

Periodic Research

Complexes of The Schiff Base Derived from 4–Aminophenyl Benzimidazole and 4–Methyl Benzaldehyde With Zn(II), Cd(II) And Hg(II) Halides



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Abstract

The study of complexes of the Schiff bases derived from 4–Aminophenyl Benzimidazole and 4–Methyl Benzaldehyde with Zn(II), Cd(II) and Hg(II) halides. In present work the preparation of 4–Aminophenyl Benzimidazole (4apbi) and its Schiff bases have been studied with various aldehydes. Schiff bases and benzimidazole derivatives are reported to show biological activities like antibacterial, antifungal, and antimalarial.

Keywords: Schiff bases, 4–Aminophenyl Benzimidazole, 4–Methyl Benzaldehyde, biological activities.

Chemistry

The sequence leading to the preparation of ligand and Schiff bases. 4–Aminophenyl 4–methyl benzimidazole was prepared from 4–methyl phenylenediamine and 4–aminobenzoic acid. After that the preparation of the complexes have been studied. Then the proton NMR spectra and I.R-spectra of the ligand and its complexes have been studied in the range 4000–400 cm^{-1} . Therefore the structure, molecular modeling and biological activities of complexes and its ligand have been studied

Introduction

Studies on metallo drugs acting as anticancer agents have gained momentum in recent times. Schiff bases are reported to show a variety of biological actions including antibacterial, antifungal, herbicidal, etc.⁽¹⁾ It has been suggested that the azomethine linkage is responsible for the biological activities displayed by Schiff bases.⁽²⁾

Benzimidazole and its derivatives have been shown to possess antibacterial and antimalarial activities. The benzimidazole moiety is reported to be toxic to fungi and a large number of benzimidazole derivatives have been synthesized and patented as fungicides⁽³⁾. The physiological activity and commercial application of 2–amino benzimidazole have received much attention⁽⁴⁾. A number of aldehydes and ketones are found to react with 2–amino benzimidazole derivatives leading to the formation of azomethines with a broad spectrum of biological activity.^(5,6)

In the present study, we have prepared 4–aminophenyl benzimidazole (4apbi) and its Schiff bases with various aldehydes. We report herein the synthesis, characterization, molecular modeling studies and biological activity of complexes of zinc chloride and chlorides and bromides of cadmium(II) and mercury(II) with the Schiff base derived from 4–aminophenyl benzimidazole and 4–methyl benzaldehyde (MBenz–4apbi)

Experimental:

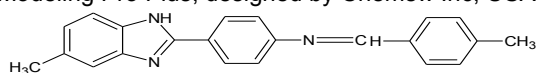
Preparation of the Ligand (M.Benz–4apbi)

All the chemicals used were of high purity. 4–Aminophenyl 4–methyl benzimidazole was prepared from 4–methyl phenylenediamine and 4–aminobenzoic acid by reported procedure⁽⁵⁾. The Schiff base was prepared by taking equimolar quantities of 4apbi (2.10 g) and 4–methyl–benzaldehyde (1mL) in about 40mL of ethanol. The solution was refluxed for about 4h. The solvent was evaporated to dryness to obtain a buff coloured solid. It was recrystallised from ethanol and dried overnight at about 100°C in vacuum for 4 h. The elemental analysis (Table 9.1) corresponds to the molecular formula ($\text{C}_{22}\text{H}_{19}\text{N}_3$).

Preparation of the Complexes

Each of the metal salts CdCl_2 , CdBr_2 , HgCl_2 , HgBr_2 and ZnCl_2 (0.33 M) was refluxed separately with the ligand (0.66 M) in about 20 mL of

ethanol for 4–6 h. The reaction mixture was evaporated to minimum volume. About 10 mL of ether was then added to it and kept overnight in a refrigerator when the complex crystallized out. It was collected by filtration, washed with ether and dried under vacuum for 4h. Conductivity data were obtained using freshly prepared N,N-dimethylformamide solution of the complex (10.3 M) at 25°C with a digital conductivity meter (model-CIS 13). Elemental analyses were carried out using a Carlo-Erba Strumentazione (model 1106). The infrared spectra in the range 4000–400 cm⁻¹ were recorded with KBr pellets using a Nicolet impact 400D spectrometer. The far infrared spectra in the range 400–200 cm⁻¹ were recorded using Thermo Nicolet (model IR 100) spectrometer using high density polyethylene. The proton NMR spectra were recorded using a Bruker-400 instrument using DMSO₆ as the solvent and TMS as internal reference. Molecular modeling was carried out using the software. Molecular Modeling Pro Plus, designed by Chemsw Inc, USA.



(x)
Table 9.1

Analytical Data of Complexes of Zn, Cd, Hg Halides with M-Benz-4-Apbi (L)

Comp.	Found (Calc.) %			$\Delta_{mol} S$ cm ² /mol
	Carbon	Nitrogen	Hydrogen	
L(C ₂₂ H ₁₉ N ₃)	81.05 (81.23)	12.77 (12.92)	5.70 (5.84)	–
Zn ₂ L ₂ .Cl ₄	57.09 (57.22)	9.0 (9.10)	4.0 (4.11)	62
Cd ₂ L ₂ .Cl ₄	51.77 (51.92)	8.12 (8.26)	3.60 (3.73)	59
Cd ₂ L ₂ .Br ₄	44.02 (44.10)	6.90 (7.03)	3.02 (3.18)	59
Hg ₂ L ₂ .Cl ₄	44.12 (44.25)	6.87 (7.04)	3.02 (3.18)	67
Hg ₂ L ₂ .Br ₄	38.40 (38.50)	5.93 (6.12)	2.70 (2.77)	68

L-(C₂₂H₁₉N₃)

The biological screening was conducted by filter paper disc method. The nutrient agar was prepared separately for bacterial strains and fungus from the commercially available nutrients (Hi MEDIA). The test solutions consisting of 5 and 10 ppm of the metal ion were prepared by dissolving accurately weighed amounts of the complexes in DMF. Whatmann filter paper discs of about 6 mm were placed on the nutrient broth at appropriate spots, properly labeled, on the petriplates. The test solutions, ligand solution, DMF and phenol as control were inoculated into these different filter paper spots. The plates were then incubated at 37°C for 24 h. The clear zones of inhibition of the respective test solutions and control were measured in mm using a scale and tabulated.

Results and Discussion

The analytical data of the complexes are given in Table 9.1. All the complexes are insoluble in common organic solvents except DMF and DMSO.

The ligand and the complexes have melting point above 250°C. The molar conductance of 10⁻³ M DMF solutions of the complexes calculated for the monomer was found to be in the range of about 59–68 S cm² mol⁻¹. The higher values of conductivity than those expected for non-electrolytes indicate the solvation of the complexes resulting in the slight displacement of anion from the coordination sphere by the stronger donor DMF molecules. The complexes may hence be regarded as non-electrolytes.

(i) NMR Spectra

The ¹H NMR spectra of the ligand MBenz4apbi, shows the chemical shift for the –NH proton at δ 12.43 ppm as a singlet and that of N=CH proton at δ 8.17 ppm as another singlet. The aromatic protons are observed in the region δ 6.67 to δ 7.83 ppm. The protons of the benzidene ring show chemical shifts at δ 3.22 ppm (m) and δ 3.43 ppm (m).

The proton NMR spectra of the complexes show a marginal or no shift in the chemical shifts of the aromatic benzidene and N=CH protons. Only the signal corresponding to –NH proton in the complexes show a large deviation and is not observed in the spectrum recorded up to δ 15 ppm. This indicates that the complexation of the ligand with the metal atom occurs through the imidazole nitrogen atom and suggests that the ligand is monodentate. The bond between the tertiary nitrogen and the metal desields, inducing a major shift in the –NH proton.

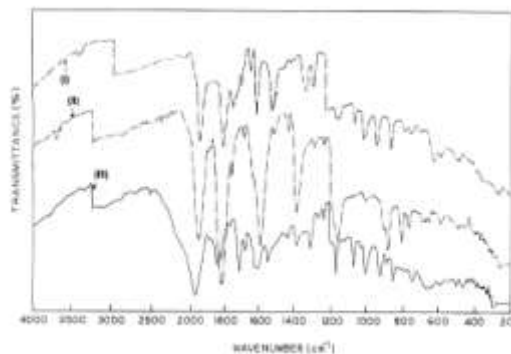
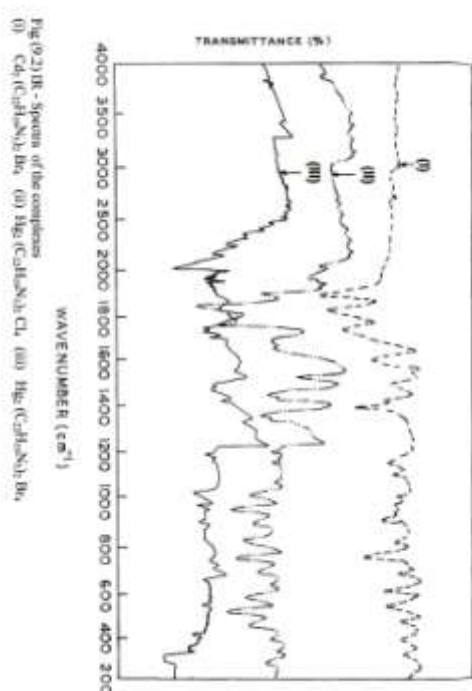


Fig (9.1) IR - Spectra of the complexes
 (i) L-(C₂₂H₁₉N₃) (ii) Zn₂L₂.Cl₄ (iii) Cd₂L₂.Br₄

IR Spectra

The IR spectra of the ligand and the complexes were studied in the range 4000–200 cm⁻¹. The absorption at 3359 cm⁻¹ is assigned to the stretching vibration of N–H bond of the imidazole ring(7). It shows a considerable shift of 5–31 cm⁻¹ in the complexes. The absorptions at 1657 and 1616 cm⁻¹ due to N=CH and C=N stretching modes also show a shift of 5–15 and 16 cm⁻¹ respectively in the complexes. These shifts indicate the bonding of imidazole nitrogen of benzimidazole to the metal atom(8). The bands due to the stretching vibrations of metal–nitrogen bonds in all the complexes are observed in the region 286–313 cm⁻¹ as reported in the literature(9). In the chloride complexes, the

stretching modes of M–Cl (terminal) bonds are observed in the region 210–350 cm^{-1} as expected(10). The bands due to bridging chlorides in these complexes are observed below 200 cm^{-1} . The ratio of $\nu\text{M–Cl(b)}$, $\nu\text{M–Cl(t)}$ is 0.54 : 0.63 as expected. However, in the case of bromo complexes of cadmium(II) and mercury(II), the Cd–Br and Hg–Br stretching frequencies are probably near the limit of the spectrometer and hence were not observed. Similar results have been reported by Coates and Ridley(11) in their observations on low– frequency infrared spectra of some complex halides of zinc(II), cadmium(II) and mercury(II). Considering that normally the complexes analyzing as MLX₂ are dimeric with a halogen as bridge, we propose dimeric structure for all the complexes.



Structure of the Complexes

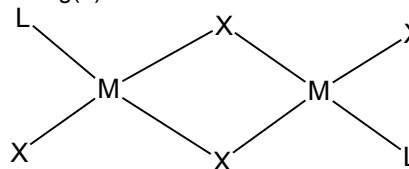
Studies on Schiff base complexes derived from salicylidene–2–amino– benzimidazole with metals such as Fe(III), Cu(II), Zn(II), Cd(II) etc., have shown coordination of the ligand to the metal ions in a tridentate manner with donor sites O, N, N of the phenolic–OH, benzimidazole–N3 and azomethine–N⁽¹²⁾.

Salicylidene–2–aminomethylbenzimidazole also acts as a tridentate ligand⁽²⁾. However, salicylidene–2–(2–aminophenyl) benzimidazole acts as a bidentate ligand bonding through the phenolic oxygen and the tertiary N of the imidazole ring of benzimidazole⁽¹³⁾. In certain cases as in the complexes of benzilidene–2– (2–aminophenyl) benzimidazole and salicylidene–2(2–aminophenyl) benzimidazole with Ti(IV), V(IV) and Sn(IV), the ligand acts as monodentate with imidazole nitrogen as the donor atom⁽¹⁴⁾. Our studies indicate that a related

ligand Mbenz4apbi, also acts as monodentate with the azomethine nitrogen. This may be probably due to steric hindrance. The molecular modeling studies also indicate very high strain on the metal ion when the ligand coordinates as a bidentate. Hence, complexes with dimeric structure as shown in structure(II) is suggested, where the metal ion has a tetrahedral environment.

Molecular Modeling Studies

Molecular modeling studies were carried out with an interactive graphics molecular modeling program Molecular Modeling Pro Plus⁽¹⁵⁾. Energy minimization was repeated several times to find the global minimum. The Jones–Leonard potential was applied on M–N bonds to obtain a configuration with minimum repulsion and, hence, minimum steric strain. Representative structure of a chloride and a bromide complex with minimum global energy is shown in Figs 1 and 2. The results show that the arrangement of the ligand around the metal atom, in space, varies in a chloride and a bromide complex due to the change in size of the halides. After the configuration with global minimum is attained, the total energy of the molecule and the percentage strain on the metal atom was computed. They are collected in Table 9.2. The total energy of these complexes varies between 696 and 846 kJ/mol and the strain on the metal atom is 34–38%. From the results it is seen that the strain on the metal ion for the chloride complexes increases from Hg(II) to Cd(II) to Zn(II). The values of total energy do not show any specific trend. The molar volume of the complexes increases with the increase in the ionic radii of the metal ions in the order Zn(II), Cd(II) and Hg(II).



(II)

The calculated metal–nitrogen and metal–halide bond lengths and the relevant bond angles are given in Table 9.2. The Zn–N bond lengths in dibromobis (nicotina–mide)zinc(II) and dibromobis–(benzimidazole)zinc(II) complexes are reported from single crystal x–ray studies to lie between 2.008 and 2.065 Å^(16,17).

The Zn ion has distorted tetrahedral geometry in these complexes. The Zn–N bond lengths obtained in the present calculations are somewhat lower. It is suggested that this decrease in the bond length may be due to the bridging of the metal ions through the halide.

It is found that in the case of Cd(II) and Hg(II) complexes also, the M–N bond length is lower than those reported in the literature⁽¹⁸⁾.



Fig. 1—Molecular energy configuration of $Hg_2L_2Cl_4$ (Color code: Black = C, Blue = N, Yellow = H, Green = Cl, Magenta = Hg)

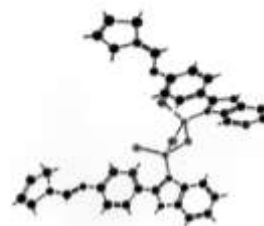


Fig. 2—Molecular energy configuration of $Cd_2L_2Cl_4$ (Color code as given to Fig. 1; Orange = Cl, Purple = Cd)

complexes. The N-M-X bond angles show a small deviation from tetrahedral angle whereas the bond angles M-X_b-M and X_b-M-X_b show large deviations.

Table 9.2 Molecular Modeling Data on Complexes Of Zn, Cd, Hg Halides With M-Benz4apbi(L)

Compound	Total energy kJ/mol	Strain on metal	Molar vol. cm ³ /mol	Bond length, Å						Bond angle deg.					
				M-N		M-X ₁		M-X _b		N-M-X ₁		M-X _b -M		X _b -M-X _b	
Zn ₂ L ₂ .Cl ₄	824	37.39 38.37	576.81	1.78	1.75	2.03	2.03	1.84 1.93	1.96 1.96	116	102	73	70	102	100
Cd ₂ L ₂ .Cl ₄	846	37.38 35.83	580.33	1.65	1.78	2.22	2.14	2.08 2.07	2.07 1.97	106	114	73	73	93	100
Cd ₂ L ₂ .Br ₄	696	34.11 34.23	594.10	1.89	1.93	2.37	2.37	2.25 2.23	2.24 2.28	115	113	83	82	93	92
Hg ₂ L ₂ .Cl ₄	777	34.03 32.59	584.13	1.93	1.78	2.28	2.25	2.09 2.14	2.13 2.13	115	110	80	81	93	92
Hg ₂ L ₂ .Br ₄	784	33.42 35.45	592.39	1.80	1.85	2.40	2.43	2.29 2.23	2.30 2.26	112	115	78	77	96	98
L-(C ₂₂ H ₁₉ N ₃)	136		247.41	-											

The metal halogen bond lengths are about 0.3–0.4Å shorter than those reported from the single crystal X-ray studies of such complexes. The N–M–X bond angles show a small deviation from tetrahedral angle whereas the bond angles M–X_b–M and X_b–M–X_b show large deviations. These deviations indicate the bridging through halogen and may arise from the bulky Schiff base ligand due to steric consideration⁽¹⁹⁾.

(v) Biological activity⁽²⁰⁾

The ligand and its complexes were tested for their activity against a set of microorganisms. Representative bacterial strains from Gram-positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram-negative bacteria (*Escherichia coli* and *Pseudomonas fluorescens*) were tested. They were also investigated for anti-fungal activity against the fungus *Fusarium*.

All the complexes^(21,22) show moderately enhanced activity against the fungus *Fusarium* as compared to that for phenol as a standard and also for the free ligand at both 5 and 10 ppm concentrations. According to the chelation theory, the formation of a complex decreases the polarisability of the metal enhancing the lipophilicity of the complexes. It facilitates the interaction of the complexes with the amino acids of the microorganism. Therefore, a higher activity of the complexes as compared to that of the free ligand is expected. Studies indicate increased antibacterial activity of the complexes towards *Pseudomonas fluorescens* when compared to that of the free ligand.^(23,24)

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