluorescent with emission in the highly useful region (550 to 600 nm) with reasonable quantum yield(Φ) approximately 0.2. The water solubility, emission properties, planarity and charged nature of the compound are comparable with popular

¹ Brown, D. J.; Taylor, E. C.; Wipf, P. *The Chemistry of Heterocyclic Compounds: Quinoxalines*; Wiley: New York, 2004; Vol. 61, Supplement II.

² Koner, R. R.; Ray, M. *Inorg. Chem.* **2008**, 47, 9122

³ (a) Sinan, M.; Panda, M.; Ghosh, A.; Dhara, K.; Fanwick, P. E.; Chattopadhyay, D. J.; Goswami, S. *J. Am. Chem. Soc.* **2008**, 130, 5185. (b) Sinan, M.; Ghosh, K.; Goswami, S. *J. Org. Chem.* **2010**, 75, 2065.

⁴ Goswami, S.; Adak, A. K. *Chem. Lett.* **2003**, 32, 678.

⁵ Chernavskaya, L. N.; Kholodova, N. V.; Blagorodov, S. G.; Dmitrieva, N. A. *Pharm. Chem. J.*, **1984**, 18, 413.

⁶ Duffy, K. J.; Haltiwanger, R. C.; Freyer, A. J.; Li, F.; Luengo, J. I.; Cheng, Y. H. *J. Chem. Soc., Perkin Trans 2*. **2002**, 181

fluorescent dyes including cationic dyes known for their DNA intercalation properties such as acridine orange, ethidium bromide and phenanthridine.⁷

Koner and Ray had proposed that the formation of $[P^1](ClO_4)$ was a result of oxidation of the Schiff base precursor at the expense of reduction of Cu(II), forming a cationic radical intermediate which underwent cyclization. Ligand oxidation due to metal reduction has been of current interest and recently *Reedijk et al.* reported⁸ the synthesis of a leuco-verdazyl ring as a result of Mn(III) reduction. Thus considering the newness of the molecule, the potential use of pyrido[1,2-*a*]quinoxalium derivatives as fluorescent heterocyclic dyes and the recent development of metal-mediated cyclization providing a new type of heterocyclic compounds, we had decided to investigate the chemistry of *Koner and Ray* further centered on three aspects: (i) whether the cyclization can be extended to other than imines (ii) finding the factors that determine the choice of metal ions and (iii) finding the role of metal ion in the reaction. This thesis contains the results of our investigation on these aspects.

The thesis has been divided into six chapters. Brief synopsis of each chapter has been provided below:

Chapter 1. This chapter summarizes the literature on the synthesis of quinoxalines with emphasis on cyclization including reactions involving metal ions and the known chemistry of the Schiff bases used in this thesis. Based on this information, the objectives of the thesis have been defined.

Chapter 2. In the proposed reaction mechanism, *Koner and Ray* suggested initial formation of a short lived cation radical on the precursor at the expense of reduction of metal ion. If this is correct then reduction of imine should make the reduced Schiff base precursor more vulnerable to oxidation. To address this, in this chapter, we have reported the synthesis and characterization of four new precursors (L^2 to L^5 , Scheme 1) and their cyclization products. Two metal complexes with L^2 were also synthesized to understand the initial binding of precursors to the metal ions. Some of the precursors, the cyclized products except $[P^5]^+$ and metal complexes were

⁷ Williams, A. T. R.; Winfield, S. A.; Miller, J. N. *Analyst*, **1983**, 108, 1067.

⁸ Tang, J.; Nayak, S.; Costa, J. S.; Robertazzi, A.; Pievo, R.; Mutikainen, I.; Roubeau, O.; Teat, S. J.; Gamez, P.; Reedijk J. *Dalton Trans.* **2010**, 39, 1361.

structurally characterized. For all of the organic compounds, ^1H NMR spectroscopic data and ESI-mass spectroscopic data in methanol were reported.

The results presented in this chapter showed increasing the number of amines at the expense of imines that the precursors cyclizes preferably with $\text{Fe}(\text{NO}_3)_3$. In fact, L^3 with a bis-amine unit cyclizes with $\text{Fe}(\text{III})$, but form complexes with $\text{Cu}(\text{II})$. Characterization of two metal complexes with L^2 supports that binding of metal ion perhaps the first step in the reaction. As the oxidation of L^2 , necessary for the cyclization, occurs at the expense of reduction of metal ion, it does not occur with either $\text{Co}(\text{II})$ or $\text{Mn}(\text{II})$. The cyclized products $[\text{HP}^3]^{2+}$ and $[\text{P}^5]^+$ are fluorescent.

Chapter 3. In the previous chapter we observed that Schiff bases as well as reduced Schiff bases of *p*-phenylenediamine undergo a cyclization reaction forming quinoxalinium type heterocyclic compounds in presence of metal salts. We surmized that similar cyclizations might be possible by aromatic rings other than *p*-phenylenediamine provided that the ring is as easily oxidizable as *p*-phenylenediamine. We found that redox potential of *p*-aminophenol ($E^0 +0.76$ V vs NHE) is closer to that of *p*-phenylenediamine ($E^0 +0.59$ V vs NHE) than either aniline ($E^0 +1.02$ vs NHE) or halogen derived anilines ($E^0 +1.01$ to 1.04 vs NHE for *p*-chloro to iodo substitution).⁹ Thus in this chapter we chose *p*-aminophenol and *p*-methoxyaniline to form Schiff bases with pyridine-2-carboxaldehyde and performed their cyclization reactions (Scheme 2).

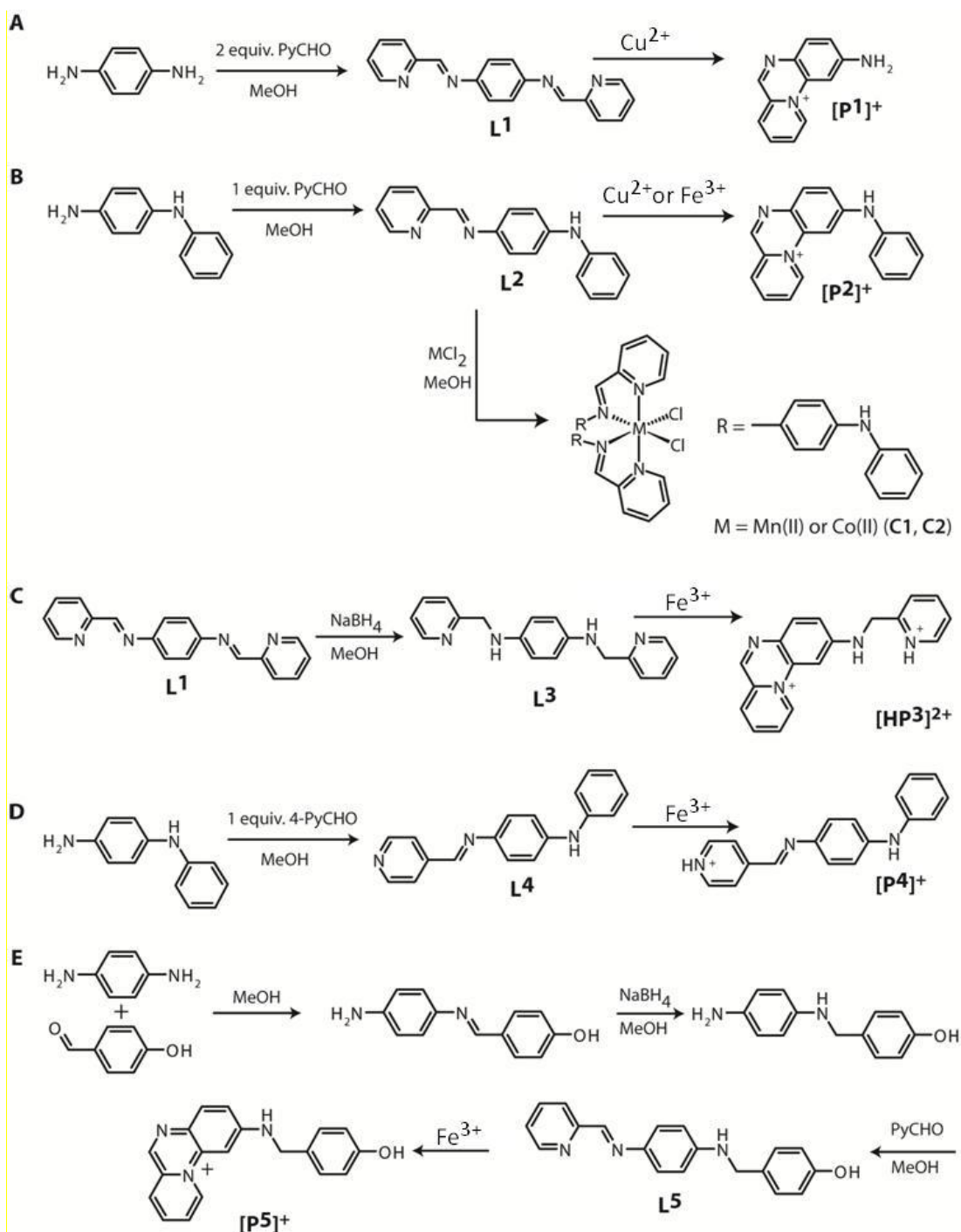
On Substitution of an amino group to a hydroxyl group, the cyclization process occurs similarly to L^2 described in the previous chapter (Scheme 1). The cyclization occurs with $\text{Fe}(\text{III})$ for L^6 . However, L^7 required a stronger oxidizer, bromine (Redox potential¹⁰ of $\text{Br}_2/2\text{Br}^-$ at 1.08 V vs NHE is higher than $\text{Fe}^{3+}/\text{Fe}^{2+}$ at $+0.771$ vs NHE). Using bromine as the oxidant with L^6 , results in the formation of a number of compounds where bromination of the ring also occurs.

Chapter 4. In the previous chapter we had observed that bromine can be used for cyclization. In this chapter we investigated the effect of bromine on the cyclization reactions of L^1 - L^3 and L^5 . Additionally, we used iodine as an oxidizing reagent ($E^0 +0.53$ V vs NHE) on L^3 as it is likely to be most vulnerable to oxidation as observed in Chapter 2. Cyclization did occur with bromine but the reactions are far from clean. Isolation and purification proved to be difficult as number of

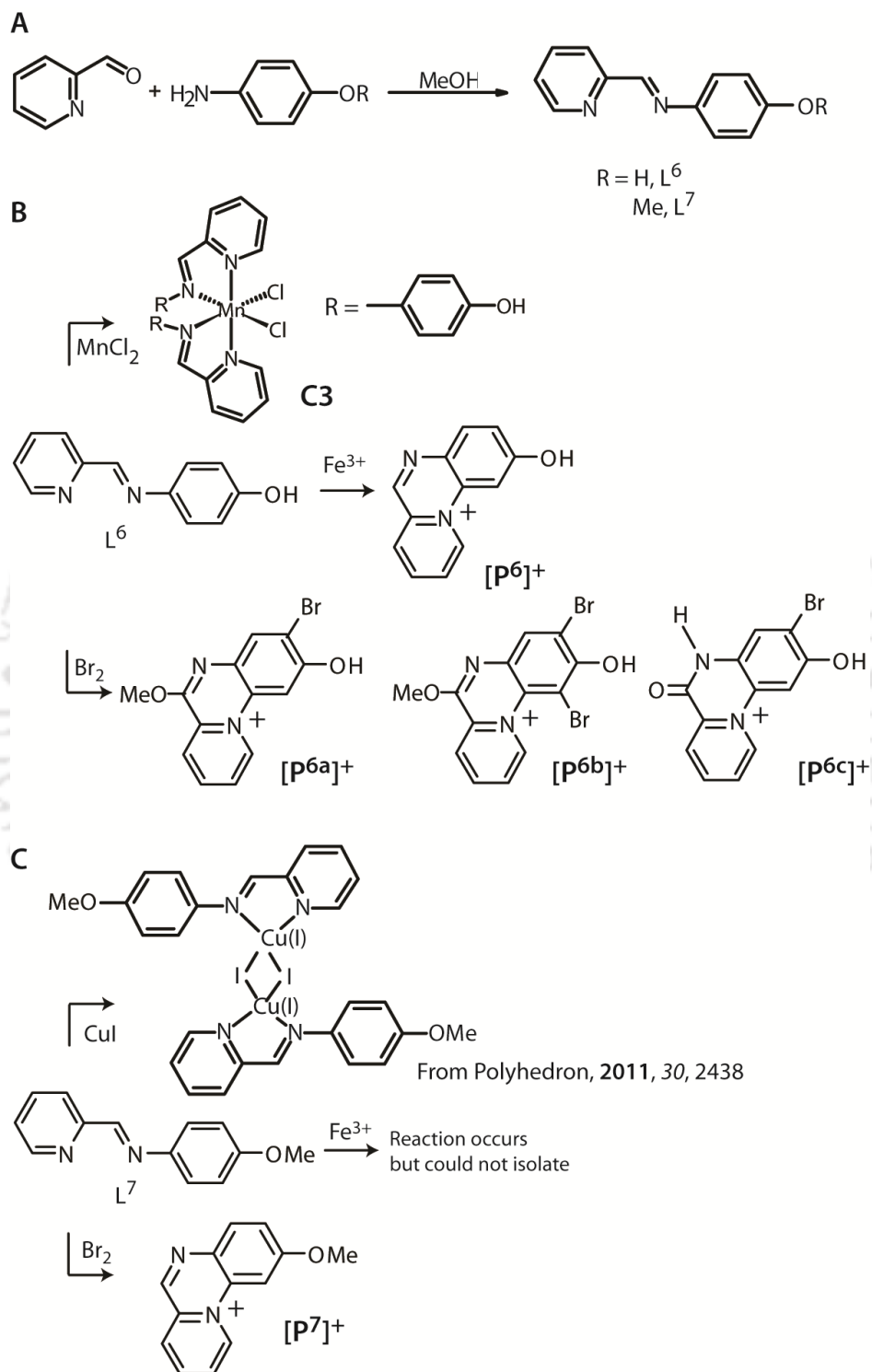
⁹ Jonsson, M.; Lind, J.; Eriksen, T. E., and Merényi, G. *J. Am. Chem. Soc.*, **1994**, *116*, 1423.

¹⁰ Electrochemical Methods; Fundamentals and applications, A. J. Bard & L. R. Faulkner, 2nd edition, Wiley, **2004**, 808.

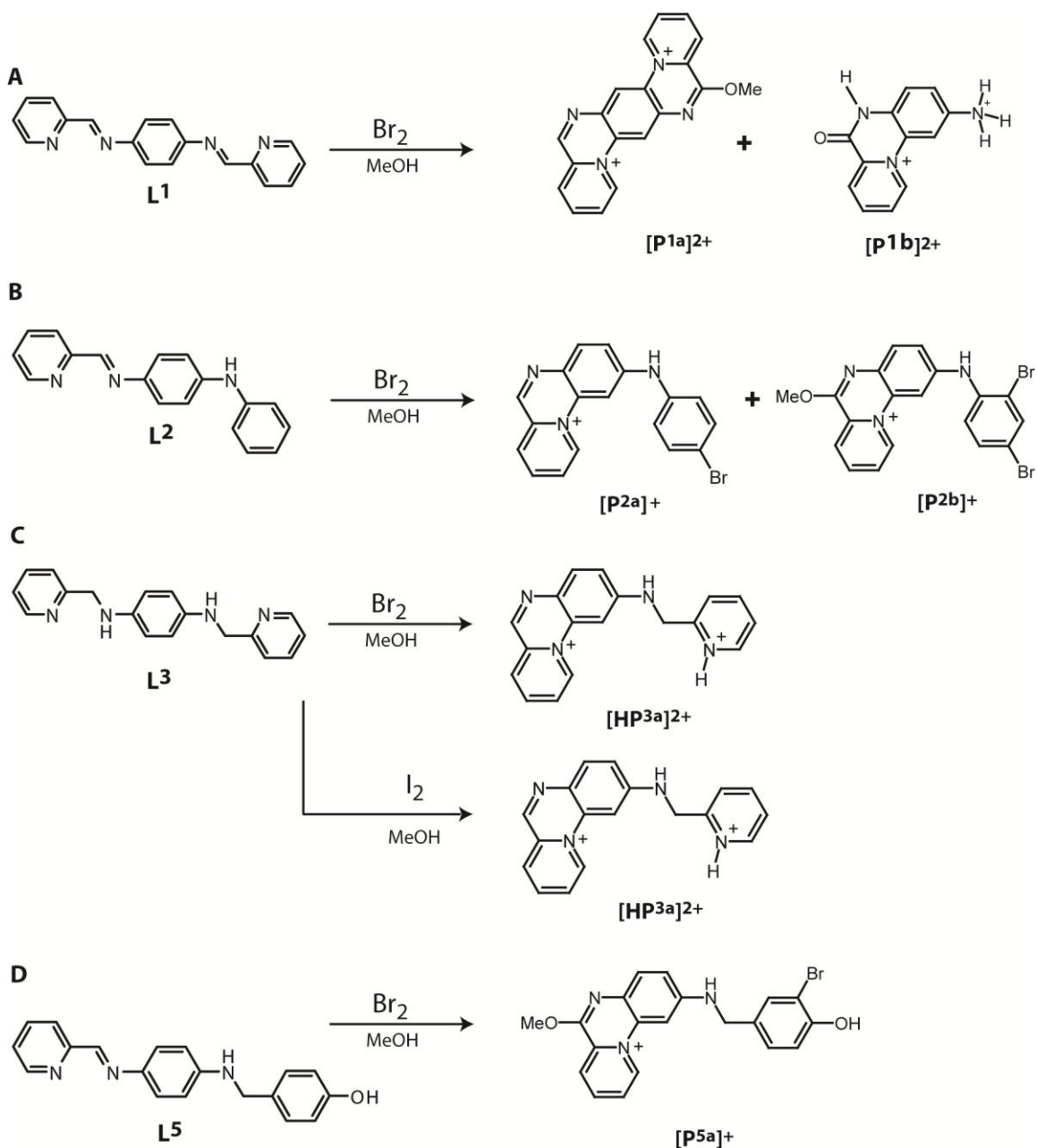
other products form and ring bromination is somewhat unpredictable (Scheme 3). The compounds presented in the scheme 3 are the ones which we could isolate and characterize through either crystallography or have evidence through ^1H NMR and ESI-mass spectral data.



Scheme 1. Synthesis and characterization of precursors and their cyclization products including metal complexes reported in Chapter 2.



Scheme 2. Synthesis and characterization of the precursors and their cyclized product as well as metal complexes presented in chapter 3.



Scheme 3. Synthesis and characterization of the cyclized product isolated using halogens as oxidizer presented in chapter 4.

Chapter 5. Most of the cyclized products have strong charge transfer bands in their UV-visible spectra and showed fluorescence. In this chapter we have studied the UV-visible and fluorescent properties of the products in MeOH (except $[P^{1a}]^{2+}$ which is only soluble in water) and determined their quantum yields using quinine sulfate as reference (Table 1). Results showed that P^1 to P^3 have similar emission characteristic while P^5 and P^6 emissions are red shifted and

P^{1a} and **P⁷** are blue shifted (Figure 2). Bromo derivatives also have emission characteristics and showed shifts as well.

Table 1. Fluorescent properties of the cyclization products

Compounds	λ_{ex} , nm	λ_{em} , nm	Quantum yield(Φ)	Fluo. Solvent	Q.Y.(Φ) Solvent
[P ¹](ClO ₄) ^a	470	580	0.23	MeOH	MeOH
[P ^{1a}] Br ₂	400	463	0.75	H ₂ O	H ₂ O
[P ²](NO ₃)	b	b	b	b	b
[HP ³](NO ₃) ₂	480	590	0.45	MeOH	H ₂ O
[HP ³] Br ₂	480	590	0.93	MeOH	H ₂ O
[HP ³] I ₂	480	584	0.55	MeOH	H ₂ O
[P ⁵] NO ₃	530	623	0.43	MeOH	H ₂ O
[P ⁶] NO ₃	550	625	0.35	MeOH	H ₂ O
[P ⁷] Br	400	473	0.83	MeOH	H ₂ O
Bromo-derivatives					
[P ^{1b}] Br	480	593	0.75	MeOH	H ₂ O
[P ^{2a}] Br	b	b	b	b	b
[P ^{2b}] Br	b	b	b	b	b
[P ^{5a}] Br	480	623	0.36	MeOH	H ₂ O
[P ^{6a}] Br	490	598	0.41	MeOH	H ₂ O
[P ^{6b}] Br	482	515	0.38	MeOH	H ₂ O

^a from ref.² ^b Non fluorescent.

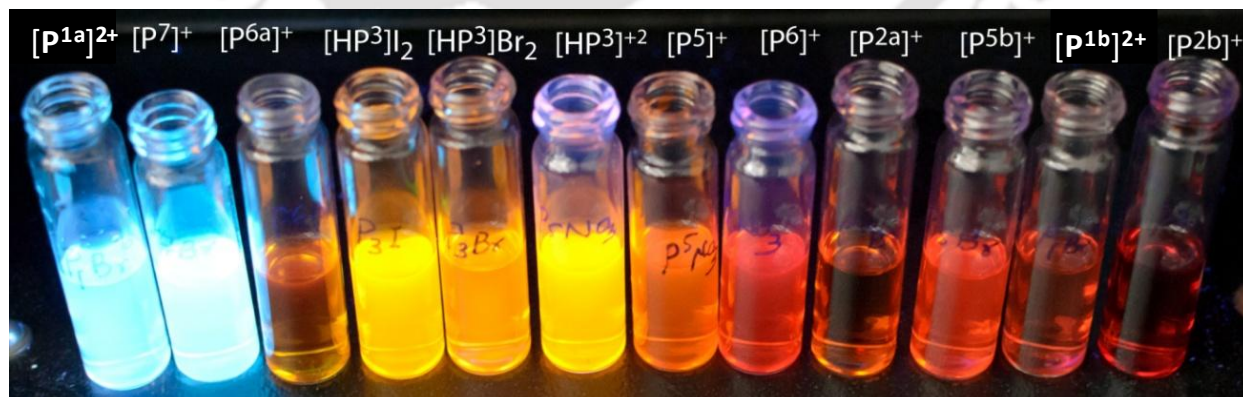


Figure 2. Fluorescent from blue to red taken in methanol except **[P^{1a}]²⁺** (H₂O), and compound **[P^{2a}]⁺**, **[P^{2b}]⁺** are non fluorescent in this condition.

Chapter 6. From the results presented in the Chapters 2-4, we hypothesized that oxidation of the precursor is the first step. As a result we performed cyclic voltammetry on the precursors. Almost all of the precursors showed irreversible oxidation which did not allow measurement of the redox potential. Thus In this chapter we have compared the first oxidation potential or anodic peak potential (E_{pa}) with the reported potentials for the oxidizers (Table 2). The results show that non-complexing strong oxidizers such as Br_2 and ceric ammonium nitrate can initiate cyclization in almost all the precursors whereas reagents having complexing capability show different behaviour.

Table 2. Summarizes electrochemical behaviours of the ligands (L^1 - L^7) with different oxidising agent to their quinoxaline derivatives pyrido[1,2-*a*]quinoxalin-11-ylum.

Precursors	E_{pa}	$\text{Ce}^{4+}/\text{Ce}^{3+}$ (1.61)	$\text{Br}_2/2\text{Br}^-$ (1.087)	Ag^+/Ag (0.799)	$\text{Fe}^{3+}/\text{Fe}^{2+}$ (0.771)	$\text{I}_2/2\text{I}^-$ (0.535)	$\text{Cu}^{2+}/\text{Cu}^+$ (0.159)
L^7	+1.26	R	R,iso, bro	N	N	N	N^a
L^1	+1.18	R	R^b ,iso, bro	N^c	R, sl	R	R^d ,iso
L^6	+1.06	R	Riso, bro	R,sl	R,iso	Rsl	N^a
L^2	+1.07	R	Riso, bro	R,iso	R,iso	R, iso	N
L^3	+0.52	R	R, iso	R,iso	R,iso	R,iso	N^a

^ametal complex formation detected¹¹, ^b ring halogenations occurred, ^cred fluorescence observed after a day in air. Iso = isolated, sl = slow reaction, bro= bromination.

Potentials of precursors measured in ethanol with a glassy carbon electrode with a scan speed of 50 mV/s and potentials are reported with respect to Ag/Ag^+ reference electrode. Reagent potentials are taken from reference 10 which were measured in aqueous medium and are reported vs NHE (Normal Hydrogen Electrode).

Conclusions. In this thesis work we chose a known reaction where cyclization of a Schiff base precursor in presence of Cu(II) resulted in a new type of heterocyclic compound and explored the reaction further. The results presented in this thesis show that (a) such reaction can occur with variety of precursors with assortment of reagents, (b) modification of this reaction can be used to make number of new fluorescent molecules with quantum yield(Φ) comparable to known fluorescent dyes, (c) more importantly, factors such as metal complexation, strength of oxidizer and side reactions with respect to reagent choice for a particular precursor were identified.

¹¹ Wu, H. C.; Thanasekaran, P.; Tsai, C. H.; Wu, J. Y.; Huang, S. M.; Wen, Y. S.; Lu, K. L. *Inorg. Chem.* **2006**, 45, 295.

Contents

I. Statement	i
II. Certificate	ii
III. Acknowledgments	iii
IV. Abstract	v
V. Contents	xiii
VI. Chapter I – Introduction	
1.1 Background	1
1.2 Literature survey	2
1.2.1 Heterocyclic compounds structurally similar to P ¹	2
1.2.2 Selected examples of quinoxaline or heterocyclic compound synthesis involving metal or metal oxides	4
1.2.3 Biological activities of quinoxaline derivative	6
1.2.4 Fluorescent dyes commonly used for DNA binding	10
1.3 Conclusions from literature survey and objectives of the thesis	12
References	13
VII. Chapter II - Synthesis and characterization of pyrido[1, 2-a] quinoxalin-11-ylum derivatives from Schiff base or reduced Schiff base by Fe(III) salt	
2.1 Experimental section	
2.1.1 Solvents and reagents	18
2.1.2 Measurements	18
2.2 Syntheses of precursors L ² - L ⁵	19
2.2.1 Synthesis of L ²	19
2.2.2 Synthesis of L ³	19
2.2.3 Synthesis of L ⁴	20
2.2.4 Synthesis of 4-aminophenyliminomethylphenol	20
2.2.5 4-aminophenylaminomethylphenol	21
2.2.6 Synthesis of L ⁵	21
2.3. Synthesis of pyrido[1,2-a]quinoxaline derivatives P ² - P ⁵	22
2.3.1 Synthesis of P ²	22

2.3.2 Synthesis of P^3	22
2.3.3 Synthesis of P^4	23
2.3.4 Synthesis of P^5	23
2.4 Syntheses of complexes $C^1 - C^2$	24
2.4.1 Synthesis of C^1	24
2.4.2 Synthesis of C^2	25
2.5 X-ray Data Collection, Structure Solution and Refinement	25
2.6 Results and discussion	40
2.6.1 Synthesis and characterization of precursors L^2 to L^5	40
2.7 Cyclization reaction of precursors $L^2 - L^5$ and L^4	42
2.7.1 Cyclization reaction of precursor L^2	42
2.7.2 Cyclization reaction of precursor L^3	42
2.7.3 Protonation reaction of precursor L^4	44
2.7.4 Cyclization reaction of precursor L^5	44
2.8 Molecular structure of precursors $L^2 - L^5$	45
2.8.1 Molecular structure of precursor L^2	45
2.8.2 Molecular structure of precursor L^3	45
2.8.3 Molecular structure of precursor L^5	47
2.9 Molecular structures of $P^2 - P^5$ and metal complexes	47
2.9.1 Molecular structure of $[P^2](NO_3).H_2O$	47
2.9.2 Molecular structure of $[HP^3](NO_3)_2.H_2O$	49
2.9.3 Molecular structure of $[P^4](NO_3)$	50
2.10 Molecular structures of complexes $C1 - C2$	52
2.10.1 Molecular structure of $Mn(L^2)_2Cl_2 (C1)$	52
2.10.2 Molecular structure of $Co(L^2)_2Cl_2 (C2)$	53
2.11 1H NMR analysis	54
Conclusion	54
References	56

**VIII. Chapter III - Synthesis and characterization of pyrido[1,2-a] quinoxalin-11-
ylium derivatives from phenol derived Schiff base by Fe(III) salt or
molecular bromine**

3.1 Experimental Section	58
3.1.1 Solvent and Reagents	58
3.2 Syntheses of precursors $L^6 - L^7$	60
3.2.1 Synthesis of L^6	60
3.2.2 Synthesis of L^7	60
3.3 Syntheses of pyrido[1,2-a]quinoxalines derivatives $P^6 - P^7$	61
3.3.1 Synthesis of $[P^6]NO_3$	61
3.3.2 Synthesis of $[P^{6a}]Br$	61
3.3.3 Synthesis of $[P^{6b}]Br$	62
3.3.4 Synthesis of $[P^{6c}]Br$	62
3.3.5 Synthesis of $[P^7]Br$	63
3.4 Synthesis of manganese complex $[Mn(L^6)Cl_2]$ (C3)	63
3.5 X-ray Data Collection, Structure Solution and Refinement	63
3.6 Results and Discussion	64
3.6.1 Synthesis and characterization of precursors L^6 and L^7	79
3.7 Cyclization reaction of precursors $L^6 - L^7$	80
3.7.1 Cyclization reactions of L^6	80
3.7.2 Cyclization reactions of L^7	80
3.7.3 Cyclization reactions of L^6 with Bromine	82
3.8.1 Structure of $[P^6]NO_3.H_2O$	83
3.8 Molecular structures of $P^6 - P^7$ and metal complex (C3)	83
3.8.2 Structure of $[P^{6a}]Br.H_2O$	84
3.8.3 Structure of $[P^7]Br$	85
3.8.4 Structure of $Mn(L^6)_2Cl_2$ (C3)	86
3.9 1H NMR analysis	87
Conclusion	88
References	88

IX. Chapter IV – Synthesis and characterization of pyrido[1,2-*a*]quinoxalin-11-ylum derivatives from Schiff base or reduced Schiff base by molecular bromine and iodine

4. 1 Experimental Section	90
4.1.1 Solvents and Reagents	90
4.2 Syntheses of pyrido[1,2- <i>a</i>]quinoxaline derivatives P ¹ - P ⁵	92
4.2.1 Syntheses of [P ^{1a}](Br) ₂ (1) and [P ^{1b}](Br) ₂	92
4.2.2 Syntheses of [P ^{2a}](Br) (3) and [P ^{2b}](Br)	92
4.2.3 Syntheses of [HP ³](Br) ₂	93
4.2.4 Syntheses of [HP ³](I) ₂	94
4.2.5 Syntheses of [P ^{5a}](Br) ₂	94
4.3 X-ray Data Collection, Structure Solution and Refinement	95
4.4 Results and discussion	108
4.4.1 Synthesis and characterization of precursors L ¹ - L ⁵	108
4.5 Cyclization reaction of precursors L ² - L ⁵	108
4.5.1 Cyclization reaction of precursor L ¹ with Br ₂	108
4.5.2 Cyclization reaction of precursor L ² with Br ₂	109
4.5.3 Cyclization reaction of precursor L ³ with Br ₂	109
4.5.4 Cyclization reaction of precursor L ³ with I ₂	110
4.5.5 Cyclization reaction of precursor L ⁵ with Br ₂	110
4.6 Molecular structure of [P ^{2a}](Br) - [P ³](I) ₂	110
4.6.1 Molecular structure of [P ^{2a}](Br)	110
4.6.2 Molecular structure of [P ^{2b}](Br)	112
4.6.3 Molecular structure of [P ³](Br) ₂ .3H ₂ O	113
4.6.4 Molecular structure of [P ³](I) ₂ .3H ₂ O	113
4.7 ¹ H NMR analysis	115
Conclusion	115
References	116

X. Chapter V – UV/vis and Fluorescence Spectroscopic study of precursor and product pyrido[1,2-*a*]quinoxalin-11-ylum derivatives

5.1 Experimental Section	117
5.1.1 Electronic spectral measurements	117
5.1.2 Fluorescence spectral measurements	117

5.2 Results and discussions	118
5.2.1 Absorption spectra of precursors	118
5.2.2 Absorption spectra of cyclized products	118
5.3 Fluorescence properties of cyclized products	128
Conclusion	129
References	129
X1. Chapter VI – Cyclic Voltammetric study of precursor and product pyrido[1,2-<i>a</i>]quinoxalin-11-ylum derivatives	
6.1 Electrochemical analysis	131
6.1.1 Setup	131
6.2 Results and discussion	132
6.2.1 Oxidizability of the precursors	132
6.2.2 Oxidizability of precursor versus Reagents redox potential	135
Conclusion	137
References	137
X11. Findings of the thesis	
X111. List of publications	

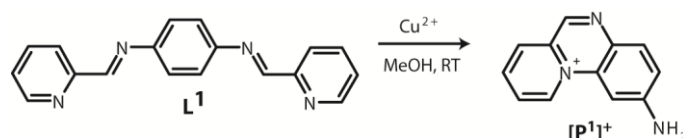
Chapter - 1



Introduction

1.1 Background

Quinoxalines are an important class of heterocyclic compounds which are used as dyes, pharmaceuticals and the moiety is present in number of antibiotics (Table 1.3).¹ Earlier Koner *et al.* had communicated the synthesis of a new fluorescent tricyclic quinoxaline derivative, pyrido[1,2-*a*]quinoxalin-11-ylum perchlorate (**[P¹]**ClO₄), formed by the Cu(II)-mediated cyclization of a simple Schiff base precursor (**L¹**) (Scheme 1).²



Scheme 1.1 Synthesis of pyrido[1,2-*a*]quinoxalin-11-ylum salt.

Only four tricyclic heterocycles including **a** having similar structure are known (Figure 1.1).³⁻⁵ Compound **b** benzo[*e*]pyrido[2,1-*c*][1,2,4]triazin-11-ium salts reported by Goswami *et al.* are highly fluorescent and showed strong binding with calf thymus DNA.³ Compound **c** was reported by Goswami and Adak.⁴ Compound **d** pyrido[1,2-*a*]quinoxalinium ion was reported by Chernavskaya *et al.*^{5a} and further structurally characterized by Duffy *et al.*^{5b} showed antimicrobial activity as well as pH sensitive fluorescence. None of the syntheses of compounds **b-d** involved metal ions.

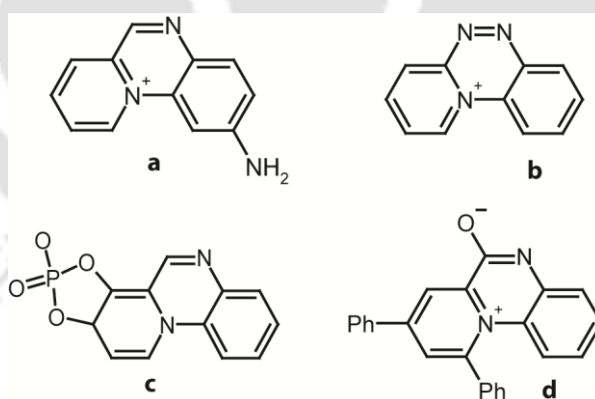
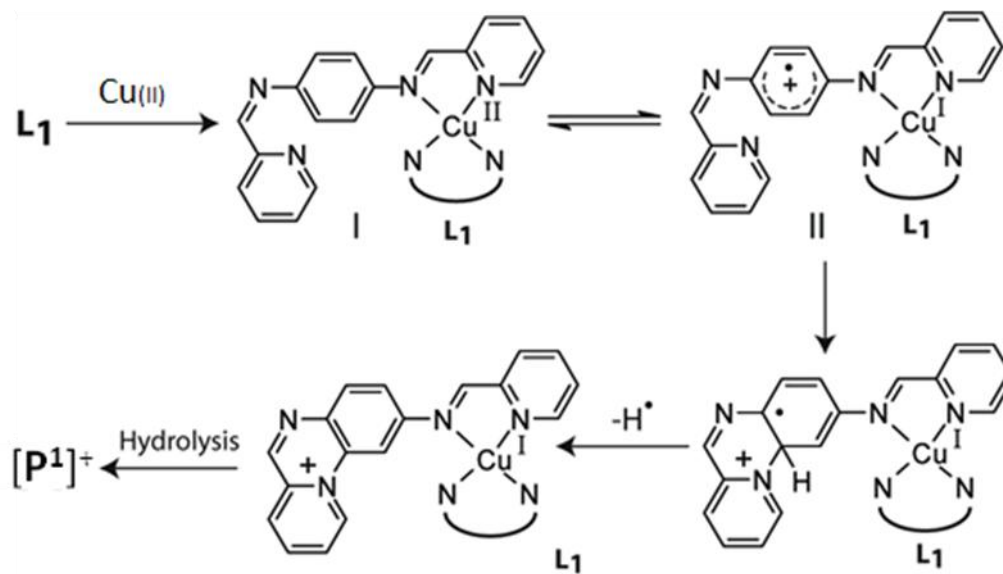


Figure 1.1 Tricyclic heterocyclic compounds **b - d** structurally similar to **[P¹]⁺** (**a**).

The proposed mechanism for the formation of **[P¹]⁺** was that in the reaction, **L¹** is oxidized at the expense of reduction of Cu(II) forming a cationic radical intermediate which undergoes cyclization (Scheme 1.2).² Ligand oxidation due to metal reduction is of current interest⁶ and recently Reedjik *et al.* reported⁷ synthesis of a leuco-verdazyl ring cyclization as a result of Mn(III) reduction. Thus considering the newness of **[P¹]⁺**, the potential use of pyrido[1,2-*a*]quinoxalinium derivatives as fluorescent heterocyclic dyes and the recent development of

metal mediated cyclization providing new type of heterocyclic compounds, we have decided to investigate the reaction with different precursors and reagents.



Scheme 1.2 Proposed mechanism of formation of $[P^1]^+$.

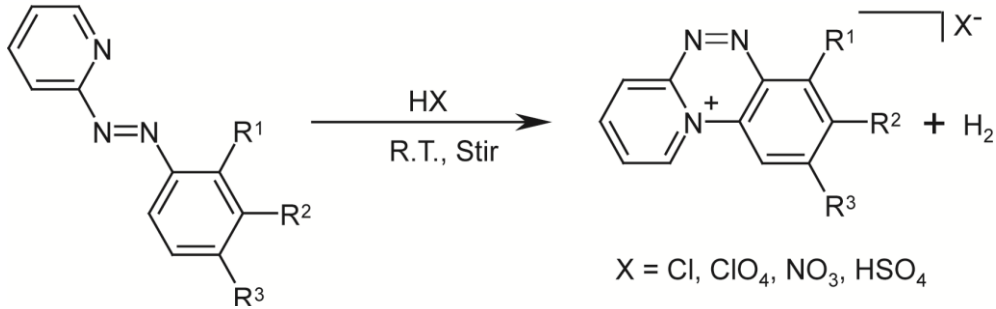
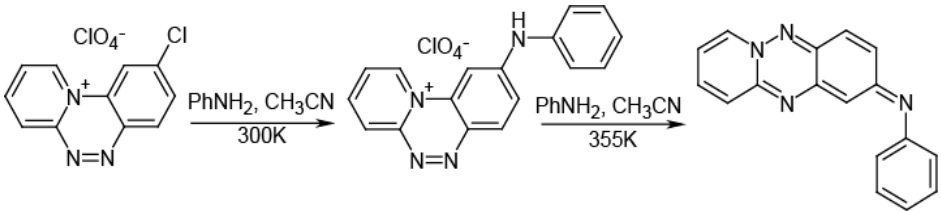
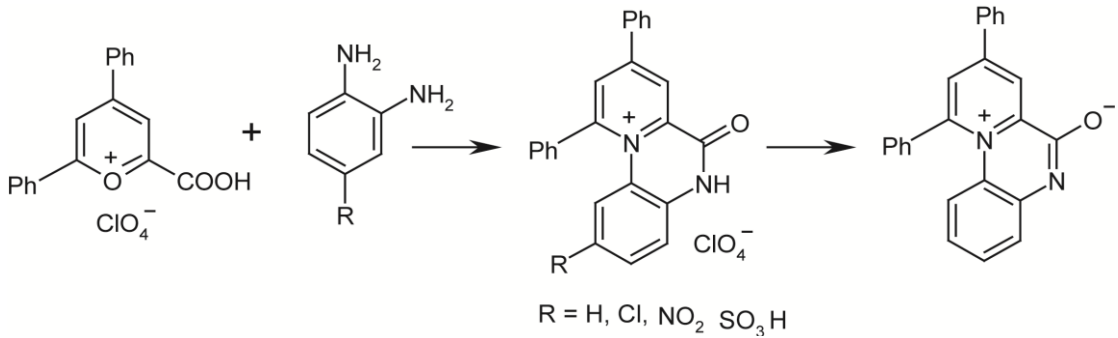
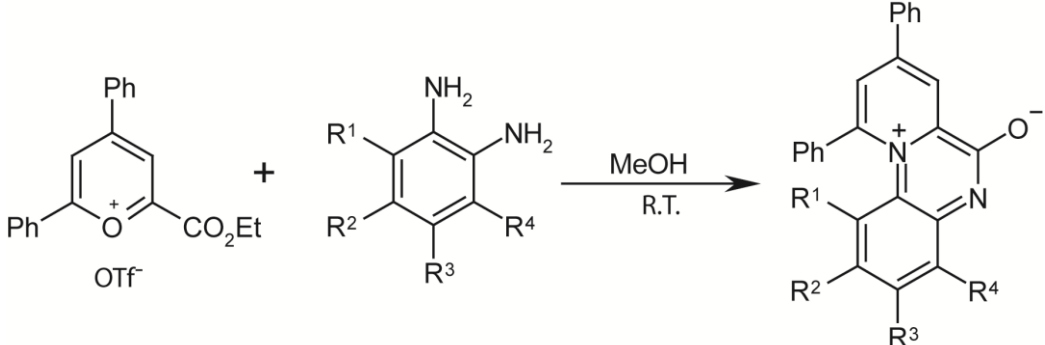
1.2 Literature survey

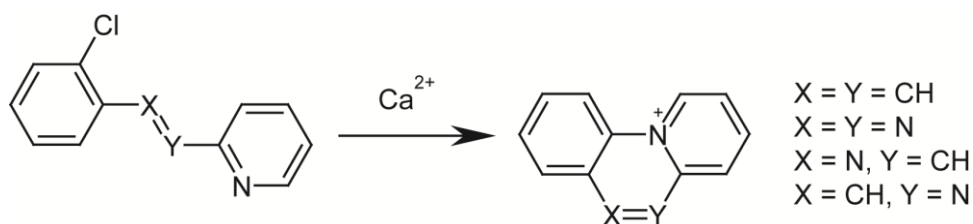
In the following sections we have compiled an overview of (1) the synthesis of quinoxaline derivatives directly related to this work, (2) selected examples of quinoxaline or heterocyclic compound synthesis involving metal or metal oxides, (3) a comprehensive list of quinoxaline derivatives reported to have practical utility and (4) fluorescent dyes commonly used for DNA binding.

1.2.1 Heterocyclic compounds structurally similar to P^1

Out of the following five examples (Table 1.1), four are synthesis of tricyclic heterocycle while the work by Sinan *et al.* reports the transformation of a tricyclic to a different tricyclic compound.^{3b} Synthesis reported by Chernavskaya *et al.* produces tricyclic structure closest to $[P^1]^+$ which does not involve any redox reaction.^{5a} Out of five only one used metal ion (Ca^{2+}),⁷ none used any redox active metal ions. Except the example given by Sinan *et al.* none are cationic.^{3a}

Table 1.1 Synthesis of heterocyclic compounds

 (3a) Sinan, M.; Panda M.; Ghosh A.; Dhara K.; Fanwick, P. E.; Chattopadhyay D. J.; Goswami, S. <i>J. Am. Chem. Soc.</i> 2008, <i>130</i>, 5185.	 (3b) Sinan, M.; Ghosh, K.; Goswami, S. <i>J. Org. Chem.</i> 2006, <i>71</i>, 2687.
 (5a) Chernavskaya¹, L. N.; Kholodova¹, N. V.; Blagorodov, S. G.; Dmitrieva¹, N. A. <i>J. Pharm. Chem.</i> 1984, <i>18</i>, 413.	 (5b) Duffy, K. J.; Haltiwanger, R. C.; Freyer, A. J.; Li, F.; Luengo, J. I.; Cheng, Y. H. <i>J. Chem. Soc., Perkin Trans. 2</i> 2002, 181.

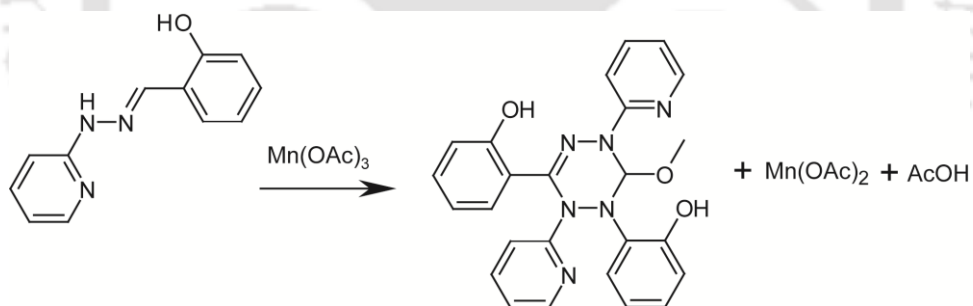


(7) Jankowiak, A.; Obijalska, E.; Kaszynski, P.; Pieczonka A.; Young, V. G.J. *Tetrahedron* **2011**, 67, 3317.

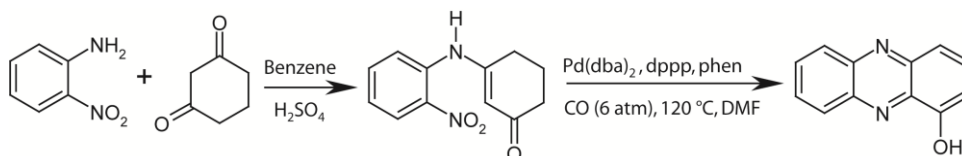
1.2.2 Selected examples of quinoxalin or heterocyclic compound synthesis involving metal or metal oxides

Out of five examples (Table 1.2), two involve redox active metal ions.^{8,12} Although role of Mn(III) was not elaborated by Tang *et al.* the generation of Mn(II) in the reaction indicated the involvement of reduction of Mn(III) in the cyclization process.⁸

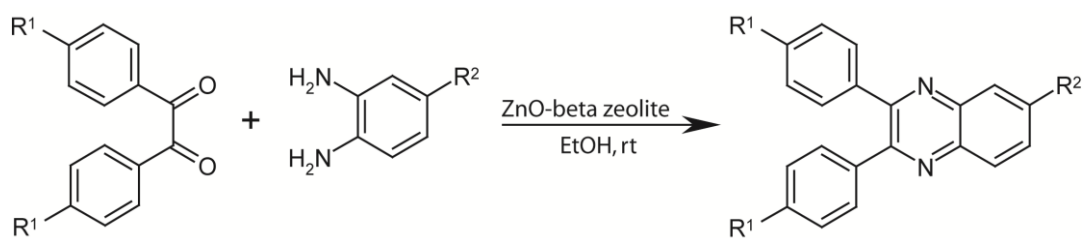
Table 1.2 Synthesis of heterocyclic compounds involving metal



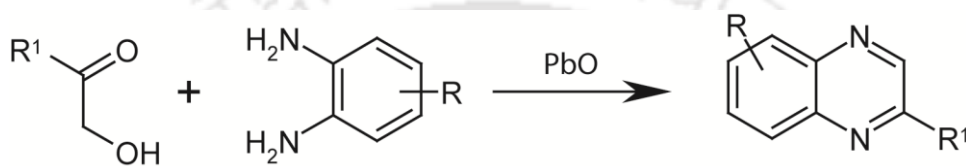
(8) Tang, J.; Nayak, S.; Costa, J. S.; Robertazzi, A.; Pievo, R.; Mutikainen, I.; Roubeau, O.; Teat, S. J.; Gamez, P.; Reedijk J. *Dalton Trans.* **2010**, 39, 1361



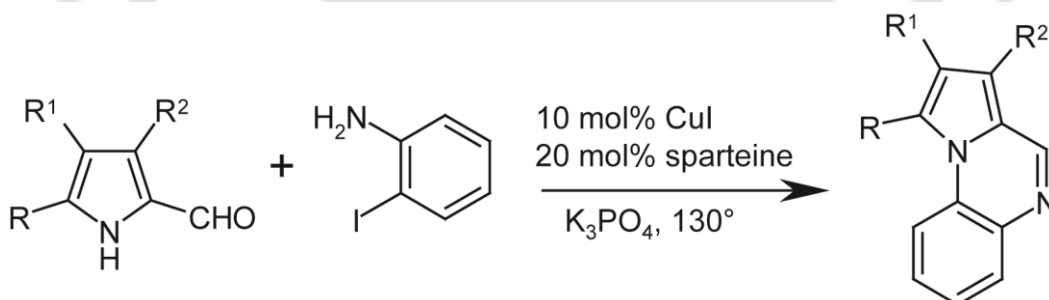
(9) Wallace, J. M.; Soderberg, B. C. G.; Tamariz, J.; Akhmedov, N. G.; Hurley, M. T. *Tetrahedron*, **2008**, 64, 9675.



(10) Katkar, S. S.; Mohite, P. K. H.; Gadekar, L. S.; Arbad, B. R.; Lande, K. M. *Cent. Eur. J. Chem.* **2010**, 8, 320.



(11) Kotharkar, S. A.; Shinde, D. B. *J. Iranian Chem. Soc.* **2006**, 3, 267.

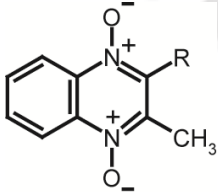
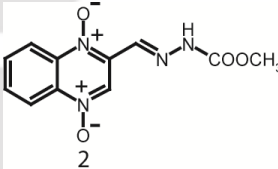
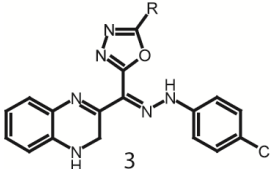
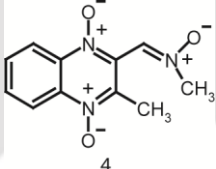
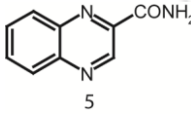
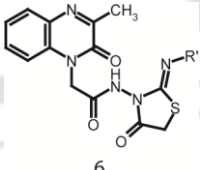
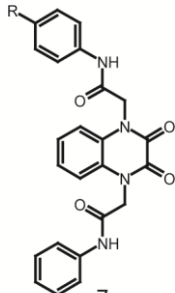
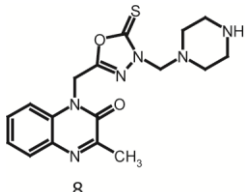


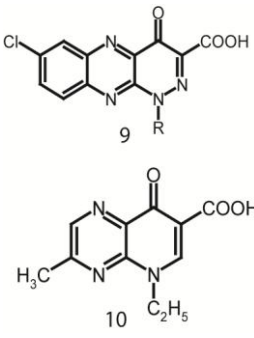
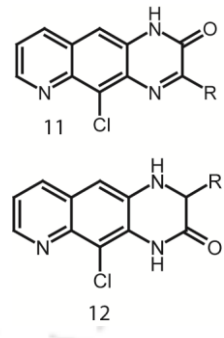
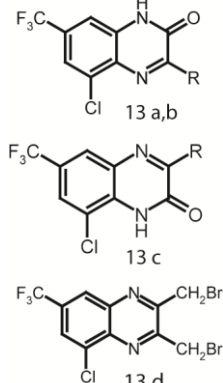
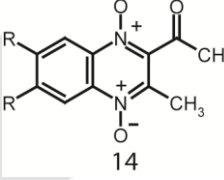
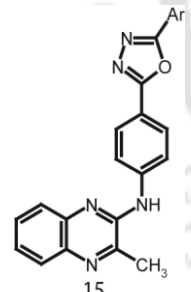
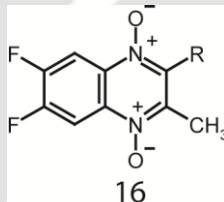
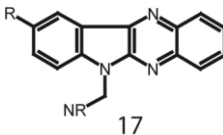
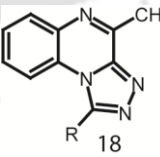
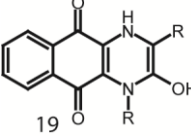
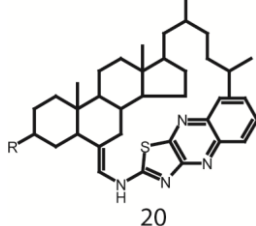
(12) Reeves, J. T.; Fandrick, D. R.; Tan, Z.; J. J.; Song, Lee, H.; Yee, N. K.; Senanayake, C. H. *J. Org. Chem.* **2010**, 75, 992.

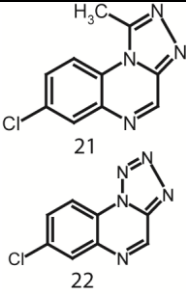
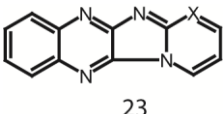
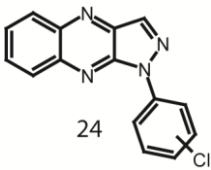
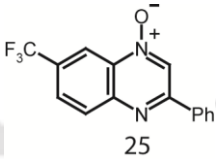
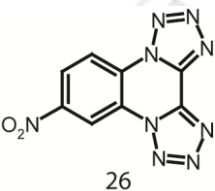
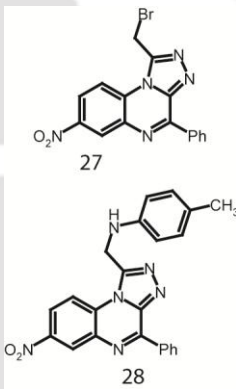
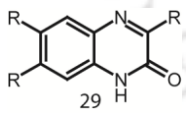
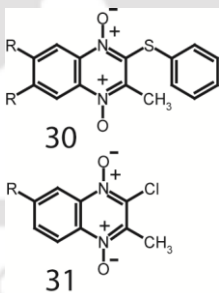
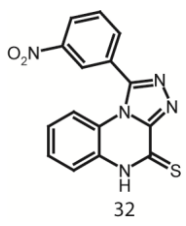
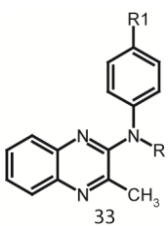
1.2.3 Biological activities of quinoxaline derivatives

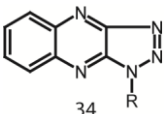
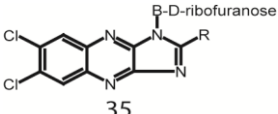
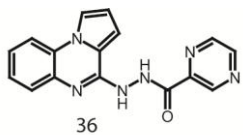
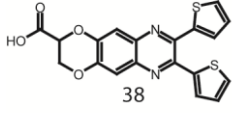
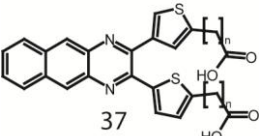
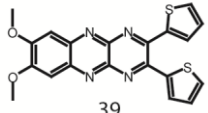
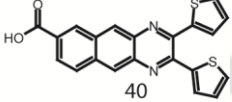
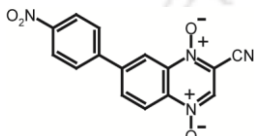
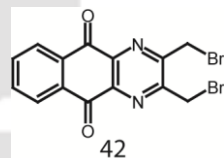
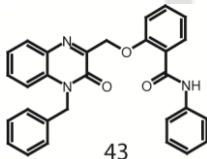
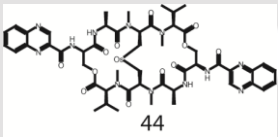
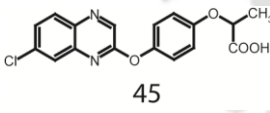
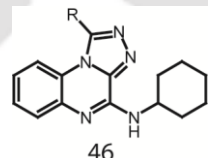
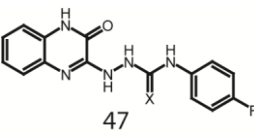
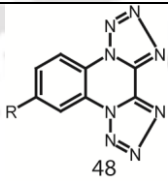
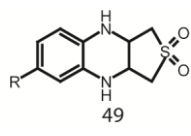
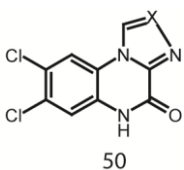
Table 1.3 compiled a list of quinoxaline derivatives along with their known activities. The survey showed that substituted quinoxaline derivatives exhibit a wide variety of biological activities. Quinoxalines demonstrated antibacterial,¹³⁻¹⁸ antifungal^{15, 25,26, 31-39} antiviral,⁴⁰⁻⁴² antineoplastic,^{20,43-46} antidepressant,⁴⁷ hypoglycemic,⁴⁸ anti-inflammatory,^{27,33,49} excitatory amino acid antagonistic,⁵⁰ antiglaucoma,⁵¹ antiparasite,⁵² antituberculosis,^{24,37,53} and anticancer,^{22, 36, 54-57} activities. Antibacterial and antifungal studies seem to be the most common. Unlike heterocyclic compounds reported in this thesis, only one example **6** is ionic in nature. Rest are neutral species.

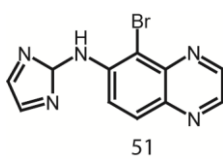
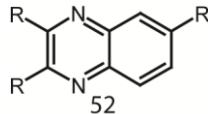
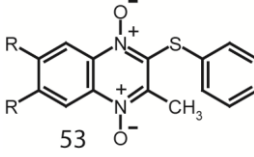
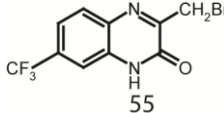
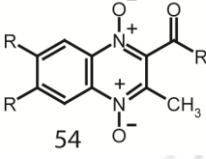
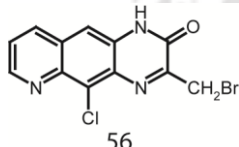
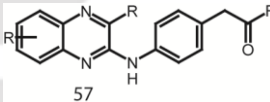
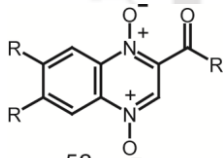
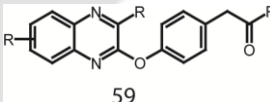
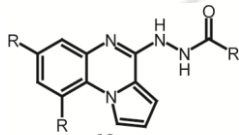
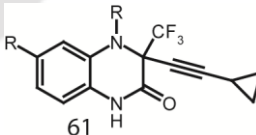
Table 1.3 Quinoxaline derivatives with known biological activity

Compound	Activity	Compound	Activity
	Highly active against Gram negative bacteria. Ref.13		Carbadox (2): usually used in research as a reference antibacterial agent. Ref.14
	Demonstrated marked antibacterial activity. Ref.15		Showed exceptional activity against <i>prot. mirabilis</i> and different <i>Salmonella</i> species in experimental infections in mice. Ref.16
	This is a well known synthetic antibacterial agent and still being used for treatment of tuberculosis. Ref.17		This was synthesized as potential antibacterial agents due to the combined biological effect of quinoxaline and thiazolidinone moiety. Ref.18
	In 1996, a new series were prepared and tested for antibacterial activity. These compounds were found to possess remarkable antibactericidal activity against <i>E. coli</i> and <i>B. subtilis</i> . Ref.19		This showed considerable antibacterial activity against the Gram positive bacteria <i>B. subtilis</i> . Ref.20

Compound	Activity	Compound	Activity
 9 10	These were prepared as analogues of nalidixic acid. However, these compounds proved to be inferior to nalidixic acid as antibacterial agents. ^{Ref. 21}	 11 12	In 2001, these were synthesized and submitted to a preliminary in vitro evaluation for antibacterial, anticandida and anticancer activities, and showed great effect against the all selected strains ^{Ref. 22}
 13 a,b 13 c 13 d	These series of quinoxaline derivatives (13a-d) and showed that compound have activity against vib. alginolyticus. compared with ciprofloxacin. ^{Ref.23}	 14	These derivatives of quinoxaline showed antitubercular activity. ^{Ref.24}
 15	Antibacterial activities were evaluated. ^{Ref.25}	 16	This was prepared and evaluated as antibacterial, antifungal, antitrichomonas and antimycoplasma activities. ^{Ref.26}
 17	This was described as antibacterial and anti-inflammatory agents. ^{Ref.27}	 18	These triazoloquinoxaline derivatives showed antimicrobial activity ^{Ref.28}
 19	Showed in vitro antibacterial activity against <i>Klebs. pneumoniae</i> and <i>E. coli</i>. ^{Ref.29}	 20	This steroidal thiazoloquinazolinone derivatives as Antibacterial agents against <i>E. coli</i>., better than amoxicillin. ^{Ref.30}

Compound	Activity	Compound	Activity
 21 22	Triazolo and tetrazolo quinoxaline derivatives showed antifungal activity. Ref.31	 23	Imidazo quinoxaline derivatives possess remarkable fungicidal activity. Ref.32
 24	Compound 24 shows antifungal activity Ref.15	 25	Anti-candida parapsilosis in vitro activity. Ref.33
 26	Compound 26 shows mild antifungal activity against certain fungi. Ref.34	 27 28	Significant antifungal activity exceeding that of nystatin. Ref.35
 29	Inhibition activity against various strains of candida. Ref.36	 30 31	These showed antitubercular activity. In addition they have anti-candida activity, while compound (30) and (31) were the most active against <i>C. krusei</i> . Ref.37
 32	Showed moderate antifungal activity against <i>Candida. albicans</i> Ref.38	 33	This was tested for the antifungal activity which showed moderate activities against <i>Candida. albicans</i> Ref.25

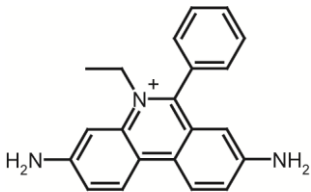
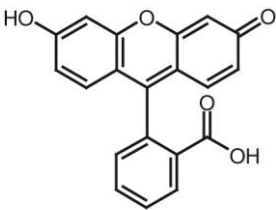
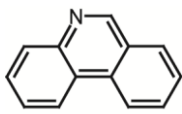
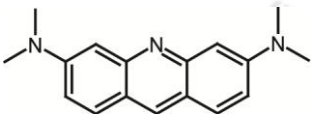
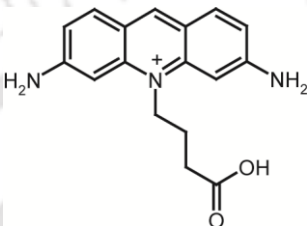
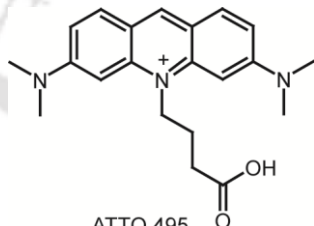
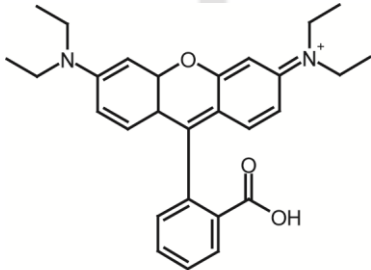
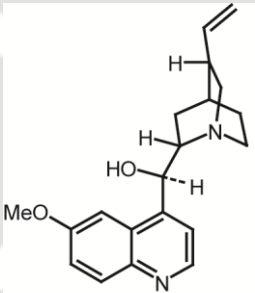
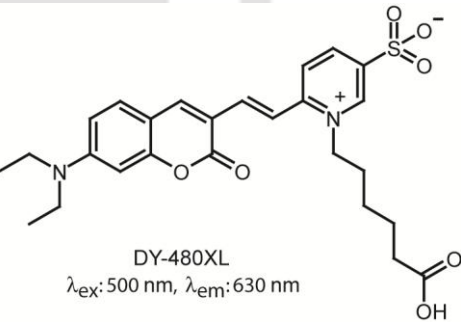
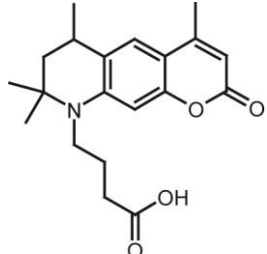
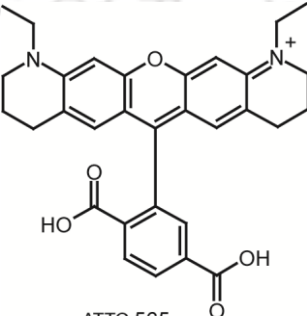
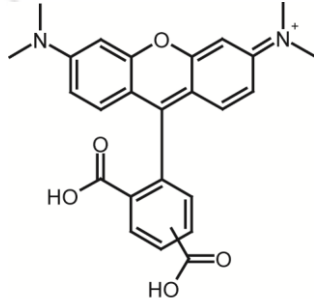
Compound	Activity	Compound	Activity
 34	This showed moderate to excellent antifungal activities against <i>Rhiz. solani</i> and <i>Rhiz. pythium</i> under different concentrations. ^{Ref.39}	 35	This showed significant antiviral activity against human cytomegalovirus and herpes virus. ^{Ref.40}
 36	This was prepared as a prototypic antiviral agent of a new class of reverse transcriptase inhibitors. This finding led to a new generation of potent HIV replication inhibitors. ^{Ref.41}	 38	The example (37 - 40) prepared as SRPK- 1 inhibitors with advantageous physicochemical properties. ^{Ref.42}
 37		 39	
 40			
 41	This was found to be highly active as a cytotoxic agent. ^{Ref.43}	 42	This showed remarkable cytotoxic effect against different sarcoma types. ^{Ref.20}
 43	This was reported as a synergistic chemotherapeutic agent for the treatment of resistant neoplastic diseases. ^{Ref.44}	 44	Shown remarkable cytotoxicity against various human-tumor cell lines. ^{Ref.45}
 45	One of the most highly and broadly active antitumor agents. ^{Ref.46}	 46	Found to possess potent antidepressant activity by virtue of their selective adenosine antagonistic activity. ^{Ref.47}
 47	Reported as mild hypoglycemic agents comparable to that of tolbutamide. ^{Ref.48}	 48	These were found to possess anti-inflammatory activity. ^{Ref.33}
 49	This has been reported as a potent anti-inflammatory agent. ^{Ref.49}	 50	the new neurological damage associated with disorders such as cerebral ischemia, Huntington's chorea, epilepsy and Alzheimer's disease. ^{Ref.50}

Compound	Activity	Compound	Activity
 51	This drug acts through reducing the intraocular pressure, thus alleviating The symptoms of glaucoma. ^{Ref.51}	 52	This showed interesting activities against several parasites. ^{Ref.52}
 53	This showed antituberculosis activity exhibiting MIC between 0.39 and 0.78 $\mu\text{g mL}^{-1}$ (rifampicin MIC= 0.25 $\mu\text{g mL}^{-1}$). ^{Ref.37} The compound [54] has been found to exhibit good antituberculosis activity. ^{Ref.24,53}	 55	This is submitted to preliminary in vitro evaluation for anticancer and results showed interesting anticancer activity for compound. ^{Ref.36}
 54			
 56	The compound (56) has encouraging anticancer activity at a concentration of 10^{-4} M. ^{Ref.22}	 57	This series was prepared and tested for anticancer in vitro and the results showed that compound was the most active agent. ^{Ref.54}
 58	Antitumor activity against a 3-cell line panel. ^{Ref.55}	 59	In vitro anticancer activity, and the results following decreasing order of activity were recorded. ^{Ref.56}
 60	Moderately active against colon cancer cell lines, while compound (60) was highly active in all cells. ^{Ref.57}	 61	As HIV-1 reverse transcriptase inhibitors. Compounds displayed activity comparable or better than Efavirenz and GW420867X. ^{Ref.58}

1.2.4 Fluorescent dyes commonly used for DNA binding

Following table 1.4 lists some of the well-known fluorescent dyes. Most of them are planar and a significant number are cationic in nature. Emission ranges from 500-650 nm.

Table 1.4 Fluorescent dyes commonly used for DNA binding

 Ethidium Bromide λ_{ex}: 510 nm, λ_{em}: 595 nm	 Fluorescein λ_{ex}: 498 nm, λ_{em}: 518 nm	 Phenanthridine λ_{ex}: 236 nm, λ_{em}: 370 nm
 Acridine Orange λ_{ex}: 502 nm, λ_{em}: 526 nm	 ATTO 465 λ_{ex}: 390 nm, λ_{em}: 479 nm	 ATTO 495 λ_{ex}: 495 nm, λ_{em}: 527 nm
 Rhodamine G λ_{ex}: 526 nm, λ_{em}: 555 nm	 Quinine λ_{ex}: 348 nm, λ_{em}: 455 nm	 DY-480XL λ_{ex}: 500 nm, λ_{em}: 630 nm
 ATTO 390 λ_{ex}: 390 nm, λ_{em}: 479 nm	 ATTO 565 λ_{ex}: 563 nm, λ_{em}: 592 nm	 5/6-TAMRA λ_{ex}: 545 nm, λ_{em}: 575 nm

1.3 Conclusions from literature survey and objectives of the thesis

From the literature we found that only three other structurally similar units were reported. Out of these, benzo[e]pyrido[2,1-c][1,2,4]triazin-11-ium salts are highly fluorescent and showed strong binding with calf thymus DNA. The compound oxopyrido[1,2-*a*]quinoxalinium ions reported first by Chernavskaya *et al.* and structurally characterized recently by Duffy *et al.* showed antimicrobial activity as well as pH sensitive fluorescence (Table 1.1). Similarly, the numbers of heterocycles formed using redox active metal ions are also few (Table 1.2). Quinoxalins derivatives showed wide variety of biological activity (Table 1.3). Structurally the quinoxalinium compound synthesized by Koner *et al.* had certain aspects; planarity, N-based heterocycle, cationic charge with common fluorescent dyes used for DNA binding. Thus the fluorescent tricyclic heterocyclic pyrido[1,2-*a*]quinoxalin-11-ylum unit synthesized by Koner *et al.* is unique in number of ways:

- Very few examples of structurally similar tricyclic heterocyclic compounds are known (Table 1.1).
- Very few examples of quinoxaline derivatives are known where a redox active metal ion was necessary for the cyclization (Table 1.1 and 1.2).
- Very few quinoxaline derivatives are cationic in nature.

Comparison of quinoxaline derivatives with known biological activity (Table 1.3) showed a very few are of ionic in nature. Thus it is somewhat uncertain if this moiety has any biological activity or not. But comparison with fluorescent dyes (Table 1.4) showed that several structural aspect and fluorescent property are quite similar. Thus considering all this aspect we had decided to explore the reaction reported by Koner *et al.*² further with the following objectives:

- Extending the cyclization to other than imines (Schiff base).
- Whether the reaction works with anything other than copper(II).
- Finding the factors that determine the choice of metal ions.
- Determine the fluorescent properties of the new compounds.

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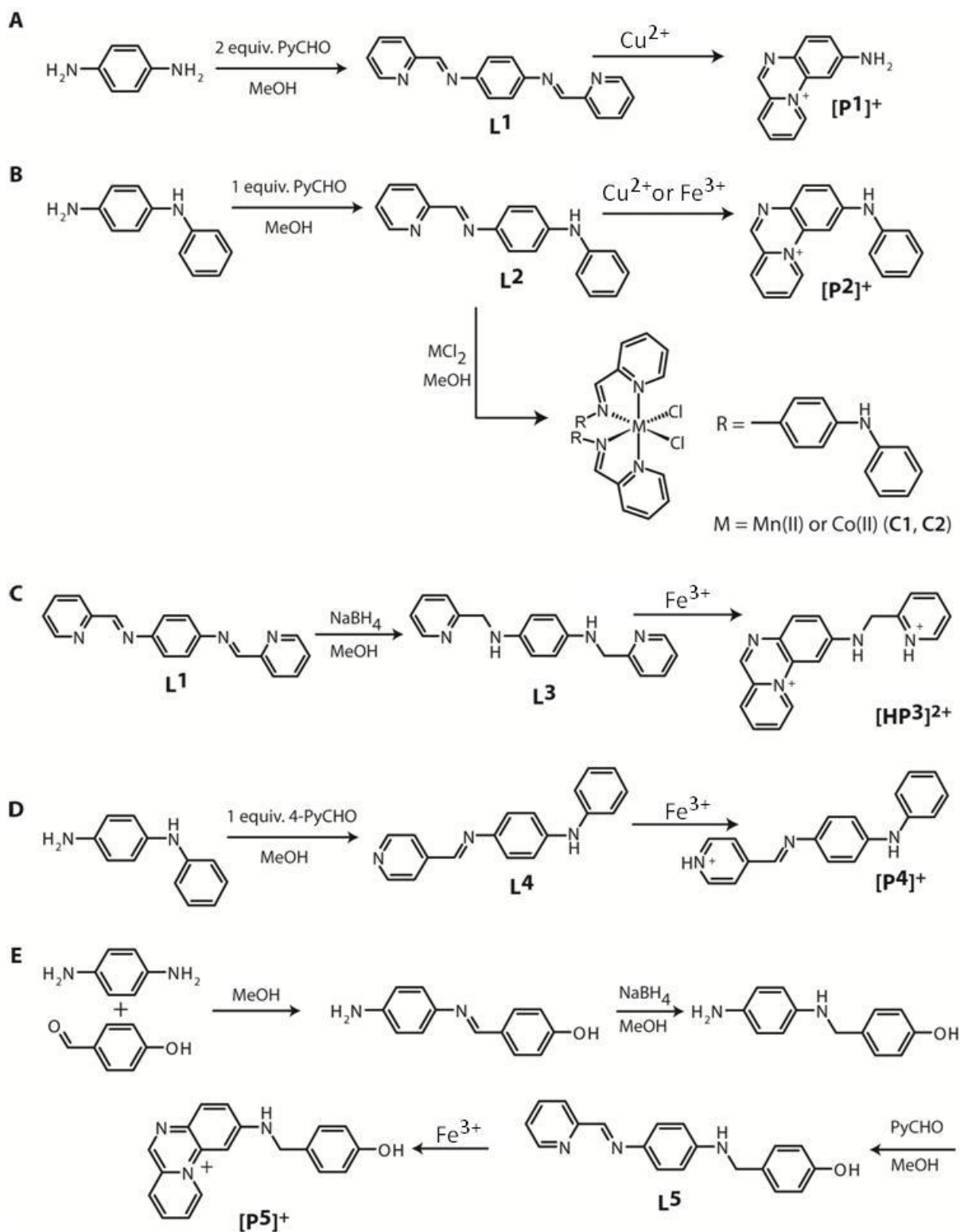
Chapter – 2

**Synthesis and characterization of
pyrido[1,2-*a*]quinoxalin-11-ylum derivatives
from Schiff base or reduced Schiff base by
Fe(III) salt**

Previously, it was reported that compound **L**¹ undergoes oxidative ring cyclization in presence of a Cu(II) salt followed by the hydrolysis of one imine bond (Scheme 2.1).¹ The proposed reaction mechanism suggested the initial formation of a short lived cation radical on **L**¹ at the expense of the reduction of Cu(II). The imine conjugated with the pyridine moiety, owing to its similarity with bipyridine, stabilizes the Cu(I) state which drives the reaction in the forward direction. If this hypothesis is correct then reduction of imine should prevent the reaction from occurring with Cu(II). Further, reduction of imine should, in principle, make the reduced **L**¹ more vulnerable to oxidation. In that case we might be able to perform the cyclization with milder oxidizers. Further, product **P**¹ contained a free amine group, so our initial attempts to derivatise the **P**¹ by reacting it with different aldehydes failed; this might be because of the lone pair of electron on the positively charged aromatic ring and thereby reducing the nucleophilicity of amine.

To investigate these issues we selected **L**² and **L**³ as precursor (Scheme 2.1). In **L**¹ to **L**³, the number of imine groups on the both side of *p*-phenylene ring were sequentially reduced to increase the vulnerability of the ring to oxidation. At the same time, incorporation of an amine in lieu of the imine in **L**² and **L**³ also ensures that the cyclized product will not be subjected to hydrolysis as was the case in **L**¹. We chose **L**⁴ to check if an intermolecular radical reaction occurs or not. Further, we chose **L**⁵ to establish if more unsymmetrical derivatization at the amine of **P**¹ is possible or not.

Thus in this chapter we present the results of the reactions of **L**² to **L**⁵ as precursors with Cu(II) and Fe(III) as oxidizer. We chose Cu(II) and Fe(III) as it is possible to reduce these ions by one electron. We knew from a previous report¹ that Mn(II) and Co(II) do not facilitate the cyclization process thus these two metal ions were used to form the corresponding metal complexes to understand metal binding capability of **L**².



Scheme 2.1 Syntheses of the Schiff base precursors, corresponding cyclization products and metal complexes.

2.1 Experimental Section

2.1.1 Solvents and Reagents

Solvents and reagents were obtained from commercial sources and used without further purification unless otherwise stated. Methanol was distilled over magnesium methoxide $[\text{Mg}(\text{OCH}_3)_2]$. Sodium hydrosulfite ($\text{Na}_2\text{S}_2\text{O}_4$) and ammonium peroxodisulfate $((\text{NH}_4)_2\text{S}_2\text{O}_8)$, pyridine-2-carboxaldehyde, pyridine-4-carboxaldehyde and N-phenyl-1, 4-diamino benzene were purchased from Aldrich Chemical Co. and used as received. *p*-Phenylenediamine was purchased from Loba Chemie Pvt. Ltd., India and was purified by recrystallizing from hot water in the presence of sodium hydrosulfite.² 4-Hydroxybenzaldehyde was purchased Loba Chemie Pvt. Ltd., India. *N*, *N'*-bis-pyridine-2-ylmethylene-benzene-1,4-diamine (**L**¹) and 2-aminopyrido[1, 2-*a*]quinoxalin-11-ylum perchlorate (**[P**¹](ClO₄) were synthesized as before.¹ Iron nitrate ($\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$) and manganese chloride ($\text{MnCl}_2 \cdot 6\text{H}_2\text{O}$) salts were purchased from Loba chemie Pvt. Ltd., India and used as received. Cobalt chloride ($\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$) was purchased from Central Drug House Pvt. Ltd., India and used as received. Sodium borohydride was purchased from Acros Organics (New Jersey, USA) and used as received.

2.1.2 Measurements

The IR spectra were recorded on Perkin-Elmer Spectrum One FT-IR spectrophotometer with KBr discs in the range 4000-400 cm^{-1} . Electronic spectra were recorded on Perkin-Elmer Lambda 25 UV-Vis spectrophotometer. The ¹H NMR spectra were recorded using Varian Mercury Plus 400 MHz spectrometer. Solid-state magnetic susceptibilities of the metal complexes at room temperature were recorded using a Sherwood Scientific Magnetic balance MSB-1. Solution electrical conductivities were measured with Eutech Instruments CON 5/ TDS 5 Conductivity Meter. X-band EPR spectra were recorded with a Jeol JES-FA series spectrometer fitted with a quartz Dewar for measurements at liquid nitrogen temperature. The spectra were calibrated with 2,2-diphenyl-1-picrylhydrazyl (DPPH, *g* = 2.0036). Electrospray ionization mass spectra (ESI-MS) were recorded on a Waters (Micromass MS Technologies) Q-TOF-Premier mass spectrometer. High-resolution mass spectra (HRMS) were recorded on an Agilent 6500 Q-TOF LC/MS system. The deviation from the observed *m/z* value to the theoretical value is less than 5 ppm in each case. Fluorescence measurements were carried out on

a Varian Cary eclipse spectrofluorometer using 10 mm path length quartz cuvettes with the slit width of 5 nm at 298 K.

2.2 Syntheses of precursors L^2 - L^5

Detailed synthetic procedures along with characterization data have been provided below:

2.2.1 *N*-Phenyl-*N'*-pyridin-2-ylmethylenbenzene-1,4-diamine (L^2)

Pyridine-2-carbaldehyde (0.29 g, 2.71 mmol) was added dropwise to a methanolic solution (50 mL) of *N*-phenyl-*p*-phenylenediamine (0.50 g, 2.71 mmol). The reaction mixture was stirred for 3 h at room temperature and filtered. The resulting yellow solid powder was washed with methanol (2×3 mL) and hexane (3×10 mL) respectively. The recrystallization was done in hot MeOH to give yellow crystals, which was dried in vacuum desiccators to give the pure product (0.60 g, 80%). Characterization data for L^2 : Melting point 137-139 °C. ESI-MS ($M+H^+$): Calcd 274.13; Found 274.21. UV/vis (MeOH): λ_{max} , nm (ϵ , $M^{-1} cm^{-1}$): 205 (40,000), 280 (18,000), 398 (18,000). IR (KBr, cm^{-1}): $\nu(N-H)$ 3259, $\nu(HC=N)$ 1618. 1H NMR (400 MHz DMSO- d_6) δ (ppm) 8.67 (1H, d, $J = 4.8$ Hz), 8.41 (1H, s, $HC=N$), 8.12 (1H, d, $J = 4.4$ Hz), 7.90 (1H, t, $J = 8.0$ Hz), 7.46 (1H, t, $J = 7.6$ Hz), 7.35 (2H, d, $J = 3.6$ Hz), 7.25 (2H, t, $J = 3.6$ Hz), 7.2 (2H, m, $J = 7.2$), 7.12 (2H, m), 6.86 (1H, t). HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{15}N_3$: 274.1339 found: 274.1349.

2.2.2 *N,N'*-Bis-pyridin-2-ylmethyl-benzene-1,4-diamine (L^3)

Pyridine-2-carbaldehyde (0.99 g, 9.20 mmol) was added dropwise to a stirred methanolic (50 mL) solution of *p*-phenylenediamine (0.50 g, 4.60 mmol). The solution was heated over a hot water bath for several minutes. The compound was precipitated as yellow solid. The yellow solid was filtered through Büchner funnel, washed with methanol (2×3 mL) and hexane (3×10 mL) respectively. The recrystallization was done in hot MeOH to give yellow crystals (0.99 g, 80%). This structure was reported previously.³ Melting point 153 –156 °C. IR (KBr, cm^{-1}): $\nu(HC=N)$ 1617(s) and $\nu(p$ -disubstituted benzene ring) 844.

The ligand L^1 (0.50 g 1.75 mmol) was taken in methanol (50 mL) and two equivalent of sodium borohydride (0.13 g, 3.44 mmol) was added portionwise with stirring at room

temperature for 4 h. The solvent was evaporated to dryness, the sticky residue was dissolved in 15 mL of water and neutralized with HCl (pH 6-7), washed with excess water and hexane (2 × 10 mL) respectively. A light orange powder thus obtained was dried in a vacuum desiccator to give the ligand (0.40 g, 78%). Characterization data for **L**³: Melting point 171-173 °C. ESI-MS ($M+H^+$): Calcd 291.15; Found 291.14. UV/vis (MeOH): $\lambda_{\max}$, nm (ϵ , $M^{-1} \text{ cm}^{-1}$): 205 (35,000), 261(22,000), 321 (sh). IR (KBr, cm^{-1}): ν_{NH} 3365. ¹H NMR (400 MHz, $\text{CDCl}_3\text{-d}_1$) δ (ppm): 8.56 (d, 2H, $J = 4.4$ Hz), 7.62 (t, 2H, $J = 8.0$ Hz), 7.33 (d, 2H, $J = 8.8$ Hz), 7.16 (t, 2H, $J = 8.0$ Hz), 6.59 (s, 4H), 4.39 (s, 4H). HRMS (ESI) m/z $[M+H]^+$ calcd for $\text{C}_{18}\text{H}_{18}\text{N}_4$: 291.1531 found: 291.1605.

2.2.3 *N*-Phenyl-*N'*-pyridin-4-ylmethylene-benzene-1,4-diamine (**L**⁴)

Pyridine-2-carbaldehyde (0.29 g, 2.71 mmol) was added dropwise to a methanolic solution (50 mL) of *N*-phenyl-*p*-phenylenediamine (0.50 g, 2.71 mmol) with constant stirring at room temperature. The reaction mixture was stirred for 3 h at room temperature and solvent was evaporated to approx 10 mL. The resulting yellow solid powder obtained within 3 h was filtered off and washed sequentially with methanol (2 × 2 mL) and hexane (3 × 10 mL), respectively. Finally, the yellow powder was dried in vacuum desiccator to give the ligand (0.60 g, 81%). Characterization data for **L**⁴: Melting point 139-141°C. ESI-MS ($M+H^+$): Calcd 274.13; Found 274.13. UV/vis (MeOH): $\lambda_{\max}$, nm (ϵ , $M^{-1} \text{ cm}^{-1}$): 204 (40,000), 277 (18,000), 407 (20,000). IR (KBr, cm^{-1}): $\nu(\text{HC=N})$ 1621, $\nu(\text{N-H})$ 3263. ¹H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.68 (2H, d, $J = 4.8$ Hz), 8.41 (1H, s, HC=N), 7.80 (2H, d, $J = 4.4$ Hz), 7.35 (2H, d, $J = 8.0$ Hz), 7.25 (2H, t, $J = 7.6$ Hz), 7.11 (2H, d, $J = 3.2$ Hz), 7.10 (2H, d, $J = 3.6$ Hz), 6.87 (1H, t, $J = 7.2$). HRMS (ESI) m/z $[M+H]^+$ calcd for $\text{C}_{18}\text{H}_{15}\text{N}_3$: 274.1339 found: 274.1344.

2.2.4 Synthesis of 4-aminophenyliminomethylphenol

The ligand 4-aminophenyliminomethylphenol was prepared by equimolar mixture of *p*-phenylenediamine (1.00 g, 9.26 mmol) and *p*-hydroxybenzaldehyde (1.13g, 9.26 mmol) in methanol (60 mL). On stirring for 2 h at room temperature, a yellow solid precipitated out from the reaction mixture which was filtered off and washed with methanol (2 × 2 mL) and hexane (3 × 10 mL) respectively. The resulting yellow solid powder product was dried in vacuum desiccator to give the ligand (1.4 g, 71%). Characterization data for **4-**

aminophenyliminomethylphenol: Melting point 134-136 °C. ESI-MS ($M+H^+$): Calcd 213.12; Found 213.13. UV/vis (MeOH): $\lambda_{\max}$, nm (ϵ , $M^{-1} \text{ cm}^{-1}$): 281(15,000), 350 (18,000). IR (KBr, cm^{-1}): $\nu(\text{N-H})$ 3287, $\nu(\text{HC=N})$ 1625, $\nu(\text{O-H})$ 3400. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.4 (1H, s, CH=N), 7.7 (2H, d, $J = 8.4$ Hz), 7.0 (2H, d, $J = 8.4$ Hz), 6.8 (2H, d, $J = 8.4$ Hz), 6.6 (2H, d, $J = 8.4$ Hz), 5.1 (NH_2).

2.2.5 Synthesis of 4-aminophenylaminomethylphenol

The ligand 4-aminophenylaminomethylphenol was prepared by equimolar mixture of *p*-phenylenediamine (1.00 g, 9.20 mmol) and *p*-hydroxybenzaldehyde (1.10 g, 9.20 mmol) in methanol (150 mL). The reaction mixture was stirred for 3 h at room temperature, but no precipitate was formed. The sodium borohydride (0.30 g, 9.20 mmol) was added portion wise to the reaction mixture. The color of the solution was changed immediately from yellow to grey and deep red within 3 h. The solvent was evaporated to dryness, the resulting sticky compound was dissolved in 10 mL of water and neutralized with HCl (pH 6-7). The resulting light grey solid was filtered off and washed with excess hot water and hexane (2×10 mL) respectively. Finally, the grey solid powder dried in desiccator to give the ligand (1.40 g, 70%). Characterization data for **4-aminophenylaminomethylphenol**: Melting point 139-140 °C. ESI-MS ($M+H^+$): Calcd 214.13; Found 214. UV/vis (MeOH): $\lambda_{\max}$, nm (ϵ , $M^{-1} \text{ cm}^{-1}$): 224 (21,000), 251 (17,000) 350 (10,000). IR (KBr, cm^{-1}): $\nu(\text{N-H}) + \nu(\text{O-H})$ 3391 (br). ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 7.1 (2H, d, $J = 8.4$ Hz), 6.6 (2H, d, $J = 8.0$ Hz), 6.4 (4H, s), 4.0 (2H, d, $J = 5.6$ Hz), 5.1 (N-H), 4.2 (NH_2), 9.3 (O-H). HRMS (ESI) m/z [$M+H$] $^+$ calcd for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}$: 215.1179 found: 215.1182.

2.2.6 Synthesis of 4-(pyridine-2-ylmethyleneamino)phenylamino methyl phenol (L^5)

The ligand L^5 was prepared from an equimolar mixture of 4-aminophenylaminomethylphenol (0.50 g, 2.3 mmol) and pyridine-2-carbaldehyde (0.20 g, 2.30 mmol) in (50 mL) methanol. The yellow color reaction mixture was stirred for 3 h at room temperature and solvent was evaporated to 5 mL. The resulting yellow solid was isolated by filtration, washed with cold water and methanol mixture (2×5 mL) and hexane (2×10 mL) respectively. The compound was recrystallized from hot methanol. Finally, the yellow solid was dried in vacuum desiccator to give the ligand (0.50 g, 70%). Characterization data for L^5 :

Melting point 173 - 175 °C. ESI-MS ($M+H^+$): Calcd 304.37; Found 304.14. UV/vis (MeOH): $\lambda_{\max}$, nm (ϵ , $M^{-1} \text{ cm}^{-1}$): 258 (13,000), 383 (16,000). IR (KBr, cm^{-1}): $\nu(\text{C}=\text{N})$ 1625, $\nu(\text{N}-\text{H})$ 3265. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ (ppm) 8.6 (1H, s, $\text{CH}=\text{N}$), 7.4 (1H, s), 7.8 (1H, t, $J = 8.4$, 6.8 Hz), 8.0 (1H, d, $J = 6.4$ Hz), 8.5 (1H, s), 6.7 (2H, d, $J = 6.0$ Hz), 6.6 (2H, d, $J = 6.4$ Hz), 4.1 (2H, s), 7.1 (2H, d, $J = 6.4$ Hz), 7.2 (2H, d, $J = 6.4$ Hz), 9.3 (-OH), 6.5 (NH). HRMS (ESI) m/z $[M+H]^+$ calcd for $\text{C}_{19}\text{H}_{17}\text{N}_3\text{O}$: 304.1444 found: 304.1455.

2.3 Syntheses of pyrido[1,2-a]quinoxalines derivatives P^2 - P^5

Detailed synthetic procedures along with characterization data have been provided below:

2.3.1 Synthesis of 2-[benzyl-amino]-pyrido[1,2-a]quinoxalin-11-ylum nitrate (P^2)

$\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (0.29 g, 0.72 mmol) was added to a solution of L^2 (0.10 g, 0.37 mmol) in (10 mL) methanol and stirred for 2 h. at room temperature. The red color solution was evaporated to dryness, washed with hexane and acetone respectively. The sticky solid compound was obtained. The needle-like red crystals were formed within 24 h by slow evaporation of methanolic solution. The crystals were collected, washed with diethyl ether and dried over silica gel in vacuum desiccator. Yield: (0.09 g, 74%). Characterization data for P^2 : Melting point 230-232 °C. Λ_M (MeOH): 89.98 $\text{S cm}^2 \text{ mol}^{-1}$. ESI-MS (M^+): Calcd 272.12; Found: 272.14. UV-vis (MeOH): $\lambda_{\max}$, nm (ϵ , $M^{-1} \text{ cm}^{-1}$): 254 (16,000), 291 (21,000), 372 (5,000), 488 (13,000). IR (KBr, cm^{-1}): $\nu(\text{HC}=\text{N})$, 1617 $\nu(\text{N}-\text{H})$, 3266 $\nu(\text{NO}_3^-)$ 1384. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ (ppm) 10.03, (1H, d, $J = 6.4$ Hz) 9.63 (NH, s) 9.51 (1H s), 8.84 (1H, d, $J = 8.4$ Hz), 8.77 (1H, t, $J = 8.0$ Hz), 8.41 (1H, t, $J = 6.4$ Hz) 8.25 (1H, m), 8.23 (1H, m), 7.44 (4H, m), 7.18 (1H, t, $J = 6.8$ Hz). HRMS (ESI) m/z $[M]^+$ calcd for $\text{C}_{18}\text{H}_{14}\text{N}_3$: 272.1188 found: 272.1187.

2.3.2 Synthesis of 2-[(Pyridin-2-ylmethyl)-amino]-pyrido[1,2-a]quinoxalin-11-ylum nitrate (P^3)

$\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (0.14 g, 0.35 mmol) was added to a solution of L^3 (0.10 g, 0.34 mmol) in (10 mL) methanol and stirred for 2 h at room temperature. The color of solution was red with orange fluorescence. The reaction mixture was evaporated to dryness where upon a sticky and hygroscopic compound was obtained. The compound was extracted from the reaction mixture

with acetone and allowed to crystallization at room temperature. Fine needle-shaped red crystals were formed in 24 h. The crystals were collected, washed with diethyl ether and dried over silica gel in vacuum desiccator. Yield: (0.02 g, 20%). Characterization data for **P³**: Melting point 235-237 °C. Λ_M (MeOH): 157 S cm² mol⁻¹. ESI-MS (M^+): Calcd 288.1297; Found 287.1316. UV/vis (MeOH): λ_{max} , nm (ϵ , M⁻¹ cm⁻¹): 265 (61,000) 310 (sh), 367 (12,000), 473 (35,000). IR (KBr, cm⁻¹): ν (N-H) 3338, ν (NO₃⁻) 1384. Fluorescence (MeOH): λ_{ex} , 480; λ_{em} , 590. ¹H NMR (400 MHz, DMSO-d₆) δ (ppm) 10.12 (1H, d, J = 7.2 Hz), 9.44 (1H, s), 8.80 (1H, d, J = 8.4 Hz), 8.74 (2H, m), 8.42 (1H, t, J = 7.2 Hz), 8.15 (1H, m), 8.14 (1H, m), 7.82 (1H, s), 7.70 (1H, d, J = 8.0 Hz) 7.61 (1H, m), 7.61 (1H, m), 4.93 (2H, s). HRMS (ESI) m/z [M]⁺ calcd for C₁₈H₁₅N₄: 287.1297 found: 287.1296.

2.3.3 Synthesis of 4-[(4-Phenylamino-phenylimino)-methyl]-pyridinium nitrate (**P⁴**)

Fe(NO₃)₃·9H₂O (0.29 g, 0.72 mmol) was added to a solution of **L⁴** (0.10 g, 0.37 mmol) in 10 mL methanol and stirred for 3 h under ice cold condition. The red colored solution was evaporated to dryness, washed with hexane and acetone respectively. A sticky solid compound was obtained. Fine needle-like red crystals were formed within 24 h by slow evaporation from a methanolic solution. The crystals were washed with diethyl ether and dried over silica gel in a vacuum desiccator. Yield: (0.07 g, 70%). Characterization data for **P⁴**: Melting point 239-240 °C. Λ_M (MeOH): 73 S cm² mol⁻¹. ESI-MS (M^+): Calcd 274.13; Found 274.13. UV/vis (MeOH): λ_{max} , nm (ϵ , M⁻¹ cm⁻¹): 205 (38,000), 284 (5,000), 409 (6,000). IR (KBr, cm⁻¹): ν (N-H) 3259, ν (NO₃⁻) 1384. ¹H NMR (400 MHz, DMSO-d₆) δ (ppm) 8.68 (2H, d, J = 4.8 Hz), 8.42 (1H, s, HC=N), 7.80 (2H, d, J = 4.4 Hz), 7.35 (2H, d, J = 8.0 Hz), 7.26 (2H, t, J = 7.6 Hz) 7.12 (2H, d, J = 3.6 Hz), 7.10 (2H, d, J = 3.6 Hz), 6.86 (1H, t, J = 7.2 Hz). HRMS (ESI) m/z [M]⁺ calcd for C₁₈H₁₆N₃: 274.1344 found: 274.1348.

2.3.4 Synthesis of 4-[(hydroxybenzyl-methyl)-amino]-pyrido[1,2-a]quinoxalin-11-ylum nitrate [**P⁵**]**P⁵**)

Fe(NO₃)₃·9H₂O (0.27 g, 0.66 mmol) was added to a solution of **L⁵** (0.20 g, 0.66 mmol) in (20 mL) methanol and was stirred for 2 h at room temperature. The color of the solution changed from yellow to red with red fluorescence of the reaction mixture was continued. The reactions stirring for another 2 h in the open atmosphere. The red colored solution was

evaporated to dryness, washed with hexane and acetone respectively. The fine needle-like red crystals were formed within 24 h by slow evaporation of a methanolic solution. The crystals were collected, washed with diethyl ether and dried over silica gel in a vacuum desiccator. The quality of crystal was not good for the X-ray data collection. Yield: (0.09 g, 37%). Characterization data for **P⁵**: Melting point 138-140 °C. Λ_M (MeOH): 80 S cm² mol⁻¹. ESI-MS (**M⁺**): Calcd 302.40; Found 302.36. IR (KBr, cm⁻¹): ν (N-H) 3259, ν (NO₃⁻) 1384. UV/vis (MeOH): $\lambda_{\max}$, nm (ϵ , M⁻¹ cm⁻¹): 270 (37,000), 320 (sh), 385 (4,000), 495 (2,000). Fluorescence (MeOH): λ_{ex} , 530; λ_{em} , 623. ¹H NMR (400 MHz, DMSO-d₆) δ (ppm) 10.13 (1H, d, J = 6.8 Hz), 9.36 (1H, s, HC=N), 9.45 (OH, br), 8.76 (1H, d, J = 7.6 Hz), 8.68 (1H, d, J = 8.0 Hz), 8.39 (1H, t, J = 7.2 Hz) 8.06 (1H, d, J = 8.8 Hz), 8.01 (NH, broad), 7.73 (1H, s), 7.52 (1H, d, J = 8.0 Hz), 7.28 (2H, d, J = 8.0 Hz), 6.75 (2H, d, J = 8.4 Hz), 4.50 (CH₂, d, J = 5.2 Hz). HRMS (ESI) m/z [**M**]⁺ calcd for C₁₉H₁₆N₃O: 302.1293 found: 302.1299.

2.4 Syntheses of complexes C1-C2

2.4.1 Synthesis of manganese complex [Mn(L²)Cl₂] (**C1**)

MnCl₂.6H₂O (0.04s g, 0.17 mmol) was added to a solution of **L²** (0.10 g, 0.37 mmol) in (20 mL) methanol and stirred for 2 h at room temperature. The color of solution was changed from yellow to red within minutes. The mixture was concentrated to 10 mL, solid compound precipitated out, which was filtered off, washed with methanol and dried in vacuum desiccator. The dark red-colored block-like crystals were formed in 48 h by slow evaporation of methanol. The crystals were collected, washed with methanol and diethyl ether respectively and dried over silica gel in vacuum desiccator. Yield: (0.25 g, 74%). Characterization data for [Mn(**L²**)₂Cl₂] (**C1**): Magnetic moment (μ_{eff}): 5.61 B.M. EPR (solid state at room temperature): g_{av} , 2.006, A_{av} , 183G. Λ_M (MeOH): 104 S cm² mol⁻¹. UV/vis (MeOH): $\lambda_{\max}$, nm (ϵ , M⁻¹ cm⁻¹): 278 (57,000), 396 (59000). IR (KBr, cm⁻¹): 1650 (C=N_{im}), 1600 (C=N_{py}).

2.4.2 Synthesis of cobalt complex $[\text{Co}(\text{L}^2)\text{Cl}_2]$ (C2)

$\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (0.04 g, 0.18 mmol) was added to a solution of L^2 (0.10 g, 0.36 mmol) in (20 mL) methanol and stirred for 2 h at room temperature. The color of solution changed from yellow to red within a minute. The mixture was concentrated to 10 mL, solid compound was precipitated out, which was filtered off, washed with methanol and dried in desiccator. The dark red-colored block-like crystals obtained after few days by slow evaporation of methanol. The crystals were collected, washed with methanol and diethyl ether respectively and dried over silica gel in vacuum desiccator. Yield: (0.25 g, 74%). Characterization data for $[\text{Co}(\text{L}^2)_2\text{Cl}_2]$ (C2): Magnetic moment (μ_{eff}) 4.40 B.M. Λ_{M} (MeOH): $104 \text{ S cm}^2 \text{ mol}^{-1}$. UV/vis (MeOH): λ_{max} , nm (ϵ , $\text{M}^{-1} \text{ cm}^{-1}$): 282 (94,000), 406 (59,000). IR (KBr, cm^{-1}): 1652(C=N_{im}), 1610(C=N_{py}).

2.5 X-ray Data Collection, Structure Solution and Refinement

The crystal structures of L^2 , L^3 , L^5 , P^2 , P^3 , P^4 , C1 and C2 were obtained by single crystal X-ray diffraction technique. Single crystals of all compounds were obtained by slow evaporation of methanolic solution except P^3 which was grown by slow evaporation of the acetone solution of the compounds. Selected crystallographic data of L^2 , L^3 , L^5 , P^2 and P^3 , P^4 , C1, C2 are given in Table 2.1 and Table 2.2 respectively. The crystals of all compounds were mounted on glass fiber. All geometric and intensity data for the crystals were collected at room temperature using a Bruker SMART APEX CCD diffractometer equipped with a fine focus 1.75 kW sealed tube Mo $\text{K}\alpha$ ($\lambda = 0.71073 \text{ \AA}$) X-ray source, with increasing ω (width of 0.3° per frame) at a scan speed of 3 s/frame. The SMART software was used for data acquisition and the SAINT software for data extraction. Structures were solved and refined using SHELX97.⁴ All non-hydrogen were refined isotropically.

Table 2.1 Crystallographic data and refinement parameters for compounds^a

Compounds	L ²	L ³	L ⁵	P ⁴
Empirical formula	C ₁₈ H ₁₅ N ₃	C ₁₈ H ₁₈ N ₄	C ₁₉ H ₁₇ N ₃ O	C ₁₈ H ₁₆ N ₄ O ₃
<i>M</i>	273.33	290.36	303.36	336.35
Wavelength Å	0.71073	0.71073	0.71073	0.71073
Crystal system	Orthorhombic	Orthorhombic	Monoclinic	Monoclinic
Space group	<i>Pbca</i>	<i>Pbca</i>	<i>P2₁/c</i>	<i>Cc</i>
<i>a</i> , Å	16.8838(5)	7.4512(4)	10.5652(7)	10.8196(18)
<i>b</i> , Å	9.7056(3)	10.1650(6)	7.9136(6)	17.1220(3)
<i>c</i> , Å	17.9541(6)	19.9519(11)	18.3207(12)	8.8963(14)
α , deg	90.000	90.000	90.000	90.000
β , deg	90.000	90.000	92.072(4)	96.832(8)
γ , deg	90.000	90.000	90.000	90.000
<i>V</i> /Å ³	2942.09(15)	1511.19(15)	1530.77(18)	1636.32
<i>Z</i>	8	4	4	4
ρ /g cm ⁻³	1.234	1.276	1.316	1.365
μ /mm ⁻¹	0.075	0.079	0.084	0.096
Reflns collected	18750	11407	6999	5097
Indep reflns	2379	542	1753	1883
GOF	1.035	1.089	0.631	1.013
Final R indices [<i>I</i> >2 σ (<i>I</i>)]	R1 = 0.0388	R1 = 0.0388	R1 = 0.0420	R ₁ = 0.0478
	wR2=0.0993	wR2=0.1039	wR2 = 0.0719	wR ₂ = 0.0999
R indices (all data)	R1= 0.0602	R1= 0.0505	R1 = 0.0956	R ₁ = 0.0785
	wR2=0.1099	wR2=0.1104	wR2 = 0.2176	wR ₂ = 0.1168

^aRefinement methods: full-matrix least-square on *F*².

Table 2.2 Crystallographic data and refinement parameters^a

Compounds	[P ²]NO ₃	[HP ³](NO ₃) ₂	[Mn(L ²) ₂ Cl ₂]	[Co(L ²) ₂ Cl ₂]
Empirical formula	C ₁₈ H ₁₆ N ₄ O ₃	C ₁₈ H ₁₈ N ₆ O ₇	C ₃₆ H ₃₀ Cl ₂ MnN ₆	C ₃₆ H ₃₀ Cl ₂ CoN ₆
<i>M</i>	336.35	430.38	672.50	676.49
Wavelength Å	0.71073	0.71073	0.71073	0.71073
Crystal system	Orthorhombic	Triclinic	Monoclinic	Orthorhombic
Space group	<i>Fdd2</i>	<i>P</i> -1	<i>P</i> 2 ₁ / <i>c</i>	<i>Pbcn</i>
<i>a</i> , Å	13.0161(10)	7.4629(4)	15.9810(16)	10.9078(9)
<i>b</i> , Å	79.761(5)	8.3156(4)	10.8265(12)	18.9290(14)
<i>c</i> , Å	6.1998(3)	15.5626(7)	19.354(2)	15.9883(13)
α , deg	90.000	90.413(4)	90.000	90.000
β , deg	90.000	90.289(4)	91.129(4)	90.000
γ , deg	90.000	103.564(4)	90.000	90.000
<i>V</i> / Å ³	6436.5(7)	1511.1115	3372.0(4)	3301.2(5)
<i>Z</i>	8	2	4	4
ρ /g cm ⁻³	1.413	1.523	1.435	1.361
μ /mm ⁻¹	0.101	0.120	0.595	0.717
Reflns collected	18540	7738	5579	1015
Indep reflns	3731	1953	3181	768
GOF	1.092	1.007	1.090	1.073
Final R indices [<i>I</i> >2 σ (<i>I</i>)]	R1 = 0.0615 wR2=0.1150	R1=0.0498 wR2 = 0.1342	R1 = 0.0466 wR2 = 0.1053	R1 = 0.0452 wR2 = 0.1202
R indices (all data)	R1 = 0.0687 wR2=0.1649	R1=0.0677 wR2=0.1498	R1 = 0.0607 wR2 = 0.1124	R1 = 0.0636 wR2 = 0.1415

^aRefinement methods: full-matrix least-square on *F*².

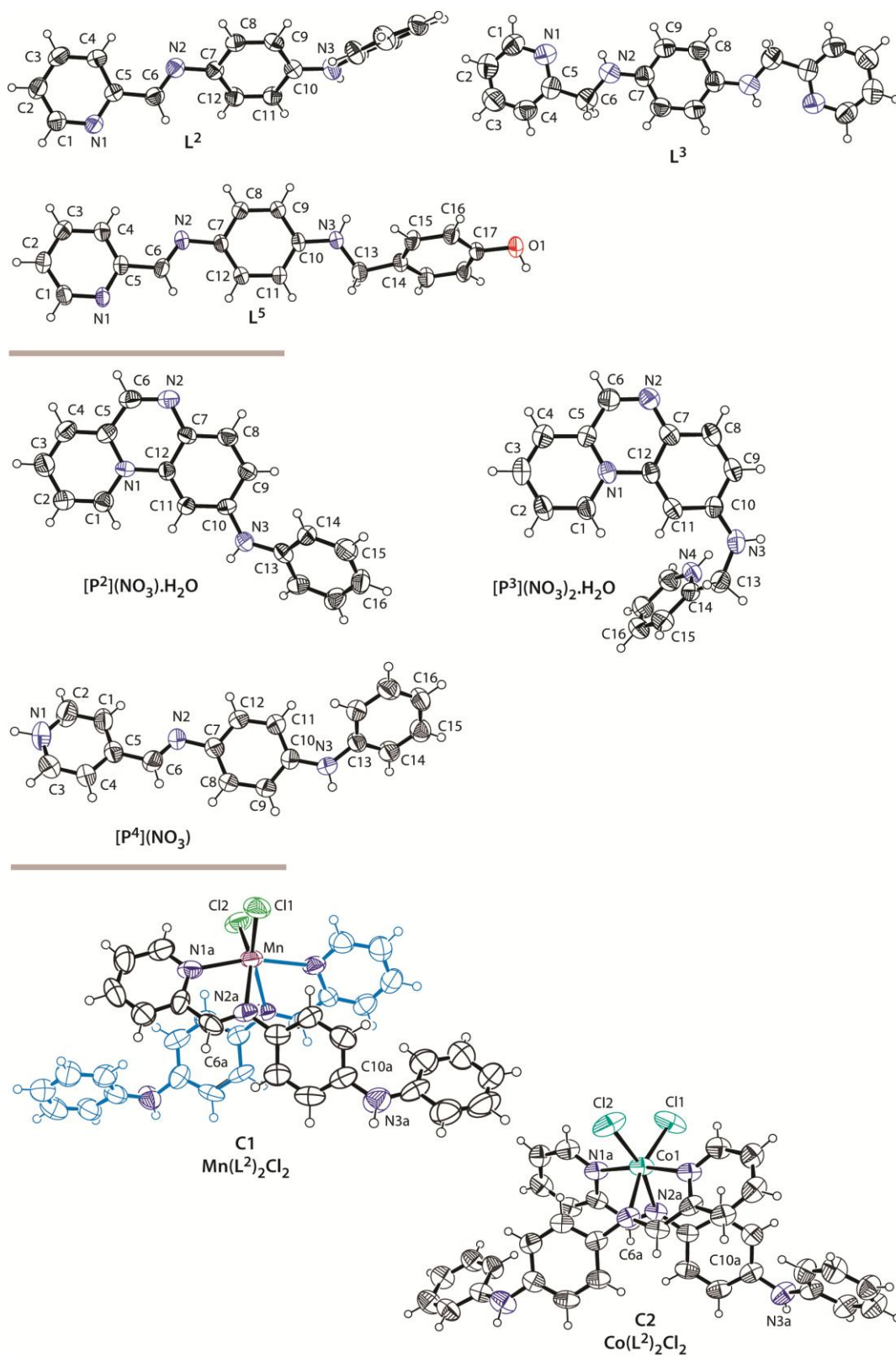


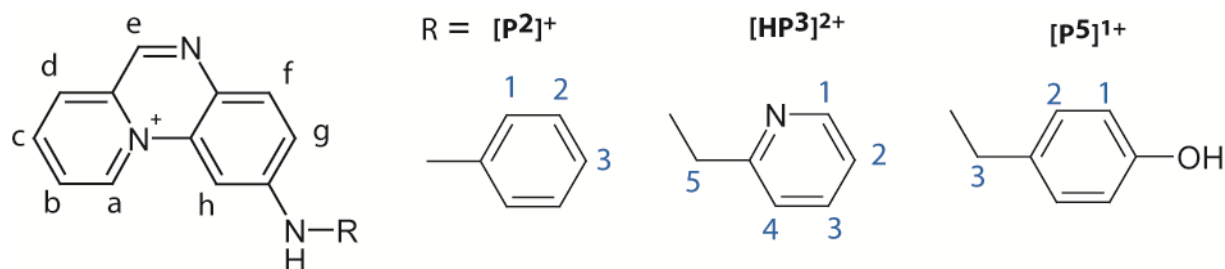
Figure 2.1 ORTEP drawing of ligands **L²**, **L³**, **L⁵** compounds **P²**, **P³**, **P⁴** and complexes **C1**, **C2** with 40% probability thermal ellipsoids.

Table 2.3 Selected bond distances (Å) of compounds

L²							
N1-C1	1.336(2)	C1-C2	1.364(2)	C2-C3	1.372(2)	C3-C4	1.369(2)
C5-C4	1.384(2)	C5-N1	1.338(19)	C6-C5	1.469(2)	C6-N2	1.269(19)
C7-N2	1.412(19)	C7-C8	1.389(2)	C9-C8	1.370(2)	C10-C9	1.396(2)
C1-C11	1.392(2)	C1-C12	1.380(2)	C7-C12	1.391(2)	C10-N3	1.394(19)
C13-N3	1.395(19)	C1-C14	1.388(2)	C1-C15	1.381(2)	C16-C15	1.376(2)
C16-C17	1.371(2)	C18-C17	1.372(2)	C13-C18	1.395(2)		
L³							
C1-N1	1.341(4)	C2-C1	1.359(5)	C3-C2	1.356(5)	C4-C3	1.365(5)
C5-C4	1.382(5)	C5- N1	1.345(4)	C5- C6	1.505(5)	C6-N2	1.401(4)
C7-N2	1.395(4)	C8-C7	1.396(5)	C9-C7	1.386(5)	C8-C9	1.365(5)
L⁵							
N1-C1	1.347(2)	C2-C1	1.369(3)	C3-C2	1.375(3)	C4-C3	1.389(3)
C5-C4	1.383(3)	C6-C5	1.463(3)	N1-C5	1.346(2)	N2-C6	1.257(2)
N2-C7	1.411(2)	C7-C8	1.383(2)	C8-C9	1.373(2)	C10-C9	1.390(3)
C10-C11	1.391(2)	C11-C12	1.385(2)	C12-C7	1.379(3)	N3-C10	1.373(2)
N3-C13	1.435(2)	C14-C13	1.520(2)	C15-C14	1.384(3)	C16-C15	1.389(2)
C17-C16	1.369(2)	C18-C17	1.371(2)	O1-C17	1.393(2)	C18-C19	1.386(2)
C14- C19	1.380(3)						
P⁴							
C2-N1	1.323(7)	C1-C2	1.370(8)	C5-C1	1.377(7)	C5-C4	1.385(7)
C3-C4	1.384(8)	N1-C3	1.326(8)	C5-C6	1.477(7)	N2-C6	1.265(6)
C7-N2	1.419(6)	C7-C8	1.387(6)	C9-C8	1.394(7)	C10-C9	1.388(6)
C10-N3	1.391(6)	C10-C11	1.401(7)	C12-C11	1.385(7)	C12 -C7	1.388(7)
N3-C13	1.402(6)	C14-C13	1.401(7)	C14-C15	1.386(7)	C15-C16	1.368(8)
C17-C16	1.371(7)	C17-C18	1.400(7)	C18- C13	1.375(7)		
P²							
N1-C1	1.379(3)	C1-C2	1.358(4)	C3-C2	1.382(5)	C3-C4	1.360(5)
C5-C4	1.381(4)	N1-C5	1.369(4)	C5-C6	1.429(4)	N2-C6	1.290(4)
N2-C7	1.391(4)	C12-C7	1.397(4)	N1-C12	1.420(4)	C7-C8	1.395(4)
C9-C8	1.358(4)	C10-C9	1.413(4)	C11-C10	1.380(4)	C12-C11	1.391(4)
N3-C10	1.375(4)	N3-C13	1.407(4)	C13-C14	1.378(4)	C15-C14	1.377(5)
C15-C16	1.356(5)	C17-C16	1.393(5)	C18-C17	1.386(5)	C13-C18	1.373(4)
P³							
N1-C1	1.381(5)	C1-C2	1.347(6)	C3-C2	1.398(6)	C3-C4	1.358(6)
C5-C4	1.386(6)	C5-C6	1.426(6)	N1-C5	1.368(5)	N2-C6	1.295(5)
N2-C7	1.380(5)	C8-C7	1.389(6)	C8-C9	1.352(5)	C10-C9	1.421(6)
C11-C10	1.396(6)	C12-C7	1.407(6)	C12-C11	1.385(5)	N1-C12	1.424(5)
N3-C10	1.354(5)	N3-C13	1.434(6)	C14-C13	1.498(6)	C15-C14	1.332(5)
C15-C16	1.314(6)	C17-C16	1.374(7)	C17-C18	1.361(7)	N4-C18	1.397(6)
C14-N4	1.392(6)						

Table 2.4 Selected bond distances (Å) and angles (°) of complexes **C1** and **C2**

Compounds	[Mn(L ²) ₂ Cl ₂](C1)	[Co(L ²) ₂ Cl ₂](C2)
M-Cl(1)	2.437(2)	2.376(2)
M-Cl(2)	2.430(2)	2.382(2)
M-N(2) _{imine}	2.369(6)	2.224(6)
M-N(2A) _{imine}	2.405(7)	2.224(6)
M-N(1) _{py}	2.256(7)	2.150(6)
M-N(1A) _{py}	2.242(7)	2.143(6)
N(2A)-C(6A)	1.273(9)	1.288(9)
N(2A)-C(7A)	1.421(10)	1.423(9)
C(10A)-N(3A)	1.398(11)	1.412(10)
Cl(2)-M-Cl(1)	100.16(8)	97.86(10)
N(2) -M-Cl(2)	92.32(17)	93.60(15)
N(2)-M-N(2A)	74.1(2)	77.27(19)
N(2A)-M-Cl(1)	98.25(15)	93.58(16)
N(1)-M-N(2)	71.2(4)	75.4(3)
N(1A)-M-N(2A)	71.0(4)	75.4(2)
N(1A)-M-N(1)	162.8(4)	170.3(2)
N(2)-M-Cl(1)	161.3(3)	164.47(19)
N(2A)-M-Cl(2)	156.1(2)	164.63(19)



Scheme 2.2 The quinoxaline derivatives with ^1H NMR labeling scheme.

Table 2.5 ^1H NMR chemical shift data for quinoxaline derivatives

Chemical Shifts (ppm)									
Compounds	Solvent	H ^a	H ^b	H ^c	H ^d	H ^e	H ^f	H ^g	H ^h
[P ¹](NO ₃)	d ₄ -CD ₃ OD	9.76d	8.25m	8.56m	8.61m	9.18s	8.01d	7.38m	7.66d
[P ²](NO ₃)	d ₄ -CD ₃ OD	9.76d	8.24t	8.63m ⁱ	8.58m ⁱ	9.26s	8.11d	7.65d	8.04s
[P ²](NO ₃)	d ₆ -DMSO	10.03d	8.41t	8.77t	8.84d	9.51s	8.23m ⁱ	7.74d	8.25m ⁱ
[HP ³](NO ₃) ₂	d ₆ -DMSO	10.12d	8.42t	8.74m ⁱ	8.80d	9.44s	8.15m ⁱ	7.70d	7.82s
[P ⁵](NO ₃)	d ₆ -DMSO	10.13d	8.39t	8.68t	8.76d	9.36s	8.06d	7.52d	7.73s
		>CH ₂	H ¹	H ²	H ³	H ⁴	>NH		
[P ²](NO ₃)	d ₄ -CD ₃ OD	-	7.43m ⁱ	7.43m ⁱ	7.17t	-	n.o.		
[P ²](NO ₃)	d ₆ -DMSO	-	7.44m ⁱ	7.44m ⁱ	7.18t	-	9.63s		
[HP ³](NO ₃) ₂	d ₆ -DMSO	4.93s	8.74m ⁱ	7.61m ⁱ	8.14m ⁱ	7.61m ⁱ	n.o.		
[P ⁵](NO ₃)	d ₆ -DMSO	4.50d	7.28d	6.75d	-	-	8.00t		
Coupling Constants (Hz)		J _{ab}	J _{bc}	J _{cd}	J _{fg}				
[P ¹](NO ₃)	d ₄ -CD ₃ OD	7.0	7.5	8.0	9.0				
[P ²](NO ₃)	d ₄ -CD ₃ OD	7.2	7 ⁱⁱ	8.0	9.2				
[P ²](NO ₃)	d ₆ -DMSO	6.4	7 ⁱⁱ	8.4	8.8				
[HP ³](NO ₃) ₂	d ₆ -DMSO	7.2	7 ⁱⁱ	8.0	8.0				
[P ⁵](NO ₃)	d ₆ -DMSO	6.8	7 ⁱⁱ	7.6	8.8				

Coupling constant values are within ± 0.4 Hz. ⁱ Overlapped with other proton. ⁱⁱ Approximate value due to multiplet nature. n.o. = not observed.

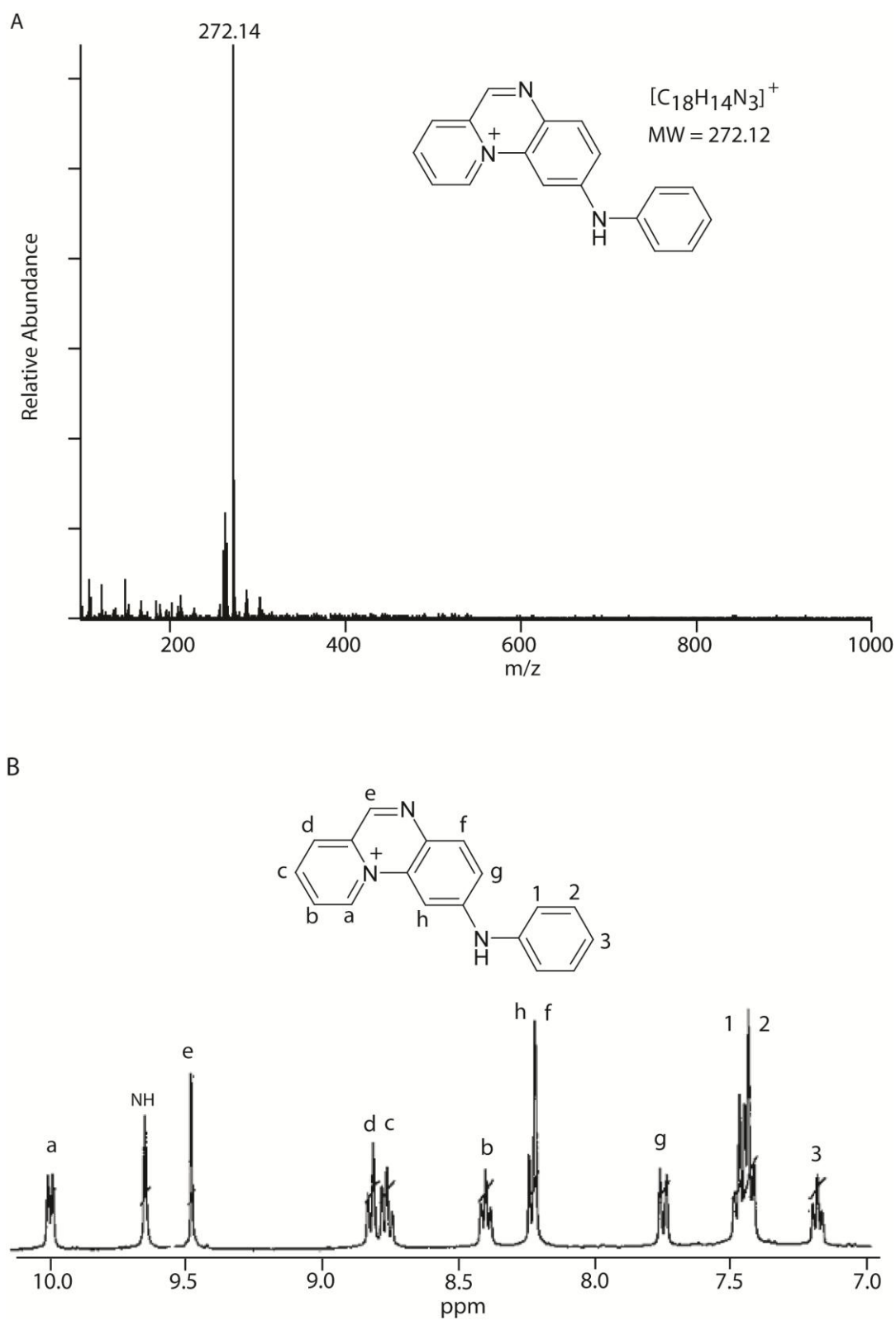


Figure 2.2 (A) ESI mass spectrum and (B) ^1H NMR spectrum with numbering scheme of $[\text{P}^2]\text{NO}_3$.

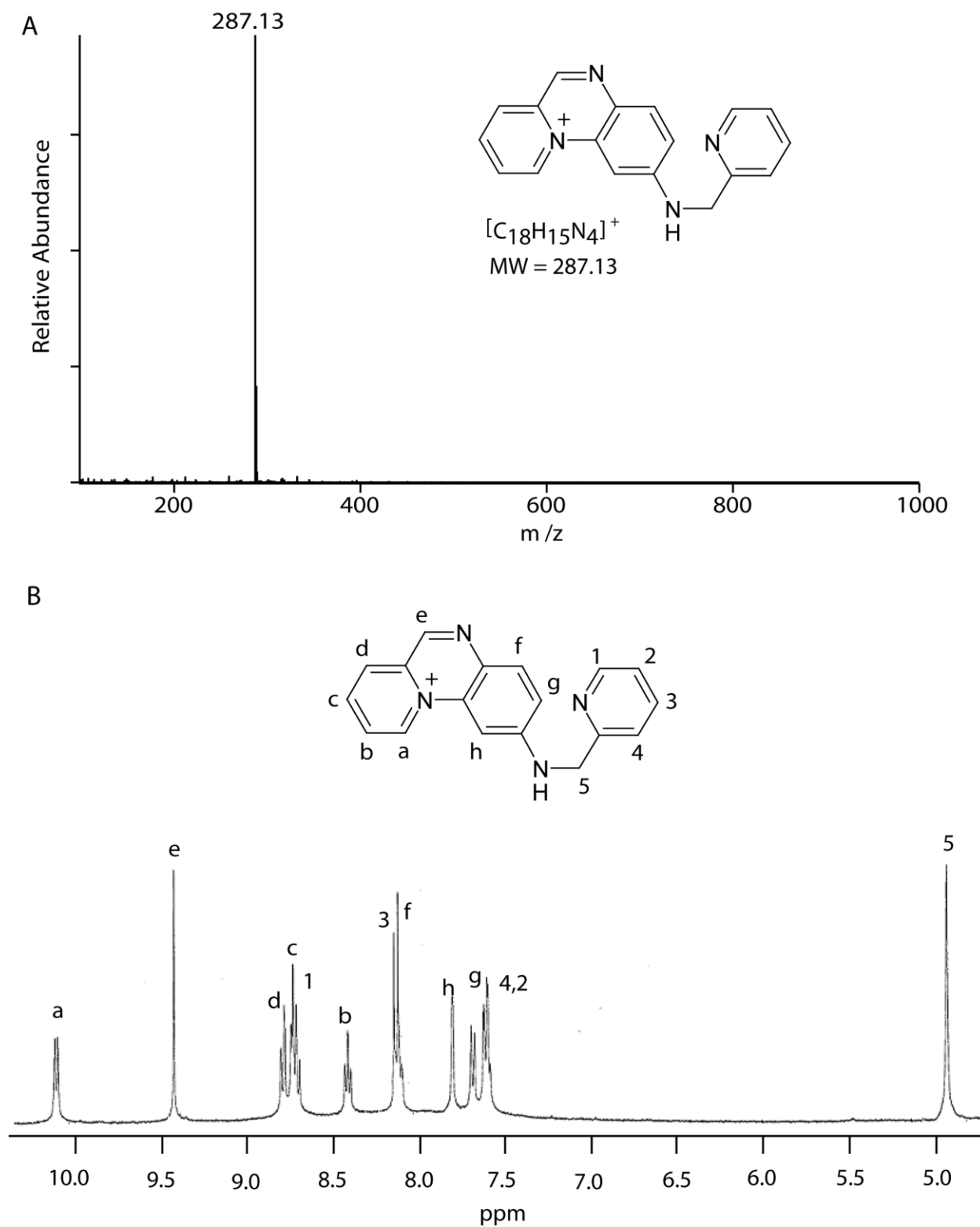


Figure 2.3 (A) ESI mass spectrum and (B) ^1H NMR spectrum with numbering scheme of $[\text{HP}^3](\text{NO}_3)_2$.

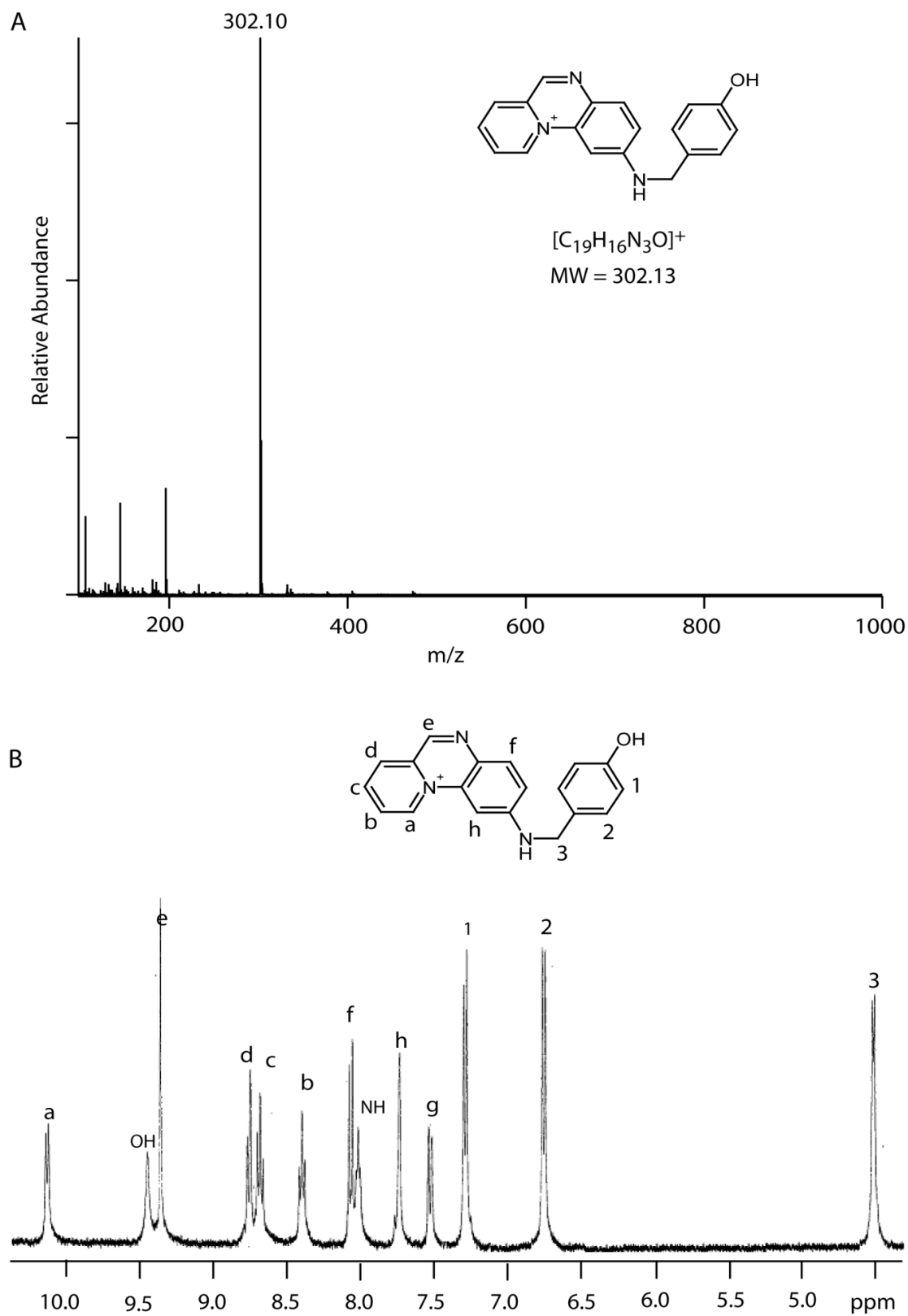


Figure 2.4 (A) ESI mass spectrum and (B) ^1H NMR spectrum with numbering scheme of $[\text{P}^5]\text{NO}_3$.

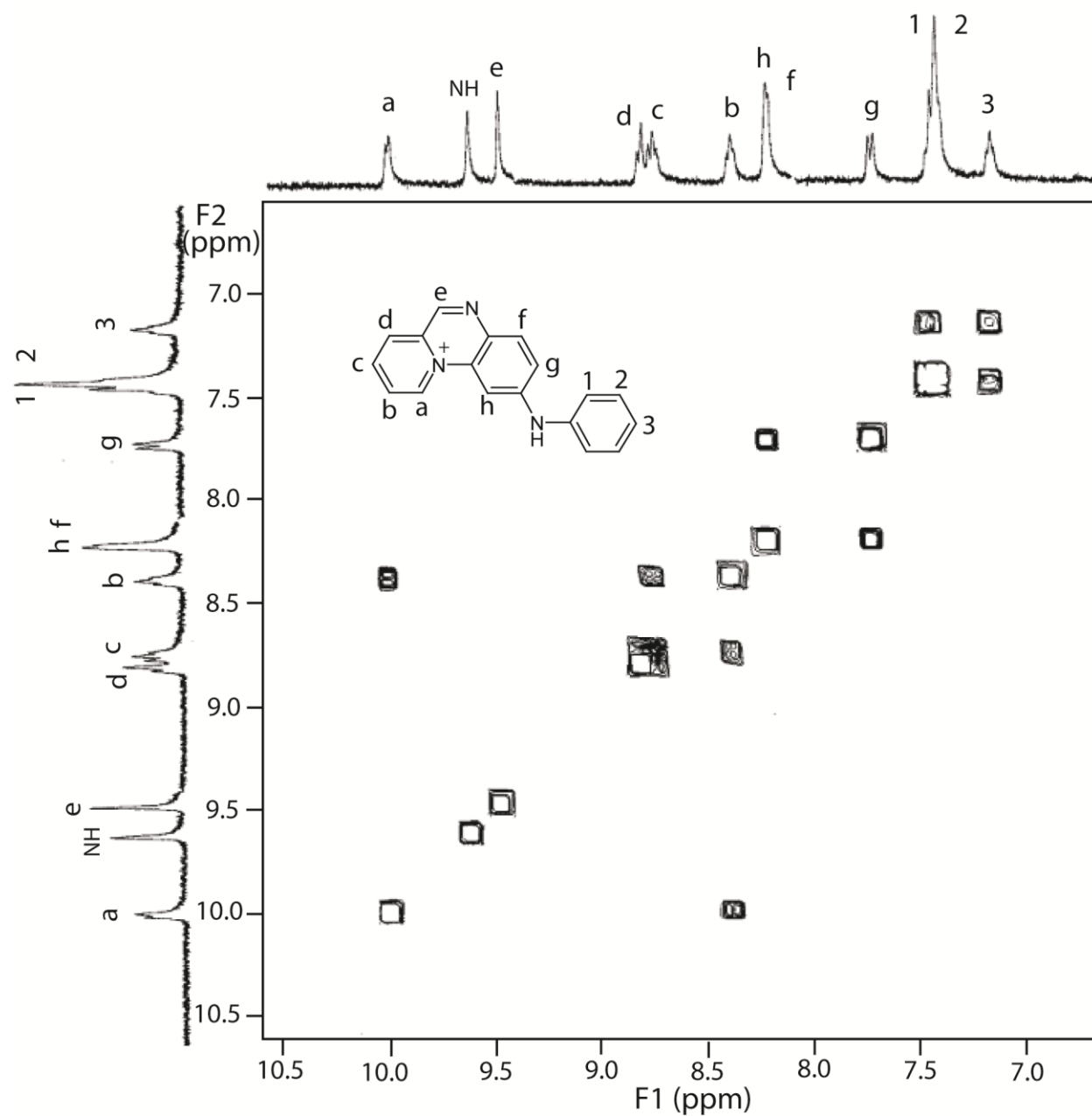


Figure 2.5 The ^1H ^1H -COSY NMR spectrum of 2-[benzyl-amino]-pyrido[1,2-*a*]quinoxalin-11-yl cation nitrate ($[\text{P}^2]\text{NO}_3$) in d_6 -DMSO at 400 MHz.

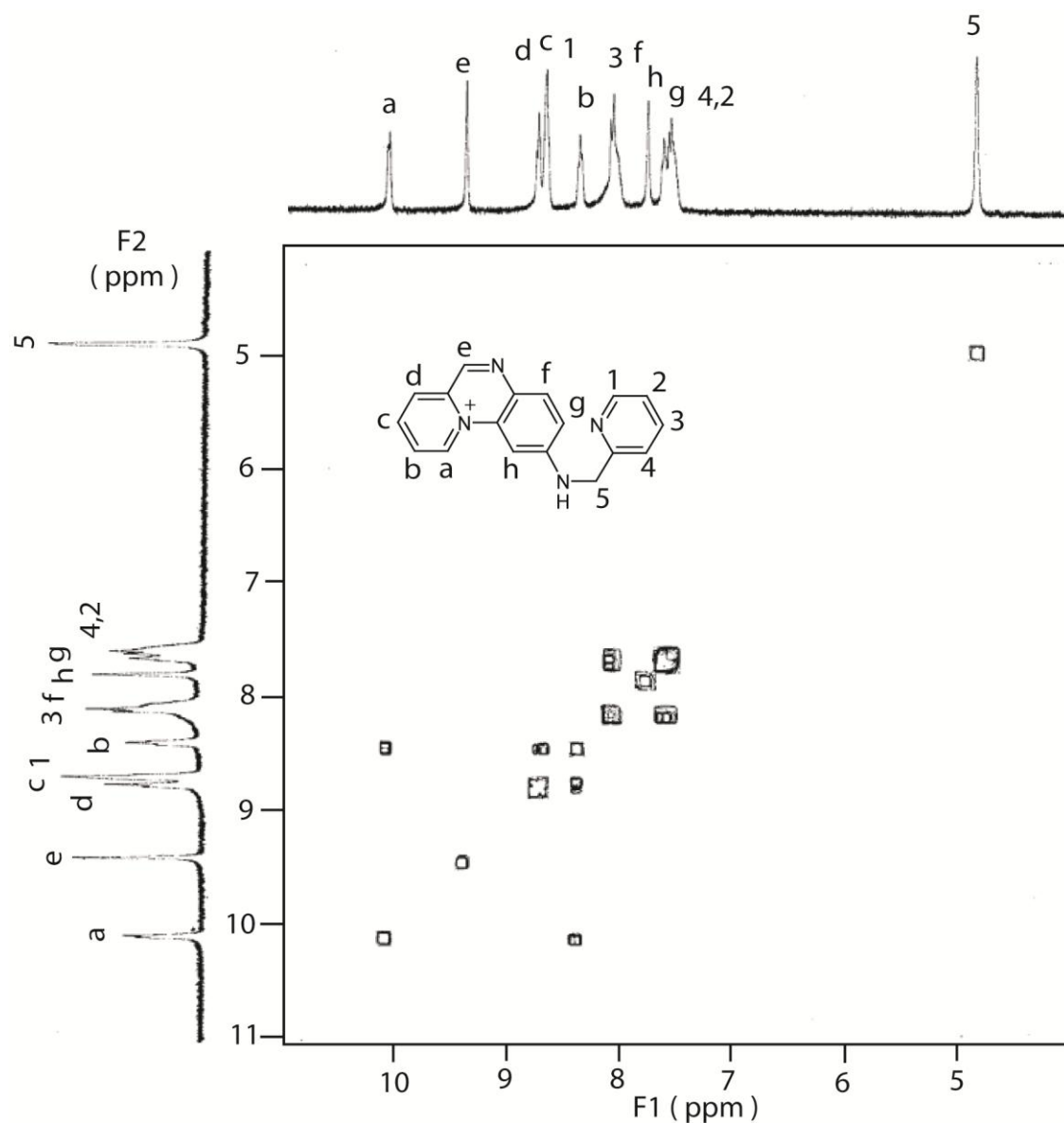


Figure 2.6 The ^1H ^1H -COSY NMR spectrum of 2-[(Pyridin-2-ylmethyl)-amino]-pyrido[1,2-*a*]quinoxalin-11-ylum nitrate ($[\text{HP}^3](\text{NO}_3)_2$) in d_6 -DMSO at 400 MHz.

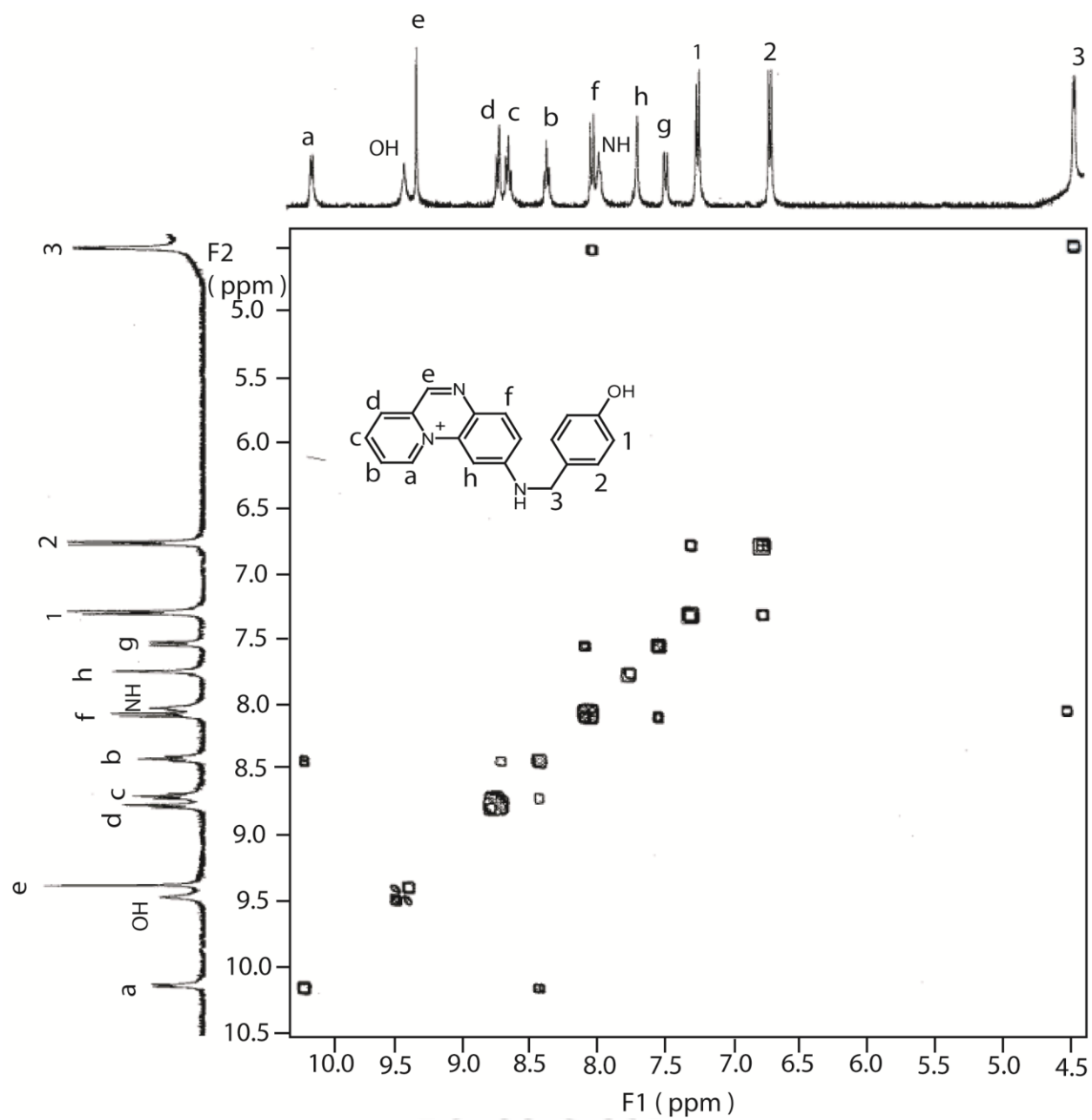


Figure 2.7 The ^1H ^1H -COSY NMR spectrum of 4-[(hydroxybenzyl-methyl)-amino]-pyrido[1,2-*a*]quinoxalin-11-ylum nitrate ($[\text{P}^5]\text{NO}_3$) in d_6 -DMSO at 400 MHz.

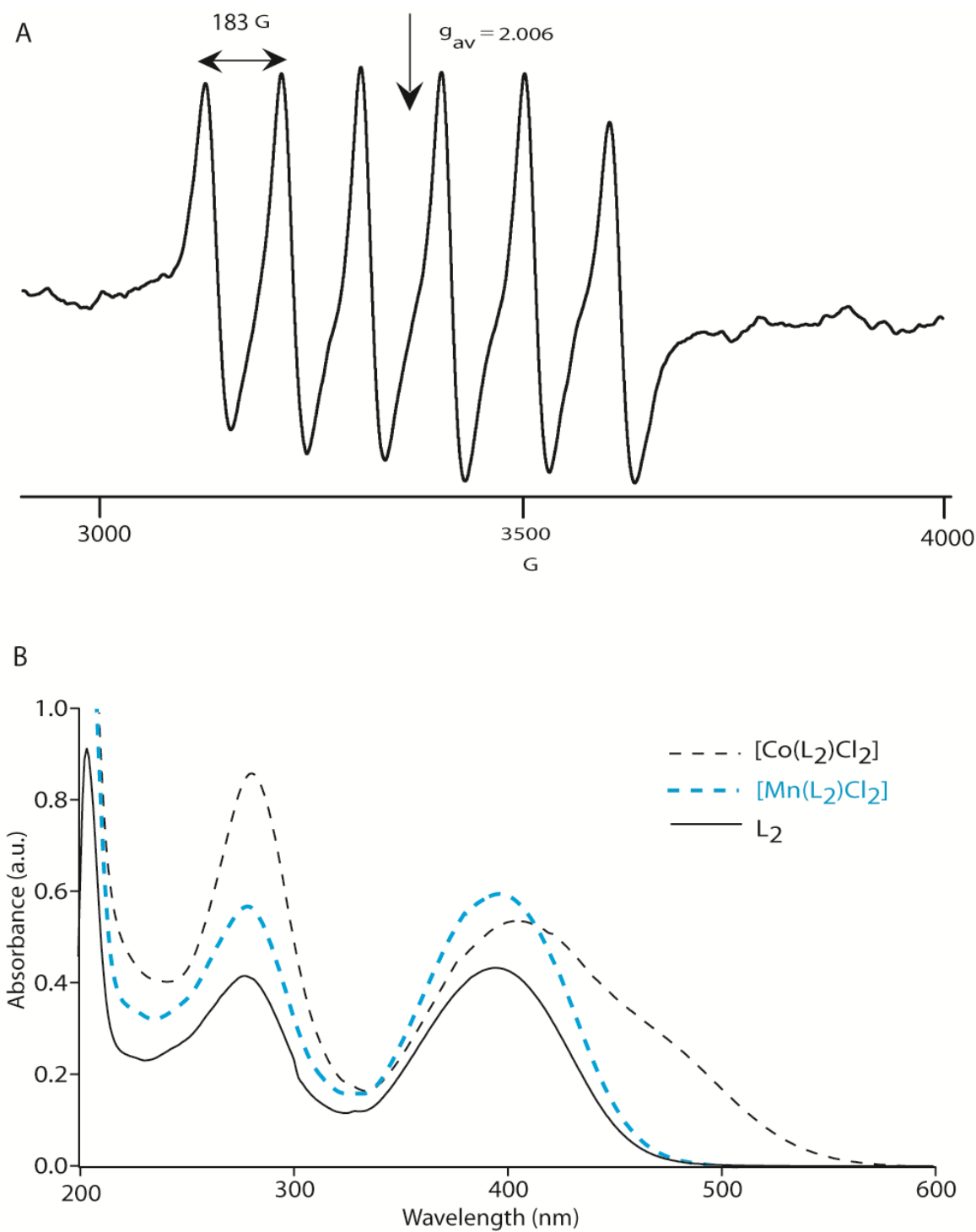


Figure 2.8 (A) EPR spectrum of complex $[\text{Mn}(\text{L}^2)_2\text{Cl}_2]$ (C1) (B) UV/vis spectra of $[\text{Co}(\text{L}^2)_2\text{Cl}_2]$ (C2), L^2 and $[\text{Mn}(\text{L}^2)_2\text{Cl}_2]$ (C1).

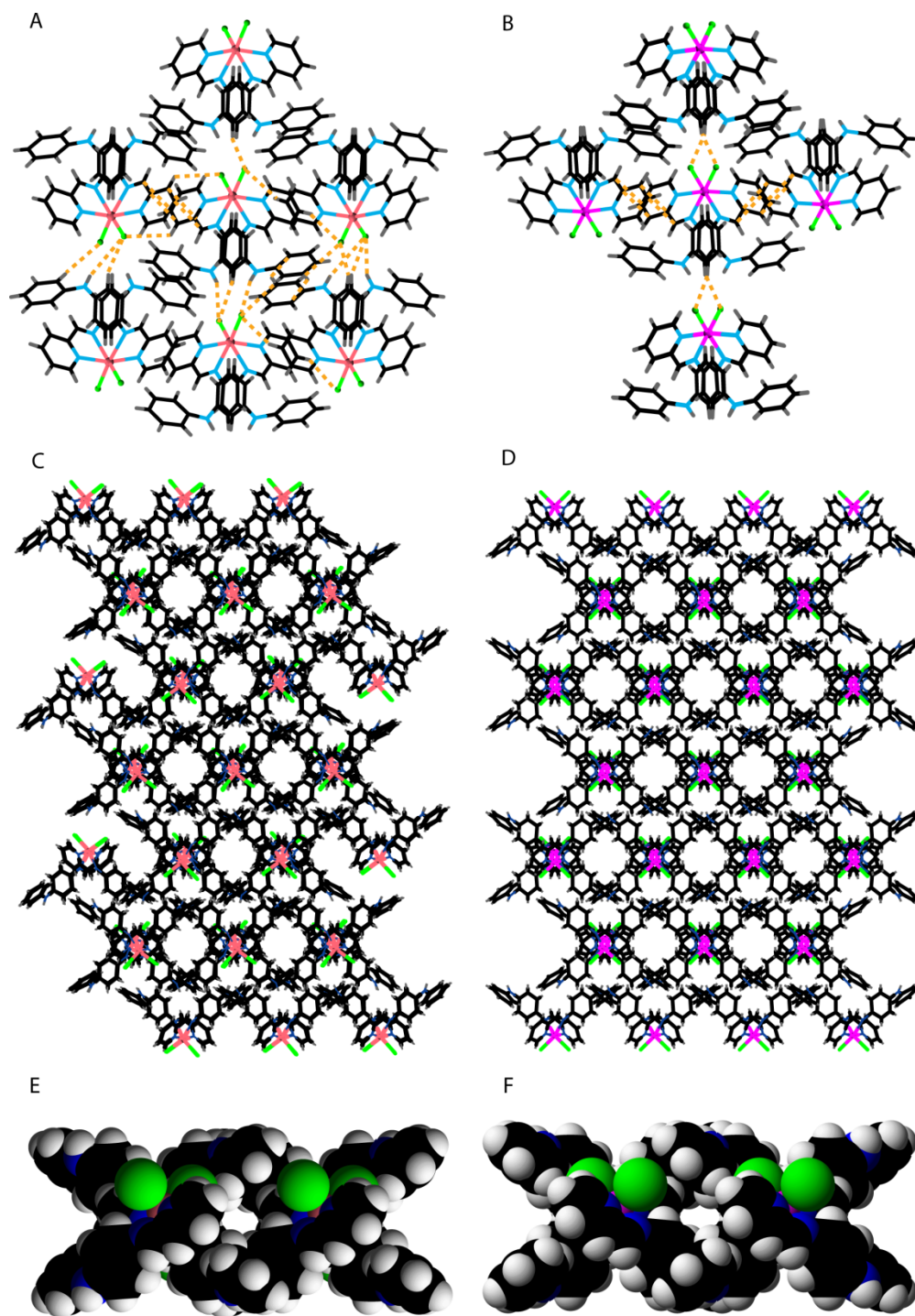


Figure 2.9 (A) H-bond attraction present in Complex [Mn(L²)₂Cl₂] (C1) (B) H-bond attraction present in Complex [Co(L²)₂Cl₂] (C2) (C) Lattice arrangement of the complex [Mn(L²)₂Cl₂](C1) (D) Lattice arrangement of the complex [Co(L²)₂Cl₂] (C2) (E) Spacefill model of [Mn(L²)₂Cl₂](C1) and molecular void (F) Spacefill model of [Co(L²)₂Cl₂] (C2) and molecular void.

2.6 Results and Discussion

2.6.1 Synthesis and characterization of precursors L^2 to L^5

The Schiff-base precursor L^2 and L^4 were prepared by condensation of either pyridine-2-carbaldehyde or pyridine-4-carbaldehyde with N-phenyl-*p*-phenylenediamine in a 1:1 molar ratio in methanol. The formation of the Schiff-base was indicated by strong yellow coloration of the solution. The reaction is facile and readily applicable to multi gram scale synthesis. The FTIR of the products showed bands at 1619 and 1621 cm^{-1} assigned as imine vibration (reported for L^1 at 1617 cm^{-1}). The reduced Schiff-base precursor L^3 was synthesized by treatment of Schiff-base L^1 with NaBH_4 . The absence of imine vibration of 1617 cm^{-1} and presence of new vibration at 3365 cm^{-1} for ν_{NH} in the FTIR of L^3 confirms the reduction. The ESI-mass and ^1H NMR spectra of all four compound supports the formulation (Experimental Section). Further, L^2 and L^3 were also structurally characterized (Sections 2.8.1 and 2.8.2).

The precursor L^5 was prepared in three steps (Scheme 2.1). The formation of unsymmetrical Schiff-base was carried out with aldehyde and *p*-phenylenediamine in a 1:1 ratio in relatively dilute solution. Although we have recrystallized the product from hot methanol, a small quantity of diimine formation cannot be ruled out. Formation of the Schiff-base is supported by an imine band in the FTIR as well as ESI-MS and ^1H NMR spectrum. Reduction of the unsymmetrical Schiff-base using NaBH_4 was performed directly in the solution, without isolation of the unsymmetrical Schiff-base. We found this procedure provided better purity of the product (Figure. 2.10). The isolated reduced Schiff-base was again subjected to condensation with pyridine-2-carbaldehyde to obtain L^5 . The FTIR of L^5 shows ν_{imine} at 1615 cm^{-1} but due to broadness of the region N-H stretches could not be identified. The L^5 was characterized using ^1H NMR spectroscopy, ESI-MS (Experimental section) and X-ray diffraction (section 2.8.3).

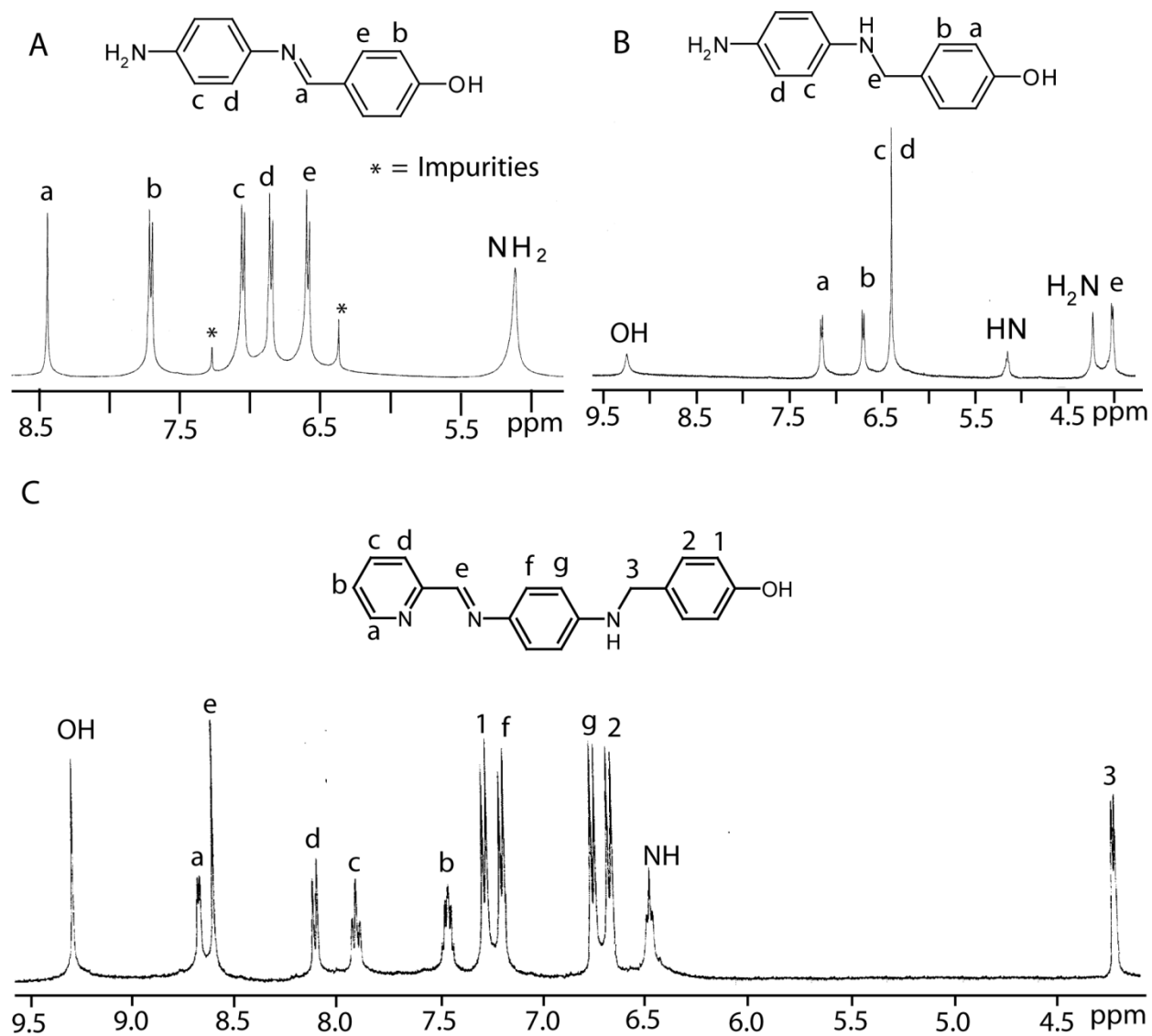


Figure 2.10 (A) ^1H NMR spectrum of 4-aminophenyliminomethylphenol with numbering scheme (B) ^1H NMR spectrum of 4-aminophenylaminomethylphenol with numbering scheme (C) ^1H NMR spectrum of L^5 with numbering scheme.

2.7 Cyclization reaction of precursors L^2 - L^5 and protonation reaction of L^4

2.7.1 Cyclization reaction of precursor L^2

Addition of a light yellow methanolic ferric nitrate solution to a light yellow methanolic L^2 solution in air turned the color of the solution to dark orange immediately. Unlike P^1 , the cyclized product P^2 is not fluorescent. Thus it was not possible to monitor the progress of the reaction using ultraviolet lamp. Both the product P^2 and the byproduct ferrous nitrate, which is likely to stay in solution as a polymeric oxo bridged ferric product due to the aerobic atmosphere, are ionic in nature. These, as well as starting material, do not move on a silica gel thin layer chromatography (TLC) plate, with a number of different solvent combination. Because of these factors we continued the reaction for two hours, even though in all likelihood the reaction was complete within minutes. The isolated product crystallizes well from methanol. All further spectroscopic analysis including structural characterization were performed on these crystals. The molar conductance of P^2 in methanol at $90 \text{ S cm}^2 \text{ mol}^{-1}$ is well within the range $80\text{--}115 \text{ S cm}^2 \text{ mol}^{-1}$ expected for a 1:1 electrolyte.⁵ The FTIR spectrum showed the 1384 cm^{-1} peak characteristic for nitrate. The $\nu_{C=N}$ stretch identified in L^2 (1619 cm^{-1}) remained in P^2 at 1617 cm^{-1} . The structure of P^2 was elucidated from single crystal X-ray diffraction (Section 2.9.1).

Reactions of L^2 with reagents other than ferric nitrate were attempted. In each case ESI-Mass (Figure 2.2 A) of the reaction mixture was used to detect formation of P^2 (m/z 272.1, scanning for +ve ion) The cyclization occurs with nitrate or chloride salts of Cu(II), AgNO_3 and ammoniumceric nitrate but not with Mn(II) or Co(II) chlorides. With MnCl_2 and CoCl_2 , L^2 forms *bis*-complexes (Scheme 2.1). Both of which were structurally characterized (Section 2.10.1 and 2.10.2).

2.7.2 Cyclization reaction of precursor L^3

Addition of a Fe(III) salt to a methanolic solution of L^3 causes immediate darkening of the colour along and the product formation is indicated by the fluorescence under ultraviolet light. The isolation of the product was difficult as both the products and resulting iron salts were highly soluble in water, methanol and most other common solvents. This resulted in a poor yield

(~20%) even though all the filtrates were highly fluorescent. Due to ionic nature of the product chromatography was not possible (immovable on TLC). We attempted to separate the components using cation exchange resins but the compound once passed through the resin could not be released from the resin with mineral acids. The molar conductance of $\mathbf{P}^3$ in methanol was found to be $157 \text{ S cm}^2 \text{ mol}^{-1}$ is closer to the range $160\text{--}220 \text{ S cm}^2 \text{ mol}^{-1}$ expected for 1:2 electrolyte.⁵ The FTIR spectrum of $\mathbf{P}^3$ showed a band at 1621 cm^{-1} identified as $\nu_{\text{C=N}}$. A broad stretch observed at 3337 cm^{-1} was identified as $\nu_{\text{N-H}}$. The characteristic peak for nitrate is also present in FTIR spectrum. The ESI-MS (Figure 2.3A) shows a molecular ion peak at 287.13 (calculated for M^+ 287.1296). The conductance value indicated $\mathbf{P}^3$ as a dication rather than monocationic species. The FTIR spectrum indicated a cyclized product similar to $\mathbf{P}^2$ which is also supported by ESI-Mass data (Figure 2.3A). The confusion about its identity was eventually solved using single crystal X-ray crystallographic analysis (Section 2.9.2). The isolated $\mathbf{P}^3$ is a dicationic species ($[\text{HP}^3]^{2+}$) owing to the protonation of the pyridine. The pK_a of the protonated pyridine was determined using pH titration (10mL of 1mM Vs 0.1M LiOH in H_2O) and found to be ~3.8 (Figure 2.11). Thus dissolving $[\text{HP}^3]^{2+}$ in neutral pH, a small portion will remain as $[\mathbf{P}^3]^+$ due to hydrolysis which explains the ESI-MS analysis. The structural characterization also supported the C=N bond formation in the $\mathbf{P}^3$.

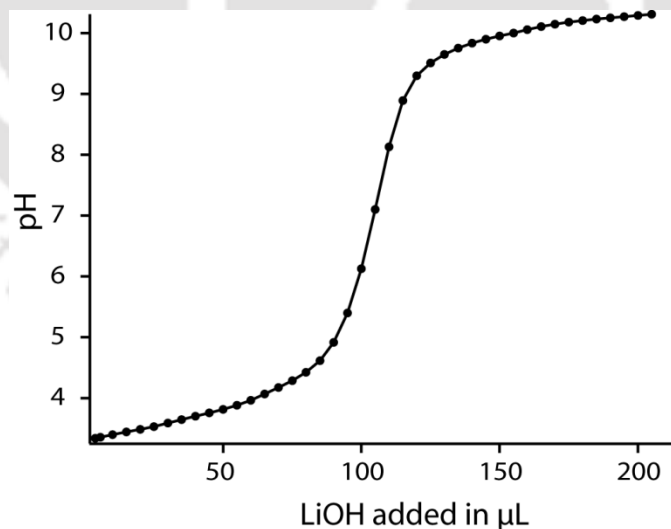


Figure 2.11 pH titration curve for compound $[\text{HP}^3]^{2+}$ in water.

Overall, $\mathbf{L}^3$ undergoes cyclization in presence of Fe(III) salt yielding $\mathbf{P}^3$ as a dicationic $[\mathbf{HP}^3]^{2+}$ form. The $[\mathbf{HP}^3]^{2+}$ salt has a tricyclic ring identical to that in $\mathbf{P}^1$ and $\mathbf{P}^2$ (Scheme 2.1) which means the cyclization of $\mathbf{L}^3$ also involves reoxidation of the reduced amine presumably by oxygen. Reoxidation / rearomatization of a cyclic product in air have also been cited as reason by others.⁶ The addition of Cu(II) salts yields a green brown solid without fluorescence. The solid is soluble in DMF and electronic spectra show a peak at 428 nm with tails in the visible band, presumably a charge transfer band which somewhat covers the d-d transitions expected for a Cu(II) complex. Attempts to purify or crystallization did not yield any tangible results yet. Addition of MnCl_2 or CoCl_2 resulted in darkening of the solution but did not show any sign (fluorescence) of $\mathbf{P}^3$ formation within 3 h but addition of AgNO_3 (Cloudy solution, fluorescence within 30 minutes) or ammonium ceric nitrate (clear dark red solution, strong fluorescence immediately) showed sign of $\mathbf{P}^3$ formation.

2.7.3 Protonation reaction of precursor $\mathbf{L}^4$

A cyclization reaction with $\mathbf{L}^4$, which is analogous to $\mathbf{L}^2$ except the position of the pyridine N, using ferric nitrate under similar condition yielded $\mathbf{P}^4$ as $[\mathbf{P}^4](\text{NO}_3)$ (Scheme 2.1). The ESI- MS and conductance (1:1) is consistent with the formulation of $[\mathbf{P}^4](\text{NO}_3)$ as $[\mathbf{L}^4](\text{NO}_3)$ (Scheme 2.1). Structural characterization eventually (Section 2.9.3) confirms that the product is only protonated $[\mathbf{HL}^4](\text{NO}_3)$ and no cyclization took place. Addition of acid (HNO_3) to $\mathbf{L}^4$ yielded a species identical to $[\mathbf{HL}^4](\text{NO}_3)$ and confirmed from IR and UV/vis spectra. Because of the *para* position of pyridine N, we expected intermolecular cyclization but apparently it did not happen. We are not sure of the reason.

2.7.4 Cyclization reaction of precursor $\mathbf{L}^5$

The precursors $\mathbf{L}^1$ and $\mathbf{L}^3$ are symmetrical around the diamine, which limits the type of derivative possible at the uncyclized arm. The precursor $\mathbf{L}^2$ overcomes this using a commercially available unsymmetrical derivative of *p*-phenylenediamine but the product is not fluorescent. From the standpoint of applications this limits the synthesis of fluorescent tricyclic product with

different derivatives at the open end. Precursor $\mathbf{L}^5$ was synthesized to check if we can make a relatively flexible design, where different derivatives can be made at the open amine. Precursor $\mathbf{L}^5$ reacts with Fe(III) salt in the same way as $\mathbf{L}^2$ yielding $\mathbf{P}^5$ as $[\mathbf{P}^5](\text{NO}_3)$ salt. The product is crystalline but crystals did not diffract well enough to solve the structure. Thus the characterization is limited to ESI-MS (Figure 2.4 A), IR and conductance, all of which support the formation of the tricyclic moiety (Experimental Section). Assignments of ^1H NMR signals (Section 2.11) and positions relative to other cyclized products confirm to the proposed structure (Scheme 2.1)

2.8 Molecular structure of precursors $\mathbf{L}^2$ - $\mathbf{L}^5$

2.8.1 Molecular structure of precursor $\mathbf{L}^2$

Ligand $\mathbf{L}^2$ crystallized in the *Pbca* space group with one molecule of the compound in the asymmetric unit. The ORTEP diagram, selected bond lengths and angles are given in Figure 2.1 and Table 2.3 respectively. The molecule is non-planar. The angle between phenylenediamine ring (plane containing C9, C10, C11, N3) and phenyl ring (N3, C13, C18, C14) is 50.32° . The pyridyl ring (N1, C1, C2, C3, C4, C5) and phenylenediamine ring (C7, C8, C9, C10, C11, C12) are also not coplanar at 43.95° the angle between them. The imine C6-N2 distance is $1.2695(19)$ Å and is in the range of accepted carbon-nitrogen double bond⁷⁻⁹ and almost the same as those in the previously described compounds.¹⁰⁻¹¹ The intermolecular H-bond interaction present in the crystal structure of $\mathbf{L}^2$ is found between pyridyl nitrogen (N1), amine nitrogen (N3) of the neighboring molecule at a distance of 3.058 Å and lattice arrangement along *a*-axis (Figures 2.12 A and 2.12 B).

2.8.2 Molecular structure of precursor $\mathbf{L}^3$

Ligand $\mathbf{L}^3$ crystallized in the *Pbca* space group with half of the molecule of the compound in the asymmetric unit. The ORTEP diagram, selected bond lengths and angles are given in Figure 2.1 and Table 2.3 respectively. It shows that each half of the molecule is related to the other half by symmetry. The bond length of N2-C6 at $1.401(4)$ Å confirms the reduction of the imine (imine length ~ 1.27 Å in $\mathbf{L}^2$). The molecule is almost planar. The angle between the planes containing terminal rings is 0° but angle between the planes containing pyridine and central aromatic ring at 2° giving a slightly zigzag shape to the molecule.

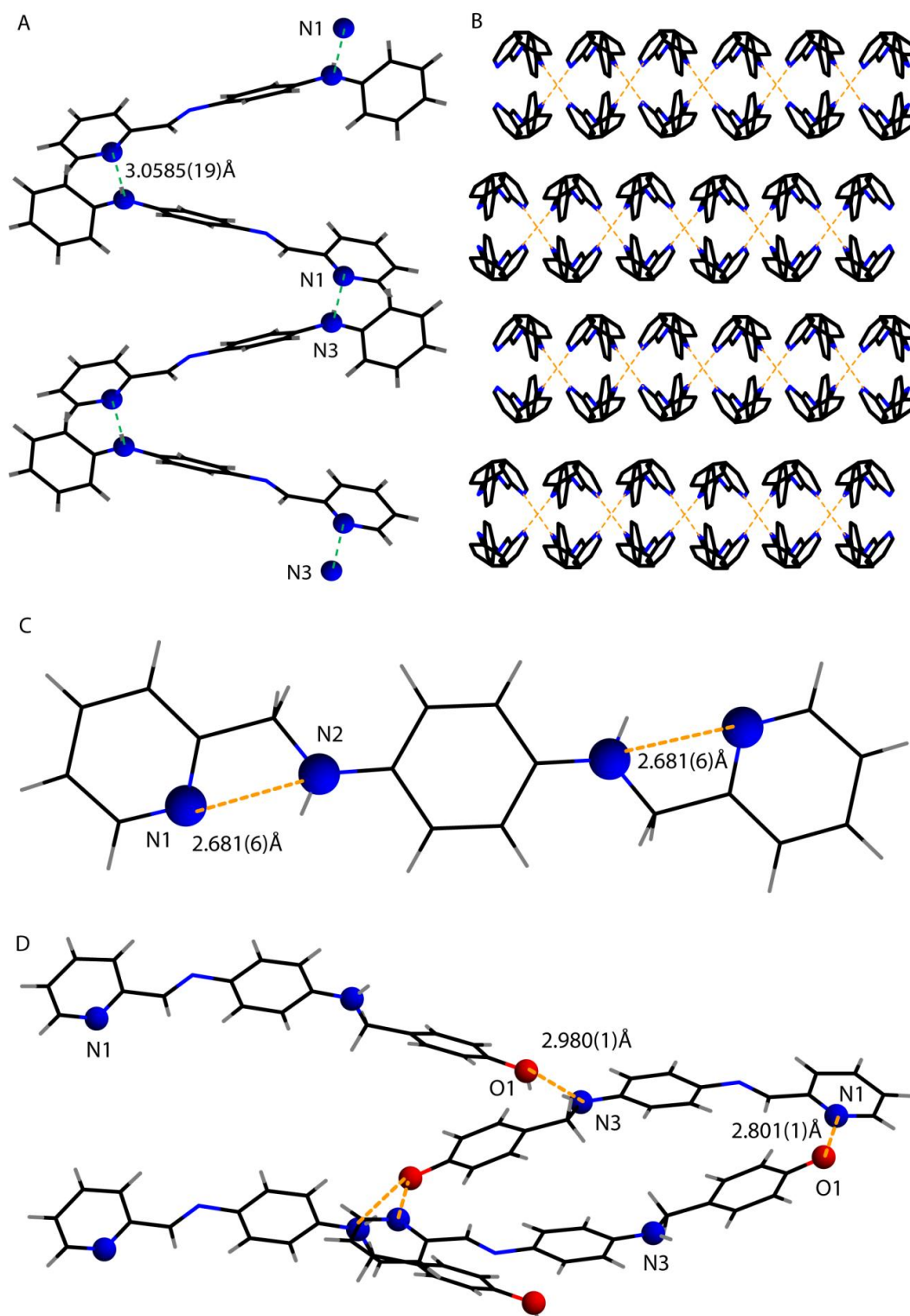


Figure 2.12 H-bond interactions present in (A) L^2 between pyridyl (N1) and imine (N3) (B) the crystal lattice of L^2 (C) L^3 and (D) L^5 .

The only H-bond interaction (Figure 2.12 C) present in the $\mathbf{L}^3$ is an intra-molecular H-bond between pyridyl (N1) and amine (N2) at a distance of 2.681(6) Å. The crystal is devoid of any other significant weak interactions.

2.8.3 Molecular structure of precursor $\mathbf{L}^5$

$\mathbf{L}^5$ crystallized in monoclinic $P2_1/c$ space group with one molecule in the asymmetric unit. The ORTEP diagram, selected bond lengths and angles are given in Figure 2.1 and Table 2.3 respectively. The bond lengths of N3-C13 at 1.435(2) Å and N2-C6 at 1.257(2) Å confirm the amine (reduced imine) and imine nature of the bonds. The molecule is almost planar starting from pyridine end to N4. However, the phenol ring is rotated out of the plane by $\sim 56.6^\circ$ compared to phenyl ring. The lattice contains number of H-bonds (Table 2.6), which generates interesting arrangement (Figure 2.12 D).

Table 2.6 H-bond distances in $\mathbf{L}^5$

D-H $\cdots$ A	$d(\text{D-H})(\text{\AA})$	$d(\text{H}\cdots\text{A})(\text{\AA})$	$d(\text{D}\cdots\text{A})(\text{\AA})$	$\angle \text{D-H}\cdots\text{A}(^\circ)$
$\mathbf{L}^5$				
N1-H24 $\cdots$ O1	0.82	1.98	2.801(1)	175
N3-H91 $\cdots$ O1	0.86	2.13	2.980(1)	170

2.9 Molecular structures of $\mathbf{P}^2$ - $\mathbf{P}^5$ and metal complexes

Detailed synthetic procedures along with characterization data have been provided below.

2.9.1 Molecular structure of $[\mathbf{P}^2](\text{NO}_3)\cdot\text{H}_2\text{O}$

Nitrate salt of $\mathbf{P}^2$ cation was crystallized in orthorhombic space group $Fdd2$ (#43) with one molecule each of $\mathbf{P}^2$ cation, nitrate and water. The ORTEP diagram, selected bond lengths and angles are reported in Figure 2.1 and Table 2.3 respectively. The tricyclic part of the molecule is essentially planar. The angle between the planes containing pyridine and phenylenediamine ring is only 3.70° . The angle between tricyclic ring (plane containing C11, C10, C9, N3) and phenyl ring (N3, C14, C13, C18) at 41.27° is not planar. The N2-C6 bond length (imine in ring) at 1.290(4) Å is slightly elongated from 1.2695(19) Å observed in corresponding Schiff base precursor ($\mathbf{L}^2$) but still considerably shorter than N2-C7 (1.391(4) Å).

This means that the imine bond retains its double bond character even after cyclization reaction i.e. N2-C7 double bond is localized and tricyclic ring is not fully aromatic. This has been observed in the case of **P¹** as well. The bonds C-N bonds around amine (N3-C10, 1.375(4); N3-C13, 1.407(4) Å) are more symmetrical and longer than observed for **P¹** (1.357(3) Å) or **P³** (Table 2.3). We think this reflects the delocalization of lone pair on amine N to both tricyclic ring and phenyl rings of **P²**. The absence of phenyl ring in **P¹** and intervening sp³ C13 in **P³** prevents this delocalization. This lone pair is withdrawn on the cationic tricyclic ring and hence the N3-C10 bond in **P¹** and **P³** gains some double bond character.

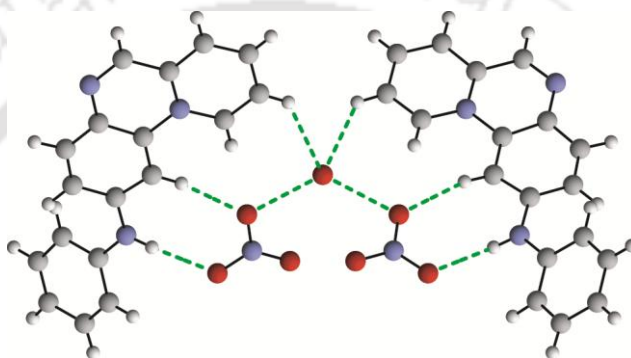


Figure 2.13 H-Bonding scheme in **[P²](NO₃).H₂O** involving amine, pyridinium, water and nitrates.

Table 2.7 H-bond distances in **[P²](NO₃).H₂O**

D-H...A	<i>d</i> (D-H)(Å)	<i>d</i> (H...A)(Å)	<i>d</i> (D...A)(Å)	<D-H...A(°)
P2				
N3-H5...O3	0.858(5)	2.197(4)	3.006(7)	157.2(4)
O2-H12...O4	0.930(6)	1.950(5)	2.862(6)	166.0(5)
O4-H12...O2	0.93(6)	1.950(5)	2.862(6)	166.0(5)
O3-H5...N3	0.858(5)	2.197(4)	3.006(7)	157.2(4)
C11-H35...O2	0.930(6)	2.265(5)	3.177(8)	166.9(4)
C1-H27...O2	0.930(6)	2.546(6)	3.476(9)	178.0(4)
C2-H30...O4	0.932(7)	2.558(8)	3.260(1)	132.5(5)
C4-H34...O1	0.930(6)	2.347(5)	3.266(8)	169.1(4)
C6-H23...O3	0.930(6)	2.608(5)	3.508(8)	162.9(4)
C3-H29...O1	0.931(8)	2.564(4)	3.221(8)	127.9(5)

The bonds C-N bonds around amine (N3-C10, 1.354(5); N3-C13, 1.434(6) Å) are less symmetrical than observed for **P²** (1.375(4), 1.407(4) Å respectively). The short nature of C-

N_{amine} attached to tricyclic ring was observed in **P**¹ (1.357(3) Å) as well. We think this reflects the delocalization of lone pair on amine N (N3) to tricyclic ring in case of alkyl substitution or no substitution but delocalizes to both aromatic ring in case of aromatic substitution. The presence of nitrate, water and amine N3 generated number of H-bonding within the lattice. The table 2.7 lists such interactions present in the lattice and figure 2.13 shows some of the resultant pattern formed with the lattice as a result of those interactions.

2.9.2 Molecular structure of [P³](NO₃)₂.H₂O

Dinitrate salt of **P**³ cation was crystallized in monoclinic space group *P*-1 (#2) with one molecule each of **P**³ cation, two nitrate anion and water molecule in the asymmetric unit. The ORTEP diagram,¹² selected bond lengths and angles are reported in Figure 2.1 and Table 2.3 respectively. The tricyclic part of the molecule is essentially planar. The angle between the planes containing pyridine and phenylenediamine ring is only 1.46° (3.70° in **P**²). Overall molecule, with angle between tricyclic ring (plane containing (C11, C10, C9, N3) and pyridyl ring (N4, C14, C13, C15) at 83.95° is not planar. The C6-N2 bond at 1.295(5) Å is clearly a double bond similar to that in **P**² (C6-N2 in **P**², 1.290(4) Å). This confirmed the formation of double bond from single bond during the cyclization process from **L**³ (C6-N2 in **L**² 1.401(4) Å).

Unlike **P**², the presence of two nitrate anion in the asymmetric unit indicated the dicationic nature of **P**³ which is supported by molar conductance. As the tricyclic ring contains one of the charges, it is likely that the other charge is because of protonation of either of amine (N3) or pyridine (N4). The pH titration supported the protonation. The pK_a values of N-methyl aniline (pK_a 4.84) and pyridine (pK_a 5.25), representing environment at N3 and N4 in **P**³ respectively, suggest that pyridine should be protonated first due to higher pK_a value. However, values are close to confirm solely on the basis of pK_a values of similar but different molecules. In **P**³, we have located the proton on pyridine from the difference Fourier map. The presence of the proton is further supported by the H-bonding (N4···O6, 2.825 Å). In fact, both pyridinium N-H, amines, water and nitrates form an extensive H-bonded network (Figure 2.14). One curious observation is N4···O2 distance at 2.924 Å is within H-bonding distance but no H could be located. H-bond distances calculated using PLATON¹³ is in table 2.8.

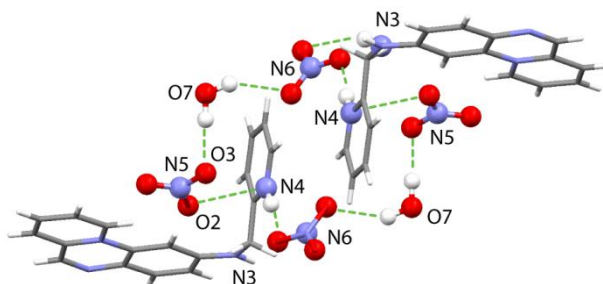


Figure 2.14 H-Bonding scheme in $[\mathbf{P}^3](\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ involving amine, pyridinium, water and nitrates.

Table 2.8 H-bond distances in $[\mathbf{P}^3](\text{NO}_3)_2 \cdot \text{H}_2\text{O}$

D-H...A	$d(\text{D-H})(\text{\AA})$	$d(\text{H...A})(\text{\AA})$	$d(\text{D...A})(\text{\AA})$	$\angle \text{D-H...A} (^{\circ})$
P3				
N3-H22...O4	0.86	2.31	3.019(4)	140
N3-H22...O6	0.86	2.50	3.208(4)	140
N4-H23...O5	0.86	2.54	3.160(4)	129
N4-H23...O6	0.86	1.97	2.825(4)	176
O7-H24...O5	0.91(3)	2.22(3)	3.030(4)	149(4)
O7-H25...O3	0.91(3)	1.90(3)	2.820(5)	178(10)
C1-H1...O2	0.93	2.30	3.215(4)	170
C2-H2...O1	0.93	2.49	3.191(5)	133
C6-H6...O7	0.93	2.48	3.403(5)	169
C11-H8...O2	0.93	2.33	3.254(5)	176
C8-H10...N2	0.93	2.61	3.519(5)	167
C18-H16...O5	0.93	2.45	3.283(6)	150
C15-H19...O3	0.93	2.37	3.234(5)	153
C13-H21...O4	0.97	2.46	3.424(4)	173

2.9.3 Molecular structure of $[\mathbf{P}^4](\text{NO}_3)$

The nitrate salt of $[\mathbf{P}^4]^+$ crystallized in the non-centrosymmetric space group Cc of monoclinic system with one molecule along with nitrate ion in the asymmetric unit. The ORTEP diagram of the compound, selected bond lengths and angles are reported in figure 2.1 and Table 2.3 respectively. The molecular structure confirms that $[\mathbf{P}^4]^+$ is protonated $\mathbf{L}^4$. No ring cyclization has been taken place. $[\mathbf{P}^4]^+$ is protonated at pyridine nitrogen (N1). The position of proton at the N1 is supported by H-bonding between pyridine and nitrate ($\text{N1} \cdots \text{O2}$ 2.731 Å). The molecular geometry is almost identical with $\mathbf{L}^2$ except the position of substitution in the pyridine

ring (*p*-substituted pyridine in $[\mathbf{P}^4]^+$. The imine (N2-C6, 1.265(6)Å) in $\mathbf{P}^4$ is identical to imine bond in $\mathbf{L}^2$ (Table 2.3).

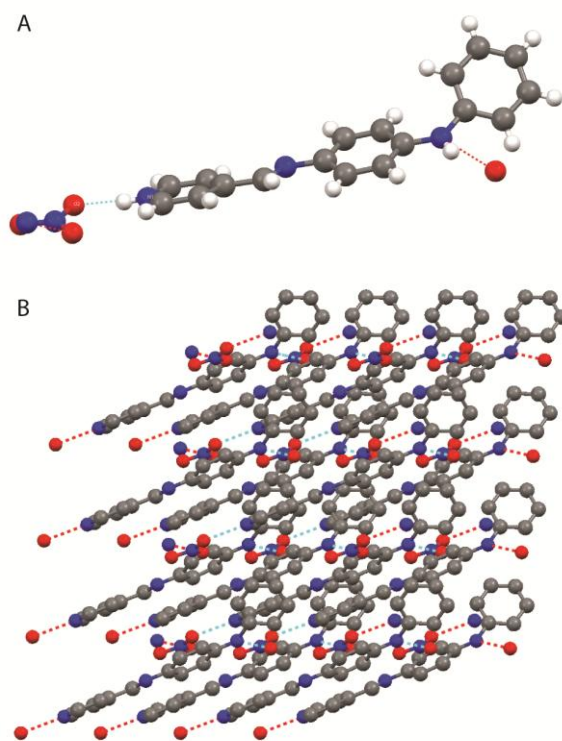


Figure 2.15 H-Bonding scheme in (A) $[\mathbf{P}^4](\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ involving amine, pyridinium, water and nitrates (B) the lattice of $[\mathbf{P}^4](\text{NO}_3)_2 \cdot \text{H}_2\text{O}$.

Table 2.9 H-bond distances in $[\mathbf{P}^4](\text{NO}_3)_2 \cdot \text{H}_2\text{O}$

D-H $\cdots$ A	$d(\text{D-H})(\text{\AA})$	$d(\text{H}\cdots\text{A})(\text{\AA})$	$d(\text{D}\cdots\text{A})(\text{\AA})$	$\angle\text{D-H}\cdots\text{A} (^{\circ})$
$\mathbf{P}^4$				
N1-H3 $\cdots$ O1	1.01(6)	2.34(6)	3.129(7)	135(4)
N1-H3 $\cdots$ O2	1.01(6)	1.74(6)	2.726(7)	163(5)
N3-H11 $\cdots$ O1	0.80(3)	2.23(4)	2.981(7)	157(3)
C9-H8 $\cdots$ O3	1.02(5)	2.50(5)	3.453(7)	155(3)

The lattice structure of $\mathbf{P}^4$ possesses an interesting feature. All the molecules in the lattice form linear chains through H-bonded interactions, between nitrate, amine H and pyridinium H, aligned in one direction (Figure 2.15). This asymmetric alignment and presence of charge transfer band

in **P**⁴ make the crystal suitable for second order nonlinear optical property studies.¹⁴ all the H-bonds and other weak interactions present in the molecule are provided in Table 2.9.

2.10 Molecular structures of complexes C1-C2

2.10.1 Molecular structure of Mn(L²)₂Cl₂ (C1)

The complex **C**¹ crystallized in monoclinic *P*2₁/*c* space group with one molecule of the complex in the asymmetric unit. The ORTEP diagram of the complex and selected bond lengths and angles are reported in Figure 2.1 and Table 2.4 respectively. The complex consists of octahedral manganese coordinated by two bidentate **L**² and two chloride ions. The chlorides are *cis* oriented. The pyridine donors from **L**² are *trans* to each other and imine donors are *cis* to each other. The overall molecule is *C*₂ symmetric without any σ plane making the molecule chiral. However, as the space group *P*2₁/*c* is achiral, both the enantiomers are within the unit cell connected through a plane of symmetry, making the crystal achiral. The geometry around manganese is distorted from ideal octahedral as is evident from the deviation of *cis* bond angles from 90° and *trans* bond angles from 180° expected for perfect octahedron (Table 2.4). The Mn-N_{pyridine} and Mn-Cl lengths are consistent with similar Mn(II) Schiff base complexes.¹⁵

Table 2.10 H-bond distances in complexes **C1** and **C2**

D-H...A	<i>d</i> (D-H)(Å)	<i>d</i> (H...A)(Å)	<i>d</i> (D...A)(Å)	<D-H...A (°)
Mn(L²)₂Cl₂ (C1)				
N3-H5...Cl1	0.86	2.69	3.531(9)	167
N3A-H6A...Cl1	0.86	2.81	3.584(9)	150
C1-H1...Cl1	0.93	2.82	3.429(13)	124
C9-H9...Cl2	0.93	2.73	3.626(8)	162
Co(L²)₂Cl₂ (C2)				
C1-H1...Cl	0.93	2.81	3.372(11)	120
C9-H9...Cl	0.93	2.67	3.522(9)	153

The Mn-Cl bond length is longer than observed for similar complexes but well within the range observed for other halide complexes. The lattice contains considerable number of $\pi\cdots\pi$, CH $\cdots$ Cl and NH $\cdots$ Cl interactions. Significant among those are multiple interactions between halides and amine NH and aromatic CH as well as $\pi\cdots\pi$ edge interactions between pyridine rings (Table

2.9). The lattice also contains solvent accessible hydrophobic voids ($V = 117 \text{ \AA}^3$) in the form of narrow one dimensional channels along a axis. The complex shows 6 lines EPR spectrum which confirmed the existing of Mn(II) (Figure 2.8 A). The UV-vis spectra of Mn (II) Complex only shows charge transfer band (Figure 2.8 B).

2.10.2 Molecular structure of $\text{Co}(\text{L}^2)_2\text{Cl}_2$ (C2)

The complex **C2** crystallized in the orthorhombic *Pbcn* space group (#60) with half of the complex in the asymmetric unit. Thus one of the ligands and the halide are identical to the other ligand and halide. The ORTEP diagram of the complex and selected bond lengths and angles are reported in Figure 2.1 and Table 2.4 respectively. The coordination environment around Co(II) and geometry of the molecule is almost identical with the Mn(II) analogue. The complex consists of octahedral cobalt coordinated by two bidentate L^2 and two chloride ions similar to the Mn(II) analogue. The chloride ions are cis oriented. The pyridyl donors from the L^2 are trans to each other and imine donors are cis to each other. The overall molecule is C_2 symmetric without any σ plane making the molecule chiral. However, both the enantiomers are within the unit cell connected through plane of symmetry, making the crystal achiral. The geometry around cobalt is distorted from ideal octahedral as it is evident from the deviation of cis bond angles from 90° and trans bond angles from 180° expected for perfect octahedral (table 2.4). The metal-ligand bond lengths (Co-N_{pyridyl}, 2.145(7); Co-N_{imine}, 2.218(7); Co-Cl, 2.378(2) all in $\text{\AA}$) are either similar or well within the range compared to reported Co(II) Schiff base complexes (example, Co-N_{py} 2.146(10) and 2.158(10); Co-N_{imine} 2.2514(10) and 2.1759(10) $\text{\AA}$).¹⁷ The bond length are slightly shorter compared to the Mn(II) analogue (**C1**) due to the difference in size of the metal ions (Table 2.4). Compared to Mn(II) analogue, the inter-molecular weak interactions (Table 2.10) are organized in a slightly different manner resulting in a reduction of solvent accessible void space within the lattice ($38 \text{ \AA}^3$ per unit cell). The figure 2.9 shows a comparison of the two lattices. The comparison of UV-visible spectra of Co(II) complex with L^2 is given in figure 2.8.B.

2.11 ^1H NMR analysis

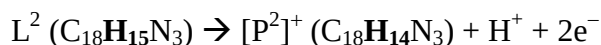
The ^1H NMR spectral assignments of the precursors and **P**⁴ were done based on peak position, integration and comparison with known (**L**¹) precursor (Experimental section). The assignments corroborates well with the structural characterization. Assignments of cyclization products (Figures 2.2 B, 2.3 B, 2.4 B) were additionally corroborated with the help of 2D COSY experiments as some of the proton absorptions overlapped (Table 2.5, Figures 2.5-2.7). This also confirms the structure of [**P**⁵](NO₃), which was not structurally characterized, as a tricyclic product similar to other products. Comparison among cyclization products showed that for same compound (**P**²) H^a, H^d, H^e & H^h, the protons nearer to the charged nitrogen, shift considerably to downfield upon changing the solvent from methanol (polarity index 5.1) to DMSO (polarity index 7.2). On the other hand protons H^f, H^g are least effected by solvent polarity change. Comparison between tricyclic part of the assignments shows that shifts of a proton among all the products in same solvent are almost identical (Table 2.5). This means that the effect of substitution at -NH has minimal effect on electron density distribution within the tricycle.

Conclusion

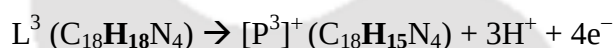
Contrary to an earlier report,¹ the results presented in this chapter shows that the cyclization process is not limited to Cu(II) mediated one. It is applied not only on Schiff base like **L**¹ but also on reduced Schiff base **L**³. The cyclization works both on the Schiff base as well as on the reduced version as long as the *ortho*-pyridyl methyl unit is connected to an aromatic diamine or at least one imine. The difference that an imine vs. an amine makes is the requirement a different reagent. Thus moving from diimine (**L**¹) to diamine (**L**³) stepwise by reducing number of imines by one (**L**² and **L**⁵), the reagent requirement shifts from Cu(II) to Fe(III). Thus **L**¹ cyclized exclusively by Cu(II), **L**² and **L**⁵ cyclized in presence of either Fe(III) or Cu(II) but **L**³ requires Fe(III) exclusively. The position of substitution on pyridine is also important. Thus **L**⁴ where pyridine has substitution at *para* position does not undergo cyclization.

The reactions can be better understood if we consider oxidation of *p*-substituted phenylene ring as the first step in the cyclization process as proposed by some of us in earlier report (Scheme 1.1).¹ According to that proposal; the *p*-substituted phenylene ring gets oxidized

by loss of one electron to a cation radical which is then become susceptible to attack by electron rich pyridine followed by loss of a proton and an electron. The total process for $\mathbf{L}^2$ can be written as follows:



In case of $\mathbf{L}^1$, at least the first oxidation was by concomitant reduction of Cu(II). In the present cases, the first oxidation is presumably through reduction of Fe(III) to Fe(II). We suspect the second oxidation needs the presence of oxygen. Reactions performed in absence of O_2 , produces the cyclized product but isolated amount decreases considerably. The need for oxygen in a similar reaction is also noted by Hequan Yao and coworkers.¹⁶ Detailed of kinetic or mechanistic studies with or without oxygen has not been performed due to the lack of proper anaerobic setup. What is surprising is that cyclization of $\mathbf{L}^3$ produced $\mathbf{P}^3$ which require further oxidation, yet it could be isolated without problem.



The isolation of $\mathbf{P}^3$ as dication was the result of protonation of the product in acidic conditions produced either by the acidic Fe(III) salt hydrolysis or by the acid produced due to the reaction. We did not observe any H_2 gas evolution.

The requirement of Cu(II) vs. Fe(III) have to do with first oxidation to generate the cation radical essential for the cyclization to start. We think that in case of pyridyl imine containing precursor, the Cu(II) complexation takes place¹⁸ which is expected to stabilize Cu(I) similar to bipyridine (redox potential $>1\text{V}$). Complexation followed by reduction of Cu(II) at the expense of ligand oxidation which then proceed via attack of pyridine followed by oxidation with oxygen. Reducing imines to amine, the precursor become vulnerable to oxidation (diamines are known to get oxidized in air) and is oxidized by Fe(III). Oxidation by Fe(III) may or may not proceed via coordination. The donors in the $\mathbf{L}^3$ being intermediate soft (pyridine N) and hard (amine) would not support stabilization of Cu(I) and thus does not support initial oxidation needed for cyclization. Addition of Cu(II) to $\mathbf{L}^3$ produces green solution reminiscent of a complex. The complex could not be isolated and characterized as of now.

Overall, the original reaction between L^1 and Cu(II) producing P^1 could be extended to amines as well. By changing the imine to an amine, the requirement for metal ion changes from Cu(II) to Fe(III). One of the goals of having derivatives at the amine end could be solved through reduction of the precursor (L^3). A method to synthesize unsymmetrical precursor for further derivatization at the amine end (P^5) has been shown.

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Chapter - 3

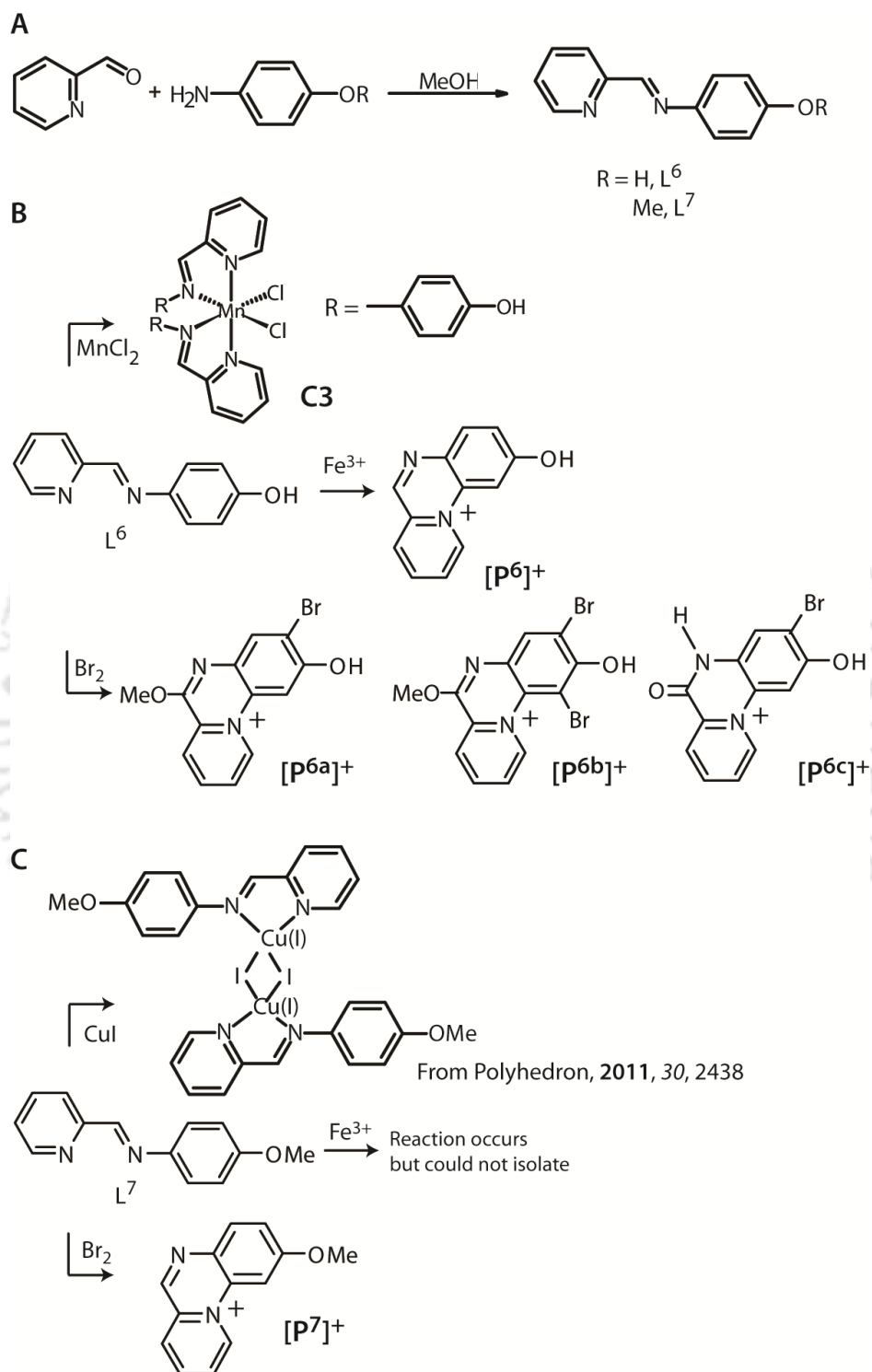
**Synthesis and characterization of
pyrido[1,2-*a*]quinoxalin-11-ylum derivatives
from phenol derived Schiff base by Fe(III) salt
or molecular bromine**

Chemistry described in the previous chapters we have observed that Schiff bases as well as reduced Schiff bases of *p*-phenylenediamine, undergo cyclization reaction forming quinoxalinium type heterocyclic compounds in presence of metal salts. Based on the experimental results, we have observed that the key step in the cyclization process is the formation of cation radical by oxidation of the *p*-phenylenediamine ring and then attacked by pyridine. Finally cyclized product is formed by air oxidation. We surmised that a similar cyclization might be possible by aromatic rings other than *p*-phenylenediamine provided that the ring is as easily oxidizable as *p*-phenylenediamine. We found that redox potential of *p*-aminophenol ($E^0 +0.76$ V vs NHE) is closer to that of *p*-phenylenediamine ($E^0 +0.59$ V vs NHE) than either aniline ($E^0 +1.02$ vs NHE) or halosubstituted anilines ($E^0 +1.01$ to 1.04 vs NHE for *p*-chloro to iodo substitution).¹ Thus in this chapter we choose to form Schiff base of *p*-aminophenol and *p*-methoxyphenol with pyridine-2-carbaldehyde and perform their cyclization reactions (Scheme 3.1).

3.1 Experimental section

3.1.1 Solvent and Reagents

Solvents used were purified prior to use following standard literature procedure. KBr was purchased from Aldrich Chemical Co. Molecular bromine and iodine were purchased from Sisco Research Laboratories Pvt. Ltd. (SRL), India and used as received. Details of the instruments used have already been described in Chapter 2. The *p*-aminophenol and *p*-methoxyaniline were purchased from Sisco Research Laboratories Pvt. Ltd. (SRL), India and used as received.



Scheme 3.1 Syntheses of the Schiff base precursors (A), corresponding cyclization products and metal complexes of precursor L^6 (B) and L^7 (C).

3.2 Syntheses of precursors L^6 – L^7

Detailed synthetic procedures along with characterization data have been provided below:

3.2.1 Synthesis of 4-Pyridin-2-ylmethyleaminophenol (L^6)

Pyridine-2-carbaldehyde (0.49 g, 4.50 mmol) was added dropwise to a methanolic solution (20 mL) of *p*-aminophenol (0.50 g, 4.50 mmol) at room temperature. A light yellow precipitate appeared within minutes and stirring of the reaction mixture was continued for 2 h. The solvent was concentrated to 5 mL and the ppt. filtered; washed with methanol (2×3 mL) and hexane (3×10 mL) respectively. The yellow powder was obtained and recrystallised from methanol, dried in vacuum desiccator. The yield of the compound was found (0.73 g, 80%). Characterization data for L^6 : Melting point 195-197 °C. ESI-MS ($M+H^+$): Calcd 199.09; Found 199.04. UV/vis (MeOH): λ_{max} , nm (ϵ , $M^{-1} cm^{-1}$): 345 (13,000) 285 (9,000), 238 (12,000). IR (KBr, cm^{-1}): $\nu(O-H)$ 3443, $\nu(HC=N)$ 1600, $\nu(C=N)$ 1580. 1H NMR (400 MHz, $CDCl_3-d_1$) δ (ppm) 9.76 (OH, br), 8.67 (d, 1H, $J = 4.4$ Hz), 8.59 (1H, s, $CH=N$), 8.12 (1H, t, $J = 7.6$ Hz) 7.90 (1H, t, $J = 7.6$ Hz), 7.46 (1H, t, $J = 6.4$ Hz) 7.29 (2H, d, $J = 6.8$ Hz), 6.83 (2H, d, $J = 6.8$ Hz). HRMS (ESI) m/z [$M+H$] $^+$ calcd for $C_{12}H_{10}N_2O$: 199.0866 found: 199.0886.

3.2.2 Synthesis of 4-Methoxy-N-pyridine-2ylmethylebenzenamine (L^7)

Pyridine-2-carbaldehyde (0.43 g, 4.10 mmol) was added dropwise to a methanolic solution (20 mL) of *p*-methoxyaniline (0.50 g, 4.10 mmol). The reaction mixture was stirring for 2 h at room temperature, the product did not precipitate. The solvent was completely removed through high vacuum and a light yellow liquid was obtained. The compound was extracted from reaction mixture by hexane (3×10 mL) and evaporated to dryness a light yellow compound was obtained. A dark crystalline compound was obtained from a vacuum desiccator after 2 days. The yield of the product was found (0.50 g, 58%). Characterization data for L^7 : Melting point 52-53 °C. ESI-MS ($M+H^+$): Calcd 213.09; Found 213.09. UV/vis (MeOH): λ_{max} , nm (ϵ , $M^{-1}cm^{-1}$): 341 (15,000) 286 (12,000) 237 (16,000). IR (KBr, cm^{-1}): $\nu(HC=N)$ 1631, 1H NMR (400 MHz, $CDCl_3-d_1$) δ (ppm) 8.70 (1H, d, $J = 4.8$ Hz), 8.63 (1H, s, $HC=N$), 8.19 (1H, d, $J = 8.0$ Hz), 7.79 (1H, t, $J = 7.6$ Hz), 7.34 (1H, m) 7.34 (2H, m), 6.95 (2H, d, $J = 8.8$ Hz). HRMS (ESI) m/z [$M+H$] $^+$ calcd for $C_{13}H_{12}N_2O$: 213.1022 found: 213.1029.

3.3 Syntheses of pyrido[1,2-a]quinoxalines derivatives P^6 - P^7

Detailed synthetic procedures along with characterization data have been provided below:

3.3.1 Synthesis of 2-Amino-pyrido[1,2-a]quinoxalin-11-ylum nitrate [P^6] NO_3

$Fe(NO_3)_3 \cdot 9H_2O$ (0.41 g, 1.00 mmol) was added to a solution of L^6 (0.20 g, 1.00 mmol) in 10 ml methanol and stirred for 2 h at room temp. The color of solution immediately changed from yellow to purple and then to red with orange fluorescence. The solvent was evaporated to dryness; a sticky product was obtained. The compound was extracted from reaction mixture with acetone (3×5 mL) and solvent was evaporated to dryness and a solid product was obtained. The fine needle-like red crystals were formed in 24 h by slow evaporation of methanol. The crystals were collected, washed with diethyl ether and dried over silica gel in vacuum desiccator. Yield: (0.08 g 30%). Characterization data for [P^6] NO_3 : Melting point 190 -192 °C. Λ_M (MeOH): 103 S $cm^2 mol^{-1}$. ESI-MS (M^+): Calcd 197.07; Found 197.07. UV/vis (MeOH): λ_{max} , nm (ϵ , $M^{-1} cm^{-1}$): 262 (21,000), 321 (4,000), 388 (4,000), 497 (11,000). IR (KBr, cm^{-1}): $\nu(NO_3^-)$ 1384. Fluorescence (MeOH): λ_{ex} , 550 nm; λ_{em} , 625 nm. 1H NMR (400 MHz, DMSO- d_6) δ (ppm) 10.27 (1H, d, J = 6.8 Hz), 9.63 (1H, s), 8.91 (1H, d, J = 7.6 Hz), 8.86 (1H, t, J = 8.0 Hz), 8.51 (1H, t, J = 6.4 Hz), 8.33 (1H, s), 8.29 (1H, d, J = 8.8 Hz), 7.65 (1H, d, J = 8.8 Hz). HRMS (ESI) m/z [M] $^+$ calcd for $C_{12}H_9N_2O$: 197.0715 found: 197.0728.

3.3.2 Synthesis of 2-hydroxy-3-bromo-pyrido[1,2-a]quinoxalin-11-ylum bromide [P^{6a}] Br

The filtrate of the reaction for [P^{6b}] Br (experimental sections 3.4.3) was evaporated to dryness; an orange red sticky compound was formed. The compound was isolated with acetone and solvent was evaporated to dryness, solid compound was obtained. The remaining sticky residue after the acetone washings was preserved for [P^{6c}] Br . The fine needle shaped yellow crystals were formed in 24 h by slow evaporation of methanol. The crystals were collected, washed with diethyl ether and dried over silica gel in vacuum desiccator. Yield: (0.05 g, 16%). Characterization data for [P^{6a}] Br : Melting point 285-287 °C. Λ_M (MeOH): 119 S $cm^2 mol^{-1}$. ESI-MS (M^+): Calcd 306.13, 304.99; Found 304.99, 306.99. UV/vis (MeOH): λ_{max} , nm (ϵ , $M^{-1} cm^{-1}$): 263 (13,000), 319 (3,000), 387 (21,000) 490 (7,000). IR (KBr, cm^{-1}): $\nu(C=N)$ 1618. Fluorescence (MeOH): λ_{ex} , 490 nm; λ_{em} 598 nm. 1H NMR (400 MHz, DMSO- d_6) δ (ppm) 11.85 (OH, br), 10.13 (1H, d, 6.8 Hz), 8.58 (1H, t, J = 5.2 Hz), 8.90 (1H, m), 8.92 (1H, m), 8.33 (1H, s) 8.20 (

1H, s), 4.25 (3H, s). HRMS (ESI) m/z $[M]^+$ calcd for $C_{13}H_{10}BrN_2O_2$: 304.9905/306.9906. found: 304.9901/306.9902.

3.3.3 Synthesis of 2-hydroxy-3-bromo-6-methoxy-pyrido[1,2-a]quinoxalin-11-ylum bromide [P^{6b}]Br

Molecular bromine (0.16 g, (52.0 μ L) 1.00 mmol) was added dropwise to a methanolic solution (10 mL) of L^6 (0.20 g, 1.00 mmol). The color of the solution was changed immediately from yellow to red with red fluorescence. A yellow precipitate was formed within a minute and stirring of the reaction mixture was continued for another 2 h at room temperature. The solvent was evaporated to 5 mL, yellow powder was obtained, washed with acetone and dried in vacuum desiccator. The fine yellow colored needle-like crystals were formed in 48 h by slow evaporation of methanol. The crystals were collected, washed with diethyl ether and dried over silica gel in vacuum desiccator. Yield: (0.07 g, 19%). Characterization data for [P^{6b}]Br: Melting point 183-186 °C. Λ_M (MeOH): 94 S $cm^2 mol^{-1}$. ESI-MS (M^+): Calcd 385.03/382.90; Found 382.93/384.92/386.92. UV/vis (MeOH): λ_{max} , nm (ϵ , $M^{-1} cm^{-1}$): 401 (13,000) 303 (5,000) 272 (14,000). IR (KBr, cm^{-1}): $\nu(C=N)$ 1615. Fluorescence (MeOH) : λ_{ex} , 482 nm; λ_{em} 515 nm. 1H NMR (400 MHz, DMSO- d_6) δ (ppm) 10.54 (1H, d, J = 6.8 Hz), 8.96 - 8.89 (2H, m), 8.53 (1H, t, J = 6.8 Hz), 8.36 (1H, s), 4.26 (3H, s). HRMS (ESI) m/z $[M]^+$ calcd for $C_{13}H_9Br_2N_2O_2$: 382.9031/384.9011/386.8992 found: 382.9030/384.9012/386.9004.

3.3.4 Synthesis of 2-hydroxy-3-bromo-pyrido[1,2-a]quinoxalin-11-ylum bromide [P^{6c}]Br

Remaining sticky residue after acetone washing given in (Experimental sections 3.4.2) was dissolved in methanol. The fine yellow coloured needle-like crystals were formed in 36 h. The crystals were collected, washed with diethyl ether and dried over silica gel in vacuum desiccator. Yield: (0.02 g, 9%). Characterization data for [P^{6c}]Br : Melting point 285-287°C. Λ_M (MeOH): 80 S $cm^2 mol^{-1}$. ESI-MS (M^+): Calcd 292.11; Found 290.88, 292.88. UV/vis (MeOH): λ_{max} , nm (ϵ , $M^{-1} cm^{-1}$): 440 (5,000) 318 (6,000) 246 (19,000). IR (KBr, cm^{-1}): $\nu(C=N)$ 1618. Fluorescence (MeOH) : λ_{ex} , 399 nm; λ_{em} 471 nm. 1H NMR (400 MHz, DMSO- d_6) δ (ppm) 12.98 (OH, br), 11.20 (1H, s), 8.96 (1H, d, J = 8.4 Hz), 8.86 (1H, t, J = 8.0 Hz), 8.53 (1H, t, J = 8.0 Hz) 8.04 (1H, s), 7.71 (1H, s). HRMS (ESI) m/z $[M]^+$ calcd for $C_{12}H_8BrN_2O_2$: 290.9769/292.9763 found: 290.9769/292.9764

3.3.5 Synthesis of 2-methoxy-pyrido[1,2-a]quinoxalin-11-ylum bromide [**P**⁷]**Br**

Molecular bromine (0.15 g, (49.0 μ L) 1.00 mmol) was added dropwise to a methanolic solution (10 mL) of **L**⁷ (0.20 g, 1.00 mmol). The color of the solution was changed immediately from yellow to red with highly intense blue fluorescence and a yellow precipitate was formed within a minute. The reaction mixture was continued stirring for another 2 h. The solvent was concentrated to 5 mL, a yellow powder was obtained and was washed with acetone. Fine needle-like yellow crystals were formed in 48 h by slow evaporation from a methanolic solution. The crystals were collected, washed with diethyl ether and dried over silica gel in vacuum desiccator. Yield: (0.14 g, 52%). Characterization data for [**P**⁷]**Br**: Melting point 285-287 °C. Λ_M (MeOH): 119 S cm² mol⁻¹ ESI-MS (**M**⁺): Calcd 211.09; Found 211.11. UV/vis (MeOH): $\lambda_{\max}$, nm (ϵ , M⁻¹ cm⁻¹): 272 (22,000), 243 (14,000), 305 (sh), 401(13,000). IR (KBr, cm⁻¹): ν (C=N)1615. Fluorescence (MeOH) : λ_{ex} , 400 nm; λ_{em} 473 nm. ¹H NMR (400 MHz, DMSO-d₆) δ (ppm) 10.50 (1H, d, J = 6.8 Hz), 9.71 (1H, s), 8.95 (1H, d, J = 8.0 Hz), 8.90 (1H, t, J = 8.4 Hz), 8.57 (1H, t, J = 6.8 Hz) 8.51 (1H, s), 8.57 (1H, d, J = 9.2 Hz), 7.81 (H, d, J = 9.2 Hz), 4.12 (3H, s). HRMS (ESI) m/z [**M**]⁺ calcd for C₁₃H₁₁N₂O: 211.0871 found: 211.086

3.4 Synthesis of manganese complex [**Mn**(**L**⁶)Cl₂] (**C3**)

MnCl₂.6H₂O (0.04 g, 0.17 mmol) was added to a solution of **L**⁶ (0.10 g, 0.37 mmol) in 20 mL methanol and stirred for 2 h at room temperature. The color of solution was changed from yellow to red within minutes. The mixture was concentrated to 10 mL, the product precipitated out and was filtered off, washed with methanol and dried in vacuum desiccator. The dark red block-like crystals were formed in 48 h by slow evaporation from methanol. The crystals were collected, washed with methanol and diethyl ether consecutively and dried over silica gel in vacuum desiccator. Yield: (0.15 g, 55%). Characterization data for [**Mn**(**L**⁶)Cl₂] (**C3**) Magnetic moment (μ_{eff}): 5.69 B.M.² EPR g , A_{I1} / G 2.008 / 5.69. Λ_M (MeOH): 121 S cm² mol⁻¹. ESI-MS (**M**⁺): Calcd 424.034; Found 425.07. UV/vis (MeOH): $\lambda_{\max}$, nm (ϵ , M⁻¹ cm⁻¹): 344 (14,000). IR (KBr, cm⁻¹): 1624 (C=N_{im}), 1586 (C=N_{py}).

3.5 X-ray Data Collection, Structure Solution and Refinement

Crystals of the complexes $[\mathbf{P}^6]\text{NO}_3$ (**1**), $[\mathbf{P}^{6a}]\text{Br}$ (**2**), $[\mathbf{P}^7]\text{Br}$ (**3**), $[\text{Mn}(\mathbf{L}^6)_2\text{Cl}_2]$ (**C3**) obtained during synthesis were used for X-ray analysis. The crystals were mounted on glass fiber. The instrumental parameters used for data collections are same as described in the Chapter 2. Absorption corrections were done using SADABS only as either kinds of absorption did not help.³ After the initial solution and refinement with SHELXL, the final refinements were performed on WinGX environment using SHELX97.⁴ Selected crystallographic data have been summarized in Table 3.1. The crystals of all compounds were mounted on glass fiber. All geometric and intensity data for the crystals were collected at room temperature using a Bruker SMART APEX CCD diffractometer equipped with a fine focus 1.75 kW sealed tube Mo $\text{K}\alpha$ ($\lambda = 0.71073 \text{ \AA}$) X-ray source, with increasing ω (width of 0.3° per frame) at a scan speed of 3 s/frame. The SMART software was used for data acquisition and the SAINT software for data extraction. Structures were solved and refined using SHELX97. All non-hydrogen atoms were refined isotropically.

Table 3.1 Crystallographic data and refinement parameters for compounds^a

Compounds	[Mn(L ⁶) ₂ Cl ₂]	[P ⁶] ₂ NO ₃	[P ^{6a}] ₂ Br	[P ⁷] ₂ Br
Empirical formula	C ₂₄ H ₂₀ Cl ₂ Mn N ₄ O ₄	C ₁₂ H ₁₁ N ₃ O ₅	C ₁₂ H ₁₀ Br ₂ N ₂ O ₃	C ₁₃ H ₁₁ BrN ₂ O
<i>M</i>	554.28	277.24	402.05	291.15
Wavelength Å	0.71073	0.71073	0.7107	0.71073
Crystal system	Orthorhombic	Triclinic	Triclinic	Monoclinic
Space group	<i>Pbcn</i>	<i>P</i> -1	<i>P</i> -1	<i>P</i> 2 ₁ / <i>n</i>
<i>a</i> , Å	15.3910(16)	7.4515(3)	7.4200(13)	7.7851(8)
<i>b</i> , Å	9.7266(10)	7.5197(3)	10.3229(17)	9.9092(10)
<i>c</i> , Å	16.8779(16)	11.8223(4)	10.6823(16)	15.3579(16)
α , deg	90.000	86.699(3)	61.279(9)	90.000
β , deg	90.000	85.416(3)	86.634(7)	94.872(7)
γ , deg	90.000	64.540(3)	86.789(7)	90.000
<i>V</i> /Å ³	1511.11(15)	596.0 (4)	716.0(2)	1180.2(2)
<i>Z</i>	4	2	2	4
ρ /g cm ⁻³	1.276	1.545	1.865	1.638
μ /mm ⁻¹	0.079	0.123	5.669	3.466
Reflns collected	458	2980	7786	2155
Indepreflns	380	1661	3427	3763
GOF	0.867	0.922	0.998	0.939
Final R indices	R1 = 0.0342	R1 = 0.0443	R1 = 0.0492	R1 = 0.0667
[<i>I</i> > 2 σ (<i>I</i>)]	wR2 = 0.0919	wR2 = 0.1071	wR2 = 0.1208	wR2 = 0.1560
R indices (all data)	R1 = 0.0430	R1 = 0.0802	R1 = 0.1261	R1 = 0.1545
	wR2 = 0.1001	wR2 = 0.1169	wR2 = 0.1503	wR2 = 0.1980

^aRefinement methods: full-matrix least-square on *F*².

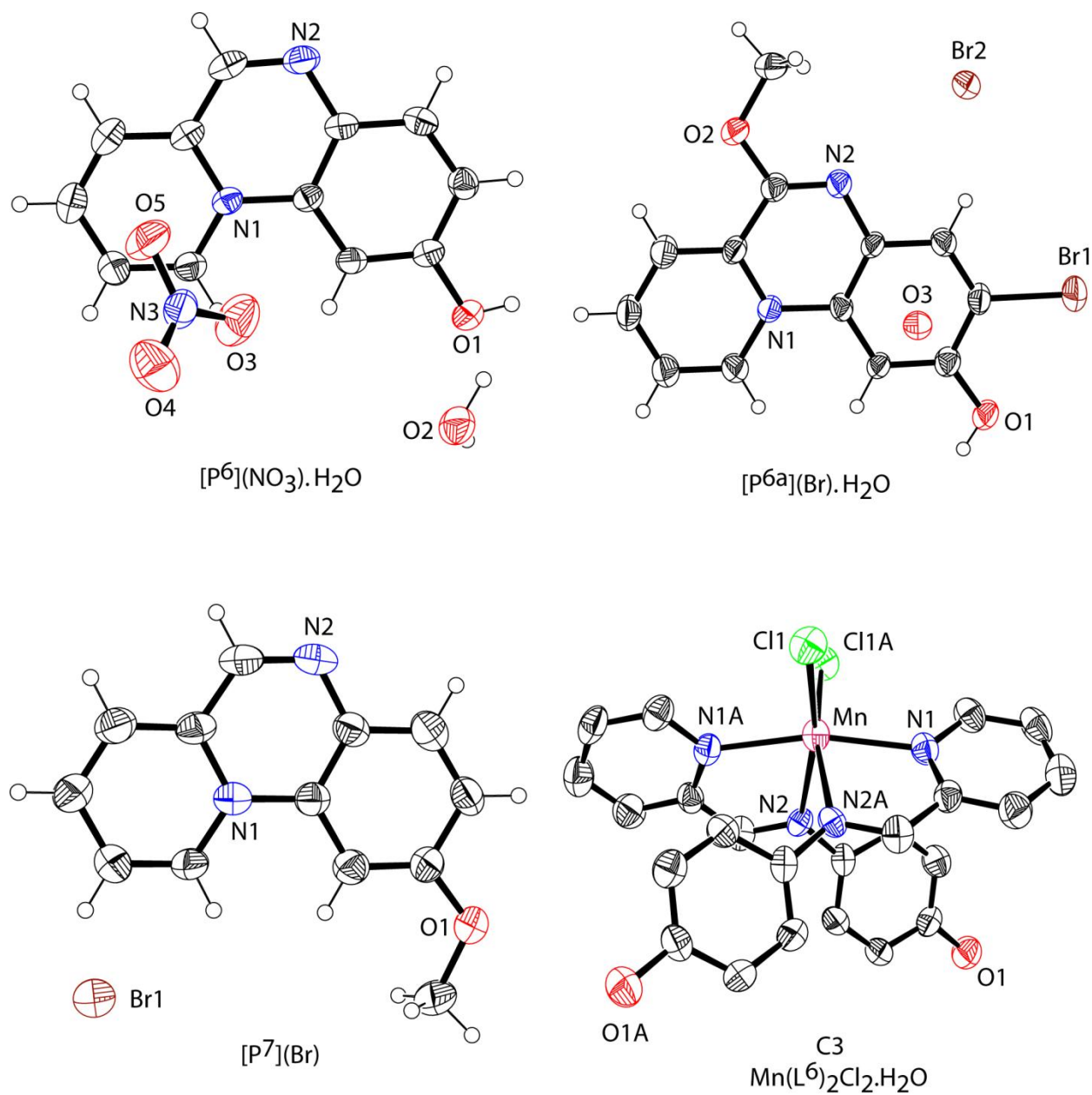


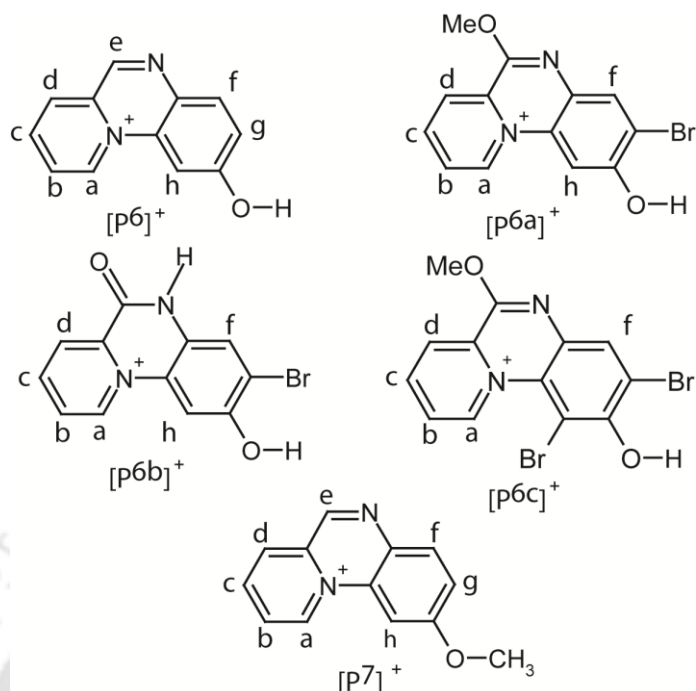
Figure 3.1 ORTEP drawing of compounds $[P^6]NO_3$, $[P^{6a}]Br$, $[P^7]Br$ and complex $[Mn(L^6)_2Cl_2]$ (C3) (solvent and H-atoms are omitted for clarity) with 40% probability thermal ellipsoids.

Table 3.2 Selected bond distances (Å) of compounds

[P⁶]NO₃							
C1-C2	1.3594(18)	C2-C3	1.385(2)	C4-C3	1.362(2)	C5-C4	1.3937(18)
C5-C6	1.4270(2)	C7-C8	1.4002(18)	C9-C8	1.3612(19)	C9-C10	1.3944(19)
C11-C10	1.3813(18)	C11-C12	1.3859(18)	C12-C7	1.4036(19)	C10-O1	1.3516(15)
N3-C1	1.3613(17)	N3-C5	1.3734(17)	N3-C12	1.4300(15)	N2-C6	1.2893(18)
N2-C7	1.3801(17)	N1-O2	1.2177(17)	N1-O3	1.2276(17)	N1-O4	1.2389(16)
[P^{6a}]Br							
C1-C2	1.367(8)	C1-N1	1.370(6)	C3-C2	1.368(8)	C3-C4	1.371(8)
C5-C4	1.386(7)	C5-C6	1.455(7)	C5-N1	1.365(6)	O2-C6	1.333(6)
O2-C13	1.446(6)	C7-N2	1.381(6)	C7-C12	1.387(7)	C7-C8	1.422(6)
C9-C8	1.341(7)	C9-C10	1.413(7)	Br1-C9	1.890(5)	C10-C11	1.389(7)
C12-C11	1.395(7)	C12-N1	1.431(6)	C10-O1	1.345(6)	O2-C6	1.333(6)
O2-C13	1.446(6)	N2-C6	1.282(6)				
[P⁷]Br							
C1-N1	1.358(6)	C2-C1	1.344(7)	C2-C3	1.420(7)	C3-C4	1.362(7)
C5-C4	1.400(8)	C5-C6	1.414(7)	C5-N1	1.391(6)	C6-N2	1.307(7)
C7-C8	1.391(8)	C9-C8	1.349(6)	C9-C10	1.414(6)	C10-C11	1.359(7)
C12-C11	1.411(6)	C12-C7	1.402(7)	C7-N2	1.386(6)	C12-N1	1.400(6)
C13-O1	1.457(6)	C10-O1	1.376(6)				

Table 3.3 Selected bond distances (Å) and angles (°) of complex **C3**

M-Cl(1)	2.482(3)	N(2)-M-N(2A)	74.1(2)
M-N(2) _{imine}	2.352(8)	N(2A)-M-Cl(1)	98.25(15)
M-N(1) _{py}	2.245(9)	N(1)-M-N(2)	71.2(4)
N(2)-C(6)	1.315(13)	N(1A)-M-N(2A)	71.0(4)
N(2)-C(7)	1.417(14)	N(1A)-M-N(1)	162.8(4)
Cl(2)-M-Cl(1)	100.16(8)	N(2)-M-Cl(1)	161.3(3)
N(2)-M-Cl(2)	92.32(17)	N(2A)-M-Cl(2)	156.1(2)



Scheme 3.2 The quinoxaline derivatives with ^1H NMR labeling scheme.

Table 3.4 ^1H NMR shift data for quinoxaline derivatives^a

Chemical Shifts (ppm)								
Compound	H ^a	H ^b	H ^c	H ^d	H ^e	H ^f	H ^g	H ^h
[P ⁶](NO ₃)	10.27d	8.51t	8.86m ⁱ	8.91m ⁱ	9.63s	8.29d	7.65d	8.33s
[P ^{6a}](Br)	10.13d	8.58t	8.58m	8.58m	-	8.19s	-	8.25m ⁱ
[P ^{6b}](Br)	9.97d	8.53t	8.86t	8.96d	-	7.71s	-	8.04s
[P ^{6c}](Br)	10.54d	8.53t	8.91m	8.91m	-	8.36s	-	-
[P ⁷](Br)	10.50d	8.57t	8.90t	8.95d	9.71s	7.81d	8.57d	8.51s
	-OCH ₃	OH						
[P ⁶](NO ₃)	-	n.o.						
[P ^{6a}](Br)	4.25s	9.63s						
[P ^{6b}](Br)	-	12.98						
[P ^{6c}](Br)	4.26s							
[P ⁷](Br)	4.12s							
Coupling Constants (Hz)								
	J _{ab}	J _{bc}	J _{cd}	J _{fg}				
[P ⁶](NO ₃)	6.8	7 ⁱⁱ	8.0	8.8				
[P ^{6a}](Br)	6.4	7 ⁱⁱ	8.4	-				
[P ^{6b}](Br)	6.4	8 ⁱⁱ	8.0	-				
[P ^{6c}](Br)	6.8	7 ⁱⁱ	7.6	-				
[P ⁷](Br)	6.8	6.8	8.4	8.0				

Coupling constant values are within ± 0.4 Hz.ⁱ Overlapped with other proton.

ⁱⁱ Approximate value due to multiplet nature. n.o. = not observed.

^a All ^1H NMR performed in d_6 -DMSO.

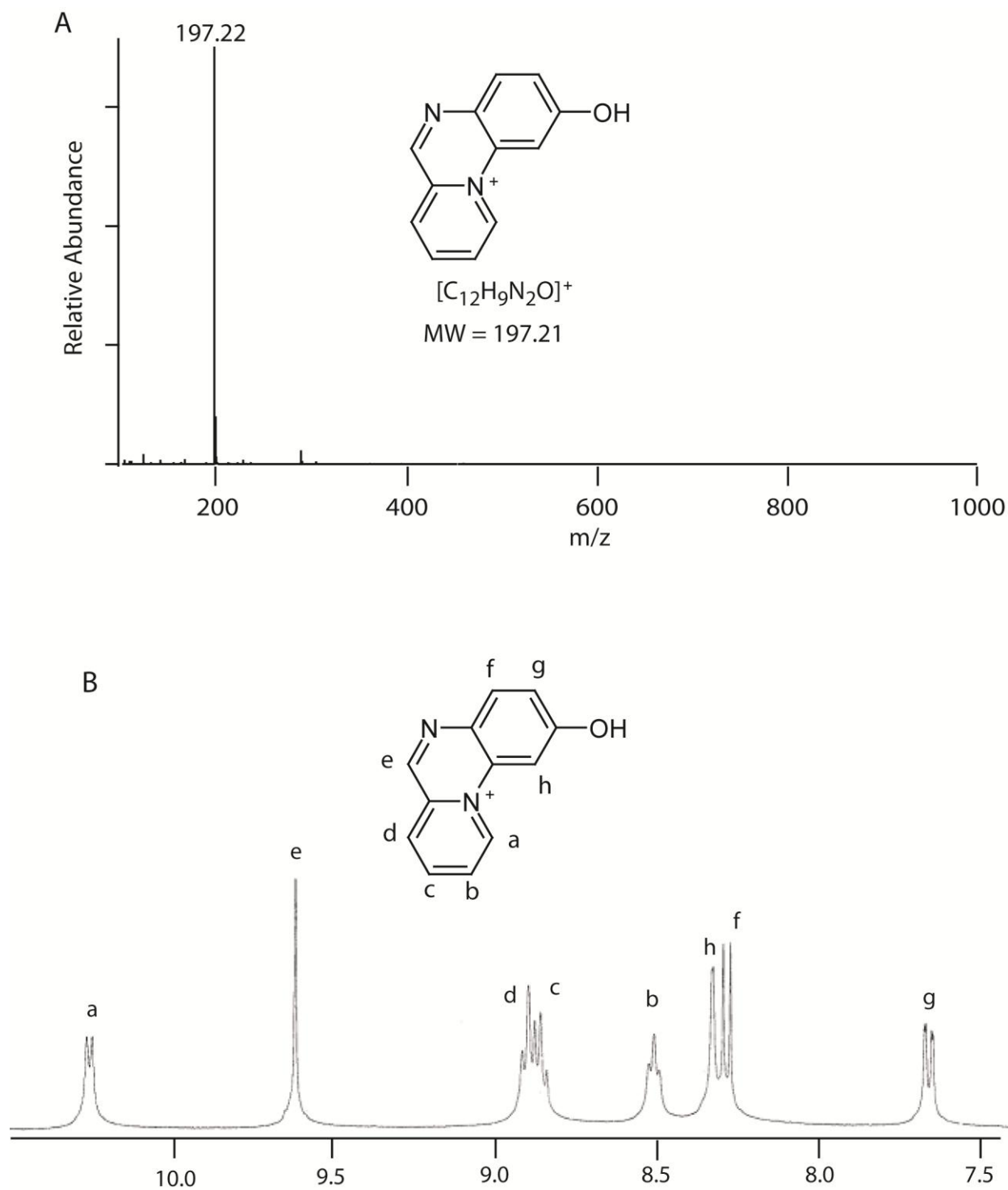


Figure 3.2 (A) ESI mass spectrum and (B) ^1H NMR spectrum with numbering scheme of $[\text{P}^6]\text{NO}_3$.

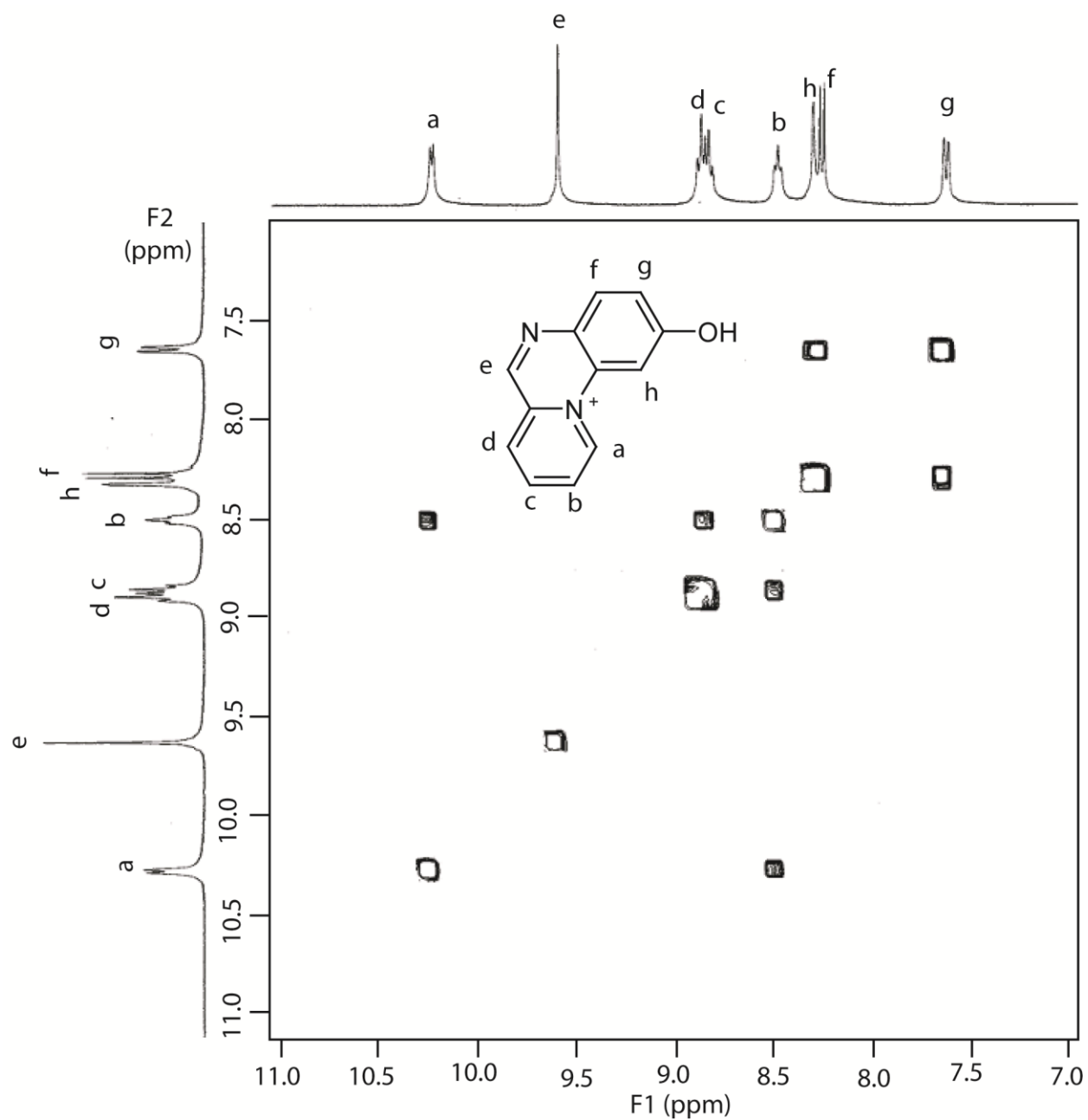


Figure 3.3 The ^1H ^1H -COSY NMR spectrum of 2-hydroxy-pyrido[1,2-a]quinoxalin-11-ylum nitrate ($[\text{P}^6](\text{NO}_3)$) in DMSO-d_6 at 400 MHz.

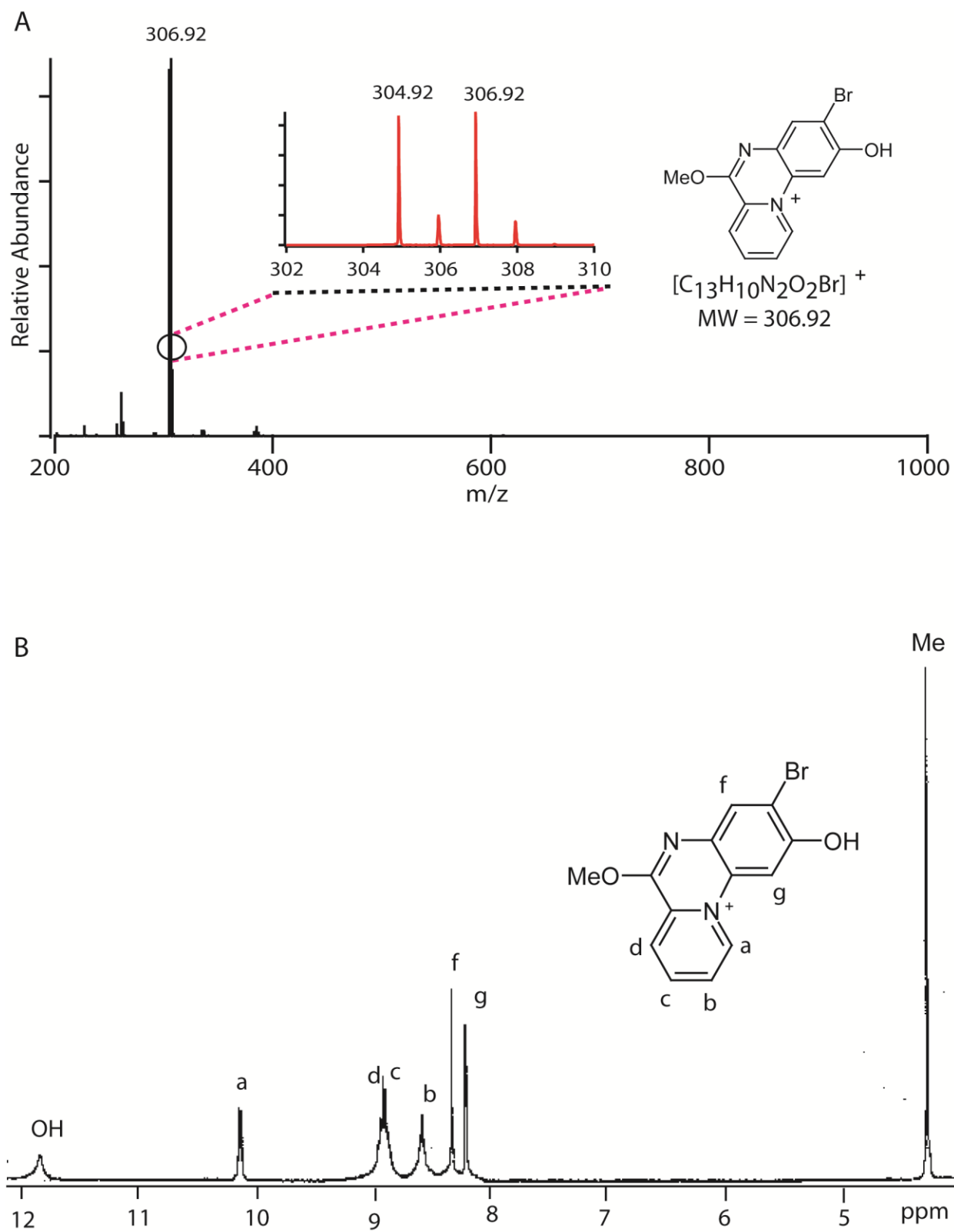


Figure 3.4 (A) ESI mass spectrum and isotopic abundance pattern calculated (red) and experimental (black) of $[P^{6a}]Br$ and (B) 1H NMR spectrum with numbering scheme of $[P^{6a}]Br$.

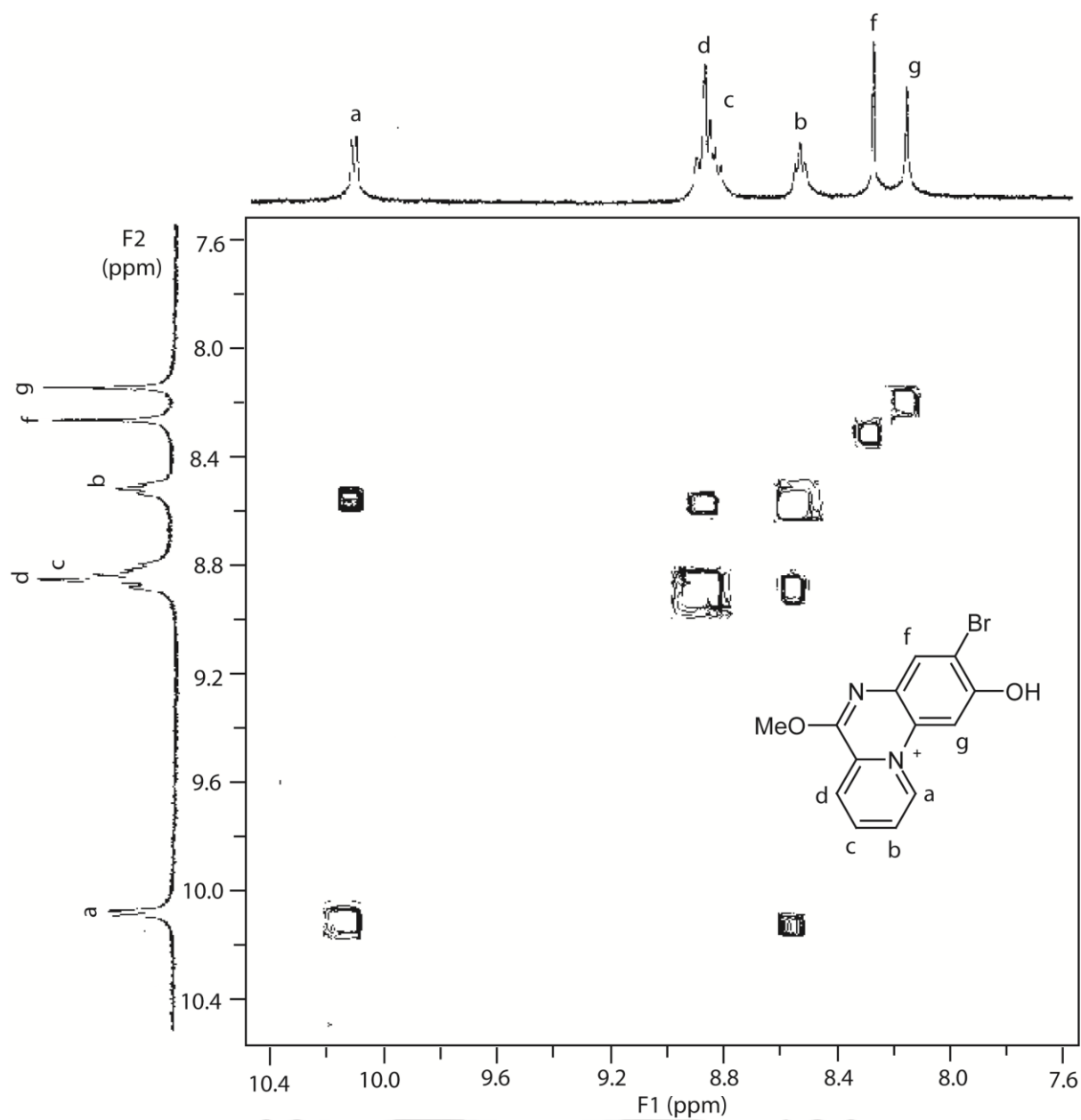


Figure 3.5 The ^1H ^1H -COSY NMR spectrum of 6-methoxy-3-bromo-2-hydroxy-pyrido[1,2-*a*]quinoxalin-11-ylum bromide ($[\text{P}^{6a}]\text{Br}$) in $\text{DMSO}-d_6$ at 400 MHz.

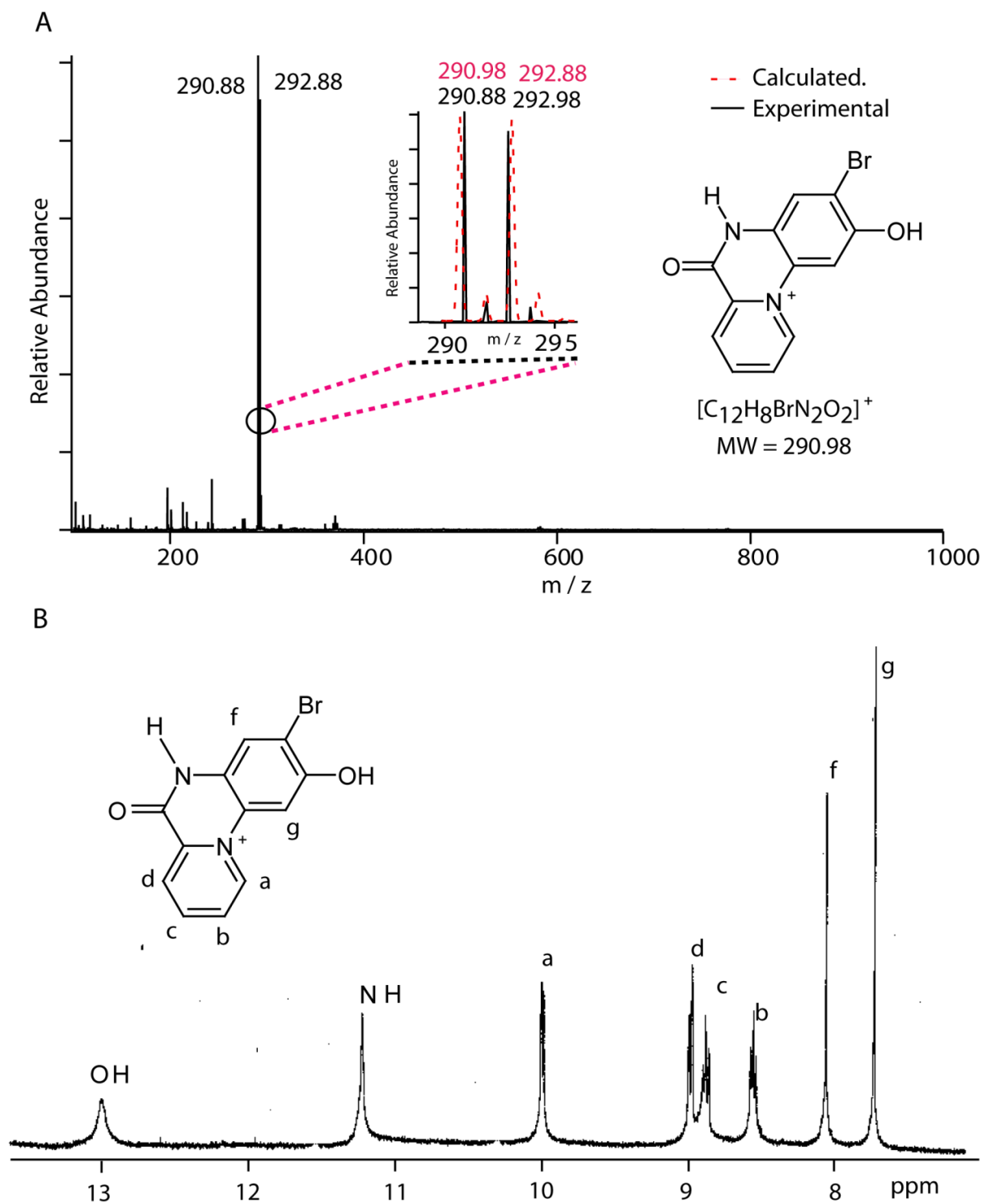


Figure 3.6 (A) ESI mass spectrum and isotopic abundance pattern calculated (red) and experimental (black) of $[P^{6b}]Br$ and (B) 1H NMR spectrum with numbering scheme of $[P^{6b}]Br$.

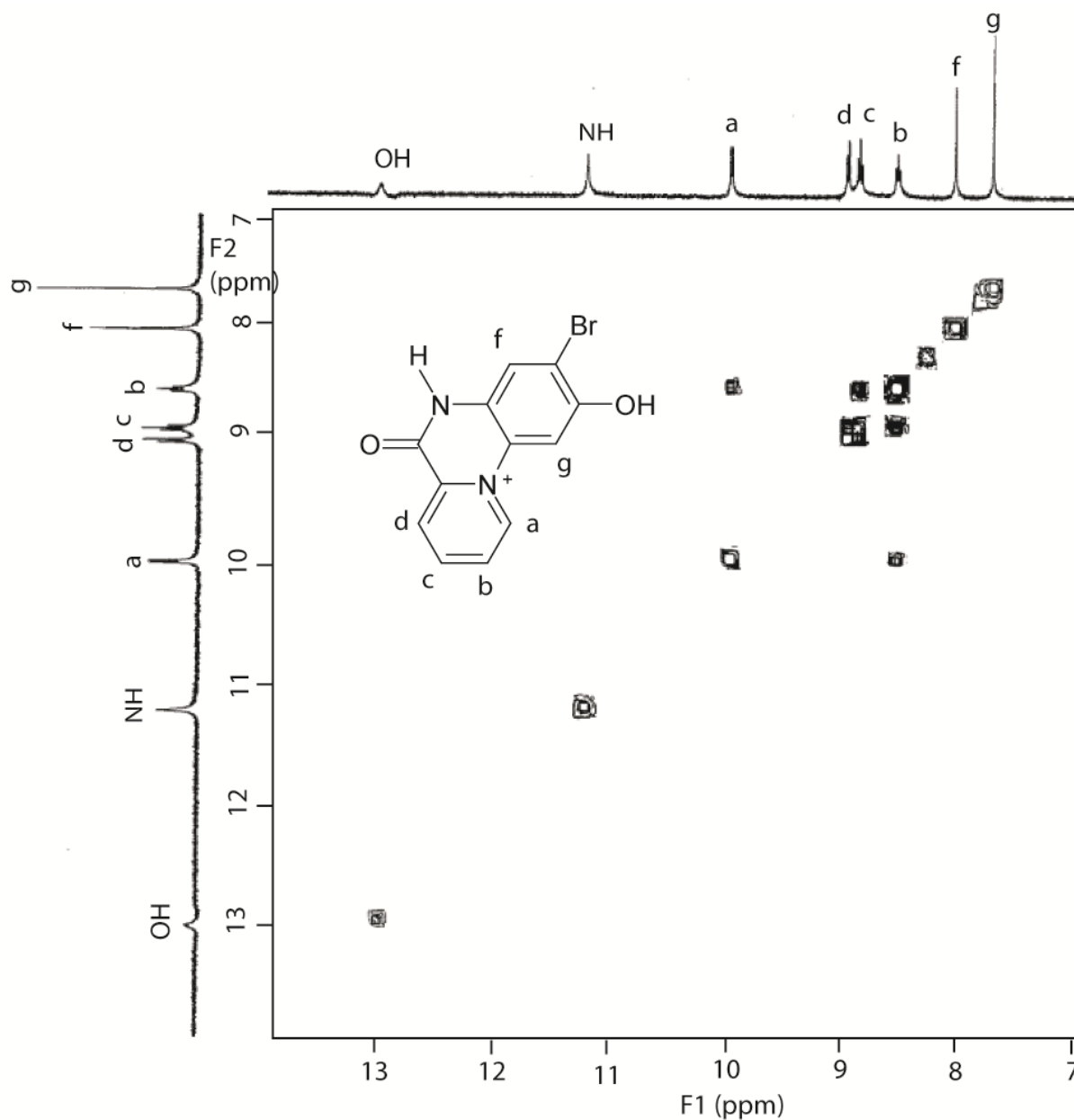


Figure 3.7 The ^1H ^1H -COSY NMR spectrum of 6-keto-2-bromo-2-hydroxy-pyrido[1,2-*a*]quinoxalin-11-ylum bromide ($[\text{P}^{6b}]\text{Br}$) in $\text{DMSO}-d_6$ at 400 MHz.

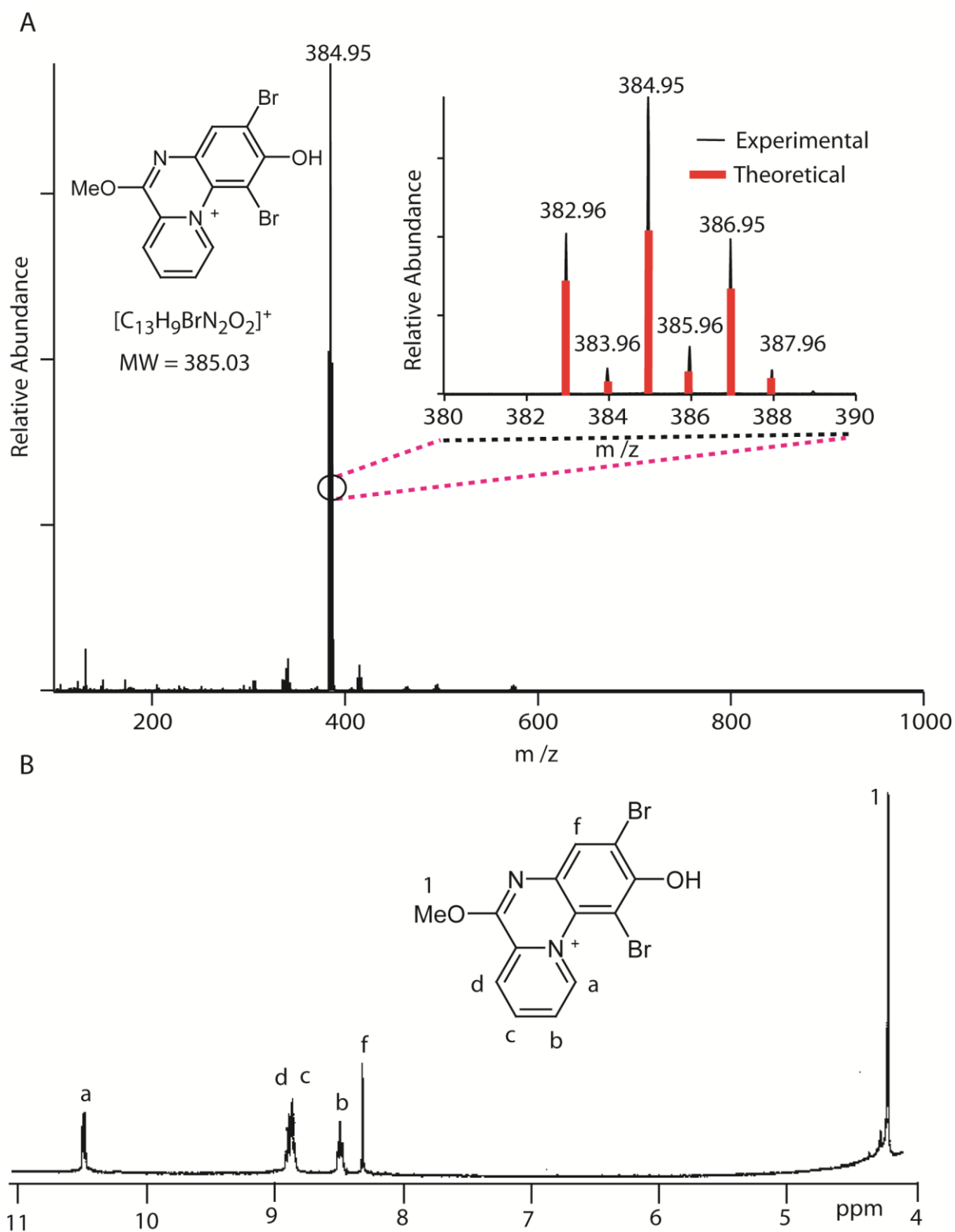


Figure 3.8 ESI mass spectrum and isotopic abundance pattern calculated (red) and experimental (black) of $[P^{6c}]Br$ and (B) 1H NMR spectrum with numbering scheme of $[P^{6c}]Br$.

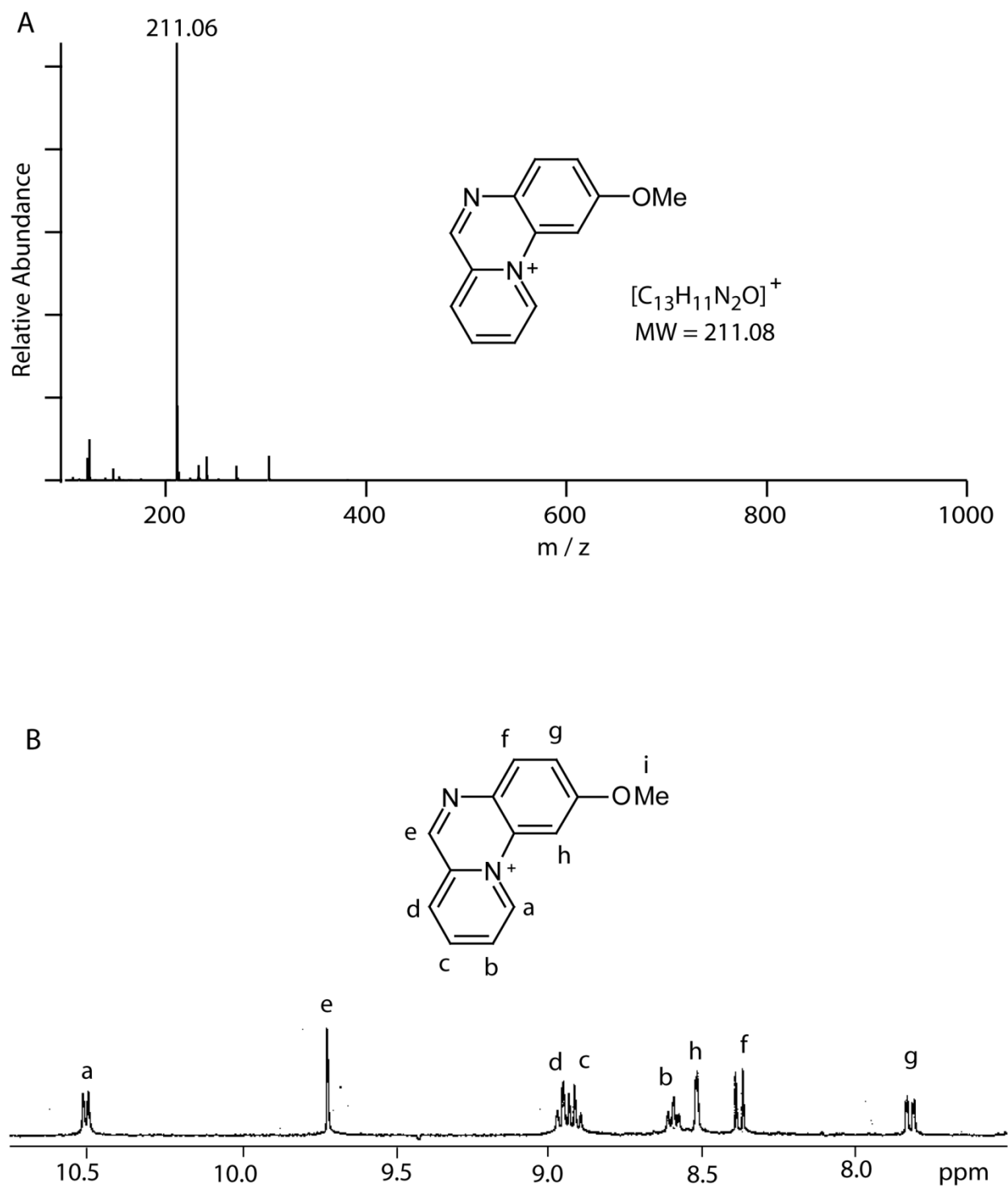


Figure 3.9 (A) ESI mass spectrum and (B) ^1H NMR spectrum with numbering scheme of $[\text{P}^7]\text{Br}$ (only the aromatic region is shown for clarity).

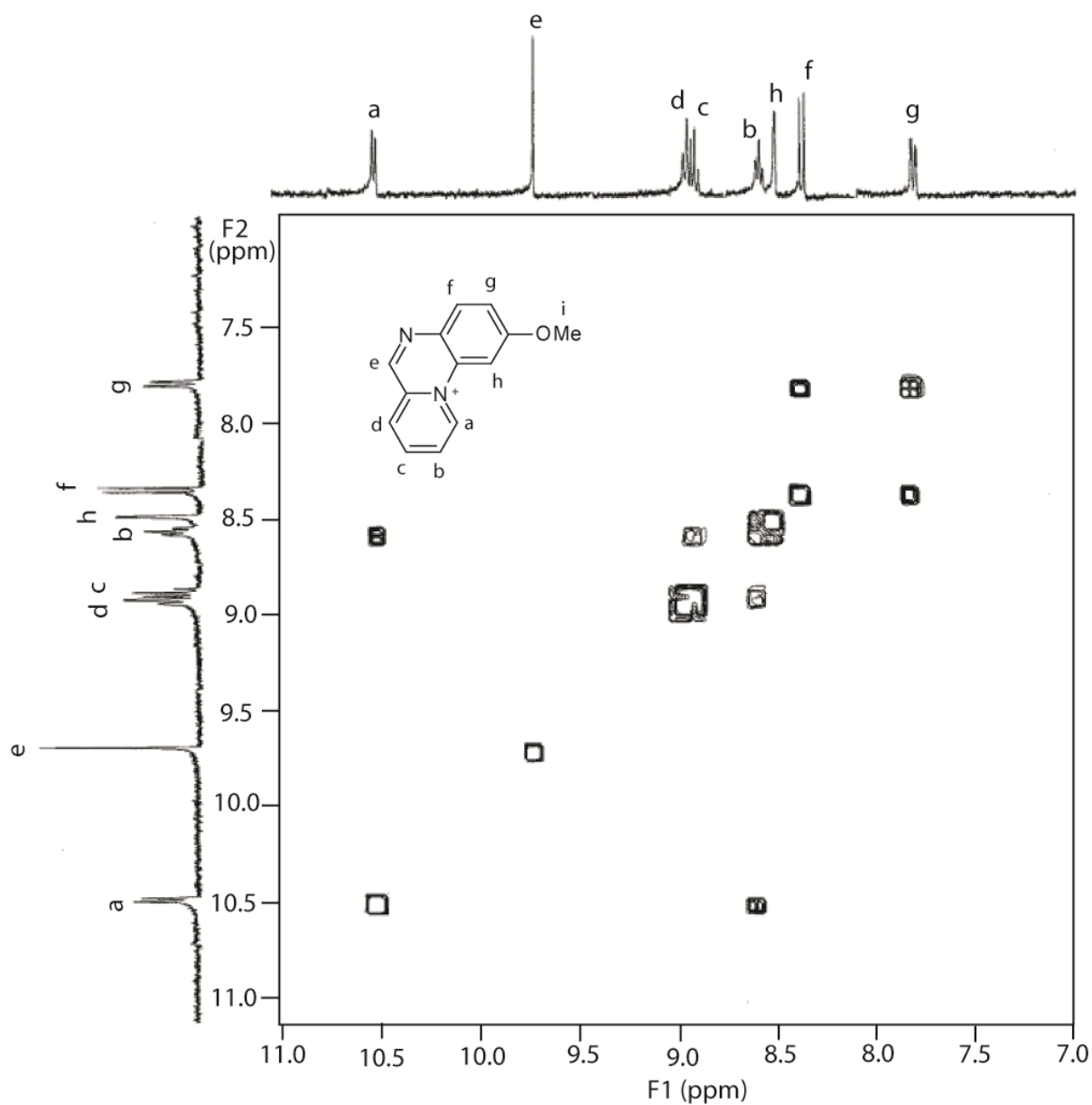


Figure 3.10 The ^1H ^1H -COSY NMR spectrum of 2-methoxy-pyrido[1,2-*a*]quinoxalin-11-ylum bromide ($[\text{P}^7]\text{Br}$) in $\text{DMSO}-d_6$ at 400 MHz (only the aromatic region is shown for clarity).

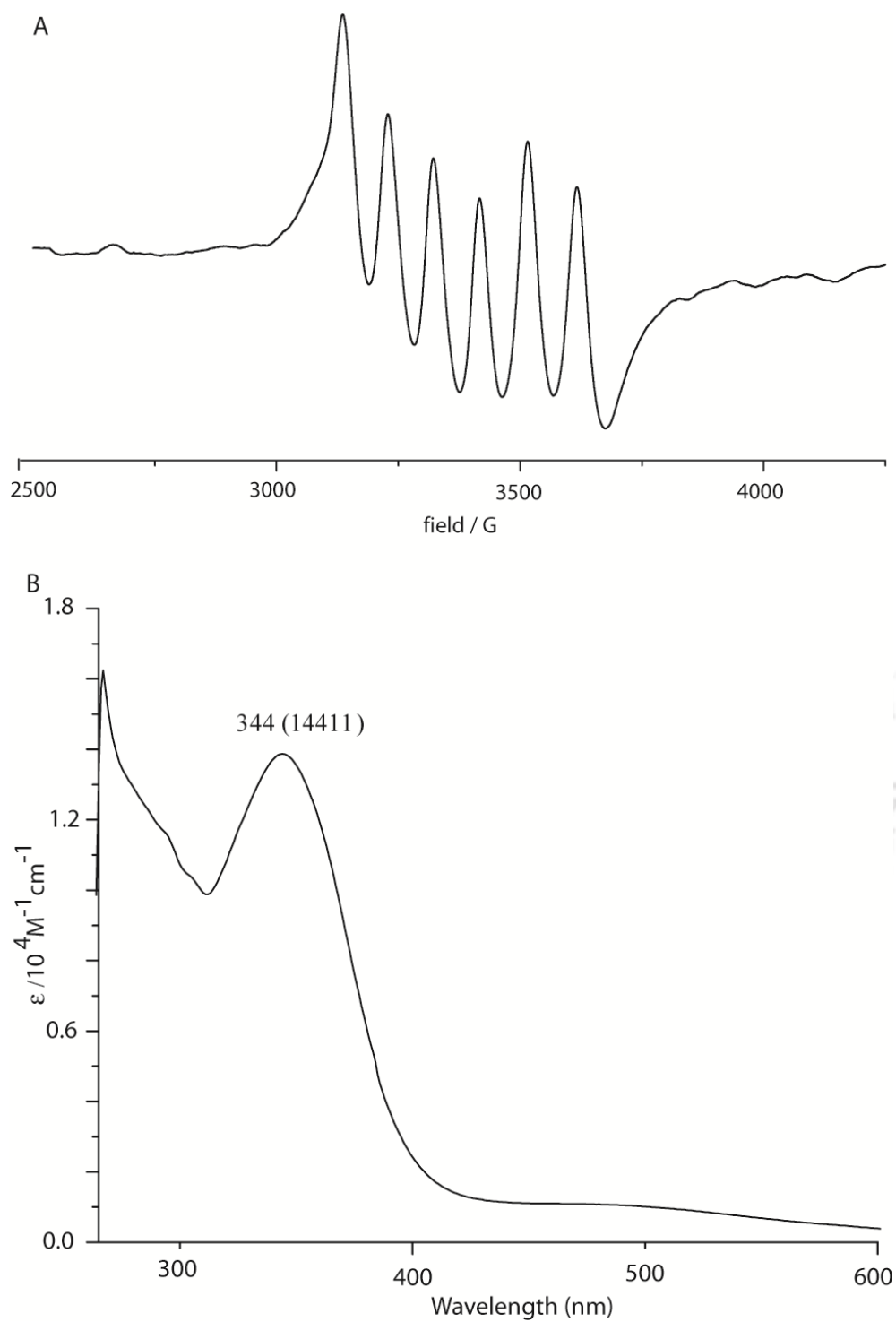


Figure 3.11 (A) EPR spectrum of $[\text{Mn}(\text{L}^6)_2\text{Cl}_2]$ complex (B) UV/vis spectra of $[\text{Mn}(\text{L}^6)_2\text{Cl}_2]$ complex in DMF.

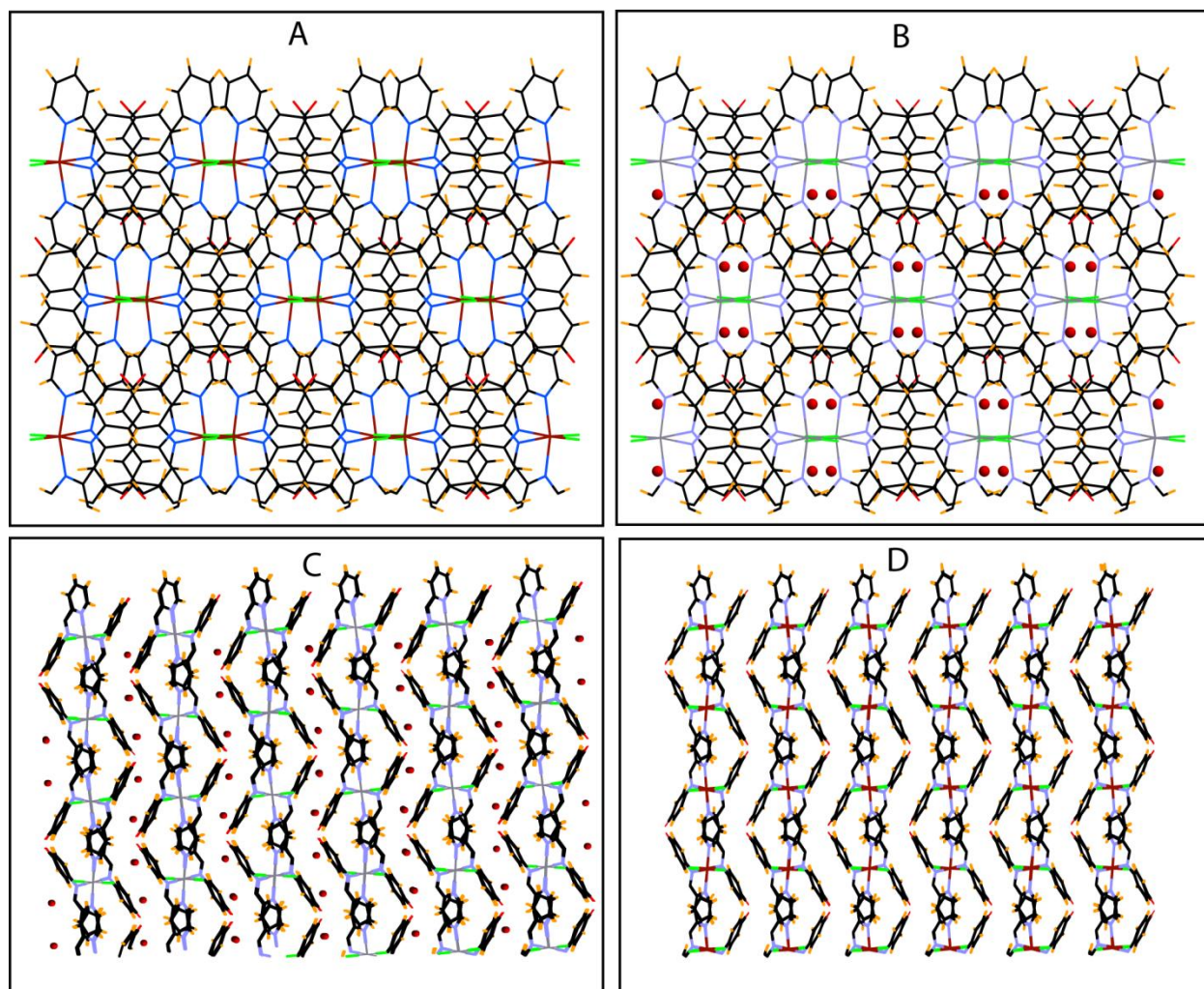


Figure 3.12 (A) Lattice arrangement of the complex $[\text{Mn}(\text{L}^6)_2\text{Cl}_2]$ along c-axis without water (B) with water (C) channel filled with water and (D) channel without water.

3.6 Results and Discussion

3.6.1 Synthesis and characterization of precursors L^6 and L^7

The Schiff base precursors L^6 and L^7 were prepared by condensation of pyridine-2-carbaldehyde with *p*-aminophenol and *p*-methoxyaniline respectively in a 1:1 molar ratio in methanol. The protocol for synthesis is similar to the Schiff bases synthesized in the earlier chapter. The reactions are facile and scalable to multi gram quantity. The FTIR of the products showed band at 1625 and 1623 cm^{-1} assigned as imine vibration (reported for L^1 1617 cm^{-1}). The ESI-MS and ^1H NMR of compound L^6 and L^7 supports the formulation (Experimental Section).

3.7 Cyclization reaction of precursors L^6 - L^7

Detailed procedure for the cyclization of precursors to pyrido[1,2-a]quinoxaline derivatives have been provided below:

3.7.1 Cyclization reactions of L^6

Addition of a light yellow methanolic ferric nitrate solution to a light yellow methanolic L^6 solution in air turned the colour of the solution initially to a dark purple which started turning red after 10 min. The cyclized product $[P^6](NO_3)$ is highly fluorescent. Thus it was possible to monitor the progress of the reaction using ultraviolet lamp. The product was isolated by crystallizing from methanol. The isolated yield is ~30%. Both the product P^6 and the byproduct iron salts, which are likely to stay in solution as a polymeric oxo-bridged ferric product due to the oxidation by oxygen, are ionic in nature. Because of ionic nature and solubility of both product and metal salts, this does not move on silica gel thin layer chromatographic (TLC) plate. Because of these factors we continued the reaction for two hours, even though in all likelihood the reaction was complete within minutes. All further spectroscopic analysis including structural characterization were performed on these crystals. The molar conductance of $[P^6](NO_3)$ in methanol at $103\text{ S cm}^2\text{ mol}^{-1}$ is well within the range $80\text{--}115\text{ S cm}^2\text{ mol}^{-1}$ expected for 1:1 electrolyte.⁵ The FTIR showed the 1384 cm^{-1} peak characteristic for nitrate.⁶ The structure of $[P^6](NO_3)$ was elucidated from single crystal X-ray diffraction (Section 3.8.1).

The reactions of L^6 with reagents other than ferric nitrate were attempted. In each case ESI-Mass of the reaction mixture was used to detect formation of $[P^6](NO_3)$ (m/z 197.22, scanning for ESI+ve ion). The cyclization occurs with $AgNO_3$ and ammonium ceric nitrate but not with $Mn(II)$ or $Co(II)$ chlorides or chloride salts of $Cu(II)$. With $MnCl_2$, L^6 forms complex (Scheme 3.1)⁷. $Mn(II)$ complex was structurally characterized (Section 3.8.4).

3.7.2 Cyclization reactions of L^7

Addition of $Fe(NO_3)_3$ solution to a methanolic L^7 solution in air turned the colour of the solution to a dark purple. Stirring the solution for over two hours showed no sign of fluorescence. Attempt to isolate the product through solvent evaporation followed by addition of

diethyl ether resulted in a purple colored sticky solid. The ESI-MS of this purple solid in methanol showed one strong mass ion peak at 302.32 which could be matched (both ESI-MS value and isotopic abundance pattern) with $C_{13}H_{12}N_2OFe(OH)_2 \sim [(L^7)Fe(OH)_2]^+$. The lability of Fe(III) high-spin complexes might be a reason to fragment the metal complex in solution into this observation of a <6 coordinate complex. Although the lack of fluorescence does not necessarily indicate that the cyclization did not occur, our efforts to isolate complex or cyclized product proved futile. Because of these we looked for a slightly stronger oxidizer. We chose bromine as the redox potential of $Br_2/2Br^-$ at 1.08 V vs NHE is higher than Fe^{3+}/Fe^{2+} (+0.771 vs NHE).⁸

Addition of molecular bromine to the methanolic solution of L^7 yielded a yellow precipitate of $[P^7](Br)$ immediately. Both the precipitate and the solution are fluorescent with a blue colour. Thus the product formation could be monitored by fluorescence using ultraviolet light. The isolation of the product was less difficult in comparison to $[L^6](NO_3)$ with ferric nitrate. The isolated product was soluble in water, methanol and most other common solvents. Although the product precipitated from the solution, the yield is $\sim 30\%$ due to the soluble nature of the product. The filtrates remained highly blue fluorescent. We did not use any precipitant to increase yield to avoid precipitation of impurity.

The molar conductance of $[P^7](Br)$ in methanol at $119\text{ S cm}^2\text{ mol}^{-1}$ is closer to the range $80\text{--}115\text{ S cm}^2\text{ mol}^{-1}$ expected for 1:1 electrolyte. The FTIR of $[P^7](Br)$ showed a band at 1621 cm^{-1} identified as $\nu(C=N)$. The ESI-MS shows molecular ion peak at 211.13 (calculated for M^+ 211.129). The identity of the product was eventually solved using single crystal X-ray crystallographic analysis (section 3.8.3).

The reactions of L^7 with reagents other than ferric nitrate were attempted. In each case ESI-Mass of the reaction mixture was used to detect formation of $[P^7](Br)$ (m/z 211.13), scanning for ESI+ve ion). The cyclization occurs with ammonium ceric nitrate but not with $AgNO_3$ (yellow colour without fluorescence) and Mn(II) or Co(II) chlorides or chloride salts of Cu(II). With $MnCl_2$, L^7 forms complex. Mn(II) complex was magnetically characterized. The magnetic moment at room temperature shows μ_{eff} 6.10 B.M. which corresponds to five unpaired electron present in the system this support the formation of Mn(II) complex. Furthermore

electron paramagnetic resonance spectrum shows six peak at room temperature like **C3** complex which is given in figure 3.11.

3.7.3 Cyclization reactions of **L⁶** with Bromine

Addition of molecular bromine to a light yellow methanolic **L⁶** solution in air turned the color of the solution immediately from yellow to red with red fluorescence. The yellow precipitate was formed within a minute. The yellow precipitate was filtered off and dried in a desiccator. The yellow solid compound was dissolved in methanol and kept for crystallization. Unfortunately, the quality of the crystals was not good enough for X-ray data collection although we have tried several times with different solvent combinations but our best efforts proved futile. So, our characterization is limited to NMR and mass spectrometry. A compound with two bromines shows a distinct M+4 peak with an approximate ratio of 1:2:1. The product $[\text{C}_{13}\text{H}_9\text{Br}_2\text{N}_2\text{O}_2]\text{Br}$ formation is indicated by ESI-MS (M^+) at 382.93, 384.92, 386.92. (Calculated: 387.03 / 385.03 / 382.90).

The molar conductance of $[\text{P}^{6b}]$ in methanol at $94 \text{ S cm}^2 \text{ mol}^{-1}$ is closer to the range 80 - 115 $\text{S cm}^2 \text{ mol}^{-1}$ expected for 1:1 electrolyte. The FTIR of $[\text{P}^{6b}]$ showed a band at 1620 cm^{-1} identified as $\nu(\text{C}=\text{N})$.

The filtrate was evaporated and redissolved in methanol after a few days yellow color needle-like crystals formed which were isolated from the reaction mixture and mounted on glass fiber for data collection. Finally, the structure was solved and formulation of compound confirmed as $[\text{C}_{13}\text{H}_9\text{BrN}_2\text{O}_2]\text{Br}$. Molar conductance and X-diffraction studies suggest that the compound is ionic nature. NMR data also support the formulation of compounds. A compound with one substituted bromine shows a distinct M+2 peak with an approximate ratio of 1:1. The ESI-MS shows molecular ion peak at 304.99, 306.99. (calculated for M^+ 306.13, 304.99). The identity of the product was eventually solved using single crystal X-ray crystallographic analysis.

The molar conductance of $[\text{P}^{6a}]$ in methanol at $85 \text{ S cm}^2 \text{ mol}^{-1}$ is closer to the range 80 - 115 $\text{S cm}^2 \text{ mol}^{-1}$ expected for 1:1 electrolyte. The FTIR of $[\text{P}^{6a}]$ showed a band at 1621 cm^{-1} identified as $\nu(\text{C}=\text{N})$.

We have also isolated one more compound by repetitive crystallization from the same reaction mixture. Unfortunately the crystal quality is not suitable for X-ray diffraction so the formulation of compound was confirmed by ESI-MS as well as NMR spectral studies. This compound is also ionic in nature $[\text{C}_{12}\text{H}_9\text{BrN}_2\text{O}_2]\text{Br}$ which is confirmed by molar conductance measurement. The molar conductance of $[\text{C}_{12}\text{H}_9\text{BrN}_2\text{O}_2]\text{Br}$ in methanol at $80 \text{ S cm}^2 \text{ mol}^{-1}$ is well within the range $80\text{--}115 \text{ S cm}^2 \text{ mol}^{-1}$ expected for 1:1 electrolyte. ESI-MS (M^+): Calcd 290.11, 292.11; Found 290.88, 292.88 (Figure. 3.6).

3.8 Molecular structures of $\text{P}^6\text{--P}^7$ and metal complexes (C3)

3.8.1 Structure of $[\text{P}^6]\text{NO}_3\cdot\text{H}_2\text{O}$

Nitrate salt of $[\text{P}^6]\text{NO}_3\cdot\text{H}_2\text{O}$ crystallized in a triclinic space group $P\bar{1}$ with one molecule each of P^6 cation, nitrate and water. The positive charge is located on the N(1) atom. The ORTEP diagram and selected bond lengths and angles are reported in Figure 3.1 and Table 3.2 respectively. The tricyclic part of the molecule is essentially planar. The angle between the planes containing pyridine and aminophenol ring is only 0.98° . The N2-C6 bond length (imine in ring) at $1.2887(19) \text{ \AA}$ is slightly elongated from $1.2695(19) \text{ \AA}$ observed in Schiff base (L^2) but still considerably shorter than N2-C7 $1.381(6) \text{ \AA}$. This means that the imine bond retains its double bond character even after cyclization reaction i.e., N2-C7 double bond is localized and tricyclic ring is not fully aromatic. The presence of nitrate, water and phenolic oxygen are generated number of H-bonding within the lattice. The Table 3.5 lists such interactions present in the lattice and Figure 3.13 shows some of the resultant pattern formed with the lattice as a result of those interactions.

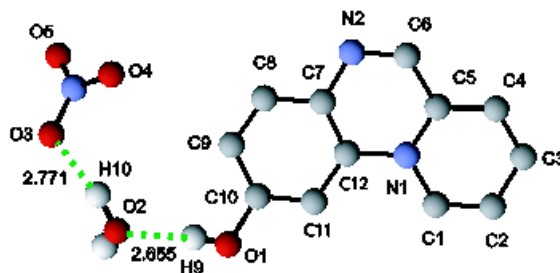


Figure 3.13 H-Bonding scheme in $[\mathbf{P}^6](\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ involving hydroxyl OH, water and nitrate.**Table 3.5** H-bond distances in $[\mathbf{P}^6](\text{NO}_3)_2 \cdot \text{H}_2\text{O}$

D-H...A	$d(\text{D-H})(\text{\AA})$	$d(\text{H...A})(\text{\AA})$	$d(\text{D...A})(\text{\AA})$	$\angle \text{D-H...A}(\text{\AA})$
$[\mathbf{P}^6]\text{NO}_3 \cdot \text{H}_2\text{O}$				
O3-H5...C5	0.930(1)	2.563(1)	3.463(2)	162.79(9)
O3-H10...C9	0.930(1)	2.771(9)	3.360(2)	161.60(9)
O3-H4...O5	0.820(1)	1.842(1)	2.655(2)	171.19(9)
C5-H5...O4	0.930(1)	2.563(1)	3.463(2)	162.79(9)
O2-H9...O1	0.930(1)	2.655(2)	3.327(2)	142.49(9)
C2-H2...N2	0.930(1)	2.632(1)	3.502(2)	155.9(1)
N2-H2...C2	0.930(1)	2.632(1)	3.502(2)	155.9(1)
C7-H7...O1	0.930(1)	2.479(1)	3.313(2)	149.4(1)
C12-H15...O2	0.930(2)	2.547(1)	3.234(2)	130.9(1)

3.8.2 Structure of $[\mathbf{P}^{6a}]\text{Br} \cdot \text{H}_2\text{O}$

Bromide salt of $[\mathbf{P}^{6a}]\text{Br} \cdot \text{H}_2\text{O}$ was crystallized in triclinic space group $P-1$ with one molecule each of $[\mathbf{P}^{6a}]^+$ cation, bromide and water. The positive charge is located on the N(1) atom. The ORTEP diagram and selected bond lengths & angles are in Figure 3.1 and Table 3.2 respectively. The tricyclic part of the molecule is essentially planar. The angle between the planes containing pyridine and aminophenol ring is only 1.60° . The N2-C6 bond length (imine in ring) at $1.276(6) \text{ \AA}$ is slightly elongated from $1.2695(19) \text{ \AA}$ observed in corresponding Schiff base precursor ($\mathbf{L}^6$) but still considerably shorter than N2-C7 ($1.381(6) \text{ \AA}$). This means that the imine bond retains its double bond character even after cyclization reaction i.e., N2-C7 double bond is localized and tricyclic ring is not fully aromatic. The presence of bromide ion, water and phenolic oxygen are generated number of H-bonding within the lattice. The Table 3.6 lists such interactions present in the lattice and Figure 3.14 shows some of the resultant pattern formed with the lattice as a result of those interactions.

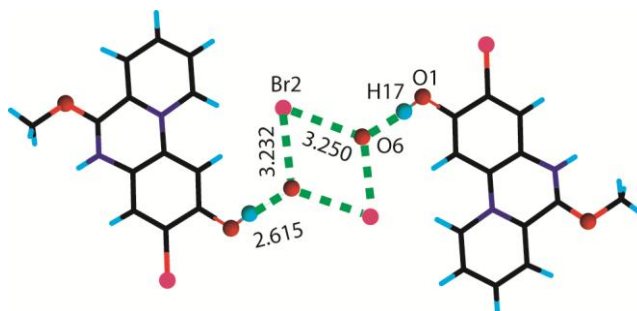


Figure 3.14 H-Bonding scheme in $[\mathbf{P}^{6a}](\text{Br}).\text{H}_2\text{O}$ involving hydroxy, water and Bromide ion.

Table 3.6 H-bond distances in $[\mathbf{P}^{6a}]\text{Br}.\text{H}_2\text{O}$

D-H $\cdots$ A	$d(\text{D-H})(\text{\AA})$	$d(\text{H}\cdots\text{A})(\text{\AA})$	$d(\text{D}\cdots\text{A})(\text{\AA})$	$\angle\text{D-H}\cdots\text{A}(^\circ)$
$[\mathbf{P}^{6a}]\text{Br}.\text{H}_2\text{O}$				
O1-H7 $\cdots$ O6	0.820	1.800(5)	2.615(7)	172.1(3)
N1-H5 $\cdots$ C13	0.860(6)	2.824(9)	3.50(1)	136.3(4)
C13-H10 $\cdots$ N1	0.961(8)	2.0645(3)	2.824(9)	126.4(5)

3.8.3 Structure of $[\mathbf{P}^7]\text{Br}$

Bromide salt of $[\mathbf{P}^7]\text{Br}$ was crystallized in triclinic space group $P2_1/n$ with one molecule each of $\mathbf{P}^7$ cation and bromide. The positive charge is located on the N(1) atom. The ORTEP diagram and selected bond lengths and angles are in Figure 3.1 and Table 3.6 respectively. The tricyclic part of the molecule is essentially planar. The angle between the planes containing pyridine and aminophenol ring is only 0.00° . The N2-C6 bond length (imine in ring) at 1.304(6) Å is slightly elongated from 1.2695(19) Å observed in corresponding Schiff base precursor ($\mathbf{L}^7$) but still considerably shorter than N2-C7 1.381(6) Å. The reason of this shortening of bond is given in (Section 3.8.2). The presence of delocalization of electron on quinoxaline moiety generated weak interaction between the tricyclic ring within the lattice. The Table 3.7 lists such interactions present in the lattice and Figure 3.15 shows some of the resultant pattern formed with the lattice as a result of weak bond interactions.

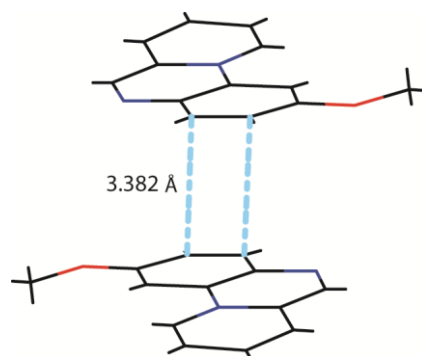


Figure 3.15 Weak bond interactions in $[P^7](Br)$ between quinoxalinium tricyclic rings. .

Table 3.7 H-bond distances in $[P^7]Br$

D-H...A	$d(D-H)(\text{\AA})$	$d(H...A)(\text{\AA})$	$d(D...A)(\text{\AA})$	$\angle D-H...A(^{\circ})$
$[P^7]Br \cdot H_2O$				
C2-H2...Br1	0.930(5)	2.828(6)	3.710(5)	158.9(3)
C6-H6...Br1	0.930(5)	2.989(5)	3.915(5)	173.8(3)
C11-H11...O1	0.930(5)	2.561(3)	3.440(6)	157.8(3)
C10-H10...Br1	0.930(5)	2.641(5)	3.534(5)	160.9(3)
C11-H11...O1	0.930(5)	2.561(3)	3.440(6)	157.8(3)
C12-H12...Br1	0.929(6)	2.882(6)	3.741(6)	154.3(4)
C8-H8...Br1	0.930(5)	2.890(5)	3.753(5)	154.9(3)

3.8.4 Structure of $Mn(L^6)_2Cl_2$ (C3)

The complex **C3** crystallized in the *pbcn* space group with half molecule of the complex in the asymmetric unit. The ORTEP diagram¹⁰ of the complex and selected bond lengths and angles are in Figure 3.1 and Table 3.4 respectively. The complex consists of octahedral manganese coordinated by bidentate L^6 and two chloride ion. The chlorides are *cis* oriented. The pyridine donors from the L^6 are *trans* to each other and imine donors are *cis* to each other. The overall molecule is C_2 symmetric without any σ plane making the molecule chiral. However, as the space group *pbcn* is achiral, both the enantiomer is within the unit cell connected through plane of symmetry making the crystal achiral. The geometry around manganese is distorted from ideal octahedral as is evident from the deviation of *cis* bond angles from 90° and *trans* bond angles from 180° expected for perfect octahedron (Table 3.3). The Mn-N_{pyridine} and Mn-Cl lengths are consistent with similar Mn(II) Schiff base complexes.¹¹ The Mn-Cl bond length is

longer than observed for similar complexes but well within the range observed for other halide complexes.¹² The lattice contains considerable number of $\pi\cdots\pi$, $\text{CH}\cdots\text{Cl}$ and $\text{NH}\cdots\text{Cl}$ interactions. Significant among those are multiple interactions between halides and amine NH and aromatic CH as well as $\pi\cdots\pi$ edge interactions between pyridine rings (Table 3.8). The lattice also contains solvent accessible hydrophobic voids ($V = 117\text{\AA}^3$) in the form of narrow one dimensional channels along a -axis (Figure. 3.12). The complex shows 6 lines EPR spectra characteristic of Mn (II) and show only charge transfer band in the UV-visible spectrum (Figure. 3.11).

Table 3.8 H-bond distances in complex **C3**

D-H $\cdots$ A	$d(\text{D-H})(\text{\AA})$	$d(\text{H}\cdots\text{A})(\text{\AA})$	$d(\text{D}\cdots\text{A})(\text{\AA})$	$\angle\text{D-H}\cdots\text{A}(^\circ)$
Mn(L⁶)₂Cl₂ (C3)				
N3-H5 $\cdots$ Cl1	0.86	2.69	3.531(9)	167
N3A-H6A $\cdots$ Cl1	0.86	2.81	3.584(9)	150
C1-H1 $\cdots$ Cl1	0.93	2.82	3.429(13)	124
C9-H9 $\cdots$ Cl2	0.93	2.73	3.626(8)	162

3.9 ¹H NMR analysis

The ¹H NMR spectroscopic assignments of the precursors and products were performed based on peak position, integration and spectra given in (Figures. 3.2 B, 3.4 B, 3.6 B and 3.8 B).¹³ All peak assignments corroborates well with the structural characterization. Assignments of the products were additionally corroborated with the help of 2D COSY spectra (Table 3.4, Figures 3.3, 3.5, 3.7 and 3.10). This also confirms the structure of [P^{6b}](Br) and [P^{6c}](Br) both were not structurally characterized by X-ray crystallography, as a tricyclic product similar to other products. Comparisons among the products show that the protons H^a, H^d, H^e and H^h protons shifts considerably to downfield as observed in (Chapter 2) ¹H NMR analysis. The result shows that counter ions do not affect chemical shifts. Comparison between tricyclic part of the assignments shows that shifts of a proton among all the products in same solvent are almost identical (Table 3.4). This means that the effect of substitution of bromine and methoxy group on quinoxalinium ring has minimal effect on electron density distribution within the tricycle.

Conclusion

The results presented in this chapter confirm our initial guess that the cyclization is possible as long as the central *p*-disubstituted aromatic ring is vulnerable to oxidation is correct. The requirement of a stronger oxidizer, bromine, for **L**⁷ shows that the oxidation is sensitive to minor changes in the redox potential (higher for *p*-methoxyaniline derivative)¹ of the precursor. The reaction of Br₂ with **L**⁶ on the other hand produced number of products, some of which were identified from ESI-MS, where bromine got incorporated in the product. It is possible that if the reaction with **L**⁶ is faster than local concentration of excess bromine had a chance to brominated the product. We will explore the reaction with bromine further in the next chapter.

Overall, we have now been able to extend the cyclization reaction to *p*-aminophenol derivatives which resulted in number of new derivatives. The changes in the derivative also resulted in fluorescent dyes having different range of coloured emission. The details analysis of the fluorescent spectra along with all the other fluorescent derivatives will be presented in chapter V.

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Chapter - 4

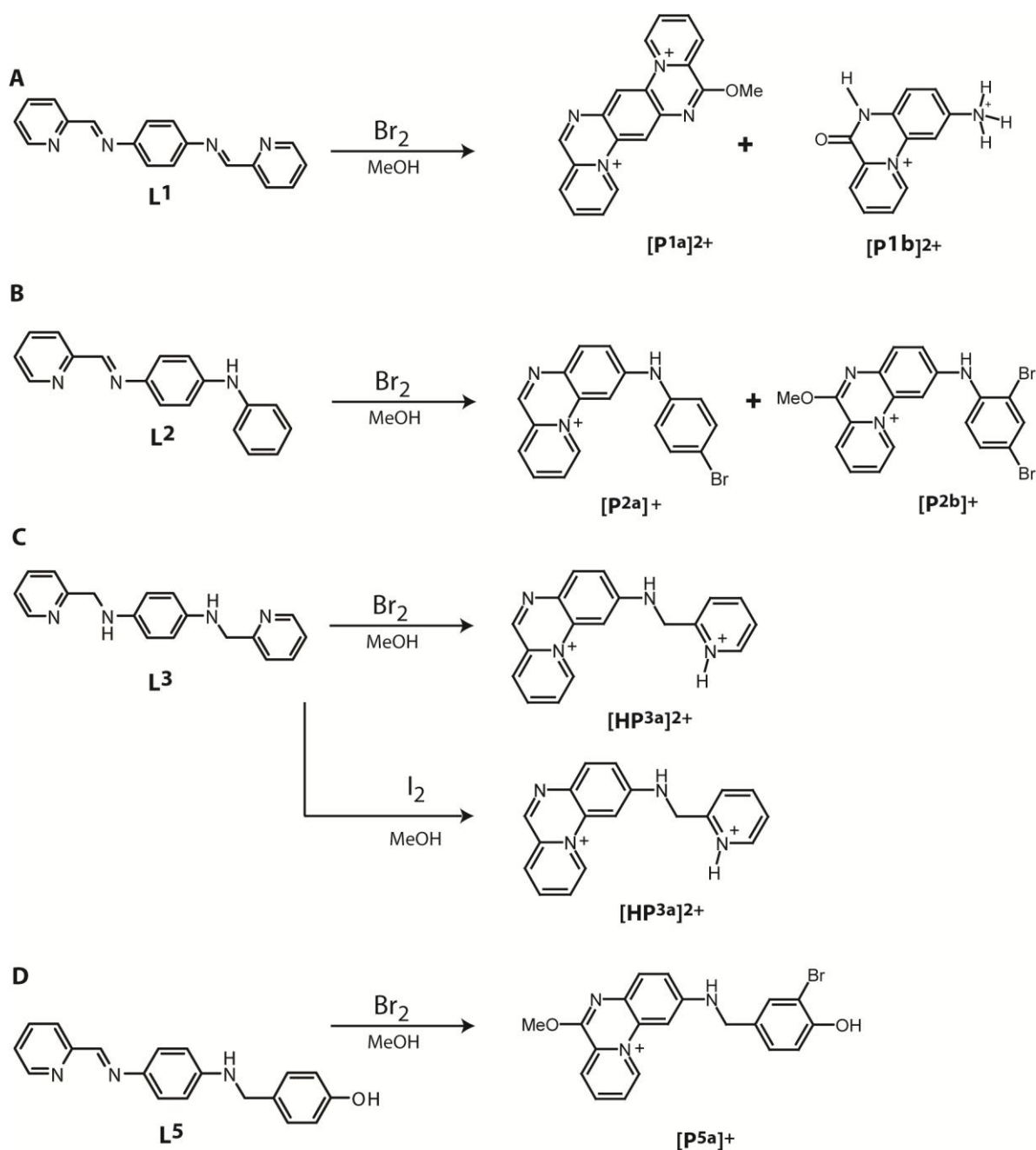
**Synthesis and characterization of
pyrido[1,2-*a*]quinoxalin-11-ylum derivatives
from Schiff base or reduced Schiff base by
molecular bromine and iodine**

In the previous chapters, we have observed that instead of metal salts, molecular bromine ($\text{Br}_2/2\text{Br}$ potential 1.08V Vs. NHE in aqueous solution)¹ could be used to facilitate the cyclization reaction of Schiff bases derived from *p*-aminophenols. In this chapter we have explored the cyclization reaction of Schiff bases as well as reduced Schiff bases of *p*-phenylenediamine derivatives (Chapter 2) using molecular bromine. The molecular iodine used as an oxidizing agent in heterocyclic synthesis has received attention in organic synthesis because of its low cost, non-toxicity and ready availability.² There are no reports on the direct oxidation of Schiff base and reduced Schiff base to the corresponding cyclized product pyrido[1,2-*a*]quinoxaline derivatives by using iodine or molecular bromine reagents either catalytic amount or stoichiometric amount.

4.1 Experimental Section

4.1.1 Solvents and Reagents

Solvents used were purified prior to use following standard literature procedure. Molecular bromine and molecular iodine were purchased from Sisco Research Laboratories Pvt. Ltd. (SRL), India and used as received. KBr was purchased from Aldrich Chemical Co. India and used as received. The ligands **L**¹-**L**⁴ were synthesized and characterized by different spectroscopic techniques which are given in the previous chapter 2.



Scheme 4.1 Syntheses of substituted and unsubstituted brominated compounds of pyrido[1,2-a]quinoxalin-11-yl cations from Schiff base and reduced Schiff base precursors. Charges are counter balanced by bromide and iodide ions which are omitted for clarity.

4.2 Syntheses of pyrido[1,2-a]quinoxalines derivatives P^1 - P^5

Detailed synthetic procedures along with characterization data have been provided below:

4.2.1 Syntheses of 5-methoxypyrido[1,2-a]pyrido[1'2':1,6]pyrazino[2,3-g]quinoxaline-8,16-diiumbromide[P^{1a}](Br)₂ (1) and 2-ammonio-6-oxo-5,6-dihydropyrido[1,2-a]quinoxali-11-iumbromide[HP^{1b}](Br)₂ (2)

[P^{1a}](Br)₂(1). Molecular bromine (0.22 g, 72.0 μ L, 1.40 mmol) was added dropwise to a methanolic solution (10 mL) of **L¹** (0.20 g, 0.70 mmol). The color of the solution was immediately changed from yellow to orange. The yellow solid product which precipitated out within a minute, was filtered off, and washed with hexane (3 $\times$ 5 mL) and acetone (3 $\times$ 5 mL) successively. The filtrate and washings were preserved. Finally, the compound was dried in vacuum desiccator. Yield: (0.08 g, 10%). Characterization data for [**P^{1a}**](Br)₂(1): Melting point >400 °C. Λ_M (MeOH): 165 S cm² mol⁻¹. ESI-MS (M^{2+}): Calcd 157.0; Found 157.0. UV-vis (H₂O): λ_{max} , nm(ϵ , M⁻¹ cm⁻¹): 266 (23,000), 304 (14,000), 402 (12,000), 425 (13,000), 490 (3,000). IR (KBr, cm⁻¹): ν (C=N) 1610. Fluorescence (H₂O): λ_{ex} , 400 nm; λ_{em} , 463 nm. ¹H NMR (400 MHz, D₂O-d₂) δ (ppm) 10.55 (1H, d, J = 6.4 Hz), 10.45 (1H, d, J = 6.8 Hz), 9.80 (1H, s), 9.78 (1H, s), 9.58 (1H, s), 9.20 (1H, d, J = 8.4 Hz), 9.11 (2H, t, J = 6.8 Hz), 9.03 (1H, d, J = 8.0 Hz), 8.73 (2H, m), 4.50 (3H, s). HRMS (ESI) m/z [M]⁺ calcd for C₁₉H₁₄N₄O: 314.1168/157.0584 found: 314.1174/157.0584

[HP^{1b}](Br)₂(2). The filtrate and washings of above reaction (1) was evaporated to dryness; the resulting compounds was highly sticky in nature. A dark red coloured crystalline compound was obtained within a week by slow evaporation of methanol, washed with diethyl ether and dried in vacuum desiccator. Yield: (0.16 g, 31%). Characterization data for [**P^{1b}**](Br)₂(2): Melting point 140-143 °C. Λ_M (MeOH): 167 S cm² mol⁻¹. ESI-MS (M^+): Calcd 212.25; Found 212.09. UV/vis (MeOH): λ_{max} , nm(ϵ , M⁻¹ cm⁻¹): 258 (26,000), 304 (6,000), 502 (4,000). IR (KBr, cm⁻¹): ν (C=O) 1710. Fluorescence (MeOH): λ_{ex} , 480 nm; λ_{em} , 593 nm. ¹H NMR (400 MHz, DMSO-d₆) δ (ppm) 12.94 (OH), 9.94 (1H, d, J = 6.8 Hz), 8.94 (1H, d, J = 6.8 Hz), 8.80 (1H, t, J = 8.0 Hz), 8.51 (1H, t, J = 6.8 Hz), 7.84 (1H, d, J = 6.8 Hz), 7.38 (1H, d, J = 8.0 Hz) 7.25 (1H, d, J = 6.8 Hz).

4.2.2 Syntheses of 2-((4-bromophenyl)amino)pyrido[1,2-a]quinoxali-11-iumbromide [**P^{2a}**](Br) (3) and 2-((2,4-dibromophenyl)amino)-6-methoxypyrido[1,2-a]quinoxalin-11-iumbromide [**P^{2b}**](Br) (4)

[P^{2a}](Br)(3). Molecular bromine (0.23 g, 75.0 μ L, 1.46 mmol) was added dropwise to a methanolic solution (10 mL) of **L²** (0.20 g, 0.73 mmol). The color of the solution changed immediately from yellow to red. A sticky solid compound precipitated out within minutes, which was washed with methanol and acetone successively. The remaining solid compound after filtration and washings were preserved. The filtrate was evaporated and washed with hexane. Fine red needle-like crystals were formed in 48 h by slow evaporation of the methanolic solution. The crystals were collected, washed with diethyl ether and dried over silica gel in vacuum desiccator. Yield: (0.16 g, 15%). Characterization data for **[P^{2a}](Br)(3)**: Melting point: 332-334 °C. Λ_M (MeOH): 81 S cm² mol⁻¹. ESI-MS (M^+): Calcd 349.97/350.03; Found 349.98/351.98. (Figure 4.5) UV/vis (MeOH): λ_{max} , nm (ϵ , M⁻¹ cm⁻¹): 246 (39,000), 298 (54,000), 373 (14,000), 485 (31,000). IR (KBr, cm⁻¹): ν (C=N) 1619, ν (N-H) 3259. ¹H NMR (400 MHz, DMSO-d₆) δ (ppm) 10.10 (1H, d, J = 6.8 Hz), 9.55 (1H, s, C=N), 9.71 (N-H), 8.87 (1H, d, J = 6.8 Hz), 8.80 (1H, t, J = 8.0 Hz) 8.43 (1H, t, J = 7.2 Hz), 8.30 (1H, s), 8.25 (1H, d, J = 8.0 Hz), 7.75 (1H, d, J = 8.5 Hz), 7.61 (2H, d, J = 8.4 Hz), 7.39 (2H, d, J = 8.8 Hz). HRMS (ESI) m/z [M]⁺ calcd for C₁₈H₁₃BrN₃: 350.0293/352.0274 found: 350.0287/352.0267

[P^{2b}](Br)(4). The solid compound from the above reaction **[P^{2a}]** was dried in vacuum desiccator. Yield: (0.16 g, 30%). Single crystals of **[P^{2b}]** were successfully grown by slow evaporation of methanolic solution. Characterization data for **[P^{2b}](Br)(Br₃)(4)**. Melting point: 216-218°C. Λ_M (MeOH): 114 S cm² mol⁻¹. ESI-MS (M^+): Calcd 353.03 / 459.95 / 460.95. Found 458 / 460.03 / 461.03 (Fig. 4.7). UV/vis (MeOH): λ_{max} , nm (ϵ , M⁻¹ cm⁻¹): 246 (50,000), 297 (68,000), 372 (17,000), 484 (39,582). IR (KBr, cm⁻¹): ν (C=N) 1615, ν (N-H) 3289. ¹H NMR (400 MHz, DMSO-d₆) δ (ppm) 10.8 (1H, d, J = 6.7 Hz), 9.70 (m, N-H), 8.85 (1H, d, J = 6.7 Hz), 8.81 (1H, t, J = 7.8 Hz) 8.44 (1H, t, J = 7.3 Hz), 8.31 (1H, s), 8.22 (1H, d, J = 7.8 Hz), 7.76 (1H, d, J = 8.4 Hz), 7.60 (1H, s), 7.39 (2H, m,) 4.20 (OMe) . HRMS (ESI) m/z [M]⁺ calcd for C₁₉H₁₄Br₂N₃O: 457.9503/459.9503/461.9503 found: 457.9536/459.955/461.9498.

4.2.3 Syntheses of 2-((pyridine-1-ium-2-ylmethyl)amino)pyrido[1,2-a]quinoxalin-11-ium bromide[HP³](Br)₂ (5)

[HP³](Br)₂ (5) Molecular bromine (0.22 g, 71.0 μ L, and 1.38 mmol) was added dropwise to a methanolic solution (10 mL) of **L³** (0.20 g, 0.69 mmol). The colour of the solution changed immediately from light orange to red with orange fluorescence. The

reaction mixture was stirred for 2 h. The solvent was concentrated to 5 mL, and 10 mL of acetone was added. A yellow solid product precipitated out, which was filtered off, washed with hexane and diethyl ether sequentially. Finally, the compound was dried over silica gel in vacuum desiccator. Yield: (0.16 g, 31%). A suitable crystal for single crystal data collection was grown through slow evaporation of methanol at room temperature under open atmosphere. Characterization data for $[\text{HP}^3](\text{Br})_2$ (**5**): Melting point 250-254 °C. Λ_{M} (MeOH): $165 \text{ S cm}^2 \text{ mol}^{-1}$. ESI-MS (M^+): Calcd: 287.13; Found: 287.13. UV-vis (MeOH): λ_{max} , nm (ϵ , $\text{M}^{-1} \text{ cm}^{-1}$): 272 (11,000), 325 (2,000), 384 (2,000), 487 (5,873). IR (KBr, cm^{-1}): $\nu(\text{C}=\text{N})$ 1621, $\nu(\text{N-H})$ 3259. Fluorescence (MeOH): λ_{ex} , 480 nm; λ_{em} , 590 nm. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 10.15 (1H, d, $J = 6.7 \text{ Hz}$), 9.47 (1H, t, 7.0 Hz) 9.44 (1H, s, $\text{HC}=\text{N}$), 8.82 (1H, t, $J = 8.4 \text{ Hz}$), 8.75 (1H, t, $J = 7.6 \text{ Hz}$) 8.44 (1H, m), 8.26 (1H, m), 8.17 (2H, m), 7.79 (1H, s), 7.69 (1H, m), 7.44 (1H, m), 4.99 (2H, s), 6.8 (s, N-H). HRMS (ESI) m/z $[\text{M}]^+$ calcd for $\text{C}_{18}\text{H}_{15}\text{N}_4$: 287.1297 found: 287.1297

4.2.4 Syntheses of $[\text{HP}^3](\text{I})_2$ (**6**)

$[\text{HP}^3](\text{I})_2$ (**6**). Molecular iodine (0.16 g, 1.00 mmol) was added to a methanolic solution (10 mL) of L^3 (0.20 g, 1.00 mmol). The colour of the solution changed immediately from light orange to red with red fluorescence. The reaction mixture was stirred for 2 h. The solvent was evaporated to 5 mL, and 10 mL acetone was added, a yellow solid was precipitated out, filtered off, washed with hexane and diethyl ether successively. Finally, the product was dried over silica gel in vacuum desiccator. Yield: (0.16 g, 41%). The suitable yellow crystal for single crystal data collection was successfully grown by slow evaporation of methanol. Characterization data for $[\text{P}^3](\text{I})_2$ (**6**): Λ_{M} (MeOH): $162 \text{ S cm}^2 \text{ mol}^{-1}$. ESI-MS (M^+): Calcd 287.13; Found 287.13. UV-vis (MeOH): λ_{max} , nm (ϵ , $\text{M}^{-1} \text{ cm}^{-1}$): 270 (11,000), 326 (2,000), 380 (2,000), 485 (6,000). IR (KBr, cm^{-1}): $\nu(\text{C}=\text{N})$ 1619, $\nu(\text{N-H})$ 3259. Fluorescence (MeOH): λ_{ex} , 480 nm; λ_{em} , 584 nm. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 10.27 (1H, d, $J = 5.6 \text{ Hz}$), 9.38 (1H, s, $\text{C}=\text{N}$), 8.83 (1H, t, $J = 7.0 \text{ Hz}$), 8.77 (1H, t, $J = 8.0 \text{ Hz}$), 8.74 (1H, m), 8.50 (1H, d, $J = 6.4 \text{ Hz}$), 8.14 (1H, m), 7.81 (1H, d, $J = 7.6 \text{ Hz}$), 7.68 (1H, d, $J = 10.4 \text{ Hz}$), 7.61 (2H, m), 7.43 (1H, m), 4.20 (2H, s). HRMS (ESI) m/z $[\text{M}]^+$ calcd for $\text{C}_{18}\text{H}_{15}\text{N}_4$: 287.1297 found: 287.1297

4.2.5 Syntheses of $[\text{P}^{5a}](\text{Br})_2$ (**7**)

$[\text{P}^{5a}](\text{Br})_2$ (**7**) Molecular bromine (0.21 g, 68 μL , 1.32 mmol) was added to a methanolic solution (10 mL) of L^5 (0.20 g, 0.66 mmol). The colour of the solution

immediately changed from yellow to red with dark red fluorescence. A solid precipitated out within 2 h, filtered off, washed with acetone and hexane respectively. Finally, the compound was dried over silica gel in vacuum desiccator. Yield: (0.10 g, 38%). The quality of crystal is not suitable for X-ray data collection. Characterization data for $[\mathbf{P}^{5a}](\text{Br})$ (**7**): Melting point 227-228 °C. Λ_M (MeOH): 90 S cm² mol⁻¹. ESI-MS (M^+): Calcd 409.98/411.98; Found 410.05/ 412.05 (Figure 4.9). UV/vis (MeOH): λ_{max} , nm (ϵ , M⁻¹ cm⁻¹): 262 (11,000), 485 (2,000). IR (KBr, cm⁻¹): $\nu(\text{O-H})$ 3445, $\nu(\text{N-H})$ 3285, $\nu(\text{C=N})$ 1620, $\nu(\text{C=C})$ 1513, $\nu(\text{C-O})$ 1258. Fluorescence (MeOH): λ_{ex} , 480 nm; λ_{em} , 623 nm. ¹H NMR (400 MHz, DMSO-d₆) δ (ppm) 10.27 (1H, d, J = 6.8 Hz), 8.83 (1H, d, J = 3.6 Hz), 8.77 (1H, t, J = 8.0 Hz), 8.50 (1H, t, J = 8.0 Hz), 7.81 (1H, m), 7.68 (2H, m), 7.59 (1H, m), 7.42 (1H, d, J = 7.2), 7.50 (1H, d, J = 4.4 Hz), 7.30 (1H, d, J = 4.4 Hz), 4.32 (s, N-H), 4.21 (s, 2H, CH₂), 4.25 (s, OMe). HRMS (ESI) m/z [M]⁺ calcd for C₂₀H₁₇BrN₃O₂: 410.0504/412.0486 found: 410.0488/412.0482

4.3 X-ray Data Collection, Structure Solution and Refinement

Crystals of the products $[\mathbf{P}^{2a}](\text{Br})$ (**2**), $[\mathbf{P}^{2b}](\text{Br})$ (**3**), $[\mathbf{HP}^3](\text{Br})_2$ (**4**), and $[\mathbf{HP}^3](\text{I})_2$ (**5**) obtained during synthesis were used for X-ray analysis. The crystals were mounted on glass fiber. The instrumental parameters used for data collections are same as described in the Chapter 2. Absorption corrections were done using SADABS only as either kinds of absorption did not help.⁴ After the initial solution and refinement with SHELXL, the final refinements were performed on WinGX environment using SHELX97.⁵ Selected crystallographic data have been summarized in Table 4.1. The crystals of all compounds were mounted on glass fibre. All geometric and intensity data for the crystals were collected at room temperature using a Bruker SMART APEX CCD diffractometer equipped with a fine focus 1.75 kW sealed tube Mo K α (λ = 0.71073 Å) X-ray source, with increasing ω (width of 0.3° per frame) at a scan speed of 3 s/frame. The SMART software was used for data acquisition and the SAINT software for data extraction. Structures were solved and refined using SHELX97. All non-hydrogen atoms were refined isotropically.

Table 4.1 Crystallographic data and refinement parameters for compounds^a

Compounds	[P ^{2a}](Br)	[P ^{2b}](Br) ₄	[HP ³](Br) ₂	[HP ³](I) ₂
Empirical formula	C ₃₆ H ₂₈ Br ₄ N ₆ O	C ₁₉ H ₁₄ Br ₄ N ₃ O	C ₃₆ H ₃₂ Br ₄ N ₈ O ₃	C ₃₆ H ₃₂ I ₄ N ₈ O ₃
<i>M</i>	880.24	619.97	944.30	1132.30
Wavelength Å	0.71073	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic	Triclinic	Triclinic
Space group	<i>C</i> 2/c	<i>C</i> 2	<i>P</i> -1	<i>P</i> -1
<i>a</i> , Å	13.0739(7)	15.664(2)	11.4659(3)	11.4796(4)
<i>b</i> , Å	6.1910(3)	7.6248(10)	13.3158(3)	13.3182(5)
<i>c</i> , Å	41.499(2)	18.047(3)	14.6807(4)	14.6721(5)
α , deg	90.000	90.000	79.7120(10)	79.764(2)
β , deg	90.836(3)	112.318(9)	89.2490(10)	89.269(2)
γ , deg	90.000	90.000	66.8380(10)	66.803(2)
<i>V</i> /Å ³	3358.6(3)	1993.9(5)	2023.57(9)	2024.95(12)
<i>Z</i>	4	4	2	4
ρ /g cm ⁻³	1.741	2.065	1.550	1.857
μ /mm ⁻¹	4.833	8.088	4.020	13.122
Reflns collected	20554	9260	28647	24289
Indepreflns	3185	2276	9359	9375
GOF	1.020	1.026	1.097	1.027
Final R indices [<i>I</i> >2 σ (<i>I</i>)]	R1=0.0372 wR2=0.0742	R1=0.0547 wR2=0.1162	R1=0.0724 wR2=0.2135	R1=0.0678 wR2=0.1562
R indices (all data)	R1=0.0648 wR2=0.0870	R1=0.0901 wR2=0.1446	R1=0.0817 wR2=0.2256	R1=0.0731 wR2=0.2150

^aRefinement methods: full-matrix least-square on *F*².

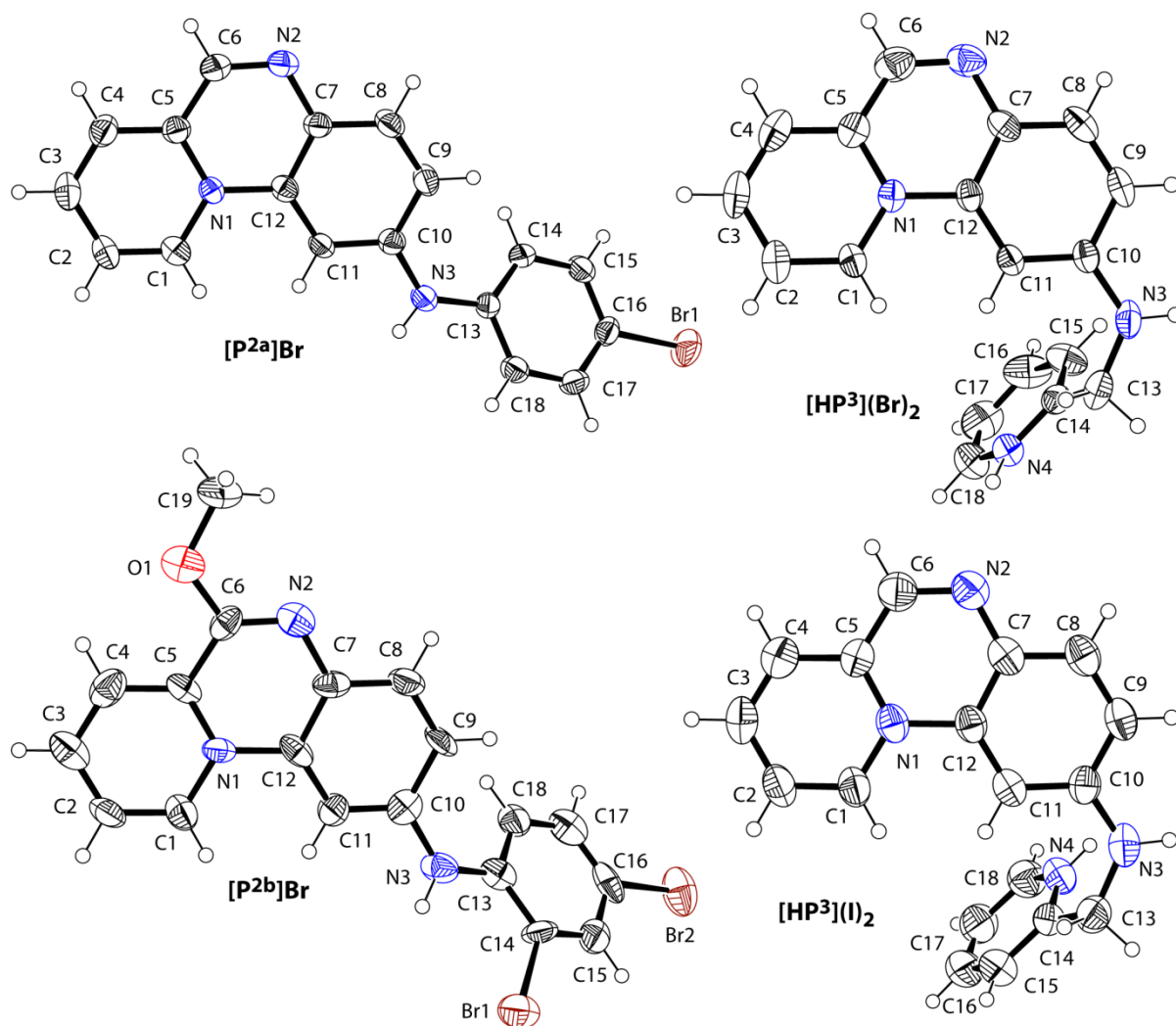
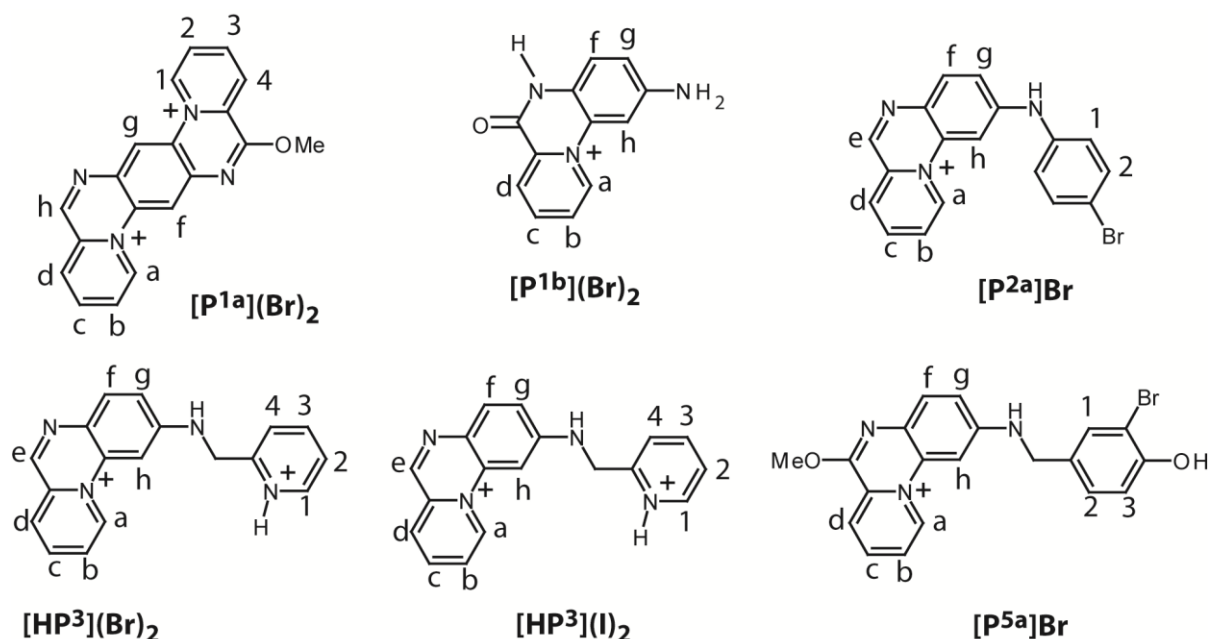


Figure 4.1 ORTEP⁶ drawing of brominated and non-brominated compounds of [P^{2a}]Br, [HP^{2b}](Br)(Br)₃, [HP³](Br)₂ and [HP³](I)₂ with 40% probability thermal ellipsoids. Solvent and counter ions (bromide / iodide) are omitted for clarity.

Table 4.2 Selected bond distances (Å) of cyclized compounds

[P^{2a}](Br)							
N1-C1	1.369(4)	C1-C2	1.352(5)	C2-C3	1.393(6)	C3-C4	1.358(6)
C5-C4	1.392(5)	N1-C5	1.375(5)	C5-C6	1.418(5)	N2-C6	1.296(5)
N2-C7	1.382(5)	C12-C7	1.410(5)	N1-C12	1.427(5)	C7-C8	1.400(5)
C8-C9	1.358(4)	C9-C10	1.413(5)	C10-C11	1.392(5)	C11-C12	1.382(5)
N3-C10	1.369(5)	N3-C13	1.396(5)	C13-C14	1.390(5)	C14-C15	1.389(5)
C15-C16	1.378(6)	C16-C17	1.380(5)	C17-C18	1.380(5)	C13-C18	1.395(5)
Br2-C16	1.898(4)						
[P^{2b}](Br)							
N1-C1	1.359(19)	C1-C2	1.361(2)	C2-C3	1.351(2)	C3-C4	1.361(2)
C5-C4	1.391(2)	N1-C5	1.326(17)	C5-C6	1.441(2)	N2-C6	1.290(17)
N2-C7	1.391(18)	C12-C7	1.411(2)	N1-C12	1.446(18)	C7-C8	1.411(2)
C8-C9	1.321(18)	C9-C10	1.431(2)	C10-C11	1.361(2)	C11-C12	1.367(19)
N3-C10	1.364(17)	N3-C13	1.383(19)	C13-C14	1.369(19)	C14-C15	1.381(2)
C15-C16	1.391(2)	C16-C17	1.361(2)	C17-C18	1.341(2)	C13-C18	1.421(2)
C6-O1	1.349(17)	O1-C19	1.467(19)	Br1-C14	1.896(16)	Br2-C16	1.905(18)
[HP³](Br)₂							
N1-C1	1.359(8)	C1-C2	1.371(9)	C3-C2	1.363(11)	C3-C4	1.363(11)
C5-C4	1.418(10)	C5-C6	1.393(10)	N1-C5	1.364(8)	N2-C6	1.321(10)
N2-C7	1.371(8)	C8-C7	1.375(9)	C8-C9	1.358(9)	C10-C9	1.406(8)
C11-C10	1.383(7)	C12-C7	1.416(8)	C12-C11	1.384(8)	N1-C12	1.417(7)
N3-C10	1.406(8)	N3-C13	1.409(9)	C14-C13	1.506(9)	C15-C14	1.329(8)
C15-C16	1.332(9)	C17-C16	1.334(12)	C17-C18	1.382(13)	N4-C18	1.380(11)
C14-N4	1.356(9)						
[HP³](I)₂							
N1-C1	1.369(7)	C1-C2	1.363(7)	C3-C2	1.402(8)	C3-C4	1.354(9)
C5-C4	1.403(7)	C5-C6	1.418(8)	N1-C5	1.374(6)	N2-C6	1.300(7)
N2-C7	1.367(6)	C8-C7	1.404(7)	C8-C9	1.358(7)	C10-C9	1.413(7)
C11-C10	1.392(6)	C12-C7	1.410(7)	C12-C11	1.389(6)	N1-C12	1.406(6)
N3-C10	1.390(6)	N3-C13	1.406(7)	C14-C13	1.513(7)	C15-C14	1.367(7)
C15-C16	1.407(8)	C17-C16	1.341(10)	C17-C18	1.371(10)	N4-C18	1.343(7)
C14-N4	1.326(7)						



Scheme 4.2 Quinoxaline derivatives with labelling scheme for ¹H NMR chemical shifts.

Table 4.3 ¹H NMR chemical shift data for quinoxaline derivatives

Chemical Shifts (ppm)								
Compound	Solvent	H ^a	H ^b	H ^c	H ^d	H ^e	H ^f	H ^h
[P ^{1b}](Br) ₂	DMSO-d ₆	09.94d	8.51t	8.80t	8.94d	-	7.38d	7.25d 7.84s
[P ^{1a}](Br) ₂	D ₂ O	10.55d	8.73m	9.11m	9.20d	-	9.80s	9.78s 9.58s
[P ^{2a}](Br)	DMSO-d ₆	10.10d	8.43t	8.80t	8.87d	9.55s	7.75d	8.25d 8.30s
[HP ³](Br) ₂	DMSO-d ₆	10.15d	9.47t	8.82t	8.75d	9.44s	8.26m	8.17d 7.79s
[HP ³](I) ₂	DMSO-d ₆	10.27d	8.83t	8.77t	8.50d	9.38s	7.81d	7.68d 7.43 m ⁱ
[P ^{5a}](Br)	DMSO-d ₆	10.27d	8.50t	8.77t	8.83d	9.34s	7.81m	7.42d 7.68 m ⁱ
		>CH ₂	H ¹	H ²	H ³	H ⁴	>NH	OMe
[P ^{1b}](Br) ₂	DMSO-d ₆	-	-	-	-	-	n.o.	n.o.
[P ^{1a}](Br)	D ₂ O	-	10.45d	-	9.11m ⁱ	9.05d	n.o.	4.23
[P ^{2a}](Br)	DMSO-d ₆	-	7.61d	7.39d	-	-	9.71s	n.o.
[HP ³](Br) ₂	DMSO-d ₆	4.99s	8.44m ⁱ	7.44m ⁱ	8.18m ⁱ	7.69m ⁱ	9.63s	n.o.
[HP ³](I) ₂	DMSO-d ₆	4.20s	8.74m ⁱ	7.61m ⁱ	8.14m ⁱ	7.61m ⁱ	n.o.	n.o.
[P ^{5a}](Br)	DMSO-d ₆	4.21s	7.59m ⁱ	7.30d	7.50d	7.68s	4.32s	4.25
Coupling Constants (Hz)		J _{ab}	J _{bc}	J _{cd}	J _{fg}			
[P ^{1b}](Br)	DMSO-d ₆	6.8	7.2	8.0	8.5			
[P ^{1a}](Br) ₂	D ₂ O	6.4	-	-	-			
[P ^{2a}](Br)	DMSO-d ₆	7.2	7 ⁱⁱ	8.0	8.0			
[HP ³](Br) ₂	DMSO-d ₆	6.7	7 ⁱⁱ	8.4	-			
[HP ³](I) ₂	DMSO-d ₆	5.6	7 ⁱⁱ	8.0	7.6			
[P ^{5a}](Br) ₂	DMSO-d ₆	6.8	8.0	8.0	-			

Coupling constant values are within ±0.4 Hz.ⁱ Overlapped with other proton.ⁱⁱ Approximate value due to multiplet nature. n.o. = not observed.

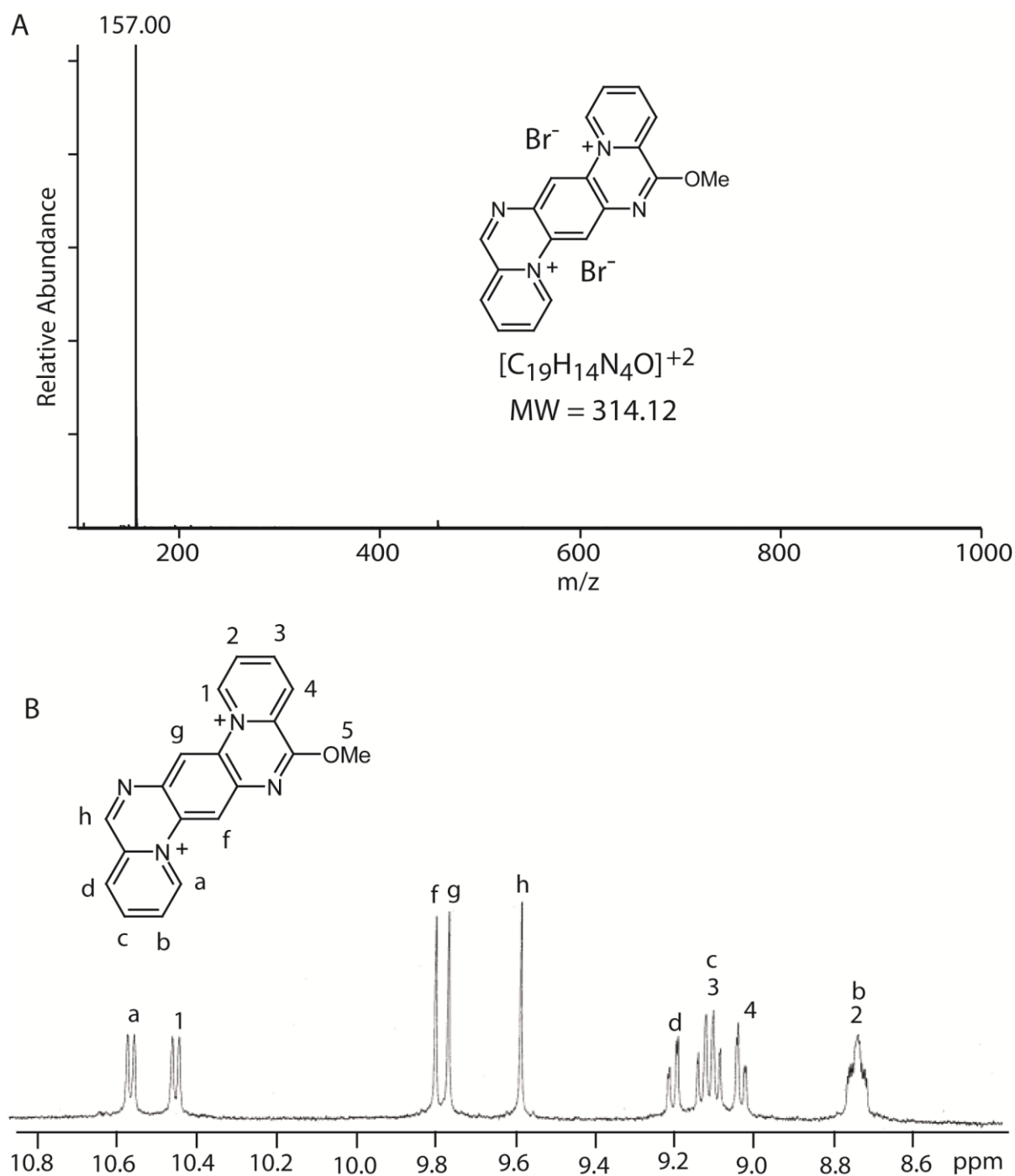


Figure 4.2 (A) ESI mass spectrum and (B) ^1H NMR spectrum with numbering scheme of $[\text{P}^{1a}](\text{Br})_2$ (only the aromatic region is shown for clarity).

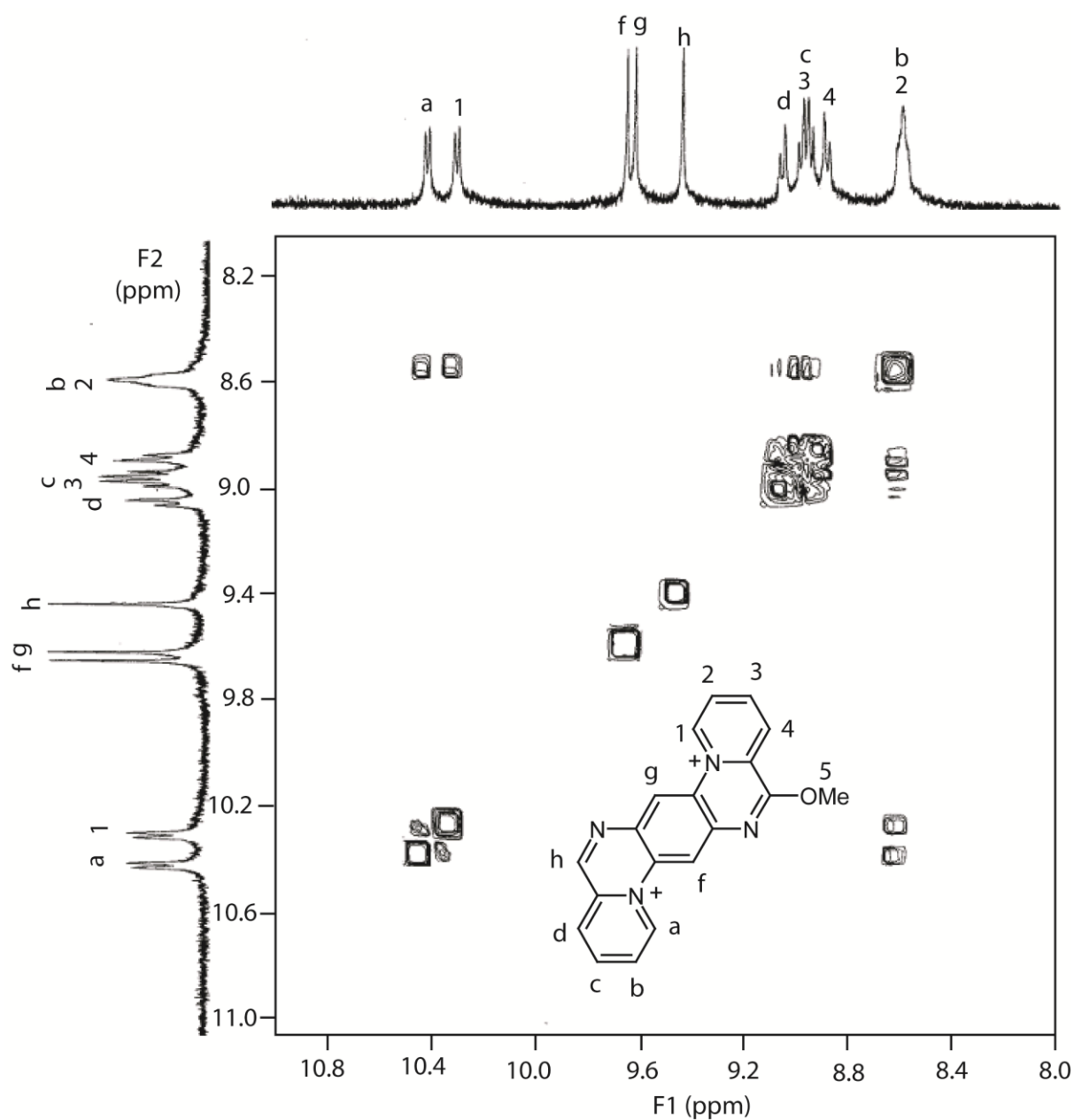


Figure 4.3 The ^1H ^1H -COSY NMR spectrum of 5-methoxypyrido[1,2-*a*]pyrido[1'2':1,6]pyrazino[2,3-*g*]quinoxaline-8,16-diiumbromide $[\text{P}^{1a}](\text{Br})_2$ in D_2O at 400 MHz (only the aromatic region is shown for clarity).

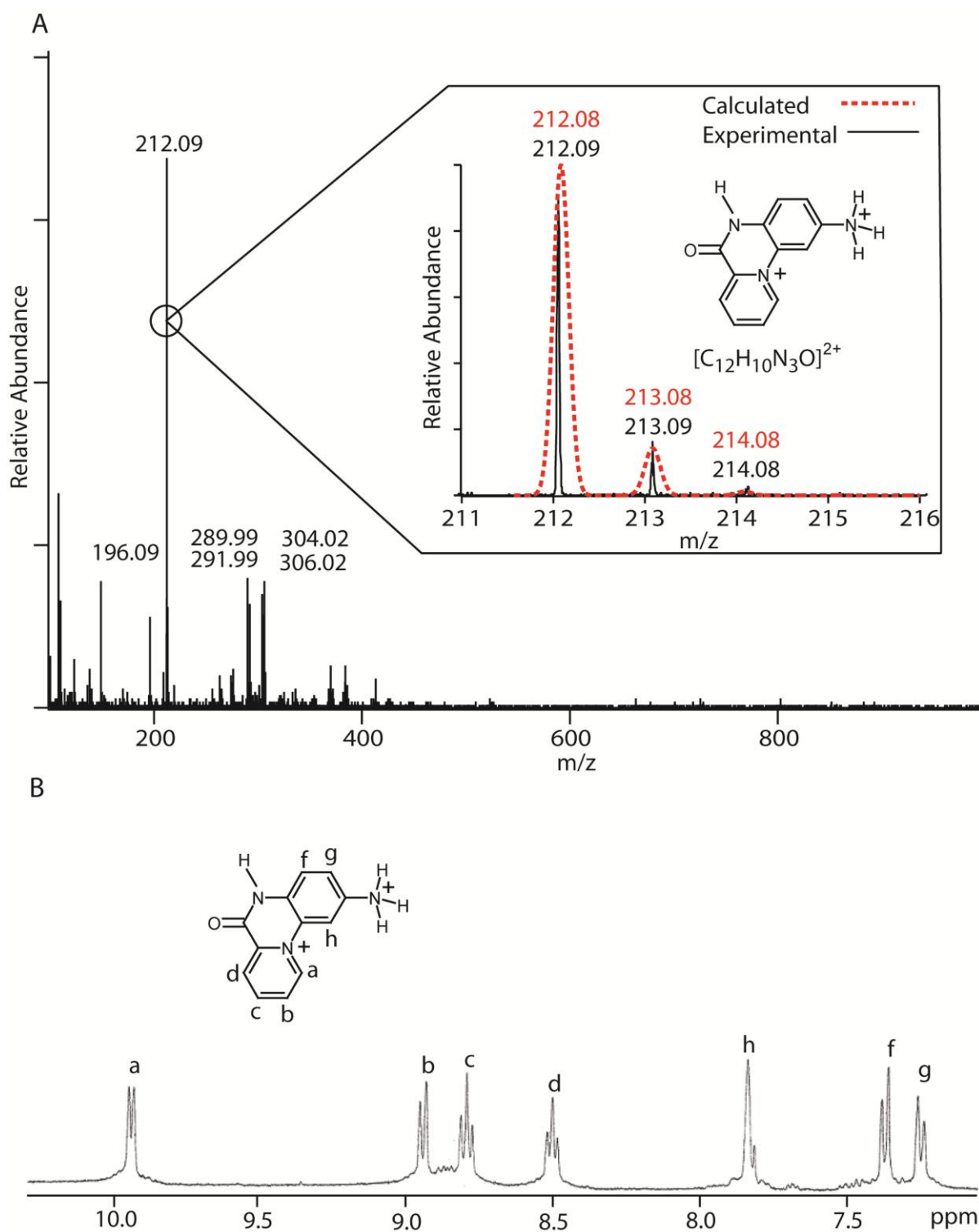


Figure 4.4 (A) ESI mass spectrum and (B) ^1H NMR spectrum with numbering scheme of $[\text{HP}^{1b}](\text{Br})_2$.

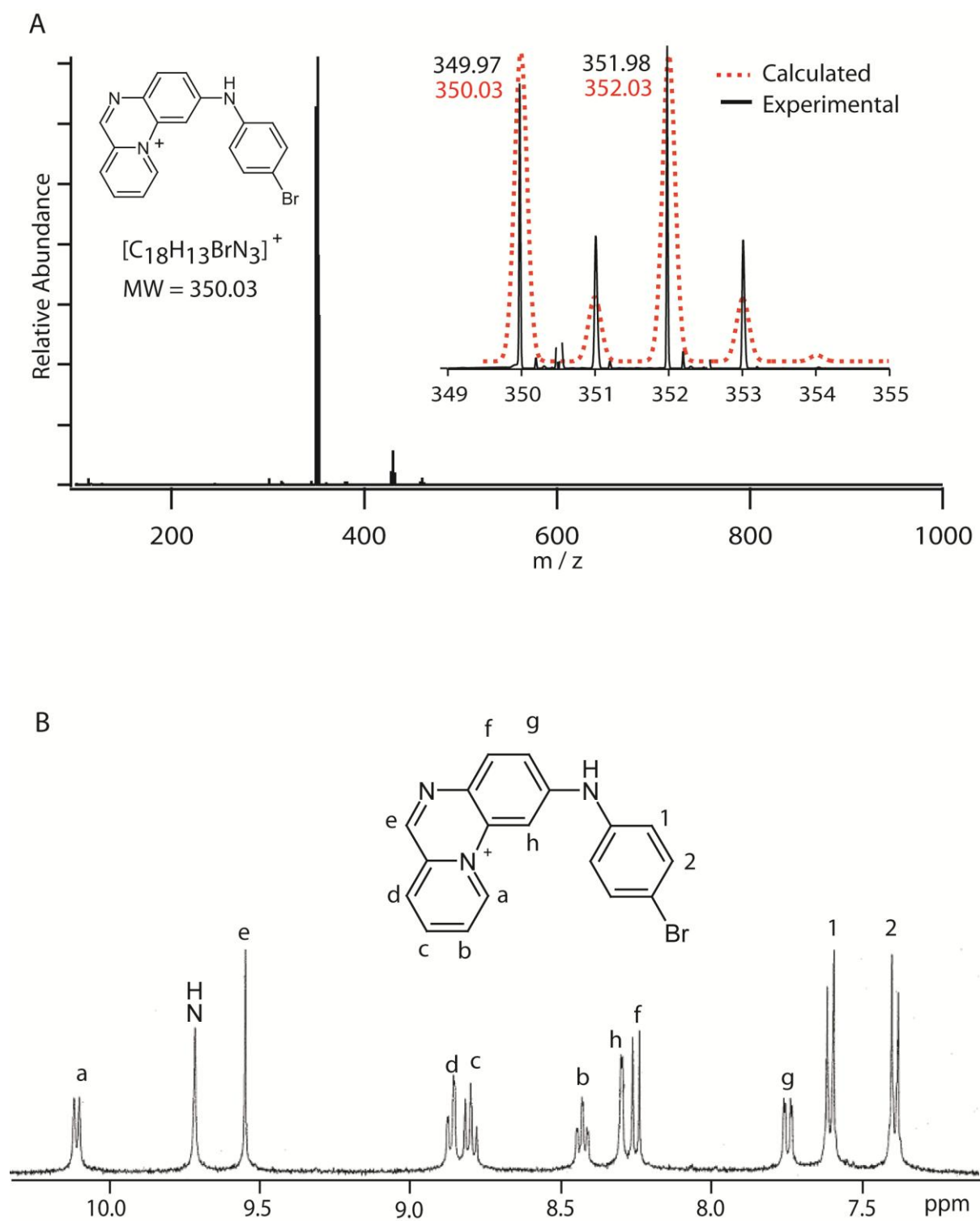


Figure 4.5 (A) ESI mass spectrum and (B) ^1H NMR spectrum with numbering scheme of $[\text{P}^{2a}](\text{Br})$.

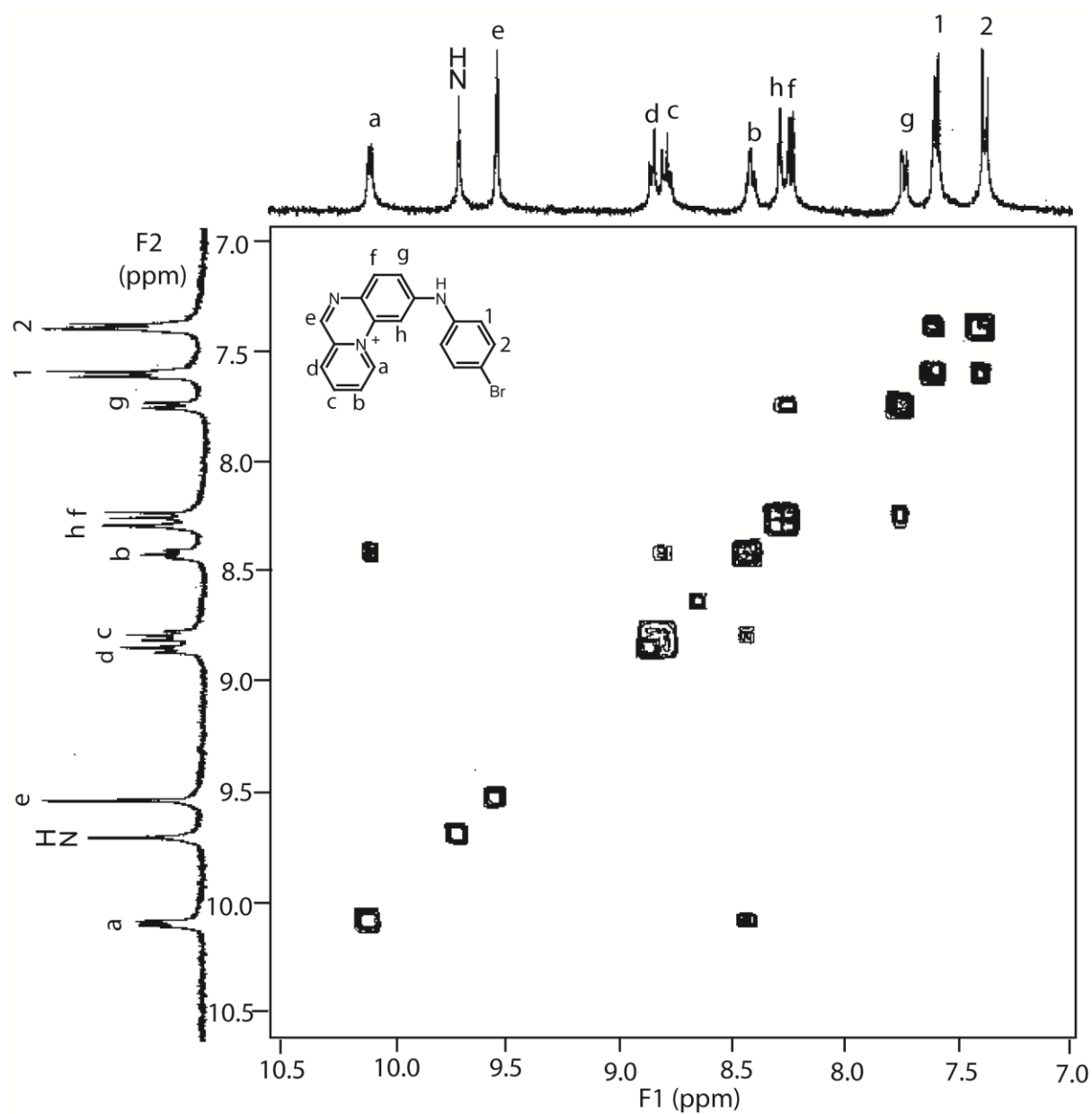


Figure 4.6 The ^1H ^1H -COSY NMR spectrum of 4-[(bromobenzyl)-amino]-pyrido[1,2-*a*]quinoxalin-11-ylum bromide [P^{2a}](Br) in DMSO-d_6 at 400 MHz.

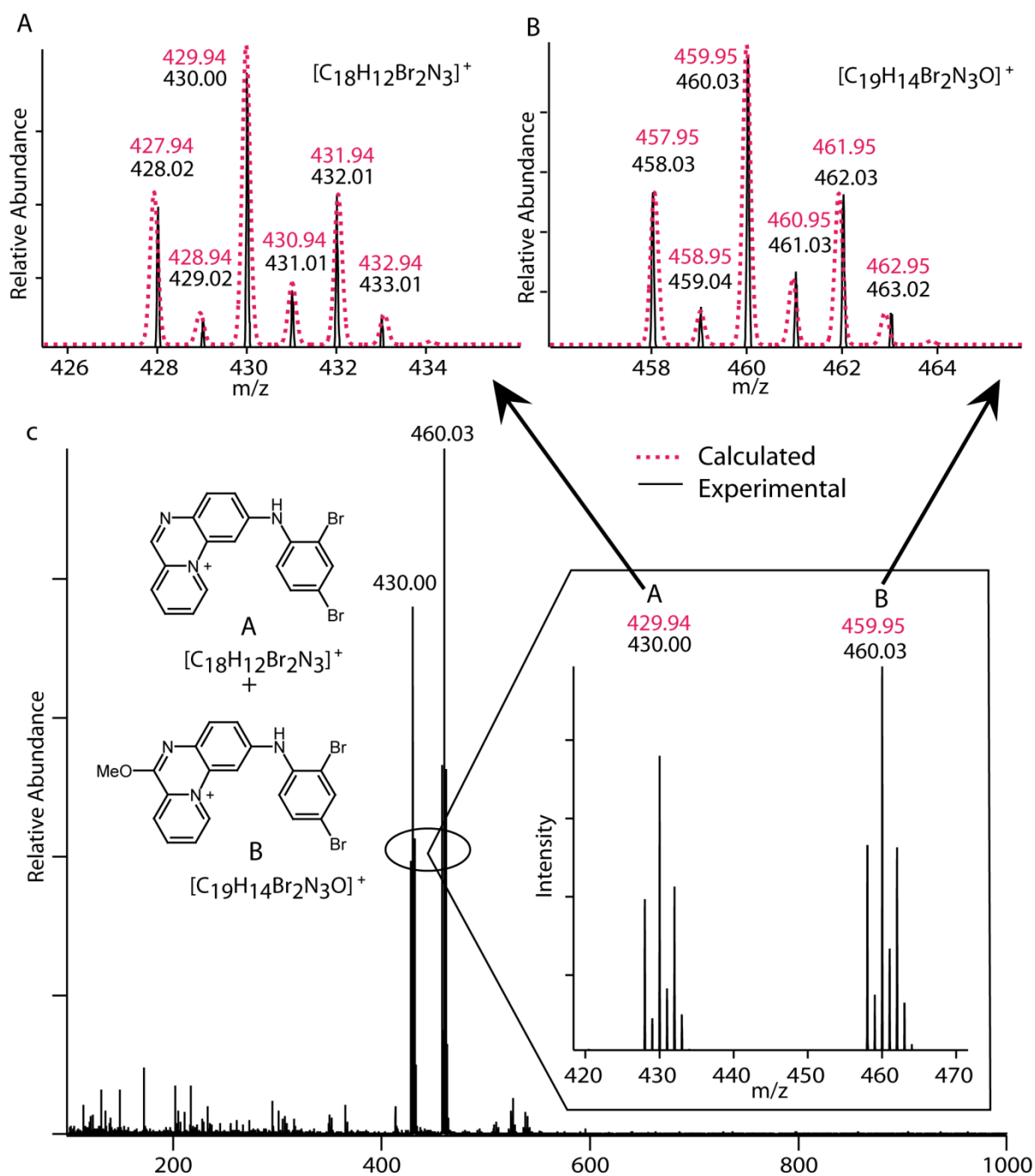


Figure 4.7 (A) Isotopic abundance pattern calculated (red) and experimental (black) of $[P^{2b'}]^+$ (B) Isotopic abundance pattern calculated (red) and experimental (black) of $[P^{2b}]^+$ (C) ESI (+Ve) mass spectrum with expansion of region 420-470 (m/z) of $[P^{2b'}]^+$ and $[P^{2b}]^+$.

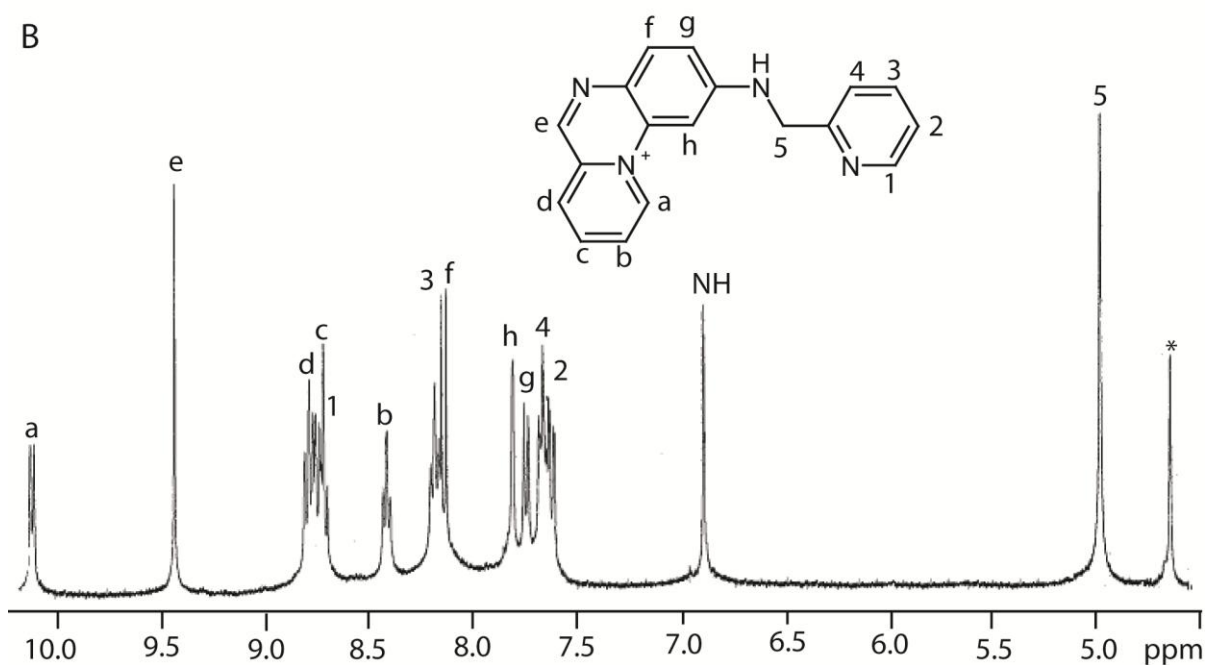
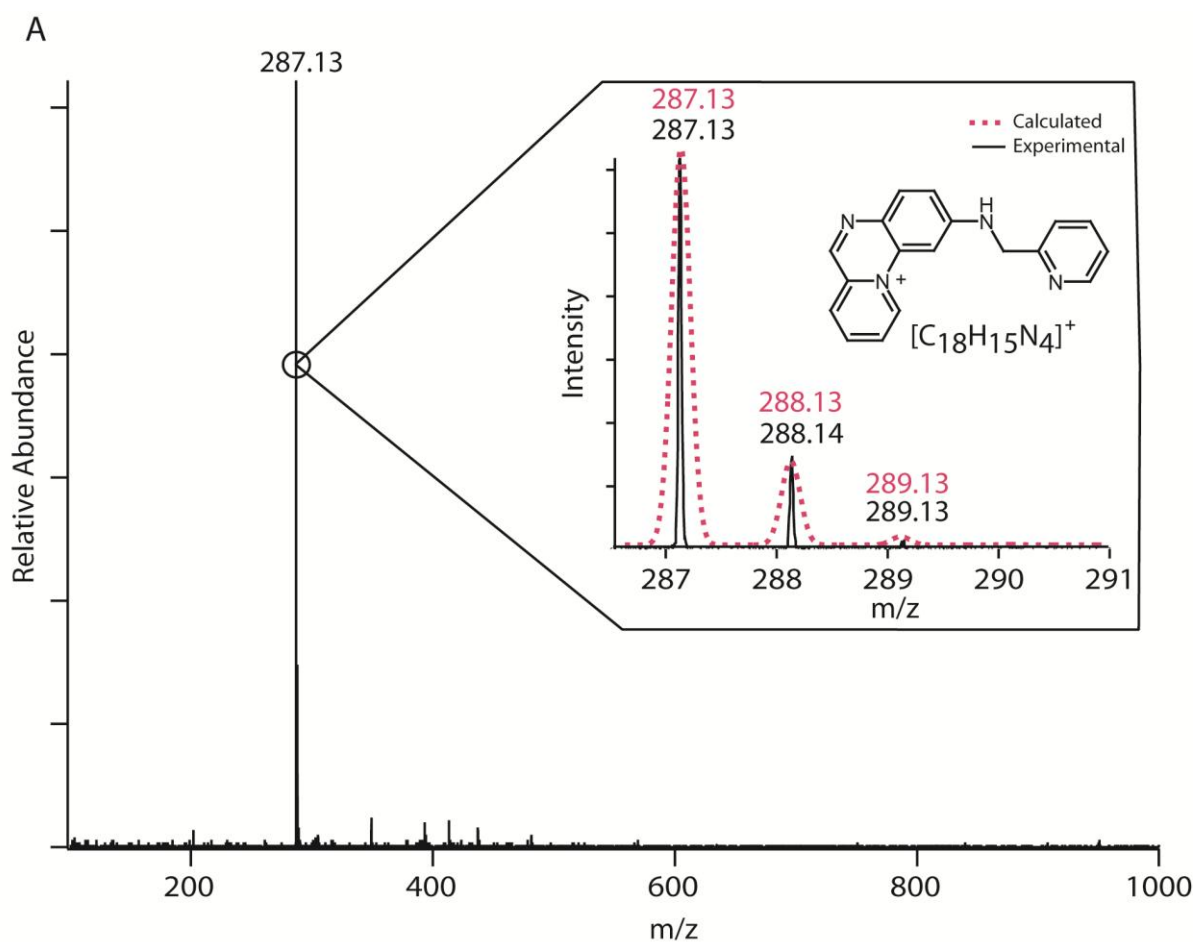


Figure 4.8 (A) ESI mass spectrum and (B) ^1H NMR spectrum with numbering scheme of $[\text{HP}^3](\text{Br})_2$.

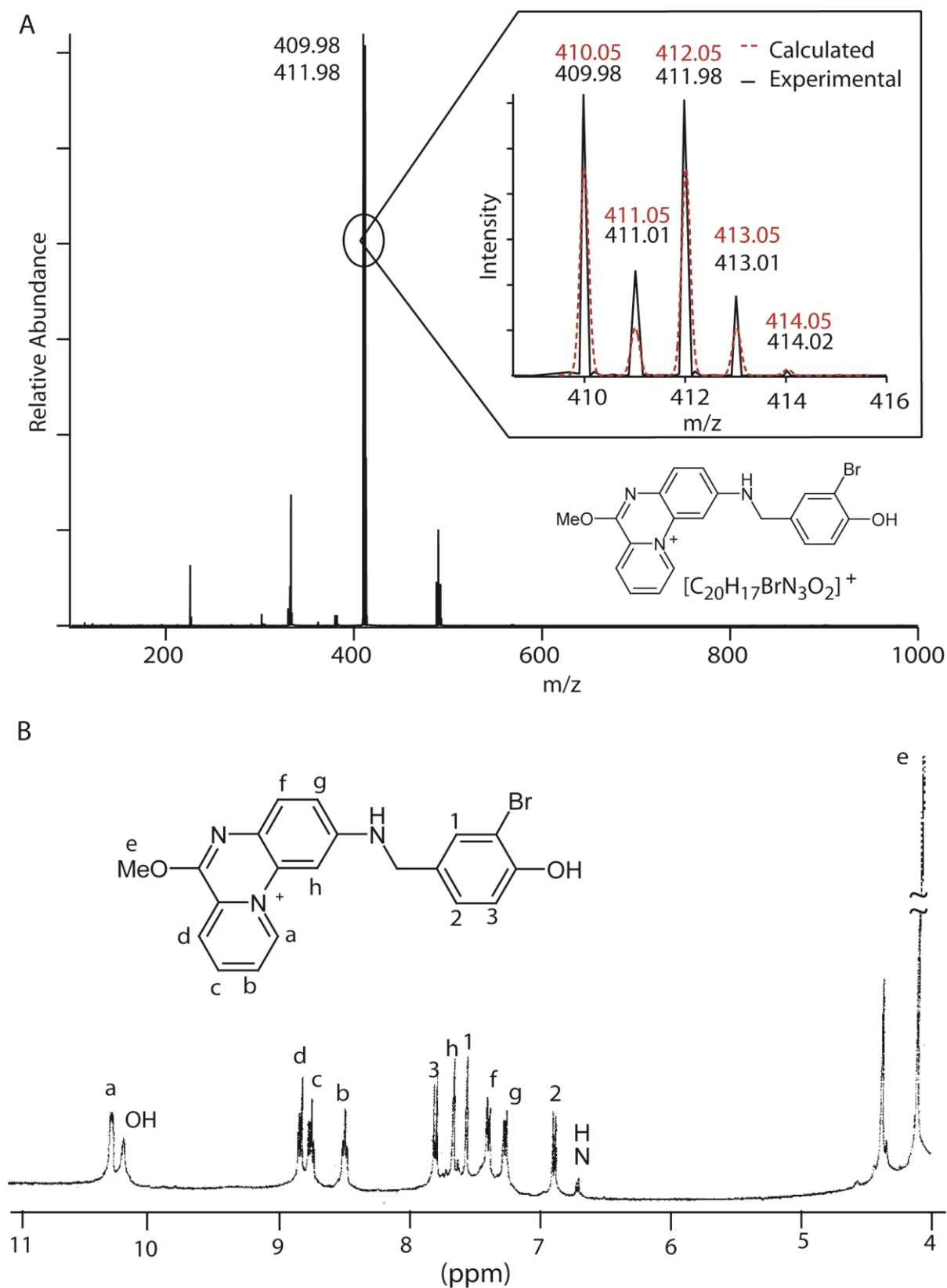


Figure 4.9 (A) ESI mass spectrum and (B) ^1H NMR spectrum with numbering scheme of $[\text{P}^{5a}](\text{Br})$.

4.4 Results and Discussion

4.4.1 Syntheses and characterization of precursors L^1 - L^5

The syntheses and characterization of L^1 - L^5 are given in the chapter 2.

4.5 Cyclization reactions of precursors L^2 - L^5

4.5.1 Cyclization reactions of precursor L^1 with Br_2

Addition of dark brown molecular bromine to yellow methanolic solution of L^1 at room temperature the colour of the solution turned orange with orange fluorescence. Thus it was possible to monitor the progress of the reaction by fluorescence. The reactive nature of reaction always result a mixture of products. The presence of multiple products in the reaction mixtures were initially confirmed by ESI-MS. One of the products [P^{1a}] obtained as crystalline solid, soluble in water, very hygroscopic in nature and its aqueous solution shows strong blue fluorescence. The other product [P^{1b}] isolated from the filtrate of the reaction, which is soluble in methanol and shows orange fluorescence. The purity of both compounds were confirmed by 1H NMR spectra. The molar conductance of [P^{1a}] $^{2+}$ in methanol was found to be $165\text{ S cm}^2\text{ mol}^{-1}$.³ Molar conductance support di-cationic nature of compound [P^{1a}] $^{2+}$. The cyclized product [P^{1a}] has been characterized by ESI-MS. The positive-ion ESI-MS of [P^{1a}] in MeOH showed a single peak at $m/z = 157.00$ for a [P^{1a}] $^{2+}$ species. The result is contrary to previously reported hydrolysis of imine bond after cyclization. The result [P^{1a}] also shows that no hydrolysis occurs after cyclization. The mixture of product was confirmed by mass spectrum as shown in (Figure 4.4.A). Another hydrolysed product [P^{1b}] isolated from same reaction and confirmed by spectroscopic analysis including ESI-MS. The positive-ion ESI-MS of [P^{1b}] showed one peak at $m/z = 212.02$ which is attributed to [P^{1b}] $^+$ (Figure 4.2). The molar conductance of [HP^{1b}] $^{2+}$ in methanol at $167\text{ S cm}^2\text{ mol}^{-1}$ is well within the range $160\text{--}220\text{ S cm}^2\text{ mol}^{-1}$ expected for 1:2 electrolyte.³ Finally, we have succeeded in the isolation and characterization of two new compounds from L^1 by cyclization with bromine oxidizer. Both compounds are highly soluble in water and showed fluorescence. None of them were structurally characterized but supported by NMR, ESI-MS technique. L^1 is also reacting slowly with molecular iodine compared to molecular bromine and afforded fluorescence compound, but due to a sticky solid nature of compound, we could not isolated the pure product.

4.5.2 Cyclization reaction of precursor L^2 with Br_2

Addition of molecular bromine to yellow methanolic L^2 solution turned the colour of the solution to red. The precipitate was formed within a minute. The precipitate was filtered off and characterized by NMR and ESI-MS. The mixture of products was confirmed by ESI-MS. Isolation of $[P^{2a}]$ and $[P^{2b}]$ was also accomplished by fractional crystallization of the crude brominating product. The isotopic pattern in 1:3:1 ratio (Figure 4.7) confirmed the two bromine atoms present in the $[P^{2b}]$ and supported the formulation of compound $[C_{13}H_9Br_2N_2O_2]Br$. The another product $[C_{13}H_9Br_2N_2O_2]Br$ is also indicated by ESI-MS (M^+) 382.93/384.92/386.92,^{7,8} but we have characterized one of the product structurally $[P^{2b}]$. The ionic nature of compounds $[P^{2a}]^+$ and $[P^{2b}]^+$ were confirmed by conductance measurement data given in (Experimental section 4.2.2). The problems of isolation of single brominated compound have been reported in the literature.⁹ The isolated product crystallizes well from methanol. All further spectroscopic analysis including structural characterization were performed on these crystals. The molar conductance of $[P^{2a}]^+$ and $[P^{2b}]^+$ in methanol at 103-120 $S\ cm^2\ mol^{-1}$ are well within the range 80-115 $S\ cm^2\ mol^{-1}$ expected for 1:1 electrolyte.³ The $\nu_{C=N}$ stretch identified in L^2 ($1619\ cm^{-1}$) remained in $[P^{2a}]^+$ at $1617\ cm^{-1}$. The structure of $[P^{2a}]$ and $[P^{2b}]$ was elucidated from single crystal X-ray diffraction (Section 4.6.1 and 4.6.2). The reaction of L^2 with iodine was observed but problem was same as mention in (Section 4.5.1).

4.5.3 Cyclization reaction of precursor L^3 with Br_2

Addition of molecular bromine to the methanolic solution causes immediate darkening of the colour along with the product formation is indicated by the fluorescence under ultraviolet light. The isolation of the product was difficult as both the products were highly soluble in water, methanol and most other common solvents. This resulted in poor yield (~20%) even though all the filtrates were highly fluorescent. The molar conductance of $[HP^3]^{2+}$ in methanol at 156 $S\ cm^2\ mol^{-1}$ is closer to the range 160-220 $S\ cm^2\ mol^{-1}$ expected for 1:2 electrolyte.³ The FTIR spectrum of $[HP^3]$ showed a band at $1621\ cm^{-1}$ identified as $\nu_{C=N}$. A broad stretch observed at $3337\ cm^{-1}$ was identified as ν_{N-H} . The ESI-MS shows molecular ion peak at 287.13 (calculated for M^+ 287.13). The conductance value indicated $[HP^3]^{2+}$ as a dication rather than monocationic species. The identity of compound was solved

by using single crystal X-ray crystallographic analysis (Section 4.6.3). The pK_a of compound was calculated by base titration and we found 3.8.

4.5.4 Cyclization reaction of precursor L^3 with I_2

Addition of molecular iodine to the methanolic solution causes immediate darkening of the colour along with the product formation is indicated by the fluorescence under ultraviolet light. The isolation of the product was difficult as given in (Section 4.5.3) above procedure. The molar conductance of $[HP^3]^{2+}$ showed 1:2 electrolyte.³ The conductance value indicated $[HP^3]$ as a dication rather than monocationic species. The structure was solved using single crystal X-ray crystallographic analysis (Section 4.6.4).

4.5.5 Cyclization reaction of precursor L^5 with Br_2

The precursor L^5 reacts with molecular bromine and afforded $[P^{5a}](Br)$ salt. The product is crystalline but crystals did not diffract well enough to solve the structure. Thus the characterization is limited to ESI-MS, IR and conductance, all of which support the formation of the tricyclic moiety (Experimental Section). Assignments of 1H NMR signals (Table 4.3) and positions relative to other cyclized products confirm to the proposed structure (Scheme 4.1). The bromination reaction was carried out in a nucleophilic solvent. Use of a present solvent that is itself nucleophilic, such as methanol, results in a methoxy substituted product. The reaction of L^5 with iodine was observed but problem was same as mention in (Section 4.5.1).

4.6 Molecular structures of $[P^{2a}](Br)$ - $[P^3](I)_2$

Details of molecular structures are given below:

4.6.1 Molecular structure of $[P^{2a}](Br)$

Bromide salt of $[P^{2a}](Br)$ was crystallized in monoclinic $C2/c$ space group with one molecule each of $[P^{2a}]^+$ cation, one bromide and water. The ORTEP diagram and selected bond lengths and angles are in Figure 4.1 and Table 4.3 respectively. The tricyclic part of the molecule is planar. The angle between the planes containing pyridine and phenylene ring is

7.10°. The N2-C6 bond length (imine in ring) of 1.296(5) Å is slightly elongated from 1.2695(19) Å observed in corresponding Schiff base precursor **L**² but still considerably shorter than N2-C7 1.381(6) Å. This means that the imine bond retains its double bond character even after cyclization reaction i.e., N2-C7 double bond is localized and tricyclic ring is not fully aromatic. This has been observed in case of **P**² (Chapter 2). The angle between tricyclic ring (plane containing C11, C10, C9, N3 atoms) and phenyl ring (N3, C14, C13, C18 atoms) is 35.71°. In the lattice, bromide ion, water and amine-N involved in non covalent interactions. The (Table 4.4) lists such interactions present in the lattice and Figure 4.10 shows some of the resultant pattern formed with the lattice as a result of H-bond interactions.

Table 4.4 H-bond distances present in [**P**^{2a}](Br)

D-H...A	<i>d</i> (D-H)(Å)	<i>d</i> (H...A)(Å)	<i>d</i> (D...A)(Å)	<DHA(°)
[P^{2a}](Br)				
N3...H19...Br1	0.83(4)	2.58(4)	3.405(4)	174(4)
O1...H20...Br1	0.79(6)	2.72(6)	3.494(4)	166(7)
C1...H1...O1	0.93	2.59	3.270(6)	130
C17...H17...N	0.93	2.62	3.357(5)	137

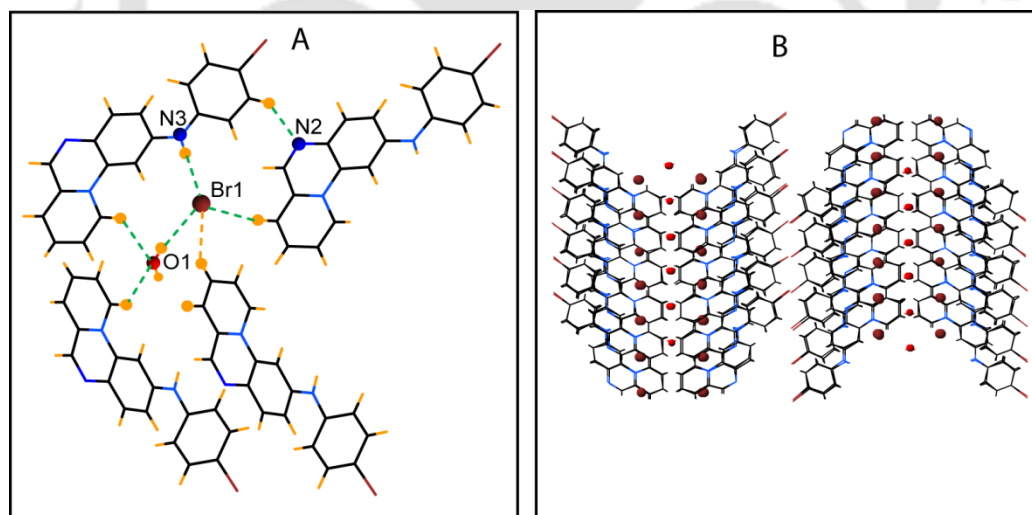


Figure 4.10 (A) Non-covalent interactions (B) Lattice arrangement along *a*-axis present in the lattice of [**P**^{2a}]⁺.

4.6.2 Molecular structure of $[\mathbf{P}^{2b}](\text{Br})$

Bromide salt of $[\mathbf{P}^{2b}](\text{Br})$ was crystallized in monoclinic space group $C2$ with one molecule each of $[\mathbf{P}^{2b}]^+$ cation, one bromide ion and tribromide ion. The ORTEP diagram and selected bond lengths and angles are in Figure 4.1 and Table 4.3 respectively. The tricyclic part of the molecule is planar. The angle between the planes containing pyridine and phenylene ring is only 5.2° . The N2-C6 bond length (imine in ring) at $1.288(6)$ Å is slightly elongated from $1.2695(19)$ Å observed in corresponding Schiff base precursor $\mathbf{L}^2$ but still considerably shorter than N2-C7 $1.392(6)$ Å. This means that the imine bond retains its double bond character even after cyclization reaction i.e. N2-C7 double bond is localized and tricyclic ring is not fully aromatic. This has been observed in case of $\mathbf{P}^2$ as well. The angle between tricyclic ring (plane containing C11, C10, C9, N3 atoms) and phenyl ring (N3, C14, C13, C18 atoms) is 47.46° . The presence of bromide and amine N3 generates number of non-covalent interactions within the lattice. The figure 4.11 shows some of the resultant pattern formed with the lattice as a result of weak bond interactions.

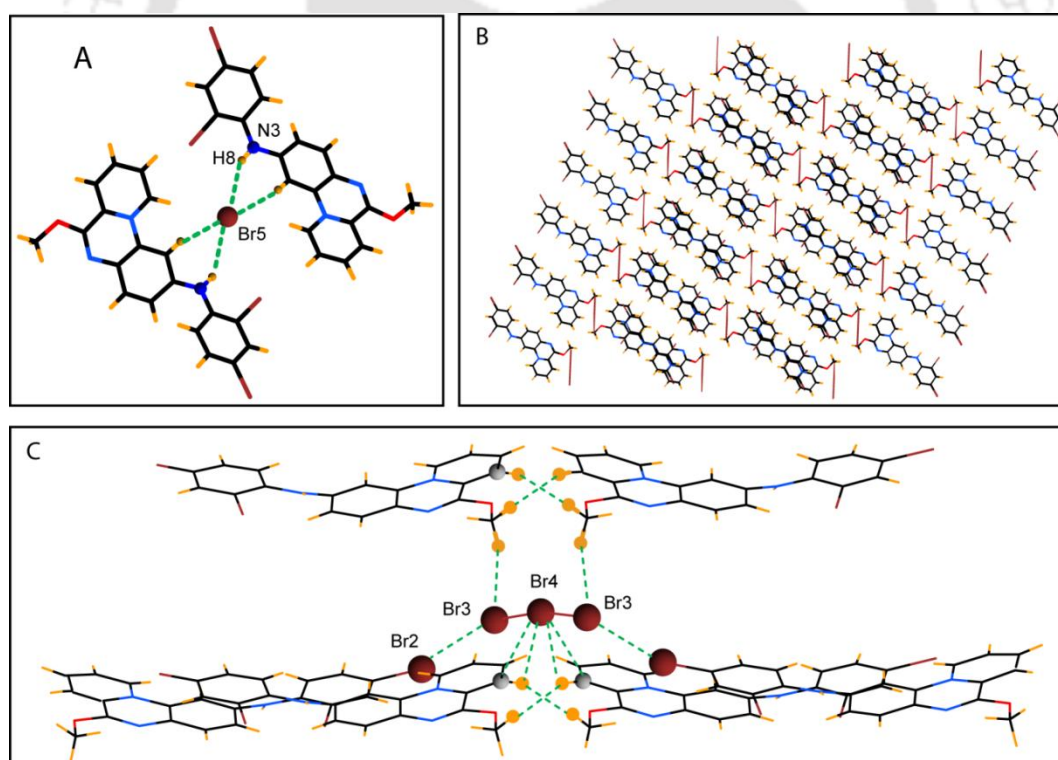


Figure 4.11(A) Intramolecular weak interactions around bromide counter ion (B) Lattice arrangement along *b*-axis (C) Intramolecular weak interaction around tribromide and substituted bromine present in the crystal of $[\mathbf{P}^{2b}]^+$.

4.6.3 Molecular structure of $[P^3](Br)_2 \cdot 3H_2O$

Bromide salt of $[P^3](Br)_2 \cdot 3H_2O$ was crystallized in triclinic space group $P-1$ with two molecules of $[HP^3]^{2+}$ cation, four bromide ion and three water molecules. The asymmetric unit contains two molecules. The ORTEP diagram and selected bond lengths and angles are in Figure 4.1 and Table 4.3 respectively. The tricyclic part of the molecule is planar. The angle between the planes containing pyridine and phenylene ring are different in both the cations present in the unit cell by 6.91° and 5.20° respectively. The N2-C6 bond length (imine in ring) at 1.320(6) Å and 1.321(6) Å is slightly elongated from 1.2695(19) Å observed in corresponding Schiff base precursor (L^1), but still considerably shorter than N2-C7 1.381(6) Å. This means that the imine bond retains its double bond character even after cyclization reaction. The presence of bromide ions, water molecules and amine N3 generates number of non-covalent interactions within the lattice. The table 4.6 lists such interactions present in the lattice and Figure 4.12 A shows some of the resultant pattern formed with the lattice as a result of those interactions.

Table 4.5 H-bonds in $[P^3](Br)_2 \cdot 3H_2O$.

D-H...A	$d(D-H)(\text{\AA})$	$d(H...A)(\text{\AA})$	$d(D...A)(\text{\AA})$	$\angle D-H...A(^{\circ})$
$[P^3](Br)_2 \cdot 3H_2O$				
N8-H8A...N5	0.86	2.60	2.883(10)	100
N8-H8A...N6	0.86	2.59	3.383(10)	154
N9-H9...N1	0.86	2.47	2.820(8)	105
N9-H9...N2	0.86	2.13	2.934(7)	156
N5-H51...Br3	0.86	2.73	3.541(6)	158
N1-H53...Br1	0.86	2.76	3.591(5)	162
C31-H31...O1	0.93	1.83	2.750(9)	169
C37-H37...O2	0.93	2.46	3.215(13)	138
C38-H38...O(50)	0.93	2.41	3.164(13)	138

4.6.4 Molecular structure of $[P^3](I)_2 \cdot 3H_2O$

Bromide salt of $[P^3](I)_2 \cdot 3H_2O$ was crystallized in triclinic space group $P-1$ with one molecule each of $[P^3]^{2+}$ cation, iodide ion and water molecule. The asymmetric unit contains two crystallographically independent salts related by a centre of inversion. The ORTEP diagram and selected bond lengths and angles are in Figure 4.12B and Table 4.6 respectively. The structure is identical with the bromide salt (Section 4.6.3). Tricyclic part of the molecule is planar. The structure is identical with bromide salts.

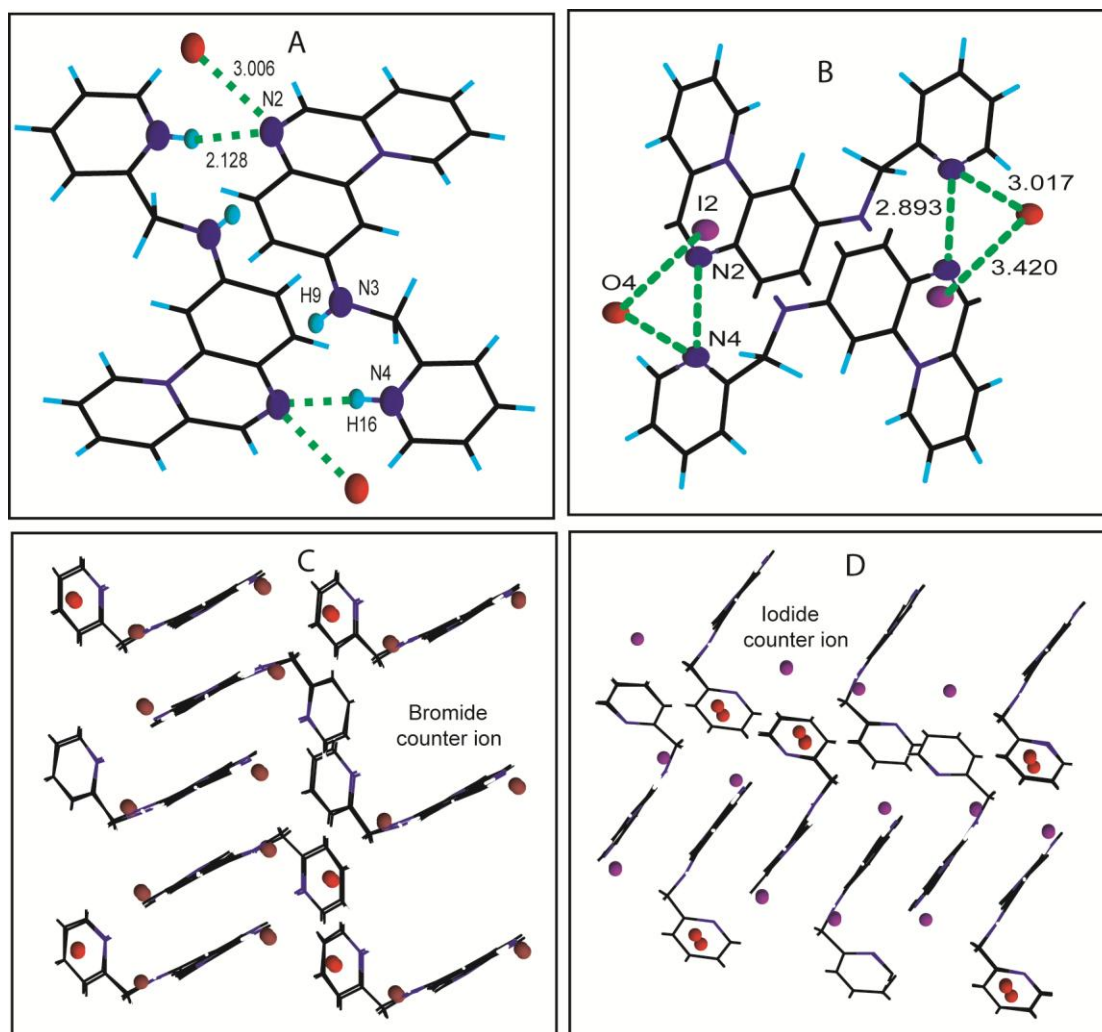


Figure 4.12 Non covalent interaction present in (A) [HP³](Br)₂ and (B) [HP³](I)₂. Lattice arrangement along *b*-axis in (C) [HP³](Br)₂ and (D) [HP³](I)₂.

In the lattice of [HP³](Br)₂, the H-bond interactions of 3.006 Å between amine-N (donor) and nitrate-O (acceptor) as well as different short range interactions results a ladder like structure and short interaction between the bromide counter anion and water of crystallization are depicted in the Figure 4.12A.

Table 4.6 H-bonds in $[\mathbf{P}^3]\cdot(\mathbf{I})_2\cdot 3\mathbf{H}_2\mathbf{O}$

D-H...A	$d(\text{D-H})(\text{\AA})$	$d(\text{H...A})(\text{\AA})$	$d(\text{D...A})(\text{\AA})$	$\angle \text{D-H...A}(^\circ)$
$[\mathbf{P}^3]\cdot(\mathbf{I})_2\cdot 3\mathbf{H}_2\mathbf{O}$				
O4-H5...C5	0.930(1)	2.563(1)	3.463(2)	162.79(9)
O4-H9...C9	0.930(1)	2.4641(9)	3.360(2)	161.60(9)
O4-H4...O5	0.820(1)	1.842(1)	2.655(2)	171.19(9)
C5-H5...O4	0.930(1)	2.563(1)	3.463(2)	162.79(9)
C1-H1...O1	0.930(1)	2.541(2)	3.327(2)	142.49(9)
C2-H2...N2	0.930(1)	2.632(1)	3.502(2)	155.9(1)
N2-H2...C2	0.930(1)	2.632(1)	3.502(2)	155.9(1)
C7-H7...O1	0.930(1)	2.479(1)	3.313(2)	149.4(1)
C12-H15...O2	0.930(2)	2.547(1)	3.234(2)	130.9(1)

4.7 ^1H NMR analysis

The ^1H NMR spectra of all isolated compounds show calculated number of protons. The presence of methoxy group in $[\mathbf{P}^{1a}]$ and $[\mathbf{P}^{5a}]$ are confirmed by ^1H NMR and support the formulation of compounds. The compound $[\mathbf{P}^{2b}]$ does not show clean ^1H NMR as bulk of the compound is mixture of two products, which is also confirmed by ESI-MS (Figure 4.7). The observed signals have been assigned to individual aromatic hydrogen with the aid of ^1H NMR correlation spectroscopic (COSY) experiments. The assignments corroborates well with the structural characterization. Assignments of cyclization products were additionally corroborated with the help of 2D COSY spectra as some of the proton positions overlapped (Table 4.3, Figures 4.3-4.6). This also confirms the structured of $[\mathbf{P}^{1a}](\text{Br})_2$, $[\mathbf{HP}^{1b}](\text{Br})_2$ and $[\mathbf{P}^{5a}](\text{Br})$, those are not structurally characterized, as a tricyclic product similar to other products. Comparisons between tricyclic part of the assignments shows that shifts of a proton among all the products in same solvent are almost identical (Table 4.3). This means that the effect of substitution at $-\text{NH}$ has minimal on electron density distribution within the tricycle.

Conclusion

The results presented in this chapter shows that the cyclization process is not limited to Fe(III) and Cu(II) mediated.¹⁰ The molecular iodine and molecular bromine can be used as an oxidizing agent in this synthesis. The cyclization works both on Schiff base as well as with reduced species. A number of new derivatives were synthesized and characterized using ^1H NMR, ESI-Mass and X-ray crystallography. The major difference between reactions with

metal ion and halogens is the isolation of multiple compounds from same reactions. Although we were able to characterize few, many could not be isolated in the pure form. It was evident from the products that halogens, especially bromine, not only oxidizes the precursor to form cyclized product but also brominates the aromatic ring. Some of the reactions with bromine are difficult to reproduce and very much sensitive to the reaction condition.

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Chapter 5

**UV/vis and Fluorescence Spectroscopic study of
precursor and product
pyrido[1,2-*a*]quinoxalin-11-ylum derivatives**

One of the impetus of this thesis work, besides synthesizing new organic compounds, was the observation of fluorescence upon excitation in the visible region by earliest member of this group [$\mathbf{P}^1$]¹. The compound [$\mathbf{P}^1$](NO₃) showed fluorescence at 580 nm upon excitation at 470 nm with a quantum yield (Φ) value of 0.23.¹ As it could be excited using common blue LED light (450 to 500 nm), soluble in number of different solvent and the difference between excitation and emission is over 100 nm, it had the potential to be used in multiple ways.^{2,3} In this respect, it's fluorescent properties comparable with other popular fluorescent dyes like acridine orange (λ_{em} . 525 nm, quantum yield(Φ) 0.20), fluorescein (λ_{em} . 500-600 nm, quantum yield(Φ) 0.79) and quinine sulfate (λ_{em} . 400-600 nm, quantum yield(Φ) 0.54).⁴ In this chapter we have presented electronic spectral and fluorescence data for cyclized products, isolated and characterized in preceding chapters, and compared their spectral property.

5.1 Experimental Section

5.1.1 Electronic spectral measurements

The absorption spectra were recorded on Perkin-Elmer Lambda 25 UV-vis spectrophotometer using methanolic solution of the samples. The solutions used were diluted from a ~1 mM solution to concentrations ranges between 1×10^{-5} to 3×10^{-5} M. Quartz cuvettes with 10 mm path length were used for all the measurements.

5.1.2 Fluorescence spectral measurements

Fluorescence measurements were carried out on a Cary Eclipse Spectrofluorometer using 10 mm path length quartz cuvettes with the slit width of 5 nm at 298 K. Optimum condition for fluorescence were determined by (a) first exciting the molecules at lowest energy λ_{max} found in absorption spectra (Table 5.2), (b) excitation profile was recorded by monitoring the corresponding emission followed by (c) excitation of the molecule at the lowest energy peak in excitation profile, the final emission profile were recorded. Quantum yield(Φ) were measured using comparative methods of *Williams et al.* using Quinine sulfate in 0.1 M H₂SO₄ as standard.⁴

5.2 Results and discussions

5.2.1 Absorption spectra of precursors

Schiff bases usually show multiple strong absorptions between 200-400 nm where strong absorption ~ 400 nm is the reason behind characteristic yellow/orange colour. The origin of these bands were identified as $n-\pi^*$ and $\pi-\pi^*$ transitions.⁵ The Schiff base precursors reported in this thesis confirm to this expectation (Table 5.1). For salicylaldimine type Schiff bases, the band ~ 400 nm is due to tautomerism between the phenol-imine and the keto-amine forms.⁵ However, in the present set of Schiff bases such transition is not possible due to the absence of phenol moiety. We assume this transition is a $\pi-\pi^*$ from $-C=N-$ bond whose energy is lowered to ~ 400 nm due to extensive delocalization. This band disappears upon reduction of $-C=N-$ as observed in L^3 .

5.2.2 Absorption spectra of cyclized products

Unlike precursors (previous section) almost all the cyclized products have a strong characteristic absorption maximum ~ 500 nm (Table 5.2). The overall spectral features are similar as well. Two Strong absorptions centered around 250 nm & 480 nm and two weaker transitions around 320 and 390 nm, indicative of the structural similarity (Fig. 5.3 and 5.4). The weaker transitions sometime appear as shoulder. The strong absorption near 500 nm is likely to be due to the intra-molecular charge transfer from amine to pyridinium unit proposed earlier.¹ To further substantiate this we had performed quantum mechanical calculation on $[P^1]^+$ using help from a collaborator.⁶

The ground state geometric structure of $[P^1]^+$ in gas phase was determined on the basis of Hartree-Fock *ab initio* geometry optimization method using STO 3-21G basis set. This calculation was done using SPARTAN '06 software. The excited state calculation of same ligand was performed using Gaussian 03 version program.⁷ for the estimation of excited state energy, we have preferred time dependent density function theory (TDDFT)⁸,⁹ calculation, which was performed using combination of the Becke's three parameter hybrid¹⁰ exchange potential with the correlation function of Lee *et al.*¹¹ (B3LYP). From this calculations, the lowest energy transition was found to be originating from (HOMO) mainly amine to (LUMO) pyridinium part of the molecule. The electron density distribution of the HOMO and LUMO is in figure 5.2. The comparison of HOMO and LUMO clearly shows

transfer of electron density centered in the phenyl amine unit (HOMO) to pyridinium unit (LUMO) during electronic transition (Figure 5.2).

The spectra of compounds $[\mathbf{P}^{1a}]^{2+}$ and $[\mathbf{P}^7]^+$ are somewhat different compared to the other compounds (Table 5.2, Figure 5.3 and 5.4). The structural difference of $[\mathbf{P}^{1a}]^{2+}$ compared to other cyclized product might be the reason for the difference. The difference between the spectra of $[\mathbf{P}^7]^+$ with respect to $[\mathbf{P}^6]^+$, despite substitution of a methoxy group with phenol, was somewhat unexpected. However, the phenol in $[\mathbf{P}^6]^+$ can be deprotonated easily (earlier chapter) providing electron density at the phenol end which can be transferred toward cationic part during electronic transition. This is similar to situation in $[\mathbf{P}^1]^+$ to $[\mathbf{P}^3]^+$ where the transition occurs from electron rich amine to electron deficient pyridinium unit. In case of $[\mathbf{P}^7]^+$, the transition of lone pair of ether oxygen to pyridinium are less favorable due to higher electronegativity of oxygen. Thus it occurs at a higher energy (~ 400 nm instead of ~ 500 nm). A point to note about $[\mathbf{HP}^3]^{+2}$ is that even though it is dicationic in the solid state, it exist mostly as $[\mathbf{P}^3]^+$ in solution. Support comes from pK_a determination in neutral solution using pH titration which points out pK_a as 3.8 (Chapter 2).

We like to mention that in table 5.2 three of the compounds might not be pure in the bulk. Our conclusion is based on the minor impurity observed in the proton NMR spectra. Thus data on these three may not be reliable. We have used the data only for comparison.

Table 5.1 Absorption spectral data of precursors $\mathbf{L}^1$ - $\mathbf{L}^7$

Compounds		Solvent	$\lambda_{\max}$, nm (ϵ , $M^{-1}cm^{-1}$)
$\mathbf{L}^1$	Schiff Base	MeOH	204 (34,000), 247 (16,000), 285 (sh), 365 (21,000).
$\mathbf{L}^2$	Schiff Base	MeOH	205 (40,000), 280 (18,000), 398 (18,000)
$\mathbf{L}^3$	Reduced Schiff Base	MeOH	205 (35,000), 261(22,000), 321 (sh)
$\mathbf{L}^4$	Schiff Base	MeOH	204 (40,300), 277 (18,000), 407 (20,000)
$\mathbf{L}^5$	Schiff Base	MeOH	258 (13,000), 383 (16,000)
$\mathbf{L}^6$	Schiff Base	MeOH	238 (12,000), 285 (9,000), 345 (13,000)
$\mathbf{L}^7$	Schiff Base	MeOH	237 (16,000), 286 (12,000), 341 (15,000)

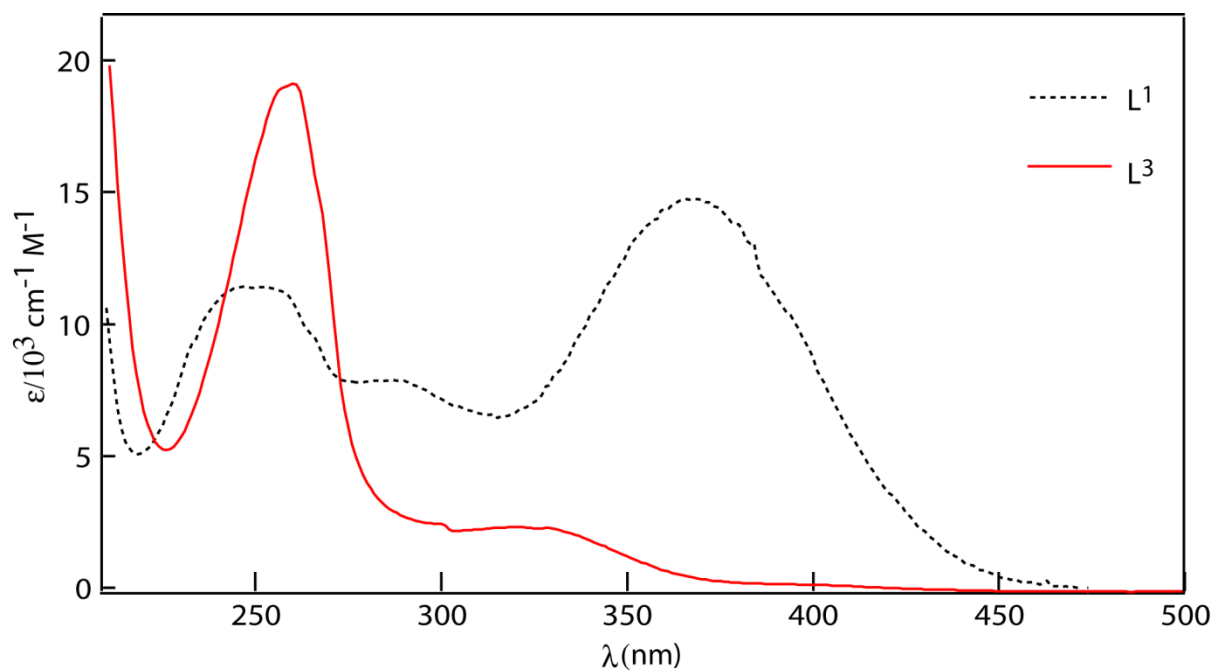


Figure 5.1 Comparative absorption spectra of Schiff base (L^1) and reduced Schiff base (L^3)

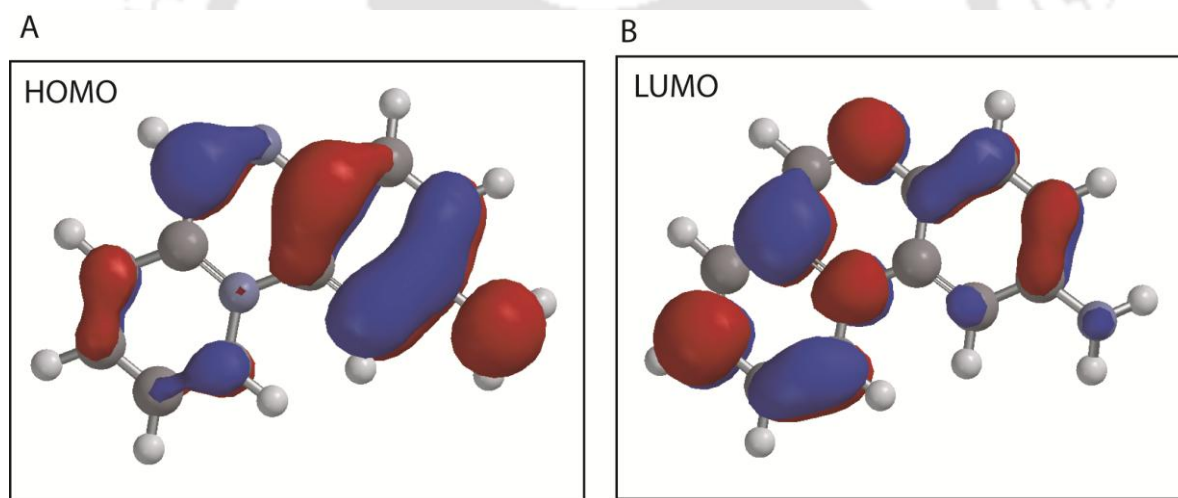


Figure 5.2 The electron density distribution of $[P^1]^+$ (A) HOMO (B) LUMO.

Table 5.2 Absorption spectral data of cyclized products^a

Compounds	Solvent	λ_{max} , nm (ϵ , M ⁻¹ cm ⁻¹)	X-ray	NMR	Mass	Bulk Quality
[P ¹]ClO ₄	MeOH	204 (22,000), 259 (9,000), 367 (9,000) 470(25,000)	Y		Y	
[P ^{1a}]Br	H ₂ O	266 (23,000), 304 (14,000) (sh), 402 (12,000), 425 (13,000), 490 (3,000)		2D	Y	
[P ^{1b}]Br	MeOH	258 (26,000), 304 (6,000), 502 (4,000)		2D	Y	
[P ²]NO ₃	MeOH	254 (16,000), 291 (21,000), 372 (5,000), 488 (13,000)	Y	2D	Y	
[P ^{2a}]Br	MeOH	246 (39,000), 298 (54,000), 373 (14,000), 485 (31,000)	Y	2D	Y	
[P ^{2b}]Br	MeOH	246 (50,000), 297 (68,000), 372 (17,000), 484 (39,000)	Y	NMR	Y	Mix. possible
[HP ³](NO ₃) ₂	MeOH	265 (61,000) 310 (sh), 367 (12,000), 473 (35,000)	Y	2D	Y	
[HP ³](Br) ₂	MeOH	272 (11,000), 325 (2,000), 384 (2,000), 487 (6,000)	Y	NMR	Y	
[P ⁵]NO ₃	MeOH	270 (37,000), 320 (sh), 385 (4,000), 495 (2,000)		2D	Y	
[P ^{5a}]Br		262 (11,000), 485 (2,000)		NMR	Y	Mix. Possible
[P ⁶]NO ₃	MeOH	262 (21,000), 321 (4,000), 388 (4,000), 497 (11,000)	Y	2D	Y	
[P ^{6a}]Br	MeOH	263 (13,000), 319 (3,000), 387 (21,000) 490 (7,000)	Y	2D	Y	Mix. Possible
[P ⁷]Br	MeOH	272 (22,000), 243 (14,000), 305 (sh), 401(13,000)	Y	2D	Y	

^a Scan range in MeOH 200 - 800 nm.

Table 5.3 Fluorescent properties of the cyclized products recorded in MeOH

Compounds	λ_{ex} , nm	λ_{em} , nm	Quantum yield (Φ)	Fluo. Solvent	Quantum Yield(Φ) Solvent
[P¹](ClO₄)^a	470	580	0.23	MeOH	MeOH
[P^{1a}]Br₂^c	400	463	0.75	H ₂ O	H ₂ O
[P²](NO₃)	b	b	b	b	b
[HP³](NO₃)₂	480	590	0.45	MeOH	H ₂ O
[HP³]Br₂	480	590	0.93	MeOH	H ₂ O
[HP³]I₂	480	584	0.55	MeOH	H ₂ O
[P⁵]NO₃	530	623	0.43	MeOH	H ₂ O
[P⁶]NO₃	550	625	0.35	MeOH	H ₂ O
[P⁷]Br	400	473	0.83	MeOH	H ₂ O
Bromo-derivatives					
[P^{1b}]Br	480	593	0.75	MeOH	H ₂ O
[P^{2a}]Br	b	b	b	b	b
[P^{2b}]Br	b	b	b	b	b
[P^{5a}]Br	480	623	0.36	MeOH	H ₂ O
[P^{6a}]Br	490	598	0.41	MeOH	H ₂ O
[P^{6b}]Br	482	515	0.38	MeOH	H ₂ O

^a from ref.¹, ^b Non fluorescent and ^c H₂O

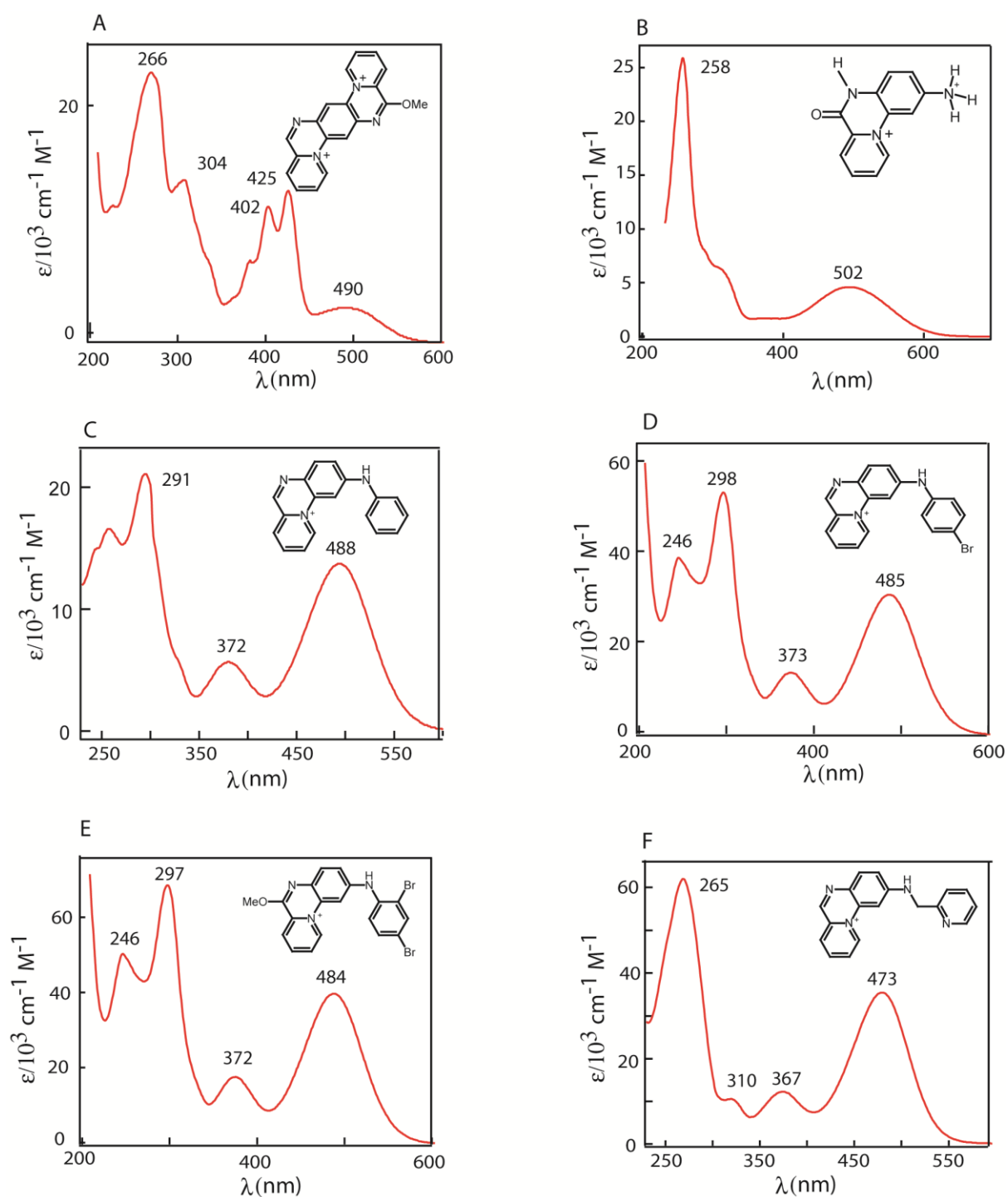


Figure 5.3 Electronic absorption spectra of (A) $[\mathbf{P}^{1a}](\text{Br})_2$, (B) $[\mathbf{P}^{1b}](\text{Br})_2$, (C) $[\mathbf{P}^2]\text{NO}_3$, (D) $[\mathbf{P}^{2a}]\text{Br}$, (E) $[\mathbf{P}^{2b}]\text{Br}$ and (F) $[\mathbf{HP}^3](\text{NO}_3)_2$.

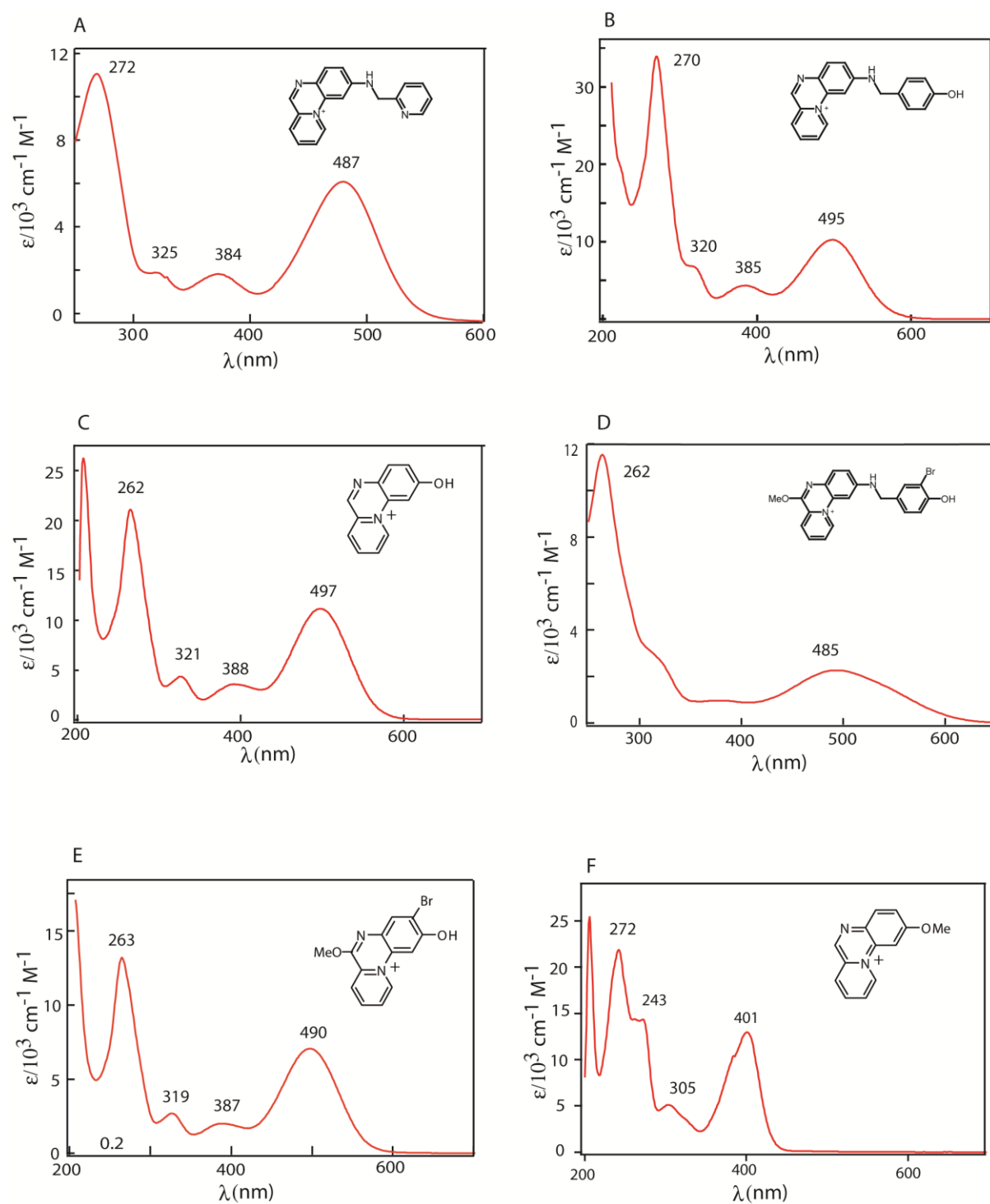


Figure 5.4 Electronic absorption spectra of (A) $[\text{HP}^3](\text{Br})_2$, (B) $[\text{P}^5]\text{NO}_3$, (C) $[\text{P}^6]\text{NO}_3$, (D) $[\text{P}^{5a}]\text{Br}$, (E) $[\text{P}^{6a}]\text{Br}$ and (F) $[\text{P}^7]\text{Br}$.

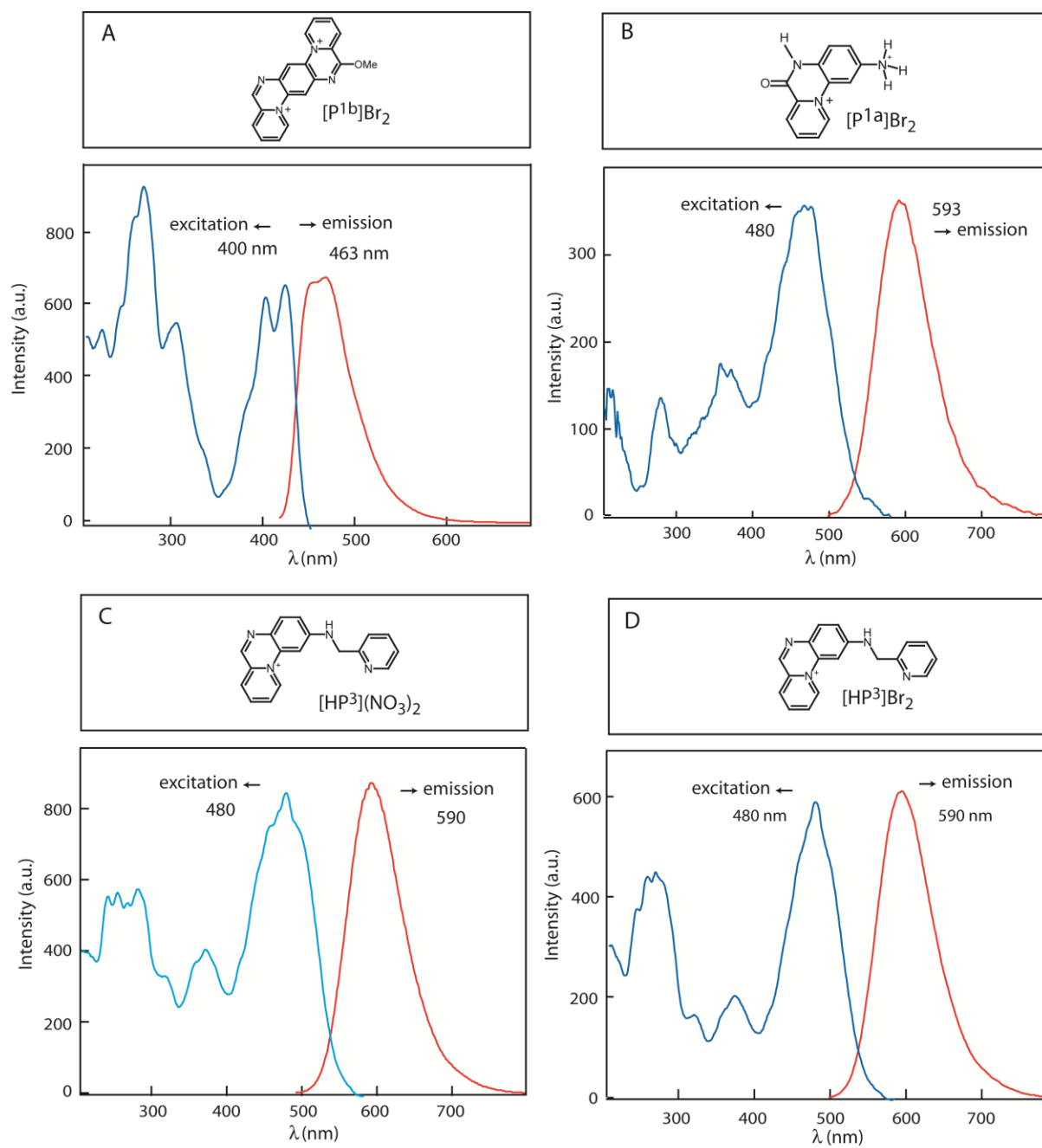


Figure 5.5 Absorption and emission spectra of (A) $[P^{1a}](Br)_2$, (B) $[P^{1b}](Br)_2$, (C) $[HP^3](NO_3)_2$ and (D) $[HP^3](Br)_2$.

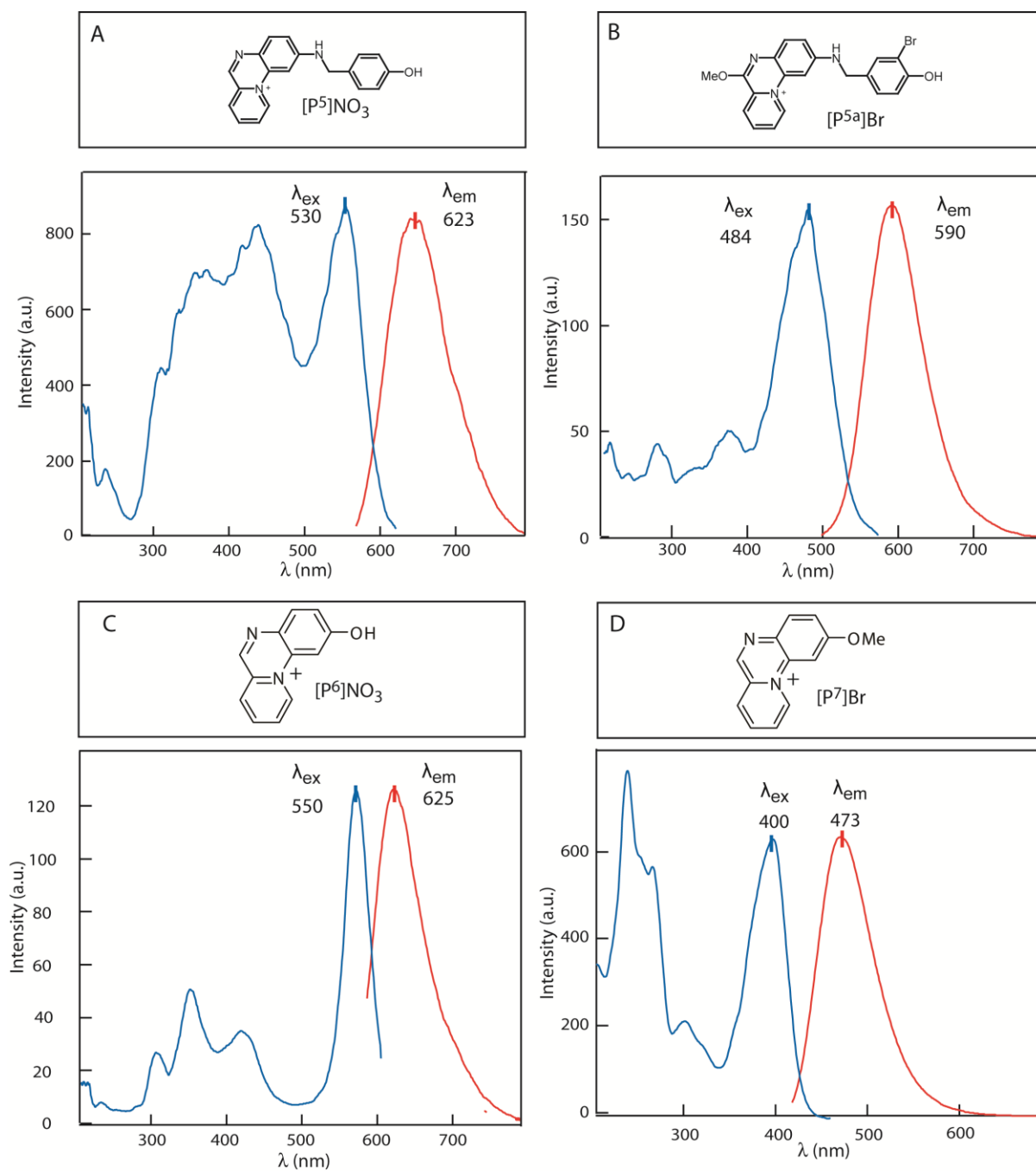


Figure 5.6 Absorption and emission spectra of (A) [P⁵]NO₃, (B) [P^{5a}]Br, (C) [P⁶]NO₃ and (D) [P⁷]Br.

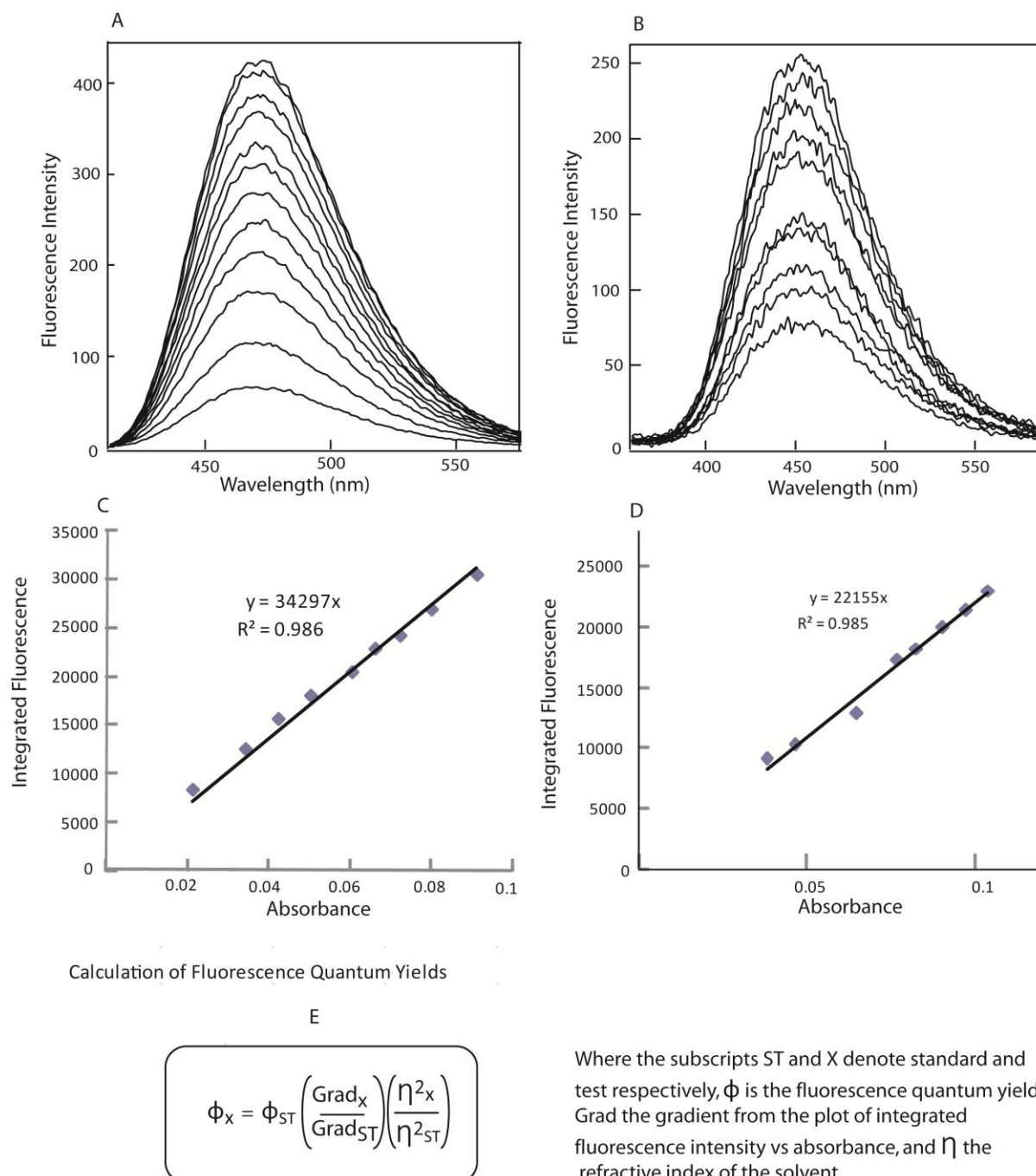


Figure 5.7 (A) Emission spectrum of $[\text{HP}^3](\text{NO}_3)_2$, (B) Emission spectrum of quinine sulphate, (C) Linear graph of compounds, (D) Linear graph of standard and (E) Formula of quantum yield.

5.3 Fluorescence properties of cyclized products

All the cyclized products, other than those from L^2 , are found to be fluorescent. The emission profile and excitation profiles for all were recorded as described in the experimental section. Emission data and spectra are presented in Table 5.3 and Figures 5.5 & 5.6. Except $[P^1]^+$ and $[P^7]^+$, all other compounds show emission between 580-625 nm (Orange to Red) upon excitation between 470-550 nm. The $[P^1]^+$ and $[P^7]^+$ emits ~ 470 nm upon excitation at ~ 400 nm. Both excitation and emission of all the compounds falls in the visible region. The difference between excitation and emission in all the cases are between 70-100 nm. The region of excitation and the relatively high difference between excitation and emission are advantages in terms of application.^{2,3}

The different spectroscopic properties of $[P^1]^+$ and $[P^7]^+$ compared to other compounds in the series were also observed in absorption spectra and explained in the previous section.

The quantum yield (Φ) as a measure of fluorescence efficiency were measured in water (Figure 5.7). The reference used for measurement was quinine sulfate in aqueous 0.1M H_2SO_4 . The values compared well with well known fluorescent dyes; acridine orange (λ_{em} . 525 nm, Q. yield 0.20), fluorescein (λ_{em} . 500-600 nm, quantum yield (Φ) 0.79) and quinine sulfate (λ_{em} . 400-600 nm, quantum yield (Φ) 0.54).

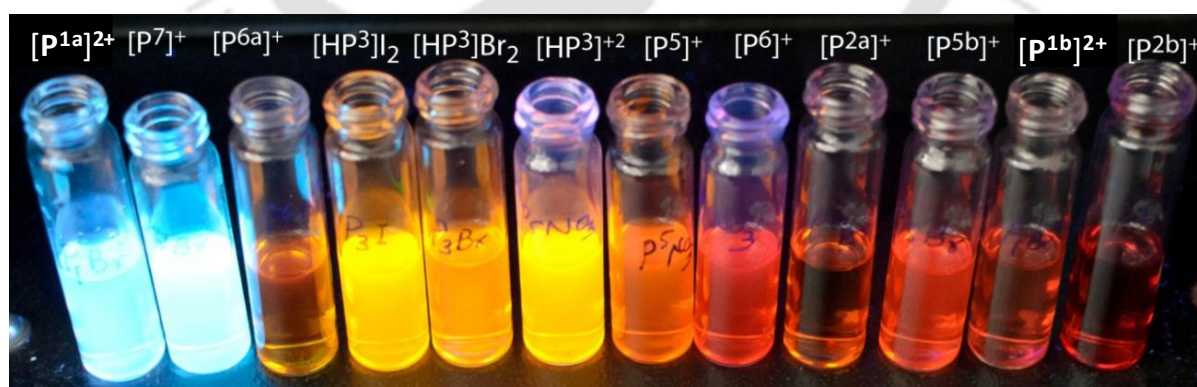


Figure 5.8 Fluorescent from blue to red taken in methanol except $[P^{1a}]^{2+}$ (H_2O) and compound $[P^{2a}]^+$, $[P^{2b}]^+$ are non fluorescent in this condition.

Conclusion

The results presented in this chapter showed that the cyclization process is associated with generation of mostly fluorescent heterocycle from non fluorescent organic precursor. The cyclized products derived from the precursor **L**² are the only exception. It might be due to the free rotation of phenyl ring at -NHPH that allows other radiative pathway for the energy. All other compounds have -NH-CH₂-R (R = H or other) unit which presumably does not allow this. Most of the compounds showed emission in the orange to red region (Figure 5.8) upon excitation in the visible region. Two of the compounds showed blue emission which perhaps is a reflection of their different electronic transitions as identified from their electronic spectra.

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Chapter 6

Cyclic Voltammetric study of precursor and product Pyrido[1,2-*a*]quinoxalin-11-ylum derivatives

The cyclization reactions presented in earlier chapters proceeds through oxidation of Schiff base or reduced Schiff base precursors. Thus it was necessary to measure and compare their oxidation potential to better understand the reaction mechanism. Oxidation potential of a compound depends on several factors¹ including measurement conditions. We choose to measure the oxidation potentials in ethanol, as methanol where all of these reactions conducted, has a very limited measurement window before solvent gets oxidized or reduced. In this chapter we present the cyclic voltammetric measurement results on the precursors and two of the cyclic products and compared the oxidation potential of the precursors.

6.1 Electrochemical analysis

6.1.1 Setup

Ethanol used in the electrochemical experiments was purified by refluxing over calcium ethoxide followed by distillation. Cyclic voltammetric measurements were carried out using CH Instruments model CH-660 electrochemical analyzer. All measurements were performed under dry nitrogen. The sample to supporting electrolyte, electrochemical grade tetrabutylammonium perchlorate (TBAP) procured from SIGMA, and ratio was kept at 1:150 throughout the measurements. All measurements were performed using a glassy carbon working electrode (CH instruments) at a scan rate of 50 mV/s unless stated otherwise. Potentials were initially measured at ~25°C relative to AgNO₃/Ag non-aqueous reference electrode. The system was calibrated against ferrocene. The $E_{1/2}$ and the peak to peak separation (ΔE_p) values of Fc⁺/Fc using this setup were found to be +0.08 V (vs Ag⁺/Ag), +0.45 V (vs SCE) and 70 mV. Redox potentials are reported vs NHE after converting with a factor of +0.61 V ({0.45-0.08}(Ag⁺/Ag to SCE) +0.241 V (SCE to NHE)). Scan range used was +1.6 V to -0.4 V (vs. NHE). Direct use of SCE as reference electrode was avoided due to aqueous nature of SCE.

6.2 Results and discussion

6.2.1 Oxidizability of the precursors

The cyclic voltammetric experiments results were summerized in table 6.1 and selected voltammograms has been presented in figure 6.1. *p*-phenylenediamine and amino phenols showed quasi-reversible oxidation. In general, both the precursors as well as two of the cyclic products analyzed showed multiple irreversible oxidations. Most of these oxidations were overlapped. The nature of the overlapping oxidations as well as variation in current height suggested possible irreversible chemical transformation of the initially oxidized species to other species during scanning. Thus reduction during the reverse scan was either absent or with negligible current height. Because of these we have compared anodic peak potential (E_{pa}) of the first oxidation to determine their relative oxidizability (Table 6.1). Among L^1 to L^3 , all derivatives of *p*-phenylenediamine, the E_{pa} shifts from +1.18 to 0.52 V as the number of imine decreases. The E_{pa} of L^3 and the parent moiety *p*-phenylenediamine are identical as both contain amine only. Although, the identical value probably is a coincident but similarity is present. We can conclude from this is that compared to free amines (a) Schiff base formation shifts the potential to high positive value making oxidation of the precursor difficult and (b) L^3 is much more susceptible to oxidation than either L^2 or L^1 . This observation holds true for the L^6 and L^7 as well. Both of them have much higher positive potential compared to their starting aminophenols. Comparing E_{pa} of L^1 - L^3 , L^6 and L^7 , the oxidizability of the precursors in the decreasing order is found to be L^7 , L^1 , L^6 , L^2 and L^3 . Compared to precursors, both the product oxidizes at potential higher than L^6 (Table 6.1). This is most likely due to the cationic nature of the cyclised product. Thus cyclization, which is an oxidation process, led to products less susceptible to further oxidation.

Table 6.1 Electrochemical data^a

Sample	Other oxidations	Second oxidation				First oxidation			
	E_{pa}	E_{pa}	E_{pc}	$E_{1/2}$	ΔE_p	E_{pa}	E_{pc}	$E_{1/2}$	ΔE_p
<i>p</i> -phenylenediamine		0.97	0.80	0.88	170	0.52	0.40	0.46	120
L ¹		1.55				1.18			
L ²		1.46				1.07			
L ³	1.49, 0.84	0.64				0.52			
<i>p</i> -methoxyaniline		0.90				0.54	0.45	0.49	90
L ⁷		1.41				1.26			
<i>p</i> -aminophenol		0.91	0.64	0.77	270	0.64	0.32	0.48	320
L ⁶		1.27				1.06			
P ₂ NO ₃						1.40			
P ₃ NO ₃		1.53				1.39			

^aAll potential values are in V and vs NHE. ΔE_p values are in mV.

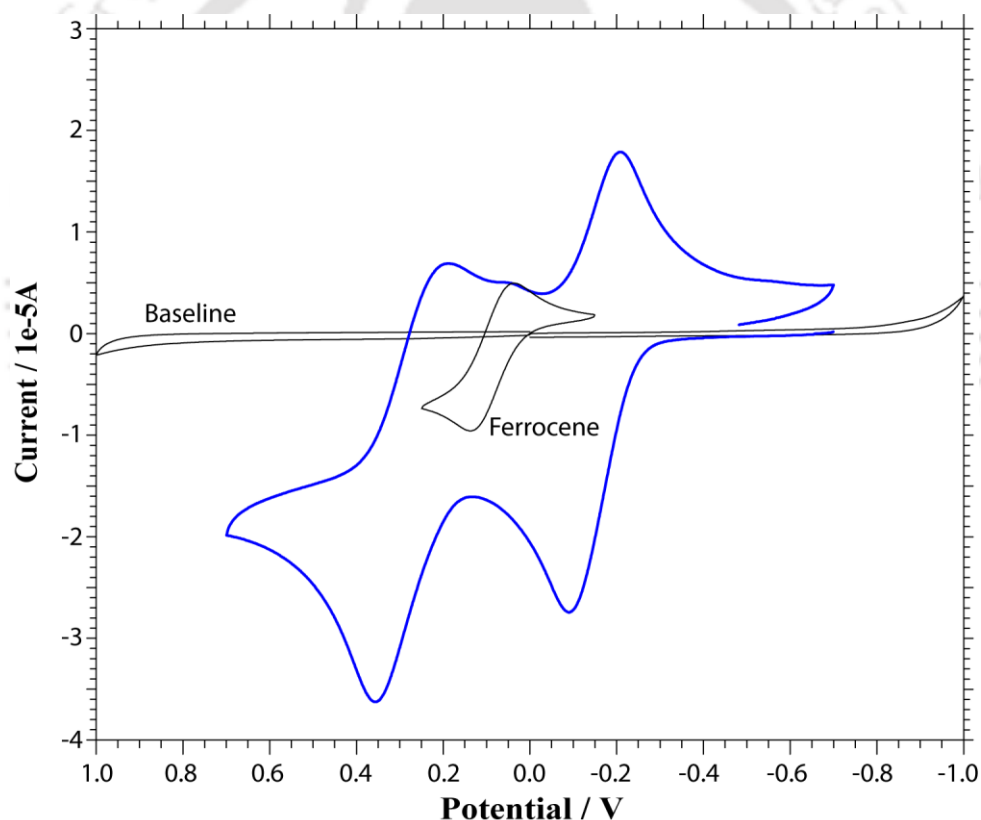


Figure 6.1. Cyclic voltammograms of PPD in EtOH at scan rate 50 mV along with solvent baseline and ferrocene reference. Scale for this figure are uncorrected for factor used for NHE conversion as explained in the experimental section. A factor of +0.61V have to be added to match with the value shown in table 6.1.

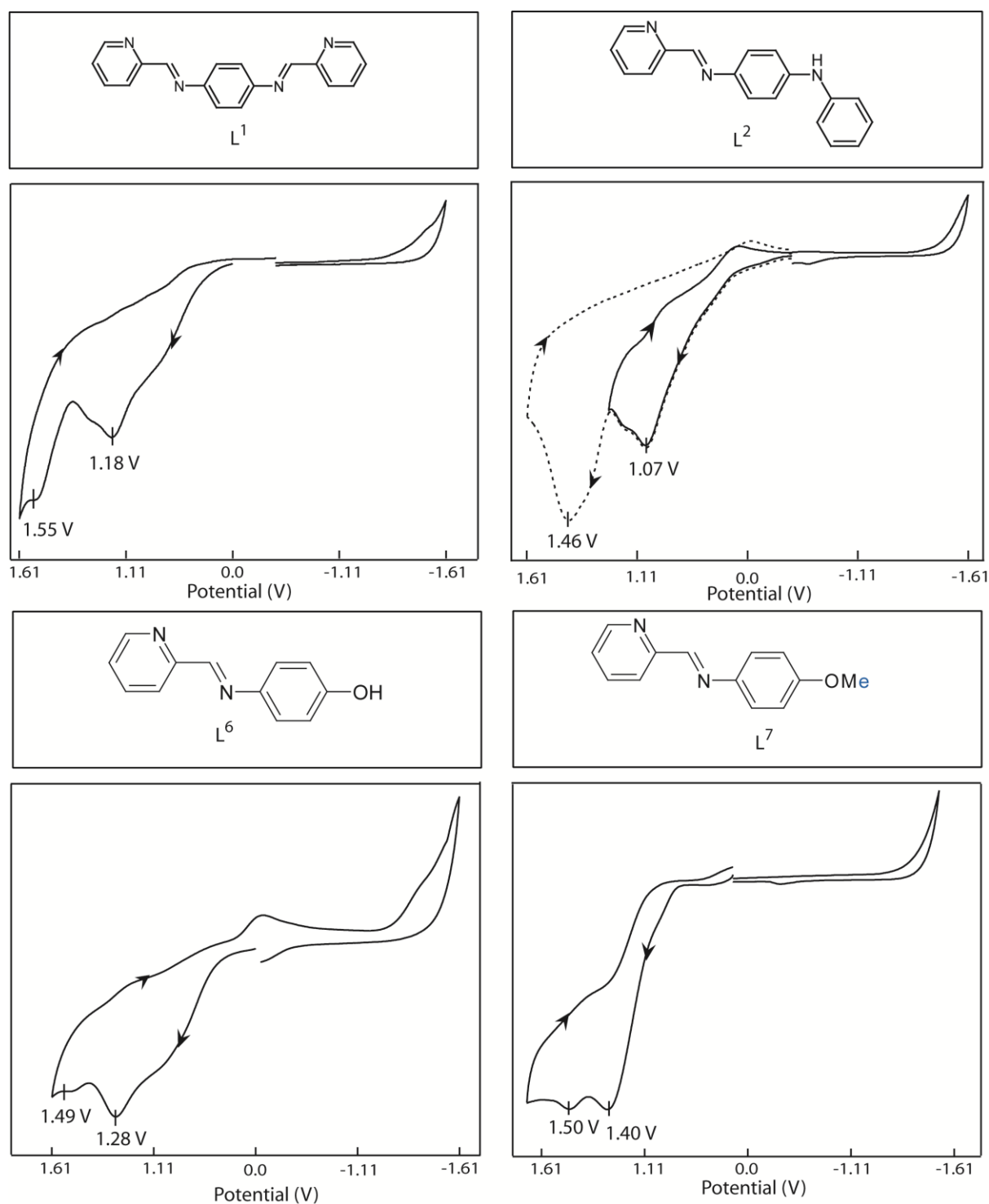


Figure 6.2. Cyclic voltammograms of **L¹**, **L²**, **L⁶** and **L⁷** in EtOH at scan rate 50 mV.

6.2.2 Oxidizability of precursor vs Reagents redox potential

In table 6.2 we have compared the oxidation potential (E_{pa} of first oxidation) with reported redox potential (E_o) of the reagents used. It is to be noted that the reagents potentials were for aqueous solutions, whereas the precursor potentials were measured in ethanol. As irreversible oxidations are susceptible on measurement conditions, our comparisons are limited on finding trends. In general, the Ce^{4+} being the strongest oxidizer among the reagents tested, it is able to oxidize all the precursors that we have tested with. However, isolation of product from these reactions proved to be difficult due to presence of multiple components in the reaction mixture. We think, the unstable radical nature of the intermediate perhaps allows side reactions leading to multiple products. On the other end, Cu^{2+}/Cu^+ being the mildest oxidizer, it does not oxidize any of the precursors except L^1 . Formation of P^1 from L^1 cannot be just oxidation of precursor. It was explained before ² that Cu(II) complex formation with the L^1 is the first step, followed by oxidation of bound L^1 at the expense of Cu(II) driven by stability of Cu(I) complexes with L^1 . In chapter 2 we have shown that metal complexation is very much possible with L^2 , as well (Chapter II). In fact, except L^3 , all the other precursors contain pyridine conjugated with imine providing coordination environment similar to bipyridine which is known to stabilize lower oxidation state (Fe^{2+} instead of Fe^{3+} , Cu^+ instead of Cu^{2+}). Thus reactions with metal ion with these precursors and eventual oxidation of the precursor, depends on the redox potential of the Cu(II) or Fe(III) complexes formed in solution which could not measure as these could not be isolated. The case of L^3 is somewhat different. Besides pyridine (intermediate soft donor), it has a amine donor (weak, hard base) which does not stabilize Cu(I) state thus stability of Cu(I) as a means of oxidizing precursor is unlikely to happen. In fact, we had observed formation of green solution indicative of Cu(II) complex which could not be isolated at this time. Halogens on the other hand have multiple ways to react with organic molecules. It could be through homolytic cleavage forming radicals first followed by oxidation of precursor by radical or forming addition complex followed by radical formation. We have not explored the details of this as of now.

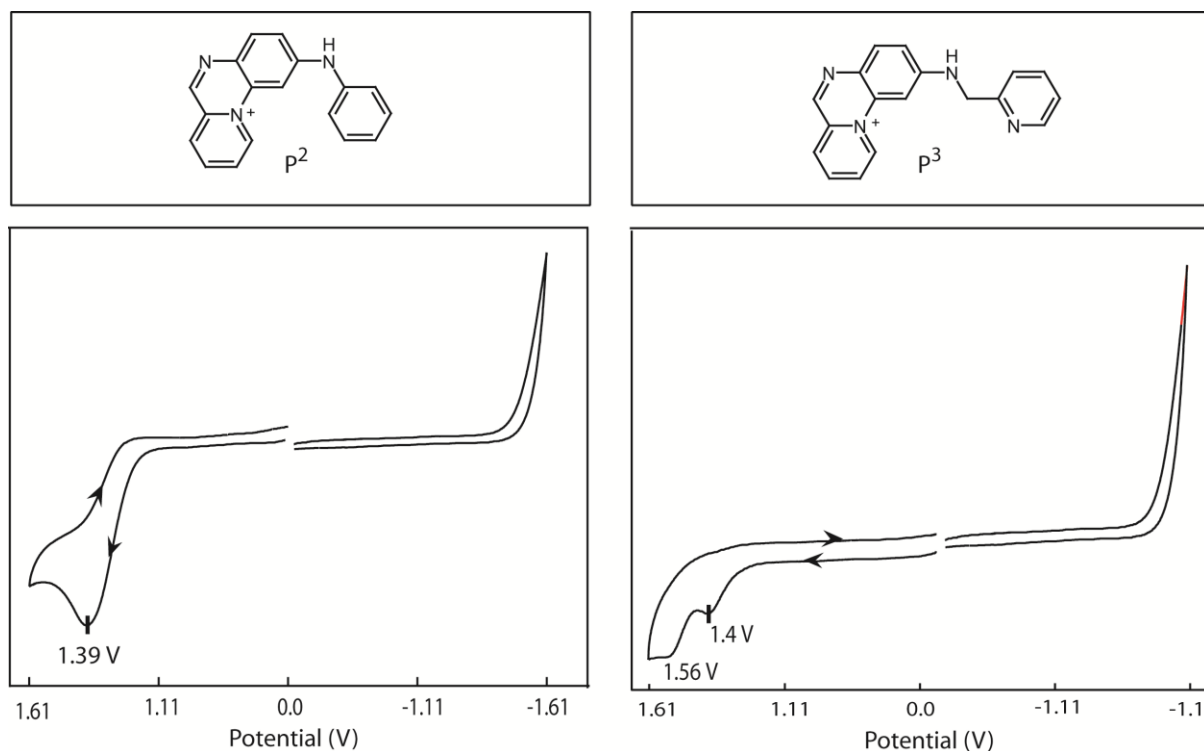


Figure 6.3. Cyclic voltammograms of **P²** and **P³** in EtOH at scan rate 50 mV sec⁻¹.

Table 6.2 Comparison of precursor oxidation potential with reagent redox potentials

Precursors	E _{pa}	Ce ⁴⁺ /Ce ³⁺ (1.61)	Br ₂ /2Br ⁻ (1.087)	Ag ⁺ /Ag (0.799)	Fe ³⁺ /Fe ²⁺ (0.771)	I ₂ /2I ⁻ (0.535)	Cu ²⁺ /Cu ⁺ (0.159)
L⁷	+1.26	R	R, iso, bro	N	N	N	N ^a
L¹	+1.18	R	R ^b , iso, bro	N ^c	R, sl	R	R ^d , iso
L⁶	+1.06	R	R iso, bro	R, sl	R, iso	R sl	N ^a
L²	+1.07	R	R iso, bro	R, iso	R, iso	R, iso	N
L³	+0.52	R	R, iso	R, iso	R, iso	R, iso	N ^a

^a metal complex formation detected, ^b ring halogenations occurred, ^c metal complex reported.
Iso = isolated, sl = slow reaction, bro= bromination.

Conclusion

From the cyclicvoltametry results presented above, we conclude that the reactions might have proceeded through mainly three different route: (i) direct oxidation of the precursor forming radical with stronger oxidant such as Ce^{4+} generating mixture of compound due to uncontrolled reactions of radicals which inhibit isolation of products, (ii) oxidation by either halogen radical or addition of halogen followed by radical formation generating mixture of cyclised product along with halogenated product usually isolable due to lower solubility of the products and (iii) complexation with metal ions followed by internal oxidation of ligand where the radical gets some stabilization depending on the nature of the ligand providing reasonable yield of the cyclised products.

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FINDINGS OF THE THESIS

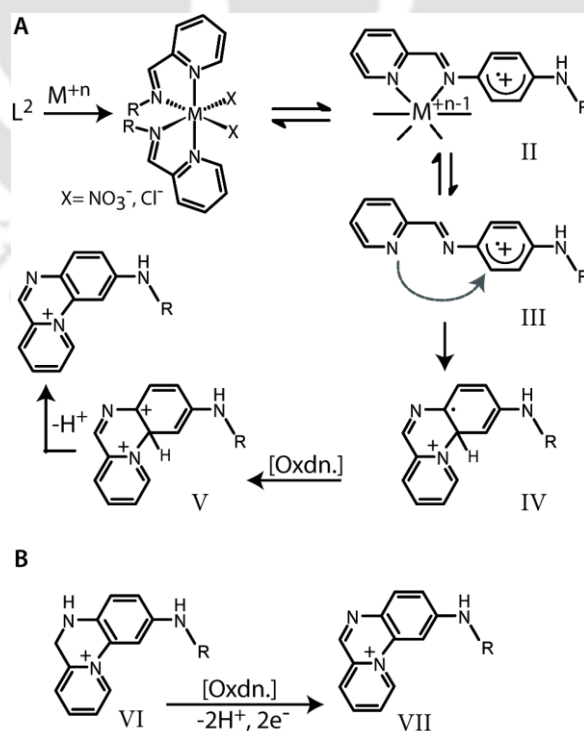
The work presented in this thesis originated from an earlier observation of transformation of a simple Schiff base to a fluorescent tricyclic heterocyclic upon addition of Cu(II) salt (Chapter 1). The reaction produced previously unknown quinoxalinium derivative. Only three other structurally similar units were reported. Out of these, benzo[e]pyrido[2,1-c][1,2,4]triazin-11-ium salts are highly fluorescent and showed strong binding with calf thymus DNA. The compound oxopyrido[1,2-*a*]quinoxalinium ions reported first by Chernavskaya *et al.* and structurally characterized recently by Duffy *et al.* showed antimicrobial activity as well as pH sensitive fluorescence. The synthesis of benzo[e]pyrido[2,1-c][1,2,4]triazin-11-ium salts involved involves either addition of acid to the organic precursor or produced in the solution from Au(III) complex of the precursor. The oxopyrido[1,2-*a*]quinoxalinium ions were synthesized from 1,2 phenylenediamine and pyrilium-2-carboxylate under refluxing condition. Another compound pyrido[1,2-*a*]quinoxalin phosphate was prepared by phosphorylation of the quinoxalin derivative of a sugar. The pyrido[1,2-*a*]quinoxalin-11-ium perchlorate has been synthesized recently in a Ca²⁺ assisted cyclization from fluoro derivatised Schiffbase precursor.

In contrast, our reaction was simple to perform and the product was highly fluorescent. It was produced due to ligand oxidation. Ligand oxidation due to metal reduction has been of current interest and recently Reedjik *et al.* reported synthesis of a leuco-verdazyl ring cyclization. They proposed that the reaction proceeds via ligand oxidation at the expense of reduction of metal ion. Thus considering the recent development of redox active metal mediated cyclization providing new type of heterocyclic compounds and the potential use of pyrido[1,2-*a*]quinoxalinium derivatives as fluorescent heterocyclic dyes, we had decided to further investigate the reaction with different precursors and reagents chosen to vary redox potential of both the precursor and reagents. During the course of this thesis we had focussed mainly on three aspect of the reaction: (i) extending the reaction to other than Schiff base (ii) extending the reaction anything other than copper(II) and (iii) if we can understand the factors that determine the choice of metal ions as well as precursors.

The results presented in Chapter 2-4 showed that the cyclization reaction is neither limited Schiff base nor Cu(II). The reactions could be extended to diamines as well as metal could be changed to Fe(III) as well (Chapter 2). The reaction even occurred with simple

addition of halogens. In the process we have synthesized number of new derivatives of the original tricyclic compound (Chapter 2-4).

The observations described in the thesis allowed us to hypothesise on the mechanism of the reaction (Scheme below). Overall, the formation of product from Schiff Base precursor is a oxidation process where two electron and one protons are lost. Structural characterization of two metal complexes showed that complexation does occur initially. Isolation of Mn(II) and Co(II) complexes also supports the requirement of a metal that can be easily reduced (Intermediate II). As pyridyl-imine is chelating ligand, it is preferably binded the metal. However, the cyclization requires pyridyl arm to be available for cyclization. The reaction occurs with first row transition metal ions which are coordinatively labile in nature. Thus we propose the intermediate III which stays in equilibrium with II and can undergo cyclization. The oxidation of intermediate IV to V perhaps requires oxygen. The reaction proceeds very slowly if performed under anaerobic condition. Performing the reactions under strict anaerobic condition or isolation and characterization under strict anaerobic condition was beyond our available facility. In case of $[\mathbf{P}^3]^+$, which did not have a imine had to undergo further reoxidation in air (Scheme, B). We observed that if this reaction is performed under nitrogen purged close container, the fluorescence is negligible compared to the reaction performed in open air.



Scheme. Proposed mechanism of the metal assisted reaction (A) and aerobic reoxidation of the $[\mathbf{P}^3]^+$.

The reactions with the halogens showed that product can be formed without the metal as well. We think halogens directly oxidizes precursor to intermediate III. Direct production of III which is a unstable radical also facilitates side reactions as well as halogenation resulting in multiple product in some cases. We are not sure whether the halogenation occurs before or after the cyclization but it is likely to be due to higher local concentration of halogen. We have used either solid/liquid halogen or concentrated methanolic solution of halogen where it is difficult to control the local concentration of halogen especially as the reaction of the radical produced is expected to be fast. Due to the difference in redox potential, bromine with higher redox potential reacted with all the precursors compared to iodine.

Thus the most important findings are new understanding about the reaction which can be used in future for synthesizing new compounds (Chapter 5). These are: (a) the relationship between a precursor and the reagent for facile cyclization depends on the oxidizability of the precursor with that particular reagent specially if there is no metal complexation involved, (b) in case the precursor act as a ligand to a metal ion (reagent) then the redox stability of the complex have to be considered i.e., if the bound metal ion can get reduced at the expense of oxidation of the ligand then cyclization can occur, (c) ortho substituted pyridine helps in the cyclization process over para-substituted one (Chapter 2) as the former facilitate intra-molecular attack, (d) between the reactions involved metal and the ones with halogen, metal ions provide cleaner reaction whereas bromine initiate side reactions resulting in multiple components depending on changes in reaction conditions (difficult to reproduce and purify).

Further, Fluorescent properties were investigated for several of these compounds (Chapter 5) and most of them are strongly fluorescent and retains the potential of future use as fluorescent dyes.

At the end we have new question as well. All along we had performed the reaction under aerobic condition at room temperature. The isolation and structural characterization of $[\text{HP}^3]^{2+}$ from L^3 (Chapter 2) showed that during the cyclization process the imine bond has formed from amine in L^3 . Compared to cyclization of $[\text{P}^1]^+$ (Chapter 1, Scheme 1), this needs extra oxidation. Does this mean that re-aromatization of the cyclization requires oxygen? Due to the inadequate setup and time limit we don't have an answer for this. The role of oxygen and kinetic studies of the reaction are aspects that can be studies in future.

List of publications

1. "Tuning one dimensional chiral channel interior in mixed ligand Cu(II) complexes of L- histidine derivative and substituted pyridine"
Koner, R. R.; Faizi, Md. S. H.; Ray, M. *Inorg. Chim. Acta*, **2011**, 372, 367.
2. Three manuscript based on the results presented in this thesis are under preparation.

Conferences

1. National Conference on frontiers in chemical sciences (FICS), Dec 2010, held at Indian Institute of Technology Guwahati, Assam, India - **Poster presentation.**
2. International symposium on Frontier in Inorganic Chemistry, Dec 2010 held at IACS Jadavpur, Kolkata, West Bengal, India - **Poster presentation**
3. 13th CRSI National Symposium in chemistry, Feb 2011 held at NISER and KIIT University Bhubaneswar, Odisha, India - **Poster presentation.**