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Volume 6, Number 2, June 2017

Synthesis , Characterization , Antimicrobial New 2,2'-[(1*E*,2*E*)-ethane-1,2-diylidenedi(2*E*)hydrazin-1-yl-2-ylidene]bis (5-methyl-1,3,4-oxadiazole) and their transition metal complexes

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Abstract

Transition metal complexes of new legend 2,2'-[(1*E*,2*E*)-ethane-1,2-diylidenedi(2*E*) hydrazin-1-yl-2-ylidene] bis (5-methyl-1,3,4-oxadiazole) with some transition metal ion such as Cr^{3}, Co^{3+}, Ni^{2+} were synthesis ,characterization by magnetic susceptibility measurements, conductance, elemental analyses, 1HNMR, IR, and mass spectra. The electrolytic behavior were confirmed from their conductance. data spectral study of transition metal complexes suggest octahedral geometry for Cr^{3+}, Co^{3+} ion , square planer geometry for Ni^{2+}.The effective magnetic moment of cobalt complex is 0.91 that mean the Co^{2+} oxidation to Co^{3+}. The complexes and ligand were tested against two types of bacteria (*Staphylococcus aureus*, *Escherichia coli*) all prepared complexes showed good biological activity.
Keywords: - Oxadiazole, Transitions metal complexes, biological activity.

الخلاصة

حضر الليكاند الجديد 2,2'−[(1*E*,2*E*)−ethane−1,2−diylidenedi(2*E*) hydrazin−1−yl−2−ylidene]bis(5−methyl−1,3,4−oxadiazole) مع بعض العناصر الانتقالية مثل Cr^{3}, Co^{3+}, Ni^{2+} وشخصت باستخدام قياسات الحساسية المغناطيسية وقياسات التوصيلية والتحليل الدقيق للعناصر (CHN) وتقنيات أخرى منها طيف الاشعة تحت الحمراء (IR) وطيف البروتون النووي المغناطيسي (H^{1}NMR) وطيف الكتلة . ومن النتائج التي تم الحصول عليها اقترح الشكل الثماني السطوح لمعقد Co^{3+} Cr^{3}, والشكل المربع المستوي لمعقد Ni^{2+} . العزم المغناطيسي الفعال لمعقد الكوبلت بين Co^{2+} الى Co^{3+} تأكسد . اختبار الفعالية البيولوجية لليكاند ومعقداته ضد نوعين من البكتريا (*Staphylococcus aureus*, *Escherichia coli*) أعطت نتائج جيدة .

1. Introduction

1, 3, 4 -oxadiazole is classify as heterocyclic aromatic chemical compound of

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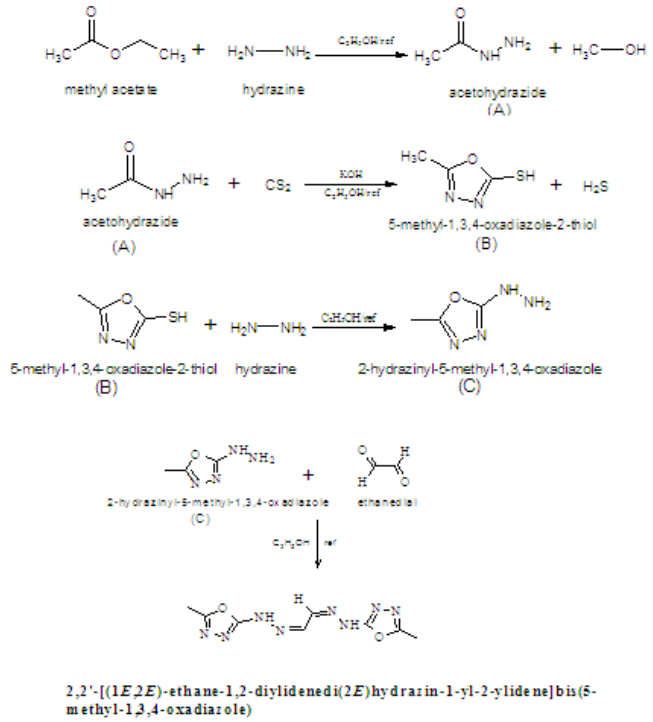
the azole family; with the molecular formula $C_2H_2N_2O$. The1,3.4- oxadiazole exist in different isomeric forms such as 1,2,4- oxadiazole, 1,2,5- oxadiazole, 1,2,3- oxadiazole and 1,3,4-oxadiazole(Kumar et al. 2012) . The 1,3,4- oxadiazole heterocyclic compound which has been commonly used as a privileged scaffold to produce various novel pharmaceutical drug such as : Antimicrobial(Prakash et al. 2009) P, Antifungal(Frank & Kalluraya 2005), anticancer (Rao & Anto 2013), P Antihypertensive(ILANGOVAN et al. 2015) , Anti-inflammatory(Burbuliene et al. 2004) and Anticonvulsant(Akbarzadeh et al. 2003) . This class of material also has gained the worth of modern application such as Insecticidal (Kolli 2016), Antioxidant (Kuş et al. 2008) , Dyes (Hunger 2003) and Polymers (de Oliveira et al. 2012) (de Oliveira, Lira, Barbosa-Filho, Lorenzo, & de Athayde-Filho, 2012) materials[11] .1,3,4-oxadiazole derivatives are as well used as employed electron conducting and hole blocking materials in organic light-emitting diodes(LEDS)[12], Also use in the extraction of transition metal complexes .

2. Experimental

2.1. Synthesis of the ligand:

New ligand 2, 2'-[(1*E*, 2*E*)-ethane-1, 2-diylidenedi (2*E*) hydrazin-1-yl-2-ylidene] bis (5-methy l-1,3,4-oxadiazole) (Scheme 1) was prepared as follows:-
ethyl acetate (0.1mol,10.5ml) was added to hydrazine monohydrate (0.15mol,7.5ml) in ethanol absolute (100ml). The resulting mixture was heated under reflux for (6hours). The mixture was concentrated**,** The product was filtered and washed with ethanol to give the **product** (A) **Acetic acid hydrazide** (liquid) , colorless ,boiling point 129 °C, yield 90%) (Manjunath et al. 2015).

Acetic acid hydrazide (A) (0.1mol, 10ml) mix with (0.1mol, 5.6g)of Potassium Hydroxide dissolved in(100 ml) absolute ethanol then added carbon disulfide (0.1mol,6ml). The resulting mixture was mixing by shaking and heated at (80) °C under reflux for (20hours). The resultant was concentrated, and carefully acidified with hydrochloric acid HCl (5%) to give yellow precipitate. The product was filtered and washed with cold water and ethanol to give the desired product 5-methyl-1,3,4-oxadiazole-2-thiol (B) (solid, yellow, melting point 188 °C, yield %89)(Khiati et al. 2007)(Hayal 2014).
5-methyl-1,3,4-oxadiazole-2-thiol (B)(0.1mol, 11.6g) was mixed with access of hydrazine (0.1mol,4ml) dissolved in (50ml) ethanol and refluxed to (10hours) then allowed to cool, the yellow precipitate of 2-hydrazinyl-5-methyl-1,3,4-oxadiazole(C) was filtered off and recrystallized from ethanol (solid, pale yellow, melting point 222°C, yield 90%) (Moustafa et al. 2002). The Schiff bases have been synthesized by condensation of 2-hydrazinyl-5-methyl-1, 3, 4-oxadiazole(C) and glyoxal in 2:1 molar proportions in ethanol absolute (100ml) for (3hours). The brown precipitate of ligand formed were filtered, washed with cold ethanol absolute and recrystallized from hot ethanol absolute(solid, brown, melting point 197°C, yield 80%) (Hanif & Chohan 2013). scheme1



Scheme 1. Synthesis of ligand (L)

2.2. Preparation of complexes

A solution of $CoCl_2.6H_2O$, $CrCl_3.6H_2O$ and $NiCl_2.6H_2O$((0.001 mol) was mixed with (L) (0.001 mol) in ethanol absolute and refluxed for 2 hrs. the precipitated complex was filtered, washed with ethanol absolute.

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2.3. Measurements

Elemental microanalysis CHN were carried out on a Thermofinigan flash analyzer, the FTIR spectra in the range (200-4000) cm^{-1} were recorded as CsI discs using a Shimadzu FTIR spectrophotometer, molar conductance measurements were made in anhydrous DMSO at 25 ^{o}C using Inolabcond 720.The ^{1}H NMR spectra were recorded on a Mercury-300BB NMR 300 spectrometer, relative to the internal standard tetramethylsilane (TMS), DOSO-d6 used as solvent. Melting points were determined in open capillary tubes using an electro thermal melting point /SMP3 apparatus. Mass spectra were recorded in the range (0-800) m/e on a 5973 network mass selective detector. Balance Magnetic susceptibility were recorded inModel MSB-MKI.

3. Results & Discussion

The physical properties of ligand and its complexes are presented in table 1. Elemental microanalysis CHN shown in table 2.

Table 1. conductance, physical properties data of the ligand and its complexes .

No	Compound	Molecular formula	Color	Λ $Scm^2 mol^{-1}$	Melting Point °C	μeff B.M.
1	Ligand	$C_8H_{10}N_8O_2$	brown	------	197-198	-----
2	$[Cr(L)_2Cl_2]Cl$	$Cr(C_8H_{10}N_8O_2)_2Cl_3$	Dark Green	35	136-135	4.28
3	$[Co(L)Cl_2]$	$Co(C_8H_{10}N_8O_2)_2Cl_2$	Dark grey	12	194-192	0.91
4	$[Ni(L)Cl_2]$	$Ni(C_8H_{10}N_8O_2)Cl_2$	brown	10	201-200	0.29

Table 2. Elemental microanalysis CHN for the ligand .

Experimental			Theoretical		
C	H	N	C	H	N
44.78%	4.03%	38.40%	44.75%	3.94%	38.38%

3.1. Infra-Red Spectroscopy

Infrared spectroscopy is one of the most commonly used tools for the detection of functional groups in pure compounds and complexes. The spectra for L shows a characteristic stretching absorption bands at (3452, 3421, 2934, 1523, 1627, 1475,1365, 1025,) cm^{-1} assigned to υ(N-H) ,υ(N–H) , υ(N–H) , υ(C=N), υ(C=N) (Field et al. 2012), symmetrical and Asymmetrical C-O-C stretching respectively(Huang et al. 2003) . The C=N and C-O-C are important to predict the bonding mode of the ligand ,these bands shift higher wavenumber in the spectra of complexes compare with ligand, observed changes are the evidences of complexation had happened . The IR data of the ligand and complexes are shown in Table (3) and figure (8),(9) and(10) . The Table lists the stretching frequency (υ) for some of the characteristics groups exhibited by the ligand and complexes.

Table 3 . Characteristic absorption bands of ligand and its complexes .

NO	υ(NH)	υ(CH) aliphatic	υ(C=N)	υ(C=N)	υ (C-O-C)	Stru. Movement	M-N	M-Cl	M-O
L	3452	2934	1627	1523	1365 1475	1025	-----	-----	-----
1	3455	2934	1649	1425 1475	1025	1025	592	293	-----
2	3453	2935	1680	1532			593	321	
3	3450	2933	1668	1525	1366 1475	1030	560	291	-----

3.2. Nuclear Magnetic Resonance

The H^{1} NMR spectral data for the 2,2'-[(1*E*,2*E*)-ethane-1,2-diylidenedi(2*E*)hydrazin-1-yl-2-ylidene]bis(5-methyl-1,3,4-oxadiazole) gave additional support for the suggested structure of the ligand. The spectra exhibit a triplet at (2.6ppm,6H) due to two methyl group (Laskar et al. 2016), singlet peaks exhibit at (6.1 ppm, 2H) due to NH group (Singh et al. 2012), another singlet peaks observed at(9.3ppm,2H) due to CH=N(Rezki et al. 2015) .The H^{1}NMR of ligand shown in figure (11).

3.3. Mass spectra

The mass spectra of the ligand and its transition metal complex were recorded at room temperature ,The mass spectrum of the ligand shows a molecular ion peak [M0] at m/z =250 . The fragmentation pathways of ligand give the peaks at different mass numbers at m/z = (218,167, 136, 125, 98 and 83)due to $[C_8H_{10}N_8]^{+\cdot}$, $[C_5H_7N_6O]^{+\cdot}$, $[C_4H_4N_6]^{+\cdot}$, $[C_4H_5N_4O]^{+\cdot}$, $[C_3H_4N_3O]^{+\cdot}$, $[C_3H_3N_2O]^{+\cdot}$ Respectively. The intensity of these peaks reflects the stability and abundance of the ions . as shown in Figure (12-17) and (Scheme 2). The complex [Cr(L) Cl_2]Cl showed a molecular ion peak at m/z [M0]= (659) which is equivalent to molecular mass of the complex. This complex shows another a fragmentation peak with loss of chlorine atom at

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Figure 2 . Electrostatic potential 2D for Ligand

to $[Cr(L)_2Cl]^{+\cdot}$ and $[Cr(L)_2]^{+\cdot}$ respectively .

The mass spectrum of the complex [Co (L) Cl_2] shows a molecular ion peak at m/z [M0] (380) which is equivalent to molecular mass of the complex. This complex spectrum shows fragment ion peak with loss chlorine atom at m/z (345, 309) due to $[Co (L) Cl]^{+\cdot}$ and $[Co (L)_2]^{+\cdot}$ respectively.

The mass spectrum of the complex $[Ni(L)Cl_2]$ shows a molecular ion peak at m/z [M0](380), This complex shows another a fragment ion peak with loss of chlorine atom at m/z (345)and (309). the mass spectra of the complexes shown in figure(12), (13),(14),(15) .

3.4. Magnetic susptibility

The value of the effective magnetic moment of the complexes is tabulated in table 1 by using Balance Magnetic susceptibility. The Results are shown in the table above all the complexes given low value of effective magnetic moment. Chromium ion Cr^{3+} shows the highest value (4.28) M.B due to the presence of three single electrons compare the low value (0.91) M.B for Co^{3+} ion and (0.42) M.B for nickel ion Ni^{2+} because there is no single electron for cobalt ion Co^{3+} and nickel ion Ni^{2+} . We conclude that the ligand works as strong ligand (strong field).

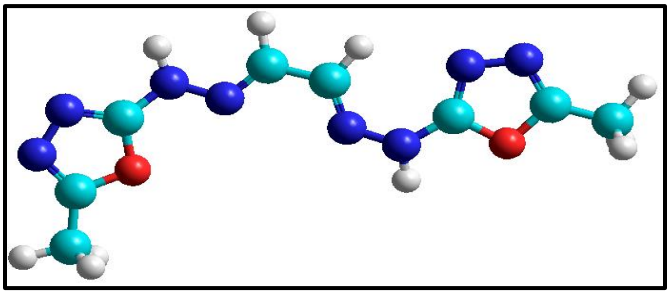
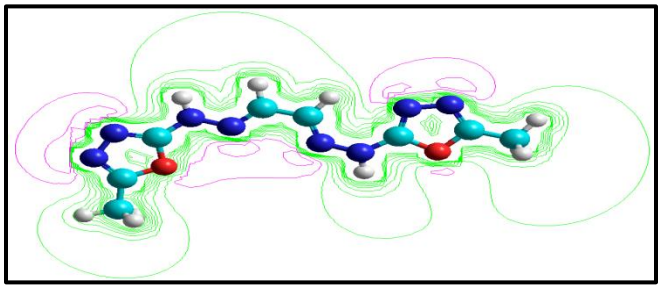
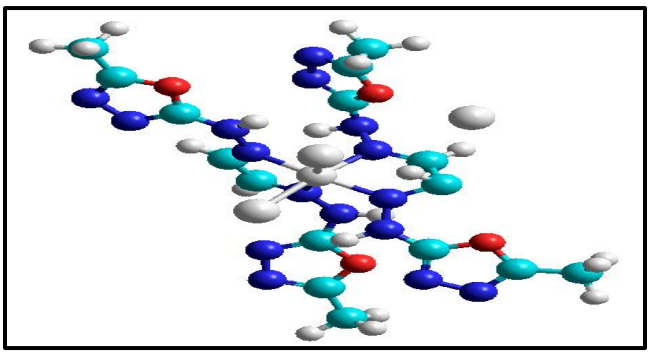


Figure 1 . Graphical presentation of stereochemistry of the Ligand ($C_{16}H_{14}N_4SO$)





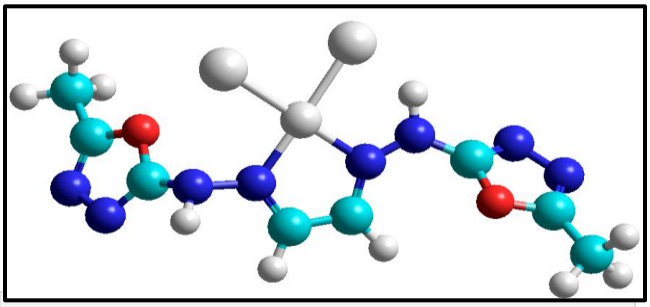
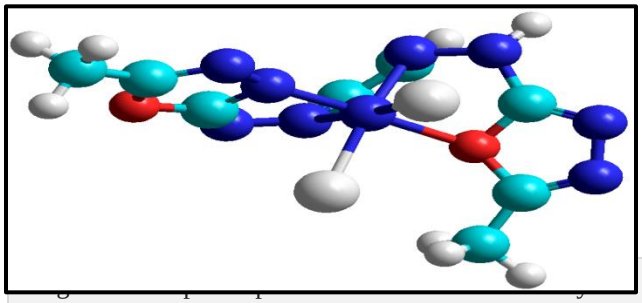
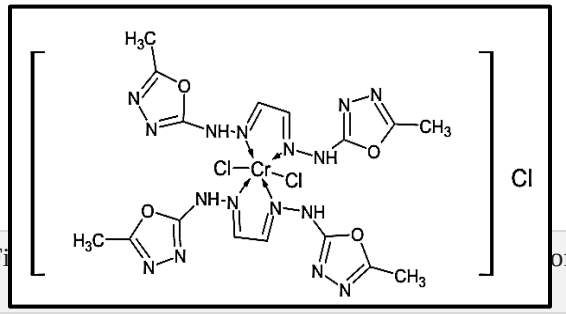


Figure 3 . Graphical presentation of stereochemistry of the $[Cr(L)_2Cl_2]Cl$



the $[Ni(L_1)Cl_2]$



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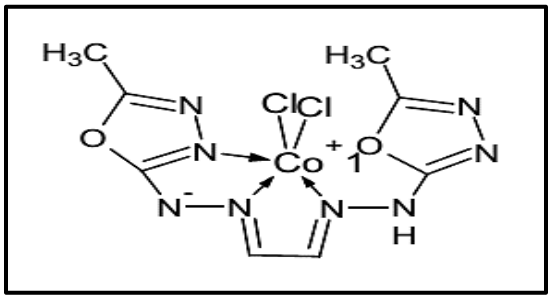

Figure 7 . $[Co(L_1)Cl_2]$

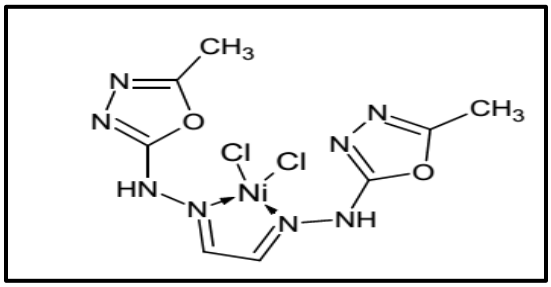

Figure 8 . $[Ni(L_1)Cl_2]$

Analytical and spectral data (^{1}H NMR, IR, mass spectra) of all synthesized compounds were in full agreement with the proposed structure.

3.5. Biological Study

The ligand and its transition metal complexes were evaluated for antimicrobial activity against gram positive bacteria such as Staphylococcus aureus and gram negative bacteria Escherichia coli, by using agar well diffusion method. All the microbial cultures were adjusted to 0.5 McFarland standard, dimethyl sulphoxide (DMSO) were used to prepared all the test solution. The area of inhibition was measured in millimeter. nutrient agar used as culture medium (Balouiri et al. 2016) , the values of the investigated compounds are tabulated in Table.4.The observe result showed transition metal complexes enhanced antimicrobial activity than that of free ligand. This result can be due to the greater lipophilic nature of the complexes and favors its permeation through the lipoid layers of the bacterial membranes. The activity of transition metal complexes can be expound on the basis o hen et al. 2(

Figure 6 . $[Cr(L)_2Cl_2]Cl$

Table 4 . Antibacterial screening data of the ligand and its metal complexes

Compound	Escherichia coli Inhibition zone(mm)	Staphylococcus Aurens Inhibition zone(mm)
L= $C_5H_{10}N_8$	22	18
$[Cr(L)_2Cl_2]Cl$	15	-
$[Co(L)Cl_2]$	21	15
$[Ni(L)Cl_2]$	20	-

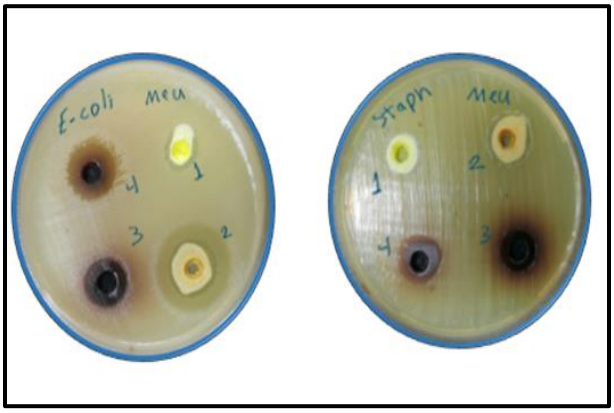

Figure 9 . Antibacterial of the ligand and its metal complexes

4. Conclusion

The ligand 2, 2'-[(1*E*, 2*E*) -ethane-1,2-diylidenedi(2*E*)hydrazin-1-yl-2-ylidene]bis(5-methyl-1,3,4-oxadiazole) was successfully synthesized. Elemental microanalysis CHN, IR, ^{1}H NMR and mass spectral observations suggest the octahedral geometry for the Cr(III), Co(III). Square planar geometry was proposed for Ni(II) .

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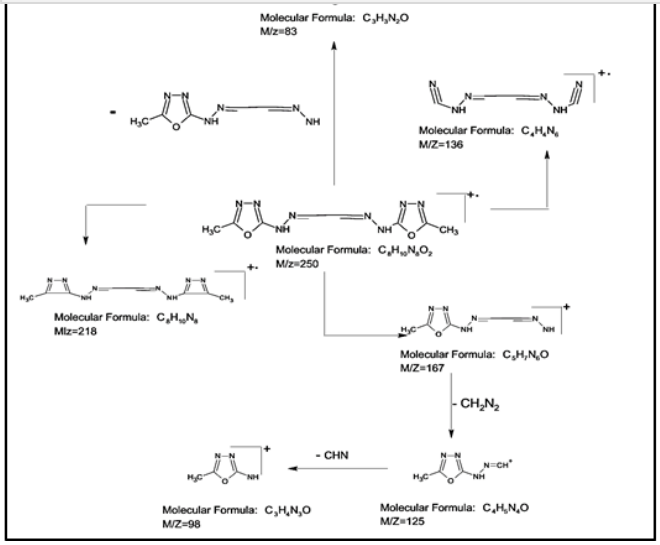
Figure 11 . IR spectra of [Cr(L)2Cl2]Cl



Scheme 2. Suggested mass fragmentation of ligand.

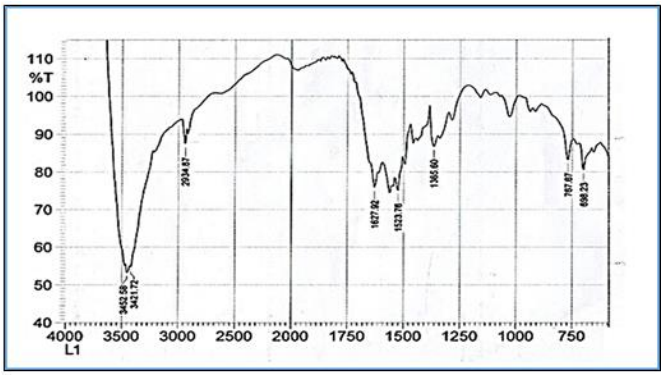
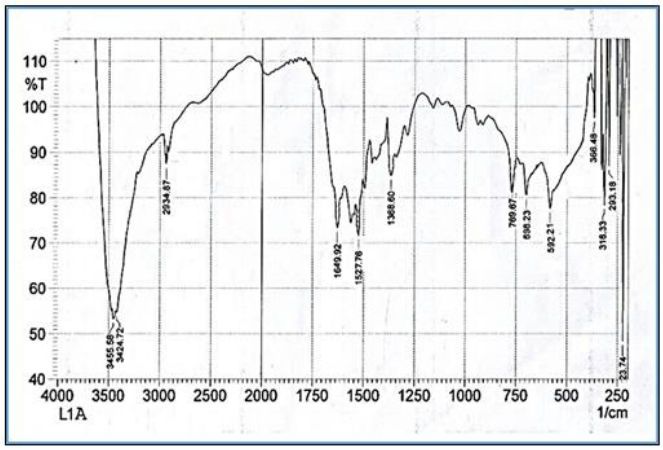


Figure 10 . IR spectra of Ligand ($C_8H_{10}N_8O_2$)



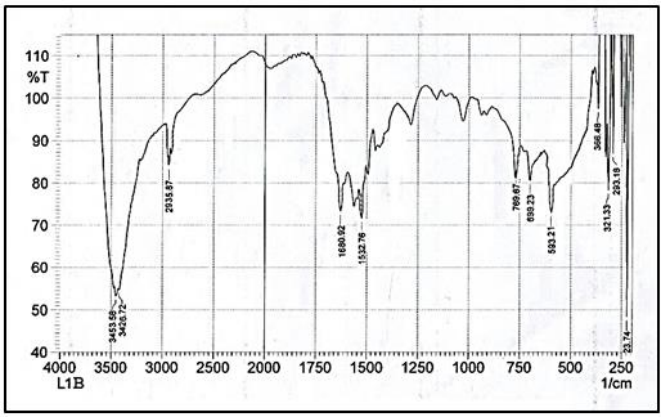


Figure 12 . IR spectra of [Co(L)Cl2]

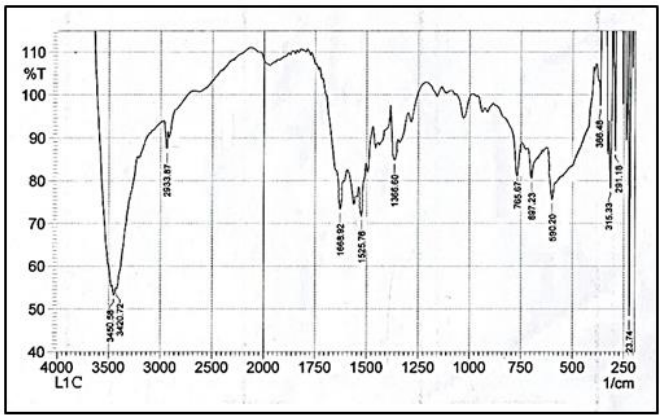


Figure 13 . IR spectra of [Ni(L)Cl2]

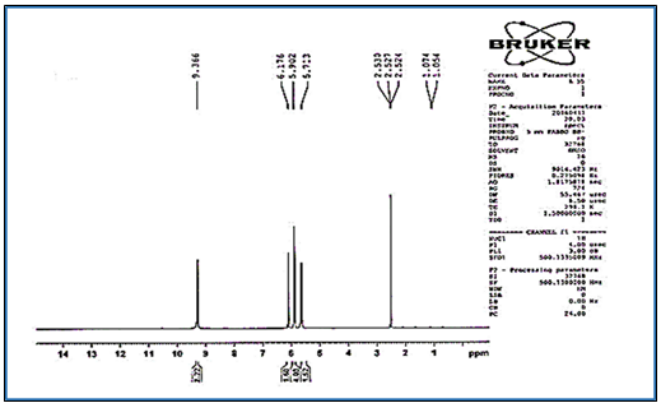


Figure 14 . NMR spectra of the ligand (C8H10N8O2)

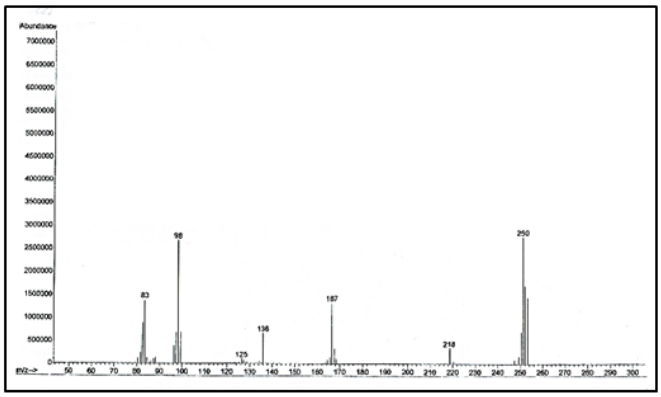


Figure 15 . mass spectra of ligand ($C_8H_{10}N_8O_2$)

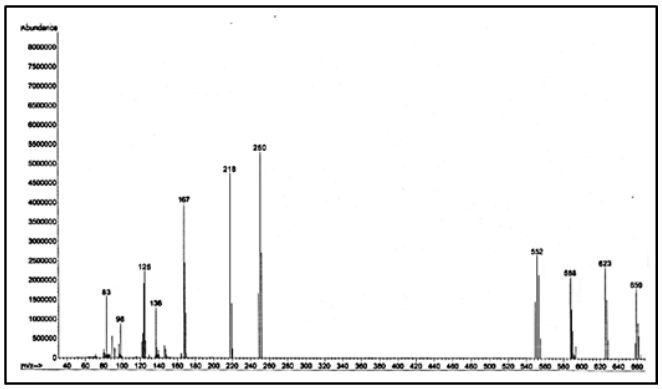


Figure 16 . mass spectra of $[Cr(L)_2Cl_2]Cl$

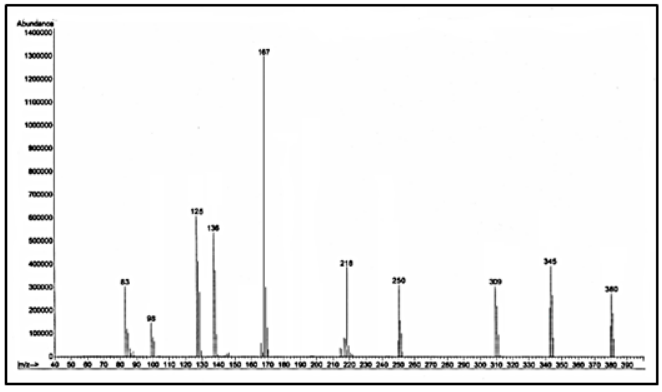


Figure 17 . mass spectra of $[Co(L)Cl_2]$

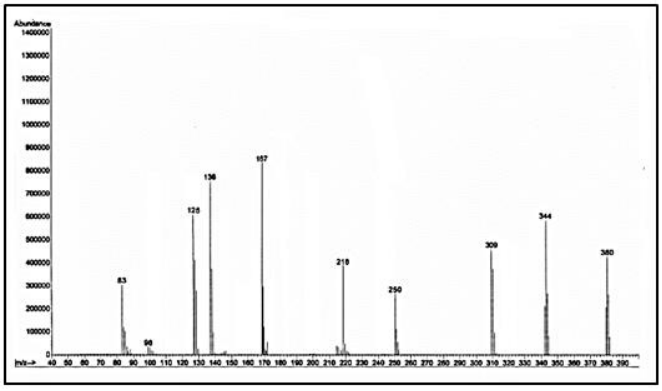


Figure 18 . mass spectra of $[Ni(L)Cl_2]$

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