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Synthesis, characterization and biological activity of new mixed-ligand divalent metal complexes derived from 1,3,4-thiadiazole Schiff base and 2,2′-bipyridine

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Abstract

New mixed-ligand complexes of Cu(II), Ni(II), Co(II), Zn(II), Pt(II) and Pd(II) transition metals were synthesized from a Schiff base 5-((Z)-((E)-3-phenylallylidene)amino)-1,3,4-thiadiazole-2-thiol obtained by the condensation reaction between cinnamaldehyde and 5-amino-1, 3, 4-thiadiazol-2-thiol as a primary ligand (LH^1) and the heterocyclic base 2,2′-bipyridine (2,2′-bipy) as a secondary ligand (L^2). The prepared ligand and their metal complexes have been characterized by elemental analysis, molar conductivity measurement, magnetic susceptibility, infrared (FT-IR), proton nuclear magnetic resonance (^{1}H-NMR), electronic (UV-Vis), mass spectrometry (MS), thermal gravimetric analysis (TGA), and screened in vitro for their potential as biological activity by the agar well diffusion method against Gram-negative *Escherichia coli* (*E. coli*) and Gram-Positive *Staphylococcus aureus (S. aureus)* strain. The mixed-ligand complexes were found to have the following formulas $[M(L^1)(L^2)]Y \cdot H_2O$ L^1 = Schiff base, L^2 = 2,2′-bipy, (M = Cu(II), Ni(II), Co(II), Zn(II), Y=NO_3), (M=pd(II), Y=Cl_2) and (M= pt(II), Y=Cl) for metallic complexes. L^1 acts as a bidentate ligand and coordinates to a metallic ion center through imine nitrogen and a deprotonated sulfur atom. Similarly, L^2 acts as a neutral bidentate ligand coordinating to the metallic ions via two nitrogen atoms. The resultant data have shown that the mixed-ligand complexes have an electrolytic nature and Co(II), Pt(II), and Pd(II) metal complexes have square planer structure, as well as tetrahedral geometry, has been proposed for the complexes of Cu(II), Ni(II) and Zn(II). Thus, the biological activity data indicated that the Cu(II), Co(II), Zn(II), and Pd(II) complexes have a much higher biological activity than the Schiff base. It was found that the Zn(II) complex was more effective than the other metal complexes used against both types of the bacteria tested.

Introduction

The study of transition metal ions in coordination chemistry with various types of ligands in the fields of bioinorganic chemistry and medicine has been enhanced by the current advancements ***[1]***. Particularly those formed with transition metals, due to their important roles in biological processes in the human body ***[2].*** Consequently, the preparation of new Schiff bases from any primary amine and active carbonyl compounds is a vital precursor of ligands that coordinate to metal ions through imine nitrogen which exhibits unique properties and novel reactivity ***[1]***. The C═N linkage in azomethine is excellent for biological activity due to the coordination to transition metal ions to form the stable complexes. Numerous azomethine have been reported to have marked antibacterial, antifungal, antimalarial, and anticancer activities ***[3]***. The ability to reversibly bind oxygen to an inhibitor of corrosion ***[4]***, transfer of an amino group ***[5]***, complexing ability towards some toxic metals ***[6]***, and catalytic activity in hydrogenation of olefins ***[7]***; all of these many important applications of a large number of Schiff bases ligand and their metals chelates that previously have been studied. Mixed-ligand complexes also play an essential role in the biological field in which is reported to exhibit good enzyme activation, as well as the storage and transportation of active substances through the membrane ***[2]***. Schiff base ligands that are derived from heterocyclic compounds such as 1,3,4-thiadiazole derivatives have attracted increased interest in the field of biological inorganic chemistry. Previously, it has been shown that 1,3,4-thiadiazole derivatives possess interesting industrial, pharmaceutical and biological applications activities due to the presence of =N-C-S- linkages such as anti-corrosion, optical brightening and fluorescent properties ***[8]***, anti-inflammatory, anti-bacterial ***[9]***, and anticancer ***[10]***. Cinnamaldehyde is the main component of the bark extract of cinnamon. It has been widely researched that cinnamaldehyde antimicrobial activity has been used in medicine, food, and wood preservation. However, there are some application limits due to several drawbacks such as its strong odor and high volatility. Many researchers have attempted to solve this problem through chemical modification ***[11]***. Schiff bases which contain cinnamaldehyde moieties are an important class of ligands in coordination chemistry and were widely reported ***[12]***. A large number of mixed-ligand complexes were reported by many researchers that containing heterocyclic bases such as 2,2'-bipyridine and 1,10-phenanthroline due to their bioinorganic applications and thermal stability ***[13]***. 2,2′-bipyridine is a bidentate strong field ligand that has been used widely in coordination chemistry and mainly in the formation of mixed-ligand complexes because of its strong redox steadiness and relative easiness of functionalization [3]. Mixed-ligand complexes incorporating 2,2′-bipyridine with other bidentate chelators have been reported as antibacterial, antineoplastic, antitumor cytotoxicity, and genotoxicity agents ***[14]***.

Nowadays, the increasing microbial resistance to antibiotics in use, necessitates the search for new compounds with potential effects against pathogenic bacteria. Hence in this research work, we reported the synthesis of new metal complexes of a Schiff base ligand derived from 5-amino-1, 3, 4-thiadiazol-2-thiol with cinnamaldehyde in the presence of 2,2′-bipyridine. The prepared compounds were characterized by elemental analysis, molar conductance, magnetic susceptibility, thermographic analysis, spectroscopic techniques (IR, ^{1}H-NMR, UV–Vis, and Mass), and evaluated the antibacterial activity of the synthesized compounds in vitro.

Materials and Methods

A. Materials

The compounds included Cinnamaldehyde (Merck), 5-amino-1,3,4-thiadiazole-2-thiol (EXIR), and 2,2′-bipyridine (GPR). $Cu(NO_3)_2.3H_2O$, $Ni(NO_3)_2$ $.6H_2O$, $Co(NO_3)_2.6H_2O$, and $Zn(NO_3)_2.6H_2O$ are products of Merck. Compounds $K_2[PtCl_4]$ and $PdCl_2$ were purchased from ALDRICH. Anhydrous grade methanol and ethanol (Merck), dimethyl sulfoxide (DMSO) (Fisher Scientific Company), Diethyl ether (Biochem), and Tetrahydrofuran (THF) (Alfa Chemika) were used. All the chemicals were analytically pure and used without further purification.

B. Instrumentation

Melting points were conducted in an open glass capillary tubes using Electro-thermal digital melting point machine Model 1102D. The proton NMR spectra were recorded on Varian INOVA 500 MHz spectrophotometer, United States instrument. Chemical shifts for the NMR measurement were obtained concerning tetramethylsilane (TMS) equally as an internal standard. The elemental (C, H, N, S) compositions of the compounds were determined using a Euro vector analyzer EA 3000 series. The FTIR spectra of the synthesized compounds were recorded on Perkin–Elmer spectrometer in the region 400-4000 cm^{-1} using the KBr disc method. The electron ionization mass spectra (EI-MS) fragmentation pattern of the Schiff base was determined on an Agilent technologies model 5975C spectrometer. Magnetic susceptibility measurements of the complexes were carried out by the Sherwood Scientific Auto Guoy balance instrument at 20°C, while the diamagnetic corrections stood evaluated using Pascal’s constants. The molar conductance of the complexes in DMSO was measured with Fisher Scientific Multimeter Model XL600 and Electronic spectra of the ligands and the complexes were recorded in a 1:9 ratio DMSO: H_2O mixture in the range 200–800 nm using Cary Eclipse UV-Visible Spectrophotometer–Agilent Technologies. Thermal gravimetric analysis TGA of samples were conducted on a Perkin- Elmer Diamond thermal apparatus using an alumina pan as reference. The TGA curves were obtained at a heating rate of 10°C/min.

Experimental Procedures

A.Synthesis of Schiff Base Ligand

The Schiff base LH^1 was synthesized using a one-step reaction. Equimolar amounts of trans-cinnamaldehyde (3-phenyl-2-propenal) (10 mmol, 1.3216 gm) were added dropwise to a refluxed methanol solution (40 ml) of (10 mmol, 1.3319 gm) 5-amino-1,3,4-thiadiazole-2-thiol with few drops of formic acid. The solution mixture was refluxed for 40 hours. After that, the reflexed solution was evaporated using a rotary evaporator. The residue was washed several times with diethyl ether and hot methanol. Finally, the yellow precipitate was obtained after filtration. (Yield, 86%).

B.Synthesis of Divalent Mixed-Ligand Complexes

The Schiff base (2 mmol, 0.4947 gm) liquefied in 10 ml of THF as a primary ligand, were mixed with equimolar concentrations of 2,2′-bipy in 5 ml THF as a secondary ligand. Following that, metal salt, (2 mmol, 0.4832gm of $Cu(NO_3)_2.3H_2O$, 0.4362gm of $Ni(NO_3)_2.6H_2O$, 0.5821gm of $Co(NO_3)_2.6H_2O$, 0.5949gm of $Zn(NO_3)_2.6H_2O$, and 0.5884gm of $Na_2[PdCl_4]$) in 10ml of THF were added dropwise to the mixed-ligands with stirring. For Pt(II) complex, (0.7 mmol, 0.1731 gm) of Schiff base was mixed with a solution of 2,2′-bipy (0.7 mmol, 0.1093 gm) in THF and then (0.7 mmol, 0.2910 gm) of $K_2[PtCl_4]$ was dissolved in a mixed solvent of (6ml D.W: 4ml THF) and was added dropwise to the mixture of ligands. The mixtures were refluxed with stirring for 48 and 72 hours for Ni(II) and Co(II) chelates, respectively. Meanwhile, the other reaction mixtures were refluxed and mixed for 24 hours. The precipitates were filtered, washed several times with THF, water, and diethyl ether. Finally, they were dried under a vacuum desiccator.

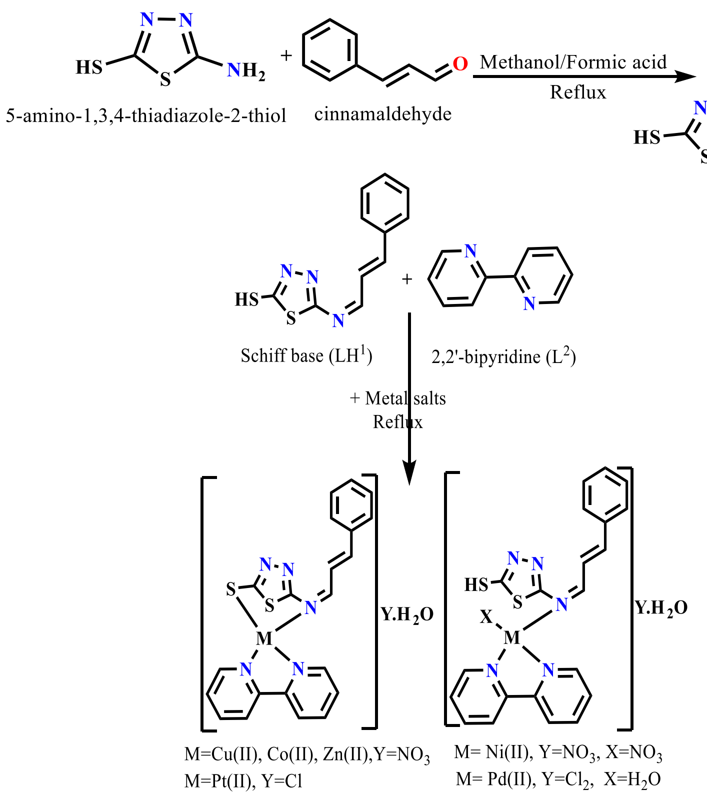


Figure-1: Schematic Synthesis of Schiff Base and Divalent Mixed-Ligand Complexes

C. Biological activity

The biological screening of the newly prepared Schiff base, its mixed-ligand chelates, and standard antibiotic were examined in vitro against *E. coli* (Gram-negative) and *S. aureus* (Gram-positive) by the agar well diffusion method using Muller Hinton agar medium [15]. A bacteria-old culture was swabbed uniformly on the agar plate surface. The labeled wells were made in the medium agar plates filled with 40 µL the test solutions were prepared by dissolving 20mg/ml in DMSO. The DMSO and Gentamicin were used as a control of the solvent and standard compound respectively for comparison and incubated the plate for 24 hours at 37^{0}C. After the incubation time, the biological activity of each sample was determined by measuring the diameter inhibition zone around each well in terms of mm by comparing it with the standard drug.

Results and Discussion

The reactions of prepared Schiff base ligand and 2,2′-bipy with transition metal salts (Cu(II), Ni(II), Co(II), Zn(II), Pt(II), and Pd(II)) gave a colored complex in moderate yields (32–79%) that are presented in Table 1 with other physical and analytical data such as melting/decomposition temperature and conductance. The elemental (C, H, N, S) analyses results are in good agreement with the proposed chemical composition of the compounds. Also, the elemental analysis indicated the coordination of the ligands (Schiff base and 2,2′-bipy) to metal ions in a 1:1:1 molar ratio. The measurements of molar conductance obtained in 10^{-3} M DMSO for the prepared divalent mixed-ligand complexes were in the range 31.22–85.5 $\Omega^{-1}cm^2mol^{-1}$. These values confirmed an ionic nature since values above 23 $\Omega^{-1}cm^2mol^{-1}$ and 80 Ω^{-1} cm^2mol^{-1} were usually expected for 1:1 and 1:2 electrolytes respectively ***[16]***.

Table-1: Physical and Chemical Properties of the Ligands and their Mixed-Ligand Metal Complexes

Compounds	Appearance	M.Wt	%Yield	M.p/dec. Temp.(°C)	% Found (Calculated)				Λm (Ω^{-1} $.cm^2.mol^{-1}$)
					C	H	N	S	
LH^1	Light Yellow	247.34	86	196-198	54.03 (53.42)	3.20 (3.67)	15.08 (16.99)	25.57 (25.93)	11.7
L^2	White	156.18	-	70-72					–
$[Cu(L^1)(L^2)]NO_3.H_2O$	Pale Green	546.08	72	340-342	45.16 (46.19)	3.57 (3.32)	14 (15.39)	11.72 (11.74)	50.49
$[Ni(LH^1)(L^2)(NO_3)]NO_3.H_2O$	Green Olive	604.24	41	246-248	42 (41.74)	2.93 (3.17)	16.14 (16.23)	9.07 (10.61)	39.39
$[Co(L^1)(L^2)]NO_3.H_2O$	Deep Brown	541.47	32	232-234	44.64 (46.58)	2.93 (3.35)	13.43 (15.52)	13.82 (11.84)	31.22
$[Pt(L^1)(L^2)]Cl.H_2O$	Yellow	651.06	56	~314^d	37.54 (38.74)	2.67 (2.79)	10.86 (10.76)	8.99 (9.85)	41.73
$[Zn(L^1)(L^2)]NO_3.H_2O$	White	547.91	65	>360	45.69 (46.03)	3.37 (3.31)	14.38 (15.34)	10.08 (11.70)	51.3
$[Pd(LH^1)(L^2)H_2O]Cl_2.H_2O$	Pale Orange	616.87	79	~248^d	39.21 (40.89)	2.58 (3.43)	11.03 (11.35)	10.34 (10.39)	85.5

(M.P) melting point, (dec.Temp.) decomposition temperature, (LH^1) Schiff base, (L^1) deprotonated LH^1

A. Magnetic Susceptibility Measurements

The measurement of magnetic susceptibility is important to identify the numbers of unpaired electrons and to determine their geometric structures, which are shown in Table 2. The Ni(II) complexes magnetic susceptibility were generally given values less than zero in the square planar environment due to their diamagnetic nature. While the tetrahedral nickel complexes are usually paramagnetic with moments in the range 3.20–4.20 B.M. and octahedral complexes should have moments between 2.80–3.30 B.M. ***[17]***. In our study, the magnetic moment of $3d^8$ Ni(II) complex was 3.61 B.M. and hence assigned a four coordinate tetrahedral geometry ***[18]***.

The magnetic momentum measurement indicates that high spin Co(II) complexes are (4.2-4.6 B.M.) with three unpaired electrons which suggest a tetrahedral environment around the Cobalt ion. However, octahedral high spin Co (II) complexes by (4.8-5.2 B.M.) are the most common ***[19]***. The effective magnetic moment in the range 1.73–2.73 B.M. are often expected to have a low spin Square planner, dsp^2 cobalt complexes. The study of divalent heteroleptic cobalt complex has a magnetic at 1.83 B.M. since it is expected for square planner rearrangement ***[20]***.

Moment values for mononuclear Cu(II) complexes regardless of geometry are expected to exhibit 1.9–2.2 B.M. The value of magnetic susceptibility of the synthesis Copper complex is 2.20 B.M. which suggests tetrahedral geometry around the metal ions. The magnetic moment is expectedly higher than the spin-only moment 1.73 B.M.; for the unpaired electron due to spin-orbit coupling and orbital contributions. However, this can be attributed to electronic spectra measurements ***[13]***.

The displayed magnetic moments of Zn(II), Pd(II), and Pt(II) complexes are expected for zero unpaired electrons. The synthesized Zn(II), Pd(II), and Pt(II) complex exhibited a magnetic moment value of 0.25, 0.35, 0 B.M. respectively which was supportive of its diamagnetism nature ***[21]***.

B. Electronic Spectra Measurements

The results of electronic transitions are often used to complement the data obtained from other physical measurements for easier structural investigations. The bands of absorption spectra and their assignments are collected in Table 2. The ultraviolet spectrum of the free Schiff base gave absorption peaks at 250 nm,313nm and 410 nm, which were consistent to $\pi\rightarrow\pi^*$ transition of the aromatic and thiadiazole ring and $n\rightarrow\pi^*$ electronic transitions of the azomethine and thiadiazole ring. During the formation of all heteroleptic divalent complexes, the band at 250 nm are not affected by metal complexation, because they are remaining in the same position while other peaks were found to be shifted to a lower wavelength, suggesting that the nitrogen atom of the azomethine group is coordinated to the metal ions ***[22]***. However, the absorption peak at 285 nm in the free 2,2′-bipyridine ligand shifted to higher wavenumber in the spectra of all complexes, due to the π-π^* transitions of coordinated 2,2′-bipy ligand to metallic ions center via two nitrogen atoms ***[23]***.

In the electronic spectrum of the copper(II) complex the bands at 249 nm, 301 nm, and 309 nm were observed. These are assigned to the intra-ligand and ligand to metal charge transitions respectively. These observations suggest that the mixed-ligand complex has a tetrahedral structure. Tetrahedral Cu(II) complexes usually have a single absorption band below 1000 nm which is attributed to $^2T_2 \rightarrow {}^2E$ transition, which was not seen as it tailed into the infrared section [24] [25]. The nickel(II) complex exhibited three bands in the regions 250 nm, 295 nm, and 306 nm due to $\pi\rightarrow\pi*$ and $n\rightarrow\pi*$ transitions respectively. The visible regions of the studied Ni(II) mixed-ligand complex showed bands at 414 and 788 nm which were consistent with $^3T_1(F)\rightarrow{}^3T_1(P)$ and $^3T_1(F)\rightarrow{}^3A_2$ transitions respectively in four coordinate tetrahedral environments ***[18]***.

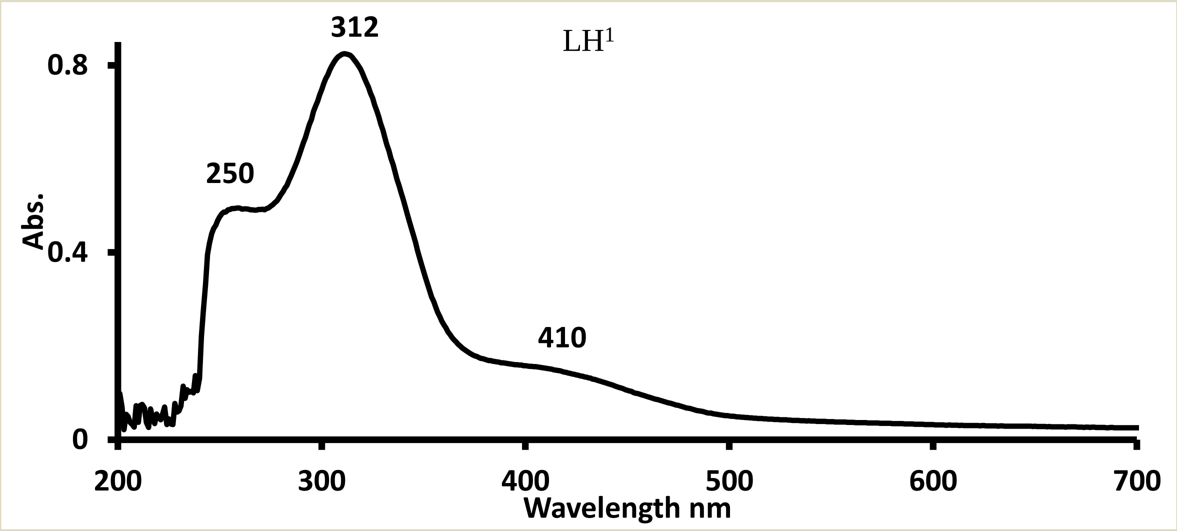
The ultraviolet spectrum of the Co(II) complex displayed three absorptions around 248 nm, 299 nm, and 304 nm assigned to $n\rightarrow\pi^*$ and $\pi\rightarrow\pi^*$ transitions respectively. In the visible/near-infrared spectrum of the low spin heteroleptic Co(II) chelates studied, three absorption bands at 507 nm, 642 nm, and 800 nm were observed. The observed absorption bands were typical to $^2A_1g \rightarrow {}^2Eg$ and $^2A_1g \rightarrow {}^2B_1g$ transitions, respectively, in d^7 low spin square geometry ***[26][27]***. Zn(II) complex regularly does not have any d-d transition band in the visible spectrum due to the filled 3d–orbital. The intra-ligand and charge transfer bands observed in the UV spectrum at 246 nm, 295 nm, and 306 nm region are due to $\pi\rightarrow\pi^*$, $n\rightarrow\pi^*$ charge transfer transitions, which are compatible with a tetrahedral structure ***[21] [25]***.

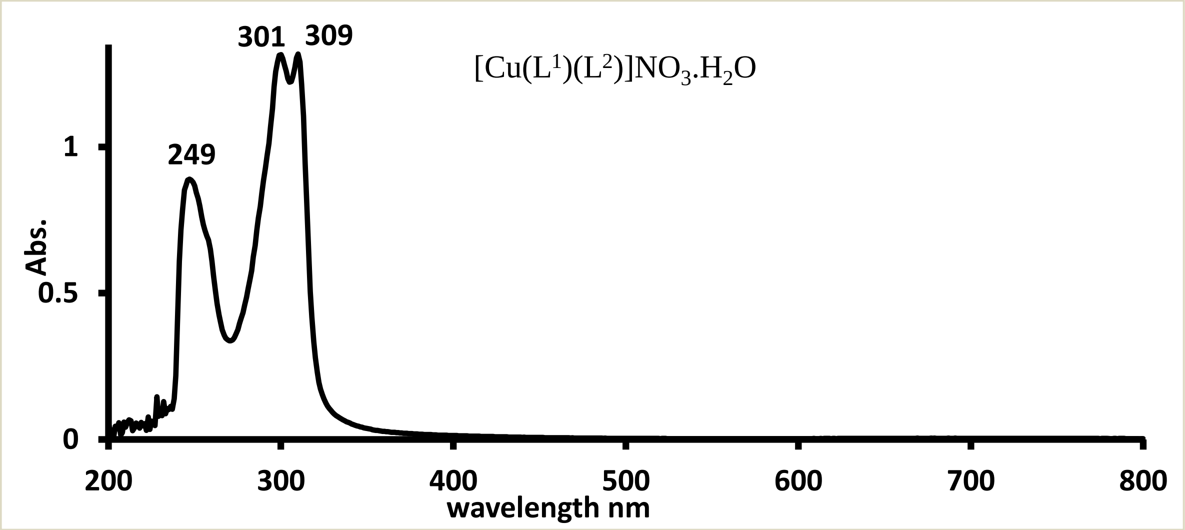
Electronic spectra of the divalent heteroleptic Platinum and Palladium chelates, show two bands in the range of 250-247 nm and 305 nm. The higher-energy band is an internal $\pi\rightarrow\pi^*$ transition of the ligand, while the lower is assigned as a Pt, Pd $\rightarrow\pi^*$ charge transfer ***[28]***. The noticeable strong bands in the range 300- 400 nm are assigned to a combination of intra-ligand and LMCT absorptions and d–d bands. This supports the idea of a square-planar environment for metal ions ***[29]***.

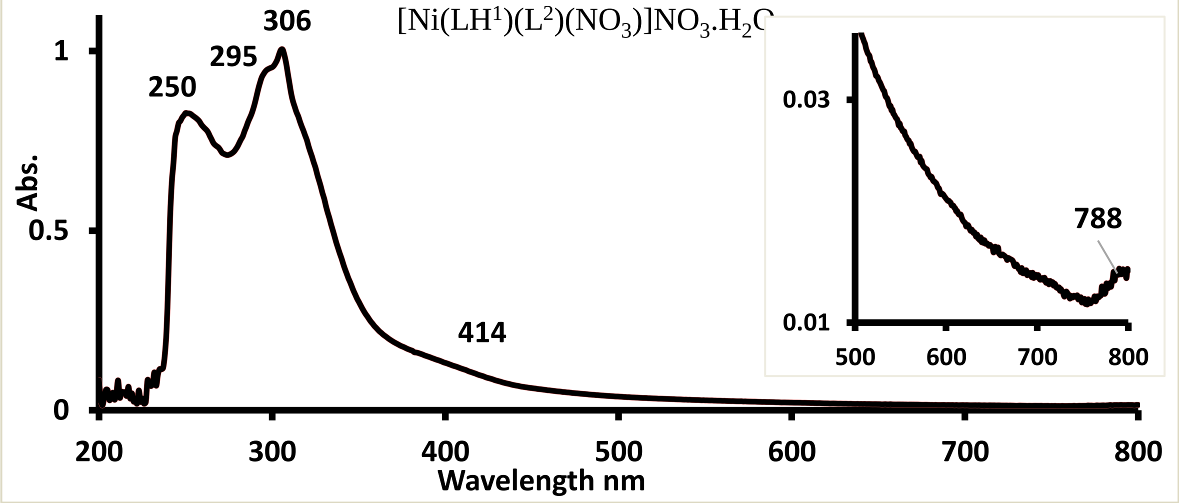
Table-2: The Magnetic Susceptibility and UV-Vis Spectral Data for the Ligands and their Mixed-Ligand Metal Complexes

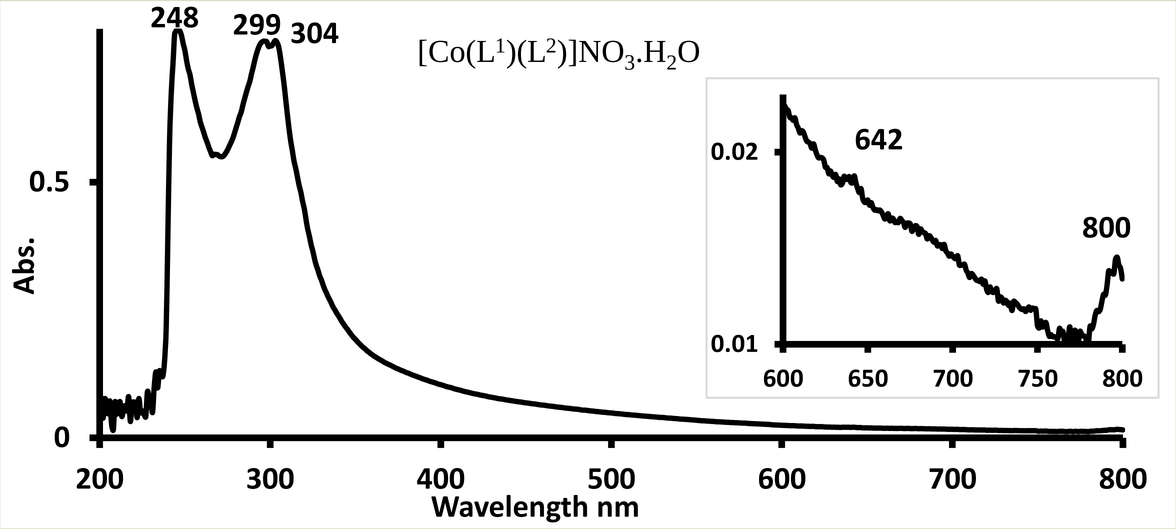
Compounds	***Absorption Bands***		***Assignment***	***μeff (B.M)***
	nm	***ε***		
LH^1	*250*	*4200*	$\pi\rightarrow\pi^*$	-
	313	*7175*	$n\rightarrow\pi^*$	
	410	*1313*	$n\rightarrow\pi^*$	
L^2	*285*	*2023*	$\pi\rightarrow\pi^*$	-
$[Cu(L^1)(L^2)]NO_3.H_2O$	*249*	*15400*	*C.T*	*2.20* *T.h*
	301	*22785*	*C.T*	
	309	*22820*	*C.T*	
$[Ni(LH^1)(L^2)(NO_3)]NO_3.H_2O$	*250*	*14525*	*C.T*	*3.61* *T.h*
	295	*16450*	*C.T*	
	306	*17325*	*C.T*	
	414	*1925*	$^3T_1(F)\rightarrow{}^3T_1(P)$	
	788	*245*	$^3T_1(F)\rightarrow{}^3A_2$	
$[Co(L^1)(L^2)]NO_3.H_2O$	*248*	*13825*	*C.T*	*1.83* *Sq.pl*
	299	*13475*	*C.T*	
	304	*13475*	*C.T*	
	507	*805*	$^2A_1g\rightarrow{}^2E_g$	
	642	*368*	$^2A_1g\rightarrow{}^2B_{1g}$	
$[Pt(L^1)(L^2)]Cl.H_2O$	*250*	*14525*	*C.T*	*Dia* *Sq.pl*
	305	*12425*	$Pt\rightarrow\pi^*$	
$[Zn(L^1)(L^2)]NO_3.H_2O$	*246*	*14350*	*C.T*	*Dia* *T.h*
	295	*22400*	*C.T*	
	306	*20300*	*C.T*	
$[Pd(LH^1)(L^2)H_2O]Cl_2.H_2O$	*247*	*14000*	*C.T*	*Dia* *Sq.pl*
	305	*12425*	$Pd\rightarrow\pi^*$	

Dia: diamagnetic, Sq.pl: Squier planaer, T.h: Tetrahedral, ε: molar absorptivity

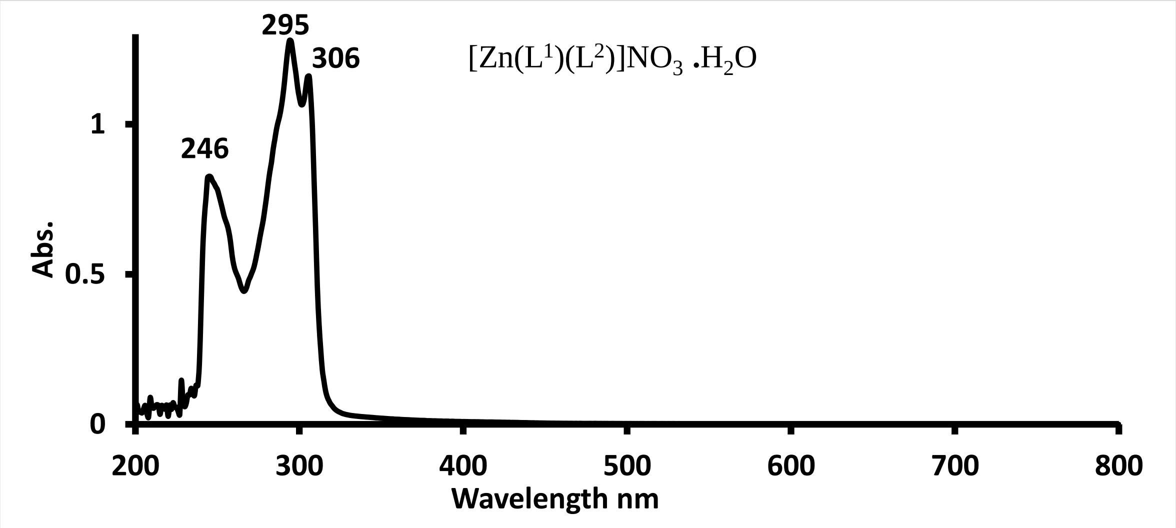

LH^1
312
250
410
Abs.
0.8
0.4
0
200
300
400
500
600
700
Wavelength nm


[Cu(L^1)(L^2)]NO$_3$.H$_2$O
301
309
249
Abs.
1
0.5
0
200
300
400
500
600
700
800
wavelength nm

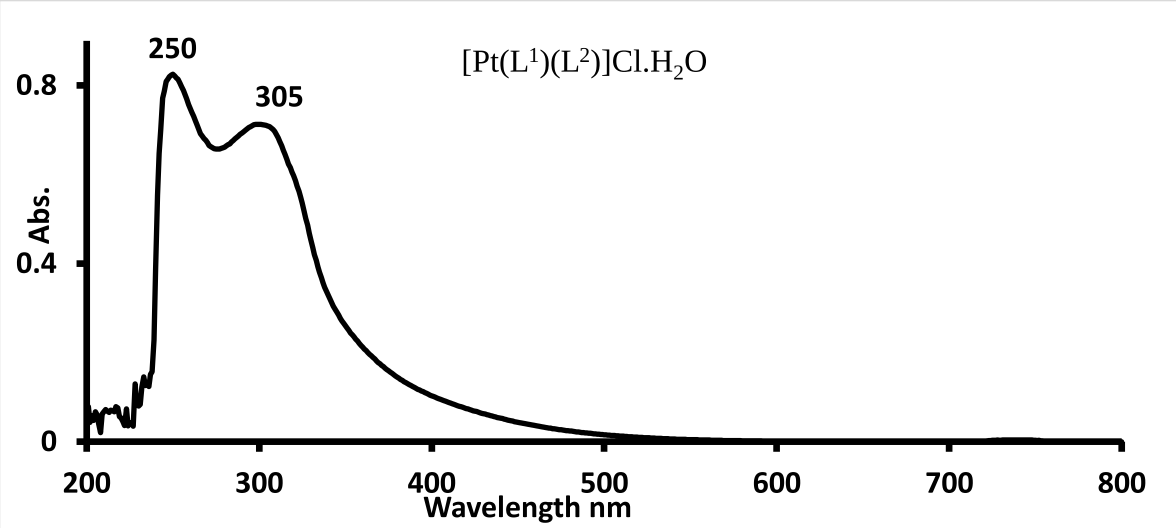

[Ni(LH^1)(L^2)(NO$_3$)]NO$_3$.H$_2$O
306
295
250
414
Abs.
1
0.5
0
200
300
400
500
600
700
800
Wavelength nm
0.03
0.01
788
500
600
700
800



248
299
304
$[Co(L^1)(L^2)]NO_3.H_2O$
0.5
0
Abs.
200
300
400
500
600
700
800
Wavelength nm
0.02
0.01
642
800
600
650
700
750
800



295
306
246
$[Zn(L^1)(L^2)]NO_3 .H_2O$
1
0.5
0
Abs.
200
300
400
500
600
700
800
Wavelength nm



250
305
$[Pt(L^1)(L^2)]Cl.H_2O$
0.8
0.4
0
Abs.
200
300
400
500
600
700
800
Wavelength nm

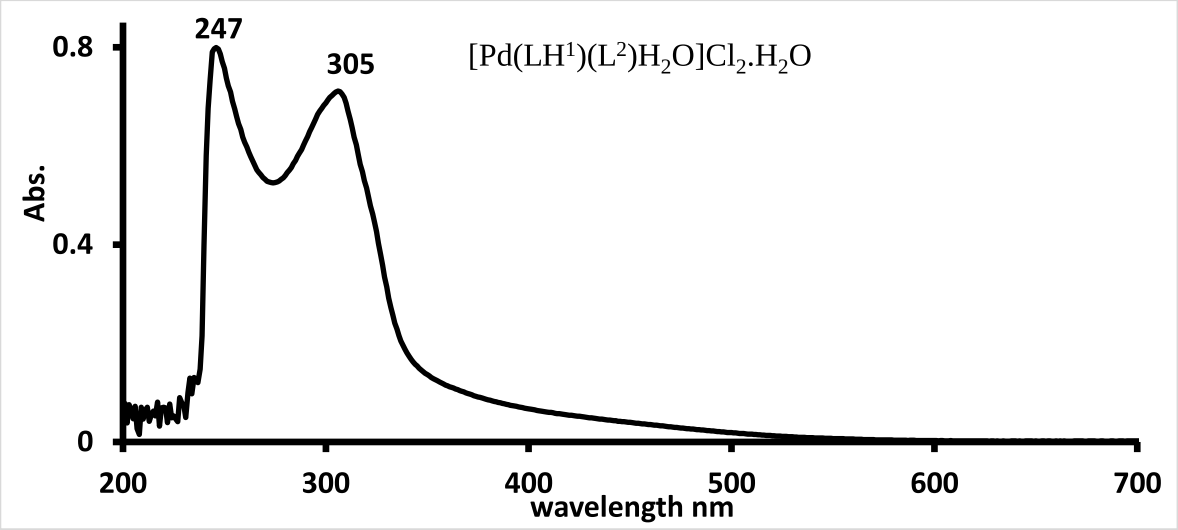


Figure-2: UV-Vis. Spectrum of Schiff Base Ligand and Mixed-Ligand Complexes

C. IR Spectral Studies

The important IR bands of ligands and their mixed-ligand complexes along with their assignments are given in Table 3. The infrared spectrum of Schiff base did not show any band at 2570 cm^{-1} for (-SH) group, while the presence of a broad stretching band at 3423 cm^{-1} for (NH) indicates that in the solid-state, it existed in the thione form and the sharp absorption band for C-S group was formed around 754 cm^{-1} ***[30]***. As well as the formation of Schiff base ligand as indicated by the presence of the high-intensity aliphatic azomethine (CH=N) stretching band at 1560 cm^{-1} which is not present in precursor reactants according to their IR spectra (Figure 10). This was combined with the disappearance of the NH_2 stretching band at (3343 cm^{-1} and 3250 cm^{-1}) which appeared in the IR spectrum of 5-amino-1,3,4-thiadiazole-2-thiol ***[31]***. In addition, another evidence about the correct structure of the Schiff base ligand was obtained through detection of bands at (3057 cm^{-1} and 2854 cm^{-1}) which are characteristics for C-H stretching of aromatic and aliphatic, respectively ***[32]***, and observed a band at 668 cm^{-1} for -CH = CH- stretching. The result can prove that cinnamaldehyde was connected with 5-amino-1,3,4-thiadiazole-2-thiol ***[33]***.

The IR spectra of the complexes are compared with those of the free ligands to determine the coordination groups involved in the complexation. Both Spectra of Schiff ligand and their complexes exhibited an absence of band at 1678 cm^{-1} due to carbonyl (C=O) stretching band ***[34]***. The bands at 1560 of C=N of azomethine group in the spectra of all mixed-ligand complexes shifted to lower/higher frequency while endocyclic C=N remained in the same region 1605 cm^{-1} without significant changes. This suggested that the coordination took place through nitrogen atoms of the azomethine group ***[35]***. The coordination via thiolate Sulphur after deprotonation was shown by the disappearance of any ν(SH) or ν(NH) vibrations and the appearance of a band due to ν(C–S) at lower wavenumbers (719-736 cm^{-1}) in mixed-ligand complexes as compared to the Schiff base ligand at 754 cm^{-1}. But in the spectrum of nickel and palladium complexes, small broadband was observed at 2427 and 2376 cm^{-1} respectively due to the thiol (SH) group which indicated that the sulfur did not participate in the chelation ***[36]***.

The characteristics of absorption bands of the free 2,2′-bipyridine L^2 ligand appear due to ν(C=N) at 1579 cm^{-1}, and δ(C-H) at (993 cm^{-1},757 cm^{-1}). The band of C=N in the 2,2′-bipyridine shifted to lower/higher frequencies and in same prepared metal complexes overlapped with the band of C=N of the azomethine group and the bending C-H deformation bands shifted to higher frequencies (1024-1038 cm^{-1}) and (765-771 cm^{-1}). This suggested that the donor nitrogens hetero atom of bipyridine are coordinated to the metal ion ***[37]***.

Broadband in the infrared spectra of all metal complexes at (3455-3389 cm^{-1}) suggests the presence of lattice or coordinated water molecules which is confirmed by TG analysis ***[30]***. Furthermore, in the spectra of mixed-ligand complexes, the new weak bands appear in the range (410-420 cm^{-1}) and (451-478 cm^{-1}) referred to as the ν(M-S) and ν(M-N) respectively ***[38] [29]***. This indicates that the ligands were coordinated with the metal ions through nitrogen and sulfur of the thiol group. While in the complexes of Ni(II) and Pd(II) new bands at (534 cm^{-1}) attributed to the ν(M-O cm^{-1}) were observed instant ν(M-S) ***[13]***. The IR spectra of Cu(II), Ni(II), Co(II), and Zn(II) complexes showed strong absorption bands at 1384-1385 cm^{-1} can be assigned to ν(NO) of the NO_3^- groups ***[32]***.

Table-3: Selected IR Spectral Bands for the Ligands and their Mixed-Ligand Metal Complexes

Compounds	***OH*** $_{(H_2O)}$	***ν(SH)*** ***ν(NH)***	***C=N of thiadiazole ring***	***C=N of bipy ring***	***C=N of imine***	***C-S***	***δ(C-H) bipy***	***M-N***	***M-S***	***M-O***
LH^1	-	3423	1605	-	1560	754	-	-	-	-
L^2	-	-	-	1579	-	-	993-757	-	-	-
$[Cu(L^1)(L^2)]NO_3.H_2O$	3450	-	1604	1575	1567	732	1036-771	474	416	-
$[Ni(LH^1)(L^2)(NO_3)]NO_3.H_2O$	3400	2427	1604	1567	1525	736	1024-767	478	-	534
$[Co(L^1)(L^2)]NO_3.H_2O$	3431	-	1606	1573	1525	727	1032-768	467	420	-
$[Pt(L^1)(L^2)]Cl.H_2O$	3389	-	1606	*Overlap with C=N of azomethine group*	1530	720	1028-766	452	419	-
$[Pd(LH^1)(L^2) H_2O]Cl_2.H_2O$	3422	2376	1604		1567	719	1038-765	451	-	534
$[Zn(L^1)(L^2)]NO_3.H_2O$	3455	-	1608	1599	1567	732	1030-765	461	412	-

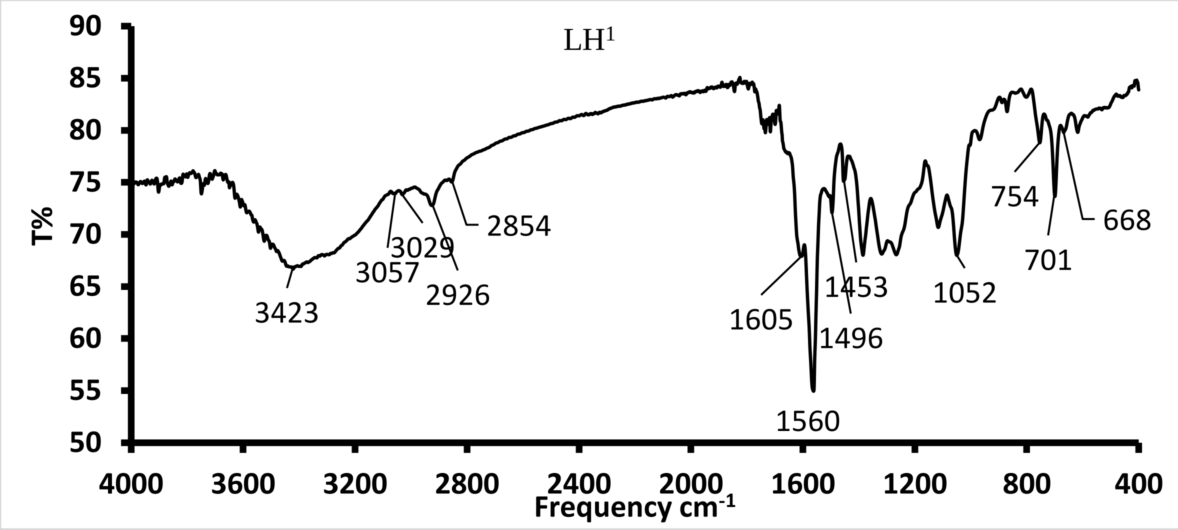


Figure-3: FTIR Spectrum of Schiff Base LH^1

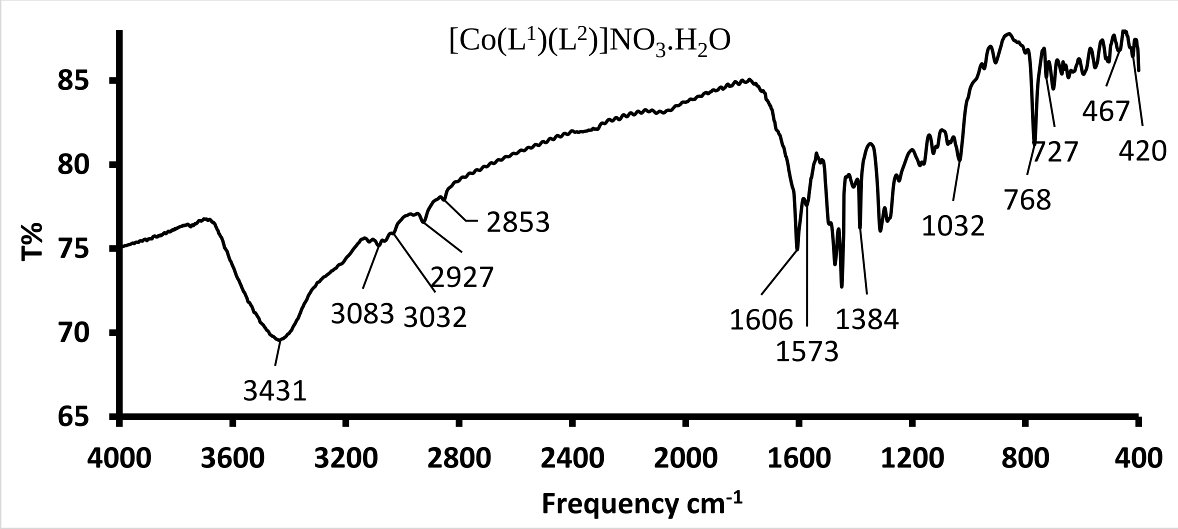


Figure-4: FTIR Spectrum of Co(II)-Complex

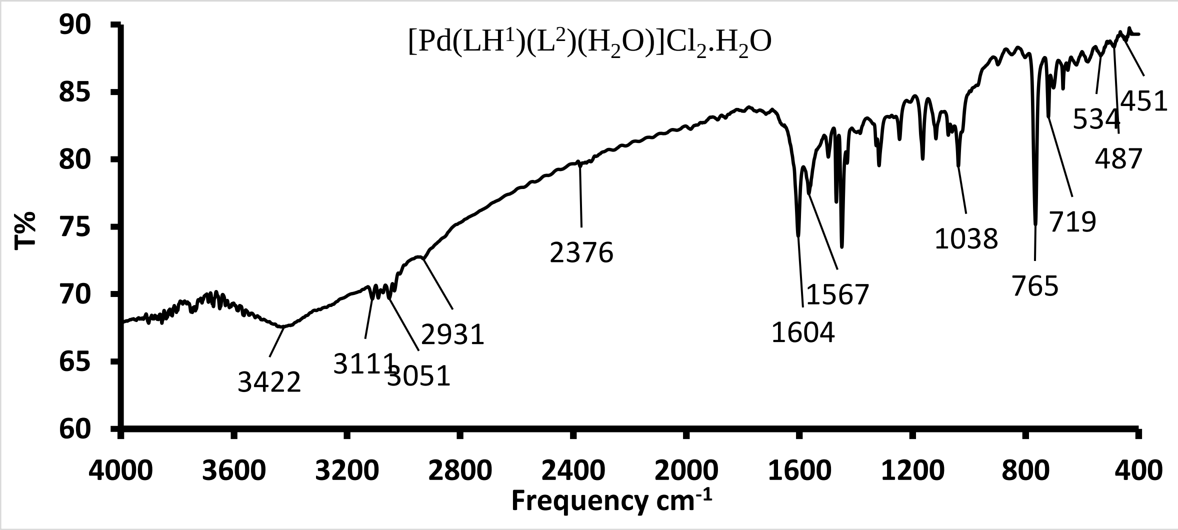


Figure-5: FTIR Spectrum of Pd(II)-Complex

D. ^{1}H-NMR Spectra

The chemical shifts of the different positions of protons in the ^{1}H-NMR spectra are used to elucidate the structure of the Schiff base and its diamagnetic Pt(II), Zn(II), and Pd(II) heteroleptic complexes are listed in Table 4. The ^{1}H-NMR spectra of the Schiff base LH^1 show the resonance at 8.5 ppm which is due to the azomethine (-CH=N-) proton. The thione and thiol forms of the Schiff base exist as a mixture of both isomers in solution. A singlet corresponding to one proton (-NH) of thione form was observed at 9.7 ppm, the (S-H) thiol proton appeared as a singlet at 13.2 ppm in the spectrum. The ligand also reveals multiples signals in the range 7.2–8.2 ppm which is attributed to aromatic protons ***[31]***. Moreover, the C-H proton at position 2 is observed as a doublet and doublet at 6.9 ppm, as it is coupling to both the aldehyde proton and the other alkene proton at position 3. The C-H proton at position 3 should resonate as a doublet as, but it is signal is overlapping with the signal of the aromatic proton ***[39]***. These indicating the formation of a ligand.

On complexation, the azomethine position signal is shifted to a higher region of 9.48ppm, 8.9 ppm, and 9.1ppm, for Pt(II), Zn(II), and Pd(II) complexes, respectively. This is indicated the complexation occurs through azomethine nitrogen atom comparison with the free ligand. The signal that appeared at 13.2 ppm in Schiff base was not observed in the spectra of Pt(II) and Zn(II) complexes, further supporting the chelation through the S atom of the thiol group, while in the spectrum of Pd(II) complex this group does not contribute in chelation due to remain the signal at 13.18 ppm ***[40]***. Also, the protons of pyridine and aromatic ring are displaced multiples around the region 7.2-8.6 ppm, which indicates the involvement of nitrogen of the bipyridine ring in the coordination ***[41]***. It was found the chemical shifts at position 7 resonate as a doublet at 8.6 ppm and proton position 10 at 8.4 ppm. In addition, the overlap of C-H proton at positions 8 and 9 with the signal at locations 4, 5, and 6 of the aromatic ring at 7.2-7.8 ppm ***[42] [43]***.

Table 4: Major ^{1}H.NMR Spectral Data for the Ligand and its Mixed-Ligand Metal Complexes

Hydrogen	***Chemical Shifts (ppm)***			
	LH^1	$[Pt(L^1)(L^2)]Cl.H_2O$	$[Zn(L^1)(L^2)]NO_3.H_2O$	$[Pd(LH^1)(L^2)(H_2O)]Cl_2.H_2O$
H-2	*6.9 dd, 1H*	*6.9 dd, 1H*	-	*6.9 dd, 1H*
H-8, H-9, H-4, H-5, H-6	*7.2-8.2 m, 5H H4, H5, H6*	*7.3-7.8 m, 9H*	*7.2-7.8 m, 9H*	*7.2-7.8 m, 9H*
H-3	*d, 1H, overlapped with signal pyridine & aromatic protons*			
H-7	-	*8.6 d, 2H*	*8.6 d, 2H*	*8.6 d, 2H*
H-10	-	*8.48 t, 2H*	*8.24 t, 2H*	*8.37 t, 2H*
H-1(CH=N)	*8.5 d, 1H*	*9.49 d, 1H*	*8.86 d, 1H*	*9.1 d, 1H*
N-H thione form	*9.7 s, 1H*	-	-	*9.7 s, 1H*
S-H thiol form	*13.2 s, 1H*	-	-	*13.18 s, 1H*

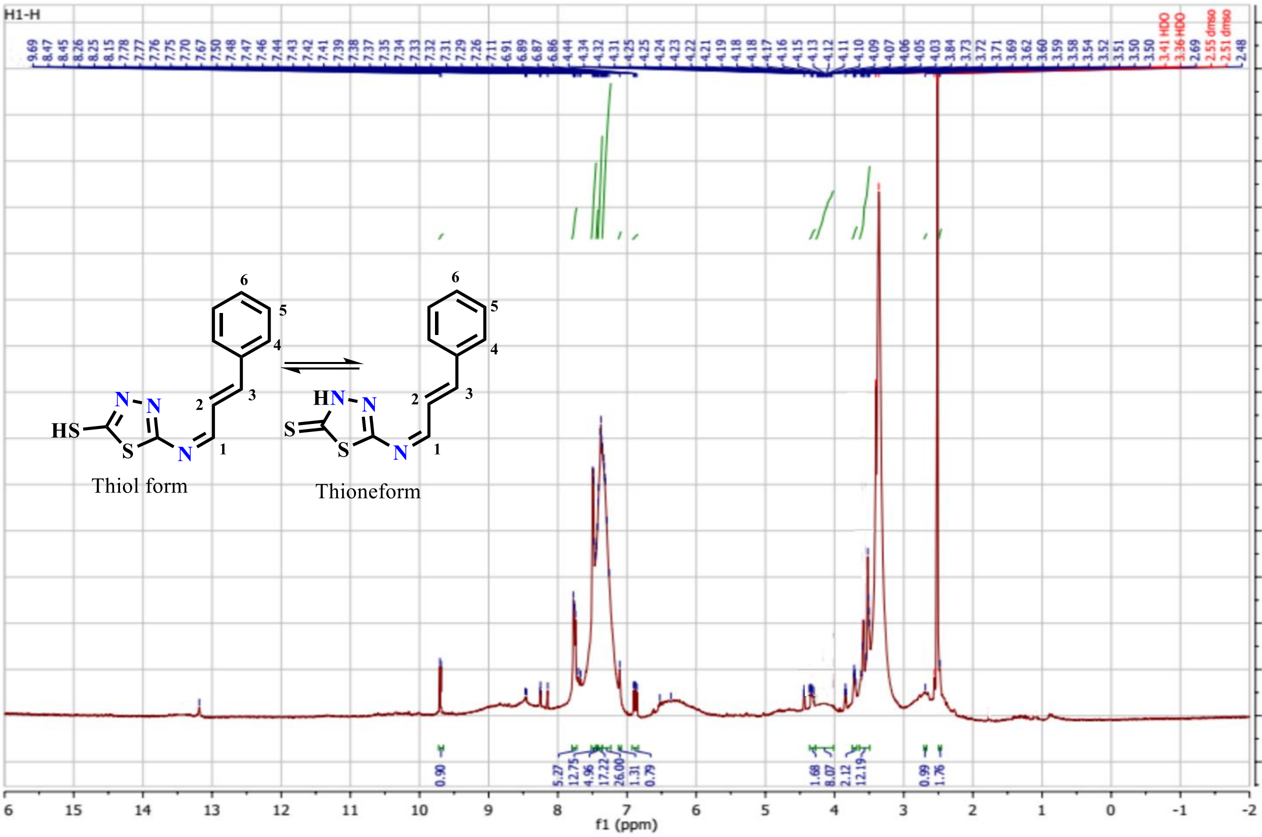


Figure-6: ^{1}H-NMR Spectrum of Schiff Base Ligand

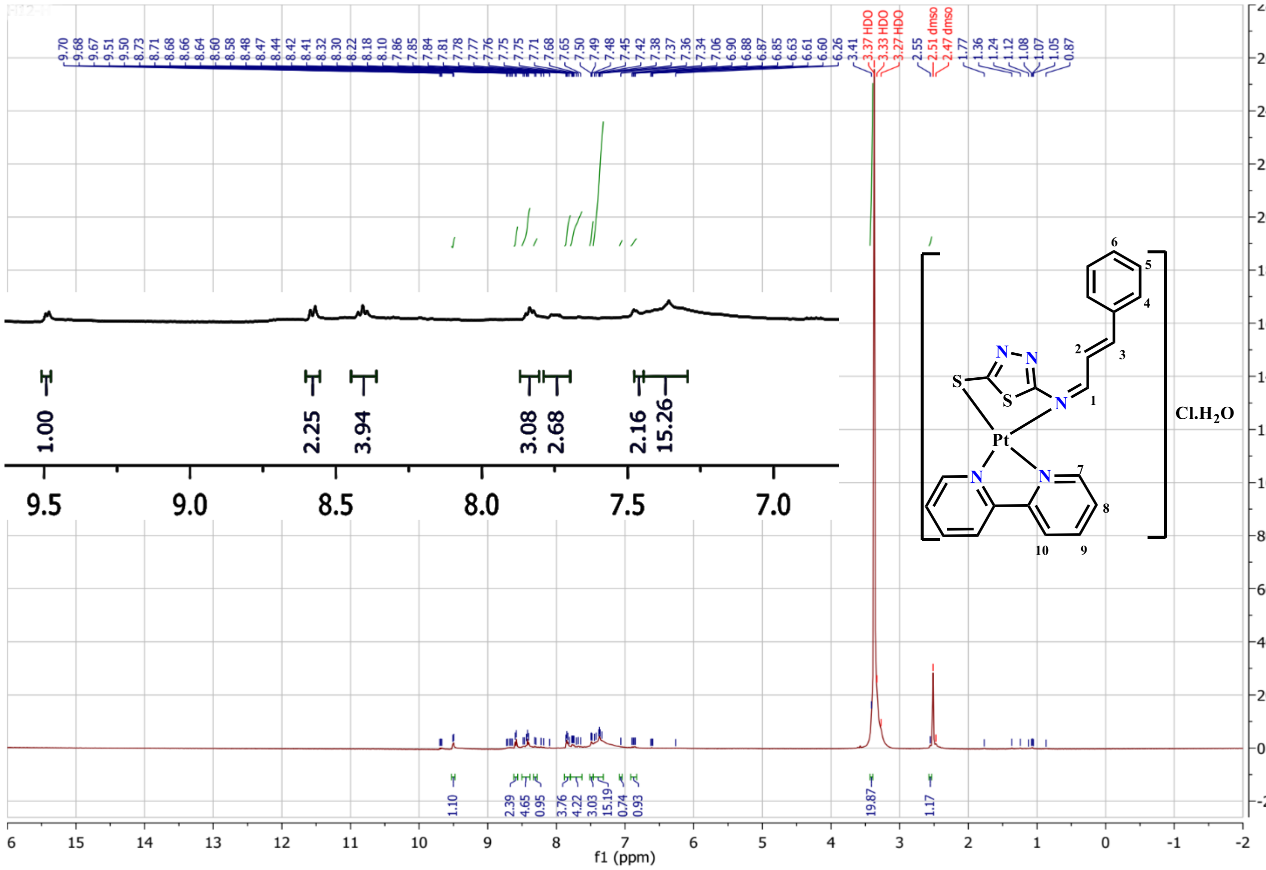
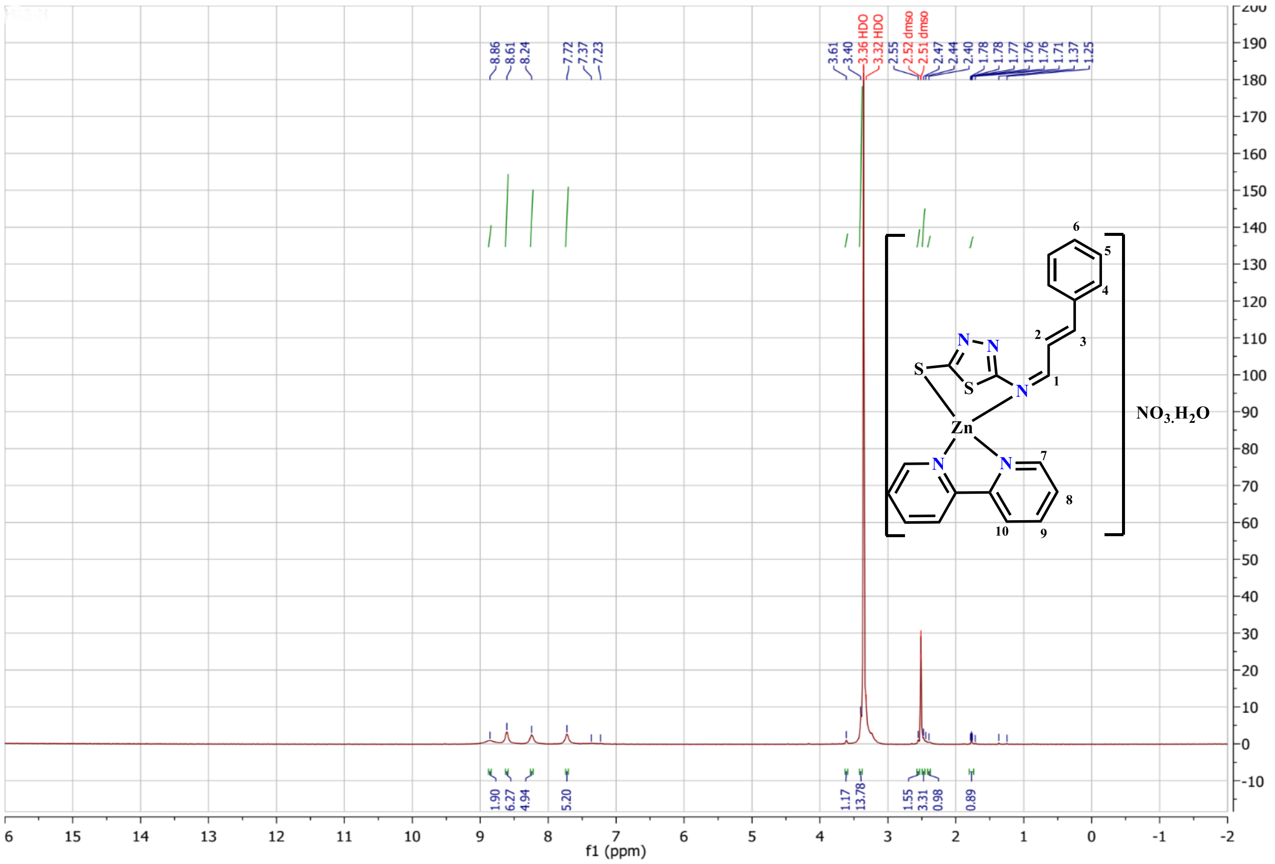


Figure-7: ^{1}H-NMR Spectrum of Pt(II)-Complex



H-NMR Spectrum of Zn(II)-Complex

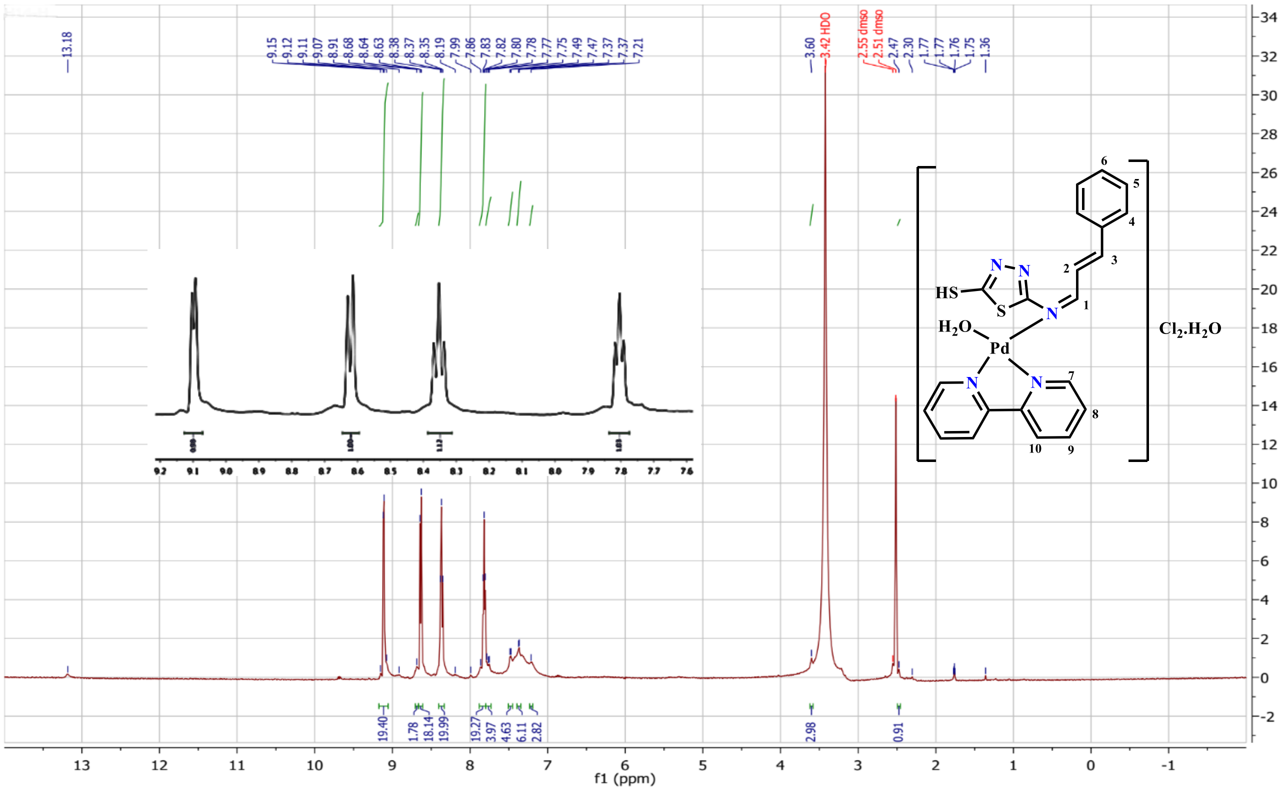


Figure-9: ^{1}H-NMR Spectrum of Pd(II)-Complex

E. Mass spectroscopy

The mass spectrum of Schiff base ligand displayed three main pathways of fragmentation with the parent molecular ion at m/z, 247, which is parallel with the proposed molecular weight (247.34) of the new synthesized ligand $C_{11}H_9N_3S_2$. This supports the condensation of 5-amino-1,3,4-thiadiazole-2-thiol and the cinnamaldehyde to produce the L^1 ligand. The further peaks that appeared in the mass spectrum are related to the fragmentation of ligand molecules obtained from the break of different bonds inside the Schiff base molecule**.** The ions peak at m/z 246 and 130 corresponding to the ions $[C_{11}H_8N_3S_2]^+$ and $[C_9H_8N]^+$ respectively, these showed the fragmentation none-bonding electrons of a thiol and imine group in the Schiff base. In addition, some molecular ions were detected in the Mass spectrum of Schiff base ligand like (m/z, 51, 65, 77), characteristic to ions $[C_6H_5]^+$, $[C_5H_5]^+$and $[C_4H_3]^+$ though the metastable ion peak at m/z (77 → 51) for the fragmentation of the aromatic nucleus. Besides, fragments at m/z, 144, and 170 molecular weight-matched to ions $[C_3H_2N_3S_2]^+$ and $[C_5H_4N_3S_2]^+$ moieties that display the fragmentation of conjugated double bond. Furthermore, the spectrum exhibited an M+1 peak at m/z, 248. Besides, a low-intensity peak was observed at m/z, 249 which could be attributed to extra mass units, a consequence of isotope carbon-13 presence [19]. Figure 10 and Figure 11 show the mass spectrum and the fragmentation pattern of 5-((Z)-((E)-3-phenylallylidene)amino)-1,3,4-thiadiazole-2-thiol respectively.

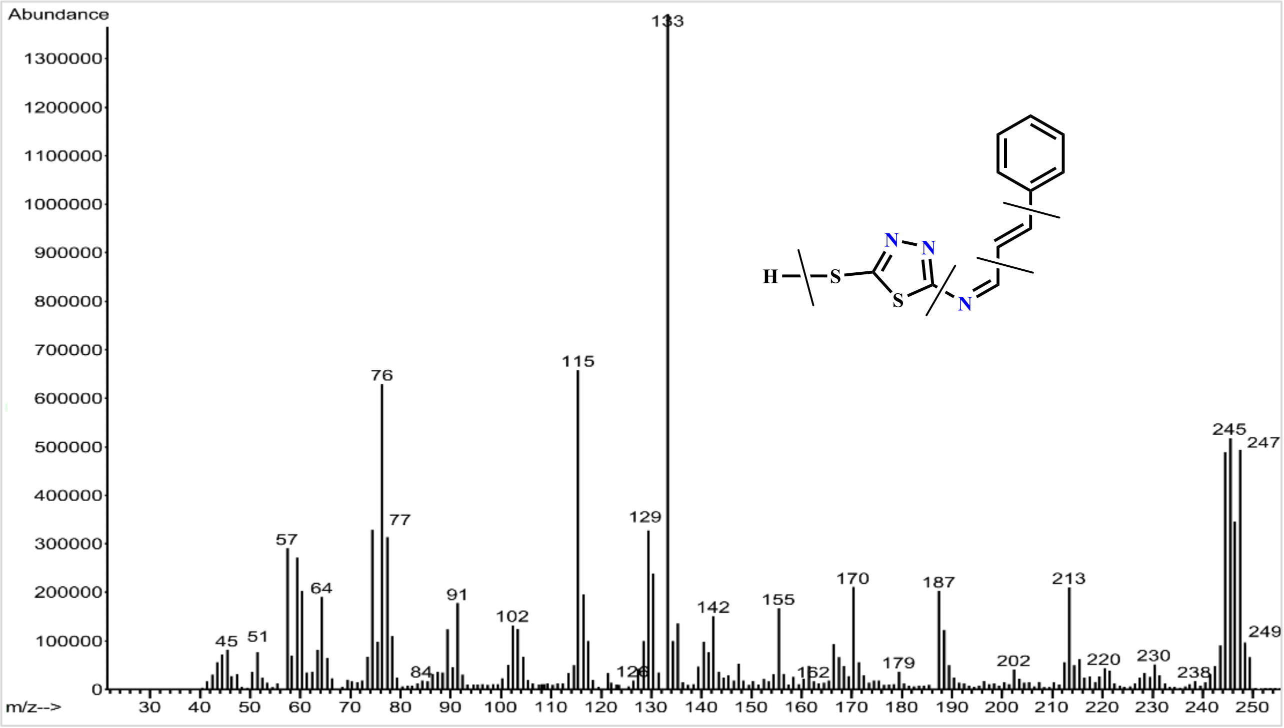


Figure-10: Mass Spectrum of Schiff Base Ligand

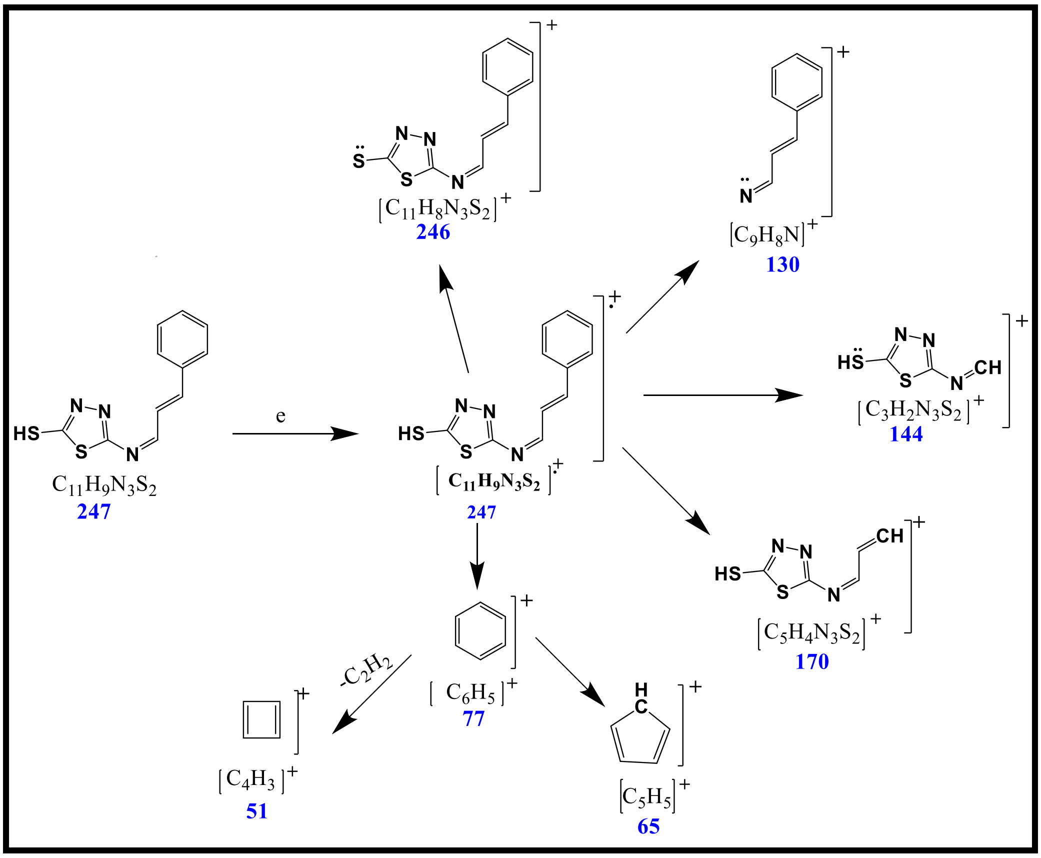


Figure-11: Schematic of the Fragmentation Pattern of Schiff Base Ligand.

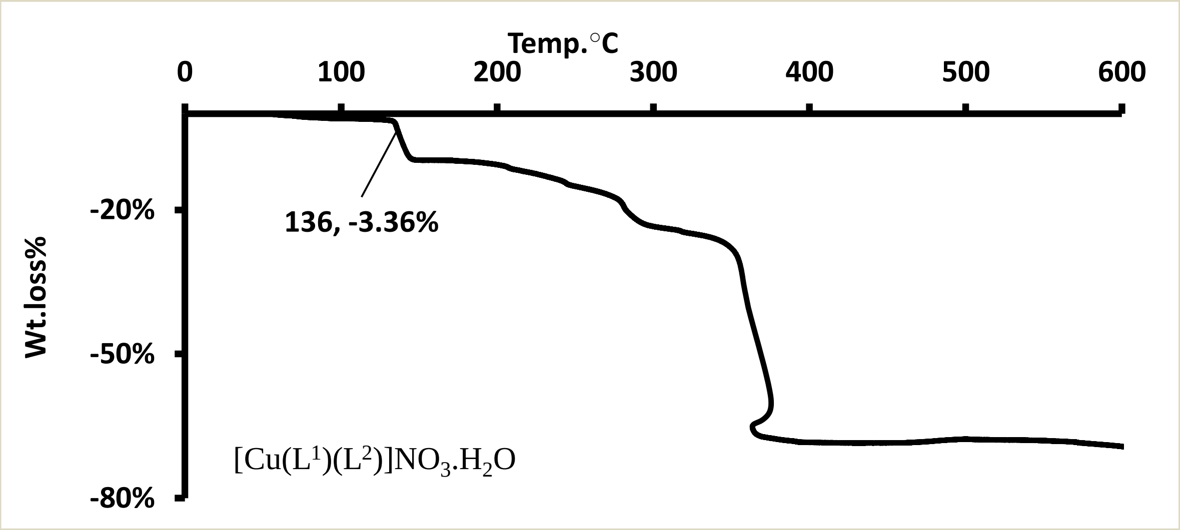
F. Thermal Gravimetric Analysis

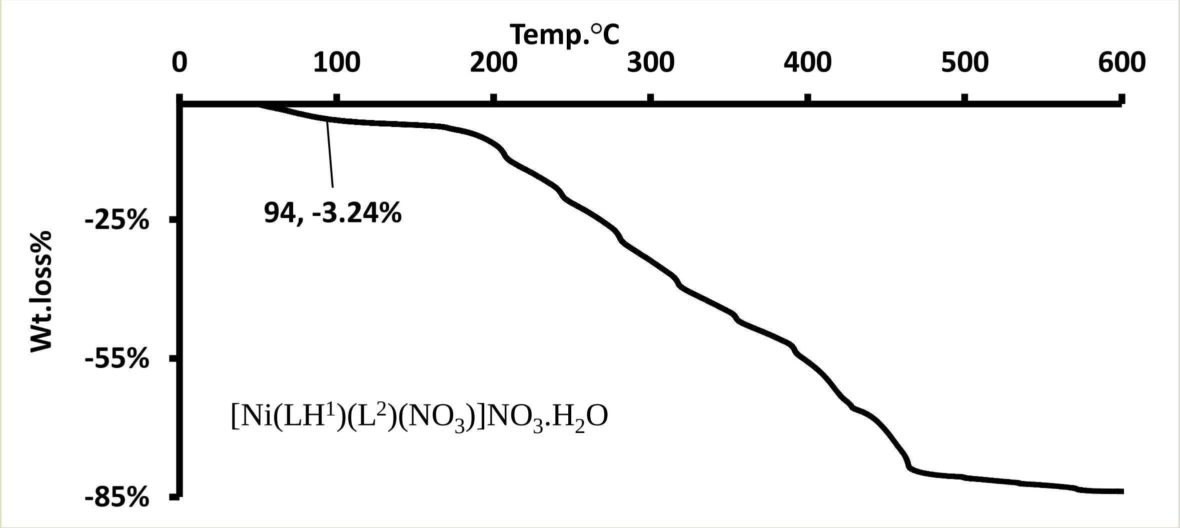
The TGA curves were obtained at a heating rate of 10◦C/min. over the temperature range of r.t– 600◦C. The calculated and estimated mass losses with temperature ranges of all metal complexes are shown in Table 5. Generally, two kinds of water molecules are associated with the chelates, hydrated water, and coordinated water. It is not possible to distinguish between them from the IR spectral data; hence, the thermal gravimetric analysis was used to investigate and determine water molecules by using of TGA instrument. Hydrated water is found outside of the inner coordination sphere. The dehydration of this form of water is normally carried out at a temperature range of 50-160°C. Meanwhile, the coordinated water molecules are removed at a higher temperature than the lattices water molecule, which was usually eliminated at below 250°C ***[23] [44]***. The dehydration step of divalent mixed-ligand complexes was observed below 180°C. The small weight loss percentages of Cu(II), Ni(II), Co(II), Zn(II), Pt(II), and Pd(II) complexes matched with the loss of one lattice water molecule. One coordinated water molecule was observed in the Pd(II) complex that was lost at 204°C. The weight loss in the ranges of 180–600° C is attributed to the decomposition of complexes.

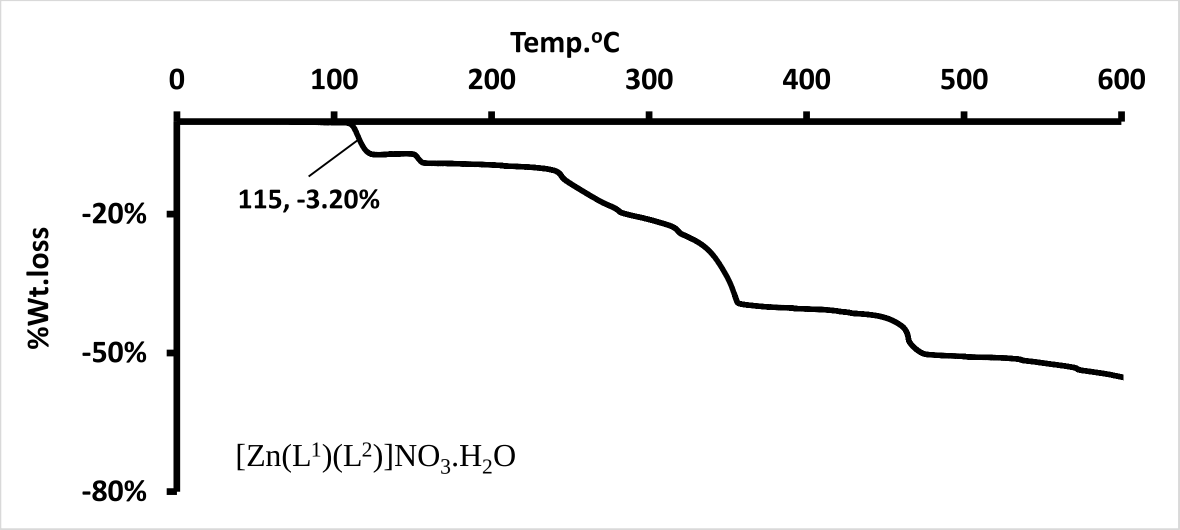
Table-5: Weight Loss with Temperature Ranges of Water Molecules in Metal Mixed-Ligand Complexes

Compounds	***TG Range ºC***	***n***	***Mass Loss of H_2O Theo. % (Est. %)***	***Total Mass Loss%***
$[Cu(L^1)(L^2)]NO_3.H_2O$	*51-136*	1^h	*3.30 (3.36)*	*70.14*
$[Ni(LH^1)(L^2)(NO_3)]NO_3.H_2O$	*50-94*	1^h	*2.98 (3.24)*	*83.87*
$[Co(L^1)(L^2)]NO_3.H_2O$	*37-180*	1^h	*3.32 (2.89)*	*71.65*
$[Pt(L^1)(L^2)]Cl.H_2O$	*70-180*	1^h	*2.7 (2.09)*	*55.29*
$[Zn(L^1)(L^2)]NO_3.H_2O$	*43-115*	1^h	*3.28 (3.20)*	*55.28*
$[Pd(LH^1)(L^2)H_2O]Cl_2.H_2O$	*50-175* *175-204*	1^h 1^c	*2.91 (2.87)* *5.84 (5.77)*	*55.44*

n= no. of moles of water molecule h, c = hydrated and Coordinated water molecule respectively







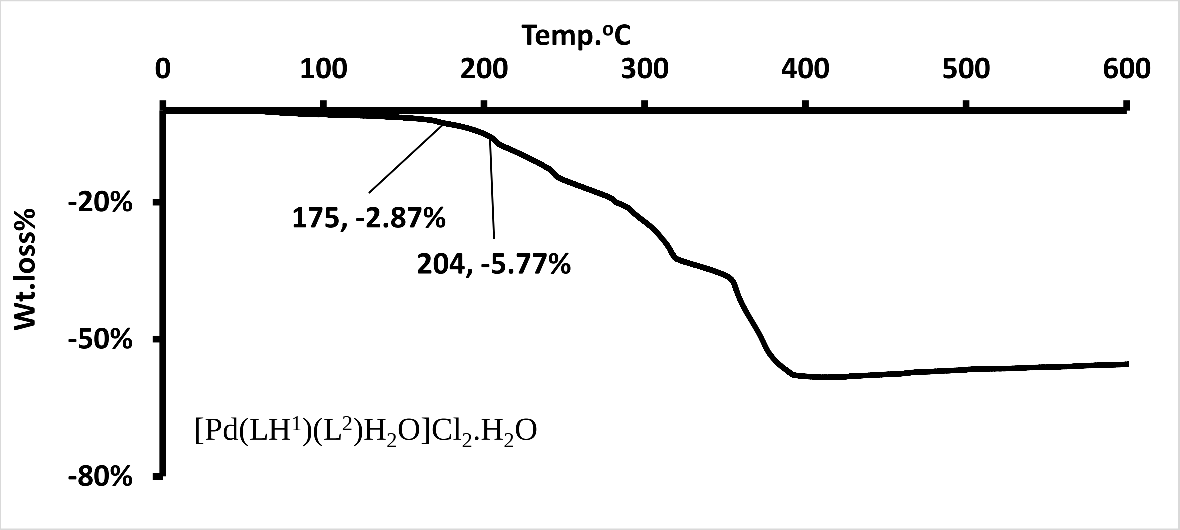


Figure-12: TGA Curve for Mixed-Ligand Complexes

G. Biological Activity

Biological activities of the ligands and their metal complexes are arranged in Table 6 against gram-negative bacteria (*E. coli*) and gram-positive bacteria (*S. aureus*) by Well Diffusion Methods using DMSO as solvent. The Schiff base (LH^1) ligand and 2,2′-bipyridine are resistant against these two bacteria (Escherichia coli and Staphylococcus aureus) with inhibitory zones of 3-16 mm and 22-37 mm respectively due to the presences of imine group, thiol group, and donor nitrogen hetero atom which has been enhancing the antibacterial activity ***[45]***. The complexes of Zn(II), Cu(II), Pd(II), and Co(II) complexes respectively showed good activity against the two bacterial species, but Ni(II) and Pt(II) are found to have no biological activity. These metal complexes are found to have sensitivity for inhibition of Gram-positive more than Gram-negative bacteria. The complex Zn(II) is high activity against both types of bacteria while the other complexes are moderate. It is concluded that the activity of the Schiff base ligand is enhanced when it is coordinated to some of these metal centers ***[13] [19]***. The increased activities of metal complexes might be due to the decline of the polarity of the metal ions as a result of complexation partial positive charge of a metal ion with Schiff base ligand and increase delocalization of π electron over the chelate ring. Chelation rises the liposolubility nature of metal(II) complexes which afterward favors its permeation through the lipid layer of the bacterial membrane system. Moreover, such metal complexes might be inhibiting the enzyme activity of the bacteria that is necessary for metabolic pathways in the microbe, thus improving biological activity ***[36]***.

Table-6: Antibacterial Assay Data in Terms of Inhibition Zone(mm) for the Ligands and their Mixed-Ligand Metal Complexes

Compounds	***Inhibition Zone (mm)***	
	***Escherichia coli* Gram(-)**	***Staphylococcus Aureus* Gram(+)**
LH^1	*3*	*16*
L^2	*22*	*37*
$[Cu(L^1)(L^2)]NO_3.H_2O$	*12*	*27*
$[Ni(LH^1)(L^2)(NO_3)]NO_3.H_2O$	-	-
$[Co(L^1)(L^2)]NO_3.H_2O$	*8*	*21*
$[Pt(L^1)(L^2)]Cl.H_2O$	-	-
$[Zn(L^1)(L^2)]NO_3.H_2O$	*14*	*29*
$[Pd(LH^1)(L^2)H_2O]Cl_2.H_2O$	*10*	*24*
Gentamicin	*18*	*40*
DMSO	*12*	-

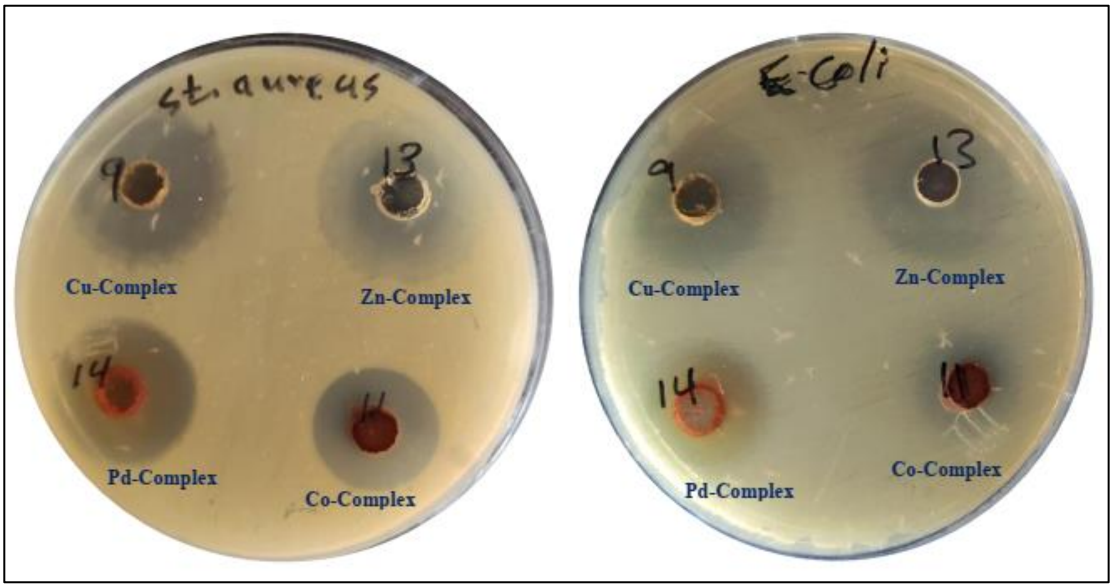


Figure-13: The Inhibition Zone of Mixed-Ligand Complexes on the Plate.

Conclusion

The synthesis of new 5-((Z)-((E)-3-phenylallylidene)amino)-1,3,4-thiadiazole-2-thiol Schiff base ligand and its Cu(II), Ni(II), Co(II), Zn(II), Pt(II), and Pd(II) mixed-ligand complexes with 2,2′-bipyridine were prepared and characterized based on analytical and spectroscopic data in the present study. The experimental data have shown that the mixed-ligand complexes are electrolytic in nature and the Cu(II), Ni(II) and Zn(II) complexes have tetrahedral structures while Co(II), Pt(II), and Pd(II) metal complexes have square planer geometry. Both Schiff base and 2,2′-bipyridine ligands coordinated through thiolate sulphur and nitrogen atom of azomethine and pyridine to the metal ions. The antimicrobial activities of the ligand and the mixed-ligand chelates were tested against (*E. coli*) and (*S. aureus*) bacterial. It has been observed that the new prepared mixed-ligand complexes showed more antibacterial activity than Schiff base ligand. Usually, the Zn(II) complexes exhibited a better antimicrobial activity compared to the Schiff base and other complexes and moderately concerning the activity standard drugs. Surprisingly the Pt(II) and Ni(II) complexes are found to have no antibacterial activity.

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