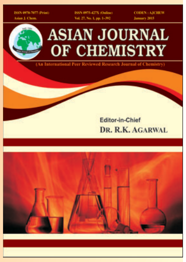
Asian Journal of Chemistry; Vol. 27, No. 3 (2015), 941-948

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2015.17627



Synthesis, Characterization and Antimicrobial Properties of Some Transition Metal Complexes with NS-Chelating Schiff Base Ligand Incorporating Thiophene and Sulfonamide Moieties

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Received: 19 March 2014; *Accepted*: 25 May 2014; *Published online*: 19 January 2015; AJC-16701

Schiff base namely 4-[(thiophene-2-yl)methyleneamino]phenyl sulfonamide (L) and its Co(II), Ni(II), Cu(II) and Zn(II) complexes were synthesized and characterized by UV-visible, IR, ^{1}H NMR, MS-EI, elemental analysis and TGA. Molar conductance and magnetic susceptibility of the complexes were also analyzed. Elemental analyses confirmed a 2:1 molar ratio of ligand to metal ion of the complexes. IR spectra revealed that the ligand is coordinated to the metal ions through azomethine-N and thiophene-S. On the basis of experimental data octahedral geometry was proposed for all complexes. Thermal studies together with IR showed the presence of lattice and coordinated water molecules in all complexes. The *in vitro* antimicrobial activities of the compounds were tested against *S. aureus*, *K. pneumoniae*, *C. albicans* and *C. krusei* by the agar well diffusion assay. The result indicated that the ligand become antimicrobially active on chelation with metal ions. It was found that Cu(II) complex showed the highest antibacterial activity among all complexes.

Keywords: Transition metal(II) complexes, 4-[(Thiophene-2-yl)methyleneamino]phenyl sulphonamide, Octahedral geometry.

INTRODUCTION

In recent years, different families of organic-inorganic chemicals are being investigated extensively because of their medicinal applications. Sulfonamides and their derivatives are one of those families. They were the first effective drugs found to act selectively and could be used systematically as preventive and therapeutic agents against various diseases[1-7]. The development of sulfonamides is a fascinating and informative area in medicinal chemistry[8-10]. Many chemotherapeutically important sulpha drugs, like sulphadia-zine, sulphathiazole and sulphamerazine possess -SO_2NH- moiety as an important toxophoric functional group.

Amino substituted sulfonamide undergoes condensation reaction with carbonyl compounds to form sulfonamide Schiff bases[11-13]. These schiff bases have been reported to posses antimicrobial[14-17], anticancer cell[18], antimalarial[19,20] and antihelmintic activities[21]. The presences of azomethine and sulfonyl functional group are responsible for antimicrobial activity.

Sulfonamide containing Schiff bases and their transition metal complexes had been previously prepared, characterized with different analytical and spectroscopic techniques and tested for their antimicrobial activities. It has been reported that the biological activities of Schiff bases get enhanced on coordination with metals. Though many schiff base metal complexes have been synthesized and tested for their antimicrobial activities against different disease causing bacteria and fungi, they however not satisfactory in acting against the same effectively[22-25]. To design effective chemotherapeutic agents and better antimicrobial drugs, it is essential to explore the interactions of metal with different Schiff bases. Hence, in the present work, we report the synthesis and characterization of a Schiff base derived from 2-thiophenecarboxaldehyde and sulfanilamide and it's Co(II), Ni(II) Cu(II) and Zn(II) complexes to gain more information about related structural and spectral properties. They were thoroughly characterized on the basis of their melting point, TLC, FT-IR, ^{1}H NMR, elemental analysis, UV-visible, MS, TGA, Magnetic moment and molar conductivity. Based on the spectral and analytical data geometry of the complexes was proposed. Furthermore, antimicrobial activity of the sulfonamide-imine and its M(II) complexes were evaluated against two pathogenic bacterial and two fungal strains by the agar well diffusion assay.

EXPERIMENTAL

All chemicals used in this investigation were of the analytical reagent grade (AR) and of highest purity available. They included 2-thiophenecarboxaldehyde (spectrochem), sulfanilamide (LOBA Chemie), copper(II) chloride (Fisher Scientific), cobalt(II) chloride (Fisher Scientific), nickel(II) chloride (Fisher Scientific), zinc chloride (Fisher Scientific), absolute ethanol (Hayman), dimethyl formamaide (SRLA), tetrahydrofuran (Fisher), dichloromethane (Fisher), dimethyl sulphoxide (SRLA), glacial acetic acid (Fisher), acetonitrile (Fisher) and chloroform (Fisher).

Physical measurements: The purity of the compounds was checked using precoated TLC plates using hexane:ethyl acetate (3:1) solvent system. The developed chromatographic plates were visualized under ultraviolet light. Melting point of the ligand and decomposition temperature of complexes were determined by open capillary on Stuart Melting point, SMP10, instrument. IR spectra of the ligand and complexes were recorded using KBr pellets in the range (4000-400 cm^{-1}) on FT-IR spectrometer Perkin-Elmer Infrared model 337. Elemental analyses were performed on a Perkin Elmer Model 240C Elemental Analyzer. ^1H NMR spectrum of the ligand in DMSO-d_6 was recorded on a 500 MHz FT NMR Spectrometer using TMS as internal standard. Electronic absorption spectra were obtained on a Perkin-Elmer Lambda 35 UV-visible spectrophotometer using a prepared CH_3CN solution (10^{-5} mol/L). The EI mass spectrum of the ligand was recorded on waters ESI mass spectrometer. Metal estimation in the complexes and consequently molar ratio of metal to ligand of the complexes were obtained from complexometric titration against standard EDTA solution at a suitable pH value using the suitable indicators. The conductivity measurements were measured in acetonitrile solutions (0.001 M) using digital conductivity meter-611. Room magnetic susceptibilities of the complexes were determined on well ground solid samples by using MSB-AUTO, Sherwood scientific magnetic susceptibility balance using Hg $[Co(NCS)_4]$ as standard. Thermogravimetric analysis of complexes has been carried on SDT Q600 V8.0 Build 95 instrument in the temperature range of 30-800 °C.

Synthesis of Schiff base (L): Sulfanilamide (1.84 g, 0.0107 mol) dissolved in a 40 mL of mixture of THF/EtOH in a ratio of 1:4, v/v was mixed with 2-thiophenecarboxaldehyde (1 mL, 0.0107 mol), which was dissolved in 30 mL of a mixture of same solvent followed by addition of glacial acetic acid (2.5 mL) to prepare a Schiff base 4-[(thiophene-2-yl)methyleneamino]phenyl sulphonamide. The reaction mixture was refluxed on oil bath at 75 °C for 6 h with continuous stirring. The progress of the reaction was monitored by TLC. The mixture was cooled and poured into ice-cooled water to precipitate Schiff base. The resulting coloured precipitate was filtered and dried in vacuum oven at 80 °C. The dried solid product was recrystallized twice from hot ethanol and then dried under reduced pressure over anhydrous $CaCl_2$ in a desiccator. The product isolated as shiny yellow powder in 92 % yield. The melting point of the product was found to be 217 °C.

Synthesis of metal complexes: All the Schiff base metal complexes were prepared by the same general procedure with stoichiometric amount of ligand and metal salts in a 2:1 mole ratio. To a 40 mL of CH_2Cl_2 solution of Schiff base ligand (0.05012 g, 0.000188 mole), 20 mL of methanolic solution of corresponding Co(II), Ni(II), Cu(II) and Zn(II) chlorides (0.000188 mole) was added drop wise. Then the mixture was refluxed with continuous stirring for 2 h and then pH of the solution was adjusted to 7-7.5 using aqueous solution of 0.1 N NaOH and further refluxed with stirring for about 8-16 h. The completion of the reaction was monitored by TLC. The resulting solution was reduced to 1/3rd of its volume and kept aside for one day. On standing, solid metal complexes were obtained and collected by vacuum filtration, washed with water, diethyl ether followed by ethanol. The final products were kept in an oven for drying. All complexes were stable up to 300 °C.

Determination of metal content of the chelates: 10 mg of each of the synthesized chelates was accurately weighed and placed in Kjeldahl flask. 10 mL of concentrated nitric acid was added initially to the powdered chelates, to start the fast wet oxidation digestion. This mixture had been digested by a gradual heating with dropping of H_2O_2 solution. This treatment was conducted until most of the powdered complexes were diminished and the remained solution had the colour of the corresponding metal salt. This solution was diluted up to 35 mL with distilled water and the metal content was determined by complexometric titration against standard EDTA solution at a suitable pH value using the suitable indicator.

Chloride ion test in the complexes: The test for ionizable chloride (s) in each of the metal complexes was determined by the titration of the samples, whose concentrations are unknown, with standard solution of silver nitrate in the presence of 1 mL of potassium chromate as an indicator[26]. The end point of the titration was determined by the formation of a red precipitate. The number of moles of chloride was thus calculated based on titration value.

Biological activity: The antimicrobial activity of the synthesized Schiff base ligand, L and its Co(II), Ni(II), Cu(II) and Zn(II) complexes were determined by the agar well diffusion assay[27]. The bacteria strains: *Klebsiella pnuemonia* and *Staphylococcus aureus* and the fungal strains: *Candida albicans* and *Candida krusei* were selected because of their clinical relevance. The bacterial and fungal strains used for the assay were maintained on Nutrient agar and Sabouard dextrose agar, respectively. In the agar diffusion method, Muller-Hinton agar and Sabouard dextrose agar were sterilized in flasks and poured into sterile petriplates and allowed to solidify. The inoculum was prepared by suspending the colonies of the organisms to be tested in 0.9 % sterile saline and turbidity adjusted to 0.5 McFarland standard (10^8 UFC/mL). Sterile swabs were used for inoculating the surface of the petriplates and wells of 7 mm diameter were aseptically bored into the culture medium and 50 μL of compounds dissolved in DMSO were added to these wells. DMSO alone was used as negative control along with the antimicrobials. Voriconazole and ampicillin were used as positive controls for fungi and bacteria, respectively. The plates were incubated aerobically at 37 °C for 24 h and the antimicrobial activity was assessed by measuring the inhibition halo of microbial growth around the well.

RESULTS AND DISCUSSION

Schiff base characterization: The structure of the synthesized ligand was confirmed on the basis of its elemental analysis and spectral data. The result of elemental analyses (C, H, N) with molecular formula and melting point are presented in

Table-1. The elemental analysis of the prepared ligand is consistent with the calculated results from the empirical formula of the ligand and the melting point is sharp indicating the purity of the prepared Schiff base. The structure of the Schiff base under study is given in Fig. 1.

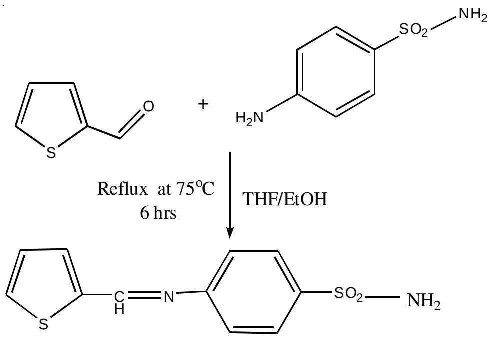


Fig. 1. General scheme for the synthesis of Schiff base (L)

The mass spectrum of the Schiff base ligand (Fig. 2) showed a signal with *m/z* ratio of 266.35 (R.I.100 %, base peak) which is same as the calculated formula *m/z* = 266.35.

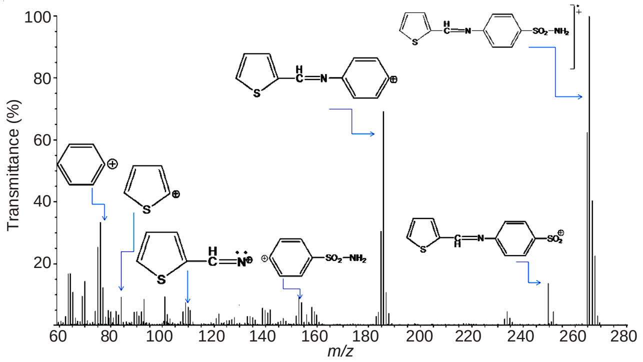


Fig. 2. Mass spectrum of the ligand

This *m/z* ratio of 266.35 confirms its molecular formula $C_{11}H_{10}N_2O_2S_2$. It is obvious that, the molecular ion peak is in good agreement with its suggested empirical formula as indicated from elemental analyses (Table-1). Peaks of *m/z* ration at 250.35 (15 %), 234.35 (10 %), 186 (76 %), 156 (10 %) and 76 (34 %) confirm the suggested structure illustrated in Fig. 1. The other peaks appeared in the mass spectrum are attributed to the fragmentation of L molecule obtained from the rupture of different bonds inside the molecule as shown in Fig. 3. The fragments were in good agreement with the proposed formula of the Schiff base ligand.

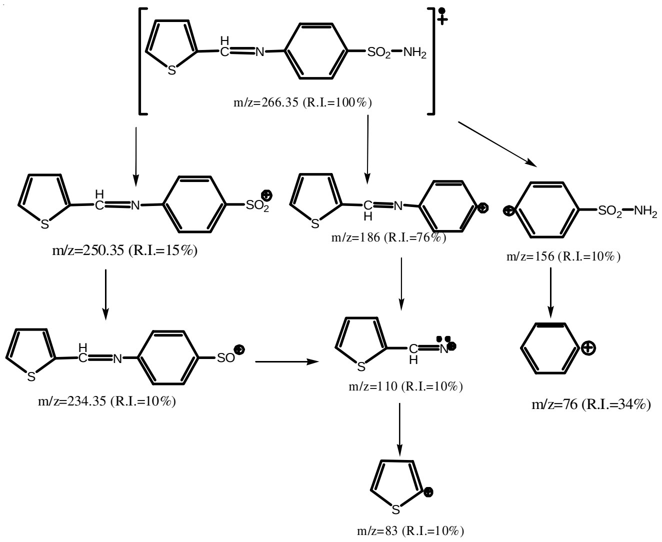


Fig. 3. Suggested mass fragmentation of the ligand

The structure of the Schiff base is also confirmed by IR, UV-visible and ^{1}H NMR spectra.

Composition and structure of metal complexes: The isolated solid metal complexes of Co(II), Ni(II), Cu(II) and Zn(II) ions with Schiff base ligand (L) were subjected to elemental analyses (C, H, N and metal), IR, magnetic studies, thermal analyses, electronic spectra, ^{1}H NMR and molar conductance to identify their tentative formulae in a trial to elucidate their molecular structures. The elemental analyses of the complexes are consistent with the calculated results from the empirical formula of each compound. The elemental analyses confirmed that the complexes have 2:1 molar ratio of the ligand to metal ion. The results of elemental analyses listed in Table-1 suggest the proposed general formulae of the prepared complexes as:$[M(L)_2(H_2O)_2]Cl_2.nH_2O$ (n = 0.5 for M = Ni(II), Co(II), Cu(II) and n = 1 for M = Zn(II)).

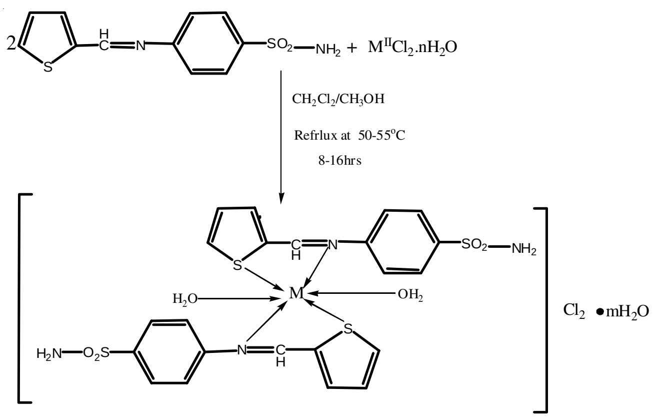
Colour change of the complexes along with decomposition point show characteristic differences between Schiff base and metal complexes. The melting points of the complexes are higher than the ligand revealing that the complexes are

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

	Compound {Empirical formula}	Color	Yeld: (%)	m.p. (°C)	Elemental analysis (%): Found (calcd.)				
					C	H	N	M	Λ_m
L	$C_{11}H_{10}O_2N_2S_2$	Shiny yellow	(92)	217	49.52	3.77	10.48	-	-
					(49.56)	(3.75)	(10.51)		
1	$[Co(L)_2(H_2O)_2]Cl_2{\cdot}0.5H_2O$	Black	(66)	> 300	37.29	3.58	7.97	8.31	269
	$\{C_{22}H_{25}CoCl_2N_4S_4O_{6.5}\}$				(37.33)	(3.54)	(7.92)	(8.33)	
2	$[Ni(L)_2\,(H_2O)_2]Cl_2{\cdot}0.5H_2O$	Black	(64)	> 300	37.30	3.55	7.91	8.27	
	$\{C_{22}H_{25}NiCl_2N_4S_4O_{6.5}\}$				(37.34)	(3.54)	(7.92)	(8.30)	287
3	$[Cu(L)_2(H_2O)_2]Cl_2{\cdot}0.5H_2O$	Black	(72)	> 300	37.12	3.53	7.82	8.94	
	$\{C_{22}H_{25}CuCl_2N_4S_4O_{6.5}\}$				(37.09)	(3.51)	(7.87)	(8.92)	255
4	$[Zn(L)_2\,(H_2O)_2]Cl_2{\cdot}H_2O$	Dark green	(66)	> 300	36.51	3.58	7.77	9.11	
	$\{C_{22}H_{26}ZnCl_2N_4S_4O_7\}$				(36.53)	(3.60)	(7.75)	(9.05)	231

Λ_m = Molar conductance ($cm^2\Omega^{-1}mol^{-1}$)

much more stable than the ligand. All compounds are stable in air. The chemical equations concerning the formation of the Schiff base and its metal complexes are represented in Figs. 1 and 4, respectively. The interaction of the ligand with the appropriate metal chlorides in a mixture of CH_2Cl_2/CH_3OH solvents in a molar ratio of 2:1 under reflux conditions gave the products presented in Table-1.



m=0.5 for M= Ni(II),Co(II),Cu(II) and m=1 for M= Zn(II)

Fig. 4. General scheme for the synthesis of M(II) complexes

Molar conductance measurements: Table-1 shows the molar conductance values of metal complexes. The molar conductance values of the synthesized complexes were determined at room temperature using 1×10^{-3} M concentration in acetonitrile as solvent, are in the range of 220-300 Ω^{-1} cm^2 mol^{-1}. These values suggested electrolytic nature of the complexes with a cation to anion ratio of 1:2 and the anions present are not coordinated to the metal ions. This is in accordance with the fact that conductivity values for an electrolytes are above 220 Ω^{-1} cm^2 mol^{-1} in acetonitrile solution[28].

IR spectra and mode of bonding: The IR spectra of the complexes are compared with that of the free ligand in order to determine the coordination sites that may be involved in chelation. There are some guide peaks, in the spectra of the ligand, which are of good help for achieving this goal. The position and/or the intensities of these peaks are expected to be changed upon chelation. The new peaks in the IR spectra of the complexes are also guide peaks in chelation. These guide/characteristic peaks are listed in Table-2 together with the assignments for most of the major peaks. The ligand used in this investigation is a neutral one having two coordination sites, N of azomethine and S of thiophene, that can bind to the metal ion.

In the IR spectrum of the ligand, N-H (primary amine) and C=N (azomethine) stretching vibrations and N-H bending; NH_2 were observed at 3290, 1607 and 1579 cm^{-1}, respectively. These values are in agreement with those observed for similar compounds[11,12,22]. The azomethine vibration of the ligand at 1607 cm^{-1} was shifted to lower or higher frequencies after complexation, 1630, 1624, 1628 and 1602 cm^{-1} for Co(II), Ni(II), Cu(II) and Zn(II) complexes, respectively. This clearly indicates coordination of the Schiff bases through the azomethine nitrogen[26,29-32].

In addition, the free ligand exhibits two bands at 1335 and 1314 cm^{-1} due to ν_{asym}(S=O) and ν_{sym}(S=O) stretching vibration of $-SO_2-$ moiety, respectively. These bands remain unchanged in all complexes up on complexation. This indicates the non participation of O of sulfonyl group of sulfonamide,$-SO_2-NH_2$, in coordination of the complexes[33].

The band at 1153 cm^{-1} in the free ligand is observed at almost the same region in complexes spectra. These bands can be attributed to the ν(ph-N) and the slight change in wave numbers may be understood as a result of changing the electron density of the aromatic system due to complexation[20, 23,25]. The free ligand also exhibits two bands at 846 and 721 cm^{-1} due to ν(C-S-C) asymmetric and symmetric stretching vibration of thiophene moiety, respectively. These bands shifted to higher or lower stretching frequency, 831-826 and 765-710 cm^{-1}, in the complexes. This indicates the involvement of thiophene sulfur in coordination using its lone pair electrons[34,35].

Appearance of a broad and strong band in the region 3480-3463 cm^{-1} in the spectra of all complexes considerably supports the presence of coordinated water molecules. The coordination of water in Co(II), Ni(II), Cu(II) and Zn(II) complexes is further confirmed by the strong broad absorption band at 3462, 3478, 3480 and 3464 cm^{-1} and the medium sharp band at 900, 892,

TABLE-2
CHARACTERISTIC INFRARED FREQUENCIES[a] (cm^{-1}) AND TENTATIVE ASSIGNMENTS FOR THE SCHIFF BASE WITH ITS METAL COMPLEXES

L	1	2	3	4	Assignments[b]
3290s,sh	-	-	-	-	ν(N-H) ;$-NH_2$
-	3462s,br	3478s,br	3480s,br	3464s,br	ν(O-H) ;H_2O
1607s,sh	1630s,sh	1624s,sh	1628m,sh	1602s,sh	C=N stre
1335m,sh	1335m,sh	1334m,sh	1335m,sh	1334s,sh	ν_{asym}(S=O)
1314m,sh	1314m,sh	1312m,sh	1311s,sh	1314m,sh	ν_{sym}(S=O)
1153s,sh	1151s,sh	1152s,sh	1150s,sh	1151s,sh	ν(C-N); aromatic
846m,sh	829m,sh	826m,sh	831m,sh	829m,sh	ν(C-S-C) asym
721m,sh	710m,sh	758m,sh	765m,sh	712m,sh	ν(C-S-C) sym
-	1466w,sh	1482w,sh	1466m,sh	1499m,sh	δ(H_2O) in plane bending of coo.H_2O
-	900m,sh	892w,sh	901m,sh	902m,sh	δr (H_2O) of coo.H_2O
-	562w,sh	560w,sh	555vw,sh	563w,sh	ν(M-N)
-	542w,sh	540m,sh	538vw,sh	542m,sh	ν(M-S)
-	599w,sh	568w,sh	565vw,sh	596vw,sh	ν(M-O); O of coord.H_2O

[a]s, strong; m, medium; w, weak; vw, very weak; br, broad; s, sharp ; [b]ν, stretching; δ,deformation, 1. $[Co(L)_2(H_2O)_2]Cl_2\cdot0.5H_2O$; 2. $[Ni(L)_2(H_2O)_2]Cl_2\cdot0.5H_2O$; 3. $[Cu(L)_2(H_2O)_2]Cl_2\cdot0.5H_2O$, 4. $[Zn(L)_2(H_2O)_2]Cl_2\cdot H_2O$

901, and 902 cm^{-1}, respectivelly. These bands are attributed to the stretching and rocking vibrations of coordinated water molecules of the complexes, respectively[36, 37]. In addition to these bands in the spectra of the complexes, a band around 3500 cm^{-1} is appeared due to OH stretching frequency of uncoordinated water molecule. This is attributed to the presence of water of hydration.

The band due to N-H stretching of -NH_2 of the ligand in the complexes was difficult to be interpreted due to overlapping of its band with the more intense O-H stretch of coordinated H_2O molecule that absorbed and appeared in the same region.

Apart from these bands, the far IR spectra of Co(II), Ni(II), Cu(II) and Zn(II) complexes showed non-ligand bands of low intensity in the region 599-560, 563-555 and 542-538 cm^{-1} can be assigned to ν(M-O) (coordinated water-O), ν(M-N) (imine-N) and ν(M-S) (Thiophene-S) vibrations, respectively. The IR spectra revealed that L coordinated to the metal ions *via* azomethin-N and thiophene-S. Therefore, the above arguments together with the elemental analyses indicated that the behaviour of Schiff base ligand as neutral NS type bidentate ligand.

Electronic spectra and magnetic susceptibility measurements: The electronic spectral data along with magnetic susceptibility measurements gave adequate support in establishing the geometry of the metal complexes. The electronic absorption spectra for 10^{-5} M solution of the ligand and its metal complexes in acetonitrile at λ ranging from 200 to 800 nm, against the same solvent as a blank, were recorded at room temperature. These electronic absorption spectra of the ligand and its metal complexes are presented in Fig. 5. The ligand showed two bands at 269 and 328 nm which may be assigned to the aromatic and C=N chromophore $\pi \rightarrow \pi^*$ and non-bonding electrons $n \rightarrow \pi^*$ transitions, respectively[6,7,13,26].

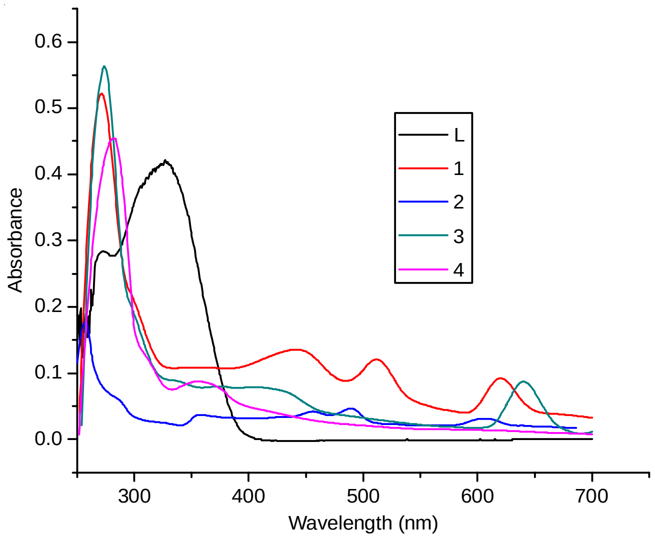


Fig. 5. Electronic absorption spectra of L and its complexes

Up on complexation, shift of the ligand bands and appearance of new bands in the visible region are expected. The band at 328 nm due to $n \rightarrow \pi^*$ transition of the non-bonding electrons on the N of the azomethine group in the free ligand shifted to shorter wavelength, indicating the involvement of the imine group in metal complexation[11,12,22].

The electronic spectrum of Co(II) complex gave three bands in the visible region at 16, 207 cm^{-1}: $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)(\nu_1)$, 19, 531 cm^{-1} : $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ (ν_2) and 22, 883 cm^{-1}; $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ (ν_3). These data along with room temperature magnetic moment value, 4.58 B.M., (normal range for octahedral Co(II) complexes is 4.30-5.20 B.M.), is an indicative of octahedral geometry.

The electronic spectrum of Ni (II) complex also displayed three bands in the visible region. These bands at 16, 393, 19,841 and 21, 368 cm^{-1} are assigned to octahedral $^3A_{2g} \rightarrow {}^3T_{2g}(F)$, $^3A_{2g} \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g} \rightarrow {}^3T_{1g}(p)$ transitions, respectively. The band at 27, 174 cm^{-} is due to charge transfer. These data along with room temperature magnetic moment value of 3.31 B.M, μeff = 3.33 B.M., are compatible and considered as an evidence for octahedral geometry around nickel(II) ion.

The electronic spectrum of Cu(II) chelate consists of a broad, low intensity shoulder band centered at 23,980 cm^{-1} and another band at 15,625 cm^{-1}. The ^2E_g and $^2T_{2g}$ states of the octahedral Cu(II) ion (d^9) split under the influence of the tetragonal distortion and the distortion can be such as to cause the three transitions $^2B_{1g} \rightarrow {}^2B_{2g}$; $^2B_{1g} \rightarrow {}^2E_g$ and $^2B_{1g} \rightarrow {}^2A_{1g}$ to remain unresolved in the spectra. This assignment is in agreement with the general observation that Cu(II) d-d transitions are normally close in energy. The magnetic moment value of 2.11 B.M. falls within the range normally observed for octahedral Cu(II) complexes.

The electronic absorption spectrum of Zn(II) complex showed only intraligand transition and no d-d transition is expected for a d^{10} configuration. The band at 28,090 cm^{-1} is due to charge transfer. The colour the complex is due to this charge transfer. According to the empirical formula and in analogy with those described for Zn(II) complexes containing N-S donor Schiff bases[29-31], the diamagnetic Zinc(II) complex is likely to be Octahedral. Therefore we proposed an octahedral geometry for Zn(II) complex.

^{1}H NMR spectra: The chemical shift of the different types of protons in the ^{1}H NMR spectra of the L was recorded in DMSO-d_6 using TMS as internal standard.

The ^{1}H NMR spectrum of the Schiff base ligand revealed its formation by the presence of azomethine, -CH=N, proton signal at $\delta = 8.82$ ppm. This is further supported by the appearance of stretching vibration band ν(CH =N) azomethine at 1607 cm^{-1}. The resonance of amine proton downfield shifted to 10.3 ppm due to the strong electron withdrawing effect of the sulphonyl group. Also the multiple signals lying in range 7.255-7.895 and 7.757-7.895 ppm were attributed to resonance of Thiophene and benzene protons[6,7,13,26].

Thermal analysis: Fig. 6 shows the TGA of Schiff base L and its metal chelates. The TGA was recorded from 30 to 800 ºC. In all samples of the metal complexes there was a rapid initial mass loss between temperatures of 30-100 ºC. This lower dehydration temperature suggests the presence of non coordinated water molecule to the metal ions. This is characteristics of desorption or drying, usually moisture, amounts to 7.0, 8.86, 10.61 and 19.45 % for Co(II), Ni(II), Cu(II) and Zn(II) complexes, respectively.

The ligand is stable up to 200 ºC. The TGA curve of the Schiff base refers to two stages of mass losses at temperature range 200-780 ºC. These stages involved an experimental and

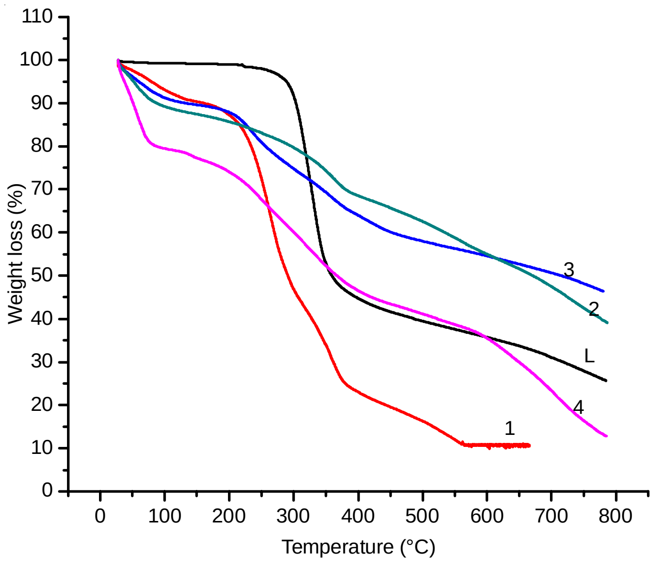


Fig. 6. Thermograms of L and its metal complexes

calculated mass loss of 71.11 and 70.9 %, respectively. These mass losses are due to the successive losses of part of $C_{11}H_{10}O_2N_2S_2$ molecule (NH_2, SO_2, CN and C_6H_5-) as gases at the given temperature range. The remaining part, 28.89 % (calc. 29.1 %) of the ligand decomposes above 800 ºC.

The complexes of the present study illustrated different thermal degradation patterns. The thermograms of Co(II), Ni(II) and Cu(II) chelates showed four decomposition steps within the temperature range 100-800 ºC. The first step of decomposition within the temperature range 100-130 ºC corresponds to the loss of lattice water molecule ($1/2H_2O$) with a mass loss of 1.33 % (calcd.1.30 %), 1.26 % (calc.1.27 %) and 1.29 % (calcd.1.26 %), respectively. The second step of decomposition occurred for Co(II), Ni(II) and Cu(II) complexes at 130-210, 130-202 and 130-250 ºC corresponds to the loss of two moles of coordinated water molecules with a mass loss of 5.05 % (calc. 5.08 %), 5 % (calc. 5.08 %) and 5.03 (calc. 5.05 %), respectively. The third step occurred at 210-387, 202-462 and 250-392 ºC corresponds to the removal part of Co(II) complex as SO_2, SO, N_2, 2HCl, 2CN and $2C_4H_3S$, Ni(II) complex as N_2, 2HCl, SO_2 and SO and Cu(II) complex as N_2 and 2HCl with a mass loss of 60.78 % (calc. 60.91 %), 29.98 % (calc. 30.11 %) and 14.17 % (calcd.14.18 %), respectively. In a similar way, the fourth step of decomposition occurred for the same complexes at 387-572, 462-800 and 392-800 ºC involved the loss of Co(II) complex as $2C_6H_5$-, Ni(II) complex as C_6H_5CN and Cu(II) complex as SO_2, SO and C_6H_5CN with mass loss of 14.98 % (calc. 15.10 %), 14.55 % (calc. 14.56 %) and 30.18 % (calcd. 30.20 %), respectively. The overall weight losses that occurred between temperature range of 100-800 ºC for Co(II), Ni(II) and Cu(II) complexes amount to 82.14 % (calcd. 82.39 %), 50.79 % (calcd. 51.00 %) and 50.67 % (calcd. 50.69 %), respectively.

Unlike others, the TGA curves of the Zn (II) chelate gave five decomposition steps as illustrated in Fig. 6. The first and second steps of decomposition correspond to the loss of one mole of lattice and two coordinated water molecules within the temperature range 100-135 and 135-218 ºC with mass loss of 2.55 % (calcd. 2.50 %) and 5 % (calcd. 4.98 %), respectively. The third, fourth and fifth steps of decomposition within the temperature range 218-429, 429-586 and 586-800 ºC correspond to the removal of the chelates as SO_2, SO, 2HCl and N_2 and 2CN and $2C_4H_3S$ with mass loss of 29.44 % (calcd. 29.47 %), 7.11 % (calcd 7.2 %) and 23.13 % (calcd. 23.10 %), respectively. The total mass losses of the decomposition steps within the temperature range 100-800 ºC were 67.23 % (calcd. 67.25 %).

From the TGA, it was interesting to observe that the complexes of the present study illustrated different thermal degradation patterns. The weight loss amounts 49.21, 49.33 and 32.77 % occurred above 800 ºC for Ni (II), Cu(II) and Zn(II) complexes, respectively. While no weight loss was occurred above 800 ºC for Co(II) complex. Weight loss amounts 82.14 % (calcd. 82.39 %) of Co(II) complex decomposes below 800 ºC leaving CoO as a residue. Among all the complexes under study, Cu(II) complex showed the highest and Co(II) complex showed the least thermal stability with delayed and fast degradations, respectively. Nickel(II) complex exhibited comparable thermal stability with that of Cu(II) complex. This is in accordance to Irving-William's series of stability[38]. For a given ligand, the stability of the complexes with dispositive metal ions follows the order; Co(II) < Ni(II) < Cu(II) > Zn(II). This order arises in part from a decrease in size across the series and in part from ligand field effect. The smaller the size of the metal ion the greater electro negativity will be. An increase in electro negativity of the metal ions will decrease electro negativity difference between the metal ions and the donor atom of the ligand. Thus, the M-L bond would be having more covalent character, which may lead to greater stability of metal chelates. Hence Cu(II) complex can be used for applications which involve higher thermal stability.

Chloride ion test in the complexes: The test for chloride ion was positive for all metal complexes under study indicating that chloride ion was outside the coordination sphere of the central metal. The result confirmed the presence of two moles of chloride ions outside the coordination sphere for charge balance. This indicated the chlorides in metal complexes were ionizable, which remain uncoordinated to the metal ions.

Metal content of the chelates: The metal content in each of the metal complexes was determined by complexometric titration against standard EDTA solution at a suitable pH value using the suitable indicator. The result indicated that molar ratio of metal to ligand of the complexes was 1:2.

Biological activity: The Schiff base ligand and its complexes (1-4) were tested for their inhibitory effects against growth of bacteria: *S. aureus* and *K. pneumoniae* and fungi: *C. albicans* and *C. krusei* by the agar well diffusion assay. The results of antibacterial and antifungal activities of the ligand and its coordinated compounds are listed in Table-3 and are represented graphically in Fig. 7. Photograph as well showing the antifungal behaviour of L and its metal complexes against *C. krusei* was also shown in Fig. 8.

The results indicated that all the compounds have showed weak to strong antimicrobial activities against all organisms used in this study except L, 2 and 4 compounds that showed no antimicrobial activity against *K. pneumoniae*. Complex 3 and L have, respectively shown the best antibacterial and antifungal activities among all. The bacteria *S. aureus* and the

TABLE-3
ANTIMICROBIAL ACTIVITY OF SCHIFF BASE LIGAND AND ITS COMPLEXES (CONCENTRATION 50 μg/mL)

Compounds	Diameter of inhibition zone (in mm)			
	S. aureus	*K. pneumoniae*	*C. albicans*	*C. krusei*
Ligand	16	-	40	15
1	15	11	38	14
2	18	-	39	24
3	20	15	32	15
4	17	-	35	13
DMSO	-	-	-	-
Ampicillin	40	12	-	-
Voriconazole	-	-	56	36

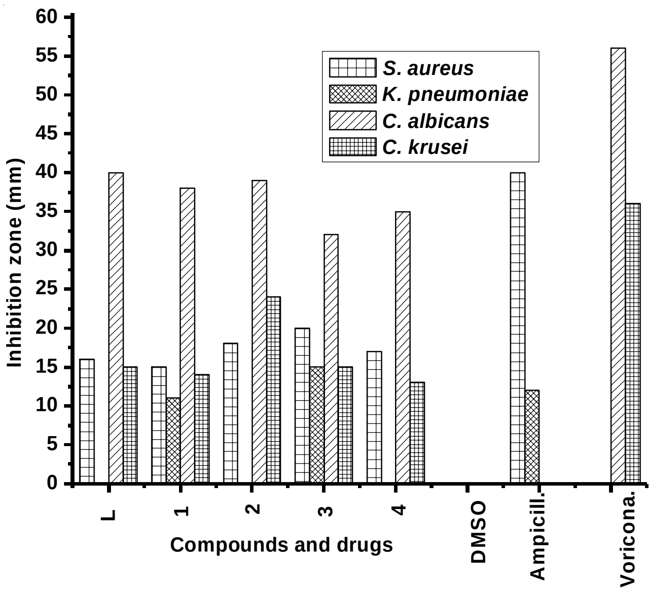


Fig. 7. Zone of inhibitions of reported compounds and standards against four types of microorganisms (two bacteria and two fungi

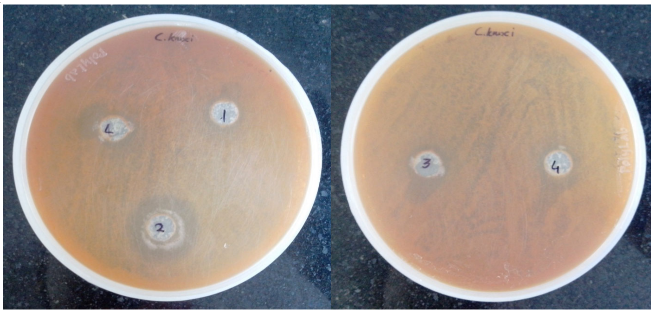


Fig. 8. Photograph showing antifungal studies of L and its metal complexes against *C. krusei*

fungi *C. albicans* were more sensitive than *K. pneumoniae* and *C. krusei* to the synthesized compounds due to the different components of the bacterial and fungal cell wall. In general the biological activity of the synthesized compounds follow the order 2 > 3 > 1 > L > 4. It is evident from the data that there is a considerable increase in toxicity of complexes as compared to the ligand. A possible mode of enhancing toxicity of complexes could be speculated in the light of "Chelation Theory"[39]. This would suggest that chelation could facilitate the ability of the complexes to cross a cell membrane. On chelation or coordination, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π-electrons over the whole chelate ring. This process thus increases the lipophilic nature of the compound which, in turn, favors penetration through the bacterial and fungal wall of the microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organisms. Complex 3 showed the best effective antibacterial activity among all due to a highest stability constant and this appears to be an ideal antibacterial complex providing non-conducive environment for the growth of bacteria. On the other hand, the difference in the magnitude of antimicrobial activity came from other factors, such as solubility and the charge of the complexes. Thus, it was apparent that the antimicrobial activity of complexes of the Schiff base was not only dependent on the charge, but also on the nature of the counter ions that neutralize the complex, the geometrical structure of the complex and nature of metal ions[40-42].

Conclusion

The present study reports on the synthesis, characterization and antimicrobial evaluation of Schiff base ligand (L) and its Co(II), Ni(II), Cu(II) and Zn(II) complexes. The synthetic procedure in this work resulted in the formation of complexes in molar ratio (2:1) (L:M), respectively. The IR spectra revealed that L coordinated to the metal ions *via* azomethine-N and thiophene-S. The synthesized schiff base acts as a neutral NS type bidentate ligand. On the basis of elemental analyses data, UV-visible spectra and magnetic susceptibility measurements octahedral geometry was proposed for all complexes where the fifth and sixth coordination sites were occupied by water molecules. The molar conductance studies indicated the electrolytic nature of the complexes with a cation to anion ratio of 1:2, respectively. Among all the complexes under study, Cu(II) complex showed the highest and Co(II) complex showed the least thermal stability with delayed and fast degradations, respectively. Nickel(II) complex exhibited comparable thermal stability with that of Cu(II) complex. Hence Cu(II) complex can be used for applications which involve higher thermal stability. The *in vitro* biological activities result showed that the ligand become antimicrobially active on chelation with metal ions and the antibacterial activity of 3 and the antifungal activities of 1 and 2 could be further studied for the treatment of infections caused by any of the above organisms.

ACKNOWLEDGEMENTS

Financial support from the Indian Council for Cultural Relation (ICCR) is gratefully acknowledged. The authors are also thankful to Department of Chemistry and SAIF, IIT Madras, India for recording elemental analyses, ^{1}H NMR and MS. Other Instrumentation facility provided by DST-FIST sponsored Department of Chemistry, Anna University, Chennai, India is acknowledged with thanks.

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