

Synthesis, Characterization and Antibacterial Studies of Some Transition Metal Complexes with the Schiff Base of a Heterocyclic Aldehyde

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Metal complexes of Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) with a new Schiff base derived from 2-acetylpyrrole and *o*-phenylenediamine are reported. The complexes have been characterized using chemical analysis, spectroscopic methods (IR, UV-VIS, ¹H NMR), conductometric and magnetic data. According to these data, an octahedral geometry for metal (II) complexes are proposed. Antibacterial activity of the ligand and its metal complexes were studied against to *Staphylococcus aureus*, *Bacillus subtilis*, *Salmonella typhi* and *E. coli*.

Key Words: Schiff base, Metal complexes, Antibacterial activity.

INTRODUCTION

The synthesis of transition metal complexes with Schiff base ligands are extensively studied due to synthetic flexibility, selectivity and sensitivity towards a variety of metal atoms¹. They are found useful in catalysis, in medicine as antibiotics and anti-inflammatory agents and in the industry as anticorrosion²⁻⁸. Literature is abundant on physico-chemical properties of various symmetrical Schiff bases and chelates with their pyridine, 2,2'-bipyridine and 1,10-phenanthroline adducts⁹⁻¹³, while comparatively little is known on asymmetric Schiff base transition metal complexes. In the present paper we describe the behaviour of the bidentate aromatic Schiff base ligands with various transition metal(II) ions. All these compounds with the ligands (Fig.1) are new, being reported for the first time. The structures of all these complexes have been investigated by using elemental analysis, FTIR, ¹H NMR, UV-VIS, magnetic susceptibility and conductivity measurements. Antibacterial activities were determined as MICs values using the micro dilution broth method against *Staphylococcus aureus*, *Bacillus subtilis*, *Salmonella typhi* and *Escherichia coli*.

EXPERIMENTAL

All reagents were supplied by Merck and were used without further purification. Melting points were determined in a electro thermal 9200. ¹H NMR spectra in CDCl₃ and DMSO were recorded on NMR spectrophotometer. The IR spectra (nujol/KBr) were recorded in the range 4000-400 cm⁻¹ by KBr pellet using Perkin-Elmer 457 spectrophotometer. Conductance

was measured in DMF at room temperature using a Digital conductivity bridge. The UV-Visible spectra in CH₃OH were recorded on a shimadzu UV 1800 spectrophotometer. The metal contents were determined gravimetrically.

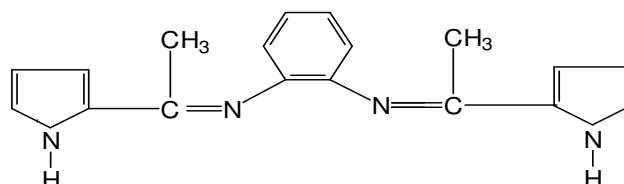


Fig.1. Structure of bis(2-acetylpyrrole)phenylene diamine

Synthesis of Schiff base ligands: The Schiff base ligand was prepared by equimolar mixture of 2-acetylpyrrole (2 mmol) and the *o*-phenylenediamine (1 mmol) in methanol for 3 h. TLC examination suggested the complete conversion of the starting materials to the Schiff base. Upon cooling, the obtained crystalline precipitates were filtered, washed with ethanol and recrystallized from absolute ethanol and finally dried. They are colourless and light yellow crystalline solids, stable at normal condition and soluble in DMSO, DMF and poorly soluble in benzene and water.

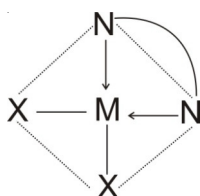
Synthesis of transition metal(II) complexes: All the metal complexes are prepared by the following general method. A hot methanoic solution of the corresponding metal(II) salt was mixed with a hot methanoic solution of the Schiff base ligand in 1:2 molar ratio, respectively. The reaction mixture was refluxed on a water bath for ca. 2 h. On cooling the reaction

mixture at room temperature the coloured complexes precipitated out in each case. The complexes were filtered out, recrystallized, washed with methanol and dried over P_2O_5 under vacuum.

Procedure for antibacterial activity: The *in vitro* antibacterial activity of the free ligands and their complexes were tested against *S. aureus*, *Bacillus subtilis*, *E. coli* and *Salmonella typhi*. Minimum inhibitory concentrations (MICs) were determined by the micro dilution broth method following the procedures recommended by the National committee for clinical laboratory standards^{14,15}. MICs were defined as the lowest concentrations of compounds which inhibit the growth of micro organisms. All tests were performed in Nutrient broth (NB) dissolved in DMSO, which lacked anti bacterial activity against any of the test bacteria. The micro plates were incubated at 37 °C and read visually after 24 h for MICs¹⁶. The results were recorded according to the presence and absence of growth.

RESULTS AND DISCUSSION

The transition metal(II) complexes with bidentate aromatic Schiff base ligands were prepared in good yield by stirring stoichiometric amounts of metal(II) chloride and bidentate aromatic Schiff base ligand. Analytical data and physical properties of the metal complexes are listed in Table-1. The complexes are stable in air and light and are soluble in organic solvents such as DMF and DMSO. Elemental analysis ($\pm 0.5\%$ for C, H and N) and molar conductance data (Less than $60 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ in acetone) suggest the complexes to be non-electrolyte with composition of $\text{MX}_2\text{-SB}^{17}$.



Schematic representation of metal complex

Structural interpretation

Infrared spectra: The infrared spectra of the complexes taken in the region $4000\text{-}400 \text{ cm}^{-1}$ were compared with those of the free ligand. There are some significant changes between the metal(II) complexes and their free ligand for chelation as expected. The IR bands observed at $1660\text{-}1610 \text{ cm}^{-1}$ of all the ligands and the complexes are assigned to $\nu(\text{C}=\text{N})$ vibration¹⁸.

The ligand bands around 1610 cm^{-1} ($\text{C}=\text{N}$) shifted to $1660\text{-}1635 \text{ cm}^{-1}$ in the complexes due to an increase of bond order on co-ordination¹⁹. The bands at $420\text{-}390$ and $344\text{-}210 \text{ cm}^{-1}$ in the complexes may be assigned to $\nu(\text{M-N})$ and $\nu(\text{M-Cl})$ modes²⁰, respectively. The IR spectra of $[\text{ML}_2]\text{Cl}_2$ complexes, the ligands act as a neutral bidentate through the azomethine and carbonyl groups²¹. The azomethine band is shifted to lower frequency in all metal complexes, suggesting that this group takes part in coordination. The co-ordination of nitrogen to the metal atom would be expected to reduce the electron density on the azomethine link and thus cause a shift in the $\text{C}=\text{N}$ band.

Moreover, in the spectra of the complexes, a considerable negative shift in $\nu(\text{C}=\text{O})$ are observed indicating a decrease in the stretching force constant of $\text{C}=\text{O}$ as a consequence of coordination through the carbonyl oxygen atom of the free ligands²².

¹H NMR spectra: ¹H NMR spectra of the metal complexes show all the expected signals. In all the spectra, a singlet corresponding to a single proton is observed in the range $\delta 9.1, 11.5$ ppm, which is attributed to the azomethine proton ($-\text{HC}=\text{N}$) in metal(II) complexes respectively. The ¹H NMR spectra of the $[\text{ML}_2]\text{Cl}_2$ complexes show a negative shift of the signal due to the NH group. This signal is observed at $\delta 8.0, 11.2$ ppm in metal complexes, suggesting that the coordination proceeds through the carbonyl oxygen or azomethine nitrogen groups. The downfield shifts of the methyl group signal at 2.3, 2.1 ppm for the metal(II) complexes, support the coordination *via* the azomethine nitrogen. The multi signals within the range $\delta 8\text{-}7.1, 8.3\text{-}7.6$ ppm are assigned to the aromatic protons of ring in metal(II) complexes, respectively.

Electronic spectra: The formation of the metal(II) complexes was also confirmed by UV-VIS spectra. The absorption spectra of the diamagnetic metal(II) complexes were recorded as 10^{-4} M CH_3OH solutions in the range 200-800 nm using a quartz cuvette of 1 cm path length. The complexes show only the charge transfer transitions, which can be assigned to charge transfer from the ligand to metal and *vice-versa*, no *d-d* transition are expected for d^{10} Hg(II) complexes²³. When compared complexes with the free ligands values have shifts frequency. The data of the spectra of the metal(II) complexes in CH_3OH solutions are shown that absorption band observed at 275 and 316 nm is attributed to $n \rightarrow \pi^*$ electronic transition of azomethine group involving the whole conjugation.

Antibacterial activity of the ligand and its metal complexes: The antibacterial activity of bidentated aromatic Schiff base ligand and its metal(II) complexes were tested against

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF THE LIGAND AND COMPLEXES

Compound	Colour/yield (%)	m.p. (°C)	Calculation (found %)				Λ_m^* ($\Omega^{-1}\text{cm}^2\text{mol}^{-1}$)	μ_{eff} (BM)
			C	H	N	M		
Schiff base	Yellow/(65)	190	32.4 (32.7)	3.2 (3.5)	10.8 (10.9)			
$[\text{CoL}_2\text{Cl}_2]$	Brown/(70)	240	38.2 (38.4)	3.0 (3.2)	9.6 (9.9)	9.03 (9.00)	3.88	
$[\text{NiL}_2\text{Cl}_2]$	Green/(75)	210	29.4 (29.6)	2.6 (2.8)	11.4 (11.5)	8.9 (8.8)	3.10	
$[\text{CuL}_2\text{Cl}_2]$	Brown/(80)	220	35.4 (35.9)	2.2 (2.6)	10.4 (10.4)	9.57 (9.55)	1.88	
$[\text{ZnL}_2]\text{Cl}_2$	Yellow/(60)	200	29.4 (29.5)	3.0 (3.1)	14.4 (14.2)	8.5 (8.6)	–	
$[\text{CdL}_2]\text{Cl}_2$	Yellow/(75)	180	32.4 (32.9)	2.2 (2.5)	10.2 (14.4)	15.82 (15.81)	32	
$[\text{HgL}_2]\text{Cl}_2$	White/(65)	200	38.6 (38.7)	2.2 (2.5)	14.8 (14.4)	37.2 (37.5)	–	

*in 10^{-3} M DMF solution at room temperature

microorganism. The microorganisms used in the present investigations include bacteria: *Staphylococcus aureus*, *Bacillus subtilis*, *Salmonella typhi* and *E. coli*. Minimum inhibitory concentrations (MICs) method was used to determine the antibacterial activity of the synthesized compounds. The diffusion method is simple and routinely used in hospital laboratories; it requires commercial disks, the medium used is Mueller-Hinton agar with 2 % of glucose and the diameter of inhibition zone is visually read at 24 h after incubation at 37 °C. The antibacterial activity was estimated on the basis of the size of the inhibition zone formed around the paper disks on the seeded agar plates. Streptomycin was used as a standard. The results are presented in Table-2.

TABLE-2
ANTIBACTERIAL ACTIVITY OF THE LIGAND
AND ITS COMPLEXES

Compound* C*	<i>E. coli</i>	<i>Salmonella typhi</i>	<i>B. subtilis</i>	<i>S. aureus</i>
Schiff base L	++	+	+	+
[Co L ₂ Cl ₂]	++++	+++	+++	++
[Ni L ₂ Cl ₂]	+++	++	++	++
[Cu L ₂ Cl ₂]	++++	++	++	++
[Zn L ₂ Cl ₂]	+++	++	++	++
[Cd L ₂ Cl ₂]	++	++	++	++
[Hg L ₂ Cl ₂]	++	++	++	++

C* = 5 mg/L Inhibition zone diameter mm (% inhibition) "+, 6-10 (27-45 %); ++10-14 (45-64 %); +++ 14-18 (64-82 %); ++++18-22 % (82-100 %)

Per cent inhibition values are relative to the inhibition zone (22 mm) of the most active compound with 100 % inhibition. The Schiff base and the complexes exhibited varying degrees of inhibitory effects on the growth of the tested bacteria species. The values reveal that the Schiff base become more effective when coordinated to the metal ions. The biological activity of the complexes follows the order: Co(II) > Ni(II) ≈ Cu(II) ≈ Zn(II) > Cd(II) ≈ Hg(II). Furthermore, the data show that *E. coli* was inhibited to a greater degree by the Co(II) and Cu(II) complexes. In conclusion the complexes prepared with the new Schiff base could reasonable be used for the treatment of some common diseases caused by *E. coli*.

Conclusion

Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) complexes of the Schiff base derived from 2-acetyl pyrrole and *o*-phenylenediamine were prepared and characterized. The study reveal that (1) complexes are non-electrolytes (2) Schiff base behaves as a neutral Bidentate ligand and is coordinated to the central

metal ion through the azomethine N (3). The metal(II) complexes have octahedral geometry (4). The biological activity of all the complexes is higher that of the free Schiff base ligand and follows the order: Co(II) > Ni(II) ≈ Cu(II) ≈ Zn(II) > Cd(II) ≈ Hg(II). This means that metal chelation significantly affects the antimicrobial behaviour of the organic ligand.

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