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Study on the Synthesis, Characterization and Antimicrobial Activity of the New Mannich Base Benzimidazolyl Phenyl Methyl Acetamide and its Metal Complexes

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ABSTRACT

Abstract: In this paper, we report the synthesis of a new Mannich base derived from acetamide and its transition metal complexes. We synthesized the base by reacting acetamide with benzaldehyde and benzimidazole. The so formed base is complexed with transition metals. The structure of the synthesized compounds is characterized by UV, IR, and 1H NMR spectroscopic techniques. The antibacterial activity of the ligand and the complexes were examined using different bacteria's.

1. INTRODUCTION

Mannich base complexes are important and popular area of research due to their amicable synthesis, adaptability, and wide range of applications. From the survey of existing literature, it appears that metal complexes of Mannich bases are playing a vital role in the development of coordination chemistry [1-3]. Many potent antibacterial and antifungal compounds synthesized by the condensation of aldehyde, amine and amide have been reported. Organic chelating ligands containing amide moiety as a functional group have a strong ability to form metal complexes and exhibit a diverse range of biological activities [4-7]. Literature studies revealed 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 [8]. Mannich bases are known to possess potent activities like antifungal [9, 10], anticonvulsant [11], anthelmintic [12], antitubercular [13,14], analgesic [15], anti-HIV [16], antimalarial [17], antipsychotic [18], antiviral [19] activities and so on. Mannich bases and their derivatives are intermediates for the synthesis of bioactive molecules [20, 23].

In the present work, Mannich base was derived from the condensation of benzaldehyde, benzimidazole and acetamide, and made complexation with CuII), Co(II) and Ni(II) ions. The ligand and the complexes were characterized using different physicochemical techniques. The ligand and its metal complexes were tested for their antimicrobial activity against various bacterial species by disc diffusion method.

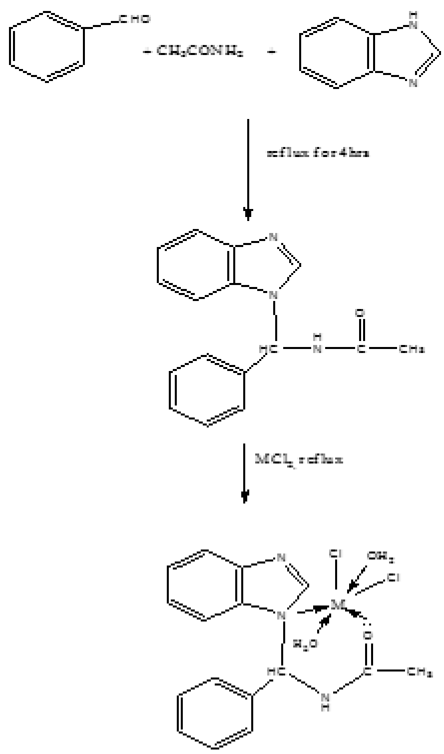
2. MATERIALS & METHODS

2.1. General

Reagents such as benzaldehyde, acetamide and benzimidazole were of sigma-Aldrich products and were used as such. The melting point of all the synthesized compounds was determined in open capillaries and is uncorrected. The UV-Vis spectra were recorded in DMSO solvent on Shimadzu UV mini-1240 spectrophotometer, IR spectra were recorded on Agilent FT-IR spectrophotometer using KBr pellets and ^{1}H NMR spectra were recorded with Bruker AMX400 NMR spectrophotometer using DMSO solvent.

2.2 Synthesis of the Ligand Benzimidazolyl phenyl methyl acetamide (BIPMA)

0.05 mol of benzimidazole and 0.05 mol of benzaldehyde are dissolved in 50mL of ethanol and taken in a 100mL Round Bottom Flask (RBF). Then 0.05 mol of the acetamide dissolved in 20 mL ethanol added in small aliquots to the reaction mixture kept in ice bath and the stirring was continued for about 4 hrs and kept in refrigerator for overnight. On the next day, the contents of the mixture were refluxed for 3-5 hr and kept in refrigerator again for overnight. The solvent was recovered from the mixture by distillation. Mannich base separates out as colorless precipitate. It is filtered and washed with hot water, recrystallized in alcohol and dried in air-oven at 60°C.The scheme of the reaction is given below.



Where M – Cu(II), Co(II) or Ni(II)

Scheme 1: Synthesis of the ligand and the metal complexes

2.3 Synthesis of the complexes

Hot ethanolic solution of the ligand (1 equivalent) was slowly mixed with hot ethanolic solution of metal chloride (1 equivalent) under reflux condition with constant stirring. The mixture was refluxed for 1-2 hr and after that, it was cooled and kept in refrigerator for few hours. The colored solid complexes were separated out in each case, it was filtered washed with alcohol and finally dried in air oven.

Table 1: Physical data of the ligand and the complexes

Compound	Yield (%)	Colour	Mp (°C)
BIPMA-Ligand	70	Colorless	247
BIPMA -Co	72	Pale pink	234
BIPMA -Ni	68	Pale green	230
BIPMA -Cu	74	Pale blue	256

2.4 Antibacterial activity

For the antibacterial study, nutrient agar was used as the medium. The ligand, as well as the complexes, were screened for antibacterial activity against certain pathogenic bacteria by disc diffusion method at concentration of 10µg / ml in DMSO using gram positive *Bascillus subtilis, Staphylococcus aureus,* and gram negative *Proteus vulgaris, Klebsiella pneumoniae* The paper disc containing the compound (10, 20 and 30 µg/disc) was placed on the surface of the nutrient agar plate previously spread with 0.1 mL of sterilized culture of microorganism. After incubating this at 37ºC for 24 hrs, the diameter of inhibition zone around the paper disc was measured.

The zone of inhibition was measured in mm and the activity was compared with Gentamycin in 1 µg / disc A comparison of the diameters of inhibition zones of the compounds investigated shows that Cu (II) complex exhibit highest antibacterial activity against all the bacterial species studied. The results are tabulated in Table.2.

Table 2: Antibacterial activity

Sr. No.	Bacteria	Standard Antibiotic Disc (Gentamycin)	Zone of inhibition mm in diameter (10 μg/disc)			
			BIPMA -L	BIPMA-Co	BIPMA-Ni	BIPMA-Cu
1	*Staphalyococcus aureas*	20	13	16	15	18
2	*Bascillu susbtilis*	18	14	13	12	15
3	*Proteus vulgaris*	24	15	17	14	19
4	*Klesiella pneumoniae*	14	11	10	09	12

3. RESULTS AND DISCUSSION

3.1 UV-Visible spectra

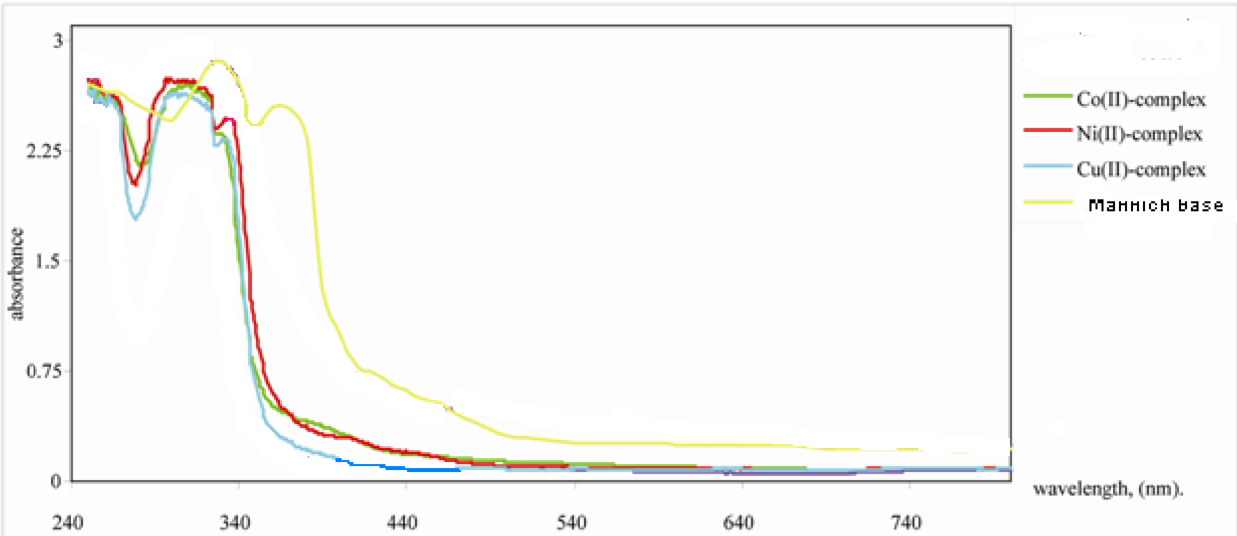


Fig.1. UV Spectra of the ligand and metal complexes

The UV-Visible spectra of the complexes were recorded in the range of 200-1100 nm. The UV spectrum mostly showed two intense maxima bands around 47530cm^{-1} and 29900cm^{-1} which belong to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions respectively. The Cu (II) complex under present study exhibit a broadband in the region 26710cm^{-1} due to transition between $^2E_g \rightarrow {}^2T_{2g}$ which indicated the distorted octahedral geometry. The Ni (II) complex showed broad signals at 26260 cm^{-1} and 28545 cm^{-1}which is assigned to $^3A_{2g} \rightarrow {}^3T_{1g}$ and $^3A_{2g} \rightarrow {}^3T_{2g}$ transitions respectively which further confirms its octahedral geometry. The position of bands observed for Co (II) complex also showing that it is also having the octahedral geometry.

3.2 IR Spectra

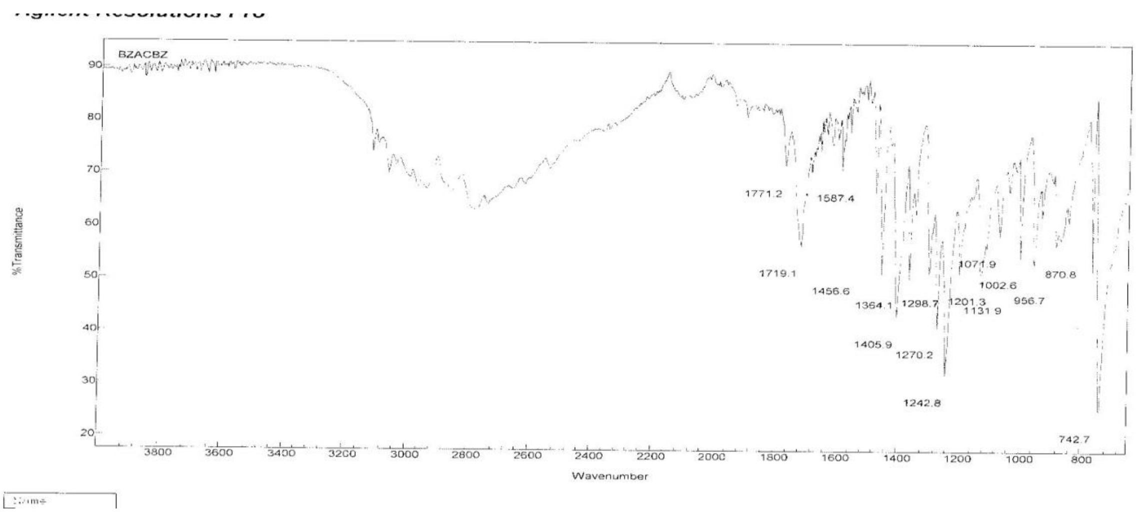


Fig 2. IR Spectra of the ligand

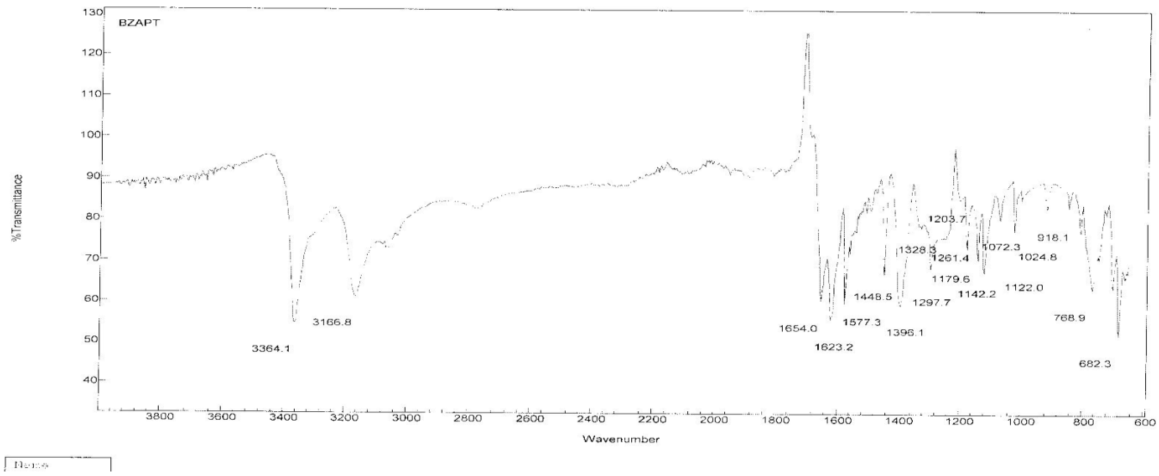


Fig 3.IR Spectra of the metal complex

Table 3: IR Spectral data of the ligand and the complexes

Compound	Vibrational frequency of various functional groups (in cm-1)				
	-OH	-C=O	CNC	M-O	M-N
BIPMA - Ligand	--	1719	1131	----	----
BIPMA-Co	3363	1654	1121	767	662
BIPMA-Ni	3364	1654	1122	766	662
BIPMA-Cu	3366	1655	1115	752	667

The important observation is the presence of an intense band at ~ 1719 cm^{-1} which is due to νC=O carbonyl group. The most notable change in the IR spectra is the disappearance of the amide – NH stretching vibration and appearance of an intense band at 1131 cm^{-1} due to νC-N-C stretching which is formed due to condensation between aldehyde, amide and the amine moieties. These results confirm the formation of the Mannich base. In all the complexes, band due to νC=O and νC-N shifted towards lower frequency clearly indicating the nitrogen and carbonyl oxygen are involved in coordination with metal ions. Further, the appearance of new bands around 760cm^{-1} corresponding to M-O bond and a signal around 660 cm^{-1} corresponding to M-Nbond confirms the formation of the metal complex.

3.3 ^{1}H NMR Spectra

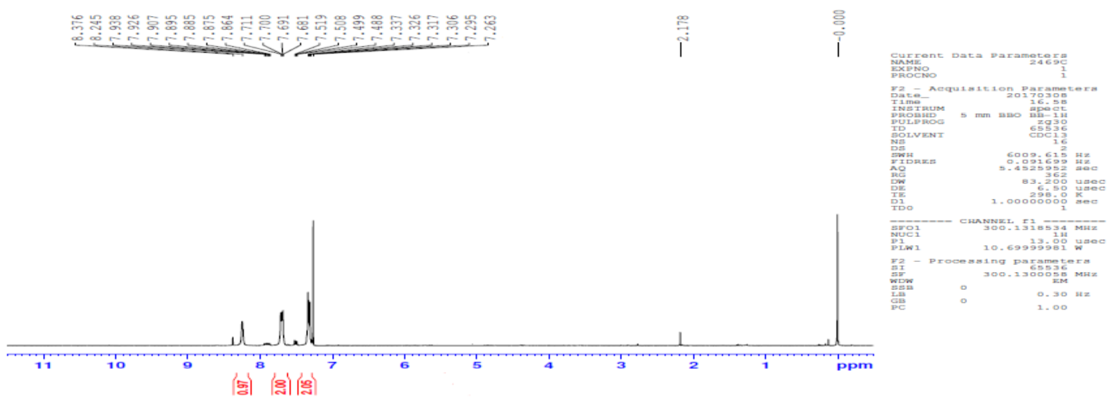


Fig 4. ^{1}H NMR spectra of the ligand

The ^{1}H NMR spectra of the Mannich base under study exhibit a multiplet around 7.2 ppm observed aromatic hydrogens. The appearance of peak at 2.1 ppm indicates the methine hydrogen attached to the nitrogen. The signal at 8.3 ppm corresponds to the amido proton after deprotonation. Further, the formation of the ligand is ascertained by the disappearance of a signal at ~6.5 ppm corresponding to the –NH proton of secondary amine as it was eliminated in the Mannich reaction.

3.4 Antimicrobial activity

The synthesized compounds were screened for antibacterial activity against certain pathogenic bacteria by disc diffusion method at concentration of 10µg / ml in DMSO using gram positive *Bacillus subtilis, Staphylococcus aureus,* and gram negative *Proteus vulgaris, Klebsiella pneumoniae*. The zone of inhibition was measured in mm and the activity was compared with Gentamycin in 1 µg / disc. The results showed that the chelating tends to makes the ligand act as more potent bactericidal agents, thus destroying more bacteria than the free ligand.

4. CONCLUSION

A new Mannich base ligand has been synthesised and made complexation with transition metals. All the compounds were characterized by physicochemical and spectroscopic methods.It has been observed that the ligand behaves as a bidentate chelating agent through the N and O donor sites and the spectroscopic data is in support of our proposed structure. The cobalt and nickel complexes were of octahedral geometry whereas the copper complex exhibits distorted octahedral geometry. The antimicrobial property of the ligand and the complexes were studied and found that complexes possess better antibacterial activity than that of the free ligand.

5. ACKNOWLEDGEMENT

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