



Synthesis, characterization and biological investigations of novel Schiff base ligands containing imidazoline moiety and their Co(II) and Cu(II) complexes

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ARTICLE INFO

Article history:

Received 22 December 2017

Received in revised form

24 March 2018

Accepted 25 March 2018

Available online 28 March 2018

Keywords:

Imidazolines

Schiff base

DFT

Thermal analyses

Antimicrobial activity

ABSTRACT

Novel imidazoline based Schiff base ligands L¹ and L² were synthesized from o-phenylenediamine/o-aminophenol with creatinine. The ligands were complexed with Co(II) and Cu(II) by direct reaction with metal salts. The synthesized ligands and the metal complexes were characterized by elemental analysis, FT-IR, ¹H NMR, mass, electronic, thermal analyses, conductivity and magnetic susceptibility measurements. The conductivity measurements showed the non-electrolytic nature of the complexes. The thermogravimetric analyses confirmed the presence of lattice and coordinated water molecules in the complexes. The DFT calculations were carried out at B3LYP/6-31G(d,p) level for the determination of the optimized structure of the ligands. The synthesized ligands and the metal complexes were screened for their antimicrobial activity against two gram positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and two gram negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) and two fungal strains (*Aspergillus niger* and *Candida albicans*). The outcomes revealed that the metal complexes showed pronounced activity than the ligands.

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1. Introduction

Schiff bases are an interesting class of compounds having azo-methine linkage (C=N) and are called as privileged ligands due to their stability and chelating properties [1]. These are the most expedient and versatile ligands which are easily synthesized in a one step procedure through condensation of common aldehydes with amines with virtually quantitative yields. Heterocyclic Schiff base ligands containing nitrogen, sulphur and oxygen donor atoms and their transition metal complexes are of great interest as simple structural models of biological system due to the presence of multifunctional groups [2–5]. Schiff base ligands easily form complexes with almost all the metal ions [6]. These compounds exhibit broad spectrum of pharmacological activities, such as antiviral, anticancer, antibacterial, antifungal, anticonvulsant and anti-inflammatory activities that can be well illustrated by the large number of drugs in the market containing their functional group [7]. A broad array of medicinal applications of these compounds has

been investigated, and some of them are found to be useful both as clinical diagnostic agents and in chemotherapeutic applications [8–18].

Many synthetic drugs such as cimetidine, azomycin and metronidazole contain imidazole ring. The substituted imidazole derivatives like ketoconazole, miconazole and clotrimazole are valuable antifungals. It is also present in the anticancer medication mercaptopurine, which combats leukemia by interfering with DNA activities. Metals like cobalt, nickel and copper have great affinity for coordination because of their smaller size, higher nuclear charge [19].

Following all these observations we were interested to incorporate imidazole moiety in Schiff base ligands. Herein we report the synthesis and characterization of two Schiff base ligands derived from creatinine and o-phenylenediamine/o-aminophenol. The study has been extended to synthesize Co(II) and Cu(II) complexes with the prepared ligands. All the prepared ligands and the complexes have been characterized by IR, ¹H NMR, UV–Vis, in addition to elemental analysis, molar conductivity and magnetic susceptibility. As part of the ongoing studies, DFT calculations were carried out to study the optimized structure, frontier molecular orbitals (FMOs) and molecular electrostatic potential (MEP) of the

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ligands.

The antimicrobial activities of Schiff bases and their metal complexes were tested against gram positive and gram negative bacteria and fungal strains. The activity results showed that Co(II) complexes were more potent against the microbes.

2. Experimental

2.1. Materials and methods

All the chemicals used were AR grade and of high purity. Creatinine (sigma Aldrich), o-phenylenediamine (sigma Aldrich), o-aminophenol (sigma), Cobalt(II) and Copper(II) chlorides (Merck) were used as received. Organic solvents used were ethyl alcohol, methyl alcohol and DMSO. Elemental analyses of the ligands and the metal complexes were carried out using micro analytical techniques on an Elementar Vario EL III CHN analyzer at STIC cochin. FT IR spectra were recorded in the region 4000–400 cm^{-1} on Shimadzu IR affinity 1 spectrophotometer. ^1H NMR spectra of the ligands were recorded in $\text{DMSO}-d_6$ using Bruker Avance III 400 MHz FT – digital NMR spectrometer. The mass spectra were recorded using electron ionization technique with WATER ACQUITY - TQD mass spectrometer at SITRA, Coimbatore. Melting points were determined in open capillaries in electrical melting point apparatus and are uncorrected. Magnetic susceptibility of the metal complexes were measured at room temperature using Gouy's method. The molar conductivities of the metal complexes in DMSO solution (1×10^{-3} M) were obtained using Elico digital conductivity meter (model CM180) having a dip type cell calibrated with KCl solution. Metals were estimated with standard EDTA solution. Electronic spectra of the ligands and the metal complexes were recorded on Shimadzu model UV-1601 spectrophotometer in the range 200–800 nm at room temperature in DMSO. Thermogravimetric analyses (TGA/DTA) of the solid complexes were carried out using a Perkin Elemer STA 6000 thermal analyzer from room temperature to 800 °C.

2.2. Synthesis

2.2.1. Synthesis of Schiff base ligand, L^1 : N^1, N^2 -bis(4-imino-1-methylimidazolidin-2-ylidene)benzene-1,2-diamine

A hot ethanolic solution of creatinine (2-imino-1-methylimidazolidin-4-one) (2 mmol) was added to an ethanolic solution of o-phenylenediamine (1 mmol) in a round bottomed flask. The reaction mixture was stirred under reflux for 6 h. The reaction mass was degassed on a rotary evaporator, over a water bath which led to the isolation of solid product (Scheme 1). The solid obtained was thus filtered, washed with ethanol and dried in vacuum over anhydrous calcium chloride.

2.2.2. Synthesis of Schiff base ligand, L^2 : $E-2$ -((4-imino-1-methylimidazolidin-2-ylidene) amino)phenol

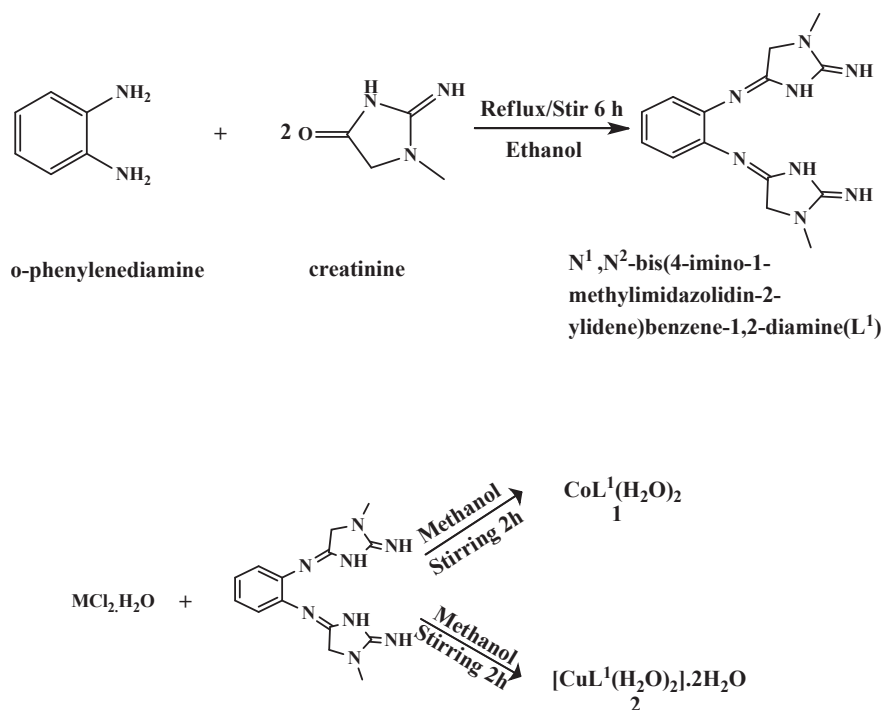
The ligand was prepared in a similar method as that of ligand L^1 by adding a hot ethanolic solution of creatinine (2-imino-1-methylimidazolidin-4-one) (1 mmol) to an ethanolic solution of o-aminophenol (1 mmol) (Scheme 2).

2.2.3. Synthesis of metal complexes

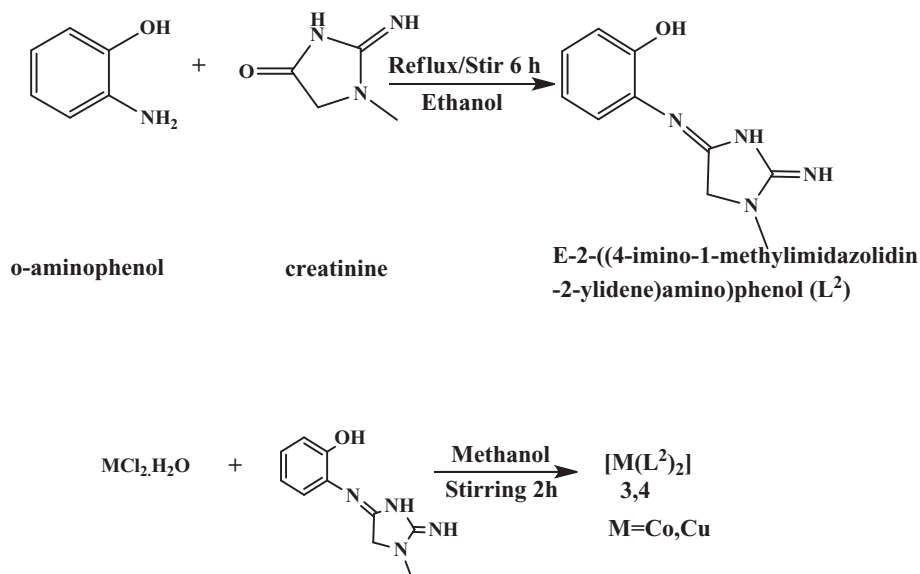
The Schiff base ligands L^1 and L^2 (1 mmol) were dissolved in methanol (15 ml). The methanolic solution of the metal chlorides $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ and $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (1 mmol, 15 ml) was added dropwise to the magnetically stirred solution of the ligands. The solution was stirred thoroughly for 2 h. The solid complexes separated out was filtered, washed several times with cold methanol and finally dried in vacuum over anhydrous calcium chloride.

2.3. DFT studies

The structures of ligands have been optimized in gas phase using DFT methods. Becke's hybrid function [20] with Lee-Yang-Parr (LYP) correlation function [21] was used throughout the studies. Geometry optimization, molecular energy, Mulliken charges, dipole moments, molecular electrostatic potential



Scheme 1. Synthesis of Schiff base ligands L_1 and its Co(II) and Cu(II) metal complexes **1** & **2**.



Scheme 2. Synthesis of Schiff base ligand L_2 and its Co(II) and Cu(II) metal complexes **3** & **4**.

calculations were performed using DFT-B3LYP with 6-31G(d,p) basis set [22] as incorporated in Gaussian09W program [23].

2.4. In – vitro antimicrobial activity

The prepared ligands and the metal complexes were screened for the antibacterial activity against gram positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and gram negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) by disc diffusion method. The antifungal activities were tested against two fungal species (*Aspergillus niger* and *Candida albicans*). The inoculums were standardized by adjusting the turbidity of the culture to that of Mc Farland standards. The standardized inoculums were inoculated in the sterile plates. The sterile sample discs measuring 6 mm diameter, soaked in known concentration (100 µg/ml) of the test compounds were placed in the nutrient agar medium. The reference drug ciprofloxacin (10 µg/ml) was used as positive control. The plates were placed at room temperature for 1 h for diffusion and incubated at 37 °C for 24 h. The diameters of the zone of inhibition were recorded. Compounds showing promising antimicrobial activity were selected for minimum inhibitory concentration studies. The minimum inhibitory effect of the Schiff base and its metal complexes were determined by micro well dilution technique using

Muller – Hinton broth as culture media by two fold serial dilutions. The test compounds were prepared at various concentrations (1000, 500, 250, 125, 62.5, 31.25, 15.625 µg/ml) and the test tubes were incubated at 37 °C for 24 h. The experiments were done in triplicate and the optical density values were determined by spectrophotometric method [24].

3. Results and discussion

Schiff base ligands L^1 and L^2 were synthesized by condensation of o-phenylenediamine and o-aminophenol with creatinine in 1:2 and 1:1 molar ratio respectively in ethanol. The complexes were synthesized by the interaction of the ligands L^1 and L^2 with $CoCl_2 \cdot 6H_2O$ and $CuCl_2 \cdot 2H_2O$ in 1:2 molar ratio in methanol (Schemes 1 and 2). All the complexes were stable at room temperature and soluble in organic solvents like DMF and DMSO.

3.1. Molar conductance

The molar conductivities of the complexes in DMSO (1×10^{-3} M) at 25 °C were found to be in the range $23\text{--}38 \Omega^{-1} \text{mol}^{-1} \text{cm}^2$. These results reveal that the complexes were non-electrolytic in nature (Table 1). This is in accordance with the

Table 1
Analytical and physical data of the ligand and its metal complexes.

Compound	Color	Yield (%)	M.pt (°C)	Mol. Wt	Elemental analysis calcd. (found)%				$\Lambda_m \Omega^{-1} \text{mol}^{-1} \text{cm}^2$
					C	H	N	M	
$C_{14}H_{18}N_8 L^1$	Pale yellow	83	216	298.35	56.36 (56.41)	6.08 (6.04)	37.56 (37.58)	–	–
$[Co L^1 (H_2O)_2 Cl_2] (1)$	Blue	75	>250	464.22	36.62 (36.65)	4.78 (4.72)	24.14 (24.17)	12.70 (12.68)	23
$[Cu(H_2O)_2 L^1 Cl_2] \cdot 2H_2O (2)$	Greenish yellow	70	>250	504.86	33.31 (33.34)	5.19 (5.16)	22.20 (22.24)	12.59 (12.62)	36.4
$C_{10}H_{12}N_4 O L^2$	Dark Yellow	89	229	204.23	58.81 (58.77)	5.92 (5.85)	27.43 (27.41)	–	–
$[Co(L^2)_2] (3)$	Blue	73	>250	465.38	51.62 (51.58)	4.76 (4.79)	24.08 (24.12)	12.66 (12.63)	24.2
$[Cu(L^2)_2] (4)$	Greenish yellow	76	>250	469.99	51.11 (51.13)	4.72 (4.69)	23.84 (23.81)	13.52 (13.54)	38.3

Table 2

IR spectral data of the ligands and their metal complexes.

Compound	$\nu(\text{C}=\text{N})$	Phenolic $\nu(\text{C}-\text{OH})$	$\nu(\text{C}=\text{NH})$	Ring $\nu(\text{NH})$	$\nu(\text{NH}_2)$	$\nu(\text{M}-\text{N})$	$\nu(\text{M}-\text{O})$	$\nu(\text{M}-\text{Cl})$
$\text{C}_{14}\text{H}_{18}\text{N}_8$ L ¹	1659	—	1567	3241	—	—	—	—
[Co L ¹ (H ₂ O) ₂ Cl ₂] (1)	1637	—	—	—	3333 3192	420	—	353
[Cu(H ₂ O) ₂ L ¹ Cl ₂]·2H ₂ O (2)	1640	—	—	—	3341 3174	410	—	369
$\text{C}_{10}\text{H}_{12}\text{N}_4\text{O}$ L ²	1665	1222	1577	3239	—	—	—	—
[Co(L ²) ₂] (3)	1640	1187	—	—	3339 3193	425	503	—
[Cu(L ²) ₂] (4)	1642	1175	—	—	3341 3173	440	510	—

fact that conductivity values for non-electrolyte are below $50 \Omega^{-1}\text{mol}^{-1}\text{cm}^2$ [25].

3.2. Infrared spectra

The prominent modes of bonding in Schiff bases and their metal complexes have been studied by FT-IR spectral data (Table 2), (Fig. 1a and b).

The IR spectra of the Schiff base ligands L¹ and L² show a strong band at $1659\text{--}1665 \text{ cm}^{-1}$ which was assigned to azomethine $\nu(\text{C}=\text{N})$ group. In comparison with the spectra of the Schiff bases, the $\nu(\text{C}=\text{N})$ band exhibit downward shift in the range $1637\text{--}1642 \text{ cm}^{-1}$ in the FT-IR spectra of the complexes, which is in accordance with the coordination of the azomethine function to the metal ion for all the complexes [26,27]. In addition presence of medium intensity bands at $1567\text{--}1577 \text{ cm}^{-1}$ and $3239\text{--}3241 \text{ cm}^{-1}$ in ligands may be assigned to $\nu(\text{C}=\text{NH})$ and ring NH respectively [28]. The coordination of the ligand to the metal atoms through the azomethine nitrogen atom is further confirmed by the appearance of medium intensity bands in the range of $480\text{--}450 \text{ cm}^{-1}$ due to $\nu(\text{M}-\text{N})$ vibrations [29]. The intense band at 1222 cm^{-1} in the ligand L² has been assigned to the phenolic $\nu(\text{C}-\text{O})$ and it is shifted to lower wave numbers $1175\text{--}1184 \text{ cm}^{-1}$ in the complexes 3 & 4 suggesting the coordination of phenolic OH to the metal after deprotonation, which is further confirmed by the appearance of a medium intensity band in the range of $500\text{--}510 \text{ cm}^{-1}$ due to $\nu(\text{M}-\text{O})$ vibration [30]. The disappearance of two bands corresponding to $\nu(\text{C}=\text{NH})$ and ring NH at $1567\text{--}1577 \text{ cm}^{-1}$ and $3239\text{--}3241 \text{ cm}^{-1}$ in complexes 1–4 and appearance of two bands at $3333\text{--}3340 \text{ cm}^{-1}$ and $3174\text{--}3193 \text{ cm}^{-1}$ indicates the existence of tautomerism. Creatinine exist in tautomeric forms as keto-amino imidazolines and keto-imino imidazolines. The absence of $-\text{NH}_2$ bands in the ligands L¹ and L² proves that creatinine in the form of keto-imino imidazoline has reacted with the corresponding amines. But in the complexes, the appearance of the $-\text{NH}_2$ bands proves that the ligands L¹ and L² has undergone tautomerism to keto-amino form. The coordinating water in the complexes 1 & 2 are characterized by the appearance of two bands at $924\text{--}945 \text{ cm}^{-1}$ and $840\text{--}875 \text{ cm}^{-1}$ [31]. The appearance of band at $353\text{--}369 \text{ cm}^{-1}$ for complexes 1 & 2 may be assigned to $\nu(\text{M}-\text{Cl})$ vibration [32].

3.3. NMR spectral studies

¹H NMR spectra of Schiff base ligands were recorded in DMSO-*d*₆, using TMS as an internal standard. The ¹H NMR spectrum of L¹ shows a singlet at δ 2.915 ppm corresponding to CH₂ protons. The signals around δ 3 ppm correspond to two CH₃ protons and multiplet around δ 7.440 ppm corresponds to aromatic protons. The signal at δ 10.2 ppm corresponds to NH proton. The ¹H NMR spectrum of L² shows a singlet at δ 2.914 ppm corresponding to CH₂ proton. The singlet at δ 3.678 ppm, δ 10.6 ppm and δ 11.3 ppm

corresponds to CH₃, NH and OH protons [33]. The multiplet at δ 7.434 ppm corresponds to aromatic protons [34] (Fig. 2a and b).

3.4. Mass spectral studies

The mass spectrum of the ligands L₁ and L₂ displayed prominent

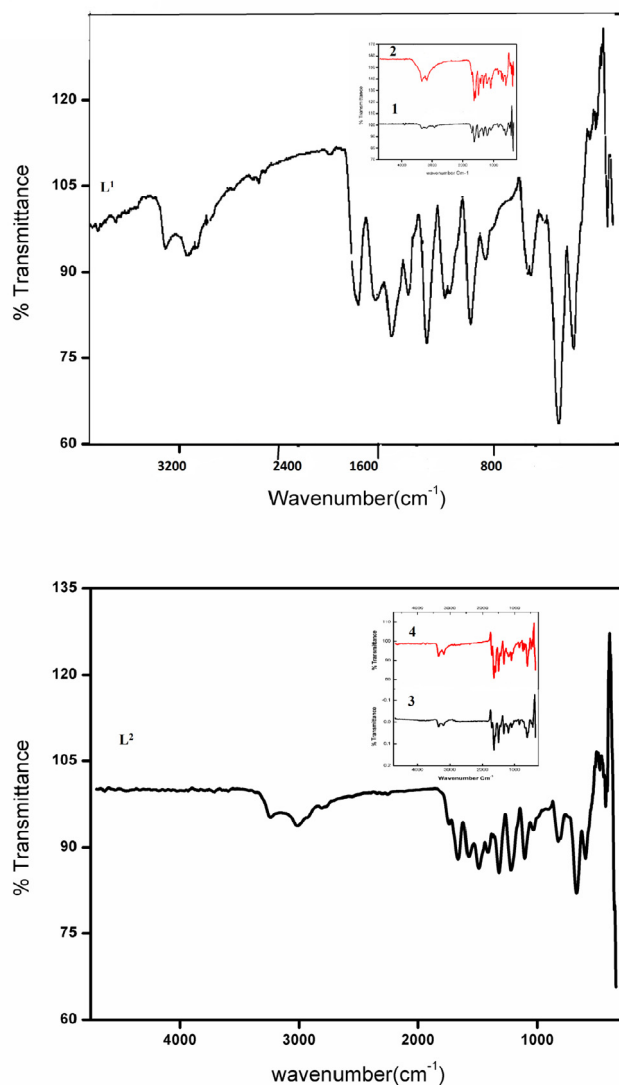


Fig. 1. IR spectra of Schiff base ligands and metal complexes L¹, 1 & 2 (a) & L², 3 & 4 (b).

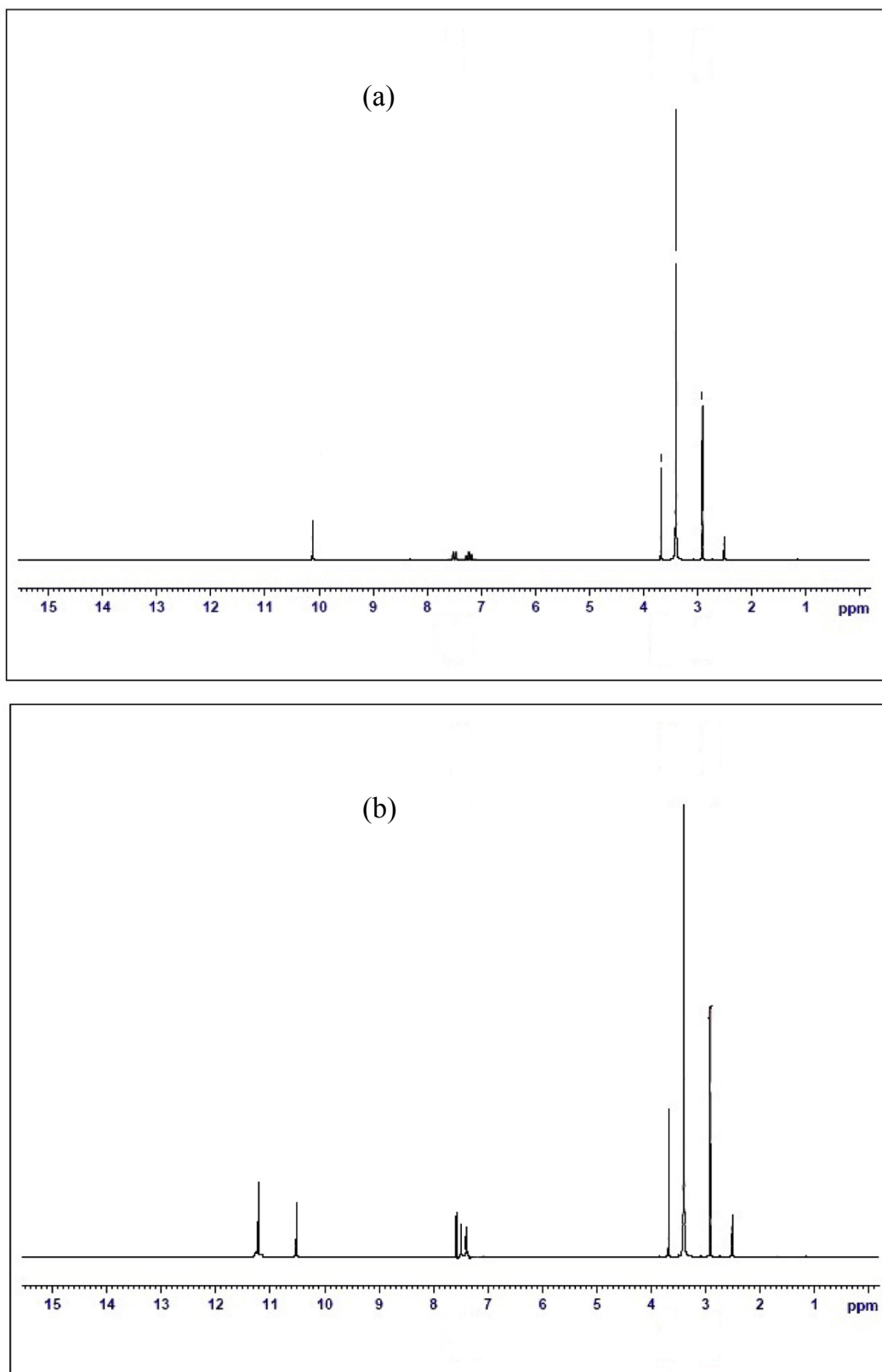


Fig. 2. ^1H NMR spectrum of Schiff base ligands L^1 (a) & L^2 (b).

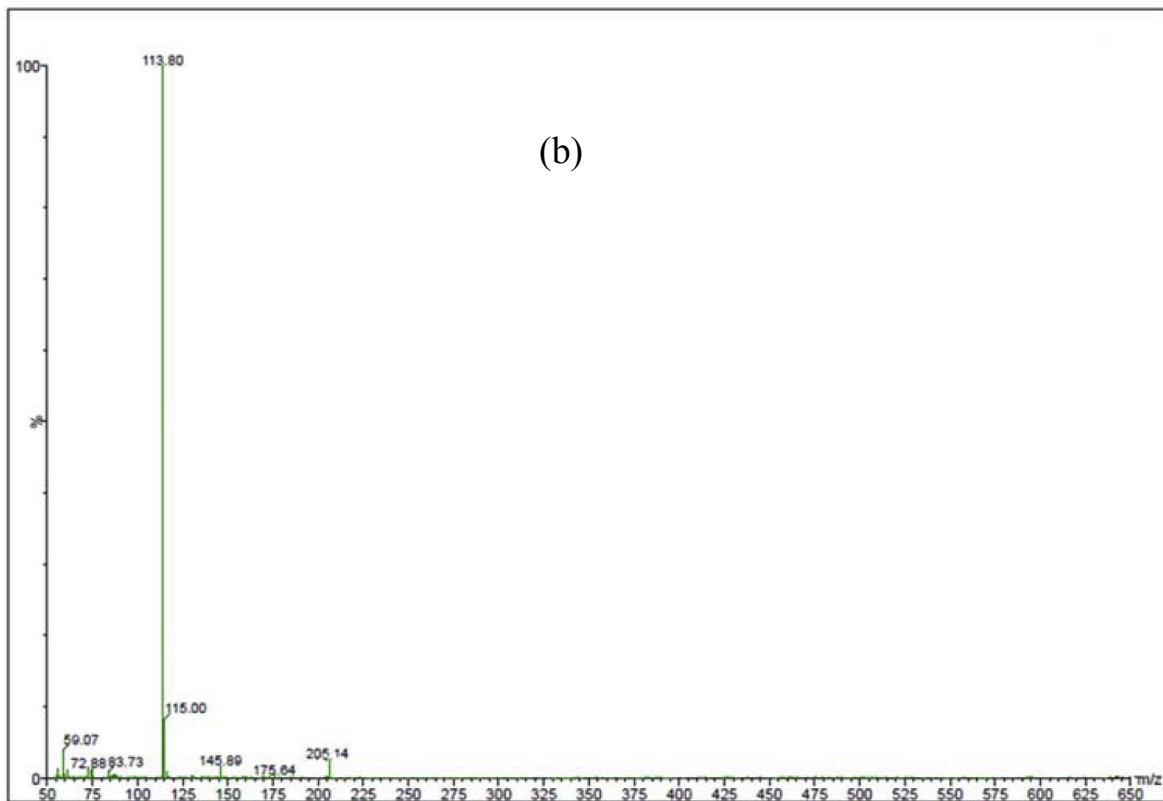
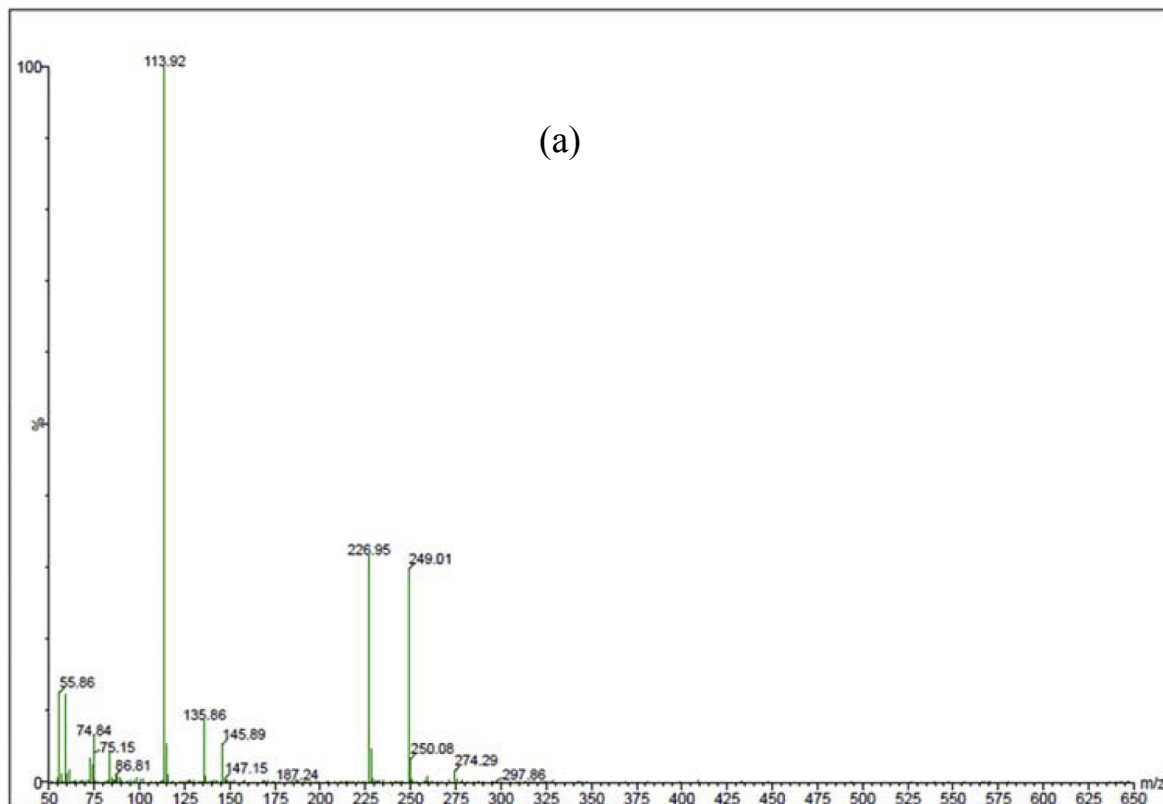


Fig. 3. Mass spectra of ligands L¹ (a) & L² (b).

Table 3
Electronic spectral data of the ligand and its metal complexes.

Compounds	λ_{\max} (nm)	Band assignments	Geometry
$C_{14}H_{18}N_8$ L ¹	242 284	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	–
[Co L ¹ (H ₂ O) ₂ Cl ₂] (1)	734 505 368	$4T_{1g}(F) \rightarrow 4T_{2g}(F)$ $4T_{1g}(F) \rightarrow 4A_{2g}(F)$ $4T_{1g}(F) \rightarrow 4T_{1g}(P)$	Octahedral
[Cu(H ₂ O) ₂ L ¹ Cl ₂]·2H ₂ O (2)	737 367	$2B_{1g} \rightarrow 2E_g$ $2B_{1g} \rightarrow 2B_{2g}$	Octahedral
$C_{10}H_{12}N_4O$ L ²	245 437	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	–
[Co(L ²) ₂] (3)	664 505	$4A_2 \rightarrow 4T_1(F)$ $4A_2 \rightarrow 4T_1(P)$	Tetrahedral
[Cu(L ²) ₂] (4)	595	$2B_{1g} \rightarrow 2A_{1g}$	Square planar

Table 4
Thermal studies of the metal complexes (1–4).

Complexes	Decomposition Temp. (°C)	Weight loss (%)		Metal oxide (%)		Inference
		Obsd.	Calcd.	Obsd.	Calcd.	
[Co L ¹ (H ₂ O) ₂ Cl ₂] (1)	250 °C	8.85	7.76	–	–	Loss of coordinated H ₂ O
	346 °C	35.76	37.69	–	–	Loss due to C ₆ H ₄ + Cl ₂
	610 °C	40.71	41.39	–	–	Loss due to C ₈ H ₁₂ N ₆
[Cu(H ₂ O) ₂ L ¹ Cl ₂]·2H ₂ O (2)	106 °C	7.44	7.14	–	–	Loss due to remaining organic moiety.
	229 °C	20.53	21.18	–	–	Loss of lattice H ₂ O
	312 °C	35.03	38.07	–	–	Loss due to coordinated H ₂ O + Cl ₂
	565 °C	22.04	20.61	–	–	Loss due to C ₈ H ₁₂ N ₆
		–	–	–	–	Loss due to C ₆ H ₄ N ₂
[Co(L ²) ₂] (3)	350 °C	41.59	41.74	14.68	16.14	Loss due to remaining organic moiety.
	692 °C	33.32	32.70	–	–	Loss due to C ₈ H ₁₄ N ₆
[Cu(L ²) ₂] (4)	281 °C	47.88	47.29	–	–	Loss due to C ₁₂ H ₈
		37.47	39.19	–	–	Loss due to remaining organic moiety.
	587 °C	–	–	15.09	16.10	Loss of C ₈ H ₁₄ N ₈
				–	–	Loss due to C ₁₂ H ₈ O ₂
				14.65	16.92	Loss due to remaining organic moiety.

peaks supporting the proposed empirical formula. The mass spectrum of Schiff base ligand L¹ shows molecular ion peak at m/z 297.86 consistent with the proposed molecular formula. The ligand L² displayed the molecular ion peak at m/z 205.14 which is equivalent to its molecular weight (Fig. 3).

3.5. Magnetic moment and electronic spectra

The electronic spectra of the ligands and complexes were recorded in DMSO at room temperature. The electronic transitions and band assignments are presented in (Table 3). The electronic spectra of the ligands showed two transitions at 242, 245 and 284, 437 for L¹ and L² respectively which corresponds to $\pi - \pi^*$ and $n -$

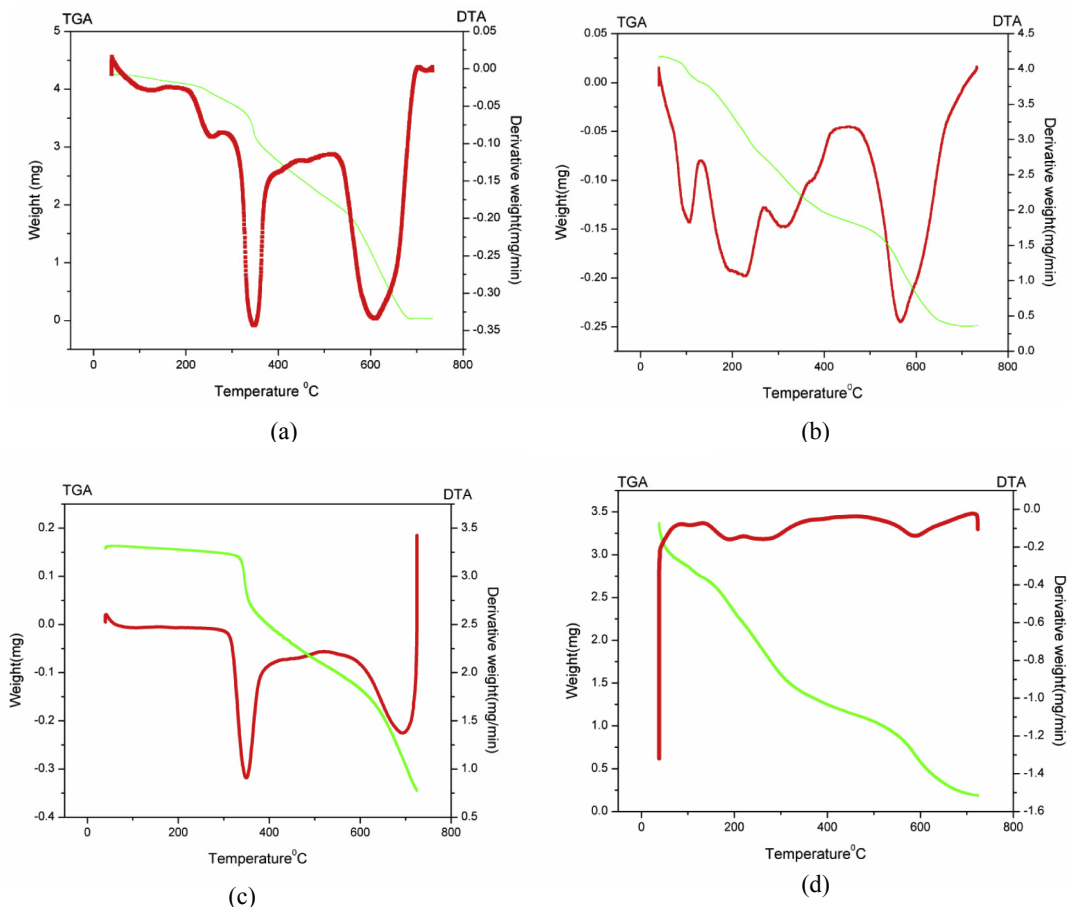


Fig. 4. (a–d). Thermograms of complexes 1–4.

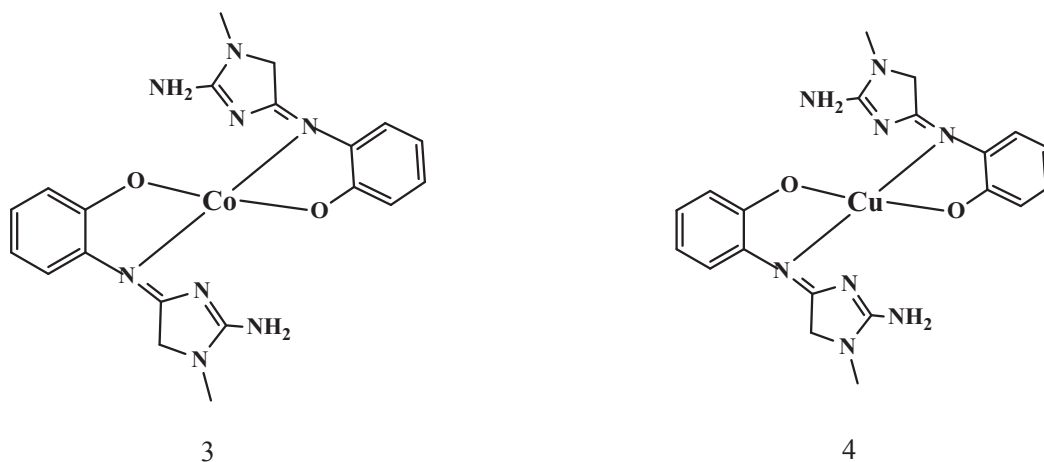
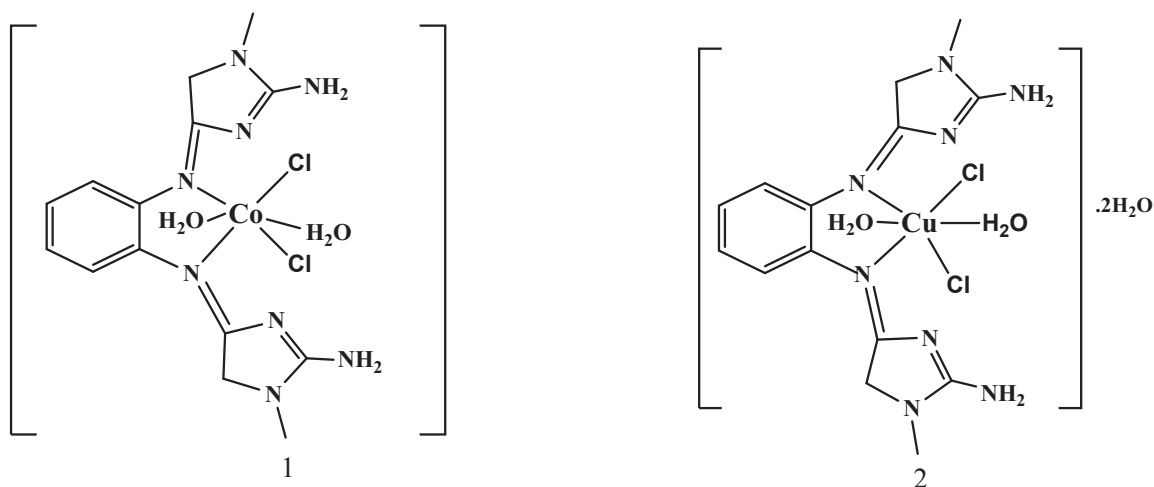


Fig. 5. Proposed structures of the complexes 1–4.

π^* transitions [35]. The Co(II) complex **1** showed three bands at 734, 505, 368 nm. These bands may be assigned to ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$,

${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transitions indicating the octahedral geometry of the complex [36,37]. The magnetic moment value of 4.8 BM also suggest the octahedral geometry of the complex. The Cu(II) complex **2** showed two bands at 737, 367 nm corresponding to ${}^2B_{1g} \rightarrow {}^2E_g$ and ${}^2B_{1g} \rightarrow {}^2B_{2g}$ transitions indicating the

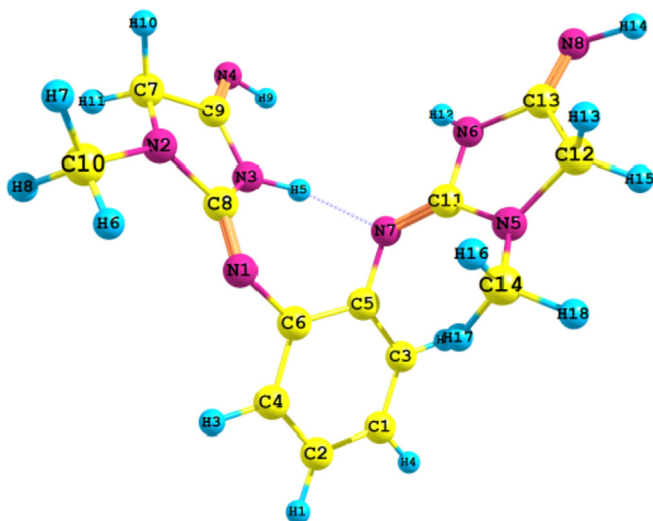
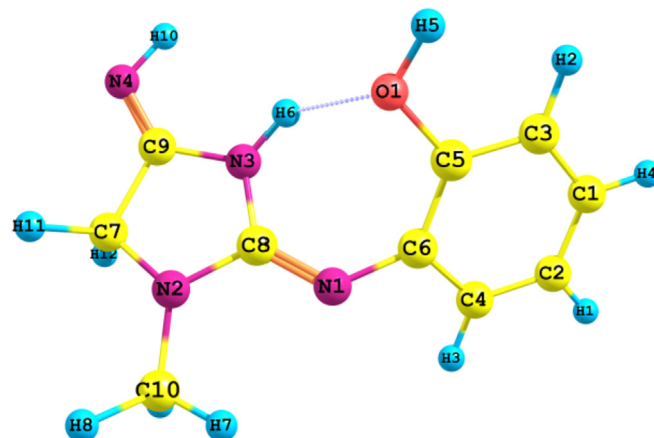
Fig. 6. Optimized geometry of ligand L¹.Fig. 7. Optimized geometry of ligand L².

Table 5
Calculated energy for the frontier molecular orbitals of the ligands L¹ & L².

Energy (eV)	C ₁₄ H ₁₈ N ₈ L ¹	C ₁₀ H ₁₂ N ₄ O L ²
LUMO +5	1.90073	2.59925
LUMO +4	1.30942	2.00903
LUMO +3	0.79267	1.53882
LUMO +2	0.36845	0.68981
LUMO +1	0.06476	0.31484
LUMO	-0.26450	-0.18694
HOMO	-5.19524	-5.31878
HOMO -1	-5.98900	-6.26846
HOMO -2	-6.21241	-6.37214
HOMO -3	-6.35282	-6.65079
HOMO -4	-6.81868	-7.33217
HOMO -5	-6.86412	-8.02769

octahedral geometry of the complex [38]. This is further corroborated by the observed magnetic moment value of 1.96 BM. The Co(II) complex **3** showed two bands at 664 and 505 nm. These bands may be assigned to $^4A_2 \rightarrow ^4T_1(F)$ and $^4A_2 \rightarrow ^4T_1(P)$ transitions indicating the tetrahedral geometry of the complex. The

magnetic moment value of 4.15 BM suggest the tetrahedral geometry of the Co(II) complex **3** [39]. The Cu(II) complex **4** showed a band at 595 nm corresponding to $^2B_{1g} \rightarrow ^2A_{1g}$ transition indicating the square planar geometry of the complex. The magnetic moment value of 1.75 BM also supports the square planar geometry of the complex.

3.6. Thermal studies

The thermal properties of the metal complexes were characterized on the basis of TG and DTG methods within a temperature range from room temperature to 800 °C (Table 4) (Fig. 4a–d). These methods provide information about the thermal stability of the complexes and suggest a general scheme for thermal decomposition of these complexes. The TG curves of Co(II) complex **1** (Fig. 4a) undergoes thermal decomposition in three steps within the range 40–635 °C. The first decomposition step within the temperature range 40–271 °C represent the loss of two coordinated water molecules [40] with an estimated mass loss of 8.85% (calcd. 7.76%). The second step of decomposition is attributed to the loss of

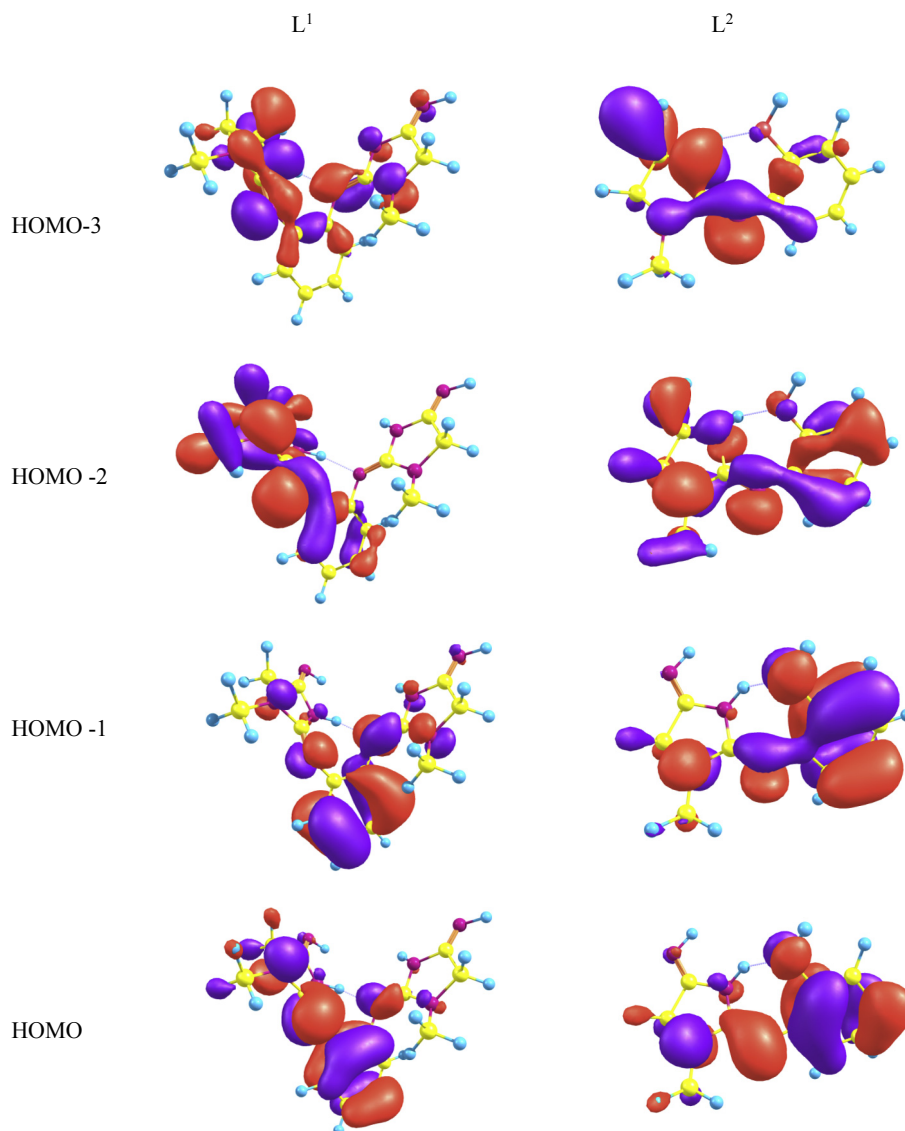


Fig. 8. The shapes of selected frontier molecular orbitals (HOMO) of ligands L¹ & L².

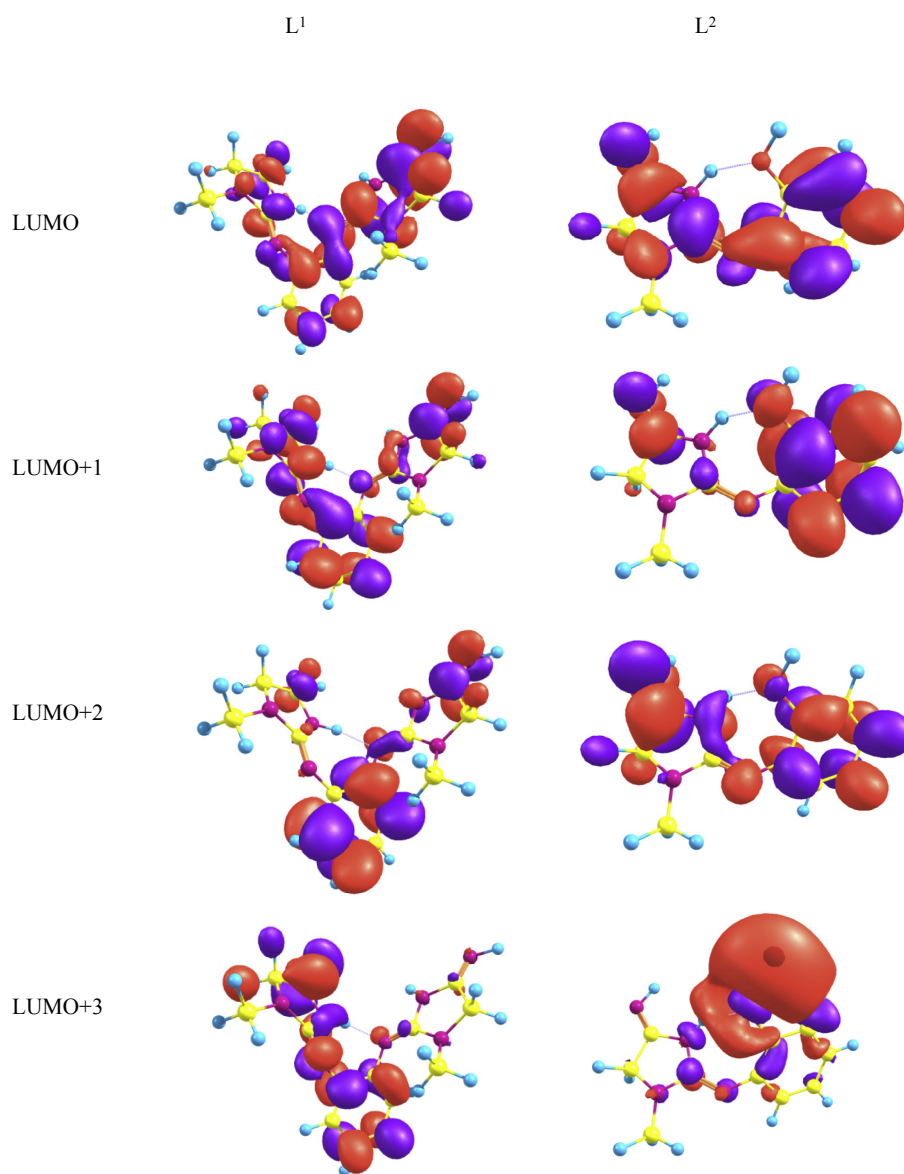


Fig. 9. The shapes of selected frontier molecular orbitals (LUMO) of ligands L¹ & L².

Table 6
Chemical reactivity parameters of the ligands L¹ & L².

Molecular properties (ev)	C ₁₄ H ₁₈ N ₈ L ¹	C ₁₀ H ₁₂ N ₄ O L ²
Etotal	-982.36609	-682.53248
EHOMO	-5.19524	-5.31878
ELUMO	-0.26449	-0.18694
ΔEHOMO-LUMO	-4.93074	-5.13184
Ionization Potential (IP)	5.19524	5.31878
Electron Affinity (EA)	0.26449	0.18694
Chemical Hardness (η)	2.4655	2.56592
Electronegativity (χ)	2.7299	2.75286
Chemical Potential (μ)	-2.7299	-2.75286
Global Softness (S) ev ⁻¹	0.20279	0.19486
Electrophilicity index (ω)	1.51133	1.47671
Dipole moment (Debye)	4.4806	1.3553

chlorine atoms along with part of ligand moiety within the range 271–465 °C with mass loss of 35.76% (calcd. 37.69%). The third step of decomposition occur within the range 465–635 °C corresponding to the loss of remaining organic moiety of the ligand with mass

loss of 40.71% (calcd. 41.39%) leaving behind CoO as the residue.

The thermogram of Cu(II) complex **2** (Fig. 4b) shows decomposition in four steps within the range 40–621 °C. The first decomposition step within the range 40–120 °C corresponds to the loss of two lattice water molecules with mass loss of 7.44% (calcd. 7.14%). The second decomposition step within the range 120–236 °C corresponds to the loss of two coordinated water molecules and chlorine atoms with an estimated mass loss of 20.53% (calcd. 21.18%). The third and the fourth decomposition steps within the range 236–621 °C corresponds to the loss of organic moieties with mass loss 35.03% (calcd. 38.07%) and 22.04% (calcd. 20.61%) respectively leaving behind CuO as the product of decomposition.

The thermogram of Co(II) complex **3** (Fig. 4c) shows no weight loss upto 300 °C indicating the absence of coordinated water molecules. The first decomposition step within the range 300–590 °C represents the elimination of organic moiety with mass loss of 41.59% (calcd. 41.74%). The second decomposition step within the range 590–725 °C corresponds to the loss of remaining

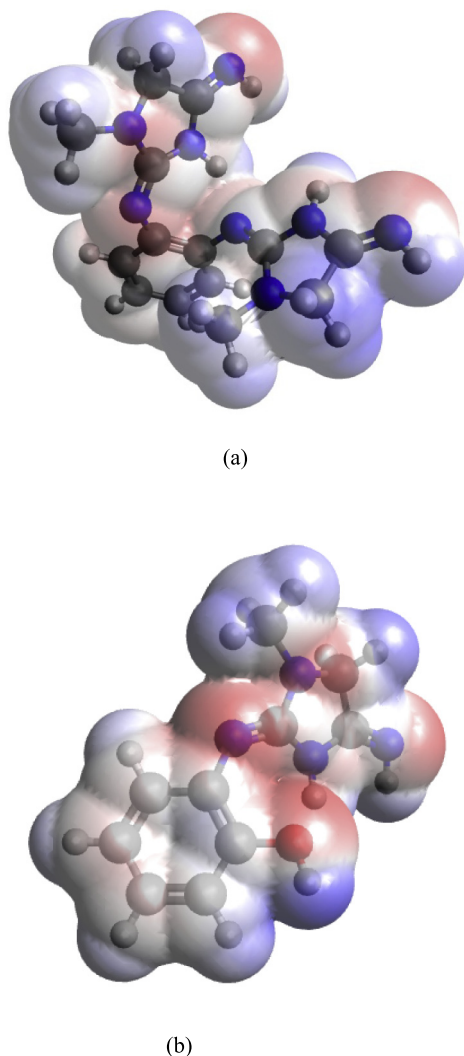


Fig. 10. Molecular electrostatic potential map of L¹(a) & L²(b).

organic moiety with weight loss of 33.32 (calcd. 32.70%) leaving behind CoO as the product of decomposition.

From the thermogram of Cu(II) complex **4** (Fig. 4d), it is evident that decomposition takes place in two steps within the range 50–689 °C. The first decomposition step within the temperature range 50–321 °C indicates the loss of imidazole moiety with mass loss of 47.88% (calcd. 47.29%). The second decomposition step in the range 321–689 °C corresponds to the loss of remaining organic

moiety with mass loss of 37.47% (calcd. 39.19%) leaving behind CuO as the product of decomposition. The proposed geometry of the complexes are given in (Fig. 5).

3.7. DFT studies

3.7.1. Geometry optimization

The geometry of the ligands L¹ and L² were optimized using B3LYP function with 6-31G(d,p) basis sets as incorporated in the Gaussian 09W programme in gas phase. The optimized geometries and the atom numbering scheme of L¹ and L² are shown in (Figs. 6 and 7).

3.7.2. Frontier molecular orbital analysis

The frontier molecular orbitals play a major role in electrical and optical properties [41,42]. The energy gap has been calculated from HOMO and LUMO levels. Chemically stable molecules have large energy gap. Soft molecules have small energy gap and hard molecules have large energy gap and hence they are stable than the soft molecules. Soft molecules having smaller energy gap are more polarizable and are more reactive than the hard molecules [43]. The frontier molecular orbitals (HOMO and LUMO) energy level of the ligands L¹ & L² have been calculated and presented in (Table 5) (Figs. 8 and 9). By using Koopmans theorem the frontier molecular orbital descriptors such as ionization potential, electron affinity, global hardness, electronegativity, chemical potential, softness, global electrophilicity index were calculated [44,45]. The chemical reactivity parameters are shown in (Table 6).

3.7.3. Molecular electrostatic potential

The sites of electrophilic attack and nucleophilic reactions can be determined using MEP maps [46,47]. The electron rich areas are represented by red color (negative potential) while the electro-positive sites are represented by blue color (positive potential). As seen in (Fig. 10a and b), the negative electrostatic potential regions (red) are mainly localized over the nitrogen atoms and oxygen atom. These atoms serve as the co-ordination sites. However, the positive potential regions (blue) are localized on H atoms. These results reveal that the negative potential sites are on electronegative atoms and the positive potential sites are around the hydrogen atoms respectively [48,49].

4. In – vitro antimicrobial activity

A study on the antimicrobial activity of the prepared Schiff base ligands L¹ and L² and their metal complexes (**1–4**) were carried out against gram positive and gram negative bacterial and fungal strains using *ciproflaxacin* and *clotrimazole* as positive control reference drug for antibacterial and antifungal activities respectively. The diameter of zone of inhibition (mm) are presented in

Table 7
Zone of inhibition of the Schiff base ligands and its metal complexes.

Compounds	Bacterial species Std (Ciprofloxacin)				Fungal species Std (Clotrimazole)	
	Gram +ve		Gram –ve		<i>C. albicans</i>	<i>A. niger</i>
	<i>S. aureus</i>	<i>B. subtilis</i>	<i>E. coli</i>	<i>P. aeruginosa</i>		
C ₁₄ H ₁₈ N ₈ L ¹	12	22	17	11	12	11
[Co L ¹ (H ₂ O) ₂ Cl ₂] (1)	21	25	28	15	20	20
[Cu(H ₂ O) ₂ L ¹ Cl ₂]·2H ₂ O (2)	14	16	22	12	17	15
C ₁₀ H ₁₂ N ₄ O L ²	10	12	11	11	9	8
[Co(L ²) ₂] (3)	25	26	27	20	23	19
[Cu(L ²) ₂] (4)	17	17	25	17	12	13
Standard	32	30	28	19	23	29

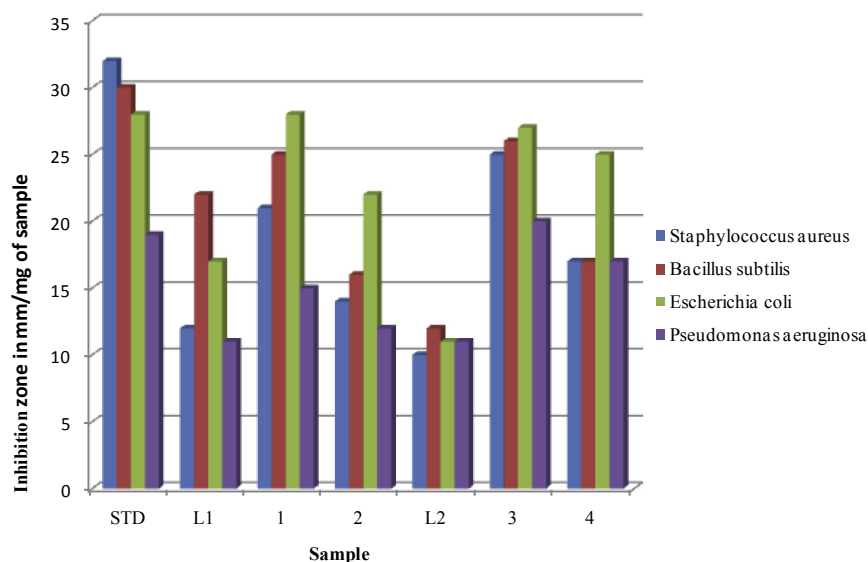


Fig. 11. Antibacterial activity of Schiff base ligands L¹ & L² and its Co(II) & Cu(II) complexes 1–4.

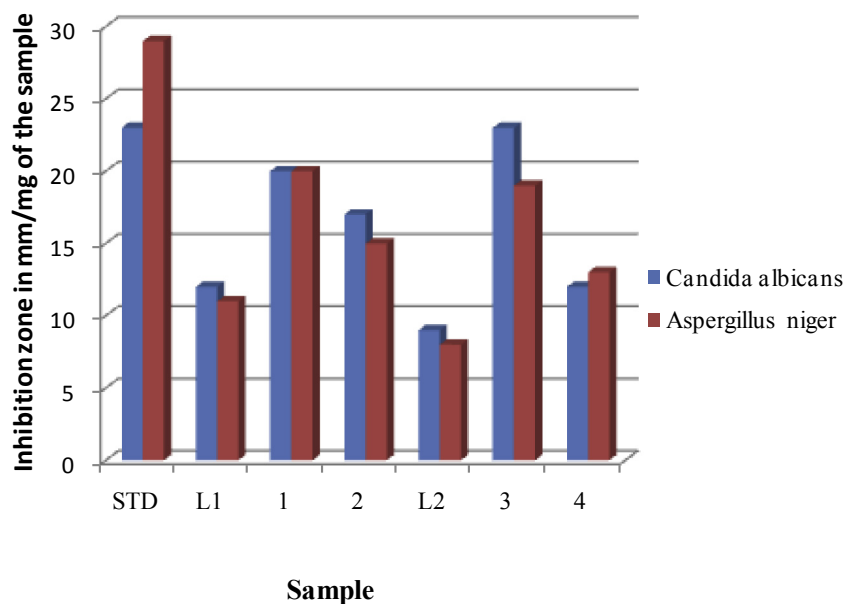


Fig. 12. Antifungal activity of Schiff base ligands L¹ & L² and its Co(II) & Cu(II) complexes 1–4.

Table 8

Minimum inhibitory concentration of Co(II) complexes 1 & 3.

Organism	[Co L ¹ (H ₂ O) ₂ Cl ₂] (1)	[Co(L ²) ₂] (3)
<i>B. subtilis</i>	31.25	62.5
<i>E. coli</i>	31.25	62.5
<i>C. albicans</i>	31.25	62.5

(Table 7) and compared with standards as shown in (Figs. 11 and 12). The results revealed that all the complexes showed enhanced activity than the ligands. Among all the metal complexes, complexes 1 and 3 exhibited better activity against *B. subtilis* with zone diameter 25 mm and 26 mm respectively. In case of *E. coli* complex 1 and 3 showed potential inhibition with zone diameter 28 mm and 27 mm respectively compared to complexes 2 and 4. However

metal complexes 1 and 3 exhibited good activity against *C. albicans* with inhibition zone diameter 20 mm and 23 mm respectively.

The MIC's of the metal complexes 1 and 3 against *B. subtilis*, *E. coli* and *C. albicans* are given in (Table 8). And it is clear from the data that the complex 1 (MIC 62.5 µg/ml) have shown best antibacterial and antifungal activity than complex 3.

A comparative study of the antimicrobial activities reveal that the metal complexes showed enhanced activity than the Schiff base ligands, which can be explained by Tweedy's chelation theory [50]. Chelation enhances the metal complexes to act as powerful antimicrobial agents. The partial sharing of the positive charge of the metal ion with the hetero donor atoms of the ligand reduces the polarity of the metal complexes. The diminution in polarity enhances the lipophilic character of the chelates which subsequently favours its permeation through the lipid layer of cell membrane. It has been reported that metal complexes containing Schiff base

ligand with nitrogen and oxygen donor atoms might hinder enzyme production and that result in cell death [1]. Other than chelation various other factors such as solubility, dipole moment, size, coordinating sites, redox potential of metal ion, solubility, bond length between metal and ligand, geometry of complexes, steric effect, concentration and hydrophobicity have substantial influence on the antimicrobial activity [51–54].

5. Conclusion

The Schiff base ligands L^1 & L^2 and their Co(II) and Cu(II) complexes (1–4) were synthesized and characterized by different spectroscopic techniques. The electronic, spectra, magnetic susceptibility, molar conductance data confirmed the octahedral geometry of the complexes. The TGA/DTA analysis were carried out to study the presence of co-ordinated and lattice water molecules in the complexes and also to confirm their thermal stability. DFT calculations of the ligands were performed to investigate the optimized structures. Moreover frontier molecular orbitals and molecular electrostatic potential were visualized to predict the co-ordination sites. The in-vitro antimicrobial studies revealed that Co(II) complexes exhibit significant activities compared to Cu(II) complexes and the parent ligands.

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