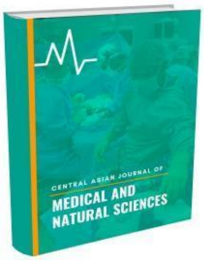

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Article

Synthesis, Characterization, Antioxidant, and Theoretical Studies of the Schiff Base Derivative of (4H-1,2,4-Triazole-3,5-Diamine) and Its Complexes With Co(II) & Cu(II) Ions

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Abstract: Schiff bases are widely studied for their potential biological activities, particularly as antioxidants. This study synthesized a Schiff base derivative from (4H-1,2,4-triazole-3,5-diamine) through condensation with o-vanillin and investigated its metal complexes with Co (II) and Cu (II) ions. Despite the known antioxidant properties of Schiff bases, there is limited information on their metal complexes' antioxidant and structural behaviors. The aim was to synthesize, characterize, and assess the antioxidant activity of the ligand and its metal complexes. The compounds were characterized using elemental analysis, FTIR, 1H-NMR, mass spectrometry, magnetic susceptibility, and molar conductivity. DFT calculations using B3LYP/6-31+G(d,p) were performed for geometry optimization and energy gap analysis. The ligand exhibited significant antioxidant activity, while Co (II) complexes adopted a tetrahedral geometry and Cu (II) complexes a square planar geometry. These findings highlight the Schiff base's potential in antioxidant applications and contribute to understanding metal-ligand interactions.

Keywords: Ligand, Heterocyclic, Schiff base, Antioxidant, Energy gab

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1. Introduction

Heterocyclic chemistry is wide and important studied of medicinal chemistry[1]. Triazoles are a significant group of the organic heterocyclic compounds that had attracted widespread attention of the chemical research[2]. Bladin in 1885 was the one who first came up with the name triazole to describe the five-membered compounds with two carbon atoms and three nitrogen atoms with molecular formula $C_2H_3N_3$[3]. Triazole appears in two types of isomeric forms, namely 1,2,3-triazole and 1,2,4-triazole[4] as shown Figure (1). 1,2,4-triazole has attracted the interest of researchers suitable to its wide range of biological performance, such as antimicrobial[5], antifungal[6], anticonvulsant[7], antiviral[8], anti-inflammatory[9], anticancer[1011] and antioxidant[12]. Triazoles can form various noncovalent interactions with various enzymes, proteins, and receptors, such as hydrogen bond, hydrophobic interactions, dipole-dipole bond & van der Waals forces[13] [1].

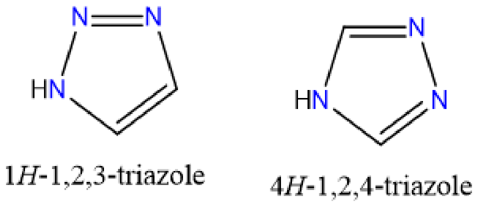


Figure 1. Triazole isomers

2. Materials and Methods

Experimental

2.1. Materials and instruments

All the chemical materials used were purchased from Sigma-Aldrich., ^{1}H-NMR was recorded on 400 MHz Bruker NMR spectrometer, the FTIR were used an IR Affinity-1-Shimadzu IR spectrometer. Work mass selective Detector 5973. micro-analyses (C.H.N.S) was used Vario ELV5 Elemental analyzer model 11086109 Germany. Thin layer chromatography was frequently used to verify the purity of produced substances [2].

2.2. Synthesis Schiff base (ligand)

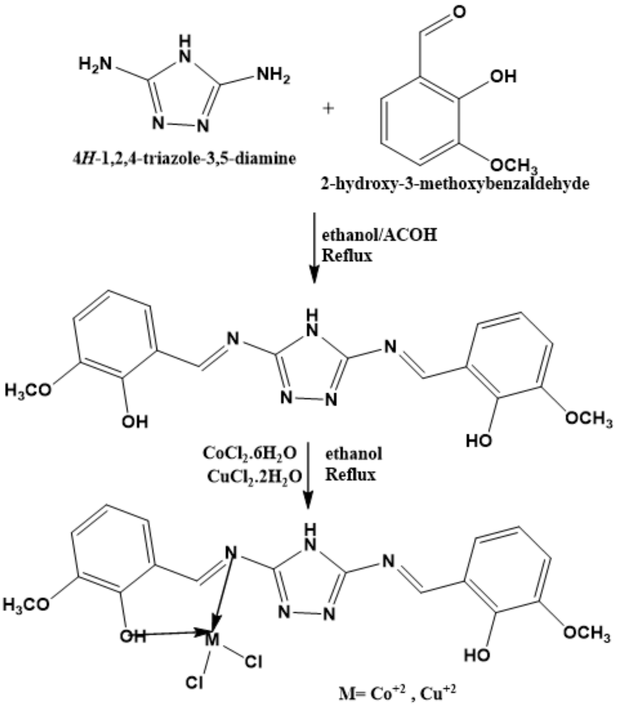
After mixing (15ml) ethanolic solution of (0.02mol, 3.04g) (2-hydroxy-3-methoxybenzaldehyde) with three drops of glacial acetic acid and (10ml) ethanolic solution of (0.01mol,0.99g) (4H-1,2,4-triazole-3,5-diamine), the reaction mixture was refluxed for three (hours) [3]. TLC was used to monitor the reaction. The resulting solid products underwent filtration separation and crystallization from ethanol to purify them 14, The yield of the yellow Schiff base product is 77% [4].

2.3. Synthesis of the complexes

Ethanolic solutions of (0.237g, 0.001mol) CoCl2.6H2O and (0.170g, 0.001mol) CuCl2.2H2O were combined with a hot solution of the (0.367 g, 0.001mol) ligand, then the reaction was refluxed for three (hours) [5]. Next, collect the suspended solid metal complex by filtering it, wash it multiple times with distilled water, and crystallize it using a heated ethanol solution[15].

3. Results and Discussion

The synthesized (ligand) and its complexes with cobalt and copper are schematically represented in scheme (1) [6]. An elemental microanalysis (CHN), atomic absorption, conductivity measurements, magnetic susptibility and physical properties data are gathered in the table (1). An analysis of the data revealed the formation of (1:1) (metal:ligand) for the complexes with Co(II) and Cu(II) ions. The molar conductance values of the complexes determined by measuring them in 10^{-3} M DMSO, fall between (11 and 15) $\Omega^{-1}cm^2mol^{-1}$, suggesting that they are not electrolytic [7]. The magnetic moment of Cu d^9 is 1.7 B.M. For that the geometry of copper complex was proposed square planar, while the magnetic moment of Co d7 is 4.62 B.M, therefor, the suggested geometry of cobalt complex was tetrahedral [8].



Scheme 1. Synthesis the ligand and its complexes

Table 1. Elemental microanalysis (CHN), molar conductance, magnetic susptibility and physical properties

comp	color	m.p °C	μeff B.M	Λ Scm2. mol-1	C% exp C%(cal)	H% exp H%(cal)	N% exp N%(cal)	M%
$C_{18}H_{17}N_5O_4$ Ligand (L)	Yellow	D> 165			59.37 (58.85)	4.13 (4.66)	20.79 (19.06)	
$Co(L)Cl_2$	brown	D> 194	4.6	15				12.68
$Cu(L)Cl_2$	green	D> 213	1.7	11				13.92

D= Decomposition

3.1. Infrared spectra

FTIR frequencies of the ligand and its complexes are listed in Table (2) [9]. The characteristic FT-IR spectrum of the ligand exhibited stretching vibration bonds at the following frequencies (cm^{-1}) at ν (O-H 3453), ν (N-H 3069), ν (C-H aro. 3017), ν (C=N 1663 imine and 1592endo ring), ν (C-N-C 1363 asy,1295sy). The stretching vibration of the complexes demonstrated the shift of azomethine groups (νC = N) to the lower frequencies as shown in Table (2). The spectra of complexes demonstrated new band vibrational modes to the M-N, and M-O group frequencies as a result of bonding the metal ion with the ligand [10]. This indicates that the coordination occurred through the azomethine group and hydroxyl group with metal ion to make a stable chelate ring as shown in fig. (2)-(4)

Table 2. FTIR frequencies data for the ligand and its metal complexes in (cm^{-1})

Comp.	ν(O-H)	ν(N-H)	ν(C-H) aromatic	ν(C=N) imine	ν(C=N) endo	ν(C-N-N) asy and (sy)	ν(M-N)	ν(M-O)
ligand	3453	3069	3017	1663	1592	1363 (1295)		
Co(L)Cl_2	3452	3070	3042	1643	1592	1304 (1283)	533	427
Cu(L)Cl_2	3447	3127	3020	1634	1605	1344 (1301)	539	425

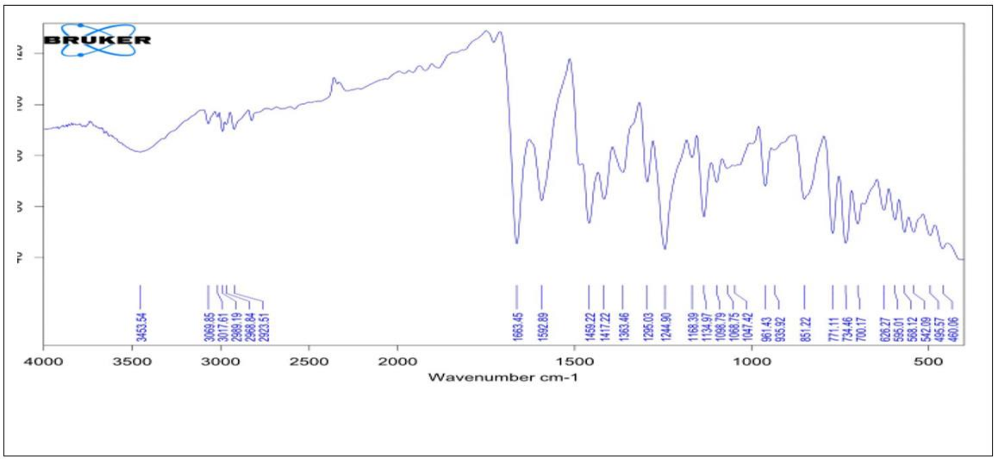


Figure 2. Ft.IR of the ligand spectrum

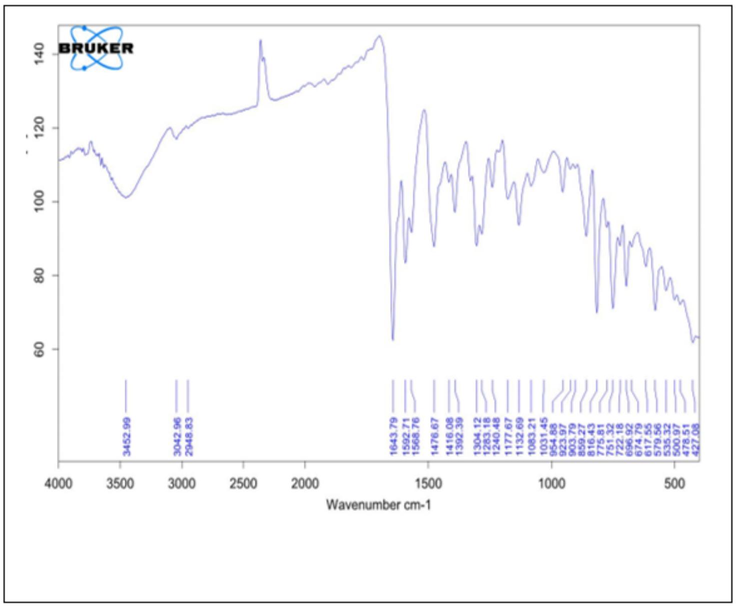


Figure 3. Ft.IR of the complex [Co(L)Cl2] spectrum

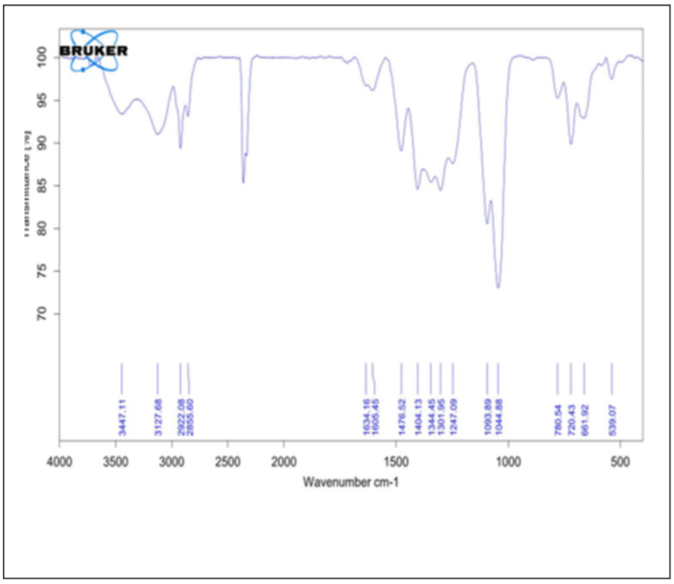


Figure 4. Ft.IR of complex [Cu(L)Cl2] spectrum

3.2. Nuclear Magnetic Resonance of ligand (L)

^{1}H- NMR Spectrum of the ligand in DMSO-d6 peak assignments characterized by the presence of signal at δ (1H, 14.34) ppm due to (N-H) protons of thioamide group, δ (1H, 11.20) ppm due to (O-H) proton of phenolic group, azomethine group (N = CH) appeared signal at δ (1H, 9.41) ppm, signal at δ (6.80-7.37) ppm belong to aromatic protons, (O-CH3) protons seemed at δ (3H, 3.82) ppm. As shown in fig. (5) [11]

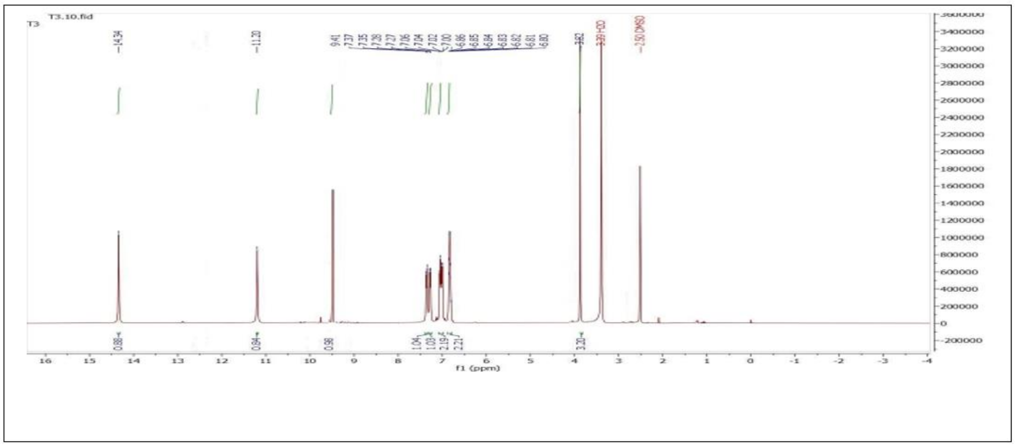


Figure 5. 1H-NMR spectrum of the ligand

3.3. Mass spectra

The mass spectrum exhibited molecular ion of the ligand at 367 m/z corresponding to its chemical formula $[C_{18}H_{17}N_5O_4]^+$, the spectrum showed a high intensity peak at 69 m/z in a good agreement with chemical formula $[C_2H_3N_3]^+$, which corresponding to the ring of triazole. Other peaks are due to the subsequent fragments like $[C_{18}H_{15}N_5O_2]^+$ = 333 m/z, $[C_{16}H_{11}N_5O_2]^+$ = 305 m/z, $[C_{16}H_{13}N_5]$= 271 m/z and $[C_{10}H_9N_4O_2]^+$ = 217 m/z. As shown in Fig. (6) [12]

The structure of complexes is confirmed by the help of mass spectra, the spectrum exhibited a peak at 497 m.z which is due molecular ion of Co (II) complex $[Cu(L)C_{12}]^+$. This complex showed fragment ion peaks with loss of two chlorine atoms at (461 and 421) m/z due to $[Co(L)Cl]^+$ and $[Co(L)]^+$ respectively. As shown in Fig. (7)

the mass spectrum appear peak at 501 m.z which is due molecular ion of Cu(II) complex [Cu(L)Cl2]+. This complex showed fragment ion peaks with loss of two chlorine atoms at (466 and 430) m/z due to [Cu(L)Cl]+ and [Cu(L)]+ respectively [13]. As shown in Fig. (8).

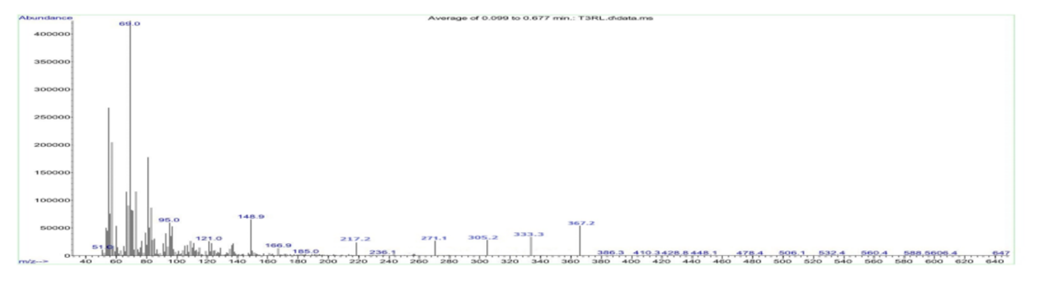


Figure 6. Mass spectrum of the ligand

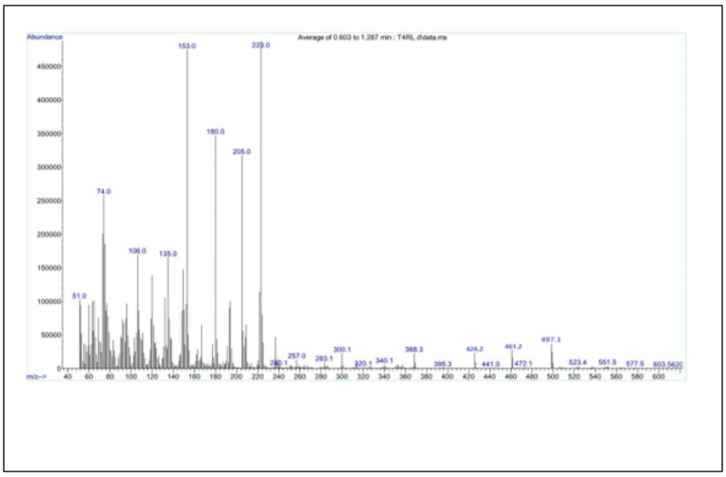


Figure 7. Mass spectrum of the [Co(L)Cl2]

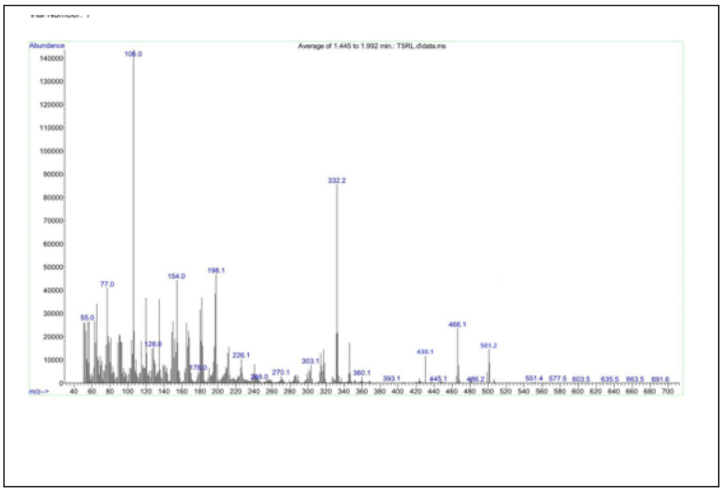


Figure 8. Mass spectrum of the [Cu(L)Cl2]

3.4. Antioxidant Activity

The phenolic reference used in the investigation of the ligand's antioxidant activity was ascorbic acid [14]. Five a normal solution with different concentrations of the ligand (200, 100,50, 25 and 12.5 µg/ml) in ethanol so that from standard ascorbic acid solutions. (6 ml) of 45 (µg/ml) ethanolic solution of DPPH was added to each (100 µl) normal solutions of the ligand. The mixed solution was incubated at room temperature and in the dark for (30 min). Then, the change in the concentration of DPPH solution was defined by measuring the absorbance at maximum wavelength (517 nm) using UV-vis spectrophotometer. Compounds' ability to scavenge DPPH radicals can be seen visually as a change in the solution's color [15]. The DPPH color shifts from violet to yellow when DPPH-H is reduced to its non-radical state by a proton or electron donor. It has been noted that when ligand concentration rises, so does the free radical scavenging activity. (Table 3). The ligand gave a good activity but lower than ascorbic acid [16]. as shown in figure (9). The percentage of a free radical scavenger is calculated according to the equation (1) 16 ,17 :

DPPH scavenging ability (%) = [A control−A sample / A control] × 100 ………(1)

Table 3. DPPH scavenging activity of Ascorbic acid and the ligand

Concentration µg mL^{-1}	Scavenging activity %	
	ascorbic acid	ligand
200	82.7	77.77
100	74.80	71.142
50	67.09	65.702
25	53.74	52.70
12.5	23.03	42.55

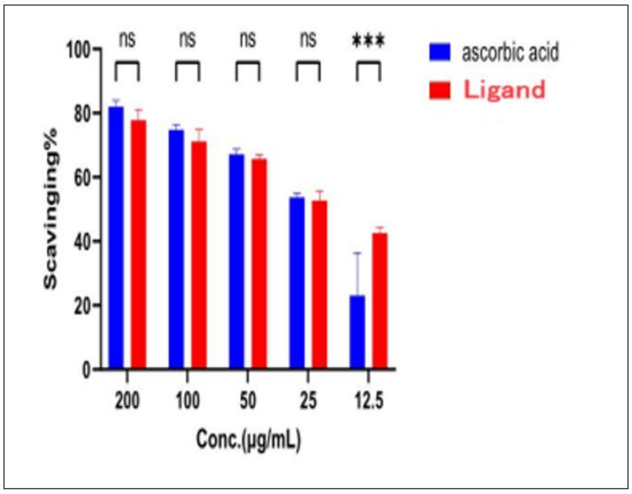


Figure 9. DPPH scavenging activity of Ascorbic acid and the ligand

3.5. Theoretical study

The Calculations of theoretical study were done by using density functional theory (DFT) method at B3LYP level with 6-31+G (d,p) bases set by using Gaussian 09 programs18 [17] . Geometry optimization for the ligand and its complexes focus on a local minimum of each structure having the lowest energy level, as shown in Figures (10 and 11). HOMO (highest molecular occupied orbital) and LUMO (lowest molecular unoccupied orbital) were computed by B3LYP / 6-31+G (d,p) level as shown in Fig. (12),. The values of the EHOMO, ELUMO and Energy gap (ΔE) are displayed in Table (4). The capacity of a molecule on interaction with other molecules is generally represented by the values of energies (EHOMO & ELUMO) of molecular orbitals [18]. The electron-donating capability of a molecule is explained by the term EHOMO. A molecule with a high EHOMO value has a strong capacity to donate electrons to a lower energy molecule (an empty orbital). The capacity of a molecule to receive electrons from an energetic molecule is greatest when it has a low ELUMO value (an unoccupied orbital)19. Energy gap (ΔE) was calculated) by the equations (2): The calculations of electronic transition energy for ligand correctly predicted the absorption at maximum wavelength values (390) nm that were close to maximum wavelength values experimentally determined values at (386) nm, as shown in Figures (13 and 14) [19].

$$\Delta E = E_{LUMO} - E_{HOMO} \quad \ldots\ldots\ldots.. (2)$$

Table 4. The value energy of (HOMO and LUMO) orbital and Energy gap

Compound	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE (eV)
$C_{18}H_{17}N_5O_4$ (L)	-5.6142	-2.0601	3.5541
$Co(L)Cl_2$	-7.6847	-4.0349	3.6498
$Cu(L)Cl_2$	-6.2281	-4.1475	2.0806

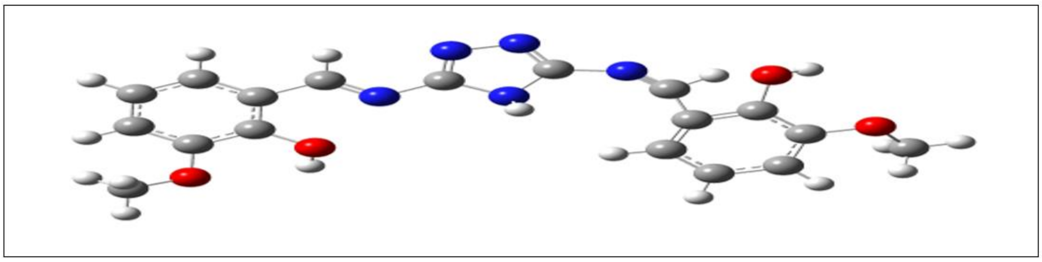


Figure 10. Geometry optimization of the ligand

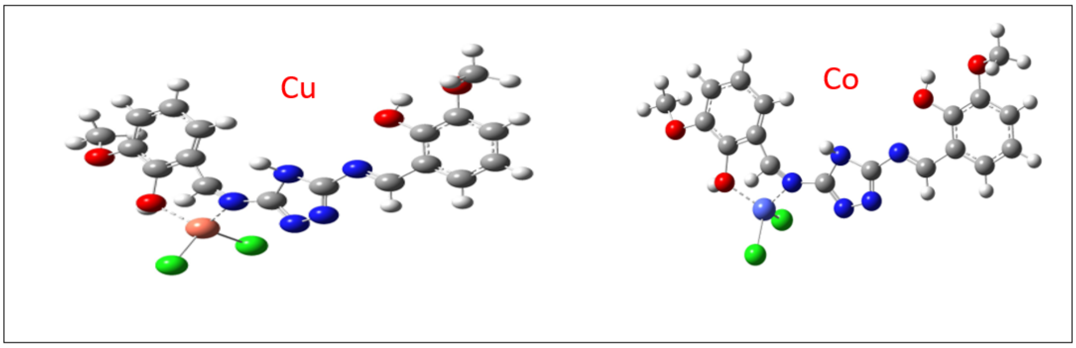


Figure 11. Geometry optimization of the [Co(L)Cl2] and [Cu(L)Cl2]

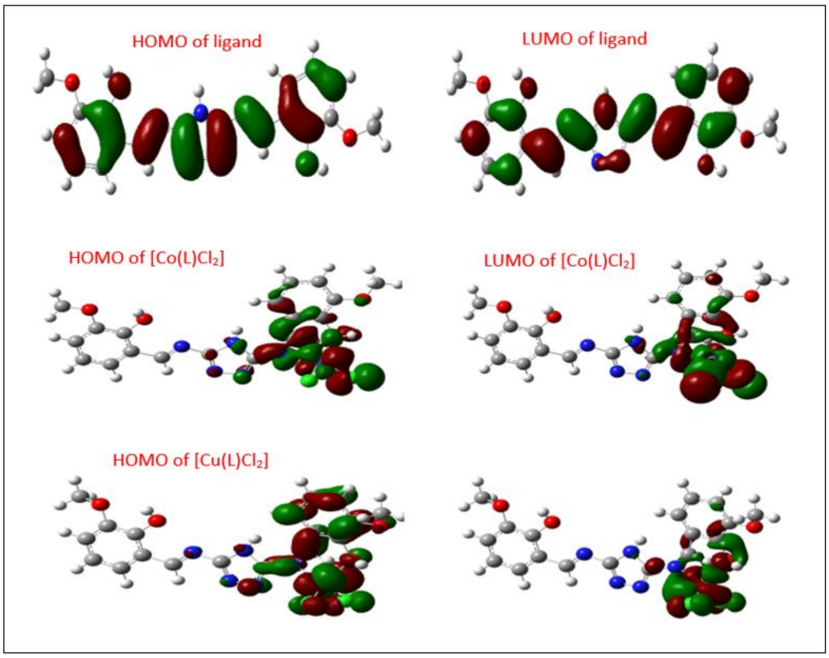


Figure 12. Molecular orbitals (LUMO-HOMO) of the ligand and its complexes

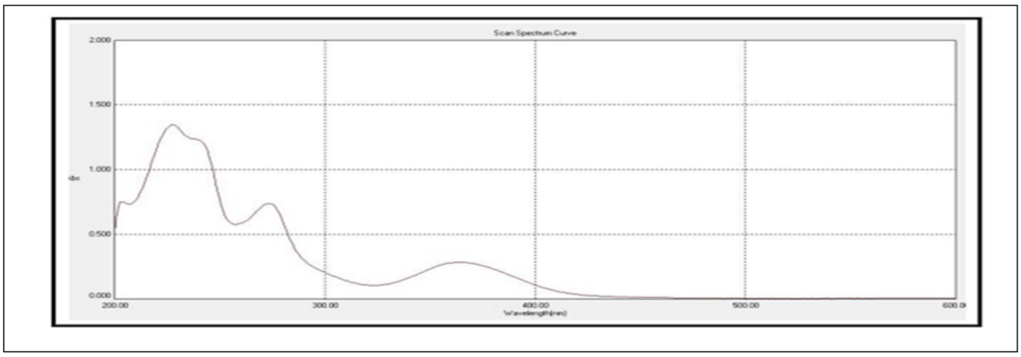


Figure 13. The experimental absorption spectrum of the ligand

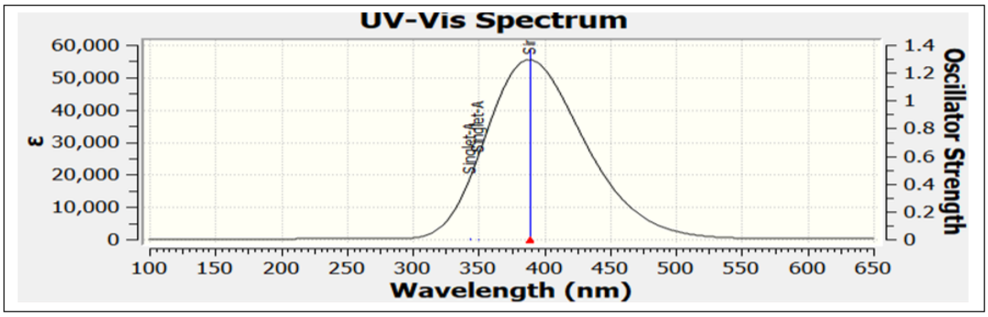


Figure 14. The theoretical absorption spectrum of the ligand

4. Conclusion

The Schiff base (ligand) and its complexes were synthesized, and their structure were confirmed by the data observed of ^{1}H-NMR, FTIR and Mass spectra, the ligand behavior as bidentate through C=N and O-H groups. molar conductivity was indicating to the non-electrolytic nature, while the magnetic measurements investigated the tetrahedral environment around cobalt (II) ion and square planer around copper (II) ion. The ligand gave a good antioxidant activity.

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