RESEARCH PAPER | Chemistry | Volume : 3 | Issue : 4 | April 2013 | ISSN - 2249-555X



Synthesis, Physico Chemical and Antimicrobial Studies on Schiff Base Complexes of Sulfa Drug with Metals of Life

KEYWORDS: Sulfa drug, Schiff base, Antibacterial, Antifungal

V. Gomathi
PG and Research Department of Chemistry, Seethalakshmi Ramaswami College, Tiruchirappalli-620 002, Tamil Nadu, India.

R. Selvameena
PG and Research Department of Chemistry, Seethalakshmi Ramaswami College, Tiruchirappalli-620 002, Tamil Nadu, India.

ABSTRACT *The new coordination complexes of Co(II), Ni(II) and Cu(II) have been synthesized from Schiff base derived from sulfapyridine and 2-hydroxynaphthaldehyde. 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, ^{1}H &^{13}C NMR, UV-Vis, Cyclic Voltammetry , EPR and fluorescence spectral studies. The spectral data of the complexes have revealed bidentate complexing nature of the Schiff base through azomethine nitrogen atoms and phenolic oxygen. These Schiff base and its metal complexes were screened for their antimicrobial activity. The complexes exhibited enhanced antimicrobial activity compared to uncomplexed Schiff base.*

Introduction

The Schiff base and their metal complexes have more importance recently because of their applications as biological, biochemical, analytical, antimicrobial, anticancer, antibacterial, antifungal and antitumour activity[1-3]. They have been studied as a class of ligands and are known to coordinate with metal ions through the azomethine nitrogen atom[4]. The synthesis of transition metal complexes with Schiff base ligands are studied due to sensitivity, selectivity and synthetic flexibility towards metal atoms [5]. They were used as catalyst, in medicine like antibiotics and anti-inflammatory agents and in the industry as anticorrosion agents [6-12]. Schiff bases derived from sulfa drugs have acquired interest for their useful applications in biological systems. Compounds containing the sulphonamide group have long been used us drugs for diseases. Sulpha drugs with aldehydes, ketones or their derivatives are biologically very active, besides having good complexing ability, their activity has also been shown to increase on complexation with metal ions[13].

EXPERIMENTAL

Materials and Methods

All the reagents used were of AR grade (BDH / E. Merck/ Sigma Aldrich). 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 ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz FT- PMR Spectrometer (DMSO-d_6). Magnetic susceptibilities were determined using Guoy method-PICO make. 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. Cyclic Voltammetric measurements for the complexes were measured using Princeton applied Research –Multichannel Versastat-II.EPR spectra were recorded on Bruker EMX plus with RT.

Synthesis of Schiff Base (HNSP):

To a hot stirred solution of sulfapyridine (0.0025 mol) in ethanol was added a solution of 2-hydroxy naphthaldehyde (0.0025 mol) in ethanol. The reaction mixture was refluxed for 4hrs. The yellow coloured solid mass formed during refluxing was cooled to room temperature, filtered and washed thoroughly with ethanol. The purity of the ligand was checked by 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 5-6hrs 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 $CaCl_2$. The coloured solids obtained were mostly insoluble in some common organic solvents and soluble in polar solvents like DMF and DMSO.

Results and discussion

Physical character:

The physical characteristics of the Schiff base and its complexes are given in Table 1.

Table -1 Physical Characteristics of the Schiff base and its complexes

S. No	Schiff base & Complexes	Molecular Formula	Colour	M.Pt (°C)	Yield	Λ_m (ohm^{-1} cm^2 mol^{-1})
1	HNSP	$C_{22}H_{17}N_3O_3S$	Yellow	238	82	-
2	$[Co(HNSP\text{-}H)_2(H_2O)_2]$	$C_{44}H_{36}N_6O_8S_2Co$	Merun	298	73	15.20
3	$[Ni(HNSP\text{-}H)_2(H_2O)_2]$	$C_{44}H_{36}N_6O_8S_2Ni$	Chrome yellow	296	66	12.00
4	$[Cu(HNSP\text{-}H)_2(H_2O)_2]$	$C_{44}H_{36}N_6O_8S_2Cu$	Dark green	294	71	16.00

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:HNSP) complexes of general formula of $[M(HNSP\text{-}H)_2(H_2O)_2]$ [M=Co^{2+}, Ni^{2+} and Cu^{2+}]. (Table-2)

Molar Conductance:

The molar conductance of metal complexes are measured using 10^{-3}M DMF solutions and are found within the range 12.00-16.00 ohm^{-1} cm^2 mol^{-1} suggesting the non-electrolytic nature[14] and indicate that no anions are present outside the coordination sphere. (Table-2)

Volume : 3 | Issue : 4 | April 2013 | ISSN - 2249-555X

Table-2
Analytical data and cyclic voltammetric data of Schiff base and its complexes

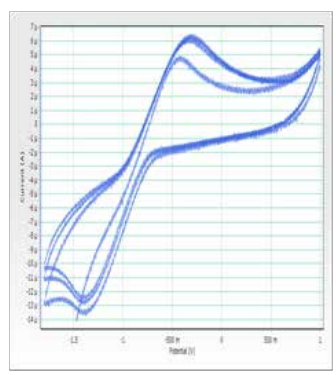
S.No	Schiff base & Complexes	Elemental analysis % Found (Calcd)				μ_{eff} (BM)	Cyclic voltammetric data(V)		
		C	H	N	S		E_{pa}	E_{pc}	ΔE
1	HNSP	65.50 (65.51)	4.00 (4.22)	9.84 (10.42)	7.63 (7.94)		-	-	-
2	$[Co(HNSP-H)_2(H_2O)_2]$	58.06 (58.74)	4.78 (4.00)	8.86 (9.34)	7.32 (7.12)	4.04	-0.44	-1.50	1.06
3	$[Ni(HNSP-H)_2(H_2O)_2]$	58.71 (58.75)	4.63 (4.00)	9.92 (9.35)	7.77 (7.12)	3.68	-0.20	-1.55	1.35
4	$[Cu(HNSP-H)_2(H_2O)_2]$	57.82 (58.44)	3.95 (3.98)	8.55 (9.30)	7.65 (7.08)	1.70	-0.4	-1.45	1.05

IR Spectra:
In order to study the bonding mode of Schiff base to the metal complexes, the IR spectrum of the free ligand is compared with the spectra of its complexes. In the IR spectrum of the Schiff base a band at 1618 cm^{-1} is assigned to ν(-CH=N) mode. This band shifts to 7-18 cm^{-1} after complexation, indicating the coordination of azomethine nitrogen to metal ion. The coordination of azomethine nitrogen is further supported by the appearance of the non ligand band in the region 450-460 cm^{-1}due to ν(M-N) in the complexes. The coordination of hydroxyl oxygen is revealed by the disappearance of the band at 3428 cm^{-1}. This is further confirmed by the appearance of the new band at 574-575 cm^{-1}due to ν (M-O). The bands at 1358 cm^{-1} and 1133 cm^{-1} in the ligand is assigned to $\nu_{as}(SO_2)$ and $\nu_s(SO_2)$[15]. This band remains almost at the same position in the complexes suggesting that the sulfonamide oxygen is not taking part in coordination.

^{1}H and ^{13}C NMR Spectra
^{1}H NMR Spectra of free ligand and its Zn(II) complex were recorded in DMSO-d_6. The ligand showed peak at δ = 8.9 ppm, suggests the presence of –CH = N linkage [15]. The peaks at δ = 10.81 ppm and 6.53 – 8.47 ppm indicate hydroxyl and aromatic protons. The coordination of the azomethine nitrogen is inferred by the shifting of the >CH = N proton signal from 8.9 ppm in the ligand to 8.49 ppm in the complexes. The disappearance of peak at δ = 10.81 ppm indicates the deprotonation of hydroxyl proton and co-ordination of oxygen to the metal[16]. ^{13}C NMR spectral data of the free ligand was recorded in the DMSO-d_6. The peak at 156.53 ppm and 170.95 ppm are assigned to azomethine and phenolic carbon.

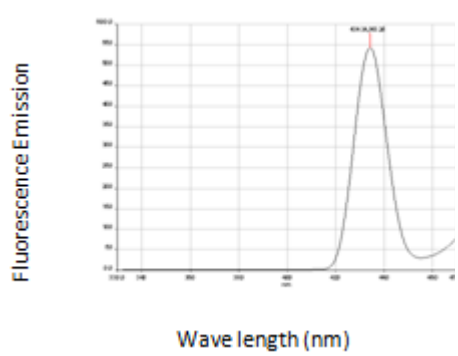
Electronic Spectra and magnetic susceptibility measurements:
The electronic spectrum of Co(II) complex exhibited four bands at 37610 cm^{-1}, 37145 cm^{-1} 31970 $cm^{-1}$and 24226 cm^{-1}. The three high energy bands are due to 4T1g(F) → T_1g(P) and the fourth low energy band is due to $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ transition . The magnetic moment of Co(II) complex was 4.04 B.M suggesting octahedral geometry. The Ni(II) complex exhibited bands at 38795 cm^{-1}, 37120cm^{-1} and 24412 cm^{-1}. The first two bands are due to n → σ* transition, and the third band is due to n → π* intraligand transition[17] and the magnetic moment at 3.68 B.M confirms the octahedral geometry. The Cu(II) complex exhibited strong high energy band at 36706 cm^{-1} , 31251 cm^{-1} and 24186 cm^{-1} is due to intraligand transition,$^2B_{1g} \rightarrow {}^2E_g$ transition and $^2E_{(g)} \rightarrow {}^2T_{2g}$ transition respectively. The magnetic moment value of 1.70 B.M measured for the Cu(II) complex lies in the range expected for d^9 system, which contains one unpaired electron with octahedral geometry.

Cyclic Voltammetry:
Electrochemical cyclic voltammetry measurements were performed at room temperature in an airtight three electrode cell by using glassy carbon electrode with 0.071 cm^2 surface area as a working electrode, a platinum wire served as the counter electrode and a Ag/AgCl in a saturated KCl solution as reference electrode. The electrochemical reaction was charged with 10 ml DMF solution of all the complexes ($1x10^{-4}$M) and n-Bu_4NClO_4 [18] (0.1M) as supporting electrolyte. Measurements were made over a potential range between -2 V to +1.5 V for Co(II) Ni(II) andCu(II) complexes with a scan rate of 0.1 V/s. Cyclic voltammetric parameters for all compounds are summarized in Table 2. The difference between forward and backward peak potential can provide a rough evaluation of the degree of the reversibility of one electron transfer of the metal centre. The analysis of cyclic voltammetric responses gives the evidence for a quasi-reversible one electron reduction. The separation in peak potentials for the complexes are in the order Ni(II)>Co(II) >Cu(II). The cyclic voltammogram of $[Ni(ESSP-H)_2(H_2O)_2]$ is given in Figure (1).



Cyclic voltammagram of [Co(HNSP-H)2(H2O)2] Figure(1)

Fluorescence Spectra:
The photoluminescence emission spectra of the Schiff base and its nickel complex were recorded in DMSO at room temperature (Figure 2). Schiff base exhibited a fluorescence emission at 434 nm with excitation at 319 nm. The nickel complex exhibited strong fluorescence emission at 345nm with excitation at 269 nm. The quenching in this Ni(II) complex indicate that the that the ligand has a potential for trace analysis of some transition metals with fluorometric method[19].

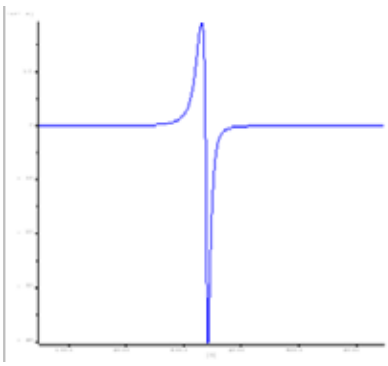


Fluorescence Spectra of HNSP Figure(2)

EPR Spectra:
EPR spectra of powdered samples were recorded on Bruker EMX plus with room temperature at 9782 MHz with 6000 G.(Figure 3). Both parallel and perpendicular features of

Volume : 3 | Issue : 4 | April 2013 | ISSN - 2249-555X

Cu are resolved in the spectra, which are characteristics of axial symmetry. The g value of Cu(II) complex is found to be around 3.5 confirms the presence of unpaired electron in the dx^2-y^2 orbital of Cu(II) complex. The lines of this type usually observed are either due to the intermolecular spin exchange, which may broaden the lines or to the occupancy of the unpaired electron in the degenerate orbital. The nature and pattern of the EPR spectra suggests an almost octahedral environment around the Cu(II) complex. (Figure 3)



EPR spectrum of [Cu(HNSP-H)2(H2O)2] Figure (3)

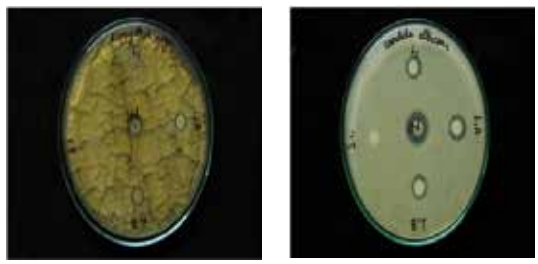
Antibacterial activity:
The synthesized Schiff base and its metal (II) complexes were screened(Table-3and Figure 4) in-vitro for antibacterial activity against gram positive (Staphylococcus aureus) and gram negative (Pseudomonas aeruginosa) bacterial strains using the disc diffusion technique [20]. The test was carried out in DMSO solution at a concentration of 100ppm using Muller Hinton agar media. Ciprofloxacin was used as the standard drug. Here it is evident that overall potency of uncoordinated compound is enhanced on coordination with metal ions. However the Ni(II) complex is observed to be the most active against various species.

Table-3
Antimicrobial Activity of Schiff base and its complexes

Antimicrobial activity of the ligand and complexes	Staphylococcus aureus	Pseudomonas aeruginosa	Candida albicans	Aspergillus niger
HNSP	15	14	14	12
$[Co(HNSP\text{-}H)_2(H_2O)_2]$	15	12	16	16
$[Ni(HNSP\text{-}H)_2(H_2O)_2]$	20	22	16	15
$[Cu(HNSP\text{-}H)_2(H_2O)_2]$	15	20	20	15

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

Highly active = inhibition zone > 15mm ; Moderatively active = inhibition zone >10mm; Slightly active = inhibition zone > 5mm ; Inactive = -<5 mm



Antifungal Activity of HNSP(L1), [Co(HNSP-H)2(H2O)2] (L1A)and [Ni(HNSP-H) 2(H2O)2](L1B)
Figure(4)

Antifungal Activity:
Antifungal activity of Schiff base and metal complexes were studied against two fungal cultures Candida albicans and Aspergillus niger species at concentration of 100 ppm using Sabouraud dextrose agar media disc diffusion technique [21]. Nystatin was used as the standard drug. Here it is evident that overall potency of uncoordinated compound is enhanced on coordination with metal ions. However the Cu(II) complex is observed to be the most active against various species.

Conclusion:
Based on the analytical and spectral data, it is found that the Schiff base acts as a bidendate ligand and the resulting complexes have octahedral geometries and the probable structure of the complexes proposed in the present work is given in Figure 5.

Proposed structure of the complexes

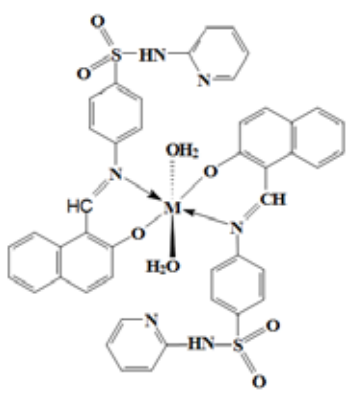


Figure (5)
M=Co(II), Ni(II) and Cu(II)

Acknowledgements
The authors are thankful to the University Grants Commission, Hyderabad, India, for the financial support. Laboratory facilities provided by the Management and all the Faculties, PG and Research Department of Chemistry, Seethalakshmi Ramaswami College, Tiruchirappalli are gratefully acknowledged.

REFERENCE 1.Mishra, Lallan and Sinha, Indian J. Chem., A,29, 1131(2000) 2.Uday and Ray, Indian J. Chem., A,40, 228 (2001) 3.K. Krishnankutty and Ummathur Mohammed Basheer, J. Indian Chem Soc.,83,663 (2006) 4.K. Arora, K.P.Sharma., Synth.React.Inorg.Met-Org.Chem.,32,913 (2003) 5.C. Spinu and A. Kriza, Acta Chim Slow,47,179 (2000) 6.B.Sun, J. Chen, J.Y. Hu and Lix, J.Chin Chem Lett.,12(11)1043 (2001) 7. Boghaei D.M. and Mohebi S, Tetrahedron., 58 (26), 5357 (2002) 8. Liu J, Wu B, Zhang B and Liu Y, Turk. J. Chem., 30, 41 (2006) 9. Britovsek G J P, Gibson V. V., Mastroianni S, Oakes D C H, Red Shaw C, Solan G. A., White A. J. P. and Williams D. J., Eur. J. Inorg.Chem., (2), 431 (2001) 10. Budakoti A., Abid M. and Azam A, Eur. J. Med. Chem., 41(l), 63 (2006) 11. Jin V.X., Tan S.I. and Ranford J.D., Inorg. Chim. Acta.,358(3), 677 (2005) 12. Mehta N.K. and Agarwala V.S., Int. Corros. Cong. Proc.,13 (319), 1 (1996) 13. G.T. Morgan, and H.D. Kdrew,; J. Chem. Soc, 1920, 117, 1456. 14.V. Gomathi and R.Selvameena, IJSR,2013,2(3),24-25. 15. V. Gomathi and R.Selvameena, Asian Journal of Chemistry2013,25(4),2083-2086. 16. V.L. Chavan and B.H. Mehta, Asian J. Chem,, 22(8) 5976-5980 (2010) 17.Maurya R C &Patel S & Rajput S , Synth React Inorg Met-org Chem, 2003,33,801. 18.Hamdi Temel, Salih Ilhan, Mehmet Aslanoglu, Ahmet Kilic, Esref Tas, J.chin.Chem.Soc,2006,53,1027-1031. 19. Gulnur Kesr Karaoglan, Ulvi Avciata and Ahmet Gul, Indian Journal of Chemistry,46A,2007,1273-1276. 20. Zahid H Chohan and Sabuhi mushtaq, Pakistan Journal of Pharmacetical Sciences 13(1);21-27(2000) 21. J. H. Chohan and M. M. Naseer, Appl. Organomet. Chem, 21,728-738 (2007)