



## **Synthesis, characterisation and antimicrobial activity of Mannich base derived from pyridine-2-carboxaldehyde and its metal complexes**

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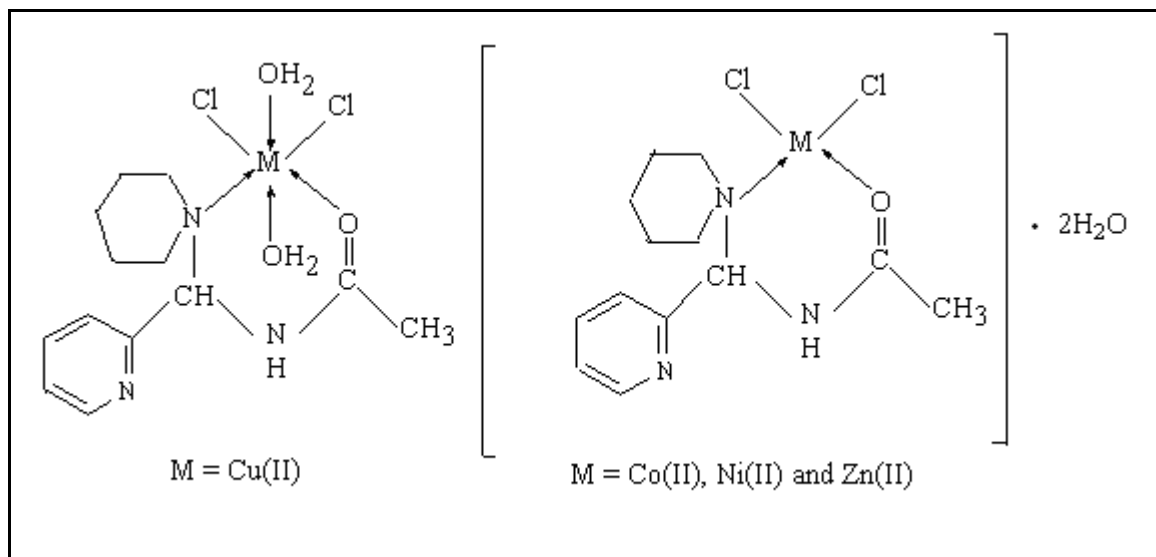
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**Abstract :** The present study deals with the synthesis, characterization and antimicrobial properties of Mannich base N-[1-piperidino(pyridine-2-carboxyl)]acetamide (**PPCA**) and its metal [Cu(II), Co(II), Ni(II) and Zn(II)] complexes. The ligand forms 1:1 (metal:ligand) type of complexes with Cu(II), Co(II), Ni(II) and Zn(II) metal salts. The structural features have been arrived from their microanalytical, IR, UV-Vis., CV, EPR spectral data. The electrolytic behaviour of the chelates was assessed from their molar conductance data. The magnetic susceptibility measurements suggested that all the complexes were paramagnetic except Ni and Zn, which were diamagnetic, and the magnitude of magnetic moment values were useful to find out the number of unpaired electrons which in turn were useful to further support the geometry suggested by electronic spectral data. The magnetic susceptibility and electronic absorption spectra of copper complex indicates an octahedral geometry around the central metal ion while cobalt, zinc complexes exhibit tetrahedral geometry and nickel complex shows square-planar structure. Both the ligand and its metal complexes were tested against some microorganisms for their antimicrobial activity. It has been found that all the complexes have higher activity than the free ligand and the standard.

### **Introduction**

Studies on the chemistry of Mannich bases are of interest in various areas of application. Many researchers have studied the numerous applications of Mannich reactions<sup>1-7</sup>. Mannich bases are very reactive; infact, they can easily be transformed into numerous other compounds. Mannich reaction consists of the condensation of substrate possessing one active hydrogen with an aldehyde/ketone and a primary/secondary amine. Many research articles are available in the literature for the synthesis of Mannich bases using formaldehyde, benzaldehyde and substituted benzaldehydes. Organic chelating ligands containing amide moiety as a functional group have a strong ability to form metal complexes and exhibit wide range of biological activities<sup>4-6</sup>. Keeping the above facts in mind and as part of our continuing efforts to investigate transition metal(II) complexes using Mannich bases<sup>8-11</sup>, in this paper we describe the synthesis, characterization and antimicrobial studies of Cu(II), Co(II), Ni(II) and Zn(II) complexes containing bidentate Mannich base derived by condensing piperidine, pyridine-2-carboxaldehyde and acetamide. The ligand system coordinates to the metal ion in a bidentate manner through the amide carbonyl oxygen and the nitrogen atom of piperidine group. The proposed structure of the complexes is shown below.



## Experimental

### Synthesis of Mannich base

Acetamide (5.9 g, 0.1 mol) dissolved in water and was mixed with piperidine (10 mL, 0.1 mol) and stirred to get a clear solution. Pyridine-2-carboxaldehyde (10.4 mL, 0.1 mol) was added in drops and the reaction mixture was kept in an ice bath that was placed over a magnetic stirrer and stirred for an hour. Compound formed was filtered and then recrystallised from ethanol. Purity of the compound was checked by TLC and the melting point of the compound was determined in an open capillary tube and were uncorrected.

### General Synthesis of metal complexes

The Mannich base dissolved in methanol and methylene chloride(1:1) and the metal chlorides,  $MCl_2$  [where  $M = Cu(II), Co(II), Ni(II)$  and  $Zn(II)$ ] dissolved in methanol were mixed in 1:1 molar ratio. The reaction mixture was warmed gently on a water bath for an hour. The metal complexes formed were filtered, washed with ethanol and dried in vacuum.

### Antimicrobial activity

The antimicrobial activities of the synthesised compounds and metal complexes have been studied by well-diffusion test against the selected organisms. The zone of inhibition values were found out at the end of 24 h at 37°C for the bacterial stains. The values are presented in Table 1.

## Results and Discussion

All the metal complexes are stable at room temperature. They are insoluble in water but soluble in MeCN, DMF and DMSO. The ligand L, on interaction with Cu(II), Co(II), Ni(II) and Zn(II) chlorides, yields complexes corresponding to the general formula  $[ML]$ . This stoichiometric assignment is supported by the microanalytical data. The low molar conductance values of the complexes ( $3.1-5.9 \text{ mho cm}^2 \text{ mol}^{-1}$ ) support their neutral nature<sup>12</sup>.

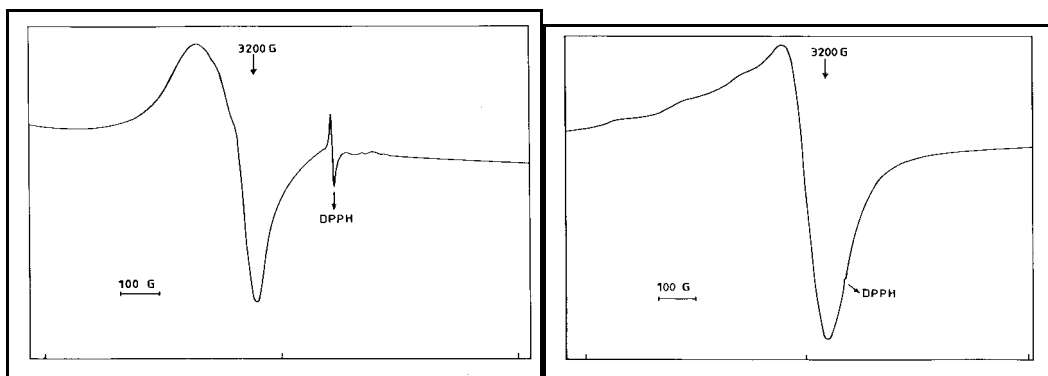
In order to study the binding mode of Mannich base to metal in the complexes, IR spectrum of the free ligand was compared with the spectra of the metal complexes. Infrared spectrum of the ligand and its metal complexes were recorded in KBr medium. Upon chelation with metal salts, the amide  $\nu_{C=O}$  and  $\nu_{C-N-C}$  of piperidine bands at  $1640 \text{ cm}^{-1}$  and  $1160 \text{ cm}^{-1}$  are shifted to lower frequencies *viz.*,  $1620-1640 \text{ cm}^{-1}$  and  $1110-1130 \text{ cm}^{-1}$  respectively. The lowering in frequencies observed in all the complexes shows the involvement of carbonyl oxygen and tertiary piperidine nitrogen atom in coordination to the metal ion. Several evidences<sup>12-14</sup> on the coordination of substituted acetamide through carbonyl oxygen have been reported.

The IR spectra of the metal complexes also show some new bands in the region 530-540  $\text{cm}^{-1}$  and 440-450  $\text{cm}^{-1}$  due to M-O and M-N bonds respectively which further confirm that the ligand is bidentate in nature. In all the complexes, an additional medium band found at 340  $\text{cm}^{-1}$  is assigned to M-Cl stretching vibration. In the spectra of all the complexes, the N-H band remained at the same position as in the free ligand, indicating that the secondary nitrogen is not coordinated.

The electronic absorption spectra of the Mannich base and its Cu(II), Co(II), and Ni(II) complexes were recorded at room temperature using DMSO as solvent. The electronic spectrum of green Cu(II) complex shows a broad band at 14,850  $\text{cm}^{-1}$  assignable to  ${}^2E_g \rightarrow {}^2T_{2g}$  transition, suggests an octahedral geometry for the complex. Though three transitions are expected in this case, they are very close in energy and often appear in the form of one broad band envelope. The Co(II) complex exhibits a band with maxima at 16,890  $\text{cm}^{-1}$  which is assigned to  ${}^4A_2 \rightarrow {}^4T_1(P)$  for tetrahedral geometry for the complex. The Ni(II) complex showed band at 16,680  $\text{cm}^{-1}$  which is assigned as  ${}^1A_{1g} \rightarrow {}^1A_{2g}$  transition confirming a square-planar geometry for the complex. The absence of any band below 10000  $\text{cm}^{-1}$  eliminates the possibility of a tetrahedral environment in this complex.

The magnetic moment value of Cu(II) complex is 1.9 B.M. which suggests an octahedral geometry around the metal ion. The magnetic moment of Co(II) complex is 3.9 B.M. which suggests the high spin four coordinated tetrahedral arrangement of ligand molecules around the metal ion. The Zn(II) complex is found to be diamagnetic as expected for  $d^{10}$  configuration.

The EPR spectrum of copper complex provides information which are important in studying the metal ion environment. The EPR spectra of the Cu(II) complex (Figure 1) were recorded in DMSO at LNT and at RT.



**Figure 1. X-band EPR spectrum of copper complex in DMSO at 300 K (a) and 77 K (b)**

The spectrum of the copper complex at RT shows one intense absorption band in the high field and is isotropic due to the tumbling motion of the molecules. However, this complex at LNT shows four well resolved peaks with low field region. The copper complex exhibits the  $g_{\parallel}$  value of 2.34 and  $g_{\perp}$  value of 2.18. These values indicate that the Cu(II) lies predominantly in the  $d_{x^2-y^2}$  orbital[29]. The spin-orbit coupling constant,  $\lambda$  value ( $-496 \text{ cm}^{-1}$ ) calculated using the relations,  $g_{av} = 1/3[g_{\parallel} + 2g_{\perp}]$  and  $g_{av} = 2(1 - 2\lambda / 10Dq)$ , is less than the free Cu(II) ion ( $-836 \text{ cm}^{-1}$ ) which also supports covalent character[30] of M-L bond in the complex. The G value of 3.94 indicates negligible exchange interaction of Cu-Cu in the complex. The covalency parameter  $\alpha^2$  is calculated ( $\alpha^2 = 0.85$ ) using the following equation:

$$\alpha^2_{cu} = -(A_{\parallel}/0.036) + (g_{\parallel} - 2.0023) + 3/7(g_{\perp} - 2.0023) + 0.04$$

If the value of  $\alpha^2 = 0.5$ , it indicates a complete covalent bonding, while the value of  $\alpha^2 = 1.0$  suggests a complete ionic bonding. The observed value of  $\alpha^2$  (0.88) of the complex is less than unity which indicates that the complex has some covalent character in the ligand environment<sup>15</sup>.

Antibacterial activity of the ligand and its complexes have been carried out against the Gram positive bacteria like *S. aureus*, *B. subtilis* and Gram negative bacteria such as *E.coli*, *P. auroginosa* using Mueller-Hinton agar by well-diffusion method using DMF as solvent. Ampicillin was used as the standard for comparing the results. The zone of inhibition values was determined at the end of an incubation period of 24 h

at 35°C. It has been observed from the result (Table 1) that the metal complexes have a higher activity than that of the free ligand and the standard. Probably this may be due to the greater lipophilic nature of the complexes<sup>16-20</sup>.

**Table 1. Antibacterial activity of ligand and its metal complexes**

No.	Compound	Inhibition zone (mm)			
		<i>S.aureus</i>	<i>E.coli</i>	<i>P.auroginosa</i>	<i>B.subtilis</i>
1.	Ligand	10	12	12	11
2.	[CuCl <sub>2</sub> .PPCA.(H <sub>2</sub> O) <sub>2</sub> ]	17	22	21	20
3.	[CoCl <sub>2</sub> .PPCA] (H <sub>2</sub> O) <sub>2</sub>	17	21	19	18
4.	[NiCl <sub>2</sub> .PPCA] (H <sub>2</sub> O) <sub>2</sub>	18	20	21	19
5.	[ZnCl <sub>2</sub> .PPCA] (H <sub>2</sub> O) <sub>2</sub>	18	22	20	21
6.	Ampicillin	10	11	10	11

PPCA = Mannich base ligand

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