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Spectral, magnetic, thermal, molecular modelling, ESR studies and antimicrobial activity of (E)-3-(2-(2-hydroxybenzylidene))hydrazinyl)-3-oxo-n(thiazole-2-yl)propanamide complexes

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ABSTRACT

(*E*)-3-(2-(2-hydroxybenzylidene)hydrazinyl)-3-oxo-*n*(thiazole-2-yl) propane-mide (H₂L) has been prepared and its structure confirmed by elemental analysis, IR and ¹HNMR spectroscopy. It has been used to produce diverse complexes with Ni(II), Co(II) and Cu(II) ions. The complexes obtained have been investigated by thermal analysis, spectral studies (IR, UV–visible, ESR), and magnetic measurements. IR spectra suggest that the H₂L acts as a bidentate ligand coordinating via (C=N)₁ and (OH)_{phenolic} or deprotonated enolized carbonyl oxygen (=C-O-)₁. The electronic spectra of the complexes and their magnetic moments provide information about geometries. The room temperature solid state ESR spectra of the Cu(II) complexes show d_{x2-y2} as a ground state, suggesting tetragonally distorted octahedral or square-planar geometries around Cu(II) centre. The molar conductance measurements proved that the complexes are non-electrolytes. The bond length, bond angle, HOMO, LUMO, dipole moment and charges on the atoms have been calculated to confirm the geometry of the ligand and the investigated. The interpretation, mathematical analysis and evaluation of kinetics of all compounds are investigated. The interpretation, mathematical analysis and evaluated using Coats–Redfern and Horowitz–Metzger methods. Finally, the antimicrobial activity has been tested.

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1. Introduction

The coordination chemistry of substituted hydrazones has received much impetus by the remarkable anticancer, amoebicidal, antibacterial, antimicrobial and antileukaemic activities exhibited by these compounds which can be related to their metal complexing abilities [1–3]. Aroylhydrazone possess strong pharmacological properties and may inhibit many enzymatic reactions catalysed by transition metals. The chemical and pharmacological properties of aroylhydrazone have been extensively investigated owing to their potential applications as antineoplastic, antiviral, antiinflammatory and antitumor agents [4–6]. Also, hydrazones have been used for the analytical determination of wide variety of metal ions [7–9]. Hydrazones have interesting ligation properties due to presence of several coordination sites. The metal complexes formed by the combination of transition metal ion with a potent acylhydrazone ligand should be more biologically active than the metal salts or

* Corresponding author. Tel.: +20 122247712. *E-mail address:* drroka78@yahoo.com (T.A. Yousef). the ligand individually. Therefore, we report here the synthesis and characterization of Ni(II), Co(II) and Cu(II) complexes with (*E*)-3-(2-(2-hydroxybenzylidene)hydrazinyl)-3-oxo-*n*(thiazole-2-yl)propanamide (H₂L). The antifungal and antibacterial properties of the ligand and its complexes were tested.

2. Experimental

2.1. Apparatus and reagents

The IR absorption spectra were recorded on a Mattson 5000 FTIR Spectrophotometer. The electronic spectra were measured on a Unicam UV/vis Spectrometer UV₂. Thermogravimetric analysis was performed using an automatic recording thermobalance type (951 DuPont instrument). Samples were subjected to heat on a rate of 10 °C/min (25–800 °C) in N₂. ¹H NMR spectra for H₂L and diamagnetic complexes, in DMSO, were recorded on EM-390 (200 MHz) Spectrometer. Carbon and hydrogen content for the ligand and its complexes was determined at the Microanalytical Unit, Mansoura University, Egypt. Co(II), Ni(II), Cu(II), Cl⁻ and

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 SO_4^{2-} contents in the complexes were determined by the well known standard methods [10]. ESR spectra were obtained on a Bruker EMX Spectrometer working in the X-band (9.78 GHz) with 100 kHz modulation frequency. The microwave power was set at 1 mW and modulation amplitude was set at 4 Gauss. The low field signal was obtained after 4 scans with a 10-fold increase in the receiver gain. A powder spectrum was obtained in a 2 mm quartz capillary at room temperature. All metal salts used were pure (Fluka, Aldrich or Merck).

2.2. Preparation of the ligand

(*E*)-3-(2-(2-hydroxybenzylidene)hydrazinyl)-3-oxo-*n*(thiazole-2yl)propan-mide (Scheme 1) was prepared by heating a mixture of 3-hydrazinyl-oxo-*N*-(thiazole-2-) propanamide (0.01 mol; 2.00 g) and salicyladehyde (0.01 mol; 1.36 g) under reflux in absolute ethanol for 3 h. On heating, white crystals were formed, filtered

off, washed with EtOH and Et_2O and recrystallized from EtOH (M.p.: 225 °C; yield 90%). The purity of the compound was checked by TLC.

2.3. Preparation of complexes

The complexes were prepared by mixing equimolar amounts of H_2L with ethanolic and/or aqueous solution of chloride salt of Cu(II); acetate salt of Ni(II), Co(II) and Cu(II) and sulphate salt of Cu(II) (Scheme 1). The reaction mixture was heated under reflux on a water bath for 1–3 h. The isolated complexes were washed several times with water, ethanol and finally with diethyl ether and the pure complexes thus obtained were dried in a desiccator over anhydrous CaCl₂. The isolated complexes are powder-like, stable in the normal laboratory atmosphere, and soluble in DMF or DMSO. The characterization of these complexes was based on the physical and spectroscopic techniques.



Scheme 1. The outline of the synthesis of ligand and its complexes.

2.4. Molecular modelling

An attempt to gain a better insight on the molecular structure of the ligand and its complexes, geometry optimization and conformational analysis has been performed by the use of MM+ force-field as implemented in hyperchem 8.0 [11]. The low lying obtained from MM+ was then optimized at PM3 using the Polak–Ribiere algorithm in RHF-SCF, set to terminate at an RMS gradient of 0.01 kcal mol⁻¹.

2.5. Antimicrobial activity

The compounds, Gentamycin and Colitrimazole were dissolved in DMSO at concentration of 1 μ g/ml. The twofold dilutions of the solution were prepared. The microorganism suspensions [12] at 10 CFU/ml (colony forming unit/ml) concentration were inoculated to the corresponding wells. The plates were incubated at 36 °C for 24 and 48 h for the bacteria and *Candida albicans*, respectively. The MIC values were determined as the lowest concentration that completely inhibited visible growth of the microorganism as detected by unaided eye.

3. Results and discussion

The isolated solid complexes are stable in air and easily soluble in DMF and DMSO only. All complexes decompose on heating at >300 °C. The molar conductance value, in DMSO, is $3-6 \,\Omega^{-1}$ cm² mol⁻¹ indicating that the all complexes are non-electrolytes Table 1.

3.1. IR and ¹H NMR spectral studies

The ¹H NMR spectrum of H₂L (Fig. 1) in d_6 -DMSO shows three signals at 12.89, 11.20 and 13.06 ppm assignable to the protons of (N_1H) , (N_2H) and $(OH)_{phenolic}$, respectively. The appearance of the signal attributed to the proton of OH group at a high value downfield from TMS suggests the presence of intramolecular hydrogen bonding. The multiple signals observed in the 6.96–7.78 ppm region are assigned to the aromatic and (-N=C-H)protons. The signal at δ 3.69 ppm is assigned to the protons of methylene group ($-CH_2-$). The infrared spectrum of H_2L exhibits characteristic bands at 1692, 1649, 1615, 1566, 3215, 3153 and 3425 cm⁻¹ assigned to $v(C=0)_1$, $v(C=0)_2$ [13], $v(C=N)_1$, $v(C=N)_2$ [14], v(N₁H), v(N₂H) [15] and (OH) [16] vibrations, respectively Table 2. The appearance of (OH) as a broad band at lower wavenumber and the two weak broad bands in the 1900-2080 and 2150-2230 cm⁻¹ regions suggest intramolecular hydrogen bonding $(O-H \cdots O)$ [17].

On comparison of the spectrum of the ligand with that of $[Ni(H_2L)(OAc)_2]\cdot H_2O$, $[Co(H_2L)(OAc)_2]\cdot 2H_2O$ and $[Cu(H_2L)Cl_2]\cdot H_2O$ complexes, we found that there are negative shift of both v(OH) and $v(C=N)_1$ vibrations. While, the $v(C=O)_1$, $v(C=O)_2$, $v(C=N)_2$, $v(N_1H)$ and $v(N_2H)$ vibrations remain at more or less at the same position Table 2, which indicates that they does not participate in coordinating via (OH) and azomethine nitrogen (C=N)_1 atoms. Also, new bands were observed in 518–521 and 460–470 cm⁻¹ regions which assigned to v(M=O) and v(M=N) [16], respectively.

Moreover, the IR spectra of $[Cu(HL)_2(H_2O)_2]$ and [Cu(HL)(OAc)]complexes reflect that the H₂L acts as a monoanionic bidentate ligand coordinating via the deprotonated enolized carbonyl oxygen $(=C-O^-)_1$ and azomethine nitrogen $(C=N)_1$. This mode of complexation is supported by the following observations: (i) the shift of $v(C=N)_1$ to lower wave numbers, (ii) the disappearance of both $v(C=O)_1$ and $v(N_1H)$ with simultaneous appearance of new band at 1125 and 1614 cm⁻¹ which assignable to $v(C-O)_{1(eno$ $lic)}$ and v(C=N), respectively and (iii) the appearance of new bands at 523 and 478 cm⁻¹ which may be attributed to v(Cu-O) and v(Cu-N), respectively [18].

In metal acetate complexes, the acetate group coordinates to the metal ions in a bidentate manner where the difference between the two acetate bands is $\Delta v \leq 180 \text{ cm}^{-1}$ [19]. Also, the bands of coordinated water observed at 854 and 595 cm⁻¹, are assigned to $\rho_r(\text{H}_2\text{O})$ and $\rho_w(\text{H}_2\text{O})$, respectively [19]. Moreover, strong evidence for the presence or absence of water of crystallization and/or coordinated water supported by the thermogram of all complexes.

3.2. Electronic spectra and magnetic moment measurements

The electronic spectrum of $[Ni(H_2L)(OAc)_2] \cdot H_2O$ complex shows two bands at 13,605 and 22,727 cm⁻¹ attributed to ${}^{3}A_{2g} \rightarrow {}^{3}T_{1g}(F)$ and ${}^{3}A_{2g} \rightarrow {}^{3}T_{1g}(P)$ transitions, respectively, in an octahedral geometry [20]. The calculated values of D_q , B, β and v_2/v_1 lie in the range reported for an octahedral structure Table 3 [20]. The position of v_1 (8146 cm⁻¹) is calculated theoretically. The value of the magnetic moment ($\mu_{eff.}$ = 3.13 B.M.) is additional evidence for an octahedral geometry.

The electronic spectrum of $[Co(H_2L)(OAc)_2]\cdot 2H_2O$ complex exhibits two bands at 14,065 and 17,241 cm⁻¹ attributed to ${}^{4}T_{1g} \rightarrow {}^{4}A_{2g}(F)$ and ${}^{4}T_{1g} \rightarrow {}^{4}T_{1g}(P)$ transitions, respectively, in an octahedral configuration [20]. The calculated D_q , B, β and v_2/v_1 values are in the range reported for an octahedral environment around Co(II) complexes. The position of v_1 (6541 cm⁻¹) is calculated theoretically. Also, the value of the magnetic moment (4.97 B.M.) is additional evidence for an octahedral geometry around the Co(II) ion.

| Table 1 | |
|--|----|
| Analytical and physical data of H ₂ L and its metal complexes | š. |

| Compound empirical formula (F.wt.) | Colour | MP (°C) | Yield (%) | %Found (Calo | Λ_m^* | | |
|--|--------|---------|-----------|--------------|---------------|---------|---|
| | | | | С | Н | М | |
| H ₂ L | White | 225 | 90 | 51.42 | 4.11 | - | - |
| C ₁₃ H ₁₂ O ₃ N ₄ S (304.3) | | | | (51.30) | (3.97) | - | |
| $[Ni(H_2L)(OAc)_2] \cdot H_2O$ | Green | >300 | 80 | 40.84 | 4.35 | 11.82 | 4 |
| NiC ₁₇ H ₂₀ O ₈ N ₄ S (499.1) | | | | (40.91) | (4.04) | (11.76) | |
| $[Co(H_2L)(OAc)_2] \cdot 2H_2O$ | Green | >300 | 85 | 39.61 | 4.40 | 11.36 | 4 |
| CoC ₁₇ H ₂₂ O ₉ N ₄ S (517.3) | | | | (39.46) | (4.28) | (11.39) | |
| $[Cu(H_2L)Cl_2] \cdot H_2O$ | Green | >300 | 80 | 34.32 | 3.15 | 14.01 | 6 |
| CuC ₁₃ H ₁₄ O ₄ N ₄ SCl ₂ (456.7) | | | | (34.15) | (3.09) | (13.91) | |
| $[Cu(HL)_2(H_2O)_2]$ | Green | >300 | 78 | 44.24 | 3.80 | 9.01 | 3 |
| CuC ₂₆ H ₂₆ O ₈ N ₈ S ₂ (706.1) | | | | (44.18) | (3.71) | (8.99) | |
| [Cu(HL)(OAc)] | Green | >300 | 82 | 42.28 | 3.36 | 14.94 | 4 |
| CuC ₁₅ H ₁₄ O ₅ N ₄ S (425.9) | | | | (42.30) | (3.32 | (14.92) | |



Fig. 1. ¹H NMR spectrum of (E)-3-(2-(2-hydroxybenzylidene)hydrazinyl)-3-oxo-n(thiazole-2-yl) propanamide (H₂L).

Table 2

Most important IR spectral bands of H₂L and its metal complexes in cm⁻¹.

| Compound | v(OH) | $\nu(N_1H)$ | $\nu(N_2H)$ | v(C=0)1 | v(C=0)2 | $v(C=N)_1$ | $v(C=N)_2$ | $\nu(CH_2)$ | v(CO) ₁ | $\nu(C=N^{*})_{2}$ | v(M-O) | v(M-N) |
|--------------------------------|-------|-------------|-------------|---------|---------|------------|------------|-------------|--------------------|--------------------|--------|--------|
| H ₂ L | 3425 | 3215 | 3153 | 1692 | 1649 | 1615 | 1566 | 2933 | - | - | - | - |
| $[Ni(H_2L)(OAc)_2] \cdot H_2O$ | 3385 | 3208 | 3174 | 1691 | 1648 | 1606 | 1581 | 2935 | - | - | 521 | 460 |
| $[Co(H_2L)(OAc)_2]\cdot 2H_2O$ | 3380 | 3209 | 3150 | 1692 | 1646 | 1601 | 1574 | 2937 | - | - | 521 | 470 |
| $[Cu(H_2L)Cl_2] \cdot H_2O$ | 3385 | 3217 | 3116 | 1692 | 1646 | 1606 | 1570 | 2937 | - | - | 519 | 472 |
| $[Cu(HL)_2(H_2O)_2]$ | 3419 | 3261 | - | 1700 | - | 1595 | 1566 | 2933 | 1125 | 1614 | 523 | 478 |
| [Cu(HL)(OAc)] | 3428 | 3275 | - | 1701 | - | 1596 | 1574 | 2934 | 1125 | 1614 | 523 | 478 |

Table 3

Magnetic moments, electronic spectra and ligand field parameters of metal complexes of H₂L.

| Complex | $\mu_{\rm eff}$ (B.M.) | Band position (cm ⁻¹) | $D_q ({ m cm}^{-1})$ | <i>B</i> (cm ⁻¹) | β | v_2/v_1 |
|--------------------------------|------------------------|-----------------------------------|----------------------|------------------------------|------|-----------|
| $[Ni(H_2L)(OAc)_2] \cdot H_2O$ | 3.13 | 13,605; 22,727 | 903 | 813 | 0.78 | 1.67 |
| $[Co(H_2L)(OAc)_2]\cdot 2H_2O$ | 4.97 | 14,065; 17,241 | 763 | 803 | 0.83 | 2.15 |
| $[Cu(H_2L)Cl_2] \cdot H_2O$ | 1.92 | 14,709 | - | - | - | - |
| $[Cu(HL)_2(H_2O)_2]$ | 1.98 | 14,749; 16,667 | - | - | - | - |
| [Cu(HL)(OAc)] | 2.01 | 14,285 | - | - | - | - |

Table 4

ESR data of the copper (II) complexes at room temperature.

| Complex | g_ | g_{\perp} | $A_{/\!\!/} 	imes 10^{-4} ({ m cm}^{-1})$ | G | α^2 | β^2 |
|--|------|-------------|--|-----|------------|-----------|
| $\begin{tabular}{l} [Cu(HL)_2(H_2O)_2] \\ [Cu(H_2L)Cl_2]\cdot H_2O \\ [Cu(HL)(OAc)] \end{tabular}$ | 2.23 | 2.05 | 160 | 4.6 | 0.75 | 0.6 |
| | 2.26 | 2.08 | 174 | 3.2 | 0.81 | 0.70 |
| | 2.20 | 2.06 | 168 | 3.3 | 0.37 | 0.58 |

The Cu(II) complexes have magnetic moment values (1.92–2.01 B. M.) which correspond to those reported for d^9 -systems. The electronic spectra of $[Cu(H_2L)Cl_2] \cdot H_2O$ and [Cu(HL)(OAC)] complexes exhibit a broad band with a maximum at 14,709 and 14,285 cm⁻¹, respectively, assigned to ${}^{2}B_{1g} \rightarrow {}^{2}A_{1g}$ transition as reported for square planar Cu(II) complexes [21]. The electronic spectrum of $[Cu(HL)_2(H_2O)_2]$ complex shows a broad band at 16,667 cm⁻¹ with a shoulder at 14,749 cm⁻¹ which may assign to ${}^{2}B_{1g} \rightarrow {}^{2}E_{g}$ and ${}^{2}E_{g} \rightarrow {}^{2}A_{1g}$ transitions, respectively, in a tetragonally distorted octahedral configuration [21].

3.3. ESR spectra

The solid state ESR spectra of some complexes exhibit axially symmetric *g*-tensor parameters with $g_{y} \leq g_{\perp} > 2.0023$ indicating that the copper site has a d_{x2-y2} ground-state characteristic of tetrahedral, square planar or octahedral stereochemistry [22]. The spin Hamiltonian parameters of these complexes were calculated Table 4. In axial symmetry the *g*-values are related by the

expression, $G = (g_{\parallel} - 2)/(g_{\perp} - 2) = 4$, where *G* is the exchange interaction parameter. According to Hathaway and Billing [23], if the value of *G* is greater than 4, the exchange interaction between Cu(II) centres in the solid state is negligible, whereas when is less than 4, a considerable exchange interaction is indicated in the solid complex. The calculated *G* values for [Cu(HL)₂(H₂O)₂], [Cu(H₂L)Cl₂]·H₂O and [Cu(HL)(OAc)] complexes are 4.5, 4.4 and 4.2, respectively (Fig. 2), suggesting that there are no copper–copper exchange interactions.

The tendency of A_{\parallel} to decrease with an increase of g_{\parallel} is an index of an increase of the tetrahedral distortion in the coordination sphere of copper [24]. In order to quantify the degree of distortion of the Cu(II) complexes, we selected the f factor $g_{\parallel}/A_{\parallel}$ obtained from the ESR spectra. Although the *f* factor, which is considered as an empirical index of tetrahedral distortion [25]. Its value ranges between 105 and 135 for square planar complexes, depending on the nature of the coordinated atoms. In the presence of a tetrahedrally distorted structure the values can be much larger [26]. For $[Cu(H_2L)Cl_2] \cdot H_2O$ and [Cu(HL)(OAc)] complexes the $g_{\parallel}/A_{\parallel}$ quotient is 129 and 130, respectively, evidence in support of the square planar geometry with no appreciable tetrahedral distortion. But, the ratio $g_{\parallel}/A_{\parallel}$ for the complex $[Cu(HL)_2(H_2O)_2]$ is 139 demonstrating the presence of significant dihedral angle distortion in the xy-plane and indicating a tetrahedral distortion from square planar geometry and the results are consistent with distorted octahedral geometry around the copper site.

Molecular orbital coefficients, α^2 (covalent in-plane σ -bonding) and β^2 (covalent in-plane π -bonding) were calculated [27–30]:

Fig. 2. Room temperature X-band ESR spectra of (a) $[Cu(H_2L)Cl_2]\cdot H_2O$ (b) [Cu(HL)(OAc)] and (c) $[Cu(HL)_2(H_2O)_2].$

$$\alpha^{2} = \left(\frac{A_{\#}}{0.036}\right) + \left(g_{\#}2.0023\right) + \frac{3(g_{\perp} - 2.0023)}{7} + 0.04$$

where $\lambda = 828 \text{ cm}^{-1}$ for the free ion and *E* is the ${}^{2}B_{1g} \rightarrow {}^{2}A_{1g}$ transition.

As a measure of the covalency of the in-plane σ -bonding $\alpha^2 = 1$ indicates complete ionic character, whereas $\alpha^2 = 0.5$ denotes 100% covalent bonding, with the assumption of negligibly small values of the overlap integral. The β^2 parameter gives an indication of the covalency of the in-plane π -bonding. The smaller the β^2 , the larger the covalency of the bonding.

The values of α^2 and β^2 for $[Cu(HL)_2(H_2O)_2]$ complex indicate that the in-plane σ -bonding and in-plane π -bonding are apprecia-

Table 5

Thermal behaviour of metal complexes of H₂L.

 $-8\lambda\alpha^2$

bly covalent and are consistent with very strong in-plane π -bonding in this complex, but in [Cu(H₂L)Cl₂]·H₂O and [Cu(HL)(OAc)] complexes, the results indicate that the in-plane σ -bonding and in-plane π -bonding are appreciably ionic. These results are anticipated because there are appropriate ligand orbitals to combine with the d_{xy} orbital of the Cu(II) ion. For the square planar geometry complexes, the lower values of β^2 compared to α^2 indicate that the in-plane π -bonding is more covalent than the in-plane σ -bonding. These data are well consistent with other reported values [31,32].

3.4. Thermal analysis

The TG of the isolated complexes was taken as a proof for the existing of water molecules as well as the anions to be coordination sphere. The water of crystallization lost in 30-110 °C regions while those coordinated lost at 235 °C. The complexes show thermal stability rather than the ligand where the beginning of its decomposition shifts to higher temperature (246-700 °C). In general, all complexes are thermally stable; $[Cu(HL)_2(H_2O)_2]$ is the highest one. It is thermally stable up to 238 °C above which the dehydration begins. In the temperature range 238-350 °C, the TG curve displays 45.1% weight loss which could be ascribed to the elimination of the two coordinated water molecules [33] as well as the two loosely bound $(C_5H_5ON_2S)$ fragments. The second weight loss stage (350–446 °C) is due to decomposition of the two organic portions (2C₆H₅O). The final weight loss of 34.3% ending at 600 °C. is largely attributed to complete decomposition of the remaining more two tightly bound fragment $(2C_2HN_2)$ as well as the release of half oxygen molecule. The remaining final fired product is CuO, representing 11.2%. The data of the different decomposition steps of all isolated complexes are shown in Table 5.

3.5. Kinetic data

The kinetic and thermodynamic parameters of thermal degradation process have been calculated using Coats-Redfern and

| Complex (M.wt.) | Temp. range (°C) | Decomp. prod. (F.wt.) | Wt. loss (%) | | |
|---|------------------|--|--------------|-------|--|
| | | | Found | Calcd | |
| [Ni(H ₂ L)(OAc) ₂]·H ₂ O (499.1) | 35-105 | H ₂ O (18.015) | 3.8 | 3.6 | |
| | 145-246 | 2C ₂ H ₃ O ₂ (118.092) | 23.6 | 23.7 | |
| | 246-393 | C ₃ H ₄ N ₂ S (100.136) | 20.0 | 20.1 | |
| | 393-700 | $C_{10}H_8O_2N_2$ (188.176) | 37.5 | 37.6 | |
| | >700 | Residue, NiO (74.709) | 15.1 | 15.0 | |
| [Co(H ₂ L)(OAc) ₂]·2H ₂ O (517.3) | 32-109 | 2H ₂ O (36.032) | 6.9 | 7.0 | |
| | 139–284 | 2C ₂ H ₃ O ₂ (118.092) | 22.7 | 22.8 | |
| | 284-398 | C ₃ H ₄ N ₂ S (100.136) | 19.3 | 19.4 | |
| | 398–595 | $C_{10}H_8O_2N_2$ (188.176) | 36.6 | 36.4 | |
| | >595 | Residue, CoO (74.929) | 14.5 | 14.4 | |
| [Cu(H ₂ L)Cl ₂]·H ₂ O (456.7) | 30-110 | H ₂ O (18.015) | 3.9 | 4.0 | |
| | 110-255 | Cl ₂ (70.906) | 15.5 | 15.5 | |
| | 255-365 | C ₃ H ₄ N ₂ S (100.136) | 22.0 | 21.9 | |
| | 365-675 | $C_{10}H_8O_2N_2$ (188.176) | 41.2 | 41.2 | |
| | >675 | Residue, CuO (79.540) | 17.4 | 17.4 | |
| [Cu(HL) ₂ (H ₂ O) ₂] (706.1) | 238-350 | 2H ₂ O + 2(C ₅ H ₅ ON ₂ S)(318.119) | 45.1 | 45.1 | |
| | 350-446 | 2C ₆ H ₅ O (186.089) | 26.4 | 26.4 | |
| | 446-600 | 2C ₂ HN ₂₊ ¹ / ₂ O ₂ (122.018) | 17.3 | 17.3 | |
| | >600 | Residue, CuO (79.540) | 11.2 | 11.2 | |
| [Cu(HL)(OAc)] (425.9) | 160-330 | C ₂ H ₃ O ₂ (59.054) | 13.9 | 13.9 | |
| | 330–380 | $C_5H_5ON_2S$ (141.045) | 33.1 | 33.2 | |
| | 380–510 | C ₈ H ₆ N ₂₊ ¹ / ₂ O ₂ (146.156) | 34.3 | 34.2 | |
| | >510 | Residue, CuO (79.540) | 18.7 | 18.7 | |
| | | | | | |



Table 6

Kinetic parameters of complexes evaluated by Coats-Redfern equation.

| Complex | Peak | Mid temp (K) | Ea (kJ/mol) | $A(S^{-1})$ | ΔH^* (kJ/mol) | ΔS^* (kJ/mol K) | ΔG^* (kJ/mol) |
|--------------------------------|------|--------------|-------------|-------------|-----------------------|-------------------------|-----------------------|
| $[Co(H_2L)(OAc)_2]\cdot 2H_2O$ | 1st | 344 | 444.9 | 7.2862E7 | 442.1 | -0.0955 | 474.9 |
| | 2nd | 484 | 27.0 | 1.4872E-5 | 22.9 | -0.3414 | 188.2 |
| | 3rd | 616 | 476.7 | 20887.45 | 471.5 | -0.1682 | 575.2 |
| | 4rd | 767 | 174.4 | 3.4683E7 | 168.1 | -0.1084 | 251.2 |
| $[Ni(H_2L)(OAc)_2] \cdot H_2O$ | 1st | 343 | 30.9 | 0.30654 | 28.1 | -0.2559 | 115.9 |
| | 2nd | 468 | 72.4 | 53.23621 | 68.6 | -0.2156 | 169.5 |
| | 3rd | 591 | 131.4 | 7.4560E6 | 126.5 | -0.1190 | 196.9 |
| | 4th | 823 | 648.3 | 233861.8 | 641.5 | -0.1505 | 765.4 |
| $[Cu(HL)_2(H_2O)_2]$ | 1st | 563 | 108.9 | 52210.3 | 104.3 | -0.1598 | 194.3 |
| | 2nd | 683 | 198.6 | 145.9 | 192.9 | -0.2103 | 336.6 |
| [Cu(HL)(OAc)] | 1st | 529 | 65.9 | 7.66498 | 61.6 | -0.2327 | 184.7 |
| | 2nd | 628 | 215.0 | 5.4965E12 | 209.8 | -0.0072 | 214.3 |
| | 3rd | 710 | 98.3 | 94.46723 | 92.4 | -0.2143 | 244.6 |
| $[Cu(H_2L)Cl_2] \cdot H_2O$ | 1st | 360 | 45.2 | 61.00084 | 42.2 | -0.2123 | 118.7 |
| | 2nd | 460 | 41.3 | 0.04279 | 37.5 | -0.2747 | 163.9 |
| | 3rd | 575 | 126.6 | 1.8189E6 | 121.8 | -0.1305 | 196.9 |
| | 4rd | 742 | 88.2 | 8.5545 | 82.1 | -0.2346 | 256.2 |
| | | | | | | | |

Table 7

Kinetic parameters of complexes evaluated by Horowitz-Metzger equation.

| Complex | Peak | Mid temp (K) | Ea (kJ/mol) | $A(S^{-1})$ | ΔH^* (kJ/mol) | ΔS^* (kJ/mol K) | ΔG^* (kJ/mol) |
|---|------|--------------|-------------|-------------|-----------------------|-------------------------|-----------------------|
| [Co(H ₂ L)(OAc) ₂]·2H ₂ O | 1st | 344 | 444.7 | 7.3729E7 | 441.8 | -0.0954 | 474.6 |
| | 2nd | 484 | 27.5 | 1.5191E-5 | 23.5 | -0.3411 | 188.6 |
| | 3rd | 616 | 476.7 | 19667.38 | 471.6 | -0.1687 | 251.0 |
| | 4rd | 767 | 174.3 | 3.4931E7 | 167.9 | -0.1083 | 251.0 |
| [Ni(H ₂ L)(OAc) ₂]·H ₂ O | 1st | 343 | 30.3 | 0.30516 | 27.5 | -0.2559 | 115.2 |
| | 2nd | 468 | 72.5 | 55.64061 | 68.6 | -0.2152 | 169.3 |
| | 3rd | 591 | 131.4 | 6.8283E6 | 126.5 | -0.1197 | 197.3 |
| | 4th | 823 | 648.5 | 237173.6 | 641.7 | -0.1504 | 765.5 |
| $[Cu(HL)_2(H_2O)_2]$ | 1st | 563 | 108.6 | 57356.8 | 103.9 | -0.1591 | 193.5 |
| | 2nd | 683 | 198.8 | 145.1 | 193.1 | -0.2104 | 336.8 |
| [Cu(HL)(OAc)] | 1st | 529 | 65.8 | 8.00962 | 61.4 | -0.2323 | 184.4 |
| | 2nd | 628 | 215.3 | 5.485E12 | 210.0 | -0.0072 | 214.6 |
| | 3rd | 710 | 98.6 | 90.30893 | 92.7 | -0.2146 | 245.1 |
| $[Cu(H_2L)Cl_2] \cdot H_2O$ | 1st | 360 | 45.6 | 56.94588 | 42.6 | -0.2128 | 119.3 |
| | 2nd | 460 | 41.3 | 0.04366 | 37.5 | -0.2745 | 163.8 |
| | 3rd | 575 | 126.9 | 1.8612E6 | 122.1 | -0.1303 | 197.0 |
| | 4rd | 742 | 88.3 | 8.46765 | 82.1 | -0.2347 | 256.3 |

Z

Horowitz-Metzger models [34,35]. Coats-Redfern relation is as follows:

$$\ln\left[-\frac{\ln(1-\alpha)}{T^2}\right] = \ln\left(\frac{AR}{\beta E}\right) - \frac{E}{RT}$$
(1)

where α represents the fraction of sample decomposed at time *t*, defined by: $\alpha = \frac{w_0 - w_t}{w_0 - w_{propo}}$, w_o , w_t and w_∞ are the weight of the sample before the degradation, at temperature *t* and after total conversion, respectively. *T* is the derivative peak temperature. β is the heating rate = dT/dt, *E* and *A* are the activation energy and the Arrhenius pre-exponential factor, respectively. A plot of $\ln[-\frac{\ln(1-\alpha)}{T^2}]$ versus 1/T gives a straight line whose slope (*E/R*) and the pre-exponential factor (*A*) can be determined from the intercept. The Horowitz–Metzger relation [35] used to evaluate the degradation kinetics is:

$$\ln[-\ln(1-\alpha)] = \frac{E\theta}{RT_c^2}$$
(2)

where $\theta = T - T_s$, T_s is the DTG peak temperature, T is the temperature corresponding to weight loss Wt. A straight line should be observed between $\ln[-\ln(1 - \alpha)]$ and θ with a slope of $\frac{E}{RT_s^2}$. A number of pyrolysis processes can be represented as a first order reaction. Particularly, the degradation of a series of H₂L complexes was suggested to be first order [36], therefore we assume n = 1 for the

remainder of the present text. The other thermodynamic parameters of activation can be calculated by Eyring equation [37]:

| (3) |) |
|-----|--------------|
| (| (3) |

$$\Delta S = R \ln \frac{hA}{k_B T} \tag{4}$$

$$\Delta S = \Delta H - T \Delta S \tag{5}$$

Thermodynamic parameters such as activation energy (*Ea*), preexponential factor (*A*), entropy of activation (ΔS), enthalpy of activation (ΔH) and free energy of activation (ΔG) of decomposition steps were calculated using Coats–Redfern [34] and Horowitz–Metzger [35] methods Tables 6 and 7. In both methods, the lift side of Eqs. (3) and (4) are plotted against 1/*T* and θ , respectively (Figs. 3 and 4). From the results, the following remarks can be pointed out:

- The high values of the energy of activation, *E* of the complexes reveals the high stability of such chelates due to their covalent bond character [38].
- The positive sign of ΔG for the investigated complexes reveals that the free energy of the final residue is higher than that of the initial compound, and all the decomposition steps are non-spontaneous processes. Also, the values of the activation,



Fig. 3. Coats-Redfern plots of (A) [Co(H₂L)(OAc)₂]-2H₂O, (B) [Cu(HL)(OAc)], (C) [Cu(H₂L)Cl₂]·H₂O (D) [Cu(HL)₂(H₂O)₂] and (E)[Ni(H₂L)(OAc)₂]·H₂O.

 ΔG increases significantly for the subsequent decomposition stages of a given complex. This is due to increasing the values of *T* ΔS significantly from one step to another which overrides the values of ΔH [39–41].

- The negative values of ΔS for the degradation process indicates more ordered activated complex than the reactants or the reaction is slow [37].

3.6. Molecular modelling

The molecular numbering of ligand and its metal complexes are shown in Figs. 5–7. Some parameters like total energy, binding energy, electronic energy, heat of formation, dipole moment, highest occupied molecular orbitals (HOMO) and lowest unoccupied molecular orbitals (LUMO) of each ligand and its complexes have been calculated and presented in Tables (Supplementary Materials) (1S – 7S).

The lower HOMO energy values show that molecules donating electron ability is the weaker. On contrary, the higher HOMO energy implies that the molecule is a good electron donor. LUMO energy presents the ability of a molecule receiving electron [42].

Analysis of the data in Tables 1S–7S (Supplementary Materials) calculated for the bond lengths and angles for the bond, one can conclude the following remarks:

1. The C(8)—N(6) bond length becomes slightly longer in complex as the coordination takes place via N atoms of -C--N-N=C-group that is formed on deprotonation of OH group in [Cu(H-L)(OAc)] complex [43].



 $\textbf{Fig. 4.} Horowitz-Metzger plots of (A) [Co(H_2L)(OAc)_2] \cdot 2H_2O, (B) [Cu(HL)(OAc)], (C) [Cu(H_2L)Cl_2] \cdot H_2O (D) [Cu(HL)_2(H_2O)_2] and (E) [Ni(H_2L)(OAc)_2] \cdot H_2O (D) [Cu(H_2L)(H_2O)_2] + (H_2O)_2] \cdot H_2O (D) [Cu(H_2L)(H_2O)_2] + (H_2O)_2 + (H_2$

- 2. There is a large variation in N(10)—N(16) bond lengths on complexation. It becomes slightly longer as the coordination takes place via N(6) atom and O(8) in case of [Cu(H₂L)Cl₂]·H₂O complex while becomes shorter in case of [Cu(HL)(OAc)] complex.
- 3. The C(11)—O(18) bond distance in [Cu(HL)(OAc)] complex becomes longer due to the formation of the M—O bond which makes the C—O bond weaker [44].
- 4. The bond angles of the hydrazone moiety of *L* are altered somewhat upon coordination but the angles around the metal undergo appreciable variations upon changing the metal centre [45]. the largest change affects C(8)–N(16)–N(10),

C(1)—C(2)—O(7), and N(16)—C(8)—C(1) angles which are reduced or increased on complex formation as a consequence of bonding.

5. The bond angles in complexes namely, $[Cu(H_2L)Cl_2]$ ·H₂O and [Cu(HL)(OAc)] are quite near to a square planar geometry predicting dsp² hybridization.

3.7. Antimicrobial activity

Minimum inhibitory concentration (MIC) [46,47] was determined for each of the active compounds along with Gentamycin and Colitrimazole as standard controls; results are shown in



Fig. 5. Molecular modelling of the ligand.



Fig. 6. Molecular modelling of [Cu(HL)(OAc)].



Fig. 7. Molecular modelling of [Cu(H₂L)Cl₂]·H₂O.

Table 8. This screening was performed against the Gram-negative and *Escherechia coli*, in addition to the pathogenic fungi *C. albicans*. The following standard organisms used in the antimicrobial screening were obtained from IFO (Institute Fermentation of Osaka); *E. coli* IFO 3301 and *C. albicans* IFO 0583. The tested compounds were dissolved in dimethylsulphoxide (DMSO) at a concentration of 1 mg/ml. Amongst all the compounds tested, $[Cu(H_2L)Cl_2]$ ·H₂O demonstrated the most potent antimicrobial

Table 8

Antimicrobial and antimycotic activities in terms of MIC (mg/ml) after 48 h.

| Compound | E. coli | C. albicans |
|--|---------|-------------|
| H ₂ L | 3000 | 3000 |
| $[Co(H_2L)(OAc)_2] \cdot 2H_2O$ | 1500 | 3000 |
| [Ni(H ₂ L)(OAc) ₂]·H ₂ O | 750 | 375 |
| $[Cu(HL)_2(H_2O)_2]$ | 3000 | 1500 |
| [Cu(HL)(OAc)] | 750 | 1500 |
| $[Cu(H_2L)Cl_2] \cdot H_2O$ | 187.5 | 3.75 |
| Gentamycin | 375 | - |
| Colitrimazole | - | 5.85 |

activity against E. coli and C. albicans. It is noteworthy that the observed antimicrobial activity was highly dependent on the metal complex, in which copper complex played an important role in achieving an excellent level of biological activity. It is observed from these studies that most of the metal chelates have a higher activity than the free ligand. Such increased activity of the metal chelates can be explained on the basis of Overtone's concept and chelation theory [48]. According to Overtone's concept of cell permeability the lipid membrane that surrounds the cell favours the passage of only lipid soluble materials due to which liposolubility is an important factor that controls antimicrobial activity. On chelation, the polarity of the metal ion is 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 *p*-electrons over the whole chelate ring and enhances the lipophilicity of the complex. This increased lipophilicity enhances the penetration of the complexes into lipid membranes and blocking of metal binding sites on the enzymes of the microorganism. It was observed from the Table 8, complexes demonstrated the lowest potent antimicrobial activity.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molstruc.2011.06.050.

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