FULL PAPER



Synthesis, spectral characterization, density functional theory studies, and biological screening of some transition metal complexes of a novel hydrazide-hydrazone ligand of isonicotinic acid

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Tahani I. Kashar, Chemistry Department, Faculty of Science, Menoufia University, Shebin El-Kom 13829, Egypt. Email: tahanikashar@science.menofia. edu.eg Novel Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), and Hg(II) complexes (1-7) of hydrazide-hydrazone ligand (H_2L) derived from the condensation of isonicotinic acid hydrazide with (Z)-N'-(2-nitrobenzylidene)-3-oxobutanehydrazide have been prepared. The ligand and its chelates were characterized based on elemental analysis, spectral, thermal analysis, molar conductance, and magnetic moment measurements. Besides, density functional theory (DFT) computations have been conducted to study structures and energetics of the ligand and its complexes. The IR spectra showed that the ligand was chelated with the metal ion in a monobasic tridentate manner using ONO donors in all complexes except Zn(II) complex (5) where the ligand binds with Zn(II) ion as a dibasic tridentate utilizing ONO donors. The magnetic moment and electronic spectral data revealed octahedral and square pyramidal geometries for complexes (1, 7) and (2, 4, 5), respectively, whereas a square planar geometry was suggested for 3. DFT studies show that the Cd(II) center reveals interesting structural deviations from regular octahedral geometry in the resulting hexa-coordinated complex $[Cd(H_2L)_2].2H_2O$ (6) assumes a trigonal prismatic (TP) structure for this complex. The antibacterial and antifungal activities of the ligand and its complexes have been investigated with different bacterial and fungal strains. The data revealed that Hg(II) complex (7) demonstrated a very good antibacterial and antifungal activity than others.

Highlights

- A new hydrazide-hydrazone ligand of isonicotinic acid was synthesized.
- Seven mononuclear Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), and Hg(II) complexes of the new ligand were prepared and characterized by different tools.

- DFT studies have been carried out to study the structure of the ligand and its complexes.
- Antimicrobial activities of the ligand and its complexes were studied against a variety of bacterial and fungal strains by using disk diffusion method and results were compared with standard drugs.

KEYWORDS

DFT calculations, hydrazide, metal complexes, Schiff base, spectral studies

1 | INTRODUCTION

Designing new antimicrobial agents with different chemical characteristics from currently used antibiotics and chemotherapeutic agents is considered as a critical demand to overcome the rising rates of antibacterial resistance.^[1] Consequently, there is a need to search for novel compounds with significant antibacterial and antifungal activity.^[2,3] Hydrazine, hydrazone, and their analogs are potential group of compounds that have significant biological and pharmacological activities.^[4-10] The most important activity reported for hydrazine and its derivatives is the free radicals scavenging effect.^[4-7] Also, the antibacterial and antifungal potentials of such nitrogenous compounds against different types of bacteria were studied by various researchers.^[8,10,11] The hydraplay also a vital role as a zine derivatives agent for the management of chemotherapeutic tuberculosis.^[12–14] Further, the hydrazide–hydrazones with (-CO-NH-N=CH-) moiety have gained an important place in medicinal chemistry as antibacterial, antifungal, antitumor, anticonvulsant, anti-inflammatory, antimalaria,l and antituberculosis agents.^[15-30] Moreover, isonicotinic acid and its derivatives showed important properties like antibacterial, antioxidant, and anticancer agents.^[14,31-33] Isonicotinic acid hydrazide (isoniazid; INH) is widely applied as a first line drug for the treatment of tuberculosis and still the most effective antituberculosis drug, recommended by WHO.^[14,31-33] Designing derivatives from this molecule has been a challenge taken up by several research groups^[31–33] as the pharmacokinetic properties and cellular permeability of the drug can be enhanced by derivatization to bioreversible forms of this drug as hydrazones.^[34] On the other hand, organic antibiotics generally have a single molecular target.^[35] One of the approaches to overcome this problem is the use of metal ions and metal compounds as alternatives for traditional antibiotics.[35-38] These metal-containing compounds possess various mechanisms of action as antimicrobial agents. Chelation of organic compounds with metal causes important changes in the biological properties of both metal and the ligand moiety.^[35–39]

In the present work, a new hydrazide-hydrazone ligand (H₂L) was prepared from condensation of isonicotinic with (Z)-N'-(2acid hydrazide nitrobenzylidene)-3-oxobutanehydrazide, which was further reacted with Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), and Hg(II) chlorides to form the corresponding metal complexes. The structures of the targeted ligand and its complexes were characterized by different analytical and spectroscopic tools. The antimicrobial and antifungal activities of these compounds were measured against different bacterial and fungi strains. Quantum chemical calculations also have been carried out to support and interpret experimental findings. In this project, density functional theory (DFT) calculations have been performed aiming to determine the stability of the complexes formed, binding energies, ligand and complexes geometries in addition to various quantum chemical parameters of the free ligand (H_2L) and its complexes.

2 | EXPERIMENTAL

2.1 | Analytical and physical measurements

All chemicals and solvents were pure chemicals from BDH or Aldrich and used as received. Melting points were determined using Fisher–Johns melting point apparatus. The infrared spectra were recorded using Mattson–5000 Fourier transform infrared (FTIR) spectrometer with KBr disk method at the Faculty of Science, Cairo University. The ¹H NMR and ¹³C NMR spectra were obtained in DMSO- d_6 on a Varian XL Gemini 300 spectro-photometer at 300 MHz at room temperature. MS were run on a GCMS-Q1000-EX Shimadzu and GCMS 5988-A HP spectrometer at 70 eV. Elemental analyses (C, H, and N) were carried out at the Microanalytical Unit of the University of Cairo. Metal ions were determined using atomic absorption with a Perkin Elmer (model 2380)

spectrophotometer. Additionally, the chloride ions were evaluated by argentometry.^[40] Molar conductivity was made in DMF solution (10^{-3} M) utilizing a type CD6N Tacussel conductmeter. Electronic absorption spectra in the 200- to 1000-nm region were recorded on a Perkin-Elmer 550 spectrophotometer in DMF solution. The thermal analyses (thermogravimetry analysis [TGA]\ differential thermogravimetry [DTG]) were carried out on a Shimadzu TG-50 thermal analyzer from room temperature to 1000°C range at a heating rate of 10°C min⁻¹. Powder X-ray diffraction (XRD) patterns collected by 18-kW diffractometer (Bruker; model D8Advance) with monochromated Cu-Ka radiation (1.54178 Å). Magnetic susceptibilities were measured at room temperature by Gouy method employing Johnson Matthey Magnetic Susceptibility Balance. Diamagnetic corrections were determined using Pascal's constants.^[41] The effective magnetic moments were ascertained from the relation $\mu_{eff} = 2.84$ $(X_M^{corrt} T)^{1/2}$ where, X_M^{corrt} is the molar magnetic susceptibility corrected for diamagnetism of all atoms in the compounds. The antimicrobial screening of H_2L ligand and its complexes was carried out against gram-positive bacteria (Staphylococcus aureua) and gram-negative bacteria (Escherichia coli), while the antifungal activity was measured against Aspergillusflavus and Candida albicans.

2.2 | Synthesis of the ligand

Synthesis of the ligand occurred via four steps. The first and second steps involve the preparation 3-ketobutanehydrazide (a) and isonicotinic acid hydrazide (isoniazid, **d**) as reported previously.^[42] After that, a mixture of 3-ketobutanehydrazide (0.01 mol) and 2-nitro benzaldehyde (b) (0.01 mol) was added in ethanol (20 ml). The mixture was refluxed for 8 h, concentrated, and cooled. The precipitate which formed (Z)-N'-(2nitrobenzylidene)-3-oxobutanehydrazide (c) was filtered off, washed several times with cold ethanol, and dried under vacuum. The last step involves the addition of the resulting Schiff base (c) (0.01 mol) and isonicotinic acid hydrazide (d) (0.01 mol) in ethanol (30 ml), and then the mixture was refluxed for 4 h; the yellow precipitate formed was filtered off, recrystallized from dilute ethanol. and dried under vacuum (Scheme 1).

2.3 | Synthesis of metal complexes

An ethanolic solution (20 ml) of the metal chlorides salt of Cu(II), Co(II), Ni(II), Mn(II), Zn(II), Cd(II), and Hg(II) were added to an ethanolic solution (20 ml) containing an equimolar concentration of the ligand (H_2L).





 $SCHEME 1 \quad \text{Synthesis of ligand} (H_2L)$

The reaction mixture was magnetically stirred and refluxed for about 3–5 h. The refluxed solution was cooled overnight and filtered. The solid product formed was washed several times with ethanol then dried under vacuum.

2.4 | Antimicrobial activity

Antimicrobial activity of the ligand and its metal complexes were determined using a modified Kirby-Bauer disk diffusion method.^[43] Briefly, 100 µl of the bacterial/ fungi under investigation were grown in 10 ml of fresh media until they reached a count of approximately 10^8 cells/ml for bacteria or 10⁵ cells/ml for fungi. One hundred microliters of microbial suspension was spread onto agar plates. The tested compounds were dissolved in DMSO giving stock solutions. Blank paper disks (Schleicher & Schuell, Spain) with a diameter of 8.0 mm were impregnated with 10 µl of the required concentration of the tested compounds (100 mg ml $^{-1}$). After that, the filter paper disk, impregnated with the tested compounds, was placed on the agar. The compounds were diffused from the disk into the agar. Standard disks of ampicillin (antibacterial agent) and amphotericin B (antifungal agent) served as positive controls for antimicrobial activity but filter disks impregnated with 10 µl of solvent dimethylsulfoxide (DMSO) were used as a negative control. Plates inoculated with filamentous fungi as Aspergillus flavus at 25°C for 48 h; Gram (+) bacteria and Gram (-) bacteria as Staphylococcus aureua was incubated at 35-37°C for 24-48 h, and yeast as Candida albicans was incubated at 30°C for 24-48 h, and then the diameters of the inhibition zones were measured in millimeters.

2.5 | Computational methods

The quantum mechanical study using DFT^[44,45] was carried out using the Gaussian 09 package.^[46] Geometry

optimizations were carried out utilizing B3LYP functional^[47,48] with LANL2DZ^[49] basis set for metals and 6-311G(d) basis set for other atoms. Frequency calculations were performed for all optimized geometries at the same level of theory to verify their nature as minima or transition states on the potential energy surface of these systems. In our systems, absence of negative eigenvalues in the force constant matrices indicates that all of the obtained stationary points are minima. The vibrational modes were examined by using the ChemCraft program.^[50] The calculated vibrational frequencies were scaled by 0.9682 to account for the anharmonicity of the experimental frequencies. Thermodynamic parameters such as the energy (E), enthalpy (H = E + PV), entropy (S), and Gibbs energy (G = H - TS for T = 298.15 K) were calculated using the same level of theory. The distribution of the highest occupied and lowest unoccupied frontier molecular orbitals (HOMO, LUMO, and FMO) as well as the molecular electrostatic potential (MEP) of the ligand and its complexes has been analyzed. The ChemCraft program was used for displaying the computational results and plotting FMOs.

3 | RESULTS AND DISCUSSION

3.1 | Chemistry

The preparation of the hydrazide–hydrazone ligand occurred via four steps as shown in Scheme 1. Initially, 3-ketobutanehydrazide and isonicotinic acid hydrazide (isoniazid) were prepared as reported previously.^[42] After that, the 3-ketobutanehydrazide was reacted with 2-nitro benzaldehyde in equimolar ratio in EtOH followed by the elimination of one water molecule results in the formation of the Schiff base (**c**). Finally, The formed Schiff base (**c**) was reacted with isonicotinic acid hydrazide in equimolar ratio in EtOH affording *N'*-((*E*)-4-(2-((*Z*)-2-nitrobenzylidene)hydrazineyl)-4-oxobutan-2-ylidene) isonicotinohydrazide ligand **H**₂**L** (Figure 1). The structure of the ligand was elucidated using elemental analyses and spectral methods.

An ethanolic solution of H_2L reacts with an EtOH solution of Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), and Hg(II) chlorides and forms the corresponding coordination compounds, 1–7 (Figure 2). Complexes (5–7) have yellowish white and white colors, whereas complexes (2–4) are colored complexes (Table 1). All the complexes are stable towards air and insoluble in most common organic solvents but soluble in DMF and/or DMSO. The elemental analysis shows 1 L:1 M except complexes (1 and 6) are 2 L:1 M stoichiometry (Table 1). The measured values of the molar conductance of the complexes



FIGURE 1 Amido-imido tautomers of the hydrazide hydrazone ligand

in 10^{-3} M DMF solution at room temperature of $10-31 \ \Omega \ cm^{-2} \ mol^{-1}$ reveal that all complexes are nonelectrolyte.^[36,51] The analytical and physical data are compatible with the suggested structures.

3.2 | Infrared studies

The IR spectrum of the free ligand (H_2L) is compared with IR spectra of its metal complexes, to investigate the mode of bonding of the hydrazine-hydrazone ligand to the metal ions. The IR spectral results of H_2L ligand, its metal complexes and their assignments are collected in Table 2. An inspection of H₂L ligand spectrum (Supplementary Information) reveals several fundamental weakbroad bands at 3435, 3295 and 3191, and 3107-2855 cm⁻¹ assigned to stretching vibrations of adsorbed water molecule, two amide v(N-H), and aromatic and aliphatic (C-H), respectively. The additional bands located at 1413, 1040 and 1065, and 689 and 744 cm⁻¹ correspond to bending deformation of (CH₃) group, (C-H) in-plane deformation, and out-of-plane (C-H) bending for the aromatic benzene skeleton.^[35,51,52] Furthermore, the H₂L IR spectrum illustrates strong and medium bands at 1516 and 1354, 930, and 1439 cm^{-1} assignable to stretching vibrations of (NO₂), pyridine ring breathing, and (NH) in-plane deformation vibration, respectively.



FIGURE 2 Structure of complexes (1–7)

Moreover, the IR spectrum of H₂L ligand displays strong and medium bands at 1678 and 1146 and 578 cm^{-1} attributed to the C=O stretching and in-plane, out-of-plane bending vibrations (v and δ , γ) of the amide carbonyl groups. For the free ligand, four bands appeared at 1678, 1440, 1272, and 853 cm^{-1} attributable to amide I {C=O stretching + C-N stretching}, amide II {N-H bending + C-N stretching}, amide III {N-H deformation + C-N stretching}, and amide IV band that mainly results from δ (C=O).^[36,53,54] Besides, the ligand spectrum displays a medium intensity band at 1608 cm⁻¹ assignable to stretching frequency of azomethine group ν (C=N). In general, the spectrum of the ligand shows the appearance of characteristic bands of ν (N–H) and ν (C=O), these observations suggest that the hydrazidehydrazone ligand exists in the amido form (Figure 1).

The IR spectra of all metal complexes show a shift in ν (C=N) (azomethine) stretching to a lower value by 7–11 cm⁻¹, indicating coordination through the azomethine N atom. In addition, the spectra of all metal complexes except complex (5) revealed the presence of only one v(N-H) band in the range (3180–3214 cm⁻¹) with disappearance of the other v(N-H) band compared

with the ligand. Moreover, a new band appeared in the range (1214–1223 cm⁻¹) could be assigned to ν (C–O) of the coordinated carbonyl group after enolization with complexation to the metal ion. Furthermore, in complex (5), the intense peaks due to ν (N–H) and ν (C=O) appeared for the ligand, disappeared upon complexation with Zn(II) ion, whereas new bands appeared at 1264 and 1298 cm⁻¹ attributed to ν (C–O) of the two carbonyl groups after enolization. The intensity and position of the amide bands (I, II, III, and IV) change relative to the ligand, the amide I, which is mainly arising from ν (C=O) undergoes downshift by (5-30 cm⁻¹) in all complexes confirming the coordination through the carbonyl group O2 (suggested by DFT studies). For complex (5), the spectrum does not show any characteristic bands for the amide group (I, II, III, IV) indicating that H₂L ligand coordinates with Zn(II) ion through deprotonated carbonyl groups (O1 and O2). Thus, H₂L behaves as a monobasic tridentate ONO donor ligand in all complexes except 5 in which the ligand coordinates through its azomethine N, enolic O1 atom, and carbonyl O2 atom. On the other hand, the ligand binds with Zn(II) ion in complex 5 as a dibasic tridentate ONO donor ligand through azomethine N and both enolic O1 and O2 atoms. The coordination of carbonyl O and azomethine N atoms is further supported by the appearance of new nonligand bands between 470-500 and 411–419 cm⁻¹ due to the v(M–O) and v(M–N) vibrations in all complexes.^[35,36] These bands are in the expected order as v(M-N) occurs at lower energy than v(M-O) as expected due to greater electronegativity of the O atom than N atom, the greater dipole moment of M-O bond, and shorter M-O bond length than the M-N bond length,^[55,56] which confirmed later with DFT studies. The absorptions due to the presence of water molecules in all complexes are evidenced by the broad absorptions around 3400 cm⁻¹.

3.3 | ¹H and ¹³C NMR of the ligand

The ¹H NMR (DMSO- d_6 ; , ppm) spectral data of H_2L ligand illustrate two singlet peaks at 2.26 and 2.44 ppm for the three protons of CH₃ and the two protons of (-CH₂--), respectively^[36,42] Also, multiplet signals that appeared in the range of δ 7.50–8.86 ppm are attributed to four aromatic protons (Supplementary Information). In addition to two doublets at δ 8.08 and 8.12 ppm corresponding to pyridine protons and three singlets at 8.80, 8.89, and 12.39 ppm attributed to the three protons of -CH=N, NHCO (adjacent to aliphatic moiety), and NHCO (adjacent to aromatic moiety), respectively.^[36,56]

						Anal. Found (calc.)%			
No	Compound	Color	Empirical formula weight	M.P. (°C)	Yield%	c	Н	Ν	М	cı
	H ₂ L.H ₂ O	Pale yellow	C ₁₇ H ₁₈ N ₆ O ₅ 386.37	215	90	53.49 (52.85)	4.50 (4.70)	21.8 (21.75)	I	I
1	$[Mn (HL)_2].H_2O$	Yellow	C ₃₄ H ₃₄ N ₁₂ O ₉ Mn 809.66	>300	78	50.8 (50.50)	4.09 (4.11)	20.61 (20.79)	6.52 (6.79)	I
7	[Co (HL)Cl(H ₂ O)].2H ₂ O	Green	C ₁₇ H ₁₉ N ₆ O ₆ CoCl 497.76	>300	75	39.51 (39.59)	3.97 (4.10)	16.30 (16.29)	11.41 (11.43)	6.90 (6.87)
ŝ	[Ni (HL)Cl].2H ₂ O	Pale green	C ₁₇ H ₁₉ N ₆ O ₆ NiCl 497.52	>300	80	39.87 (41.04)	3.59 (3.85)	16.71 (16.89)	11.50 (11.80)	6.78 (7.13)
4	[Cu (HL)Cl (H ₂ O)].H ₂ O	Brown	C ₁₇ H ₁₉ N ₆ O ₆ CuCl 502.37	>300	83	40.71 (40.64)	3.80 (3.81)	16.33 (16.73)	12.44 (12.65)	6.84 (7.06)
ŝ	$[Zn (L)(H_2O)_2]H_2O$	Yellowish White	C ₁₇ H ₂₂ N ₆ O ₇ Zn 487.78	>300	85	42.14 (41.86)	3.96 (4.55)	17.27 (17.23)	13.61 (13.40)	I
9	[Cd (HL) ₂].2H ₂ O	Yellowish White	$C_{34}H_{36}N_{12}O_{10}Cd$ 886.17	>300	79	46.10 (46.14)	3.96 (4.10)	19.00 (18.99)	12.72 (12.70)	I
2	[Hg (HL)Cl (H ₂ O) ₂]	White	C ₁₇ H ₁₉ N ₆ O ₆ HgCl	>300	81	31.70 (31.93)	3.08 (3.00)	13.08 (13.14)	30.92 (31.37)	5.40 (5.54)

 $\mathbf{TABLE} \ \mathbf{1} \quad \text{Elemental analysis and color of } \mathbf{H_{2}L} \text{ ligand and its metal complexes}$

ر(M_N) ر س(M_0) ر		I	I		422w	497w		433W	510w	413w	470w		411w	481w		413W	500W		419w	497w		415w	500W	
$\frac{\nu_{\rm as}(\rm NO_2^-)}{\nu_{\rm s}(\rm NO_2^-)}$		1516s	1354s		1530	1355		1526s	1340s	1526s	1343s		1530s	1334s		1526s	1354s		1527s	1354s		1528s	1351s	
Py.Ring breathing,	C—H in-plane-, out-plane bending	930w	689m		932w	705w		934w	700w	932w	700w		926w	696w		942w	680w		936w	700w		935w	705w	
	<i>ν</i> (C−0)	I			1221w			1220w		1220W			1214m			1298w	1264w		1223w			1221w		
	N	853m	808	787	844m	782m		845m	786w	842m	793w		857m	838w	789w	I			845m	781w		845m	780m	
	III	1272m			1298m			1286w		1281w			1288m						1307m	1281m		1309w	1278w	
dno	ч П	1440m			1422m			1417m		1441m			1437	1415		I			1422m			1417m		
Amide gi	I	1680m			1670s			1672m				1650s	1664s						1674s			1675s		
ν(C=N)	·	1608s			1616w			1616s		1619m			1615w			1617s			1601m			1602m		
µ(C−H)		3107w	3011w	2855w	3074w	3050w	2953w	3058w	2955w	3100w	3074w	2864w	3100w	3050w	3018w	3036w	2970w	2828w	3073w	3050w	2968w	3073w	2960w	2900w
HN1		3295m	3191m		3180w			3188w		3200w				3214m							3183br		3187br	
НОл		3435br			3431br			3426br		3400br				3431br		3422br			3354br			3460br		
Compound	4	$H_2L.H_2O$			$[Mn (HL)_2].H_2O$			[Co (HL)Cl(H ₂ O)].2H ₂ O		[Ni (HL)Cl].2H ₂ O				[Cu (HL)Cl(H ₂ O)].H ₂ O		$[Zn (L)(H_2O)_2].H_2O$			[Cd (HL) ₂].2H ₂ O			$[Hg (HL)Cl (H_2O)_2]$		
No.					1			7		ŝ			4			5			9			2		

TABLE 2 Infrared spectral bands (cm^{-1}) of H_2L ligand and its metal complexes

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TABLE 3	Electronic spectral data	and magnetic moments	s of H₂L ligand and its me	tal complexes
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No.	Compound	Spectral bands (nm)	Assignment	µeff. (B.M.) per metal ion
	H ₂ L. H ₂ O	220,314	$\pi - \pi^*$	—
		390,460	$n-\pi^*$	
1	[Mn (HL) ₂].H ₂ O	212,310	Intraligand transitions	6.02
		396		
2	[Co (HL)Cl(H ₂ O)].2H ₂ O	220,312	Intraligand transitions	
		395		5.06
		418	LMCT	
		524	${}^{4}A_{2}{}'(F) \rightarrow {}^{4}A_{2}{}'(P)$	
		600	${}^{4}\!A_{2}^{'}(F) \rightarrow {}^{4}\!E^{\prime\prime}(P)$	
		680	${}^4\!A_2^{'}(F) \to {}^4\!E'(F)$	
3	[Ni (HL)Cl].2H ₂ O	210,310	Intraligand transitions	Diamagnatic
		394		
		430	$LMCT + {}^{1}A_{2g} \rightarrow {}^{1}A_{1g}$	
4	[Cu (HL)Cl (H ₂ O)].H ₂ O	216,314	Intraligand transitions	1.82
		346,390		
		430	$LMCT + {}^{2}B_{1g} \rightarrow {}^{2}E_{g}$	
		680	$^{2}B_{1\mathrm{g}} ightarrow ^{2}B_{2\mathrm{g}}$	
		776	${}^{2}B_{1g} \rightarrow {}^{2}A_{1g}$	
5	[Zn (L)(H ₂ O) ₂].H ₂ O	212,314	Intraligand transitions	Diamagnetic
		396		
		418	LMCT	
6	[Cd (HL) ₂].2H ₂ O	212,312	Intraligand transitions	Diamagnetic
		394		
7	$[\mathrm{Hg}(\mathrm{HL})\mathrm{Cl}(\mathrm{H}_2\mathrm{O})_2]$	210,310	Intraligand transitions	Diamagnetic
		374		

The ¹C NMR (DMSO- d_6 ; , ppm) spectral data of H_2L ligand ((DMSO- d_6 ; , ppm) exhibit peaks at 14 and 17 ppm for CH₃ and --CH₂--, respectively. Also, the signals corresponding to the aromatic and pyridine carbon atoms are observed at δ 112, 121, 124, 128, 130, 133, 140, and 144 ppm. On the other hand, the peaks at 148, 149, 150, and 161 are attributed to carbon atoms of CH=N, C=N, C=O (adjacent to aliphatic moiety), and C=O (adjacent to aromatic moiety), respectively.^[56]

3.4 | Mass spectra

The mass spectra of the ligand and complexes 2 and 4 (Supplementary Information) have been performed. The molecular ion peaks observed for these compounds are found to be at m/z = 386.47, 497.86 and 502.66 amu, respectively, in complete agreement with results of elemental analysis and indicating that the complexes have monomeric nature.



FIGURE 3 UV–Vis absorption spectra of ligand H_2L and its transition metal complexes (1–7) in DMF

		TG temp		Mass los	ss (%)		
No.	Compound	range (°C)	DTG (°C)	Found	Calcd	Assignment	$T_{\rm s}$
	H ₂ L. H ₂ O	20-180	171	4.17	4.07	Loss of 1 mol of crystallized H ₂ O ^a	
		181-1000	277	89.73	89.72	Complete ligand pyrolysis ^b	
		At 1000		6.10	6.21	2C ^c	
1	[Mn (HL) ₂]. H ₂ O	20-100	50	2.20	2.22	Loss of one mol of crystallized H_2O^a	260
		100-260				stable zone	
		260-301	294	53.01	52.80	Partial ligand pyrolysis, –(2 mol of C_5H_4N and 2 mol of $C_7H_5NO_2)^b$	
		301-600	313, 531	38.91	38.16	Complete ligand pyrolysis $(C_{10}H_{12}N_8O_4)^b$	
		At 600		5.86	6.80	(Mn) ^c	
2	[Co (HL)Cl	20-220	65, 120	7.11	6.97	Loss of 2 mol of crystallized $(H_2O)^a$	220
	(HO)].2H ₂ O	220-290	254	24.94	25.30	loss of coordinated H ₂ O, 0.5 Cl ₂ and partial ligand pyrolysis (–C ₅ H ₃ N) ^b	
		290-500	317,400	23.51	23.46	Partial ligand pyrolysis (-C ₆ H ₃ NO ₂) ^b	
		500-1,000	725	32.46	32.84	Complete ligand pyrolysis ^b	
		At 1000		11.98	11.43	(Co) ^c	
3	[Ni (HL)Cl].2H ₂ O	20-195	72, 167	7.30	7.23	Loss of 2 mol crystallized H_2O^a	195
		195–304	267	22.69	22.61	loss of 0.5 Cl ₂ and partial ligand pyrolysis (–C ₅ H ₃ N) ^b	
		304-395	385	24.19	24.32	Partial ligand pyrolysis –(C ₆ H ₃ NO ₂) ^b	
		395-1000	620, 750, 950	33.64	33.98	Complete ligand pyrolysis ^b	
		At 1000		12.18	11.80	(Ni) ^c	
4	[Cu (HL)Cl	20-200	40, 130	3.68	3.58	Loss of 1 mol crystallized H ₂ O ^a	200
	$(H_2O)] H_2O$	200-256	224	7.19	7.06	Loss of 0.5 Cl ₂ ^b	
		256-1,000	264, 802	63.61	63.97	Loss of 1 mol of coordinated (H ₂ O) ^b and complete ligand pyrolysis ^b	
		At 1000		25.52	25.09	$(CuO + 4C)^{c}$	
6	[Cd (HL) ₂]. 2H ₂ O	20-200	77, 175	4.25	4.06	Loss of 2 mol of crystallized H_2O^a	260
		200-440	308	49.95	49.23	Partial ligand pyrolysis; –(2 mol of C ₅ H ₄ N and 2 mol of C ₇ H ₅ NO ₂) ^b	
		440-950	590	34.54	34.90	Complete ligand pyrolysis $(C_{10}H_{12}N_8O_4)^b$	
		At 950		11.25	12.71	(Cd) ^c	
7	[Hg (HL)Cl	20-150		_	—	Stable zone	150
	$(H_2O)_2]$	150-350	187, 226, 302	98.5	100	Complete ligand pyrolysis ^b and sublimation of Hg.	

 $TABLE\ 4 \quad \ \ \text{Thermal analyses}\ (TG/DTG)\ \text{data for hydrazide-hydrazone}\ (H_2L)\ \text{metal complexes}$

Abbreviations: DTG, differential thermogravimetry; $T_{\rm S}$: thermal stability.

^cFinal residue.

3.4.1 | UV-Vis absorption and magnetic measurements

The ultraviolet and visible (UV–Vis) spectra of all complexes were recorded at room temperature in highperformance liquid chromatography (HPLC) grade DMF solvent. The UV–Vis data and magnetic moments of metal complexes were collected in Table 3 and depicted in Figure 3. The electronic spectra of the Schiff base ligand consisted of relatively intense bands in the region of 220 and 314 nm assigned to π - π * transitions and bands at 400 and 460 nm due to n- π * transitions of the C=N and C=O moieties. Mn^{II}, Co^{II}, Ni^{II}, Cu^{II}, Zn^{II}, Cd^{II}, and Hg^{II} chelates show three bands at 208–220, 308–314, and

^aDehydration.

^bDecomposition.



390–396 nm, which are attributed to the π - π * and n- π * transitions, respectively, within the H_2L ligand. The shift to a lower wavelength of $n-\pi^*$ bands in the complexes were attributed to the coordination of M(II) ion with the imine nitrogen and carbonyl oxygen atoms. In the electronic spectra of some complexes, there is a band around 418-430 nm. This band is assigned as a LMCT transition.^[57–59] The electronic spectrum of complex **2** [Co (H₂L)Cl(H₂O)]H₂O shows d-d bands at 680, 600, and 500 nm, which were consistent with five-coordinate cobalt complexes.^[59-61] The electronic spectra of **3** [Ni(H_2L) Cl].2H₂O shows one d-d transition band of lower intensity at 430 nm. A lack of any electronic transition at longer wavelength, due to forbidden d-d transition, compatible with the square planar geometry of Ni(II) complexes.^[62] In general, three bands corresponding to ${}^{1}A_{2g} \rightarrow {}^{1}A_{1g}$, ${}^{1}B_{1g} \rightarrow {}^{1}A_{1g}$ and ${}^{1}E_{g} \rightarrow {}^{1}A_{1g}$ transitions are expected for square planar diamagnetic nickel(II) complex.^[63,64] But the long tail of strong interligand and charge transfer transitions hide some or all of these bands in many cases.^[65] Complex (4) $[Cu(H_2L)Cl(H_2O)]H_2O$ reveals three absorption bands at 776, 680, and 430 nm attributed to $^2B_{1\mathrm{g}}
ightarrow \, ^2A_{1\mathrm{g}}, \,\, ^2B_{1\mathrm{g}}
ightarrow \, ^2B_{2\mathrm{g}}, \,\, \mathrm{and} \,\, ^2B_{1\mathrm{g}}
ightarrow \, ^2E_{\mathrm{g}} \,\, \mathrm{transitions}$ affording distorted square pyramidal geometry around Cu(II) ion.^[35,36] It is well known that the d-d transitions in d^5 system are spin forbidden and hence, in complex 1, one low intensity broad band can be observed in the range 600-700 nm which may be attributed to octahedral Mn(II) d–d transition.^[66,67]

Magnetic measurements were recorded at room temperature. The effective magnetic moment (μ_{eff}) values of the complexes are given in Table 3. The μ_{eff} value at room temperature of the Mn (II) complex is 6.03 BM, which is

SCHEME 2 Thermal decomposition mechanism of complexes (1) and (6)

in the normal range observed for octaherdal Mn(II) complexes.^[66,67] This indicates that Mn(II) complex is probably octahedral. On the other hand, the μ_{eff} value (5.06 and 1.82 BM) for Co(II) and Cu(II) complexes, respectively, falls within the range normally observed for five coordinate Co(II) and Cu(II) complexes.^[35,36] Magnetic susceptibility measurements reveal that Ni(II) complex are diamagnetic which is quite obvious for square planar nickel(II) complexes.^[62–64] The zinc, cadmium, and mercury complexes are diamagnetic, the elemental analysis shows that Zn(II) complex (**5**) has five-coordinate structure,^[68,69] whereas Cd(II) and Hg(II) complexes have hexa-coordinate structures.^[70–72]

Based on elemental analyses and spectral methods, the suggested chemical structures for the synthesized metal complexes are displayed in Figure 3.

3.4.2 | Thermal studies

Thermal studies were undertaken in order to study the thermal stability for the complexes and as supportive data for the proposed molecular formulae. The results of such analysis have been summarized in Table 4. The thermal behavior of the ligand and its complexes was characterized on the basis of TGA/ DTG method (Supplementary Information).

The TG curve of the free ligand (H_2L) shows two decomposition steps. The first stage includes the thermal dehydration of the ligand, which starts between 25°C and 180°C with a mass loss (found: 4.15; calc.4.07:%) due to the loss of lattice water molecule with DTG peak at 171°C, whereas the second step starts between 181°C and

SCHEME 3 Thermal decomposition mechanism of complexes (2) and (3)



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1000°C with DTG peak at 277°C due to complete decomposition of the ligand.

The TG curves of complexes (1) and (6) reveal three decomposition steps within temperature ranges 20–200°C. 200–440°C, and 310–950°C (Table 4) (Scheme 2). The first step shows mass losses of 2.20% and 4.25%, respectively, is assigned to the liberation of lattice water and complete desolvation within the temperature range 20–200°C. The second step of decomposition within temperature range 200-440°C with DTG peaks at 294°C and 308°C corresponding to the loss of 2 mol of C₅H₄N (pyridine moiety) and 2 mol of C₇H₅NO₂ from the two ligand molecules with weight loss of 53.01% and 49.95%, respectively. The final step involves complete ligand pyrolysis leaving free metallic residue.^[73-77]

The TG curves of complexes (2) and (3) show four steps within temperature decomposition ranges 20-220°C, 195-304°C, 290-500°C, and 395-1,000°C (Scheme 3). The first step is accompanied with estimated mass losses of 7.11% and 7.30%, respectively, attributable to complete desolvation with DTG peaks at 120°C and 167°C. After that, the decomposition of the complexes started at 220°C and 195°C, respectively, in the second step with DTG peaks at 400°C and 385°C associated with mass loses of 24.94% and 22.69%, respectively, assignable to the removal of coordinated chloride ion as well as partial ligand pyrolysis $(-C_5H_3N)$ in addition to the loss of coordinated water complex 2 (Table 4). The next step is followed by complete pyrolysis of ligand leaving free metallic residue at high temperatures.^[73–77]

The thermal behavior of the square pyramidal Cu(II) complex (4) occurs in three decomposition stages within temperature ranges 20-200°C, 200-256°C, and 256-1000°C. The first one is the desolvation step which is associated with weak DTG peaks at 40, 130°C attributed to a loss of 1 mol of crystallized water and complete desolvation with weight losses (found: 3.68; calc. 3.58%). Afterward, the coordinated chloride ion is lost in the second stage corresponding to DTG peak at 224°C. Finally, complete ligand pyrolysis takes place associated with the removal of the rest coordinated water molecule with weight loss 63.61%. This step is ended with the formation of CuO contaminated with carbon residue^[35,74] (Table 4). The thermal decomposition is observed as follows:

$$\begin{bmatrix} Cu(C_{17}H_{16}N_{6}O_{4})(Cl)(H_{2}O) \end{bmatrix} H_{2}O \xrightarrow{(I) 20-200^{\circ}C} \begin{bmatrix} Cu(C_{17}H_{16}N_{6}O_{4})(Cl)(H_{2}O) \end{bmatrix} + H_{2}O \xrightarrow{(II) 20-356^{\circ}C} \\ (II) 200-356^{\circ}C \xrightarrow{(III) 256-1000^{\circ}C} \begin{bmatrix} Cu(C_{17}H_{16}N_{6}O_{4})(H_{2}O) \end{bmatrix} + Cl \xrightarrow{(III) 256-100^{\circ}C} \begin{bmatrix} Cu(C_{17}H_{16}N_{6}O_{4})(H_{2}O) \end{bmatrix} \end{bmatrix} + Cl \xrightarrow{(III) 256-100^{\circ}C} \begin{bmatrix} Cu(C_{17}H_{16}N_{6}O_{4})(H_{2}O) \end{bmatrix} + Cl \xrightarrow{(III) 256-100^{\circ}C} \begin{bmatrix} Cu(C_{17}H_{16}N_{6}O_{4})(H_{2}O) \end{bmatrix} \end{bmatrix} + Cl \xrightarrow{(III) 256-100^{\circ}C} \begin{bmatrix} Cu(C_{17}H_{16}N_{6}O_{4})(H_{2}O) \end{bmatrix} \end{bmatrix} + Cl \xrightarrow{(III) 256-10^{\circ}C} \begin{bmatrix} Cu(C_{17}H_{16}N_{6}O_{4})(H_{2}O) \end{bmatrix} \end{bmatrix} \end{bmatrix} = Cl \xrightarrow{(III)$$



FIGURE 4 X-ray diffraction (XRD) pattern of copper oxide obtained from the thermal decomposition of complex **4**

The mercury complex (7) was found to be an anhydrous one by elemental analysis and was confirmed by the thermogravimetric studies. It is stable up to 150° C and decomposes in a single step, which is represented by the DTG peaks at 188, 226, 280, 302 °C (Table 4). As expected, for mercury complexes, sublimation of Hg and only traces of carbon residue was left on heating up to 800° C.^[78]

3.4.3 | XRD of the copper oxide

Copper oxide (CuO) obtained from the thermal decomposition of copper(II) complex (**4**) was confirmed by the characteristic peaks observed in the XRD pattern, as shown in Figure 4. XRD analysis showed intense peaks at 36.5° , 42.0° , 44.59° , 58.9° , and 64.9° , consistent with



 $FIGURE \ 5 \quad \ \ {\rm Optimized\ structures\ of\ the\ ligand\ } (H_2L)\ tautomers$

the standard values of JCPDS file no. 00-003-0897. The observed diffraction reflections were comparable with other literature data.^[79,80] In addition, XRD is a convenient method for determining the mean size of nano crystallites. The average crystalline size (D) of the nano CuO particles was calculated by Scherer's equation affording diameter of 19 nm. CuO NPs is broadly used in number of fields such as catalysis, sensing materials, ceramics, thermoelectric materials, glass, superconducting materials, and antimicrobial activity.^[81] The XRD spectrum also shows diffraction peaks characteristic for cuprous oxide that consistent with the JCPDS file no 00-003-0892.

3.5 | DFT studies

In order to provide a more comprehensive analysis of the metal ligand bonding in some selected complexes, a DFT computational study was carried out on the ligand and complexes (2, 4, 5-7).

3.5.1 | Structure of the ligand

Due to the presence of labile hydrogens, double bond, and protonable heteroatoms in the ligand, the

 $\begin{array}{lll} T\,A\,B\,L\,E\,\,5 & \mbox{The relative energies (kcal/mol) calculated for} \\ \mbox{different tautomers of the ligand (H_2L) at $B3LYP$/ 6-311G(d,p)$} \end{array}$

Tautomer	$\Delta \boldsymbol{E}$	$\Delta \boldsymbol{E_0}$	ΔE_{298}	ΔH_{298}	ΔG_{298}
Α	0	0	0	0	0
В	6.67	6.52	6.43	6.43	6.78
С	7.94	7.77	7.76	7.17	6.71
D	23.45	22.97	23.18	23.18	21.90
Ε	8.27	8.28	8.16	8.16	60.53
F	16.18	16.27	16.09	16.09	16.02

TABLE 6 NBA charges of the ligand and the studied complexes

studied hydrazide-hydrazone molecule can exist in different tautomeric forms. Hydrazide-hydrazone ligand (H_2L) can exist either in the amido (keto) or in imido form as illustrated in Figure 1. The (enol) optimized structures of the investigated tautomers are shown in Figure 5. The B tautomer involves proton transfer from N2 to O1, whereas in the C and D tautomers, the proton transfers from N5 to O2 and from C17 to O2, respectively. Proton transfer between N2 and O1 and between N5 and O2 takes place in the di-enol tautomer E, whereas the di-enol tautomer F involves transfer of protons from N2 to O1 and from C17 to O2. Among all forms, the di keto tautomer A is the most stable structure in the gas phase as presented in Table 5. However, the enol tautomer **B** is more stable than other enol tautomers, whereas the enol form **D** is less stable than tautomer **C** by 15.51 kcal mol⁻¹. From theoretical point of view, the studied ligand exists in the diketo form A, which agrees with the experimental finding. Natural bond orbital (NBO) analysis was carried out to shed light on the electronic structures of the ligand and its complexes. The atomic natural charges for the optimized geometries over some atoms in the ligand forms and its complexes are listed in Table 6. The negative charge on the oxygen atoms O1 and O2 (-0.590, -0.580 e) is larger than that on the nitrogen atoms N2, N3, N4, and N5 as given in Table 6. Therefore, it is expected that the metal ion will bind preferably with the oxygen atoms than with nitrogen atoms.

In order to further understand the interaction between the ligand and metal ions, the frontier molecular orbitals (FMO) are calculated as depicted in Figure 6. HOMO, the highest energy orbital containing electrons, represents the ability to donate electrons where LUMO is the lowest energy orbital that can accept electrons. HOMO spreads over benzene ring, N4, N5, and O2, whereas there is no

Compound	01	02	N2	N3	N4	N5	Μ	Cl
Α	-0.590	-0.580	-0.437	-0.319	-0.447	-0.230	—	_
В	-0.697	-0.575	-0.349	-0.347	-0.443	-0.217	—	—
2	-0.758	-0.622	-0.441	-0.344	-0.428	-0.229	0.958	-0.604
4	-0.545	-0.352	-0.313	-0.349	-0.316	0.110	0.576	-0.557
5	-0.601	-0.616	-0.309	-0.439	-0.317	-0.235	1.069	_
6	-0.554	-0.407	-0.344	-0.399	-0.315	-0.108	1.028	_
7	-0.541	-0.374	-0.329	-0.333	-0.312	-0.110	0.829	-0.582



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spatial HOMO distribution on O1, N2, and N3 in the diketo tautomer **A**. After enolization of O1 in the most stable enol form **B**, the HOMO was located on N3 and N2 in addition to the benzene ring, N4, N5, and O2 as shown in Figure 6. These results confirm that the metal ion will prefer binding with O2 in its keto form while the deprotonation after enolization is essential for coordination of metal ion



FIGURE 6 Density functional theory (DFT) computed highest occupied molecular (HOMO) and lowest unoccupied molecular orbital (LUMO) diagrams of ligand (H₂L) tautomers (A and B) and its complexes 4 and 6

with O1, which supports our experimental finding that the chelation with metal ions takes place through the enol form of the ligand. The DFT studies predicted that the enol tautomer \mathbf{B} is the most stable enol form.

Also, the energy gap between HOMO and LUMO characterizes the chemical stability, reactivity and hardness of the molecule.^[35,82] Hardness is one of the highly useful concepts for understanding the behavior and reactivities of chemical systems. It is coupled with the softness, electronic chemical potential, or absolute electronegativity in this respect.^[83,84] Hardness is a direct measure of the stability of molecules, whereas softness is a direct measure of reactivity of molecules. From the data of HOMO and LUMO energies, the energy gap, ΔE , absolute electronegativity, χ , chemical potentials, Pi, absolute hardness, η , absolute softness, σ , global electrophilicity, ω , global softness, S, and additional electronic charge, $\Delta N_{\rm max}$, have been calculated and presented in Table 7 to give indications about the stability and reactivity of the ligand and its complexes. The calculations demonstrated that the free ligand has a small HOMO-LUMO energy gap (3.85 eV) which increases its softness and reactivity toward the reaction with the metal ions and it has high biological activity due to high ω value.

3.5.2 | Structure of the complexes

The geometries of the optimized structures of the studied complexes (2, 4–7) are depicted in Figure 7. Complexes 2, 4, and 5 adopted mononuclear, distorted

five-coordinate geometries. The two common geometries for five-coordinate species are trigonal bipyramidal (tbp) and square-based pyramidal (sp) metal environments. Complexes 2, 4, and 5 are not homoleptic compounds, so they are expected to undergo deviations from the ideal geometries. It is possible to assign approximate tbp or sp metal coordination geometry using a simple quantitative measure derived from a simple calculation of the angular structural parameter (τ). τ defined as $\tau = [(\theta -)/60]$, where θ and are the two largest coordination angles and $\tau = 0$ for perfect sp and one for ideal tbp. The deviations from ideal geometries can happen when the metal center is displaced out of the ligand plane or due to ligand bite angle restrictions. For complexes 2, 4, and 5, the τ parameters are 0.15, 0.45, and 0.31 respectively, indicating that these complexes adopted coordination geometries that can best be described as distorted square-based pyramidal (sp). Moreover, the sum of the bond angles around Co(II), Cu(II), and Zn(II) are 340°, 360°, and 343°, which implies a pyramidization degree of 42° , 0° , and 17° for complexes 2, 4, and 5, respectively. In Complex 2, the basal plane was defined by one imine nitrogen donor (N3), carbonyl oxygen donor (O2), enolic oxygen donor (O1) of the H₂L ligand, and oxygen donor (O5) of water molecule. The pseudo-apical position is occupied by chloride ion. In case of complex 4, the basal plane is occupied by one imine nitrogen donor (N3), enolic oxygen donor (O1) of the H_2L ligand, oxygen donor (O5) of water molecule, and chloride ion, whereas the carbonyl oxygen donor (O2) stays in the pseudo-apical position. On the other hand, in complex 5, the Zn ion coordinated to imine nitrogen donor (N3), two enolic oxygen atoms of the H₂L ligand (O1 and O2), and oxygen donor

<i>E</i> (a.u)	H ₂ L(A)	2	4	5	6	7
Dipole moment (D)	3.55	15.02	9.92	9.00	3.851	12.22
E _{HOMO} (eV)	-6.38	-6.21	-6.44	-5.93	-5.80	-6.17
E _{LUMO} (eV)	-2.59	-3.52	-3.77	-2.80	-3.30	-3.40
$\Delta E (eV)$	3.79	2.69	2.67	3.13	2.50	2.77
χ (eV)	4.485	4.865	5.105	4.365	4.550	4.785
η (eV)	1.895	1.345	1.335	1.565	1.250	1.385
$\sigma ({\rm eV}^{-1})$	0.527	0.743	0.749	0.638	0.800	0.722
Pi (eV)	-4.485	-4.865	-5.105	-4.365	-4.550	-4.785
$S (eV^{-1})$	0.527	0.743	0.748	0.638	0.800	0.722
ω (eV)	5.300	8.798	9.76	6.087	8.281	8.265
$\Delta N_{ m max}$	2.366	3.617	3.823	2.789	3.640	3.454

TABLE 7	Various quantum
chemical para	meters of free ligand
(H ₂ L) and its	complexes



FIGURE 7 Optimized structures of the complexes

(O6) of the water molecule in the basal plane. These four atoms form a distorted plane with the oxygen atom

of the H_2O ligand (O5) coordinated to Zn(II) ion in Z axis. Starting the optimization process with a regular

octahedral structure for complex (5) where there are two water molecules coordinated to Zn(II) ion in the *z* axis leads gradually to the distorted square pyramidal structure where one water molecule leaves the coordination sphere.

The DFT studies show that the Cd(II) complex has trigonal prismatic geometry. Although octahedral coordination geometries are the most common fundamental geometries of transition metal hexa-coordinated complexes, the trigonal prismatic geometry for a metal ion with a d¹⁰ electronic configuration is not rare because there is no crystal field stabilization energy (CFSE).^[85,86] The majority of metal complexes without CFSE were predicted to have structures with twist angles $<5^{\circ}$, suggesting that experimentally they will have trigonal prismatic structures.^[87] Perfectly prismatic structure of Cd(II) was observed in the potassium salt of the tris (acetylacetonato) complex^[87], and distorted trigonal prisms were found with other ligands such as nitrates, carboxylates, triamines, oxalato, and a derivative of triazacyclonon.^[88-90] Another examples of trigonal prismatic complexes containing saturated amine ligands such as $[Cd((Me)_5 tricosane))]$ (PF₆)₂ and $[Hg((Me)_5 tricosane))]$ $(PF_6)_2$ $((Me)_5 tricosane = 1,5,9,13,20$ -pentamethyl-3,7,11,15,18,22-hexaazabicvclo[7,7,7] tricosane) were studied previously.^[89] Janiak and coworkers showed that the Cd(II) complex with tetradentate pyridyl di-Schiff-base ligands, N,N0-bis-(1-pyridin-2-yl-ethylidene)propane-1,3-diamine has trigonal prismatic geometry.^[85] The ideal octahedron consists of two exactly parallel, staggered equilateral triangles of side (s) with an intertriangular distance (h) (Figure 8). The trigonal distortion for the hexa-coordinated complexes can be measured by evaluating the s/h ratio and twist angle () value.^[85,89] In complex 6, Cd(II) ion coordinated to two tridentate ligand (H_2L) , the coordination sphere can be described as being constituted of two triangles

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(O5, O2, N3 and O1, O6, N6) with an average side (s) of 3.791 Å. Triangles are slightly tilted with a dihedral angle of 9.4° and an intertriangular separation between the centroids (distance between O2 and 06) of 3.204 Å (h). The torsion angles N3-O2-O6-O1 and N9-O6-O2-O5 are 9.9° and 14.9° are close to that of a regular trigonal prismatic geometry (= 0). The s/h ratio in complex 6 is 1.18, revealing an elongation relative to an ideal trigonal prism with square faces (s = h, s/h = 1.00).^[82] On the other side, in complex 7, Hg(II) ion coordinated to O1, O2, and N3 from the tridentate ligand (H_2L) and chloride ion in the equatorial plane while coordinated with two water molecule in the z axis forming octahedral structure. The angles O5-Hg-O6, N3-Hg-Cl, and O2-Hg-O1 are 167°, 155°, and 135°, which are deviated from the ideal octahedral structure (180°). Moreover, the torsion angles O2-O6-Cl-O5 and N3-O1-O5-Cl are 42° and 79°, predicting distortion than regular octaheral geometry (= 60), while the s/h ratio in complex 7 is 1.3 matching with octahedral structures shown in the literature.^[85]

The calculated binding energies of the complexes in the gas phase are collected in Table S1. The negative sign of the binding energies indicates that the investigated complexation reactions are thermodynamically favored. The binding energy is more negative for copper complex (4) which implies that it is formed more spontaneously than the other complexes. The order of thermodynamic stability of the investigated complexes is Cu(II) > Co(II) > Hg(II) > Cd(II) > Zn(II). Selected bond lengths and bond angles for the complexes are listed in Table 8. The calculations indicated that the bond length between the metal ion and enolic oxygen (M–O1) is the shortest compared with M–N3 and M–O3 bond distances. The negative charges on O1 and O2 increased in complexes

FIGURE 8 Octahedron and trigonal prism with enhanced triangular faces and relevant parameters for the assessment of their relationship and distortion. is the twist angle between the enhanced triangles around the C3 axis^[85]



regular octahedron

trigonal prism

Compound	C6-01	C9-02	C6—N2	C7-N3	C9—N4	M—01	M-02	M—N3	6NW	M-CI	M-05	M—06
H_2L	1.213	1.209	1.392	1.277	1.386	I	I	I	I	I	I	I
2	1.289	1.228	1.320	1.284	1.364	2.029	2.198	2.116	I	2.296	2.142	I
4	1.287	1.218	1.319	1.286	1.377	1.998	2.302	2.008	I	2.371	2.045	
5	1.287	1.292	1.321	1.287	1.312	2.016	2.092	2.143	I		2.135	2.086
6	1.275	1.223	1.327	1.286	1.366	2.257	2.358	2.395	2.381	I	2.287	2.394
7	1.274	1.222	1.329	1.288	1.368	2.462	2.526	2.433	I	2.552	2.553	2.804

Selected bond lengths (B, \dot{A}) for the complexes

TABLE 8

2 and **4** relative to their values in the free ligand. Besides, the negative charge on N3 increased in all complexes that revealed the back donation between metal center and ligand nitrogen atom (N3) in addition to O1 and O2 (in complexes **2** and **4**), which leads to a significant increase in its negative charge. Moreover, the charges on the metal ions in the complexes are equal or less than +1 e; this indicates charge transfer from the ligands to the central metal ion. The dipole moments (D) for the complexes except complex **6** range from 9.0–15.02 Debye (Table 7), implying that these complexes are highly polar compounds.

Wiberg bond order for each of the five different metal-ligand interactions, M-O1, M-O2, M-N3, M-Cl, and M-O(H₂O), is presented in Table 9. The total bond order is further resolved into contributions from the d-orbital occupancy for the α - and β -electrons Co(II) to the overall bond order for and Cu(II) complexes. A low degree of covalency for M-O and M-N bonds, which is less than 0.45, was observed in all complexes. The Co(II) and Cu(II) complexes show higher M-O and M-N bond order than d¹⁰ metal complexes which is consistent with the values of bond lengths as the Cu-O1 and Cu-N3 are the shortest compared with the other complexes. In contrast, the bond orders for M-Cl interaction is larger than M-O and M-N bond orders which can be attributed to the fact that the chloride ligand displays both σ and π donation to the metal centers. When this feature is considered, the overall bond order is also rather low with average total values of only 0.66 for Co(II) and Cu(II) complexes while 0.43 for Hg(II) complex. In general, the wiberg bond orders obtained for the M–O1, M–O2, and M-N3 moieties correlate with our calculated bond length variations.

Regarding HOMO and LUMO energies in the free ligand and complexes, the HOMO level in all complexes is destabilized by 0.21-0.81 eV, whereas LUMO is stabilized by 0.17-0.58 eV relative to the ligand which causes a decrease in energy gap in these complexes. Besides, the electron cloud of the HOMO in complexes 2 and 4 is spread over the metal and its coordination sphere, whereas in complexes 5-7, HOMO is localized on the coordination sphere surrounded the metal only and there is no HOMO observed on the metal (Figures 6 and S7). This observation arises from the strong interaction between the metal and the ligand in complexes 2 and 4 than other complexes, which elucidated before by the higher M-N and M-O bond order in complexes 2 and 4 than the studied d¹⁰ metal complexes (5-7).

TABLE 9	computed wiberg bond
order for met	al–nitrogen, metal–oxygen
and metal ch	oro bonds from the
optimized str	uctures of the studied
metal comple	xes

Compound/bond	M01	M02	M—N3	M—Cl	M-O(H ₂ O)
2	0.298 ^a	0.190 ^a	0.260 ^a	0.574 ^a	0.209 ^a
	0.059 ^b	0.039 ^b	0.052 ^b	0.124 ^b	0.044 ^b
	0.358 ^c	0.229 ^c	0.312 ^c	0.698 ^c	0.253 ^c
4	0.311 ^a	0.159 ^a	0.297 ^a	0.474 ^a	0.227^{a}
	0.120 ^b	0.042 ^b	0.130 ^b	0.158 ^b	0.081 ^b
	0.431 ^c	0.201 ^c	0.427 ^c	0.632 ^c	0.308 ^c
5	0.255	0.188	0.224	—	0.185
					0.198
6	0.170	0.119	0.158	—	—
7	0.177	0,119	0.204	0.431	0.1149
					0.0025

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 $^a\mbox{Contributions}$ from the $\alpha\mbox{-electron}$ orbital occupancy.

 $^{b}\mbox{Contributions}$ from the $\beta\mbox{-electron}$ orbital occupancy.

^cTotal contributions.

MEP provides the key to predict the reactive sites towards electrophilic and nucleophilic attack and in studies of biological recognition and hydrogen bonding interactions.^[91] The MEP of the ligand (H_2L) and the complexes are shown in Figure 9. The negative sites (red) of the MEP are related to electrophilic reactivity while the positive sites (blue) are related to nucleophilic reactivity. It can be seen from Figure 9 that the negative MEP regions of the ligand are concentrated on the carbonyl oxygen atom, azomethine nitrogen atom in addition to the pyridine nitrogen atom. The electrostatic potential was shifted to more positive values with the coordination of the ligand to the metal ion, which is consistent with the higher global electrophilicity (ω) of the complexes in comparison with the ligand. The usefulness of electrophilicity index in unraveling the toxicity of many compounds has been analyzed as there is a linear correlation between the electrophilicity and the biological activity of molecules.^[92] The higher values of the electrophilicity of the complexes relative to the ligand give a sign for the higher biological activity of the studied complexes compared with the ligand.

The IR frequencies of the ligand and its complexes were obtained theoretically by DFT using the hybrid B3LYP functional. The calculated values of the vibrational spectra were compared with the corresponding experimentally measured values in the gas phase (Table 10). The computed N—H, C=O, and C=N stretching vibrational modes of the ligand of 3260,1711–1737 and 1602–1668 cm⁻¹ match well with the corresponding experimental values at 3295, 1680, and 1608 cm⁻¹, respectively. In the complexes, C=O group of ligand actively participates in chelation, and it shows a change in frequency to lower value, corresponding to the partial loss of double bond character, whereas C=N is shifted to higher or lower values in the complexes compared to ligand. Theoretically, the stretching of coordinated C=O and C=N bonds is shifted toward lower frequencies compared with the uncoordinated ones on the other side of the ligand. Besides, the stretching vibrations of M-O and M-N occurred at 411-510 cm⁻¹ in the FTIR spectrum match well with the calculated vibrational frequencies. The good agreement between the calculated values of the vibrational spectra with the experimentally observed data shows that the method used in this study is well adapted to predict the FTIR spectrum of the ligand and its complexes.

3.6 | Biological studies

The antibacterial and antifungal activities of the hydrazide-hydrazone ligand and its metal complexes were measured as the diameter of the inhibition zone, and the data were listed in Table 11 and represented graphically in Figure 10. The H_2L ligand was found to have moderate activity against *Staphylococcus aureus* (G + ve) bacteria but less than the standard antibiotics, whereas low activity against *Esherichia coli* (G -ve) bacteria. The complexes were found to have remarkable antimicrobial activity compared with that of the free ligand. It was noticed

 H_2L





6



7



that Hg(II) complex (7) showed higher antibacterial activity against both gram +ve and gram -ve bacteria followed by the Cu(II) complex, whereas Mn(II) (1) and Zn(II) (5) complexes show the lowest antibacterial activity compared with the other complexes. The antibacterial activity has the order: (7) > (4) > (2) > (3) > (6) > (5) > (1). The better activity of metal complexes can be explained based on

the chelation theory.^[36,93] This suggested that chelation could increase the lipophilic nature of the metal and promote the ability of such complexes to pass through the cell membrane of the microorganism to be destroyed. On the other hand, Hg(II) complex was found also to possess higher antifungal activity against *Aspergillus flavus* and *Candida albicans* comparing with all the studied compounds and the standard.

TABLE 10 Selected vibrational modes and IR of the ligand and its complexes

	ν(N—H)		ν(C=0)		ν(C=N)		ν (M—O) and ν (M—N)	
Compd	Calcd. ^a	Exp.	Calcd. ^a	Exp.	Calcd. ^a	Exp.	Calcd. ^a	Exp.
H_2L	3260	3295(br) ^b	1711, 1737	1680	1602-1668	1608	—	—
	3118	3191(br) ^b						
2	3309	3188(br) ^b	1669	1672	1602–1628	1616	474–590	433-510
4	3306	3214(br) ^b	1693	1664	1622–1627	1615	415-548	411-481
5	—	_	—	—	1597–1627	1617	455-614	413-500
6	3309	3183(br) ^b	1630, 1692	1674	1601–1627	1601	450-526	419–497
	3308							
7	3308	3187(br) ^b	1677	1675	1607–1629	1602	467–594	415-500

^aCalculated at the B3LYP/LANL2DZ for metal ions and 6-311G(d,p) for other atoms (scale factor 0.9682). ^bBroad band centered at this position.

TABLE 11 Antimicrobial and antifungal activities of H₂L ligand and its metal complexes

	Inhibition zone diameter (mm)						
	Fungi		G(+ve)	G(-ve)			
Compound	Aspergillus flavus	Candida albicans	Staphylococcus aureus	Escherichia coli			
H_2L	0	0	14	0			
1	0	0	11	9			
2	13	0	20	20			
3	20	0	21	18			
4	12	12	25	24			
5	0	0	12	11			
6	20	16	17	16			
7	34	23	30	28			
Ampicillin	—	—	18	22			
Amphotericin B	17	18	_	—			





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4 | CONCLUSIONS

A new hydrazide-hydrazone ligand (H₂L) was successfully prepared from condensation of isonicotinic acid hydrazide with (Z)-N'-(2-nitrobenzylidene)-3-oxobutanehydrazide. The investigated ligand was used to synthesize a new series of Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), and Hg(II) transition metal complexes that were fully characterized by thermal and elemental analyses, FTIR, mass and electronic spectra. FTIR spectra indicated that the ligand acts as a tridentate and coordinated to the metal ion through ONO donors in all complexes with 1 L:1 M stoichiometry except complexes (1) and (6) where the ligand binds to Mn(II) and Cd(II) ions in 2 L:1 M stoichiometry. Spectral characterization of the novel complexes suggested octahedral geometry for complexes (1, 7) and square pyramidal geometry for complexes (2, 4, 5). However, complexes (3) and (6) adopt square planar and trigonal prismatic geometrical structure, respectively. DFT calculations have been carried out to study the structure of the ligand tautomers and metal complexes of the most stable form. The antimicrobial screening assay revealed that the metal chelates show greater inhibitory effects than the parent hydrazide-hydrazone ligand towards the studied bacterial and fungal organisms.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the supplementary material of this article.

AUTHOR CONTRIBUTIONS

Dina Tolan: Formal analysis; methodology; resources; software; validation. **Tahani Kashar:** Formal analysis; methodology; resources; software; validation. **Kazunari Yoshizawa:** Formal analysis; methodology; resources; software; validation. **Ahmed El-Nahas:** Conceptualization; formal analysis; methodology; project administration; resources; software; validation; visualization

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