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Syntheses, Characterization of a New Legend 2-Hydroxy-N'-(5-Phenyl-1,3,4-Oxadiazol-2-yl) Benzohydrazide with Some Transition Metal Complexes

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Abstract

In the current study, many new derivatives for 1.3.4-oxadiazole with its complexes using salts of transition metals such as nickel, copper, iron, cadmium, cobalt and chromium, were synthesized. The prepared ligands and their complexes were and identified using H-NMR and mass spectrometry in addition to FT-IR spectroscopy. Magnetic susceptibility and conductivity measurements were also performed. The hyperchem application was also used to perform theoretical calculations using the MP3 method[1] to study the stability energy of the compounds to determine the binding sites of the ligand with the metallic elements to form complexes.

Key words: ligand, complexes, characterization, Hyperchem, electrostatic potential

Introduction

Oxadiazole and its derivatives were pentagonal heterocyclic compounds containing one oxygen and two nitrogen atoms. Oxadiazole was present in various forms as 1,2,5-oxadiazole, 1,2,4-oxadiazole, 1,2,3-oxadiazole and 1,3,4-oxadiazole [2]. The 1,3,4-oxadiazole isomer is attributed to the (unstable) diazoxitonotomer[3].

Figure 1: Oxadiazole Isomers

The compounds containing the nucleus 1,3,4-oxadiazole have an important benefit in the biological field as they have many biological activities such as anti-bacterial [4,5], anti-fungal [6], anti-inflammatory [7], anti-cancer [8], anti-cancer [8].

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anticonvulsant [9], interferon stimulator [10], anti-HIV [11], anti-diabetes [12], anti-tuberculosis [13], lipid peroxidation inhibitor [14], insecticides [15] and antioxidants [16]. They were also used in many equipments and devices such as corrosion inhibitors [17], fluorescent and color chemical sensors [18], dyes [19], polymers [20], and light-emitting diodes [21].

Experimental

Synthesis of Benzohydrazide (A)

A mixture of Methyl benzoate (50.5 ml, 0.4 mol) and hydrazine monohydrate (20ml, 0.4 mol) in absolute ethanol (100 ml) were refluxed for 6 hours, the mixture was evaporated to half volume, cooled, filtered and washed with absolute ethanol[22], the solid (A) was lighting white with melting point 115^{0}C, yield 95% .

Synthesis of 5-phenyl-1,3,4-oxadiazole-2-thiol (B) and checked with TLC.

Benzohydrazide (A) (13.6 gm, 0.1 mol), potassium hydroxide (5.6 gm, 0.1 mol) and carbon disulfide (6ml, 0.1 mol) were refluxed in absolute ethanol (100 ml), the solvent was evaporated and acidified with HCl (10%), then the precipitate was filtered and the solid result was recrystallized from ethanol absolute [23]. The solid (B) was white yellowish, melting point 220 ^{0}C, yield 92.3%.and checked with TLC

Synthesis of 2-hydrazinyl-5-phenyl-1,3,4-oxadiazole(C)

5-phenyl-1,3,4-oxadiazole-2-thiol (B) (9gm, 0.5 mol) and hydrazine monohydrate (5ml , 0.1 mol) in ethanol absolute as solvent (50 ml) were refluxed for 15 hours. White precipitate was appeared in round bottom[24]. The precipitate was filtered and recrystallized from absolute ethanol, melting point 226^{0}C, yield 72% .and checked with TLC.

Synthesis of 2-hydroxy-*N*'-(5-phenyl-1,3,4-oxadiazol-2-yl)benzohydrazide

The ligand was synthesized by condensation of 5g 0.028 mole of 2-hydrazinyl-5-phenyl-1,3,4-oxadiazole(C) and 2.5ml 0.028 methyl salicylate (2-methylhydroxy benzoate) in absolute ethanol (50 ml), then the mixture was refluxed for 10 hours (monitored by TLC) [25][26]. The ligand was precipitated, filtered and recrystallized from absolute ethanol to get yellow-brown ligand melted at 230^{0}C, yield 88%.and checked with TLC.

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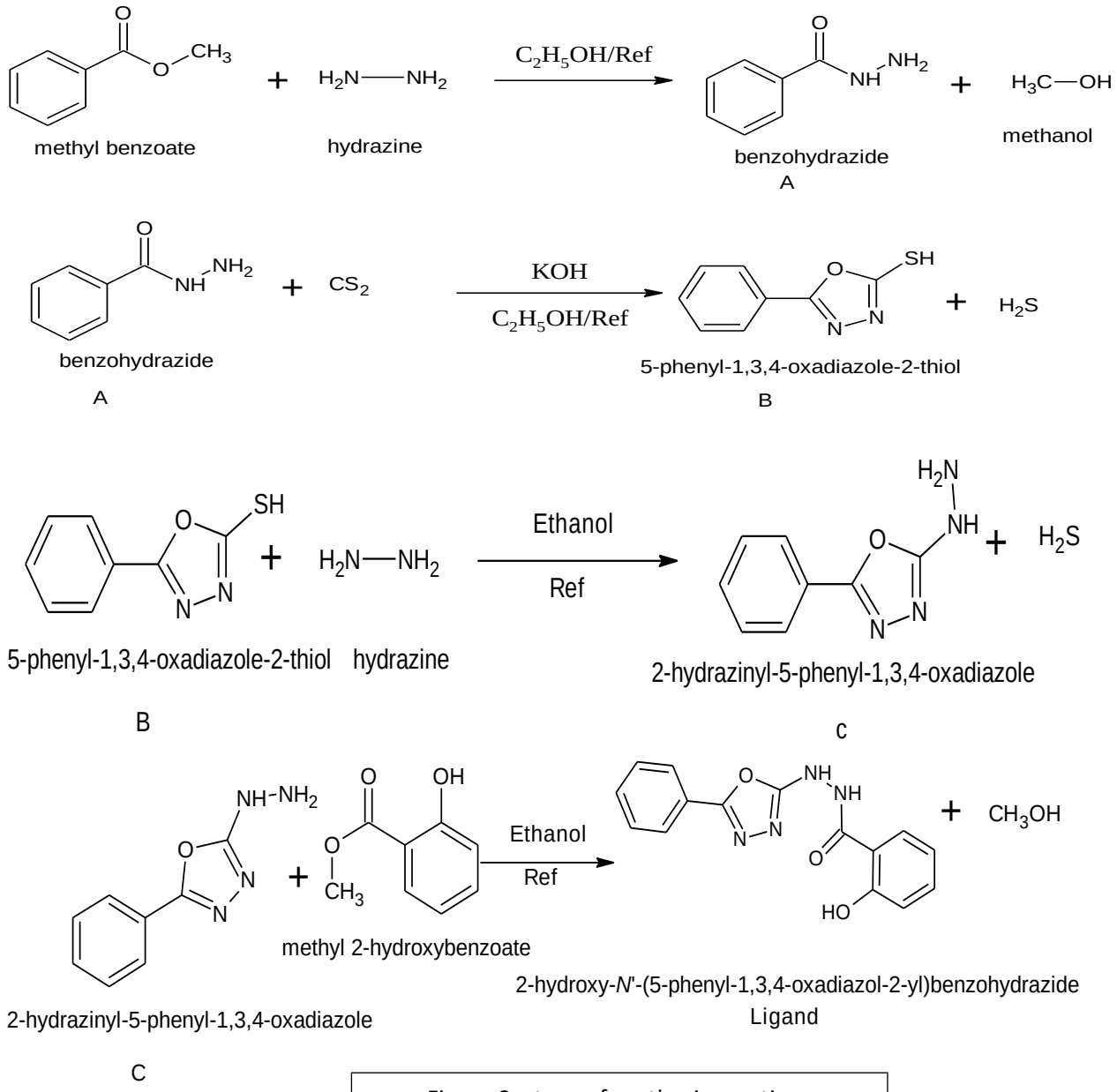

Figure 2: steps of synthesis reactions

Preparation of complexes

The complexes were synthesized by mixing of (0.001 mol) from the ligand with salts ($COCl_2.6H_2O$, $CdCl_2.6H_2O$, $CuCl2.6H_2O$ and $NiCl_2.6H_2O$) in (100 ml) absolute ethanol and refluxed for 2 hrs. The precipitate was filtered and wash several times with ethanol or aqueous ethanol to removed unreacted salts or ligand, then the precipitated complexes were dried, and checked with TLC[27] .

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Analysis and physical measurements

No	formula	Color	M.Wt	M.p °C	Λ Scm^2 mol^{-1}
1	C15H12N4O2 (L)	white	296	230	------
2	Cr(L) Cl_3	green	454	323	**10**
3	Co (L) Cl_2H_{2O}	White yellowish	444	215	**12**
4	Ni(L)Cl_2	Light green	425	220	**11**
5	Cu(L)Cl_2	Light gray	430	217	**10**

Table 1: Analysis and physical measurements

3.1 FT-IR spectral

FT-IR of the synthesized ligand and its complexes were carried out using KBr disc to ligand and CsI for complexes . The free ligand (L) exhibited six major bands which ware attributable to (υOH) (3298) cm^{-1} (υNH_2) (3194) cm^{-1}, (υC=N) (14481) cm^{-1}, (υC-O-C) sym (1230Cm^{-1}), (υ C-O-C) asy (1319Cm^{-1}) and (1072Cm^{-1}) structure movement bands respectively, as shown below (table 2). New bands were formed Attributed to the coordinated (M- N) and (M-Cl) bonds and appeared at the region(601-327)cm^{-1}and (277-235)cm^{-1} respectively. This indicated that the coordinate occurred through the (N), and (Cl) atoms .

	OH	NH	C-H aromatic	C=O	C=C aromatic	C=N Hetro	C-O-C ASY	C-O-C SY	Str movment	M-N	M-Cl
L1	3298	3194	3055	1631	1531	1481	1319	1230	1072		
L1Co	3298	3194	3055	1631	1531	1500	1319	1230	1072	327	235
L1Ni	3302	3236	3055	1616	1558	1431	1327	1288	1076	601	277
L1Cu	3271	3116	3055	1639	1531	1481	1384	1303	1010	482	270

Table 2 FT-IR spectra of ligand and it is complexes

The ^{1}H-NMR spectra of the ligand showed signals at (13.94ppm, H) and (5.81ppm, 2H) due to O-H protons and NH-NH protons respectively .signals at [(6.99-8.03)ppm, 9H] due to chemical shifts of aromatic ring protons linking the oxadiazole ring[29] as showed in the figure below [figure 15] .

3.3 Mass spectra

The mass spectra of ligand showed the molecular ion peak at 296 m/z which was in conformity with the molecular formula $C_{15}H_{12}N_4O_3$. Other peaks ware due to the subsequent fragments like $[C_{15}H_{11}N_4O_2]^+$=279 m/z , $[C_{15}H_{11}N_4O]^+$=263 m/z , $[C_8H_7N_4O]^+$=175 m/z , $[C_8H_6N_3O]^+$=160 m/z ,

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$[C_8H_5N_2O]^+$=145 m/z , $[C_7H_5O_2]^+$=121 m/z , $[C_7H_5NO]^+$=119 m/z , $[C_7H_3O]^+$=103 m/z, $[C_6H_6]^+$=77 m/z,$[C_4H_3]^+$=51 m/z.

The mass spectral of the Cr(III) complexes showed molecular ion peaks at 454 m/z corresponding to $[[Cr(L)\ Cl_3]^{\cdot+}$ stoichiometry. This complex showed another fragmentation peaks at 419 m/z ,383 m/z , 348 m/z due to loss one , two and three chlorine atom respectively. The mass spectral of the Co (II) complexes showed molecular ion peaks at 444 m/z corresponding to $[Co(L)H_2OCl_2]^{\cdot+}$ stoichiometry. This complex showed another fragmentation peaks at 426 m/z ,390 m/z due to loss one and two chlorine atom respectively . The mass spectral of the Ni(II) complexes showed molecular ion peaks at 424 m/z corresponding to $[Ni(L)Cl_2]^{\cdot+}$ stoichiometry . This complex showed another fragmentation peaks at 390 m/z ,354 m/z due to loss one and two chlorine atom respectively . The mass spectral of the Cu(II) complexes showed molecular ion peaks at 430 m/z corresponding to $[Cu(L)Cl_2]^{\cdot+}$ stoichiometry . This complex showed another fragmentation peaks at 395 m/z ,359 m/z due to loss one and two chlorine atom respectively .

3-3: Molecular Electrostatic potential(MEP) .

Electrostatic potential is a very important in parameter finding the active site in the molecule system with a positive charge. The species that have positive charge tend to attack a molecule where the electrostatic potential is strongly negative (electrophilic attack). Electrostatic potential of free ligands were measured and plotted as 2D contour to find the active site of molecule[30] as shown in figures[4-9].

4.1 Biological Study

The antibacterial and antifungal efficiency of ligand and its complexes were evaluated by using agar spread method. Two type of bacteria have been used, Gram positive bacteria as (*Staphylococcus aureus*) and Gram negative bacteria as(*Pseudomonas aeruginosa*), using Ampicillin as standard drug ,and tow type of fungi (*Candida albicans*) and (*Candida kruse*), using Flucanazole and Itraconazole as standard drug.

The bacteria and fungi inhibition was calculated in millimeter. nutrient agar was used as culture medium .dimethyl Sulfoxide used as diluent the concentration of all compounds in this dilwent was 10^{-3}, using disc susceptibility test. The dishes were put in the incubator for 24hr. at 37℃[31] . according to the results in table (3), all compound possessed good anti-bacterial and anti-fungal activity. Out of all the synthesis compounds Nickel(II) complex mor more bactericidal than others even the standard drug.

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Candida kruse	Itraconazole C2	Flucanazole Control 1	Candida albicans	Itraconazole Control 2	Flucanazole Controle 1	DMSO		NO
15	22	14	10	20	15	0	L3	1
10	22	14	11	20	15	0	L3Cr	2
12	22	14	11	20	15	0	L3Co	3
12	22	14	11	20	15	0	L3Ni	4
12	22	14	10	20	15	0	L3Cu	5

Table(3)Anti-fungal data of ligand and its complexes, data represented the diameter of the zone growth inhibition (mm)

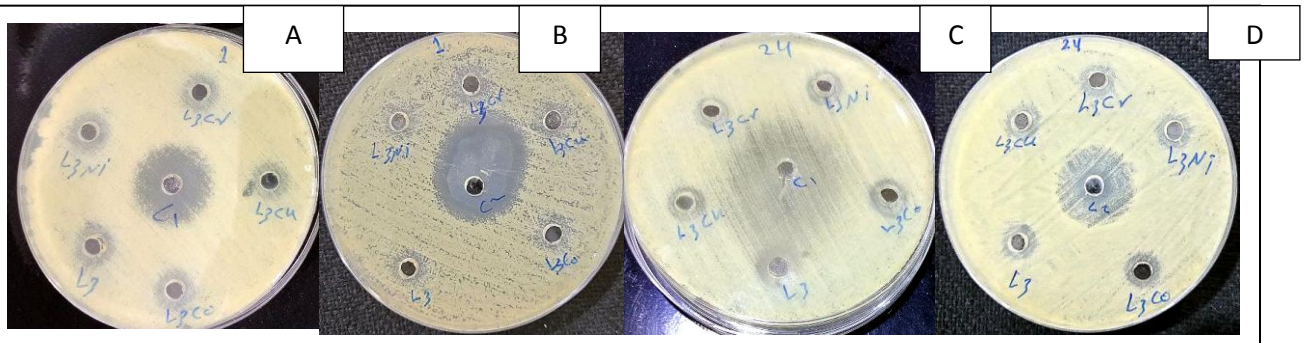

Figure 2 anti-fungi

A: Candida albians with Fluconazole control1

B: Candida albians with Itraconazole control2

C: Candida kruse with Fluconazole control1

D: Candida kruse with Itraconazole control2

Psedo -Ve	Staph +Ve	Ampicilline Controle	DMSO		NO
18	18	15	0	L3	1
0	8	15	0	L3Cr	2
16	0	15	0	L3Co	3
0	14	15	0	L3Ni	4
18	16	15	0	L3Cu	5

anti-bacterial data of ligand and its complexes, data represented the diameter of Table(4) the zone growth inhibition (mm)

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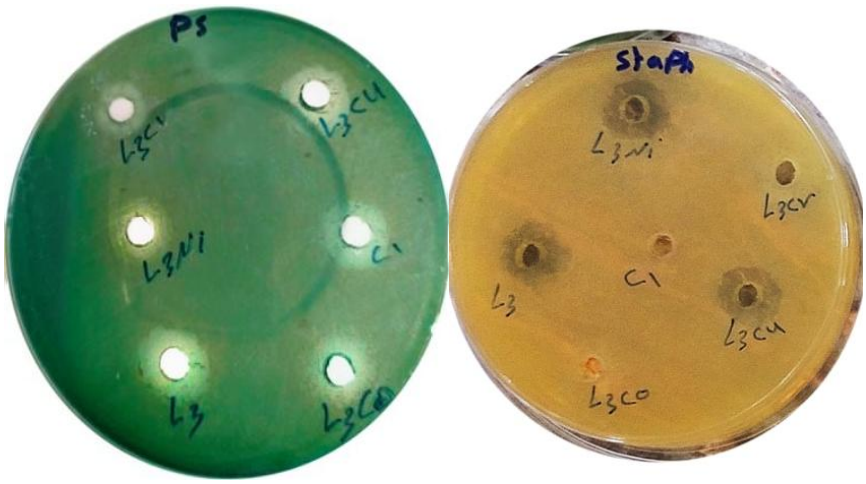


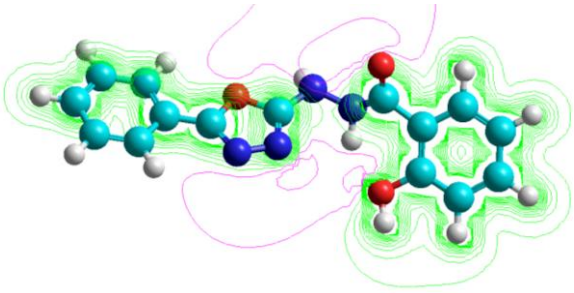
Figure 3 anti – bacterial

A: against *Staphylococcus aureus.*

A B: against *Pseudomonas aeruginosa* B

conclusion

A 1,3,4-oxidiazole derivative acts as a two-chelated ligand. The spectral data show the participation of two groups of N-H and C-N-C in coordination with a central transition metal ion. Various techniques such as 1H.NMR spectra as well as molar conductivity .



Figure(5) HOMO Electrostatic Potential as Contours for L

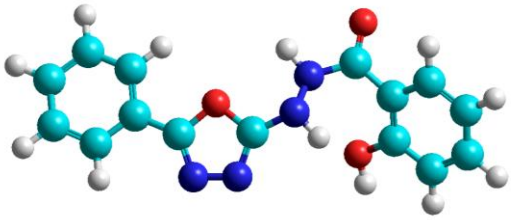


Figure 4 . Graphical presentation of stereochemistry of the Ligand

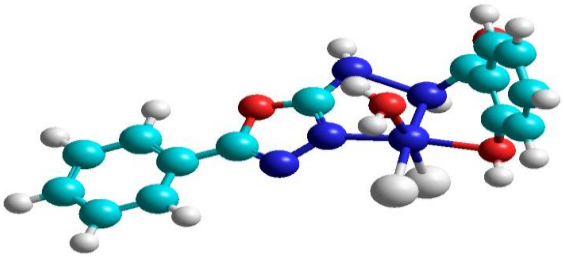


Figure 7 . Graphical presentation of stereochemistry of the complex $[Co(L_1)Cl_2H_2O]$

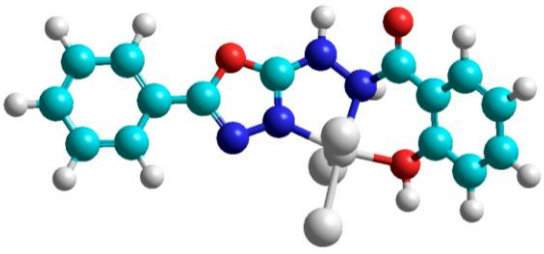


Figure 6 . Graphical presentation of stereochemistry of the complexes $[Cr(L_1)\ Cl_3]$

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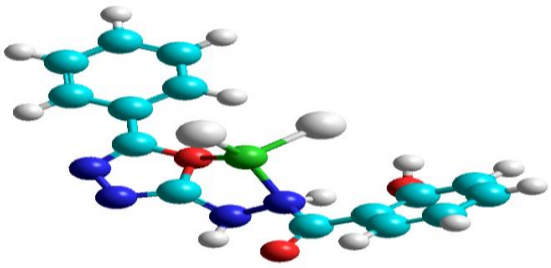


Figure 9 . Graphical presentation of stereochemistry of the complexes $[Cu(L_1)\ Cl_2]$

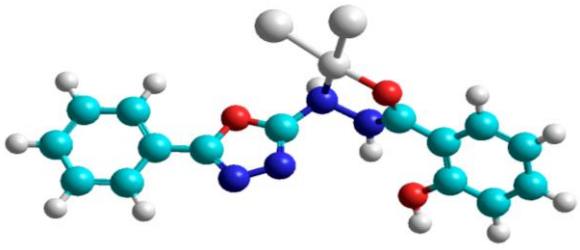
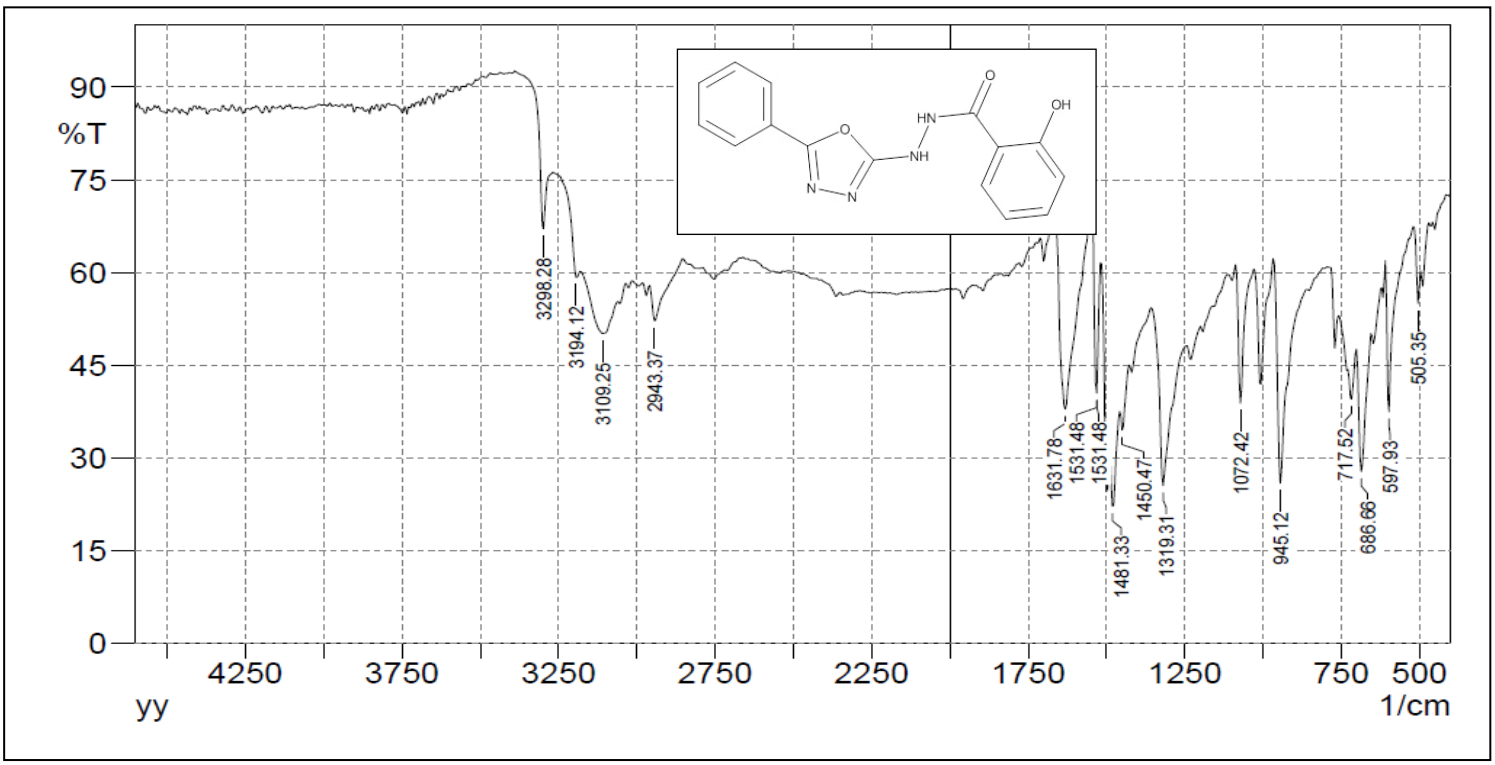


Figure 8 . Graphical presentation of stereochemistry of the complexes $[Ni(L_1)\ Cl_2]$



L

Figure 10

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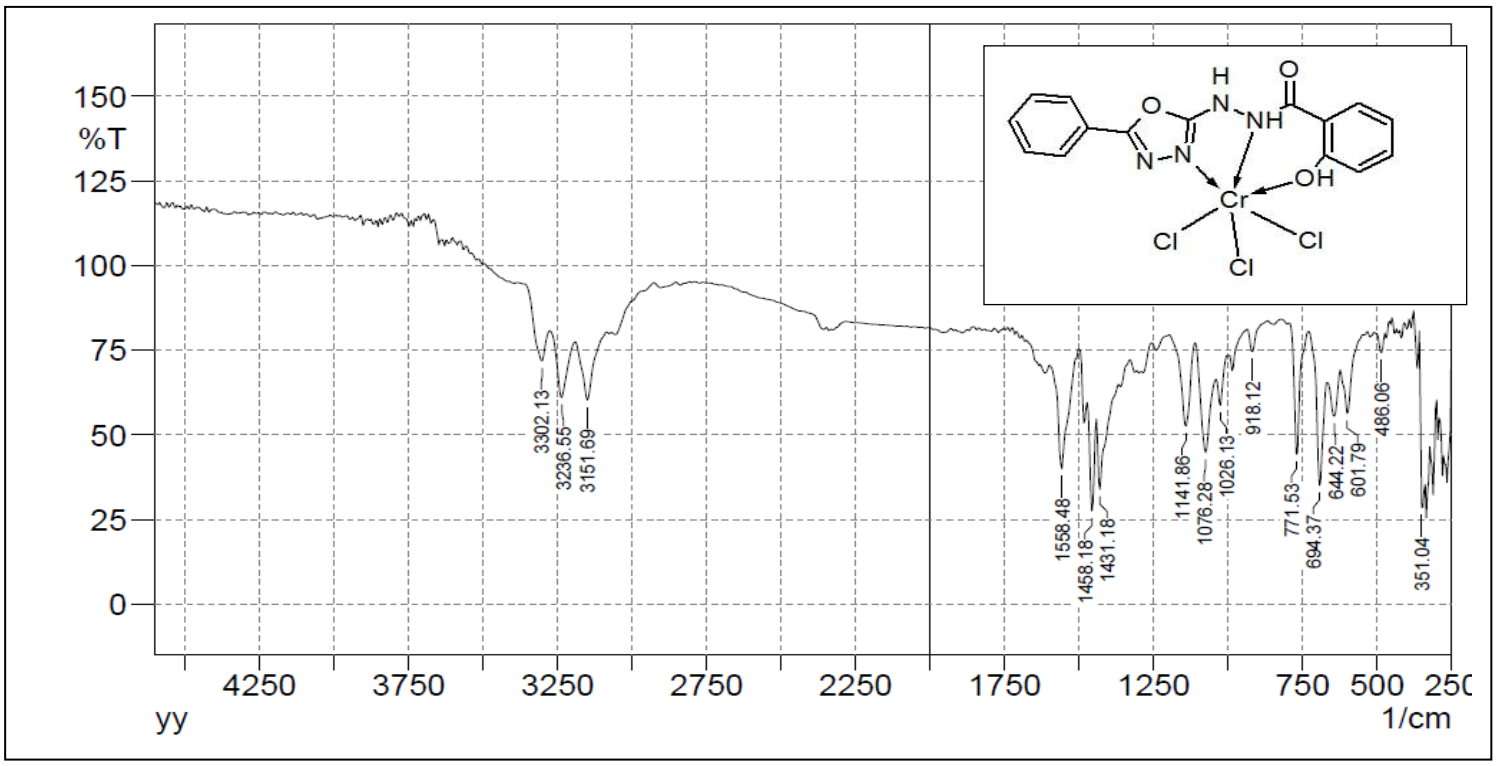
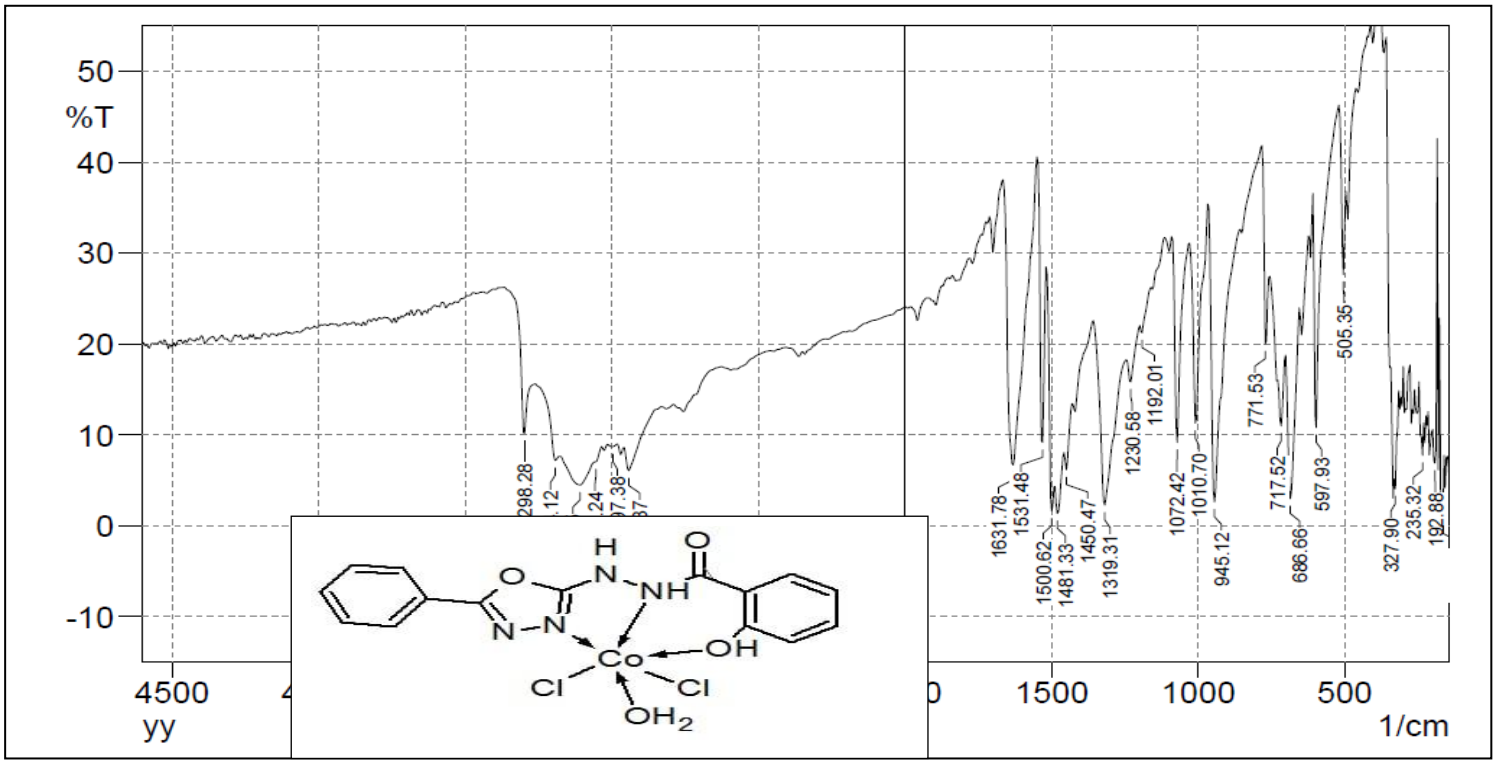


$Cr(L_1)Cl_3$

Figure 11



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$Co(L)Cl_2H_2O$

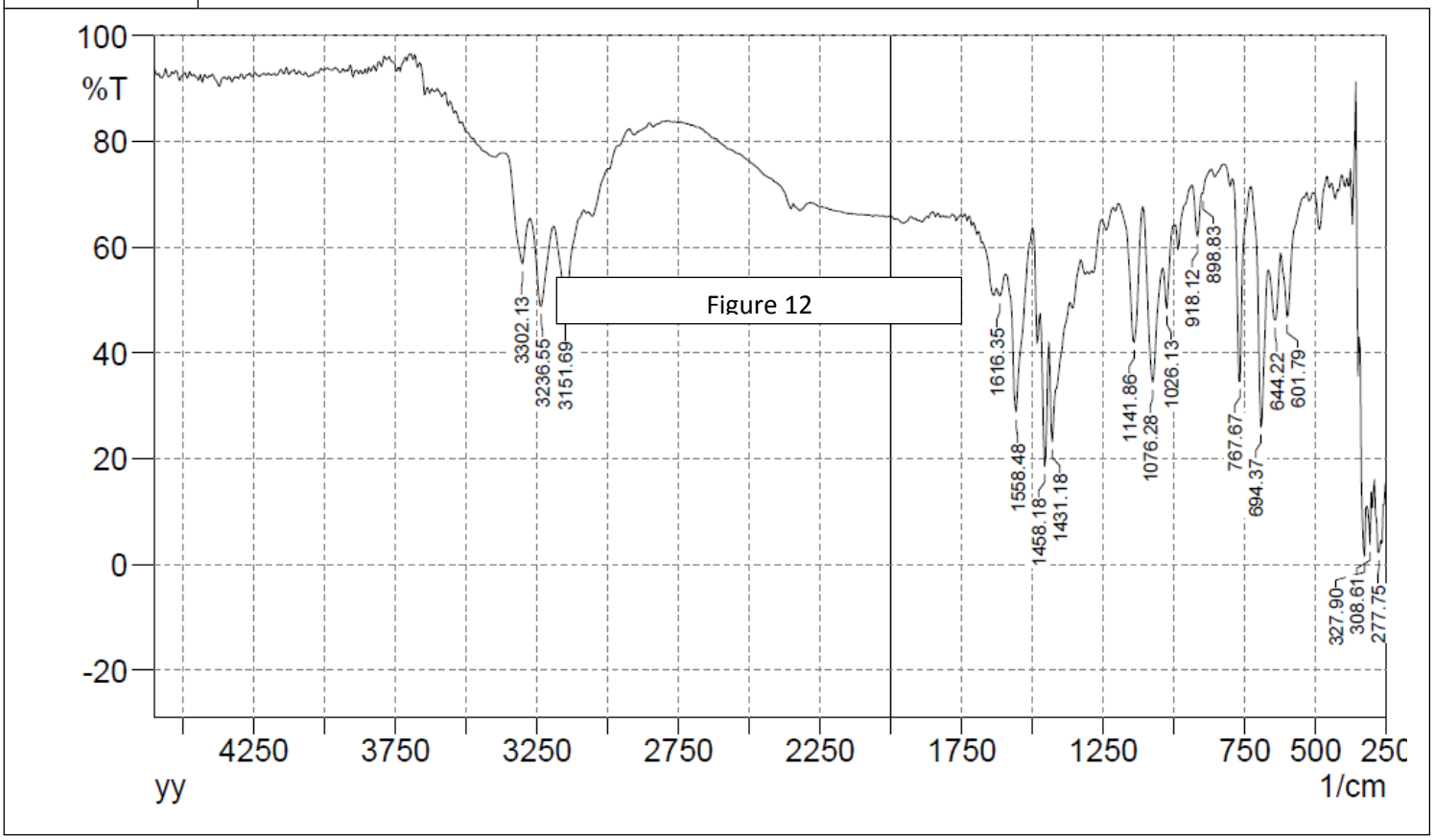
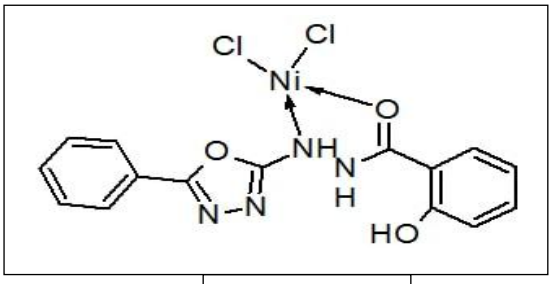


Figure 12



$Ni(L_1)Cl_2$

Figure 13

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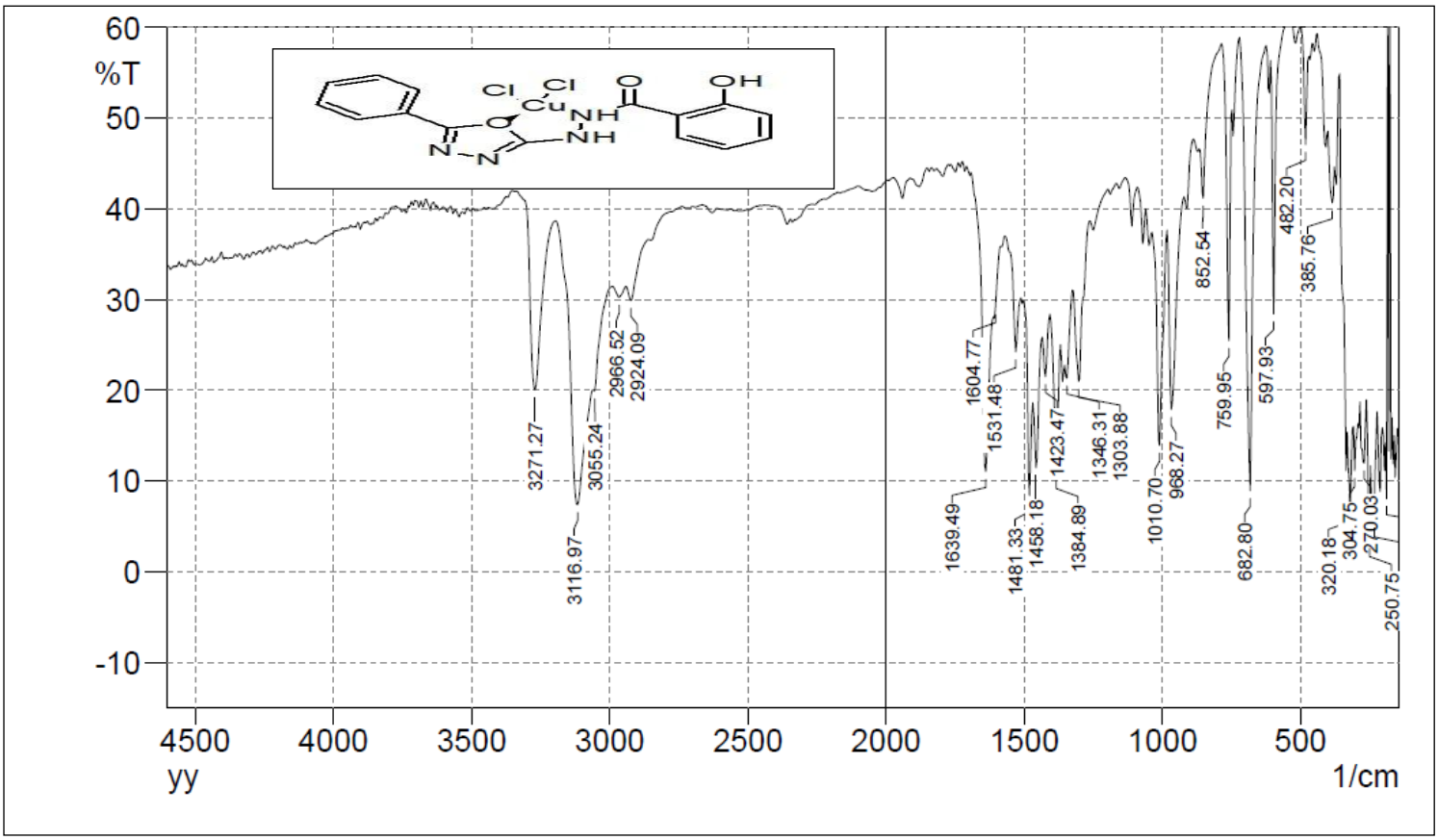

Cu(L_1)Cl

Figure 14

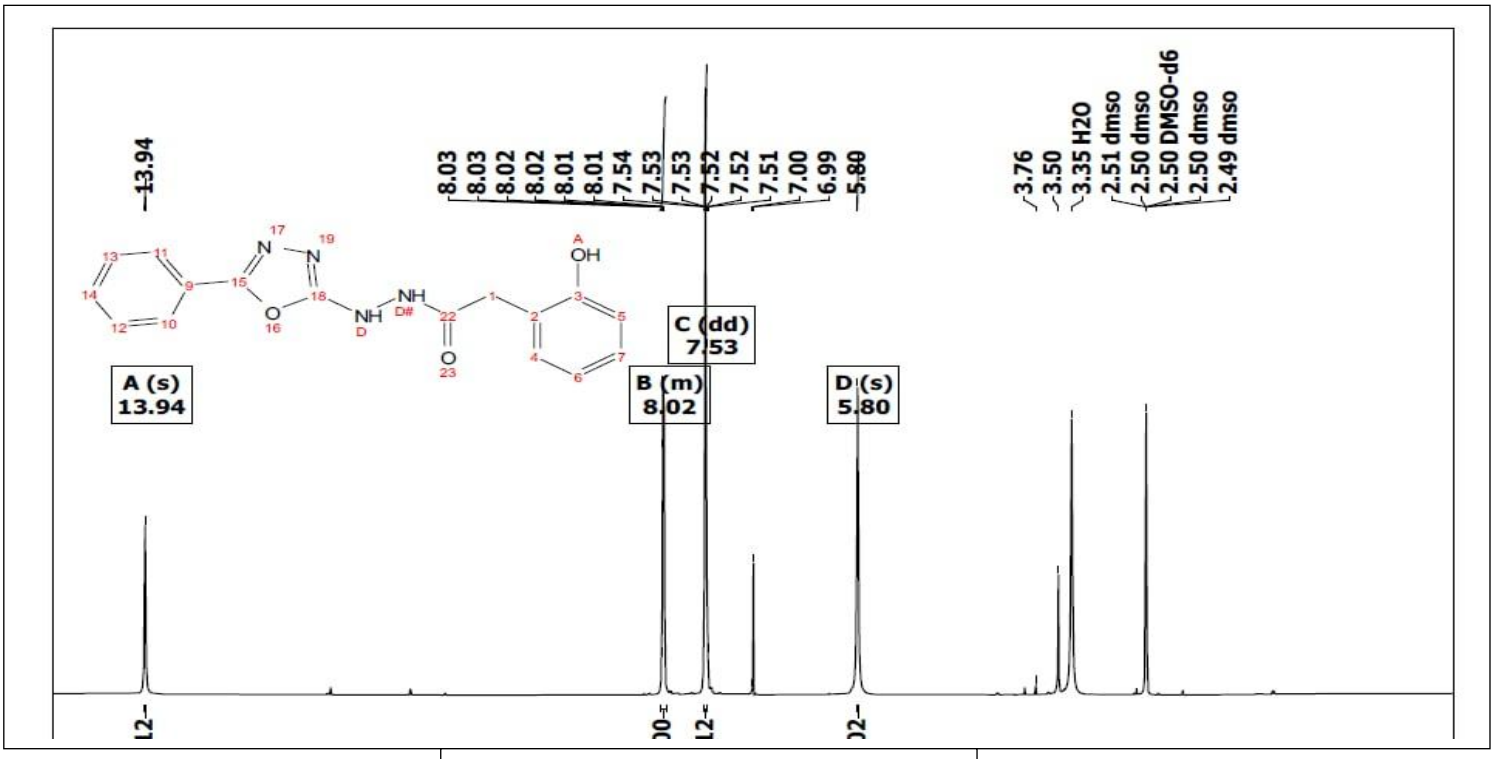

Figure 15 H-NMR spectra of Ligand

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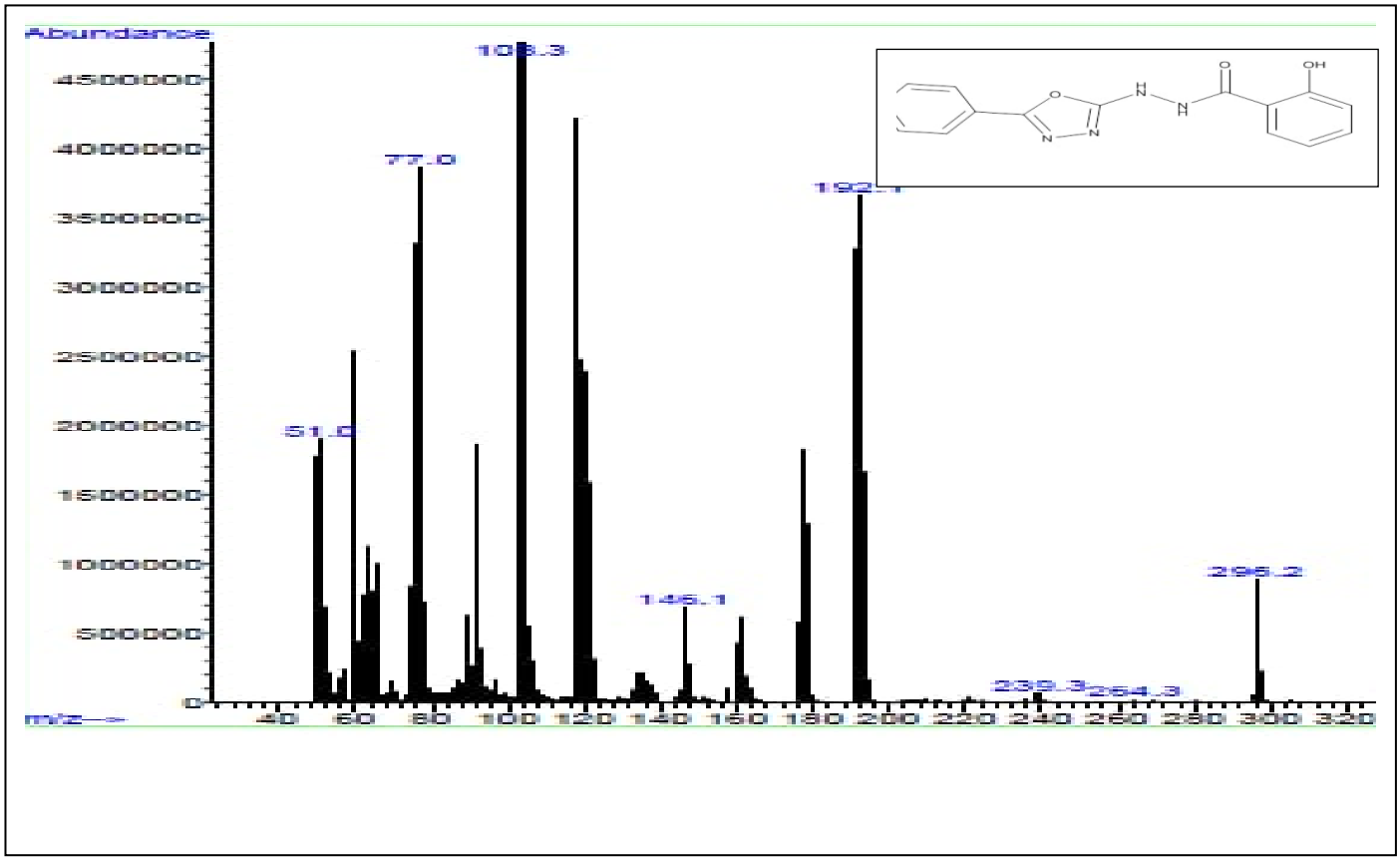

Figure16 Mass spectra of ligand

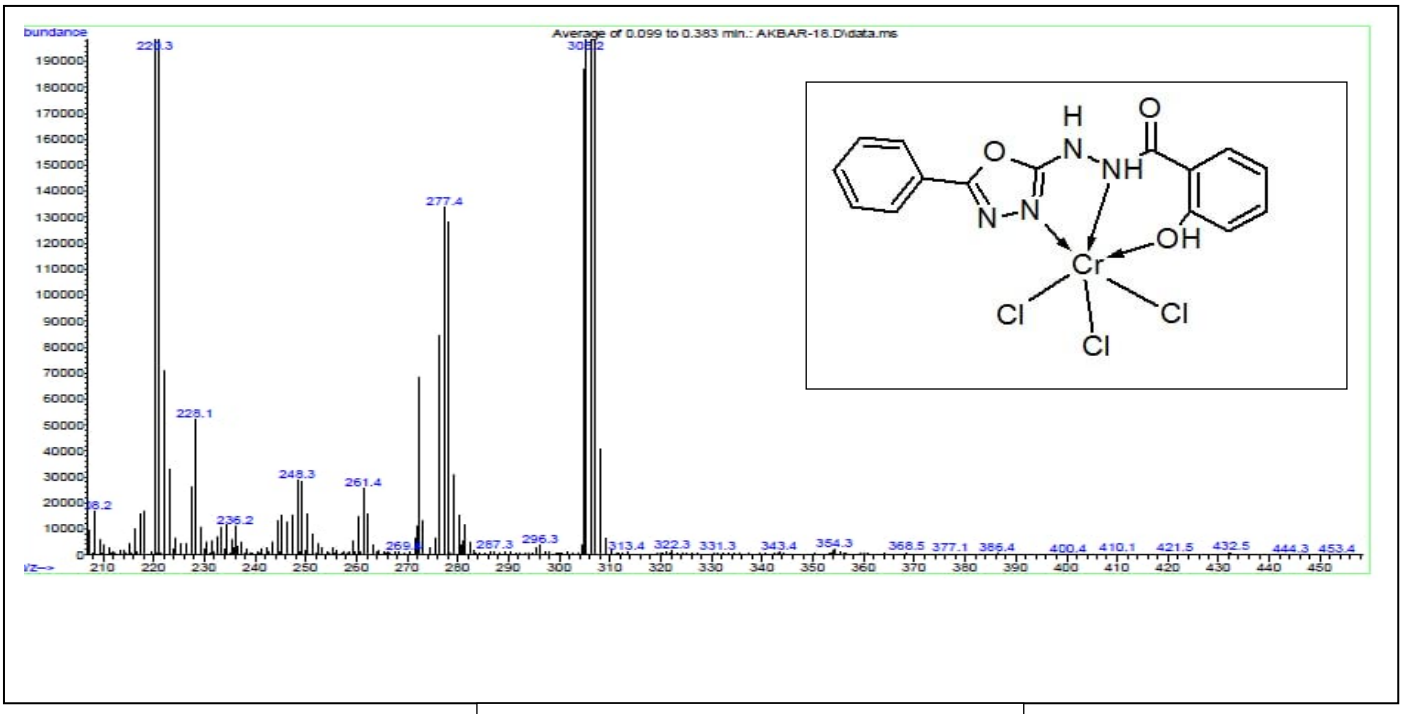

Figure 17 Mass spectra of $Cr(L)Cl_3$

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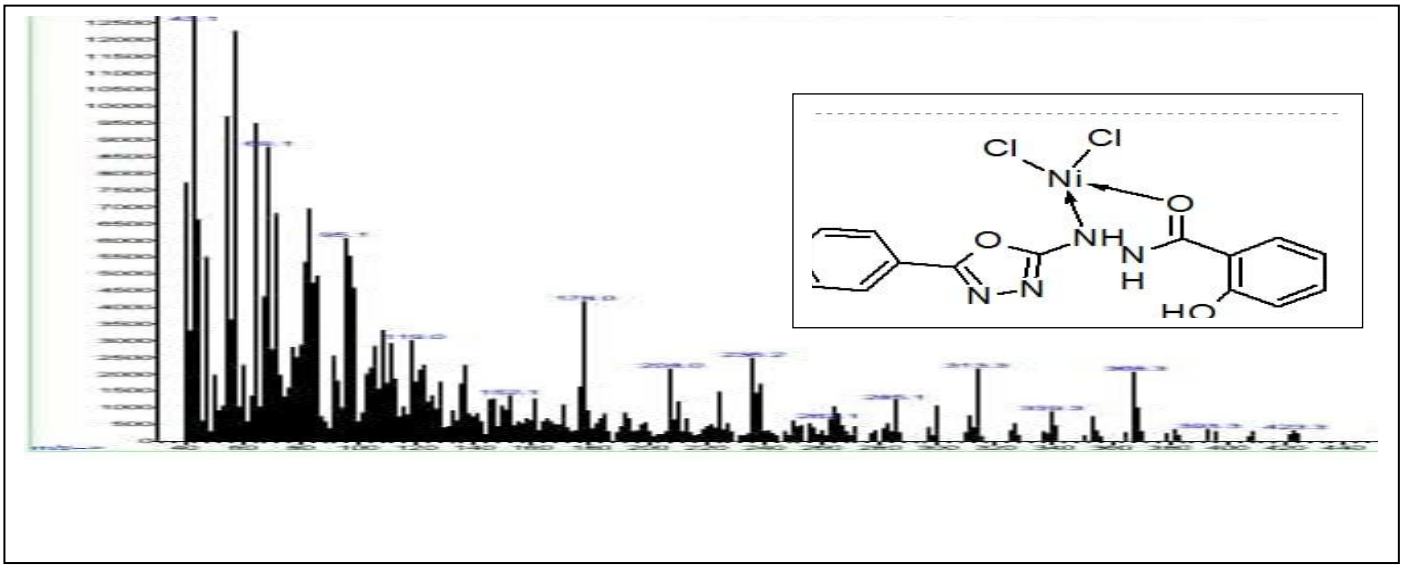

Figure 18 Mass spectra of $Ni(L)Cl_2$

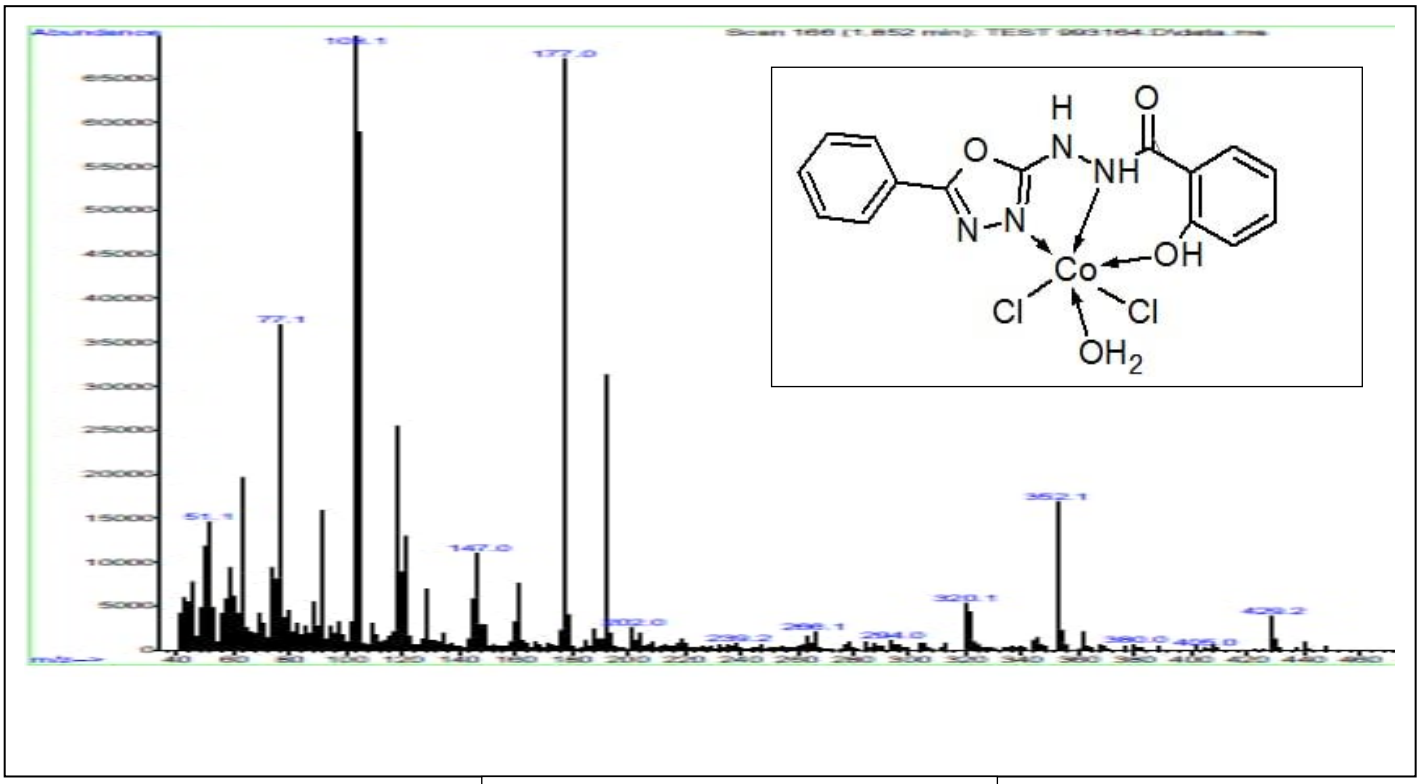

Figure 19 Mass spectra of $Co(L)Cl_2H_2O$

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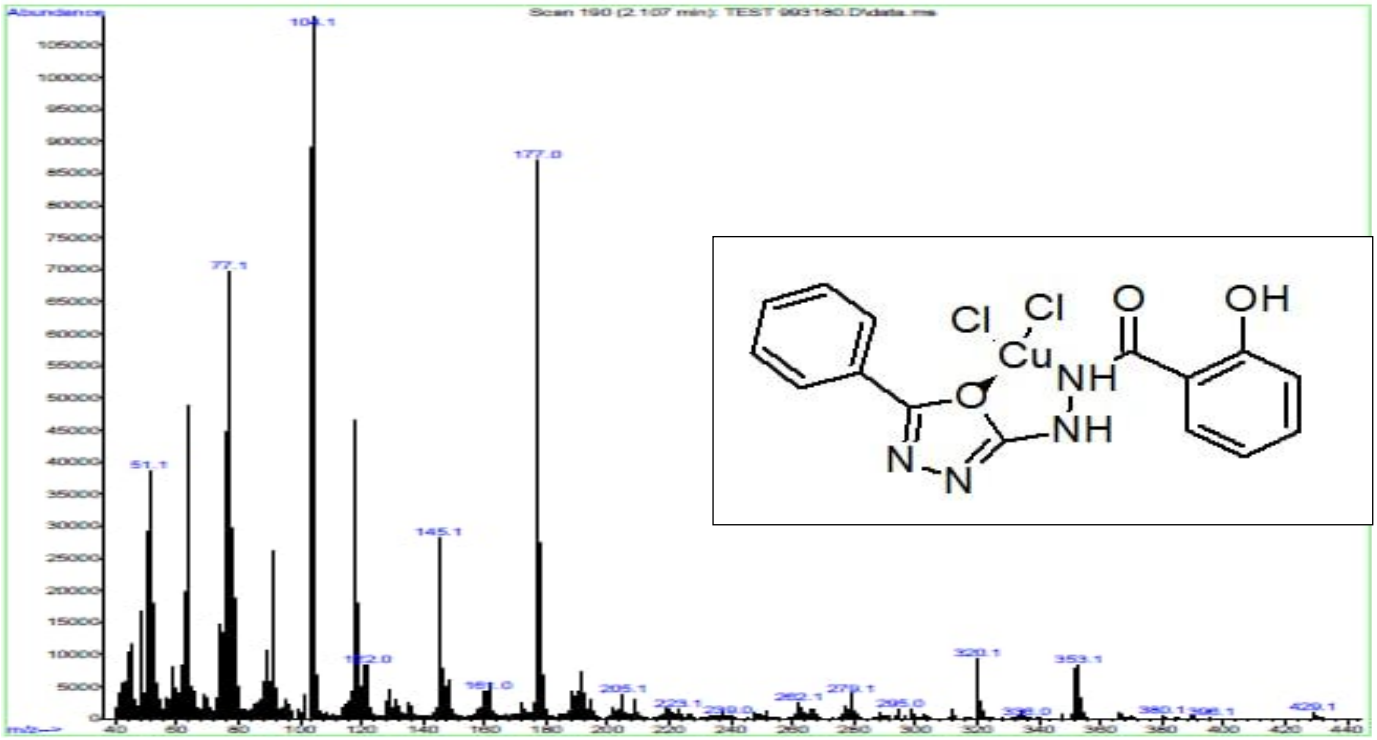

Figure 20 Mass spectra of $Cu(L)Cl_2$

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