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Syntheses, Characterization and biological Activity of a new ligand [4-[(1*E*)-ethylideneamino]-5-phenyl-4*H*-1,2,4-triazole-3-thiol with some transition metals complexes

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Abstract

Anew Ligand **4-[(1*E*)-ethylideneamino]-5-phenyl-4*H*-1,2,4-triazole-3-thiol**e with its ($CrCl_3.6H_2O$,$FeCl_3.6H_2O$,$CoCl_3$,$NiCl_2.6H_2O$and$CuCl_2.6H_2O$)complexes were synthesized .The authenticity of the ligand and its transition metal complexes were established by elemental analyses, conductance, as well as spectroscopic (IR, 1HNMR, mass It may be concluded that the ligand coordinate through Nitrogen(N^1) and sulfer(S^{12}) atoms as shown in figure (1). This view is further supported by the appearance of a band corresponding to the metal–nitrogen stretching at 410–555 cm^{-1} in the complexes. the Ni and Cu atoms leading to the formation tetrahedral geometry .Octahedral geometry was proposed for the(Cr(III),Fe(III) and Co(III) prepared complex. Figure(2). All complexes and their parent organic moiety have been screened for antibacterial (Table4) by using spread method and measurement inhibition zone by using (DMSO). this studying showed positivity results. By appear lager inhibition zone against E-coli and staph aurens. Figure(3)

تحضير وتشخيص ودراسة الفعالية البايلوجية لليكاند الجديد 4-[(E1)- ايثايلدين امينو]- 5- فنيل -H4-4,2,1- ترايازول-3-ثايول الجديد ومعقداته

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**المعهد التقني – الشطرة

الخلاصة

تم تحضير ليكاند جديد **4-[(1*E*)-ethylideneamino]-5-phenyl-4*H*-1,2,4-triazole-3-thiol**e ومعقداته مع بعض العناصر ألانتقالية ($CrCl_3.6H_2O$,$FeCl_3.6H_2O$,$CoCl_3$,$NiCl_2.6H_2O$,$CuCl_2.6H_2O$) . وتم التأكد من الصيغ الجزيئة والتركيبية لليكاند

ومعقداته باستخدام تقنيات التحليل العنصري ، التوصيلية ، الحساسية المغناطيسية وكذلك أطياف (Mass H−NMR,IR) وتم الاستنتاج بأن الليكاند يتآصر من خلال ذرات N^1 و S^{12} وهذا الاستنتاج يدعمه ظهور حزمة عند (555−410)سم$^{-1}$ تعزى الى (M−N) في طيف المعقدات. وتم التأكد من البيانات التي تم الحصول عليها بأن معقدات Cu(II), Ni(II) رباعية السطوح بينما معقدات Co(III) ، Fe(III) و Cr(III) ثمانية السطوح. وتم اختبار الفعالية البايلوجية لليكاند المحضر ومعقداته باستخدام طريقة الانتشار وذلك بقياس منطقة التثبيط وباستخدام مذيب ثنائي مثيل اوكسيد الكبريت (DMSO) ، وأعطت اختبارات الفعالية نتائج ايجابية حيث لوحظ ظهور تثبيط جيد ضد بكتريا E−coli و Staphylococcus .

1- Introduction

A literature survey revealed triazole derivatives belonging to an important group of heterocyclic compounds that have been the subject of extensive study in the recent past. Aromatic nitrogen heterocycles represent an important class of compounds which can acts as ligands towards metal ions[1]. Ligands containing nitrogen such as 1,2,4-triazole derivatives and their metal complexes played an major role in the expansion of coordination chemistry resulting in an large number of publications, extent from pure synthetic work to physicochemical [2] , biochemically relevant studies of metal complexes [3–4] and magnetic materials and photo chemically driven molecular devices [5]. this compound display a broad range of biological activity, acting as antitumor, antibacterial, antifungal and antiviral agents [6]. the synthesis of these heterocycles has received considerable attention in recent years. In coordination chemistry pyrazole and triazole derived ligands exhibit various coordination modes and have received considerable attention for the synthesis of transition metal complexes with various nuclear ties[7].

2.1 Preparation of the ligand

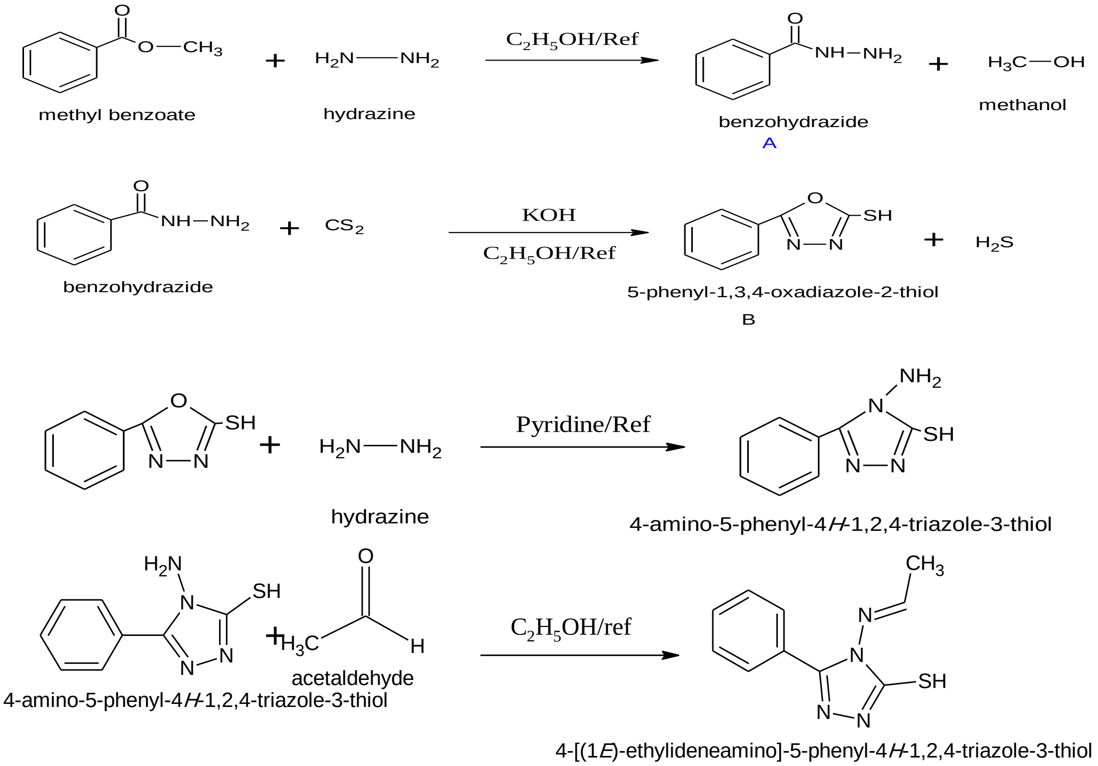
The new ligand 4-[(1*E*)-ethylideneamino]-5-phenyl-4*H*-1,2,4-triazole-3-thiol (Scheme1) was prepared as follows:

A mixture of methyl benzoate(15gm, 0.1mole) and hydrazine hydrate (0.1mole,11ml) dissolved in ethanol (100ml) was refluxed on a water bath for 6 hrs, The resultant mixture[A] was concentrated and the white solid which separated was filtered and recrystallised from ethanol. The purity of the compound was followed by TLC on precoated silica gel. Yield: 93 %, m. p. 138-140°C[8-9].

A mixture of [A](0.09mol,13gm) ,KOH (0.05mol, 3gm) in 100ml ethanol and CS_2 (0.05mol,4ml)was refluxed on a water bath for 15 hrs, until the evolution of H_2S gas ceased [10-11]. The excess CS_2 was removed under reduced pressure. The resultant mixture[B] was acidified with acetic acid and the white solid which separated was filtered and recrystallised from ethanol. The purity of the compound was followed by TLC on precoated silica gel. Yield: 88 %, m. p. 220-222 °C[8-9].

A mixture[B] (0.1mol,18gm) and hydrazine hydrate (0.2mol, 7ml) dissolved in pyridine (50ml) was refluxed on a water bath for 5 hrs . The resultant mixture[C] was concentrated and the light brown solid which separated was filtered and recrystallised from ethanol. The purity of the compound was followed by TLC on precoated silica gel. Yield: 91.6 %, m. p. 190-192°C.

A mixture[C] (0.01mol, 2gm) and Acetaldehyde (0.02mol, 1ml) dissolved in ethanol (50ml) was refluxed on a water bath for 3 hrs. The resultant mixture[ligand] was concentrated and the pale brown solid which separated was filtered and recrystallised from ethanol. Yield: 66.6 %, m. p. 200-203°C.



Scheme (1) preparation of ligand

2.2 Preparation of complexes

The Cr(III), Co(III), Fe(III), Ni(II) and Cu(II) complexes were prepared by refluxing the respective hydrated metal chloride ($1*10^{-3}$ mole) in 15 ml ethanol with 50 ml of an ethanolic solution of the ligand (0.0009 mole, 0.2 gm) for 3 hrs. The resultant solids which separated were filtered, washed with ethanol and dried in air.

2.3 Measurements

Elemental C, H and N analysis 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 nuclear magnetic resonance 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 /SMP3I apparatus. Mass spectra were recorded in the range (0-800) m/e on a 5973 network mass selective detector .

3. Results & Discussion

The purity of the ligand and its complexes were checked by TLC . Elemental analysis tabulated in Table (1), Melting point, physical properties and molar conductance of all the compounds studied are tabulated in Table (2). The calculated values were in a good agreement with the experimental values.

Table 1.Analitical data for the ligand

Experimental			**Theoretical**		
C%	**H%**	**N%**	**C%**	**H%**	**N%**
55.08	**4.72**	**25.75**	**55.02**	**4.62**	**25.67**

Table 2. conductance, physical properties data of the ligand and its complexes

No	Compound	Molecular formula	Color	Λ Scm^2 mol^{-1}	Melting Point
1	Ligand	$C_{10}H_{10}N_4S$	Brown	-------	201-203
2	$[Cr(L)_2Cl_2]Cl$	$[Cr(C_{10}H_{10}N_4S)_2Cl_2]Cl$	pale pink	35	213-215
3	$[Fe(L)_2Cl_2]Cl$	$[Fe(C_{10}H_{10}N_4S)_2Cl_2]Cl$	pale Green	34	216-218
4	$[Co(L)_2Cl_2]Cl$	$[Co(C_{10}H_{10}N_4S)_2Cl_2]Cl$	Pale yellow	39	198-200
5	$[Ni(L)Cl_2]$	$[Ni(C_{10}H_{10}N_4S)Cl_2]$	White	14	208-210
6	$[Cu(L)Cl_2]$	$[Cu(C_{10}H_{10}N_4S)Cl_2]$	Dark Gray	15	230d*

d*=decomposition

3.1 Infra-Red Spectroscopy

The FTIR spectrum for L shows a characteristic stretching absorption bands at 3136 cm^{-1}, 3099cm^{-1}, 2700 cm^{-1},1350 cm^{-1}, 1446 cm^{-1} and 1610 cm^{-1}. assigned to C=N proton Izomethein ,υ(C-H) Aromtic, υ(S-H) , symmetrical C-N-C, asymmetrical C-N-C stretching and C=N of the triazole ring respectively . The C=N and N-N stretching vibrations are important to predict the bonding mode of the ligand ,these bands shift lower wavelength in the spectra of complexes compare with ligand, observed changes are the evidences of complexion had happened . The IR data of the complexes are shown in Table (3) and figure(4)(5)(6). 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	Compound	υC-H Aliphatic	υC-H Aromatic	SH	υC=N	υ C-N-C	Structural movement	M-S υ	M-N υ	M-Cl υ
L_2	$C_{10}H_{10}N_4S$	2954	3099	2700	1610	1350(sy) 1446(asy)	1060			
1	$[Cr(L_2)_2Cl_2]Cl$	2955	3151	2762	1610	1352(sy) 1489(asy)	1062	482	555	354
2	$[Fe(L_2)_2Cl_2]Cl$	2955	3159	2854	1610	1352(sy) 1448(asy)	1076	480	555	335
3	$[Co(L_2)_2Cl_2]Cl$	2956	3151	2854	1610	1352(sy) 1489(asy)	1078	482	555	322
4	$[NiL_2Cl_2]$	2954	3101	2854	1610	1352(sy) 1417(asy)	1062	482	555	351
5	$[CuL_2Cl_2]$	2953	3143	2762	1606	1352(sy) 1431(asy)	1070	381	410	324

3.2 Nuclear Magnetic Resonance

The data of proton NMR of the ligand 4-[(1*E*)-ethylideneamino]-5-phenyl-4*H*-1,2,4-triazole-3-thiol displayed good solubility in DMSO. The proton nuclear magnetic resonance spectral data gave additional support for the composition of the ligand. The spectra also exhibit a singlet – CH_3 peaks at 2.85ppm due to methyl group, another peaks exhibit at 3.73ppm due to singlet –SH[12]. the aromatic ring[13-14-15]exhibit peaks at (7.52-8.03) ppm and peaks exhibit at 8.96ppm due to singlet – Proton Iso methein[16]the proton NMR of the ligand shown in figure(7) .

3.3Mass spectra

The mass spectrum of the ligand exhibits a molecular ion peak $[M^{+\cdot}]$ at m/z 218,the ligand spectra shows fragment the spectra peaks at m/z (203,192,177,144,115,103and100) due to ($C_9H_7N_4S$) ,($C_8H_8N_4S$) , ($C_8H_7N_3S$), ($C_8H_6N_3$), ($C_3H_5N_3S$),(C_7H_5N)and($C_2H_2N_3S$) respectively as shown in Figure (8).The mass spectrum of thecomplex $[Cr(L)_2Cl_2]Cl$ shows a molecular ion peak at m/z $[M^{+\cdot}]$ 595 which is equivalent to molecular mass of the complex. This complex shows another a fragment ion peak with loss of chlorine atom at m/z 560. the ligand spectra shows fragment ion peak with loss two chlorine atom at m/z (524,489) due to $[Cr(L)_2Cl]$and $[Cr(L)_2]$ respectively.

The mass spectrum of the complex $[Fe(L)_2Cl_2]Cl$ shows a molecular ion peak at m/z $[M^{+\cdot}]$ 599 which is equivalent to molecular mass of the complex. This complex shows another a fragment ion peak with loss of chlorine atom at m/z 563. the ligand spectra shows fragment ion peak with loss two chlorine atom at m/z (528,492) due to $[Fe(L)_2Cl]$and $[Fe(L)_2]$ respectively.

The mass spectrum of the complex $[CuLCl_2]$ shows a molecular ion peak at m/z $[M^{+\cdot}]$ 353, This complex shows another a fragment ion peak with loss of chlorine atom at m/z 317 and 282. Respectively the mass spectra of the ligand shown in figure(9) , (10),(11).

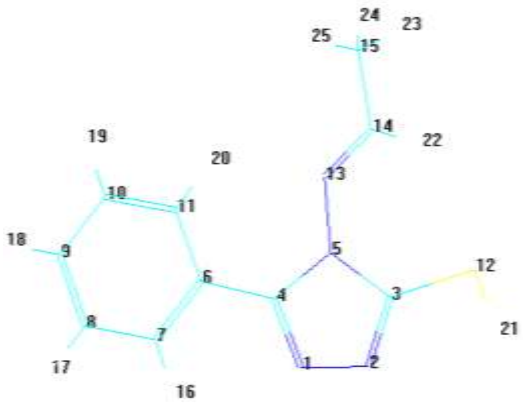
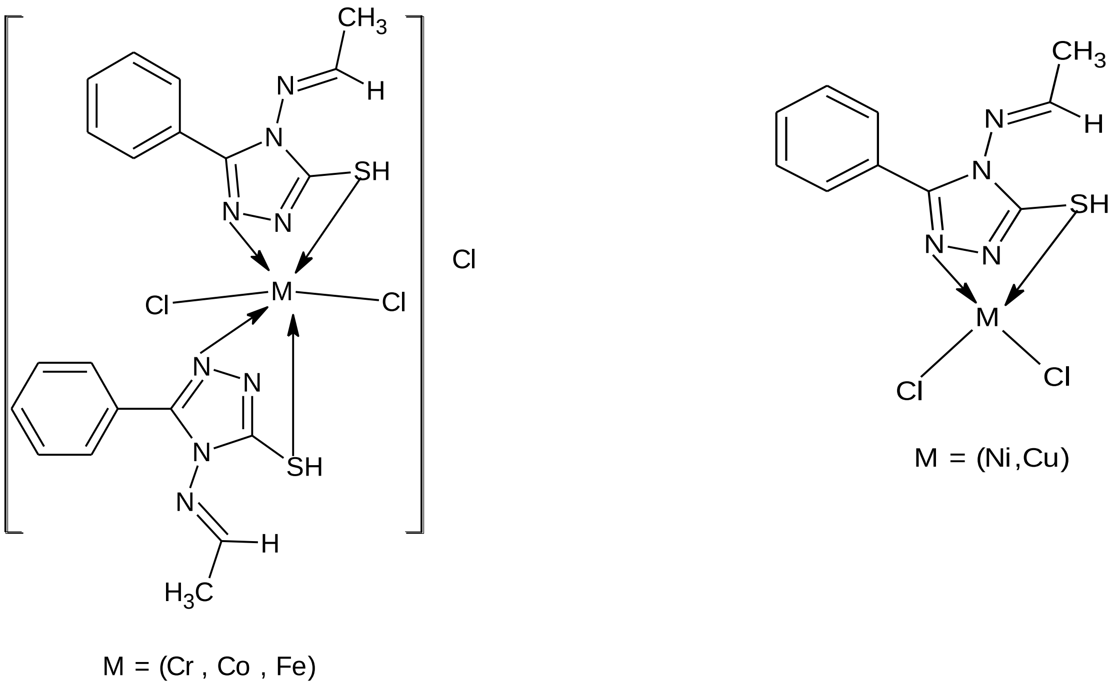


Figure (1)



M = (Cr , Co , Fe)

M = (Ni,Cu)

Figure (2)

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

3-4 – Biological Activity.

The antibacterial activity of all the synthesized complexes was evaluated by using agar well diffusion method. All the microbial cultures were adjusted to 0.5 McFarland standard, which is visually comparable to a microbial suspension of approximately 1.5 × 108 cfu/mL. 20mL of Mueller Hinton agar medium was poured into each Petri late and plates were swabbed with 100 μL inocula of the test microorganisms and kept for 15 min for organism [17-18]. figure (3) adsorption. Using sterile cork borer of 8mm diameter, wells were bored into the seeded agar plates, and these were loaded with a 100 μL volume with concentration of 4.0mg/mL of each compound.

Reconstituted in the dimethyl sulphoxide (DMSO). All the plates were incubated at 37◦C for 24 hrs. Antibacterial activity of each compound was evaluated by measuring the zone of growth inhibition against the test organisms with zone reader (HiAntibiotic zone scale). DMSO was used as a negative control whereas Ciprofloxacin was used as positive control. This procedure was performed in three replicate plates for each

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

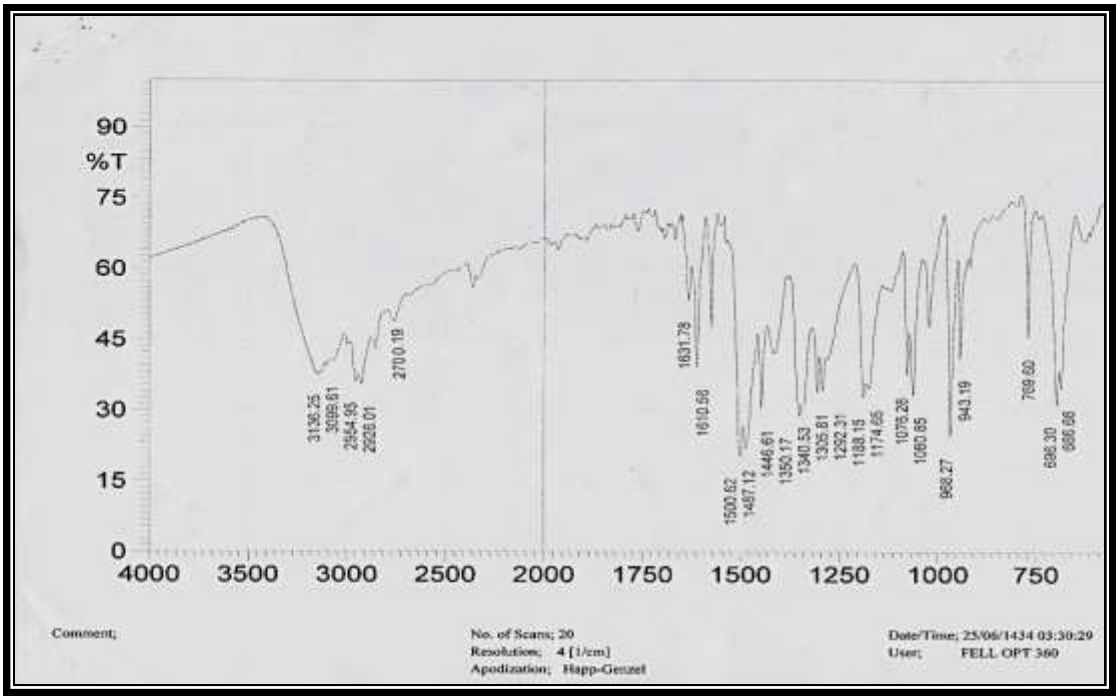
Compound	Escherichia coli	Staphylococcus Aurens
	Inhibition zone(mm)	Inhibition zone(mm)
Antibiotic Ciprodar	35++++++	25++++
The solvent DMSO	-	-
L= $C_{10}H_{10}N_4S$	13+	20+++
1=$[Cr(L)_2Cl_2]$ Cl	10+	15++
2=$[Fe(L)_2Cl_2]$ Cl	18++	12+
3=$[Co(L)_2Cl_2]$ Cl	20+++	20+++
4=$[Ni(L)Cl_2]$	12+	20+++
5= $[Cu(L)Cl_2]$	17++	10+

**(+ = Weak Inhibition , ++ =Medium Inhibition , +++ = Good Inhibition)

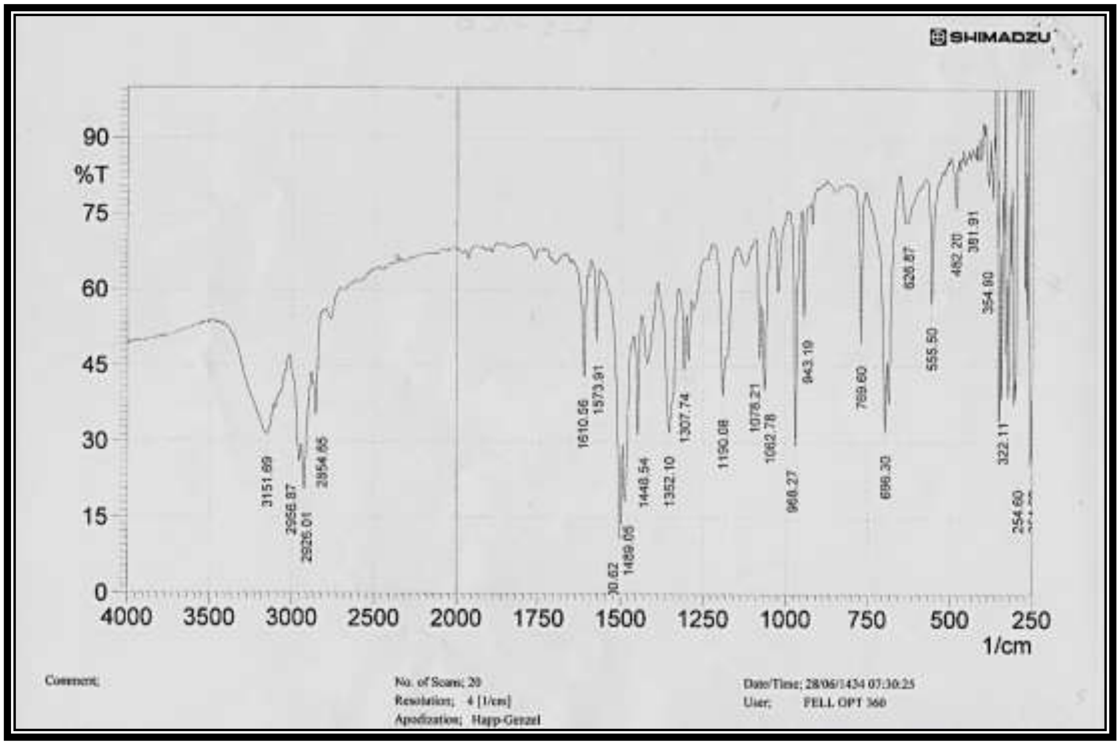
Figure (3)

4.Conclution

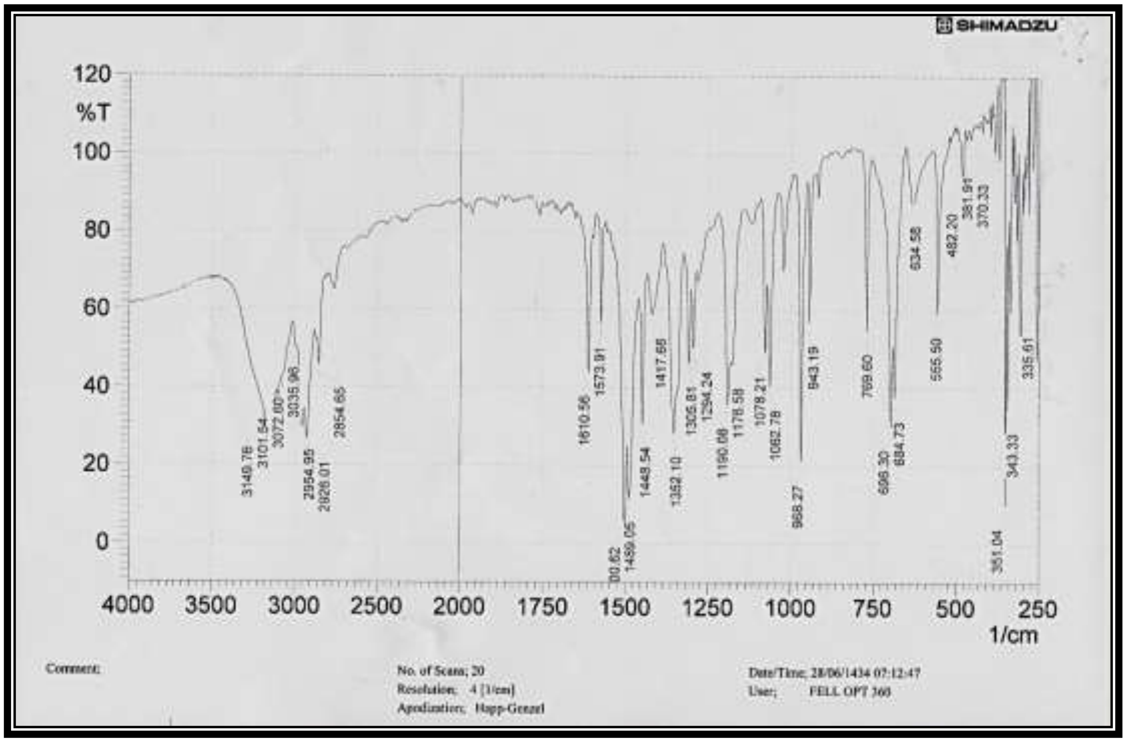
The ligand 4-[(1*E*)-ethylideneamino]-5-phenyl-4*H*-1,2,4-triazole-3-thiol was successfully synthesized. The elemental analysis, , IR, ^{1}H NMR and mass spectral observations suggest the octahedral geometry for the Cr(III), Co(III),Fe(III). Tetrahedral geometry was proposed for Ni(II),Cu(II) .



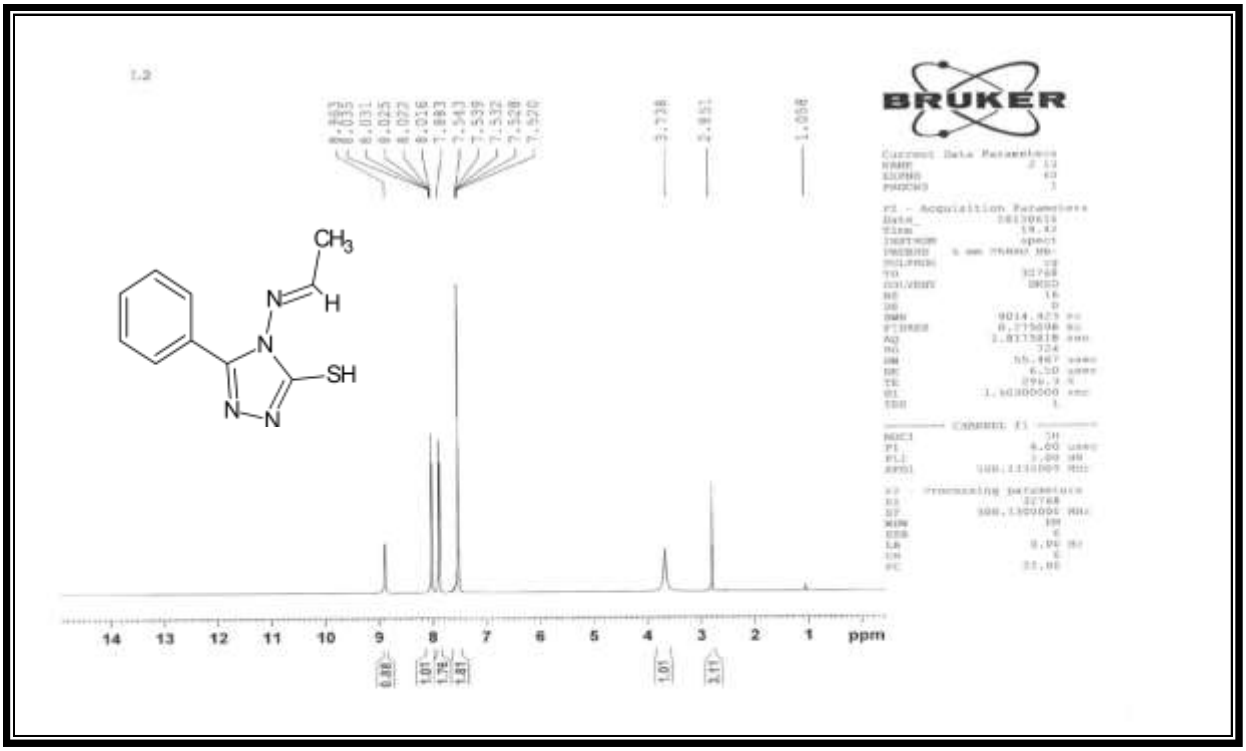
Figure(4) IR spectrum of Ligand ($C_{10}H_{10}N_4S$)



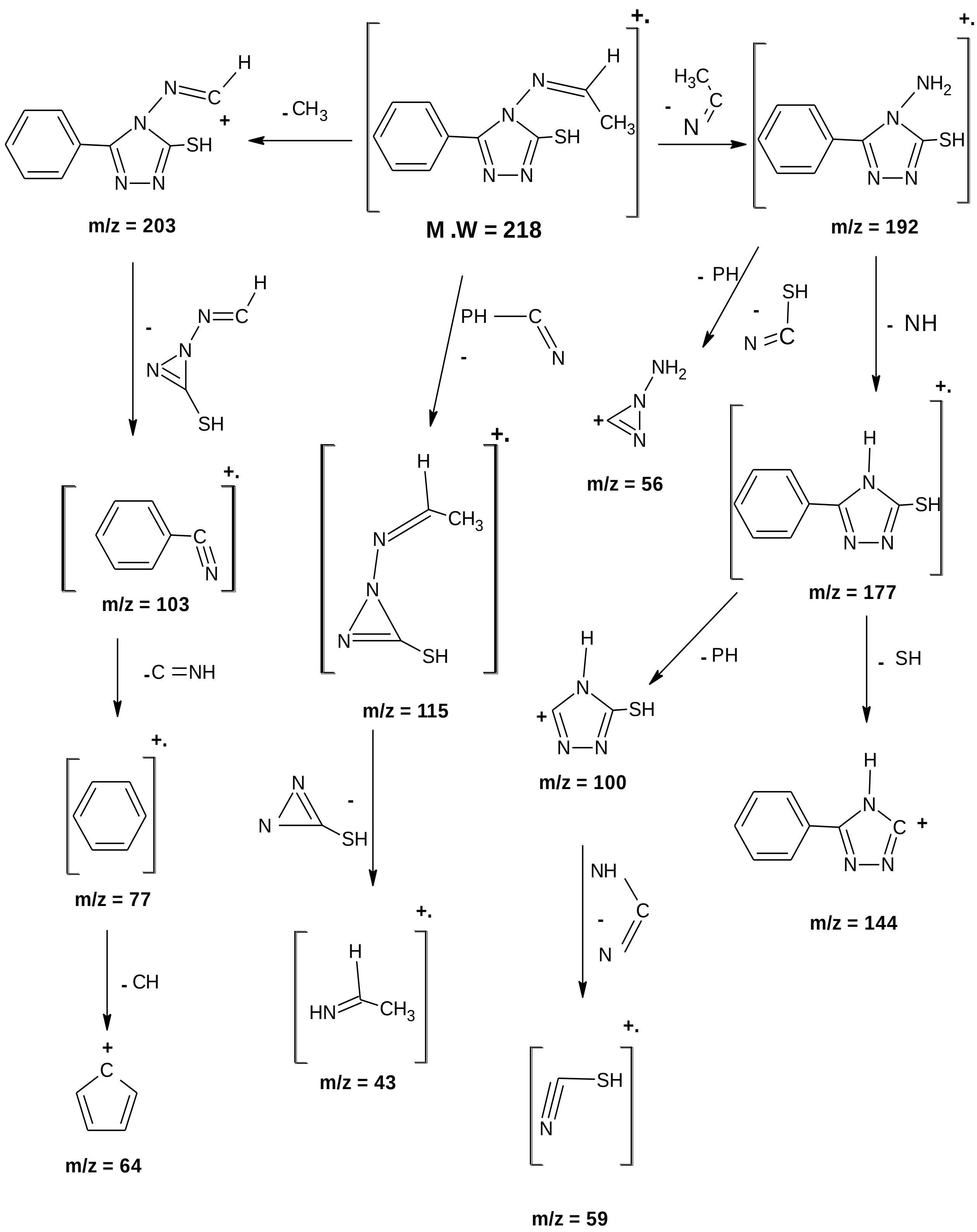
Figure(5) IR spectrum of $[Co(L)_2Cl_2]$ Cl



Figure(6) IR spectrum of [Ni(L) Cl$_2$]



Figure(7) ^{1}H NMR spectrum of the ligand ($C_{10}H_{10}N_4S$)



Scheme (2) Mechanism of fragmentation of ligand

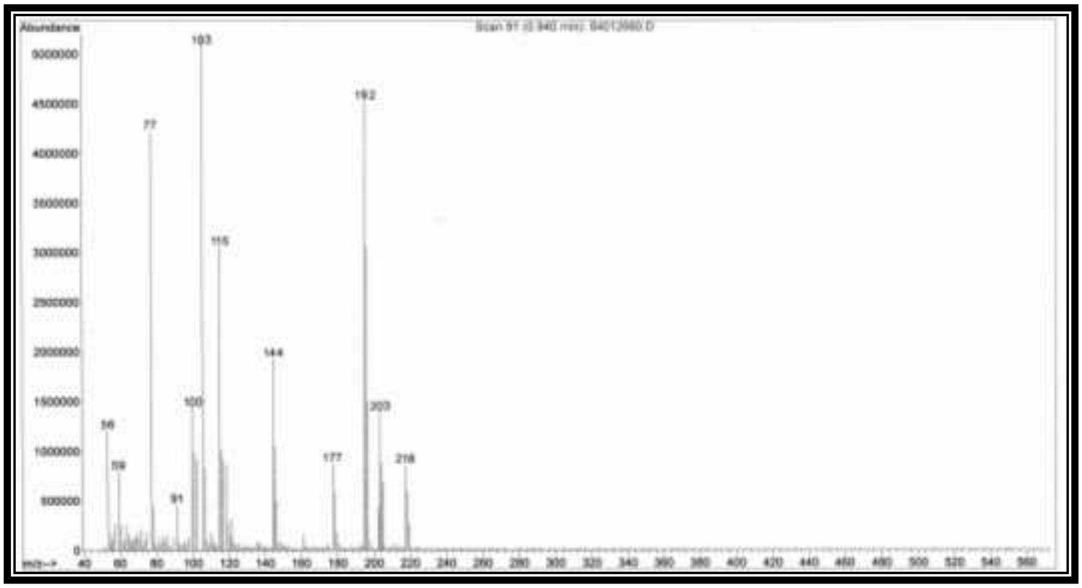


Figure (8) mass spectrum of ligand

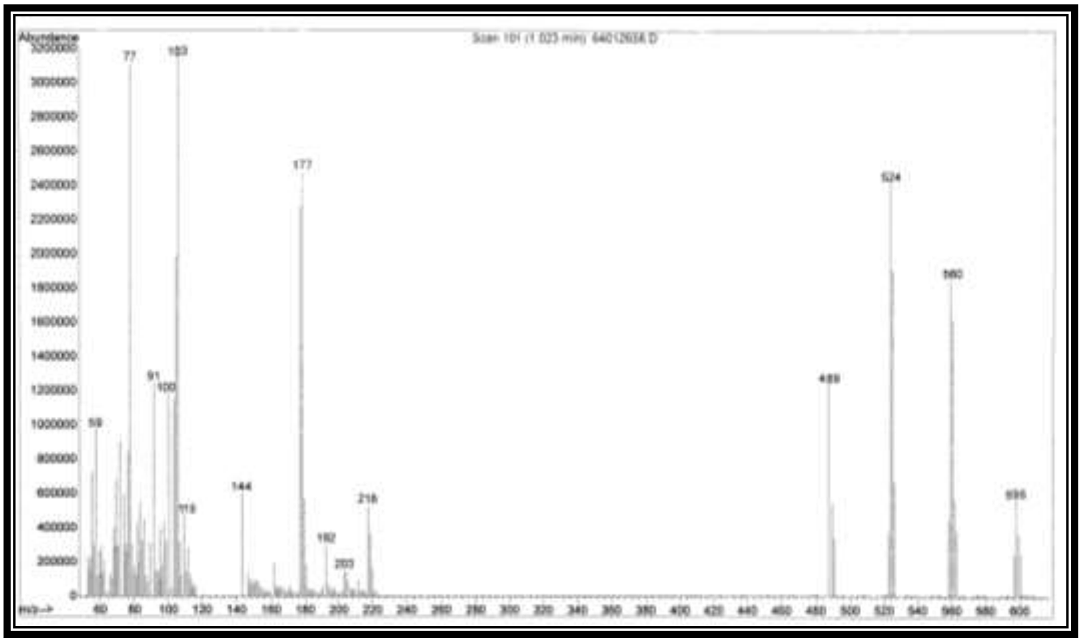


Figure (9)mass spectrum of $[Cr(L)_2Cl_2]Cl$

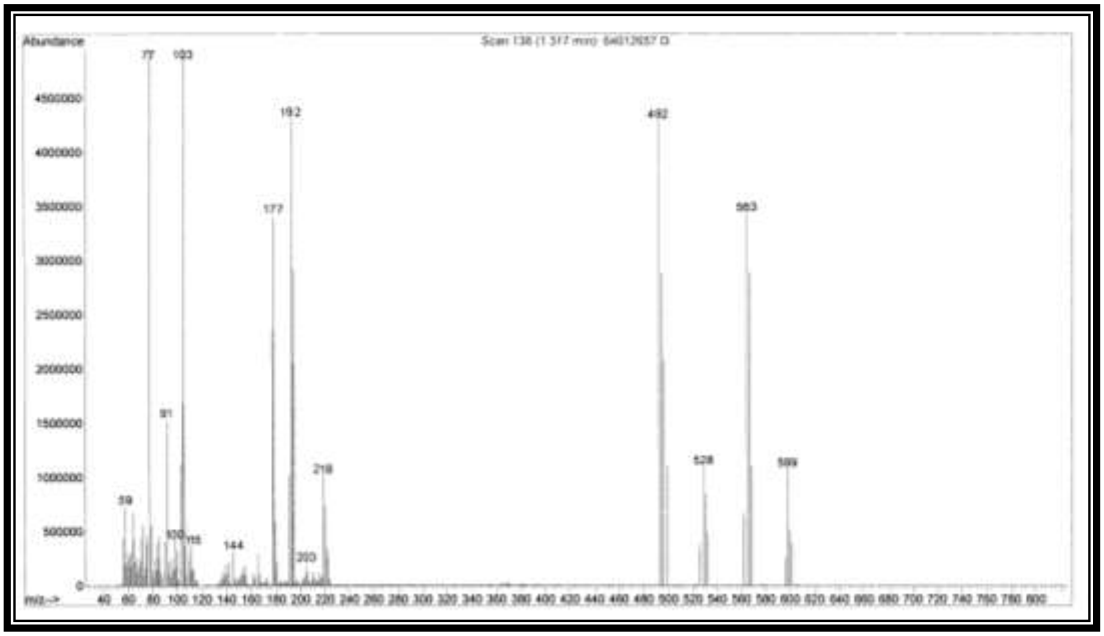


Figure (10) mass spectrum of [Fe(L)$_2$Cl$_2$]Cl

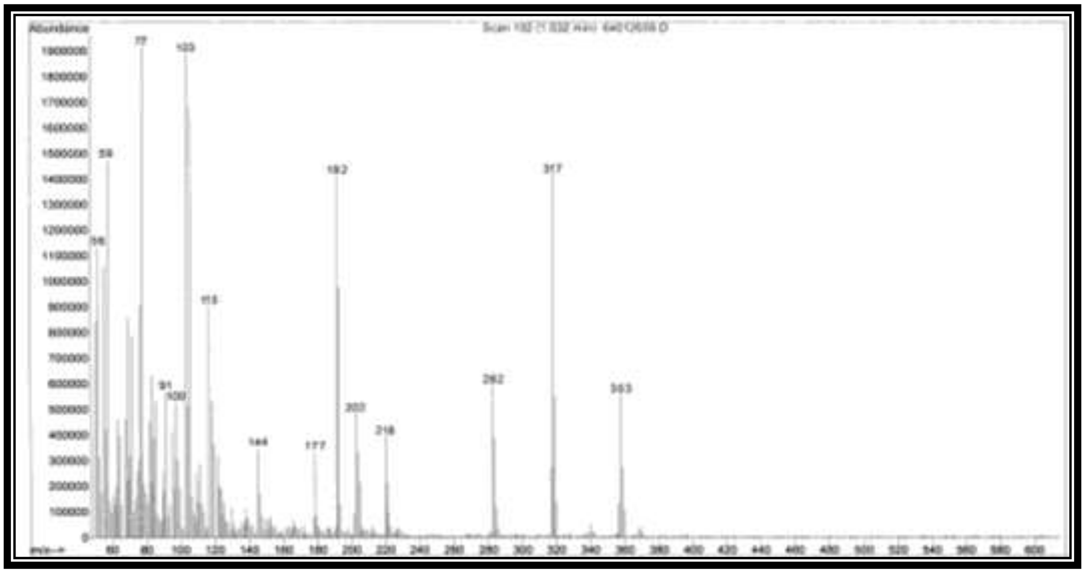


Figure (11) mass spectrum of [Cu(L)$_2$Cl$_2$]

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