

Syntheses, spectral characterization and antimicrobial activity of novel mixed ligand Schiff base complexes

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Abstract Novel mixed ligand complexes of metal ions Co(II) and Ni(II) have been successfully prepared with a Schiff base ligand obtained from Isatin monohydrazone and 2-Acetyl thiophene with 1,10-phenanthroline. The complexes have been investigated with elemental analysis, Conductance measurement, magnetic studies, electronic, vibrational and mass spectroscopic techniques. Infra-Red spectral measurements reveal that the coordination of the Schiff base (L) to the metal atom was found to be through the azomethine nitrogen and the carbonyl oxygen. The nitrogen present in 1,10-phenanthroline also coordinated with the metal ion in this mixed ligand complexes. All the complexes were assigned octahedral geometry on the basis of magnetic moment and electronic spectroscopic data. The ligand and their complexes were checked for their antimicrobial activities against four bacterial strains and three fungal strains by disc diffusion method and agar plate technique.

Keywords — Schiff base, Isatin monohydrazone, 2-acetylthiophene, 1,10-phenanthroline mixed ligand complex, spectra

I. INTRODUCTION

Exclusive pharmaceutical importance of transition metal complexes has fascinated the attention many researchers around the globe leading to their usage in numerous areas of contemporary medication [1]. Transition metals, in view of their stereochemical versatility and rich redox reactivity, have an active part in small molecule binding and transport, electron transfer triggering, fine and selective catalysis. Due to these features, transition metals play an essential role in many biological processes and constitute the active sites in most enzymes. [2] Isatin, an endogenous indole and its derivatives exhibit a wide range of biological activities. [3] Isatin-based Schiff base copper(II) complex is related to the antiviral drug, methisazone. Schiff bases derived from isatin exhibit many neurophysiological and neuropharmacological effects like antimicrobial, antiviral, anticonvulsant, anticancer, antimycobacterial, antimalarial, cysticidal, herbicidal and antiinflammatory activity. [4–9] They also have anti-HIV, antiprotozoal and antihelminthic activities. [10–12] Transition metal coordination complexes show better DNA cleavage [13]. In this context, mixed-ligand compounds with transition metal ions were observed to be predominantly valuable because of its ability to bind DNA molecule through many types of interactions and to cleave the duplex by nature of their inherent physico-chemical, photochemical and electrochemical reactivity [14–19]. Current research on the combination of good intercalators, such as 1,10-phenanthroline, 2,2'-bipyridine

and more compounds observed high affinity between nucleobase pairs and their planar structure through stacking interaction [20]. A remarkable benefit in the usage of such compounds is that the ligand or the coordinating metal species can be varied easily in controlled manner to enable specific applications [21, 22]. Varied applications of this type of Schiff base ligand and its complexes encouraged us for the synthesis, characterization and biological activity studies of some mixed ligand transition metal complexes of Schiff bases ligand L (derived from Isatin monohydrazone and 2-acetyl thiophene) and 1,10-phenanthroline.

II. EXPERIMENTAL

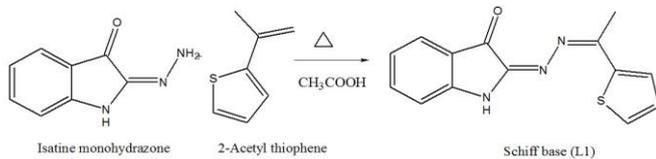
A. Chemicals and Reagents

Isatin, Hydrazine hydrate, were obtained from Himedia. 2-acetyl thiophene, ammonium acetate and acetic acid were purchased from Merck India Pvt. Ltd.. 1,10-Phenanthroline, Co(II) and Ni(II) acetates were procured from Sigma and used as such. Further chemicals and solvents were obtained as AR grade. The general solvents like chloroform, ethanol and methanol were purified by standard methods.

B. Synthesis of Schiff Base Ligand (L)

Isatine monohydrazone (5mmol) in methanol (25 mL) was poured into a 100 mL round bottomed flask. A solution of 2-acetylthiophene (5 mmol) in absolute methanol (25 mL) was slowly mixed to the flask. Added few drops of acetic acid and were heated at reflux for 8h with continuous

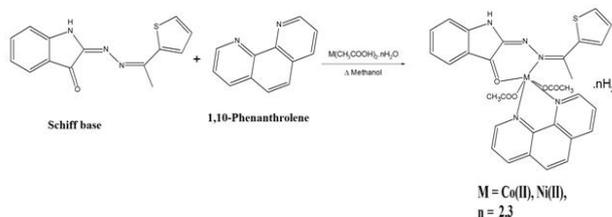
stirring. The mixture was condensed to half of the original volume under reduced pressure and an excess of anhydrous ether was introduced. A reddish precipitate was formed, which was collected in vacuo filtration and washed many times with anhydrous ether and dried in vacuum over anhydrous calcium chloride. The purity of the resultant Schiff base ligand was inspected by TLC (Thin Layer Chromatography). The yield of the resultant ligand was observed as 65% (Scheme – 1).



Scheme 1. Synthesis of Schiff base ligand

C. Mixed ligand Metal Complexes with Ligand L and 1,10-Phenanthroline ($[MLP(CH_3COO)_2] \cdot nH_2O$) $M = Co(II) \& Ni(II)$, $P = 1,10$ -Phenanthroline

The Schiff base ligand L (1mmol) in methanol (20mL) was taken in a 100 mL round bottomed flask. A solution of metal (II) acetate (1 mmol) in aqueous methanol (10 mL) and solution of 1,10-phenanthroline (1 mmol) in aqueous methanol (10 mL) was slowly introduced drop-by-drop to the flask and the reaction mixture was refluxed for 4 h on a water bath. Cool the reaction mixture. The volume of the mixture was reduced to half of the initial volume under reduced pressure and an excess of anhydrous ether was added. The precipitate formed was filtered off, washed several times with ether and with little cold ethanol, and then dried in vacuum in presence of anhydrous $CaCl_2$. The yield of the chemical reaction is 60-65% (Scheme – 2).



Scheme 2. Synthesis of metal complexes

D. Instruments and Methods

Microanalysis of carbon, hydrogen, and nitrogen contents present in the samples were recorded on Perkin Elmer Elemental Analyzer. The FAB-mass spectra of the Schiff base ligands/complexes were recorded on a JEOL SX 102/DA-6000 mass spectrometer. A Coranation Digital Conductivity Meter was employed to measure the molar conductance of the complexes. The infrared spectra of the solid samples were recorded on JASCO/FT-IR 410 spectrometer in the range $4000-400\text{ cm}^{-1}$. Electronic spectra of the samples were recorded using Perkin Elmer Lambda-25 UV/Visible spectrometer. Magnetic susceptibility measurements of the powdered complexes were carried out by employing the Guoy's method at room temperature. Microbial activity against bacterial and fungal strains of the

ligand and its metal complexes were confirmed by in vitro studies with the bacterial strains, viz., *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis*; with the fungal strains, viz., *Aspergillus flavus*, *Aspergillus niger* and *Candida albicans* by the disc diffusion method.

III. RESULTS AND DISCUSSIONS

Elemental analysis and other physical data of $[MLP(CH_3COO)_2] \cdot nH_2O$ complexes are provided in Table 1. The listed values in the table show that the metal, ligand and 1,10-phenanthroline ratio is 1:1:1 in all the complexes. The common chemical formula of the complexes is $[ML(CH_3COO)_2] \cdot nH_2O$, where L is the novel Schiff base ligand, P is 1,10-phenanthroline, M is Co(II) and Ni(II) and n is 2 or 3. The metal complexes are soluble in methanol, chloroform, dichloromethane, DMF, DMSO etc. Non-electrolytic behaviour of the metal coordination complexes I confirmed from the low molar conductance values as detailed in the table [23].

Electronic Spectra and Magnetic Properties

The electronic spectrum of Co(II) complex (Figure –1) shows two absorption bands (Table -1) at 550–640 nm region, which are assignable to the overlap of ${}^4T_1g(F) \rightarrow {}^4A_2g(F)$ and ${}^4T_1g(F) \rightarrow {}^4T_2g(F)$ transitions in an octahedral environment around the metal ion [24, 25]. The magnetic susceptibility value is found to be 4.90 BM for Co(II) complex (Table -1) (normal range for octahedral Co(II) complexes is 4.3–5.2 BM), which indicated the octahedral geometry of the complex.

The electronic spectrum of the Ni(II) complex is shown in Figure 2. The two peaks at 420 and 640 nm (Table 1) is attributed to ${}^3A_2g(F) \rightarrow {}^3T_1g(F)$, and ${}^3A_2g(F) \rightarrow {}^3T_1g(P)$ transitions, respectively. It suggests an octahedral geometry around Ni(II) ion [26]. The mixed ligand nickel(II) complex has a magnetic moment value of 3.15 BM at room temperature. The value is observed to be in normal range for octahedral Ni(II) coordination (μ_{eff} 2.9 – 3.3 BM).

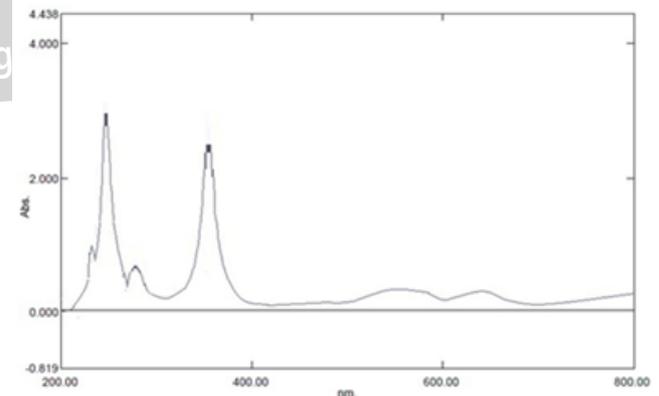


Figure .1 UV-Vis spectrum of Co(II) complex $[CoLP(CH_3COO)_2] \cdot 3H_2O$

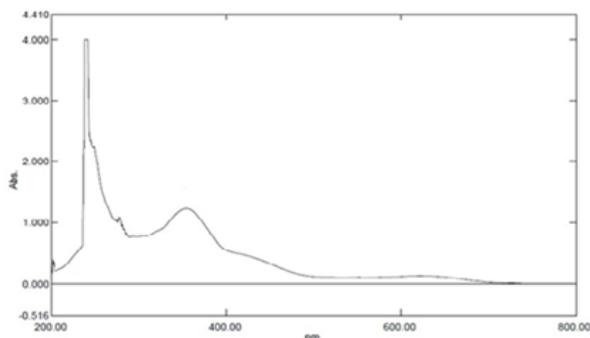


Figure.2 UV-Vis spectrum of Ni(II) complex [NiLP(CH₃COO)₂].2H₂O

IR Spectral data

In Cobalt(II) complex (Figure 3), the vibrational mode at 1614 cm⁻¹ for the azomethine group of free ligand is shifted to lower band at 1613 cm⁻¹ in the complex. It is attributed to the coordination of the N atom of the azomethine group to the metal ion. On complexation, the stretching bands of the carbonyl group at 1723 cm⁻¹ is shifted to lower frequency at 1719 cm⁻¹ is the indicative of the coordination of carbonyl oxygen. The band is little big in the range around 1720 cm⁻¹ is due to the coordination of carboxylato group of acetic acid as well. The vibrational mode observed at ~3400 cm⁻¹ can be attributed to the stretching vibration of the coordinated water molecules. A peak at ~751 cm⁻¹ for the complexes is also assigned to the coordinated water molecule [26]. New bands at 663 and 510 cm⁻¹ are due to the formation of M-O and M-N bonds, respectively [27].

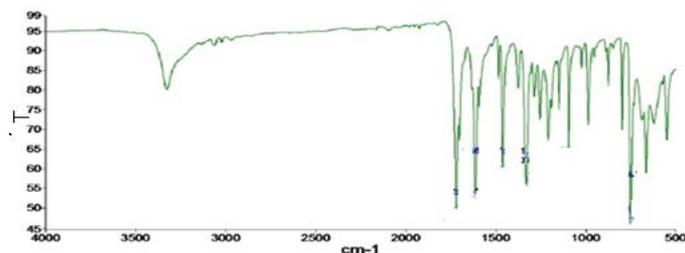


Figure. 3 – IR spectrum of Co(II) complex [CoLP(CH₃COO)₂].3H₂O

In the mixed ligand Nickel(II) complex (Figure 4), the band of azomethine group is shifted to lower frequency at 1612 cm⁻¹ in the complex which reveals the coordination of the azomethine nitrogen atom to the Nickel(II) ion. The stretching bands of the carbonyl group shifted from 1723 cm⁻¹ to 1719 cm⁻¹ is the indication of the coordination of carbonyl oxygen. The water coordination with the metal ions is normally appeared at ~3400 cm⁻¹. A band at ~750 cm⁻¹ in the complexes is also assigned to the coordinated water molecule [26]. The IR Peaks of the Ni(II) complex shows new bands in 663 and 515 cm⁻¹ regions, which is indicative of the formation of Metal-Oxygen and Metal-Nitrogen coordination, respectively [27].

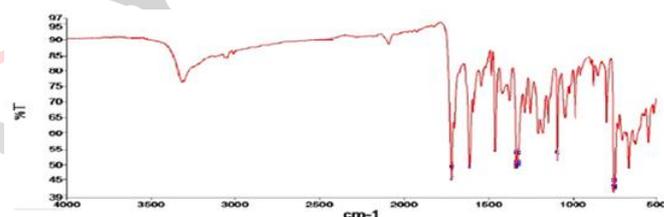


Figure.4 – IR spectrum of Ni(II) complex [NiLP(CH₃COO)₂].2H₂O

Table 1. Analytical and physical parameters of the new Schiff base ligand (L) and its metal complexes

Compound	Empirical formula	Colour	M.W.	Elemental analysis				$\Delta\epsilon$ (Ohm ⁻¹ cm ² mol ⁻¹)	λ (nm)	μ_{eff}
				C	H	N	M			
L	C ₁₄ H ₁₁ N ₃ O ₅ S	Red	269.32	62.86 (62.44)	3.92 (4.12)	16.02 (15.60)	-		353-248	-
CoL(CH ₃ COO) ₂ .3H ₂ O	C ₃₀ H ₃₁ N ₃ O ₈ SCo	Reddish brown	680.59	52.01 (52.94)	4.52 (4.59)	9.79 (10.2)	7.96 (8.66)	11	351, 247, 550, 640	4.90
NiL(CH ₃ COO) ₂ .2H ₂ O	C ₃₀ H ₃₀ N ₃ S Ni	Reddish yellow	662.34	55.70 (54.40)	4.89 (4.41)	9.61 (10.57)	8.02 (8.86)	11	350, 248, 420, 640	3.15

Mass Spectral data

The mass spectra of the Cobalt(II), Nickel(II), complexes (Figures. 5 and 6) show molecular ion peaks at m/z = 681.74771 [M+H]⁺ (28 %), m/z = 663.30140 [M+H]⁺ (36 %), respectively, which coincide with the formula weights of the Schiff base complexes.

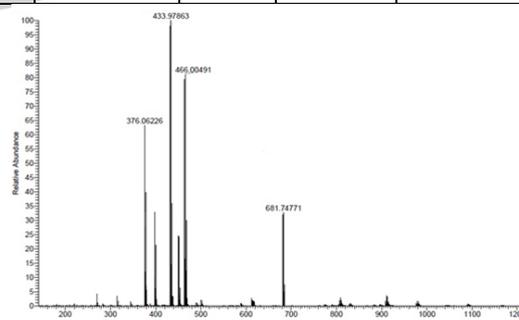


Figure.5 – Mass spectrum of Co(II) complex [CoLP(CH₃COO)₂].3H₂O

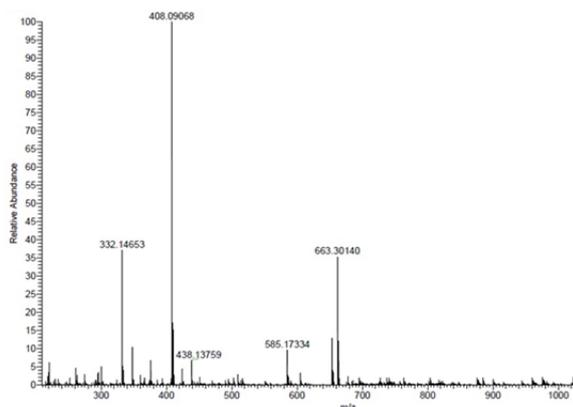


Figure.6 – Mass spectrum of Ni(II) complex $[\text{NiLP}(\text{CH}_3\text{COO})_2] \cdot 2\text{H}_2\text{O}$

Antimicrobial studies

The results of the antimicrobial activities of the synthesized compounds are summarized. Amikacin and Nystatin were taken as references for antibacterial studies (as positive standard) and antifungal studies, respectively and DMSO was used as a negative control. These

Table 2. *In vitro* antimicrobial activity (MIC, $\mu\text{g/mL}$) of the mixed ligand (L) complexes

Compound	Bacterial species				Fungal species		
	<i>E. coli</i>	<i>B. subtilis</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	<i>A. niger</i>	<i>A. flavus</i>	<i>C. albicans</i>
L	24	>100	61	90	48	71	91
$[\text{CoLP}(\text{CH}_3\text{COO})_2] \cdot 3\text{H}_2\text{O}$	72	61	33	>100	56	49	35
$[\text{NiLP}(\text{CH}_3\text{COO})_2] \cdot 2\text{H}_2\text{O}$	55	42	37	21	>100	84	44
Amikacin ^a	05	05	04	05	-	-	-
Nystatin ^a	-	-	-	-	06	06	05

IV. CONCLUSION

A new Schiff base ligand was successfully synthesized from Isatin monohydrazone and 2-Acetyl thiophene and new mixed ligand (1,10-phenanthroline) metal coordination complexes of Co(II) and Ni(II) were also derived. The complexes have been analysed by spectral and thermal characterization techniques. Spectral studies revealed that the coordination of the Schiff base (L) to the metal atom was found to be through the azomethine nitrogen and the carbonyl oxygen. All the complexes were observed to be in octahedral geometry with reference to the magnetic and spectral studies. The antimicrobial activities against four bacterial strains and three fungal strains by disc diffusion method and agar plate technique suggest the possible use of the synthesized compounds for pharmaceutical screenings.

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compounds show moderate to strong activity against microbes. The antibacterial activity is observed to be relatively better than the antifungal activity. The activity studies show that the activity of the metal complexes is better than those of the free ligand (L), which indicates that the complexation to metal enhances the activity of the ligand. These synthesized compounds shows moderate to strong antimicrobial activity. In the antibacterial activity, the two metal complexes show very good activity against all the bacteria and specially against *E. coli* and *B. subtilis*. Against *E. coli* bacteria, the activity of Ni(II) complex is better than the negative standard amikacin. Co(II) complexes also displays moderate activity against the bacteria and also the fungal species. In the case of antifungal activity, Ni(II) complex is more active than the other complexes and the free ligand (L). Here, the Co(II) complex exhibit significant activity against the Gram-negative bacteria, viz., *E. coli* and *B. subtilis*. So the complex reported in this work may possess a possible antitumour effect.

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