



Synthesis of Cobalt (II), Nickel(II), Copper(II) and Zinc(II) Complexes of N-(1-Morpholinosalicylyl)benzohydrazide and their Antimicrobial Activities

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Abstract

A new Mannich base, N-(1-Morpholinosalicylyl)benzohydrazide (MSB), formed by the condensation of morpholine, benzohydrazide and salicylaldehyde and its Co(II), Ni(II), Cu(II) and Zn(II) complexes have been synthesised. Their structures have been elucidated on the basis of analytical, magnetic, electrical conductivity and spectral methods. On the basis of colour, magnetic moments and spectral data, the geometries of Co(II), Ni(II), Cu(II) and Zn(II) complexes have been assigned. The electrochemical property of the ligand and its complexes in acetonitrile solution was studied by cyclic voltammetry. The X-band ESR spectra of the Cu(II) complex in DMSO at 300 and 77 K were recorded and their salient features are reported. Antibacterial activities of the ligand and its complexes were tested against some selected bacteria. The ligand and all the complexes showed antimicrobial activities.

Keywords: Antimicrobial activities; Mannich base; Metal complexes.

1. INTRODUCTION

Metal complexes of Mannich base have been studied (Shanmugapriya *et al.* 2012; Haidu, 1990; Cleare, 1974; Singh *et al.* 1985) extensively in recent years due to selectivity and sensitivity of the ligand towards various metal ions. From the survey of existing literature, it appears that metal complexes of Mannich base has played a vital role in the development of coordination chemistry (Desai *et al.* 1993; Kasim *et al.* 1999; Jameel *et al.* 2006). A search through the literature reveals that no work has been done on the condensation

of morpholine, salicylaldehyde and benzohydrazide. It is well known from the literature that benzohydrazide compounds containing the amide moiety have a strong ability to form metal complexes. In the present work, a new Mannich base derived from the condensation of morpholine, salicylaldehyde and benzohydrazide and its metal complexes with Cu(II), Co(II), Ni(II) and Zn(II) were synthesized and characterized using different physicochemical techniques. The proposed structure of the synthesized Mannich base is given in the Figure 1. The ligand and its metal complexes have biological activities against various microbes such as *Bacillus subtilis*, *staphylococcus aureus*, *pseudomonas aeruginosa*, *Escherichia coli*, *candida albicans* and *Aspergillus niger*.

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2. MATERIALS & METHODS

2.1 Chemicals

Reagents such as morpholine, salicylaldehyde, benzohydrazide, various Metal (II) chlorides were of Merck products. The melting points of all compounds were determined in open capillaries and are uncorrected. Purity of the compound was checked by TLC using Silica gel G coated glass plates with chloroform and ethyl acetate (1:1) as eluent and iodine vapour as visualizing agent and confirmed by retention factor (R_f) value. The IR spectra were recorded in KBr pellets using FT-IR shimadzu IR affinity 1. The ^1H NMR and ^{13}C NMR Spectra were recorded on Bruker AMX400 NMR spectrophotometer using TMS as internal standard and chemical shifts were expressed in ppm. The elemental analysis were performed on Perkin Elmer Series C, H, N & S analyser 2000. Mass Spectra were recorded on a JEOL-8X 102. UV-visible spectra of the complexes were recorded on perkin Elmer Lambda EZ201 spectrophotometer in DMF solution. Molar conductivity was determined using Systronic Conductivity Bridge with a dip type cell using 10^{-3} M solution of complexes in DMSO. Cyclic voltammogram of the complexes were recorded in acetonitrile solution at 300 K using a three-electrode cell comprising reference

Ag/AgCl, auxiliary Pt and working glass carbon electrodes. Magnetic susceptibility measurements of the complexes were done using a Gouy balance. The ESR spectral studies were made in JEOL-DPS-2000.

2.1.1 Synthesis of Mannich base

In a typical procedure (Raman *et al.* 2003), an ethanolic solution of salicylaldehyde, morpholine and benzohydrazide were taken in 1:1:1 mole ratio. Morpholine 4.4 mL (0.05 mol), benzohydrazide 6.8 g (0.05 mol) and 6.1 mL of salicylaldehyde (0.05 mol) were mixed and continuously stirred for 3 hours under ice-cold condition. Compound formed was filtered and then recrystallized from methanol. Purity of the compound was checked with TLC. The melting point of the recrystallized sample was determined in an open capillary tube and was uncorrected. Yield: 68%, m.p. 187°C .

2.1.1.1 Synthesis of metal complexes

The Mannich base (dissolved in CHCl_3) and the metal chlorides in ethanol were mixed in 1:1 molar ratio. The reaction mixture was gently warmed on a water-bath for one hour. The resulting solution was concentrated to a third of its volume and cooled to 0°C

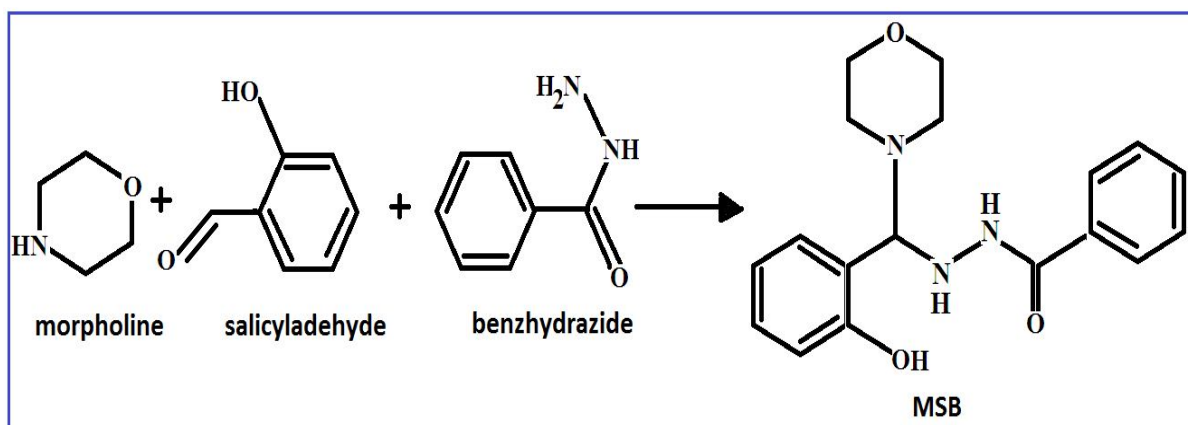


Fig. 1: Formation of Mannich base

Table 1. Physical Characterization, Analytical, molar conductance, Magnetic susceptibility data

Compound	Colour	Found/(Calculated)					Mol. Wt.	Yield %	λ_m^{-1} $\text{cm}^2 \text{Mol}^{-1}$	μ_{eff} BM
		M%	C%	H%	N%	Cl %				
$\text{C}_{18}\text{H}_{21}\text{N}_3\text{O}_3$	Colourless	-	66.04(66.12)	6.24(6.35)	12.38(12.45)	-	327	68	-	-
Cu(II) complex	Green	12.70(12.82)	43.54(43.65)	5.04(5.13)	8.46(8.57)	14.11(14.24)	496	61	4	1.6
Co(II) complex	Pink	12.93(12.98)	47.36(47.43)	4.60(4.72)	9.21(9.32)	15.35(15.43)	456	60	1.8	3.9
Ni(II) complex	Pale green	12.74(12.82)	47.47(47.53)	4.61(4.76)	9.23(9.32)	15.38(15.45)	455	59	2.7	-
Zn(II) complex	Colourless	14.06(14.12)	46.75(46.83)	4.54(4.67)	9.09(9.12)	15.15(15.54)	462	60	1.6	-

for 6 hours. The precipitated complexes were filtered, washed with ethanol and dried in vacuo. The proposed structures of the complexes are given in Fig. 2.

3. ANTIMICROBIAL ACTIVITY

The invitro biological screening effects of the synthesized Mannich base and its Cu(II), Co(II), Ni(II) and Zn(II) complexes have been studied for their antibacterial and antifungal activities by disc diffusion method at concentration of 10 $\mu\text{g}/\text{ml}$ in DMSO using both gram positive *S.aureus*, *B.Subtilis*, gram negative *E.Coli*, *P.Aeruginosa* and antifungal activity against *C.albicans* and *A.niger*. The zone of inhibition was measured in mm and the activity was compared with Ciprofloxacin 1g/disc for bacteria, Nystatin 10g / disc for fungi as standard drugs. The compounds possess appreciable antibacterial activities against selected organisms but lesser when compared with their standards. The zone of inhibition values are presented in Table 2.

4. RESULT & DISCUSSION

The elemental analyses show 1:1 (Metal:Ligand) stoichiometry for all the complexes. The analytical data of the ligand and the complexes are given

in Table 1. They correspond well with the general formula ML , where $\text{M} = \text{Cu(II), Ni(II), Co(II) and Zn(II)}$; $\text{L} = (\text{C}_{18}\text{H}_{21}\text{N}_3\text{O}_3)$. The low conductance of the chelates supports the non-electrolytic nature of the metal complexes.

4.1 Infrared spectra

The IR spectra of the Mannich base ligand (MSB) and its complexes are recorded. The IR spectra of the complexes were compared with those of the free ligand in order to determine the coordination sites that may be involved in coordination. In MSB, the infrared bands observed at 3056, 1612 and 1205 cm^{-1} have been assigned to $\nu_{\text{N-H}}$ amide, $\nu_{\text{C=O}}$ and $\nu_{\text{C-N-C}}$ of morpholine group respectively. In IR spectra of all the complexes, the $\nu_{\text{N-H}}$ band remained at the same position as in the free ligand, indicating that the secondary nitrogen is not coordinated. A band due to $\nu_{\text{C-N-C}}$ stretching vibration of the morpholine ring appearing at 1205 cm^{-1} in the metal complex remained at the same position as in the free ligand indicating the nitrogen atom from the morpholine ring is not coordinated. A band due to $\nu_{\text{N-H}}$ adjacent to methyne carbon have stretching vibration appearing at 1148 cm^{-1} in the ligand is shifted to 1126 cm^{-1} in the metal complex, suggesting the coordination of the nitrogen atom adjacent to methyne

carbon to central metal ion. It is observed that the band appearing at 1612 cm^{-1} due to $\nu_{C=O}$ in the ligand is shifted to 1604 cm^{-1} in the metal complex indicating the involvement of carbonyl oxygen in coordination.. The new bands at 496 and 472 cm^{-1} in the spectra of the metal complexes were assigned to ν_{M-O} and ν_{M-N} stretching vibrations (Lever *et al.* 1971; Narng *et al.* 1974). The presence of coordinated water molecules in Cu(II) complex is determined by the appearance of bands at $3200-3400\text{ cm}^{-1}$ and a peak at 863 cm^{-1} is assignable to the OH stretching and rocking mode of coordinated water molecules. The rocking vibration of water is not observed in the IR spectra of Ni(II), Co(II) and Zn(II) complexes. This is confirmed that water molecule is not coordinated in these complexes.

4.1.1 Magnetic moment and UV-Visible spectra

Electronic spectra and magnetic measurements were recorded in order to obtain information about the geometry of the complexes. The μ_{eff} (1.6 BM) value of the Cu(II) represents distorted octahedral geometry of the ligand around the central metal ion. The four coordinated Co(II) complex shows μ_{eff} value of 3.9 BM which indicates the presence of three unpaired electrons and it supports the tetrahedral geometry. The observed zero magnetic moment value confirms the square planar environment for the Ni(II). The Zn(II) complex is found to be diamagnetic as expected for d^{10} configuration.

The electronic spectra of the ligand and its complexes were recorded in DMSO solution. The Cu(II) ion with d^9 configuration in a complex can be either octahedral or tetrahedral or rarely square planar. The octahedral coordinated Cu(II) ion has the ground state ${}^2E_g(t_{2g})^6(e_g)^3$. The only excited state should then be ${}^2T_{2g}(t_{2g})^5(e_g)^4$, the energy difference being $10Dq$. The Cu(II) complex under the present study exhibits a broad band in the region 13790 cm^{-1} . The broadness of the band may be due to Jahn-Teller distortion (Reddy *et al.* 2006). This observation indicate that the complex has distorted octahedral structure. Co(II) complex display a band at

15834 cm^{-1} which is assigned to ${}^4A_2 \rightarrow {}^4T_1$ for tetrahedral geometry (Figgis *et al.* 1959). The Ni(II) complex is diamagnetic suggesting a square planar geometry (Albert cotton *et al.* 1999). It showed a broad band at 16611 cm^{-1} which is assigned to ${}^1A_{1g} \rightarrow {}^1B_{1g}$. The spectrum of this complex is consistent with this assignment. No transitions were observed in the visible region for the Zn(II) complex consistent with the d^{10} configuration of the Zn^{2+} ion. This complex is also found to be diamagnetic as expected for d^{10} configuration.

4.1.1.1 ESR, 1H -NMR spectra and ${}^{13}C$ -NMR spectra

The EPR spectrum of the Cu(II) complex shows $g_{||} > g_{\perp} > 2.0023$ and a g value within the range of $2.08-4.49$ is consistent with the $d_{x^2-y^2}$ ground state in an distorted octahedral geometry. Evidence for the bonding mode of the ligand is also provided by the 1H -NMR spectra of the Mannich base and the diamagnetic Zn(II) complex, which were recorded in $CDCl_3$. The 1H -NMR spectrum of the MSB displayed the following signals: a multiplet at 7.6δ (Ar-H), 7.9δ (d, H, NH), 7.3δ (q, H, NH), 2.2δ (d, H, CH), 2.5δ (morpholine N- CH_2), 3.4δ (morpholine O- CH_2) and a multiplet at 6.9δ (Ar-H). The peak at 12.1 ppm is attributed to the phenolic $-OH$ group present in salicylaldehyde. The presence of this peak noted for Zn(II) complex, confirms that the $-OH$ proton is free from complexation. In Zn(II) complex, the doublet of the N-H proton shifted slightly down field to 8.4δ , reveals the coordination of carbonyl oxygen to Zn(II) ion. The signal due to ν_{N-H} adjacent to methyne carbon is also slightly shifted downfield and appeared at 7.5δ in the complex. This is an indication of the coordination of the nitrogen atom adjacent to methyne carbon to central metal ion. Therefore, it is concluded that the Mannich base behaves as a neutral bidentate ligand in all the complexes.

The ${}^{13}C$ -NMR spectrum indicates the amide C=O carbon appears at 157 ppm . The signal observed between $132 - 127\text{ ppm}$ is due to aromatic CH-carbon and 119 ppm for N-CH carbon. The signals due to the O- $(CH_2)_2$ and N- $(CH_2)_2$ carbons of Morpholine are obtained at 40 and 38 ppm respectively.

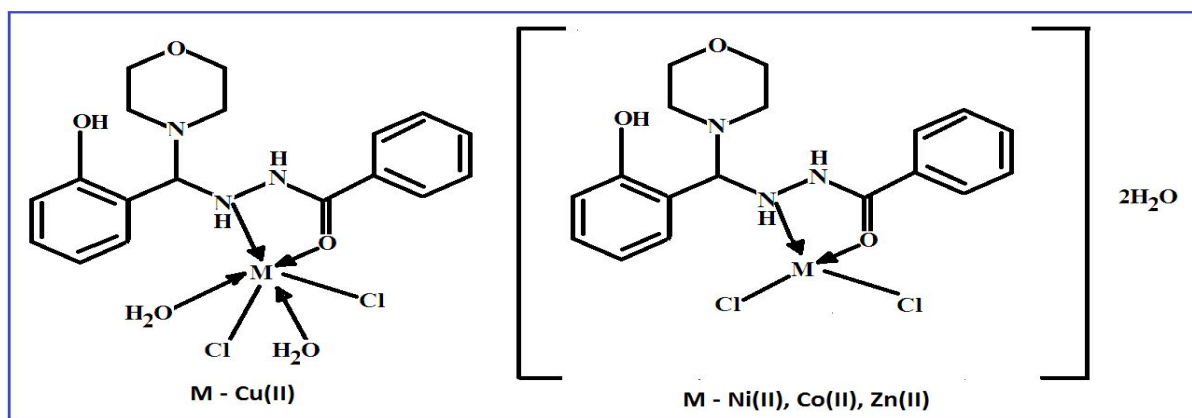


Fig. 2: Proposed structure of metal complexes

Table 2. Antimicrobial Activities of Metal Complexes of MSB

Compound	Diameter Zone of Inhibition (mm)					
	Gram Positive		Gram Negative		Fungi	
	<i>S.aureus</i>	<i>B.Subtilis</i>	<i>E.Coli</i>	<i>P.aeruginosa</i>	<i>C.albicans</i>	<i>A.niger</i>
MSB	20	18	16	18	18	16
Cu(II)	18	17	17	16	17	14
Co(II)	19	16	19	18	19	19
Ni(II)	20	22	20	16	20	20
Zn(II)	21	20	21	17	22	18
Standard	27*	30*	26*	28*	30**	31**
DMSO (Solvent)	NI	NI	NI	NI	NI	NI

NI= No Inhibition * Ciprofloxacin ** Nystatin

4.1.1.1.1 Electrochemical Study

The cyclic voltammetry is the most versatile electro analytical technique for the study of electro active species. The cyclic voltammogram of the copper complex is recorded over a potential range -0.4V to -1.1V shows two quasi-reversible peaks, one at cathodic direction and another at anodic direction. The quasi-reversible reduction peak at -0.92V due to the formation of Cu(II)/Cu(I) while the other quasi-reversible oxidation peak at -0.56V is due to formation of Cu(I)/Cu(II).

4.1.1.1.1 Antimicrobial study

For *in vitro* antimicrobial activity, the synthesized compounds were tested against the bacteria *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* and fungi *Candida albicans* and *Aspergillus niger* (Zotta, 1985). The minimum inhibitory concentration (MIC) values of the investigated compounds with the standard drugs are presented in Table 2. Antimicrobial activity of metal chelates can be explained on the basis of chelation

theory (Srivastava, 1944). On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of charge of the metal ion with donor groups. Further, it increases the delocalization of π -electrons over the whole chelate ring and enhances the presentation of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganism. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organism.

5. CONCLUSION

A new mannich base, N-(1-Morpholinosalicylyl)benzohydrazide (MSB) and its metal complexes have been synthesized and characterized by elemental analysis and spectral studies.

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