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College of Science for Women
Department of Chemistry

Preparation and Characterization of Nickel(II), Copper(II), and Zinc(II)ion Complexes Using a New Schiff Base Ligand, and Study of Their Biological Activity

A Thesis

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By

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بِسۡمِ ٱللَّهِ ٱلرَّحۡمَٰنِ ٱلرَّحِيمِ

قُل لَّآ أَقُولُ لَكُمۡ عِندِى خَزَآئِنُ ٱللَّهِ وَلَآ أَعۡلَمُ ٱلۡغَيۡبَ وَلَآ
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ٱلۡأَعۡمَىٰ وَٱلۡبَصِيرُۚ أَفَلَا تَتَفَكَّرُونَ ٥٠

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Supervisor Certification

I certify thesis entitle

Preparation and Characterization of Nickel(II), Copper(II), and Zinc(II) ion Complexes Using a New Schiff Base Ligand, and Study of Their Biological activity

Was prepared under my supervision at the University of Babylon / College of Science for Women as a partial Requirement for the degree of Master in Chemistry.

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Dedication

To…..

Al-Imam Ali ben Abi Taleb

Zaynab

Acknowledgements

Before every beginning and after every end and between every line and between every letter Thank you, love and praise to my dear Lord (**Allah**) Thanks to the owner of my soul, my heart and my love.....

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List of Abbreviations

Abbreviations	Full name
^{13}CNMR	Carbon nuclear magnetic resonance
^{1}HNMR	Proton nuclear magnetic resonance
6-APA	6-Aminopencillic acid
BI	Benzoyl isothiocyanat.
CA	Cinnamaldehyde
CTX-M	Cefotaximase-Munich
DCM	Dichloromethane
DMSO	Dimethyl Sulfoxide
DTG $_{max}$	Differential thermogravimetric maximum
GGA	Glacial Acetic Acid
HMBA	2-hydroxy-4-methoxybenzaldehyde
m/e or m/z	Mass to charge
MIC	Minimum inhibitory concentration.
PPA	Propanoic acid
UV-Visible	Ultraviolet-visible radiation
υ	Frequencies
ZI	Zone of inhibition
λ_{max}	Wavelength for maximum absorption

Chapter One

1.1.Introdaction

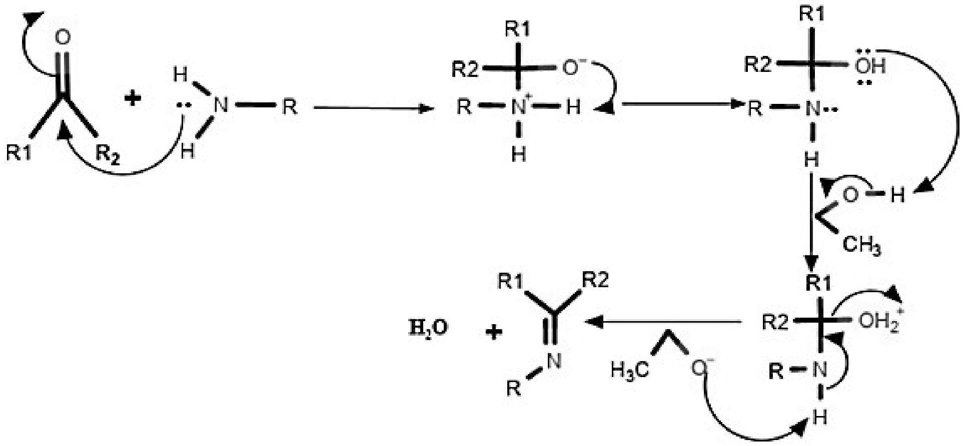
Coordination Chemistry is one of the main pillars of inorganic chemistry which is both an intriguing and experimentally difficult frontier in modern chemical sciences the most active area of researches in inorganic chemistry today is coordination compounds, which has resulted in the development of innovative products with equally novel applications in a variety of industries including medicines, fungicides, pigments, paints, polymers and photoconductors (Kubra,N.K.,*et al.,*2018). A coordination complex is made up of a core atom or ion that is coordinated by one or more molecules or ions (Ligands) that operate as Lewis bases and form coordinate bonds with the central atom or ion, which then functions as a Lewis acid(Soldatović, T.,2020). Donor atoms are those in the ligands that are directly bound to the primary atom or ion (Sinha,S., *et al.*,2022).The central atom is a metal or metalloid and the compound that results from bond formation is called a Coordination compound, the Coordination complex or often simply a Complex (Khan, M. W.,*et al*,2021). The species that donates the electron pair, also known as the ligand, is assumed to be coordinated with the species that will receive the single pair of electrons (the electron-pair acceptor)The traditional prerequisite for the creation of what we have referred to as coordinate bonds, leading to a coordination compound, is a central atom or ion with vacant or empty orbitals and connected ionic or neutral atoms or molecules, with each bringing lone pairs of electrons(Rahaman ,M.S., *et al.,*2022).

Since coordination chemistry has many interests and is involved in many fields, therefore, coordination compounds is not very new in the field of medicine and drug discovery ,in the world of medicine and drug discovery, coordination compounds are not a particularly new concept, This field, which interconnects the line between medicine and inorganic chemistry, encompasses metal-based therapeutically significant chemicals, agents that isolating or mobilize metal, diagnostic tools that contain metal, and the therapeutic recruitment of endogenous metal ions, also a regular biological process requires hundreds of inorganic complexes and metals, which are found in our body and biological system in the form of various enzymes and protein cofactors(Chen, K., & Arnold, F. H., 2020). Chemists are constantly drawn to the fields of the synthesis and use of coordination compounds and organometallics due to their biological significance and crucial role in maintaining important biological processes, and other interests the biological activity of many coordination compounds activities against bacteria and fungi (Tripathi,H.S.M.V.D.,2020) the type of heterocyclic compounds has been of considerable interest in terms of structural chemistry, catalysis and biological functions. The field has undergone spectacular growth due to the synthesis of multidentate ligands from heterocyclic compounds and the complexes of such ligands form with metal ions . There are a number of multidentate ligands that play important roles in coordination chemistry and catalyst designing (Taghreed . H. Al-Noor., *et al.,*2013), and due to the large and diverse range of ligands, including heterogeneous ligands, and the Heterocycles have played a prominent role among pharmaceuticals, as they have been essential in the perpetuation, propagation, and evolution of life in molecular forms such as nucleotides, carbohydrates, hemes, and amino acids (Scriven,E.,& Ramsden,C.A., 2017).

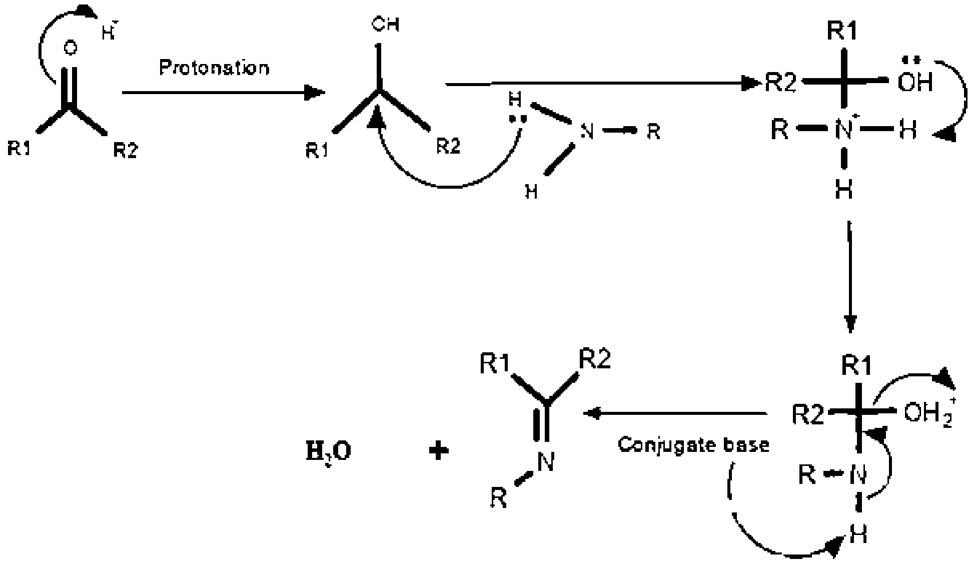
1.2.Schiff Bases

The organic compounds which includes several active groups such as azomethine (C=N) Schiff base is the condensation product of aldehydes or ketones with the primary amines,The Schiff base was named after the scientist *Hugo Schiff*, and These compounds are stable. Schiff bases contain azomethine group and have the general syntactic formula (RHC = N-R1). The groups(-R) may be aliphatic, aromatic, homogeneous or heterogeneous and other various substitutes for Schiff bases (Shah,S.S.,*et al.,*2020) , (Arumugam AP,*et al.,*2017).There are important compounds in coordination chemistry, such as that the symmetrical Schiff base compounds that produce stable molecules, schiff base compounds are bonded to metal ions through azomethine nitrogen .In the field of coordination chemistry, schiff base ligands have gained a lot of attention due to their simple production, accessibility, and electronic features .The importance of Schiff base compounds in inorganic synthesis, analytical chemistry, metal refining, metallurgy, electroplating and photography has led to a lot of interest in these compounds (More,M.S., *et al.,*2019). It also has multiple applications in the medical field, including anti-cancer (Sama A. Al-Aghbari,*et al.,*2019),(Ranjan K., *et al.,*2018), antibacterial (Mohamed Gabera,*et al.,*2018),antifungal (T.F.F.Magalhaes,*et al* 2020),anti-inflammatory(T.J.Saritha,*et al.,*2021),anti-tumor and antiviral products(Domenico Iacopetta,*et al*.,2021) and ureases inhibitory(de Fátima,*et al,*2018).The complexes of Schiff base have attracted special attention (Obaid,S.M.H.*,et al.,*2020) especially the presence of multifunctional groups, containing nitrogen, sulfur, and oxygen donor atoms, as well as their transition metal, (Diana,R & Panunzi,B.,2020).

The general mechanism of the Schiff base reaction in the basic medium **(** Uddin, M. N.,*et al.,*2020),is represented by the **Scheme (1-1)**:



In the acidic medium:



Scheme(1-1):Mechanism of the Schiff base Reaction in the Basic and acidic Medium

1.2.1. Methods for Synthesis Schiff Bases

(A) Condensation Reaction Method

One of the most popular methods for preparing Schiff bases is the condensation reaction method, in which the reaction is stimulated by the presence of droplets of glacial acetic acid ,hydrochloric acid, or Para-sulfonic acid colorant ,reflux for carbonyl compounds with an amine. Several researchers have explained that the acid gives a proton to the carbonyl group, forming the carbonate ion, which is then fastly added to the amine(Aurora Reiss,*et al.,*2021), and the **Figure (1-1)** shows this compound forming by this way .Schiff base ligands have been known about for a very long time and can be easily synthesized by condensation reactions of primary amines and carbonyl compounds in which the characteristic azomethine bond is formed (Viviana Bressi ,*et al.,*2022)

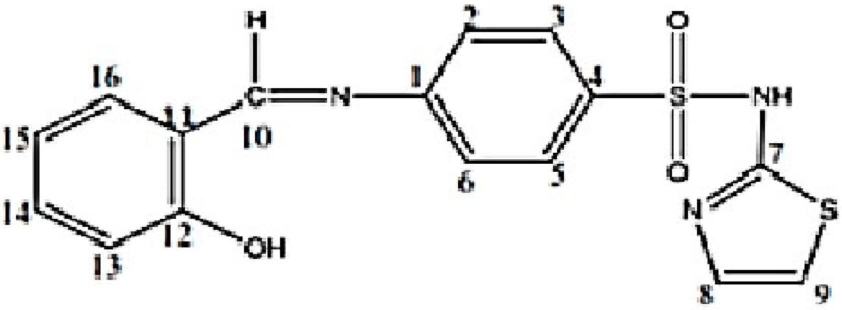
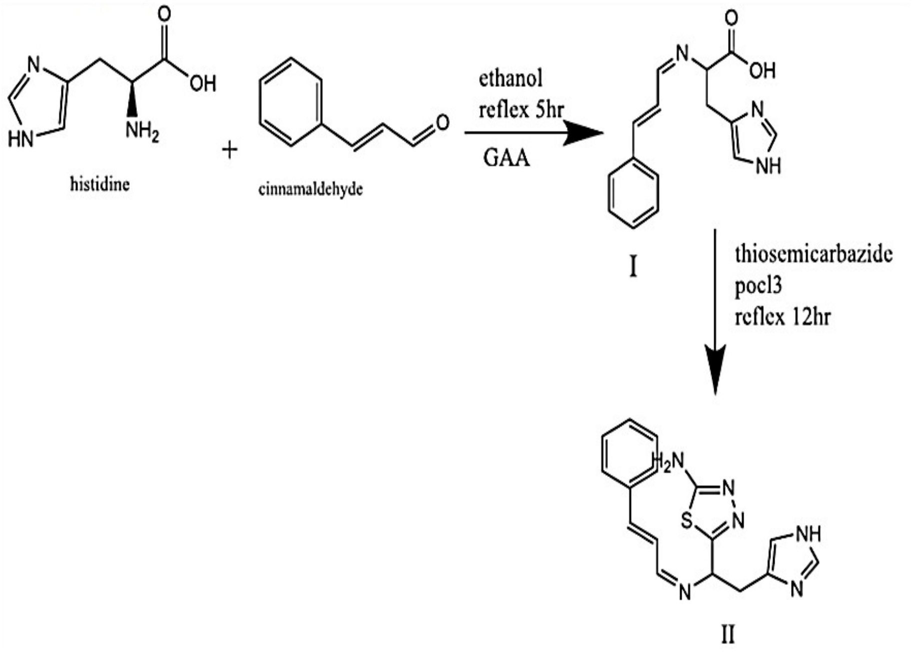


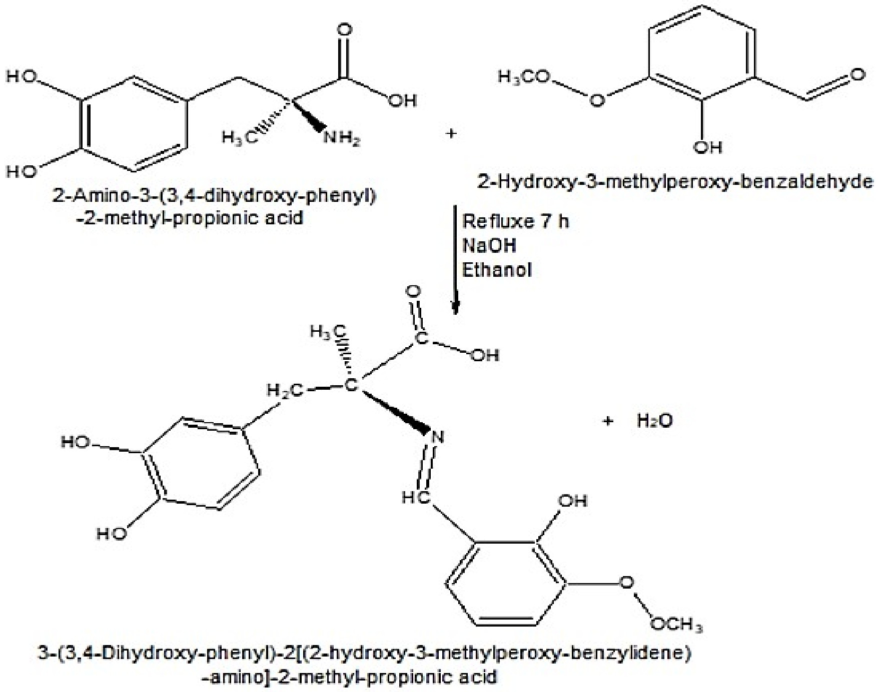
Figure (1-1): Schiff base Prepared by Condensation Reaction Method

In the study (Mahmood Ibrahim,*et al*.,2020) was synthesised a new Schiff base from the cinnamaldrhyde by condensation reaction method and detection of these new compounds by different techniques and also measured antimicrobial activity, **Scheme(1-2)** shows how to prepare these compounds



Scheme (1-2):Synthesis of Intermediate and Final Compounds from the Cinnamaldrhyde by Condensation Reaction Method

In the study (Obaid,S.M.H.,*et al.,*2020) the Schiff base ligand (L) was prepared through react (1mmol) of methyldopa (2-amino-3- (3,4-dihydroxy-phenyl)-2-methyl-propionic acid) in ethanol with (1 mmol) of sodium hydroxide to the solution and was added (1 mmol) of o-vanillin (2-hydroxy-3-methoxybenzaldehyde) dissolved in ethanol the mixture was refluxed with stirring the of methyldopa and o-vanillin in ethanol gives according to the following reaction by condensation method the, **Scheme (1-3)**Shows the Schiff base reaction.

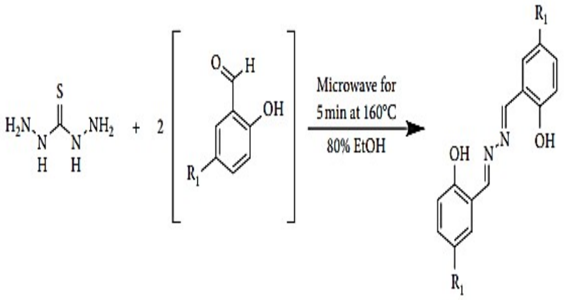


Scheme(1-3):Synthesis of Schiff base Ligand (3-(3,4-Dihydroxy-phenyl)-2](2-hydroxy-3-methylperoxy-benzylidene-amino-[2-methyl-propionic acid

(B) Microwave Irradiation Method

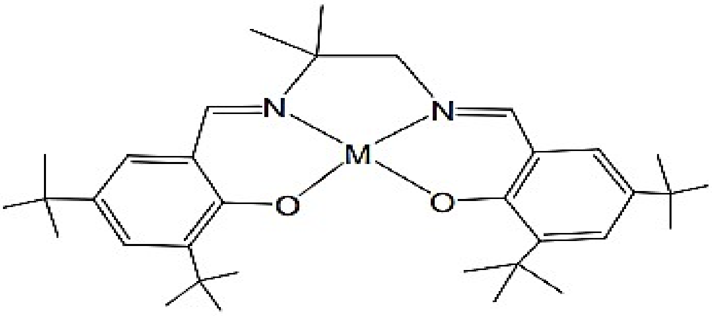
The invention of microwave-mediated organic processes in 1986 posed a significant challenge to a wide range of scientists and engineers .A Microwave oven emission non-ionizing radiation, which causes dielectric heating of the reactants (Bandyopadhyay,D.,*et al.,* 2021). Microwaves are electromagnetic waves with a wavelength range that fall between far-infrared and radio rays, Microwave waves are non-ionizing rays of insufficient energy to break bonds and form photons ,they are not thermal energy, but they convert to heat while they interact with the medium in which they are reflected, implemented or absorbed, due to the ability of some liquid or solid materials to convert electromagnetic waves into heat, which causes chemical reactions (Mishra,A. P., *et al.,* 2012). Microwave-assisted synthesis is a branch of green chemistry, microwave-assisted synthesis has gained much attention in recent years .The applications of microwave irradiation are used for carrying out chemical transformations, which are pollution-free, eco-friendly, low cost and offer high yields together with simplicity in processing and handling .The salient features of the microwave approach are shorter reaction times, This forces solvents and reactants to cause molecular interactions. Microwave-induced methods have advantages over common heating systems when products are formed through the acceleration of reaction following mild conditions, good selectivity and environmentally benign processes (Schütz, M. B.*,et al*.,2018).

There are some controversies regarding the rate acceleration in the microwave oven when microwave irradiation was used for the preparation of these *β*-lactam derivatives, It was seen that low-power microwave irradiation produces *cis-β*-lactam in higher proportions than *trans-β*-lactams.However, high-power microwave-induced reactions of the same substrates produced trans-*β*-lactams as a major proportion. Pure cis-*β-lactams* on exposure to high power microwave irradiation in the presence of tertiary base did not isomerize(Banik, B.K.,2018). In the study(Kassim, K.,*et al.,*2019) synthesis a new Schiff base by microwave method, and the **Scheme (1-4)** shows these compounds.



Scheme (1-4): Schiff base Synthesis by Microwave Method.

In the study (Said, M. A.,*et al*,2020) for the preparation of H_2L: 2-methylpropane-1,2-diamine and two equivalents of 3,5-di-tert-butyl-2-hydroxybenzaldehyde in ethanol were placed in a microwave reactor vessel and irradiated for 5 minutes at 100ºC. Ethanol was completely removed, and the yellow solid was dissolved in DCM to which 10 mL of n-hexane was added. The solution was placed in a freezer (-80°C) to yield light yellow crystals of pure H_2L,**Figure(1-2)** Shows ligand and its metal complexes.



Figure(1-2):Unsymmetrical Salen(tBu)H2 (H_2L) and its Metal Complexes, M= Pd, Zn, Cu, Fe, Ni, Mn and V

Another study in (Chauhan,D.S.,*et al*,2020) synthesis A new Schiff base of chitosan with cinnamaldehyde (Cinn-Cht) was synthesized in a single step using microwave irradiation and characterized using spectroscopic techniques.In this context, we herein report the synthesis of cinnamaldehyde cross-linked chitosan to prepare a Schiff base (Cinn-Cht),**Figure(1-3)** Shows synthesis of Schiff base.

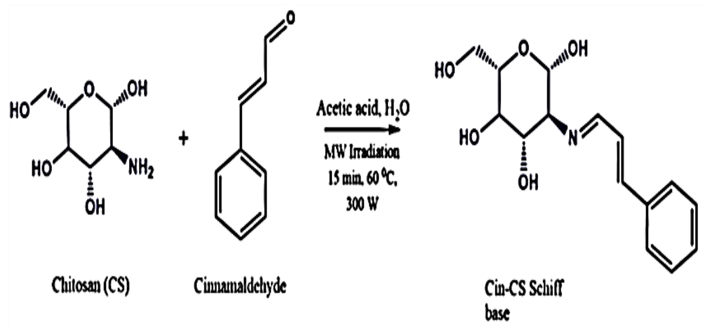
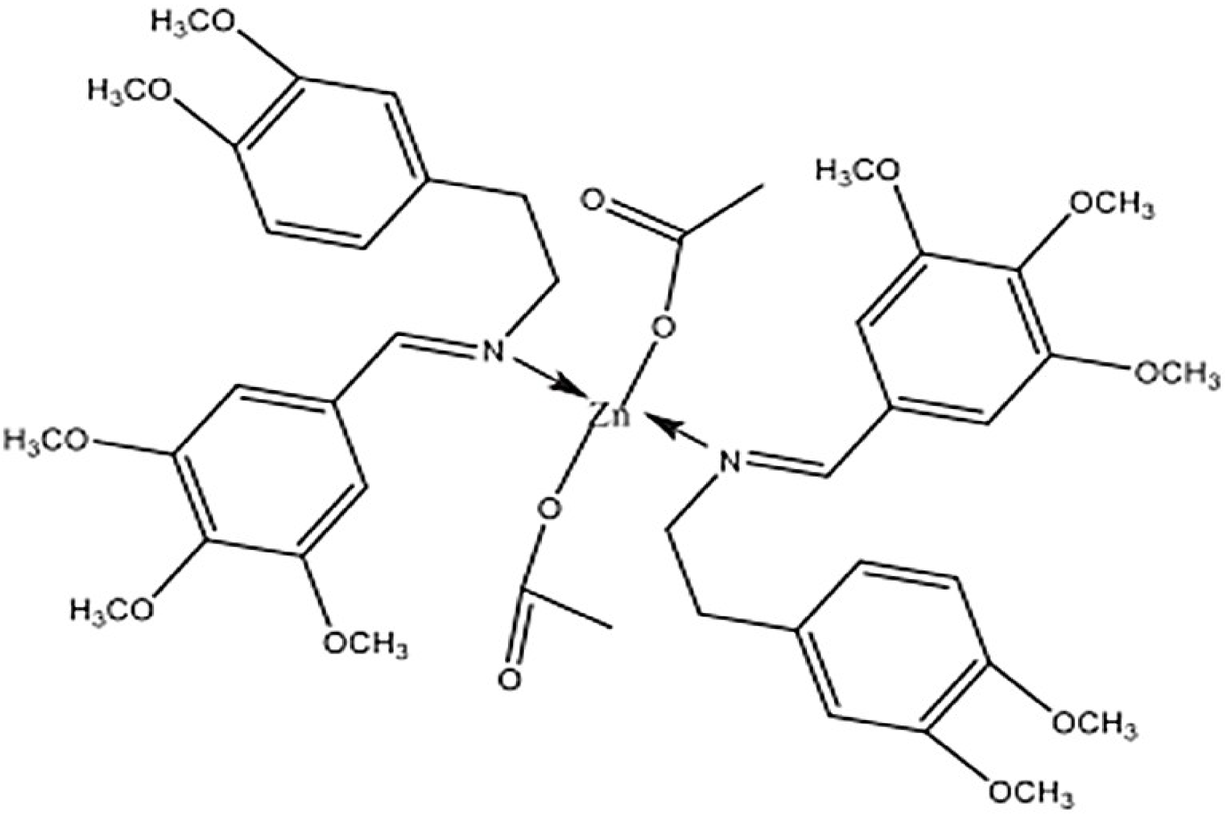


Figure (1-3): Synthesis of Schiff base from Chitosan with Cinnamaldehyde

1.2.2.Classification of Schiff base

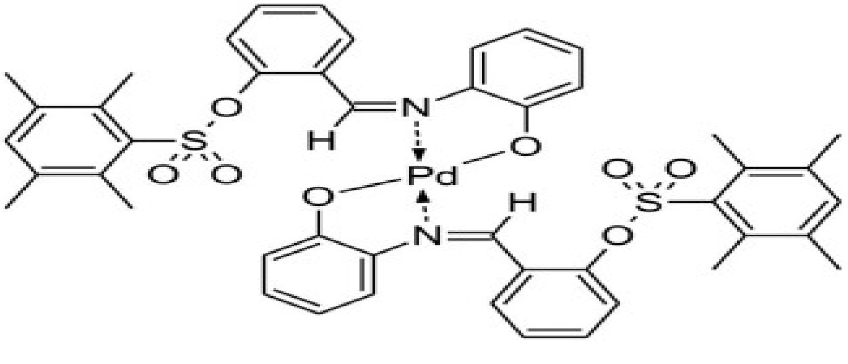
Schiff bases are Classification as donor ligands depending on the number of donor atoms present in the Schiff base ,This classification explains that coordination is the result of a Lewis acid-base reaction in which neutral molecules or anions (Ligands) form coordinate covalent bonds with a (Central metal atom/ion).Ligands are Lewis bases with at least one electron pair to donate to a Metal atom/ion. The consistency is affected by the nature of the metal ion and the metal ion's position in the periodic table, the charge and the radius.

-Monodentate Schiff Bases: These ligands contain one donor atom has one electron pair to donate to the metal ion, the (Bushra Naureena.,*et al*.,2021)Synthesis Monodentate Schiff Base,**Figure (1-4)** shows the structure for Monodentate Schiff Base of ligand.



Figure(1-4):Synthesis of Zinc (II) Complex with Monodentate Schiff Base of Ligand

-Bidentate Schiff base: These Schiff base ligands contain two electron-donating atoms (two pairs of electrons) to the metal ion. In the study (Gizem Selvi,*et al* 2020) synthesis a complex of Pd(II) with a ligand that has two donor atoms, **Figure (1-5)** shows the structure of the bidentate Schiff base ligand.



Figure(1-5):Synthesis Complex Pd(II) from Bidentate Schiff base Ligand

Schiff bases derived from Amoxicillin trihydrate with Cinnamaldehyde and p-Chlorobenzaldehyde and their complexes with bivalent transition metal ions were screened for antibacterial activity against several bacterial.The metal complexes showed enhanced antibacterial activity compared to uncomplexed ligand(Joshi,S.,*et al.,*2011),**Figure(1-6)** Shows the reaction.

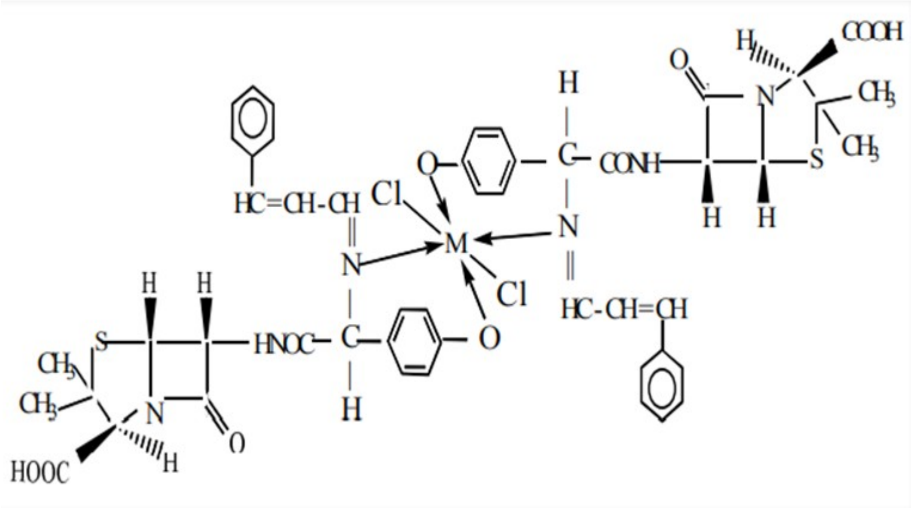


Figure (1-6):Synthesis of Schiff base from Amoxicillin trihydrate with Cinnamaldehyde

-Tridentate Schiff base: These Schiff bases contain three donor atoms (three pairs of electrons) to the metal ions. researcher(Kordestani ,N.,*et al.,* 2021) have synthesised the copper complex Cu(II) with ligand has three atoms can be donated,**Figure (1-7)** shows the structure for tridentate Schiff base ligand.

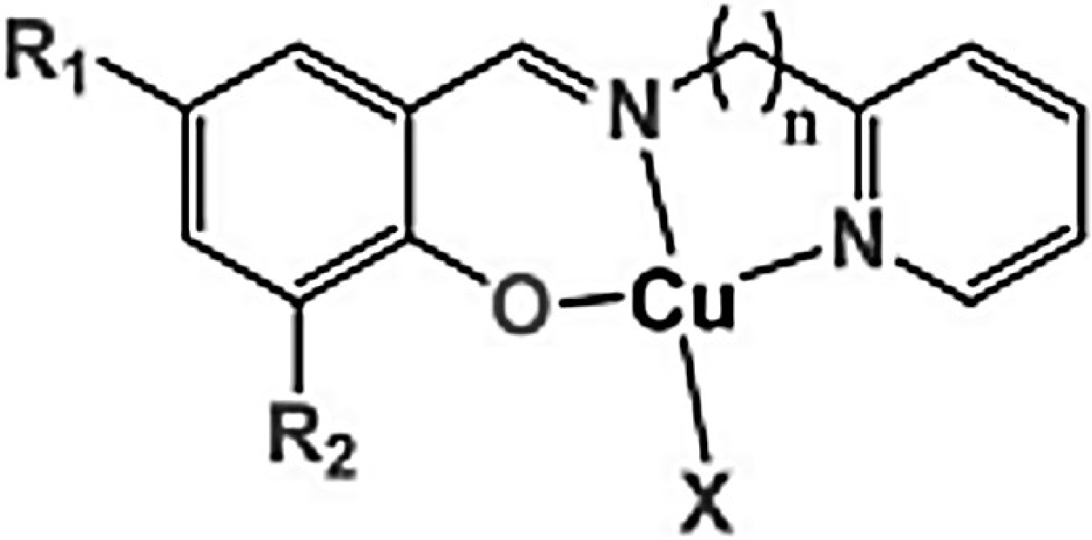
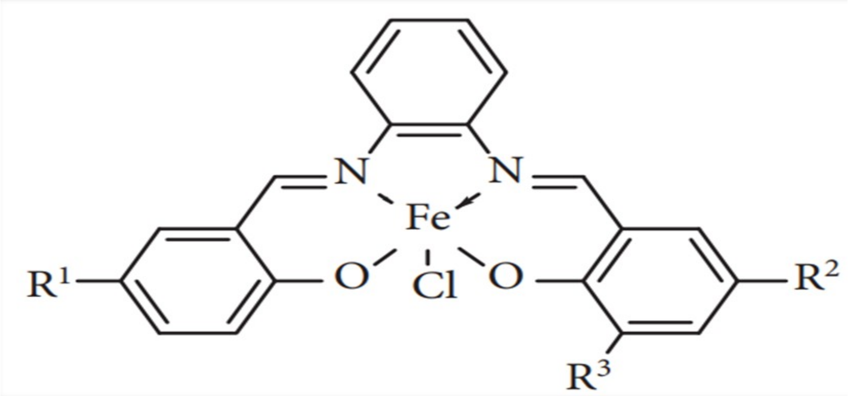


Figure (1-7):Synthesis the Copper Complex Cu(II) with Tridentate Schiff base Ligand

-Tetradentate & Polydentate Schiff Base: These Schiff base ligands contain four or more donor atoms (four or more pairs of electrons) to the metal ion, in the study (Quang Trung Nguyen.,*et al.,* 2021),have synthesis the complex of Fe(III) with ligand has four donor atoms,**Figure (1-8)** Showing the structure for tetradentate Schiff base ligand



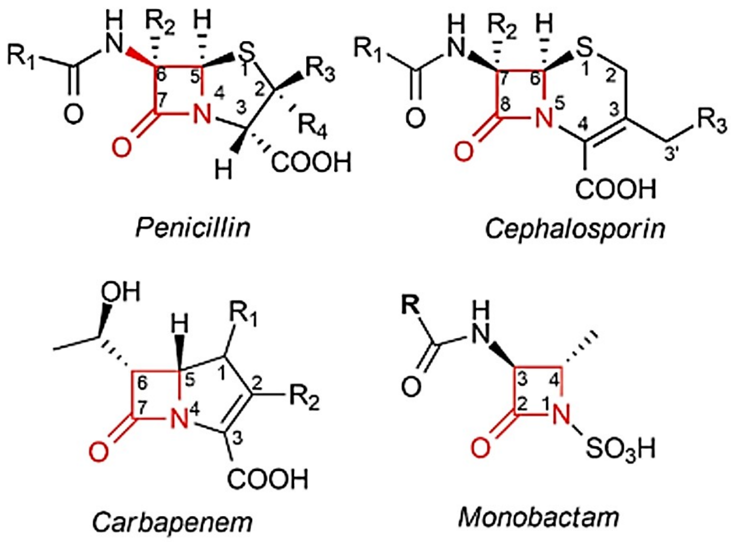
Figure(1-8):Synthesis the Iron Complex Fe(III) with Tetradentate Schiff base Ligand

1.3.Antibiotic

Antibiotics are used to treat infections in humans and animals by either killing or inhibiting the growth of bacteria(Vanessa Minden,*et al.,*2017). Often, resistance develops to antibiotics, which target bacterial cell wall synthesis mechanisms (Ott Scheler,*et al.,*2020). This is how, over time more antibiotic-resistant bacteria spring up, with multiple resistance mechanisms resulting in lower antibiotic effectiveness and increased morbidity and mortality in the population due to bacterial infections . As a result, bacterial resistance is one of the most pressing problems confronting humanity today (Díaz-García, V., & Retamal-Morales.,2020),This is what prompted researchers to continue developing existing antibiotics or creating new ones.

1.3.1.*β*-Lactam

β-lactam antibiotics are the most commonly used antibiotics in human medicine (Marco E,*et al.,*2018).Since the discovery of the *β*-lactam antibiotic,it has had extensive application in the therapies of microbial diseases. However, almost all *β*-lactams are resistant to bacteria (Subhendu sekhar,*et al* .,2017).The types of *β*-lactam antibiotics (penicillins, cephalosporins, carbapenems, and monobactams) are one of the most efficient classes of antibiotics for treating bacterial infections (Catia Longhi,*et al.,*2022),(Ahmad,M.M.U.,*et al.,*2019), and are a diverse family of antibiotics, **Figure(1-9)** Shows these structures of different classes of *β*-lactam antibiotics.

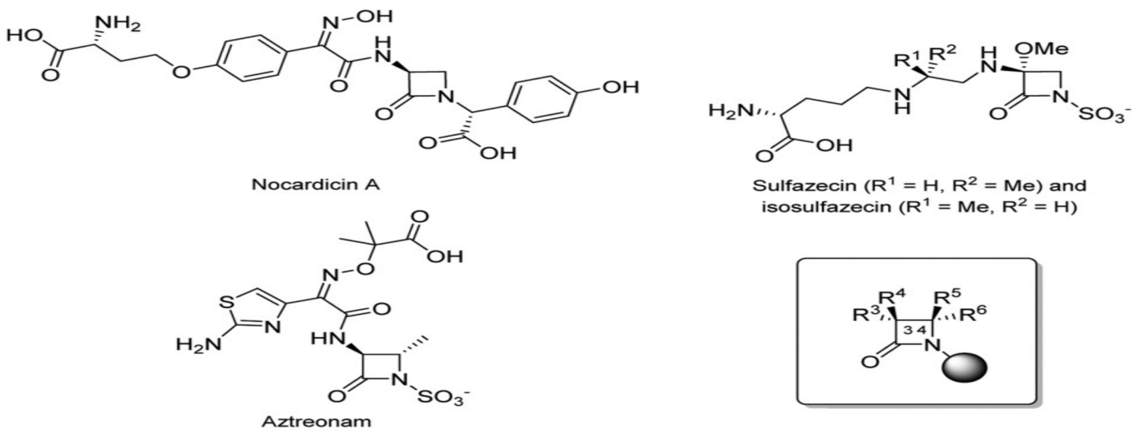

Penicillin Cephalosporin

Carbapenem Monobactam

Figure (1-9):Different Classes of *β*-lactam Antibiotics

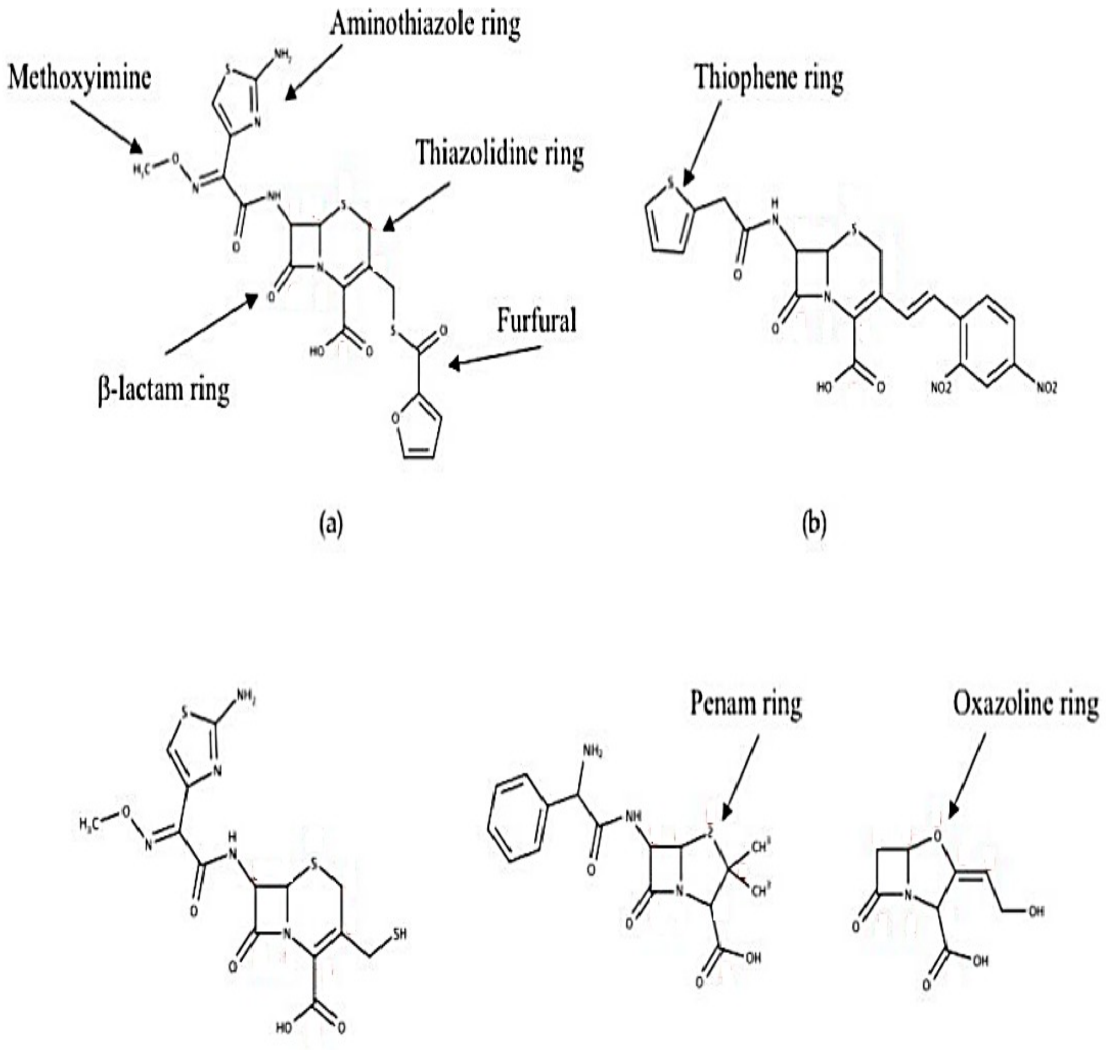
All of these compounds have a four-member ring with an amidic functional group, also known as the " β-lactam ring" or "azetidine." In penicillins, Cephalosporins, and Carbapenems, this ring is fused to another 5- or 6-member ring, but not in monobactams. The ***β***-lactam moiety in Penicillins is fused to a five-member Thiazolidine ring; in Cephalosporins, it is fused to a six-member Dihydrothiazine ring; in Carbapenems, it is fused to a Pyrroline ring; and in monobactams, the ***β***-lactam ring is not fused to any other ring (Bradford, K.B.,*et al.*,2016).

The results of efforts Previous were evident in the discovery of numerous natural and semi-synthetic monocyclic β-lactam containing antibacterial agents. Cimarusti and Sykes have provided a well-documented overview on the structure–activity relationships for many of these monocyclic β-lactams developed before 1984 .A semiempirical quantum chemical study of the structure–activity relationship in monocyclic β-lactam antibiotics has been reported by (Decuyper, L.,*et al.,*2018), as showing in **Figure(1-10).**



Figure(1-10):Some Renowned Monocyclic *β*-lactam Antibiotics and the General Structure of Azetidin-2-ones, Depicting the Categorization According to their N-Substituent

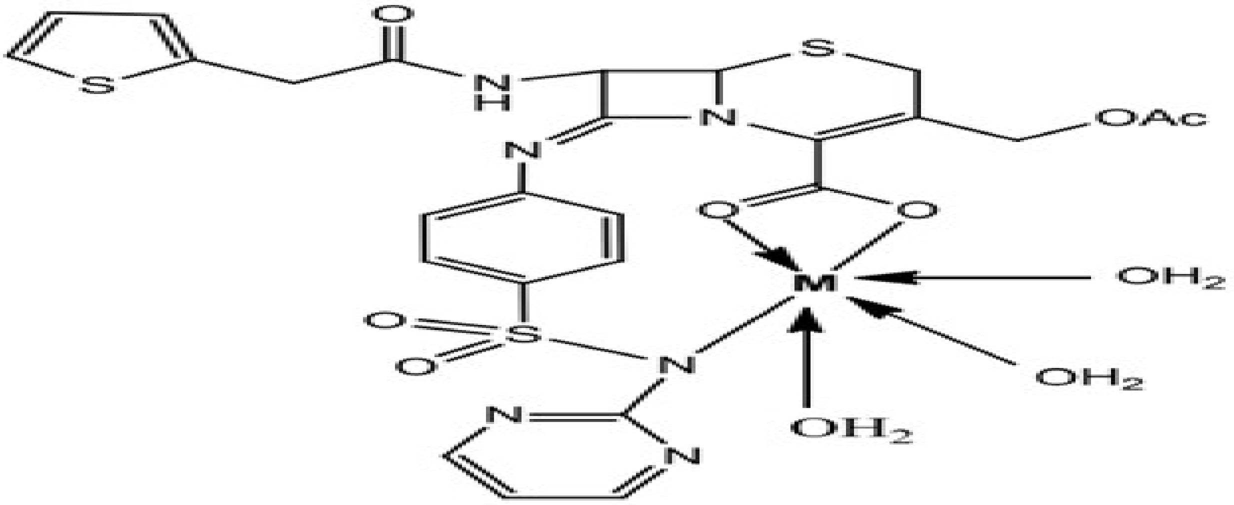
The interaction of the below compound (CTX-M-15) with four bicyclic β-lactam compounds from the cephalosporin and penicillin families, as well as one β-lactumase inhibitor, in the study of (Ahmadvand, P., *et al.*,2022), investigated compounds have a five- or six-membered heterocyclic ring attached to a four-membered β-lactam ring with a secondary amino group in common, **Figure (1-11)** shows structures of bicyclic β-lactam.



(a) (b)

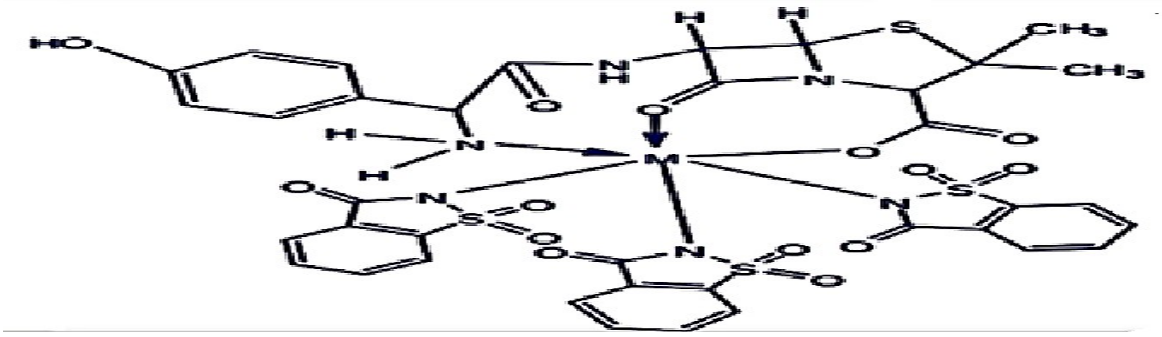
Figure(1-11):Chemical Structures of Bicyclic *β*-lactam Compounds Synthesised

The arrival of a new chemotherapeutic Schiff base has piqued the interest of medicinal chemists. Many studied (J.R. Anacona, N.N., Juan Camus, 2014), have been published on Schiff bases biological activities, including their anticancer, antibacterial, antifungal, and herbicidal characteristics,the synthesis and characterization, and antibacterial activity of a tridentate Schiff base derived from cephalothin and sulfadiazine, as well as its transition metal (M(II) = Mn, Co, Ni, Cu, Zn) Complexes,**Figure (1-12)** Shows the Schiff base ligand and their complexes.



Figure(1-12): Cephalothin and Sulfadiazine, and its Transition Metal M(II) = Mn, Co, Ni, Cu, Zn Complexes

Derivatives of amoxicillin, a *β*-lactam antibiotic, have been extensively used as a potential bactericidal agent due to their role in the treatment of bronchitis, tonsillitis, throat infection, ear infection, typhoid, pneumonia and urinary tract infections. However, biological property of amoxicillin enhanced upon chelation with metal ions(Taghreed . H. Al-Noor,*et al* 2021),**Figure (1-13)** Shows derivatives of amoxicillin.



Figure(1-13):Representation Preparation of the Complexes Semi-synthetic Penicillins(6-APA,7-ADCA)

Amoxicillin's bio-functional activity is related to the *β*-lactam ring in the study (Sahar S.,*et al.,*2019) studied the interactions of some ligands containing Amoxicillin's,**Figure(1-14)** Shows prepared Amoxicillin as a ligand.

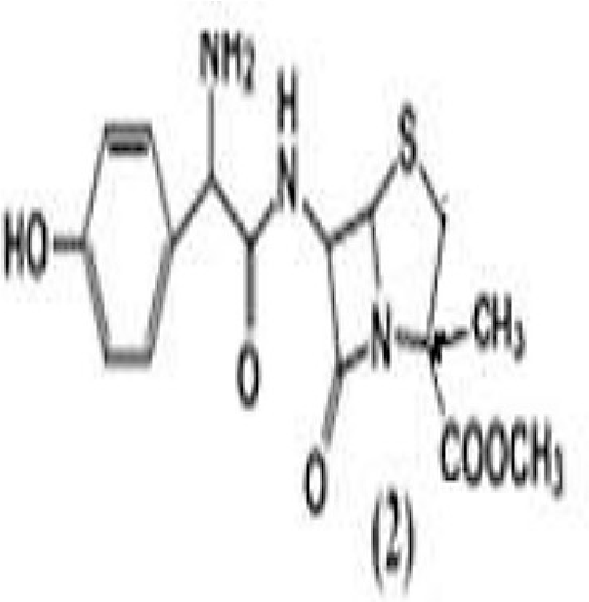
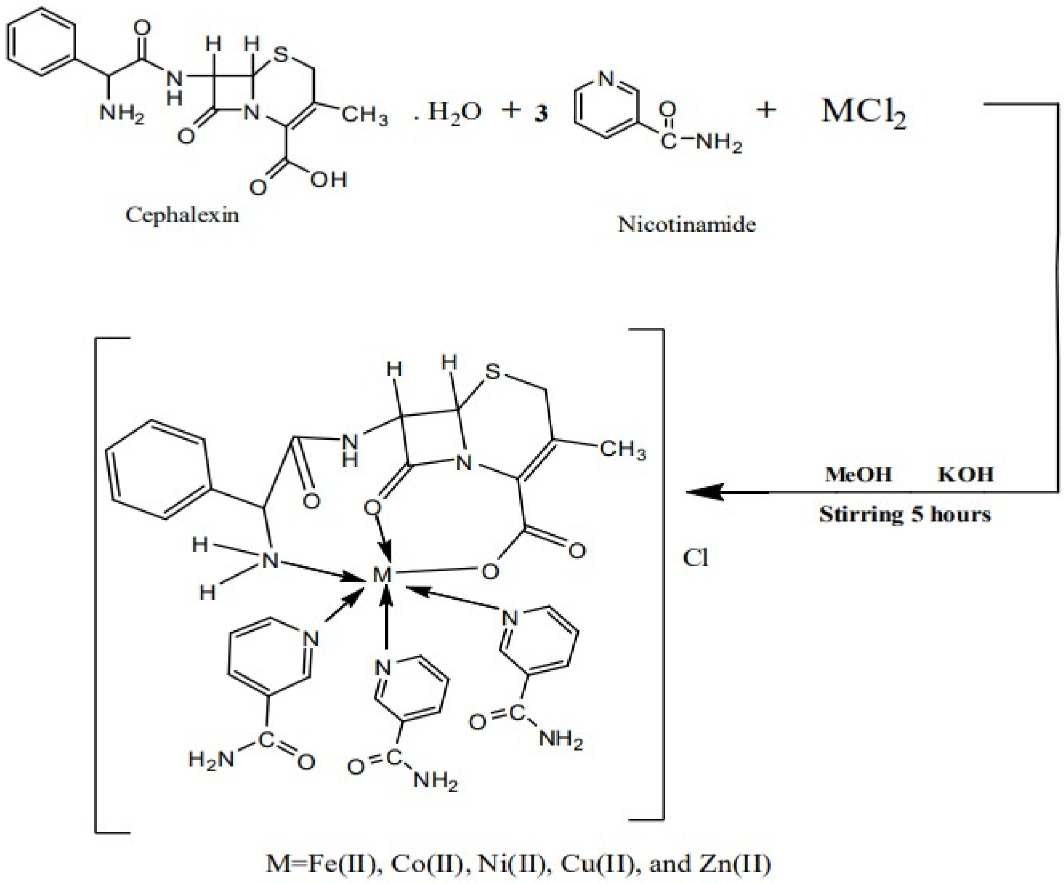


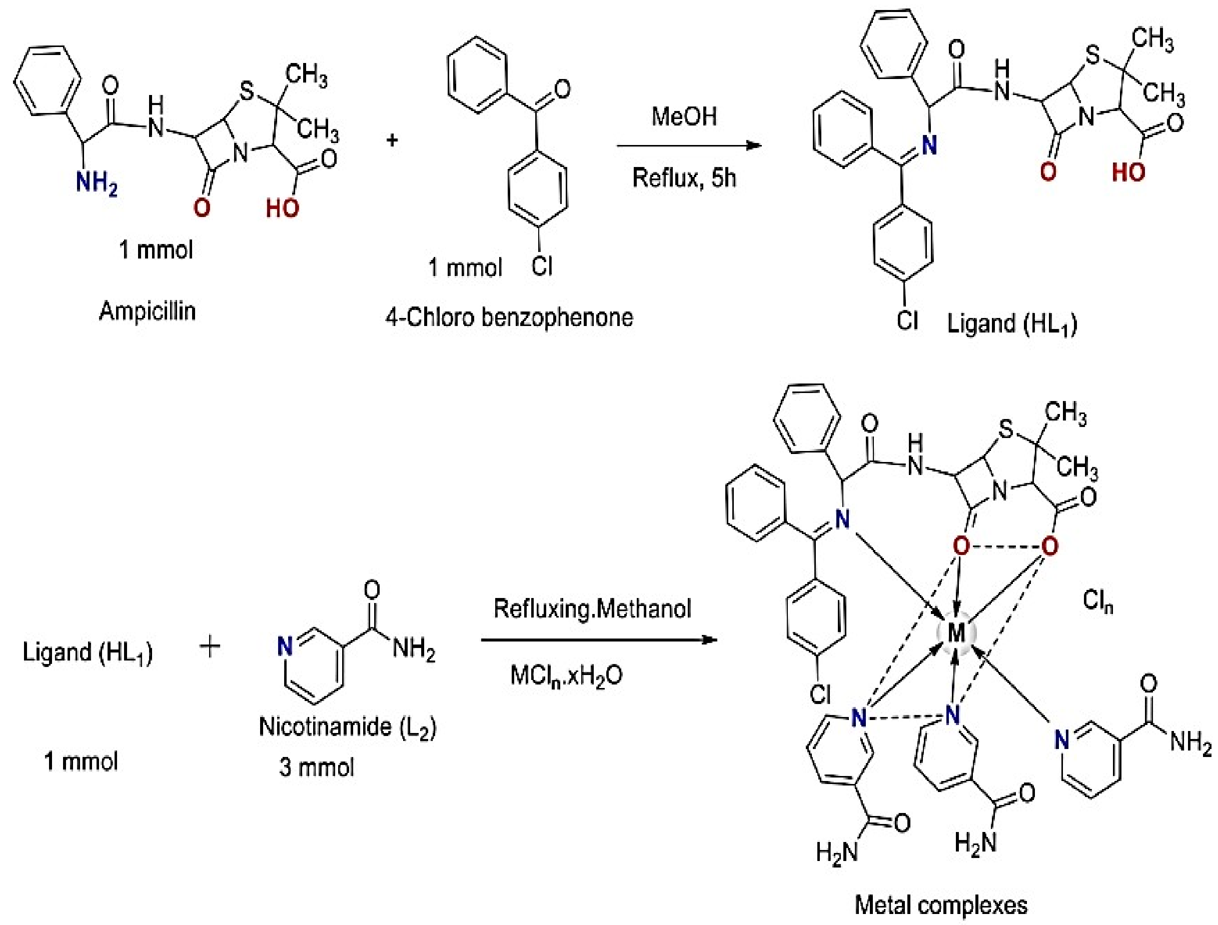
Figure (1-14):Proposed Structure for the Amoxicillin as Ligand

Because of its broad antibacterial activity, cephalexin is one of the most commonly used first-generation cephalosporin-based antibiotics for treating infections ,there is studied by the(Taghreed. H. Al-Noor,*et al* 2013),**Scheme(1-5)** Shows structure and synthesis of cephalexin ligand and their complexes .



Scheme(1-5): Synthesis of Mixed ligand Complexes from Cephalexin Ligand

The Schiff base derivatives from ampicillin has been study in (Taghreed H. Al-Noor.,*et al*,2021),been noticed these ligand act as multi-dentate ligands and forms several stable metal complexes and this compoundes from ligand and complexes were have a high antibacterial activity, **Scheme(1-6)**Shows the ligand and their complexes.



[M= Cr(III), Fe(III), Co(II),Ni(II), Cu(II), Cd(II) and Hg(II), n = 2, 3]

Scheme(1-6):Schiff Base Derivatives from Ampicillin and their Complexes

1.3.2.Penicillin

Penicillin is a common antibiotic used to treat bacterial infections. Penicillin is a member of the β-lactam cyclic amine antibiotic family (Paul J. Weldrick., *et al.,*2020). Anciently the true story began in 1928 with Alexander Fleming, a Scottish bacteriologist(Fleming, A.,1926), and he first pictured the mould and its growth temperatures, and observed that it has a rapid production at 20^0C. Then he studied other types of molds to check if their antibacterial activity and to confirm the unique nature of the strain he discovered, **Figure(1-15)**Shows the penicillium colony.

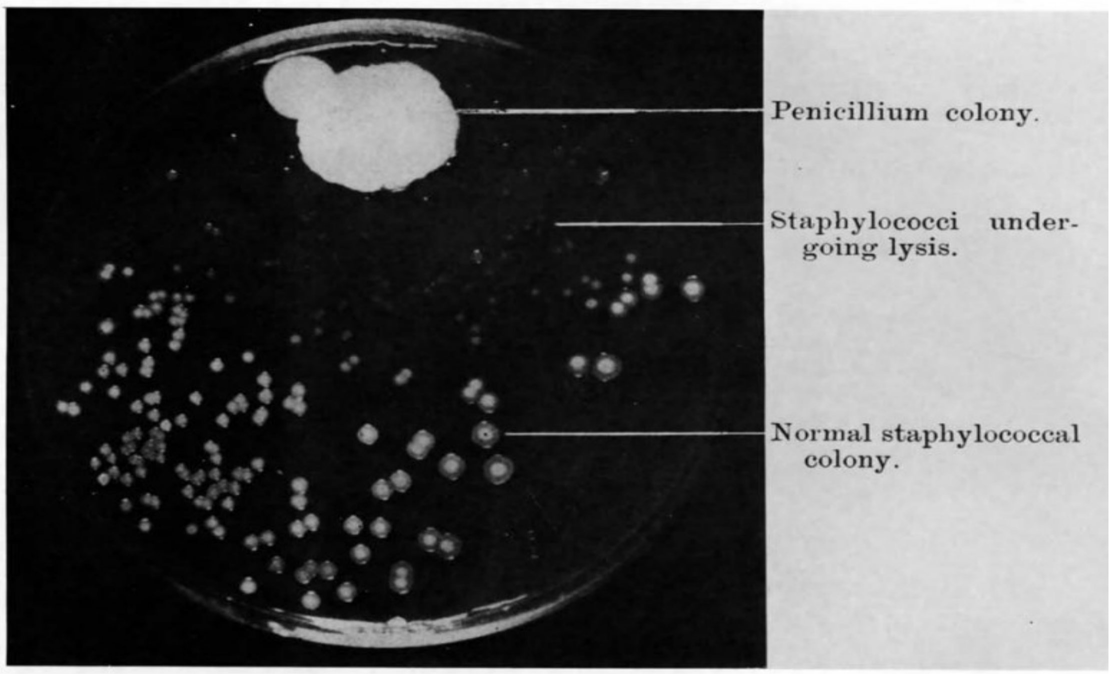
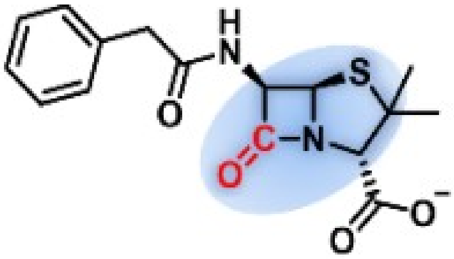


Figure (1-15): Photograph of a Culture-plate Showing the Dissolution of *Staphylococcal* Colonies in the Neighbourhood of a Penicillium Colony

Penicillin and other *β*-lactam antibiotics are widely regarded as the most important drugs ever developed. This implies that resistance to *β*-lactam antibiotics is a serious threat. Penicillin G (benzyl penicillin) was the first *β*-lactam to be clinically used, primarily to treat streptococcal infections, against which it shows excellent activity(Hossein Salami,*et al.,*2020). Penicillin G (PenG) contains a rigid bicyclic *β*-lactam core structure (i.e. the penam structure) and a bulky ,flexible, phenylacetamido (PAA) side chain as well as a negatively charged carboxylate group. (Kozuch, J.,*et al.,*2021),(Pupin,R.R.,*et al,*2020),**Figure(1-16)**Shows the structure of Penicillin **G**.



Figure(1-16):Chemical Structure for Penicillin G

And another type of penicillin, Penicillin V (phenoxymethyl penicillin) is another naturally occurring penicillin whose oral formulation is applied therapeutically and prophylactically in pediatric patients with mild to moderate infections(Catia Longhi., *et al.,*2022). PVA hydrolyzes the side chain of phenoxymethyl penicillin (Pen V) and there is used in the production of the pharmaceutical intermediate 6-aminopenicillanic acid (6-APA)(Amol M., *et al.,*2020).The difference between PnG and PnV stability in an aqueous acid medium can be shown in the study (Lima,L.M., *et al*.,2020), **Figure (1-17)** shows the structure of penicillin V.

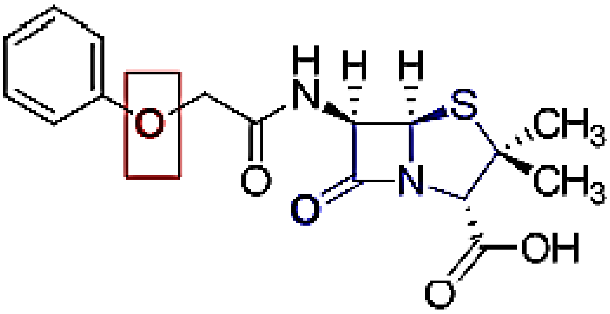
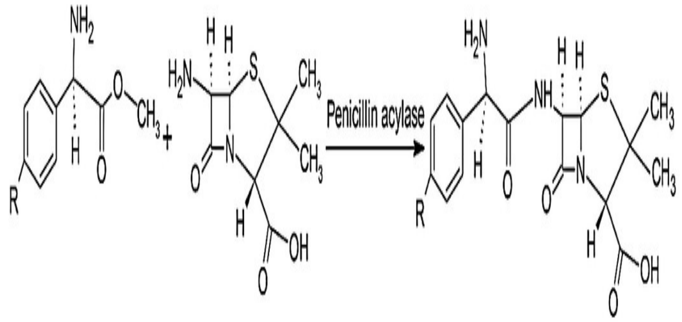


Figure (1-17) :Chemical Stracture of Penicillin V

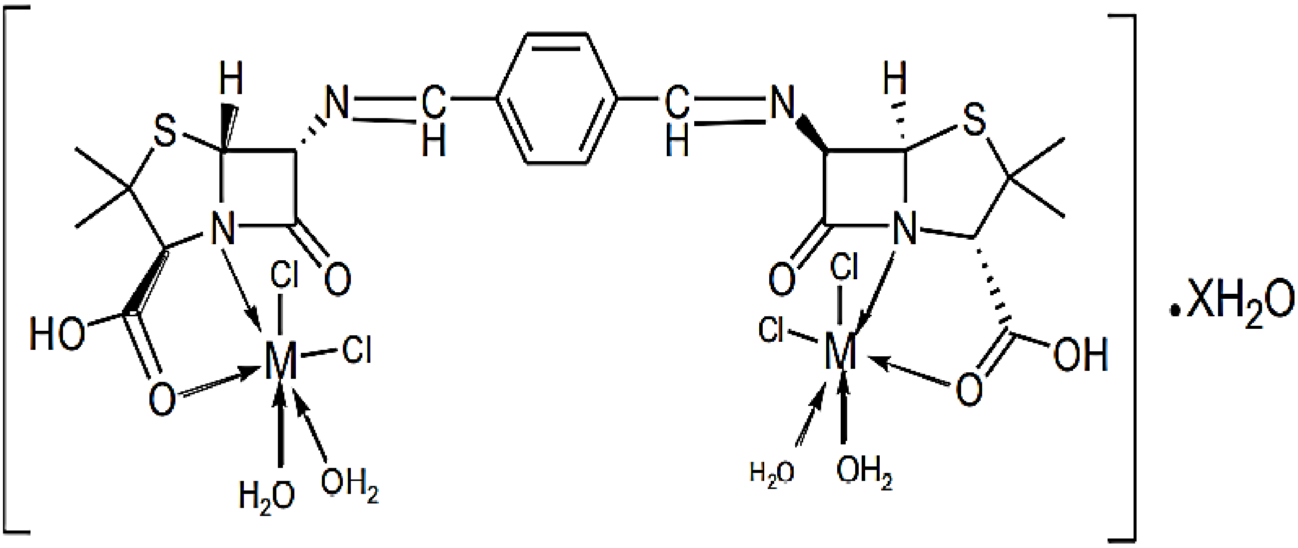
1.3.3.6-aminopenicillic acid(6-APA)

The 6-aminopenicillanic acid (6-APA) is an important active pharmaceutical intermediate that can be integrated and repurposed into semisynthetic antibiotics such as amoxicillin, ampicillin, and cephalosporin antibiotics cefadroxil and cephalexin. Antibiotic resistance has increased the demand for semisynthetic antibiotics(Amol M.,*et al.,*2020),6-Amino Penicillinic acid is a key compound in the production of β-lactam antibiotics.The 6-aminopenicillin acid is one important pharmaceutical and therapeutic application, in the study of (Meghwanshi,G.K.,*et al.,*2020) has been used penicillin acylase in the synthesis of semi-synthetic β-lactam antibiotics. **Scheme(1-7)** shows the synthesis of semi-synthetic β-lactam antibiotics by penicillin acylase.



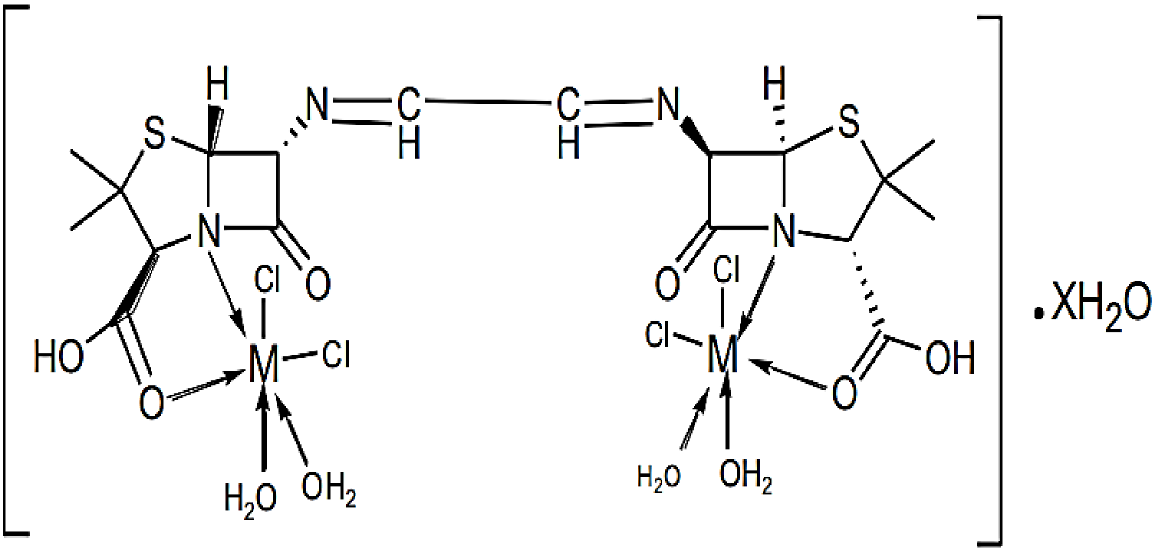
Scheme(1-7):Penicillin Acylase Catalyzed Synthesis of some Important Semi-Synthetic *β*-lactam Antibiotics

The (6-APA) have a wide range of pharmacological activities, including antiviral, antibacterial, antifungal, anticonvulsant, and anti-inflammatory properties, as well as chemotherapeutic applications. In the study (Sabah, A.J.A.a.Y.H. ,2016) a new ligand has been synthesised and it is complexed by the interaction of bifunctional aldehyde(terephthaldehyde), (glyoxal) with the 6-amino penicillanic acid.The minimum inhibitory concentration (**MIC**) of the raw material **6-APA**, and synthesized compounds were evaluated,they discovered that at the selected concentrations, the synthesized compounds are more active and sensitive against both Gram-positive and Gram-negative organisms and he found the microbiological activity is highest with complexes from ligands alone. **Figure(1-18)**, and **(1-19)**Show the chemical formula of the synthesised compounds (ligand and complexes) along with the suggested geometrical shape.



$[M_2L_1Cl_4(H_2O)_4].XH_2O$, X:Natural number , M = Co, Cu or Zn

Figure(1-18):Chemical Formula of the Co(III),Cu(II),and Zn(II) Complexes Synthesized from Terephthaldehyde Ligand

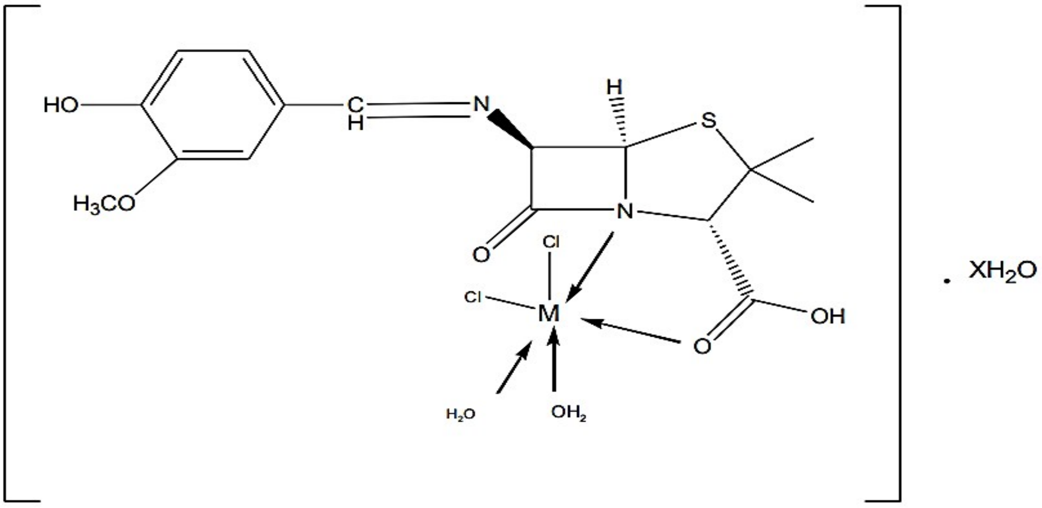


$[M_2L_2Cl_4(H_2O)_4].XH_2O$, X: Natural number , M = Co, Cu or Zn

Figure (1-19):Chemical Formula of Co(III),Cu(II),and Zn(II) Complexes Synthesized from Glyoxal Ligand

The study (Yasser Hussam Sabah.,2016) developed two new ligands by the interaction of bifunctional aldehyde (Vanillin) with the antibacterial

6-aminopenicillanic acid, and compared the minimum inhibitory concentration (**MIC**) of the raw material 6-APA, with synthesized compounds, he also concluded that at the selected concentrations, the synthesized compounds are more active and sensitive against both Gram-positive and Gram-negative than the raw material 6-APA, **Figure(1-20)** shows the structure of the synthesized compounds



$[ML_3Cl_2(H_2O)_2].XH_2O$, X:Natural number , M = Co, Cu or Zn

Figure(1-20):Chemical Formula of Complexes Synthesized from Vanillin Ligand

In the study (Ibtisam M Ali., *et al.*,2021), prepared the four new ligands by the reaction of 6-amino penicillanic acid (6-APA) with Schiff bases to produce azo-azomethine ligands HL_1, HL_2 HL_3, and HL_4 , then prepared complexes of these ligands with Copper (II), Nickel (II), and Iron (II) metal ion, the ligands act as tridentate ligands to form the octahedral complexes, the prepared ligands and their complexes show good biological activity,**Figures (1-21)**,**(1-22)**,**(1-23)**,**(1-24)** show the prepared compounds.

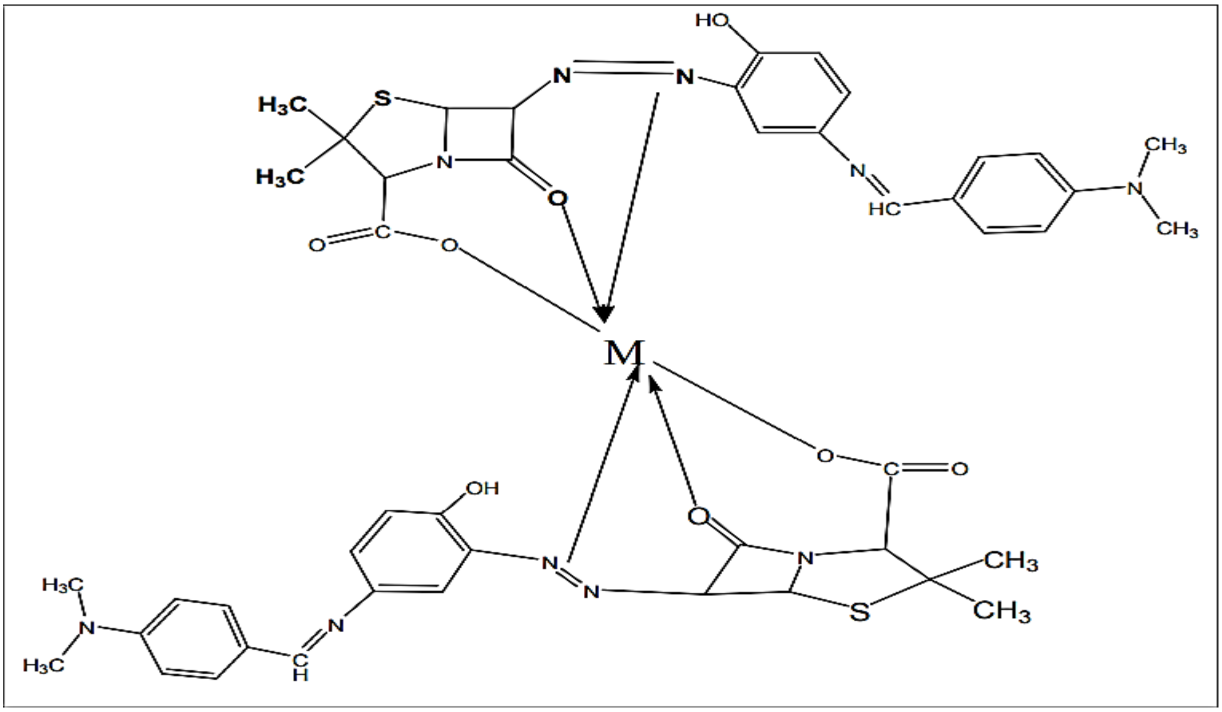


Figure (1-21):Chemical Formula of Copper (II), Nickel (II), and Iron (II) Complex with (HL_1) Ligand

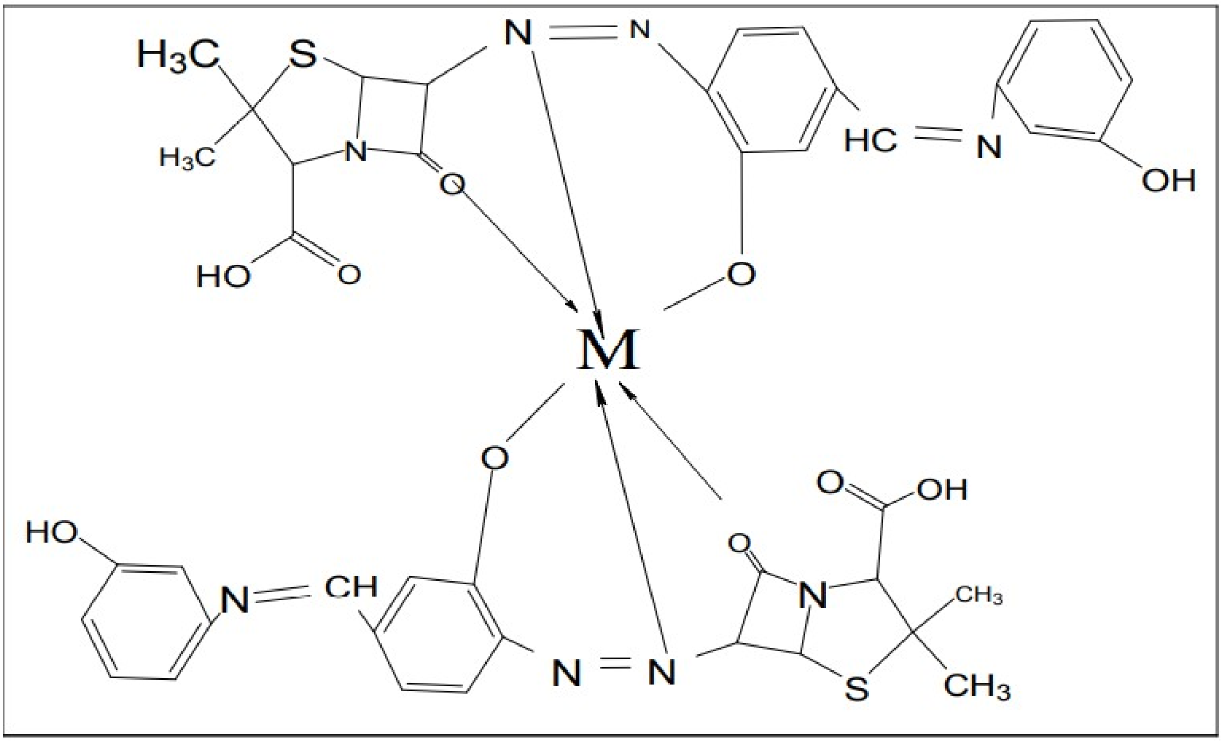


Figure (1-22):Chemical Formula of Copper (II), Nickel (II), and Iron (II) Complex with (HL_2) Ligand

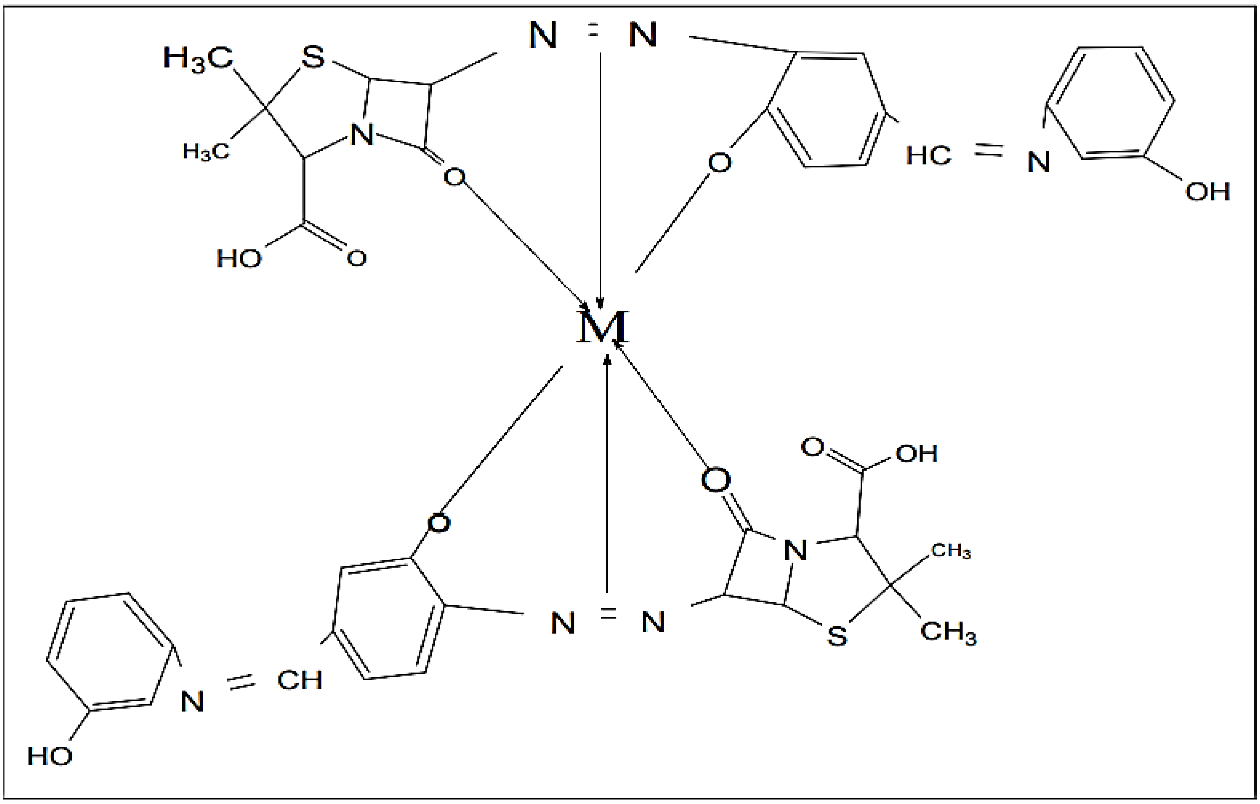


Figure (1-23):Chemical Formula of Copper (II), Nickel (II), and Iron (II) Complexes with (HL_3) Ligand

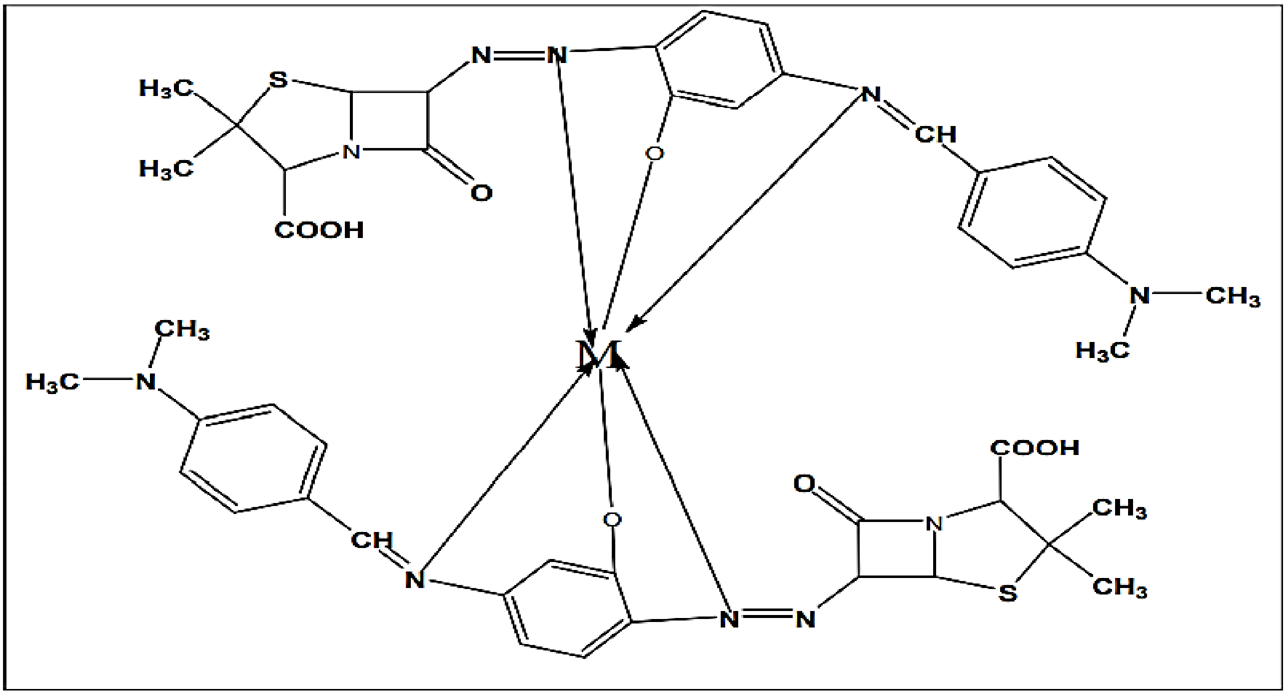
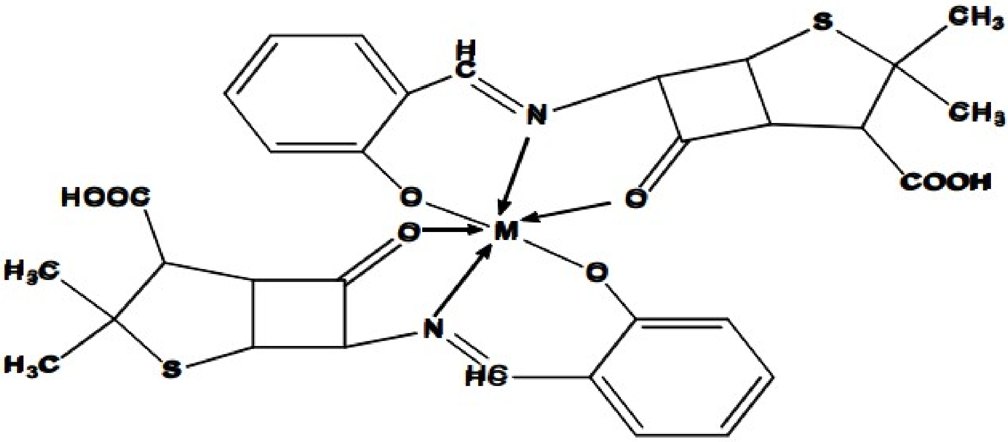


Figure (1-24):Chemical Formula of Copper (II), Nickel (II), and Iron (II) Complexes with(HL$_4$) Ligand

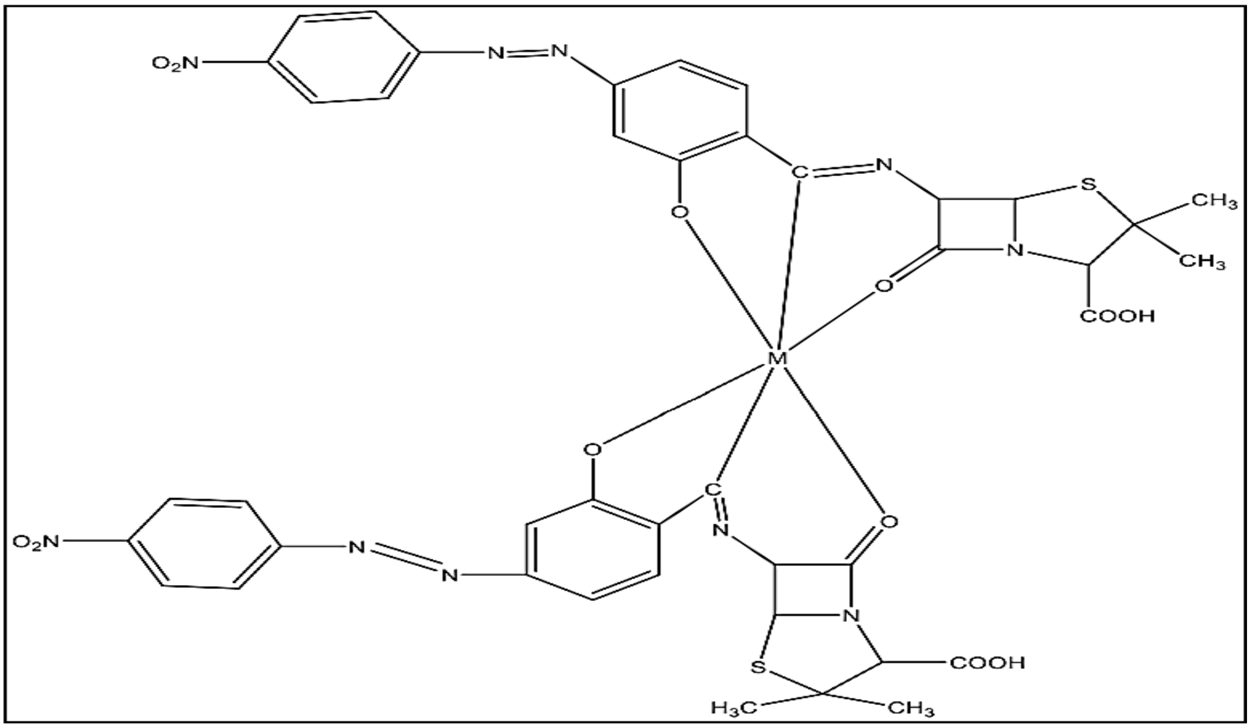
In the study (Rasha Hasan Jasim, et al.,2017) synthesis and characterization of a new biological activity compound from the interaction between 6-APA and Salicyldehyde, and after that the ligand has been associated with metal ions to form the claw complexes to get an octahedral shape, and blow **Figure(1-25)** Showing their complexes.



M=Cu(II) , Co(II) , Ni(II) and Zn(II)

Figure(1-25):Stracture of Complexes that Synthesis from Ligand that Interaction of 6-aminopenicillic acid and Salicyldehyde

In the study (N. Ghufran Kareem, Mohammed Hamid Said.,2021), the synthesis of the new azo-azomethine ligand [6[2-hydroxy-4-((3-nitrophenyl)diazenyl)-1-phenyl]imine penicillanic acid] [HNDIP], and it was used to prepare new complexes with [Cu(II), Ni(II), Co(II), Zn(II), and Fe(II)] metal ions, and also tested that the biological activity of the ligand and its complexes, found have high inhibitory activity against bacteria,**Figure(1-26)** Shows the ligand and their complexes..



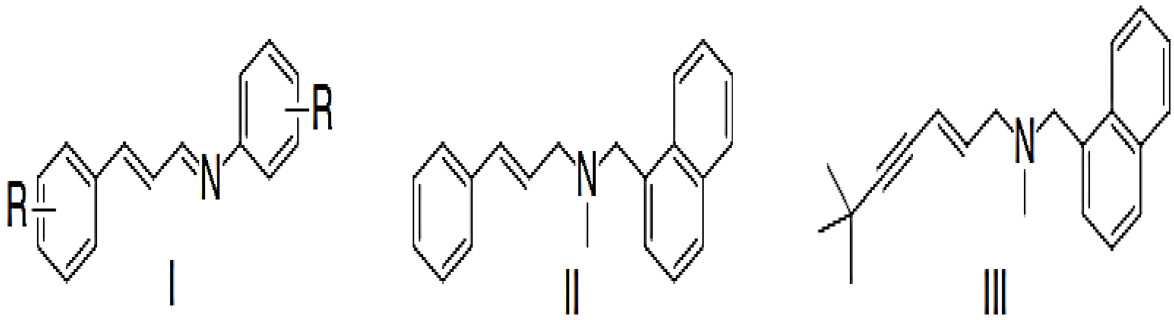
Figure(1-26):Structure of Complex M= (Cu^{+2}, Co^{+2}, Ni^{+2}, Zn^{+2}, Fe^{+2}) with[6[2-hydroxy-4-((3-nitrophenyl)diazenyl)-1-phenyl]imine penicillanic acid] Ligand

1.4.Cinnamaldehyde

Cinnamon oil is a natural antifungal agent with the main component (Cinnamaldehyde) (Abourehab,M.A.,*et al.*,2022). Cinnamaldehyde has been shown in numerous studies to inhibit the growth of pathogenic microorganisms, and has also been shown to have anti-tumor and anti-diabetic properties. However, because of its high volatility and strong odors, cinnamaldehyde has many practical limitations as an antimicrobial agent or food additive. As a result, many researchers have shifted their focus to cinnamaldehyde derivatives. Cinnamaldehyde derivatives and cinnamaldehyde Schiff base and its complexes were synthesized in the study (Joshi,S., *et al.,*2011).Cinnamaldehyde Schiff base is an important class of cinnamaldehyde derivatives with high bioactivity that can be easily synthesized, Many researchers have reported on the bioactivity of cinnamaldehyde Schiff base compounds.

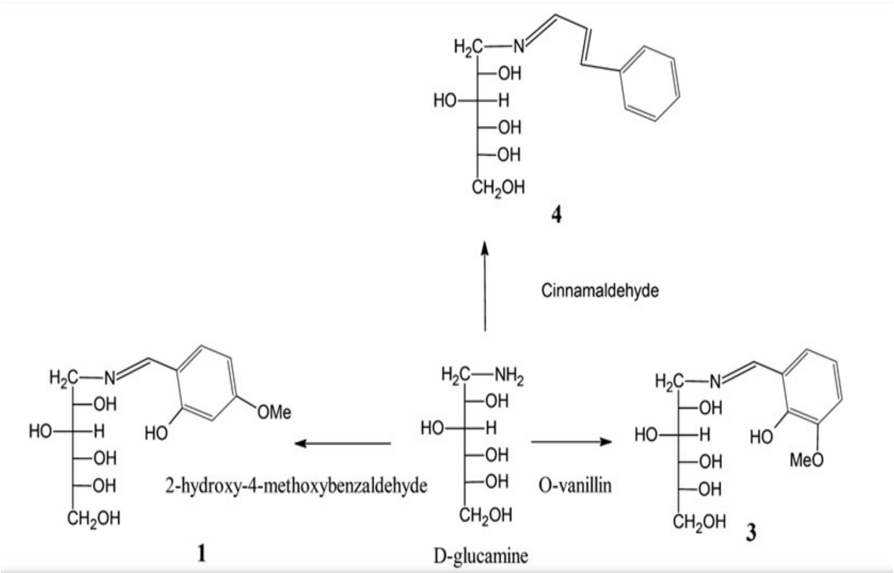
Schiff base for cinnamaldehyde compound and their metal complex have bioactivity test revealed that cinnamaldehyde Schiff base and metal complex were more active than cinnamaldehyde (Hui Wang.,*et al*.,2021). through chemical modification, Cinnamaldehyde (**CA**) has been widely researched as an antimicrobial substance for use in medicine, food, and wood preservation. The imine bond (C=N) formed in Schiff base compounds confers specific properties on the cinnamaldehyde Schiff base compounds(Hui Wang.,*et al*.,2016).

In the study (T.F.F. Magalhaes.,*et al,*2020)have synthesized and evaluated the antifungal activities of 23 cinnamyl Schiff base derivatives. Some of the compounds showed promising antifungal activity, **Figure(1-27)** Shows Some cinnamyl Schiff base derivatives.



Figure(1-27):General Structure of some Cinnamyl Schiff base (I) and Structures of Allylamines naftifine (II) and Terbinafine (III)

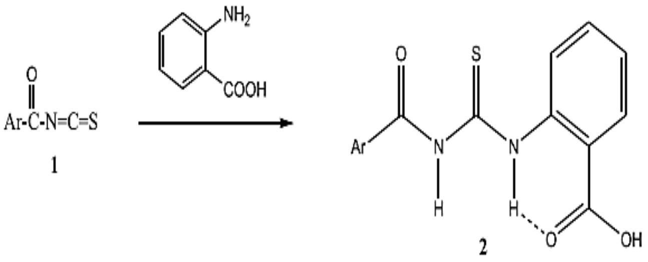
In the study(Nanishankar V.,et al.,2017)have attempted to enhancement of antiaflatoxigenic and antimicrobial properties of HMBA, cinnamaldehyde, and similar molecules via Schiff base formation accomplished from condensation reaction with amino sugar (D-glucamine). the HMBA-derived Schiff bases exhibited commendable antiaflatoxigenic activity, **Scheme (1-8)** Shows the reaction.



Scheme(1-8):Synthesis of Schiff bases (Cinnamldehyde) Formation Accomplished from Condensation Reaction with Amino sugar (D-glucamine).

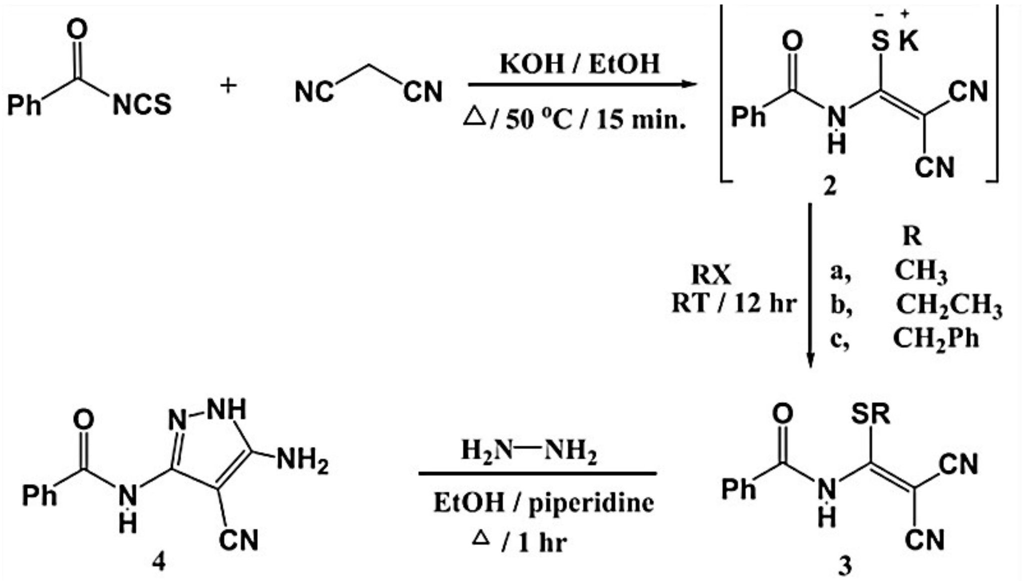
1.5.Benzoyl isothiocyanat

Benzoyl isothiocyanate **(BI)**, as a new type of comonomer, has attracted special attention because the structure of **(BI)** contains not only benzene ring but also amino group. Remarkably, the introduction of benzene ring and amino groups in **(BI)** were bonded(Huinan Che .,*et al,*2021).Extensive studies on the chemistry of aroyl isothiocyanates have established the value of these reagents as starting materials for the synthesis of a wide variety of heterocyclic compounds and thiourea derivatives,and this study is the one from studies (Magdy,M.Hemdan&Amira,A.Al-sayed*.,*2016), The interaction of equimolar quantities of 2-(1,3-dioxisoindolin-2-yl)benzoyl isothiocyanate,**Scheme (1-9)** Shows the reaction.



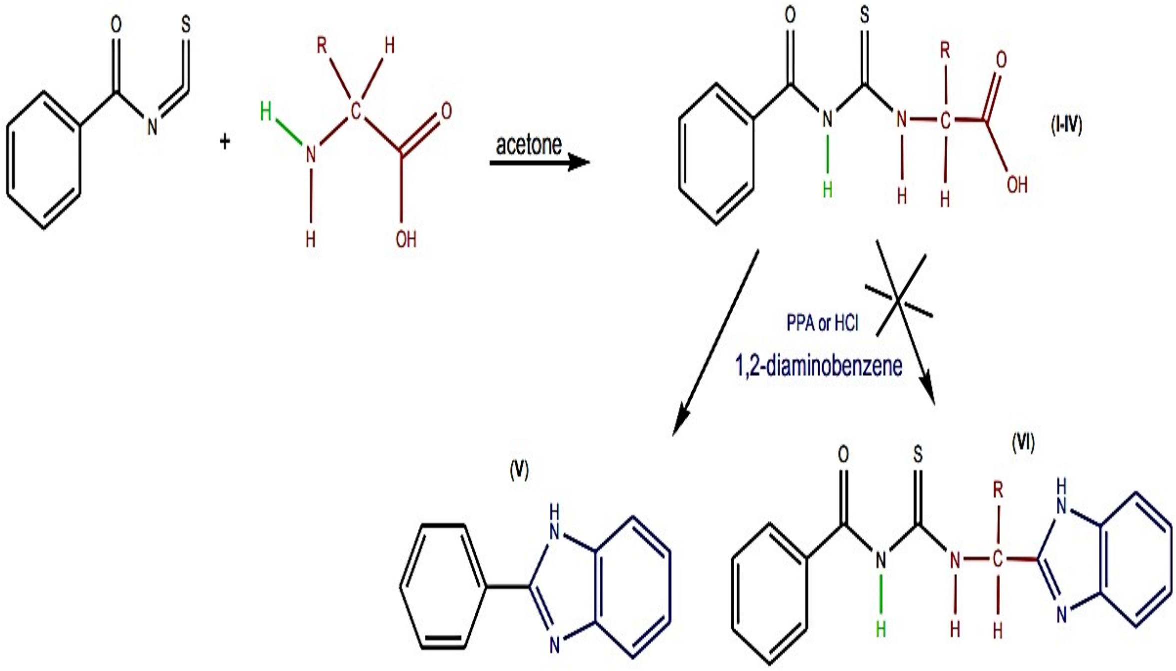
Scheme(1-9):Reaction of Equimolar Quantities of 2-(1,3-dioxisoindolin-2-yl) Benzoyl isothiocyanate

In the study(Ali M. S.,*et al*.,2020) the N-(pyrazolo[5,1-c][1,2,4]triazin-7-yl)benzamides 6a,b; were synthesized by reacting benzoyl isothiocyanate with malononitrile in KOH/EtOH, then alkylation with alkyl halides and eventually hydrazine, were noticed to have significant antiviral activity against bird flu-influenza (H_5N_1),with viral reductions ranging from 85 to 65 percent as shows in **Scheme(1-10).**

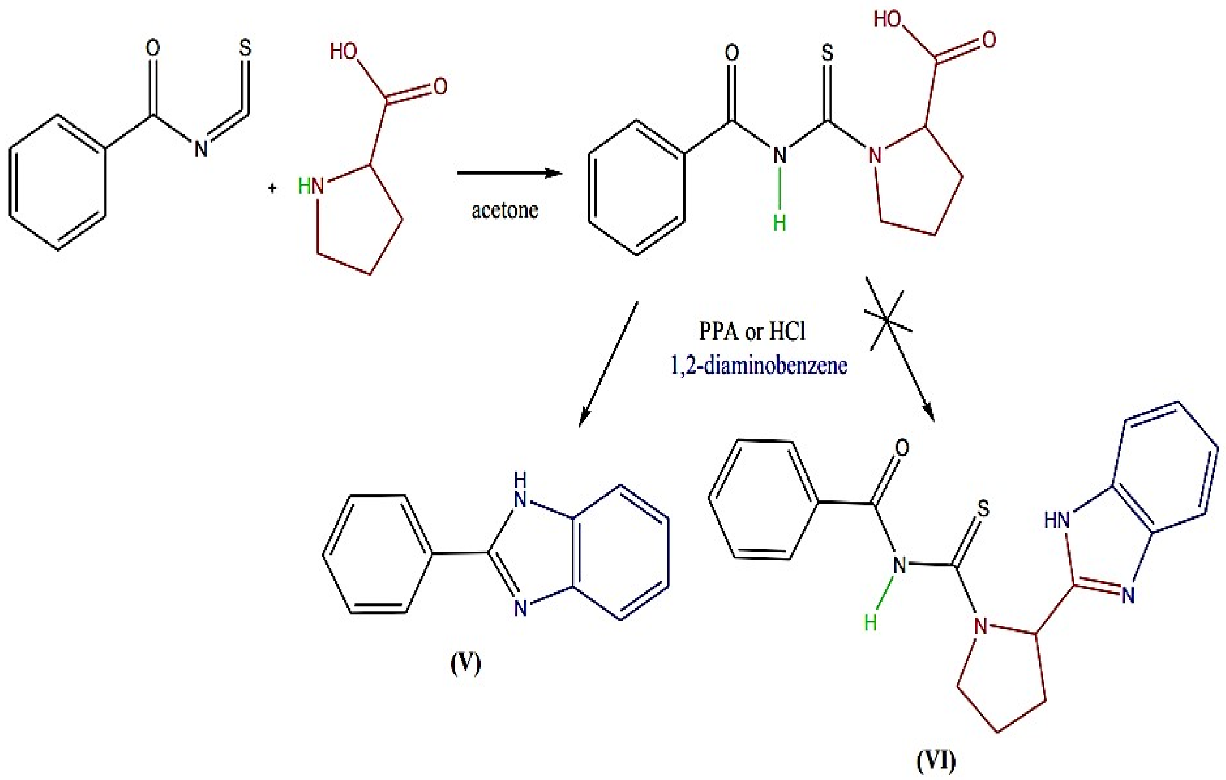


Scheme(1-10):Synthesis of N-(pyrazolo[5,1-c][1,2,4]triazin-7-yl) benzamides 6a,b

Benzoyl isothiocyanate amino acid derivatives can be used as intermediates in the synthesis of other biologically active molecules with a thiourea backbone,the fallowing compound prepared from reaction of benzoyl isothiocyanate with L-serine, L-proline, D-methionine and L-alanine(Odame, F.,*et al.*,2015) the results different compound show in the **Scheme(1-11)**,**(1-12)**.



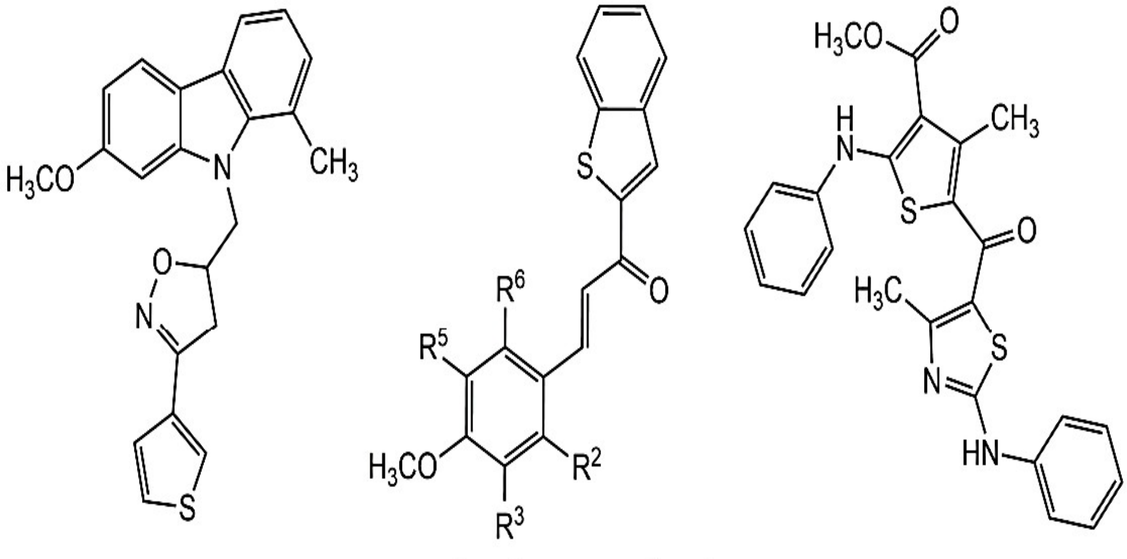
Scheme (1-11):Synthesis for Compounds I and IIIV



Scheme(1-12):Synthesis for Compounds II and V

1.6. 5-bromothiophene-2-carbaldehyde

Thiophene derivatives are preferred structures for drug design and discovery. Anti-inflammatory properties are known for thiophene-based compounds, such as the commercial drugs Tinoridine and Tiaprofenic acid. The current review updates the role of thiophene-based derivatives in inflammation (da Cruz,R.M.D.,*et al.,*2021), **Figure(1-28)** shows the structures of compounds.



1

$2\ R^2 = R^6 = OCH_3, R^3 = R^5 = H$

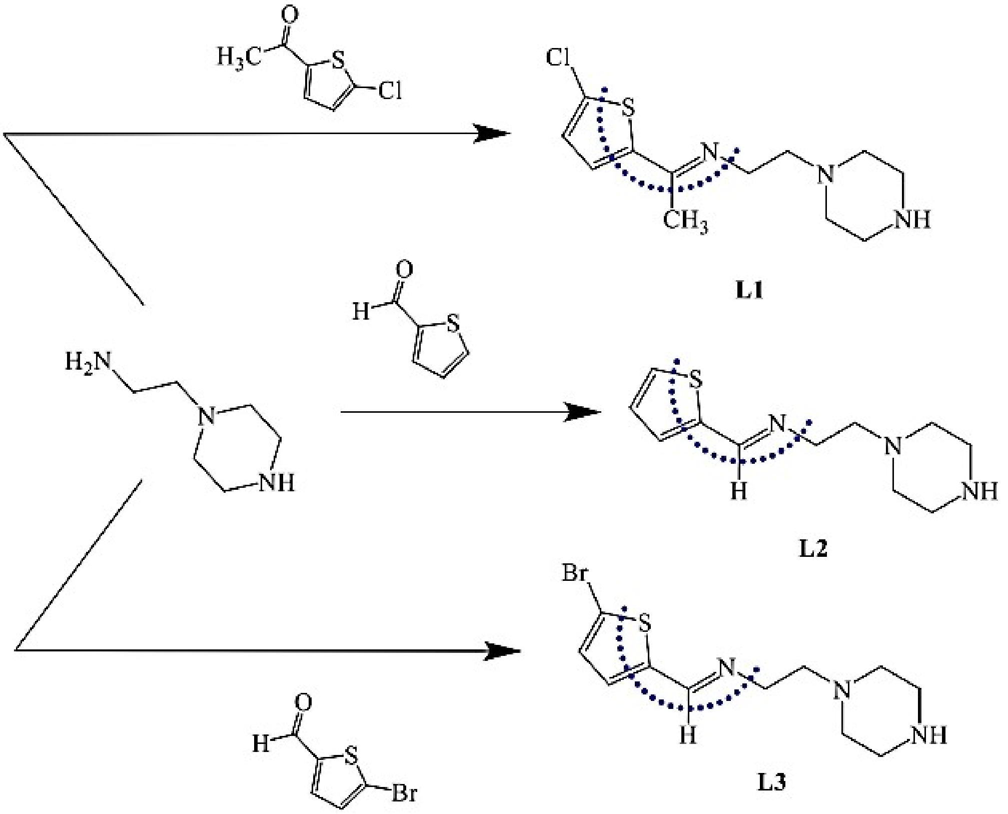
$3\ R^2 = R^6 = H, R^3 = OCH_3, R^5 = OH$

4

Figure(1-28):Chemical Structures of Thiophene-based Compounds Active Against COX and LOX Enzymes

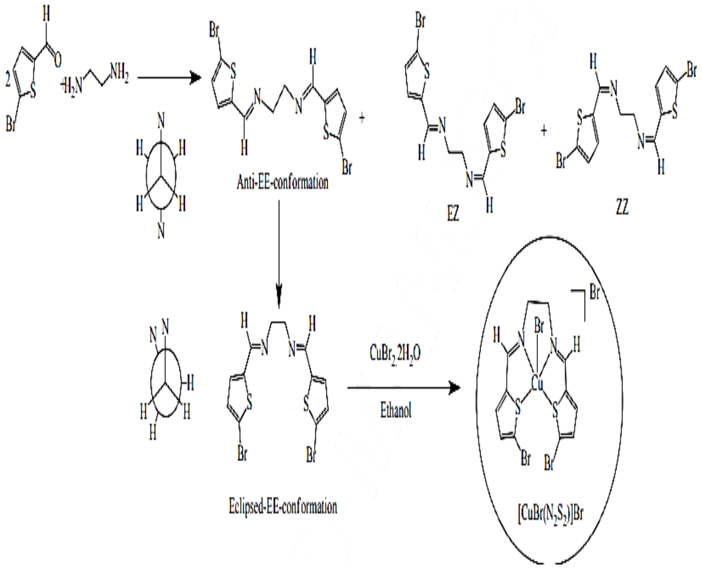
Several Schiff base ligands with N, O, S, and P atoms have recently been made available for analysis and biological applications. Furthermore, these types of Schiff bases have numerous applications in the life sciences, such as catalysts and photochromic sensors, and also have impressive biochemical applications, including antifungal, antiviral, antitumor, and antibacterial properties.

In 2020 was prepared new Schiff base by condensation of 1 mole of 2-(piperidin-4-yl) ethanamine with 1.2 moles of aldehydes as: 1-(5-chlorothiophen-2-yl)thenone,thiophene-2-carbaldehyde, and 5-bromothiophene-2-carbaldehyde,which afforded the good yields formation of N-(1-(5-chlorothiophen-2-yl)ethylidene)-2-(piperazin-1-yl)ethanamine (**L1**), 2-(piperazin-1-yl)-N-(thiophen-2-ylmethylene)-ethanamine (**L2**), and N-((5-bromothiophen-2-yl)methylene)-2-(piperazin1-yl)ethanamine (**L3**), respectively. The synthesized ligands were found soluble in common organic solvents (Ismail Warad,*et al.,*2020), **Scheme(1-13)** shows the Synthesised compound.



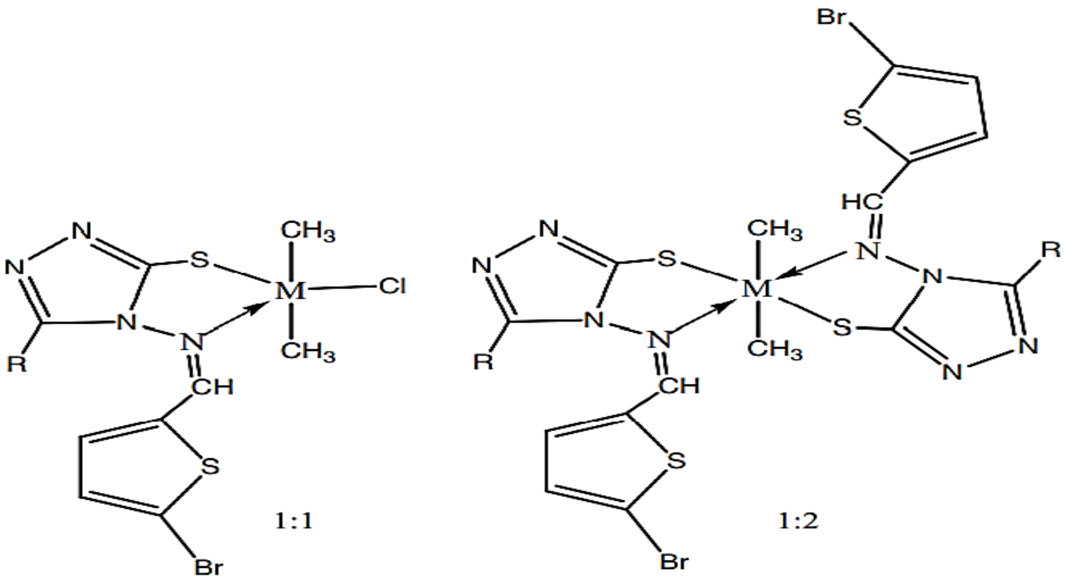
Scheme (1-13):Synthesis of the Schiff Synthesis of the Schiff bases (N-(1-(5-chlorothiophen-2-yl)ethylidene)-2-(piperazin-1-yl)ethanamine, 2-(piperazin-1-yl)-N-(thiophen-2-ylmethylene)-ethanamine,N-((5-bromothiophen-2-yl)methylene)-2-(piperazin1-yl)Ethanamine

In coordination chemistry, N- and S-containing Schiff base ligands interact with a wide range of metal ions, resulting in the formation of a variety of complexes with intriguing biological and physicochemical properties, in the study(Ismail Warad,*et al.,*2017) synthesis of A new tetradentate N_2S_2 Schiff base ligand derived from 5-bromothiophene-2-carbaldehyde and its [CuBr(N2S2)]Br complex were synthesized in good yield and its complex, [CuBr(N2S2)]Br,by Condensation of 5-bromothiophene-2-carbaldehyde with ethylenediamine in a 2:1 molar ratio afforded the tetra-dentate Schiff base (N1E, N2E)-N1 ,N2-bis((5-bromothiophen-2-yl)methylene)ethane1,2-diamine [N2S2] ligand, the **Scheme(1-14)** shows Synthesis of compounds



Scheme (1-14):Synthesis of the N_2S_2 and its Desired Monocationic [CuBr(N_2S_2)]Br Complex

In the study (Kiran Singh.,*et al.,*2013) was synthesis a new Schiff base and their complex and tested for biological activity, The Schiff bases (imines) HL_1 and HL_2 by the reaction of 5-bromothiophene-2-carboxaldehyde with 4-amino-5-mercapto-1,2,4-triazole and 4-amino-3-ethyl-5-mercapto-1,2,4-triazole, respectively, Organosilicon(IV) and organotin(IV)Complexes,**Figure(1-29)**Shows stracture for ligand's Complexes.



$R = -H, -CH_2CH_3$

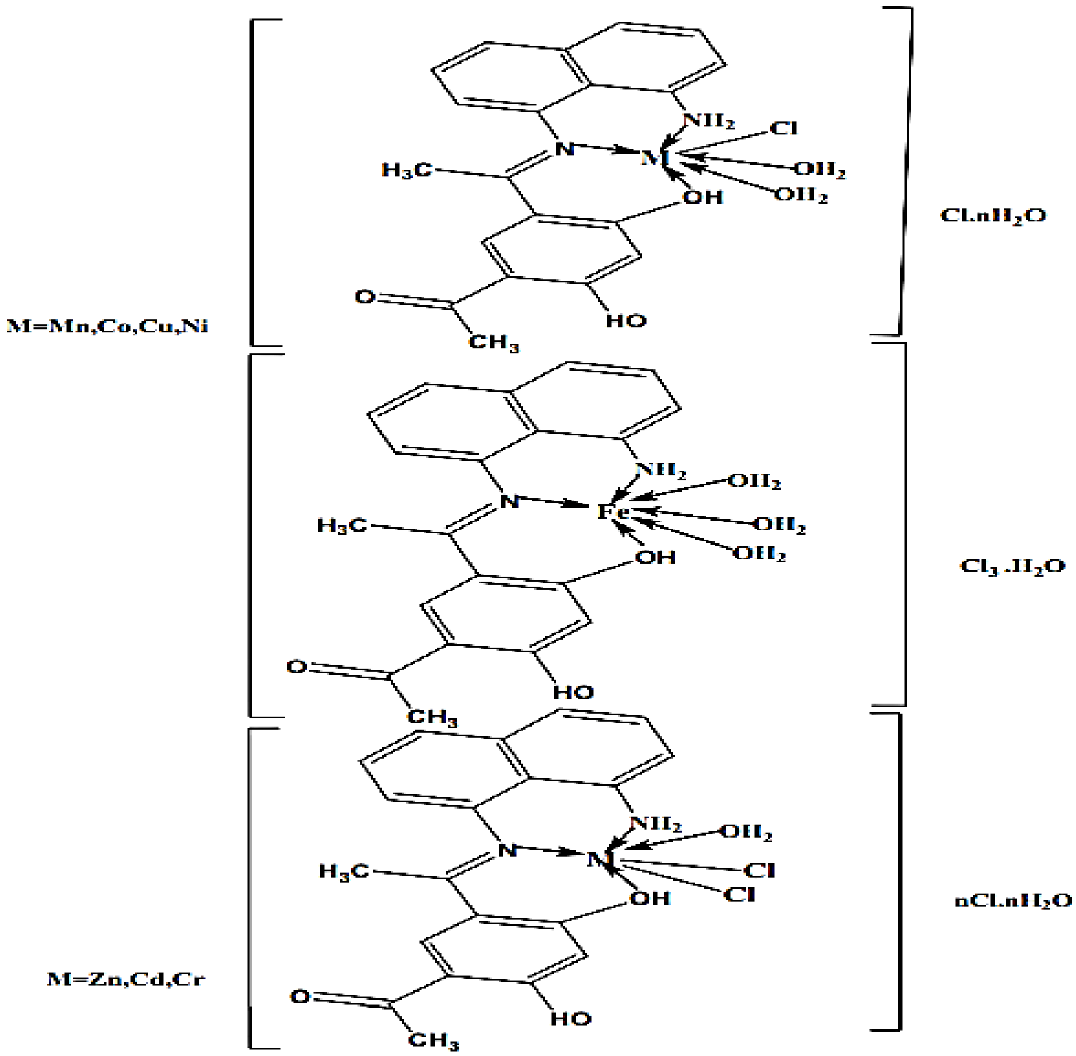
M= Si, Sn

Figure (1-29):Proposed Structures of the 1:1 and 1:2 Complexes from HL_1 and HL_2 Ligand

1.7.Methods for Synthesis of Complexes

(A) Conventional or wet chemical method

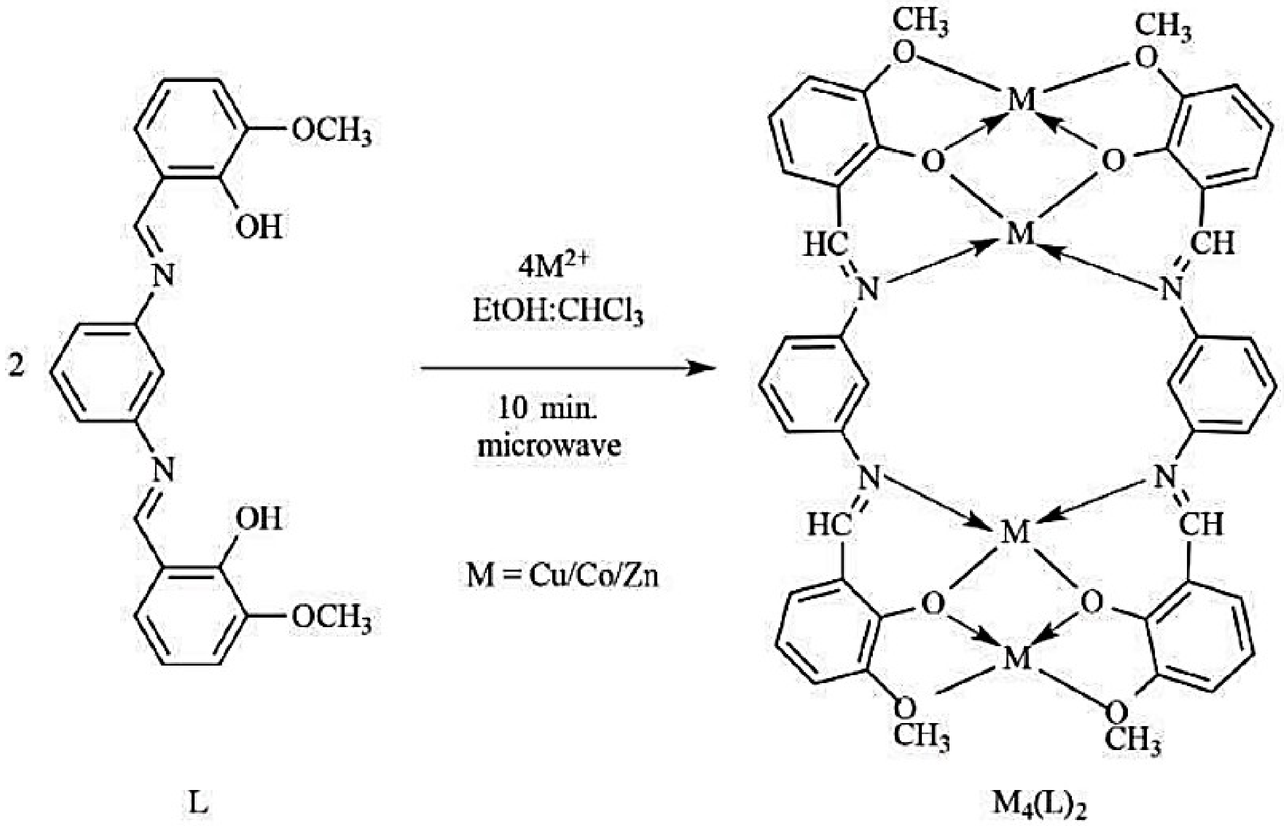
In the study(Ahmed, Y. M., et al.,2021)has been synthesised metal complexes by stirring and then refluxing a mixture of the metal salt for the Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) metal ions with ligand *Schiff* Bases ligand by using a suitable solvent, **Figure(1-30)** shows the structure of complexes.



Figure(1-30):Structures of Metal Complexes from 4,6-Diacetylresorcinol and 1,8-naphthalenediamine in 1:1Molar Ratio

(B) Microwave-assisted method

Microwave-assisted techniques involve simple handling, making them a cheaper and quicker synthetic method than the classical methods (Hijji, Y,*et al*.,2021). Schiff base ligands were complexed with Cu and Ni metal centres using the microwave synthesis method in the study (Moeketse, T. N.,*et al*.,2022) to produce metal-ligand complexes with enhanced capabilities for NO detection, A Schiff base (3 mmol) was added to a propionic solution of copper(II) chloride (1.5 mmol). The same procedure was followed for the other metal (Ni).and in the other study using the same method (Khaidir, S. S.,,*et al*.,2022) the ligand was synthesized via condensation of o-vanillin and m-phenylenediamine. Its tetranuclear Cu(II), Co(II), and Zn(II) complexes were obtained through microwave-assisted complexation with corresponding acetate salts in a 1:2 ratio of L:M. as shown at **Scheme (1-15)**.



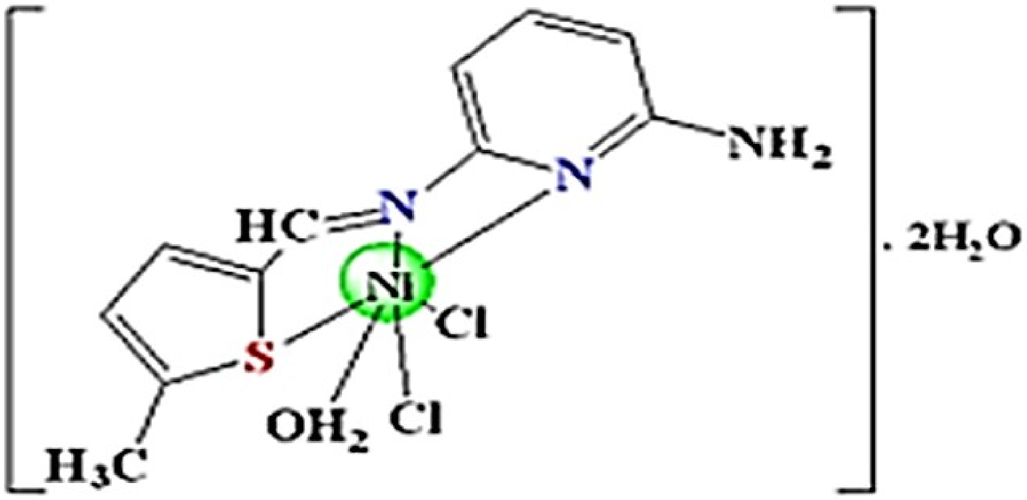
Scheme(1-15):Synthesis of Tetranuclear Metal Complexes M_4 $(L)_2$ Where M = Cu, Co and Zn

1.7.1.The Coordination Chemistry of Ni, Cu, and Zn

Nickel chemistry: The reactivity of Ni metal resembles that of Co , and is resistant to aqueous alkalis. Ni(II) is far the most important oxidation state for the metal, Ni(II) complexes with coordination numbers from 4 to 6 being common ,octahedral and square planar geometries are most usual ,For some Ni(II) complexes, there is only a small energy difference between structure types (Catherine.E.,*et al.,*2008),Some structures of the Ni(II) complexes are complicated by interconversions between square planar and tetrahedral, or square planar and octahedral coordination (Li, Y. J.*et al.,*2021),(Kaya, Y.,*et al.,*2020).

$NiCl_2$ is made by direct combination of the elements. The chloride is a useful precursor in Ni(II) chemistry and can be purchased as the yellow anhydrous salt or green hydrate. hydrated nickel(II) salts and their aqueous solutions usually contain green $[Ni(H_2O)_6]^{2+}$ (Ashraf,A.Aly., *et al.*,2020)

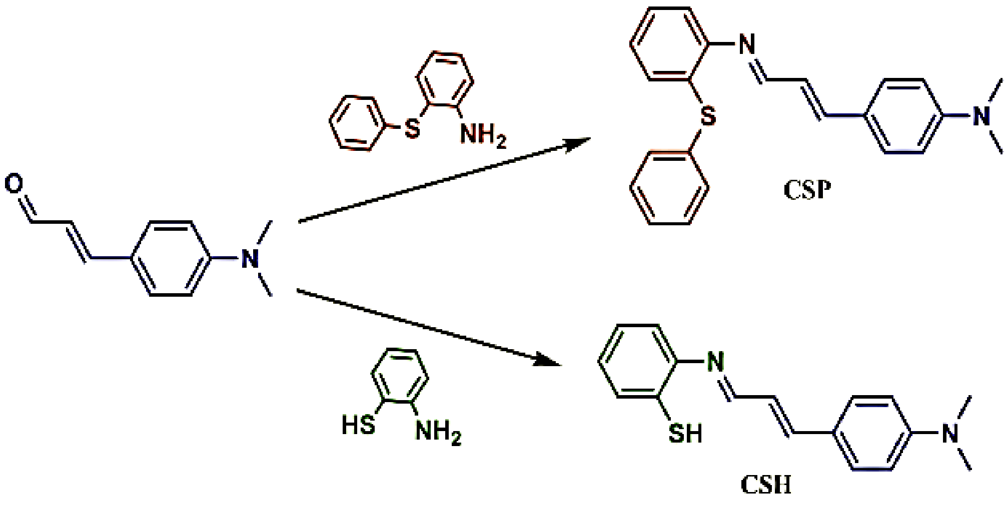
In the study (Nassar,D.A.,*et al*.,2022) synthesis a new Schiff base ligand N 2 -((5-methylthiophen-2-yl) methylene) pyridine-2,6-diamine (L) was prepared by condensation of 5-Methyl-2-thiophenecarboxaldehyde and 2,6-diaminopyridine in ethanol in a molar ratio 1:1. The ligand and its complexes ,**Figure(1-31)** shows the stracture of Ni(II) complex .



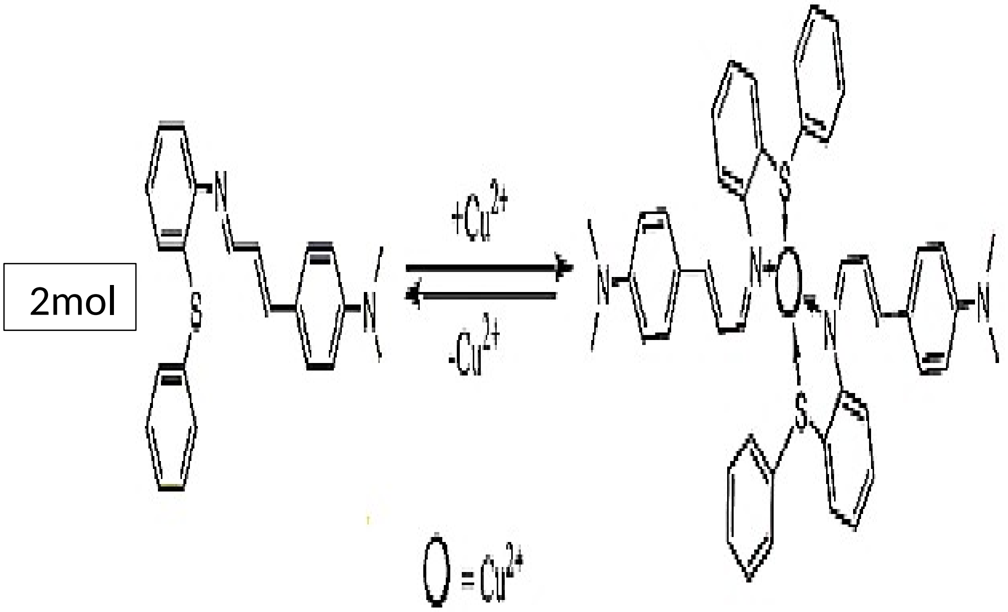
Figure(1-31):Propose Structure of the Schiff base Ligand and its Ni(II) Complexes

Copper chemistry:*Cupric* is the old name for Copper(II),Copper is the least reactive of the first row metals. Copper is the only first row d-block metal to exhibit a stable +1 oxidation state, in aqueous solution, Cu(I) is unstable by a relatively small margin with respect to Cu(II) (Wells, A. F. ,2012), It is not attacked by non-oxidizing acids in the absence of air, but it reacts with hot concentrated sulfuric acid, Copper(II) chloride forms yellow or brown deliquescent crystals and forms the green-blue $CuCl_2.2H_2O$ on standing in moist air (Catherine, E.*et al.,*2008),Complexes containing N- and O-donor ligands are very common, and coordination numbers of 4, 5 and 6 predominate (Kalarani, R.*,et al.,*2020).,A practical application of the coordination of N,O-donors to Cu(II) is the biuret test for peptides and proteins(Denholm, K.,*et al.,*2021)

In the study (Aydin, Z., & Keles, M,2020) the N,N-dimethyl-4-((2-(phenylthio) phenyl)imino)propenyl)aniline (CSP) and 2-(4-(dimethylamino) phenyl) allylidene) amino)benzenethiol (CSH) were synthesized as new Schiff base derivatives and the (CSP) shows high sensitivity and selectivity to Cu^{2+} over a wide range of other metal ions in acetonitrile, Show in **Scheme (1-16),(1-17)**.



Scheme (1-16):Synthesis of the Probes, CSP and CSH



Scheme (1-17):Proposed Reversible Binding Mechanism between CSP and Cu^{2+}

Two new metal complexes of general formula $M(Ha\alpha ft)_2$ [M = Ni(II) and Cu(II)] of asymmetrical Schiff base ligand (HL = Haαft) derived from amoxicillin and α-formylthiophene have been prepared in the study (Chaudhary,N.K.&Mishra,P.,*et al.*,2015),**Figure (1-32)** shows Schiff base ligand and metal complexes.

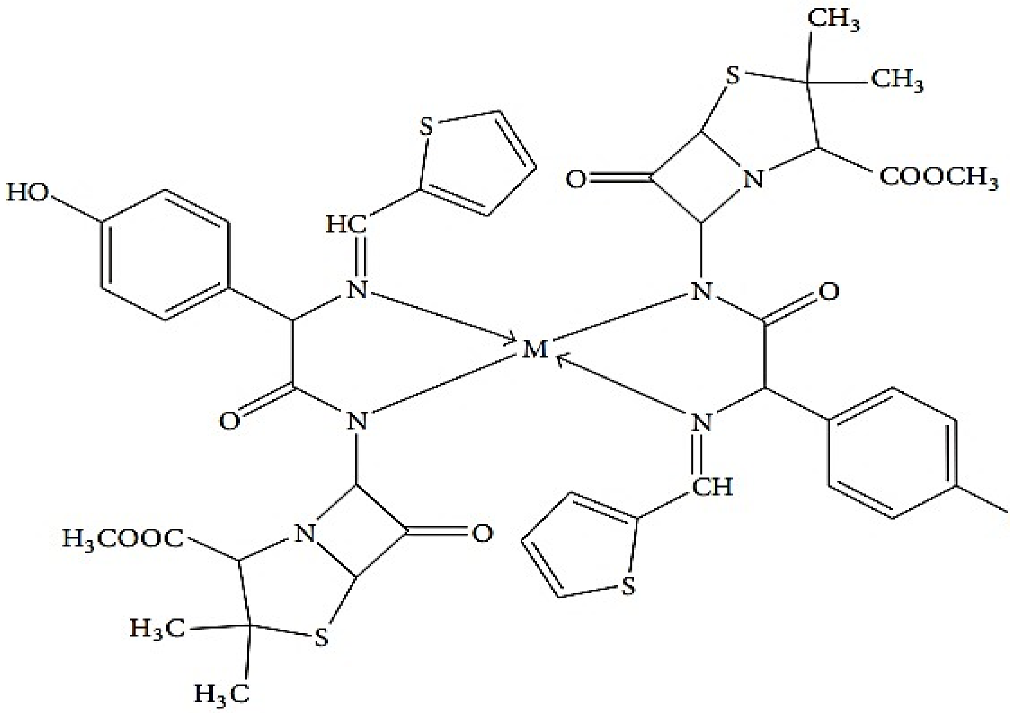
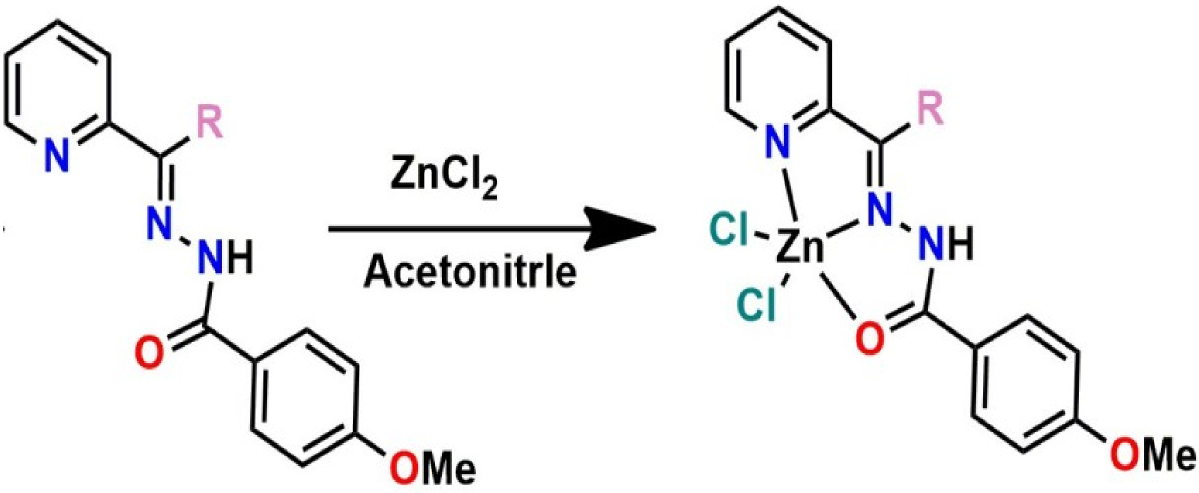


Figure (1-32):Structure of Metal Complex (M = Ni(II) & Cu(II))

Zinc Chemistry: The first (**Sc**) and last (**Zn**) members of the first row of the d-block exhibit a more restricted range of oxidation states than the other metals, and the chemistry of **Zn** is essentially confined to that of **Zn**(II),since the electronic configuration of **Zn**$^{2+}$ is d^{10}, compounds are diamagnetic proparties. Zinc reacts with all the halogens to give ZnX_2, and combines with elemental **S** and **P**.

The water Solubility of $ZnCl_2$ is highe soluble,uses of $ZnCl_2$ are varied, e.g. in some fire proofings, wood preservation, as an astringent. Zinc is not attacked by air or water at room temperature, but the hot metal burns in air and decomposes steam, forming ZnO. Zinc is much more reactive than Copper(Catherine. E.*et al.,*2008), znic with ligands containing a range of donor atoms, e.g. hard N- and O- and soft S-donors (Monkcom, E. C.,*et al.,*2021),(Liu, X., & Hamon, J. R. ,2019).

In the study (Dasgupta, S.,*et al.,*2020) mononuclear zinc(II) complexes namely [Zn(L_1)Cl_2] was synthesized from acyl hydrazone Schiff base ligand with and this compound have anti-cancer activity ,**Scheme(1-18)** show Schiff base ligand and its complexe.



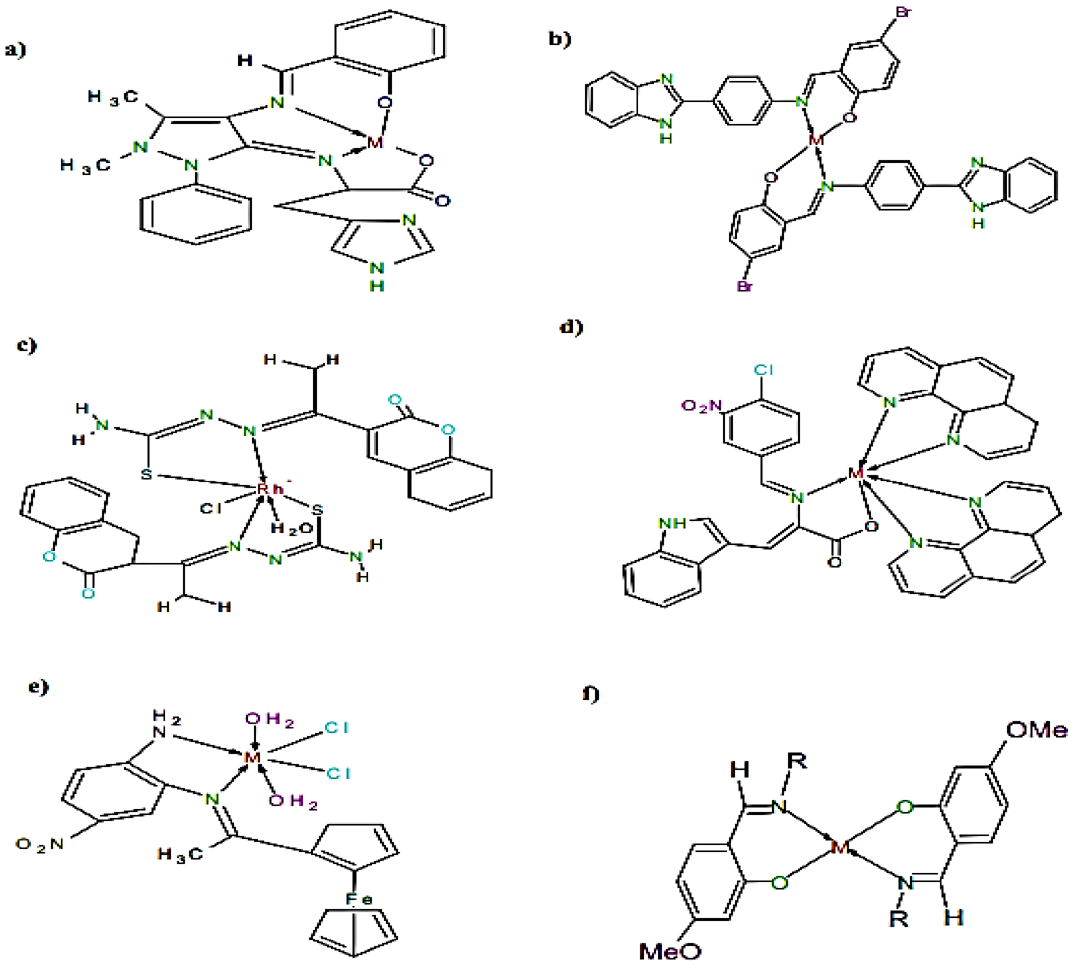
Scheme(1-18):Representation of Zinc Complexe from Schiff base Ligand

1.7.2.Applications of Complexes

There are many applications for complexes, so we will discuss some of them:

(A) Biological application

Transition metal complexes have thus emerged as an elective wellspring of chemotherapeutic antimicrobial agents(Shekhar, S.,*et al.,*2021) complexes of this study are shown in **Figure (1-33).** Chelation may make it much easier for a complex to cross a cell membrane, increasing antibacterial activity, chelation reduces metal ion polarity by partially sharing its positive charge with donor groups and electron delocalization over the chelate ring, bacterial strains become toxic to the Schiff base and its metal complexes,most metal chelates have polar and nonpolar properties, It has multiple applications in the medical field (Devi, J.,*et al.,*2022), Anticancer(Deswal, Y.,*et al*.,2022), antioxidant(Yernale, N. G.,*et al*.,2022), antifungal(Graur, V.,*et al*.,2022).



Figure(1-33):Structure Representation of few Schiff Metal Complexes Demonstrating Antibacterial Activity

Coordination compounds are anti-cancer drugs, Also, many of the coordination compounds are anti-bacterial. The coordination compounds have been showed effective behaviour against many diseases like Alzheimer's and malaria, recently coordination compounds used as antivirus such as coronavirus, in present review for (Mohammed, H. S., & Tripathi, V. D.,2020), we highlighted the most important coordination complexes that show a significant role in the field of medicine, many coordination compounds exhibited biological activities against bacteria and fungi. The mix ligands of piperaquine, acetaminophen and acetylsalicylic of Copper (II), Cobalt (II), Zinc (II), and Iron (II) ions exhibited biological activity against *Escherichia coli* and *Staphylococcus aureus* ,**Figure(1-34**) shows the Stracture of Complexes.

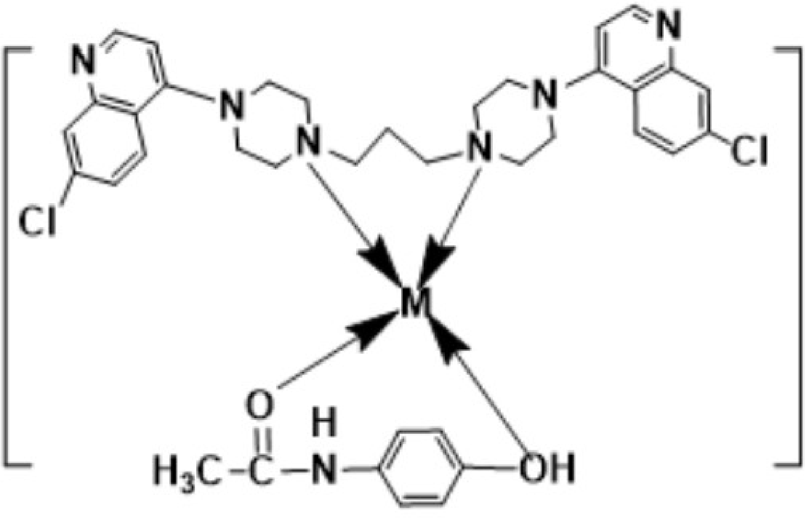
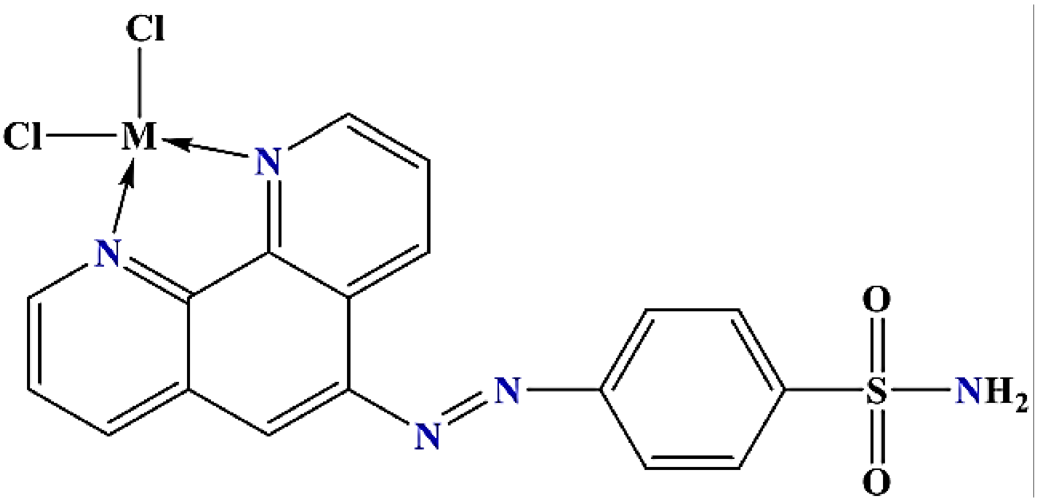


Figure (1-34):Stracture of Cu(II),Co(II),Zn(II),Fe(II)Complexes

Industrial application (B)

Metal complexes are widely used in industrial applications as catalysts, pigments and dyes, organic synthesis intermediates, polymer stabilizers, and corrosion inhibitors(Uddin, M. N.,*et al*.,2020).The metal complexes with Schiff bases have numerous applications in everyday life, including essential cost-effective synthetic substrates, excellent analytical tools, and efficient catalytic, photochromic, thermochromic, stereo-chemical, and anti-corrosive materials Some bivalent metal complexes (Cobalt, Nickel, Copper, and palladium) have been studied for their ability to act as mesogens, industrial & biochemical catalysts, and optical & magnetic behavior in electronic media(Kargar, H.,*et al.,*2021).

In the study by (Al-Saidi, H. M. *et al.,*2022),synthesis dye by coordination of M(II) through (L) ligand N-atoms should produce complexes which should maintain the stability and redox properties of traditional 1,10-o-phenanthroline complexes , The (L) ligand was coordinated to a M(II) metal center through the 1,10-o-phenanthrolin binding to form a stable complex ,**Figure(1-35)** Shows the stracture of synthetic complexes.



Figure(1-35):Proposed Structure of Synthetic Metal Complexes of the L, where M = Ni(II), Cu(II) and Zn(II) Ions

1.8.Aims Of The Work

1- Synthesis of Schiff base biologically effective organic compounds by linking the 6-aminopenicillic acid compound with various aldehydes and ketones, with aromatic aldehyde(cinnamaldehyde), an isothiocyanate aromatic ketone(benzoyl isothiocyanat), and sulfur- heterocyclic aldehyde(5- bromothiophene -2-carbaldehyde.

2- Characterized these compounds by different techniques and many physical measurements.

3- Preparation Complexes of these ligands with a d-block of transition element metals (Ni,Cu,Zn)with oxidation state (+2) as chloride salts.

4- Characterization of prepared metal complexes by using diagnostic techniques many physical measurements to arrive at the geometry of the complexes .

5- study of biological activity of the prepared ligands and ligand's (Ni(II),Cu(II),Zn(II)) complexes and study of the inhibitory against deferent type of bacteria.

Chapter Two

2.1.Materials

Chemicals of a high degree of purity and from different international origins were used, **Table(2-1)**shows materials used in the research and the companies producing

Table(2-1):Materials Used in the Research and the Companies Producing

	Chemicals	Formula	M.wt	Company	Purity
1	6-Aminopenicilic acid	$C_6H_{12}O_3N_2S$	216.26	Sigma Aldrich	99.98 %
2	Cinnamaldehyde	C_9H_8O	132.16	Verdean House	98%
3	Benzoyl isothiocyanate	C_8H_5NOS	163.19	Macklin	97%
4	5-Bromothiophen -2-carbaldehyde	$C_5H_3BrO_2$	191.05	Macklin	97%
5	Absolute ethanol	C_2H_5OH	46	Honeywell	99.9%
6	DMSO	C_2H_6OS	78.14	B.D.H	99%
7	Nickel (II)chloride hexa-hydrate	$NiCl_2.6H_2O$	237.71	Univar	99%
8	Copper (II) chloride dehydrate	$CuCl_2.2H_2O$	170.48	Qrec	98%
9	Zinc(II) chloride	$ZnCl_2$	136.30	Sigma Aldrich	98%
10	Hydrochloric acid	HCl	36.45	Sigma Aldrich	35%
11	Acetone	C_3H_6O	58.08	B.D.H	98%
12	Molar Hinton	-	-	B.D.H	98%
13	Pyridine	C_5H_5N	79.101	B.D.H	98%

2.2.Apparatuses

Melting points.2.2.1

By using a electro thermal SMP30-melting point 9300 M.P apparatus The melting points of all prepared compounds were determined by open capillary tube,at the College of Science for women, University of Babylon.

2.2.2.Fourier Transform Infrared Spectra (FTIR)

The FTIR Spectra were obtained by using KBr discs using a Biotic 600 FTIR Spectrophotometer in the range 4000-400 cm $^{-1}$ on a Shimadzu FTIR-8400S, which, were measured at the College of Science for women University of Babylon.

2.2.3.Conductivity Measurement

Electrical conductivity measurements of the complexes were made with Absolute Ethanol solutions at 25 C^0 using , on a Hennu HI 9811-5 conductivity meter. at College of AL-Mustaqbal university , Department of Medical laboratory techniques.

2.2.4.UV-Visible Spectra

UV-visible spectra of prepared ligand solutions and it's complexes were measuring in Absolute ethanol solvent on PEAK instruments C-7200 at College of, Science for Women, University of Babylon.

2.2.5.(^{13}C, ^{1}H) NMR Spectra Measurements

The nuclear magnetic resonance spectra for ligand were measured at Tahran University of Iran using an instrument 10-Bruker Biospin GmbH spectrometer Operating at (400Hz) with (DMSO-d^6).

2.2.6.Flame atomic absorption spectroscopy

The atomic absorption analysis was used to determine the metal contents in the complexes by Shimadzu AA-7000 Spectrophotometer, at the Ministry of Science and Technology, Baghdad.

2.2.7.Liquid Chromatography-Mass spectrometry

This devise fracture the molecular wight of the samples, were measured at Tehran/Iran, on day petronic company, by the waters Alliance 2695 HPLC-Micro mass Quattro micro API Mass spectrometer.

2.2.8.Magnetic susceptibility apparatus

Measurements of magnetic susceptibility have been made for the prepared complexes by using Faraday method with Balance Magnetic Susceptibility by Sherwood scientific ,Model – 3003, at the College of Sciences ,Al-Mustansiriyah University.

2.2.9. Microelemental analysis (C.H.N.S)

The ratios of the elements carbon, hydrogen, nitrogen and sulfur were determined for the ligands on Euro vector A3000 at College of Sciences, university of Babylon.

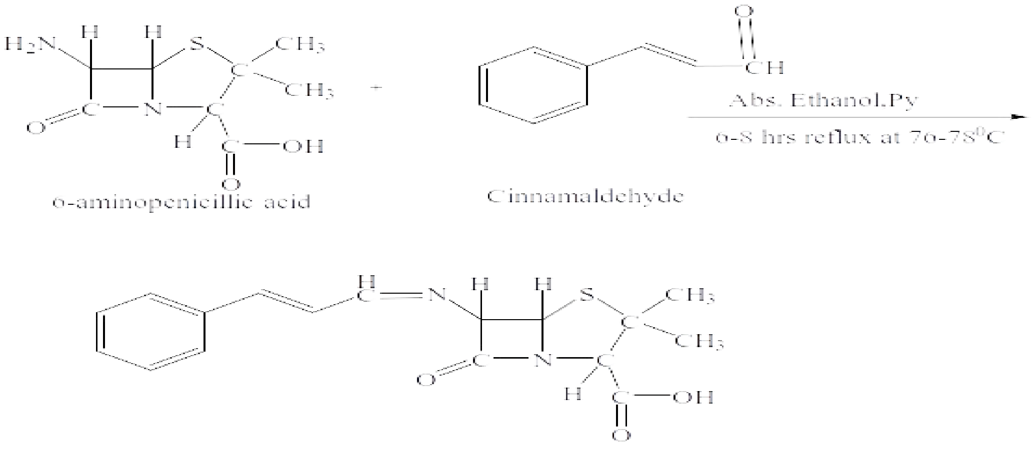
2.2.10.Thermogravimetric analysis (TGA)

The (TGA) used to measure of the complexes, on ShimadzuTA-60WS, at the College of Science for Women, University of Babylon.

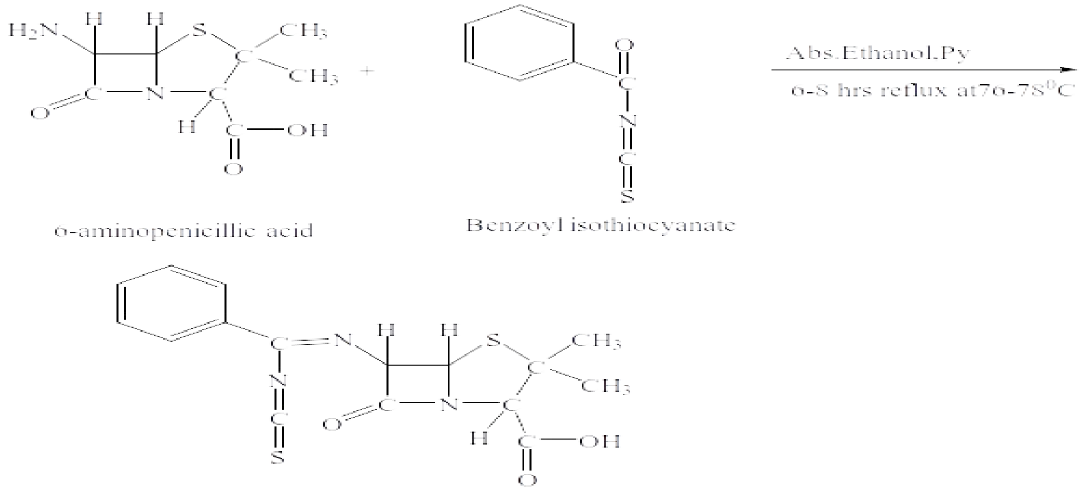
2.3.Experimental

2.3.1.Synthesis of Ligands (L_1, L_2,L_3)

The ligands (Schiff base) were prepared using the general method (Issa, Y. M.,*et al.*,2021), (Srivastava, A. K.,*et al.*,2021) where(2.162g) from 6-aminopenicilic acid(0.01 mol) was weighed and then dissolved in 50 ml absolute ethanol in around bottom 250 ml .Should the mixture was heated to 76^0C and 4-5 drops of pure pyridine were added , then a volume(1.283 ml) of Cinnamaldehyde ,(1.363ml) of benzoyl isothiocyanate and (1.188 ml) of 5-Bromothiophene-2-carbaldehyde (0.01mol), were added to the solutions ,Then the mixture was reflux for period ranging for 6-8 hours at a temperature 76-78^0C. A color change from light yellow to dark brown in (L_1), light yellow to dark red in (L_2) and brown-green to brown-orange in (L_3) After the reaction was completed, dried the product at room temperature mixture and recrystallized by using Ethanol, **Scheme(2-1)**,**(2-2)** and **(2-3)** show the preparation reaction for Ligands (L_1,L_2 and L_3) .



Scheme(2-1):Preparation of Ligand(3,3-dimethyl-7-oxo-6-(((1Z,2E)-3-phenylallylidene) amino)-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid (L_1)



Scheme (2-2):Preparation of Ligand (Z)-6-((isothiocyanate(phenyl) methylene)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid (L₂)

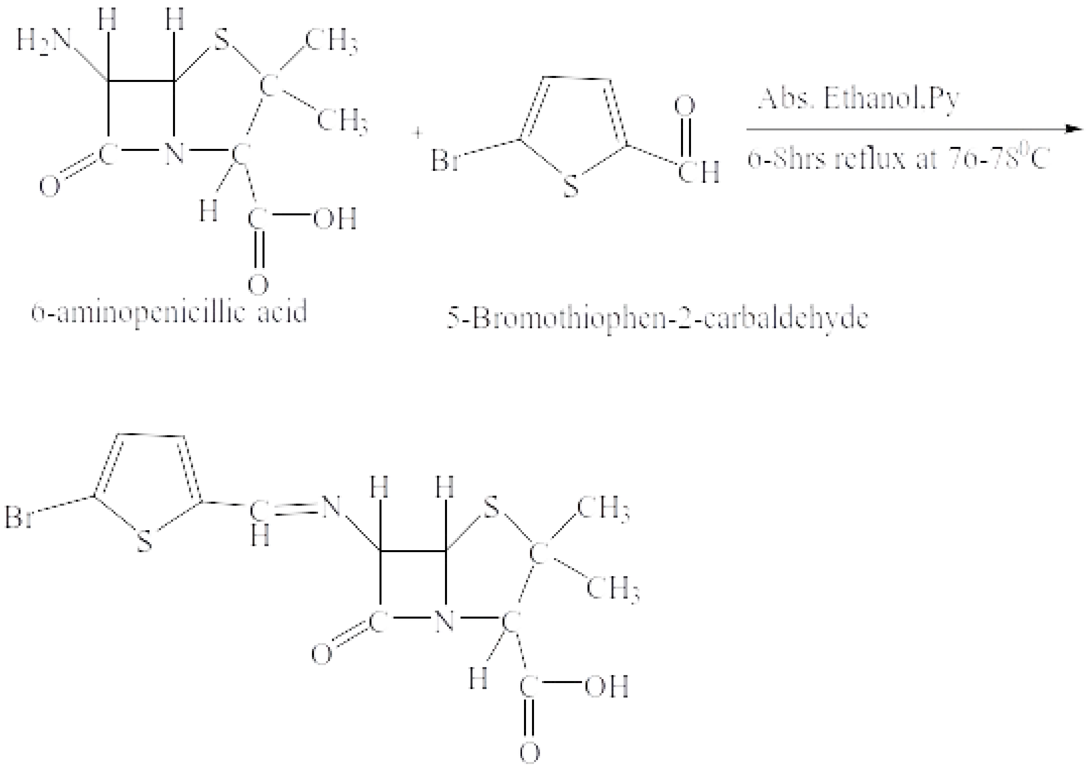


Figure:(2-3):Preparation of Ligand (E)-6-(((5-bromothiophen-2 yl)

methylene)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid(L_3)

2.3.2.Preparation of Complexes with Ligand(L_1)

The complexes were prepared using the general method for the preparation of complexes(Issa, Y. M.,*et al.*,2021),(Nassar,*et al.*,2022), where (0.660)g from a ligand(L_1) (0.002mol) were weighed and then dissolved in 20 ml of absolute ethanol, the solution was mixed with (0.170 g, 0.237 g, and 0.137 g) of $CuCl_2 . 2H_2O$, $NiCl_2 .6H_2O$, and $ZnCl_2$ (0.001mol) respectively. The mixtures were still with stirring 24-48 hours at room temperature, After the reactions were completed, and dried at room temperature mixtures and the colored complexes got precipitated slowly, which was filtered, washed repeatedly with distilled water and ethanol, the chemical equations below show the preparation of ligand's complexes.

$$2C_{17}H_{18}N_2O_3S + NiCl_2.6H_2O \rightarrow [Ni(C_{17}H_{18}N_2O_3S)_2Cl_2]+6H_2O$$

$$2C_{17}H_{18}N_2O_3S+CuCl_2.2H_2O \rightarrow [Cu(C_{17}H_{18}N_2O_3S)_2Cl_2]+2H_2O$$

$$2C_{17}H_{18}N_2O_3S + ZnCl_2 \rightarrow [Zn (C_{17}H_{18}N_2O_3S)_2Cl_2]$$

2.3.3.Preparation of Complexes with Ligand (L_2)

In (L_2) ligand (0.722 g,0.002 mol) were weighed and then dissolved in 20 ml of absolute ethanol ,that solution was mixed with of (0.170 g, 0.237 g, and 0.137 g) of $CuCl_2 . 2H_2O$, $NiCl_2 .6H_2O$, and $ZnCl_2$ (0.001 mol) respectively, for 24-48 hours . After the reactions were completed, dried the product was at room temperature, filtered, and washed repeatedly with distilled water and ethanol (Kuate, M.,*et al.*,2020), the chemical equations show the preparation of ligand's complexes.

$$2C_{16}H_{15}N_3O_3S_2 + NiCl_2.6H_2O \rightarrow [Ni(C_{16}H_{15}N_3O_3S_2)_2Cl_2] + 6H_2O$$

$$2C_{16}H_{15}N_3O_3S_2 + CuCl_2.2H_2O \rightarrow [Cu(C_{16}H_{15}N_3O_3S_2)_2Cl_2] + 2H_2O$$

$$2C_{16}H_{15}N_3O_3S_2 + ZnCl_2 \rightarrow [Zn(C_{16}H_{15}N_3O_3S_2)_2Cl_2]$$

2.3.4.Preparation of Complexes with Ligand (L_3)

A (0.778 g) from a ligand (L_3) (0.002mol) was weighed and then dissolved in 20 ml of absolute ethanol ,that solution was mixed with (0.170 g, 0.237 g, and 0.137 g) of $CuCl_2 . 2H_2O$, $NiCl_2 .6H_2O$, and $ZnCl_2$ (0.001mol) respectively ,the chemical equations show the preparation of ligand complexes.

$$2C_{13}H_{13}BrN_2O_3S_2 + NiCl_2.6H_2O \rightarrow [Ni(C_{13}H_{13}BrN_2O_3S_2)_2Cl_2] + 6H_2O$$

$$2C_{13}H_{13}BrN_2O_3S_2 + CuCl_2.2H_2O \rightarrow [Cu(C_{13}H_{13}BrN_2O_3S_2)_2Cl_2] + 2H_2O$$

$$2C_{13}H_{13}BrN_2O_3S_2 + ZnCl_2 \rightarrow [Zn(C_{13}H_{13}BrN_2O_3S_2)_2Cl_2]$$

2.4.Antibacterial Activity

The antibacterial activity for the ligands and their complexes were be tested by used tow type from bacteria were be isolated and diagnosed in the laboratory by using the microscopic and biochemical tests. Since the purpose of this process is to know the extent of biological resistance that these types of bacteria show towards each of the ligands and their complexes, and thus we can be sure that the compounds that have been prepared have biological activity or not.From this types Gram-positive represented of (*Staphylococcus aurous*) is the most dangerous of all the different and common types of staphylococcal bacteria.(Portela, R.,*et al*.,2020)they often cause skin infections, but can cause pneumonia, heart valve infections, and bone infections ,So most *S. aurous* strains are now resistant to first-generation penicillins, second-generation penicillins such as oxacillin ,nafcillin, and methicillin are used(Paul J. Weldrick*., et al.,*2020).,and the other type Gram-Negative represented of *Pseudomonas* has become an important cause of infection,and it is a frequent cause of nosocomial infections(Doghri, I.,2020). Pseudomonal infections are complicated and can be life-threatening

2.4.1-Preparation of the Media

The media were prepared by dissolving (8.7)g of molar Hinton agar in 250 ml distilled water, then set in the autoclave at 121 ^{0}C and 1atm for 15-20 minute, later that the media took off and cold to 54^{0}C. After complete solidification, and distributed into Petri dishes with a view to leaving bacteria and then used for tests, made 5 mm gap between the wells was made aseptically using sterile gel borer.(Zhang, F., *et al.,*2020).

-Well Diffusion Method (Mat Method)

The antibacterial of the(L_1,L_2,L_3) and their complexes against as tow Bactria Gram-positive *staphylococcus* ,Gram-negative *pseudomonas* the bactria cultures were grown and maintained in the media(Miragaia, M.,2018).

Five millimeters in diameter were cut using sterile gel borer, samples were filled in the wells with the help of micropipette at the dilution $3x10^{-3}M$ (Taghreed H. Al-Noor.,*et al.,*2021) for the different type of the ligands and their complexes then left for 24 hour at 37 ^{0}C.After incubation the antibacterial activity was determined by measuring the diameter of the zone of inhibition (**ZI**) by the ruler (singh A.,*et al*.,2012).

Chapter Three

3.1.Complexes

The term metal complex include s-block, p-block and all d-block elements and lanthanides, as well as the post-transition metals gallium, indium, tin, thallium, lead, and bismuth. It excluded actinides and rare/radioactive d-elements with atomic numbers greater than 100, as well as the radioactive elements technetium and promethium(Frei,A.,*et al*.,2022) However, metal-based coordination complexes have played an important role in medicine throughout history, including the use of arsenic for the first effective treatment of (Salvarsan), mercury in the topical antiseptic mercurochrome and the vaccine preservative thiomersal, and gold in the treatment of rheumatoid arthritis (Auranofin).Metal complexes are currently being tested in clinical trials to treat cancer and other diseases. With the approval of the chemotherapeutic platinum-based drug Cisplatin (1978), which is still used in the majority of cancer treatments today, metal complexes became a cornerstone of medicinal chemistry. Several more platinum, iron, ruthenium, copper, and gallium-based metal complexes have entered human clinical trials as cancer and other disease treatments in the last two decades (Frei,A.,*et al*.,2020).

3.2.Physical Properties

The physical properties of the prepared compounds, such as melting point, color ,molecular Wight and product yield , were calculated,**Tab1e (3-1)** shows the results of these calculations.

Tab1e (3-1):Physical Properties of Prepared Compounds

Compounds	**M.p** (^{0}C)	**M.wt** (g/mol)	**Color**	**Yield%**
L_1	190-192 ^{0}C	330.40	Brown-bright	76.8%
$]Ni(L_1)_2\ Cl_2[$	210-220 ^{0}C	790.43	Brown-golden	67.3%
$]Cu(L_1)_2\ Cl_2[$	198-200 ^{0}C	795.25	Yellow-green	44.9%
$]Zn(L_1)_2Cl_2[$	220-230 ^{0}C	797.08	Gray-brown	78.2%
L_2	93-97 ^{0}C	361.43	Black-red	91.5%
$]Ni(L_2)_2\ Cl_2[$	118-120 ^{0}C	852.45	Red	62.8%
$]Cu(L_2)_2\ Cl_2[$	100-102 ^{0}C	857.31	Bronzy	44%
$]Zn(L_2)_2Cl_2[$	110-112 ^{0}C	859.14	Light-Red	78.9%
L_3	91-93^{0}C	389.177	Brown-red bright	79%
$]Ni(L_3)_2\ Cl_2[$	100-110 ^{0}C	907.944	Brown-bright	52.5%
$]Cu(L_3)_2\ Cl_2[$	98-100 ^{0}C	912.804	Brown-black	51.5%
$]Zn(L_3)_2Cl_2[$	120-129 ^{0}C	914.734	Brown-orangey	66.4%

3.3.Solubility

The Solubility of Ligands and their Complexes Ni (II), Cu (II) and Zn (II) were studied in different polar and non-polar solvents. The compounds are Soluble in absolute ethanol and slightly soluble in methanol, while it was found that all compounds are insoluble in water. Table (3-2) shows the solubility of prepared compounds in different solvents.

Table (3-2):Solubility of Prepared Compounds in Different Solvents

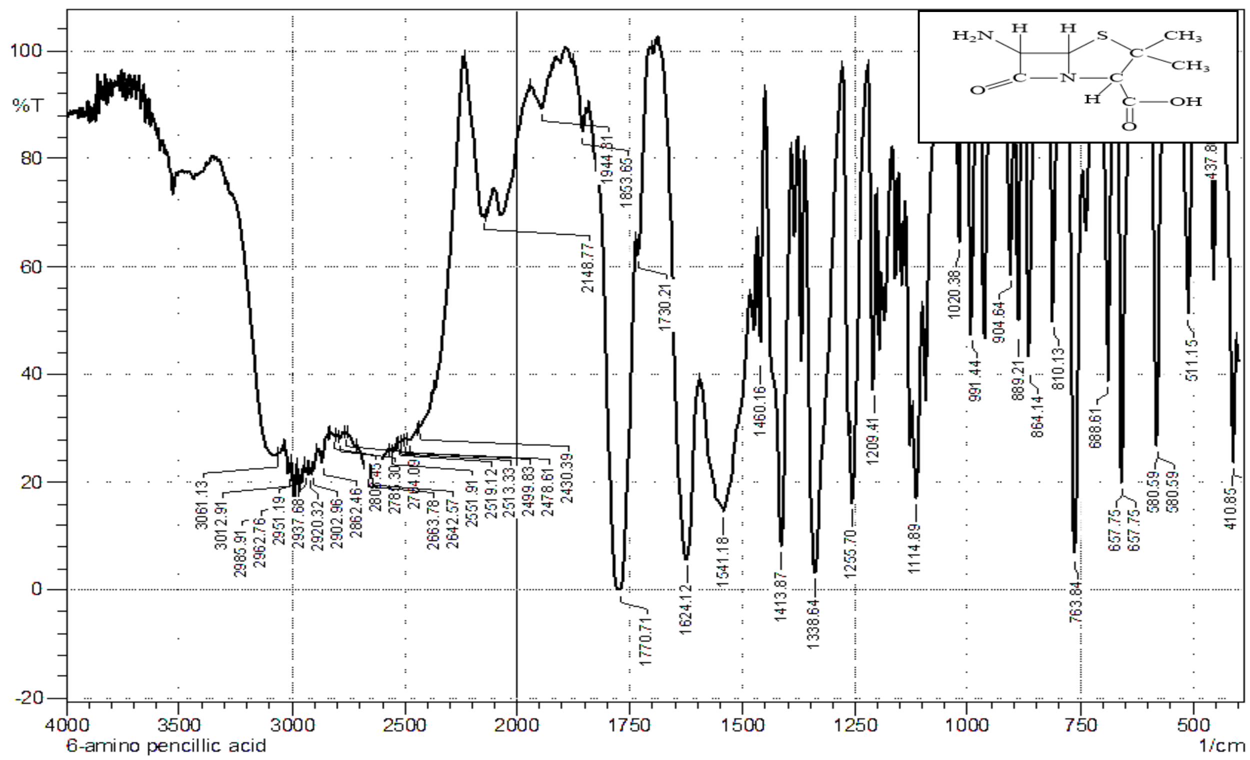
Compound	Acetone	Water	Abs.Ethanol	DMSO	Methanol	Chloroform
L_1	++	--	++	++	+ -	--
]Ni $(L_1)_2Cl_2$[	+ -	--	++	++	+ -	--
]Cu $(L_1)_2Cl_2$[	+ -	--	+ +	++	+ -	--
]Zn$(L_1)_2Cl_2$[	--	--	++	++	+ -	--
L_2	++	--	++	++	+ -	--
]Ni $(L_2)_2Cl_2$[	+-	--	++	++	+ -	--
]Cu $(L_2)_2Cl_2$[	+-	--	++	++	+ -	--
]Zn$(L_2)_2Cl_2$[	+-	--	++	++	+ -	--
L_3	--	--	++	++	+ -	--
]Ni $(L_3)_2Cl_2$[	+-	--	++	++	+ -	--
]Cu $(L_3)_2Cl_2$[	+-	--	++	++	+ -	--
]Zn$(L_3)_2Cl_2$[	++	--	++	++	+ -	--

(++) Soluble,(+ -) Slightly soluble,(--)Insoluble.

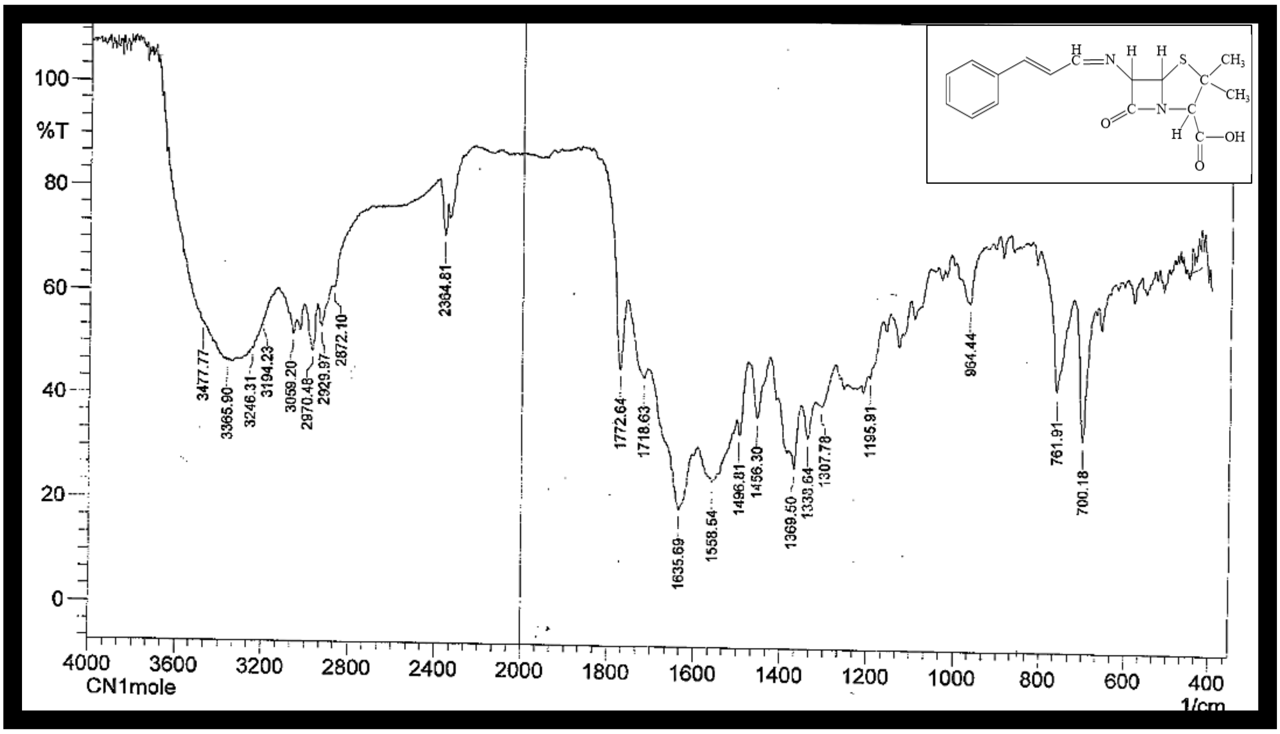
3.4.Characterization of Ligands

3.4.1.The FTIR Spectrum for Ligands (L_1, L_2,L_3)

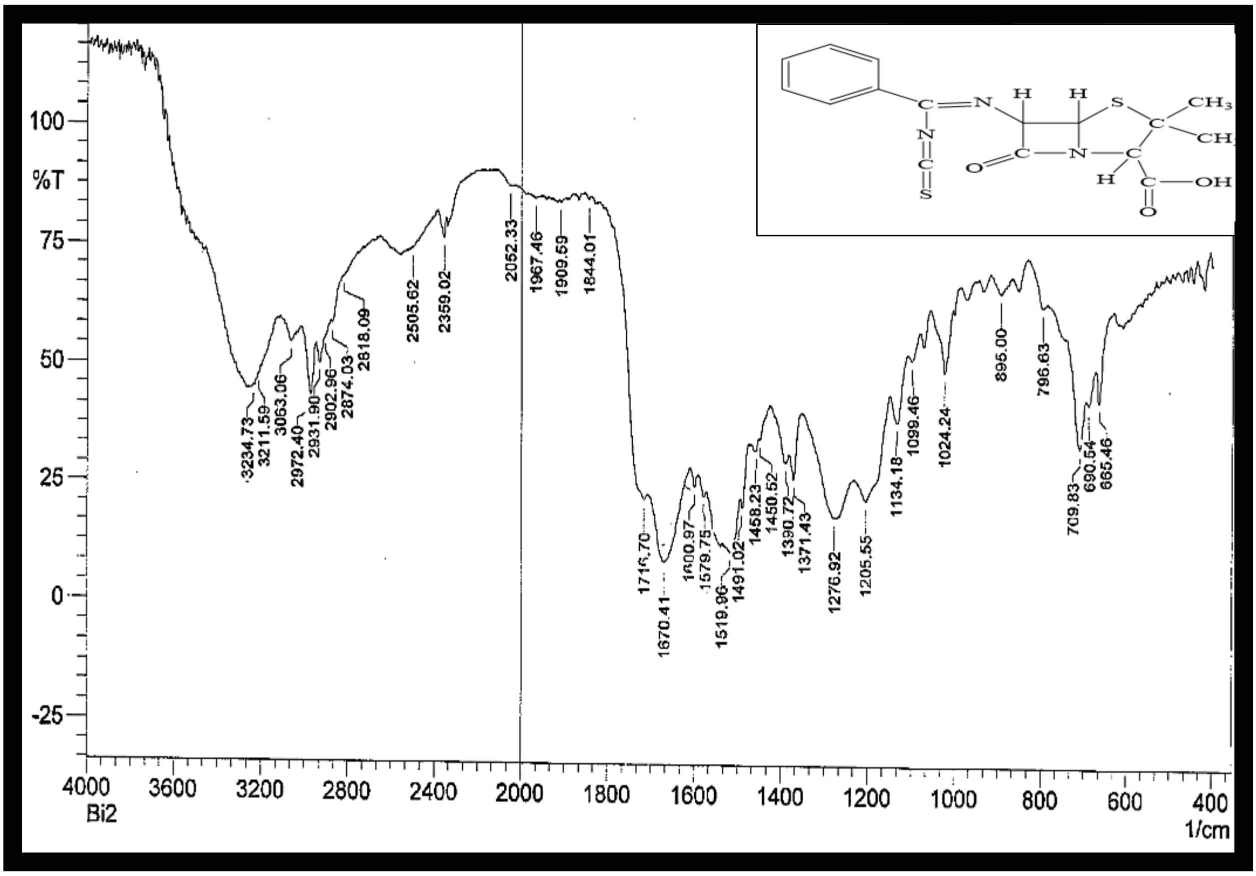
The FTIR Spectrum of (6-aminopencilinic acid) exhibited a band 3477.77 cm^{-1} referring to υ(-NH_2) group,and the band at 1624.12 cm^{-1} was referred to υ(-C=O) of the *β*-lactam group (Juan Roberto Anacona *et al.,*2019), (Bhal,2015). The FTIR Spectrum for the ligand (**L_1**) display of a new band at 1602 cm^{-1} assigned to υ(-C=N) for the Schiff base ligand(**L_1**), and absence of the band due to υ(-NH_2) suggested the occurrence of the condensation reaction The band at 1635.64 cm^{-1} was attributed to the stretching vibration υ(-C=O) of *β*-lactam group (Hui Wang *et al.*,2016),(Hui Wang*,et al,*.,2018), The FTIR Spectrum for the ligand (**L_2**) display of a new band at 1579.75 cm^{-1} assigned to υ(-C=N) for the Schiff base ligand, The band at 1670.41cm^{-1} was attributed to the stretching vibration υ(-C=O) of *β*-lactam group(Magdy M. Hemdan., &Amira,A.Al-sayed.,2016) (Mohammad Azam *et al.,*2020) .The FTIR Spectrum for the ligand (**L_3**) display of a new band at 1618.1 cm^{-1} assigned to υ(-C=N) for the Schiff base ligand ,the band at 1670 cm^{-1} was attributed to the stretching vibration υ(-C=O) of *β*-lactam group (Ismail Warad *et al*.,2020), (K. Nakamoto,J.W.S.,2009) .Supporting Information in **Table(3-4),(3-5),(3-6)** ,and the **Figures (3-1)**,**(3-2)**,**(3-3)**,and**(3-4)** show the FTIR Spectrum of 6-Aminopenicilic acid ,and Schiff base ligands (**L_1,L_2,L_3**) respectively.



Figure(3-1): FTIR Spectrum for 6-Aminopenicilic acid



Figure(3-2):FTIR Spectrum for Ligand (L_1)



Figure(3-3):FTIR Spectrum for Ligand (L_2)

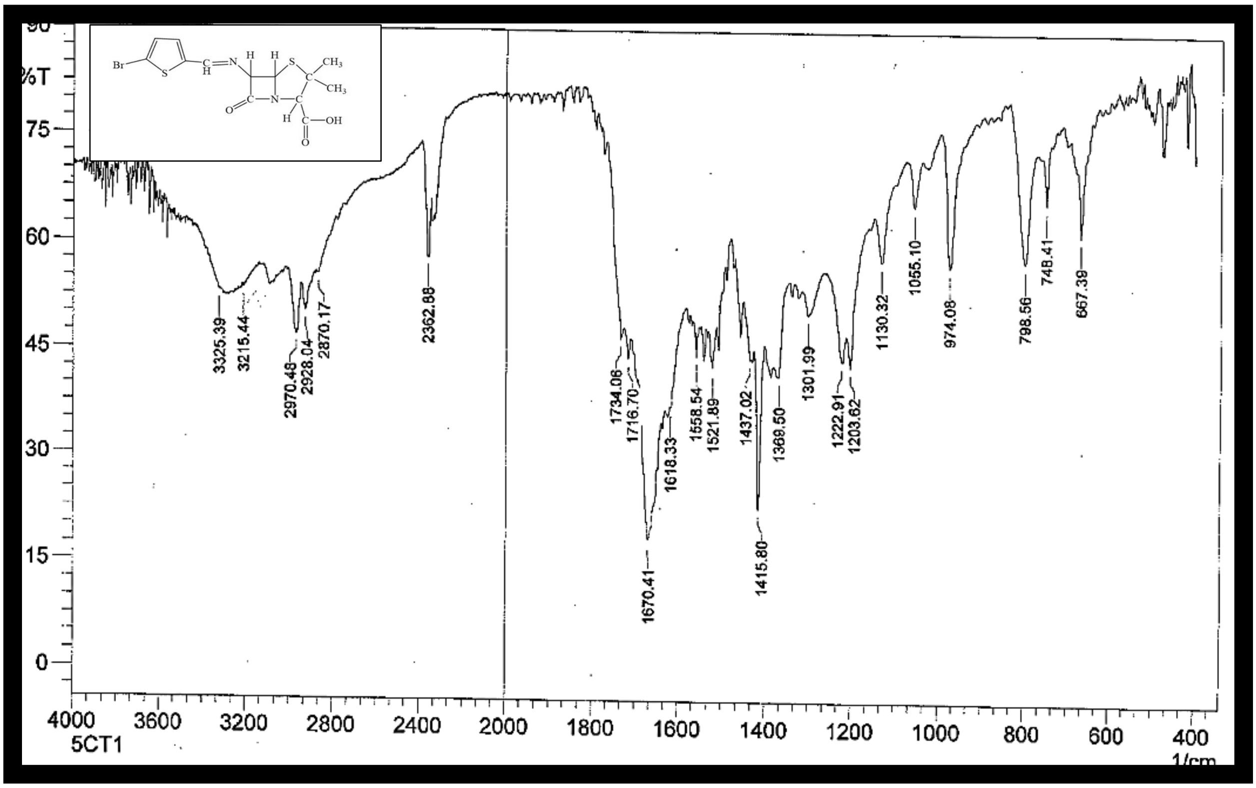


Figure (3-4): FTIR Spectrum for Ligand (L_3)

3.4.2.The ^{1}HNMR Spectrum of the Ligands (L_1,L_2,L_3)

The DMSO-d^6 was used as solvent to measure the ^{1}HNMR Spectrum of the Ligand (**L_1**)**.** The peakes at δ7.4-8.2 ppm (m) ascribed the aromatic ring ,and δ8.3-8.5 ppm (d) ascribed to proton of *β*-lactam ring(Taghreed H. Al-Noor., *et al*.,2021) The signals at δ 8.8- 8.9 ppm (d) and δ 9.0(s) ppm were observed due to azomethine protons in the spectra, and COOH, respectively,(Hui Wang.,*et al.*,2016),(Hui Wang.,*et al*.,2018),(Bhal,2015),(Donald L. pavia *et al*.,2001),**Figure(3-5)** shows the ^{1}HNMR for ligand(**L1**).

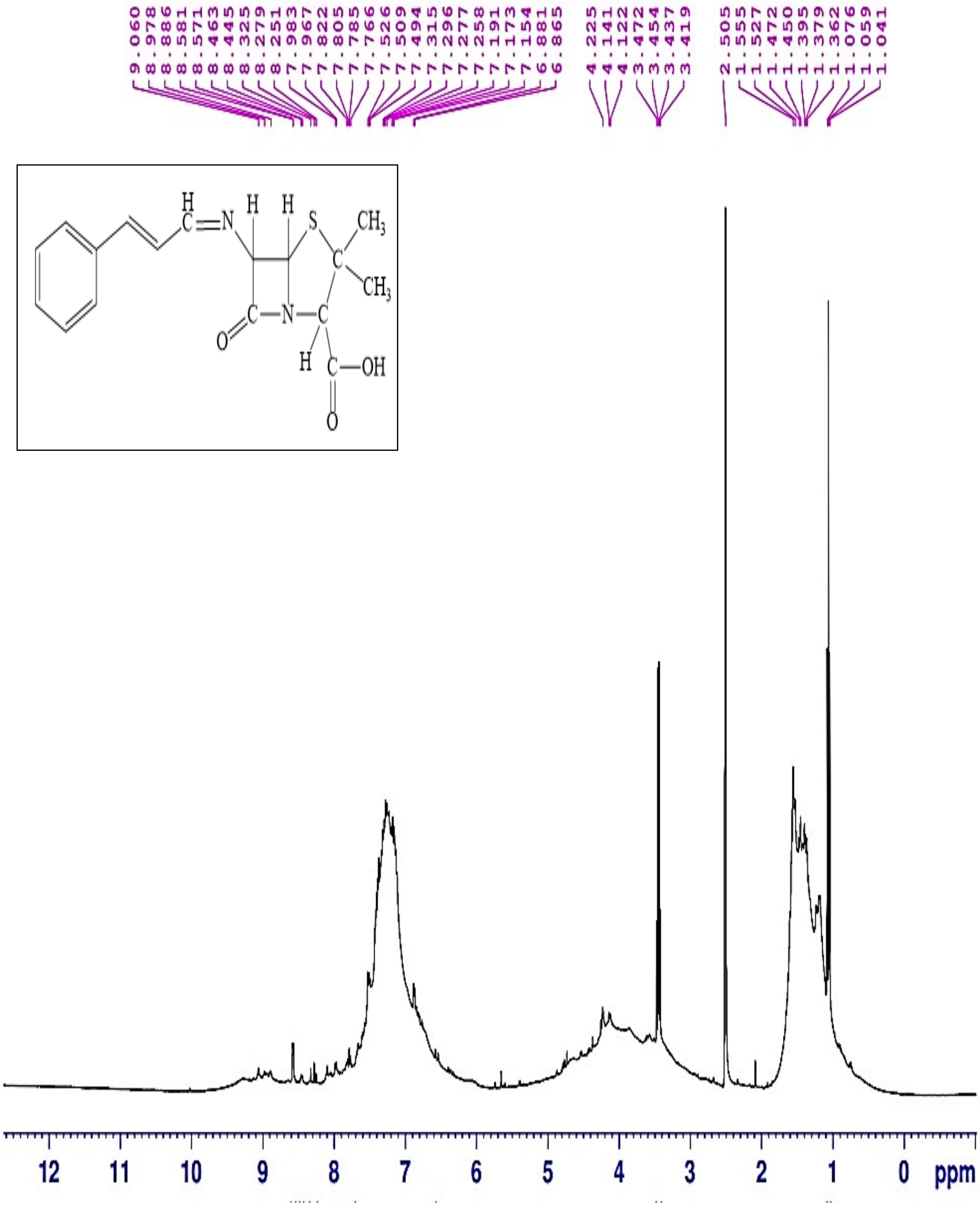


Figure (3-5): ^{1}HNMR Spectrum for Ligand (L1)

(**d**)deplet,(**t**) triplet,(**S**) singlet,(**m**) multi.

The ^{1}HNMR Spectrum for the ligand(**L₂**). Showing Peakes at δ7.3-7.9 ppm (m) ascribed to proton of aromatic ring, and δ8.4-8.5 ppm (d) accredit to the *β*-lactam ring, The signals at δ 8.6 ppm (s) were observed due to proton of COOH group(Mohammad Azam., *et al*.,2020), **Figure(3-6)** shows^{1}HNMR spectrum for ligand(**L2**).

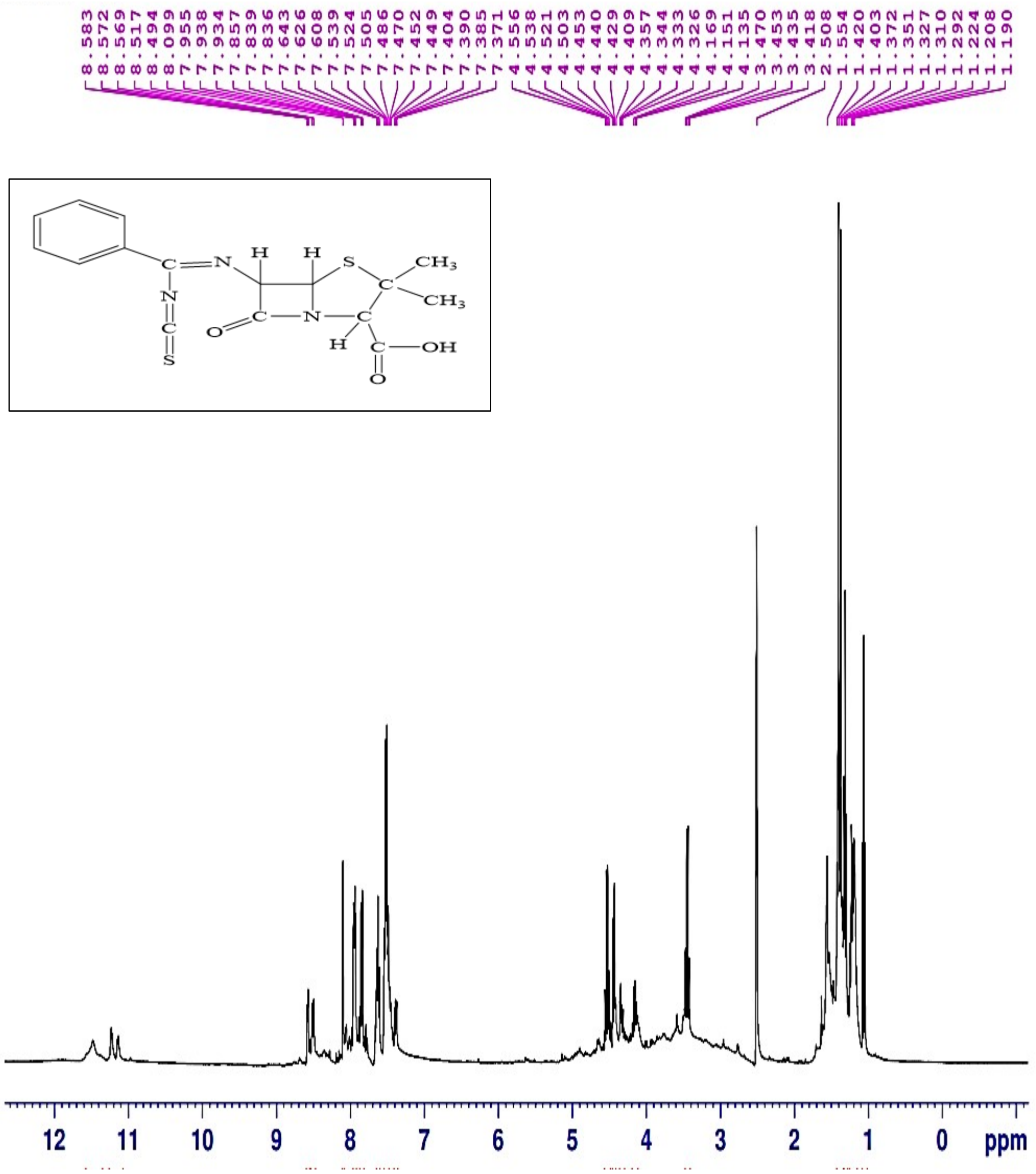


Figure (3-6): ^{1}HNMR Spectrum for Ligand(L2)

The ^{1}HNMR Spectrum of the ligand (**L**$_3$) shows peaks at δ7.043-7.17 ppm (d) attributed to proton of *β*-lactam ring protons, the peaks at δ 7.49-7.50 and δ 7.88-7.89 ppm (d) attributed that to protons for thiophene ring, The signals at δ 9.26 ppm (s) and δ9.827 ppm(s) were observed due to azomethine proton, and COOH, respectively (Ismail Warad., *et al*.,2020), **Figure(3-7)** shows ^{1}HNMR spectrum for Schiff base ligand (**L**$_3$).

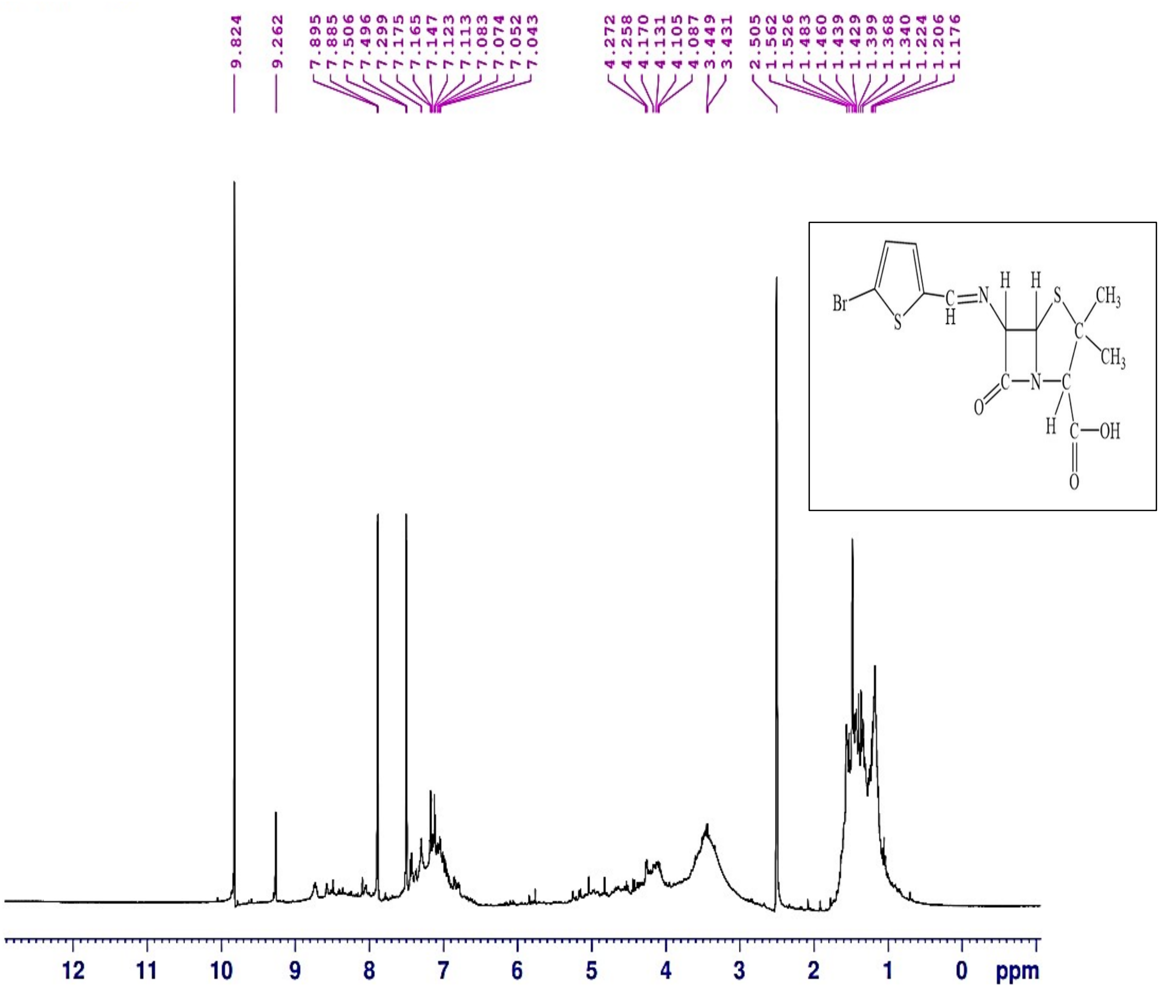


Figure (3-7):^{1}HNMR Spectrum for Ligand (L_3)

3.4.3.The ^{13}CNMR Spectrum of the Ligands (L_1,L_2,L_3)

The ^{13}CNMR spectrum of the ligand (**L_1**) showing The carbon signal in (**L_1**) at the δ124.39-127.45 ppm attribute the aromatic ring and δ128.32,128.82,129.30 ppm referred to carbon atom for *β*-lactam ring (Taghreed H. Al-Noor., *et al*.,2021). The signals at δ 136.36 ppm and δ 150.07 ppm were observed due to azomethine, and **C**OOH, respectively, (Mohammad Azam.,*et al*.,2020),(Donald L. pavia.,*et al*.,2001),**Figure(3-8)** shows ^{13}CNMR spectrum for Schiff base ligand (**L_1**)

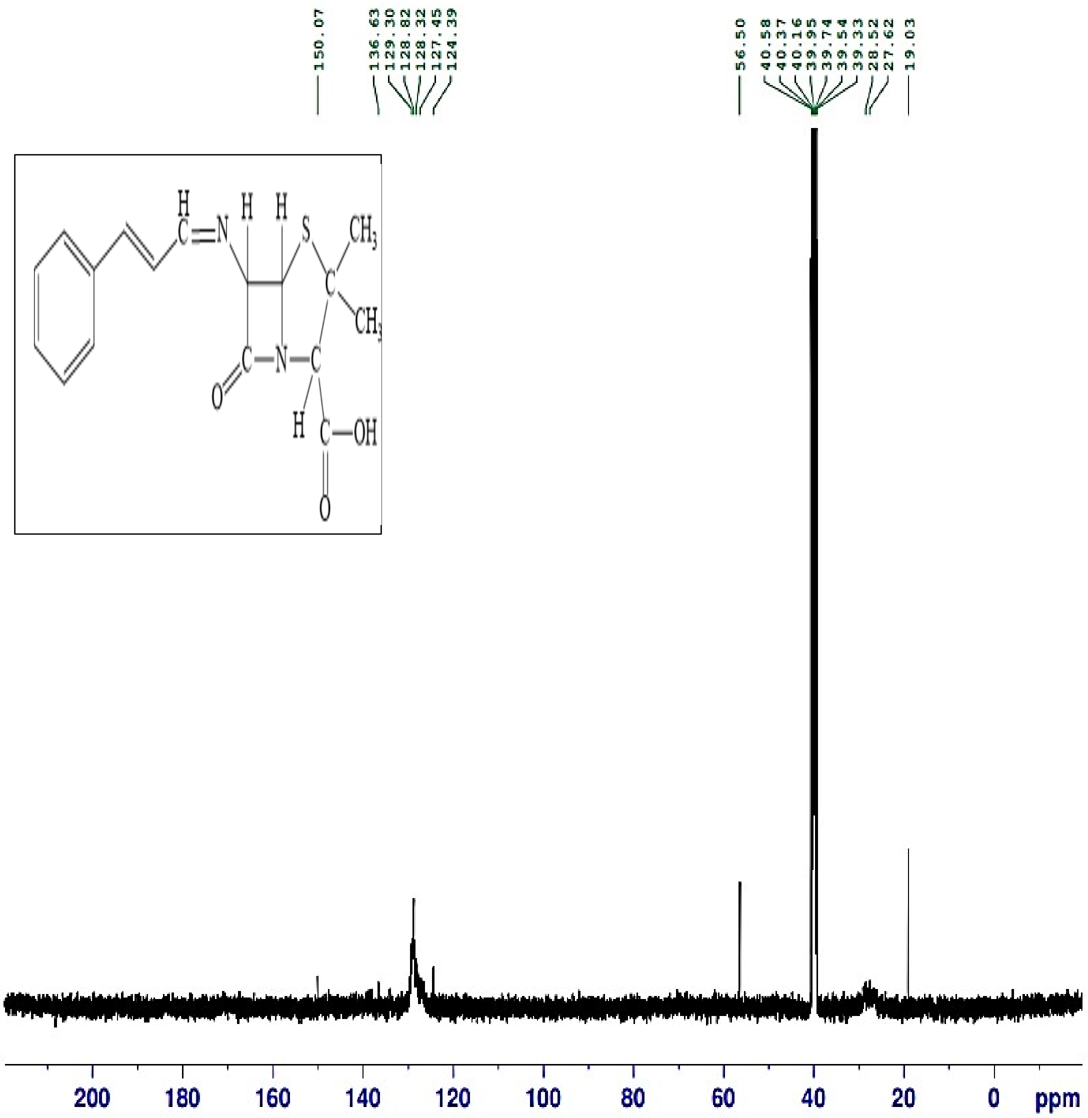


Figure (3-8):^{13} CNMR Spectrum for Ligand (L_1)

The ^{13}**CNMR** Spectrum for (**L_2**) Showing peakes at the δ124.39-129.73ppm referred to the aromatic ring , the δ132.59 ,133.69 ,136.64 ppm attributed to carbon atom for *β*-lactam ring, The signals at δ 150.05 ppm and δ 168.55-168.81 ppm ,δ170.25-171.34 ppm (d),190.10 ppm were observed due to azomethine ,**C**=S,**C**-S and **C**OOH, respectively. (Magdy M. Hemdan&Amira,A.Al-sayed., *et al.,*2016),(Felix Odame., *et al.,*2015),(Mohammad Azam *et al.,*2020),**Figure(3-9)** shows ^{13}CNMR spectrum for ligand (**L_2**).

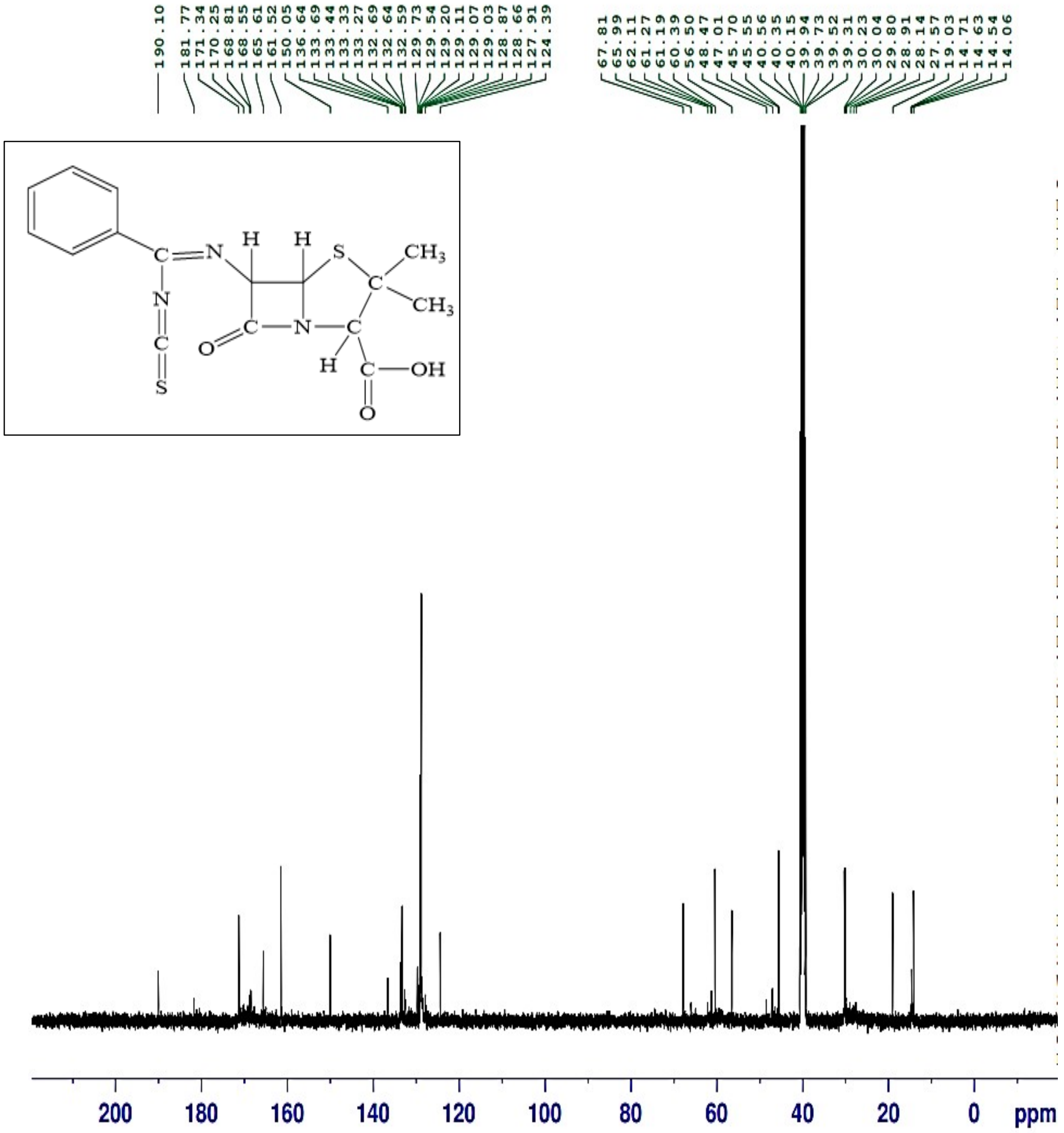


Figure (3-9): ^{13}CNMR Spectrum for Ligand (L$_2$)

The^{13}**CNMR** spectrum of the ligand (**L$_3$**) show The signals 128.99,133.09,139.18 ppm refered to carbons atom for *β*-lactam ring , the signal 145.31ppm attributed for azomethine and the signal 184.02 ppm for (**C**OOH),(Mohammad Azam.,*et al*.,2020),(N. Ghufran Kareem, Mohammed Hamid Said,(2021**)**, (Ismail Warad.,*et al*.,2020),**Figure(3-10)** shows the ^{13}CNMR Spectrum of (**L$_3$**).

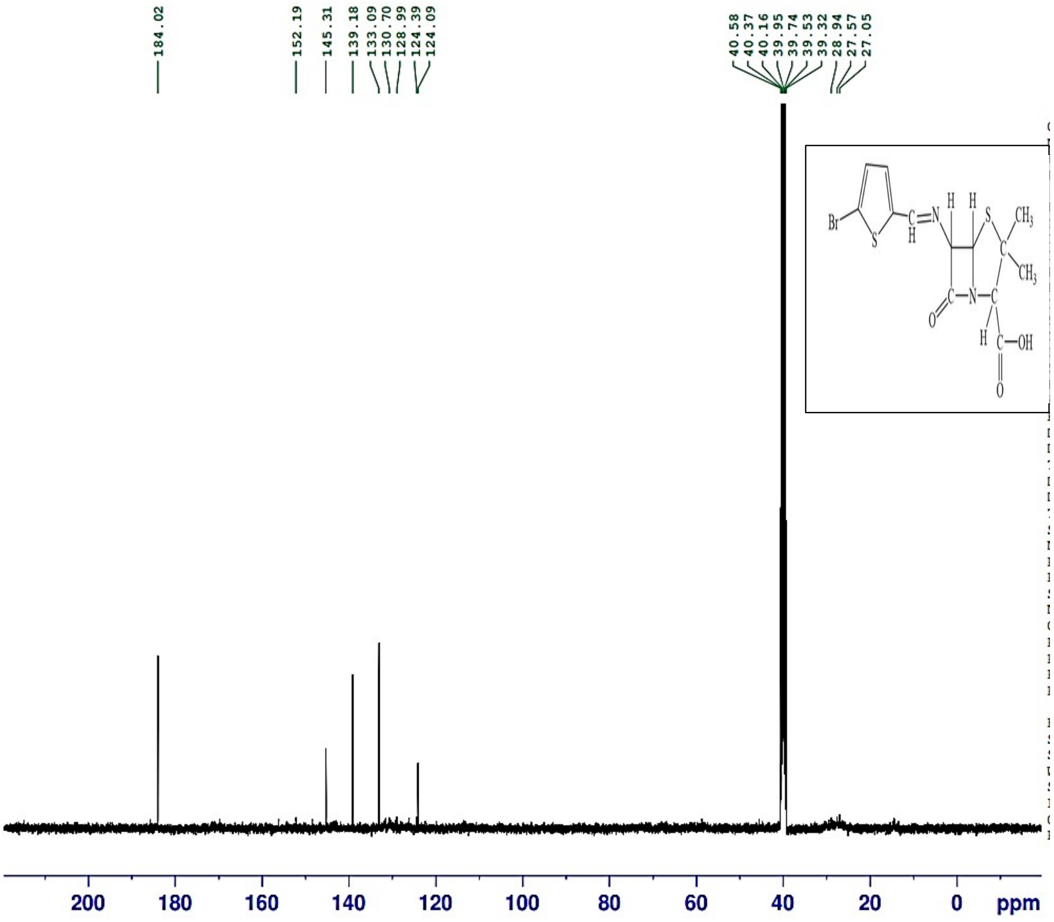


Figure (3-10):^{13}CNMR Spectrum for Ligand (L_3)

3.4.4.Micro Elemental Analysis for Ligands

The micro elemental analysis of the prepared ligands(**L_1,L_2,L_3**) was measured. There was a correspondence between the practical ratio value that was the result of experimental work with the theoretically calculated ratios from the relative equations of the elements obtained from this measurement,**Table(3-3)** shows the practical and theoretically data of Ligands (**L_1,L_2,L_3**), respectively.

Table(3-3):Value for Measurements of C.H.N.S Technique of Ligands (L_1,L_2,L_3)

Compounds	%C		%H		%N		%S	
	Cal.	Exp.	Cal.	Exp.	Cal.	Exp.	Cal.	Exp.
L_1	61.8	57.82	5.45	6.49	8.48	8.97	9.7	8.089
L_2	53.18	54.62	4.15	7.165	11.63	15.22	17.7	20.306
L_3	40.12	39.066	3.34	3.72	7.19	7.076	16.478	16.85

3.4.5.UV-Visible Spectrum for Ligands

The ligand spectrum is associated mainly with bonds in the metal complexes spectrum. often the organic molecules behave as ligands, especially when these molecules contain (**π**) electron systems, these molecules have distinct absorption bands that usually appear in the ultraviolet region, and they generally take the form of strong bands because it has permissible transitions of the type ($\pi \rightarrow \pi^*$) and non-allow able transitions of the type ($n \rightarrow \pi^*$).

3.4.5.1.UV-Visible Spectrums for Ligands (L_1,L_2,L_3)

The electronic spectrum of the ligand and their complexes have been measured by using absolute ethanol in the range between 200-800 nm at room temperature.

The UV-Visible spectra of ligand (**L_1**) include absorption peak at wave lengths 308 nm which is assigned to π-π^* transition for nonbonding pair of electron of nitrogen azomethine group, **Figure(3-11)** shows UV-Visible spectrum for (**L_1**) ligand.

The UV-Visible spectra of ligand(**L_2**) include absorption peaks at wave lengths369nm,271nm and 238 nm, which are assigned to n-π* transition for nonbonding pair of electron of nitrogen azomethene group and π-π* transition for nonbonding pair of electron in the isothiocyanat group and π-π * transition for unsaturated bonding, respectively (Issa, Y. M.,*et al.*,2021), **Figure (3-12)** shows UV-Visible spectrum for ligand(**L_2**).

The UV-Visible spectra of ligand (**L_3**) include absorption peaks at wave lengths 297 nm and 220 nm which are assigned to n-π* transition for nonbonding pair of electron of nitrogen azomethine group and π- π * transition for unsaturated bonding, respectively(Donald L. pavia., *et al.*,2001),**Figure(3-13)** shows UV-Visible spectrum for ligand(**L_3**), Supporting Information in **Tables(3-7),(3-8),(3-9).**

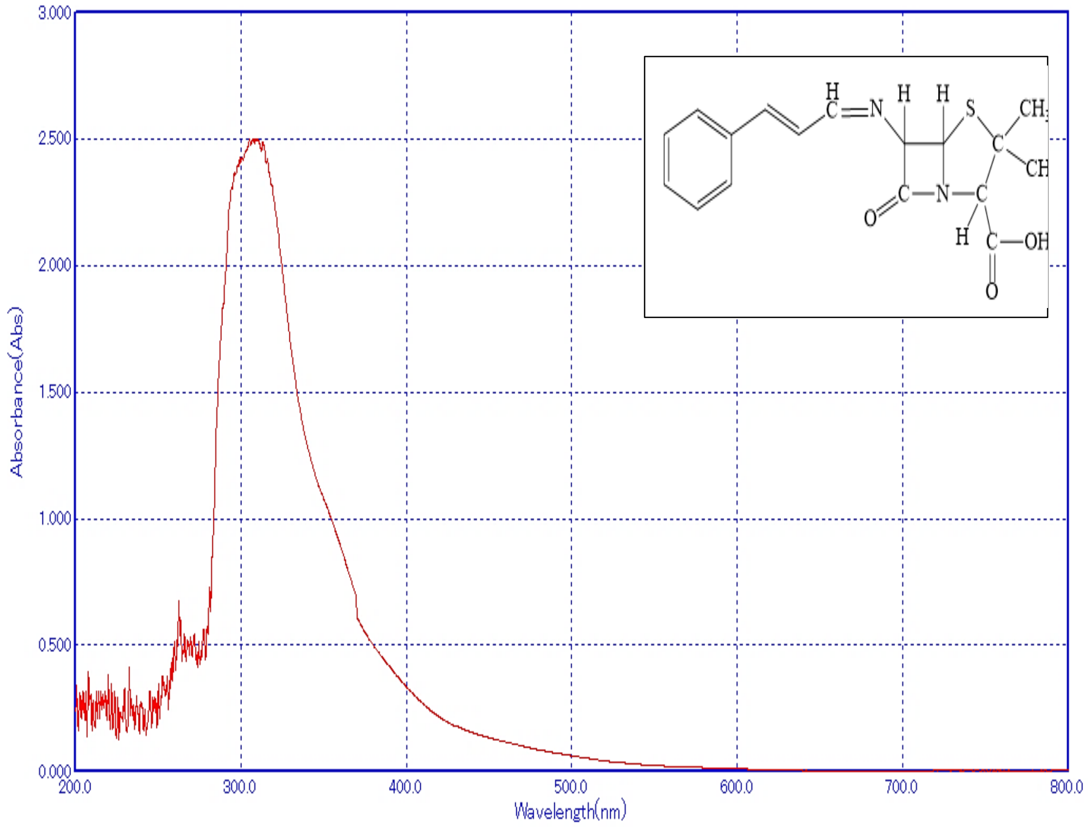
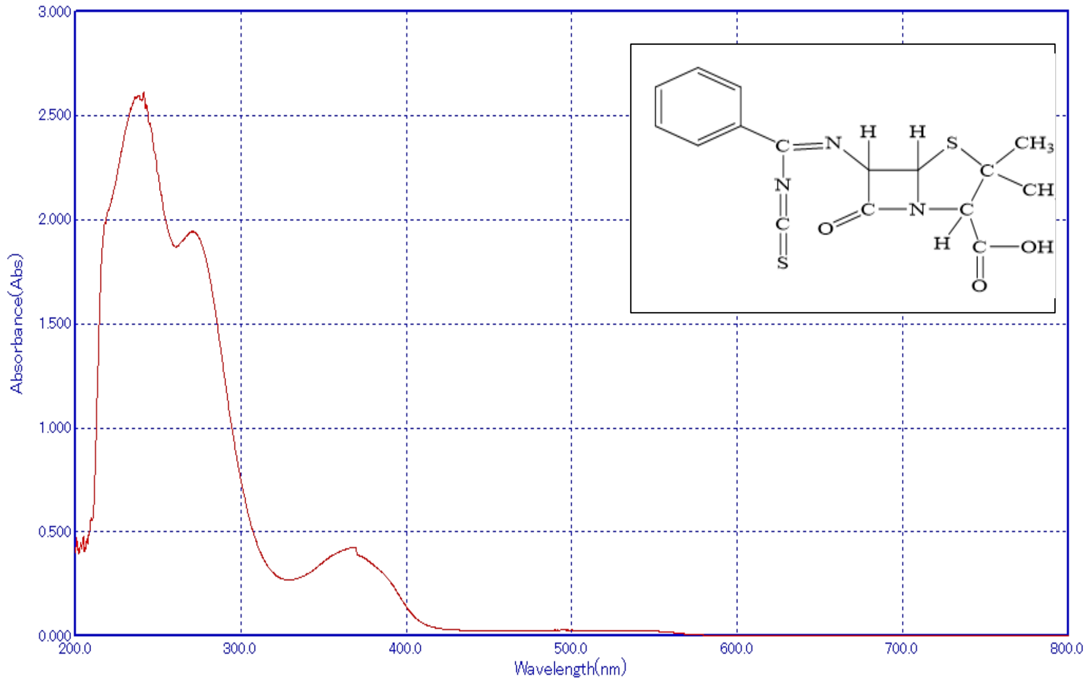


Figure (3-11): UV-Visible Spectrum for Ligand (L₁)



Figure(3-12):UV-Visible Spectrum for Ligand (L_2)

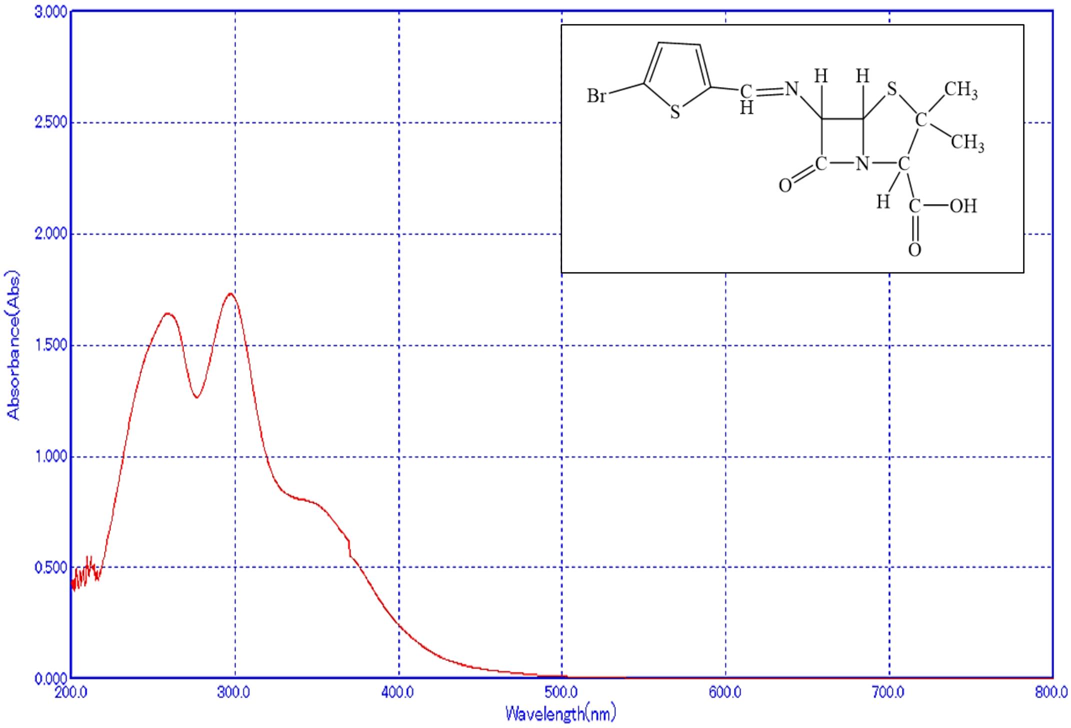


Figure (3-13):UV-Visible Spectrum for Ligand (L_3)

3.4.6.Mass Spectroscopy

Organic molecules are vaporized and bombarded with beams of extremely high-energy electrons in a mass spectrometer. The energy imparted by the collisions is significant, and the molecule emits electrons to produce positively charged ions. These ions have so much energy that they commonly fragment through various bond cleavages to produce new positively charged ions. Through passing the positive ions through a magnetic field, which deflects the ion, they are accelerated toward a negatively charged plate. Ions of lighter mass are deflected more than heavier ions. Each type of ion has a unique mass to charge (*m/e*) ratio. Most ions produced during molecule fragmentation have a charge of(+1), so(*m/e*)usually represents the ion's mass. (Bahl, A.,2015).

Mass Spectrum for Ligands (L_2,L_3).3.4.6.1

The mass spectrum of the ligands (**L_2**), and (**L_3**) shows the appearance of a peak at (360 M/Z^+), and (390 M/Z^+) respectively which is attributed to the parent molecular ion, which corresponds to the proposed molecular formula of the ligands(**L_2**),(**L_3**). These spectrums recorded other peaks, most of which agree with what was mentioned in the prevue's studies (Rasha Hasan Jasim., *et al*.,2017). the diagrams below **Scheme (3-1)**and **Scheme(3-2)** show the proposed fragmentations paths for two ligands and **Figure (3-14)**, and **(3-15)** shows the mass spectrums of the ligands (**L_2**), (**L_3**).

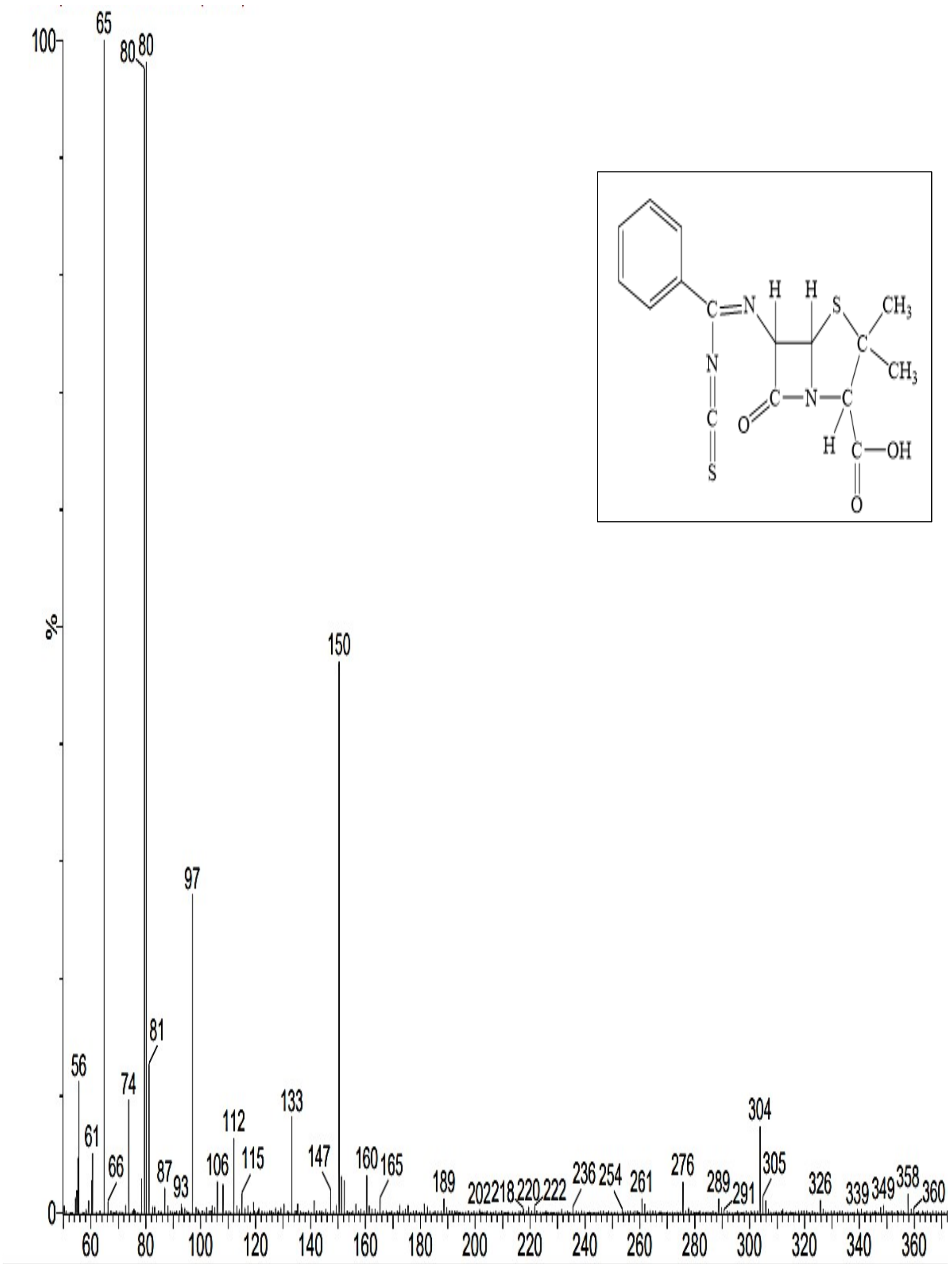
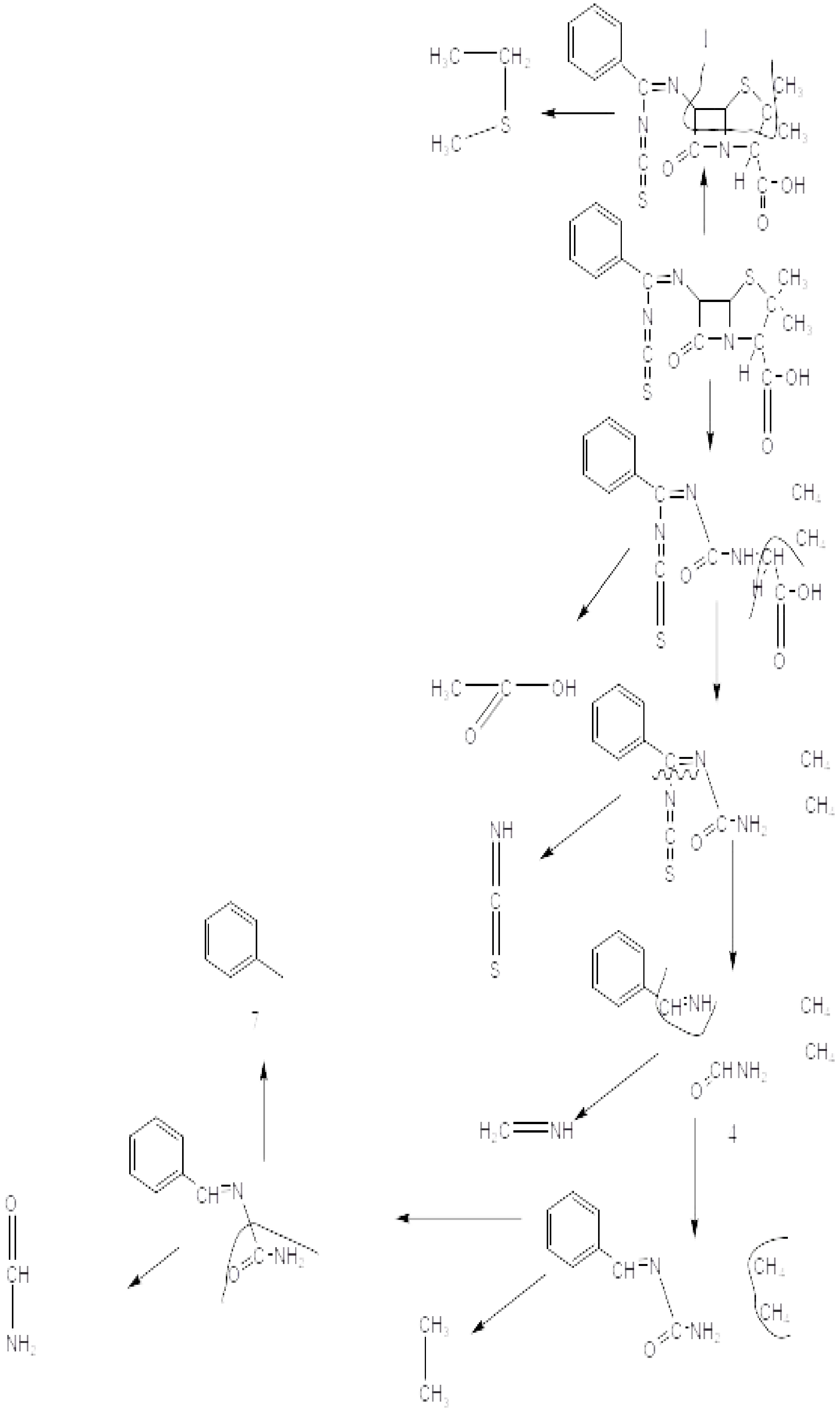


Figure (3-14) :Mass Spectrum of Ligand (L_2)


H3C—CH2
S
H3C
H3C—C—OH
O
NH
C
S
H2C=NH
CH3
CH3
O
CH
NH2
C=N
CH=N
O=C-NH2
CH NH2
CH4
7
4

Scheme (3-1): Fragmentation of the ligand(L₂)

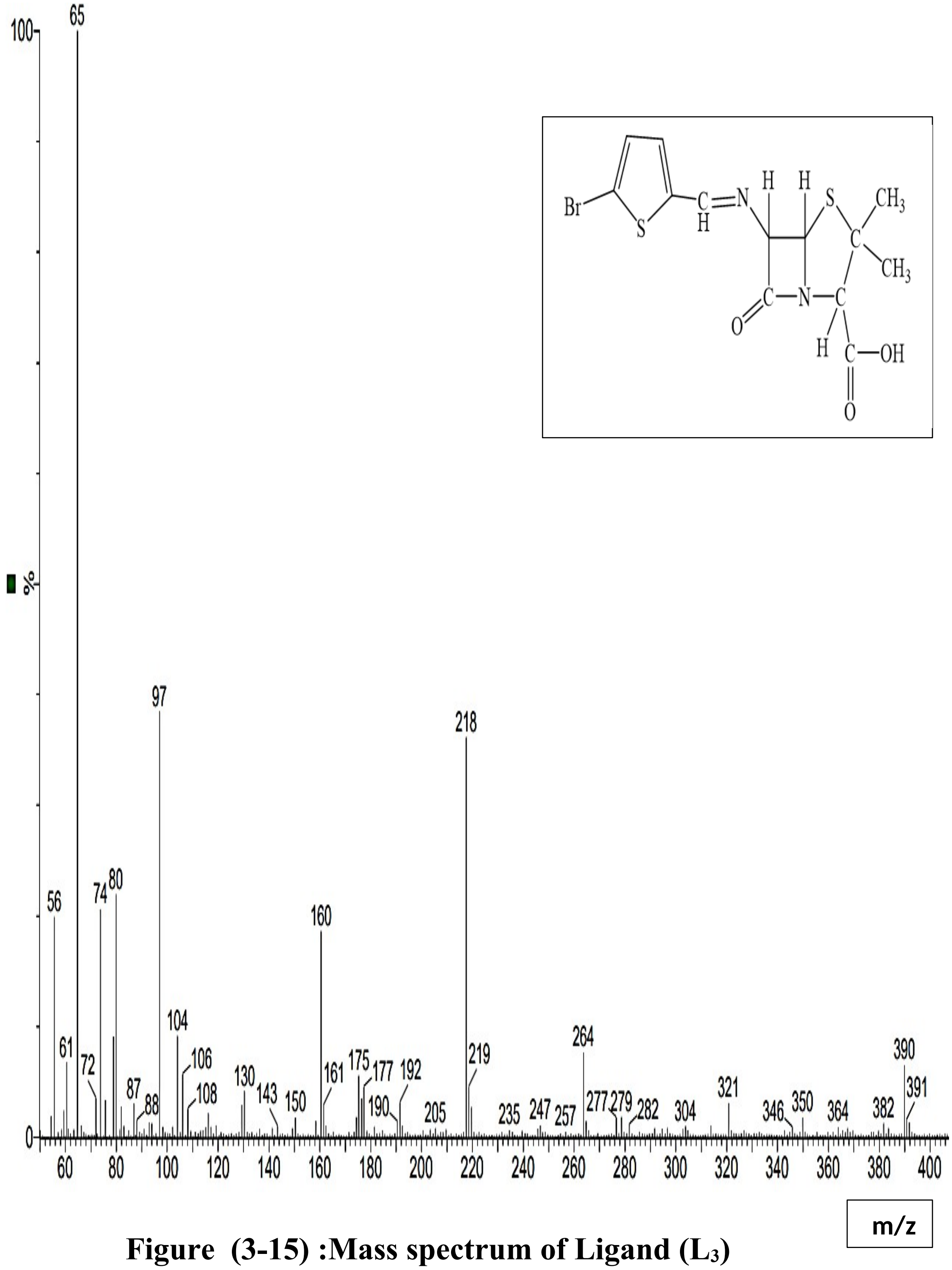
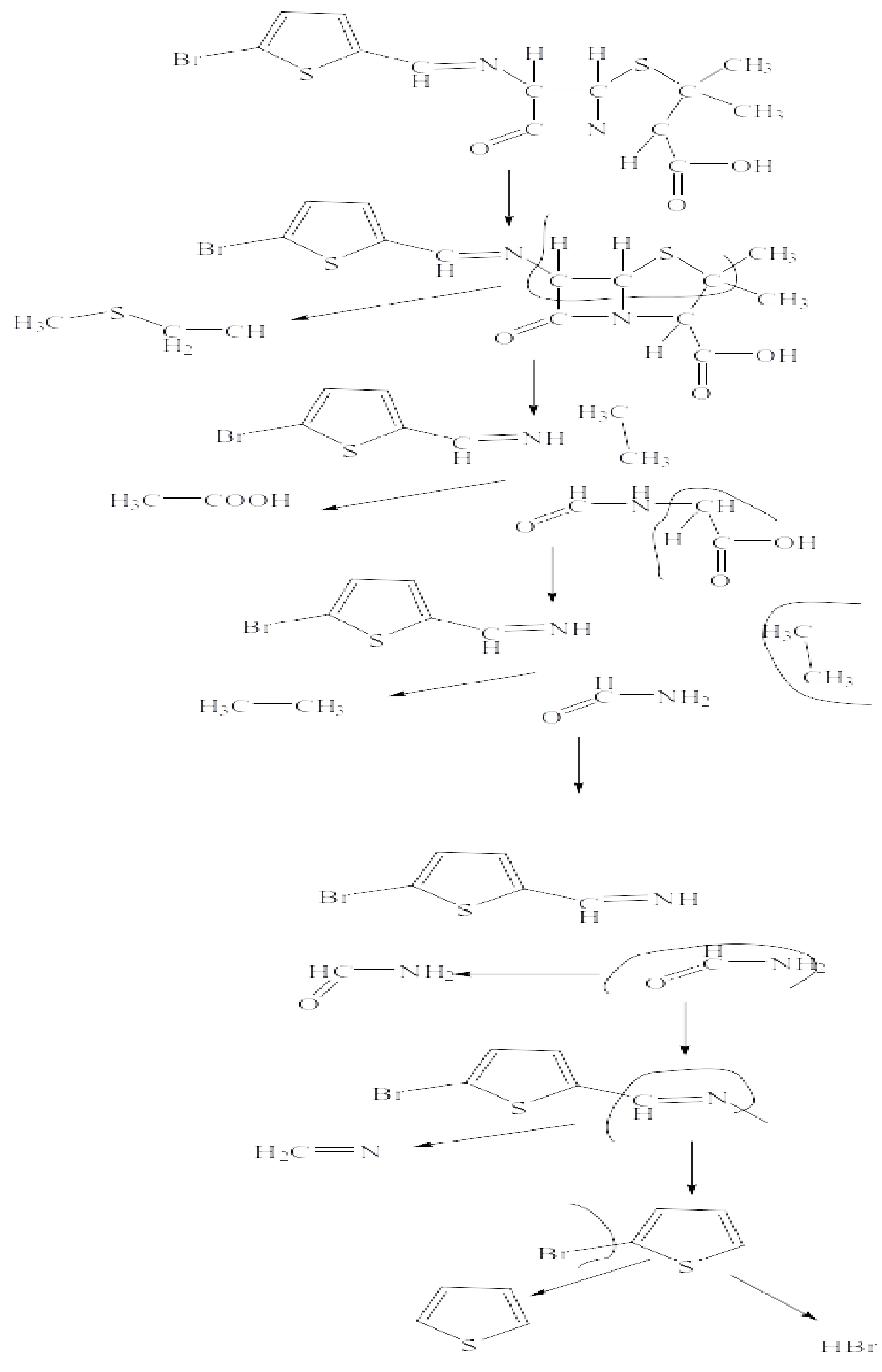


Figure (3-15) :Mass spectrum of Ligand (L₃)



Scheme (3-2): Fragmentation of the ligand(L_3)

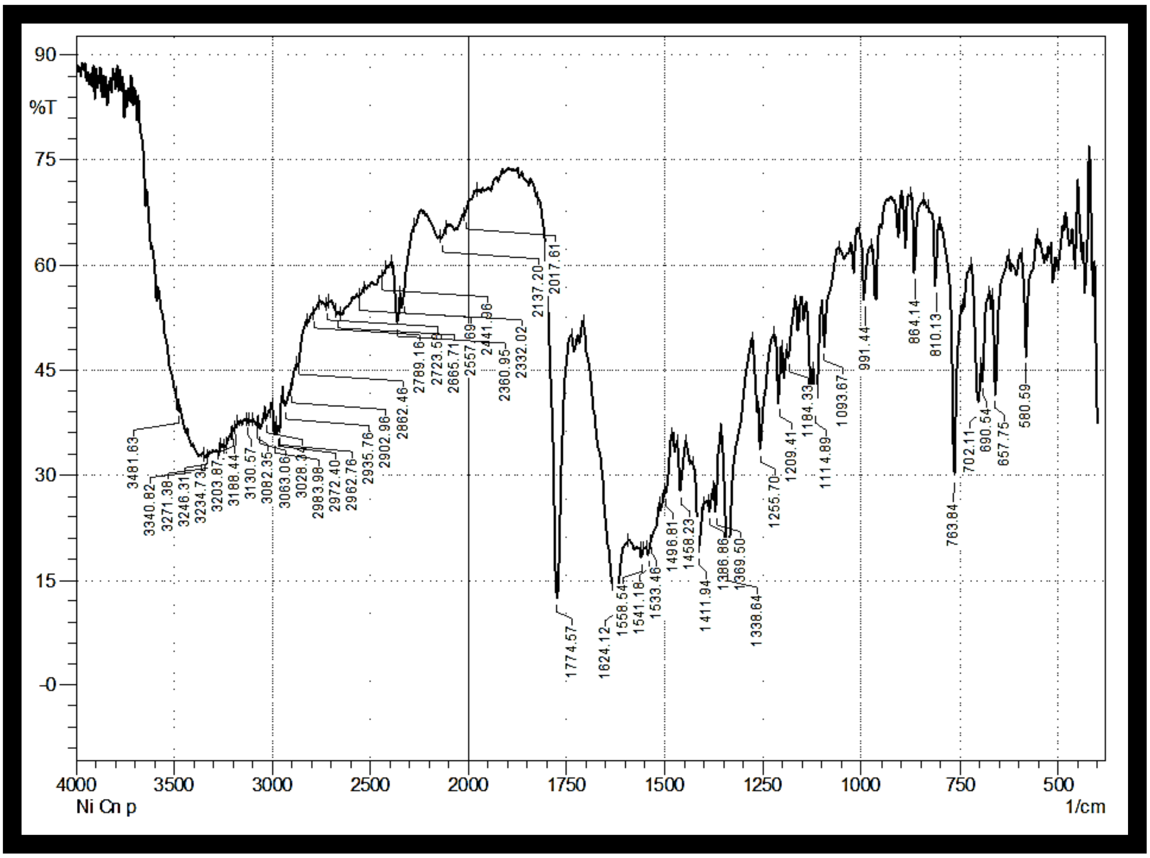
3.5.Characteriziation of Complexes

3.5.1.1.The FTIR Spectrums of Ni(II),Cu(II), and Zn(II) Complexes for Ligand (L_1)

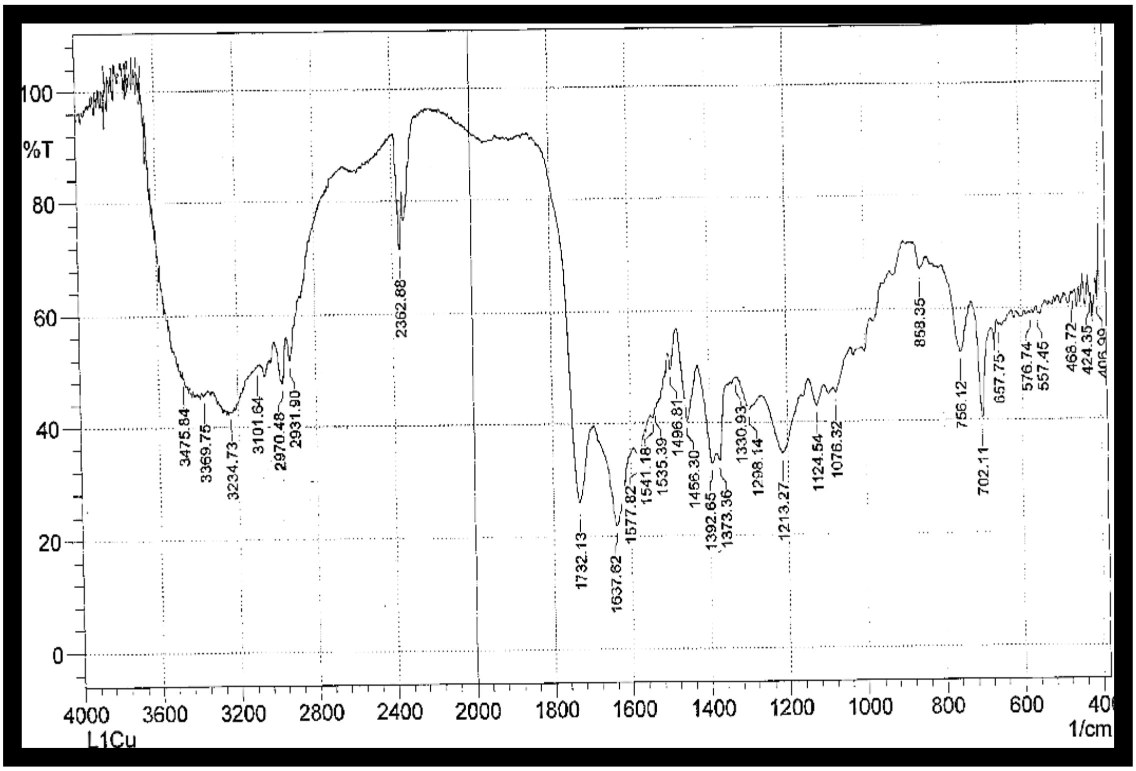
The FTIR spectrum for complexes of Ni(II), Cu(II) and Zn(II) with ligand (L1) shows shifted the band of the azomethine group to a lower frequency in all the complexes which appeared in the range of 1579-1573.97 cm^{-1}, those indicating its participation in complexation. The stretching vibrations at 16624.12 -1637.62 cm^{-1} for the υ (-C=O) group in the *β*-lactam ring were shifted to a higher frequency in the metal complexes thus showing the coordination is done by the oxygen atom for the υ(C=O) group in the *β*-lactam ring. Furthermore, the weak bands observed at 567.04-551.66 cm^{-1} and 470.18-460 cm^{-1} were assigned to υ(M–N) and υ(M–O),(Mohammad Azam,*et al.*,2017),(K.Nakamoto, J.W.S.,2009), the **Figures (3-16)**,**(3-17)**, and **(3-18)** show the FTIR spectrum for complexes of Ni(II), Cu(II) and Zn(II) with ligand (L_1) and **Table (3-4)** showing frequencies of the band for the prepared ligand (L_1) and their complexes.

Table(3-4):Value of the Band in FTIR Spectrum of the Prepared Ligand (L_1) and their Complexes

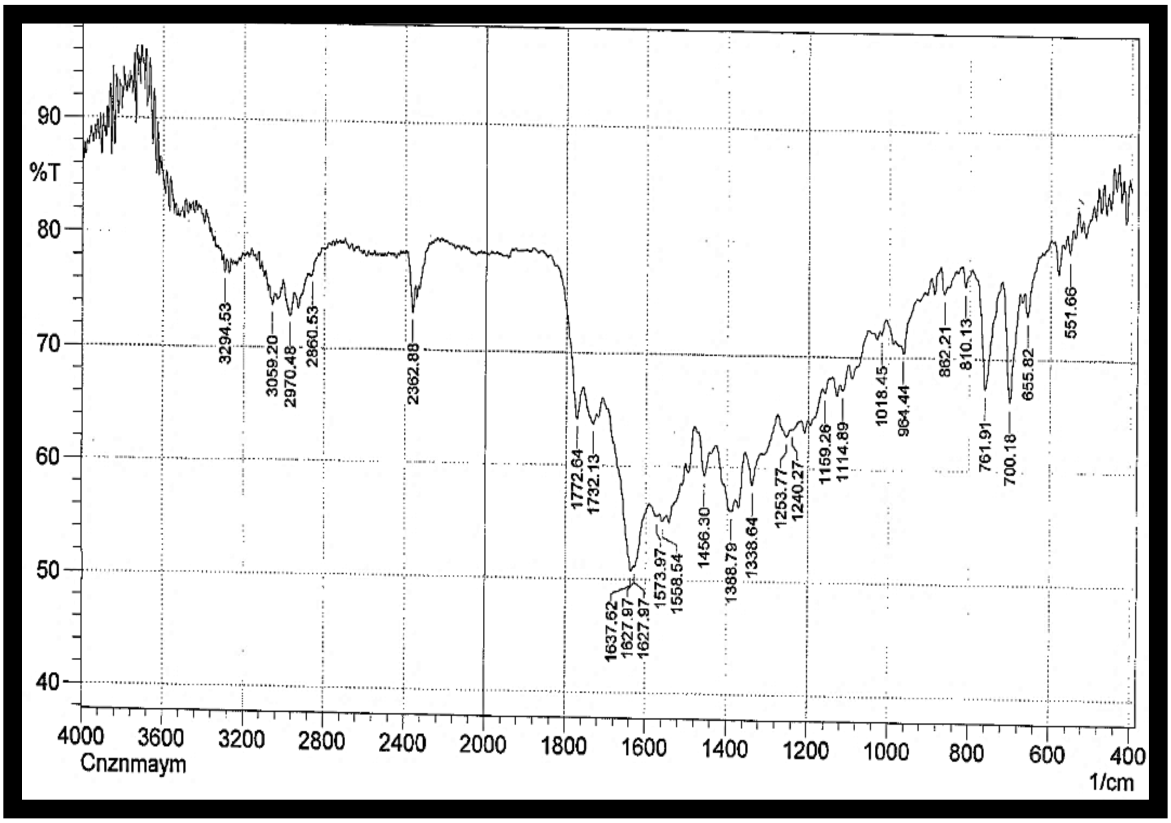
Compound	υ (-OH)	υ (-SH)	υ(C=O)	*β*-lactam υ(C=O)	υ (HC=N)	υ (C-N)	υ (C-O)	υ (C=C)	υ (M-N)	Y M-O
L_1	3330	2640	1772.64	1635.69	1602	1338.9	1114.89	1558.54	-	-
L_1-Ni	3340.82	2665.71	1774.57	1624.12	1579	1338.64	1114.89	1558.54	567.04	470.65
L_1-Cu	3234.73	2650	1732.13	1637.62	1577.82	1330.93	1124.54	1541.18	557.45	468.72
L_1-Zn	3294.53	2650	1772.64	1627.97	1573.97	1338.64	1114.89	1558.54	551.66	460



Figure(3-16):FTIR Spectrum for Ni^{+2} Complex with Ligand (L1)



Figure(3-17):FTIR Spectrum for Cu^{+2} Complex with Ligand (L$_1$)



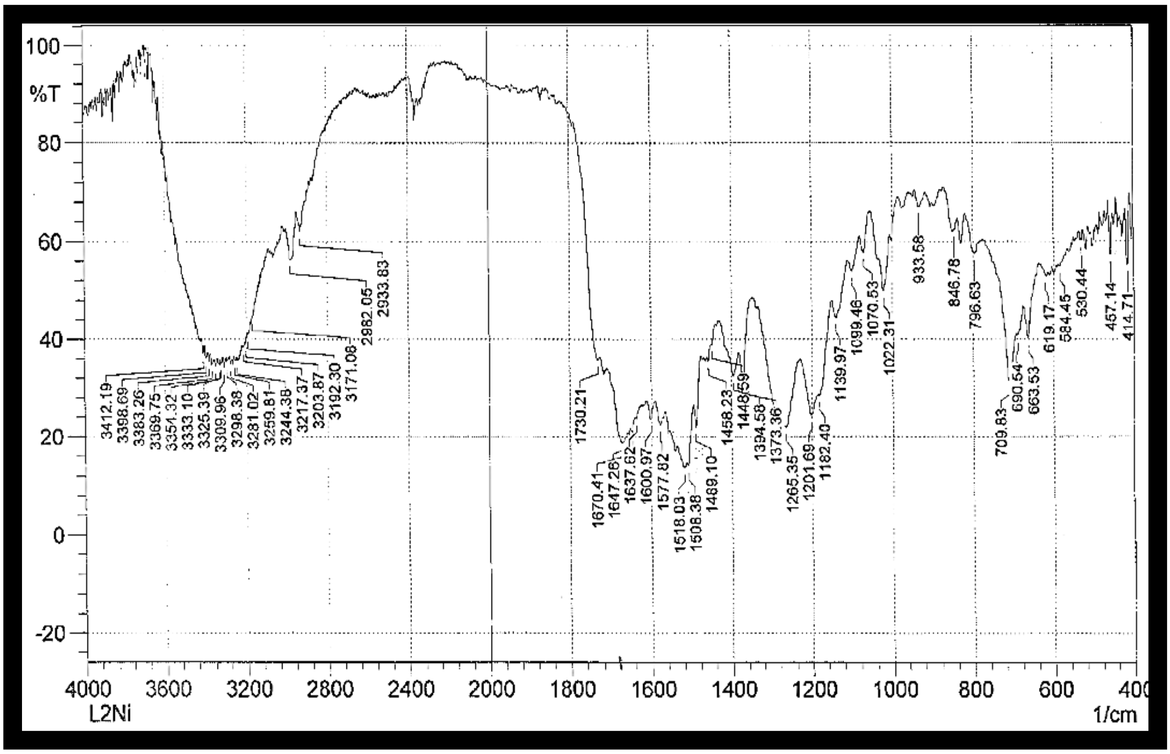
Figure(3-18):FTIR Spectrum for Zn^{+2} Complex with Ligand (L1)

3.5.1.2.The FTIR Spectrum of Ni(II),Cu(II),Zn(II) Complexes for ligand (L$_2$)

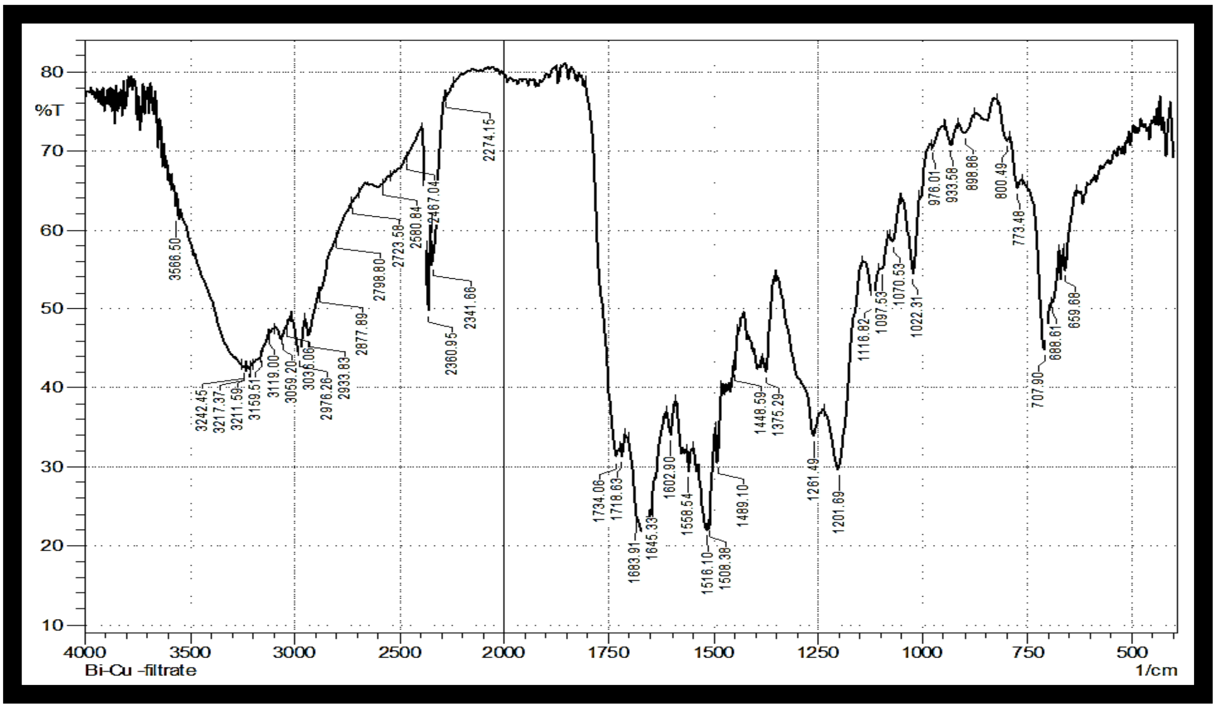
The **Figures (3-18)**,**(3-19)** and **(3-20)** show the FTIR Spectrum for Complexes of Ni(II), Cu(II) and Zn(II) with ligand (**L$_2$**). From these figures noticed the azomethine group was shifted to a higher frequency in all complexes and appeared in the range of 1570–1581.68 cm^{-1}, indicating its involvement in the complexation. The stretching vibrations at 1647.26-1683.91 cm^{-1} for the υ(C=O) group in the *β*-lactam ring were shifted to a higher frequency in the spectrum of metal complexes compared with the spectrum of free ligand this indicates their subscriptions to coordination through the oxygen atom of the υ(C=O) group. Also observed, the new weak bands at 599-520 cm^{-1} and 518-420 cm^{-1} were attributed to υ (M–N) and υ(M–O) which confirms the occurrence of coordination through the nitrogen atom of the azomethine group and the oxygen atom of the carbonyl group, **Table (3-5)** shows the frequencies of the band for the ligand (L2) and their complexes.

Table(3-5) :Value of Frequencies for the Band in FTIR Spectrum of Prepared Ligand (L_2) and thier Complexes

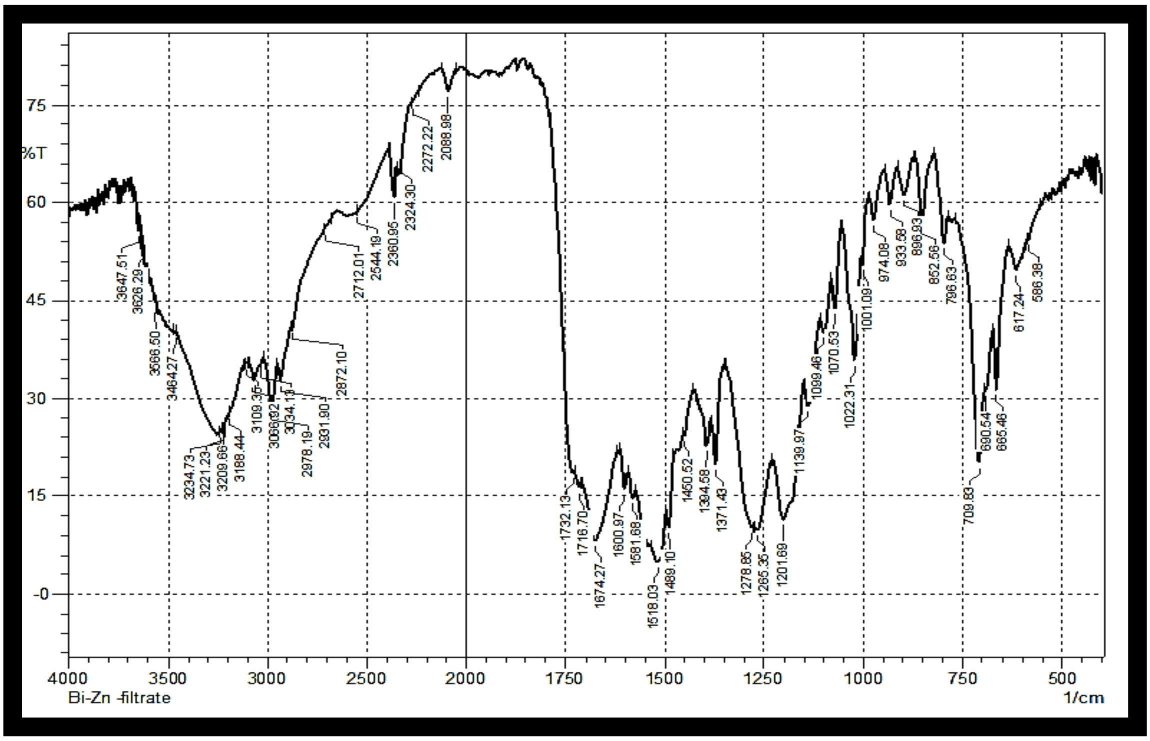
Compound	υ (OH)	υ (SH)	υ (C=O)	*β*-lactam υ(C=O)	υ (C=N)	υ (C-N)	υ (C-O)	υ (C=S)	υ (M-N)	υ (M-O)
L_2	3234.73	2505	1716.70	1670.41	1579.75	1371	1134	1276-1205	-	-
L_2-Ni	3298.38	2650	1718	1647.26	1577.82	1373	1139	1265-1201	520	414
L_2-Cu	3242.46	2560	1718.63	1683.91	1570	1373.	1116	1261-1202	599	518
L_2-Zn	3234.73	2550	1716.70	1647.27	1581.68	1371.43	1139.97	1278-1201	530	420



Figure(3-19):FTIR Spectrum for Ni^{+2}Complex with Ligand (L_2)



Figure(3-20):FTIR Spectrum for Cu^{+2}Complex for Ligand (L_2)



Figure(3-21):FTIR Spectrum for Zn^{+2}Complex with Ligand(L_2)

3.5.1.3.The FTIR Spectrum of Ni(II),Cu(II),Zn(II) Complexes for Ligand (L_3)

In the FTIR Spectrum of (**L_3**) ligand, the band of the azomethine group is shifted to a lower frequency in all of the complexes that emerged in the range of 1635-1560 cm^{-1}, those showing its participation in complexation. The frequency of the υ(-C=O) group in the *β*-lactam ring, shifting to 1668.48-1653.05 cm^{-1} (a lower frequency) in the metal complexes, the FTIR Spectra for complexes of Ni(II), Cu(II), and Zn(II) with ligand (**L_3**) are shown in **Figures (3-21), (3-22)** and **(3-23)**, and **Table (3-6)**, respectively.

Table(3-6):Value of Frequencies for the Band in the FTIR Spectrum of the Prepared Ligand (L_3) and their Complexes

Compound	υ (OH)	υ (-SH)	υ (C=O)	υ (C=O) β-lactam	υ (HC=N)	υ (C-N)	υ (C-O)	υ (C-S)	υ (M-N)	υ (M-O)
L_3	3210	2650	1716.70	1670	1618.33	1369.9	1222.91	1130.32	-	-
L_3-Ni	3269.45	2600.13	1716	1668.48	1635.69	1375.23	1220.91	1130.32	590	520
L_3-Cu	3147.34	2650	1716	1668.48	1590	1373.36	1220.98	1116.82	590	550
L_3-Zn	3228.95	2600	1716	1653.05	1560	1390.72	1222.91	1130.32	550	518

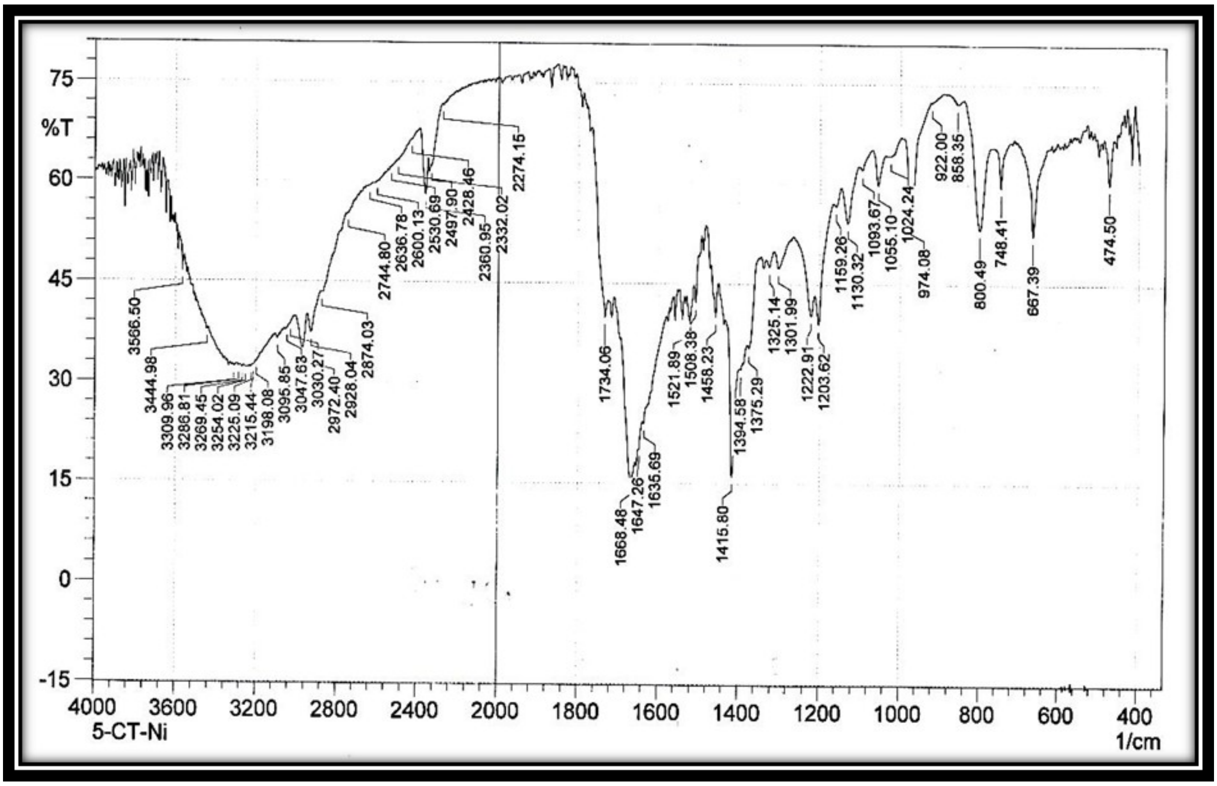


Figure (3-22):FTIR Spectrum for Ni+2 Complex with Ligand (L_3)

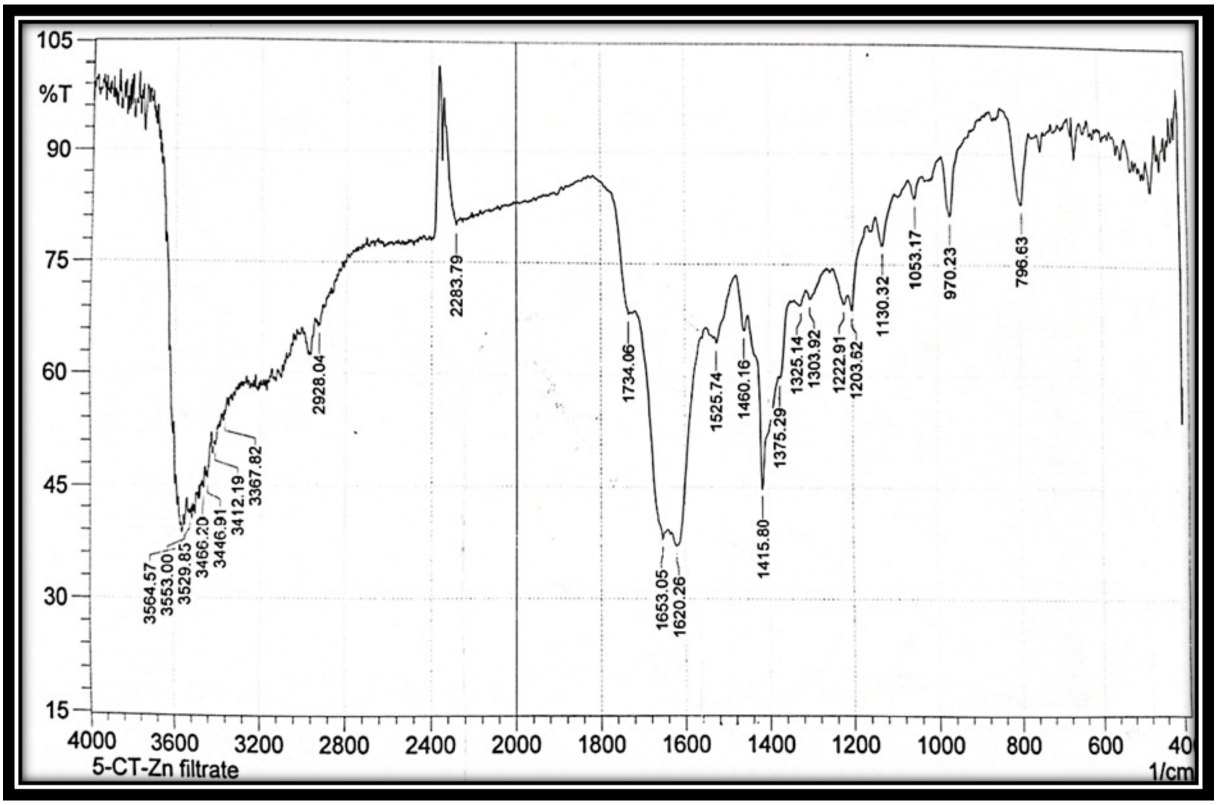


Figure (3-23): FTIR Spectrum for Cu^{+2} Complex with Ligand (L_3)

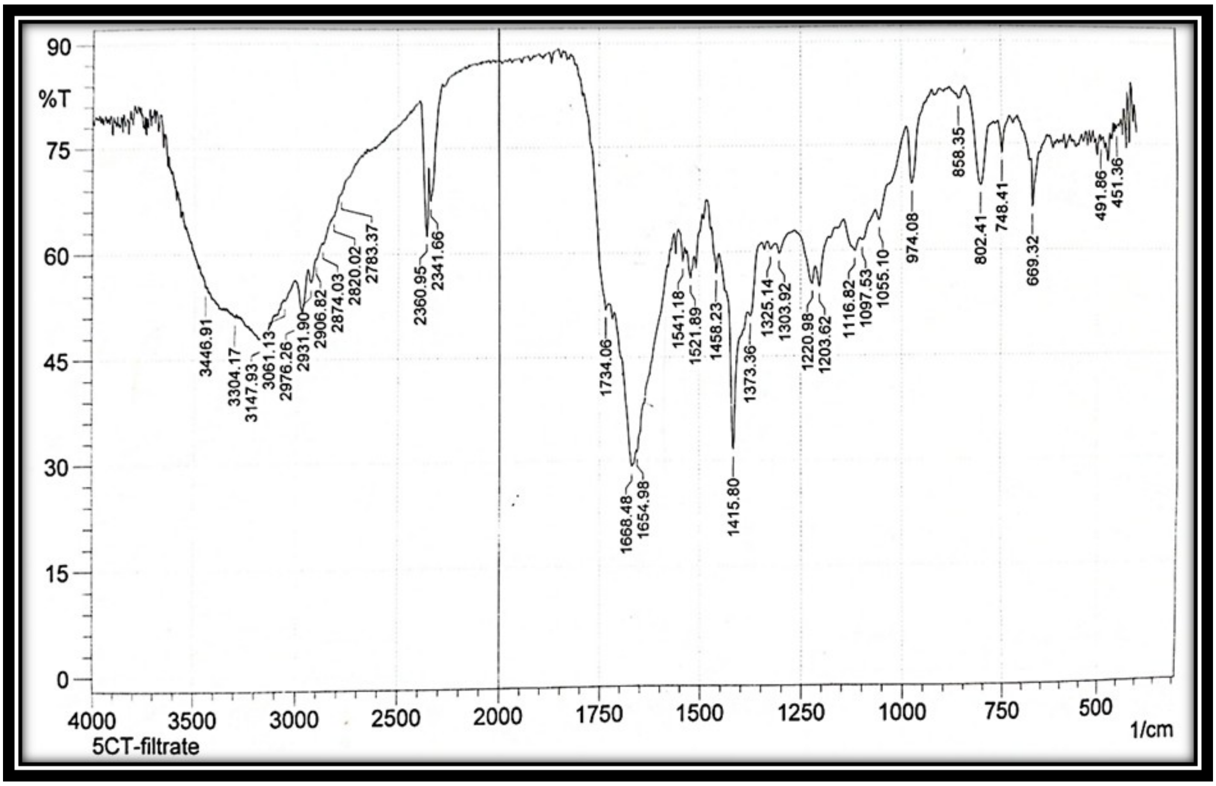


Figure (3-24): FTIR Spectrum for Zn^{+2} Complex with Ligand (L_3)

3.5.2.UV-Visible spectrum for complexes

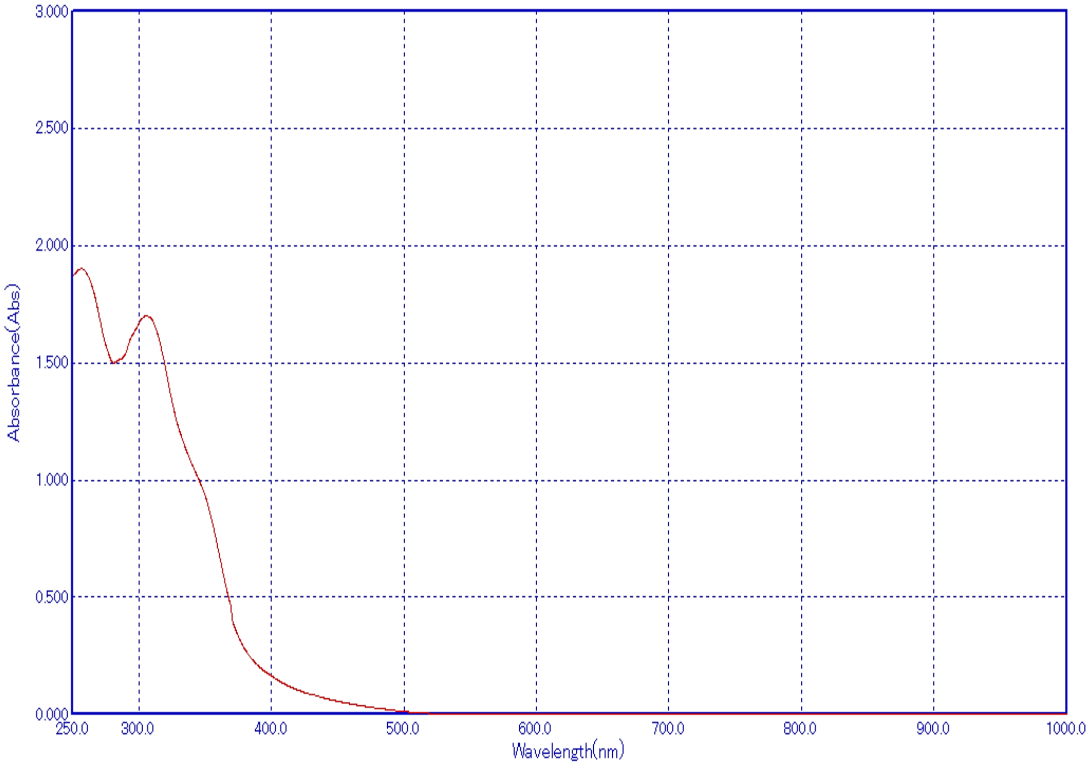
The UV- Vis spectra for most complexes of transition elements are colored because they contain functional groups that absorb visible or ultraviolet light, called chromophores so it appears as absorptions at certain wavelengths in the visible region of the spectrum usually other absorptions in the near-infrared and far ultraviolet adjacent to this is the reason for the interest of the UV- Vis spectra from coordination chemistry.

3.5.2.1.Electronic Spectra of Ni(II),Cu(II),and Zn(II) Complexes for Ligand (L_1)

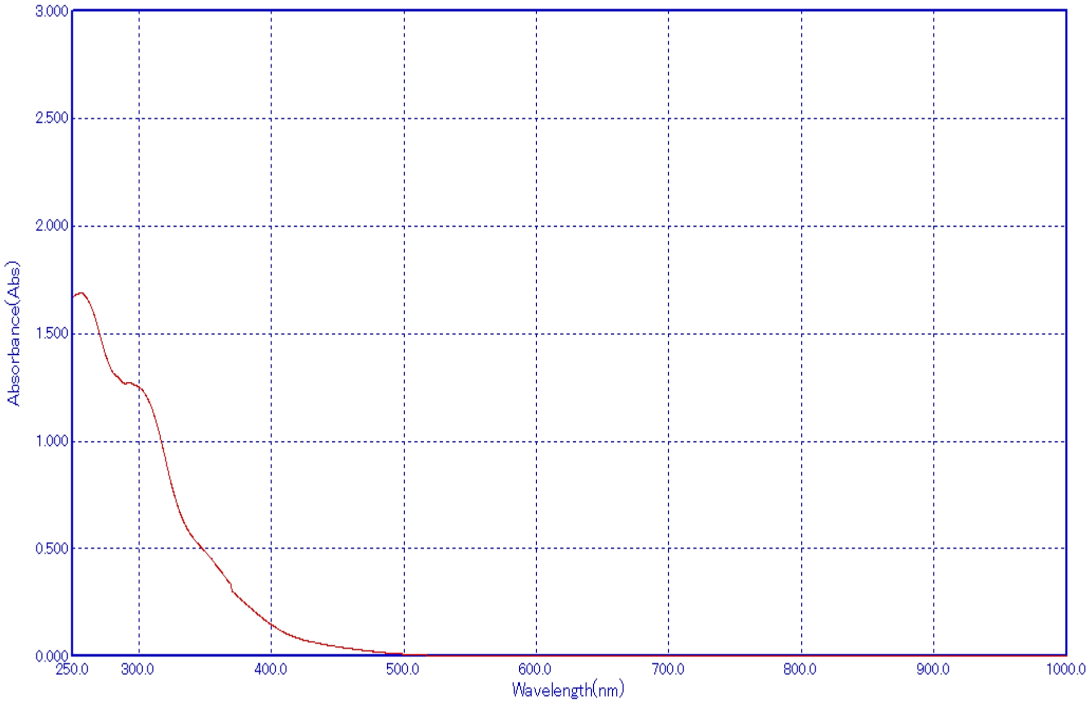
To investigate the occurrence of coordination between the ligand and the metal ion, the ligand's spectrum was compared to a complexes spectrum, and it was found in Ni(II) complex, that the azomethine group shifted to a lower wavelength at 306.4nm (Blue shift), with appearances a new band at 270 nm due to the ligand field transitions (L.F) and charge transfer (C.T), respectively.

In **Cu(II)** complex, that the azomethine group shifted to a lower wavelength at 307.2nm(Blue shift), with appearances a new band at 259.1 nm,and the second band due to the ligand field transitions (L.F), respectively.

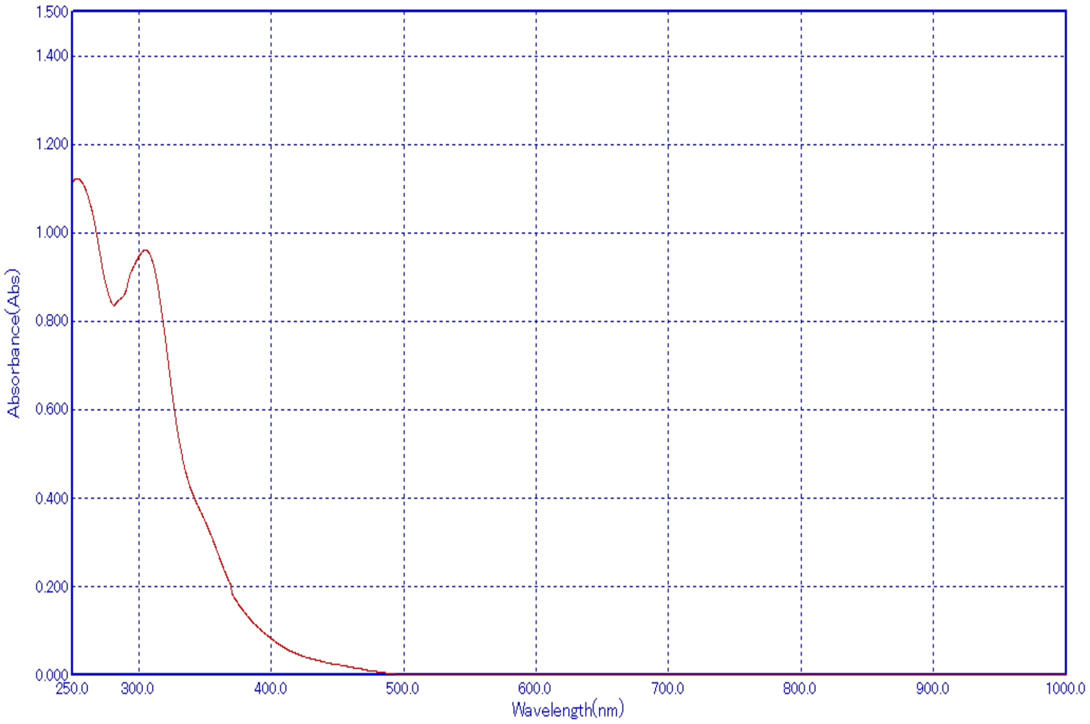
In the **Zn(II)** complex, that the azomethine group shifted to a higher wavelength at 311.4nm (Red shift), with appearances a new band at 259.1 nm due to the ligand field transitions (L.F) and charge transitions (C.T), respectively(Socrates, G. (2004),**Figures(3-25),(3-26),(3-27)** show the UV-Visible spectrum for the ligand's complexes, and The **Table(3-7)** shows The electronic transition and wavelength, values of the ligand(**L**$_1$)and its complexes.



Figure(3-25):UV-Visible Spectrum for Ni^{+2} Complex with Ligand (L1)



Figure(3-26):UV-Visible Spectrum for Cu^{+2} Complex with Ligand (L_1)



Figure(3-27):UV-Visible Spectrum for Zn^{+2} Complex with Ligand (L_1)

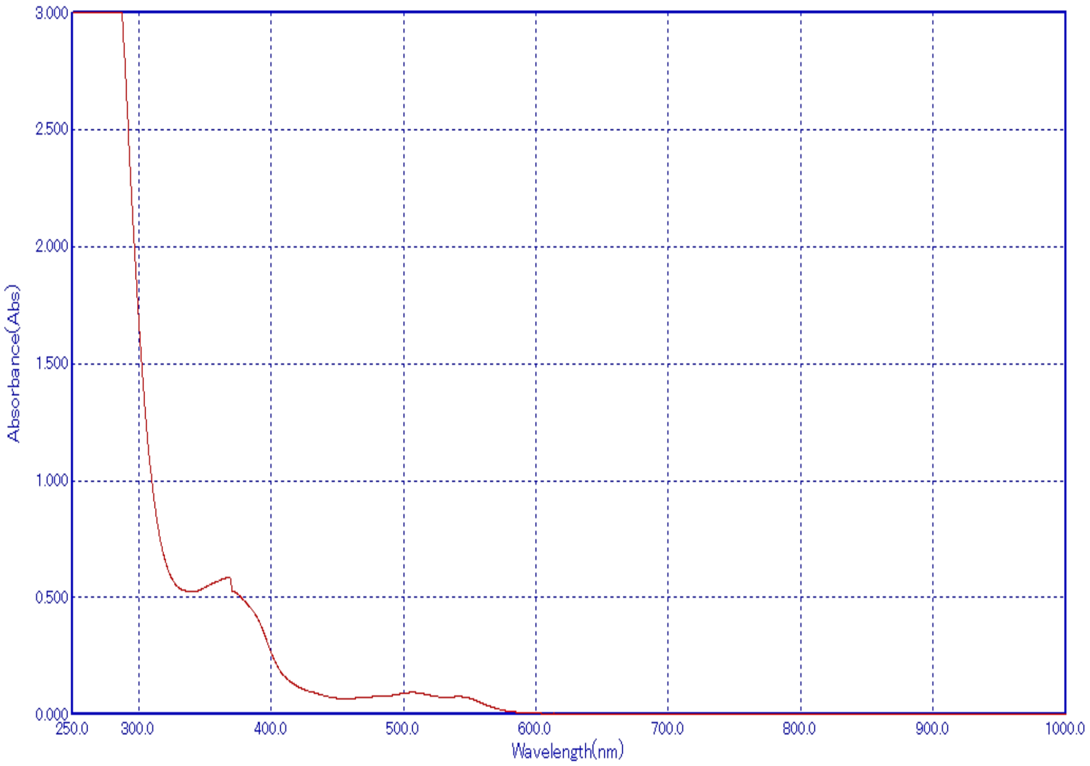
Table (3-7):Electronic Transition of the Ligand(L_1) and its Complexes

Compounds	ג max	ʋ cm-1	Assignment	Shifted
L_1	308.4nm	3242.5cm$^-$	π-π*	-
[Ni(L)$_2$Cl$_2$]	306.4nm 270nm	3263.7cm$^-$ 3703.7cm$^-$	L.F C.T	Blue shift
[Cu(L)$_2$Cl$_2$]	307.2nm 259.1nm	3255.2cm$^-$ 3859.5cm$^-$	L.F L.F	Blue shift
[Zn(L)$_2$Cl$_2$]	311.4nm 259.1nm	3211.3cm$^-$ 3859.5cm$^-$	L.F C.T	Red shift

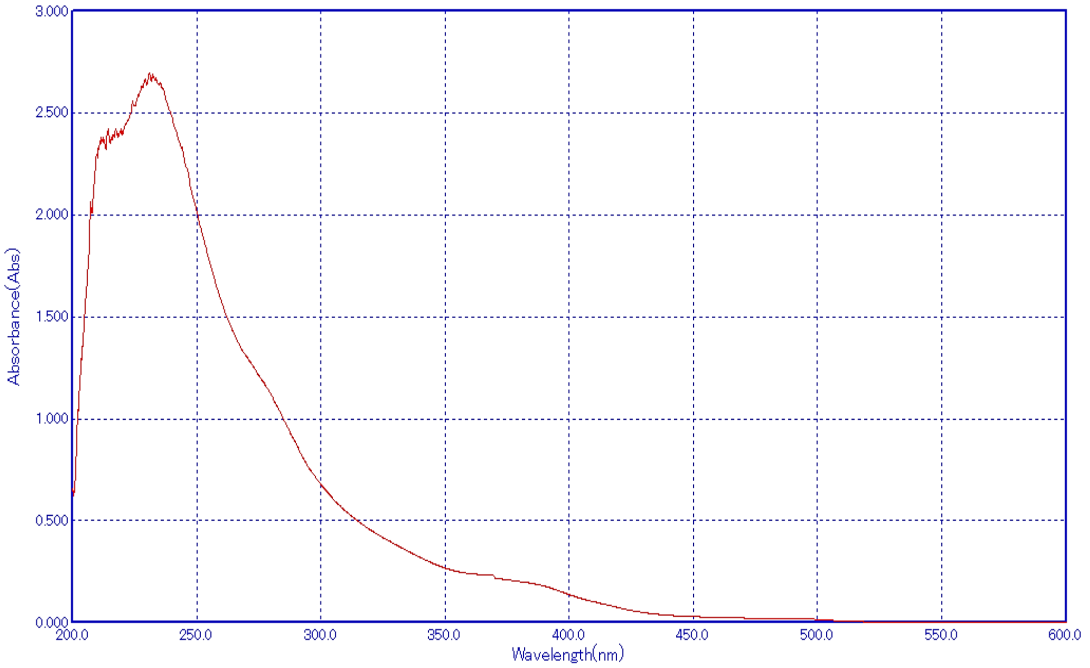
3.5.2.2.Electronic spectra of Ni(II),Cu(II),Zn(II) Complexes for ligand (L_2)

The spectrum of ligand (L2) was compared with complexs spectrums, and it was found in Ni(II) and **Cu**(II) complexs, that the azomethine group shifted to a lower wavelength at 366.2 nm and 214.5 nm respectively (Blue shift), due to the ligand field transitions (L.F).and appearance a new band 231.5 nm in **Cu**(II) complex due to the L.F, with disappearances a band at 369 nm in the spectrum of the free ligand.

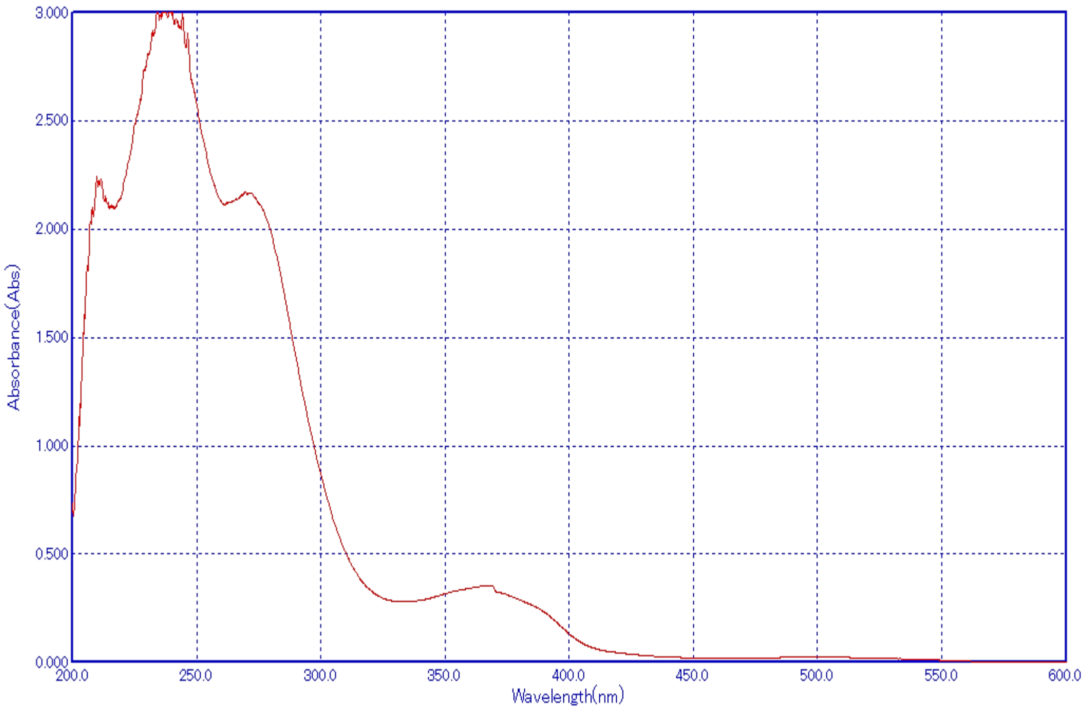
while In the spectrum of the Zn(II) complex, the azomethine group shifted to a higher wavelength at 369.2nm (Red shift), with appearances a new band at 210.2nm due to the ligand field transitions (L.F) and charge transfer (C.T), respectively,**Figures(3-28)**,**(3-29)**, and **(3-30)** show the UV-Visible spectrum of the Ni(II), Cu(II) and Zn(II) complexes with ligand (L_2), and the data has been listed in the **Table(3-8)**.



Figure(3-28):UV-Visible Spectrum for Ni^{+2} Complex with Ligand (L_2)



Figure(3-29):UV-Visible Spectrum for Cu^{+2} Complex with Ligand (L_2)



Figure(3-30):UV-Visible Spectrum for Zn^{+2} Complex with Ligand (L$_2$)

Table (3-8):Electronic transition of the ligand(L$_2$) and its Complexes

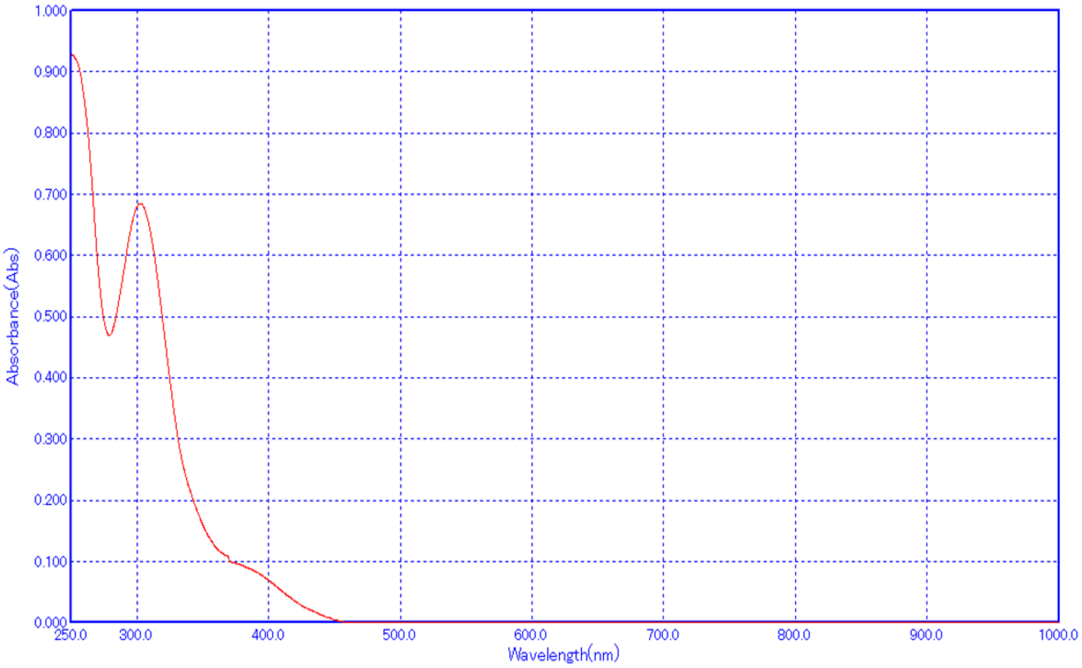
Compounds	λ max	ʋ cm-1	Assignment	Shifted
L$_2$	369nm 271nm 238nm	2710cm^{-} 3690cm^{-} 4201.68cm^{-}	n-π* π- π* π- π*	
[Ni(L$_2$)$_2$Cl$_2$]	366.2nm	2730.74cm^{-}	L.F	Blue shift
[Cu(L$_2$)$_2$Cl$_2$]	231.5nm 214.5nm	4319.65cm^{-} 4662cm^{-}	L.F L.F	Blue shift
[Zn(L$_2$)$_2$Cl$_2$]	369.2nm 271nm	2708.55cm^{-} 3690cm^{-}	L.F L.F	Red shift

	238.3nm	4196.4cm^{-}	C.T	
	210.2nm	4757.4cm^{-}	C.T	

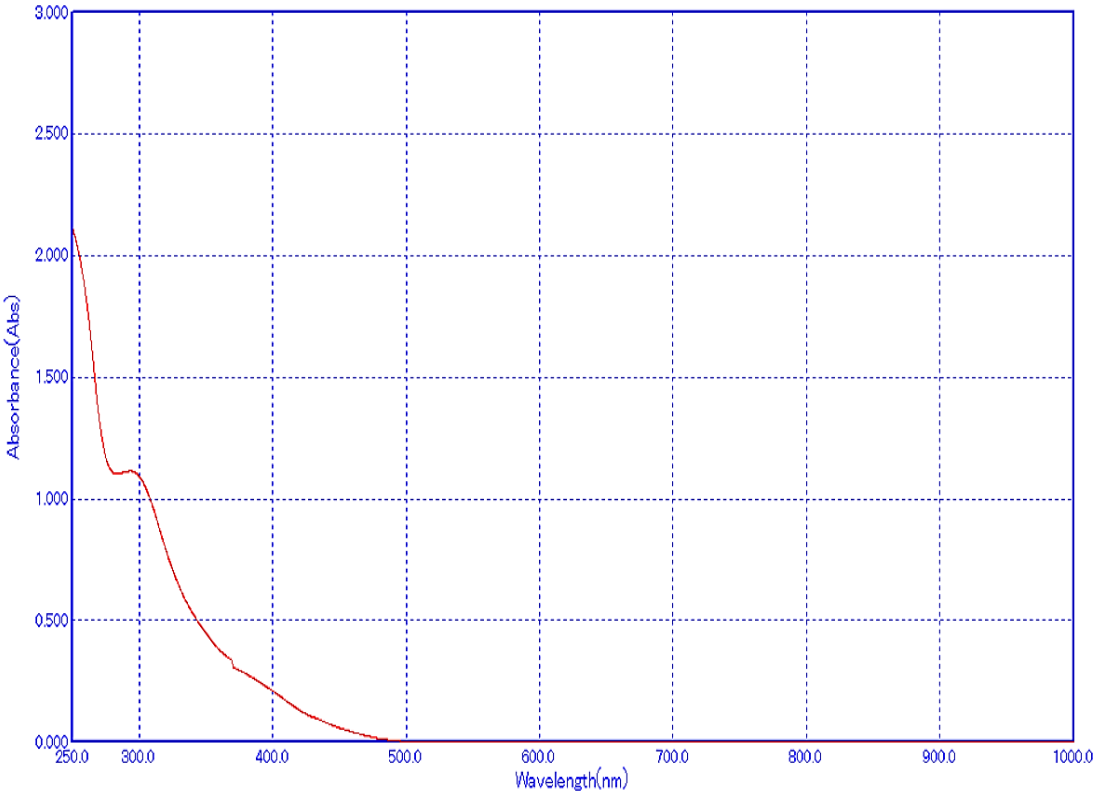
3.5.2.3.Electronic spectra of Ni(II),Cu(II),Zn(II) Complexes for ligand (L_3)

The Spectrum of ligand (**L_3**) was compared with complexs spectrums, and it was found in **Ni**(II) and **Cu**(II) complexs, the azomethine group shifted to a higher wavelength at 303.4nm and 297.6nm ,respectively (Red shift), due to the ligand field transitions (L.F).and in **Cu**(II) complex due to the L.F.

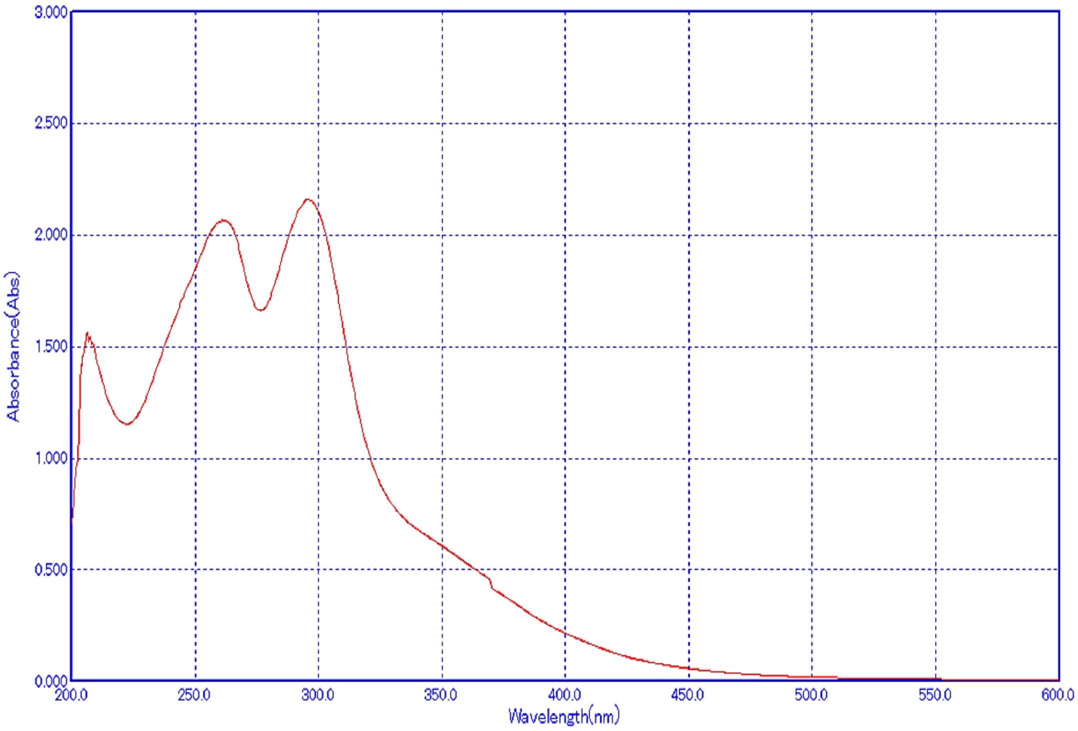
In the **Zn**(II) complex spectrum, the azomethine group shifted to a lower wavelength at 295.7nm,206.4 (Blue shift), with appearances a new band at 261.4nm due to the ligand field transitions (L.F) and charge transfer (C.T) respectively ,**Figures(3-31),(3-32),(3-33)** show the UV-Visible spectrum for the ligand's complexes ,**Table (3-9)** shows The electronic transition of the ligand(**L_3**) and its complexes



Figure(3-31):UV-Visible spectrum for Ni^{+2} complex with ligand (L$_3$).



Figure(3-32):UV-Visible spectrum for Cu^{+2} complex with ligand (L$_3$)



Figure(3-33):UV-Visible spectrum for Zn^{+2} complex with ligand (L_3)

Table (3-9):Electronic Transition of the Ligand(L_3) and its Complexes

Compounds	λ_{max}	υ_{cm-1}	Assignment	Shifted
L_3	297nm 220nm	3367cm^{-1} 4545.4cm^{-}	π -π* π- π*	
$[Ni(L)_2Cl_2]$	303.4nm	3295.9cm^{-}	L.F	Red shift
$[Cu(L)_2Cl_2]$	300nm	3333.3cm^{-}	L.F	Red shift
$[Zn(L)_2Cl_2]$	370nm	2702.7cm^{-}	L.F	Blue shift

	295nm 261.7nm 206nm	$3389.8cm^{-}$ $3821.1cm^{-}$ $4854cm^{-}$	L.F C.T C.T	

3.5.3.Atomic Absorption Spectroscopy

This technique is considered a quantitative technique as it relies on the principle of absorption spectroscopy to determine the concentration of the metal present in the complex depending on the extent to which it absorbs the radiation applied to it. The results have shown in the same case between practical and theoretical values, this indicates the correctness of the proposed formulas, as well as the correctness of the mixing ratios between metals and ligand.**Table (3-10)** shows theoretical and Practical values for the ratio of metal to the ligand and the suggested formula of the prepared complexes.

Table (3-10): Theoretical and Practical Values for the Ratio of Metal Ions in the Complexes, and Suggested Formula of the Prepared Complexes

Complexes	%Metal		Suggested formula
	Exp.	Cal.	
L_1-Ni	6.0	7.4	]Ni $(L_1)_2Cl_2$[
L_1-Cu	11.0	8.0	]Cu $(L_1)_2Cl_2$[
L_1-Zn	8.7	8.2	]Zn$(L_1)_2Cl_2$[
L_2-Ni	6.3	6.9	]Ni $(L_2)_2Cl_2$[
L_2-Cu	11.4	7.4	]Cu $(L_2)_2Cl_2$[

L_2-Zn	8.8	7.6	$]Zn(L_2)_2Cl_2[$
L_3-Ni	6.3	6.5	$]Ni\ (L_2)_2Cl_2[$
L_3-Cu	10.1	7.0	$]Cu\ (L_2)_2Cl_2[$
L_3-Zn	8.1	7.1	$]Zn(L_2)_2Cl_2[$

3.5.4. Magnetic Susceptibility for Coordination Complexes

Magnetic measurements have been widely used in the study of transition metal complexes, as most transition metals possess single electrons and show paramagnetic properties. In addition, the greater the number of lone electrons, the greater the magnetic moment of the ion ,as it gives information about the compound in terms of electronic structure and oxidative state of atoms. The transition metals produce the magnetic properties of the complexes as a result of the orbital motion and the Permian motion.

$$\mu=\sqrt{4S(S+1)}+L(L+1)=B.M$$

S=spin quantum number

L=orbital quantum number

$$\mu=\sqrt{n(n+2)}=B.M$$

(The number of unpaired electrons)=n

Bohr Magneton=B.M.

The value of the magnetic susceptibility of the prepared complexes was measured at room temperature by using magnetic balance and the value of the effective magnetic moment(μ_{eff}) was found from the following relationship

$\mu_{eff}=2.828\sqrt{XA.T}=$¿ $B.M$

$X_A=X_M+D$

$X_M=Xg$ **x** M.wt

Absolute temperature=T

Atomic sensitivity=X_A

molarity sensitivity =X_M

gram sensitivity =Xg

Effective magnetic moment =μ_{eff}

Correction factor for the compounds prepared in the study =D

The practical values for the effective magnetic moment obtained from the above equations showed convergence with the theoretical value, the results were included in **Table (3-11).**

3.5.5.Molar Conductivity for Coordination Complexes

Absolute ethanol was used as a solvent for the complexes, which were prepared at a concentration of 1 x 10^{-3} M. To measure molar conductivity, it has been found that all complexes are either substructural or non-conductive (the behavior of these complexes was neutral), The molar conductivity value was confined to between 0-10 (ohm^{-}.cm^{2}.mole^{-1}), and these results are in agreement with what was observed in the study. (Ahmed, A. A.,*et al.,*2021) and **Table (3-11)** shows the molar conductivity results for all complexes.

Table(3-11):Magnetic Susceptibility,Molar Conductivity, and Hybridization for Complexes

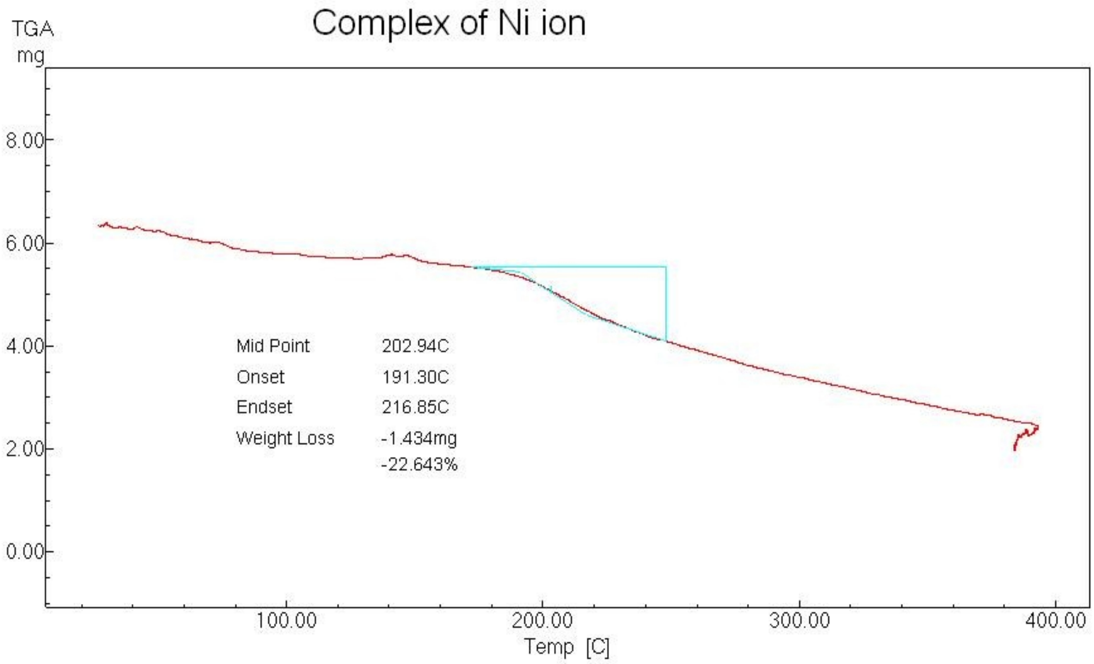
Complexes	μeff (B.M)		Molar conductance (Ω^{-1} cm^2 mol^{-1})	Shape	Hybridization
	Cal.	Exp.			
$[Ni(L_1)_2Cl_2]$	2.82	0.17	2	Octahedral	$sp^3 d^2$
$[Cu(L_1)_2Cl_2]$	1.73	1.196	3	Octahedral	$sp^3 d^2$
$[Zn(L_1)_2Cl_2]$	0	0	0	Octahedral	$sp^3 d^2$
$[Ni(L_2)_2Cl_2]$	2.82	0.17	10	Octahedral	$sp^3 d^2$
$[Cu(L_2)_2Cl_2]$	1.73	2.327	2	Octahedral	$sp^3 d^2$
$[Zn(L_2)_2Cl_2]$	0	0	0	Octahedral	$sp^3 d^2$
$[Ni(L_3)_2Cl_2]$	2.82	0.17	0	Octahedral	$sp^3 d^2$
$[Cu(L_3)_2Cl_2]$	1.73	1.66	0	Octahedral	$sp^3 d^2$
$[Zn(L_3)_2Cl_2]$	0	0	0	Octahedral	$sp^3 d^2$

3.5.6.Thermogravimetric Analysis (TGA)

Thermogravimetric analysis (TGA) is an experimental technique that measures mass and/or rate changes as a function of temperature or time as a sample undergoes an athermal event. Unlike other thermal analysis techniques, TGA has the advantages of being relatively easy to use, quick, and only requiring a small amount of sample. For these advantages, TGA-based experiments have become a popular analytical method to study the reactivity and kinetics of char gasification. (Zhang, Y.,*et al*.,2019). TGA curves of compounds measure the amount and rate of change in the weight of a material from room temperature to 400C^0 in an air atmosphere. TGA is a useful technique for determining complexes' thermal stability and mode of decomposition.

3.5.6.1.Thermogravimetric Analysis for Complexes of Ni (II) Ion with (L$_2$) ligand

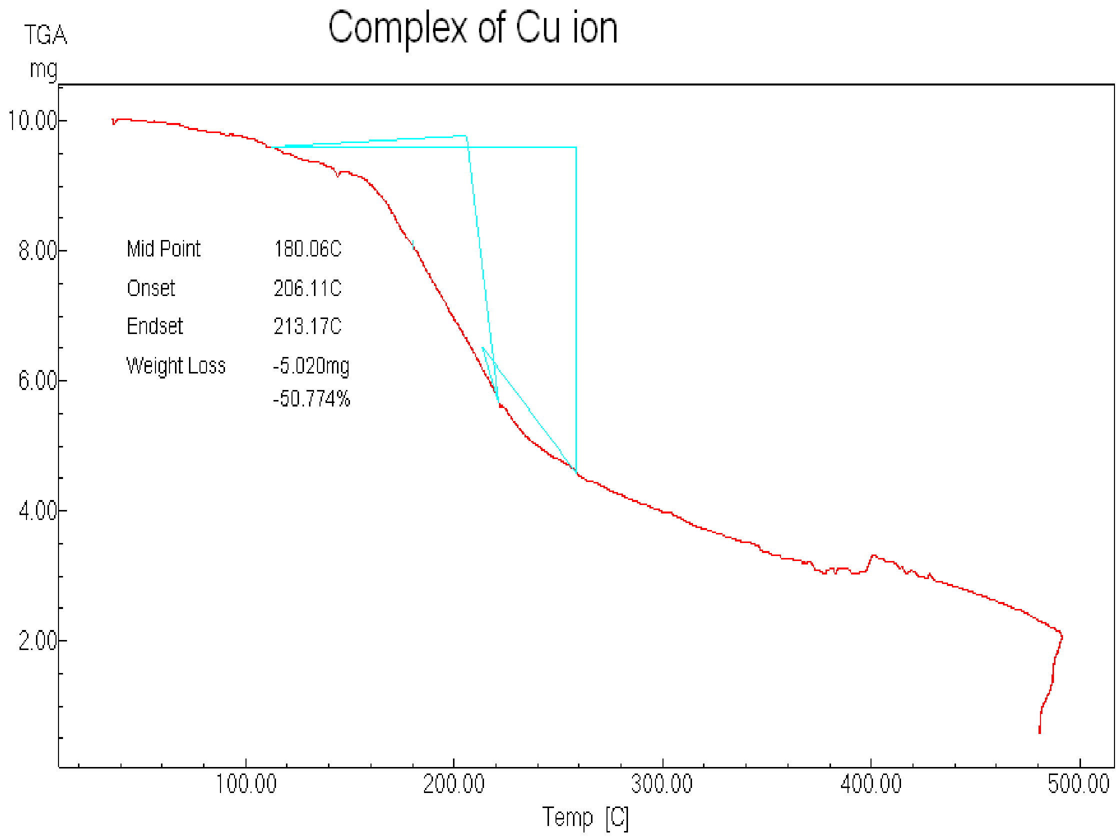
The structural formula of the Ni(II) complex was proposed from the TG and differential thermal analysis. The TGA curve indicated that the Nickel (II) complex degraded in one principal decomposition stage. In the stage, the weight loss was 22.643% with a DTG$_{max}$ (differential thermo gravimetric maximum) of 202.94^{0}C within a temperature range of 191.30–216.85^{0}C,The complexes mass loss.thus,this measurement confirms that there is absence of water molecule inside or outside the coordination sphere for nickel complexes, the **Figure(3-34)** shows The TGA curve for Ni(II)ion complexes with (**L$_2$**)ligand.



Figure(3-34): Thermogravimetric Analysis Curve for Ni^{+2} Complexe with Ligand(L_2)

3.5.6.2.Thermogravimetric analysis for Complexes of Cu(II) ion with (L_2) ligand

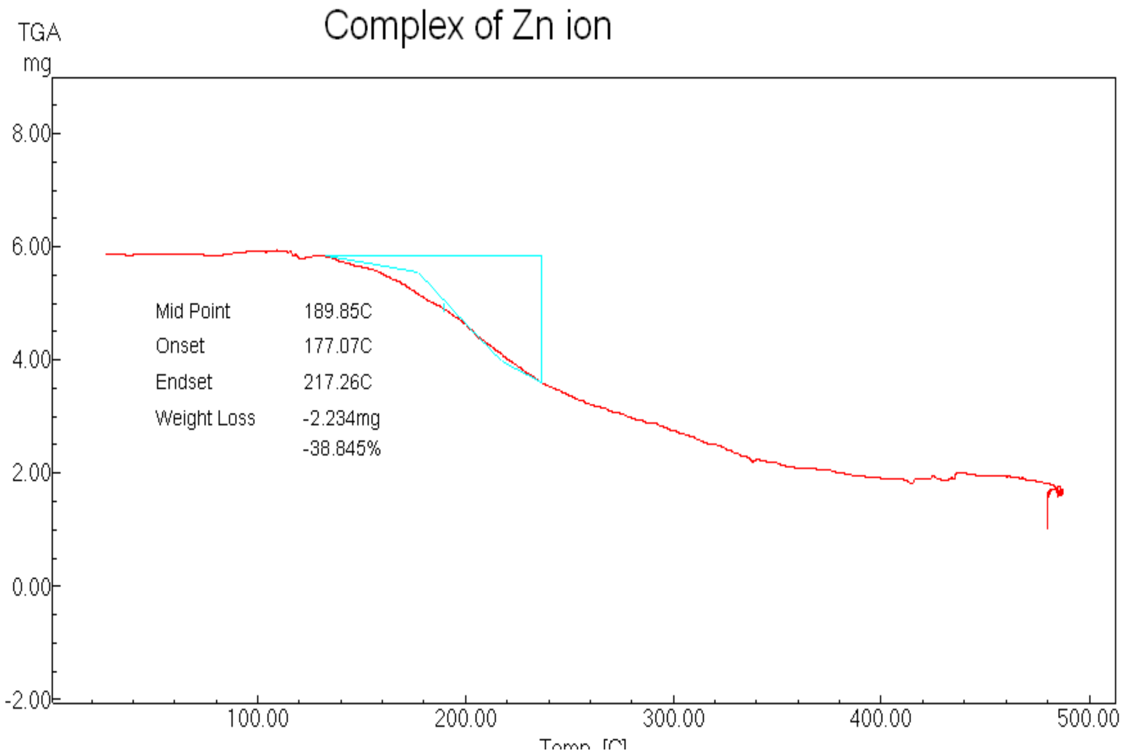
The TGA curve indicated that the copper (II) complexes degraded in one principal decomposition stage. In the stage, the weight loss was 50.774% with a DTG_{max} of 180.04C^0 within a temperature range of 206.11-213.17C^0,The complexes mass loss .thus ,this measurement confirms that there is absence of water molecule inside or outside the coordination sphere for copper complexes, **Figure(3-35)** shows The TGA curve for Cu (II) complexe of ligand (**L_2**)



Figure(3-35): Thermogravimetric analysis curve for Cu^{+2} complexes

3.5.6.3.Thermogravimetric analysis for Complexes of Zn(II) ion with ligand (L_2)

The Zinc(II) complex decomposed in one primary breakdown stage, according to the TGA curve. With a DTGmax of 189.85 ^{0}C and a temperature range of 177.07-217.26 ^{0}C, the complexes' mass loss in the stage was 38.845%. The TGA curve for Zn (II) complexes of ligand(L_2) is show in **Figure (3-36)** and this measurement demonstrates that there are water molecules not present both inside or outside the coordination sphere for zinc complexes.



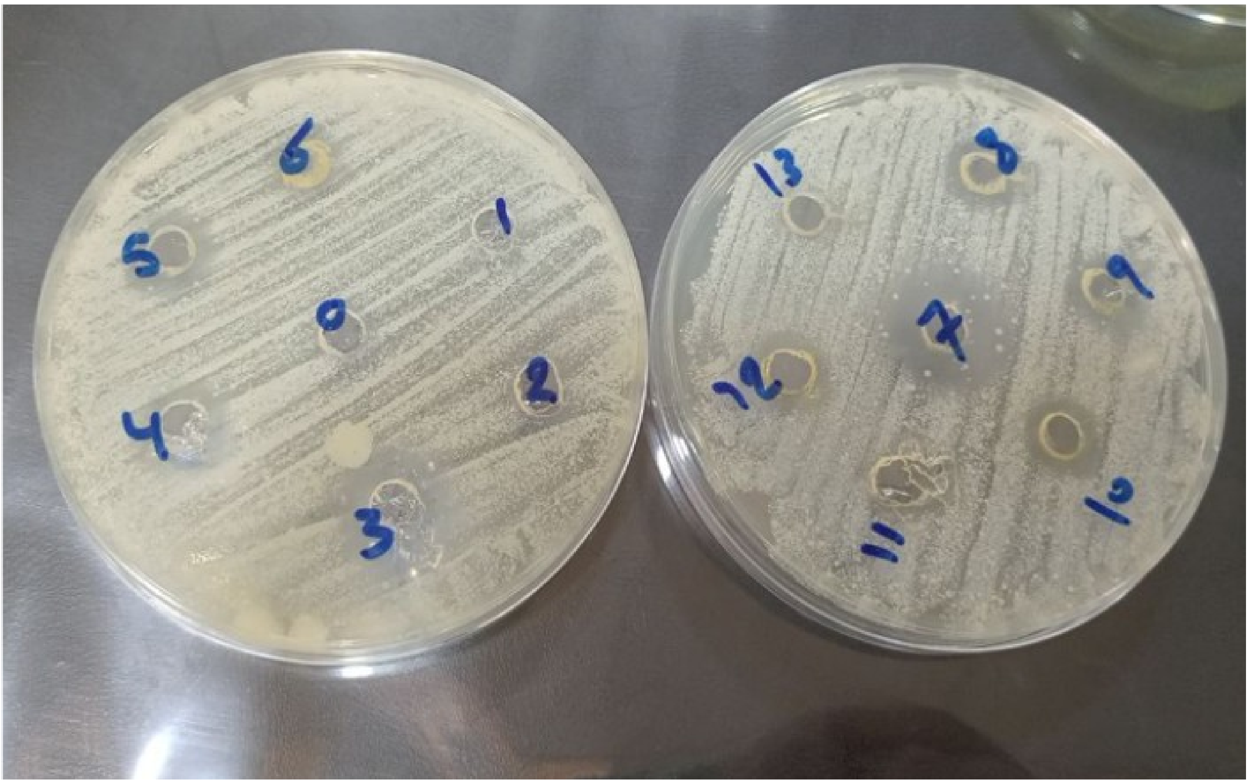
Figure(3-36): Thermogravimetric Analysis Curve for Zn^{+2} Complexe with Ligand (L$_2$)

3.7.Antibacterial Activity

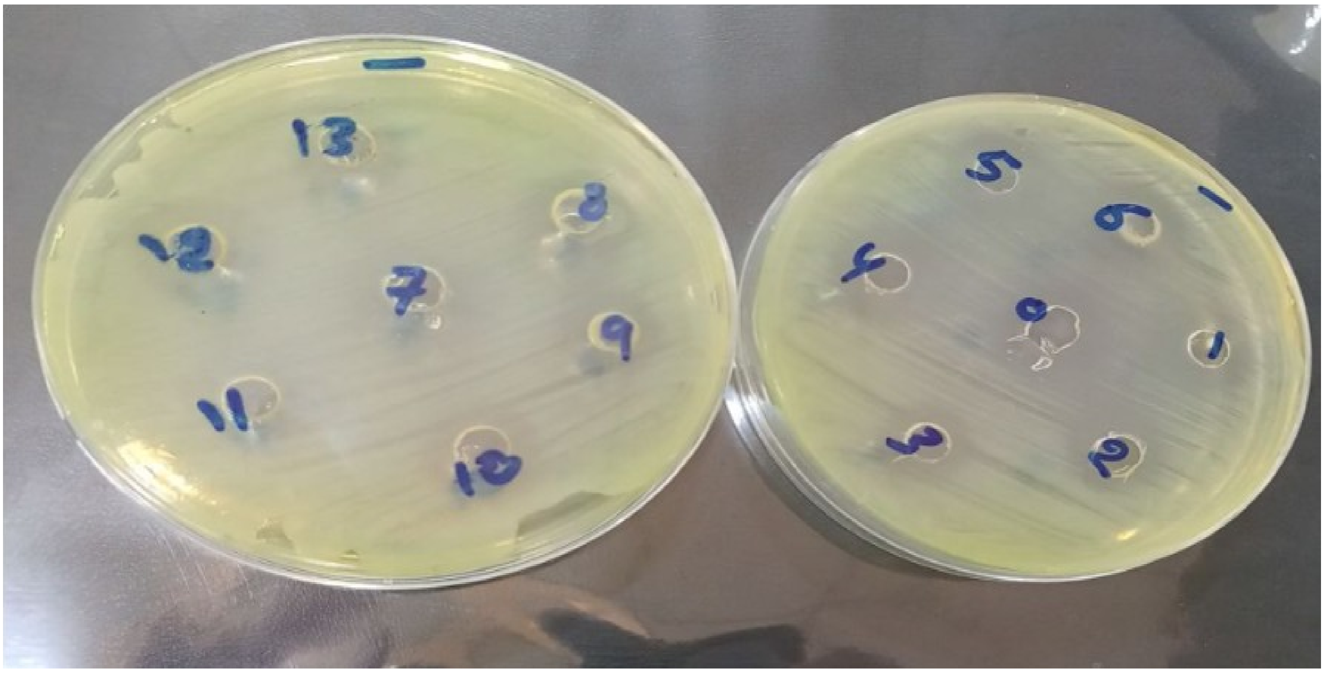
The antibacterial activities of newly synthesized compounds. According to this method, an increase in the growth of microbial cells increases the microbial number, The prepared complexes of the ligands(L_1,L_2,L_3) with Ni(II), Cu(II), Zn(II) were studied against the biological activity of two different types of bacteria (*Staphylococcus aureus* and *Pseudomonas*), at the concentration of 1×10^{-3} *M* ,and compare to the inhibitory effect of the original ligands (L_1,L_2,L_3) toward same types of bacteria.The three complexes (Ni(II),Cu(II),Zn(II) of the (L_2,L_3) recorded an elevation in the inhibition ability in comparison to the original ligands which was the precursor of these complexes studied at the concentration ($1\times10^{-3}M$) when the ligand and its complexes were applied on the plantation of(*Staphylococcus aureus* and *Pseudomonas*) as shown in **Figure (3-37)** and **(3-38)** .The ligand (**L_1**) illustrated the highest inhibitory effect among it's complexes ,andThe ligand (L_2) the complex of Zinc illustrated the highest inhibitory effect among the tow complexes and the original ligand(Catia Longhi.,*et al*,2022). the (L_3) The complex of Nickel illustrated the highest inhibitory effect among the two complexes and the original ligand(Ryldene Marques Duarte da Cruz.,*et al.,*2021),on the other hand, the complex of Zinc showed approximate inhibitory effects at the concentration (1×10^{-3} *M*) than the complex of Copper at the concentration(1×10^{-3} *M*) .The **Table(3-12)**shows inhibitory of the ligands and their metal complexes against tow type from bacterial.

Table(3-12):Minimum Inhibitory Concentration (MIC) in (g/mL) of the Ligands and their Metal Complexes

Compounds	*pseudomonas*	*Staphylococcus*
L_1	15	21
$[Ni(L_1)_2 Cl_2]$	15	10
$[Cu(L_1)_2Cl_2]$	12	12
$[Zn(L_1)_2Cl_2]$	15	12
L_2	15	0
$[Ni(L_2)_2 Cl_2]$	15	12
$[Cu(L_2)_2Cl_2]$	13	15
$[Zn(L_2)_2Cl_2]$	16	12
L_3	15	0
$[Ni(L_3)_2Cl_2]$	17	12
$[Cu(L_3)_2Cl_2]$	13	12
$[Zn(L_3)_2Cl_2]$	16	15



Figure(3-37): Ligands(L_1,L_2,L_3) and its complexes were applied on the plantation of *Staphylococcusaureus*



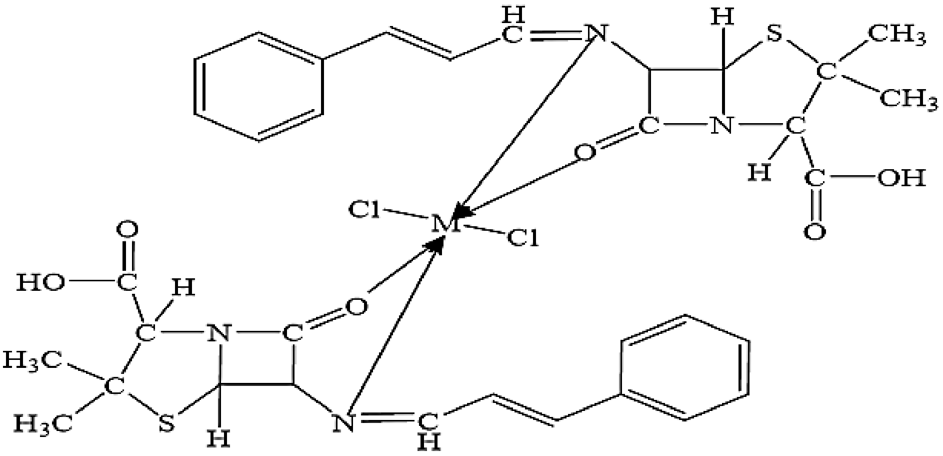
Figure(3-38):Ligands(L_1,L_2,L_3) and its Complexes were Applied on the Plantation of *pseudomonas*

3.8.Conclusions

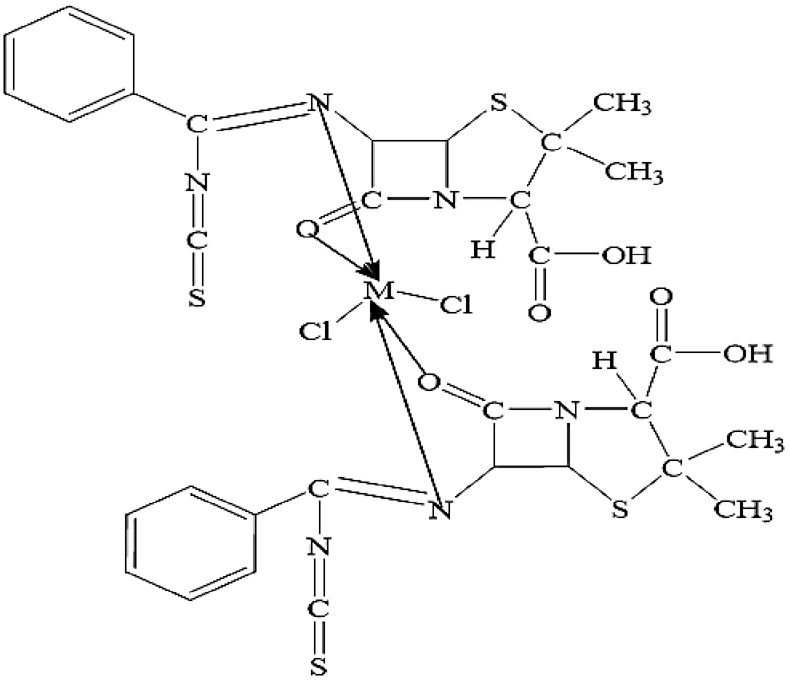
The basic *β*-lactam compounds of penicillin, 6-aminopenicillanic acid (6-APA), are an important active pharmaceutical intermediate that can be incorporated and redirected into semi-synthetic antibiotics.

1- The ligand (L_1) was synthesized by Schiff base reaction between 6-aminopenicillin acid and Cinnamaldehyde to form the(3,3-dimethyl-7-oxo-6-(((1Z,2E)-3-phenylallylidene)amino)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid) ligand,and The ligands(L_2) was synthesized by Schiff base reaction between 6-aminopenicillin acid and benzoyl isothiocyanat to form ((Z)-6-((isothiocyanato(phenyl) methylene)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid) ligand ,and The ligands(L_3) was synthesized by Schiff base reaction between 6-aminopenicillin acid and 5-Bromo-2-thiophene carboxaldehyde to form((E)-6-(((5-bromothiophen-2-yl) methylene)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid)ligand, and all synthesized ligands were bi-dentate, It showed coordination with the central metal ion via N-atoms of azomethine group and O- atoms of carbonyl group for the β-lactam ring .

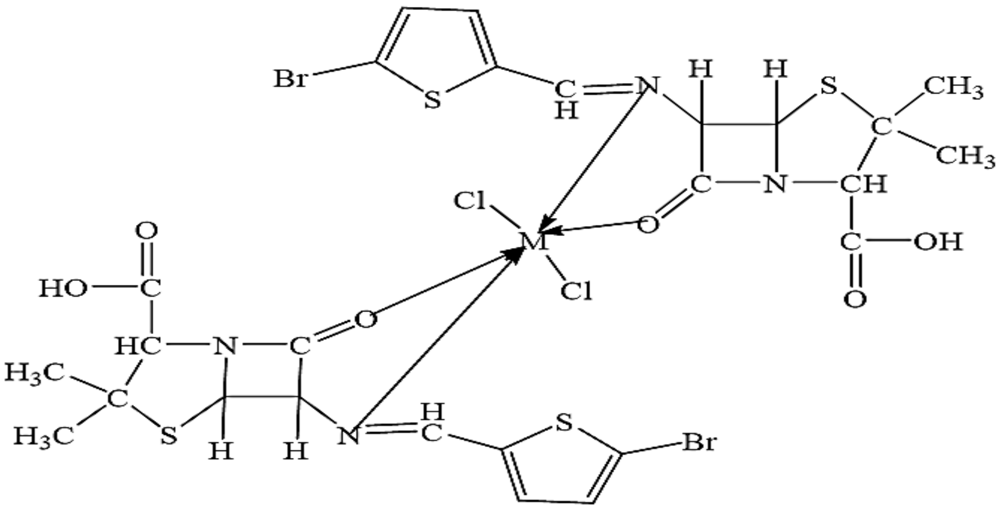
2-As a result,Three new metal(II) complexes with the Schiff base derived from these ligands. And showed octahedral geometry for the Ni(II), Cu(II), and Zn(II) complexes, the complexes were prepared with ligands from Schiff's base where they were mixed and thus obtained in a molar ratio [1:2] from[M(II):L],**Figures(3-39),(3-40)**,and**(3-41)** show the suggested shape for complexes.



Figure(3-39):Suggested Shape of Metal ion Complexes with Ligand(L1) ,M=Ni(II),Cu(II), and Zn(II)



Figure(3-40):Suggested Shape of Metal ion Complexes with Ligand(L2),M=Ni(II),Cu(II),and Zn(II)



Figure(3-41):Suggested Shape of Metal ion Complexes with Ligand(L3),M=Ni(II),Cu(II), and Zn(II)

3-Finally, each of the ligands and their complexes were biologically applied against two different types of Gram-positive and Gram-negative bacteria (*Pseudomonas*, *Staphylococcus*) ,Where all the prepared ligands and complexes showed an increase in biological activity compared to the basic materials

3.9.Future Work

1-Synthesis of compounds from new Schiff base reactions using aldehydes and ketones it has a distinctive chemical environment with 6-Aminopencilinic acid (for its high biological activity against bacteria.

2-Synthesis of stable complexes from central metals of great vital importance.

3- Connecting a biological efficacy test against different types of bacteria to determine their resistance to these compounds.

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الخلاصة

تضمن هذا العمل تحضير وتشخيص معقدات جديدة من ليكاندات ثنائية المخلب مع ثلاث املاح من فلزات للنيكل والنحاس والزنك, حيث ان تحضير ثلاث ليكاندات قواعد شف الجديدة مشتقة من التفاعل (6-امينوبنسلانك اسيد) مع(سينمالديهايد,بنزويل ايزوثايوسيانات, 5-برومو2-ثايوفين كاربوكسالديهايد) كل على حدة لتكوين (L_1,L_2,L_3))على التوالي .

يتم تشخيص الليكاندات المحضرة باستخدام تقنيات التحليل الطيفي(مطيافية الاشعة تحت الحمراء ($^1H,^{13}C$) مطيافية الرنين النووي المغناطيسي ,مطيافية الاشعة الفوق البنفسجية والمرئية,والتحليل الطيفي للكتلة والتحليل الدقيق للعناصر (C.H.N.S) والقياسات الفيزيائية. يتم تحضير المعقدات من خلال مزج الليكاندات الجديدة مع الاملاح الفلزية(حيث ان النسبة المولية من كلوريد الفلز الى الليكاند هي [2:1] وهذا بما يتناسب مع تكوين معقدات النيكل والنحاس والزنك ومن خلال دراسة التقنيات التحليل الطيفية وتقنيات(الحساسية المغناطيسية ,والتوصيلية الكهربائية المولارية والامتصاص الذري والتفكك الحراري) تم اقتراح الاشكال الفراغية للمعقدات المحضرة واعتمادا على النتائج كانت جميع المعقدات ثمانية السطوح وقد اظهرت الليكاندات الثلاثة ان التناسق مع ايون الفلز عبر ذرات النايتروجين لمجموعة شف وذرات الاوكسجين لحلقة البيتا لاكتام حيث يكون التهجين الناتج في شكل ثماني السطوح هو (sp^3d^2).

وتم دراسة الفعالية البايلوجية لكل من اليكاندات والمعقدات حيث ضد نوعين من البكتريا موجبة الكرام وسالبة الكرام (الزائفة ومكورات العنقودية الذهبية) حيث اظهرت كل من الليكاندات المحضرة والمعقدات فعالية بايلوجية كبيرة مقارنة مع المواد الاساسية .

جمهورية العراق
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قسم الكيمياء

تحضير وتشخيص المعقدات الفلزية لايونات النيكل والنحاس والزنك ثنائية التكافؤ بواسطة ليكاندات جديدة من قواعد شف ودراسة فعاليتها البايلوجية

رسالة

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كجزء من متطلبات نيل شهادة الماجستير في الكيمياء

تقدمت بها

زينب فالح عباس صالح

بكالوريوس علوم الكيمياء, كلية العلوم للبنات, جامعة بابل

2019

بأشراف

الاستاذ الدكتور (محمد حامد سعيد)

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