

**Synthesis ,characterization and antibacterial study Of new 2-ethyl-5-
{[(3-phenyl-5- sulfanyl-4H-1,2,4-triazol-4-yl)imino]methyl}benzene-
1,4-diol and their transition metal complexes**

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Abstract

Transition metal complexes of new legend 2-ethyl-5-{[(3-phenyl-5- sulfanyl-4H-1,2,4-triazol-4-yl)imino]methyl}benzene-1,4-diol such as Cr^{3+} , Fe^{3+} , Co^{3+} , Ni^{2+} , Cu^{2+} were synthesis ,characterization by magnetic susceptibility measurements, conductance , elemental analyses, ^1H NMR , 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+} , Fe^{3+} and Co^{3+} ion , square planer geometry for Ni^{2+} and Cu^{2+} ion. The complexes and ligand were tested against two types of bacteria (Staphylococcus aureus, Escherichia coli).all prepared complexes showed good biological activity.

Keywords: - Triazole, Transitions metal complexes, biological activity.

1- Introduction

Introduction1. 1,2,4 triazole which is six –electron aromatic system of five – member heterocyclic ring.1,2,4 triazole and its derivatives have one of the most promising ligand ,and show with transition metal ion widely applied in luminescence ,magnetic and ion precursor properties[1-3].The derivatives of 1,2,4 –triazole has attractive whispered attention due to biological activity such as antimicrobial ,anti-inflammatory ,analgesic , antitumor, [4-10],anti HIV [11] , anti-cancer [12-13] and materials field [14]. The ability of transition metals to assume a wide range of oxidation states and coordination geometries provides unique opportunities for catalysis .1,2,4- triazole derivatives play excellent role as anti-corrosion iron [15]. The effectiveness of these compounds as corrosion inhibitors mainly depends on its functional groups, steric effects, electronic density of donor atoms, and p-orbital character of donating electrons [16-19]. Complexes of 1, 2, 4-triazoles are being developed for potential use such as magnetic material and photo chemical chemically driven molecular devices [20].

2.Experimental

2.1 Preparation of the ligand

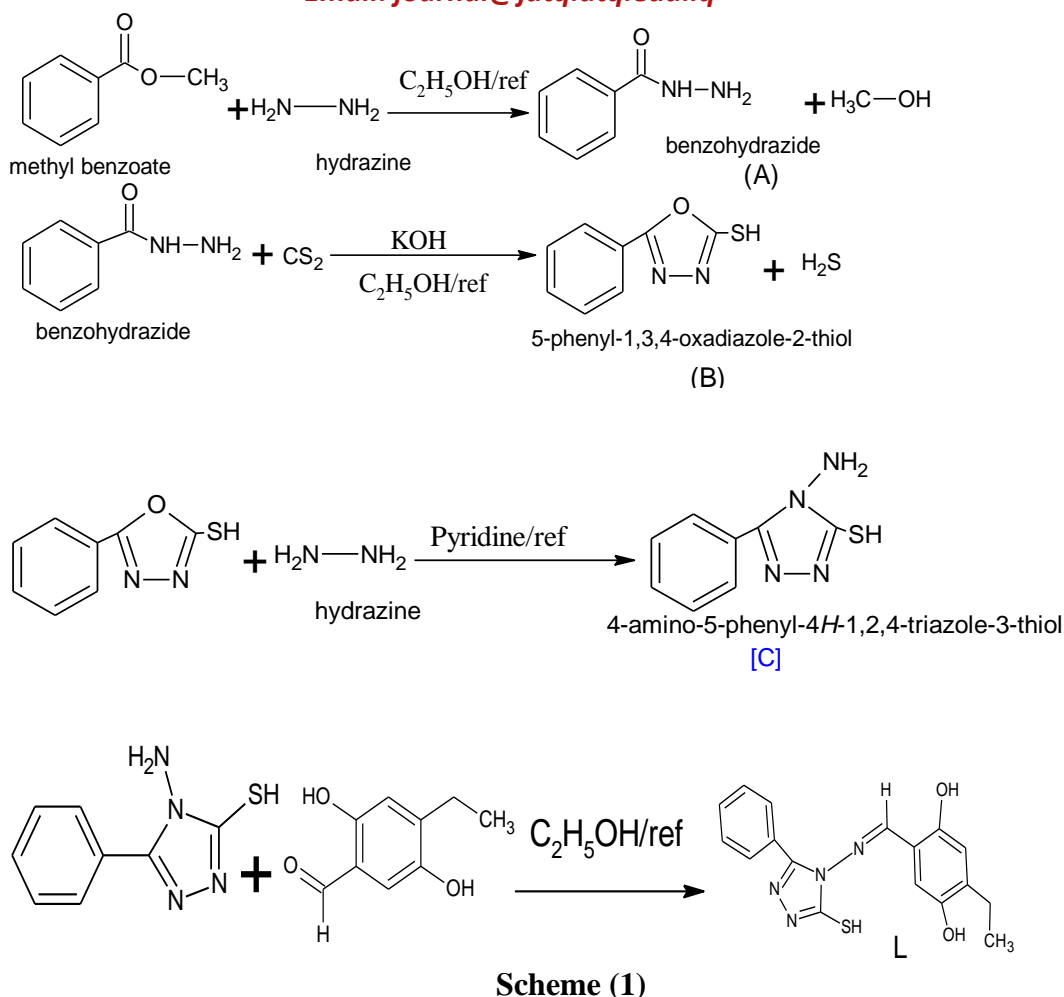
Novel ligand 2-ethyl-5-[[[(3-phenyl-5-sulfanyl-4H-1,2,4-triazol-4-yl)imino]methyl]benzene-1,4-diol (Scheme 1) was prepared as follows:-

A mixture of (13.6 g, 0.1mol) of methyl benzoate and (10ml, 0.2mol) of hydrazine was dissolved in (100ml) ethanol. The resulting mixture was heated under reflux for (6hours).The resultant mixture was concentrated , The crude product was filtered(size of 6 µm) and washed with ethanol to give the desired product benzo hydrazide(A) as White needles, yield(91%), Melting point(m.p.) (138-140) °C [21,22] A mixture(A)(13.6 gm .1mol) and (5.6,g.1mol)of Potassium Hydroxide dissolved in(100 ml) absolute ethanol of this solution (7.5 ml, 0.1mol) of carbon disulfide was added. The resulting mixture was mixing by shaking and heated at (80) °C under reflux for (20hours).The resultant mixture was concentrated , and carefully acidified with hydrochloric acid HCl(5%) to give paleWhite precipitate. The crude product was filtered and washed with cold water and ethanol to give the desired product 5-phenyl-1,3,4-oxadiazole-2-thiol (B), as White solid, yield(90.5%),m.p.

(220-222) ° C[21,22].

A mixture(B) (17.8gm .0.1 mol,) and excess of hydrazine (0.15mol, 7ml) dissolved in Pyridine (100ml) was refluxed on a water bath (80) °C for(20) hrs. . The resultant mixture was concentrated , and carefully acidified with hydrochloric acid(5%) HCl to give pale light Brown precipitate. The crude product was filtered and washed with cold water, recrystallized from ethanol to give the desired product(4-amino-5-phenyl-4H-1,2,4-triazole-3-thiol)(C)as Brown crystal ,yield(90%), m.p.(189-191)°C.

A mixture(C) (0.01mol,1.92gm) and (4-ethyl-2,5-dihydroxybenzaldehyde) (0.01mol,2ml) dissolved in (50ml) ethanol, And was refluxed for (3hrs) the solution is evaporated to half and cooled output when nominated and returned crystallized using absolute ethanol to give crystals of Light brown color of the output [ligand]. Yield: (73 %), m.p. (202-204)°C.(scheme1)



Scheme (1)

2.2 Preparation of complexes

The metal complexes were obtained by reflux (1 mmol) of transition metal chloride (1mmol) Cr(III), Co(III), Fe(III), Ni(II) and Cu(II) in 50 ml ethanol with the ligand (1mmol, 0.2 gm) for 2 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 $(200-4000) \text{ cm}^{-1}$ were recorded as CsI discs using a Shimadzu FTIR spectrophotometer, molar conductance measurements were made in anhydrous DMSO at 25°C using Inolabcond 720. The ^1H 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.

3. RESULTS & DISCUSSION

The purity of the ligand and its complexes were checked by TLC using silica gel-G as adsorbent., 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.Elemental analysis for the ligand

Experimental			Theoretical		
C%	H%	N%	C%	H%	N%
60.08	4.72	16.61	59.98	4.74	16.46

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

No	Compound	Molecular formula	Color	Λ Scm ² mol ⁻¹	Melting Point °C	μ_{eff} B.M.
1	Ligand	C ₁₇ H ₁₆ N ₄ SO ₂	Light brown	-----	202-204	-
2	[Cr(L) ₂ Cl ₂].Cl	Cr(C ₁₇ H ₁₆ N ₄ SO ₂) ₂ Cl ₃	yellow	34	228-230	3.9
3	[Fe(L) ₂ Cl ₂].Cl	Fe(C ₁₇ H ₁₆ N ₄ SO ₂) ₂ Cl ₃	Dark brown	36	221-223	2.3
4	[Co(L) ₂ Cl ₂].Cl	Co (C ₁₇ H ₁₆ N ₄ SO ₂) ₂ Cl ₃	Dark Green	31	210d*	0.42

5	[Ni(L) Cl ₂]	Cu(C ₁₇ H ₁₆ N ₄ SO ₂) Cl ₂	Light yellow	18	188- 191	0.16
6	[Cu(L) Cl ₂]	Ni(C ₁₇ H ₁₆ N ₄ SO ₂) Cl ₂	Dark brown	15.6	192- 194	1.8

d*=decomposition

3.1 magnetic susceptibility :

The value of The effective magnetic moment of the complexes is tabulated in table[2] by using Balance Magnetic susceptibility .from 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(3.9)M.B due to the presence of three single electrons compare the low value(0.42) for nickel ion Ni⁺² because there is no single electron for nickel ion Ni⁺² . we conclude that the ligand works as strong ligand (strong field).

3.2 Infra-Red Spectroscopy

Infrared spectroscopy is one of the most commonly used tools for the detection of functional groups in pure compounds and mixtures. The spectra for L shows a characteristic stretching absorption bands at (3115,2740 ,1633,2940 and 1404) cm⁻¹ assigned to ν (C-H.Ar.) , ν (S-H) [23] , ν (C=N), ν (C-H) , and symmetrical C-N-C stretching respectively [24]. The C=N and S-H stretching 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 (ν) for some of the characteristics groups exhibited by the ligand and complexes.

Table 3: Characteristic absorption bands of ligand and its complexes

N O	ν O _H	ν C – H.alf	ν C – H.ar o	ν SH	ν C =N	ν C-N- C	Stru. Mov eme nt	ν M -N	ν M- S	ν M- Cl
L	330	2940	3115	2740	163	1477	1076	—	—	—

	2				3					
1	331 0	2933	3120	2788	163 9	1494	1072	686	401	308
2	330 3	2941	3116	2830	163 5	1479	1074	688	402	343
3	330 0	2977	3133	2814	163 7	1492	1074	680	433	312
4	329 2	2945	3122	2801	162 0	1489	1078	692	398	300
5	330 4	2970	3128	2744	163 7	1499	1074	688	405	341

3.3 Nuclear Magnetic Resonance

The ^1H NMR spectral data for the 2-ethyl-5-[(3-phenyl-5- sulfanyl-4H-1,2,4-triazol-4- yl) imino]methyl}benzene-1,4-diol displayed good solubility in DMSO. The proton nuclear magnetic resonance spectral data gave additional support for the suggested structure of the ligand. The spectra exhibit a triplet at (1.6)ppm due to methyl group, another singlet peaks exhibit at (2.5)ppm due to CH_2 , The ^1H NMR spectrums of ligand shows multiplets peak were observed around (7.5-8.06)are due to phenyl protons .the spectra exhibit also beaks at(3.8) , ,(8.9) and (9.95) due to SH[25], C-H.Ar , C=N-H and OH respectively[26,27]. the proton NMR of the ligand shown in figure(11) .

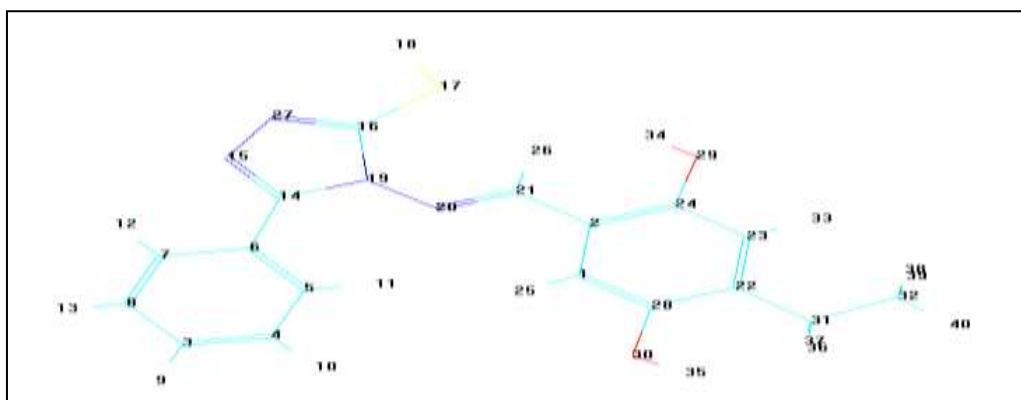
3.4 Mass spectra :

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 $m/z = 340$, The fragmentation pathways of ligand give the peaks at different mass numbers at $m/z = (295, 281, 267, 252, 238, 175, 165, 143, 117, 103, 99, 66, \text{ and } 65)$ due to $[\text{C}_{16}\text{H}_{15}\text{N}_4\text{O}_2]^+$, $[\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}_2]^+$, $[\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}_2]^+$, $[\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2]^+$, $[\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}_2]^+$, $[\text{C}_8\text{H}_5\text{N}_3\text{S}]^+$, $[\text{C}_9\text{H}_{11}\text{NO}_2]^+$, $[\text{C}_8\text{H}_5\text{N}_3]^+$, $[\text{C}_7\text{H}_5\text{N}_2]^+$, $[\text{C}_7\text{H}_5\text{N}]^+$, $[\text{C}_2\text{HN}_3\text{S}]^+$, $[\text{C}_2\text{N}_3]^+$, $[\text{C}_5\text{H}_5]^+$ Respectively. The intensity of these peaks reflects the stability and abundance of the ions. It is also supported by the mass spectra of the other complexes. as shown in Figure(12-17)and(Scheme 2). the complex $[\text{Cr}(\text{L})\text{Cl}_2]\text{Cl}$ showed a molecular ion peak at $m/z [\text{M}0] = (840)$ which is equivalent to molecular mass of the complex. This complex shows another a fragmentation peak with loss of chlorine atom at $m/z(804)$. the complex spectrum shows fragment ion peak with loss two chlorine atom at $m/z (768, 733)$ due to $[\text{Cr}(\text{L})_2\text{Cl}]^+$ and $[\text{Cr}(\text{L})_2]^+$ respectively.

The mass spectrum of the complex $[\text{Fe}(\text{L})_2\text{Cl}_2]\text{Cl}$ shows a molecular ion peak at m/z $[\text{M}^0]$ (843) 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 (808). the complex spectrum shows fragment ion peak with loss two chlorine atom at m/z (772, 737) due to $[\text{Fe}(\text{L})_2\text{Cl}]^+$ and $[\text{Fe}(\text{L})_2]^+$ respectively.

The mass spectrum of the complex $[\text{Co}(\text{L})_2\text{Cl}_2]\text{Cl}$ shows a molecular ion peak at m/z $[\text{M}^0]$ (845) 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 (811). the complex spectrum shows fragment ion peak with loss two chlorine atom at m/z (775, 740) due to $[\text{Co}(\text{L})_2\text{Cl}]^+$ and $[\text{Co}(\text{L})_2]^+$ respectively.

The mass spectrum of the complex $[\text{NiLCl}_2]$ shows a molecular ion peak at m/z $[\text{M}^0]$ (470), This complex shows another a fragment ion peak with loss of chlorine atom at m/z (435) and (399). The mass spectrum of the complex $[\text{CuLCl}_2]$ shows a molecular ion peak at m/z $[\text{M}^0]$ (475), This complex shows another a fragment ion peak with loss of chlorine atom at m/z (439) and (404). the mass spectra of the complexes shown in figure(13), (14), (15), (16), (17).



Figure(1):The stereochemistry of the Ligand

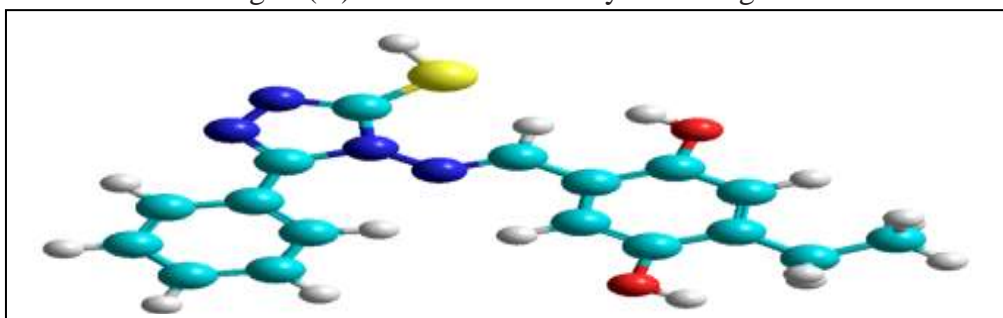


Figure (2): Graphical presentation of stereochemistry of the Ligand
($C_{16}H_{14}N_4SO$)

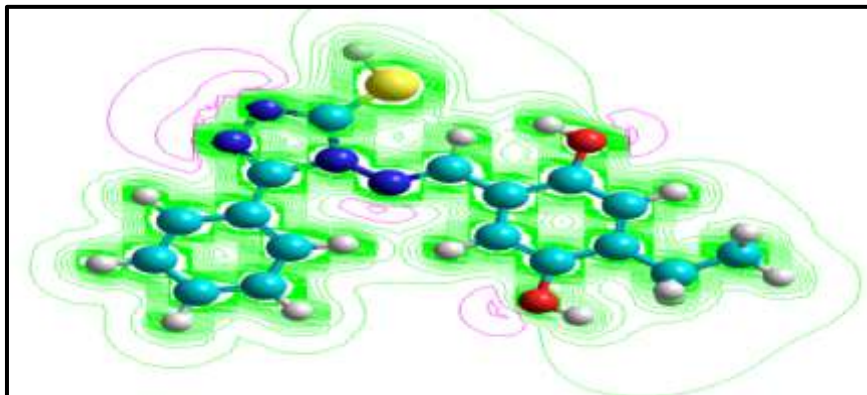


Figure (3): Electrostatic potential 2D for Ligand

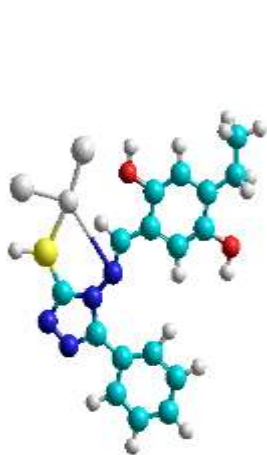


Figure 4:[Ni(L)Cl₂]

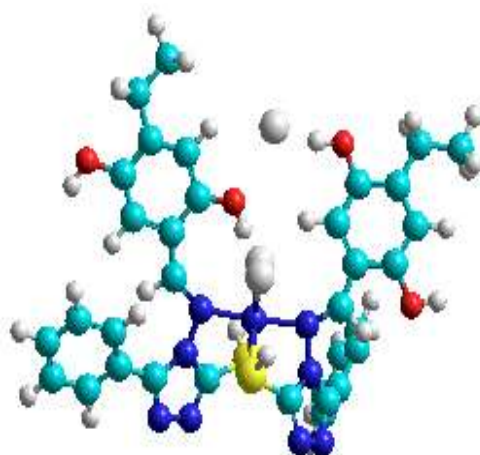


Figure 5:[Co(L)₂Cl₂]Cl

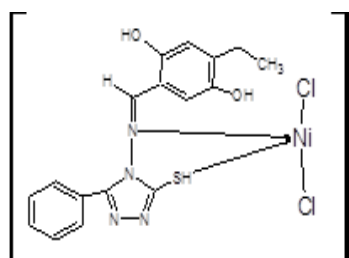


Figure 6

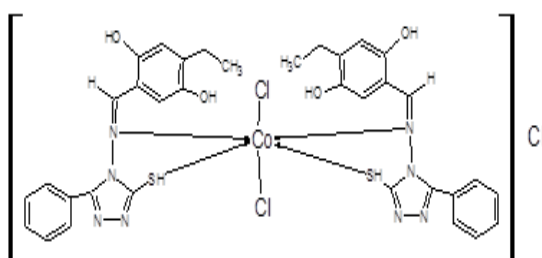


Figure 7

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

3-4 – 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[28] , 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 lipid layers of the bacterial membranes. The activity

of transition metal complexes can be expound on the basis of Overton's concept [29] and Chelation theory [30]

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

Compound	Escherichia coli Inhibition zone(mm)	Staphylococcus Aureus Inhibition zone(mm)
L= C ₁₇ H ₁₆ N ₄ SO ₂	10++	15+++
[Cr(L) ₂ Cl ₂]Cl	18++++	15+++
[Fe(L) ₂ Cl ₂]Cl	20+++++	10++
[Co(L) ₂ Cl ₂]Cl	18++++	10++
[Ni(L)Cl ₂]	13+++	10++
[Cu(L)Cl ₂]	15+++	10++

****(+ = Weak Inhibition , ++ =Medium Inhibition , +++ = Good Inhibition ,++++ =Very good**

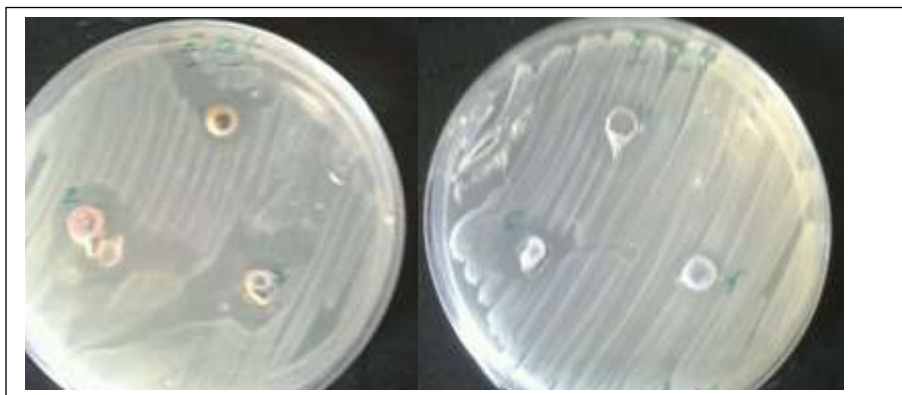
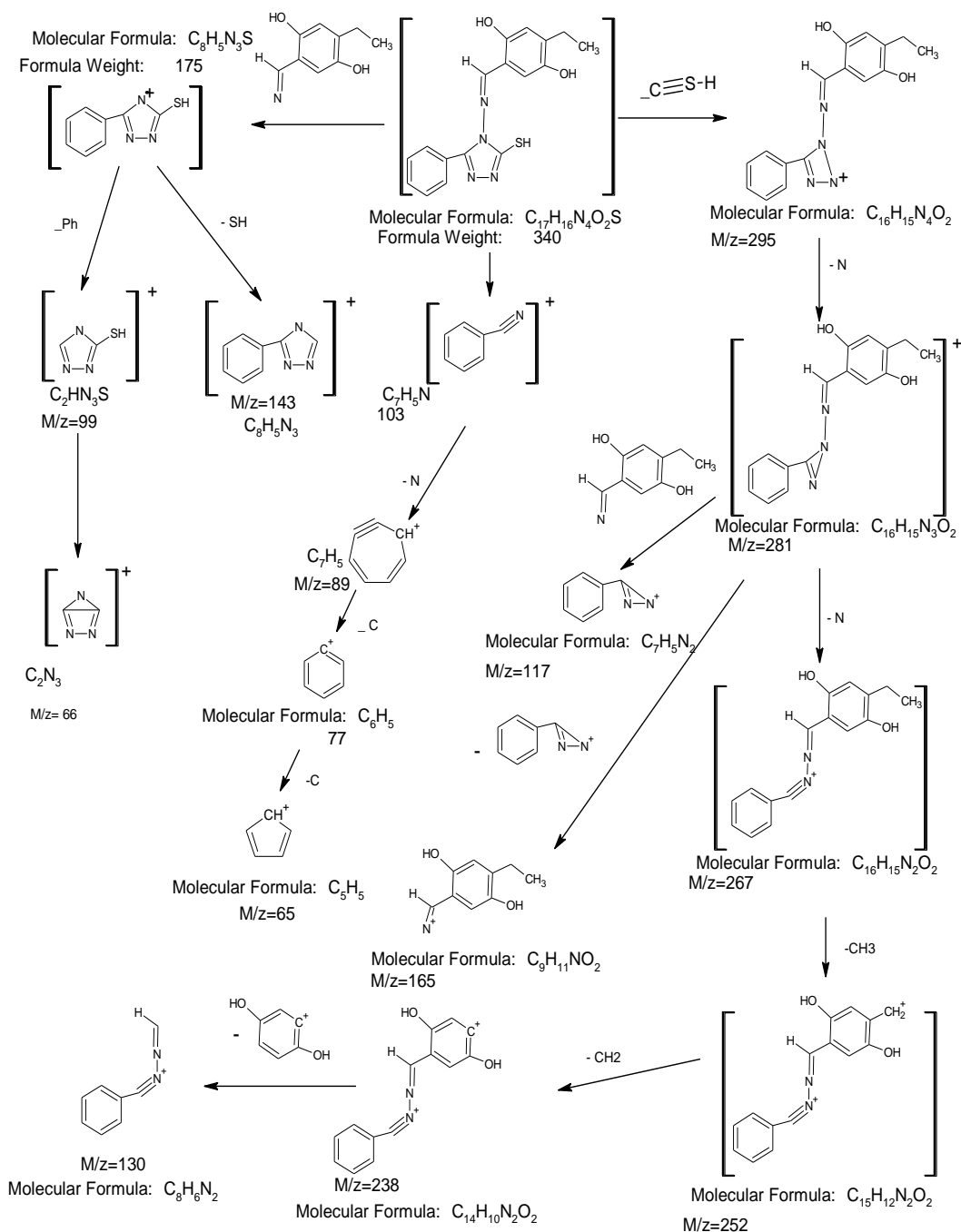


Figure (8) biological study

4. Conclusion:

The ligand 4-{[(Z)-(2-methoxyphenyl) methylidene] amino}-5-phenyl-4H-1,2,4-triazole-3-thiol. was successfully synthesized. The elemental analysis, IR, ^1H 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) .



Scheme2

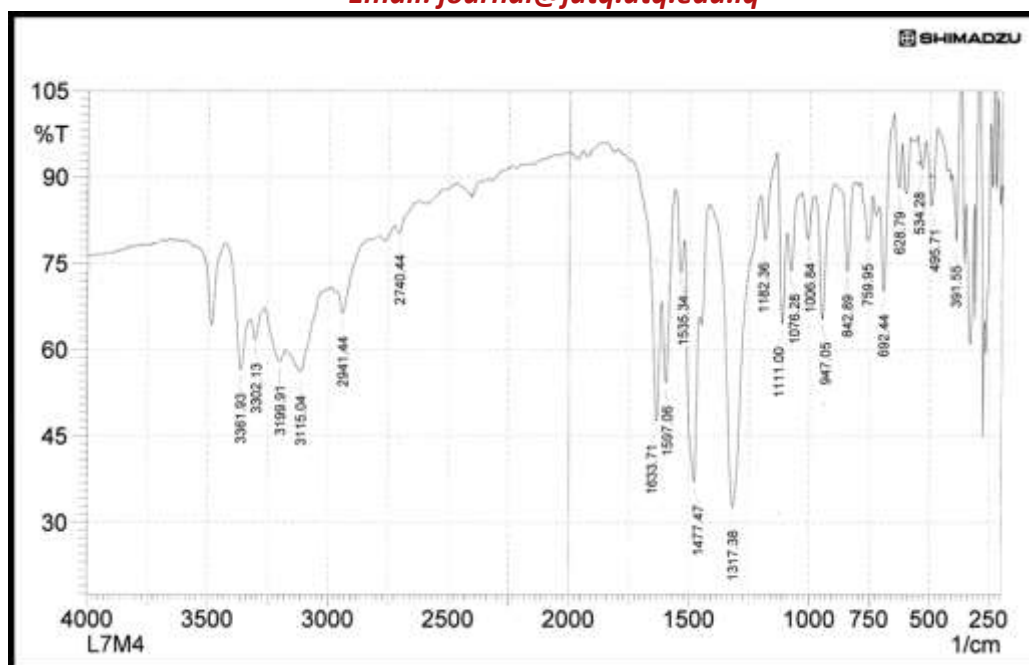


Figure 8: IR spectra of Ligand ($C_{17}H_{16}N_4SO_2$)

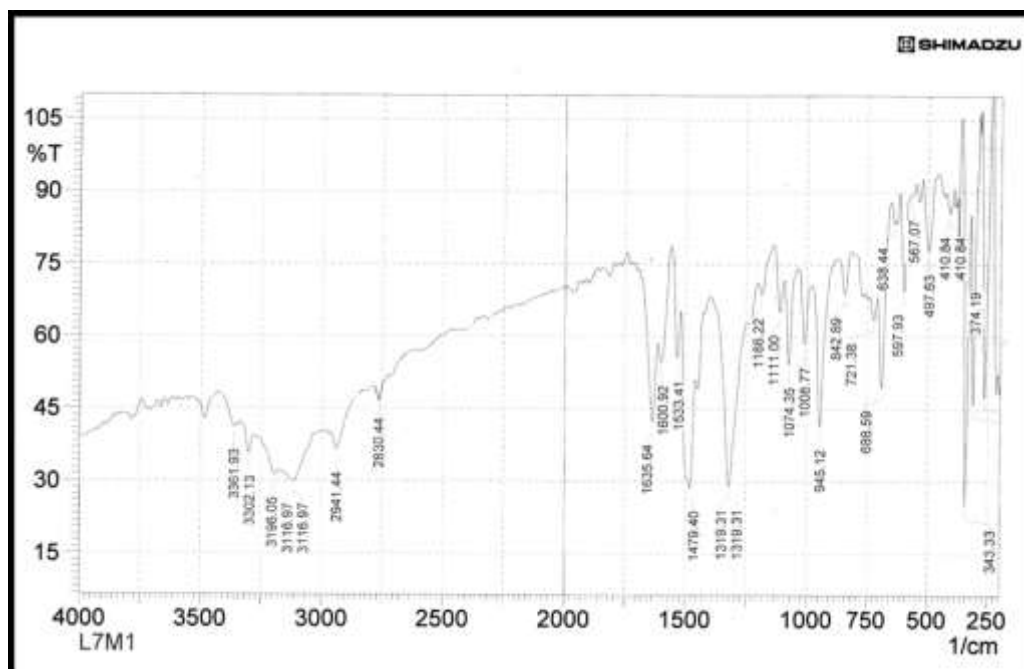


Figure 9: IR spectra of $[Fe(L)_2Cl_2]Cl$



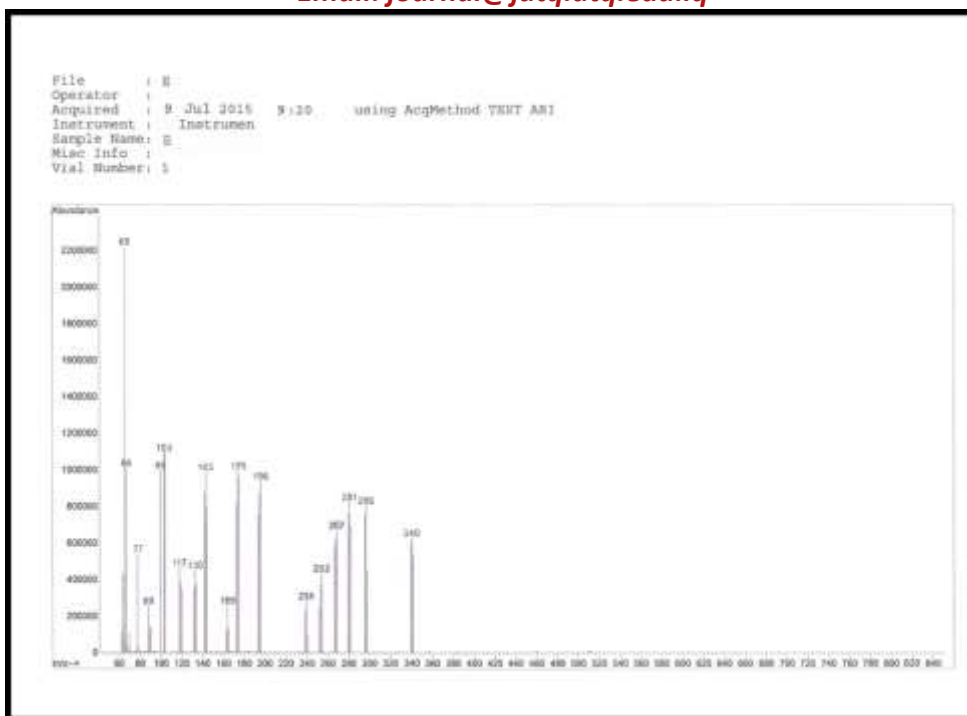


Figure 12: mass spectra of ligand

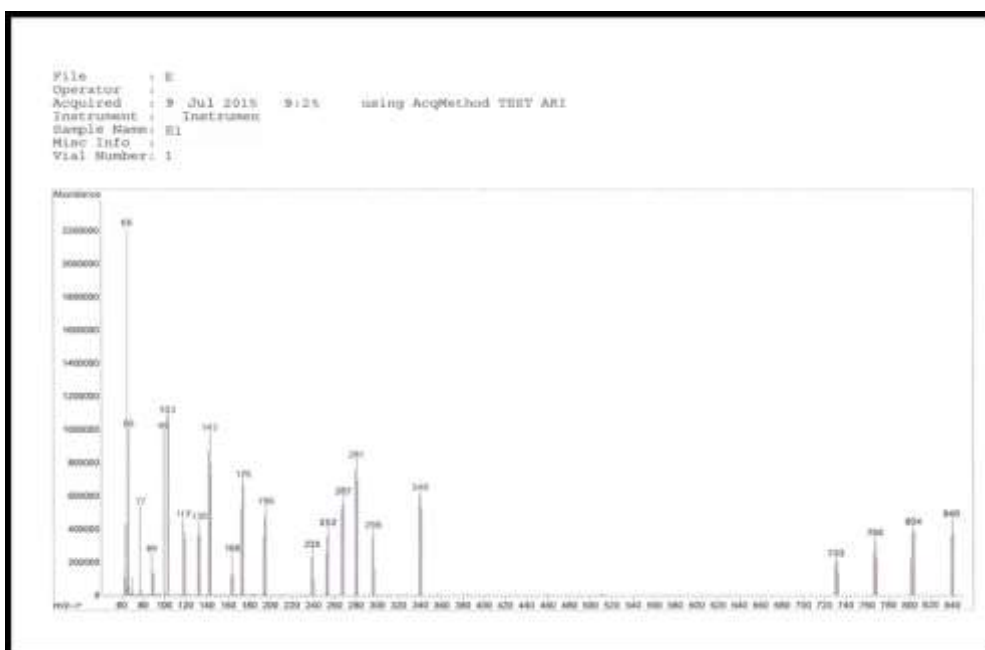
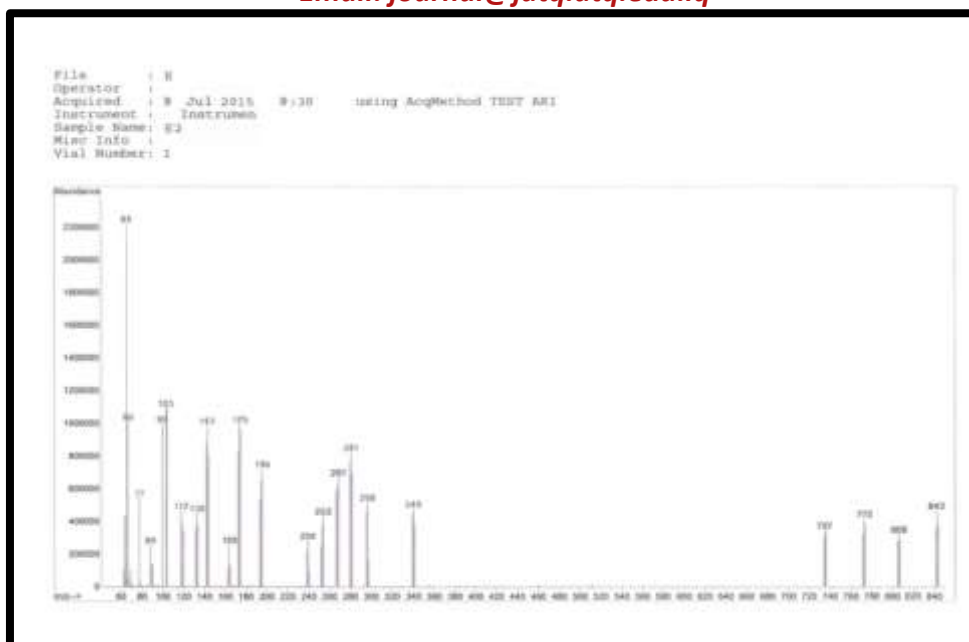


Figure 13: mass spectra of $[\text{Cr}(\text{L})_2\text{Cl}_2]\text{Cl}$



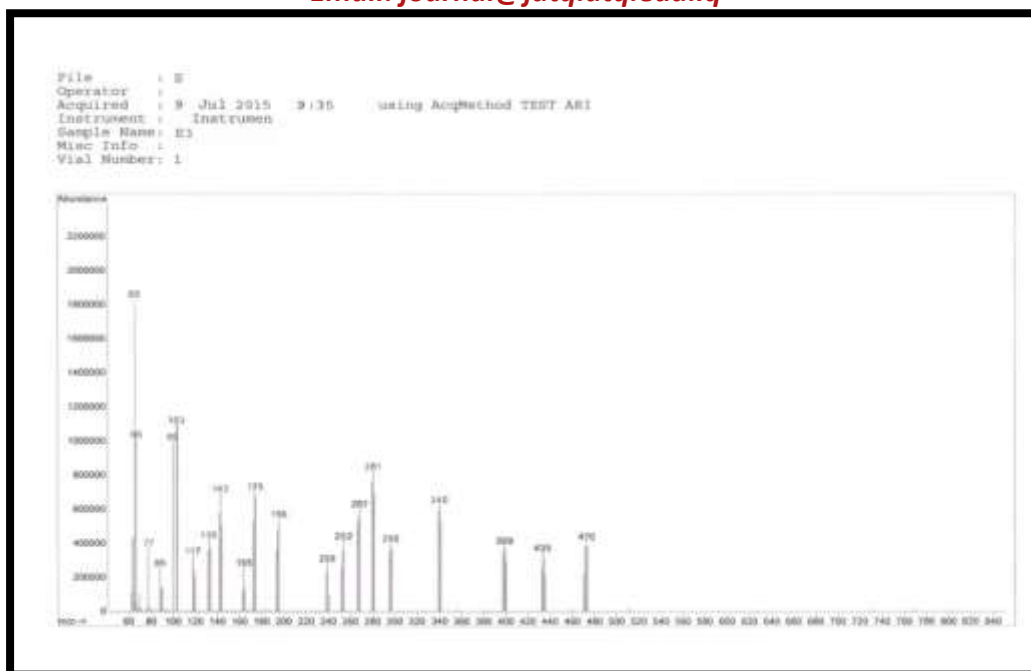


Figure 16: mass spectra of $[\text{Ni}(\text{L})\text{Cl}_2]$

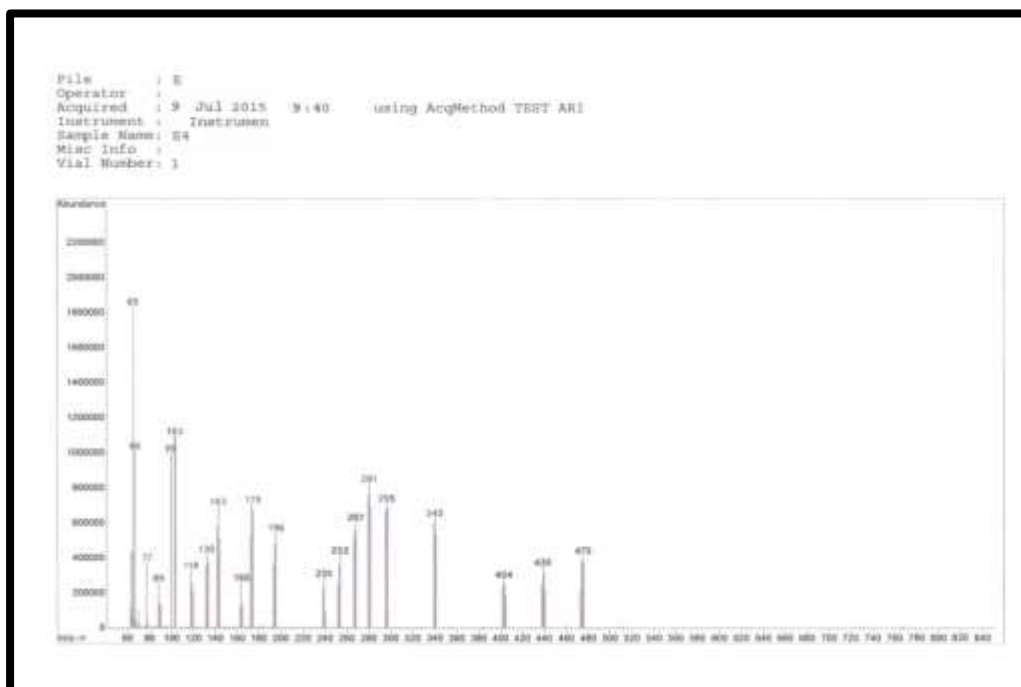


Figure 17: mass spectra of $[\text{Cu}(\text{L})\text{Cl}_2]$

References

- [1].Ouellette, W.; Hudson, B. S.; Zubieta, J. Inorg. Chem.,46, 4887, (2007)
- [2]. Liu, J. C.; Fu, D. G.; Zhuang, J. Z.; Duan, C. Y.; You, X. Z. J.Chem. Soc., 2337, (1999).
- [3]. Abramovitch, R. A.; Gibson, H. H.; Olivella, S. J. Org. Chem., 66, 1242, (2001)
- [4]: Neslihan, D.; Ahmet, D.; Sengul, A.and Sancak, K., "Synthesis and antimicrobial activities of some new 1,2,4-triazole derivatives", Eur. J. Med. Chem. 39:793-804. (2004).
- [5]: Neslihan, D.; Ahmet, D.; Sengul, A., and Elif. C. "Synthesis and antimicrobial activities of some new [1,2,4] triazolo [3,4-b] [1,3,4] thiadiazines", 75- 91. (2005)
- [6]: Neslihan, D.; Ahmet, D.and Sengul, A. K. "Synthesis and biological activity of new 1,2,4-triazol-3-one derivatives", Russian J. Bioorg. Chem. 39: 387- 97, (2005).
- [7]: Sabir, H.; Gyoti, S.and Mohd, H. "Synthesis and antimicrobial activities of 1,2,4-triazole and 1,3,4-thiadiazole derivatives of 5-amino-2-hydroxybenzoic acid", E. J. Chem. 5 (4), 963- 968, (2008).
- [8]: Aiyalu, R. and Kalasalingam, A. R., "Synthesis of some novel triazole derivatives as anti-nociceptive and anti-inflammatory agents", 59: 355- 364, (2009)
- [9]: Mudasir, R. B.and Abdul, R. "Substituted 1,2,4-triazoles and thiazolidinone from fatty acids: Spectral Characterization and antimicrobial activity", Indian J. Chem., 48 B, 97-102, (2009).
- [10]: Malii, R. R.; Somani, R. R.; Toraskar, M. P.; Mali, K. K.and Shirodkar, P. Y. "Synthesis of some antifungal and Anti-tubercular 1,2,4-triazole analoges", Int. J. Chem Tech Res., 1 (2). 168-173, (2009).
- [11]Abdel-Aziz, H. A., Abdel-Wahab, B. F., Badria, F. A., Arch.Pharm., 343, 152-159, (2010).
- [12]Bennet L, Baker H I; J. Org. Chem., , 22, 707, (1957).
- [13] Nishio H, Yamamota I, Kaziya K, Han O K; Chem. Pharm. Bull., , 17, 539, (1969).
- [14] Liu D., Zheng Y., Steffen W., Wagner M., Buttand H.-J. Ikeda T., Macromol. Chem. Phys., , 214, 56–61. (2013).
- [15]- El-Sayed M. Sherif, Int. J. Electrochem. Sci., 7 4834 – 4846, (2012).
- [16]. E.M. Sherif, S.-M. Park, J. Electrochem. Soc., 152 B428, (2005).
- [17]. El-Sayed M. Sherif, J. Appl. Surf. Sci., 252 ,8615. (2006).
- [18]. E.M. Sherif, S.-M. Park, Corros. Sci., 48 ,4065. (2006)

- [19]. El-Sayed M. Sherif, A.H. Ahmed, Synthesis and Reactivity in Inorganic, Metal-Organic and Nano Metal Chemistry, 40 ,365. (2010)
- [20] C. D. Brandt, J. A. Kitchen, U. Beckmann, N. G. White, G.B. Jameson, and S. Brooker, "Synthesis and structures of 3,5-disubstituted 1,2,4-triazole head units and incorporation of 3,5-dibenzoyl-1,2,4-triazolate into new [2 + 2] Schiff-base macrocyclic complexes," *Supramolecular Chemistry*, vol. 19, no. 1-2, pp. 17–27, (2007).
- [21] Z.Khiati, A . A . Othman and B . Guessas and S . *Afr.J.Chem.*, 60 ,20-24,(2007).
- [22] A . vogel, " Text book of practical organic chemistry " Longman, 4th ed,65,395,(1978).
- [23] K.M.Daoud and M.A.Eisa .*Nat. J. of chemistry*,7, 438-445, (2002).
- [24] Nakamoto, N. "Infrared spectra of inorganic and coordination compound " 6th ed; Wiley Interscience; New York (1997)
- [25] S. George and *Acta oham.*, 58, 119-129, (2008).
- [26] A Huang, J.J.Kodanko, L.E.Overman and *J.Am.Chem.Soc.*, 126, 14043-4053, (2004).
- [27] George S., *Acta omarm.*, 58, 119-129, (2008).
- [28] Andrews M. , *J.antimicrobail chemotherapy J.*, 48(1), 5-16, (2001).
- [29] P. Knopp, K. Weighardt, B. Nuber, J. Weiss, , *Inorg. Chem.* 29, , 363. (1990).
- [29] Y. Anjaneyalu, R.P. Rao, *Synth. React. Inorg. Met.-Org. Chem.*, 26, , 257. (1986).

تحضير وتشخيص ودراسة الفعالية البايولوجية للكاند مع بعض معقدات العناصر
الانتقالية

2-ethyl-5-[[(3-phenyl-5-sulfanyl-4H-1,2,4-triazol-4-
yl)imino]methyl]benzene-1,4-diol

رشا ناصر الجابري

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كلية العلوم / قسم الكيمياء

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تم تحضير سلسلة جديدة من معقدات العناصر الانتقالية (Cu(II) و ethyl-5-[[[(3-phenyl-5-sulfanyl-4H--2-lyl)imino]methyl} benzene-1,4-diol مع Cr(III), Fe(III), Co(III), Ni(II) تم تشخيص الليكاندات والمعدقات المحضرة باستخدام تحليل العناصر الدقيق، التوصيلية المولارية، أطياف الأشعة تحت الحمراء، وبروتون الرنين النووي المغناطيسي وطيف الكتلة والحساسية المغناطيسية. السلوك الالكتروليتي للمعدقات تم تأكيده باستخدام تقنية التوصيل المولاري. وتم الاستنتاج بان الليكاند يتناسق من خلال ذرتي النتروجين والكبريت كما موضح في الجدول (3) , في جميع المعقدات وجد ان الليكاند يعمل كليكند ثنائي السن ويتناسق من خلال [S] و [N] وهذه الرؤية تضيف دعما اخر من خلال ظهور حزمة تقابل حزمة امتصاص M-N بحدود cm^{-1} (692-680). من النتائج التي تم الحصول عليها اقترح الشكل مربع مستوي للـ Ni(II) ورباعي السطوح (Cu(II) بينما لمعدقات Cr(III), Fe(III), Co(III) شخصلت على انها ثمانية السطوح. وتم اختبار الفعالية البايولوجية للليكاند 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 .