

Synthesis, Characterization and Biological Activity of Schiff Base Complexes Derived from Sulfadiazine



CHEMISTRY

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ABSTRACT

The new coordination complexes of Co(II), Ni(II) and Cu(II) have been synthesized from Schiff base derived from sulfadiazine and 3-ethoxysalicylaldehyde. The nature of bonding and the structural features of the Schiff base and its complexes have been deduced from elemental analysis, molar conductance, magnetic susceptibility measurements, IR, ¹H NMR, UV-Vis and fluorescence spectral studies. The spectral data of the complexes have revealed bidentate complexing nature of the Schiff base through phenolic oxygen and azomethine nitrogen atoms. These Schiff base and metal complexes were screened for their antimicrobial activity. The complexes exhibit enhanced antimicrobial activity compared to uncomplexed Schiff base

Introduction

Schiff bases are considered as a very important class of organic compounds, which have wide applications in many biological aspects [1]. Schiff bases and their metal complexes have exhibited biological activities as antibiotics, antiviral and antitumour agents because of their specific structure [2-3]. The sulfa drugs are well known for their biological activity. The sulfonamides were the first effective chemotherapeutic agents to be employed systematically for the prevention and cure of bacterial infection in human beings. Compounds containing the sulfonamide group have long been used as drugs for diseases. It has now been observed that some of these drugs show increased biological activity when administered in the form of metal complexes [4]. However complexes containing sulfa drugs are limited. In this paper, we therefore, present the synthesis, characterization and biological studies of Co(II), Ni(II) and Cu(II) complexes of Schiff base derived from sulfadiazine and 3-ethoxysalicylaldehyde.

EXPERIMENTAL materials and Methods

All the reagents used were of AR grade (BDH / E. Merck). Solvents were purified and dried according to the standard procedures. Elemental analysis (C,H,N) were performed using elemental analyser. IR spectra of the ligand and its complexes were recorded in KBr pellets with Perkin Elmer IR RXI Spectrometer in the 4000-400 cm⁻¹ range. The ¹H NMR and ¹³C NMR spectra were recorded on a Bruker 400 MHz

FT- PMR Spectrometer (DMSO-d₆). Magnetic susceptibilities were determined with a magnetic susceptibility meter (MSB-Auto). Melting points were determined using Elico melting point apparatus. The electronic spectra were recorded in Perkin Elmer Lambda 35 spectrometer in the 190-1100 nm range. Fluorescence spectra were detected using Perkin Elmer LS 45 Spectrofluorometer. Conductivity measurements for the complexes were carried out using Elico conductivity bridge and dip type conductivity cell.

Synthesis of Schiff Base (ESSD): To a hot stirred ethanolic solution of sulfadiazine (0.0025 mol) in minimum amount of dimethyl formamide, an ethanolic solution of 3-ethoxysalicylaldehyde (0.0025 mol) was added. The reaction mixture was refluxed for 3hrs. The orange coloured solid mass formed during refluxing was cooled, filtered, washed and dried in a desiccator. The purity of the ligand was checked by melting point, TLC and spectral data.

General method for preparation of metal complexes: To a hot magnetically stirred ethanolic solution of Schiff base (0.002 mol) in minimum quantity of dimethyl formamide, an ethanolic solution of the M(II) acetates (0.001 mol) was added. The mixture was refluxed for 5 hrs on a water bath. The precipitates formed during refluxing were cooled in an ice bath and collected by suction filtration, washed thoroughly with ethanol and pet ether, dried in desiccator over CaCl₂. The coloured solids ob-

tained were mostly insoluble in some common organic solvents and soluble in polar solvents like DMF and DMSO.

Results and discussion

Analytical data: The analytical data obtained for the Schiff base and its complexes agree very well with the proposed molecular formulae and also indicates the formation of 1:2 (M:ESSD) complexes of general formula of

[M(ESSD-H)₂(H₂O)₂] [M=Co²⁺, Ni²⁺ and Cu²⁺] (Table-1).

S. No	Schiff base & Complexes	Elemental analysis % Found (Calcd)				μ_{eff} (BM)
		C	H	N	S	
1	ESSD	57.20 (57.29)	4.50 (4.52)	14.34 (14.07)	8.79 (8.04)	-
2	[Co(ESSD-H) ₂ (H ₂ O) ₂]	51.53 (51.30)	4.49 (4.27)	12.01 (12.60)	8.26 (7.20)	4.64
3	[Ni(ESSD-H) ₂ (H ₂ O) ₂]	50.84 (51.31)	4.90 (4.28)	12.01 (12.60)	6.78 (6.20)	3.46
4	[Cu(ESSD-H) ₂ (H ₂ O) ₂]	51.11 (51.03)	4.77 (4.25)	12.05 (12.53)	7.92 (7.16)	1.98

Molar Conductance: The molar conductance of metal complexes were measured using 10-3M DMF solutions and were found within the range 6-10 ohm⁻¹ cm² mol⁻¹ suggesting the non-electrolytic nature[5] and indicate that no anions are present outside the coordination sphere. (Table-2).

S. No	Schiff base & Complexes	Molecular Formula	Colour	M.Pt (°C)	Yield	μ_{eff} (ohm ⁻¹ cm ² mol ⁻¹)
1	ESSD	C ₁₀ H ₁₀ N ₄ O ₂ S	Orange	190	70	-
2	[Co(ESSD-H) ₂ (H ₂ O) ₂]	C ₃₈ H ₃₈ N ₈ O ₁₀ S ₂ Co	Pale yellow	215	67	9
3	[Ni(ESSD-H) ₂ (H ₂ O) ₂]	C ₃₈ H ₃₈ N ₈ O ₁₀ S ₂ Ni	White	222	55	6
4	[Cu(ESSD-H) ₂ (H ₂ O) ₂]	C ₃₈ H ₃₈ N ₈ O ₁₀ S ₂ Cu	Olive green	225	68	10

IR Spectra: In order to study the bonding mode of Schiff base to the metal complexes, the IR spectrum of the free ligand was compared with the spectra of its complexes.

In the IR spectrum of the Schiff base a band at 1581 cm⁻¹ is assigned to $\nu(\text{-CH=N})$ mode. Evidence of the nitrogen coordination of the azomethine $\nu(\text{-CH=N})$ group to the central metal atom stems from the shift of the frequency from 1581 cm⁻¹ in the ligand to 1660-1694 cm⁻¹ in the metal complexes[6]. The coordination of azomethine nitrogen is further supported by

the appearance of the non ligand band in the region 435-460

cm⁻¹ due to $\nu(M-N)$ in the complexes [7].

The coordination of hydroxyl oxygen is revealed by disappearance of the band at 3349 cm⁻¹. This is further confirmed by the appearance of the new band at 524-579 cm⁻¹. The bands at 1342 cm⁻¹ and 1157 cm⁻¹ in the ligand is assigned to $\nu(SO_2)$ and $\nu(SO_2)$. This band remains almost at the same position in the complexes suggesting that the sulfonamide oxygen is not taking part in coordination.

1H and 13C NMR Spectra: 1H NMR Spectra and 13C NMR Spectra of Schiff base were recorded in DMSO-d₆. The Schiff base showed peak at $\delta = 8.96$ ppm, suggesting the presence of -CH = N linkage. The peaks at $\delta = 12.68$ ppm and 6.88-7.62 ppm indicate hydroxyl and aromatic protons. The peaks in the region at 1.36-1.33 ppm, which is a triplet, is assigned to -CH₃ group of ethoxy substituent on the benzene ring while peaks in the region 4.05-4.10 ppm, which is a quartet, is attributed to -CH₂ protons of the ethoxy substituent [8]. The peaks at 157.19 ppm and 150.77 ppm in the 13C NMR are assigned to azomethine and phenolic carbon. The peak at 64.12 ppm and 14.68 ppm in the 13C NMR are attributed to methylene and methyl carbon of ethoxy substituent.

Electronic Spectra and magnetic susceptibility measurements: The electronic spectrum of Co(II) complex exhibited bands at 36495 cm⁻¹ and 38127 cm⁻¹ corresponding to 4T_{1g}(F) T_{1g}(P) transition and metal to ligand charge transfer transition. The magnetic moment of Co(II) complex was 4.64 B.M suggesting octahedral geometry. The Ni(II) complex exhibited bands at 36496 cm⁻¹, 29478 cm⁻¹ and 12642 cm⁻¹. The first band is due to metal to ligand charge transfer transition, and the other two bands are due to

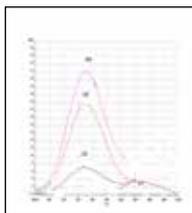
3A_{2g}(F) 3T_{2g}(F) and

3A_{2g}(F) 3T_{2g}(P) transition and the magnetic moment at 3.46 B.M confirms the octahedral geometry. The magnetic moment value of 1.98 B.M measured for the Cu(II) complex lies in the range expected for d₉ system, which contains one unpaired electron with octahedral geometry [9]. The Cu(II) complex exhibited a band at 36115cm⁻¹ and 38210 cm⁻¹ due to

2B_{1g} 2A_{1g} and metal to ligand charge transfer transition.

Fluorescence Spec tra:

The photoluminescence emission spectra of the Schiff base and its metal complexes were recorded in DMSO at room temperature (Figure 1).



Schiff base exhibited a fluorescence emission at 296 nm with excitation at 296 nm. The complexes displayed enhanced emis-

sion intensities compared to the ligand. The metal complexes exhibited strong fluorescence emission at 276, 278, and 277 nm for Co(II), Ni(II) and Cu(II) complexes respectively with excitation around 274 nm. Significant differences in the positions of emission maximum of Schiff base and its complexes establish the coordination of the metal ion to the ligand. The fluorescence spectral results reveal that fluorescence emission intensity of Schiff base increases dramatically on complex formation with transition metal ions. Enhancement of fluorescence through complexation is much interesting as it opens up the opportunity for photochemical applications of these complexes [10]. The order of emission maxima is Ni (II) < Cu(II) < Co(II) < L

Antimicrobial activity:

Antibacterial and antifungal activity of Schiff base and its Co(II), Ni(II) and Cu(II) acetate complexes were investigated against bacterial species like gram positive bacteria Staphylococcus aureus and Klebsiella sp and gram negative bacteria E.Coli and Pseudomonas aeruginosa and fungi Aspergillus niger and Mucor by disc diffusion method [11].

(Table-3).

S. No	Schiff base & Complexes	Staphylococcus aureus	Klebsiella sp	E.Coli	Pseudomonas aeruginosa	Aspergillus niger	Mucor sp
1	ESSD	++	++	+++	+++	++	++
2	[Co(ESSD-H) ₂ (H ₂ O) ₂]	+++	+++	+++	+++	++	+++
3	[Ni(ESSD-H) ₂ (H ₂ O) ₂]	+++	+++	+++	+++	+++	+++
4	[Cu(ESSD-H) ₂ (H ₂ O) ₂]	++	+++	+++	+++	+++	+++

Standard = Ciprofloxacin 5 µg/ disc for bacteria; Nystatin = 100 units/disc for fungi.

Highly active = +++ (inhibition zone > 15mm) Moderately active = ++ (inhibition zone >10mm) Slightly active = + (inhibition zone > 5mm) Inactive = - (<5 mm)

The test was carried out in DMSO solution at a concentration of 100 ppm. Results were compared with standard drug Ciprofloxacin for bacteria and Nystatin for fungi at the same concentration. Metal complexes exhibit higher antimicrobial activities than the uncomplexed ligand. This enhancement in antimicrobial activity of the metal complexes as compared to free ligand can be explained on the basis of chelation therapy [12]. The order of antimicrobial activity was Ni (II) > Co(II) = Cu(II) > L

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