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Preparation, Characterization, and Biological Evaluation of New azo and azo-Schiff Ligands and their Metal Ion Complexes

A Thesis Submitted to the College of Science, University of Babylon as a partial fulfillment of the requirements for Degree of Doctorate of philosophy in Science/ Chemistry

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قسم الكيمياء

تحضير وتشخيص والتقييم البيولوجي لليكاندات ازو وازو شف الجديدة ومعقدات فلزاتها الايونية

اطروحة مقدمة إلى
كلية العلوم- جامعة بابل
وهي جزء من متطلبات نيل درجة دكتوراه فلسفة في العلوم/ كيمياء

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بإشراف

أ.م. د. سعد مدلول مهدي

١٤٤٤ هـ ٢٠٢٢ م

بسم الله الرحمن الرحيم

﴿ وَمَا أُوتِيتُم مِّنَ الْعِلْمِ إِلَّا قَلِيلًا ﴾

صدق الله العلي العظيم

سورة الاسراء / الآية (٨٥)

Dedication

To my father, may God have mercy on him, who always wanted me to complete my graduate studies.

To my family who are faraway.

To whom I had help and support.... I dedicate my humble effort.

Thikra

Acknowledgment

First, praise is to Allah who enabled me to accomplish this project. Also my deep gratitude for the Department of Chemistry College of Science / Babylon University, which afforded me this opportunity to achieve the Ph.D. degree.

I would like to thank all people who aid and encouraged me in this work, First, I thank my academic advisor, Assist. Prof. Dr. Saad Madlool Mahdi for their valuable guidance throughout this project.

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Finally, I must express my very profound acknowledgment to my family who are faraway, for their unlimited support, persistent encouragement, and long patience throughout all the years of study and research, this work would not have been possible without them, thank you very much.

Thikra Jawad

Supervisor Certification

I certify that Thesis entitled "**Preparation, Characterization, and Biological Evaluation of New azo and azo-Schiff Ligands and their Metal Ion Complexes**" was prepared by "**Thikra Jawad Hashim Mutter"** under our supervision at the Department of Chemistry, College of Science, University of Babylon, as a partial fulfillment of the requirements for the degree of Doctor of philosophy in Science of Chemistry, and that this work has never been published anywhere. According, we recommend this study for discussion.

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Certification of the Examination Committee

We are the examiner committee, certify that we have read the thesis entitled **"Preparation, Characterization, and Biological Evaluation of New azo and azo-Schiff Ligands and their Metal Ion Complexes"** presented by the student **"Thikra Jawad Hashim Mutter"** and examined her in its contents and, in our opinion, it is accepted as a thesis for Doctorate degree in the Philosophy of Science of Chemistry/ Inorganic Chemistry with **Excellent** degree.

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الخلاصة: -

شغلت كيمياء مركبات الازو، قواعد شف والازو- قاعدة شف حيزا كبيرا من اهتمام الباحثين في حقل الكيمياء اللاعضوية نظرا لدورها الفاعل في المجالين الأكاديمي والتطبيقي، ومن هذا المنطلق تضمنت الدراسة خطين لتحضير الليكاندات العضوية، تضمن الخط الاول تحضير ليكاندات الازو-اميدازول وهي: -

(L_1)= (E)-2-((2, 4-difluorophenyl) diazenyl)-4, 5-diphenyl-1H-imidazole.

(L_2)= (E)-2-((4-chloro-2-fluorophenyl) diazenyl)-4, 5-diphenyl-1H-imidazole.

(L_3)= (E)-2-((4-bromo-2-fluorophenyl) diazenyl)-4, 5-diphenyl-1H-imidazole.

وذلك من خلال تفاعل ازدواج املاح الدايزونيوم لثلاثة من مشتقات الأمين ثنائية التعويض **(٢، ٤- ثنائي فلورو انيلين، ٢- فلورو، ٤- كلورو انيلين، ٢- فلورو، ٤- برومو انيلين)**

مع قاعدة الاقتران **(٤، ٥- ثنائي فنيل اميدازول)** والتي تكون مؤهلة للتناسق مع مجموعة مختارة من ايونات العناصر الانتقالية ثنائية التكافؤ **Co(II)، Ni(II)، Cu(II)، Pd(II) ، Pt(II)** من خلال موقعين للتناسق **(N, N)** من قبل الليكاندات لتحضير المعقدات. فيما تضمن الخط الثاني من هذه الدراسة تحضير ثلاث ليكاندات من الازو- قاعدة شف عبرتفاعل ازدواج املاح الدايزونيوم لثلاثة من مشتقات الأمين ثنائية التعويض والمذكورة اعلاه مع قاعدة شف **DCSS** (والتي حضرت من التفاعل التكثيفي بين **٢، ٥- ثنائي كلورو انيلين** و **السالساليديهايد** بوجود حامض الخليك الثلجي كعامل مساعد) والتي تعتبر كقاعدة اقتران لتحضير ثلاثة ليكاندات من الازو-قاعدة شف وهي: -

(L_4)-2-((E)-((2,5-dichlorophenyl)imino)methyl)-4-((E)-(2,4-difluorophenyl)diazenyl)phenol.

(L_5)-4-((E)-(4-chloro-2-fluorophenyl)diazenyl)-2-((E)-((2,5-dichlorophenyl)imino)methyl)phenol.

(L_6)-4-((E)-(4-bromo-2-fluorophenyl)diazenyl)-2-((E)-((2, 5-dichlorophenyl)imino)methyl)phenol.

والتي تعمل كليكاندات ثنائية السن وذلك عبر ذرة نيتروجين مجموعة الازوميثين وذرة اوكسجين مجموعة الهيدروكسيل لحلقة الفنيل **(N, O)** مع نفس ايونات العناصر الانتقالية المختارة

والمذكورة أعلاه لتحضير معقدات الازو- ميثين، حيث حضرت جميع المعقدات الصلبة بعد معرفة الظروف المثلى للتحضير من تركيز ودالة حامضية PH ودراسة تأثير المذيب على الليكاند ومعرفة النسبة المولية اللازمة **(M: L)** عمليا لتحضير المعقدات، حيث كانت جميع المعقدات الفلزية بنسب مولية **1:1**، من ناحية أخرى، النسبة المولية لمعقدات الكوبلت هي **2:1** مع ليكاندات الازو-اميدازول وليكاندات الازو- قاعدة شف، كذلك معقدات النحاس مع ليكاندات الازو-قاعدة شف.

شخصت جميع الليكاندات العضوية والمعقدات الفلزية المحضرة مع تقنيات طيفية عديدة مثل **(طيف الاشعة تحت الحمراء، طيف الرنين النووي المغناطيسي، طيف الكتلة، طيف الاشعة فوق البنفسجية والمرئية والتحليل الدقيق للعناصر)** للتأكد من صحة التحضير للمعقدات، فيما استخدمت تقنيات تكميلية أخرى مثل **(الامتصاص الذري، التوصيلية الكهربائية المولارية والحساسية المغناطيسية)** لاقرار الصيغة البنائية الهندسية لها، ومن خلال النتائج مجتمعة أمكن اقتراح الاشكال الهندسية للمعقدات المحضرة، حيث اتخذت جميع معقدات **النيكل والبلاديوم والبلاتين** لليكاندات الازو-اميدازول والازو- قاعدة شف شكل **المربع المستوي** باستثناء معقد **الكوبلت** لنفس الليكاندات المذكورة حيث اتخذ شكل **ثماني السطوح**، فيما اتخذ معقد **النحاس** شكل **رباعي السطوح** مع ليكاندات الازو-اميدازول وشكل **ثماني السطوح** مع ليكاندات الازو-قاعدة شف .

كذلك تم دراسة الفعالية البيولوجية لليكاندات المحضرة وبعض معقداتها الفلزية المختارة قيد الدراسة

- إمكانية استخدامها كمضادات حيوية لنوعين من البكتريا، الموجبة لصبغة كرام (***Staphylococcus aureus***)، والسالبة لصبغة كرام (***Escherichia coli***) وبأستخدام **metronidazole** و **tetracycline**كمحلول قياسي ومذيب **DMSO** ككاشف، حيث اعطت المركبات المحضرة نتائج جيدة ومتباينة بالمقارنة مع الدواء المستخدم،
- كذلك تم استخدام نفس المركبات المحضرة كمضادات لعملية الاكسدة ضد الجذور الحرة بأستخدام **tannic acid** كمحلول قياسي وDPPH ككاشف، حيث اعطت المركبات المحضرة نتائج جيدة ومختلفة من خلال قيمة ($\mathbf{IC_{50}}$) بالمقارنة مع tannic acid من جهة، ومن جهة اخرى تزداد عملية الاكسدة بزيادة التركيز للمركبات المحضرة.
- واخيرا واستنادا الى ماجاء في الادبيات لما الى أهمية مركبات **البلاديوم والبلاتين** واستخدامها كدواء ضد مرض السرطان وقع اختيارنا على استخدام كل من معقدي

البلاديوم والبلاتين وامكانية المقارنة بينهما من خلال قيمة **(IC_{50})** وامكانية استخدامهما كدواء ضد مرض السرطان، حيث تبين ان **معقدي البلاتين** يعطي فعالية دوائية أفضل من معقدي البلاديوم وفقا للنتائج المستحصلة من هذه الدراسة.

Summary:-

The chemistry of azo compounds, Schiff bases, and azo-Schiff bases occupied a great deal of interest by researchers in the field of inorganic chemistry due to their active role in both of academic and applied fields, for this reason, our study included two ways for preparing ligands, the first way combined the synthesis of azo-imidazole ligands, which are:-

(L_1)= (E)-2-((2, 4-difluorophenyl) diazenyl)-4, 5-diphenyl-1H-imidazole.

(L_2)= (E)-2-((4-chloro-2-fluorophenyl) diazenyl)-4, 5-diphenyl-1H-imidazole.

(L_3)= (E)-2-((4-bromo-2-fluorophenyl) diazenyl)-4, 5-diphenyl-1H-imidazole.

This coupling reaction for preparation of azo compounds was carried out through diazonium salts of three di-substituted aniline derivatives **(2, 4-difluoroaniline, 4-chloro-2-fluoroaniline, and 4-bromo-2-fluoroaniline),** with coupling component **(4, 5-diphenyl-1H-imidazole)**, which is qualified to coordinate with a selection of ions of divalent transition elements **Co(II), Ni(II), Cu(II), Pd(II), and Pt(II),** by two sites for coordination **(N, N)** of the ligands to prepare the complexes, while the second way of this study included preparation of three azo - Schiff base ligands, using coupling reaction of diaz onium salts of three di-substituted aniline derivatives above mentioned with Schiff base **DCSS** (which was prepared from the condensation reaction between **2, 5-dichloroaniline** and **salicylaldehyde** in the presence of glacial acetic acid as a catalyst) which is considered a coupling component for the preparation of three of the azo-Schiff base ligands which are:-

(L_4)-2-((E)-((2,5-dichlorophenyl)imino)methyl)-4-((E)-(2,4-difluorophenyl)diazenyl)phenol.

(L_5)-4-((E)-(4-chloro-2-fluorophenyl)diazenyl)-2-((E)-((2,5-dichlorophenyl)imino)methyl)phenol.

(L_6)-4-((E)-(4-bromo-2-fluorophenyl)diazenyl)-2-((E)-((2, 5-dichlorophenyl)imino)methyl)phenol.

That as a bidentate chelating ligand through two sites for coordination via the azo-methine nitrogen atom and the oxygen atom of the phenyl ring **(N, O)** with the same ions of the transition elements were selected and above mentioned to prepare azo-Schiff base complexes. All solid complexes were prepared after knowing some of the optimum conditions for the preparation like optimum concentration, acidic function pH study, effect of the solvent on the synthesized ligands, and knowing the molar ratio **(M: L)** needed to prepare the complexes practically, all the metal complexes had molar ratios of **(1:1)**, on the other hand, the molar ratio for the cobalt(II) complexes was **(1:2)** with the azo-imidazole, azo-Schiff base ligands, as well as the copper(II) complexes with the azo-Schiff base ligands.

All the prepared organic ligands and their metal complexes were characterized with many techniques such as **(FTIR, ^{1}H-NMR, Mass, UV-Visible spectra, and Elementary Analysis)** to ensure their preparation, additionally, complementary techniques, such as **Atomic Absorption**, **Molar Electrical Conductivity**, and **Magnetic Susceptibility**, to determine its geometric structural formula. Through the combined results, it was possible to suggest the geometric shapes of the prepared complexes, where all the **Nickel(II)**, **Palladium(II)**, and **Platinum(II)** complexes of the azo-imidazole,

azo-Schiff base ligands took the shape of a **square planar**, except for the **cobalt(II)** complexes of the same ligands mentioned, where it took the form of **octahedral**, while the **copper(II)** complex took the form of a **tetrahedral** with azo-imidazole ligands and **octahedral** with azo-Schiff base ligands.

The biological activity of the prepared ligands and some of their selected metal complexes under study were also studied

- The possibility of using them as antibiotics for two types of bacteria, gram-positive **(*Staphylococcus aureus spp*)** and gram-negative **(*Escherichia coli spp*)**, using **metronidazole** and **tetracycline** as **standard** solution and solvent **DMSO** as **control**, where the prepared compounds gave excellent and different results compared to the used drug.
- The same prepared compounds were also used as antioxidants against free radicals using **tannic acid** as a **standard** solution and **DPPH** as a **control**, as the prepared compounds gave excellent and different results through the value of **(IC_{50})** compared to tannic acid, and on the other hand, the oxidation process increases with the increasing concentration of the prepared compounds.
- Finally, and based on what was stated in the literature regarding the importance of **Palladium(II)** and **Platinum(II)** compounds and their use as a drug against cancer disease, we chose to use both the palladium(II) and platinum(II) complexes and the possibility of comparing them through the value of **(IC_{50})** and the possibility of using them as a medicine against cancer, where it was found that the platinum(II) complexes give a more efficient pharmacological effect than the palladium(II) complexes, according to the results obtained from this study.

Table of Contents

Contents

Contents

Contents

Contents

Contents

List of Tables

Contents

List of Figures

Contents

Contents

Lists of Scheme:

Contents

List of Abbreviations:

Symbol	Definition
(HPASASN)	4,5 - dihydroxy - 3- (phpnyl azo) -2,7- disulfonic acid disodium naphthalene salt
(NASAR)	4-((E)-(4-((E)-1-((4-nitrophenyl)imino)ethyl)phenyl)diazenyl)benzene-1,3-diol
MTT	(3-(4,5-dimethylthiazol-2-y1)-2,5-diphenyl tetrazolium bromide)
MTS	(3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium)
XTT	2,3-bis-(2-mehoxy-4-niro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide
WST	(2-(2-methoxy-4-nitrophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfophenyl)-2H-tetrazolium)
(DCSS)	(E)-2-(((2,5-dichlorophenyl)imino)methyl)phenol
DPPH	2, 2-diphenyl-1-picrylhydrazyl
ELISA	Enzyme Linked Immunosorbent Assay
ESI	Electrospray Ionization

Declaration

I am, **Thikra Jawad Hashim**, who conducted this study entitled "**Preparation, Characterization, and Biological Evaluation of New azo and azo-Schiff Ligands and their Metal Ion Complexes",** and submitted it as a partial fulfillment of the requirements for doctor degree in science of chemistry.

The research was carried out at the Department of Chemistry, College of Science, University of Babylon; the study was performed under the supervision of Assist.Prof. Dr.Saad Madlool Mahdi, Chemistry Department/ College of Science/ University of Babylon.

I confirm that the work presented in this thesis has not been previously submitted for a doctorate, Master, and Diploma thesis at any higher education institution, likewise, I declare that all information in this document has been obtained and presented in accordance with the academic rules and ethical conducts. I further state, that as required by these rules and conducts, I have fully cited and documented all methods, figures and results that are not original to this work, or any information that is not derived from this work.

I affirm that this been indicated in this thesis.

Conclusions and Recommendations

Conclusions

Based on the results of the spectroscopic and analytical characterize of the azo-imidazole ligands and the azo-imidazole ligands - the prepared Schiff base and their metal complexes under study, we conclude the following: -

- This work is characterized by the ease of preparing the azo-imidazole ligands and their prepared metal complexes, while there is a relative difficulty in preparing the azo-imidazole ligands with a Schiff base due to the intra-molecular effects or the effect of the solvent.
- The possibility of preparing new azo-Schiff ligands starting from the preparation of a Schiff base (DCSS) containing a hydroxyl group, which is a coupling component for each of the dihalide amines (2, 4-difluoroaniline, 4-chloro- 2-fluoroaniline, 4-bromo-2). - fluoroaniline), respectively, and in the usual way.
- Prove the formation of new ligands during their characterizes by possible spectroscopic methods such as (TLC, FTIR, ^{1}H-NMR, Mass spectra, Uv-Visible, and elementary analysis) to ensure their preparation, additionally, complementary techniques, such as atomic absorption, molar electrical conductivity, and magnetic susceptibility.
- Preparing five solid complexes for each ligand according to the best molar ratios and characterizing them using the

available technical means such as molar conductivity and magnetic susceptibility from which it is possible to know the number of lone electrons and suggest the geometric structures of the complexes through knowing the results of the study side by side.

- Suggesting the geometrical structure of a square planar with hybridizations (dsp^2) for nickel, palladium, and platinum complexes for all azo-imidazole and azo- Schiff base ligands, octahedral hybridization (sp^3d^2) for the cobalt complex with the same aforementioned ligands, while the copper complex takes the octahedral structure with azo-Schiff ligands, and It is tetrahedral and hybridization (sp^3) with azo-imidazole ligands.
- All the prepared ligands of both types behave as bi-dentate ligands by coordinating the nitrogen atom of the imidazole ring (N_3) and the nitrogen atom of the azo-bridge group for the azo-imidazole ligands, and the nitrogen atom of the azo-methine group with the oxygen atom of the hydroxyl group in salicylaldehyde ring for azo-Schiff ligands.
- The results of the study agree with the structures of the ligands and their solid complexes largely.
- Clarification of the biological effect of the prepared compounds and the possibility of their use in the medical field through:

- Their effect on inhibiting the growth of two types of bacteria such as (***Staphylococcus aureus***) represented by gram-positive bacteria and (***Escherichia coli***) represented

by gram-negative bacteria in comparison with metronidazole and tetracycline as a standard and (DMSO) as control.

- The possibility of using the prepared compounds to dispose of free radicals, as they proved to have an excellent inhibiting activity compared to tannic acid as a standard solution and (DPPH) as control and using methanol as a solvent.
- Study of the bioactivity and toxicity assays of these compounds on human cells with breast cancer and the possibility of using them as drugs for the treatment of cancer disease. Palladium(II) and platinum(II) complexes with the azo-imidazole and azo-Schiff ligands were selected in conducting tests on the cancer cell line of breast cancer using the MTT assay, where it was found that the platinum complexes (PtL_1 and PtL_5) has a higher selectivity than the palladium complexes (PdL_2 and PdL_4) and depends on the value of (IC_{50}).

Recommendations

Based on the foregoing conclusions, the following recommendations can be proposed:-

- The possibility of preparing new azo-base Schiff ligands derived from homogeneous or heterocyclic compounds instead of salicylaldehyde to obtain a new type of azo-Schiff base ligands and study the resulting differences in coordination behavior.
- The use of azo-Schiff base ligands in analytical chemistry for spectroscopic estimation, or to extract the ions of the elements under study, because they have the ability to form color chelate complexes.
- Studying the biological effect of other types of bacteria, fungi, and cancers for these ligands and their complexes, especially those that contain in their composition components of known biological effects such as groups of fluorine, chlorine, and bromine.
- The possibility of using azo ligands in the field of industry as dyes that have high stability in the direction of moisture, light, and heat.
- Study of the thermal behavior of these ligands and their metal complexes.

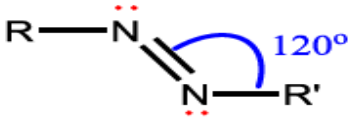
Chapter One - Introduction

1.1. General Introduction

Recently, researchers have been interested in azo compounds for their wide use in multiple fields due to their high stability, sensitivity, and high selectivity when interacting with many metal ions [1, 2], azo compounds have been used in many industrial fields [3], including agriculture [4], in addition to their biological effect in inhibiting the growth of bacteria and germs, which enabled them to be used as medicines in the field of medicine [5]. As for Schiff's bases, they are from the organic compounds that contain the azo-methane group, which are used in several fields, in the field of inorganic chemistry, ligands are used to form complexes with transitional and non-transition metal ions [6], in the field of biochemistry, its importance has emerged, and its use as anti-bacterial [7, 8], anti-fungal [9] and anti-cancer [10], among the organic compounds of wide popularity in this field are the derivatives of imidazole and benzimidazole, which have been used in the development of many anti-cancer drugs, anti-bacterial, anti-viral, fungi, and antihypertensive drugs [11], it was also used in the field of analytical chemistry [12] to detect many transitional and non-transition elements as organic ligands. Among the organic compounds of great importance in many fields are the azo and azo-Schiff compounds, which are known for their wide use in inhibiting the growth of bacteria and germs [13, 14] and anti-corrosion [15] and as organic reagents where they are used to detect many metal ions, whether they are transitional or non- transition and good extraction reagents for some transition element ions from aqueous solutions [16].

1.2. Azo Compounds

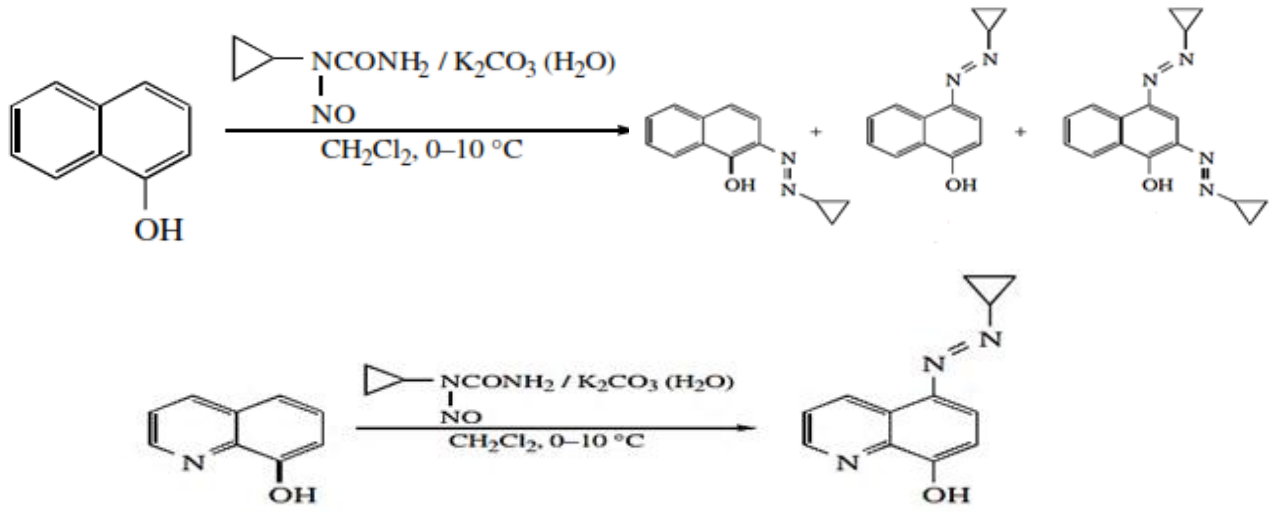
Organic compounds containing the azo bridge group bearing the formula (RN = N-R'), hybridization of an azo nitrogen atom, SP^2 where it exists in two types, one aromatic is stable due to resonance [17] between the aromatic rings and the other is unstable aliphatic and decomposes into nitrogen and hydrocarbon [18], as in figure (1-1).



R, R' = Aliphatic or Aromatic groups

Fig (1-1): Shows the position of the Trans isomer of the azo compound

In spite of this, there are many aliphatic azo compounds, so Tomilov and his group [19] were able to prepare the unstable diazonium salt of the compound N-cyclopropyl-N-nitrosourea in the presence of potassium carbonate and cooling and its coupling with 2-naphthol and 8-hydroxyquinoline to form stable azo compounds, as in scheme (1-1).



Scheme (1-1): Shows Preparation of the azo of the diazonium salt of the aliphatic compound N-cyclopropyl-N-nitrosourea

Azo compounds have bright, brilliant colors that vary according to their molecular structure and substituent groups on the aromatic rings, including yellow, orange, red, and green to blue [20]. Most of the azo compounds are stable dyes used in dyeing woolen and cotton fabrics and synthetic fibers [21], and some of them have a strong sensitivity to acids and bases and appear in each of them special colors that are clearly distinguished from each other for this reason they are used as indicators in analytical chemistry [22] not to mention its biological effect as an anti-fungal and anti-bacterial [23, 24] as it entered the pharmaceutical and drug industry to inhibit the action of germs [25], as an anti-cancer [26, 27], and played a key role in the field of chemical coordination in the formation of stable chelating complexes [28, 29], in addition to its important role in the field of green chemistry [30].

1.2.1. Classification of Azo Compounds

The azo compounds can be classified:

1.2.1.1. Depending on the Number of Azo Groups Included in Its Composition

1.2.1.1.1. Mono-Azo Compounds

This class of organic compounds includes one azo group that may coordinate with some metal ions through one of the two nitrogen atoms of the aforementioned group and thus these compounds behave as mono-chelated ligands as in the azobenzene compound, but if the compound contains electron-donating groups that can coordinate through their non-bonding-electronic pairs, then they can be classified into di-chelated ligands as in the ligand [7-hydroxyl-8-phenyl azo-1,3-disulfonic acid disodium naphthalene] [31], as in Figure (1-2), and tri-chelates as in two ligands (Z)-2-acetyl-2-(1-hydroxyethylidene)-1-(2-hydroxyphenyl)hydrazin-2-ium-1-ide and (Z)-2-

acetyl-1-(2-carboxyphenyl)-2-(1-hydroxyethylidene)hydrazin-2-ium-1-ide [32], as in Figures (1-3) and (1-4).

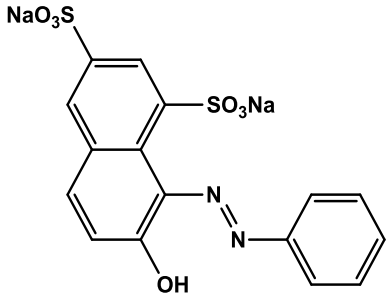


Fig (1-2): Shows structural formula of [7-hydroxyl-8-phenyl azo-1, 3-disulfonic acid disodium naphthalene]

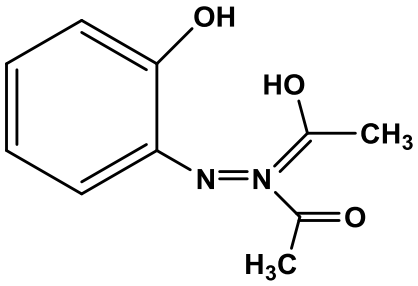


Fig (1-3): Shows structural formula of (Z)-2-acetyl-2-(1-hydroxyethylidene)-1-(2-hydroxyphenyl) hydrazin-2-ium-1-ide

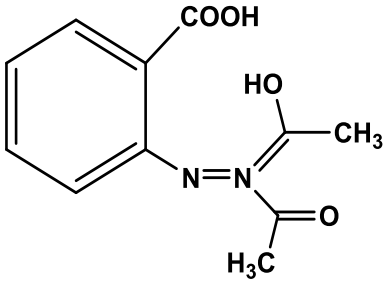


Fig (1-4): Shows structural formula of (Z)-2-acetyl-1-(2-carboxyphenyl)-2-(1-hydroxyethylidene) hydrazin-2-ium-1-ide

1.2.1.1.2. Di-Azo Compounds

These compounds contain two azo groups linked on either side by homogeneous or heterogeneous organic rings, so the name differs at that time, and depending on the type of rings and the nature of the donor atoms, Tanushri was able to prepare 2,6-di(phenyl diazo)pyridine [33], which its formula is given in figure (1-5).

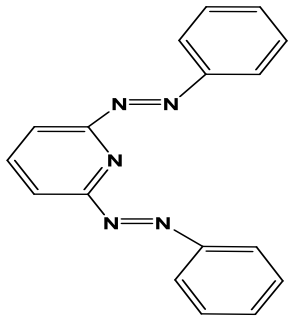


Fig (1-5): Shows structural formula of 2, 6-di (phenyl diazo) pyridine

These compounds are prepared from the reaction of one mole of the diaz onium salt of a diamine compound with a two mole of a coupling component compound, taking into account the control of the acidity function. Many di-azo ligands have been prepared for amino-base bases and at a relatively low acidity function (pH<5) but if the base of phenolic pairs is chosen, the pairing process must be completed in a base medium (pH >8), an example of these types of ligands is the compound 2,2-((H1-1,2,4-triazole-3,5-diyl)bis(diazene-1,2-diyl))bis(benzene-1,3,5-triol) [34], it has the following formula in figure (1-6).

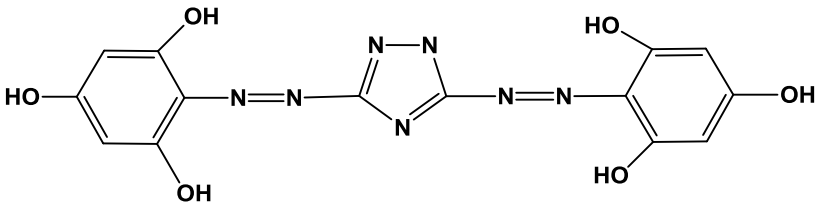


Fig (1-6): Shows structural formula of 2,2-((H1-1,2,4-triazole-3,5-diyl)bis(diazene-1,2-diyl))bis(benzene-1,3,5-triol)

1.2.1.1.3. Multi-Azo Compounds

This type of ligands include three or more azo-bridge groups linked together by similar or different aromatic rings and may contain substituted groups of different chemical nature, whether acidic or basic, these groups may also differ in the positions of their substitution on the rings, the compound example shown in figure (1-7) [35].

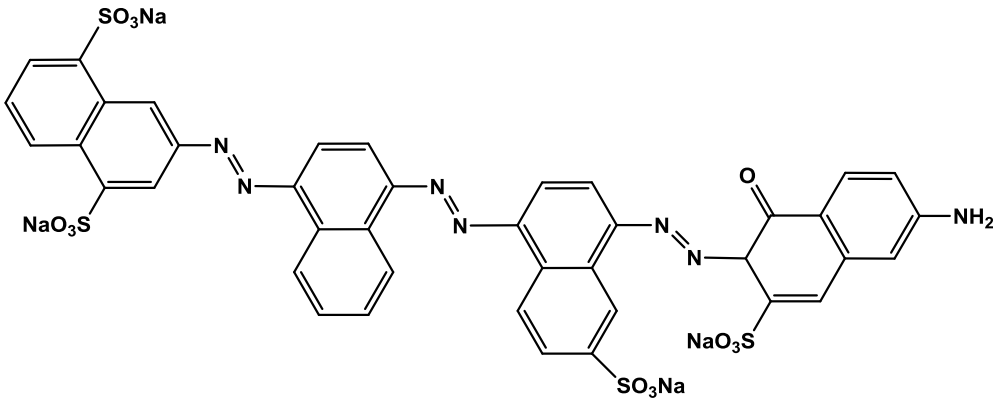


Fig (1-7): Shows structural formula of sodium 3-((E)-(4-((E)-(4-((E)-(6-amino-1-oxo-3-sulfonato-1, 2-dihydronaphthalen-2-yl) diazenyl)-6-sulfonatonaphthalen-1-yl) diazenyl) naphthalen-1-yl)diazenyl)naphthalene-1,5-disulfonate

An example of a tetra-azo ligand is (Tetrakis azo), and its structural formula is shown in figure (1-8) [20]:

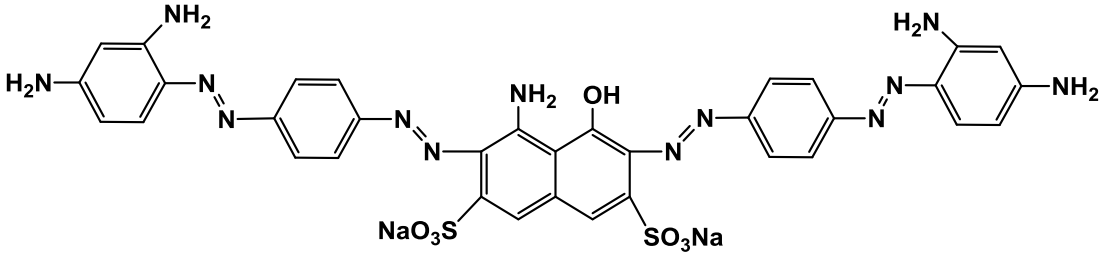


Fig (1-8): Shows structural formula of sodium 4-amino-3, 6-bis ((E)-(4-((E)-(2, 4-diaminophenyl)diazenyl)phenyl)diazenyl)-5-hydroxynaphthalene -2,7-disulfonate

1.2.1.2. Depending on the Type of Rings Connected at the Ends of the Azo Group of Bridges

1.2.1.2.1. Homocyclic Azo Compounds

In this type of compound, the bridge azo group is linked to two homogeneous rings that do not contain heteroatoms such as (O, N, and S) and may not contain substitutes, the simplest type of these compounds is azo benzene, whose formula is shown in figure (1-9) [36]: -

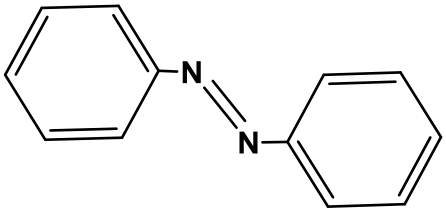


Fig (1-9): Shows structural formula of azo benzene

In addition, this type is limited in effectiveness because of the lack of sites for bonding, but the bonding is through the azo bridge group, which is the only site available for bonding with metal ions if these compounds are free of compensated groups.

The aromatic rings may be substituted by one or more acidic or basic groups (OH, -COOH, -SH, -NH_2, -NHR-) and others. A simple example of this type of compound is the 4, 5-dihydroxy-3- (Phenylazo)-2, 7-Disodium Naphthalene Sulfonic Acid (HPASASN) [37], as shown in its structural formula in figure (1-10).

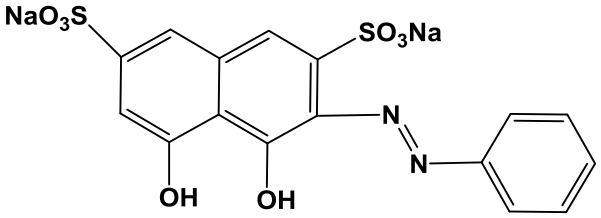


Fig (1-10): Shows structural formula of 4, 5-dihydroxy-3-(Phenylazo)-2, 7-Disodium Naphthalene Sulfonic Acid

1.2.1.2.2. Heterocyclic Azo Compounds

The use of this type of ligand has become popular in recent times due to its distinct properties, as it is coordinated through the nitrogen atom of the azo group with the metal ion, which has an empty orbital with an energy symmetry similar to the orbital of the ligand donor atom, and if these ligands contain one substituted group or more in a suitable location for the azo group that qualifies for consistency through which it produces a chelating ligand [38].

The simple examples of this type of ligands are the ligands (E)-5-amino-4-(4-(dimethylamino)phenyl(diazinyl)-1H-pyrazole-3-ol and (E)-5-amino-4 -((4-(Dimethyl amino)phenyl(diazinyl)-1-phenyl-1H-pyrazole-3-ol [39], these formulas is given in figures (1-11) and (1-12).

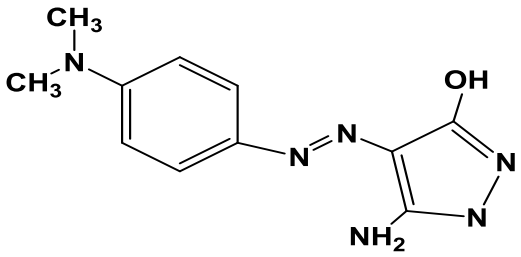


Fig (1-11): Shows structural formula of (E)-5-amino-4-(4-(dimethylamino) phenyl (diazinyl)-1H-pyrazole-3-ol

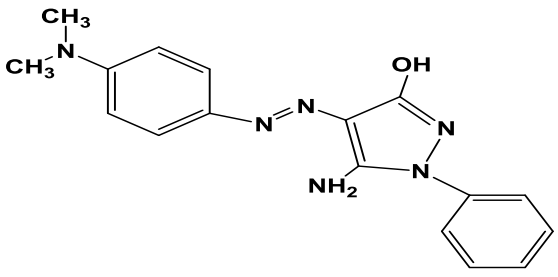


Fig (1-12): Shows structural formula of (E)-5-amino-4 - ((4-(Dimethyl amino) phenyl (diazinyl)-1-phenyl-1H-pyrazole-3-ol

As for the azo compound 2-[(4-aminoantipyrene) azo [naphthol], it is a clear example of a heterogeneous pentagonal dinitrogen ring ligand, as shown in its structural formula in figure (1-13) [40]:-

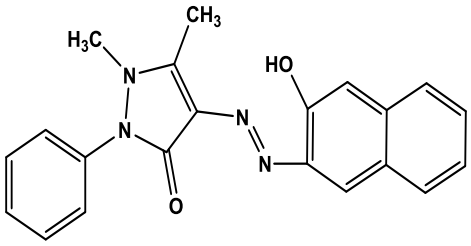


Fig (1-13): Shows structural formula of (E)-4-((3-hydroxynaphthalen-2-yl) diazenyl) - 1, 5-dimethyl-2-phenyl-1, 2-dihydro-3H-pyrazol-3-one

A simple example of the compound heterocyclic pentagonal ligand [11], as shown in its structural formula in figure (1-14).

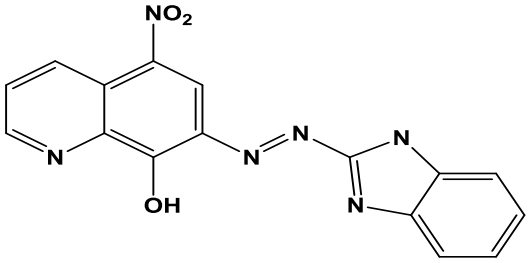


Fig (1-14): Shows structural formulaof 7-((1H-benzo [d]imidazol-2-yl) diazenyl)-5-nitroquinolin-8-ol

The pentagonal ring may contain two different hybrid atoms, such as nitrogen and sulfur, such as 1-(4-amino-(3-benzothiazole) azo) acetophenone [41], whose formula is shown figure (1-15).

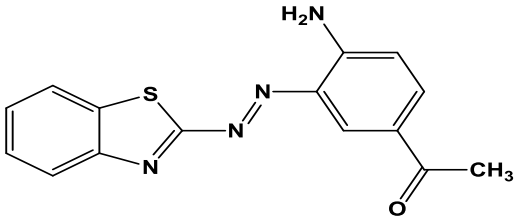


Fig (1-15): Shows structural formula of 1-(4-amino-3-(benzo[d]thiazol-2-yldiazenyl) phenyl)ethanone

Also, the compound 5-[5-mercapto-(1, 2, 4-triazolyl azo)-2, 4-dihydroxybenzaldehyde] [42] with the following structural formula is one of the simple examples of the heterocyclic pent acyclic ligand, whose formula is shown in figure (1-16).

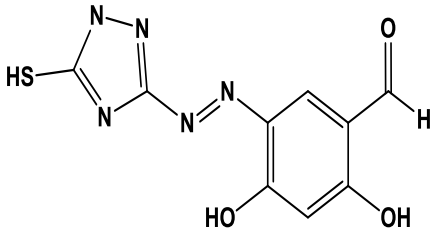


Fig (1-16): Shows structural formula of 2, 4-Dihydroxy-5-[(5-mercapto-1H-1, 2, 4-triazole-3-yl) diazenyl] benzaldehyde

There are heterocyclic ligands of the hexagonal ring of pyridine [43, 44], whose structural formulas are shown in figures (1-17) and (1-18).

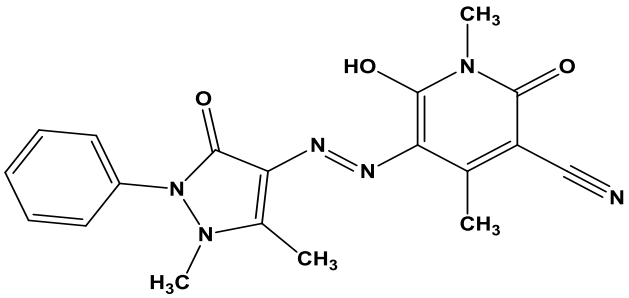


Fig (1-17): Shows structural formula of 5-[(1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-yl) diazenyl]-6-hydroxy-1, 4-dimethyl-2-oxo-1, 2-dihydropyridine-3-carbonitrile

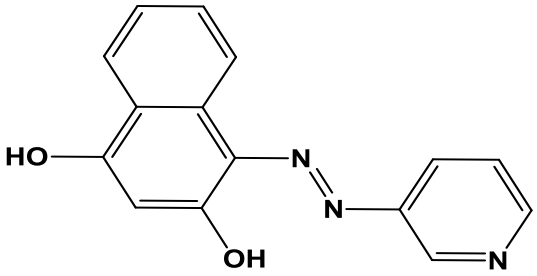


Fig (1-18): Shows structural formula of (E)-4-(pyridine -3-yldiazenyl) naphthalene-1, 3-diol

1.2.2. Some Methods of Preparing Azo Compounds

Researchers have been finding new and multiple ways to obtain these compounds at a high rate, due to the importance of azo compounds from an academic and applied point of view, and the following are some of the methods used in preparing these compounds.

1.2.2.1. The Classic Traditional Method

This method is one of the most widely used and common methods for its ease of preparation. It includes two steps:

1.2.2.1. a. Diazotization

This step includes the preparation of diazonium salts resulting from the reaction of the primary amine with sodium nitrite $NaNO_2$ dissolved in a dilute solution of HCl or H_2SO_4 acid at a temperature (0-5) ^0C. This reaction is called diazotization [45, 46], and it can be represented by the following equation:-

$$ArNH_2 + NaNO_2 + 2\,HX \xrightarrow{(0\text{-}5)^oC} ArN_2^+X^- + NaX + 2\,H_2O$$

X= (Cl, Br, NO_2, HSO_4, etc….)

This reaction is one of the exothermic reactions, and all the reactants and the resulting substances are in an ionic state in the aqueous solution. The nitrification reaction takes place at pH < 2 as the high pH works to return the enilinium ion to the original amine that is slightly soluble in water unless it contains effective groups in addition the lack of acidity leads to the reaction of the formed diazonium salt with the unreacted amine. the amount of sodium nitrite should be equivalent to the primary amine, as its increase leads to an increase in the amount of nitrous acid, which affects the stability of the resulting diazonium salt, and to break down the excess of nitrous acid, urea is

used (which reacts slowly). The isolation of diazonium salts is relatively slow and characterized by its instability, as it is rarely isolated, so it is used immediately after preparation in solution.

1.2.2.1. b. Coupling

In this step, the diazonium salt prepared in the previous step is reacted with the coupling component, which is often homogeneous or heterocyclic aromatic compounds, as in the reaction of the diazonium salt produced from the denitrification of omoxylene with -1-naphthol-4-benzene [47], the following figure (1-19) shows the structural formula of the prepared azo compound.

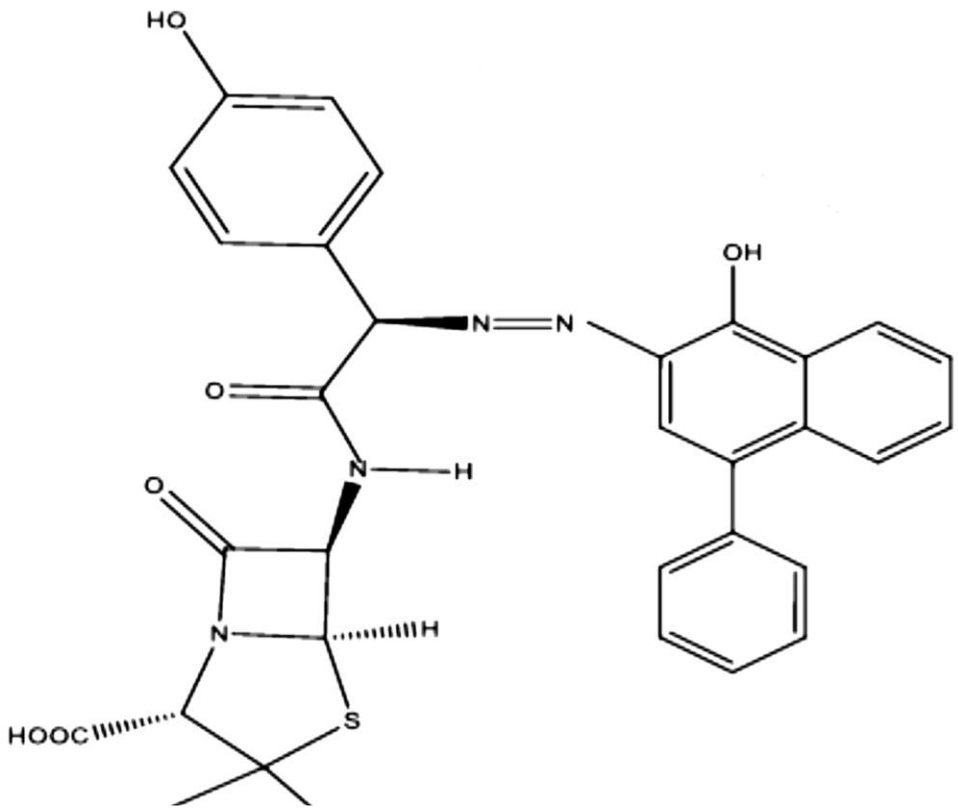
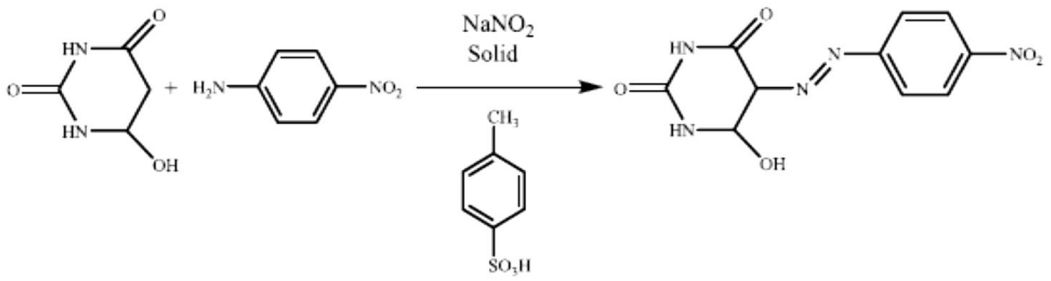


Fig (1-19): Shows structural formula of a heterocyclic azo compoundderived from omoxylene

1.2.2.2. Solvent Exclusion Method

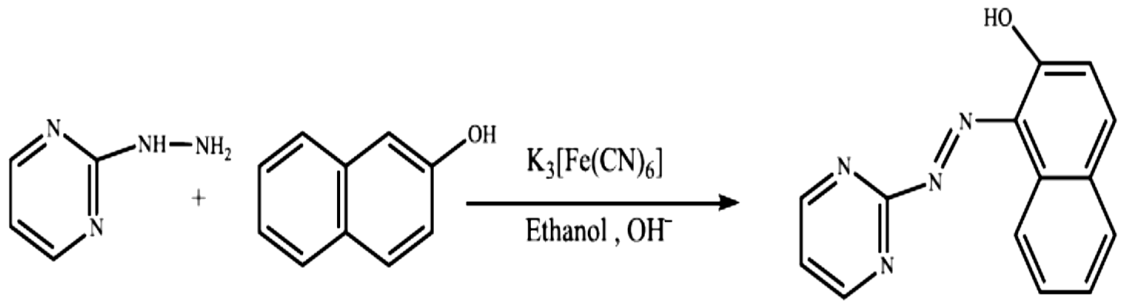
This method includes grinding the primary amine with sodium nitrite $NaNO_2$ in its solid state at room temperature and in the presence of para methyl sulfonic acid, followed by adding the resulting diazonium salt with coupling component [48], as shown in the following scheme (1-2).



Scheme (1-2): Shows azo compound prepared by thesolvent exclusion method

1.2.2.3. Couples Method Using the Oxidation Process

Several heterocyclic azo compounds were prepared in this way, as researcher S.V. Hunig [49] was able to prepare a heterocyclic azo compound by reacting naphthol (coupling base) in ethanol solvent with 2-hydrazaninopyrimidine in the basic medium and using Potassium ferricyanide as an oxidizing agent, as shown in the following scheme (1-3).



Scheme (1-3): Shows azo compound prepared by the couplingmethod using oxidation

1.3. Imidazole Chemistry

Imidazole is one of the compounds found in chemical and biological systems, and it is a planar molecule consisting of a five-membered ring containing three carbon atoms and two nitrogen atoms, where two nitrogen atoms are present in the 1 and 3 positions [50, 51], and the nitrogen atom in the (1) position is pyrrole of type (N). While the nitrogen atom in position (3) is pyridine of type (N3, 1), as shown by the structural formula in figure (1-20).

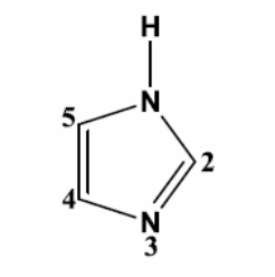


Fig (1-20): Shows the structural formula of Imidazole ring

The designation of the regular imidazole molecule is 1, 3-diazole, where one of the two nitrogen atoms is attached to a hydrogen atom. One of the properties of imidazole is that it has the ability to dissolve in water and other polar solvents and exhibits amphoteric behavior due to the presence of the lone pair of electron on the nitrogen atom, which gives it the basic properties and at the same time contains one proton capable of losing it easily and this makes it have acidic properties and is less acidic than carboxylic acids and amides, but more acidic than alcohols [52]

Imidazole is an important type of heterocyclic aromatic compound that is involved in many chemical and biological fields; The process of introducing the imidazole molecule in the process of preparing compounds has been of great importance, especially in the field of medicine, during the past decade, imidazole derivatives occupied a unique and distinguished position in the

field of medicinal chemistry, as they have a wide range of biological activity, which are well-known analgesics, anti-inflammatory antibiotics, platelet aggregation inhibitors, and anti-epileptic drugs, and can be found in many other drug combinations such as Cimetidine, Flumazenil, and Decarbonize. Imidazole compounds and their derivatives are used in various fields, as brightly colored azo-imidazole dyes are used in dyeing wool, cotton, rubber, and (polyester), as well as antioxidants and cofactors in many important industries. They are also considered antibacterial [53].

1.3.1. Imidazole Azo Compounds- Structure, Importance and Application

Azo-imidazole compounds are highly effective heterocyclic aromatic compounds that have different atoms such as nitrogen and oxygen that contribute to bonding with different elements and that a small amount of these elements inhibit biological activity. It has an important role in the field of spectral determination to estimate very small quantities of elements, especially ions of transition elements, due to the high sensitivity and selectivity of this type of compound towards ions of transition elements, such as the compound 1- alkyl-2(naphthyl-alpha-azo) imidazole [54], as shown in the Figure (1-21).

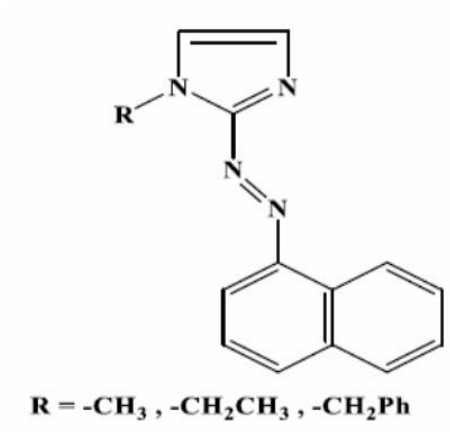


Fig (1-21): Shows the structural formula of 1- alkyl-2(naphthyl-alpha-azo) imidazole

One of the essential features of Azo-imidazole compounds is that it contains an azomethine group (N=N-C=N-) and one of the benefits of this group is its use in stabilizing the low-oxidation state of metals when they are linked with azo ligands. Towards oxidation and reduction, as shown in the palladium complex with a ligand 1- alkyl-2(naphthyl-para-azo) imidazole [55], as shown in the Figure (1-22).

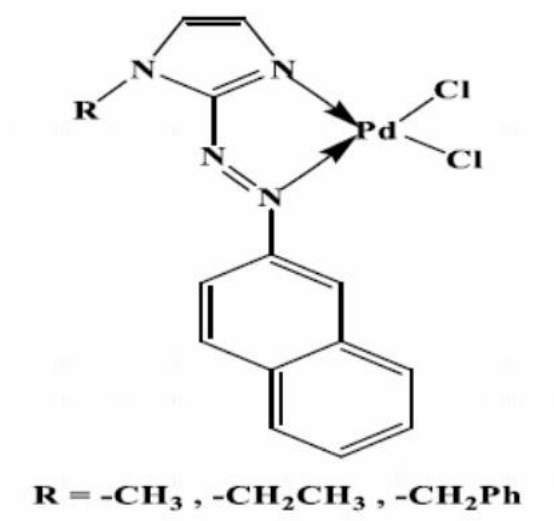


Fig (1-22): Shows the structural formula of palladium complex with a ligand 1- alkyl-2(naphthyl-para-azo) imidazole

Among the things that have been invested in azo-imidazole ligands and their metal complexes is the dominant characteristic color in organic and aqueous solutions in the field of analytical chemistry, as well as another important characteristic of azo-imidazole compounds, which is a selective complexity with positive ions of some ions of selective elements, where some ions of transitional elements were extracted, such as binary cobalt by solvent extraction in the form of an ionic atomic complex using the compound 2-[2-(1,4- dimethyl phenyl) azo]- imidazole [56], the composition of which is shown in the Figure (1-23).

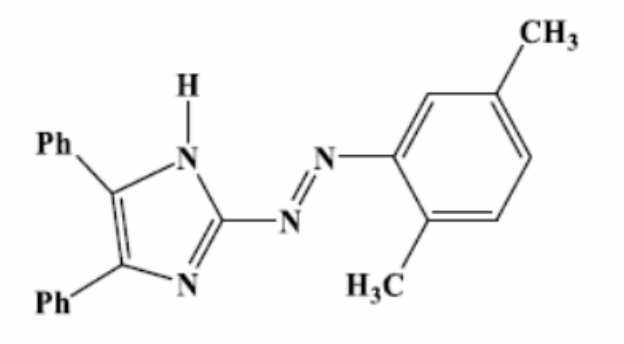


Fig (1-23): Shows the structural formula of 2-[2-(1, 4- dimethyl phenyl) azo] - imidazole

The azo-imidazole aromatic compounds are used in the field of acidic and basic indicators, as many of these compounds were prepared in the form of chelating reagents, spectroscopic analysis was studied and the quantification of elements was determined. These complexes have the ability to bind with the DNA bases of cancer cells through N-N-chelating bonds [57, 58].

In the field of industry, a large number of polymeric dyes of the type polyazoimidazole, which contains azobenzene, have been prepared, as well as in optical data storage applications and optical electrolyte switches, as the azo-optical compounds reflect light when exposed to rays and show cis and trans isomers when exposed to radiation. During thermal relaxation, this causes a change in the properties of the molecules [59]. The process of change in chemical and physical properties as a result of exposure to radiation occurs widely in the field of optics and optoelectronics [60].

1.3.2. Biological and Chemical Significance of Imidazole Residential Complexes

The imidazole compound is characterized by having a very good pharmacological benefit, as it was discovered that there is a possibility of

using it as medicine in the treatment of cancer and types of microorganisms such as viruses and bacteria. Studying its pharmacological effects, where imidazole was used as an anti-cancer. Recent research has been able to prepare compounds called nucleosides derived from (Tiazofurin), and it was found that the imidazofurin compound has the ability to treat cancer [61]. In addition, many other compounds containing imidazole were prepared, and the results of the tests showed that these compounds have a strong effect [62]. As it has been shown that these compounds have the ability to treat different types of cancers such as leukemia, lung cancer, neck cancer, as well as liver enlargement, and there are many of these important compounds, such as (pentacyclicnaphthalimides) [63]. In addition, new imidazole compounds were prepared, as these compounds showed their effectiveness against breast cancer, as the results showed that the nature of the chemical group's presents within the structure of the compounds has a major role in determining the effectiveness of these compounds. If this group was basic, these compounds had great effectiveness in limiting the spread of this disease[64], as well as lymphoma cell cancer, among these compounds 2-naphthyl-1-(3,4,5-trimethoxyphenyl)-1H-imidazole[65], whose formula is shown in the following figure (1-24).

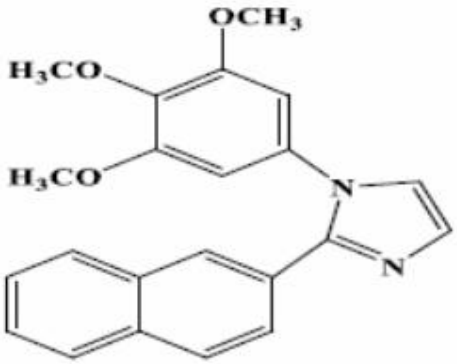


Fig (1-24): Shows the structural formula of 2-naphthyl -1-(3, 4, 5-trimethoxyphenyl)-1*H*-imidazol

Imidazole was also used as an inhibitor of the carboxypeptidase enzyme, as it is one of the important enzymes that produce carboxypeptidase in the pancreas. This enzyme plays an essential role in many vital processes in the human body, including digestion and blood clotting. To eliminate this problem, compounds containing imidazole were prepared in their composition, which proved to be highly effective against carboxypeptidase enzyme inhibitors. Among these compounds is the compound 2-(4-imidazoyl) hydrocinnamic acid [66], whose formula is shown in the following figure (1-25).

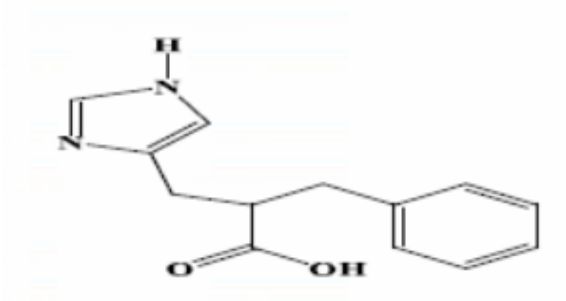


Fig (1-25): Shows the structural formula of 2- (4-imidazoyl) hydrocinnamic acid

In addition, imidazole was used as an inhibitor of the heme oxygenase enzyme. To address the problem of inhibiting the heme oxygenase enzyme, new imidazole compounds were prepared, which, after conducting tests, proved to have great efficacy against the heme oxygenase inhibitor. Among these compounds is the compound 2-oxy-floro 1-(1H-imidazol-1- yl)-4-phenylbutanes [67], whose formula is shown in the following figure (1-26).

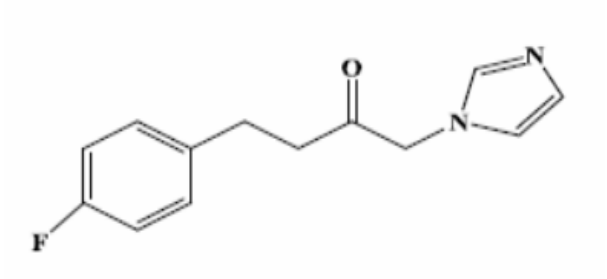


Fig (1-26): Shows the structural formula of 2-oxy-floro 1-(1H-imidazol-1- yl)-4-phenylbutanes

Imidazole was also used as an antidote to stroke and heart attacks, as new compounds were prepared containing imidazole, an imidazole acid derivative, where it was found that it had good anti-thrombotic efficacy. Among these compounds is the compound cyclic amino alkyl imidazole acetic acid [68], whose formula is shown in the following figure (1-27).

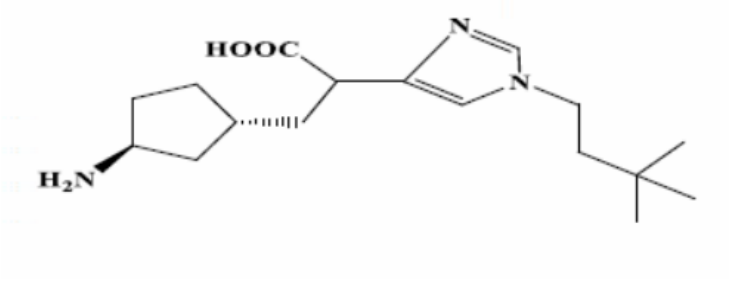


Fig (1-27): Shows the structural formula of cyclic amino alkyl imidazole acetic acid

In addition, imidazole was used as an anti-inflammatory, as new compounds containing imidazole were prepared, which were found to be effective in treating infections. Among these compounds is 7-methyl-5-thioxo-1, 5, 6, 7, 8, 8a-hexahydroimidazo [1, 2-f] pyrimidine-2, 3-dicarbonitrile [69], whose formula is shown in the following figure (1-28).

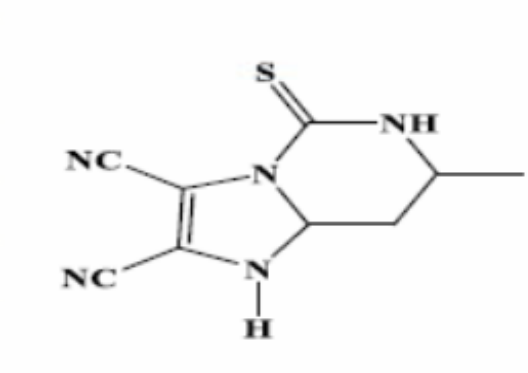


Fig (1-28): Shows the structural formula of 7-methyl-5-thioxo-1, 5, 6, 7, 8, 8a-hexahydroimidazo [1, 2-f] pyrimidine-2, 3-dicarbonitrile

In addition, imidazole was used as an antibacterial, as it is known that work in the field of antibiotics is one of the most important fields in the field of medicine. Its predecessors and the most important types of bacteria that imidazole compounds are used to eliminate are ***(Escherichia coli spp)*** and ***(Staphylococcus aureus spp)***. Among these compounds is the compound 1-(3-chlorophenyl)-5-(4-phenoxyphenyl) pyrazole [70], whose formula is shown in the following figure (1-29).

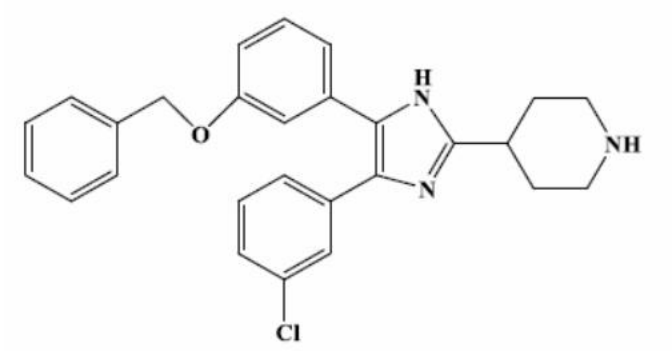


Fig (1-29): Shows the structural formula of 1-(3-chlorophenyl) -5-(4-phenoxyphenyl) pyrazole

1.4. Schiff's Base

The organic compounds that contain in their chemical structures the azomethine group (C=N) as an active group are known as Schiff bases [71], and its name is due to Hugo Schiff [72], who is credited with preparing the first organic compound containing in its composition the azomethine group (-C=N-), from the reaction of condensation of some carbonyl derivatives with primary amines in different solvents that have the ability to pull water molecules, these compounds are characterized by the general formula (R''R'C=NR) and each (R' and R'') represents an aliphatic or aromatic group or a hydrogen atom, and when (R) represents a substituted or unsubstituted benzene ring, the Schiff bases are called an anilates or benzanyls [73]

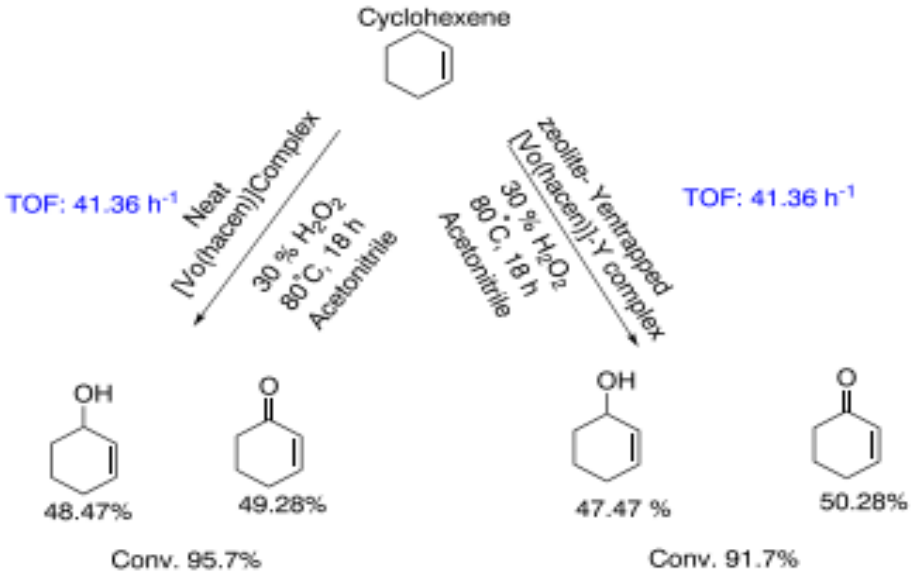
Schiff bases have many physical and chemical properties that qualify them to enter into many applications, such as bonding with many ions of elements to form complexes or preparing ring-closure derivatives, which have proven their usefulness in many practical applications in several fields [74], as researchers in recent years have focused their studies on their use as catalysts in the fields of organic and industrial chemistry [75]. The effectiveness of Schiff's bases may be attributed to the presence of a non-symbolic sp^2-hybridized electron pair of the nitrogen atom of the aforementioned azomethine group.

Schiff bases have many advantages, the most important of which is relatively high stability, and this stability is related to the compounds needed to prepare these bases (carbonyls and amines) in terms of aromatic properties, which are often solids. It has relative thermal stability [76]. While Schiff bases derived from aliphatic compounds [77] were characterized by their liquid properties. The stability of the aromatic Schiff bases is attributed to the resonance state of the linked groups on both ends of the azomethine group [78]

Many of these bases were used as ligands for the presence of the azomethine group and were classified under the name of a ligand (donor-acceptor) [79] in order to give it a partial charge of the electron pair of the nitrogen atom of the group referred to above by the σ-Donor bond which leads to an increase in the density electron on the atom or metal ion, which leads the ion to return part of the excess charge to the orbital (π*) of the azomethine group (C=N), then it is true to call it the ligand (π-Acid ligand).

The importance of paying attention to the development of Schiff bases lies in their multiplicity of use in many areas, so we preferred to mention some of them:

In the industrial field, it was found that some of them have an important effect in inhibiting the corrosion process [80], and others as an accelerator for hardening rubber [81], and some of the complexes of Schiff bases related to polymers [82] have an effect on the decomposition of hydrogen peroxide and the oxidation of ascorbic acid, or as a catalyst in the oxidation of many From organic compounds [83], where the scheme (1-4) shows oxidation of cyclohexane to alleles using Schiff base complexes



Scheme (1-4): Shows oxidation of cyclohexene to corresponding allylic products

In the field of analytical chemistry, it has been used in the manufacture of selective electrodes for many metal ions [84]. In the qualitative and quantitative determination of many metal ions, for their ability to form stable and colored aggregate complexes [85], and in the field of extraction, some of them were used in the extraction of uranium (VI) and thorium (VI) [86].

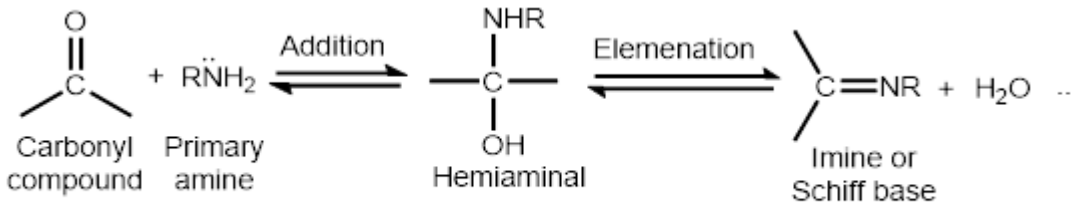
The importance of Schiff bases and their complexes has increased after the application of many of them in the medical and pharmaceutical fields, due to their high impact in this vital aspect, as many of them found effectiveness against microorganisms, such as the effect of Schiff bases derived from heterocyclic ketones [87] and the effect of quaternary molybdenum and binary manganese complexes of Schiff base derived from hydrazine carboxamide and hydrazine carbothiamide [88] on (***E.coli spp*** and ***X.Compestris spp***) bacteria, and the mono silver [89] had a significant effect on (***Cucumber mosai)c*** virus.

Schiff bases describe thiazole derivatives [90] as having high activity as anti-inflammatory and analgesic, and complexes of Schiff bases of (Co, Ni, Cu, and Zn) elements of Schiff bases produced from salicyldehyde and 2,4-dihydroxybenzaldehyde [91] with the amino acids glycine and alanine have antitumor activity and in the order Co>Zn>Cu>Ni, and the azo-Schiff-aryl base derivatives have a high inhibitory activity against cancer cells [92].

1.4.1. Methods of Preparing Schiff Bases

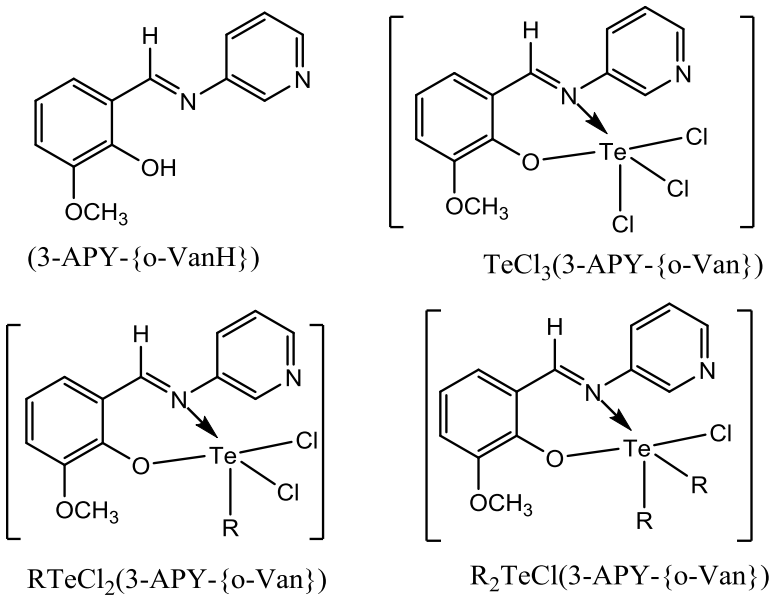
The methods of preparing Schiff- bases differ according to the nature of the reactants materials for the reaction and the physical conditions of pressure and temperature, in addition to the role of the catalyst to obtain a higher product percentage. Below we explain the necessary methods for preparation.

1.4.1.1. Preparation of Schiff bases by condensing stoichiometric amounts of aldehydes or ketones (aliphatic or aromatic) with primary, aliphatic, aromatic amines or ammonia, in the presence of glacial acetic acid or hydrochloric acid as a catalyst [93, 94]. It is the most common method for preparing Schiff bases, while it should be noted that this method has been used to detect or quantify aldehydes or ketones, as well as to purify amino or carbonic compounds or protect these groups [95], the mentioned preparation method shown in the following scheme (1-5).



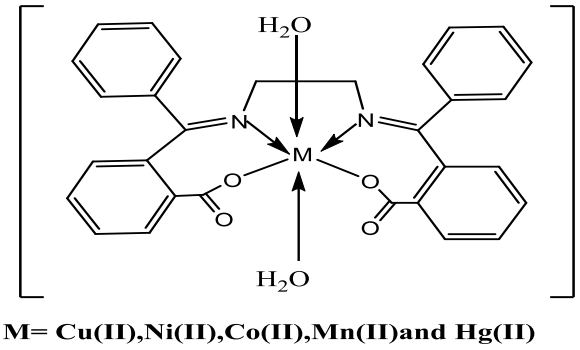
Scheme (1-5): Shows the preparation method of Schiff-base

Malik etal [96] were prepared a Schiff base by reaction of O-Vanillin with 3-aminopyridine, from which he was able to prepare several quaternary tellurium complexes and characterized them by spectroscopic methods, as he suggested the geometrical form (Two-dimensional trigonometric pyramid with pentagonal coordination) for its prepared complexes in addition to studying its biological activity, whose formula is shown in the following figures (1-30).



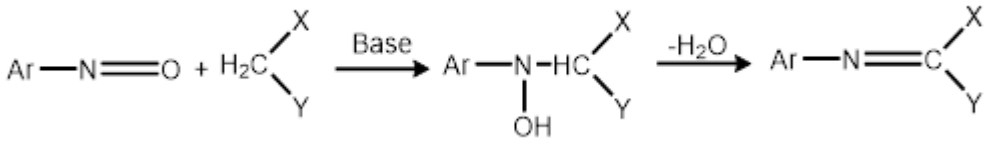
Figs (1-30): Show the structural formula of quaternary tellurium complexes

From the condensation of benzoic acid 2-benzoyl with ethylene diamine it was possible to prepare a new base [97], where many complexes of this base were prepared for the ions of manganese, cobalt, nickel, copper and mercury with a positive charge, with measurements of the biological activity of many bacteria and fungi whose formula is shown in the figure (1-31).



Figs (1-31): Show the structural formula of prepared complexes

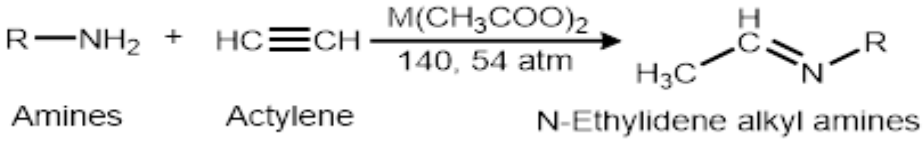
1.4.1.2. Schiff bases are prepared from condensing aromatic nitrous compounds and compounds containing a reactive methylene group such as malonic esters, beta-ketone esters (β-ketoesters), and fluorine's and β-dike tones in a basic environment to give the intermediate hydroxylamine derivatives followed by the withdrawal of the water molecule to obtain the azomethine group, and bases (sodium hydroxide, carbonate or pyridine) were used for the desired purpose [98]. As the scheme (1-6) shows the course of the reaction.



X, Y=Electron withdrawing groups

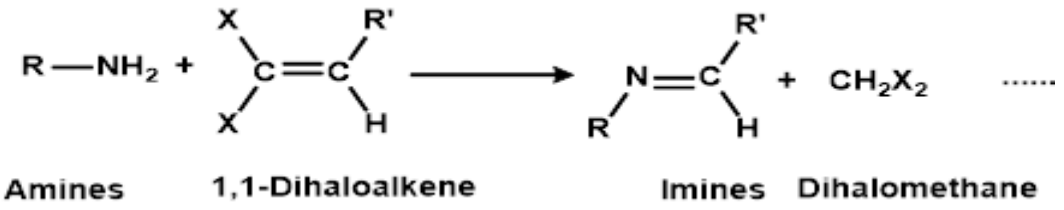
Scheme (1-6): shows the course of the reaction to prepare Schiff-base

1.4.1.3. The reaction of acetylene [99] with primary amines under vigorous conditions of high temperature and pressure and in the presence of acetate salt of some (IIB) elements as catalysts to prepare Schiff bases, as shown in the following scheme (1-7).



Scheme (1-7): shows the course of the reaction to prepare Schiff-base in the presence of acetate salt of some (IIB) elements as catalysts

1.4.1.4. Di-halide alkenes can be used as a starting material prepared of Schiff bases when reacting with secondary amines [100] and the scheme (1-8) can explain the reaction process.



Scheme (1-8): shows the course of the reaction to prepare Schiff-base by using di-halide alkenes as a starting material

1.4.2. Schiff Bases Derived From Salicyladehyde

Salicyladehyde can be classified as a monomeric di-chelated ligand of the type (O, O) that has the ability to bond with the represented transitional metal ions and form chelate complexes. A simple and well-known example of the above is the complex of the mentioned organic molecule with the beryllium ion (II), and its composition is a tetrahedral complex with the stereoscopic shape shown in figure (1-32).

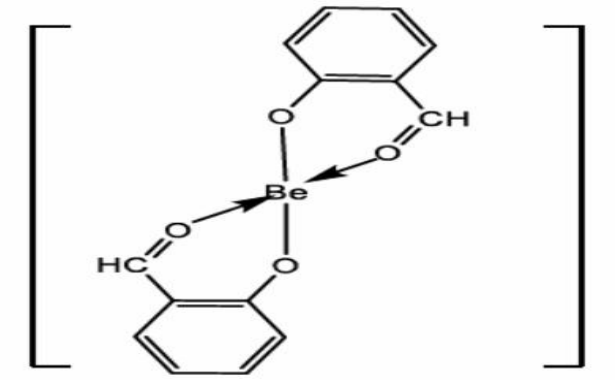
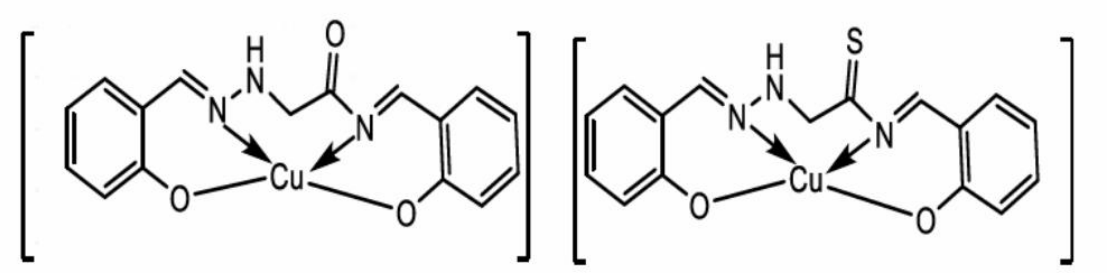


Fig (1-32): Shows the structural formula of the Beryllium complex

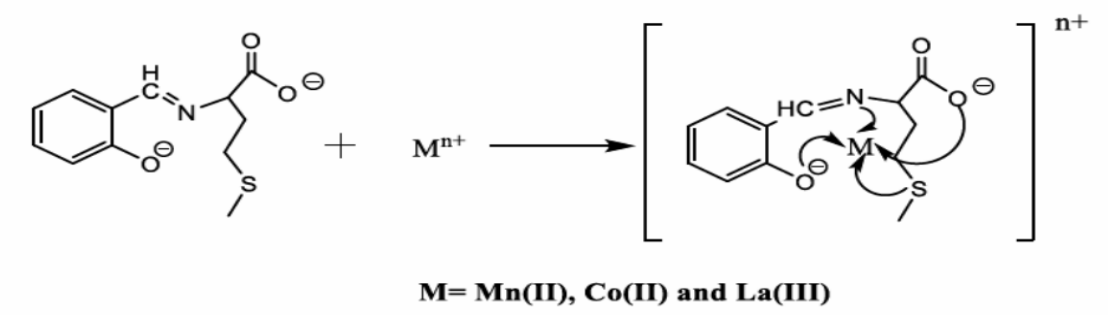
Shamly, et al, [101] prepared a series of Schiff bases derived from the condensation of salicylaldehyde with aniline, ethylene diamine, and 3-aminobenzoic acid in an aqueous medium, also, their complexes were prepared with positively charged magnesium and nickel ions. The ligands and their chelating complexes were tested for their biological activity. They were selected for this purpose, and the metal complexes outperformed their ligands in their ability to inhibit these vital organisms.

As for the researcher Md Saddam [102], he prepared two Schiff bases from the reaction of salicylaldehyde with semicarbazide and thiosemicarbazide, and then reacted these two bases with the copper ion (II). The thermal behavior of these two complexes was studied to knowledge of the dissociation steps, as well as their biological activity. Figure (1-33) shows the thermal formula for both the aforementioned complexes.



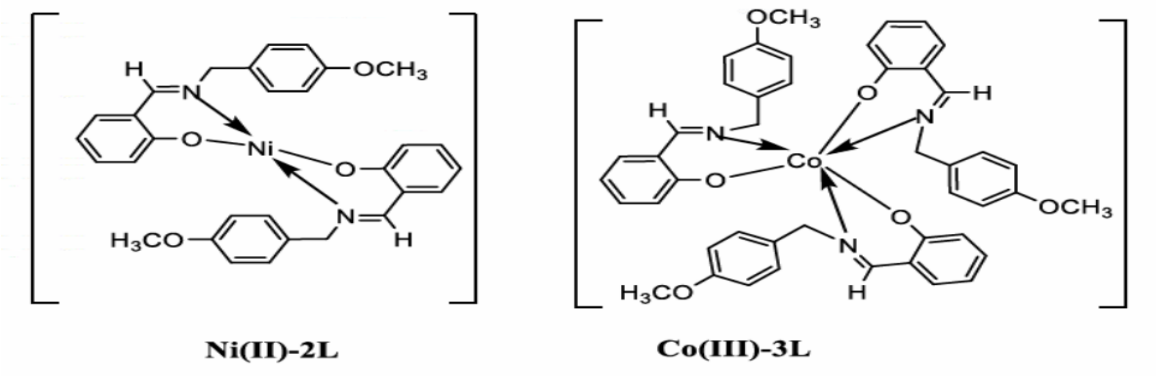
Figs (1-33): Show the thermal formula for the mentioned complexes

Shaiful, et al, [103] prepared a series of chelating complexes of internal and external transition metal ions, which are divalent manganese, cobalt, and trivalent lanthanum with a Schiff-base ligand derived from the condensation of salicylaldehyde with amino acid (methionine). The prepared chelate complexes were characterized by several spectroscopic and analytical techniques, scheme (1-9) shows the geometrical formula for the prepared complexes.



Scheme (1-9) shows the geometrical formula for the prepared complexes

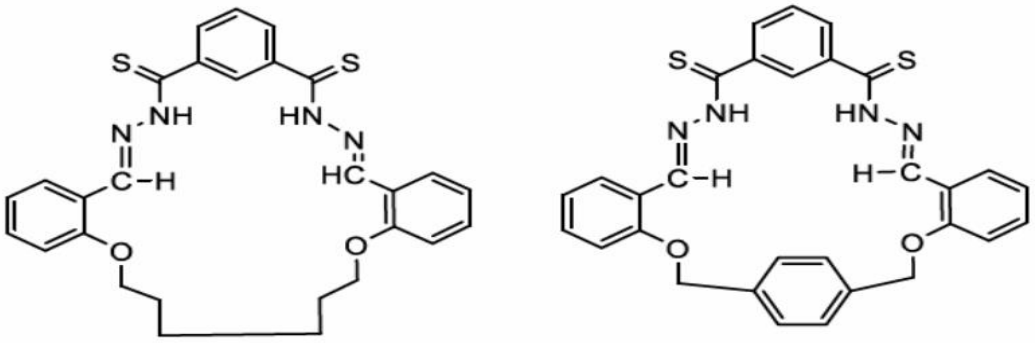
In another recent study, Ali, et al, [104] prepared metal complexes for the two positively charged nickel and triple positively charged cobalt, which are derived from the two-chelated azomethine ligand of type (N, O), It was prepared from salicylaldehyde with 4-methoxybenzylamine. Identification of the ligand and its chelate complexes with the infrared, ultraviolet-visible spectrum, ^{1}HNMR spectrum, and the ^{13}C spectrum, as well as the calculation of the percentage of elements in their compounds (C.H.N), figures (1-34) show the two forms of the aforementioned complexes .



Figs (1-34): Show the structural formula of the Nickel and Cobalt complexes

The ligands of the large rings have had great luck in terms of their preparation and use, Hamid [105] was able to prepare several large rings of Schiff- bases derived from 1, 3-di-thiocarbohydrazide, which proved their biological activity against selected types of bacteria, as well as their

feasibility in inhibiting corrosion processes. The structural formula of this type of two ligands is presented in figures (1-35).



Figs (1-35): Show the structural formula of the large rings of Schiff-bases derived from 1, 3-di-thiocarbohydrazide

1.5. Azo-azomethine Compounds

1.5.1. Methods of Preparing Azo-azomethine Compounds

Azo- Schiff or azo-azomethine are those organic compounds that contain in their chemical structures both active groups (azo-bridge) and (azomethine), and they are relatively recent compounds when compared to azo compounds and Schiff bases [106]. In addition, when we look at the composition of the two groups, we find that both of them have a nitrogen atom with a non-contact electron pair that gives them many properties. There are three general methods for preparing these types of ligands, which are:

1.5.1.1. The azo compound is first prepared from the preparation of the aromatic diazonium salt, followed by a condensation step with a carbonyl compound. Naturally, the resulting azo-Schiff base compounds differ according to the groups of azomethine, and it is the most famous method for preparing such compounds.

Tuncel and Serine [83] prepared the azo-Schiff compound by coupling the diazonium salt of 2-hydroxy aniline (and its chlorine derivative) with 4-

amino 5-hydroxy2, 7-naphthalene sulfonic acid and then condensing with ortho-vanillin to prepare the azo- Schiff and the preparation of many of its metallic complexes, whose formula is shown in figure (1-36).

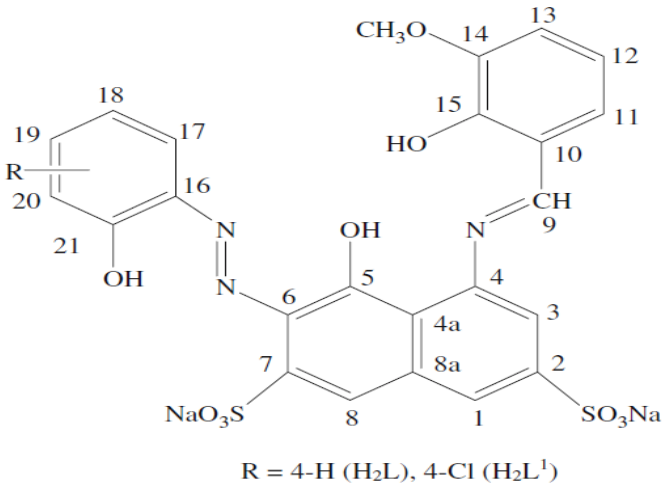


Fig (1-36): Shows the structural formula of the azo and azo-Schiff ligand derived from the diazonium salt of 2-hydroxy aniline with 4-amino 5-hydroxy2, 7-naphthalene sulfonic acid and then condensing with ortho-vanillin

In the same way, the compound 2-(3-phenyl azo-2-hydroxybenzylideneamino) benzoic acid [107] was prepared by condensing the compound 5-(phenyl azo) salicyladehyde with anthranilic acid, as shown in the figure (1-37).

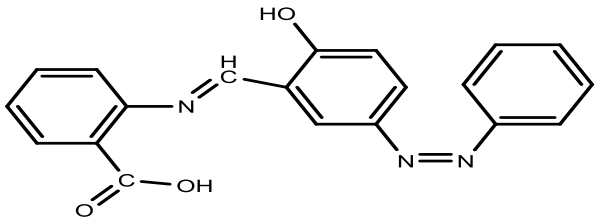


Fig (1-37): Shows the structural formula of the azo and azo-Schiff ligand of 2-(3-phenyl azo-2-hydroxybenzylideneamino) benzoic acid

1.5.1.2. Prepare Schiff base first by condensing the primary amine and carbonyl groups in order to prepare the resulting compound containing the amine, from which an aromatic diazonium salt is prepared to be added to the prepared coupling base in a suitable solvent and at an appropriate acidic function to obtain the ligand (azo-azomethine) required in the second step. It is less common than the previous one.

The method was followed by [108] Saad and Ali to prepare the amine of the Schiff base by condensing 4-aminoacetophenone with 4-nitro-aniline, and pairing the diazonium salt with resorcinol in an alkaline medium to prepare the azo-Schiff (NASAR) and characterizing it by spectrophotometric means, and then preparing three complexes of ions of transition elements The positive charge binary (Co, Ni, and Cu) and the knowledge of their geometric structures, whose formula is shown in figure (1-38).

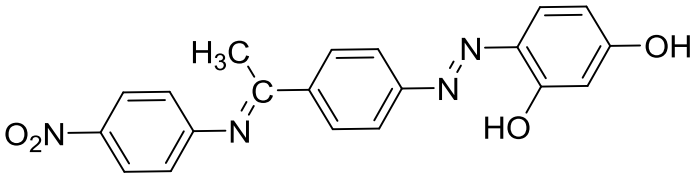
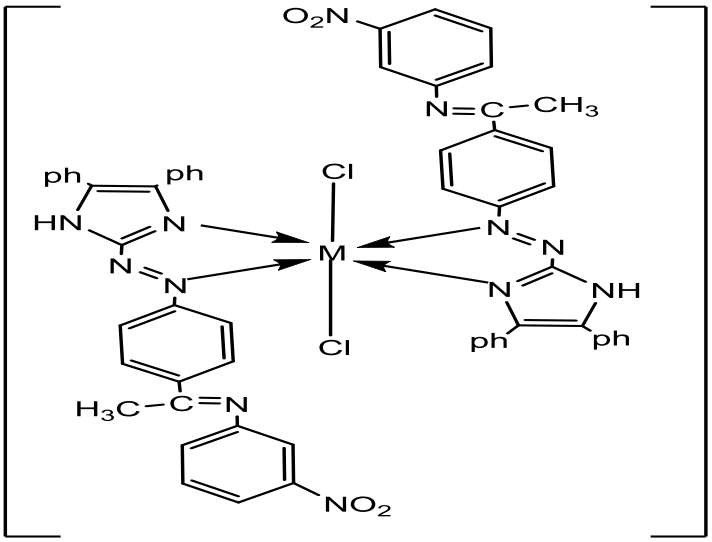


Fig (1-38): Shows the structural formula of the azo and azo-Schiff ligand of 4-((E)-(4-((E)-1-((4- nitrophenyl) imino) ethyl) phenyl)diazenyl)benzene-1,3-diol

Zainab [109] and her group were also able to prepare a di-chelated ligand (azo-azomethine) by coupling the diazonium chloride salt of the compound 1-(4-aminophenyl) ethylidene-3-nitroaniline with 5,4-diphenylimidazole and after verifying the correct chemical composition. The prepared ligand complexes were prepared for many positively charged dimeric ions and these complexes were characterized to suggest their geometrical structure when tested biologically, it was found that they have the ability to inhibit several

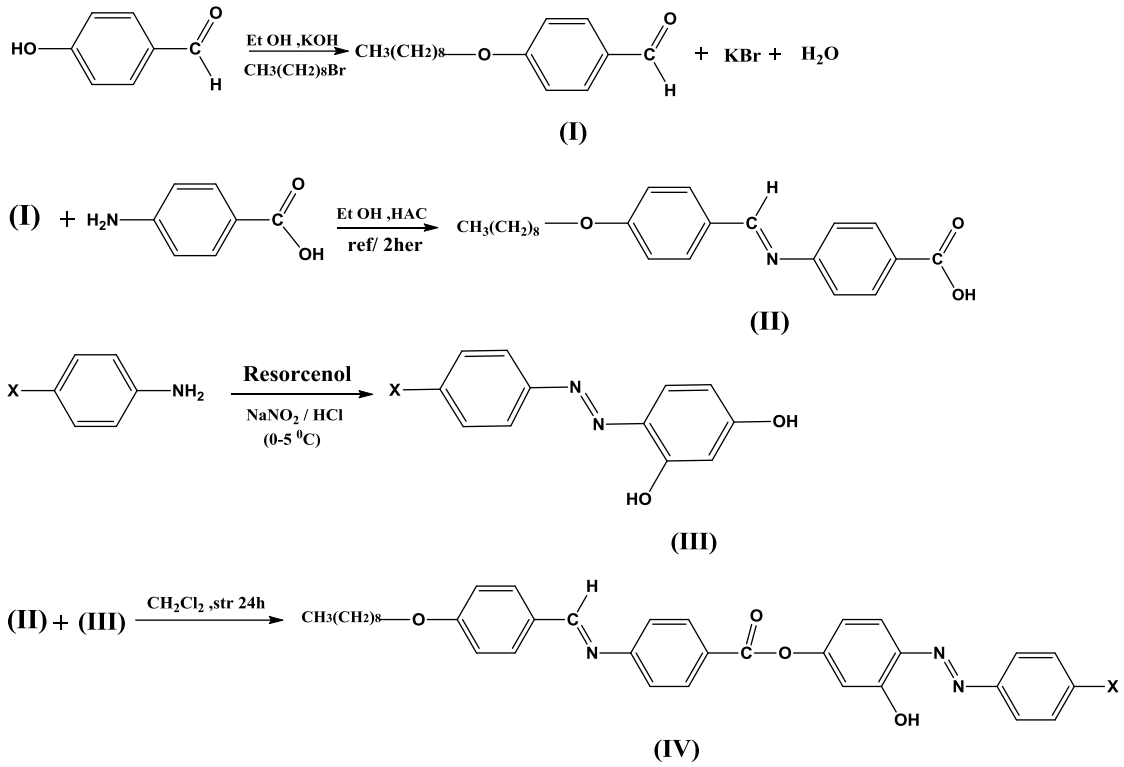
types of gram-positive and gram-negative bacteria, whose formula is shown in figure (1-39).



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

Fig (1-39) shows the structural formula of the azo and azo-Schiff complexes of the di-chelated ligands

1.5.1.3. There is a third way to obtain some of the azo compounds - Schiff base by preparing each of the Schiff base and the azo compound separately and then linking them together to form the azo-azomethine compound. In this way, seven ligands [110] were obtained. The prepared compounds were characterized by many spectroscopic and analytical methods, through which it was found that these organic compounds and their complexes possess the character of liquid crystals, as one of these ligands, as shown in the following scheme (1-10).



Scheme (1-10): Shows the steps used to prepare one of the ligands

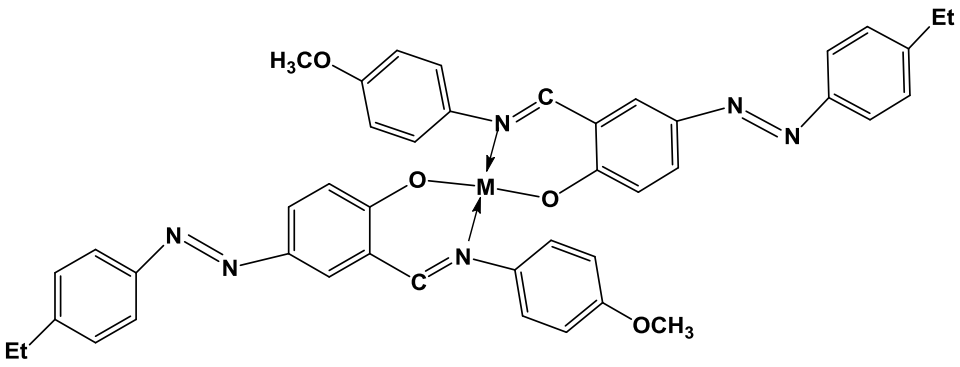
1.5.2. Coordination Methods of Azo-azomethine Ligands

The Azo-azomethine ligands can coordinate with one or both groups if favorable conditions are provided for that from the nature of the ligand and the number and type of donor atoms and their location relative to the azo or azomethine group, as both groups are effective for coordination with the central ion and as follows:

1.5.2.1. Coordination through Nitrogen Atom of the Azomethine Group

The coordination between the ligand and the metal ion is through the nitrogen atom of the azomethine group, in addition to the donor atom of another active group, and it is mostly in the ortho site relative to the azomethine group, examples of these are the complexes of cobalt, copper, and

zinc metal ions, which have a positive double charge with the ligand (E)-(4-ethylphenyl)diazenyl)-2-((E)-(4-))-4-methoxyphenyl(amino)methyl)phenol. The prepared complexes showed inhibition in killing cancer cells against three cancer lines: breast cancer line MCF-7, prostate cancer line PC3, and lung H2126. The geometrical formula for this type of complex has been suggested, which is a square planar [14], as shown in figure (1-40).

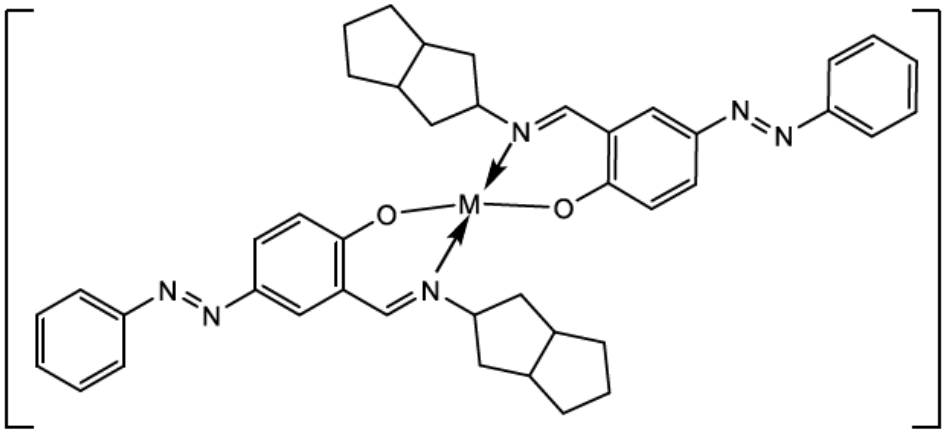


M = Co(II), Cu(II) and Zn(II)

Fig (1-40) shows the structural formula of the complexes of metal ions with the ligand (E)-(4-ethylphenyl) diazenyl)-2-((E)-(4-))-4-methoxyphenyl(amino)methyl)phenol.

Depending on this fact as well, the researcher Selma [111] prepared azomethine ligand and its complexes for some positive double charge ions of the first transition series such as cobalt, nickel, and copper, these ions were bonded with a nitrogen atom of the azomethine group and an oxygen atom of the hydroxyl group after losing their protons to form a hexagonal ring, the tetra coordination complexes were characterized by many spectral and analytical means, including ultraviolet, infrared, nuclear magnetic resonance, and carbon spectra. The behavior of the

double-chelated ligand with a single negative charge was shown, the geometric formula for the prepared complexes as shown in figure (1-41).



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

Fig (1-41) shows the geometrical formula of the cobalt, nickel, and copper complexes

1.5.2.2. Coordination through Nitrogen Atom of the Azo Group

This title includes bonds that contain other coordination sites in addition to the nitrogen atom of the azo bridge group, for example, a hydroxyl group, an amine or a thiol, or a heterocyclic donor atom such as an imidazole or pyridine nitrogen atom, which has the ability to bond by a coordination bond with the metal ion to form a chelating ring and depending on this structure, So, researcher Saad [112] was able to prepare the ligands azo-Schiff imidazole by condensing the amine of the Schiff base first by condensing 4-aminoacetophenone with both (4-chloroaniline and 4-bromoaniline), followed the coupling of this amine with the coupling component 4, 5-

biphenylimidazole, It was diagnosed by spectroscopic methods, including six complexes of positively charged transitional metal ions (cobalt, nickel, copper, cadmium, mercury and zinc), and it was found that the molar ratio of the prepared complexes (M:L,1:2) and non-ionic complexes with octahedral geometric structure, whose formula is shown in figure (1-42).

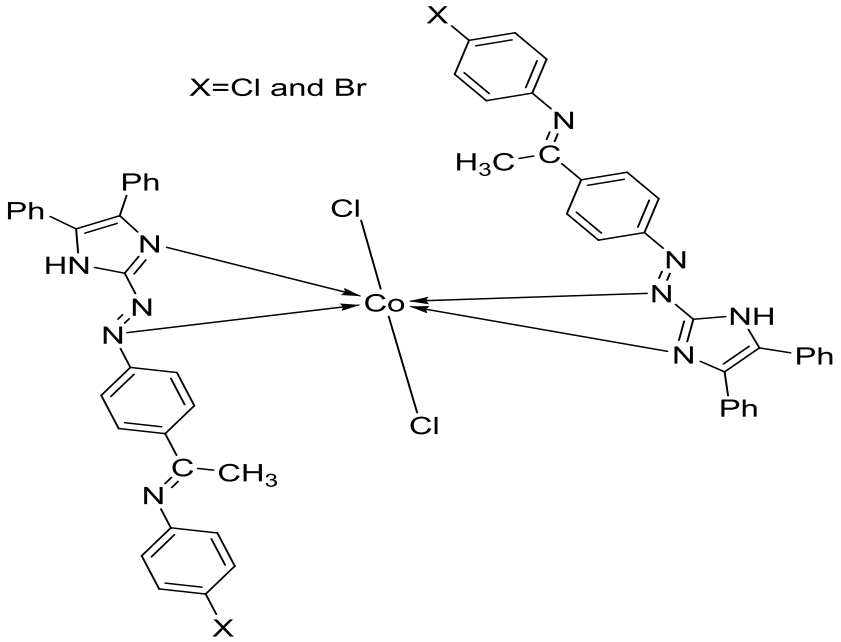
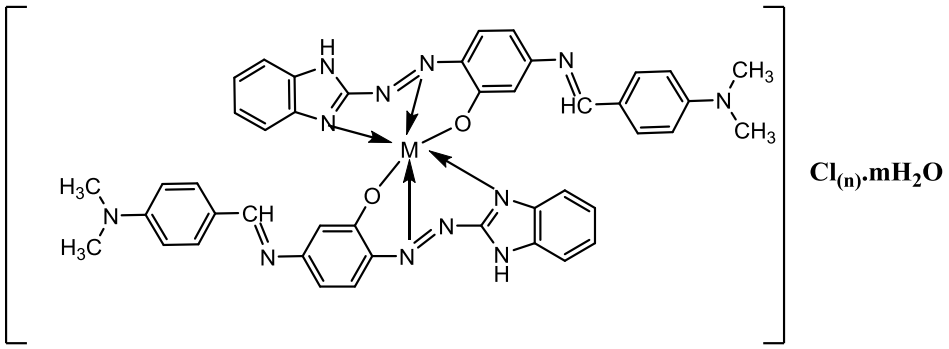


Fig (1-42) shows the geometrical formula for the complex of the cobalt ion with the ligands azo-Schiff imidazole

Khalid and Hayder [113] prepared chelating complexes of ions of Zn (II), Pd(II), Pt(IV), Cu(II), Co(II), Ni(II) with ligand (E). - ((4-((E)-(1H-benzo[d]imidazol-2-))-4yl)diazenyl)phenyl)imino)methyl)-N,N-dimethylaniline and characterize the ligand and its complexes spectroscopically and analytically and depending on the results of these analysis and their inclusion with the results of magnetic susceptibility and molar electrical conductivity of the metal complexes, their stereotyped forms were proposed, and these compounds gained their effect in evaluating their biological activity against selected types of bacteria and fungi. Below are the

structural formulas of the prepared complexes, as shown in figures (1-43) and (1-44).



M= Co(II), Ni(II), Cu(II) and Zn(II), ; n=0 ,m=1
M=Pt(IV), n=2 , m=0

Fig (1-43) shows the geometrical formula for the chelating complexes of ions of Zn (II), Pt(IV), Cu(II), Co(II), Ni(II) with ligand (E). - ((4-((E)-(1H-benzo[d]imidazol-2-))-4yl)diazenyl)phenyl)imino)methyl)-N,N-dimethylaniline

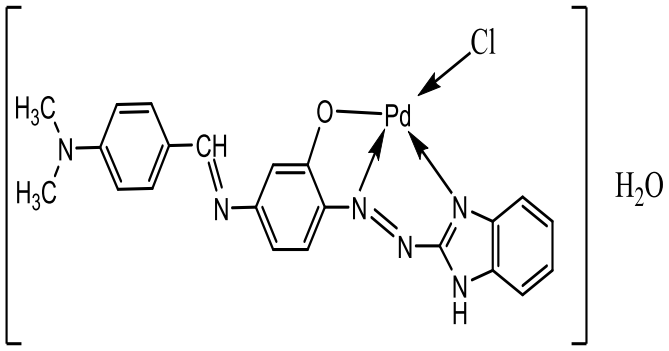


Fig (1-44) shows the geometrical formula for the chelating complex of ion of Pd (II) with ligand (E) - ((4-((E)-(1H-benzo[d]imidazol-2-))-4yl)diazenyl)phenyl)imino)methyl)-N,N- dimethylaniline

1.5.2.3. Coordination by the Two Nitrogen Atoms of the Two Azo-azomethine Groups

We can find this kind of coordination in the participation of both active groups in coordination with the metal ion with the involvement of the lone pair of electrons for each of the nitrogen atoms in the two mentioned groups

to form a chelating ring and confirmation of this fact, the researcher Abbas and his group [114] prepared azo-Schiff ligand in two steps, condensing 4-amino antipyrine with 5-methyltryptamine as a first step, while in the second step, the resulting compound was chlorinated and paired with 3-hydroxybenzoic acid, and the researcher prepared vanadyl (II) complexes for both ligands using vanadyl sulfate $VOSO_4$ in isolation from oxygen, and the geometrical formula of the complexes is given in figure (1-45).

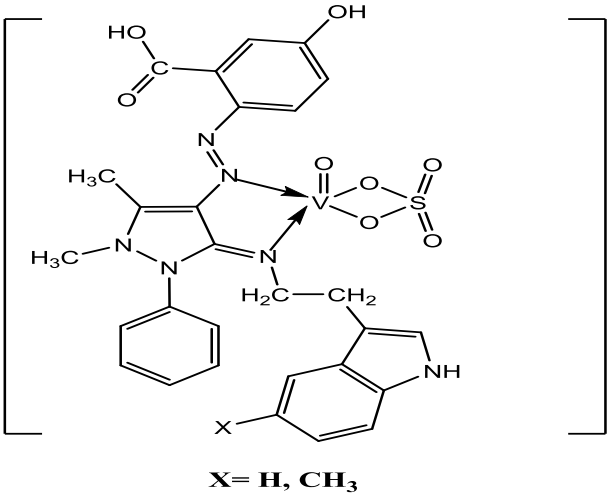
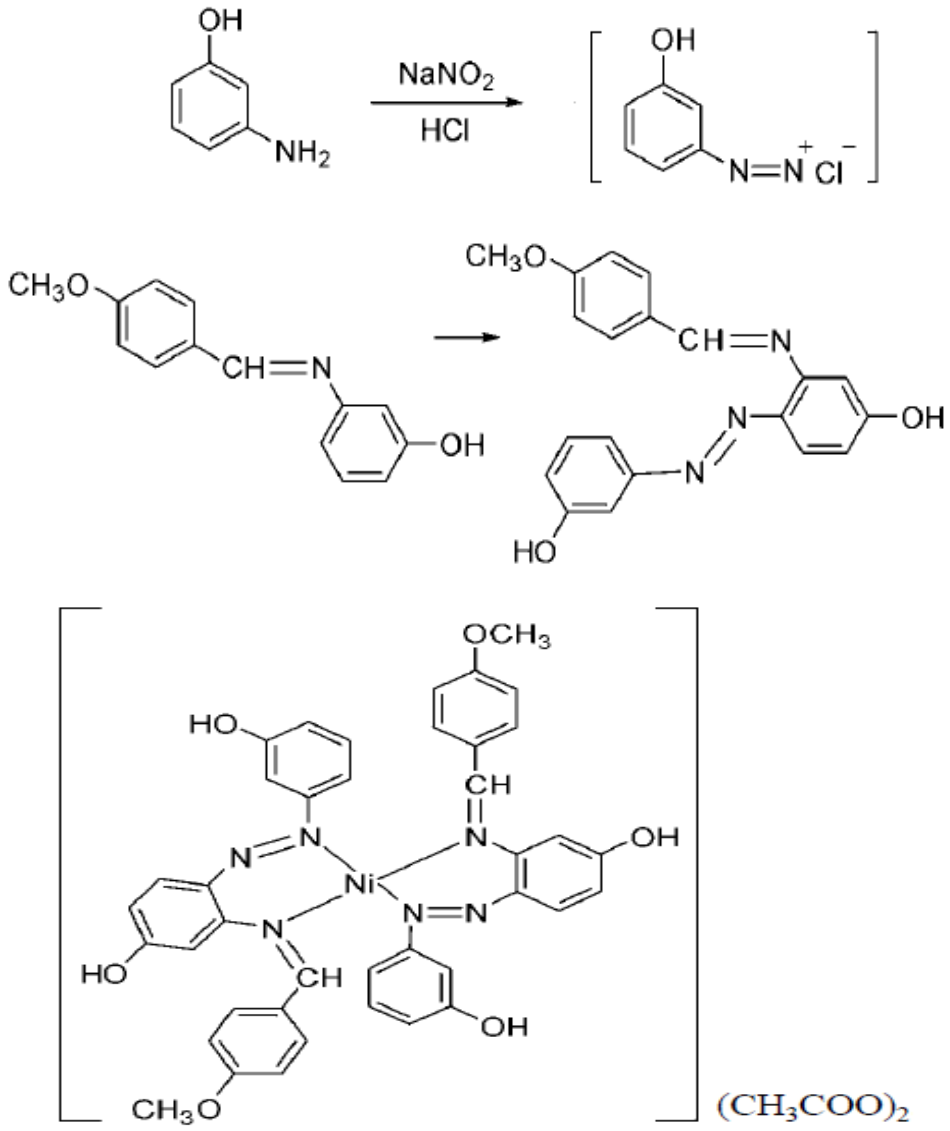


Fig (1-45) shows the geometrical formula for the chelating complex of vanadyl (II) ion

The tetra-chelated azo-Schiff ligand [115] was prepared by preparing the Schiff base first from condensing the 4-methoxybenzaldehyde with 3-aminophenol, and pairing the diazonium salt of 3-aminophenol with the prepared Schiff base to form the azo-Schiff ligand and preparing a nickel complex. Scheme (1-11) shows the steps for preparing a nickel complex.



Scheme (1-11) shows the steps for preparing a nickel complex

1.6. Bioinorganic Chemistry

Biological inorganic chemistry has witnessed a very rapid development, due to the development of techniques in instrumental analysis and the need to discover the properties of complexes with biological effects present in the living system and prepared as samples or therapeutic materials, as it is now known that metal ions control a wide range of life processes [116]. Some

diseases occur when there is an increase or decrease in the concentration of metal ions inside the body or the entry of pollutants such as lead, cadmium, and mercury. Metal ions are considered the best measure of drugs, as the action of many of them is based on the ability of complex compounds for these metal ions to penetrate cell membranes. In contrast, most aqueous ions lack this ability.

It was found that the effectiveness of antibiotics increases in the presence of metal ions [117]. Zhang has indicated in the case of treatment against cancerous tumors that the metal complexes exploit the difference between cancerous and normal cells by identifying harmful cells [118], it was also possible to use metal complexes to increase the pharmacological effects of some drugs within what is known as the synergic effect of effectiveness [119].

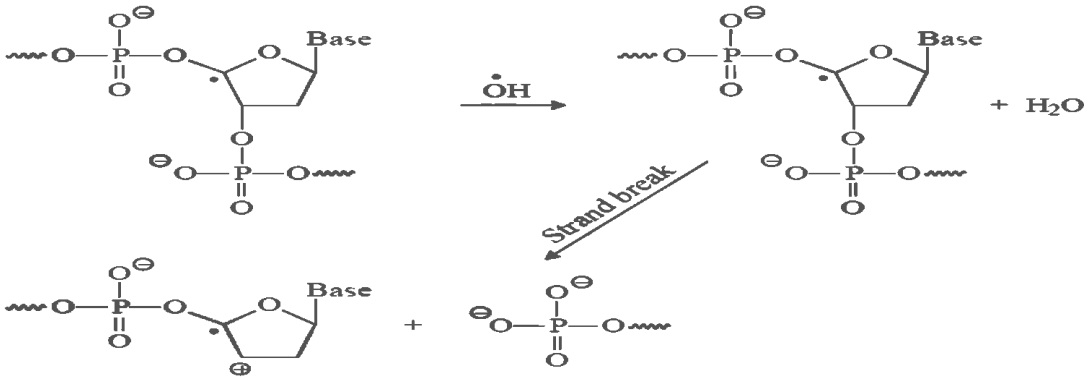
The study of the complexes of transition elements is due to the possession of these elements with special properties, including the ability to possess multiple oxidation states, in addition to their tendency to form ionic or neutral complexes [120].

In a study by researchers Chow and Geake, they suggested that the metal facilitates the injury of oxidative tissues through the intermediate pathway of the free radical, which is similar to the Fenton reaction [121] by applying the ESR technique (metal trapping) and it occurs through the formation of the intermediate hydroxyl radical in vivo, which is obtained from (ROS) produced through the Fenton-type reaction as in the following equations:

$$LM(II) + H_2O_2 \rightarrow LM(I) + {}^{\cdot}OOH + H^+$$

$$LM(I) + H_2O_2 \rightarrow LM(II) + {}^{\cdot}OH + OH^-$$

Where the metal acts as a double-edged sword by damaging the DNA and inhibiting its currency by the interaction of hydroxyl radicals with the sugars and bases of the DNA, where the OH radical works by pulling the hydrogen atom from C4 from the sugar deoxyribose to get the sugar radical and by this mechanism the bonds are broken and released in the form of free bases, the attack on the bases of DAN is by degenerate electrons, and this is a reaction similar to the direct effects of radiation on DNA [122], as shown in scheme (1-12).



Scheme (1-12): Shows the mechanism of the Fenton reaction

1.7. Biological Activity

Bacteria are prokaryotic microorganisms with a diameter ranging between (0.5-1.0) µm and dimensions between (1-6) µm, and due to their small size, the ratio between their sizes to their personal area is greater than that of similar large-sized organisms through which nutrients enter or excrete waste, water is approximately (80-90) percent of its weight. The solid materials in the cell contain carbon, nitrogen, phosphorous, sulfur, oxygen and hydrogen. Bacteria need other elements, but in smaller quantities, such as iron, manganese, magnesium, potassium, zinc, cadmium, and cobalt [123, 124]. The types of bacteria are either Gram-positive, such as (***Micrococcus***

spp, Staphylococcus aureus spp, and Streptococcus spp) or Gram-negative, such as (***Escherichia coli spp, Klebsiella spp, Pseudomonas spp, Proteus spp***) [125]. Below we will show a brief explanation of some types of isolated pathogenic bacteria that were used in the study of biological activity: -

1.7.1. *Escherichia coli*

Gram-negative bacilli, which are motile, produced from the fermentation of the sugar lactose, are widespread in nature, are present in the soil and surface water, and live normally in the intestine. Intestines, or may lead to inflammation of the kidneys, bladder, or acute stomach and intestines in children, the bacilli may be a cause of inflammation of the bile sac, and in rare cases may cause sepsis and inflammation in the inner lining of the heart [126, 127].

1.7.2. *Staphylococcus aureus*

They are Gram-positive staphylococci, non-motile, and may be mono or even pairs, and are present in a wide range, especially in the air and dust, where by the sick person or the vector of germs they reach these sites, and multiply abundantly in the nose and soon colonize this type newly born in the hospital, as They carry these germs in their noses within two weeks of birth. Staphylococcus aureus is one of the most important causes of infection in the teeth and infects the skin or its appendages such as pustules, boils and pimples, and among other diseases that can be caused by bronchial pneumonia and intestinal disorders, and it is one of the causes of food poisoning. The feeder Mueller-Hinton and on other familiar media under aerobic conditions [127, 128].

1.8. Breast Cancer

Breast cancer is the most common type of cancer among women in the United States and worldwide [129]. Its signs include a change in the shape of the breast, the appearance of a lump in the breast, the discharge of fluid from the nipple, or the appearance of a red spot with scales. Among the signs that appear in the body in the event of the spread of the disease are pain in the bones, shortness of breath, swollen lymph nodes, and yellowing of the skin [130].

Breast cancer specifically refers to cancer formed in the breast tissue, often from the ducts that carry milk to the nipples and lobules (milk-forming glands). Breast cancer affects both women and men, but cases of infection among men are rarer than women. A picture of normal and other abnormal breast cells is shown in figure (1-46)

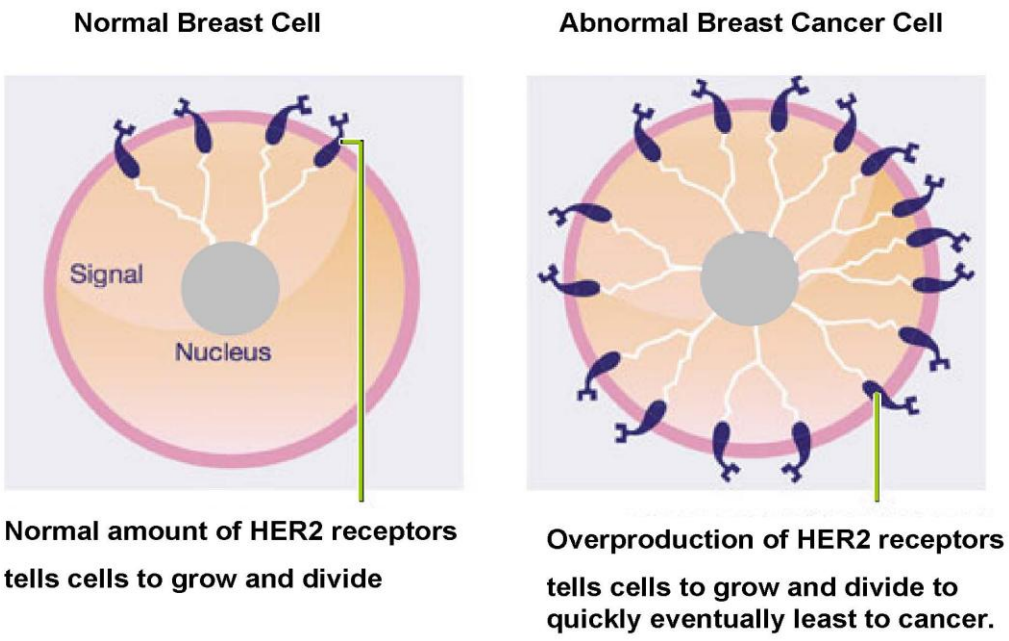


Fig (1-46): Picture of normal and other abnormal breast cells

The main factor for developing breast cancer is gender (women are more likely than men), advanced age (the likelihood increases with age), lack or absence of children, lack of breastfeeding, increase in the proportion of certain hormones in the body, some diet, obesity, and heredity. Studies showed Recent studies have shown that exposure to light pollution is a factor in breast cancer [131].

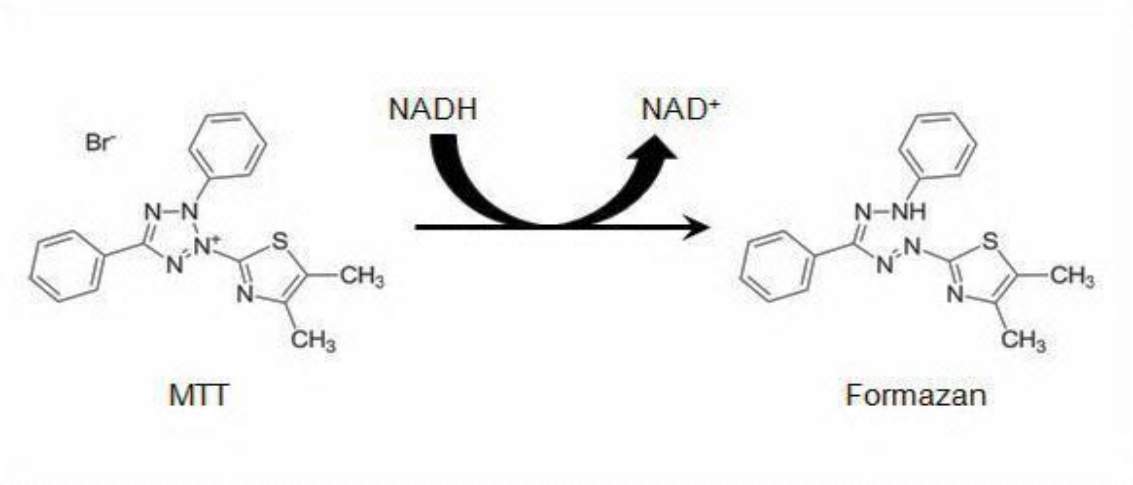
1.9. Cell Viability and Cytotoxicity Assays

Biological and cytotoxicity tests are used for drug tests and cytotoxicity tests. These tests depend on various cell functions, such as enzyme activity, cell membrane permeability, nucleotides, adenine triphosphate synthesis, enzyme facilities, cell adhesion, and nucleotide intake. To calculate the number of living cells, many scientists discovered [132] there are many methods for this purpose, such as the method of colony formation, the method of violet crystal, and the method of tetrazolium salts dissolved in water.

Tetrazolium salts are colorless compounds that become colored when converted to formazan. These salts are used as an indicator to measure the level of cell activity in prokaryotic and eukaryotic organisms. [133].

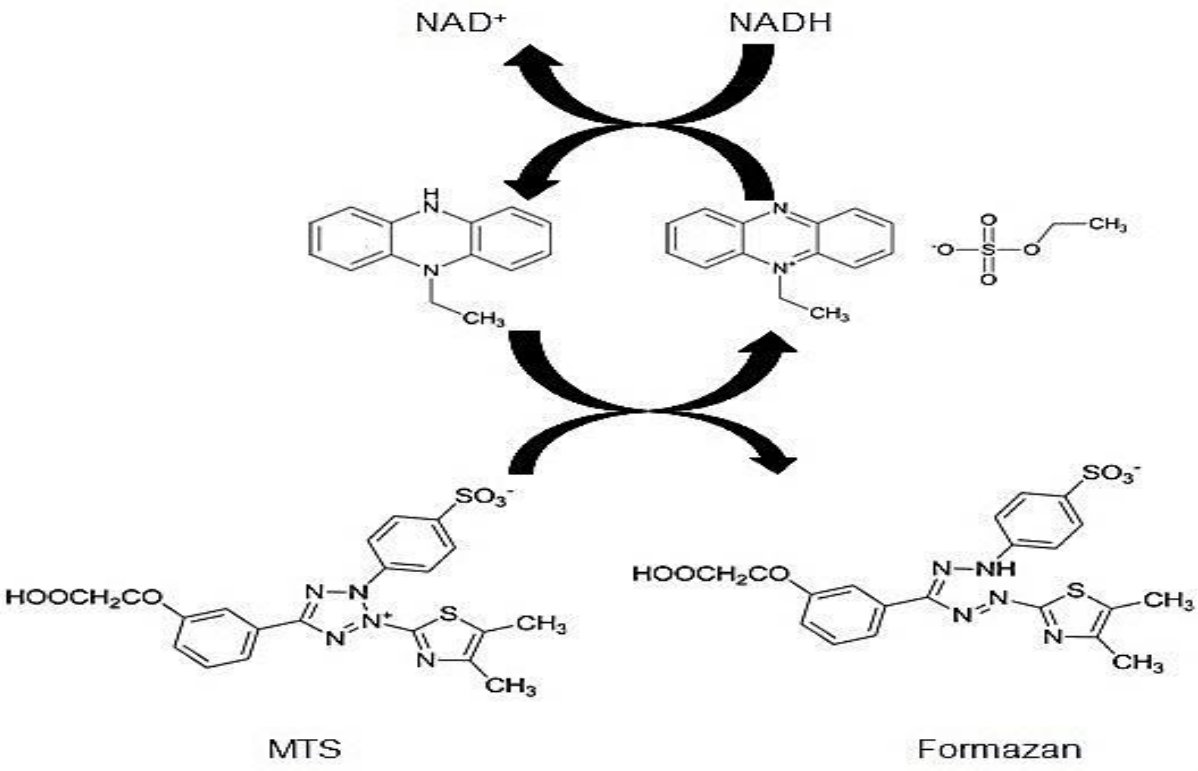
The mechanism of action of reducing tetrazolium salts in eukaryotic organisms occurs inside and outside the cell depending on the ability of tetrazolium to reduce the cell wall and permeate into the cell. A variety of tetrazonium salt compounds has been used to detect living cells. The most common vehicles are MTT, MTS, XTT and WST. These compounds are divided into two basic groups, the first being the positively charged MTT compound or dye, which easily penetrates the living eukaryotic cells. Some studies indicated that NADH is responsible for the reduction of MTT, as the percentage of live cells (cells viability) is calculated, since living cells change the color of MTT dye from yellow to blue or violet, as the size of the blue

color expands, the number of living cells increases, this color change occurs as a result of the production of the dehydrogenase enzyme in living cells by mitochondria, which breaks the tetrazolium rings in MTT dye [134]. Scheme (1-13) shows the mechanism of action of the MTT dye used to detect the toxicity of compounds on cells.



Scheme (1-13): Mechanism of action of the (MTT) dye used to detect the toxicity of compounds on cells

As for the second group, it represents dyes (MTS, XTT, WST) characterized by being negatively charged and having high permeability. Its reduction occurs on the surface of the cell or within the plasma membrane through the activity of electron transfer in the plasma membrane. This group of salts is used by bonding with an electron acceptor medium such as phenazine methyl sulfate (PMS) or phenazine ethyl sulfate (PES), which penetrates into living cells and converts the salts to soluble formazan. MTS is an example of these salts, whose name is5-(3-Carboxymethoxyphenyl)-2-(4, 5-d: methylthiazolyl)-3-(4-sulphophenyl) tetrazolium.In addition. Scheme (1-14) shows the mechanism of action of the (MTS) dye used to detect the toxicity of compounds on cells.



Scheme (1-14): Mechanism of action of the (MTS) dye used to detect the toxicity of compounds on cells

Aims of the Research:

The azo and azomethine groups added to their organic compounds many physical and chemical properties. Therefore, it is natural that we find these compounds have different uses in various fields and based on what was stated in the introduction to our work, our research could be summarized as follows:

1- Synthesis of two types of new compounds, the first type is three heterocyclic azo-imidazole as derivative of 4, 5-diphenylimidazole, while the second one is three compounds of homocyclic azo-azomethine.
2- Studying the coordination ability of these newly synthesized compounds with cobalt, nickel, copper, palladium, and platinum ions.
3- Study of ligand properties and pure solid complexes of these new ligands with the mentioned ions after studying some of the optimum conditions of the coordination process such as the pH of the coordination medium, the range of concentration used in the UV-vis spectral study, as well as the mole ratio (M: L), and some of the physicochemical properties of the complexes.
4- Characterization of the ligands and their complexes by available analytical and spectral methods such as Mass, ^{1}HNMR, FT-IR, UV-vis, accurate analysis of elements, Magnetic susceptibility, and Molar conductivity.
5- We also seek in this research to study the biological activity of each of the azo and azo-azomethine ligands and some of their prepared complexes against two types of bacteria, Gram-negative (***Escherichia coli***) and Gram-positive (***Staphylococcus aureus***) using Metronidazole, and tetracycline as a reference antibiotic, in

addition to the possibility of using the same prepared compounds mentioned above as anti-oxidation compounds and using tannic acid as a reference standard solution and making a comparison between them for the possibility of using them in the biological aspect, and based on what was mentioned in the literature regarding the importance of the organic compounds of palladium and platinum in the medical field, we decided in this research to seek to study the biological and toxicological examinations of some of the palladium and platinum complexes with azo and Azo-azomethine ligands on human cells with breast cancer and the possibility of using it as a drug treatment for cancer patients and a comparison between them for the possibility of using this type of compound in the medical and pharmaceutical aspects.

2.1. Chemicals:

Chemicals that prepared by the following companies were used without any additional purification processes. Table (2-1) shows the most important chemicals used in the research and their degree of purity.

Table (2-1): Chemicals Used, the Companies that Supply them, and their Purity.

Compounds	Company	Purity
2,4- Difluoroaniline	Fluorochem	99%
2,5- Dichloroaniline	Fluorochem	98%
4- Bromo - 2- fluoroaniline	Fluorochem	99%
4- Chloro- 2- fluoroaniline	Fluorochem	98%
4,5- diphenyl- 1H- imidazole	Fluorochem	98%
Aceton	B.D.H	99%
Acetonitrile	B.D.H	99%
Ammonium acetate	Aldrich	98%
Bis(acetonitrile) palladium(II) chloride	Fluorochem	99%
Chloroform	B.D.H	98%
Cobalte(II)chloride hexahydrate	B.D.H	98%
Copper(II) Chloride dihydrate	Sigma- Aldrich	99%
Diethyl ether	Scharlau	99%
Dimethyl formamide	Scharlau	99%
Dimethyl sulphoxide	Riedel-deHaën	99%
DPPH	B.D.H	99.9%
Ethanol Absolute	Scharlau	99%
Glacial Acetic acid	Merck	99%
Hydrochloric acid	B.D.H	36.5%
Methanol	Sigma- Aldrich	99%
Muller-Hinton agar	Indian manufacture	
Nickel(II) Chloride hexahydrate	Himedia	96%
Potassium tetrachloroplatinate(II)	Fluorochem	99+%
Salicyladehyde	Himedia	98%
Sodium hydroxide	B.D.H	98%
Sodium nitrite	Merck	99%
Tannic acid	B.D.H	99.9%

2.2. Instrumentations:

The following devices were used in the analytical, spectroscopic, and Physical measurements of the prepared organic ligands and their complexes as follows:

2.2.1. Melting Point Device

The melting point of all chemical compounds was determined using a device of the type (Stuart CL7-9) at the University of Babylon college of Science – Department of Chemistry.

2.2.2. Infrared Spectra Spectrophotometer

The infrared spectra of the ligands and their metal complexes were measured in their solid state and mixed with potassium bromide in the form of tablets using the device (BRUKER, type: Tensor27, TNo: 3534) of German origin in the laboratories of the College of Pharmacy / University of Babylon.

2.2.3. UV-Visible Spectrophotometer

The UV-visible spectra of the preparing compound were recorded by (UV_6100PC Double beam spectrophotometer, EMC LAB, Germany) within the range 200-800 nm, using quartz cells with a light path (1) cm at the University of Babylon college of Science – Department of Chemistry.

2.2.4. Electric Balance

The required weights of chemical substances were adjusted by the sensitive four decimal order (Denver is 9001) electrical balance in the

Inorganic Chemistry Laboratory / Department of Chemistry - College of Science - University of Babylon.

2.2.5. PH Measurement

The pH of the prepared solutions was measured using a device (pH meter, 315i, Germany) in the Department of Chemistry – College of Science - University of Babylon.

2.2.6. Molar Conductivity Measurements

The molar electrical conductivity values of all prepared complexes were recorded in Dimethylsulfoxide and dimethylformamide solvents using a (Conductivity Meter 740, WTW, Germany) and at ($1x10^{-3}$) molar concentration for each solution at room temperature in the laboratories of the University of Babylon / College of Science - Department of Chemistry.

2.2.7. Magnetic Susceptibility Measurements

Magnetic susceptibility of the prepared complexes were recorded in Al-Mustansiriya University were carried out using the (Auto Magnetic susceptibility Balance, Sherwood, England).

2.2.8. ^{1}HNMR Spectroscopy Measurements

^{1}HNMR spectra of the prepared compounds were recorded in DMSO-d6 solvent using a device (Varian-500 Hz) at the Central Laboratory of the University of Tehran - Islamic Republic of Iran.

2.2.9. Mass Spectrometry Measurements

The mass spectrometry of the Ligand was measured using the device (MSD Direct probe using ACQ method low energy M) in the Central Laboratory of Tehran University - Islamic Republic of Iran. ESI-MS technology was used to measure the mass spectrometry of the complexes.

2.2.10. Atomic Absorption Device

The atomic absorption spectra of the prepared complexes were measured in (Atomic Absorption Spectrophotometer AA_6300, Shimadzu, Japan). At Ibn Sina Company - Baghdad / Iraq.

2.2.1.1. Elemental Analysis Measurements

The ratios of carbon, hydrogen, and nitrogen elements (C.H.N) for the prepared ligands and their metal complexes were determined using the Eager 300 for EA1112) analyzer in the Central Laboratory of Tehran University - Islamic Republic of Iran.

2.3. Preparation of Organic Ligands

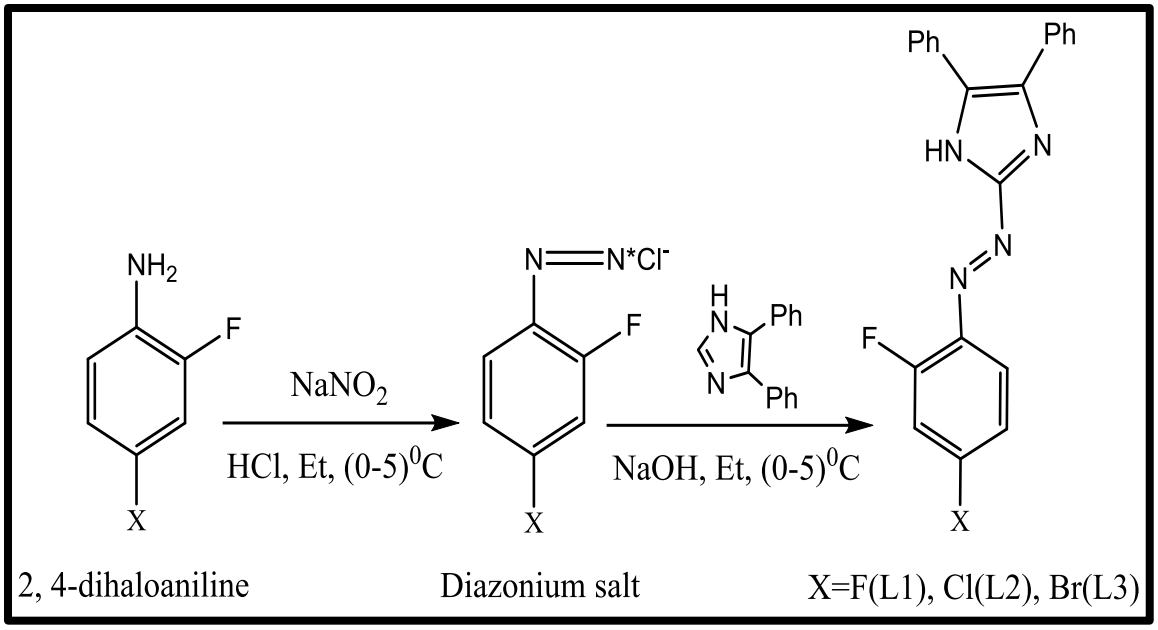
2.3.1. Preparation of Azo-imidazole Ligands (L1- L3)

L1- (E)-2-((2, 4-difluorophenyl) diazenyl)-4, 5-diphenyl-1H-imidazole.

L2-(E)-2-((4-chloro-2-fluorophenyl)diazenyl)-4,5-diphenyl-1H-imidazole.

L3-(E)-2-((4-bromo-2-fluorophenyl)diazenyl)-4,5-diphenyl-1H-imidazole.

The azo ligand was prepared according to the method proposed by Shibata, *et al*, [135], (0.01) mole (1.291) gm of 2, 4-Difluoroaniline was dissolved in an alcoholic acid solution consisting of (4) ml of concentrated hydrochloric acid and (30) ml of distilled water and amount of alcohol to complete the dissolution, the mixture was cooled to a degree of $(0\text{-}5)^0$C, (0.01) mole (0.690) gm of $NaNO_2$ dissolved in (10) ml of distilled water were added dropwise with continuous stirring and cooling, noting that the temperature did not rise above $(5)^o$C, the solution was left to settle for (15) min to complete the nitrogenization process, the resulting diazonium chloride solution was then added dropwise with continuous stirring to a solution (0.01) mole (2.203) gm of the 4, 5-diphenyl-1H-imidazole dissolved in an alcoholic base solution of (10)% NaOH with a temperature not exceeding $(5)^0$C, the color of the solution changed, and the precipitation of the azo derivative were observed at the end of the addition, the same method was used to prepare the rest of the azo-imidazole ligands, the yield and melting point for azo-imidazole ligands were recorded in table (2-2), scheme (2-1) shows the reaction equations:



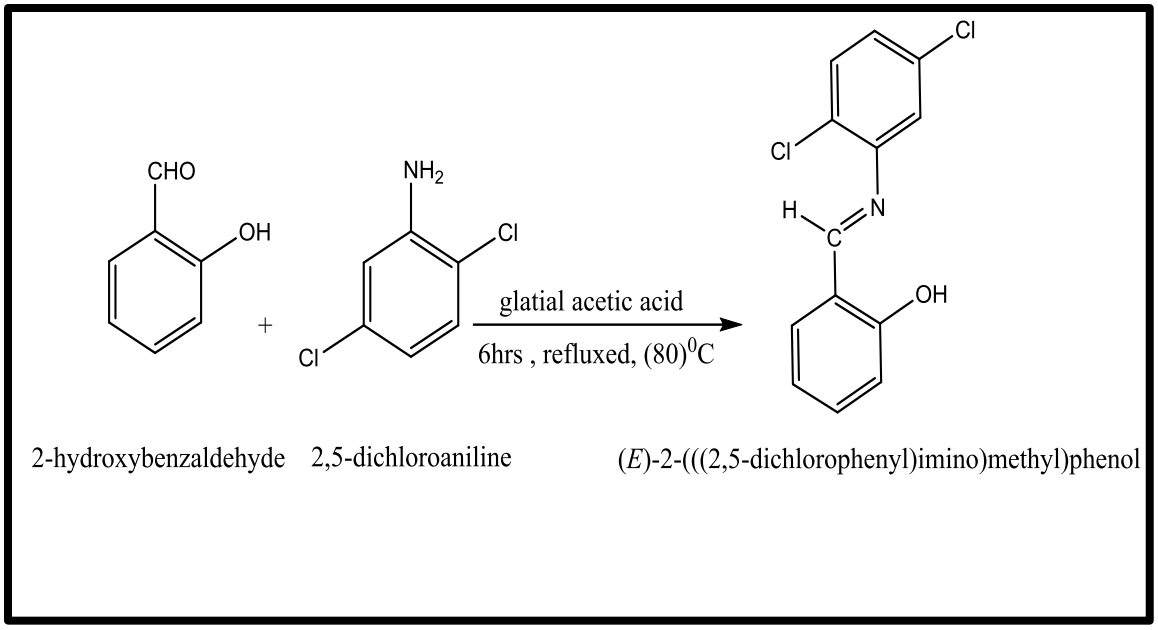
Scheme (2-1): Preparation of Azo-imidazole ligands (L1- L3)

2.3.2. Preparation of Azo-Schiff-base Ligands (L4- L6)

Azo-azo-Schiff base ligands were prepared in two steps

2.3.2.1. The First Step:-Preparation of Schiff Base Ligand (DCSS) [136]

Schiff-base was prepared from the condensation reaction of a solution of (0.01) mole (1.620) gm of aromatic amine (2, 5- dichloroaniline) dissolved in (25) ml of absolute ethanol and (0.01) mole (1.221) gm of (o-hydroxy-benzaldehyde) dissolved in (25) ml of the same solvent, (3) drops of glacial acetic acid were added as a catalyst, the mixture was refluxed for (6) hrs at $(80)^0$C, and left to cool, yellow crystals were observed, filtered and washed, dried in the air, and recrystallized by hot ethanol to obtain a pure Schiff-base ligand (DCSS) in its pure form, the yield and melting point for Schiff-base ligand were recorded in the table (2-3), scheme (2-2) shows the reaction equations:



Scheme (2-2): Preparation of Schiff-base ligand (DCSS)

2.3.2.2. The Second Step:-Preparation of Azo-Schiff-base Ligands (L4 - L6) [135]

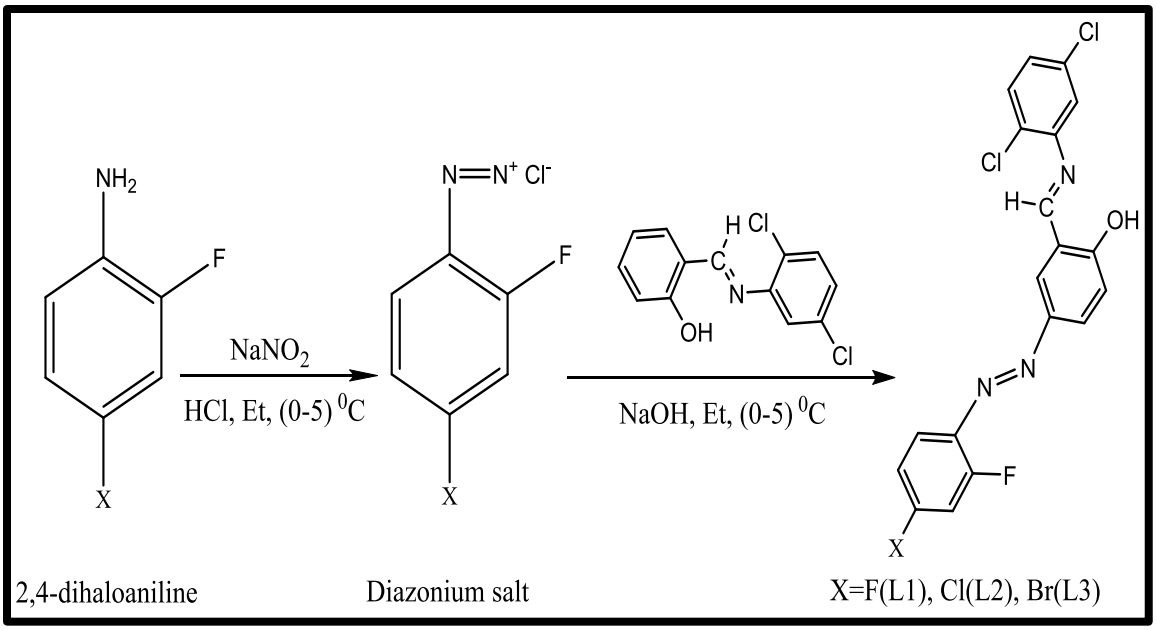
L4-2-((E)-((2,5-dichlorophenyl)imino)methyl)-4-((E)-(2,4-difluorophenyl)diazenyl)phenol.

L5-4-((E)-(4-chloro-2-fluorophenyl)diazenyl)-2-((E)-((2,5-dichlorophenyl)imino)methyl)phenol.

L6-4-((E)-(4-bromo-2-fluorophenyl)diazenyl)-2-((E)-((2, 5-dichlorophenyl)imino)methyl)phenol.

(0.01) mole (1.291) gm of 4-Difluoroaniline was dissolved in an alcoholic acid solution consisting of (4) ml of concentrated hydrochloric acid and (30) ml of distilled water and amount of alcohol to complete the dissolution, the mixture was cooled to a degree of (0-5)^{0}C, (0.01) mole (0.690) gm of $NaNO_2$ dissolved in (10) ml of distilled water were added

dropwise with continuous stirring and cooling, noting that the temperature did not rise above (5)ºC, the solution was left to settle for (15) min to complete the nitrogenization process, the resulting diazonium chloride solution was then added dropwise with continuous stirring to a solution (0.01) mole (2.662) gm of the coupling component DCSS that prepare is in the first step dissolved in an alcoholic base solution of (10)% NaOH with a temperature not exceeding (5)^{0}C, the color of the solution changed, and the precipitation of the azo derivative were observed at the end of the addition, the same method was used to prepare the rest of the azo-Schiff base ligands, the yield and melting point for azo-Schiff ligands were recorded in table (2-3), scheme (2-3) shows the reaction equations:



Scheme (2-3): Preparation of Azo-Schiff-base ligands (L4- L6)

2.4. Preparation of Buffer Solutions

Buffer solutions were prepared at a concentration of (0.01) molar by dissolving (0.7708) gm of ammonium acetate in (1) L of deionized water and the required pH was obtained from adding ammonia solution or concentrated acetic acid to the ammonium acetate solution.

2.5. Preparation of Metal Salt Solution

2.5.1. Preparation of Salt Solutions of the Metals Cobalt (II), Nickel (II), Copper (II), and Platinum (II) [137]

The solutions of salts of the ($CoCl_2.6H_2O$), ($NiCl_2.6H_2O$), ($CuCl_2.2H_2O$), and (k_2PtCl_4) were prepared at a concentration of (1×10^{-3}) molar by dissolving (0.0273) gm, (0.0237) gm, (0.0170) gm, and (0.0415) gm respectively in (100) ml of the buffer solutions that prepared in paragraph (2-4). While the concentrations within the ranges (1×10^{-5}-1×10^{-4}) molar were prepared by diluting the standard stock solution.

2.5.2. Preparation of the Palladium (II) Salt Solution [137]

A solution of palladium salt was prepared by dissolving (0.0259) gm of ($C_4H_6C_{l2}N_2Pd$) in (100) ml of acetonitrile and from this standard solution; other standard solutions were prepared by successive dilution.

2.6. Preparation of Ligand Solutions

The stock solutions for each ligand (L_1- L_6) were prepared at (1×10^{-3}) M, by dissolving (0.036) gm, (0.0376) gm, (0.0421) gm, (0.0406) gm, (0.0422) gm, and (0.0467) gm for each of them, respectively in (100) ml of absolute

ethanol. The ranges (1×10^{-5}-1×10^{-4}) M of each one of these ligands prepared by dilution from the stock solutions.

2.7. Determine Some of the Best Conditions

For the purpose of reaching the optimal conditions for the preparation of solid metal complexes, a set of experiments were carried out for solutions of the ligands complexes with the ions under study referred to as follows: -

2.7.1. Initial Tests of the Interaction of Ligands with Selected Metal Ions

A set of test tubes were taken and placed in each of them (1) ml of a solution of each of the selected metal ion salts, then (1) ml of the ligand solution was added dropwise with shaking, using multiple concentrations of each of the selected metal salt solution and the ligand until the volume of solution of the added ligand became (3) ml. Noting a change such as the appearance of a new color or the formation of a precipitate during the addition process, after that, the mixture was divided into two parts, to one of which drops of the acidic buffer solution were added, and to the other drops of the basic buffer solution were added, in order to know the effect of the pH function on the reaction and to record the obtained results, then the mixture was heated to a temperature of $(60)^0$C in a water bath for (10) minutes. The purpose of this study is to know the ions that interact with the ligands under study and to determine the initial conditions that necessary for each ligand to interact with the metal ions.

2.7.2. Determine the Best Solvent

This study was conducted to find out the effect of changing the solvent on the solubility of the prepared ligands, choosing the best solvent for the studied ligands, and use it to conduct all experiments, where different polar solvents were used, including ethanol, methanol, chloroform, DMSO, and DMF, at a concentration (1×10^{-4}) molar at laboratory temperature, and by dissolving the weight required from each ligand in one of the solvents mentioned in a volumetric bottle (25) ml, then perform the spectrum scan for the ligand solution against the solvent as a reference.

2-7-3- Identification the Best Rang of Concentrations

A set of concentrations of the prepared ligands and metal ions were prepared, ranging from (1×10^{-6} - 1×10^{-3}) molar and a set of preliminary tests was conducted to reach the optimal range of concentrations that appropriate for electronic spectral study in UV-visible region. It was found that the concentrations located between (9×10^{-3} - 1×10^{-3}) molar showed deposits of metal complexes now of mixing the solutions, which called for their exclusion from the measurement process. Whereas, the mixing solutions at (1×10^{-6} - 1×10^{-5}) molar concentrations showed weak absorption that is difficult to measure. From here, it is clear that the best solutions were within the range (3×10^{-4} - 9×10^{-4}) molar, being clear solutions and showing acceptable absorption that we can rely on in the measurement process.

2.7.4. The Proposed Structural Formulas of the Prepared Complexes

The mole ratio method was adopted for identifying the ratio of [Metal: Ligand] [M: L] the method included measuring the absorbance of a group of solutions of a mixture of metal salt and ligand prepared according to the best conditions that were previously reached. These solutions contained a fixed amount of a specific concentration of one of the two components (the metal salt solution) with variable amounts of the same concentration of the second component (the ligand solution). From drawing the graphs between the molar ratio of the metal: the ligand on the x-axis and the molar absorptivity on the y-axis, and the point of intersection represents the molar ratio of the complex solutions.

2.8. Preparation of Solid Metal Complexes

According to the optimum conditions that were reached in terms of concentration and acidity function, and after determining the molar ratio of the ligands in their complexes, it became easy to prepare the solid complexes of the metal ions under study with all the prepared ligands. Tables (2-2) and (2-3) show some of the physical properties of these ligands and their prepared metal complexes, which will be mentioned later.

2.8.1. Preparation of Solid Azo-imidazole Complexes

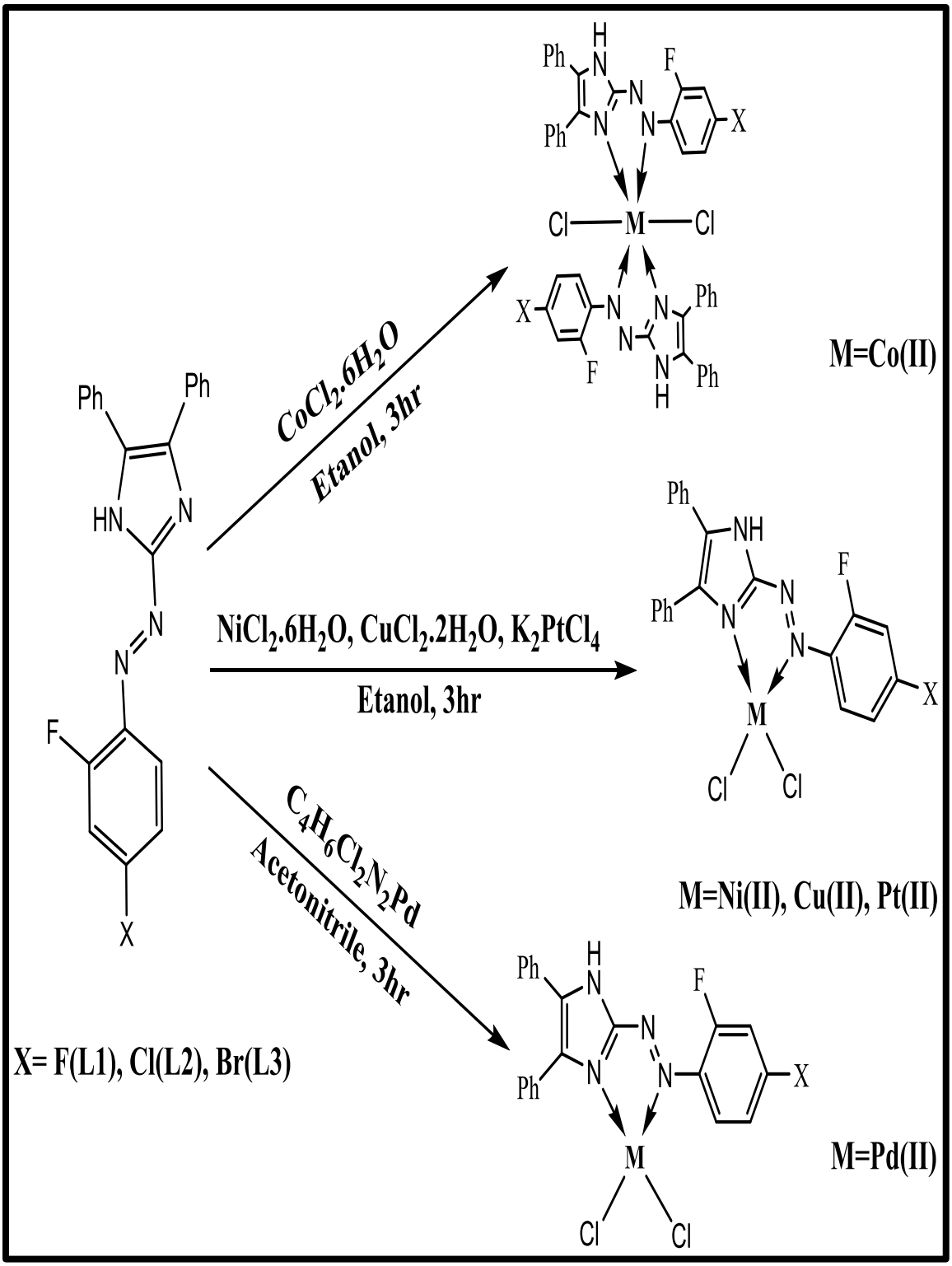
2.8.1.1. Preparation of Solid Azo-imidazole Complexes for Co (II), Ni (II), Cu (II), and Pt (II) Ions

Divalent azo-imidazole complexes for Co(II), Ni(II), Cu(II), and Pt(II) ions were prepared, in molar ratios [M: L] equal to [1:1] except for the cobalt complex, which equal to [1:2], by adding a mixing solution of each ligand dissolved in (50) ml of absolute ethanol to aqueous solutions of salts

of metal ions Co(II), Ni(II), Cu(II), and Pt(II) with weights appropriate to the molar ratios [M: L] after dissolving them in (25) ml of distilled water, these solutions were refluxed for (3) hours, when the reaction was complete, the solution was reduced to a minimum and cooled with an ice bath, the colored solid complexes were developed and they were filtered and dried in an oven $(50)^0$C, their yields and M.P were determined, as shown in the table (2-2), scheme (2-4) shows the reaction equations:

2.8.1.2. Preparation of Solid Azo-imidazole Complex for Pd (II) Ion

Divalent palladium complex was prepared by adding a mixture of each ligand of azo-imidazole ligands dissolved in (50) ml of acetonitrile [137] to a solution of palladium salt dissolved in (25) ml of acetonitrile with weights that matched the molar ratio (1:1), these solutions were refluxed for (3) hours to complete the reaction, when the reaction was complete, the solution was reduced to a minimum and cooled with an ice bath, the colored solid complexes were developed and they were filtered and dried in an oven $(50)^0$C, their yields and M.P were determined, as shown in the table (2-2), scheme (2-4) shows the reaction equations:



Scheme (2-4): Preparation of Azo-imidazole complexes for Co (II), Ni (II), Cu (II), Pd (II), and Pt (II) ions

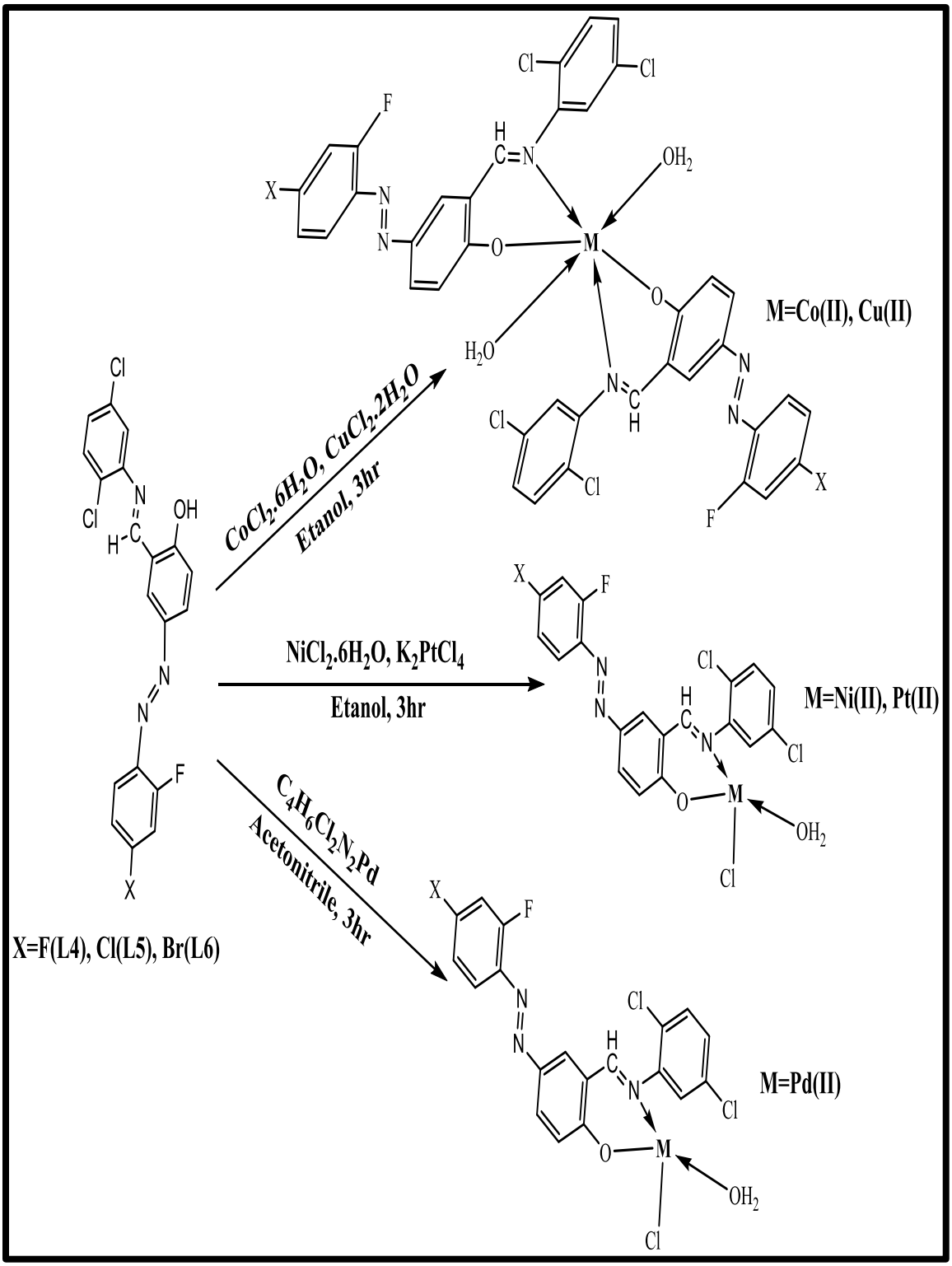
2.8.2. Preparation of Solid Azo-Schiff Complexes

2.8.2.1. Preparation of Solid Azo-Schiff Complexes for Co (II), Ni (II), Cu (II), and Pt (II) Ions

Divalent azo-Schiff base complexes for Co(II), Ni(II), Cu(II), and Pt(II) ions were prepared, in molar ratios [M: L] equal to [1:1] for the nickel and platinum complexes, While the molar ratio of cobalt and copper complexes was [1:2], by adding a mixing solution of each ligand dissolved in (50) ml of absolute ethanol to aqueous solutions of salts of metal ions Co(II), Ni(II), Cu(II), and Pt(II) with weights appropriate to the molar ratios [M: L] after dissolving them in (25) ml of distilled water, these solutions were refluxed for three hours to complete the reaction, when the reaction was complete, the solution was reduced to a minimum and cooled with an ice bath, the colored solid complexes were developed and they were filtered and dried in an oven $(50)^0$C, their yields and M.P were determined, as shown in the table (2-3), scheme (2-5) shows the reaction equations:

2.8.2.2. Preparation of Solid Azo-Schiff Base Complex for Pd (II) Ion

The divalent palladium complex was prepared by adding a mixture of each ligand of azo-Schiff base ligands dissolved in (50) ml of acetonitrile [137] to a solution of palladium salt dissolved in (25) ml of acetonitrile with weights that matched the molar ratio (1:1), these solutions were refluxed for three hours to complete the reaction, and monitoring by TLC techniques (ethanol: chloroform 2:1), when the reaction was complete, the solution was reduced to a minimum and cooled with an ice bath, the colored solid complexes were developed and they were filtered and dried in an oven $(50)^0$ C, their yields and M.P were determined, as shown in the table (2-3), scheme (2-5) shows the reaction equations:



Scheme (2-5): Preparation of Azo-Schiff complexes for Co (II), Ni (II), Cu (II), Pd (II), and Pt (II) ions.

Table (2-2): Some Physical Properties of the Azo-imidazole Ligands (L_1- L_3) and their Metal Ion Complexes at the Molar Ratio [M: L].

No.	Molecular formula	color	m.p °C	%Yield
1	**L1 ($C_{21}H_{14}N_4F_2$)**	Deep-orange	120-121	82
2	**[Co($C_{42}H_{28}N_8F_4Cl_2$)]**	Brown	160-162	75
3	**[Ni($C_{21}H_{14}N_4F_2Cl_2$)]**	Reddish brown	172-173	71
4	**[Cu($C_{21}H_{14}N_4F_2Cl_2$)]**	Deep- red	148-150	82
5	**[Pd($C_{21}H_{14}N_4F_2Cl_2$)]**	Deep- red	153-155	86
6	**[Pt($C_{21}H_{14}N_4F_2Cl_2$)]**	Orange	148-150	81
7	**L2 ($C_{21}H_{14}N_4F$ Cl)**	Orange	125-127	88
8	**[Co($C_{42}H_{28}N_8F_2Cl_4$)]**	Reddish orange	158-160	77
9	**[Ni($C_{21}H_{14}N_4FCl_3$)]**	Deep- brown	175-176	69
10	**[Cu($C_{21}H_{14}N_4FCl_3$)]**	dark brown	151-153	86
11	**[Pd($C_{21}H_{14}N_4FCl_3$)]**	Deep- red	158-160	88
12	**[Pt($C_{21}H_{14}N_4FCl_3$)]**	Deep- orange	142-144	80
13	**L3($C_{21}H_{14}N_4FBr$)**	Reddish orange	128-130	85
14	**[Co($C_{42}H_{28}N_8F_2Cl_2Br_2$)]**	reddish brown	165-166	86
15	**[Ni($C_{21}H_{14}N_4FCl_2Br$)]**	light brown	177-179	77
16	**[Cu($C_{21}H_{14}N_4FCl_2Br$)]**	Dark brown	149-151	90
17	**[Pd($C_{21}H_{14}N_4FCl_2Br$)]**	Deep- red	154-156	89
18	**[Pt($C_{21}H_{14}N_4FCl_2Br$)]**	Reddish-purple	146-148	84

Table (2-3): Some Physical Properties of the Azo-Schiff Base Ligands (L_4- L_6) and their Metal Complexes at the Molar Ratio [M: L].

No.	Molecular formula	color	m.p °C	%Yield
1	**Schiff base (DCSS)**	Yellow	125-127	88
2	**L4 ($C_{19}H_{11}Cl_2F_2N_3O$)**	Orange	144-145	78
3	**Co[$C_{38}H_{24}Cl_4F_4N_6O_4$]**	Deep Brawn	176-177	80
4	**Ni[$C_{19}H_{12}N_3Cl_3F_2O_2$]**	Greenish- Brown	183-185	75
5	**Cu[$C_{38}H_{24}Cl_4F_4N_6O_4$]**	Dark- red	187-189	82
6	**Pd[$C_{19}H_{12}N_3Cl_3F_2O_2$]**	Deep- Brawn	154-156	86
7	**Pt[$C_{19}H_{12}N_3Cl_3F_2O_2$]**	Dark- Orange	150-151	88
8	**L5($C_{19}H_{11}Cl_3FN_3O$)**	Light- Brown	146-147	75
9	**Co[$C_{38}H_{24}Cl_6F_2N_6O_4$]**	Dark- Pink	155-156	77
10	**Ni[$C_{19}H_{12}Cl_4FN_3O_2$]**	Brawn	166-167	75
11	**Cu[$C_{38}H_{24}Cl_6F_2N_6O_4$]**	Reddish- Brown	174-176	82
12	**Pd[$C_{19}H_{12}Cl_4FN_3O_2$]**	Dark- Red	149-150	86
13	**Pt[$C_{19}H_{12}Cl_4FN_3O_2$]**	Reddish orange	156-158	89
14	**L6 ($C_{19}H_{11}BrCl_2FN_3O$)**	Brown	149-151	78
15	**Co[$C_{38}H_{24}Br_2Cl_4F_2N_6O_4$]**	Dark- Pink	155-157	74
16	**Ni[$C_{19}H_{12}BrCl_3FN_3O_2$]**	Dark- Brown	161-163	71
17	**Cu[$C_{38}H_{24}Br_2Cl_4F_2N_6O_4$]**	Reddish- Lead	158-160	72
18	**Pd[$C_{19}H_{12}BrCl_3FN_3O_2$]**	Reddish- Brown	153-155	78
19	**Pt[$C_{19}H_{12}BrCl_3FN_3O_2$]**	light brown	159-161	83

2.9. Spectral Measurements of the Complexes

Complexes were identified using FT-IR spectrophotometers, and the infrared spectra of these compounds were recorded in the form of hard disks of potassium bromide (KBr) in the range of (400-4000) cm^{-1}. UV-Visible spectra measurements were performed. The solutions of ligands and their metal complexes were prepared and dissolved in absolute ethanol and the solvent of acetonitrile for the palladium and platinum ion ligands using quartz cells with optical path length (1) cm, where measurements were made at the greatest wavelength (λmax). ^{1}H-NMR was studied to find out the structural formula of the ligands (L1- L6) and some of their complexes using the solvent (DMSO-d6) and using TMS as a standard reference. Mass spectra were recorded for all the ligands and some of their metal complexes under study. In addition, the flame atomic absorption spectrometer was used using (air/acetylene) as fuel to calculate the percentage of metal ions in their prepared complexes, by measuring the absorbance of the metals present in the complexes and at the corresponding wavelengths.

2.10. Measurements of Conductivity

The molar electrical conductivity (Λ_m) was measured for solutions of chelate complexes prepared in (DMSO, and DMF) solvents at a concentration of (1×10^{-3}) molarity and at a temperature of (25) °C.

2.11. Magnetic Susceptibility Measurements

The magnetic susceptibility of solid metal complexes was measured at a temperature of $(25)^{0}$C, and by using the Faraday method, the model to be measured is placed in a small tube of thermal glass (Pyrex) hanging from the cuff of a sensitive balance scale in the center of a strong electromagnet, in

preparation for obtaining the values of the gram sensitivity (Xg), which has been converted to the molar sensitivity (Xm), then to the atomic sensitivity (XA) after extracting the value of the correction factor (D) from tables of Pascal constants, so that the values of the effective magnetic moment (μef) can be calculated according to the following law: -

$$\mu_{eff} = 2.828 \sqrt{X_A \; T} \quad B.M$$

The BM represents the Bohr Magneton, which is the unit of measurement of the magnetic moment, T = absolute temperature in Kelvin. The information obtained will be included in the third chapter.

2.12. Biological Study

2.12.1. Biological Efficiency

The biological activity of the prepared ligands and some of their metal complexes were conducted under study. This study included the use of two types of pathogenic bacteria isolated and diagnosed in the laboratory using chemical and microscopic tests. These isolated bacteria are pathogens of many diseases. It included two different types of gram-negative bacteria (***Escherichia coli spp***) and gram-positive bacteria (***Staphylococcus aureus spp***), and the causes of many common diseases [138].

2.12.1.1. Preparation of Culture Media

The culture medium (agar) of the Muller-Hinton type was prepared according to the instructions of the Indian manufacturer (BLOMARK LABORATORIES) by dissolving (38) gm of the culture medium in (1000)

ml of boiled distilled water in a glass flask and mixing well, to completely dissolve the culture medium, then place in an autoclave at a temperature of (121)°C and at a pressure of (15) pounds / inch^2 for (15) minutes, then pour the medium into sterilized glass dishes at a rate of (15-20) milliliters per dish and leave until solidification is complete, then the dishes were placed in the incubator for a period of (24) hours and at a temperature of (37) degrees Celsius to ensure that there was no contamination in them.

2.12.1.2. Preparation of Solutions

The solutions of the ligands and their complexes under study were prepared by dissolving (0.01) gm of each compound in (5) ml of DMSO solvent for each ligand and its metal complexes, which were tested for their biological activity.

2.12.1.3. Processing Method [139]

Bacteria were spread in the dishes and on the surface of the food medium using Muller Hinton agar using (loopful), and three holes with a diameter of (6) mm were made in these dishes by using an alcohol-sterilized cork- borer, taking into account leaving an appropriate distance between one spot and another to avoid overlapping areas of inhibition among them. The prepared solutions were added to these pits for (0.1) ml using a micropipette and placed in the incubator for (24) hours at a temperature of (37) °C. Then measure the zone of inhibitor for the prepared compounds using the millimeter ruler.

2.12.2. Antioxidant Study

The electron-donating ability of samples and standard tannic acid were determined from bleaching of purple-colored methanol solution of DPPH. Free radical scavenging activity of test samples was measured according to Brand-Williams, *et al*, [140, and 141]. DPPH (5mg /100 ml) was prepared as a normal solution in methanol with DPPH was used as a control. Different concentrations (25, 50, and 75) µg /ml of samples were taken in separate test tubes and volumes were made up to (20) µl using methanol. Then (200) µl of DPPH solution was added in each test tube and these solutions were kept in dark for thirty minutes. The same procedure was followed for tannic acid as well. All the samples were tested in triplicate. Later optical density was recorded at (517) nm using a spectrophotometer. From linear curve to obtained (IC50) value by drawing between concentration and percent inhibition. The decrease in absorbance indicates increased radically scavenging activity, which was determined by the following formula [142].

$$\textbf{Inhibition (\%)} = \frac{\textbf{A control} - \textbf{A test}}{\textbf{A control}} \times \textbf{100}$$

2.12.3. Cell Cytotoxicity and Viability Assays

MCF-7 human breast cancer cell line was obtained from the American Type Culture Collection (ATCC, Manassas, VA, USA). Cells were grown and maintained in Dulbecco's Modified Eagle Medium (DMEM; Gibson, Life Technologies, Waltham, MA, USA) supplemented with (10%) fetal bovine serum (FBS; Bio West SAS, Nubile, France) and (1%) PSF

(antibiotic antimitotic solution, Sigma-Aldrich®, St. Louis, MO, USA) in a humidified incubator with (5%) CO_2 in air at (37) °C [143]. After reaching (~75%) confluence, cells were detached using (0.25%) trypsin (Gibson, Invitrogen, Waltham, MA, USA) and (0.1%) ethylenediaminetetraacetic acid (Merck, Darmstadt, Germany) in phosphate-buffered saline (PBS) at (37)°C. Cells were then re-suspended in DMEM with (10%) FBS and (1%) PSF. Cells were seeded onto the 96-well plates at a density of 5000 cells per well and incubated for (24) h prior to the experiments. The Cells were washed with PBS (phosphate-buffered saline, pH 7.4) and incubated in a fresh medium containing different concentrations of samples (1000, 500, 250, 125, 62.5, 31.25, 0 µg/ml) for (72) h. The cell viability assay was measured using the 3-(4, 5dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) dye reduction assay. MTT was performed to determine the cytotoxic effect of the samples at various concentrations. After (72) h of incubation (37)℃, (5%) CO_2 in a humid atmosphere), MTT (5 mg/mL in PBS) was added to each well, and the plate was incubated for a further 4h at (37)℃. The resulting formazan was dissolved in (100) µl of DMSO [144] with gentle shaking at (37)℃, and absorbance was measured at (570) nm with an ELISA reader. The results were given as the mean of three independent experiments. Concentrations of samples showing a (50%) reduction in cell viability (i.e., IC50 values) were then calculated.

Preface:

The study included two ways to prepare the ligands; the first one includes the preparation of three new compounds containing azo-imidazole ligands (L_1, L_2, and L_3) through the coupling reaction of diazonium salts of each of di-substituted halogen anilines (2,4- difluoroaniline, 4- chloro- 2-fluoroaniline, and 4- bromo - 2- fluoroaniline) with 4, 5-diphenyl-1H-imidazole that qualified for coordination with the divalent transition ions Co(II), Ni(II), Cu(II), Pd(II), and Pt(II) through neutral bidentate chelate sites (N, N) for the preparation of complexes, while the second way of study includes preparation of three new azo-Schiff ligands via the coupling of the diazonium salts of three previously mentioned di-substituted halogen anilines with first derivative which were previously mentioned (DCSS) as a coupling component to form three new azo-Schiff ligands (L_4, L_5, and L_6) respectively that serve as a bidentate chelating ligand via the azomethine nitrogen atom and the monobasic oxygen atom of the salicylaldehyde (N, O) with the same divalent transition ions in the first way of study.

The measurements of the mass spectra, the proton nuclear magnetic resonance spectra of these organic ligands and some of their metal complexes, the infrared, and UV-visible spectra, in addition to the measurements of micro-elemental analysis, the percentage of metal, molar conductivity, and magnetic sensitivity, proved the validity of the proposed structures for both ligands and chelate-metal complexes alike, as well as studying the effect of the solvent on the prepared ligands. The biological evaluation of these new compounds were studied via-

- Study of the bioactivity of antimicrobials and antioxidants for azo and azo-Schiff base ligands and some of their metal complexes.

- Study of the cytotoxicity effect for palladium complexes with ligands L_2 and L_4 and platinum complexes with ligands L_1 and L_5 on cancer cells of breast cancer.

Below we review the most important results obtained:

3.1. Mass Spectra

Mass spectrometry is one of the important measurements through which it is possible to prove the molecular weight and molecular formula of the prepared new compounds. It can also be used to study the mechanism of reactions or to suggest ways of dissociating the compounds studied with this technique, which devices have greatly varied to keep pace with the needs and multiple research purposes [145]. There are many factors affecting the experiments performed using this method, the type of detector used, solvent, temperature, bombardment energy, and the kind of bombardment plays a significant role in the shape of the spectrum obtained, in addition to the molecular weight of the compound and the number of heterogeneous atoms present in it [146, 148].

When the vapor of a substance is exposed to a bundle of electrons, that material absorbs the energy of this bundle, then one or more electrons are separated and a process of ionization for that molecule occurs, accompanied by the cracking of weak bonds and the formation of small ions known as “fragments” [149].

The fragments differ in the ratio of their molecular weights to their charge (Mass/Charge) and according to this difference, the fragments are separated either by the influence of a magnetic field or by the effect of a double magnetic field with an electric field and accordingly the results of the analysis will appear in the form of a mass spectrometer [150].

3.1.1. Mass Spectra of Azo-imidazole Ligands and their Chelating Complexes

The mass spectra of the prepared azo-imidazole ligands L_1, L_2, and L_3 was measured using mass spectrometry, where the mass fragmentation spectrum of the ligands for L_1, L_2, and L_3 showed the parent ion fragment at the value of m/z = 360.2[M], 376.2 (It appeared in less than 1% due to the large molecular weight, high bombardment energy, and a large number of heterogeneous atoms present in this ligand) [146], and 421.2[M], (which are values equivalent to the mass of the mentioned ligands) [151], respectively, also, the spectra of these ligands showed the ion radical fragment of 4,5- diphenyl- 1H- imidazole with a value of m/z = 218 [112] and the phenyl ring fragment at m/z = 77 for each ligand, which led us to prove the formation of the above-mentioned azo-imidazole ligands and thus prove the proposed formulas for the prepared compounds, figures (3-1) to (3-3) and schemes (3-1) to (3-3) show the mass spectra of these ligands and the proposed mass fragmentation pathways for them.

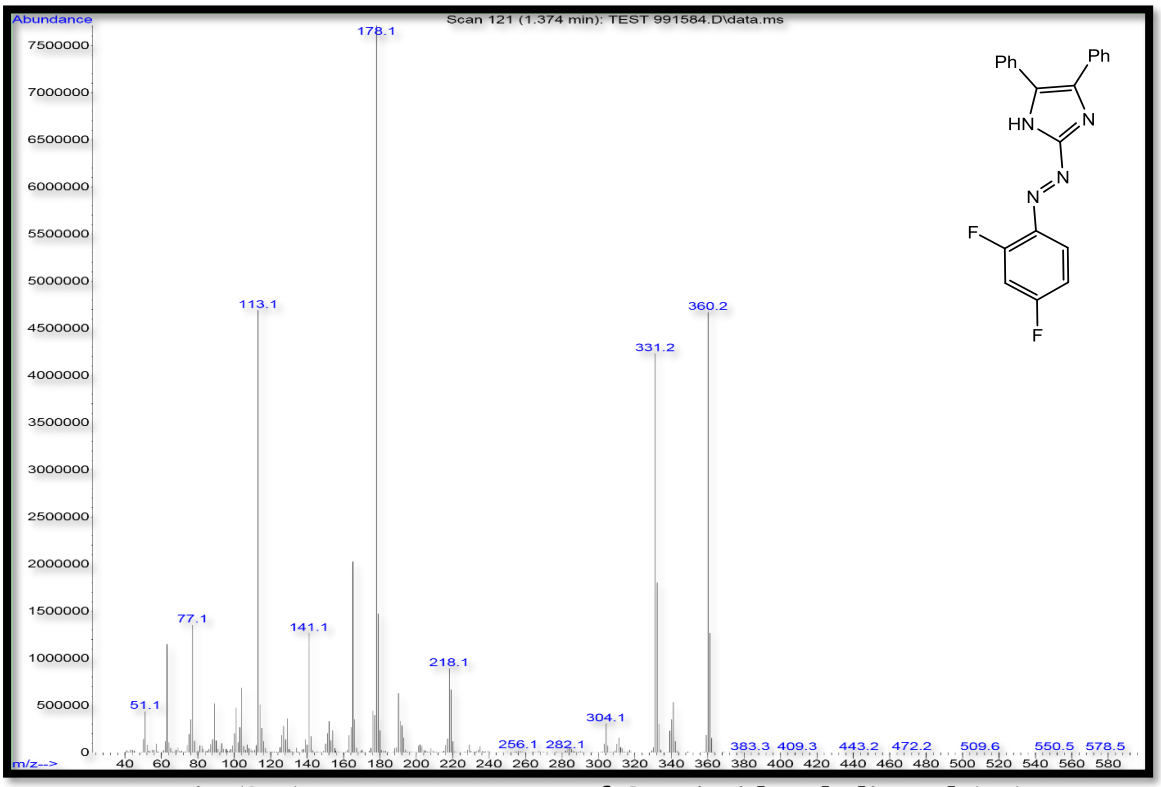


Fig (3-1): Mass spectrum of Azo-imidazole ligand (L_1)

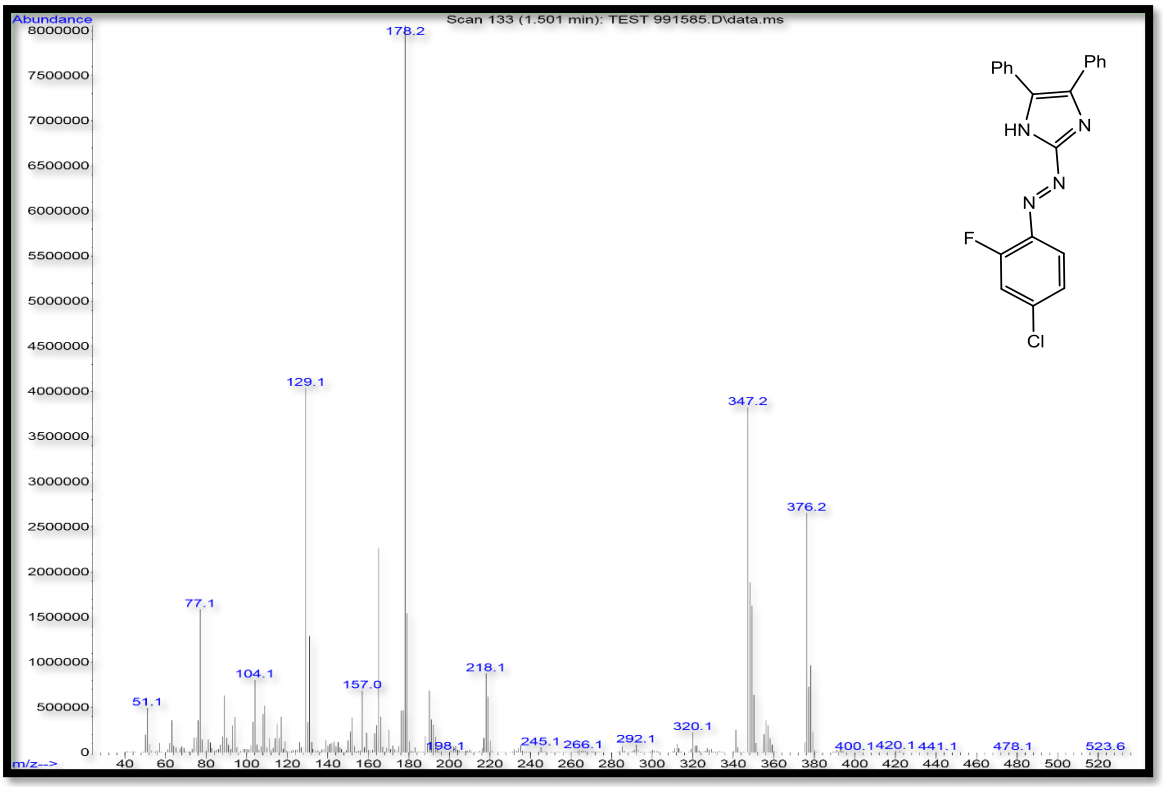


Fig (3-2): Mass spectrum of Azo-imidazole ligand (L_2)

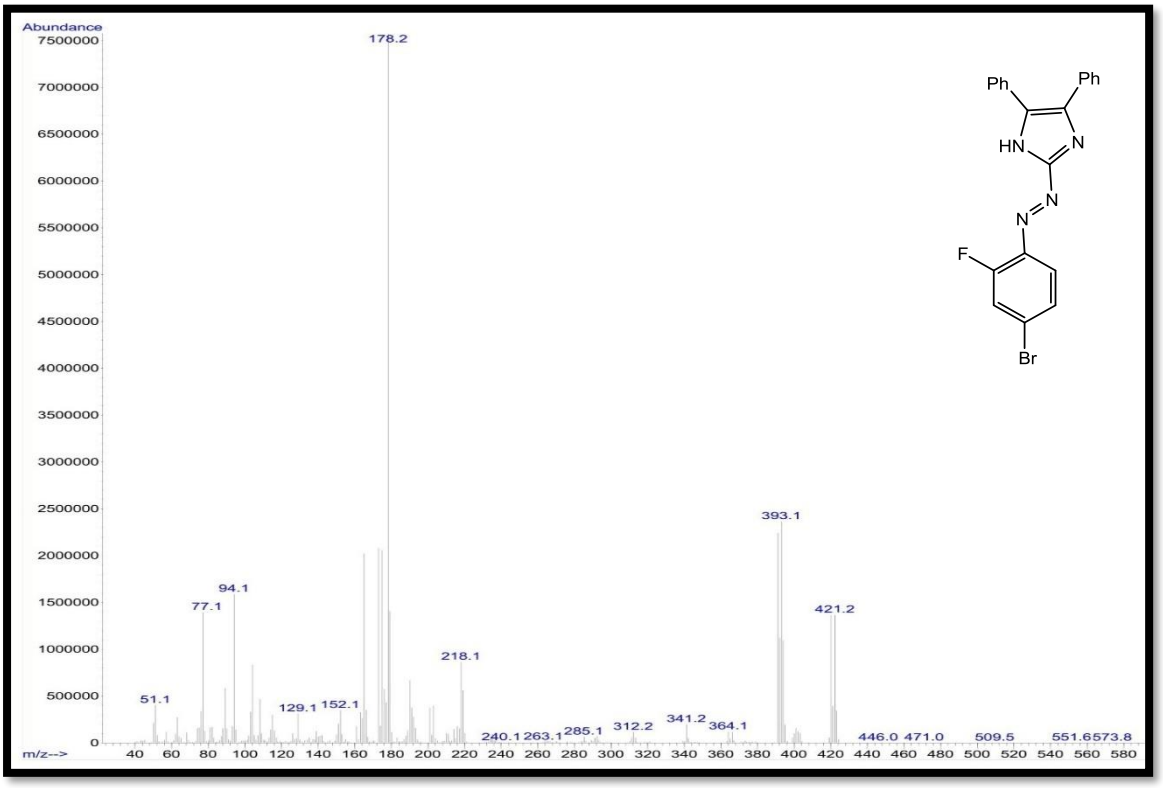
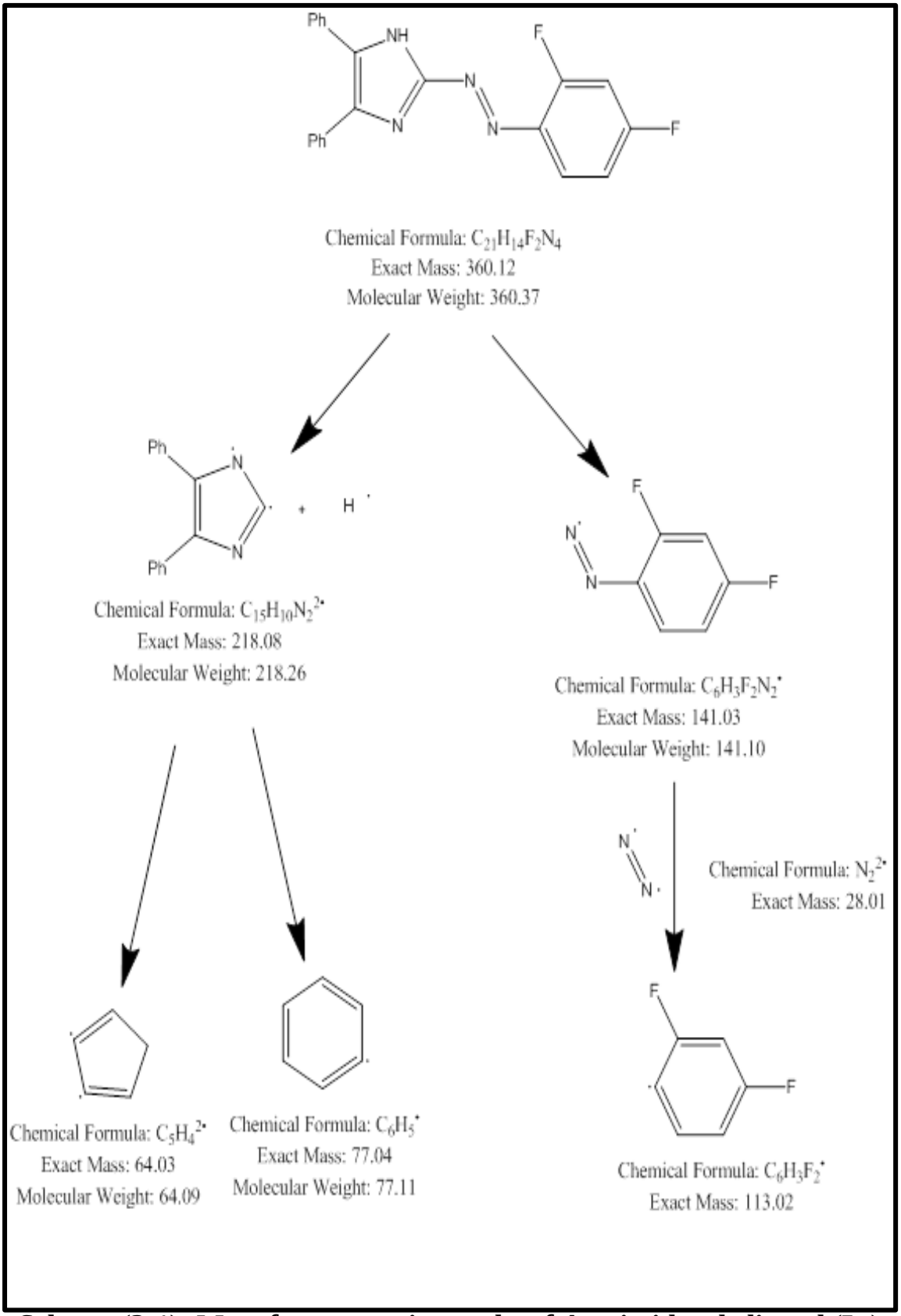
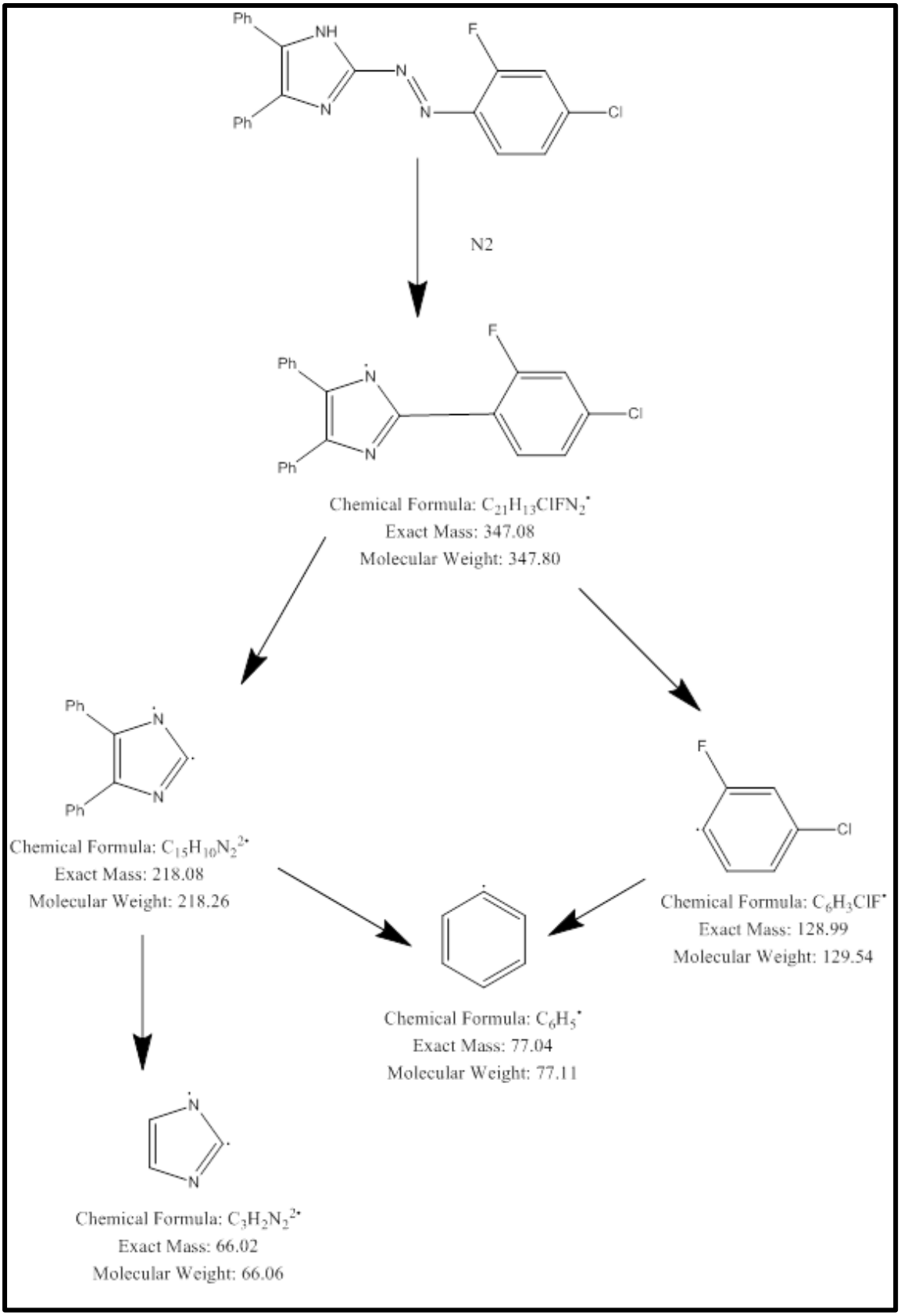


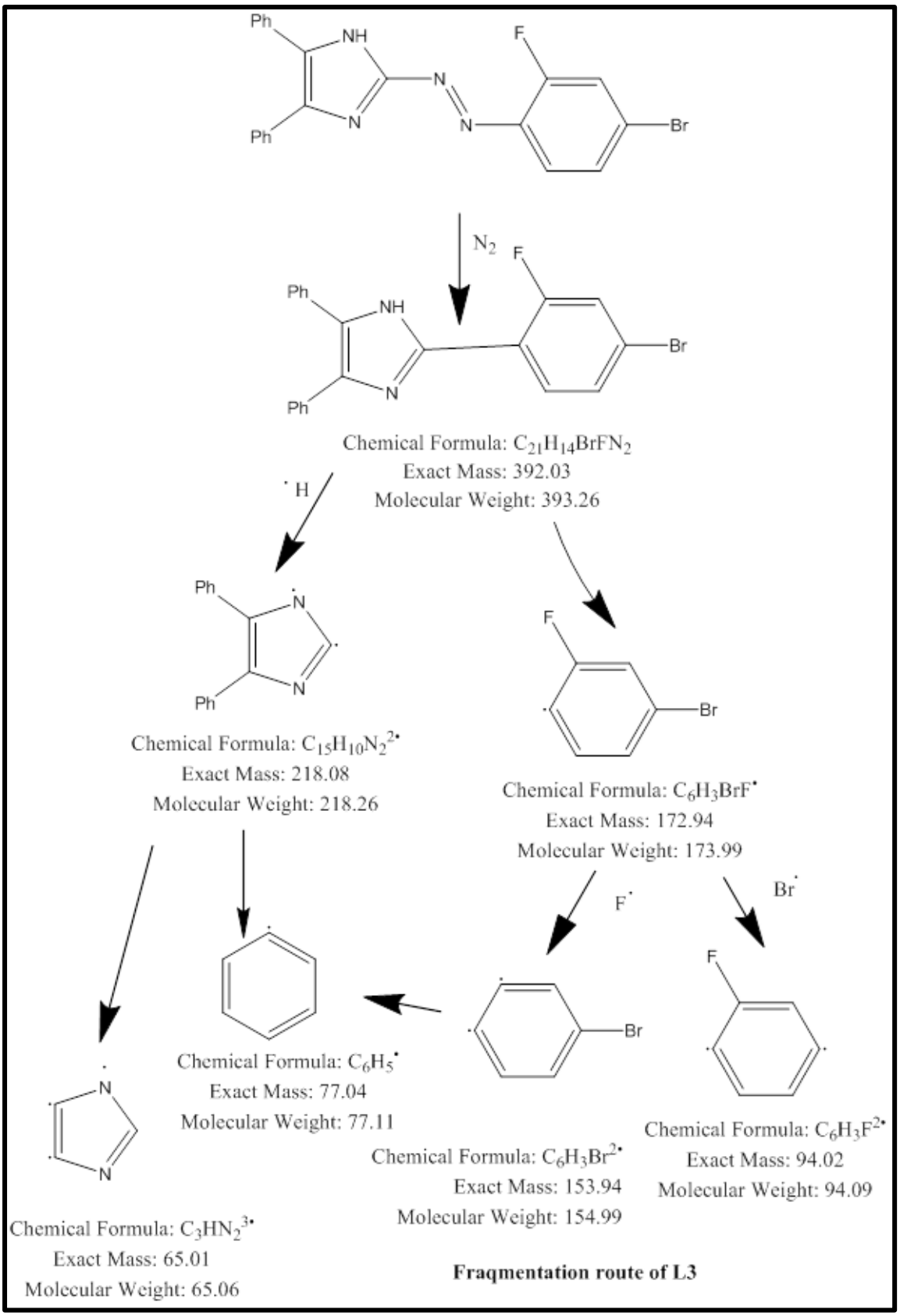
Fig (3-3): Mass spectrum of Azo-imidazole ligand (L_3)



Scheme (3-1): Mass fragmentation paths of Azo-imidazole ligand (L_1)



Scheme (3-2): Mass fragmentation paths of Azo-imidazole ligand (L_2)



Scheme (3-3): Mass fragmentation paths of Azo-imidazole ligand (L_3)

The most important thing that distinguishes these spectra from the previous ones is the large gradient in the molecular weights of the visible fragments, and this is mainly due to the difference in the energy used in the electronic bombardment. In general, it is noted that the proposed mass fragmentation paths varied between the exit of chlorine ions (if any), then the exit of the metal ion from the complex, followed by the fragmentation of the organic ligand or keeping the ligand bound to the metal ion during the complex dissociation reaction [152, 153].

It was possible to use the ESI technique, which deals with the inorganic parts along with the organic ligand [154] to know the mass of the azo-imidazole ligand complexes, as follows. The mass fragmentation spectrum of the complexes of CuL_1, PdL_2, and NiL_3 was measured. Fragments with an m/z = 494.2, 554.2, and 550.4, respectively, and with a molecular ion appearance ratio of less than 1% (due to the large molecular weight of the prepared complexes and the ease of their fragmentation in view of a large number of hybrid atoms) [148] for each of $CuL_1$and NiL_3, and others with a value of 360.2, 376.2, and 421.1 equivalent to the [M] of the derived ligand for each complex, respectively. In addition, that values are supporting evidence of the value of the molecular weight of the mentioned complexes and enhance the formation of the complexes with a molar ratio (M: L, 1:1), figures (3-4) to (3-6) and diagrams (3-4) to (3-6) show the mass spectra of some of the prepared metal complexes and the proposed mass fractionation paths for some of these complexes.

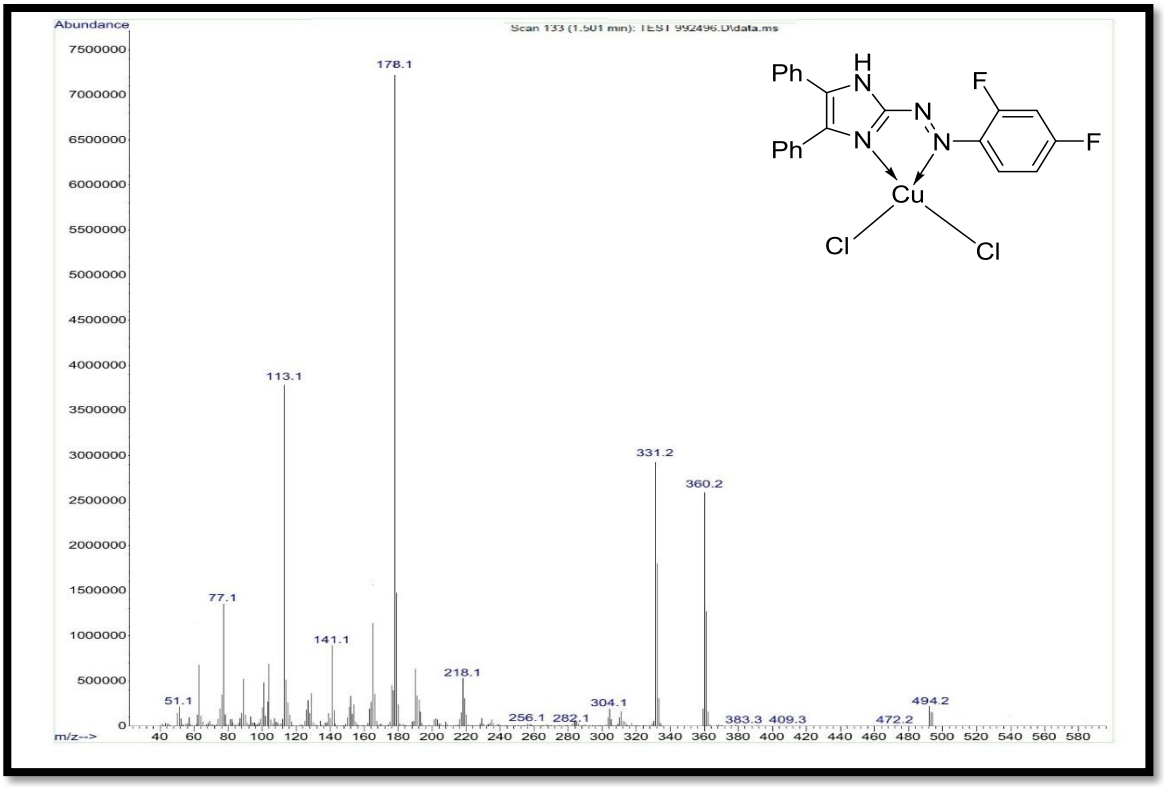


Fig (3-4): Mass spectra of Azo-imidazole complex (CuL_1)

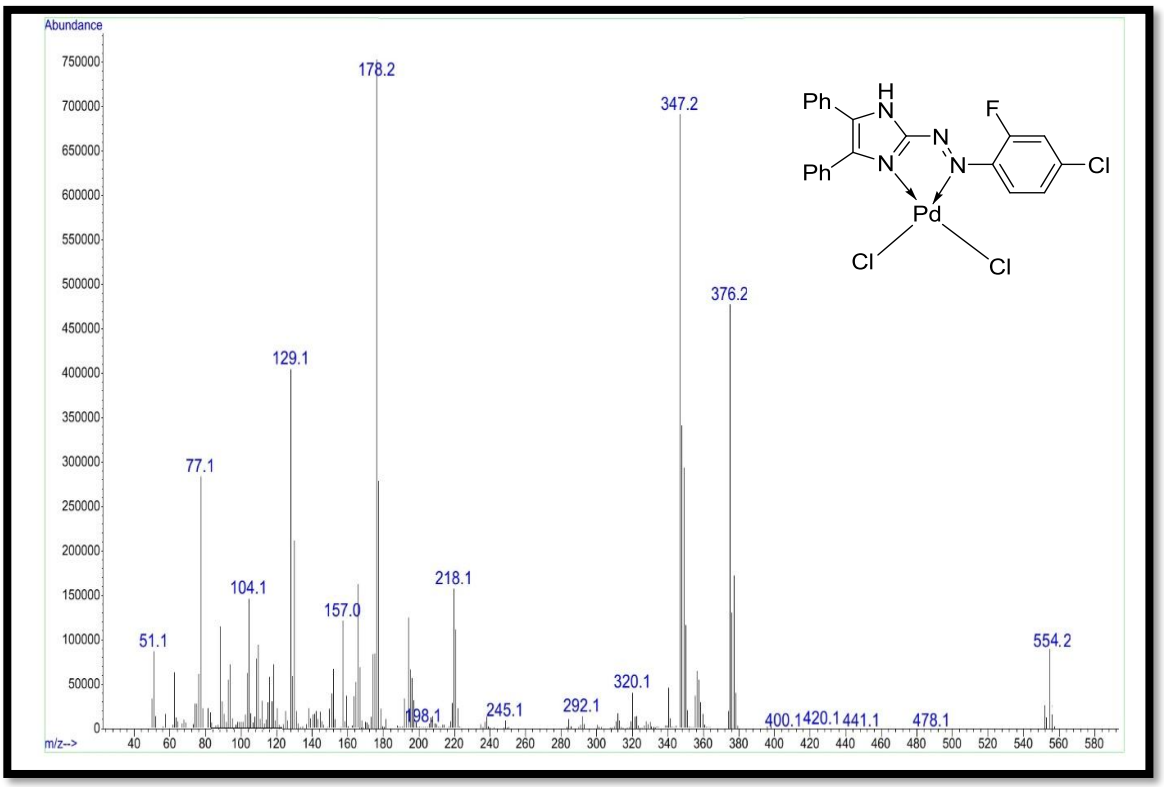


Fig (3-5): Mass spectra of Azo-imidazole complex (PdL_2)

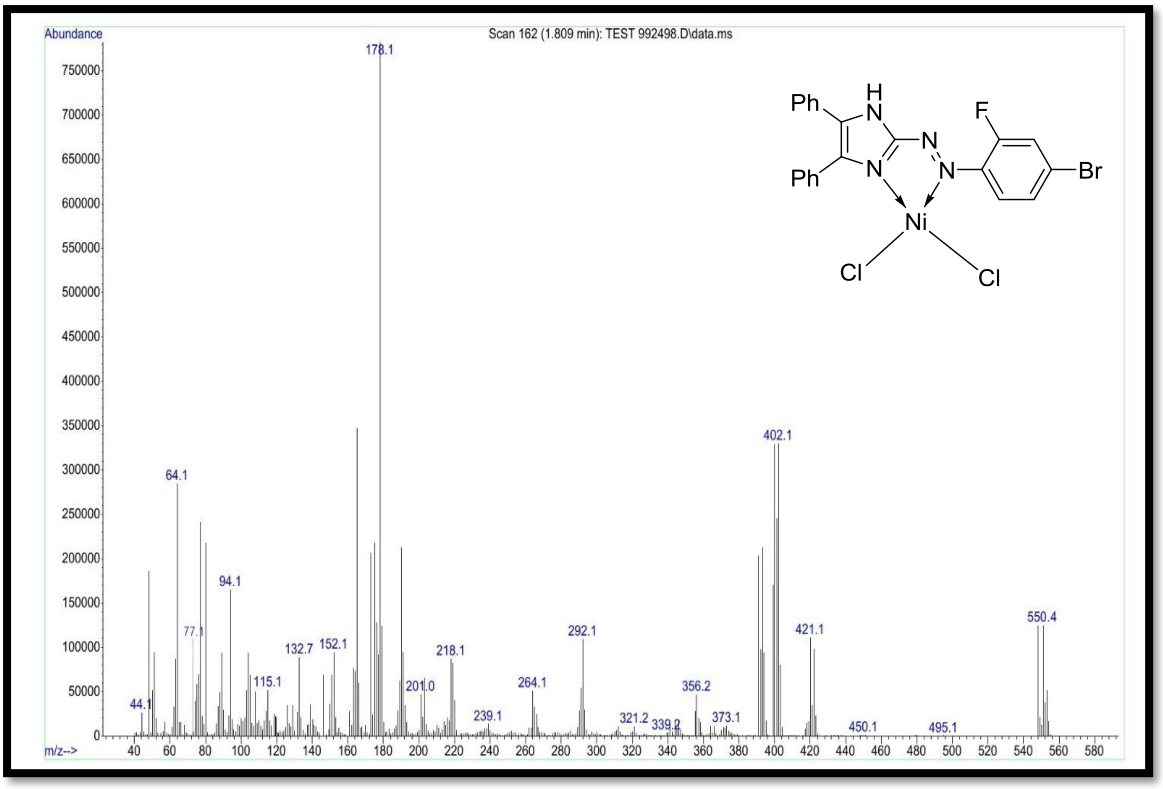
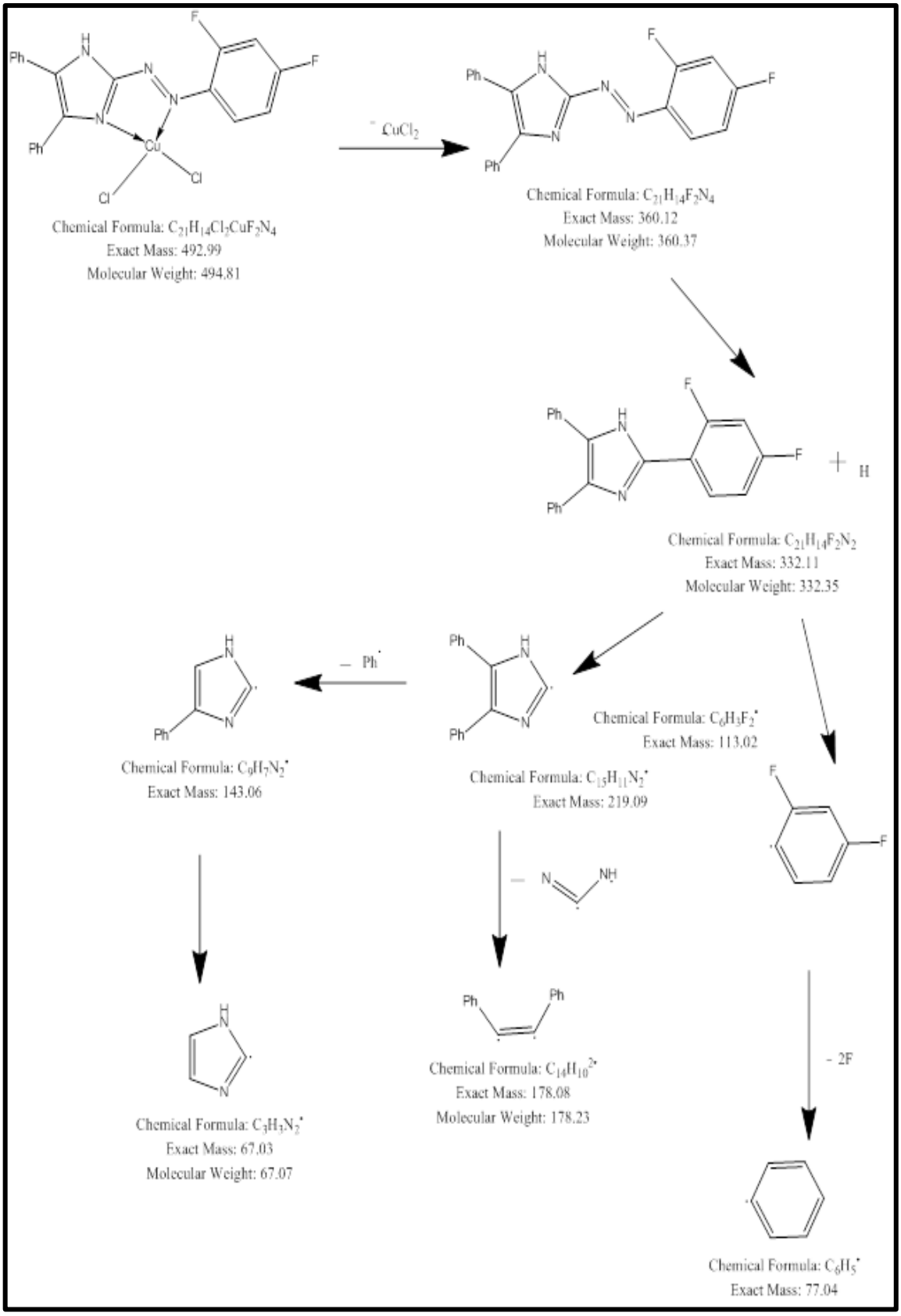
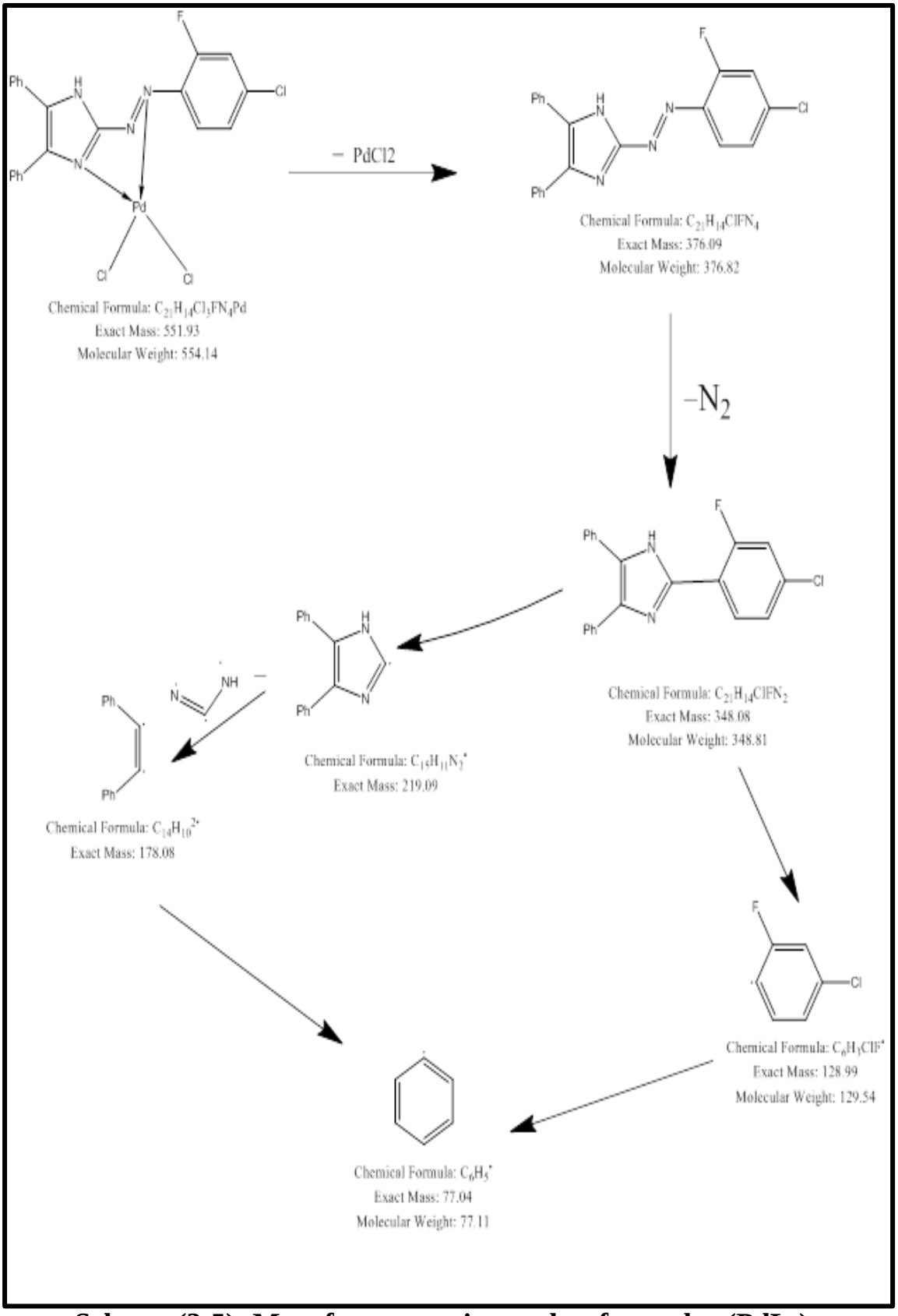


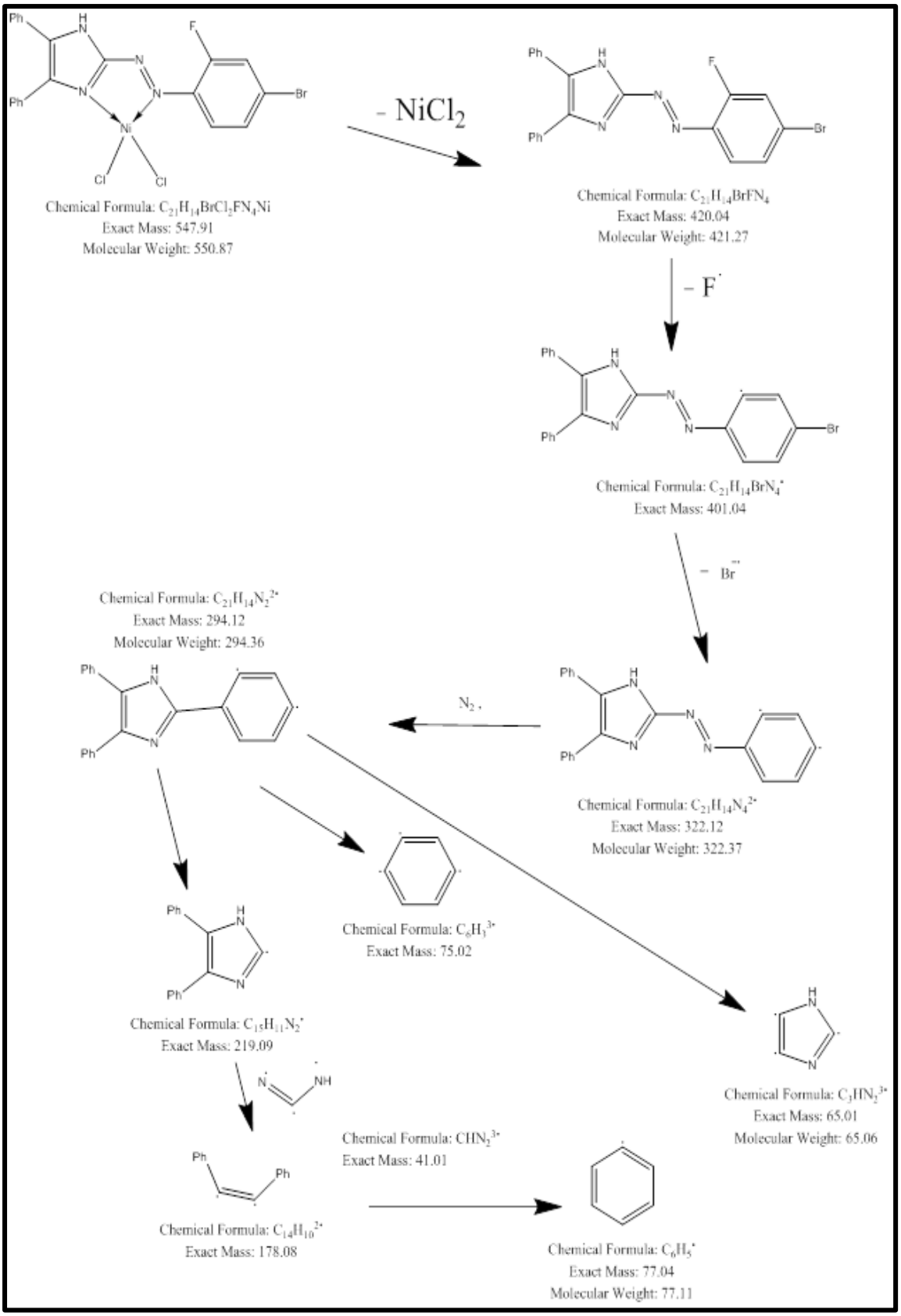
Fig (3-6): Mass spectra of Azo-imidazole complex (NiL_3)



Scheme (3-4): Mass fragmentation paths of complex (CuL_1)



Scheme (3-5): Mass fragmentation paths of complex (PdL_2)



Scheme (3-6): Mass fragmentation paths of complex (NiL_3)

3.1.2. Mass Spectra of Azo-Schiff Base Ligands and their Chelating Complexes

Molecular species (organic, inorganic, and polymers) [155] can be precisely detected by using an adequate technique such the mass spectrometry, that able to give successive degradation of the target compounds, the molecular masses can easily be informed, the stability of the fragments can be expressed by their intensities.

The mass spectra of the new organic ligands, the subject of our study, were recorded using mass spectrometry. All of these spectra showed the mother molecular ions at m/z = 406.1, 422.4, and 467.0 for L_4, L_5, and L_6, respectively, with a small relative abundance of less than 1% (the reason for this phenomenon may be due to their high molecular weights and a large number of heterogeneous atoms present in their chemical structures), in addition to the exposure of these ligands to high bombardment energy. The disintegration of these molecules, which in their paths correspond to what is, stated in the literature regarding the fragmentation of this type of organic compound [156]. Figures (3-7) to (3-9) show the recorded spectra of the three azo-Schiff ligands.

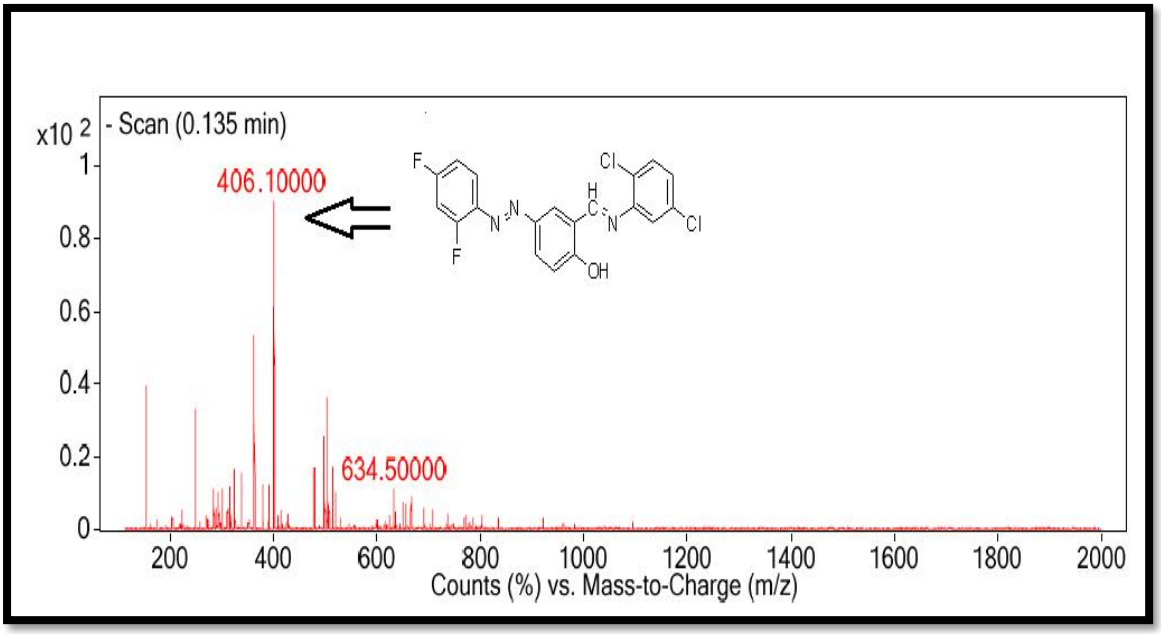


Fig (3-7): Mass spectra of Azo-Schiff ligand (L_4)

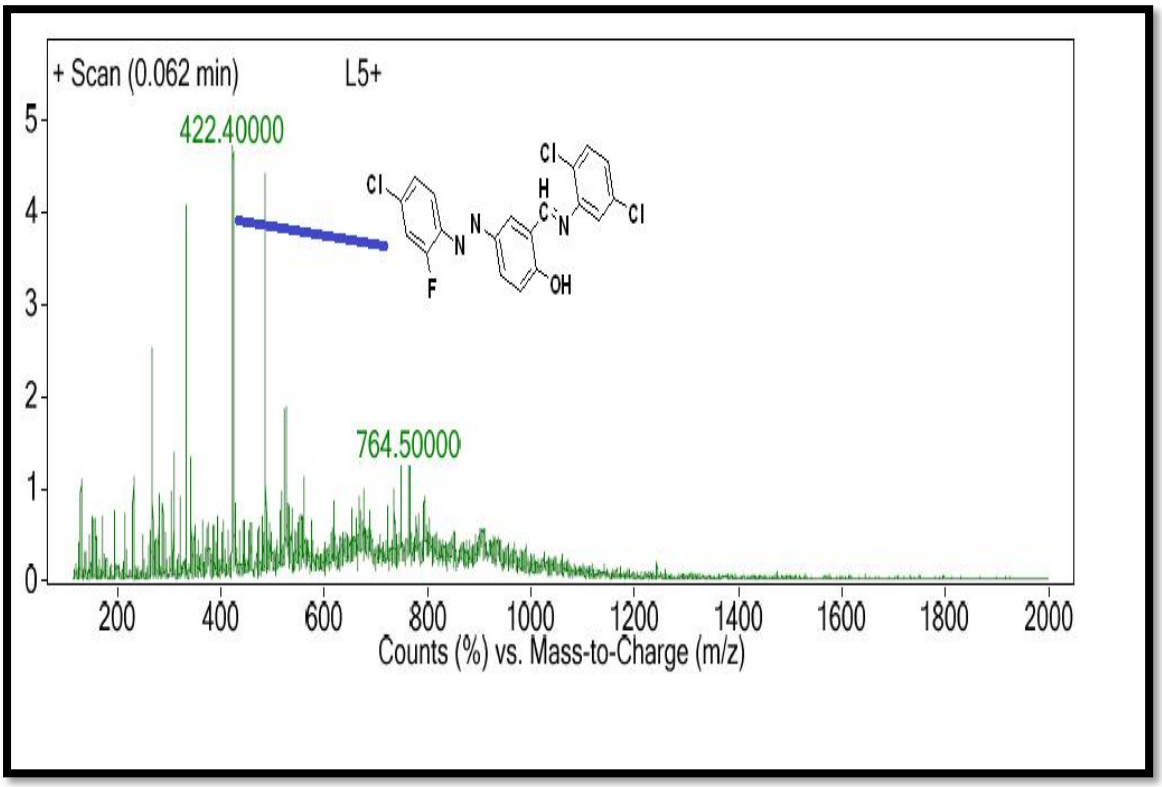


Fig (3-8): Mass spectra of Azo-Schiff ligand (L_5)

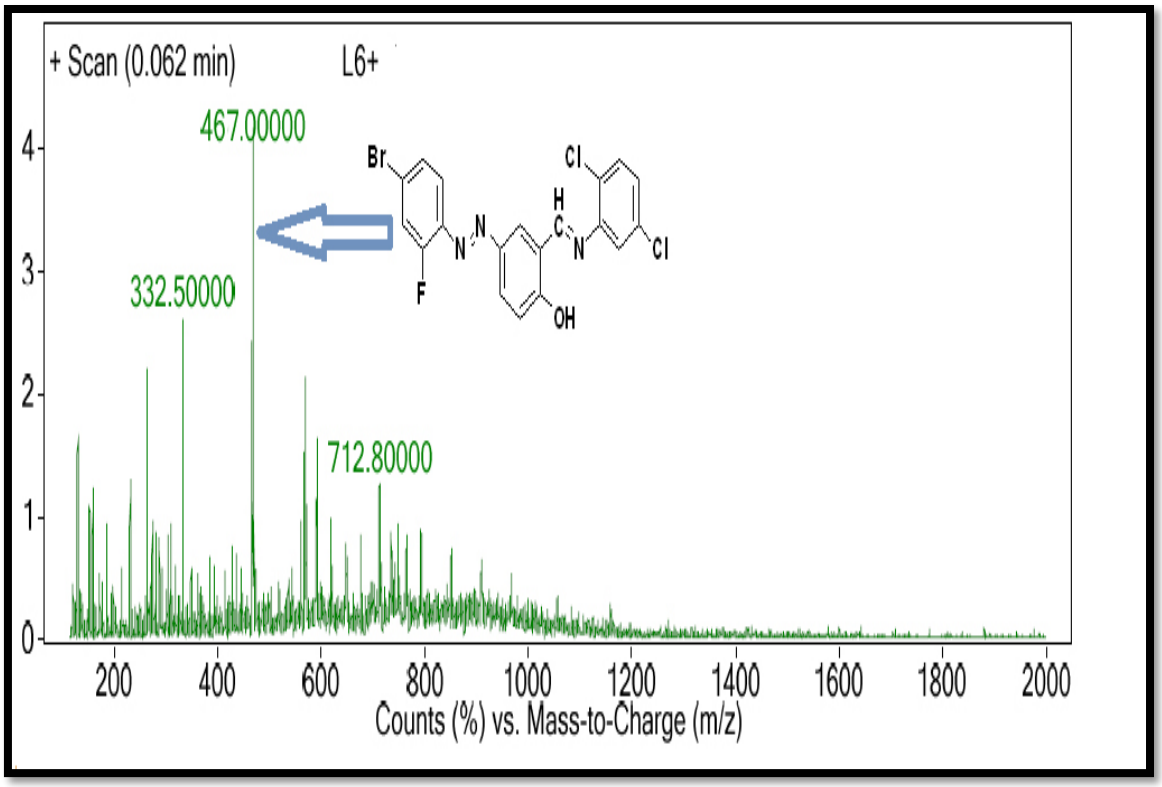


Fig (3-9): Mass spectra of Azo-Schiff ligand (L_6)

Mass spectrometry analysis were carried out for the prepared metal complexes, which showed the mass spectrum of the complexes the mother molecular ions at m/z = 565.1, 670.2, and 578.2 for PdL_4, PtL_5, and NiL_6, respectively, with a small relative abundance of less than 1% (the reason for this phenomenon may be due to their high molecular weights and a large number of heterogeneous atoms present in their chemical structures), in addition to the exposure of these ligands to high bombardment energy. The disintegration of these molecules, which in their paths correspond to what is, stated in the literature regarding the fragmentation of this type of organic compound [156]. Figures (3-10) to (3-12) show the recorded spectra of the three azo-Schiff ligands complexes.

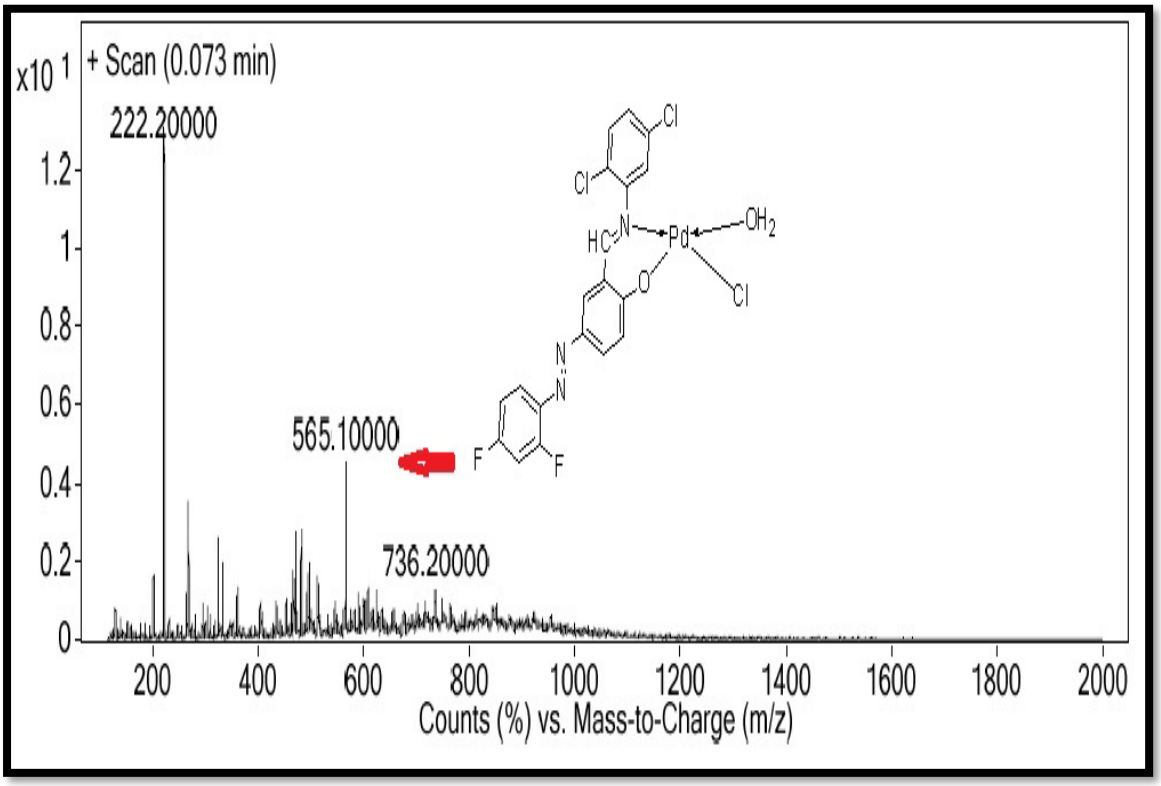


Fig (3-10): Mass spectra of Azo-Schiff complex (PdL_4)

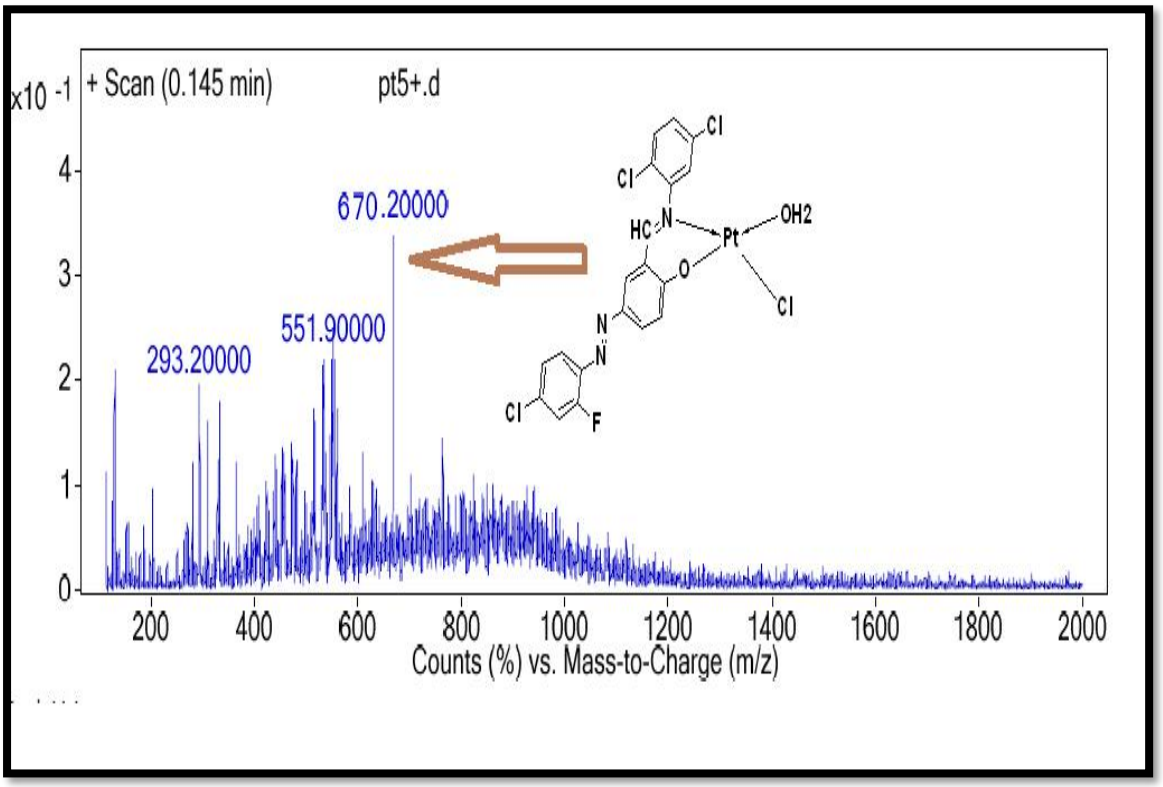


Fig (3-11): Mass spectra of Azo-Schiff complex (PtL_5)

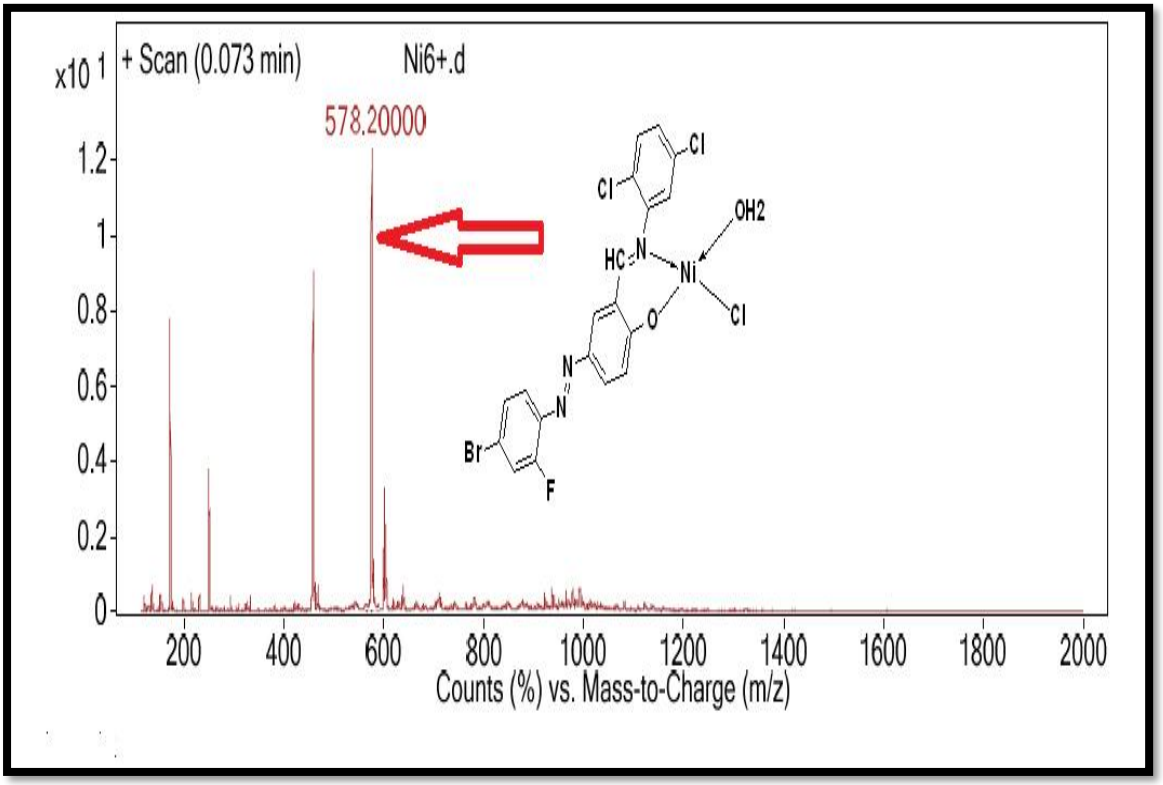


Fig (3-12): Mass spectra of Azo-Schiff complex (NiL_6)

3.2. ^{1}HNMR Spectroscopy

Nuclear magnetic resonance technology is one of the important techniques in determining the structure of organic compounds in solutions [157]. Nuclear magnetic resonance spectroscopy, in turn, gives information about the number of magnetically distinct atoms of the protons of the hydrogen atoms under study [155], in addition to knowing the environment of each of them.

3.2.1. ^{1}HNMR Spectroscopy of Azo-imidazole Ligands and their Chelating Complexes

^{1}HNMR spectra of the three new ligands prepared for L_1, L_2, and L_3 showed a single signal at (8.99 ppm, 9.26 ppm, and 10.76 ppm) respectively, related to the NH imidazole protons [158, 159], which shifted to a lower frequency due to imidazole-imidazole intermolecular hydrogen bonding [160], The spectra of ligands also showed multiple signals within the range (6.74-7.83ppm, 7.32-7.78ppm, and 7.31-7.89ppm) for each of L_1, L_2, and L_3 respectively, which related to the aromatic ring protons for each ligand, in some spectra (L_2, L_3), the moisture signal observed at 3.5ppm. In addition, each of the spectra of the all ligands showed a single signal at (2.5 ppm) that related to the protons of the DMSO-d6 solvent [161]; figures (3-13) to (3-15) show the nuclear proton magnetic resonance spectra of the azo-imidazole ligands.

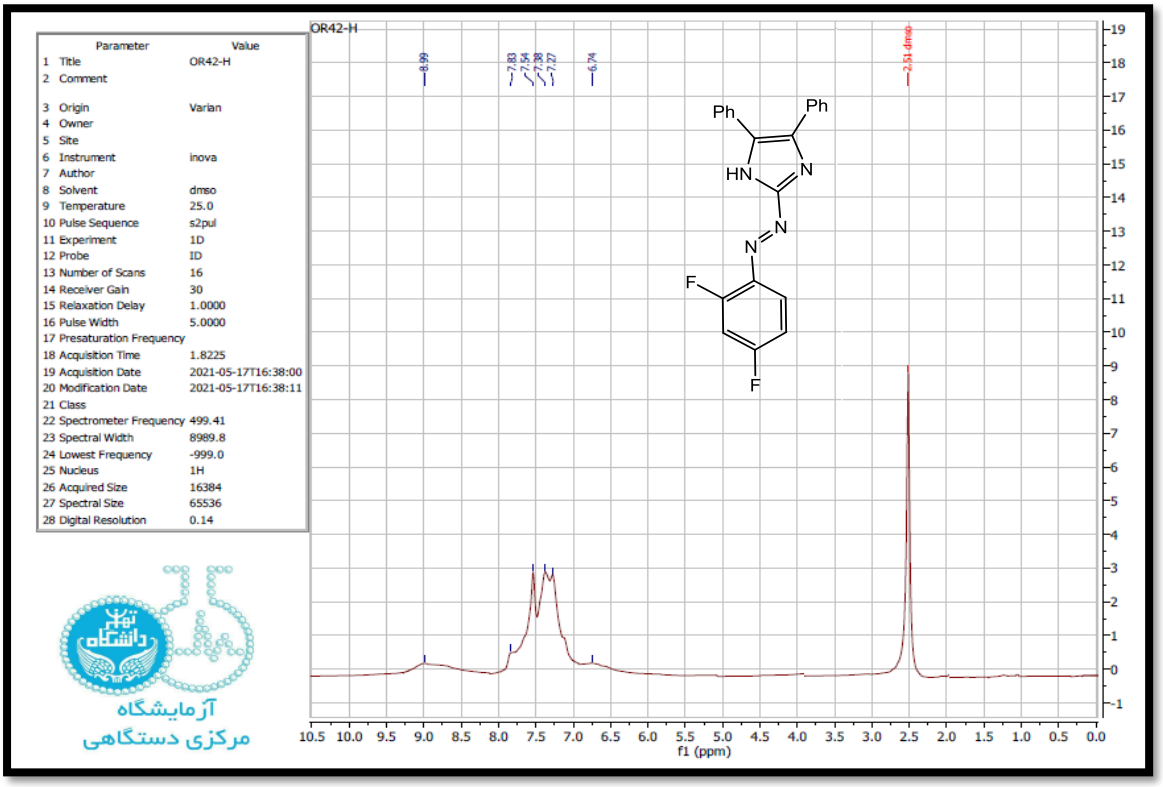


Fig (3-13): ^{1}HNMR spectra of Azo-imidazole ligand (L_1)

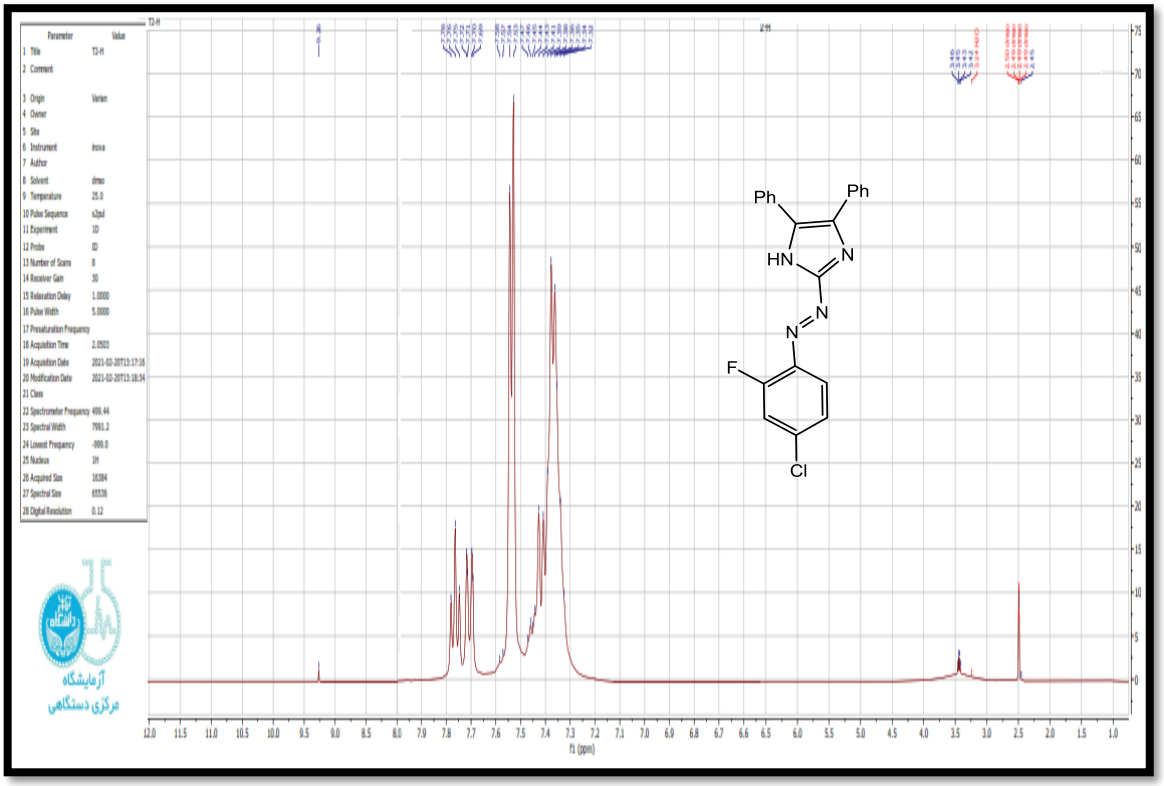


Fig (3-14): ^{1}HNMR spectra of Azo-imidazole ligand (L_2)

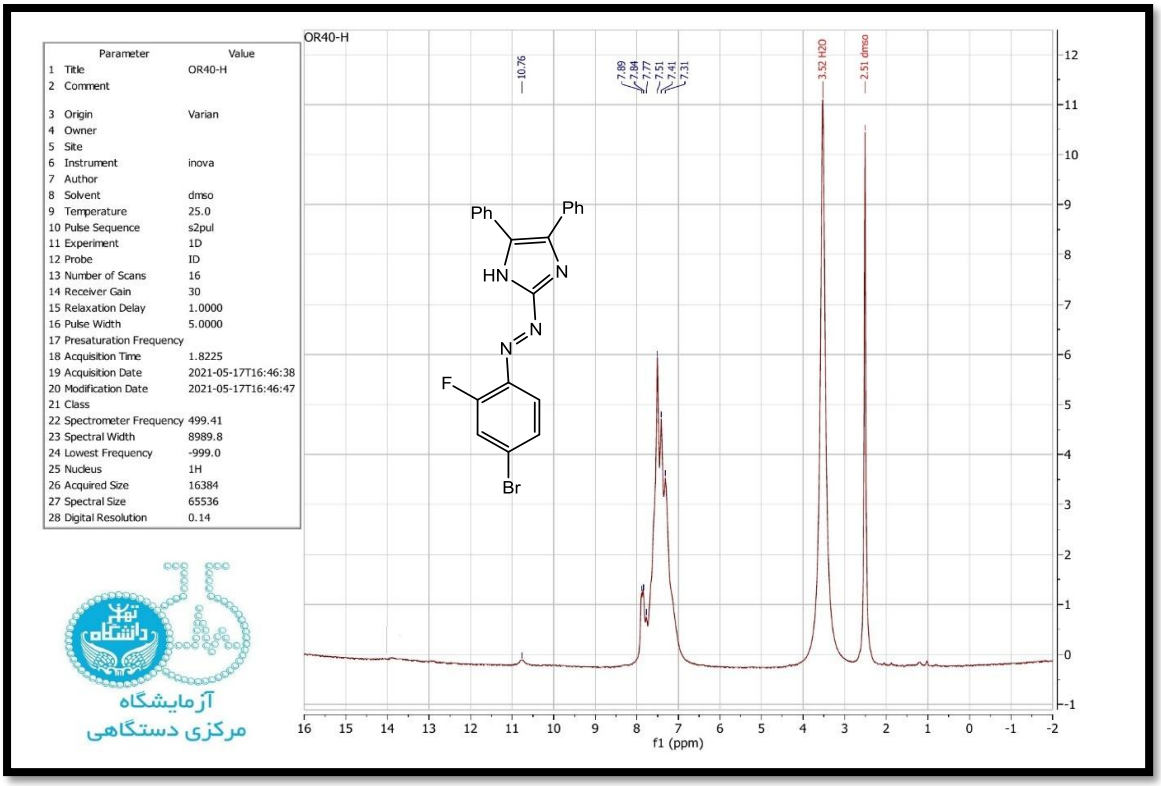


Fig (3-15): ^{1}HNMR spectra of Azo-imidazole ligand (L_3)

The complexes (NiL_1, PtL_2, and PdL_3) to find out the proton environment and contribute to the determination of the complex's shape after completing the remaining tests, where the resonance spectrum of each complex showed the disappearance of the proton signal of the NH imidazole to an exchange process with the protons of the solvent, as for the other indications of the spectrum of all the aforementioned complexes, they do not differ much from the spectra of their ligands, noting that there are few displacements in their apparent signals, and this is the result of the complexity with the metal ion [162, 163], figures (3-16) to (3-18) show the nuclear proton magnetic resonance spectra of the new prepared complexes with nickel, platinum and palladium ions.

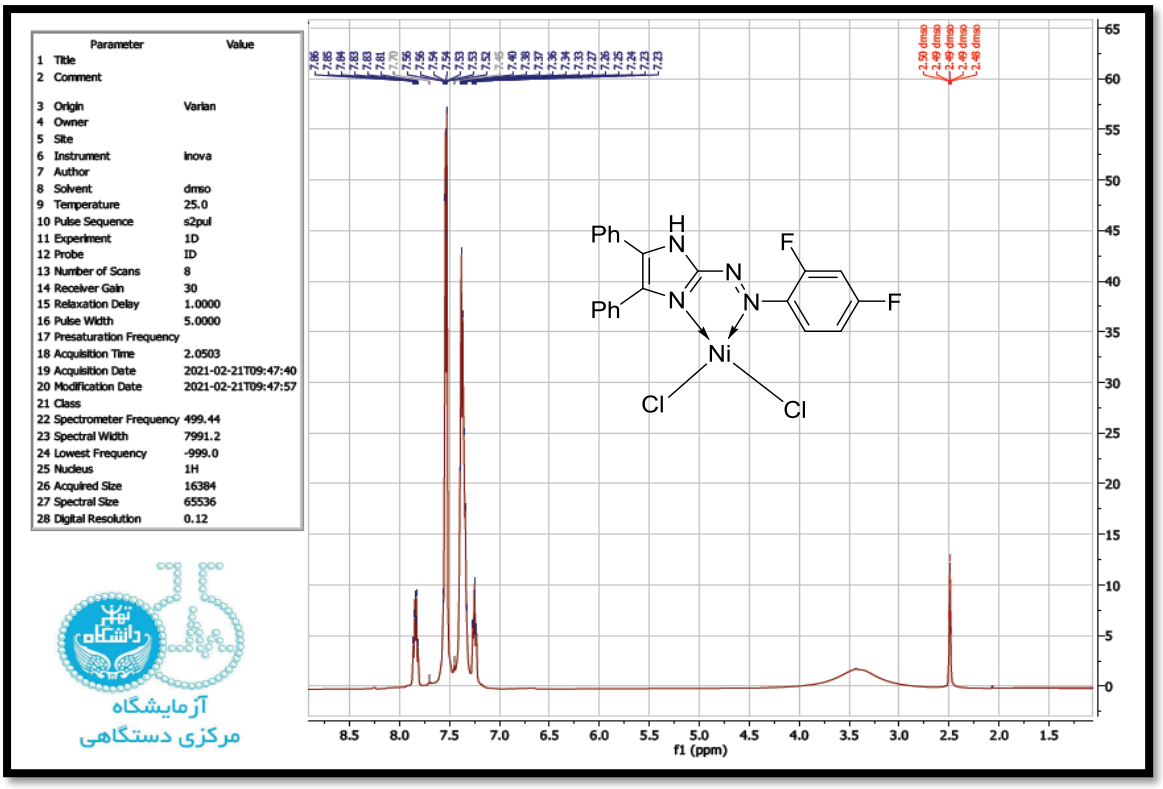


Fig (3-16): ^{1}HNMR spectra of Azo-imidazole complex (NiL_1)

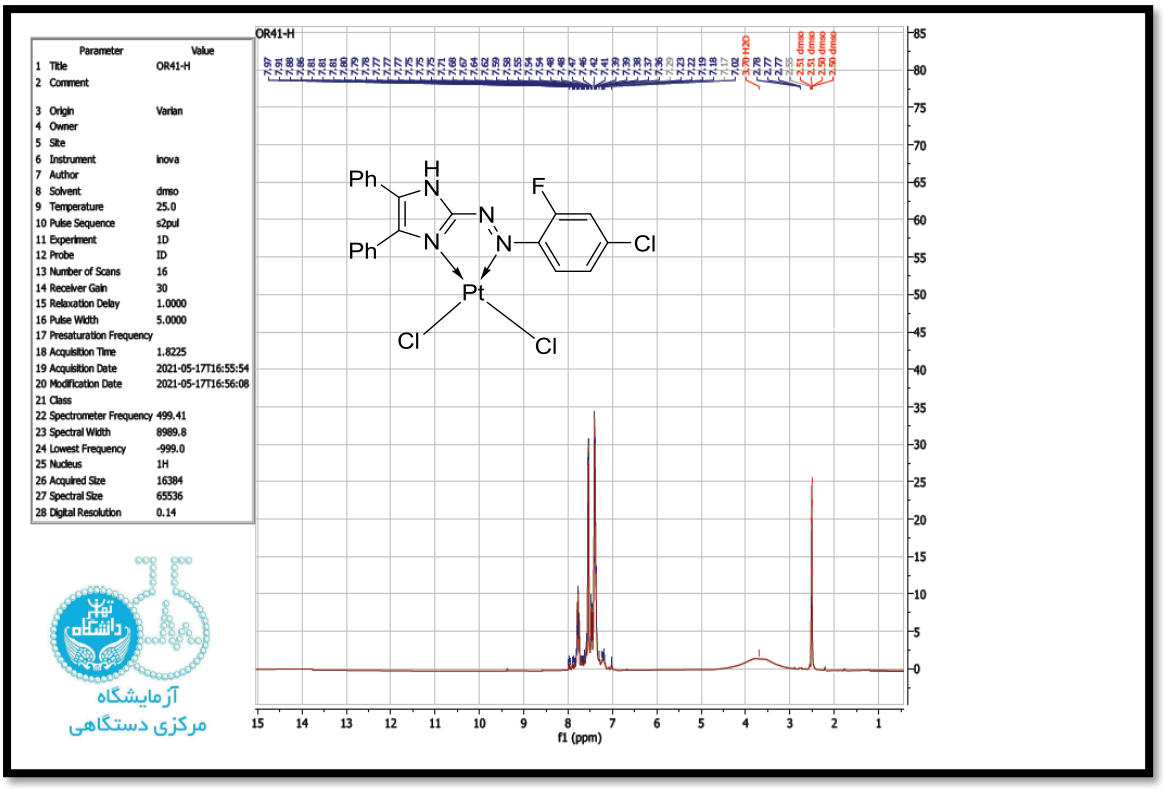


Fig (3-17): ^{1}HNMR spectra of Azo-imidazole complex (PtL_2)

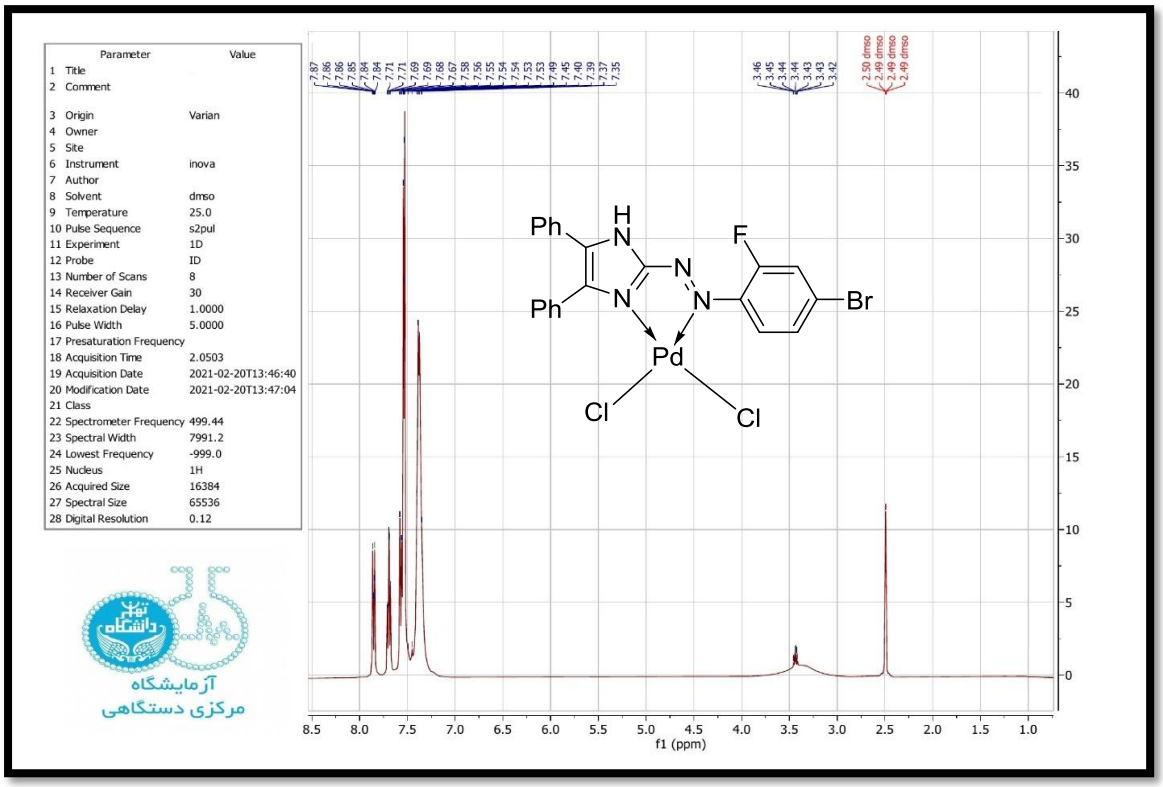


Fig (3-18): ^{1}HNMR spectra Azo-imidazole complex of (PdL_3)

3.2.2. ^{1}HNMR Spectroscopy of Azo-Schiff Base Ligands and their Chelating Complexes

The spectra of ligands for L_4, L_5, and L_6 showed many separate signals, including a single signal at (12.74ppm, 12.87ppm, 13.02ppm) related to the protons of the hydroxyl group of the phenol ring [164, 165] and a single signal at (9.05ppm, 9.07ppm, 9.17ppm) related to the azomethine group protons(HC=N-) [166] and multiple signals Within the range (7.47 – 7.39ppm, 7.66-7.51ppm, and 7.68-7.66ppm) related to the aromatic rings protons for each of (L_4, L_5, and L_6), respectively, it is believed that there is moisture in the samples, so it gave the signal at (3.32ppm), as well as to the protons of the solvent DMSO-d6 at (2.5ppm) for each ligand [161], respectively, figures (3-19) to (3-21) show the nuclear proton magnetic resonance spectra of the new azo-Schiff ligands.

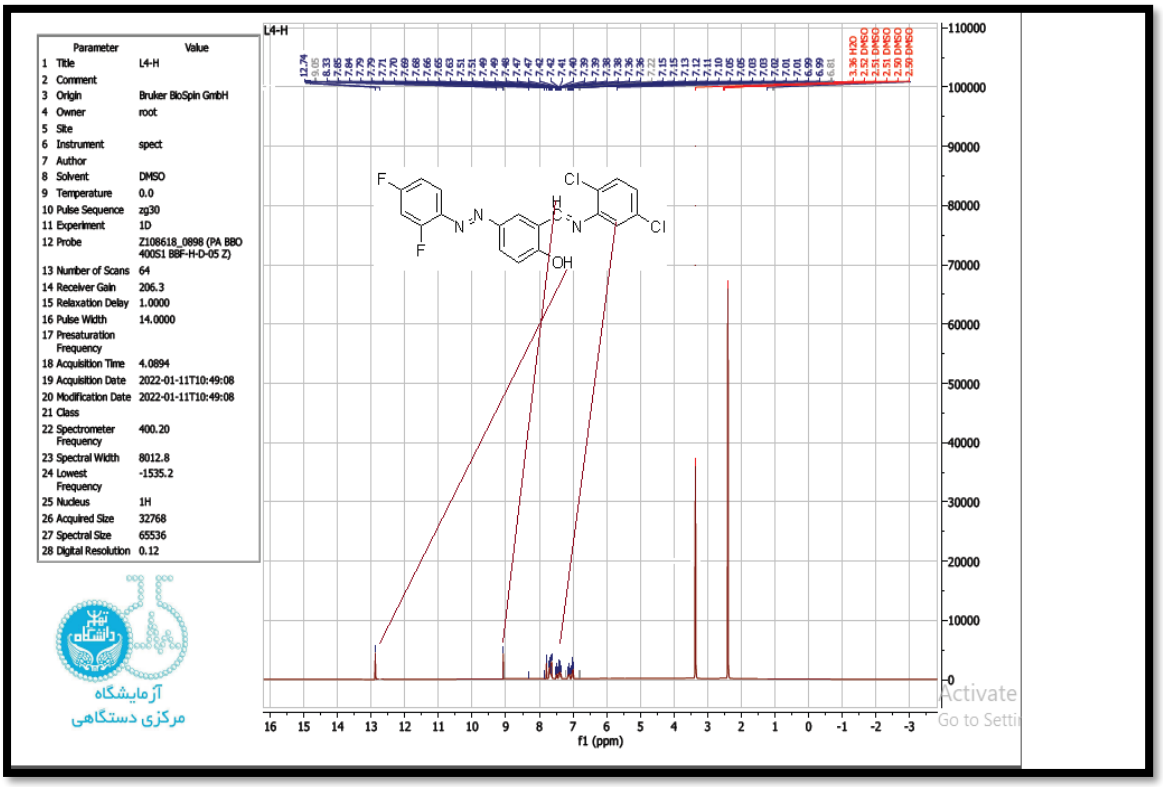


Fig (3-19): ^{1}HNMR spectra of Azo-Schiff ligand (L_4)

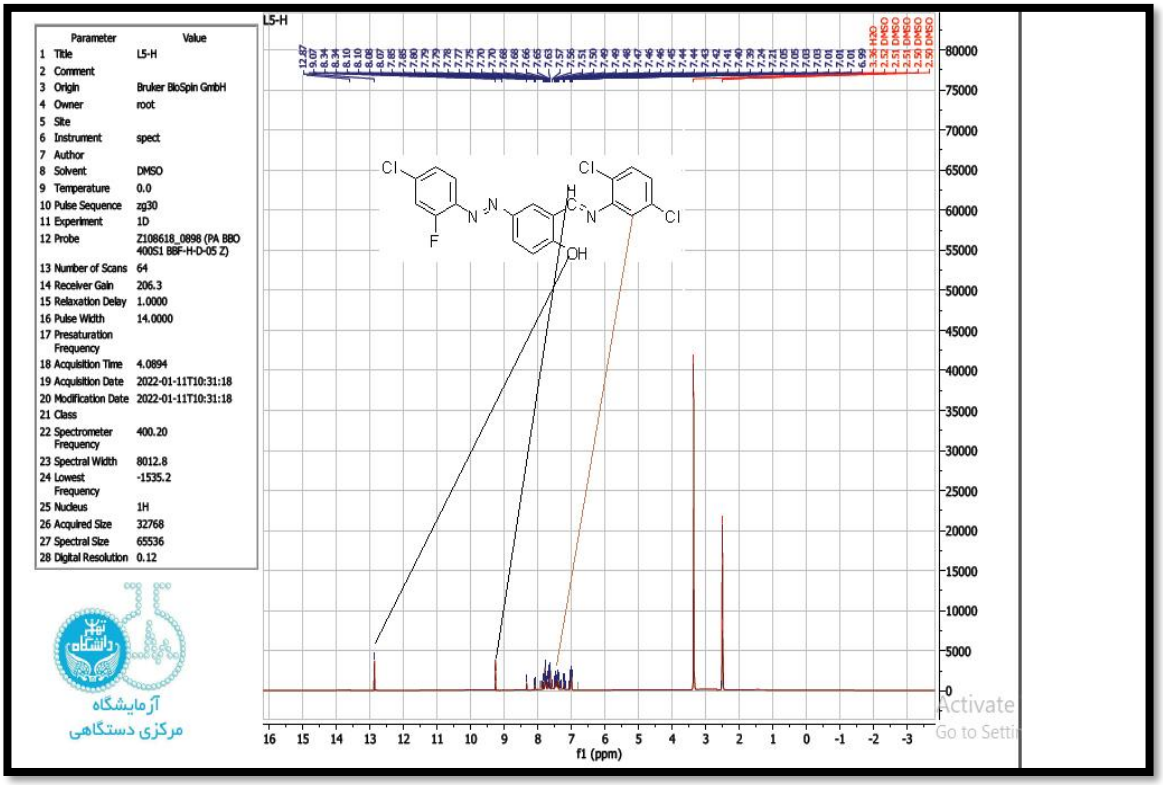


Fig (3-20): ^{1}HNMR spectra of Azo-Schiff ligand (L_5)

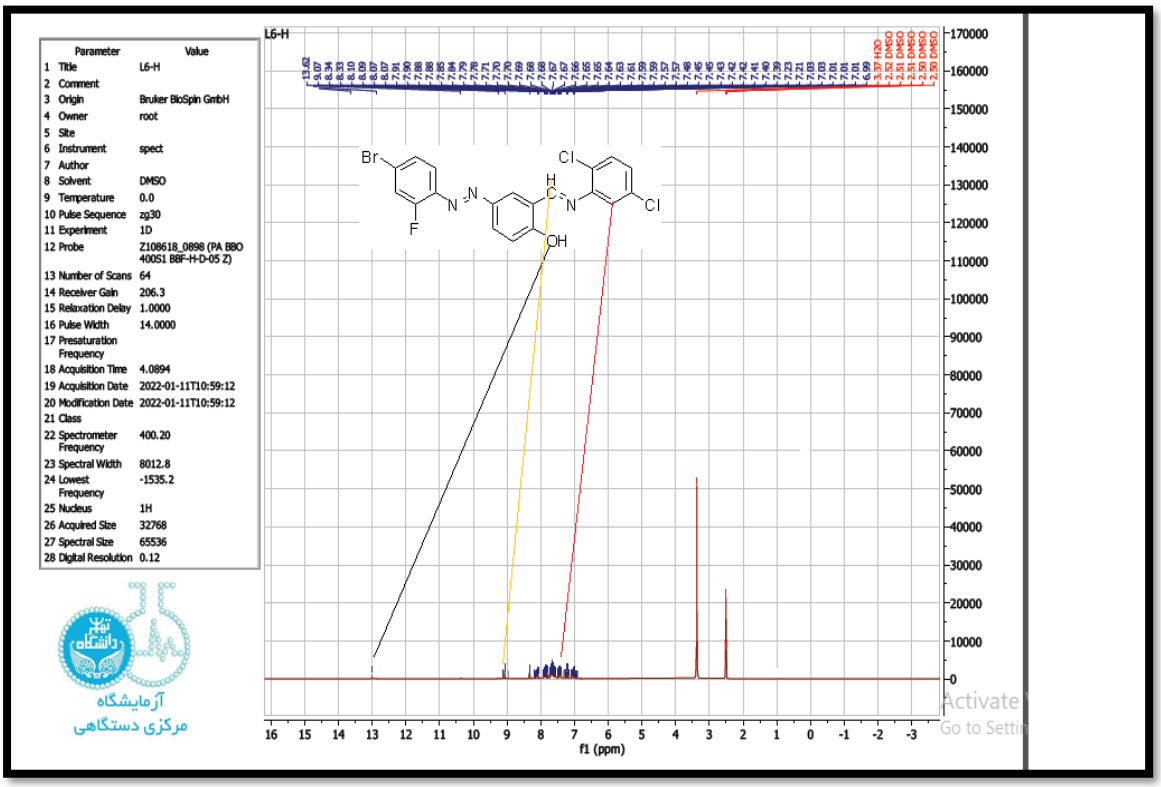


Fig (3-21) ^{1}HNMR spectra of Azo-Schiff ligand (L_6)

From the spectrum of each complex chosen for the same reasons mentioned above, all the spectra of (PdL_4, PtL_5, and CuL_6) azo-Schiff complexes showed the disappearance of the signal of protons related to the hydroxyl group in the phenol ring, and this is evidence of their participation in the coordination process with the metal ion (due deprotonated and confirm the bonding between the oxygen and ions) [167, 168], we also note the appearance of large signals at (3.42ppm, 3.36ppm, and 3.36ppm) for each complex (PdL_4, PtL_5, and CuL_6), indicative of the coordination of water with the metal ion (and this enables us to suggest the form of complexes later), as for the other indications of the spectrum of all the aforementioned complexes, they do not differ much from the spectra of their ligands, noting that there are few displacements in their apparent signals, and this is the result of the complexity with the metal ion

[162, 163], figures (3-22) to (3-24) show the nuclear proton magnetic resonance spectra of the new prepared complexes with palladium, platinum, and copper ions.

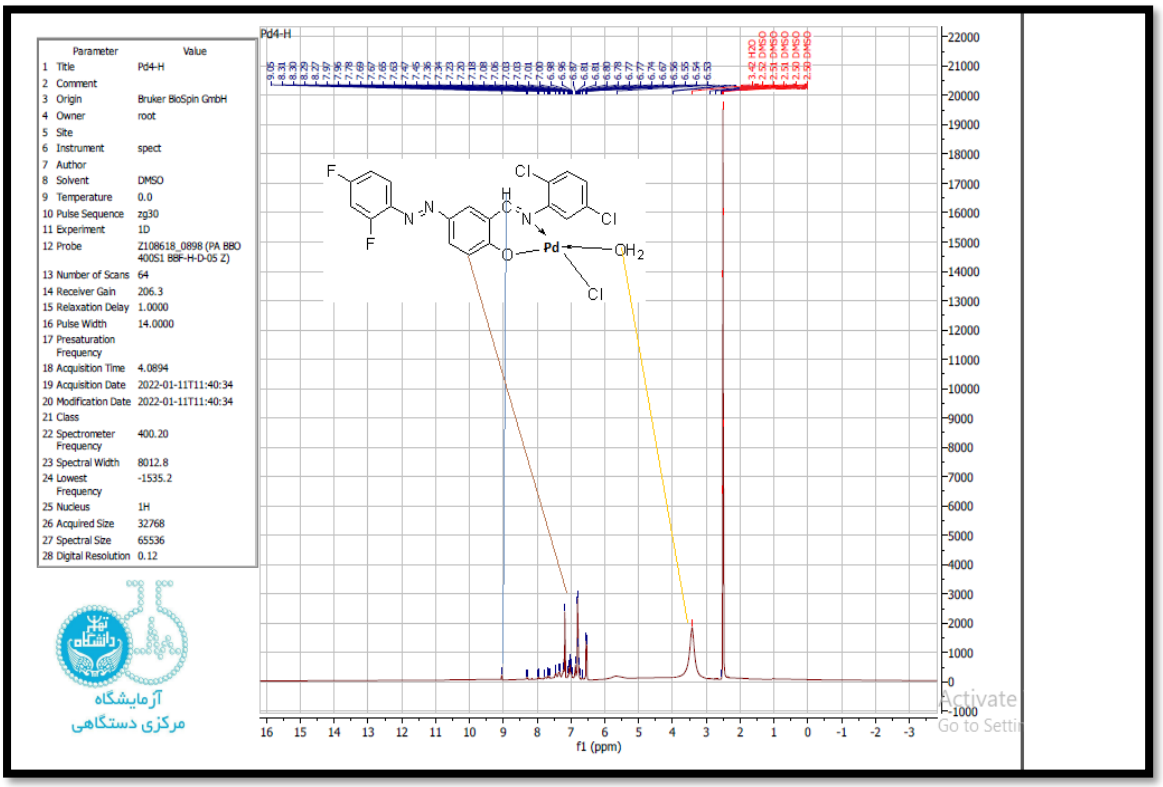


Fig (3-22): ^{1}HNMR spectra of Azo-Schiff complex (PdL_4)

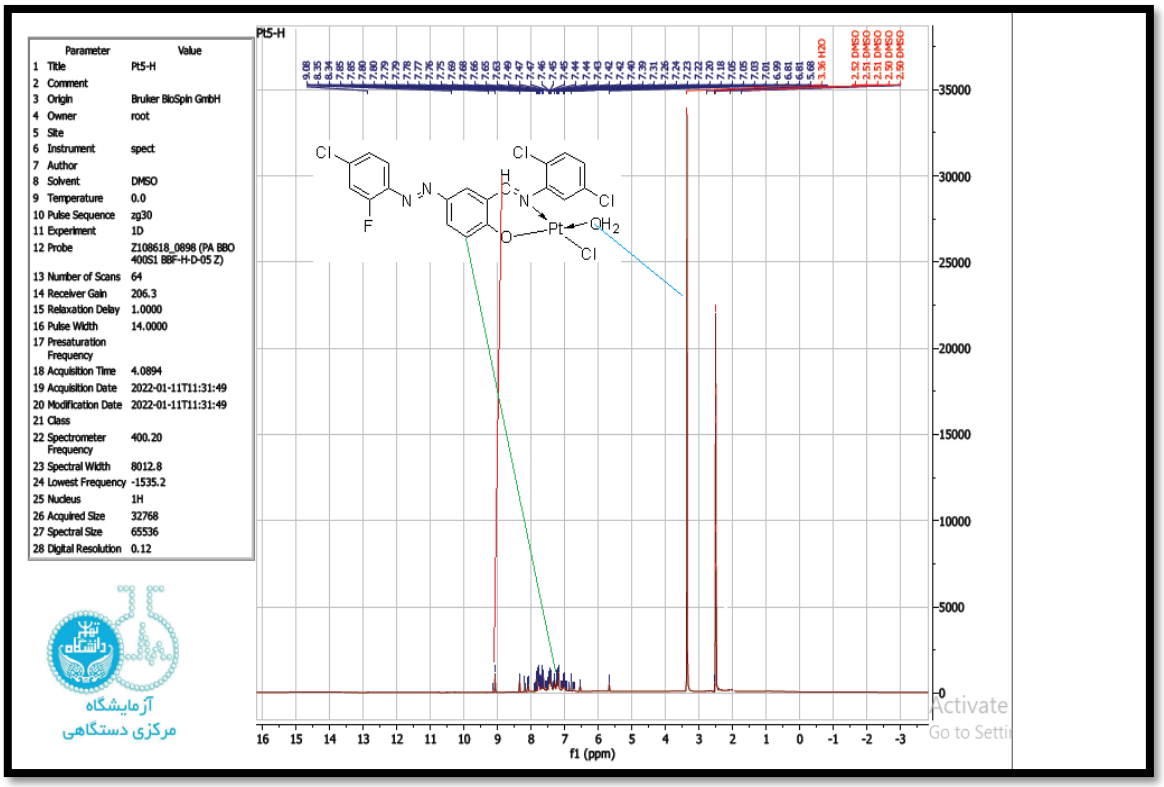


Fig (3-23): ^{1}HNMR spectra of Azo-Schiff complex (PtL_5)

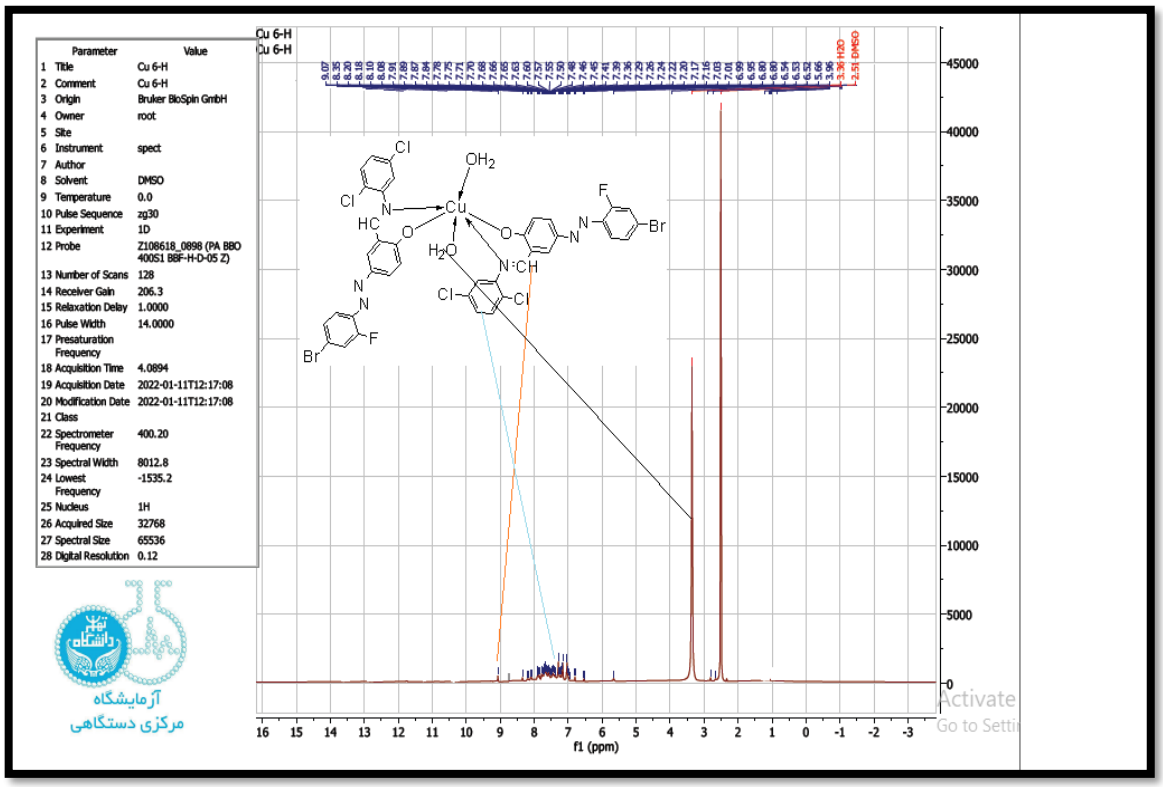


Fig (3-24): ^{1}HNMR spectra of Azo-Schiff complex (CuL_6)

3.3. Infrared Spectra

Infrared spectra are widely used in coordination chemistry to determine the changes in the absorption bands of effective groups before and after the coordination of the ligand and its complexes. It is known that the emergence of the coordination bond leads to changes in the structure and energy level of the electrons, in particular the participation of electrons in the coordination process, in addition to changes in the symmetry of that molecule, which leads to the emergence of clear differences in the intensity of the main absorption beam sites, which is an indication of interaction and formation of the desired product [169. 171], the infrared spectra of the ligand are also affected by the nature of the aggregates associated with it in terms of electronic density, space orientation, and symmetry, as well as the presence or absence of implicit hydrogen bonds, as well as the strength of

the coordination bond after the coordination process between the ligand molecule and the metal ion. We also do not rule out the effects that occur from the presence of metal ions outside the coordination sphere [172, 173].

Infrared spectra of pure solid chelate complexes were recorded after being formatted as KBr discs and within the range (400-4000 cm-1) and the locations of the stretching bands have been determined for the number of effective groups that are likely to enter the process of coordination with metal ions, and an attempt has been made to explain them based on what is mentioned in the literature, noting the changes that occur to these bands in the shape, intensity, and location when these ligands interact with metal ions to form their chelating complexes.

In general, the infrared spectra showed the appearance of distinct bands for ν (N-H), ν(C=N), ν (N=N), ν (M–N), ν (M–O) and other bands. These stretch bands related to each ligand were compared separately, noting the changes in these bands in shape, intensity, and location before and after the coordination with the metal ions under study. In general, a similarity was observed between the spectra of the chelating complexes in some cases, but they differ in nature from the spectrum of the free ligand, and the reason may be due to the presence of the same effects on the stretching vibrations of the ligands prepared in this study.

3.3.1. Infrared Spectra of Azo-imidazole Ligands and their Chelating Complexes

The infrared spectra of L_1, L_2, and L_3 were showed weak intensity bands at stretching frequencies (3427, 3445, 3450) cm^{-1}, respectively, which related to the bond of (N–H) imidazole [174], when compared infrared spectra for azo-imidazole ligands with the spectra of complexes of the cobalt, nickel, copper, palladium, and platinum ions, there was no appearance of stretching frequency that related to the bond of (N–H)

imidazole, the reason may be due intermolecular hydrogen bonding [175], which leads to their lack of participation in the coordination process with the metal ions, also the spectra of the above-mentioned ligands were showed weak intensity absorption bands at frequencies (1613.76, 1608.93, 1644.33) cm^{-1}, which related to the bond of (C=N) group [176] for heterogeneous imidazole rings, and regarding the bands of the weak intensity absorption at frequencies (1491.74, 1490.55, 1489.37)cm-1 these related to the bond of (N=N) of the azo-bridge group [177]. While these bands suffered noticeable changes in the infrared spectra of the metal complexes by shifting them towards a lower frequency with some changes in their intensity, this shows the participation of the nitrogen atom for the azomethine group of the imidazole [178] and the nitrogen atom of the azo-bridge group [179, 180] in the coordination process with the metal ion to form bidentate chelating (N, N) complexes for all synthesized complexes. In addition, the infrared spectra of the metal complexes showed new absorption bands that related to the bond (M–N) at a frequency range from (694.71- 695.31) cm_{-1} starting from the first complex of the first ligand (CoL_1) to the last complex of the third ligand (PtL_3) [181, 183], table (3-1) shows the values of stretching frequencies of effective groups of ligands and their metal complexes, figures (3-25) to (3-42) show the infrared spectra of azo-imidazole ligands and their metal ion complexes.

Table (3-1): The values of infrared frequencies spectra in units (cm^{-1}) of the ligands (L_1, L_2, and L_3) and their chelating complexes.

Ligands/complexes	υ (N-H_{im})	υ (C=N_{im})	υ (N=N)	υ(M-N)
L1 ($C_{21}H_{14}N_4F_2$)	3427.13	1613.76	1491.74	---------
[Co($C_{42}H_{28}N_8F_4Cl_2$)]		1598.22	1483.47	694.71
[Ni($C_{21}H_{14}N_4F_2Cl_2$)]		1606.54	1485.44	697.18
[Cu($C_{21}H_{14}N_4F_2Cl_2$)]		1604.21	1483.13	693.46
[Pd($C_{21}H_{14}N_4F_2Cl_2$)]		1604.39	1488.98	693.11
[Pt($C_{21}H_{14}N_4F_2Cl_2$)]		1606.12	1482.77	694.52
L2 ($C_{21}H_{14}N_4F$ Cl)	3445.18	1608.93	1490.55	---------
[Co($C_{42}H_{28}N_8F_2Cl4$)]		1595.51	1487.85	697.04
[Ni($C_{21}H_{14}N_4FCl_3$)]		1597.92	1482.83	694.03
[Cu($C_{21}H_{14}N_4FCl_3$)]		1594.88	1461.24	693.72
[Pd($C_{21}H_{14}N_4FCl_3$)]		1600.86	1480.06	695.11
[Pt($C_{21}H_{14}N_4FCl_3$)]		1597.29	1476.27	696.43
L3($C_{21}H_{14}N_4FBr$)	3450.15	1644.33	1489.37	---------
[Co($C_{42}H_{28}N_8F_2Cl_2Br_2$)]		1589.72	1461.90	696.01
[Ni($C_{21}H_{14}N_4FCl_2Br$)]		1589.09	1477.90	693.78
[Cu($C_{21}H_{14}N_4FCl_2Br$)]		1587.41	1479.38	693.21
[Pd($C_{21}H_{14}N_4FCl_2Br$)]		1586.53	1484.11	692.97
[Pt($C_{21}H_{14}N_4FCl_2Br$)]		1590.13	1470.09	695.31

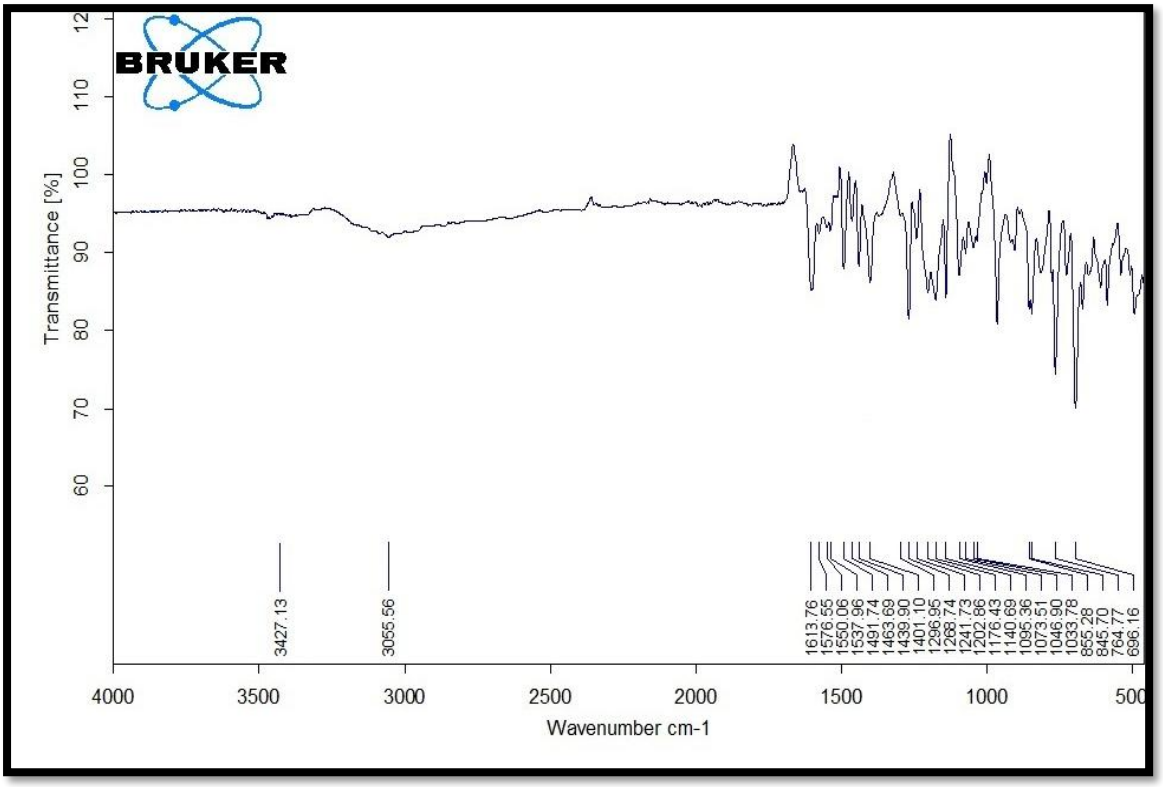


Fig (3-25): FTIR spectra of Azo-imidazole ligand (L_1)

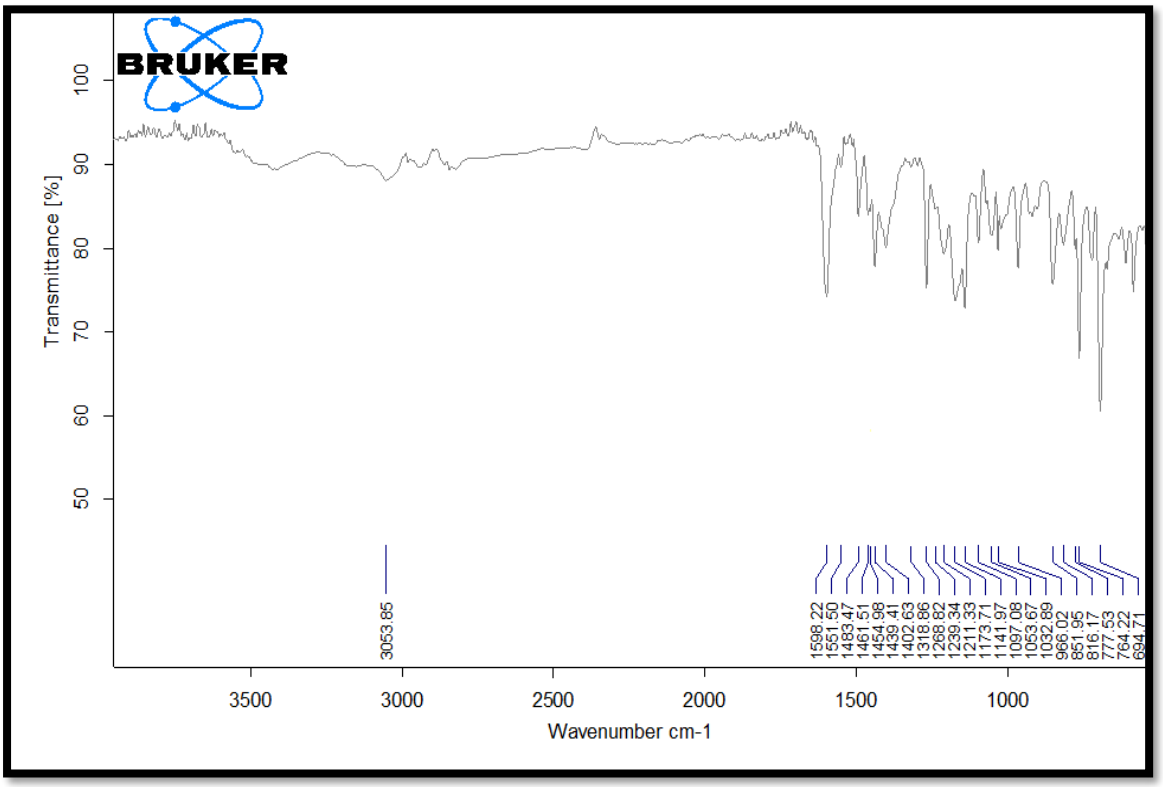


Fig (3-26): FTIR spectra of Azo-imidazole ligand complex (CoL_1)

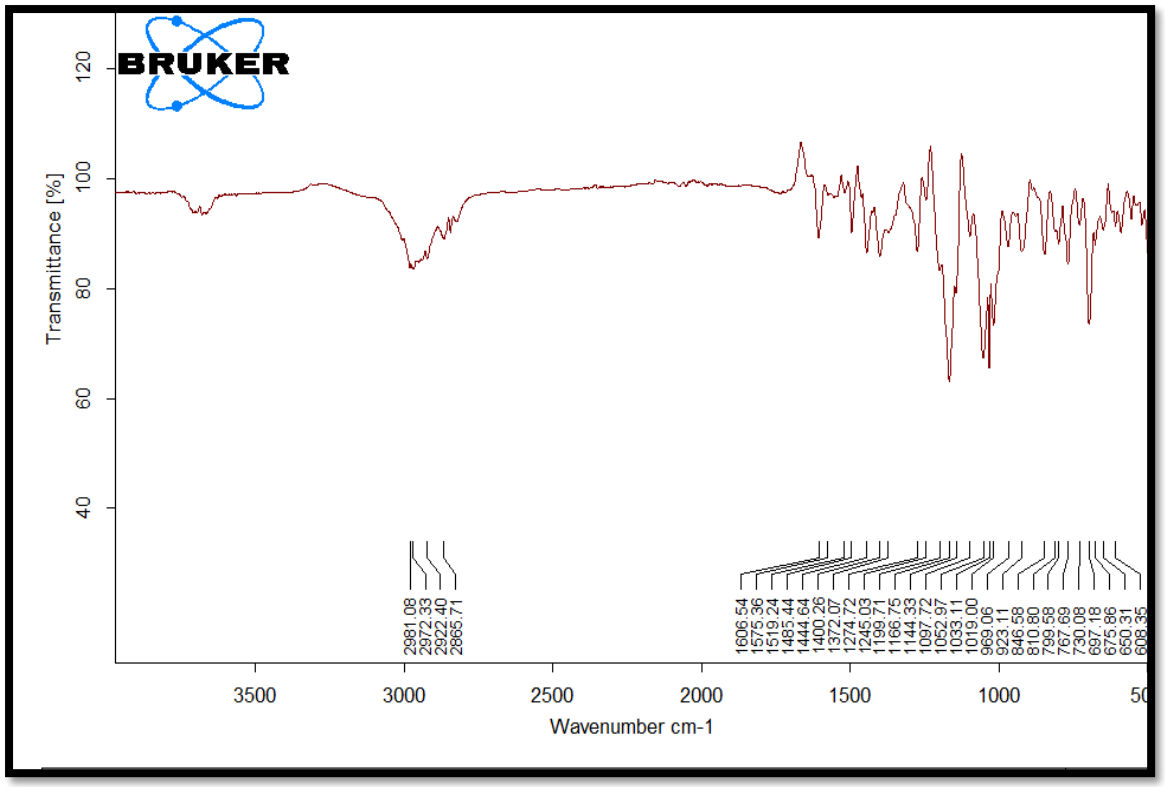


Fig (3-27): FTIR spectra of Azo-imidazole ligand complex (NiL_1)

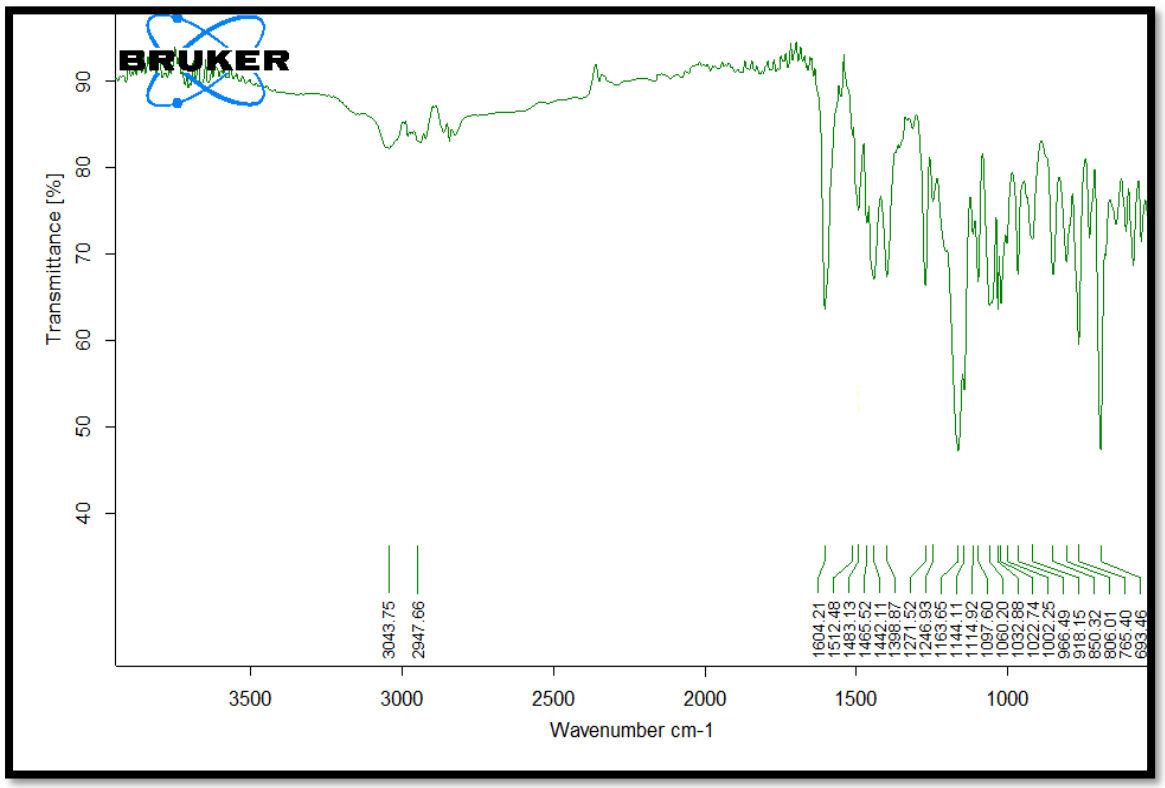


Fig (3-28): FTIR spectra of Azo-imidazole ligand complex (CuL_1)

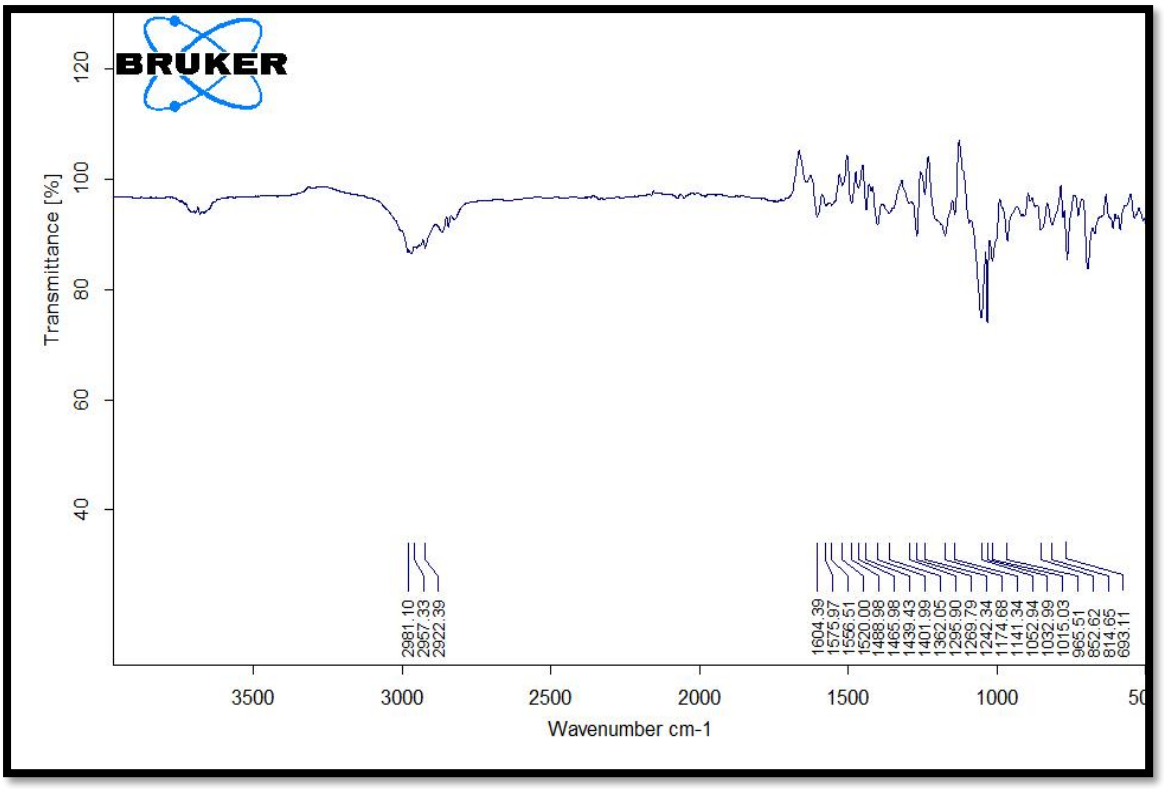


Fig (3-29): FTIR spectra of Azo-imidazole ligand complex (PdL_1)

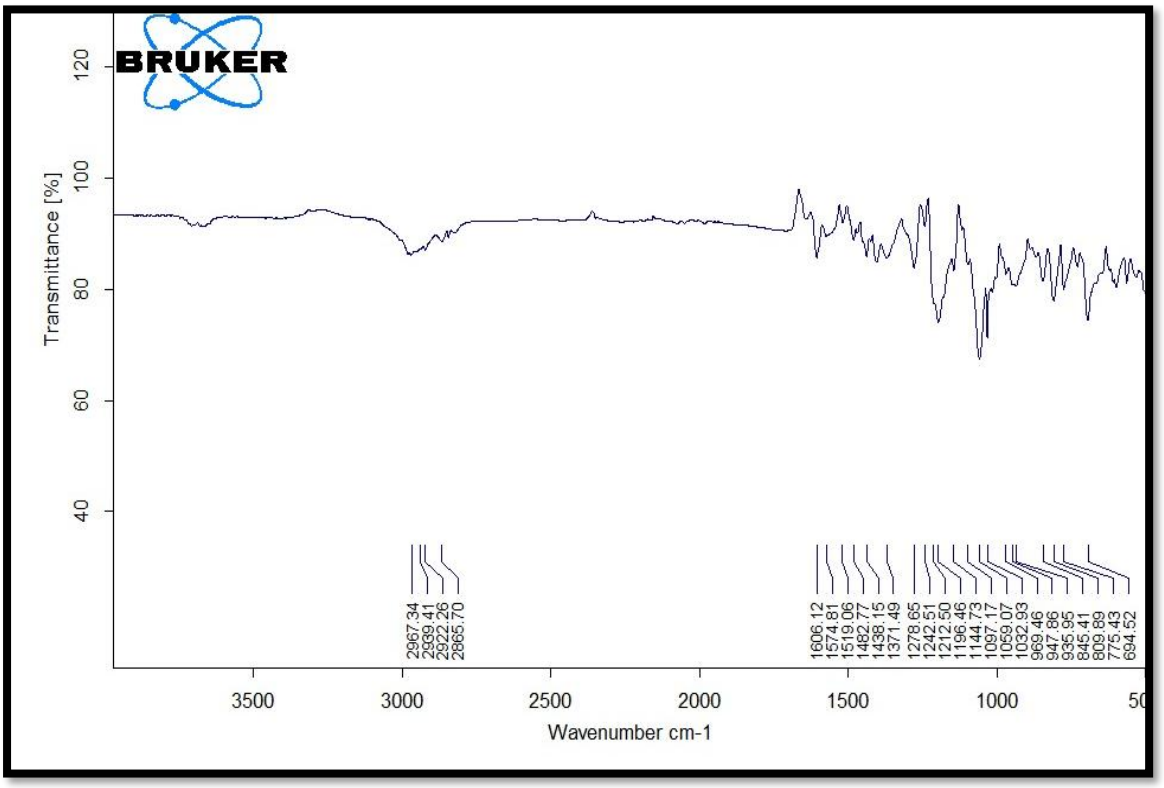


Fig (3-30): FTIR spectra of Azo-imidazole ligand complex (PtL_1)

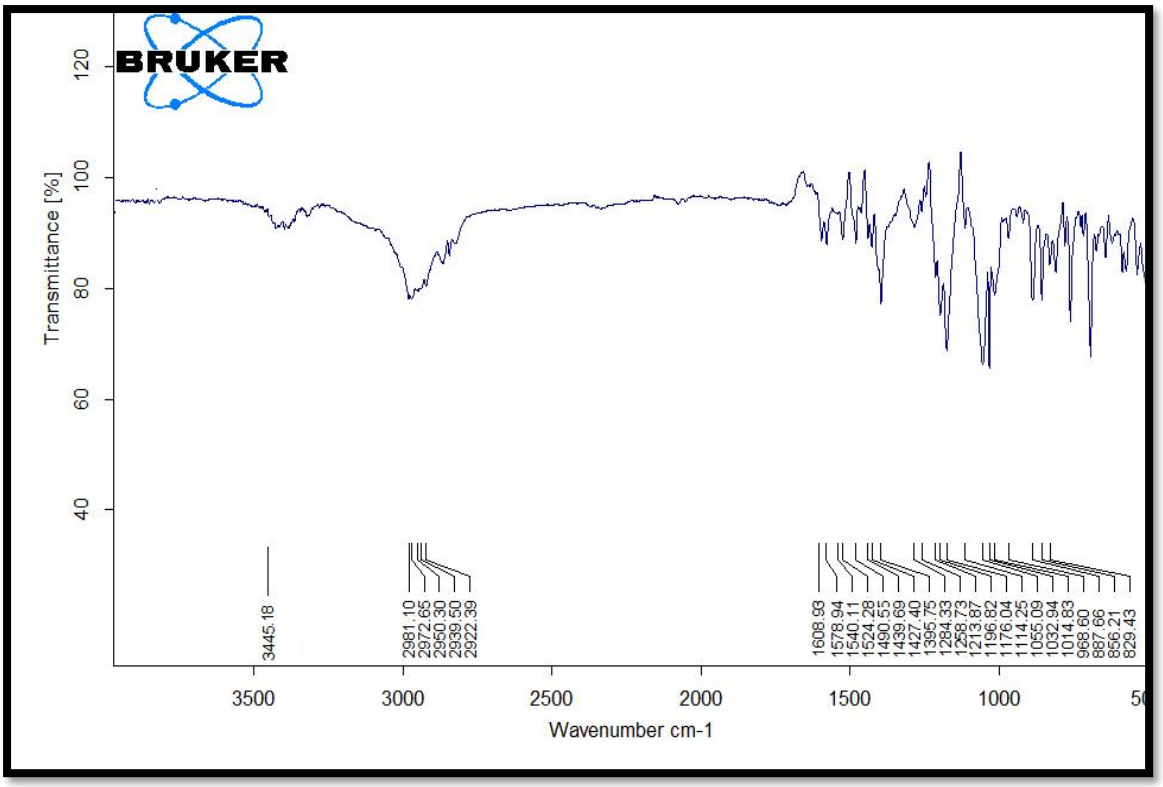


Fig (3-31): FTIR spectra of Azo-imidazole ligand (L_2)

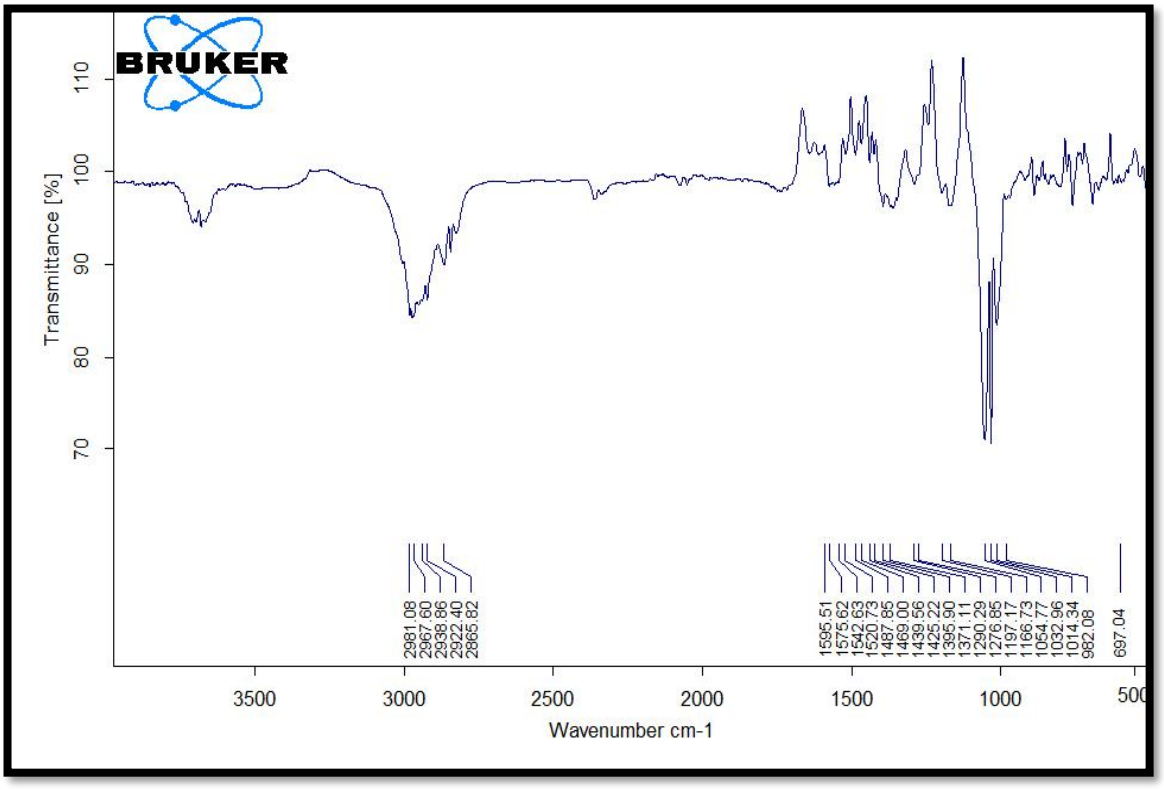


Fig (3-32): FTIR spectra of Azo-imidazole ligand complex (CoL_2)

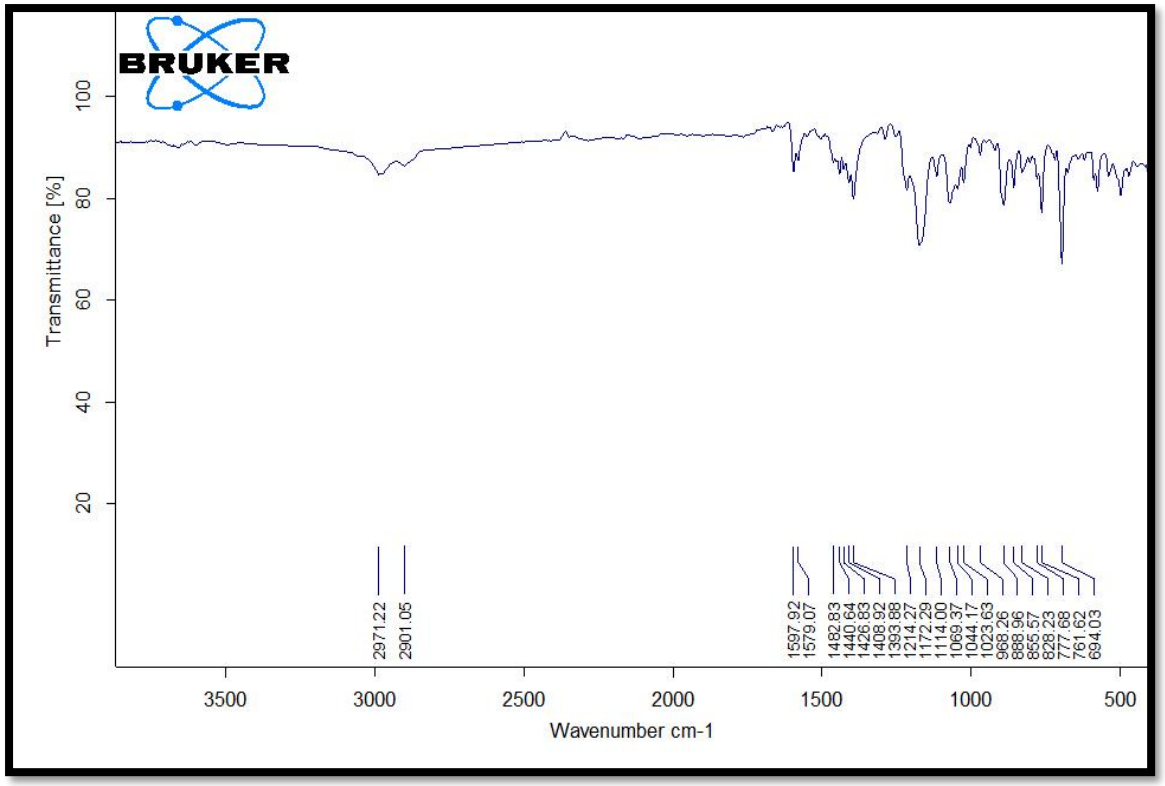


Fig (3-33): FTIR spectra of Azo-imidazole ligand complex (NiL_2)

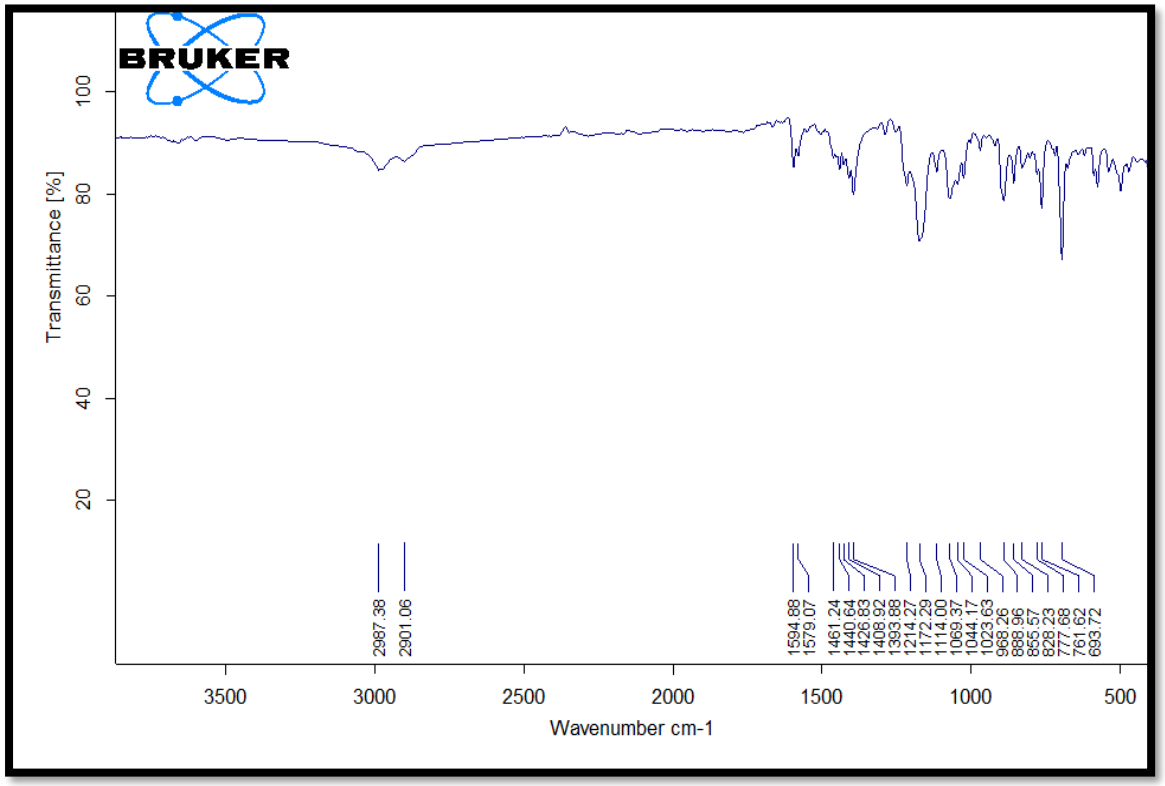


Fig (3-34): FTIR spectra of Azo-imidazole ligand complex (CuL_2)

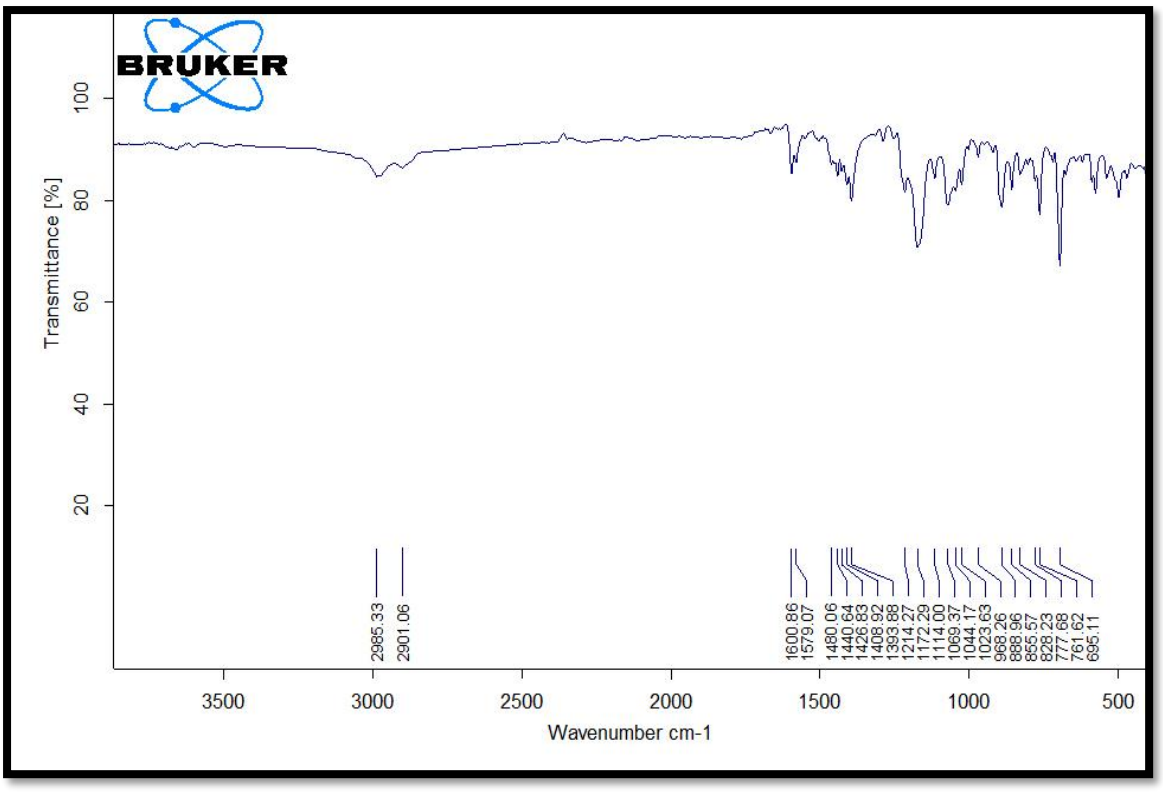


Fig (3-35): FTIR spectra of Azo-imidazole ligand complex (PdL_2)

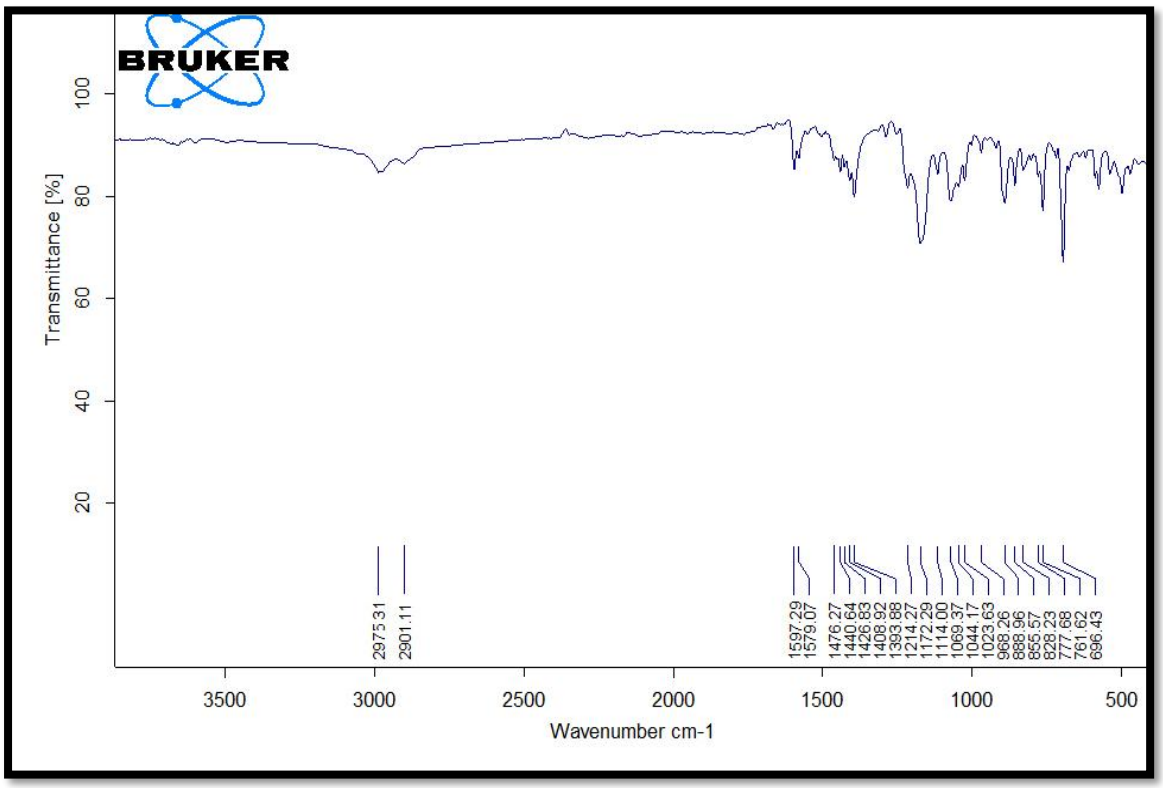


Fig (3-36): FTIR spectra of Azo-imidazole ligand complex (PtL_2)

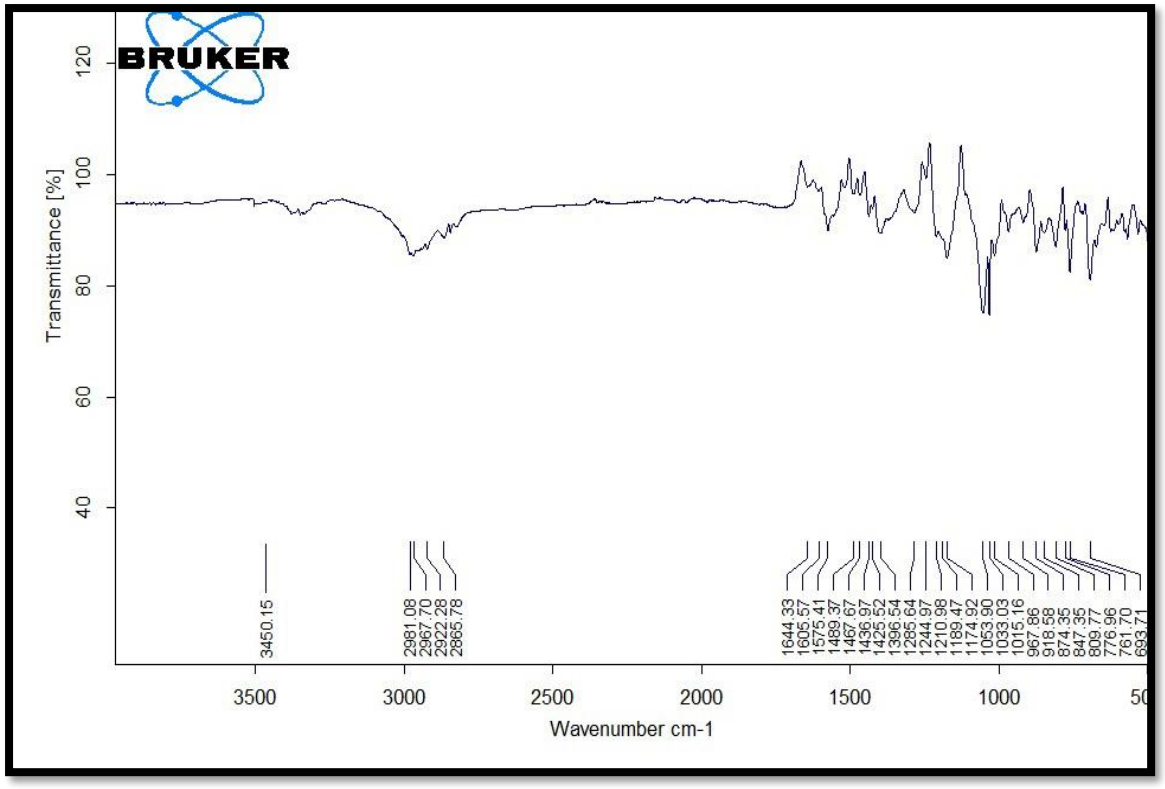


Fig (3-37): FTIR spectra of Azo-imidazole ligand (L_3)

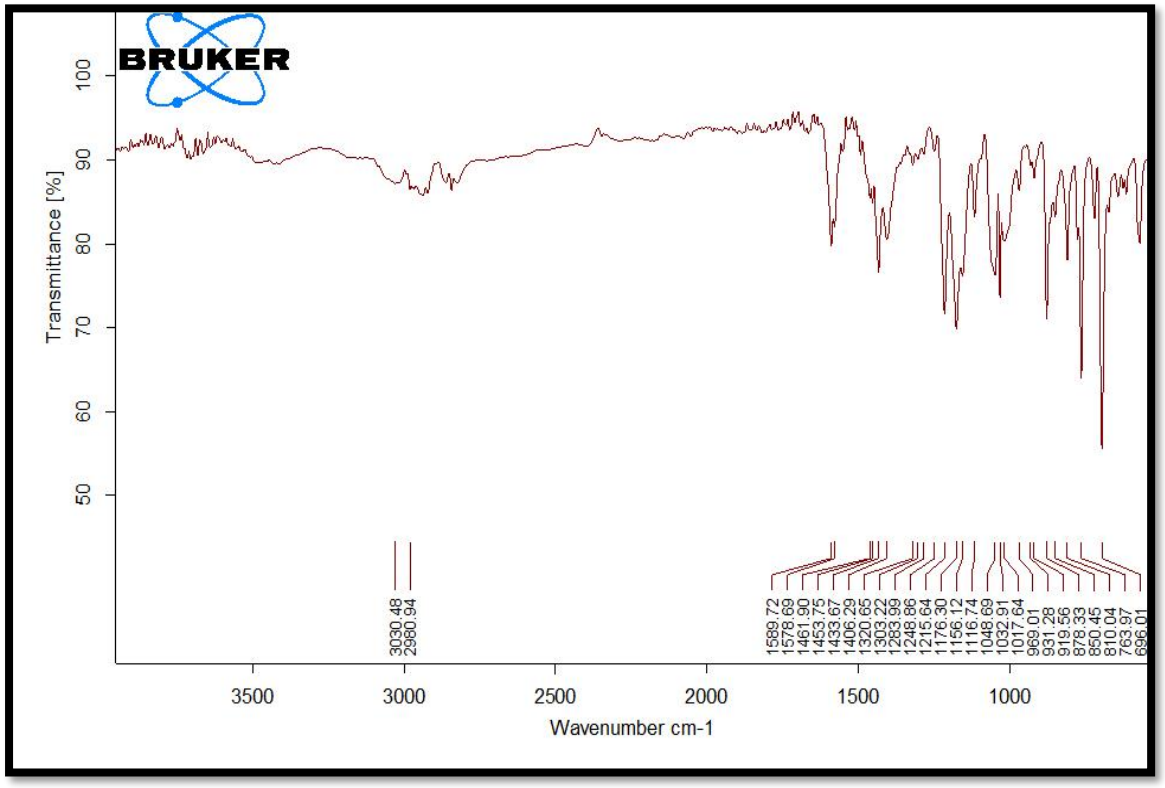


Fig (3-38): FTIR spectra of Azo-imidazole ligand complex (CoL_3)

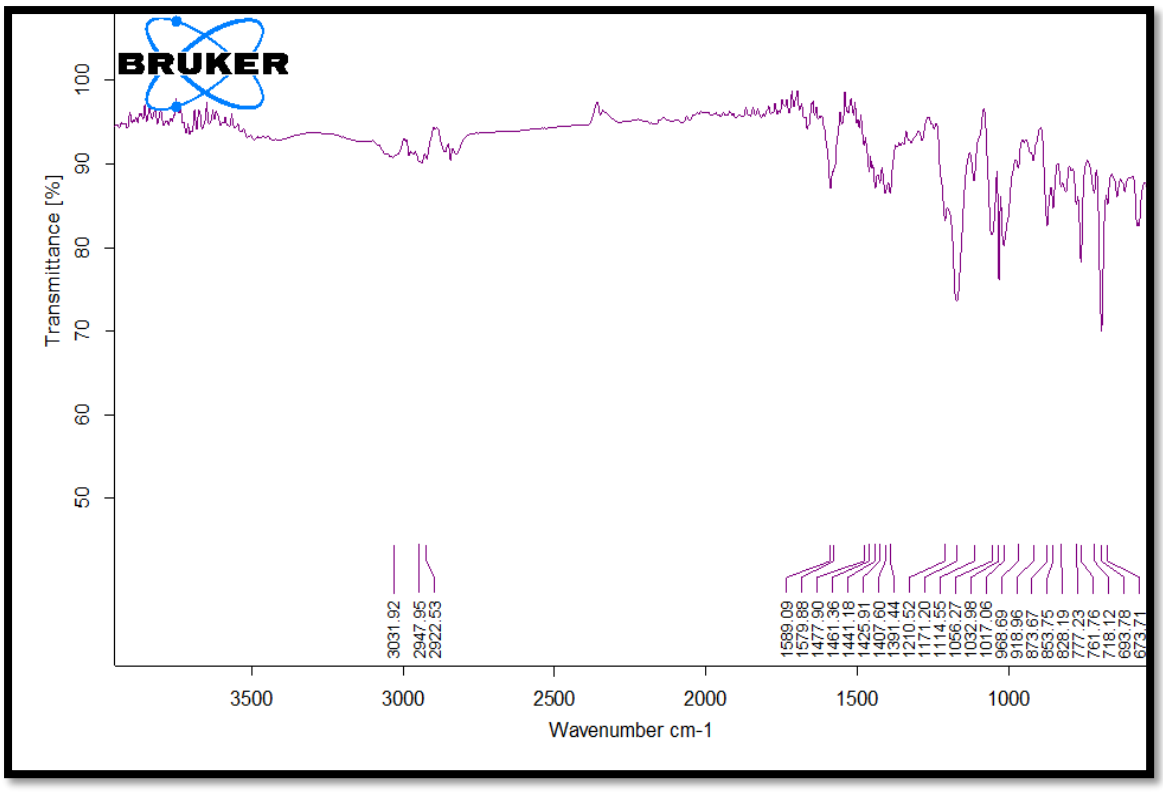


Fig (3-39): FTIR spectra of Azo-imidazole ligand complex (NiL_3)

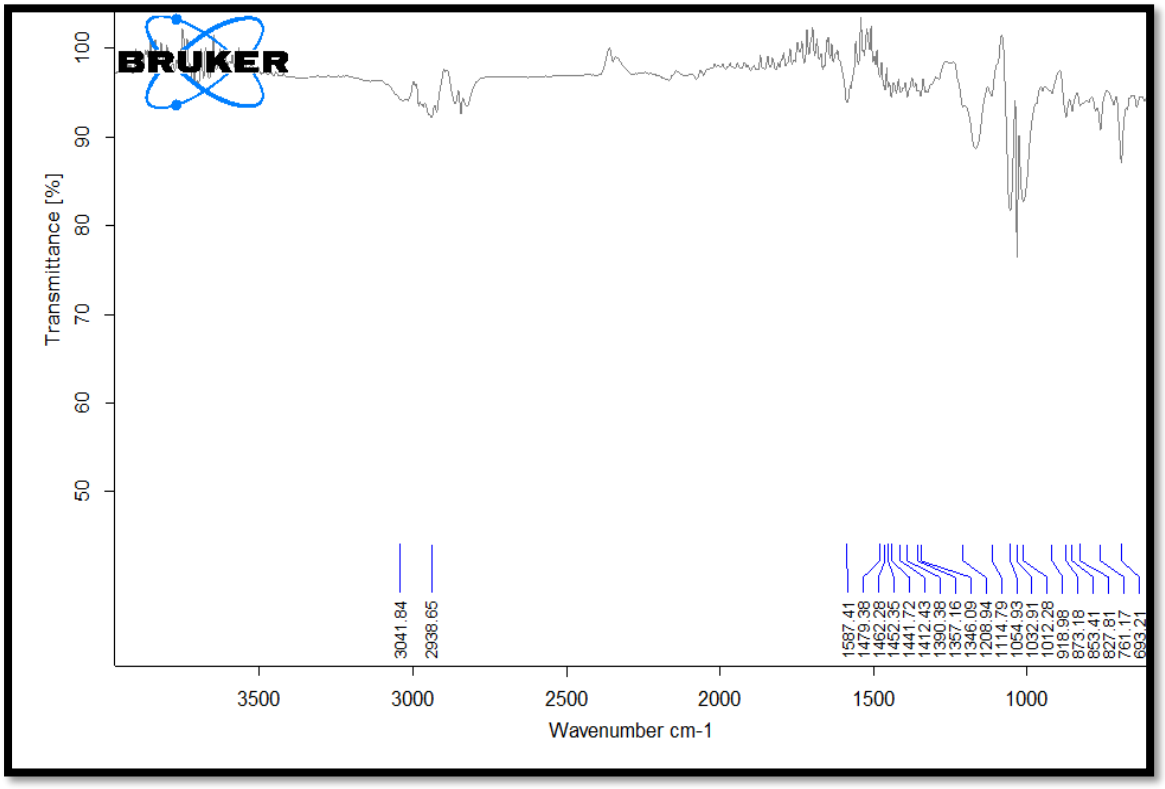


Fig (3-40): FTIR spectra of Azo-imidazole ligand complex (CuL_3)

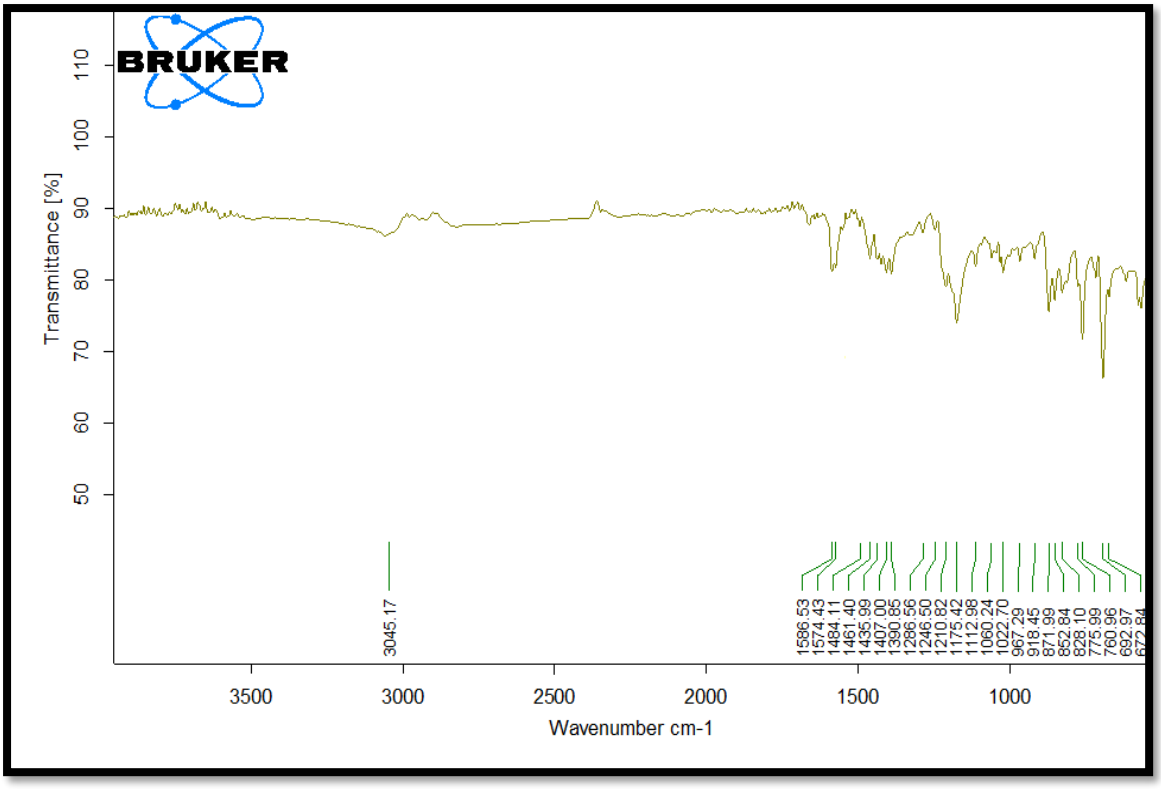


Fig (3-41): FTIR spectra of Azo-imidazole ligand complex (PdL_3)

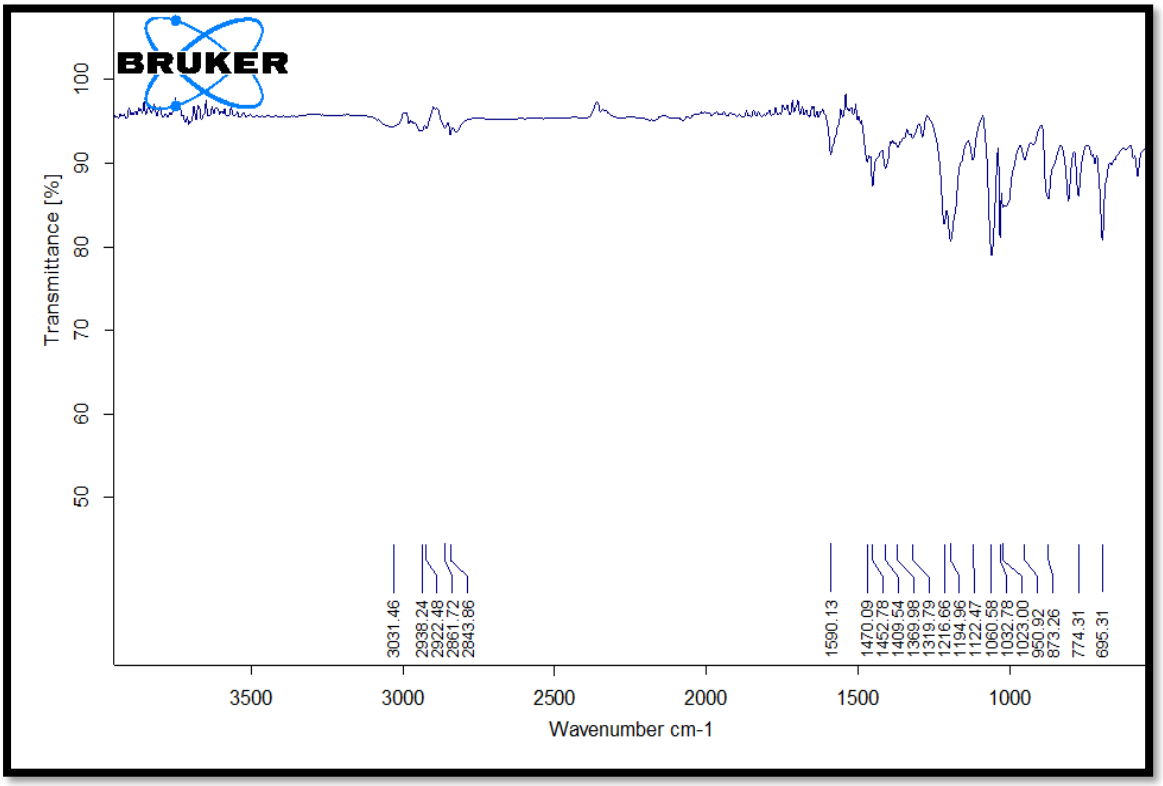


Fig (3-42): FTIR spectra of Azo-imidazole ligand complex (PtL_3)

3.3.2. Infrared Spectra of Azo-Schiff Base Ligands and their Chelating Complexes

Before starting to explain the spectra of the organic azo-Schiff ligands (L_4, L_5, and L_6) and their metal ion complexes, it is better for us to refer to the infrared spectra of the basic compounds that participated in the preparation of the above-mentioned ligands, where the azo-Schiff ligands were prepared by preparing the Schiff base first, which is considered a coupling component for the diazonium salts resulting from the dihalide amines (2,4- difluoroaniline, 4-chloro-2- fluoroaniline, and 4- bromo - 2-fluoroaniline) to prepare three azo-Schiff ligands[(2-((E)-((2,5-dichlorophenyl)imino)methyl)-4-((E)-(2,4-difluorophenyl)diazenyl)phenol) (L_4), (4-((E)-(4-chloro-2-fluorophenyl)diazenyl)-2-((E)-((2,5-dichlorophenyl)imino)methyl)phenol) (L_5), and (4-((E)-(4-bromo-2-fluorophenyl)diazenyl)-2-((E)-((2,5-dichlorophenyl) imino)methyl) phenol) (L_6), respectively.

Schiff base (DCSS) was prepared by condensing 2, 5- dichloroaniline With 2-hydroxy-benzaldehyde in absolute ethyl alcohol and using glacial acetic acid as a catalyst, figure (3-43) shows the infrared spectrum of Schiff base ligand ((E)-2-(((2,5-dichlorophenyl)imino)methyl)phenol (DCSS).

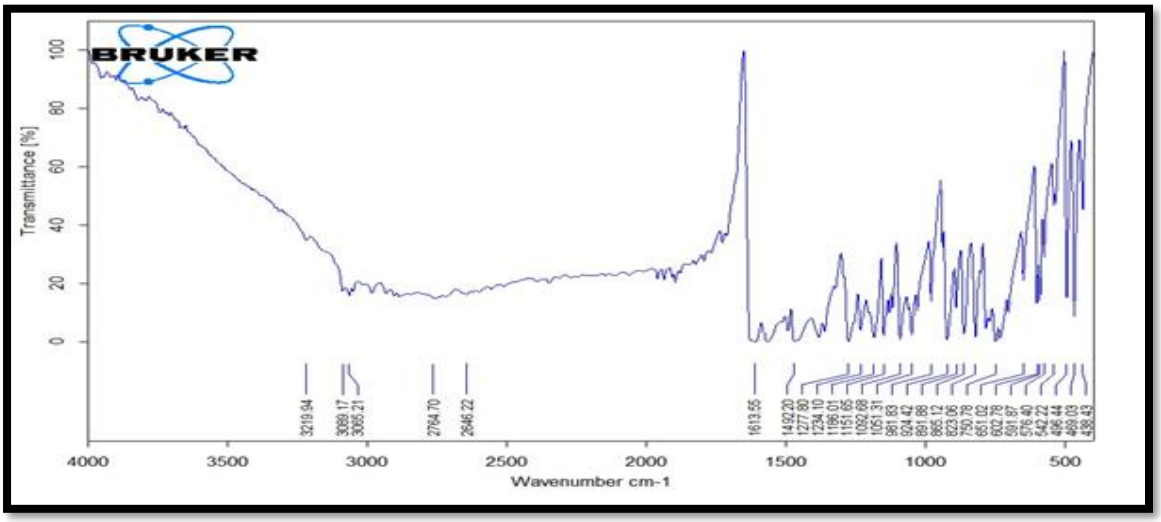


Fig (3-43): FTIR spectra of Schiff base ligand (DCSS).

From the spectrum of the Schiff-base ligand, there is broadband at the frequency (3219.94) cm^{-1} which is related to the hydroxyl group, also, a weak intensity absorption band at the frequency of (1613.56) cm^{-1}, which is related to the bond of (C=N) group [184], and this indicates the formation of the Schiff-base compound.

While in the azo-Schiff base ligands spectra, we noticed that new bands at frequencies (1471.62, 1472.58, and 1471.77) cm^{-1} [185] which is related to the bond of azo groups (N=N) for each ligand (L_4, L_5, and L_6), respectively, with these mentioned in the Schiff base spectra.

For the azo Schiff ligand complexes spectra, it is found a clear change in the intensity and location of the bands of some of their functional groups (shifting somewhat) due to the coordination [186] between the lone pair of the azomethine nitrogen atom and the hydroxyl oxygen atom with the vacant orbitals of the metallic ions, forming bidentate chelation, while the azo group still in their regions i.e. non-sharing in the coordination. In addition to the appearance of broad bands of the hydroxyl group of some complexes, which is due to the presence of moisture in the sample, indeed to the appearance of the M-N and M-O frequencies [187] that indicate the coordination, and the water of coordination frequencies [188] was present in the complexes spectra's, table (3-2) shows the stretching bands of the effective groups of ligands and their metal ion complexes, figures (3-44) to (3-61) show the infrared spectra of azo- Schiff base ligands and their metal ion complexes.

Table (3-2): The values of infrared frequencies spectra in units (cm^{-1}) of the ligands (L_4, L_5, and L_6) and their chelating complexes.

Ligands/complexes	υ (OH) Coor. H_2O	υ (C=N)	υ (N=N)	υ(M-N) υ(M-O)
Schiff base (DCSS)	3219.94	1613.56	---------	---------
L4 ($C_{19}H_{11}Cl_2F_2N_3O$)	3376.67	1614.21	1471.62	---------
[Co($C_{38}H_{24}Cl_4F_4N_6O_4$)]	3400.19	1597.29	1472.67	591.88 490.72
[Ni($C_{19}H_{12}N_3Cl_3F_2O_2$)]	3404.98	1605.18	1471.84	588.72 468.35
[Cu($C_{38}H_{24}Cl_4F_4N_6O_4$)]	3432.60	1608.53	1468.80	587.41 498.89
[Pd($C_{19}H_{12}N_3Cl_3F_2O_2$)]	3409.36	1608.14	1473.01	593.99 469.07
[Pt($C_{19}H_{12}N_3Cl_3F_2O_2$)]	3407.38	1603.85	1479.78	584.01 476.32
L5($C_{19}H_{11}Cl_3FN_3O$)	3551.23	1615.42	1472.58	---------
[Co($C_{38}H_{24}Cl_6F_2N_6O_4$)]	3526.34	1597.29	1472.67	591.88 490.72
[Ni($C_{19}H_{12}Cl_4FN_3O_2$)]	3304.98	1605.18	1471.84	588.72 468.35
[Cu($C_{38}H_{24}Cl_6F_2N_6O_4$)]	3332.60	1608.53	1468.80	587.41 498.89
[Pd($C_{19}H_{12}Cl_4FN_3O_2$)]	3407.38	1603.85	1479.78	584.01 476.32
[Pt($C_{19}H_{12}Cl_4FN_3O_2$)]	3445.60	1608.14	1473.01	593.99 469.07
L6 ($C_{19}H_{11}BrCl_2FN_3O$)	3301.25	1616.95	1471.77	---------
[Co($C_{38}H_{24}Br_2Cl_4F_2N_6O_4$)]	3530.12	1600.04	1472.02	651.42 468.28
[Ni($C_{19}H_{12}BrCl_3FN_3O_2$)]	3386.37	1605.89	1472.14	580.93 460.53
[Cu($C_{38}H_{24}Br_2Cl_4F_2N_6O_4$)]	3334.18	1608.54	1469.31	580.62 469.93
[Pd($C_{19}H_{12}BrCl_3FN_3O_2$)]	3432.71	1594.30	1480.96	582.43 480.59
[Pt($C_{19}H_{12}BrCl_3FN_3O_2$)]	3392.56	1601.82	1473.65	581.68 469.97

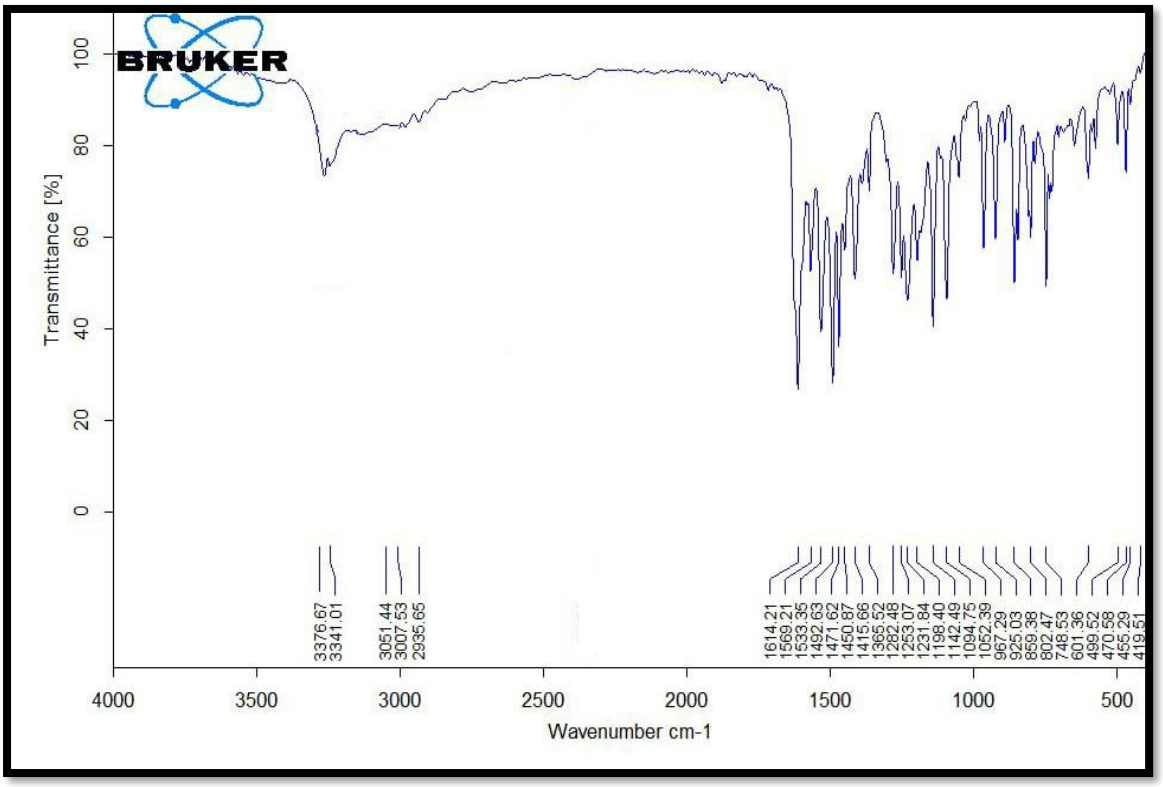


Fig (3-44): FTIR spectra of Azo-Schiff base ligand (L_4)

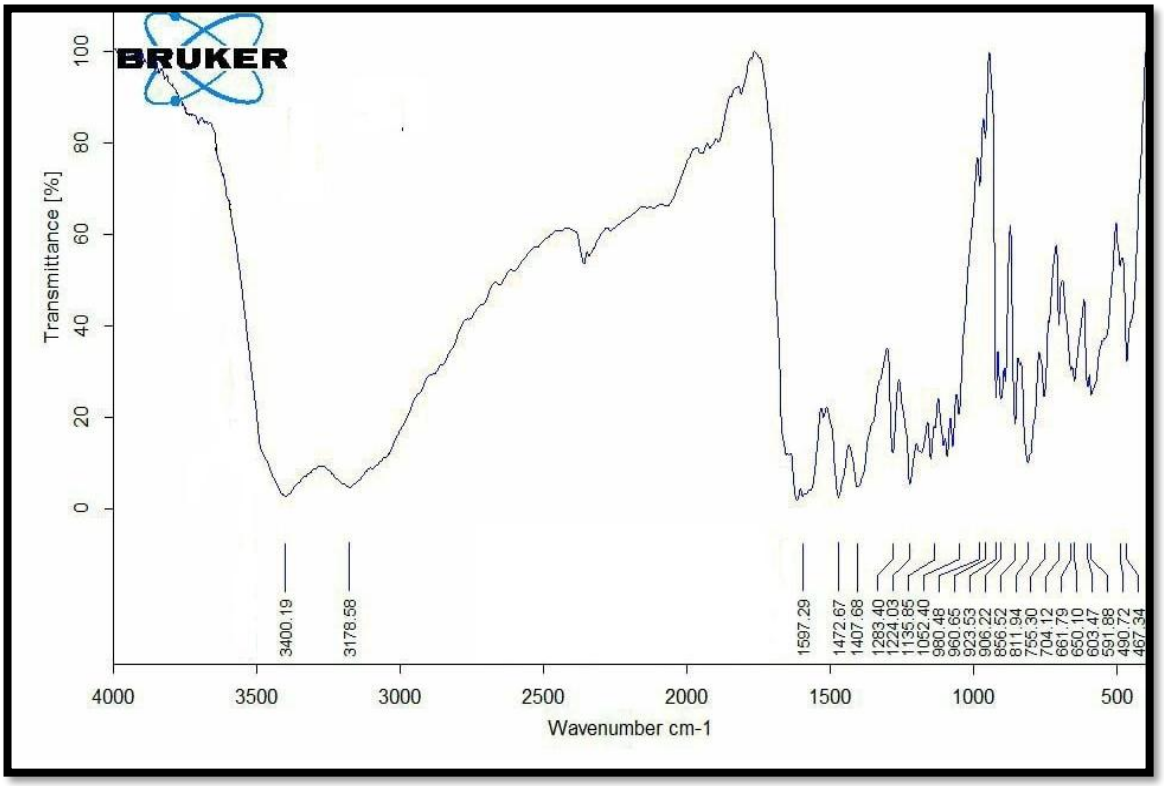


Fig (3-45): FTIR spectra of Azo-Schiff base ligand complex (CoL_4)

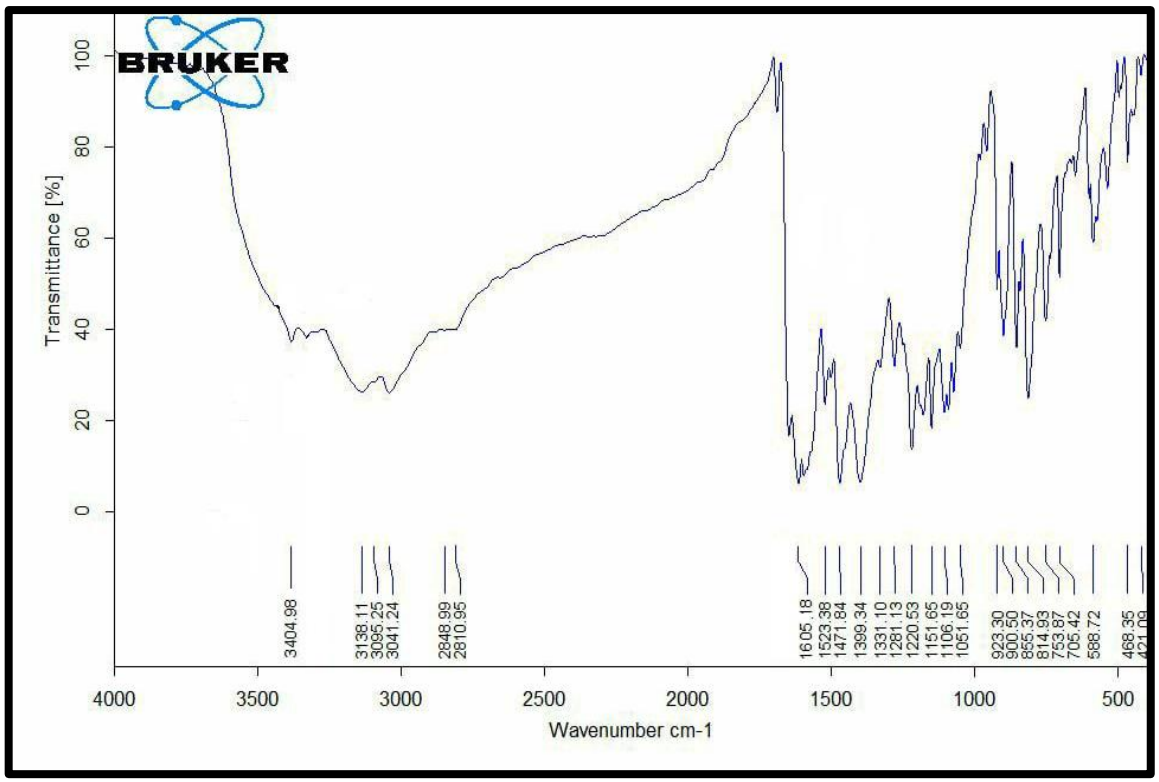


Fig (3-46): FTIR spectra of Azo-Schiff base ligand complex (NiL_4)

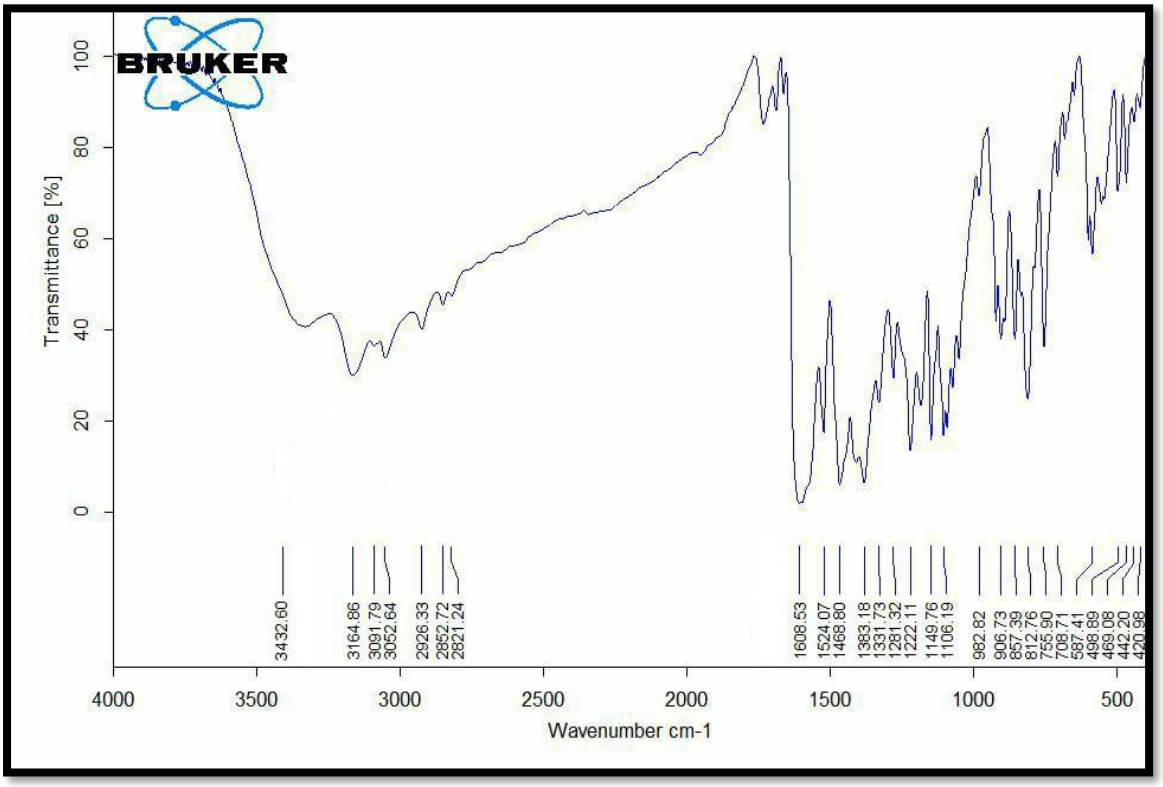


Fig (3-47): FTIR spectra of Azo-Schiff base ligand complex (CuL_4)

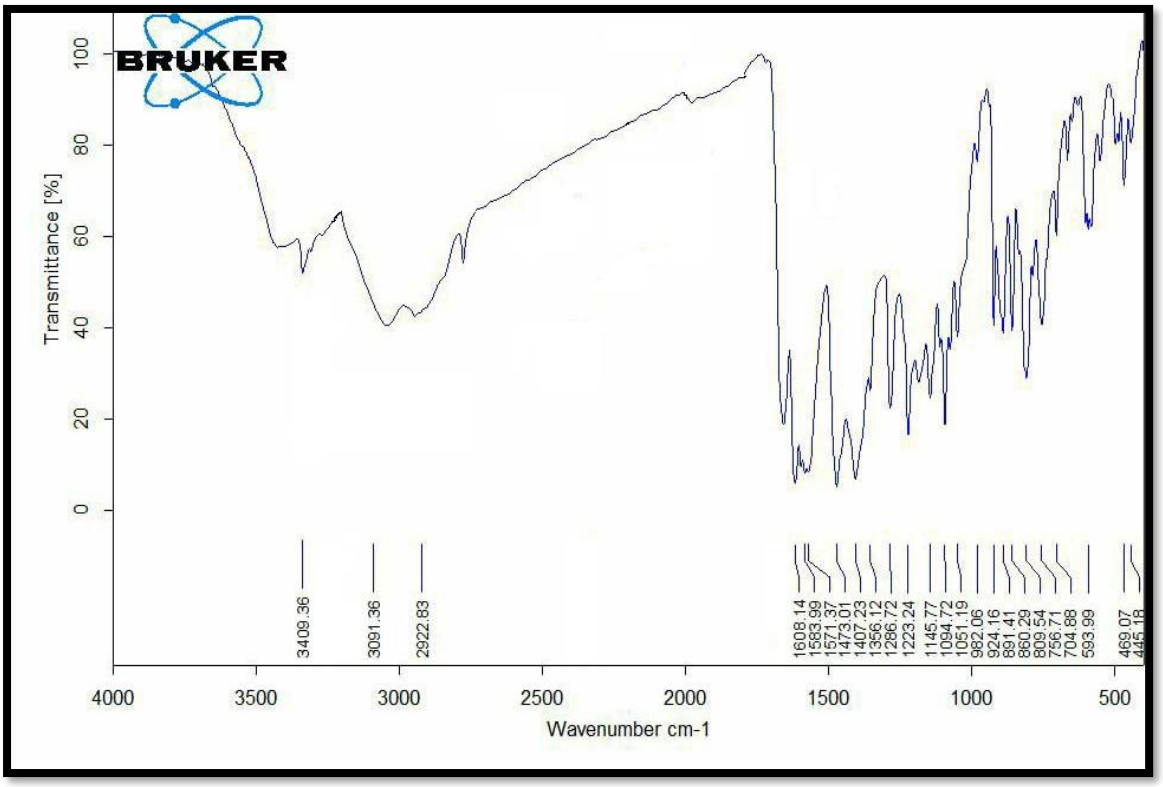


Fig (3-48): FTIR spectra of Azo-Schiff base ligand complex (PdL_4)

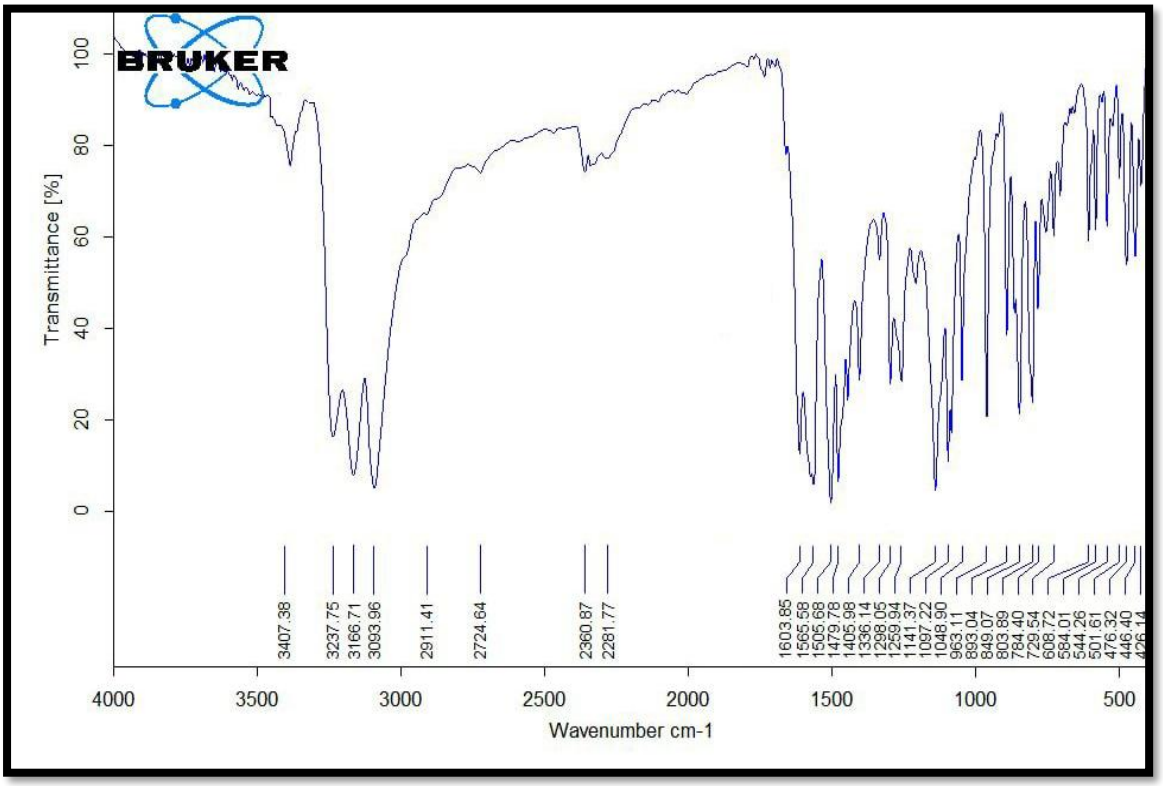


Fig (3-49): FTIR spectra of Azo-Schiff base ligand complex (PtL_4)

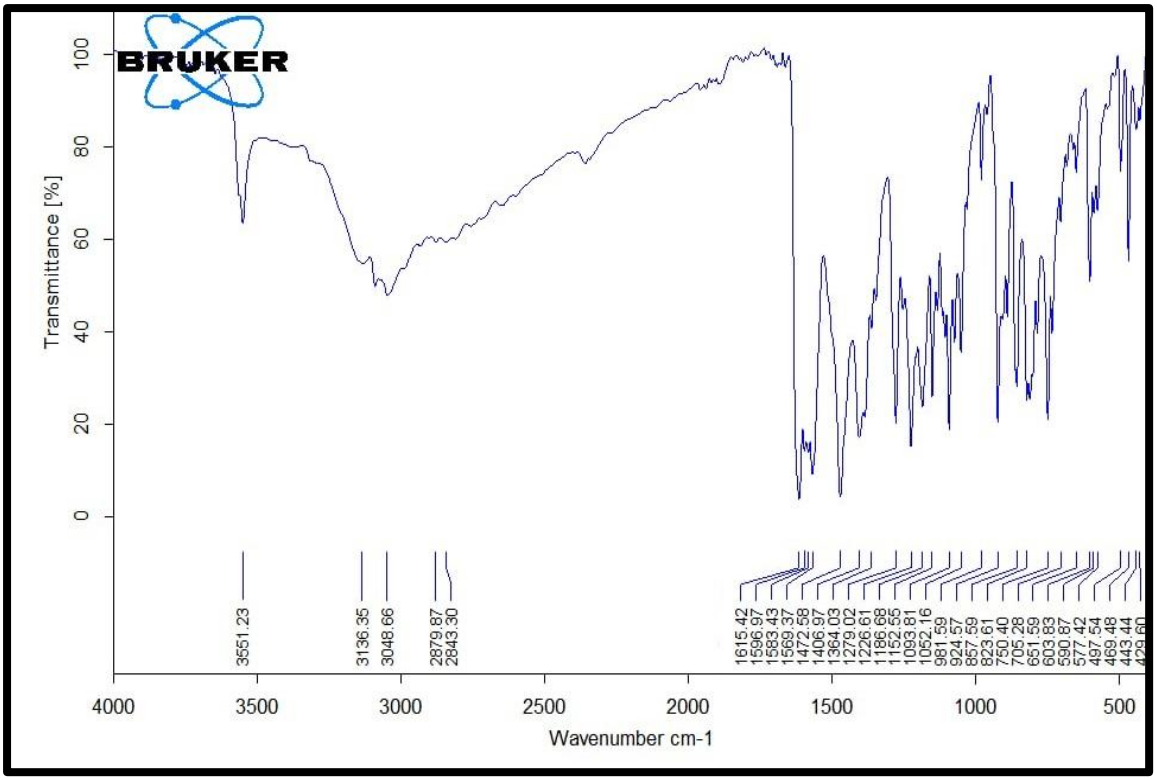


Fig (3-50): FTIR spectra of Azo-Schiff base ligand (L_5)

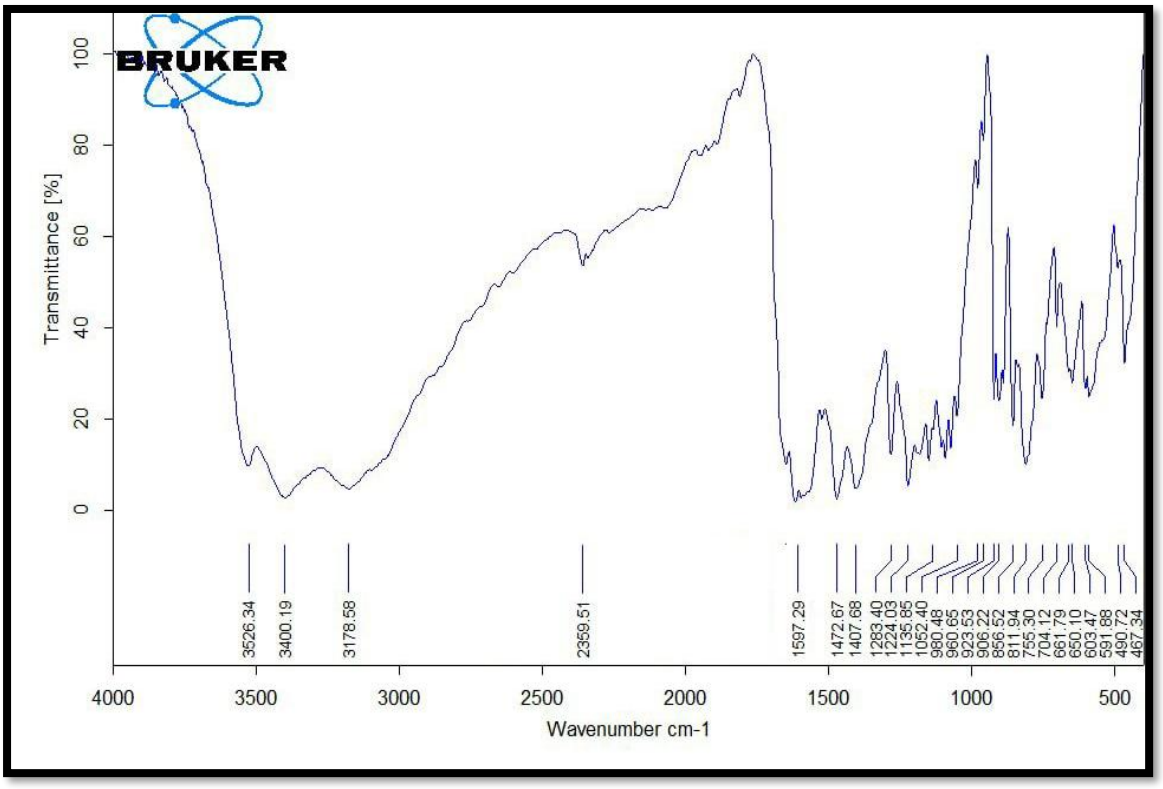


Fig (3-51): FTIR spectra of Azo-Schiff base ligand complex (CoL_5)

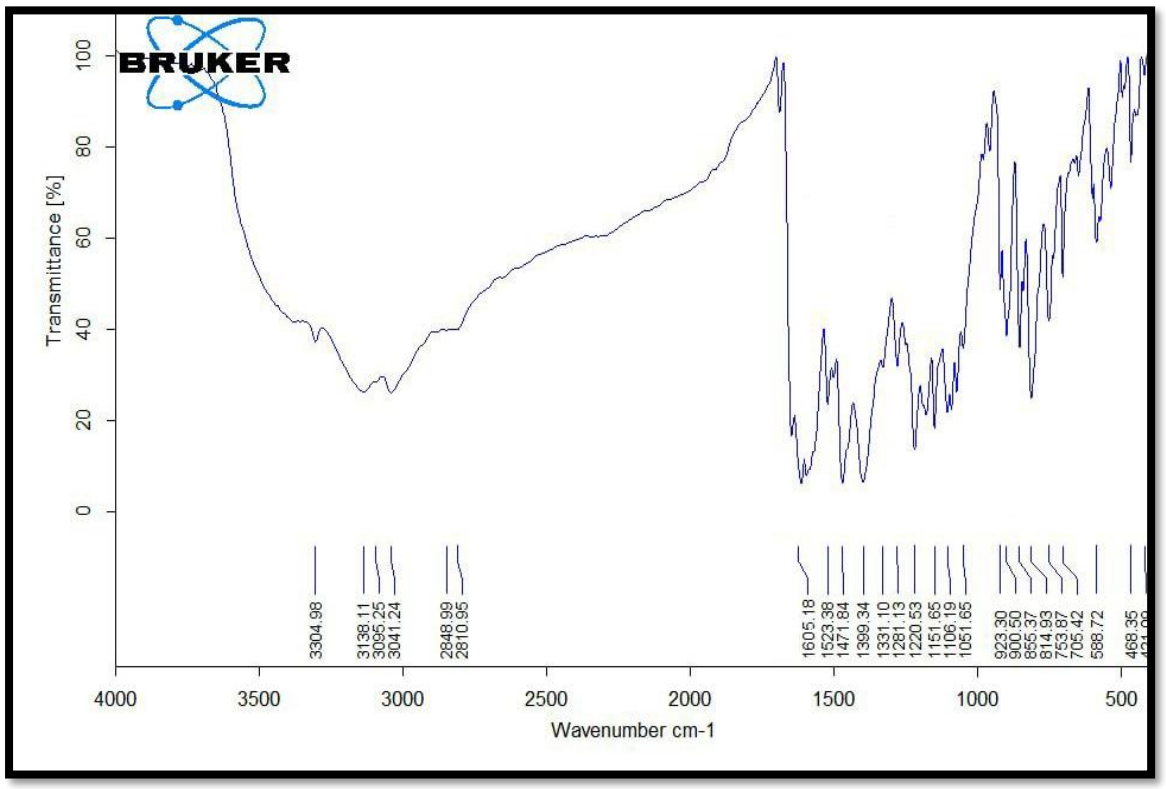


Fig (3-52): FTIR spectra of Azo-Schiff base ligand complex (NiL_5)

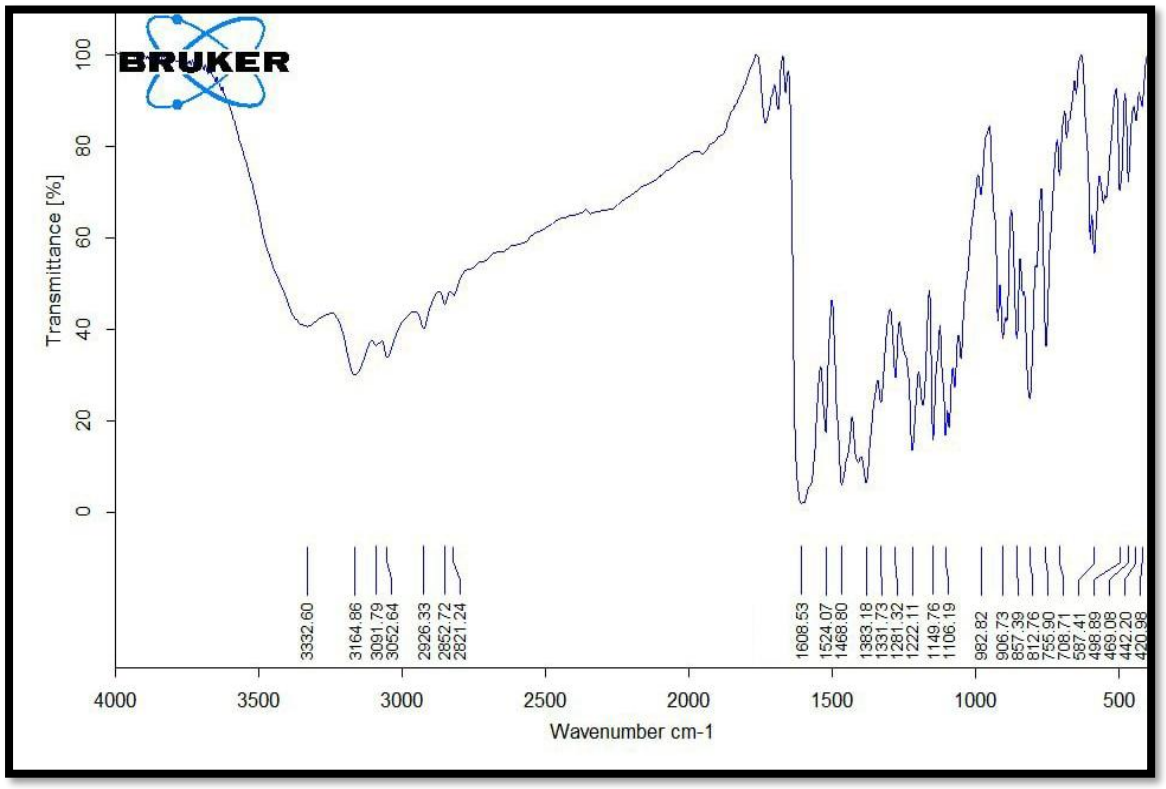


Fig (3-53): FTIR spectra of Azo-Schiff base ligand complex (CuL_5)

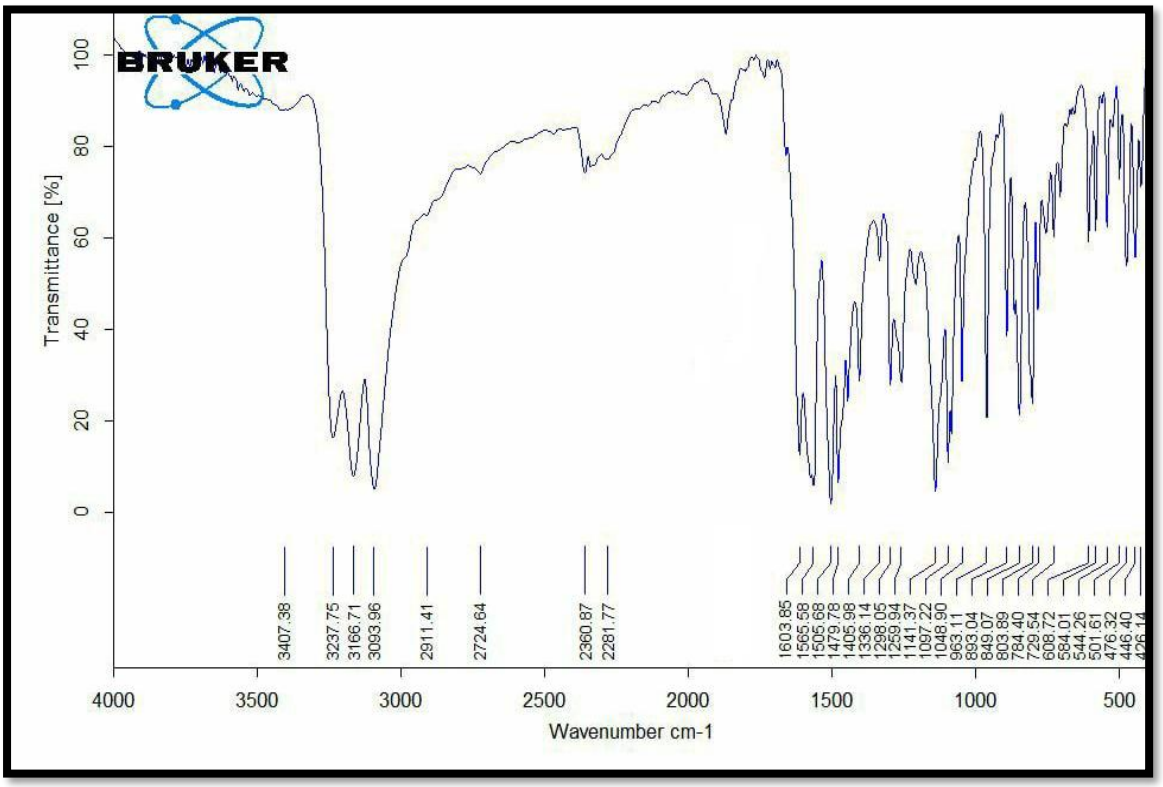


Fig (3-54): FTIR spectra of Azo-Schiff base ligand complex (PdL_5)

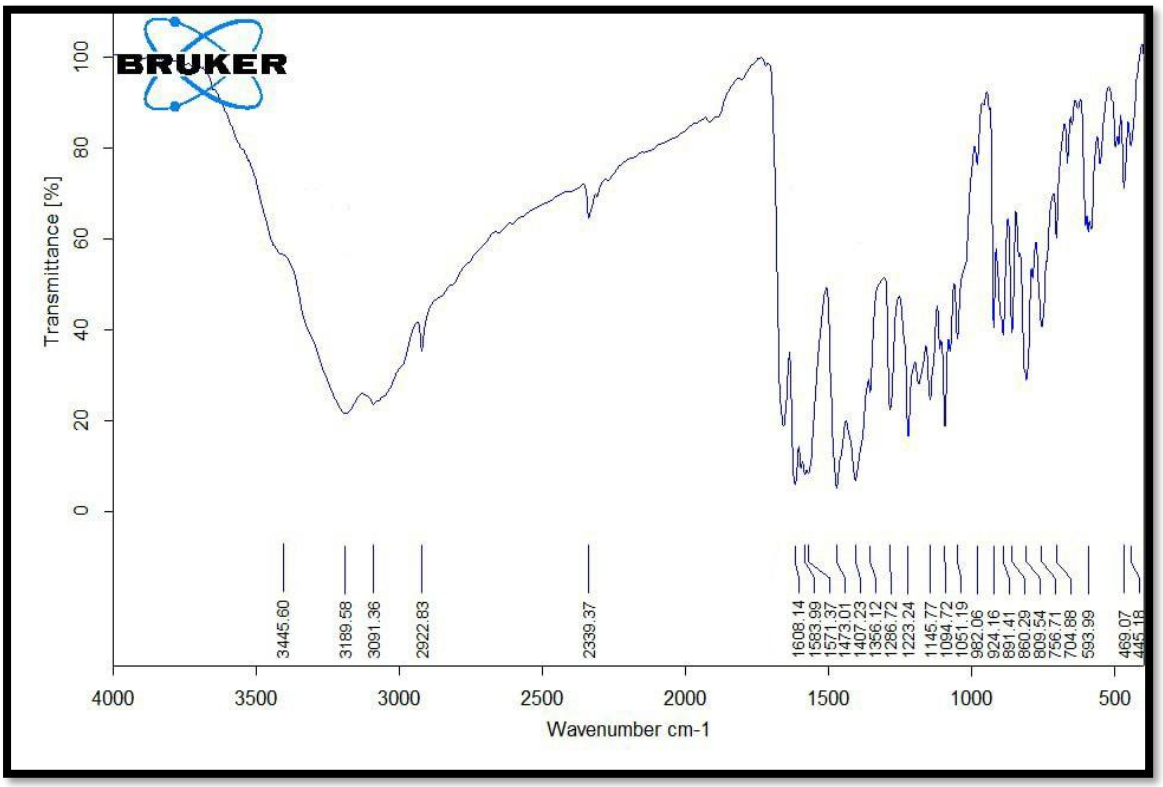


Fig (3-55): FTIR spectra of Azo-Schiff base ligand complex (PtL_5)

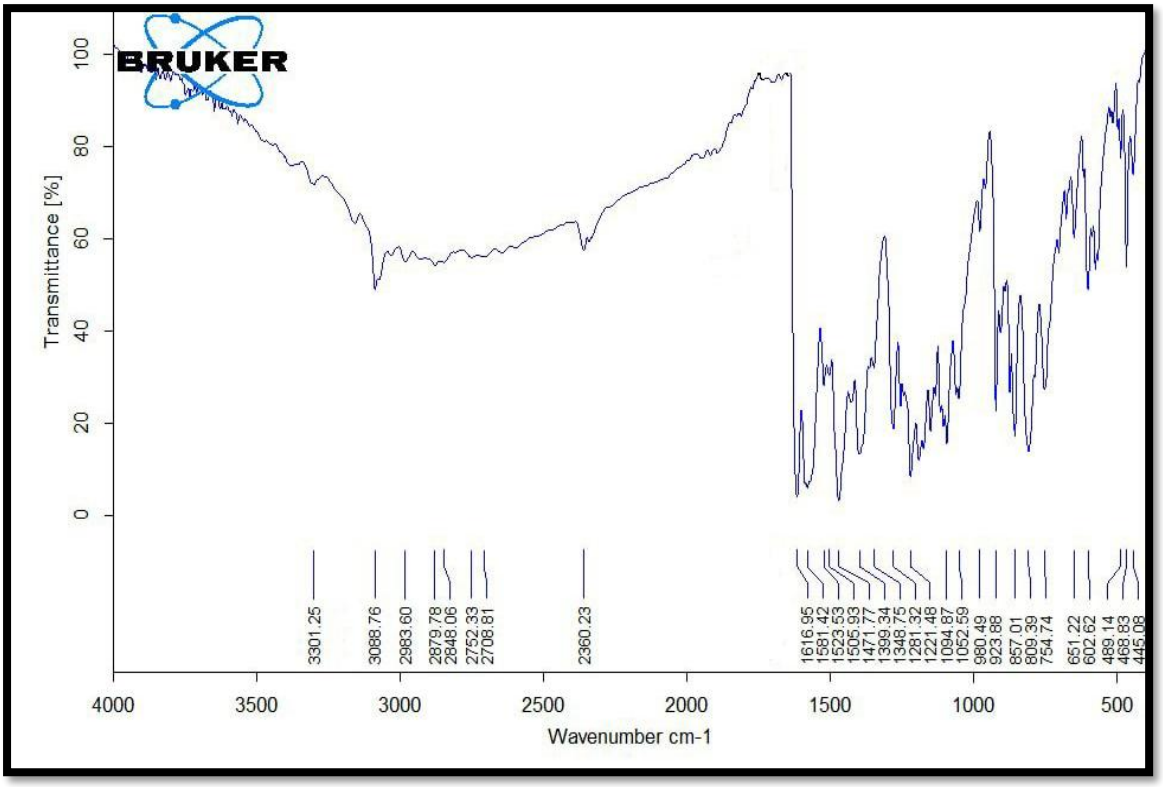


Fig (3-56): FTIR spectra of Azo-Schiff base ligand (L_6)

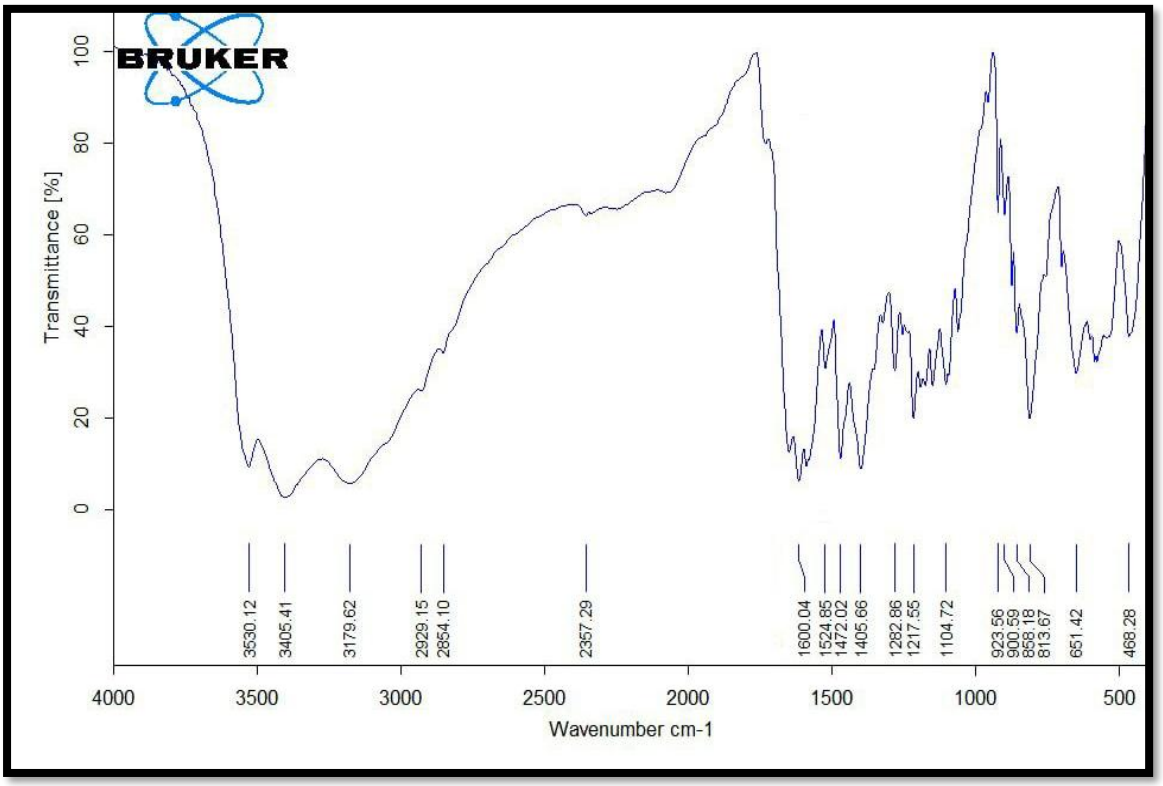


Fig (3-57): FTIR spectra of Azo-Schiff base ligand complex (CoL_6)

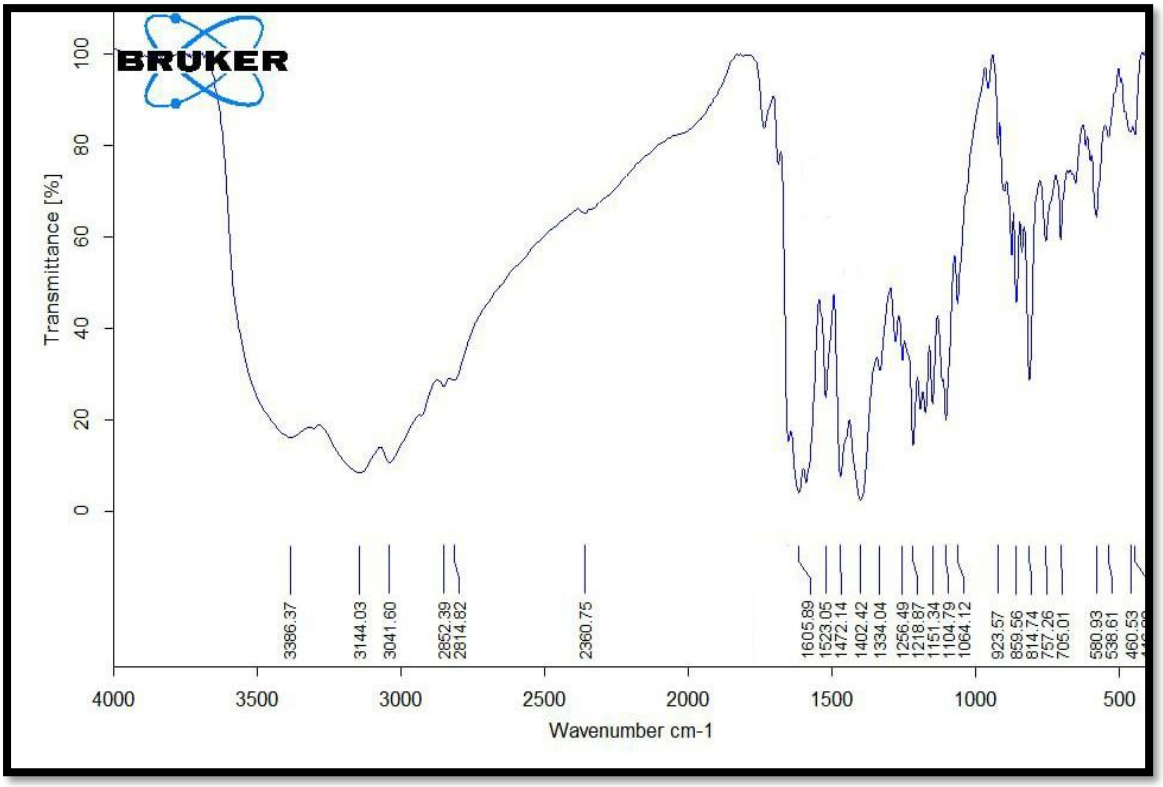


Fig (3-58): FTIR spectra of Azo-Schiff base ligand complex (NiL_6)

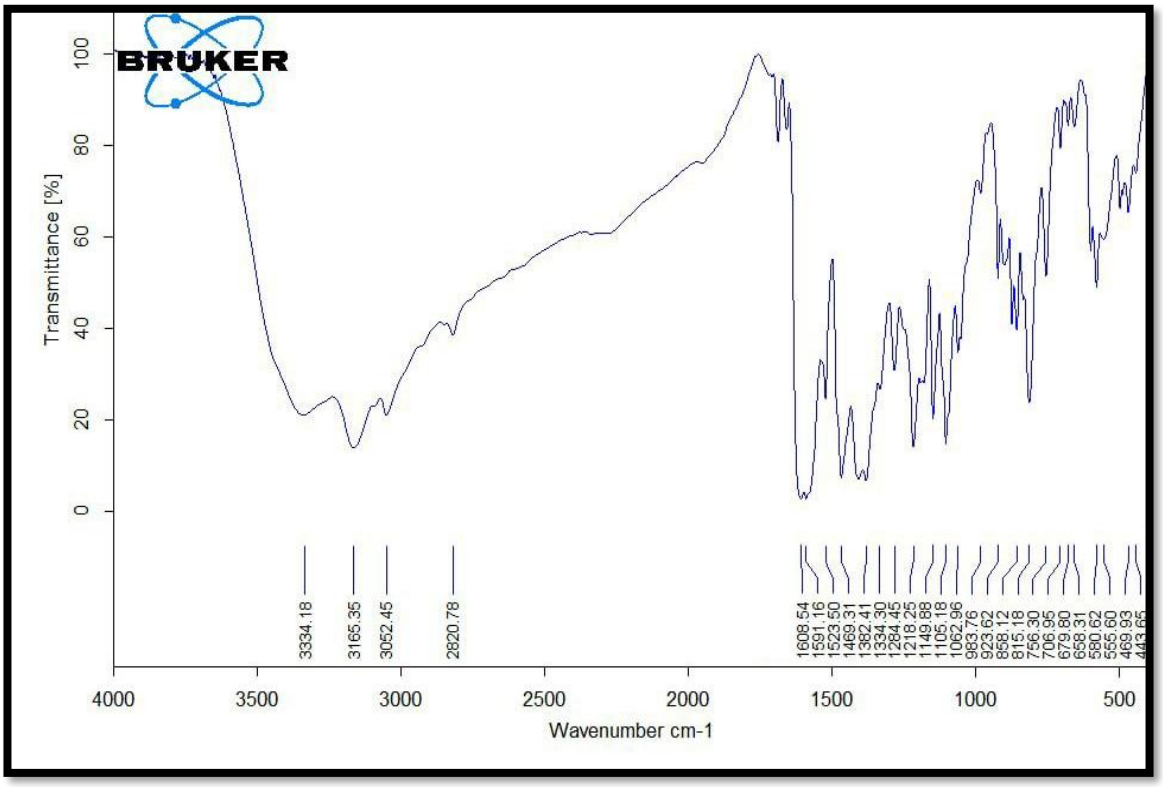


Fig (3-59): FTIR spectra of Azo-Schiff base ligand complex (CuL_6)

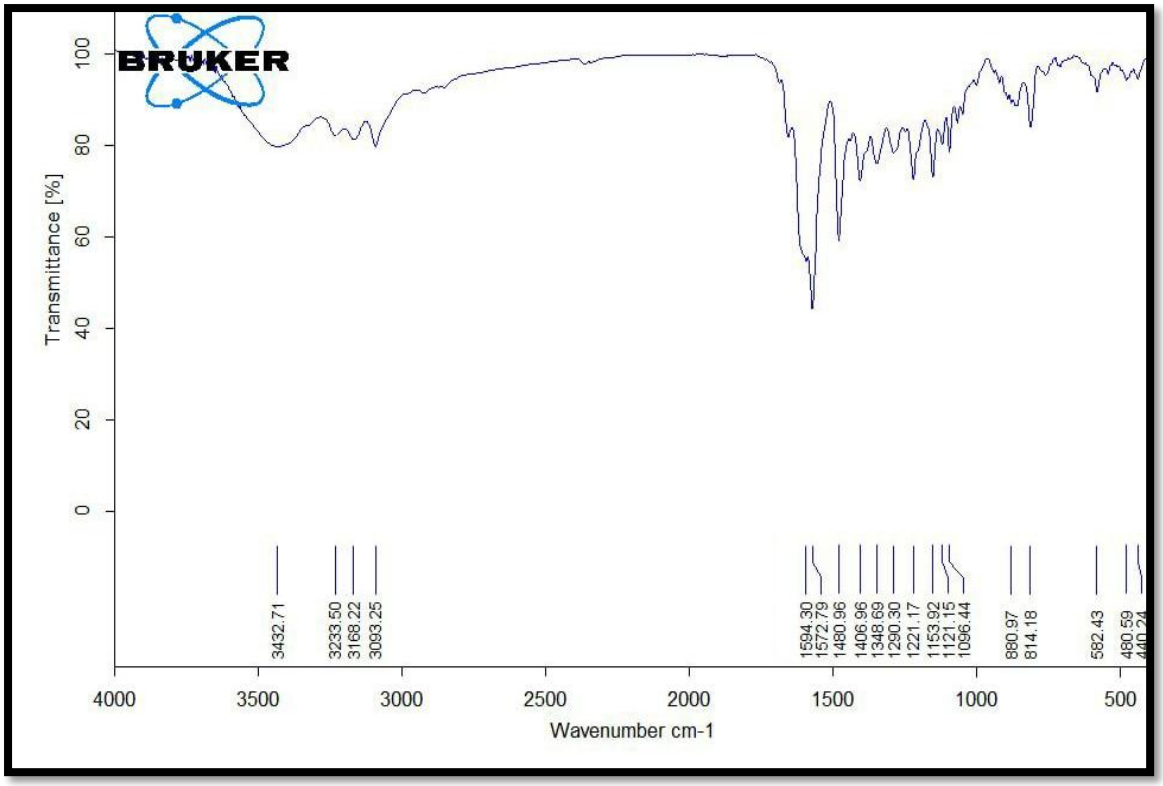


Fig (3-60): FTIR spectra of Azo-Schiff base ligand complex (PdL_6)

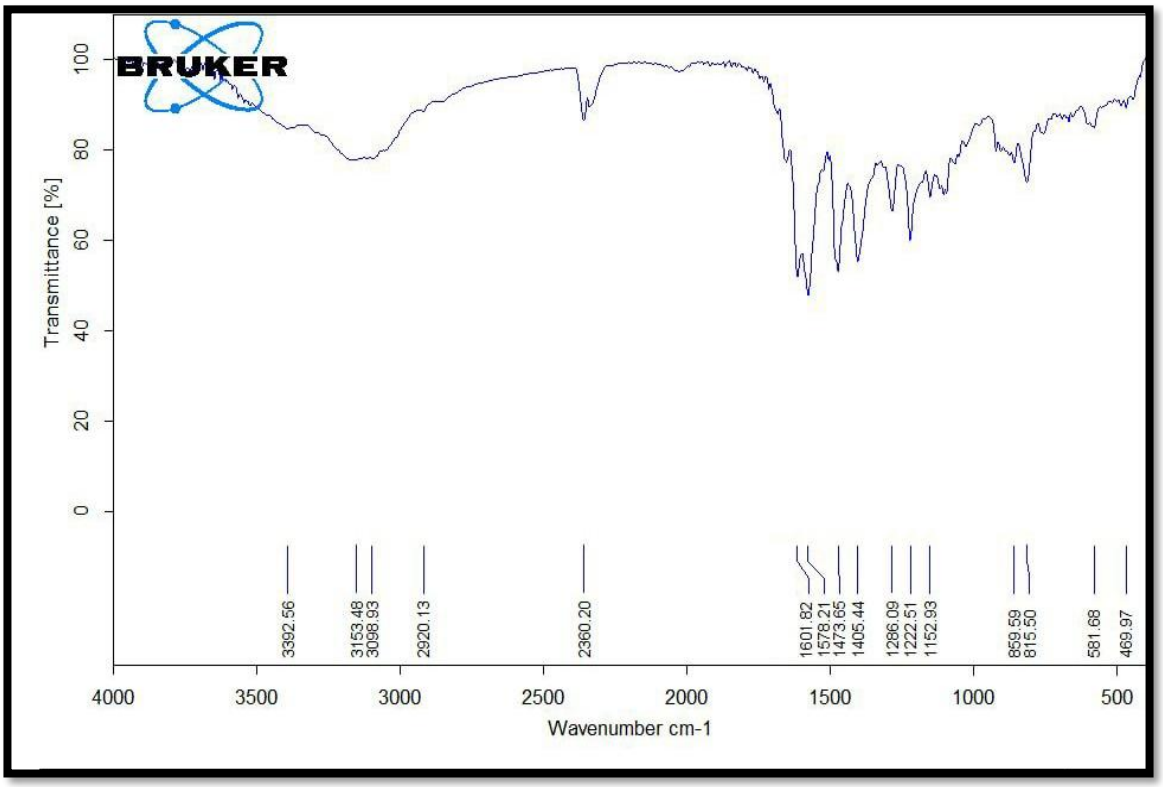


Fig (3-61): FTIR spectra of Azo-Schiff base ligand complex (PtL_6)

3.4. Electronic Spectra

One of the distinguishing characteristics of most solutions of metal complexes of the transition elements is their bright colors, which are due to absorptions in the visible region of the spectrum for those solutions [189], and they are often accompanied by other absorptions in the ultraviolet and near and near-infrared regions. Despite the imprecision in the interpretation of the spectra, their study imparts useful information about the structure and affinity of coordination compounds. The scientific need to explain the phenomena of color and magnetic properties in the metal complexes of the transitional elements led to the emergence of theories, some of which have succeeded in explaining the two mentioned phenomena, so the interest in the chemistry of this class of compounds has increased. The fact that the atom or transition metal ion contains orbitals (d) partially filled with electrons led to the difference in colors and magnetic properties [190]. The reason for the emergence of the electronic spectra of complex compounds is attributed to the electronic transitions between energy levels, which can be summarized as follows.

1- Ligand Spectra

Some inorganic or unsaturated organic molecules often show absorption bands in the ultraviolet region of the spectrum because they have anti-synergy (π^*) orbitals that have certain stability that can accept electrons. Many metallic complexes. The strong absorption bands in the ultraviolet region of the spectrum are caused by ($\pi \rightarrow \pi^*$) or ($n \rightarrow \pi^*$) transitions. [189].

2- Charge-Transfer Spectra

This type of spectra is due to the electronic transitions arising between the metal and the ligand because of the interaction between them. Whatever

the case, if the metal orbitals are more acceptors than donors, then it is easier to transfer the charge from the ligand to the metal ion (L→M), and the transfer of charge increases by increasing the oxidation state of the metal ion and increasing the stability of its vacant and accepting orbitals, which leads as a result to (reduction the metal), and vice versa when the electron is transferred from the metal with a low oxidation state to the ligand (M→L), this will inevitably lead to (the oxidation of the metal) and when the inorganic compound contains two metal ions in two different oxidation states, then the charge transfer occurs between these two ions [191] (M→M).

3- Counter – Ion Spectra

The absorption spectra of complexes containing the accompanying ions attached to the complex ion show absorption bands that sometimes overlap with (d→d) spectra, such as the ions of nitrate, nitrite, and negative oxy ions, which show strong absorption bands in the ultraviolet region, so it is preferable to exclude such accompanying ions and replace them with ions It does not absorb radiation in the ultraviolet region, such as chloride, perchlorate and sulfate ions [189].

4- Ligand –Field Spectra

They are the spectra resulting from the excitation of an electron between two energy levels, the transition occurs between the d orbitals of a metal. This type of transfer is not permitted according to the Laporta Rule. Therefore, this type of transition appears weekly in the visible region of the spectrum. The number of beams and their locations depend on the nature of the metal and its oxidation state. In addition, the complex shape of the metal ion has a great influence on the spectrum, relative to not only the number and locations of the beams but also depends on the intensity of

absorption of those beams. This is evident when comparing the spectra of octahedral and tetrahedral complexes.

In general, the electron spectra absorption bands are often wide due to the short period required for the absorption of the photon by the molecule, which occurs in a time (8-10) seconds compared to the period required for the occurrence of vibrational or rotational movements of the relatively slow molecule [191].

3.4.1. Electronic Spectra of Azo-imidazole Ligands and their Chelating Complexes

The UV-visible spectra of the ligands L_1, L_2, and L_3 and mixture solutions were studied with five solutions of positively charged dimeric transition elements (for cobalt, nickel, copper, palladium, and platinum), where the concentrations (1×10^{-4} - 1×10^{-5}) molarity of Beer-Lambert law for dilute solutions were studied, the concentrations were excluded from that, as they were not sensitive to the device or higher, due to the precipitation and turbidity of their complexes.

Each spectrum of the ligands L_1, L_2, and L_3 gave two absorption bands, the first of which was in the visible region of the spectrum at ($23529cm^{-1}$, $22371cm^{-1}$, and $21691cm^{-1}$) respectively, as a result of the electronic transition (**n→π***), which is the greatest wavelength of the ligand (λmax), while the second absorption bands were in the ultraviolet region of the spectrum at ($34602cm^{-1}$, $34364cm^{-1}$, and $34129cm^{-1}$) for each ligand respectively, in succession as a result of the electronic transition (**π→π***), this is consistent with what is stated in the literature [192]. While the second band in the spectra of the above-mentioned ligands, which is related to the internal charge transitions (charge transfer), suffered a redshift towards a longer wavelength in its metal complexes [193] for cobalt, nickel, copper, palladium, and platinum, due the coordination [194]

between the lone pairs of nitrogen ligands to the vacant orbitals of the selected ion. As for the spectra of the ligand field or the spectra of (d → d), they were not studied for these complexes due to their occurrence at the top of the charge transfer (M-L, CT) in the metal complexes. Figures (3-62) to (3-79) show the electronic spectra of the azo-imidazole ligands(L_1, L_2, and L_3) with their metal complexes, while the obtained results for these spectra were included in the table (3-3) .

Table (3-3): Electronic spectra of ligands (L_1, L_2, and L_3) and their complexes in ethanol solvent at laboratory temperature.

Compound/Complexes	Absorption Bands(nm)	Absorption Bands(cm^{-1})	Transition	Geometry	Hybridization
L_1 ($C_{21}H_{14}N_4F_2$)	289 425	34602 23529	π→π* n→π*	---------	--------
[Co($C_{42}H_{28}N_8F_4Cl_2$)]	302 482	33112 20746	M→L,CT	Octahedral	sp^3d^2
[Ni($C_{21}H_{14}N_4F_2Cl_2$)]	289 467	34602 21413	M→L,CT	square- planar	dsp^2
[Cu($C_{21}H_{14}N_4F_2Cl_2$)]	292 479	34246 20876	M→L,CT	Tetrahedral	Sp3
[Pd($C_{21}H_{14}N_4F_2Cl_2$)]	294 535	34013 18691	M→L,CT	square- planar	dsp^2
[Pt($C_{21}H_{14}N_4F_2Cl_2$)]	298 460	33557 21739	M→L,CT	square- planar	dsp^2
L_2 ($C_{21}H_{14}N_4F$ Cl)	291 447	34364 22371	π→π* n→π*	--------	--------
[Co($C_{42}H_{28}N_8F_2Cl4$)]	302 493	33112 20283	M→L,CT	Octahedral	sp^3d^2
[Ni($C_{21}H_{14}N_4FCl_3$)]	292 470	34246 21276	M→L,CT	square- planar	dsp^2
[Cu($C_{21}H_{14}N_4FCl_3$)]	279 491	35842 20366	M→L,CT	Tetrahedral	Sp3
[Pd($C_{21}H_{14}N_4FCl_3$)]	294 475	34013 21052	M→L,CT	square- planar	dsp^2
[Pt($C_{21}H_{14}N_4FCl_3$)]	297 469	33670 21321	M→L,CT	square- planar	dsp^2
L_3($C_{21}H_{14}N_4FBr$)	293 461	34129 21691	π→π* n→π*	--------	--------
[Co($C_{42}H_{28}N_8F_2Cl_2Br_2$)]	294 486	34013 20576	M→L,CT	Octahedral	sp^3d^2
[Ni($C_{21}H_{14}N_4FCl_2Br$)]	283 471	35335 21231	M→L,CT	square- planar	dsp^2
[Cu($C_{21}H_{14}N_4FCl_2Br$)]	288 488	34722 20491	M→L,CT	Tetrahedral	Sp3
[Pd($C_{21}H_{14}N_4FCl_2Br$)]	300 470	33333 21276	M→L,CT	square- planar	dsp^2
[Pt($C_{21}H_{14}N_4FCl_2Br$)]	303 470	33003 21276	M→L,CT	square- planar	dsp^2

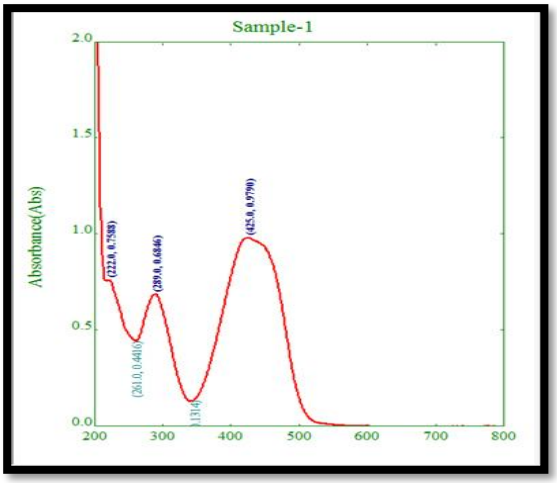


Fig (3-62): Electronic Spectra of Azo-imidazole ligand (L_1)

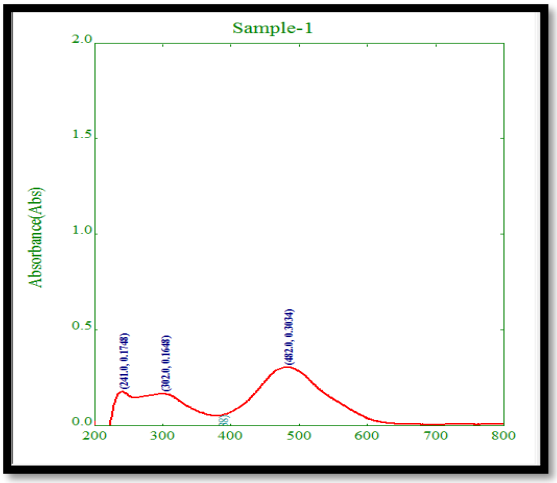


Fig (3-63): Electronic Spectra of Azo-imidazole complex (CoL_1)

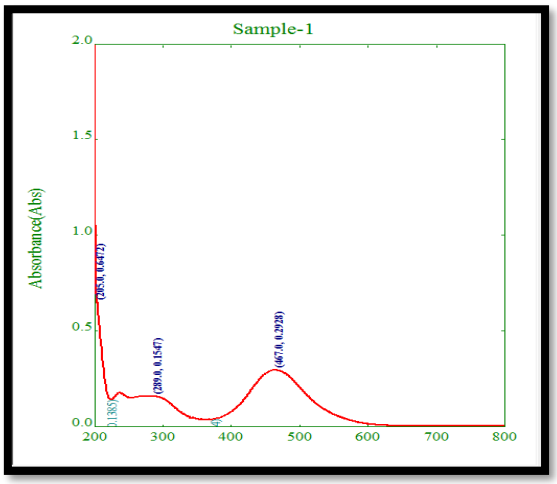


Fig (3-64): Electronic Spectra of Azo-imidazole complex (NiL_1)

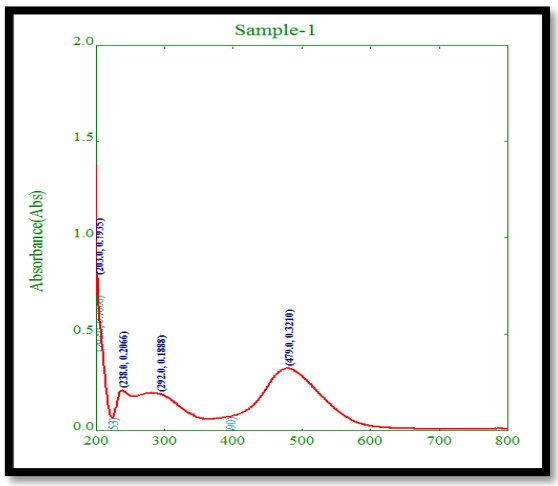


Fig (3-65): Electronic Spectra of Azo-imidazole complex (CuL_1)

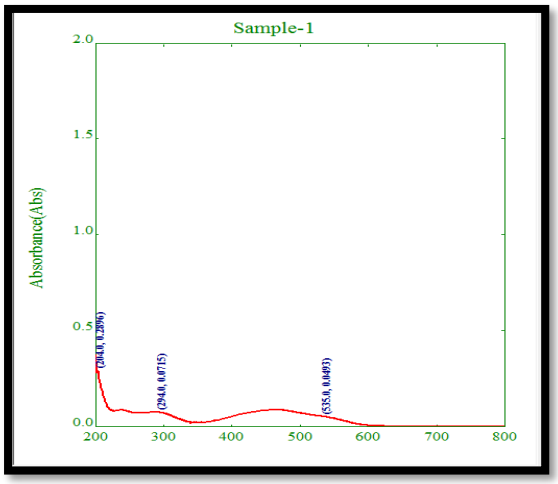


Fig (3-66): Electronic Spectra of Azo-imidazole complex (PdL_1)

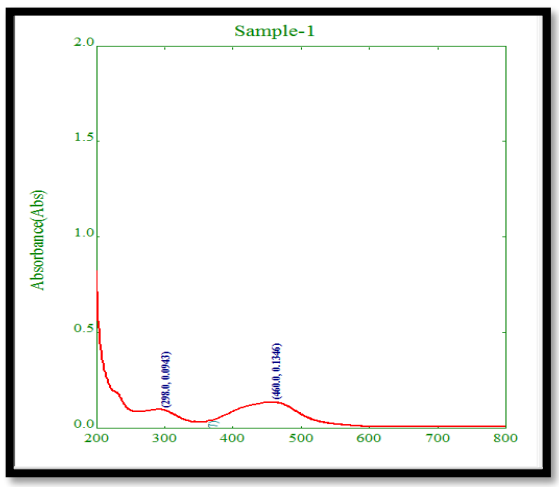


Fig (3-67): Electronic Spectra of Azo-imidazole complex (PtL_1)

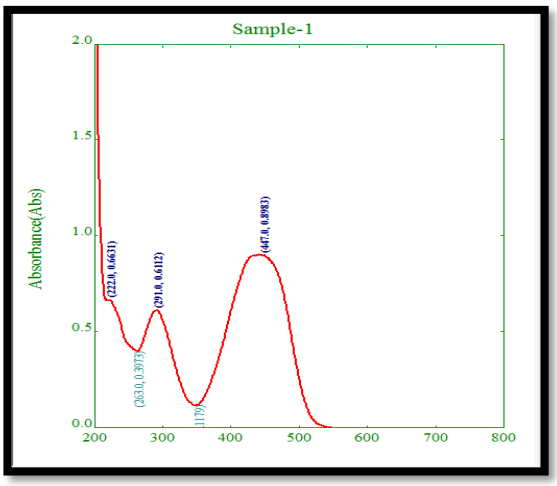


Fig (3-68): Electronic Spectra of Azo-imidazole ligand (L_2)

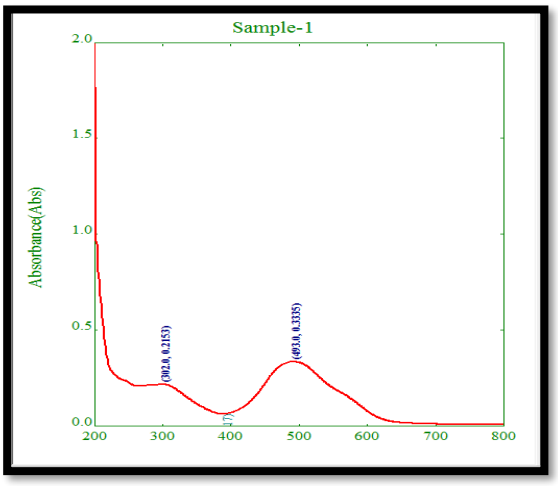


Fig (3-69): Electronic Spectra of Azo-imidazole complex (CoL_2)

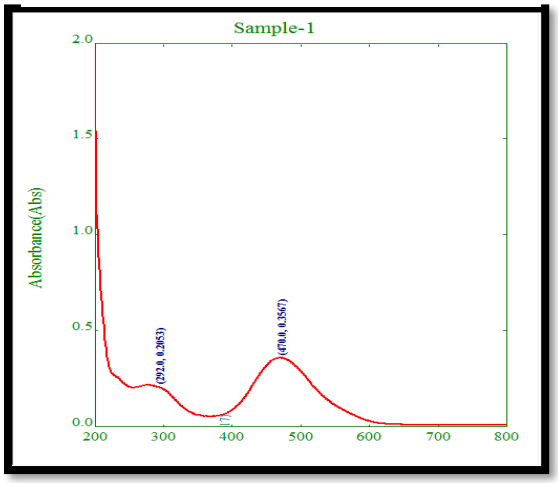


Fig (3-70): Electronic Spectra of Azo-imidazole complex (NiL_2)

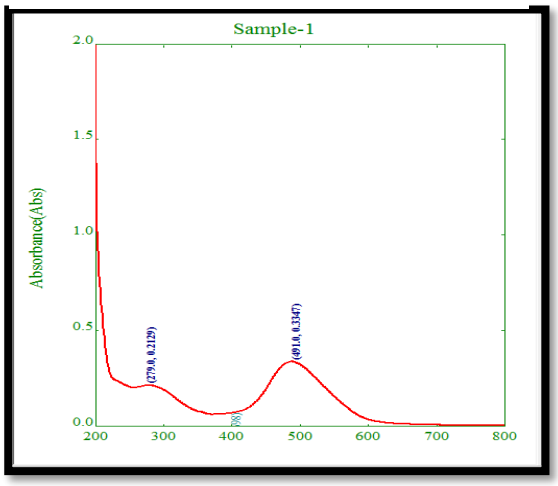


Fig (3-71): Electronic Spectra of Azo-imidazole complex (CuL_2)

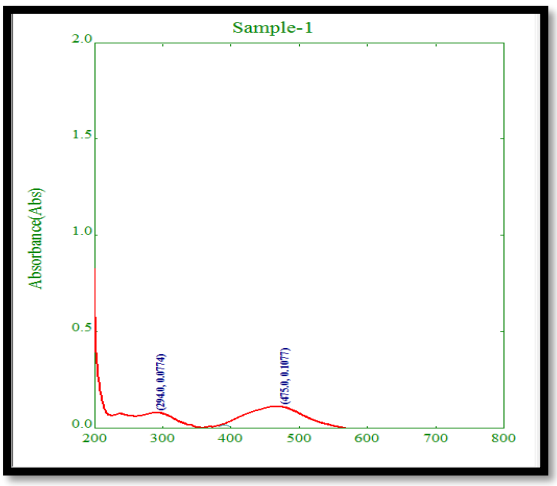


Fig (3-72): Electronic Spectra of Azo-imidazole complex (PdL_2)

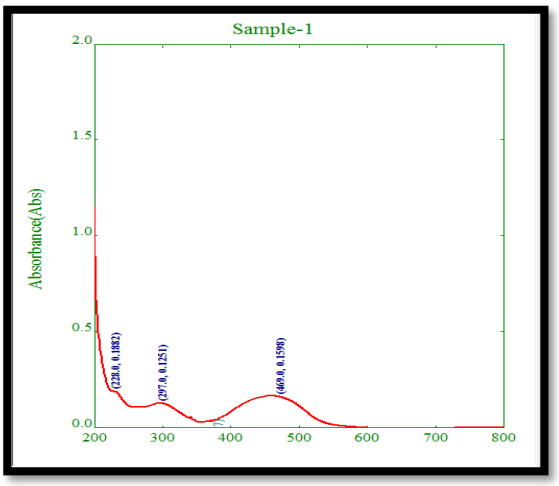


Fig (3-73): Electronic Spectra of Azo-imidazole complex (PtL_2)

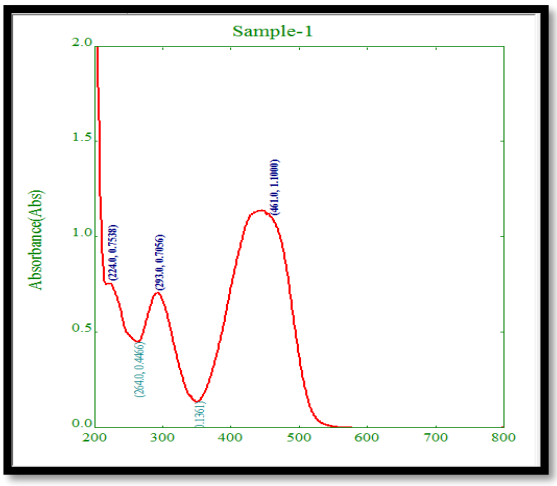


Fig (3-74): Electronic Spectra of Azo-imidazole ligand (L_3)

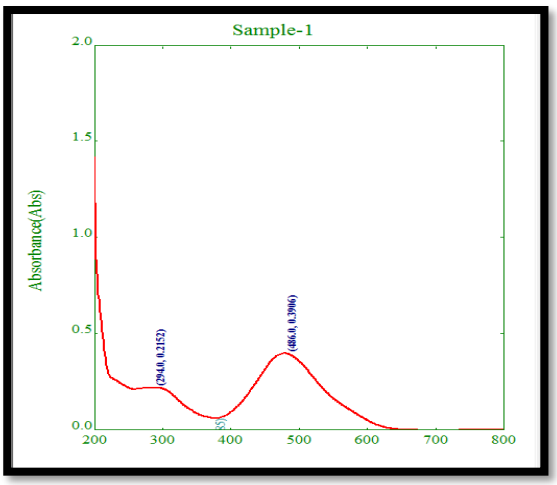


Fig (3-75): Electronic Spectra of Azo-imidazole complex (CoL_3)

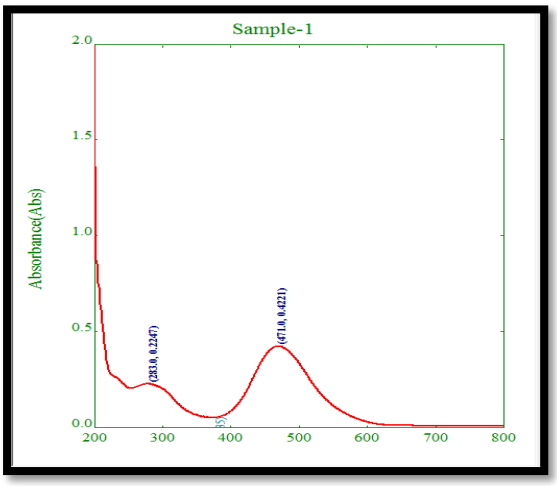


Fig (3-76): Electronic Spectra of Azo-imidazole complex (NiL_3)

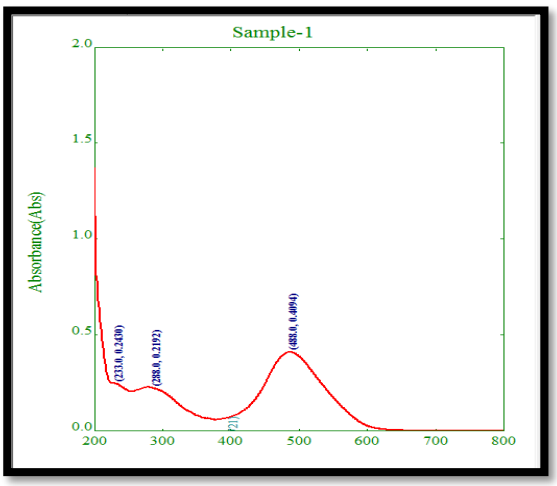


Fig (3-77): Electronic Spectra of Azo-imidazole complex (CuL_3)

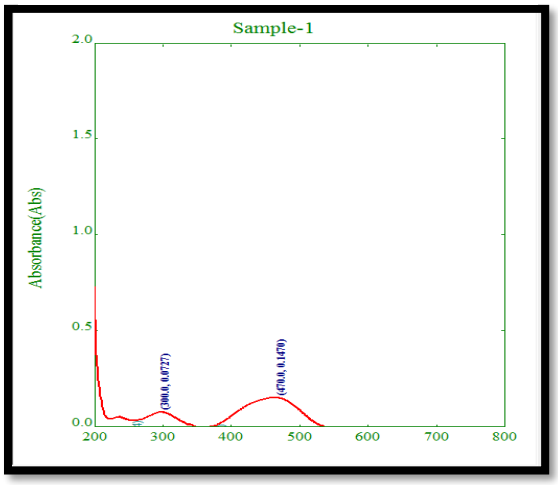


Fig (3-78): Electronic Spectra of Azo-imidazole complex (PdL_3)

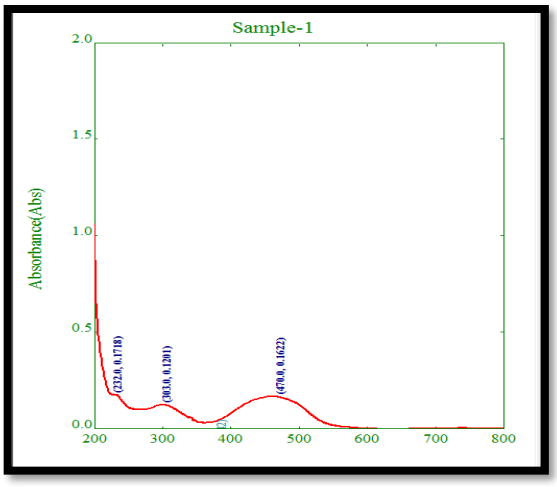


Fig (3-79): Electronic Spectra of Azo-imidazole complex (PtL_3)

3.4.2. Electronic Spectra of Azo-Schiff Base Ligands and their Chelating Complexes

With regard to the azo-Schiff ligands L_4, L_5, and L_6, the electronic spectra of their solutions and complexes of their solid metal ions were recorded using an ethanol solvent, and the electronic transitions and charge transfer bands were characterized, the UV-visible spectra of the solutions of selected ion complexes (cobalt, nickel, copper, palladium, and platinum) for each of the above-mentioned ligands showed new absorption bands at different wavelengths from the spectra of their free ligands (a red shifting in their complexes transitions was taken due to the coordination between the nitrogen ligands and lone pairs of oxygen to the vacant orbitals of the selected ions) [193, 194] . Where each spectrum of the ligands L_4, L_5, and L_6 showed two principle absorption bands at (28328cm^{-1}, 47169 cm^{-1}), (27932cm^{-1}, 47619cm-1)**,**(27247cm-1, 41666cm-1), which related to the electronic transitions (n→π*, π→π*), respectively. Figures (3-80) to (3-97) show the electronic spectra of the azo-Schiff base ligands (L_4, L_5, and L_6) with their metal complexes, while the obtained results for these spectra were included in the table (3-4).

Table (3-4): Electronic spectra of ligands (L_4, L_5, and L_6) and their complexes in ethanol solvent at laboratory temperature.

Compound/Complexes	Absorption Bands(nm)	Absorption Bands(cm^{-1})	Transition	Geometry	Hybridization
L_4 ($C_{19}H_{11}Cl_2F_2N_3O$)	212 353	47169 28328	π→π* n→π*	---------	--------
[Co($C_{38}H_{24}Cl_4F_4N_6O_4$)]	302 448	33112 22321	M→L,CT	Octahedral	sp^3d^2
[Ni($C_{19}H_{12}N_3Cl_3F_2O_2$)]	289 401	34602 24937	M→L,CT	square- planar	dsp^2
[Cu($C_{38}H_{24}Cl_4F_4N_6O_4$)]	292 411	34246 24330	M→L,CT	Octahedral	sp^3d^2
[Pd($C_{19}H_{12}N_3Cl_3F_2O_2$)]	294 450	34013 22222	M→L,CT	square- planar	dsp^2
[Pt($C_{19}H_{12}N_3Cl_3F_2O_2$)]	298 453	33557 22075	M→L,CT	square- planar	dsp^2
L_5($C_{19}H_{11}Cl_3FN_3O$)	210 358	47619 27932	π→π* n→π*	--------	--------
[Co($C_{38}H_{24}Cl_6F_2N_6O_4$)]	302 432	33112 23148	M→L,CT	Octahedral	sp^3d^2
[Ni($C_{19}H_{12}Cl_4FN_3O_2$)]	293 404	34129 24752	M→L,CT	square- planar	dsp^2
[Cu($C_{38}H_{24}Cl_6F_2N_6O_4$)]	279 451	35842 22172	M→L,CT	Octahedral	sp^3d^2
[Pd($C_{19}H_{12}Cl_4FN_3O_2$)]	294 425	34013 23529	M→L,CT	square- planar	dsp^2
[Pt($C_{19}H_{12}Cl_4FN_3O_2$)]	297 402	33670 24875	M→L,CT	square- planar	dsp^2
L_6 ($C_{19}H_{11}BrCl_2FN_3O$)	240 367	41666 27247	π→π* n→π*	--------	--------
[Co($C_{38}H_{24}Br_2Cl_4F_2N_6O_4$)]	294 435	34013 22988	M→L,CT	Octahedral	sp^3d^2
[Ni($C_{19}H_{12}BrCl_3FN_3O_2$)]	293 422	34129 23696	M→L,CT	square- planar	dsp^2
[Cu($C_{38}H_{24}Br_2Cl_4F_2N_6O_4$)]	288 455	34722 21978	M→L,CT	Octahedral	sp^3d^2
[Pd($C_{19}H_{12}BrCl_3FN_3O_2$)]	300 445	33333 22471	M→L,CT	square- planar	dsp^2
[Pt($C_{19}H_{12}BrCl_3FN_3O_2$)]	303 456	33003 21929	M→L,CT	square- planar	dsp^2

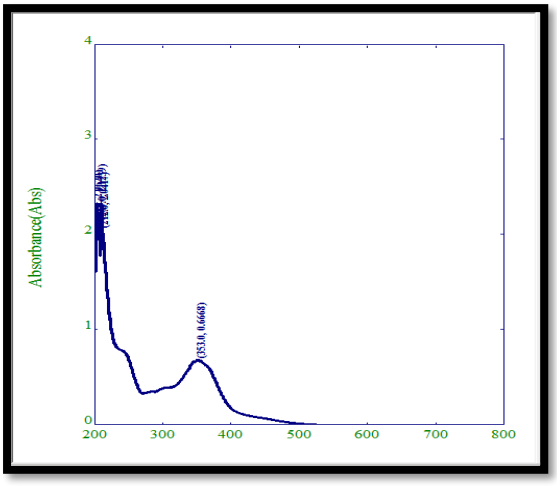


Fig (3-80): Electronic Spectra of Azo-Schiff ligand (L_4)

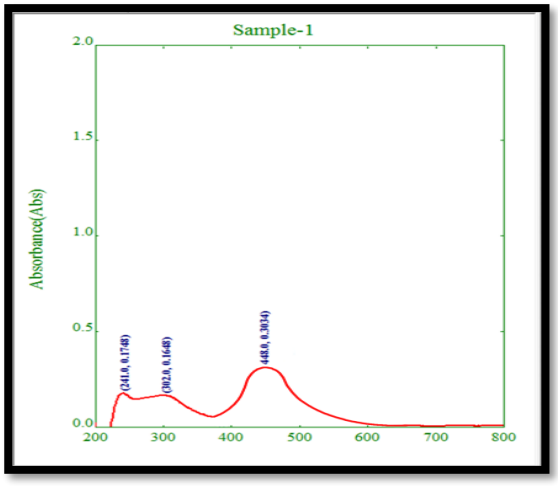


Fig (3-81): Electronic Spectra of Azo-Schiff complex (CoL_4)

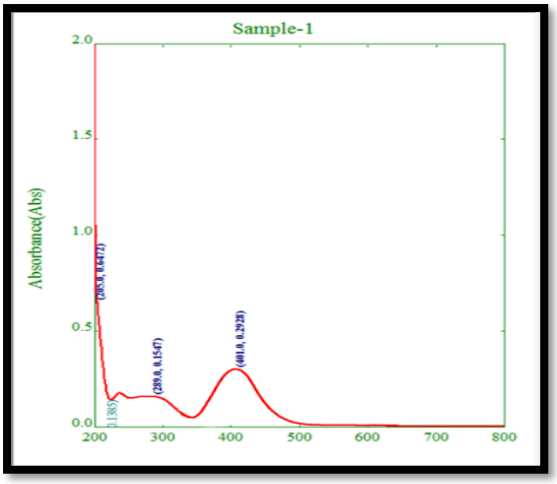


Fig (3-82). Electronic Spectra of Azo-Schiff complex (NiL_4)

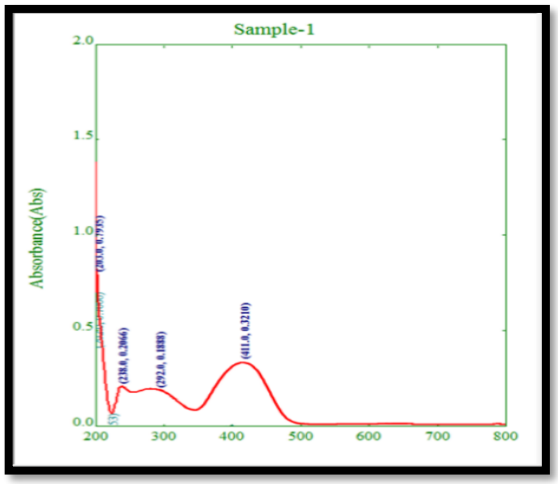


Fig (3-83): Electronic Spectra of Azo-Schiff complex (CuL_4))

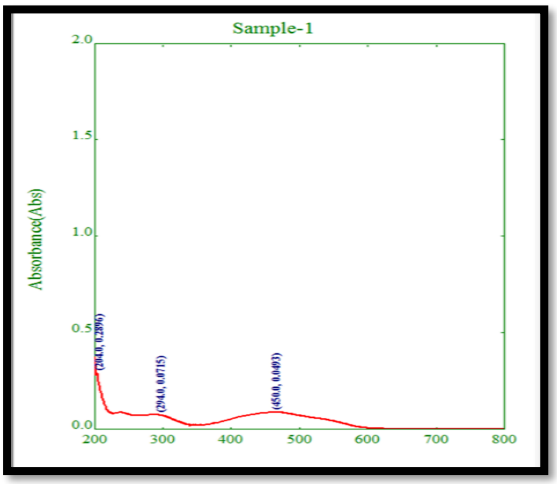


Fig (3-84): Electronic Spectra of Azo-Schiff complex (PdL_4)

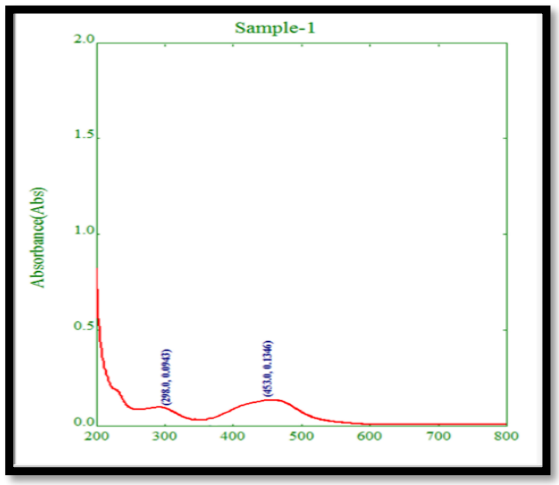


Fig (3-85): Electronic Spectra of Azo-Schiff complex (PtL_4)

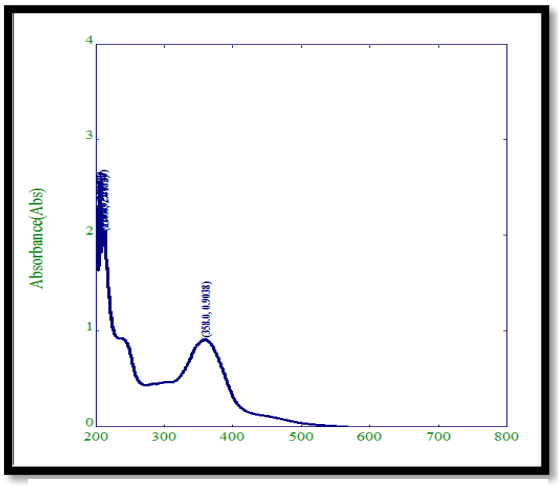


Fig (3-86): Electronic Spectra of Azo-Schiff ligand (L_5)

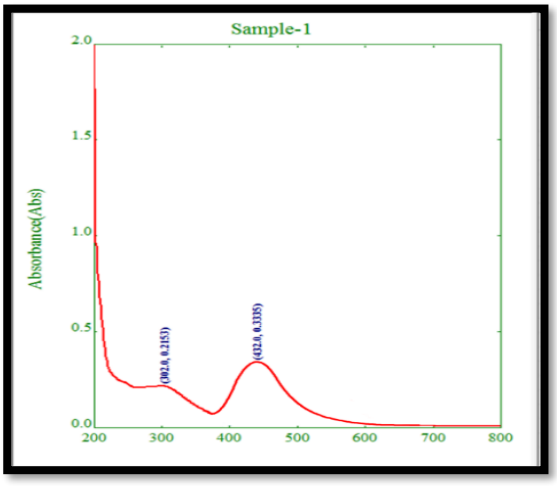


Fig (3-87): Electronic Spectra of Azo-Schiff complex (CoL_5)

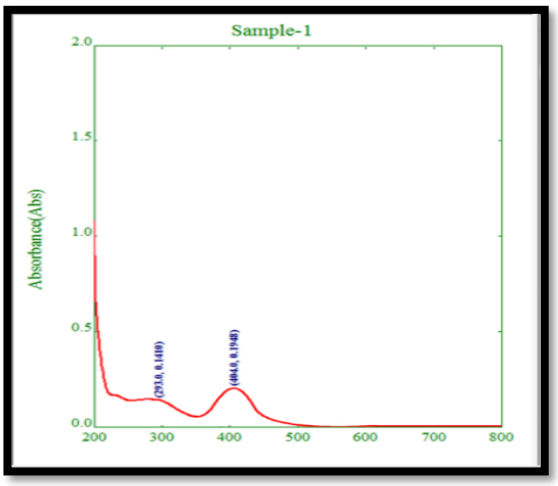


Fig (3-88): Electronic Spectra of Azo-Schiff complex (NiL_5)

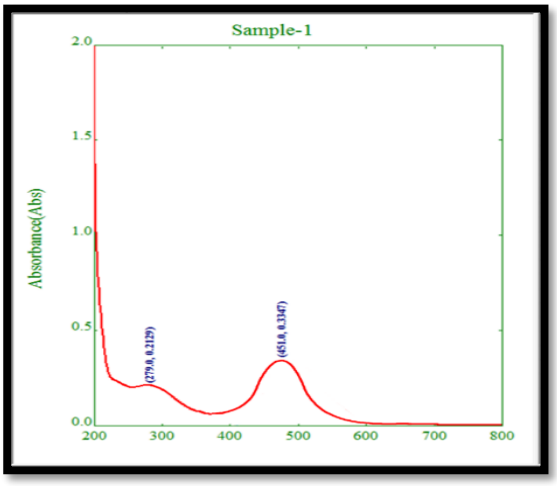


Fig (3-89): Electronic Spectra of Azo-Schiff complex (CuL_5)

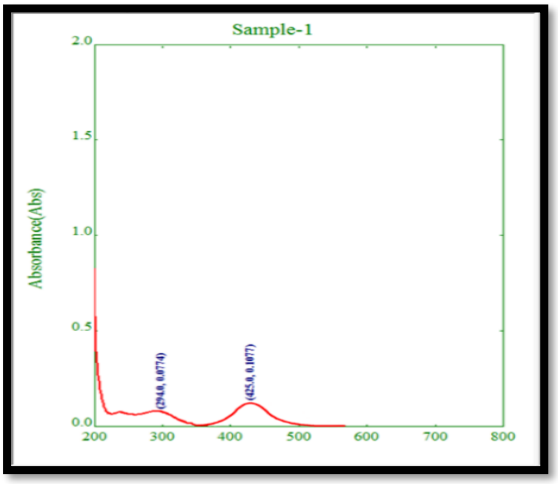


Fig (3-90): Electronic Spectra of Azo-Schiff complex (PdL_5)

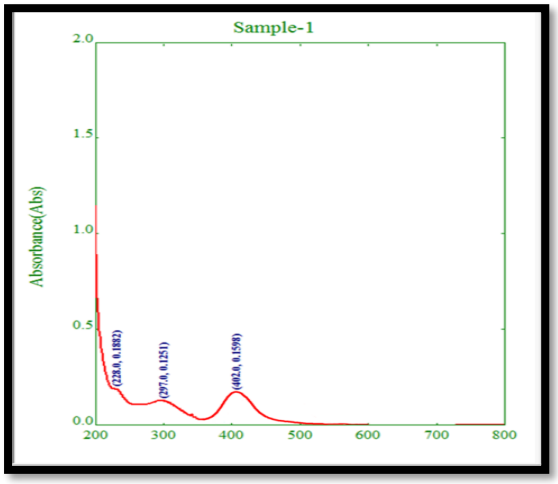


Fig (3-91): Electronic Spectra of Azo-Schiff complex (PtL_5)

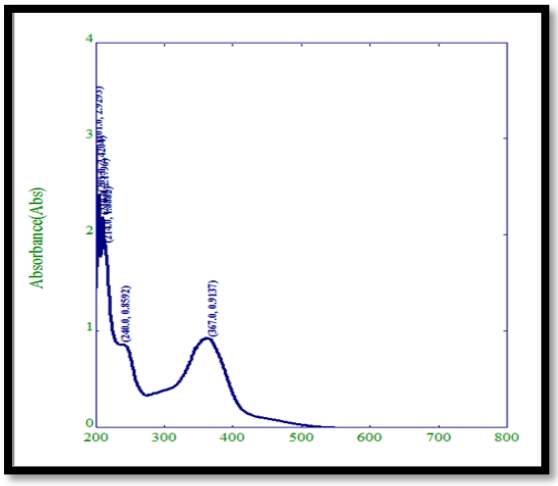


Fig (3-92): Electronic Spectra of Azo-Schiff ligand (L_6)

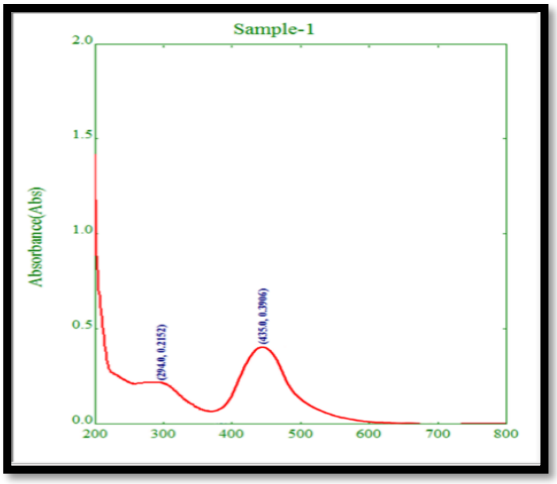


Fig (3-93): Electronic Spectra of Azo-Schiff complex (CoL_6)

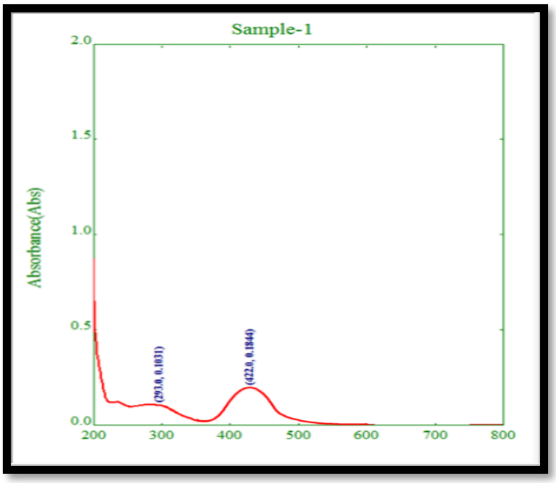


Fig (3-94): Electronic Spectra of Azo-Schiff complex (NiL_6)

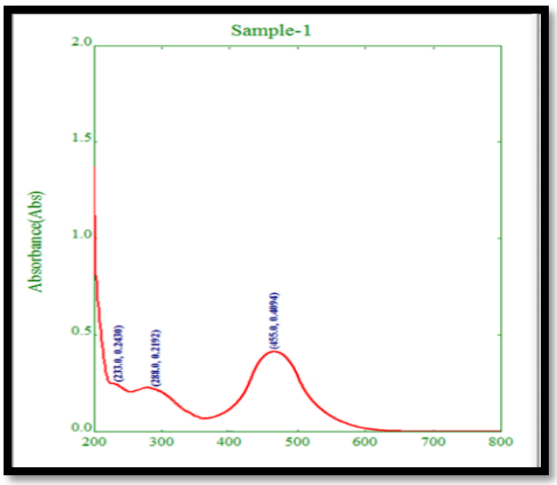


Fig (3-95): Electronic Spectra of Azo-Schiff complex (CuL_6)

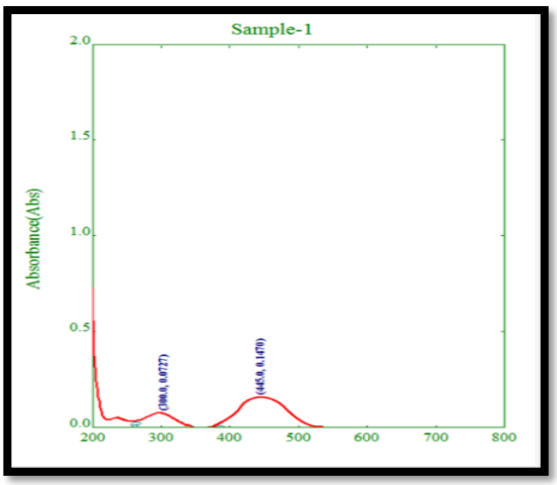


Fig (3-96): Electronic Spectra of Azo-Schiff complex (PdL_6)

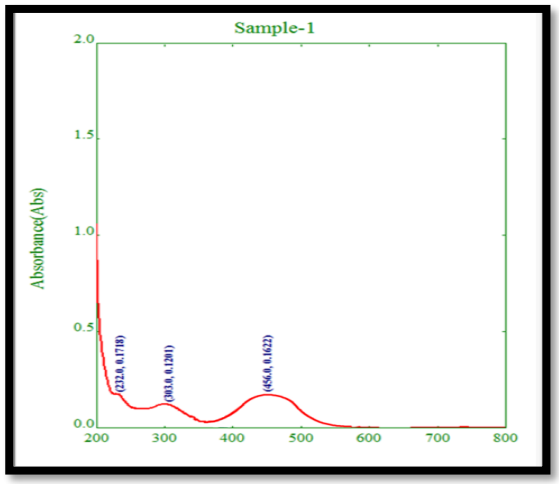


Fig (3-97): Electronic Spectra of Azo-Schiff complex (PtL_6)

3.5. Elemental Analysis

Carbon, hydrogen, and nitrogen elements were calculated for each of the ligands L_1, L_2, L_3, L_4, L_5, and L_6, and the metal complexes derived from them using the microanalysis technique, which is one of the common techniques for characterizing chemical compounds. The proportions of metallic elements in their complexes were also calculated using the flame atomic absorption technique.

When comparing the practically obtained values with those calculated theoretically, a great convergence was observed between them, which supports the validity of the added ratios of (metal: ligand), it was also found through these measurements the presence of water molecules for some of the prepared complexes, which supports the validity of the proposed formulas for the solid metal complexes, the results were included in tables (3-5) and (3-6) show the values of the precise analysis of the elements for each of the ligands, their metal complexes.

Table (3-5): Elemental analysis and theoretical molecular weight of the Azo-imidazole ligands and their metal complexes.

Ligands/complexes	Mwt	Found (Calc.) %			
		C %	H %	N %	M %
L1 ($C_{21}H_{14}N_4F_2$)	360.2613	69.99 (69.81)	3.92 (3.88)	15.55 (15.50)	-----
[Co($C_{42}H_{28}N_8F_4Cl_2$)]	850.4558	59.31 (58.95)	3.32 (3.24)	13.17 (12.88)	6.93 (6.71)
[Ni($C_{21}H_{14}N_4F_2Cl_2$)]	489.9547	51.48 (50.97)	2.88 (2.81)	11.44 (11.27)	11.98 (11.75)
[Cu($C_{21}H_{14}N_4F_2Cl_2$)]	494.8073	50.97 (50.82)	2.85 (2.79)	11.32 (11.13)	12.84 (12.66)
[Pd($C_{21}H_{14}N_4F_2Cl_2$)]	537.6813	46.91 (46.85)	2.62 (2.55)	10.42 (10.28)	19.79 (19.53)
[Pt($C_{21}H_{14}N_4F_2Cl_2$)]	626.3463	40.27 (40.11)	2.25 (2.18)	8.95 (7.98)	31.15 (30.85)
L2 ($C_{21}H_{14}N_4F$ Cl)	376.8117	66.94 (65.33)	3.75 (3.38)	14.87 (13.50)	-----
[Co($C_{42}H_{28}N_8F_2$Cl4)]	883.5566	57.10 (56.96)	3.19 (2.93)	12.68 (11.72)	6.67 (6.26)
[Ni($C_{21}H_{14}N_4FCl_3$)]	506.5051	49.81 (49.74)	2.79 (2.68)	11.06 (10.95)	11.59 (11.35)
[Cu($C_{21}H_{14}N_4FCl_3$)]	511.3577	49.33 (49.21)	2.76 2.63	10.96 (10.91)	12.43 (12.37)
[Pd($C_{21}H_{14}N_4FCl_3$)]	554.2317	45.52 (45.41)	2.55 (2.47)	10.11 (10.02)	19.20 (19.05)
[Pt($C_{21}H_{14}N_4FCl_3$)]	642.8967	39.24 (39.15)	2.20 (2.16)	8.72 (8.55)	30.35 (29.98)
L3($C_{21}H_{14}N_4FBr$)	421.2157	59.87 (59.85)	3.35 (3.21)	13.30 (13.15)	-----
[Co($C_{42}H_{28}N_8F_2Cl_2Br_2$)]	972.3646	51.88 (51.55)	2.90 (2.79)	11.52 (11.25)	6.06 (5.88)
[Ni($C_{21}H_{14}N_4FCl_2Br$)]	550.9091	45.79 (45.14)	2.56 (2.34)	10.17 (9.96)	10.65 (10.18)
[Cu($C_{21}H_{14}N_4FCl_2Br$)]	555.7617	45.39 (44.98)	2.54 (2.15)	10.08 (9.94)	11.43 (11.25)
[Pd($C_{21}H_{14}N_4FCl_2Br$)]	598.6357	42.14 (41.98)	2.36 (2.27)	9.36 (9.17)	17.78 (17.44)
[Pt($C_{21}H_{14}N_4FCl_2Br$)]	687.3007	36.70 (36.57)	2.05 (2.02)	8.15 (7.97)	28.39 (27.95)

Table (3-6): Elemental analysis and theoretical molecular weight of the Azo-Schiff ligands and their metal complexes.

Ligands/complexes	Mwt	Found (Calc.) %			
		C %	H %	N %	M %
Schiff base (DCSS)	266.2163	58.65 (58.46)	3.40 (3.32)	0.053 (0.047)	-----
L4 ($C_{19}H_{11}Cl_2F_2N_3O$)	406.2089	56.18 (56.01)	2.73 (2.55)	10.34 (10.22)	-----
[Co($C_{38}H_{24}Cl_4F_4N_6O_4$)]	905.3656	50.41 (50.11)	2.67 (2.39)	9.28 (9.17)	6.51 (6.42)
[Ni($C_{19}H_{12}N_3Cl_3F_2O_2$)]	517.4096	44.11 (43.98)	2.14 (2.04)	8.12 (8.09)	11.34 (11.28)
[Cu($C_{38}H_{24}Cl_4F_4N_6O_4$)]	909.9784	50.16 (50.13)	2.66 (2.51)	9.24 (9.16)	6.98 (6.79)
[Pd($C_{19}H_{12}N_3Cl_3F_2O_2$)]	565.1362	40.38 (39.97)	2.14 (2.07)	7.44 (7.32)	18.83 (18.76)
[Pt($C_{19}H_{12}N_3Cl_3F_2O_2$)]	653.8012	34.91 (34.55)	1.85 (1.77)	1.85 (1.77)	29.84 (29.1)1
L5($C_{19}H_{11}Cl_3FN_3O$)	422.7593	53.99 (53.89)	2.62 (2.54)	9.94 (9.86)	-----
[Co($C_{38}H_{24}Cl_6F_2N_6O_4$)]	938.4664	48.64 (48.42)	2.58 (2.49)	8.96 (8.75)	6.28 6.20
[Ni($C_{19}H_{12}Cl_4FN_3O_2$)]	533.96	42.75 (41.98)	2.27 (2.12)	7.87 (7.75)	11.00 (10.87)
[Cu($C_{38}H_{24}Cl_6F_2N_6O_4$)]	943.0792	48.41 (48.31)	2.57 (2.55)	8.91 (8.79)	6.74 (6.62)
[Pd($C_{19}H_{12}Cl_4FN_3O_2$)]	581.6866	39.24 (38.99)	2.08 (2.00)	7.23 (7.11)	18.30 (18.24)
[Pt($C_{19}H_{12}Cl_4FN_3O_2$)]	670.3516	34.05 (33.96)	2.83 (2.67)	6.27 (6.14)	29.11 (29.07)
L6 ($C_{19}H_{11}BrCl_2FN_3O$)	467.1633	48.85 47.99	2.37 2.12	9.00 8.87	-----
[Co($C_{38}H_{24}Br_2Cl_4F_2N_6O_4$)]	10272744	44.43 (44.32)	2.36 (2.22)	8.18 (8.13)	5.74 (5.65)
[Ni($C_{19}H_{12}BrCl_3FN_3O_2$)]	578.364	39.46 (39.37)	2.09 (2.01)	7.27 (6.97)	10.15 (10.10)
[Cu($C_{38}H_{24}Br_2Cl_4F_2N_6O_4$)]	10318872	44.24 44.11	2.34 2.28	8.15 8.06	6.16 6.09
[Pd($C_{19}H_{12}BrCl_3FN_3O_2$)]	626.0906	36.46 36.33	1.93 1.59	6.71 6.44	17.00 16.89
[Pt($C_{19}H_{12}BrCl_3FN_3O_2$)]	714.7556	31.93 31.55	1.69 1.57	5.88 5.71	27.30 27.21

3.6. The Effect of Solvent

To find out the best solvent to be adopted during the preparation of the ligands and their metal complexes, as well as conducting laboratory measurements, its effect was studied in several solvents, including ethanol, methanol, chloroform, DMF, and DMSO. The UV-visible spectrum of organic ligands prepared at laboratory temperature and optimum concentration and for all used solvents showed, the effect of the solvent in changing the maximum wavelength values (λmax) because of the polarity of the solvents used [195]. Figures (3-98) to (3-103) show the UV-visible spectra of the six prepared ligands in the above-mentioned solvents, and the obtained absorbance values are shown in Tables (3-7) to (3-12).

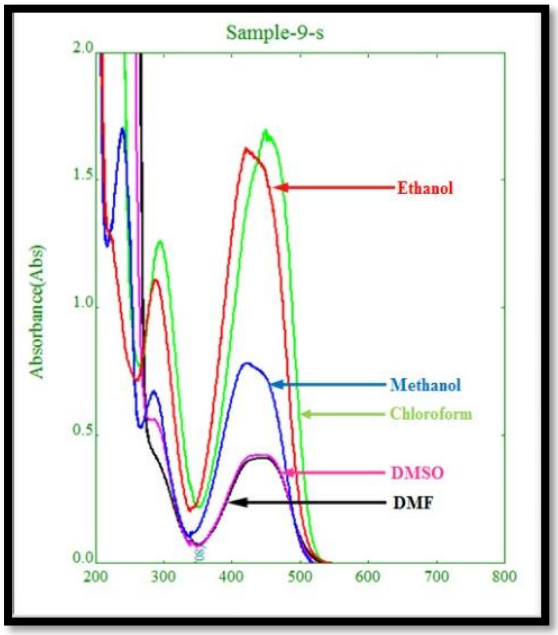


Fig (3-98): UV-visible spectra of (L_1) at different solvents.

Table (3-7): Maximum absorbance and wavelength values for (L_1).

Solvents	λ_{max} (nm)	Absorption
Ethanol	425	1.58
Methanol	437	0.79
Chloroform	467	1.62
DMSO	448	0.421
DMF	450	0.404

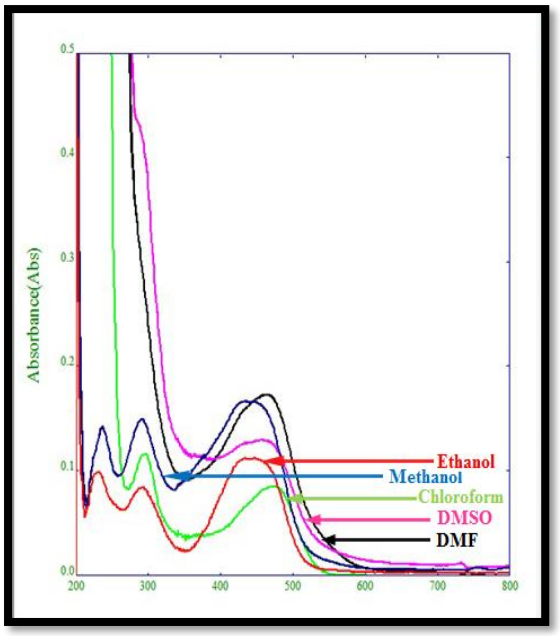


Fig (3-99): UV-visible spectra of (L_2) at different solvents.

Table (3-8): Maximum absorbance and wavelength values for (L_2).

Solvents	λ_{max} (nm)	Absorption
Ethanol	448	0.109
Methanol	435	0.169
Chloroform	472	0.083
DMSO	460	0.128
DMF	462	0.175

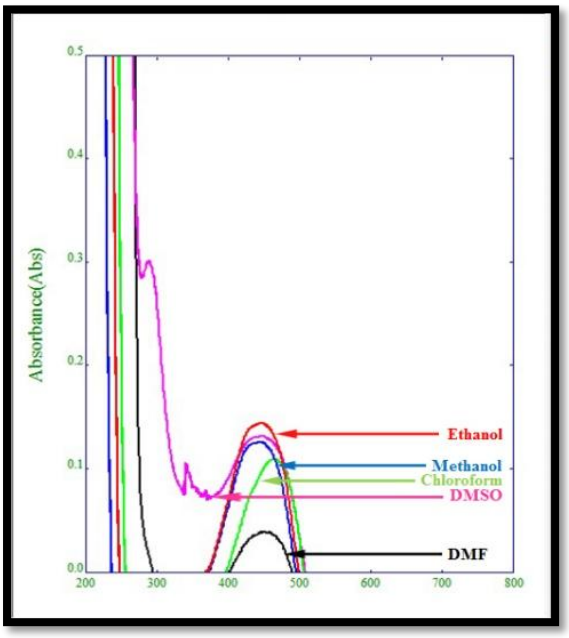


Fig (3-100): UV-visible spectra of (L_3) at different solvents.

Table (3-9): Maximum absorbance and wavelength values for (L_3).

Solvents	λ_{max} (nm)	Absorption
Ethanol	446	0.1442
Methanol	449	0.1258
Chloroform	469	0.109
DMSO	450	0.131
DMF	457	0.034

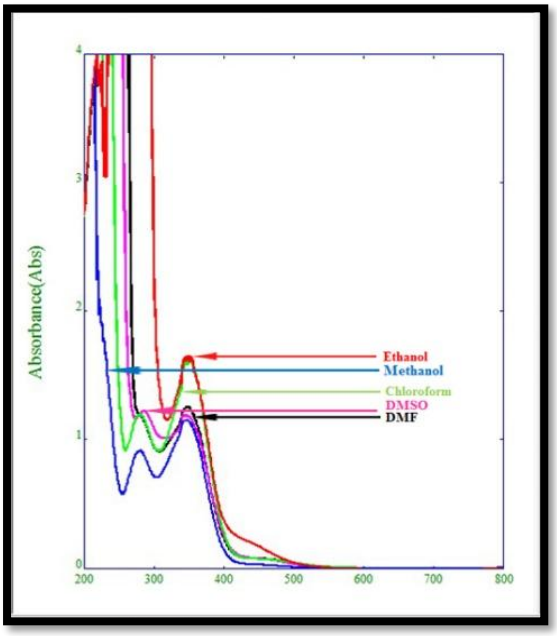


Fig (3-101): UV-visible spectra of (L_4) at different solvents.

Table (3-10): Maximum absorbance and wavelength values for (L_4).

Solvents	λ_{max} (nm)	Absorption
Ethanol	347	1.51
Methanol	350	1.14
Chloroform	352	1.48
DMSO	347	1.2
DMF	349	1.2449

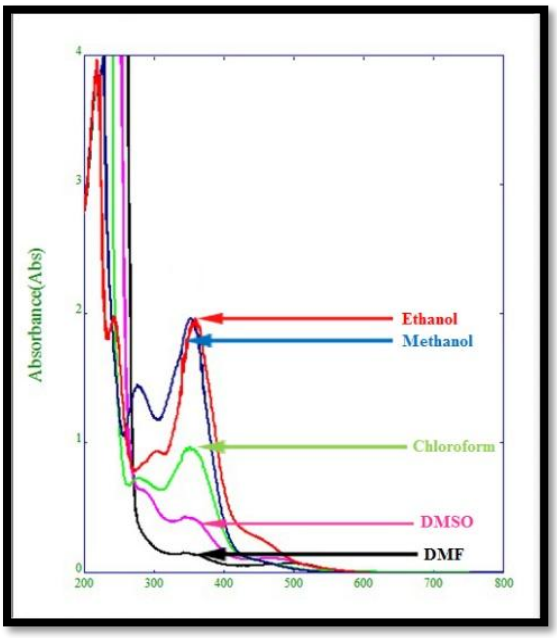


Fig (3-102): UV-visible spectra of (L_5) at different solvents.

Table (3-11): Maximum absorbance and wavelength values for (L_5).

Solvents	λ_{max} (nm)	Absorption
Ethanol	360	1.8
Methanol	358	1.78
Chloroform	359	0.9
DMSO	357	0.4
DMF	351	0.06

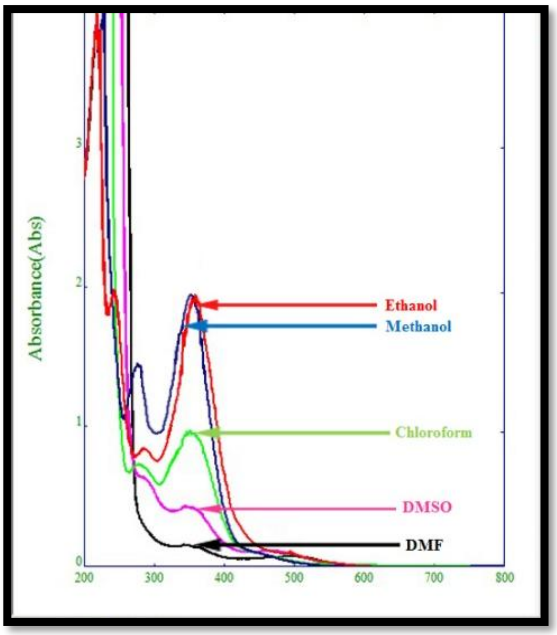


Fig (3-103): UV-visible spectra of (L_6) at different solvents.

Table (3-12): Maximum absorbance and wavelength values for (L_6).

Solvents	λ_{max} (nm)	Absorption
Ethanol	357	1.83
Methanol	354	1.85
Chloroform	355	0.93
DMSO	352	0.412
DMF	348	0.067

3.7. Molar Conductivity Measurements

Molar conductivity measurements are one of the important methods for knowing the structural formula of the complex, and this method is characterized by its simplicity [196], and by adding the results of this technique to the results of other techniques such as UV-visible and infrared spectra and the precise analysis of the elements as well as the values of the magnetic standard, the researcher can guess the stereotype of coordination complexes.

The value of molar electrical conductivity increases with the increase of the charged species in the solution [196], and solvents with high dielectric constants and low viscosity used, such as methanol, ethanol, dimethyl sulfur dioxide, dimethylformamide, nitromethane, methyl cyanide, and others [197], It is not recommended to use water as a solvent due to the difficulty of dissolving complexes in water or the ability to dissolve them

in it [198]. In order to arrive at the ionic formula of a compound, the molar electrical conductivity measurement at a concentration (1×10^{-3} M) is used, the molar conductivity values for many solvents can be shown in table (3-13).

Table (3-13):Molar electrical conductivity values at (1×10^{-3}) molar concentration for different types of electrolytes in different solvents.

Solvent	Non - Electrolyte	Electrolyte type			
		1 : 1	1 : 2	1 : 3	1 : 4
Water	0.0	120	240	360	480
Ethanol	0-20	35-45	70–90	120	160
Nitro methane	0-20	75-95	150–180	220-260	290–330
Methyl cyanide	0-30	120-160	220–300	340-420	500
DMF	0-30	65-90	130-170	200-240	300
DMSO	0-20	30-40	70–80	----	----

3.7.1. Molar Conductivity Measurements of Azo-imidazole Complexes

The molar electrical conductivity of solutions of solid metal complexes with azo-imidazole ligands (L_1), (L_2), and (L_3) at a concentration of (1×10^{-3}) M for each complex and at room temperature was measured using the dimethyl formamide (DMF) and dimethyl sulfoxide (DMSO) solvents, the results showed that the obtained values ranged between (22.88-27.21) $S.cm^2.mol^{-1}$,(9.63-16.07) $S.cm^2.mol^{-1}$ for the ligand complexes (L_1), (19.13-26.27) $S.cm^2.mol^{-1}$,(9.70-14.43) $S.cm^2.mol^{-1}$ for the ligand complexes (L_2), and (18.18-24.86) $S.cm^2.mol^{-1}$,(5.07-12.52) $S.cm^2.mol^{-1}$ for ligand (L_3) complexes, for (DMF) and, (DMSO), respectively, it was found closeness in the values when comparing these results with what was mentioned in the literature [199, 200], for complexes that are free of ionic character [201], this confirms the validity of the

proposed formulas, and the results of this study were included in the table (3-14)

3.7.2. Molar Conductivity Measurements of Azo-Schiff Base Complexes

The molar electrical conductivity of solutions of solid metal complexes with ligands (L_4), (L_5), and (L_6) at a concentration of (1×10^{-3})M for each complex and at room temperature was measured using the dimethyl formamide (DMF) and dimethyl sulfoxide (DMSO) solvents, the results showed that the obtained values ranged between (10.36-25.33) $S.cm^2.mol^{-1}$,(6.01-12.94) $S.cm^2.mol^{-1}$ for the ligand complexes (L_4), (15.42-27.23) $S.cm^2.mol^{-1}$,(8.10-16.74) $S.cm^2.mol^{-1}$ for the ligand complexes (L_5), and (15.64-26.22) $S.cm^2.mol^{-1}$,(7.78-16.44) $S.cm^2.mol^{-1}$ for ligand (L_6) complexes, for (DMF) and, (DMSO), respectively, it was found closeness in the values when comparing these results with what was mentioned in the literature[199, 200], for complexes that are free of ionic character [201], this confirms the validity of the proposed formulas, and the results of this study were included in the table (3-15).

3.8. Magnetic Susceptibility Measurements

In order to reach to propose the forms of metal complexes, it is necessary to know and study the magnetic properties of those complexes under study, and magnetic susceptibility is one of the successful methods used for many transition metal complexes [202], as a result of the effects resulting from the outer shells partially filled with electrons, through which you know the electronic arrangement and the oxidation state of the metal, and specifying the number of single electrons for the metal ion indicates the state of the complexes, whether they have high or low spin [203].

The magnetic properties are known as a result of the orbital motion and the spin motion of the complexes. The theoretical magnetic moment of the first transition series of metal ions can be known by the relation [204, 205].

$$\mu_{S+L} = \sqrt{4S(S+1) + L(L+1)} \qquad \ldots\ldots\ldots\ldots\ldots (1)$$

as that

S= Sum of the total spin

L= Quantum number of total orbital angular momentum

When the value of the magnetic moment is limited to the spin motion only when (L= 0)

The previous relationship is reduced to the spin formula _ only

$$\mu_S = \sqrt{4S(S+1)}.B.M \qquad \ldots\ldots\ldots\ldots\ldots (2)$$

When $S = \frac{n}{2}$ the relationship is written:

$$\mu_S = \sqrt{n(n+2)} \qquad \ldots\ldots\ldots\ldots\ldots (3)$$

Where is n= the number of lone electrons for the central atom

While it is practical to know the value of the magnetic susceptibility of the prepared complexes according to room temperature, the effective magnetic moment was found from the relationship

$$\mu_{eff} = 2.828\sqrt{X_A T}.B.M \qquad \ldots (4)$$

$$X_A = X_m + D \qquad \ldots (5)$$

$$X_m = X_g \times M.wt \qquad \ldots (6)$$

Where each represents

T= Absolute temperature.

X_A= Atomic susceptibility.

X_M= Molar susceptibility.

Xg= Gamic (weight) susceptibility.

D= Diamagnetic correction factor.

Meff = Effective magnetic moment.

M.wt= Gram molecular weight.

B.M = Magnetic moment unit (Bor. magneton).

Dia magnetic results from the inductive effect of the magnetic field affecting the electronic value, so the correction must be made within molecule [189, 206]. The metal ion may have a magnetic moment that is very close to the spin value as it does for the ions of the first transition series. As for the magnetic moment of the ions of the second and third series, it is less than the value of the calculated moment of the spin formula, and the reason is due to the large size of the (4d) and (5d) orbitals compared to the (3d) orbitals, which leads to a lack of repulsion between the electrons in these orbitals, also, heavy ions have high values of the orbital-spin coupling constant (ג), so they show lower moments than the calculated values of the spin formula only.

The magnetic susceptibility measurements were carried out for all the compounds concerned in the study and for all the organic imidazole and azo-Schiff ligands at (298) absolute temperature. The magnetic days of atoms in organic molecules, metal ions, and inorganic radicals were corrected according to Pascal's tables [207], and magnetic moment values were calculated according to the previously mentioned relationships.

3.8.1. Magnetic Susceptibility Measurements of Azo-imidazole Complexes

The results of the magnetic susceptibility of the azo-imidazole complexes were included in the table (3-14), as the magnetic moment values of the cobalt complexes for (L_1, L_2, and L_3) equal to (4.43, 5.19, and 5.33) B.M, respectively, these values are in agreement with the results of many highly spin octahedral ($t2g^5$, eg^2)complexes of cobalt [208, 209], which range from (3.87- 5.20) B.M, this clearly indicates the presence of the paramagnetic characteristic of cobalt complexes, as there are three odd electrons in (3d). As for the copper (II) complexes of the ligands as above mentioned, they possessed magnetic moments of (1.88, 2.14, 1.93) B.M, respectively, this indicates the paramagnetic property resulting from the presence of an odd electron for the copper (II) ion in its complexes that may suggest a tetrahedral copper complexes [210], while the other (Nickle, Palladium, and Platinum) [211, 212] complexes didn't give a reliable value due to their diamagnetic properties because (the lake of the odd electron in the 3d orbitals).

3.8.2. Magnetic Susceptibility Measurements of Azo-Schiff Base Ligand Complexes

The results of the magnetic susceptibility of the azo-Schiff complexes were included in the table (3-15), as the magnetic moment values of the cobalt and copper ligands complexes L_4, L_5, and L_6 reached an amount equal to (5.33, 4.41, and 5.04) B.M, (1.98, 2.24, and 1.83) B.M, respectively. Where cobalt complexes gave values that were equivalents to the presence of three odd electrons in the 3d orbitals that were compatible with the octahedral cobalt complexes [213]. The copper complexes gave values that agreed with the presence of a single electron, which may suggest an octahedral copper complex [214], while the d8 ions (Nickle,

Palladium, and Platinum) [211, 212] complexes did not give a reliable value due to their diamagnetic properties.

Table (3-14): Molar electrical conductivity and magnetic susceptibility of Azo-imidazole complexes.

Complexes	Λ_m (S.mol^{-1}.Cm^2) DMF	DMSO	Magnetic Susceptibility μ_{eff} B.M
CoL1	27.21	13.34	4.43
NiL1	24.54	10.25	0
CuL1	22.88	9.63	1.88
PdL1	26.50	16.07	0
PtL1	24.75	15.83	0
CoL2	23.53	12.30	5.19
NiL2	19.21	11.66	0
CuL2	26.27	12.25	2.14
PdL2	19.13	9.70	0
PtL2	22.69	14,43	0
CoL3	20.37	8.96	5.33
NiL3	18.18	5.07	0
CuL3	24.86	12.52	1.93
PdL3	21.55	8.15	0
PtL3	23.73	7.57	0

Table (3-15): Molar electrical conductivity and magnetic susceptibility of Azo-Schiff complexes.

Complexes	Λ_m (S.mol^{-1}.Cm^2) DMF	DMSO	Magnetic susceptibility μ_{eff} B.M
CoL4	15.18	10.84	5.33
NiL4	10.36	6.01	0
CuL4	17.68	11.58	1.98
PdL4	18.45	10.27	0
PtL4	25.33	12.94	0
CoL5	15.42	9.07	4.41
NiL5	21.88	13.35	0
CuL5	27.23	13.83	2.24
PdL5	16.39	8.10	0
PtL5	24.63	16.74	0
CoL6	22.33	10.15	5.04
NiL6	15.64	13.90	0
CuL6	21.37	16.44	1.83
PdL6	20.16	10.55	0
PtL6	26.22	7.78	0

3.9. The Proposed Structure of Chelate Complexes

The difference in the geometric shapes of the azo and Schiff bases complexes is attributed to several factors, including the difference in the available coordination centers that participate in the composition of the ligand, the nature of the metal ion involved in the composition of the complex, in addition to the nature of the compensated groups on the rings constituting the Schiff base in terms of its type and location [215, 217].

In general, various stereo forms have been suggested, including octahedron, square planar, tetrahedron, square-base pyramid, triangular base pyramid, and other stereotypes. The technique of X-ray spectroscopy is used to determine the spatial shape of the complex [218, 221].

Based on the results of the aforementioned analytical and spectroscopic measurements of the prepared chelating ligands complexes in this study, and their comparison of what was stated in the literature about the coordination sites involved in the composition of azo and azo Schiff bases compounds and the nature of their bonding sites with various metal ions, According to the results that were reached in a consensual manner in this study, where the complexes took three different geometric shapes which are the octahedral shape of the positively charged dichotomous cobalt complexes with all the azo-imidazole and azo- Schiff ligands, while the positively charged copper dimer complex took two forms, namely the tetrahedral shape with each of (L_1, L_2, and L_3) The second form is octahedral with ligands (L_4, L_5, and L_6), and finally, the complexes of each of the nickel, palladium and platinum ions have taken the shape of a square planar and for all the ligands mentioned above, Figure(3-104) shows all the proposed stereotypes for the azo-imidazole and azo-Schiff complexes prepared in this study.

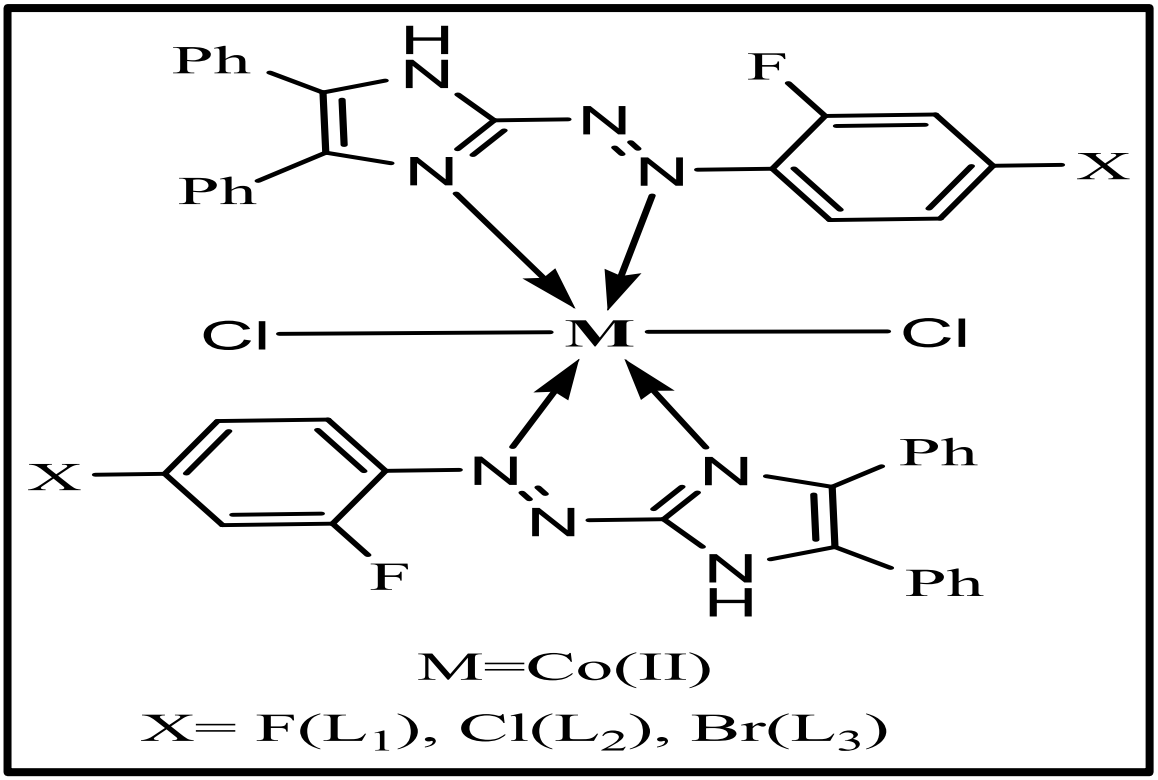


Fig (3-104): The proposed geometry of the complex of Co (II) with Azo-imidazole ligands L_1 (F), L_2 (Cl), and L_3 (Br).

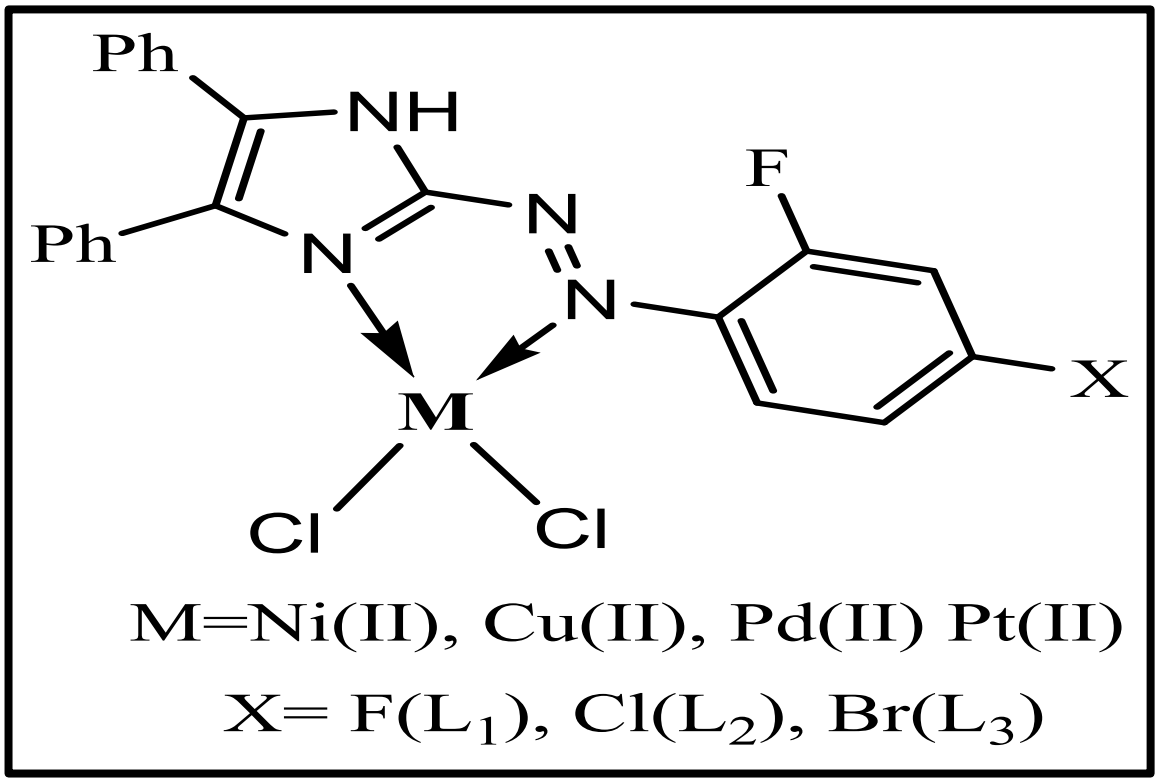
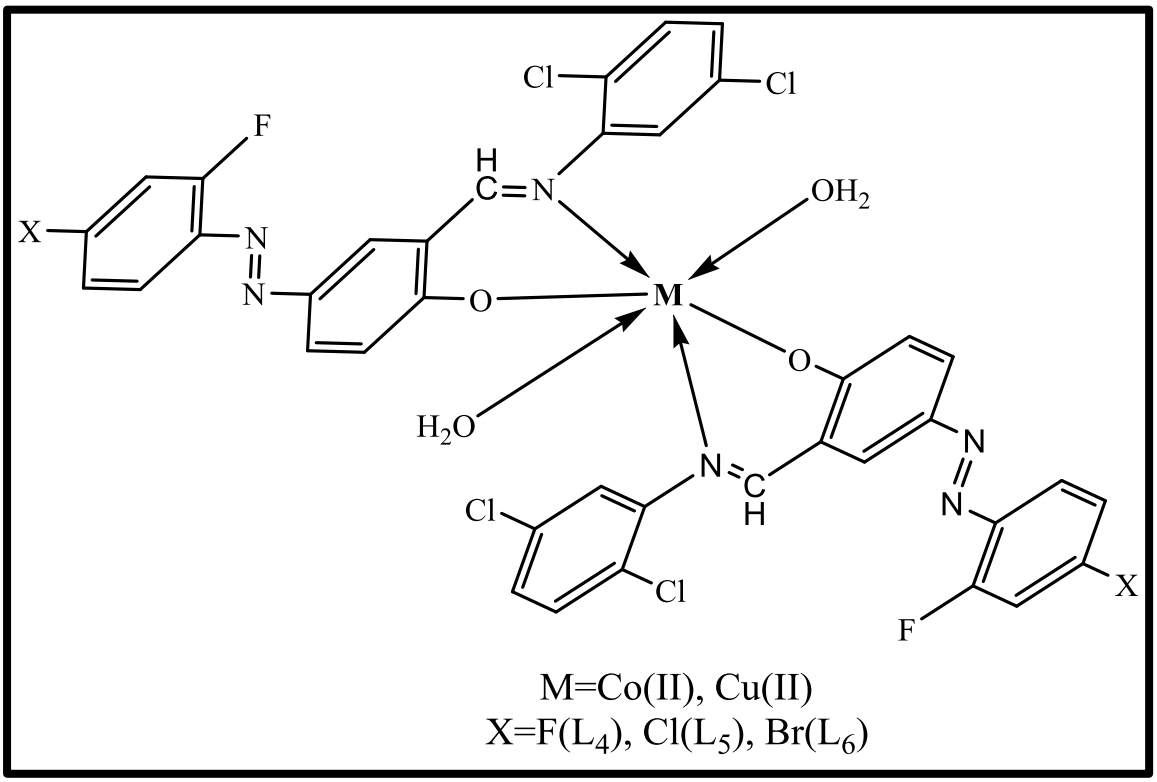


Fig (3-105): The proposed geometry of the complexes of Ni (II),Cu(II), Pd(II), and Pt(II) with Azo-imidazole ligands L_1 (F), L_2 (Cl), and L_3 (Br).



Fig(3-106): The proposed geometry of the complexes of Co (II), Cu (II) with Azo-Schiff ligands L_4 (F), L_5 (Cl), and L_6 (Br).

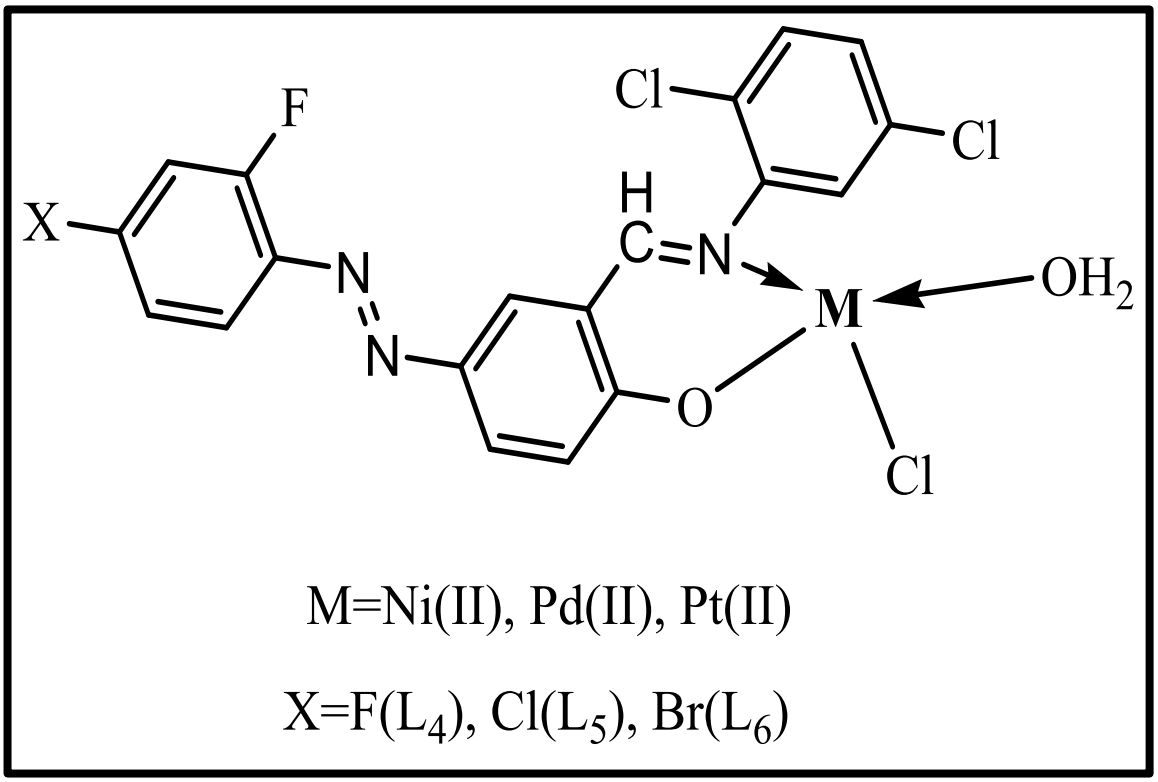


Fig (3-107): The proposed geometry of the complexes of Ni (II), Pd(II), and Pt (II) with Azo-Schiff ligands L_4 (F), L_5 (Cl), and L_6 (Br).

Preface:

The study included a biological evaluation of some of the prepared compounds under study. Where the synthesized ligands and some of their metal ion complexes were screened for their antimicrobial bioactivity against two strains of bacteria (***Staphylococcus aureus spp***) and (***Escherichia coli spp***), metronidazole (Flagyl) and tetracycline were used as reference antibiotics STD for azo-imidazole and azo-Schiff base ligands with some of their metal ion complexes, respectively, and DMSO as control. Where the prepared compounds showed varying inhibition compared to metronidazole and tetracycline antibiotics, also the complexes showed an inhibition rate over those of their ligands. In addition, the effect of the aforementioned ligands with some of their selected complexes as anti-oxidants was studied, DPPH with methanol was used as a control, whereas tannic acid was used as a standard STD solution, it also showed varying rates of inhibition compared with tannins acid, and the inhibition rates of complexes are higher than the ligands.

The study also included biological and toxicological assays of some platinum and palladium complexes for azo-imidazole and azo-Schiff ligands, represented by complexes selection (PtL_1 and PdL_2) for azo-imidazole ligands and (PtL_5 and PdL_4) for aze-Schiff base ligands prepared in the experimental part on human breast cancer cells MCF-7 by using MTT assay, and comparison was made between the complexes of each of palladium and platinum, where the platinum complexes of azo-imidazole and azo-Schiff ligands showed a higher selectivity in killing cancer cells than the palladium complexes of the same ligands mentioned above, where the complexes of (PtL_1 and PtL_5) need (42.68µg/ml and 56.78 µg/ml) respectively, to kill half the cancerous cells, and this concentration is symbolized by IC_{50} and it is likely to be very safe with normal uninfected

cells, as it does not target healthy cells and for the same concentration, while the palladium complexes (PdL_2 and PdL_4) need (67.29 μg/ml and 74.64 μg ml) respectively, and as a result, platinum complexes (PtL_1 and PtL_5) can be considered a new treatment for breast cancer, with relatively high selectivity and efficacy compared to palladium complexes (PdL_2 and PdL_4) for the same above mentioned ligands.

4.1. Biological Evaluation

4.1.1. Antibacterial Screening

The synthesized of azo-imidazole and azo-Schiff base ligands and some of their metal ion complexes were screened for their antimicrobial bioactivity against two strains of bacteria (***Staphylococcus aureus spp***) and (***Escherichia coli spp***) by the wells method. Mueller-Hinton agar was used as a culture medium for bacterial growth. All compounds were dissolved in DMSO. Metronidazole and tetracycline were used as a reference antibiotic (STD) for each of the azo-imidazole and azo-Schiff base ligands and some of their metal ion complexes, respectively, and DMSO as a control. The zones of inhibition were determined at the end of an incubation period of 24 hr. at 35◦ C. During this period, the test solution diffused and the growth of inoculated microorganisms was affected.

Below we review the most important results obtained:

4.1.1.1. Antibacterial Screening for Azo-imidazole Ligands and Some of their Metal Ion Complexes

Through the results obtained from this study, the azo-imidazole ligands with some of their complexes showed high activity at the values (10-13mm) [222, 224] against (***Staphylococcus aureus***), except for (L_1), and (L_2), which showed low activity at the values (8 mm), and (9 mm), respectively compared with (STD). While for bacterial strain (***E. coli***), the

azo dyes ligands and their chelates displayed a high activity at values (14-17 mm), except for (L_1, NiL_1, L_2, and L_3) which showed credible activity (Somewhat) at values (12, 13, 13, and 13 mm), respectively compared with the same drug.

And from the collected data, it is clear that the formation of complexes enhances antimicrobial activity [225, 226], Such increased activity of complexes may be related to the chelation theory and the concept of overtone.

According to the concept of overtone [227] cell permeability, the lipid membrane around the cell wall favors the passage of lipid-soluble substances only because of the important factor of lipid solubility to control the antimicrobial activity of bacteria. Regarding the chelation [227, 228] the ligand orbital overlap and the partial participation of the metal ion with the donor groups and more reduces the polarity of the metal ion and increases the spread of electrons on all the chelating rings and thus enhancing the fatty alpha of the complex and in turn, leads to breaking the permeability barrier of the cell and thus delays the normal cellular processes, the table (4-1) shows the inhibition of the growth of the bacteria (Inhibition Zone) for azo-imidazole ligands and some of their metal ion complexes recorded in millimeter unit, while the figures (4-1) and (4-2) show the biological effect and relationship of azo-imidazole ligands and some of their metal ion complexes with the bacteria under study.

Table (4-1): The inhibition of the growth of the bacteria (Inhibition Zone) for Azo-imidazole ligands and some of their metal ion complexes recorded in millimeter unit.

Compounds	S.aureus (Gram positive)	E.coli (Gram negative)
Metronidazole (STD)	12	18
L_1 ($C_{21}H_{14}N_4F_2$)	8	12
[Ni($C_{21}H_{14}N_4F_2Cl_2$)]	11	13
[Pd($C_{21}H_{14}N_4F_2Cl_2$)]	10	14
[Pt($C_{21}H_{14}N_4F_2Cl_2$)]	13	18
L_2 ($C_{21}H_{14}N_4F$ Cl)	9	13
[Ni($C_{21}H_{14}N_4FCl_3$)]	10	15
[Pd($C_{21}H_{14}N_4FCl_3$)]	12	15
[Pt($C_{21}H_{14}N_4FCl_3$)]	13	16
L_3($C_{21}H_{14}N_4FBr$)	11	13
[Ni($C_{21}H_{14}N_4FCl_2Br$)]	12	14
[Pd($C_{21}H_{14}N_4FCl_2Br$)]	12	16
[Pt($C_{21}H_{14}N_4FCl_2Br$)]	13	17

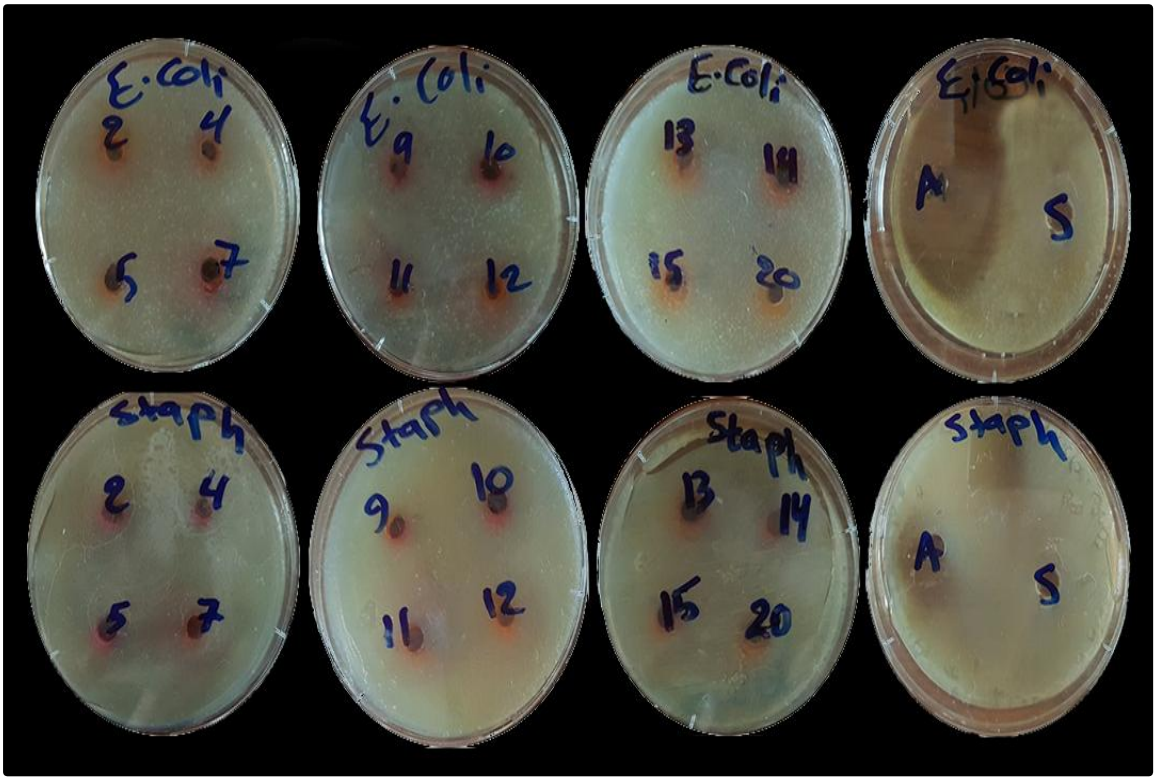


Fig (4-1): The biological effect of Azo-imidazole ligands and some of their metal ion complexes with the bacteria under study.

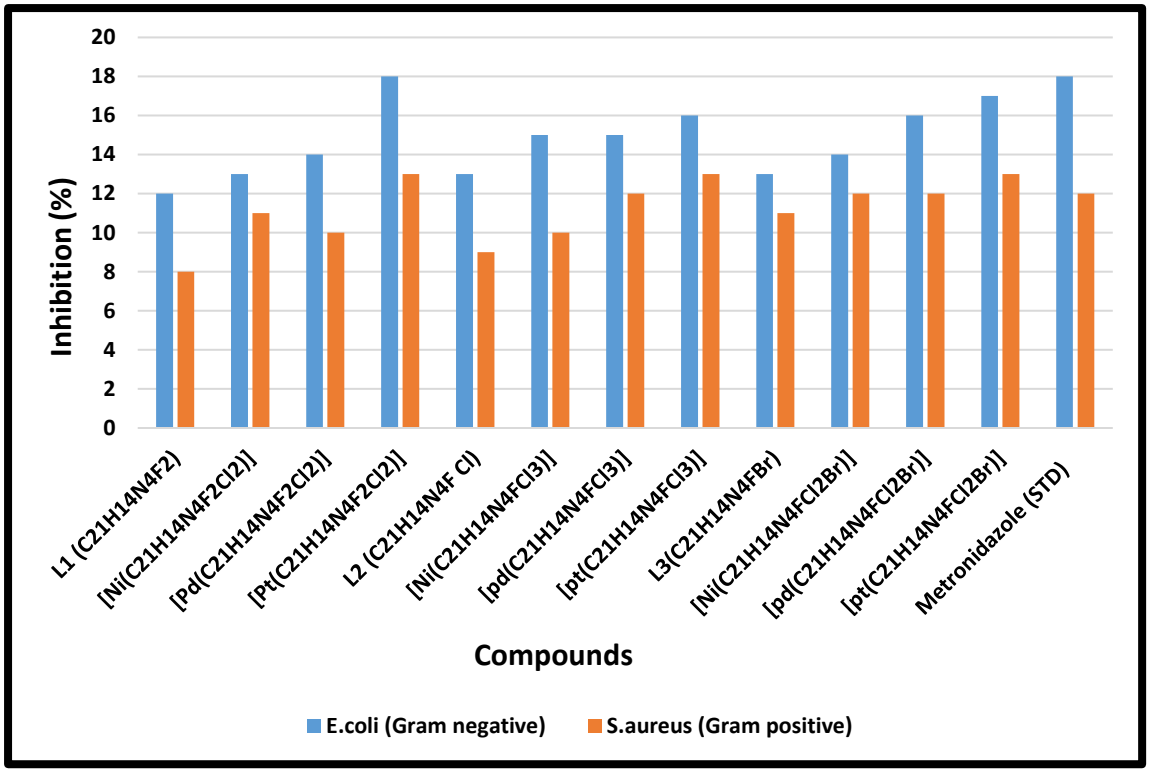


Fig (4-2): The relationship of Azo-imidazole ligands and some of their metal complexes with the bacteria under study.

4.1.1.2. Antibacterial Screening for Azo-Schiff Ligands and Some of their Metal Ion Complexes

From collected data, the azo-Schiff ligands with some of their complexes showed moderate activity (Somewhat) at the values (10-13mm) against (***Staphylococcus aureus***), except for (PtL_5, PdL_6, and PtL_6) which showed high activity (Somewhat) at the values (15, 16, and 17mm), respectively compared with (STD), While for bacterial strain (***E. coli***), the azo-Schiff ligands and their chelates displayed high activity at the values (14-17mm), except for (L_4, NiL_4, and L_5) which showed moderate activity at the values (11, 13, and 13mm), respectively compared with the same drug.

On the other hand, it is clear that the formation of complexes enhances antimicrobial activity; such increased activity of complexes may be related to the chelation theory and the concept of overtone.

According to the concept of overtone [227] cell permeability, the lipid membrane around the cell wall favors the passage of lipid-soluble substances only because of the important factor of lipid solubility to control the antimicrobial activity of bacteria. Regarding the chelation [227, 228] the ligand orbital overlap and the partial participation of the metal ion with the donor groups and more reduces the polarity of the metal ion and increases the spread of electrons on all the chelating rings and thus enhancing the fatty alpha of the complex and in turn, leads to breaking the permeability barrier of the cell and thus delays the normal cellular processes, the table (4-2) shows the inhibition of the growth of the bacteria (Inhibition zone) for azo-Schiff ligands and some of their metal ion complexes recorded in millimeter unit, while the figures (4-3) and (4-4) show the biological effect and relationship of azo-Schiff ligands and some of their metal complexes with the bacteria under study.

Table (4-2): The inhibition of the growth of the bacteria (Inhibition Zone) for Azo-Schiff ligands and some of their metal ion complexes recorded in millimeter unit.

Compounds	S.aureus (Gram positive)	E.coli (Gram negative)
Tetracycline antibiotic (STD)	25	27
L_4 ($C_{19}H_{11}Cl_2F_2N_3O$)	10	11
[Ni ($C_{19}H_{12}N_3Cl_3F_2O_2$)]	11	13
[Pd ($C_{19}H_{12}N_3Cl_3F_2O_2$)]	11	15
[Pt ($C_{19}H_{12}N_3Cl_3F_2O_2$)]	12	16
L_5 ($C_{19}H_{11}Cl_3FN_3O$)	11	13
[Ni ($C_{19}H_{12}Cl_4FN_3O_2$)]	12	14
[Pd ($C_{19}H_{12}Cl_4FN_3O_2$)]	13	17
[Pt ($C_{19}H_{12}Cl_4FN_3O_2$)]	15	18
L6 ($C_{19}H_{11}BrCl_2FN_3O$)	12	14
[Ni ($C_{19}H_{12}BrCl_3FN_3O_2$)]	13	14
[Pd ($C_{19}H_{12}BrCl_3FN_3O_2$)]	16	18
[Pt ($C_{19}H_{12}BrCl_3FN_3O_2$)]	17	20

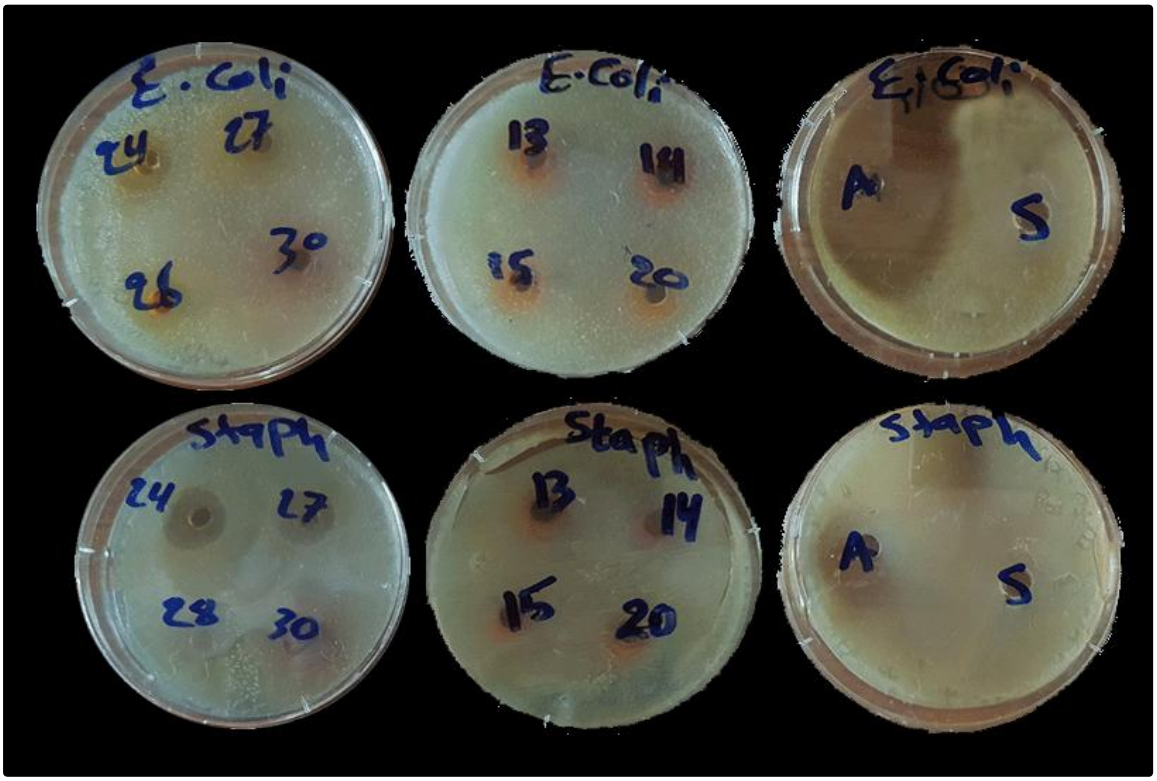


Fig (4-3): The biological effect of Azo-Schiff ligands and some of their metal complexes with the bacteria under study.

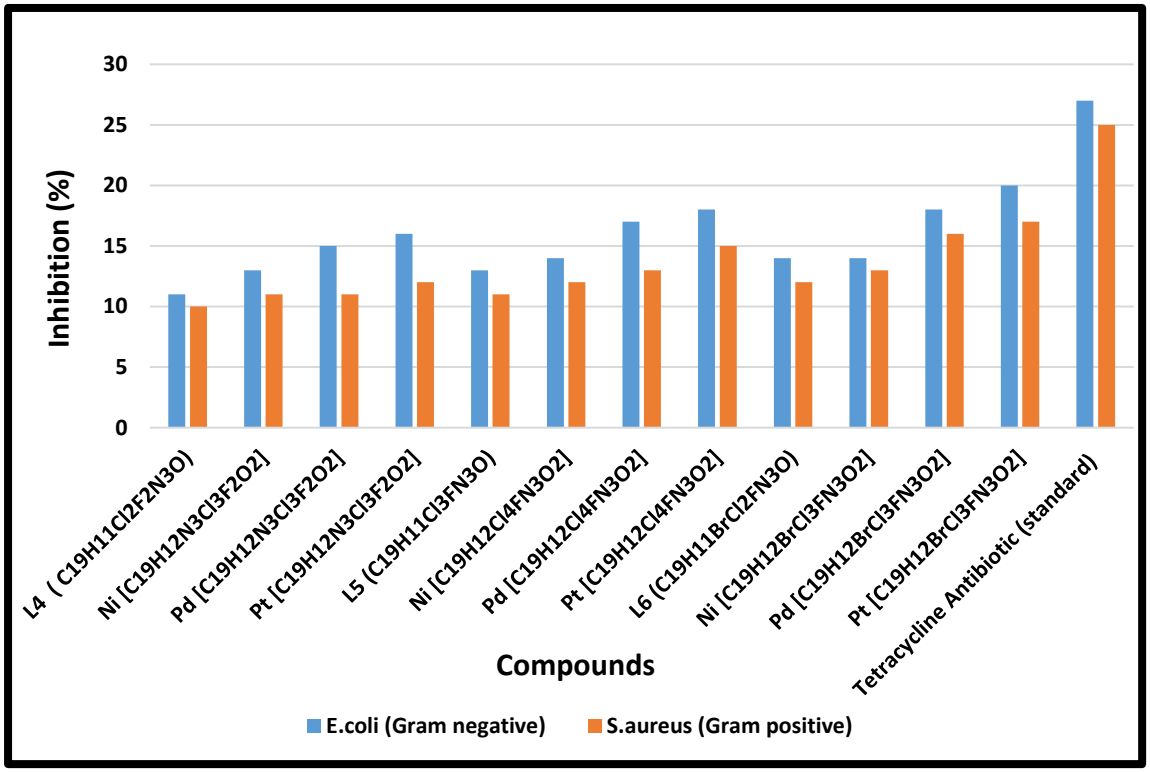


Fig (4-4): The relationship of Azo-Schiff ligands and some of their metal complexes with the bacteria under study.

4.1.2. Antioxidant Activity by DPPH Method

The application of the DPPH process provides a simple and rapid way to measure antioxidants by spectrophotometry. The synthesized of azo-imidazole, azo-Schiff base ligands and some of their metal complexes were measured as antioxidants using DPPH as a control, and tannic acid as a standard (STD), where all tested compounds demonstrated nearly the same radical scavenging ability in the presence of 25, 50, and 75 µg /ml. The DPPH scavenging effect increased with the increasing concentrations of the compounds studied. Below we review the most important results obtained:

4.1.2.1. Antioxidant Activity by DPPH Method for Azo-imidazole Ligands and Some of their Metal Ion Complexes

From the results, it is clear that all the azo-imidazole ligands with some of their complexes showed excellent inhibiting activity compared with tannic acid, depending on the values of (IC_{50}), which showed similar results for the value of (IC_{50}) for tannic acid on the one hand, and on the other hand, depending on the use of different concentrations under study, we note an increase in the inhibitory ratio for the same compound was increased by increasing the concentration [229], and the azo-imidazole complexes showed a higher rate of inhibition than their ligands. It is believed that the metal moiety will enhance that activity [230, 232]. Because the ligand's proton donor capacity was improved by the addition of the metallic moiety, add that all the synthesized compounds having electron-donating groups like nitrogen, exhibited free radical scavenging capacity in comparison with the standard [226], table (4-3) shows the antioxidant activity of azo imidazole ligands (L_1, L_2, L_3) and their metal complex, while the figure (4-5) shows the DPPH scavenging activity of azo imidazole ligands (L_1, L_2, L_3) and their ion metal complexes.

Table (4-3): Antioxidant activity of Azo-imidazole ligands (L_1, L_2, L_3) and their metal complex.

Compounds	Conc.			IC_{50}
	25 µg\ml	50 µg\ml	75 µg\ml	
L_1 ($C_{21}H_{14}N_4F_2$)	57.14	59.25	63.61	5.11
[Ni($C_{21}H_{14}N_4F_2Cl_2$)]	61.88	63.77	66.33	7.40
[Pd($C_{21}H_{14}N_4F_2Cl_2$)]	69.13	70.33	72.56	14.09
[Pt($C_{21}H_{14}N_4F_2Cl_2$)]	70.66	72.13	74.76	12.98
L_2 ($C_{21}H_{14}N_4F$ Cl)	59.11	62.95	66.34	5.54
[Ni($C_{21}H_{14}N_4FCl_3$)]	62.12	64.97	68.14	7.00
[Pd($C_{21}H_{14}N_4FCl_3$)]	66.86	68.76	71.78	10.02
[Pt($C_{21}H_{14}N_4FCl_3$)]	69.66	70.34	73.45	12.98
L_3($C_{21}H_{14}N_4FBr$)	63.14	65.92	68.23	8.20
[Ni($C_{21}H_{14}N_4FCl_2Br$)]	63.99	66.12	68.11	9.80
[Pd($C_{21}H_{14}N_4FCl_2Br$)]	68.11	72.43	77.98	6.63
[Pt($C_{21}H_{14}N_4FCl_2Br$)]	70.66	73.45	78.55	8.14
Tannic acid (STD)	56.1	57.4	62.74	4.63

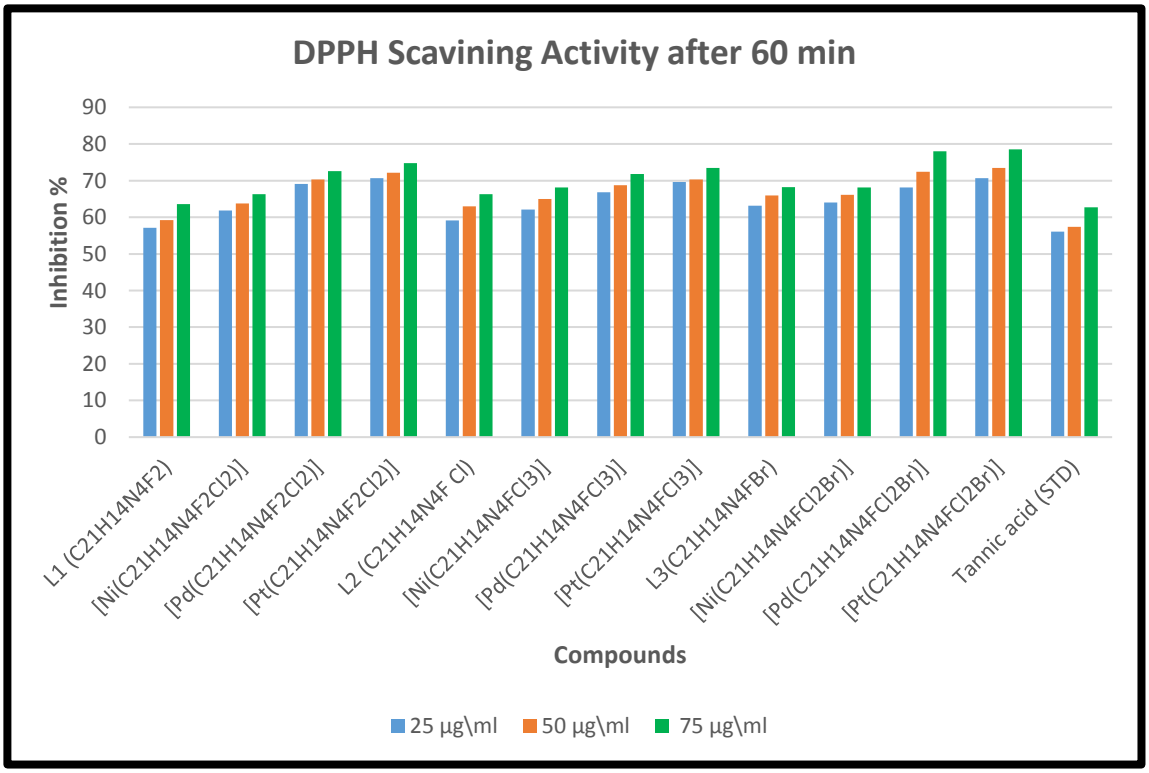


Fig (4-5): DPPH scavenging activity of Azo-imidazole (L_4, L_5, L_6) and their complexes.

4.1.2.2. Antioxidant Activity by DPPH Method for Azo-Schiff Ligands and Some of their Metal Ion Complexes

From collected data, the azo-Schiff base ligands with some of their complexes showed excellent inhibiting activity compared to tannic acid through the value of (IC_{50}) for each of them, it is clear that all the synthesized compounds showed excellent inhibiting activity compared to the standard because all synthesized compounds contain electron donor groups such as nitrogen and oxygen, which have the ability to scavenge free radicals and thus increase the antioxidant activity of ligands and their metal complexes [226], addition there have been reports in the literature of metallic complexes with antioxidant activity in the ligand, it is believed that the metal moiety will enhance that activity [230. 232] because the addition of the metallic moiety improved the ligand's proton donor capacity, table (4-4) shows the antioxidant activity of azo-Schiff base ligands (L_4, L_5, L_6) and their metal complex, while the figure (4-6) shows the DPPH scavenging activity of azo- Schiff base ligands (L_4, L_5, L_6) and their metal ion complexes.

Table (4-4): Antioxidant activity of Azo-Schiff ligands (L_4, L_5, L_6) and their metal complex.

Compounds	Conc.			IC_{50}
	25 µg\ml	50 µg\ml	75 µg\ml	
L_4 ($C_{19}H_{11}Cl_2F_2N_3O$)	58.13	59.27	61.61	7.55
[Ni($C_{19}H_{12}N_3Cl_3F_2O_2$)]	62.85	63.75	64.37	19.96
[Pd($C_{19}H_{12}N_3Cl_3F_2O_2$)]	65.23	67.46	69.55	10.06
[Pt($C_{19}H_{12}N_3Cl_3F_2O_2$)]	67.68	69.18	70.14	17.44
L_5($C_{19}H_{11}Cl_3FN_3O$)	58.87	59.95	62.34	8.00
[Ni($C_{19}H_{12}Cl_4FN_3O_2$)]	61.14	62.81	63.77	11.60
[Pd($C_{19}H_{12}Cl_4FN_3O_2$)]	64.12	67.66	69.87	8.00
[Pt($C_{19}H_{12}Cl_4FN_3O_2$	68.12	69.45	71.11	15.13
L_6 ($C_{19}H_{11}BrCl_2FN_3O$)	60.34	61.34	62.11	14.80
[Ni($C_{19}H_{12}BrCl_3FN_3O_2$)]	62.86	64.17	66.53	9.93
[Pd($C_{19}H_{12}BrCl_3FN_3O_2$)]	63.67	64.22	67.13	10.67
[Pt($C_{19}H_{12}BrCl_3FN_3O_2$)]	68.44	70.11	71.53	15.00
Tannic acid(STD)	56.1	57.4	62.74	4.63

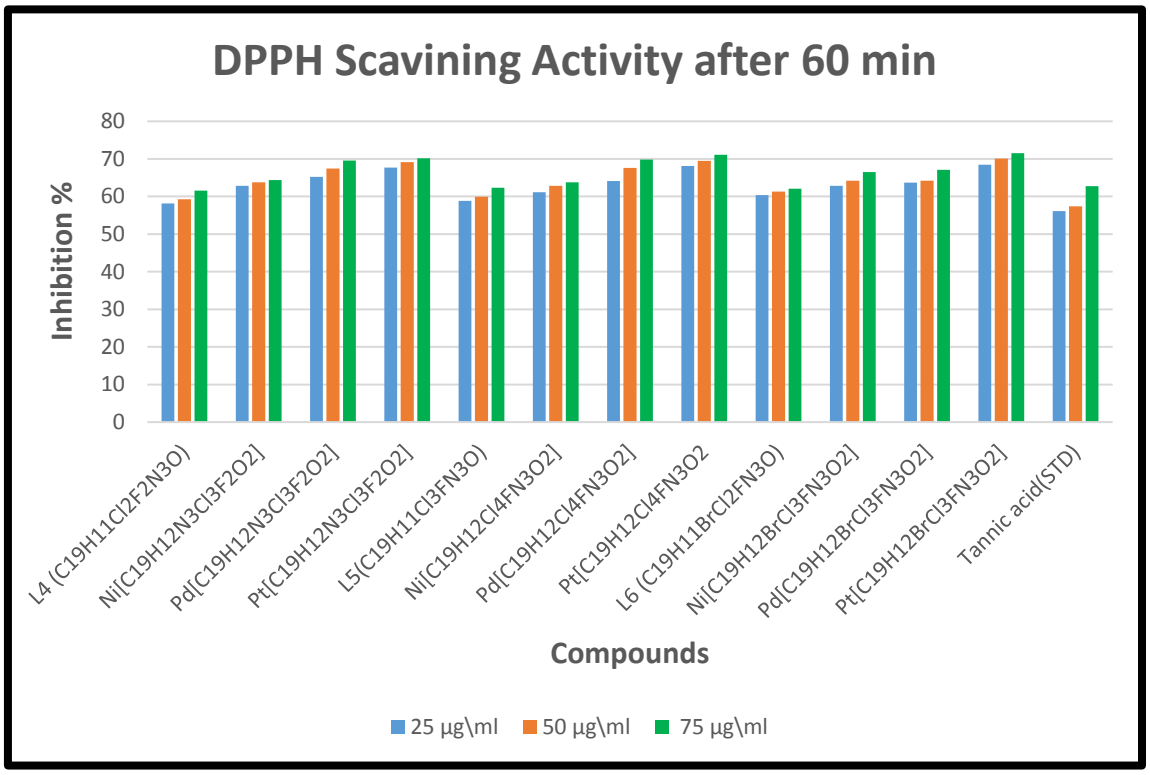


Fig (4-6): DPPH scavenging activity of Azo-Schiff (L_4, L_5, L_6) and their complexes

4.1.3. MCF-7 Cell Line Breast Cancer Assay

One of the important matters that must be referred to, and which was reached through the tests that were conducted for some of the platinum and palladium complexes on the cells of the breast cancer line is the so-called toxicological and viability percentage of the prepared compound and the half-inhibitory concentration, which is symbolized by the symbol (IC_{50}), as this concentration kills half of the cancer cells.

In this study, the toxicity and viability of some of the platinum and palladium complexes were estimated for each of the azo-imidazole and azo-Schiff base ligands under study, and a comparison was made between them by finding a value (IC_{50}). Where the results proved that the platinum complexes (PtL_1 and PtL_5) had a more inhibition effect on cancer cells than the palladium complexes (PdL_2 and PdL_4). Below we review the most important results obtained:

4.1.3.1. MCF-7 Cell Line Breast Cancer Assay for Azo-imidazole Complexes with Platinum and Palladium (PtL_1 and PdL_2)

Two azo imidazole complexes (PtL_1 and PdL_2) were selected for breast cancer MCF-7 cell line assay for estimation of their abilities for breast cancer inhibition, the results are observed with their IC_{50} values, in table (4-5) and figures (4-7), (4-8), and (4-9).

Table (4-5): Breast cancer MCF-7 cell line for PtL_1 & PdL_2 complexes.

Concentration µg/ mL.	Log Conc. µg/ mL.	PtL_1 MC7 cell line		PdL_2 MC7 cell line	
		IC_{50} =42.68 µg/ mL		IC_{50} = 67.29 µg/ mL	
		Viability %	Cytotoxicity %	Viability %	Cytotoxicity %
31.25	**1.49**	94.74035	5.26	96.08323	3.91677
62.5	**1.79**	89.68043	10.32	92.77846	7.22154
125	**2.09**	86.48469	13.516	86.29131	13.70869
250	**2.39**	73.03595	26.965	80.04896	19.95104
500	**2.69**	50.99867	49.002	66.74533	33.5247
1000	**3**	34.82024	65.18	39.6679	60.3321

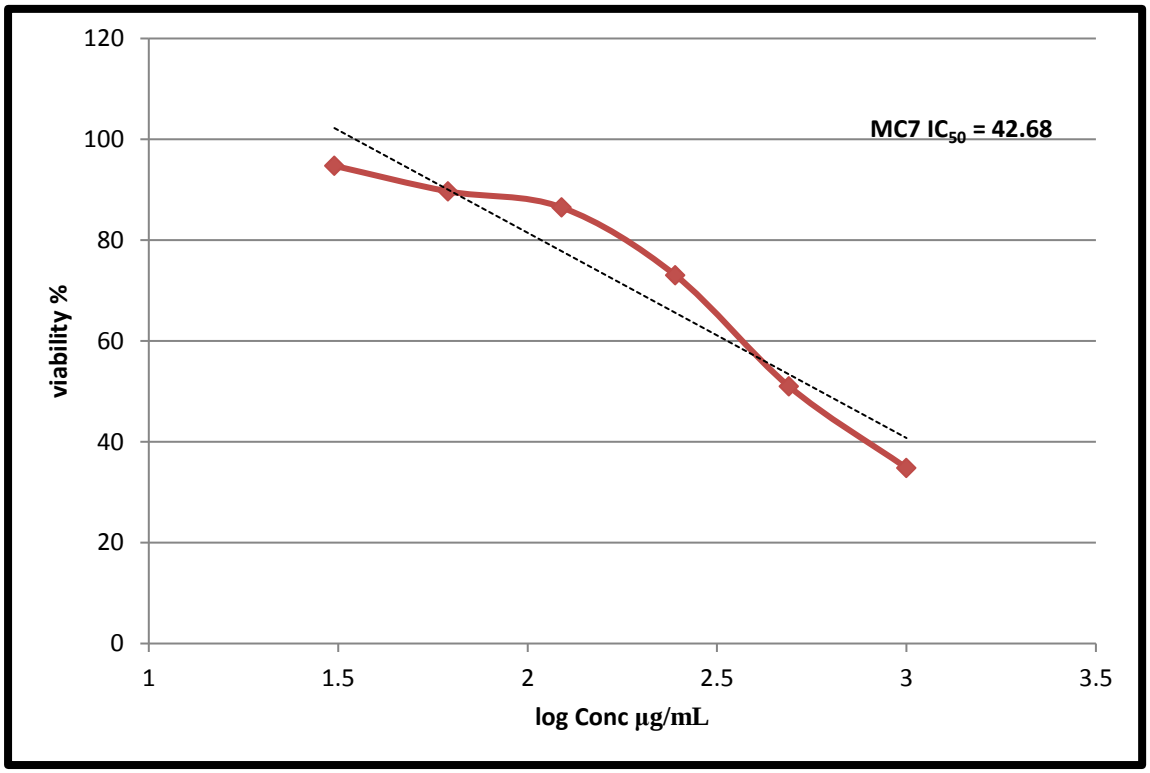


Fig (4-7): Viability relation with the PtL_1complex concentration.

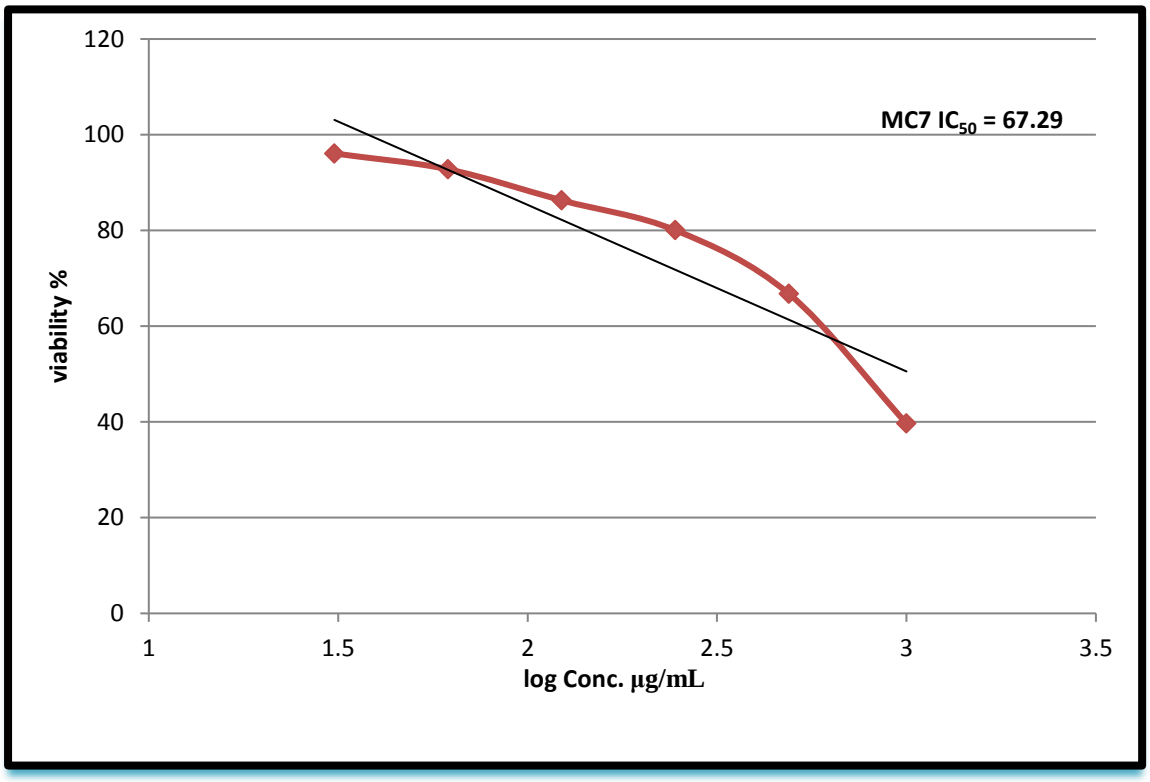


Fig (4-8): Viability relation with the PdL_2 complex concentration.

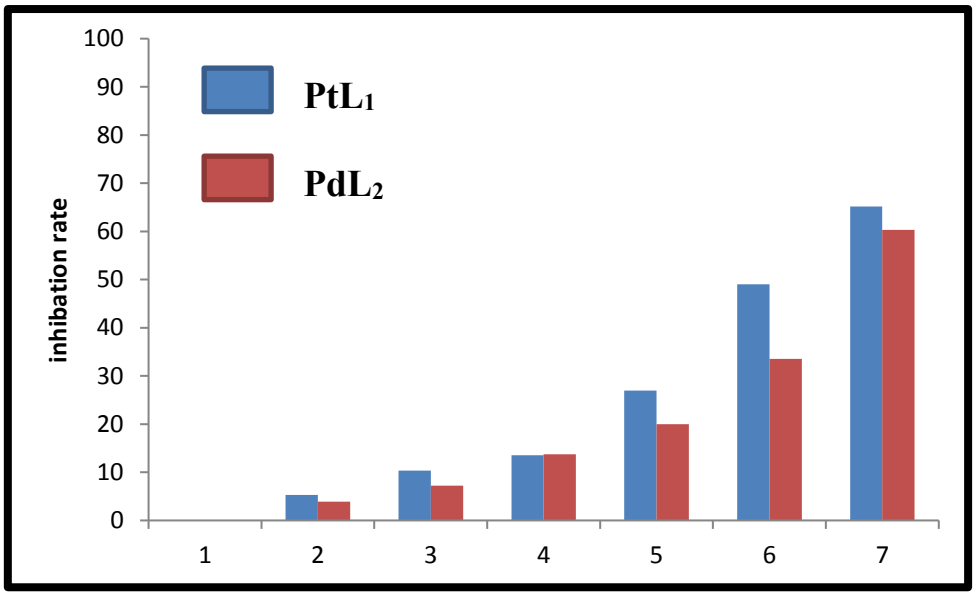


Fig (4-9): Breast cancer inhibition rate for (PtL_1 & PdL_2) complexes.

From the results above, it was noticed that the azo complexes' IC_{50} values (the minimal concentration required for 50% inhibition in vitro) and expressed as molar concentration.

In this study, the platinum azo complex (PtL_1) IC_{50} value was 42.68 µg /mL and a cytotoxicity percent of 65.18%, this regard a moderate value due to the presence of the platinum ion (Pt^{+2}) as these present in cis- Platin and its analogs drugs[233, 234], indeed another ligand component such as imidazole ring is (somewhat) used as safe anticancer drugs such as decarbonize, temozolomide, and mercaptopurine [235] and the substituted fluoride ions, as in fluorinated anticancer agents [236].

The other azo imidazole complex (PdL_2) IC_{50} value was 67.29 µg /mL and a cytotoxicity percent of 60%, showing less value than platinum complexes, these types of halogenated compounds can develop a sensible anticancer ability [237], indeed to the previously mentioned reasons.

4.1.3-2. MCF-7 Cell Line Breast Cancer Assay for Azo-Schiff Complexes with Platinum and Palladium (PtL_5 and PdL_4)

Two of the azo-Schiff base complexes (PdL_4 and PtL_5) were examined for breast cancer MCF-7 cell line assay to estimate their abilities for breast cancer inhibition, the results are observed with their IC_{50} values, in table (4-6) and figures (4-10), (4-11), and (4-12).

Table (4-6): Breast cancer MCF-7 cell line for PdL_4 & PtL_5 complexes.

Concentration µg/ mL.	Log Conc. µg/ mL.	PdL_4 MC7 cell line		PtL_5 MC7 cell line	
		IC_{50} =74.64 µg/ mL		IC_{50} = 56.78µg/ mL	
		Viability %	Cytotoxicity %	Viability %	Cytotoxicity %
31.25	**1.49**	97.546	2.4533	94.369	5.631
62.5	**1.79**	93.145	6.855	90.457	9.543
125	**2.09**	88.451	11.549	88.984	11.016
250	**2.39**	80.048	19.952	81.596	18.403
500	**2.69**	63.578	36.422	61.811	38.189
1000	**3**	49.744	50.256	43.766	56.234

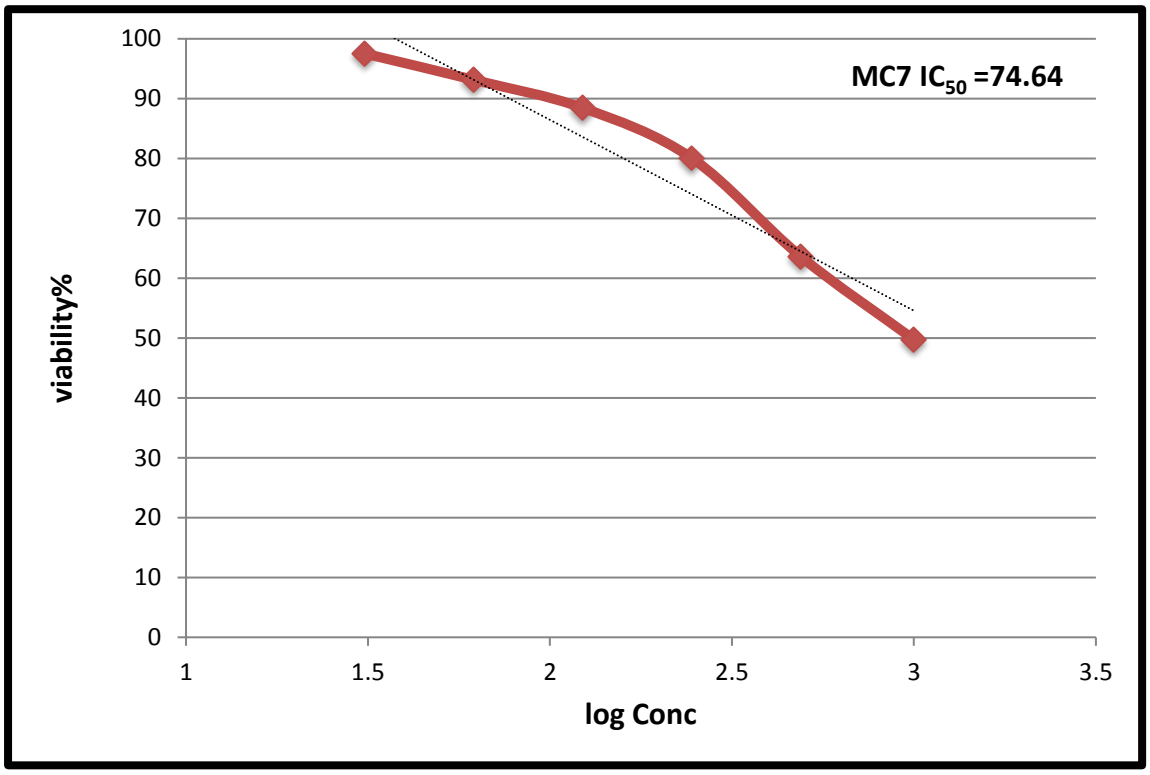


Fig (4-10): Viability relation with the PdL_4 complex concentration.

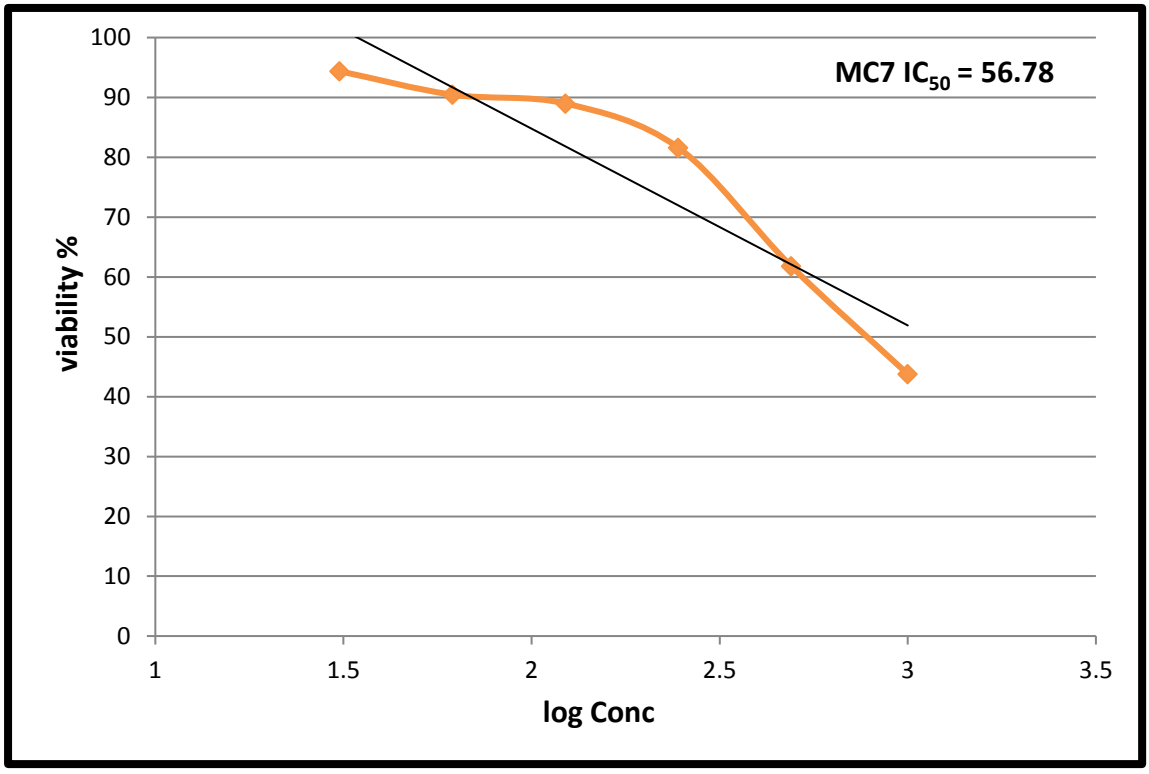


Fig (4-11): Viability relation with the PtL_5 complex concentration.

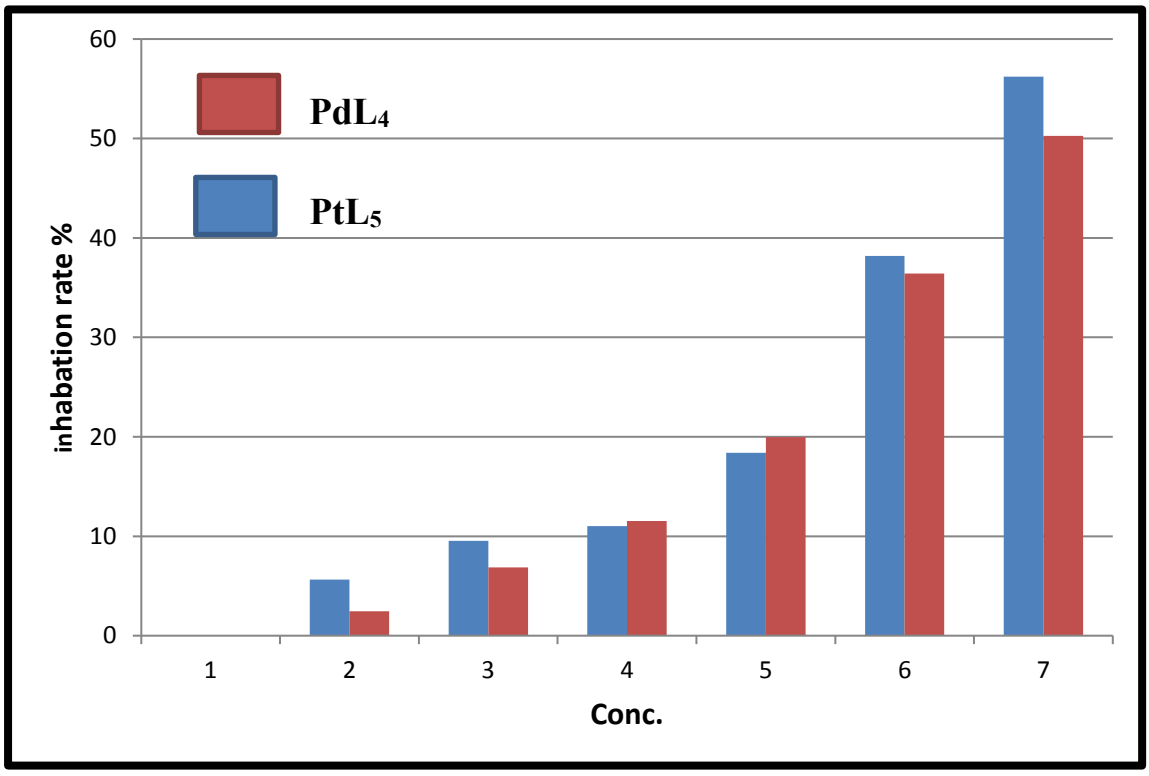


Fig (4-12): Breast cancer inhibition rate for (PdL_4, and PtL_5) complexes.

In this study, the platinum azo-Schiff complex (PtL_5) IC_{50} value (the minimum concentration required for 50% inhibition in vitro) was 56.78 µg /mL and a cytotoxicity percent of 56.23%, this regard a moderate value due to the presence of the platinum ion (Pt^{+2}) as these present in cis- Platin and its analogs drugs [233, 234] and the substituted fluoride ions, as in fluorinated anticancer agents [236].

The other azo-Schiff complex (PdL_4) IC_{50} value was 74.64 µg /mL and a cytotoxicity percent of 50.25 %, showing less value than platinum complexes, and these types of halogenated compounds can develop a sensible anticancer ability[237], indeed to the previously mentioned reasons.

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