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Synthesis, Spectroscopic and Antimicrobial studies of binuclear transition metal complexes with tetradentate Schiff base.

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ABSTRACT

A binucleating Schiff base, H₂L, ligand was synthesized by reaction of 5-bromo-3-fluorosalicylaldehyde and p-phenylenediamine in the molar ratio 1:1 forms stable complexes with transition metal ions such as Cu(II), Ni(II), V(IV), Mn(II) and Co(II). The elemental analysis, conductivity, IR, electronic, ¹H NMR, and magnetic moments were used to characterize the isolated ligand and its metal complexes. The molar conductivity data indicate that the complexes are non-electrolytes. Analytical data suggest 1:1 (M:L) stoichiometry. The ligand acts as dibasic with two N₂O₂ tetradentate sites and can coordinate with metal ions to form binuclear complexes. The bonding sites are nitrogen atoms of the azomethine groups and oxygen atoms of the phenolic groups. The metal complexes exhibit different geometrical arrangements such as square planar, square pyramidal and tetrahedral. The Schiff base ligand and its metal complexes were tested against four pathogenic bacteria (*S. aureus* and *B. subtilis*) as Gram-positive bacteria and (*E. coli* and *K. pneumoniae*) as Gram-negative bacteria and one pathogenic fungi (*A. fumigatus*) to assess their antimicrobial properties.

Keywords: Binuclear complexes, Spectroscopic study, Antimicrobial activity

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INTRODUCTION

Metal complexes of Schiff bases derived from substituted salicylaldehyde and various amines have been extensively investigated. The binucleating Schiff base complexes have numerous applications, such as in the treatment of cancer [1], as antibactericide agents [2], as antifungicide agents [3] and for other biological properties [4]. Several applications have been related for these complexes in chemical analysis, homogeneous and heterogeneous catalysis for oxidation and polymerization of organic compounds [5]. The interest in Schiff base complexes as analytical reagents is increasing since they enable simple and inexpensive determinations of different organic and inorganic substances. The term “binucleating ligands” was first introduced in 1970 by Robson to describe the class of polydentate chelating ligands which able to bind simultaneously two metal ions. Among many different types of binucleating ligands, the salen ligands attracted particularly wide attention of scientists. The high affinity for the chelation of Schiff bases towards the transition metal ions is utilized in preparing their solid complexes. In view of recent interest in the biological activities of the metal-ligand chelates involving Schiff base ligands, we started to study the biological activities of Schiff base complexes derived from tetradentate ligands involving an N_2O_2 donor atom.

This paper describes the synthesis, spectral and magnetic studies of Schiff base derived from 5-bromo-3-fluorosalicylaldehyde and p-phenylenediamine its binuclear Cu(II), Ni(II), V(IV), Mn(II) and Co(II) complexes. Indeed, the biological activity of the ligand and its complexes were screened against selected kinds of bacteria and fungi.

MATERIALS AND METHODS

Experimental

Chemicals were purchased from Sigma-Aldrich and were used without further purification. Methanol, Ethanol, Dimethylsulphoxide and DMF were HPLC grade and were used after purification by the standard methods as described in the literature [6].

Physical measurements

C, H, N micro analysis was carried out with a Perkin-Elmer 2400II elemental analyzer. The FT-IR spectra ($4000-400\text{ cm}^{-1}$) of the compounds were recorded using Bruker Optik GmbH – Tensor 27 of OPUS version 6.5 with solid KBr disc. The electronic spectra were recorded at 300 K on a Perkin-Elmer Lambda 40 (UV-Vis) spectrometer using HPLC grade DMF as solvent in the range 200–800 nm. ^1H NMR spectra was recorded on a Bruker 300 MHz spectrometer using tetramethylsilane as an internal standard. The molar conductance values at room temperature were measured in DMF ($10^{-3}\text{ moldm}^{-3}$) on an Elico digital direct conductivity meter model CM-180. The magnetic studies were carried out at room temperature on a PAR vibrating sample magnetometer (Model-155).

Table 1. Physical and analytical data for the Schiff base, H₂L, ligand and its metal complexes

	Compound	Molecular formula	Colour	Yield (%)	M.P (°C) ^a	Elemental analysis, found (Calc.) ^b [%]			
						C	H	N	M
	H ₂ -BrFsalppd	C ₂₀ H ₁₂ O ₂ N ₂ F ₂ Br ₂	Orange	80	240	39.78 (47.05)	2.37 (2.35)	6.30 (6.27)	–
1	[Cu ₂ (BrFsalppd) ₂]	C ₄₀ H ₂₀ O ₄ N ₄ F ₄ Br ₄ Cu ₂	Dark brown	60	>250	42.12 (41.95)	1.67 (1.74)	4.91 (4.89)	11.23 (11.18)
2	[Ni ₂ (BrFsalppd) ₂]	C ₄₀ H ₂₀ O ₄ N ₄ F ₄ Br ₄ Ni ₂	Light green	62	>250	42.40 (42.35)	1.85 (1.76)	4.91 (4.94)	10.29 (10.34)
3	[VO ₂ (BrFsalppd) ₂]	C ₄₀ H ₂₀ O ₄ N ₄ F ₄ Br ₄ (VO) ₂	Green	65	>250	41.83 (42.94)	1.84 (1.78)	4.55 (5.00)	8.59 (9.10)
4	[Mn ₂ (BrFsalppd) ₂]	C ₄₀ H ₂₀ O ₄ N ₄ F ₄ Br ₄ Mn ₂	Brown	70	>250	42.10 (42.63)	1.69 (1.77)	4.54 (4.97)	9.31 (9.75)
5	[Co ₂ (BrFsalppd) ₂]	C ₄₀ H ₂₀ O ₄ N ₄ F ₄ Br ₄ Co ₂	Greenish brown	65	>250	42.25 (42.33)	1.71 (1.76)	4.75 (4.93)	10.30 (10.38)

^aMelting point of the compound at their decomposition

^b Elemental analyses for C, H and N were within ± 0.4% of the theoretical value

Synthesis of the Schiff base, H₂L, ligand

A solution of 5-bromo-3-fluorosalicylaldehyde (2 mmol) in methanol (30 ml) was slowly added over a solution of p-phenylenediamine (1 mmol) in the same solvent (30 ml). The reaction mixture was heated to reflux for 2 h at 80 °C. The resulting diimine precipitated as an orange solid was filtered off and washed with methanol. The Schiff base ligand so obtained was dried over anhydrous CaCl₂ in a dessicator.

Synthesis of the Schiff base metal complexes

The Ni(II), Cu(II), V(IV), Mn(II) and Co(II) complexes were synthesised by the addition of appropriate metal acetate / sulphate (2 mmol) in ethanol (30 ml) to the hot solution (60 °C) of Schiff base (2 mmol) in the same solvent (30 ml). The resulting mixture was refluxed on a water bath for 3 h were upon the complexes precipitated. They were collected by filtration and purified by washing with ethanol, diethylether and dried over anhydrous CaCl₂.

ANTIMICROBIAL ACTIVITIES

The standardized disc-agar diffusion method [7] was followed to determine the activity of the synthesized compounds against the sensitive organisms *S. aureus* and *B. subtilis* as Gram-positive bacteria, *E. coli* and *K. pneumoniae* as Gram-negative and the fungi *A. fumigatus*. The antibiotic ampicillin was used as standard reference in the case of bacteria and fluconazole was used as a standard antifungal reference.

The tested compounds were dissolved in DMSO (which has no inhibition activity), to get concentration of 2 and 1 mgmL⁻¹. The test was performed on medium potato dextrose agar (PDA) which contains infusion of 200 g potatoes, 6 g dextrose and 15 g agar Uniform size filter

paper disks (three disks per compound) were impregnated by equal volume (10 μL) from the specific concentration of dissolved test compounds and carefully placed on incubated agar surface. After incubation for 36 h at 27 $^{\circ}\text{C}$ in the case of bacteria and 48 h at 24 $^{\circ}\text{C}$ in the case of fungi, inhibition of the organisms which evidenced by clear zone surround each disk was measured and used to calculate mean of inhibition zones.

RESULTS AND DISCUSSION

The resulting solids are intensely coloured and stable in air. The ligand is partially soluble in common organic solvents but the complexes are soluble only in DMF and DMSO.

Elemental analysis

The elemental analysis is in good agreement with that calculated for the proposed formula.

Molar Conductance

Conductivity measurements were carried out in 10^{-3} mol/dm³ DMF solution at 25 $^{\circ}\text{C}$. The room temperature molar conductivity values are given in Table 3. The molar conductance values of the complexes indicate that they are non-electrolytic [8].

¹H NMR Spectra

The ¹H NMR spectra of the free ligand was recorded in DMSO-d₆. The free ligand exhibits sharp low field signal for the phenolic proton between 13.34 and 13.30 ppm. This shows that the Schiff base forms intramolecular hydrogen bonds [9] involving the phenolic proton and the azomethine nitrogen atom, thus implying a phenol-iminic structure. Signal for the methine proton of the azomethine group –N=C(H)– was observed between 8.4–8.7 ppm. In the region of 7.6–6.8 ppm were assigned to chemical shifts for protons of the aromatic ring. The total number of protons present in the Schiff base exhibited signals of the protons in their expected regions and these data are in good agreement with that previously reported for similar compounds.

IR spectra

IR spectra of metal complexes of the Schiff base ligand were compared with that of the Schiff base in order to determine the coordination sites that may involved in chelation. The O–H stretching frequency of the ligand exhibits broad weak intensity band in the 2500–3500 cm⁻¹ range, which is assigned to the intra molecular hydrogen bond O–H ...N=C. This band disappeared in the spectra of the complexes. A strong sharp absorption band around 1631 cm⁻¹ in the spectrum of the Schiff base ligand can be assigned to the C=N stretching. In all the complexes, this band is shifted to lower frequencies in the range 1615–1595 cm⁻¹ upon

complexation with the metal, which can be attributed to the coordination of the imine nitrogen to the metal centre [10].

Table 2. Infrared spectral data of the ligand and its metal complexes (cm⁻¹) and their assignments

	(C=N)	$\nu(\text{C-O})$	$\nu(\text{O-H...N})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$
H ₂ L	1631	1335	3125	–	–
1	1614	1313	–	535	466
2	1614	1315	–	526	449
3	1613	1319	–	530	464
4	1615	1319	–	528	452
5	1595	1316	–	502	446

The frequency of the aromatic carbon and phenolic oxygen of the free ligand at 1335 cm⁻¹ was shifted to lower frequency ($\Delta\nu = 10\text{--}25\text{ cm}^{-1}$) in the binuclear complexes, suggesting the participation of phenolic –OH group in chelation. The band at 982 cm⁻¹ is assigned to $\nu(\text{V=O})$ this band is observed as a new peak for the complexes and is not present in the spectrum of the free ligand. Finally, the appearance of two non-ligand bands in the two ranges 500–550 cm⁻¹ and 440–470 cm⁻¹ in all the complexes could be assigned to the stretching frequencies of $\nu(\text{M-O})$ and $\nu(\text{M-N})$ respectively [11]. Therefore, from the IR spectra, it is concluded that H₂L behaves as a tetradentate ligand with ONNO donor sites coordinating to the metal ions via the azomethine N and deprotonated phenolic O atoms.

Electronic spectra and magnetic moment measurements

UV-Vis spectra provide the most detailed information about the electronic structure. The UV-Vis spectrum of the Schiff base ligand (H₂L) exhibits two charge transfer (CT) bands at 260 nm and 325 nm attributed to $\pi\text{--}\pi^*$ and $n\text{--}\pi^*$ transition within the Schiff base ligand. In the spectrum of the complexes, the CT band at 260 nm remains as such, in agreement with the $\pi\text{--}\pi^*$ transition of the Schiff base ligand. The band observed at 325 nm observed in the spectrum of the free ligand (H₂L) is red shifted to 350–365 nm in complexes in the form of ligand to metal charge transfer (LMCT) transition. Similarly much weaker and less well defined broad bands are found in the spectrum of the complexes at 520–650 nm which are assigned to the d-d transitions. The absorption spectrum of copper complexes show a broad band at about 590 nm attributed to ${}^2B_{1g} \rightarrow {}^2A_{2g}$ transition which is well within the range of 610–555 nm expected for square planar CuO₂N₂ chromophore. The magnetic moment (μ_{eff}) for this complex was found to be 1.74 B.M. per Cu ion which was in usual range for square planar copper complexes and indicating no direct interaction between the two copper centers in the solid state at room temperature [12].

The electronic spectra of the binuclear Ni(II) complexes show a band at 520 nm that may be assigned to the ${}^1A_{1g} \rightarrow {}^1A_{2g}$ transition, indicating a square planar environment around the nickel(II) metal ions [13] which is confirmed by the diamagnetic properties of the complexes.

The binuclear vanadyl complex exhibits only one band in addition to the intense charge transfer band, in the 585 nm region owing to the ${}^2B_{2g} \rightarrow {}^2E$ transition characteristic of square pyramidal geometry. The magnetic moment data of the V(IV) complex was 1.79 B.M. which confirms the binuclear structure of the complex [14].

Table 3. Electronic spectral data and magnetic moment values of the metal complexes

Complex	Electronic spectral bands (nm)	Tentative assignments	Magnetic moments μ_{eff} (B.M.) ^a	Molar conductance ($\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$) in DMF
1	590	${}^2B_{1g} \rightarrow {}^2A_{2g}$	1.74	8.5
2	520	${}^1A_{1g} \rightarrow {}^1A_{2g}$	Diamagnetic	9.8
3	585	${}^2B_{2g} \rightarrow {}^2E$	1.79	15.7
4	545	${}^6A_{1g} \rightarrow {}^4E(G)$	5.71	10.2
5	645	${}^4A_2(F) \rightarrow {}^4T_1(F)$	4.2	12.4

^a B.M. Bohr magneton

The peaks at 415 and 545 nm, which may be assigned to ${}^6A_1 \rightarrow {}^4A_1(G)$ and ${}^6A_1 \rightarrow {}^4E(G)$ respectively are characteristic of four coordinated tetrahedral Mn(II) complex [15]. The magnetic moment of manganese(II) complex is 5.71 B.M. which suggest that the complex is four coordinated.

The cobalt(II) complex shows two weak bands from d-d transitions were observed at 610 and 645 nm which may be assigned to ${}^4A_2(F) \rightarrow {}^4T_1(F)$ correspond to a tetrahedral environment around the Co^{2+} ion. The magnetic moment of Co(II) complex was found to be 4.2 B.M. which is at the lower end of magnetic moments expected for tetrahedral Co(II) complex suggest the dimeric nature of the complex [16].

From the interpretation of elemental analysis, infrared, electronic spectra, EPR, magnetic measurements and molar conductivity, it is possible to draw up the tentative structures of the transition metal complexes. Fig. 4 depicts the representative structure of the metal complexes.

ANTIMICROBIAL ACTIVITY

To contribute in the field of bioinorganic chemistry, the Schiff base ligand, H_2L and its metal complexes were evaluated for antimicrobial activity against two strains Gram-positive bacteria (*S. aureus* and *B. subtilis*), Gram-negative bacteria (*E. coli* and *K. pneumoniae*) and fungi (*A. fumigatus*). The obtained antimicrobials are presented in Table 4. The Schiff base ligand was found to be biologically active. Table 4 shows that all metal complexes exhibit antimicrobial activity in one or more strain and enhanced it comparing with the parent Schiff base. Complexes 1, 2 and 5 showed high activity than complexes 3 and 4. These complexes showed a high activity in Gram-positive, Gram-negative bacteria and intermediate activity for fungi in high and low concentrations. The activity of the Schiff base ligand and its metal

complexes increases as the concentration increases because it is a well known fact that concentration plays a vital role in increasing the degree of inhibition. The structure of the tested compounds seems to be the principal factor influencing the antimicrobial activity. Other factors such as solubility, conductivity and dipole moment, which affected by the presence of metal ions, which may also be possible reasons for increasing the biological activity of the metal complexes as compared to the ligand from which they are derived.

Table 4. Antimicrobial activity of the Schiff base, H₂L, ligand and its Cu(II), Ni(II), V(IV), Mn(II) and Co(II) complexes against different bacteria and fungi

Ligand / Complexes	Diameter of growth of Inhibition Zone (mm)									
	Gram-positive bacteria				Gram-negative bacteria				Fungi	
	S. aureus		B. subtilis		E. coli		K. pneumonia		A. fumigatus	
	A	B	A	B	A	B	A	B	A	B
H ₂ L	20	13	19	12	17	14	17	11	21	17
1	30	21	27	20	28	19	29	19	19	12
2	28	20	26	19	30	22	25	17	23	15
3	25	19	23	16	21	15	19	12	16	11
4	23	17	22	14	20	12	16	11	22	17
5	29	20	24	18	28	19	25	14	29	20
Ampicillin	32	25	30	22	35	25	38	23	–	–
Fluconazole	–	–	–	–	–	–	–	–	37	25

The concentration of A is 2 mgmL⁻¹ and B is 1 mgmL⁻¹

SUMMARY AND CONCLUSION

In the present study, the Schiff base, H₂L, ligand is dibasic with two sets of N₂O₂⁻ tetradentate sites. The Schiff base was allowed to react with metal ions in 1:1 molar ratio (ligand:metal ion) to form the binuclear complexes. For this ligand, copper(II) and nickel(II) exhibit a square planar geometry, oxovanadium(IV) exhibits square pyramidal and tetrahedral geometry for manganese (II) and cobalt (II) complexes respectively. The bonding sites are the azomethine nitrogen atoms and the phenolic oxygen atoms. The ligand and its metal complexes enhanced a moderate antimicrobial activity compared with standard antifungal and antibacterial agents.

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