

Research Article

Coordination Modes of a New Mannich Base *N*-[Phenyl(pyrrolidin-1-yl)methyl]acetamide and its Metal Complexes with Zn^{II}, Cd^{II} and Hg^{II} Ions: Synthesis, Spectroscopic and Antimicrobial Studies

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Abstract

Zinc(II), cadmium(II) and mercury(II) complexes having the general formula MLX.H₂O and MLX.2H₂O (M=Zn^{II}, Cd^{II} and Hg^{II}, L= ligand and X = 2Cl⁻ and SO₄²⁻) have been prepared with *N*-[Phenyl(pyrrolidin-1-yl)methyl]acetamide(PBA). The complexes have been characterized by elemental analysis, molar conductance values and various spectral studies.

The biological activities of the ligand and its complexes have been screened *in vitro* against some bacteria and pathogenic fungi to study their capacity to inhibit their growth.

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Introduction

Synthetic heterocyclic complexes of transition metals have attracted much attention as promising compounds in coordination chemistry [1]. Transition metal complexes of Mannich base ligands are also widely studied due to their potential therapeutic uses[2] because these species display a variety of reactivity mode. They also possess catalytic and biological activity [3]. They have been investigated for their antitumor, anti-HIV and antifungal activities [4]. They find use in health and skin care products and in paint manufacturing [5].

In this paper, we report the results of the structure, functions, and relationship under lying metal ion binding by the bidentate and tridentate nitrogen and oxygen donor ligand with Zn^{II}, Cd^{II} and Hg^{II}.

Experimental

All the chemicals and solvents were of AR grade. Metal salts were purchased from Merck and Loba chemie Mumbai, India. Ethanol, methanol and the solvents were dried by the standard procedures [6]. Metal contents were estimated by usual procedure after digesting them with con. HNO₃ and the results were further confirmed by atomic absorption spectroscopy. Sulphate was estimated gravimetrically as BaSO₄ and chlorides were estimated volumetrically by Volhard's method[6]. The elemental analyses were performed using Carlo Erba

1108 elemental analyzer at RSIC, CDRI, Lucknow. IR spectroscopy analyses were recorded on Spectrum-one Perkin Elmer FT-IR spectrometer by using KBr pellets. The UV visible spectra were recorded on a Shimadzu UV spectrometer in the wavelength range 200-800 nm. The ¹H and ¹³C NMR of the ligand and its d¹⁰ metal complexes were recorded on a Bruker instrument and on a JEOL-GSX 400 spectrometer. The FAB mass recorded for the ligand was carried out using a JEOL -GC mate mass spectrometer. The conductance data were obtained in ~10⁻³ M DMF solutions of the complexes at room temperature using a Systronics direct reading digital conductivity meter-304 with dip type conductivity cell. The thermal analyses were recorded on universal V4.3A TA instrument. The antimicrobial activity was determined with the disc diffusion method.

Synthesis and characterization of the ligand

The ligand *N*-[Phenyl(pyrrolidin-1-yl)methyl]acetamide (PBA) was prepared by Mannich condensation[7] reaction between acetamide, benzaldehyde and pyrrolidine in 1:1:1 mol ratio. Acetamide(5.90 g, 0.1 mol) was dissolved in minimum quantity of ethanol and mixed with benzaldehyde(10 mL, 0.1 mol) and pyrrolidine (7.1 mL, 0.1 mol) with constant stirring in an ice bath. After 12 days, a yellow solid obtained was washed with water and with acetone. The compound was dried in an air oven and recrystallised from ethanol. It was insoluble in water and soluble in organic solvents.

Molecular formula: $C_{13}H_{18}N_2O$, Yield: 93%, MP: 120-124°C, Mol.wt: 218, FT-IR KBr in cm^{-1} : 3306(NH), 1646(C=O), 3053, 3035(ν_{CH} aromatic), 2971, 2876(ν_{CH} alicyclic), 2821(ν_{CH} aliphatic), 1149(C-N-C), 1601(ν_{C-C} , ν_{C-N}), 1531(δ_{NH} secondary amide), 1029(δ_{CH} i.p.b benzene), 986 (δ_{CH} + o.p.b of pyrrolidine), 879, 851(δ_{NH} wagging and twisting), 732(δ_{CH} o.p.b benzene), 704(o.p.b ring C=C). 1H NMR (300MHz, DMSO- d_6): δ 8.42(s, NH), 5.86 & 5.83 (d, CH), 7.39 - 7.26(m, CH benzene ring) 2.51(s, $N(CH_2)_2$ at α , α'), 1.65(s, $(CH_2)_2$ at β , β'). ^{13}C NMR (300MHz, DMSO- d_6): 169.62 (s, C=O), δ 141.62-127.68(m, 6C phenyl ring), 49.23(s, pyrrolidine $N(CH_2)_2$ at α , α'), 23.59(s, pyrrolidine $(CH_2)_2$ at β , β'). UV-Vis(DMF): 287($n \rightarrow \pi^*$), 226($\pi \rightarrow \pi^*$). FABMS: $m/z = 218$ ($C_{13}H_{18}N_2O$), $m/z = 127$ ($C_6H_{11}N_2O^+$), $m/z = 99$ ($C_5H_{10}N_2^+$), $m/z = 70$ ($C_4H_8N^+$).

Calculated: C 71.60%, H 8.26% and N 12.84%. Found: C 71.53%, H 8.31% and N 12.97%.

Synthesis of the metal complexes

The ligand was dissolved in ethanol and warmed and mixed with metal salts in methanol solution at hot condition with constant stirring in 1:2 mol ratio. The insoluble precipitate settled down, was filtered, washed first with ethanol and then with methanol to remove the unreacted ligand and metal, dried in an air oven at 80°C.

Antibacterial and antifungal studies

The ligand as well as the metal complexes were tested *in vitro* against the bacterial species viz *E.coli*, *P.aeruginosa*, *S.typhi*, *B.subtilis*, *S.pyogenes*, *S.aureus* and the fungal species *A.niger* and *A.flavus* by disc diffusion method[8] using agar nutrient as medium and gentamycin as control. The paper disc containing the compound was placed on the surface of the nutrient agar plate, previously spread with sterilized culture of microorganism. After incubating this, at 37°C for 24 hrs, the diameter of inhibition zone around the paper disc was measured.

Results and Discussion

To find out the stoichiometry[9] of the complexes, the percentage of the metal ions, anions and CHN were determined(Table 1). The molar conductance values " Λ_M " suggest that, all the complexes are non-electrolytes. The CHN analyses are also in good agreement with the calculated values.

In the IR spectra of all the PBA complexes(Table 2), the stretching frequencies of C=O and C-N-C bonds are found lowered, indicating that both carbonyl oxygen and CNC nitrogen atoms are coordinated to the metal ions. So the ligand acts as ON donor[10]. But in Zn(II) sulphato complex, in addition to

the C=O and C-N-C bonds the amido NH bond was also shifted to lower frequency, which indicates the tridentate bonding nature of the ligand. The IR spectrum of the sulphato complexes shows the presence of coordinated sulphato group[10]. The bands at the ranges of 1150, 1000 and 900 cm^{-1} are due to 'SO' stretching mode, ν_3 of sulphato group and the triply degenerate 'OSO' bending mode, ν_4 and splits up into its components at the ranges of 650, 600 and 580 cm^{-1} in the complex. The frequencies 750(ν_1) and 500(ν_2) cm^{-1} are also observed. These frequencies due to coordinated sulphato group are associated with bidentate chelation[11]. The bands around 3300-3500, 1600-1650, 800-880, 600-690 and 460-530 cm^{-1} found in the spectra of all the complexes of PBA indicate the presence of coordinated water molecule[12]. The Far-IR absorption bands observed around 591&522, 467, 400&360 and 240 cm^{-1} are assignable to the M-O, M-N and M-Cl stretching modes respectively for Hg^{II} chloro complex.

The important resonance signals obtained in the 1H NMR spectra[13] of the Zn^{II} , Cd^{II} & Hg^{II} chloro and Hg^{II} sulphato complexes were recorded in DMSO- d_6 . The signal due to amide NH is shifted to upfield when compared with that of the free ligand, which occurs at δ 8.42 ppm. This may be due to the modification of the electron density upon coordination of the carbonyl O and the deshielding zone developed around these protons. This suggests that the amide N is not involved in coordination. But in Zn(II) sulphato complex the amide NH is shifted to lower frequency indicates the coordination with metal centers. The complexes experiences a downfield shift in the cases of $-CH_3$ and $N(CH_2)_2$ protons which are directly attached to CO and amine N. This can be explained on the basis of the reduction in electron density around the proton, which leads to deshielding. The proton signal moves to a higher frequency. The signals due to benzene protons of the ligand are not affected due to complexation[14]. The new peaks are formed at the range of δ 3.35 ppm indicating the presence of water molecules in all the complexes (Table 3). These results support the coordination suggested by IR data.

The thermograms of the Zn^{II} , Cd^{II} and Hg^{II} sulphates and Hg^{II} chloro complexes show three stage decomposition. All the above complexes do not show weight loss below 120°C, indicating the absence of lattice filled water in the metal complexes[15]. The first stage decomposition is obtained in the temperature range 140 - 210°C. The % weight loss in this range corresponds to the loss of coordinated water molecules[16]. The second stage decomposition is obtained in the temperature range 210 - 400°C. The % weight loss in this range corresponds to % weight loss of Mannich base ligand. The third stage decomposition range is obtained in the temperature range 400 - 900°C. The % weight loss in this range corresponds to % weight loss of metal oxide residue.

Table 1 Analytical and Conductance Data for Zn^{II}, Cd^{II} and Hg^{II} Complexes of PBA

Complex	% C	% H	% N	%Metal	%Anion	Λ_M
	Obs. (Cal.)	Obs. (Cal.)	Obs. (Cal.)	Obs. (Cal.)	Obs. (Cal.)	$\text{ohm}^{-1}\text{cm}^2$ mol^{-1}
ZnSO ₄ .PBA.H ₂ O	30.12 (29.97)	2.91 (3.44)	4.80 (5.34)	12.92 (12.48)	17.83 (18.32)	6.99
CdSO ₄ .PBA.2H ₂ O	34.00 (33.77)	4.25 (3.90)	5.62 (6.06)	24.48 (24.33)	20.17 (20.78)	25.68
HgCl ₂ .PBA.2H ₂ O	29.91 (29.66)	3.32 (3.42)	5.84 (5.32)	37.86 (38.13)	13.55 (13.48)	20.00
HgSO ₄ .PBA.2H ₂ O	29.02 (28.31)	3.50 (3.27)	4.37 (5.08)	36.05 (36.40)	18.00 (17.42)	11.55

Table 2 Important IR Absorption Bands (cm⁻¹) of PBA and Zn^{II}, Cd^{II} and Hg^{II} Complexes

Compound	ν_{NH}	$\nu_{\text{C=O}}$	ν_{CNC}	ν_3	ν_4	ν_1	ν_2
PBA	3306	1646	1149	-	-	-	-
ZnSO ₄ .PBA.H ₂ O	3233	1616	1103	1151, 1010, 984	631, 611, 576	872	463
CdSO ₄ .PBA.2H ₂ O	3408	1622	1108	1108, 992, 894	656, 617, 591	860	521
HgCl ₂ .PBA.2H ₂ O	3424	1620	1040	-	-	-	-
HgSO ₄ .PBA.2H ₂ O	3526	1614	1112	1112, 1026, 1020	620, 604	820	465

Table 3 ¹H NMR Resonance Signals (δ ppm) for PBA and Zn^{II}, Cd^{II} and Hg^{II} Complexes

Compound	Amide - NH	Methyl -CH ₃	Methylene -N(CH ₂) ₂	Methine - CH	Water
PBA	8.42	1.89	2.51	6.69	-
ZnSO ₄ .PBA.H ₂ O	-	2.50	2.52	-	3.35
CdSO ₄ .PBA.2H ₂ O	-	2.50	2.52	-	3.35
HgCl ₂ .PBA.2H ₂ O	8.04	2.50	3.76	7.00	3.33
HgSO ₄ .PBA.2H ₂ O	8.04	2.64	3.77	6.88	3.35

Based on the above observations, the tentative structures for the ligand and its complexes are depicted in **Figures 1- 4**.

The antimicrobial property of the ligand was compared with that of the complexes. The Zn(II) complex shows good activity against the strains of bacteria and fungi undertaken for study, when compared to the ligand and other metal complexes. The zones of inhibition based upon zone size around the discs were measured. The measured zone of inhibition against the growth of various microorganisms is listed in **Table 4 & 5**. The increased activity of the metal complexes can also be explained on the basis of chelation theory[17]. Chelation reduces the polarity of the zinc ion mainly

because of the partial sharing of its positive charge with the donor groups and possibly the π -electron delocalization within the whole chelate ring system thus formed during coordination. This process of chelation thus increases the lipophilic nature of the zinc ion, which in turn favors its permeation through the lipid layer of the membrane. This in turn is responsible for increasing the hydrophobic character and liposolubility of the molecule in crossing cell membrane of the microorganism. Hence this property enhances the biological utilization ratio and activity of the testing drug/compound. The enhanced activity of the complexes may also be explained on the basis of their solubility, fineness of the particles, size of the metal ion and the presence of bulkier organic moieties [18].

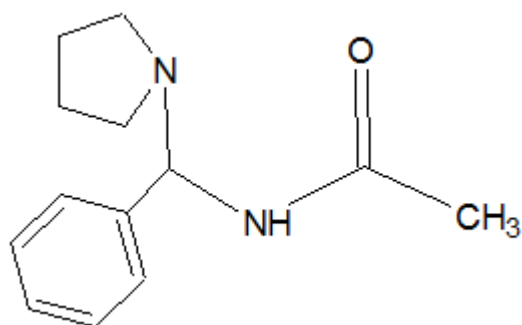


Figure 1 PBA

(Tentative structure proposed for N-[Phenyl(pyrrolidin-1-yl)methyl]acetamide)

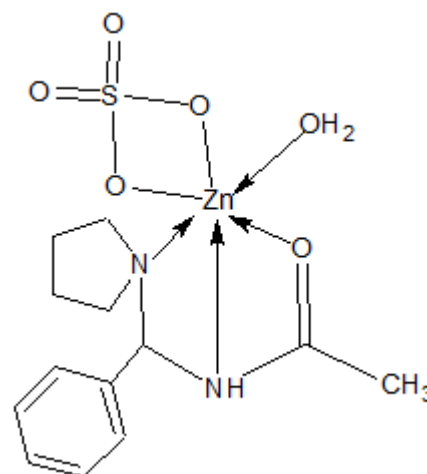


Figure 3 ZnSO₄.PBA.H₂O

(Tentative structure proposed for Zn sulphato complex)

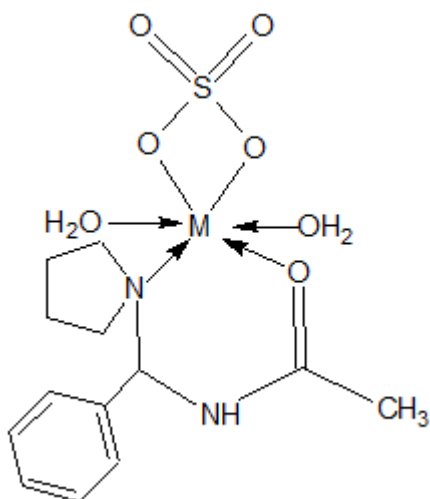


Figure 2 M.SO₄.PBA.2H₂O (M = Cd and Hg)

(Tentative structure proposed for Cd and Hg sulphato complex)

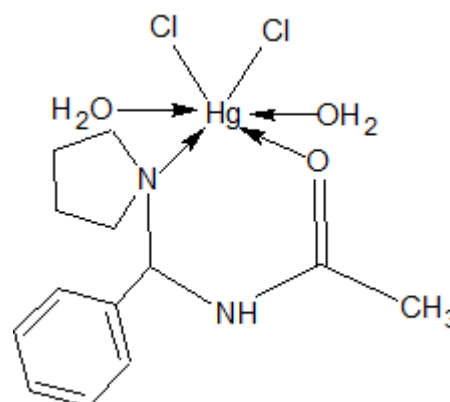


Figure 4 HgCl₂.PBA.2H₂O

(Tentative structure proposed for Hg chloro complex)

Table 4 Antibacterial Activity of Ligand and its Complexes

Compound	Escherichia coli			Pseudomonas aeruginosa			Salmonella typhi			Bacillus subtilis			Streptococcus pyogenes			Staphylococcus aureus		
	10	20	30	10	20	30	10	20	30	10	20	30	10	20	30	10	20	30
Conc.(µg/disc)	10	20	30	10	20	30	10	20	30	10	20	30	10	20	30	10	20	30
Control	09	11	14	08	10	13	08	09	12	09	11	12	08	11	13	08	09	11
PBA	12	16	21	14	16	20	11	17	23	13	15	19	10	15	22	13	17	20
ZnSO ₄ .PBA.H ₂ O	27	32	46	23	29	40	26	32	45	19	27	39	21	26	37	20	31	43
CdSO ₄ .PBA.2H ₂ O	18	25	31	14	20	28	18	24	36	15	21	23	14	22	31	15	18	25

Table 5 Antifungal Activity of Ligand and its Complexes

Compound	A. niger			A. flavus		
Conc. (µg/disc)	10	20	30	10	20	30
Control	08	09	12	05	08	10
PBA	11	14	17	13	18	21
ZnSO ₄ .PBA.H ₂ O	23	31	40	25	34	47
CdSO ₄ .PBA.2H ₂ O	18	26	32	18	23	28

Conclusion

The elemental analysis, IR & ¹H NMR spectral observations and thermal analysis suggest the octahedral geometry for the Cd(II) sulphato, Hg(II) chloro and sulphato complexes. Zn(II) sulphato complex exhibit tetrahedral geometry. The Mannich base shows some antimicrobial activity to certain extent but their complexes exhibit comparatively greater amount of activity against the microorganisms.

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