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Synthesis, characterization and biological activity of Co(II), Ni(II), Cu(II) and Cd(II) complexes with new imidazole derivatives [ethyl {[5-oxo-1-(phenylcarbonyl)-4-(prop-1-en-2-yl)-4,5-dihydro-1H-imidazol-2-yl]sulfanyl}acetate]

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Abstract
The new imidazole ligand have been synthesized from reaction of benzoyl chloride with thiourea, then the resulting product reacted with ethylchloroacetate to produced [ethyl {[4-oxo-1-(phenylcarbonyl)-5-(prop-1-en-2-yl)-4,5-dihydro-1H-imidazol-2-yl]sulfanyl}acetate], This ligand was characterized by C.H.N.S (Elemental analysis), 1H-NMR spectrum, FT-IR spectrum and UV-visible spectra . Metal complexes of this ligand were synthesized and characterized by C.H.N.S (elemental analysis), Magnetic susceptibility, electrical conductance, UV-Vis spectra and FT-IR spectra. The synthesized compounds were screened for its antibacterial and antifungal activity. The result showed that these complexes inhibited the growth of the tested organism.

Key words: 1H-imidazol compounds, coordination compound of 1H-imidazol, spectral data, antimicrobial activity.

1. Introduction

Imidazole is a heterocyclic compound that contains nitrogen and classified as a diazole. Its refers to a large family of derivatives. (1-3) Imidazole have an important attractive in organic and bioinorganic chemistry for the reason that it play an important position in synthesis of organic compounds and inorganic complexes since it have an active site of N chelating atoms in imidazole as a ligands molecule. (4-8) Imidazole having a great pharmacological activity. (9) Biologically activity of imidazole compounds including the anticancer, antiviral. (10-11) In recent times, imidazole used in drug development for the treatment of hypertension, HIV infections and as microbial inhibitors. (12-13)

2. Experimental

Physical Measurements

Melting points were registered on a GallenkampMF B600 melting point apparatus. Elemental analyses (C.H.N.S) were carried out on EA-034.mth. For ligand and its complexes. The contents of metal complexes were predictable by using Flame atomic absorption Shimadzu-670 AA Spectrophotometer. FT-IR spectra were registered using FT-IR-8300 Shimadzu in the range of (4000-350)cm-1, samples were measured as (CsI)disc. ^{1}H-NMR spectra were acquired with Bruker spectrophotometer model ultra-shield at 300MHz in d6 DMSO solution with TMS as internal standard. Magnetic susceptibilities of samples were calculated by using Magnetic Susceptibility Balance of Sherwood Scientific. The molar conductance of metal complexes were recorded using Electrolytic Conductivity Measuring model (MC-1-Mark)V using platinum electrode (EDC 304) with (1cm-1) cell constant, and the concentration was (10-3 M) in (DMF) dimethylformmide as a solvent at room temperature. UV-Vis spectra were recorded by using UV-1650PC-Shimadzu Spectrophotometer at room temperature; the concentration of the ligand and their metal complexes was (10^{-3}M).

Methods and Materials section

Synthesis of ligand (L)

A(A (0.01 mol, 1.8g) of benzoyl chloride was added to the solution of thiourea (0.01 mole, 0.76g)) in 50 mL dioxane). The reaction mixture was refluxed for 7 hrs., the resulting product was filtered off and recrystallized from ethanol. Scheme (1).

B(To the mixture of product (0.01 mol, 1.8 g) in (30ml) acetone, (0.03 mol, 3.675g) of

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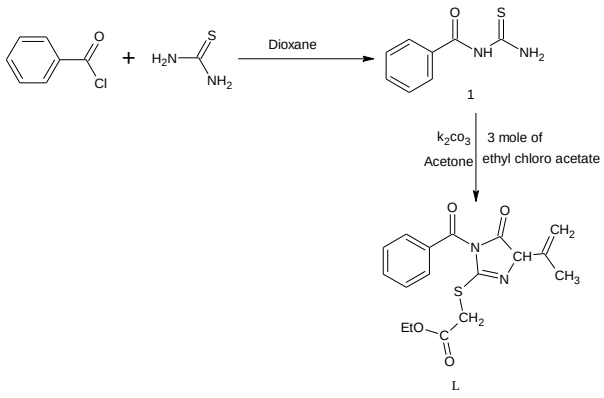
ethylchloroacetate and (0.01 mol, 1.38 g) (K_2CO_3) potassium carbonate were added, then the mixture was refluxed for 12hr. the precipitate was filtered off and recrystallized from ethanol and water (7:3). Scheme (1).



Scheme (1): Synthesis of Ligand (L)

Synthesis of metal complexes (S_1-S_4)

A) An Ethanolic solution of (0.05 mmol) [$CuCl_2.4H_2O$] was added to an ethanolic solution (0.346 g, 1 mmole) of (L). The mixture reaction was refluxed for (3) hrs., and then during this time period a precipitate was formed. The product was filtered off, washed with hot ethanol, followed by cold water and dried.

4. Study of antimicrobial activities for ligand(L)and its Complexes (S1 –S4)

B) The antimicrobial activities of the ligand (L) and its complexes (S_1-S_4) were estimated against (E. coli) and ((Bacillusubtilis) cultured in Nutrient agar medium, DMSO served as control, the compounds concentration were (10-3M). The new complexes (S_1-S_4) were screened for its in vitro growth inhibitory activity against other pathogenic fungi, i.e., [P. chrysogenum and Aspergillus niger] on potato dextrose agar medium and incubated at 30 °C for 72 hours. DMSO served as control and as a solvent for both techniques. The complexes concentrations were (10^{-3}M).The percentage of inhibition of fungal growth expressed, were estimated on the growth in test plates as compared with the control plates.

Results and Discussion

1. Elemental Analyses

The analytical and physical properties data of ligand (L) and its complexes (S_1-S4) were specified in Table (1). The results showed that elemental analysis is good coincidence with the calculated value. The new complexes (S_1-S_4) were soluble in (CH_2Cl_2, $CHCl_3$, DMF and DMSO). They are thermal stable and unaffected by the moisture.

2. ^{1}H-NMR Spectrum of Ligand (L)

^{1}H-NMR spectrum of synthesized ligand, figure (2), in DMSO-d6 shows signals at (7.52 – 8.17ppm, 5H) assigned to protons of aromatic ring, signals at 5.00 ppm, (s, 2H) attributed to) -S-CH_2-CO) group protons, signal at 4.60ppm, (s, 1H) refer to (CH–CO-N(group proton of imidazole ring, while the signals at 4,15-4.21ppm, (q, 2H,) assigned to (O –CH2) group protons of ester, signals at 2.27 ppm, (s, 3H,) may be attributed to (C = CH2) groups protons and finally, signals at 1.23-1.42 ppm (t, 3H,). Referred to protons of methyl groups.(14).

Table (1):Some analytical and physical property

Comp. symbol	General formula	Mwt g.mol^{-1}	Color	M.P (°C)	Elemental analysis(%) Calculated (Found)				
					C	H	N	S	M
(L_1)	$C_{17}H_{18}O_4N_2S$	346.4	Yellow	120-122	58.89 (57.90)	5.19 (5.39)	8.08 (7.99)	9.23 (9.11)	-----
S_1	$[Co(L)_2(Cl)_2]$	822.73	Brown	188dec	49.59 (49.38)	4.37 (4.41)	6.80 (6.92)	7.77 (7.59)	7.16 (7.13)
S_2	$[Ni(L)_2]Cl_2$	822.49	Light green	221dec	49.60 (48.86)	4.37 (4.22)	6.80 (6.65)	7.78 (7.80)	7.13 (7.58)
S_3	$[Cu(L)_2Cl_2].4H_2O$	899.3	Dark brownish	264dec	45.36 (44.97)	2.89 (3.02)	6.22 (5.89)	3.55 (3.43)	7.06 (6.98)
S_4	$[Cd(L_1)_2Cl_2].4H_2O$	948.22	Off white	204dec	43.02 (42.87)	4.74 (4.68)	5.90 (5.82)	3.37 (3.22)	11.63 (11.74)

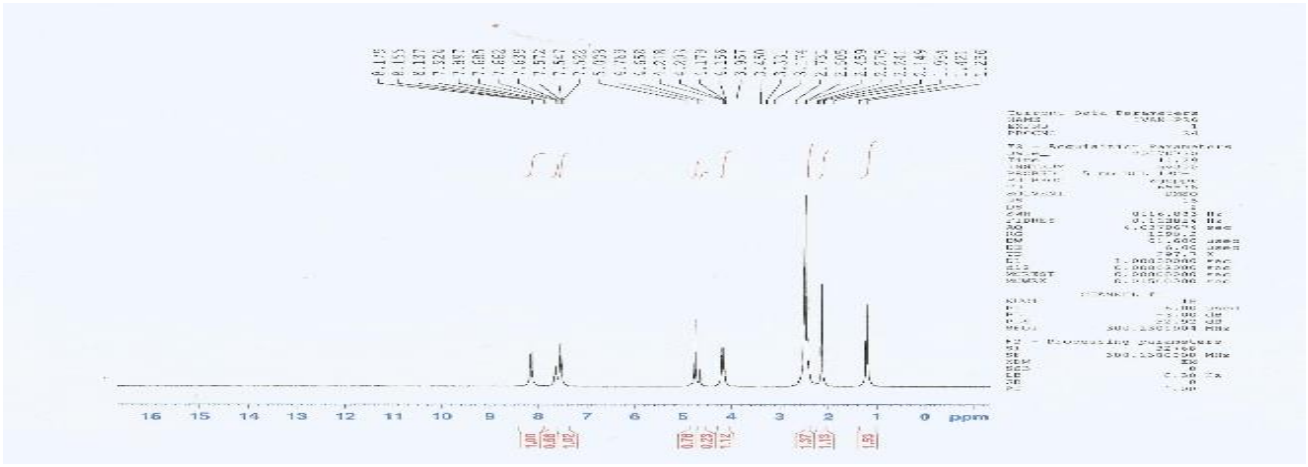


Figure (2): ^{1}H-NMR spectrum of prepared ligand (L) in DMSO-d6

3. FTIR Spectra of the prepared ligand (L) and its metal complexes (S1-S4)

FTIR spectra of the ligand and their metal complexes and main vibration modes were listed in Table (2).

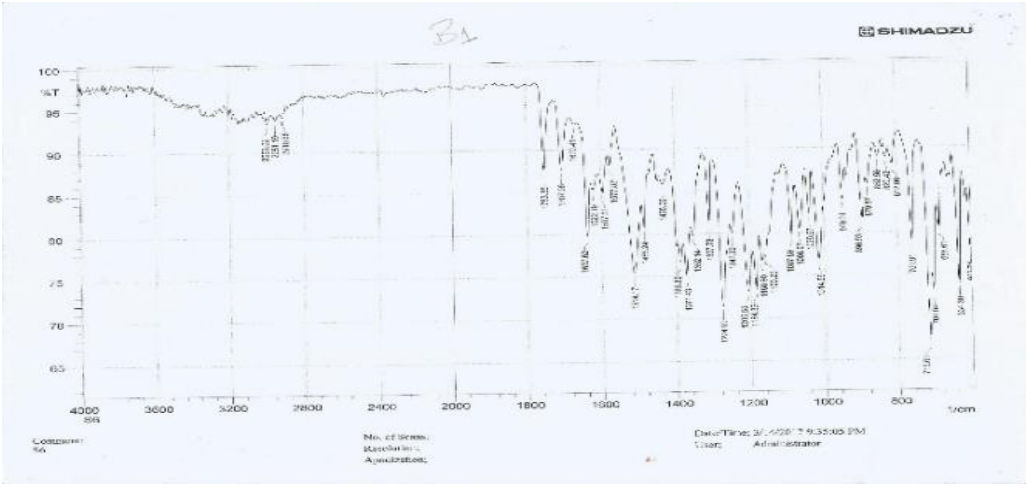
FTIR spectrum of the prepared ligand display bands at (2993 cm-1) in FTIR spectrum attributed to υ(C-H) vibration, also observed(14,15) at all metal complexes spectra. Spectrum of the free ligand also shows band at (1753cm-1) due to carbonyl group of ester υ(C=O) vibration , This band was not changed in all metal complexes of the prepared ligand. Band at (1707cm-1) referred to amide carbonyl group. While band at (1670cm-1) assigned to carbonyl group of benzene ring. These two carbonyl bands were changed in all complexes because it was participated in coordination process with metal ions. Band at (1637cm-1) may be attributed to (C=N) of Schiff base. Different alteration have take place at frequencies of two υ(C=O) vibrations of carbonyl groups was observed at (1707 cm-1 and 1670cm-1) in the spectrum of ligand these bands were shifted by (15-28) cm-1 to a lower frequencies in all metal complexes spectra as shown in table (2), The υ(C-S) vibration which showed at (1014 cm-1) in free ligand and its not shifted in all complexes, while the frequencies of (C=C) and (C-O) appears at(1637 cm-1) and (1274 cm-1) respectively.

Table (2): FTIR spectral data (cm-1) of the of ligand and their complexes (S1-S4)

comp.	*L*	*S_1(Co)*	*S_2(Ni)*	*S_3(Cu)*	*S_4(Cd)*
υ(N-H)	3300	3296(w)	3303(w)	3299(w)	3292(w)
υ(O-H)	-----	3435(s)	------	3444(s)	3402(s)
υ(C-H)	2993(w) 2951(w)	2993(w) 2951(w)	2990(w) 2948(w)	2987(w) 2953(w)	2985(w) 2944(w)
υ(C=O)	1753(s)	1743(s)	1743(s)	1743(s)	1739(s)
υ(C=N) Schiff	1707(s)	1647(s)	1651(s)	1641(s)	1661(s)
υ(C-S)	1014(m)	1020(m)	1003(m)	1016(m)	1011(m)
υ(C-O)	1274(s)	1274(s)	1276(s)	1274(s)	1272(s)
υ(C=C)	1637(s) 1514(s)				
υ(M–N)	--------	547(w)	565(w)	552(w)	554(w)
υ(M–O)	-------	476(w)	480(w)	468(w)	472(w)

Where : S=strong, W=weak, M=medium

The frequencies of υ(M–O) in the spectra of complexes were estimated at (545-523) cm-1(16).



4. Electronic spectra, Magnetic moment, and Molar conductance measurements

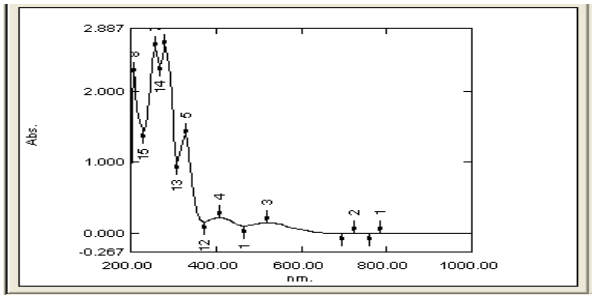
The (U.V-Vis) spectrum of ligand, in absolute ethanol exhibited three absorption bands at (252 nm, 39682 cm-1), (288 nm, 34722 cm-1) attributed to ($\pi\rightarrow\pi^*$) transitions, while band at (343 nm, 29154 cm-1) referred to ($n\rightarrow\pi^*$) transitions[14,17]. Complexation of prepared free ligand (L) with metal ions forms new bands in the visible region and UV. These bands were belonged to M-L charge transfer and to ligand field transitions (17).Table (3) show bands of maximum absorption of metal complexes (S_1-S_4) in $CHCl_3$ with its assignments

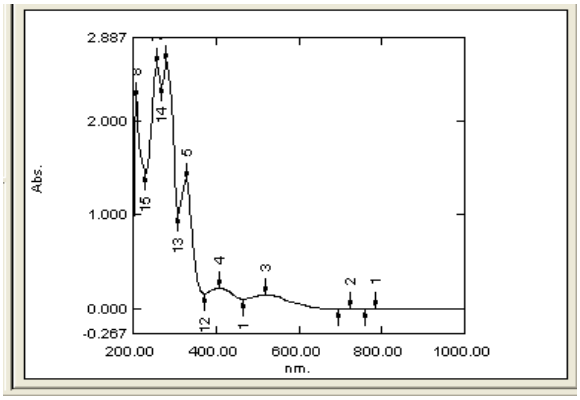
The UV-Vis spectrum of the brown cobalt complex (S_1) shows transitions at (408nm, 24510 cm-1) attributed to charge transfer (MLCT) and (560nm, 17857cm-1) may be assigned to $^4T_1g\rightarrow 4T_1g$ pF) transition, these indicate an octahedral geometry. The magnetic moment and molar conductance measurement suggested that this compound have being a paramagnetic (4.74 B.M) and non electrolytic nature.

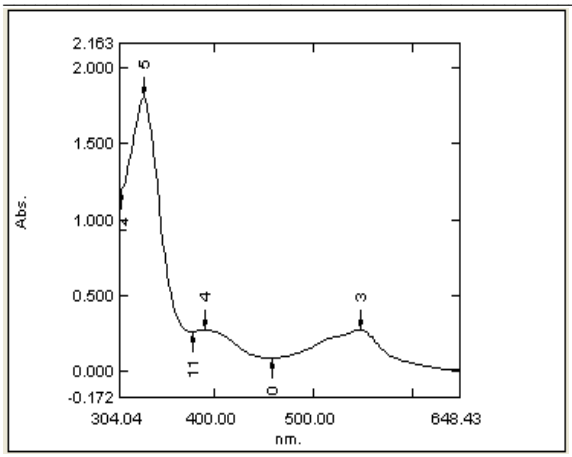
The UV-Vis spectrum of the light green nickel(II) (S_2) complex exhibit absorption bands at (550nm,18181cm-1) and (400nm, 25000cm-1) referred to $^1A_1g \rightarrow {}^1A_2g$, and $^1A_1g \rightarrow {}^1B_1g$ transitions, which related to a square-planar geometry. The complex has a diamagnetic properties, this value be suitable for a square-planar geometry concerning Ni (II) ion. The molar conductivity measurements estimated that this complex have an ionic behaviour.

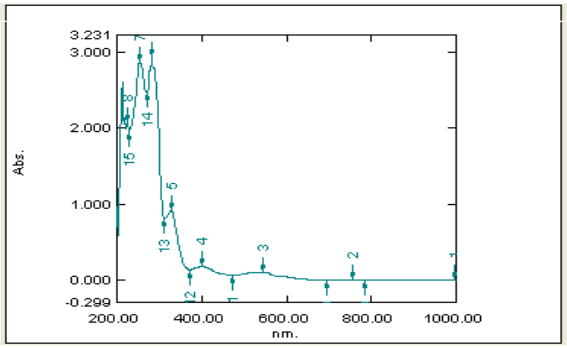
The UV-Vis spectrum of dark brownish copper complex (S_3) showed bands at (595 nm, 16806 cm-1), belongs to $^2Eg \rightarrow {}^2T_2g$ transition, and bands at (390 nm, 25641 cm-1), which attributed to Metal to Ligand Charge Transfer transition. These bands and their position indicated an octahedral geometry. Magnetic susceptibility for this complex to be (1.78 B.M), this value agreed with distorted octahedral shape about Cu(II) complex. While the molar conductance measurement in DMF referred to that the complex has non-ionic nature

. According to the UV-Vis spectrum of off white cadmium (S_4) complex, no d-d transition related to d^{10}. The synthesized complex are off white colour with the diamagnetic properties, The spectrum of (S_4), in $CHCl_3$, showed bands at (277nm, 36101cm-1), (335 nm, 29850 cm-1) and (400 nm, 25000cm-1), respectively, belonged to ($\pi\rightarrow\pi^*$), ($n\rightarrow\pi^*$) and (MLCT) transitions(18--25).The molar conductance measurements referred to that complex have non-ionic behaviour









Co complex

Table (3): Electronic spectra, Magnetic moment conductance in (DMF) for (S1-S4) complexes (B.M)

No.	Maximum absorption υ_{max}(cm^{-1})	Band assignment	Molar Cond. $S.cm^2.mol^{-1}$	µeff. B.M	Suggested geometry
(S_1)	24510 17857	LMCT $^4T_1g \rightarrow {}^4A_2g$ (pF)	20.31	4.74	O.h
(S_2)	18181 25000	$^1A_{1g} \rightarrow {}^1A_{2g}$ $^1A_{1g} \rightarrow {}^1B_{1g}$	171.24	Dia	S.p
(S_3)	16806 25641	$^2Eg \rightarrow {}^2T_2g$ LMCT	19.23	1.78	O.h
(S_4)	36101 29850 25000	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$ MLCT	21.25	Dia	O.h

Suggested Chemistry Structure of Metal complexes (S1-S4)

According to the outcome acquired from elemental and spectral analysis as well as Magnetic susceptibility and the results of the molar conductance measurement, the structure of the complexes that aforesaid above can be illustrated as follows, figure(4).

Biological activity

The synthesized free ligand (L) and their metal complexes (S1-S4) were estimated in vitro for their ability to reduce the growth of [(E.coli) as gram negative] and [(Bacillusubtilis) as gram positive] are exposed in table (4). Another study of the same ligand and its metal complexes was made against (P. chrysogenum and Aspergillus niger) fungus, DMSO and cwas used as a solvent, table (4). The results showed, that the prepared ligand (L) was active toward E.coli . and no active toward Bacillusubtilis. All prepared metal complexes (S1-S4) were very active toward free ligand (L) . While the results of the antifungal activity of the prepared complexes, Table (4) displayed so as to the metal complexes (S_1-S_4) selected kinds of bacteria compared with the prepared were more toxic compared with prepared free ligand (L) against the same fungi and under the same empirical conditions. The increasing of antifungal effectiveness of prepared metal complexes could be related to the effect of the metal ion on the processing of normal cells. The activity of antifungal could be illustrated by Tweedy's Chelation theory (26). The chelation process between the metal ions and the ligands reduces the polarity of the metal ions, because of the partial participation of its positive charge with the donor groups of the ligand, this process make the penetration of the complexes during the lipid layer of cell membrane easy (26-30).

Figure (4): Suggested Chemistry Structure of Metal complexes (S_1-S_4)

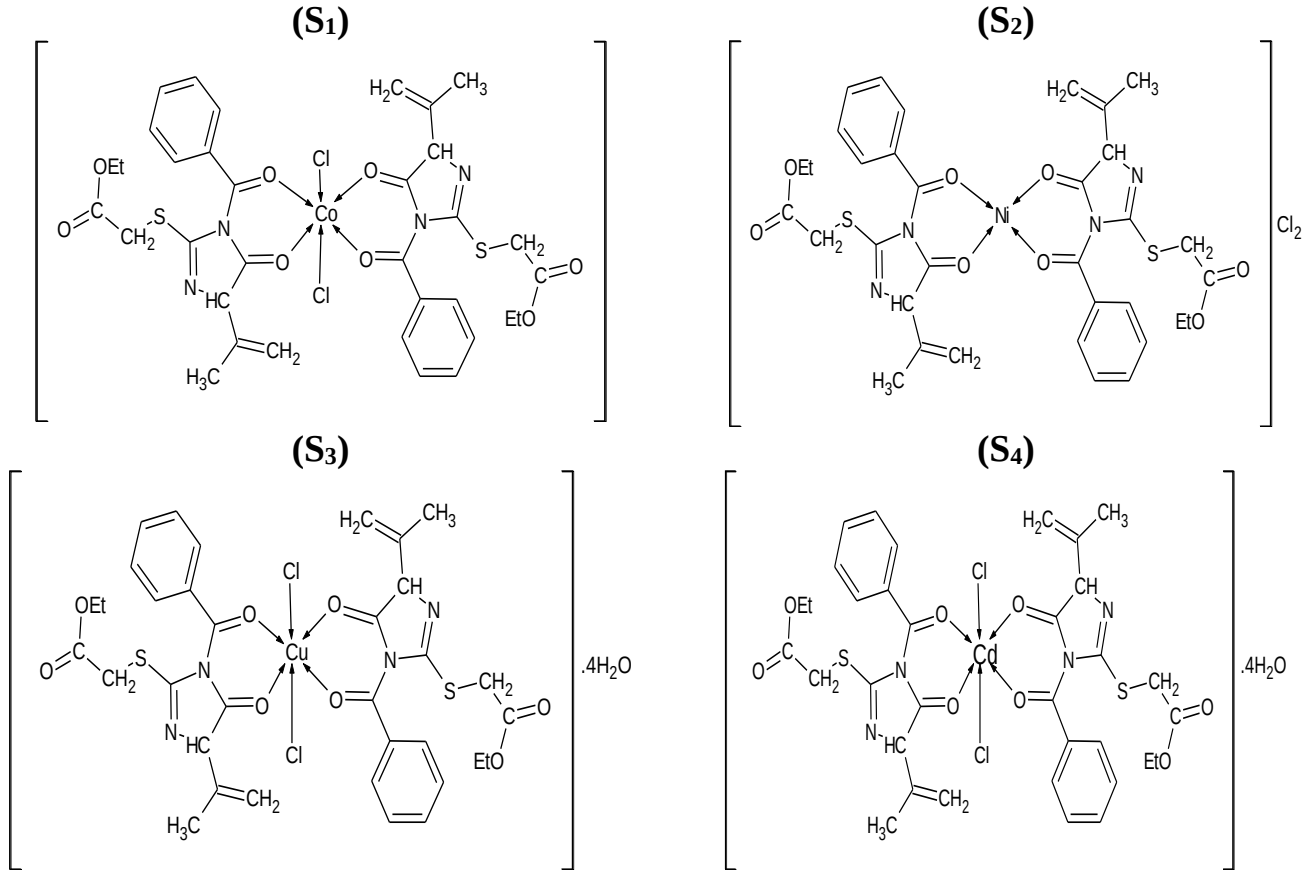


Table (4): Antibacterial and antifungal activities for ligand (L) and their metal (S1-S4) (10-3 µgm.ml-1)

Comp. No.	*E. coli*	*Bacillusubtilis*	*A. niger*	*P. chrysogenum*
Control DMSO	-	-	-	-
(L)	+	+	++	++
(S_1)	++	++	++	++
(S_2)	+++	++	+++	+++
(S_3)	+++	+++	++	+++
(S_4)	++	++	+++	+++

Where : + represent that inhibition zone equal to or less 6mm
++ represent that inhibition zone equal to or less 12mm
+++ represent that inhibition zone equal to 30mm

Conclusion:

The novel imidazole ligand (L) and their metal complexes were synthesized and characterized. The mode of bonding and overall structure of the complexes was determined through physio-chemical and spectroscopic methods. The free ligand (L) and its metal complexes display important antibacterial and antifungal activity; the metal complexes showed highly effectiveness compared with the free ligand. From all above data it was suggested that all complexes have octahedral geometry except nickel complex has a square planer structure, with coordination number 4, while the cupper complex and cadmium complex has an octahedral structure with coordination number 6, that includes four molecules of coordinated water coming from the hydrated salt that used in the preparation process. This supported by the elemental analysis data and the water peaks were detected in the FTIR spectrum.

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