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SYNTHESIS, CHARACTERISATION AND ANTIBACTERIAL ACTIVITY OF A NEW MANNICH BASE, N–(1–PIPERIDINOBENZYL) BENZAMIDE AND ITS TRANSITION METAL (II) COMPLEXES

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ABSTRCT

Solid complexes of a new Mannich base, N–(1–piperidinobenzyl) benzamide (PBB) with Cu (II), Co (II), Ni (II) and Zn (II) complexes have been synthesised and characterised by spectral studies, molar conductance, magnetic susceptibilty and elemental analyses. The electrolytic behaviour of the chelates was assessed from ther molar conductance data. The monomeric nature of the chelates was confirmed from their magnetic susceptibility values. The cyclic voltammogram of copper complex in MeCN solution shows quasi–reversible peak. The X–band ESR spectra of the copper complex in DMSO at 300 and 77 K were recorded and their salient features are reported. The antibacterial activity of the complexes have also been studied. Most of the complexes have higher activity than that of the free Mannich base ligand.

Key words : Mannich base, Antibacterial, Cu (II), Co (II), Ni (II), Zn (II)

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[1–3]. 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. Studies of metal complexes of the benzaldehyde based Mannich bases have been reported in literature[4,5]. However, there is no report of any metal complex of N–(1–piperidinobenzyl) benzamide. In continuation of our earlier work[6–8], in the present paper an attempt is made to synthesise N–(1–piperidinobenzyl) benzamide and to study its complexation characteristics with Cu (II), Co (II), Ni (II) and Zn (II) salts. The ligand system coordinates with the metal ion in a bidentate manner through the oxygen atom of the carbonyl group and nitrogen atom of piperidine ring. The proposed structure of the ligand, PBB is given in Figure 1.

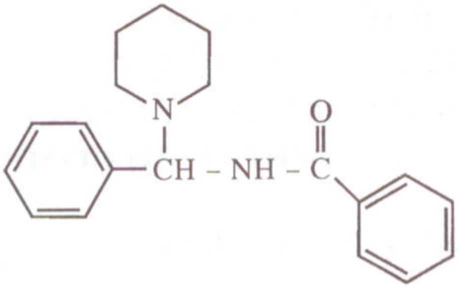


Figure 1. Structure of the Mannich base, PBB

EXPERIMENTAL

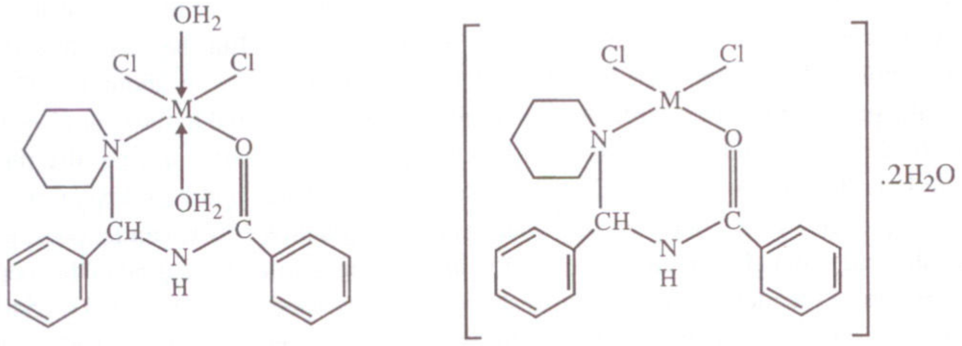
All the chemicals used were of AR grade. Carbon, hydrogen and nitrogen contents were determined at the Regional Sophisticated Instrumentation Centre, Central Drug Research Institute, Lucknow. IR spectra were recorded on a Perkin–Elmer 783 spectrophotometer. KBr disc method was used for recording the IR spectra. UV–vis spectra of the complexes were recorded on Shimadzu 1601 spectrophotometer. The ^{1}H–NMR spectra were recorded at Madurai Kamaraj University, on a Brucker instrument using TMS as internal standard. The molar conductivity of the complex was measured on a Systronic conductivity bridge with a dip type cell using 10^{-3} M solution of complexes in DMSO. Electrochemical measurements were carried out with Electrochemical analyser model BAS–27 Voltammogram. ESR spectra of the copper complex was recorded on a Varian E112 X–band spectrometer at the Regional Sophisticated Instrumentation Centre, Indian Institute of Technology, Mumbai using TCNE as the g–marker. Magnetic susceptibility measurements were carried out using the Gouy balance. Mercury (II) tetrathiocyanatocobaltate (II) was used as calibrant. Muller–Hinton agar was used for testing the susceptibility of microorganisms to antibacterial agents using the well–diffusion technique. Ampicillin was used as the standard.

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 dropwise and stirred in ice–bath. Then the resulting reaction mixture was kept at room temperature for about five days. The solid product formed was filtered, washed with water to remove the unreacted benzamide and piperidine followed by CCl_4 to remove any unreacted benzaldehyde. The product, PBB was then dried and recrystallised in methanol. Yield : 55%; m.p. : 159°C.

Synthesis of metal complexes using PBB : Ni (II), Cu (II), Co (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 mixed with an ethanolic solution of the metal salt, MCl_2 [where M = Ni (II), Cu (II), Co (II) and Zn (II)] in 1:1 mole ratio. The reaction mixture was gently warmed on a water–bath for 1/2 h. The resulting solid complex formed was filtered, washed with water and recrystallised in ethanol and dried *in vacuo*.

RESULTS AND DISCUSSION

All the complexes are coloured and stable at room temperature. They are insoluble in water but soluble in $CHCl_3$, DMF and DMSO. The analytical data of the complexes alongwith some physical properties are summarised in Table 1. An examination of the elemental analysis of the products listed in Table 1 reveals the formation of 1 : 1 (metal : ligand) complexes. The proposed structure of the complexes is given in Figure 2.



M = Cu (II) **M = Co (II), Ni (II) and Zn (II)**

Figure 2. Structure of the complexes

Table 1. Analytical data of the ligand and its complexes

Complex (Colour)	% Analysis, Found (calcd)				Yield %	μ_{eff} (B.M)	λ_m (mho $cm^{-2}mol^{-1}$)
	M	C	H	N			
PBB	–	76.8 (77.5)	7.1 (7.4)	8.9 (9.5)	59	–	–
[$CuCl_2$.PBB.$(H_2O)_2$] (green)	13.4 (13.7)	48.9 (49.1)	5.2 (5.6)	5.8 (6.0)	60	1.9	5.2
[$CoCl_2$.PBB.$(H_2O)_2$] (pink)	12.5 (13.4)	48.0 (50.8)	4.9 (5.4)	5.2 (6.3)	58	4.2	3.4
[$NiCl_2$.PBB]$(H_2O)_2$ (green)	12.1 (12.8)	47.9 (49.8)	5.1 (5.2)	6.7 (6.3)	57	–	2.6
[$ZnCl_2$.PBB] $(H_2O)_2$ (yellow)	14.1 (14.6)	49.4 (50.8)	4.8 (5.3)	5.7 (6.2)	53	–	1.9

The low molar conductance values of the complexes reveal their non–electrolytic nature[9]. The monomeric nature of the chelates was confirmed from their magnetic susceptibility values.

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 3285, 1626 and 1120 cm^{-1} which have been assigned to ν_{NH}, amide $\nu_{C=O}$ and $\nu_{C\text{-}N\text{-}C}$ of piperidine group, respectively[10]. In the IR spectra of all the complexes, the ν_{NH} band remained at the same position as in the free ligand, indicating that the secondory nitrogen is not coordinated. In all the complexes, the amide $\nu_{C=O}$ and $\nu_{C\text{-}N\text{-}C}$ 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 at 3450–3000 cm^{-1} characteristics for coordinated water molecules[11]. However, a band around 880 cm^{-1}, characteristic of coordinated water, is not observed in the IR spectra of Ni (II), Co (II) and Zn (II) complexes. The thermal decomposition studies of Ni (II), Co (II) and Zn (II) complexes show appreciable change at 110°C, when heated. The thermal analytical data of the Co (II) complex shows a 12.7% loss in weight (theor. 13.9%), Ni (II) complex shows a 12.1% loss in weight (theor. 13.3%) and Zn (II) complex shows a 13.7% loss in weight (theor. 14.6%) equivalent to the elimination of two lattice water molecules[12] in these complexes. But the thermal analysis of Cu (II) complex shows that there is a loss of two water molecules at about 170°C, which suggests the presence of two coordinated water molecules coordinated to the central metal ion, which is further confirmed from its characteristic IR spectrum. It clearly indicates that the water molecule is lattice held in Ni (II), Co (II) and Zn (II) complexes and coordinated in Cu (II) complex. According to Nikolaev *et al.*[13] water eliminating below 150°C can be considered as lattice water and water eliminating above 150°C may be due to its coordination to the metal ion. The IR spectra of the metal complexes also show some new bands in the region 530–540 cm^{-1} and 440–450 cm^{-1}, which are probably due to the formation of M–O and M–N bonds, respectively[14,15]. In all the complexes, an additional medium band, found at 325 cm^{-1} is assigned to M–Cl stretching vibration[16,17]

The ^{1}H–NMR spectra of PBB displayed the expected signals. PBB exhibits a multiplet signal at 7.2–7.5 δ (m, Ar–H), 7.7–7.8 δ (d, CH), 5.8–5.9 δ (d, sec. amide NH), 2.5–2.6 δ (piperidine N–CH_2), and 1.5 δ (piperidine CH_2). In Ni (II) and Zn (II) complexes, the doublet of N–H proton is shifted slightly downfield to 5.9–6.0 δ, which reveals the coordination of carbonyl oxygen to Ni (II) and Zn (II) ion. The signal due to piperidine N–CH_2 protons is also shifted slightly downfield and appeared at 2.7 δ in those complexes. This is an indication of the coordination of piperidine nitrogen. This observation is consistent with our earlier report[6]. Thus, ^{1}H–NMR and IR results confirm the bidendate nature of PBB ligand.

The ^{13}C–NMR spectra were recorded by employing TMS as internal reference and $CDCl_3$ as solvent at ambient temperature. The number of signals of sharp peaks represent the number of carbons of the compound, which are chemically non–equivalent. The spectra exhibit the resonance of carbonyl carbon at 170 ppm. The chemical shift of aromatic carbons appear at 139 128, 127 and 126 ppm. The substituted aromatic carbon can be distinguished from other carbons by its decreased peak hight. The peak at 139 ppm may be assigned to the substituted carbon in the ring. The methine carbon, which is directly bonded to benzene ring, exhibits, a signal at 63 ppm. The peaks at 49, 25 and 24 ppm are assigned to α, β and λ carbons of piperidine ring, respectively.

The FAB mass spectra of the ligand and its Cu(II) complex were compared as regarding their stoichiometric composition. The Mannich base shows a molecular ion peak at m/z=294. The molecular ion peak for the Cu (II) complex was observed at m/z = 464, which confirms its stoichiometry as $[CuCl_2.PBB.(H_2O)_2]$.

The electronic absorption spectra of the ligand and its copper (II), cobalt (II), nickel (II) and zinc (II) complexes were recorded in DMSO solution. The green Cu (II) complex showed a broad band at 11961 cm^{-1}, which is assigned to $^2E_g \rightarrow {}^2T_{2g}$ transition indicating octahedral geometry[18] of the complex. The Co (II) complex exhibits a band at 15576 cm^{-1}, assigned as $^4A_2 \rightarrow {}^4T_1$ transition, which supports tetrahedral geometry[19] for the complex. The Ni (II) complex showed bands at 14556 and 20190 cm^{-1}, which are assigned as $^1A_{1g} \rightarrow {}^1B_{1g}$ and $^1A_{1g} \rightarrow$ 1A2g transitions confirming a square planar geometry[20] for the complex. The absence of any band below 10000 cm^{-1} eliminates the possibility of a tetrahedral environment in this complex.

The magnetic moment value for Cu (II) complex (1.91 B.M.) 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 B.M., which indicates the presence of three unpaired electrons, supporting tetrahedral structure. The observed zero magnetic moment value confirms the square planar environment for the Ni (II) complex, in conformity with the fact that all known square planar complexes of Ni (II) are diamagnetic. The Zn (II) complex is also found to be diamagnetic as expected for d^{10} configuration.

The ESR spectrum of copper complex provides informations which are important in studying the metal ion environment. The X–band ESR 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 $g_{||}$ value of 2.276 and $g_{\perp}$ value of 2.074. These values indicate that the ground state[21] of Cu (II) is predominantly $d_{x^2-y^2}$. The observed $g_{||}$ value is less than 2.3 for the complex indicating its covalent nature[22]. The spin–orbit coupling constant, λ value (– 498 cm^{-1}) calculated by using the relations, $g_{av} = 1/3[g_{||}+2g_{\perp}]$ and $g_{av} = 2(1-2\lambda/10Dq)$, is less than the free Cu (II) ion (– 832 cm^{-1}) which also supports covalent character of M–L bond in the complex. The G values of 3.80 indicates negligible exchange interaction of Cu–Cu in the complex. The in–plane σ–bond strength represented by molecular orbital coefficient, α^2 (covalent in–plane σ–bonding) and β^2 (covalent in–plane π–bonding) were calculated using the following equations :

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

$$\beta^2 = (-g_{\parallel} - 2.0023)\, E / -8\lambda\alpha^2$$

If the value of $\alpha^2 = 0.5$, it indicates complete covalent bonding, while the value of $\alpha^2 = 1.0$ suggests complete ionic bonding. The observed value of α^2 (0.82) of the complex[23] is less than unity, which indicates that the complex has some covalent character in the ligand environment.

The cyclic voltammogram of the Cu (II) complex (0.01 M) in MeCN solution in 0.8 to –1.2V potential range. It shows a well defined redox process corresponding to the anodic peak at $Ep_a = 0.48$ V and the associated cathodic peak at $Ep_c = 0.25$ V. This couple is found to be quasi–reversible and the ratio of anodic to cathodic peak currents ($Ip_a/Ip_c = 0.84$) which suggests that the process is simple one electron transfer, quasi–reversible process[24,25].

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 method[26], using DMF as solvent, at a concentration of 100μg/10μL against Gram positive (*Staphylococcus aureus* and *B. subtilis*) and Gram negative (*Escherichia coli* and *P. auroginosa*) bacteria. 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 2. A comparative study of the ligand and its complexes indicates that the metal complexes are more active than the free ligand and the standard.

Table 2. Antibacterial activity of metal complexes of PBB

No.	Compound	Inhibition zone (mm) at concentration (100 μg/10 μL)			
		S. aureus	*B. subtilis*	*P. auroginosa*	*E. coli*
1.	PBB	11	10	12	13
2.	$[CuCl_2.PBB(H_2O)_2]$	21	19	22	25
3.	$[CoCl_2.PBB](H_2O)_2$	19	17	20	21
4.	$[NiCl_2.PBB](H_2O)_2$	18	17	19	19
5.	$[ZnCl_2.PBB](H_2O)_2$	15	13	20	22
6.	Ampicillin	7	8	10	10

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REFERENCES

1. P. S. Desai and K. R. Desai, J. Indian Chem. Soc., **70**, 177 (1993).
2. R. C. Paul, P. Kapila Bedi and K. K. Vasisht, J. Indian. Chem. Soc., **53**, 768 (1976).
3. V. H. Shah, H. H. Patel and A. R. Parikh, J. Indian Chem. Soc., **59**, 678 (1982).
4. A. N. M. Kasim, D. Venkappayya and G. V. Prabhu, J. Indian Chem. Soc., **76**, 67 (1999).
5. D. Venkappayya and G. V. Prabhu, J. Indian Chem. Soc., **72**, 511 (1995).
6. N. Raman and S. Ravichandran, Asian J. Chem., **14**, 1551 (2002).
7. N. Raman and S. Ravichandran, Asian J. Chem., **14**, 1766 (2002).
8. N. Raman and S. Ravichandran, Asian J. Chem., **15**, 255 (2003).
9. W. J. Geary, Coord. Chem. Rev. **7**, 81 (1971).
10. D. H. K. Kerridge, Chem. Soc. Rev., **17**, 181 (1988).
11. K. Nakamoto, "Infrared and Raman Spectra of Inorganic and Coordination Compounds", 3rd Ed., John Wiley, New York, (1977), p. 296.
12. A. N. Verma, S. B. Gholse and S. P. Sangal, J. Indian Chem. Soc., **69**, 331 (1992).
13. A. V. Nikolaev, V. A. Logvinenko and L. I. Myachina "Thermal Analysis", Academic, New York, **2**, (1969) p. 779.
14. K. Nakamoto, "Spectroscopy and Structure of Metal Chelate Compounds", John Wiley, New York, (1988), p. 214.
15. K. K. Narang and A. Agarwal, Inorg. Chim. Acta., **9**, 137 (1974).
16. D. M. Adams, "Metal–Ligand and Related Vibrations", St. Martin's Press, New York, (1968).
17. J. R. Ferraro, "Low Frequency Vibrations of Inorganic and Coordination Compounds", Plenum, New York, (1971), p. 187.
18. A. B. P. Lever, "Inorganic Electronic Spectroscopy", 2nd Ed., Elsevier, Amsterdam, (1968), p. 257.
19. B. N. Figgis and R. S. Nyholm, J. Chem. Soc., 338 (1959).
20. H. G. Gray and Ballhausen, J. Am. Chem. Soc., **85**, 260 (1963).
21. R. M. Silverstein, G. C. Bassler and T. C. Movril, "Spectroscopic Identification of Organic Compounds", 4th Ed., Wiley, New York, (1981), p. 112.
22. B. J. Hathway and D. E. Billing, Coord. Chem. Rev., **5**, 143 (1961).
23. D. Kevelson and R. J. Niedman, Chem. Phys., **35**, 149 (1961).

24. Z. Shirin and R. M. Mukherjee, Polyhedron, **11**, 2625 (1992).
25. A. Shyamala and A. R. Chakravarty, Polyhedron, **12**, 1545 (1993).
26. C. H. Collin and P. M. Lyne, "Microbiological Methods", 3rd Ed., Butterworth, London, (1970).

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