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Synthesis, characterization and antimicrobial activity of new cobalt (II), nickel (II) and copper (II) complexes with 2-(2-hydroxy-1, 2-diphenylethylideneamino) benzoic acid

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ABSTRACT

The new Schiff base ligand 2-(2-hydroxy-1, 2-diphenylethylideneamino) benzoic acid [HL] and its Co(II), Ni(II) and Cu(II) metal complexes were synthesized. The ligand and metal complexes were characterized by elemental analysis, UV-visible, IR, ^{1}H NMR spectroscopy, thermal studies and magnetic susceptibility measurement. The ligand [HL] was synthesized by condensation of benzoin and 2-amino benzoic acid. On the basis of electronic spectral data and magnetic susceptibility measurement the octahedral geometry has been proposed for Cu(II), Ni(II) and Co(II) complexes. The ligand and metal (II) complexes were also screened for their antimicrobial activity against microorganisms *Staphylococcus aureus* and *Pseudomonas aeruginosa* and antifungal activity against the fungi *Candida albicans* and *Aspergillus niger.*

Arylazo compounds are very interesting because they are involved in a number of biological activities [1]**;** they are also used in analytical chemistry as a complexing agent to detect various types of metal ions. The Schiff base complexes are important as medicine and show a variety of interesting biological activities such as antibacterial and antifungal activity [2–4]. Benzoin and its derivatives are used as intermediates for the synthesis of organic compounds and as a catalyst in photo polymerization. They are used in anticratering in powder coating. It has been reported that the benzoin can be used in skin disorders as an antibacterial and antifungal agent. Arylamines are attractive targets for chemical synthesis because of their wide applications in fine chemicals, polymers and dyes. These are important components in many important biologically active natural products as well as medicinally important compounds. [5,6]**.** Transition metal complexes with various donor groups have been used in organometallic chemistry [7]. A large number of Schiff base compounds have been synthesized and structurally characterized [8–14]**.**

The various classes of Schiff bases that can be prepared by condensation of different types of amines and carbonyl compounds are very popular due to diverse chelating ability. Several transition metal complexes have been screened for their medicinal properties [5–19]. The first row transition metals have attracted much attention due to their biological importance [20]**.**These factors prompted us to carry out a study on synthesis of Schiff base and its complexes with Co(II), Ni(II) and Cu(II) metal ions.

In this paper we report the synthesis of new benzoin ligand 2-(2-hydroxy-1,2-diphenylethylideneamino) benzoic acid [HL] and its legation behavior with Co(II), Ni(II) and Cu(II) metals. The synthesized ligand and metal complexes were characterized by elemental analysis, UV–Vis, IR, ^{1}H NMR, TG-DTG, magnetic susceptibility. They are also screened for their biological activities against the microorganism *Staphylococcus aureus, Pseudomonas aeruginosa* and fungi *Aspergillus niger and Candida albicans.*

All reagents used were pure AR grade such as benzoin, 2-amino benzoic acid, copper chloride, nickel chloride and cobalt chloride. The solvents used were ethanol, petroleum ether, ethyl acetate etc. The synthesis of Schiff base ligand and metal complexes is shown in Scheme 1.

The benzoin (10.6 g, 0.05 mol) and 2-amino benzoic acid (6.85 g, 0.05 mol) were dissolved in ethanol (25 ml) separately in 1:1 molar ratio. The ethanolic solutions were mixed together. The mixture was refluxed on water bath for 3 h. On cooling, a crystalline complex was separated by filtration and the crystals were washed with ethanol and anhydrous diethyl ether and dried over anhydrous $CaCl_2$ [21–25].

A ligand (3.31 g, 0.01 mol) [HL] was dissolved in (25 ml) ethanol and added to a metal salt [nickel chloride (2.37 g, 0.01 mol), copper chloride (1.70 g, 0.01 mol) and cobalt chloride (2.37 g, 0.01 mol)] ethanolic solution (25 ml). The metal-ligand molar ratio was (1:1). The mixture was refluxed for 2 h. On cooling, a crystalline complex was separated by filtration and the crystals were washed and dried as above [21–25].

Analytical and physical data of the compounds studied are reported in Table 1. The ligand and the metal (II) complexes are

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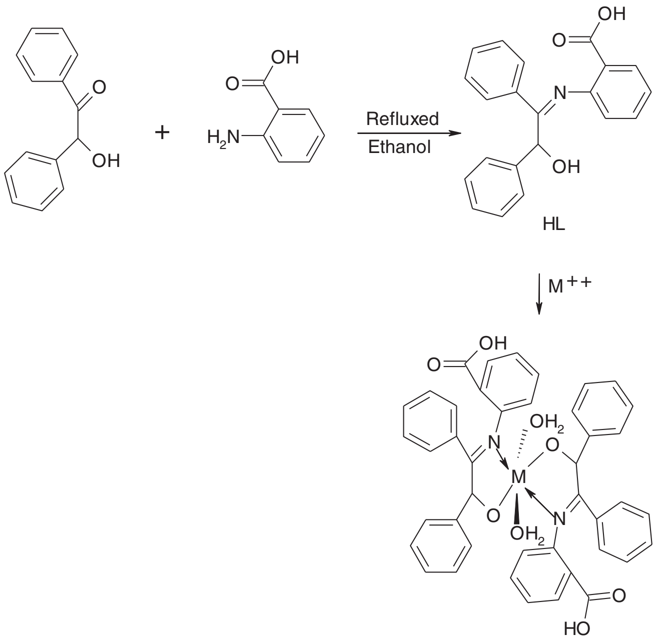

Where **M = Co^{2+}, Ni^{2+} and Cu^{2+}**

Scheme 1. Synthesis of Schiff base and metal complexes.

soluble in common polar solvents like methanol, ethanol and chloroform. They are soluble even in DMF and acetone. The ligand and the metal (II) complexes synthesized were stable at room temperature. The synthesized ligand and the metal complexes were characterized by elemental and spectral analysis. Biological activity of the ligand and the metal complexes were also studied. Based on their elemental and spectral studies the geometry of the synthesized compounds has been elucidated.

By the elemental analysis, the stoichiometry of ligand and their metal complexes is confirmed. The elemental analysis of ligand and the metal complexes are found in agreement with the proposed structure of ligand and the metal complexes are listed in Table 1.

The electronic spectra and magnetic moment are very useful in the evaluation of results obtained by other methods of structural investigation. Information regarding the geometry of the complexes around the Co(II), Ni(II) and Cu(II) ions was obtained from electronic spectral studies and magnetic moments. The electronic spectra of ligand and their metal complexes were recorded at room temperature using methanol as a solvent.

The electronic spectra of ligand show bands in the region of 204 nm and 248 nm but in the complexes they are slightly shifted to higher frequencies. The band between 325 nm can be assigned to $n \rightarrow \pi^*$ of transition of azomethine group. In the spectra of complexes the bands of azomethine chromophore $n \rightarrow \pi^*$ transition that are shifted to lower frequencies indicate that imine nitrogen is involved in the co-ordination of metal ion. A very weak low intensity absorption band associated with d-d transition for Cu(II) complexes at 465, 532 nm (typical octahedral transition) Co(II) complexes at 450 nm $[^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)]$, 525 nm $[^4T_{1g} \rightarrow {}^4A_{2g}]$ and 734 nm $[^4T_{1g} \rightarrow {}^4T_{2g}]$ and for Ni(II) complexes at 470 nm (charge transfer), 525 nm $[^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)]$, 985 nm $[^3A_{2g} \rightarrow {}^3T_{1g}(F)]$ respectively supports the octahedral geometry of metal complexes [26].

The magnetic moment obtained at room temperature is as shown in Table 2. The magnetic moment obtained at room temperature indicates paramagnetism. The Co(II) complex shows a magnetic moment of 4.94 B.M., the spin free octahedral complex of Co(II) is reported to exhibit magnetic moment in the range of 4.46–5.53 B.M. [27–30]. Hence, the observed magnetic moment for the Co(II) complex under study indicates that it has an octahedral configuration. The Ni(II) complex shows a magnetic moment of 3.04 B.M. The magnetic moment of octahedral Ni(II) complexes are reported to exhibit magnetic moment in the range of 2.80–3.40 B.M. [28–31] indicating spin orbital coupling contribution from $^3A_{2g}$ and higher $^3T_{2g}$ states. Hence, the observed magnetic moment for the Ni(II) complex suggests that it may have octahedral geometry. The observed magnetic moment of Cu(II) complex is 1.73 B.M. and it indicates an octahedral geometry [29–32]. Thus the electronic spectral data and magnetic moment data support the octahedral geometry of the complexes.

The IR spectral data of Schiff base [HL] and their metal complexes are presented in Table 2. The IR spectra of complexes are compared with those of ligand in order to determine the coordination sites that may be involved in chelation. A strong band observed at 1620 cm^{-1} in a ligand [HL] is a characteristic band of (HC N) azomethine group. The shifting of this band towards lower frequency region by 15–20 cm^{-1} in complexes indicates involvement of azomethine nitrogen in coordination with metal ion [33–35]. The assignment of the proposed coordination sites is further supported by appearance of a band at 453–462 cm^{-1} suggesting the υ (M—N) bond. The presence of υ (M—O) stretching vibration at 542–588 cm^{-1} supports the involvement of oxygen atom in complexation with metal ions. The ligand and metal complexes were characterized mainly using the azomethine and —OH bands. In the complexes, the broad band in the range of 3379–3385 cm^{-1} is attributed to the presence of water molecules. Presence of water molecules was also confirmed by thermal analysis. The presence of band in the range of 1314–1393 cm^{-1} (OH in-plane bending vibration of carboxylic group) in ligand and metal complexes confirms that the carboxylic functional group remains unchanged. Therefore, from the IR spectra, it is concluded, that the ligand coordinated to the metal ions via azomethine nitrogen and deprotonated oxygen atom from benzoin.

The ^1H NMR spectra of Schiff base are recorded in $CDCl_3$, using Tetramethylsilane (TMS) as an internal standard at IIT, Mumbai. The ^1H NMR spectra of benzoin show signals at δ 6.03 ppm assignable to —OH group, δ 6.09 ppm assignable to —CH-group and δ 7.06-8.01 ppm assignable to aromatic protons. In the NMR spectra of ligand, the signal due to —OH of benzoin shifts to δ 5.960 ppm [36]. The signal at 11 ppm

Table 1
Analytical and Physical data of the compounds studied.

Name of compounds	Molecular formula/ formula weight	Color	M.P. 0 °C	Found (calculated) %			
				C	H	N	Metal
HL	$C_{21}H_{17}NO_3$ 331	Faint yellow	148	77.06 (76.12)	4.83 (5.17)	4.73 (4.23)	–
HL—Co	$C_{42}H_{36}N_2O_8Co.2H_2O$ 755	Yellowish brown	>250	67.38 (66.70)	5.12 (4.80)	4.09 (3.70)	7.66 (7.80)
HL—Ni	$C_{42}H_{36}N_2O_8Ni.2H_2O$ 755	Yellowish brown	>250	67.59 (66.78)	4.88 (4.80)	4.20 (3.71)	7.26 (7.77)
HL—Cu	$C_{42}H_{36}N_2O_8Cu.2H_2O$ 760.29	Grey	>250	66.04 (66.30)	5.39 (4.74)	4.16 (3.68)	8.45 (8.36)

Table 2
IR spectral data and Magnetic moment data.

Name of Compound	ν (C=N)	ν (C—O)	ν (M—N)	ν (M—O)	ν (C—O—H)	ν (H_2O)	$\mu_{eff.}$ B.M.
HL	1620	1090	_	_	1393	3379	_
HL—Co	1600	1112	462	588	1314	3385	4.94
HL—Ni	1595	1112	453	542	1315	3383	3.04
HL—Cu	1603	1111	460	560	1318	3385	1.73

is assignable to —OH of carboxylic acid. Since, Co^{2+}, Ni^{2+} and Cu^{2+} complexes are paramagnetic; their ^1H NMR spectra could not be obtained [31].

The typical thermogram of nickel complex is shown in Fig. 1. Thermal decomposition of Co(II), Ni(II) and Cu(II) metal complexes have been studied as a function of temperature by TGA and DTG. It exhibited three step decomposition for the Schiff base metal (II) complexes. The first decomposition takes place around 200 °C due to total cleavage of the base metal complex along with hydroxide to oxide transformation followed by concomitant release of water molecules corresponding to loss of coordinated water molecules (calc. 4.76%;found 5.2%). An endothermic peak of DTA confirmed the loss of water molecules. The second decomposition takes place around 400 °C, attributed to the release of intermediate organic moiety. The third slow and broad decomposition around 510–530 °C can be attributed to total decomposition of organic moiety into carbon dioxide and other gasses. The remaining 11% weight is totally due to the presence of inorganic metal oxide [27,37].

The antibacterial and antifungal activity of the Schiff bases and their metal complexes was tested on *S. aureus, P. aeruginosa, A. niger and C. albicans.* The method used for antibacterial activity was Agar Well-Diffusion method [38] and for antifungal activity was Agar-Ditch method [39,40]. The stock solution 1 mg/ml was prepared and was used to prepare concentrations of 0.8, 0.6, 0.4 and 0.2 mg/l. The bacteria and fungi were inoculated on the surface of Nutrient agar and Sabouraud's agar, respectively. The various concentrations of the compounds were inoculated in the wells prepared on the agar plates. The plates were incubated at room temperature for 24 h. In order to clarify the effect of DMF on the biological screening, separate studies were carried out with DMF and showed no activity against any bacteria and fungi. The results are as summarized in the Table 3.The ligand shows less activity against the microorganisms and fungi. The $C_{42}H_{36}N_2O_8Cu.2H_2O$ complex shows maximum activity against bacteria as well as fungi. The cobalt complex ($C_{42}H_{36}N_2O_8Co.2H_2O$) is weakly active against the microorganism but is moderately active against fungi. The $C_{42}H_{36}N_2O_8Ni.2H_2O$ complex is highly active against *S. aureus* and moderately active against *P. aeruginosa* and *fungi.* The results were compared with standard antibiotics like Gentamycin and Streptomycin.

The hemolytic activity of the synthesized ligand and its metal complexes were determined using Wister rat erythrocytes. The RBCs were prepared as follows. 2–3 ml of rat blood was drawn into 12 ml of heparinized 5 mM HEPES buffer pH 7.4 containing 150 mM NaCl and centrifuged at 4000 rpm for 5 min. The cell pellate was washed three times with buffer and the buffy coat was removed. A working stock of RBCs was made by diluting the RBCs pellate (0.5–0.8 ml) to about 15 ml with buffer. For standardization of the volume for lysis assay,

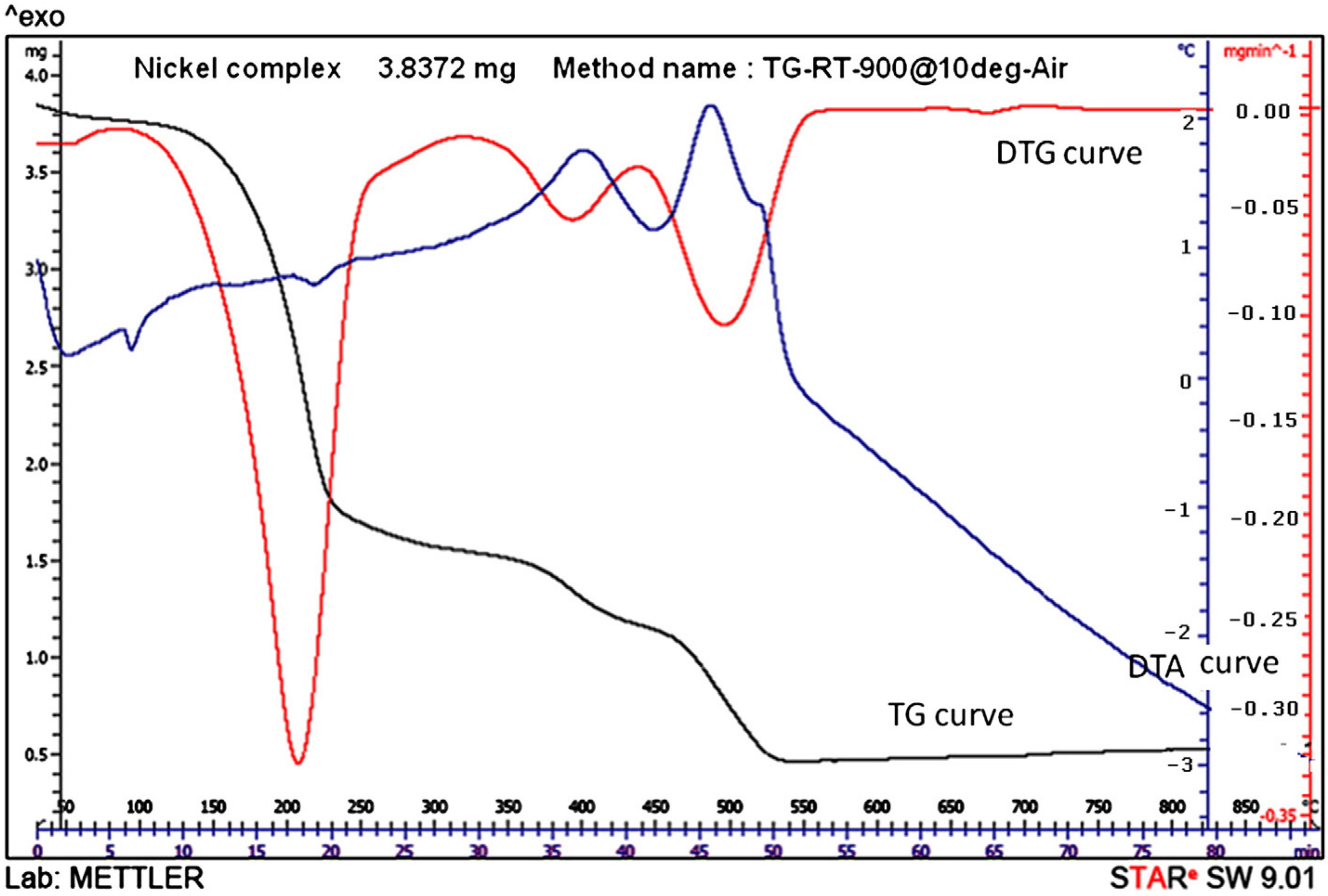

Fig. 1. Thermal analysis of nickel complex.

Table 3
Biological activity data of complexes.

Name of compd.	Conc. mg/lit.	*Staphylococcus Aureus*	*Pseudomonas Aeruginosa*	*Aspergillus niger*	*Candida albicans*
HL	0.2	Inactive	Inactive	Weakly active	Weakly active
	0.4	Inactive	Inactive	Weakly active	Weakly active
	0.6	Weakly active	Weakly active	Weakly active	Weakly active
	0.8	Weakly active	Weakly active	Weakly active	Moderately active
	1.0	Weakly active	Weakly active	Weakly active	Moderately active
HL—Co	0.2	Weakly active	Inactive	Weakly active	Weakly active
	0.4	Weakly active	Inactive	Weakly active	Weakly active
	0.6	Weakly active	Inactive	Moderately active	Moderately active
	0.8	Weakly active	Weakly active	Moderately active	Moderately active
	1.0	Moderately active	Weakly active	Moderately active	Moderately active
HL—Ni	0.2	Moderately active	Weakly active	Weakly active	Weakly active
	0.4	Moderately active	Weakly active	Weakly active	Weakly active
	0.6	Moderately active	Moderately active	Weakly active	Weakly active
	0.8	Highly active	Moderately active	Moderately active	Moderately active
	1.0	Highly active	Moderately active	Moderately active	Moderately active
HL—Cu	0.2	Moderately active	Weakly active	Weakly active	Weakly active
	0.4	Moderately active	Weakly active	Weakly active	Weakly active
	0.6	Highly active	Moderately active	Moderately active	Moderately active
	0.8	Highly active	Moderately active	Moderately active	Moderately active
	1.0	Highly active	Moderately active	Moderately active	Moderately active

Inhibition
Less than 5 mm = Inactive
6–10 mm = Weakly active
11–14 = Moderately active
15 and above = Highly active

different volumes (5–40 μl) of diluted blood samples were drawn into 1 ml of water containing 0.1% of Triton X-100 and buffer with RBCs was used as blank. The solution was centrifuged at 4000 rpm. Hemoglobin released in the supernatant was measured spectrophotometrically at 540 nm. The volume of RBCs was standardized so as the absorbance was about ~0.2 OD (about 2×10^6 cells/ml) range. This suitable volume was used for the hemolysis assay with synthesized compounds.

Different volumes of compounds were taken in 1.5 ml eppendorf tubes containing 5 mM HEPES buffer pH 7.4 containing 150 mM NaCl. To this, diluted blood suspension (volume as determined above) was added and total volume in the reaction tube was made up to 1 ml with buffer. The tubes were incubated at 37 °C for 30 min in a gentle shaking water bath. After incubation, the samples were centrifuged in a Kubota centrifuge at 4000 rpm for 5 min to remove the unhemolysed cells. The absorbance of the supernatant was measured at 540 nm. Buffer containing RBCs suspension was taken as buffer blank (A_0). The lysis obtained with 0.1% of Triton X-100 with RBCs was taken for 100% lysis control (A_{100}). The assay was carried out in duplicates and was repeated thrice. The average values were taken for plotting. The percentage hemolysis was calculated by using following equation

$$H\% = \left(A_{sample} - A_0\right) X\ 100/(A_{100} - A_0)$$

where A_{100} and A_0 are absorbance of 100% and 0% hemolysed cells respectively.

Table 4
Hemolytic activity data.

Name of compound	% RBC Lysis	
	Rat	Human
HL	24	20
HL—Co	15	15
HL—Ni	22	23
HL—Cu	30	20

The same procedure was repeated for human erythrocytes also and the results are recorded in Table 4. The cobalt complex shows less hemolytic activity. The results are very interesting and much helpful for drug designing.

All the complexes have octahedral geometry and paramagnetic nature. The cobalt ($C_{42}H_{36}N_2O_8Co.2H_2O$) and the nickel complexes ($C_{42}H_{36}N_2O_8$-$Ni.2H_2O$) are moderately active against the *S. aureus* fungi *C albicans* and *A. niger*, The highest activity is observed for copper complex.

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