

Synthesis, Characterization and Antimicrobial Study of a New Mannich Base, N-(1-Piperidinobenzyl)benzamide and its Transition Metal(II) Complexes

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This paper describes the synthesis of a new type of Mannich base, N-(1-piperidinobenzyl)benzamide (PBB) and its complexation behaviour with Cu(II), Co(II), Ni(II) and Zn(II) ions. The structural features of the complexes are characterized by microanalytical data, IR, UV-Vis, NMR, EPR and TGA techniques. The electrolytic behaviour of the chelates was assessed from their molar conductance data. The monomeric nature of the chelates was confirmed from their magnetic susceptibility values. The X-band EPR spectra of the copper complex in DMSO at 300 and 77 K were recorded and their salient features are reported. The antimicrobial activity of the ligand and its complexes has been extensively studied on microorganisms such as *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* and the fungi *Aspergillus niger* and *Rhizoctonia bataicola* by well-diffusion technique using DMF as solvent. The values of zone of inhibition were found out at 37 °C for a period of 24 h. It has been found that all the complexes have higher activity than the free ligand and the standard.

Key Words: Mannich base, N-[1-Piperidinobenzyl]benzamide, 1,2-Diaminobenzene, Antimicrobial activity.

INTRODUCTION

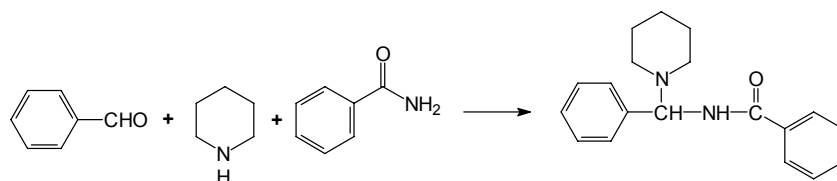
Organic chelating ligands containing amide moiety as a functional group have a strong ability to form metal complexes and exhibit a wide range of biological activities. Literature survey reveals that during the past decades, there has been a great deal of interest in the synthesis and structural elucidation of transition metal complexes containing amide moiety. A number of studies have been done on the Mannich base complexes formed by the condensation of morpholine with different aldehydes^{1,2}. Similarly, a few works^{3,4} have been carried out on the Mannich base complexes formed by the condensation of benzamide with different amines. Studies on metal complexes of the benzaldehyde based Mannich bases have been reported

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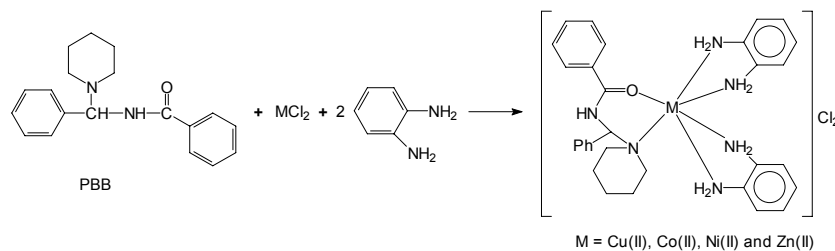
in literature⁵⁻¹². However, there is no report on metal complexes of N-(1-piperidinobenzyl)benzamide. As a part of our continuing efforts to investigate the transition metal(II) complexes using Mannich bases, this work describes the synthesis and characterization of Cu(II), Co(II), Ni(II) and Zn(II) complexes from the Mannich base, N-(1-piperidinobenzyl) benzamide.

EXPERIMENTAL

General procedure for the preparation of PBB: In the preparation of PBB ligand, benzamide (12.1 g, 0.1 mol), piperidine (10 mL, 0.1 mol) and benzaldehyde (10 mL, 0.1 mol) were taken in 1:1:1 mole ratio in ice-cold condition. Benzamide was mixed with piperidine and stirred to get a clear solution. Benzaldehyde was then added in dropwise and stirred in ice-bath. Then the resulting reaction mixture was kept at room temperature for *ca.* 5 d. The solid product formed was filtered, washed with water to remove the unreacted benzamide and piperidine followed by CCl₄ to remove any unreacted benzaldehyde. The product, PBB was then dried and recrystallized in methanol. Yield: 65 %; m.p. 159°C.



Synthesis of metal complexes using PBB: Cu(II), Co(II) Ni(II) and Zn(II) complexes have been synthesised using PBB as ligand. The ligand PBB being insoluble in water, all the complexes were prepared in non-aqueous medium. In a typical procedure PBB was dissolved in chloroform and 1,2-diaminobenzene are mixed with an ethanolic solution of the metal salt, MCl₂ [where M = Ni(II), Cu(II), Co(II) and Zn(II)] in 1:1:1 mole ratio. The reaction mixture was gently warmed on a water-bath for 1 h. The resulting solid complex formed was filtered, washed with distilled water and dried *in vacuo*.



RESULTS AND DISCUSSION

All the complexes are stable at room temperature. They are insoluble in water and sparingly soluble in common organic solvents but soluble in DMSO. The analytical data of the complexes along with some physical properties, the elemental analysis of the products, molar conductance and magnetic susceptibility are listed in Table-1. The high molar conductance values of the complexes reveal their electrolytic nature¹³.

TABLE-1
PHYSICAL CHARACTERIZATION, ANALYTICAL, MOLAR
CONDUCTANCE, MAGNETIC SUSCEPTIBILITY
DATA OF THE COMPLEXES

Complex	Found/(Calcd.) %			m.w.	Yield (%)	λ_m mho	μ_{eff} (BM)
	C	H	N				
PBB	77.52	7.53	9.52	294.4	65.0	–	–
Cu(II)	56.70 (57.70)	5.18 (5.94)	12.19 (13.02)	645.1	55.8	252	1.9
Co(II)	57.19 (58.13)	5.21 (5.88)	12.15 (13.11)	640.49	56.2	267	4.2
Ni(II)	57.21 (58.16)	5.13 (5.98)	12.25 (13.12)	640.25	67.2	257	2.8
Zn(II)	56.30 (57.55)	5.11 (5.92)	12.11 (12.99)	646.9	63.4	300	–

The IR spectra provide valuable information regarding the nature of the functional group attached to the metal atom. In order to study the binding mode of the Mannich base to the metal in the complexes, the IR spectrum of the free ligand was compared with the spectra of the complexes. The ligand PBB shows its characteristic bands at 3366, 1636 and 1121 cm^{-1} which have been assigned to $\nu(\text{NH})$, amide $\nu(\text{C}=\text{O})$ and $\nu(\text{C}-\text{N}-\text{C})$ of piperidine group, respectively¹⁴. In the IR spectra of all the complexes, the $\nu(\text{NH})$ band remained at the same position as in the free ligand, indicating that the secondary nitrogen is not involved in the coordination to the metal ion. In all the complexes, the amide $\nu(\text{C}=\text{O})$ and $\nu(\text{C}-\text{N}-\text{C})$ of piperidine bands displayed substantial negative shifts with fairly low intensity indicating coordination through the oxygen of amide moiety and nitrogen of piperidine entity present in the ligand. The metal complexes showed a hump in 3355-3338, 1623-1627 and 1096-1097 cm^{-1} region, respectively shows that the bands are shifted to lower frequencies characteristics for the amide NH_2 , amide $\text{C}=\text{O}$ and $\text{C}-\text{N}-\text{C}$ of piperidine complexed with metal salts.

The ^1H NMR spectrum of PBB displayed the expected signals. It exhibits a multiplet signal at 7.2-7.7 δ (m, Ar-H), 7.9 δ (CH), 5.8-5.9 δ (d, sec.amide NH), 2.3-2.6 δ (piperidine N-CH₂) and 1.4-1.8 δ (piperidine CH₂). In Zn(II) complex, the doublet of N-H proton is shifted slightly downfield to 6.1-6.3 δ which reveals the coordination of carbonyl oxygen to Zn(II) ion. The signal due to piperidine N-CH₂ protons is also shifted slightly downfield and appeared at 2.5-2.9 δ in those complexes. This is an indication of the coordination of piperidine nitrogen.

The ^{13}C NMR spectra of the ligand and its zinc complex recorded by employing TMS as internal reference at ambient temperature. The number of signals of sharp peaks represents the number of carbons of the compound, which are chemically non-equivalent. The spectra exhibit the resonance of carbonyl carbon at 154 ppm. The chemical shift of aromatic carbons appears at 136, 128, 127 and 123 ppm. The substituted aromatic carbon can be distinguished from other carbons by its decreased peak height. The peak at 136 ppm may be assigned to the substituted carbon in the ring. The methane carbon which is directly bonded to benzene ring exhibits signal at 54 ppm. The peaks at 48, 25 and 24 ppm are assigned to α , β and γ carbons of piperidine ring respectively.

The electronic absorption spectra of the ligand and its copper(II), cobalt(II) and nickel(II) complexes recorded in DMSO solution. The green Cu(II) complex showed a broad band at 15151 cm^{-1} which is assigned to $^2\text{E}_g \rightarrow ^2\text{T}_{2g}$ transition indicating octahedral geometry¹⁵ of the complex. The Co(II) complex exhibits a band at 18867 cm^{-1} , assigned as $^4\text{A}_2 \rightarrow ^4\text{T}_1$ transition which supports octahedral geometry¹⁶ for the complex. The Ni(II) complex showed a bands at 19268 cm^{-1} which is assigned as $^1\text{A}_{1g} \rightarrow ^1\text{A}_{2g}$ transitions, confirming octahedral geometry¹⁷ for the complex. The absence of any band below 10000 cm^{-1} eliminates the possibility of tetrahedral environment in the nickel complex. The above facts are also supported by the magnetic susceptibility data.

The magnetic moment value for Cu(II) complex (1.9 BM) indicates the octahedral arrangement of the ligand around the central metal ion. The four coordinated Co(II) complex shows μ_{eff} value of 4.2 BM which indicates the presence of three unpaired electrons, supporting octahedral structure. The observed 2.8 BM magnetic moment value confirms the octahedral environment for the Ni(II) complex. The Zn(II) complex is also found to be diamagnetic as expected for d^{10} configuration and on the basis of analytical and spectral data six coordinated octahedral geometry is proposed for the Zn(II) complex.

The X-band EPR spectra of the Cu(II) complex, recorded in DMSO at liquid nitrogen temperature and at room temperature. The spectrum of the copper complex at room temperature shows one intense absorption band in the high field and is isotropic due to the tumbling motion of the

molecules. However, this complex at liquid nitrogen temperature shows four well-resolved peaks with low intensities in the low field region and one intense peak in the high field region. The copper complex exhibits the g_{\parallel} value of 2.276 and g_{\perp} value of 2.074. These values indicate that the unpaired electron lies predominantly in the $d_{x^2-y^2}$ orbital¹⁸.

The ligand PBB and its Cu(II), Co(II), Ni(II) and Zn(II) complexes were tested for antibacterial activity. Mueller-Hinton agar was used for testing the susceptibility of microorganisms to antibacterial agents by well diffusion method¹⁹, using DMF as solvent, at a concentration of 0.01 M against Gram positive (*Staphylococcus aureus* and *B. subtilis*) and Gram negative (*Escherichia coli* and *P. auroginosa*) bacteria. Ampicillin was used as the standard for comparing the results (Table-2). Study of anti-fungal activity of the ligand and its complexes has been carried out using the fungi such as *A. niger* and *R. bataicola* by well-diffusion technique using DMF as solvent. For the antifungal activity potatoes dextrose agar (PDA) medium was used as the standard for comparing the results. Amphotericin was used as the standard. The zone of inhibition values were found out at the end of an incubation period of 24 h at 37 °C and the results are presented in Table-3. A comparative study of the ligand and its complexes indicates that the metal complexes are more active than the free ligand and the standard. The increase in antibacterial activity is due to faster diffusion of metal complexes as a whole through the cell membrane or due to the combined activity effect of the metal and ligand²⁰.

TABLE-2
ANTIBACTERIAL ACTIVITIES OF METAL(II) COMPLEXES

Complex	Inhibition zone (mm)			
	<i>S. aureus</i>	<i>E. coli</i>	<i>P. auroginosa</i>	<i>B. subtilis</i>
PBB	11	12	12	10
Cu(II)	15	16	14	15
Co(II)	13	14	13	14
Ni(II)	14	16	15	13
Zn(II)	19	22	18	20
Ampicillin	11	11	11	10

TABLE-3
ANTIFUNGAL ACTIVITY OF METAL(II) COMPLEXES

Complex	Inhibition zone (mm)	
	<i>Aspergillus niger</i>	<i>Rhizoctonia bataicola</i>
PBB	12	14
Cu(II)	15	16
Co(II)	18	17
Ni(II)	16	16
Dextrose agar	10	11

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