



## Synthesis, characterization and biological activities of Schiff base complexes of Cu(II), Ni(II), and Co(II) with 4-pyridine carboxaldehyde and 3-aminopyridine

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### ABSTRACT

Schiffbase complexes of the Cu(II), Ni(II), and Co(II) 4-pyridine carboxaldehyde 3-amino pyridine complexes were synthesized and characterized by elemental analysis, magnetic susceptibility, conductivity measurements, FT-IR, electronic, spectral measurements, XRD studies antimicrobial and nuclease activity studies. The conductance measurements indicate that all the complexes are non-electrolytes. The IR spectra indicate the coordination of pyridine nitrogen and M-N bonds. The powder XRD analysis indicates that the complex is nanocrystalline. The results indicate that all the above mentioned metal ions are hexacoordinated and having moderate antimicrobial and nuclease activity.

**Key words:** 4-pyridine carboxaldehyde, 3-amino pyridine, Schiff base, Antimicrobial activity, Nuclease activity

### INTRODUCTION

Heterocyclic compounds are widely distributed in nature and essential too much biochemical processes. These compounds are worth attention because of their biological activities and clinical usage. Schiffbase ligand of 4-pyridine carboxaldehyde and 3-amino pyridine forms a stable complex with different transition metal ions. In particular, the transition metal complexes have been the subject for thorough investigation because of their extensive application in wide ranging areas from material science to biological sciences[1-3]. Schiffbase complexes of transition metals are often useful as chemical nucleases due to their structure and physico-chemical properties. The interaction of these complexes with DNA has gained much attention due to their possible applications as new therapeutic agents. Because ligands both influence the reactivity of transition metal complexes with DNA and can also be varied in an easily controlled fashion, their presence and manipulation greatly facilitate the interaction between the complexes and DNA[4-6]. Many potent antibacterial and antifungal Schiff base compounds of heterocyclic compounds were reported[7-10]. Some heterocyclic Schiff bases [11-12] can act as antibacterial agent. The present investigation involves the synthesis and characterization of the Schiff base ligand of 4-pyridine carboxaldehyde and 3-amino pyridine and its complexes with Cu(II), Ni(II) and Co(II) ions.

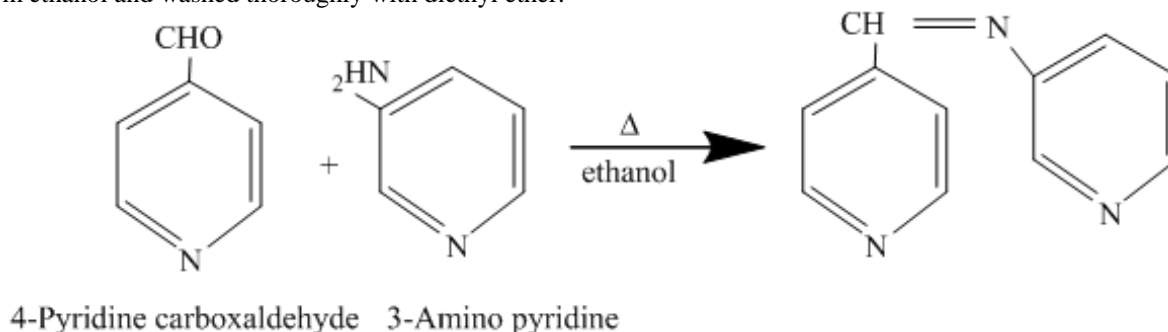
### EXPERIMENTAL SECTION

All the chemicals and solvents used were of AR grade. All the reagents used for the preparation of the Schiff bases were obtained from Sigma Aldrich. Metal salts were purchased from Loba Chemie.

IR spectra of the ligand and their complexes have been recorded in KBr pellets at Shimadzu FT-IR 8201 spectrophotometer in 4000-200  $\text{cm}^{-1}$ . Magnetic susceptibility measurements were recorded with a Gouy's balance by using mercuric tetra thiocyanatocobaltate (II) as a calibrant. Elemental analysis was performed with Perkin Elmer 240 analyzer.

**Preparation of Schiff base ligand**

The Schiff base ligand was prepared by mixing equimolar quantities of 3-amino pyridine with 4-pyridine carboxaldehyde in ethanol and refluxed for 1 hour. The Schiff base ligand formed was separated and recrystallized from ethanol and washed thoroughly with diethyl ether.

**Preparation of Schiff base complexes**

Schiff base complex was prepared by the addition of hot ethanolic solutions (60<sup>0</sup>C) of ligand and aqueous solutions nitrates of Cu(II), Ni (II), and Co(II) in drop by drop in 2:1 molar ratio. The mixture was stirred for 8 hours at 60<sup>0</sup>C. The precipitated solid was washed thoroughly by ethanol and then by diethyl ether. The solid complexes were dried in vacuum desiccator.

**Determination of antimicrobial activity**

The in- vitro biological activity of the Schiff base and its metal complexes in DMSO were tested against the bacteria *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *E.Coli*, *Staphylococcus aureus* and *Proteus* by disc diffusion method using nutrient agar as medium and *Amikacin* as control. The inhibition zone was developed at which the concentration was noted. The antimicrobial activity was estimated based on the size of inhibition zone in the discs [13-16]. From the results, the activity index was calculated using the following formula.

$$\text{Activity Index (AI)} = \frac{\text{Inhibition zone of the sample}}{\text{Inhibition zone of the standard}}$$

**Nuclease Activity studies****Gel Electrophoresis**

Cleavage reactions were run between complexes and the calf thymus DNA performed by gel electrophoresis [17] experiment and the solutions were diluted with loading dye using 1% agarose gel. After electrophoresis, the gel was photographed under UV transluminator [18].

**RESULTS AND DISCUSSION**

All the complexes are stable at room temperature, non-hygroscopic, insoluble in water but slightly soluble in methanol and ethanol and soluble in DMF and DMSO.

Analytical data suggest that the metal to ligand ratio in all the complexes to be 1:2 (Table 1). Conductivities, Magnetic susceptibilities of the complexes are also shown in Table 2, 3. All the complexes are non-electrolytes because their conductivity values were in the range 14-23 ohm<sup>-1</sup> cm<sup>2</sup> mol<sup>-1</sup>. Magnetic susceptibility data of the complexes showed the octahedral coordination of the complexes.

**Table 1 Physical characteristics and analytical data of ligand and its complexes**

Compound	Colour Yield (%)	Empirical formula	Melting point (°C)	Elemental Analysis Calculated (found) %		
				C	H	N
C <sub>11</sub> H <sub>9</sub> N <sub>3</sub> (L)	Colourless (85%)	C <sub>11</sub> H <sub>9</sub> N <sub>3</sub>	175	72.13 (71.99)	4.91 (4.01)	22.95 (21.98)
[CuL (NO <sub>3</sub> ) <sub>2</sub> ]	BluishGreen (65%)	CuC <sub>11</sub> H <sub>9</sub> N <sub>5</sub> O <sub>6</sub>	201	35.62 (33.82)	2.42(2.01)	18.89 (18.11)
[NiL (NO <sub>3</sub> ) <sub>2</sub> ]	Green (40%)	NiC <sub>11</sub> H <sub>9</sub> N <sub>5</sub> O <sub>6</sub>	187	36.09 (34.11)	2.46 (2.02)	19.14 (18.04)
[CoL (NO <sub>3</sub> ) <sub>2</sub> ]	Black (45%)	CoC <sub>11</sub> H <sub>9</sub> N <sub>5</sub> O <sub>6</sub>	210	36.07(34.10)	2.45(1.97)	19.13(18.12)

Table 2 Magnetic Susceptibility data of the complexes

Complex	Magnetic susceptibility(BM)
[CuL (NO <sub>3</sub> ) <sub>2</sub> ]	1.8
[NiL (NO <sub>3</sub> ) <sub>2</sub> ]	3.1
[CoL (NO <sub>3</sub> ) <sub>2</sub> ]	5.0

Table 3 Molar conductance data of ligand and complexes

Ligand/complex	Molar conductance	Nature
C <sub>11</sub> H <sub>9</sub> N <sub>3</sub> (L)	23	Non- electrolyte
[CuL (NO <sub>3</sub> ) <sub>2</sub> ]	16	Non- electrolyte
[NiL (NO <sub>3</sub> ) <sub>2</sub> ]	15	Non- electrolyte
[CoL (NO <sub>3</sub> ) <sub>2</sub> ]	15	Non- electrolyte

### Electronic spectra

The UV – Visible data of ligand and its complexes are given in Table.4 The UV– visible spectrum of the ligand shows a absorption bands at 270nm, 389nm which is assigned to  $\pi$ -  $\pi^*$  transition of the –C=N- bond. This supports the possible involvement of azomethine group in coordination.

The UV – Visible spectrum of Cu(II) complex of ligand shows absorption bands at 297 nm 591 nm. The bands have been assigned  ${}^2E_g \rightarrow {}^2T_{2g}$  transition. The nature of the band suggests distorted octahedral geometry [19]. Ni (II) complex of ligand shows absorption bands at 345nm, and 551nm which are assigned to  ${}^3A_{2g} \rightarrow {}^3T_{2g}$ ,  ${}^3A_{2g} \rightarrow {}^3A_{1g}$ , (F),  ${}^3A_{2g} \rightarrow {}^3T_{1g}$  respectively. Thus Ni(II) complex of is assigned an octahedral geometry [20].

In the spectrum of Co(II) shows absorption bands at 221nm, 419nm which are assigned to  ${}^4T_{1g} \rightarrow {}^4T_{1g}(p)$ ,  ${}^4T_{1g} \rightarrow {}^4A_{2g}$ , transitions respectively. Thus Co(II) complex is assigned an octahedral geometry [21].

Table 4 Electronic spectral data of the ligand/complexes

Ligand/complex	$\lambda_{max}$ (nm)
C <sub>11</sub> H <sub>9</sub> N <sub>3</sub>	270,389
[CuL (NO <sub>3</sub> ) <sub>2</sub> ]	297,591
[NiL (NO <sub>3</sub> ) <sub>2</sub> ]	345,551
[CoL (NO <sub>3</sub> ) <sub>2</sub> ]	221, 419

Fig 1 UV- Visible spectrum of Schiff base ligand

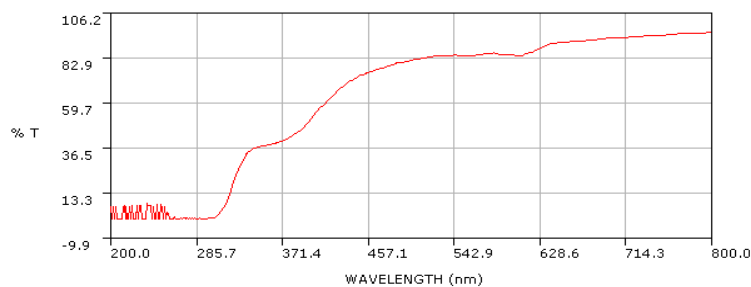


Fig 2 UV- Visible spectrum of Cu (II) complex

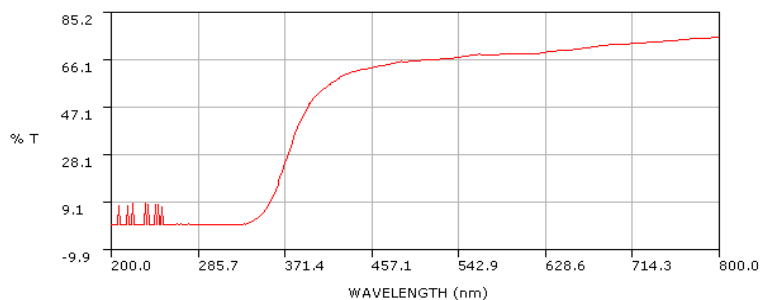


Fig 3 UV- Visible spectrum of Ni (II) complex

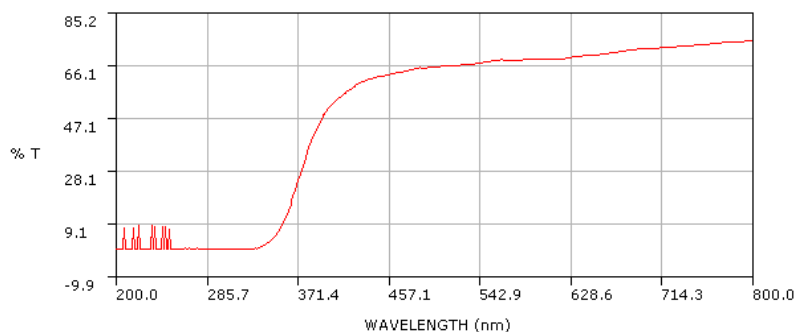


Fig 4 UV- Visible spectrum of Co(II) complex

### IR-Spectra

The IR spectra of the ligand and its complexes are shown in Fig 5-8. Selected IR spectral band for the ligand and its complexes are given in Table.5 The IR spectrum of the free ligand is characterized mainly by the strong bands at  $2832\text{ cm}^{-1}$ ,  $2910\text{ cm}^{-1}$  and  $1590\text{ cm}^{-1}$  which are attributed to the stretching frequencies of C – O, C – H and C = N respectively. The Schiff base shows a peak in the free ligand at  $810\text{ cm}^{-1}$  and  $744\text{ cm}^{-1}$  corresponding to the presence of 3-substituted and 4-substituted pyridine groups. The IR spectra of the free ligand were compared with the spectra of metal complexes. The characteristic absorption bands  $3423\text{ cm}^{-1}$ - $3373\text{ cm}^{-1}$  range was attributed to –OH group of the coordinated or lattice water [22]. The absorption bands in the range  $2853$ - $2810\text{ cm}^{-1}$ ,  $2923\text{ cm}^{-1}$ - $2900\text{ cm}^{-1}$  and  $1607$ - $1602\text{ cm}^{-1}$  are assigned to C – O, C – H and C = N respectively[23]. The band observed at  $1590\text{ cm}^{-1}$  region is assigned to the azomethine group of ligand. This band is shifted towards higher frequencies region to the extent of  $10$ - $20\text{ cm}^{-1}$  in the metal complex indicating the involvement of pyridine nitrogen in coordination sphere. This fact is also supported by the results of elemental analysis of complexes. Another absorption band in the range  $776\text{ cm}^{-1}$  -  $701\text{ cm}^{-1}$  is assigned to the coordinated nitrate group with the central metal atom [24].

Table 5 IR spectral data of ligand and its complexes

Ligand/Complex	$\nu_{\text{O-HH}_2\text{O}}$	$\nu_{\text{C-O}}$	$\nu_{\text{C-H}}$	$\nu_{\text{C=N}}$	$\nu_{\text{M-N}}$
$\text{C}_{11}\text{H}_9\text{N}_3$	-	2832.12	2910.34	1590.89	-
$[\text{CuL}(\text{NO}_3)_2]$	3423.74	2852.10	2923.08	1604.87	717.56
$[\text{NiL}(\text{NO}_3)_2]$	3373.98	2810.15	2900.10	1607.71	701.70
$[\text{CoL}(\text{NO}_3)_2]$	3385.72	2853.50	2905.12	1602.14	776.81

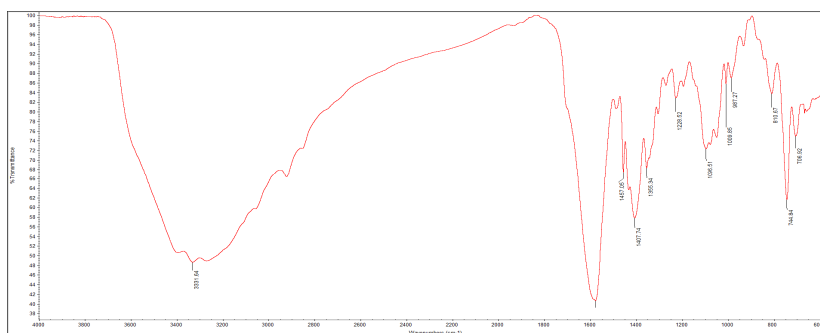
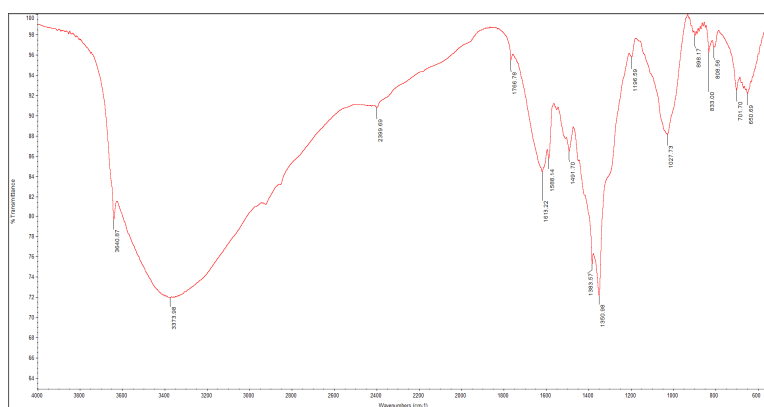
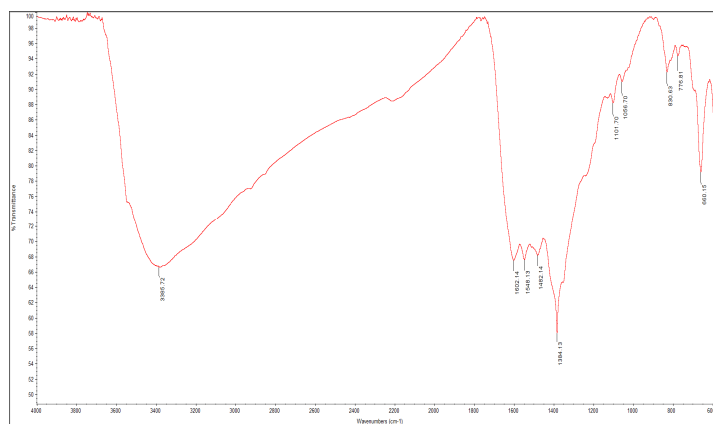
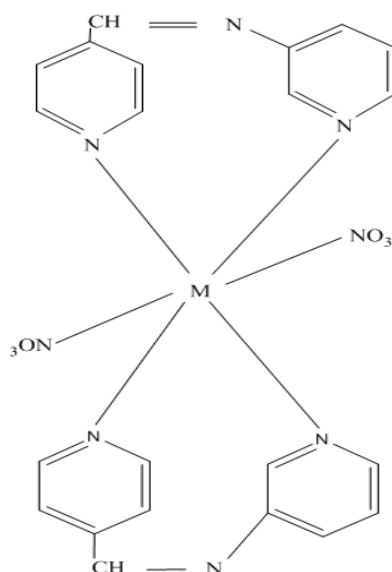


Fig 5 FT-IR spectrum of Schiff base ligand

**Fig 6 FT-IR spectrum of Cu(II) complex****Fig 7 FT-IR spectrum of Ni(II) complex****Fig 8 FT-IR spectrum of Co(II) complex**

On the basis of the above observation the probable structure of Cu(II), Ni(II) and Co(II) complexes may be presented as follows Fig 9.

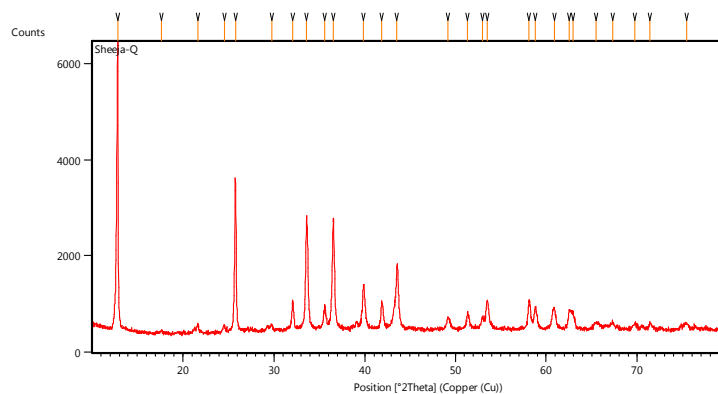


**Fig 9 Proposed structure of schiff base complex of Cu(II) , Ni(II), and Co(II)ions**  
M = Cu(II), Ni(II), and Co(II)

### XRD Analysis

The powder XRD analysis of Co(II) complex was carried out. The diffractogram is given in Fig 10. The strong and broad peak confirms the complex formation and the appearance of large feeble peaks indicates that the complex is nano crystalline [25]. The grain size of the complexes is calculated using Scherer's formula. The calculated grain size is 5.34 nm suggested that the complexes are in nano crystalline state.

$$\text{Particle size (D)} = \frac{K\lambda}{\beta \cos \theta}$$



**Fig 10 XRD Spectrum of Co(II) complex**

### Antimicrobial activity

The results of antibacterial activity substantiate the findings of earlier researchers that biologically active compounds become more active and less biologically active compounds become more active upon coordination. Such enhancement in biological activity of metal complexes can be explained on the basis of Overtone's concept and chelation theory.

The present investigation suggest that all the metal complexes of the ligand bearing metal ion, pyridine ring, -N = CH- group, have comparatively more biological activity. This antibacterial activity serves as a basis for the chemical modification directed towards the development of new class of antimicrobial agents.

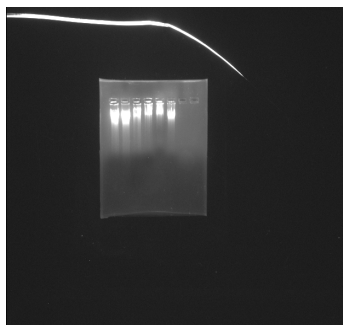
**Table 6 Antimicrobial activities of ligand and its complexes**

Ligand/ complex	Antibacterial activity (mm)			Antifungal activity (mm)		
	<i>Staphylococcus aureus</i>	<i>E.Coli</i>	<i>Klebsiella pneumonia</i>	<i>Candida albicans</i>	<i>Aspergillus niger</i>	<i>Pencilium SP</i>
C <sub>11</sub> H <sub>9</sub> N <sub>3</sub> (L)	9	7	8	9	7	7
[CuL(NO <sub>3</sub> ) <sub>2</sub> ]	13	10	10	10	9	10
[NiL(NO <sub>3</sub> ) <sub>2</sub> ]	11	9	9	12	9	8
[CoL(NO <sub>3</sub> ) <sub>2</sub> ]	11	9	10	11	12	9

**Nuclease Activity**

The nuclease activity of Cu(II), Ni(II) and Co(II) complexes were studied using gel electrophoresis and the respective photograph is shown in Fig 11. The cleavage efficiency of the complexes is compared with the control DNA to study the binding ability.

The presence of smear in the gel diagram indicates the radical cleavage [26] by the abstraction of hydrogen from sugar units of DNA. The metal complexes were able to convert super coiled DNA into open circular DNA [27]. The reaction is modulated by the metallo complexes bound hydroxyl or peroxy radical generated from the oxidant H<sub>2</sub>O<sub>2</sub>. All the complexes showed enhanced nuclease activity.



**Fig 11** Gel diagram for M(II) complexes  
M=Cu(II), Ni(II) and Co(II)

**CONCLUSION**

The Schiff base ligand synthesized from 4-pyridine carboxaldehyde with 3-amino pyridine. They formed stable complexes with transition metal ions such as Cu(II), Ni(II) and Co(II) in ethanol. The ligand and their complexes were characterized using spectral and analytical data. From the spectral and stoichiometric analysis, a hexacoordinated nature was assigned for the metal complexes. Antimicrobial study showed that all the complexes have moderately active. DNA cleavage activity studies of all complexes showed nuclease activity.

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