SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL ACTIVITY OF MANNICH BASE METAL COMPLEXES

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Abstract:

*Neutral complexes of Cu(II), Co(II), Ni(II) and Zn(II) have been synthesized from a new Mannich base, N-[1-morpholino(4-diphenylaminobenzyl)]acetamide (**MDABB**) derived by the condensation of morpholine, 4-diphenylaminobenzaldehyde and benzamide. 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 behavior 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. The electrochemical behavior, the anodic and cathodic potential and the number of electron transfer were calculated using cyclic voltammogram. The cyclic voltammogram of copper complex in MeCN solution at 298 K was studied. The X-band EPR spectra of copper complex in DMSO at 300 K and 77 K were recorded and their salient features are discussed. 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 by well-diffusion technique using DMSO as solvent. The values of zone of inhibition were found out at 37^0C for a period of 24 h. It has been found that all the complexes have higher activity than the free ligand and the standard.*

Introduction:

From the survey of existing literature, it appears that metal complexes of Mannich bases have played a vital role in the development of coordination chemistry. It is well known from the literature that the compounds containing amide moiety have a strong ability to form metal complexes and exhibit a wide range of biological activities[1-10]. Earlier work reported that some drugs showed increased activity when administered as metal chelates rather than as organic compounds. Keeping the above facts in mind and as part of our continuing efforts to investigate transition metal(II) complexes using Mannich bases[11-15], in this paper we describe the synthesis, characterization, redox and antimicrobial studies of Cu(II), Co(II), Ni(II) and Zn(II) complexes containing bidentate Mannich base derived by condensing morpholine, 4-diphenylaminobenzaldehyde and benzamide. The ligand system coordinates to the

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metal ion in a bidentate manner through the amide carbonyl oxygen and the nitrogen atom of morpholine group. The proposed structure of the complexes is shown below:
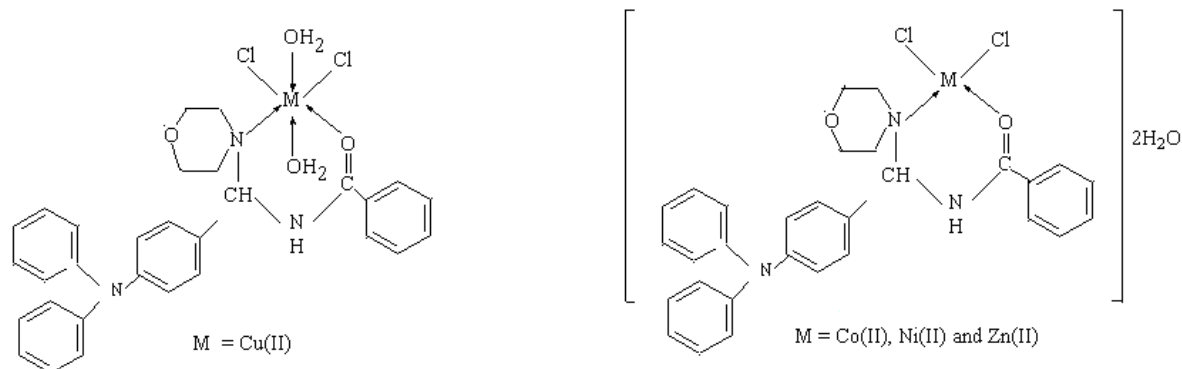
Synthesis of Mannich Base:

The Mannich base, was synthesised by the condensation of an ethanolic solution of morpholine, 4-diphenylaminobenzaldehyde and benzamide were taken in 1:1:1 mole ratio. 4-diphenylaminobenzaldehyde (2.73 g, 0.1 mol) was mixed with morpholine (10 mL, 0.1 mol) and stirred to get a clear solution. Benzamide (1.21 g, 0.1 mol) was then added in small quantities to the mixture and stirred under ice-bath condition. At first, a yellow sticky mass appeared. It was kept aside with the mother liquor open to atmosphere for 5 days. The yellow solid formed was separated by filtration, washed with distilled water, carbon tetrachloride and recrystallised from ethanol.Yield: 62 %; m.p:188 ^{0}C.

Synthesis of Complexes:

An ethanolic solution of Mannich base (5 mM) was mixed with metal (II) chloride (5 mM) in ethanol (20 mL) solution keeping ligand-metal ratio 1:1. The reaction mixture was then warmed for 1 h on a water bath till the complex precipitated out. The solid complex obtained was removed by filtration, successively washed with water, dried at room temperature and recrystallised from ethanol.

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 (Table 1). The low molar conductance values of the complexes (3.4-8.2 mhocm^{2}mol^{-1}) support their neutral nature[16].

Table 1: Physical characteristics and analytical data of the complexes

Compound	Analysis, found (calcd) (%)				Yield (%)	μ_{eff} (B.M)
	M	C	H	N		
MDABB	----	72.76 (77.74)	6.31 (6.26)	10.29 (9.07)	62	----
Cu complex	10.87 (9.96)	51.86 (52.68)	5.23 (5.22)	7.23 (6.64)	54	1.9
Co complex	10.66 (10.34)	51.12 (52.88)	5.53 (5.51)	7.12 (6.92)	58	3.9

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Ni complex	10.72	51.42	5.34	7.54	60	----
	(10.44)	(52.81)	(5.39)	(6.84)		
Zn complex	10.27	51.12	4.45	6.78	58	----
	(10.72)	(52.68)	(5.89)	(7.62)		

MDABB = Mannich base ligand

The FAB mass spectra of the Mannich base ligand and its copper complex are used to compare their stoichiometric composition. The Mannich base ligand shows a molecular ion peak M+ at m/z =463. The molecular ion peak for [CuCl$_2$.MDABB.(H$_2$O)$_2$] complex was observed at m/z = 632, which confirms the stoichiometry of metal chelates as [ML].

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, N-[1-morpholino (4-diphenylaminobenzyl)]benzamide and its metal complexes were recorded in KBr medium. Upon complexation with metal salts, the amide $\nu_{C=O}$ and ν_{C-N-C} of morpholine bands at 1640 cm^{-1} and 1160 cm^{-1} are shifted to lower frequencies *viz.*, 1620-1630 cm^{-1} and 1120-1130 cm^{-1} respectively. The lowering in frequencies observed in all the complexes shows the involvement of carbonyl oxygen and tertiary morpholine nitrogen atom in coordination to the metal ion. Several evidences[17-21] on the coordination of substituted amides through carbonyl oxygen have been reported.

The IR spectra of the metal complexes also show some new bands in the region 530-540 cm^{-1} and 440-450 cm^{-1} due to M-O and M-N bonds respectively which further confirm that the ligand is bidentate in nature. Nakamota[22] has reported assignments of M-O and M-N in the similar range. In all the complexes, an additional medium band found at 320 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 of MDABB shows a broad band at 14,970 cm^{-1} assignable to $^2E_g \rightarrow {}^2T_{2g}$ transition, suggests an octahedral geometry[23] 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 of MDABB exhibits a band with maxima at 15,580 cm^{-1} which is assigned to $^4A_2 \rightarrow {}^4T_1(P)$ for tetrahedral geometry[24] for the complex. The Ni(II) complex of MDABB showed band at 16,580 cm^{-1} which is assigned as $^1A_{1g} \rightarrow {}^1A_{2g}$ transition confirming a square-planar geometry[25,26] 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 of Cu (II) complex is 1.9 B.M. which suggests an octahedral geometry [27] 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[28]. 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 found to be diamagnetic as expected for d^{10} configuration.

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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.
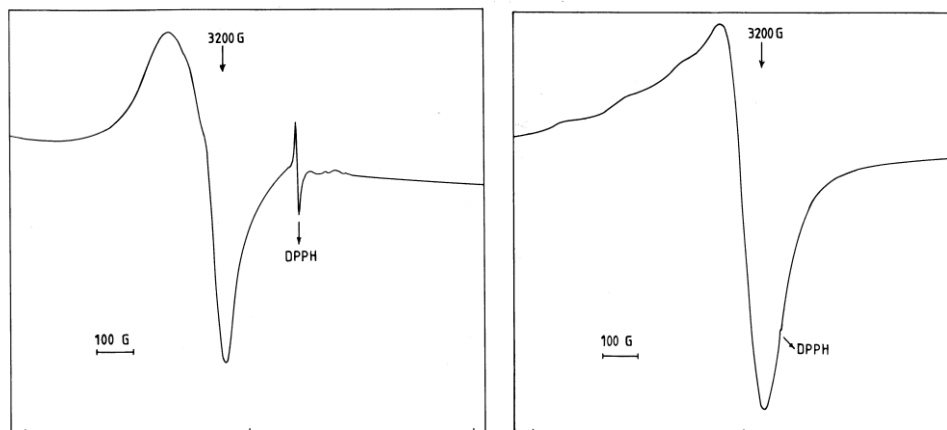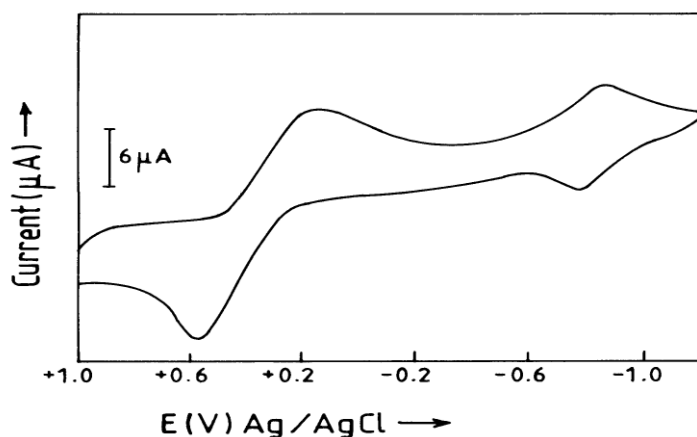

Figure 1: The EPR spectrum of the copper complex in DMSO at 300 K (a) and 77 K (b)

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 2.32 and $g_\perp$ value of 2.17. These values indicate that the Cu (II) lies predominantly in the $d_{x^2-y^2}$ orbital[29]. The spin-orbit coupling constant, λ value (-498 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 (-838 cm^{-1}) which also supports covalent character[30] of M-L bond in the complex. The G value of 3.92 indicates negligible exchange interaction of Cu-Cu in the complex. The covalency parameter α^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 α^2 (0.87) of the complex is less than unity which indicates that the complex has some covalent character in the ligand environment[31]. The cyclic voltammogram of the Cu(II) complex (0.01 M) in MeCN solution in the absence of molecular oxygen at room temperature in 1.0 to –1.2 V potential range indicates quasi-reversible one-electron process[32]. A noteworthy feature has been observed in the cyclic voltammogram of Cu(II) complex (Figure 2).

Figure 2: Cyclic voltammogram of copper complex in MeCN

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During the forward scan, it shows two cathodic reduction peaks, one at +0.24 V and another at –0.86 V which are attributed to reduction of Cu(II) → Cu(I) and Cu(I) → Cu(0) respectively. During the reverse scan, it shows two anodic oxidation peaks, one at –0.76 V and another at +0.55 V which are attributed to oxidation of Cu(0) → Cu(I) and Cu(I) → Cu(II) respectively.

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[33] 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 $35\,^0$C. During this period, the test solution diffused and the growth of the inoculated microorganisms was affected. It has been observed from the result (Table 2) 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.

Table 2: Antibacterial activity of the Mannich base ligand and its metal complexes

No.	Compound	Inhibition Zone (mm)			
		S.aureus	*E.coli*	*P.auroginosa*	*B.subtilis*
1.	Ligand	12	13	12	11
2.	$[CuCl_2.MDABB.(H_2O)_2]$	19	21	20	21
3.	$[CoCl_2.MDABB] (H_2O)_2$	18	22	19	17
4.	$[NiCl_2.MDABB] (H_2O)_2$	17	20	22	18
5.	$[ZnCl_2.MDABB] (H_2O)_2$	19	21	22	20
6.	Ampicillin	10	11	11	10

MDABB = Mannich base ligand

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