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Research Article

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL EVALUATION OF 3d TRANSITION METAL Co(II), NI(II), Cu(II) & Zn(II) COMPLEXES DERIVED FROM 4-[(2-HYDROXY-3-METHOXYPHENYL)METHYLENEIMINO]-3*H*-1,2,4-TRIAZOLE-3-THIONE

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ABSTRACT

New nitrogen-containing Schiff base ligand (**H_2L**) was synthesized by the condensation of an equimolar amount of 4-amino-1,2,4-triazole-3-thione and ortho vanillin. The synthesized ligand was characterized by physical constant, FT- IR, ^{1}H NMR, ^{13}C NMR, mass spectrometry. It was further coupled with various transition metal Co(II), Ni(II), Cu(II) and Zn(II) ions. The synthesized metal complexes were confirmed with the help of FT-IR, ^{1}H NMR,elemental analysis, mass spectrometry, UV and TGA methods. The spectral data revealed that the ligand acts as binegative and tridentate in the metal complexes. The results of antimicrobial studies showed that the complexes exhibited good antimicrobial activity as compared with the free ligand.

Keywords: SNO Donor, Ligand, Metal complex, Antimicrobial

1. INTRODUCTION

Coordination chemistry of Schiff bases is the topic of great importance since long ago. Schiff bases are able to form co-ordinate bonds with many transition metal ions via phenolic, thiolic and azomethine groups; therefore have been used for the synthesis of metal complexes on account of their easy synthesis and strong metal binding capability. Generally an enhancement in the biological activities has been observed due to chelation of Schiff base ligands and the metal moiety. A number of ligand metal complexes [1,2] have been studied to possess antibacterial [3], antifungal [4], herbicidal [5] and anticancer [6] activities. The chemistry of 1, 2, 4-triazole and its heterocyclic derivatives has received significant attention owing to their synthetic and effective biological importance. Schiff bases of 1,2,4-triazole derivatives have also been found to possess extensive biological activity.

The role of N and S atoms in the coordination of ligands to metal at the active sites of various metallo-biomolecules is well known. From literature survey, the metallic element enhances the biological activity and in some cases the complex possesses even more healing properties than the parent drug [7].

Transition metals like cobalt, nickel, copper and zinc have great affinity for coordination due to their smaller size and higher nuclear charge. In the present study, we report synthesis, characterization of a new SNO donor ligand, its metal complexes and their antimicrobial activity.

In continuation of our research on the synthesis and antimicrobial evaluation of several Schiff bases and their metal complexes [8-10]; herein we report the synthesis of SNO donor ligand and its transition metal complexes and their antimicrobial activity.

2. EXPERIMENTAL

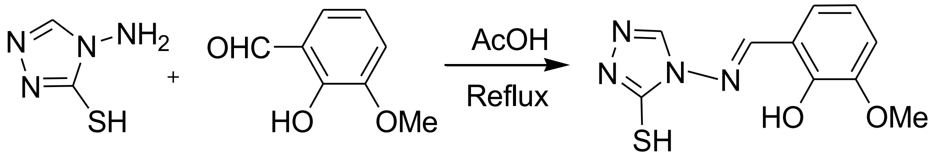
2.1. Material and methods

All the chemicals used were SD fine or Spectrochem made and used without further purification. The 4-amino-1, 2, 4-triazole-3-thione was synthesized according to the literature method [11]. Melting points were determined on PLT-276 digital melting point apparatus. Elemental analysis data were recorded using Perkin Elmer-240 elemental analyser. IR spectra were scanned on Bruker spectrometer in the range 4000-400 cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO-d6 with Bruker Avance 200 MHz using TMS as the internal standard. UV absorption spectra and thermogravimetric analysis were recorded on Shimadzu UV-1800 and Shimadzu TGA 50 spectrometers respectively.

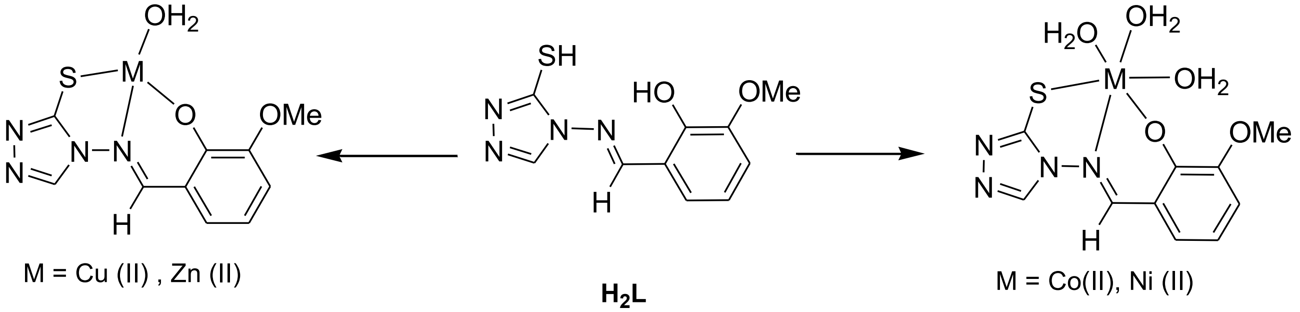
2.2. Synthesis of 4-[(2-hydroxy-3-methoxyphenyl)methyleneimino]-3*H*-1,2,4-triazole-3-thione (H_2L)

An equimolar quantity of 4-amino-1,2,4-triazole-3-thione (0.580 g,5 mmol) and ortho vanillin (0.760 g, 5 mmol) were dissolved in 2 mL acetic acid and the resultant mixture was refluxed for 4 h under constant stirring. The progress of reaction was monitored by TLC (30% Ethyl acetate: n-hexane) and after the completion of reaction; the mixture was poured onto crushed ice and filtered off. The obtained product was recrystallized in absolute ethanol as pure $\mathbf{H_2L}$ ligand (**Scheme 1**).

Color: Pale yellow, Yield: 88%, ***MP:***243℃; ***FT-IR (cm^{-1}):*** 3657 ν(-OH), 2609 ν(-SH), 1602 ν(C=N); ***^1H NMR (200 MHz, DMSO-d_6):*** δ ppm13.96 (s, 1H, triazole-SH), 10.18 (s, 1H, -OH), 9.67 (s, 1H, HC=N), 8.97 (s, 1H, triazole ring), 7.35 (d, *J* = 7.9 Hz, 1H, Ar-H), 7.16 (d, *J* = 6.9 Hz, 1H,Ar-H), 6.92 (t, *J* = 7.9 Hz, 1H,Ar-H), 3.85 (s, 3H,-OMe); ***^{13}C NMR (500 MHz, DMSO-d_6, δ ppm):*** 162.73 (s, quat, Ar), 158.16 (s,-HC=N),148.22(s, quat, Ar), 148.21(s, quat, triazole), 138.05 (s, triazole,CH), 119.64 (s, Ar,CH), 119.45 (s, Ar,CH), 118.16(s,quat, Ar), 115.47 (s, Ar, CH), 56.01 (s, OCH_3); ***Mass spectrum (ESI):*** $[M+1]^+$=251.1.



Scheme 1: Schematic route for synthesis of H_2L ligand



Scheme 2: Synthesis of metal (II) complexes

2.3. General procedure for the synthesis of metal complexes (1-4)

Schiff base transition metal(II) complexes (**1**-**4**) of ligand $\mathbf{H_2L}$ were synthesized from $\mathbf{H_2L}$ (0.25 g, 1mmol) in methanol (20 mL) with analogous metal(II) salts [i.e. chloride of Co(II) (0.24g, 1mmol), Ni(II) (0.24 g, 1 mmol), Cu(II) (0.17 g, 1 mmol) and Zn(II) (0.14 g, 1mmol)] in methanol (10 mL) in 1:1 stoichiometric ratio (**Scheme 2**). pH of the solution was turned slightly alkaline by adding aqueous ammonia. The solution was refluxed for 10-12 hrs. The solid product separated out, which was vacuum filtered, washed with cold methanol, diethyl ether (Yield: 60-76%).

3. RESULTS AND DISCUSSION

All the synthesized metal complexes derived from H_2L were colored, non-hygroscopic & air stable solids. They were insoluble in water, but soluble in DMF and DMSO. The physical and analytical data of the ligand and its metal complexes are shown in **Table 1**.

3.1. FT-IR spectra

The functionalities of free ligand and their coordinating ability to form metal complexes were studied by IR spectroscopy. The characteristics IR peak values of ligand and its metal complexes are summarized in **Table 2**. In infrared spectrum of H_2L, the characteristic band at 1602 cm^{-1} for azomethine group was shifted to lower side in metal complexes by 05-09 cm^{-1}, indicating the coordination of azomethine nitrogen with metal ion [12]. This was also confirmed by the presence of new bands in the spectra of metal complexes in the range between 420-478 cm^{-1}corresponding to the ν(M–N) bond.

Table1: Physical and analytical data of H_2Land its metal complexes.

Compound	Mol. Formula (F.W.)	M.P. (°C)	Color	Elemental analysis found (calculated.)% % C (cal.)	% H (cal.)	% N (cal.)	% M (cal.)
Ligand (H_2L)	$C_{10}H_{10}N_4O_2S$ (250.05)	243°C	Light yellow	47.89 (47.99)	4.08 (4.03)	22.46 (22.39)	-
[Co(H_2L)(H_2O)$_3$]	$C_{10}H_{14}CoN_4O_5S$ (361.24)	>280°C	Brown	33.16 (33.25)	3.80 (3.91)	15.64 (15.51)	16.22 (16.31)
[Ni(H_2L)(H_2O)$_3$]	$C_{10}H_{14}N_4NiO_5S$ (360.00)	>280°C	wheat	33.26 (33.27)	3.80 (3.91)	15.59 (15.52)	16.40 (16.26)
[Cu(H_2L) (H_2O)]	$C_{10}H_{10}CuN_4O_3S$ (329.82)	>280°C	Green	36.49 (36.42)	3.10 (3.06)	16.80 (16.99)	19.15 (19.27)
[Zn(H_2L)(H_2O)]	$C_{10}H_{10}N_4O_3SZn$ (330.00)	>280°C	yellow	36.29 (36.21)	3.15 (3.04)	16.81 (16.89)	19.60 (19.72)

Table 2: Infrared frequencies and electronic transitions of ligand (H_2L) and its metal complexes

Compound Name	ν(HC=N)	ν(–OH)	ν(–SH)	ν(M-N)	ν(M–O)	Elect. transition (cm^{-1})
H_2L	1602	3214	2609	-	-	
[Co(H_2L)(H_2O)$_3$]	1597	-	-	430	490	10510,19760(dd)
[Ni (H_2L)(H_2O)$_3$]	1599	-	-	420	499	11035,16305,25510(dd)
[Cu (H_2L)(H_2O)]	1593	-	-	450	501	19490 (dd)
[Zn (H_2L) (H_2O)]	1595	-	-	478	545	24937(CT)

An appearance of new broad band in the region 3338-3371 cm^{-1} indicates the presence of coordinated water in metal complexes [13]. The band at 3214 cm^{-1} which corresponds to ν(-OH) stretch in ligand disappeared in the metal complex, showing the deprotonation of phenolic-OH during complexation. Appearance of a new band at 499-545 cm^{-1} was assigned to metal-oxygen bond [13]. The thiolic-SH stretching vibration was absent in metal complex, due to deprotonation of thiol group and thiol sulphur coordinated to metal ion [12].

Thus IR spectral data supports that the ligand acts as a binegative tridentate ligand with SNO donor sites in the complexes coordinating through the azomethine N, deprotonated thiol sulphur and O atom of phenolic -OH to the metal (II) ions.

3.2. ^{1}H NMR spectra

The ^{1}H NMR spectra were recorded for ligand (**Fig. 1**) and Zn(II) complex in DMSO solvent. The signal for azomethine (-CH=N) proton in ligand displayed as singlet at δ 9.67 ppm was slightly deshielded and appeared at δ 9.18 ppm in the Zn(II) complex This might be due to the transfer of electron density from nitrogen to the Zn (II). There is formation of coordination bond between azomethine nitrogen and zinc (Zn←N) [14]. The characteristic proton signals of phenolic (-OH) and thiolic (-SH) disappeared in the NMR of zinc complex which indicates the deprotonation of -OH and -SH proton during complexation. All other aromatic protons in the NMR spectrum of zinc complex appeared at almost the same chemical shift, as they appear in the spectrum of the ligand. The signals of all the protons of the ligand H_2L and Zn(II) complexes were found as to be in their expected region.

3.3. Electronic spectra

The electronic absorption spectra of the Co(II), Ni(II), Cu(II) and Zn(II) complexes were recorded in DMSO at room temperature and the results are listed in **Table 2**. The electronic spectra of Co(II) complex shows two transitions in the range of 10510 cm^{-1} and 19760 cm^{-1}, corresponding to $^4T_{1g}(F)\rightarrow{}^4T_{2g}(F)$ (ν1); $^4T_{1g}(F)\rightarrow{}^4T_{1g}(P)$ (ν3), ν2 which is very close to (ν3) transition is not observed, but it can be calculated [15] by using relation ν2 = ν1+10Dq. It strongly supports the octahedral geometry around Co(II) ion. The electronic spectral data of Ni(II) complex exhibited three d-d bands in the region 11,035, 16,305 and 25,510 cm^{-1}, respectively due to $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$,$^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g}(F) \rightarrow$

$^3T_{1g}$(P) transitions. The position of these bands suggests an octahedral geometry around Ni(II) ion.

In case of the copper complex, d-d transition was observed at 19,490 cm^{-1}, which can be assigned as the $^2B_{1g} \rightarrow {}^2A_{1g}$ transition, indicating that the Cu(II) complex exists in square planar geometry [16-17].

3.4. Thermogravimetric analysis

Thermal stability of the synthesized metal complexes was done up to 1000ºC at a heating rate of 10ºC/min in inert atmosphere of nitrogen. Metal complexes (**1-4**) exhibit similar decomposition patterns as evident from their TGA graphs. Cobalt complex decomposes in three steps within temperature range of 130-610ºC. First step corresponds to the loss of three coordinated water molecules (Found 14.99 %, calcd. 14.95 %) in temperature range of 130-160ºC. The second step corresponds to the loss of C_8H_7NO (Found 43.87 %, calcd. 43.97 %) in temperature range of 160-380ºC. A peak corresponding to mass loss of 56.10 % (calcd.56.25 %) at 380-610ºC was due to the loss of triazole moiety in the third step and as a final product, it leaves the metal oxide as residue. Similar behavior was observed in the TGA curve of metal complexes (2-4). Thermal analysis data of all metal complexes (**1-4**) is collectively summarized in **Table 3**.

Table 3: Thermal analysis data of metal complexes (1-4)

Comp.no.	Molecular formula	Stages	Temp (ºC)	Possible evolved species	Residual species	Mass loss	
						Found	Calc.
1	$C_{10}H_{14}CoN_4O_5S$ (361.24)	1st	130-160	$3H_2O$		14.99	14.95
		2nd	160-380	C_8H_7NO		36.87	36.84
		3rd	380-610	Triazole moiety		27.46	27.42
					CoO	20.61	20.77
2	$C_{10}H_{14}N_4NiO_5S$ (360.00)	1st	135-165	$3H_2O$		15.10	15.00
		2nd	165-360	C_8H_7O		33.15	33.05
		3rd	360-690	Triazole moiety		31.30	31.60
					NiO	20.35	20.40
3	$C_{10}H_{10}CuN_4O_3S$ (329.82)	1st	140-160	H_2O		5.56	5.47
		2nd	160-415	C_8H_7NO		40.30	40.42
		3rd	415-670	Triazole moiety		30.10	30.09
					CuO	24.00	24.01
4	$C_{10}H_{10}N_4O_3SZn$ (330.00)	1st	125-160	H_2O		5.45	5.43
		2nd	160-390	C_8H_7NO		40.25	40.18
		3rd	390-680	Triazole moiety		29.95	29.90
					ZnO	24.38	24.36

3.5. Antimicrobial activity

In vitro antimicrobial screening of the synthesized ligand and metal complexes was carried out against four bacteria (*S. Aureus, S. Pyogenes, E. Coli & S. Typhi*) and two fungi (*C. Albicans & T. Rubrum*) by petri-plate containing 30 mL potato dextrose agar and nutrient agar medium. The plates were incubated for 20-24hr and 24-48 hr for bacteria and fungi stains, respectively. The activities were measured in terms of zone of inhibition in mm. Cefotaxime, Azithromycin and Clotrimazole were used as the standard drugs for bacteria and fungi, respectively at 500 ppm concentration of sample as well as drugs.

Results of antimicrobial activity of the ligand and metal complexes are shown in **Table 4**. The metal complexes exhibit higher inhibition against tested microorganism compared to the free ligand. The antimicrobial activity of metal complexes depends on the following factors such as the chelate effect, nature of coordinated ligand, total charge of complex, nature of the ion neutralizing the ionic complex and nuclearity of the metal center in the complex [18-19].

The increased activity of the metal complex than the free ligand can also be explained on the basis of chelation theory [20].

Table 4: Results of antimicrobial activity of synthesized compounds

Compounds	**Zone of Inhibition in mm**					
	Antibacterial Activity				**Antifungal Activity**	
	S. Aureus	***S. Pyogenes***	***E. Coli***	***S. Typhi***	***C. Albicans***	***T. Rubrum***
Ligand (H_2L)	-	-	-	-	-	-
$[Co(H_2L)(H_2O)_3]$	-	-	10	10	-	-
$[Ni(H_2L)(H_2O)_3]$	-	-	-	-	-	-
$[Cu(H_2L)(H_2O)]$	14	16	-	10	16	16
$[Zn(H_2L)(H_2O)]$	14	-	-	11	-	12
Cefotaxime	-	-	**25**	**20**	-	-
Azithromycin	**26**	**24**	-	-	-	-
Clotrimazole	-	-	-	-	**18**	**25**

4. CONCLUSION

The synthesized ligand H_2L coordinates in a binegative tridentate manner to the metal (II) ion in the metal complexes. On the basis of different spectral techniques results, an octahedral geometry has been assigned for Co(II) and Ni(II) complexes, while Cu(II) complex exists in square planer and tetrahedral for Zn(II) complexes. The presence of coordinated water was confirmed by the TGA and IR data. Antibacterial activity results revealed that all the synthesized metal complexes show moderate to significant inhibition on the tested strains. On the basis of results of activity against bacteria and fungi the Cu(II) complex was found to be the most effective. Metal complexes show enhanced activity in comparison to free ligand.

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