Synthesis, Characterization and Antimicrobial Studies of Mannich Base Derived from 2-Methyl Benzimidazole and its Metal Complexes

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A ligand derived from 2-methyl benzimidazole, nicotinic acid hydrazide and benzaldehyde and its metal complexes with Cu(II), Co(II), Ni(II), Zn(II) and Fe(III) have been synthesized and characterized by IR, UV-visible, ¹H NMR, ¹³C NMR. The antimicrobial activities of the ligand and its metal complexes were determined against the bacteria *Escherichia coli*, *Salmonella paratyphi* A and *Staphylococcus aureus*.

Keywords: Transition metal complexes, 2-Methyl benzimidazole, Nicotinic acid hydrazide, Antimicrobial activity.

INTRODUCTION

Benzimidazole is an important pharmacophore in modern drug discovery. Mannich bases of benzimidazole derivatives exhibits diverse pharmacological activities like antimicrobial [1], analgesic [2], antiinflammatory [3], anthelmintic [4], antiviral [5] as well as antitumor [6], etc., The benzimidazole contains a phenyl ring fused with imidazole ring [7]. In addition to their biological importance, benzimidazoles form stable complexes with various transition metals [8]. Transition metal complexes of 2-substituted benzimidazole and benzimidazole based mixed ligands have been reported with mono-, bi-, and tridentate coordination behaviour [9-13]. The continuous increase in bacterial resistance to the existing drugs have been resulted due to wide spread use of antibacterial agents leading to research on new substances possessing antimicrobial activity [14,15]. Several benzimidazoles are commercially available as pharmaceuticals veterinary products and fungicides.

EXPERIMENTAL

All the reagents and solvents were purchased from Sigma-Aldrich and used as received. IR spectra were recorded with KBr pellets using FT-IR Shimadzu instrument. Electronic spectra were recorded by using a Shimadzu-UV-Vis-Spectrophotometer in 10⁻⁵ M solution of the compound in dimethyl formamide (DMF) at 25 °C with 1 cm quartz cell. ¹³C NMR and ¹H NMR were recorded in DMSO-*d*₆ on Bruker NMR spectrometer using TMS as internal reference.

Synthesis of Mannich base (BNH): To the ethanolic solution of nicotinic acid hydrazide (**3**), (6.857 g, 0.05 mol), 2-methyl benzimidazole (**1**), (6.608 g, 0.05 mol) was added and then benzaldehyde (**2**) (5 mL, 0.05 mol). The reaction mixture was then adjusted to pH 3.5 with conc. HCl and refluxed with constant stirring at 60-70 °C for about 6 h. The colourless solid formed was filtered and washed with ethanol. The crude solid obtained was dried and recrystallized using absolute alcohol. The recrystallized product was dried over in vacuum get the quantitative yield.

Synthesis of metal complexes: To a hot magnetically stirred methanolic solution of Mannich bases (0.1 mol), the methanolic solution of metal(II) salt (0.05 mol) was added. The mixture was then refluxed around 2 h. The complexes were precipitated immediately. The precipitated complexes were allowed to stand for an hour, then filtered, washed with methanol then dried and cooled in a desiccator.

RESULTS AND DISCUSSION

The IR spectra of the complexes indicate that ligand behaves as a bidentate and coordinate to metal *via* N-(C-NH). In the ligand, band appearing at 3456 cm⁻¹ due to NH stretching is shifted to lower wave number at 3456-3211 cm⁻¹ in the complexes by confirming the coordination through the nitrogen atom. All the complexes exhibit 695-622 and 548- 466 cm⁻¹ assignable to ν(M-O) and ν(M-N), respectively (Table-1).

Electronic spectra: The electronic spectra of the ligand and its metal complexes were recorded in DMF solution. The

Scheme-I: Synthesis of Mannich base (BNH)

TABLE-1

Compounds	$\nu(\text{NH}) \text{ cm}^{-1}$	$\nu(\text{CH}) \text{ cm}^{-1}$	$\nu(\text{C=O}) \text{ cm}^{-1}$	$\nu(\text{C=N}) \text{ cm}^{-1}$	$\nu(\text{M-O}) \text{ cm}^{-1}$	$\nu(\text{M-N}) \text{ cm}^{-1}$
BNH (Ligand)	3456	3057	1628	1198	—	—
Cu-BNH	3402	3077	1651	1197	654	548
Zn-BNH	3219	3170	1648	1200	694	510
Co-BNH	3211	3103	1648	1199	686	466
Fe-BNH	3418	3062	1598	1195	695	470
Ni-BNH	3248	3189	1676	1121	622	503

electronic spectra of the ligand showed an absorption bands at 324 and 282 nm attributed to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions. The electronic spectra of ligand and its metal complexes were summarized in Table-2.

TABLE-2

Compounds	$\lambda_{\text{max}} \text{ (nm)}$	Transition assignment	Geometry
BNH	282	$\pi \rightarrow \pi^*$	—
	324	$n \rightarrow \pi^*$	—
Fe-BNH	366	$n \rightarrow \pi^*$	Octahedral
	280	$\pi \rightarrow \pi^*$	—
Ni-BNH	325	$n \rightarrow \pi^*$	Octahedral
Co-BNH	311	$n \rightarrow \pi^*$	Octahedral
	273	$\pi \rightarrow \pi^*$	—
Cu-BNH	270	$\pi \rightarrow \pi^*$	Octahedral
Zn-BNH	278	$n \rightarrow \pi^*$	Octahedral

^1H NMR spectra: The ^1H NMR spectra of ligand shows CH_3 proton signal at $\delta = 2.56$ ppm. The NH proton signal was observed as $\delta = 8.127$ ppm for benzimidazole. The phenyl proton signals of phenyl ring was located at $\delta = 7.26$ ppm and the pyridine proton signals of pyridine ring was located at $\delta = 8.59$ ppm.

^{13}C NMR spectra: The ^{13}C NMR shows a peak at 149 ppm is for $-\text{CH}$ carbon, the peaks at 126-134 ppm signifies aromatic carbon. A peak at 164.1 ppm indicates the presence of amide carbon. The proton ^1H NMR and ^{13}C NMR of ligand have confirmed the suggested structure of the ligand.

Antibacterial activity: All the compounds were screened *in vitro* for their antibacterial activity against *Salmonella typhi*, *Staphylococcus aureus* and *Escherichia coli* by well diffusion method. The zone of inhibition values were found out at the end of 24 h at 37°C for the bacterial stains. The antibacterial data (Table-3) suggested that Mannich base derivative of benzimidazole were found to be biologically active. It is observed that growth inhibiting activity of metal complexes of Mannich bases is superior when compared with the ligand.

Conclusion

The ligand (BNH) and its metal complexes have been synthesized and characterized by IR, UV and NMR spectral techniques. It is revealed from the IR studies that the ligand coordinated to metal as a bidentate ligand. The UV spectral studies confirm the octahedral geometry of the complexes (Fig. 1). The ^1H NMR and ^{13}C NMR spectra showed that the number of hydrogen atoms present in the ligand were exacted when compared with the numbers of hydrogen atoms in the

Fig. 1 Suggestive structures of Metal complexes

TABLE-3
ANTI BACTERIAL ACTIVITY OF LIGAND
AND ITS METAL COMPLEXES

Compounds	Conc. ($\mu\text{g mL}^{-1}$)	<i>Escherichia coli</i>	<i>Solmonella typhi</i>	<i>S. aureus</i>
BNH (Ligand)	100	73	63	61
Fe-BNH	100	84	80	64
Ni-BNH	100	70	76	60
Co-BNH	100	81	72	57
Cu-BNH	100	79	77	65
Zn-BNH	100	86	80	79
Standard	100	100	100	100

expected compounds. The antibacterial screening of ligand and its metal complexes showed the excellent activity.

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