

Synthesis, spectral and biological behaviour of bivalent transition metal complex of tridentate (NNO donor) Schiff base ligand

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ABSTRACT

Complex of 2-Aminobenzimidazole-salicylaldehyde(L) with chloride of manganese(II) was synthesized. The molar ratio metal:ligand in the reaction of the complex formation was 1:2. It should be noticed that the reaction of the metal salt yielded bis (ligand) complex of the general formula $[M(L)_2] \cdot 2H_2O$ ($M = Mn^{II}$). The complex was characterized by elemental analysis, molar conductivity measurements, magnetic susceptibility measurements, Infra-Red, electronic spectra and mass spectral studies. The complex behaves as non-electrolyte and has octahedral configuration around the metal ion. In the complex, ligand act as tridentate (NNO donor) coordinating by participation of the imidazole nitrogen of the benzimidazole ring, nitrogen of the azomethine group and oxygen of the deprotonated hydroxyl group. Both Schiff base and its metal complex have been screened *in vitro* for their antibacterial activity against two gram positive *B. subtilis* and *S. aureus* and two gram negative *E. coli* and *K. pneumoniae* bacterial strains by agar well-diffusion method.

Keywords: 2-Aminobenzimidazole, complex, manganese(II), spectroscopic studies, antibacterial activity.

1. INTRODUCTION

Benzimidazole and its derivatives play an important role in analysis and in several biological reactions. Benzimidazole derivatives exhibit antibacterial, antihelmintic and insecticidal activities^[1-3]. Transition metal complexes containing benzimidazole are widely used as catalysts for hydrogenation, hydroformylation, oxidation and other reactions^[4-6].

A wide variety of benzimidazole derivatives have been described for their chemotherapeutic importance. These compounds have shown biological activity against parasites and bacteria. Some of them are known to possess antibacterial, antiviral, anti-inflammatory, antihypertensive, arteriosclerosis and fungicidal activities. Various benzimidazoles are effective inhibitors for the growth of lactobacilli, vaccinia virus, influenza virus and HIV-virus^[7-13]. Benzimidazole and its derivatives act as bacteriostats or bactericides, anticarcinogens etc^[14,15].

Several thousands of analogs of imidazole and benzimidazole have been synthesized and screened for pharmacological activity. Sanja O.

Podunavac and coworkers have reported the synthesis and antimicrobial activity of 2-Aminobenzimidazole with Cu(II), Co(II) and Ni(II)^[16]. Moreover, Schiff bases possess anticancer activity in animal screening, since the -N=CH group is a structural modification of the azomethine linkage^[17]. The pyrimidino[1,2-a]benzimidazoles are known to exhibit CNS depressant and anti-inflammatory activity^[18].

2. EXPERIMENTAL

2.1. Chemicals

All the chemicals used were of AR/GR grade. Pure sample of 2-Aminobenzimidazole (ABZ), molecular formula $C_7H_7N_3$, molecular weight 133.15 g/mol, melting point 229-231°C and metal salt of $MnCl_2 \cdot 4H_2O$ were obtained from Himedia Pharmaceuticals Ltd. Solvents used were ethanol, acetone and DMF.

2.2. Instrumentation

Elemental analysis was carried out on VarioMICRO V2.20 ElementarAnalysenSysteme GmbH, from IIIM, Jammu. Metal content was determined gravimetrically. The infrared spectra

was recorded on FT-InfraRed Spectrophotometer Model RZX (Perkin Elmer) using KBr pellets, from SAIF, Panjab University, Chandigarh. Molar conductance measurement was made in 10^{-3} M DMF solution on a Systronics direct reading Conductivity Meter (Model 303). The melting points of the ligand and the complex were recorded in open capillaries on a capillary melting point apparatus. Electronic spectra was recorded on a Perkin Elmer UV WinLab Spectrophotometer at Sadhu Vaswani College, Bairagarh, Bhopal. The magnetic susceptibility measurements was carried out on a Vibrating Sample Magnetometer (VSM) from IIT, Roorkee. The mass spectra was recorded at SAIF/CIL, PU, Chandigarh by LC-MS spectrometer Model Q-ToF MicroWaters.

2.3. Synthesis of Schiff base

Equimolar solutions of pure samples of 2-Aminobenzimidazole (0.1 M) and Salicylaldehyde (0.1 M) were prepared in pure ethanol separately. Both the solutions were mixed (pH 7.4) and refluxed for 4 hours. Temperature for reflux was set at 60-70°C. The reaction mixture was kept for two days. Concentration of the solution was done to reduce the volume upto 1/3rd of its original volume. The resulting reaction mixture was kept without disturbing for 4-5 days when deep yellow needle like crystals gets formed in the reaction vessel / beaker. These crystals were dried and further recrystallised with acetone. Yellow needle like Crystals appear. The yellow Schiff base product obtained (m.p. 142°C) produced in 54% yield was subjected to analysis.

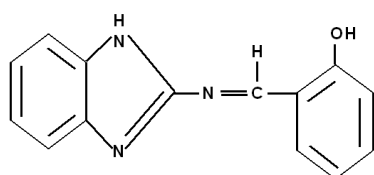


Figure - 1: Structure of Schiff base.

2.4. Synthesis of the complex

For the synthesis of complex, Ab-S-Mn, ligand-metal ratio was determined by conductometric titration using monovariation method on systronics conductivity meter using dip type electrode. 20ml of the ligand (0.01M) was diluted to 200ml using pure ethanol and titrated against $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ (0.02M) solution prepared in the same solvent. Conductance was recorded after each addition of metal salt solution. Graph is plotted between corrected conductance and volume of metal salt added. From the equivalence point in the graph, it has been concluded that the complex formation of the ligand with the metal takes place in the ratio 2:1 (L:M). Conductometric titration supported 2:1 (L:M) ratio in the complex, which was further supported by Job's method of

continuous variation^[19] as modified by Turner and Anderson^[20].

0.05 M solution of Ab-S and 0.025 M solution of manganese chloride were prepared separately in pure ethanol. On mixing both the solutions, dark gray solution was obtained (pH 6.5). pH was adjusted to 7.5 by adding N/10 NaOH solution. Colour of the resulting solution was olive green. The resulting mixture was refluxed for 4 hours and then kept for three days when walnut green coloured product was obtained. Product was filtered, washed with the same solvent, dried and weighed. Product obtained (m.p. 240°C) produced in 68% yield was subjected to analysis.

2.5. In vitro antibacterial activity

Qualitative analysis for screening of antibacterial activity of Schiff base and its complex was carried out by Agar-well diffusion method^[21,22] with modifications. The compounds were tested against two Gram positive and two Gram negative bacteria at concentration 10^{-3} M. 20 ml of sterilized nutrient agar was inoculated with 100 ml of bacterial suspension (10^8 CFU/ml) and then, poured on to sterilized petri plate. The agar plate was left to solidify at room temperature. A well of 6 mm was aseptically bored into the agar plate. Then, 20 ml of the complexes (diluted with DMSO, 1:1) was added in each well. Chloramphenicol (10 μg) was used as a positive reference to determine the sensitivity of bacteria. The plates were kept at 4°C for 2 hours to allow the dispersal and then incubated.

Definite volumes of peptone (5 gm), beef extract (3 gm) and agar (15 gm) were dissolved in distilled water to prepare the nutrient agar and pH was adjusted to 7.2. This solution was sterilized by autoclaving at 15 psi for 20 minutes.

3. RESULTS AND DISCUSSION

Through a condensation reaction, an amino group available in the pure compound was allowed to react with salicylaldehyde to form a Schiff base ligand (L) which was subsequently, reacted with metal ion to form Schiff base metal complex. The ligand and the metal(II) complex were isolated pure from EtOH in good yields and they are of various colours. The ligand is yellow whereas the complex formed is walnut green in colour. The complex gets decomposed at 240°C. The analytical data of the complex correspond to 1:2 (metal: ligand) stoichiometry. Thus, the general formula $[\text{M}(\text{L}_2)] \cdot 2\text{H}_2\text{O}$ where (M=Mn^{II}), has been assigned to the metal complex. The complex is stable at room temperature without decomposition for a long time. The complex is non-hygroscopic, insoluble in water and other common organic solvents but soluble in DMF and

DMSO. The molar conductance value (measured in 10^{-3}M DMF) is $15.3 \text{ Scm}^2\text{mol}^{-1}$, indicating / revealing the non-electrolytic nature^[23] of the

Table - 1: Analytical and physico-chemical data of Schiff base and its metal complex

Ligand / Complex	Mol. Wt.	Elemental Analysis Found (calcd.) (%)				Colour (yield%)	M.Pt. (°C)	Scm ² mol ⁻¹
		C	H	N	M			
[HL] C ₁₄ H ₁₁ N ₃ O	237.25	70.87 (70.30)	4.67 (4.40)	17.71 (17.3)	---	Yellow (54%)	142	---
C ₂₈ H ₂₄ N ₆ O ₄ Mn	(563.45)	58.70 (59.68)	4.10 (4.29)	14.87 (14.91)	10.05 (9.75)	Walnut green (68)	240 (Decomposition)	15.3

Table - 2: Important IR spectral bands (cm⁻¹) of the ligand and its complex

Ligand/ Complex	$\nu_{\text{HC=N}}$	$\nu_{\text{CyclicC=N}}$	$\nu_{\text{CyclicC-N}}$	ν_{CO}	$\nu_{\text{(H}_2\text{O)-OH}}$ (rocking)	$\nu_{\text{M-N}}$	$\nu_{\text{M-O}}$	$\nu_{\text{chelate ring}}$
Ab-S	1609 s	1569 s	1439 s	1273 s	---	---	---	---
[Mn(Ab-S) ₂].2H ₂ O	1646 m	1438s	1462 s	1269 s	849 w	502 m	619 s	1349 s

complex. The magnetic moment data indicated the complex to be paramagnetic in nature. The analytical data and molar conductance values are given in table 1.

3.1. IR spectra and mode of bonding

The IR spectrum of the Schiff base showed a sharp band near 1609 cm^{-1} which may be due to the azomethine linkage^[24], which was shifted to higher frequency at 1646 cm^{-1} in the metal complex, indicating coordination of the metal ion through the azomethine nitrogen^[25]. The ligand showed a strong band at 3566 cm^{-1} due to the phenolic -OH group^[26]. This band was absent in the spectra of the complex, indicating involvement of this group in the formation of the complex^[27]. The appearance of the M-N band at 502 cm^{-1} and the M-O band at 619 cm^{-1} in the complex indicates that metal complex was coordinated through an O and a N atom^[28,29]. The weak bands observed at 1273 cm^{-1} and at 1269 cm^{-1} are characteristics of $\nu_{\text{C-O}}$ (phenolic) ^[30] in the Schiff base and the metal complex, respectively. The shift of about 4 cm^{-1} of $\nu_{\text{(C-O)}}$ band to lower region in complex was observed indicating participation of the carbonyl oxygen in coordination. The appearance of bands for $\nu_{\text{cyclic (C-N)}}$ at 1439 cm^{-1} in ligand which gets shifted to higher frequencies by 1462 cm^{-1} in the complex indicates coordination of the imidazole nitrogen to the metal in the complex formation. The IR spectral data and their tentative assignments are given in table 2.

3.2. Electronic spectra

The electronic spectra of the complex were recorded in the solution state. The energies of the

observed spin allowed bands in the complex agreed with the octahedral geometry. The electronic spectrum of paramagnetic Mn(II) complex shows four weak bands at 26738 cm^{-1} , 20704 cm^{-1} , 19802 cm^{-1} and 16000 cm^{-1} which can be assigned to ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g} \nu_1$, ${}^6\text{A}_{1g} \rightarrow {}^4\text{E}_g \nu_2$, ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g} \nu_3$ and ${}^6\text{A}_{1g} \rightarrow {}^6\text{T}_{1g} \nu_4$, respectively, for an Mn (II) ion in an octahedral field. These transitions along with μ_{eff} value of 5.62 B.M. agrees with the proposed octahedral^[31,32] configuration.

3.3. Mass spectra

The mass spectrum of $[\text{Mn}(\text{C}_{28}\text{H}_{24}\text{N}_6\text{O}_4)]$ shows a molecular ion peak (m^+) at m/z 567.65(I) due to $[\text{Mn}(\text{L})_2]^+$ which suggests the monomeric nature and confirms the molecular weight and the proposed formula for the complex. Besides this peak, the complex showed the fragment ion peak at m/z 267.9 (IV) corresponding to L^+ with other atoms $(\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_2)^+$. other peaks of appreciable intensity have been observed at m/z values 100.9, 104.9, 132.0, 170.8, 231.1, 308.7 and 403.7 that indicates the fragmentation pattern. The peaks observed at m/z 403.7(II) due to loss of $(\text{C}_7\text{H}_9\text{N}_3\text{O}_2)^+$ from (I) indicative of 2-Aminobenzimidazole ring with two water molecules, at 308.7 (III) due to loss of $(\text{C}_7\text{H}_5)^+$ from (I) and at m/z 231.9 (V) due to loss of $[(\text{C}_8\text{H}_6\text{N}_3\text{O}_2)\text{Mn}]^+$ from (I). Intense peaks at 170.8 (VI) is due to loss of $(\text{CH}_2\text{N}_2\text{O})^+$ from (V) and at m/z 132.0 (VII) due to loss of $(\text{C}_7\text{H}_5\text{N}_3)^+$ from (II)

indicating the loss of second molecule of 2-Aminobenzimidazole ring. The peaks at m/z 104.9

(VIII) due to loss of $(C_7H_5O)^+$ from (II) and base peak at 100.9 (IX) due to metal ion linked to the

Table - 3: Antibacterial activity of pure compound, ligand and its metal complex.

Compounds/Complexes (100 $\mu\text{g/ml}$)	<i>B. subtilis</i>	<i>S. aureus</i>	<i>E. Coli</i>	<i>K. pneumonia</i>
Ab	-	-	-	-
Ab-S	0.9	-	1.15	1.15
$[\text{Mn}(\text{Ab-S})_2] \cdot 2\text{H}_2\text{O}$	1.2	1.15	1.25	-
Chloramphenicol 10 μg (4mm)	2.0	2.15	2.0	2.5

donor atoms, $[\text{Mn}(\text{NNO})]^+$. The relative intensities of these peaks give an idea of the stabilities of the various fragments [33,34].

3.4. Antibacterial activity study

For antibacterial activity the ligand and its metal complex were screened against two gram positive and two gram negative bacterial strains and the findings are given in table 4. The complex showed higher activity with 1.15-1.25 mm inhibition zone than the ligand which showed only 0.9-1.15 mm inhibition zone [35,36] at the same concentration whereas in case of *K. pneumoniae* the complex showed zero activity. Although, the pure compound showed no activity against these bacterial strains. However, ligand and its complex [37] showed lower activity as compared to standard drug chloramphenicol with 2.0-2.5 mm inhibition zone at the same concentration.

4. CONCLUSION

Based on stoichiometry and analytical data, it is concluded that the ligand is neutral, tridentate coordinating through the "N", "N" and "O" of the azomethine group, imidazole ring and phenolic group, respectively. The complex possesses 1:2 (M:L) stoichiometry based on analytical and spectral data and octahedral structure has been proposed for the complex. The ligand and its complex showed very good activity against all bacterial strains.

Hence, the proposed tentative structure for the metal complex is given as below:

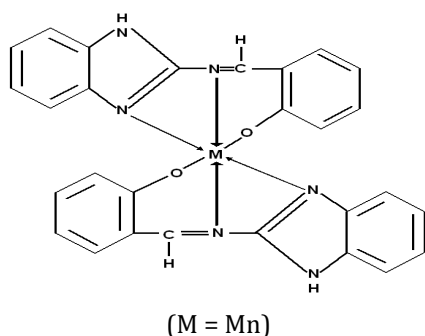


Figure - 2: Structure of metal complex.

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